June 2021 Volume 80 Supplement 1

Annals of the Rheumatic Diseases

The EULAR Journal

eular
EUROPEAN CONGRESS OF RHEUMATOLOGY
2021 | 2–5 JUNE

Abstracts

ard.bmj.com

THE HOME FOR INNOVATIVE RHEUMATOLOGY RESEARCH

eular
EUROPEAN ALLIANCE OF ASSOCIATIONS FOR RHEUMATOLOGY

BMJ

Annals of the Rheumatic Diseases

Annual European Congress of Rheumatology

EULAR 2021

2–5 June 2021

Abstracts

The EULAR Journal

ARD
The EULAR Journal

Editor
Josef S Smolen (Austria)

Associate Editors
Francis Berenbaum (France)
Dimitrios Boumpas (Greece)
Gerd Burmester (Germany)
Mary Crow (USA)
Kimme Hyrich (UK)
Rik Lories (Belgium)
Iain McInnes (UK)
Thomas Pap (Germany)
David Pisetsky (USA)
Désirée van der Heijde (The Netherlands)
Kazuhiko Yamamoto (Japan)

Methodological and Statistical Advisors
Guro Giskeødegård (Norway)
Stian Lydersen (Norway)

Social Media Advisors
Alessia Alunno (Italy)
Javier Rodriguez Carrio (Spain)
Peter Korsten (Germany)
Caroline Ospelt (Switzerland)
Christophe Richez (France)
Paul Studenic (Austria)

Guidelines for Authors and Reviewers

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

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

Editorial Board

Daniel Aletaha (Austria)
Johan Askling (Sweden)
Sang-Cheol Bae (Korea)
Xenofon Baraliakos (Germany)
Anne Barton (UK)
Maarten Boers (The Netherlands)
Maxine Breban (France)
Matthew Brown (Australia)
Maya Buch (UK)
Frank Buttgereit (Germany)
Loreto Carmona (Spain)
Carlo Chizzolini (Switzerland)
Bernard Combe (France)
Philip Conaghan (UK)
Maurizio Cutolo (Italy)
Nicola Dalbeth (Australia)
Christian Dejaco (Austria)
Oliver Distler (Switzerland)
Thomas Dörner (Germany)
Dirk Elewaut (Belgium)
Axel Finckh (Switzerland)
Rebecca Fischer-Betz (Germany)
Roy Fleischmann (USA)
Mary Goldring (USA)
Laure Gossec (France)
Walter Grassi (Italy)
Ahmet Gül (Turkey)
Frederic Houssiau (Belgium)
Tom Huizinga (The Netherlands)
Arthur Kavanaugh (USA)
Margreet Kloppenburg (The Netherlands)
Robert Landewé (The Netherlands)
Zhan-Gou Li (China)
Rik Lories (Belgium)
Ingrid Lundberg (Sweden)
Gary MacFarlane (UK)
Xavier Mariette (France)
Alberto Martini (Italy)
Marco Mattuci Cerinic (Italy)
Dennis McGonagle (UK)
Fred Miller (USA)
Peter Nash (Australia)
Michael Nurmohamed (The Netherlands)
Caroline Ospelt (Switzerland)
Monika Østensen (Norway)
Constatino Pitzalis (UK)
Jane Salmon (USA)
Georg Schett (Germany)
Philipp Sewerin (Germany)
José da Silva (Portugal)
Hendrik Schulze-Koops (Germany)
Nan Shen (China)
Greg Silverman (USA)
Alexander So (Switzerland)
Hiroshi Takayanagi (Japan)
Tsutomu Takeuchi (Japan)
Yoshiya Tanaka (Japan)
Dimitrios Vassilopoulos (Greece)
Douglas Veale (Ireland)
Jiri Vencovsky (Czech Republic)
Ronald van Vollenhoven (Sweden)
Erwin Wagner (Spain)
Michael Ward (USA)
Kevin Winthrop (USA)
Huji Xu (China)

Chairman of Advisory Committee

Johannes Bijlsma (The Netherlands)

Advisory Committee

Ferry Breedveld (The Netherlands)
Marco Matucci Cerinic (Italy)
Michael Doherty (UK)
Maxime Dougados (France)
Paul Emery (UK)
Daniel Furst (USA)
Steffen Gay (Switzerland)
Marc Hochberg (USA)
Joachim Kalden (Germany)
Edward Keystone (Canada)
Lars Klareskog (Sweden)
Tore Kvien (Norway)
Zhan-guo Li (China)
Peter Lipsky (USA)
Sir Ravinder Maini (UK)
Emilio Martín-Mola (Spain)
Haralampos Moutsopoulos (Greece)
Karel Pavelka (Czech Republic)
Yehuda Shoenfeld (Israel)
Leo van de Putte (The Netherlands)
Frank Wollheim (Sweden)
Anthony Woolf (UK)

Subscription Information

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

Institutional Rates 2021

Print
£1,121

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

Personal Rates 2021

Print (includes online access at no additional cost)
£431

Online only
£241

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

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

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

For more information on subscription rates or to subscribe online please visit ard/bmj.com/pages/contact-us/

Contact Details

Editorial Office
Annals of the Rheumatic Diseases
BMJ Journals, BMA House, Tavistock Square
London WCIH 9JR,UK
E: **ard@bmj.com**

Production Editor
Teresa Jobson
E: **production.ard@bmj.com**

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

Customer support
For general queries and support with existing and new subscriptions:
W: **support.bmj.com**
T: **+44 (0)20 7111 1105**
E: **support@bmj.com**

Self-archiving and permissions
W: **bmj.com/company/products-services/rights-and-licensing/**
E: **bmj.permissions@bmj.com**

Advertising
W: **bmj.com/company/for-advertisers-and-sponsor/**

Display Advertising ROW
Sophie Fitzsimmons
T: **+44 (0)20 3655 5612**
E: **sfitzsimmons@bmj.com**

Online Advertising ROW
Marc Clifford
T: **+44 (0) 20 3655 5610**
E: **mclifford@bmj.com**

Display & Online Advertising Americas
Jim Cunningham
T: **+1 201 767 4170**
E: **jcunningham@cunnasso.com**

Reprints

Author Reprints
BMJ Reprints Team
E: **admin.reprints@bmj.com**

Commercial Reprints ROW
Nadia Gurney-Randall
M: **+44 07866 262344**
E: **ngurneyrandall@bmj.com**

Commercial Reprints Americas
Ray Thibodeau
T: **+1 267 895 1758**
M: **+1 215 933 8484**
E: **ray.thibodeau@contentednet.com**

For all other journal contacts
ard.bmj.com/contact-us

EULAR 2021 Abstracts Reviewers

ABHISHEK, Abhishek (United Kingdom)
ABLIN, Jacob (Israel)
ADAMI, Giovanni (Italy)
ALIVERNINI, Stefano (Italy)
ALLAART, Cornelia (Netherlands)
ALLANORE, Yannick (France)
ALPIZAR-RODRIGUEZ, Deshiré (Mexico)
ALUNNO, Alessia (Italy)
AMOURA, Zahir (France)
ANDRÉS, Mariano (Spain)
ANTON, Jordi (Spain)
APPEL ESBENSEN, Bente (Denmark)
ARAUJO, Filipe (Portugal)
ARINGER, Martin (Germany)
ASHISH J., Mathew (India)
ASKLING, Johan (Sweden)
ATSUMI, Tatsuya (Japan)
AVCIN, Tadej (Slovenia)
AVOUAC, Jérôme (France)
BACKHOUSE, Mike (United Kingdom)
BAERWALD, Christoph (Germany)
BALAGUE, Federico (Switzerland)
BALINT, Peter (Hungary)
BARALIAKOS, Xenofon (Germany)
BARTON, Anne (United Kingdom)
BATTICCIOTTO, Alberto (Italy)
BEARNE, Lindsay (United Kingdom)
BELIZNA, Cristina (France)
BENAVENT, Diego (Spain)
BERGSTRÖM, Maria (Sweden)
BERTI, Alvise (Italy)
BERTSIAS, George (Greece)
BIJLSMA, Hans (Netherlands)
BLUEML, Stephan (Austria)
BOLETO, Goncalo (Portugal)
BOONEN, Annelies (Netherlands)
BOOTSMA, Hendrika (Netherlands)
BOURS, Sandrine (Netherlands)
BOYD, Peter (Ireland)
BOZEC, Aline (Germany)
BREBAN, Maxime (France)
BRIDGES, Louis (United States)
BROUWER, Elisabeth (Netherlands)
BRUCE, Ian (United Kingdom)
BUCH, Maya (United Kingdom)
BUCKLEY, Chris (United Kingdom)
BUKILICA, Mirjana (Serbia)
BULTINK, Irene E.M. (Netherlands)
BURDEN, Andrea (Switzerland)
BURKARD, Theresa S. (Switzerland)
BURMESTER, Gerd (Germany)
BUTTGEREIT, Frank (Germany)
CABRAL DA FONSECA, Joao Eurico (Portugal)
CALABRESE, Leonard (United States)
CAPORALI, Roberto (Italy)
CARDIEL, Mario (Mexico)
CARMONA, Loreto (Spain)
CARRON, Philippe (Belgium)
CARUBBI, Francesco (Italy)
CAÑETE, Juan D. (Spain)
CHANDRAN, Vinod (Canada)
CHAPMAN, Victoria (United Kingdom)
CHIGHIZOLA, Cecilia (Italy)
CHINOY, Hector (United Kingdom)
CHRIST, Lisa (Switzerland)
CID, Maria (Spain)
CIMAZ, Rolando (Italy)
CIUREA, Adrian (Switzerland)
CLARKE, Alex (United Kingdom)
COATES, Laura (United Kingdom)
CODREANU, Catalin (Romania)
COMBE, Bernard (France)
CONAGHAN, Philip (United Kingdom)
CONSOLARO, Alessandro (Italy)
CONSTANTINO, Félicie (France)
COPE, Andrew (United Kingdom)
COSTEDOAT-CHALUMEAU, Nathalie (France)
COURVOISIER, Delphine (Switzerland)
CROFFORD, Leslie (United States)
CRONIN, Owen (United Kingdom)
CROWSON, Cynthia S. (United States)
CUTOLO, Maurizio (Italy)
CZIRJÁK, László (Hungary)
D'AGOSTINO, Maria-Antonietta (France)
DAIEN, Claire (France)
DE BENEDETTI, Fabrizio (Italy)
DE COCK, Diederik (Belgium)
DE PABLO, Paola (United Kingdom)
DE VLAM, Kurt (Belgium)
DE WIT, Maarten (Netherlands)
DEANE, Kevin (United States)
DENIS, Poddubnyy (Germany)
DENTON, Christopher (United Kingdom)
DEODHAR, Atul (United States)
DISTLER, Oliver (Switzerland)
DOLEZALOVA, Pavla (Czech Republic)
DUFTNER, Christina (Austria)
DUREZ, Patrick (Belgium)
DÖRNER, Thomas (Germany)
EATHAKKATTU ANTONY, Benny (Australia)
EDWARDS, Christopher (United Kingdom)
ELEWAUT, Dirk (Belgium)
ESTEVEZ-LOPEZ, Fernando (Spain)
FAUTREL, Bruno Jean (France)
FEARON, Ursula (United Kingdom)
FEIST, Eugen (Germany)
FERREIRA, Ricardo (Portugal)
FILER, Andrew (United Kingdom)
FILIPPUCCI, Emilio (Italy)
FILLATREAU, Simon (France)
FINCKH, Axel (Switzerland)
FIRINU, Davide (Italy)
FISCHER-BETZ, Rebecca (Germany)
FITZGERALD, Oliver (Ireland)
FONTES, Francisca (Portugal)
FRAGOULIS, George (Greece)
FRANCISCA, Sivera (Spain)
GAFFNEY, Karl (United Kingdom)
GARCÍA DE YÉBENES, Maria Jesus (Spain)
GATTO, Mariele (Italy)
GAUJOUX-VIALA, Cecile (France)
GENEVAY, Stéphane (Switzerland)
GENOVESE, Mark (United States)
GENSLER, Lianne (United States)
GIACOMELLI, Roberto (Italy)
GJERTSSON, Inger (Sweden)
GOSSEC, Laure (France)
GUANABENS, Nuria (Spain)
GUERMAZI, Ali (United States)
GUILLEVIN, Loic (France)
GUNNARSSON, Iva (Sweden)
GUNNARSSON, Ragnar (Norway)
HAAVARDSHOLM, Espen A (Norway)
HARAOUI, Boulos (Canada)
HAUGEN, Ida Kristin (Norway)
HELLIWELL, Philip (United Kingdom)
HERMANN, Walter (Germany)
HERRERO-BEAUMONT, Gabriel (Spain)
HIEPE, Falk (Germany)
HILBERDINK, Bas (Netherlands)
HOEPER, Kirsten (Germany)
HOFFMANN-VOLD, Anna-Maria (Norway)
HOLERS, V. Michael (United States)
HORNEFF, Gerd (Germany)
HUGHES, Michael (United Kingdom)
HUIZINGA, Tom (Netherlands)
HUSNIE, Elaine (United States)
HYRICH, Kimme (United Kingdom)
IAGNOCCO, Annamaria (Italy)
IONESCU, Ruxandra (Rumania)
ISAACS, John (United Kingdom)
JAVAID, Kassim (United Kingdom)
KAY, Jonathan (United States)
KLOPPENBURG, Margreet (Netherlands)
KOK, Marc (Netherlands)
KOUTSIANAS, Christos (United Kingdom)
KOWAL-BIELECKA, Otylia (Poland)
KROON, Feline (Netherlands)
KRÖNKE, Gerhard (United Kingdom)
KUO, Chang-Fu (Taiwan)
LAMBOVA, Sevdalina (Bulgaria)
LAMOT, Lovro (Croatia)
LAMPRECHT, Peter (Germany)
LARGO, Raquel (Spain)
LAUPER, Kim (Switzerland)
LIEW, Jean (United States)
LORIES, Rik (Belgium)
LUBRANO, Ennio (Italy)
LUQMANI, Raashid Ahmed (United Kingdom)
MACHADO, Pedro (Portugal)
MARIETTE, Xavier (France)
MARQUES, Andrea (Portugal)
MARTINEZ LAGUNA, Daniel (Spain)
MARZO-ORTEGA, Helena (United Kingdom)
MCBETH, John (United Kingdom)
MCGONAGLE, Dennis (United Kingdom)
MEESTERS, Jorit (Netherlands)
MERRIMAN, Tony (New Zealand)
METSIOS, George (United Kingdom)
MOSCA, Marta (Italy)
MOSOR, Erika (Austria)
MYASOEDOVA, Elena (Russia)
NAJM, Aurelie (United Kingdom)
NAREDO, Esperanza (Spain)
NAVARRO, Victoria (Spain)
NDOSI, Mwidimi (United Kingdom)

NIKIPHOROU, Elena (United Kingdom)
OGDIE-BEATTY, Alexis (United States)
OLIVÉ, Alejandro (Spain)
OMETTO, Francesca (Italy)
OROZCO, Gisela (United Kingdom)
OSTOJIC, Predrag (Serbia)
PADYUKOV, Leonid (Sweden)
PALMER, Deborah (United Kingdom)
PEENE, Isabelle (Belgium)
PENTEK, Marta (Hungary)
PEREIRA DA SILVA, José Antonio (Portugal)
PERPETUO, Ines (United Kingdom)
PERS, Yves-Marie (France)
PIMENTEL SANTOS, Fernando (Portugal)
PODDUBNYY, Denis (Germany)
PORTER, Duncan (United Kingdom)
PRIMDAHL, Jette (Denmark)
PROFT, Fabian (Germany)
QUARTIER, Pierre (France)
QUARTUCCIO, Luca (Italy)
RADNIC , Tatjana (Serbia)
RAMIREZ, Giuseppe A. (Italy)
RAMONDA, Roberta (Italy)
RAMOS CASALS, Manuel (Spain)
RAUSCH OSTHOFF, Anne-Kathrin (Switzerland)
RAVELLI, Angelo (Italy)
RAVINDRAN, Vinod (India)
REGIERER, Anne (Germany)
REYNOLDS, Gary (United Kingdom)
RICHETTE, Pascal (France)
RITSCHL, Valentin (Austria)
RIVELLESE, Felice (United Kingdom)
RODRIGUES MANICA, Santiago (Portugal)
ROELOFS, Anke (United Kingdom)
ROMAO, Vasco C. (Portugal)
ROTH, Johannes (Germany)
ROVERE-QUERINI, Patrizia (Italy)
RUARO, Barbara (Italy)
RUBBERT-ROTH, Andrea (Switzerland)
RUDWALEIT, Martin (Germany)
SALLUSTO, Federica (Switzerland)
SALVARANI, Carlo (Italy)
SANCHEZ-SANTOS, Maria (United Kingdom)
SANTOS, Eduardo (Portugal)
SCHEINECKER, Clemens (Austria)
SCHULZE-KOOPS, Hendrik (Germany)
SCHÄFER, Valentin Sebastian (Germany)
SELLAM, Jeremie (France)
SENGUPTA, Raj (United Kingdom)
SENOLT, Ladislav (Czech Republic)
SEPRIANO, Alexandre (Portugal)
SEWERIN, Philipp (Germany)
SIEBERT, Stefan (United Kingdom)
SIEPER, Joachim (Germany)
SKAPENKO, Alla (Germany)
SMITH, Eve (United Kingdom)
SMITH, Vanessa (Belgium)
SPARKS, Jeffrey (United States)
SPIERINGS, Julia (Netherlands)
STAINES, Katherine (United Kingdom)
STENOVA, Emoke (Slovakia)
STUDENIC, Paul (Austria)
SVENSSON, Camilla (Sweden)
SWART, Joost F. (Netherlands)
SYTSKE, Anne Bergstra (Netherlands)
SZ?CS, Gabriella (Hungary)
SZEKANECZ, Zoltan (Czech Republic)
SZODORAY, Peter (Norway)
TAKEUCHI, Tsutumu (Japan)
TAYLOR, Peter C. (United Kingdom)
TERRIER, Benjamin (France)
TROLDBORG, Anne Margrethe (Denmark)
TSOKOS, George (United States)
VAN DER HORST-BRUINSMA, Irene (Netherlands)
VAN GAALEN, Floris A. (Netherlands)
VAN LAAR, Jacob (Netherlands)
VAN ONNA, Marloes (Netherlands)
VAN VOLLENHOVEN, Ronald (Sweden)
VASSILOPOULOS, Dimitrios (Greece)
VENCOVSKY, Jiri (Czech Republic)
VIEIRA-SOUSA, Elsa (Portugal)
VINCENT, Tonia (United Kingdom)
VOJINOVIC, Jelena (Serbia)
VONKEMAN, Harald (Netherlands)
WEBERS, Casper (Netherlands)
WENZEL KRAGSTRUP, Tue (Denmark)
WESTHOVENS, René (Belgium)
WILKIE, Ross (United Kingdom)
WINTHROP, Kevin (United States)
YAZICI, Yusuf (United States)
ZAVADA, Jakub (Czech Republic)
ZIMBA, Olena (Ukraine)
ŽIGON, Polona (Slovenia)

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

Contents

Scientific Abstracts

Welcome Address
EULAR 2021 Abstracts Reviewers

Oral Presentations

OP0002	New perspectives on therapeutic immune tolerance	1
OP0003–OP0004	Autoimmune diseases by abnormal T cell function	1
OP0005	What the rheumatologist needs to know to interpret studies in 2021	2
OP0006–OP0013	Opening Plenary Abstract session	2
OP0014–OP0021	Genomics, genetic basis of disease and functional genomics	8
OP0022–OP0029	Adaptive immunity (T cells and B cells) in rheumatic diseases and Innate immunity in rheumatic diseases	12
OP0030–OP0037	Of mice and man: insights into pathophysiology of rheumatoid arthritis and spondyloarthritis	16
OP0038–OP0045	Molecular mechanisms in Connective Tissue Disease	20
OP0046–OP0053	Clinical aspects of axial spondyloarthritis – science meets daily practice	24
OP0054–OP0061	Vasculitis - I	28
OP0062–OP0070	Vasculitis - II	33
OP0072–OP0073	New toys in rheumatology: single cell RNA and epigenetic sequencing, the holy grail?	38
OP0074–OP0081	Education	39
OP0083–OP0089	The origins of pain in RMDs	45
OP0090–OP0097	Infection-related rheumatic and orphan diseases	49
OP0098–OP0105	Rheumatoid arthritis - comorbidity and clinical aspects - I	54
OP0106–OP0113	Bone & Joints	59
OP0114–OP0120	Rheumatoid arthritis - biological DMARDs	63
OP0122–OP0128	Rheumatoid arthritis - non biologic treatment and small molecules	68
OP0129–OP0136	SLE, Sjögren's and APS - treatment and SLE, Sjögren's and APS - clinical aspects (other than treatment)	74
OP0137–OP0144	Spondyloarthritis - treatment	80
OP0145–OP0152	Diagnostics and imaging procedures	86
OP0161–OP0168	Advances in Pediatric Rheumatology	97
OP0170–OP0177	Progress in myositis and scleroderma research - I	101
OP0178–OP0185	Rheumatoid arthritis - prognosis, predictors and outcome	106
OP0186–OP0187	Oncorheumatology: the crossroads of cancer and musculoskeletal diseases	112
OP0189–OP0190	Joint Session EULAR ESCMI and EANM (European Association of Nuclear Medicine) – State-of-the-art nuclear imaging in RMDs	114
OP0193	Comorbidities in gout and hyperuricaemia	116
OP0194–OP0195	Immune events with checkpoint inhibitors	117
OP0196–OP0197	The aftermath of metabolic imbalance in OA	118
OP0199–OP0200	Emerging molecular targets in OA	120
OP0201	Origin and role of myeloid cells during homeostasis and inflammation	121
OP0202–OP0209	Crystal diseases	122
OP0210–OP0217	Rheumatoid arthritis - comorbidity and clinical aspects - II	126
OP0218–OP0225	Unrevealing the impact of PsA and comorbidity prevention	130
OP0226–OP0233	Psoriatic arthritis - treatment	136
OP0234–OP0241	Epidemiology and public health	144
OP0242–OP0249	Systemic sclerosis, myositis - etiology, pathogenesis and animal models	148
OP0250–OP0257	Imaging in axial spondyloarthritis – what is new?	152
OP0266–OP0273	Progress in myositis and scleroderma research - II	162
OP0281–OP0288	New Developments in COVID-Research	170
OP0289–OP0297	SLE, Sjörgen's and APS - Clinical Aspects	177
OP0298–OP0299	Difficult to treat RA: definitions and mechanisms	183
OP0300	Quantitative imaging	184
OP0301	Let's consider Biologic Immunogenicity	185
OP0305–OP0306	Controversies on phenotypes in PsA	187
OP0307	Pharmacology and Microbiota	188
OP0308	What can we learn from the tissue	189

OP0309	EULAR Projects in musculoskeletal imaging	189
OP0310–OP0311	What's new: Latest advances in treatment and care in vasculitis and fibromyalgia	190
OP0312	Stress, inflammation & autoimmunity	191
OP0313–OP0314	Hyperinflammation and Covid19	191
OP0315	Metabolic pathways during the regulation of inflammation and immunity	192
OP0316	Let's work. Together.	193
OP0318–OP0319	Deconditioning in rheumatic disease, time to recognise and tackle it	194
OP0320–OP0321	EFIS session: Emerging concepts how B cells drive systemic autoimmunity: from bench to clinic	196

Late breaking abstracts

LB0001	.....	198
LB0002	.	199
LB0003	.	200
LB0004	.	201

Poster Tours

POS0001–POS0010	Adaptive immunity (T cells and B cells) in rheumatic diseases	203
POS0011–POS0020	Epidemiology and treatment of pain in RMDs	207
POS0021–POS0031	Epidemiology: Big Questions - Big studies	212
POS0032–POS0039	Imaging in axial spondyloarthritis	221
POS0040–POS0046	Molecular and structural changes of bone turnover during inflammatory disease	225
POS0047–POS0056	New Developments in COVID research	228
POS0067–POS0074	Pediatric Rheumatology – Basic and translational science	240
POS0075–POS0085	Pediatric Rheumatology - Clinical	244
POS0086–POS0092	Rheumatoid arthritis - non biologic treatment and small molecules - PART 1	251
POS0093–POS0100	Rheumatoid arthritis - prognosis, predictors and outcome	256
POS0101–POS0111	SLE, Sjögren's and APS - clinical	260
POS0112–POS0121	Translating vasculitis	267
POS0122–POS0131	Central pain and other extra-articular associations to KOA	272
POS0132–POS0141	Crystal arthritis	277
POS0142–POS0151	Fine-tuning strategies (beyond treatments) to reduce the impact of PsA	282
POS0162–POS0171	Metabolic bone disease / Osteoporosis	293
POS0172–POS0180	Molecular profiles in connective tissue disease outcome	298
POS0181–POS0191	PROMs and markers	304
POS0192–POS0201	PsA treatment: what is new?	310
POS0202–POS0209	Rheumatoid arthritis - biological DMARDs	317
POS0210–POS0219	Rheumatoid Arthritis - comorbidity and clinical aspects - Part 1	322
POS0220–POS0225	Rheumatoid arthritis - non biologic treatment and small molecules - PART 2	328
POS0226–POS0235	Spondyloarthritis - treatment	332
POS0236–POS0245	Clinical aspects of spondyloarthritis	339
POS0246–POS0255	Clinical vasculitis	344
POS0256–POS0265	Diagnostics and imaging procedures	350
POS0276–POS0285	New drugs and therapies	362
POS0286–POS0295	Oncorheumatology	368
POS0296–POS0304	Public Health, Health Services and Health Economics	373
POS0305–POS0314	Rheumatoid Arthritis - comorbidity and clinical aspects - Part 2	378
POS0315–POS0325	Scleroderma, myositis and related syndromes	383
POS0326–POS0335	Systemic sclerosis, myositis - etiology, pathogenesis and animal models	390
POS0336–POS0343	Vasculitis - Large vessel vasculitis	395

POSTERS only

POS0344–POS0362	Genomics, genetic basis of disease and functional genomics	401
POS0363	Adaptive immunity (T cells and B cells) in rheumatic diseases	411
POS0364–POS0370	Innate immunity in rheumatic diseases	412
POS0371–POS0376	Osteo arthritis, aetiology, pathology and animal models	416
POS0377–POS0403	Rheumatoid arthritis - aetiology, pathogenesis and animal models	419
POS0404–POS0415	Spondyloarthritis - aetiology, pathogenesis and animal models	431
POS0416–POS0421	SLE, Sjögren's and APS - aetiology, pathogenesis and animal models	437
POS0422–POS0433	Systemic sclerosis, myositis and related syndromes - aetiology, pathogenesis and animal models	440
POS0434	Basic and translational pain science	445
POS0434–POS0504	Rheumatoid arthritis - prognosis, predictors and outcome	446

POS0505–POS0589	Rheumatoid arthritis - comorbidity and clinical aspects	485
POS0590–POS0645	Rheumatoid arthritis - biological DMARDs	527
POS0646–POS0679	Rheumatoid arthritis - non biologic treatment and small molecules	561
POS0680–POS0704	SLE, Sjögren's and APS – treatment	585
POS0705–POS0795	SLE, Sjögren's and APS - clinical aspects (other than treatment)	602
POS0796–POS0821	Vasculitis – large vessel vasculitis	650
POS0822–POS0831	Vasculitis – small vessel vasculitis	664
POS0832-POS0894	Scleroderma, myositis and related syndromes	669
POS0895–POS0941	Spondyloarthritis – treatment	704
POS0942–POS1019	Spondyloarthritis - clinical aspects (other than treatment)	734
POS1020–POS1058	Psoriatic arthritis – treatment	777
POS1059–POS1086	Psoriatic arthritis - clinical aspects (other than treatment)	808
POS1087–POS1119	Osteoarthritis	822
POS1120–POS1150	Crystal diseases, metabolic bone diseases other than osteoporosis	839
POS1151–POS1160	Infection-related rheumatic diseases	854
POS1161–POS1268	COVID-19	858
POS1269–POS1291	Spine, mechanical musculoskeletal problems, local soft tissue disorders	919
POS1292–POS1334	Paediatric rheumatology	927
POS1335–POS1385	Other orphan diseases	949
POS1386–POS1410	Diagnostics and imaging procedures	976
POS1411–POS1417	Public health, health services research, and health economics	989
POS1418–POS1441	Epidemiology, risk factors for disease or disease progression	992
POS1442–POS1445	Validation of outcome measures and biomarkers	1005
POS1446–POS1447	Rehabilitation	1007
POS1448–POS1451	Education	1008
POS1452–POS1453	Educational cases	1010

Publication Only

AB0001–AB0015	Genomics, genetic basis of disease and functional genomics	1036
AB0016–AB0028	Adaptive immunity (T cells and B cells) in rheumatic diseases	1042
AB0029–AB0034	Innate immunity in rheumatic diseases	1048
AB0035–AB0041	Osteo arthritis, aetiology, pathology and animal models	1050
AB0042–AB0069	Rheumatoid arthritis - aetiology, pathogenesis and animal models	1053
AB0070–AB0076	Spondyloarthritis - aetiology, pathogenesis and animal models	1065
AB0077–AB0088	SLE, Sjögren's and APS - aetiology, pathogenesis and animal models	1068
AB0089–AB0095	Systemic sclerosis, myositis and related syndromes - aetiology, pathogenesis and animal models	1074
AB0096–AB0098	Vasculitis - aetiology, pathogenesis and animal models	1076
AB0099–AB0150	Rheumatoid arthritis - prognosis, predictors and outcome	1078
AB0151–AB0194	Rheumatoid arthritis - comorbidity and clinical aspects	1103
AB0195–AB0246	Rheumatoid arthritis - biological DMARDs	1121
AB0247–AB0277	Rheumatoid arthritis - non biologic treatment and small molecules	1148
AB0278–AB0296	SLE, Sjögren's and APS – treatment	1165
AB0297–AB0351	SLE, Sjögren's and APS - clinical aspects (other than treatment)	1175
AB0352–AB0400	Vasculitis – small vessel vasculitis	1220
AB0401–AB0461	Scleroderma, myositis and related syndromes	1229
AB0462–AB0486	Spondyloarthritis – treatment	1257
AB0487–AB0520	Spondyloarthritis - clinical aspects (other than treatment)	1270
AB0521–AB0565	Psoriatic arthritis – treatment	1286
AB0566–AB0581	Psoriatic arthritis - clinical aspects (other than treatment)	1320
AB0582–AB0605	Osteoarthritis	1328
AB0606–AB0627	Osteoporosis	1339
AB0628–AB0646	Crystal diseases, metabolic bone diseases other than osteoporosis	1347
AB0647–AB0650	Infection-related rheumatic diseases	1356
AB0651–AB0712	COVID-19	1358
AB0713–AB0719	Pain in rheumatic diseases, including fibromyalgia	1388
AB0720–AB0755	Paediatric rheumatology	1391
AB0756–AB0786	Other orphan diseases	1406
AB0787–AB0802	Diagnostics and imaging procedures	1419
AB0803–AB0811	Public health, health services research, and health economics	1426
AB0812–AB0833	Epidemiology, risk factors for disease or disease progression	1430
AB0834–AB0845	Validation of outcome measures and biomarkers	1441
AB0846–AB0852	Education	1446

AB0853–AB0858 Educational cases 1450

Health Professionals in Rheumatology Abstracts

Oral Presentations

OP0071-HPR Like a gearwheel: HPR's research, education, and practice 38
OP0100-HPR Rheumatoid arthritis - comorbidity and clinical aspects - I 55
OP0153-HPR–OP0160-HPR HPR Abstract Session (I) 92
OP0198-HPR Monitoring and restoring health: Should we have a core set for multidisciplinary care in rheumatology 119
OP0258-HPR–OP0265-HPR HPR Abstract Session (II) 157
OP0302-HPR Context matters: Placebo and nocebo effects for pain management 185
OP0303-HPR Myths and taboos around relationships: strategies for a sexy life 186
OP0322-HPR [Joint session HPR/ PARE/ ARP] Mastering Self-management: State of art in a New Era 197

Poster Tours

POS0152-HPR–POS0161-HPR HPR - Adapting and individualising care 289
POS0266-HPR–POS0275-HPR HPR - Understanding and measuring: expanding the toolbox 356

POSTERS only

POS1454-HPR–POS1464-HPR HPR Measuring health (development and measurement properties of PROs, tests, devices) 1011
POS1465-HPR–POS1469-HPR HPR Epidemiology and public health (including prevention) 1017
POS1470-HPR–POS1473-HPR HPR Interventions (educational, physical, social and psychological) 1020
POS1474-HPR–POS1486-HPR HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative) 1022
POS1487-HPR–POS1489-HPR HPR Service developments, innovation and economics in healthcare 1028
POS1490-HPR–POS1493-HPR HPR Professional education, training and competencies 1029
POS1494-HPR–POS1496-HPR HPR Interdisciplinary research 1031

Publication Only

AB0859-HPR–AB0865-HPR HPR Measuring health (development and measurement properties of PROs, tests, devices) 1453
AB0866-HPR–AB0871-HPR HPR Epidemiology and public health (including prevention) 1456
AB0872-HPR–AB0883-HPR HPR Interventions (educational, physical, social and psychological) 1459
AB0884-HPR–AB0902-HPR HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative) 1465
AB0903-HPR–AB0909-HPR HPR Service developments, innovation and economics in healthcare 1474
AB0910-HPR–AB0911-HPR HPR Professional education, training and competencies 1477
AB0912-HPR HPR Interdisciplinary research 1478

People with Arthritis and Rheumatism in Europe Abstracts

Oral Presentations

OP0009-PARE Opening Plenary Abstract session 5
OP0082-PARE Challenges for Patients and Patients' Organisations in Times of the Pandemic 44
OP0169-PARE Challenges for working people with RMDs in pandemic times 101
OP0191-PARE Improving collaborative research and patients' participation in health decision-making 115
OP0274-PARE–OP0280-PARE PARE Abstract session 166
OP0304-PARE Myths and taboos around relationships: strategies for a sexy life 187
OP0317-PARE Let's work. Together. 193
OP0323-PARE–OP0324-PARE Members and Volunteers – Unknown beings? How to explore their interests, establish contacts and support 197

Poster Tours

POS0057-PARE–POS0066-PARE PARE Poster Tour 235

POSTERS only

POS1497-PARE Patient information and education 1033
POS1498-PARE Building patient led organisations 1033
POS1499-PARE Arthritis research 1034

Publication Only

AB0913-PARE–AB0922-PARE	Patient information and education	1478
AB0923-PARE	Building patient led organisations	1482
AB0924-PARE–AB0925-PARE	Arthritis research	1483
AB0926-PARE	Psychosocial support	1484
AB0927-PARE	Work and rehabilitation	1484

Author Index 1486

Oral Presentations

New perspectives on therapeutic immune tolerance

OP0002 IMMTOR NANOPARTICLES ENHANCE THE TOLEROGENIC ENVIRONMENT OF THE LIVER IN MICE

P. Ilyinskii[1], C. Roy[1], J. Leprevost[1], K. Kishimoto[1]. [1]*Selecta Biosciences, Biology, Watertown, United States of America*

Background: Tolerogenic ImmTOR biodegradable nanoparticles encapsulating rapamycin have been shown to mitigate the formation of anti-drug antibodies against pegadricase, a pegylated uricase enzyme, which enabled monthly dosing and sustained reduction of serum uric acid levels in a Phase 2 clinical trial of SEL-212, a combination of pegadricase + ImmTOR, in patients with symptomatic gout with hyperuricemia. Prior mechanism of action studies showed selective biodistribution of ImmTOR to the spleen and liver following intravenous (IV) administration in mice. In the spleen, ImmTOR has been demonstrated to induce tolerogenic dendritic cells and antigen-specific regulatory T cells and inhibit antigen-specific B cell activation. Splenectomized mice showed a partial but incomplete abrogation of the tolerogenic immune response mediated by ImmTOR.
Objectives: Here we evaluated the ability of ImmTOR to enhance the tolerogenic environment in the liver.
Results: All the major resident populations of liver cells, including liver sinusoidal endothelial cells (LSECs), Kupffer cells (KC), stellate cells (SC), and hepatocytes, actively took up fluorescent-labeled ImmTOR particles, which resulted in downregulation of MHC class II and co-stimulatory molecules and upregulation of the PD-L1 checkpoint molecule. The LSEC, known to play an important role in hepatic tolerance induction, emerged as a key target cell for ImmTOR. The tolerogenic environment led to a multi-pronged modulation of hepatic T cell populations, resulting in an increase in T cells with a regulatory phenotype, upregulation of PD-1 on $CD4^+$ and $CD8^+$ T cells, and the emergence of a large population of $CD4^-CD8^-$ (double negative) T cell population. Modulation of T cell phenotype was seen to a lesser extent after administration by empty nanoparticles, but not free rapamycin. The upregulation of PD-1, but not the appearance of double negative T cells, was inhibited by antibodies against PD-L1 or CTLA-4.
Conclusion: These results suggest that the liver may contribute to the tolerogenic properties of ImmTOR in mitigating anti-drug antibody responses to biologic therapies, such as pegadricase.
Disclosure of Interests: Petr Ilyinskii Shareholder of: Selecta Biosciences, Employee of: Selecta Biosciences, Christopher Roy Shareholder of: Selecta Biosciences, Employee of: Selecta Biosciences, Julie LePrevost Shareholder of: Selecta Biosciences, Employee of: Selecta Biosciences, Kei Kishimoto Shareholder of: Selecta Biosciences, Employee of: Selecta Biosciences
DOI: 10.1136/annrheumdis-2021-eular.1920

Autoimmune diseases by abnormal T cell function

OP0003 AUTOREACTIVE CD4+ T CELLS AND THEIR TCR REPERTOIRE IN PR3-ANCA ASSOCIATED VASCULITIS

R. Kumar[1], N. Yoosuf[1], A. Bartoletti[2], A. Avik[3], B. Raposo[1], A. Jonasdottir[4], B. Lövström[1], K. Chemin[1], A. Bruchfeld[4], I. Gunnarsson[1], V. Malmström[1]. [1]*Karolinska Institutet, Division of Rheumatology, Department of Medicine, Stockholm, Sweden;* [2]*The University of Pavia, Medicine, Pavia, Italy;* [3]*Danderyds hospital, Rheumatology, Stockholm, Sweden;* [4]*Karolinska University Hospital, CLINTEC, Stockholm, Sweden*

Background: ANCA-associated vasculitis (AAV) with proteinase 3 (PR3) ANCA is genetically associated with HLA-DP [1], is often relapsing in nature, and has a predisposition for kidneys, lungs and ear-nose-throat involvement [2]. Despite the presence of PR3+ANCA, indicating CD4+T-cell help in the disease, the knowledge about autoreactive CD4+T cells is scarce. Activated T cells have been shown at site of inflammation [3] and involvement of proinflammatory cytokines in circulation is also reported [4, 5].
Objectives: Identification of autoreactive T cells may help to identify the drivers of the immune responses and chronicity. We therefore aimed to investigate PR3-specific CD4+T-cell responses in peripheral blood of AAV patients with a focus on both phenotype and T-cell receptor (TCR) repertoires.
Methods: The study included sixty-six patients: 26 with active PR3 autoantibody+ AAV, 21 with inactive but PR3+ AAV and 19 with inactive PR3- AAV. *In-vitro* cultures with PR3 protein were established to assess antigen-specific cytokine responses in a 3-color fluorospot assay. Deep immunophenotyping was performed by flow cytometry. Antigen-responsive CD4+ T cells were isolated and single cell TCR$\alpha\beta$ sequences were generated and analyzed from PR3+ AAV patients (n=5) using a previously published protocol [6].
Results: PBMCs from AAV patients demonstrated an HLA-DP associated cytokine responses to PR3 stimulation including IFN-γ and IL-10, but not IL-17A. This T-cell autoreactivity was found to be confined to a highly differentiated CD4+ T cell population characterized by perforin and GPR56 expression, implicating a cytotoxic feature of the response. Active disease involved a reduction in expression of several markers associated with cytotoxicity amongst the CD4+GPR56+ T cells. Their frequency was also negatively associated with the doses of prednisolone. A similar phenotype was shared with T cells activated by human cytomegalovirus (HCMV) peptides in the same patient cohort. Single cell sequencing of paired alpha beta T-cell receptors (TCRs) revealed different patterns of gene usage between PR3 and HCMV reactive T cells. Moreover, we could identify shared (public) PR3-reactive T-cell clones between different HLA-DPB1*04:01+ patients.
Conclusion: PR3 is an autoantigen which provokes ANCA responses in AAV patients. Our study identified PR3-reactive CD4+ T cells at the level of their phenotype and TCR repertoire. The autoreactive CD4+ T cells, present in both active and inactive disease, implicate chronic antigen exposure and the persistence of long-lived T-cell clones. The presence of public autoreactive clones between HLA-DPB1*04:01+ patients suggests an active role for these cells in pathogenesis of AAV and validates the link with predisposed genotype.
REFERENCES:
[1] Lyons PA, Rayner TF, Trivedi S, Holle JU, Watts RA, Jayne DR, et al. Genetically distinct subsets within ANCA-associated vasculitis. New England Journal of Medicine. 2012; 367(3):214-223.
[2] Kumar Sharma R, Lövström B, Gunnarsson I, Malmström V. Proteinase 3 autoreactivity in Anti-Neutrophil Cytoplasmic Antibody-associated vasculitis–immunological versus clinical features. Scandinavian Journal of Immunology. 2020:e12958.
[3] Wilde B, Thewissen M, Damoiseaux J, van Paassen P, Witzke O, Tervaert JWCJAr, et al. T cells in ANCA-associated vasculitis: what can we learn from lesional versus circulating T cells? 2010; 12(1):204.
[4] Hoffmann JC, Patschan D, Dihazi H, Müller C, Schwarze K, Henze E, et al. Cytokine profiling in anti neutrophil cytoplasmic antibody-associated vasculitis: a cross-sectional cohort study. Rheumatology international. 2019; 39(11):1907-1917.
[5] Berti A, Warner R, Johnson K, Cornec D, Schroeder D, Kabat B, et al. Circulating Cytokine Profiles and ANCA Specificity in Patients with ANCA-Associated Vasculitis. Arthritis & rheumatology (Hoboken, NJ). 2018; 70(7):1114.
[6] Han A, Glanville J, Hansmann L, Davis MM. Linking T-cell receptor sequence to functional phenotype at the single-cell level. Nature biotechnology. 2014; 32(7):684-692.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.41

OP0004 AUTOIMMUNE AND INFLAMMATORY MANIFESTATIONS IN COMMON VARIABLE IMMUNODEFICIENCY DISORDERS

K. López-Aldabe[1], L. Hidalgo[2], A. Antolí[2], G. Rocamora[2], X. Corbella[2], X. Solanich[2]. [1]*Bellvitge University Hospital, Bellvitge Biomedical Research Institute-IDIBELL, Internal Medicine, L'Hospitalet de Llobregat, Spain*; [2]*Bellvitge University Hospital, Bellvitge Biomedical Research Institute-IDIBELL, Internal Medicine, Hospitalet de Llobregat, Spain*

Background: Common variable immunodeficiency (CVID) disorders are the second most frequent immunodeficiency worldwide and autoimmune diseases (AD) are present in 20% of such patients, cytopenia being the most frequent manifestation [1]. Defects in central and peripheral tolerance, activation/proliferation of B cells, and hypogammaglobulinemia are key features of the disease, along with a reduction in CD4+T cells, abnormalities in Treg and defective secretion of regulatory cytokines, that could perpetuate autoimmune - autoinflammatory phenomena.
Objectives: To describe immune and inflammatory disorders in our CVID cohort.
Methods: Retrospective analysis of 33 patients who fulfill the European Society for Immunodeficiencies (ESID) Registry – Work criteria for CVID diagnosis [2] treated in the immunodeficiency unit of our tertiary university hospital. After getting an informed consent form, medical records were revised to obtain clinical, analytical and immunological data.
Results: Of the 33 CVID patients analysed, 11 had some autoimmune/inflammatory manifestation. Seven patients presented autoimmune thrombocytopenia (AIT), and one of them also had non-severe neutropenia. Two patients also had seronegative spondyloarthropathy, one patient had cutaneous psoriasis, and

two patients had alopecia. There were no cases of type 1 diabetes, vitiligo or thyroid disorders. Interestingly, four patients had lung involvement, two of them with granulomatous-lymphocytic interstitial lung disease (GLILD), one with organising pneumonia and one with usual interstitial pneumonia. Five of the eleven patients required immunosuppressive treatment, mostly with steroids. One case of AIT required concomitant treatment with azathioprine and the patient with psoriasis was treated with methotrexate. In six patients, autoimmune disorder was the first manifestation.

Conclusion: 33% of the CVID patients had autoimmune or inflammatory manifestations in our cohort; six patients had one immune/inflammatory phenomena, four had two different disorders and one patient presented with three different ones. The most frequent manifestation was AIT, as seen in previous reports. In six cases, the autoimmune-inflammatory manifestation was the first symptom attributable to CVID. In conclusion, AD are common in CVID patients, so clinicians must be aware of possible immunodeficiencies in this type of patients.

REFERENCES:

[1] Amaya-Uribe L, Rojas M, Azizi G, Anaya JM, Gershwin ME. Primary immunodeficiency and autoimmunity: A comprehensive review. J Autoimmun. 2019 May;99:52-72.

[2] ESID Registry – Working Definitions for Clinical Diagnosis of PID, January 22, 2019.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2696

What the rheumatologist needs to know to interpret studies in 2021

OP0005 DIETARY HYPERINSULINEMIC POTENTIAL AND RISK OF INCIDENT GOUT: 3 PROSPECTIVE COHORT STUDIES OF US MEN AND WOMEN

N. McCormick[1,2,3,4], C. Yokose[1,3,4], L. Lu[2,5], A. Joshi[3,4,6], H. Choi[1,2,3,4]. *[1]Massachusetts General Hospital, Clinical Epidemiology Program, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; *[2]Arthritis Research Canada, -, Richmond, Canada*; *[3]Massachusetts General Hospital, The Mongan Institute, Boston, United States of America*; *[4]Harvard Medical School, Medicine, Boston, United States of America*; *[5]Brigham and Women's Hospital, Channing Division of Network Medicine, Boston, United States of America*; *[6]Massachusetts General Hospital, Clinical & Translational Epidemiology Unit, Boston, United States of America*

Background: Gout and the metabolic (insulin resistance) syndrome frequently coexist. Intravenous insulin has been shown to raise serum urate (SU) levels in physiologic studies and a Mendelian Randomization study also showed a causal role of insulin on the risk of gout. However, it is unknown whether habitual hyperinsulinemic dietary intake confers gout risk.

Objectives: Prospectively examine the relation between two distinct insulin-related dietary indices and risk of incident gout in three large cohorts of US women and men over 30 years.

Methods: We studied 164,090 women from Nurses Health Study I (1986-2016) and II (1989-2017) and 40,598 men from Health Professionals Follow-up Study (1986-2016), who were free of gout at baseline. Dietary intake and covariates were assessed by validated questionnaires every 4 years. Insulinemic potential of diet was evaluated using 1) food-based empirical dietary index for hyperinsulinemia (EDIH) score that was pre-defined based on circulating C-peptide levels[1] and reflects *insulin resistance*;[2] and 2) dietary insulin index (DII), which reflects *transient, postprandial insulin secretion*.[2] We assigned EDIH and DII scores for each participant, adjusted for total energy intake, and prospectively examined the association between scores and incident gout (using ACR survey criteria for gout[3]), adjusting for potential confounders.

Results: We ascertained 2,874 incident gout cases over 5,124,490 person-years of follow-up. In pooled multivariable-adjusted analyses, those in the highest EDIH quintile had 1.76-times (95% CI: 1.56 to 1.99) higher gout risk, compared with the lowest (Table 1). This attenuated with further adjustment for BMI (a likely causal intermediate) but remained positive (RR 1.30, 1.15 to 1.48). DII scores were inversely associated with gout risk (RR 0.66, 0.58 to 0.74) (Table 1).

Conclusion: EDIH scores, reflecting chronic hyperinsulinemia (i.e., greater insulin resistance with reduced clearance), were positively associated with the risk of incident gout, even beyond the pathway through adiposity. Conversely, higher DII scores, which reflect short-term, postprandial elevations in insulin levels (and also greater insulin clearance and sensitivity) conferred a lower risk. This corroborates human physiologic experiments and Mendelian Randomization studies showing insulin resistance can increase SU levels by decreasing renal excretion of urate, and supports lowering insulinemic potential of diet as a strategy to reduce gout risk.

REFERENCES:

[1] Tabung *et al.* PMID 27821188

[2] Lee *et al.* PMID 32618519

[3] Wallace *et al.* PMID 856219

Disclosure of Interests: Natalie McCormick: None declared, Chio Yokose: None declared, Leo Lu: None declared, Amit Joshi: None declared, Hyon Choi Consultant of: Ironwood, Selecta, Horizon, Takeda, Kowa, Vaxart, Grant/research support from: Ironwood, Horizon

DOI: 10.1136/annrheumdis-2021-eular.719

Opening Plenary Abstract session

OP0006 ASSOCIATIONS OF BASELINE USE OF BIOLOGIC OR TARGETED SYNTHETIC DMARDS WITH COVID-19 SEVERITY IN RHEUMATOID ARTHRITIS: RESULTS FROM THE COVID-19 GLOBAL RHEUMATOLOGY ALLIANCE

J. Sparks[1,2], Z. Wallace[2,3], A. Seet[4], M. Gianfrancesco[4], Z. Izadi[4,5], K. Hyrich[6,7], A. Strangfeld[8], L. Gossec[9,10], L. Carmona[11], E. Mateus[12,13], S. Lawson-Tovey[7,14], L. Trupin[4], S. Rush[4], G. Schmajuk[4,15], P. Katz[4], L. Jacobsohn[4], S. Al Emadi[16], L. Wise[17], E. Gilbert[18], A. Duarte-Garcia[19], M. Valenzuela-Almada20, T. Hsu[1], K. D'silva[2,3], N. Serling-Boyd[2,3], P. Dieudé[21], E. Nikiphorou[22], V. Kronzer[18], N. Singh[23], M. F. Ugarte-Gil[24], B. Wallace[25,26], A. Akpabio[27], R. Thomas[28], S. Bhana[29], W. Costello[30], R. Grainger[31], J. Hausmann[2,32,33], J. Liew[34], E. Sirotich[35,36], P. Sufka[37], P. Robinson[38,39], P. Machado[40,41,42], J. Yazdany[4]on behalf of COVID-19 Global Rheumatology Alliance. *[1]Brigham And Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, United States of America*; *[2]Harvard Medical School, Division of Rheumatology, Inflammation, and Immunity, Boston, United States of America*; *[3]Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; *[4]University of California, San Francisco, Division of Rheumatology, San Francisco, United States of America*; *[5]University of*

Table 1. Risk Ratio (95% CI) of Gout According to Quintiles of Insulin-Related Dietary Index

	EDIH (measure of insulin resistance)					
	Q1: lowest circulating insulin levels	**Q2**	**Q3**	**Q4**	**Q5: highest circulating insulin levels**	**P for trend**
N cases	430	482	598	631	733	
Person-years	1,025,129	1,025,285	1,025,574	1,025,301	1,023,651	
Age-adjusted RR	1.00 (Ref)	1.13 (1.00-1.29)	1.43 (1.26-1.61)	1.53 (1.36-1.73)	1.85 (1.64-2.09)	<.0001
MV-Adjusted* RR	1.00 (Ref)	1.11 (0.98-1.27)	1.39 (1.22-1.57)	1.47 (1.30-1.67)	1.76 (1.56-1.99)	<.0001
MV-Adjusted RR (+ BMI)**	1.00 (Ref)	1.03 (0.90-1.17)	1.21 (1.06-1.37)	1.21 (1.07-1.37)	1.30 (1.15-1.48)	<.0001
Dietary Insulin Index (measure of transient, post-prandial secretion and sensitivity)						
	Q1: lowest insulin sensitivity	**Q2**	**Q3**	**Q4**	**Q5: greatest insulin sensitivity**	**P for trend**
N cases	783	611	527	498	455	
Person-years	1,024,763	1,025,730	1,025,075	1,025,538	1,023,834	
Age-adjusted RR	1.00 (Ref)	0.79 (0.71-0.88)	0.69 (0.62-0.77)	0.65 (0.58-0.73)	0.59 (0.53-0.66)	<.0001
MV-Adjusted* RR	1.00 (Ref)	0.79 (0.71-0.88)	0.69 (0.62-0.77)	0.66 (0.59-0.74)	0.60 (0.53-0.67)	<.0001
MV-Adjusted RR (+ BMI)**	1.00 (Ref)	0.78 (0.70-0.87)	0.69 (0.62-0.77)	0.67 (0.60-0.75)	0.66 (0.58-0.74)	<.0001

*Multivariable (MV) models adjusted for age (month), White race, smoking, menopause (women only), hormone use (women only), physical activity, history of hypertension, and diuretic use **MV + BMI models further adjusted for BMI (a likely causal intermediate)

California, San Francisco, Department of Epidemiology and Biostatistics, San Francisco, United States of America; [6]*The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [7]*Manchester University NHS FT, National Institute of Health Research Manchester Biomedical Research Centre, Manchester, United Kingdom*; [8]*Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), ein Institut der Leibniz-Gemeinschaft, German Rheumatism Research Center, Berlin, Germany*; [9]*Institute Pierre Louis Epidemiology And Public Health, INSERM, Paris, France*; [10]*University Hospitals Pitié Salpêtrière - Charles Foix, Rheumatology Department, Paris, France*; [11]*Instituto de Salud Musculoesquelética (InMusc), Rheumatology Department, Madrid, Spain*; [12]*Portuguese League Against Rheumatic Diseases, Rheumatology Department, Lisbon, Portugal*; [13]*European League Against Rheumatism (EULAR) Standing Committee of People with Arthritis/Rheumatism in Europe (PARE), Department of Rheumatology, Kilchberg, Switzerland*; [14]*The University of Manchester, Centre for Genetics and Genomics Versus Arthritis, Manchester, United Kingdom*; [15]*San Francisco VA Medical Center, Division of Rheumatology, San Francisco, United States of America*; [16]*Hamad Medical Corporation, Rheumatology Department, Doha, Qatar*; [17]*University of Southern California, Division of Rheumatology, Los Angeles, United States of America*; [18]*Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; [19]*Mayo Clinic, Division of Rheumatology and Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, United States of America*; [18]*Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; [21]*Bichat-Claude Bernard Hospital, Rheumatology Department, Paris, France*; [22]*King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; [23]*University of Washington, Division of Rheumatology, Seattle, United States of America*; [24]*Scientific University of the South, Rheumatology Department, Lima, Peru*; [25]*University of Michigan, Department of Internal Medicine/Rheumatology, Ann Arbor, United States of America*; [26]*VA Ann Arbor Healthcare System, Center for Clinical Management Research, Ann Arbor, United States of America*; [27]*Royal Hallamshire Hospital, Rheumatology Department, Sheffield, United Kingdom*; [28]*University of Queensland, UQ Diamantina Institute, Queensland, Australia*; [29]*Crystal Run Health, Rheumatology Department, Middletown, United States of America*; [30]*Irish Children's Arthritis Network, Arthritis Department, Tipperary, Ireland*; [31]*University of Otago, Rheumatology Department, Dunedin, New Zealand*; [32]*Boston Children's Hospital, Program in Rheumatology, Boston, United States of America*; [33]*Beth Israel Deaconess Medical Center (BIDMC), Division of Rheumatology and Clinical Immunology, Boston, United States of America*; [34]*Boston University School of Medicine, Section of Rheumatology, Boston, United States of America*; [35]*McMaster University, Department of Health Research Methods, Evidence, and Impact, Hamilton, Canada*; [36]*Canadian Arthritis Patient Alliance, Arthritis Department, Toronto, Canada*; [37]*Healthpartners, Rheumatology Department, St Paul, United States of America*; [38]*University of Queensland, Faculty of Medicine, Brisbane, Australia*; [39]*Metro North Hospital and Health Service, Faculty of Medicine, Queensland, Australia*; [40]*University College London, Centre for Rheumatology & Department of Neuromuscular Diseases, London, United Kingdom*; [41]*University College London Hospitals National Health Service (NHS) Trust, National Institute for Health Research (NIHR) University College London Hospitals Biomedical Research Centre, London, United Kingdom*; [42]*Northwick Park Hospital, Department of Rheumatology, London, United Kingdom*

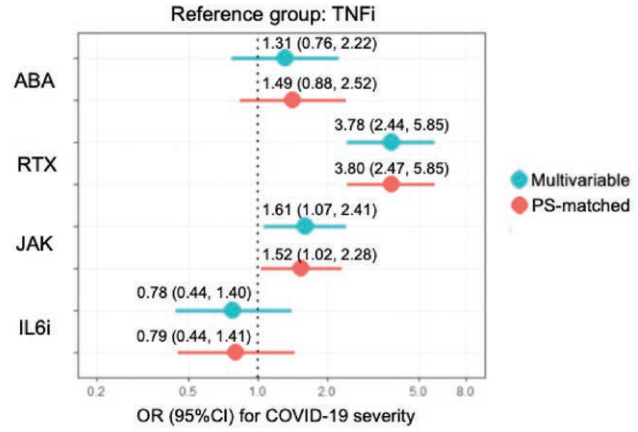
Background: Targeted DMARDs may dampen the inflammatory response in COVID-19, perhaps leading to a less severe clinical course. However, some DMARD targets may impair viral immune defenses. Due to sample size limitations, previous studies of DMARD use and COVID-19 outcomes have combined several heterogeneous rheumatic diseases and medications, investigating a single outcome (e.g., hospitalization).

Objectives: To investigate the associations of baseline use of biologic or targeted synthetic (b/ts) DMARDs with a range of poor COVID-19 outcomes in rheumatoid arthritis (RA).

Methods: We analyzed voluntarily reported cases of COVID-19 in patients with rheumatic diseases in the COVID-19 Global Rheumatology Alliance physician registry (March 12, 2020 - January 6, 2021). We investigated RA treated with b/tsDMARD at the clinical onset of COVID-19 (baseline): abatacept (ABA), rituximab (RTX), Janus kinase inhibitors (JAK), interleukin-6 inhibitors (IL6i), or tumor necrosis factor inhibitors (TNFi). The outcome was an ordinal scale (1-4) for COVID-19 severity: 1) no hospitalization, 2) hospitalization without oxygen need, 3) hospitalization with any oxygen need or ventilation, or 4) death. Baseline covariates including age, sex, smoking, obesity, comorbidities (e.g., cardiovascular disease, cancer, interstitial lung disease [ILD]), concomitant non-biologic DMARD use, glucocorticoid use/dose, RA disease activity, country, and calendar time were used to estimate propensity scores (PS) for b/tsDMARD. The primary analysis used PS matching to compare each drug class to TNFi. Ordinal logistic regression estimated ORs for the COVID-19 severity outcome. In a sensitivity analysis, we used traditional multivariable ordinal logistic regression adjusting for covariates without matching.

Results: Of the 1,673 patients with RA on b/tsDMARDs at the onset of COVID-19, (mean age 56.7 years, 79.6% female) there were n=154 on ABA, n=224 on RTX, n=306 on JAK, n=180 on IL6i, and n=809 on TNFi. Overall, 498 (34.3%) were hospitalized and 112 (6.7%) died. Among all patients, 353 (25.3%) were ever smokers, 197 (11.8%) were obese, 462 (27.6%) were on glucocorticoids, 1,002 (59.8%) were on concomitant DMARDs, and 299 (21.7%) had moderate/high RA disease activity. RTX users were more likely than TNFi users to have ILD (11.6% vs. 1.7%) and history of cancer (7.1% vs. 2.0%); JAK users were more likely than TNFi users to be obese (17.3% vs. 9.0%). After propensity score matching, RTX was strongly associated with greater odds of having a worse outcome compared to TNFi (OR 3.80, 95% CI 2.47, 5.85; Figure). Among RTX users, 42 (18.8%) died compared to 27 (3.3%) of TNFi users (Table). JAK use was also associated with greater odds of having a worse COVID-19 severity (OR 1.52, 95%CI 1.02, 2.28). ABA or IL6i use were not associated with COVID-19 severity compared to TNFi. Results were similar in the sensitivity analysis and after excluding cancer or ILD.

Figure. Odds ratios for the ordinal COVID-19 severity outcome for patients with RA on biologic or targeted synthetic DMARDs (n=1673).



The effect size is the odds of being one level higher on the ordinal scale than the reference group.

n for propensity score (PS)-matched analyses: 98 ABA and 525 TNFi; 127 RTX and 520 TNFi; 198 JAK and 527 TNFi; 107 IL6i and 525 TNFi.

Multivariable covariates and propensity score included age, sex, region, season, smoking, obesity, RA disease activity, interstitial lung disease, cancer, comorbidity count, concomitant non-biologic DMARD use, and glucocorticoid use/dose.

Table 1. Frequencies for the ordinal COVID-19 severity outcome for patients with RA on biologic or targeted synthetic DMARDs (n=1673).

COVID-19 outcomes by severity scale (n,%)	ABA n=154	RTX n=224	JAK n=306	IL6i n=180	TNFi n=809
1)Not hospitalized	113 (73.3%)	121 (54.0%)	220 (71.9%)	150 (83.3%)	666 (82.3%)
2)Hospitalization without oxygenation	10 (6.5%)	14 (6.2%)	11 (3.6%)	9 (5.0%)	53 (6.5%)
3)Hospitalization with any oxygenation or ventilation	16 (10.4%)	47 (21.0%)	52 (17.0%)	16 (8.9%)	63 (7.8%)
4)Death	15 (9.7%)	42 (18.8%)	23 (7.5%)	5 (2.8%)	27 (3.3%)

Conclusion: In this large global registry of patients with RA and COVID-19, baseline use of RTX or JAK was associated with worse severity of COVID-19 compared to TNFi use. The very elevated odds for poor COVID-19 outcomes in RTX users highlights the urgent need for risk-mitigation strategies, such as the optimal timing of vaccination. The novel association of JAK with poor COVID-19 outcomes requires replication.

Acknowledgements: The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance and do not necessarily represent the views of the ACR, EULAR, the UK National Health Service, the National Institute for Health Research, the UK Department of Health, or any other organization.

Disclosure of Interests: Jeffrey Sparks Consultant of: Bristol-Myers Squibb, Gilead, Inova, Janssen, and Optum, unrelated to this work, Grant/research support from: Amgen and Bristol-Myers Squibb, unrelated to this work, Zachary Wallace Consultant of: Viela Bio and MedPace, outside the submitted work., Grant/research support from: Bristol-Myers Squibb and Principia/Sanofi, Andrea Seet: None declared, Milena Gianfrancesco: None declared, Zara Izadi: None

declared, Kimme Hyrich Speakers bureau: Abbvie unrelated to this study, Grant/research support from: BMS, UCB, and Pfizer, all unrelated to this study, Anja Strangfeld Paid instructor for: AbbVie, MSD, Roche, BMS, Pfizer, outside the submitted work, Grant/research support from: grants from a consortium of 13 companies (among them AbbVie, BMS, Celltrion, Fresenius Kabi, Lilly, Mylan, Hexal, MSD, Pfizer, Roche, Samsung, Sanofi-Aventis, and UCB) supporting the German RABBIT register, outside the submitted work, Laure Gossec Consultant of: Abbvie, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sanofi-Aventis, UCB, unrelated to this study, Grant/research support from: Lilly, Mylan, Pfizer, all unrelated to this study, Loreto Carmona: None declared, Elsa Mateus Grant/research support from: grants from Abbvie, Novartis, Janssen-Cilag, Lilly Portugal, Sanofi, Grünenthal S.A., MSD, Celgene, Medac, Pharmakern, GAfPA; grants and non-financial support from Pfizer, outside the submitted work, Saskia Lawson-Tovey: None declared, Laura Trupin: None declared, Stephanie Rush: None declared, Gabriela Schmajuk: None declared, Patti Katz: None declared, Lindsay Jacobsohn: None declared, Samar Al Emadi: None declared, Leanna Wise: None declared, Emily Gilbert: None declared, Ali Duarte-Garcia: None declared, Maria Valenzuela-Almada: None declared, Tiffany Hsu: None declared, Kristin D'Silva: None declared, Naomi Serling-Boyd: None declared, Philippe Dieudé Consultant of: Boerhinger Ingelheim, Bristol-Myers Squibb, Lilly, Sanofi, Pfizer, Chugai, Roche, Janssen unrelated to this work, Grant/research support from: Bristol-Myers Squibb, Chugaii, Pfizer, unrelated to this work, Elena Nikiphorou: None declared, Vanessa Kronzer: None declared, Namrata Singh: None declared, Manuel F. Ugarte-Gil Grant/research support from: Janssen and Pfizer, Beth Wallace: None declared, Akpabio Akpabio: None declared, Ranjeny Thomas: None declared, Suleman Bhana Consultant of: AbbVie, Horizon, Novartis, and Pfizer (all <$10,000) unrelated to this work, Wendy Costello: None declared, Rebecca Grainger Speakers bureau: Abbvie, Janssen, Novartis, Pfizer, Cornerstones, Jonathan Hausmann Consultant of: Novartis, Sobi, Biogen, all unrelated to this work (<$10,000), Jean Liew Grant/research support from: Yes, I have received research funding from Pfizer outside the submitted work., Emily Sirotich Grant/research support from: Board Member of the Canadian Arthritis Patient Alliance, a patient run, volunteer based organization whose activities are largely supported by independent grants from pharmaceutical companies, Paul Sufka: None declared, Philip Robinson Speakers bureau: Abbvie, Eli Lilly, Janssen, Novartis, Pfizer and UCB (all < $10,000), Consultant of: Abbvie, Eli Lilly, Janssen, Novartis, Pfizer and UCB (all < $10,000), Pedro Machado Speakers bureau: Yes, I have received consulting/speaker's fees from Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, all unrelated to this study (all < $10,000)., Consultant of: Yes, I have received consulting/speaker's fees from Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, all unrelated to this study (all < $10,000)., Jinoos Yazdany Consultant of: Eli Lilly and AstraZeneca unrelated to this project

DOI: 10.1136/annrheumdis-2021-eular.1632

OP0007

MUC5B PROMOTER VARIANT AND LONG-TERM INCIDENCE OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A POPULATION BIOBANK STUDY OF 250,000 INDIVIDUALS

A. Palomäki[1], T. Laitinen[2], J. Koskela[3], A. Palotie[3,4,5], N. Mars[3]on behalf of FinnGen. *[1]Turku University Hospital, Centre for Rheumatology and Clinical Immunology, Turku, Finland*; *[2]Tampere University Hospital, Administration Center, Tampere, Finland*; *[3]University of Helsinki, Institute for Molecular Medicine Finland, FIMM, HiLIFE, Helsinki, Finland*; *[4]Massachusetts General Hospital, Analytic and Translational Genetics Unit, Department of Medicine, Boston, United States of America*; *[5]Broad Institute of MIT and Harvard, Stanley Center for Psychiatric Research, Cambridge, MA, United States of America*

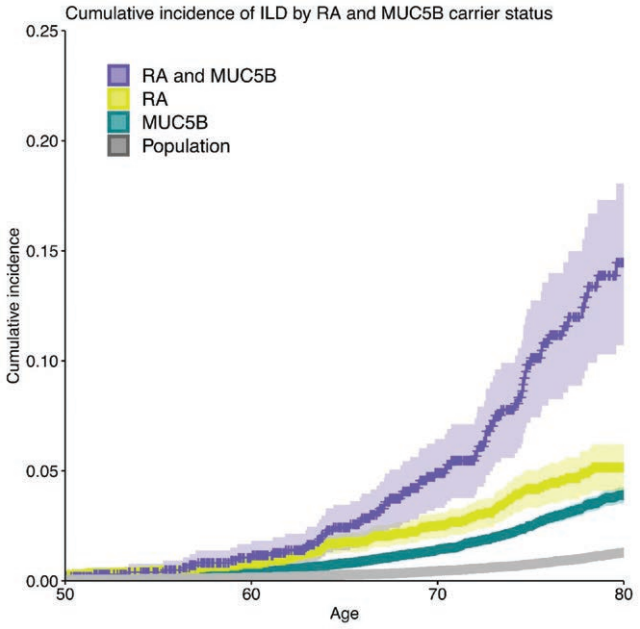
Background: The promoter variant rs35705950 in *MUC5B* is the strongest known genetic risk factor for rheumatoid arthritis-associated interstitial lung disease (RA-ILD) [1]. There is, however, no large-scale data on the impact of *MUC5B* on the long-term incidence of RA-ILD.

Objectives: To describe long term risk of RA-ILD in RA patients carrying *MUC5B* variant compared to non-carriers with RA.

Methods: FinnGen is a collection of epidemiological cohorts and hospital biobank samples, linking genotypes with up to 46 years of follow-up within nationwide registries. Diagnoses of RA and ILD were identified from the Finnish national hospital discharge, medication reimbursement and cause-of-death registries. We estimated lifetime risks of ILD by age 80. *MUC5B* is a common variant and has an allele frequency of 0.1 in the Finnish population.

Results: Out of the 248,400 individuals, 5534 patients have been diagnosed with RA, out of whom 178 (3.2%) developed ILD. *MUC5B* was a strong predictor of ILD in RA patients (HR 2.14, 95%CI 1.56-2.92). In patients with RA, *MUC5B* conferred a lifetime risk of 14.5% (95%CI 10.7-18.1%), compared to 5.2% (4.1-6.2%) in *MUC5B* non-carriers with RA (Figure). In the population, *MUC5B* carriers and *MUC5B* non-carriers had lifetime risks of 3.9% and 1.3%, respectively. The risk difference started to emerge at age 65. The risk was highest in men with RA who are *MUC5B* carriers: 18.5% (11.1-25.2%) developed ILD, compared to 8.5% (6.1-10.9%) of *MUC5B* non-carriers with RA.

Conclusion: We report findings from a large longitudinal study, showing that *MUC5B* confers a considerable lifetime risk of RA-ILD, and contributes to increased morbidity. These findings have clinical implications for improving identification of RA patients at high risk of developing ILD.



REFERENCES:

[1] Juge P-A, Lee JS, Ebstein E, et al. MUC5B Promoter Variant and Rheumatoid Arthritis with Interstitial Lung Disease. N Engl J Med 2018;379:2209–19

Disclosure of Interests: Antti Palomäki Speakers bureau: MSD, Pfizer, Sanofi, Consultant of: Pfizer, Abbvie, Tarja Laitinen: None declared, Jukka Koskela Speakers bureau: Pfizer, Aarno Palotie: None declared, Nina Mars: None declared

DOI: 10.1136/annrheumdis-2021-eular.619

OP0008

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III TRIAL OF IVIG 10% IN PATIENTS WITH DERMATOMYOSITIS. THE PRODERM STUDY: RESULTS ON EFFICACY AND SAFETY

R. Aggarwal[1], C. Charles-Schoeman[2], J. Schessl[3], Z. Bata-Csorgo[4], M. Dimachkie[5], Z. Griger[6], S. Moiseev[7], C. V. Oddis[8], E. Schiopu[9], J. Vencovský[10], I. Beckmann[11], T. Levine[12], E. Clodi[13], A. T. Proderm Investigators[14]. *[1]University of Pittsburgh, Rheumatology, Pittsburgh, United States of America*; *[2]UCLA Health, Rheumatology, Los Angeles, United States of America*; *[3]Friedrich Baur Institute, University of Munich, Neurology, Munich, Germany*; *[4]University of Szeged, Faculty of Medicine, Dermatology, Szeged, Hungary*; *[5]Univeristy of Kansas, Medical Center, Neurology, Kansas City, United States of America*; *[6]University of Debrecen, Department of Internal Medicine, Debrecen, Hungary*; *[7]First Moscow State Medical University, Department of Internal Medicine, Moscow, Russian Federation*; *[8]University of Pittsburgh, Rheumatology, Piitsburgh, United States of America*; *[9]Michigan Medicine, Rheumatology, Ann Arbor, United States of America*; *[10]Charles University, Rheumatology, Prague, Czech Republic*; *[11]Octapharma PPG, Clinical R&D, Vienna, Austria*; *[12]Phoenix Neurological Associates, Neurology, Phoenix, United States of America*; *[13]Octapharma PPG, Global Medical & Scientific Affairs, Vienna, Austria*; *[14]Hospitals in different countries worldwide, Rheumatology-Dermatology-Neurology, Vienna, Austria*

Background: Dermatomyositis (DM) is a rare chronic systemic autoimmune disease with characteristic skin rash and progressive proximal muscle weakness. Current therapies encompass corticosteroids and other immunosuppressants and intravenous immunoglobulins (IVIg), however, none of these therapies are proven by randomized controlled phase 3 studies. There have been no large randomized clinical trials supporting the efficacy and safety of IVIg in DM.

Objectives: The ProDERM study aimed to evaluate the efficacy and safety/tolerability of IVIg in DM patients in a double-blind, randomized, placebo-controlled, international multi-center, phase III clinical trial.

Methods: The trial consisted of a double-blind, placebo-controlled First Period (16 weeks), in which adult patients with definite or probable DM (according to Bohan and Peter criteria) were randomized 1:1 to either high dose IVIg (2g/kg every 4 weeks) or placebo. Patients on placebo and patients without clinical worsening while on IVIg treatment entered the open label Extension Period (24 weeks) and received 2g/kg IVIg infusions every 4 weeks. To be included, subjects must have active disease with a manual muscle testing-8 (MMT-8) score < 142/150. Patients who showed clinical worsening (defined according to Oddis et al, 2013 - with slight adaptation) at 2 consecutive visits between week 8 and week 16 were switched to the alternate treatment arm.
Primary endpoint was the proportion of responders in the IVIg vs. placebo arm at week 16, where response was defined per 2016 ACR/EULAR Myositis response criteria of at least minimal improvement [Total Improvement Score (TIS) ≥ 20 points)] and without clinical worsening at 2 consecutive visits up to week 16.
Results: A total of 95 adult DM patients (mean age: 53 years; 75% females; 92% Caucasian) were enrolled, with 47 and 48 randomized to IVIg and placebo, respectively. Baseline clinical characteristics (including medical history and prior DM medication) were balanced between the 2 arms.
The study met the primary endpoint at week 16, with the proportion of responders being significantly higher in the IVIg group (37/47; 78.7%) as compared to the placebo group (21/48; 43.8%; p-value 0.0008; Table 1).

Table 1. Total Improvement Score – Analysis of Proportion of Responders at Week 16 (Full Analysis Set, N=95)

TIS Response	*octagam 10%* N=47	Placebo N=48	Difference *octagam 10%* – placebo
Number (%) of responders	37 (78.72%)	21 (43.75%)	
Difference in response rates [95% CI] p-value[a]			34.97 [16.70, 53.24] 0.0008

[a]Cochran-Mantel-Haenszel TestCI=confidence interval; N=number of patients; TIS=total improvement score

In the analysis of responders per improvement category at Week 16, a 45.2% higher response rate for at least moderate improvement (TIS ≥n40 points; p < 0.0001) and a 23.6% higher response rate for at least major improvement (TIS ≥060 points; p < 0.0062) was observed in the IVIG group as compared to the placebo group.
The mean (SD) TIS was significantly higher in IVIg group [48.4 (24.4)] than in placebo arm [21.6 (20.2)] at week 16 (Fig 1).

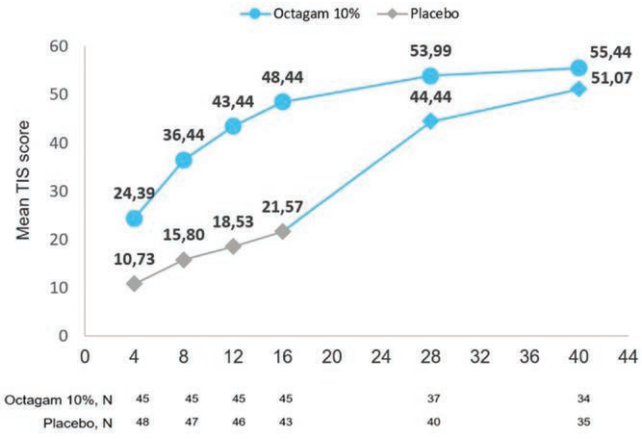


Figure 1.

After switching to IVIG in the Extension Period the placebo group attained a similar response rate at Week 40 as did the IVIg treated patients at Week 16, i.e approx. 70% for minimal improvement.
In line with the overall primary endpoint, secondary end points including all of the sub-components of TIS except muscle enzyme (MMT-8, MD global, Extramuscular global, patient global, HAQ,) as well as CDASI (Cutaneous Dermatomyositis Disease Area and Severity Index), also showed statistically significant improvement under IVIg treatment compared to placebo treatment.
The safety and tolerability profile of IVIg was consistent with previously reported safety outcomes for IVIg administration.
Conclusion: This is the first large international phase III randomized, placebo-controlled trial demonstrating the efficacy and safety of IVIg as a treatment for patients with DM.
REFERENCES:
[1] Oddis, C. V. *et al. Arthritis Rheum* (2013), **65,** 314–324

Acknowledgements: Acknowledgments to all participating investigators, centers and patients and their families
Disclosure of Interests: Rohit Aggarwal Consultant of: Q32, Alexion, Argenx, AstraZeneca, BMS, Boehringer Ingelheim, Corbus, Csl Behring, EMD Serono, Janssen, Kezar, Mallinckrodt, Kyverna, Octapharma, Orphazyme, Pfizer., Grant/research support from: BMS, Mallinckrodt, Pfizer, EMD Serono, Christina Charles-Schoeman Consultant of: Pfizer, Abbvie, Octapharma, Gilead, Regeneron-Sanofi, Grant/research support from: Bristol Myers Squibb, Pfizer, Abbvie, Octapharma, Joachim Schessl Speakers bureau: Octapharma, Grifols, CSL Behring, Consultant of: Octapharma, Zsuzsanna Bata-Csorgo Speakers bureau: Novartis, Sanofi-Genzyme, Ewopharma, Consultant of: Sanofi-Genzyme, Novartis, Ewopharma, Mazen Dimachkie Consultant of: ArgenX, Catalyst, Cello, CSL-Behring, EcoR1, Kezar, Momenta, NuFactor, Octapharma, RaPharma/UCB, RMS Medical, Sanofi Genzyme, Shire Takeda, Spark Therapeutics and UCB Biopharma., Grant/research support from: Alexion, Alnylam Pharmaceuticals, Amicus, Biomarin, Bristol-Myers Squibb, Catalyst, Corbus, CSL-Behring, GlaxoSmithKline, Genentech, Grifols, Kezar, Mitsubishi Tanabe Pharma, Novartis, Octapharma, Orphazyme, Ra Pharma/UCB, Sanofi Genzyme, Sarepta Therapeutics, Shire Takeda, Spark Therapeutics, UCB Biopharma, Viromed/Healixmith., Zoltán Griger Speakers bureau: Abbvie, CSL-Behring, Eli-Lilly, Roche, Boehringer Ingelheim, Consultant of: Octapharma, Sergey Moiseev: None declared, Chester V Oddis Consultant of: EMD Serono; Alexion Pharmaceuticals, Inc, Grant/research support from: Genentech (Clinical trial support); Bristol Myers Squibb (Clinical trial support), Elena Schiopu Consultant of: Octapharma, Grant/research support from: Octapharma, Janssen (Johnson & Johnson), BMS, Pfizer, Abbvie, Jiří Vencovský Speakers bureau: Abbvie, Biogen, MSD, Pfizer, Roche, Sanofi, UCB, Consultant of: Abbvie, Boehringer, Eli Lilly, Octapharma, Gilead, Irene Beckmann Employee of: Octapharma, Todd Levine Shareholder of: Corinthian Reference Labs, CND Life Sciences, Consultant of: Grifols, Octapharma, Alexion, Elisabeth Clodi Employee of: Octapharma PPG, Vienna Austria, and the ProDERM Investigators: None declared
DOI: 10.1136/annrheumdis-2021-eular.1389

OP0009-PARE

SUCCESSFUL PATIENT EDUCATION ON COVID-19 VACCINE SAFETY IN A LARGE RHEUMATOLOGY COHORT USING INTERACTIVE MOBILE-PHONE VIDEO TECHNOLOGY: CONTEXT, RESULTS, AND NEXT STEPS

L. Rajagopala[1], M. Ford[1], M. Jasim[1], D. Mulherin[1], S. Venkatachalam[1], T. Sheeran[1], J. Bateman[1]. [1]*The Rheumatology Centre,Cannock Wolverhampton,The Royal Wolverhampton NHS Trust,UK, Rheumatology, Wolverhampton, United Kingdom*

Background: There are reported concerns of patient misunderstanding of the COVID-19 pandemic and vaccination safety. It is particularly important that these are understood in patients taking complex immunusuppressive therapies. Rapid delivery of targeted and up-to-date video messages from clinicians sent directly to patients could address patient uncertainty, and improve COVID-19 vaccination uptake. Innovative SMS (short message service) based video message has already shown promise in delivering COVID-19 information to patients [1]. We present our experience in creating a tailored vaccine information video sent directly to our large cohort of patients in the UK with a range of rheumatic diseases and report on the learning points going forward.
Objectives: Our three objectives were: (1) educate our patients using an interactive mobile video information resource outlining the safety of the COVID vaccination in these patient groups; (2) better understand our patients' views of the COVID-19 vaccine; (3) evaluate the patient experience of this approach.
Methods: We designed and recorded an 8-minute interactive web-based video delivered education resource designed for mobile phones. This included: aims of the video; details of licenced vaccines; UK vaccination schedule; frequently asked questions; links to national charity resources; our clinician recommendations; a rheumatologist being vaccinated; case studies; and summary data. We produced a simple mobile phone web-based evaluation of the resource, including anonymised patient demographics, their understanding of the safety of the vaccine pre/ post video, and their user experience. Resource and evaluation were piloted by local healthcare professionals, our Patient Participation Group, a national charity, and approved by senior management. We distributed this to our follow-up patient cohort via our hospital SMS provider on 21.12.20, at the start of roll-out of UK vaccines, containing a link to the resource and evaluation.
Results: Of a cohort of 10,981 patients, we had 8886 mobile phone numbers. At Day 14, we recorded 2358 video views (26.3%) and 664/2358 completed evaluations (28.1%). Only one person reported being unable to watch the video. Before watching the video, 348/664 patients (52.4%) were unsure if the vaccine was safe and/or recommended for them, rising to 626/664 (94.3%) post-video. Reasons for uncertainty after the video (38/664) included drug allergy and fertility concerns. Following the video, 509/664 patients (76.6%) reported that they were more likely to have the vaccination. The majority of the patients (614/660, 93.0%)

agreed that the method was a helpful method to share such information.Age distribution of our whole cohort, patients with mobile phones, and responders were similar: Age >50 was 80.4%,76.3%,and 88.6% respectively. A large proportion was treated with immunosuppressive medication (61.3% conventional DMARD, 39.4% biological DMARD and 17.6% corticosteroids). Gender and case mix for responders were similar to published data from our cohort: female 74.0%; rheumatoid arthritis commonest disease (389/664, 58.5%).

Conclusion: To our knowledge, this is the first study to show the potential for SMS linked interactive multimedia message for patient education. The multimedia component allows users to easily navigate to relevant sections, and access a choice of linked resources. We demonstrate this low-cost technology is simple, effective and well placed to assist physicians in educating patients during a time when face-to-face contact is proving to be difficult. We have shown high levels of patient satisfaction, reassurance, and self-reported behaviour change. Such technology has potential utility for national bodies, primary and secondary care groups, and merits further research.

REFERENCES:

[1] The Lancet Rheumatology. Rapid distribution of information by SMS-embedded video link to patients during a pandemic. June 2020,Volume2,Number 6,e309-e368

Acknowledgements: We would like to thank the Hibbs Lupus Trust, and our Patient Participation Group.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1778

OP0010 EFFICACY AND SAFETY OF FAECAL MICROBIOTA TRANSPLANTATION FOR ACTIVE PERIPHERAL PSORIATIC ARTHRITIS: A RANDOMISED SHAM-CONTROLLED TRIAL

M. Skov Kragsnaes[1], J. Kjeldsen[2], H. C. Horn[1], H. L. Munk[1], J. K. Pedersen[3], S. A. Just[3], P. Ahlquist[4], F. Moeller Pedersen[2], M. De Wit[5], S. Möller[6], V. Andersen[7], K. Kristiansen[8], H. M. Holt[9], D. Kinggaard Holm[10], R. Christensen[11], T. Ellingsen[1]. [1]Odense University Hospital, Department of Rheumatology, Odense, Denmark; [2]Odense University Hospital, Department of Medical Gastroenterology, Odense, Denmark; [3]Svendborg Hospital OUH, Section of Rheumatology, Department of Medicine, Svendborg, Denmark; [4]Reumaklinik Fyn, Reumaklinik Fyn, Odense, Denmark; [5]Amsterdam, Patient Research Partner, Amsterdam, Netherlands; [6]Odense University Hospital, OPEN – Open Patient data Explorative Network, Odense, Denmark; [7]University Hospital of Southern Denmark, IRS-Centre Sønderjylland, Aabenraa, Denmark; [8]University of Copenhagen, Laboratory of Genomics and Molecular Biomedicine, Department of Biology, Copenhagen, Denmark; [9]Odense University Hospital, Department of Clinical Microbiology, Odense, Denmark; [10]Odense University Hospital, Department of Clinical Immunology, Odense, Denmark; [11]Bispebjerg and Frederiksberg Hospital, Musculoskeletal Statistics Unit, the Parker Institute, Copenhagen, Denmark

Background: Although causality remains to be established, targeting dysbiosis of the intestinal microbiota by faecal microbiota transplantation (FMT) has been proposed as a novel therapeutic option for treatment of extra-intestinal inflammatory diseases.[1]

Objectives: In this proof-of-concept study, we evaluated efficacy and safety of FMT in psoriatic arthritis (PsA).[2]

Methods: In this double-blind, parallel-group, sham-controlled, superiority trial, we randomly allocated (1:1) adults with active peripheral PsA (≥3 swollen joints) despite ongoing treatment with methotrexate to one gastroscopic-guided FMT or sham transplantation into the duodenum. The transplants (50 g faeces) came from one of four healthy, thoroughly screened, anonymous stool donors.3 The primary efficacy endpoint was the proportion of participants experiencing treatment failure (i.e., needing treatment intensification) through 26 weeks. The first key secondary endpoint was change in Health Assessment Questionnaire Disability Index (HAQ-DI) score from baseline to week 26. Safety was monitored throughout the trial. Trial registration number: NCT03058900, ClinicalTrials.gov.

Results: Of 97 screened, 31 (32%) underwent randomisation (15 allocated to FMT), all received the assigned intervention, and 30 (97%) completed the 26-week clinical evaluation (Table 1). Treatment failure occurred more frequently in the FMT group than in the sham group (9 [60%] vs 3 [19%]; risk ratio, 3.20; 95% CI, 1.06 to 9.62; P=0.018). During the entire 26 weeks of observation, the rate of the treatment failures was significantly higher in the FMT than in the sham group, see figure 1. Improvement in HAQ-DI score differed between groups (0.07 vs 0.30) by 0.23 points (95% CI, 0.02 to 0.44; P=0.031) in favour of sham. No serious adverse events were observed.

Conclusion: In this first interventional randomised controlled trial of FMT in immune-mediated arthritis, FMT was inferior to sham in treating active peripheral PsA. FMT did not appear to result in serious adverse events.

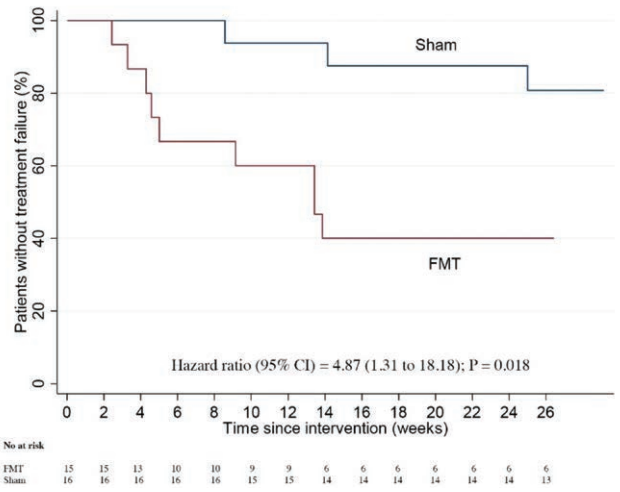


Figure 1. Time-to-event curves by intervention group from baseline to week 26.FMT, faecal microbiota transplantation.

Table 1. Baseline demographics and disease characteristics.

Characteristic	FMT (n=15)	Sham (n=16)
Female sex, no. (%)	8 (53%)	12 (75%)
Age, yr.	48.9 (16.1)	52.4 (11.0)
Height, cm	175.2 (7.0)	169.8 (8.6)
Weight, kg	93.6 (15.4)	92.4 (24.8)
Time since diagnosis, yr.[a]	2.6 (0.3 to 5.8)	5.6 (0.5 to 8.8)
Rheumatoid factor IgM negative, no. (%)[b]	13 (93%)	15 (94%)
Anti-citrullinated peptide antibody negative, no. (%)[b]	14 (100%)	16 (100%)
HLA-B27 negative, no. (%)	15 (100%)	13 (81%)
C-reactive protein, mg/L	4.98 (7.18)	5.54 (5.87)
HAQ-DI	0.89 (0.51)	0.78 (0.50)
Swollen joint 66 count	7.5 (3.0)	6.7 (2.7)
Tender joint 68 count	14.9 (8.9)	17.3 (8.8)
SPARCC enthesitis index		
Score ≥1, no. (%)	13 (87%)	15 (94%)
Score in patients with a score ≥1	8.1 (4.3)	7.2 (3.3)

Data are mean (SD) or n (%) unless otherwise stated.FMT, faecal microbiota transplantation.[a] Time since diagnosis of psoriatic arthritis is presented as median and interquartile range (IQR).[b] Presence of rheumatoid factor (IgM) and anti-citrullinated peptide antibody was not accessed in one patient from the FMT group.

REFERENCES:

[1] Manasson J, Blank RB, Scher JU. The microbiome in rheumatology: Where are we and where should we go? *Ann Rheum Dis* 2020;79:727-33.

[2] Kragsnaes MS, Kjeldsen J, Horn HC, et al. Efficacy and safety of faecal microbiota transplantation in patients with psoriatic arthritis: protocol for a 6-month, double-blind, randomised, placebo-controlled trial. *BMJ Open* 2018;8:e019231.

[3] Kragsnaes MS, Nilsson AC, Kjeldsen J, et al. How do I establish a stool bank for fecal microbiota transplantation within the blood- and tissue transplant service? *Transfusion* 2020;60:1135-41.

Acknowledgements: We thank all participants for their contribution. We thank CS Klinkby, trial nurse, for assistance in relation to the conduct of the trial visits. We also thank L Albjerg, biomedical laboratory technologist, AC Nilsson, consultant, KF Rasmussen, consultant, and J Georgsen, consultant, at the Department of Clinical Immunology, Odense University Hospital, Denmark, for assisting in the implementation of the FMT stool bank.

Disclosure of Interests: Maja Skov Kragsnaes Grant/research support from: Novartis 2017 (unrestricted research grant) to support 3 months PhD salary related to the conduct of the trial., Jens Kjeldsen: None declared, Hans Christian Horn: None declared, Heidi Lausten Munk: None declared, Jens Kristian Pedersen: None declared, Søren Andreas Just: None declared, Palle Ahlquist: None declared, Finn Moeller Pedersen: None declared, Maarten de Wit: None declared, Sören Möller: None declared, Vibeke Andersen: None declared, Karsten Kristiansen: None declared, Hanne Marie Holt: None declared, Dorte Kinggaard Holm: None declared, Robin Christensen: None declared, Torkell Ellingsen Grant/research support from: Novartis 2017 (unrestricted research grant)

DOI: 10.1136/annrheumdis-2021-eular.2046

OP0011

INTEGRATION OF FLOW AND DIGITAL CYTOMETRY IN EARLY TREATMENT-NAÏVE RHEUMATOID ARTHRITIS IDENTIFIES DISTINCT IMMUNOPHENOTYPES IN PERIPHERAL BLOOD AND DISEASE TISSUE

F. Rivellese[1,2], E. Pontarini[1], L. Fossati-Jimack[1], R. A. Moura[3,4], V. C Romão[3,4], J. E. Fonseca[3,4], A. Nerviani[1,2], C. Cubuk[1], K. Goldmann[1], M. Bombardieri[1,2], M. Lewis[1,2], C. Pitzalis[1,2]on behalf of Pathobiology of Early Arthritis Cohort (PEAC) investigators. [1]*William Harvey Research Institute, Centre for Experimental Medicine and Rheumatology, London, United Kingdom*; [2]*Barts Health NHS Trust, Department of Rheumatology, London, United Kingdom*; [3]*Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon Academic Medical Centre, Department of Rheumatology, Lisbon, Portugal*; [4]*Instituto de Medicina Molecular, Faculdade de Medicina, Rheumatology Research Unit, Lisbon, Portugal*

Background: The study of synovial tissue in patients with Rheumatoid Arthritis (RA) has led to the identification of synovial patterns of immune cell infiltration and specific cellular subsets associated that have been disease activity and clinical outcomes(*1–3*). However, the relationship of circulating and synovial immune cell sub-sets with histopathological features and clinical outcomes remains to be defined.

Objectives: To assess the relationship of peripheral blood and synovial immune cells with RA histopathology and clinical outcomes, by performing flow and digital cytometry in matched peripheral blood and synovial samples from patients with early RA.

Methods: 70 patients with early (<12 months) untreated RA (2010 criteria) recruited in the pathobiology of early Arthritis Cohort (PEAC) at the Barts Health NHS Trust were included(*1*). Peripheral blood mononuclear cells (n=70) were analysed by flow cytometry. Matched synovial tissues (n=70) obtained by minimally invasive ultrasound-guided synovial biopsy underwent semi-quantitative scoring (0-4) of immune cell infiltration and classification into lympho-myeloid (LM), diffuse-myeloid (DM) and pauci-immune (PI) pathotypes, as previously described(*1*). 49 synovial and 36 matched peripheral blood samples underwent RNA-sequencing and were analysed by digital cytometry (Xcell) (*4*) and Singular Value Decomposition (SVD).

Results: Circulating B cells and their subsets showed significant inverse correlations with inflammatory markers (ESR, CRP), disease activity (swollen joints, four components and two components(*5*) DAS28) and ultrasound scores (Fig 1A). Among T cell subsets, CXCR5-PD1hiICOS+CD4+ T cells (T peripheral helper cells, Tph) had strong positive correlations with inflammatory markers (ESR and CRP), disease activity (DAS28) and ultrasound scores (Fig 1B). Tph in the peripheral blood also correlated with immune cell infiltration in synovia (Fig 1C) and were significantly higher in patients with a LM pathotype (Fig 1D). Accordingly, circulating Tph were associated with synovial LM pathotype independently of clinical features such as DAS28, ACPA positivity, Body Mass Index (BMI) and age (AUC 0.821). By applying digital cytometry in matched synovial and peripheral blood samples, synovial B and T cells were significantly higher in patients with a LM pathotype, in line with the histological definition of the LM pathotype – rich in B and T cells. On the contrary, circulating B cells and total CD4 and CD8 T cells were significantly lower in patients with a synovial LM pathotype (Fig 1E). The Tph signature in synovia derived by Singular Value Decomposition (SVD) correlated with baseline ESR (R 0.38, p<0.0001) and DAS28 (R 0.35, p <0.0001) and with delta-DAS28 after 6 months of treatment with conventional synthetic DMARDs (R 0.27, p 0.026). Finally, the baseline synovial Tph signature was significantly higher in patients who progressed to the use of biologics and was predictive of future biologic DMARDs use, independently of baseline DAS28, ACPA positivity, BMI and age (AUC 0.703).

Conclusion: By combining conventional flow cytometry in the peripheral blood and digital cytometry on matched synovial and peripheral blood samples, we highlight diverging associations of circulating immune cell subsets with synovial inflammation and pathotypes. Tph cells, in particular, emerge as predictors of lympho-myeloid synovial inflammation and disease progression.

Figure 1

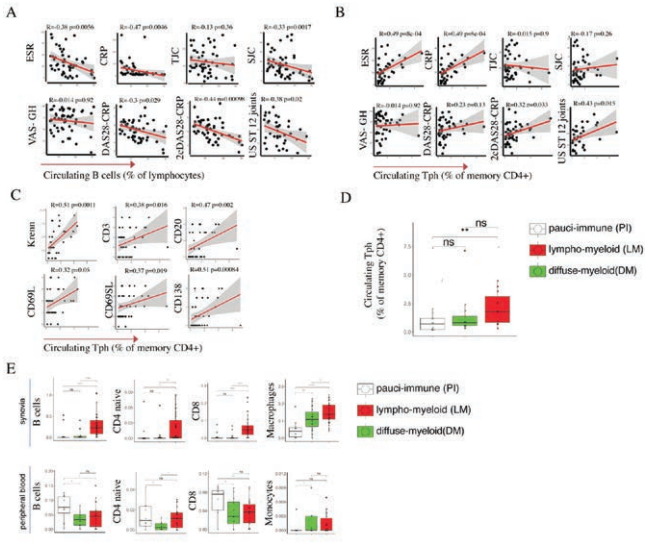


Figure 1.

REFERENCES:

[1] F. Humby *et al.*, *Ann. Rheum. Dis.* 78, 761–772 (2019), doi:10.1136/annrheumdis-2018-214539.

[2] M. J. Lewis *et al.*, *Cell Rep.* 28, 2455-2470.e5 (2019), doi:10.1016/j.celrep.2019.07.091.

[3] D. a Rao *et al.*, *Nat. Publ. Gr.* 542, 110–114 (2017), doi:10.1038/nature20810.

[4] D. Aran *et al.*, *Genome Biol.* 18, 220 (2017), doi:10.1186/s13059-017-1349-1.

[5] E. M. A. Hensor *et al.*, *Rheumatology*. 58, 1400–1409 (2019), doi:10.1093/rheumatology/kez049.

Acknowledgements: The Pathobiology of Early Arthritis Cohort (PEAC) was supported by the MRC (grant 36661). Versus Arthritis provided funding infrastructure support (grant 20022). F. Rivellese is funded by an NIHR Transitional Research Fellowship (TRF-2018-11-ST2-002). We would like to thank the patients and the clinical and laboratory team (core team) at Queen Mary University of London.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.438

OP0012

ASSOCIATION BETWEEN PASSIVE SMOKING IN CHILDHOOD AND ADULTHOOD, AND RHEUMATOID ARTHRITIS: RESULTS FROM THE FRENCH E3N-EPIC COHORT STUDY

Y. Nguyen[1,2], C. Salliot[2,3], X. Mariette[4,5], M. C. Boutron-Ruault[2], R. Seror[4,5]. [1]*AP-HP.Nord - Hôpital Beaujon, Department of Internal Medicine, Clichy, France*; [2]*Centre for Research in Epidemiology and Population Health (CESP), Université Paris Sud, INSERM U1018, Villejuif, France*; [3]*Centre Hospitalier Régional D'Orléans, Department of Rheumatology, Orléans, France*; [4]*AP-HP Hôpital Bicêtre, Department of Rheumatology and National Reference Center for Rare Systemic Autoimmune Diseases, Le Kremlin-Bicêtre, France*; [5]*Université Paris Sud - Faculty of Medicine, INSERM UMR1184, Le Kremlin-Bicêtre, France*

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease of multifactorial aetiology, which preferentially affects women. To date, active smoking has been the most reproducibly reported risk factor for anti-citrullinated protein antibodies (ACPA) positive RA, particularly persons who carry the HLA-DRB1-shared epitope (SE) alleles.

Objectives: We aimed to investigate the relationships between passive smoking in childhood (PSc) or in adulthood (PSa), and the risk of incident RA in a large prospective cohort of healthy French women.

Methods: The E3N-EPIC (*Etude Epidémiologique auprès des femmes de la Mutuelle générale de l'Education Nationale*) is a French prospective cohort study that investigates environmental factors associated with chronic diseases. It follows 98,995 healthy French women since 1990 covered by a national health insurance primarily involving teachers. RA cases have been previously identified with specific questionnaires and medication reimbursement database. Women were considered exposed to PSc if they self-declared staying in a smoky room several hours a day during childhood, and to PSa if they self-declared being exposed at least one hour a day to passive smoking while adults. We used Cox multivariable regression models with age as the timescale (model 1), adjusted on smoking status (never, current, or former smoker) and on the two types of passive smoking (model 2), and on educational level, and BMI (model 3). Stratified analyses were conducted depending on the active smoking status (never or ever-smoker).

Results: 79,806 women were included in the study. Mean (± SD) age at cohort entry was 49.0 (± 6.4) years. Among them, 698 incident RA cases were identified, diagnosed after a mean of 11.7 (± 5.8) years after baseline. In the whole cohort, 10,810 (13.5%) women were exposed to PSc, 42,807 (53.6%) to PSa, 6,581 (8.25%) were exposed to both, and 47,036 (58.9%) were exposed to either. In the whole population, PSc was positively associated with the risk of RA in all three models (HR 1.24; 95% CI [1.01 to 1.51] in Model 3). In stratified analyses

on smoking status, PSc was associated with RA among never-smoking women (HR 1.42; 95% CI [1.07 to 1.88]), but not among ever-smoking women (HR 1.10; 95% CI [0.83;1.46]).
In the whole population, PSa was also positively associated with the risk of RA in all three models (HR 1.19; 95% CI [1.02 to 1.40] in Model 3). In stratified analyses on the smoking status, PSa was associated with an increased RA risk only among never-smoking women (HR 1.27; 95% CI [1.02 to 1.57]) and not among ever-smoking women (HR 1.16; 95% CI [0.93;1.44]).
Conclusion: In this large population-based prospective cohort study of French women, we reported that passive exposure to smoking during childhood or adulthood increased the risk of RA. The association was principally observed among never smoking women. These results suggest that smoking by-products, whether actively or passively inhaled absorbed, could generate autoimmunity, at least towards antigens involved in RA pathogenesis.
REFERENCES:
[1] Karlson EW, Chang S-C, Cui J, et al. Gene-environment interaction between HLA-DRB1 shared epitope and heavy cigarette smoking in predicting incident rheumatoid arthritis. Ann Rheum Dis 2010;69:54–60.
[2] Seror R, Henry J, Gusto G, et al. PSc increases the risk of developing rheumatoid arthritis. Rheumatology 2019;58:1154–62.
[3] Nguyen Y, Salliot C, Gusto G, et al. Improving accuracy of self-reported diagnoses of rheumatoid arthritis in the French prospective E3N-EPIC cohort: a validation study. BMJ Open 2019;9:e033536.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1260

OP0013 **SEX DIFFERENCES IN AUTOIMMUNE DISEASE SUSCEPTIBILITY; A MULTI-OMIC APPROACH**

G. Robinson[1,2], K. Waddington[2], J. Peng[1], A. Radziszewska[1], H. Peckham[1], D. Isenberg[1,2], Y. Ioannou[2], I. Pineda Torra[3], C. Ciurtin[1], E. Jury[2]. *[1]University College London, Centre for Adolescent Rheumatology Versus Arthritis London, London, United Kingdom*; *[2]University College London, Rheumatology, London, United Kingdom*; *[3]University College London, Centre for Cardiometabolic and Vascular Science, London, United Kingdom*

Background: Males and females have altered immune responses resulting in variation in autoimmune and cardiovascular disease risk (CVR). Recently, these differences have played a role in the inflammatory response to COVID-19. Sex differences exist in the frequency and activity of immune-cell subsets but mechanisms underlying sexual dimorphism remain unknown. Juvenile-onset systemic lupus erythematosus (JSLE) is an autoimmune disorder that commonly emerges during puberty, has a strong female prevalence (female:male ratio, 4.5:1) and results in an increased CVR. JSLE is characterised by chronic inflammation and dyslipidaemia, where cardiovascular disease is a leading cause of mortality for patients. Our previous work identified a link between immune cell function and lipid metabolism in adult-onset SLE. We hypothesised that sex hormones could influence both lipid metabolism and immune cell function and this could determine sex-specific susceptibility to JSLE and associated CVR.
Objectives: We investigated the role of sex hormones in modifying systemic lipid metabolism and inflammation.
Methods: Nuclear magnetic resonance spectroscopy based serum metabolomics measuring over 130 lipoproteins (14-subsets with lipid compositions), flow cytometry measuring immune-cells, and RNA-sequencing were used to assess the metabolic and immune profile in young, pre/post-pubertal males (n=10/17) and females (n=10/23) and in individuals with gender-dysphoria (GD) under cross-hormone treatment (trans-male/female, n=26/25). This analysis was also performed on a cohort of post-pubertal male (n=12) and female (n=23) JSLE patients. Data was analysed by logistic regression, balanced random forest machine learning (BRF-ML), differential gene expression (DEG) and pathway analysis.
Results: Post-pubertal males had significantly reduced cardio-protective high-density lipoprotein (HDL) subsets ($p<0.0001$) and increased cardio-pathogenic very-low-density lipoprotein subsets ($p<0.0001$) compared to females. These differences were not observed pre-puberty and were reversed significantly by cross-hormone treatment in GD individuals, suggesting that sex hormones regulate lipid metabolism *in-vivo*.
BRF-ML (28 immune-cell subsets) identified an increased frequency of anti-inflammatory regulatory T-cells (Tregs) in post-pubertal males compared to females ($p=0.0097$). These Tregs were also more suppressive in males compared to females. Differences in Treg frequency were seen pre-puberty and were not altered by sex hormone treatment in GD individuals. However, Treg DEGs and functional transcriptomic pathways altered between post-pubertal males and females, including those involved in inflammatory signalling, overlapped with those altered by hormones in GD, suggesting hormones may also drive Treg functional changes. In addition, HDL metabolites modified by hormones showed differential associations with Treg phenotypes between post-pubertal males and females.
Strikingly, sex differences in lipoproteins and Tregs were lost in JSLE, suggesting hormone signalling could be dysregulated in the pathogenesis of autoimmunity and could increase CVR for patients.
Conclusion: Sex hormones drive altered lipoprotein metabolism and functional transcriptomic pathways in Tregs. Males have a lipoprotein profile associated with increased CVR, but a more anti-inflammatory immune profile compared to females. Together, this could explain sex differences in inflammatory disease susceptibilities and inform future sex-specific therapeutic strategies for the management of both JSLE and CVR.
Acknowledgements: Lupus UK
Rosetrees Trust
Versus Arthritis
NIHR UCLH Biomedical Research Centre
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1405

Genomics, genetic basis of disease and functional genomics

OP0014 **HLA ASSOCIATIONS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS AND CLINICAL SUBTYPES**

M. Tordoff[1], S. Smith[1], E. Lopez Isac[1], A. Morris[1], S. Eyre[1,2], W. Thomson[1,2], J. Bowes[1,2]on behalf of Centre for Genetics and Genomics Versus Arthritis.. *[1]The University of Manchester, Centre for Genetics and Genomics Versus Arthritis, Manchester, United Kingdom*; *[2]National Institute of Health Research Manchester Biomedical Research Centre, Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust, Manchester, United Kingdom*

Background: Juvenile idiopathic arthritis (JIA) is a childhood onset rheumatic disease which is classified into seven different clinical subtypes based upon the ILAR classification criteria. The most common extra articular manifestation of JIA is its associated uveitis (JIAU); particularly chronic anterior uveitis (CAU). Uveitis is a serious complication with the potential to lead to visual impairment and blindness. The rheumatoid factor negative polyarthritis and oligoarthritis ILAR subtypes, often referred to as the "polygo" subgroup, are at a higher risk for developing JIAU, with up to 30% of polygos afflicted by CAU. The HLA region has long been reported as a genetic risk factor for JIA susceptibility, with evidence suggesting that different amino acids of HLA genes infer risk to different JIA subtypes.
Objectives: Investigate the association of amino acids and genetic variants in the HLA region with susceptibility to JIAU and the ILAR clinical subtypes.
Methods: Samples were genotyped using the Illumina Infinium CoreExome and Infinium Onmiexpress arrays. Samples were excluded based on <98% call rate, discrepancy between genetically inferred sex and database records, inferred relatedness (identify-by-descent) and ancestral outliers based on principal component analysis (PCA). SNPs were excluded based on <0.01 minor allele frequency (MAF), and call rate <98%. SNP2HLA was used to impute HLA amino acids, SNPs and alleles. Analysis was then executed on markers with an information score >0.9 and MAF >.01 using logistic regression or an omnibus test for multiallelic markers, including 3 PCs as covariates. Independent associations were identified using forward stepwise logistic regression including previously identified variants as covariates. Comparison of regression models was performed using a likelihood ratio test (LRT).
Results: We analysed 7425 markers within the HLA region in 450 JIAU and 2024 JIA cases without uveitis. The most significant association was to amino acid positions 13 of HLA-DRB1 ($p=2.9\times10^{-30}$). Conditional analysis on DRB1 position 13 revealed an independent signal at DRB1 position 67 ($p=2.4\times10^{-6}$). Conditioning on all DRB1 alleles revealed an independent signal at HLA-DPB1 position 69 ($p=5.3\times10^{-7}$). As expected, ILAR subtype was found to be associated with JIAU ($p=1.58\times10^{-6}$). We used LRT to test if genetics provided further information above ILAR subtype alone and found that including residues at DRB1 position 13 significantly improved the fit of a model based on ILAR subtype alone (LRT $p = 3.6\times10^{-27}$). The reciprocal analysis, adding ILAR subtype to a model based on DRB1 position 13 alone, did not significantly improve the fit of a model (LRT $p=0.83$). Exploring associations in the polygo subgroup (n=1646) we found significant associations to the three previously described amino acids and JIAU (DRB1 position 13 $p=3.4\times10^{-20}$, DRB1 position 67 $p=3.3\times10^{-4}$, DPB1 position 69 $p=2.2\times10^{-6}$).
Conclusion: This is largest analysis of HLA markers in JIAU patients to date and we identify two independent associations to amino acids in HLA-DRB1 and a further independent association to HLA-DPB1. This analysis demonstrates that including data on genetic risk factors adds further information to that captured

by ILAR subtype alone. It also reveals that the previously validated associations at position 13 of HLA-DRB1 are also correlated with JIAU in the polygo subtype suggesting that genetic risk factors will help refine risk within clinical subtypes. Conditioning on DRB1 alleles reveals that the secondary independent DRB1 position 69 association is also strongly associated in the polygo subset of this cohort. Together these results highlight the potential future use of genetics risk factors for risk classification for uveitis in patients with JIA

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.430

OP0015 GENOMIC RISK SCORE FOR ADVANCED OSTEOARTHRITIS IN OLDER ADULTS

P. Lacaze[1], G. Polekhina[1], A. Bakshi[1], M. Riaz[1], A. Owen[1], A. Franks[1], Y. Wang[1], J. Abidi[2], J. Tiller[1], S. Orchard[1], J. Mcneil[1], F. Cicuttini[1]. *[1]Monash University, School of Public Health and Preventive Medicine, Melbourne, Australia*; *[2]Alfred Hospital, Department of Medicine, Melbourne, Australia*

Background: Osteoarthritis (OA) is a major cause of disability, with treatment options mostly limited to advanced disease when joint replacement is indicated. Recent genome-wide association analysis more than doubled the number of OA-associated variants identified (1, 2), extending the feasibility of identification of high-risk individuals.

Objectives: Including these variants, we calculated polygenic risk scores (PRSs) and performed validation in a well-characterised population of older individuals.

Methods: We calculated PRSs for knee and hip OA respectively, using joint replacement surgeries as markers of advanced disease in 12,724 older individuals of European descent in the ASPREE trial. We considered in-trial joint replacement (hospitalizations during median 4.7 years follow-up) and pre-trial joint replacement from self-reported medical history. Multivariable models examined the effect of PRS as a continuous variable (per standard deviation [SD]) and categorical variable (low-risk [0-20%], medium-risk [21-80%], high-risk [81-100%] groups), adjusting for age, sex and BMI.

Results: Mean population age at baseline was 75 years and 54.9% of participants were female. In total, 1478 (11.6%) participants had knee replacements and 1324 (10.4%) had hip replacements. Female sex, higher BMI and age were associated with higher risk of knee and hip replacements. PRSs as continuous variables per SD were associated with knee (odds ratio [OR] 1.11, 95% confidence interval [CI] 1.04-1.17) and hip (OR 1.18, 95% CI 1.11-1.25) replacements. We found meaningfully different rates of knee or hip joint replacement occurring between low-, medium- and high-risk PRS groups. Participants in the high-risk PRS group, compared with the low, had a higher risk of knee replacements (OR=1.35, CI 1.12-1.62), and hip replacements (OR 1.66, 95% CI 1.37-2.02). We found no interaction between PRS and sex, and no collinearity between PRS and BMI, suggesting PRS is an independent risk factor for OA.

Conclusion: Joint-specific genomic risk scores predict advanced OA in older adults, independent of age, sex and BMI. Stronger associations are observed for hip versus knee OA. Our study provides some of the first evidence of potential clinical utility of genomic risk prediction for OA, which may help identify individuals who would benefit most from targeted clinical management and preventive intervention.

REFERENCES:

[1] Tachmazidou I, Hatzikotoulas K, Southam L, *et al.* 2019. Identification of new therapeutic targets for osteoarthritis through genome-wide analyses of UK Biobank data. *Nat Genet,* 51, 230-236

[2] Zengini E, Hatzikotoulas K, Tachmazidou I, *et al.* 2018. Genome-wide analyses using UK Biobank data provide insights into the genetic architecture of osteoarthritis. *Nat Genet,* 50, 549-558

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2918

OP0016 IDENTIFICATION OF FUNCTIONAL VARIANTS IN THE RHEUMATOID ARTHRITIS ASSOCIATED JAZF1 LOCUS IN SYNOVIAL FIBROBLASTS

M. Houtman[1], X. Ge[2], A. Mcgovern[2], K. Klein[1], G. Orozco[2], M. Frank Bertoncelj[1], M. Marks[3], O. Distler[1], P. Martin[2], S. Eyre[2], C. Ospelt[1]. *[1]University Hospital Zurich, University of Zurich, Center of Experimental Rheumatology, Department of Rheumatology, Zurich, Switzerland; [2]The University of Manchester, Versus Arthritis Centre for Genetics and Genomics, School of Biological Sciences, Faculty of Biology, Medicine and Health, Manchester, United Kingdom; [3]Schulthess Klinik, Department of Teaching, Research and Development, Zurich, Switzerland*

Background: Over the past decade, genome wide association studies (GWAS) have identified the *JAZF1* locus as a risk locus for several autoimmune diseases, including rheumatoid arthritis (RA)[1]. However, the exact causal variants in the *JAZF1* locus and their underlying regulatory events contributing to RA are still not known. Here, we focus on the effect of these variants on gene expression in synovial fibroblasts (SF).

Objectives: To characterize the functional consequences of RA-causal variants in the *JAZF1* locus in SF.

Methods: Genetic fine-mapping of RA loci was conducted by computing sets of credible variants driving GWAS signals. These credible variant sets were integrated with DNA architecture (ChIP-seq), 3D chromatin interactions (3C, HiC and capture HiC), DNA accessibility (ATAC-seq) and gene expression (RNA-seq and CAGE-seq) datasets to select putative RA-causal variants in SF. Selected variants in the *JAZF1* locus were tested for regulatory function by luciferase reporter assays and electrophoretic mobility shift assays (EMSA) in the fibrosarcoma cell line HT1080. The JASPAR2020 database was used to identify putative transcription factors (TF) binding to the selected variants. The expression of *HOTTIP* was measured by quantitative PCR in hand SF (n=23). Genotyping was done by pyrosequencing.

Results: Genetic fine mapping revealed 47 variants in the *JAZF1* locus. Integration of these variants with the chromatin datasets prioritized rs2158624, rs57585717 and rs186735625 as the top candidates (posterior probability of causality >0.1) in the *JAZF1* locus. We found that rs2158624 and rs186735625 are located in the vicinity of enhancer elements in SF as determined by ATAC-seq. In addition, the region of rs2158624 exhibited strong chromatin interactions with the genomic region of *HOTTIP* and *HOXA13*. Both these transcripts were previously shown to be specifically expressed in SF isolated from hands and feet[2]. Based on this, we selected rs2158624 as the most promising candidate in the *JAZF1* locus. We found that the rs2158624-C allele (risk) is associated with lower expression of *HOTTIP,* but not *HOXA13*, in hand SF compared to the rs2158624-T allele (non-risk) (p=0.02). Luciferase assays in HT1080 cells demonstrated enhancer activity with both the rs2158624-C allele (p=0.006) and T allele (p=0.04), with no significant difference in enhancer activity between the rs2158624-C and T allele. EMSAs identified stronger specific binding of HT1080-cell nuclear extract for the rs2158624-T allele than for the C allele (risk). Based on the JASPAR2020 database, we identified NFAT5 as a potential TF that can bind to rs2158624 and may regulate the expression of *HOTTIP*.

Conclusion: We were able to substantially narrow down the potential functional variants in the *JAZF1* locus using our data integration approach and functional assays. We suggest that the risk allele of rs2158624 influences the binding of TFs controlling the expression of the long non-coding RNA *HOTTIP* in SF, which might confer specific risk to develop RA in hands.

REFERENCES:

[1] Okada Y *et al.* Genetic of rheumatoid arthritis contributes to biology and drug discovery. *Nature* 2014;506:376.

[2] Frank-Bertoncelj M *et al.* Epigenetically-driven anatomical diversity of synovial fibroblasts guides joint-specific fibroblast functions. *Nat Commun* 2017;8:14852.

Disclosure of Interests: Miranda Houtman: None declared, Xiangyu Ge: None declared, Amanda McGovern: None declared, Kerstin Klein: None declared, Gisela Orozco: None declared, Mojca Frank Bertoncelj: None declared, Miriam Marks: None declared, Oliver Distler Speakers bureau: Bayer, Boehringer Ingelheim, iQone, Medscape, MSD, Novartis, Pfizer and Roche, Consultant of: Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Bayer, Baecon Discovery, Boehringer, CSL Behring, ChemomAb, Corbus Pharmaceuticals, Galapagos NV, GSK, Glenmark Pharmaceuticals, Horizon Pharmaceuticals, Inventiva, Italfarmaco, iQvia, Kymera, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Pfizer, Roche, Roivant Sciences, Sanofi and UCB, Grant/research support from: Kymera Therapeutics and Mitsubishi Tanabe, Paul Martin: None declared, Stephen Eyre: None declared, Caroline Ospelt: None declared

DOI: 10.1136/annrheumdis-2021-eular.1400

OP0017 VALIDATION OF GWAS-IDENTIFIED VARIANTS FOR ANTI-TNF DRUG RESPONSE IN RHEUMATOID ARTHRITIS: A META-ANALYSIS OF THREE LARGE COHORTS

J. M. Sánchez-Maldonado[1], R. Cáliz Cáliz[2], M. Á. López-Nevot[3], A. Moñiz-Díez[1], A. J. Cabrera-Serrano[1], H. Canhão[4], R. Ter Horst[5], A. Escudero Contreras[6], S. Sorensen[7], M. L. Hetland[8], M. Á. Ferrer González[2], B. Glintborg[8,9], I. Filipescu[10], E. Perez-Pampín[11], P. Conesa-Zamora[12], J. Swierkot[13], A. Den Broeder[14], S. De Vita[15], S. E. Hove Jaconsen[16], L. Quartuccio[15], Y. LI[5], M. Netea[5], M. J. H. Coenen[14], V. Andersen[8,9], J. E. Fonseca[17], K. Bogunia-Kubik[18], E. Collantes Estevez[6], J. Sainz[1,19]on behalf of REPAIR consortium. *[1]GENYO. Center for Genomics and Oncological Research, Genomic Oncology, Granada, Spain; [2]Virgen de las Nieves University Hospital, Rheumatology Deparment, Granada, Spain; [3]Virgen de las Nieves University Hospital, Immunology Department, Granada, Spain; [4]Universidade Nova de Lisboa, CEDOC, EpiDoC Unit, NOVA Medical School and National School of Public Health, Lisboa, Portugal; [5]Radboud University*

Nijmegen Medical Center, Department of Internal Medicine and Radboud Center for Infectious Diseases, Nijmegen, Netherlands; [6]Reina Sofía Hospital/IMIBIC/University of Córdoba, Rheumatology Deparment, Córdoba, Spain; [7]Hospital of Southern Jutland, Focused Research Unit for Molecular Diagnostic and Clinical Research, Aabenraa, Denmark; [8]Rigshospitalet, The DANBIO Registry, The Danish Rheumatologic Biobank and Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology ad Spine Diseases, Centre of Head and Orthopaedics, Glostrup, Denmark; [9]University of Copenhagen, Department of Clinical, Faculty of Health and Medical Sciences, Copenhagen, Denmark; [10]University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Rheumatology Department, Cluj-Napoca, Romania; [11]University Hospital of Santiago de Compostela, Rheumatology Unit, Santiago de Compostela, Spain; [12]Santa Lucía University Hospital, Clinical Analysis department, Cartagena, Spain; [13]Wroclaw Medical University, Department and Clinic of Rheumatology and Internal Medicine, Warsaw, Poland; [14]Radboud University Medical Center, Radboud Institute for Health Sciences, Department of Human Genetics, Nijmegen, Netherlands; [15]University of Udine, Department of Medical Area, Udine, Italy; [16]University Hospital of Southern Jutland, Department of Biochemistry and Immunology, Aabenraa, Denmark; [17]Hospital de Santa Maria, CHLN, Rheumatology and Metabolic Bone Diseases Department, Lisbon, Portugal; [18]Polish Academy of Sciences Wrocław, Hirszfeld Institute of Immunology and Experimental Therapy, Warsaw, Poland; [19]University of Granada, Department of Medicine, Granada, Spain

Background: The interplay between genetics and drug response in rheumatoid arthritis (RA) has shown that response to biologics varies between individuals and that a large proportion of patients show no clinical improvement (Plenge and Bridges, 2011). Despite the disappointing scenario, to date, only a few genetic markers have been consistently identified and we are far from being able to optimize drug dosing or prioritize drug combinations based on genetic findings.
Objectives: With this background, we sought to validate the association of GWAS-identified variants for response to TNF inhibitors (TNFi) in a two-stage case control association study and to shed some light into the functional role of the most interesting markers.
Methods: The discovery population consisted of 1361 RA patients ascertained through the REPAIR consortium and the DANBIO registry. RA patients fulfilled the 1987 revised American College of Rheumatology (ACR) and the ACR/EULAR 2010 classification criteria. The validation cohort included 706 Dutch RA patients from the DREAM registry. The study followed the Declaration of Helsinki and study participants gave their written informed consent to participate in the study, which was approved by the ethical review committee of participant institutions. Twenty-seven single-nucleotide polymorphisms (SNPs) were selected through a literature search of relevant GWAS. Linear regression analysis adjusted for age, sex and country of origin was used to determine the association between GWAS-identified SNPs and changes in DAS28 (ΔDAS28) after 3 or 6 months of treatment. The meta-analysis of both populations was performed using a fixed effect model. Correction for multiple testing was performed using the Bonferroni method but also considering the number of inheritance models tested (P=0.0009). To assess the role of the most interesting markers in modulating immune responses, stimulation experiments in whole blood, peripheral mononuclear cells (PBMCs) and monocyte-derived macrophages using a large number of pathogens and microbiome bacteria were performed in 408 subjects from the Human Functional Genomic Project cohort. We also evaluated the correlation of these SNPs with plasmatic levels of 108 inflammatory proteins, 7 serum steroid hormones and counts of 91 blood-derived immune cell populations.
Results: The meta-analysis of the discovery cohort and DREAM registry including 2067 RA patients treated with TNFi revealed an overall association of the $LINC02549_{rs7767069}$ SNP with a decreased drop in DAS28 that remained significant after correction for multiple testing (per-allele OR_{Meta}=0.83, P_{Meta}=0.000077; P_{Het}=0.61). In addition, the meta-analysis of these large cohorts showed that each copy of the $LARRC55_{rs717117G}$ allele significantly decreased the drop in DAS28 in RF-positive patients (per-allele OR_{Meta}=0.67, P=0.00058; P_{Het}=0.06) whereas an opposite but not significant effect was found in RF-negative subjects (per-allele OR_{Meta}=1.38, P=0.10; $P_{Interaction}$=0.00028; P_{Het}=0.45). Interestingly, the meta-analysis also showed potentially interesting but not statistically significant overall and RF-specific associations for the $MAFB_{rs6071980}$ and $CNTN5_{rs1813443}$ SNPs with ΔDAS28 (per-allele $OR_{Meta_rs6071980}$=0.84, P=0.0059; P_{Het}=0.63 and $OR_{Meta_rs1813443_RF+}$=0.81, P=0.0059; P_{Het}=0.69 and $OR_{Meta_rs1813443_RF-}$=1.00, P=0.99; P_{Het}=0.12; $P_{Interaction}$=0.032). Although analysis of functional data is ongoing, so far, we found that carriers of the $LARRC55_{rs717117G}$ allele showed decreased levels of IL6 after stimulation of PBMCs with *Borrelia burgdorferi* and *Escherichia Coli* bacteria (P=0.00046 and 0.00044), which suggested a reduced IL6-mediated anti-inflammatory effect of this marker to worsen the response to TNFi.
Conclusion: This study confirmed the influence of the *LINC02549* and *LARRC55* loci to determine the response to TNFi in RA patients and a weak effect of the *MAFB* and *CNTN5* loci that needs to be further investigated.
REFERENCES:
[1] Plenge RM et al 2011. Arthritis Rheum 63, 590-3.
ACKNOWLEDGEMENTS: We thank all participants who have agreed to participate in this study. Authors also thank María Dolores Casares, Ángeles Molina, Carmen Oloriz for the collection of Spanish samples and Hans Jurgen Hoffmann, Marianne Thomsen, Vibeke Østergaard Thomsen, Malene Rohr Andersen, Lise Lotte B. Laursen, Helle Jørgensen, Ram Benny Christian Dessau, Niels Steen Krogh, Ulla Vogel, Paal Skytt Andersen, Ivan Brandslund, Steffen Bank, Frederik Trier Møller, Nikolai Toft and Niels Møller Andersen for the participation in collection and purification of Danish samples. We also thank the Danish Departments of Rheumatology for their implication in the collection of clinical data from RA patients included in the DANBIO cohort and the Danish Rheumatologic Biobank. Likewise, we would like to thank Teun van Herwaarden for steroid hormone measurements in serum samples from subjects ascertained through the HFGP initiative.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2248

OP0018 PREDICTING RESPONSES TO ANTI-TNF TREATMENTS IN RHEUMATOID ARTHRITIS PATIENTS FROM GENETIC AND CLINICAL DATA USING A MACHINE LEARNING APPROACH

S. Ju[1], M. Hudson[2], I. Colmegna[3], S. Bernatsky[3], Y. LI[1]. *[1]McGill University, School of Computer Science, Montréal, Canada*; *[2]Jewish General Hospital, Rheumatology, Montréal, Canada*; *[3]MUHC Research Institute, Medicine, Montréal, Canada*

Background: Tumor necrosis factor (TNF) inhibitors are key therapies in rheumatoid arthritis (RA). However, a third of patients fail to respond to these agents, and there are no reliable predictors for response. Predictive models, potentially based on clinical and genomic data, are vital to personalizing therapy. The Dialogue for Reverse Engineering Assessments and Methods (DREAM) RA Responder Challenge invited research teams to create models for patient response to anti-TNF therapy. The winning model relied heavily on limited genetic input and was unable to correctly predict responses in a large number of individuals.
Objectives: We compared non-linear and linear analytic methods to predict response and non-response to anti-TNF treatment for RA patients in the DREAM database, using moth clinical variables and a large number of potential genome-wide predictors.
Methods: DREAM data on anti-TNF treated RA patients were accessed through Synapse (synapse.sagebase.org). Analogously to the DREAM challenge, we were provided with the clinical and genomic data of 2706 patients with at least moderate disease activity according to their composite disease activity scores for 28 joints (DAS28). In contrast to the previous analysis that focused on single nucleotide polymorphisms (SNPs) based on existing knowledge of RA, we used the full genome-wide dataset of 2.5 million SNPs. We first reduced this to 284 SNPs by considering the marginal p-value of 0.001 for each SNP based on whether or not it predicted response. Then, we removed SNPs with borderline significant p-values if they were in linkage disequilibrium with the most significant SNPs. Instead of predicting a binary outcome of responder or non-responder, we trained both linear (e.g. least absolute shrinkage and selection operator, or LASSO) and non-linear models (e.g. Random Forest) to predict a continuous outcome, the change in DAS28 from baseline to 3-12 months after initiation of anti-TNF therapy. We split the patients into training (N=2031) and testing (N=675) subsets and used the predicted response scores to evaluate the true binary response labels for the test patients.
Results: The best performing method was Random Forest (RF), a non-linear model that uses decision trees to progressively separate subjects into groups based on the most predictive features. Support Vector Regression (SVR) also out-performed linear methods. Compared to only clinical covariates such as age and sex, adding SNPs improved the prediction from an area under the receiver operating curve (AUROC) of 0.63 to 0.67, i.e., 0.04 improvement. This AUROC of 0.67 was 0.046 greater than the DREAM challenge winner.
Conclusion: Non-linear methods such as RF and SVR gave larger predictive improvements compared to linear methods. This may imply some interaction between SNPs and clinical covariatesas potential predictors of response to anti-TNF therapy in RA. We are further investigating these 284 SNPs and their interactions in this regard.

REFERENCES:

[1] Guan, Y., Zhang, H., Quang, D., Wang, Z., Parker, S., Pappas, D. A., Kremer, J. M., & Zhu, F. (2019). Machine Learning to Predict Anti-Tumor Necrosis Factor Drug Responses of Rheumatoid Arthritis Patients by Integrating Clinical and Genetic Markers. Arthritis & rheumatology (Hoboken, N.J.), 71(12), 1987–1996. https://doi.org/10.1002/art.41056

[2] Sieberts, S. K., Zhu, F., García-García, J., Stahl, E., Pratap, A., Pandey, G., Pappas, D., Aguilar, D., Anton, B., Bonet, J., Eksi, R., Fornés, O., Guney, E., Li, H., Marín, M. A., Panwar, B., Planas-Iglesias, J., Poglayen, D., Cui, J., Falcao, A. O., … Mangravite, L. M. (2016). Crowdsourced assessment of common genetic contribution to predicting anti-TNF treatment response in rheumatoid arthritis. Nature communications, 7, 12460. https://doi.org/10.1038/ncomms12460

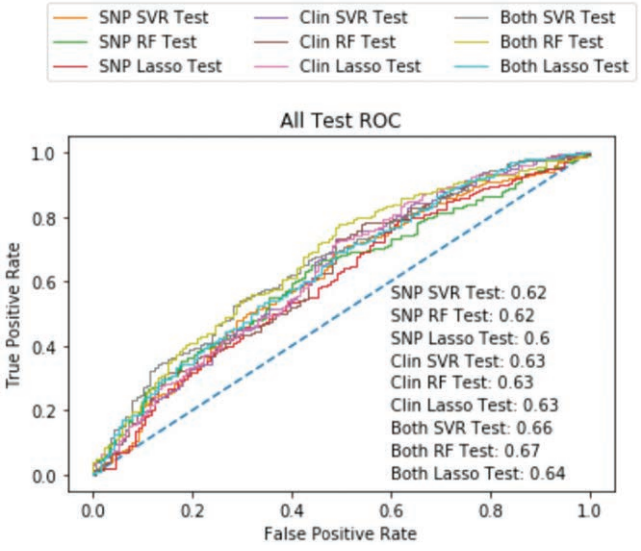


Figure.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1107

OP0019 DEFINING SYSTEMIC LUPUS ERYTHEMATOSUS MOLECULAR TAXONOMY THROUGH DATA-DRIVEN RESTRATIFICATION AND IDENTIFICATION OF CLUSTER-TAILORED DRUGS FOR A PERSONALIZED MEDICINE APPROACH

P. Garantziotis[1,2], D. Nikolakis[3], S. Doumas[1], E. Fragou[1], A. Fanouriakis[4], A. Filia[1], T. Witte[2], G. Bertsias[5], D. Boumpas[1,6]. [1]*Biomedical Research Foundation Academy of Athens, Athens, Greece, Center of Clinical, Experimental Surgery & Translational Research, Athens, Greece*; [2]*Medical University Hannover, Department of Clinical Immunology and Rheumatology, Hannover, Germany*; [3]*University of Amsterdam, Department of Experimental Immunology, Amsterdam, Netherlands*; [4]*Asklepieion' General Hospital, Department of Rheumatology, Athens, Greece*; [5]*University of Crete, Medical School, Department of Rheumatology, Clinical Immunology and Allergy, Crete, Greece*; [6]*National and Kapodistrian University of Athens, Medical School, 4th Department of Medicine, Attikon University Hospital, Athens, Greece*

Background: Systemic Lupus Erythematosus (SLE) is characterized by lack of treatment diversity, largely empirical treatment decisions, and paucity of novel compound development.
Objectives: We sought to stratify SLE patients based on their molecular phenotype and predict personalized therapeutic compounds, tailored to the molecular fingerprint of each subgroup.
Methods: We performed a co-expression analysis using our publicly available whole blood RNA-seq data of 120 SLE patients. Modules of commonly regulated genes were established and used to re-stratify patients through hierarchical clustering, in a data-driven, clinically independent, manner. Next, we established an in silico, subgroup signature-based, drug prediction pipeline. Investigated drugs included both those currently in practice and those who have been tested in SLE clinical trials and are listed in the iLINCS prediction databases. Finally, drug repurposing analysis was performed, to identify novel perturbagens that counteract group-specific SLE signatures.
Results: Molecular taxonomy identified five distinct lupus molecular endotypes, each characterized by a unique gene module enrichment pattern. A group defined by strong neutrophilic signature encompassed almost exclusively patients with active nephritis, while a B-cell expression group included patients with severe lupus phenotype. Metabolic processes enrichment defined a group of patients with disease of moderate severity and serologic activity. Finally, patients with mild lupus features were distributed in two groups, which demonstrated enhanced basic cellular functions, myelopoiesis, and autophagy. The ability of different compounds to reverse the transcriptomic aberrancies observed in each patient group was examined. Bortezomib efficiently reversed disturbances in the "neutrophilic" cluster. Azathioprine and ixazomib might be a reasonable option for patients of the "B-cell" cluster, whereas fostamatinib appeared efficacious for the "Metabolism" patient subgroup.
Conclusion: The clinical spectrum of SLE encompasses distinct molecular endotypes, each defined by unique pathophysiologic aberrancies, which can be utilized to guide personalized care and direct novel compound development.
Acknowledgements: This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 742390).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1636

OP0020 HOMEOBOX D TRANSCRIPTION FACTORS SHAPE DIFFERENTIAL JOINT ENVIRONMENT BETWEEN ANTERIOR FINGER JOINTS AND THUMB

M. Mirrahimi[1], K. Klein[1], M. Houtman[1], M. Maciukiewicz[1], M. Frank Bertoncelj[1], A. Juengel[2], M. Berli[3], M. Marks[4], O. Distler[1], C. Ospelt[1]. [1]*University Hospital of Zürich, Department of Rheumatology, Zürich, Switzerland*; [2]*Universitätsklinik Balgrist, Research Rheumatology, Zürich, Switzerland*; [3]*Universitätsklinik Balgrist, Technical Orthopedics, Zürich, Switzerland*; [4]*Schulthess Klinik, Department of Research and Development, Zürich, Switzerland*

Background: The expression of embryonic Homeobox (HOX) genes is tightly regulated based on anatomic location in human adult dermal and synovial fibroblasts. Previously, we showed that HOX-D10,-D11 and -D13 are higher expressed in synovial fibroblasts from small distal joints from the hands and feet, in particular in digits II-V and wrists compared to thumb and that this expression pattern is epigenetically imprinted[1]. The consequences of the tightly restricted expression of these transcription factors are largely unknown.
Objectives: To elucidate the function of HOXD10, -D11 and -D13 in synovial fibroblasts.
Methods: Synovial tissues were isolated from paws of naïve C57BL/6 mice (n=8), from patients with rheumatoid arthritis (RA), osteoarthritis (OA) and from healthy controls. Synovial fibroblasts were cultured and transfected with GapmeR to silence HOXD10, -D11, and -D13, respectively or with control GapmeR. RNA sequencing was performed on the NovaSeq platform and pathway analysis was done using R packages and web-based tools (GSEA, EnrichR, Cytoscape). HOXD target gene expression was measured by qPCR (n=3-6).
Results: To confirm and further analyze the distinctive expression pattern of HOXD genes, we measured their expression in healthy synovial tissues of different joints of human feet and mouse paws. Similar to what we had found in hands, *HOXD10*, *-D11* and *-D13* were less abundant in the joints of the first digit of human feet compared to digits II-V (n=3-4 in each joint). Measurements in joints of mouse paws showed lower expression of *HoxD10*, *-D11* and *-D13* in distal interphalangeal joints compared to proximal interphalangeal joints and metacarpophalangeal (MCP) joints, respectively. Silencing of HOXD10, -D11 and –D13, affected the expression of 5333, 2217 and 7347 genes, respectively, in cultured RA synovial fibroblasts from human wrists (n=3).
There were more transcripts equally regulated by HOXD10 and -D13 (40% of all HOXD10 and 31% of all HOXD13 regulated transcripts), than by HOXD11 and either -D10 or -D13 (18% of all HOXD10 regulated genes and 16% of all HOXD13 regulated genes), suggesting most redundancy between HOXD10 and -D13 (Figure 1). Among genes differentially expressed in SF isolated from MCP II-V versus thumb joints, 19%, 4% and 33% were regulated by HOXD10, -D11 or –D13, respectively, supporting a role for HOXD13 in particular in shaping the joint specific environment. All three HOXD transcription factors regulated genes involved in cell cycle progression, demonstrating dependence of synovial fibroblasts on these HOX genes for cell division. Other enriched pathways were Toll-like receptor and integrin signaling pathways, regulation of unsaturated fatty acid synthesis and autophagy and extra-cellular matrix protein organization. We could

confirm several targets of HOXD10, -D11, and –D13 by qPCR, e.g. *NR4A1*, *ROR2, LIF, ATF3*.

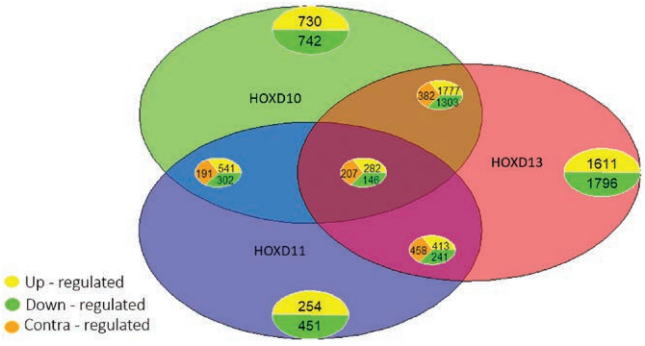


Figure 1. Comparison of the genes which were differentially expressed after HOXD10-11-13 silencing

Conclusion: The expression of HOXD10, -D11 and –D13 in synovial fibroblasts and tissues strikingly overlaps with predilection sites for RA. Silencing experiments suggested that these embryonic HOX transcription factors have a crucial role in regulating fibroblast functions and might shape a joint specific environment that modulates the development and course of RA in specific joints.

REFERENCES:

[1] Klein K, et al. Ann Rheum Dis 2018;77(Suppl 1):P126

Disclosure of Interests: Masoumehalsadat Mirrahimi: None declared, Kerstin Klein: None declared, Miranda Houtman: None declared, Malgorzata Maciukiewicz: None declared, Mojca Frank Bertoncelj: None declared, Astrid Juengel: None declared, Martin Berli: None declared, Miriam Marks: None declared, Oliver Distler Speakers bureau:

1-Speaker fee on Scleroderma and related complications: Bayer, Boehringer Ingelheim, Medscape, Novartis, Roche

- Speaker fee on rheumatology topic other than Scleroderma: MSD, iQone, Novartis, Pfizer, Roche, Consultant of:
- Consultancy fee for Scleroderma and its complications: Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Bayer, Baecon Discovery, Boehringer, CSL Behring, ChemomAb, Corbus Pharmaceuticals, Horizon Pharmaceuticals, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, Kymera, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Roivant Sciences, Sanofi, UCB
- Consultancy fee for rheumatology topic other than Scleroderma: Abbvie, Amgen, Lilly, Pfizer, Grant/research support from:. OD has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued “mir-29 for the treatment of systemic sclerosis” (US8247389, EP2331143).
- Research Grants to investigate the pathophysiology and potential treatment of Scleroderma and its complications: Kymera Therapeutics, Mitsubishi Tanabe, Caroline Ospelt: None declared

DOI: 10.1136/annrheumdis-2021-eular.2095

OP0021 IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES IN EARLY RHEUMATOID ARTHRITIS PATIENTS RESPONDING TO TOCILIZUMAB

I. Muller[1], M. Verhoeven[2], H. Gosselt[1], M. Lin[1], T. De Jong[3], E. Mantel[3], K. Chatzidionysiou[4], G. Jansen[3], L. Padyukov[4], P. Welsing[2], F. Lafeber[2], R. De Jonge[1], C. J. Van der Laken[3]. *[1]Amsterdam UMC, locatie VUmc, Clinical Chemistry, Amsterdam, Netherlands*; *[2]University Medical Center Utrecht, Department of Rheumatology and Clinical Immunology, Utrecht, Netherlands*; *[3]Amsterdam UMC, locatie VUmc, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands*; *[4]Karolinska Institutet and Karolinska University Hospital, Department of Medicine, Stockholm, Sweden*

Background: Tocilizumab (TCZ) is a monoclonal antibody that binds to the interleukin 6 receptor (IL-6R), inhibiting IL-6R signal transduction to downstream inflammatory mediators. TCZ has shown to be effective as monotherapy in early rheumatoid arthritis (RA) patients (1). However, approximately one third of patients inadequately respond to therapy and the biological mechanisms underlying lack of efficacy for TCZ remain elusive (1). Here we report gene expression differences, in both whole blood and peripheral blood mononuclear cells (PBMC) RNA samples between early RA patients, categorized by clinical TCZ response (reaching DAS28 < 3.2 at 6 months). These findings could lead to identification of predictive biomarkers for TCZ response and improve RA treatment strategies.

Objectives: To identify potential baseline gene expression markers for TCZ response in early RA patients using an RNA-sequencing approach.

Methods: Two cohorts of RA patients were included and blood was collected at baseline, before initiating TCZ treatment (8 mg/kg every 4 weeks, intravenously). DAS28-ESR scores were calculated at baseline and clinical response to TCZ was defined as DAS28 < 3.2 at 6 months of treatment. In the first cohort (n=21 patients, previously treated with DMARDs), RNA-sequencing (RNA-seq) was performed on baseline whole blood PAXgene RNA (Illumina TruSeq mRNA Stranded) and differential gene expression (DGE) profiles were measured between responders (n=14) and non-responders (n=7). For external replication, in a second cohort (n=95 therapy-naïve patients receiving TCZ monotherapy), RNA-seq was conducted on baseline PBMC RNA (SMARTer Stranded Total RNA-Seq Kit, Takara Bio) from the 2-year, multicenter, double-blind, placebo-controlled, randomized U-Act-Early trial (ClinicalTrials.gov identifier: NCT01034137) and DGE was analyzed between 84 responders and 11 non-responders.

Results: Whole blood DGE analysis showed two significantly higher expressed genes in TCZ non-responders (False Discovery Rate, FDR < 0.05): urotensin 2 (UTS2) and caveolin-1 (CAV1). Subsequent analysis of U-Act-Early PBMC DGE showed nine differentially expressed genes (FDR < 0.05) of which expression in clinical TCZ non-responders was significantly higher for eight genes (MTCOP12, ZNF774, UTS2, SLC4A1, FECH, IFIT1B, AHSP, and SPTB) and significantly lower for one gene (TND2P28M). Both analyses were corrected for baseline DAS28-ESR, age and gender. Expression of UTS2, with a proposed function in regulatory T-cells (2), was significantly higher in TCZ non-responders in both cohorts. Furthermore, gene ontology enrichment analysis revealed no distinct gene ontology or IL-6 related pathway(s) that were significantly different between TCZ-responders and non-responders.

Conclusion: Several genes are differentially expressed at baseline between responders and non-responders to TCZ therapy at 6 months. Most notably, UTS2 expression is significantly higher in TCZ non-responders in both whole blood as well as PBMC cohorts. UTS2 could be a promising target for further analyses as a potential predictive biomarker for TCZ response in RA patients in combination with clinical parameters (3).

REFERENCES:

[1] Bijlsma JWJ, Welsing PMJ, Woodworth TG, et al. Early rheumatoid arthritis treated with tocilizumab, methotrexate, or their combination (U-Act-Early): a multicentre, randomised, double-blind, double-dummy, strategy trial. Lancet. 2016;388(10042):343-55.

[2] Bhairavabhotla R, Kim YC, Glass DD, et al. Transcriptome profiling of human FoxP3+ regulatory T cells. Human Immunology. 2016;77(2):201-13.

[3] Gosselt HR, Verhoeven MMA, Bulatovic-Calasan M, et al. Complex machine-learning algorithms and multivariable logistic regression on par in the prediction of insufficient clinical response to methotrexate in rheumatoid arthritis. Journal of Personalized Medicine. 2021;11(1).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3668

Adaptive immunity (T cells and B cells) in rheumatic diseases and Innate immunity in rheumatic diseases

OP0022 RHO EXPRESSION FACILITATES T CELL MIGRATION TO LYMPH NODES IN RESPONSE INFLAMMATION

E. Malmhäll-Bah[1], K. M. Andersson[1], M. C. Erlandsson[1], M. Brisslert[1], O. Khan[2], M. Akula[2], I. M. Jonsson[1], M. Bergö[2,3], M. I. Bokarewa[1,4]. *[1]University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; *[2]University of Gothenburg, Department of Molecular and Clinical Medicine, Gothenburg, Sweden*; *[3]Karolinska Institute, Department of Biosciences and Nutrition, Gothenburg, Sweden*; *[4]Sahlgrenska University Hospital, Rheumatology, Gothenburg, Sweden*

Background: Deficiency in geranylgeranyltransferase type I (GGTase-I) results in accumulation of active Rho family proteins RhoA, Rac1 and Cdc42, responsible for cell communication and migration. We reported that mice with GGTase-I deficient macrophages (GLC mice) develop a spontaneous and age-dependent arthritis, reproducing pathology of RA [1].

Objectives: We study how GGTase-I deficiency in Mø changes T cell phenotype to facilitate their translocation to joints and the development of arthritis.

Methods: GLC mice were developed on a mixed genetic background (129Ola/Hsd-C57BL/6) by Cre-technology using LysM-promotor to knockout the *Pggt1b* gene in Mø[2]. $CD4^+$ cells were isolated from spleen and lymph node (LN) of 16 weeks-old mice (GLC n=7, wt n=5) expected to have high prevalence of arthritis. RNA was extracted to measure expression of the Rho proteins and signature genes to characterize differences in Th-subtypes and migration abilities of $CD4^+$ cells between GLC and wt mice. Furthermore, Illumina RNAseq analyzed the transcriptome of LN $CD4^+$ cells. In a separate experiment we treated GLC mice with CTLA4-FP (n=12) or PBS (n=11) for 20 weeks from the age of 5 weeks. Rationale was to disrupt Mø/T cell contact to prevent arthritis. To study Rho-protein dependent phenotype in human RA, we performed RNAseq of sorted $CD4^+$ cells of RA patients.

Results: RNAseq showed that $CD4^+$ cells in LN of GLC mice had IFN-γ dependent cytotoxic profile and upregulated numerous pro-inflammatory genes including *Eomes*, *Cxcr3*, *Tigit*, *Tnfsf10*, *Il-1rl1*, *Stat1*, *Jak3*, *Irf7*, *Irf5*, *Ptpn13*. Furthermore, the over-represented genes often depended on the IRF family in their transcription.

GLC mice overexpressed *Cdc42* and *Rac1* in spleen $CD4^+$ compared to wt (p=0.005 and p=0.048 resp.). Spleen GLC $CD4^+$ cells had higher levels of $\alpha5\beta1$ and $\alpha2\beta2$ integrins, strongly correlating to *Cdc42* (r= 0.61 p=0.0027 and r=0.50, p=0.018) and arthritis (r=0.64, p=0.0015 and r=0.69, p=0.0004). Importantly, *Cdc42*, *Rac1*, and *RhoA* were higher expressed in LN $CD4^+$ compared to spleen (p=0.016, p=0.031 and p=0.016). In addition, *Itgb1* coding for $\beta1$ integrin, was upregulated in GLC $CD4^+$ cells of both spleen and LN (p=0.003 p=0.03, resp.), suggesting Rho proteins are important for migration of $CD4^+$ cells to the joint draining LN and for arthritis development. $CD4^+$ cells that migrated to the LN had high proportion of $Foxp3^+$ cells. This also correlated to the expression of *Itgb1* (r=0.84, p=0.0012) presenting a plausible mechanism for increased influx of Tregs into joints. Several observations are in favor of this notion. First, GLC mice expressed more *Foxp3* in LN compared to spleen $CD4^+$ cells (p=0.016). Second, transcription of *Foxp3* in LN $CD4^+$ cells was higher in GLC mice compared to wt (p=0.015). Third, this high *Foxp3* coexisted with low transcription of *Lef1* (p=0.03), required for Treg immunosuppression. Last, *Foxp3* correlated negatively to both *Lef1* (r=-0.72, p=0.017), and its cofactor *Tcf1* (r=-0.75, p=0.01).

CTLA4-FP reduced inflammation in GLC mice evident as lower IFN-γ, IL-6 and TNF-α production (p=0.0002, p<0.0001 and p<0.0001 resp.) and the number of $CD25^+CD4^+$cells in spleen (p=0.027). In contrast, we observed increased IL-17A production (p=0.056). However, CTLA4-FP treatment did not affect migration of $CD4^+$ cells enriched with Rho-protein into draining LN nor alleviate arthritis.

Similar to the GLC mice, $CD4^+$ cells of RA patients with high expression of RhoA, Rac1 and Cdc42 demonstrated enrichment for Th1 signature genes including *IFNG*, *TBX21*, *Eomes*, *IL2RA*, *IL2RB*, *IL12RB2*, *TNF*, *IL18RAP* (all, adj. p<0.05).

Conclusion: This study shows that accumulation of Rho-proteins in $CD4^+$ cells results in pro-inflammatory IFN-γ dependent phenotype in mice and human RA. Accumulation of RhoA, Rac1 and Cdc42 proteins trigger the migration of $CD4^+$ cells into joint draining LN and facilitates arthritis. Inhibiting Mø/T cell contact in GLC mice did not suffice to prevent migration of Rho-protein expressing cells and arthritis

REFERENCES:

[1] Khan, O.M., et al. J Clin Invest, 2011. **121**(2): p. 628-39.
[2] Akula, M.K., et al. Nat Commun, 2019. **10**(1): p. 3975.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1323

OP0023 GENERATION OF PT101, A HIGHLY SELECTIVE IL-2 MUTEIN FOR TREATMENT OF AUTOIMMUNE DISEASES

J. Visweswaraiah[1], E. Sampson[2], P. Petaipimol[1], A. Monsef[3], K. Kis-Toth[4], K. L. Otipoby[2], J. Sundy[3], N. Higginson-Scott[1], J. Viney[5]. *[1]Pandion Therapeutics, Biotherapeutics, Watertown, United States of America*; *[2]Pandion Therapeutics, Immunology, Watertown, United States of America*; *[3]Pandion Therapeutics, Clinical, Watertown, United States of America*; *[4]Pandion Therapeutics, Translational Sciences, Watertown, United States of America*; *[5]Pandion Therapeutics, R&D, Watertown, United States of America*

Background: Regulatory T cells (Tregs) play a critical role in immune homeostasis and are dysfunctional in many autoimmune diseases. Interleukin 2 (IL-2) drives the proliferation and function of Tregs. via the heterotrimeric IL-2 receptor (CD25/CD122/CD132). As a result, CD25 loss-of-function in mice is associated with Treg deficiency and widespread autoimmunity. Low dose IL-2 is being evaluated for treatment of autoimmune diseases and has been shown to expand Tregs, however it has a narrow selectivity window before activating conventional T cells and natural killer cells. To enhance IL-2 selectivity and improve its therapeutic utility for activating and expanding Tregs, mutations can be introduced that reduce CD122/CD132 affinity thus creating a dependency on CD25 binding for signaling through CD122/CD132 upon IL-2 facilitated CD25/CD122/CD132 trimer formation.

Objectives: To generate a highly selective IL-2 mutein that activates and expands Tregs selectively that can be used for treatment of autoimmune diseases

Methods: Using a structure guided approach, we introduced mutations in IL-2 that significantly decreased CD122 binding affinity in addition to other mutations that increased CD25 binding affinity. Finally, we explored additional mutations, format, orientation, and linker lengths to generate the most potent, selective molecule with drug-like manufacturability. These structure activity relationship efforts culminated in the generation of PT101, a mutant IL-2 Fc fusion that is selective in activating and expanding Tregs in vitro and in vivo.

Results: PT101 selectively induced STAT5 phosphorylation in human and cynomolgus monkey Tregs in vitro. In humanized NOD-scid IL-2Rg-null (NSG) mice and cynomolgus monkeys, administration of PT101 dose-dependently and selectively expanded Tregs without significant effects on other immune cell types, and without eliciting proinflammatory cytokine production. The Tregs from PT101-dosed humanized mice have increased expression of FOXP3 and CD25, suggesting enhanced function and stability. In a Phase 1a single ascending dose clinical trial, PT101 was well-tolerated and selectively expanded total Tregs, with a mean maximal increase of up to 3.6-fold over baseline in healthy volunteers. There was no evidence of expansion of natural killer cells nor pro-inflammatory conventional T cells at any of the doses studied.

Conclusion: PT101 selectively activated and expanded Tregs without significant effects on other immune cell types, and without eliciting proinflammatory cytokine production. These Tregs have enhanced function and stability as seen by increase in expression of FOXP3 and CD25 in these cells. PT101 maintained selectivity in Phase 1 a clinical trial with no evidence of expansion of natural killer cells nor pro-inflammatory conventional T at any dose studied. A Phase 1b/2a clinical trial in patients with ulcerative colitis and a Phase 2 clinical trial in patients with systemic lupus erythematosus are planned to further evaluate PT101.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2097

OP0024 DECREASED LEVELS OF T FOLLICULAR HELPER (CD4+CXCR5+) CELLS AND CD27+CD38+ AND CD27+CD38- B CELLS IN ANKYLOSING SPONDYLITIS PATIENTS CORRELATE WITH MARKER OF INFLAMMATION

H. Forsblad-D'elia[1], U. Hellman[2], A. Kumar[2], K. Lejon[3]. *[1]Institute of Medicine, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; *[2]Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden*; *[3]Department of Clinical Microbiology, Infection and Immunology, Umeå University, Umeå, Sweden*

Background: The role of different lymphocyte subsets in ankylosing spondylitis (AS) is still to be elucidated. It has previously been reported contradictory data concerning the levels of T Follicular Helper (TFH) cells and differentiated B cells in peripheral blood of AS patients. In addition, the connection to disease related parameters is still to be fully revealed.

Objectives: The purpose of this study was to investigate the level of CD4+TFH cells and CD27+CD38+/CD38- B cells in patients with AS from northern Sweden and to compare the levels with age and sex-matched controls. We also studied associations between these cell subsets and disease related factors.

Methods: Peripheral blood mononuclear cells (PBMSc) from a cohort of 50 patients with AS from Region Västerbotten (mean age 52±9.1 years, 33 (66 %) men, 50 (100 %) HLAB27 positive) and 50 pair wise matched blood donor controls (mean age 54±8.8 years, 33 (66 %) men) were stained with a combination of antibodies allowing for the detection of CD27, CD38, CD19, CD3, CD4 and CXCR5 markers and analyzed by flow cytometry. In addition, the patient with AS were examined with spinal x-ray for radiographic alterations assessed with mSASSS. CRP and ESR were measured and physical function and disease activity were registered with BASMI and BASFI respectively ASDAS-CRP and BASDAI.

Results: When comparing AS patients and controls pair wise, we observed on average a 50% reduction of TFH (CD3+CD4+CXCR5+) cells among CD45+ lymphocytes in PBMCs from patients (p=0,000008). Furthermore, a 20-30% reduction among memory/plasma cells (CD19+CD27+CD38+ and CD19+CD27+CD38-) among CD45+ lymphocytes in PBMCs from patients (p=0,002 and p=0,007 respectively). For female patients a correlation between TFH and ESR (R_s=-0,551 p=0,022) was observed. Moreover, negative correlations between the two B cell subsets (CD19+CD27+CD38+ and CD19+CD27+CD38-) and ESR were observed for female patients (R_s =–0,476 p=0,053 and R_s =–0,522 p=0,032 respectively).

Conclusion: TFH cells was reduced in AS patients and this reduction correlated with a reduction in differentiated (CD27+CD38+ and CD27+CD38-) B cells. In

addition, the inflammation marker ESR was negatively correlated with TFH as well as with the differentiated B cell subsets in female patients. Our observations indicates a role of the humoral immune response in AS.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.785

OP0025 CD209+/CD14+ DENDRITIC CELLS ARE ENRICHED AND ACTIVATED AT THE SITE OF INFLAMMATION AND ARE MODULATED BY JAK/STAT SIGNALLING

V. Marzaioli[1,2], A. Floudas[1,2], M. Canavan[1,2], S. Wade[1,2], K. Murray[2], R. Mullan[3], D. Veale[1,2], U. Fearon[1,2]. [1]*Trinity Biomedical Sciences Institute, 1Molecular Rheumatology, Dublin, Ireland*; [2]*Centre for Arthritis and Rheumatic Diseases, SVUH, EULAR Centre of Excellence for Rheumatology, Dublin, Ireland*; [3]*Adelaide and Meath Hospital, Department of Rheumatology, Dublin, Ireland*

Background: Dendritic cells (DCs) are a heterogeneous population of professional antigen-presenting cells which are at the interface between innate and adaptive immunity. A specific subset of DCs is known to derive from monocyte and has a key role in inflammation and infection.

Objectives: This study aimed to characterize the phenotype and function of a distinct $CD209^+/CD14^+$ DC subset in the periphery and at the site of inflammation in patients with rheumatoid (RA) and psoriatic arthritic (PsA), in addition to examining the effect Tofacitinib and TNF inhibitor on their development.

Methods: Peripheral blood and synovial fluid mononuclear cells (PBMC and SFMC) were isolated by Ficoll density gradient from healthy subject (HC), and patients with RA and PsA. Single cell synovial tissue suspension (ST) from RA and PsA patients were also established using enzymatic/mechanical digestion. PBMC, SFMC and ST were analysed by flow cytometry to identify the $CD209^+/CD14^+$ DC subset, its frequency and the cell surface expression of chemokines receptors (CCR6, CCR7, CXCR3, CXCR4 and CXCR5) and activation markers (CD40 and CD80). In addition, PBMC were stimulated with different TLR (LPS, CPG, R848, Poly I:C) and intracellular staining for IL12, TNFα, IL1β and IL6 was performed by flow cytometry. Lineage negative cells ($CD3/CD19/CD56^-$) were stimulate with GMCSF/IL4 in the presence or absence of the JAK/STAT inhibitor Tofacitinib or the TNF inhibitor Humira, and the CD209+/CD14+ DC development was evaluated by flow cytometry.

Results: We identified, for the first time, a distinct CD209+/CD14+ DC population in PBMC of patients with RA and PsA, with similar frequency across the groups. However, when PBMC were stimulated with TLRs, an increase of IL12 and TNFα was observed in RA and PsA PBMC when compared to HC. Interestingly, this distinct DC population was significantly enriched at the site of inflammation, in both SFMC and ST, displaying a more mature phenotype, evident by the observed significant increase in CD40 and CD80 expression. SPICE analysis further identified differential expression and co-expression of chemokine receptors at the periphery of RA and PsA patients, when compared to the HC. Furthermore synovial tissue single cell analysis from RA/PsA demonstrated a unique chemokines receptors profile demonstrating increased single expression and co-expression of CXCR3 and CXCR5 compared to periphery. Finally, we have previously observed that JAK/STAT is involved in monocyte-derived dendritic cells population development (1,2), therefore we performed CD3, CD19 and CD56 depletion of RA/PsA PBMC followed by stimulation with GMCSF/IL4, to spike the Mo-DC population, in the presence of Tofacitinib or Humira. Interestingly, we observed that JAK/STAT inhibition, but not TNF inhibitor, reduced the generation and development of CD209+/CD14+ DC.

Conclusion: We identify for the first time a distinct monocyte-derived DC population characterized as $CD209^+/CD14^+$ in the periphery of RA and PsA patients. This population was enriched at the site of inflammation and displayed a unique chemokine receptor profile and activation markers, suggesting that these cells are already activated in the periphery of IA patients, and are recruited and further activated in the inflamed joint. In addition, we showed that the $CD209^+/CD14^+$ DC development is regulated by JAK/STAT signalling, but not TNF inhibition.

REFERENCES:

[1] Marzaioli V, Canavan M, Floudas A, et al. Monocyte-Derived Dendritic Cell Differentiation in Inflammatory Arthritis Is Regulated by the JAK/STAT Axis via NADPH Oxidase Regulation. *Front. Immunol.* 2020;11:1406.

[2] Marzaioli V, Hurtado-Nedelec M, Pintard C, et al. NOX5 and p22phox are 2 novel regulators of human monocytic differentiation into dendritic cells. *Blood*. 2017;130(15):1734–1745.

Acknowledgements: The authors also wish to thank all the patients who volunteered to participate into this study and the funding

Disclosure of Interests: Viviana Marzaioli: None declared, Achilleas Floudas: None declared, Mary Canavan: None declared, Siobhan Wade: None declared, Kieran Murray: None declared, Ronan Mullan: None declared, Douglas Veale Speakers bureau: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Consultant of: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Grant/research support from: Janssen, Abbvie, Pfizer, UCB, Ursula Fearon Speakers bureau: Abbvie, Grant/research support from: Janssen, Abbvie, Pfizer, UCB

DOI: 10.1136/annrheumdis-2021-eular.2122

OP0026 IGF1R DEPENDENT CELL INTERACTION AND REGULATION OF AUTOANTIBODY PRODUCTION IN RHEUMATOID ARTHRITIS

S. Erdogan[1], M. Erlandsson[1,2], N. Oparina[1], C. Lundquist[1], C. Wasen[1], M. Svensson[1], M. Bemark[3], K. M. Andersson[1], M. I. Bokarewa[1,2]. [1]*Gothenburg University, Rheumatology and Inflammation Research, Göteborg, Sweden*; [2]*Sahlgrenska University Hospital, Rheumatology Clinic, Göteborg, Sweden*; [3]*Göteborg University, Microbiology and Immunology, Göteborg, Sweden*

Background: The insulin-like growth factor 1 receptor (IGF1R) signalling mediates numerous developmental processes acting through downstream adaptor molecules IRS1/2, which activate Akt and inhibit the family of forkhead box class O (FoxO). Inhibition of IGF1R signalling alleviates rheumatoid arthritis (RA) (Erlandsson et al., 2017), however, the role of IGF1R signalling in the regulation of immune function is poorly understood.

Objectives: To investigate the link between IGF1R signalling and antigen presentation in experimental arthritis.

Methods: Arthritis was induced by immunising Balb/c mice with methylated bovine serum albumin (mBSA, n=18) and DBA/1 mice with type II collagen (CII, n=18). The mice were treated with a synthetic IGF1R inhibitor NT157 or with short hairpin RNA targeting IGF1R (shIGF1R) from the day prior to immunisation. Controls were treated with cyclodextrine vehicle/ non-targeting (nt)RNA, respectively. Flow cytometry was used for spleen cell phenotype. Antibody levels were measured by ELISA. Immunohistochemistry (IHC) of spleen was performed for assessment of marginal zone (MZ) and location of pS^{612}IRS1+ and pS^{256}FoxO1+ cells. IHC images were acquired by fluorescent confocal microscopy, and analysed using ZEN2009 and Cell Profiler soft ware.

Results: The inhibition of IGF1R resulted in an 80% increase in MZ area in NT157-treated mice compared to controls (p=0.0001). This was supported by a significant increase of CD21+ (p=0.034) and CD23+ cell populations (p=0.00059), both among the CD19+ B cells and antigen-presenting MHCII+CD19- cells, implying that IGF1R expression regulates the populations of MZ and follicular cells. Additionally, there was a strong positive correlation between the decrease of IGF1R+ and ICOSL+ population on CD21+ cells (r=0.70, p=0.0071), which retained them in the MZ and prolonged communication with macrophages. Insufficient feedback from ICOSL- B cells limited expression of CXCR5 on CD4 cells. The IHC analysis displayed that, IGF1R inhibition led to abundance of inactivate pS^{612}IRS1+ and pS^{256}FoxO1+ cells within the MZ, compared with controls (p=0.0002). Alongside the increase of IgM+ B cell population (p=0.0022), we observed significant increase in number of antigen-presenting F4/80+ cells (p=0.043) and MARCO expression (p=0.043) after IGF1R intervention. Finally, the NT157- treated mice displayed a significant pleiotropic increase in IgM autoantibody production, with anti-CCP IgM (p=0.027), RF-IgM (p=0.0085), anti-DNA IgM (p=0.066) and in total IgM (p=0.027) levels, which correlated positively with $pS^{256}FoxO1^+$ cells (r=0.51, p=0.03). Levels of IgG were not changed.

Conclusion: We show that IGF1R signalling is important for immune cell communication after antigen challenge. IGF1R controls ICOSL dependent trafficking of B cells through the MZ and facilitates interaction with T cells. Retention of B cells in the MZ tips the balance from T cell to macrophage-dependent processes, which permits the formation of autoantibody producing B cells.

REFERENCES:

[1] Erlandsson, M., et.al., 2017. IGF-1R signalling contributes to IL-6 production and T cell dependent inflammation in rheumatoid arthritis. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*, 1863(9), pp.2158-2170.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2440

OP0027 AS-RELATED TCR BETA CLONOTYPES ARE PRESENT IN DIFFERENT INFLAMED TISSUES OF PATIENTS WITH SPONDYLOARTHROPATHIES

E. Komech[1], A. Barinova[1], E. Shmidt[2], T. Korotaeva[3], A. Koltakova[3], N. Nikitina[4], E. Belousova[4], M. Shapina[5], S. Rodionovskaya[6], I. Nikishina[7], S. Vahlyarskaya[8], D. Atarshchikov[9], E. Klescheva[10], D. Chudakov[1,11], S. Lukyanov[12], I. Zvyagin[1,11]. [1]*Pirogov Russian National Research Medical University, Institute of Translational Medicine, Center for Precision Genome Editing and Genetic Technologies for Biomedicine, Moscow, Russian Federation*; [2]*Pirogov Russian National Research Medical University, City Clinical Hospital #1, Moscow, Russian Federation*; [3]*Nasonova Research Institute of Rheumatology, Lab of spondyloarthritis and psoriatic arthritis, Moscow, Russian Federation*; [4]*Moscow Regional Research Clinical Institute, Gastroenterology Department, Moscow, Russian Federation*; [5]*State Scientific Center of Coloproctology, Gastroenterology Department, Moscow, Russian Federation*; [6]*Children's Clinical Hospital of*

the Federal Medical-Biological Agency No.38, Rheumatology Department, Moscow, Russian Federation; *[7]Nasonova Research Institute of Rheumatology, Pediatric, Moscow, Russian Federation*; *[8]Pirogov Russian National Research Medical University, Russian Children's Clinical Hospital, Moscow, Russian Federation*; *[9]Central Clinical Hospital under President Affairs, Opthalmology, Moscow, Russian Federation*; *[10]Medical Academy of Postgraduate Education, Ophtalmology, Moscow, Russian Federation*; *[11]Shemyakin-Ovchinnikov institute of bioorganic chemistry, Genomics of adaptive immunity, Moscow, Russian Federation*; *[12]Pirogov Russian National Research Medical University, Head of the University, Moscow, Russian Federation*

Background: Recently a group of T-cell clones with characteristic T-cell receptor (TCR) motif was identified in peripheral blood and synovial fluid of HLA-B*27+ patients with ankylosing spondylitis (AS) [1-2] - a prototypic disease from a wider group of spondyloarthropathies (SpAs). Extraarticular manifestations of AS could involve skin, intestine or eye. Emerging data indicate linkage between intestinal and joint inflammation, including expression of gut-associated integrins on synovial T-cells [3-4]. However, clonal T-cell composition and presence of identical clones in different inflamed sites in SpAs remains poorly studied.
Objectives: To investigate clonal T-cell repertoire and presence of AS-related TCR motif in different sites of inflammation of patients with SpA.
Methods: Samples of synovial fluid (SF) were obtained from HLA-B*27+ and HLA-B*27- patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA), as well as gut biopsy samples from patients with AS and Crohn's disease (AS/CD) or ulcerative colitis (AS/UC), and conjunctival swabs from patients with uveitis (Uv) and with or without articular manifestations (Table 1). Also SF and gut biopsy samples were obtained from HLA-B*27+ patients with juvenile idiopathic arthritis (JIA). For one patient PsA patient paired samples of SF and gut biopsy were obtained.

Table 1. Detection of the AS-related motif TRBV9_CASS[V/A/L/P][G/A][L/T/V][F/Y]STDTQYF_TRBJ2-3 in bTCR repertoires of samples from different inflamed sites of patients with SpA

Tissue	Diagnosis	B27+	B27-	AS-related TCR motif+ among all samples from B27+ donors
Synovial fluid	AS PsA JIA	20	12	
Intestinal biopsy	AS/CD AS/UC JLA	4	3	3 / 4
Conjunctival swab	Uv	8	0	4 / 8

SF and gut samples were processed to isolate mononuclear cells, while conjunctival swabs were directly lysed in the lysis buffer. CD3+ β7-intergin+ cells were isolated from SF by fluorescence-activated cell sorting. Deep TCR repertoire profiling was carried out using UMI-based cDNA library preparation technology [1].
Results: Identical T-cell clonotypes were detected between paired SF and gut samples of the same patient with psoriatic arthritis and intestinal inflammation. The subpopulation of β7-intergin+ SF T-cells shared significantly more identical clonotypes with gut biopsy repertoire compared to the bulk SF T-cell repertoire. Clonotypes belonging to the AS-related TCR beta motif TRBV9_CASS[V/A/L/P][G/A][L/T/V][F/Y]STDTQYF_TRBJ2-3 were detected in all inflamed tissues tested: synovial fluid, intestinal biopsies and conjunctival swabs of SpA patients (Table 1). Importantly, we observed these clonotypes exclusively in samples from HLA-B*27+ donors (n=26), but not in HLA-B27- context (n=15) with comparable analysis depth, thus confirming strong HLA-B*27-restriction of the clonotypes. The AS-related clonotypes were detected in the subpopulation of β7-intergin+ SF T-cells from HLA-B*27+ patients with PsA.
Conclusion: For the first time we directly report the T-cell clonal sharing between synovial fluid and inflamed gut tissue of SpA patients. In sum our data suggests involvement of identical T-cell clones in inflammation in different anatomical sites in SpA.
REFERENCES:
[1] Komech et al. Rheumatology (Oxford). 2018;57(6):1097-1104.
[2] Faham et al. Arthritis Rheumatol. 2016;11(10):300-308.
[3] Guggino et al.*Ann Rheum Dis*. Published Online First: 18 October 2019. doi:10.1136/annrheumdis-2019-216456.
[4] Qaiyum et al *Ann Rheum Dis*. 2019;78(11):1566-1575.
Acknowledgements: We thanks all the patients and medical personnel involved in the study
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3535

OP0028 CD206+CD163+ PATHOGENIC MACROPHAGES ENRICHED IN RHEUMATOID ARTHRITIS SYNOVIAL TISSUE WITH DISTINCT TRANSCRIPTIONAL SIGNATURES

M. Hanlon[1], M. Canavan[1], Q. Song[2], N. Neto[3], P. Gallagher[4], R. Mullan[5], C. Hurson[6], M. Monaghan[3], S. Nagpal[2], D. Veale[4], U. Fearon[1]. *[1]Trinity Biomedical Sciences Institute, Molecular Rheumatology Research Group, Dublin, Ireland*; *[2]Janssen Research and Development Spring House, Immunology & Discovery Sciences, Spring House, United States of America*; *[3]Trinity Biomedical Sciences Institute, Mechanical and Manufacturing Engineering, Dublin, Ireland*; *[4]St. Vincent's University Hospital, Centre for Arthritis & Rheumatic Diseases, Dublin, Ireland*; *[5]Tallaght Hospital, Department of Rheumatology, Dublin, Ireland*; *[6]St. Vincent's University Hospital, Department of Orthopaedics, Dublin, Ireland*

Background: Synovial tissue macrophages are an exquisitely plastic pool of innate cells that play a key role in RA disease progression. However, the precise nature, diversity, and function of macrophage subsets within the inflamed joint remains unexplored.
Objectives: Therefore, the aims of this study are to phenotypically, transcriptionally and functionally characterise synovial tissue macrophages residing within the inflamed joint.
Methods: Rheumatoid Arthritis, Psoriatic Arthritis, Osteoarthritis and healthy control synovial-tissue biopsies and synovial-fluid mononuclear cells were analysed using the following panel (CD40,-CD45,-CD64,-CD68,-CD163,-CD206,-CD253,-CCR4,-CCR7,-CXCR1,-CXCR3). CD206+CD163+ and CD206-CD163- macrophages were sorted from RA synovial-tissue by FACSAria sorter; RNAseq and FLIM analysis, autologous T-cell co-culture and heathy fibroblast experiments performed. Cytokine expression was measured by MSD immunoassay.
Results: RA synovial tissue and fluid macrophages display markers typical of both M1 (CD40+CD253+) and M2 (CD206+CD163+) macrophages with a spectrum of macrophage activation states identified. Within this spectrum, significant enrichment of dominant CD206+CD163+ macrophage-subtype is present in synovial tissue versus fluid ($p<0.05$). CD206+CD163+ synovial tissue macrophages express significantly more CD40 than synovial fluid ($p<0.0003$), positively correlate with disease activity ($r=0.6$, $p<0.01$), with baseline levels predicting response to therapy ($p<0.05$). Moreover, CD206+CD163+CD40+ macrophages are enriched in RA synovial tissue compared to PsA and OA pathotypes ($p<0.05$). While the CD206+CD163+ subset is present in healthy synovial tissue, expression of CD40 is completely absent in healthy synovium ($p<0.05$) with dramatically decreased expression of CX3CR1 on RA macrophages. RNAseq analysis indicates that CD206+CD163+ population is transcriptionally distinct from synovial tissue CD206-CD163-, synovial fluid CD206+CD163+, and RA monocyte-derived M1/M2 macrophages, with unique tissue-resident gene signatures. Moreover, differing metabolic demands between CD206+CD163+ and CD206-CD163- subsets was demonstrated by RNAseq and FLIM analysis. CD206+CD163+ macrophages enhance autologous T-cell responses, spontaneously secrete high levels of pro-inflammatory cytokines and activate healthy fibroblasts towards pro-inflammatory mechanisms thus further contributing to the local inflammatory response. Finally, inhibition of CD40 activity abrogates the expression of pro-inflammatory mediators (TNFa, IL-1B, IL-6, IFNy) and induces IL-10 expression in sorted CD206+CD163+ synovial tissue-macrophages suggesting a key role for CD40 in driving this pathogenic phenotype.
Conclusion: This data identifies for the first-time enrichment of a previously undescribed dysfunctional dominant and transcriptionally distinct macrophage subtype in RA synovial tissue. Taken together, this data provides a greater understanding of the critical role tissue-resident macrophages play in perpetuating inflammation in RA. Further investigation of the molecular patterns and cues that shape specific synovial macrophage subsets may provide opportunities to reinstate RA joint homeostasis.
Disclosure of Interests: Megan Hanlon: None declared, Mary Canavan: None declared, Qingxuan Song Employee of: Janssen Research & Development, Nuno Neto: None declared, Phil Gallagher: None declared, Ronan Mullan: None declared, Conor Hurson: None declared, Michael Monaghan: None declared, Sunil Nagpal Employee of: Janssen Research & Development, Douglas Veale Speakers bureau: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Consultant of: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Grant/research support from: Janssen, Abbvie, Pfizer, UCB, Ursula Fearon Speakers bureau: Abbvie, Grant/research support from: Janssen, Abbvie, Pfizer, UCB
DOI: 10.1136/annrheumdis-2021-eular.1431

OP0029 NEUTROPHIL EXTRACELLULAR TRAPS IN GIANT CELL ARTERITIS INFLAMED TEMPORAL ARTERIES: LOCALIZATION, CO-EXPRESSION OF INFLAMMATORY CYTOKINES AND ASSOCIATION WITH DISEASE EXTENSION

O. Argyropoulou[1], D. Palamidas[1], N. Georgantzoglou[2], E. Karatza[3], E. Xingi[4], E. Kapsogeorgou5, C. D. Anagnostopoulos[6], A. C. Lazaris[2], K. Ritis[7], A. Goules8, K. Kambas[9], A. Tzioufas8. *[1]School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece*; *[2]School of Medicine, National and Kapodistrian University of Athens, 1st Department of Pathology, Athens, Greece*; *[3]National and Kapodistrian University of Athens, 2nd Propaedeutic Department of Surgery, Athens, Greece*; *[4]Hellenic*

Pasteur Institute, Light Microscopy Unit, Athens, Greece; [1]*School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece*; [6]*Biomedical Research Foundation Academy of Athens, Clinical, Experimental Surgery & Translational Research, Athens, Greece*; [7]*Democritus University of Thrace, First Department of Internal Medicine, Alexandroupolis, Greece*; [1]*School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece*; [9]*Hellenic Pasteur Institute, Laboratory of Molecular Genetics, Athens, Greece*

Background: Giant cell arteritis (GCA) represents the most prevalent form of systemic vasculitis in elderly, characterized by a remarkable heterogeneity in terms of clinical and histological phenotype, the pathogenetic mechanisms and treatment selection (1). An interplay between cells of both innate and adaptive immunity, appear to govern the pathophysiologic mechanisms (2). Among the different cellular populations, neutrophils may hold a central role in GCA pathogenesis, since they are present in abundance in tissue injury (3,4). Most importantly, they are a source of neutrophil extracellular traps (NETs) that may deliver immunocompetent substances, necessary for the perpetuation of the inflammatory response (5). The detection and function of NETs have not been studied in GCA.
Objectives: To explore the presence and clinical significance of NETs in temporal artery biopsies (TABs) of patients with GCA.
Methods: Ten patients with GCA [5 with limited cranial vasculitis (CV) and 5 with associated generalized large vessel vasculitis (LVV), as defined by ^{18}F-fluorodeoxyglucose (FDG) positron-emission tomography with computed tomography (PET/CT)] and 8 patients with polymyalgia rheumatica (PMR) were studied. GCA and PMR patients fulfilled the 1990 ACR and 2012 EULAR/ACR provisional classification criteria, respectively. The presence, location, quantitation and decoration of NETs with IL-6, IL-1β, and IL-17A were assessed in TABs at the time of disease diagnosis by tissue immunofluorescence and confocal microscopy. Quantification of NETs in tissue sections was performed using the Imaris v.9.3 software that counts the total measure volume instead of only the projection area (6). Serum levels of IL-6 and IL-17A around the time of tissue biopsy were also evaluated in all patients.
Results: All temporal artery biopsies from GCA patients had NETs located mainly in the adventitia, adjacent to the vasa vasorum, whereas TABs from PMR patients had no NET structures. LVV was associated with a higher NETs to total tissue volume ratio, compared to CV-GCA [p=0.0317]. NETs decorated with IL-6 were present in TABs of all LVV and 3 of 5 CV-GCA patients, while IL-17A positive NETs were observed in all GCA patients. IL-1β-positive NETs were not detected in any GCA patient. No relation was found between serum IL-6 and IL17A levels and NETs containing IL-6 and/or IL-17A.
Conclusion: NETs bearing IL-6 and IL-17A cytokines are present in inflamed GCA-TABs. IL-6 positive NETs are associated with the LVV phenotype and might be useful as a tissue biomarker for disease severity and extent.
REFERENCES:
[1] K. S. M. van der Geest et al. Arthritis Rheumatol, 2018;70:1366-76.
[2] C. Salvarani et al. Lancet, 2008;372:234-45.
[3] D. Chatelain et al. Ann Rheum Dis, 2009;68:84-8.
[4] S. Nadkarni et al. Circ Res, 2014;114:242-8.
[5] V. Mutua et al. Clin Rev Allergy Immunol, 2020.
[6] S. V. Costes et al. Biophys J, 2004;86:3993-4003.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.735

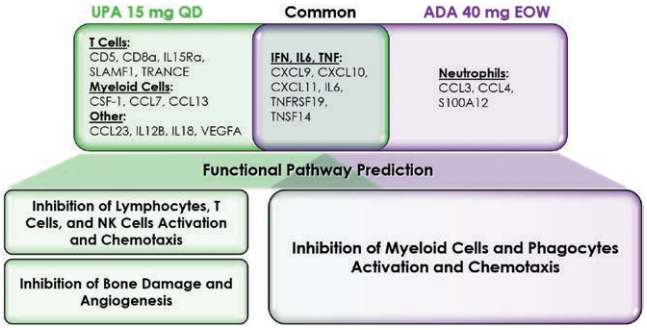
Of mice and man: insights into pathophysiology of rheumatoid arthritis and spondyloarthritis

OP0030

TREATMENT OF NON-BIOLOGIC-DMARD-IR PSA PATIENTS WITH UPADACITINIB OR ADALIMUMAB RESULTS IN THE MODULATION OF DISTINCT FUNCTIONAL PATHWAYS: PROTEOMICS ANALYSIS OF THE SELECT-PSA 1 PHASE 3 STUDY

T. Sornasse[1], J. Anderson[2], K. Kato[2], A. Lertratanakul[2], C. T. Ritchlin[3], I. McInnes[4]. [1]*AbbVie, Precision Medicine Immunology, Redwood City, United States of America*; [2]*AbbVie, Immunology Clinical Development, North Chicago, United States of America*; [3]*University of Rochester, Allergy/Immunology and Rheumatology, Rochester, United States of America*; [4]*University of Glasgow, College of Medical, Veterinary and Life Sciences, Glasgow, United Kingdom*

Background: Treatment of non-biologic-DMARD-IR (DMARD-IR) PsA patients with upadacitinib (UPA) at 15 mg QD, an oral JAK1 selective inhibitor, resulted in improvement in musculoskeletal symptoms, psoriasis, physical function, fatigue, quality of life, and inhibited radiographic progression; improvements were observed as early as Week 2 (ACR20 and ACR50). UPA 15 mg QD was non-inferior to adalimumab (ADA) 40 mg EOW for ACR20[1]
Objectives: To determine the relative biological pathway modulation of UPA compared with ADA in patients with PsA via the evaluation of a pre-defined set of plasma proteins associated with inflammation.
Methods: Patients from the SELECT-PsA1 study (DMARD-IR PsA patients) were randomly selected (PBO, n=100; UPA 15 mg QD, n=100; ADA 40 mg EOW, n = 100). The levels of 92 inflammation related protein biomarkers (pBM) were analyzed using a multiplexed Proximity Extension Assay platform in plasma samples collected at baseline, week 2, and 12; change from baseline in protein levels were expressed as Log_2 Fold Change; a Repeated Measure Mixed Linear Model identified proteins modulated by UPA and ADA compared to Baseline. Functional pathway prediction was performed in silico with a commercially distributed software where 52 significantly modulated pBM (mean $|Log_2$ FC$| \geq 0.1$ AND FDR ≤ 0.05) were selected; results were summarized based on 3 core biological groups: 1) adaptive immune system, 2) innate immune system, and 3) non-immune connective and vascular systems.
Results: At the single pBM-level, at the week 2 and 12 time points, treatment with UPA 15 mg QD resulted in distinct down modulation of T cell-associated (CD5, CD8a, IL15Ra, SLAMF1, TRANCE) and myeloid cell-associated pBM (CSF-1, CCL7, CCL13) that was not observed in the ADA treated group. Reciprocally, treatment with ADA 40 mg EOW resulted in a specific down modulation of a subset of neutrophil associated pBM (CCL3, CCL4, and S100A12). Both treatments resulted in the down modulation of IFN-, IL6-, and TNF-related pBM (CXCL9, CXCL10, CXCL11, IL6, TNFRSF19, and TNSF14) suggesting a common node of activity related to these pivotal cytokine-signaling pathways.
Functional pathway prediction based on the pBM data revealed that treatment with UPA is preferentially associated with the inhibition of T cells, but also NK cells and lymphocytes, compared to the predicted effects of treatment with ADA. Treatment with UPA also preferentially inhibited pathways related to bone damage and angiogenesis, as compared to the predicted effect of treatment with ADA. Finally, both treatments were predicted to inhibit multiple pathways associated with the activity of myeloid cells and phagocytes.
Conclusion: Consistent with previous observations in RA[2], UPA is predicted to inhibit multiple functional pathways associated the pathobiology of PsA belonging to the general categories of adaptive and innate immunity but also non-immune vascular and connective tissue biology. In contrast, treatment with ADA appears to affect more specifically functional pathways associated with the innate immune system.
REFERENCES:
[1] McInnes, I. et al. **Annals of the Rheumatic Diseases 79**, 16-17 (2020).
[2] Sornasse, T., Song, I.H., Radstake, T. & McInnes, I. **Annals of the Rheumatic Diseases 79**, 581-582 (2020).



Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship.
Disclosure of Interests: Thierry Sornasse Shareholder of: AbbVie, Employee of: AbbVie, Jaclyn Anderson Shareholder of: AbbVie, Employee of: AbbVie, Koji Kato Shareholder of: AbbVie, Employee of: AbbVie, Apinya Lertratanakul Shareholder of: AbbVie, Employee of: AbbVie, Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Grant/research support from: AbbVie, Amgen, UCB, Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sanofi Regeneron, UCB Pharma, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sanofi Regeneron, UCB Pharma
DOI: 10.1136/annrheumdis-2021-eular.1462

OP0031

SHARED AND DISTINCT GUT MICROBIOME SIGNATURES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND ITS RELATED IMMUNE-MEDIATED DISEASES

V. Rios Rodriguez[1], M. Essex[2,3], J. Rademacher[1,4], F. Proft[1], U. Löber[2,3], L. Marko[3,5], U. Pleyer[6], B. Siegmund[1], D. Poddubnyy[1,7], S. Forslund[2,3,5,8]. [1]*Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Gastroenterology, Infectiology and Rheumatology, Berlin, Germany*; [2]*Helmholtz Association of German Research Centers e.V., Max Delbrück Center for Molecular Medicine (MDC), Berlin, Germany*; [3]*Experimental and Clinical Research Center, a Joint Cooperation Between the Charité Medical Faculty and the Max Delbrück Center for Molecular Medicine, Experimental and Clinical Research Center, Berlin, Germany*; [4]*Berlin Institute of Health, Clinical Research Unit, Berlin, Germany*; [5]*German Center for Cardiovascular Research (DZHK), Partner Site Berlin, Berlin, Germany*; [6]*Charité Campus Virchow Clinic, Oftalmology, Berlin, Germany*; [7]*Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), ein Institut der Leibniz-Gemeinschaft, Epidemiology, Berlin, Germany*; [8]*EMBL Heidelberg, Structural and Computational Biology Unit, Heidelberg, Germany*

Background: Immune-mediated diseases such as spondyloarthritis (SpA) consistently coincide with dysbiosis of the gut microbiota and frequently present with additional inflammatory pathologies such as Crohn's disease (CD) and acute anterior uveitis (AAU). Deep profiling of gut microbiota may reveal new pathways of how SpA and its related diseases are initiated and perpetuated.
Objectives: To identify the presence of shared and specific gut microbiota signatures for SpA and its related diseases as a whole, as well as for the individual diseases, relative to healthy controls.
Methods: Patients were recruited with a definite diagnosis of axial SpA, AAU or CD and were compared to controls (patients with back pain and previously ruled out SpA/CD/AAU diagnosis). All patients were naïve to or did not receive treatment with biological disease-modifying antirheumatic drugs for at least 3 months before enrollment of the study. Fecal samples were collected and microbiota composition was determined by 16S rRNA gene sequencing, followed by computational analysis referencing the SILVA138 database. Nonparametric Wilcoxon tests were used to calculate differential abundances between binary groups, and the Spearman correlation was used with continuous covariates. Nested linear models and likelihood ratio tests were used to assess confounding with respect to patient characteristics, HLA-B27 expression, inflammatory markers, and the presence of other immune-mediated diseases.
Results: A total of 300 patients were recruited for the study: 111 axial SpA, 110 AAU, and 79 CD patients and were compared to 63 control individuals. Fifty-three of patients were males with an age (mean±SD) of 39.1±12.3 years. The prevalence of HLA-B27 was 63.0% by patients compared to 7.9% by control individuals. A multivariate PERMANOVA test between the groups was significant ($p<0.001$), revealing a difference in overall composition between the groups.
At the phylum level, patients with axial SpA, AAU and CD contained higher abundances of Proteobacteria, Bacteroidetes and Fusobacteria, and lower abundances of Firmicutes and Actinobacteria compared to the control group. At the genus level, patients (with axial SpA, AAU and CD) displayed a shared gut microbiome signature differing from that of control individuals. Patients samples were strongly depleted in *Blautia* compared to the control group. Many of the differentially abundant taxa also correlated with increased inflammation as measured by C-reactive protein (CRP), including a depletion of *Fusicatenibacter*, *Lachnospiraceae FCS020* and *Roseburia*, as well as an enrichment of *Lactobacillus* and *Veillonella*. By looking at each separate disease phenotype, CD patients differed significantly from the control individuals with respect to many genera. These primarily consisted of depletions in Clostridiales (*Roseburia*, *Coprococcus*, *Ruminococcaceae*), and enrichments of pathogen-harboring genera such as *Escherichia-Shigella* and *Fusobacterium*. Axial SpA patients were uniquely enriched in *Collinsella* and *Holdemanella* and depleted in *Cupriavidus*; the enrichment of *Lactobacillus* and depletion of *Blautia* observed in all patient groups was also associated to the presence of axial SpA, though confounded by CRP. There were strong taxa associations to the presence of HLA-B27, including enrichment of *Asteroleplasma*, *Coprococcus*, *Faecalibacterium*, *Rominococcaceae, Lachnospiraceae NK4A136* and *Rikenellaceae*.
Conclusion: There is a robust shared taxonomic signature among related immune-mediated diseases, in addition to individual disease phenotype signatures. Patients frequently exhibited a strong depletion in *Blautia* and an enrichment in *Lactobacillus* as well as pathogen-harboring genera such as *Escherichia-Shigella* and *Fusobacterium*.

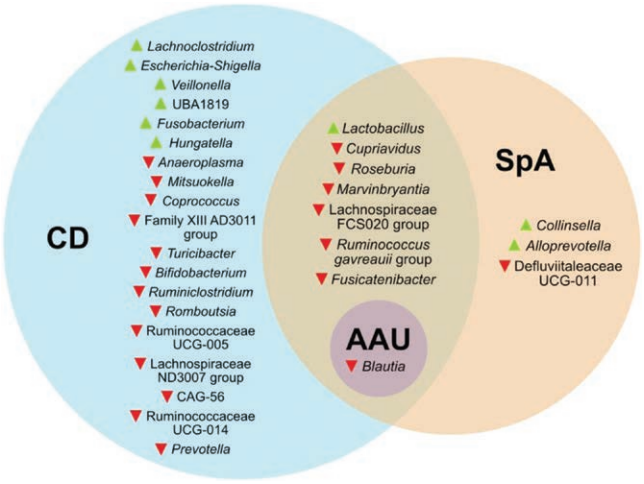


Figure 1. Taxa associations within and between the groups resulting from comparing each with the control group and accounting for disease concomitance and patient characteristics (FDR ≤ 0.05). AAU, anterior acute uveitis; CD, Crohn's disease; SpA, spondyloarthritis.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1965

OP0032

SINGLE CELL ANALYSIS OF SPONDYLOARTHRITIS REGULATORY T CELLS IDENTIFIES DISTINCT SYNOVIAL GENE EXPRESSION PATTERNS AND CLONAL FATES

D. Simone[1,2], F. Penkava[1], A. Ridley[1], S. Sansom[3], H. Al Mossawi[1], P. Bowness[1]. [1]*University of Oxford, NDORMS, Oxford, United Kingdom*; [2]*Università della Campania "Luigi Vanvitelli," Dipartimento Medicina di Precisione, Naples, Italy*; [3]*University of Oxford, Kennedy Institute of Rheumatology, Oxford, United Kingdom*

Background: Regulatory T cells (Tregs) play an important role in controlling inflammation and limiting autoimmunity, but their phenotypes at inflammatory sites in human disease are poorly understood. Whilst the phenotype and transcriptional profile of Tregs have been studied in some immune mediated conditions, they have been little studied (especially at the single cell level) in synovial fluid in the course of inflammatory arthritis. In Spondyloarthritis (SpA), in particular, where pathogenesis and inflammation is driven by dysregulated effector immunity, the role of the regulatory arm of immunity is largely unknown.
Objectives: We aimed to draw an atlas of Tregs in the context of SpA joint inflammation using single cell RNA sequencing of blood and SF Tregs of patients with Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA). Functionally distinct specialised Treg subtypes, and specific changes in transcriptional profile occurring in synovial fluid Tregs, providing an insight on Treg adaptation during inflammation. Furthermore, by coupling gene expression analysis with TCR sequencing, we aimed to describe clonally expanded and likely antigen-driven Tregs in the SF.
Methods: Fluorescent activated cell sorting (FACS) was used to isolate 13,400 memory CD3+ CD45RA-ve CD25+127low Tregs from the blood and synovial fluid (SF) of 2 patients with HLA-B27+ AS presenting with active knee arthritis. Single-cell RNA sequencing (scRNA-seq) using 5' V(D)J 10x Genomics technology allowed both transcriptional definition of Tregs, and exploration of their immune TCR repertoire. Findings were compared to >3,000 SF and blood Tregs from 3 patients with olygoarticular PsA [1]. Multicolor flow cytometry and in vitro cell-based assays using patient-derived cells were used to confirm and expand, at protein and functional level, the findings that emerged from the gene expression analysis.
Results: We report a large scRNAseq dataset (approx. 17,000 cells) comparing Tregs from SpA blood and joints. We identify multiple Treg clusters with distinct transcriptomic profiles, including, among others, a regulatory CD8+ subset expressing cytotoxic markers/genes, and a Th17-like *RORC*+ Treg subset characterized by IL-10 and LAG-3 expression. Synovial Tregs show upregulation of interferon signature and TNF receptor superfamily genes, and marked clonal expansion, consistent with tissue adaptation and antigen contact respectively. Individual synovial Treg clones map to different clusters indicating cell fate divergence. Finally, we demonstrate that LAG-3 directly inhibits IL-12/23 and TNF

secretion by patient-derived monocytes, a mechanism with translational potential in SpA.

Conclusion: Our detailed characterization of Tregs at an important inflammatory site illustrates the marked specialization of Treg subpopulations and identifies a broad transcriptional profile upregulated across all synovial regulatory cells. Our TCR analysis provides evidence of Treg clonal expansion, which may be driven by antigen, and confirms functional specialisation of individual clones. We also propose a new insight into a Treg functional mechanism through LAG-3 that suggests a novel therapeutic approach to immune-driven diseases.

REFERENCES:

[1] Penkava et al., Nature Communications, 2020

Disclosure of Interests: Davide Simone: None declared, Frank Penkava: None declared, Anna Ridley: None declared, Stephen Sansom: None declared, Hussein Al Mossawi Employee of: UCB, Paul Bowness Grant/research support from: Regeneron, Celgene/BMS and GSK

DOI: 10.1136/annrheumdis-2021-eular.4278

OP0033 REGULATORY T CELL CD39 EXPRESSION AS A PREDICTOR OF EARLY REMISSION-INDUCTION WITH METHOTREXATE IN NEW-ONSET RHEUMATOID ARTHRITIS

P. Brown[1,2], A. Anderson[1], B. Hargreaves[1,2], A. Morgan[3,4], J. D. Isaacs[1,2], A. Pratt[1,2]. [1]*Translational and Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, United Kingdom*; [2]*Musculoskeletal Unit, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom*; [3]*Leeds Institute of Cardiovascular and Metabolic Medicine, Discovery and Translational Science Department, School of Medicine, University of Leeds, Leeds, United Kingdom*; [4]*National Institute for Health Research, Leeds Biomedical Research Centre, Leeds, United Kingdom*

Background: The long term outcomes for patients with rheumatoid arthritis (RA) depend on early and effective disease control. Methotrexate remains the key first line disease modifying therapy for the majority of patients, with 40% achieving an ACR50 on monotherapy(1). There are at present no effective biomarkers to predict treatment response, preventing effective personalisation of therapy. A putative mechanism of action of methotrexate, the potentiation of anti-inflammatory adenosine signalling, may inform biomarker discovery. By antagonism of the ATIC enzyme in the purine synthesis pathway, methotrexate has been proposed to increase the release of adenosine moieties from cells, which exert an anti-inflammatory effect through interaction with ADORA2 receptors(2). Lower expression of CD39 (a cell surface 5-'ectonucleotidase required for the first step in the conversion of ATP to adenosine) on circulating regulatory T-Lymphocytes (Tregs) was previously identified in patients already established on methotrexate who were not responding (DAS28 >4.0 vs <3.0)(3). We therefore hypothesised that *pre*-treatment CD39 expression on these cells may have clinical utility as a predictor of early methotrexate efficacy.

Objectives: To characterise CD39 expression in peripheral blood mononuclear cells in RA patients naïve to disease modifying therapy commencing methotrexate, and relate this expression to 4 variable DAS28CRP remission (<2.6) at 6 months.

Methods: 68 treatment naïve early RA patients starting methotrexate were recruited from the Newcastle Early Arthritis Clinic and followed up for 6 months. Serial blood samples were taken before and during methotrexate therapy with peripheral blood mononuclear cells isolated by density centrifugation. Expression of CD39 by major immune subsets (CD4+ and CD8+ T-cells, B-lymphocytes, natural killer cells and monocytes) was determined by flow cytometry. The statistical analysis used was binomial logistic regression with baseline DAS28CRP used as a covariate due to the significant association of baseline disease activity with treatment response.

Results: Higher pre-treatment CD39 expression was observed in circulating CD4+ T-cells of patients who subsequently achieved clinical remission at 6 months versus those who did not (median fluorescence 4854.0 vs 3324.2; p = 0.0108; Figure 1-A). This CD39 expression pattern was primarily accounted for by the CD4+CD25 high sub-population (median fluorescence 9804.7 vs 6455.5; p = 0.0065; Figure 1-B). These CD25 high cells were observed to have higher FoxP3 and lower CD127 expression than their CD39 negative counterparts, indicating a Treg phenotype. No significant associations were observed with any other circulating subset. A ROC curve demonstrates the discriminative utility of differential CD39 expression in the CD4+CD25 high population for the prediction of DAS28CRP remission in this cohort, showing greater specificity than sensitivity for remission prediction(AUC: 0.725; 95% CI: 0.53 - 0.92; Figure 1-C). Longitudinally, no significant induction or suppression of the CD39 marker was observed amongst patients who did or did not achieve remission over the 6 months follow-up period.

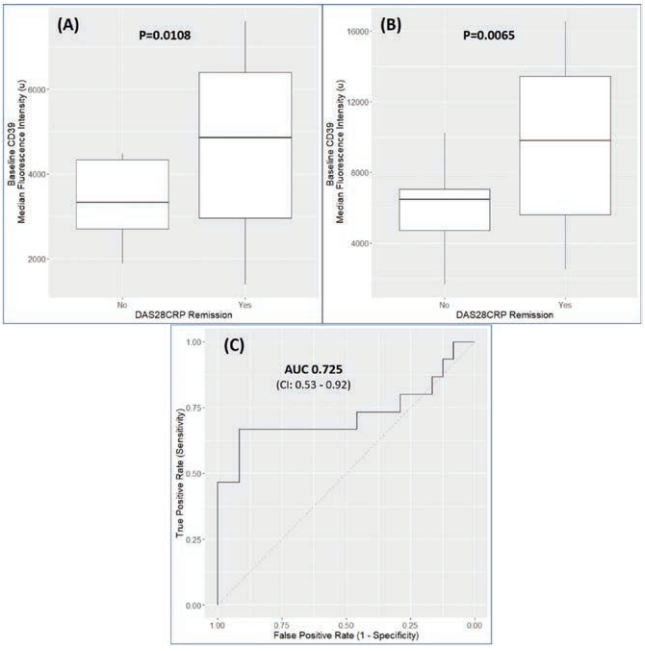


Figure 1. Six month DAS28CRP remission versus pre-treatment median fluorescence of CD39 expression on CD4+ T-cells (A); CD25 High expressing CD4+ T-cells (B); and ROC curve of predictive utility of pre-treatment CD39 expression on CD25 High CD4+ T-cells (C).

Conclusion: These findings support the potential role of CD39 in the mechanism of methotrexate response. Expression of CD39 on circulating Tregs in treatment-naïve RA patients may have particular value in identifying early RA patients likely to respond to methotrexate, and hence add value to evolving multi-parameter discriminatory algorithms.

REFERENCES:

[1] Hazlewood GS, et al. BMJ. 2016 21;353:i1777
[2] Brown PM, et al. Nat Rev Rheumatol. 2016;12(12):731-742
[3] Peres RS, et al. Proc Natl Acad Sci U S A. 2015;112(8):2509-2514

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2030

OP0034 STP938, A NOVEL, POTENT AND SELECTIVE INHIBITOR OF CTP SYNTHASE 1 (CTPS1) DEMONSTRATES EFFICACY IN RODENT MODELS OF INFLAMMATION AND ARTHRITIS

H. Asnagli[1], A. Novak[2], L. Birch[2], R. Lane[2], N. Minet[3], D. Laughton[2], P. George[4], G. De Ribains[5], S. Latour[3], A. Fischer[6], T. Bourne[7], A. Parker[1]. [1]*Step Pharma, Pharmacology, Archamps, France*; [2]*Sygnature Discovery, Discovery Building-Biocity Building, Nottingham, United Kingdom*; [3]*Institut Imagine, Laboratory of Lymphocyte Activation & EBV Susceptibility, INSERM-U1163, Paris, France*; [4]*Independent consultant, Drug Discovery & Development, Paris, France*; [5]*Gamut, Therapeutics, Paris, France*; [6]*INSERM-U1163, AP-HP, Paris, France*; [7]*Milvuswood, Consultancy, High Wycombe, United Kingdom*

Background: The final rate-limiting step in pyrimidine synthesis is the conversion of UTP to CTP which is catalyzed by cytidine triphosphate synthase 1 (CTPS1) or CTPS2. A hypomorphic mutation in the CTPS1 gene has highlighted the essential and non-redundant role of CTPS1 in T and B lymphocyte proliferation[1]. These patients exhibit no effects on non-hematopoietic tissues. Thus, selective inhibition of CTPS1 represents a novel targeted approach to dampen pathological T- and B-cell lympho-proliferation. STP938 is an orally bioavailable, small molecular weight, selective inhibitor of CTPS1 developed by Step Pharma.

Objectives: To demonstrate the in vitro effects of CTPS1 inhibition on T and B cell proliferation and the therapeutic potential of STP938 using in vivo models of disease.

Methods: The *in vitro* anti-proliferative activity of STP938 was investigated using cell lines and primary human PBMCs. STP938 was assessed *in vivo* using the DTH-KLH rat model and the mouse collagen-induced arthritis (CIA) model. For the KLH-DTH model, Lewis rats were immunized with KLH, a week later, challenged locally at the ear with KLH antigen, ear swelling was assessed after 24 hours. Blood samples were collected for detection of KLH-specific IgG levels at day 8. STP938 was given orally one-hour prior to immunization and then b.i.d. for 7 days. For the CIA model, DBA-1 mice were immunized with Collagen type II and complete Freund's adjuvant and received a booster immunization three

weeks later. STP938 was administered to mice developing signs of arthritis from Day 28 to 45 orally daily b.i.d.

Results: STP938 inhibited *in vitro* proliferation of HEK_{wt} but not $HEK\text{-}CTPS1_{KO}$ cells as well as Jurkat and human PBMCs. STP938 demonstrated a significant and dose-dependent inhibition of KLH-specific T and B cell responses *in vivo*. STP938 significantly reduced the disease severity in the CIA model in a dose-dependent manner as determined by clinical and histopathological readouts.

Conclusion: Our preliminary *in vitro* and *in vivo* results indicate that inhibition of CTPS1 specifically blocks proliferation of cells derived from the lymphocyte lineage and reduces the T cell driven inflammatory response. These data highlight the therapeutical potential of STP938 in treating patients with autoimmune diseases such as rheumatoid arthritis.

REFERENCES:

[1] Martin et al, JCI Insight. 2020, 12;5(5):133880

Disclosure of Interests: Hélène ASNAGLI Employee of: Step Pharma, Andrew Novak: None declared, Louise Birch Shareholder of: Step Pharma, Rebecca Lane: None declared, Norbert Minet Employee of: employee as Ph D student under CIFRE grant, David Laughton: None declared, Pascal George Shareholder of: Step Pharma, Geoffroy de Ribains Shareholder of: as former employee of Step Pharma, Employee of: former employee of Step Pharma, Sylvain Latour: None declared, Alain Fischer: None declared, Tim Bourne Shareholder of: UCB, Step Pharma, Sitryx Therapeutics, Consultant of: a range of biotech companies, Employee of: former employee of Step Pharma and Sitryx Therapeutics, Andrew Parker Employee of: Step Pharma

DOI: 10.1136/annrheumdis-2021-eular.148

OP0035 ASSESSMENT OF THE INTESTINAL PERMEABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS USING COLONIC TISSUES AND SERA

R. Audo[1,2], P. Sanchez[1], J. Mielle[2], L. Macia[3], B. Rivière[4], C. Lukas[1], B. Combe[1], J. Morel[1], C. Daien[1]. [1]*CHU Montpellier, Department of Rheumatology, Montpellier, France*; [2]*UMR5535, IGMM, Montpellier, France*; [3]*University of Sydney, Charles Perkins Center, Montpellier, France*; [4]*CHU Montpellier, Laboratoire d'Anatomie et de Cytologie Pathologiques, Montpellier, France*

Background: Patients with rheumatoid arthritis (RA) have an altered gut microbiota (dysbiosis) (1-3). This microbiota interacts with intestinal epithelium which can lead to an increased intestinal permeability, responsible for the passage of antigens and inflammatory molecules, and can therefore promote systemic inflammation. Gut microbiota tends to normalize with disease control (2), suggesting that systemic inflammation may directly influence the composition of microbiota and the gut barrier. It was shown in many inflammatory diseases that intestinal permeability is impaired, but to date there is very little data in RA.

Objectives: In the present study, we evaluate the intestinal permeability in RA patients by analyzing tight junctions in colonic biopsies and serum markers.

Methods: Colonic biopsies from 20 RA patients who underwent coloscopy for screening with normal histology were compared with those from 20 age and sex matched controls. ZO-1, occludin and claudin 2 junction proteins were evaluated by immunohistochemistry. The staining intensity was assessed by two blinded independent readers. The serum concentrations of LPS-binding protein (LBP), CD14s and zonulin were evaluated by ELISA in 25 patients naive of DMARDs, 41 patients before and after introduction of a DMARDs and 21 controls. Elevated zonulin in serum indicates an increase in intestinal permeability while LBP and CD14s indicate bacterial translocation.

Results: ZO-1 expression was significantly lower in biopsies from patients with RA than controls (mean score ± SD of 1.6 ± 0.56 vs 2.0 ± 0.43; p = 0.01). Age, sex, disease duration and immunological status did not significantly influence the expression of colonic junction proteins. LBP and CD14s were higher in serum from RA patients naive of DMARDs than controls (p = 0.002 and p = 0.003). LBP, CD14s and zonulin levels significantly correlated with DAS28 (r = 0.61, p = 0.005; r = 0.51, p = 0.030 and r = 0.46, p = 0.049, respectively). After treatment, unlike non-responders, LBP and CD14s were significantly reduced in DMARD responders and variations in LBP and CD14s significantly correlated with changes in DAS28 (r = 0.46, p = 0.002 and r = 0, 33 and p = 0.030, respectively).

Conclusion: This work is one of the first to explore intestinal permeability in RA and to show altered tight junction in colonic tissue from RA. This increased intestinal permeability appears to be related to the systemic inflammation. Improving the gut microbiota through food or probiotics could enhance the effect of treatments by limiting this amplification loop of inflammation.

REFERENCES:

[1] Horta-Baas G, Romero-Figueroa MDS, Montiel-Jarquin AJ, Pizano-Zarate ML, Garcia-Mena J, Ramirez-Duran N. Intestinal Dysbiosis and Rheumatoid Arthritis: A Link between Gut Microbiota and the Pathogenesis of Rheumatoid Arthritis. J Immunol Res. 2017;2017:4835189.

[2] Zhang X, Zhang D, Jia H, Feng Q, Wang D, Liang D, et al. The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment. Nat Med. 2015;21(8):895-905.

[3] Maeda Y, Kurakawa T, Umemoto E, Motooka D, Ito Y, Gotoh K, et al. Dysbiosis Contributes to Arthritis Development via Activation of Autoreactive T Cells in the Intestine. Arthritis Rheumatol. 2016;68(11):2646-61.

Disclosure of Interests: Rachel Audo: None declared, Pauline Sanchez: None declared, Julie Mielle: None declared, Laurence Macia: None declared, Benjamin Rivière: None declared, Cédric Lukas: None declared, Bernard Combe: None declared, Jacques Morel: None declared, Claire Daien Speakers bureau: Pfizer roche chugai fresenius BMS msd Novartis galapagos, Consultant of: Abivax abbbvie BMS roche chugai, Grant/research support from: Pfizer, roche-chugai, fresenius, msd

DOI: 10.1136/annrheumdis-2021-eular.2642

OP0036 IL-6 ACTIVATES YES-ASSOCIATED PROTEIN (YAP) IN FIBROBLASTS AND INDUCES YAP-SNAIL COMPLEX FORMATION TO DRIVE SYNOVIAL LINING PATHOLOGY IN INFLAMMATORY ARTHRITIS

R. Symons[1], F. Colella[1], F. Collins[1], A. Roelofs[1], C. De Bari[1]. [1]*Arthritis and Regenerative Medicine Laboratory, Institute of Medical Sciences, University of Aberdeen, Aberdeen, United Kingdom*

Background: In rheumatoid arthritis (RA), the fibroblast-like synoviocytes (FLS) in synovial lining become invasive and cause joint destruction. The molecular mechanisms underpinning this pathogenic FLS phenotype are incompletely understood. The FLS descend from *Growth differentiation factor 5* (*Gdf5)*-expressing joint interzone cells in the embryo, and we showed that conditional ablation of the transcriptional co-activator Yes associated protein (Yap) in *Gdf5*-lineage cells prevents synovial lining hyperplasia after traumatic cartilage injury in mice [1].

Objectives: Here, we investigated a potential role for Yap in pathogenic FLS in immune-mediated inflammatory arthritis.

Methods: Immunohistochemistry was used to detect Yap in human RA synovium and Yap, Snail and Ctgf in mouse synovium following antigen-induced arthritis (AIA). To determine the effect of Yap knockout (KO) in synovial stromal cells, AIA was induced in *Gdf5-Cre;tdTomato;*$Yap^{fl/fl}$ (*Yap* cKO) and *Gdf5-Cre;tdTomato;*$Yap^{wt/wt}$ (control) mice, or in *Pdgfrα-CreER*;$Yap^{fl/fl}$ (*Yap* ciKO, targeting *Pdgfrα*-expressing fibroblasts) and $Yap^{fl/fl}$ or $Yap^{WT/fl}$ (control) mice after adult tamoxifen induction. Yap KO in both models was confirmed by immunohistochemistry. After nine days, arthritis severity was determined by histological scoring of synovial lining hyperplasia, immune infiltrates, cellular exudate, and marginal erosions. TdTomato+ *Gdf5*-lineage cells in synovium were quantified. *In vitro*, Yap reporter cells were treated with inflammatory cytokines to evaluate their ability to stimulate Yap-induced GFP expression by flow cytometry. Snail overexpression, siRNA-mediated Yap knockdown, and IL-6/sIL-6R stimulation were performed on normal mouse FLS, AIA-FLS or human RA-FLS, and cell invasion through a matrigel-coated transwell was quantified. A proximity ligation assay was utilised to detect Yap/Snail complex formation.

Results: Average expression levels of Yap (p<0.0001), its transcription factor partner Snail (p=0.002), and their downstream target Ctgf (p=0.0003), were increased in mouse synovium after AIA (n=5), and Yap was highly expressed by FLS in human RA synovium. Yap cKO mice (n=24) showed a significantly decreased arthritis severity (p=0.002) after AIA compared to controls (n=22), with significant reductions in synovial lining hyperplasia (p<0.001), synovial immune cell infiltrates (p=0.026) and marginal erosions (p=0.002). Similarly, Yap ciKO mice (n=6) showed a significant decrease in arthritis score (p=0.039) after AIA compared to controls (n=9). However, both control mice (p<0.001) and Yap cKO mice (p<0.001) showed an extensive expansion of tdTomato+ *Gdf5*-lineage synovial cells after AIA, with no significant difference between control and Yap cKO mice. *In vitro*, Yap knockdown prevented IL-6/sIL-6R-induced invasion of normal mouse FLS (p=0.037) and decreased the invasiveness of AIA-FLS (p=0.0057). Using Yap reporter cells, we found that Yap was activated by IL-6/sIL-6R (p=0.016), but not TNFα or IL-1β. Finally, IL-6/sIL-6R treatment of normal mouse FLS (p=0.033) or human RA-FLS (p=0.036) induced Yap-Snail complex formation, and Yap knockdown prevented FLS invasion induced by Snail overexpression (p=0.027).

Conclusion: These data demonstrate that via activation by IL-6, and co-operation with the transcription factor Snail, Yap acts as a key modulator of the invasive and destructive phenotype of FLS in inflammatory arthritis. Therapeutic targeting of Yap could reduce joint destruction in RA.

REFERENCES:

[1] A. J. Roelofs *et al.*, "Joint morphogenetic cells in the adult mammalian synovium," *Nat. Commun.*, vol. 8, no. May, p. 15040, 2017. DOI: 10.1136/annrheumdis-2018-213799

Acknowledgements: This work was funded by the Medical Research Council (MR/L020211/1 and MR/L022893/1) and Versus Arthritis (20775 and 21156).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2530

OP0037

ABATACEPT AND OTHER DMARDS HAVE COMMON TRANSCRIPTOMIC EFFECTS ON RA SYNOVIAL TISSUE

C. Triaille[1,2], T. Gaelle[3], T. Sokolova[1], L. Meric de Bellefon[1,3], C. Galant[4], P. Durez[1,3], B. Lauwerys[1,3], N. Limaye[5]. [1]*Université Catholique de Louvain, Pôle de Pathologies Rhumatismales Systémiques et Inflammatoires, Institut de Recherche Expérimentale et Clinique, Brussels, Belgium*; [2]*Cliniques Universitaires Saint-Luc, Service d'Hématologie, Oncologie et Rhumatologie pédiatrique, Brussels, Belgium*; [3]*Cliniques Universitaires Saint-Luc, Service de Rhumatologie, Brussels, Belgium*; [4]*Cliniques Universitaires Saint-Luc, Service d'Anatomie Pathologique, Brussels, Belgium*; [5]*Université catholique de Louvain, Genetics of Autoimmune Diseases and Cancer, de Duve Institute, Brussels, Belgium*

Background: Modes of action of DMARDs (disease-modifying antirheumatic drugs) in rheumatoid arthritis (RA) are not completely understood at the level of the synovium. Studying treatment-induced modifications in RA synovial tissue can provide unique insights into the pathways modulated downstream of different DMARDs.

Objectives: Our goal was to assess histological and transcriptomic effects of Abatacept (ABA) on RA synovium, and to compare them with previously published data obtained by our group using the same study design on other DMARDs: Tocilizumab (TCZ), Rituximab (RTX), Methotrexate (MTX) and Adalimumab (ADA).

Methods: Synovial tissue was obtained using ultrasound-guided biopsy from affected joints before (W0) and 16 weeks (W16) after treatment with subcutaneous Abatacept 125mg per week on a MTX background. Paraffin-sections were stained for CD3, CD20 and CD68 and scored by a pathologist for T cell, B cell and macrophage infiltration. Transcriptional profiling was performed using GeneChip Human Genome U133 Plus 2.0 arrays (Affymetrix), and analyzed on Genespring GX (Agilent). Pathway analyses were performed on Genespring GX, Metascape (https://metascape.org/) and EnrichR (https://maayanlab.cloud/Enrichr/). Protein-Protein Interaction (PPI) networks were generated on STRING (https://string-db.org/).

Results: 14 RA patients were included (female: 9, ACPA/RF positive: 8, erosive disease: 12, median disease duration in years (± SD): 11.7 (± 8.1), median DAS28CRP (± SD): 4.78 (± 1.11)). Median DAS28CRP significantly decreased between W0 and W16, as did US GS score. Evaluation of histological slides (n=11 pairs of samples) showed no significant effect of Abatacept on T cell, B cell or macrophage infiltration. Gene expression analysis (n=10 pairs of samples) identified 304 transcripts differentially expressed (129 downregulated, 175 upregulated) between W0 and W16 (FC≥1.5 and p<0.05, paired Mann-Whitney). Downregulated genes were significantly enriched for immune processes and included several key T cell regulatory genes (*IL2RA, CD28, IL7, IL7R*), strongly overlapping with data from previous studies on TCZ (n= 12 pairs), RTX (n=12 pairs), MTX (n=8 pairs) and ADA (n=8 pairs). Thus, each treatment shares 31 to 48% of its downregulated genes with the others, with genes downregulated by at least three involved in key RA-associated pathways such as *leukocyte activation*, *NF-kappa B signaling*, *TNF signaling and JAK-STAT signaling*. Given their seemingly overlapping effects, data were pooled across these studies, markedly improving power thanks to their paired-design. This revealed that genes downregulated by DMARDs (n=573, Benjamini-Hochberg corrected p-value<0.05, paired Mann-Whitney) were significantly enriched for both *T cell* and *myeloid leukocyte activation* pathways. Interestingly, DMARDs seem to have a coordinate effect on the two pathways (correlation of mean Log_2FC: r=0.8558, p<0.0001), with a stronger impact ($Log_2FC_{W16\text{-}W0}$) in good responders to therapy (n=17) as compared to moderate (n=20) and to non-responders (n=13) (p<0.0001, Mann-Whitney). Finally, Transcription Factor enrichment and PPI network analyses point to a central role for molecules including JAK/STATs as mediators of all studied therapies.

Conclusion: We provide evidence that the effects of five DMARDs on RA synovium culminate in the same pathways (namely, *T cell* and *myeloid leukocyte activation*). This confirms previous studies suggesting the existence of common mediators downstream of DMARDs, independent of their primary targets, and suggests attractive new therapeutic targets.

Acknowledgements: This work was funded in part by unrestricted grants from Cap48 (RTBF) and Bristol-Myers Squibb. Clément Triaille is funded by the Fonds National de la Recherche Scientifique (FNRS, Communauté française de Belgique) and Fondation Saint-Luc (Cliniques Universitaires Saint-Luc).

Disclosure of Interests: Clément Triaille: None declared, Tilman Gaelle: None declared, Tatiana Sokolova: None declared, Laurent Meric de Bellefon: None declared, Christine Galant: None declared, Patrick Durez Grant/research support from: unrestricted research grant from Bristol-Myers Squibb, Bernard Lauwerys Employee of: currently employed at UCB Biopharma, Nisha Limaye: None declared

DOI: 10.1136/annrheumdis-2021-eular.2088

Molecular mechanisms in Connective Tissue Disease

OP0038

SPLICEOSOME ALTERATIONS IN LEUCOCYTES FROM APS, SLE AND SLE+APS PATIENTS ARE CLOSELY RELATED TO THEIR MAIN CLINICAL FEATURES

A. M. Patiño-Trives[1], C. Perez-Sanchez[1], A. Ibañez-Costa[2], P. S. Laura[1], M. Luque-Tévar[1], I. Arias de la Rosa[1], M. C. Ábalos-Aguilera[1], D. Ruiz[1], P. Seguí Azpilcueta[1], M. Espinosa[1], N. Barbarroja Puerto[1], E. Collantes Estevez[1], J. P. Castaño[2], R. M. Luque Huertas[2], M. A. Aguirre[1], C. Lopez-Pedrera[1]. [1]*IMIBIC, Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, Córdoba, Spain*; [2]*IMIBIC, Department of Cell Biology, Physiology and Immunology, University of Cordoba, Spain, Córdoba, Spain*

Background: To date, although multiple molecular approaches have illustrated the various aspects of Primary Antiphospholipid Syndrome (APS), systemic lupus erythematosus (SLE) and antiphospholipid syndrome plus lupus (APS plus SLE), no study has so far fully characterized the potential role of posttranscriptional regulatory mechanisms such as the alternative splicing.

Objectives: To identify shared and differential changes in the splicing machinery of immune cells from APS, SLE and APS plus SLE patients, and their involvement in the activity and clinical profile of these autoimmune disorders.

Methods: Monocytes, lymphocytes and neutrophils from 80 patients (22 APS, 35 SLE and 23 APS plus SLE) and 50 healthy donors (HD) were purified by immunomagnetic selection. Then, selected elements of the splicing machinery were evaluated using a microfluidic qPCR array (Fluidigm). In parallel, extensive clinical/serological evaluation was performed, comprising disease activity, thrombosis and renal involvement, along with autoantibodies, acute phase reactants, complement and inflammatory molecules. Molecular clustering analyses and correlation/association studies were developed.

Results: Patients with primary APS, SLE and APS plus SLE displayed significant and specific alterations in the splicing machinery components in comparison with HD, that were further specific for each leukocyte subset. Besides, these alterations were associated with distinctive clinical features.

Hence, in APS, clustering analysis allowed to identify two sets of patients representing different molecular profile groups with respect to the expression levels of splicing machinery components. Principal component analyses confirmed a clear separation between patients. Clinically, cluster 1 characterized patients with higher thrombotic episodes and recurrences than cluster 2 and displayed a higher adjusted global APS score (aGAPSS). Accordingly, these patients showed higher levels of inflammatory mediators than cluster 2.

Similarly, in patients with APS plus SLE, clustering analysis allowed to identify two sets of patients showing differential expression of splicing machinery components. Clinical and laboratory profiles showed that cluster 2 characterized patients that had suffered more thrombotic recurrences, most of them displaying an aGAPSS over 12 points and expressing higher levels of inflammatory mediators than cluster 1. The incidence of lupus nephropathy was similarly represented in both clusters.

Lastly, in SLE patients, molecular clustering analysis identified two sets of patients showing distinctive clinical features. One cluster characterized most of the patients positive for anti-dsDNA antibodies, further suffering lupus nephropathy, and a high proportion of them also presenting atheroma plaques and high levels of inflammatory mediators.

Correlation studies further demonstrated that several deranged splicing machinery components in immune cells (i.e. SF3B1tv1, PTBP1, PRP8 and RBM17) were linked to the autoimmune profile of the three autoimmune diseases, albeit in a specific way on each disorder. Accordingly, *in vitro* treatment of HD lymphocytes with aPL-IgG or anti-dsDNA-IgG changed the expression of spliceosome components also found altered *in vivo* in the three autoimmune diseases. Finally, the induced over/downregulated expression of selected spliceosome components in leukocytes modulated the expression of inflammatory cytokines, changed the procoagulant/adhesion activities of monocytes and regulated NETosis in neutrophils.

Conclusion: 1) The splicing machinery, profoundly altered in leukocytes from APS, APS plus SLE and SLE patients, is closely related to the activity of these diseases, their autoimmune and inflammatory profiles. 2) The analysis of the splicing machinery allows the segregation of APS, APS plus SLE and SLE, with specific components explaining the CV risk and renal involvement in these highly related autoimmune disorders.

Acknowledgements: Funded by ISCIII, PI18/00837 and RIER RD16/0012/0015 co-funded with FEDER

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2485

OP0039

ALPN-303, AN ENHANCED, POTENT DUAL BAFF/APRIL ANTAGONIST ENGINEERED BY DIRECTED EVOLUTION FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND OTHER B CELL-RELATED AUTOIMMUNE DISEASES

S. R. Dillon[1], L. S. Evans[2], K. E. Lewis[1], J. Yang[3], M. W. Rixon[4], J. Kuijper[5], D. Demonte[5], J. Bhandari[4], S. Levin[2], K. Kleist[1], S. Mudri[1], S. Bort[2], D. Ardourel[5], M. A. Seaberg[6], R. Wang[6], C. Gudgeon[1], R. Sanderson[6], M. F. Wolfson[4], J. Hillson[3], S. L. Peng[3]. [1]*Alpine Immune Sciences, Translational Sciences, Seattle, United States of America*; [2]*Alpine Immune Sciences Inc, Immunology, Seattle, United States of America*; [3]*Alpine Immune Sciences Inc, Clinical Development, Seattle, United States of America*; [4]*Alpine Immune Sciences Inc, Protein Therapeutics, Seattle, United States of America*; [5]*Alpine Immune Sciences Inc, Protein Engineering, Seattle, United States of America*; [6]*Alpine Immune Sciences Inc, Bioanalytical Sciences, Seattle, United States of America*

Background: BAFF and APRIL are TNF superfamily members that form homo- and heteromultimers that bind TACI and BCMA on B cells; BAFF also binds BAFF-R. BAFF and APRIL support B cell development, differentiation, and survival, particularly for plasmablasts and plasma cells, and play critical roles in the pathogenesis of B cell-related autoimmune diseases. In nonclinical models, inhibition of either BAFF or APRIL alone mediates relatively modest effects, whereas their co-neutralization dramatically reduces B cell function, including antibody production. Fc fusions of wild-type (WT) TACI (e.g. atacicept and telitacicept) target both BAFF and APRIL and have demonstrated promising clinical potential in e.g. systemic lupus erythematosus (SLE) and IgA nephropathy but have not yet clearly exhibited long-term and/or complete disease remissions.
Objectives: To generate a dual BAFF/APRIL antagonist with inhibitory activity superior to WT TACI and BCMA and with the potential to improve clinical outcomes in B cell-mediated diseases.
Methods: Our directed evolution platform was used to identify a potent variant TNFR domain (vTD) of TACI that exhibits significantly enhanced affinity for BAFF and APRIL as compared to WT TACI; this TACI vTD domain was fused to a human IgG Fc to generate the therapeutic candidate ALPN-303. ALPN-303 was evaluated for functional activity in: 1) human lymphocyte assays, 2) the NOD.*Aec1Aec2* spontaneous model of Sjogren's syndrome (SjS), 3) the bm12-induced mouse model of lupus, 4) the (NZB/NZW)F_1 spontaneous model of lupus, and 5) preclinical rodent and cynomolgus monkey pharmacokinetic/pharmacodynamic studies.
Results: ALPN-303 inhibited BAFF- and APRIL-mediated signaling *in vitro* in human lymphocyte assays, with significantly lower IC_{50} values than WT TACI-Fc and belimumab comparators. In all mouse models evaluated, administration of ALPN-303 rapidly and significantly reduced key lymphocyte subsets including plasma cells, germinal center B cells, and follicular T helper cells. ALPN-303 significantly reduced autoantibodies and sialadenitis in the spontaneous SjS model, inhibited glomerular IgG deposition in the bm12-induced model of lupus, and potently suppressed anti-dsDNA autoAbs, blood urea nitrogen levels, proteinuria, sialadenitis, kidney lesions, and renal immune complex deposition in the NZB/W lupus model. As compared to WT TACI-Fc, ALPN-303 exhibited higher serum exposure and significantly and persistently decreased titers of serum IgM, IgG, and IgA antibodies in mice and cynomolgus monkeys (Figure 1).

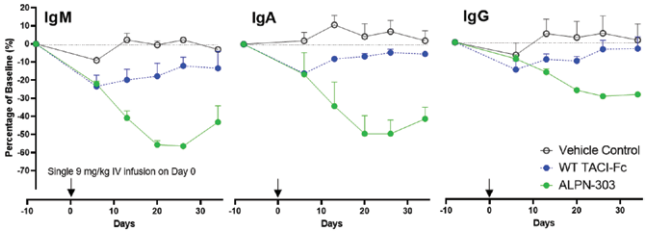


Figure 1. ALPN-303 induces more potent suppression, as compared to WT TACI-Fc, of serum immunoglobulins following a single 9 mg/kg IV infusion (on Day 0; arrows) in female cynomolgus monkeys.

Conclusion: ALPN-303 is a potent BAFF/APRIL antagonist derived from our directed evolution platform that consistently demonstrates encouraging immunomodulatory activity and efficacy *in vitro* and *in vivo*, superior in preclinical studies to anti-BAFF antibody and WT TACI-Fc. This novel Fc fusion molecule demonstrates favorable preliminary developability characteristics, including higher serum exposures and more potent immunosuppressive activities, which may enable lower clinical doses and/or longer dosing intervals than WT TACI-Fc therapeutics. ALPN-303 may thus be an attractive development candidate for the treatment of multiple autoimmune and inflammatory diseases, particularly B cell-related diseases such as SLE, SjS, and other connective tissue diseases. Preclinical development is underway to enable the initiation of clinical trials later this year.

Disclosure of Interests: Stacey R. Dillon Shareholder of: Alpine Immune Sciences, Bristol Myers Squibb, Employee of: Alpine Immune Sciences, Bristol Myers Squibb, Lawrence S. Evans Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Katherine E. Lewis Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Jing Yang Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Mark W. Rixon Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Joe Kuijper Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Dan Demonte Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Janhavi Bhandari Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Steve Levin Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Kayla Kleist Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Sherri Mudri Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Susan Bort Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Daniel Ardourel Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Michelle A. Seaberg Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Rachel Wang Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Chelsea Gudgeon Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Russell Sanderson Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Martin F. Wolfson Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Jan Hillson Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences, Stanford L. Peng Shareholder of: Alpine Immune Sciences, Employee of: Alpine Immune Sciences
DOI: 10.1136/annrheumdis-2021-eular.727

OP0040

HIPPOCAMPAL IMMUNE CELL TRAFFICKING AND A MYELOID PREDOMINANT INFLAMMATORY RESPONSE WITH ENHANCED ANTIGEN PRESENTATION AND DECREASED LEVELS OF NEUROTRANSMITTERS UNDERLY THE NEUROPSYCHIATRIC PHENOTYPE OF THE NZW/NZB MURINE LUPUS MODEL

D. Nikolopoulos[1,2], T. Manolakou[1], A. Filia[1], M. Nakos-Bimpos[1], A. Polissidis[1], D. Boumpas[1,2]. [1]*Biomedical Research Foundation Academy of Athens, Center of Translational Research, Athens, Greece*; [2]*National and Kapodistrian University of Athens, Rheumatology and Clinical Immunology Unit, 4th Department of Medicine, Athens, Greece*

Background: Neuropsychiatric events are common in patients with systemic lupus erythematosus (SLE), yet the underlying pathogenesis remains ill-defined, as the access to brain tissue is limited. We have previously shown that NZW/NZB F1 murine lupus model recapitulates the neuropsychiatric lupus phenotype including depressive-like behavior, increased rates of anxiety, cognitive dysfunction and motor disturbances, both at pre-nephritic and nephritic stages of the disease.
Objectives: To dissect specific regions in the brain, which account for this phenotype and elucidate inflammatory and non-inflammatory mechanisms involved.
Methods: Four distinct brain regions (hippocampus, amygdala, striatum and pre-frontal cortex) were dissected from brains of female C57BL/6 (WT) and NZW/NZB F1 mice at the age of 3 months (pre-nephritic) and 6 months (nephritic stage) (n=5-8/condition/experiment). Since most of the behavioral phenotype corresponds to the hippocampus, we first examined in depth the hippocampal pathology by bulk RNA sequencing, measurements of neurotransmitters levels via high-performance liquid chromatography (HPLC) and by immunophenotyping via flow cytometry analyses. For comparisons, statistical significance was indicated as a two-sided P<0.05.
Results: Transcriptomic analysis revealed aberrant immune mediated response in the hippocampus of 6 month-old lupus mice compared to WT. Specifically, inflammatory pathways including both innate and adaptive immune responses, increased cytokine production, increased antigen presentation and immune cell trafficking, along with increased apoptosis and decreased cell proliferation suggest that immune aberrancies may lead to neuronal damage. These aberrancies were present in mice at 3 month-old, yet were progressed with time being more prominent at 6 month of age in lupus hippocampus. The RNA sequencing date were validated by immunophenotyping on lupus hippocampus demonstrating increased reactive GFAP+ astrocytes both at 3 and 6-month old mice. Activated IBA1+ microglia and CD11b+CD45hi CNS myeloid cells were increased only at 6 months of age. Furthermore, increased immune cell infiltration from the periphery including lymphocytes (CD45+CD11b-) mainly T cells (CD4+/CD8+) and monocytes (CD45+CD11b+Ly6G-Ly6C+), was evident only in 6 month-old lupus hippocampus compared to WT. Importantly, microglia cells in lupus hippocampus at 6 but not at 3 month of age, exhibited increased expression of antigen presenting markers including CD80, CD86 and MHC-II

indicating that microglia cells may carry out the antigen presentation process seen in transcriptomic data. Low levels of serotonin and noradrenaline were observed at both 3 and 6 months of age in lupus mice; these aberrancies were mainly attributed to decreased serotonin synthesis as evidenced by intact serotonin metabolism (no differences were observed at its metabolite: 5-hydroxyindoleacetic acid). Analysis of the remaining regions of the brain combined with studies of metabolic activities of various brain regions by PET-CT scanning is in progress.

Conclusion: Immune cell trafficking from the periphery combined with marked inflammatory response in the hippocampus underlie the neuropsychiatric phenotype in NZW/B murine lupus. Our data indicate increased expression of activated myeloid cells -including microglia- in the hippocampus of lupus mice culminating in increased antigen presentation and decreased neurotransmitter levels.

REFERENCES:

[1] Nikolopoulos, D., et al. "THU0223 THE NEUROPSYCHIATRIC PHENOTYPE OF NZB/W LUPUS-PRONE MOUSE MODEL AT PRE-NEPHRITIC AND NEPHRITIC STAGES OF THE DISEASE: MURINE MODEL RECAPITULATES HUMAN DISEASE." (2020): 334-335.

Acknowledgements: This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 742390)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3972

OP0041 SALIVA AND SERUM LEVELS OF CXCL13: ASSOCIATION WITH THE SEVERITY OF SALIVARY GLAND LESIONS AND LYMPHOMA IN PATIENTS WITH SJÖGREN'S SYNDROME (SS)

L. Chatzis[1], A. Goules[1], A. Tzioufas[1], E. Kapsogeorgou[1]. [1]*School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece*

Background: CXCL13 has been implicated in the formation of ectopic germinal centers (GC) in minor salivary gland (MSG) inflammatory lesions of SS patients. Recent studies suggest that serum CXCL13 levels associate with disease severity and risk for non-Hodgkin's lymphoma (NHL) development.

Objectives: To validate the clinical utility of CXCL13 by investigating potential associations of saliva and serum CXCL13 levels with various histopathologic (including severity of MSG autoimmune infiltrates and GC formation), serologic and clinical features of the disease, as well as NHL.

Methods: CXCL13 levels were measured by a commercially available ELISA (sensitivity: 1 pg/ml; Abcam, Cambridge, UK) in paired serum and saliva specimens from 25 SS patients (9 with NHL; SSL), 9 sicca controls (SC; sicca-complaining individuals with no infiltrates in diagnostic MSG biopsy and negative autoantibody profile) and 6 healthy controls (HC). From the 16 SS patients without evidence of NHL, 5 had mild, 6 intermediate and 5 severe lesions at MSGs, as arbitrarily defined by focus (FS) and Tarpley (TS) biopsy scores (mild: FS:1-1.7, TS:1, intermediate: FS:1.8-2.95, TS:2 and severe: FS: 3.0-11, TS: 3-4). Furthermore, the organization of the MSG infiltrates to GCs has been evaluated in 23 patients revealing 10 with GCs.

Results: Kruskal-Wallis analysis revealed that serum CXCL13 levels were significantly increased in SS patients without or with NHL (median: 94.83 pg/ml and 96.70 pg/ml, respectively), compared to SC and HC (35.44 and 40.92 pg/ml respectively; $p<0.05$), whereas saliva levels were only marginally increased (76.47, 84.10, 55.98 and 65.30 pg/ml in SS, SSL, SC and HC, respectively, $p=0.051$). Among SS patients with distinct MSG lesion severity, only those with severe lesions were found to express significantly higher serum CXCL13 levels (149.3 pg/ml) from SC and HC (p: 0,0051 and 0.0166, respectively). Spearman's Rank correlation analysis showed that both serum and saliva levels correlated with SG biopsy focus score (r: 0.6889, $p=0.0001$ and r: 0.4222, $p=0.01$, respectively). Mann-Whitney test revealed that serum CXCL13 levels were significantly elevated in patients with GCs at MSG lesions (156.1 *vs* 69.64 pg/ml, p:0.0015), rheumatoid factor (105.0 *vs* 53.72 pg/ml, p: 0.015) and marginally with anti-Ro/La antibodies (121.8 *vs* 65.05 pg/ml, p: 0.06) compared to those without. Furthermore, CXCL13 levels were significantly increased in SS patients at high risk to develop NHL compared to low risk (149.3 *vs* 71.54 pg/ml, respectively, p: 0.0275). Saliva levels were not found to associate with the studied features.

Conclusion: Serum and to a lesser extend saliva CXCL13 levels are increased in SS and SSL patients and associate with the degree of MSG infiltration, as assessed by focus score. Serum, but not saliva, CXCL13 associates with various disease features, including GC formation, and may have a clinical utility in identifying SS patients at high risk to develop lymphoma.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2119

OP0042 BLOCKING OF CD103+ TISSUE RESIDENT MEMORY T CELLS (TRM) AS A THERAPEUTIC STRATEGY IN SJOGREN'S SYNDROME

D. Mauro[1], X. Lin[2], G. Guggino[3], D. Chong[2], S. Raimondo[4], D. MA[5], F. Xiao[2], W. Du[2], M. Lo Pizzo[3], L. Zhang[5], A. Rizzo[6], R. Alessandro[4], L. Lu[2], F. Ciccia[1]. [1]*University of Campania "L. Vanvitelli", Rheumatology Unit, Department of Precision Medicine, Naples, Italy*; [2]*The University of Hong Kong, Department of Pathology and Shenzhen Institute of Research and Innovation, Hong Kong, China*; [3]*University of Palermo, Mother and Child Care, Department of Health Promotion, Rheumatology Section, Internal Medicine and Medical Specialties, Palermo, Italy*; [4]*Università degli Studi di Palermo, Dipartimento di Biopatologia e Biotecnologie Mediche e Forensi, Palermo, Italy*; [5]*Shanxi Medical University, Department of Rheumatology, Shanxi Bethune Hospital and Shanxi Academy of Medical Sciences, Taiyuan, China*; [6]*Azienda Ospedaliera "Ospedali Riuniti Villa Sofia-Cervello", Pathology Unit, Palermo, Italy*

Background: Tissue-resident memory T cells (TRM), are a recently identified T cells population featuring tissue localization and expression of markers of tissue homing, CD69 and CD103. Recently, the expansion of CD8+ TRMs and their involvement in the sialadenitis was described in a murine model of SS. However, CD4+ and CD8+ TRM's functional relevance in pSS is still not fully understood, and the TRM therapeutic targeting unexplored.

Objectives: The study aimed to address the role of $CD4^+$ and $CD8^+$ TRMs in the pathogenesis of pSS and to explore the therapeutic targeting of the tissue residency marker of TRM CD103.

Methods: An animal model of experimental (ESS) obtained by immunization of female C57BL/6 mice (n=10) with salivary glands (SG) protein extract and Freund's complete adjuvant used to investigate the dynamic of infiltration of SG by $CD4^+$ and $CD8^+$ TRMs, their frequency, and the impact of CD103 blockade. For the therapeutic intervention, at 10-weeks post-immunization, the salivary gland was cannulated via Wharton's duct, and an anti-CD103 neutralizing antibody or vehicle-injected. The mice's saliva flow rate was assessed, and SGs were analyzed by Flow-cytometry and immunohistochemistry (IHC).

The frequency and localization of TRMs was analyzed in minor SG of sicca syndrome (nSS) and pSS patients (n=39) by flow cytometry and IHC. The expression of genes involved in the tissue retention of TRMs was assessed in SG by RT-PCR.

Results: Upon the ESS progression, a significant progressive increase in $CD45^+CD103+$ cells frequency was observed from 5wk to 20wk post-immunization ($p<0.001$), where the $CD8^+$ were the most abundant, followed by $CD4^+$. Consistently, $CD103^+CD8^+$ T cells were detected within the lymphocytic infiltration of SG from ESS mice. Sorted purified SG $CD10^+CD3^+CD8^+$ T cells showed higher Granzyme B, TNF-alpha expression compared to $CD103^-CD3^+CD8^+$ at both mRNA and protein levels. Notably, ESS mice treated with anti-CD103 showed improvement in salivary function ($p<0.05$) and reduced lymphocytic infiltrations measured as focus score (FS) ($p<0.01$) and area-fraction ($p<0.01$). Consistently, anti-CD103 treatment consistently reduced $CD103^+$ cells and IFN-gamma$^+$, Granzyme B^+, and $TNFa^+$ $CD8^+$ cells. We next performed phenotypic analysis of $CD45^+CD103^+$ immune cells in the SG of pSS patients observing an increase in both with $CD8^+CD103^+CD69^+$ and $CD4^+CD103^+CD69^+$ ($p<0.05$). Finally, IHC showed that the expansion of TRMs in pSS salivary glands was accompanied by a down-regulation of E-cadherin glandular expression and their migration outside the epithelium in the context of inflammatory infiltrates. SG of patients with pSS showed a significant up-regulation of BLIMP1, KFL-2, and S1PR1 and down-regulation of ITGB2. CXCL9 and CXCL10, and IL-15 involved in the tissue recruitment and long-term survival of TRMs were significantly modulated in pSS salivary glands.

Conclusion: TRM are expanded and activated in the SG of pSS and ESS, participating in the organization of tissue inflammation. Although the mechanisms behind this expansion are still not fully understood, CD103 could be a valuable novel therapeutic target to prevent lymphocytic infiltrations and glandular destruction in Sjogren syndrome.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2649

OP0043 INCREASED RISK OF SEVERE INFECTIONS AND MORTALITY IN PATIENTS WITH NEWLY DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS: A POPULATION-BASED STUDY

K. Zhao[1,2], H. Xie[1,2], L. Ll[2,3], A. Aviña[2,3], J. Esdaile[2,3]. [1]*Simon Fraser University, Health Sciences, Burnaby, Canada*; [2]*Arthritis Research Canada, Biostatistics, Richmond, Canada*; [3]*The University of British Columbia, Experimental Medicine, Vancouver, Canada*

Background: Systemic lupus erythematosus (SLE) is a chronic disease with a broad spectrum of autoantibodies and clinical manifestations. As much as 45%

of SLE patients were reported to suffer from severe infections[1,2]. However, due to the high cost of recruiting patients, we still do not have a holistic picture of the SLE-infection association. Administrative data which encompass all provincially funded healthcare service data shows promising opportunities to advance the knowledge and management of the SLE patients which cannot be evaluated by the conventional clinical setting with small sample size and selective samples[3,4,5].

Objectives: To evaluate the risk of severe infection and infection-related mortality among patients with newly diagnosed systemic lupus erythematosus.

Methods: We conducted an age- and gender- matched cohort study of all patients with incident SLE between January 1, 1997 and March 31, 2015 using administrative health data from British Columbia, Canada. Primary outcome was the first severe infection after SLE onset necessitating hospitalization or occurring during hospitalization. Secondary outcomes were total number of severe infections and infection-related mortality.

Results: We identified 5,169 SLE patients and matched them with 25,845 non-SLE individuals from the general population, yielding 955 and 1,986 first severe infections during 48,367 and 260,712 person-years follow-up, respectively. The crude incidence rate ratios for first severe infection and infection-related mortality were 2.59 (95% CI, 2.39-2.80) and 2.20 (95% CI, 1.76-2.73), respectively. The corresponding adjusted hazard ratios were 1.82 (95% CI 1.66-1.99) and 1.61 (95% CI, 1.24-2.08). SLE patients had an increased risk of a greater total number of severe infections with crude rate ratio of 3.24 (95% CI, 3.06-3.43) and adjusted rate ratio of 2.07 (95% CI, 1.82-2.36).

Conclusion: SLE is associated with increased risks of first severe infection (1.8-fold), a greater total number of severe infections (2.1-fold) and infection-related mortality (1.6-fold).

REFERENCES:

[1] Yurkovich M, Vostretsova K, Chen W, Aviña-Zubieta JA. Overall and cause-specific mortality in patients with systemic lupus erythematosus: a meta-analysis of observational studies. Arthritis Care Res (Hoboken) 2014;66(4):608-16.

[2] Petri M. Infection in systemic lupus erythematosus. Rheum Dis Clin North Am 1998;24(2):423-56.

[3] Cervera R, Khamashta MA, Font J, et al. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: a comparison of early and late manifestations in a cohort of 1,000 patients. Medicine (Baltimore) 2003;82(5):299-308.

[4] Goldblatt F, Chambers S, Rahman A, Isenberg DA. Serious infections in British patients with systemic lupus erythematosus: hospitalisations and mortality. Lupus 2009;18(8):682-9.

[5] Bosch X, Guilabert A, Pallares L, et al. Infections in systemic lupus erythematosus: a prospective and controlled study of 110 patients. Lupus 2006;15(9):584-9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.17

OP0044 ANA POSITIVITY IS ASSOCIATED WITH COMPLEX IMMUNE DISTURBANCE EVEN IN INDIVIDUALS WHO DO NOT DEVELOP CLINICAL AUTOIMMUNE DISEASE

S. U. Hassan[1,2], Z. Wigston[1], A. Burska[1], M. Y. MD Yusof[1,2], E. Vital[1,2]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine, Rheumatology, Leeds, United Kingdom*; [2]*NIHR Leeds Musculoskeletal Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Study of pre-clinical autoimmunity can reveal immune changes that initiate or prevent clinical disease. We previously reported an At Risk cohort of ANA positive individuals referred to secondary care, of whom 16% progressed to SLE or Sjogren's syndrome during follow up[1]. Recently, we also reported that even ANA positive individuals who do not develop clinical autoimmunity, have defective pDC function and non-haematopoietic interferon-production[2].

Objectives: To describe the immunophenotype of ANA-positive progressors and non-progressors compared to healthy controls.

Methods: We conducted a prospective observational longitudinal study of At-Risk individuals in Leeds (n=150) over 3 years with annual follow up. Those who met classification criteria for autoimmune connective tissue disease (AI-CTD) during follow up were termed progressors and others; non-progressors. Among the non-progressors, those with no clinical diagnostic criteria at any time point were called absolute non-progressors (ANP).

At baseline we analysed two IFN-stimulated gene expression scores previously described[3] and flow cytometry performed for major circulating subsets. Association between progression group and biomarkers were tested using independent samples t-test.

Results: 3 year follow up data were available in 148/150 patients. Outcomes were: progressors: 30/148 (20%) [SLE=25; pSS=5] and non-progressors: 118/148 (80%). Within the non-progressors, 69/148 (47%) were ANP.

A detailed analysis of baseline biomarkers is included in Table 1. Despite not developing clinically significant disease, non-progressors had significant alterations in several biomarkers. This was also evident in the ANP sub-group.

Table 1.

Biomarker	Healthy Controls Mean (95% CI)	Non-progressors Mean (95% CI)	Difference from healthy controls p	Absolute non-progressors Mean (95% CI)	Difference from healthy controls p	Progressors Mean (95% CI)	Difference from healthy controls p
IFN score A	-6.27 (-6.88, -5.65)	-5.22 (-5.64, -4.80)	0.016	-5.11 (-5.91, -4.32)	0.120	-4.14 (-5.11, -3.18)	0.001
IFN score B	-5.43 (-6.00, -4.85)	-5.30 (-5.62, -4.98)	0.193	-4.96 (-5.45, -4.47)	0.949	-4.27 (-4.90, -3.65)	0.136
% Monocytes	14.80 (10.50, 19.11)	15.46 (12.96, 17.97)	0.187	14.94 (11.42, 18.47)	0.738	10.36 (7.42, 13.30)	0.227
% CD4 T cells	62.90 (57.75, 68.05)	64.89 (60.86, 68.92)	0.001	68.72 (62.97, 74.47)	0.267	60.93 (53.64, 68.21)	0.001
% CD8 T cells	32.18 (27.47, 36.90)	28.60 (25.12, 32.09)	0.135	25.02 (20.28, 29.77)	0.044	31.51 (25.63, 37.40)	0.875
% Naïve B cells	65.59 (56.56, 74.61)	73.74 (70.02, 77.46)	0.001	76.86 (72.21, 81.51)	0.128	68.86 60.62, 75.84)	0.173
% Memory B cells	29.56 (20.42, 38.72)	19.72 (15.84, 23.61)	<0.000	23.13 (16.65, 29.61)	0.054	25.57 (17.18, 33.96)	0.163
% Plasmablasts	1.12 (0.81, 1.43)	0.91 (0.58, 1.24)	0.964	1.01 (0.44, 1.58)	0.457	0.81 (0.53, 1.10)	0.112
% NK cells	13.65 (9.65, 17.65)	12.30 (8.90, 15.71)	0.480	12.35 (6.65, 18.05)	0.781	11.90 (8.65, 15.14)	0.195

Conclusion: Clinically benign ANA positivity is a complex immune state with many features seen in active SLE, including pDC exhaustion, keratinocyte interferon production and strong skin interferon score, increased blood interferon score, and disturbance of B cell subsets. These findings suggest that other factors are necessary for clinical disease, or that regulatory mechanisms stabilise autoimmunity. Further work in this cohort will address these questions.

REFERENCES:

[1] Md Yusof et al. Ann Rheum Dis 2018

[2] El-Sherbiny et al. Sci Rep 2018

[3] Psarras et al. Nat Commun. 2020

Disclosure of Interests: Sabih-Ul Hassan: None declared, Zoe Wigston: None declared, Agata Burska: None declared, Md Yuzaiful Md Yusof: None declared, Edward Vital Grant/research support from: Honoraria and research grant support from Roche, GSK and AstraZeneca.

DOI: 10.1136/annrheumdis-2021-eular.1414

OP0045 NLRP12 INVOLVES IN THE LUPUS WITH POSITIVE INTERFERON SIGNATURE

Y. P. Tsao[1], F. Y. Tseng[2], C. W. Chao[2], M. H. Chen[1], S. T. Chen[2]. [1]*Taipei Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Department of Medicine, Taipei, Taiwan, Republic of China*; [2]*National Yang-Ming University, Institutes of Clinical Medicine, Taipei, Taiwan, Republic of China*

Background: Systemic lupus erythematous (SLE) is a systemic autoimmune disease with diverse etiological factors. It was recognized that interferon (IFN) signature involved in the progress of SLE. NLRP12 (NOD-like receptor family (NLR) pyrin domain containing 12) is a pyrin containing NLR protein that we had linked its new biological function to the cross-regulation of Toll like receptor (TLRs) and Rig-I like receptor (RIG-I) pathways. NLPR12 acts as an innate immune check-point in regulating type I IFNs expression during TLRs and RIG-I activation. The importance of NLRP12 in lupus disease activity remained to be elucidated.

Objectives: To clarify the role of NLRP12 in regulating the interferon signature.

Methods: Peripheral blood mononuclear cells (PBMCs) were collected from SLE patients and healthy donors for analysis of *NLRP12* and IFN-α gene expression by RT-QPCR. PBMCs were applied for Chromatin immunepreciptation (ChIP) assay and electrical mobility shift assay (EMSA) to determine the putative transcription factor that regulates *NLRP12* expression. An involvement of epigenetic regulation of NLRP12 expression in SLE patients was also analyzed. Bone marrow derived dendritic cells (BMDCs) were collected from wild type mouse and Nlrp12 knocked-out mice. Another CD14+ monocytes were isolated from 10 cases of lupus patients and 8 cases of healthy control, following by stimulating different type of nucleic acids, and IFN-α and IL-6 were measured with ELISA assay. CD14+ monocytes in lupus patients were also pre-treated with IFNAR2 antibody for further nucleic acid stimulation. Two mice models were applied for evaluation the role of Nlrp12: intraperitoneal injection of TMPD (2,6,10,14-tetramethylpentadecane, or pristane) in C57BL/6 mice and Fas^{lpr} mice. Both models were conducted with and without Nlrp12 knockout.

Results: *NLRP12* expression was significantly lower in PBMC isolated from SLE patients compared to healthy donors. The inverse correlation was observed in *NLRP12* and *IFNA* gene expression as well as *NLRP12* expression and amount of double-stranded DNA autoantibody in SLE patients. *NLRP12* expression showed negative correlations with IFN-α treatment, as well as herpes simplex virus-1 (HSV-1) infection. Results from ChIP and EMSA analysis indicated a potential transcription factor 1 (TF-1) regulating NLRP12 promoter activity. TF-1 lead to transcriptional suppression of *NLRP12* in SLE PBMC, and it was gradually induced after IFN treatment. Recruitment of TF-1 to NLRP12 promoter in SLE PBMC compared to the healthy PBMC was detected, and increased when treating with IFN. Human CD14+ monocytes collected from lupus and healthy control stimulating with different type of nucleic acids revealing significant increasing level of *IFN-α* and *IL-6* in lupus patients. Among animal models, both pristine induced mice and Fas^{lpr} mice revealed increasing autoantibodies production and severity of glomerulonephritis in *Nlrp12*-/- group in comparison with *Nlrp12*+/+ ones, indicating the role of NLRP12 in maintaining positive interferon signature as well as disease activity.

Conclusion: Expression level of *NLRP1.2* has been demonstrated to be a biomarker of disease activity in SLE patients. The NLRP12 was involved in the interferon signature, which was also negatively regulated by TF-1. Both clinical samples and animal models revealed NLRP12 in maintaining the positive interferon signature, indicating the possible role of exacerbating factor for lupus disease activity.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4215

Clinical aspects of axial spondyloarthritis – science meets daily practice

OP0046 CAN PATIENTS WITH AXIAL SPONDYLOARTHRITIS INDICATE WHETHER PAIN IS MAINLY RELATED TO INFLAMMATION OR STRUCTURAL DAMAGE?

A. Kampman[1], F. Wink[1,2], M. Carbo[2], F. Maas[2], A. Spoorenberg[2], S. Arends[2].
[1]*Medical Center Leeuwarden, Rheumatology, Leeuwarden, Netherlands*;
[2]*University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*

Background: Patients with axial spondylarthritis (axSpA) mainly rate disease activity on experienced symptoms such as pain (1). Pain is also included in the assessments (ASDAS and BASDAI) used to monitor disease activity in axSpA. However, besides disease activity, also other factors including the presence of structural damage may be related to experienced pain and discomfort.

Objectives: To explore to what extent axSpA patients relate their experienced pain in neck, back and hips to inflammation and/or structural damage.

Methods: Patients from the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort visiting the out-patient clinic between May 2016 and October 2019 were included in this cross-sectional analysis. Patients filled out two additional questions related to question 2 of the BASDAI: To what extent do you think pain in your neck, back and hips is related to: 1. inflammation caused by axSpA?, 2. damage of spine and joints caused by axSpA? These questions were answered on a NRS from 0 (none) to 10 (very much). A difference of ≥2 points was considered as clinically relevant. Patients who differentiated the cause of their pain were allocated to an inflammation or damage group, in favour of their highest score. Furthermore, patient characteristics and clinical assessments were compared between the inflammation and damage groups.

Results: In total, 688 axSpA patients were included, 62.4% were male, mean age was 47.9 years, median symptom duration was 19 years, 77.9% were HLA-B27+, mean BASDAI was 3.9 and mean $ASDAS_{CRP}$ was 2.3. Respectively 13% and 14% of the patients reported a score of 0 on the additional questions about inflammation or damage.

In total, 517 (75%) patients could not differentiate between inflammation or damage. 102 (15%) patients interpreted experienced pain as mainly related to inflammation and 69 (10%) patients interpreted their pain as mainly related to structural damage.

Patients who interpreted pain as mainly related to inflammation were significantly younger, had shorter symptom duration, were more frequently diagnosed as non-radiographic axSpA and had higher $ASDAS_{CRP}$, which was driven by the patient-reported questions as the objective marker CRP was not significantly different between both groups (Table 1).

Table 1. Patients characteristics and clinical assessments of axSpA patients who related pain mainly to inflammation versus to structural damage.

	Inflammation group (n = 102)	Structural damage group (n = 69)	P-value
Age (years)	39.5 ± 12.4	48.9 ± 12.4	<0.001
Symptom duration (years)	12 (6 – 20)	28 (17 – 35)	<0.001
Diagnosis non-radiographic axSpA	39 (40%)	8 (13%)	<0.001
Male gender	60 (59%)	44 (64%)	0.627
BASDAI	4.2 ± 1.8	3.9 ± 2.0	0.371
BASDAI – Q2	6 (3 – 7)	4 (2 – 6)	0.005
Patient global disease activity	4 (3 – 7)	3 (2 – 5)	<0.001
$ASDAS_{CRP}$	2.6 ± 0.9	2.2 ± 0.8	0.003
CRP	3.0 (2.0 – 8.0)	2.5 (2.0 – 4.4)	0.094
Occiput wall distance (cm)	0.0 (0.0 – 4.0)	4.0 (0.0 – 10.0)	<0.001
Chest expansion (cm)	5.8 (4.0 – 7.0)	4.0 (3.0 – 6.0)	0.006
Modified Schober test (cm)	14.0 ± 1.6	13.5 ± 1.6	0.052
Lateral flexion mean (cm)	15.3 ± 6.5	12 ± 5.9	0.001
Cervical rotation mean (degrees)	80 (70 – 90)	70 (45 - 81)	<0.001
mSASSS *	3.0 (0.0 – 9.0)	8.0 (1.8 – 26.0)	0.061

* only available in a subgroup of patients. Inflammation group (n=31), structural damage group (n=39).

Patients who reported their pain as mainly related to structural damage showed significantly worse spinal mobility on almost all spinal mobility tests. In the subgroup of patients with available mSASSS data, there was also a trend towards more spinal radiographic damage (Table 1).

Conclusion: In our large observational cohort of axSpA patients, the vast majority (75%) could not rate whether experienced pain in neck, back and hips was more related to inflammation or structural damage. However, if patients were able to relate pain to inflammation or damage, it seems in accordance with the outcome of their clinical assessments.

REFERENCES:

[1] Spoorenberg A *et al*. Rheumatology (Oxford), 2005;44(6):789-95.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.293

OP0047 IDENTIFICATION OF CLINICAL PHENOTYPES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, PERIPHERAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS ACCORDING TO PERIPHERAL MUSCULOSKELETAL MANIFESTATIONS: A CLUSTER ANALYSIS IN THE INTERNATIONAL ASAS-PERSPA STUDY

C. López-Medina[1], S. Chevret[2], A. Moltó[1], J. Sieper[3], M. T. Duruöz[4], U. Kiltz[5], B. Zorkany[6], N. Hajjaj-Hassouni[7], R. Burgos-Vargas[8], J. Maldonado-Cocco[9], N. Ziade[10], M. Gavali[11], V. Navarro-Compán[12], S. F. Luo[13], A. Biglia[14], T. J. Kim[15], M. Kishimoto[16], F. Pimentel Dos Santos[17], J. Gu[18], L. Muntean[19], F. A. Van Gaalen[20], P. Géher[21], M. Magrey[22], S. Ibáñez[23], W. Bautista-Molano[24], W. P. Maksymowych[25], P. M. Machado[26], R. B. M. Landewé[27], D. Van der Heijde[20], M. Dougados[1]. [1]*Cochin Hospital, Rheumatology, Paris, France*; [2]*University of Paris, INSERM (U1153): Clinical Epidemiology and Biostatistics, Paris, France*; [3]*Charité University, Department of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany*; [4]*Marmara University School of Medicine, PMR Department, Rheumatology Division, Istanbul, Turkey*; [5]*Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Rheumatology, Herne, Germany*; [6]*Cairo University, Cairo, Cairo, Egypt*; [7]*Health Sciences College, International University of Rabat (UIR), Rabat, Morocco*; [8]*Hospital General de México Eduardo Liceaga, Rheumatology, Mexico City, Mexico*; [9]*Buenos Aires School of Medicine, Rheumatology, Buenos Aires, Argentina*; [10]*Rheumatology, Saint-Joseph University and Mount Lebanon Hospital, Beirut, Lebanon*; [11]*Nizam's Institute of Medical Sciences, Rheumatology, Hyderabad, India*; [12]*Rheumatology, University Hospital La Paz, Madrid, Spain*; [13]*Chang Gung Memorial Hospital-Linkou, Rheumatology, Allergy and Immunology, Taoyuan, Taiwan, Republic of China*; [14]*Fondazione IRCCS Policlinico S. Matteo, University of Pavia, Rheumatology, Pavia, Italy*; [15]*Chonnam National University Medical School and Hospital, Rheumatology, Donggu Gwangju, Korea, Rep. of (South Korea)*; [16]*Kyorin University School of Medicine, Department of Nephrology and Rheumatology, Tokyo, Japan*; [17]*Nova University of Lisbon, NOVA Medical School, Lisboa, Portugal*; [18]*Third Affiliated Hospital of Sun Yat-Sen University, Rheumatology, Guangzhou, China*; [19]*Iuliu Hatieganu University of Medicine and Pharmacy, Rheumatology, Cluj-Napoca, Romania*; [20]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [21]*Semmelweis University, Rheumatology, Budapest, Hungary*; [22]*Cases Western Reserve University School of Medicine, Rheumatology, Cleveland, United*

States of America; [23]*Facultad de Medicina Clínica Alemana – Universidad del Desarrollo, Rheumatology, Santiago, Chile*; [24]*University Hospital Fundación Santa Fé de Bogotá and Universidad El Bosque, Rheumatology, Bogotá, Colombia*; [25]*University of Alberta, Rheumatology, Alberta, Canada*; [26]*Centre for Rheumatology and Department of Neuromuscular Diseases; University College of London, Rheumatology, London, United Kingdom*; [27]*Amsterdam Rheumatology Center, AMC, Rheumatology, Amsterdam, Netherlands*

Background: Patients with a diagnosis of Spondyloarthritis (SpA) and Psoriatic Arthritis (PsA) may have predominant axial or peripheral symptoms, and the frequency and distribution of these symptoms may determine the clinical diagnosis by the rheumatologist ("clinical clusters"). Clustering analysis represents an unsupervised exploratory analysis which tries to identify homogeneous groups of cases ("statistical clusters") without prior information about the membership for any of the cases.
Objectives: To identify "statistical clusters" of peripheral involvement according to the specific location of these symptoms in the whole spectrum of SpA and PsA (without prior information about the diagnosis of the patients), and to evaluate whether these "statistical clusters" are in agreement with the "clinical clusters".
Methods: Cross-sectional and multicentre study with 24 participating countries. Consecutive patients considered by their treating rheumatologist as suffering from either PsA, axial SpA (axSpA) or peripheral SpA (pSpA) were enrolled. Four different cluster analyses were conducted: the first one using information about the specific location from all the peripheral musculoskeletal manifestations (i.e., peripheral arthritis, enthesitis and dactylitis), and thereafter a cluster analysis for each peripheral manifestation individually. Multiple correspondence analyses and k-means clustering methods were used. Distribution of peripheral manifestations and clinical characteristics were compared across the different clusters.
Results: 4465 patients were included in the analysis. Two clusters were found with regard to the *location of all the peripheral manifestations* (Fig. 1). Cluster 1 showed a low prevalence of peripheral manifestations in comparison with cluster 2; however, when peripheral involvement appeared in cluster 1, this was mostly represented by arthritis of hip, knee and ankle, as well as enthesitis of the heel. Patients from cluster 1 showed a higher prevalence of males (63% vs 44%), HLA-B27 positivity (69% vs 38%) and axial involvement (80% vs 52%), as well as more frequent diagnosis of axSpA (66% vs 21%) and more frequently fulfilling the ASAS axSpA criteria (69% vs. 41%). Patients from cluster 2 showed a higher prevalence of psoriasis (63% vs 25%), a more frequent diagnosis of PsA (61% vs 19%), and they fulfilled more frequently the peripheral ASAS (26% vs 11%) and the CASPAR criteria (57% vs 19%).

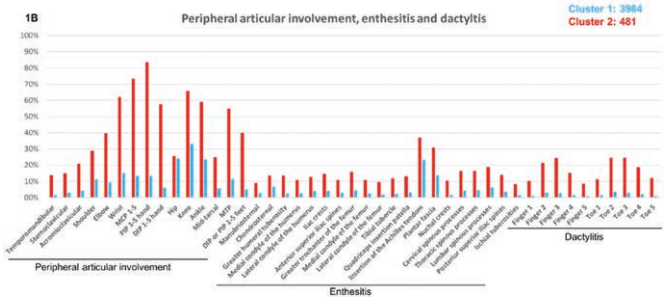


Figure 1. Distribution of the peripheral involvement across clusters

Three clusters were found with regard to the *location of the peripheral arthritis.* Clusters 2 and 3 showed a high prevalence of peripheral joint disease, although this was located more predominantly in the lower limbs in cluster 2, and in the upper limbs in cluster 3. Cluster 1 showed a higher prevalence of males, HLA-B27 positivity, axial involvement, a lower presence of psoriasis, a more frequent diagnosis of axSpA and fulfilling the ASAS axSpA criteria in comparison with clusters 2 and 3, respectively. Clusters 2 and 3 showed a higher prevalence of enthesitis and dactylitis in comparison with cluster 1, a more frequent diagnosis of PsA and fulfillment of the CASPAR criteria. Information about the *location of enthesitis* exhibited three groups: cluster 1 showed a very low prevalence of enthesitis, while cluster 2 and 3 showed a high prevalence of enthesitis, with a predominant involvement of axial enthesis in cluster 2 and peripheral enthesitis in cluster 3.
Finally, the *analysis of dactylitis* also exhibited three clusters that showed a very low prevalence of dactylitis, predominantly toes and predominantly fingers involvement, respectively.
Conclusion: These results suggest the presence of heterogeneous patterns of peripheral involvement in SpA and PsA patients without clearly defined groups, confirming the clear overlap of these peripheral manifestations across the different underlying diagnoses.
Acknowledgements: This study was conducted under the umbrella of ASAS with unrestricted grant of Abbvie, Pfizer, Lilly, Novartis, UCB, Janssen and Merck.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.805

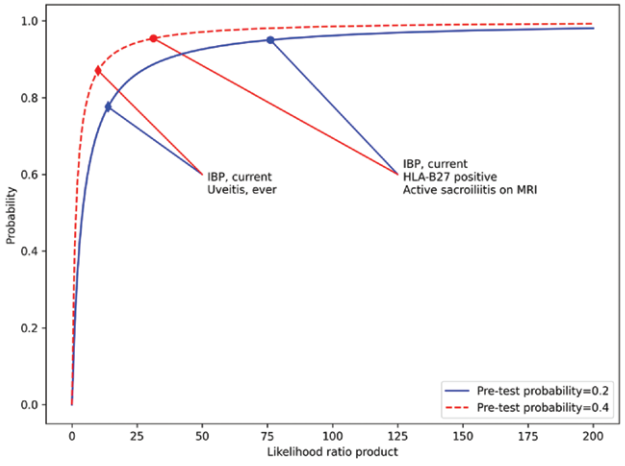
OP0048

DIAGNOSING AXIAL SPONDYLOARTHRITIS: ESTIMATION OF THE DISEASE PROBABILITY IN PATIENTS WITH A PRIORI DIFFERENT LIKELIHOODS OF THE DIAGNOSIS

D. Poddubnyy[1,2], F. Proft[1], L. Spiller[1], M. Protopopov[1], V. Rios Rodriguez[1], B. Muche[1], J. Rademacher[1], M. Torgutalp[1], J. L. Vahldiek[3], J. Sieper[1], I. Redeker[2]. [1]*Charité – Universitätsmedizin Berlin, Division of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany*; [2]*Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), ein Institut der Leibniz-Gemeinschaft, Epidemiology Unit, Berlin, Germany*; [3]*Charité – Universitätsmedizin Berlin, Division of Radiology, Berlin, Germany*

Background: The diagnostic approach in axial spondyloarthritis (SpA) relies on a estimation of the post-test disease probability that is based on evaluation of positive and negative results of diagnostic tests in the context of the pre-test disease probability.
Objectives: To evaluate the diagnostic value of SpA parameters and their combination for the diagnosis of axial SpA in patients with an *a priori* different probability of the diagnosis.
Methods: A total of 361 patients with chronic back pain and suspicion of axial SpA (181 referred by primary care physicians or orthopaedists, 180 recruited via an online screening tool) received a structured rheumatologic examination as a part of the OptiRef study [1], which resulted into a diagnosis or exclusion of axial SpA. The prevalence of axial SpA indicating the pre-test probability was 40% in the physician-referred subgroup and 20% in the online screening subgroup. Sensitivities, specificities, and likelihood ratios (LRs) for SpA features were determined in both subgroups and the respective post-test probabilities of axial SpA were calculated.
Results: The relative diagnostic value of single SpA features varied substantially between the groups with different referral pathways – see the online disease probability calculator http://www.axspa.de/calculator.html. It can be seen that the diagnostic values of the SpA parameters vary substantially between the groups. For instance, HLA-B27 positivity increased the probability of the presence of axial SpA by 35% to 55% in online-screened patients and by 22% to 62% in physician-referred patients. Furthermore, the absence of HLA-B27 resulted in a sharp decrease in the probability of the presence of axial SpA in physician-referred patients (from 40% to 6%). This decrease was less sharp in the online screening group (from 20% to 10%). Furthermore, combinations of parameters performed differently in the studied subgroups. Figure 1 illustrates that the observed differences in the diagnostic values of the SpA parameters in different subgroups were only clinically relevant in the presence of a low number of positive test results. For instance, combining IBP with anterior uveitis increased the post-test probability for axial SpA to 78% in the online screening group and to 87% in the physician-referred group, whereas using HLA-B27 positivity and active sacroiliitis on MRI in combination with IBP resulted in a surge in the post-test probability of the presence of axial SpA to around 95% in both groups.

Figure 1. The relationship between the likelihood ratio product and the post-test probability of axial SpA in patients with different pre-test disease probability.



The relationship between the likelihood ratio product and the post-test probability of axial SpA is depicted for patients referred via an online screening tool (pre-test probability of axial SpA = 20%) and in patients referred via a physician-based referral tool (pre-test probability of axial SpA = 40%).

IBP: inflammatory back pain; MRI: magnetic resonance imaging; SpA: spondyloarthritis.

Conclusion: The diagnostic value of a single diagnostic test in the clinical practice is not fixed and a number of factors including the referral pathway can affect it. Fluctuation of the diagnostic values is especially relevant when the number of positive parameters is low (1-2).

REFERENCES:

[1] Proft F, et al. Semin Arthritis Rheum. 2020;50:1015-1021.

Acknowledgements: The OptiRef study was supported by a research grant from Novartis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3550

OP0049 COMPARISON OF BASELINE DISEASE ACTIVITY AND PATIENT (PT)-REPORTED OUTCOMES (PROS) BETWEEN PTS WITH PSORIATIC ARTHRITIS AND AXIAL INVOLVEMENT (AXIAL PSA) AND AXIAL SPONDYLOARTHRITIS (AXIAL SPA) FROM THE CORRONA PSA/SPA REGISTRY

P. J. Mease[1], M. Marchese[2], R. Mclean[2], T. Blachley[2], L. Anatale-Tardiff[2], C. Saffore[3], E. Lesser[3], A. Ogdie[4]. [1]*Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, United States of America*; [2]*Corrona, LLC, Waltham, United States of America*; [3]*AbbVie Inc., North Chicago, United States of America*; [4]*University of Pennsylvania, Philadelphia, United States of America*

Background: Although pts with axial PsA and axial SpA share some common clinical characteristics, there are also potential differences that may influence disease assessment and treatment response. Identifying differences between the two pt populations is important for assessment of disease characteristics and severity as well as informing treatment decisions. There has been little comparative characterization of these conditions in a US population.

Objectives: To compare characteristics of pts with axial PsA and axial SpA.

Methods: Pts ≥18 years of age diagnosed with axial PsA or axial SpA at enrollment in the prospective, multicenter, observational Corrona PsA/SpA Registry between March 2013 and August 2020 were included. Enrollment visit demographics, clinical characteristics, treatment history, disease activity measures, and PROs were compared between disease groups. Continuous measures were reported using means and standard deviations; means for disease groups were compared using two-sample *t* tests or Wilcoxon rank sum tests. Categorical measures were reported as frequencies and percentages; frequencies in disease groups were compared using chi-square or Fisher exact tests.

Results: A total of 1044 pts (470 with axial PsA and 574 with axial SpA) were identified (Table). Pts with axial PsA were older with a higher percentage being female vs pts with axial SpA. Time since symptom onset and diagnosis were shorter for pts with axial PsA vs axial SpA (12.0 vs 15.6 years [*P*<0.001] and 6.8 vs 8.3 years [*P*=0.01]). Pts with axial PsA were less likely than pts with axial SpA to have current or historical uveitis (4% vs 14% [*P*<0.001]) or inflammatory bowel disease (5% vs 10% [*P*=0.005]). Prior biologic synthetic disease-modifying antirheumatic drug (bDMARD) and conventional synthetic DMARD use was more prevalent in the axial PsA vs axial SpA groups (64% vs 52% [*P*<0.001]/59% vs 32% [*P*<0.001]), while mean dactylitis (measured by Dactylitis Count) and enthesitis (measured by Spondyloarthritis Research Consortium of Canada [SPARCC] Enthesitis Index) counts were higher (0.4 vs 0.1 [*P*<0.001]/1.7 vs 1.2 [*P*<0.001]). Mean pt-reported pain and spinal pain were lower in pts with axial PsA vs axial SpA (49.4 vs 53.9 [*P*=0.015]/40.8 vs 49.7 [*P*<0.001]) (Figure). The proportion of pts with morning stiffness along with mean fatigue and work impairment scores were similar between disease groups.

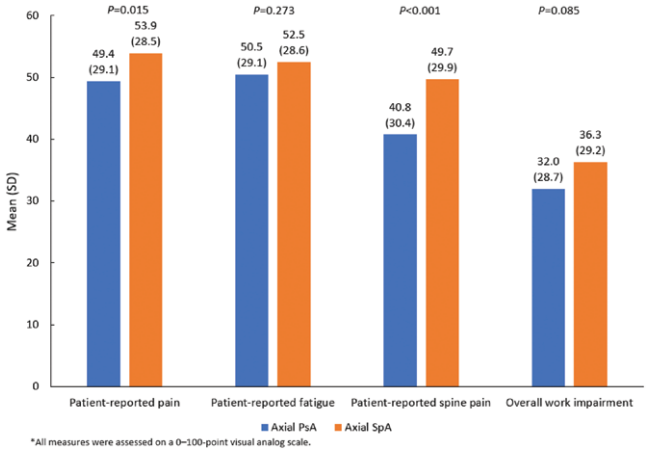
Table.

Baseline demographics and clinical characteristics	Axial PsA N=470	Axial SpA N=574	*P* value
Age (years), mean ± SD	51.6 ± 13.2	47.7 ± 14.0	<0.001
Female, n (%)	265 (57)	248 (44)	<0.001
White, n (%)	428 (94)	507 (91)	0.089
Years since symptom onset, mean ± SD	12.0 ± 11.6	15.6 ± 12.1	<0.001
Years since diagnosis, mean ± SD	6.8 ± 9.0	8.3 ± 10.5	0.010
HLA-B27 positive status, n/n (%)	52/189 (28)	214/295 (73)	<0.001
Abnormal CRP, n (%)	88 (19)	140 (24)	0.033
Uveitis, n (%)	20 (4)	80 (14)	<0.001
IBD, n (%)	25 (5)	59 (10)	0.005
Dactylitis count, mean ± SD	0.4 ± 1.5	0.1 ± 0.7	<0.001
SPARCC enthesitis count, mean ± SD	1.7 ± 2.9	1.2 ± 2.4	<0.001
Morning stiffness, n (%)	439 (95)	537 (96)	0.923
BASDAI (0–10), mean ± SD	4.8 ± 2.5	4.9 ± 2.4	0.463
BASDAI Q2 (0–10): spinal pain, mean ± SD	5.0 ± 2.9	5.7 ± 2.9	<0.001
BASDAI Q3 (0–10): peripheral pain/swelling, mean ± SD	4.5 ± 2.9	4.0 ± 3.1	0.010
Modified BASDAI (0–10), mean ± SD	5.0 ± 2.5	5.4 ± 2.4	0.013
Prior bDMARDs, n (%)	300 (64)	299 (52)	<0.001
Prior csDMARDs, n (%)	275 (59)	181 (32)	<0.001
Prior prednisone use, n (%)	54 (12)	73 (13)	0.611
Prior NSAID use, n (%)	52 (11)	46 (8)	0.115

Conclusion: Findings from this descriptive real-world analysis suggest there may be meaningful differences between pts with axial SpA and axial PsA but future studies are needed to better understand these differences.

Acknowledgements: Medical writing services provided by Alan Saltzman of Fishawack Facilitate Ltd, part of Fishawack Health, and funded by AbbVie.

Figure. Patient-reported outcomes*



This study was sponsored by Corrona, LLC. Corrona has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Crescendo, Eli Lilly and Company, Genentech, Gilead, GSK, Janssen, Merck, Momenta Pharmaceuticals, Novartis, Pfizer, Regeneron, Roche, Sun, UCB, and Valeant. The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract. No honoraria or payments were made for authorship.

Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Janssen, Lilly, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Galapagos, Gilead, GlaxoSmithKline, Janssen, Lilly, Novartis, Pfizer, Sun, and UCB, Grant/research support from: AbbVie, Amgen, BMS, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, and UCB, Maya Marchese Employee of: Corrona, Robert McLean Employee of: Corrona, Taylor Blachley Employee of: Corrona, Laura Anatale-Tardiff Employee of: Corrona, Christopher Saffore Shareholder of: AbbVie, Employee of: AbbVie, Elizabeth Lesser Shareholder of: AbbVie, Employee of: AbbVie, Alexis Ogdie Consultant of: Amgen, AbbVie, BMS, Celgene, Corrona, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB, Grant/research support from: National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, Rheumatology Research Foundation, National Psoriasis Foundation, Pfizer, and Novartis

DOI: 10.1136/annrheumdis-2021-eular.137

OP0050 TWO-YEAR DIAGNOSTIC CONSISTENCY IN PATIENTS WITH CHRONIC BACK PAIN SUSPECTED OF AXIAL SPONDYLOARTHRITIS IN PROTOCOLISED FOLLOW-UP: DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY COHORT

A. Boel[1], M. Van Lunteren[1], K. M. Fagerli[2], U. Lindström[3], R. Ramonda[4], M. G. H. Van de Sande[5], F. A. Van Gaalen[1], D. Van der Heijde[1]. [1]*Leiden University Medical Centre, Rheumatology, Leiden, Netherlands*; [2]*Diakonhjemmet Hospital, Rheumatology, Oslo, Norway*; [3]*University of Gothenburg, Rheumatology and Inflammation Research, Gothenburg, Sweden*; [4]*University of Padova, Rheumatology Unit, Padova, Italy*; [5]*Amsterdam University Medical Center, Clinical Immunology and Rheumatology, Amsterdam, Netherlands*

Background: A diagnosis of (early) axial spondyloarthritis (axSpA) is based on pattern recognition, which can be challenging and may change over time.

Objectives: To investigate consistency of diagnosis over two years in patients with chronic back pain (<2 years symptoms) suspected of axSpA.

Methods: In the SPACE cohort, patients over 16 years of age referred to the rheumatology outpatient clinic with chronic back pain (CBP) (≥3 months and <2 years) starting before the age of 45, suspected of axSpA were included. Follow-up was performed only in patients with at least two SpA features or one SpA feature with a positive likelihood ratio ≥6.4[1].

According to protocol, all SpA features as well as MRI and radiographs of the sacroiliac joints were performed at baseline and two years. Physicians were asked to report whether the diagnosis was axSpA or no axSpA at both timepoints, for which they had information available on all SpA features and locally

read imaging. Only patients with complete data on diagnosis and imaging at baseline and 2 years were included.
Patients were labelled with a consistent axSpA diagnosis if they had a diagnosis of axSpA at baseline and at two-year follow-up. Those patients whose diagnosis switched from axSpA to no axSpA; or from no axSpA to axSpA were labelled inconsistent axSpA diagnosis.
Results: Over two years, in 295 patients with CBP the diagnostic consistency rate was 84%, of whom 184 patients (62%) had a diagnosis axSpA and 66 (22%) a diagnosis no axSpA at both timepoints. 26 patients changed from axSpA to no axSpA (9%) and 19 patients from no axSpA to axSpA (7%).
The patients who only had an axSpA diagnosis at baseline were more often male and less often HLA-B27 positive compared to the other two groups (Table). Furthermore, both groups with an inconsistent diagnosis had fewer SpA features and a lower level of confidence of the diagnosis (LoC) compared to the group with a consistent diagnosis of axSpA, especially at baseline.

Table 1. Characteristics at baseline and 2-year follow-up of the group with a consistent axSpA diagnosis over 2 years and the groups whose diagnosis (axSpA/no axSpA) changed

	Consistent diagnosis axSpA AxSpA at baseline and 2yrs *(N=184)*		Inconsistent diagnosis AxSpA at baseline only *(N=26)*		Inconsistent diagnosis AxSpA at 2yrs only *(N=19)*	
	Baseline	2-year	Baseline	2-year	Baseline	2-year
Female	45%		15%		42%	
Inflammatory Back Pain	69%	74%	69%	77%	68%	84%
HLA-B27 positive	75%	75%	27%	27%	68%	68%
Sacroiliitis radiographs*	27%	38%	0%	0%	5%	5%
Sacroiliitis MRI*	69%	81%	23%	27%	5%	21%
Number of SpA features, mean (SD)	5 (2)	7 (2)	3 (1)	5 (2)	3 (1)	5 (1)
LoC diagnosis axSpA/no axSpA, mean (SD)	8.1 (2.0)	8.6 (1.8)	5.8 (1.7)	7.5 (1.9)	5.6 (2.2)	6.1 (2.3)

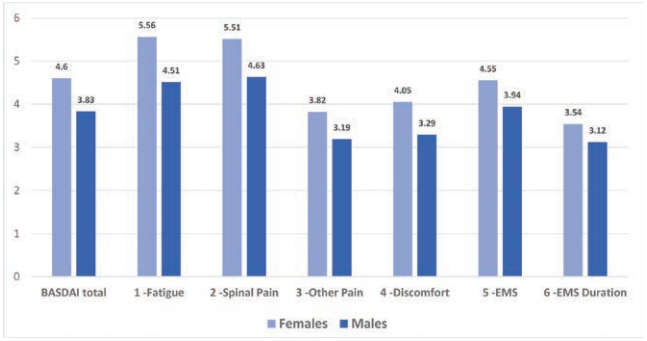
* Based on local reading axSpA, axial Spondyloarthritis; HLA-B27, Human Leucocyte Antigen B27; LoC, Level of Confidence regarding diagnosis; MRI, Magnetic Resonance Imaging; SpA, Spondyloarthritis.

At two-year follow-up the LoC in the group with an axSpA diagnosis at 2 years only was much lower than in the other two groups. In the group that only had an axSpA diagnosis at baseline, the LoC regarding the diagnosis increased most compared to baseline: physicians were more certain of the diagnosis no axSpA at two-year follow-up than they were of the diagnosis axSpA at baseline.
The number of patients with sacroiliitis on radiographs and MRI was much higher in the group with a consistent diagnosis of axSpA. Although the percentage of patients with sacroiliitis on MRI increased in the group with a diagnosis of axSpA at two-year follow-up only, this was still much lower (21%) compared to the patients with a consistent diagnosis (81%). This was in line with a low LoC in this group.
Conclusion: In a cohort of patients with CBP suspected of axSpA the diagnostic consistency rate was high. Interestingly, in the group that only had a diagnosis axSpA at baseline, rheumatologists were more certain about the absence of axSpA at two years than the presence of axSpA at baseline.
REFERENCES:
[1] Rudwaleit et al. (2004). How to diagnose axial spondyloarthritis early. *Ann Rheum Dis*
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.349

OP0051 LOOKING BEYOND BASDAI TOTAL SCORES: ANALYSIS OF THE BASDAI ON THE BASIS OF SEX

S. Maguire[1,2], P. Gallagher[3], F. B. O'shea[1,2]. [1]*St James' Hospital, Department of Rheumatology, Dublin, Ireland*; [2]*Trinity College Dublin, School of Medicine, Dublin, Ireland*; [3]*St Vincent's Hospital, Department of Rheumatology, Dublin, Ireland*

Background: Females with axial spondyloarthropathy (axSpA) average scores on patient reported outcomes (PROs) than males. However, this does not necessarily correlate to worse clinical findings. The Ankylosing Spondylitis Registry of Ireland (ARSI) is a national registry on patients with axSpA in Ireland and a source of epidemiological data.
Objectives: The purpose of this study was to compare the scores of each sex across the individual components of the BASDAI to understand why females report worse scores than males.
Methods: Analysis of the ASRI was preformed using IBM SPSS version 26. Patients were analyzed on the basis of gender. Comparison of baseline characteristics and mean BASMI, BASFI, HAQ and ASQoL were tested for significance using an independent two tailed t-test and a Mann Whitney U test. Mean total BASDAI score and mean score for each component of the BASDAI were compared and tested for significance with the same statistical tests. A chi-squared test for independence was used to determine significance in variation of HLA-B27 status and radiographic findings.
Results: A total of 857 patients were included in the analysis. Patient population was 24.9% (213) female and 75.1% (644) male with a mean age of 45.9 years and mean disease duration of 19.4 years (means: BASDAI 4.02, BASMI 4, BASFI 3.67, HAQ 0.53, ASQoL 6.48). Females had worse BASDAI(4.6 vs 3.83, p<0.01), HAQ(0.6 vs 0.51, p=0.03) and ASQoL scores (7.62 vs 6.12, p<0.01) than males. BASFI scores were worse in females which did not reach significance (3.89 vs 3.63, p=0.26). However, females had significantly better BASMI scores than males (3.51 vs 4.16, p<0.01). Within the BASDAI, females scored significantly worse than males across all components (Fatigue: 5.56 vs 4.51, p<0.01; Spinal pain: 5.51 vs 4.63, p<0.01; Other pain: 3.82 vs 3.19, p=0.01; Discomfort: 4.05 vs 3.29, p<0.01; EMS: 4.55 vs 3.94, p=0.01), however duration of EMS did not reach significance (3.54 vs 3.12, p=0.07)(graph 1). Within the BASDAI, females recorded highest mean scores for fatigue (5.56), while males recorded highest mean scores for spinal pain(4.63). Lowest mean scores for both genders was for EMS duration (3.54 vs 3.12). Ranking of the BASDAI components by mean scores show similarity in the ranking of discomfort, EMS, other pain and EMS duration(Table 1).



Graph 1. Breakdown of BASDAI scores in Females compared to Males

Table 1. Ranking in order of severity by mean score

	Females	Males
1 -most severe	Fatigue	Spinal pain
2	Spinal Pain	Fatigue
3	EMS	EMS
4	Discomfort	Discomfort
5	Other pain	Other pain
6 -least severe	EMS duration	EMS duration

Conclusion: AxSpA females have consistently worse PROs but have better spinal mobility than males. Despite females recording worse BASDAI scores than males, the pattern of active disease is similar in 4 of the 6 components of the BASDAI. However, fatigue is the most problematic symptom in females with active axSpA while spinal pain is the most problematic symptom for males. This variation by gender should be kept in consideration when evaluating a patient with suspected active axSpA.
References:
Disclosure of Interests: Sinead Maguire Grant/research support from: Recipient of the Gilead Inflammation Fellowship, Phil Gallagher: None declared, Finbar Barry O'Shea: None declared
DOI: 10.1136/annrheumdis-2021-eular.633

OP0052 FACTORS ASSOCIATED WITH REMISSION AT 5 YEARS OF FOLLOW-UP IN EARLY ONSET AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE DESIR COHORT

L. Pina Vegas[1,2], E. Sbidian[1,3,4], D. Wendling[5,6], P. Goupille[7], S. Ferkal[3,4], P. Le Corvoisier[4,8], B. Ghaleb[9], A. Luciani[10], P. Claudepierre[1,2]. [1]*Université Paris Est Créteil, EpiDermE, Créteil, France*; [2]*Hôpital Henri Mondor, Rhumatologie, Créteil, France*; [3]*Hôpital Henri Mondor, Dermatologie, Créteil, France*; [4]*Hôpital Henri Mondor, INSERM, Centre d'Investigation Clinique 1430, Créteil, France*; [5]*CHRU de Besançon, Rhumatologie, Besançon, France*; [6]*Université de Franche-Comté, EA 4266 « Agents pathogènes et inflammation », Besançon, France*; [7]*CHU de Tours, Rhumatologie, Tours, France*; [8]*Université Paris Est Créteil, Ecole Nationale*

Vétérinaire d'Alfort, Inserm, U955-IMRB, Équipe 03, Créteil, France; [9]*Université Paris Est Créteil, INSERM, U955 équipe 03, Créteil, France*; [10]*Université Paris Est Créteil, INSERM, U955 équipe 18, Créteil, France*

Background: The disease course of axial SpA (axSpA) is highly variable and can be characterized by ongoing axial inflammation and radiographic progression associated with restricted mobility of the spine, reduced function and disability leading to impairment in quality of life. Control of disease activity is a primary aim in axSpA management. To assess disease activity the Ankylosing Spondylitis Disease Activity Score-C-reactive protein (ASDAS-CRP) is often considered as a reference tool. The data on remission are spare in axSpA and the identification of long-term remission factors, enabling the patient's management to be adapted, seems necessary but remains unclear.
Objectives: To evaluate the proportion of patients in remission according to ASDAS-CRP at 5 years of follow-up, to describe their characteristics in comparison with patients with active disease at that time, and to identify baseline factors associated with remission at 5 years of follow-up.
Methods: We included all patients from the DESIR (*Devenir des Spondylarthropathies Indifférenciées Récentes*) cohort with available data on ASDAS-CRP at 5-year follow-up and TNFα inhibitors exposure. Patients in remission, defined as an ASDAS-CRP<1.3, and with active disease were compared according to their main demographic, clinical, biological and radiological characteristics. A logistic model stratified on TNFα inhibitors exposure was used in the main analysis. Sensitivity analyses among patients with axSpA diagnosis confirmed by rheumatologist at 5-years were performed.
Results: A total of 614 patients were followed in the DESIR cohort at M60. After excluding those with missing data on ASDAS score (n= 163) and TNFα inhibitors exposure (n= 2), analyzed patients were 449 (73%). Excluded patients had similar baseline characteristics to those included in the analysis. Among patients unexposed to TNFα inhibitors (n=247), 77 (31%) were in remission (37,8±8,3 years; 55% men, 58% NSAID users), 170 (69%) weren't (39,8±8,6 years; 42% men, 81% NSAID users). Among exposed patients (n=202), 34 (17%) were in remission (36,1±8,1 years; 71% men, 29% NSAID users), 168 (83%) weren't (39,5±9,0 years; 41% men, 63% NSAID users) (Figure 1). Overall, patients in remission were more frequently men, HLA-B27+, with high education and lower BMI at 5-year of follow-up. The baseline factors associated with remission at 5 years of follow-up from the multivariate analysis are presented in Table 1.

Table 1. Baseline factors associated with remission at 5-year follow-up (multivariate analysis)

	Baseline factors positively associated with 5-year remission	Baseline factors negatively associated with 5-year remission
Unexposed to TNFα inhibitors	• Past history of **arthritis** (OR_a=2.1, 95%CI 1.2-5.3)	• Low **BASDAI** (OR_a=0.9, 95%CI 0.8-0.9)
Exposed to TNFα inhibitors	• High **education** (OR_a=2.9, 95%CI 1.6-5.1)	• Low **BASDAI** (OR_a=0.9, 95%CI 0.9-0.9) • Low **BMI** (OR_a=0.8, 95%CI 0.7-0.9) • Low **enthesitic index** (OR_a=0.8, IC95% 0.7-0.9)

Conclusion: The overall remission rate at 5 years was 25%, 31% among patients unexposed to TNFα inhibitors and 17% among those exposed. This study reveals the difficulty in achieving 5-year remission in recent axSpA, especially in the most active forms at baseline; socio-educational factors and overweight also appear to be related.
Acknowledgements: L Pina Vegas received a Master 2 grant from the French Society of Rheumatology (Bourse Master 2ème Année 2019)
Disclosure of Interests: Laura Pina Vegas: None declared, Emilie Sbidian: None declared, Daniel Wendling: None declared, Philippe Goupille: None declared, Salah Ferkal: None declared, Philippe Le Corvoisier: None declared, Bijan Ghaleh: None declared, Alain Luciani: None declared, Pascal Claudepierre Speakers bureau: Abbvie, Janssen, Lilly, MSD, Novartis, Pfizer, Consultant of: Abbvie, Pfizer, Roche-Chugai, Bristol-Myers Squibb, MSD, UCB, Novartis, Janssen, Lilly, Celgene (consulting fees, less than 10,000 $ each)., Employee of: Roche Chugai, Sanofi Aventis, Celgene, Pfizer, MSD, Novartis and BMS (investigator).
DOI: 10.1136/annrheumdis-2021-eular.305

OP0053

IMPACT OF CORRECTING CRP THRESHOLD ACCORDING TO BMI ON DIAGNOSIS, DISEASE ACTIVITY, INDICATION OF BIOLOGICAL TREATMENT AND PREDICTION OF THERAPEUTIC RESPONSE, IN PATIENTS SUSPECTED OF AXIAL SPONDYLOARTHRITIS. RESULTS FROM DESIR COHORT

O. Facorat[1], J. Morel[2], B. Combe[2], P. Richette[3], C. Lukas[2]. [1]*University Hospital of Martinique, Rheumatology, Fort de France, France*; [2]*University Hospital of Montpellier, Rheumatology, Montpellier, France*; [3]*Lariboisière Hospital, Rheumatology, Paris, France*

Background: Acute phase reactants are crucial parameters to consider for management of chronic inflammatory back pain (IBP) patients suspect of axial spondyloarthritis (ax-SpA). Indeed, C-reactive protein (CRP) is part of ASAS classification criteria for SpA, impacts on assessment of disease activity by ASDAS-CRP score, and should be elevated when a bDMARD is discussed in patients without radiological sacroiliac lesions. Moreover, elevated CRP is regarded predictive of favorable therapeutic response. Obesity in otherwise healthy people is associated with high CRP values. An adjusted definition of normal CRP threshold based on gender and BMI has been proposed.
Objectives: The aim of this study was to assess whether correcting CRP threshold with patient's BMI would change classification according to ASAS criteria for ax-SpA, presence of clinically relevant activity according to ASDAS-CRP, indication for TNF inhibitor (TNFi) and, as primary endpoint, improve prediction of therapeutic response to first TNFi.
Methods: The study was conducted in DESIR cohort, which included 708 patients with early IBP suspect of ax-SpA. We included all patients with available data on BMI and CRP. High CRP level was defined either according to usual threshold (5 mg/L) or to the formula using BMI for adjustment. With this formula, CRP could be considered "normal" or due to obesity if: ≤ 1 + (BMI-25)/25 for men and ≤ 1 + (BMI-25)/12.5 for women (with CRP in mg/dL). We reported distribution of CRP levels in patients with high level according to usual threshold but below BMI adjusted threshold, as it is potentially suggestive of false-positive CRP due to overweight/obesity. Among them, we identified those who had no objective sign of disease activity (defined as arthritis, dactylitis, active uveitis or inflammatory bowel disease). To evaluate the impact on classification/diagnosis, we examined HLAB27-positive patients with only 2 ASAS criteria, including high CRP (the second being IBP, since it was mandatory for inclusion in DESIR cohort). Then, we calculated ASDAS-CRP score. We presented proportions of patients with ASDAS-high or very high disease activity but high CRP level possibly due to BMI only, and among those, the number concerned by a change of disease activity level when adjusting ASDAS-CRP score with minimal value for CRP (2mg/l). Among patients treated by TNFi during first 24-month follow-up, we excluded those with sacro-iliitis, and studied in others, CRP levels at last visit before treatment initiation using both thresholds. We compared proportion of ASAS40 responders using logistic regression analysis, with abnormal CRP defined after correction for BMI in patients without any sign of activity, beside other classical predictive factor of therapeutic response (age, gender, sacro-iliitis, HLAB27, psoriasis, arthritis, smoking).
Results: Data were available for 634 patients. 205 had a high CRP level using usual threshold, of which 73 (35.6%) had a high CRP possibly due to BMI alone as they had no objective sign of disease activity. There were no differences in diagnosis as no patient had as only ASAS criteria: HLAB27 associated with high CRP and IBP. ASDAS-CRP score could be calculated in 626 patients. By correcting ASDAS score for patients with high CRP possibly due to BMI, 95.3% remained with same activity level (kappa for the ASDAS levels was 0.93). For impact of CRP on indication of bDMARD, 178 patients were treated by TNFi during first 24 months of follow-up: 61% of patients had an indication of TNFi according to EMA, with usual CRP threshold, and 56% with the adjusted one. Regarding response to TNFi, there were no association between any of the 2 CRP thresholds and ASAS40 response. Only sacro-iliitis on MRI was associated with ASAS40 response.
Conclusion: Adjustment of CRP threshold according to BMI has a very limited impact on diagnosis, evaluation of disease activity of SpA, indication of TNFi initiation and prediction of TNFi response.
Disclosure of Interests: Odile Facorat: None declared, Jacques Morel Speakers bureau: Abbvie, Biogen, BMS, Fresenius Kabi, Lilly, Mylan, Novartis, Pfizer, Sanofi, Consultant of: Abbvie, BMS, Boerhinger Ingelheim, Galpaagos, GSK, Lilly, Novartis, Sanofi, Grant/research support from: Biogen, BMS, Lilly, Novartis, Pfizer, Sanofi, Servier, Bernard Combe Speakers bureau: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Consultant of: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Novartis, Pfizer, and Roche-Chugai, Pascal Richette Consultant of: AbbVie, Amgen, Biogen, BMS, Celgene, Janssen-Cilag, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, SanofiAventis, UCB, Cédric Lukas Speakers bureau: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Consultant of: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Grant/research support from: Pfizer, Novartis and Roche-Chugai
DOI: 10.1136/annrheumdis-2021-eular.609

Vasculitis - I

OP0054

NEW ROLE FOR PROTEINASE 3 IN IL-16 BIOACTIVITY CONTROL IN GRANULOMATOSIS WITH POLYANGIITIS

A. Kerstein-Staehle[1], C. Alarcin[1], J. Luo[1], G. Riemekasten[1], P. Lamprecht[1], A. Müller[1]. [1]*University of Luebeck, Department of Rheumatology and Clinical Immunology, Lübeck, Germany*

Background: The immunomodulatory cytokine IL-16 is increased in several inflammatory and autoimmune diseases[1]. IL-16 recruits and activates CD4+ immune cells such as T cells, dendritic cells, or monocytes. IL-16 is produced by various immune and non-immune cells, but synthesis and storage of IL-16 is regulated differentially depending on the cell type and stimulation. For its biological activity, IL-16 cleavage by caspase-3 is required[1]. Necrotizing granulomatous inflammation is a hallmark of granulomatosis with polyangiitis (GPA) with neutrophil dysregulation as a central driver of chronic inflammation and autoimmunity[2]. Earlier studies showed a correlation between increased serum IL-16 and disease parameters in AAV, including GPA[3], but functional evidence for a direct link between IL-16 and neutrophils in granulomatous inflammation is missing so far.
Objectives: In this study we aim to identify a functional link between increased IL-16, neutrophils, and the autoantigen proteinase 3 (PR3) with regard to chronic inflammation and autoimmunity in GPA.
Methods: IL-16 was measured in sera of GPA patients (n = 40) and healthy controls (HC, n = 50) by ELISA and correlated with clinical features, such as disease activity (BVAS), creatinine, GFR, VDI and PR3-ANCA status. IL-16 protein expression was analyzed in peripheral blood mononuclear cells (PBMC) and polymorphonuclear cells (PMN) from GPA patients and HC (n = 5, each) by SDS-PAGE and western blot. Binding affinity of recombinant pro-IL-16 to native human PR3 was assessed by microscale thermophoresis. Cleavage of pro-IL-16 by active human PR3 was performed at various time points at 37°C. Cleavage products were analyzed by SDS-PAGE and western blot.
Results: Circulating IL-16 was significantly increased in GPA patients compared to HC. Elevated IL-16 positively correlated with BVAS, creatinine, VDI and PR3-ANCA status and negatively correlated with GFR. In PMBC and PMN from GPA and HC we identified different expression patters of precursor and active forms of IL-16. In healthy PBMC we found high amounts of precursor (80kD), pro-IL-16 (55kD) and active IL-16 (17kD). In contrast, PBMC from GPA patients had lower amounts of pro-IL-16 and no active IL-16, indicating activation and secretion of IL-16 due to inflammatory stimulation, as shown earlier[5]. In GPA PMN we detected no precursor IL-16, but pro-IL-16 and its active form, in contrast to very low amounts of all IL-16 forms in healthy PMN. Processing and release of IL-16 in neutrophils has been linked to apoptosis and secondary necrosis[5]. By interaction studies we demonstrated direct binding of pro-IL-16 to PR3 with a Kd of 10 nM. In a subsequent cleavage assay we confirmed IL-16 processing by PR3 in a time-dependent manner.
Conclusion: Correlation of serum IL-16 with clinical features of GPA suggests that IL-16 is associated with markers of disease activity, tissue damage and autoreactivity. We showed that PBMC and PMN represent a source of IL-16 in GPA. By the identification of PR3 as an additional IL-16-activating enzyme we could demonstrate a potential link between excessive PR3 expression, cell death and IL-16-dependent mechanisms, contributing to chronic granulomatous inflammation and autoimmunity in GPA.

REFERENCES:

[1] Glass, W. G. et al. Not-so-sweet sixteen: The role of IL-16 in infectious and immune-mediated inflammatory diseases. J. Interf. Cytokine Res. 26, 511–520 (2006).
[2] Millet, A. et al. Proteinase 3 on apoptotic cells disrupts immune silencing in autoimmune vasculitis. J. Clin. Invest. 125, 4107–4121 (2015).
[3] Yoon, T. et al. Serum interleukin-16 significantly correlates with the Vasculitis Damage Index in antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Res. Ther. 22, 1–6 (2020).
[4] Elssner, A. et al. IL-16 Is Constitutively Present in Peripheral Blood Monocytes and Spontaneously Released During Apoptosis. J. Immunol. 172, 7721–7725 (2004).
[5] Roth, S. et al. Secondary necrotic neutrophils release interleukin-16C and macrophage migration inhibitory factor from stores in the cytosol. Cell Death Discov. 1, 15056 (2015).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1314

OP0055 ULTRASOUND HALO SIGN AS A POTENTIAL MONITORING TOOL FOR PATIENTS WITH GIANT CELL ARTERITIS: A PROSPECTIVE ANALYSIS

C. Ponte[1,2], S. Monti[3,4], C. A. Scirè[5,6], P. Delvino[3,4], N. Khmelinskii[1,2], A. Milanesi[3], V. Teixeira[1,7], F. Brandolino[3], F. M. Diamantino Saraiva[1], C. Montecucco[3], J. E. Fonseca[1,2], W. A. Schmidt[8], R. Luqmani[9]. *[1]Hospital de Santa Maria - Centro Hospitalar Universitário Lisboa Norte, Department of Rheumatology, Lisboa, Portugal*; *[2]Instituto de Medicina Molecular (IMM), Reumatology Research Unit, Lisboa, Portugal*; *[3]Fondazione I.R.C.C.S. Policlinico San Matteo, Department of Rheumatology, Pavia, Italy*; *[4]University of Pavia, PhD in Experimental Medicine, Pavia, Italy*; *[5]Italian Society for Rheumatology, Epidemiology Research Unit, Milan, Italy*; *[6]University of Ferrara, Rheumatology Unit, Department of Medical Sciences, Ferrara, Italy*; *[7]Centro Hospitalar Universitário do Algarve, Department of Rheumatology, Faro, Portugal*; *[8]Immanuel Hospital Berlin, Medical Centre for Rheumatology Berlin-Buch, Berlin, Germany*; *[9]University of Oxford, Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*

Background: Ultrasound of the temporal ± axillary arteries showing a non-compressible halo sign is recommended for diagnosing patients with giant cell arteritis (GCA); however, its value for monitoring disease activity is still poorly understood.
Objectives: To assess the sensitivity to change of ultrasound halo features and their association with disease activity and glucocorticoid (GC) treatment in patients with newly diagnosed GCA.
Methods: Two centre prospective study of new patients with ultrasound confirmed-GCA who underwent serial ultrasound assessments of the temporal (TA) and axillary (AX) arteries at fixed time-points. The number of arterial segments with halo and the maximum halo intima-media thickness (IMT) per segment was recorded at each visit. Only time-points in which >80% of patients were assessed were considered for analysis. Sensitivity to change of the halo sign was calculated as standardised mean difference (SMD) for each time-point separately. Correlation between ultrasound findings and erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Birmingham Vasculitis Activity Score (BVAS), and GC treatment was performed using Spearman's correlation coefficient. Logistic regression was used to determine the probability of being in remission for each unit increase (standardised) of the halo feature of interest. Remission was defined as the absence of relapse with a prednisolone dose <30 mg/day, and relapse as the recurrence of GCA-related symptoms or rise of CRP/ESR values not otherwise explained and requiring GC increase. Halo features at disease onset and first relapse were compared using Wilcoxon test.
Results: A total of 49 patients (73.5% females) with a mean age of 78.2 ± 7.4 years at baseline were assessed at 354 visits. TA involvement was reported in 47 (95.9%) patients and AX involvement in 11 (22.4%); 220 arterial segments with halo were recorded (201 TA, 19 AX). Halo sensitivity to change was calculated for weeks 1, 3, 6, 12 and 24, and showed a significant SMD between all time-points and baseline for the TA halo features, but only after week 6 for the AX halo features (Table and Figure). The number of TA segments with halo, sum of TA halo IMT and maximum TA halo IMT showed a significant correlation with ESR (0.41; 0.44; 0.48), CRP (0.34; 0.39; 0.41), BVAS (0.29; 0.36; 0.35) and GC cumulative dose (-0.34; -0.37; -0.32). The likelihood of achieving disease remission was lower in patients with a higher number of TA segments with halo (OR 0.39, p<0.05) and increased values of sum and maximum TA halo IMT (OR 0.34, p<0.05). By contrast, AX halo features showed no correlation with disease activity, nor any association with attaining clinical remission. During the study period, 32 relapses were observed (mean time for first relapse of 31.8 weeks ± 18.5 days). Halo sign was present in 16/17 (94.1%) cases of first disease relapse, all showing an increased halo IMT (sum and maximum) in relation to the previous ultrasound assessment performed. When compared to disease onset, a lower mean number of segments with halo and mean sum of halo IMT was reported for patients presenting with their first clinical relapse (2.93 ± 1.59 vs. 4.85 ± 1.51, p=0.0012; 2.01 ± 1.13 vs. 4.49 ± 1.95 mm, p=0.0012).

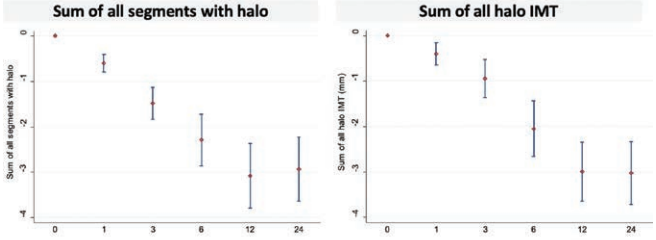
Table 1. SMD of halo features between baseline and different time-points

	Week 1	Week 3	Week 6	Week 12	Week 24
N of arterial segments					
Sum of all segments with halo (n=49)	**-0.51**	**-0.78**	**-1.13**	**-1.69**	**-1.52**
Sum of TA segments with halo (n=47)	**-0.49**	**-0.78**	**-1.18**	**-1.87**	**-1.69**
Sum of AX segments with halo (n=11)	-0.35	-	-0.62	-0.73	-0.91
Halo thickness (mm)					
Sum of all halo IMT (n=49)	**-0.98**	**-1.44**	**-1.37**	**-1.60**	**-1.48**
Sum of TA halo IMT (n=47)	**-1.01**	**-1.55**	**-1.54**	**-1.81**	**-1.69**
Sum of AX halo IMT (n=11)	-0.15	-0.45	**-0.81**	-0.84	-0.98
Max. TA halo IMT (n=47)	**-1.07**	**-1.32**	**-1.47**	**-1.91**	**-2.19**
Max. AX halo IMT (n=11)	-0.04	-0.29	**-0.94**	**-1.13**	-1.01

In bold p<0.05; n=n at baseline

Conclusion: Ultrasound is a reliable imaging tool to assess disease activity and response to treatment in patients with GCA. Future clinical trials in GCA should evaluate direct treatment effect on halo features as an outcome measure of interest.

Figure: Mean variation (not standardised) of halo features at different time-points



Eight arterial segments were evaluated at each time-point: bilateral common superficial temporal arteries, parietal and frontal branches, and bilateral axillary arteries

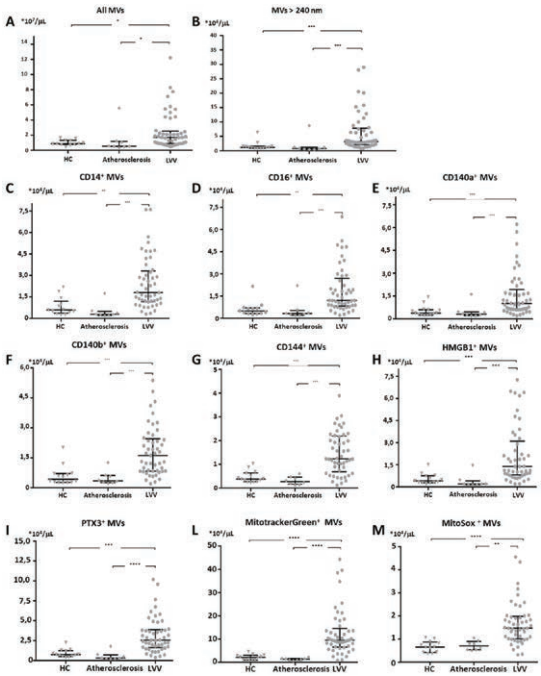
Acknowledgements: The first two authors contributed equally to this work
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1273

OP0056

PLASMA MICROVESICLES AS LIQUID BIOPSIES OF THE ARTERIAL WALL IN LARGE VESSEL VASCULITIS

E. Tombetti[1], K. H. Chun[2], C. Iannone[3], E. M. Baldissera[4], J. Mason[5], A. Manfredi[6]. [1]*Milan University, Biomedical and Clinical Sciences Luigi Sacco, Milan, Italy*; [2]*Vita-Salute San Raffaele University, Milan, Italy*; [3]*Vita-Salute San Raffaele University, Autoimmunity and Vascular Inflammation, Milan, Italy*; [4]*Ospedale San Raffaele, UniRAR, Milan, Italy*; [5]*Hammersmith Hospital, Vascular Sciences and Rheumatology - NHLI, London, United Kingdom*; [6]*Vita-Salute San Raffaele University, Autoimmunity and Vascular Inflammation; UniRAR, Milan, Italy*

Background: Large-vessel vasculitides comprise Takayasu arteritis (TA)and giant cell arteritis (GCA). Arterial stenosis and dilatation directly affect prognosis but the mechanism(s) underlying remodeling of the vessel wall have not been identified. Microvesicles (MVs) are membrane-enclosed extracellular vesicles released upon cellular activation and stress and as a consequence of environmental inflammation. MVs maintain features and constituents of their parental cells. They have been proposed to serve as potential liquid biopsies in oncology.
Objectives: To verify whether arterial wall derived-MVs are recognizable in the blood of TA patients and express bioactive molecules potentially involved in arterial injury, inflammation and remodeling.
Methods: Platelet was obtained from 112 LVV pts (73 TA, 39 GCA), 42 age and age- and sex-matched healthy controls (HC) and 30 pts with severe carotid atherosclerosis requiring vascular surgery. Plasma flow cytometry was performed with anti-CD14, CD16, anti-CD144 (VE-cadherin, an endothelial marker), anti-CD140a/b (PDGF receptor A/B a vascular stromal marker), anti-HMGB1, anti-PTX3, mitotracker green (that identifies mithochondrial moieties) and mitosox (that revels mitochondrial reactive oxygen species). MVs were identified by physical parameters using Gigamix beads. Medium- to large-sized MVs were defined as MVs with >240nm-eq diameter.
Results: Preliminary results are available for 49 LVV (42 TA, 7 GCA), 8 severe carotidatherosclerosis and 14 age- and sex-matched HC. As compared to HC or CA, LVV plasma contains a higher number of MVs and in particular of medium- to large- sized MVs ($p<0.001$ for all comparisons) (Figure, panels A-B). Next, we evaluated the MVs surface expression of markers of leukocytic, endothelial and stromal/vascular stromal lineages. Total counts of CD14+, CD16+, CD66b+, CD140a+, CD140b+, CD144+ MVs were increased in LVV plasma with very high level of significance (Figure, panels C-G) while higher percentage of CD16+ and CD140a+ medium-to large-sized MVs was found in atherosclerosis. Expression of molecules involved in inflammation or repair, PTX3 or HMGB1 mitochondrial antigens and mitochondrial ROS all were consistently higher in LVV (Figure, panels H-M).
Conclusion: MVs, including those expressing arterial stromal biomarkers, are increased in LVV plasma, suggesting a communication between the vessel wall and peripheral blood. MV express signals that may in turn contribute to persisting vascular inflammation in large vessel vascultis Further analysis is required to dissect their potential use as disease biomarkers



REFERENCES:
[1] van Niel G et al, Nat Rev Mol Cell Biol. 2018
[2] Mason JC. Nat Rev Rheumatol. 2010
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4300

OP0057

A PERSONALISED RITUXIMAB RETREATMENT APPROACH BASED ON CLINICAL AND B-CELL BIOMARKERS IN ANCA-ASSOCIATED VASCULITIS

J. Arnold[1], E. Vital[1], S. Dass[1], A. Aslam[1], A. Rawstron[2], S. Savic[1], P. Emery[1], M. Y. MD Yusof[1]. [1]*Chapel Allerton Hospital, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [2]*St James's University Hospital, Haematological Malignancy Diagnostic Service, Leeds, United Kingdom*

Background: Time-to-relapse after rituximab for ANCA-associated vasculitis (AAV) is variable and optimal retreatment strategy has been unclear. We previously showed that repopulation of naïve B-cells at 6 months predicts sustained response [1].
Objectives: In AAV following rituximab induction, to evaluate clinical and B-cell predictors of relapse in order to develop a retreatment algorithm.
Methods: An observational study was conducted in 60 rituximab-treated AAV patients followed for over 10 years. Complete response (CR) was defined as Birmingham Vasculitis Activity Score v3.0 = 0. Retreatment was given on clinical relapse, defined as new features or worsening of persistent disease (not by biomarker status). Peripheral B-cell subsets were measured using highly sensitive flow cytometry. Predictors were tested using multivariable Cox-Regression.
Results: Median times-to-retreatment for rituximab cycles 1-5 were 87, 71, 65, 59 and 86 weeks. Over 417 patient-years follow-up, 137 relapses occurred in 50 patients; 16 (in 14 patients) were major (renal=7, neurological=4, ENT=3 and respiratory=2). The major-relapse rate was 3.8/100 patient-years. In multivariable analysis, concomitant immunosuppressant [HR 0.48 (95% CI 0.24–0.94)], achieving CR [0.24 (0.12–0.50)] and naïve B-cell repopulation at 6 months [0.43 (0.22–0.84)] were associated with longer time-to-relapse. Higher baseline memory B-cells [1.01 (1.00–1.02)] were associated with a shorter time-to-relapse. AUROC for prediction of time-to-relapse was greater if guided by naïve B-cell repopulation than if ANCA and/or CD19+ return at 6 months had been used, 0.82 and 0.52 respectively.
Conclusion: These data suggest that all patients should receive concomitant oral immunosuppressant. Those with incomplete response or with absent naïve B-cells should be retreated at 6 months. Patients with complete response and naïve repopulation at 6 months should not receive fixed retreatment. This algorithm could reduce hypogammaglobulinaemia due to unnecessary retreatment.

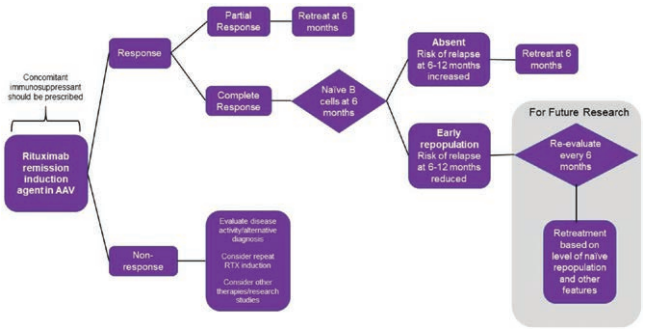


Figure 1. A personalised retreatment algorithm for rituximab in ANCA-associated vasculitis

REFERENCES:
[1] Md Yusof et al. Annals of rheumatic diseases (2015) PMID: 25854586.
Disclosure of Interests: Jack Arnold: None declared, Edward Vital Speakers bureau: Roche, GSK and AstraZeneca, Consultant of: Roche, GSK and AstraZeneca, Grant/research support from: Roche, GSK and AstraZeneca, Shouvik Dass Speakers bureau: Roche and GSK, Aamir Aslam: None declared, Andrew Rawstron: None declared, Sinisa Savic: None declared, Paul Emery Speakers bureau: BMS, Abbott, Pfizer, MSD, Novartis, Roche and UCB, Consultant of: BMS, Abbott, Pfizer, MSD, Novartis, Roche and UCB, Grant/research support from: Abbott, BMS, Pfizer, MSD and Roche., Md Yuzaiful Md Yusof: None declared
DOI: 10.1136/annrheumdis-2021-eular.2193

OP0058

CARDIOVASCULAR AND CEREBROVASCULAR RISK IN PATIENTS WITH SMALL VESSEL VASCULITIDES: A COMPARATIVE ANALYSIS BETWEEN AORTIC STIFFNESS, CAROTID SONOGRAPHY AND SCORE

K. Triantafyllias[1], L. E. Thiele[2], M. De Blasi[1], A. Schwarting[2,3]. [1]*ACURA Clinics, Rheumatology, Bad Kreuznach, Germany*; [2]*Johannes Gutenberg University Medical Center, Internal Medicine I, Department of Rheumatology and Clinical Immunology, Mainz, Germany*; [3]*ACURA Clinics, Rheumatology, 55543, Germany*

Background: Cardiovascular (CV) and cerebrovascular (CVB) risk have not been adequately examined in the setting of patients with small vessel vasculitides. In particular, data on CV/CVB surogate markers are scarce and the diagnostic value of traditional CV risk scores, such as the Systematic COronary Risk Evaluation (SCORE) and ist EULAR modified version (mSCORE) is unknown.
Objectives: Aims of this study were to examine gold standard surrogates of CV risk and subclinical atherosclerosis (1), as well as novel duplex-sonographic markers of CVB risk in a cohort of patients with small vessel vasculitides. Moreover, we sought to evaluate for the first time the diagnostic value of SCORE and mSCORE in identifying patients at high CV and CVB risk.
Methods: SCORE/mSCORE and the gold standard marker of aortic stiffness (carotid-femoral pulse wave velocity; cfPWV) were examined in patients with small vessel vasculitides and healthy controls across 3 Rheumatology Centers. Moreover, sonography of the common- (CCA), internal- (ICA) and external- (ECA) carotid arteries was performed in subsets of both groups, evaluating carotid intima-media-thickness (cIMT), plaque presence and duplex-sonographic indices of CBV risk, such as the resistance- (RI) and pulsatility-index (PI). Disease characteristics, clinical and serological activity markers, as well as traditional CV risk factors were also documented.
Results: We recruited 46 patients with small vessel vasculitides [granulomatosis with polyangiitis (n=33), eosinophilic granulomatosis with polyangiitis (n=6), microscopic polyangiitis (n=4), cryoglobulinemic vasculitis (n=1), urticaria vasculitis (n=2): 76.1% female, median age 61.5 years (52-72.25, IQR)] and 105 healthy controls [76.1% female, median age 61.5 years (52-72.25, IQR)]. cfPWV was significantly higher in the patient group compared to the control group, even after statistical corrections for confounding factors (i.e. age, gender: different in the two groups) (8.4 m/s vs. 6.8 m/s; p_{adj}<0.001). Moreover, carotid sonography revealed higher CVB surrogates in the patient subgroup, compared to controls.
According to SCORE and (EULAR)-mSCORE, 0.9% and 15.8% of the patients had high CV risk (defined as SCORE/mSCORE >5), respectively. However, cfPWV revealed an increased CV risk in 28.2% of the patients. Moreover, carotid sonography showed signs of subclinical carotid arteriosclerosis in 50% (plaques) and 71.7% (cIMT >0.9 mm) of the patients, respectively.
Conclusion: Herein, we could show that patients with small vessel vasculitides had higher aortic stiffness and subclinical carotid atherosclerosis, compared to controls and could thus have higher CV and CVB risk. Moreover, we were able to demonstrate for the first time that SCORE/mSCORE performed poorly in identifying patients at high CV risk and carotid atherosclerosis compared to cfPWV and carotid sonography respectively. Thus, cfPWV and carotid sonography could improve CV and CBV screening in patients with small vessel vasculitides.

Table 1. Descriptive characteristics.

	Controls	Patients	Significance
	(n=105)	*(n=46)*	*(p)*
cfPWV† (m/s)	6.80 (6.05-7.5)	8.40 (7.26-10.66)	<0.001*
Age† *(years)*	50 (39.50-56.5)	61.50 (52-72.25)	<0.001*
Gender *(female)*	95 (90.5%)	35 (76.1%)	0.019*
Nicotin *(smokers)*	21 (20%)	5 (11.1%)	0.190
Antihypertensive drugs	18 (17.1%)	27 (65.9%)	<0.001*
BMI†	23.73 (21.1-27.1)	25.14 (22.81-28.70)	0.074
Mean art. pressure¶	93.45±10.68	96.19±10.68	0.150
ESR† *(mm/h)*	-	20.00 (11– 41.5)	-
ANCA	-	25 (54.3%)	-
Creatinine†	0.77 (0.72-0.81)	0.94 (0.8-1.31)	<0.001*
Cholesterol¶ *(mg/dL)*	-	216.88±40.16	-
Prednisolone† *(mg)*	-	5.63 (1.75-16.38)	-
Lung involvement		17 (37%)	-
Kidney involvement		17 (37%)	-
Ear-nose-throat (ENT)		16 (34.8%)	-

†median (IQR): Mann Whitney test¶ mean±standard deviation: t test*p<0.05

REFERENCES:

[1] Vlachopoulos C et al., Prediction of Cardiovascular Events and All-Cause Mortality With Arterial Stiffness: A Systematic Review and Meta-Analysis. *J Am Coll Cardiol 2010* 30;55(13):1318-27

Disclosure of Interests: Konstantinos Triantafyllias Speakers bureau: Pfizer, Novartis, Janssen, Chugai, Leif-Erik Thiele: None declared, Michele De Blasi: None declared, Andreas Schwarting: None declared
DOI: 10.1136/annrheumdis-2021-eular.3603

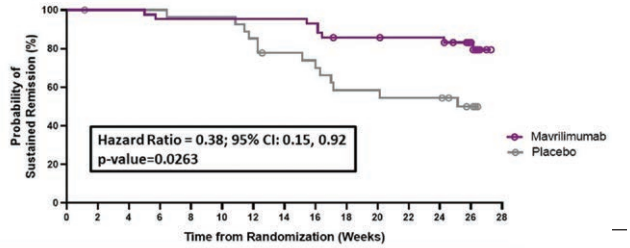
OP0059

MAVRILIMUMAB (ANTI GM-CSF RECEPTOR A MONOCLONAL ANTIBODY) REDUCES RISK OF FLARE AND INCREASES SUSTAINED REMISSION IN A PHASE 2 TRIAL OF PATIENTS WITH GIANT CELL ARTERITIS

M. C. Cid[1], S. Unizony[2], L. Pupim[3], F. Fang[3], J. Pirrello[4], A. Ren[5], M. Samant[3], T. Zhou[3], J. F. Paolini[3]. [1]*Hospital Clínic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Vasculitis Research Unit, Department of Autoimmune Diseases, Barcelona, Spain*; [2]*Massachusetts General Hospital, Vasculitis and Glomerulonephritis Center, Department of Rheumatology, Allergy and Immunology, Boston, United States of America*; [3]*Kiniksa Pharmaceuticals Corp., Clinical Development, Lexington, United States of America*; [4]*Kiniksa Pharmaceuticals Corp., Business Development, Lexington, United States of America*; [5]*Kiniksa Pharmaceuticals Corp., Clinical Operations, Lexington, United States of America*

Background: T helper (Th)1 and Th17 lymphocytes play a role in the pathogenesis of giant cell arteritis (GCA). Current treatments primarily target the Th17 axis, possibly leaving residual Th1 activity. Granulocyte macrophage colony stimulating factor (GM-CSF), a mediator of Th1 and Th17 cells, is a pathogenic factor in GCA.
Objectives: To evaluate the efficacy and safety of the GM-CSF inhibitor mavrilimumab in patients with GCA.
Methods: Randomized, double-blind, placebo-controlled phase 2 trial enrolling patients with active, biopsy- or imaging-proven new onset (N/O) or relapsing refractory (R/R) GCA. Active disease: GCA symptoms and erythrocyte sedimentation rate (ESR) (>30 mm/hr) and/or C-reactive protein (CRP) (≥1 mg/dL) elevation within 6 weeks from randomization. Corticosteroid-induced remission (resolution of GCA symptoms and CRP <1 mg/dL or ESR <20 mm/hr) was required by baseline. 3:2 randomization to mavrilimumab 150 mg or placebo subcutaneously every 2 weeks and protocol-defined 26-week prednisone taper starting at 20-60 mg/day.
Primary efficacy endpoint: time to first adjudicated flare (ESR ≥30 mm/hr and/or CRP ≥1 mg/dL and GCA symptoms or new/worsening vasculitis on imaging) by Week 26 in all treated patients. Key secondary endpoint: sustained remission through Week 26. Safety up to Week 38 was assessed.
Results: 70 patients (35 N/O, 35 R/R) were enrolled (mavrilimumab [N=42] or placebo [N=28]). Mean (SD) age was 69.7 (7.48) years and 71.4% were female. Flare by Week 26 occurred in 8 (19%) and 13 (46.4%) patients receiving mavrilimumab and placebo, respectively (27.4 percentage points reduction). Median time to flare by Week 26 could not be estimated in the mavrilimumab group due to too few events (Not Estimable) and was 25.1 weeks [95% CI: (16.0, NE)] in the placebo group (HR [95% CI] 0.38 [0.15, 0.92]; p=0.0263) (Figure). Sustained remission at Week 26 occurred in 83.2% of patients receiving mavrilimumab and 49.9% of those receiving placebo (33.4 percentage points increase; p=0.0038). Results were consistent across disease type subgroups (HR for flare: N/O 0.29 [95% CI: 0.06, 1.31; nominal p= 0.0873]; R/R 0.43 [95% CI: 0.14, 1.30]; nominal p=0.1231), although not powered for significance (Table). Adverse events (AEs), mostly mild to moderate, were comparable between groups. There were 5 serious AEs (mavrilimumab 2 [4.8%], placebo 3 [10.7%]), none drug-related. No deaths or vision loss occurred. No adjudicated cases of pulmonary alveolar proteinosis were observed.

Figure 1. Time to Flare by Week 26 after randomization in All Patients.



	Patients at Risk, n														
Week	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28
Mavrilimumab	42	42	42	40	40	40	40	40	39	35	35	34	34	28	0
Placebo	28	27	27	27	26	26	23	20	19	15	15	14	14	10	0

Conclusion: Mavrilimumab was superior to placebo on the primary and secondary efficacy endpoints of time to flare and sustained remission at week 26 in patients with GCA. Mavrilimumab was well tolerated, and no new safety signals were observed.
Disclosure of Interests: Maria C. Cid Speakers bureau: meeting attendance support from Roche and Kiniksa, Paid instructor for: educational from GSK and Vifor, Consultant of: consulting for Janssen, GSK, and Abbvie, Grant/research support from: research grant from Kiniksa, Sebastian Unizony Consultant of: consulting for Janssen and Kiniksa, Grant/research support from: research support from Genentech, Lara Pupim Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals, Fang Fang Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals, Joseph Pirrello Shareholder of: Kiniksa

Table 1. Efficacy at Week 26

	All Patients [1]		Subgroups			
			N/O		R/R	
	Mavrilimumab (N=42)	Placebo (N=28)	Mavrilimumab (N=24)	Placebo (N=11)	Mavrilimumab (N=18)	Placebo (N=17)
Patients with Flare, n (%)	8 (19.0)	13 (46.4)	3 (12.5)	4 (36.4)	5 (27.8)	9 (52.9)
Time to Flare (weeks) [2]						
Median, 95% CI	NE (NE, NE)	25.1 (16.0, NE)	NE (NE, NE)	NE (11.7, NE)	NE (16.4, NE)	22.6 (16.0, NE)
HR (Mavrilimumab vs Placebo), 95% CI [3]	0.38 (0.15, 0.92)		0.29 (0.06, 1.31)		0.43 (0.14, 1.30)	
P-value [4] [5]	0.0263		0.0873		0.1231	
Sustained Remission (%), 95% CI [6]	83.2 (67.9, 91.6)	49.9 (29.6, 67.3)	91.3 (69.3, 97.7)	62.3 (27.7, 84.0)	72.2 (45.6, 87.4)	41.7 (17.4, 64.5)
Difference in Proportions (95% CI) [7]	33.3 (10.7, 55.8)		28.9 (-2.7, 60.5)		30.6 (-2.1, 63.2)	
P-value [5] [7]	0.0038		0.0727		0.0668	

NE = Not estimable.[1] Total mITT population. Stratified by randomization strata.[2] Kaplan-Meier.[3] Cox proportional-hazards model; treatment as covariate.[4] Log-rank test.[5] N/O and R/R subgroups not powered for significance; nominal p values reported.[6] Kaplan-Meier Survival Estimates with standard error.[7] Two-sided p-value for the difference in sustained remission between 2 arms using normal approximation. Placebo arm is reference.

Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals, Ai Ren Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals, Manoj Samant Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals, Teresa Zhou Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals, John F. Paolini Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals
DOI: 10.1136/annrheumdis-2021-eular.1915

OP0060

COMPARATIVE STUDY ON ANTI-TNF VS TOCILIZUMAB FOR TREATMENT OF REFRACTORY UVEITIC CYSTOID MACULAR EDEMA DUE TO BEHCET'S DISEASE. MULTICENTER STUDY OF 49 PATIENTS

B. Atienza-Mateo[1], I. Ferraz-Amaro[2], E. Beltrán[3], A. Adan[4], M. Hernández-Garfella[5], L. Martinez-Costa[6], M. Cordero-Coma[7], M. Díaz-Llopis[8], J. M. Herreras[9], O. Maiz-Alonso[10], I. Torre-Salaberri[11], D. Díaz Valle[12], A. Atanes-Sandoval[13], F. Francisco[14], S. Insua[15], J. Sánchez[16], R. Almodovar[17], O. Ruiz-Moreno[18], M. Gandia Martinez[19], J. M. Nolla[20], J. L. Martín-Varillas[21], V. Calvo-Río[1], D. Prieto-Peña[1], M. A. González-Gay[1], R. Blanco[1]. *[1]Hospital Universitario Marqués de Valdecilla, IDIVAL, Rheumatology, Santander, Spain*; *[2]Hospital Universitario de Canarias, Rheumatology, Santa Cruz de Tenerife, Spain*; *[3]Hospital del Mar, Rheumatology, Barcelona, Spain*; *[4]Hospital Clinic, Ophthalmology, Barcelona, Spain*; *[5]Hospital General Universitario de Valencia, Ophthalmology, Valencia, Spain*; *[6]Hospital Peset, Ophthalmology, Valencia, Spain*; *[7]Hospital de León, Ophthalmology, León, Spain*; *[8]Hospital Universitario La Fe, Ophthalmology, Valencia, Spain*; *[9]Hospital Universitario IOBA, Ophthalmology, Valladolid, Spain*; *[10]Hospital Universitario de Donostia, Rheumatology, San Sebastián, Spain*; *[11]Hospital Universitario de Basurto, Rheumatology, Bilbao, Spain*; *[12]Hospital Clínico San Carlos, Ophthalmology, Madrid, Spain*; *[13]Complejo Hospitalario Universitario de A Coruña, Rheumatology, A Coruña, Spain*; *[14]Hospital Doctor Negrín, Rheumatology, Las Palmas de Gran Canaria, Spain*; *[15]Hospital Universitario Santiago de Compostela, Rheumatology, A Coruña, Spain*; *[16]Hospital Universitario 12 de Octubre, Rheumatology, Madrid, Spain*; *[17]Hospital Universitario Fundación de Alcorcón, Rheumatology, Madrid, Spain*; *[18]Hospital Universitario Miguel Servet, Ophthalmology, Zaragoza, Spain*; *[19]Hospital Puerta del Mar, Rheumatology, Cádiz, Spain*; *[20]Hospital Universitario de Bellvitge, Rheumatology, Barcelona, Spain*; *[21]Hospital Sierrallana, Rheumatology, Torrelavega, Spain*

Background: Posterior segment involvement is the most serious affection of uveitis in Behçet's disease (BD), with cystoid macular edema (CME) being the leading cause of blindness. Anti-TNF, especially adalimumab (ADA) and infliximab (IFX), have demonstrated efficacy as first-line biologic agents in BD-related uveitis **[1,2]**. Moreover, the anti-IL6R tocilizumab (TCZ) has shown excellent results in highly refractory BD-uveitis and noninfectious uveitic CME **[3-6]**.
Objectives: To compare the efficacy of ADA vs IFX vs TCZ in patients with refractory CME due to BD.
Methods: Observational multicenter study of patients with BD-associated CME refractory to conventional and/or biological immunosuppressive drugs. From a cohort of 177 patients treated with anti-TNF and 14 patients treated with TCZ, we selected those with CME at baseline. CME was defined as macular thickness > 300µm (measured by optic coherence tomography). We analyzed in the 3 groups of treatment (ADA, IFX, TCZ) from baseline up to 4 years the evolution of macular thickness (main outcome) and best-corrected visual acuity (BCVA). Differences between basal and final follow-up were evaluated. Multivariable linear regression was used to assess the differences between the 3 groups.
Results: A total of 49 patients were included. ADA was used in 25 patients (40 eyes with CME), IFX in 15 (21 eyes with CME) and TCZ in 9 (11 eyes with CME). No statistically significant baseline differences were observed between the 3 groups (Table) except for previous anti-TNF therapy, which was used only in patients treated with TCZ (5 patients received ADA, 1 received IFX and 2 received both ADA and IFX, in different times). Most patients from all groups had received several conventional immunosuppressive drugs. Biological therapy was used in monotherapy or combined with azathioprine (n=10, 5 and 1 in ADA, IFX and TCZ group, respectively), cyclosporine A (n=10, 5 and 1) or methotrexate (n=4, 2 and 3). Macular thickness progressively decreased in the 3 groups, with no signs of CME after 1 year of treatment. Similarly, BCVA improvement and inflammatory ocular remission was reached in all groups (Figure).

Table 1. Demographic and clinical characteristics of 49 patients with cystoid macular edema due to Behçet's disease receiving ADA, IFX or TCZ.

	ADA (n=25)	IFX (n=15)	TCZ (n=9)
Eyes with cystoid macular edema, n	40	21	11
Age, years	41 ± 11	38 ± 9	43 ± 16
Sex, men/women	12/13	7/8	5/4
HLA–B51 +, n	19	10	6
Duration of uveitis before anti-TNF/ anti-IL6R, months	30 [12-82]	15 [8-60]	32 [24-144]
Ocular features at start of anti-TNF/anti-IL6R			
Macular thickness, µm	432 ± 118	483 ± 126	417 ± 113
Visual acuity, BCVA	0.4 ± 0.2	0.3 ± 0.2	0.2 ± 0.2
Tyndall, inflammation grade	2 [1-3]	1 [0-1.5]	1 [0-1.5]
Vitritis, inflammation grade	2.5 [1.5-3]	1 [0-2]	2 [1-2]
Previous treatment, n			
Oral glucocorticoids // i.v. pulse methylprednisolone	18 // 13	4 // 9	7 // 8
MTX //CsA //AZA	13 // 22 // 14	8 // 13 // 8	8 // 6 // 2
ADA // IFX	0 // 0	0 // 0	7 // 3
Prednisone dosage at start of anti-TNF/anti-IL6R, mg/day	45 [30-60]	30 [20-60]	30 [30-30]
Combined treatment, n			
CsA // AZA // MTX	10 // 10 // 4	5 // 5 // 2	1 // 1 // 3

Data are presented as mean ± SD or median [IQR] when data were not normally distributed. ADA, adalimumab; AZA, azathioprine; CsA, cyclosporine A; MTX, methotrexate; IFX, infliximab; TCZ, tocilizumab.

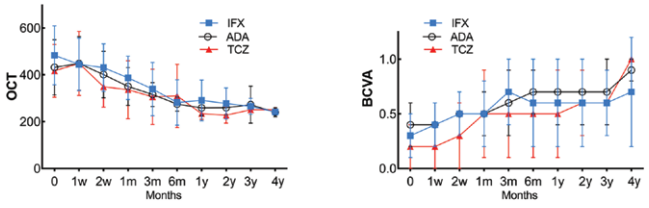


Figure 1. Evolution of ocular parameters in 49 patients with cystoid macular edema due to Behçet's disease receiving ADA, IFX or TCZ.

Conclusion: Refractory CME associated to BD's uveitis can be effectively treated with ADA, IFX or TCZ. Moreover, TCZ is effective in patients resistant to anti-TNF therapy.

REFERENCES:

[1] *Arthritis Rheumatol.* 2019;71(12):2081-2089. doi: 10.1002/art.41026
[2] *Ophthalmology.* 2018;125(9):1444-1451. doi: 10.1016/j.ophtha.2018.02.020
[3]*Rheumatology (Oxford).* 2018;57(5):856-864. doi: 10.1093/rheumatology/kex480
[4] *Am J Ophthalmol.*2019;200:85-94. doi: 10.1016/j.ajo.2018.12.019
[5] *Clin Exp Rheumatol.* 2014;32(4 Suppl 84): S54-7. PMID: 25005576
[6] *Clin Exp Rheumatol.* 2016;34(6 Suppl 102): S34-S40. PMID:27054359

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.307

OP0061

A PROOF-OF-CONCEPT STUDY TO ASSESS THE EFFICACY OF TOCILIZUMAB MONOTHERAPY AFTER ULTRA-SHORT GLUCOCORTICOID ADMINISTRATION TO TREAT GIANT CELL ARTERITIS - THE GUSTO TRIAL

L. Christ[1], L. Seitz[1], G. Scholz[1], A. C. Sarbu[1], J. Amsler[1], L. Bütikofer[2], C. Tappeiner[3], F. Kollert[1], S. Reichenbach[1], P. Villiger[1]. *[1]Inselspital, Bern University Hospital, Department of Rheumatology, Immunology and Allergology, Bern, Switzerland*; *[2]Inselspital, University of Bern, Clinical Trial Unit (CTU), Bern, Switzerland*; *[3]Inselspital, Bern University Hospital, Department of Ophthalmology, Bern, Switzerland*

Background: Two randomised controlled trials [1, 2] demonstrated a glucocorticoid (GC)-sparing effect of tocilizumab (TCZ) of at least 50%. Long-term GC treatment leads invariably to numerous side effects, particularly in elderly giant cell arteritis (GCA) patients.
Objectives: The GUSTO (GCA treatment with ultra-short GC and TCZ) trial was set up to evaluate the efficacy and safety of TCZ-monotherapy after ultra-short GC treatment in new-onset GCA.
Methods: Eighteen patients with newly diagnosed GCA were enrolled in this investigator-initiated, single-arm, single-center, open-label clinical trial with Simon's two stage design (NCT03745586). Patients received 500 mg methylprednisolone intravenously for 3 consecutive days. Thereafter, GC treatment was discontinued and TCZ (8 mg/kg body-weight) was administered intravenously, followed by weekly subcutaneous TCZ injections (162 mg) from day 10 until week 52. The primary endpoint was defined as the proportion of patients who achieved remission within 31 days and showed no relapse at week 24; the secondary endpoint included the proportion of patients with complete relapse-free remission of disease at week 52. Remission was defined as disappearance of GCA symptoms, whereas partial remission included the presence of mild symptoms (defined as non-ischemic with NRS<5/10, reported as mild, not occurring on most days of the week). An interim analysis of the primary endpoint was performed after the first 12 patients reached the primary endpoint.
Results: At baseline there were 12/18 female patients, and the median age was 71 (range 64-78) years. Overall, 15/18 had cranial symptoms (10/18 had jaw claudication, 6/18 had visual symptoms), 10/18 suffered from polymyalgia rheumatica (PMR)-symptoms, 16/18 had positive cranial ultrasound, and 13/18 had positive histopathology.
At interim analysis, only 25% (3/12) of patients achieved remission within 31 days and stayed relapse-free up to week 24. Thus, the null hypothesis that the proportion of responders would be smaller than 40% (p=0.92) was not rejected. Of the 18 patients recruited at the time of interim analysis, 14 achieved remission within 24 weeks (mean duration 11.1 (95% CI 8.3-13.9) weeks) and 13 showed no relapses up to 52 weeks (72%, 95% CI 47-90%). Overall, 3/18 patients were non-responders (2/3 with persistent cranial symptoms including one new-onset of an anterior ischemic optic neuropathy (AION); 1/3 with persistent PMR symptoms) and started on rescue GC-treatment, and 2/18 discontinued the study due to an adverse event (hepatopathy and diverticulitis, respectively; 1/2 after induction of remission).
Figure 1 demonstrates remission status over time.
Conclusion: After a 3-days pulse of methylprednisolone, ensuing TCZ monotherapy induced and maintained remission until week 52 in 13/18 patients. The data add an important piece of evidence regarding the potency of blocking the interleukin-6 pathway in GCA and suggest that a substantial reduction of concomitant GC treatment in TCZ-treated GCA patients is feasible.

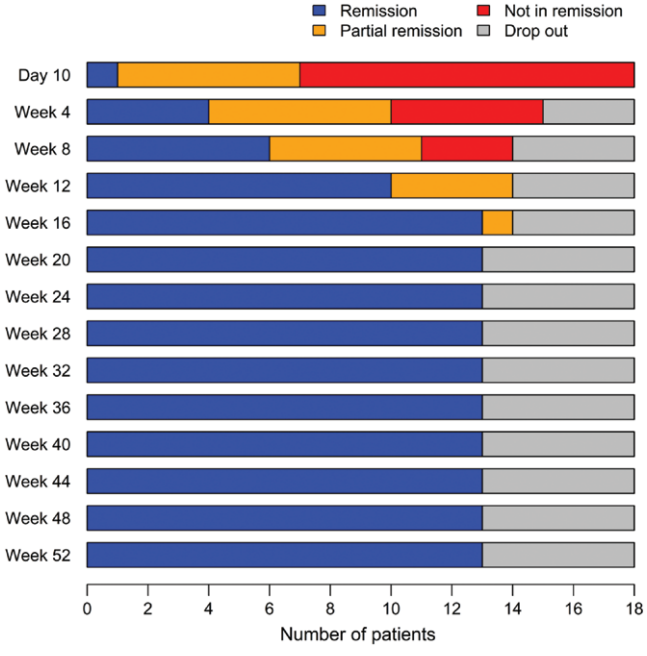


Figure 1. Disease status of patients at each visit (Day 10 - week 52, n=18).

REFERENCES:
[1] Villiger, P.M., et al., Tocilizumab for induction and maintenance of remission in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet, 2016. **387**(10031): p. 1921-7.
[2] Stone, J.H., et al., Trial of Tocilizumab in Giant-Cell Arteritis. N Engl J Med, 2017. **377**(4): p. 317-328.

Disclosure of Interests: Lisa Christ Shareholder of: F. Hoffmann-La Roche, Grant/research support from: Gilead Sciences; F. Hoffmann-La Roche; Pfizer, Luca Seitz: None declared, Godehard Scholz: None declared, Adela-Cristina Sarbu: None declared, Jennifer Amsler: None declared, Lukas Bütikofer: None declared, Christoph Tappeiner: None declared, Florian Kollert Shareholder of: Roche, Consultant of: Yes (Actelion, BMS, Boehringer-Ingelheim, Pfizer), Grant/research support from: Yes (Gilead, Pfizer), Employee of: Yes, I am currently employed by Roche and previously by Novartis, Stephan Reichenbach: None declared, Peter Villiger Speakers bureau: Roche, MSD, Abbvie, Pfizer, Novartis, Grünenthal, Celgene, Sanofi, Chugai, Consultant of: Roche, MSD, Abbvie, Pfizer, Novartis, Celgene, Sanofi, Grant/research support from: Roche, MSD, Abbvie
DOI: 10.1136/annrheumdis-2021-eular.522

Vasculitis - II

OP0062

CYTOKINE PRODUCING B CELLS SKEW MACROPHAGES TOWARDS A PRO-INFLAMMATORY PHENOTYPE IN GIANT CELL ARTERITIS

J. C. Graver[1], W. F. Jiemy[1], D. Altulea[1], A. Boots[1], P. Heeringa[2], W. Abdulahad[1], E. Brouwer[1], M. Sandovici[1]. *[1]University of Groningen, University Medical Center Groningen, Rheumatology & Clinical Immunology, Groningen, Netherlands*; *[2]University of Groningen, University Medical Center Groningen, Pathology & Medical Biology, Groningen, Netherlands*

Background: Giant cell arteritis (GCA) is the most frequent form of systemic vasculitis affecting the temporal artery (TA) and the aorta. Macrophages and T cells are well recognized players in the pathogenesis of GCA while B cells are often not taken into account. Recently, changes in the circulating B cell compartment were documented in GCA and B cells were found to organize into tertiary lymphoid organs at the site of vascular inflammation (TA and aorta).[1,2] The exact role of B cells in GCA is still unknown as no disease-specific antibodies have been defined. However, beside their role in humoral immunity, B cells can also produce various cytokines. In GCA, peripheral B cells of treated GCA patients, showed an enhanced capacity to produce pro-inflammatory cytokine Interleukin (IL)6[3] which is nowadays an important target of treatment in GCA.[4] We hypothesize that B cells help shape the inflammatory response in GCA by producing effector and regulatory cytokines.
Objectives: We aimed to assess the cytokine profile of circulating and lesional B cells in GCA and studied the effects on macrophage skewing.
Methods: To assess B cells with the capacity to produce cytokines, cryopreserved peripheral blood mononuclear cells of 11 untreated GCA patients and 15 age- and sex-matched healthy controls (HC) were cultured for 3 days in the presence of CpG-ODN 2006. During the last 5 hours phorbol myristate acetate and Calcium Ionophore were added. Thereafter, intracellular effector (IL6, TNFa, IFNy, LTb) and regulatory B cell-related cytokines (IL10) were measured with flow cytometry. To assess potential skewing of macrophages by B cell products, THP-1 cells were differentiated into macrophages and stimulated for 24 hours with supernatant from stimulated B cells (n=6). Expression of IL23, IL6, IL1b, TNFa, MMP9 and YKL40 was assessed on mRNA level with qPCR. To assess local cytokine production, TA (n=11) and aorta tissue samples (n=10) of histologically-proven GCA patients were stained to detect CD20, IL6, TNFa, IFNy, LTb, and IL10 expression. For comparison, 14 aorta tissues samples of patients with an atherosclerosis-related aortic aneurysm were included.
Results: *In vitro* stimulated B cells from untreated GCA patients showed an enhanced percentage of IL6+ B cells (median (IQR); 44 (41-52)) and of IL6+TNFa+ B cells (12 (8-24)) compared to stimulated B cells from HC (IL6+: 28 (23-39), IL6+TNFa+: 6 (4-24)). In addition, soluble factors, secreted by GCA derived and stimulated B cells, skewed macrophages towards a pro-inflammatory phenotype with enhanced expression of IL23, IL6, IL1b, and TNFa. Furthermore, these macrophages also showed higher expression of the tissue remodelling factor MMP9 and the pro-angiogenic factor YKL40. At the site of vascular inflammation, B cells were detected in the regions with clear TNFa, IL6, IFNY, LTb and IL10 expression in both the TA and aorta of GCA patients.

Conclusion: This study demonstrates that circulating B cells of patients with GCA have the capacity to express pro-inflammatory cytokines (IL6 and TNFa) which can influence other cellular players in GCA. Specifically, B cell secreted soluble factors were able to skew macrophages towards a pro-inflammatory phenotype. In addition, this study provides evidence for an active role of B cells in shaping the cytokine milieu at the site of inflammation thereby revealing the B cell as a new target of intervention in GCA.

REFERENCES:

[1] Ciccia, F. *et al.* Ectopic expression of CXCL13, BAFF, April and LT-β is associated with artery tertiary lymphoid organs in giant cell arteritis. *Ann. Rheum. Dis.* **76**, 235–243 (2017)
[2] Graver, JC. *et al.* Massive B cell Infiltration and Organization Into Artery Tertiary Lymphoid Organs in the Aorta of Large Vessel Giant Cell Arteritis. *Front. Immunol.* **10**, 83 (2019)
[3] Van Der Geest, KSM. *et al.* Disturbed B cell homeostasis in newly diagnosed giant cell arteritis and polymyalgia rheumatica. *Arthritis Rheumatol.* **66**, 1927–1938 (2014)
[4] Stone, JH. *et al.* Trial of tocilizumab in giant-cell arteritis. *N. Engl. J. Med.* **377**, 317–328 (2017)

Disclosure of Interests: Jacoba Carolien Graver: None declared, William Febry Jiemy: None declared, Dania Altulea: None declared, Annemieke Boots Consultant of: Grunenthal, Peter Heeringa: None declared, Wayel Abdulahad: None declared, Elisabeth Brouwer Speakers bureau: Roche, fees paid to UMCG, Maria Sandovici: None declared
DOI: 10.1136/annrheumdis-2021-eular.1984

OP0063 SINGLE CENTRE EXPERIENCE OF THE CLINICAL SPECTRUM, AETIOLOGIES AND MANAGEMENT OF NON-INFECTIOUS AORTITIS

R. S. Andev[1,2], N. Ahmad[2], A. Verdiyeva[2], R. Luqmani[1,2], S. Dubey[2].
[1]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom; *[2]Oxford University Hospitals NHS Foundation Trust, Department of Rheumatology, Oxford, United Kingdom*

Background: Aortitis, a rare form of large vessel vasculitis, may occur in the context of a primary systemic vasculitis, as a part of systemic autoimmune disease or in isolation. The evidence and guidelines to diagnose, manage and monitor aortitis remain limited. However, PET CT and vascular MRI scans have facilitated our ability to make the diagnosis more readily. The optimal management strategy and complication rates remain uncertain.

Objectives: Our aim was to explore the clinical, laboratory and radiological features of aortitis. We sought to review the management and complications of this illness by collecting detailed information on the outcomes and treatments used, including disease modifying agents (DMARDs) and biologics.

Methods: Patients diagnosed with aortitis since 2006 that had been managed in a single tertiary centre were identified using the Rheumatology Assessment Database Innovation in Oxford (RHADIO). Their medical notes were retrospectively reviewed using a local electronic patient record system and the following information was obtained: demographics, underlying risk factors, imaging and laboratory results (including biopsy reports if available), management and outcome.

Results: We identified 155 patients who met the inclusion criteria. There was a female preponderance of 57.4% (n=89). At the time of diagnosis, the average age was 69 (range 30-92) and the mean symptomatology length prior to diagnosis was 12 months (range 0-120). The majority of patients (60.4%, n=94) had aortitis secondary to giant cell arteritis (GCA), isolated aortitis was identified in 29.7% (n=46) and IgG4-related disease aortitis was uncommon (2.6%, n=4). Those with cranial GCA-like symptoms were diagnosed on average 3.9 months before those who presented differently (10.1 months versus 14.0 months).

Common presentations comprised: systemic inflammatory response syndrome (49.0%, n=76), cranial GCA-like symptoms (26.5%, n=41) and unexplained weight loss (24.5%, n=38). Importantly, 18.7% (n=29) of patients presented with ischaemic symptoms that included angina, TIAs/strokes and claudication. Aortic dissection was the primary presentation for 6.5% (n=10) of patients.

At presentation, the mean CRP was 84 mg/L (range 1-249) and the ESR was 72 mm/hr (range 2-164). Most (73.5%, n=114) had diagnostic PET CT changes. For those patients with GCA, diagnostic ultrasound changes were seen in 27.7% (n=26).

Nearly all were treated with prednisolone (92.3%, n=143) and all but 8 (5.1%) received a DMARD at some point. Methotrexate was the most commonly used DMARD (93.9%, n=138), followed by leflunomide (22.3%, n=35) and azathioprine (19.1%, n=28). Cyclophosphamide was used in 23.8% of patients (n=38) and 15 patients (9.7%) received tocilizumab.

Around a third (34.1% n=53/155) had received at least two DMARDs during their treatment course. On average, patients required 3.46 drugs to manage their aortitis. Those who relapsed (43.2%, n=67) were more likely to have GCA (65.7%, n=44).

Vascular sequelae were present in 37.4% (n=58). The most common complications were ischaemic in nature with stroke/TIA and claudication reported in 16.8% (n=26). Aortic aneurysms were recorded in 11.6% (n=18) of cases and 5.1% (n=8) developed dissections despite being on treatment for their aortitis. One patient developed renal infarcts and ischaemic bowel leading to intestinal failure because of florid vasculitis.

Conclusion: Aortitis has a varied presentation with systemic inflammatory response syndrome being the most common. Delayed diagnosis remains a problem and especially for those with non-GCA related aortitis, which is likely to contribute to the risk of subsequent vascular complications. Vascular events including dissection are common, many of which could be preventable, emphasising the importance of early diagnosis and good disease control.

REFERENCES:

[1] Koster M *et al*. Large-vessel giant cell arteritis: diagnosis, monitoring and management. Rheumatology [Internet]. 2018 Feb 1;57(suppl_2):ii32–42. Available from: https://doi.org/10.1093/rheumatology/kex424

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1546

OP0064 TOCILIZUMAB IN CRANIAL AND EXTRACRANIAL REFRACTORY GIANT CELL ARTERITIS: A MULTICENTER STUDY OF 312 CASES

L. Sanchez-Bilbao[1], J. Loricera[1], V. Aldasoro[2], J. P. Valdivieso-Achá[3], I. Villa-Blanco[4], O. Maiz[5], R. Melero[6], C. Moriano[7], J. Sánchez[8], E. De Miguel[9], E. Perez-Pampín[10], J. R. De Dios[11], J. C. Nieto González[12], E. Galíndez-Agirregoikoa[13], P. Moya[14], F. Sivera[15], J. L. Andréu Sánchez[16], V. Pinillos[17], A. García-Valle[18], P. Vela-Casasempere[19], N. Alvarez-Rivas[20], M. Revenga[21], S. Manrique Arija[22], C. Fernández-López[23], E. Raya[24], C. Hidalgo[25], R. López-González[26], C. Campos Fernández[27], A. Juan-Mas[28], B. Arca[20], I. Rua-Figueroa[29], M. D. Boquet[30], A. García[31], A. Gallego[32], E. Salgado-Pérez[33], M. A. González-Gay[1], R. Blanco[1]on behalf of Tocilizumab in Giant Cell Arteritis Spanish Collaborative Group: Santos Castañeda (H La Princesa), Arantxa Conesa (HU de Castellón), Carmen Ordás (H Cabueñes), Alejandro Olivé-Marqués (H Trías i Pujol), Carles Galisteo (H Parc Taulí), Francisco Navarro (H General Universitario de Elche), Javier Toyos (HU Virgen Macarena), Guillén Sada (Complejo Hospitalario de Navarra), José Andrés Román Ivorra (HU y Politécnico La Fe), Francisco Ortiz-Sanjuán (HU y Politécnico La Fe), Pau Lluch (H Mateu Orfila), Carmen Torres (Complejo Asistencial de Ávila), Elena Becerra (HU de Torrevieja), Luisa Marena (H La Mancha Centro), Roser Solans Laqué (H Valle de Hebrón), Javier Narváez (H de Bellvitge), Cristina Luna (HU Nuestra Señora de La Candelaria), Nagore Fernández-Llanio (H Arnáu de Vilanova), Susana Romero-Yuste (Complejo Hospitalario Universitario de Pontevedra), Mónica Calderón-Goercke (HU Marqués de Valdecilla-IDIVAL), Eztizen Labrador (H San Pedro). *[1]Hospital Universitario Marqués de Valdecilla-IDIVAL, Rheumatology, Santander, Spain*; *[2]Complejo Hospitalario de Navarra, Rheumatology, Pamplona, Spain*; *[3]Hospital de La Princesa, Rheumatology, Madrid, Spain*; *[4]Hospital Sierrallana, Rheumatology, Torrelavega, Spain*; *[5]Hospital de Donostia, Rheumatology, San Sebastián, Spain*; *[6]Complexo Hospitalario de Vigo, Rheumatology, Vigo, Spain*; *[7]Complejo Asistencial Universitario de Leon, Rheumatology, León, Spain*; *[8]Hospital 12 de Octubre, Rheumatology, Madrid, Spain*; *[9]Hospital La Paz, Rheumatology, Madrid, Spain*; *[10]Hospital Universitario de Santiago, Rheumatology, Santiago de Compostela, Spain*; *[11]Hospital del Alto Deba, Rheumatology, Mondragón, Spain*; *[12]Hospital Gregorio Marañón, Rheumatology, Madrid, Spain*; *[13]Hospital de Basurto, Rheumatology, Bilbao, Spain*; *[14]H Sant Pau, Rheumatology, Barcelona, Spain*; *[15]Hospital Universitario de Elda, Rheumatology, Alicante, Spain*; *[16]HU Puerta de Hierro, Rheumatology, Madrid, Spain*; *[17]Hospital SAN PEDRO, Rheumatology, Logroño, Spain*; *[18]Complejo asistencial universitario de Palencia, Rheumatology, Palencia, Spain*; *[19]Hospital General Universitario de Alicante, Rheumatology, Alicante, Spain*; *[20]Hospital Universitario San Agustín, Rheumatology, Avilés, Spain*; *[21]Hospital Ramón y Cajal, Rheumatology, Madrid, Spain*; *[22]Hospital Regional de Málaga, Rheumatology, Málaga, Spain*; *[23]Hospital Universitario Juan Canalejo, Rheumatology, La Coruña, Spain*; *[24]Hospital San Cecilio, Rheumatology, Granada, Spain*; *[25]Complejo Asistencial Universitario de Salamanca, Rheumatology, Salamanca, Spain*; *[26]Complejo Hospitalario de Zamora, Rheumatology, Zamora, Spain*; *[27]Hospital General Universitario de Valencia, Rheumatology, Valencia, Spain*; *[28]Hospital Universitario Son Llàtzer, Rheumatology, Palma de Mallorca, Spain*; *[29]Hospital Doctor Negrin, Rheumatology, Las Palmas, Spain*; *[30]Hospital Arnau de Vilanova, Rheumatology, Lleida, Spain*; *[31]Hospital Virgen de las Nieves, Rheumatology, Granada, Spain*; *[32]Complejo Hospitalario Universitario de Badajoz, Rheumatology, Badajoz, Spain*; *[33]Complejo Hospitalario Universitario de Ourense, Rheumatology, Ourense, Spain*

Background: Giant cell arteritis (GCA) may be divided into cranial, and extracranial GCA. Tocilizumab (TCZ) has shown efficacy and safety in GCA and other large-vessel vasculitis (LVV) (1-5).
Objectives: To compare the efficacy of TCZ in cranial and extracranial GCA.
Methods: Multicenter observational study of 312 patients with GCA treated with TCZ. They were divided into 3 groups a) only cranial (cGCA), b) only extracranial (ecGCA), c) mixed affection (mixGCA). GCA was diagnosed by a) ACR criteria, and/or b) positive temporal artery biopsy, and/or c) LVV by imaging. Remission and sustained remission was defined according to EULAR definitions (1). In ecGCA and mixGCA we also studied the improvement (complete or partial) by imaging techniques.
Results: We studied 312 patients (218 females; mean age, 73.4±9.6 years). TABLE shows the main features of the 3 groups. Remission at month 6 was higher in cGCA, as well as the sustained remission at month12 (FIGURE). At 18 and 24months, were similar in the 3 groups. Improvement by imaging techniques was partial/complete at 6,12,18 and 24 months, in 50%/0%,71%/0%, 61%/15% and 67%/17% respectively, in ecGCA, and in 75%/0%,53%/18%, 64%/12% and 50%/28% in mixGCA.

Table 1. Main features of 312 patients at TCZ onset.

	Cranial GCA	Extracranial GCA	Mixed GCA	Cranial vs Extracranial GCA
	(n=152)	(n=49)	(n=111)	p
Age at TCZ onset, years, mean± SD	76.0±8.2	65.4±12.2	73.5±8.1	**0.000***
Sex, female/male, n (% female)	105/47 (69)	33/16 (67)	80/31 (72)	0.960
Time from diagnosis to TCZ onset (months, median [IQR]	6 [2-21]	7 [2-20]	9 [3-25]	0.765
Biopsy-proven GCA, n (%)	87/128 (68)	0 (0)	50/87 (57)	**0.000***
Systemic manifestations at TCZ onset	109 (72)	32 (65)	84 (76)	0.501
Fever, n (%)	18 (12)	1 (2)	8 (7)	**0.048***
Constitutional syndrome, n (%)	52 (34)	16 (33)	47 (42)	0.933
PmR, n (%)	88 (58)	29 (59)	71 (64)	0.999
Ischemic manifestations at TCZ onset	117 (77)	0 (0)	70 (63)	**0.000***
Visual involvement, n (%)	31 (20)	0 (0)	16 (14)	**0.000***
Headache, n (%)	103 (85)	0 (0)	63 (57)	**0.000***
Jaw claudication, n (%)	39 (26)	0 (0)	21 (19)	**0.000***
Acute phase reactants				
ESR, mm/1st hour, median [IQR]	28 [9-53]	24 [10-43]	28 [15-48]	0.462
CRP, mg/dL, median [IQR]	1.2 [0.3-3.4]	0.7 [0.4-1.8]	1.6 [0.4-3.8]	0.153
Prednisone dose at TCZ onset, mean ± SD	26.2±17.6	15.4±14.2	20.1±14.9	**0.000***
TCZmono/TCZcombo, n (% TCZ mono)	116/36 (76)	26/23 (53)	69/42 (62)	**0.003***
Follow-up (months), mean ± SD	27.3±21.1	32.7±23.3	27.9±22.0	0.143

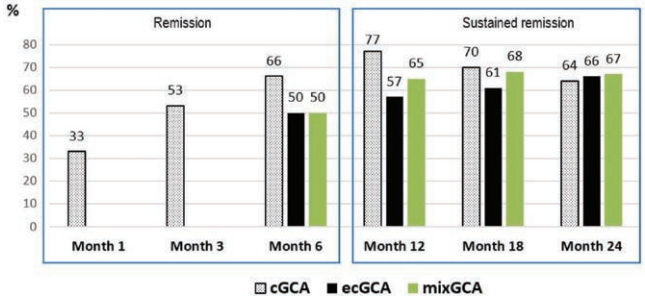


Figure 1. Remission and sustained remission of cGCA, ecGCA and mixGCA according to EULAR **(1).** In the first 3 months we only could assess cGCA because in ecGCA and mixGCA a control imaging was not performed

Conclusion: TCZ seems to be effective in all phenotypes but it is faster in cGCA in reaching remission. However, improvement by imaging techniques was partial and very rarely complete in ecGCA and mixGCA.
REFERENCES:
[1] Hellmich B, et al. Ann Rheum Dis. 2020; 79: 19-30.
[2] Stone JH, et al. N Engl J Med. 2017; 377: 317-28.
[3] Calderón-Goercke M, et al. Semin Arthritis Rheum 2019; 49:126-35. https://doi.org/10.1016/j.semarthrit.2019.01.003.
[4] Prieto Peña D et al. Clin Exp Rheumatol 2020 Nov 27. PMID: 33253103.
[5] Loricera J, et al. Clin Exp Rheumatol 2016; 34:S44-53. PMID: 27050507

Disclosure of Interests: Lara Sanchez-Bilbao: None declared, Javier Loricera: None declared, Vicente Aldasoro: None declared, Juan Pablo Valdivieso-Achá: None declared, Ignacio Villa-Blanco: None declared, Olga Maiz: None declared, Rafael Melero: None declared, Clara Moriano: None declared, Julio Sánchez: None declared, Eugenio de Miguel: None declared, Eva Perez-Pampín: None declared, Juan Ramón De Dios: None declared, Juan Carlos Nieto González: None declared, Eva Galíndez-Agirregoikoa: None declared, Patricia Moya: None declared, Francisca Sivera: None declared, José Luis Andréu Sánchez: None declared, Valvanera Pinillos: None declared, Andrea García-Valle: None declared, Paloma Vela-Casasempere: None declared, Noelia Alvarez-Rivas: None declared, Marcelino Revenga: None declared, Sara Manrique Arija: None declared, Carlos Fernández-López: None declared, Enrique Raya: None declared, Cristina Hidalgo: None declared, Ruth López-González: None declared, Cristina Campos Fernández: None declared, Antonio Juan-Mas: None declared, Beatriz Arca: None declared, Iñigo Rua-Figueroa: None declared, María Dolors Boquet: None declared, Antonio García: None declared, Adela Gallego: None declared, Eva Salgado-Pérez: None declared, Miguel A González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Grant/research support from: Abbvie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: Abbvie, Lilly, Pfizer, Roche, Bristol-Myers, Janssen, UCB Pharma and MSD, Grant/research support from: Abbvie, MSD and Roche
DOI: 10.1136/annrheumdis-2021-eular.2139

OP0065

TOCILIZUMAB IN VISUAL INVOLVEMENT OF GIANT CELL ARTERITIS. MULTICENTER STUDY OF 312 PATIENTS OF CLINICAL PRACTICE

L. Sanchez-Bilbao[1], J. Loricera[1], V. Aldasoro[2], R. Melero[3], S. Castañeda[4], O. Maiz[5], C. Moriano[6], I. Villa-Blanco[7], E. Labrador-Sánchez[8], C. Hidalgo[9], S. Manrique Arija[10], E. Galíndez-Agirregoikoa[11], E. Perez-Pampín[12], A. García-Valle[13], C. Campos Fernández[14], J. R. De Dios[15], C. L. Iñíguez[16], J. L. Andréu Sánchez[17], J. Sánchez[18], M. Calderón-Goercke[1], M. A. González-Gay[1], R. Blanco[1]on behalf of Tocilizumab in Giant Cell Arteritis Spanish Collaborative Group: Francisca Sivera (HU de Elda), Eugenio de Miguel (HU La Paz), Juan Pablo Valdivieso-Achá (H La Princesa), Marcelino Revenga (HU Ramón y Cajal), Guillén Sada (Complejo Hospitalario de Navarra), Carlos Fernández-López (HU Juan Canalejo), Beatriz Arca (HU San Agustín), Ruth López (Complejo Hospitalario de Zamora), Patricia Moya (H Sant Pau), María Dolors Boquet (H Arnau de Vilanova), Adela Gallego (Complejo Hospitalario Universitario de Badajoz), Paloma Vela (H General Universitario de Alicante), Juan Carlos Nieto (HU Gregorio Marañón), Enrique Raya (H San Cecilio), María Noelia Álvarez-Rivas (HU San Agustín), Íñigo Rúa-Figueroa (H Doctor Negrín), Antonio García (H Virgen de Las Nieves), Carlos Vázquez (H Miguel Servet), Arantxa Conesa (HU de Castellón), Carmen Ordás (H Cabueñes), Alejandro Olivé-Marqués (H Trías i Pujol), Carles Galisteo (H Parc Taulí), Francisco Navarro (H General Universitario de Elche), Javier Toyos (HU Virgen Macarena), José Andrés Román Ivorra (HU y Politécnico La Fe), Francisco Ortiz-Sanjuán (HU y Politécnico La Fe), Pau Lluch (H Mateu Orfila), Carmen Torres (Complejo Asistencial de Ávila), Elena Becerra (HU de Torrevieja), Luisa Marena (H La Mancha Centro), Roser Solans Laqué (H Valle de Hebrón), Javier Narváez (H de Bellvitge), Cristina Luna (HU Nuestra Señora de La Candelaria), Nagore Fernández-Llanio (H Arnáu de Vilanova), Susana Romero-Yuste (Complejo Hospitalario Universitario de Pontevedra), Valvanera Pinillos (H San Pedro). *[1]Hospital Universitario Marqués de Valdecilla-IDIVAL, Rheumatology, Santander, Spain*; *[2]Complejo Hospitalario de Navarra, Rheumatology, Pamplona, Spain*; *[3]Complexo Hospitalario de Vigo, Rheumatology, Vigo, Spain*; *[4]Hospital de La Princesa, Rheumatology, Madrid, Spain*; *[5]Hospital de Donostia, Rheumatology, San Sebastián, Spain*; *[6]Complejo Asistencial Universitario de Leon, Rheumatology, León, Spain*; *[7]Hospital Sierrallana, Rheumatology, Torrelavega, Spain*; *[8]Hospital SAN PEDRO, Rheumatology, Logroño, Spain*; *[9]Complejo Asistencial Universitario de Salamanca, Rheumatology, Salamanca, Spain*; *[10]Hospital Regional de Málaga, Rheumatology, Málaga, Spain*; *[11]Hospital de Basurto, Rheumatology, Bilbao, Spain*; *[12]Hospital Universitario de Santiago, Rheumatology, Santiago de Compostela, Spain*; *[13]Complejo asistencial universitario de Palencia, Rheumatology, Palencia, Spain*; *[14]Hospital General Universitario de Valencia, Rheumatology, Valencia, Spain*; *[15]Hospital del Alto Deba, Rheumatology, Mondragón, Spain*; *[16]Hospital Universitario Lucus Augusti, Rheumatology, Lugo, Spain*; *[17]HU Puerta de Hierro, Rheumatology, Madrid, Spain*; *[18]Hospital 12 de Octubre, Rheumatology, Madrid, Spain*

Background: Visual involvement is one of the most feared complication of Giant Cell Arteritis (GCA).Tocilizumab (TCZ) has shown efficacy and safety in large-vessel vasculitis (LVV) including GCA **(1-4).**
Objectives: To assess the efficacy of TCZ to: **a)** prevent the appearance of new ocular involvement, and **b)** to improve visual symptoms if present.

Methods: Observational, multicenter study of 312 patients with GCA treated with TCZ. Patients were diagnosed with GCA accordingly to **a)** ACR criteria, and/or **b)** biopsy of temporal artery, and/or **c)** presence of LVV by imaging.
Patients were divided into two subgroups: **a)** with, and **b)** without visual involvement at any time. Visual manifestations were classified as: **a)** Transient visual loss (TVL) (amaurosis fugax), **b)** Permanent visual loss (PVL) (longer than 24 hours) (partial or complete; unilateral or bilateral), **c)** diplopia, and **d)** blurred vision. Accordingly to visual duration up to TCZ onset, we considered: **a)** 1-10 days, **b)** 11-30 days, and **c)** more than 30 days.
Results: We studied 312 (218 women/94 men; mean age73.4±9.6 years). Visual manifestations at any time (before and/or after TCZ) were observed in 78 (25%). In 47 of them visual manifestations were present at TCZ onset, and in the remaining 31 patients had had a complete recovery. Main clinical features of GCA with and without visual involvement are shown in TABLE. Patients with visual involvement were older, with other ischemic complications, and requiring more corticosteroids dose.

Table 1. Main features of 312 patients at TCZ onset.

	Overall N= 312	GCA with visual involvement (n= 78)	GCA without visual involvement (n=234)	p
General features				
Age (mean±SD)	73.4±9.6	76.6±8.0	72.4±9.8	**0.001***
Female/Male(% of female), n	218/94 (70)	47/31 (60)	171/63(73)	**0.046***
Time from GCA diagnosis to TCZ onset (months), median [IQR]	8 [3-24]	5 [1-14]	10 [3-24]	**0.040***
Positive TAB, n (%)	137/229 (60)	33/60 (55)	104/169 (61)	0.444
Ischemic manifestations				
Visual involvement, n (%)	47 (15)	47 (60)	0	**0.000***
Headache, n (%)	166 (53)	59 (76)	107 (46)	**0.000***
Jaw claudication	60 (19)	26 (33)	34 (14)	**0.001***
Systemic manifestations				
Fever, n (%)	27 (9)	8 (10)	19 (8)	0.743
Constitutional syndrome, n (%)	115 (37)	30 (38)	85 (36)	0.878
PmR, n (%)	188 (60)	46 (59)	142 (61)	0.830
Acute phase reactants				
ESR, mm/1st hour, median [IQR]	27 [10-50]	34.5 [15.2-58]	26.0 [10.0-48.0]	0.193
CRP (mg/dL), median [IQR]	1.4 [0.4-3.3]	1.5 [0.3-5.5]	1.3 [0.4-2.9]	0.134
Prednisone dose, mg/day, mean±SD	22.3±16.6	27.1±18.6	20.8±15.6	**0.008***
TCZmono/TCZcombo, n (%)	211/101	57/21	154/80	0.295
Follow-up (months), mean±SD	28.4±21.8	25.8±22.4	29.3±21.6	0.119

After TCZ onset, none patient developed new visual involvement. At TCZ onset 47 patients had the following visual manifestations; PVL (n= 28; unilateral/bilateral; 22/6), TVL (n=15; unilateral/bilateral; 9/6), diplopia (n=2) and blurred vision (n=2).
None of the patients with TVL presented new episodes after TCZ onset, while 8 out of 28 patients with PVL experienced partial improvement (FIGURE). The 2 patients with diplopia and 1 of 2 patients with blurred vision improved.

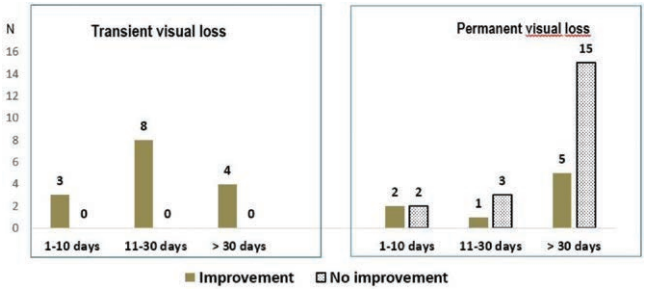


Figure 1. Efficacy of TCZ in 47 patients with GCA and visual involvement at TCZ onset.

Conclusion: TCZ seems to prevent the appearance of new ocular manifestations. When they are present, TCZ may improve totally TVL and partially PVL.
REFERENCES:
[1] Stone JH, et al. N Engl J Med. 2017; 377: 317-28.
[2] Calderón-Goercke M, et al. Semin Arthritis Rheum 2019;49:126-35. https://doi.org/10.1016/j.semarthrit.2019.01.003.
[3] Prieto Peña D et al. Clin Exp Rheumatol 2020 Nov 27. PMID: 33253103.
[4] Loricera J, et al. Clin Exp Rheumatol 2016; 34:S44-53. PMID: 27050507.
Disclosure of Interests: Lara Sanchez-Bilbao: None declared, Javier Loricera: None declared, Vicente Aldasoro: None declared, Rafael Melero: None declared, Santos Castañeda: None declared, Olga Maiz: None declared, Clara Moriano: None declared, Ignacio Villa-Blanco: None declared, Eztizen Labrador-Sánchez: None declared, Cristina Hidalgo: None declared, Sara Manrique Arija: None declared, Eva Galíndez-Agirregoikoa: None declared, Eva Perez-Pampín: None declared, Andrea García-Valle: None declared, Cristina Campos Fernández: None declared, Juan Ramón De Dios: None declared, Carlota Laura Iñíguez: None declared, José Luis Andréu Sánchez: None declared, Julio Sánchez: None declared, Monica Calderón-Goercke: None declared, Miguel A González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Consultant of: Abbvie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Grant/research support from: Abbvie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: Abbvie, Lilly, Pfizer, Roche, Bristol-Myers, Janssen, UCB Pharma and MSD, Consultant of: Abbvie, Lilly, Pfizer, Roche, Bristol-Myers, Janssen, UCB Pharma and MSD, Grant/research support from: Abbvie, MSD and Roche
DOI: 10.1136/annrheumdis-2021-eular.2169

OP0066

METABOLIC PROFILE AND COMORBIDITIES IN GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA PATIENTS BEFORE AND AFTER TREATMENT

I. Esen[1,2], P. Therkildsen[3], B. Dalsgaard Nielsen[4], A. Van 't Ende[1], A. Boots[1,2], P. Heeringa[2,5], E. M. Hauge[4], E. Brouwer[1,2], Y. Van Sleen[1,2]. *[1]University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*; *[2]University Medical Center Groningen, Vasculitis Expertise Center Groningen, Groningen, Netherlands*; *[3]Aarhus University Hospital, Department of Rheumatology, Aarhus, Denmark*; *[4]Aarhus University Hospital, Department of Rheumatology and Department of Clinical Medicine, Aarhus, Denmark*; *[5]University Medical Center Groningen, Department of Pathology and Medical Biology, Groningen, Netherlands*

Background: Giant cell arteritis (GCA) is a granulomatous vasculitis that affects the large vessels, occurring in people over 50 years of age. GCA frequently overlaps with polymyalgia rheumatica (PMR), which affects the proximal joints in the shoulders and hips. Both GCA and PMR patients require long-term treatment with glucocorticoids (GCs). Investigation of new treatment options is required because many GCA and PMR patients experience GC-related adverse events. These include hypercholesterolemia, hypertension, diabetes mellitus, cataract, and infections.(1) Previous studies suggest that unhealthy metabolic features and a higher Body Mass Index (BMI) might be protective in the development of GCA (2). However, data are limited.
Objectives: We aimed to elaborate more-in depth on the metabolic features, BMI and prevalence of comorbidities of GCA and PMR patients at the time of diagnosis and during treatment, to characterize patients for improved treatment options.
Methods: This study included two independent cohorts: the GPS (Groningen) cohort, and the Aarhus cohort for validation of baseline data (Table 1). Patients in the GPS cohort were prospectively followed with visits at 3 months, 1, 2, and 5 years. Laboratory measurements, metabolic co-morbidities were assessed at every visit. At baseline, we assessed whether comorbidities and BMI predicted the duration of GC treatment.

Table 1. Baseline characteristics. P-values were calculated with Mann-Whitney U test and Fischer Exact test. Numbers in bold: significance between HC and GCA/PMR patients from GPS cohort. *: significance between GCA and PMR of GPS cohort. [a]: significance between two cohorts.

	GCA GPS cohort (n=50)	*PMR GPS cohort (n=44)*	*HCs GPS cohort (n=65)*	**GCA Aarhus cohort (n=52)**	**PMR Aarhus cohort (n=25)**
Age, median	71	73	70	67	68
Female, %	35	26	43	32	13
Follow-up duration in months, median	42	40	NA	NA	NA
BMI, median	24.3	26.6	25.4	24	26.4
Systolic BP (mmHg), median	140	140	145	135	143
Diastolic BP (mmHg), median	**79.5***	80	80	76.5	83
HbA1c (mmol/mol), median	**43**	**40**	39	43	40
CRP (mg/L), median	**54**	**42**	4	76	53
ESR (mm/h), median	**94***	**57**	9	77	51
Diabetes mellitus, %	12	23	12	15	8
Hypercholesterolemia, %	22	14	17	15	24
Hypertension, %	66[a]	55	60	38	36
Cataract, %	**14**	**16**	34	NA	NA

Results: Frequencies of metabolic features in GCA/PMR patients from the GPS cohort were not significantly different in comparison to healthy controls (HCs). Higher HbA1c levels were detected in GCA patients than in HCs. Data on metabolic features from the Aarhus cohort compared well with the GPS cohort data and thus validated these findings (Table 1). Next, the effect of co-existing co-morbidities on the clinical manifestations was investigated. GCA patients with cataract had reduced CRP and ESR whereas PMR patients with cataract had a higher ESR than

patients without cataract (p=0,034). Analysis of GC treatment effect on co-morbidities revealed a significant increase in prevalence of diabetes (after 3 months) and cataract (after 5 years) compared to baseline. BMI was significantly higher after one year and five years of GC treatment. PMR patients with cataract at baseline required longer treatment with GCs (p=0.023). Presence of other metabolic features at the time of GCA or PMR diagnosis did not affect the treatment duration (Figure 1).
Conclusion: Newly-diagnosed GCA and PMR patients did not appear to have a healthier metabolic profile than HCs. As expected, GC treatment resulted in the development of an unhealthier metabolic profile in GCA patients. In PMR patients, the presence of cataract at baseline was predictive for a prolonged treatment period which could be explained by higher ESR levels in PMR patients with cataract. Together, our findings emphasize the importance of novel GC sparing therapeutic agents and personalized medicine in GCA and PMR.
REFERENCES:
[1] Buttgereit F,et al. Prevention of glucocorticoid morbidity in giant cell arteritis. Rheumatol (United Kingdom). 2018.
[2]Ungprasert P, et al. Lower body mass index is associated with a higher risk of giant cell arteritis: A systematic review and meta-analysis. Ann Transl Med. 2015.
Disclosure of Interests: Idil Esen: None declared, Philip Therkildsen: None declared, Berit Dalsgaard NIelsen: None declared, Anna van 't Ende: None declared, Annemieke Boots Consultant of: Grunenthal, Peter Heeringa: None declared, Ellen-Margrethe Hauge: None declared, Elisabeth Brouwer Speakers bureau: Roche, fees paid to UMCG, Yannick van Sleen: None declared
DOI: 10.1136/annrheumdis-2021-eular.2425

OP0068 EFFICACY AND SAFETY OF TNF-A ANTAGONISTS AND TOCILIZUMAB IN TAKAYASU ARTERITIS: MULTICENTER WORLDWIDE RETROSPECTIVE STUDY OF 209 PATIENTS

A. Mekinian[1], L. Biard[2], L. Dagna[3], P. Jégo[4], C. Salvarani[5], M. Sergey[6], O. Espitia[1], S. Sciascia[7], P. Hernan[8], P. Cacoub[1], O. Fain[1], D. Saadoun[9]on behalf of TAK FRENCH GROUP. *[1]Saint Antoine, Internal Medicine, Paris, France; [2]Saint Antoine, SDF, Paris, France; [3]Saint Antoine, QF, Paris, Italy; [4]Saint Antoine, SFD, Paris, France; [5]Saint Antoine, Internal Medicine, Itale, Italy; [6]Saint Antoine, Internal Medicine, Moscou, Russian Federation; [7]Saint Antoine, Internal Medicine, Paris, Italy; [8]Saint Antoine, Internal Medicine, Paris, Spain; [9]Pitie, Internal Medicine, Paris, France*

Background: In this large worldwide TAK registry, we report 209 patients treated with TNF-α antagonists and tocilizumab aiming to compare their safety and efficacy, and determine the predictive factors of treatment response and relapse.
Objectives: To assess safety and efficacy of TNF-α antagonists and tocilizumab in patients with Takayasu arteritis (TAK).
Methods: We conducted a retrospective multicenter study in referral centers from France, Italy, Spain, Israel, Japan, Tunisia and Russia about biological-targeted therapies in TAK during the period from January 2017 to September 2019 for the data collection.
Results: Two-hundred nine patients with TAK [median age of 29 years [7-62], and 186 (89%) females] were included. They received either TNF-α antagonists [n=132 (63%) with 172 lines; infliximab (n=109), adalimumab (n=45), golimumab (n=8), certolizumab (n=6) and etanercept (n=5)], or tocilizumab [n=77 (37%) with 121 lines; intravenous and subcutaneous in 95 and 26 cases, respectively]. A complete response at 6 months was evidenced in 101/152 (66%) on TNF-α antagonists and 75/107 (70%) on tocilizumab, respectively. Age ≥ 30 years [OR= 2.09 [1.09; 3.99]] was associated with complete response, whereas vascular signs [0.26 [0.1;0.65]], baseline prednisone ≥ 20 mg/day [0.51 [0.28;0.93]] were negatively associated with the complete response to TNF-α antagonists or tocilizumab. During a median follow-up of 36 months, 103 relapses were noted. Supra-aortic branches and thoracic aorta involvements [HR 2.44 (1.06;5.65) and 3.66 (1.18;11.4), respectively], and systemic signs at baseline [HR 2.01 (1.30;3.11)] were significantly associated with relapse. The cumulative incidence of treatment discontinuation and relapse were similar in TNFα antagonists and tocilizumab. Fifty-eight (20%) adverse effects occurred on biological-targeted therapies of whom 37 (21%) and 21 (17%), (p=0.4) on TNF-α antagonists and tocilizumab, respectively
Conclusion: This large multicenter study shows high efficacy of biological-targeted treatments in refractory TAK. Efficacy, relapse and drug retention rate were equivalent with TNF-α antagonists and tocilizumab.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2843

OP0069 THE ROLE OF POSITRON EMISSION TOMOGRAPHY/ COMPUTED TOMOGRAPHY (PET/CT) IN DISEASE ACTIVITY ASSESSMENT IN PATIENTS WITH LARGE VESSEL VASCULITIS

E. Galli[1], F. Muratore[2], L. Boiardi[2], M. I. Casali[3], A. Versari[3], G. Besutti[4], L. Spaggiari[4], P. Mancuso[5], P. Giorgi Rossi[5], C. Salvarani[1,2]. *[1]University of Modena and Reggio Emilia, Department of Rheumatology, Modena, Italy; [2]Rheumatology Unit, Azienda USL-IRCCS di Reggio Emilia, Department of Specialistic Medicine, Reggio Emilia, Italy; [3]Nuclear Medicine Unit, Azienda USL-IRCCS di Reggio Emilia, Department of Oncology and Advanced Technology, Reggio Emilia, Italy; [4]Radiology Unit, Azienda USL-IRCCS di Reggio Emilia, Department of Imaging and Laboratory Medicine, Reggio Emilia, Italy; [5]Epidemiology Unit, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Department of Epidemiology Service, Reggio Emilia, Italy*

Background: Assessment of disease activity in large vessel vasculitis (LVV) is still an unmet need. PET Vascular Activity Score (PETVAS) is a new composite score aimed at quantifying the overall inflammatory burden by adding together PET qualitative visual scores (0-3, according to Meller) in nine selected arterial regions (1). In two independent cohorts, PETVAS showed to be effective in discriminating between patients with clinically active and inactive vasculitis.
Objectives: To assess the role of PET/CT and the performance of PETVAS in differentiating between clinically active and inactive vasculitis in a single center cohort of patients with LVV.
Methods: One-hundred patients with radiographic evidence of LVV were enrolled by the Rheumatology Unit of Reggio Emilia Hospital (Italy) between June 2007 and September 2020. All subjects underwent full clinical, laboratory and imaging evaluation (including PET/CT) at baseline, annually and when a relapse was suspected. Medical records of recruited patients were retrospectively reviewed from baseline visit until 30 September 2020, last follow-up or death.
For each PET/CT test, the nuclear medicine physician's interpretation of scans (active/inactive vasculitis) was compared with disease activity clinical judgement (active disease/remission). The latter was based on comprehensive signs/symptoms assessment, laboratory and imaging (excluding PET/CT) data and was considered the reference standard.
For each PET/CT scan, PETVAS score was calculated and its performance in discriminating between patients with active and inactive disease was compared to clinical judgement.
Results: In the study period 100 LVV patients [51 giant cell arteritis (GCA), 49 Takayasu arteritis (TAK)] underwent a total of 474 PET scans. Nuclear medicine physician's interpretation of PET/CT was able to discriminate between patients in clinically active LVV (n 167) and those in clinical remission (n 307) with a sensitivity of 60% (95% CI, 51 to 69%) and a specificity of 80% (95% CI, 75 to 84%). The following sensitivity and specificity values were found in LVV subgroups: 73% (95% CI, 59 to 84%) and 77% (95% CI, 70 to 83%) for TAK, and 51% (95% CI, 38 to 63%) and 82% (95% CI, 76 to 88%) for GCA, respectively.
LVV patients with higher PETVAS scores were more frequently classified as having active disease: age and sex adjusted OR 1.15 (95% CI, 1.11 to 1.19), p<0.0001. Similar results were found in LVV subgroups, [age and sex adjusted OR 1.12 (95% CI, 1.08 to 1.17) for GCA and 1.22 (95% CI, 1.14 to 1.31) for TAK, all p<0.0001].
The area under receiver operating characteristics (ROC) curve (AUC) of PETVAS in differentiating between clinically active and inactive LVV was 0.73 (95% CI, 0.68 to 0.79). Similar results were found in LVV subgroups, [0.70 (95% CI, 0.62 to 0.78) for GCA, and 0.79 (95% CI, 0.71 to 0.87) for TAK]. A PETVAS ≥10 provided 61% sensitivity and 80% specificity in differentiating between clinically active and inactive LVV (52% sensitivity and 82% specificity in GCA subgroup and 73% sensitivity and 78% specificity in TAK subgroup).
Conclusion: In our cohort PET/CT has shown to be useful in monitoring LVV disease activity.
PETVAS seems to be a reliable tool in helping clinicians to discriminate between LVV patients with active disease and those in remission.
REFERENCES:
[1] Grayson PC, Alehashemi S, Bagheri AA, Civelek AC, Cupps TR, Kaplan MJ, Malayeri AA, Merkel PA, Novakovich E, Bluemke DA, Ahlman MA. 18 F-Fluorodeoxyglucose-Positron Emission Tomography as an Imaging Biomarker in a Prospective, Longitudinal Cohort of Patients with Large Vessel Vasculitis. Arthritis Rheumatol. 2018 Mar;70(3):439-449. doi: 10.1002/art.40379. Epub 2018 Feb 6. PMID: 29145713; PMCID: PMC5882488.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3713

OP0070 ONSET TO DIAGNOSIS TIME PREDICTS SURVIVAL RATE IN TAKAYASU ARTERITIS

A. Popov[1], I. Borodina[2], L. Shardina[3]. *[1]Ural State Medical University, Hospital Therapy and Urgent Medical Care Service, Ekaterinburg, Russian Federation; [2]Sverdlovsk Regional Clinical Hospital 1, Therapy, Yekaterinburg, Russian Federation; [3]Ural State Medical University, Higher Medical Nurse and Social Education, Yekaterinburg, Russian Federation*

Background: Takayasu arteritis (TA) is large vessel vasculitis. In spite of relatively high 5 to 15 years survival rate, TA affects young persons and causes major cardiovascular events, disability and preterm deaths [1]. Nowadays, though new

high-resolution visualization and effective treatment options are available, quite a large number of TA patients remain undiagnosed and untreated for years [2].
Objectives: To assess the influence of timely TA diagnosis and treatment initiation on the survival rate and cardiovascular events risk.
Methods: A retrospective cohort study included 183 patients (139 females, 44 males), enrolled during the period from 1979 to 2018 after TA diagnosis verification according to ACR1990 criteria [3]. All subjects have been followed up at the Sverdlovsk Regional Clinical Hospital 1. Cox regression model was used to compare survival rate.
Results: By enrollment, females median age was 35 [25%-75%: 24 - 44] and in males median age was 34 [26 -42]. Median time duration from the first symptoms onset to the diagnosis verification was 3 [1-7] years in females and [1.5 - 8] years in males. The most common affected arteries were subclavian (55%), carotid (53%), and renal (42%). 5-year survival rate was 92%; 10-year survival rate was 90%; 15-year survival rate was 80%. The median term of survival was 34 [20 - 41] years. 31 deaths (18 males and 13 females) occurred during the follow-up period. Median age of death was 36 [32-44] in females, and 50 [40-57]) in males. The average disease course duration at the time of death was 9.25 years, median term being 6.5 [3-16] in females and 5 [3-10] in males. Also a total of 72 cardiovascular events were recorded during the follow-up period: 27 in men and 45 in women. The median duration of AT course by the development of the first ever event was 10 (5 -20). There were 24 cases of ischemic stroke, 3 transient ischemic attacks, 4 cases of hemorrhagic stroke. Median age of the first ever event was 38 (30 - 49.5). Time duration 4 years or more from AT symptoms onset to diagnosis was associated with significantly more frequent cardiovascular events (OR 1.8; 95% CI 1.07 – 3.34); and premature deaths (see table) by the 5^{th} year of follow up (OR 2.9; 1.27- 6.55).
Conclusion: In a retrospective cohort, time duration 4 years or more from TA symptoms onset to diagnosis verification was associated with higher risk of cardiovascular events and lower survival rate.
REFERENCES:
[1] Mirouse C. et al. Ann. Rheum. Dis. 2018; 77(2): 10-48
[2] Dejaco C. et al. Ann. Rheum. Dis. 2018;77: 636-643
[3] Arend W.P. et al. Arthritis Rheum. 1990; 3(8): 1129-1134.
Disclosure of Interests: Artem Popov Speakers bureau: Novartis, Menarini, AstraZeneca, Pfizer, Severnaya Zvezda, Romepharm, Irina Borodina: None declared, Lubov Shardina: None declared
DOI: 10.1136/annrheumdis-2021-eular.3964

Like a gearwheel: HPR's research, education, and practice

OP0071-HPR **PILOT IMPLEMENTATION OF ENHANCEMENTS IN SUPERVISED GROUP EXERCISE FOR PEOPLE WITH AXIAL SPONDYLOARTHRITIS (AXSPA) IN THE NETHERLANDS**

B. Hilberdink[1], F. Van der Giesen[2], T. P. M. Vliet Vlieland[1], L. Van Bodegom-Vos[3], S. Van Weely[1]. [1]*Leiden University Medical Center, Department of Orthopaedics, Rehabilitation and Physical Therapy, Leiden, Netherlands*; [2]*Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; [3]*Leiden University Medical Center, Department of Biomedical Data Sciences, section Medical Decision Making, Leiden, Netherlands*

Background: Supervised group exercise (SGE) for people with axSpA is widely available in the Netherlands [1]. Its contents have barely changed over the past 30 years, despite new evidence-based insights to improve the quality of SGE [1,2].
Objectives: To evaluate the process and effect of the implementation of enhancements in SGE for people with axSpA in the Netherlands.
Methods: This implementation study was executed in four regions, organising nine axSpA-specific SGE classes. The implemented enhancements included: 1. Exercise personalisation based on periodic assessments, including the 6-Minute Walk Test (6MWT) and the Ankylosing Spondylitis Performance Index (ASPI; improved/not improved); 2. High intensity aerobic exercise including intensity monitoring (e.g. by heartrate or BORG-scale); 3. Group education on home exercise and physical activity (e.g. promotion of an app). The implementation strategy was executed over a period of one year and consisted of a one-day training for the supervisors and bimonthly telephone support.
To evaluate the implementation effect, a survey was sent to 95 SGE participants, including two questions evaluating changes in the programme and in own functioning, as well as the 'ASAS Health Index' (ASAS HI) and the 'Short Questionnaire to Assess Health-enhancing physical activity' (SQUASH), which were also administered at baseline. In addition, the data from the periodic assessments (6MWT and ASPI) were used. Changes were analysed with the Wilcoxon Signed-Rank Test.
To evaluate the implementation process, apart from specific questions in the patient survey, semi-structured interviews with supervisors from each region were conducted.
Results: The survey was returned by 60/95 (63%) SGE participants (72% male, median age 60 years).
Effects: As shown in Table 1, 33% experienced improved functioning, 37% improved performance on ASPI and the improvements on 6MWT were statistically significant, $p < .05$, whereas there were no significant changes in ASAS HI and SQUASH.

Table 1.

	SGE Participants (n=60)
Effect evaluation	
Self-reported improvements in functioning, n (%)	20/60 (33)
Change in 6MWT score, median (IQR)	10 (-20;62)*
Improved on ASPI, n (%)	20/54 (37)
Change in ASAS HI score, median (IQR)	0 (-1;1.9)
Change in number of days with exercise (SQUASH), median (IQR)	0 (-1;2)
Evaluation of enhancements	
Satisfied with overall programme changes, n (%)	35/60 (58)
Satisfied with amount of exercise personalisation, n (%)	51/58 (88)
Assessment is applied, n (%)	50/58 (86)
Assessment is favourable, n (%)	47/50 (94)
Satisfied with amount of aerobic exercise, n (%)	39/56 (70)
Satisfied with exercise intensity, n (%)	44/57 (77)
Heartrate monitoring is applied, n (%)	29/59 (49)
Heartrate monitoring is favourable, n (%)	27/29 (93)
Familiar with axSpA-specific home exercise app, n (%)	12/56 (21)
Exercises at home using the app, n (%)	1/56 (2)

*$p < .05$

Process: The semi-structured interviews with the SGE supervisors (n=4, 25% male, aged 28-56 years, SGE experience 8-30 years) showed that: 1. exercise personalisation was difficult and periodic assessments were only maintained in two regions; 2. all regions increased focus on high intensity aerobic exercise and three monitored intensity; 3. none provided structural group education on home exercise. Table 1 shows that the majority of participants was satisfied with the overall programme changes, the personalisation, the assessments and the high intensity aerobic exercise and that heartrate monitoring and education on a home exercise app were applied in less than half of the participants.
Conclusion: After a training for SGE supervisors and telephone support, a set of enhancements was only partially implemented. However, the majority of participants was satisfied with applied changes and about a third improved functioning. For a nationwide implementation, a more extensive strategy addressing specific barriers is warranted.
REFERENCES:
[1] Hilberdink B, et al. Rheumatol Int. 2021;41(2):391-401.
[2] Millner JR, et al. Semin Arthritis Rheum. 2016;45(4):411-427.
Acknowledgements: The authors thank The Dutch Arthritis Society and all participants, coordinators, boards, and guiding therapists from the four included SGE regions.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.739

New toys in rheumatology: single cell RNA and epigenetic sequencing, the holy grail?

OP0072 **SINGLE CELL SEQUENCING REVEALS CLONALLY EXPANDED CYTOTOXIC CD4+ T CELLS IN THE JOINTS OF ACPA+ RA PATIENTS**

A. Argyriou[1], M. H. Wadsworth II[2], A. Lendvai[1], S. Christensen[2], A. Hensvold[1,3], C. Gerstner[1], K. Kravarik[2], A. Winkler[2], V. Malmström[1], K. Chemin[1]. [1]*Division of Rheumatology, Center for Molecular Medicine (CMM), Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden*; [2]*Inflammation & Immunology Research Unit, Pfizer Inc., Cambridge, MA, United States of America*; [3]*Center for Rheumatology, Academic Specialist Center, Stockholm Health Region, Stockholm, Sweden*

Background: CD4+ T cells with cytotoxic functions (CD4+ CTL) have gained attention in recent years. Accumulating evidence supports their importance in defense against human viral infections such as CMV[1], EBV[2], dengue[3], HIV[4, 5] and SARS-CoV-2[6]. Moreover, expansion of so called CD28null cytotoxic CD4+ T cells have been reported in the blood of patients with rheumatic diseases such as rheumatoid arthritis (RA)[7], myositis[8] and vasculitis[9] as well as in cardiovascular diseases[10].
Objectives: Here, we aimed to investigate the presence and clonal expansion of CD4+ CTL in the peripheral blood (PB) and synovial fluid (SF) of RA patients using single cell technologies.

Methods: We assessed the expression of cytotoxic effector molecules and transcription factors in CD4+ T cells in synovial fluid (n=21) and paired peripheral blood (n=16) from ACPA- and APCA+ RA patients by multi-parameter flow cytometry. We performed single cell sequencing, in combination with 5´ TCRab sequencing, on purified CD4+ T cells from the peripheral blood (PB) and synovial fluid (SF) of ACPA+ RA patients (n=7).
Results: Flow cytometry experiments show that Granzyme-B+ Perforin-1+ CD4+ CTL are significantly increased in the SF of ACPA+ RA patients as compared to ACPA- RA patients (p=0.0072). The presence of CD4+ CTL could be confirmed by single cell sequencing in SF of each ACPA+ RA patient tested (n=7). Moreover, we found that the adhesion G-protein coupled receptor GPR56 is selectively expressed on the recently described peripheral helper (T_{PH}) T-cell subset[11] and associates with the expression of tissue resident memory markers LAG-3, CXCR6 and CD69. In blood, we confirmed a previous report[12] showing that GPR56 delineates cytotoxic CD4+ T cells. Finally, expanded TCR clones expressing cytotoxic effector molecules were identified in synovial fluid of ACPA+ RA patients and, for some patients, in their corresponding peripheral blood.
Conclusion: We identified GPR56 as a marker of T_{PH} cells in SF of ACPA+ RA patients that associates with tissue residency receptors. The combination of single cell sequencing and multi-parameter flow cytometry highlights the importance of CD4+ CTL in ACPA+ RA and suggests a potential therapeutic target (Figure 1).
REFERENCES:
[1] Casazza J. P. et *al*., *J Exp Med* **2006,** *203* (13), 2865-77.
[2] Landais E. et al., *Blood* **2004,** *103* (4), 1408-16.
[3] Kurane I. et *al*. *J Exp Med* **1989,** *170* (3), 763-75.
[4] Appay V. et *al*. *J Immunol* **2002,** *168* (11), 5954-8.
[5] Juno J. A. et *al*. *Front Immunol* **2017,** *8*, 19.
[6] Meckiff B. J. et *al*. *Cell* **2020,** *183* (5), 1340-1353 e16.
[7] Schmidt D. et *al*. *J Clin Invest* **1996,** *97* (9), 2027-37.
[8] Fasth A. E. et *al*. *J Immunol* **2009,** *183* (7), 4792-9.
[9] Moosig F. et *al*. *Clin Exp Immunol* **1998,** *114* (1), 113-8.
[10] Sato K. et *al*. *J Exp Med* **2006,** *203* (1), 239-50.
[11] Rao D. A., et *al*. *Nature* **2017,** *542* (7639), 110-114.
[12] Peng Y. M. et *al*. *J Leukoc Biol* **2011,** *90* (4), 735-40.
Acknowledgements: We thank the patients who donated samples and the medical staff at the Rheumatology Clinic of Karolinska University Hospital. Julia Boström, Gloria Rostvall, and Susana Hernandez Machado are acknowledged for organizing the sampling, storage, and administration of biomaterial. This study is supported by grants from Dr. Margaretha Nilssons, the Nanna Svartz, the Ulla and Gustaf af Ugglas foundations and the Swedish association against rheumatism.

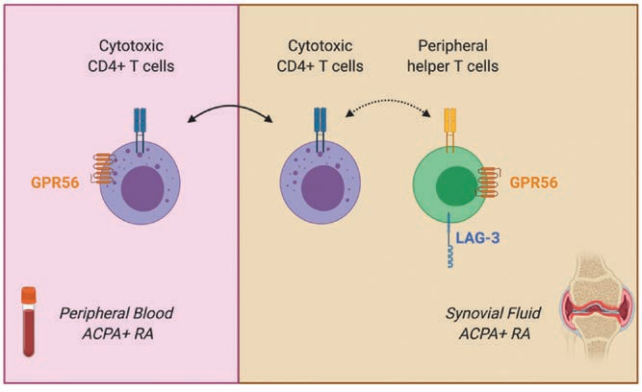


Figure 1. Cytotoxic CD4+ T cells and GPR56+ peripheral helper CD4+ T cells are two T-cell subsets identified in SF of ACPA+ RA patients.

Disclosure of Interests: Alexandra Argyriou: None declared, Marc H Wadsworth II Employee of: Pfizer, Inc, Cambridge, MA 02139, United States, Adrian Lendvai: None declared, Stephen Christensen Employee of: Pfizer, Inc, Cambridge, MA 02139, United States, Aase Hensvold: None declared, Christina Gerstner: None declared, Kellie Kravarik Employee of: Pfizer, Inc, Cambridge, MA 02139, United States, Aaron Winkler Employee of: Pfizer, Inc, Cambridge, MA 02139, United States, Vivianne Malmström: None declared, Karine Chemin: None declared
DOI: 10.1136/annrheumdis-2021-eular.1403

OP0073

SINGLE-CELL TRANSCRIPTOMICS UNCOVERS DEFECTIVE BONE MARROW EARLY B CELL DEVELOPMENT IN A SUBSET OF LUPUS PATIENTS ASSOCIATED WITH AGGRAVATED INFLAMMATION

C. Dong[1], X. Gu[1], J. Ji[1], X. Zhang[2], Z. Gu[1]. [1]*Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*; [2]*Institute Pasteur of Shanghai Chinese Academy of Sciences, Key Laboratory of Molecular Virology & Immunology, Shanghai, China*

Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that occurs when the body's immune system attacks own tissues and organs. B cells play a central role in SLE pathogenesis by producing autoantibodies as well as antibody-independent functions. Peripheral B cell abnormality is well known in lupus patients such as expansions of plasmablasts and atypical memory B cells, which are associated with active diseases. However, little is known about the B cell development in the bone marrow of lupus patients.
Objectives: We conduct this survey to explore the disorder of the B cell development in the bone marrow of lupus patients.
Methods: In this study, we have performed the scRNASeq to profile the bone marrow B cell compartment in lupus patients and healthy donors.
Results: We identified that in a subset of lupus patients, the early B cells (proB and preB cells) were strongly decreased, which were confirmed by flow cytometry in an expanded cohort. Furthermore, bone marrow B cells from these patients showed a strong proinflammatory signature revealed by pathway analysis. Interestingly, BCR repertoire analysis showed that the IGHV-4-34 was highly enriched in these patients, indicating an enhanced B cell tolerance defect. Finally, a panel of proinflammatory cytokines (TNF-a, IL-1a, IL-12p70, IFN-g, et al.) were strongly increased in the bone marrow plasma of these patients compared with early B normal patients and healthy donors, confirming a localized proinflammatory microenvironment.
Conclusion: Altogether, the current study has revealed that a defective early B cell development in lupus patients is associated with a more severe B cell tolerance defect and aggravated inflammation, which may shed new light on developing novel therapies by targeting relevant pathways.
REFERENCES:
[1] Min Wang, Hua Chen, Jia Qiu, et al. Antagonizing miR-7 suppresses B cell hyperresponsiveness and inhibits lupus development. J Autoimmun 2020.
[2] A M Jacobi, D M Goldenberg, F Hiepe, et al. Differential effects of epratuzumab on peripheral blood B cells of patients with systemic lupus erythematosus versus normal controls. Ann Rheum Dis, 2008.
Acknowledgements: This work was funded by Special project of clinical medicine of Nantong University (Grant/Award number: 2019LQ001), National Natural Science Foundation of China (Grant/Award number: 81671616, 81871278 and 82071838).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3061

Education

OP0074

A FRAMEWORK OF POTENTIAL INTERVENTIONS TO ACCELERATE GENDER-EQUITABLE CAREER ADVANCEMENT IN ACADEMIC RHEUMATOLOGY

P. V. Ovseiko[1], L. Gossec[2], L. Andreoli[3], U. Kiltz[4], L. Van Mens[5], N. Hassan[6], M. Van der Leeden[7], H. J. Siddle[8], A. Alunno[9], I. Mcinnes[10], N. Damjanov[11], F. Apparailly[12], C. Ospelt[13], I. Van der Horst-Bruinsma[14], E. Nikiphorou[15], K. Druce[16], Z. Szekanecz[17], A. Sepriano[18], T. Avcin[19], G. Bertsias[20], G. Schett[21], A. M. Keenan[8], L. C. Coates[22]on behalf of EULAR Task Force on Gender Equity in Academic Rheumatology. [1]*University of Oxford, Radcliffe Department of Medicine, Oxford, United Kingdom*; [2] *Sorbonne Universite, Institut Pierre Louis d'Epidémiologie et de Santé Publique, INSERM, Paris, France*; [3] *University of Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy*; [4] *Ruhr-University Bochum, Rheumatology, Rheumazentrum Ruhrgebiet, Herne, Germany*; [5]*University of Amsterdam, Clinical Immunology and Rheumatology, Amsterdam Rheumatology and Immunology Center, Academic Medical Center, Amsterdam, Netherlands*; [6] *University of Bristol, Musculoskeletal Research Unit, Bristol, United Kingdom*; [7]*VU University Amsterdam, Rehabilitation Medical Clinic, Amsterdam, Netherlands*; [8]*University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [9]*University of Perugia, Rheumatology Unit, Department of Medicine, Perugia, Italy*; [10]*University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; [11]*University of Belgrade, Faculty of Medicine, Belgrade, Serbia*; [12]*University of Montpellier, INSERM, IRMB, Montpellier, France*; [13]*University Hospital Zurich, University of Zurich, Center of Experimental Rheumatology, Department of Rheumatology, Zurich, Switzerland*; [14]*Amsterdam University Medical Center, Location VU Medical Center, Department of Rheumatology, Amsterdam, Netherlands*; [15]*King's College London, Centre for Rheumatic Diseases, School of Immunology and Microbial Sciences, London, United Kingdom*; [16]*University of Manchester, Arthritis Research UK Centre for Epidemiology, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; [17]*University of Debrecen, Division of Rheumatology, Faculty of Medicine, Debrecen, Hungary*;

[18]*Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; [19]*University Children's Hospital, University Medical Center Ljubljana, Department of Allergology, Rheumatology and Clinical Immunology, Ljubljana, Slovenia*; [20]*University of Crete Medical School, Department of Rheumatology, Clinical Immunology and Allergy, Heraklion, Greece*; [21]*Friedrich-Alexander-University Erlangen-Nuremberg (FAU), Universitätsklinikum Erlangen, Department of Internal Medicine 3, Erlangen, Germany*; [22]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*

Background: A growing number of professional societies in clinical and medically related disciplines investigate evidence, make recommendations, and take action to advance gender equity. Evidence on women's advancement and leadership in the context of the European Alliance of Associations for Rheumatology, EULAR, is limited [1].
Objectives: The objective of the EULAR Task Force on Gender Equity in Academic Rheumatology was to establish the extent of the unmet need for support of female rheumatologists, health professionals and non-clinical scientists in academic rheumatology and develop a framework to address this through EULAR and Emerging EULAR Network (EMEUNET).
Methods: Potential interventions to accelerate gender-equitable career advancement in academic rheumatology were gathered from a narrative review of the relevant literature, expert opinion of a multi-disciplinary Task Force (comprised of 23 members from 11 countries), data from the surveys of EULAR scientific member society leaders, EULAR and EMEUNET members, and EULAR Executive Committee members. These interventions were rated by Task Force members, who ranked each according to perceived priority on a five-point numeric scale from 1 = very low to 5 = very high.
Results: A framework of 29 potential interventions was formulated, which covers six thematic areas, namely, EULAR policies, advocacy and communication, EULAR Congress and associated symposia, training courses, mentoring/peer support, and EULAR funding (Figure 1).

Theme	Intervention	Level of priority, Mean	SD
EULAR policies	Requirements for EULAR Centres of Excellence to demonstrate commitment to gender equity	4.5	0.8
	Gender-equitable EULAR committees, working groups, and task forces	4.4	0.8
	Gender-equitable grants committees	4.0	0.9
	Gender-equitable editorial boards and peer-review in rheumatology journals	3.9	1.0
Advocacy and communication	Campaigns to increase visibility of female role models and promote women's leadership	4.5	0.7
	Raising awareness of unconscious bias and gender equity issues in rheumatology	4.3	1.0
	Promoting gender-sensitive clinical practice, research and training	4.1	1.0
	Engaging national rheumatology groups to develop country-specific support	3.6	1.2
EULAR Congress and associated symposia	Monitoring gender equity of chairs and invited speakers (invitees and acceptances)	4.6	0.7
	Increasing visibility of female role models	4.4	0.7
	Family- and child-friendly policies	4.1	1.2
	Code of Conduct expressing and enforcing the values of diversity and inclusion	4.1	0.9
	EULAR no male only panel pledge	4.0	1.1
	Collating a register of female experts in field	3.5	1.3
Training courses (open to men and women)	Leadership skills training	4.2	0.7
	Training and support for writing grant applications	4.0	0.8
	High-impact scientific writing masterclasses	3.8	1.0
	Effective work-life balance management training	3.8	0.9
	Speaking/presentation/communication skills training	3.7	0.9
	Unconscious bias training	3.7	1.0
	Promotion and salary negotiation training	3.6	1.0
Mentoring/ peer support (open to men and women)	Peer to peer mentorship programmes	4.5	0.6
	Establishing a EULAR network for women in rheumatology	4.2	1.1
	Information on training/career pathways	4.0	1.0
	Senior sponsorship programmes	3.8	1.0
	Effective work-life balance training	3.6	1.1
EULAR funding	Monitoring gender equity in EULAR funding	4.3	0.7
	Career grants for mid/senior women academics	4.0	1.1
	Funding calls for research on gender-sensitive clinical practice, research, and training	4.0	1.1

Figure 1. A framework of potential interventions with the levels of priority, mean and standard deviation (SD)

Conclusion: The framework provides structured interventions for accelerating gender-equitable career advancement in academic rheumatology.
REFERENCES:
[1] Andreoli L, Ovseiko PV, Hassan N, et al. Gender equity in clinical practice, research and training: Where do we stand in rheumatology? Joint Bone Spine 2019;86(6):669-72.
Acknowledgements: The task force is grateful to EULAR for funding this activity under project number EPI 024.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1765

OP0075

EVALUATION OF A VIRTUAL REALITY TEACHING CONCEPT FOR MEDICAL STUDENTS DURING THE SARS-COV-2 PANDEMIC

A. Pfeil[1], F. Marcus[2], T. Hoffmann[1], P. Klemm[3], P. Oelzner[1], U. Müller-Ladner[3], A. Hueber[4], U. Lange[3], G. Wolf[1], G. Schett[5,6], D. Simon[5,6], A. Kleyer[5,6]. [1]*Jena University Hospital – Friedrich Schiller University Jena, Department of Internal Medicine III, Jena, Germany*; [2]*Jena University Hospital – Friedrich Schiller University Jena, Department of Internal Medicine I, Jena, Germany*; [3]*Campus Kerckhoff, Justus-Liebig University Gießen, Department of Rheumatology, Immunology, Osteology and Physical Medicine, Bad Nauheim, Germany*; [4]*Sozialstiftung Bamberg, Section Rheumatology, Bamberg, Germany*; [5]*University Hospital Erlangen, Department of Internal Medicine 3, Rheumatology and Immunology, Erlangen, Germany*; [6]*University Hospital Erlangen, German Center Immune Therapy, Erlangen, Germany*

Background: The ongoing COVID-19 pandemic has disrupted face-to-face teaching of medical students and forced efforts in finding alternative approaches. In order to help maintain high-quality education, a new virtual reality (VR)-based concept for training medical students in rheumatic and musculoskeletal diseases (RMD) has been developed. This VR training concept is based on the integration of real patient data with two- and three-dimensional visualized pathological joints from X-ray and computed tomography generated images.
Objectives: To evaluate the practicability and acceptance of the VR training application in the digital curricular education of medical students during the COVID-19 pandemic.
Methods: A short refresher lecture on rheumatic diseases (duration 60 minutes) was followed by presenting the VR training concept to the students. The VR training concept included the demonstration of three virtual patients with early rheumatoid arthritis, rheumatoid arthritis psoriatic arthritis regarding the symptoms, current medical problems, disease patterns at the imaging (conventional radiographs and high-resolution computed tomography) and therapy options. The practicability and acceptance of the VR was evaluated by medical students using a survey.
Results: The study encompassed 237 medical students (163 female, 73 male, one diverse, age range 20 to 40 years). 72 % of the participants rated the virtual teaching as good or very good. 87 % presented an expanded knowledge for rheumatoid arthritis and psoriatic arthritis through the VR. Moreover, 91 % reported that the lecture provided a deeper understanding of RMD. Furthermore, 60 % of the students asked for additional courses by VR.
Conclusion: The study highlighted the usefulness of innovative VR tools for teaching medical students digitally about RMD. VR applications can be a complementary educational modality for medical students, especially during the COVID-19 pandemic, to provide students with the best possible clinical experience while ensuring that patient, student, and staff safety is not compromised.

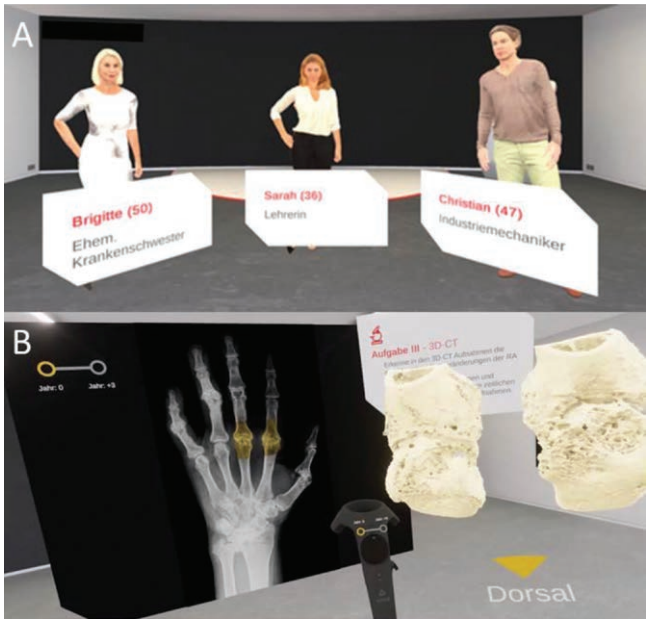


Figure 1. ***A*** Screen view of virtual reality included three virtual patients with early rheumatoid arthritis (RA), RA, and psoriatic arthritis (PsA) and ***B*** demonstration of structural damage in RA and PsA using hand X-ray and high-resolution quantitative computed tomography images.

Disclosure of Interests: Alexander Pfeil Speakers bureau: Lilly Pharma Deutschland GmbH, Franz Marcus: None declared, Tobias Hoffmann: None declared, Philipp Klemm Consultant of: Lilly Pharma Deutschland GmbH, Peter Oelzner: None declared, Ulf Müller-Ladner Consultant of: Lilly Pharma Deutschland GmbH, Axel Hueber Consultant of: Lilly Pharma Deutschland GmbH, Uwe Lange: None declared, Gunter Wolf: None declared, Georg Schett: None declared, David Simon Consultant of: Lilly Pharma Deutschland GmbH, Arnd Kleyer Consultant of: Lilly Pharma Deutschland GmbH
DOI: 10.1136/annrheumdis-2021-eular.2578

OP0076

HOW TO SELF-EXAMINE FOR TENDER AND SWOLLEN JOINTS: CO-DEVELOPMENT OF A TRAINING VIDEO FOR PEOPLE WITH RHEUMATOID ARTHRITIS

C. Sharp[1,2], K. Staniland[3], T. Cornell[4], W. Dixon[3,5]. [1]*The University of Manchester, Centre for Epidemiology Versus Arthritis, & Centre for Primary Care and Health Services Research, Manchester, United Kingdom*; [2]*Manchester Royal Infirmary, Kellgren Centre for Rheumatology, Manchester, United Kingdom*; [3]*The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [4]*Poole Hospital, Rheumatology, Poole, United Kingdom*; [5]*Salford Royal NHS Foundation Trust (Formerly Hope Hospital), Rheumatology, Salford, United Kingdom*

Background: COVID-19 has catalysed the transformation of healthcare services, with outpatient services increasingly dependent upon remote models of care. Healthcare professionals now have to make clinical assessments based on remote patient examinations. The number of tender and swollen joints a patient has drives decision-making in RA, making it particularly important that people with RA and HCPs have a shared understanding of these examinations.
Even before remote consultations became widespread, long gaps between clinic visits create challenges in enabling HCPs to form an accurate picture of disease activity over time. The REMORA (REmote MOnitoring of Rheumatoid Arthritis) app aims to address this issue by asking people with RA to track disease activity, including counting the number of tender or swollen joints, weekly(1). Data are integrated into the electronic patient record for clinicians to access with patients during clinical consultations. As part of the supporting materials for the REMORA app, we planned to develop a video to train people with RA how to examine their own joints. This video may now help meet the need created by the recent expansion in remote consultations.
Objectives: To describe the co-production, implementation and evaluation of a video to train patients how to examine their own joints.
Methods: The need for the video to fill a current gap in patient education was identified by the REMORA patient and public involvement and engagement (PPIE) group. A core working group comprising the PPIE lead, a nurse consultant, rheumatology clinicians, project and communications managers was formed. A storyboard was drafted and feedback gained from the PPIE group and wider REMORA team. Images were sourced from licenced suppliers, or co-developed with the PPIE group where necessary. No ethical approval was required as the PPIE group lead was acting as an equal member of the research term. Written informed consent was gained from video participants. Filming took place between two national lockdowns during the COVID-19 pandemic, providing a challenge to ensure social distancing and requiring the use of masks.
Results: A 15 minute video to train people with RA to self-examine for tender and swollen joints was developed. An introduction outlining the rationale behind self-examination is followed by a nurse consultant coaching an RA patient in individual joint self-examination. Shoulders, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints and knees are included, all of which are counted in disease activity scores.
Early feedback from stakeholders has been overwhelmingly positive. The video will be publicly available on YouTube from February 2021. A survey of patients and HCPs aims to obtain more formal feedback on the video, with a view to a further iteration, if required. Leading national organisations in rheumatology will promote the video, as it supports national programmes including the British Society for Rheumatology national early inflammatory arthritis audit and ePROMS (electronic patient report outcome measure) platform, both of which include entry of patient reported tender and swollen joint counts.
Conclusion: This video was co-designed by people with RA, aiming to support self-examination of tender and swollen joint counts. Hits on YouTube and survey responses will help assess its impact. Evaluation to assess whether the video affects patients' ability to self-examine for tender and swollen joints before and after watching is planned. We hope the video will support remote consultations and help people with arthritis to better understand and self-manage their arthritis, and to have shared decision making conversations with their clinicians.

REFERENCES:

[1] Austin L, Sharp CA, van der Veer SN, Machin M, Humphreys J, Mellor P, et al. Providing 'the bigger picture': benefits and feasibility of integrating remote monitoring from smartphones into the electronic health record: findings from the Remote Monitoring of Rheumatoid Arthritis (REMORA) study. Rheumatology. 2020;59(2):367-78.

Disclosure of Interests: Charlotte Sharp: None declared, Karen Staniland: None declared, Trish Cornell Shareholder of: shares in Abbvie, Employee of: Abbvie, working as a Rheumatology Nurse Consultant, Will Dixon Consultant of: Google and Abbvie, unrelated to this work.

DOI: 10.1136/annrheumdis-2021-eular.1990

OP0077

THE EMERGING EULAR NETWORK (EMEUNET): AN INTERNATIONAL SURVEY REFLECTING ON A TEN-YEAR JOURNEY

M. de Hooge[1], M. Hanlon[2], A. Alunno[3], A. Sepriano[4], K. Lauper[5], F. Rivellese[6]. [1]*Ghent University Hospital, Rheumatology, Ghent, Belgium*; [2]*Trinity University College, Rheumatology, Dublin, Ireland*; [3]*University of Perugia, Rheumatology, Perugia, Italy*; [4]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [5]*University Hospitals of Geneva, Rheumatology, Geneva, Switzerland*; [6]*Queen Mary University, Rheumatology, London, United Kingdom*

Background: The Emerging EULAR NETwork (EMEUNET), founded in 2009, aims to promote education, foster research collaborations and facilitate the integration of young researchers and rheumatologists within EULAR.
Objectives: After 10 years, we aimed to interview our members to assess how EMEUNET is fulfilling its goals, understand if there are unmet needs and explore new ideas.
Methods: In July 2019 a survey was circulated for 3 months among EMEUNET members via its social media channels. The survey contained 18 closed and 2 open items, in addition to general questions on age, job and country of origin and work.
Results: Out of 124 total respondents, most completed all items (120/124) and only a minority had some missing items (4/124). A little over half of the respondents were female (n=69, 54.8%) and median age was 33y (range 25y-42y). Most respondents were born (n=109, 88.6%) and/or worked in Europe (n=114, 92.7%) (fig. 1), although there was also a representation from extra-European countries, which is in line with the general EMEUNET membership (https://emeunet.eular.org/map.cfm).

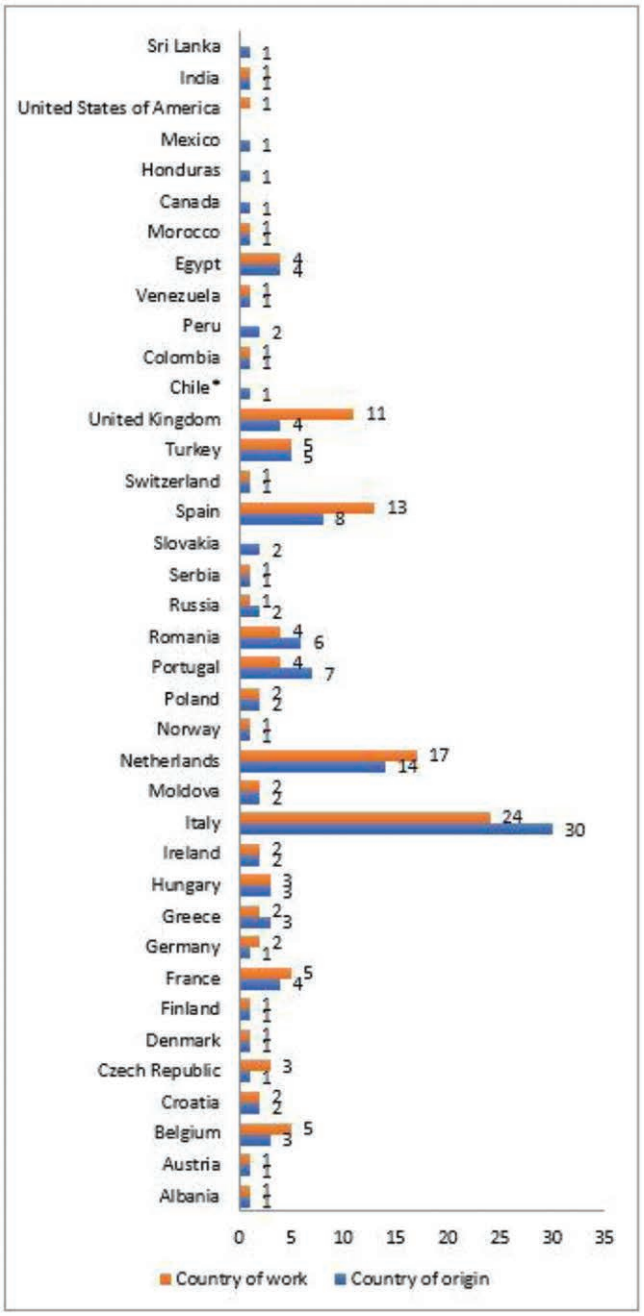


Figure 1. Country of origin and where respondents work at the time of completing the EMEUNET VISE questionnaire.

11 (9.1%) had been EMEUNET members for less than 2 years, 81 (66.9%) for 2-5years and 29 (24.0%) for more than 5 years.
Figure 2 shows a clear link between the respondents' perception of EMEUNET aim(s) and the actual aims of EMEUNET set out in our mission statement (https://emeunet.eular.org/mission_statement.cfm).

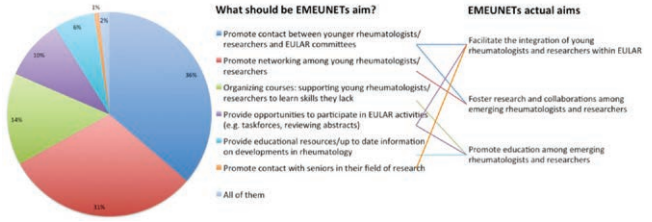


Figure 2. The links between what participants would like to see as EMEUNET aims and the aims of EMEUNET as they are now

Most of the respondents got to know about EMEUNET through a friend/colleague in Rheumatology (n=67, 54.0%), at EULAR/ACR annual conferences (n=32, 25.8%), via social media (n=9, 7.3%), other international meeting (n=6, 4.8%), national Rheumatology meeting (n=6, 4.8%) or via the EMEUNETs country liaisons (n=4, 3.2%).
29 respondents (24%) were part of the EMEUNET working group (WG), 43% (n=53) applied before to be part of the WG, 24% (n=29) never applied and 15% (n=19) did not know what the WG was. Most of the respondents who never applied to the WG thought it to be too time consuming. Only 21 (16.9%) felt there was a subgroup in the WG missing and most of those (n=8, 38.1%) found this should fully focus on research collaborations, which is actually part of the general aims of EMEUNET and a focus of all Working Groups.
Only a relatively small portion of EMEUNET of respondents (<5%) stated to have approached EMEUNET with their ideas. Although 90.2% (n=110) felt that the opportunity to submit new ideas is a good initiative, only 52.5% (n=..) knew that such possibilities exists. This suggests that EMEUNET could do more to make members aware of this possibility. Additionally, while the main reasons for not contacting EMEUNET with an idea were 'not having one' (41.9%) or having 'no time' (34.9%), 20.9% feels their ideas would not be received well, which is another aspect offering room for improvement.
Twice a year, EMEUNET organises networking events (NE) for their members to discuss their work in an informal setting. We found that 56/120 (46.7%) of the respondents prefer a low-budget (<€20) event, including an activity and the possibility to network, accompanied by drinks and bites. This is much in line with EMEUNETs past NE. In addition, past NEs were often mentioned as an example of ideal events.
Conclusion: Awareness on EMEUNET often comes from colleagues and international conferences in rheumatology, which coincides with one of the focuses of EMEUNET to increase visibility in the last 10 years. Expectations about NE are in line with the previously organised NE.
Areas for improvement are dissemination of information on the EMEUNET WG, the possibility to submit ideas -which is open to all members- and the increased focus on research collaboration, an aspect on which we are actively working as EMEUNET is fully engaged with the newly launched EULAR Virtual Research Centre.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2706

OP0078 HIGH MEDIAN NERVE LESION SECONDARY TO SEVERE GIANT CELL ARTERITIS (GCA)

K. Iqbal[1,2], J. Miller[3], M. Lai[4], M. Charnley[2], M. Meraj[2], B. Thompson[1,2].
[1]*Newcastle University, Faculty of Medical Sciences, Newcastle upon Tyne, United Kingdom*; [2]*Freeman Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, Rheumatology, Newcastle upon Tyne, United Kingdom*; [3]*Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Neurology, Newcastle upon Tyne, United Kingdom*; [4]*Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Neurophysiology, Newcastle upon Tyne, United Kingdom*

Background: Giant cell arteritis (GCA) is a systemic vasculitis affecting large to medium-sized vessels. Cranial nerve lesions are frequently documented secondary to GCA, however peripheral nerves are rarely involved.

Objectives: We present an unusual case of a GCA-associated isolated high median nerve palsy.
Methods: Case report.
Results: A 76 year old white British female presented in Spain with three weeks of frontotemporal headaches, mandibular claudication, photopsia and constitutional symptoms, followed by acute-onset right hand paresis and dysaesthesia. Acute-phase reactants were elevated. COVID-19 PCR was negative. Shortly after admission she developed acute bilateral anterior ischaemic optic neuropathy and tongue necrosis with autoamputation. Temporal artery ultrasound and biopsy confirmed GCA. PET-CT showed no evidence of a diffuse large-vessel vasculitis. She was repatriated to the UK for ongoing inpatient care. Upper limb neurophysiology two months later demonstrated an isolated right high median nerve lesion, with reduced median motor responses and absent sensory responses with denervation in extensor carpi radialis. Imaging excluded a central lesion. The timing of her symptoms suggested the lesion was secondary to GCA. Treatment was with tocilizumab, methotrexate and tapering corticosteroids, alongside PEG feeding and careful multi-disciplinary rehabilitation.
Conclusion: We suggest there are two important learning points from this complex case. Firstly, peripheral nerve lesions can occur in GCA, although they are rare. A literature search identified a modest number of case reports of brachial plexus or lower cervical nerve lesions[1,2]. Neurologic manifestations in GCA are attributed to vasculitis of the vasa nervorum, or extension of inflammation from arteries to contiguous nerves[1,2]. The restriction of clinical involvement to the median nerve alone would appear to favour the former mechanism. Functional recovery of neurological deficits is typically partial at best.
Secondly, this case highlights the difficulty faced by clinicians in recognising GCA and the importance of urgent treatment with glucocorticoids. The patient developed GCA during the ongoing COVID-19 pandemic when Spain was the second-worst affected European country (5% seroprevalence; 95% CI 4.7-5.4)[3]. The partial overlap in symptoms between GCA and COVID-19 (e.g. headache, pyrexia, malaise, elevated acute-phase reactants) can cause diagnostic confusion and treatment delay[4]. GCA should be considered in the differential diagnosis of older patients with suspected COVID-19, or the non-specifically unwell elderly patient.
REFERENCES:
[1] Blaise S, et al. Horton's disease revealed by brachial C5 plexopathy [French]. Rev Med Interne. 2005;26(7):578-82.
[2] Merianos P, et al. Giant cell arteritis of the median nerve simulating carpal tunnel syndrome. Hand. 1983;15(3): 249-251.
[3] Pollán M, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet. 2020; 396(10250): 535-544.
[4] Monti S, Delvino P, et al. Impact of delayed diagnoses at the time of COVID-19: increased rate of preventable bilateral blindness in giant cell arteritis. Ann Rheum Dis. 2020;79:1658-1659.

Table 1.

Area/movement	Result
Abductor pollicis brevis	Grade 2 weakness
Opponens pollicis	Grade 4 weakness
Pronator teres/quadratus	Grade 4 weakness
Flexor pollicis longus	Grade 1-2 weakness
Flexor digitorum profundus (digit 2 and 3)	Grade 1-2 weakness
Finger abduction	Preserved
Finger extension	Preserved
Other comments	
Dysaesthesia in distribution of median nerve	

Disclosure of Interests: Kundan Iqbal: None declared, James Miller Speakers bureau: Dr Miller has participated in pharmaceutical-sponsored symposiums previously but not in last five years., Consultant of: Dr Miller has participated in pharmaceutical-sponsored consultancy previously but not in last five years., Ming Lai: None declared, Mia Charnley: None declared, Muhammad Meraj: None declared, Ben Thompson Speakers bureau: Dr Thompson has participated in educational talks for Roche, Novartis, Lilly and UCB., Consultant of: Dr Thompson has participated in advisory boards for Roche, Novartis, Lilly, Gilead, Abbvie and UCB.
DOI: 10.1136/annrheumdis-2021-eular.2043

OP0079 **LIMB GIRDLE MUSCULAR DYSTROPHY TYPE 2B - A RARE MYOSITIS MIMIC**

A. Merriman[1], S. Boyle[1]. *[1]Western General Hospital, Rheumatic Diseases Unit, Edinburgh, United Kingdom*

Background: Proximal muscle weakness with associated raised creatine kinase (CK) commonly leads to referral to Rheumatology for the investigation of Idiopathic Inflammatory Myopathy (IIM). Some genetic myopathies can have a similar presentation with investigations that suggest inflammatory disease, leading to difficulty with accurate diagnosis (Amato & Brown, 2011; Harlan & Mammen, 2019).
Objectives: To describe the case of a patient with Limb Girdle Muscular Dystrophy Type 2B (LGMD2B), whose initial presentation mimicked an inflammatory myopathy.
Methods: Case report.
Results: A 43-year-old patient was reviewed by Rheumatology due to proximal muscle weakness with a raised CK. Muscle biopsy was suggestive of inflammatory myopathy. Therefore, he was started on treatment with corticosteroids. Corticosteroid treatment resulted in no improvement in his weakness or CK. His diagnosis was reviewed, and he was referred to the Neurology and Genetics services. Following molecular genetic analysis, a diagnosis of Limb Girdle Muscular Dystrophy Type 2B was made.
Conclusion: Muscle biopsies can suggest an inflammatory aetiology in some genetic myopathies (Amato & Brown, 2011; Harlan & Mammen, 2019). If a patient with suspected IIM presents with atypical features, or they do not respond as expected to treatment, then consider a genetic myopathy such as LGMD2B as a cause and involve the Neurology and Genetics services in the case.
REFERENCES:
[1] Amato, A. A., & Brown, R. H., Jr. (2011). Dysferlinopathies. *Handb Clin Neurol*, *101*, 111-118. https://doi.org/10.1016/b978-0-08-045031-5.00007-4
[2] Harlan, M & Mammen A. L (2019). Myositis Mimics: The Differential Diagnosis of Myositis. In: R. Aggarwal and C. V. Oddis (Eds.) *Managing Myositis* (pp. 209-223). Springer, Cham.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1251

OP0080 **OSTEOPOIKILOSIS IN PATIENT WITH ANKYLOSING SPONDYLITIS**

V. Omelchenko[1,2], E. Letyagina[1,2], Y. Kurochkina[1], A. Akimova[1], M. Korolev[1,2]. *[1]RICEL - Branch of IC&G SB RAS, Rheumatology Department, Novosibirsk, Russian Federation*; *[2]Novosibirsk State University, Internal Medicine Section, Novosibirsk, Russian Federation*

Background: Osteopoikilosis (OPK) – a rare congenital genetic-mediated benign sclerosing disease of skeleton. OPK is usually clinically asymptomatic and is most often an incidental finding during an X-ray study [1]. The lesions are from 2 to 10 mm and are located in the area of the ischial, pubic bones, metaepiphyseal regions of the tubular bones. The axial skeleton is usually not affected in OPK. As early described, OPK may be associated with inflammatory rheumatic diseases, such as rheumatoid arthritis, spondyloarthritis, reactive arthritis and scleroderma [2–4]. Ankylosing spondylitis is a chronic rheumatic disease from the group of spondyloarthritis with obligatory involvement of the sacroiliac joints and frequent involvement of entheses and peripheral joints. Although a significant mutual influence of OPK and AS has not been proven, their combination can lead to unreasonable over-examination in real clinical practice.
Objectives: To present a clinical case of rare coexisting of osteopoikilosis and ankylosing spondylitis.
Methods: Case report. The patient was treated and examined based on real clinical practice.
Results: A 33-year-old man was admitted to our rheumatology department with a three-year history of inflammation pain in cervical region of spine and hip, knees and shoulder joints and long morning stiffness duration (up to 3 hours). AS was earlier verified based on modified New York criteria (1984) and Nonsteroidal anti-inflammatory drugs were prescribed promptly. On the outpatient basis he also received sulfasalazine and methotrexate due to arthritis and enthesitis. Nevertheless he had high disease activity (ESR 66 mm/h, CRP 77.5 mg/l, BASDAI = 7.5), severely limited range of motion in the cervical, thoracic and lumbar spine, arthritis, enthesitis when he entered in our clinic. He had been treated with secukinumab 150 mg for fourteen months and then he was switched to golimumab 50 mg per month because of lack of efficacy. Low disease activity has now been achieved.
During the assessment of radiographs of the pelvic bones and spine, typical changes of the late stage of ankylosing spondylitis (syndesmophytes, stage 4 sacroiliitis) were revealed at the first visit in our clinic. At the same time, a number of phenomena were discovered that were not related to the course of the AS, which required expanding the differential diagnosis range. The tumor process and endocrine pathologies were excluded. OPK was diagnosed on the basis of characteristic changes in various parts of the skeleton, especially in phalanges, wrists and pelvis bones (fig.1).

Figure 1. OPK spots in phalanges and wrists.

Conclusion: We've reported rare case of AS and OPK coexisting in young patient. The identification of typical radiological phenomena and correct evaluation of clinical data may allow to avoid unnecessary expensive examinations.
REFERENCES:
[1] Carpintero P. et al. Clinical features of ten cases of osteopoikilosis // Clin. Rheumatol. 2004. Vol. 23, № 6. P. 505–508.
[2] Joseph R.O., Thomas J., Shenoy P. Osteopoikilosis and ankylosing spondylitis: Strange bedfellows: A case report // Int. J. Rheum. Dis. 2019. Vol. 22, № 6. P. 1162–1164.
[3] Akgul O. et al. Osteopoikilosis and ankylosing spondylitis: A rare coexistence and good response to TNF blocker adalimumab // Int. J. Rheum. Dis. 2015. Vol. 18, № 3. P. 372–374.
[4]Ruaro B. et al. Coexistence of osteopoikilosis with seronegative spondyloarthritis and Raynaud's phenomenon: first case report with evaluation of the nailfold capillary bed and literature review. // Reumatismo. 2012. Vol. 64, № 5. P. 335–339.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2267

OP0081 **A CASE OF ATYPICAL MYCOBACTERIUM INFECTION COMPLICATING EXTRA-NODAL ROSAI-DORFMAN DISEASE IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)**

K. Su[1], G. Hagan[2], S. Tosounidou[1], C. Gordon[1,3], J. Reynolds[1,3]. *[1]Sandwell and West Birmingham NHS Trust, Rheumatology, Birmingham, United Kingdom*; *[2]Sandwell and West Birmingham NHS Trust, Respiratory, Birmingham, United Kingdom*; *[3]University of Birmingham, Institute of Inflammation and Aging, Birmingham, United Kingdom*

Background: We present the case of a 28 year old Black-British female with severe SLE requiring treatment with rituximab in 2012 due to persistent low-grade activity and severe episodes of pleuro-pericardial effusions, pancytopaenia, fever and weight loss

Her other background includes beta-thalassaemia trait and excision of calcific fibrotic tissue on bilateral anterolateral orbits in 2015.
In 2018 she reported an 18-month history of non-tender, non-fluctuant, slow growing left thigh mass with USS revealing a well demarcated subcutaneous complex cystic lesion of ~2x4x7cm. There was no preceding trauma or skin infection. Histology from a needle biopsy revealed diffuse histiocytosis with positive immunohistochemistry (ICH) for S100, CD68 and CD31, it was negative for CD1a, consistent with **Extra-nodal Rosai-Dorfman disease (RDD)**.
She developed constitutional symptoms after reporting months of gradual weight loss with gradual ESR, CRP rise and leucocytosis. Her SLE symptoms were stable and given lack of SLE-specific symptoms; PET-CT was used to identify systemic RDD; the thigh mass showed strong FDG avidity along with a small focus of uptake in the small bowel, thought to be RDD related with no other areas of uptake.
She had ongoing ooze from the enlarging thigh lesion (5 x 26 x 15 cm), this was sent for MCS and AAFB; which isolated **Mycobacterium avium**. She was treated with rifampicin, ethambutol and clarithromycin resulting in improved thigh lesion, constitutional symptoms and inflammatory markers.

Objectives:

[1] To describe a rare associated complication of severe SLE and to educate and inform clinicians regarding possible masquerades of disease
[2] To education and inform about the approach to diagnosis of mycobacterium infection.

Methods: Case report and literature review.

Results: Mycobacterium infections rarely complicate RDD; to date, only one case report is published involving an HIV infected patient with RDD confirmed on LN biopsy presenting with splenomegaly and treated with oral corticosteroids (OCS) complicated by *Mycobacterium avium complex* and *Salmonella enterica* confirmed on bone marrow biopsy/culture, similar to our patient, he presented with constitutional symptoms and weight loss[(2)].
Mycobacterium can also mimic RDD, a case report has described a 74 year old with tender lymphadenopathy diagnosed with RDD on LN biopsy. She was treated with IV and OCS, but was unresponsive. A repeat LN biopsy and CT imaging revealed the presence of *mycobacterium kansasii;* her biopsy was positive for CD68/S100 throughout. Of note, she had high levels of anti-interferon autoantibodies and was diagnosed with adult-onset immunodeficiency syndrome[(3)].

Conclusion: This case illustrates the need for a MDT approach for multi-system diseases such as SLE and RDD, and the need to consider atypical infections when blood tests are incongruent with clinical state.

REFERENCES:

[1] Bruce-Brand C, Schneider JW, Schubert P. Rosai-Dorfman disease: an overview. J Clin Pathol. 2020 Nov;73(11):697-705. doi: 10.1136/jclinpath-2020-206733.
[2] Olmedo-Reneaum A, Molina-Jaimes A, Conde-Vazquez E, Montero-Vazquez S. Rosai-Dorfman disease and superinfection due to *Salmonella enterica* and Mycobacterium avium complex in a patient living with HIV. IDCases. 2020 Jan 14;19:e00698.
[3] King YA, Hu CH, Lee YJ, Lin CF, Liu D, Wang KH. Disseminated cutaneous Mycobacterium kansasii infection presenting with Rosai-Dorfman disease-like histological features in a patient carrying anti-interferon-γ autoantibodies. J Dermatol. 2017 Dec;44(12):1396-1400.

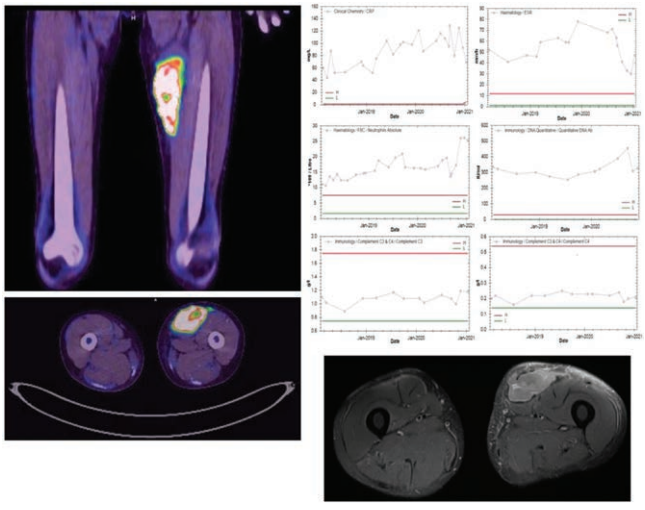


Image 1.

Table 1.

SLE Clinical History
Diagnosed 2006 ('97 ACR Classification Criteria)
Clinical
-Polyarthritis
-Glandular (lacrimal swelling)
-Pericardial effusion/Pleural Effusion
-Myositis
Serological
-Anti-nuclear antibody (ANA)
-Anti-dsDNA
-Anti-U1-RNP
-Anti- SS-A/Ro
-Lupus Anticoagulant
Previous SLE Treatment
-Hydroxychloroquine (HCQ)
-Methotrexate (MTX)
-Azathioprine (AZA)
-Rituximab (RTX)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2415

Challenges for Patients and Patients' Organisations in Times of the Pandemic

OP0082-PARE THE EFFECT COVID-19 HAS ON THE MENTAL HEALTH OF PEOPLE LIVING WITH RHEUMATIC DISEASES. FROM DATA TO INTERVENTIONS.

S. Mingolla[1], A. Celano[2], M. Santopietro[3]. [1]*APMARR APS, Communication, Lecce /Puglia, Italy*; [2]*APMARR APS, National Association of People with Rheumatic and Rare Diseases, Lecce, Italy*; [3]*WeResearch, Ricerche di Marketing, Milan, Italy*

Background: Covid-19 has had an important impact on the mental health conditions of over 5 million Italians suffering from one of the over 150 rheumatic diseases. In order to understand the psychological impact of the Covid-19 emergency and the restrictions imposed to counter it, the Italian National Association of People with Rheumatic and Rare Diseases – APMARR APS launched the research "Living with a rheumatic pathology".

Objectives: Gather data directly from Italian patients about the impact of the COVID-19 and consequent restrictions on their mental health and feelings; evaluate the most effective intervention to be implemented to face the pandemic by Patients organization.

Methods: A qualitative-quantitative survey was carried out through a questionnaire administered throughout the national territory to a sample of N = 1,001 people. The people invited to complete the questionnaire were women (55,9%) and men (44,1%), aged 18-85 years (age 18-41=26,7%; age 42-65=64%; age >65=9,3%) with at least one rheumatic pathology. The questionnaire was made up of 39 questions, of which 29 were closed and 10 were open. For the administration of the questionnaires, the CAWI (Computer Aided Web Interview) methodology of on-line survey was used. The 1,001 interviews were carried out from 7 to 14 August 2020.

Results: More than 4 out of 10 people (total sample 44.2%; male 60%, female 35,7%; age 18-41=39,1%; age 42-65=45,9%; age >65 = 50%) declared that the emergency period has somehow caused a worsening of their health condition. People declared that the deterioration of their health is due to the emergency period for the following reasons: 1) Psychological: such as stress and anxiety: "Too much stress and anxiety made the symptoms worse."; "The stress of the quarantine affected my problem"; "Insomnia. Nervousness. General ailments. Depression. Strong stress" 2) Inability to perform physiotherapy and motor activities due to the lockdown 3) Postponement of examinations, visits and checks 4) remote working, in some cases described as harmful for people's mental and physical health: "Due to Covid19 I had to do remote working and I worked even 12 hours a day including holidays to the detriment of my family life".
Furthermore, from January 31, 2020 a significant increase emerged in communication problems with rheumatology specialist compared to the period before the emergency due to Covid-19. The sharp increase may be due to the situation of severe psychological stress to which also the doctors were subjected in the emergency phase: people could not find the comfort of being empathically listened to.

Conclusion: The research shows that the most frequent symptoms among people with rheumatic diseases were depression and high levels of anxiety due to strong emotional stress. Psychological malaise caused direct effects in worsening the symptoms of rheumatic disease as well as other related effects, for example, insomnia. The forced isolation due to the lockdown has made people lack the social support that is fundamental for the psychological well-being especially for those suffering from some chronic pathology. Starting from the data collected, APMARR promptly activated a completely free psychological support service with 6 professional psychologists, two of them specialized in emergency psychology. The service is accessible online and is still going on for all who are not able to overcome the anxiety and fear related to the pandemic and its evolution. Thousands of accesses to the service have been measured to date.

References: S Mingolla[1], A Celano[1], M Santopietro[2]

[1] NATIONAL ASSOCIATION OF PEOPLE WITH RHEUMATIC AND RARE DISEASES - APMARR APS

[2] WeResearch. Ricerche di marketing

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.910

The origins of pain in RMDs

OP0083 INFECTIOUS AND AUTOINFLAMMATORY MODIC TYPE 1 CHANGES HAVE DIFFERENT PATHOMECHANISMS

I. Heggli[1,2], R. Schüpbach[3], N. Herger[1,2], T. A. Schweizer[4], A. Juengel[1,2], N. Farshad-Amacker[5], M. Betz[6], J. M. Spirig[6], F. Wanivenhaus[6], N. H. Ulrich[6], F. Brunner[2], A. S. Zinkernagel[4], M. Farshad[6], O. Distler[1,2], S. Dudli[1,2]. [1]*Center of Experimental Rheumatology, Department of Rheumatology, University Hospital, University of Zurich, Zurich, Switzerland*; [2]*Department of Physical Medicine and Rheumatology, Balgrist University Hospital, University of Zurich, Zurich, Switzerland*; [3]*Unit of Clinical and Applied Research, Balgrist University Hospital, University of Zurich, Zurich, Switzerland*; [4]*Department of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland*; [5]*Department of Radiology, Balgrist University Hospital, University of Zurich, Zurich, Switzerland*; [6]*Department of Orthopeadic Surgery, Balgrist University Hospital, University of Zurich, Zurich, Switzerland*

Background: Modic type 1 changes (MC1) are vertebral bone marrow (BM) edema that associate with non-specific low back pain (LBP). Two etiologies have been described. In the infectious etiology the anaerobic aerotolerant *Cutibacterium acnes* (*C. acnes*) invades damaged intervertebral discs (IVDs) resulting in disc infection and endplate damage, which leads to the evocation of an immune response. In the autoinflammatory etiology disc and endplate damage lead to the exposure of immune privileged disc cells and matrix to leukocytes, thereby evoking an immune response in the BM. Different etiologies require different treatment strategies. However, it is unknown if etiology-specific pathological mechanisms exist.

Objectives: The aim of this study was to identify etiology-specific dysregulated pathways of MC1 and to perform in-depth analysis of immune cell populations of the autoinflammatory etiology.

Methods: BM aspirates and biopsies were obtained from LBP patients with MC1 undergoing spinal fusion. Aspirates/biopsies were taken prior screw insertion through the pedicle screw trajectory. From each patient, a MC1 and an intra-patient control aspiration/biopsy from the adjacent vertebral level was taken. If *C. acnes* in IVDs adjacent to MC1 were detected by anaerobic bacterial culture, patients were assigned to the infectious, otherwise to the autoinflammatory etiology.

Total RNA was isolated from aspirates and sequenced (Novaseq) (infectious n=3+3, autoinflammatory n=5+5). Genes were considered as differentially expressed (DEG) if p-value < 0.01 and log2fc > ± 0.5. Gene ontology (GO) enrichment was performed in R (GOseq), gene set enrichment analysis (GSEA) with GSEA software.

Changes in cell populations of the autoinflammatory etiology were analyzed with single cell RNA sequencing (scRNAseq): Control and MC1 biopsies (n=1+1) were digested, $CD45^+CD66b^-$ mononuclear cells isolated with fluorescence activated cell sorting (FACS), and 10000 cells were sequenced (10x Genomics). Seurat R toolkit was used for quality-control, clustering, and differential expression analysis.

Transcriptomic changes (n=5+5) of $CD45^+CD66b^+$ neutrophils isolated with flow cytometry from aspirates were analyzed as for total bulk RNAseq. Neutrophil activation (n=3+3) was measured as $CD66b^+$ expression with flow cytometry. $CD66b^{high}$ and $CD66b^{low}$ fractions in MC1 and control neutrophils were compared with paired t-test.

Results: Comparing MC1 to control in total bulk RNAseq, 204 DEG in the autoinflammatory and 444 DEG in the infectious etiology were identified with only 67 shared genes (Fig. 1a). GO enrichment revealed "T-cell activation" (p = 2.50E-03) in the autoinflammatory and "complement activation, classical pathway" (p=1.1E-25) in the infectious etiology as top enriched upregulated biological processes (BP) (Fig 1b). ScRNAseq of autoinflammatory MC1 showed an overrepresentation of T-cells (p= 1.00E-34, OR=1.54) and myelocytes (neutrophil progenitor cells) (p=4.00E-05, OR=2.27) indicating an increased demand of these cells (Fig. 1c). Bulk RNAseq analysis of neutrophils from the autoinflammatory etiology revealed an activated, pro-inflammatory phenotype (Fig 1d), which was confirmed with more $CD66b^{high}$ neutrophils in MC1 (+11.13 ± 2.71%, p=0.02) (Fig. 1e).

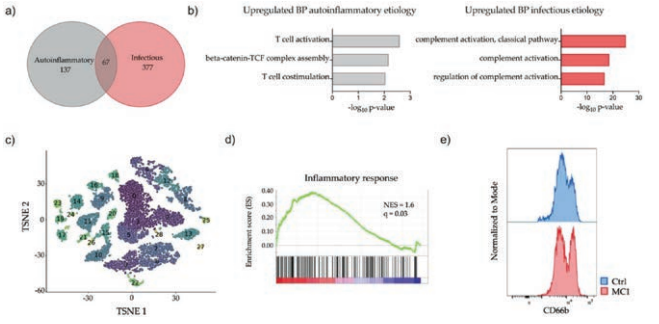


Figure 1. (a) Venn diagram of DEG from total bulk RNAseq (b) Top enriched upregulated BP of autoinflammatory (left) and infectious (right) etiology (c) Cell clustering of autoinflammatory MC1 BM (d) Enrichment of "inflammatory response" gene set in autoinflammatory MC1 neutrophils (e) Representative histogram of $CD66b^+$ expression in MC1 and control neutrophils.

Conclusion: Autoinflammatory and infectious etiologies of MC1 have different pathological mechanisms. T-cell and neutrophil activation seem to be important in the autoinflammatory etiology. This has clinical implication as it could be explored for diagnostic approaches to distinguish the two MC1 etiologies and supports developing targeted treatments for both etiologies.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.825

OP0084 CENTRAL MECHANISMS TRAIT PREDICTS PERSISTENT KNEE OSTEOARTHRITIS PAIN AT 24-MONTHS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

S. Holden[1,2,3], D. Mcwilliams[1,2,3], S. Smith[1,2,3], D. Walsh[1,2,3,4]. [1]*University of Nottingham, Pain Centre Versus Arthritis, Nottingham, United Kingdom*; [2]*University of Nottingham, NIHR Nottingham Biomedical Research Centre, Nottingham, United Kingdom*; [3]*University of Nottingham, Division of Rheumatology, Orthopaedics and Dermatology, Nottingham, United Kingdom*; [4]*Sherwood Forest Hospitals NHS Foundation Trust, Rheumatology, Mansfield, United Kingdom*

Background: In the UK, 10% of men and 18% of women over the age of 60 suffer from symptomatic osteoarthritis (OA), and rising. OA knee pain can worsen without significant radiographic changes and pain remains a major problem for up to 20% of patients after total knee joint replacement. Chronic knee OA pain is

augmented by central pain mechanisms, including central sensitisation. Measures of the level of central involvement in pain could inform clinical decision making. Self-report characteristics of depression, anxiety, cognitive difficulties, catastrophizing, sleep disturbance, fatigue, and widespread pain distribution together contribute to a Central Mechanisms Trait which is associated with central sensitisation and OA knee pain

Objectives: Using self-report questionnaire data from the Osteoarthritis Initiative Cohort Study (OAI) we aimed to evaluate the prognostic performance of baseline CMT for pain at 24-months.

Methods: OAI participants with knee OA or at risk of knee OA with pain in the same knee at both index time point (48-months) and one year prior to that date were included (n=1984). Knee pain was measured using the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) pain sub-scale, by reference to the index knee (the knee with the highest WOMAC pain sub-scale score at baseline). Questionnaire items were selected to assess the 7 available characteristics identified by Akin-Akinyosoye et al.[1], from which a single CMT factor was calculated by confirmatory factor analysis. Anxiety, fatigue and cognitive difficulties were assessed by single items, depression and sleep disturbance represented by multiple items, and catastrophising by using the Coping Strategies Questionnaire – Catastrophising sub-scale. Pain distribution was defined as a sum of other painful joints at or below the hip. A CMT factor was derived from the 7 characteristics using confirmatory factor analysis. The association between the CMT factor score and 24-month pain (adjusted for baseline pain, radiographic OA (Kellgren-Lawrence (KL) scale) and demographic confounders) was investigated using generalised linear regression with a negative binomial link function.

Results: At baseline, participants had a mean (SD) age 65(9) years, a BMI 29.6(5.1) kg/m^2, 60% were female, 19.8% were African American, KL score was 1.92(1.35) indicating that the majority of the cohort had radiographic OA. Model diagnostics informed the CMT model, with the final model having an RMSEA of 0.073 (90%CI 0.070-0.076). Data were consistent with a single factor model for CMT. In the multivariable model, higher baseline CMT scores were significantly associated with 24-month WOMAC pain scores, with or without adjustment for baseline pain and other covariates, including KL score (multivariable model; std beta=0.173 (SE=0.027), p=0.004). Association of baseline CMT was of similar strength, and over and above association of KL score with 24-month pain (std beta=0.164 (SE=0.038), p=<0.001). Adjusted regression coefficients and associated p-values are shown in Table 1.

Table 1. Adjusted regression coefficients for analysed variables against WOMAC pain at 24-months

Variables	Std beta (SE)	P
Sex	-0.096 (0.101)	0.344
Age, y	-0.001 (0.006)	0.881
BMI, kg/m^2	0.017 (0.010)	0.088
Index Knee Kellgren-Lawrence Score	**0.164 (0.038)**	**<0.001**
CMT Factor Score	**0.173 (0.060)**	**0.004**
Baseline Pain	**0.857 (0.035)**	**<0.001**

n=1421, rows in bold indicate significant association (p<0.05), associations adjusted for race and ethnicity

Conclusion: CMT predicts worse pain prognosis with a similar magnitude to radiographic OA even after adjustment for other factors. A self-report tool which included items relevant to the characteristics included in the CMT may help to select people with OA knee pain with unfavourable pain prognosis. Poor outcomes related to central pain mechanisms or to joint structural damage might be amenable to treatments addressing central or peripheral pain mechanisms respectively.

REFERENCES:

[1] Akin-Akinyosoye et al., PAIN, 2018. **159**(6): p. 1035-1044.

Acknowledgements: This abstract was prepared using an Osteoarthritis Initiative (OAI) public use data set and does not necessarily reflect the opinions or views of the OAI investigators, the NIH, or the private funding partners. The authors wish to thank the participants, principal investigators, co-investigators and staff of all the hospitals who have contributed data to the OAI. The OAI is a public-private partnership comprised of five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261; N01-AR-2-2262) funded by the National Institutes of Health, a branch of the Department of Health and Human Services, and conducted by the OAI Study Investigators. Private funding partners include Merck Research Laboratories; Novartis Pharmaceuticals Corporation, GlaxoSmithKline; and Pfizer, Inc. Private sector funding for the OAI is managed by the Foundation for the National Institutes of Health.

Disclosure of Interests: Samuel Holden: None declared, Daniel McWilliams Grant/research support from: Pfizer and Eli Lilly, Stephanie Smith: None declared, David Walsh Consultant of: Pfizer, Eli Lilly, AbbVie and GlaxoSmithKline, Grant/research support from: Pfizer and Eli Lilly

DOI: 10.1136/annrheumdis-2021-eular.1595

OP0085 ALTERED EXPRESSION OF NEUROTROPHINS AND THEIR RECEPTORS IN THE SKIN OF PATIENT WITH COMPLEX REGIONAL PAIN SYNDROME (CRPS)

S. Stroeve[1,2], S. Dudli[1,2], I. Kolm[3], I. Heggli[1,2], N. Herger[1,2], S. Catanzaro[4], A. Schweizer[5], M. Calcagni[6], O. Distler[1,2], F. Brunner[2], A. Juengel[1,2]on behalf of Experimental Rheumatology Balgrist Campus. *[1]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, Zürich, Switzerland*; *[2]Department of Physical Medicine and Rheumatology, Balgrist University Hospital, University of Zurich, Zurich, Switzerland*; *[3]University Hospital Zurich, Department of Dermatology, Zurich, Switzerland*; *[4]Balgrist University Hospital, University of Zurich, Switzerland, Unit of Clinical and Applied Research, Zurich, Switzerland*; *[5]Balgrist University Hospital, University of Zurich, Switzerland, Department of Hand surgery, Zurich, Switzerland*; *[6]University Hospital Zurich, Department of Plastic Surgery and Hand Surgery, Zurich, Switzerland*

Background: Complex regional pain syndrome (CRPS) is a rare painful condition that usually appears after trauma or surgery of the extremities. Symptoms include pain, sensory, sudomotor and vasomotor disturbances, trophic changes and impaired motor function. The course varies from mild to chronic disease with a high impact on daily functioning and quality of life. In skin tissue, sustained inflammatory, fibrotic processes together with reduced epidermal nerve fibers are reported. Neurotrophins and their receptors are mediators in cell-to-cell communication and key mediators of pain signaling

Objectives: The aim of this study was to identify differential expression of neurotrophins and their receptors in the skin and skin fibroblasts of patients with CRPS

Methods: Healthy controls (HC) and patients with acute CRPS with symptoms for less than 6 months fulfilling the Budapest criteria were recruited. Pain scores were evaluated by numeric rating scale (0=no pain, 100=maximal) and body perception was assessed using the Bath Body Perception Disturbance Scale (BBPDS) (0=no perception disturbance, 57=maximal perception disturbance).

Skin biopsies of the affected and/or non-affected side were taken. Immunohistochemistry on formalin-fixed, paraffin-embedded skin tissue slides was used to show NT3 expression in skin tissues. Blinded analysis was done by an experienced dermato-pathologist determined staining graduated by 0= none, 1= sparse, 2=moderate, 3= dense.

Skin fibroblast were isolated from skin biopsies by outgrowth cultures (CRPS, affected side, n=6 and HC, n=5). Cells (passage 3-6) were starved and subsequently stimulated with TNFα (10 ng/ml) or TGFβ (10 ng/ml) for 24 h to mimic active disease and total RNA was isolated by miRNeasy kit. Gene expression of neurotrophins (NGF, BDNF, and NT3) and neurotrophin receptors (NGFR, TrkA, TrkB and TrkC) was measured by quantitative real time PCR and quantified using the $\Delta\Delta$Cq method with GAPDH as a reference gene. ELISA was used to analyze NT3 protein expression in cell culture supernatants.

Results: In 5 of 9 patients with CRPS immunohistological staining of NT3 showed an higher expression (from low to moderate) in the affected side versus the non-affected side. In 4 of 9 patients the expression of NT3 was high in the non-affected side (moderate/dense) and stayed high in the affected side.

Of interest, the patients with increasing expression of NT3 in the affected side showed increased pain scores (max pain 80+/-10.95, n=5 versus 48.16+/-18.16, n=4, p=0.059 and changed body perception 26.8+/-8.68 n=5 versus 6.5+/-3.91, n=4, p=0.016).

Isolated skin fibroblasts from the affected side of patients with CRPS compared to healthy skin fibroblasts showed higher **basal** gene expression of NT3 ($\log_2$ fold-change= 1.9 +/- 0.4, *p= 0.005*) and NGFR ($\log_2$ fold-change= 3.6 +/- 2.1, *p=0.014*). **TNFα** stimulated CRPS skin fibroblasts showed higher expression for NT3 ($\log_2$ fold-change= 2.1 +/- 1.2, p=0.002) compared to HC. **TGFb** stimulated skin fibroblasts of patients with CRPS showed higher expression of NT3 ($\log_2$ fold-change= 1.4+/-0.8, *p=0.019*), NGFR ($\log_2$ fold-change= 2.6 +/- 1.8, *p=0.036*) and TrkC ($\log_2$ fold-change= 2.3 +/- 1.8, *p=0.032*) compared to HC.

On protein level, NT3 showed a tendency of upregulation in unstimulated fibroblasts from CRPS patients comparing to HC (CRPS mean= 8.0 +/- 2.2 pg/ml, HC

mean= 6.3 +/- 1.8 pg/ml, *p=0.25*). After **TNFα** stimulation, protein level of NT3 was significantly higher in CRPS skin fibroblasts (CRPS mean= 10.6 +/- 2.4 pg/ml, HC mean= 4.8 +/- 1.3 pg/ml, *p=0.004*).

Conclusion: These data indicate a new role of skin fibroblasts in CRPS. Differential basal and stimulated expression of NT3, the receptor for NT3 (TrkC) and NGFR, the common receptor for all neurotrophins, indicates deregulated communication of fibroblasts with the sensory nerve fibers in CRPS. This might contribute to the dysregulated healing process and sustained pain.

Disclosure of Interests: Sanne Stroeve: None declared, Stefan Dudli: None declared, Isabel Kolm: None declared, Irina Heggli: None declared, Nick Herger: None declared, Sabrina Catanzaro: None declared, Andreas Schweizer: None declared, Maurizio Calcagni Speakers bureau: Arthrex, Consultant of: Medartis, Arthrex, SilkBiomaterials, Grant/research support from: Medartis, Oliver Distler: None declared, Florian Brunner: None declared, Astrid Juengel: None declared

DOI: 10.1136/annrheumdis-2021-eular.830

OP0086

GENDER INFLUENCE ON CLINICAL MANIFESTATIONS, DEPRESSIVE SYMPTOMS AND BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) SERUM LEVELS IN PATIENTS AFFECTED BY FIBROMYALGIA

C. Gioia[1], B. Lucchino[1], C. Iannuccelli[1], G. Dolcini[1], M. Di Franco[1]. [1]*Sapienza Università di Roma, Reumatologia, Dipartimento di Scienze Cliniche, Internistiche, Anestesiologiche e Cardiovascolari, Sapienza Università di Roma, Roma, Italy*

Background: Fibromyalgia (FM) is a common rheumatic disease characterized by chronic widespread pain, sleep and mood disorders. A higher prevalence of FM in women compared with men is well known, although the specific differences in clinical manifestations related to gender are still poorly defined. Brain-Derived Neurotrophic Factor (BDNF) is an endogenous growth factor that gained attention for its potential as biomarker of several diseases, including FM and depression.

Objectives: The aims of this study were to investigate gender-related difference among males and females affected by FM in clinical manifestations, depressive features and BDNF serum level, evaluating also the diagnostic potential of the latter.

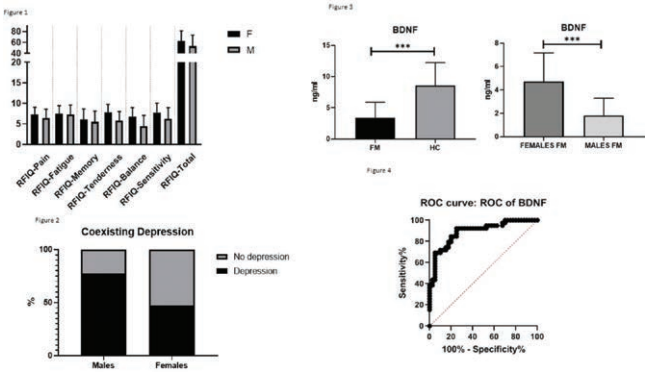
Methods: We consecutively enrolled adult patients affected by FM (ACR 2016) referring to our out-patient clinic. Each subject underwent clinical and answered to questionnaires for the severity of FM symptoms (Revised Fibromyalgia Impact Questionnaire, R-FIQ) and depressive symptoms (Beck Depression Inventory-II, BDI-II). We collected blood samples from a subgroup of patients of both sexes, matched for age, for BDNF serum level dosage through ELISA. BDNF levels were assessed also in a control group, matched for sex and age.

Results: The cohort was composed by 201 FM patients (172 F, 29 M), mean age 49.13. Females showed higher values of R-FIQ total score (p=0,0005) as well the specific items of the R-FIQ for pain (p=0,013), fatigue (p=0,014), memory problems (p=0,007), tenderness to touch (p<0,0001), balance problems (p<0,0001) and sensitivity to environmental stimuli (p=0,012) when compared with males (fig. 1). There was no difference in BDI-II between males and females, but notably male patients reported a significantly higher frequency of coexisting depressive disorder (p=0,038) (fig. 2). Serum BDNF levels were evaluated in 40 FM patients and 40 healthy controls (HC) (F:M 1:1). BDNF levels were significantly lower in FM patients compared with HC (p<0,0001). Among FM patients, BDNF levels were lower in males compared with females (p<0,0001) (fig.3). BDNF did not correlate with any clinical and clinimetric parameter. BDNF showed a good diagnostic performance (AUC=0,89, CI95%=0,82-0,9630, p<0,0001) (fig. 4). At a cut-off value <6,47 ng/dl, BDNF showed a specificity of 75% and a sensibility of 92,31%,(CI 95%=79,68-97.35) for FM identification (LR=3,692).

Conclusion: FM clinical manifestations are strongly dependant from gender. While females present a more severe disease and a higher burden of symptoms, mood disorders tend to be a major characteristic of males with FM. Reduced BDNF serum levels have been reported as typical of depressive disorders. Our findings of lower BDNF levels in male FM patients compared to females support this hypothesis. BDNF have potential as biomarker of the disease and should be validated in larger cohorts.

REFERENCES:

[1] Sarzi-Puttini et al. Nature Reviews 2020
[2] Colucci-D'Amato et al. Int J Molecular Sciences 2020
[3] Nugraha et al. Rheumatol Int 2012
[4] Schmitt et al. Ann Med 2016
[5] Melchior et al. Neuroscience 2016
[6] Stefani et al. Neuroscience Letters 2012



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3326

OP0087

COMORBIDITIES IN HAND OSTEOARTHRITIS PATIENTS: PREVALENCE AND IMPACT ON PAIN AND PAIN SENSITIZATION

E. Mulrooney[1], T. Neogi[2], H. Solveig Dagfinrud[1,3], H. Berner Hammer[1,4], P. Steen Pettersen[1], T. L. Gaarden[5,6], K. Engedal[7,8], T. K. Kvien[1,9], K. Magnusson[10], I. K. Haugen[1]. [1]*Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway*; [2]*Boston University School of Medicine, Section of Rheumatology, Boston, United States of America*; [3]*University of Oslo, Department for Interdisciplinary Health Sciences, Oslo, Norway*; [4]*University of Oslo, Department of Orthopaedics, Oslo, Norway*; [5]*Diakonhjemmet sykehus, Alderspsykiatrisk Avdeling, Oslo, Norway*; [6]*University of Oslo, Faculty of Medicine, Oslo, Norway*; [7]*Norwegian Centre of Ageing and Health, Norwegian Centre of Ageing and Health, Oslo, Norway*; [8]*University of Oslo, Department of Geriatric Medicine, Oslo, Norway*; [9]*University of Oslo, Division of Orthopaedic Surgery, Oslo, Norway*; [10]*Lund University, Department of Clinical Sciences, Lund, Sweden*

Background: Pain is a hallmark symptom of hand osteoarthritis (OA). A subset of people with hand OA display centrally driven pain characteristics. Pain is driven by person-related factors, but how comorbidities are related to the hand OA pain experience is undetermined. Changes in pain pathophysiology and pain levels by for instants low-grade inflammation, might explain the link.

Objectives: The purpose of this study was to determine whether the burden of comorbidities or the individual comorbidities were associated with pain and pain sensitization in persons with hand OA.

Methods: These cross-sectional analyses included 282 participants with hand OA from the Nor-Hand study. Comorbidities were assessed by an index (subscales: Disease, Limitation and Treatment, (0-45 scale)) by Sangha et al. The participants completed pain questionnaires; Numeric Rating Scale (NRS) hand pain (0-10) and all joints (0-10), Australian/Canadian (AUSCAN) hand pain subscale (0-20 scale), Western Ontario & McMaster Universities Arthritis Index (WOMAC) pain subscale (0-20) and homunculus (painful joint sites last six weeks, (0-18)). Pressure pain threshold (PPT, handheld algometer, kg/cm^2) at tibialis anterior and trapezius and Temporal summation (TS) at the distal radioulnar joint tapped with weighted probe (x10), assessed central pain sensitization. TS-delta was calculated of the first and peak measure of the fifth or tenth tap. Linear regression was used to examine all relations, while adjusted for age, sex, body mass index and education.

Results: The participants (89% women, median (IQR) age: 61 (57-66)) showed broad range in pain severity. Most frequent comorbidities were back pain (n=170, 60%), hypertension (n= 85, 30%), stomach ulcer/abdominal disease (n=62, 22%) and depression (n=46, 16%). 281 (99.3%) participants reported >1

Table.

B (95% confidence interval per one SD of the comorbidity index/subscale) are reported

	NRS hand pain	NRS pain all joints	AUSCAN hand pain	WOMAC knee/hip pain	Painful joints	PPT Trapezium	PPT Tibialis Anterior	TS
Comorbidity Index	**0.76 (0.12, 0.24)**	**0.76 (0.12, 0.24)**	**1.61 (0.15, 0.37)**	**2.76 (0.26, 0.50)**	**2.76 (0.42, 0.88)**	**-0.38 (-0.15, -0.04)**	-0.25 (-0.13, 0.01)	**0.25 (0.02, 0.11)**
Disease	**0.69 (0.24, 0.52)**	**0.56 (0.16, 0.46)**	**0.89 (0.22, 0.75)**	**1.34 (0.45, 1.02)**	**2.19 (0.66, 1.76)**	**-0.34 (-0.32, -0.06)**	-0.24 (-0.29, 0.04)	**0.23 (0.02, 0.23)**
Treatment	**0.56 (0.18, 0.48)**	**0.58 (0.18 0.49)**	**0.80 (0.19, 0.76)**	**1.29 (0.46, 1.06)**	**1.79 (0.47, 1.65)**	**-0.31 (-0.32, -0.44)**	-0.19 (-0.28, 0.07)	**0.22 (0.01, 0.24)**
Limitations	**0.69 (0.32, 0.70)**	**0.86 (0.44, 0.81)**	**1.16 (0.51, 1.20)**	**1.58 (0.78, 1,53)**	**3.30 (1.72, 3.13)**	**-0.41 (-0.47, -0.13)**	-0.26 (-0.41, 0.02)	**0.26 (0.04, 0.33)**
Depression	**0.96 (0.29, 1.63)**	0.66 (-0.04, 1.36)	**1.74 (0.46, 3.02)**	**0.99 (-0.38, 2.35)**	**3.43 (0.78, 6.09)**	-0.36 (-1.00, 0.29)	-0.44 (-1.25, 0.37)	0.02 (-0.50, 0.53)
Back pain	**0.89 (0.38, 1.40)**	**1.10 (0.57, 1.63)**	**1.04 (0.08, 2.00)**	**2.90 (1.87,3.93)**	**2.64 (0.65, 4.64)**	0.08 (-0.41, 0.56)	0.23 (-0.38, 0.84)	0.22 (-0.17, 0.61)
Hypertension	**0.64 (0.05, 1.22)**	0.45 (-0.17, 1.06)	1.00 (-0.12, 2.11)	**1.32 (0.13, 2.52)**	**2.74 (0.44, 5.05)**	-0.32 (-0.88, 0.23)	-0.28 (-0.97, 0.40)	0.17 (-0.28, 0.62)

comorbidity other than OA. Mean (SD) comorbidity index value was 7.73 (4.25). Higher values were statistically significantly associated with greater pain severity by each pain questionnaire, lower PPT trapezium (borderline significant for PPT tibialis anterior), and greater TS (Table). Similar results were found for subscales. Depression, back pain and hypertension associated with most measures of pain. (Table). Included in the same model, results remained similar (not shown). No statistically significant association between individual comorbidities and pain sensitization (Table).

Conclusion: Higher burden of comorbidities was associated with greater pain intensity and central pain sensitization. Hypertension, back pain and depression were associated with most pain measures. The lack of relation between individual comorbidities and pain sensitization suggest the burden of comorbidity is more important.

Disclosure of Interests: Elisabeth Mulrooney: None declared, Tuhina Neogi: None declared, Hanne Solveig Dagfinrud: None declared, Hilde Berner Hammer Speakers bureau: Speaker fee from Novartis, Lilly and AbbVie, Pernille Steen Pettersen: None declared, Torfinn Lødøen Gaarden: None declared, Knut Engedal: None declared, Tore K. Kvien Speakers bureau: Amgen, Celltrion, Egis, Evapharma, Ewopharma, Hikma, Oktal, Sandoz, Sanofi, Consultant of: AbbVie, Amgen, Biogen, Celltrion, Eli Lilly, Gilead, Mylan, Novartis, Pfizer, Sandoz, Sanofi, Grant/research support from: AbbVie, Amgen, BMS, MSD, Pfizer, UCB (to the institution)., Karin Magnusson: None declared, Ida K. Haugen Speakers bureau: Novartis, Grant/research support from: Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1884

OP0088 A COHORT STUDY ON THE BIDIRECTIONAL RELATIONSHIP BETWEEN FIBROMYALGIA AND PERIODONTITIS OVER A 15-YEAR FOLLOW-UP

K. S. K. MA[1], T. Van Dyke[2]. [1] *National Taiwan University, Taipei, Taiwan, Department of Life Science, Taipei, Taiwan, Republic of China*; [2]*Forsyth Institute, Cambridge, Center for Clinical and Translational Research, Boston, United States of America*

Background: Fibromyalgia has been proposed to be driven by chronic inflammation and infections that are associated with early rheumatoid arthritis and inflammatory arthritis. Other than the central sensitization model, our knowledge of fibromyalgia pathogenesis has been expanded with an inflammation-dependent theory, which is stimulated by prolonged spinal cord hyperexcitability.

Objectives: To determine the relationship between periodontitis and fibromyalgia.

Methods: In this cohort study, 196,428 periodontitis patients and 196,428 propensity score-matched non-periodontitis controls were enrolled. A Cox proportional hazard model was utilized to estimate the risk of fibromyalgia and survival analysis was adopted to assess the time-dependent effect of periodontitis on fibromyalgia. Subgroup analyses stratified by age, gender, and follow-up years were conducted to identify susceptible populations. A symmetrical cohort was designed to ascertain the relationship between fibromyalgia and the risk of periodontitis.

Results: Patients with history of periodontitis were more likely to develop fibromyalgia than non-periodontitis controls (HR =1.42, 95% CI =1.39–1.44, P < 0.001), which persisted in the survival analysis (log-rank test P < 0.0001). This effect was significant in both genders and all age subgroups, and was particularly evident in males (HR=1.52, 95% CI = 1.48–1.56, P < 0.001) and younger periodontitis patients (HR= 1.55, 95% CI =1.50-1.60, P < 0.001). Fibromyalgia patients who never had periodontitis presented with higher risk for periodontitis over time (HR = 1.43, 95% CI = 1.40 - 1.45, P < 0.001).

Conclusion: This is the first longitudinal study that addresses the bidirectional relationship between fibromyalgia and periodontitis, in which periodontitis may serve as a risk factor or early sign of fibromyalgia. Based on the observed relationship between fibromyalgia and periodontitis, regular follow-ups and patient education are recommended for patients with either disease.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3902

OP0089 DO PAIN CATASTROPHIZING REDUCE THE LIKELIHOOD OF REMISSION IN PATIENTS WITH CHRONIC INFLAMMATORY JOINT DISORDERS?

M. Wilk[1], K. Łosińska[1], A. H. Pripp[2], M. Korkosz[1,3], G. Haugeberg[4,5]. [1]*University Hospital, Division of Rheumatology and Immunology, Cracow, Poland*; [2]*Oslo University Hospital, Oslo Centre of Biostatistics and Epidemiology, Oslo, Norway*; [3]*Jagiellonian University Medical College, Department of Rheumatology, Cracow, Poland*; [4]*Sørlandet Hospital, Department of Rheumatology, Kristiansand, Norway*; [5]*5NTNU, Norwegian University of Science and Technology, Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, Trondheim, Norway*

Background: Rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (ax-SpA) may have a devastating impact on patients' lives, including chronic and relapsing pain. One factor contributing to bio-psycho-social model of pain in these diseases, is pain catastrophizing (PC) defined as tendency to report pain experience in exaggerated terms, to ruminate more or to feel helpless about it. In one RA study PC has been shown to be associated with patient reported outcomes e.g. reduced likelihood of remission using composite measures.[1]

Objectives: Main objective of this study was to explore if pain catastrophizing score is associated with remission rates in the chronic inflammatory joint disorders RA, PsA and ax-SpA.

Methods: Patients were recruited during routine assessment at an outpatient clinic in Norway. Variables collected included demographics, treatment, disease duration, global pain VAS, pain catastrophizing score (PCS), and disease activity scores: DAS28-CRP for RA, BASDAI for ax-SpA and DAPSA for PsA. Cut off definitions of remission was for DAS28 <2.6, for BASDAI <4.0 and for DAPSA ≤4.0. Two questions from Coping Strategies Questionnaire as recommended by Jensen et al [2] were used to describe PC, range PC total score (PCS) 0–6. Patients with PCS ≥ 4 were defined as high pain catastrophizers. Statistics included Chi-Square test and adjusted logistic regression (enter procedure).

Results: For RA (N=580), PsA (N=394) and ax-SpA (N=225) mean age (SD) was 61.5 (13.1), 54.4 (12.9) and 47.5 (12.9) years, mean disease duration 12.6 (10.9), 10.2 (8.4) and 12.2 (10.7) years and percentage of women 66.7%, 47.0% and 38.4%. Mean (SD) DAS28-CRP in RA was 2.3 (1.0), BASDAI for ax-SpA 3.7 (2.3) and DAPSA for PsA 10.8 (8.5). Mean (SD) global pain (VAS 0-100mm) was for RA 32.0 (25.6), for PsA 35.5 (25.4) and for ax-SpA 39.4 (25.4) mm.

Conventional synthetic DMARDs were used by 65.0% of RA patients, 54.8% by PsA and 9.8% in ax-SpA and for biologic DMARDs the corresponding numbers were 36.7%, 43.9%, 65.9%, respectively.

Percentage of patients in remission was significantly lower in high pain catastrophizers compared with low pain catastrophizers in RA (34.1% vs 70.3%, p<0.01) and ax-SpA patients (17.9% vs 64.5%, p<0.01) but not in PsA (10.3% vs 26.7%, p=0.06).

In analysis adjusting for age, gender, disease duration and global pain (Tab. 1), PC was independently associated with lower remission rate in RA (OR 0.79 (95% CI 0.63, 0.99), p=0.04) and in ax-SpA (OR 0.65 (95% CI 0.46, 0.93), p=0.02) but not in PsA (OR 0.83 (95% CI 0.55, 1.25), p=0.37)

Conclusion: Our data indicates that high level of patient's PC may reduce likelihood of achieving remission in RA and ax-SpA. Interestingly, this was not shown in PsA patients. Further studies are needed to reveal the importance of PC and its influence on composite disease activity measures used to define disease status e.g. remission.

Table 1. Variables and their associations with remission rates in RA, PsA, ax-SpA in logistic regression analysis.

	RA remission		PsA remission		ax-SpA remission	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
PCS	0.79 (0.63, 0.99)	0.04	0.83 (0.55, 1.25)	0.37	0.65 (0.46, 0.93)	0.02
Age	0.99 (0.97, 1.01)	0.17	1.00 (0.96, 1.04)	0.85	0.98 (0.94, 1.02)	0.27
Gender	0.87 (0.52, 1.45)	0.59	0.37 (0.15, 0.93)	0.03	0.92 (0.40, 2.14)	0.85
Disease duration	1.03 (1.00, 1.05)	0.03	0.95 (0.90, 1.00)	0.06	1.04 (0.99, 1.09)	0.09
Global pain (VAS)	0.96 (0.95, 0.97)	<0.01	0.85 (0.81, 0.89)	<0.01	0.90 (0.88, 0.92)	<0.01

REFERENCES:

[1] Hammer HB et al Pain Catastrophizing, Subjective Outcomes, and Inflammatory Assessments Including Ultrasound: Results From a Longitudinal Study of Rheumatoid Arthritis Patients. Arthritis Care Res. 2018;70: 703-12.

[2] Jensen MP, et al. One- and two-item measures of pain beliefs and coping strategies. Pain 2003;104:453-69.

Acknowledgements: Nurses and doctors from Division of Rheumatology at Sørlandet Hospital in Kristiansand, Norway contributed to data collection.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3715

Infection-related rheumatic and orphan diseases

OP0090 CLASSIFICATION OF PATIENTS WITH RELAPSING POLYCHONDRITIS BASED ON SOMATIC MUTATIONS IN UBA1

M. Ferrada[1], K. Sikora[1], Y. Lou[1], K. Wells[1], B. Patel[2], D. Ospina Cardona[3], E. Rose[1], W. Goodspeed[1], P. Hoffman[4], A. Jones[3], L. Wilson[3], N. Young[2], S. Savic[4], D. Kastner[4], A. Ombrello[4], D. Beck[4], P. Grayson[1]. [1]*NIH, NIAMS, Bethesda, United States of America*; [2] *NIH, NHLBI, Bethesda, United States of America*; [3]*NIH, NHGRI, Bethesda, United States of America*; [4]*NIHR, Leeds Biomedical Research Centre and Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*

Background: Somatic mutations in ubiquitin activating enzyme 1 (*UBA1*) cause a newly defined syndrome known as VEXAS. [1] More than fifty percent of patients currently identified with VEXAS meet diagnostic criteria for relapsing polychondritis (RP).

Objectives: To determine the prevalence VEXAS within a cohort of patients with RP, to compare their clinical, laboratory, and immunologic features and to develop a clinical algorithm to inform genetic screening for VEXAS among patients with RP.

Methods: Exome and targeted sequencing of the *UBA1* gene was performed in a prospective observational cohort of patients with RP. Clinical and immunological characteristics of patients with RP were compared based on presence or absence of *UBA1* mutations. Random forest was used to derive a clinical algorithm to identify patients with *UBA1* mutations. Immune populations were quantified by multipanel flow cytometry. Categorical and continuous variables were compared using the chi square or Kruskal-Wallis test. P<0.05 defined statistical significance.

Results: Seven of 92 patients with RP (7.6%) were confirmed to have *UBA1* mutations (VEXAS-RP). Six additional patients with VEXAS-RP from other cohorts were included for subsequent analyses. Patients with VEXAS-RP were all male, older at disease onset, and commonly had fever, ear chondritis, skin involvement, deep vein thrombosis, and pulmonary infiltrates. Patients with RP as compared with VEXAS-RP had a significantly higher prevalence of airway chondritis, costochondritis and tenosynovitis/arthralgias. (Table). Mortality was significantly greater in VEXAS-RP than RP (27% vs 2% p=0.01). Maximum ESR, CRP, and mean corpuscular volume (MCV) values were significantly greater in VEXAS-RP. Absolute monocyte, lymphocyte, and platelet counts were significantly lower in VEXAS-RP. A decision tree based on male sex, MCV>100 fl and Platelet count<200 K/ul classified between VEXAS-RP and RP with 100% sensitivity and 96% specificity.

Conclusion: Mutations in *UBA1* are causal for disease in a subset of patients with RP. These patients are defined by disease onset in the fifth decade of life or later, male sex, ear/nose chondritis and hematologic abnormalities. Early identification is important in VEXAS given the associated high mortality rate.

REFERENCES:

[1] Beck DB, Ferrada MA, Sikora KA, Ombrello AK, Collins JC, Pei W, Balanda N, Ross DL, Ospina Cardona D, Wu Z *et al*: **Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease**. *N Engl J Med* 2020, **383**(27):2628-2638.

Table 1. Clinical Characteristics of patients with RP vs VEXAS-RP

	All Patients n=98	RP n=85	VEXAS-RP n=13	p value
Demographic Characteristics				
Race, White n (%)	90 (92)	77 (91)	13 (100)	0.59
Sex, Male n (%)	26 (27)	13 (15)	13 (100)	<0.0001
Age, Symptom onset, years, Median (IQR)	38 (30-47)	37 (28-43)	56 (54-64)	<0.0001
Clinical Symptoms				
Fever n (%)	33 (34)	20 (24)	13 (100)	<0.0001
Ear chondritis n (%)	61 (62)	48 (56)	13 (100)	0.0015
Nose chondritis n (%)	83 (85)	71 (84)	12 (92)	0.68
Airway chondritis n (%)	37 (38)	37 (44)	0 (0)	0.0015
Tenosynovitis/arthalgias n (%)	83 (85)	77 (91)	6 (46)	0.0005
Skin involvement n (%)	33 (34)	22 (26	11 (85)	<0.0001
Laboratory Values				
ESR, mm/hr, median (IQR)	12 (6-22)	11 (5-19)	66.5 (42-110)	<0.0001
CRP, mg/L, median (IQR)	2.9 (0.8-9.6)	1.9 (0.6-6.3)	17.7 (9.6-99.5)	<0.0001
Platelet count (k/uL)	246(201-299)	258 (227-312)	145 (100-169)	<0.0001
MCV fL	93.05 (90-98)	92.2 (89-95)	105 (102-115)	<0.0001
Absolute lymphocyte count	1.6 (1.1-2.3)	1.78(1.4-2.4)	0.92 (0.5-1.2)	<0.0001
CT scan abnormalities				
Pulmonary infiltrates n (%)	16 (16.33)	6 (7.06)	10 (77)	<0.0001
Complications				
Death n (%)	6 (6)	3 (4)	3 (23)	0.029
Unprovoked DVT	12 (12)	4 (5)	8 (62)	<0.0001

N number; IQR = interquartile range

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3422

OP0091

TREATMENT OF OCULAR SARCOIDOSIS. STUDY OF 65 PATIENTS OF A SERIES OF 384 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL

C. Álvarez-Reguera[1], J. J. Gaitán-Valdizán[2], R. Fernández-Ramón[2], R. Demetrio-Pablo[2], J. L. Martín-Varillas[3], L. Sanchez-Bilbao[1], D. Martínez-López[1], I. González-Mazón[1], M. Á. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*; [2]*Hospital Universitario Marqués de Valdecilla, Ophthalmology, Santander, Spain*; [3]*Hospital de Sierrallana, Rheumatology, Torrelavega, Spain*

Background: Ocular involvement is a relatively frequent and potentially severe complication of sarcoidosis. Oral corticosteroids (OCS) are the first-line treatment. Conventional immunosuppressive agents (cIS) and biological therapy (BT) can be used in refractory cases **(1-5).**

Objectives: To evaluate the treatment and visual outcomes of a cohort of patients diagnosed with ocular sarcoidosis.

Methods: Study of a large cohort (n=384) of all consecutive patients diagnosed with sarcoidosis from January 1, 1999 to December 31, 2019 at a single University Hospital. Finally, 344 patients were included according the ATS/ERS/WASOG criteria *(Eur Respir J. 1999; 14:735-7).* Different ocular manifestations and the following systemic treatments were assessed: **a)** OCS, **b)** cIS), **c)** monoclonal TNF inhibitors, **d)** Etanercept (ETN), **e)** Tocilizumab (TCZ). Best Corrected Visual Acuity (BCVA) according to different systemic treatments was compared at diagnosis and after one year of follow-up (Kruskall Wallis test).

Results: 344 patients were reviewed. From these, 65 (18.9%) presented ocular manifestations as uveitis (83.1%), orbital lesions (7.7%), retinal vasculitis (6.2%), dry eye (6.2%) and scleritis (1.5%). All of them received systemic treatment. BT was particularly used in patients with retinal vasculitis (100%), panuveitis (75%) and orbital lesions (40%). Systemic treatment and BCVA outcome according to ocular manifestations are shown in table. Median BCVA at onset and after one year was 0.6 [interquartile range (IQR) 0.3-0.8] and 0.9 [0.6-1], respectively. No statistically significant differences were observed between systemic treatments in BCVA of patients with uveitis after 1 year of follow-up (Figure**).**

Conclusion: Panuveitis, intermediate uveitis and orbital lesions, require a more aggressive treatment than other manifestations of ocular sarcoidosis. In uveitis, an important improvement in BCVA after 1 year of follow-up was observed regardless of the type of treatment used.

Table 1. Median BCVA at onset and after one year according to ocular manifestations and type of systemic therapy.

Type of ocular affectation	n (%)	Median BCVA at onset [IQR]	Median BCVA after 1 year [IQR]	OCS n (%)	cIS n (%)	monoclonal TNFi n (%)	ETN n (%)	TCZ n (%)
Uveitis	54 (83.1)	0.6 [0.3-0.8]	0.9 [0.6-1]	44 (81.5)	29 (53.7)	16 (29.6)	3 (5.5)	3 (5.5)
-**Anterior**	31 (47.7)	0.7 [0.3-0.8]	0.8 [0.5-1]	22 (70.9)	12 (38.7)	2 (6.5)	2 (6.5)	0
-**Intermediate**	2 (3.1)	0.5	0.7	2 (100)	1 (50)	1 (50)	1 (50)	1 (50)
-**Posterior**	5 (5.2)	0.5 [0.1-0.9]	0.9 [0.9-1]	4 (80)	4 (80)	3 (60)	0	0
-**Panuveitis**	16 (24.6)	0.4 [0.2-0.7]	0.9 [0.5-1]	16 (100)	12 (75)	10 (62.5)	0	2 (12.5)
Orbital lesions	5 (7.7)	0.5 [0.1-0.6]	1 [0.1-1]	4 (80)	2 (40)	2 (40)	0	1 (20)
Retinal vasculitis	4 (6.2)	0.6 [0.5-0.8]	1 [0.6-1]	4 (100)	4 (100)	1 (25)	0	1 (25)
Dry eye	4 (6.2)	1	0.9	2 (50)	1 (25)	0	0	0
Scleritis	1 (1.5)	1	1	1 (100)	0	0	0	0

Abbreviations: BCVA: Best Corrected Visual Acuity; IQR: Interquartile Range; OCS: Oral Corticosteroid; cIS: Conventional Immunosuppressants; Monoclonal TNFi: monoclonal tumour necrosis factor inhibitors; ETN: Etanercept; TCZ: Tocilizumab.

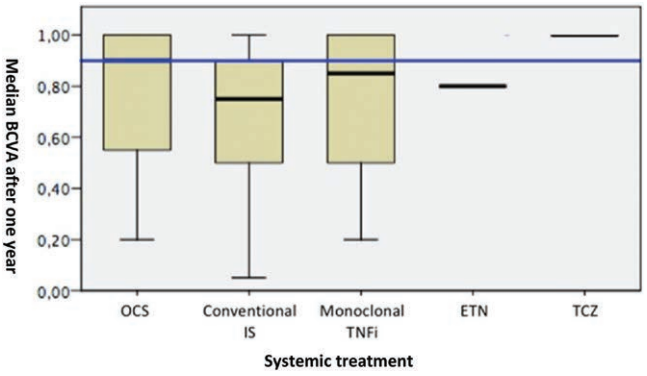


Figure 1. Median [25,75 IQR] BVCA after one year follow up according to type of systemic treatment in sarcoid uveitis.Median BCVA after one year Systemic treatment**Abbreviations:** BCVA: Best Corrected Visual Acuity; OCS: Oral Corticosteroids; Conventional IS: Conventional immunosupressants; Monoclonal TNFi: monoclonal tumour necrosis factor inhibitors; ETN: Etanercept; TCZ: Tocilizumab.

REFERENCES:

[1] Riancho-Zarrabeitia L, et al. Semin Arthritis Rheum 2015;45(3):361-8. PMID: 26092330

[2] Riancho-Zarrabeitia L et al. Clin Exp Rheumatol 2014;32(2):275-84. PMID: 24321604

[3] Vegas-Revenga N, et al. Am J Ophthalmol 2019; 200:85-94. PMID: 30660771

[4] Cordero-Coma et al. Mediators Inflamm 2014; 2014:717598. PMID: 24976689

[5] Calvo-Río V, et al. Clin Exp Rheumatol 2014; 32 (4 Suppl 84): S54-7. PMID: 25005576

Disclosure of Interests: Carmen Álvarez-Reguera: None declared, Jorge Javier Gaitán-Valdizán: None declared, Raúl Fernández-Ramón: None declared, Rosalía Demetrio-Pablo: None declared, José Luis Martín-Varillas: None declared, Lara Sanchez-Bilbao: None declared, David Martínez-López: None declared, Iñigo González-Mazón: None declared, Miguel Á. González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi and MSD., Grant/research support from: Abbvie, MSD, Janssen and Roche., Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD., Grant/research support from: Abbvie, MSD and Roche.

DOI: 10.1136/annrheumdis-2021-eular.1896

OP0092

LONG-TERM SAFETY AND EFFECTIVENESS OF CANAKINUMAB IN CRYOPYRIN-ASSOCIATED PERIODIC SYNDROMES (CAPS) – 30-MONTH DATA FROM THE RELIANCE REGISTRY

J. B. Kuemmerle-Deschner[1], B. Kortus-Goetze[2], P. Oommen[3], A. Janda[4], J. Rech[5], T. Kallinich[6], F. Weller-Heinemann[7], G. Horneff[8], I. Foeldvari[9], C. Schuetz[10], M. Borte[11], A. Braner[12], J. Weber-Arden[13], N. Blank[14]. [1]*University Hospital Tuebingen, Department of Pediatrics, Division of Pediatric Rheumatology, Tuebingen, Germany*; [2]*University of Marburg, Division of Nephrology, Marburg, Germany*; [3]*Heinrich-Heine-University Düsseldorf, Clinic of Pediatric Hematology, Oncology and Clinical Immunology, Duesseldorf, Germany*; [4]*University Hospital Ulm, Department of Pediatrics, Ulm, Germany*; [5]*Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany*; [6]*Charité University Medicine Berlin, Department of Pediatrics, Division of Pulmonology, Immunology and Critical Care Medicine, Berlin, Germany*; [7]*Klinikum Bremen-Mitte, Prof. Hess Kinderklinik, Bremen, Germany*; [8]*Asklepios Clinic Sankt Augustin, Asklepios Clinic Sankt Augustin, Sankt Augustin, Germany*; [9]*Centre for Pediatric and Adolescence Rheumatology, Centre for Pediatric and Adolescence Rheumatology, Hamburg, Germany*; [10]*Medizinische Fakultät Carl Gustav Carus, Technische Universität Dresden, Pediatrics, Dresden, Germany*; [11]*Hospital St. Georg gGmbH Leipzig, ImmunoDeficiencyCenter Leipzig (IDCL), Leipzig, Germany*; [12]*University Hospital Frankfurt, Department of Medicine II, Rheumatology, Frankfurt, Germany*; [13]*Novartis Pharma GmbH, Novartis Pharma GmbH, Nuernberg, Germany*; [14]*University Hospital Heidelberg, Rheumatology, Heidelberg, Germany*

Background: In clinical trials as well as in real-life, the IL-1ß inhibitor canakinumab leads to rapid remission of symptoms in the treatment of CAPS, a monogenic autoinflammatory disease with severe systemic and organ inflammation.

Objectives: The RELIANCE registry is designed to explore long-term safety and effectiveness of canakinumab under routine clinical practice conditions in pediatric (≥2 years) and adult patients with CAPS, including Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), and neonatal onset multisystem inflammatory disease (NOMID)/chronic infantile neurological cutaneous and articular syndrome (CINCA).

Methods: This prospective, non-interventional, observational study with a 3-year follow-up enrolls patients with clinically confirmed diagnoses of CAPS routinely receiving canakinumab. In 6-monthly visits, clinical data, physician assessments and patient-reported outcomes are evaluated starting at baseline with last update at 30 months of follow-up in the total cohort including the cohort with severe CAPS subtypes (NOMID/CINCA).

Results: 91 CAPS patients (50% female; 14 [15%] NOMID/CINCA subtypes) were enrolled by December 2020 (Table 1). At baseline, median age was 20.5 years and median duration of prior canakinumab treatment was 6 years. 11 drug related severe adverse events per 100 patient years were reported. 68% of patients

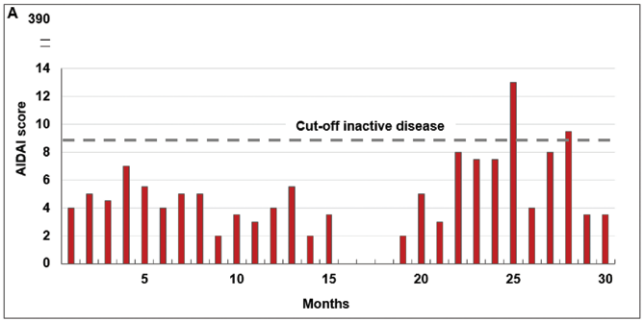
reached disease remission by physicians´ assessment along with rates of 40-61% absent disease activity in PGA. Patients reported stable low level disease activity, fatigue and Auto-Inflammatory Diseases Activity Index scores (AIDAI, figure 1). CAPS was impairing social life in 50% of patients and another 50% reported days off from school/work. Lab parameters were within normal limits.

Table 1. Patient and physician assessment of clinical CAPS disease activity and laboratory markers over time.

	Baseline		12 months		30 months	
	Total cohort	NOMID/ CINCA	Total cohort	NOMID/ CINCA	Total cohort	NOMID/ CINCA
Number of patients, N	91	14	67	8	28	4
Number (%) of patients with days absent from work/ school during last 6 months	30 (34)	4 (29)	28 (42)	2 (25)	17 (61)	4 (100)
Number (%) of patients in disease remission (physician assessment)	61 (68.5)	11 (78.6)	42 (66.7)	4 (66.7)	19 (67.9)	4 (100.0)
Physician Global Assessment, percentage of absent/mild-moderate/severe rating, %	40 / 53 / 2	57 / 36 / 0	33 / 60 / 2	33 / 50 / 0	61 / 39 / 0	75 / 25 / 0
Patient assessment of current disease activity; 0–10, median (min; max)	2.0 (0; 7)	1.0 (0; 6)	1.0 (0; 7)	1.0 (0; 5)	0.0 (0; 7)	0.0 (0; 4)
Patient assessment of current fatigue; 0–10, median (min; max)	3.0 (0; 9)	2.0 (0; 6)	3.0 (0; 8)	2.0 (0; 8)	1.0 (0; 8)	4.0 (0; 5)
Number (%) of patients without impairment of social life by the disease	32 (52.5)	4 (50.0)	31 (62.0)	3 (42.9)	11 (47.8)	1 (33.3)
CRP, median (mg/dl)	0.1	0.2	0.1	0.5	0.0	0.2
SAA, median (mg/dl)	0.3	0.4	0.5	0.9	0.3	0.1
ESR, median (mm/h)	5.0	6.0	5.0	3.5	5.0	5.5
SAE	**Number of events**		**Incidence rate per 100 patient years**			
	Total cohort	NOMID/CINCA	Total cohort	NOMID/CINCA		
All types of SAE	39	3	14.72	11.72		
SADR	20[#]	0	10.69	0.00		

[#] Alport's syndrome, appendicitis, blister, cardiovascular disorder, chest pain, circulatory collapse, erythema, febrile convulsion, glomerulonephritis, haemophilus test positive, pneumonia, premature delivery, skin discolouration, tonsillectomy, tonsillitis bacterial, tonsillitis streptococcal (all N=1 event), pyrexia (N=3 events), not yet coded (inpatient admission, N=1 event)CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; n. a., not annotated; SAA, serum amyloid A; SADR, serious adverse drug reaction; SAE, serious adverse event

Figure 1: Median AIDAI score (0-390) of the CAPS cohort (N = 91 at baseline) over 30 months



Conclusion: The 30-month interim analysis of the RELIANCE study demonstrates that long-term canakinumab treatment is safe and effective in patients with any subtype of CAPS. However, impairment of social life and days off school/work still exists.
Disclosure of Interests: J. B. Kuemmerle-Deschner Consultant of: Novartis, AbbVie, Sobi, Grant/research support from: Novartis, AbbVie, Sobi, Birgit Kortus-Goetze Consultant of: Novartis, Prasad Oommen Grant/research support from: Novartis, Ales Janda: None declared, Jürgen Rech Speakers bureau: bbvie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD; Mylan, Novartis, Roche, Sanofi, Sobi, UCB, Consultant of: Abbvie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD, Mylan, Novartis, Roche, Sanofi, Sobi, UCB, Grant/research support from: Novartis, Sobi, Tilmann Kallinich Consultant of: Sobi, Novartis, Roche, Grant/research support from: Novartis, Frank Weller-Heinemann: None declared, Gerd Horneff Speakers bureau: AbbVie, Bayer, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Grant/research support from: AbbVie, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Ivan Foeldvari Consultant of: Novartis, Catharina Schuetz: None declared, Michael Borte Grant/research support from: Pfizer, Shire, Axel Braner Consultant of: Novartis and SOBI, Julia Weber-Arden Employee of: Novartis, Norbert Blank Consultant of: Novartis, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Actelion, UCB, Boehringer-Ingelheim, Roche, Grant/research support from: Novartis, Sobi
DOI: 10.1136/annrheumdis-2021-eular.3716

OP0093 RETENTION RATE OF IL-1 INHIBITORS IN PATIENTS WITH SCHNITZLER'S SYNDROME

F. Crisafulli[1], A. Vitale[2], C. Gaggiano[2], L. Dagna[3], G. Cavalli[3], R. Cimaz[4], O. Viapiana[5], F. Iannone[6], G. Lopalco[6], R. Bortolotti[7], M. Abdel Jaber[7], C. Montecucco[8], S. Monti[8], S. Balduzzi[8], G. Emmi[9], P. Airò[1], F. Franceschini[1], L. Cantarini[2], M. Frassi[1]on behalf of Working Group of Autoinflammatory Diseases of Italian Society of Rheumatology (SIR). *[1]ASST Spedali Civili and University of Brescia, Rheumatology and Clinical Immunology Unit, Brescia, Italy; [2]University of Siena, Research Center of Systemic Autoinflammatory Diseases and Behçet's Disease Clinic, Department of Medical Sciences, Surgery and Neurosciences, Siena, Italy; [3]Vita-Salute San Raffele University, IRCCS San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UniRAR), Milano, Italy; [4]Università degli Studi di Milano, ASST Gaetano Pini-CTO Institute, Department of Clinical Sciences and Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Division of Pediatric Rheumatology, Milano, Italy; [5]University of Verona, Rheumatology Unit, Verona, Italy; [6]University of Bari "Aldo Moro," Department of Emergency and Organ Transplantations, Rheumatology Unit, Bari, Italy; [7]Santa Chiara Hospital, Department of Rheumatology, Trento, Italy; [8]IRCCS Fondazione Policlinico San Matteo, University of Pavia, Department of Rheumatology, Pavia, Italy; [9]University of Florence, Department of Experimental and Clinical Medicine, Firenze, Italy*

Background: Schnitzler's syndrome is an autoinflammatory disease characterized by monoclonal gammopathy and recurrent episodes of urticaria accompanied by clinical and laboratory signs of acute inflammation. Interleukin (IL)-1 inhibitors proved to be useful in the treatment, but data on long-term safety and efficacy of these agents are sparse.
Objectives: To evaluate the retention rate of IL-1 inhibitors in patients with Schnitzler's Syndrome.
Methods: Retrospective analysis of an Italian multicenter cohort (9 Centers). All patients fulfilled Strasbourg diagnostic criteria. Data are expressed as median [IQR].
Results: We identified 15 patients (8 females, 7 males) who received a total of 24 treatment courses with IL-1 inhibitor treatment (16 anakinra and 8 canakinumab) between January 2001 and December 2019, with a median treatment duration of 19 months [8.5-51.3]. Median age at diagnosis was 64.0 years [56.0-72.5] and median follow up was 5.0 years [2.0-8.0]. Before the biological treatment, all patients were treated with corticosteroids and 11 with at least one conventional synthetic disease-modifying antirheumatic drug (csDMARD): methotrexate (5), colchicine (5), cyclosporine (3), azathioprine (1), mycophenolate mofetil (1), cyclophosphamide (1).
Fifteen patients received 16 courses of Anakinra, which was the 1st line biological treatment in 14 patients. Seven patients continued it with benefit, while 7 patients discontinued it: 3 for secondary inefficacy; 3 for adverse events (2 injection site reactions, 1 severe allergic reaction); 1 for secondary inefficacy and leukopenia. Anakinra was used as 2nd line treatment in 1 case (after tocilizumab failure); in 1 patient anakinra was resumed after temporary discontinuation and an attempt with infliximab. One patient died for multiple myeloma progression while on treatment with anakinra. The median duration of the courses with anakinra was 20.0 months [6.0-58.3].
Seven patients received 8 courses of canakinumab (150 mg/8weeks in 5 cases and 150 mg/4weeks in 3). In 5 cases the drug was administered as 2nd line biological treatment (after anakinra failure) and in 2 cases as 3rd line treatment (1 after tocilizumab and anakinra failures and 1 after anakinra and adalimumab failure). In 1 patient, it was resumed after temporary discontinuation and an attempt with etanercept. One patient died while on treatment with canakinumab due to a presumably unrelated adverse event. The median duration of canakinumab treatment courses was 19.0 months [13.5-31.0].
At last follow-up visit, all patients were on treatment with an IL-1 inhibitor: 8 with anakinra (7 at the dosage of 100 mg/day, 1 at the dosage of 200 mg/day) and 7 with canakinumab (2 at the dosage of 150 mg/8 weeks, 4 at the dosage of 150 mg/4 weeks and 1 at the dosage of 300 mg/4 weeks). Notably, in 3 patients the dosage of canakinumab was increased since the start of the treatment.

Among 9 patients who were on treatment with prednisone at the start of the last IL-1 inhibitor, the prednisone median dose was 12.5 mg/day [10.0-18.8] while at the last follow-up visit it was 5.0 mg/day [0-7.5] (p= 0.02).
The retention rate of IL-1 inhibitors was 73.4% [SE 9.4] at 1 year and 63.6% [SE 10.4] at 2 years (Figure 1a). There was no significant difference between the retention rate of anakinra (at 1 year: 67.0% [12.2]; at 2 years: 59.6% [12.9]) and canakinumab (at 1 year: 85.7% [13.2]; at 2 years 71.4% [17.1]) (log-rank test: p=0.41) (Figure 1b).

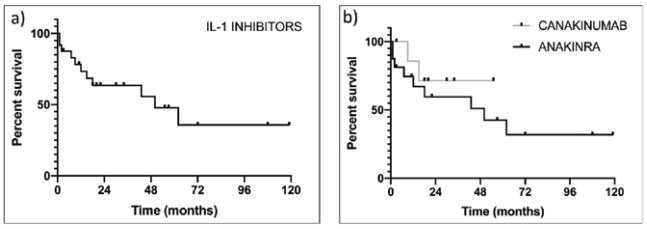


Figure 1. a) Retention rate of IL-1 inhibitors (24 courses); b) Retention rate of canakinumab (8 courses) and anakinra (16 courses).

Conclusion: In this multicentric cohort of patients affected by Schnitzler's syndrome, the treatment with IL-1 inhibitors as 1st, 2nd or 3rd line biological treatment permitted a good disease control and corticosteroid reduction in patients who did not respond to csDMARDs and/or to prior other biological DMARDs. The optimal dosage of these drugs needs to be tailored for every patient.
Acknowledgements: AIDA Network
Disclosure of Interests: Francesca Crisafulli: None declared, Antonio Vitale: None declared, Carla Gaggiano: None declared, Lorenzo Dagna: None declared, Giulio Cavalli Speakers bureau: SOBI, Novartis, Paid instructor for: SOBI, Novartis, Consultant of: SOBI, Novartis, Rolando Cimaz: None declared, Ombretta Viapiana: None declared, Florenzo Iannone: None declared, Giuseppe Lopalco: None declared, Roberto Bortolotti: None declared, Masen Abdel Jaber: None declared, Carlomaurizio Montecucco: None declared, Sara Monti: None declared, Silvia Balduzzi: None declared, Giacomo Emmi: None declared, Paolo Airò: None declared, Franco Franceschini: None declared, Luca Cantarini Speakers bureau: SOBI, Novartis, Paid instructor for: SOBI, Grant/research support from: SOBI, Novartis, Micol Frassi: None declared
DOI: 10.1136/annrheumdis-2021-eular.3071

OP0094 PULMONARY ARTERIAL HYPERTENSION IN ADULT-ONSET STILL'S DISEASE: A CASE SERIES OF 13 PATIENTS

S. Mitrovic[1,2], A. Boucly[3,4], E. Lazaro[5], N. Schleinitz[6], C. Bloch-Queyrat[7], C. Christides[8], J. Pouchot[9], M. Humbert[3,4,10], D. Montani[3], L. Savale[3], X. Jaïs[3], O. Sitbon[3,4], B. Fautrel[11,12,13,14]. *[1]Hôpital Pitié-Salpêtrière, AP-HP, Department of Rheumatology, Paris, France*; *[2]Institut Mutualiste Montsouris, Department of Medicine, Paris, France*; *[3]Hôpital Bicêtre, AP-HP, Service de Pneumologie, Centre de Référence de l'Hypertension Pulmonaire, Paris, France*; *[4]Université Paris-Sud, Université Paris-Saclay, INSERM Unité Mixte de Recherche en Santé S_999, Le Kremlin-Bicêtre, France*; *[5]CHU Bordeaux, Service de Médecine Interne et Maladies Infectieuses, Bordeaux, France*; *[6]Hôpital Timone, AP-HM, Service de Médecine Interne, Marseille, France*; *[7]Hôpital Avicennes, Médecine Interne, Bobigny, France*; *[8]Centre Hospitalier Henri Duffaut, Service de Médecine Interne, Avignon, France*; *[9]Hôpital Européen Georges Pompidou, AP-HP, Service de Médecine Interne, Paris, France*; *[10]Université Paris-Sud, Université Paris-Saclay, Le Kremlin-Bicêtre, France*; *[11] Hôpital Pitié-Salpêtrière, AP-HP, Service de Rhumatologie, Paris, France*; *[12]Centre de Référence des Maladies Auto-Inflammatoires rares et des Amyloses, (CeRéMAIA), Paris, France*; *[13]Pierre Louis Institute of Epidemiology and Public Health, INSERM UMR 1136, Paris, France*; *[14]Sorbonne Université, Department of Rheumatology, Paris, France*

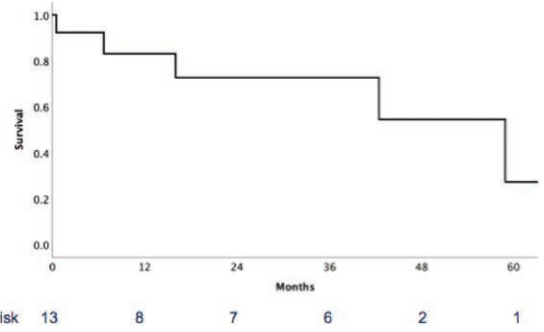
Background: Pulmonary Arterial Hypertension (PAH) is a rare but potentially fatal complication of Adult-Onset Still's Disease (AOSD) (1). To date, only isolated observations have been published.
Objectives: To establish the largest case series of AOSD patients with PAH, and to describe their clinical profile, evolution and response to treatments.
Methods: Cases were retrospectively identified from the French PAH network database and from an online call of the "Club Rhumatismes et Inflammation" (http://www.cri-net.com). To be included, all patients had to fulfil the Yamaguchi or Fautrel's criteria for AOSD and PAH had to be confirmed by right heart catheterization. The data were collected using a standardized questionnaire.
Results: Thirteen patients were identified. All were female, the mean age at PAH diagnosis was 32± 12 years, 2 (15%) patients were Caucasian, 6 (46%) from Sub-Saharan Africa, 1 (8%) from Asia and 4 (31%) from West Indies. Only 2 (15%) patients were smokers. All patients had a systemic onset of AOSD, 12 had a polycyclic and 1 a chronic articular evolution, and the mean delay between AOSD and PAH diagnosis was 2.9 (range 1.7 -5.4) years. At PAH diagnosis, patients were receiving the following treatments: 13 (100%) corticosteroids (median dose 12 mg [interquartile range (IQR) 9-18]), 3 (23%) methotrexate, 8 (61%) interleukin (IL)-1 inhibitors (exposure median duration 6.7 months [IQR 3.6-8.5]), none IL-6 inhibitors, 2 (15%) TNF inhibitors. Six (46%) patients developed PAH during an AOSD flare. PAH was severe at diagnosis: 2 (15%), 7 (54%) and 4 (31%) patients were in NYHA functional class II, III and IV, respectively, with a median 6-minute walk distance of 289 m [IQR 0-448], a mean pulmonary arterial pressure of 41 ± 12 mmHg, a mean pulmonary arterial occlusion pressure of 6 ± 3 mmHg, a mean cardiac output of 3.9 ± 1.2 L/min, a mean cardiac index of 2.5 ± 0.9 L/min/m^2 and a median pulmonary vascular resistance of 7 Wood Units [IQR 6-11]. The treatment prescribed after PAH diagnosis is detailed in the table. The median follow-up was 34 months [IQR 7-42]. Five patients (38.5 %) died. Figure 1 shows the overall survival. The haemodynamic response to PAH treatment seemed to be dissociated from the prognosis since several patients have died while their haemodynamic had improved or almost normalised.
Conclusion: PAH is a rare but potentially severe complication of AOSD, leading to death in 38.5% of our cases series. AOSD remission should be physicians' objective, since PAH seems to occur when the underlying disease is not controlled.
REFERENCES:
[1] Feist E, Mitrovic S, Fautrel B. Mechanisms, biomarkers and targets for adult-onset Still's disease. *Nat Rev Rheumatol*. 2018;1:603-618.

Table 1. Therapeutic management

Treatment	n (%)
Inotropic therapy	5 (38%)
HTAP treatment	10 (77%)
• 0Monotherapy	3
• oInitial oral dual combination therapy	3
• nDual combination therapy including intravenous (IV) prostacyclin	1
• uUpfront triple combination therapy including IV prostacyclin	3
High-dose corticosteroids	9 (69%)
Interleukin 1 inhibitors initiation	2 (15%)
Interleukin 6 inhibitors initiation	5 (38%)

Acknowledgements: The authors want to thank the Club Rhumatismes et Inflammation for the diffusion of the online call.

Figure. Overall survival



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2668

OP0095 NON-GONOCOCCAL PYOGENIC ARTHRITIS OF NATIVE JOINTS IN WESTERN AUSTRALIA. A LONGITUDINAL POPULATION-BASED STUDY OF FREQUENCY, RISK FACTORS AND OUTCOME.

J. Nossent[1], W. Raymond[1], D. Preen[2], H. Keen[1], C. Inderjeeth[1]. *[1]The University of Western Australia, Rheumatology, Crawley, Australia*; *[2]The University of Western Australia, School of Population and Global Health, Crawley, Australia*

Background: The worldwide incidence of PyA is reportedly rising due to a combination of increased longevity, multi- comorbidity, iatrogenic complications and increasing use of immunomodulating therapies, while there is limited data on longterm outcomes of PyA.
Objectives: To describe the recent incidence, risk factors and long-term outcomes in adults hospitalised with non-gonococcal pyogenic arthritis (PyA) of native joints in Western Australia (WA).

Methods: We extracted population-based longitudinally linked administrative health data for patients 16 years or older with a first diagnostic code of 711.xx (ICD9-CM) and M00.xx (ICD10-AM) in WA in the period 1990-2010. Annual incidence rates (IR), risk factors during 14.5 years lookback and outcomes including standardized mortality rates (SMR) during 10.1 years follow-up are reported.
Results: A total of 2,777 patients (67% male, mean age 49.8 ± 20.5) received a first diagnostic code for PyA. The AIR increased from 4.5 to 11.8 /100,000 over time as did age at onset (45.1 to 55.4 years) and proportion of female patients (23 to 36%). There was no seasonal variation in PyA incidence but a higher rate of predisposing comorbidities in female patients. Knees (33.6%) and hands (22%) were most frequently affected with 28.4 % of positive cultures not due to Gr+ cocci. Mean hospital stay was 8 days, 30-day readmittance and mortality rate was 12 .8% and 3.1% respectively. During ten years follow-up serious infections (43%), new diagnosis of osteoarthrosis (20%), joint replacement (10.8%), osteomyelitis (6%), and crystal arthropathy (6.3%) were the most common morbidities. SMR were increased across all age and gender categories (Table) but highest in females aged 16-40 (SMR 25.9).

Table 1. Mortality rates (MR) per 1000 person years in patients with pyogenic arthritis compared with age (at death) and gender matched categories from the general population by standardised mortality rate (SMR)

Gender	Age	Deaths	Person years	MR PyA	MR Gen pop *	SMR
Male						
	16-40	27	4015	6.72	0.892	7.53
	40-59	80	7106	11.25	2.972	3.78
	>60	331	7366	44.93	21.55	2.08
	All	**438**	**18487**	**23.69**	**5.820**	**4.07**
Female						
	16-40	11	1026	10.72	0.41	25.95
	40-59	40	2769	14.44	1.75	8.21
	>60	208	4088	50.88	24.20	2.10
	All	**259**	**7883**	**32.85**	**5.50**	**5.96**

* Based on WA death data from Australian Bureau of statistics in 2011

Conclusion: The incidence of PyA has increased significantly between 1990 and 2010 in WA. PyA associates with a 3% in-hospital mortality rate and significant late bone and joint morbidity including osteomyelitis. PyA associated with excess mortality across age and gender categories, most markedly in younger female patients.
REFERENCES:
[1] Ross JJ. Septic arthritis of native joints. Infect Dis Clin North Am 2017;31:203-18
Acknowledgements: The authors would like to acknowledge the support of the Western Australian Data Linkage Branch, the Western Australian Department of Health, and the data custodians of, the Hospital and Morbidity Data Collection, the Emergency Department Data Collection the WA Cancer Register and the WA Death Register for their assistance with the study
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1344

OP0096 EXPOSURE TO DENGUE INFECTION DO NOT RAISE RISK OF RHEUMATOID ARTHRITIS: FINDINGS FROM THE MALAYSIAN EPIDEMIOLOGICAL INVESTIGATION OF RHEUMATOID ARTHRITIS (MYEIRA) CASE-CONTROL STUDY

L. K. Tan[1,2], C. L. Too[1,10], A. F. Nurul-Aain[1], A. A. Siti-Aisyah[1], S. Wahinuddin[2], A. Osman[2], I. S. Lau[3], H. Hussein[4], N. S. Shahril[4], S. C. Gun[5], E. Mageswaren[4], M. S. Mohamed Said[6], A. Mohd. Mokhtar[7], R. Azmillah[3], M. Othman[8], L. Alfredsson[9], L. Klareskog[10], M. Shahnaz[11], L. Padyukov[10]. *[1]Allergy and Immunology Research Center, Institute for Medical Research, Ministry of Health Malaysia, Selangor, Malaysia*; *[2]Faculty of Medicine, Universiti Kuala Lumpur Royal College of Medicine Perak, Perak, Malaysia*; *[3]Department of Medicine, Selayang Hospital, Selangor, Malaysia*; *[4]Department of Medicine, Putrajaya Hospital, Putrajaya, Malaysia*; *[5]Department of Medicine, Tuanku Ja'afar Hospital, Negeri Sembilan, Malaysia*; *[6]Faculty of Medicine, University Kebangsaan Malaysia Medical Center, Kuala Lumpur, Malaysia*; *[7]Department of Medicine, Tengku Ampuan Afzan Hospital, Pahang, Malaysia*; *[8]Department of Medicine, Raja Permaisuri Bainun Hospital, Perak, Malaysia*; *[9]Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Malaysia*; *[10]Department of Medicine, Rheumatology Unit, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden*; *[11]Ministry of Health Malaysia, Federal Government Administrative Center, Putrajaya, Malaysia*

Background: Dengue infection is associated with joints pain mimicking disease onset symptom of rheumatoid arthritis (RA). However, there is lack of epidemiological studies on exposure to dengue infection and risk of future RA.
Objectives: We investigated the relationship between exposure to dengue infection and risk of developing different subsets of RA, defined by the presence of anti-citrullinated peptide antibody (ACPA) in the multi-ethnic Malaysian population.
Methods: Serum samples from 1,235 RA cases (i.e. 516 Malay, 254 Chinese, 405 Indians and 60 others/mixed-ethnicity) and 1,624 epidemiological matched population-based controls (i.e. 1,023 Malay, 208 Chinese, 297 Indians and 96 others/mixed-ethnicity) were assayed for presence of dengue IgG antibody using World Health Organization recommended ELISA kits. Positive results of dengue IgG antibodies indicates previous exposure to dengue infection(s). We performed chi-square and Mann-Whitney U analysis to determine the association of ever-exposed dengue infection with ACPA-positive/ACPA-negative RA and to investigate the antibody frequency and levels among the studied populations.
Results: We observed high occurrence of dengue IgG antibody in the overall RA cases (79.7%) and matched controls (77.3%), with no significant differences detected between the ACPA subsets of RA. Ethnicity stratification analysis revealed a decrease risk of developing ACPA-positive RA in the Indian patients with positive dengue IgG antibody (OR=0.59, 95% CI=0.37-0.94, p=0.03), and in particular patients with elevated level of dengue IgG antibody (OR=0.44, 95% CI=0.25-0.78, p<0.05). On the other hand, the significant decrease mean levels of dengue IgG antibody were observed in the ACPA-positive RA subset for all three major ethnic groups (i.e. Malay, p<0.0001, Chinese, p<0.01 and Indian<0.05) (Figure 1). No association was observed between presence of dengue IgG antibody and ACPA-negative RA subset.

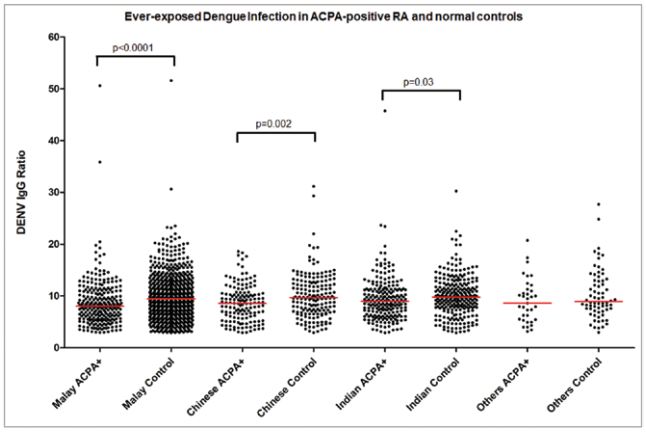


Figure 1. Comparison of mean dengue IgG antibody level between ever-exposed dengue infection RA cases, stratified by ACPA status. Comparison of median dengue IgG antibody level between the ever-exposed dengue infection ACPA-positive RA and normal controls in the four ethnic groups. The red line indicates the mean level of dengue IgG antibody level

Conclusion: Our findings demonstrated that exposure to dengue infection do not increase the risk of developing future RA in the multi-ethnic Malaysian population. The inverse associations observed in the Indian ethnic group are in line with the other studies investigating exposure to viral infection and risk of RA.
REFERENCES:
[1] Sherina et al (2017) Low levels of antibodies against common viruses associate with anti-citrullinated protein antibody-positive rheumatoid arthritis; implications for disease aetiology. Arthritis Research & Therapy 2017, 19:2169
[2] Gissel García et. al. (2011) Long-term persistence of clinical symptoms in dengue-infected persons and its association with immunological disorders. International Journal of Infectious Diseases 15 (2011) e38–e43
Acknowledgements: The authors would like to thank the Director General of Health, Ministry of Health Malaysia for supporting this study. The authors are also indebted to participants for their kind participation. This study was financially supported by the Ministry of Health, Malaysia (JPP-IMR 17-025) and the short-term research grant by UniKL RCMP (str16037).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1684

OP0097 LISTERIA MONOCYTOGENES. DESCRIPTION AND ANALYSIS OF CASES IN AN IMMUNODEPRESSED POPULATION BY RHEUMATIC DISEASES

M. Lisbona Muñoz[1], P. León[1], G. Lopez Antequera[1], E. Rubio-Romero[1]. *[1]H.U.Virgen del Rocío, Rheumatology, Seville, Spain*

Background: Listeria monocytogenes is a gram-positive bacteria that cause the invasive disease listeriosis. Human clinical syndromes are infrequent, mostly appearing in immunosuppressed individuals, newborns, the elderly, pregnant women, and occasionally healthy patients.

Objectives: We describe and analyze Listeria-related demographics and clinical features to determine the predisposing conditions for severe infections in an immunodepressed population by rheumatic diseases.
Methods: Descriptive Observational Study. A retrospective analysis of 143 patients were performed affected by listeriosis, with positive isolation of Listeria monocytogenes from blood, treated in the H.U. Virgen del Rocío (Seville- Spain) between 2003-2019. Of them 9 were rheumatic patients. The type of clinical manifestation was analyzed, paying special attention to the characteristics associated with patients with neurological complications or unfavorable outcome (death and / or abortion in pregnant women), immunosuppression (associated with cancer or rheumatic disease) was assessed as independent variables, chronic diseases (Hypertension, Diabetes Mellitus, dyslipidemia, COPD, Renal Insufficiency and Ischemic Heart Disease) as well as other baseline characteristics of the patient. (age, sex, pregnancy) and their toxic habits (tobacco and alcohol).
Results: The sample includes a similar proportion of men (70 cases) and women (73 cases), of all ages. Of the total patients, most (85%) required hospital admission, with a duration median (non-parametric data) of 11 days. 78% of the cases admitted showed a favorable evolution. However, 15.4% resulted in death and 5.6% in abortion. This percentage of abortions represented 29% of the total pregnant women admitted Of all the patients admitted, a third (33%) were immunocompromised, including patiets with cancer (79%) and rheumatic diseases (21%). Include lupus (33%), RA (22%), APs (11%), polymyalgia rheumatica (11%), panuveitis (11%) and ANCA vasculitis MPO specificity (11%). All of them required admission although the majority showed a favorable evolution, except one of the patient. which resulted in death, in which case in addition to lupus he presented with prostate cancer. Regarding the baseline treatment of these patients, 7 underwent treatment with synthetic DMARDs and three with biological DMARDs (1 Adalimumab, 1 Infliximab and 1 Rituximab) As a result of the listeria infection, most of them had fever or digestive symptoms and two of they experienced neurological manifestations (meningoencephalitis) None of these last two (with lupus and RA) had biological DMARDs.
Conclusion: Listeriosis is an uncommon but potentially serious infection usually in older people, pregnant women and immunocompromised patients. In our sample, 33% of the patients were immunocompromised. Of the 9 patients. affected by listeria with rheumatic disease we find a death for meningoencephalitis. Given the impact of this infection in immunosuppressed patients should pay attention in our patients with fever and neurological manifestations.
REFERENCE:
[1] Eleftherios Mylonakis et al. A Case Series and Review of 222 Cases. Medicine 2002; 81: 260-269.
[2] Alcoba Lez M et al.Meningitis por Listeria monocytogenes en el adulto en España. Presentación de 10 casos y revisión de la literatura. Rev Clin Esp 2002; 202 (12): 638-643.
[3] Eleftherios Mylonakis et al. Central Nervous Sistem Infection with Listeria monocytogenes. 33 Years' Experience at a General Hospital and Review of 776 Episodes from tha Literature. Medicine 1998; 77: 313-336.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4282

Rheumatoid arthritis - comorbidity and clinical aspects - I

OP0098 POLYPHARMACY IS ASSOCIATED WITH A POORER TREATMENT RESPONSE AND INCREASED RISK OF ADVERSE EVENTS IN EARLY RHEUMATOID ARTHRITIS

S. Benamar[1], C. Lukas[2], C. Daien[2], C. Gaujoux-Viala[3], L. Gossec[4], A. C. Rat[5], B. Combe[2], J. Morel[3]. [1]*CHU Montpellier, Rheumatology, Montpellier, France*; [2]*University Hospital of Montpellier, Rheumatology, Montpellier, France*; [3]*University Hospital of Nîmes, Rheumatology, Nimes, France*; [4]*La Pitié-Salpêtrière Hospital, Rheumatology, Paris, France*; [5]*CHU Caen, Rheumatology, Caen, France*

Background: Polypharmacy is steadily increasing in patients with rheumatoid arthritis (RA). They may interfere with treatment response and the occurrence of serious adverse events. Medications taken by a patient may reflect active comorbidities, whereas comorbidity indices usually used include past or current diseases.
Objectives: To evaluate whether polypharmarcy is associated with treatment response and adverse events in an early RA cohort and to establish whether polypharmacy could represent a substitute of comorbidities.
Methods: We used data from the French cohort ESPOIR, including 813 patients with early onset arthritis. Patients included the current study had to start their first disease modifying anti-rheumatic drug (DMARD) within 24 months of inclusion in the cohort. Disease activity data were collected at one, five and ten years from the initiation of the first DMARD. For each patient, treatments were collected at baseline and at five years. Medications count included all specialties other than background RA therapy, analgesics/NSAIDs and topicals. Polypharmacy was defined as a categorical variable based on the median and tertiles of distribution in the cohort. Treatment response was assessed by achieving DAS28 ESR remission (REM) at 1 year, 5 years and 10 years from the initiation of the first DMARD. The occurrence of severe adverse events (SAE) was measured by the occurrence of severe infection, hospitalization, or death during the 10-year follow-up. The association between patient's characteristics and achievement of REM and occurrence of SAE were tested in univariate analysis. A logistic regression model was used to evaluate associations between polypharmacy and REM at 1 year, 5 years and 10 years (we used baseline polypharmacy for the 1-year analysis and five years polypharmacy for the 5- and 10-years analyses). Multivariate adjustment was made for age, sex, BMI, duration of disease, initial DAS28 ESR, initial HAQ, smoking status, rheumatic disease comorbidity index (RDCI).
Results: The proportion of patients who achieved REM one year after the initiation of the first DMARD was 32.1% in the polypharmacy according to the median group (patients taken ≥2 medication) versus 67.9% in the non-polypharmacy group (p=0.07). At 5 years after the first DMARD, the proportion of patients with REM was 45.0% in the polypharmacy group versus 56.3% in the non-polypharmacy group (p=0.03). At 10 years the proportion of patients with REM was 32.5% in the polypharmacy group versus 67.5% (p=0.06). Patients who take greater or equal to 2 medications had a 40% lower probability of achieving REM (OR = 0.60 [0.38-0.94] p = 0.03) at 5 years from the first DMARD (if RDCI index was not included in the model). At 10 years, patients receiving multiple medications had a 43% lower probability of achieving REM (OR = 0.57 [0.34-0.94] p = 0.02). SAE incidence was 61 per 1000 patient-years. For patients who developed SAE all causes 71.4% where in the polypharmacy group versus 57.8% were in the non-polypharmacy group (p = 0.03; univariate analysis). These results are no longer significant after adjustment for comorbidities indices.
Conclusion: In this early RA cohort, polypharmacy is associated with a poorer treatment response and increased risk of adverse events. Polypharmacy may represent a good substitute of comorbidities for epidemiological studies.
Acknowledgements: We are grateful to Nathalie Rincheval (Montpellier) who did expert monitoring and data management and all theinvestigators who recruited and followed the patients (F. Berenbaum, Paris-Saint Antoine; MC. Boissier, Paris-Bobigny; A. Cantagrel, Toulouse; B. Combe, Montpellier; M. Dougados, Paris-Cochin; P. Fardellone and P. Boumier, Amiens; B. Fautrel, Paris-La Pitié; RM. Flipo, Lille; Ph. Goupille, Tours; F. Liote, Paris- Lariboisière; O. Vittecoq, Rouen; X. Mariette, Paris-Bicêtre; P. Dieude, Paris Bichat; A. Saraux, Brest; T. Schaeverbeke, Bordeaux; and J. Sibilia, Strasbourg).
The work reported on in the manuscript did not benefit from any financial support. The ESPOIR cohort is sponsored by the French Society for Rheumatology. An unrestricted grant from Merck Sharp and Dohme (MSD) was allocated for the first 5 years. Two additional grants from INSERM were obtained to support part of the biological database. Pfizer, Abbvie, Lilly and more recently Fresenius and Biogen also supported the ESPOIR cohort.
Disclosure of Interests: Soraya Benamar: None declared, Cédric Lukas Speakers bureau: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Consultant of: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Grant/research support from: Pfizer, Novartis and Roche-Chugai, Claire Daien Speakers bureau: AbbVie, Abivax, BMS, MSD, Roche, Chugai, Novartis, Pfizer, Sandoz, Lilly, Consultant of: AbbVie, Abivax, BMS, MSD, Roche, Chugai, Novartis, Pfizer, Sandoz, Lilly, Cécile Gaujoux-Viala Speakers bureau: Abbvie, BMS, Celgene, Janssen, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi, Roche-Chugai, UCB, Consultant of: Abbvie, BMS, Celgene, Janssen, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi, Roche-Chugai, UCB, Grant/research support from: Pfizer, Laure Gossec Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis et UCB, Consultant of: AbbVie, Amgen, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis et UCB, Anne-Christine Rat Speakers bureau: Pfizer, Lilly, Consultant of: Pfizer, Lilly, Bernard Combe Speakers bureau: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi;, Consultant of: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi;, Grant/research support from: Novartis, Pfizer, and Roche-Chugai., Jacques Morel Speakers bureau: Abbvie, BMS, Lilly, Médac, MSD, Nordic Pharma, Pfizer, UCB, Consultant of: Abbvie, BMS, Lilly, Médac, MSD, Nordic Pharma, Pfizer, UCB, Grant/research support from: BMS, Pfizer
DOI: 10.1136/annrheumdis-2021-eular.3213

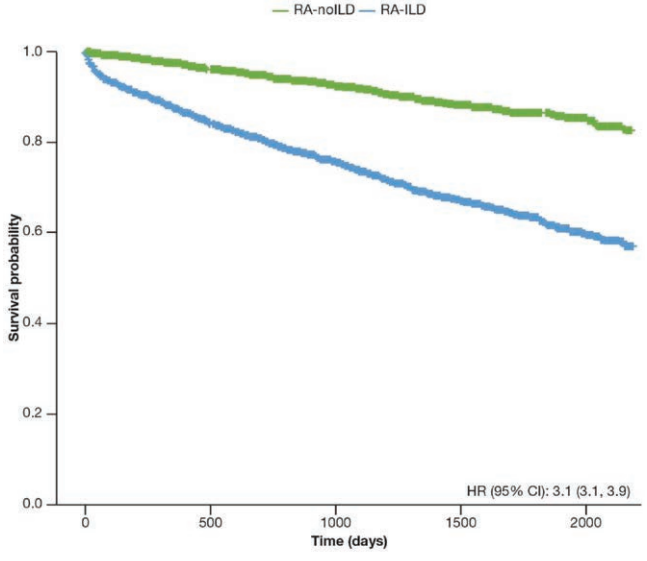
OP0099 EPIDEMIOLOGY AND MORTALITY OF RA-ASSOCIATED INTERSTITIAL LUNG DISEASE: DATA FROM A FRENCH ADMINISTRATIVE HEALTHCARE DATABASE

P. A. Juge[1], L. Wemeau Stervinou[2], S. Ottaviani[3], G. Desjeux[4], J. Zhuo[5], B. Bregman[6], V. Vannier-Moreau[7], R. M. Flipo[8], B. Crestani[9], P. Dieudé[3]. [1]*Université de Paris, AP-HP, Hôpital Bichat Claude-Bernard, Department of Rheumatology, Paris, France*; [2]*CHU Lille, Department of Pulmonology, Lille, France*; [3]*Assistance Publique-Hôpitaux de Paris, Hôpital Bichat-Claude-Bernard,*

Department of Rheumatology, Paris, France; [4]*Sanoïa, eHealth Services, Aubagne, France*; [5]*Bristol Myers Squibb, Worldwide Health Economics and Outcomes Research, Princeton, United States of America*; [6]*Bristol Myers Squibb, Health Economics and Public Health, Rueil-Malmaison, France*; [7]*Bristol Myers Squibb, Medical Affairs, France, Rueil-Malmaison, France*; [8]*Centre Hospitalier Universitaire de France, Department of Rheumatology, Lille, France*; [9]*Assistance Publique-Hôpitaux de Paris, Hôpital Bichat-Claude-Bernard, Department of Pulmonology, Paris, France*

Background: Interstitial lung disease (ILD) is a common extra-articular manifestation of RA and is associated with increased morbidity and mortality.[1-3] Studies have shown variability in the prevalence and mortality rate of patients with RA-associated ILD (RA-ILD).[4] Further studies are needed to better characterise the epidemiology of RA-ILD.
Objectives: To estimate the prevalence and incidence of clinical RA-ILD in France and to compare mortality rates between patients with RA-ILD and patients with RA without clinical ILD (RA-noILD).
Methods: A historical cohort study was conducted using data from the French national claims database (SNDS) between 1 January 2013 and 31 December 2018. Adults with an RA diagnosis (International Classification of Diseases, Tenth revision [ICD-10] codes M05, M06.0, M06.8 and M06.9) and ≥2 distinct dates of DMARD delivery were included. Onset of RA was defined as the first date of occurrence between RA codes and the first known DMARD reimbursement. ILD diagnosis was defined as having ICD-10 code J84 and ≥1 computed tomography scan after, but within 1 year of, the first date of ILD occurrence. All patients had ≥6 months' reimbursement after RA-ILD onset. The prevalence and incidence (2014–2018) of RA-ILD were estimated. The mortality rate was calculated, comparing patients with RA-ILD and patients with RA-noILD, matched 1:1 for age, sex, age at RA-ILD onset, duration of RA and presence of diabetes, arterial disease, dyslipidaemia and cardiac disease. Mortality was compared between patients with RA with and without clinical ILD in the matched population using Cox proportional hazards regression.
Results: The prevalence of RA-ILD was 6.52 per 100,000 inhabitants (incidence=1.04 per 100,000 person-years). Of the 173,138 patients with RA included in the overall population, 4330 (2.5%) had clinical ILD. Patients with RA-ILD were older at RA diagnosis (mean [SD] age: 63.3 [13.7] vs 56.9 [15.2] years) and were more likely to be male (39.8% vs 27.0%) compared with patients with RA-noILD. Patients with RA-ILD were more likely to have cardiac disease (84.9% vs 63.1%), arterial disease (38.0% vs 19.3%), diabetes (21.4% vs 12.5%) and dyslipidaemia (44.7% vs 32.9%) compared with those with RA-noILD. The mortality rate in patients with clinical RA-ILD was 1.71 per 100,000 inhabitants. The mortality rate increased according to age (0.28 per 100,000 inhabitants for patients aged <65 years, 4.60 per 100,000 inhabitants for patients aged 65–74 years and 11.4 per 100,000 inhabitants for patients aged ≥75 years). After matching, the adjusted mortality risk was three times higher (HR [95% CI]: 3.1 [3.1, 3.9]) in patients with RA-ILD than in those with RA-noILD (Figure 1).
Conclusion: This is the largest epidemiological study of RA-ILD in France. The prevalence of clinical RA-ILD in this population was towards the lower end of previous estimates (1–58%),[3] possibly due to under-reporting of claims data. However, the occurrence of clinical ILD was associated with a strong increase in mortality compared with patients with RA-noILD.

Figure 1. Mortality risk in patients with RA with versus without ILD in the matched population[a]



[a]Patients with RA-ILD and RA-noILD were matched for age, sex, age at RA-ILD onset, duration of RA and presence of diabetes, arterial disease, dyslipidaemia and cardiac disease.
HR=hazard ratio; ILD=interstitial lung disease; RA-ILD=RA-associated interstitial lung disease; RA-noILD=RA without ILD.

REFERENCES:
[1] Bodolay E, et al. *Rheumatology (Oxford)* 2005;44:656–661.
[2] Duarte AC, et al. *Rheumatology (Oxford)* 2019;58:2031–2038.
[3] Hyldgaard C, et al. Ann Rheum Dis 2017;76:1700–1706.
[4] Spagnolo P, et al. *Arthritis Rheumatol* 2018;70:1544–1554.
Acknowledgements: This study was funded by Bristol Myers Squibb. Claire Line, PhD of Caudex provided medical writing support, funded by Bristol Myers Squibb.
Disclosure of Interests: Pierre-Antoine Juge Consultant of: Bristol Myers Squibb, Lidwine Wemeau Stervinou Consultant of: Boehringer Ingelheim, Bristol Myers Squibb, Roche, Sanofi, Sebastien Ottaviani Consultant of: AbbVie, Bristol Myers Squibb, Lilly, Merck Sharp & Dohme, Novartis, Roche-Chugai, SOBI, UCB, Guillaume Desjeux: None declared, Joe Zhuo Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Bruno Bregman Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Virginie Vannier-Moreau Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Rene-Marc Flipo Speakers bureau: AbbVie, Bristol Myers Squibb, Janssen, Lilly, Medac, Merck Sharp & Dohme, Novartis, Pfizer, Roche-Chugai, Grant/research support from: Amgen, Janssen, Novartis, Pfizer, Bruno Crestani: None declared, Philippe Dieudé Consultant of: Boehringer Ingelheim, Bristol Myers Squibb, Chugaï, Lilly, Medac, Novartis, Pfizer, Sanofi, Grant/research support from: Bristol Myers Squibb, GlaxoSmithKline, Pfizer
DOI: 10.1136/annrheumdis-2021-eular.871

OP0100-HPR

THE INFLUENCE OF COMORBIDITY ON MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS 1980-2015: A LONGITUDINAL POPULATION-BASED STUDY IN WESTERN AUSTRALIA

K. Almutairi[1], J. Nossent[1], D. Preen[2], H. Keen[1], C. Inderjeeth[1]. [1]*The University of Western Australia, School of Medicine, Perth, Australia*; [2]*The University of Western Australia, School of Population and Global Health, Perth, Australia*

Background: Rheumatoid arthritis (RA) contributes to excess morbidity and mortality in RA patients compared with the general population (1). In Australia, there is a paucity of published literature on the mortality and morbidity rates in RA patients, despite the significant morbidity and mortality burden on health care costs due to RA. Linked data is the preferred method to estimate morbidity and mortality outcomes as they provide the best case-ascertainment.
Objectives: To describe temporal changes in mortality rates for patients with RA in relation to comorbidity accrual from 1980-2015 in Western Australia (WA).
Methods: Using population-level linked data from WA health administrative datasets (hospital morbidity, emergency department and death data) we followed 17,125 RA patients (ICD-10-AM M05.00–M06.99, ICD-9-CM 714) from 1980-2015. Comorbidity was ascertained using the Charlson Comorbidity Index (CCI). Mortality rate ratios (MRR) were calculated per decade between the RA cohort and the WA general population by direct age standardisation method, while temporal trends of comorbidities and in-hospital mortality were estimated per 1000 hospital separations in three consecutive decades.
Results: During 356,069 patient-years, a total of 8955 (52%) deaths occurred in the RA cohort. The leading causes of deaths were cardiovascular diseases 2386 (26.6%), cancer 1511 (16.8%), rheumatic diseases 519 (5.8%), chronic pulmonary disease 491 (5.5%), dementia 269 (3.0%) and diabetes 235 (2.6%). The highest prevalence of comorbidity (688.6 per 1000 separations) was in the period 1991-2000 following a 1.3% average annual increase since 1980. In-hospital mortality rate was also highest (26.7 deaths per 1000 separations) in the same

Table 1. Mortality rates observed among patients with rheumatoid arthritis, based on Charlson Comorbidity Index, per 1000 hospital separations, Western Australia hospitals (1980-2015).

Time period	1980-1990	1991-2000	2001-2010	2011-2015
Total number of hospital separations	82099	107731	185398	80410
Number of deaths	1620	2875	3183	1277
CCI score				
0	481 (29.7%)	1024 (35.6%)	1197 (37.6%)	565 (44.2%)
1	838 (51.7%)	1271 (44.2%)	1358 (42.6%)	467 (36.6%)
2	273 (16.8%)	518 (18%)	581 (18.3%)	232 (18.2%)
3	1 (0.1%)	4 (0.2%)	2 (0.1%)	0 (0%)
6	27 (1.7%)	58 (2%)	45 (1.4%)	13 (1%)
In-hospital RA mortality per 1000 hospital separation	19.7	26.7	17.2	15.9
Parentage of average annual change per annum in the period	0	3.8	-4.8	-2.6
Parentage of average annual change since 1980	0	1.5	-1.4	-0.2

CCI= Charlson Comorbidity Index.

period. After 2001, both RA comorbidity and mortality rates decreased annually by -0.5% and -4.8%, respectively, with annual changes of -4.4% to -2% and from 2011- 2015, respectively. The overall mortality rate in RA patients after age adjustment was 2.5-times (95%CI: 2.52-2.65) higher than the general population between 1980- 2015 and 1.5-times (95%CI: 1.39-1.81) for the period 2011-2015.
Conclusion: The annual comorbidity prevalence and mortality rates in WA have decreased significantly since 2001 reflecting improvements in the management of RA and comorbidity. Nonetheless, the mortality rate in RA patients in WA remains 1.5-times higher than their community counterparts suggesting that there is room to achieve further improvements.
REFERENCES:
[1] Meune C, Touze E, Trinquart L, Allanore Y (2009) Trends in cardiovascular mortality in patients with rheumatoid arthritis over 50 years: a systematic review and meta-analysis of cohort studies. Rheumatology (Oxford) 48:1309-1313. doi:10.1093/rheumatology/kep252

Acknowledgements: Khalid Almutairi was supported by an Australian Government Research Training Program PhD Scholarship at the University of Western Australia.

Disclosure of Interests: Khalid Almutairi: None declared, Johannes Nossent Speakers bureau: Janssen, David Preen: None declared, Helen Keen Speakers bureau: Pfizer Australia, Abbvie Australia, Charles Inderjeeth Speakers bureau: Eli Lilly.
DOI: 10.1136/annrheumdis-2021-eular.340

OP0101 RHEUMATOID ARTHRITIS DISEASE ACTIVITY OVER TIME AND SUBSEQUENT CARDIOVASCULAR RISKS.

K. Yoshida[1], H. Guan[1], S. Stryker[2], E. Karis[2], L. Harrold[3], D. Solomon[1].
[1]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, United States of America; *[2]Amgen, Inc., Thousand Oaks, United States of America*; *[3]Corrona, LLC., Waltham, MA, United States of America*

Background: Rheumatoid arthritis (RA) patients have an increased risk of cardiovascular (CV) events not fully explained by traditional CV risk factors. The relationship between fluctuating inflammation due to RA disease activity and CV events is of interest.
Objectives: To examine the influence of time-varying disease activity on the subsequent risks of CV disease.
Methods: We followed patients from a large US registry of clinically diagnosed RA patients, starting at their first visit with a Clinical Disease Activity Index (CDAI) through the end of follow-up or first CV event. Exposure of interest was disease activity measured by categorical CDAI (high, moderate, low, and remission) averaged within each 6-month window. The outcome of interest was major adverse CV events (MACE) defined as non-fatal myocardial infarction, non-fatal stroke (excluding transient ischemic attacks), and CV death. For baseline confounders we considered age, gender, race, disease duration, Health Assessment Questionnaire, hypertension, diabetes, hyperlipidemia, family history of premature (age<50) CV events, and RF/ACPA seropositivity. For time-varying variables we considered tumor necrosis factor inhibitor (TNFi), non-TNFi biologic, methotrexate, oral glucocorticoid, non-steroidal anti-inflammatory drugs, statin, and aspirin use. We used the marginal structural model (MSM) framework to examine the impact of CDAI at each 6-month interval on MACE. We estimated time-varying hazard ratios (HRs) comparing high CDAI during follow-up to CDAI remission. Several predicted survival curves were constructed under different hypothetical CDAI scenarios, such as early and late transition to CDAI remission.
Results: 40,721 patients were eligible for our analyses. 77% were female and 84% were Caucasian. The mean age was 58 (SD 13) years with mean disease duration of 8.8 (median 5) years. Mean CDAI at their first registry visit was 14 (SD 13; remission 19%, low 31%, moderate 28%, and high 22%). Other baseline characteristics include: 41% current/former smokers, 31.5% with hypertension, 8.6% with diabetes, 18% with hyperlipidemia, and 52% seropositive. The average follow-up duration after baseline was 4.4 (median 3.3; max. 17.6) years. The crude event count of MACE was 1,050 events / 180,402 person-years.
In the MSM analysis, the average HRs, assuming a constant HR, were 1.31 [0.90, 1.90] for low, 1.46 [1.01, 2.10] for moderate, and 1.43 [0.89, 2.31] for high CDAI disease activity categories during each 6-month interval. When approximating time-varying HR with linear trends, the highest estimates during the first 6 months of follow up were 1.61 [0.93, 2.77] for low CDAI, 1.97 [1.13, 3.43] for moderate CDAI, and 2.11 [1.13, 3.96] for high CDAI. These HRs gradually diminished during the follow up (Table). When we constructed hypothetical survival curves with transition to CDAI remission at different time points, earlier transition to CDAI remission was related to better event-free survival (Figure).

Table 1. Time-varying hazard ratio estimates [95% confidence intervals] by duration in study

	Disease activity measured by CDAI			
Year	Remission	Low	Moderate	High
0.5	1.00 [ref]	1.61 [0.93, 2.77]	1.97 [1.13, 3.43]	2.11 [1.13, 3.96]
1	1.00 [ref]	1.54 [0.97, 2.44]	1.85 [1.17, 2.93]	1.94 [1.13, 3.31]
2	1.00 [ref]	1.42 [1.00, 2.01]	1.63 [1.16, 2.29]	1.62 [1.04, 2.54]
3	1.00 [ref]	1.31 [0.90, 1.90]	1.43 [0.97, 2.11]	1.36 [0.80, 2.31]
4	1.00 [ref]	1.20 [0.72, 2.02]	1.26 [0.72, 2.21]	1.14 [0.55, 2.36]
5	1.00 [ref]	1.11 [0.54, 2.26]	1.11 [0.51, 2.42]	0.96 [0.36, 2.53]

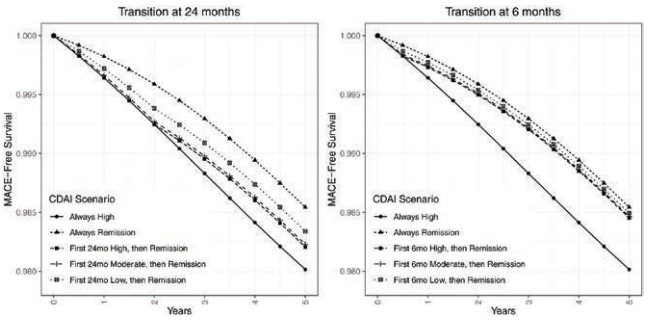


Figure 1. MACE-free survival curves under hypothetical CDAI scenarios

Conclusion: High and moderate CDAI were associated with higher hazard of MACE during the earlier period of follow-up, but the increased hazard diminished over time. In hypothetical senarios, earlier transition to CDAI remission would improve MACE free-survival.
Acknowledgements: This study was sponsored by Corrona, LLC. Corrona is supported through contracted subscriptions with multiple pharmaceutical companies. The analysis was financially supported by Amgen Inc.
Disclosure of Interests: Kazuki Yoshida Consultant of: OM1, Inc., Grant/research support from: Corrona, LLC., Hongshu Guan: None declared, Scott Stryker Shareholder of: Amgen, Inc., Employee of: Amgen, Inc., Elaine Karis Shareholder of: Amgen, Inc., Employee of: Amgen, Inc., Leslie Harrold Consultant of: AbbVie, Bristol-Myers Squibb, Genentech/Roche, Grant/research support from: Pfizer, Daniel Solomon Grant/research support from: DHS receives salary support from research contracts through Brigham and Women's Hospital with Abbvie, Amgen, Corrona, Genentech and Janssen.
DOI: 10.1136/annrheumdis-2021-eular.28

OP0102 DECLINE IN EXCESS RISK OF HEART FAILURE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN RECENT YEARS

E. Myasoedova[1,2], J. M. Davis III[1], S. Achenbach[3], K. Wright[1], R. Kurmann[4,5], R. Mankad[4], V. Roger[4], C. S. Crowson[3]. *[1]Mayo Clinic, Rheumatology, Rochester, MN, United States of America*; *[2]Mayo Clinic, Quantitative Health Sciences, Epidemiology, Rochester, United States of America*; *[3]Mayo Clinic, Quantitative Health Sciences, Biomedical Statistics and Informatics, Rochester, United States of America*; *[4]Mayo Clinic, Cardiovascular Disease, Rochester, United States of America*; *[5]Luzerner Kantonsspital, Department of Cardiology, Heart Center, Lucerne, Switzerland*

Background: Heart failure (HF) is one of the most common cardiovascular conditions in patients with rheumatoid arthritis (RA). Previous studies showed a 2-fold excess risk of HF in RA versus the general population (1). Whether this has changed over time is not known. Longitudinal studies on trends in occurrence of HF in RA patients over time, and studies comparing trends in HF in RA versus the general population are lacking.
Objectives: 1) To assess trends in incidence of HF in patients with incident RA in 1980-2009; and 2) To compare incidence of HF in RA patients and population-based comparators without RA with RA incidence/ index date in 1980-2009.
Methods: The study population comprised Olmsted County, Minnesota residents with incident RA (age ≥18 years, 1987 ACR criteria met in 1980-2009) and non-RA subjects from the same underlying population with similar age, sex and calendar year of index. All subjects were followed until death, migration, or 04/30/2019. Incident HF was defined using Framingham criteria. Patients with HF prior to RA incidence/index date were excluded. Cox proportional hazards models were used

to compare incident HF events by decade, adjusting for age, sex and cardiovascular risk factors: smoking, obesity, diabetes mellitus, hypertension, dyslipidemia. Cumulative incidence of HF adjusted for death was also computed.

Results: The study included 905 patients with RA (mean age 55.9 years; 69% female; median follow-up 13.4 years). The 10-year cumulative incidence of HF in RA cohort in the 1980s was 8.5% (95%CI 5.3-13.6%), 1990s was 10.8% (95%CI 7.7-15.1%), and 2000s was 7.1% (95%CI 4.9-10.3%). There was no difference in incidence of HF in 1990s (hazard ratio [HR] 0.91, 95% Confidence Interval [CI] 0.62-1.35) and 2000s (HR 0.73; 95%CI 0.46-1.18) compared to 1980s. Patients with incident RA were then compared to 903 individuals without RA (mean age 56.0 years; 69% female; median follow-up 13.8 years). The 10-year cumulative incidence of HF in these individuals in the 1980s was 7.4% (95%CI 4.5-12.3%), 1990s was 7.5% (95%CI 4.9-11.3%), and 2000s was 7.3% (95%CI 5.0-10.7%). Similar to RA, there was no statistically significant difference in incidence of HF in 1990s (HR 0.96, 95%CI 0.60-1.51) and 2000s (HR 0.75, 95%CI 0.44-1.30) compared to the 1980s. When comparing the risk of HF in RA and non-RA subjects, patients with RA in 2000s had no excess in HF risk as compared to the general population (HR 1.14, 95%CI 0.73-1.78, Figure 1). This is in contrast to the 2-fold excess risk of HF in patients with RA in 1980s (HR 2.20, 95%CI 1.44-3.34) and ~1.5-fold increase in risk of HF in 1990s (HR 1.54, 95%CI 1.04-2.29).

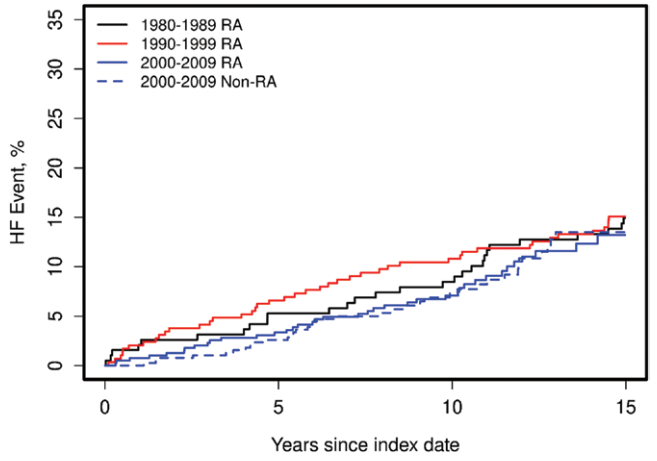


Figure 1. Cumulative incidence of any HF event in RA and non-RA patients by decade of RA incidence/index

Conclusion: We found a reduction in excess HF risk in patients with RA compared to individuals without RA in 2000s compared to 1980s. There were no statistically significant changes in incidence of HF in patients with RA and in individuals without RA over time. More studies are needed to understand the reasons and implications of these trends.

REFERENCES:

[1] Nicola PJ, et al. The risk of congestive heart failure in rheumatoid arthritis: a population-based study over 46 years. Arthritis Rheum 2005;52:412–20.

Acknowledgements: This work was supported by a grant from the National Institutes of Health, NIAMS (R01 AR46849) and NHLBI (HL120859). Research reported in this publication was supported by the National Institute of Aging of the National Institutes of Health under Award Number R01AG034676. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Disclosure of Interests: Elena Myasoedova: None declared, John M Davis III Grant/research support from: Pfizer, Sara Achenbach: None declared, Kerry Wright: None declared, Reto Kurmann: None declared, Rekha Mankad: None declared, Veronique Roger: None declared, Cynthia S. Crowson: None declared

DOI: 10.1136/annrheumdis-2021-eular.263

OP0103

5-YEAR CARDIOVASCULAR EVENT RISK IN EARLY RHEUMATOID ARTHRITIS PATIENTS WHO RECEIVED TREAT-TO-TARGET MANAGEMENT: A POPULATION-BASED COHORT STUDY

T. O. Lam[1], L. S. Tam[1]on behalf of The Clinical Rheumatology Systematic Treat-to-target in Asia Leadership (CRYSTAL). [1]*The Chinese University of Hong Kong, Department of Medicine & Therapeutics, The Prince of Wales Hospital, Hong Kong, Hong Kong (SAR)*

Background: Rheumatoid arthritis (RA) is associated with higher cardiovascular disease (CVD) risk due to the underlying inflammation [(1)]. It is uncertain if the excess CV risk could be reduced by effective suppression of inflammation using the treat-to-target (T2T) approach in patients with early RA (ERA).

Objectives: This study compared the 5-year cardiovascular event (CVE) rate among ERA patients managed by a T2T strategy with a CV risk factor-matched non-RA population.

Methods: This was an observational study using the Hong Kong Hospital Authority population-based hospital database known as the Clinical Data Analysis and Reporting System (CDARS) and the Clinical Rheumatology Systematic Treat-to-target in Asia Leadership (CRYSTAL) registry. ERA subjects from the registry with baseline disease duration less than 2 years were recruited between 2012-2016. All patients received a tight control, T2T treatment strategy aiming at remission and had been followed for at least 5 years. Each ERA subject was matched to 3 non-RA controls according to age, gender, smoking status, and the presence of diabetes mellitus (DM), hypertension (HT) and hyperlipidaemia (HL). All subjects on antiplatelet agents, with pre-existing CVD or chronic kidney disease were excluded. All subjects were analysed up to 5 years from baseline. The primary end point was the first occurence of a CVE, namely ischaemic cerebrovascular disease, ischaemic heart disease and heart failure.

Results: The study identified 261 ERA subjects and 783 matched controls. Their characteristics were shown on Table 1. The mean age was 60+/-12 years, 78% were female, 18% were smokers, 8%, 25% and 22% had DM, HT and HL respectively.

Table 1. Characteristics of ERA subjects and the matched controls

	ERA (n=261)	Controls (n=783)	*p-value*
Age (mean +/- SD)	60.2 +/- 12	60.3 +/- 12	*0.99*
Total cholesterol (mean +/- SD)	4.8 +/- 0.94	4.9 +/- 1.00	*0.34*
High density lipoprotein-cholesterol (median, IQR)	1.4 (1.2-1.6)	1.4 (1.2-1.7)	*0.612*
Low density lipoprotein-cholesterol (mean +/- SD)	2.8 +/- 0.8	2.6 +/- 0.8	*0.27*
Triglyceride (median, IQR)	0.96 (0.7-1.3)	1.2 (0.8-1.7)	*0.00*
Atherogenic index# (mean +/- SD)	-0.07 +/-0.29	-0.15 +/- 0.28	*0.48*
RA disease characteristics	**Baseline**	**last visit**	
Seropositivity	89.3%		
Disease duration (median days, IQR)	177 (96-299)	2026 (1818-2126)	
Erythrocyte sedimentation rate (mean +/- SD)	55.7 +/- 34	32.6 +/- 21.3	
C-reactive protein (median, IQR)	7.9 (3.5-22.2)	2.1 (1.0-5.0)	
Swollen joint count (median, IQR)	3 (2-6)	0 (0-1)	
Tender joint count (median, IQR)	6 (3-10)	0 (0-1)	
Patient's global assessment (mean mm +/- SD)	50.7 +/- 26.8	16.0 +/- 18.3	
DAS28-ESR (mean +/- SD)	5.2 +/- 1.3	2.4 +/- 1.8	
DAS28-CRP (mean +/- SD)	4.4 +/- 1.3	1.8 +/- 1.5	
Health assessment questionnaire (mean +/- SD)	0.77 +/- 0.74	0.38 +/- 0.51	

Atherogenic index = $\log_{10}$ (triglyceride/HDL-cholesterol)SD: standard deviation, IQR: interquartile range, DAS28: disease activity score-28

CVEs occurred in 2.3% ERA subjects and in 3.3% controls. The difference was statistically insignificant. The CVE-free survival was shown in Figure 1.

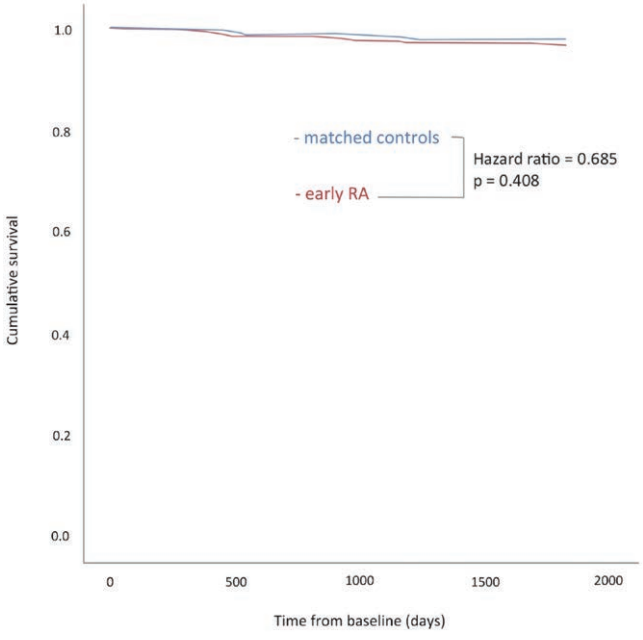


Figure 1. CVE-free survival curves of ERA subjects & matched controls

In the ERA cohort, after adjusting for baseline age and atherogenic index, cox-regression analysis showed that i) a longer DAS28 remission duration was protective for CVE with an adjusted hazard ratio (AHR) of 0.46 (95% CI 0.23-0.93),

while ii) poor baseline function as reflected by a higher health assessment questionnaire (HAQ) score was predictive of CVE with an AHR of 5.2 (95% CI 1.2-23).
Conclusion: ERA patients treated by a T2T strategy did not develop excess CVE compared to CV risk factor-matched controls over 5 years. A longer disease remission duration was protective while a higher baseline HAQ was associated with a higher CVE risk.

REFERENCES:

[1] Agca R et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Annals of the Rheumatic Diseases.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2040

OP0104 DIFFERENCES IN LOW-DENSITY LIPOPROTEIN (LDL) PARTICLE COMPOSITION AND OXIDATION MAY UNDERLIE THE PARADOXICAL ASSOCIATION OF LOW LDL WITH HIGHER CORONARY ATHEROSCLEROSIS BURDEN IN RHEUMATOID ARTHRITIS

G. Karpouzas[1,2], S. Ormseth[2], E. Hernandez[2], M. Budoff[3]. [1]*Harbor-UCLA Medical Center, Rheumatology, Torrance, United States of America*; [2]*The Lundquist Institute, Rheumatology, Torrance, United States of America*; [3]*The Lundquist Institute, Cardiology, Torrance, United States of America*

Background: The association between cholesterol and cardiovascular disease (CVD) risk is attenuated in Rheumatoid arthritis (RA). In fact, RA patients in the lowest low-density lipoprotein (LDL) group (<70mg/dl) may experience unexpectedly high CVD risk.
Objectives: We here explored whether patients with LDL<70mg/dl (Group 1) had higher coronary atherosclerosis burden compared to other LDL groups (Group 2: 70≤LDL≤130 and Group 3: LDL>130), as a reason for this risk. We further evaluated whether low LDL in group 1 associated with differences in inflammation, LDL particle composition or oxidation.
Methods: One hundred fifty RA patients without symptoms or history of CVD underwent coronary atherosclerosis evaluation with computed tomography angiography. Coronary artery calcium (CAC), number of segments with plaque (segment involvement score), stenotic severity (segment stenosis score), and extensive (>4 segments with plaque) or obstructive disease (>50% stenosis) were assessed. Lipoprotein classes and subclasses were directly measured. Oxidized LDL (oxLDL) was measured with monoclonal antibody E06. Chemiluminescence Elisa quantified IgG and IgM antibodies to oxLDL (anti-oxLDL) and apoB100 immune complexes (IC). Proinflammatory cytokines were measured with Erenna Immunoassay. Robust linear and logistic regression models-adjusted for Framingham D'Agostino score, obesity, disease activity, bDMARD and statin treatment- evaluated associations between LDL groups and plaque outcomes. Similar models evaluated adjusted differences in LDL subclasses, oxLDL, anti-oxLDL, anti-ApoB100 IC, and cytokines across LDL groups.
Results: Group 1 patients had higher coronary plaque burden (Figure 1A) and 2.8 times greater risk of extensive or obstructive disease (adjusted OR 2.82 [95% CI 1.12-7.17], *P* = 0.031) compared to LDL>70 groups. Among statin naïve patients, those with LDL<70 also had higher oxLDL (log-transformed adjusted mean 2.55 [95% CI 2.34-2.77] versus 2.27 [95% CI 2.19-2.36], *P* = 0.018 for LDL>70). Notably, Group 1 patients also had higher anti-oxLDL IgG and anti-ApoB100 IgG IC levels compared to other groups (Figure 1B). LDL subclass relative content in the LDL particle differed across groups (Figure 1C). Lp(a) was higher in LDL particles in Group 1 (adjusted mean 16.04% [95% CI 11.75-20.33], versus 10.48% [95% CI 8.20-12.75] in Group 2, *P* = 0.026 and 7.41% [95% CI 0.77-14.04] in Group 3, *P* = 0.033). Notably, Lp(a) content strongly associated with oxLDL overall (r = 0.83, *P* < 0.0001). This association was stronger for Group 1 compared to others (*P* < 0.005, Figure 1D). No differences in RA activity, CRP, TNF-α, IL-17A, or IL-17F were seen across groups. However, Group 1 had higher IL-6 (log-transformed adjusted mean 1.98 [95% CI 1.64- 2.32] versus 1.57 [95% CI 1.45-1.70], *P* = 0.028 in Group 2 and 1.32 [95% CI 0.84-1.80], *P* = 0.031 in Group 3). IL-6 associated with both IgG anti-oxLDL (*P* = 0.015) and anti-apoB100 IC (*P* = 0.016). Log-transformed IL-6 further associated with higher log-transformed CAC (adjusted B 0.41 [95% CI 0.01-0.81], *P* = 0.049).
Conclusion: RA patients with LDL<70 mg/dl had higher coronary atherosclerosis burden. Low circulating LDL in that group may reflect higher oxidation; this was mostly linked to the larger Lp(a) relative content of LDL and its significantly higher oxidation potential in that group. OxLDL immune recognition was linked to higher IgG anti-oxLDL Ab and anti-ApoB100 IC levels in the LDL<70 group, which further associated with higher IL-6 elaboration and atherosclerosis burden.
Disclosure of Interests: George Karpouzas Speakers bureau: Sanofi/ Genzyme/ Regeneron, Consultant of: Sanofi/ Genzyme/ Regeneron, Grant/research support from: Pfizer, Sarah Ormseth: None declared, Elizabeth Hernandez: None declared, Matthew Budoff Consultant of: Pfizer

DOI: 10.1136/annrheumdis-2021-eular.3397

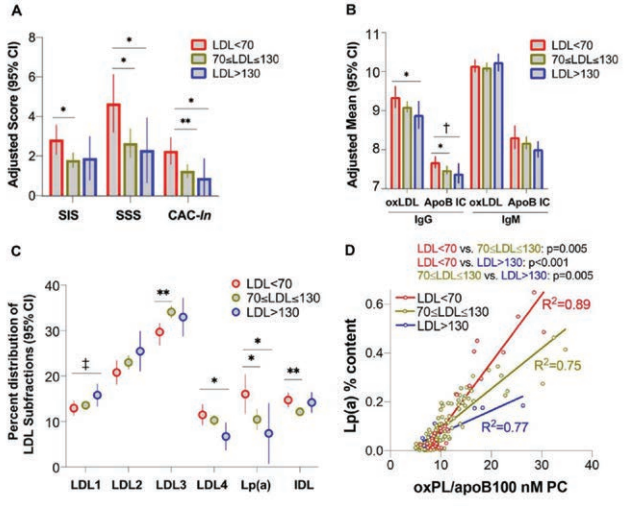


Figure 1 (A) Mean segment involvement score (SIS), segment stenosis score (SSS), and log-transformed coronary artery calcium (CAC-ln) across LDL groups, adjusted for Framingham-D'Agostino score, DAS28-CRP, waist-to-height ratio, bDMARD use, and statin use. **(B)** Mean serum levels of IgG and IgM anti-oxLDL and apoB100 immune complexes (IC) across LDL groups, adjusted for Framingham D'Agostino score and statin use. **(C)** LDL particle composition across LDL groups, adjusted for Framingham D'Agostino risk score, statin use, and total HDL-C. **(D)** Association between Lp(a) content and LDL oxidation across LDL groups, adjusted for Framingham D'Agostino score and statin use.
*p<0.050, **p<0.010, †p=0.051, ‡p=0.056

OP0105 FEASIBILITY AND USEFULNESS OF MAPPING BIOLOGIC REGISTRIES TO A COMMON DATA MODEL: ILLUSTRATION USING COMORBIDITIES

L. Kearsley-Fleet[1], K. Hyrich[1,2], M. Schaefer[3], D. Huschek[3], A. Strangfeld[3], J. Zavada[4], M. Lagová[5], D. Courvoisier[6], C. Tellenbach[7], K. Lauper[1,6], C. Sánchez-Piedra[8], N. Montero[8], J. T. Sánchez-Costa[8], D. Prieto-Alhambra[9,10], E. Burn[10,11]. [1]*The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [2]*Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, National Institute of Health Research Manchester Biomedical Research Centre, Manchester, United Kingdom*; [3]*German Rheumatism Research Center (DRFZ Berlin), Epidemiology and Health Care Research Unit, Berlin, Germany*; [4]*Institute of Rheumatology, Prague, Czech Republic*; [5]*Institute of Biostatistics and Analyses Ltd, Brno, Czech Republic*; [6]*University Hospitals of Geneva, Division of Rheumatology, Geneva, Switzerland*; [7]*Swiss Clinical Quality Management in Rheumatic Diseases, Zurich, Switzerland*; [8]*Spanish Society of Rheumatology, Madrid, Spain*; [9]*Universitat Autonoma de Barcelona and Instituto de Salud Carlos III, GREMPAL Research Group, Idiap Jordi Gol and CIBERFes, Barcelona, Spain*; [10]*University of Oxford, NDORMS, Oxford, United Kingdom*; [11]*Fundació Institut Universitari per a la recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol, Barcelona, Spain*

Background: The Observational and Medical Outcomes Partnerships (OMOP) common data model (CDM) provides a framework for standardising health data with a view towards federated analyses, thus maximising the use and power of combining disparate datasets.
Objectives: To assess feasibility and usefulness of mapping biologic registry data from different European countries to the OMOP CDM and present initial descriptive data regarding comorbidities.
Methods: Five biologic registries, as part of a funded FOREUM project, have been mapped to the OMOP CDM: 1) the Czech biologics register (ATTRA), 2) Registro Español de Acontecimientos Adversos de Terapias Biológicas en Enfermedades Reumáticas (BIOBADASER), 3) British Society for Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA), 4) German biologics register 'Rheumatoid arthritis observation of biologic therapy' (RABBIT), and 5) Swiss register 'Swiss Clinical Quality Management in Rheumatic Diseases' (SCQM). The mapping includes socio-demographic, observation period within the studies, baseline comorbidities, and baseline medications. Only patients with RA were included. Using R, registers received identical scripts to run on their mapped databases to produce an initial description of patient characteristics without the need to share patient-level data.
Results: A total of 54,458 individuals are included the five registries being mapped to the OMOP CDM, see table. Age and gender distribution was similar across registries. All registers reported on cardiovascular system comorbidities, diabetes mellitus, mental disorders, and respiratory system comorbidities. However, it was noted that results of comorbidity mapping relies on what each register collect on each patient at the point of registration.
Whilst the Charlson comorbidity index could be calculated within each registry, due to lack of the specific coding needed, such as "uncomplicated diabetes mellitus" / "end-organ damage diabetes mellitus", it was felt to be an inaccurate

measure. The granularity of the comorbidities was insufficient, as many registers coded, for example, diabetes mellitus without any extra information.

Registry	ATTRA	BIOBADASER	BSRBR-RA	RABBIT	SCQM
Country	Czechia	Spain	United Kingdom	Germany	Switzerland
Number of Participants	2334	3012	25179	13652	10281
Gender					
Female	1808 (77%)	2372 (79%)	18995 (75%)	10191 (75%)	7584 (74%)
Male	526 (23%)	640 (21%)	6184 (25%)	3461 (25%)	2697 (26%)
Age at observation start date	59 (52, 66)	56 (47, 63)	58 (49, 66)	58 (50, 67)	57 (47, 66)
First observation start date	Feb-2002	Oct-1999	Oct-2001	Aug-2006	March-1995
Number of comorbidities	1 (1, 2)	1 (0, 2)	1 (0, 2)	2 (1, 3)	2 (1, 4)
Disorder of cardiovascular system	1609 (69%)	208 (7%)	2239 (9%)	6330 (46%)	3969 (39%)
Diabetes mellitus	331 (14%)	273 (9%)	1770 (7%)	1591 (12%)	792 (8%)
Depressive Disorder	165 (7%)	0	4971 (20%)	1023 (7%)	1337 (13%)
Disorder of respiratory system	215 (9%)	209 (7%)	4125 (16%)	1282 (9%)	1630 (16%)

Conclusion: This is the first analysis of data from the newly mapped OMOP CDM across five European registers. Through mapping the registers into a CDM, and using the same script, the ability to undertake collaborative analysis without sharing patient level data outside of the country can be realised. Due to differences in study design and data capture, there needs to be a focus on harmonising the coding and analysing of the comorbidities and drugs across registries.

Disclosure of Interests: Lianne Kearsley-Fleet: None declared, Kimme Hyrich: None declared, Martin Schaefer: None declared, Doreen Huschek: None declared, Anja Strangfeld: None declared, Jakub Zavada Speakers bureau: Abbvie, Eli-Lilly, UCB, Sanofi., Consultant of: Abbvie, UCB, Sanofi, Gilead., Markéta Lagová: None declared, Delphine Courvoisier Speakers bureau: Medtalks Switzerland, Christoph Tellenbach: None declared, Kim Lauper Speakers bureau: Medtalks Switzerland, Carlos Sánchez-Piedra: None declared, Nuria Montero: None declared, Jesús-Tomás Sánchez-Costa: None declared, Daniel Prieto-Alhambra Consultant of: Amgen (speaker fees and advisory board membership fees paid to DPA's department) and UCB (consultancy fees paid to DPA's department), Grant/research support from: grants and other from AMGEN, grants, non-financial support and other from UCB Biopharma, grants from Les Laboratoires Servier, outside the submitted work., Edward Burn: None declared

DOI: 10.1136/annrheumdis-2021-eular.888

Bone & Joints

OP0106

THE ASSOCIATIONS BETWEEN BARIATRIC SURGERY AND HIP OR KNEE ARTHROPLASTY, AND HIP OR KNEE OSTEOARTHRITIS: A COHORT STUDY FROM SWEDISH NATIONWIDE HEALTHCARE REGISTRIES

T. Burkard[1], D. Holmberg[2], T. Hügle[3], A. M. Burden[1,4]. *[1]ETH Zurich, Department of Chemistry and Applied Biosciences, Zurich, Switzerland*; *[2]Karolinska University Hospital, Department of Molecular medicine and Surgery, Stockholm, Sweden*; *[3]Lausanne University Hospital (CHUV) and University Lausanne, Department of Rheumatology, Lausanne, Switzerland*; *[4]Maastricht University Medical Center+, Department of Clinical Pharmacy and Toxicology, Maastricht, Netherlands*

Background: Osteoarthritis (OA) is a slowly developing chronic joint disease mainly characterized by joint pain which may lead to physical disability. OA in weight bearing joints, such as the hip and knee, was suggested to be susceptible to high body weight. In end-stage disease, hip and knee OA are often treated with arthroplasty. The impact of weight loss among obese patients on hip and knee arthroplasty has not been assessed to date.

Objectives: To assess the association between bariatric surgery and hip or knee arthroplasty. As a secondary aim, we assessed the association between bariatric surgery and hip or knee OA in a secondary care setting.

Methods: We performed a propensity score (PS)-matched cohort study using data from Swedish nationwide healthcare registries (patient registry [secondary care], causes of death registry, prescribed drug registry). Patients aged 18-79 years who underwent bariatric surgery between 2006 and 2019 were matched to up to 2 obese bariatric surgery free patients (called unexposed patients) based on their PS. PS-matching was carried out in risk set sampling to reduce selection bias, within 4 sequential cohort entry blocks to account for time trend biases. The primary outcome was hip or knee arthroplasty. The secondary outcome was a diagnosis of hip or knee OA in secondary care. We excluded patients with differential indications for arthroplasty or OA (e.g. rheumatoid arthritis, septic arthritis). After a 1-year run-in period, patients were followed in an "as-treated" approach until the outcome or censoring due to onset of an exclusion criterion, change of exposure status, or end of study period. We applied Cox proportional hazard regression to calculate hazard ratios (HR) with 95% confidence intervals (CIs) of hip or knee arthroplasty, and separately of hip or knee OA, among bariatric surgery patients when compared to obese unexposed patients. Additionally, we performed analyses in subgroups of age, sex, joint location, bariatric surgery type, and by duration of follow-up.

Results: A total of 39 392 bariatric surgery patients were PS-matched to 61 085 obese unexposed patients. The study population had a mean age of 42 years, a mean follow-up of 6.5 years, and 72.5% of patients were women. We observed 1138 and 1108 hip or knee arthroplasties among bariatric surgery and obese unexposed patients, respectively. We observed an overall increased risk of hip or knee arthroplasty among bariatric surgery patients (HR of 1.43, 95% CI 1.32-1.55), compared to obese unexposed patients. The risk for knee arthroplasty was higher than that for hip arthroplasty among bariatric surgery patients (HR of 1.58, 95% CI 1.42-1.76, and HR of 1.21, 95% CI 1.06-1.39, respectively). Patients who underwent combined malabsorptive and restrictive bariatric surgery yielded highest risks of hip or knee arthroplasty (HR of 3.58, 95% CI 1.34-9.54). Risks of hip or knee arthroplasty decreased with duration of follow-up (highest risks 1-3 years post-bariatric surgery, HR of 1.79, 95% CI 1.56-2.07). In secondary analyses, risks of secondary care hip or knee OA were decreased among bariatric surgery versus obese unexposed patients (HR of 0.84, 95% CI 0.79-0.90). We observed lower risks for knee OA (HR of 0.82, 95% CI 0.76-0.88) than for hip OA (HR of 0.90, 95% CI 0.79-1.01) and observed lowest risks of hip or knee OA in early follow-up (1-3 years post-bariatric surgery) with a HR of 0.79, 95% CI 0.71-0.88, stable thereafter at a HR of 0.87, 95% CI 0.78-0.97.

Conclusion: Our results suggest that substantial weight loss among obese patients is associated with decreased risks of secondary care hip and knee OA. Increased risks of hip and knee arthroplasty after bariatric surgery are likely the result of increased operability of patients who have lost a substantial amount of excess body weight. Stronger associations for the knee than for the hip in both arthroplasty and OA are consistent with existing literature suggesting a stronger impact of body weight on knee than on hip joints.

Acknowledgements: We thank Prof. Dr. Jesper Lagergren (Karolinksa Institutet, Stockholm, Sweden) for hosting Dr. Theresa Burkard for a research stay at the Upper Gastrointestinal Surgery Group and making the data available for use. Furthermore, we thank Dr. Giola Santoni (Karolinksa Institutet, Stockholm, Sweden) for her technical support.

Disclosure of Interests: Theresa Burkard: None declared, Dag Holmberg: None declared, Thomas Hügle Consultant of: Pfizer, Abbvie, Novartis, Grant/research support from: GSK, Jansen, Pfizer, Abbvie, Novartis, Roche, MSD, Sanofi, BMS, Eli Lilly, UCB, Andrea Michelle Burden: None declared

DOI: 10.1136/annrheumdis-2021-eular.3974

OP0107

CLINICAL EFFICACY OF ROMOSOZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS FOR 12 MONTHS

Y. Kanayama[1], R. Sugimoto[2]. *[1]Toyota Kosei Hospital, Orthopedic surgery and Rheumatology, Toyota, Japan*; *[2]Toyota Kosei Hospital, Orthopedic surgery, Toyota, Japan*

Background: Romosozumab (ROMO), a monoclonal antibody that binds sclerostin, increases bone formation and decreases bone resorption. And although it is a novel therapeutic agent for osteoporosis, which has shown high effects of increasing bone density and inhibiting fragile fracture in overseas clinical trials. However the clinical efficacy for rheumatoid arthritis complicated with osteoporosis (RA-OP) is unknown.

Objectives: To evaluate the clinical efficacy of ROMO in patients with RA-OP for 12 months.

Methods: RA patients diagnosed according to the 2010 ACR/EULAR criteria. All patients met at least one of the following criteria were eligible; a bone mineral density T score of -2.5 or less at the lumber spine or total hip and either one or more moderate or severe vertebral fractures or two or more mild vertebral fractures. All patients were initiated ROMO from between March and December, 2019. The total number of patients was 13 cases. The ROMO dose was 210mg at once every 1 months. In all cases native or activated vitamin D has been used. We reviewed the results for 12 months about the increase and decrease of bone mineral density (BMD) of lumbar spine(LS) and total hip(TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen(PINP) and tartrate-resistant acid phopshatate form 5b(TRACP-5b).

Results: The gender was all female. The mean age was 73.2 ± 7.6; disease duration was 20.5 ± 16.9 years; the body mass index was 19.7 ± 3.0 and the FRAX was 40.5 ± 16.2. Clinical findings related to RA-OP at baseline were as follows; CRP 1.29 ± 1.66; DAS-CRP 3.43 ± 0.96; HAQ 1.59 ± 0.97 and, bone turnover markers and bone mineral density at baseline were as follows; P1NP 58.1 ± 33.5; TRACP-5b 438 ± 216; LS-BMD and T-score 0.81 ± 0.15 g/cm^2 and -2.63 ± 1.05 and TH-BMD 0.54 ± 0.08 g/cm^2 and -3.22 ± 0.64 g/cm^2. The rate of increased P1NP from baseline to 1, 3, 6 and 12 months were each 114.3 ± 90.6% at 1 month, 131.6 ± 134.3% at 3 month, 122.6 ± 174.3% at 6 month and 80.4 ± 181.6% at 12 month and decreased TRAC-5b were -10.7 ± 20.8% at 1 month, 7.9 ± 36.9% at 3 month, 25.5 ± 64.6% at 6 month and 32.5

± 77.0% at 12 month. The rate of increased LS-BMD from baseline to 6 and 12 months were 8.6 ± 8.0%, 12.5 ± 11.1% and TH-BMD were 4.3 ± 5.0%, 6.8 ± 6.9% (Fig. 1, 2).
Conclusion: Clinical efficacy of ROMO for RA-OP was extremely effective and has the high potential to be an important option in the treatment of RA-OP.

References:

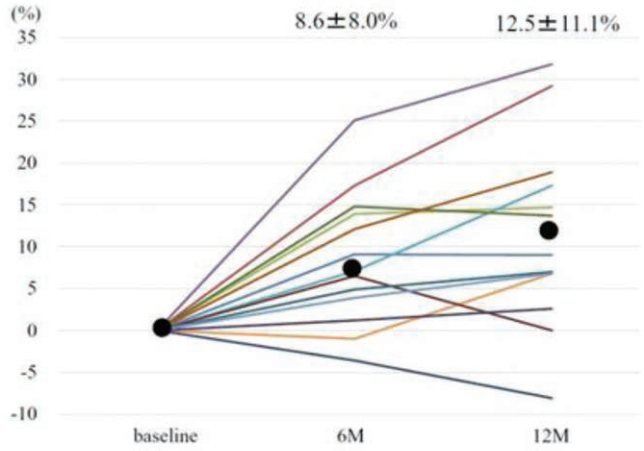


Fig.1: The rate of increased LS-BMD from baseline to 12 month

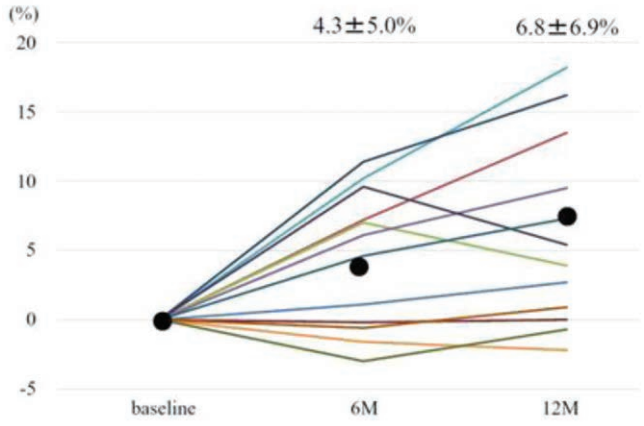


Fig.2: The rate of increased TH-BMD from baseline to 12 month

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3462

OP0108

LORECIVIVINT (SM04690), AN INTRA-ARTICULAR, SMALL-MOLECULE CLK2/DYRK1A INHIBITOR THAT MODULATES THE WNT PATHWAY, PROVIDED CARTILAGE-PROTECTIVE EFFECTS IN AN ANIMAL MODEL OF POST-TRAUMATIC OA

T. Seo[1], V. Deshmukh[1], Y. Yazici[2]. [1]*Samumed, LLC, Biology, San Diego, United States of America*; [2]*Samumed, LLC, Chief Medical Officer, San Diego, United States of America*

Background: Osteoarthritis (OA) is characterized by increased cartilage thinning, bone remodeling, and inflammation. Post-traumatic OA, which develops after acute direct trauma to the joints, accounts for approximately 12% of all OA cases.[1] Current therapeutic options focus on alleviating symptoms and pain rather than disease modification. Lorecivivint (LOR; SM04690), an intra-articular (IA), small-molecule CLK2/DYRK1A inhibitor that modulates the Wnt pathway, has been shown in animal studies to induce chondrogenesis, protect cartilage, and reduce inflammation and, thereby, improve joint health.[2]
Objectives: A single IA LOR injection was evaluated in a rat model of knee instability to determine its protective and regenerative effects when injected at different timepoints after induction of post-traumatic OA.
Methods: Knee instability/post-traumatic OA was surgically induced in rats by combining anterior cruciate ligament transection with partial medial meniscus transection (ACLT+pMMx). LOR (0.3 ug) or vehicle was injected into the IA space of the damaged knee at 2, 3, or 4 weeks after induction of OA. OA-induced (n=10/group) or sham-operated (surgery without ACLT+pMMx; n=5/group) rats were sacrificed at the injection timepoint (baseline) or 12 weeks following LOR/vehicle injection (study conclusion). Histological grades were evaluated using the summed OARSI scores (stage and grade of cartilage damage)[3] of the anterior and posterior medial femoral condyle (MFC) and medial tibial plateau (MTP). Weight distribution analysis was performed using an incapacitance meter at several timepoints. Statistical analysis was performed using one-way ANOVA with Dunnett's multiple comparison test.
Results: ACLT+pMMx surgeries led to increased OARSI scores in rats compared with sham surgeries by 2 weeks. LOR treatment at Weeks 2, 3, and 4 led to significant decreases (P<0.05) in total joint OARSI scores (Table 1) at the end of the study compared with vehicle treatment. Rats treated with LOR for 12 weeks and rats at injection baseline had similar OARSI scores, suggesting that LOR treatment arrested the progression of cartilage damage. Significant improvements (P<0.05) were also observed in the weight distribution of LOR-treated rats in the 3- and 4-week groups at 6 and 12 weeks after their respective IA injections compared with vehicle-treated rats.

Table 1. OARSI scores

Week-2 injection	**Sham-operated**	**Baseline (BL)**	**Vehicle**	**LOR**
	(14 weeks after surgery)	(2 weeks after surgery)	(12 weeks after injection)	(12 weeks after injection)
Total score	5.99	19.17	31.36	19.19
SEM	1.07	1.55	2.48	1.81
***P* value versus BL**				0.9999
***P* value versus vehicle**				0.0004
Week-3 injection	**Sham-operated**	**Baseline (BL)**	**Vehicle**	**LOR**
	(15 weeks after surgery)	(3 weeks after surgery)	(12 weeks after injection)	(12 weeks after injection)
Total score	6.09	23.17	30.45	21.20
SEM	1.25	1.36	1.42	1.00
***P* value versus BL**				0.4522
***P* value versus vehicle**				0.0001
Week-4 injection	**Sham-operated**	**Baseline (BL)**	**Vehicle**	**LOR**
	(16 weeks after surgery)	(4 weeks after surgery)	(12 weeks after injection)	(12 weeks after injection)
Total score	6.97	16.88	24.95	18.63
SEM	1.32	1.04	1.74	1.61
***P* value versus BL**				0.6257
***P* value versus vehicle**				0.0111

Conclusion: LOR exhibited cartilage-protective effects and slowed disease progression in the ACLT+pMMx model in vivo and, therefore, has potential as a structure-modifying treatment for OA.
REFERENCES:
[1] Brown TD, et al. *J Orthop Trauma*. 2006.
[2] Deshmukh V, et al. *Osteoarthr Cartil.* 2019.
[3] Pritzker KPH, et al. *Osteoarthr Cartil*. 2006.
Disclosure of Interests: Tim Seo Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Vishal Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Yusuf Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC
DOI: 10.1136/annrheumdis-2021-eular.2237

OP0109

CARTILAGE LESIONS OF THE KNEE: GAGCEST IMAGING AT 3 T MRI AND INTRAOPERATIVE VALIDATION

M. Pachowsky[1], S. Söllner[2], A. Kleyer[3], G. Welsch[4], G. Schett[3]. [1]*University Hospital of Erlangen, Erlangen, Germany, Department of Internal Medicine 3 – Rheumatology and Immunology, Department of Trauma and Orthopaedic Surgery and Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Germany, Erlangen, Germany*; [2]*University Hospital of Erlangen, Germany, Department of Trauma and Orthopaedic Surgery, Erlangen, Germany*; [3]*University Hospital of Erlangen, Erlangen, Germany, Department of Internal Medicine 3 – Rheumatology and Immunology, and Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Germany, Erlangen, Germany*; [4]*University Hospital Hamburg-Eppendorf, Hamburg, Germany, UKE Athleticum, Hamburg, Germany*

Background: Morphological Magnetic Resonance Imaging (MRI) has become the accepted diagnostic tool for non-invasive evaluation of cartilage lesions[1]. Emerging

techniques including chemical exchange saturation transfer (CEST) can be used to visualize microstructural and biochemical changes to the cartilage matrix even before morphological damage is visible[2,3]. CEST is a promising technique based on detecting the chemical exchange between bulk water protons and protons bound to solutes. This technique renders the possibility to function as a biomarker for glycosaminoglycan (GAG/gag) content for instance in cartilage of joints.

Objectives: The aim of the study was to compare glycosaminoglycan chemical exchange saturation transfer (gagCEST) of knee cartilage with intraoperative results for the assessment of early osteoarthritis (OA) and to define gagCEST values for the differentiation between healthy and degenerated cartilage.

Methods: Patients with cartilage lesions or moderate OA were preoperatively examined using 3T Magnetic Resonance Imaging (MRI). In this prospective study, regions of interest (ROIs) were examined by a sagittal gagCEST analysis and a morphological high-resolution three-dimensional, fat-saturated proton-density space sequence. Cartilage lesions were identified arthroscopically, graded by the International Cartilage Repair Society (ICRS) score in 42 defined ROIs per patient and consecutively compared with mean gagCEST values using analysis of variance and Spearman's rank correlation test. Receiver operating characteristics (ROC) curves were applied to identify gagCEST threshold values to differentiate between the ICRS grades.a

Results: Twenty-one patients with cartilage lesions or moderate OA were examined. The imaging assessment consisted of a total of 882 ROIs which were examined and graduated in ICRS score 0 (67.3%), 1 (25.2%), 2 (6.2%) and the merged ICRS 3 and 4 (1.0%). gagCEST values decreased with increasing grade of cartilage damage with a negative correlation between gagCEST values and ICRS scores. A gagCEST value threshold of 3.55% was identified to differentiate between ICRS score 0 (normal) and all other grades.

Conclusion: Conclusions. gagCEST reflects the content of glycosaminoglycan and might provide a diagnostic tool for the detection of early knee-joint cartilage damage and for the non-invasive subtle differentiation between ICRS grades by MRI even at early stages in clinical practice.

REFERENCES:

[1] Crema, M.D., M.H. Nogueira-Barbosa, F.W. Roemer, M.D. Marra, J. Niu, F.A. Chagas-Neto*, et al.*, Three-dimensional turbo spin-echo magnetic resonance imaging (MRI) and semiquantitative assessment of knee osteoarthritis: comparison with two-dimensional routine MRI. Osteoarthritis Cartilage, 2013. **21**(3): p. 428-33.10.1016/j.joca.2012.12.011

[2] Eagle, S., H.G. Potter and M.F. Koff, Morphologic and quantitative magnetic resonance imaging of knee articular cartilage for the assessment of post-traumatic osteoarthritis. J Orthop Res, 2017. **35**(3): p. 412-423.10.1002/jor.23345

[3] Liebl, H., G. Joseph, M.C. Nevitt, N. Singh, U. Heilmeier, K. Subburaj*, et al.*, Early T2 changes predict onset of radiographic knee osteoarthritis: data from the osteoarthritis initiative. Ann Rheum Dis, 2015. **74**(7): p. 1353-9.10.1136/annrheumdis-2013-204157

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1822

OP0110 A COHORT STUDY ON THE BIDIRECTIONAL RELATIONSHIP BETWEEN PERIODONTITIS AND OSTEOARTHRITIS OVER A 15-YEAR FOLLOW-UP

K. S. K. MA[1], E. Thota[1], T. Van Dyke[2]. [1]*National Taiwan University, Taipei, Taiwan, ROC, Department of Life Science, Taipei, Taiwan, Republic of China*; [2]*Forsyth Institute, Cambridge, Center for Clinical and Translational Research, Boston, United States of America*

Background: Recently, osteoarthritis has been proposed to be driven by complement-mediated inflammatory cascades. That is, in addition to the conventional degenerative model, our knowledge of osteoarthritis pathogenesis has been expanded with an inflammation-dependent theory.

Objectives: To identify the relationship between osteoarthritis and periodontitis.

Methods: 144,788 periodontitis patients and 144,788 propensity score-matched controls without history of periodontitis were enrolled in this cohort study. A Cox proportional hazard model was used to estimate the risk of osteoarthritis. Survival analysis was utilized to assess the time-dependent effect of periodontitis on osteoarthritis. Age and gender were stratified to identify susceptible subgroups. A symmetrical case-control analysis was designed to determine the relationship between periodontitis and history of osteoarthritis.

Results: Patients with periodontitis had higher risk of osteoarthritis (HR =1.15, 95% CI =1.12–1.17, P < 0.001) and severe osteoarthritis that led to total knee/hip replacement (HR =1.12, 95% CI =1.03–1.21, P < 0.01) than controls, which was time-dependent (log-rank test P < 0.01). The effect of periodontitis on osteoarthritis was significant in both genders and age subgroups over 30 years old (all P < 0.001). Among them, females (HR=1.27, 95% CI = 1.13–1.42, P < 0.001) and patients aged over 51 (HR= 1.21, 95% CI =1.10-1.33, P < 0.001) with periodontitis were predisposed to severe osteoarthritis that led to total knee/hip replacement. In addition, periodontitis patients were more likely to have a history of osteoarthritis (OR = 1.11, 95% CI = 1.06 - 1.17, P < 0.001).

Conclusion: These findings suggest a bidirectional relationship between osteoarthritis and periodontitis. Patients with periodontitis presented with a higher risk of osteoarthritis, including severe osteoarthritis that led to total knee/hip replacement. Likewise, periodontitis was more likely to develop following osteoarthritis.

REFERENCES:

[1]Wang Q, Rozelle AL, Lepus CM, et al. Identification of a central role for complement in osteoarthritis. Nat Med 2011;17:1674-9. Temoin S, Chakaki A, Askari A, et al.

[2] Identification of oral bacterial DNA in synovial fluid of patients with arthritis with native and failed prosthetic joints. J Clin Rheumatol 2012;18:117-21.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3852

OP0111 PLASMA PROTEOMICS IDENTIFIES CRTAC1 AS BIOMARKER FOR OSTEOARTHRITIS SEVERITY AND PROGRESSION

I. Szilagyi[1,2], C. Vallerga[3], J. H. Waarsing[4], D. Schiphof[2], S. M. A. Bierma-Zeinstra[2], J. Van Meurs[3]. [1]*Erasmus MC, General Practice, Rotterdam, Netherlands*; [2]*Erasmus University Medical Center, General Practice, Rotterdam, Netherlands*; [3]*Erasmus University Medical Center, Internal Medicine, Rotterdam, Netherlands*; [4]*Erasmus University Medical Center, Orthopedics, Rotterdam, Netherlands*

Background: Accurate biomarkers for diagnosis and prediction of osteoarthritis (OA) are needed. In addition, biomarkers have the potential to serve as a measure of the different pathological processes underlying OA. Here, we report on a proteomics screen targeted at two important pathways thought to underlie the etiology of OA: the inflammation and metabolic pathways.

Objectives: The aim of this study was to identify a robust biomarker for OA severity and progression.

Methods: We used data from the Rotterdam Study, a population based prospective study with participants aged 45 and older. The participants in this study underwent blood measurement at baseline and radiographic measurements at baseline as well as after a mean follow-up time of 5 years. We measured 184 proteins (inflammation and cardiometabolic panel) in plasma from 3,517 participants in the Rotterdam Study using the Olink platform.

We estimated the association for all available proteomic biomarkers with OA in knee, hip and hand in 2 ways: 1) Cross-sectionally in all joints, where we analyzed severity of OA by adding up KL-scores of both joints (knee and hip OA), and all joints of the left and right hand (total amount of joints=30); 2) Longitudinally in Knee and Hip, defining cases of progression of OA as an increase with at least 1 unit in KL-grade per person, excluding progressing from KL0 to KL1. We analyzed the relationship with multivariate regression

Figure 1. Forest plot for significantly associated proteins with severity of Hand OA

models using generalized linear models with binomial link function. In model 1 we adjusted for age, sex and cell counts, in model 2 we additionally adjusted for BMI. We report effect estimate(beta) per standard deviation (SD) change in protein levels with 95% Confidence Interval (CI) and nominal p-value (significance level<0.05) for each protein. All statistical analyses were performed in R version 3.5.2.

Results: We found in total 56 proteins that were significantly associated with one or more OA-outcomes at nominal level. Figure 1 illustrates the 19 significant associations for severity of hand OA ordered by significance level (most significant at top). We observed a very robust association between the level of circulating Cartilage acidic protein 1 (CRTAC1) and severity of OA in the knee (β=0.16, 95%CI 0.09-0.23, p=0.000013, FDR-corrected P:0.0011) hand (β=0.086, 95%CI 0.03-0.14, p=0.00085, FDR-corrected P: 0.0252), while a similar trend was seen in hip (β=0.08, 95%CI -0.02-0.18, p=0.12), although power in hip was limited in our study. The association with CRTAC1was also found for progression in knee (β=0.21, 95%CI 0.03-0.36, p=0.0156, FDR-corrected P>0.2) and hip (β=0.18, 95%CI -0.01-0.38, p=0.0624, FDR-corrected P>0.9). These associations were independent of BMI. Among the findings were several other promising biomarkers, e.g. MMP-10, which we observed to be associated with severity of hand OA (β=-0.09, 95%CI -0.15- -0.04, p=0. 00067, FDR-corrected P:0.0383) and progression of knee OA (β=-0.24, 95%CI -0.42- -0.06, p=0.0073, FDR-corrected P>0.1). Additionally, COMP, a well-known biomarker for OA, was also found significant for OA severity in hand (β=0.10, 95%CI 0.05-0.16, p<0.001, FDR-corrected P:0.0043) and knee (β=0.09, 95%CI 0.02-0.17, p=0.01, FDR-corrected P>0.2).

Conclusion: We identified the CRTAC1 protein as a robust, promising biomarker for osteoarthritis severity and progression. This protein is a glycosylated extracellular matrix protein that is found in the interterritorial matrix of articular deep zone cartilage. This protein can also be used to distinguish chondrocytes from osteoblasts and mesenchymal stem cells in culture. This suggests that CRTAC1-levels reflects a cartilage-specific process in the joint. Such a biomarker might be useful for targeting the right patients for clinical trials and designing novel therapies for OA.

Disclosure of Interests: Ingrid Szilagyi: None declared, Costanza Vallerga: None declared, J.H. Waarsing: None declared, Dieuwke Schiphof: None declared, S.M.A. Bierma-Zeinstra Consultant of: Pfizer, one day consultancy, Joyce Van Meurs: None declared

DOI: 10.1136/annrheumdis-2021-eular.1888

OP0112 FACTORS ASSOCIATED WITH OSTEOPOROSIS CARE OF MEN: A REAL-LIFE STUDY ON A NATION-WIDE DATASET

G. Adami[1], D. Gatti[1], A. Giollo[1], E. Bertoldo[1], O. Viapiana[1], P. Olivi[2], A. Fassio[1], M. Rossini[1]. [1]*University of Verona, Rheumatology Unit, Verona, Italy*; [2]*University of Verona, Orthopedic Unit, Verona, Italy*

Background: Male osteoporosis is associated with an important clinical and economic burden worldwide. Notwithstanding that, undertreatment of men with osteoporosis is common. Understanding the factors associated with less osteoporosis care utilization might help define future intervention to improve access of men to osteoporosis care.

Objectives: The aim of the study was to describe the factors associated with osteoporosis care in men.

Methods: We conducted a retrospective analysis of a nation-wide cohort (DeFRACalc79 database). DeFRACalc79 is a tool that estimates the fracture risk considering clinical and densitometric risk factors, including the presence of prior hip or vertebral and non-vertebral or non-hip fractures. We compared the clinical characteristics of male individuals with an age matched cohort of women. Propensity score generation with 2:1 matching for female and male patients was performed matching the cohorts for age, generating propensity estimates with a logistic regression model.

Results: We analyzed a sample of 4,902 men at high risk of osteoporosis. We found that the factors associated to osteoporosis care utilization in men were: the presence of comorbidities (OR 1.939, 95% CI 1.799-2.090), adjuvant hormonal therapy for prostate cancer (OR 1.482, 95% CI 1.315-1.670), the presence of vertebral or hip fractures (OR 1.490, 95% CI 1.378-1.611) and glucocorticoid treatment (OR 2.573, 95% CI 2.274-2.832) (Table 1)

Conclusion: We found that men accessed osteoporosis care with more severe osteoporosis and/or with a diagnosis of secondary osteoporosis. Male osteoporosis remains largely underdiagnosed with a dramatic latency in osteoporosis care utilization compared to women.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.257

Table 1. Clinical and densitometric characteristics of the study population and age-matched cohort of women

	Men (n=4,902)	Women (n=9,804)	OR (95% CI) – p value
Age (±SD)	65.1 (±14.2)	65.1 (±14.2)	NS
BMI (±SD)	25.31 (±4.91)	24.07 (±4.85)	**<0.0001**
Lumbar spine T-score (±SD)	-2.13 (±1.37)	-2.51 (±1.15)	**<0.0001**
Osteoporosis at lumbar spine (%)	2,601 (53.1%)	5,948 (60.7%)	**0.733 (0.684-0.785)**
Femoral neck T-score (±SD)	-1.93 (±1.04)	-2.19 (±0.91)	**<0.0001**
Osteoporosis at femoral neck (%)	1,412 (28.8%)	3,936 (40.1%)	**0.603 (0.560-0.649)**
% 10-year risk of fracture (±SD)	22.77 (±21.05)	20.26 (±4.85)	**<0.0001**
Family history of fragility fracture (%)	891 (18.2%)	2,379 (24.3%)	**0.693 (0.636-0.756)**
Secondary osteoporosis (%)	2,415 (49.3%)	3,092 (31.5%)	**2.108 (1.965-2.262)**
Glucocorticoids ≥5 mg/day >3 months (%)	768 (17.4%)	694 (7.7%)	**2.573 (2.274-2.832)**
Glucocorticoids ≥5 mg/day ≥3 months <12 months (%)	74 (2.0%)	72 (0.9%)	**2.357 (1.700-3.267)**
Glucocorticoids ≥5 mg/day ≥12 months (%)	119 (3.2%)	138 (1.6%)	**1.977 (1.543-2.534)**
Adjuvant hormonal therapy for breast cancer or prostate cancer (%)	495 (12.0%)	766 (8.4%)	**1.482 (1.315-1.670)**
Comorbidities (%)	1,778 (36.3%)	2,225 (22.7%)	**1.939 (1.799-2.090)**
Rheumatoid arthritis (%)	303 (8.8%)	511 (6.3%)	**1.439 (1.241-1.668)**
Psoriatic arthritis (%)	59 (1.9%)	103 (1.3)	**1.390 (1.006-1.919)**
Systemic lupus erythematosus (%)	22 (0.7%)	77 (1.0%)	0.693 (0.431-1.115)
Systemic sclerosis (%)	9 (0.3%)	60 (0.8%)	**0.364 (0.180-0.734)**
Other rheumatic diseases (%)	173 (5.2%)	310 (3.9%)	**1.354 (1.119-1.638)**
Inflammatory bowel diseases (%)	144 (2.7%)	126 (1.6%)	**2.773 (2.175-3.534)**
Chronic obstructive pulmonary disease (%)	281 (8.3%)	277 (3.5%)	**2.461 (2.074-2.920)**
Diabetes (%)	441 (12.4%)	478 (5.9%)	**2.238 (1.954-2.564)**
Neurological diseases (%)	236 (7.0%)	260 (3.3%)	**2.202 (1.837-2.639)**
HIV infection (%)	110 (3.4%)	23 (0.3%)	**11.603 (7.389-18.221)**
Vertebral or hip fractures (%)	1,434 (29.3%)	2,130 (21.7%)	**1.490 (1.378-1.611)**
Non-vertebral, non-hip fractures (%)	534 (10.9%)	1,477 (15.1%)	**0.689 (0.620-0.766)**

OP0113 FEMALE REPRODUCTIVE FACTORS AND RISK OF JOINT REPLACEMENT ARTHROPLASTY OF KNEE AND HIP DUE TO OSTEOARTHRITIS IN POSTMENOPAUSAL WOMEN: A NATIONWIDE COHORT STUDY OF 1.36 MILLION WOMEN

Y. Eun[1], J. E. Yoo[2], K. D. Han[3], D. H. Kim[3], J. Lee[1], D. Y. Lee[4], D. H. Lee[5], H. Kim[6], D. W. Shin[7]. [1]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medicine, Seoul, Korea, Rep. of (South Korea)*; [2]*Healthcare System Gangnam Center, Seoul National University Hospital, Department of Family Medicine, Seoul, Korea, Rep. of (South Korea)*; [3]*Soongsil University, Department of Statistics and Actuarial Science, Seoul, Korea, Rep. of (South Korea)*; [4]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Obstetrics and Gynecology, Seoul, Korea, Rep. of (South Korea)*; [5]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Orthopedic Surgery, Seoul, Korea, Rep. of (South Korea)*; [6]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medical Humanities, Seoul, Korea, Rep. of (South Korea)*; [7]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Family Medicine and Supportive Care Centre, Seoul, Korea, Rep. of (South Korea)*

Background: Previous studies on the link between female reproductive factors and osteoarthritis (OA) have shown conflicting results.

Objectives: This study attempted to explore the association between reproductive factors and joint replacement arthroplasty of knee (TKRA) and hip (THRA) in a large nationwide population-based cohort of postmenopausal women.

Methods: 1,218,257 subjects who participated in national health examination in 2009 were included in the study. The study outcomes is incident THRA or TKRA

due to severe hip or knee OA. The association of reproductive factors and THRA or TKRA was evaluated using a multivariate-adjusted proportional hazards model.
Results: During the mean follow-up duration of 8.2 years, 1,733 incident THRA cases and 65,108 incident TKRA cases were observed. Later age at menarche (aHR 1.12 in 13-14 years; aHR 1.24 in 15-16 years; aHR 1.32 in ≥ 17 years), longer breastfeeding (aHR 1.24 in < 6 months; aHR 1.24 in 6-12 months; aHR 1.50 in ≥ 12 months), HRT (aHR 1.06 in < 2 years; aHR 1.11 in 2-5 years; aHR 1.21 ≥ 5 years) and OC use (aHR 1.11 in < 1 year; aHR 1.17 ≥ 1 year) was associated with increased risk of TKRA for severe knee OA, while later age at menopause (aHR 0.93 in 45-49 years; aHR 0.89 in 50-54 years), longer reproductive span (aHR 0.91 in 30-34 years; aHR 0.87 in 35-39 years; aHR 0.91 in ≥ 40 years) was associated with decreased risk. With regard to THRA for severe hip OA, later menarche (aHR 1.21 ≥ 17 years), longer breastfeeding (aHR 1.39 in < 6 months; aHR 1.31 in ≥ 12 months), and HRT more than 5 years (aHR 1.49) were associated with higher risk. The association between reproductive factors and severe OA was more pronounced in underweight and younger subjects.
Conclusion: Our study found that shorter estrogen exposure was associated with higher risk of joint replacement therapy due to severe OA, and such association was more pronounced in underweight and younger subjects.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2871

Rheumatoid arthritis - biological DMARDs

OP0114

SHORT- AND LONGER-TERM RISKS FOR ACUTE CORONARY SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS STARTING TREATMENT WITH DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS. A COLLABORATIVE OBSERVATIONAL HEAD-TO-HEAD STUDY ACROSS FIVE NORDIC RHEUMATOLOGY REGISTERS

B. Delcoigne[1], L. Ljung[1,2], S. A. Provan[3], B. Glintborg[4,5], K. Lederballe Gron[4,5], M. L. Hetland[4,5], N. Steen Krogh[6], N. Trokovic[7], H. Relas[8], C. Turesson[9], B. Michelsen[3,10], J. Askling[1]on behalf of Nordforsk Rheumatology. *[1]Karolinska Institutet, of Medecine, Division of Clinical Epidemiology, Stockholm, Sweden*; *[2]Umeå University, Department of Public Health and Clinical Medicine/ Rheumatology, Umeå, Sweden*; *[3]Diakonhjemmet Hospital, Department of Rheumatology and Research, Oslo, Norway*; *[4]DANBIO and Copenhagen Center for Arthritis Research, COPECARE, Copenhaguen, Denmark*; *[5]Rigshospitalet, Center for Rheumatology and Spine Diseases, Centre of Head and Orthopedics, Copenhagen, Denmark*; *[6]Zitelab, Zitelab, Frederiksberg, Denmark*; *[7]Helsinki University Hospital, Department of Medicine, Helsinki, Finland*; *[8]Helsinki University Hospital, Division of Rheumatology, Helsinki, Finland*; *[9]Lund University, Rheumatology, Department of Clinical Sciences, Malmö, Malmö, Sweden*; *[10]Sorlandet Hospital, Division of Rheumatology, Department of Medicine, Kristiansand, Norway*

Background: Rheumatoid Arthritis (RA) is associated with increased cardiovascular co-morbidity including acute coronary syndrome (ACS), partly due to effects of systemic inflammation. Disease-modifying anti-rheumatic drugs (DMARDs) may reduce RA disease activity, but act through several pathways and may themselves have an impact on cardiovascular risks. Whether the risks of ACS associated with biologic (b) and targeted synthetic (ts) DMARDs differ is still unknown.
Objectives: To assess and compare incidences of ACS during treatment of RA with etanercept (ETA), adalimumab (ADA), infliximab (INF), certolizumab pegol (CTZ), golimumab (GOL), rituximab (RIT), abatacept (ABA), tocilizumab (TCZ), baricitinib (BAR) or tofacitinib (TOF).
Methods: We defined and pooled treatment cohorts of patients starting any of the above treatments between 2008 and 2017 from clinical rheumatology registers in Denmark (DK), Finland (FI), Norway (NO), and Sweden (SE). One patient could contribute several treatment episodes. Age, sex, co-medication (methotrexate, prednisolone), number of previous b/tsDMARDs, CRP, comorbidities (cardiovascular (including ACS (defined as ICD-10: I20.0, I21.0-4, I21.9) and cerebrovascular disease, thromboembolic events, diabetes, hospitalized infection, cancer, kidney failure, COPD) and associated drugs were extracted and used as adjustment in Cox regression analyses comparing the incidence of ACS between treatments. We used several follow-up lengths (1, 2, and up to 5 years) and two different risk windows (ACS on drug [ending follow-up on treatment discontinuation] and ACS ever since treatment start [disregarding any treatment discontinuation]). We also stratified by age and number of previous b/tsDMARDs.
Results: We included 40850 treatment courses in 24083 patients (DK 7271, FI 3732, NO 1540, and SE 11540; around 75% women). ETA was the most common treatment (27%) whereas BAR and TOF comprised <1%, and the other DMARDs 6-14% each. The proportions with a history of ACS at treatment start ranged from 1.2% (NO) to 1.8% (DK).

We found 780 incident ACS events during 141 326 person-years (pyrs) in the 5-year follow-up time and "ACS ever since treatment start" risk window, resulting in a crude incidence rate of 5.5 events per 1000 pyrs. No event was recorded for BAR nor TOF, which also had the shortest follow-up. Adjusted hazard ratios (HR) increased slightly with longer follow-up times, but the two risk windows provided similar HRs. For the 5-year follow-up, RIT was associated with an increased risk of ACS compared to ETA (Table), while no association was observed for shorter follow-up times. Stratifying on age did not modify the associations. Separate analyses by number of previous b/tsDMARDs suggested that ABA (HR=1.8, 95% CI 1.0-3.3), INF (HR=2.2, 95% CI 1.0-4.6) and RIT (HR=1.9, 95% CI 1.1-3.4) were associated with increased risks of ACS compared to ETA in the subgroup of patients with two or more previous bDMARDs (Figure), whereas no differences were found among patients starting either drug as 1st/2nd bDMARD.

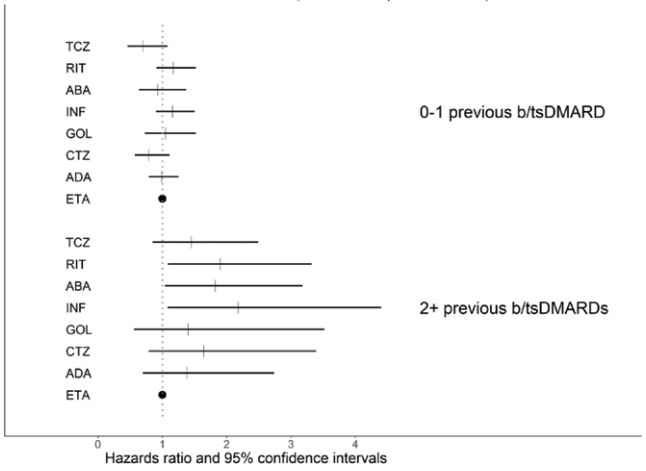
Table 1. Comparisons of risks for ACS during a 5-year follow-up since start of bDMARD treatment.

Drug	N events	pyrs	Crude incidence rate/ 1000 pyrs	HR (95% CI)[1]
ETA	175	35917	4.9	ref.
ADA	115	24093	4.8	1.0 (0.8-1.3)
CTZ	54	14158	3.8	0.9 (0.6-1.2)
GOL	40	9006	4.4	1.1 (0.8-1.5)
INF	106	17803	6.0	1.2 (0.9-1.5)
ABA	70	10795	6.5	1.1 (0.8-1.4)
RIT	158	16622	9.5	**1.3 (1.0-1.6)**
TCZ	62	12866	4.8	0.9 (0.5-1.2)
BAR	0	36		
TOF	0	30		

Pyrs: person-years; HR: hazards ratio[1] adjustment: see text.

Conclusion: In this cohort including ≥ 24,000 patients followed for up to 5 years, the ACS incidence rate was 5.5/1000 pyrs, with RIT showing an increased risk compared to ETA. In clinical practice, the choice of bDMARD does not seem to influence ACS risk in the short term. In the longer term, differences in ACS risk between bDMARDs may reflect channeling to these, or truly differential effects in subpopulations of patients.
Acknowledgements: Partly funded by Nordforsk and Foreum

Figure:
Comparisons of risks for ACS during a 5-year follow-up since start of bDMARD treatment, stratified on number of previous b/tsDMARDs:
Hazards ratio and 95% confidence intervals (with etanercept as reference)



Disclosure of Interests: Bénédicte Delcoigne: None declared, Lotta Ljung: None declared, Sella Aa. Provan Speakers bureau: Novartis, Consultant of: Novartis, Grant/research support from: Boehringer- Ingelheim, Bente Glintborg Grant/research support from: Pfizer, BMS, AbbVie, Kathrine Lederballe Gron Grant/research support from: BMS, Merete L. Hetland Consultant of: Abbvie, Biogen, BMS, Celltrion, Eli Lilly, Janssen Biologics B.V, Lundbeck Fonden, MSD, Pfizer, Roche, Samsung Biopies, Sandoz, Novartis, Grant/research support from: Abbvie, Biogen, BMS, Celltrion, Eli Lilly, Janssen Biologics B.V, Lundbeck Fonden, MSD, Pfizer, Roche, Samsung Biopies, Sandoz, Novartis, Niels Steen Krogh: None declared, Nina Trokovic: None declared, Heikki Relas Speakers bureau: Abbvie, Celgene, Pfizer, Grant/research support from: Abbvie, Celgene, Pfizer, Carl Turesson Speakers bureau: Abbvie, Bristol-Myers Squibb, Medac, Pfizer, Roche, Consultant of: Roche, Brigitte Michelsen Consultant of: Novartis (paid to employer), Grant/research support from: Novartis (paid to employer), Johan Askling Consultant of: Abbvie, Astra-Zeneca, BMS, Eli Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB. These entities have entered into

agreements with Karolinska Institutet with JA as principal investigator, mainly in the context of safety monitoring of biologics via the ARTIS national safety monitoring system.

DOI: 10.1136/annrheumdis-2021-eular.2626

OP0115 EFFICACY AND SAFETY OF ABBV-3373, A NOVEL ANTI-TNF GLUCOCORTICOID RECEPTOR MODULATOR ANTIBODY DRUG CONJUGATE, IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS DESPITE METHOTREXATE THERAPY: A PHASE 2A PROOF OF CONCEPT STUDY

F. Buttgereit[1], J. Aelion[2], B. Rojkovich[3], A. Zubrzycka-Sienkiewicz[4], T. Radstake[5], S. Chen[5], D. Arikan[5], H. Kupper[6], H. Amital[7,8]. [1]*Charité University Medicine, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; [2]*West Tennessee Research Institute, Jackson, United States of America*; [3]*Buda Hospital of the Hospitaller Order of St. John of God, Rheumatology, Budapest, Hungary*; [4]*Reumatika –Centrum Reumatologii, ARS Rheumatica sp.z.o.o, Warsaw, Poland*; [5]*AbbVie, Immunology, North Chicago, United States of America*; [6]*AbbVie Deutschland GmbH & Co. KG, Immunology, Ludwigshafen, Germany*; [7]*Sheba Medical Center, Department of Medicine 'B' and Zabludowicz Center for Autoimmune Diseases, Ramat Gan, Israel*; [8]*Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*

Background: ABBV-3373 is a novel antibody drug conjugate composed of adalimumab (ADA) linked to a proprietary and highly potent glucocorticoid receptor modulator (the anti-inflammatory payload) currently evaluated for the treatment of rheumatoid arthritis (RA).

Objectives: To assess the efficacy and safety of ABBV-3373 vs ADA in RA patients (pts).

Methods: This was a 24-week (wk) randomized, double-blind, double-dummy, active-controlled Phase 2a study of intravenously (IV)-administered ABBV-3373 100 mg (for 12 wks followed by placebo [PBO] for 12 wks) vs subcutaneous injections of ADA 80 mg every other wk (for 24 wks) in pts on background methotrexate. The primary endpoint was the change from baseline (BL) in DAS28(CRP) at Wk 12. Pre-planned statistical methods incorporating pre-specified historical ADA data both alone (pre-specified success criterion, 2-sided $P \leq 0.1$) and supplemented with in-trial ADA data (pre-specified success criterion, probability >95%) were used to achieve adequate statistical power with a reduced trial size. Assay sensitivity was evaluated through construction of a synthetic PBO arm by propensity score matching, using individual pt-level PBO data from 3 recent sponsor-run trials of similar populations and trial settings. Secondary endpoints at Wk 12 included 1) mean change from BL in CDAI, SDAI, DAS28(ESR), HAQ-DI; 2) proportion of pts achieving DAS28(CRP)≤3.2, ACR20/50/70 responses, HAQ-DI≤-0.22. Continuous and categorical efficacy variables were analyzed using mixed effect model repeated measurements and Cochran-Mantel-Haenszel test, respectively; non-responder imputation was applied to missing categorical data. Treatment-emergent adverse events were summarized through Wk 12.

Results: A total of 48 pts were randomized and treated (ABBV-3373: 31; ADA: 17); 46 pts (96%) completed 12 wks of study treatment. BL demographics and disease characteristics were indicative of established RA and similar among the 2 treatment arms and the synthetic PBO arm. ABBV-3373 demonstrated significant improvement in mean DAS28(CRP) at Wk 12 vs the pre-specified historical ADA (-2.65 vs -2.13; P=0.022) and numerically greater improvement vs the combined in-trial and historical ADA arm (-2.65 vs -2.29; probability 90%; Figure). Comparable improvements in disease activity and targets were observed for ABBV-3373 and in-trial ADA. Assay sensitivity was supported by the fact that both ABBV-3373 and ADA arms were superior to synthetic PBO (P<0.001). For secondary endpoints, greater efficacy was observed with ABBV-3373 vs historical ADA; ABBV-3373 was predicted with 79-99% probability to be better than ADA based on the combined in-trial and historical ADA data. 2 serious infections were reported with ABBV-3373 (pneumonia, upper respiratory tract infection) and none with ADA through Wk 12 (Table). 1 event of anaphylactic shock reaction was reported with ABBV-3373. After increasing the duration of IV administration from 3 min to 15-30 min, no similar events were observed.

Conclusion: These data demonstrate the clinical efficacy of ABBV-3373 and its potential to provide improved outcomes for RA pts compared to ADA. The safety profile of ABBV-3373 was generally similar to ADA.

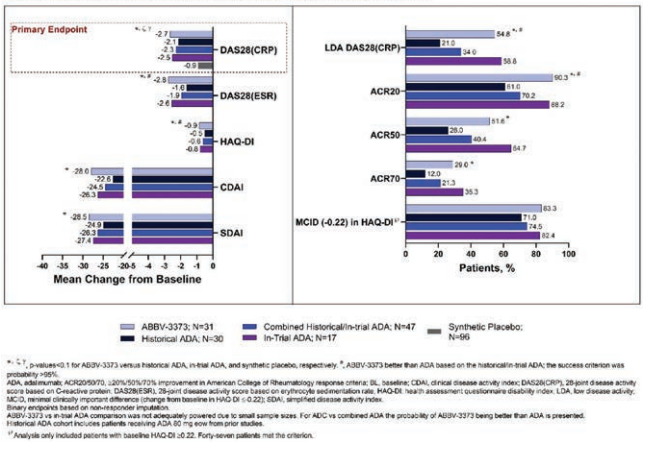
Acknowledgements: AbbVie and the authors we thank the patients, trial sites, and investigators who participated in this clinical trial. AbbVie, Inc was the trial sponsor, contributed to trial design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. No honoraria or payments were made for authorship. The authors thank Yang Yang of AbbVie Inc for supporting the statistical analysis and data reporting. Medical writing support was provided by Ramona Vladea, PhD of AbbVie, Inc.

Table 1. Treatment Emergent Adverse Events up to Week 12

Event, n (%)	ADA (N = 17)	ABBV-3373 (N = 31)
Adverse event (AE)	12 (70.6)	11 (35.5)
AE with reasonable possibility of being drug related[$]	3 (17.6)	2 (6.5)
Severe AE	0	1 (3.2)
Serious AE	0	4 (12.9) [#]
AE leading to Discontinuation of Study Drug	1 (5.9)	1 (3.2)
Serious infections	0	2 (6.5)
Opportunistic infection excluding Tuberculosis	0	0
Allergic Reactions Including Hypersensitivity, Angioedema, and Anaphylaxis	2 (11.8) [&]	1 (3.2) [^]
Systemic glucocorticoid events	0	0
All deaths	0	0

[$]As assessed by investigator.[#]Serious AEs: 1 non-cardiac chest pain, 1 pneumonia, 1 upper respiratory tract disease and 1 anaphylactic shock.[&]1 Type I hypersensitivity, 1 Pruritus[^]1 Anaphylactic shock

Figure. Analysis of Primary, Secondary, and Additional Efficacy Endpoints at Week 12



Disclosure of Interests: Frank Buttgereit Consultant of: AstraZeneca, AbbVie, Grünenthal, Horizon Pharma, Pfizer, and Roche, Grant/research support from: AbbVie, Horizon Pharma, Pfizer, and Roche, Jacob Aelion Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Eli Lilly, Galapagos/Gilead, Genentech, GlaxoSmithKline, Horizon, Janssen, Mallinckrodt, Nektar, Nichi-Iko, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, Selecta, UCB, Bernadette Rojkovich: None declared, Anna Zubrzycka-Sienkiewicz Consultant of: Astellas and Roche, Grant/research support from: AbbVie, Astellas, Galapagos NV, Gilead Sciences, Janssen, Lilly, Mabion, Pfizer, Roche, and UCB SA, Timothy Radstake Shareholder of: AbbVie, Employee of: AbbVie, Su Chen Shareholder of: AbbVie, Employee of: AbbVie, Dilek Arikan Shareholder of: AbbVie, Employee of: AbbVie, Hartmut Kupper Shareholder of: AbbVie, Employee of: AbbVie, Howard Amital Consultant of: Abbvie, Janssen, Novartis, Roche, Perrigo, Pfizer, Neopharm, Elly Lilly, Gilead, Sanofi, Teva and Rafa, Grant/research support from: Yansen, Pfizer

DOI: 10.1136/annrheumdis-2021-eular.221

OP0116 ELDERLY PATIENTS ARE NOT AT INCREASED RISK OF SERIOUS INFECTIONS WHEN RECEIVING BDMARDS OR JAK INHIBITORS COMPARED TO CSDMARD TREATMENT

A. Strangfeld[1], B. Manger[2], M. Worsch[3], T. Schmeiser[4], A. Zink[1], M. Schaefer[1]. [1]*German Rheumatism Research Centre, Epidemiology and Health Care Research, Berlin, Germany*; [2]*University Hospital Erlangen, Faculty of Medicine, Erlangen, Germany*; [3]*Private Practice, Mühlhausen, Germany*; [4]*Private Practice, Cologne, Germany*

Background: Elderly rheumatoid arthritis (RA) patients are generally at increased risk of serious infections (SI). At the same time, treatment with bDMARDs has been associated with a higher SI risk than treatment with csDMARDs (1). However, long-term use of bDMARDs did not increase the risk of SI in a small group of elderly patients over 65 (2). The extent to which elderly patients are exposed to a higher SI risk when treated with JAK inhibitors (JAKi) is an open question.

Objectives: To assess the effects of bDMARDs and specifically JAKi on the risk of SI in elderly patients with RA.

Methods: The German register RABBIT is a prospective, longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. This analysis comprises patients over 70 years of age who were enrolled between 01/2007 and 04/2020 and had at least one follow-up.

Results: Of 13,491 patients followed-up in RABBIT, 2274 with an age > 70 years were included in the analysis. 626 SI were observed in 425 of these patients. Baseline characteristics at start of the respective DMARD are shown in Table 1. In most characteristics, patients on JAKi were more comparable to patients under bDMARDs than to those on csDMARDs. JAKi patients received glucocorticoids (GC) less frequently than patients on other treatments. The HR for SI was lower than 1 in patients receiving bDMARDs or JAKi compared to csDMARDs, but without statistical significance (Figure 1). GC use (HR 1.6, 95% CI: 1.2 – 2.2 for ≤ 10 mg/d), higher DAS28-ESR values (HR 1.1, 95% CI: 1.0 – 1.2 per 1 point increase), COPD or pulmonary fibrosis (HR 1. 8, 95% CI: 1.3 – 2.4), chronic kidney disease (HR 1.5, 95% CI: 1.2 – 1.9) and diabetes mellitus (HR 1.3, 95% CI: 1.0 – 1.7) were associated with an increased risk of SI. Better physical capacity was associated with a decreased risk of SI (HR 0.9, 95% CI: 0.88 – 0.98 for a 10 point increase).

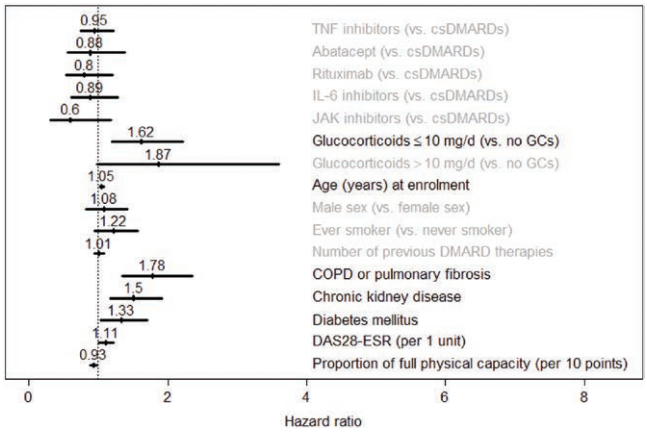


Figure 1. Hazard ratios for serious infections with 95% confidence intervals

Conclusion: Treatment with JAKi as well as treatment with bDMARDs was not associated with an increased risk of SI in elderly patients above 70 years of age. Key comorbidities such as diabetes mellitus, chronic pulmonary and kidney diseases were associated with increased risk, as was concomitant GC use and higher disease activity.

REFERENCES:

[1] Listing J et al., Rheumatology 2013; 52 (1): 53-61.
[2] Kawashima H. et al., Rheum. Intern. 2017; 37: 369-376.

Acknowledgements: RABBIT is supported by a joint, unconditional grant from AbbVie, Amgen, BMS, Celltrion, Fresenius-Kabi, Gilead, Hexal, Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi-Aventis, UCB, and Viatris.

Table 1. Patient characteristics by treatment at baseline

Parameter	csDMARDs	TNFi	RTX	ABA	IL-6i	JAKi
	N=758	N=840	N=209	N=147	N=212	N=108
Age (years)	75.9 (3.9)	75.5 (3.6)	74.8 (3.6)	76.1 (3.9)	75.9 (3.7)	76.7 (3.7)
Male sex	184 (24.3)	220 (26.2)	50 (23.9)	36 (24.5)	46 (21.7)	28 (25.9)
Ever smoker	249 (32.8)	287 (34.2)	77 (36.8)	50 (34)	73 (34.4)	39 (36.1)
Disease duration (years)	7.9 (8.8)	12.3 (11.4)	17 (11.1)	12.8 (10)	13.8 (11.7)	11.9 (10.9)
Seropositivity	487 (64.3)	671 (79.9)	201 (96.2)	126 (85.4)	182 (85.8)	79 (73.5)
Number of previous DMARDs	1.4 (0.7)	2.5 (1.3)	4.2 (1.8)	3.6 (1.9)	3.3 (1.8)	2.6 (1.5)
DAS28-ESR	4.6 (1.2)	5.1 (1.2)	5.4 (1.3)	5.3 (1.3)	5.3 (1.3)	5 (1.2)
Proportion of full physical function	64.8 (23.1)	57.1 (23.6)	50.4 (23.7)	52.9 (23.5)	55.3 (24.1)	55.2 (23.7)
Number of comorbidities	3.1 (2.5)	3.8 (2.6)	4.2 (2.6)	4.6 (2.9)	3.6 (2.4)	3.8 (2.2)
No comorbidity	52 (6.9)	29 (3.5)	4 (1.9)	4 (2.7)	9 (4.2)	5 (4.6)
Three and more comorbidities	385 (50.8)	528 (62.9)	147 (70.3)	107 (72.8)	131 (61.8)	76 (70.4)
COPD or pulmonary fibrosis	69 (9.1)	89 (10.6)	29 (13.9)	26 (17.7)	12 (5.7)	11 (10.2)
Chronic kidney disease	94 (12.4)	151 (18)	28 (13.4)	21 (14.3)	39 (18.4)	22 (20.4)
Diabetes mellitus	151 (19.9)	172 (20.5)	31 (14.8)	23 (15.6)	42 (19.8)	25 (23.1)
GCs (last 6 months)	347 (45.8)	526 (62.6)	143 (68.8)	82 (56.2)	127 (59.9)	44 (40.7)
GCs (<5mg)	447 (58.9)	384 (45.7)	101 (48.2)	88 (60)	118 (55.8)	72 (66.7)
GCs (5-9mg)	252 (33.3)	375 (44.6)	81 (38.7)	43 (29)	72 (34.2)	27 (25.1)
GCs (>=10mg)	59 (7.8)	82 (9.8)	274 (13.1)	16 (11)	21 (10)	9 (8.2)

Results are presented as mean ± SD for continuous variables and number (percentage) for discrete variables.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.763

OP0117

REAL-WORLD EFFECTIVENESS OF TNFI VERSUS NON-TNFI BIOLOGICS ON DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE ACR'S RISE REGISTRY

M. Gianfrancesco[1], J. LI[1], M. Evans[1], M. Petersen[2], G. Schmajuk[1], J. Yazdany[1]. *[1]University of California, San Francisco, Medicine, San Francisco, United States of America; [2]University of California, Berkeley, Biostatistics, San Francisco, United States of America*

Background: Our understanding of how medications such as biologic disease modifying anti-rheumatic drugs and targeted small molecules (b/tsDMARDs) influence disease activity in RA is based largely on randomized controlled trials (RCTs). However, most U.S. trials in RA are limited by small sample sizes and have often excluded patients who are older, male, and from racial/ethnic minorities. Whether effectiveness of b/tsDMARDs varies in these populations has largely been unexplored.

Objectives: We aimed to examine differences in longitudinal RA disease activity by demographic and clinical characteristics using a novel electronic health record data source of rheumatology providers across the U.S. We simulated various treatment assignments of b/tsDMARDs that have been examined in RCTs: namely, TNF-inhibitors (TNFi) and non-TNFi.

Methods: We included 16,448 individuals from the ACR's RISE registry with ≥ 2 RA diagnoses (ICD-9: 714.0) ≥ 30 days apart, who had at least 2 recorded clinical disease activity index (CDAI) scores and no historical b/tsDMARD use documented in RISE. b/tsDMARD use and CDAI scores were assessed at each quarter; covariates included sex, race (white, Black, Asian, other), ethnicity (Hispanic/non-Hispanic), age, smoking, obesity, area deprivation index, other DMARD use, RF status, anti-CCP status, and practice type. Longitudinal targeted maximum likelihood estimation estimated the average treatment effect (ATE) of cumulative TNFi vs. non-TNFi use over a 12-month period on CDAI score among the entire population and across various subgroups based on demographic and clinical characteristics, accounting for censoring and time-varying confounding.

Results: Approximately 75% of patients were female with a mean age of 65.1 (+/- 13.7) years. Sixty percent of patients were white, 8% black, 2% Asian, and 30% other/mixed or unknown race; 6% were Hispanic. The mean CDAI score at baseline was 11.3 (+/- 10.7). For the overall population, there was no significant difference in disease activity between TNFi and non-TNFi at 12 months (ATE= 0.85, 95% CI -0.26, 1.96; Table 1). Stratified analyses found higher disease activity for TNFi compared to non-TNFi among patients of Black and Asian race, non-Hispanic ethnicity, and female sex. Among Black race patients, TNFi use was associated with a 6.08 point higher CDAI score compared to non-TNFi use (95% CI 1.99, 10.17). In contrast, in Hispanic/Latino ethnicity patients, TNFi use was associated with a lower CDAI score compared to non-TNFi use (ATE= -2.64, 95% CI -3.99, -1.30).

Table 1. Average treatment effect (ATE) of cumulative TNFi vs. non-TNFi use at 12-months on CDAI score in patients with RA

	TNFi	Non-TNFi	ATE (95% CI)
Overall (n=16,448)	8.84	7.99	0.85 (-0.26, 1.96)
Race			
White (n=9,814)	8.24	6.81	1.42 (0.03, 2.81)*
Black (n=1,358)	13.91	7.83	6.08 (1.99, 10.17)*
Asian (n=301)	6.54	2.74	3.80 (2.93, 4.67)*
Ethnicity			
Non-Hispanic (n=14,216)	8.92	7.63	1.29 (0.08, 2.51)*
Hispanic (n=938)	5.69	8.33	-2.64 (-3.99, -1.30)*
Sex			
Female (n=12,527)	8.98	7.47	1.51 (0.31, 2.72)*
Male (n=3,921)	8.57	9.49	-0.92 (-3.42, 1.58)

*$P<0.05$

Conclusion: Results from this RCT simulation study suggest that non-TNFi may have an important role as first-line agents in the treatment of Black and Asian patients, but not Hispanic patients. These novel findings fill gaps where RCTs have not been conducted, highlight the need for inclusion of diverse populations in future trials, and have the potential to lead to a more personalized approach to rheumatologic care.

References:

Disclosure of Interests: Milena Gianfrancesco: None declared, Jing Li: None declared, Michael Evans: None declared, Maya Petersen: None declared, Gabriela Schmajuk: None declared, Jinoos Yazdany Consultant of: Eli Lilly and Astra

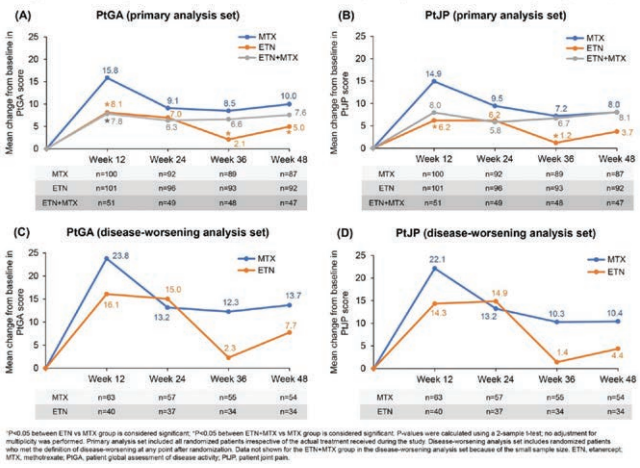
Zeneca, unrelated to this project., Grant/research support from: Gilead, unrelated to this project.
DOI: 10.1136/annrheumdis-2021-eular.1032

OP0118 EFFECT OF WITHDRAWING ETANERCEPT OR METHOTREXATE ON PATIENT-REPORTED OUTCOMES IN RHEUMATOID ARTHRITIS PATIENTS IN REMISSION ON COMBINATION THERAPY: RESULTS FROM THE SEAM-RA TRIAL

J. Curtis[1], E. Karis[2], V. Bykerk[3], G. Kricorian[4], P. Yen[5], P. Emery[6], P. Haraoui[7], D. Collier[4], B. Stolshek[8]. [1]*University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, United States of America*; [2]*Amgen Inc, Global Development, California, United States of America*; [3]*Hospital for Special Surgery, Department of Rheumatology, New York, United States of America*; [4]*Amgen Inc, Global Medical, California, United States of America*; [5]*Amgen Inc, Global Biostatistical Science, California, United States of America*; [6]*Leeds National Institute for Health Research, Biomedical Research Center at Leeds Teaching Hospitals Trust, LIRMM Leeds University, Division of Rheumatic and Musculoskeletal Disease, Leeds, United Kingdom*; [7]*Rheumatology Institute of Montreal, Department of Medicine, Montreal, Canada*; [8]*Amgen Inc, Global Health Economics, California, United States of America*

Background: Limited studies have assessed the effect of withdrawal of either methotrexate (MTX) or etanercept (ETN) on patient-reported outcomes (PROs) in rheumatoid arthritis (RA).
Objectives: To evaluate the baseline and change in PROs following withdrawal of MTX or ETN in RA patients with sustained remission receiving combination ETN+MTX.
Methods: Adult patients with RA on ETN+MTX and in remission (SDAI ≤3.3) for ≥12 months (including a 24-week, open-label, run-in period) were randomized to a 48-week double-blind period to receive ETN 50 mg weekly (N=101), oral MTX 10-25 mg weekly (N=101) or continue ETN+MTX (N=51). The primary endpoint was maintenance of SDAI remission without disease worsening (DW) at week 48 between ETN and MTX groups. Patients who experienced SDAI >11 at any time after randomization, or SDAI >3.3 and ≤11 during 2 consecutive or on 3 non-consecutive visits were considered to have DW and resumed ETN+MTX. PROs assessed were patient global assessment of disease activity (PtGA, 0-100 mm), patient joint pain (PtJP, 0-100 mm), Health Assessment Questionnaire-Disability Index (HAQ-DI), and the 36-item short-form health survey (SF-36) component and domain scores. A 2-sample t-test was used to compare the treatment differences between groups. A subgroup analysis for patients with DW was also performed (DW analysis set) and compared PROs between ETN vs MTX arms (ETN+MTX not shown given the small sample size).
Results: Of the 253 patients randomized, 121 (47.8%) experienced DW and were included in the DW analysis set. Baseline demographics were generally balanced between the 3 treatment groups. Most patients were women (76.3%), White (87.0%), and with a mean age of 55.6 years. The mean (SD) MTX dose was 16.3 (4.69) mg and the mean (SD) duration of RA was 10.3 (7.8) years. At week 48, a significantly greater proportion of patients on ETN vs MTX monotherapy maintained SDAI remission (49.5% vs 28.7%; P=0.004) after therapy withdrawal. In the overall population, PtGA and PtJP scores were very low at baseline (PtGA–MTX: 4.4, ETN: 4.5, ETN+MTX: 3.5; PtJP–MTX: 4.9, ETN: 5.5, ETN+MTX: 3.5) and showed some worsening over the study period in all treatment groups, with a mean change at week 48 ranging from 5.0 to 10.0 units for PtGA and 3.7 to 8.1 units for PtJP. Patients on ETN had less worsening, with a nominally significant treatment difference observed between ETN and MTX monotherapy groups for PtGA at almost all timepoints, and for PtJP at weeks 12 and 36 (Figure). Mean HAQ-DI (MTX: 0.32; ETN: 0.26; ETN+MTX: 0.28) and SF-36 scores (physical component [PCS]–MTX: 52.1, ETN: 52.7, ETN+MTX: 52.3; mental component [MCS]–MTX: 55.5, ETN: 55.8, ETN+MTX: 57.1) at baseline show that patients had low disability and excellent health-related quality of life compared with normative values for the general non-RA population. HAQ-DI scores were well maintained at weeks 24 and 48 (change from baseline at week 48–MTX: 0.14; ETN: 0.15; ETN+MTX: 0.21). The SF-36 PCS, MCS, and domain scores decreased minimally from baseline with treatment differences that were not nominally significant between groups. Among patients with DW during the study, those on ETN showed less PtGA and PtJP worsening from baseline than those on MTX at weeks 12, 36, and 48 (Figure). Other PROs (HAQ-DI [change from baseline at week 24–ETN: 0.34; MTX: 0.21; at week 48–ETN: 0.15; MTX: 0.15], SF-36 PCS, MCS, and domain scores) showed a similar degree of worsening in both the MTX and ETN arms.
Conclusion: In patients with sustained SDAI remission on ETN+MTX, mental and physical health as measured by SF-36 was comparable with that of the non-RA population. Withdrawal of ETN (MTX monotherapy) resulted in a greater worsening of PtGA and PtJP than withdrawal of MTX (ETN monotherapy), and patients on ETN monotherapy restored these scores close to baseline towards the end of the treatment period. These findings demonstrate that ETN monotherapy has a greater effect on maintaining overall patient assessment of disease and joint pain compared with MTX monotherapy.

Figure. Mean change from baseline in PtGA and PtJP scores (primary and disease-worsening analysis set)



[a]P<0.05 between ETN vs MTX group is considered significant; [b]P<0.05 between ETN+MTX vs MTX group is considered significant. P-values were calculated using a 2-sample t-test; no adjustment for multiplicity was performed. Primary analysis set included all randomized patients irrespective of the actual treatment received during the study. Disease-worsening analysis set includes randomized patients who met the definition of disease-worsening at any point after randomization. Data not shown for the ETN+MTX group in the disease-worsening analysis set because of the small sample size. ETN, etanercept; MTX, methotrexate; PtGA, patient global assessment of disease activity; PtJP, patient joint pain.

Disclosure of Interests: Jeffrey Curtis Speakers bureau: AbbVie, BMS, Gilead, Lilly, Novartis, Sanofi, Scipher, Amgen, Corrona, Janssen, Myriad, and Pfizer, Consultant of: AbbVie, BMS, Gilead, Lilly, Novartis, Sanofi, Scipher, Amgen, Corrona, Janssen, Myriad, and Pfizer, Grant/research support from: AbbVie, BMS, Gilead, Lilly, Novartis, Sanofi, Scipher, Amgen, Corrona, Janssen, Myriad, and Pfizer, Elaine Karis Shareholder of: Amgen Inc., Employee of: Amgen Inc., Vivian Bykerk Speakers bureau: Amgen, BMS, Gilead, Pfizer, Sanofi-Genzyme/Regeneron, Scipher Medicine, and UCB., Consultant of: Amgen, BMS, Gilead, Pfizer, Sanofi-Genzyme/Regeneron, Scipher Medicine, and UCB., Grant/research support from: Amgen and Novartis, Greg Kricorian Shareholder of: Amgen Inc., Employee of: Amgen Inc., Priscilla Yen Shareholder of: Amgen Inc., Employee of: Amgen Inc., Paul Emery Speakers bureau: AbbVie, BMS, Celltrion, Gilead, Lilly, MSD, Novartis, Pfizer, Roche, Samsung, Sandoz, and UCB., Consultant of: AbbVie, BMS, Celltrion, Gilead, Lilly, MSD, Novartis, Pfizer, Roche, Samsung, Sandoz, and UCB., Paul Haraoui Speakers bureau: AbbVie, Celgene, Janssen, Pfizer, and UCB., Consultant of: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Pfizer, Roche, Sandoz, Sanofi-Genzyme, and UCB., Grant/research support from: Roche, AbbVie, Amgen, Merck, and Pfizer, David Collier Shareholder of: Amgen Inc., Employee of: Amgen Inc., Brad Stolshek Shareholder of: Amgen Inc., Employee of: Amgen Inc.
DOI: 10.1136/annrheumdis-2021-eular.1863

OP0119 SHOULD WE USE BIODMARDS IN FIRST INTENTION IN EARLY RHEUMATOID ARTHRITIS?: RESULTS AT 5 YEARS FROM THE ERA LOUVAIN BRUSSELS COHORT

E. Sapart[1], T. Sokolova[1], S. De Montjoye[1], S. Dierckx[2], A. Nzeusseu Toukap[1], A. Avramovska[1], L. Meric de Bellefon[1], P. Durez[1]. [1]*Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCL) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Belgium*; [2]*CHU Mont-Godinne, Rheumatology, Mont-Godinne, Belgium*

Background: Early effective treatment has led to major improvements in patients with rheumatoid arthritis (ERA). Low disease activity and remission are achieved earlier and in higher frequency when the initial treatment in rheumatoid arthritis includes a combination of methotrexate (MTX) with a bDMARD compared to MTX alone.
Objectives: The aim of this study is to retrospectively analyse and compare the benefit of a treatment with methotrexate (MTX) alone or combined with a bDMARD as an induction therapy during 5 years of follow-up in early rheumatoid arthritis (ERA) patients.
Methods: We included ERA patients from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 classification criteria and were naïve to DMARDs. Treatments were initiated based on the decision of a senior rheumatologist. bDMARDs induction therapy was usually limited to 6 or 12 months. We collected patient characteristics at baseline and clinical response was analysed at 6 months, 1 year, 3 years and 5 years.
Results: Data from 470 eligible ERA patients were collected. The average age of the population is 48.9 years; 70.5% of the patients are women; 27.3% are smokers and 68.8% are positive for anti-citrullinated protein antibody (ACPA).

281 patients (59.8 %) initiated MTX as a monotherapy (MTX group) compared to 189 patients (40.2%) who received a bDMARD (Bio group).
At baseline, the disease activity is the main factor that favors the initiation of bDMARDs (DAS28-CRP 5.2 vs 4.5, p<0.001) followed by HAQ (1.32 vs 1.15, p=0.009), ACPA positivity (77.8% vs 62.5%, p=0.0006), rheumatoid factor positivity (71.5% vs 60.2%, p=0.0134). Other parameters such as age, gender, smoking habits or baseline erosion were similar between groups.
391 patients were followed up to 5 years. We then divided each of the two groups into two subgroups according to the last treatment they received at 5 years. Figure 1 shows the percentage of DAS28-CRP remission during time in each of the four groups (MTX->MTX (n=134), MTX->BIO (n=103); BIO->MTX (n=95), BIO->BIO (n=59);

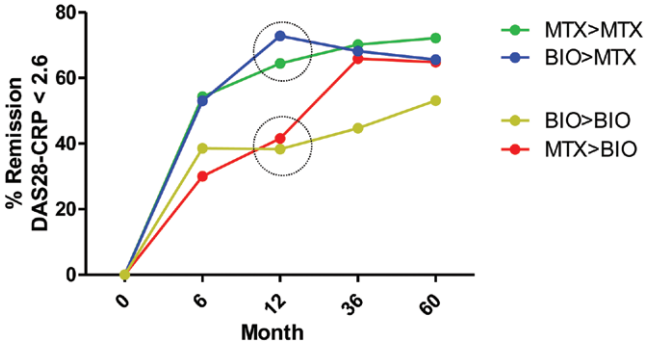


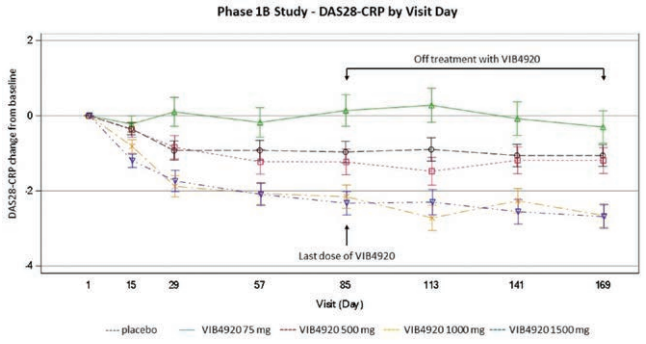
Figure 1. DAS28-CRP remission rate during time in each of the four groups (MTX->MTX (n=134), MTX->BIO (n=103); BIO->MTX (n=95), BIO->BIO (n=59).

At 12 months, DAS28-CRP response rate was statistically significantly higher in MTX>MTX and BIO>MTX groups compared to the two other groups. As expected, the remission rate was rescued in the group MTX->Bio after 12 months.
Interestingly, ERA patients initially treated by a bDMARD followed by a MTX maintenance therapy experienced a stable and sustained rate of remission.
Conclusion: Longterm remission is an achievable goal in ERA followed in daily clinic. Our results suggest that a bDMARD induction therapy followed by MTX maintenance therapy could be a good option in severe case of ERA.
REFERENCES:
[1] Smolen JS and al. D. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying anti-rheumatic drugs: 2019 update. Ann Rheum Dis. 2020 Jan 22.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2314

OP0120 DURATION OF CLINICAL EFFICACY FOLLOWING TREATMENT WITH VIB4920 IN SUBJECTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

O. Ali[1], L. Wang[2], W. Xu[2], D. Falleroni[3], J. Falloon[1], G. Illei[1]. [1]*Viela Bio, Clinical Development, Gaithersburg, United States of America*; [2]*Viela Bio, Biostatistics, Gaithersburg, United States of America*; [3]*Viela Bio, Clinical Operations, Gaithersburg, United States of America*

Background: VIB4920 binds CD40 ligand and functionally neutralizes its engagement with CD40[1]. We reported results through Day 85 of a Phase 1b, randomized, double-blind, placebo-controlled study (NCT02780388) in subjects with moderate to severe rheumatoid arthritis (RA) who had an inadequate response to methotrexate (MTX) or other disease modifying anti-rheumatic drugs (DMARDs) or tumor necrosis factor (TNF)-inhibitors[1]. We showed that at the end of the 12-week treatment period (Day 85), subjects treated with 1000 or 1500 mg VIB4920 (once every 2 weeks) had a clinically meaningful and statistically significant greater reduction in disease activity compared to placebo.
Objectives: To assess the duration of clinical efficacy following the last dose of VIB4920 in subjects with moderate to severe RA.
Methods: Subjects in the Phase 1b study (Ph1b) continued to have monthly safety and efficacy assessments between Days 85 and 169, the end of a 12-week follow-up. To estimate the subsequent duration of meaningful clinical improvement, we conducted an observational one-visit study (OS) (EudraCT 2019-002351-42) with the primary endpoint of time from last dose of VIB4920 to start of a new DMARD or biologic therapy or increase in dose of DMARD that was ongoing at Day 169 (ie, rescue therapy).
Results: At Day 169 of the Ph1b (3 months after the last dose), clinical responses achieved at Day 85 were maintained in the 1000 and 1500 mg cohorts (Figure). Of 24 subjects, 16 (6/12 treated with 1000 mg and 10/12 with 1500 mg) participated in the OS. The median (range) time from Day 169 (last visit) in the Ph1b to the OS was 21.8 (21.2 to 23.1) months in the 1000 mg group and 33.7 (32.3 to 34.8) months in the 1500 mg group. All subjects had taken DMARDs (primarily methotrexate [MTX]) for at least part of this time (Table). Rescue therapy was started in 1/6 (16.7%) subject in the 1000 mg group and 3/10 (30.0%) subjects in the 1500 mg group (Table); median time to rescue could not be estimated due to the limited number of rescues. Two subjects were on no DMARDs at the OS. All subjects, except for 1 in the 1000 mg group, who was rescued with adalimumab, and 2 in the 1500 mg group (no rescue), had active disease (DAS28-CRP ≥ 2.6) at the OS. The median DAS28-CRP at the OS was higher than at Day 169 of the Ph1b but lower than at the Ph1b baseline visit (Table). Two subjects who received 1500 mg and met DAS28-CRP criteria for low disease activity (< 3.2) at Day 169 also met these criteria at the OS without receiving any rescue therapy after a median of nearly 37 months after last treatment. Results from the Patient and Physician Global Assessment VAS showed trends similar to the DAS28-CRP.
Conclusion: Blocking CD40L with VIB4920 led to prolonged clinical benefit in patients with RA when added to stable background DMARD therapy. The exact duration of benefit could not be defined in this study, but most patients did not require rescue therapy during a prolonged follow-up period, and some patients maintained low disease activity or discontinued DMARDs, suggesting a possible long-term benefit of VIB4920. Interpretation of these data is limited because the OS did not include placebo-treated subjects from the Ph1b. The duration of clinical response needs to be confirmed in prospective, double-blind, placebo-controlled studies.
REFERENCES:
[1] Karnell JL et al. Sci Transl Med. 2019 Apr 24;11(489).
Acknowledgements: The authors thank the study participants and investigators.



Summary of Results

	VIB4920 1000 mg N = 6	VIB4920 1500 mg N = 10
Subjects who received ≥ 1 DMARD at any time between Day 169 of Ph1b and OS	6 (100%)	10 (100%)
Hydroxychloroquine (HCQ)	1 (16.7%)	0
MTX	5 (83.3%)	9 (90.0%)
Leflunomide	1 (16.7%)	2 (20.0%)
Adalimumab	1 (16.7%)	0
Etanercept	0	1 (10.0%)
Rescue therapy		
HCQ, Adalimumab	1 (16.7%)	0
MTX	0	2 (20%)
MTX, Leflunomide, Etanercept	0	1 (10%)
DAS28-CRP [median (min, max)]		
Ph1b Baseline	5.4 (4.7 – 6.3)	4.7 (4.3 - 5.7)
Ph1b Day 169	2.9 (1.1 – 4.2)	2.3 (1.1 - 3.4)
OS	3.7 (1.1 – 5.5)	3.9 (2.3 – 5.6)

Disclosure of Interests: Omar Ali Shareholder of: I own shares of Viela Bio., Employee of: I am an employee of Viela Bio., Liangwei Wang Shareholder of: I own shares of Viela Bio., Employee of: I am an employee of Viela Bio., Wenjing Xu Shareholder of: I own shares of Viela Bio., Employee of: I am an employee of Viela Bio., Dan Falleroni Shareholder of: I own shares of Viela Bio., Employee of: I am an employee of Viela Bio., Judith Falloon Shareholder of: I own shares of Viela Bio., Employee of: I am an employee of Viela Bio., Gabor Illei Shareholder of: I own shares of Viela Bio., Employee of: I am an employee of Viela Bio.
DOI: 10.1136/annrheumdis-2021-eular.2544

Rheumatoid arthritis - non biologic treatment and small molecules

OP0122 COMPARATIVE EFFECTIVENESS OF JAKI VERSUS BDMARDS; A NATIONWIDE STUDY IN RA

A. Barbulescu[1], J. Askling[1,2], K. Chatzidionysiou[2,3], H. Forsblad-D'elia[4], A. Kastbom[5], U. Lindström[4], C. Turesson[6], T. Frisell[1]on behalf of the ARTIS Study Group. *[1]Karolinska Institute, Department of Medicine Solna, Clinical Epidemiology, Stockholm, Sweden*; *[2]Nya Karolinska, Department of Rheumatology, Stockholm, Sweden*; *[3]Karolinska Institute, Department of Medicine Solna, Stockholm, Sweden*; *[4]Gothenburg University, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; *[5]Linköping University, Department of Biomedical and Clinical Sciences, Linköping, Sweden*; *[6]Lund University, Department of Clinical Sciences, Rheumatology, Malmö, Sweden*

Background: The Janus kinase inhibitors (JAKi) have been increasingly used for the treatment of rheumatoid arthritis (RA) in Sweden, with baricitinib representing ~80% of prescriptions. Evidence regarding the comparative effectiveness of JAKis versus biologics (bDMARDs), and in particular non- tumour-necrosis-factor inhibitor (TNFi) bDMARDs, in real-life is limited.
Objectives: To compare RA patients treated with bDMARDs and JAKi in Sweden, in terms of: (1) patient characteristics at treatment start; (2) proportions of patients remaining on therapy, and response rates, at 12 months.
Methods: RA patients starting treatment in 2017 and 2018 with either a TNFi, rituximab, abatacept, interleukin 6 inhibitors (IL6i) or a JAKi as different lines of treatment were identified in the Swedish Rheumatology Quality Register. One patient could contribute with more than one treatment episode.
Treatment response at 12 months was measured as EULAR good response, HAQ improvement >0.2 units, DAS28 and CDAI remission, and as 0 tender and swollen joint counts (28JC). Patients were classified as non-responders if they stopped treatment before evaluation due to safety or inefficacy. Responses for patients who stopped treatment due to pregnancy or death and patients on treatment but with missing response were imputed using multiple imputation.
Proportions of responders and differences in proportions between treatment groups, adjusted using inverse probability of treatment weighting, were estimated using linear regression with robust standard errors.
Results: JAKi were often used after bDMARDs, and less frequently prescribed in combination with methotrexate. Measured comorbidities were less frequent among JAKi initiators than among non-TNFi biologic initiators, but RA activity was similar (Table).

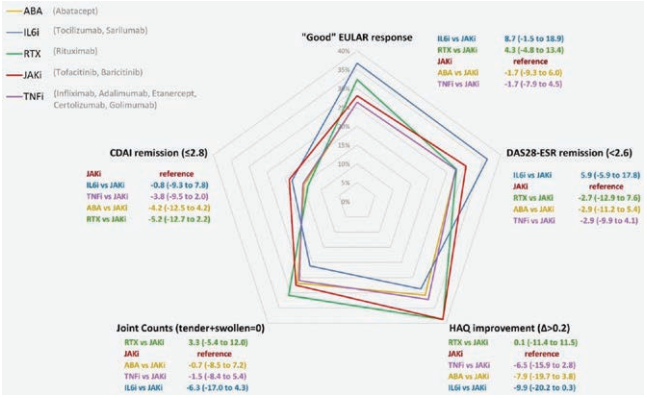
Table 1. Patient characteristics at treatment initiation

Characteristic Median (IQR) or N (%)	Abatacept	IL6i	Rituximab	TNFi	JAKi
Treatment Starts	694	534	692	3497	905
Age	63 (53-71)	59 (48-70)	65 (54-73)	59 (47-68)	60 (51-70)
Female	543 (78)	441 (83)	519 (75)	2739 (78)	759 (84)
RA duration (years)	13 (5-21)	10 (5-18)	12 (6-22)	9 (3-17)	13 (7-22)
Rheum. factor	535 (79)	385 (73)	588 (87)	2405 (70)	686 (77)
DAS28	4.8 (3.9-5.6)	4.9 (4.0-5.7)	4.7 (3.8-5.5)	4.4 (3.4-5.3)	4.7 (3.9-5.7)
HAQ	1.3 (0.8-1.6)	1.3 (0.8-1.8)	1.3 (0.8-1.8)	1.0 (0.5-1.4)	1.3 (0.8-1.8)
Tender joints	5 (2-9)	6 (3-10)	5 (2-9)	4 (2-8)	6 (2-10)
Swollen joints	4 (2-6)	4 (2-7)	4 (2-7)	3 (1-6)	4 (2-7)
ts/bDMARD line	3 (2-4)	3 (2-4)	2 (1-4)	1 (1-2)	4 (2-6)
At least one prev. TNFi	539 (78)	442 (83)	457 (66)	1448 (41)	770 (85)
At least one prev. non-TNFi	271 (39)	220 (41)	243 (35)	441 (13)	584 (65)
Methotrexate co-treatment	264 (50)	172 (40)	286 (53)	1708 (62)	296 (40)
Glucocorticoids co-treatment	247 (47)	186 (43)	275 (51)	1126 (41)	389 (53)
Cancer*	90 (2.8)	64 (2.3)	363 (7.7)	410 (1.8)	20 (2.2)
Cardio-vascular dis.*	245 (7.5)	123 (4.4)	322 (6.8)	749 (3.4)	41 (4.4)
Chronic respiratory dis.*	303 (9.3)	140 (5.0)	473 (10.0)	721 (3.2)	50 (5.4)
Diabetes*	324 (9.9)	216 (7.7)	456 (9.7)	1479 (6.7)	69 (7.5)

* any diagnosis within 5 years before startAdjusted differences in proportion with each response outcome

In a crude comparison, 65% (61%-68%) of JAKi, 62% (59%-66%) of abatacept, 58% (53%-62%) of IL6i, 80% (77%-83%) of rituximab and 68% (67%-70%) of TNFi initiators remained on treatment at 12 months after start. Also, JAKi showed lower overall responder proportions than TNFi, rituximab and IL6i.

After adjustment for demographic and socio-economic factors, RA disease activity, previous use of ts/bDMARDs, co-medication with glucocorticoids and methotrexate and comorbidities at baseline, no significant differences in responder proportions between JAKi and bDMARDs remained (Figure). Furthermore, the adjusted proportions of patients on treatment were higher for JAKi and rituximab than for the other bDMARDs.
Conclusion: This preliminary analysis of patients treated in clinical practice found no statistically significant difference in effectiveness between JAKi and bDMARDs.
Disclosure of Interests: Andrei Barbulescu: None declared, Johan Askling Grant/research support from: Abbvie, Astra-Zeneca, BMS, Eli Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB. These entities have entered into agreements with Karolinska Institutet with JA as principal investigator, mainly in the context of safety monitoring of biologics via the ARTIS national safety monitoring system, Katerina Chatzidionysiou Speakers bureau: Eli Lilly, Abbvie and Pfizer, Consultant of: Eli Lilly, Abbvie and Pfizer, Helena Forsblad-d'Elia: None declared, Alf Kastbom Employee of: Sanofi, Ulf Lindström: None declared, Carl Turesson Speakers bureau: Abbvie, Bristol-Myers Squibb, Medac, Pfizer, Roche, Consultant of: Roche, Grant/research support from: Bristol-Myers Squibb, Thomas Frisell: None declared



DOI: 10.1136/annrheumdis-2021-eular.774

OP0123 SAFETY PROFILE OF JAK-INHIBITORS VERSUS TNF-INHIBITORS IN REAL-WORLD CLINICAL PRACTICE: DATA FROM A MULTICENTER REGISTER

B. Hernández-Cruz[1], C. Sánchez-Piedra[2], M. Freire González[3], N. Busquets[4], J. García-González[5], M. Moreno[6], J. M. Blanco[7], S. Manrique Arija[8], E. Perez-Pampín[9], F. Sánchez-Alonso[2], I. Castrejon[10]on behalf of BIOBADASER. *[1]Hospital Universitario Virgen Macarena, Rheumatology, Sevilla, Spain*; *[2]Fundación Española de Reumatologia, Rheumatology, Madrid, Spain*; *[3]Complejo Hospitalario A Coruña, Rheumatology, A Coruña, Spain*; *[4]Hospital General de Granollers, Rheumatology, Granollers, Spain*; *[5]Hospital 12 De Octubre, Rheumatology, Madrid, Spain*; *[6]Hospital Clínico Universitario Virgen de la Arrixaca, Rheumatology, El Palmar, Spain*; *[7]Hospital Universitario Basurto, Rheumatology, Bilbo, Spain*; *[8]Hospital Regional Universitario de Málaga (Carlos de Haya), Rheumatology, Málaga, Spain*; *[9]Hospital Clínico Universitario de Santiago, Rheumatology, Santiago de Compostela, Spain*; *[10]Hospital Universitario Gregorio Marañón, Rheumatology, Madrid, Spain*

Background: JAK-inhibitors (JAKi) are small molecules emerging as a promising treatment for immune mediated diseases. Data from clinical trials are very promising. But long-term observational studies, with patients with diverse clinical backgrounds are required to confirm safety profile.
Objectives: To compare the safety profile of JAKi versus TNF antagonists (anti-TNF) in a multicenter real world dataset.
Methods: Data of patients enrolled in BIOBADASER 3.0 up to November 2020 with the start of anti-TNF or JAKi were analysed. Adverse events (AE) were classified according to Meddra dictionary (v19.0). For each group, demographic, clinical variables and ncidence rate ratios of AE per 1000 patients-year (PYs) and 95% confidence interval were estimated.
Results: A total of 3,729 patients on anti-TNF (5,306) or JAKi (493) were analyzed. Patients on JAKi were older and with a mean disease duration of 10 years. JAKi were prescribed as first line treatment only in 24% of patients. The main reason of stopping treatment was ineffectiveness (53-59%) followed by adverse events (25-34%) in both groups. Survival during first year was similar between groups.

Table 1. Patient characteristics and adverse events by treatment group

	Anti-TNF	JAKi
Mean age start of treatment (SD), yrs	50.8 (12.6)	57.6 (11.9)
Female, n (%)	3122 (58.8)	392 (79.5)
Disease duration, median (IQR)	7.0 (2.7-13.7)	9.9 (4.9-16.8)
First line biologic, n (%)	2614 (49.3)	117 (23.7)
Rheumatoid Arthritis	1385 (41.1)	339 (95.2)
Ankylsosing Spondylitis	1031 (30.6)	1 (0.3)
Psoriatic Arthritis	957 (28.4)	16 (4.5)
DAS28-ESR	4.3 (1.4)	4.7 (1.4)
Survival first year (IC 95%)	73.3 (71.9-74.6)	69.7 (66.0-73.0)
Charlson Index, mean (SD)	1.9 (1.3)	2.3 (1.6)
Reason to stop therapy (n)*:		
Lack of efficacy	1534 (53.2)	57 (58.8)
Adverse event	723 (25.1)	33 (34.0)
Adverse events (AE)*		
Serious infections	14.2 (12.4-16.2)	33.2 (19.3-57.3)
Herpes zoster	5.7 (4.6-7.1)	12.8 (5.3-30.7)
Tuberculosis	0.7 (0.4-1.3)	0.0 (0.0-0.0)
Malignancy/Neoplasia	10.2 (8.7-11.9)	15.3 (6.9-34.2)
Cardiac events	13.9 (12.2-16.0)	30.7 (17.4-54.0)
GI perforation	1.2 (0.8-1.9)	10.2 (3.8-27.3)
Vascular events	9.8 (8.3-11.5)	25.6 (13.8-47.5)

*Data show the incidence rate ratio per 1000 patient-years (PYs; 95% CI)

Conclusion: Serious infections and herpes zoster tend to be more frequent in patients on JAKi. However patients on JAKi were older, presented higher comorbidity and have a longer disease duration.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2645

OP0124

EFFECTS OF NINTEDANIB IN PATIENTS WITH PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS (RA-ILD) IN THE INBUILD TRIAL

C. Kelly[1], E. Matteson[2], M. Aringer[3], G. R. Burmester[4], H. Mueller[5], L. Moros[6], K. Rohr[6], M. Kolb[7] on behalf of the INBUILD Trial Investigators.. [1]*Newcastle University, Institute of Cellular Medicine, Newcatle upon Tyne, United Kingdom*; [2]*Mayo Clinic College of Medicine and Science, Division of Rheumatology, Rochester, United States of America*; [3]*University Medical Center & Faculty of Medicine, TU Dresden, Rheumatology, Medicine III, Dresden, Germany*; [4]*Charité–University Medicine Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; [5]*Boehringer Ingelheim Pharma GmbH & Co. KG, Biostatistics and Data Sciences, Biberach, Germany*; [6]*Boehringer Ingelheim International GmbH, TA Inflammation Med, Ingelheim am Rhein, Germany*; [7]*McMaster University and St. Joseph's Healthcare, Department of Medicine, Hamilton, Canada*

Background: In the INBUILD trial in subjects with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF), nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks by 57% compared with placebo.

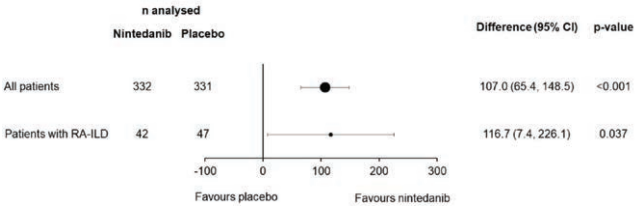
Objectives: To assess the rate of decline in FVC in subjects with RA-ILD in the INBUILD trial.

Methods: Subjects in the INBUILD trial had a chronic fibrosing ILD other than IPF, reticular abnormality with traction bronchiectasis (with or without honeycombing) of >10% extent on high-resolution computed tomography (HRCT), forced vital capacity (FVC) ≥45% predicted, diffusing capacity of the lungs for carbon monoxide ≥30%–<80% predicted, and met criteria for progression of ILD within the 24 months before screening, despite management deemed appropriate in clinical practice. Patients taking stable doses of approved medications to treat RA or connective tissue disease could participate, except that the protocol excluded those taking azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, rituximab, cyclophosphamide, or oral glucocorticoids >20 mg/day. We analysed the rate of decline in FVC (mL/year) over 52 weeks and adverse events in subjects with RA-ILD.

Results: Of 663 subjects who received trial medication, 89 had RA-ILD (42 nintedanib, 47 placebo), of whom 60.7% were male, 64.0% were current or former smokers, 86.5% had a usual interstitial pneumonia (UIP)-like pattern on HRCT; 93.3% had received confirmation of their RA diagnosis from a rheumatologist. At baseline, 21.3% of subjects were taking biologic disease-modifying anti-rheumatic drugs (DMARDs), 53.9% were taking non-biologic DMARDs and 73.0% were taking glucocorticoids (≤20 mg/day prednisone or equivalent). At baseline, mean (SD) age was 66.9 (9.6) years, time since RA diagnosis was 9.9 (9.4) years, time since ILD diagnosis was 3.6 (3.2) years, FVC was 71.5 (16.2) % predicted and C-reactive protein was 13.7 (22.5) mg/L. The adjusted mean (SE) rate of decline in FVC over 52 weeks was -82.6 (41.3) mL/year in the nintedanib group versus -199.3 (36.2) mL/year in the placebo group (difference 116.7 mL/year [95% CI 7.4, 226.1]; nominal p=0.037), consistent with findings in the overall trial population (Figure). As in the overall trial population, the most common adverse event in subjects with RA-ILD was diarrhoea (reported in 54.8% of the nintedanib group and 25.5% of the placebo group). Adverse events led to permanent discontinuation of trial drug in 19.0% of subjects in the nintedanib group and 12.8% of subjects in the placebo group.

Conclusion: In the INBUILD trial, nintedanib slowed the rate of decline in FVC in patients with progressive fibrosing RA-ILD, with adverse events that were manageable for most patients. The efficacy and safety of nintedanib in subjects with RA-ILD were consistent with those observed in the overall trial population.

Figure. Rate of decline in FVC (mL/year) over 52 weeks with nintedanib versus placebo in all subjects and in subjects with RA-ILD in the INBUILD trial.



Acknowledgements: The INBUILD trial was funded by Boehringer Ingelheim. Medical writing support was provided by Fleishman Hillard Fishburn, London, UK. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE).

Disclosure of Interests: Clive Kelly Speakers bureau: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim, Eric Matteson Speakers bureau: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim and Gilead Sciences, Grant/research support from: Sun Pharmaceuticals and Pfizer, Martin Aringer Speakers bureau: AbbVie, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Chugai, Gilead, GlaxoSmithKline, HEXAL, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi and UCB, Consultant of: AbbVie, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, GlaxoSmithKline, Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Sanofi and UCB, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead, Lilly, Merck Sharp & Dohme, Pfizer, Roche and Sanofi, Consultant of: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead, Lilly, Merck Sharp & Dohme, Pfizer, Roche and Sanofi, Heiko Mueller Employee of: Currently an employee of Boehringer Ingelheim, Lizette Moros Employee of: Currently an employee of Boehringer Ingelheim, Klaus Rohr Employee of: Currently an employee of Boehringer Ingelheim, Martin Kolb Consultant of: Algernon, Boehringer Ingelheim, Pieris Pharmaceuticals and Roche, Grant/research support from: Boehringer Ingelheim, Pieris Pharmaceuticals and Prometic

DOI: 10.1136/annrheumdis-2021-eular.969

OP0125

TOFACITINIB IN RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: EFFICACY AND SAFETY ANALYSIS FROM TREASURE REAL-LIFE DATA

U. Kalyoncu[1], E. Bilgin[1], A. Erden[2], H. Satış[3], A. Tufan[3], E. Tekgoz[4], A. Ateş[5], B. N. Coşkun[6], B. Yağız[6], O. Küçükşahin[7], V. Yazısız[8], G. Kimyon[9], C. Bes[10], A. İ. Ertenli[1], S. Kiraz[1]. [1]*Hacettepe University, Internal Medicine, Rheumatology, Ankara, Turkey*; [2]*Ankara City Hospital, Internal Medicine, Rheumatology, Ankara, Turkey*; [3]*Gazi University, Internal Medicine, Rheumatology, Ankara, Turkey*; [4]*University of Health Sciences Turkey, Gulhane Faculty of Medicine, Internal Medicine, Rheumatology, Ankara, Turkey*; [5]*Ankara University, Internal Medicine, Rheumatology, Ankara, Turkey*; [6]*Uludağ University, Internal Medicine, Rheumatology, Bursa, Turkey*; [7]*Yıldırım Beyazıt University, Internal Medicine, Rheumatology, Ankara, Turkey*; [8]*Akdeniz University, Internal Medicine, Rheumatology, Antalya, Turkey*; [9]*Mustafa Kemal University,*

Internal Medicine, Rheumatology, Hatay, Turkey; [10]*University of Health Sciences Basaksehir Can and Sakura State Hospital, Internal Medicine, Rheumatology, İstanbul, Turkey*

Background: Beyond the joints, rheumatoid arthritis (RA) may affect lungs. Especially the involvement of the paranchyme, RA-associated interstitial lung disease (RA-ILD), is a major cause of mortality and morbidity. Tofacitinib, an oral JAK 1/3 inhibitor, has been used increasingly in the management of rheumatoid arthritis (RA) in recent years. Recently, a couple of animal and human studies reported promising results (1).

Objectives: To assess the real-life efficacy and safety of tofacitinib in patients with RA-ILD in TReasure registry.

Methods: This is a multicenter, observational study included RA patients with ILD diagnosis based on the HRCT images of the lungs, and were followed in 8 different centers participated in the TReasure database. Demographic data and patients' characteristics regarding RA and RA-ILD at the visit in which tofacitinib was initiated and for the last follow-up visit under tofacitinib were recorded. Using the present study cohort, the RA patients with ILD receiving tofacitinib were compared with those without ILD receiving tofacitinib (controls) in terms of the general and disease-related characteristics and data of concomitant DMARD use. To evaluate retention rates of tofacitinib and reasons for discontinuation, data of the patients with RA-ILD in this study cohort were compared with the data of RA patients without ILD who were followed in Hacettepe University (major contributor of the TReasure registry). This research was funded by Pfizer.

Results: A total of 47 RA patients with RA-ILD and a control group of 387 patients without ILD were included. The RA patients with ILD receiving tofacitinib were mostly male, older, and had higher baseline disease activity as compared with those without ILD (Table). The ILD pattern was known in 44 (93.6%) of 47 RA-ILD: 16 (36.3%) had UIP, 24 (54.5%) had NSIP, and 4 (9.1%) had airway disease. While 15 (31.9%) of the patients was asymptomatic, most common initial symptom was shortness of breath (in 14 (29.7%) patients). 18 patients had pre- and post-treatment FVC% and FEV1% values (with a median of 12 (9-19) months). Mean FEV1%; 82.1 vs. 82.8 (pre and post-treatment, respectively, p=0.079), mean FVC%; 79.8 vs. 82.8 (pre and post-treatment, respectively, p=0.014). To evaluate retention rates and reasons for discontinuation, 47 RA-ILD and 239 RA patients without ILD were analyzed. Retention rates were similar (p=0.21, log-rank) (Figure). Most common cause of tofacitinib discontinuation in RA-ILD group was infections (5 (25%) patients). Follow-up durations under tofacitinib were 15 (7-32) and 11 (4-24) months in ILD + and – groups, respectively. The rate of drug discontinuation due to infection in the RA patients with and without ILD was 6.3 per 100 patient-years and 2.4 per 100 patient-years, respectively.

Table 1. Characteristics of the RA patients with and without ILD under tofacitinib

Variables	RA-ILD(+) n=47	RA-ILD(-) n=387	p
Male sex	20 (42.6)	69 (17.8)	<0.001
Age, years	64 (57-69)	56 (46-64)	<0.001
Disease duration for RA, months	128 (78-212)	110 (64-183)	0.171
Smoking status			
Never smoker	26 (55.3)	211 (56.4)	0.259
Current&Ex-smoker	19 (44.7)	163 (43.6)	
RF (+)	36 (78.3)	249 (68.8)	0.187
Anti-CCP (+)	30 (65.2)	196 (61.6)	0.640
RF positive or CCP (+)	41 (87.2)	242 (76.3)	0.094
Presence of comorbidity	33 (70.2)	203 (52.5)	0.021
DAS-28 before tofacitinib	5.4 (4.6-6.22)	4.36 (3.22-5.58)	<0.001
ESR before tofacitinib, mm/h	38 (19-73)	29 (17-45)	0.029
CRP before tofacitinib	6.75 (1.63-24)	9.95 (4.18-25.1)	0.065
Follow-up duration under tofacitinib	15 (7-32)	7 (3-12)	<0.001

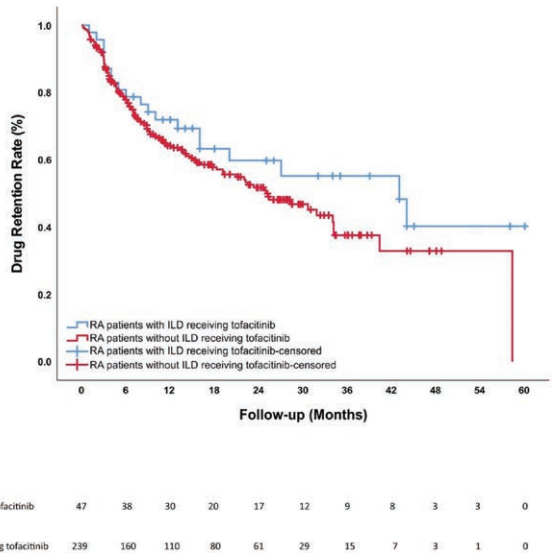


Figure 1. Tofacitinib retention rates in the RA patients with and without ILD

Conclusion: In majority of patients, pulmonary functions remained stable during follow-up. Tofacitinib seems as a promising option for RA-ILD. High rate of discontinuation due infections was observed in RA-ILD patients under tofacitinib; however, it should be kept in mind that RA-ILD patients were older than RA patients without ILD.

REFERENCES:

[1] Bejarano M, et al AB0418 ILD in Patients with RA Treated with tofacitinib. ARD;78:1672.

Disclosure of Interests: Umut Kalyoncu Speakers bureau: Pfizer, Abbvie, UCB, Amgen, Emre Bilgin: None declared, Abdulsamet Erden: None declared, Hasan Satış: None declared, abdurrahman tufan: None declared, Emre Tekgoz: None declared, Aşkın Ateş: None declared, Belkıs Nihan Coşkun: None declared, Burcu Yağız: None declared, Orhan Küçükşahin: None declared, Veli yazısız: None declared, Gezmiş Kimyon: None declared, Cemal Bes: None declared, Ali İhsan Ertenli: None declared, Sedat Kiraz: None declared

DOI: 10.1136/annrheumdis-2021-eular.1236

OP0126 INFECTIONS AND SERIOUS INFECTIONS IN THE FILGOTINIB RHEUMATOID ARTHRITIS PROGRAM

J. Galloway[1], M. H. Buch[2], K. Yamaoka[3], C. Leatherwood[4], A. Pechonkina[5], I. Tiamiyu[4], D. Jiang[6], L. Ye[6], R. Besuyen[7], D. Aletaha[8], K. Winthrop[9]. [1]*King's College London, Centre for Rheumatic Diseases, School of Immunology and Microbial Sciences, London, United Kingdom*; [2]*University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; [3]*Kitasato University School of Medicine, Department of Rheumatology and Infectious Diseases, Kanagawa, Japan*; [4]*Gilead Sciences, Inc., Clinical Research, Foster City, United States of America*; [5]*Gilead Sciences, Inc., Inflammation and Respiratory Therapeutic Area, Foster City, United States of America*; [6]*Gilead Sciences, Inc., Biostatistics, Foster City, United States of America*; [7]*Galapagos BV, Clinical Development, Leiden, Netherlands*; [8]*Medical University of Vienna, Division of Rheumatology, Department of Medicine 3, Vienna, Austria*; [9]*Oregon Health and Science University, Division of Infectious Diseases, Portland, United States of America*

Background: The Janus kinase (JAK)-1 preferential inhibitor filgotinib (FIL) improved rheumatoid arthritis (RA) signs and symptoms in 3 phase (P)3 trials.[1–3] Like other RA therapies, JAK inhibition is associated with increased infection rates.[4]

Objectives: To assess long-term safety across the FIL program regarding infections, including serious infections (SI).

Methods: Patients (pts) meeting 2010 ACR/EULAR RA criteria in pooled analysis of P2 DARWIN 1–2 (D1–2), P3 FINCH 1–3 (F1–3), and long-term extension studies (DARWIN 3, FINCH 4) were included. The placebo (PBO)-controlled as-randomised data set included pts receiving FIL 100 mg (FIL100), FIL 200 mg (FIL200), or PBO up to week (W)12 (D1–2, F1–2). The active-controlled as-randomised data set included pts receiving FIL100, FIL200, adalimumab (ADA), or methotrexate (MTX) up to W52 (F1, F3). The long-term as-treated data set included pts in all 7 studies receiving FIL100 or FIL200; data after rerandomisation were included and contributed to treatment received.

Exposure-adjusted incidence rates (EAIRs) per 100 patient-years exposure (PYE) and differences with 95% confidence intervals (CIs) were calculated using Poisson regression; EAIRs for tuberculosis (TB) in active controlled sets were calculated using an Exact Poisson method. Kaplan-Meier (KM) event probabilities with 95% CIs were provided for SI. If pts had multiple events within the same treatment period, only the first event was counted in EAIR calculation; PYE were calculated up to the last follow-up time or day before next treatment, including after first event. For KM analysis, time to event was calculated until the first event.

Results: Of 2267/1647 pts in as-treated set receiving FIL200/FIL100, 1697 had treatment-emergent infection; 118 were SI. Baseline potential risk factors for pts with SI are in Table.

Table 1. Baseline characteristics of pts with/without treatment emergent SI[a]

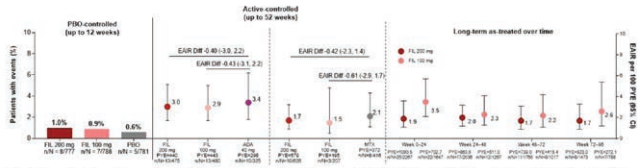
Parameter, n (%)	SI N = 92	No SI N = 2491
Medical history		
Chronic lung disease	13 (14.1)	125 (5.0)
Chronic renal disease	3 (3.3)	23 (0.9)
Infections and infestations	29 (31.5)	499 (20.0)
Baseline body mass index, kg/m^2		
<30	64 (69.6)	1749 (70.2)
≥30	28 (30.4)	742 (29.8)
Age, years		
<65	67 (72.8)	2006 (80.5)
≥65	25 (27.2)	485 (19.5)
Former/current smoker	30 (32.6)	677 (27.2)
Oral corticosteroids, mg		
<7.5	28 (56.0)	731 (66.1)
≥7.5	22 (44.0)	375 (33.9)
Missing data	42	1385

[a]Phase 3 (FINCH 1-4) studies, as randomised.SI, serious infection.

In 12W PBO-controlled period, infection rates were 17.9%/15.6%/13.3% for FIL200/FIL100/PBO. In 52W ADA-controlled period, infection EAIRs (95% CIs)/100 PYE were 46.9 (40.9, 53.7)/43.7 (38.0, 50.4)/43.4 (36.5, 51.5), FIL200/FIL100/ADA; and 38.5 (33.8, 43.9)/39.0 (31.1, 48.8)/42.2 (36.1, 49.3), FIL200/FIL100/MTX in 52W MTX-controlled period; 24.8 (23.1, 26.5)/34.4 (30.4, 38.8), FIL200/FIL100 in long-term analysis. In 12W PBO-controlled period, there was no active TB for FIL200/FIL100/PBO. In 52W ADA-controlled period, active TB EAIRs (95% CIs)/100 PYE were: 0 (0.0, 0.8)/0 (0.0, 0.8)/0.3 (0.0, 1.9), FIL200/FIL100/ADA and 0 (0.0, 0.6)/0 (0.0, 1.9)/0 (0.0, 1.0), FIL200/FIL100/MTX in 52W MTX-controlled period; 0/0.1 (0.0, 0.5), FIL200/FIL100 in long-term analysis.

SI rate or EAIRs are in Figure. Most common infections were upper respiratory tract infection and nasopharyngitis; majority were low grade. Pneumonia was most common SI (<1%). In long-term population, event probability (95% CI) of SI was 2.2% (1.6, 2.9)/2.5% (1.8, 3.4) for FIL200/FIL100 at 52W. In F1–3 (excluding data after rerandomisation), there were no significant changes in mean neutrophil and lymphocyte counts; values remained within normal limits up to W52 for all arms.

Figure. Rate or EAIR of serious infections



ADA, adalimumab; CI, confidence interval; EAIR, exposure-adjusted incidence rate/100 PYE; FIL, filgotinib; MTX, methotrexate; PBO, placebo; PYE, patient-years of exposure.

Conclusion: EAIRs of infections and SI for FIL were similar to PBO, ADA, and MTX. At 52W, incidence rates of SI were comparable for FIL100 and FIL200. Long-term SI EAIR for FIL100 was slightly higher than for FIL200.

REFERENCES:

[1] Genovese et al. *JAMA*. 2019;322:315–25.
[2] Westhovens et al. *Ann Rheum Dis*. 2021; online first.
[3] Combe et al. *Ann Rheum Dis*. 2021; online first.
[4] Strand et al. *Arthritis Res Ther.* 2015;17:362.

Disclosure of Interests: James Galloway Speakers bureau: Pfizer, Bristol-Myers Squibb, UCB and Celgene, Maya H Buch Consultant of: Pfizer; AbbVie; Eli Lilly; Gilead Sciences, Inc.; Merck-Serono; Sandoz; and Sanofi, Grant/research support from: Pfizer, Roche, and UCB, Kunihiro Yamaoka Speakers bureau: AbbVie, Actelion Pharmaceuticals Japan, Asahikasei Pharma Corp, Astellas Pharma, AYUMI Pharma Co, Boehringer Ingelheim Japan, Bristol-Myers Squibb, Chugai Pharma, Daiichi Sankyo, Eisai Pharma, Eli Lilly, GlaxoSmithKline, Gilead G.K., Hisamitsu Pharma Co., Janssen Pharma, Mitsubishi-Tanabe Pharma, MSD, Nippon Kayaku, Nippon Shinyaku, Ono Pharma, Otsuka Pharma, Pfizer, Sanofi, and Takeda Industrial Pharma, Consultant of: Asahikasei Pharma Corp., AbbVie, Gilead G.K., Pfizer, Astellas Pharma Inc, Eli Lilly Japan K.K., and Japan Tobacco Inc., Grant/research support from: Takeda Industrial Pharma, Pfizer, Astellas Pharma, Daiichi Sankyo, Eli Lilly, Eisai Pharma, Teijin Pharma, MSD, Shionogi, Chugai Pharma, Nippon Kayaku, Mitsubishi-Tanabe Pharma, and AbbVie, Cianna Leatherwood Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Alena Pechonkina Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Iyabode Tiamiyu Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Deyuan Jiang Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Lei Ye Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Robin Besuyen Shareholder of: Galapagos BV, Employee of: Galapagos BV, Daniel Aletaha Speakers bureau: AbbVie, Celgene, Lilly, Merck, Novartis, Pfizer, Sanofi Genzyme, UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Medac, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi Genzyme, Grant/research support from: AbbVie, Novartis, Roche, Kevin Winthrop Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly and Co., Galapagos NV, Gilead Sciences, GlaxoSmithKline, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, and Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1416

OP0127 CONFOUNDING EFFECTS OF CONTINUED METHOTREXATE IN PLACEBO ARMS (PLC) OF RHEUMATOID ARTHRITIS (RA) CLINICAL TRIALS – A POST-HOC ANALYSIS OF TWO RANDOMIZED CONTROLLED TRIALS (RCTS)

A. Kerschbaumer[1], Z. I. Rivai[1], J. S. Smolen[1], D. Aletaha[1]. [1]*Medical University of Vienna, Department of Medicine III / Division of Rheumatology, Vienna, Austria*

Background: Various hypotheses exist for the explanation of PLC response rates in RA clinical trials. Here we hypothesized that PLC-treated patients who continue to take methotrexate (cMTX) when entering the trial compared to those who have no cMTX would have higher response rates, because of increased adherence to MTX in the trial environment.

Objectives: To compare differences in response rates in PLC treated RA patients receiving MTX background therapy to patients receiving PLC without background conventional synthetic (cs)DMARDs in two RCTs.

Methods: To investigate the hypothesis we conducted a post-hoc analysis of two RCTs that allowed inclusion of patients with and without cMTX - the GO-AFTER and the SIRROUND-T trials, investigating golimumab and sirukumab, respectively, compared with PLC in patients who had an insufficient response to biological DMARDs.(1,2)

All PLC randomized patients of both trials were pooled and included in the analyses; we did not analyse the active treatment groups. Subsequently we stratified the pooled PLC group into patients receiving PLC on top of cMTX and patients receiving PLC without any csDMARD as background therapy. We compared American College of Rheumatology (ACR) 20/50/70% response rates and Clinical Disease Activity Index (CDAI) low disease activity (LDA, i.e. CDAI≤10) responses between the two groups using Fisher's exact test.

Similar to the primary analyses of the individual studies, non-responder imputation (NRI) for state outcomes (ACR responses, CDAI LDA) was applied in patients who initiated any csDMARD after randomization, had MTX or glucocorticoid doses increased during the study or discontinued the study. NRI was also applied for early escape patients receiving active therapy after failing to achieve a ≥20% decrease in joint counts at week (wk) 16 in GO-AFTER and at wk 18 in SIRROUND-T.

Results: Of the 398 pooled PLC patients, 285 continued their MTX and 113 had no MTX (or other background csDMARDs). Baseline characteristics were similar (Table 1).

Table 1. Baseline characteristics

	Placebo without background csDMARD	Placebo + continued MTX
n	113	285
Age (years) *	56 (48-64)	56 (45-64)
Female (%)	95 (84.1%)	236 (82.8%)
Disease duration (years)	8.4±5.2	8.8±7.5
ACPA positive (%)	88 (77.9%)	214 (75.1%)
RF positive (%)	90 (79.6%)	211 (74%)
SJC 66 (0-66)	15.9±9.9	16.2±10.8
TJC 68 (0-68)	29.1±16.8	26.7±15.7
PGA (VAS 0-10)	6.8±2.2	6.5±2.1
EGA (VAS 0-10)	6.4±1.8	6.1±1.9
Pain (VAS 0-10)	7.0±1.9	6.6±2.1
HAQ-DI (0-3)	1.6±0.7	1.6±0.6
CRP (mg/dL) *	1.2 (0.5-3.5)	1.0 (0.4-2.6)
CDAI	39.4±13.5	38.5±12.8
Concomitant GC intake (%)	67 (59.3%)	174 (61.1%)
Concomitant MTX (%)	0 (0%)	285 (100%)
MTX dosage ≥12.5mg (%)	0 (0%)	222 (77.9%)
MTX dosage <12.5mg (%)	0 (0%)	63 (22.1%)

Data is shown as mean (± standard deviation) or n (%) unless stated otherwise* median (IQR)

At wk 16, an ACR20 response was achieved by 72/285 (25.3%) of PLC+c-MTX and 14/113 (12.4%) receiving PLC only patients (p=0.005); for ACR50 these numbers were 25/285 (8.4%) vs. 1/113 (0.9%; p=0.003); and for ACR70 they were 8/285 (2.8%) vs. 0/113 (0%; p=0.112). Also, significantly more PLC+cMTX patients achieved a CDAI LDA at wk 16 (25/285, 8.8%) compared to PLC only treated patients (2/113; 1.8%; p=0.013). Results between the two arms were numerically or statistically different already from week 4 (for ACR 20) or week 8 (ACR 50, CDAI LDA) onwards (Figure 1).

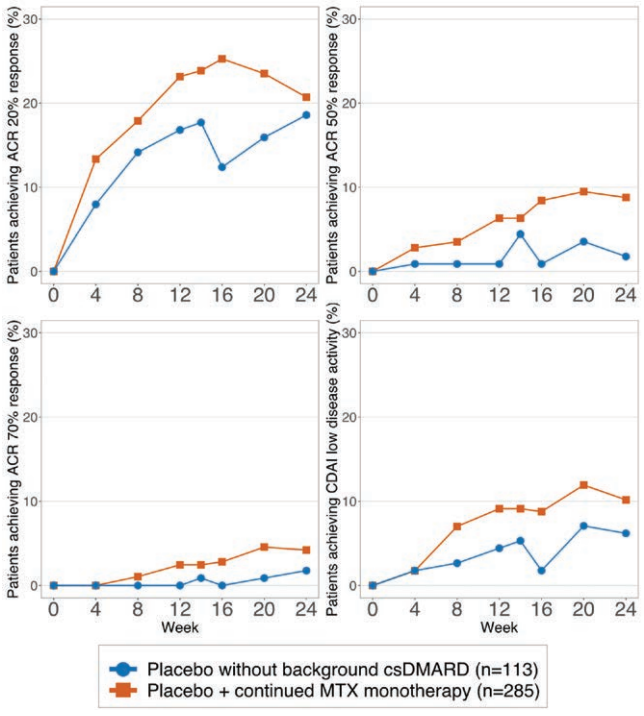


Figure 1. ACR 20/50/70 and CDAI LDA responses of PLC patients with continued MTX vs. PLC patients without csDMARD background therapy.

Conclusion: In patients randomized to placebo therapy, continued MTX background therapy increases clinical responses and achievement of good clinical states. These findings imply that pre-existing and putatively insufficient background therapy should be effectively optimized before enrollment into a clinical trial protocol.

REFERENCES:

[1] Smolen JS *et al. Lancet* 2009; **374**: 210–221.
[2] Aletaha D *et al. Lancet* 2017; **389**: 1206–1217.

Acknowledgements: This study, carried out under YODA Project # 2018-3704, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C. The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C.

Disclosure of Interests: Andreas Kerschbaumer Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli-Lilly, Gilead, Merck Sharp and Dohme, Novartis and Pfizer, Paid instructor for: Celgene, Zaida Iasha Rivai: None declared, Josef S. Smolen Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO Pharma, Janssen, Lilly, Merck Sharp & Dohme, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, and UCB, Consultant of: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO Pharma, Janssen, Lilly, Merck Sharp & Dohme, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, and UCB, Grant/research support from: Abbvie, AstraZeneca, Janssen, Lilly, Merck Sharpe & Dohme, Pfizer, and Roche, Daniel Aletaha Speakers bureau: Abbvie, Amgen, Lilly, Merck, Novartis, Pfizer, Roche, Sandoz, Consultant of: Abbvie, Amgen, Lilly, Merck, Novartis, Pfizer, Roche, Sandoz, Grant/research support from: Abbvie, Amgen, Lilly, Novartis, Roche, SoBi, Sanofi

DOI: 10.1136/annrheumdis-2021-eular.1532

OP0128

INTEGRATED LABORATORY ABNORMALITY PROFILES OF UPADACITINIB WITH UP TO 4.5 YEARS OF EXPOSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED IN THE SELECT PHASE 3 PROGRAM

C. Charles-Schoeman[1], J. T. Giles[2], N. Lane[3], E. Choy[4], D. Furst[5], J. Vencovský[6], A. G. Wilson[7], G. R. Burmester[8], T. Shaw[9], Y. Song[9], H. Camp[9], N. Khan[9], J. Yee[9], S. Anyanwu[9], I. Mcinnes[10]. [1]*University of California, Los Angeles, Rheumatology, Los Angeles, California, United States of America*; [2]*Columbia University, Rheumatology, New York, New York, United States of America*; [3]*University of California, Davis, Rheumatology, Sacramento, California, United States of America*; [4]*CREATE Centre, Cardiff University, Rheumatology, Cardiff, United Kingdom*; [5]*David Geffen School of Medicine, University of California, Los Angeles, Division of Rheumatology, Los Angeles, California, United States of America*; [6]*Institute of Rheumatology, Rheumatology, Prague, Czech Republic*; [7]*Conway Institute, University College Dublin, Center for Arthritis Research, Dublin, Ireland*; [8]*Charité University Medicine, Rheumatology, Berlin, Germany*; [9]*AbbVie Inc, Immunology, North Chicago, Illinois, United States of America*; [10]*University of Glasgow, Institute of Infection, Immunity, and Inflammation, Glasgow, United Kingdom*

Background: Upadacitinib (UPA) is an oral Janus kinase inhibitor approved for rheumatoid arthritis (RA). The safety and efficacy of UPA has been evaluated across a spectrum of patients (pts) with RA in the phase 3 SELECT clinical program.[1,2]

Objectives: To describe long-term laboratory profiles (cutoff date: June 30, 2020) associated with exposure to UPA, adalimumab (ADA), and methotrexate (MTX) in pts with RA treated in the SELECT trials.

Methods: Data were analyzed from 6 randomized controlled UPA RA trials.[1,2] The proportions of pts experiencing potentially clinically significant laboratory changes at a single time point were summarized for the following groups: pooled UPA 15 mg once daily (QD; UPA15; 6 trials), pooled UPA 30 mg QD (UPA30; 4 trials), ADA 40 mg every other week (EOW; 1 trial), and MTX monotherapy (1 trial). Pts received UPA with/without background conventional synthetic disease-modifying antirheumatic drugs. Treatment-emergent adverse events are reported as exposure-adjusted event rates (events/100 pt-years [E/100 PY]). Toxicity was graded per OMERACT criteria, or NCI CTCAE for creatine phosphokinase (CPK) and creatinine.

Results: 4413 pts received ≥1 dose of UPA (UPA15, n=3209; UPA30, n=1204). Exposures were comparable between treatment groups (Table). Proportions of pts with Grade (Gr) 3 and 4 decreases in hemoglobin were highest with UPA30 and MTX (Table). Rates of anemia, as reported by the investigator, were comparable between UPA15, ADA, and MTX groups (Figure); the frequency of UPA-treated pts who discontinued due to anemia was low in all arms. Gr 3 and 4 decreases in neutrophils and lymphocytes with UPA were dose-dependent and higher vs ADA or MTX. Discontinuations due to neutropenia and lymphopenia were rare (<0.1%). Transaminase elevations were more frequent with UPA and MTX vs ADA; however, the proportion of pts who discontinued due to increases in alanine (ALT) or aspartate aminotransferase (AST) were comparable between UPA15 and ADA, and numerically higher with UPA30 and MTX. CPK elevations were more frequent with UPA (Figure). Most events were asymptomatic, and the 1 case of rhabdomyolysis in the UPA30 group was unrelated to study drug (attributed to influenza).

Table 1. Pts with potentially clinically significant laboratory changes

Variable, n (%)	MTX monotherapy (n=314; 637.4 PY)	ADA 40 mg EOW (n=579; 1051.8 PY)	UPA 15 mg QD (n=3209; 7023.8 PY)	UPA 30 mg QD (n=1204; 3091.6 PY)
Mean (SD) exposure, weeks	106 (67)	95 (70)	114 (64)	134 (66)
Median (range) exposure, weeks	144 (1, 221)	118 (2, 231)	136 (0, 232)	160 (0, 231)
Hemoglobin, g/L				
Gr 3 (70–<80 or decreased 21–<30)	28[a] (9.0)	24[b] (4.2)	254[d] (7.9)	169[f] (14.2)
Gr 4 (<70 or decreased ≥30)	16[a] (5.1)	16[b] (2.8)	101[d] (3.2)	78[f] (6.5)
Neutrophils, 10^9/L				
Gr 3 (0.5–<1.0)	3[a] (1.0)	3[b] (0.5)	40[d] (1.2)	37[g] (3.1)
Gr 4 (<0.5)	1[a] (0.3)	1[b] (0.2)	10[d] (0.3)	5[g] (0.4)
Lymphocytes, 10^9/L				
Gr 3 (0.5–<1.0)	74[a] (23.7)	53[b] (9.2)	802[d] (25.1)	423[g] (35.5)
Gr 4 (<0.5)	5[a] (1.6)	3[b] (0.5)	75[d] (2.3)	47[g] (3.9)
ALT, U/L				
Gr 3 (3.0–8.0 × ULN)	26[a] (8.3)	13[c] (2.3)	152[e] (4.8)	71[h] (5.9)
Gr 4 (>8.0 × ULN)	5[a] (1.6)	4[c] (0.7)	26[e] (0.8)	10[h] (0.8)
AST, U/L				
Gr 3 (3.0–8.0 × ULN)	15[a] (4.8)	9[c] (1.6)	101[e] (3.2)	36[h] (3.0)
Gr 4 (>8.0 × ULN)	1[a] (0.3)	5[c] (0.9)	18[e] (0.6)	8[h] (0.7)
CPK, U/L				
Gr 3 (>5.0–10.0 × ULN)	2[a] (0.6)	3[c] (0.5)	65[e] (2.0)	36[i] (3.0)
Gr 4 (>10.0 × ULN)	0[a] (0)	3[c] (0.5)	27[e] (0.8)	15[i] (1.3)
Creatinine, µmol/L				
Gr 3 (>3.0–6.0 × ULN)	0[a] (0)	1[c] (0.2)	3[e] (<0.1)	2[j] (0.2)
Gr 4 (>6.0 × ULN)	0[a] (0)	4[c] (0.7)	8[e] (0.3)	1[j] (<0.1)

[a]n=312. [b]n=576. [c]n=577. [d]n=3201. [e]n=3199. [f]n=1193. [g]n=1192. [h]n=1195. [i]n=1196. [j]n=1197ULN, upper limit of normal

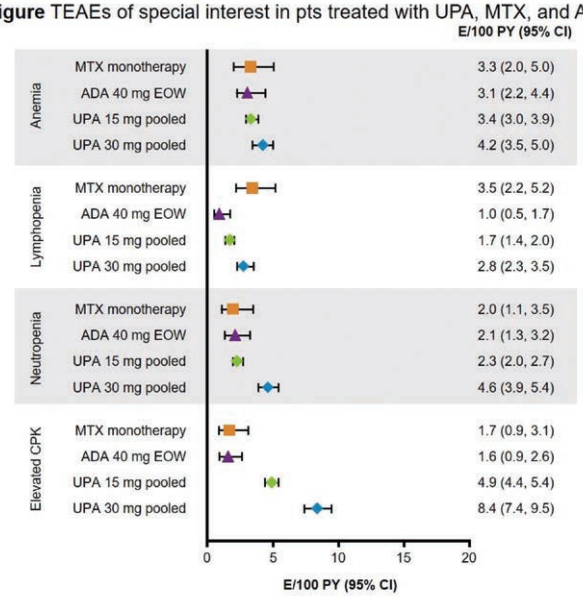
Conclusion: This long-term analysis of UPA-treated pts with RA showed dose-dependent relationships for several laboratory abnormalities. Incidences of these with UPA15 were typically higher than with ADA but similar to MTX, except for increased CPK elevations. Treatment discontinuations due to laboratory abnormalities were infrequent and similar across all treatment groups.

REFERENCES:

[1] Tanaka Y. Mod Rheumatol 2020;30:779–87; 2. Rubbert-Roth A, et al. N Engl J Med 2020;383:1511–21.

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Russell Craddock, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Figure TEAEs of special interest in pts treated with UPA, MTX, and ADA[a]



MTX: n=314, PY=637.4; ADA 40 mg EOW: n=579, PY=1051.8; UPA 15 mg pooled: n=3209, PY=7023.8; UPA 30 mg pooled: n=1204, PY=3091.6

[a]Pts who switched from placebo, ADA, or MTX to UPA were included in the UPA analysis set from the start of UPA, while those who switched from UPA to ADA were included in the ADA analysis set from the start of ADA, and were censored at time of switch. MTX monotherapy was censored at time of rescue to combination therapy (addition of UPA)

ADA, adalimumab; CI, confidence interval; CPK, creatine phosphokinase; E/100 PY, events/100 pt-years; EOW, every other week; MTX, methotrexate; pt, patient; PY, pt-years; TEAE, treatment-emergent adverse event; UPA, upadacitinib

Disclosure of Interests: Christina Charles-Schoeman Consultant of: AbbVie, Gilead, Pfizer, and Sanofi/Regeneron, Grant/research support from: AbbVie, Bristol-Myers Squibb, and Pfizer, Jon T Giles Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Gilead, Pfizer, and UCB, Grant/research support from: Pfizer, Nancy Lane Consultant of: Amgen, Mallinckrodt, Pfizer, and Roche, Ernest Choy Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Chugai, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Regeneron, Roche, Sanofi, and UCB, Consultant of: AbbVie, Amgen, Biocon, Biogen, Chugai, Eli Lilly, Gilead, Janssen, Merck Serono, Novartis, Pfizer, Regeneron, Roche, R-Pharm, and Sanofi, Grant/research support from: Bio-Cancer, Biogen, Novartis, Pfizer, Roche, Sanofi, and UCB, Daniel Furst Speakers bureau: AbbVie, Continuing Medical Education, and Novartis, Consultant of: Actelion, Amgen, Bristol-Myers Squibb, Corbus, Galapagos, Novartis, and Pfizer, Grant/research support from: Actelion, Amgen, Bristol-Myers Squibb, Corbus, Galapagos, GSK, NIH, Novartis, Pfizer, Roche/Genentech, and Sanofi, Jiří Vencovský Speakers bureau: AbbVie, Biogen, MSD, Pfizer, Roche, Sanofi, and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly, Gilead, and Octapharma, Anthony G Wilson: None declared, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Eli Lilly, Gilead, Janssen, MSD, Pfizer, Roche, and UCB, Consultant of: AbbVie, Eli Lilly, Gilead, Janssen, MSD, Pfizer, Roche, and UCB, Tim Shaw Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Heidi Camp Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Nasser Khan Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Jillian Yee Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Samuel Anyanwu Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Iain McInnes Consultant of: AbbVie, Celgene, Janssen, Novartis, and UCB, Grant/research support from: Celgene, Janssen, Novartis, Pfizer, Roche, and UCB
DOI: 10.1136/annrheumdis-2021-eular.1815

SLE, Sjögren's and APS - treatment and SLE, Sjögren's and APS - clinical aspects (other than treatment)

OP0129 BELIMUMAB AFTER RITUXIMAB SIGNIFICANTLY REDUCED IGG ANTI-DSDNA ANTIBODY LEVELS AND PROLONGED TIME TO SEVERE FLARE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

M. Shipa[1], A. Embleton-Thirsk[2], M. Parvaz[1], L. Santos Ribeiro[1], P. Muller[2], K. Chowdhury[2], D. Isenberg[1], C. Doré[2], C. Gordon[3], M. Ehrenstein[1]. [1]*University College London, Department of Rheumatology, London, United Kingdom*; [2]*University College London, Comprehensive Clinical Trials Unit, London, United Kingdom*; [3]*University of Birmingham, Rheumatology Research Team - Inflammation and Ageing, Birmingham, United Kingdom*

Background: B cell depletion with rituximab, an anti-CD20 mAb, has shown efficacy for systemic lupus erythematosus (SLE) in open-label studies but failed to meet primary endpoints in two randomised, placebo controlled trials. Rituximab increases BAFF levels which has been associated with subsequent lupus flares. We hypothesised that high BAFF levels after rituximab limit its effectiveness in SLE and that the anti-BAFF monoclonal antibody belimumab given immediately after rituximab could be a valuable therapeutic strategy.

Objectives: To assess the safety and obtain preliminary evidence for efficacy of belimumab following rituximab therapy in patients with SLE.

Methods: BEAT-LUPUS (Belimumab after B cell depletion in SLE) is a 52-week phase IIb, randomised, double-blind, placebo-controlled clinical trial investigating the safety and efficacy of intravenous belimumab after B cell depletion therapy (rituximab). The maximum permissible prednisolone dose throughout the trial was 20mg/day with encouragement to reduce by 50% from baseline by 6 months. The primary outcome measure was log IgG anti-dsDNA antibody serum levels at 52 weeks measured by ELISA. A linear regression ANCOVA model was fitted to evaluate the difference in 52-week anti-dsDNA levels between treatment arms adjusting for anti-dsDNA value at screening (before rituximab) and randomisation (4-8 weeks after the 1st infusion of rituximab), CD19 > or < $0.01x10^9$/l at randomisation, and renal involvement at screen. Secondary outcomes included measures of disease activity and incidence of adverse events. B cell (CD19) counts were measured by flow cytometry. Intention to treat analysis was adopted. Full ethical and regulatory approval was obtained. A comprehensive description of the protocol and statistical analysis plan is available[1,2].

Results: 52 patients with active SLE received rituximab (2 infusions, 2 weeks apart) and then randomised to receive either belimumab (n=26) or placebo (n=26) 4-8 weeks after their 1st dose of rituximab. 32 patients completed trial treatment protocol (belimumab or placebo) through to 52 weeks, withdrawals were equally split between belimumab and placebo. There was a significant reduction in IgG anti-dsDNA antibody levels in patients treated with belimumab compared to placebo at 52 weeks (p<0.001, Figure 1); 43 patients were included in the intention to treat analysis at 52 weeks.

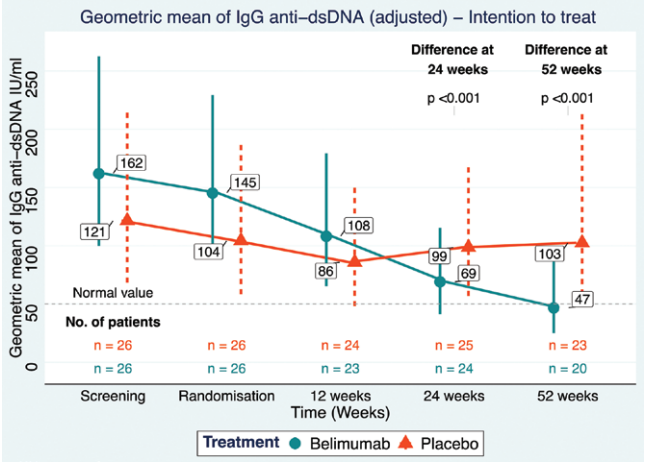


Figure 1. Serum IgG anti-dsDNA antibody levels (geometric means with 95% confidence intervals) in patients treated with rituximab, then randomised to belimumab or placebo at 1st trial infusion. An intention to treat linear regression ANCOVA model was fitted to evaluate the difference in 52-week anti-dsDNA between belimumab or placebo adjusting for baseline values and stratification factors. N= patient numbers who provided serum samples at time indicated.

Kaplan-Meier curves demonstrated that belimumab reduced the risk of severe flare (BILAG A flare) compared to placebo (hazard ratio 0.27, 95% confidence interval 0.07-0.97, unadjusted log-rank p=0.03). There were 10 and 3 severe flares in the placebo and belimumab group respectively. There was no difference in cumulative steroid dose over the course of the trial between belimumab and placebo.

Belimumab did not increase the incidence of infections, serious or total adverse events, nor withdrawals due to adverse events compared to placebo. Belimumab significantly suppressed B cell repopulation at 52 weeks compared to placebo (p=0.001), but not total serum IgG.

Conclusion: This placebo controlled double blind trial met its primary endpoint, a significant reduction in IgG anti-dsDNA antibody levels, and demonstrated that belimumab prolongs the time to severe flare compared to placebo. These results suggest that belimumab after rituximab is a safe and effective treatment for patients with SLE and supports further development of this combination as a novel therapeutic strategy.

REFERENCES:

[1] Jones A, et al. BMJ Open. 2019;9:e032569.

[3] Muller P, et al. Trials. 2020;21:652.

Acknowledgements: We acknowledge the important contribution of the BEAT Lupus Trial Steering Committee, the Data Monitoring Committee, the BEAT-LUPUS trial investigators, and all the patients participating in the trial or involved in its development.

Funding: This trial was supported by Versus Arthritis (grant number 20873) and the UCLH Biomedical Research Centre (BRC). GSK provided belimumab free of charge, as well as additional funding.

GSK had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results. Versus Arthritis and the UCLH BRC reviewed the relevant grant proposals and monitor progress of relevant aspects of the study but did not play any role in the analyses, interpretation of data, or decision to submit results.

Disclosure of Interests: Muhammad Shipa: None declared, Andrew Embleton-Thirsk: None declared, Mariea Parvaz: None declared, Liliana Santos Ribeiro: None declared, Patrick Muller: None declared, Kashfia Chowdhury: None declared, David Isenberg Speakers bureau: Paid by GSK to deliver educational talks, Consultant of: Received consultancy fees from GSK for attending advisory boards, Caroline Doré: None declared, Caroline Gordon Speakers bureau: Paid for educational speaker role by GSK, Consultant of: Received consultancy fees from GSK for attending advisory boards, Michael Ehrenstein Speakers bureau: Paid by GSK as a speaker in educational sessions, Consultant of: Received consultancy fees from GSK for attending advisory boards, Grant/research support from: GSK provided part of the funding for the BEAT-LUPUS trial

DOI: 10.1136/annrheumdis-2021-eular.553

OP0130 COMPOSITE OF RELEVANT ENDPOINTS IN SJÖGREN'S SYNDROME (CRESS): A COMPREHENSIVE TOOL FOR CLINICAL TRIALS

S. Arends[1], L. de Wolff[1], J. F. Van Nimwegen[1], G. M. Verstappen[1], J. Vehof[2], M. Bombardieri[3], S. J. Bowman[4], E. Pontarini[3], A. Baer[5], M. Nys[6], J. E. Gottenberg[7], R. Felten[8], N. Ray[9], A. Vissink[10], F. G. M. Kroese[1], H. Bootsma[1]. [1]*University Medical Centre Groningen and University of Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*; [2]*University Medical Centre Groningen and University of Groningen, Ophthalmology, Groningen, Netherlands*; [3]*Queen Mary University of London, Rheumatology, London, United Kingdom*; [4]*Queen Elizabeth Hospital, Rheumatology, Birmingham, United Kingdom*; [5]*John Hopkins University School of Medicine, Rheumatology, Baltimore, United States of America*; [6]*Bristol Myers Squibb, Brussels, Belgium*; [7]*Centre National de Référence des Maladies Auto-immunes et Systémiques rare Est/Sud-Ouest (RESO), Rheumatology, Strasbourgh, France*; [8]*Centre National de Référence des Maladies Auto-immunes et Systémiques rare Est/Sud-Ouest (RESO), Rheumatology, Strasbourg, France*; [9]*Bristol Myers Squibb, Lawrenceville NJ, United States of America*; [10]*University Medical Centre Groningen and University of Groningen, Oral and Maxillofacial Surgery, Groningen, Netherlands*

Background: Several large randomised controlled trials (RCTs) in primary Sjögren's syndrome (pSS) failed to demonstrate drug efficacy.[1-4] Many of these trials used ESSDAI as primary endpoint, showing large but similar response rates in active treatment and placebo groups.[1,3,4] Given the heterogeneous nature of pSS, there is need for a composite endpoint including multiple clinically relevant parameters.

Objectives: To develop and validate the Composite of Relevant Endpoints in Sjögren's Syndrome (CRESS).

Methods: A multidisciplinary team of pSS experts selected clinically relevant items and measurements to include in the CRESS. Definition of response of CRESS items was based on clinical relevance, previously defined minimal clinically important improvement (MCII) and data of the single-centre ASAP-III (abatacept) trial.[1] CRESS was validated in three independent RCTs: TRACTISS (rituximab) trial[2],

multi-centre abatacept trial[3] and ETAP (tocilizumab) trial[4]. CRESS response rates were assessed at the primary endpoint visit of all four trials.

Results: Five complementary items were selected to form CRESS: systemic disease activity, patient-reported symptoms, tear gland, salivary gland and serological item. Definition of response per item is presented in Table 1. Total CRESS response was defined as response on ≥3 of 5 items. Since not all trials have ocular staining score or salivary gland ultrasonography (SGUS) available, the concise CRESS (cCRESS) was developed simultaneously, leaving Schirmer's test and unstimulated whole saliva flow for the tear and salivary gland items, respectively. In the ASAP-III trial, CRESS response rates were 24/40 (60%) for abatacept vs. 7/39 (18%) for placebo at week 24 (p<0.001).

Table 1. CRESS items and definition of response

Items	*Measurements*	*Definition of response*
Systemic disease activity	ClinESSDAI	Score<5 (low disease activity)
Patient-reported symptoms	ESSPRI	Decrease of ≥1 point or ≥15%
Tear gland*	Schirmer/OSS**	-If abnormal Schirmer (≤5 mm) at baseline: increase of ≥5 mm in Schirmer -Or if abnormal OSS (≥3 points) at baseline: decrease ≥2 points in OSS -Or if both Schirmer/OSS normal scores at baseline: no change to abnormal in both
Salivary gland*	UWS/SGUS	Increase of ≥25% in UWS (or if score is 0 at baseline, any increase) Or decrease of ≥25% in total Hocevar score (SGUS)
Serological	RF/IgG	Decrease of ≥25% in RF Or decrease of ≥10% in IgG
CRESS responder	**Responder on ≥3 of 5 items**	

Ocular Staining Score (OSS), Unstimulated whole salivary flow (UWS), Salivary gland ultrasonography (SGUS), Rheumatoid factor (RF), Immunoglobuline G (IgG)***Concise CRESS (cCRESS):** CRESS without OSS and SGUS, leaving Schirmer and UWS for tear and salivary gland items, respectively**Mean of both eyes

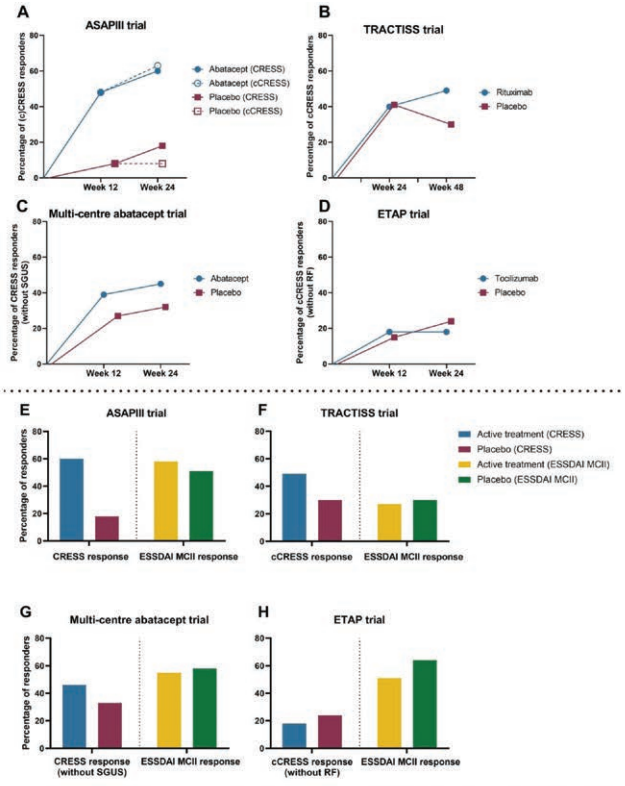


Figure 1 A. CRESS and cCRESS (=CRESS without OSS and SGUS) response rates in ASAP-III trial at week 12 and 24. At week 12, only CRESS without SGUS was available **B.** cCRESS response rates in TRACTISS (rituximab) trial at week 24 and 48 **C.** CRESS without SGUS response rates in multi-centre abatacept trial at week 12 and 24. **D.** cCRESS without rheumatoid factor response rates in ETAP (tocilizumab) trial at week 12 and 24. **E.** CRESS response rates vs. ESSDAI MCII response rates in ASAP-III trial at week 24. Median baseline ESSDAI scores for abatacept were 14.0 (IQR 9.0-16.8), for placebo 13.0 (IQR 8.0-18.0) **F.** cCRESS response rates vs. ESSDAI MCII response rates in TRACTISS trial at week 48. Mean baseline ESSDAI scores for rituximab were 5.3, SD±4.7, for placebo 6.0, SD±4.3 **G.** CRESS without SGUS response rates vs. ESSDAI MCII response rates in multi-centre abatacept trial at week 24. Mean baseline ESSDAI scores for abatacept were 8.7, SD±3.4, for placebo 10.1, SD±5.0 **H.** cCRESS without RF response rates vs. ESSDAI MCII response rates in ETAP trial at week 24. Median baseline ESSDAI scores for tocilizumab were 11.0 (IQR 8.0-13.5), for placebo 10.0 (IQR 8.0-14.8). For all trials, ESSDAI response percentages were calculated imputing missing patients as non-responders.

In the external validation trials, cCRESS response rates for TRACTISS were: 33/67 (49%) rituximab vs. 20/66 (30%) placebo at week 48 (p=0.026). CRESS response rates (without SGUS) for the multi-centre abatacept trial were: 41/92 (45%) abatacept vs. 30/95 (32%) placebo at week 24 (p=0.067). cCRESS response rates (without rheumatoid factor) for ETAP were: 10/55 (18%) tocilizumab vs. 13/55 (24%) placebo at week 24 (p=0.482) (Figure 1A-D). Compared to ESSDAI MCII of ≥3 points decrease, CRESS was able to approximately halve placebo response rates in RCTs with high baseline ESSDAI scores (>5) (Figures 1E-H).

Conclusion: CRESS shows lower placebo response rates compared to ESSDAI MCII, which is crucial for demonstrating treatment efficacy. With the CRESS, higher response rates in abatacept and rituximab treated patients compared to placebo were found in RCTs which previously showed negative primary endpoint results. CRESS confirmed that no differences were found for almost all outcome measures between tocilizumab and placebo,[4] with low response rates. The CRESS is a well-balanced, feasible, composite endpoint for use in clinical trials in pSS patients.

REFERENCES:

[1] Van Nimwegen 2020;9913(19):1–11
[2] Bowman 2017;69(7):1440–50
[3] Baer (doi:218599)
[4] Felten (doi:21846)

Acknowledgements: The authors would like to acknowledge all contributors of the included trials.

Disclosure of Interests: Suzanne Arends: None declared, Liseth de Wolff: None declared, Jolien F. van Nimwegen Speakers bureau: Bristol Myers Squibb, Consultant of: Bristol Myers Squibb, Gwenny M. Verstappen: None declared, Jelle Vehof: None declared, Michele Bombardieri Consultant of: MedImmune, GlaxoSmithKline, Grant/research support from: MedImmune, Simon J. Bowman Consultant of: AstraZenecea/MedImmune, Bristol Myers Squibb, Celgene, Eli Lilly, Glenmark, GlaxoSmithKline, MTPharma, Novartis, Ono, Pfizer, Takeda, UCB, XTLBio, Elena Pontarini: None declared, Alan Baer Consultant of: Bristol Myers Squibb, Sanofi, VielaBio, Novartis, Marleen Nys Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Jacques-Eric Gottenberg Grant/research support from: Bristol Myers Squibb, Pfizer, Renaud FELTEN: None declared, Neelanjana Ray Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Arjan Vissink: None declared, Frans G.M. Kroese Speakers bureau: Bristol Myers Squibb, Roche and Janssen-Cilag, Consultant of: Bristol Myers Squibb, Grant/research support from: Unrestricted grants from Bristol Myers Squibb, Hendrika Bootsma Speakers bureau: Bristol Myers Squibb and Novartis, Consultant of: Bristol Myers Squibb, Roche, Novartis, Medimmune, Union Chimique Belge, Grant/research support from: Unrestricted grants from Bristol Myers Squibb and Roche

DOI: 10.1136/annrheumdis-2021-eular.1113

OP0131

ANIFROLUMAB EFFECTS ON RASH AND ARTHRITIS IN PATIENTS WITH SLE AND IMPACT OF INTERFERON SIGNAL IN POOLED DATA FROM PHASE 3 TRIALS

J. T. Merrill[1], V. Werth[2], R. Furie[3], E. F. Morand[4], J. M. Kahlenberg[5], G. Abreu[6], R. Tummala[7]. *[1]Oklahoma Medical Research Foundation, Arthritis & Clinical Immunology Research Program, Oklahoma City, United States of America*; *[2]University of Pennsylvania and Corporal Michael J. Crescenz Veterans Administration Hospital, Dermatology, Philadelphia, United States of America*; *[3]Zucker School of Medicine at Hofstra/Northwell, Division of Rheumatology, Great Neck, United States of America*; *[4]Monash University, Centre for Inflammatory Disease Monash Health, Melbourne, United States of America*; *[5]University of Michigan, Division of Rheumatology, Ann Arbor, United States of America*; *[6]AstraZeneca, BioPharmaceuticals R&D, Gothenburg, Sweden*; *[7]AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, United States of America*

Background: Treatment with the type I interferon (IFN) receptor antibody anifrolumab was associated with clinical improvements in mucocutaneous and musculoskeletal disease activity in patients with systemic lupus erythematosus (SLE) in the phase 2 MUSE trial (NCT01438489) and phase 3 TULIP trials.[1–4] Because rash and arthritis are the most common manifestations of SLE, the effect of anifrolumab on these symptoms can be examined in biomarker-defined subsets, as previously reported for the MUSE trial.[2]

Objectives: To evaluate the effect of anifrolumab on rash and arthritis in patients with SLE, and the impact of IFN gene signature (IFNGS) on treatment response, using disease measures of different stringency in pooled data from the phase 3 TULIP trials.

Methods: TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) were placebo-controlled, 52-week trials of intravenous anifrolumab administered every 4 weeks in patients with moderate to severe SLE.[3,4] In this post hoc analysis, outcomes of rash and arthritis were evaluated using mucocutaneous and musculoskeletal domains of the SLE Disease Activity Index 2000 (SLEDAI-2K) and the

British Isles Lupus Assessment Group (BILAG) index. In addition, the modified Cutaneous Lupus Erythematosus Disease Area and Severity Index (mCLASI) score was used to evaluate rash, and tender and swollen joint counts were used to assess arthritis.

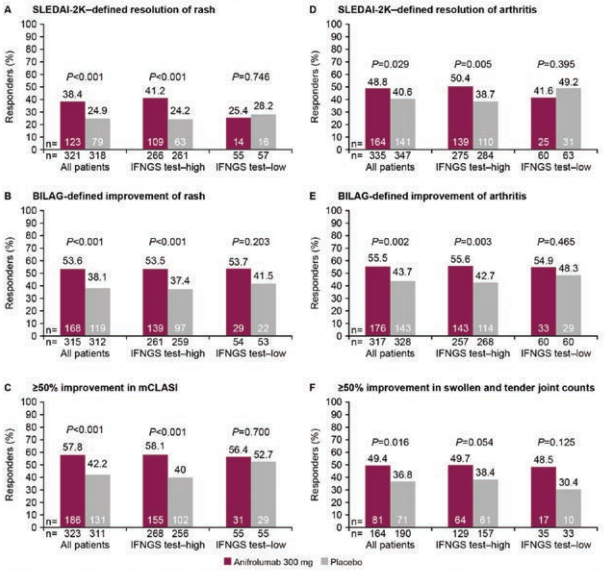
Results: 360 patients received anifrolumab 300 mg (IFNGS test–high, n=298; IFNGS test–low, n=62) and 366 patients were given placebo (IFNGS test–high, n=302; IFNGS test–low, n=64). Change from baseline to Week 52 compared with placebo was measured by outcomes, ordered by their stringency. More anifrolumab-treated patients achieved rash improvement using SLEDAI-2K (complete resolution: difference 13.5%, nominal *P*<0.001), BILAG (at least 1 severity grade lowering: difference 15.5%, nominal *P*<0.001), and mCLASI (≥50% improvement, if baseline score >0: difference 15.6%, nominal *P*<0.001). Results were comparable in the IFNGS test–high subset (SLEDAI-2K: difference 17.0%, nominal *P*<0.001, BILAG: difference 16.1%, nominal *P*<0.001; mCLASI: difference 18.1%, nominal *P*<0.001). There was a trend toward anifrolumab-associated rash improvement in IFNGS test–low patients using BILAG (Figure). More patients receiving anifrolumab had SLEDAI-2K–defined resolution in arthritis (difference 8.2%, nominal *P*=0.029), BILAG severity lessening (difference 11.8%, nominal *P*=0.002), and ≥50% decrease in tender/swollen joint counts, when ≥6 at baseline (difference 12.6%, nominal *P*=0.016). Results were comparable in the IFNGS test–high subset (SLEDAI-2K: difference 11.7%, nominal *P*=0.005; BILAG: difference 12.9%, nominal *P*=0.003; joint counts: difference 11.3%, nominal *P*=0.054). In IFNGS test–low patients, there was a trend toward anifrolumab-associated arthritis improvement when measured using BILAG, and the effect of anifrolumab on the number of swollen/tender joint counts was similar to the IFNGS test–high group, although the IFNGS test–low sample size in this analysis was very small (Figure).

Conclusion: In pooled data from the TULIP trials, anifrolumab treatment was associated with improvements in rash and arthritis using measures of different stringency. The SLEDAI-2K findings were largely driven by the subset of patients who were IFNGS test–high. However, using measures that were more sensitive to change, despite small sample sizes, IFNGS test–low patients may also have benefit.

REFERENCES:

[1] Furie R, et al. *Arthritis Rheumatol*. 2017;69:376–86.
[2] Merrill JT, et al. *Lupus Sci Med.* 2018;5:e000284.
[3] Furie RA, et al. *Lancet Rheumatol*. 2019;1:e208–19.
[4] Morand EF, et al. *N Engl J Med.* 2020;382:211–21.

Figure. Patients with SLEDAI-2K–defined resolution (A) and BILAG-defined improvement (B) in rash. Patients with ≥50% improvement in mCLASI score from baseline to Week 52 (mCLASI >0 at baseline) (C). Patients with SLEDAI-2K–defined resolution (D) and BILAG-defined improvement (E) in arthritis. Patients with ≥50% improvement in the number of swollen or tender joints from baseline to Week 52 (≥6 at baseline) (F).



BILAG, British Isles Lupus Assessment Group; IFNGS, interferon gene signature; mCLASI, modified Cutaneous Lupus Erythematosus Disease Area and Severity Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.
Data pooled from TULIP-1 and TULIP-2 trials.
Resolution defined as: SLEDAI-2K rash component=0 (patients with SLEDAI-2K rash component=2 at baseline); SLEDAI-2K arthritis component=0 (patients with SLEDAI-2K arthritis component=4 at baseline); improvement defined as: BILAG rash, mucocutaneous baseline score A change to B, C, or D, or baseline score B change to C or D; BILAG arthritis, musculoskeletal baseline score A change to B, C, or D, or baseline B change to C or D. mCLASI defined as the activity portions of CLASI that describe skin erythema, scale/hypertrophy, and inflammation of the scalp.

Acknowledgements: Writing assistance by Victoria Alikhan, PhD, of JK Associates Inc., part of Fishawack Health. This study was sponsored by AstraZeneca.

Disclosure of Interests: Joan T Merrill Consultant of: AstraZeneca, AbbVie, Amgen, Aurinia, BMS, EMD Serono, GSK, Remegen, Janssen, Provention, and UCB, Grant/research support from: BMS and GSK, Victoria Werth Speakers bureau: University of Pennsylvania, who own the copyright for the CLASI and SDASI, Consultant of: AbbVie, Amgen, Argenx, AstraZeneca, Biogen, BMS, Celgene, Chrysalis, CSL Behring, Cugene, Eli Lilly, EMD Serono, Genentech, GSK, Incyte, Idera, Janssen, Kirin, Medimmune, Medscape, Nektar, Octapharma, Pfizer, Principa, Regeneron, Resolve, and Viela Bio, Grant/research support from: AstraZeneca, Biogen, Celgene, Corbus Pharmaceuticals, Genentech, Gilead, Janssen, Pfizer, Syntimmune, and Viela Bio, Richard Furie Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Eric F. Morand Speakers bureau: AstraZeneca, Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, J Michelle Kahlenberg Consultant of: Admirex Pharmaceuticals, AstraZeneca, Aurinia Pharmaceuticals, BMS, Boehringer Ingelheim, Eli Lilly, and Ventus Therapeutics, Grant/research support from: BMS/Celgene and Q32 Bio, Gabriel Abreu Employee of: AstraZeneca, Raj Tummala Employee of: AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.1471

OP0132 EFFECT OF IBERDOMIDE ON CUTANEOUS MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF A 24-WEEK, PLACEBO-CONTROLLED, PHASE 2 STUDY

V. Werth[1], J. Merrill[2], R. Furie[3], T. Dörner[4], R. Van Vollenhoven[5], P. Lipsky[6], M. Weiswasser[7], S. Korish[7], P. Schafer[8], M. Stern[9], Z. Liu[10], S. Tang[11], N. Delev[7]. [1]*University of Pennsylvania, Michael J. Crescenz VA Medical Center, Philadelphia, United States of America*; [2]*Oklahoma Medical Research Foundation, University of Oklahoma Health Sciences Center, Oklahoma City, United States of America*; [3]*Northwell Health, Rheumatology, Great Neck, United States of America*; [4]*DRFZ and Charité University Hospitals, Rheumatology and Hemostaseology, Berlin, Germany*; [5]*Amsterdam University Medical Centers, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands*; [6]*RILITE Foundation, President, Charlottesville, United States of America*; [7]*Bristol Myers Squibb, Clinical R&D, Princeton, United States of America*; [8]*Bristol Myers Squibb, Translational Medicine, Princeton, United States of America*; [9]*Bristol Myers Squibb, Translational Development & Diagnostics, Princeton, United States of America*; [10]*Bristol Myers Squibb, Biometrics, Princeton, United States of America*; [11]*Bristol Myers Squibb, Translational Bioinformatics, Princeton, United States of America*

Background: Iberdomide is a high-affinity cereblon ligand that promotes proteasomal degradation of Ikaros (*IKZF1*) and Aiolos (*IKZF3*), transcription factors involved in innate and adaptive immune cell development and homeostasis, and linked to the genetic risk for systemic lupus erythematosus (SLE). A phase 2, placebo-controlled study evaluated the efficacy and safety of iberdomide in patients (pts) with moderate to severe SLE.

Objectives: To examine the effect of iberdomide on cutaneous manifestations in SLE pts.

Methods: Adult autoantibody-positive SLE pts with a SLE Disease Activity Index 2000 (SLEDAI 2K) score ≥6 were randomized (2:2:1:2) to oral iberdomide (0.45, 0.3, 0.15 mg) or placebo once daily (QD) for 24 weeks while continuing standard background lupus medications. The Cutaneous Lupus Area and Severity Index Activity score (CLASI-A) was assessed every 4 weeks through week 24. As prespecified, exploratory analyses, change from baseline and the proportion of pts who achieved ≥50% reduction from baseline (CLASI-50) were evaluated for all pts, pts with baseline CLASI-A ≥8, and by cutaneous lupus subtypes (acute [ACLE], subacute [SCLE], chronic [CCLE]). CLASI-A outcomes were also evaluated post hoc for subgroups with high baseline expression of *IKZF3* or the type 1 interferon (IFN) gene signatures in the blood.

Results: Of 288 randomized pts, the mean and median (range) baseline CLASI-A scores were 6.9 and 5.0 (0-49), with 28% of pts having a score ≥8. 56% of pts had ACLE, 29% CCLE, and 16% SCLE. CLASI-50 responses were not significantly different comparing iberdomide to placebo in all pts and pts with baseline CLASI-A ≥8 at week 24, where high placebo response rates were observed (Table). Numerically greater mean improvement from baseline in CLASI-A scores in pts with baseline CLASI-A ≥8 was observed for iberdomide 0.45 mg vs placebo beginning at week 4, with continuous improvement through week 24. For pts with SCLE or CCLE, CLASI-50 response rates were significantly higher with iberdomide 0.45 mg vs placebo (*P*<0.04; Table). SCLE pts had significantly greater mean change and median percent improvement in CLASI-A from baseline with iberdomide 0.45 mg vs placebo at week 24 (*P*<0.03). Treatment differences in CLASI-A between iberdomide 0.45 mg and placebo were larger for SCLE and CCLE subgroups with high baseline *IKZF3* or type 1 IFN gene signatures, with statistical significance achieved for SCLE pts but not CCLE pts (Figure).

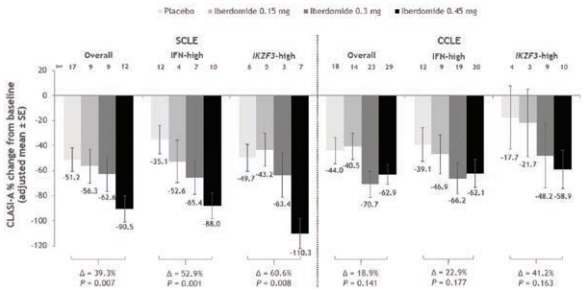
Conclusion: Iberdomide showed beneficial effects on skin manifestations in pts with SLE. Efficacy appears to be more pronounced in pts with SCLE and CCLE skin subtypes, and in pts with high *IKZF3* or IFN gene expression signatures.

Table 1. CLASI-50 Response Rates by Subgroups at Week 24

		0.15 mg QD (n=42)		0.3 mg QD (n=82)		0.45 mg QD (n=81)	
Subgroup	Placebo (n=83)	0.15 mg QD vs Placebo		0.3 mg QD vs Placebo		0.45 mg QD vs Placebo	
	n/m (%)	n/m (%)	Str Diff in % (95% CI) *P* value	n/m (%)	Str Diff in % (95% CI) *P* value	n/m (%)	Str Diff in % (95% CI) *P* value
All pts	37/83 (44.6)	19/42 (45.2)	0.4 (-17.33, 18.55) *P*=0.961	41/82 (50.0)	5.3 (-9.93, 20.11) *P*=0.499	45/81 (55.6)	10.9 (-4.30, 25.51) *P*=0.163
CLASI-A ≥8	10/20 (50.0)	8/13 (61.5)	15.9 (-17.42, 45.45) *P*=0.399	13/24 (54.2)	12.1 (-17.57, 39.97) *P*=0.458	16/24 (66.7)	15.1 (-15.51, 42.49) *P*=0.368
ACLE	23/50 (46.0)	15/30 (50.0)	4.8 (-17.22, 26.31) *P*=0.662	20/43 (46.5)	-3.3 (-22.95, 16.67) *P*=0.738	17/38 (44.7)	-3.0 (-23.20, 17.65) *P*=0.782
SCLE	9/17 (52.9)	5/9 (55.6)	2.6[a] (-33.04, 36.33) *P*=0.966	3/9 (33.3)	-6.6 (-38.98, 31.86) *P*>0.999	11/12 (91.7)	**38.7[a] (4.54, 61.75)** *P*=0.035
CCLE	5/18 (27.8)	7/14 (50.0)	22.2[a] (-10.51, 50.00) *P*=0.198	10/23 (43.5)	23.8 (-6.89, 48.88) *P*=0.129	18/29 (62.1)	**34.1 (4.43, 56.16)** *P*=0.029

CI, confidence interval; Str Diff, stratified difference.[a]Unstratified difference.

Figure. CLASI-A Percent Change From Baseline by CLE Subtype for All Patients and Patients with High Baseline Expression of *IKZF3* or Type 1 IFN Gene Signature



Δ, treatment difference of adjusted means; CCLE, chronic cutaneous lupus erythematosus; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-activity score; IFN, interferon; SCLE, subacute cutaneous lupus erythematosus.

Acknowledgements: This study was sponsored by Bristol Myers Squibb. Professional medical writing assistance was provided by Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

Disclosure of Interests: Victoria Werth Consultant of: Bristol Myers Squibb, Grant/research support from: Bristol Myers Squibb, Joan Merrill Consultant of: UCB, GlaxoSmithKline, AbbVie, EMD Serono, Remegen, Celgene/Bristol Myers Squibb, AstraZeneca, Lilly, Immupharma, Amgen, Janssen, Resolve, Alpine, Aurinia, Astellas, Alexion, and Provention, Grant/research support from: GlaxoSmithKline and AstraZeneca, Richard Furie Consultant of: Bristol Myers Squibb, Grant/research support from: Bristol Myers Squibb, Thomas Dörner Consultant of: support for clinical studies and honoraria for scientific advice: AbbVie, Bristol Myers Squibb Company, Celgene, Eli Lilly, Janssen, Novartis, Roche, Employee of: Charite Universitätsmedizin, Berlin and DRFZ Berlin, Germany, Ronald van Vollenhoven Speakers bureau: UCB, AbbVie, Galapagos, Janssen, Pfizer, Paid instructor for: support for educational programs: Pfizer, Roche, Consultant of: AstraZeneca, Biogen, Biotest, Celgene, Gilead, Servier, UCB, AbbVie, Galapagos, Janssen, Pfizer, Grant/research support from: Bristol Myers Squibb, GlaxoSmithKline, Eli Lilly, UCB, Peter Lipsky Employee of: RILITE Foundation, Michael Weiswasser Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Shimon Korish Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Peter Schafer Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Mark Stern Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Zhaohui Liu Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Shaojun Tang Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Nikolay Delev Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.2181

OP0133

THE PREVALENCE AND RISK FACTORS OF RETINAL TOXICITY ASSOCIATED WITH LONG-TERM HYDROXYCHLOROQUINE USE

S. Do[1], J. H. Du[2], J. X. An[3], J. Wang[4], A. Lin[5]. *[1]Western University of Health Sciences, School of Pharmacy, Pomona, United States of America*; *[2]Kaiser Permanente Fontana Medical Center, Department of Pharmacy, Fontana, United States of America*; *[3]Kaiser Permanente Research & Evaluation, Department of Research and Evaluation, Pasadena, United States of America*; *[4]Kaiser Permanente Fontana Medical Center, Department of Ophthalmology, Fontana, United States of America*; *[5]Kaiser Permanente Southern California, Department of Rheumatology, Fontana, United States of America*

Background: Hydroxychloroquine (HCQ) is commonly used for the treatment of various autoimmune diseases. The medication is generally well-tolerated. However, long-term use after 5 years may increase the risk of retinopathy. One study in 2014 has demonstrated the risk can be as high as 7.5%. Optical Coherence Tomography (OCT) has become a major modality in screening retinopathy.

Objectives: To evaluate the prevalence of retinal toxicity among patients using hydroxychloroquine and to determine various risk factors associated with hydroxychloroquine-associated retinal toxicity.

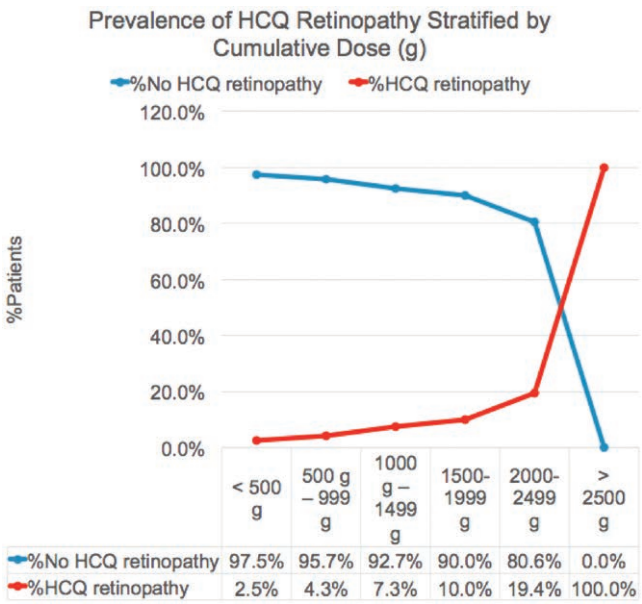
Methods: We performed a retrospective chart review on a cohort of adult patients with long-term use (≥ 5 years cumulative) of HCQ between January 1st, 2011 to December 31st, 2018 from the Kaiser Permanente San Bernardino County and Riverside medical center areas in Southern California, USA. Patients were excluded if they had previously been diagnosed with retinopathy prior to hydroxychloroquine use, were deceased, or had incomplete OCT exam. Our primary endpoint was the prevalence of patients who developed retinal toxicity detected by OCT, and later confirmed by retinal specialist. Potential risk factors (age, duration of therapy, daily consumption per actual body weight, cumulative dose, confounding diseases and medication) for developing retinopathy were also evaluated. Univariable and multivariable logistic regression analyses were used to determine risk factors associated with retinal toxicity.

Results: Among 676 patients exposed to more than 5 years of HCQ, the overall prevalence of retinal toxicity was 6.8%, and ranged from 2.5% to 22.2% depending on the age, weight-based dosing, duration of use and cumulative dose. Duration of therapy for 10 years or more increased risk of retinopathy by approximately 5 to 19 folds. Similarly, weight-based dose of 7 mg/kg/day or greater was asscciated with increased risk of retinopathy by approximately 5 times. Patients with cumulative dose of 2000 grams or more had greater than 15 times higher risk of developing retinopathy. Duration of use for10 years or more (odd ratio 4.32, 95% CI 1.99 – 12.49), age (odd ratio 1.04; 95% CI 1.01 - 1.08), cumulative dose of more than 1500 g (odd ratio 7.4; 95% CI 1.40 – 39.04) and atherosclerosis of the aorta (odd ratio 2.59; 95% CI, 1.24 – 5.41) correlated with higher risk of retinal toxicity.

Table 2. Hydroxychloroquine Treatment Exposure

	No Retinal Toxicity (N=630)		Retinal Toxicity (N=46)		
	Mean	Std Dev	Mean	Std Dev	p-value
Dose per day (mg)	326.6	96.2	337	92.8	0.479
Dose per kg/day	**4.3**	**1.4**	**4.9**	**1.7**	**0.003**
Duration of use					
Months	**99.3**	**33.4**	**141.5**	**64.5**	**< 0.0001**
Years	**8.3**	**2.8**	**11.8**	**5.4**	**< 0.0001**
Cumulative dose (mg)	**983.2**	**445.2**	**1483.6**	**891.5**	**< 0.0001**

Conclusion: The overall prevalence of retinopathy was 6.8%. Regular OCT screening, especially in patients with hydroxychloroquine use for more than 10 years, daily intake > 7 mg/kg, or cumulative dose > 1500 grams is important in detecting hydroxychloroquine-associated retinal toxicity



REFERENCES:
[1] Hobbs HE. Sorsby A, & Freedman A. Retinopathy Following Chloroquine Therapy. *The Lancet*. 1959; 2(7101): 478-480.
[2] Levy, G. D., Munz, S. J., Paschal, J., Cohen, H. B., Pince, K. J., & Peterson, T. Incidence of hydroxychloroquine retinopathy in 1,207 patients in a large multicenter outpatient practice. *Arthritis & Rheumatism: 1997*; *40*(8): 1482-1486.
[3] Ding, H. J., Denniston, A. K., Rao, V. K., & Gordon, C. Hydroxychloroquine-related retinal toxicity. *Rheumatology*. 2016; *55*(6): 957-967.
[4] Stelton, C. R., Connors, D. B., Walia, S. S., & Walia, H. S. Hydrochloroquine retinopathy: characteristic presentation with review of screening. *Clinical rheumatology*. 2013; *32*(6): 895-898.
[5] Marmor, M. F., Kellner, U., Lai, T. Y., Melles, R. B., & Mieler, W. F. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (2016 revision). *Ophthalmology*. 2016; *123*(6): 1386-1394.
[6] Melles, R. B., & Marmor, M. F. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. *JAMA ophthalmology*. 2014; *132*(12): 1453-1460.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.328

OP0134 NOVEL INTERFERON GENE EXPRESSION SCORES PREDICT REFRACTORY SEVERE CUTANEOUS DISEASE FOLLOWING RITUXIMAB THERAPY IN SLE

L. M. Carter[1], A. Alase2, Z. Wigston2, A. Psarras2, A. Burska2, M. Y. MD Yusof2, E. Hensor2, J. Reynolds[3], M. Wittmann2, I. N. Bruce[4], E. Vital2on behalf of The MASTERPLANS Consortium. *[1]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[1]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[3]University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom*; *[4]University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*

Background: We developed and validated two continuous interferon-stimulated gene (ISG) expression scores (IFN-Score-A and IFN-Score-B) that predict clinical outcomes in SLE. IFN-Score-A includes ISGs typically present in a global interferon signature while IFN-Score-B includes additional ISGs potentially responsive to multiple IFN subtypes [1].
We have previously shown that these scores associate with treatment response following rituximab (RTX) therapy within the British Isles Lupus Assessment Group (BILAG) Biologics Register (BILAG-BR), a UK wide study of patients treated with RTX for active SLE following cyclophosphamide and/ or mycophenolate mofetil treatment failure. Specifically, multivariable analysis showed higher baseline IFN-Score-B independently predicted BILAG response at 6 months post treatment [2]. We also showed that response of cutaneous lupus to RTX can be poor even when other organs respond well, and that interferons are enriched in the skin of patients with SLE where dysregulated keratinocytes are a source of IFNκ [3]. MASTERPLANS is a consortium aimed at identifying therapeutic biomarkers in SLE.
Objectives: To investigate how IFN-Score-A and -B associated with skin disease and response to RTX.
Methods: Pre-treatment whole blood samples were collected in TEMPUS tubes from subjects undergoing first RTX treatment within BILAG-BR. IFN-Scores were derived using a custom Taqman array as previously described [1]. Clinical response was defined as improvement in BILAG-2004 disease activity, with a maximum of one domain showing persistent BILAG-2004 grade B disease, and no new BILAG grade A or B disease flares at 6 months. The mucocutaneous domain of BILAG was then analysed separately.
Results: 147 patients were studied, of whom 90 had follow up data available. Baseline BILAG-2004 grade A/B disease activity predominantly affected the mucocutaneous domain in 74/147 (50.3%), musculoskeletal in 61 /147 (41.5%) and renal domain 66/147 (37.4%).
At 6 months 59/90 (65.6%) achieved an overall treatment response. Responders showed significantly higher mean IFN-Score-B compared with non-responders (-1.8 vs -2.4, p = 0.04). Among those with active grade A/B BILAG-2004 mucocutaneous disease at baseline, 38/50 (76%) showed improvement within this domain at 6 months. However, among overall non-responders, 7/31 (22.6%) had new or residual BILAG-A mucocutaneous disease at 6 months post RTX, indicating it to be a substantial component of overall treatment failure. In contrast, persistent grade A musculoskeletal disease was seen in 9.7% of non-responders. BILAG-A mucocutaneous disease is characterised by severe manifestations including extensive rashes covering > 18% of body surface area, severe bullous lupus or panniculitis and disabling deep mucosal ulceration. Neither IFN-Score-A nor IFN-Score-B were significantly associated with the severity of mucocutaneous disease at baseline. However, individuals with persistent or new BILAG-A mucocutaneous disease at six months following RTX displayed significantly lower baseline IFN-Score-B than those with improving or residual less severe disease (-3.0 vs -2.1, p = 0.04) after RTX.
Conclusion: Low IFN score-B status identified an endotype of severe mucocutaneous SLE which was resistant to RTX therapy in the BILAG-BR cohort. We previously showed that high IFN-score-B independently predicts overall therapeutic response to rituximab. Further work will aim to refine IFN status as overall and organ specific biomarkers in SLE.
REFERENCES:
[1] El-Sherbiny et al., Sci. Rep. 2018; 8: 5793.
[2] Alase et al., ARD 2019;78:763-764
[3] Psarras et al., Nat Commun. 2020; 11: 6149
Acknowledgements: We would like to thank the Medical Research Council, National Institute of Health Research, UK for funding the MASTERPLANS project
Disclosure of Interests: Lucy Marie Carter: None declared, Adewonuola Alase: None declared, Zoe Wigston: None declared, Antonios Psarras: None declared, Agata Burska: None declared, Md Yuzaiful Md Yusof: None declared, Elizabeth Hensor: None declared, John Reynolds: None declared, Miriam Wittmann Consultant of: Abbvie, Celgene, Janssen, L'Oreal, Novartis and Pfizer, Ian N. Bruce Speakers bureau: GlaxoSmithKline, UCB Pharma, Consultant of: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, MedImmune, Merck Serono, Grant/ research support from: Genzyme Sanofi, GlaxoSmithKline, Edward Vital Consultant of: Roche, GSK and AstraZeneca, Grant/research support from: Roche, GSK and AstraZeneca
DOI: 10.1136/annrheumdis-2021-eular.1098

OP0135 SAFETY AND EFFICACY OF SUBCUTANEOUS BELIMUMAB AND INTRAVENOUS RITUXIMAB COMBINATION IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A PHASE 2, RANDOMISED, PLACEBO-CONTROLLED 68-WEEK STUDY

X. Mariette[1], C. Baldini[2], F. Barone[3], H. Bootsma[4], K. Clark[5], S. De Vita[6], K. Lerang[7], P. Mistry[8], F. Morin[9], R. Punwaney[10], R. Seror[1], P. L. Van Daele[11], A. Van Maurik[12], N. Wisniacki[13], D. Roth[14]. *[1]Université Paris-Saclay, Rheumatology, Paris, France*; *[2]University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy*; *[3]University of Birmingham, College of Medical and Dental Sciences, Rheumatology, Birmingham, United Kingdom*; *[4]University of Groningen, University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*; *[5]GlaxoSmithKline, Clinical Science, Stevenage, United Kingdom*; *[6]Azienda Ospedaliera Universitaria di Udine, Rheumatology Clinic, Department of Medical Area, Udine, Italy*; *[7]Oslo University Hospital, Department of Rheumatology, Oslo, Norway*; *[8]GlaxoSmithKline, R&D Biostatistics, Stevenage, United Kingdom*; *[9]Centre de Recherche Musculo-Squelettique, Centre de Recherche Musculo-Squelettique, Trois Rivieres, Canada*; *[10]GlaxoSmithKline, Pharmaceutical Research and Development, Philadelphia, PA, United States of America*; *[11]Erasmus Medical Center, Department of Internal Medicine and Department of Immunology, Rotterdam, Netherlands*; *[12]GlaxoSmithKline, Clinical Pharmacology and Experimental Medicine, Stevenage, United Kingdom*; *[13]GlaxoSmithKline, Discovery Medicine, Stevenage, United Kingdom*; *[14]GlaxoSmithKline, Research and Development, Collegeville, PA, United States of America*

Background: B-lymphocyte stimulator (BLyS) is increased in primary Sjögren's syndrome (pSS) and plays a role in the B-cell hyperactivity thought to contribute to pSS. Belimumab (BEL, anti-BLyS) and rituximab (RTX, anti-CD20) target B cells through distinct and potentially complementary mechanisms.
Objectives: To evaluate the safety and efficacy of subcutaneous (SC) BEL/intravenous (IV) RTX combination (BEL/RTX) in patients with pSS.
Methods: This Phase 2, double-blind study (GSK Study 201842; NCT02631538) randomised 86 adults with active pSS to 4 treatment arms stratified for baseline EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) scores 5-12 or >12: placebo (PBO; N=13), BEL/RTX (N=24; BEL 200 mg SC weekly to Week [Wk] 24 followed by weekly PBO SC to Wk 52 + RTX 1000 mg IV, Wk 8 + 10), BEL monotherapy (N=24; BEL 200 mg SC weekly to Wk 52) or RTX monotherapy (N=25; RTX 1000 mg IV, Wk 8 + 10). Follow-up was at Wk 68. Safety to Wk 68 was the primary endpoint (safety population; patients received ≥1 dose of study treatment). Secondary/other endpoints (completer population; patients completed treatment and follow-up phase) were ESSDAI score, stimulated salivary flow, CD20+ B-cell count within salivary gland biopsies, patient-reported oral dryness, and EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) score.
Results: Baseline demographics and disease characteristics were similar among arms. Adverse events (AEs) were balanced across arms. Serious AEs were infrequent but occurred only in active treatment arms (Table). No unexpected safety issues were identified with BEL/RTX relative to BEL or RTX. Treatment phase and follow-up were completed by 60/86 patients. ESSDAI reductions with BEL/RTX were numerically greater over time than PBO, with greatest difference at Wk 68 (Table), but were not differentiated from monotherapy. Stimulated salivary flow showed a trend favouring BEL/RTX vs PBO over later time points (Table). In contrast with PBO, BEL, and RTX, salivary gland biopsies from BEL/RTX showed almost complete B-cell depletion (Wk 24). There was no clear evidence for a positive effect of BEL/RTX on patient-reported oral dryness or ESSPRI score.

Table 1. Key safety endpoints and selected efficacy endpoints

AEs – safety population	PBO (N=13)	BEL/RTX (N=24)	BEL (N=24)	RTX (N=25)
AEs, n (%)	13 (100)	24 (100)	23 (96)	24 (96)
Drug-related AEs, n (%)	10 (77)	17 (71)	16 (67)	14 (56)
AEs leading to discontinuation/ withdrawal, n (%)	1 (8)	5 (21)	3 (13)	5 (20)
SAEs, n (%)	0	3 (13)	2 (8)	4 (16)
Number of SAEs	0	4	2	7
Deaths, n (%)	0	1 (4)*	0	0
Infections and Infestations, n (%)†	11 (85)	19 (79)	21 (88)	18 (72)
Efficacy – completer population	**PBO (N=8)**	**BEL/RTX (N=17)**	**BEL (N=19)**	**RTX (N=16)**
ESSDAI change, LS mean (SE) from BL over time‡				
Wk 12	-2.00 (1.449)	-4.85 (0.996)	-3.87 (0.949)	-4.22 (1.048)§
Wk 24	-2.87 (1.324)	-5.32 (0.911)	-3.87 (0.869)	-5.25 (0.940)
Wk 52	-2.87 (1.294)	-5.67 (0.890)	-4.76 (0.850)	-4.32 (0.919)
Wk 68	-1.75 (1.400)	-5.73 (0.962)	-3.87 (0.918)	-4.38 (0.994)
Stimulated salivary flow (ml/min), mean (SD)				
BL	0.47 (0.247)	0.71 (0.629)	0.43 (0.329)	0.62 (0.621)
Wk 12	0.49 (0.205)	0.75 (0.834)	0.49 (0.373)	0.58 (0.527)
Wk 24	0.55 (0.305)	0.78 (0.790)	0.45 (0.411)	0.72 (0.890)
Wk 52	0.53 (0.378)	1.00 (1.146)	0.58 (0.608)	0.69 (0.781)
Wk 68	0.36 (0.163)	0.88 (0.817)	0.52 (0.450)	0.73 (0.785)§

*Aspiration (n=1); not considered related to treatment; patient died of food aspiration; †System organ class with the highest percent of AEs; ‡Analysis was performed using mixed model repeated measures; §n=15.BL, baseline; LS, Least square; SAEs, serious AEs; SD, standard deviation; SE, standard error

Conclusion: No unexpected safety issues were identified with BEL/RTX relative to BEL or RTX. BEL/RTX showed a trend towards improvement in ESSDAI and stimulated salivary flow over time, which was sustained post treatment. BEL/RTX depleted B cells in minor salivary gland biopsies.
Funding: GSK
Acknowledgements: Medical writing assistance was provided by Katalin Bartus, PhD, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.
Disclosure of Interests: Xavier Mariette Consultant of: BMS, Galapagos, Gilead, GSK, Janssen, Novartis, Pfizer, Servier, UCB, Grant/research support from: Servier, Chiara Baldini: None declared, Francesca Barone Consultant of: GSK, UCB, Roche, Actelion, Grant/research support from: GSK, UCB, Roche, Actelion, Employee of: Kintai therapeutics, Candel Therapeutics, Hendrika Bootsma Speakers bureau: BMS, Novartis, Consultant of: BMS, Roche, Novartis, MedImmune, UCB, Servier, Grant/research support from: BMS, Roche, Ken Clark Shareholder of: GSK, Employee of: GSK, Salvatore De Vita Consultant of: GSK, Roche, Karoline Lerang: None declared, Prafull Mistry Shareholder of: GSK, Employee of: GSK, Frederic Morin: None declared, Rajesh Punwaney Shareholder of: GSK, Employee of: GSK, Raphaèle Seror Consultant of: GSK, BMS, Fresenius Kabi, Boehringer, Jansen, Amgen, Pfizer, Roche, Paul LA van Daele: None declared, Andre van Maurik Shareholder of: GSK, Employee of: GSK, Nicolas Wisniacki Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK
DOI: 10.1136/annrheumdis-2021-eular.2170

OP0136

RITUXIMAB PREVENTS THE PROGRESSION OF B-CELL DRIVEN INFLAMMATORY INFILTRATE IN THE MINOR SALIVARY GLANDS OF PRIMARY SJOGREN'S SYNDROME BY DOWNREGULATING IMMUNOLOGICAL PATHWAYS KEY IN ECTOPIC GERMINAL CENTRE ORGANIZATION: RESULTS FROM THE TRACTISS TRIAL

E. Pontarini[1], F. Chowdhury[1,2], E. Sciacca[1], S. Grigoriadou[1], F. Rivellese[1], D. Lucchesi[1], K. Goldmann[1], L. Fossati-Jimack[1], P. Emery[3], W. F. Ng[4], N. Sutcliffe[5], C. Everett[6], C. Fernandez[6], A. Tappuni[2,5], M. Lewis[1], C. Pitzalis[1], S. J. Bowman[7], M. Bombardieri[1]. *[1]William Harvey Research Institute, Queen Mary University of London, Experimental Medicine and Rheumatology, London, United Kingdom*; *[2]Institute of Dentistry, Queen Mary University of London, Oral Immunobiology and Regenerative Medicine, London, United Kingdom*; *[3]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Chapel Allerton Hospital, Leeds, United Kingdom*; *[4]Translational and Clinical Research Institute, Newcastle University, Newcastle-upon-Tyne, Newcastle, United Kingdom*; *[5]Royal London Hospital, Bart's Health NHS Trust, Rheumatology department, London, United Kingdom*; *[6]Leeds Institute for Clinical Trials Research, University of Leeds, Clinical Trials Research Unit, Leeds, United Kingdom*; *[7] University Hospitals Birmingham NHS Foundation Trust, Rheumatology Department, Birmingham, United Kingdom*

Background: The pathogenic role of B-cells in primary Sjögren's Syndrome (pSS) is well established and B cell abnormalities. Because of the substantial role of B-cells, rituximab (RTX), a chimeric anti-CD20 monoclonal antibody, has been considered as a potential biologic disease modifying drug to reduce disease activity in pSS. To date, the TRial for Anti-B-Cell Therapy In patients with pSS (TRACTISS) is the largest multi-centre, placebo-controlled trial with RTX. Despite the unmet primary endpoints (30% reduction in fatigue or oral dryness, measured by visual analogue scale), RTX treated patients showed an improvement in unstimulated whole salivary flow (Bowman et al. Arthritis Rheumatol 2017;69:1440–1450).
Objectives: To provide the first longitudinal transcriptomic and histological analysis at 3 time points over 48 weeks of labial SGs of pSS patients treated with RTX, in comparison to placebo, from the TRACTISS cohort.
Methods: 26 pSS patients randomised to RTX or placebo arm consented for labial SG biopsies at baseline, weeks 16 and 48. Patients received two 1000mg cycles of RTX or placebo at baseline and week 24. SG focus score, inflammatory aggregate area fraction, B-cells (CD20+), T-cells (CD3+), follicular dendritic cells (FDCs) (CD21+) and plasma cells (CD138+) density were assessed by H&E and immunofluorescence staining. The histological analysis was performed by digital imaging using QuPath software. RNA was extracted from matched labial SG lobules and sequenced with Illumina platform. A Principal Component Analysis (PCA) and features driving the PCA were investigated along with the most influential gene loadings. The limma-voom R pipeline was used to extract Differential Expressed Genes (DEGs) between placebo and RTX group at week 48, and gene ontology (GO) enrichment analysis performed through EnrichR to derive GO terms and pathways associated with DEGs.
Results: Placebo-treated labial SGs showed a worsening of inflammation highlighted by the increment of B-cell density, development of new FDC networks, and a higher ectopic GC prevalence at week 48, compared to RTX-treated patients. No difference in total T-cells and plasma cell infiltration was observed. RTX downregulated genes involved in immune cell recruitment and inflammatory aggregate organisation (e.g. CCR7, CCL19, CD52, and PDCD1) and gene signature-based analysis of 64 immune cell types highlighted how RTX preferentially blocked class-switched- and memory-B-cells infiltration in SGs at week 48. Pathway analyses confirmed the downregulation of leukocyte migration, MHC class II antigen presentation, and T-cell co-stimulation immunological pathways, such as the CD40 receptor complex pathway. The analysis of placebo SGs transcriptomic at week 48 showed a higher expression of genes linked to ectopic GC organisation, such as CXCL13, CCL19, LTβ, in female compared to male subjects. Gender was confirmed as a key co-variate responsible for most of the variation in the PCA, together with the SG focus score and the *foci* area fraction.
Conclusion: Treatment with RTX showed beneficial effects on labial SG inflammatory infiltration in pSS, by downregulating genes involved in immune cell recruitment, activation and organisation in ectopic GCs. Class-switched-B-cells, memory-B-cells and FDC network development were primarily affected appearing to be responsible for the lack of progression in SG B cell infiltration in the RTX compared to the placebo arm in which clear worsening of SG immunopathology over 48 weeks was detected in female patients. Although a clear association with the clinical improvement in unstimulated salivary flow observed at week 48 in

RTX-treated patients could not be established given the low number of patients consenting to 3 longitudinal biopsies it is conceivable that RTX is responsible for preserving exocrine function.

Acknowledgements: SJB receives a salary contribution from the NIHR Birmingham Biomedical Research Centre.

Disclosure of Interests: Elena Pontarini: None declared, Farzana Chowdhury: None declared, Elisabetta Sciacca: None declared, Sofia Grigoriadou: None declared, Felice Rivellese: None declared, Davide Lucchesi: None declared, Katriona Goldmann: None declared, Liliane Fossati-Jimack: None declared, Paul Emery: None declared, Wan Fai Ng: None declared, Nurhan Sutcliffe: None declared, Colin Everett: None declared, Catherine Fernandez: None declared, Anwar Tappuni: None declared, Myles Lewis: None declared, Costantino Pitzalis: None declared, Simon J. Bowman Consultant of: SJB In 2020 I have received consultancy fees from Novartis, Abbvie and Galapagos., Michele Bombardieri: None declared

DOI: 10.1136/annrheumdis-2021-eular.3960

Spondyloarthritis - treatment

OP0137 TUMOR NECROSIS FACTOR INHIBITORS SHOW A DELAYED EFFECT ON RADIOGRAPHIC SACROILIITIS PROGRESSION IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: 10-YEAR RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

M. Torgutalp[1], V. Rios Rodriguez[1], M. Verba[1], M. Protopopov[1], F. Proft[1], J. Rademacher[1,2], H. Haibel[1], M. Rudwaleit[3], J. Sieper[1], D. Poddubnyy[1,4]. [1]*Charité – Universitätsmedizin Berlin, Division of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany*; [2]*Berlin Institute of Health,., Berlin, Germany*; [3]*Klinikum Bielefeld, Department of Internal Medicine and Rheumatology, Bielefeld, Germany*; [4]*Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), Epidemiology Unit, Berlin, Germany*

Background: Observational cohort studies have shown that there is low, but still detectable progression level in radiographic sacroiliitis, which might also have an impact on the function in patients with axial spondyloarthritis (axSpA). Recent data showed that tumor necrosis factor inhibitors (TNFi) might retard spinal progression when initiated earlier and taken longer in patients with axSpA. However, the question of whether they also have such an effect on radiographic progression in sacroiliac joints (SIJs) is still unclear.

Objectives: To investigate the longitudinal association between radiographic sacroiliitis progression and treatment with TNFi in patients with early axial SpA in a long-term inception cohort.

Methods: Based on the availability of at least two sets of SIJ radiographs, 301 patients (166 with nr-axSpA, symptom duration ≤5 years and 135 with r-axSpA, symptom duration ≤10 years) from the German Spondyloarthritis Inception Cohort (GESPIC) were included in this analysis. These patients contributed with a total of 737 2-year radiographic intervals. Two trained and calibrated central readers scored the radiographs according to the modified New York criteria. If both scored an image as definite radiographic sacroiliitis, the patient was classified as having r-axSpA. The sacroiliac sum score was calculated as a mean of both readers. The association between previous as well as current TNFi use and radiographic sacroiliitis progression, which was defined as the change in the sacroiliitis sum score over 2 years, was analysed using longitudinal generalized estimating equations (GEE) analysis.

Results: At baseline, 9 (3.0%) patients were treated with a TNFi, and 87 (28.9%) patients received at least one TNFi during the entire follow-up period. A total of 141 of the radiographic intervals were covered with TNFi of any duration, while 109 of them were covered with a TNFi of at least 12 months. While receiving ≥12 months TNFi in the previous interval was associated with a lower progression of the sacroiliitis sum score compared to not receiving TNFi in the previous interval, this was not the case in patients who received TNFi ≥12 months in the current 2-year interval (Figure 1). The significant association between TNF ≥12 months in the previous interval and progression in the sacroiliitis sum score were confirmed in the adjusted multivariable longitudinal GEE analysis. In addition, a similar trend for the beneficial effects was observed in different models, which included other treatment definitions with TNFi in the previous 2-year interval (Table).

Conclusion: Treatment with TNFi was associated with retardation of radiographic sacroiliitis progression in patients with axSpA. This effect becomes evident between 2 and 4 years after treatment initiation.

Figure. A) Cumulative probability plot of the 2-year progression in the sacroiliitis sum score, stratified by receiving at least 12 months TNFi in the previous and current 2-year radiographic intervals. **B)** The change in sacroiliitis sum scores over two years in patients with axial spondyloarthritis treated vs non-treated with TNFi at least 12 months in the previous and current 2-year radiographic intervals.

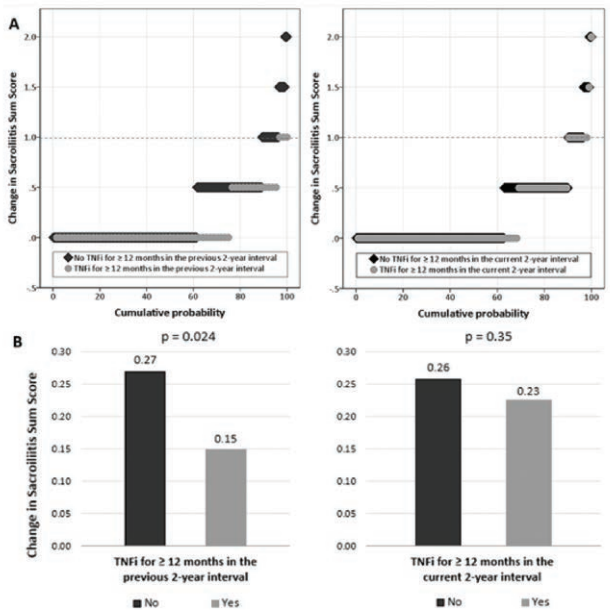


Table 1. The longitudinal GEE analysis of the association between progression in the sacroiliitis sum score and TNFi use.

TNFi treatment definition	Reference	β* (95% CI)
TNFi for ≥ 12 months in the previous 2-year interval	No TNFi for ≥ 12 months in the previous 2-year interval	**-0.09 (-0.18, -0.003)**
Any TNFi use in the previous 2-year interval	No TNFi use in the previous 2-year interval	-0.09 (-0.17, 0.002)
TNFi for ≥ 12 months in the current 2-year interval	No TNFi for ≥ 12 months in the current 2-year interval	-0.03 (-0.11, 0.06)
Any TNFi use in the current 2-year interval	No TNFi use in the current 2-year interval	0.05 (-0.05, 0.14)
TNFi for ≥ 12 months in the previous and ≥ 12 months in the current 2-year interval	No TNFi for ≥ 12 months in the previous and ≥ 12 months in the current 2-year interval	-0.08 (-0.17, 0.004)

* Parameter estimates from the multivariable models adjusted for **sex**, **age** at the beginning of the current 2-year interval, **HLA-B27** positivity, **symptom duration** at the beginning of the current 2-year interval, time-averaged elevated **CRP**, time-averaged **BASDAI**, and time-averaged **NSAID intake score** in the current 2-year interval.

References:

Acknowledgements: GESPIC was initially supported by the BMBF. As a consequence of the funding reduction by BMBF according to schedule in 2005 and stopped in 2007, complementary financial support has been obtained also from Abbott, Amgen, Centocor, Schering–Plough, and Wyeth. Starting from 2010, the core GESPIC cohort was supported by AbbVie.

Disclosure of Interests: Murat Torgutalp: None declared, Valeria Rios Rodriguez: None declared, Maryna Verba: None declared, Mikhail Protopopov: None declared, Fabian Proft: None declared, Judith Rademacher: None declared, Hildrun Haibel: None declared, Martin Rudwaleit Consultant of: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma, Joachim Sieper: None declared, Denis Poddubnyy Speakers bureau: AbbVie, Bristol-Myers Squibb, Lilly, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Biocad, Gilead, GlaxoSmithKline, Eli Lilly, MSD, Novartis, Pfizer, Samsung Bioepis, and UCB, Grant/research support from: AbbVie, MSD, Novartis, and Pfizer

DOI: 10.1136/annrheumdis-2021-eular.2926

OP0138 FEASIBILITY OF PROGRESSIVE ANTI-TNF TAPERING IN AXIAL SPONDYLOARTHRITIS PATIENTS IN LOW DISEASE ACTIVITY: RESULTS FROM THE MULTICENTER NON-INFERIORITY PROSPECTIVE RANDOMIZED CONTROLLED TRIAL SPACING

C. Lukas[1,2], A. Tournadre[3], M. C. Picot[4], E. Nogué[4], E. Dernis[5], P. Goupille[6,7], B. Combe[2], J. Morel[2]. [1]*University Montpellier, IDESP, Montpellier, France*;

[2]University Hospital Montpellier, Rheumatology, Montpellier, France; [3]University Hospital Clermont-Ferrand, Rheumatology, Clermont-Ferrand, France; [4]University Hospital Montpellier, Clinical research and epidemiology unit (Department of Medical Information), Montpellier, France; [5]Hospital Le Mans, Rheumatology, Le Mans, France; [6]University Hospital of Tours, Department of Rheumatology and CIC INSERM 1415,Tours, France; [7]University of Tours, EA 7501, GICC,Tours, France

Background: Anti-TNF treatments (TNFi) have shown high efficacy in axial spondyloarthritis (ax-SpA) with inadequate response to non-steroidal anti-inflammatory drugs (NSAIDs). However their effect remains predominantly symptomatic, and their long-term tolerance as well as significant societal cost justify investigation about a potential reduction in drug dosage, or –most feasible and comfortable for the patient– increase in intervals between doses.
Objectives: To assess if a progressive and monitored reduction of administered TNFi by increase of intervals between injections results in a comparable proportion of patients remaining after 12 months (m) in low disease activity state despite a decreased cumulative treatment dose received.
Methods: Non-inferiority randomized controlled trial, having included adult patients with ax-SpA fulfilling ASAS criteria, already treated by anti-TNF, and in stable low disease activity for at least 6 m (current and at least 6 m old BASDAI<4/10), who were randomized into 2 groups: either keeping on their usual treatment with stable doses ("unchanged" group), or progressive spacing of injections of their treatment ("spacing" group). Follow-up was done every 3 m during 12 m, with regular monitoring of disease activity and, in patients from the group "spacing", modification of the rhythm of injections according to disease activity and predefined standardized protocol (either increase or decrease (step-back) of intervals between injections). The primary endpoint was the difference of proportions of patients having a low disease activity state (BASDAI<4/10) after 12 m of follow-up between the 2 groups. It was estimated on the ITT population after multiple imputation. The 90% confidence interval associated was calculated using the Farrington-Manning method and the lower bound was compared to the non-inferiority margin of -20%. With an expected proportion of 85% patients remaining in low disease activity in the unchanged group, and α and β risks at respectively 5% and 90%, the required number of patients was calculated at 358, and thus 398 had to be included with a 10% expected proportion of patients with unavailable data.
Results: 398 patients were randomized in 23 French rheumatology units (197 and 201 in the spacing and unchanged groups respectively), and 389 included in analyses (9 did not receive the allocated treatment). Mean (SD) age was 44.3 (12.4) years, 71.2% were males. Mean (SD) BASDAI at inclusion was 1.45 (1.02). TNFi used were etanercept (35.7%), adalimumab (33.9%), infliximab (20.6%), golimumab (9.3%) and certolizumab (0.5%). For the 373 patients with complete follow-up (93.7%), 162/184 (88.0%) had a low disease activity in the "spacing" group vs. 173/189 (91.5%) in the "unchanged" group at 12 m. After multiple imputation for the 16 patients with missing data, the difference of proportion between the two groups was estimated to -4.18% [CI90% -10.0; 1.7], thus confirming the non-inferiority of the "spacing" procedure. In the "spacing" group at 12 m, 134/162 (82.7%) patients in low disease activity were still receiving a lowered TNFi dose.
Conclusion: In ax-SpA patients with BASDAI<4 for at least 6 months under TNFi, it is possible to increase intervals between injections while maintaining a low disease activity by adjusting treatment with quarterly monitoring of SpA activity.
Disclosure of Interests: Cédric Lukas Speakers bureau: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Consultant of: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Grant/research support from: Pfizer, Novartis and Roche-Chugai, Anne Tournadre Speakers bureau: Abbvie, Fresenius, Janssen, MSD, Pfizer, Roche Chugai, Sanofi, Paid instructor for: Fresenius, Consultant of: Abbvie, Fresenius, Lilly, Novartis, Sanofi, Grant/research support from: Fresenius, Novartis, Pfizer, UCB, Marie Christine Picot: None declared, Erika Nogué: None declared, Emmanuelle Dernis Speakers bureau: Roche chugai, UCB, BMS, Novartis, Lilly, Mylan, Pfizer, Celgène, Consultant of: UCB, MSD, BMS, Lilly, Novartis, Philippe Goupille Speakers bureau: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Consultant of: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Grant/research support from: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Bernard Combe Speakers bureau: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Consultant of: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Novartis, Pfizer, and Roche-Chugai, Jacques Morel Speakers bureau: Abbvie, Biogen, BMS, Fresenius Kabi, Lilly, Mylan, Novartis, Pfizer, Sanofi, Consultant of: Abbvie, BMS, Boerhinger Ingelheim, Galpaagos, GSK, Lilly, Novartis, Sanofi
DOI: 10.1136/annrheumdis-2021-eular.1354

OP0139

A TIME-SHIFTED EFFECT OF TUMOR NECROSIS FACTOR INHIBITORS ON RADIOGRAPHIC SPINAL PROGRESSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: LONG-TERM RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

D. Poddubnyy[1,2], V. Rios Rodriguez[1], M. Torgutalp[1], A. Dilbaryan[1], M. Verba[1], F. Proft[1], M. Protopopov[1], J. Rademacher[1], H. Haibel[1], J. Sieper[1], M. Rudwaleit[3]. [1]Charité – Universitätsmedizin Berlin, Division of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany; [2]Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), ein Institut der Leibniz-Gemeinschaft, Epidemiology Unit, Berlin, Germany; [3]Klinikum Bielefeld Rosenhöhe, Department of Internal Medicine and Rheumatology, Bielefeld, Germany

Background: There are inconclusive data on the effect of tumor necrosis factor inhibitors (TNFi) on radiographic spinal progression in axial spondyloarthritis (axSpA). Although inflammation and new bone formation are linked in axSpA, TNFi failed to show inhibition of radiographic spinal progression over two years compared to historical cohorts in pivotal studies in radiographic axSpA. Subsequent observational studies suggested that a longer treatment duration, earlier treatment initiation and effective inflammation suppression might be required to achieve inhibition of radiographic progression.
Objectives: The aim of the current study was to evaluate the effect of TNFi on radiographic spinal progression in patients with early axSpA in a long-term inception cohort.
Methods: A total of 266 patients with early axSpA (with r-axSpA with symptom duration ≤10 years and nr-axSpA with symptom duration ≤5 years) from the German Spondyloarthritis Inception Cohort (GESPIC) with at least two sets of spinal radiographs obtained at least 2 years apart during a 10-year follow-up were included. These patients contributed with a total of 542 2-year radiographic intervals. Spinal radiographs were evaluated by three trained and calibrated readers according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The final mSASSS was calculated as a mean of three reader scores. The association between the current TNFi, previous TNFi and radiographic spinal progression defined as the absolute mSASSS change score over 2 years was analyzed using longitudinal generalized estimating equations (GEE) analysis.
Results: Only 9 patients were treated with a tumor necrosis factor inhibitor (TNFi) at baseline, and a total of 77 patients received TNFi during the entire follow-up period that gave 103 2-year intervals covered by TNFi of any duration, and 78 intervals covered by TNFi with treatment duration of at least 12 months. Radiographic spinal progression in axSpA patients receiving TNFi in the current 2-year interval was not different from progression in patients not treated with TNFi, while TNFi in the previous 2-year interval was associated with lower progression compared to patients without TNFi in this interval (Figure 1). The latter was also evident for patients who received TNFi in both previous and current 2-year intervals, i.e. patients treated with TNFi over 4 years. The longitudinal GEE analysis confirmed no significant association between current TNFi treatment and radiographic spinal progression but a significant association between TNFi in the previous 2-year interval (especially if this was continued also in the current interval giving 4 years in total) and the progression in the current one (Table 1).

Table 1. The association between the change of the mSASSS over two years and current and/or previous treatment with TNFi in the longitudinal generalized estimation equation analysis.

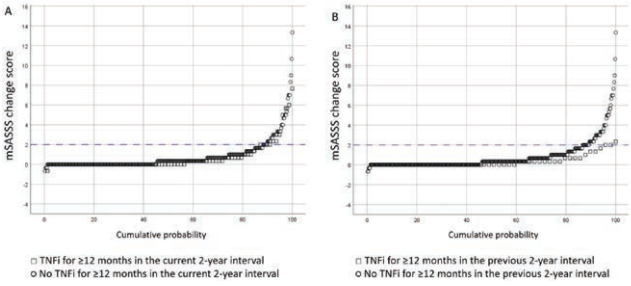
TNFi treatment definition			
TNFi for ≥12 months in the previous 2-year interval	TNFi for ≥12 months in the current 2-year interval	Reference	β* (95% CI)
	Yes	No TNFi for ≥12 months in the current 2-year interval	-0.19 (-0.56 to 0.18)
Yes		No TNFi for ≥12 months in the previous 2-year interval	**-0.56 (-0.95 to -0.17)**
Yes	Yes	No TNFi for ≥12 months in the current and previous 2-year intervals	**-0.59 (-1.03 to -0.15)**

*Parameter estimates from the multivariable models adjusted for sex, symptom duration at the beginning of the current 2-year interval, time-averaged ASDAS in the current 2-year interval, smoking in the current 2-year interval, classification as non-radiographic or radiographic axSpA, and mSASSS at the beginning of the current 2-year interval.

Conclusion: TNFi treatment exhibits a time-shifted inhibitory effect on radiographic spinal progression in axSpA that becomes evident only in the second 2-year interval after treatment initiation.

Acknowledgements: GESPIC was initially supported by the BMBF. As consequence of the funding reduction by BMBF according to schedule in 2005 and stopped in 2007, complementary financial support has been obtained also from Abbott, Amgen, Centocor, Schering–Plough, and Wyeth. Starting from 2010, the core GESPIC cohort was supported by AbbVie.

Figure 1. Cumulative probability plots depicting mSASSS change scores over 2 years in patients with axial spondyloarthritis treated vs. not treated with TNFi in the current (A) or previous (B) 2-year interval.



Disclosure of Interests: Denis Poddubnyy Speakers bureau: AbbVie, Bristol-Myers Squibb, Lilly, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Biocad, Gilead, GlaxoSmithKline, Eli Lilly, MSD, Novartis, Pfizer, Samsung Bioepis, and UCB, Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Valeria Rios Rodriguez: None declared, Murat Torgutalp: None declared, Ani Dilbaryan: None declared, Maryna Verba: None declared, Fabian Proft: None declared, Mikhail Protopopov: None declared, Judith Rademacher: None declared, Hildrun Haibel: None declared, Joachim Sieper: None declared, Martin Rudwaleit Consultant of: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma

DOI: 10.1136/annrheumdis-2021-eular.1726

OP0140

BIOLOGIC REFRACTORY DISEASE IN AXIAL SPONDYLOARTHRITIS - DEFINITION, PREVALENCE AND PATIENT CHARACTERISTICS. A COLLABORATION BETWEEN FIVE NORDIC BIOLOGIC REGISTRIES

D. DI Giuseppe[1], U. Lindström[2], K. Aaltonen[3], H. Relas[4], S. Aarrestad Provan[5], B. Gudbjornsson[6], M. L. Hetland[7], J. Askling[8], T. Schjødt Jørgensen[9], L. Dreyer[10], D. Nordström[11], B. Michelsen[12], A. J. Geirsson[13], L. T. H. Jacobsson[14], B. Glintborg[7]. *[1]Karolinska Institutet, Clinical Epidemiology Division, Department of Medicine Solna, Stockholm, Sweden*; *[2]Sahlgrenska Academy at University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; *[3]Ministry of Social Affairs and Health, Pharmaceuticals Pricing Board, Helsinki, Finland*; *[4]Helsinki University Hospital (ROB-FIN), Departments of Medicine and Rheumatology, Helsinki, Finland*; *[5]Diakonhemmet Hospital, Department of rheumatology, Oslo, Norway*; *[6]Landspitali University Hospital, and Faculty of Medicine, University of Iceland, Centre for Rheumatology Research (ICEBIO), Reykjavik, Iceland*; *[7]Center for Rheumatology and Spine Diseases, Centre of Head and Orthopedics, Rigshospitalet, DANBIO and Copenhagen Center for Arthritis Research (COPECARE), Glostrup, Denmark*; *[8]Karolinska Institutet, Clinical Epidemiology Division, Dept of Medicine Solna, Stockholm, Sweden*; *[9]The Parker Institute, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Department of Rheumatology, Copenhagen, Denmark*; *[10]Aalborg University Hospital, Department of Rheumatology, Aalborg, Denmark*; *[11]Helsinki University and Helsinki University Hospital, Department of Medicine and Rheumatology, Helsinki, Finland*; *[12]Sørlandet Sykehus, Kristiansand, Norway, Division of Rheumatology, Department of Medicine, Kristiansand, Norway*; *[13]Reykjavik University Hospital, Department of Rheumatolgy, Reykjavik, Iceland*; *[14]Sahlgrenska Academy at University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*

Background: In clinical practice, some patients with axial spondyloarthritis (axSpA) fail several consecutive biological treatments (bDMARDs). How this group of "refractory" patients should best be defined, how common they are, and what their characteristics are, is poorly understood.

Objectives: To explore the point prevalence of bDMARD refractory disease in axSpA over time, according to different definitions, and to describe the characteristics of refractory vs. not-refractory patients upon start of their first bDMARD.

Methods: Observational prospective cohort study. Patients with axSpA (ankylosing spondylitis/non-radiographic axial SpA) starting a first bDMARD 2009-2018 were identified in biologic registries in Denmark, Sweden, Finland, Norway and Iceland. Clinical characteristics and treatments were retrieved, and data were pooled for analysis.

Refractory disease was defined based on the number of different bDMARD treatments started in individual patients: mild (≥3 bDMARDs), moderate (≥4), and strict (5 or more). Restart of same bDMARD with another bDMARD in between counted as separate courses whereas switch from originator to corresponding biosimilar was ignored.

Proportions of patients fulfilling each definition of refractory disease at 2 and 5 years after the start of 1st bDMARD were calculated.

Point-prevalence per calendar-year was calculated as the number of patients with refractory disease at the end of each year, divided by the total number of patients ever having starting a first bDMARD before that time-point, and who were still alive and resident in the country.

Results: The point prevalence of refractory axSpA increased with calendar-time (Figure). Among 12,037 included axSpA patients (64% male), the point-prevalence of bDMARD refractory disease in 2018 was 16%/7%/3% according to mild/moderate/strict definitions (Table).

Table 1. Biologic refractory axSpA according to three definitions

		Refractory definition		
	Overall cohort	MILD	MODERATE	STRICT
A. Baseline characteristics upon start 1st bDMARD				
N	12037	1969	832	351
Age, years	42 (13)	41 (12)	41 (12)	41 (12)
Male, %	64%	57%	54%	56%
Disease duration, years	7 (10)	6 (9)	6 (8)	5 (8)
BASDAI, 0-100	53 (28)	60 (29)	63 (27)	66 (35)
ASDAS	3.3 (1.1)	3.5 (1.2)	3.6 (1.0)	3.7 (1.1)
CRP, mg/L	16 (23)	18 (26)	21 (28)	23 (32)
Patient global, VAS, 0-100	59 (25)	65 (22)	66 (22)	67 (23)
Patient Pain, VAS, 0-100	57 (24)	62 (22)	63 (22)	63 (22)
Fatigue, VAS, 0-100	59 (27)	66 (26)	66 (26)	68 (25)
B. Proportions of patients having refractory disease 2 and 5 years after start of their first bDMARD				
2 years, %		5%	1%	0%
5 years, %		13%	4%	1%

Numbers are means (SD) unless otherwise stated

Upon start of their 1st bDMARD, patients later fulfilling the definitions for refractory axSpA were more frequently women, had shorter disease duration, higher C-reactive protein and higher patient reported outcomes.

Overall, 5%/1%/0% had mild/moderate/strict refractory disease 2 years after start of first bDMARD, after 5 years it was 13%/4%/1% (Table).

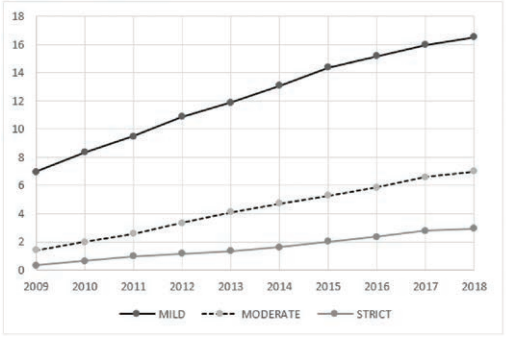
Conclusion: In this large Nordic observational cohort of axSpA patients treated in routine care, we could demonstrate that a substantial proportion of all patients had used multiple bDMARDs. In 2018, one in six patients had received ≥3 bDMARDs, indicating a bDMARD refractory disease. Multiple switching was more frequent during later years, probably due to more bDMARDs becoming available. The characteristics of refractory axSpA, including sex and disease activity, will have to be further explored, as will the impact of refractory disease on long-term outcomes.

Acknowledgements: the DANBIO, SRQ, ICEBIO, ROB-FIN and NOR-DMARD registries.

Partly sponsored by Nordforsk and Foreum.

Figure. Point prevalence of bDMARD refractory disease in AxSpA per calendar year according to three different definitions (mild ≥3 bDMARDs, moderate ≥4, strict ≥5)

X-axis: year, Y-axis: percentage



Disclosure of Interests: Daniela Di Giuseppe: None declared, Ulf Lindström: None declared, Kalle Aaltonen: None declared, Heikki Relas Speakers bureau: Abbvie, Celgene, MSD, Roche, Sella Aarrestad Provan: None declared, Björn Gudbjornsson Speakers bureau: Amgen and Novartis, Merete

L. Hetland Grant/research support from: AbbVie, Biogen, BMS, Celtrion, Eli Lilly Denmark A/S, Janssen Biologics B.V, Lundbeck Fonden, MSD, Pfizer, Roche, Samsung Biopis, Sandoz. MLH chairs the steering committee of the Danish Rheumatology Quality Registry (DANBIO), which receives public funding from the hospital owners and funding from pharmaceutical companies. MLH co-chairs the EuroSpA research collaboration, which generates real-world evidence of treatment of psoriatic arthritis and axial spondyloarthritis based on secondary use of quality data and is partly funded by Novartis., Johan Askling: None declared, Tanja Schjødt Jørgensen: None declared, Lene Dreyer Speakers bureau: Eli-Lilly and Galderma, Grant/research support from: BMS, Dan Nordström: None declared, Brigitte Michelsen: None declared, Arni Jon Geirsson: None declared, Lennart T.H. Jacobsson: None declared, Bente Glintborg Grant/research support from: Abbvie, BMS, Pfizer, Lundbeck foundation

DOI: 10.1136/annrheumdis-2021-eular.630

OP0141

EFFECTS OF FILGOTINIB ON SPINAL LESIONS IN ANKYLOSING SPONDYLITIS: MAGNETIC RESONANCE IMAGING DATA FROM THE TORTUGA TRIAL

X. Baraliakos[1], M. Østergaard[2], R. B. M. Landewé[3], W. Barchuk[4], K. Liu[5], C. Tasset[6], L. Gilles[7], T. Hendrikx[8], R. Besuyen[9], W. P. Maksymowych[10]. [1]*Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*; [2]*University of Copenhagen, Copenhagen Center for Arthritis Research, Rigshospitalet, Copenhagen, Denmark*; [3]*Maastricht University Medical Center, Department of Rheumatology, Maastricht, Netherlands*; [4]*Gilead Sciences, Inc., Inflammation Clinical Research, Foster City, United States of America*; [5]*Gilead Sciences, Inc., Biostatistics, Foster City, United States of America*; [6]*Galapagos NV, Late Stage Development, Mechelen, Belgium*; [7]*Galapagos NV, Clinical Research, Mechelen, Belgium*; [8]*Galapagos BV, Medical Affairs, Leiden, Netherlands*; [9]*Galapagos BV, Clinical Research, Leiden, Netherlands*; [10]*University of Alberta, Department of Medicine, Division of Rheumatology, Edmonton, Canada*

Background: The oral Janus kinase 1 preferential inhibitor filgotinib (FIL) significantly improved Spondyloarthritis Research Consortium of Canada (SPARCC) magnetic resonance imaging (MRI) inflammation scores (bone marrow oedema) in the spine and sacroiliac joints vs placebo (PBO) in the Phase 2 TORTUGA trial (NCT03117270) in patients with active ankylosing spondylitis (AS).[1]

Objectives: This post-hoc analysis evaluated the effects of FIL on Canada-Denmark (CANDEN) MRI measures of spinal inflammation and structural lesions in patients from the TORTUGA trial.

Methods: TORTUGA was a PBO-controlled, multicentre, double-blind, randomised trial. Patients with active AS (as per modified New York classification criteria, with sacroiliitis confirmed by central reading) were treated with FIL 200 mg (n=58) or PBO (n=58) once daily for 12 weeks. MRI of the total spine was conducted at baseline and at treatment end. Scans were re-evaluated post-hoc by 2 independent experts (blinded to time point and assigned treatment) using the CANDEN method;[2] inter-reader discrepancies were resolved by an independent adjudicator. Observed changes from baseline were evaluated using analysis of covariance, with factors for treatment, baseline value, and randomisation stratification by prior tumour necrosis factor inhibitor use. Least-squares (LS) mean changes from baseline and between-group differences with 95% confidence intervals (CI) were calculated; P values are nominal.

Results: MRI scans from 88 patients (47 FIL, 41 PBO) with an evaluable scan at baseline and Week 12 (or early termination) were re-evaluated. Baseline characteristics were generally similar between patients with/without an MRI scan. Of those with MRI scans, mean total spine inflammation score (which ranges from 0–614) was higher, and mean ankylosis score (which ranges from 0–460) was lower, in the FIL vs PBO group at baseline. Total spine inflammation scores decreased from baseline with FIL but not with PBO (Figure and Table; P=0.0003 for between-group difference). Cumulative probability plots favoured FIL over PBO for change from baseline in subregion inflammation scores, including posterolateral elements (i.e. sum of lesions in ribs, transverse processes, spinous processes, soft tissue inflammation, and postero-lateral vertebral body), facet joint, and vertebral body. Total spine fat lesion scores numerically increased from baseline in the FIL but not PBO group (P=0.0878 for between-group difference; Table). There were no significant differences between groups for changes in erosion (P=0.1956) or ankylosis (P=0.3888) scores (Table).

Table 1. Change from baseline at Week 12 in CANDEN total spine inflammation, total spine fat, total spine bone erosion, and ankylosis scores

	Treatment group	n	Sample mean (SE)	LS mean (SE)	95% CI of treatment mean	LS mean of group difference (SE)	95% CI of group difference	Between-group P value
Total spine inflammation score	Filgotinib	47	–4.98 (0.96)	–4.40 (1.13)	–6.65, –2.15	–4.49 (1.21)	–6.85, –2.12	0.0003
	Placebo	41	0.29 (0.78)	0.09 (1.13)	–2.17, 2.34			
Total spine fat score	Filgotinib	47	1.01 (0.62)	1.09 (0.66)	–0.22, 2.40	1.18 (0.69)	–0.18, 2.55	0.0878
	Placebo	41	–0.25 (0.19)	–0.09 (0.66)	–1.40, 1.21			
Total spine bone erosion score	Filgotinib	47	0.01 (0.02)	0.07 (0.03)	0.00, 0.14	0.05 (0.04)	–0.02, 0.12	0.1956
	Placebo	41	–0.02 (0.03)	0.02 (0.03)	–0.04, 0.09			
Total ankylosis score	Filgotinib	47	0.30 (0.29)	0.23 (0.31)	–0.40, 0.85	0.28 (0.34)	–0.37, 0.94	0.3888
	Placebo	41	–0.01 (0.08)	–0.06 (0.31)	–0.68, 0.56			

SE, standard error

Conclusion: This is the first PBO-controlled trial to demonstrate a decrease in inflammatory activity with FIL, not only in the spinal vertebrae but also in the postero-lateral elements of the spine and facet joints. As expected in a 12-week study period, no changes in erosion or ankylosis were seen, while fat lesions showed a tendency to increase with FIL. Larger trials are needed to confirm these results.

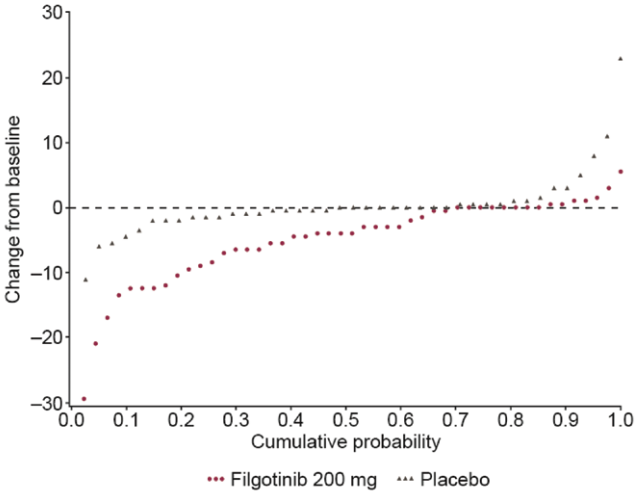
REFERENCES:

[1] van der Heijde D, et al. *Lancet* 2018;392:2378–87.

[2] Krabbe S, et al. *RMD Open* 2019;5:e001057.

Acknowledgements: The TORTUGA trial was sponsored by Galapagos NV (Mechelen, Belgium) and co-funded by Galapagos NV and Gilead Sciences, Inc. (Foster City, CA, USA). Medical writing support was provided by Debbie Sherwood BSc, CMPP (Aspire Scientific Ltd, Bollington, UK), and funded by Galapagos NV.

Figure. Change from baseline in total CANDEN spine inflammation score



CANDEN, Canada-Denmark

Disclosure of Interests: Xenofon Baraliakos Consultant of: AbbVie, Bristol Myers Squibb, Celgene, Chugai, Eli Lilly, Galapagos, Hexal, Janssen, MSD, Novartis, Pfizer, Sandoz and UCB, Grant/research support from: AbbVie, Celgene, Novartis and UCB, Mikkel Østergaard Speakers bureau: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Orion, Pfizer, Roche, Sandoz, Sanofi and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Merck and Novartis, Robert B.M.

Landewé Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering and UCB, Consultant of: AbbVie, Ablynx, Amgen, AstraZeneca, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Novo Nordisk, Pfizer, Roche, Schering, TiGenix and UCB, Grant/research support from: AbbVie, Amgen, Janssen (formerly Centocor), Novartis, Pfizer, Roche, Schering and UCB, Employee of: Director of Rheumatology Consultancy BV, William Barchuk Shareholder of: Gilead Sciences, Inc., Employee of: Currently employee of Gilead Sciences, Inc.; and former employee of AbbVie, Eli Lilly and Johnson & Johnson, Ke Liu Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Chantal Tasset Shareholder of: Galapagos, Employee of: Galapagos, Leen Gilles Employee of: Galapagos, Thijs Hendrikx Shareholder of: Galapagos, Employee of: Galapagos, Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, Walter P Maksymowych Speakers bureau: AbbVie, Janssen, Novartis, Pfizer and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Novartis, Pfizer and UCB, Employee of: Chief Medical Officer of CARE Arthritis Limited

DOI: 10.1136/annrheumdis-2021-eular.1797

OP0142

NETAKIMAB REDUCES ANKYLOSING SPONDYLITIS ACTIVITY IN PATIENTS WITH OR WITHOUT SACROILIITS ON MRI: RESULTS OF SUBANALYSIS OF PHASE 3 ASTERA TRIAL

I. Gaydukova[1,2], V. Mazurov[1], S. Erdes[3], T. Dubinina[4], A. Kundzer[5], N. Soroka[6], A. Eremeeva[7]. *[1]Mechnikov North-Western State Medical University, Department of Therapy and Rheumatology of Temporary Disability and Medical Care Quality Expertise, St-Petersburg, Russian Federation*; *[2]Clinical Rheumatology Hospital No 25, Consultative Outpatient Department, St-Petersburg, Russian Federation*; *[3]Nasonova Research Institute of Rheumatology, Laboratory of Spondyloarthritides, Moscow, Russian Federation*; *[4]Nasonova Research Institute of Rheumatology, Laboratory of Medical and Social Problems of Rheumatology, Moscow, Russian Federation*; *[5]Belarusian Medical Academy of Postgraduate Education, Department of Cardiology and Rheumatology, Minsk, Belarus*; *[6]Belarusian State Medical University, Department of Internal Diseases №2, Minsk, Belarus*; *[7]JSC BIOCAD, Clinical Development Department, St-Petersburg, Russian Federation*

Background: The presence of sacroiliitis in patients (pts) with ankylosing spondylitis (AS) on imaging can be established both by sacroiliac joint (SIJ) X-ray or MRI. Active sacroiliitis on MRI as defined by ASAS is predictor of good treatment response to biological disease modifying anti-rheumatic drugs [1, 2]. Netakimab (NTK) is a humanized anti-interleukin-17A antibody approved for the treatment of AS, psoriatic arthritis, moderate-to-severe plaque psoriasis in Russia and Belarus. The difference in treatment response to NTK in AS pts with and without active sacroiliitis on MRI (MRI+/MRI–) is unclear.

Objectives: To report the changes in AS activity in pts with and without sacroiliitis on MRI at week 16 of NTK treatment.

Methods: ASTERA (NCT03447704) is an ongoing phase 3 placebo (PBO)-controlled clinical study, aimed at evaluating NTK efficacy in AS. All pts fulfilled modified New York criteria. Evaluation of acute inflammation on SIJ MRI was performed at the baseline but was not an inclusion criterion. This analysis includes pts received subcutaneous NTK 120 mg every 2 wks with available baseline SIJ MRI. The presence of sacroiliitis on MRI was defined as SPARCC>2. Efficacy endpoints included ASAS20/40, ASAS partial remission (PR), changes from baseline in BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), ASDAS-CRP (Ankylosing Spondylitis Disease Activity Score).

Results: 67 MRI+ and 46 MRI– pts were included into analysis. Baseline characteristics were balanced across both arms. 42.4% of MRI+ pts and 38.3% of MRI– pts achieved ASAS40 at week 16 ($p \geq 0.05$), ASAS20 was observed in 65.2%/55.3% pts in the same arms respectively ($p \geq 0.05$). ASAS PR was reported for 15.2% MRI+ and 17.0% MRI– pts ($p \geq 0.05$). Improvements in BASDAI and ASDAS-CRP were similar across both arms. At wk 16, mean change from baseline in BASDAI was –2.7 vs –3.0 for MRI+ and MRI– pts respectively, mean change in ASDAS-CRP was –1.7 vs –1.4 in the same arms ($p \geq 0.05$ for all), (figure 1).

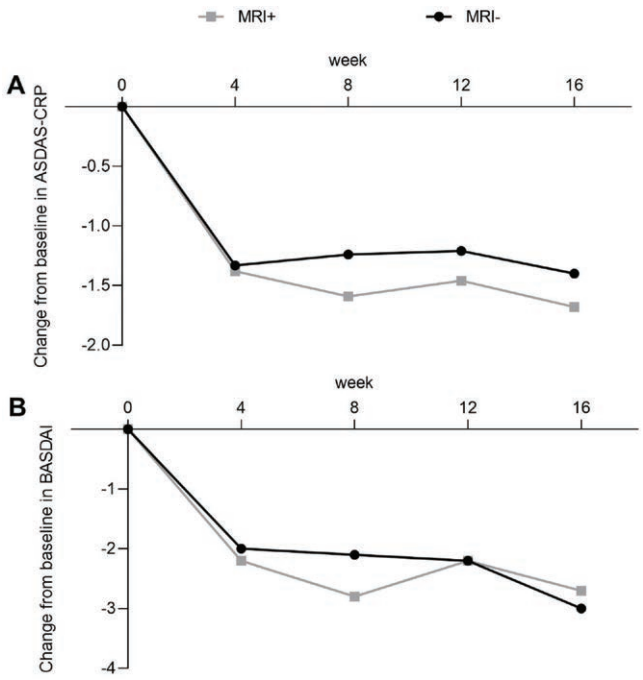


Figure 1. Clinical improvements in AS disease activity. Mean change from baseline is shown for (A) ASDAS-CRP, and (B) BASDAI

Conclusion: NTK leads to decline of disease activity in AS pts irrespectively of sacroiliitis on MRI.

REFERENCES:

[1] Rudwaleit M, et al. MRI in predicting a major clinical response to anti-tumour necrosis factor treatment in ankylosing spondylitis. Ann Rheum Dis. 2008;67(9):1276-81.

[2] Sieper J, et al. A randomized, double-blind, placebo-controlled, sixteen-week study of subcutaneous golimumab in patients with active nonradiographic axial spondyloarthritis. Arthritis Rheumatol. 2015;67(10):2702-12.

Acknowledgements: This study was sponsored by JSC BIOCAD.

Disclosure of Interests: Inna Gaydukova Speakers bureau: Abbvie, Biocad, Eli Lilly, MSD, Novartis, Pfizer, Sandoz, V Mazurov: None declared, Shandor Erdes: None declared, Tatiana Dubinina: None declared, Alena Kundzer: None declared, Nikolaj Soroka: None declared, Anna Eremeeva Employee of: Biocad

DOI: 10.1136/annrheumdis-2021-eular.2187

OP0143

IMPACT OF ADALIMUMAB VERSUS NON-BIOLOGIC THERAPY ON DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES IN ANKYLOSING SPONDYLITIS OVER 24 MONTHS – RESULTS OF THE COMPLETE-AS CANADIAN OBSERVATIONAL STUDY

L. Bessette[1], A. Chow[2], V. Pavlova[3], M. C. Laliberté[4], M. Khraishi[5]. *[1]Laval University, Centre Hospitalier de l'Université Laval, Laval University, Centre Hospitalier de l'Université Laval, Quebec City, Canada*; *[2]University of Toronto, University of Toronto, Toronto, Canada*; *[3]McMaster University, McMaster University, Hamilton, Canada*; *[4]AbbVie Corporation, AbbVie Corporation, Montreal, Canada*; *[5]Memorial University of Newfoundland, Memorial University of Newfoundland, St. John's, Canada*

Background: COMPLETE-AS was an observational study among Canadian biologic-naïve adults with active ankylosing spondylitis (AS) treated with either adalimumab or subsequent non-biologic disease-modifying anti-rheumatic drugs and/or non-steroidal anti-inflammatory drugs (nbDMARD/NSAID) after having switched from initial treatment with a preceding nbDMARD and/or NSAID due to lack of response or intolerance, as per treating physician judgement.

Objectives: To assess the impact of adalimumab on disease activity and patient-reported outcomes among adalimumab- vs. nbDMARD/NSAID-treated patients over 24 months.
Methods: Patients were enrolled between July 2011 and December 2017 and followed for up to 24 months. Treatment was per routine care and all analyses were perfomed using the intent-to-treat (ITT) approach. Between-group differences for change in patient-reported disease activity (BASDAI), morning stiffness (minutes/day), functional limitation (BASFI), quality of life (QoL: SF-12), depression (BDI-II), and work productivity (WLQ) were assessed with repeated measures models for overall treatment effect; baseline-adjusted estimates (least square means [LSM]) for each visit were produced. Achievement of, and time to the following endpoints were assessed: 50% improvement from baseline in BASDAI (BASDAI50); minimum clinically important improvements (MCIIs) in BASDAI ($\Delta \geq 1.1$); BASFI ($\Delta \geq 0.6$); SF-12 physical component score (PCS; $\Delta \geq 4.4$) and mental component score (MCS; $\Delta \geq 3.1$); and low disease activity for BASDAI (<4) and BASFI (<3.8).
Results: A total of 452 adalimumab-treated patients and 187 nbDMARD/NSAID-treated patients were enrolled in the study and included in the analyses. At baseline, mean (SD) BASDAI [6.4 (1.8) vs. 5.0 (1.8); p<0.001] and BASFI [5.5 (2.4) vs. 3.7 (2.4)] were however significantly (p<0.001) higher among adalimumab-treated patients compared to nbDMARD/NSAID-treated patients, respectively. Over 24 months, adalimumab-treated patients had significantly lower overall BASDAI scores compared to nbDMARD/NSAID-treated patients [estimate (95% CI): -0.7 (-1.2, -0.3); p=0.007]. BASFI scores were also significantly lower among adalimumab-treated patients over the course of the study [estimate (95% CI): -0.4 (-0.8, 0.0); p=0.013]. Both groups had statistically comparable outcomes for morning stiffness, BDI-II, WLQ, and SF-12.
Adalimumab-treated patients were also at significantly higher odds of achieving therapeutic response thresholds, including BASDAI50 [OR (95% CI): 1.7 (1.2-2.3)], BASDAI<4 [1.8 (1.2-2.7)], MCII for BASDAI [1.9 (13.-2.9)], and MCII for BASFI [1.6 (1.1-1.2)]. Time to achievement of each threshold was significantly shorter among adalimumab-treated patients for BASDAI50 [HR (95% CI): 1.8 (1.1-2.8)], BASDAI<4 [1.7 (1.6-3.6)], and MCII for BASDAI [1.5 (1.0-2.3)]. Time to achievement of MCII for BASFI was not statistically different between groups; for BASFI<3.8 and MCII for both SF-12 PCS and MCS, both odds of, and time to achievement, were also statistically comparable.
At month 24, baseline-adjusted BASDAI and BASFI was comparable (p>0.05): LSM (95%CI) 3.5 (3.3, 3.8) vs. 3.6 (3.2-4.0), and 2.9 (2.6-3.1) vs. 3.3 (2.9-3.7), respectively, for adalimumab-treated vs. nbDMARD/NSAID-treated patients.
Conclusion: Among Canadian patients with active AS, adalimumab-treated patients reported a greater overall reduction in disease burden related to both self-reported disease activity and functional capacity compared to nbDMARD/NSAID-treated patients, along with higher odds and shorter time to achieving therapeutic response thresholds. Despite the overall beneficial effects observed with adalimumab, residual disease burden, however, is observed for Canadian AS patients even after 24 months of treatment.
Acknowledgements: The authors wish to acknowledge JSS Medical Research for their contribution to the statistical analysis, medical writing, and editorial support during the preparation of this abstract. AbbVie provided funding to JSS Medical Research for this work.
Disclosure of Interests: Louis Bessette Speakers bureau: Speaker for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Gilead, Sandoz, Fresenius Kabi, Consultant of: Consultant for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, Gilead, Sandoz, Samsung Bioepis, Fresenius Kabi, Grant/research support from: Investigator for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Gilead, Andrew Chow Speakers bureau: Speaker for AbbVie, BMS, Janssen, Pfizer, Consultant of: Consultant for AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Grant/research support from: Investigator for AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Viktoria Pavlova Speakers bureau: Speaker for Amgen, Abbvie, BMS, Jenssen, Lilly, Merk, Novartis, Roche, UCB, and Pfizer, Consultant of: Consultant for Amgen, Abbvie, BMS, Jenssen, Lilly, Merk, Novartis, Roche, UCB, and Pfizer, Grant/research support from: Investigator for Janssen, UCB, Abbvie, and Pfizer; and received research grants from UCB, Marie-Claude Laliberté Employee of: Employee of AbbVie, Majed Khraishi Speakers bureau: Speaker for AbbVie, Consultant of: Consultant for AbbVie, Grant/research support from: Principal Investigator for AbbVie
DOI: 10.1136/annrheumdis-2021-eular.2608

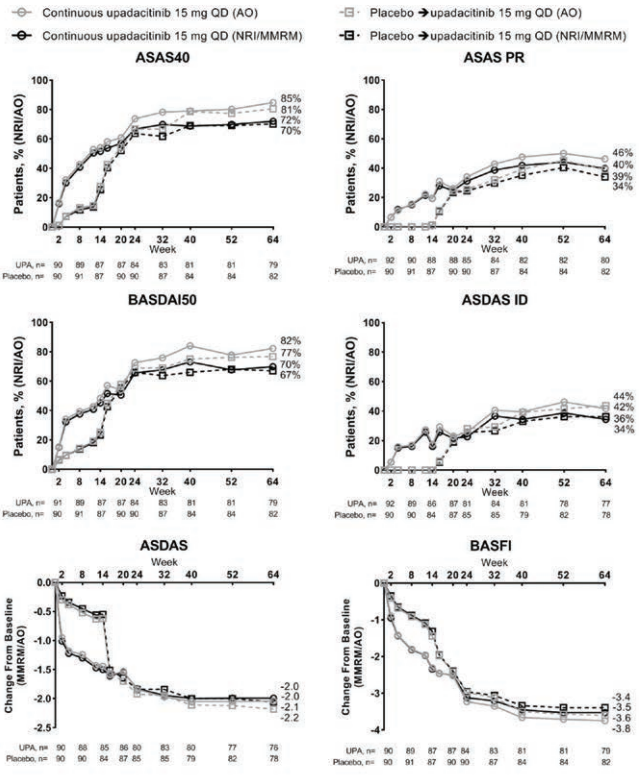
OP0144

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 1-YEAR RESULTS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY WITH OPEN-LABEL EXTENSION

A. Deodhar[1], D. Van der Heijde[2], J. Sieper[3], F. Van den Bosch[4], W. P. Maksymowych[5], T. H. Kim[6], M. Kishimoto[7], A. Ostor[8], B. Combe[9], Y. Sui[10], X. Wang[10], A. Chu[10], I. H. Song[10]. [1]*Oregon Health, Science University, Portland, United States of America*; [2]*Leiden University, Medical Center, Leiden, Netherlands*; [3]*Charité Universitätsmedizin, Medicine, Berlin, Germany*; [4]*Ghent University Hospital, Rheumatology, Ghent, Belgium*; [5]*University of Alberta, Rheumatology, Edmonton, Canada*; [6]*Hanyang University, Hospital for Rheumatic Diseases, Seoul, Korea, Rep. of (South Korea)*; [7]*Kyorin University, School of Medicine, Tokyo, Japan*; [8]*Cabrini Hospital, Monash University & Emeritus Research, Melbourne, Australia*; [9]*CHU Montpellier, Montpellier University, Montpellier, France*; [10]*AbbVie Inc., Rheumatology, North Chicago, United States of America*

Background: Upadacitinib (UPA) was efficacious and well tolerated vs placebo (PBO) during the first 14 weeks (wks) of the phase 2/3 SELECT-AXIS 1 study in patients (pts) with active ankylosing spondylitis (AS) who had an inadequate response to NSAIDs.[1]
Objectives: To report efficacy and safety of UPA through 1 year in the SELECT-AXIS 1 study.
Methods: In SELECT-AXIS 1 (NCT03178487) pts were randomized 1:1 to UPA 15 mg once daily (QD) or PBO; at wk 14, pts continued in the 90-wk open-label extension and received UPA 15 mg QD; reported here are data up to wk 64. The study enrolled pts (≥18 y) with active AS (defined as BASDAI ≥4 and pt assessment of back pain ≥4 [numeric rating scale, 0–10] at screening and baseline [BL]) who had inadequate response to ≥2 NSAIDs or intolerance to or contraindication for NSAIDs and were biologic DMARD naive. Efficacy assessments included percentage of pts with Assessment of SpondyloArthritis international Society (ASAS) 20/40 response, ASAS partial remission, BASDAI50, AS Disease Activity Score (ASDAS) and change from BL in ASDAS and BASFI. Data are reported as observed and by using non-responder imputation (NRI). Treatment-emergent adverse events (TEAEs) were reported as events per 100 patient-years (PY) up to January 31, 2020.
Results: Of 187 pts, 178 pts (each n=89 for UPA and PBO arms) completed wk 14 on study drug and entered the open-label extension; 160 pts completed wk 64. Efficacy was maintained or continued to improve throughout the study in the continuous UPA group: 85% (95% CI, 77%–93%) of pts achieved ASAS40 at wk 64 in the as-observed analysis and 72% (63%–81%) in the NRI analysis (Figure). Pts who switched from PBO to UPA at wk 14 showed similar speed of onset and magnitude of response vs pts

Figure. Efficacy Endpoints Over Time



AO, as observed; ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Scores; ID, inactive disease; MMRM, mixed-effect model repeated measures; NRI, non-responder imputation; PR, partial remission; QD, once daily; UPA, upadacitinib.
Dashed line: all patients randomized to placebo received open-label UPA starting from week 14.
N's below the graphs are for as observed analysis. N's for NRI analysis were 94 for placebo to upadacitinib and 93 for continuous upadacitinib.
160 patients completed week 64; lack of efficacy (n=10) and adverse events (n=4) were the most common reasons for discontinuation between weeks 14 and 64.

initially randomized to UPA: 81% (95% CI, 72%–89%) in the as-observed analysis and 70% (61%–80%) in the NRI analysis achieved ASAS40 at wk 64 (Figure). Similar results were observed for other efficacy endpoints (Figure). Among all 182 pts receiving UPA, 618 AEs were reported. AEs leading to discontinuation and serious AEs were low (Table). No serious infections, active tuberculosis, venous thromboembolic events, gastrointestinal perforation, major adverse cardiovascular events, renal dysfunction, or deaths were reported.

Table 1. TEAEs per 100 PYs

Events/(E/100 PY)	UPA 15 mg QD N=182 (237.6 PY)
Any AE	618 (260.1)
Serious AE	14 (5.9)
AE leading to discontinuation	15 (6.3)
Infections	205 (86.3)
Opportunistic infection*	2 (0.8)
Herpes zoster†	5 (2.1)
Creatine phosphokinase elevation‡	28 (11.8)
Hepatic disorder§	24 (10.1)
Neutropenia‖	7 (2.9)
Anemia‖	3 (1.3)
Lymphopenia‖	2 (0.8)
Malignancy¶	1 (0.4)
Death	0

AE, adverse event; PY, patient-year; QD, once daily; TEAE, treatment-emergent AE; UPA, upadacitinib.*Two non-serious events of esophageal candidiasis in the same patient.†Five events in 4 patients; all non-serious and limited to 1 dermatome.‡All events were non-serious and none led to study drug discontinuation; majority were asymptomatic.§Majority based on asymptomatic alanine aminotransferase/aspartate aminotransferase elevations; all were non-serious and none led to study drug discontinuation.‖All events were non-serious and none led to study drug discontinuation.¶Squamous cell carcinoma of tongue in 61-year-old male former smoker; no reasonable possibility to be study drug related per investigator.

Conclusion: UPA 15 mg QD showed sustained and consistent efficacy over 1 year. Pts who switched from placebo to UPA at wk 14 showed a similar efficacy response compared with pts who received continuous UPA. No new safety findings were observed compared with safety data from the UPA clinical development program in other indications.[2]

REFERENCES:

[1] van der Heijde D, et al. *Lancet*. 2019;394(10214):2108-2117.
[2] Cohen, et al. *Arthritis Rheumatol*. 2019;71(suppl 10).

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing support was provided by M Hovenden and J Matsuura of ICON plc (North Wales, PA) and was funded by AbbVie.

Disclosure of Interests: Atul Deodhar Speakers bureau: Novartis, Pfizer, Consultant of: AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer, UCB, Désirée van der Heijde Consultant of: AbbVie, BMS, Cyxone, Eisai, Galapagos, Gilead, GlaxoSmithKline, Lilly, Novartis, Pfizer, and UCB Pharma, Joachim Sieper Speakers bureau: AbbVie, Janssen, Lilly, Merck, and Novartis, Consultant of: AbbVie, Janssen, Lilly, Merck, and Novartis, Filip van den Bosch Speakers bureau: AbbVie, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB Pharma, Consultant of: AbbVie, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB Pharma, Walter P Maksymowych Consultant of: AbbVie, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Novartis and Pfizer, Tae-Hwan Kim Speakers bureau: AbbVie, Celltrion, Kirin, Lilly, and Novartis, Mitsumasa Kishimoto Consultant of: AbbVie, Amgen-Astellas BioPharma, Asahi-Kasei Pharma, Astellas, Ayumi Pharma, BMS, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Kyowa Kirin, Novartis, Pfizer, Tanabe-Mitsubishi, Teijin Pharma, and UCB Pharma, Andrew Ostor Consultant of: AbbVie, BMS, Roche, Janssen, Lilly, Novartis, Pfizer, UCB, Gilead, and Paradigm, Bernard Combe Speakers bureau: AbbVie, Lilly, Merck, Consultant of: AbbVie, Lilly, Gilead, Janssen, Novartis, Roche-Chugai, and Sanofi, Grant/research support from: AbbVie and Lilly, Yunxia Sui Shareholder of: AbbVie, Employee of: AbbVie, xin wang Shareholder of: AbbVie, Employee of: AbbVie, Alvina Chu Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie, Employee of: AbbVie

DOI: 10.1136/annrheumdis-2021-eular.473

Diagnostics and imaging procedures

OP0145

DIFFERENTIAL DIAGNOSIS OF RA AND PSA USING NEURAL NETWORKS ON THREE-DIMENSIONAL BONE SHAPE OF FINGER JOINTS

L. Folle[1], C. Liu[1], D. Simon[2], T. Meinderink[2], A. M. Liphardt[2], G. Krönke[2], G. Schett[2], A. Maier[1], A. Kleyer[2]. *[1]Friedrich-Alexander-Universität Erlangen-Nürnberg - Pattern Recognition Laboratory, Department of Computer Science, Erlangen, Germany*; *[2]Friedrich-Alexander; University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany*

Background: Early diagnosis and reliable differentiation between rheumatic diseases (RMDs) are crucial to start an adequate therapy and prevent irreversible damage. Since finger joints are commonly affected in rheumatoid arthritis (RA) and psoriatic arthritis (PsA), imaging of the peripheral skeleton is an essential step of diagnosis at a rheumatologist. High resolution peripheral quantitative computed tomography (HR-pQCT) allows an even more detailed and three-dimensional (3D) illustration of the peripheral bone than conventional radiographs. Segmented scans contain further information, such as the density, microstructure, and shape of the bones, which can be further analyzed by neural networks.
Objectives: We hypothesize that, based on the shape of the second metacarpophalangeal (MCP) joint from HR-pQCT images, a neural network can be trained to differentiate between RA, PsA, and healthy controls and to reveal regions in the bone shape characteristic for the diseases.
Methods: HR-pQCT images of MCP joints from patients with classified CCP positive RA, classified PsA, and healthy controls with low motion artifacts and appropriate scan region were selected as reported previously [3]. Scans were performed as part of the clinical routine and patients gave their informed consent to use pseudonymized data (Ethics approval 334_16B). Based on the assumption that pathognomonic changes develop over time, only images were used, where the period between classification and imaging exceeded one year.
Based on previous work [4], a pixel-wise mask of the second metacarpal bone was generated using a neural network based on the HR-pQCT scans of patients. Supervised auto-encoder [1] networks were used to predict the correct class given the bone mask only. For the neural network experiment, the patient scans were split on a patient-level into training (70%), validation (20%), and testing (10%). Guided backpropagation [2] was used as a method to investigate the regions influencing the class prediction most.
Results: In total, images of 331 patients were included in the experiments. The evaluation of the model on the 33 test cases yielded a high accuracy for the healthy control with 94%, RA patients with 84%, and PsA patients with 89%. An area under the receiver operator curve of 91% could be achieved. The regions of the bone mask influencing the network´s decision most are highlighted exemplary in Figure 1.

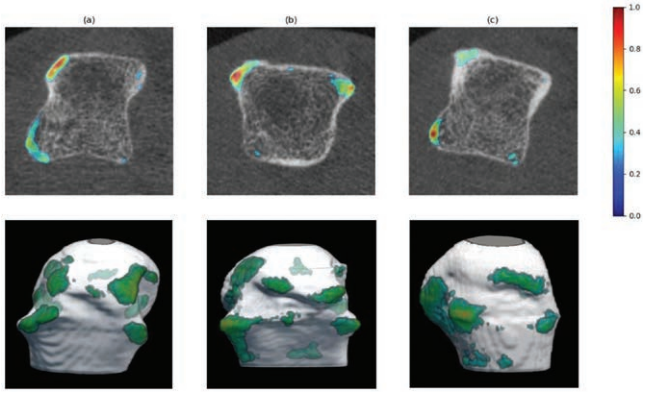


Figure 1. Visualization of the HR-pQCT slices with gradient maps. Higher values (red) represent regions that had a stronger contribution to the classification result. The HR-pQCT images are displayed for reference only. (a) Healthy patient, (b) RA diagnosed patient, and (c) PsA diagnosed patient. The first row shows the single slices with the highest values corresponding to the 3D bone masks in the second row.

Conclusion: For the first time, a neural network-based approach successfully provides a differential diagnosis of RA and PsA based only on the shape of the second MCP in HR-pQCT images. The evaluation of the test set suggests that high curvatures of the bone surface in the joint region significantly influence the prediction of the network, suggesting an in-depth investigation of these regions

for patients affected by RA and PsA. Based on these promising findings, we aim to extend the approach to seronegative RA as well as early RA and PsA.

REFERENCES:

[1] Le, L. et al. (2018). Supervised autoencoders: Improving generalization performance with unsupervised regularizers. In Advances in Neural Information Processing Systems.
[2] Springenberg, J. T. et al. (2015). Striving for simplicity: The all convolutional net. 3rd International Conference on Learning Representations, ICLR 2015 - Workshop Track Proceedings.
[3] Simon, D. et al. (2017). Age- and Sex-Dependent Changes of Intra-articular Cortical and Trabecular Bone Structure and the Effects of Rheumatoid Arthritis. Journal of Bone and Mineral Research, 32(4), 722–730.
[4] Folle, L. et al. (2021). Fully Automatic Bone Mineral Density Measurements using Deep Learning. Manuscript submitted for publication.

Acknowledgements: This work was supported by the emerging field initiative (project 4 Med 05 "MIRACLE") of the University Erlangen-Nürnberg and MASCARA - Molecular Assessment of Signatures Characterizing the Remission of Arthritis grant 01EC1903A.

Disclosure of Interests: Lukas Folle: None declared, Chang Liu: None declared, David Simon Speakers bureau: Lilly, Novartis, Consultant of: Lilly, Novartis, Gilead, BMS, Abbvie, Grant/research support from: Lilly, Novartis, Timo Meinderink: None declared, Anna-Maria Liphardt Consultant of: Mylan/Meda Pharma, Grant/research support from: Novartis, Gerhard Krönke Speakers bureau: Lilly, Novartis, Consultant of: Lilly, Novartis, Gilead, BMS, Abbvie, Grant/research support from: Lilly, Novartis, Georg Schett Speakers bureau: Lilly, Novartis, Consultant of: Lilly, Novartis, Gilead, BMS, Abbvie, Grant/research support from: Lilly, Novartis, Andreas Maier: None declared, Arnd Kleyer Speakers bureau: Lilly, Novartis, Consultant of: Lilly, Novartis, Gilead, BMS, Abbvie, Grant/research support from: Novartis, Lilly

DOI: 10.1136/annrheumdis-2021-eular.383

OP0146 TENOSYNOVITIS, SYNOVIAL HYPERTROPHY AND FEET BURSITIS ARE USEFUL ULTRASOUND BIOMARKERS FOR PREDICTING ARTHRITIS DEVELOPMENT IN A POPULATION AT-RISK FOR RHEUMATOID ARTHRITIS

Y. Kisten[1], A. Circiumaru[1], M. Loberg[1], N. Vivar-Pomiano[1], A. Antovic[2], H. Rezaei[1], E. Af Klint[1], A. Hensvold[1,2], A. Catrina[1,2]. *[1]Karolinska Institute, Department of Medicine, Rheumatology Unit and Early Arthritis Clinic of the Karolinska University Hospital, Stockholm, Sweden*; *[2]Academic Specialist Center, Center for Rheumatology, Stockholm Health Region, Stockholm, Sweden*

Background: Musculoskeletal ultrasound (MSUS) evaluation of individuals at risk for developing rheumatoid arthritis (RA) having Anti-Citrullinated Protein Antibody (ACPA) positivity and musculoskeletal complaints, may play an important role in the very early detection of RA.

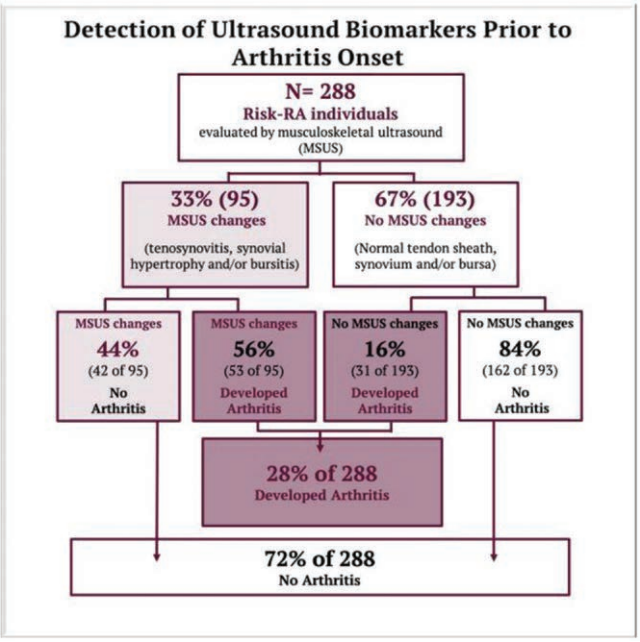
Objectives: We aimed to identify which ultrasound markers could predict arthritis development.

Methods: Individuals with musculoskeletal complaints with a positive anti-CCP2 test were referred to the rheumatology department for a detailed clinical (68 joint count) and MSUS examination of the hands, feet and any symptomatic joints. Only those without clinical and/or MSUS detected arthritis were included in the RISK RA prospective cohort and followed-up over 3 years/ or until arthritis onset. Using EULAR-OMERACT guidelines[1], MSUS markers for synovial hypertrophy (SH) and hyperemia (Doppler activity) were documented for each visit. Finger and wrist tendons were screened for any signs of tenosynovitis (TS), and between metatarsal joints for bursitis. Association of MSUS biomarkers with arthritis development was tested (comparing proportions) using Chi-Squared or Fisher's exact tests.

Results: 288 individuals were included from January 2014 to October 2019 (79% female, 35% RF positive, median age 48 years: IQR: 36-58). Within a median of 38 months (IQR: 1-72) since recruitment, 84 individuals (28%) developed an arthritis diagnosis.

Prior to obtaining any diagnosis (at inclusion and/or follow-up visit), 95 of the 288 individuals (33%) had at least one type of MSUS anatomical modification present (around the tendons, joint synovium and/or within bursal cavities), and 56% (53/95) of these individuals eventually developed arthritis. Of the remaining 193 that did not present with any obvious MSUS changes, 16% progressed towards arthritis development.

The presence of tenosynovitis was detected in 64 of 288 individuals scanned prior to diagnosis and were more frequent in those developing arthritis (44%, 37/84) as compared to those with TS not developing arthritis (13%, 27/204), p<0.0001. The extensor carpi ulnaris wrist tendons were mostly involved. Sonographic changes within the synovium were noted in 11% (32/288) of all individuals, mostly affecting the metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints. There was a higher incidence of synovial hypertrophy detected in those developing arthritis (22%, 18/24), as compared to those that remained arthritis free (7%, 14/204), p<0.0001. The MCP joints with synovial hypertrophy were more prone to arthritis development as compared to the MTP's. Furthermore, we observed a higher frequency of bursitis between the MTP joints in individuals developing arthritis, as compared to individuals having a bursitis who did not develop arthritis (13%, 11/84 versus 7%, 14/204, p=0.009).



Conclusion: Ultrasound biomarkers such as tenosynovitis of the extensor carpi ulnaris, synovial hypertrophy of the MCP joints and feet bursitis have good potential to predict arthritis development in a population at-risk for rheumatoid arthritis.

REFERENCES:

[1] Maria-Antonietta D'Agostino et al. RMD Open 2017;3:e 000428

Acknowledgements: All study participants and patients, including researchers that are part of the multidisciplinary laboratory, clinical and academic teams of the RISK RA study group, as well as all assisting this research in one form or the other are greatly acknowledged.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1676

OP0147 RHEUMATIC? - A DIGITAL DIAGNOSTIC DECISION SUPPORT TOOL FOR INDIVIDUALS SUSPECTING RHEUMATIC DISEASES: A MULTICENTER VALIDATION STUDY

R. Knevel[1], J. Knitza[2,3,4], A. Hensvold[5,6], A. Circiumaru[5,6], T. Bruce[7], S. Evans[8], T. Maarseveen[1], M. Maurits[1], L. Beaart- van de Voorde[1], D. Simon[2,3], A. Kleyer[2,3], M. Johannesson[6], G. Schett[2,3], T. Huizinga[1], S. Svanteson[8], A. Lindfors[7], L. Klareskog[5], A. Catrina[5]. *[1]LUMC, Rheumatology, Leiden, Netherlands*; *[2]Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany*; *[3]FAU Erlangen-Nuremberg and Universitätsklinikum, Deutsches Zentrum fuer Immuntherapie (DZI), Erlangen, Germany*; *[4]Université Grenoble Alpe, AGEIS, Grenoble, France*; *[5]Karolinska Institutet, Karolinska University Hospital, Division of Rheumatology, Department of Medicine, Stockholm, Sweden*; *[6]Academic Specialist Center, Center for Rheumatology, Center for Rheumatology, Stockholm Region, Sweden*; *[7]Ocean Observations, a Design Consultancy, Stockholm, Sweden*; *[8]Elsa Science, A Digital Health Company, Stockholm, Sweden*

Background: Digital diagnostic decision support tools promise to accelerate diagnosis and increase health care efficiency in rheumatology. *Rheumatic?* is an online tool developed by specialists in rheumatology and general medicine together with patients and patient organizations for individuals suspecting a rheumatic disease.[1,2] The tool can be used by people suspicious for rheumatic diseases resulting in individual advise on eventually seeking further health care.

Objectives: We tested *Rheumatic?* for its ability to differentiate symptoms from immune-mediated diseases from other rheumatic and musculoskeletal complaints and disorders in patients visiting rheumatology clinics.

Methods: The performance of *Rheumatic?* was tested using data from 175 patients from three university rheumatology centers covering two different settings: A.Risk-RA phase setting. Here, we tested whether *Rheumatic?* could predict the development of arthritis in 50 at risk-individuals with musculoskeletal complaints and anti-citrullinated protein antibody positivity from the KI (Karolinska Institutet) B.Early arthritis setting. Here, we tested whether *Rheumatic?* could predict the development of an immune-mediated rheumatic disease in i) EUMC (Erlangen) n=52 patients and ii) LUMC (Leiden) n=73 patients.
In each setting, we examined the discriminative power of the total score with the Wilcoxon rank test and the area-under-the-receiver-operating-characteristic curve (AUC-ROC).
Results: In setting A, the total test score clearly differentiated between individuals developing arthritis or not, median 245 versus 163, *P < 0.0001,* AUC-ROC = 75.3 (Figure 1**).** Also within patients with arthritis the *Rheumatic?* total score was significantly higher in patients developing an immune-mediated arthritic disease versus those who did not: median score EUMC 191 versus 107, *P < 0.0001,* AUC-ROC = 79.0, and LUMC 262 versus 212, *P < 0.0001,* AUC-ROC = 53.6.

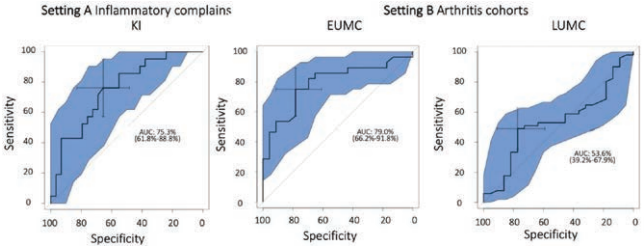


Figure 1. (Area under) the receiver operating curve for the total *Rheumatic?* score

Conclusion: *Rheumatic?* is a web-based patient-centered multilingual diagnostic tool capable of differentiating immune-mediated rheumatic conditions from other musculoskeletal problems. A following subject of research is how the tool performs in a population-wide setting.

REFERENCES:

[1] Knitza J. et al. Mobile Health in Rheumatology: A Patient Survey Study Exploring Usage, Preferences, Barriers and eHealth Literacy. JMIR mHealth and uHealth. 2020.
[2] https://rheumatic.elsa.science/en/

Acknowledgements: This project has received funding from EIT Health. EIT Health is supported by the European Institute of Innovation and Technology (EIT), a body of the European Union that receives support from the European Union's Horizon 2020 Research and Innovation program.
This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777357, RTCure.

Disclosure of Interests: Rachel Knevel: None declared, Johannes Knitza: None declared, Aase Hensvold: None declared, Alexandra Circiumaru: None declared, Tor Bruce Employee of: Ocean Observations, Sebastian Evans Employee of: Elsa Science, Tjardo Maarseveen: None declared, Marc Maurits: None declared, Liesbeth Beaart- van de Voorde: None declared, David Simon: None declared, Arnd Kleyer: None declared, Martina Johannesson: None declared, Georg Schett: None declared, Thomas Huizinga: None declared, Sofia Svanteson Employee of: Elsa Science, Alexandra Lindfors Employee of: Ocean Observations, Lars Klareskog: None declared, Anca Catrina: None declared

DOI: 10.1136/annrheumdis-2021-eular.1118

OP0148

SPATIOTEMPORAL DYNAMICS OF BONE LOSS BEFORE AND AFTER THE ONSET OF RHEUMATOID ARTHRITIS

K. Tascilar[1], D. Simon[1], A. M. Liphardt[1], T. Meinderink[1], S. Bayat[1], J. Rech[1], A. Hueber[2], G. Krönke[1], G. Schett[1], A. Kleyer[1]. *[1]Friedrich-Alexander; University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, 91054 Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany*; *[2]Solzialstiftung Bamberg, Sektion Rheumatologie, Bamberg, Germany*

Background: Rheumatoid Arthritis (RA) is preceded by a clinically silent pre-phase characterized by autoimmunity against anti-modified protein antibodies including anti-citrullinated protein antibodies (ACPA). At this pre-stage patients already experience significant loss of volumetric peripheral bone mineral density (vBMD) compared to healthy controls measured by high-resolution peripheral quantitative computed tomography (HR-pQCT) (1-2). However, the longitudinal course of vBMD changes during the preclinical phase, after diagnosis, and its association with time to disease onset have not been investigated.

Objectives: To longitudinally characterize the changes of metacarpal and radial vBMD before and after the clinical onset of RA and its association with time to onset of arthritis.
Methods: To explore the development of arthritis, we initiated a RA-at-risk cohort in 2011. (Ethics 334_16B). This prospective cohort includes adults positive for CCP-AB with or without musculoskeletal symptoms, excluding arthritis. Participants are regularly followed with clinical examination and HR-pQCT imaging of the MCP and radial bone to monitor early bone changes. HR-pQCT images with low motion grade artefacts were analyzed to obtain the total (D100), cortical (DComp) and trabecular (DTrab) vBMD (D100) in mg HA cm^3.
We descriptively analyzed the vBMD time course in patients who developed RA by fitting regression curves separately for the pre-clinical and clinical periods and estimated time-conditional marginal mean VBMDs for the 5-year peri-RA period. We analyzed time to diagnosis of clinical RA defined by the 2010 ACR/EULAR classification criteria using Cox regression models. Hazard ratios indicate the relative risk of clinical disease onset associated with 1 standard deviation reduction in bone density.
Results: 130 subjects (mean [SD] age 47.0 [12.2], 89 female [68%]) between 2011 and 2020 were analyzed. Median (IQR) follow-up duration for the cohort was 18.6 (4.6-47.6) months. Participants underwent 233 HR-pQCT scans and 58 (45%) underwent 2 to 6 scans with a median interval of 16.2 (12.2-21.2) months. 49 (38%) patients who developed RA had a pre-diagnosis follow-up of 4.1 (2.5-13.4) months and post-diagnosis follow-up of 22.0 (8.8-38.9) months. The time course of scaled bone mineral densities depicted in Figure 1A suggest that bone

Table 1. Relative risk of RA development in the total cohort; crude and age/sex adjusted hazard ratios for one standard-deviation reduction in vBMD.

	Crude		Adjusted	
	HR (95%CI)	P	HR (95%CI)	P
MCP.D-Comp	1.16 (0.86 to 1.57)	0.336	1.20 (0.89 to 1.63)	0.229
MCP.D-Trab	1.14 (0.83 to 1.57)	0.405	1.17 (0.85 to 1.62)	0.341
MCP.D100	1.16 (0.83 to 1.61)	0.392	1.21 (0.86 to 1.71)	0.265
Rad.D-Comp	1.42 (0.97 to 2.07)	0.071	1.66 (1.07 to 2.55)	0.023
Rad.D-Trab	1.20 (0.87 to 1.66)	0.257	1.23 (0.88 to 1.71)	0.223
Rad.D100	1.43 (0.99 to 2.06)	0.056	1.52 (1.03 to 2.25)	0.033

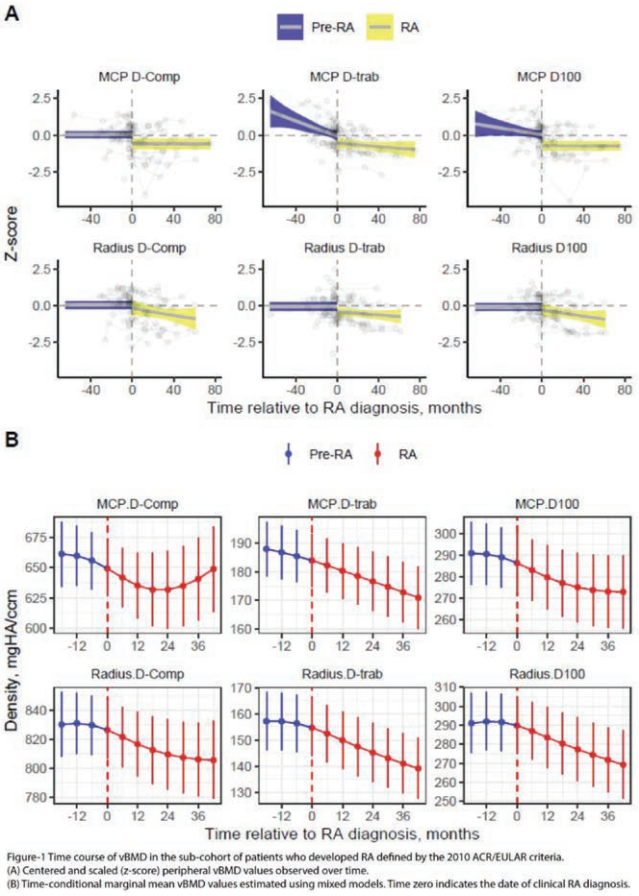


Figure-1 Time course of vBMD in the sub-cohort of patients who developed RA defined by the 2010 ACR/EULAR criteria.
(A) Centered and scaled (z-score) peripheral vBMD values observed over time.
(B) Time-conditional marginal mean vBMD values estimated using mixed models. Time zero indicates the date of clinical RA diagnosis.

density around the MCP joints deteriorate in the preclinical phase of RA, which is mostly prominent in the trabecular bone. Modelling (Figure 1B) suggests that trabecular bone loss around the MCP joints has a constant pace regardless of the clinical status. Whereas the radial bone densities are relatively stable in the preclinical phase and show a reduction after the clinical onset of RA. Age and sex adjusted hazard ratios (95%CI) for the risk of RA clinical onset were 1.52 (1.03 to 2.25) for radius D100 and 1.66 (1.07 to 2.55) for radius DComp (Table-1).
Conclusion: Metacarpal bone showed a constant decline that started already in the pre-phase of RA and continued after its clinical onset. In contrast, bone loss in the radius was not observed in the pre-phase but started at onset of RA. Low radial vBMD in the pre-clinical phase, however, was associated with a higher risk of RA onset. These findings suggest different spatiotemporal dynamics of bone loss before and after RA onset

REFERENCES:

[1] Kleyer A. et. al. Ann Rheum Dis. 2014, 73:854-60
[2] Simon D. et. al. Ann Rheum Dis. 2020, doi:10.1002/art.41229

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4176

OP0149 RELIABILITY AND RESPONSIVENESS OF TWO OMERACT WHOLE-BODY MRI SCORES OF ENTHESEAL AND JOINT INFLAMMATION IN THE KNEE REGION IN SPONDYLOARTHRITIS

M. Wetterslev[1,2], W. P. Maksymowych[3,4], R. G. Lambert[5,6], I. Eshed[7], S. Juhl Pedersen[1], M. Stoenoiu[8], S. Krabbe[1], P. Bird[9], V. Foltz[10], A. J. Mathew[1,2], F. Gandjbakhch[10], J. Paschke[4], P. Carron[11,12], G. De Marco[13,14], H. Marzo-Ortega[13,14], A. E. F. Poulsen[1], J. L. Jaremko[5], P. G. Conaghan[13,14], M. Østergaard[1,2]on behalf of the OMERACT MRI in Arthritis Working Group.
[1]Rigshospitalet, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Copenhagen, Denmark; *[2]University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark*; *[3]University of Alberta, Department of Medicine, Edmonton, Alberta, Canada*; *[4]CARE Arthritis, Edmonton, Alberta, Canada*; *[5]University of Alberta, Department of Radiology and Diagnostic Imaging, Edmonton, Alberta, Canada*; *[6]Medical Imaging Consultants, Edmonton, Alberta, Canada*; *[7]Tel-Aviv University, Department of Diagnostic Imaging, Sheba Medical Center, Affiliated to the Sackler School of Medicine, Israel*; *[8]Université catholique de Louvain, Department of Rheumatology, Cliniques Universitaires Saint-Luc, Institut de Recherche Expérimentale et Clinique, Brussels, Belgium*; *[9]University of New South Wales, Division of Medicine, Sydney, Australia*; *[10]Sorbonne University, Department of Rheumatology, APHP, Pitié-Salpêtrière Hospital, Paris, France*; *[11]Ghent University Hospital, Department of Rheumatology, Ghent, Belgium*; *[12]Ghent University, VIB Inflammation Research Centre, Ghent, Belgium*; *[13]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal medicine, Leeds, United Kingdom*; *[14]NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Inflammation in peripheral joints and entheses is common in spondyloarthritis (SpA). Whole-body magnetic resonance imaging (WB-MRI) allows assessment of the overall inflammatory status of arthritis patients including joints and entheses. The OMERACT MRI Whole-body scoring system for Inflammation in Peripheral joints and Entheses (MRI-WIPE) [1] has been developed and validated for the entire body assessment, including the knee, but not separately validated for the knee joint region. Detailed MRI scoring systems exist for heels, hands and feet, but although knee arthritis is a key cause of functional impairment, no detailed scoring system has been validated for inflammatory arthritides. The Knee Inflammation MRI Scoring System (KIMRISS) [2] was developed and validated in osteoarthritis and demonstrated good reliability.
Objectives: To perform region-based development of whole-body MRI through validation of two knee region scoring systems in SpA.
Methods: Assessment of inflammation was performed in the knee region on sagittal WB-MRIs using 2 scoring systems, MRI-WIPE and KIMRISS (Figure 1), in 4 iterative multi-reader exercises. In the final exercise, images (psoriatic arthritis, axial and peripheral SpA) were obtained before and after TNF-inhibitor.

Figure 1

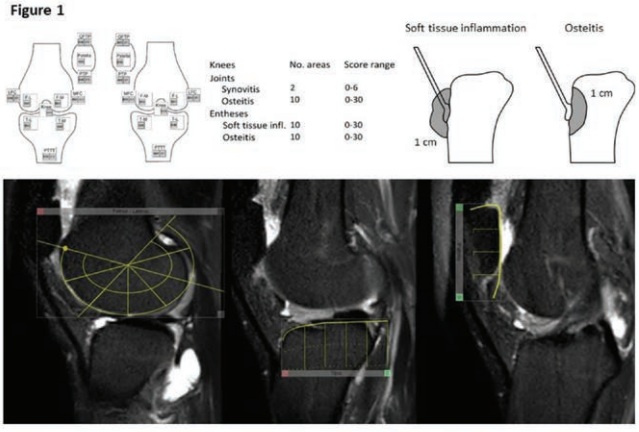


Figure 1. Upper row, left: MRI-WIPE schematic and scoring ranges for the knee-region from Krabbe, et al. [1]; Upper row, right: schematic drawing of the principle of scoring osteitis and soft tissue inflammation illustrated by the tibial insertion of the patellar ligament.
Lower row: Sagittal WB-MRI of a knee with the web-based superimposed interactive overlays used in KIMRISS for osteitis scoring positioned for femur, tibia and patella.

Results: In the final exercise (exercise 4), reliability was mostly good for experienced readers with the overall highest interreader agreement in the previous exercise (exercise 3). Median pairwise single measure intraclass correlation coefficients for osteitis and synovitis/effusion for status/change were 0.71/0.48 (WIPE osteitis), 0.48/0.77 (WIPE synovitis/effusion), 0.59/0.91 (KIMRISS osteitis) and 0.92/0.97 (KIMRISS synovitis/effusion) (Table 1). Wilcoxon signed-rank test showed significant change in synovitis/effusion for both methods and they correlated significantly regarding status in osteitis (0.92, p<0.001) and synovitis/effusion (0.89, p=0.001) and change in synovitis/effusion (0.89, p<0.001). Standardized response mean was 0.74 (WIPE synovitis/effusion) and 0.78 (KIMRISS synovitis/effusion).
Conclusion: MRI-WIPE and KIMRISS may both be useful as part of modular whole-body evaluation in clinical studies.

REFERENCES:

[1] Krabbe S et al. J Rheum. 2019;46(9):1215-21
[2] Jaremko JL et al. RMD Open. 2017;3(1):e000355

Acknowledgements: We thank CARE Aarthritis Limited (carearthritis.com) for help with setting up the web-based scoring interface, the scoring exercises, and the web-based meetings. We thank all who participated in the SIG (Special Interest Group) virtual OMERACT meeting 29 October 2020. HMO, GDM and PGC are supported in part by the National Institute for Health Research (NIHR) Leeds Biomedical Research Centre, United Kingdom. The views expressed in this study are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Disclosure of Interests: Marie Wetterslev: None declared, Walter P Maksymowych Speakers bureau: AbbVie, Janssen, Novartis, Pfizer and UCB,

Table 1. MRI-WIPE knee and KIMRISS interreader reliability for OMERACT exercises 3 and 4

			MRI-WIPE Knee				KIMRISS			
			Osteitis		Synovitis/effusion		Osteitis		Synovitis/effusion	
Variables	**No. patients**	**Type of score**	**Mean score**	**ICC**	**Mean score**	**ICC**	**Mean score**	**ICC**	**Mean score**	**ICC**
Exercise 3	11	Status	3.6 (0-16)	0.57 (-0.06-0.98)	1.8 (0-4)	0.47 (0.05-0.85)	32.3 (1-224)	0.87 (0.66-0.99)	29.9 (11-60)	0.34 (-0.62-0.87)
	11	Change	1.1 (-2-6)	0.53 (0.03-0.90)	0 (-2-1)	0.32 (-0.13-0.76)	27.7 (-9-131)	0.58 (-0.30-0.96)	-1.6 (-33-11)	0.48 (-0.32-0.95)
9 readers										
Exercise 3	11	Status	3.1 (0-16)	0.83 (0.71-0.97)	2.5 (0-5)	0.59 (0.51-0.71)	34.4 (0-233)	0.89 (0.83-0.99)	36.5 (16-78)	0.59 (0.08-0.86)
	11	Change	0.9 (-3-6)	0.72 (0.57-0.83)	0 (-2-1)	0.63 (0.49-0.76)	19.3 (-23-86)	0.46 (0.18-0.83)	-1.8 (-45-17)	0.89 (0.82-0.95)
3 readers										
Exercise 4	10	Change	-0.25 (-4-5)	0.38 (-0.35-0.94)	-1.0 (-3-1)	0.30 (-0.43-0.89)	-0.45 (-37-65)	0.26 (-0.86-0.97)	-14.7 (-48-0.20)	0.48 (-0.39-0.99)
	20	Status	2.9 (0-7)	0.50 (-0.01-0.84)	2.1 (0-4)	0.44 (-0.21-0.79)	15.2 (0-66)	0.35 (-0.04-0.89)	55.6 (1-122)	0.54 (0.01-0.96)
9 readers										
Exercise 4	10	Change	0.2 (-2-6)	0.48 (0.16-0.66)	-1.4 (-5-0)	0.77 (0.70-0.82)	5.8 (-27-111)	0.92 (0.90-0.94)	-20.7 (-65-28)	0.97 (0.96-0.98)
	20	Status	2.3 (0-6)	0.71 (0.60-0.80)	2.7 (0-5)	0.48 (0.42-0.57)	11.4 (0-36)	0.59 (0.39-0.71)	69.4 (1-153)	0.91 (0.87-0.93)
3 readers										

Sum scores are mean (range) of the patients scores. ICC values are mean (range). ICC is 2-way mixed model, single measure, by absolute agreement.

Consultant of: AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Novartis, Pfizer and UCB, Robert G Lambert Consultant of: Parexel and Pfizer, Iris Eshed: None declared, Susanne Juhl Pedersen Speakers bureau: MSD, Pfizer, AbbVie, Novartis and UCB, Consultant of: AbbVie and Novartis, Grant/research support from: AbbVie, MSD, and Novartis, Maria Stoenoiu: None declared, Simon Krabbe: None declared, Paul Bird Speakers bureau: Janssen, Abbvie, UCB, Celgene, BMS, Novartis, Pfizer, Gilead, Eli-Lilly, Consultant of: Janssen, Abbvie, UCB, Celgene, BMS, Novartis, Pfizer, Gilead, Eli-Lilly, Violaine Foltz: None declared, Ashish Jacob Mathew: None declared, Frederique Gandjbakhch: None declared, Joel Paschke: None declared, Philippe Carron Speakers bureau: Pfizer, MSD, Novartis, BMS, AbbVie, UCB, Eli Lilly, Gilead and Celgene, Consultant of: Pfizer, MSD, Novartis, BMS, AbbVie, UCB, Eli Lilly, Gilead and Celgene, Grant/research support from: UCB, MSD and Pfizer, Gabriele De Marco: None declared, Helena Marzo-Ortega Speakers bureau: AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer, Takeda and UCB, Grant/research support from: Janssen and Novartis, Anna Enevold Fløistrup Poulsen: None declared, Jacob L Jaremko: None declared, Philip G Conaghan Speakers bureau: AbbVie, AstraZeneca, BMS, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, Gilead, Novartis, Pfizer and Stryker, Consultant of: AbbVie, AstraZeneca, BMS, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, Gilead, Novartis, Pfizer and Stryker, Mikkel Østergaard Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Consultant of: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB

DOI: 10.1136/annrheumdis-2021-eular.755

OP0150

MACHINE LEARNING APPROACHES FOR RISK MODELLING IN INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS USING HIGH DIMENSIONAL IMAGE ANALYSIS

M. Maciukiewicz[1], J. Schniering[1], H. Gabrys[2], M. Brunner[1], C. Blüthgen[3], C. Meier[1], M. Guckenberger[2], H. Fretheim[4], A. M. Hoffmann-Vold[4], O. Distler[1], T. Frauenfelder[3], S. Tanadini-Lang[2], B. Maurer[1,5]. *[1]Center of Experimental Rheumatology, Department of Rheumatology, University of Zurich, Zurich, Switzerland*; *[2]Department of Radiation Oncology, University Hospital Zurich, University of Zurich, Zurich, Switzerland*; *[3]Institute of Diagnostic and Interventional Radiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland*; *[4]Institute of Clinical Medicine, University of Oslo, Rheumatology, Oslo University Hospital, Oslo, Norway*; *[5]Department of Rheumatology and Immunology, University Hospital Bern, Bern, Switzerland*

Background: The interstitial lung disease (ILD) associated with connective tissue diseases including systemic sclerosis (SSc) is heterogenous disease characterized by reduced survival of approximately 3 years (1). “Radiomics” is a field of research which describes the in-depth analysis of tissues by computational retrieval of high-dimensional quantitative features from medical images (2). Our previous study suggested capacity of radiomics features to differentiate between “high” and “low” risk groups for lung function decline in two independent cohorts (3).

Objectives:

- bTo develop robust, machine learning (ML) workflow for “radiomics” data in SSc-ILD to select optimal methods for prediction.
- oTo predict the time to individual lung function decline defined as defined by the time to a relative decline of ≥ 15% in Forced Vital Capacity (FVC)% as previously (3), using workflow.

Methods: We investigated two cohorts of SSc-ILD: 90 patients (76.7% female, median age 57.5 years) from the University Hospital Zurich and 66 patients (75.8% female, median age 61.0 years) from Oslo University Hospital’s. Patients were retrospectively selected if (3): a) diagnosed with early/mild SSc according to the Very Early Diagnosis of Systemic Sclerosis (VEDOSS) criteria, b) presence of ILD on HRCT as determined by a senior radiologist. For every subject, we defined 1,355 robust radiomic features from HRCT images. The follow-up period was defined as the time interval between baseline visit and the last available follow-up visit.

We have developed a systematic computational workflow to build predictive ML models. To reduce the number of redundant radiomic features, we applied correlation thresholds. We applied distinct methods including 1) Lasso Penalized Regression for feature selection, and 2) Random Forest (RF) for modeling using the R package ‘caret’. To select the optimal ML model, we randomly divided derivation cohort into Training (70%) and Holdout (30%) sets and applied fivefold cross-validation (5kCV) for feature and classifier selection on Training set only.

Results: We have investigated various methods to select the optimal set of predictive radiomic features. Since the ML model performance is affected by both, feature, and classifier selection, we assessed these factors first.

Results from feature filtering and selection, suggested that the combination of correlation threshold of 0.9 with Lasso regression proved best. As we perform feature selection in 5k CV workflow, features present in at least 2 sets entered model optimization step.

During model selection, we selected RF classifier. We detected positive correlation between actual and predicted values with Spearman’s rho = 0.313, p = 0.167 and Spearman’s rho = 0.341, p = 0.015 in Oslo and Holdout sets respectively, as shown on Figure 1. The percentage of variance remained modest for both Holdout (Rsq = 0.104) and Oslo (Rsq = 0.126) datasets.

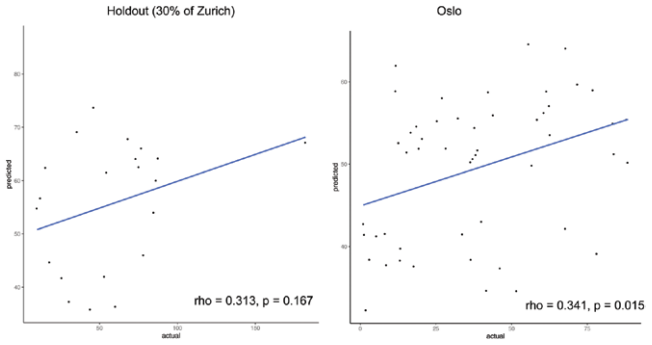


Figure 1. Performance of the best, RF classifier shown as scatterplot between actual and predicted values of individual time to lung decline.

Conclusion: In summary, we: (1) developed ML workflow that allowed to select o optimal methodology for modeling (i.e., feature and classifier selection), and (2) provide models that predicted time to individual lung function decline, characterized by significant correlation between predicted and actual values.

REFERENCES:

[1] Hansell DM, Goldin JG, King TE, Jr., Lynch DA, Richeldi L, Wells AU. CT staging and monitoring of fibrotic interstitial lung diseases in clinical practice and treatment trials: a position paper from the Fleischner Society. Lancet Respir Med. 2015;3(6):483-96.

[2] Lambin, P. et al. Radiomics: extracting more information from medical images using advanced feature analysis. Eur. J. Cancer 48, 441–446 (2012).

[3] Schniering J. et al. Resolving phenotypic and prognostic differences in interstitial lung disease related to systemic sclerosis by computed tomography-based radiomics. https://www.medrxiv.org/content/10.1101/2020.06.09.20124800v1

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2517

OP0151

AUTOANTIBODIES AGAINST DENSE-FINE-SPECKLED 70 (DFS70) DO NOT ENTIRELY EXCLUDE CONNECTIVE TISSUE DISEASES

L. M. Mockenhaupt[1], R. Dolscheid-Pommerich[2], C. Behning[3], B. Stoffel-Wagner[2], P. Brossart[1], V. Schäfer[1]. *[1]University Hospital Bonn, Clinic of Internal Medicine III, Department of Oncology, Hematology, Rheumatology and Clinical Immunology, Bonn, Germany*; *[2]University Hospital Bonn, Institute of Clinical Chemistry and Clinical Pharmacology, Bonn, Germany*; *[3]University Hospital Bonn, Institute of Medical Biometry, Informatics and Epidemiology, Bonn, Germany*

Background: Antinuclear antibodies (ANA) are serological markers for the presence of rheumatic diseases [1]. In some patients, a pattern can be detected in ANA immunofluorescence that resembles an anti-dense-fine-speckled-70 antibody [2]. This is detected less frequently in patients with connective tissue diseases (CTD) and is therefore often used as an exclusion criteria for a CTD [2]. To date, however, it is not clear how the presence of an anti-DSF70 autoantibody will reliably rule out CTDs.

Objectives: To examine the degree to which CTDs can be excluded from either a positive test and whether there are discrepancies between patients with CTDs and a negative anti-DSF70 test and those with CTDs and a positive anti-DSF70 test.

Methods: We analyzed data of 460 patients who were tested for the presence of the DSF70 antibody at the University Hospital Bonn, Germany. Patients were examined with regard to clinical symptoms and signs, type of disease, type of CTD, fulfillment of the classification criteria for the particular CTD, DSF70 antibodies, other autoantibodies and ANA titer. Gold standard for presence of a CTD was the diagnosis of the treating rheumatologist.

In addition to variations between patients with CTD and positive or negative DSF70 antibodies, specificity, sensitivity and positive predictive value were calculated for different ANA titers.

Results: Of the 460 patients, 79.8% were female and 182 were diagnosed with a CTD. 354 patients (77.0%) were tested negative, 81 (17.6%) positive and 25 (5.4%) had a borderline anti-DSF70 autoantibody result.

We identified 21 patients with a positive test result in the presence of a CTD, which accounts for 25.9% of all anti-DSF70 autoantibody positive tested patients. We found no significant differences in DSF70-positive patients with CTD in regard to age, gender, symptoms, clinical signs and also disease-specific antibodies compared to patients with negative DSF70 status and present CTD.

Of the 21 DSF70-positive patients with CTD, 12 (57.1%) were tested for the presence of disease-specific autoantibodies. Specific autoantibodies could be detected in all of the tested patients with systemic lupus erythematosus, systemic sclerosis, Sjögren's syndrome and mixed connective tissue disease.

DSF70 autoantibodies had a specificity of 86.8%, a sensitivity of 26.9% and a positive predictive value of 68.2% at an ANA titer of ≥1:160, with respect to the absence of a connective tissue disease.

Table 1. Sensitivity, specificity and positive predictive value of anti-DSF70 autoantibody in different ANA titers (borderline patients excluded)

a) ANA-Titer ≥ 1:80		
N=362	*No present CTD*	*Present CTD*
DSF70 positive	52	21
DFS70 negative	145	144
	Sensitivity: 26.4%	Specificity: 87.3%
Positive predictive value= 71.2%		
b) ANA-Titer ≥ 1:160		
N=326	*No present CTD*	*Present CTD*
DSF70 positive	45	21
DSF70 negative	122	138
	Sensitivity: 26.9%	Specificity: 86.8%
Positive predictive value= 68.2%		
c) ANA-Titer ≥ 1:640		
N=167	*No present CTD*	*Present CTD*
DSF70 positive	17	14
DSF70 negative	48	88
	Sensitivity: 26.2%	Specificity: 86.3%
Positive predictive value= 54.8%		

Conclusion: Autoantibodies to DSF70 often occur in CTD patients and are therefore not a valid exclusion criteria for a CTD. We observed no CTD in 68.2% of patients who were tested positive. Thus, in difficult situations, the DSF70 test may be helpful and the additional exclusion of other autoantibodies may render CTD even less probable.

REFERENCES:

[1] Mahler M, Fritzler MJ. Epitope specificity and significance in systemic autoimmune diseases: Epitope specificity. *Ann N Y Acad Sci*. 2010;1183(1):267-287.

[2] Mahler M, Hanly JG, Fritzler MJ. Importance of the dense fine speckled pattern on HEp-2 cells and anti-DFS70 antibodies for the diagnosis of systemic autoimmune diseases. *Autoimmun Rev*. 2012;11(9):642-645.

Disclosure of Interests: Louisa-Marie Mockenhaupt: None declared, Ramona Dolscheid-Pommerich: None declared, Charlotte Behning: None declared, Birgit Stoffel-Wagner: None declared, Peter Brossart: None declared, Valentin Schäfer Speakers bureau: AbbVie, Novartis, BMS, Chugai, Celgene, Medac, Sanofi, Lilly, Hexal, Pfizer, Janssen, Roche, Schire, Onkowissen, Royal College London, Consultant of: Novartis, Chugai, AbbVie, Celgene, Sanofi, Lilly, Hexal, Pfizer, Amgen, BMS, Roche, Gilead, Medac, Grant/research support from: Novartis, Hexal, Lilly, Roche, Celgene, Universität Bonn

DOI: 10.1136/annrheumdis-2021-eular.934

OP0152

COMPARISON OF DIAGNOSTIC CRITERIA IN BEHÇET DISEASE AND SENSITIVITY IN DIAGNOSING SEVERE MANIFESTATIONS.

C. Álvarez-Reguera[1], A. Herrero-Morant[1], L. Sanchez-Bilbao[1], D. Martínez-López[1], J. L. Martín-Varillas[2], G. Suárez Amorín[3], C. Mata-Arnaiz[4], M. Á. González-Gay[1], R. Blanco[1]. *[1]Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*; *[2]Hospital de Sierrallana, Rheumatology, Sierrallana, Spain*; *[3]Hospital Universitario Marqués de Valdecilla, Ophthalmology, Santander, Spain*; *[4]Hospital de Laredo, Rheumatology, Laredo, Spain*

Background: Behçet disease (BD) is characterized by painful recurrent oral aphthosis genital ulcers and skin lesions. Nevertheless, the major causes of morbidity result from ocular, vascular and neurological involvement. Diagnosis of BD is usually performed according to the International Study Group (ISG*) (Lancet 1990; 335:1078-80).* Recently, criteria proposed by the International Team for the Revision of the International Criteria for BD (ITR-ICBD) have demonstrated a higher sensitivity *(J Eur Acad Dermatology Venereol 2014;28:338-47).*

Table 1. Main clinical features according to different diagnostic criteria. Patients characteristics, data are in n (%)

	Expert rheumatologists (N=120)	ISG criteria (N=59)	ICBD criteria (N=96)
Age, mean years / (SD)	38 (13.8)	35.6 (13)	37 (13)
Gender, men/women, N (%)	62/58 (52.1/47.9)	29/30 (49.1/50.8)	48/48 (50/50)
Oral aphthosis, N (%)	113 (94.2)	59 (100)	94 (97.9)
Genital aphthosis, N (%)	71 (78.5)	46 (78)	71 (74)
Skin manifestations N (%)	76 (63.3)	52 (88.1)	64 (71.6)
Ocular lesions, N (%)	54 (45)	31 (52.5)	50 (52.1)
Joint manifestations, N (%)	78 (65)	38 (64.4)	62 (64.6)
Neurological manifestations, N (%)	23 (19.2)	9 (15.2)	20 (21.1)
Vascular manifestations, N (%)	14 (11.6)	7 (11.9)	14 (14.6)
Gastrointestinal features, N (%)	8 (6.6)	3 (5.1)	5 (5.3)

Objectives: To assess **a)** the concordance and differences between ISG and ICDB criteria **b)** sensitivity in diagnosing severe manifestations (ocular, vascular and neurological).

Methods: The study included 120 patients diagnosed with definitive or possible BD by expert rheumatologists. They were diagnosed at a well-defined population in Northern Spain between January 1980 and December 2019. The ISG and ICBD diagnostic criteria for BD were applied to all patients and compared among them.

Results: 120 patients (62 men/ 58 women) were studied. Mean age at diagnosis was 37.6±13.8 years. 59 (49.2%) patients fulfilled ISG criteria and 96 (80%) ICBD criteria. Concordance between both criteria was moderate (Kappa 0.41). ICBD criteria diagnosed more patients with neurological (χ^2=49.1, p<0.01), vascular (χ^2= 56.7, p<0.01) and ocular manifestations (χ^2=84.4 p<0.01) (Figure**).**

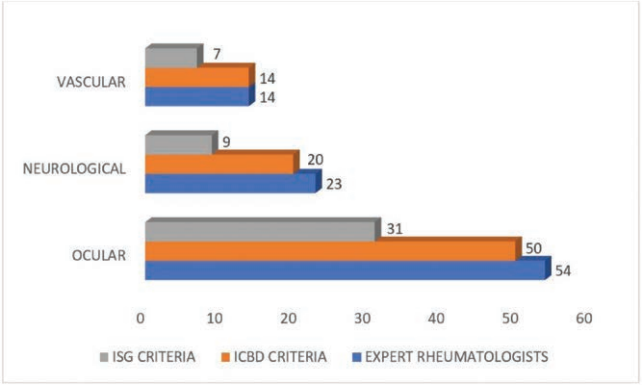


Figure 1. Number of patients with vascular, neurological or ocular manifestations diagnosed with BD by different criteria. **Abbreviations: ITRC-ICBD:** International Team for the Revision of the International Criteria for BD; **ISG:** International Study Group for Behçet Disease.

Conclusion: ICBD criteria are more likely to diagnose BD and classify more patients with severe manifestations of the disease.

REFERENCES:

[1] Atienza-Mateo B, et al. Rheumatology (Oxford) 2018;57(5):856-864. doi: 10.1093/rheumatology/kex480.
[2] Vegas-Revenga N, et al. Am J Ophthalmol. 2019; 200:85-94. doi: 10.1016/j.ajo.2018.12.019
[3] Calvo-Río V, et al. Clin Exp Rheumatol. 2014;32(4 Suppl 84):S54-7. PMID: 25005576
[4] Santos-Gómez M, et al. Clin Exp Rheumatol. 2016;34(6 Suppl 102): S34-S40. PMID:27054359
[5] Atienza-Mateo B, et al. Arthritis Rheumatol. 2019; 71(12):2081-2089. doi: 10.1002/art.41026.
[6] Martín-Varillas JL, et al. Ophthalmology. 2018;125(9):1444-1451. doi: 10.1016/j.ophtha.2018.02.020

Disclosure of Interests: Carmen Álvarez-Reguera: None declared, Alba Herrero-Morant: None declared, Lara Sanchez-Bilbao: None declared, David Martínez-López: None declared, José Luis Martín-Varillas: None declared, Guillermo Suárez Amorín: None declared, Cristina Mata-Arnaiz: None declared, Miguel Á. González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi and MSD., Grant/research support from: Abbvie, MSD, Janssen and Roche., Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Bristol-Myers, Janssen, Lilly and MSD., Grant/research support from: Abbvie, MSD and Roche.
DOI: 10.1136/annrheumdis-2021-eular.3331

HPR Abstract Session (I)

OP0153-HPR BRIDGING GAPS ACROSS LEVELS OF CARE IN REHABILITATION OF PATIENTS WITH RHEUMATIC - AND MUSCULOSKELETAL DISEASES: RESULTS FROM A STEPPED WEDGE CLUSTER RANDOMISED CONTROLLED TRIAL

G. Berdal[1], A. L. Sand-Svartrud[1], M. Azimi[2], I. Bø[3], T. Nygaard Dager4, S. Eppeland[5], G. Ohldieck Fredheim[6], A. Sirnes Hagland[7], A. Klokkeide[8], A. D. Linge[9], K. Tennebø[10], H. Lindtvedt Valaas[6], A. M. Aasvold[11], J. Sexton[12], I. Kjeken[1]. *[1]National Advisory Unit on Rehabiliation in Rheumatology, Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*; *[2]Diakonhjemmet Hospital, Dept. of Rheumatology, Oslo, Norway*; *[3]Hospital for Rheumatic Diseases, Dept. of Rehabilitation, Lillehammer, Norway*; *[1]National Advisory Unit on Rehabiliation in Rheumatology, Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*; *[5]Sørlandet Hospital, Dept. of Rheumatology, Arendal, Norway*; *[6]Vikersund Spa Rehabilitation Centre, Dept. of Rehabilitation, Vikersund, Norway*; *[7]Haugesund Sanitetsforening's Rheumatism Hospital, Dept. of Rehabilitation, Haugesund, Norway*; *[8]Rehabilitation West Rehabilitation Centre, Dept. of Rehabilitation, Haugesund, Norway*; *[9]Muritunet Rehabilitation Centre, Dept. of Rehabilitation, Ålesund, Norway*; *[10]Valnesfjord Health Sports Centre, Dept. of Rehabilitation, Valnesfjord, Norway*; *[11]Meråker Spa Rehabilitation Centre, Dept. of Rehabilitation, Meråker, Norway*; *[12]Diakonhjemmet Hospital, Dept. of Rheumatology, Oslo, Norway*

Background: Previous research show that patients with rheumatic and musculoskeletal diseases (RMDs) benefit from rehabilitation, but the health effects are small and decline over time. Later reports reveal that the quality of rehabilitation services varies largely, with lack of coordination and continuity across levels of care. This may weaken the effect on patients' long-lasting health, ability to self-manage their conditions and achieve their goals. We therefore developed a new, evidence-based rehabilitation program to strengthen the quality and bridge the gaps in rehabilitation services for this patient group.

Objectives: To evaluate if a new rehabilitation program (the BRIDGE program) designed to improve the quality and continuity of rehabilitation across levels of care, was more effective than traditional rehabilitation in improving goal achievement, function, self-assessed health and health related quality of life (HR-QoL) in patients with RMDs.

Methods: In a stepped wedge cluster randomised controlled trial 8 rehabilitation centres organised in secondary health care and located across all health regions of Norway recruited a total of 374 patients with rheumatic and musculoskeletal diseases. These patients received either traditional rehabilitation (control) (n=206), or traditional rehabilitation extended with an individually adapted complex intervention consisting of structured goal setting, plans for self-management, motivational interviewing, self-monitored digital feedback, and tailored follow-up support after discharge according to patients' needs and available resources in primary healthcare (the BRIDGE program) (n=168). Patient-reported data were collected electronically on admission and discharge from rehabilitation, and after 2, 7, and 12 months. The primary outcome measure was patients' goal achievement measured by the Patient Specific Functional Scale (PSFS) (0-10, 10=best) seven months after rehabilitation stay. Secondary outcome measures were function measured by the 30-seconds Sit-To-Stand Test (30secSTS), self-assessed health and HR-QoL measured by the EuroQol instruments EQ-5D-5L-VAS (0-100, 100=best) and EQ 5D-5L-index (-1 to 1, 1=best). The main comparative analysis was performed on the intention to treat population, using all available data, by linear mixed models adjusted for the baseline scores and for the potentially confounding effects of calendar time and data clustering. Sensitivity analyses were performed on data provided by the per protocol population according to predefined criteria, in addition to centerwise comparisons of the control and intervention groups.

Results: No significant treatment effects of the BRIDGE-program were demonstrated either for patients' goal achievement (mean difference 0.1 [95% CI: -0.5, 0.8], p=0.70) (Figure 1), function (mean difference 0.9 [95% CI: - 0.4, 2.2], p=0.18), self-assessed health (mean difference -0.1 [95% CI: -4.1, 3.9], p=0.98), or HR-QoL (mean difference 0.0 [95% CI: -0.0, 0.0], p=0.99) seven months after rehabilitation. Sensitivity analyses confirmed the findings from the primary analysis. A significant proportion of missing data for the primary outcome measure (29% in the control and 41% in the intervention group), caused by errors in the digital data collection system, may impair the reliability of the results.

Conclusion: The BRIDGE program was not shown to be more effective than traditional rehabilitation in terms of improving goal achievement, function, self-assessed health and HR-QoL in patients with RMDs. There is still a need for more knowledge about factors that can improve the quality, continuity and long-term health effects of rehabilitation for this patient group.

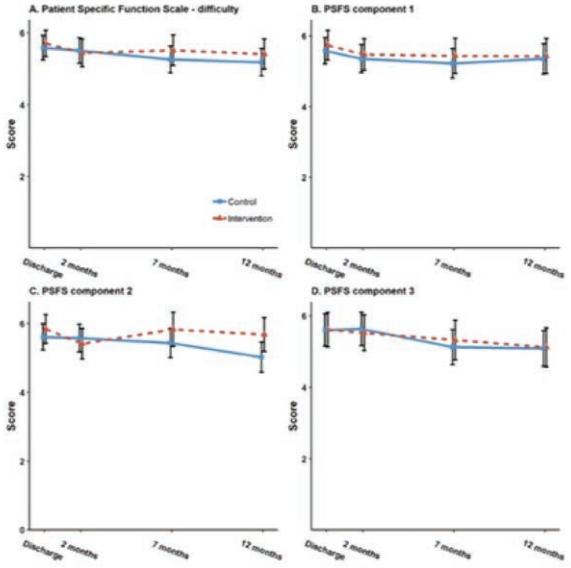


Figure 1. Goal achievement measured with PSFS (0-10, 10 best) indicated by difficulty to perform goal at 4 time-points: discharge from rehabilitation (baseline for this particular outcome) and after 2, 7 and 12 months. Vertical lines indicate the estimated mean values (center) with 95% confidence interval. Horizontal lines show the fluctuating mean PSFS values from baseline to 12 months after discharge. Graph A shows the average of the first three goals set by the patients, measured over time, while the graphs B, C and D show the results separately for the first, second and third goal, respectively.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.987

OP0154-HPR FEASIBILITY OF A WEB-BASED, PEER-SUPPORTED EXERCISE PROGRAM FOR PEOPLE WITH HIP OR KNEE OSTEOARTHRITIS

K. L. Joseph[1,2], H. Solveig Dagfinrud[1], K. B. Hagen[3], K. Røren Nordén[1], C. Fongen[1], O. M. Wold[4], A. T. Tveter[1]. *[1]Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology,The division of Rheumatology and Research, Oslo, Norway*; *[2]University of Oslo, Faculty of Medicine, Institute of Health and Society, Oslo, Norway*; *[3]Norwegian Institute of Public health, Division of Health Service, Oslo, Norway*; *[4]Norwegian Association for Rheumatic diseases, Norwegian Association for Rheumatic diseases, Oslo, Norway*

Background: Long-term physical activity (PA) and exercise is recommended as a cornerstone in the treatment of people with osteoarthritis (OA) (1), yet adherence to exercise is challenging (2). The treatment needs for this large group of patients cannot be fully managed within the health-care system, thus developing innovative and effective follow-up strategies is urgently needed.

Objectives: To explore the feasibility and preliminary efficacy of a web-based, peer-supported exercise program for people with hip or knee OA.
Methods: This study was a single-group, pre-post feasibility study. Patients aged 40-80 years with hip or knee OA who were not candidates for surgery were eligible. The 12-week intervention was delivered through a patient-organizations (The Norwegian Association for Rheumatic Diseases) web-based platforms, and included weekly exercise programs, weekly motivational messages, an OA and exercise website and assigned peer-supporters. Feasibility was evaluated by calculating the proportion of eligible patients who were enrolled and retained at follow-up, as well as time resources used on delivery of the intervention. Acceptability was evaluated by calculating proportion of patients who had valid baseline accelerometer data and completed the maximal cardiorespiratory exercise test according to protocol. Primary efficacy measures were change in PA assessed by accelerometers and change in exercise capacity (VO2peak) assessed by indirect maximal cardiorespiratory exercise test. Secondary efficacy measures were change in patient reported outcomes assessed by HOOS and KOOS (www.koos.nu) (a 10-point change in normalized scores was considered a minimally important change). Data was analysed using paired sample t-test, given as mean change (95% confidence interval) and p-values.
Results: We identified 49 eligible patients of which 35 (71%) consented and were enrolled. Among those who consented, 22 (63%) were retained. Time resources used on delivery of the exercise programs and motivational messages were mean (SD) 7.3±1.1 min per week/patient. Compliance with wearing the accelerometer was mean (SD) 6.1±1.0 valid days (mean (SD) 13.8±1.3 hours/day). Twenty (67%) out of 30 patients who attended baseline testing performed the maximal cardiorespiratory exercise test, of which 18 completed according to protocol. Due to Covid-19 restrictions, follow-up testing of primary efficacy measures included only eight patients. For these patients there was a significant increase from baseline to follow-up on moderate-to-vigorous PA (mean change 16.4 minutes/day; 95% CI 6.9, 25.9, p=0.005) and VO2peak (mean change 1.83 ml/kg/min; 95% CI 0.29, 3.36, p=0.026). Across all secondary efficacy measures 30-52% of the patients (n=21) improved from baseline to follow-up (Figure 1).

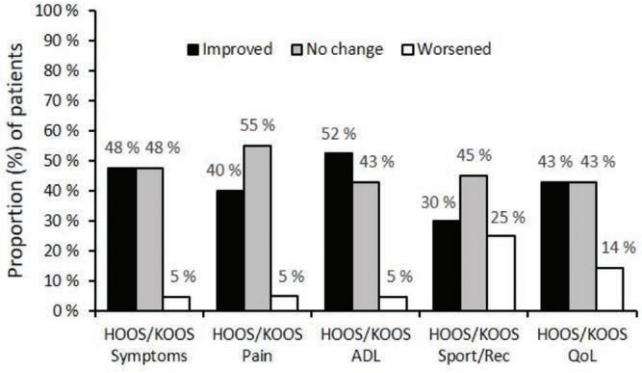


Figure 1. Proportion (%) of patients with Minimally Important Change (from baseline to follow-up) in normalized scores in subdomains of Hip disability and Osteoarthritis Outcome Score (HOOS) / Knee injury and Osteoarthritis Outcome Score (KOOS).

Conclusion: Overall, the examined study processes were considered to be feasible and acceptable. Some minor amendments should be applied to improve the recruitment and retention rate before it can be carried out in a larger trial. The efficacy results should be interpreted with caution due the small sample size. However, if the positive results in this study are confirmed in a power-calculated randomised controlled trial, our novel follow-up strategy may be implemented and recommended for long-term management of hip and knee OA.
REFERENCES:
[1] Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis Rheumatol. 2020;72(2):220-33.
[2] Williamson W, Kluzek S, Roberts N, Richards J, Arden N, Leeson P, et al. Behavioural physical activity interventions in participants with lower-limb osteoarthritis: a systematic review with meta-analysis. BMJ Open. 2015;5(8):e007642.
Acknowledgements: The authors wish to acknowledge all patients for participating, the patient representative who gave invaluable input on interventional components and the peer-supporters for volunteering to provide interventional support.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1313

OP0155-HPR

REMOTE MANAGEMENT OF RHEUMATOID ARTHRITIS VS ROUTINE OUTPATIENT FOLLOW-UP: A PROSPECTIVE, LONGITUDINAL REAL-WORLD STUDY

M. Ndosi[1], S. Kingsbury[2], P. G. Conaghan[2]. [1]*University of the West of England, Faculty of Health and Applied Sciences, Bristol, United Kingdom*; [2]*University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*

Background: Remote management of rheumatoid arthritis (RA) using patient self-assessment of disease and patient-reported outcomes has potential to inform timely clinical decisions on disease management, reduce burden on busy rheumatology services and promote effective self-management. However, it is unclear how patients' self-reporting relates to treatment decisions.
Objectives: To determine the agreement between remote treatment decisions based on patient self-assessment questionnaire assessed blindly by a health professional and treatment decisions based on routine outpatient monitoring appointments.
Methods: This was a prospective real-world study including patients (who gave informed consent) enrolled in an observational study of RA patients starting a new biologic therapy.
Enrolled patients continued with their usual care and usual clinic monitoring. In addition, they completed at home, self-assessment questionnaires at monthly intervals, including: two self-reported components which are collected as part of routine clinical practice (joint stiffness and flare), visual analogue scales for pain, global health and fatigue; and HAQ-DI and self-efficacy scales (Arthritis Self-Efficacy Pain and Other Symptoms subscales) at inclusion visits, 12 and 24 months. Remote treatment decisions were made by an independent (blinded) health professional, based on the self-assessment questionnaires and information collected in the study: medical history, ongoing therapies for RA, clinical outcomes, adverse events and toxicity. In this analysis, the independent blinded clinician did not have the same information as the routine hospital visit clinician (blood results and joints assessment).
The remote decisions were matched with the hospital visit decisions (within 2 weeks) and the measure of agreement between the 2 raters (independent blinded health professional and clinician at outpatient appointment) were evaluated using kappa coefficient: <0.2, 0.21-0.40, 0.41-0.60, 0.61-0.80 and 0.81-0.99 representing poor, fair, moderate, substantial and almost perfect agreement respectively.
Results: A total of 72 RA patients were recruited into the sub-study: mean (SD) age 57.8 (11.6), disease duration 11.7 (10.3) and 52 (87%) were female. The pre-categorised remote decisions were: no change to biologic, stop biologic, add concomitant DMARD, reduction/removal of a concomitant DMARD and bring in for review. There were 57 matched decisions between the independent health professional and the outpatient clinicians. The outpatient clinician made 7 changes to biologic and 18 non-biologic therapy changes, while the remote health professional made 1 change to biologic and 17 changes to a non-biologic DMARD including bringing in for review. The self-assessment questionnaires reported 34 RA flares of which 21 had resolved. In the matched decisions, there was only one adverse event that needed stopping treatment, identified by both the remote and the outpatient treatment. The independent health professional and the outpatient clinician had a 'fair' agreement on changes to biologic therapy (Kappa = 0.226, p = 0.007) and overall changes to RA therapy (Kappa = 0.24, p = 0.07).
Conclusion: Remote RA monitoring using patient self-assessment and outcome measures was feasible with fair agreement on treatment decisions. Further work is required on understanding the importance of adding blood test monitoring to remote decision-making.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3356

OP0156-HPR

THE EFFECT OF A PERSON-CENTERED SMOKING CESSATION PROGRAM IN RHEUMATOID ARTHRITIS PATIENTS IN A RHEUMATOLOGY OUTPATIENT CLINIC SETTING – RESULTS OF AN INTERVENTIONAL FEASIBILITY STUDY

M. L. Karlsson[1,2], K. Hertzberg-Nyquist[3], S. Saevarsdottir[2], I. E. Lundberg[1,2], I. Demmelmaie[4], S. Pettersson[1], K. Chatzidionysiou[2,5]. [1]*Karolinska University Hospital, Department of Gastroentorogy, Dematology and Rheumatology, Stockholm, Sweden*; [2]*Karolinska Institute, Department of medicine Solna, Stockholm, Sweden*; [3]*Centre of Rheumatology, Rehumatology, Stockholm, Sweden*; [4]*Uppsala University, Department of Public health and Caring Science, Uppsala, Sweden*; [1]*Karolinska University Hospital, Department of Gastroentorogy, Dematology and Rheumatology, Stockholm, Sweden*

Background: Smoking is associated with worse treatment response[1] and higher mortality[2] in rheumatoid arthritis (RA).

Objectives: To assess the effect of a smoking cessation intervention in a rheumatology setting.
Methods: We designed a smoking cessation interventional feasibility study. RA patients who were active smokers were asked to participate. A nurse-delivered program consisting of behavioural changes techniques and voluntary pharmacotherapy was executed. The intervention was at baseline and at several time points during a 24 month period, based on the individual patient's needs. Smoking status was collected at baseline, 6, 12, 18 and 24 months. Smoking cessation was verified by 7-days abstinence and carbon monoxide in expiratory air. The main outcome was the proportion of patients who quit smoking (QS) at 24 months.
Results: A total of 99 patients were included in the study between 2011-2020. Median (IQR) age of patients was 58 (50 - 64), 69 % were female and 82% were RF and/or ACPA positive. 59% of patients had a newly diagnosed RA, (included from the early RA-track), with a median (IQR) symptom duration of 5 (2-9,5) months. Patients with established RA 41% (included from regular rheumatology department) had a median disease duration of 4 (2-8) years. After 24 months 21% quit smoking (QS) (Table 1). At months 6, 12, 18 and 24 the proportion of QS patients was 12, 13, 15 and 21, respectively. The proportion of QS patients at month 12 and continued being in the QS group throughout the study period was 10%. In the subgroup of patients who continued smoking (CS) the median number of cigarettes per day was significantly reduced at all follow-up time points (Table 1). No significant differences were observed at baseline between CS at 24 months and QS, apart from the proportion of patients who reported anxiety (extracted from EQ-5D and defined as absent or present), which was significantly fewer in the QS group (Table). In the QS group at month 24, the proportion of females was numerically lower compared to CS (52% vs. 73%, p=0.07).

Table 1. Baseline demographical, clinical characteristics and number of cigarettes at specific time-points for patients who were non-smokers (QS) and smokers (CS) at month 24.

	QS N=21 (21%)	CS N=78 (79%)	Difference between QS and CS (p-value)
Age*(median, IQR)	60 (53-62)	57 (50-64)	0.94
Symptom duration in early RA patients (months) (median, IQR)	6 (2-12)	4.5 (2-8.5)	0.49
Disease duration of patients with established RA (years) (median, IQR)	8 (3.5-16.5)	3 (2-6)	0.12
% females	52	73	0.07
% RF and/or ACPA positive	85	81	0.70
DAS28* (median, IQR)	4.24 (3.13-5.72)	4.11 (2.88-5.36)	0.69
HAQ* (median, IQR)	0.75 (0.25 -1.38)	0.88 (0.38-1.25)	0.74
VAS pain* (median, IQR)	46.0 (11-60)	34.5 (12-70)	0.90
% of patients with reported anxiety* (part of EQ5D)	28	58	0.02
Smoking duration (years) (median, IQR)	40 (30-50)	40 (34-49)	0.92
Median number of cigarettes per day			
-at baseline	10 (7-15)	12 (10-20)	0.22
-at 6 months	0 (0-3)	6 (3-10)	0.006
-at 12 months	0 (0-5)	6 (3-10)	0.0003
-at 18 months	0 (0-0)	6 (2-10)	0.00
-at 24 months	0 (0-0)	6 (3-10)	0.00

*=measured at baseline

Conclusion: Smoking cessation intervention in a rheumatology clinic setting may facilitate reduced smoking or complete cessation in patients with RA. Patient who did not report anxiety were more likely to quit smoking.
REFERENCES:
[1] Saevarsdottir, S., et al (2011). Patients with early rheumatoid arthritis who smoke are less likely to respond to treatment with methotrexate and tumor necrosis factor inhibitors: observations from the Epidemiological Investigation of Rheumatoid Arthritis and the Swedish Rheumatology Register cohorts. *Arthritis Rheum, 63*(1), 26-36.
[2] Joseph, R´., et al (2016) Smoking-Related Mortality in Patients With Early Rheumatoid Arthritis: A Retrospective Cohort Study Using the Clinical Practice Research Datalink Arthritis Care Res (Hoboken) 68 (11) 1598-1606
Acknowledgements: This study was partly funded by grants from Swedish Reumatism Association.
Disclosure of Interests: Marie-Louise Karlsson Speakers bureau: MLK has recivied fee form Novartis Sverige AB, Grant/research support from: MLK had recivied finical grants from Novartis Sverige. Abbvie has fincial support brochure wich was used in the study, Katarina Hertzberg-Nyquist: None declared, Saedis Saevarsdottir Employee of: S is a part-time employee of deCODE genetics Inc., unrelated to this work., Ingrid E. Lundberg Consultant of: I Lundberg har recieved consulting fees from Corbus Pharmaceutical, EMD Serono Research & Development Institute, Octapharma AG, Orphazyme, Janssen, Kezar Life Sciences Inc., Ingrid Demmelmaie: None declared, Susanne Pettersson: None declared, Katerina Chatzidionysiou Consultant of: KC has received consultancy fees from Eli Lilly, AbbVie and Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.1310

OP0157-HPR

CHANGES IN PAIN AND HAND FUNCTION AFTER MULTIMODAL OCCUPATIONAL THERAPY AND/OR SURGERY IN PATIENTS WITH CARPOMETACARPAL OSTEOARTHRITIS

A. T. Tveter[1], N. Osteras[1], R. Nossum[2], R. E. Mehl Eide[3], Å. Klokkeide[4], K. Hoegh Matre[3], M. Olsen[4], I. Kjeken[1]. *[1]Diakonhjemmet Hospital, Department of Rheumatology, National advisory unit on rehabilitation in rheumatology, Oslo, Norway*; *[2]Trondheim University Hospital, St.Olavs Hospital, Clinic for Clinical Service functions, Trondheim, Norway*; *[3]Haukeland University Hospital, Department of Rheumatology, Bergen, Norway*; *[4]Haugesund Rheumatism Hospital AS, Department of Rheumatology, Haugesund, Norway*

Background: Carpometacarpal osteoarthritis (CMC1 OA) is a subset of hand OA, often leading to pain and functional limitations. The EULAR recommends conservative treatment as first-line management, and a recent study showed significant short-term effect of multimodal occupational therapy on pain and hand function in patients referred to surgical consultation[1]. However, long-term results are lacking.
Objectives: To explore the long-term effect of multimodal occupational therapy on pain and hand function in patients with CMC1 OA, and to assess the differences between those undergoing surgery or not in the two groups.
Methods: This project presents secondary analyses of a multicentre RCT. Patients referred by their general practitioner to surgical consultation due to CMC1 OA at three Norwegian hospitals from 2013-2015 were eligible. During the waiting period between referral and surgical consultation, 180 patients were randomized to usual care (information, n=90) or a 3-month multimodal occupational therapy intervention (patient education, hand exercises, orthoses and assistive devices, n=90). Patients were assessed at baseline, and 4 (before surgical consultation), 18 and 24 months. Pain at rest was assessed using a 11-point numeric rating scale, and hand function was self-reported with the MAP-Hand (1-4, 1=no problem). The long-term within- and between-group differences on pain and hand function were assessed using repeated measure ANOVA. Sub-analyses were done among those undergoing surgery or not in the two groups. P-value <0.05.
Results: 163 patients (63 (8) years, 81% women) were included in the analyses. Both groups showed a significant reduction in pain and improvement in hand function over time (p<0.001), with a significant between-group difference for pain (F (1, 161) = 8.56, p = 0.004), in favour of the intervention group, but not hand function.
After 2 years, 22 patients had undergone surgery in the intervention group vs 29 in the control group. No significant difference over time were found in pain or hand function between those undergoing surgery or not in the two groups. However, at the time of the surgical consultation, significantly higher pain (Figure 1) and poorer hand function were reported among those later undergoing surgery in the control group (p≤0.001). Surgery did not lead to further improvement in pain and hand function in the intervention group.

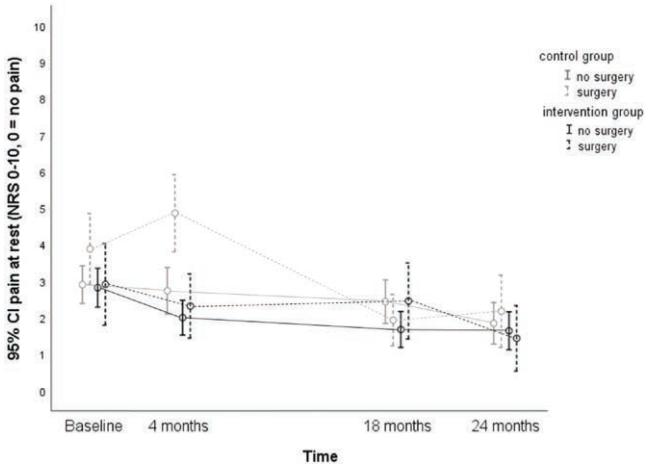


Figure 1. Between-group difference on pain over a 2-year period. The control group is marked in light grey and the intervention group in black. Those who underwent surgery are marked with dotted lines, while those who did not are marked with solid lines (n=163)

Conclusion: The results showed that the positive effect of multimodal occupational therapy on pain and hand function persisted over the 2-year period, however, no significant between-groups difference over time was found. No significant between-group differences were found when dividing into sub-groups, however, those later undergoing surgery in the control group scored significantly worse on pain and hand function at the time of surgical consultation. The results may imply that patients who would benefit from surgery were identified, and that surgery does not give an additional benefit in patients who have received multimodal occupational therapy. This needs to be further investigated.

REFERENCES:

[1] Tveter AT, Østerås N, Nossum R, Eide REM, Klokkeide Å, Hoegh Matre K, et al. Short-term effects of occupational therapy on hand function and pain in patients with carpometacarpal osteoarthritis: secondary analyses from a randomized controlled trial. *Arthritis care & research.* 2020:10.1002/acr.24543

Acknowledgements: We would like to acknowledge Øyvor Andreassen for her contribution throughout the project as a patient representative.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2857

OP0158-HPR THE FALL PREVENTION PROGRAMME 'SICHER DURCH DEN ALLTAG' IS EFFECTIVE AND COST-EFFECTIVE

K. Niedermann Schneider[1], A. Meichtry[1], B. Zindel[2], B. Brunner[3], M. Ernst[1], V. Krafft[2], R. Mattli[3], I. Nast[1], M. Wirz[1], S. Wieser[3]. *[1]Zurich University of Applied Sciences, Institute of Physiotherapy, Winterthur, Switzerland*; *[2]Swiss League Against Rheumatism, Swiss League Against Rheumatism, Zurich, Switzerland*; *[3]Zurich University of Applied Sciences, Winterthur Institute of Health Economics, Winterthur, Switzerland*

Background: Falls in older people are frequent and have often severe health consequences. Reinforced by population ageing, they represent a substantial challenge for health care systems. Falls are often due to a combination of intrinsic and extrinsic risk factors. For these reasons, the Swiss League Against Rheumatism (SLAR) developed the multidimensional, home-based fall prevention programme 'Sicher durch den Alltag' ('Safely Through Everyday Life'). The programme has been implemented nationwide since 2013 and is financed by selected health insurance companies. Trained physiotherapists (PTs) or occupational therapists (OTs) visit the senior at home for a 60-90 minutes session. They perform a detailed assessment of the senior's individual risk of falling and subsequently eliminate identified environmental risk factors and provide tailored exercises. After 4 weeks, the PT/OT calls the senior to discuss further needs. The cost of the intervention is at 500 Swiss Francs (approximately 460 Euro) per senior.

Objectives: Assess the effectiveness and cost-effectiveness of this fall prevention programme.

Methods: A prospective, longitudinal observational study was performed. Baseline study data was assessed at the home visit, including the self-reported number of falls during a) the year and b) the month before the visit. The participants of the programme were monitored for one year after the home visit by bi-monthly telephone calls. Participants were asked to report the falls that they continuously documented in a diary. Questionnaires administered orally included the Falls Efficacy Scale-International (FES-I), a Quality of Life Questionnaire (EQ-5D-5L), and the amount of moderately intensive physical activity (PA).To compare the falls during the years before and after the home visit, the mean number of falls before the visit was calculated based on reported falls during a) the year and b) the month (multiplied by 12) before the visit. A 2:1 weighted mean from a) and b) was calculated, considering that retrospective reporting over one year or over one month may underestimate or overestimate, respectively, the number of falls. Statistical analysis fitted a GEE-Poisson-Modell (Generalized Estimating Equations) to the data for number of falls and a Linear Mixed Model (LMM) for fear of falling, quality of life and PA. Falls related health care spending in the years before and after the intervention were compared based on health insurance claims data.

Results: Overall, 639 person-years of observation time were available for analysis. Participants were mainly female (59%) and had a mean age of 81.8+/- 5.2 years. On average, rate of falling decreased from 1.35 to 1.02 per person year (-23.9%), fear of falling decreased by -1.27 (95%CI -1.50, -1.05), quality of life improved by -0.88 (95%CI -1.09, -0.68), PA increased by 9.87 minutes per day (95%CI 5.65, 14.09). Health insurance claims data showed a 48.0% reduction (95%CI 30.5%, 61.0%) of medically treated falls. The average cost per prevented medically treated fall was estimated at 1317 Swiss Francs (approximately 1200 Euro) and the probability of the intervention being cost-saving at 47%.

Conclusion: This low-threshold fall prevention programme was found to be very effective and cost-effective. Home visits by trained PTs or OTs contribute substantially to reduce falls in the elderly. The high cost-effectiveness is explained by a substantial reduction of severe falls.

REFERENCES:

[1] Swiss Council for Accident Prevention BFU (2019); https://www.bfu.ch/de/die-bfu/medien/statistik-der-nichtberufsunfaelle-1. Downloaded 15 Dec. 2020.

[2] Kempen G et al. The Short FES-I: a shortened version of the falls efficacy scale-international to assess fear of falling. *Age and Ageing*, *37*(1)

[3] Herdman M et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res. 2011;20(10): 1727.

[4] Craig CL et al: International physical activity questionnaire: 12-country reliability and validity. Medicine and science in sports and exercise 2003, 35(8):1381-1395

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3453

OP0159-HPR IMPACT OF NON-PHARMACOLOGICAL INTERVENTIONS TARGETING SLEEP DISTURBANCES OR DISORDERS IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED TRIALS

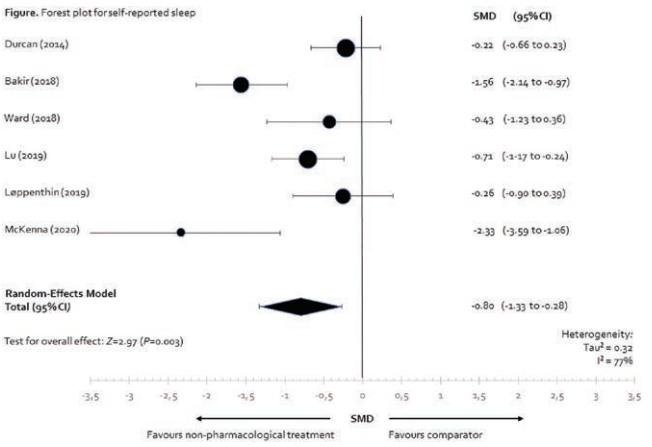
K. M. Latocha[1], K. Løppenthin[2,3], S. Al-Bazy[1], T. Albrechtsen[1], H. Jensen[1], M. Østergaard[1,3], P. Jennum[3,4], B. A. Esbensen[1,3], R. Christensen[5,6]. *[1]Rigshospitalet, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Glostrup, Denmark*; *[2]Rigshospitalet, Research Unit for Cancer Late Effect, Department of Oncology, Copenhagen, Denmark*; *[3]Copenhagen University, Department of Clinical Medicine, Faculty of Health and Medical Sciences, København, Denmark*; *[4]Rigshospitalet, Danish Center for Sleep Medicine, Department of Clinical Neurophysiology, Glostrup, Denmark*; *[5]The Parker Institute, Musculoskeletal Statistics Unit, Copenhagen, Denmark*; *[6]University of Southern Denmark, Department of Clinical Research, Faculty of Health Sciences, Odense, Denmark*

Background: Patients with inflammatory arthritis (IA) often present limitations in daily life due to unpredictability, severity and chronicity of the disease, reduced functional ability and health-related quality of life. Moreover, sleep disturbances or disorders have been reported in up to 40-90% of patients with IA [1-3]. Sleep disturbances are further associated with pain, fatigue, mental well-being and disease activity [4]. As chronic us of hypnotic drugs are associated with tolerance and side effects, there is growing interest in non-pharmacological management to improve sleep.

Objectives: With a systematic review and meta-analysis, our primary objective was to evaluate the evidence of non-pharmacological interventions targeting sleep in patients with IA. Primary outcome was sleep domains, while secondary objectives were based on the core outcome domains for IA trials and harms.

Methods: Following protocol closure, a systematic search was undertaken in MEDLINE, CENTRAL, PsycINFO, CINAHL, ClinicalTrials.gov, ACR and EULAR in September 2020. Eligible studies were randomised trials with adults with IA and concomitant sleep disturbances or disorders, comparing a non-pharmacological intervention targeting sleep disturbances or disorders to another non-pharmacological intervention, a pharmacological intervention or standard care. Screening of titles, abstracts, and subsequent full text assessment were conducted independently by two reviewers using the Covidence tool. Randomisation, blinding, and adequacy of analyses was assessed using the Cochrane's RoB tool and the overall quality of evidence was rated using GRADE methodology. Disagreements were resolved at consensus meetings with last authors. Effect sizes for continuous outcomes were based on the standardised mean difference (SMD), combined using standard random-effects meta-analysis (all with 95% CIs).

Results: Six trials (308 patients) were included in the quantitative synthesis. Two trials included patients with the sleep disorder insomnia and the remaining four trials included patients with sleep disturbances. Sleep domains were measured with Pittsburgh Sleep Quality Index (PSQI) or Insomnia Severity index (ISI). Three trials reported improvement on sleep following foot reflexology, auricular plaster therapy, and exercise. The overall meta-analysis presented in the figure of forest plot for self-reported sleep suggests that non-pharmacological interventions have a potentially large effect size of -0.80 (95% CI, -1.33 to -0.28) on sleep. However, the quality of the evidence was assessed as corresponding to low, given that the body of the evidence was rated down twice, due to serious study limitations and inconsistency.



Conclusion: Although the effect of non-pharmacological interventions targeting sleep disturbances or the sleep disorder insomnia was statistically highly significant, the implication for clinical practice is questionable because of the overall quality evidence. None of the core outcomes used in contemporary IA trials have indicated clinical benefit in favour of non-pharmacological interventions targeting sleep disturbances or disorders.

In conclusion, more rigorous research on non-pharmacological management of sleep disturbances and disorders is urgently needed, also aimed at specific sleep disorders, in order to fully reveal the clinical utility of these novel treatment options. At this point, non-pharmacological treatment of sleep disturbances or disorders is promising and potentially highly effective, and may have the potential to persistently decrease the symptom burden and increase the quality of life of patients with IA.

REFERENCES:

[1] Li et al., Psychol Health Med. 2019 Sep;24(8):911-924
[2] Haugeberg et al., Arthritis Res Ther. 2020 Aug 26;22(1):198
[3] Wali et al., J Clin Sleep Med. 2020 Feb 15;16(2):259-265
[4] Løppenthin et al., Clin Rheumatol. 2015 Dec;34(12):2029-39

Disclosure of Interests: Kristine Marie Latocha: None declared, Katrine Løppenthin: None declared, Safa Al-Bazy: None declared, Tannie Albrechtsen: None declared, Helle Jensen: None declared, Mikkel Østergaard Speakers bureau: Abbvie, Celgene, Eli-Lilly, Janssen, Novartis, Pfizer, Roche, Sanofi and UCB, Consultant of: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: Abbvie, BMS, Merck, Celgene, Novartis, Poul Jennum: None declared, Bente Appel Esbensen: None declared, Robin Christensen: None declared

DOI: 10.1136/annrheumdis-2021-eular.836

OP0160-HPR

PREFERENCES FOR TREATMENTS TO PREVENT RHEUMATOID ARTHRITIS: DISCRETE CHOICE SURVEY OF GENERAL POPULATIONS IN UNITED KINGDOM, GERMANY, AND ROMANIA

G. Simons[1], J. Veldwijk[2], R. DI Santostefano[3], M. Englbrecht[4], C. Radawski[5], L. Valor[6], K. Raza[7], M. Falahee[7]. [1]*University of Birmingham, Rheumatology Research Group, Institute of Inflammation and Ageing, Birmingham, United Kingdom*; [2]*Erasmus University Rotterdam, Erasmus School of Health Policy and Management, Rotterdam, Netherlands*; [3]*Janssen R&D, Janssen R&D, NJ, United States of America*; [4]*Freelance data scientist, Freelance data scientist, Eckental, Germany*; [5]*Eli Lilly & Company, Eli Lilly & Company, Indianapolis, United States of America*; [6]*Friedrich-Alexander-University Erlangen, Department of Internal Medicine, Erlangen, Germany*; [7]*University of Birmingham, Rheumatology Research Group, Institute of Inflammation and Ageing, Birmingham, United Kingdom*

Background: There is increasing research focus on intervention for rheumatoid arthritis (RA) at the earliest stages of disease development, including treatment to prevent RA in at-risk groups. Novel cellular therapies are in development, and the effectiveness of existing immunomodulatory agents to prevent RA in those at risk is under investigation. Quantitative evidence of likely uptake of preventive treatments, and preferences for benefits and risks of such treatments is limited.

Objectives: To quantify preferences for preventive therapies for RA.

Methods: A web-based survey (n = 2959) was administered to an age- and gender- stratified sample of adults in the general population from online survey panels in the UK, Germany, and Romania. After receiving information about RA, questions to check comprehension of background information, an introduction to the survey tasks and warm-up questions, participants were asked to imagine that they were experiencing arthralgia (without swelling) and had positive autoantibody tests indicating a 60% chance of developing RA in the next two years. Using a discrete choice experiment with a Bayesian D-efficient design, participants were offered a series of 15 choices between no treatment and two unlabeled hypothetical treatments to lower risk of RA development. Treatments were defined by six attributes with varying levels including benefits, risks, and frequency/route of administration (Table 1). One choice task with fixed levels described treatments representative of those under investigation for RA prevention (abatacept, hydroxychloroquine, atorvastatin and tolerogenic cell-based therapy). Attribute selection and presentation was informed by previous qualitative research, ranking surveys, systematic literature review, and expert opinion. Survey design was informed by patient research partners. The survey was pretested during qualitative interviews and revised. A pilot of the final survey with 100 respondents was conducted to obtain priors for the final experimental design. Random parameters logit (RPL) models were used to estimate relative importance of treatment attributes and likely treatment uptake rates in each country.

Table 1. Treatment attributes and levels

Attribute	Levels
Chance of developing RA reduced from 60% to	10%; 20%; 30%; 40%
How the treatment is taken	A shallow injection under the skin A drip into the vein One or two tablets
How often the medication has to be taken	Daily Weekly Monthly Every 6 months
Chance of mild side effects	2%; 5%; 10%
Chance of a serious infection due to treatment	0%; 1%; 5%
Chance of a serious side effect that is potentially irreversible	1 in 100,000 people 20 in 100,000 people 100 in 100,000 people

Results: Across all three countries, effectiveness was the treatment attribute that had most impact on treatment choice (Figure 1). Method of administration was second most important for respondents from the UK and Romania but less important for German respondents. Risks of serious infection and serious side effects were more important determinants of treatment choice for respondents in Romania than they were in the UK and Germany. Percentage choice of fixed profiles reflecting abatacept, atorvastatin, hydroxychloroquine, tolerogenic cell-based therapy and no treatment differed across countries (χ^2=78.90; p<0.001): 28.3%, 20.6%, 22.2% 18.5% and 10.4% respectively in the UK; 31.3%, 18.8%, 11.2%, 23.4% and 15.3% in Germany; and 27.6%, 20.5%, 15.8%, 21.7% and 14.4% in Romania.

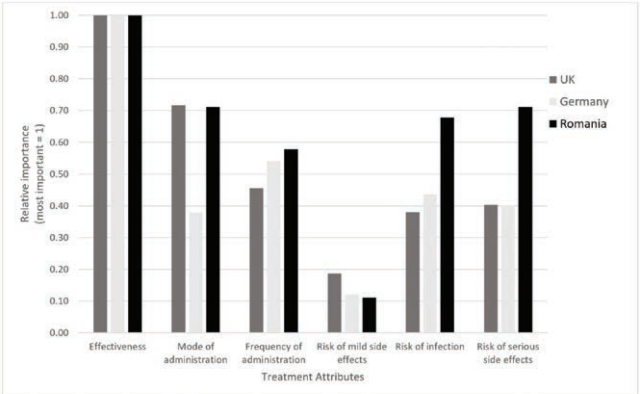


Figure 1: Relative importance of treatment attributes stratified by country; UK (N=982), Germany (N =984) and Romania (N =993). Separate RPL models were used for each country.

Conclusion: This study suggests that effective preventive treatments for RA are acceptable to members of the general population told to assume up a 60% chance of developing RA. The relative importance of treatment attributes and likely uptake of fixed treatment profiles differed across countries. These findings are informative for the design of prevention trials, and the development of informational resources and efficient preventive strategies for those at risk of developing RA.

Acknowledgements: On behalf of the PREFER project. PREFER received funding from the IMI 2 Joint Undertaking (grant No. 115966), which receives support from the EU's Horizon 2020 research and innovation program and European Federation of Pharmaceutical Industries and Associations (EFPIA). K. Raza is supported by the NIHR Birmingham Biomedical Research Centre.

Disclosure of Interests: Gwenda Simons: None declared, Jorien Veldwijk: None declared, Rachael Di Santostefano Shareholder of: Johnson & Johnson, Employee of: Janssen R&D (of Johnson & Johnson), Matthias Englbrecht Speakers bureau: AbbVie, Chugai, Eli Lilly, Novartis, Roche, Sanofi, Mundipharma, Paid instructor for: AbbVie, Chugai, Roche, Consultant of: AbbVie, Novartis, Roche, Sanofi, Grant/research support from: Roche, Chugai, Christine Radawski Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, Larissa Valor: None declared, Karim Raza Consultant of: Personal fees from Abbvie, Pfizer, Sanofi, Lilly, Bristol Myers Squibb, UCB, Janssen, and Roche Chugai, Grant/research support from: Abbvie and Pfizer, M. Falahee: None declared
DOI: 10.1136/annrheumdis-2021-eular.2168

Advances in Pediatric Rheumatology

OP0161 PREDICTIVE VALUE OF MUSCULOSKELETAL ULTRASOUND IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN CLINICAL REMISSION

M. Mazzoni[1], S. Merlo[1,2], C. Morreale[1,2], A. Pistorio[3], S. Viola[2], S. Ancona[1,2], F. Magnaguagno[4], A. Consolaro[1,2], A. Ravelli[1,2], C. Malattia[1,2]. *[1]Università degli Studi di Genova, Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili, Genoa, Italy*; *[2]IRCCS Istituto Giannina Gaslini, Clinica Pediatrica e Reumatologia, Genoa, Italy*; *[3]IRCCS Istituto Giannina Gaslini, Epidemiologia e Biostatistica, Genoa, Italy*; *[4]IRCCS Istituto Giannina Gaslini, UOC Radiologia, Genoa, Italy*

Background: The accurate assessment of remission status in JIA patients is of utmost relevance to taper medications and prevent side effects from their long-term administration. In RA patients in clinical remission (CR), musculoskeletal ultrasound (MSUS) allows to detect persistent joint inflammation (subclinical synovitis), which predicts disease flare and structural damage progression. Although subclinical synovitis has been reported in a substantial proportion of JIA patients with inactive disease, its prognostic value is still being defined.
Objectives: 1) to investigate the prevalence of MSUS-detected subclinical synovitis in JIA patients in CR; 2) to establish which and how many joints should be scanned to reliably assess remission; 3) to evaluate the persistence of subclinical synovitis over the time; 4) to investigate whether subclinical synovitis entails a risk of disease flare and whether it should affect the therapeutic strategy.
Methods: 135 consecutive JIA patients who met the Wallace criteria for CR were included in this 3-years prospective study. All patients underwent MSUS assessment of 56 joints at study entry and at 6 months follow-up visit. Joints were scanned for synovial hyperplasia, joint effusion and Power Doppler (PD) signal by two independent ultrasonographers. Patients were followed clinically for 3 years. A flare of synovitis was defined as a recurrence of clinically active arthritis. The association between clinical and MSUS variables with flare, was evaluated by adjusted logistic regression models.
Results: 135 patients (78.5% F; median age 11.3 y; median disease duration 5.7 y; median CR duration 1.4 y) were included. Fifty-seven/135 (42.2%) patients had persistent oligoarthiritis; 41/135 (30.4%) extended oligoarthiritis; 32/135 (23.7%) polyarthiritis; 5/135 (3.7%) systemic arthritis. Seventy-eight/135 (57.7%) patients were in CR on medication. Subclinical synovitis was detected in 32/135 (23.7%) patients and in 53/7560 (0.7%) joints. Subclinical tenosynovitis was present in 20/135 (14.8%) patients. Subclinical synovitis was found more frequently in the ankle and wrist joints. 58.6% of patients showed persistent subclinical synovitis at 6 month follow up MSUS examination. During the 3-year follow up 45/135 (33.3%) patients experienced a disease flare (median survival time 2.2 y). PD positivity in tendons was the stronger independent risk factor of flare on multivariable regression analysis (HR: 4.8; P=0.04). Other predictors of flare were the JIA subtype (oligo-extended form: HR: 2.3; P=0.031) and the status of CR on medication (HR: 3.7; P=0.002).
Conclusion: our results confirm that MSUS is more sensitive than clinical evaluation in the assessment of persistent synovial inflammation in JIA patients. Subclinical tenosynovitis was the best predictor of disease flare. To date, the role of tenosynovitis in the diagnosis and prognosis of JIA has been poorly investigated. Our results further support the role of MSUS, especially of the wrist and the ankle, in monitoring JIA patients in clinical remission and to predict disease flare.
REFERENCES:

[1] De Lucia O, et al. Baseline ultrasound examination as possible predictor of relapse in patients affected by juvenile idiopathic arthritis (JIA). Ann Rheum Dis. 2018 Oct;77(10):1426-1431.
[2] Filippou G, et al. The predictive role of ultrasound-detected tenosynovitis and joint synovitis for flare in patients with rheumatoid arthritis in stable remission. Results of an Italian multicentre study of the Italian Society for Rheumatology Group for Ultrasound: the STARTER study. Ann Rheum Dis 2018;77:1283-9.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3823

OP0162 ETANERCEPT RESPONSE CLUSTERS IN JUVENILE IDIOPATHIC ARTHRITIS

S. Shoop-Worrall[1,2], K. Hyrich[1,3], L. Wedderburn[4,5,6], W. Thomson[3,7], N. Geifman[2]on behalf of BSPAR-ETN Study, BCRD Study, CAPS, CHARMS, CLUSTER. *[1]The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; *[2]The University of Manchester, Centre for Health Informatics, Manchester, United Kingdom*; *[3]Manchester University NHS FT, Manchester Academic Health Science Centre, NIHR Manchester BRC, Manchester, United Kingdom*; *[4]UCL Great Ormond Street Institute of Child Health, Centre for Adolescent Rheumatology Versus Arthritis, London, United Kingdom*; *[5]Great Ormond Street Hospital NHS Foundation Trust, Paediatric Rheumatology, London, United Kingdom*; *[6]Great Ormond Street Biomedical Research Centre, NIHR, London, United Kingdom*; *[7]The University of Manchester, Centre for Genetics and Genomics Versus Arthritis, Manchester, United Kingdom*

Background: In children and young people (CYP) with JIA, we have previously identified clusters with different patterns of disease impact following methotrexate (MTX) initiation. It is unclear whether clusters of treatment response following etanercept (ETN) therapy exist and whether, in a group of CYP who have responded inadequately to or had adverse events on methotrexate, similar treatment response patterns exist. Novel response patterns would aid stratified treatment approaches through better understanding and potential forecasting of more specific response patterns across multiple domains of disease.
Objectives: To identify and characterise trajectories of juvenile arthritis disease activity score (JADAS) components following ETN initiation for JIA.
Methods: ETN-naïve CYP with non-systemic JIA were selected if enrolled prior to January 2019 in at least one of four CLUSTER consortium studies: BSPAR-ETN, BCRD, CAPS and CHARMS, at point of starting ETN as their first biological therapy. JADAS components (active joint count, physician's global assessment (0-10cm), parental global evaluation (0-10cm) and standardised ESR (0-10) were collected at ETN initiation and during the following year.
Multivariate group-based trajectory models, that identify clusters of CYP with similar patterns of change over time, were used to explore ETN response clusters across the different JADAS components. Censored-normal (global scores, ESR) and zero-inflated Poisson (active joint count) models were used, adjusting for year of ETN initiation. Optimal models were selected based on a combination of model fit (BIC), parsimony, and clinical plausibility.
Results: Of the 1003 CYP included, the majority were female (70%) and of white ethnicity (90%), with rheumatoid factor-negative JIA the most common disease category (39%).
The optimal model identified five trajectory clusters of disease activity following initiation of ETN (Figure 1). Clusters following ETN were similar and covered similar proportions of CYP to those previously identified following MTX: Fast (Group 1: 13%) and Slow (Group 2: 10%) response, active joint count improves but either physician (Group 3: 6%) or parent global scores (Group 4: 34%) remain persistently raised and a group with persistent raised scores across all JADAS components (Group 5: 36%). Compared to the persistent disease cluster, those with greater improvement had lower age and higher functional ability at ETN initiation and those with persistent raised parent global scores had lower ESR levels and were less likely to be RF-positive at ETN initiation.

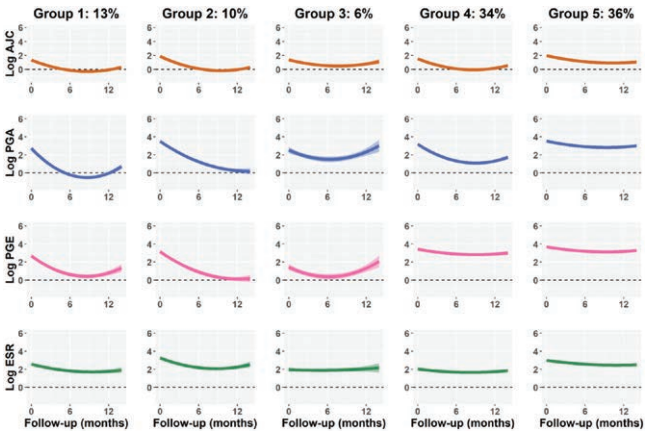


Figure 1. Clusters identified following ETN initiation in children and young people recruited to the UK BSPAR-ETN, BCRD, CAPS and CHARMS studies.

Conclusion: This study has identified that within CYP initiating ETN, similar response clusters are evident to those previously identified following MTX. This commonality suggests a new framework for understanding treatment response, beyond a simple responder/non-responder analysis at a set point, which applies across multiple drugs despite different mechanisms of action and previous unfavourable treatment outcomes. Understanding both clinical factors associated with, and biological mechanisms underpinning, these clusters would aid stratified medicine in JIA.

Acknowledgements: We thank the children, young people and families involved in CLUSTER, as well as clinical staff, administrators and data management teams. Funding for CLUSTER has been provided by generous grants from the MRC, Versus Arthritis, GOSH children's charity, Olivia's vision and the NIHR Manchester and GOSH BRC schemes.

Disclosure of Interests: Stephanie Shoop-Worrall: None declared, Kimme Hyrich Speakers bureau: Abbvie, Grant/research support from: BMS, UCB, Pfizer, Lucy Wedderburn Speakers bureau: Pfizer, Grant/research support from: Abbvie, Sobi, Wendy Thomson Grant/research support from: Abbvie, Sobi, Nophar Geifman Grant/research support from: Abbvie, Sobi

DOI: 10.1136/annrheumdis-2021-eular.2505

OP0163 COMPARATIVE ANALYSIS OF ETANERCEPT BIOSIMILAR AND ORIGINATOR USE IN CLINICAL PRACTICE: DATA FROM THE GERMAN BIKER-REGISTRY

G. Horneff[1], D. Windschall[2], T. Hospach[3], S. Mrusek[4], M. Rühlmann[5], A. Klein[1]on behalf of BIKER-Registry collaborative group. [1]*Sankt Augustin, Paediatrics, Sankt Augustin, Germany*; [2]*Sendenhorst, Paediatric Rheumatology, Sendenhorst, Germany*; [3]*Klinikum Stuttgart - Olga Hospital / Women's Hospital, Paediatrics, Stuttgart, Germany*; [4]*Baden-Baden, Paediatric rheumatology, Baden-Baden, Germany*; [5]*Göttingen, Paediatrics, Göttingen, Germany*

Background: In 2017, 2 Etanercept biosimilars became approved. Comparative studies performed in adult patients with rheumatoid arthritis, ankylosing spondylitis or psoriasis by extrapolation led to approval for juvenile idiopathic arthritis (JIA).

Objectives: So far there is limited experience with Etanercept biosimilars in JIA: The large national data base of the BIKER-registry was used to describe experience with Etanercept biosimilars in clinical practice.

Methods: In this retrospective analysis patients exposed to ETA were identified in the German BIKER-registry and grouped into cohorts according to initiation of treatment after 2017, use of the originator and of biosimilars. The course of JADAS10, Physician global assessment VAS 0–100-mm, Parent/patient global assessment VAS 0–100-cm, Active joint count 0-71, truncated at 10, ESR and CHAQ-DI was analyzed. Descriptive statistics was used for demographic, clinical data, drug exposure, adverse events (AEs) and events of special interest (ESI).

Results: Until 31.10.2020, 2917 JIA patients were reported to have received Etanercept. Since January 1 2017, in 39 centres treatment with Etanercept was started in 439 patients (377 (85.9%) started with the originator and 62 (14.1%) started a Biosimilar). Biosimilars were prescribed n 17 centres (44%). In 12 centres (31%), Etanercept biosimilars were used first line in 62 patients. In 17 centres (44%), 63 patients switched for the originator to a biosimilar. 3 patients reswitched from the biosimilar to the originator. 4 patient switched from a biosimilar to the originator). 22 centres (56%) had not prescribed a biosimilars so far.

In not a single centre, initiation of a biosimilar was more frequent than of the originator.

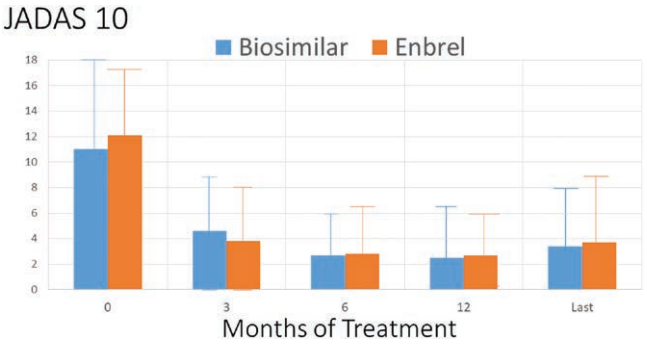
The patients' characteristics and disease activity parameters were widely comparable. Patients receiving biosimilar first line were slightly older at disease onset and had a longer disease duration. Patients receiving biosimilar first line had more often rheumatoid factor (RF) negative polyarthritis while extended oligoarthritis was more frequent in the originator cohort. In the switching cohort, more patients had extended oligoarthritis and fewer had RF negative polyarthritis and ERA JIA.

No difference in disease activity parameters was noted, neither at baseline, during the course of treatment nor at last observation upon treatment. A decrease of the JADAS10 indicates improvement in both groups (Figure 1). At the time of switching, 68% had JADAS minimal disease activity (MDA) and 43% were in JASDAS remission. At month 6 and 12 these numbers increased to 74%/65% and 62%/50%.

In total, 66 adverse events (AE) were reported in 45 patients upon biosimilar treatment.

33 patients had 1, 5 patients 2, 5 patients had 3 and 2 reported 4 events. Adverse event of special interest were hypersensitivity n=1, injection site reaction n=1, new onset of psoriasis n=1, celiac disease n=1, Crohn's diesease n=1, elevated transaminases n=2, depression n=1 and disease deterioration (arthritis flare) in n=21. In 20 patients, the etanercept biosimilar was discontinued.

Conclusion: This analysis is the first attempt to present a large data sample on JIA patients exposed to Etanercept biosimilars. Biosimilar were used in a minority of patients and by a minority of centers although no difference in efficacy or safety was noted from our analysis. Until today, the use of the originator is by far exceeding the use of biosimilars. The prescription of a biosimilar either first line or by switching from the originator is limited to a part of centres. Differences in efficacy between first line biosimilar users and originator users could not be observed. Also, after switching, no loss of efficacy was observed.



Disclosure of Interests: Gerd Horneff Speakers bureau: Pfizer, Daniel Windschall: None declared, Toni Hospach: None declared, Sonja Mrusek: None declared, Michael Rühlmann: None declared, Ariane Klein: None declared

DOI: 10.1136/annrheumdis-2021-eular.1003

OP0164 LONG-TERM SAFETY OF ANAKINRA IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS FROM THE PHARMACHILD REGISTRY

G. Giancane[1,2], R. Papa[1,2], S. Vastert[3], F. Bagnasco[4], J. F. Swart[3], P. Quartier[5], M. Hofer[6,7], J. Anton[8], S. Kamphuis[9], H. Sanner[10], M. Glerup[11], F. De Benedetti[12], E. Tsitsami[13], A. Remesal[14], E. Moreno Ruzafa[15], J. De Inocencio[16], C. Myrup[17], C. Pallotti[1], I. Koné-Paut[18], K. Franck-Larsson[19], H. Malmstrom[19], S. Cederholm[19], A. Pistorio[4], N. Wulffraat[3], N. Ruperto[1]. [1]*IRCCS Istituto Giannina Gaslini, Clinica Pediatrica e Reumatologia, Genoa, Italy*; [2]*Università degli Studi di Genova, Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DiNOGMI), Genoa, Italy*; [3]*Wilhelmina Kinderziekenhuis, Department of Pediatric Immunology and Rheumatology, Utrecht, Netherlands*; [4]*IRCCS Istituto Giannina Gaslini, Servizio di Epidemiologia e Biostatistica, Genoa, Italy*; [5]*Université de Paris, Institut IMAGINE, Centre de référence national pour les Rhumatismes inflammatoires et les maladies Auto-Immunes Systémiques rares de l'Enfant (RAISE), Unité d'Immunologie, Hématologie et Rhumatologie Pédiatrique, Hôpital Necker-Enfants Malades, Assistance Publique Hôpitaux de Paris, Paris, France*; [6]*Unité Romande d'Immuno-Rhumatologie Pediatrique, CHUV, University of Lausanne, Lausanne, Switzerland*; [7]*Unité Romande d'Immuno-Rhumatologie Pediatrique, University Hospital of Geneva, Geneva, Switzerland*; [8]*Hospital Sant Joan de Déu, Universitat de Barcelona, Division of Pediatric Rheumatology, Esplugues de Llobregat (Barcelona), Spain*; [9]*Sophia Children's Hospital, Department of Paediatric Rheumatology/Department of Rheumatology, Erasmus University Medical Centre, Rotterdam, Netherlands*; [10]*Oslo University Hospital, Dept. of Rheumatology - Norwegian National Advisory Unit on Rheumatic Diseases in Children and Adolescents, Oslo, Norway*; [11]*Aarhus University Hospital, Pediatric Rheumatology Unit, Aarhus, Denmark*; [12]*IRCCS Ospedale Pediatrico Bambino Gesù, Division of Rheumatology, Rome, Italy*; [13]*Aghia Sophia Childrens Hospital, First Department of Pediatrics, University of Athens Medical School, Athens, Greece*; [14]*University Hospital La Paz, Rheumatology Unit, Madrid, Spain*; [15]*University Hospital Valle de Hebron, Rheumatology Unit, Barcelona, Spain*; [16]*12 de Octubre University Hospital, Department of Pediatric Rheumatology, Madrid, Spain*; [17]*Rigshospitalet, Pediatric Rheumatology Unit, Copenhagen, Denmark*; [18]*National Referral Centre of Auto-Inflammatory Diseases and inflammatory amyloidosis, CEREMAIA, CHU de Bi¢etre, APHP, University of Paris Sud Saclay, Department of Pediatric Rheumatology, le Kremlin Bicêtre, Paris, France*; [19]*SOBI, Swedish, Stockholm, Sweden*

Background: Systemic juvenile idiopathic arthritis (SJIA) is characterized by extra-articular manifestations, as fever and rash, and rarely associated by a potentially lethal complication as macrophage activation syndrome (MAS). Anakinra is a recombinant human interleukin (IL)-1 receptor antagonist whose efficacy and safety profile has been studied for patients with SJIA.

Objectives: To evaluate the long-term safety profile of anakinra in patients with SJIA.

Methods: Data from patients with SJIA enrolled in the Pharmachild registry before 30 September 2018 and treated with anakinra were analyzed. The study

endpoints were the occurrence of non-serious adverse events (AEs) of at least moderate severity and serious AEs (SAEs), including macrophage activation syndrome (MAS), and the duration of anakinra treatment with reasons for discontinuation. All endpoints were analyzed overall, by 6 month-time windows and in different treatment sets represented by those patients continuously treated with anakinra for at least 12, 18 and 24 months (set-12, -18, -24, respectively).
Results: 306 patients were enrolled. 46%, 34% and 28% of them had been treated for at least 12, 18 and 24 months, respectively. 201 AEs, mostly represented by infections, were reported for 509.3 patient-years (py) with an overall incidence rate (IR) of 39.5/100 py. Among 56 SAEs (IR 11.0/100 py), (Table 1) 23.2% were infections and 19.6% MAS episodes. The IR of AEs was higher during the first 6 months of anakinra, followed by decreasing IR in the different long-term treatment sets. Treatment discontinuation occurred in 76% of patients, most in the first 6 months, due to inefficacy (43%), remission (31%) or AEs/intolerance (15%). No deaths or malignancies occurred during anakinra treatment.

Table 1. Number of SAEs and incidence rates (95% CI) by overall PT decreasing order and time window in the complete set (events with a frequency >1 by overall SOC and >1 by overall PT were reported) Only time windows <13 months were reported in the present table.

	Time window	1-6 months		7-12 months		Overall	
	N	306		194		306	
	Patient-time (years)	117.3		80.2		509.3	
SOC	PT	n	Rate (95% CI)	n	Rate (95% CI)	n	Rate (95% CI)
All	All	33	28.1 (19.1-41.5)	4	5.0 (1.9-13.2)	56	11.0 (7.9-15.2)
Infections and infestations	All	7	6.0 (2.9- 12.4)	1	1.2 (0.2- 8.8)	13	2.6 (1.4- 4.8)
	Pneumonia	2	1.7 (0.4- 6.8)	1	1.2 (0.2- 8.8)	4	0.8 (0.3- 2.1)
Immune system disorders	All	7	6.0 (2.8- 12.5)	1	1.2 (0.2- 8.8)	11	2.2 (1.1- 4.1)
	Haemophagocytic lymphohistiocytosis	7	6.0 (2.8- 12.5)	1	1.2 (0.2- 8.8)	11	2.2 (1.1- 4.1)
Injury, poisoning and procedural complications	All	5	4.3 (1.8- 10.2)	-	-	9	1.8 (0.9- 3.4)
	Infusion related reaction	1	0.9 (0.1- 6.0)	-	-	2	0.4 (0.1- 1.6)
	Injection related reaction	4	3.4 (1.3- 9.1)	-	-	6	1.2 (0.5- 2.6)
Metabolism and nutrition disorders	All	3	2.6 (0.8- 7.9)	-	-	4	0.8 (0.3- 2.1)
Skin and subcutaneous tissue disorders	All	3	2.6 (0.8- 7.9)	1	1.2 (0.2- 8.8)	4	0.8 (0.3- 2.1)
Blood and lymphatic system disorders	All	1	0.9 (0.1- 6.1)	-	-	2	0.4 (0.1- 1.6)
General disorders and administration site conditions	All	1	0.9 (0.1- 6.1)	1	1.2 (0.2- 8.8)	2	0.4 (0.1- 1.6)
Investigations	All	2	1.7 (0.4- 6.8)	-	-	2	0.4 (0.1- 1.6)
Nervous system disorders	All	1	0.9 (0.1- 6.0)	-	-	2	0.4 (0.1- 1.6)
Surgical and medical procedures	All	1	0.9 (0.1- 6.0)	-	-	2	0.4 (0.1- 1.5)

Abbreviations: SAE, serious adverse event; SOC, system organ class; PT, preferred term, MedDRA version 21.1; N, number of patients ever treated with anakinra during the time window irrespectively of the length of any unexposed periods; 95% CI, 95% Confidence Interval.

Conclusion: The results of the present study confirm the long-term safety profile of anakinra in SJIA patients and show a decreasing overall incidence rate of AEs over time.
Disclosure of Interests: Gabriella Giancane Grant/research support from: The study was funded by SOBI Swedish, Riccardo Papa Grant/research support from: The study was funded by SOBI Swedish, Sebastian Vastert Grant/research support from: The study was funded by SOBI Swedish, Francesca Bagnasco Grant/research support from: The study was funded by SOBI Swedish, Joost F. Swart Grant/research support from: The study was funded by SOBI Swedish, Pierre Quartier Grant/research support from: The study was funded by SOBI Swedish, michael hofer Grant/research support from: The study was funded by SOBI Swedish, Jordi Anton Grant/research support from: The study was funded by SOBI Swedish, Sylvia Kamphuis Grant/research support from: The study was funded by SOBI Swedish, Helga Sanner Grant/research support from: The study was funded by SOBI Swedish, Mia Glerup Grant/research support from: The study was funded by SOBI Swedish, Fabrizio De Benedetti Grant/research support from: The study was funded by SOBI Swedish, Elena Tsitsami Grant/research support from: The study was funded by SOBI Swedish, Agustin Remesal Grant/research support from: The study was funded by SOBI Swedish, Estefania Moreno Ruzafa Grant/research support from: The study was funded by SOBI Swedish, Jaime de Inocencio Grant/research support from: The study was funded by SOBI Swedish, Charlotte Myrup Grant/research support from: The study was funded by SOBI Swedish, Chiara Pallotti Grant/research support from: The study was funded by SOBI Swedish, Isabelle Koné-Paut Grant/research support from: The study was funded by SOBI Swedish, Karin Franck-Larsson Employee of: I am employee of SOBI pharmaceutical company, Hakan Malmstrom Employee of: I am employee of SOBI pharmaceutical company, Susanna Cederholm Employee of: I am employee of SOBI pharmaceutical company, Angela Pistorio Grant/research support from: The study was funded by SOBI Swedish, Nico Wulffraat Grant/research support from: The study was funded by SOBI Swedish, Nicolino Ruperto Speakers bureau: NR has received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, Astrazeneca-Medimmune, Bayer, Biogen, Boehringer, Bristol Myers and Squibb, Celgene, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche,Janssen, Merck, Novartis, Pfizer, R-Pharma, Sinergie, Sobi and UCB., Consultant of: NR has received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, Astrazeneca-Medimmune, Bayer, Biogen, Boehringer, Bristol Myers and Squibb, Celgene, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche,-Janssen, Merck, Novartis, Pfizer, R-Pharma, Sinergie, Sobi and UCB., Grant/research support from: The IRCCS Istituto Giannina Gaslini (IGG), where NR works as full-time public employee has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmith-Kline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties.
DOI: 10.1136/annrheumdis-2021-eular.1731

OP0165 RISK FOR UVEITIS EVENTS AFTER WITHDRAWAL OF DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN THE TREATMENT OF PATIENTS WITH EXTENDED OLIGOARTHRITIS OR RHEUMATOID FACTOR NEGATIVE POLYARTHRITIS

J. Klotsche[1], A. Klein[2], M. Niewerth[1], T. Kallinich[3], D. Windschall[4], J. P. Haas[5], F. Weller-Heinemann[6], T. Hospach[7], F. Dressler[8], K. Minden[1], G. Horneff[2]. *[1]German Rheumatism Research Centre Berlin, a Leibniz Institute, Epidemiology unit, Berlin, Germany*; *[2]Asklepios Kinderklinik Sankt Augustin, Department of General Pediatrics, Sankt Augustin, Germany*; *[3]Charité - Universitätsmedizin Berlin, Pediatric Pneumology and Immunology, Berlin, Germany*; *[4]St Josef-Stift Sendenhorst, Kinder- und Jugendrheumatologie, Sendenhorst, Germany*; *[5]Deutsches Zentrum für Kinder- und Jugendrheumatologie, Kinder- und Jugendrheumatologie, Garmisch-Partenkirchen, Germany*; *[6]Klinikum Bremen-Mitte gGmbH, Prof.-Hess-Kinderklinik, Bremen, Germany*; *[7]Olgahospital Stuttgart, Department of Paediatric Rheumatology, Stuttgart, Germany*; *[8]Medizinische Hochschule Hannover, Kinderklinik, Hannover, Germany*

Background: Juvenile idiopathic arthritis (JIA) associated uveitis is an extra-articular manifestation of the JIA disease that may cause vision-threatening complications and an uncontrolled uveitis may even lead to blindness. Uveitis occurs in up to 20% of patients with JIA, depending on the JIA category. The majority of patients develop uveitis within the first two years after JIA symptom onset, but uveitis can continue into adulthood.
Objectives: The main objective of this study was to analyze the risk for uveitis events after discontinuing disease-modifying antirheumatic drugs (DMARD) in patients with extended oligoarthritis and rheumatoid factor (RF)-negative polyarthritis.
Methods: Data of the two ongoing multicenter biologic registers: German Biologics in Pediatric Rheumatology (BiKeR) and the Juvenile arthritis Methotrexate/Biologics long-term Observation (JuMBO) were used to analyze the adverse-event (AE) and events of special interest (ESI) reports about uveitis events during treatment and after discontinuation of DMARDs. Biker started recruitment of children and adolescent patients with JIA exposed to biological (b) or conventional (cs) DMARD's in 2001. The patients were further followed in JuMBO after reaching the age of 18 or transitioning to an adult rheumatologist. Disease characteristics, treatment data, AE's and ESI's were reported by the pediatric or adults rheumatologist, respectively.
Results: A total of 2,041 patients with RF-negative polyarthritis (n=1,280) or extended oligoarthritis (n=761) were included into the analyses. The mean follow-up of this study was 7.6 years (SD 5.3). About half of the patients were enrolled in BiKeR with start of etanercept (1,137, 55.7%), followed by 635 (31.1%) patients with start of methotrexate (MTX) monotherapy or adalimumab (ADA, n=198, 9.7%). A history of uveitis was reported for 238 (11.7%) patients

at enrolment in BiKeR. More patients with a history of uveitis treated with ADA were included in BiKeR initiating ADA (n=98 of 238, 41.2%). Patients with uveitis had a lower age at JIA onset in comparison to patients without uveitis (mean 3.6 (SD 3.0) versus 7.0 (SD 4.5) years). A total of 142 recurrent (84% of 169) uveitis events were reported in 93 patients and for 27 patients (1.3% of 2,041) was an incident uveitis reported during follow-up. More than one uveitis event was reported for 32 patients with a maximum number of 4 uveitis flares in 3 patients. Nineteen uveitis flares (11.2% of 169) were reported for patients after the age of 18. The longer the time since DMARD discontinuation the fewer uveitis events occurred. Uveitis events were significantly more often reported in the first 24 months after MTX discontinuation (<6 months: OR=3.19, 95%CI: 1.70 to 5.96; 6 to <12 months: OR=2.06, 95%CI: 1.01 to 4.66; 12 to <24 months: OR=2.20, 95%CI: 1.14 to 4.25) and in the first three months after biological DMARD discontinuation (OR=5.4, 95%CI: 1.56 to 18.33). Patients with a MTX dose of ≤ 10 mg/m^2 at last MTX intake had a higher likelihood for uveitis events (OR=1.40, 95%CI: 1.02 to 1.92).

Conclusion: This is the first study that analyzed the risk of uveitis after DMARD withdrawal. Uveitis relapses are common. Patients who discontinued DMARD therapy were at high risk for uveitis within the first 3 to 24 months after discontinuation. Rheumatologists and ophthalmologists should be aware about this risk which should lead to a regular uveitis screening after DMARD withdrawal.

Disclosure of Interests: Jens Klotsche: None declared, Ariane Klein: None declared, Martina Niewerth: None declared, Tilmann Kallinich: None declared, Daniel Windschall: None declared, Johannes-Peter Haas: None declared, Frank Weller-Heinemann Speakers bureau: Pfizer, Abbvie, SOBI, Roche, Novartis, Toni Hospach: None declared, Frank Dressler: None declared, Kirsten Minden: None declared, Gerd Horneff: None declared

DOI: 10.1136/annrheumdis-2021-eular.4014

OP0166 DISEASE ACTIVITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS AFTER SIMULTANEOUS PCV13 AND HIB VACCINATION: A COHORT STUDY

O. Lomakina[1], E. Alexeeva[1,2], T. Dvoryakovskaya[1], K. Isaeva[1], A. Chomakhidze[1], R. Denisova[1], A. Mamutova[1], A. Fetisova[1], M. Gautier[1], K. Chibisova[1], D. Vankova[1], E. Krekhova[1,2], M. Shingarova[2], I. Kriulin[1,2], I. Tsulukiya[1], I. Zybkova[1], N. Tkachenko[1]. *[1]National Medical Research Center of Children's Health, Department of Rheumatology, Moscow, Russian Federation*; *[2]Sechenov First Moscow State Medical University (Sechenov University), Pediatrics and pediatric rheumatology, Moscow, Russian Federation*

Background: The safety of vaccination of children with rheumatic diseases is determined not only by the risk of adverse events but also by the risk of exacerbation of the disease. The simultaneous administration of several vaccines can increase the likelihood of these events.

Objectives: To evaluate the clinical and laboratory signs of disease activity in children with juvenile idiopathic arthritis (JIA) after simultaneous vaccination against pneumococcal and Haemophilus influenzae type b (Hib) infections.

Methods: We included hospitalized patients with JIA ages 2 through 18 without serious comorbidity, immunized with polysaccharide conjugate vaccines against pneumococcal (PCV13) and Hib infections. Vaccines were administered (0.5 ml each) concurrently subcutaneously into the deltoid area. In all children before and 3 weeks after vaccination, clinical (joints with active arthritis, uveitis activity) and laboratory signs (increased ESR, concentrations of highly sensitive C-reactive protein – hsCRP, and calprotectin) of JIA activity were assessed. Serum hsCRP and calprotectin were quantified by ELISA. The upper limit of the reference interval for hsCRP was considered (according to the manufacturer's instructions) a value of 8.2 mg/L, for calprotectin – 2.9 µg/ml, and for ESR – > 10 mm/h.

Results: The study included 430 patients with JIA (girls 60.9%), median (IQR) age – 11.1 years (7.3 to 14.4), onset of JIA – 4.7 years (2.4 to 8.6). Patients with persistent oligoarticular JIA numbered 149 (34.7%), polyarticular RF-negative – 148 (34.4%), systemic – 101 (23.4%), enthesitis-related – 20 (4.7%), and polyarticular RF-positive JIA – 12 (2.8%). Biologic disease-modifying antirheumatic drugs (DMARDs) were administered to 278 (64.7%), non-biologic DMARDs (mostly methotrexate) – 282 (65.6%), corticosteroids – 45 (10.5%), and NSAIDs – 18 (4.2%) patients. Three weeks after vaccination, out of 100 (23.3%) patients with initially active joints, signs of active arthritis remained in 96 patients, of which 16 patients had a decrease in the median (IQR) number of active joints by 4 (2 to 8). Among patients without active joints at baseline, signs of active arthritis were not subsequently detected. Before vaccination, 9 patients had uveitis in the exacerbation phase, 7 - in the subactive phase, and 41 - in the remission phase. After vaccination, exacerbation of uveitis persisted in 4 patients. There were no new cases of uveitis or its exacerbation. The dynamics of laboratory signs of JIA activity are presented in Table 1. Initially, the high concentration of calprotectin was found in 191 (44.4%) patients, and after vaccination – in 220 (51.2%) patients; the difference was 6.7% (95% CI 1.0 - 12.5); hsCRP - in 34 (7.9%) and 51 (11.9%) patients; the difference was 4.0% (95% CI 0.6 - 7.3); high ESR – in 76 (17.7%) and 41 (9.5%) patients; the difference was -8.1% (95% CI -11.6 to -4.7), respectively. An independent predictor of new cases of high concentration of hsCRP (n = 36), but not new cases of high concentration of calprotectin (n = 94), was the initial number of joints with active arthritis – odds ratio 2.37 (95% CI 1.14 - 4.93).

Table 1. Laboratory signs of JIA activity after simultaneous administration of vaccines against pneumococcal (PCV13) and Hib-infections

	Baseline	After 3 weeks		
Variables	Geometric mean (95% CI)		**Ratio***	**p****
Calprotectin, µg/ml	2.93 (2.70 – 3.17)	3.15 (2.92 – 3.40)	1.08 (0.99 – 1.17)	0.087
hsCRP, mg/L	0.69 (0.60 – 0.78)	0.79 (0.69 – 0.90)	1.15 (0.99 – 1.33)	0.073
ESR, mm/h	4.4 (4.0 – 4.8)	3.7 (3.4 – 4.0)	0.84 (0.78 – 0.90)	0.001

Note. CI – confidence interval. * Ratios of paired observations (95% CI). ** P-value calculated in paired samples t-test.

Conclusion: Simultaneous vaccination against pneumococcal (PCV13) and Hib-infections in children with JIA produced no negative dynamics of the traditional indicators of disease activity (joint activity, uveitis, high ESR). At the same time, 3 weeks after vaccination, an increase in the concentration of calprotectin and hsCRP was found in a small number of patients (<10%).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3457

OP0167 THE ROLE OF LUNG ULTRASOUND IN THE DIAGNOSIS OF INTERSTITIAL LUNG DISEASE IN CHILDREN WITH DERMATOMYOSISTIS

R. Dertkgil[1], C. Cappello[1], S. Dertkigil[1], R. Marini[2], S. Appenzeller[3]. *[1]UNICAMP, Radiology, Campinas, Brazil*; *[2]UNICAMP, Pediatrics, Campinas, Brazil*; *[3]UNICAMP, Orthopedics, Rheumatology and Traumatology, Campinas, Brazil*

Background: Dermatomyositis is a multi organ autoimmune disease wich is commonly complicated with interstitial lung disease. Chest high-resolution computed tomography (HRCT) is still considered the diagnostic gold standard for interstitial lung disease and is quantification, however he increasing use of lung ultrasound may play an important role in the future.

Objectives: The aim of our study was to determine the diagnostic value of lung ultrasound in the detection and progression of interstitial pulmonary disease in patients with dermatomyositis.

Methods: Twenty two subjects with dermatomyositis diagnosed according to the American College of Rheumatology criteria were enrolled (6 males, 16 females; mean age: 15,8 ± 8.8 years; range: 6 to 29 years). All subjects underwent high resolution computed tomography followed by transthoracic ultrasound for comet tail sign detection and pleural irregularity in order to predict the degree of interstitial lung disease. The modified transthoracic ultrasound assessment was performed at 06 thoracic regions each side. The Warrick score was calculated according standard high-resolution chest computed tomography images that were evaluated independently from each other by two thoracics radiologists.

Results: A significantly positive correlation between transthoracic ultrasound and the severity of pulmonary involvement, as seen by the number of B lines (Spearman 's correlation coefficient = 0.80, p < 0.001), and the number of positive areas (regions wih more than 3 B lines) (Spearman 's correlation coefficient = 0.75, p < 0.001) were found. When compared with high-resolution chest computed tomography as the gold standard method, the sensitivity, specificity, of transthoracic ultrasound was 96.4%, 83,3% respectively. Addicionally the number of B lines (sum of 35 or more B lines) and a number of B lines positive areas (7 or more regions with at least 3 B lines) cut of allowed to discriminate the inflamatory pattern (ground glass) to those with structural pattern (honeycomb and pulmonary cysts).

Conclusion: Our study showed that transthoracic ultrasound comet tails scoring system could be useful in the assessment of the pulmonary involvement in patients with dermatomyositis, and should be considered as a primary screening exam to exclude lung involvement, rather than routine chest CT scans in assimptomatic patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4033

OP0168 THE ROLE OF VASCULAR INFLAMMATION MARKERS IN DEFICIENCY OF ADENOSINE DEAMINASE 2

U. Kaya Akca[1], E. Sag2, Ş. Ünal[3], M. Kasap-Cuceoglu2, Y. Bilginer2, S. Özen2. *[1]Hacettepe University School of Medicine, Pediatric Rheumatology, Ankara, Turkey*; *[1]Hacettepe University School of Medicine, Pediatric Rheumatology, Ankara, Turkey*; *[3]Hacettepe University School of Medicine, Pediatric Hematology, Ankara, Turkey*

Background: Deficiency of adenosine deaminase 2 (DADA2) is a monogenic autoinflammatory disease whose pathogenesis has not been clearly elucidated.
Objectives: To investigate the role of vascular inflammatory factors in the pathogenesis of DADA2, to compare the vascular inflammation profiles of DADA2 patients with different phenotypes, and to compare DADA2 patients with classic polyarteritis nodosa (PAN).
Methods: The study included eighteen DADA2 patients, ten PAN patients, and eight healthy controls. Plasma levels of sST2, sRAGE, Tie-2, sCD40L, Tie-1, sFlt-1, LIGHT, TNF-α, PlGF, IL-6, IL-18, IL-10, MCP-1 were studied by cytometric bead-based multiplex assay panel.
Results: Among the DADA2 patients, five had hematological manifestations, 13 had vasculitic findings, and accompanying immunological findings were present in seven patients. Nine patients had neurological findings, five of whom had neuropathy. Hematological findings were Diamond-Blackfan anemia-like phenotype in four patients and bicytopenia (anemia and thrombocytopenia) in one patient. Disease characteristics of DADA2 and PAN patients revealed that neurological involvement and livedo reticularis were more frequent in DADA2 patients (p=0.034 and p=0.009, respectively), while myalgia was more common in PAN patients (p:0.001).
Plasma levels of Tie-1 and sFlt-1 were higher in the overall DADA2 patients compared to healthy controls and PAN patients (p<0.001 and p=0.004, respectively). DADA2 patients with PAN-like features had higher sRAGE, Tie-2, and TNF-α levels compared to PAN patients (p=0.013, p=0.003, and p=0.001, respectively). There was no significant difference in the levels of vascular inflammation markers between DADA2 patients with vasculitis and hematological involvement except IL-18. The plasma IL-18 levels were higher in the DADA2 patients with hematological findings compared to vasculitic phenotype (p=0.001). Finally DADA2 patients with neuropathy had higher sRAGE concentrations than patients without neuropathy and healthy controls (p=0.03 and p=0.008, respectively).
Conclusion: We suggest that the high plasma IL-18 levels may be associated with an activated IFN pathway, the pathogenesis of hematologic manifestations, and unresponsive to anti-TNF treatment. Higher concentrations of Tie-1, Tie-2, sFlt-1, sRAGE, and TNF-α distinguished DADA2 patients with PAN-like features from PAN patients. We identified sRAGE as a potential biomarker of neuropathy in DADA2 patients.
REFERENCES:
[1] Pesciotta EN, Lam H-S, Kossenkov A, et al. In-Depth, Label-Free analysis of the erythrocyte cytoplasmic proteome in Diamond Blackfan Anemia identifies a unique inflammatory signature. PLoS One 2015;10(10):e0140036.
[2] Haslbeck KM, Bierhaus A, Erwin S, et al. Receptor for advanced glycation endproduct (RAGE)–mediated nuclear factor-κB activation in vasculitic neuropathy. *Muscle Nerve* 2004;29(6):853-60.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2504

Challenges for working people with RMDs in pandemic times

OP0169-PARE **DEVELOPMENT OF POINTS TO CONSIDER WHEN SUPPORTING PERSONS WITH REUMATIC AND MUSCULOSKELETAL DISEASES TO PARTICIPATE IN HEALTHY AND SUSTAINABLE PAID WORK**

A. Boonen[1], S. Verstappen[2], M. Butink[1], C. Webers[1], N. Betteridge[3], T. Stamm[4], D. Wiek[5], A. Woolf[6], G. R. Burmester[7], H. Bijlsma[8]. [1]*Academic Hospital Maastricht, Rheumatology, Maastricht, Netherlands*; [2]*University of Manchester, Centre for Musculoskeletal Research, Manchester, United Kingdom*; [3]*University of Liverpool, Public Health, Liverpool, United Kingdom*; [4]*Medical University of Vienna, Section of Outcome Research; Center for Medical Statistics, InformaticsArticial Intelligence, Vienna, Austria*; [5]*EULAR, PARE, Zurich, Switzerland*; [6]*Royal Cornwall Hospital, Bone and Joint Resreach Group, Truro, United Kingdom*; [7]*Charité – Universitätsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany*; [8]*UMC Utrecht, Rheumatology, Utrecht, Netherlands*

Background: Despite earlier diagnosis and improved management of rheumatic and musculoskeletal diseases (RMDs), a work participation gap remains when compared to the general population. To bridge this work participation gap, EULAR's current strategy states that *'by 2023, EULAR's activities and related advocacy will have increased participation in work by people with RMDs'*. To achieve this goal, guidance is needed how to support people with RMDs to remain in paid work or (re)-enter the labour force.
Objectives: To develop Points to Consider (PtC) when supporting people with RMD to participate in healthy and sustainable paid work.
Methods: An international expert group, established by Eular in 2019, convened twice to agree on a protocol for the development of PtC. EULAR's standard operating procedures were followed. The group (a) defined the target audience, (b) identified areas from which knowledge should be derived to enable formulation of the PtC, (c) agreed on a strategy to collect evidence, (d) established an international taskforce to formulate and agree on the PtC, and (e) proposed an implementation plan.
Results: The target audience are professionals involved in clinical care for patients with RMDs as well as their organisations, persons with RMDs and their organisations, and administrators responsible for healthcare and work policies. Six knowledge areas are identified (Table). Depending on the specific knowledge area, strategies for collecting evidence comprise synthesis of published and grey literature, surveys among various organisations and collection of case studies from employers. Whenever evidence in RMDs is limited, evidence from other chronic diseases will be sought. The international taskforce includes experts from different disciplines in rheumatology (one in other chronic diseases), EU policy makers, and representatives of PARE, HCP, EULAR Public Affairs and EMEUNET. As part of the implementation, close cooperation with national professional and patients societies is planned. Additionally, results will be included in EULAR's activities at the EU policy level.

Table 1. Knowledge areas and strategy to retrieve evidence

	In persons with RMDs:	Sources of evidence
1	Is work relevant for the clinical outcome of disease	LR; Review of managament recommendations and Care Standards
2	What are barriers and facilitators to enter or stay in the labor force	SLR
3	What is the effectiveness of interventions to enter or stay in the labor force	SLR; Survey among professional and patient organisations
4	Which social security systems are more effective when entering or staying in the labor force	LR
5	How does disease influence the cycle of work	SLR; Grey literature
6	What (not) to do by employers to let patients enter or stay in the work force	SLR; Survey among large companies; case studies

LR: Literature review; SLR: Systematic literature review

Conclusion: The proposed initiative to develop PtC should ultimately result in improvement of healthy and sustainable labor force participation of people with RMDs.
Disclosure of Interests: Annelies Boonen Grant/research support from: Abbvie, Suzanne Verstappen: None declared, Maarten Butink: None declared, Casper Webers: None declared, Neil Betteridge: None declared, Tanja Stamm: None declared, Dieter Wiek: None declared, Anthony Woolf: None declared, Gerd Rüdiger Burmester: None declared, Hans Bijlsma: None declared
DOI: 10.1136/annrheumdis-2021-eular.2995

Progress in myositis and scleroderma research - I

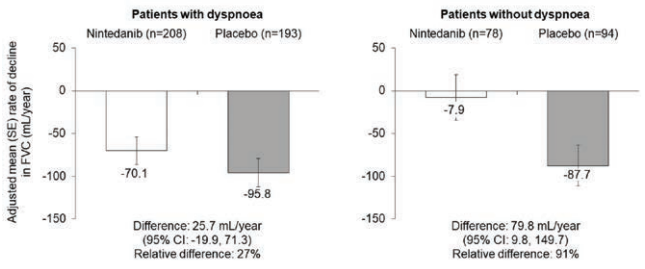
OP0170 **DECLINE IN FORCED VITAL CAPACITY (FVC) IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) WITH AND WITHOUT DYSPNOEA: DATA FROM THE SENSCIS TRIAL**

E. Volkmann[1], M. Kreuter[2], A. M. Hoffmann-Vold[3], M. Wijsenbeek[4], V. Smith[5], D. Khanna[6], C. Denton[7], W. Wuyts[8], C. Miede[9], M. Alves[10], S. Sambevski[10], Y. Allanore[11]on behalf of the SENSCIS trial investigators.. [1]*University of California, David Geffen School of Medicine, Department of Medicine, Division of Rheumatology, Los Angeles, United States of America*; [2]*Thoraxklinik, University of Heidelberg, Member of the German Center for Lung Research, Center for Interstitial and Rare Lung Diseases, Pneumology and Respiratory Care Medicine, Heidelberg, Germany*; [3]*Oslo University Hospital, Department of Rheumatology, Oslo, Norway*; [4]*Erasmus MC, University Medical Centre, Department of Respiratory Medicine, Rotterdam, Netherlands*; [5]*Ghent University Hospital, Department of Rheumatology and Internal Medicine, Ghent, Belgium*; [6]*University of Michigan, Department of Medicine, Ann Arbor, United States of America*; [7]*University College London Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom*; [8]*University Hospitals Leuven, Unit for Interstitial Lung Diseases, Department of Pulmonary Medicine, Leuven, Belgium*; [9]*mainanalytics GmbH, Statistics, Sulzbach (Taunus), Germany*; [10]*Boehringer Ingelheim International GmbH, TA Inflammation Med, Ingelheim am Rhein, Germany*; [11]*Descartes University, APHP, Cochin Hospital, Department of Rheumatology A, Paris, France*

Background: Some patients with SSc-ILD develop dyspnoea secondary to parenchymal lung disease, while others do not report dyspnoea even when their

lung function is impaired. It is unclear whether the presence of dyspnoea is associated with a worse course of SSc-ILD or with response to therapy.
Objectives: To investigate the rate of decline in FVC in patients with SSc-ILD in the SENSCIS trial in subgroups by patient-reported dyspnoea at baseline.
Methods: The SENSCIS trial enrolled patients with SSc-ILD with first non-Raynaud symptom within ≤7 years before screening, extent of fibrotic ILD ≥10% on HRCT and FVC ≥40% predicted. Patients were randomised to receive nintedanib or placebo until the last patient reached week 52. In post-hoc analyses, we analysed the rate of decline in FVC (mL/year) over 52 weeks in patients with and without dyspnoea at baseline based on the question about dyspnoea in the St. George's Respiratory Questionnaire (SGRQ). Patients who reported having shortness of breath "most days a week", "several days a week" or "a few days a month" (rather than "only with chest infection" or "not at all") over the last month were considered to have dyspnoea at baseline. A random slope and intercept model was used to assess the rate of decline in FVC (mL/year) and an interaction test was applied to assess potential heterogeneity in the treatment effect of nintedanib between the subgroups.
Results: Of 576 patients, 69.8% had dyspnoea at baseline. At baseline, in patients with and without dyspnoea, respectively, mean (SD) extent of fibrotic ILD on HRCT was 37.7 (21.7)% and 31.6 (19.4)%; mean (SD) FVC was 71.0 (16.3) and 76.5 (16.8) % predicted; 50.7% and 44.8% were taking mycophenolate; 53.5% and 41.9% were taking corticosteroids. In the placebo group, the rate of decline in FVC (mL/year) was similar in patients with and without dyspnoea at baseline (Figure). The effect of nintedanib versus placebo on reducing the rate of decline in FVC (mL/year) was numerically more pronounced in patients without dyspnoea (difference: 79.8 [95% CI: 9.8, 149.7]) than with dyspnoea (difference: 25.7 [-19.9, 71.3]), but the exploratory interaction p-value did not indicate heterogeneity in the treatment effect between subgroups (p=0.20).
Conclusion: In the SENSCIS trial, patients with SSc-ILD who had dyspnoea at baseline had a numerically greater extent of fibrotic ILD on HRCT and numerically lower FVC % predicted at baseline. The rate of decline in FVC in the placebo group was similar in patients with and without dyspnoea. Nintedanib had a numerically greater treatment effect in patients without dyspnoea. These data suggest that the presence of dyspnoea should not be used as a criterion for starting nintedanib in patients with SSc-ILD.

Figure. Rate of decline in FVC (mL/year) over 52 weeks in subgroups by dyspnoea at baseline in the SENSCIS trial.



Treatment-by-time-by-subgroup interaction p=0.20.
The presence of dyspnoea was based on this question from the St George's Respiratory Questionnaire: "Over the last month, I have had shortness of breath:". Patients who ticked boxes for "most days a week", "several days a week" or "a few days a month" were considered to have dyspnoea.

Acknowledgements: The SENSCIS trial was funded by Boehringer Ingelheim. Medical writing support was provided by Fleishman Hillard Fishburn, London, UK. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE).
Disclosure of Interests: Elizabeth Volkmann Consultant of: Boehringer Ingelheim, Grant/research support from: Corbus and Forbius, Michael Kreuter Speakers bureau: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim, Grant/research support from: Boehringer Ingelheim and Roche, Anna-Maria Hoffmann-Vold Speakers bureau: Actelion, Boehringer Ingelheim, Lilly, Merck Sharp & Dohme and Roche, Consultant of: Actelion, Arxx Therapeutics, Bayer, Boehringer Ingelheim, Lilly, Medscape, Merck Sharp & Dohme and Roche, Grant/research support from: Boehringer Ingelheim, Marlies Wijsenbeek Speakers bureau: Boehringer Ingelheim (fees paid to institution) and Hoffmann-La Roche (fees paid to institution), Consultant of: Boehringer Ingelheim (fees paid to institution), Bristol-Myers Squibb (fees paid to institution), Galapagos NV (fees paid to institution), Hoffmann-La Roche (fees paid to institution), NeRRe Therapeutics (fees paid to institution), OncoArendi Therapeutics (fees paid to institution), Respivant Sciences (fees paid to institution) and Savara (fees paid to institution), Grant/research support from: Boehringer Ingelheim (fees paid to institution) and Hoffmann-La Roche (fees paid to institution), Vanessa Smith Speakers bureau: Boehringer Ingelheim and Janssen-Cilag NV, Consultant of: Boehringer Ingelheim, Grant/research support from: Belgian Fund for Scientific Research in Rheumatic diseases (FWRO), Boehringer Ingelheim, Janssen-Cilag NV and Research Foundation - Flanders (FWO), Dinesh Khanna Shareholder of: Eicos Sciences, Inc. (less than 5%), Consultant of: Acceleron Pharma, Actelion, AbbVie, Amgen, Bayer, Boehringer Ingelheim, CSL Behring, Corbus, Gilead Sciences, Galapagos NV, Genentech/Roche, GlaxoSmithKline, Horizon Therapeutics, Merck Sharp & Dohme, Mitsubishi Tanabe Pharma, Sanofi-Aventis and United Therapeutics, Grant/research support from: Bayer, Bristol-Myers Squibb, Horizon Therapeutics, Immune Tolerance Network, National Institutes of Health and Pfizer, Employee of: Chief Medical Officer- CiviBioPharma/Eicos Sciences, Inc., Christopher Denton Speakers bureau: Boehringer Ingelheim, Corbus, Janssen, and Mallinckrodt Pharmaceuticals, Consultant of: Acceleron Pharma, Arxx Therapeutics, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos NV, GlaxoSmithKline, Horizon Therapeutics, Janssen, Mallinckrodt Pharmaceuticals, Roche, Sanofi and UCB, Grant/research support from: Arxx Therapeutics, GlaxoSmithKline and Servier, Wim Wuyts: None declared, Corinna Miede Employee of: Currently an employee of mainanalytics GmbH, contracted by Boehringer Ingelheim, Margarida Alves Employee of: Currently an employee of Boehringer Ingelheim, Steven Sambevski Employee of: Currently an employee of Boehringer Ingelheim, Yannick Allanore Consultant of: Boehringer Ingelheim, Medsenic, Menarini and Sanofi, Grant/research support from: Alpine Pharmaceuticals
DOI: 10.1136/annrheumdis-2021-eular.834

OP0171 PHASE 3 TRIAL OF LENABASUM, A CB2 AGONIST, FOR THE TREATMENT OF DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC)

R. Spiera[1], M. Kuwana[2], D. Khanna[3], L. Hummers[4], T. Frech[5], W. Stevens[6], J. Gordon[7], S. Kafaja[8], M. Matucci-Cerinic[9], O. Distler[10], E. B. Lee[11], Y. Levy[12], J. B. Jun[13], S. Constantine[14], N. Dgetluck[14], B. White[14], D. Furst[8], C. Denton[15].
[1]Hospital for Special Surgery, Department of Medicine, New York, United States of America; *[2]Nippon Medical School Graduate School of Medicine, Department of Allergy and Rheumatology, Tokyo, Japan*; *[3]University of Michigan School of Medicine, Scleroderma Program, Ann Arbor, United States of America*; *[4]Johns Hopkins University School of Medicine, Division of Rheumatology, Baltimore, United States of America*; *[5]University of Utah, Division of Rheumatology, Salt Lake City, United States of America*; *[6]St. Vincent's Hospital, Department of Rheumatology, Melbourne, Australia*; *[7]Hospital for Special Surgery, Department of Rheumatology, New York, United States of America*; *[8]David Geffen School of Medicine at University of California, Department of Rheumatology, Los Angeles, United States of America*; *[9]University of Florence, Department of Experimental Rheumatology, Florence, Italy*; *[10]University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland*; *[11]Seoul National University Hospital, Division of Rheumatology, Seoul, Korea, Rep. of (South Korea)*; *[12]Israel Sackler School of Medicine, Tel Aviv University, Department of Internal Medicine, Tel Aviv, Israel*; *[13]Hanyang University Hospital for Rheumatic Diseases, Department of Rheumatology, Seoul, Korea, Rep. of (South Korea)*; *[14]Corbus Pharmaceuticals, Clinical, Norwood, United States of America*; *[15]Royal Free Hospital, University College London, Division of Medicine, London, United Kingdom*

Background: Lenabasum is an oral CB2 agonist that attenuates inflammation and fibrosis in SSc animal models and showed clinical benefit with acceptable safety in a Phase 2 trial in dcSSc.
Objectives: Test efficacy and safety of lenabasum in a Phase 3 trial in dcSSc.
Methods: Subjects ≥18 years old with disease duration ≤ 6 years were randomized 1:1:1 to lenabasum 5 mg, 20 mg, or placebo (PBO), all BID, with stable background immunosuppressant therapy (IST) allowed. The primary efficacy endpoint was ACR CRISS score, and secondary endpoints were ΔmRSS, ΔHAQ-DI, and ΔFVC, all at Week 52 for lenabasum 20 mg vs PBO.
Results: 363 adults were dosed; 37 (10%) stopped study drug early, with only 1 subject (PBO cohort) stopping due to adverse event (AE). Baseline demographics were similar among groups. Disease duration was ≤ 3 years in 60% and 66%, mean mRSS score was 22.0 and 23.3, and background IST was used by 89% and 84% of lenabasum 20 mg and PBO groups, respectively.
Safety results showed serious AEs and severe AEs occurred in 9.2% and 5.8% vs 14.6% and 13.0%, respectively, of lenabasum 20 mg and PBO groups.
Efficacy results (Table) demonstrated:

- No significant differences were seen in primary and secondary efficacy endpoints. Primary MMRM analyses with treatment-by-time-by-subgroup interactions showed that background mycophenolate (MMF) significantly influenced the outcome
- oSubjects on no IST with disease duration ≤3 years were only 7% of PBO subjects and showed little improvement on PBO, in line with other dcSSc trials in which IST was restricted. Post-hoc subgroup analyses of these subjects on no IST suggested improvement in ΔmRSS and ΔHAQ-DI, for lenabasum 20 mg vs PBO
- uUnexpectedly high improvement occurred in PBO subjects receiving IST, notably those on MMF started within 2 years of baseline
- nPost-hoc analyses of subjects on established IST (MMF or, if no MMF, ≥ 1 non-MMF IST started > 2 years before baseline)

Table 1. Primary and secondary efficacy endpoints and post-hoc analyses, Week 52

Group, by IST treatment	Cohort	N	ΔmRSS, mean (SD)	ΔFVC% mean (SD)	ΔFVC, mL mean (SD)	ΔHAQ-DI mean (SD)	ACR CRISS median
mITT population, MMRM primary analysis method							
All	Placebo	123	-8.1 (7.72)	-1.0 (8.68)	-51 (317)	-0.13 (0.468)	0.887
	Lenabasum 20 mg	120	-6.7 (6.59)	-1.6 (6.91)	-78 (265)	-0.13 (0.436)	0.888
Placebo subjects, per protocol completers, LOCF							
No IST	Placebo	16	-2.3 (9.4)	-2.8 (7.4)	-97 (244)	0.12 (0.34)	0.417
All IST	Placebo	97	-8.9 (7.07)	-1.0 (9.2)	-43 (330)	-0.17 (0.474)	0.936
MMF, no other IST	Placebo	29	-10.7 (8.1)	-0.58 (7.1)	-37 (235)	-0.12 (0.456)	0.935
MMF ≤ 2 years, no other IST	Placebo	23	-11.7 (8.1)	-0.3 (6.0)	-41 (197)	-0.13 (0.495)	0.935
Non-MMF ≤ 2 years	Placebo	24	-6.7 (6.2)	-1.4 (7.87)	-52 (281)	-0.15 (0.357)	0.931
Post-hoc comparisons, per protocol completers, LOCF							
No IST	Placebo	16	-2.3 (9.4)	-2.8 (7.4)	-97 (244)	0.12 (0.34)	0.417
	Lenabasum 20 mg	10	-6.3 (6.02)	-2.3 (5.58)	-99 (209)	-0.06 (0.498)	0.811
Established IST1	Placebo	26	-6.1 (5.35)	-4.6 (10.11)	-170 (350)	-0.17 (0.445)	0.619
	Lenabasum 20 mg	38	-7.4 (5.08)	-0.4 (5.70)[2]	-21 (233)[3]	-0.07 (0.357)	0.941
Established IST, subjects with ILD	Placebo	22	-5.9 (5.28)	-3.7 (5.43)	-133 (206)	-0.10 (0.372)	0.553
	Lenabasum 20 mg	33	-7.2 (5.70)	-1.0 (10.5)	-47 (365)	-0.06 (0.391)	0.819

[2] P = 0.0386 two-sample t-test; [3] P = 0.0481 two-sample t-test; other comparisons were not significant

suggested improvement in ΔFVC% (nominal P = 0.0386) and ΔFVC mL (nominal P = 0.0481) for lenabasum 20 mg vs PBO. Improvement in FVC was also seen in subjects on established IST who had ILD at baseline, lenabasum 20 mg vs PBO

- mACR CRISS score demonstrated a ceiling effect and correlated most highly with ΔmRSS (r = -0.739) and moderately with MDGA (-0.432), HAQ-DI (-0.362), FVC% (0.366), and PtGA (-0.288)

Conclusion: Lenabasum was safely used in this study. Unexpectedly high improvement on background IST, especially MMF, has not been previously reported at this level. The primary endpoint was not met. Post-hoc analyses showed greater improvement in lenabasum- vs PBO-treated subjects who were not on background IST and those on established IST, including subjects with ILD.

Disclosure of Interests: Robert Spiera Consultant of: Abbvie, Roche-Genetech, GSK, CSL Behring, Sanofi, Janssen, Chemocentryx, Formation Biologics, Mitsubishi Tanabe, Grant/research support from: Roche-Genetech, GSK, Boehringer Ingelheim, Chemocentryx, Corbus, Formation Biologics, Sanofi, Inflarx, Astra Zeneca, Kadmon, Masataka Kuwana Speakers bureau: Boehringer-Ingelheim, Chugai, Janssen, Consultant of: Boehringer-Ingelheim, Chugai, Corbus, Grant/research support from: Boehringer-Ingelheim, Chugai, MBL, Ono Pharmaceuticals, Tanabe-Mitsubishi, Dinesh Khanna Shareholder of: Eicos Sciences, Inc (less than 5%). Leadership/Equity position – Chief Medical Officer, CiviBioPharma/Eicos Sciences, Inc, Consultant of: Acceleron, Actelion, Abbvie, Amgen, Bayer, Boehringer Ingelheim, CSL Behring, Corbus, Gilead, Galapagos, Genentech/Roche, GSK, Horizon, Merck, Mitsubishi Tanabe Pharma, Sanofi-Aventis, and United Therapeutics, Grant/research support from: NIH, Immune Tolerance Network, Bayer, BMS, Horizon, Pfizer, Laura Hummers Consultant of: CSL Behring, Boehringer Ingelheim, Grant/research support from: Investigator for study sponsored by Corbus Pharmaceuticals. Corbus, Boehringer Ingelheim, Medpace, Kadmon, Cumberland, CSL Behring, Tracy Frech Grant/research support from: Investigator for study sponsored by Corbus Pharmaceuticals, Wendy Stevens Grant/research support from: Investigator for study sponsored by Corbus Pharmaceuticals, Jessica Gordon Grant/research support from: Investigator for study sponsored by Corbus Pharmaceuticals. Research funding for EICOS Pharmaceuticals and Cumberland Pharmaceuticals., Suzanne Kafaja Grant/research support from: Investigator for study sponsored by Corbus Pharmaceuticals, Marco Matucci-Cerinic Consultant of: Actelion, Janssen, Inventiva, Bayer, Biogen, Boehringer, CSL Behring, Corbus, Galapagos, Mitsubishi, Samsung, Regeneron, Acceleron, MSD, Chemomab, Lilly, Pfizer, Roche, Grant/research support from: Investigator for study sponsored by Corbus Pharmaceuticals, Oliver Distler Consultant of: Consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB., Eun Bong Lee Grant/research support from: Investigator for study sponsored by Corbus Pharmaceuticals, Yair Levy Grant/research support from: Investigator for study sponsored by Corbus Pharmaceuticals, Jae-Bum Jun Consultant of: Consultant to Boehringer Ingelheim Korea, Jeil Pharma, Dae Woong Pharma, Kwangdong Pharma, and Sama Pharma., Grant/research support from: Investigator for study sponsored by Corbus Pharmaceuticals, Scott Constantine Employee of: Employee of Corbus Pharmaceuticals, Nancy Dgetluck Employee of: Employee of Corbus Pharmaceuticals, Barbara White Employee of: Employee and stockholder of Corbus Pharmaceuticals, Daniel Furst Consultant of: Corbus, Galapagos, Pfizer, CSL Behring, Mitsubishi Tanabi, Actelion, Amgen, Novartis, Roche/Genentech, Gilead, Talaris, and Boehringer Ingelheim., Grant/research support from: grants from Corbus, Galapagos, GSK, Pfizer, Talaris, CSL Behring, Mitsubishi Tanabi, Christopher Denton Consultant of: Consultancy fees and/or honoraria from Corbus, Actelion, GlaxoSmithKline, Bayer, Sanofi, Galapagos, Inventiva, Boehringer Ingelheim, Roche, CSL Behring, Acceleron, Horizon, Arxx Therapeutics

DOI: 10.1136/annrheumdis-2021-eular.1795

OP0172

BRENTUXIMAB VEDONTIN FOR SKIN INVOLVEMENT IN REFRACTORY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS, INTERIM RESULTS OF A PHASE IIB OPEN-LABEL TRIAL

A. Fernandez-Codina[1,2,3], T. Nevskaya[1], J. Pope[1]. *[1]Western University, Medicine, Rheumatology division, London, Canada*; *[2]Windsor Regional Hospital - Ouellette Campus, Medicine, Windsor, Canada*; *[3]Hospital Clínic de Barcelona, Systemic Autoimmune Diseases, Barcelona, Spain*

Background: Systemic sclerosis (SSc) is an autoimmune disease affecting multiple organs causing morbidity and mortality. Treatments targeting SSc skin often have limited success. The presence of CD30+ lymphocytes in skin biopsies and increased levels of serum CD30 have been reported in SSc patients[1]. This could constitute a new therapeutic target.

Objectives: To explore the efficacy and safety of brentuximab vedotin, a chimeric anti-CD30 antibody drug conjugate, in patients with severe active diffuse cutaneous SSc who failed multiple treatments.

Methods: This Phase IIb, single center, open-label, investigator-initiated trial will recruit 10 patients. Brentuximab vedotin 0.6 mg/Kg was infused intravenously every 3 weeks for 48 weeks. Inclusion criteria were age ≥18 years, meeting the 2013 ACR/EULAR SSc classification criteria, modified Rodnan skin score (mRSS) ≥15 with <5 years since the first non-Raynaud's symptom and/or skin worsening despite immunosuppression. Patients were allowed to continue their standard of care medications for SSc except for rituximab. Patients with severe cardiac or pulmonary SSc involvement, severe infections, significant peripheral neuropathy, or active malignancy were excluded. The primary objective was a decrease in mRSS of ≥8 at 48 weeks. The main secondary endpoint was MRSS at 24 weeks. Differences were assessed by paired t tests. Data were compared to 16 age, disease duration, mRSS and past/present use of immunosuppressors-matched controls (ratio 2-3:1) from the Canadian Scleroderma Research Group (CSRG) registry.

Results: Eight of 10 patients have been recruited to date; two are in the first 8 weeks and one was withdrawn at her request after developing influenza at week 12. Five subjects (60% female) have reached week 24, and 3 have completed 48 weeks. The mRSS is shown in Table 1. The ΔMRSS for patients treated with brentuximab between weeks 0 and 24 was 8.2 ([CI 95% 2.8, 13.6], p = 0.013) and from 0 to 48 was 15.3 ([CI 95% 8.2, 22.5], p = 0.012). Whereas, the ΔMRSS for the CSRG controls was 3.1 ([CI 95% -2, 8.2], p = 0.211) at 48 weeks. Assuming that mRSS would at least be the same from week 24 to 48 in the 2 cases who are between 24 and 48 weeks with brentuximab, we compared the 5 cases vs controls (Figure 1). ΔMRSS for Brentuximab was 12.2 ([CI 95% 5.9, 18.5], p = 0.006. No cases have developed a peripheral neuropathy and only one SAE (influenza).

Table 1.

N (SD)	N	Age	Disease duration	mRSS week 0	mRSS week 24	mRSS week 48	mRSS week 48**
Case	5	60.2 (9.3)	4.5 (2.1)	33 (5.2)	24.8 (6)	15.7 (3)	20.8 (8.3)
Control	16	58.5 (8.3)	4.9 (2.1)	31.3 (5.9)	N/D	28.1 (7.5)	28.1 (7.5)
p		0.731	0.775	0.559	N/D	0.013	0.079

mRSS = modified Rodnan skin score, N/D = no data, ** = comparisons including 5 cases, assuming stability in MRSS from week 24 to 48 in cases 5 and 6

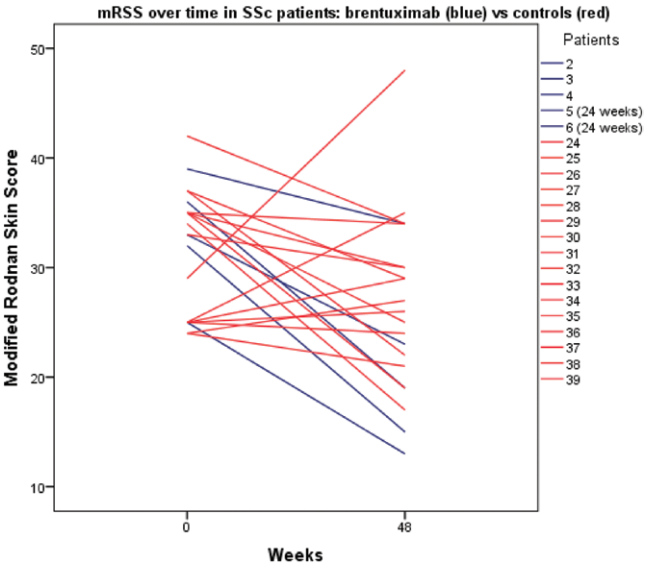


Figure 1.

Conclusion: Brentuximab vedontin already achieved the primary endpoint at 24 weeks, after half of the intended recruitment sample reached this landmark. A comparison with CSRG controls showed that mRSS only decreased significantly in patients treated with brentuximab. This interim report suggests that brentuximab vedontin might effectively improve skin involvement in patients with diffuse SSc and severe skin involvement.

REFERENCES:

[1] Mavalia C, Scaletti C, Romagnani P, et al. Type 2 helper T-cell predominance and high CD30 expression in systemic sclerosis. Am J Pathol. 1997;151(6):1751-8.

Acknowledgements: We would like to acknowledge the Canadian Scleroderma Research Group, Louise Vanderhoek, Sara Macdonald Hewitt and Jillian Bylsma for their collaboration

Disclosure of Interests: Andreu Fernandez-Codina Consultant of: Bayer, Boehringer Ingelheim, Atheneum consulting, Tatiana Nevskaya: None declared, Janet Pope Speakers bureau: Actelion, Amgen, Abbie, Bayer, Boehringer Ingelheim, BMS, Eli Lilly, Galapagos, Gilead, Janssen, Medexus, Merck, Novartis, Pfizer, Roche, Samsung, Sandoz, Sanofi, Teva, UCB., Consultant of: Actelion, Amgen, Abbie, Bayer, Boehringer Ingelheim, BMS, Eli Lilly, Galapagos, Gilead, Janssen, Medexus, Merck, Novartis, Pfizer, Roche, Samsung, Sandoz, Sanofi, Teva, UCB., Grant/research support from: Actelion, Amgen, Abbie, Bayer, Boehringer Ingelheim, BMS, Eli Lilly, Galapagos, Gilead, Janssen, Medexus, Merck, Novartis, Pfizer, Roche, Samsung, Sandoz, Sanofi, Teva, UCB.

DOI: 10.1136/annrheumdis-2021-eular.2115

OP0173 REDUCTION OF SKIN FIBROSIS IN SYSTEMIC SCLEROSIS ON RITUXIMAB TREATMENT. LONG-TERM FOLLOW-UP

L. Garzanova[1], L. Ananyeva[1], O. Koneva[1], O. Ovsyannikova[1], O. Desinova[1], M. Starovoytova[1], R. Shayakhmetova[1]. [1]*V A Nasonova Research Institute of Rheumatology, Laboratory of microcirculation and inflammation, Moscow, Russian Federation*

Background: A sound experience has been accumulated up to date with the use of rituximab (RTX) for treatment of systemic sclerosis (SSc). Some studies reported improvement of skin fibrosis following treatment with RTX, but long-term follow-ups are really few.

Objectives: to evaluate the effect of RTX on the manifestations of skin fibrosis in patients (pts) with SSc in the long-term follow-up.

Methods: This prospective study included 71 pts aged 46 years (17-66) on average, 59 (83%) pts were females, mean disease duration was 5,6±4,4 years, and mean follow-up - 42 months (12-72) (mo). Diffuse SSc was established in 42 (59%) pts. All pts received glucocorticoids in low doses. 45% of pts were receiving immunosuppressants at study entry. The following parameters were evaluated: Rodnan skin score (mRSS), interdigital space(IDS) (the distance between the tips of 1 and 5 fingers at maximum extension), oral aperture (OAp) and activity index (EScSG-AI) over the periods: 12-18 mo, 24-30 mo, 36-42 mo, 48-54 mo and 60-72 mo after initiation of RTX therapy. The results are presented as: mean values, delta (Δ), median, upper and lower quartiles.

Results: RTX therapy resulted in significant decrease of disease activity index, which statistically significantly correlated with decrease of mRSS - the main indicator of the severity of skin fibrosis (r=0,39;p=0,001). Changes in parameters by follow-up periods are presented in the Table 1.

Table 1. Changes in clinical and instrumental parameters at RTX treatment (delta; median; lower quartile; upper quartile).

Parameters	12-18 mo (n=71)	24-30 mo (n=55)	36-42 mo (n=36)	48-54 mo (n=24)	60-72 mo (n=17)
ΔmRSS	3,32 [3.3; 0; 8] p=0,001	5,4 [3; 0; 10] p=0,001	5,1 [3,5; 0; 9] p=0,001	5,3 [3; 0; 10] p=0,001	7,3 [5; 1; 14] p=0,001
ΔOAp, cm	0,24 [0,1; 0; 0,5] p=0,0009	0,26 [0,1; 0; 0,6] p=0,0006	0,39 [0,2; 0; 0,8] p=0,004	0,31 [0.3; 0; 0,7] p=0,006	0,36 [0,2; 0; 0,8] p=0,009
ΔActivity index (EScSG-AI)	1,49 [1,5; 0; 2,5] p=0,001	1,64 [1,5; 0; 2,5] p=0,001	1,11 [1; 0; 2] p=0,0001	2 [2; 1; 3] p=0,0001	2,17 [2; 1,5; 2] p=0,0001
Cumulative dose of RTX, g	1,43±0,6	2,97±0,8	3,45±1,3	3,96±1,1	5,15±1,7

Decreasing of mRSS statistically significantly correlated with increasing cumulative dose of RTX (r=0,29;p=0,01). Decreasing disease activity index correlated with increasing cumulative dose of RTX (r=-0,37; p=0,01). IDS improvement was documented at all assessment time periods, although statistically insignificant.

Conclusion: The results of this study confirm reported positive effect of RTX on the reduction of skin fibrosis in SSc. Long-term follow-up demonstrated steadily decreasing skin fibrosis and improvement of microstomia with increasing oral aperture in parallel with a decrease of the disease activity index and increasing cumulative dose of RTX.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2860

OP0174 SUBCLINICAL INTERSTITIAL LUNG DISEASE IS FREQUENT AND PROGRESSES ACROSS DIFFERENT CONNECTIVE TISSUE DISEASES

A. M. Hoffmann-Vold[1], H. Andersson[1], S. Reiseter[2], H. Fretheim[1], I. Barua[1], T. Garen[1], Ø. Midtvedt[1], R. Gunnarsson[1], M. Durheim[3], T. M. Aaløkken[4], Ø. Molberg[1]. [1]*Oslo University Hospital, Rheumatology, Oslo, Norway*; [2]*Akershus University Hospital, Internal Medicine, Oslo, Norway*; [3]*Oslo University Hospital, Respiratory Medicine, Oslo, Norway*; [4]*Oslo University Hospital, Radiology, Oslo, Norway*

Background: Based on the argument that symptoms define disease, physicians commonly apply the terms “preclinical” or “subclinical” disease to describe patients with disease-related findings but no accompanying symptoms for connective tissue disease associated interstitial lung disease (CTD-ILD). The term subclinical frequently applies to patients with mild ILD changes on high resolution chest tomography (HRCT), normal forced vital capacity (FVC), and without respiratory symptoms. Previous work in systemic sclerosis (SSc)-ILD did show that patients with even minor extent of ILD at baseline often progressed and had increased mortality risk, suggesting that it is not appropriate to define these patients as “subclinical.”

Objectives: To identify the prevalence of subclinical ILD across CTD diagnoses, and assess the rate of progression of lung fibrosis compared to CTD without ILD and with clinical ILD.

Methods: All CTD patients, including SSc, anti-synthetase syndrome (ASS) and mixed connective tissue disease (MCTD) from the Oslo University Hospital diagnosed before 2015 and assessed for the presence of ILD by HRCT were included. The year 2015 was chosen to secure an observation time of at least five years from ILD diagnosis to study end on 01.01.2021 or time of death. All patients fulfilled the respective CTD classification criteria. Subclinical ILD was defined as an ILD extent <5% by semi-quantitative assessment of baseline HRCT, preserved lung function with FVC >80% predicted and without respiratory symptoms. Clinical ILD was defined as >5% extent of ILD or <5% extent of ILD on HRCT with respiratory symtoms or FVC<80%. The outcome was ILD progression, defined as increasing extent of ILD from basline to follow-up HRCT by semi-quantitative assessment. Vital status was available in all patients and mortality was evaluated. Descriptive statistical analyses were conducted and time to ILD progression determined by Kaplan-Meier estimates.

Results: We identified 525 CTD patients, including 296 with SSc, 135 with MCTD and 94 with ASS who had conducted a baseline HRCT. Of these, 227 (43%) had no ILD, 67 (13%) subclinical and 231 (44%) clinical ILD (Table). Of the 67 subclinical ILD patients, 45 (15%) had SSc, 13 (10%) MCTD and 9 (10%) ASS of thespecific cohorts. Over a median time of 4.5 years between baseline and follow-up HRCT, 95/395 (24%) showed progression of ILD, including 72 (26%) SSc and 23 (19%) MCTD patients. Disease progression frequently occurred in both subclinical ILD (38%) and clinical ILD (51%) patients (Figure). Age, gender, underlying CTD, and baseline lung function were not predictive for the progression of lung fibrosis. Progression was too infrequent to allow for meaningful multivariable regression analyses. After a median observation period of 12 years, 153 (29%) of the patients died. The 1-, 5- and 10-year survival rates in those without ILD, subclinical and clinical ILD were 97%/97%/99%, 88%/91%/82%, and 82%/85%/68% (p<0.001), respectively.

Table 1. Clinical characteristics, demographics and outcome

	No ILD (n=227)	Subclinical ILD (n=67)	Clinical ILD (n=231)
Age, y (SD)	50 (15.4)	51 (14.4)	52 (15.3)
Male sex, n (%)	89 (39)	22 (33)	111 (48)
Deceased, n (%)	50 (22)	12 (18)	91 (39)
Observation period, y median (range)	13.7 (18.6)	13.9 (17.9)	11.5 (17.1)
FVC% (SD)	97 (18.6)	99 (17.9)	81 (20.9)
FVC decline% (SD)	-0.70 (11.1)	-0.81 (16.5)	-1.61 (15.9)
DLCO% (SD)	73 (19.4)	73 (16.9)	55 (17.4)
Extent of ILD% (SD)	0 (0)	2.3 (1.5)	19.3 (16.8)
ILD progression% (SD)	0.08 (1.0)	3.1 (6.2)	3.6 (9.9)
ILD progressors, n (%)	3 (2)	20 (38)	72 (51)

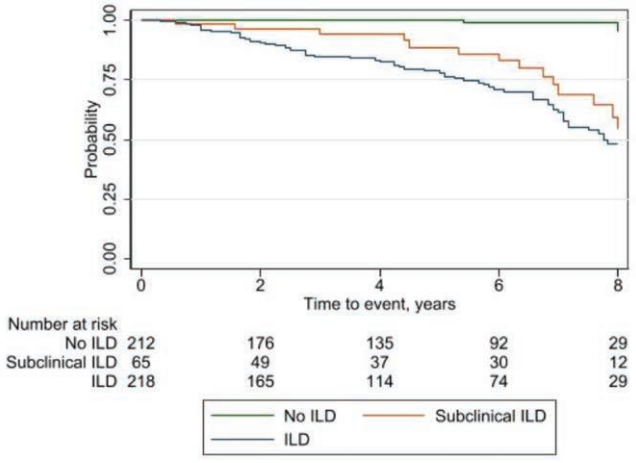


Figure 1. Time to ILD progression in CTD without ILD, with subclinical and clinical ILD

Conclusion: Subclinical ILD is frequently present across CTDs and progresses over time in a substantial subgroup of patients, comparable to patients with clinical ILD. Our findings question the terms sub- and preclinical ILD, which may potentially lead to a suboptimal "watchful waiting management strategy". Monitoring all CTD patients with any ILD is of high importance to identify disease progression early.

Disclosure of Interests: Anna-Maria Hoffmann-Vold Speakers bureau: Actelion, Boehringer Ingelheim, Roche, Merck Sharp & Dohme, Lilly and Medscape, Consultant of: Actelion, Boehringer Ingelheim, Bayer, ARXX, and Medscape, Grant/research support from: Boehringer Ingelheim, Helena Andersson: None declared, Silje Reiseter: None declared, Håvard Fretheim Consultant of: Actelion, Bayer., Imon Barua: None declared, Torhild Garen: None declared, Øyvind Midtvedt: None declared, Ragnar Gunnarsson: None declared, Mike Durheim Speakers bureau: Boehringer Ingelheim and Roche, Consultant of: Boehringer Ingelheim, Grant/research support from: Boehringer Ingelheim, Trond M Aaløkken: None declared, Øyvind Molberg: None declared

DOI: 10.1136/annrheumdis-2021-eular.3810

OP0175 INTERNATIONAL MULTICENTRIC PROSPECTIVE STUDY ON PREGNANCY IN SYSTEMIC SCLEROSIS (IMPRESS-2)

E. Tombetti[1], V. Ramoni[2], M. Betelli[3], Y. Allanore[4], M. Matucci Cerinic[5], A. Tincani[6], A. Brucato[7] on behalf of the IMPRESS-2 Working group. *[1]Milan University, Biomedical and Clinical Sciences Luigi Sacco, Milan, Italy*; *[2]ASST Lodi, Medicina Generale, Lodi, Italy*; *[3]Ospedale Papa Giovanni XXIII, Medicina, BErgamo, Italy*; *[4]Cochin Institute, Rheumatology, Paris, France*; *[5]Università Di Firenze, Rheumatology, Firenze, Italy*; *[6]Università di Brescia, Rheumatology, Brescia, Italy*; *[7]Milan University, Medicine, Milan, Italy*

Background: Data about the obstetric outcomes of pregnant women with Systemic Sclerosis (SSc) mainly derive from retrospective studies. Moreover, little evidence is available to define if pregnancy impacts on SSc course and if children of SSc mothers have a normal post-natal development.

Objectives: To assessed the obstetric, pediatric and rheumatologic outcomes of SSc pregnancies in a prospective controlled study

Methods: Prospective recruitment of three cohorts.

1) 110 pregnant women with SSc.

2) 218 control pregnancies without systemic autoimmune diseases

3) 78 non-pregnant control SSc with a matching subject in cohort-1.

SSc was characterized for disease activity, severity, cutaneous/organ involvement and therapy. Women and their offspring were followed until 21 months after enrollment (ie, 12 months after expected delivery).

Results: Gestational and neonatal outcomes

Miscarriages and fetal death occurred in 7% and 5% of SSc pregnancies. Compared to control pregnancies, SSc pregnancies had higher rates of gestational hypertension (12% Vs 4%, p=0.004), pre-eclampsia (9% Vs 1%, p=0.002), fetal growth-restriction (13% Vs 4%, p=0.004), prematurity (26% Vs 7%, p<0.001) and cesarean section (52% Vs 4%, p=0.002). Newborns from SSc mothers weighted less (2773 Vs 3243g, p<0.001), were more frequently small for gestational age (SGA, 18% Vs 12%, p=0.05) and required neonatal-intensive care unit (ICU) more frequently (12% Vs 1%, p<0.001). Rates of newborn malformation/death, and one year-pediatric outcomes were similar.

Univariate and multivariate analyses were performed for relevant outcomes. For example, pre-eclampsia positively associated with baseline skin score and its evolution during pregnancy (p=0.015 and 0.013), immunosuppressive agents, bosentan and iloprost at baseline (p=0.001, 0.041 and 0.007), and twin pregnancy(p=0.006). Multivariate logistic regression for pre-eclampsia in SSc identified baseline arterial hypertension, immunosuppressive agents or of iloprost, twin pregnancy and assisted conception as risk factors (p=0.000, 0.002, 0.0025, 0.000 and 0.027), and baseline calcium channel blockers as protective factors (p=0.001).

SSc course during pregnancy

As compared to matched non-pregnant SSc, SSc pregnant women had lower Medsger disease severity index (0.6 +/-0.9 Vs 1.0 +/-1.1, p=0.022), health assessment questionnaire (HAQ, 0.21 +/-0.38 Vs 0.40 +/-0.55, p=0.026), and lower rate of iv iloprost (21% Vs 42%, p=0.006). Pregnant and non-pregnant SSc women had a similar disease course during the 21 months of follow-up, despite a lower use of immunosuppressive agents (17% Vs 36%, p=0.014). Two scleroderma-renal-crises (SRC) occurred during pregnancy (one was a relapse of a previous SRC; the other occurred at week 33, and resolved after premature delivery of a SGA newborn and ACE-inhibitors, preventing differentiation from pre-eclampsia).

Conclusion: SSc pregnancies have generally a favorable obstetric/pediatric outcome, albeit at a higher risk of gestational hypertension, pre-eclampsia, fetal growth restriction, prematurity, delivery of SGA newborn and requirement of neonatal-ICU. Pregnancy does not impact on SSc course, although SRC during late pregnancy and pre-eclampsia might be hardly discriminated.

REFERENCES:

[1] Taraborelli M et al., Arthritis Rheum, 2012.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4273

OP0176 ULTRASOUND (US) EVALUATION OF BOWEL VASCULOPATHY IN SYSTEMIC SCLEROSIS (SSC)

L. Cometi[1], G. Bandini[2], K. El Aoufy[1], A. Domanico[3], L. Tofani[1], C. Bruni[1], S. Bellando Randone[1], S. Guiducci[1], A. Moggi Pignone[2], E. Accogli[3], M. Matucci-Cerinic[1]. *[1]University of Florence & Division of Rheumatology, Azienda Ospedaliero Universitaria Careggi, Florence, Italy*; *[2]University of Florence & Division of Internal Medicine Unit III, Azienda Ospedaliero Universitaria Careggi, Florence, Italy*; *[3]Department of Internal Medicine, Centre of Research and Learning in Ultrasound, Maggiore Hospital, Bologna, Italy*

Background: Gastrointestinal involvement is one of the most frequent features of SSc, affecting nearly 90% of patients, with a great impact on quality of life and morbidity. One of the key pathological factors of SSc bowel involvement is vasculopathy (1), although little is known about its pathophysiology and no treatments are currently available.

Objectives: to assess with abdominal US the superior mesenteric artery (SMA) and the inferior mesenteric artery (IMA) vessel characteristics and blood flow in SSc, compared to healthy controls (HC).

Methods: we performed fasting abdominal US in SSc patients fulfilling the ACR/EULAR 2013 classification criteria and HC. Patients with a history of peripheral / coronary arterial disease were excluded. For both SMA and IMA, caliber (mm), Peak Systolic Velocity – PSV (cm/sec), Reverse Velocity – RV (cm/sec), End-Diastolic Velocity – EDV (cm/sec), Mean Velocity – mV (cm/sec), Blood-flow (cm/sec), Resistive Index – RI and Pulsatility Index – PI were measured.

Results: 28 SSc patients [25 females (89.3%), mean age 48.75 ± 12.39 years; 6 (22.22%) anti-centromere and 19 (70.37%) positive for anti-topoisomerase I antibodies] and 28 HC [18 females (64.3%), mean age 36.25 ± 12.08 years] were evaluated. In SSc, the SMA caliber was significantly smaller than in HC (5.75 ± 0.62 vs. 6.45 ± 0.60 mm, p<0.0001), while IMA dimensions did not differ.

The SMA study revealed SSc patients had a significant reduction of RV (7.25 ± 6.37 vs. 18.52 ± 6.16 cm/sec, p<0.0001) and PI (3.33 ± 0.75 vs. 4.53 ± 1.03, p<0.0001) when compared to HC. In addition, in SSc the mV of SMA was significantly lower than in HC (38.03 ± 13.90 vs. 28.32 ±9.25 cm/sec, p=0.0035), as well as the RI (0.88 ± 0.04 vs. 0.91 ± 0.03, p=0.0034); EDV was significantly increased (16.34 ± 7.03 vs. 12.64 ± 5.46 cm/sec, p=0.0321). Similarly to SMA, also in IMA RV and PI were significantly lower that controls (RV: 2.69 ± 6.10 vs. 17.06 ± 5.75 cm/sec, p<0.0001; PI: 3.54 ± 0.95 vs. 6.08 ± 1.53, p<0.0001). Moreover SSc patients presented a significant reduction of PSV and RI of IMA (PSV: 72.27 ± 27.23 vs. 93.81 ± 25.73 cm/sec, p=0.0084; RI: 0.88 ± 0.04 vs. 0.91 ± 0.03, p=0.0132) when compared to HC. Although the HC group was significantly younger than the SSc group (p=0.0003), all the results were confirmed after adjustment for age (Table 1).

Table 1. comparison of the characteristics of SMA and IMA between SSc patients and HC.

	SSc		HC			Age adjusted
SMA	**N**	**Mean ± SD**	**N**	**Mean ± SD**	**p-value**	**p-value**
Caliber (mm)	28	5.75 ± 0.62	28	6.45 ± 0.60	**<0.0001**	**0.0002**
PSV (cm/sec)	28	137.50 ± 34.50	28	135.26 ± 33.81	0.8075	0.7297
RV (cm/sec)	28	7.25 ± 6.37	28	18.52 ± 6.16	**<0.0001**	**<0.0001**
EDV (cm/sec)	28	16.34 ± 7.03	28	12.64 ± 5.46	**0.0321**	0.0650
mV (cm/sec)	28	38.03 ± 13.90	28	28.32 ±9.25	**0.0035**	**0.0150**
Blood-flow (cm/sec)	28	1073.1 ± 831.16	28	913.36 ± 272.87	0.3409	0.4781
PI	28	3.33 ± 0.75	28	4.53 ± 1.03	**<0.0001**	**0.0002**
RI	28	0.88 ± 0.04	28	0.91 ± 0.03	**0.0034**	**0.0141**
IMA						
Caliber (mm)	26	2.71 ± 0.47	24	2.79 ± 0.37	0.4872	0.5385
PSV (cm/sec)	23	72.27 ± 27.23	23	93.81 ± 25.73	**0.0084**	**0.0044**
RV (cm/sec)	23	2.69 ± 6.10	23	17.06 ± 5.75	**<0.0001**	**<0.0001**
EDV (cm/sec)	23	7.87 ± 2.01	23	7.95 ± 2.10	0.8921	0.9250
mV (cm/sec)	23	17.83 ± 5.33	23	14.75 ± 5.08	0.0514	0.3938
Blood-flow (cm/sec)	23	106.70 ± 47.99	20	84.00 ± 30.13	0.0676	0.3056
PI	23	3.54 ± 0.95	23	6.08 ± 1.53	**<0.0001**	**<0.0001**
RI	23	0.88 ± 0.04	23	0.91 ± 0.03	**0.0132**	**0.0205**

SMA=superior mesentheric artery, IMA=inferior mesentheric artery, PSV=Peak Systolic Velocity, RV=Reverse Velocity, EDV=End-Diastolic Velocity, mV=Mean Velocity, PI=Pulsatility Index, RI=Resistive Index.

Conclusion: this preliminary study shows, for the first time, the presence of a significant reduction of RV, PI and RI in the intestinal arteries of SSc patients when compared to HC. These data show an increased stiffness of the gastrointestinal arterial wall, in agreement with the typical SSc vasculopathy. A larger cohort is needed to confirm the results and explore the possible relationship with other clinical features of the disease.

REFERENCES:

[1] **Sjogren, RW.** *Gastrointestinal features of scleroderma.* Curr Opin Rheumatol 1996;8:569-75.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.647

OP0177 PRESENCE AND SEVERITY OF DIGITAL OCCLUSIVE ARTERIAL DISEASE PREDICTS DIGITAL ISCHEMIC COMPLICATIONS IN SYSTEMIC SCLEROSIS

Y. Radwan[1,2], T. Gunderson[3], C. S. Crowson[2,3], D. Liedl[4], K. J. Warrington[2], P. Wennberg[4], A. Makol[2]. *[1]Michigan State University, Department of Internal Medicine, Lansing, United States of America*; *[2]Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; *[3]Mayo Clinic, Health Sciences Research, Rochester, United States of America*; *[4]Mayo Clinic, Department of Cardiovascular Disease, Rochester, United States of America*

Background: Vasculopathy is a key feature of systemic sclerosis (SSc), manifesting clinically as Raynaud's phenomenon (RP) with or without digital ischemia. Laser doppler flowmetry (LDF) with thermal challenge is a safe, noninvasive and reproducible technique to detect digital occlusive arterial disease (DOAD) with a high sensitivity and specificity of >90% (1).

Objectives: To study the prevalence and clinical correlates of DOAD assessed by LDF in patients with SSc referred for evaluation of RP at a tertiary referral center.

Methods: Medical records of all patients with SSc meeting ACR/EULAR 2013 classification criteria that underwent LDF between Jan 2001-Dec 2018 at our institution were retrospectively reviewed to abstract the presence or absence of DOAD. The presence of DOAD on LDF was confirmed if pre- and post-warming skin blood flow was ≤206 arbitrary units. Severity of DOAD was assessed based on number of digits involved. Risk factors associated with presence of DOAD in SSc, and correlation between presence and severity of DOAD with digital ischemic complications were studied.

Results: 304 patients with SSc (mean age 57.1 ± 3.3 y, 81% females, 93% Caucasians) underwent LDF during the study period. Median time between SSc diagnosis and performing LDF was 12.9 months. Majority of patients with SSc had limited cutaneous SSc (lcSSc) (79.6%) and 64.1% had a positive SSc specific antibody.

On LDF with thermal challenge, presence of DOAD was noted in 243 (79.9%) patients, of whom 78.6% had lcSSc, 42.4% had a centromere antibody (Ab), 17.3% had a Scl-70 Ab, 53.5% had interstitial lung disease, 36.6% had pulmonary arterial hypertension, and 73.3% had gastrointestinal dysmotility (GID). Of 159 patients with DOAD who also had a nailfold capillaroscopy, 70.4% had abnormalities. Large vessel occlusive disease was significantly higher in patients with DOAD in comparison to those without DOAD (29.2% vs 16.4%; p: 0.04). After adjusting for age and sex, GID (OR: 2.73 [95%CI 1.52-4.92]) and telangiectasia (OR: 2.83 [95%CI 1.23-6.40]) were significantly associated with DOAD.

Digital ischemic complications among patients with SSc with DOAD were significantly higher than among those without DOAD (79.8% vs 41.0% had digital ulcers, 53.9% vs 26.2% had pitting/scars, 31.3% vs 8.2% had gangrene/amputation; p <0.001). (Figure 1) Increasing severity of DOAD was associated with a statistically significantly higher incidence of digital ischemic complications as presented in Table 1.

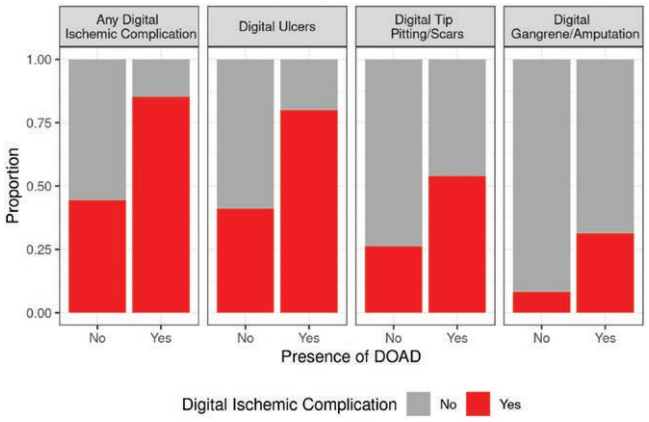


Figure 1. Correlation between the presence of digital occlusive arterial disease (DOAD) and digital ischemic complications in systemic sclerosis

Table 1. Logistic regression models for association of digital ischemic complications and severity of digital occlusive arterial disease

Digital Involvement	Odds Ratio (OR)		
Complication	**Reflects "digits vs. 0"**	**OR**	**CI 95%**
Digital Ulcer	**Unit Increase**	1.28	1.19-1.39
	1-2	2.11	0.927-4.92
	3-7	5.57	2.84-11.2
	8-10	10.9	4.98-25.4
Digital Tip Pitting/Scars	**Unit Increase**	1.17	1.10-1.26
	1-2	1.92	0.803-4.61
	3-7	2.62	1.35-5.28
	8-10	5.45	2.72-11.4
Digital Gangrene/Amputation	**Unit Increase**	1.26	1.16-1.37
	1-2	1.36	0.317-5.48
	3-7	4.10	1.62-12.6
	8-10	9.05	3.60-27.7
Any Digital Involvement	**Unit Increase**	1.35	1.24-1.49
	1-2	2.98	1.27-7.30
	3-7	6.16	3.08-12.7
	8-10	18.5	7.46-53.2

Conclusion: This is the largest single center study to describe the prevalence and predictors of DOAD on LDF in a well-defined cohort of patients with SSc. The high prevalence of DOAD on LDF noted in SSc-RP make it a valuable tool not only for evaluation of vasculopathy in SSc but also to distinguish it from Primary RP. The presence and severity of DOAD strongly correlates with digital ischemic complications and can be used as a guide to counsel patients and determine the aggressiveness of therapeutic interventions. Our study underscores the significance of LDF as a reliable non-invasive modality to detect DOAD and a prognostic tool to identify patients at highest risk of digital ischemic complications.

REFERENCES:

[1] Mahe G et al. J Vasc Surg. 2014 Apr;59(4):1051-1057.e1

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.924

Rheumatoid arthritis - prognosis, predictors and outcome

OP0178 ASSOCIATION BETWEEN ENVIRONMENTAL AIR POLLUTION AND RHEUMATOID ARTHRITIS FLARES

G. Adami[1], A. Fassio[1], O. Viapiana[1], G. Orsolini[1], E. Bertoldo[1], A. Giollo[1], D. Gatti[1], M. Rossini[1]. *[1]University of Verona, Rheumatology Unit, Verona, Italy*

Background: Environmental air pollution has been linked to the pathogenesis of Rheumatoid Arthritis (RA). Nevertheless, evidence linking higher concentrations of air pollutants with the risk of RA reactivations is missing.

Objectives: The objective of the present study was to determine the association between RA flares and air pollution.

Methods: We collected longitudinal data of patients affected by RA and of the daily concentration of air pollutants in the Verona area. We designed a case-crossover study. In case-crossover studies, instead of obtaining information from two groups (cases and controls), the exposure information is obtained comparing two different periods of time in the same group of patients followed longitudinally. We compared the exposure to pollutants in the 30-day and 60-day periods preceding an arthritic flare referent to the 30-day and 60-day preceding a low-disease activity visit. Flare was defined as an increase in DAS28-CRP of >1.2 points with current DAS28-CRP ≥3.2 (OMERACT definition).

Results: 888 patients with RA with 3,396 follow-up visits were included in the study. 13,636 daily air pollution records were retrieved. We found an exposure-response relationship between the concentration of air pollutants and the risk of having abnormal CRP levels (Figure 1). Patients exposed to greater concentrations of air pollutants were at higher risk of having CRP levels ≥5 mg/L. Patients exposed to PM10 concentrations ≥50 µg/m3 had a 70% higher risk of having CRP levels ≥5 mg/L (OR 1.696 95% CI, 1.245-2.311). Among RA patients, 440 patients (49.5%) had at least 2 follow-up visits with a difference in DAS28-CRP of more than 1.2 points (with current DAS28-CRP ≥3.2), serving as our sample for the case-crossover study. Concentrations of CO, NO, NO2, NOx, PM10, PM2.5 and O3 were higher in the 60-day period preceding a flare (Table 1). Sensitivity analyses considering geometric mean and cumulative concentrations yielded similar results (data not shown). Remarkably, we found that the cumulative exposure to NO2 in the 60 days preceding a flare was approximately 500 µg/m3 higher than the low disease activity visit, an exposure that equates to approximately to 200 passively smoked cigarettes (3.5 cigarettes per day on a 60-day period).

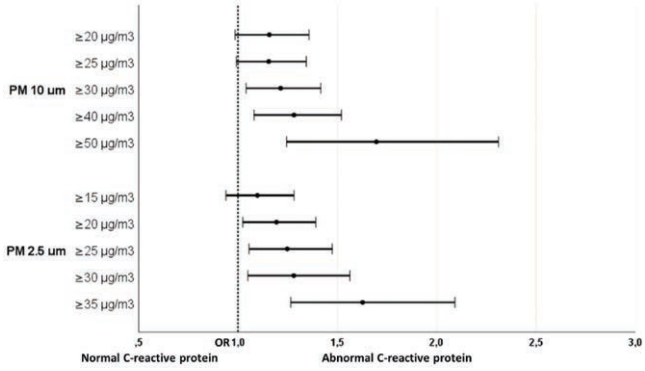


Figure 1. Odds of having abnormal CRP serum levels (≥5 mg/L) at different exposures of PM10 and PM2.5 (mean concentration in the 60 days before assessment)

Table 1. Case-crossover study. Mean concentrations (mean and Area Under the Curve) of air pollutants in the 60 days before low-disease activity visit and flare visit (DAS28-CRP difference >1.2)

Pollutant		Control period (low disease activity, n=440)	Hazard period (flare, n=440)	p value
CO µg/m^3	Mean	0.38	0.42	0.001
	AUC	22.00	24.53	0.001
NO µg/m^3	Mean	19.23	24.11	0.002
	AUC	1,120.53	1,403.88	0.002
NO_2 µg/m^3	Mean	30.91	32.44	0.042
	AUC	1,800.96	1,892.05	0.040
NO_x µg/m^3	Mean	60.34	69.35	0.004
	AUC	3,515.77	4,041.06	0.004
PM10 µg/m^3	Mean	31.21	33.65	0.011
	AUC	1,789.22	1,942.52	0.005
O_3 µg/m^3	Mean	31.08	33.79	0.002
	AUC	1,776.37	1,934.35	0.001
PM2.5 µg/m^3	Mean	23.08	24.74	0.018
	AUC	1,272.61	1,403.60	<0.001

Conclusion: We found a striking association between air pollution and RA disease severity and reactivations in a cohort of patients followed over a 5-year period. The exposure to high levels of air pollutants was associated with increased CRP levels and a higher risk of experiencing a flare of arthritis. This excessive risk was evident at very low levels of exposure, even below the proposed threshold for the protection of human health. Our study has important and direct consequences. In order to reduce the burden of RA, public and environmental health policy makers should aim to diminish gaseous and PM emissions to a larger extent as currently recommended.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.216

OP0179

DISCONTINUATION RATE OF TOFACITINIB IS SIMILAR WHEN COMPARED TO TNF INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS: POOLED DATA FROM TWO RHEUMATOID ARTHRITIS REGISTRIES IN CANADA

M. Movahedi[1], D. Choquette[2], L. Coupal[2], A. Cesta[1], X. LI[1], E. Keystone[3], C. Bombardier[1]on behalf of OBRI and RHUMADATA Investigators. *[1]UHN, Toronto General Hospital Research Institute, Toronto, Canada*; *[2]Institut de Rhumatologie de Montréal, RHUMADATA, Montreal, Canada*; *[3]University of Toronto, Medicine, Toronto, Canada*

Background: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment as the first or an alternative option to biologic disease- modifying antirheumatic drugs (bDMARDs), including tumor necrosis factor inhibitors (TNFi). The similarity in retention of TNFi and TOFA was previously reported separately by the Ontario Best Practices Research Initiative (OBRI) and the Quebec cohort RHUMADATA®.
Objectives: To increase the study power, we propose to evaluate the discontinuation rate (due to any reason) of TNFi compared to TOFA, using pooled data from both these registries.
Methods: RA patients enrolled in the OBRI and RHUMADATA initiating their TOFA or TNFi between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Time to discontinuation was assessed using adjusted Kaplan-Meier (KM) survival and Cox regression models. To deal with confounding by indication, we estimated propensity scores for covariates with a standard difference greater than 0.1. Models were then adjusted using stratification and inverse probability of treatment weight (IPTW) methods. Multiple imputation (Imputation by Chained Equation method, N=20) was used to deal with missing data for covariates at treatment initiation.
Results: A total of 1318 patients initiated TNFi (n=825) or TOFA (n=493) with mean (SD) disease duration of 8.9 (9.3) and 13.0 (10.1) years, respectively. In the TNFi group, 78.8% were female and mean age (SD) at treatment initiation was 57.6 (12.6) years. In the TOFA group, 84.6% were female and mean (SD) age at treatment initiation was 59.5 (11.5) years. The TNFi group was less likely to have prior biologic use (33.9%) than the TOFA group (66.9%). At treatment initiation, the mean (SD) CDAI was significantly ($p<0.05$) lower in the TNFi group [20.0 (11.7)] compared to the TOFA group [22.1(12.4)]. Physical function measured by HAQ-DI was also significantly lower ($p<0.05$) in the TNFi compared to the TOFA group (1.2 vs.1.3).
Over a mean follow-up of 23.2 months, discontinuation was reported in 309 (37.5%) and 182 (36.9%) of all TNFi and TOFA patients, respectively. After adjusting for propensity score deciles across 20 imputed datasets, there was no significant difference in discontinuation between treatment groups (adjusted HRs: 0.96, 95% CI: 0.78-1.18; p=0.69). The results were similar for two propensity adjustment methods. Figure 1 shows IPTW adjusted KM survival curves comparing discontinuation rates in patients treated with TNFi and TOFA.

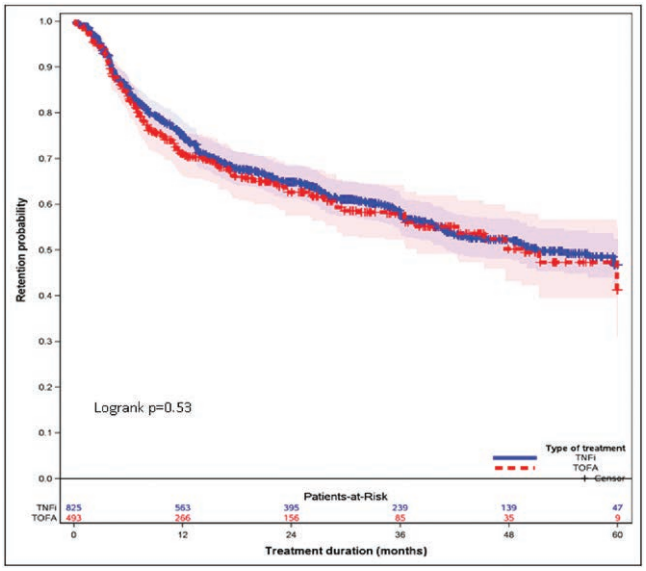


Figure 1. Note: Propensity Score Weighted (IPTW) Survival Curves was performed using one imputed dataset

Conclusion: In this pooled real -world data study, we found that TNFi and TOFA retention is similar in patients with RA. In the next step we will analysis the data for specific reasons of dicontinutaion. We will also repeat analysis comparing discontinuation in the first users versus those after one or more biologic failure.
Disclosure of Interests: Mohammad Movahedi: None declared, Denis Choquette Grant/research support from: Rhumadata® is supported by unrestricted grants from Abbvie Canada, Amgen Canada, Eli Lilly Canada, Novartis Canada, Pfizer Canada, Sandoz Canada and Sanofi Canada., Louis Coupal: None declared, Angela Cesta: None declared, Xiuying Li: None declared, Edward Keystone Grant/research support from: Amgen, Merck, Pfizer Pharmaceuticals, PuraPharm. Speaker Honoraria Agreements: AbbVie, Amgen, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis. Consulting Agreements/Advisory Board Membership: AbbVie, Amgen, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis, Claire Bombardier Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted

grants from: Abbvie, Amgen, Aurora, Bristol-Meyers Squibb, Celgene, Hospira, Janssen, Lilly, Medexus, Merck, Novartis, Pfizer, Roche, Sanofi, & UCB.
Dr. Bombardier held a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology
DOI: 10.1136/annrheumdis-2021-eular.912

OP0180

IMPACT OF RF AND ANTI-CITRULLINATED PROTEIN ANTIBODY SEROSTATUS ON 2-YEAR RETENTION OF ABATACEPT IN PATIENTS WITH RA

R. Alten[1], X. Mariette[2], R. M. Flipo[3], R. Caporali[4,5], M. H. Buch[6,7], Y. Patel[8], R. Sanmartí[9], S. Marsal[10], M. T. Nurmohamed[11], H. Griffiths[12], P. Peichl[13], B. Bannert[14], A. Forster[15], M. Chartier[16], S. Connolly[17], Y. Elbez[18], C. Rauch[19], V. Khaychuk[20], K. Lozenski[21]. [1]*Schlosspark-Klinik University, Department of Internal Medicine, Rheumatology, Berlin, Germany*; [2]*Université Paris-Saclay, AP-HP, Hospital Bicêtre, Department of Rheumatology, Paris, France*; [3]*Centre Hospitalier Universitaire de France, Department of Rheumatology, Lille, France*; [4]*University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy*; [5]*G. Pini Hospital, Clinical Rheumatology Unit, Milan, Italy*; [6]*University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [7]*University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; [8]*Hull Royal Infirmary, Rheumatology, Hull, United Kingdom*; [9]*Hospital Clinic de Barcelona, Rheumatology Department, Barcelona, Spain*; [10]*Hospital Universitari Vall d'Hebron, Rheumatology, Barcelona, Spain*; [11]*ARC Amsterdam University Hospitals – VU University Medical & Reade, Department of Rheumatology, Amsterdam, Netherlands*; [12]*University Hospital Geelong, Barwon Rheumatology Service, Geelong, Australia*; [13]*Evangelical Hospital, Department of Internal Medicine, Vienna, Austria*; [14]*Universitätsspital Basel, Rheumatologische Universitätsklinik, Basel, Switzerland*; [15]*Schulthess Klinik, Department of Rheumatology, Zürich, Switzerland*; [16]*Bristol Myers Squibb, Non-Registrational Data Generation, Rueil-Malmaison, France*; [17]*Bristol Myers Squibb, Global Drug Development, Princeton, United States of America*; [18]*Deepscover, Biostatistics, Puteaux, France*; [19]*Bristol Myers Squibb, Medical Immunology & Fibrosis, Munich, Germany*; [20]*Bristol Myers Squibb, US Medical Immunology and Fibrosis, Princeton, United States of America*; [21]*Bristol Myers Squibb, Immunology and Fibrosis, Princeton, United States of America*

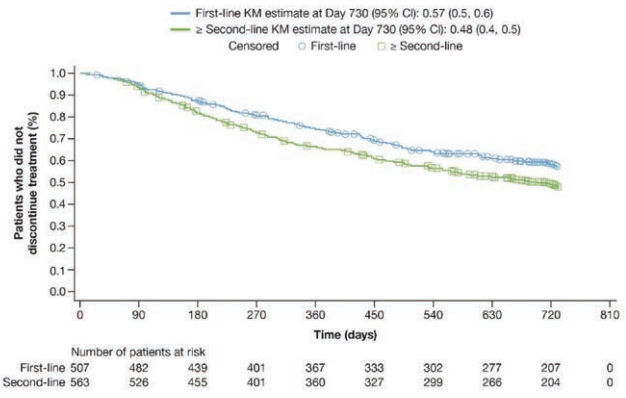
Background: Up to 50% of patients with RA discontinue DMARD treatment within 18 months.[1] However, up to 20% of patients who fail multiple treatments may have a good treatment response to another therapy.[1] Predictive biomarkers, such as RF and anti-citrullinated protein antibodies (ACPAs), may be useful to stratify patients with RA to the most appropriate treatment.[1] ASCORE (Abatacept SubCutaneOus in Routine Clinical PracticE; NCT02090556) was a 2-year, observational, prospective, multicentre study of SC abatacept for the treatment of RA in routine clinical practice.[2]
Objectives: To determine if RF/ACPA serostatus and treatment line impact abatacept retention in patients with RA in a *post hoc* analysis of ASCORE.
Methods: Eligible patients, aged ≥18 years, with active moderate-to-severe RA (ACR/EULAR 2010 criteria) who were IV abatacept-naive and initiated SC abatacept 125 mg once weekly, were enrolled into two cohorts: biologic (b) DMARD-naive patients and those with ≥1 prior bDMARD treatment failure. This *post hoc* analysis assessed abatacept retention rate at 2 years in a subset of patients with RF/ACPA serostatus data (n=1748) from the ASCORE study (N=2892; as observed). Baseline (BL) serostatus groups examined by treatment line were: RF/ACPA double positive (+/+) RA, RF/ACPA single positive (RF+/ACPA– or RF–/ACPA+) RA (data not shown) and RF/ACPA double negative (–/–) RA. Last observation carried forward (LOCF) analyses were used to assess change from BL and measures of disease remission (DAS28 [CRP] <2.6, CDAI ≤2.8, and SDAI ≤3.3) in patients with +/+ RA versus –/– RA.
Results: BL demographic and disease characteristics were similar across serostatus groups and treatment lines (Table 1). Mean age was 57.1 and 57.8 years for +/+ RA and –/– RA, respectively. Mean DAS28 (CRP) was 4.7 and 4.8 for +/+ RA and –/– RA, respectively. In patients with +/+ RA, abatacept retention was greater when given as first-line treatment (57% vs 48% when given as ≥ second-line) (Figure 1). Retention was similar in patients with –/– RA regardless of treatment line. After 2 years, mean (SE) change from BL (LOCF) in DAS28 (CRP) was –1.41 (0.06) and –0.97 (0.09) for patients with +/+ and –/– RA, respectively. For patients with +/+ RA, mean (SE) change from BL in DAS28 (CRP) was –1.62 (0.08) for those in whom abatacept was first-line and –1.19 (0.08) for those in whom abatacept was ≥ second-line. For patients with –/– RA, mean (SE) change from BL in DAS28 (CRP) was –1.03 (0.13) for those in whom abatacept was first-line and –0.93 (0.12) for those in whom abatacept was ≥ second-line. Remission rates (LOCF) were significantly (p<0.0001) higher in patients with +/+ RA vs –/– RA respectively: DAS28 (CRP) 38.4% (n=393) versus 19.3% (n=62); CDAI 50.6% (n=513) versus 33.0% (n=107); and SDAI 49.5% (n=497) versus 32.5% (n=102).
Conclusion: In this real-world analysis, patients with +/+ RA treated with first-line abatacept had higher retention than patients receiving abatacept as a ≥ second-line therapy. Remission rates on abatacept were higher in patients with +/+ RA versus –/– RA. These results support early treatment with abatacept and highlight the importance of further evaluating precision medicine approaches in RA.

Table 1. BL demographics and disease characteristics by RF/ACPA status

	+/+ RA (n=1079)		–/– RA (n=343)	
	First-line (n=511)	≥ second-line (n=568)	First-line (n=140)	≥ second-line (n=203)
Age	57.1 (13.4)	57.1 (12.2)	59.5 (14.7)	56.6 (13.2)
DAS28 (CRP)	4.7 (1.2)	4.7 (1.2)	4.8 (1.1)	4.8 (1.2)
CDAI	26.6 (12.5)	26.6 (12.4)	27.7 (12.5)	28.6 (13.8)
SDAI	28.1 (13.1)	28.1 (12.9)	29.1 (12.9)	30.2 (14.7)

Data are mean (SD). Patients with missing data for BL RF/ACPA status are excluded. ACPA=anti-citrullinated protein antibody; BL=baseline.

Figure 1. Retention rates by treatment group in patients with +/+ RA



Patients with missing data for baseline RF/ACPA status are excluded.
+/+=RF/ACPA double positive; ACPA=anti-citrullinated protein antibody; KM=Kaplan-Meier.

Acknowledgements: Professional medical writing and editorial assistance was provided by Lindsay Craik at Caudex and was funded by Bristol Myers Squibb. This study was funded by Bristol Myers Squibb.
Disclosure of Interests: Rieke Alten Speakers bureau: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Consultant of: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Grant/research support from: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Xavier Mariette Consultant of: Bristol Myers Squibb, Galapagos, Gilead, GlaxoSmithKline, Janssen, Pfizer, UCB, Rene-Marc Flipo Speakers bureau: AbbVie, Bristol Myers Squibb, Janssen, Lilly, Medac, Merck Sharp & Dohme, Novartis, Pfizer, Roche-Chugai, Grant/research support from: Amgen, Janssen, Novartis, Pfizer, Roberto Caporali Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Fresenius Kabi, Galapagos, Gilead, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Samsung Bioepis, Sanofi, UCB, Consultant of: Galapagos, Gilead, Janssen, Lilly, Merck Sharp & Dohme, Maya H Buch Speakers bureau: AbbVie, Consultant of: AbbVie, Eli Lilly, Gilead, Merck Serono, Pfizer, Roche, Sanofi, Grant/research support from: Gilead, Pfizer, Roche, UCB, Yusuf Patel: None declared, Raimón Sanmartí Speakers bureau: AbbVie, Bristol Myers Squibb, Gebro, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, Consultant of: AbbVie, Bristol Myers Squibb, Gebro, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, Grant/research support from: Bristol Myers Squibb, Merck Sharp & Dohme, Pfizer, Sara Marsal Speakers bureau: Bristol Myers Squibb, Celgene, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol Myers Squibb, Celgene, Galapagos, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, UCB, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Sanofi, UCB, M.T. Nurmohamed Speakers bureau: AbbVie, Bristol Myers Squibb, Eli Lilly, Roche, Sanofi, Consultant of: AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Mundipharma, Novartis, Pfizer, Roche, Sanofi, Hedley Griffiths Consultant of: AbbVie, Gilead, Janssen, Novartis, Peter Peichl: None declared, Bettina Bannert: None declared, Adrian Forster: None declared, Melanie Chartier Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Sean Connolly Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Yedid Elbez Consultant of: Bristol Myers Squibb, Christiane Rauch Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Vadim Khaychuk Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Karissa Lozenski Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.932

REFERENCES:
[1] Smolen JS, et al. *Ann Rheum Dis* 2020;79:685–699.
[2] Alten R, et al. *Ann Rheum Dis* 2019;78(suppl 2):A1639.

OP0181

CURRENT FAVOURABLE 10-YEAR OUTCOME OF PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: DATA FROM THE ESPOIR COHORT

B. Combe[1], N. Rincheval[2], F. Berenbaum[3], P. Boumier[4], A. Cantagrel[5], P. Dieudé[3], M. Dougados[3], B. Fautrel[3], R. M. Flipo[6], P. Goupille[7], X. Mariette[3], A. Saraux[8], T. Schaeverbeke[9], J. Sibilia[10], O. Vittecoq[11], J. P. Daures[2]on behalf of ESPOIR Cohort. *[1]Montpellier, Rhumatologie, Montpellier, France*; *[2]Montpellier, INSERM, Montpellier, France*; *[3]Paris, RHUMATOLOGIE, Paris, France*; *[4]Limoges, RHUMATOLOGIE, Limoges, France*; *[5]CHU, Rheumatology, Toulouse, France*; *[6]Lille, RHUMATOLOGIE, Lille, France*; *[7]Tours, RHUMATOLOGIE, Tours, France*; *[8]Brest, RHUMATOLOGIE, Brest, France*; *[9]Bordeaux, RHUMATOLOGIE, Bordeaux, France*; *[10]Strasbourg, RHUMATOLOGIE, Strasbourg, France*; *[11]Rouen, RHUMATOLOGIE, Rouen, France*

Background: ESPOIR is a longitudinal prospective cohort of adults with possible early RA (ClinicalTrials.gov: NCT03666091). Patients were referred by rheumatologists and general practitioners to one of the 14 regional centers in France. The objective and design of the cohort are described elsewhere (1). Patients received standard of care by their rheumatologists and were followed without predefined therapeutic strategies

Objectives: To report the current 10-year outcome of patients with early rheumatoid arthritis (RA) in the ESPOIR cohort, and predictors of outcome.

Methods: From 2003 to 2005, 813 patients were included if they had early arthritis (< 6 months) with a high probability of RA developing and had never been prescribed disease modifying anti-rheumatic drugs (DMARDs). Multivariate logistic regression analysis was used to evaluate predictors of outcome.

Results: In total, 521 (64.1%) RA patients were followed up for 10 years and 35 (4.3%) died, which appears similar to the French general population. Overall, 480 (92.1%) patients received a DMARD; 174/521 (33.4%) received at least one biologic DMARD, 13.6 and 23.4% within 2 and 5 years. At year 10 (Table), mean DAS28 ESR was 2.5 ± 1.3; 273 (52.4%) patients were in DAS28 remission, 39.7% in CDAI remission, 40.1% in DAS28 sustained remission, and 14.1% in drug-free remission. Disability was well controlled overtime (Figure) and half of the patients achieved a HAQ Disability Index < 0.5; the SF-36 physical component and pain were well controlled. Structural progression was weak, with a mean change from baseline in modified Sharp score of 11.0 ± 17.9. A total of 82 (16.5%) patients required joint surgery including arthroplasty or arthrodesis in only 6.5% of the cases. A substantial number of patients showed new comorbidities, mainly cardiovascular or metabolic diseases over 10 years. Finally, positivity for anti-citrullinated protein antibodies was confirmed as a robust predictor of long-term outcome in patients with early RA.

Table 1. Outcome in ESPOIR cohort and 1993 cohort at 10 years

	ESPOIR cohort n=521	1993 cohort n=112
DAS28 ESR	2.5 ± 1.3	
DAS44	-	2.2 ± 0.9
SDAI	7.5 ± 8.7	
CDAI	6.8 ±8.3	
DAS28 ESR remission (n (%)	273 (52.4)	
CDAI remission	207 (39.7)	
DAS28 sustained remission, n (%)	209 (40.1)	
DAS28 drug-free remission, n (%)	75 (14.1)	
DAS28 ESR LDA	336 (64.5)	
Rheumatoid nodules	39 (7.5)	
Sicca syndrome	314 (60.3)	
Patient global assessment	24.0 ± 24.0	
HAQ DI score	0.5 ± 0.6	0.75 ± 0.71
HAQ DI < 0.5, n (%)	280 (54.5)	
SF36 MCS	46.7 ± 10.5	
SF36 PCS	44.6 ± 9.2	
Pain (mm, VAS)	16.6 ± 20.6	
Fatigue (mm, VAS)	31.4 ± 27.0	23.2 ± 23.0
ESR (mm/hr)	14.4 ± 13.8	18.4 ± 16.5
CRP level (mg/l)	6.4 ± 16.5	9.3 ± 11.7
Normal CRP (< 5 mg/l), n (%)	336 (67.6)	
Total mSharp score*	13.8 ± 19.6	35.4 ± 46.1
Erosion score	4.9 ± 9.4	18.4 ± 26.5)
Joint narrowing score	8.9 ± 12.1	32.1 ±23.2
Joint surgery	82 (16.5)	26 (23.2)
Joint arthroplasty/arthrodesis	34 (6.5)	20 (17.9)

Data are mean (SD)

DAS28, disease activity in 28 joints; HAQ DI, Health Assessment Questionnaire Disability Index; SF36 MCS, Medial Outcomes Study 36-item Short Form mental component summary; SF36 PCS, Medical Outcomes Study 36-item Short Form physical component summary; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; VAS, visual analog scale; CDAI, Clinical Disease Activity Index; SDAI, Simple Disease Activity Index; *van der Heijde-modified Total Sharp score

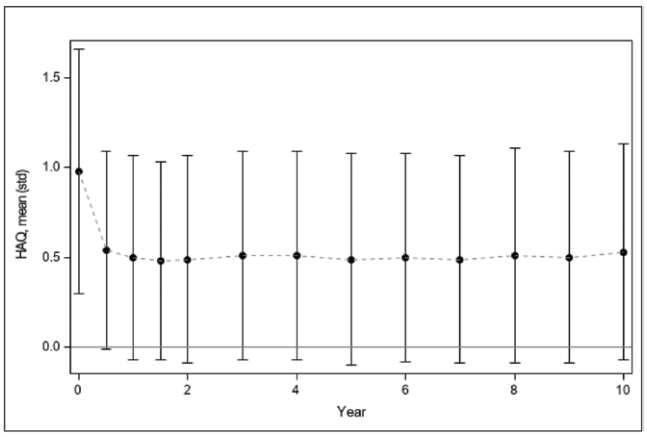


Figure 1. Health Assessment Questionnaire Disability Index (HAQ-DI) over 10 yearsData are mean (SD).

Conclusion: We report a very mild 10-year outcome of a large inception cohort of patients with early RA diagnosed in the early 2000s, which was much better than results for a previous cohort of early RA patients who were recruited in 1993. This current favourable outcome may be related to more intensive care for real-life patients than previously.

REFERENCES:

[1] Combe B et al. Jt Bone Spine Rev Rhum. 2007;74:440–5

Acknowledgements: We thank MC Boissier, G Falgaronne and F. Lioté for help in patient recruitment. An unrestricted grant from Merck Sharp and Dohme (MSD) was allocated for the first 5 years of the cohort study. Two additional grants from INSERM supported part of the biological database. The French Society of Rheumatology, Abbvie, Pfizer, Lilly and more recently Fresenius and Biogen supported the ESPOIR cohort.

Disclosure of Interests: Bernard Combe Speakers bureau: AbbVie; BMS; Gilead; Lilly; Merck; Pfizer; Roche-Chugai;, Consultant of: AbbVie; BMS; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi;, Grant/research support from: Fresenius, Novartis, Pfizer, and Roche-Chugai., Nathalie Rincheval: None declared, Francis Berenbaum Speakers bureau: Boehringer, Bone Therapeutics, Expanscience, Galapagos, Gilead, GSK, Merck Sereno, MSD, Nordic, Novartis, Regulaxis, Roche, Sandoz, Sanofi, Servier, UCB, Peptinov, TRB Chemedica, 4Moving Biotech, 4P Pharma, Consultant of: Boehringer, Bone Therapeutics, Expanscience, Galapagos, Gilead, GSK, Merck Sereno, MSD, Nordic, Novartis, Regulaxis, Roche, Sandoz, Sanofi, Servier, UCB, Peptinov, TRB Chemedica, 4Moving Biotech, 4P Pharma, Patrick BOUMIER: None declared, Alain Cantagrel Speakers bureau: AbbVie; Amgen, Bristol-Myers Squibb; Grunenthal; Lilly; Medac; MSD France; Novartis; Pfizer; Roche-Chugai; Sanofi;, Consultant of: AbbVie; Amgen, Bristol-Myers Squibb; Grunenthal; Lilly; Medac; MSD France; Novartis; Pfizer; Roche-Chugai; Sanofi;, Grant/research support from: Abbvie, Fresenius, MSD France, Novartis, Pfizer, and UCB, Philippe Dieudé Speakers bureau: Boehringer Ingelheim, Bristol-Myers Squibb, Chugai, Lilly, Medac, Novartis Roche-Genentech, Sanofi, Consultant of: Boehringer Ingelheim, Bristol-Myers Squibb, Chugai, Lilly, Medac, Novartis Roche-Genentech, Sanofi, Grant/research support from: Bristol-Myers Squibb, GlaxoSmithKline, Pfizer., Maxime Dougados Speakers bureau: Pfizer, Abbvie, Lilly, UCB, Merck, BMS, Roche, Biogen, Sanofi, Novartis, and Sandoz, Consultant of: Pfizer, Abbvie, Lilly, UCB, Merck, BMS, Roche, Biogen, Sanofi, Novartis, and Sandoz, Grant/research support from: Pfizer, Abbvie, Lilly, UCB, Merck, BMS, Roche, Biogen, Sanofi, Novartis, and Sandoz, Bruno Fautrel Speakers bureau: AbbVie, Amgen, Biogen, BMS, Celgene, Celltrion, Fresenius Kabi, Gilead, Janssen, Lilly, Medac, MSD, Mylan, NORDIC Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi-Genzyme, SOBI, UCB, Consultant of: AbbVie, Amgen, Biogen, BMS, Celgene, Celltrion, Fresenius Kabi, Gilead, Janssen, Lilly, Medac, MSD, Mylan, NORDIC Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi-Genzyme, SOBI, UCB, Grant/research support from: AbbVie, Lilly, MSD and Pfizer, René-Marc Flipo Speakers bureau: Abbvie, Biogen, BMS, Janssen, MSD, Nordic, Novartis, Pfizer, Roche-Chugai and Sanofi-Genzyme, Consultant of: Abbvie, Biogen, BMS, Janssen, MSD, Nordic, Novartis, Pfizer, Roche-Chugai and Sanofi-Genzyme, Grant/research support from: Abbvie, Janssen, Novartis, Pfizer and Roche-Chugai, Philippe Goupille Speakers bureau: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB., Consultant of: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB., Grant/research support from: Abbvie, Biogen, MSD, Pfizer, Xavier Mariette Speakers bureau: BMS, Galapagos, Gilead, GSK, Janssen, Lilly, Novartis, Pfizer,

Servier, and UCB., Consultant of: BMS, Galapagos, Gilead, GSK, Janssen, Lilly, Novartis, Pfizer, Servier, and UCB., Grant/research support from: Servier, Alain Saraux Speakers bureau: AbbVie, Bristol-Myers Squibb, Lilly, Nordic, Novartis, Pfizer, Roche-Chugai, Sanofi and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Lilly, Nordic, Novartis, Pfizer, Roche-Chugai, Sanofi and UCB, Grant/research support from: Roche-Chugai, Thierry Schaeverbeke Speakers bureau: AbbVie, BMS, Lilly, Novartis, Nordic Pharma, Pfizer, Roche, UCB, Consultant of: AbbVie, BMS, Lilly, Novartis, Nordic Pharma, Pfizer, Roche, UCB, Grant/research support from: Pfizer, AbbVie, BMS, Roche, UCB, Astra, MSD, Rigel, AB-sciences, Jean Sibilia Speakers bureau: AbbVie, Lilly, MSD, Amgen, Pfizer, BMS, Janssen, Roche, Sandoz, Sanofi-Genzyme, SOBI, UCB, Novartis., Consultant of: AbbVie, Lilly, MSD, Amgen, Pfizer, BMS, Janssen, Roche, Sandoz, Sanofi-Genzyme, SOBI, UCB, Novartis., Grant/research support from: AbbVie, Lilly, Pfizer, Roche, Olivier VITTECOQ Speakers bureau: AbbVie, Bristol-Myers Squibb, Gilead, Lilly, Merck, Novartis, Pfizer; Roche-Chugai, Mylan and Sanofi, Consultant of: AbbVie, Bristol-Myers Squibb, Gilead, Lilly, Merck, Novartis, Pfizer; Roche-Chugai, Mylan and Sanofi, Grant/research support from: Novartis, Pfizer, Merck, and Bristol-Myers Squibb, Jean-Pierre Daures: None declared

DOI: 10.1136/annrheumdis-2021-eular.1063

OP0182 IN RA PATIENTS IN REMISSION, WHICH BIOMARKERS PREDICT SUCCESSFUL TAPERING OF CSDMARDS?

H. Gul[1], F. Ponchel[1], P. Emery[1]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine, Rheumatology, Leeds, United Kingdom*

Background: Recommendations for the management of patients with RA who achieve stable clinical remission ≥6 months with conventional synthetic (cs) disease-modifying anti-rheumatic drugs (DMARDs) are to taper (with the aim of potentially stopping), although there are currently no validated biomarkers permitting prediction of sustained remission.

Objectives: To assess the rate of sustained remission over 12 months In RA patients in remission, who received either (i) structured tapering of csDMARDs or (ii) continuation of current therapy, focusing on the value of imaging and immunological biomarkers as well as patient-reported outcome measures (PROs).

Methods: RA patients (n=200) prospectively attending a remission clinic, fulfilling DAS28(3v)CRP<2.6 for ≥6 months on stable csDMARD therapy (mono or combination therapy & no corticosteroids) were included. Patients were offered the choice of structured cs-DMARD tapering according to a pre-defined protocol (Table 1) or remaining on stable therapy. Clinical, ultrasound (US), immunological (T-cell subsets) and PRO data were collected at inclusion. Loss of remission was defined as increase of DAS28(3v)CRP >2.6. Mann-Whitney-U and Chi-square tests were used to compare outcomes. After imputing missing data, regressions for predicting sustained remission were performed. AUROCs were used to compare models.

Results: The decision to taper treatment was associated with male gender, longer remission duration, normal CRP and lower grey scale scores (p<0.05). Of those who tapered 64% (75/117) remained in clinical remission at 12 months, compared to 80% (66/83, p=0.018) of patients who remained on stable treatment. At 15 months 11/117 (10%) had successfully stopped therapy.

In the tapering group, higher CRP, TJC and IRC were consistently associated with inability to sustain remission, as well as higher scores for several PROs (p<0.05) with a trend for total PD (P=0.066). Predicting sustained remission was modelled and retained RAQoL, total PD and a T-cell subset (Figure 1, 85% accuracy, AUROC 0.872).

In the non-tapering group, higher CRP/ESR, SJC and shorter disease duration (p<0.05) were associated with flare. No parameter was able to predict sustained remission.

Conclusion: In patients who chose to taper, the combination of clinical, PRO, US and T-cell parameters demonstrated added value for predicting sustained remission (85% accuracy) compared to clinical parameters alone. Different biomarkers were associated with sustained remission on continued therapy. These data may assist with informed tapering of csDMARDs.

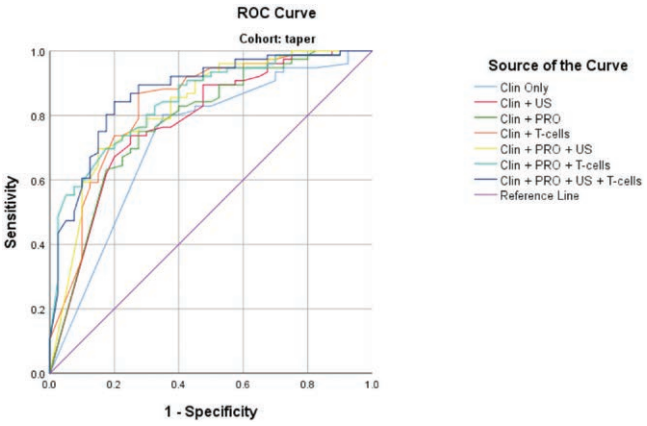


Figure 1. AUROC Analysis of tapering cohort data

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1523

OP0183 IDENTIFICATION OF A SUBGROUP OF PEOPLE WITH RHEUMATOID ARTHRITIS CHARACTERISED BY HIGH DISABILITY OVER 10 YEARS, DESPITE LOW INFLAMMATION: RESULTS FROM TWO EUROPEAN PROSPECTIVE COHORT STUDIES

J. Gwinnutt[1], S. Norton[2,3], K. Hyrich[1,4], M. Lunt[1], B. Combe[5], N. Rincheval[6], A. Ruyssen-Witrand[7], B. Fautrel[8,9], J. Chipping[10,11], A. Macgregor[10,11], S. Verstappen[1,4]. [1]*The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [2]*King's College London, Health Psychology section, Institute of Psychiatry, Psychology and Neuroscience, London, United Kingdom*; [3]*King's College London, Department of Inflammation Biology, Faculty of Life Sciences and Medicine, London, United Kingdom*; [4]*Manchester Academic Health Science Centre, NIHR Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, Manchester, United Kingdom*; [5]*The University of Montpellier, Department of Rheumatology, CHU Montpellier, Montpellier, France*; [6]*The University of Montpellier, Laboratory of Biostatistics and Epidemiology, Montpellier, France*; [7]*Hôpital Purpan, Centre de Rhumatologie, Toulouse, France*; [8]*Pitie Salpetriere Hospital, Department of Rheumatology, Assistance Publique Hôpitaux de Paris, Paris, France*; [9]*Sorbonne University, INSERM UMRS, Pierre Louis Institute of Epidemiology and Public Health, Paris, France*; [10]*University of East Anglia, Norwich Medical School, Norwich, United Kingdom*; [11]*Norfolk and Norwich University Hospitals NHS Trust, Rheumatology Department, Norwich, United Kingdom*

Background: Long-term studies in rheumatoid arthritis (RA) have reported low inflammation yet high disability over time. It is important to determine which factors are driving this disparity, so appropriate interventions can be used to reduce this gap.

Objectives: To identify a subgroup of people with RA with low inflammation yet high disability over 10 years, and describe their characteristics.

Methods: Data came from two cohorts of inflammatory arthritis with regular assessments over 10 years: the Norfolk Arthritis Register (NOAR, inclusion: ≥2 swollen joints for ≥4 weeks) from the UK and the *Etude et Suivi des Polyarthrites Indifférenciées Récentes* study (ESPOIR, inclusion: early RA) from France. Participants provided demographic data and completed patient reported outcomes (PROs, including the Health Assessment Questionnaire [HAQ]). The 2-component Disease Activity Score (DAS28-2C)[1], a measure of inflammation, was

Table 1. csDMARD tapering schedule

Drug	Baseline Dose	Taper 1	Taper 2	Taper 3	Taper 4	Taper 5
Hydroxychloroquine	200mg bd	200mg od	Stop	-	-	-
Hydroxychloroquine	200mg od	Stop	-	-	-	-
Sulfasalazine	1.5g bd	1g bd	1.5g od	500mg bd	500mg od	Stop
Sulfasalazine	1g bd	1.5g od	500mg bd	500mg od	Stop	-
Sulfasalazine	500mg bd	500mg od	Stop	-	-	-
Sulfasalazine	500mg od	Stop	-	-	-	-
Methotrexate	25mg/week	15mg/week	7.5mg/week	No change	Stop	-
Methotrexate	15mg/week	7.5mg/week	No change	Stop	-	-
Methotrexate	7.5mg/week	No change	Stop	-	-	-

NB: Patients were seen 3-monthly. If they remained in remission following tapering, they proceeded to the next taper unless there is a significant clinical reason not to taper at the time of assessment (as per standard care). Order of cs-DMARD tapering applies to patients on dual/triple therapy. All but 5 (112) were on methotrexate.

Table 1. Baseline characteristics / logistic regression analysis

	NOAR			ESPOIR		
Variable	Low HAQ trajectory, mean (SD)	High HAQ trajectory, mean (SD)	OR (95% CI)	Low HAQ trajectory, mean (SD)	High HAQ trajectory, mean (SD)	OR (95% CI)
N (%)	343 (59%)	239 (41%)	-	131 (55%)	108 (45%)	-
Age, years	54.9 (14.2)	62.1 (13.8)	1.07 (1.05, 1.08)	47.8 (13.3)	51.8 (11.2)	1.04 (1.01, 1.06)
Women, N (%)	224 (65.3%)	176 (73.6%)	1.82 (1.12, 2.78)	100 (76.3%)	95 (88.0%)	2.73 (1.20, 6.23)
Symptom duration, months	7.8 (5.1)	8 (5.4)	1.10 (0.98, 1.05)	3.4 (1.8)	3.6 (1.8)	1.16 (0.98, 1.37)
Current smoker, N (%)	77 (22.4%)	50 (20.9%)	1.19 (0.71, 2.00)	61 (46.6%)	52 (48.1%)	1.52 (0.82, 2.83)
DAS28-2C	3.14 (1.46)	3.21 (1.56)	-	4.65 (1.31)	4.41 (1.35)	-
HAQ	0.8 (0.6)	1.4 (0.5)	-	1.1 (0.6)	1.6 (0.6)	-
Pain (0-10)	3.7 (2.4)	4.6 (2.5)	1.16 (1.07, 1.26)	4.1 (2.8)	5.1 (2.6)	1.07 (0.95, 1.20)
Fatigue (0-10)	4.3 (2.8)	5.3 (2.5)	1.16 (1.06, 1.28)	5.0 (2.6)	6.5 (2.5)	1.20 (1.05, 1.36)
AIMS anxiety	3.99 (1.96)	4.42 (1.99)	1.06 (0.88, 1.29)	4.9 (2.26)	5.98 (2.25)	1.10 (0.94, 1.29)
AIMS depression	2.85 (1.87)	3.38 (1.87)	1.10 (0.94, 1.29)	3.96 (1.99)	5.08 (2.32)	1.12 (0.94, 1.33)
RF+, N (%)	142 (41.4%)	106 (44.4%)	0.94 (0.60, 1.46)	79 (60.3%)	50 (46.3%)	0.77 (0.34, 1.75)
Anti-CCP+, N (%)	113 (32.9%)	86 (36.0%)	1.35 (0.84, 2.17)	76 (58.0%)	45 (41.7%)	0.89 (0.39, 2.05)

calculated from swollen joint counts and C-reactive protein level. Inclusion criteria for this analyis: <2 years baseline symptom duration; HAQ and DAS28-2C at baseline and one other follow-up; recruited after 1/1/2000. HAQ and DAS28-2C were modelled simultaneously using a multivariate group-based trajectory model, to identify groups of participants with similar trajectories of HAQ and DAS28-2C over 10 years. Baseline demographics and PROs were compared between the trajectory groups using logistic regression. Analyses performed separately in NOAR and ESPOIR.

Results: 1001 NOAR and 767 ESPOIR participants were included. In both cohorts, a four group trajectory model had the best fit (Figure). Two subgroups were identified in each cohort that demonstrated the hypothesised relationship: similar DAS28-2C but differing HAQ scores (red trajectories in Figure), titled "High HAQ" and "Low HAQ" (mean difference in HAQ over follow-up [95% confidence interval (CI)]: NOAR 0.76 [0.73, 0.80]; ESPOIR 0.89 [0.82, 0.96]). At baseline, the High HAQ groups in both NOAR and ESPOIR were older, had a higher proportion of women, and had higher levels of fatigue (NOAR: odds ratio [OR] 1.16 [95% CI 1.06, 1.28]; ESPOIR: OR 1.20 [95% CI 1.05, 1.36] [Table]) and pain (NOAR only).

Conclusion: There is a group of people with RA with high levels of disability, despite low inflammation. These results underline the potential need for pain and fatigue management in people with RA, even when inflammation is low.

REFERENCES:

[1] Hensor et al (2019). *Rheumatology (Oxford) 58*(8)

Acknowledgements: Thanks to the participants of NOAR and ESPOIR and those working in the recruiting centres

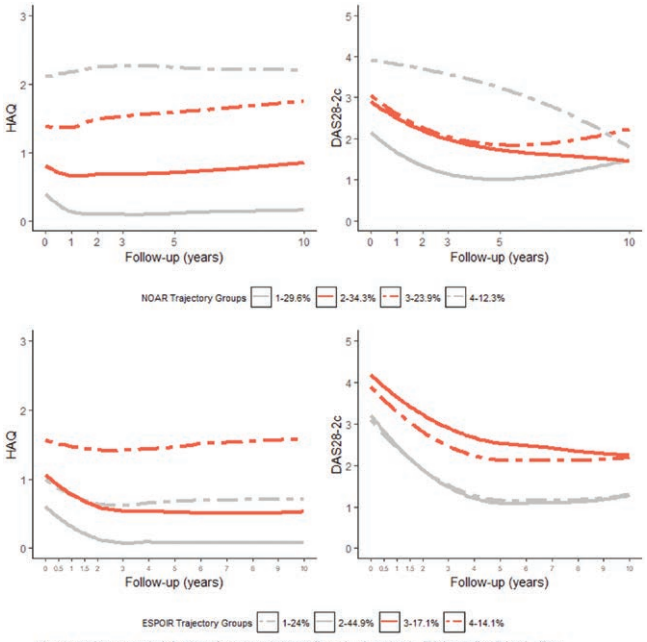


Figure - Trajectory analysis in NOAR (upper) and ESPOIR (lower) – dotted red = "high HAQ", solid red = "low HAQ", grey lines indicate other trajectory groups identified by the Group-Based Trajectory Analysis.

ESPOIR Funding: An unrestricted grant from Merck Sharp and Dohme (MSD) was allocated for the first 5 years of the cohort study. Two additional grants from INSERM supported part of the biological database. The French Society of Rheumatology, Abbvie, Pfizer, Lilly and more recently Fresenius and Biogen supported the ESPOIR cohort study.

Disclosure of Interests: James Gwinnutt Grant/research support from: Research grant from Bristol Myers Squibb unrelated to this project, Sam Norton Consultant of: Pfizer and AstraZeneca, Kimme Hyrich Consultant of: Abbvie, Grant/research support from: Pfizer and BMS, Mark Lunt: None declared, Bernard Combe: None declared, Nathalie Rincheval: None declared, Adeline Ruyssen-Witrand: None declared, Bruno Fautrel: None declared, Jacqueline Chipping: None declared, Alex MacGregor: None declared, Suzanne Verstappen: None declared

DOI: 10.1136/annrheumdis-2021-eular.1770

OP0184

PHENOTYPING OF MOLECULAR SIGNATURES IN THE SYNOVIAL TISSUE OF RHEUMATOID ARTHRITIS BY INTEGRATIVE SYSTEMS ANALYSIS

J. Qiao[1,2,3], S. X. Zhang[1,2,3], H. Wang[1,2,3], J. Q. Zhang[1,2,3], M. T. Qiu[1,2,3], M. J. Chang[1,2,3], R. Zhao[1,2,3], S. Song[1,2,3], G. Y. Liu[1], P. F. He[4], X. LI[1,2,3]. *[1]The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; *[2]Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; *[3]Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; *[4]Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Rheumatoid arthritis (RA) is an aggressive immune-mediated joint disease characterized by synovial proliferation and inflammation, cartilage destruction, and joint destruction[1]. Despite efforts to characterize the disease subsets and to predict the differential prognosis in RA patients, disease heterogeneity is not adequately translated into the current clinical subclassification[2].

Objectives: To develop and validate an integrative system approach for stratifying patients with RA according to disease status and whole-genome gene expression data.

Methods: An RNA sequencing dataset of synovial tissues from 124 RA patients (including 57 patients with early RA, 95 with established RA) and 15 healthy controls (HC) was imported from the Gene Expression Omnibus (GEO) database (GSE89408) by software package R (version 4.0.3). After filtrating of differentially expressed genes (DEGs) between RA and HC, non-negative matrix factorization, functional enrichment, and immune cell infiltration were applied to illustrate the landscapes of these patients for classification. Clinical features (age, gender, and auto-antibodies) were also compared to discover the signatures of these classifications.

Results: A matrix of 576 DEGs from RA samples was classified into 5 subtypes (early/C1–C3, established/C4-C5) with distinct molecular and cellular signatures and two sub-groups (S1 and S2) (Figure 1A-1D). New-onset patients (early C2) and established C4 patients were named as S1, they shared similar gene signatures mainly characterized by prominent immune cells and proinflammatory signatures, and enriched in the chemokine-mediated signaling pathway, lymphocyte activation, response to bacterium and Primary immunodeficiency. S2(C1, C3 and C5) were more occupied by synovial fibroblasts of destructive phenotype. They were mainly enriched in the response to external factors and PPAR signaling pathway (Figure 1E-1H). Interestingly, combined with clinical information, S1 and S2 had no significance in age and gender ($P > 0.05$). But patients in S1 had a stronger association with the presence of anti-citrullinated protein antibodies (ACPA) ($P < 0.05$) (Figure 1I-1J).

Conclusion: We successfully deconvoluted RA synovial tissues into pathobiological discrete subsets using an unsupervised machine learning method and described their distinct molecular and cellular characteristics. These results

provide important insights into divergent and shared mechanistic features of RA and serve as a template for future studies to guide drug tar-get discovery by synovial molecular signatures and de-sign stratified approaches for patients with RA.

REFERENCES:

[1] Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet 2016;388(10055):2023-38. doi: 10.1016/S0140-6736(16)30173-8 [published Online First: 2016/10/30]

[2] Jung SM, Park KS, Kim KJ. Deep phenotyping of synovial molecular signatures by integrative systems analysis in rheumatoid arthritis. Rheumatology (Oxford) 2020 doi: 10.1093/rheumatology/keaa751 [published Online First: 2020/11/25]

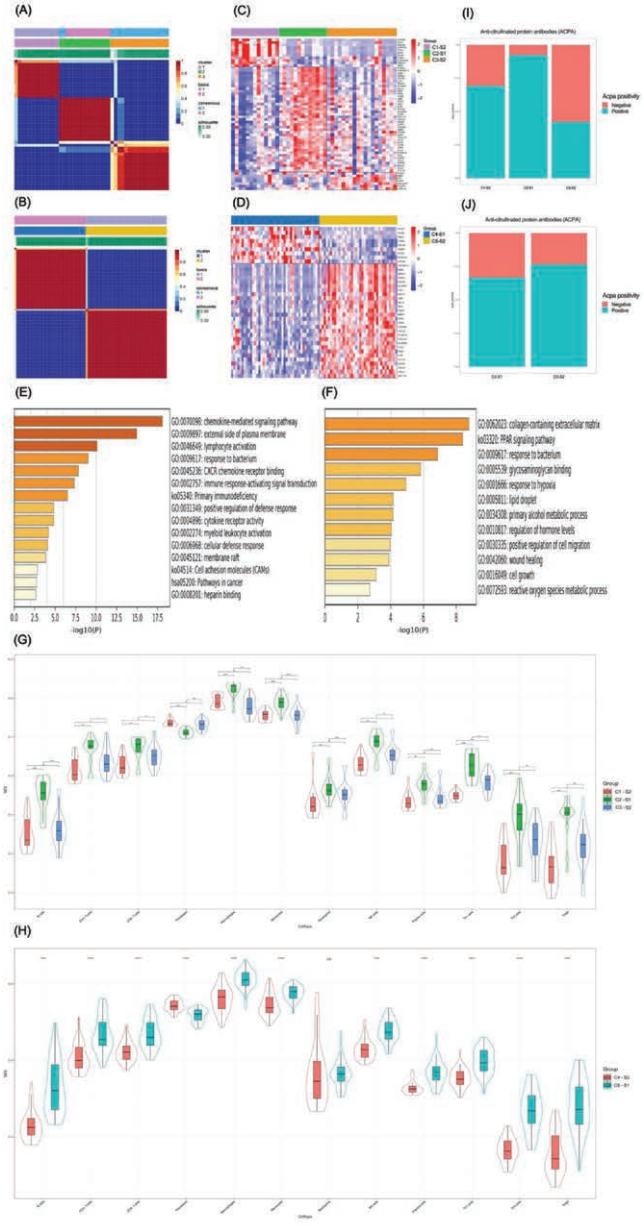


Figure1 Identification of RA patients using non-negative matrix factorization, functional enrichment, and immune cell infiltration in the differentially expressed genes set. **(A-D)** The consensus map of NMF clustering results in the total RNA sequencing dataset. Patients were divided into cluster 1-5 according to the expression profiles of 576 DEGs. Heatmap of five clusters defined by the cluster-based genes expression. **(E-F)** Gene Ontology (GO) terms and KEGG pathway related to common cluster-based gene signatures. **(G-H)** Cell subset enrichment score according to RA subgroup. **(I-J)** Distribution of the five RA subgroups by clinical phenotypes (the positivity of ACPA). (ns, not significant; * P<0.05; ** P<0.01; *** P<0.001;**** P<0.0001)

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1970

OP0185

RADIOGRAPHIC PROGRESSION DESPITE PERSISTENT LDA OR REMISSION IS INFLUENCED BY CURRENT SMOKING RATHER THAN THE RESPECTIVE DAS 28 LEVEL, RESULTS OF THE SWISS RHEUMATOID ARTHRITIS REGISTER (SCQM)

L. Brandt[1,2], H. Schulze-Koops[3], T. Hügle[4], M. J. Nissen[5], H. Paul[6], R. Muller[6]. *[1]Division of Rheumatology, Medical University Department, Kantonsspital Aarau, Aarau, Switzerland*; *[2]Ludwig-Maximilians-University Munich, Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, Munich, Germany*; *[3]Ludwig-Maximilians-University Munich, Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, Munich, Germany*; *[4]University Lausanne, Division of Rheumatology, University Hospital Lausanne (CHUV), Lausanne, Switzerland*; *[5]Geneva university hospital, Rheumatology, Geneva, Switzerland*; *[6]Kantonsspital Aarau, Division of Rheumatology, Medical University Department, Aarau, Switzerland*

Background: The therapeutic aim for rheumatoid arthritis (RA) is to control disease activity and prevent radiographic progression. Various clinical scores are utilized to describe disease activity in RA patients. The DAS28 score can define states of low disease activity (LDA) and remission. Despite achieving LDA or remission, radiographic progression may nevertheless occur. However, the rates and frequency of this occurrence have not been analyzed in detail.

Objectives: To describe the frequency and rate of radiographic progression in patients with persistent LDA or remission.

Methods: Analysis of RA patients from the SCQM cohort. Persistent LDA or remission were defined as DAS 28 ≤3.2 or <2.6 respectively, at two subsequent follow up time points in the database. We included patients with at least two sets of radiographs within these intervals of LDA and/or remission. Radiographic progression was measured with the Ratingen-score (range 0-190), which describes joint erosions numerically. Repair was defined as an improvement in the Ratingen score >5 points/year and progression as >2 or >5 points change in the Ratingen score within one year.

Results: Among 10'141 RA patients, 4'342 episodes of remission occurred in 3'927 patients with 1'776 sets of X rays available within these episodes. Similarly, 8'136 episodes of LDA in 6'765 patients and 2'358 sets of X rays were present within these intervals. For patients in LDA or remission, rates of repair were 5.5% and 4.8%, respectively, while for radiographic progression >5 points in the Ratingen score/year were 10.3% in both groups and for >2 points change of Ratingen score/year were 27.7 and 25.4%, respectively).

No differences for demographic factors or measures of disease activity, rheumatoid factor or ACPA were found comparing patients with radiographic progression or non-progression despite LDA or remission at the beginning of the episode of LDA and/or remission.

Interestingly, 42.9% of patients in LDA with progression of >5 points in the Ratingen score/year were current smokers vs 29.4% among the non-progressors (X^2 = 6.55, p = 0.01). This significant difference vanished when the cut-off for radiographic progression was set at >2 points yearly change in Ratingen score or in patients in remission.

Conclusion: Radiographic progression despite LDA or remission are more frequent than expected. No differences in radiographic progression were found comparing LDA and remission suggesting that the goal of LDA is appropriate. Smoking seems to be an independent risk factor for radiographic progression despite LDA. Why the effect of smoking could was not demonstrated in patients in remission, remains unclear.

Disclosure of Interests: Lena Brandt: None declared, Hendrik Schulze-Koops: None declared, Thomas Hügle Consultant of: GSK, Abbvie, Pfizer, Jansen, Novartis, Eli Lilly., Michael J. Nissen Consultant of: Abbvie, Celgene, Eli-Lilly, Janssen, Novartis and Pfizer, Hasler paul Consultant of: Abbvie, Lilly, Rudiger Muller Consultant of: AbbVie, Novartis, Grant/research support from: Gebro

DOI: 10.1136/annrheumdis-2021-eular.2557

Oncorheumatology: the crossroads of cancer and musculoskeletal diseases

OP0186

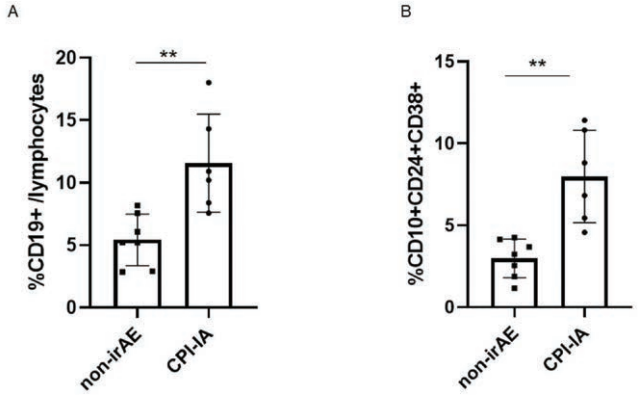
CHANGES IN CIRCULATING B CELL LEVELS AND IMMUNOPHENOTYPE ARE ASSOCIATED WITH DEVELOPMENT OF ARTHRITIS FOLLOWING TREATMENT WITH CHECKPOINT INHIBITORS

M. Gatto[1,2,2], S. Bjursten[3,4], C. Jonell[1], C. Jonsson[1], S. Mcgrath[1], A. Rudin[1], M. Levin[3,4,5], I. Gjertsson[1]. *[1]University of Gothenburg, Rheumatology and Inflammation Research, GOTHENBURG, Sweden*; *[2]University of Padova, Unit of Rheumatology, Padova, Italy*; *[3]University of Gothenburg, Oncology, Sahlgrenska University Hospital, GOTHENBURG, Sweden*; *[4]University of Gothenburg, Oncology, Institute of Clinical Sciences, Sahlgrenska Academy, GOTHENBURG,*

Sweden; [5]*University of Gothenburg, Wallenberg Laboratory for Cardiovascular Research, Department of Molecular and Clinical Medicine, Sahlgrenska Academy, GOTHENBURG, Sweden*

Background: Inflammatory arthritis (IA) is frequent among rheumatic side effects induced by checkpoint inhibitor (CPI) therapy for metastatic malignancies[1]. While T cells are likely to sustain the inflammatory process[2], fewer data are available concerning the role of B cells[3].
Objectives: To investigate the phenotype of circulating B cells in patients who develop CPI-induced IA (CPI-IA) and to compare it with features of B cells in patients not developing immune-related adverse events (irAE) upon CPI treatment.
Methods: B cell subsets at baseline (before CPI initiation) and during CPI treatment were analyzed in CPI-IA patients and in patients receiving CPI but who did not develop irAE (non-irAE). Peripheral blood mononuclear cells (PBMC) were analyzed by flow cytometry and B cells were identified as $CD19^+$ and divided into naïve ($CD27^-IgD^+$), memory ($CD27^+IgD^{+/-}$), double negative ($CD27^-IgD^-$) and transitional ($CD10^+CD24^+CD38^{+/hi}$) B cells. Levels of CD21, an activation marker on transitional B cells, were also analyzed. Non-parametric tests were used for analysis of differences between groups.
Results: Six CPI-IA and 7 non-irAE patients matched for age, gender and CPI treatment were included, who had received CPI treatment due to metastatic melanoma. Flow cytometry revealed a significant increase of circulating B cells (p=0.002) (Figure 1A) and especially of transitional B cells in CPI-IA patients vs. non-irAE (median %, range: 7.8 (4.5-11.4) vs. 3.2 (1.6-4.3),p=0.007) (Figure 1B), while no remarkable changes were seen across other subsets. Transitional B cell levels significantly decreased from active to quiescent CPI-IA in all patients (p=0.008). In two CPI-IA patients for whom baseline sampling was available, the increase of transitional levels occurred early after CPI treatment and before CPI-IA onset. Levels of expression of CD21 on transitional B cells were increased in CPI-IA vs. non-irAE (p=0.01).

Figure 1. B cells (CD19+) and transitionals are significantly increased in CPI-IA patients
Mann-whitney U test, **<0.01



Conclusion: Transitional B cells are expanded in CPI-IA patients and seem to increase early after start of CPI therapy. Monitoring this B cell subset might lead to closer follow-up and earlier diagnosis of CPI-IA.
REFERENCES:
[1] Ramos-Casals M, Brahmer JR, Callahan MK, et al. Immune-related adverse events of checkpoint inhibitors. Nat Rev Dis Primers 2020;6:38
[2] Murray-Brown W, Wilsdon TD, Weedon H, et al. Nivolumab-induced synovitis is characterized by florid T cell infiltration and rapid resolution with synovial biopsy-guided therapy. J Immunother Cancer 2020;8:e000281
[3] Das R, Bar N, Ferreira M, et al. Early B cell changes predict autoimmunity following combination immune checkpoint blockade. J Clin Invest. 2018;128:715-2
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.908

OP0187 INCIDENCE OF MALIGNANCY IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE JAPANESE IORRA PATIENT REGISTRY

M. Harigai[1], N. Sugitani[1], R. Sakai[1], E. Inoue[1,2], M. Mochizuki[3], S. Toyoizumi[4], N. Yoshii[3], N. Sugiyama[3], E. Tanaka[1], H. Yamanaka[1,5]. [1]*Tokyo Women's Medical University School of Medicine, Department of Rheumatology, Tokyo, Japan*; [2]*Showa University, Showa University Research Administration Center, Tokyo, Japan*; [3]*Pfizer Japan Inc, Inflammation and Immunology, Tokyo, Japan*; [4]*Pfizer R&D Japan, Biometrics and Data Management, Tokyo, Japan*; [5]*Sanno Medical Center, Tokyo, Japan*

Background: The risk of some types of malignancy is increased in patients (pts) with rheumatoid arthritis (RA), compared with the general population. We have previously reported the incidence of malignancy in Japanese pts with RA.[1-4]
Objectives: This analysis further evaluated the incidence of malignancy in Japanese pts with RA using recent data from the large prospective observational study, IORRA.
Methods: This analysis included all pts with RA aged ≥18 years who were enrolled in IORRA from April 2013 to October 2018, with follow-up through October 2019, and participated in ≥2 surveys. Index was defined as the date of the first entry in the IORRA database, with baseline defined as the 6-month period prior to the index date. Malignancies were identified in pt reports of biannual IORRA surveys and confirmed using medical records. Age- and sex-standardised incidence ratios (SIRs) and 95% confidence intervals (CIs) were calculated.
Results: In total, 8020 pts were included. At baseline, the majority (85.0%) of pts were female; mean disease duration was 12.8 years, 5.8% and 4.8% of pts had a past history of malignancy or comorbid malignancy at baseline, respectively, and the majority (75.9%) of pts were receiving methotrexate (Table). The SIR (95% CI) was 0.90 (0.80, 1.01). SIRs (95% CI) of site-specific malignancies were: breast cancer, 0.91 (0.69, 1.18); lung cancer, 0.67 (0.44, 0.97); colon cancer, 0.93 (0.62, 1.32); stomach cancer, 0.82 (0.56, 1.14); and lymphoma, 3.74 (2.73, 4.96).

Table 1. Patient demographics and baseline disease characteristics

	Patients with RA (N=8020)
Age (years), mean (SD)	59.3 (13.8)
Female, n (%)	6816 (85.0)
Duration of RA (years), mean (SD)	12.8 (10.3)
Never smoked, n (%)	5086 (66.2)
DAS28, mean (SD)	2.8 (1.1)
J-HAQ, mean (SD)	0.60 (0.72)
Malignancy status, n (%)	
Past history of malignancy	467 (5.8)
Comorbid malignancy at baseline	386 (4.8)
Medication use, n (%)	
MTX	6088 (75.9)
Tacrolimus	787 (9.8)
Corticosteroids	2641 (32.9)
bDMARD use	1508 (18.8)
TNFi	1163 (14.5)
Tocilizumab	311 (3.9)
Abatacept	106 (1.3)
JAK inhibitors	4 (0.05)

bDMARD, biological disease-modifying antirheumatic drug; DAS28, Disease Activity Score in 28 joints; JAK, Janus kinase; J-HAQ, Japanese Health Assessment Questionnaire; MTX, methotrexate; N, the number of patients included in the analysis, the number of patients assessed for each characteristic may be fewer than N; n, the number of patients with each characteristic; SD, standard deviation; TNFi, tumour necrosis factor inhibitor

Conclusion: Overall risk of malignancy was similar to that in the general Japanese population, although a significantly higher risk of lymphoma was identified.
REFERENCES:
[1] Sugimoto et al. Rheumatol Int 2017; 37: 1871-1878.
[2] Shimizu et al. Clin Rheumatol 2017; 36: 1237-1245.
[3] Askling et al. Ann Rheum Dis 2016; 75: 1789-1796.
[4] Yamada et al. Rheumatol Int 2011; 31: 1487-1492.
Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Anthony G McCluskey, CMC Connect, and funded by Pfizer Inc.
Disclosure of Interests: masayoshi harigai Speakers bureau: AbbVie Japan, Ayumi, Boehringer Ingelheim Japan, Bristol-Myers Squibb, Chugai, Eisai, Eli Lilly Japan, GlaxoSmithKline, Kissei, Pfizer Japan Inc, Takeda, Teijin, Consultant of: AbbVie Japan, Boehringer Ingelheim Japan, Bristol-Myers Squibb, Kissei, Teijin, Grant/research support from: AbbVie Japan, Asahi Kasei, Astellas, Ayumi, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Kissei, Mitsubishi Tanabe, Nippon Kayaku, Sekiui Medical, Shionogi, Taisho, Takeda, Teijin, Naohiro Sugitani: None declared, Ryoko Sakai Speakers bureau: Bristol-Myers Squibb, Eisuke Inoue Speakers bureau: Pfizer Japan Inc, Bristol-Myers Squibb, Michika MOCHIZUKI Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Shigeyuki Toyoizumi Employee of: Pfizer R&D Japan, Noritoshi Yoshii Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Naonobu Sugiyama Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Eiichi Tanaka Speakers bureau: AbbVie Japan, Asahi Kasei, Astellas, Ayumi, Chugai, Eisai, Eli Lilly Japan, GlaxoSmithKline, Kyowa, Janssen, Mochida, Pfizer Japan Inc, Takeda, Teijin, Hisashi Yamanaka Speakers bureau: Astellas, Bristol-Myers-Squibb, Pfizer Inc, Mitsubishi Tanabe, Teijin, YLBio, Consultant of: Corrona, LLC
DOI: 10.1136/annrheumdis-2021-eular.356

Joint Session EULAR ESCMI and EANM (European Association of Nuclear Medicine) – State-of-the-art nuclear imaging in RMDs

OP0189 MACROPHAGE PET/CT IMAGING OF THE FEET CAN CONTRIBUTE TO EARLY PREDICTION OF THERAPY OUTCOME IN RHEUMATOID ARTHRITIS

N. J. F. Verweij[1], M. Ter Wee[1,2], J. De Jongh[1], G. C. J. Zwezerijnen[3], M. Yaqub[3], D. Van Schaardenburg[1], A. Voskuyl[1], W. Lems[1], A. A. Lammertsma[3], M. Boers[1,2], C. J. Van der Laken[1]. [1]*Amsterdam Rheumatology and Immunology Center, Amsterdam UMC - Location VUmc, Department of Rheumatology, Amsterdam, Netherlands*; [2]*Amsterdam Public Health, Amsterdam UMC – location VUmc, Department of Epidemiology and Biostatistics, Amsterdam, Netherlands*; [3]*Amsterdam UMC - Location VUmc, Department of Radiology & Nuclear Medicine, Amsterdam, Netherlands*

Background: Treat-to-target strategies for rheumatoid arthritis (RA) have shown significant improvements in therapy outcomes. Nevertheless, it usually takes a minimum of 12 weeks before clinical assessment of treatment response can be made. Quantitative positron emission tomography (PET) has shown potential to predict clinical response at a very early stage in the treatment in RA patients.(1) In particular, macrophage imaging by [^{11}C]-(*R*)-PK11195 PET allows for highly sensitive and specific imaging of RA disease activity.(2,3)

Objectives: To determine whether quantitative assessment using [^{11}C]-(R)-PK11195 PET/CT imaging at 0-2 weeks is associated with subsequent clinical response to therapy with methotrexate and step-down prednisolone (COBRA-light) therapy in therapy-naive RA patients.

Methods: Whole body [11C]-(R)-PK11195 PET/CT scans were performed at baseline and after two weeks of treatment in thirty-five clinically active and therapy-naive RA patients and at least two clinically inflamed joints. All patients were DMARD-naïve and received medication according to the COBRA-light schedule. (4) Clinical follow up with DAS44 assessment was performed at 0, 2 and 13 weeks of treatment. PET/CT scans were visually assessed by two experienced readers blinded to clinical data and quantitatively analyzed using in-house software. Regions of interest (ROIs) with a fixed size per joint (on both visual PET positive and negative joints) were placed on shoulders, elbows, hips, knees and hand and feet joints, with the CT-scan as anatomical reference. Standardized uptake values (SUVs) normalized for body weight were calculated in these ROIs to determine the amount of tracer uptake per joint. SPSS version 22.0 was used to perform regression analyses. The sum of visually positive joints and the average SUV in hand joints, feet joints and all joints in the body were compared with DAS44 scores.

Results: Included patients were mostly male (51%) and aged 54 ± 12. Baseline DAS44 was 3.2 ± 1.0; all but one of the thirty-five patients demonstrated visually enhanced tracer uptake in one or more joints on PET/CT. A total of 171 (out of 1470) joints (12%) were visually PET positive at baseline. Over 90% of PET positive sites were located either in the wrists (15%), small hand joints (37%), or small feet joints (40%; Figure 1A). After 2 weeks, the number of PET positive joints had decreased to 100, with the highest decrease in quantitative uptake in feet joints (Figure 1B). Notably, both visual and quantitative PET data at baseline and differences between baseline and 2 weeks did not correlate with DAS44 at 13 weeks (DAS44-13wks). However, at 2 weeks, the average SUV in the feet (SUVfeet-2wks) – but not average SUVhands-2wks or average SUVtotalbody-2wks – was significantly correlated with DAS44-13wks (R^2 = 0.14, p = 0.04). DAS44-2wks and SUVfeet-2wks both contributed independent information to the prediction DAS44-13wks (combined R^2 = 0.297, p < 0.01).

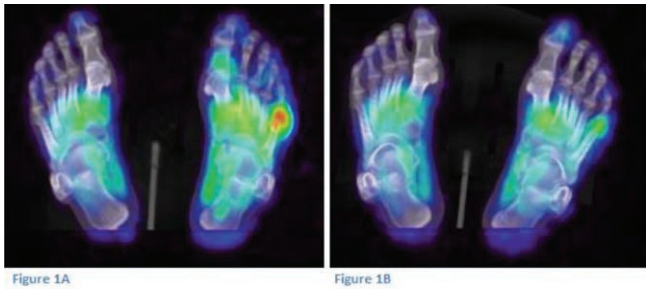


Figure 1. Changes in [^{11}C]-(R)-PK11195 uptake in MTP joints of a RA patient, before (A) and 2 weeks after initiation of COBRA light treatment (B).

Conclusion: Quantitative macrophage PET assessment in feet joints after 2 weeks of COBRA light treatment in early RA patients correlates with clinical response after 3 months of treatment. This correlation further increases when combined with the DAS44 score at 2 weeks. Therefore, quantitative, non-invasive macrophage PET/CT, especially when combined with early clinical assessment, may be useful for early assessment of response to treatment. Further studies will help optimize timing and focus of the PET examination in prediction of treatment response.

REFERENCES:

[1] Elzinga EH, et al. J Nucl Med. 2011; 52(1):77-80.
[2] Van der Laken CJ et al. Arthritis Rheum. 2008 Nov;58(11):3350-5.
[3] Gent YY, et al. J Rheumatol. 2014; 41: 2145-52
[4] Den Uyl D, et al. Ann Rheum Dis. 2014;73(6):1071-8.

Disclosure of Interests: Nicki J.F. Verweij: None declared, Marieke ter Wee: None declared, Jerney de Jongh: None declared, Gerben C.J. Zwezerijnen: None declared, Maqsood Yaqub: None declared, Dirkjan van Schaardenburg: None declared, Alexandre Voskuyl: None declared, WIllem Lems Speakers bureau: Pfizer, Galapagos, Eli Lilly, Amgen, UCB, Curaphar, Consultant of: Pfizer, Galapagos, Eli Lilly, Amgen, UCB, Curaphar, Grant/research support from: Pfizer, Adriaan A. Lammertsma Consultant of: Roche, Maarten Boers Consultant of: Novartis, BMS, Pfizer, Conny J. van der Laken Consultant of: Novartis, Pfizer, Abbvie, UCB, BMS, GSK, Galapagos, Grant/research support from: Novartis, Pfizer, Abbvie, UCB, BMS, GSK, Galapagos
DOI: 10.1136/annrheumdis-2021-eular.2189

OP0190 USEFULNESS OF 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY IN DIAGNOSING POLYMYALGIA RHEUMATICA AND LARGE-VESSEL VASCULITIS: A CASE-CONTROL STUDY

A. Desvages[1], F. Hives[2], X. Deprez[3], A. Pierache[4], R. M. Flipo[1], J. Paccou[1]. [1]*Lille University Hospital, Rheumatology, Lille, France*; [2]*Lille University Hospital, Nuclear Medicine, Lille, France*; [3]*Valenciennes Hospital, Rheumatology, Valenciennes, France*; [4]*Lille University Hospital, Biostatistics, Lille, France*

Background: Polymyalgia rheumatica (PMR) is a relatively common disease among the elderly. None of the most common imaging techniques provides diagnostic certainty of PMR. 18F-fluoro-dexoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) may be a useful candidate as it can be used to visualize articular and periarticular FDG uptake at different locations, as well as associated large-vessel vasculitis (LVV), but its usefulness needs to be evaluated in the absence of large-scale case-control studies.

Objectives: The purpose of this study was to determine the usefulness of FDG-PET/CT in diagnosing PMR and LVV.

Methods: We analysed FDG-PET/CT scans performed between January 2015 and December 2019 on patients diagnosed with PMR. For comparisons, patients with PMR were matched 1:1 to controls according to age and sex. FDG-PET/CT scans had been performed on controls over the same period for diagnosis of cancer-associated stroke. FDG uptake was scored visually using a semi-quantitative analysis (score 0-3) for 17 articular or periarticular sites, as described by Sondag *et* al. **[1]**, and for 13 vascular sites, as described by Slart *et* al. **[2]**. The case and control groups were compared using generalized linear mixed models (binomial distribution, logit function) for binary outcomes, and linear mixed models for continuous outcomes, with matched sets as a random effect. The optimal threshold for the number of sites with significant hyperfixation (score ≥ 2) was determined by maximizing the Youden index.

Results: 81 patients with a diagnosis of PMR and 81 controls were included (mean (SD) age 70.7 (9.8) years; 44.4% women). We found significant differences between the PMR and control groups at all articular or periarticular sites for: 1) FDG uptake score (p<0.0001); 2) number of patients per site with significant FDG uptake (score ≥ 2) (p<0.0001); 3) global FDG articular uptake scores (score 0-51) (31 [IQR, 21 to 37] versus 6 [IQR, 3 to 10], p<0.001); and 4) number of sites with significant FDG uptake (score ≥ 2) (score 0-17) (11 [IQR, 7 to 13] versus 1 [IQR, 0 to 2], p<0.001). Using ROC curve analysis (Figure 1), we found that the presence of 6 or more sites with significant FDG uptake (≥ 2) was associated with the diagnosis of PMR with a sensitivity of 84% and a specificity of 96% (AUC 0.96 [95% CI 0.93-0.99]). No significant differences in global FDG vascular uptake scores (score 0-39) or in number of patients with at least 1 significant uptake vascular site (score ≥ 2) were found between the PMR and control groups (1 [IQR, 0 to 4] versus 4 [0 to 6], p=0.06 and 8 (11.3%) versus 10 (14.1%), p=0.62 respectively).

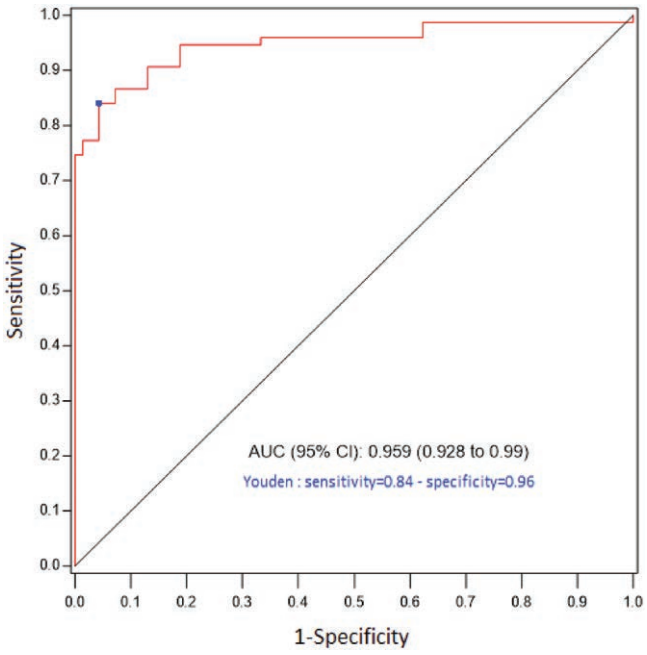


Figure 1. ROC curve analyzing performance of FDG-PET/CT for the diagnosis of PMR according to the number of sites with significant FDG uptake (≥ 2)

Conclusion: Our results demonstrate that the FDG uptake score and the number of sites with significant FDG uptake could be relevant criteria for the diagnosis of PMR. However, unlike other authors, we found no evidence suggesting that FDG-PET/CT may be useful in diagnosing silent underlying LVV in patients with isolated PMR.

REFERENCES:

[1] Sondag M, Guillot X, Verhoeven F, Blagosklonov O, Prati C, Boulahdour H, et al. Utility of 18F-fluoro-dexoxyglucose positron emission tomography for the diagnosis of polymyalgia rheumatica: a controlled study. Rheumatology (Oxford). 2016;55(8):1452-7.

[2] Slart RHJA, Writing group, Reviewer group, Members of EANM Cardiovascular, Members of EANM Infection & Inflammation, Members of Committees, SNMMI Cardiovascular, Members of Council, PET Interest Group, et al. FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (PIG), and endorsed by the ASNC. Eur J Nucl Med Mol Imaging. 2018;45(7):1250-69.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.780

Improving collaborative research and patients' participation in health decision-making

OP0191-PARE

DEVELOPMENT OF A PUBLIC AND PATIENT INVOLVEMENT (PPI) RESEARCH NETWORK FOR PEOPLE WHO HAVE RHEUMATIC CONDITIONS

L. Larkin[1], A. Moses[1], T. Raad[1], A. Tierney[1], N. Kennedy[1], W. Costello[2].
[1]*University of Limerick, School of Allied Health and Health Research Institute, Limerick, Ireland*; [2]*iCAN, Irish Children's Arthritis Network, Tipperary, Ireland*

Background: Public and patient involvement (PPI) improves quality and relevance of research (1). PPI is advocated by policy makers and funding bodies and is supported by EULAR (2). Arthritis Research Limerick (ARL) is a partnership between researchers at the University of Limerick and clinicians at University Hospitals Limerick. PPI representatives have been involved in ARL projects, however no formal PPI network had been established prior to 2020. The need for a formal PPI network to collaborate with ARL was identified by both ARL and patient representatives. This need arose from a joint ambition to promote meaningful involvement of the public and patients in ARL projects and to develop a platform through which researchers and PPI representatives could collaboratively set research priorities.

Objectives: The aim of this project was to create a formal PPI network to engage with people living with rheumatic and musculoskeletal diseases (RMDs) and their families and to identify collaborative research opportunities between ARL and PPI representatives.

Methods: A face-to-face PPI seminar was planned for October 2020. The seminar consisted of speakers from ARL providing an overview of research projects and a World Café research ideas session. Funding was obtained through a competitive, peer-review funding call from the PPI Ignite group at the University of Limerick to support the PPI seminar. The funding application was a joint application between ARL members and a PPI partner (iCAN - Irish Children's Arthritis Network). The seminar was advertised through national patient organisations (iCAN and Arthritis Ireland), social media and ARL research networks.

Results: Due to Covid-19 public health restrictions the PPI seminar was held virtually. The ARL PPI inaugural seminar was attended by N=19 researchers and people living with RMDs. The seminar speakers included ARL researchers and a PPI representative. The World Café event was modified to adapt to the virtual seminar delivery. Research ideas were noted by the seminar organiser and summarised for attendees at the end of the research ideas and priorities session. An ARL PPI mailing list was set-up post seminar as a means of communicating with seminar attendees and will serve as a formal PPI network for ARL. Research updates and opportunities will be communicated via this formal network to people living with RMDs and researchers alike.

Conclusion: This was the first PPI seminar organised by ARL in collaboration with a PPI seminar, and has led to the creation of a formal PPI network. Delivery mode of the PPI seminar was changed due to Covid-19 public health restrictions. This change may also have impacted engagement and attendance at the PPI seminar, given that virtual events are not accessible to all of the RMD population. Future PPI seminars will consider a hybrid approach of face-to-face and virtual attendance, to enhance accessibility. A formal PPI communication network has been established. Future work will focus future collaborative opportunities between the PPI panel and the ARL group, including project development, co-led research funding applications and joint research dissemination.

REFERENCES:

[1] INVOLVE. (2012). Briefing notes for researchers: Involving the public in NHS, public health and social care research. Retrieved from www.invo.org.uk 7th January 2020.

[2] de Wit MPT, Berlo SE, Aanerud GJ, et al (2011). European League Against Rheumatism recommendations for the inclusion of patient representatives in scientific projects. *Annals of the Rheumatic Diseases* 70:722-726

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.442

Comorbidities in gout and hyperuricaemia

OP0192

INCIDENT GOUT AND RISK OF FIRST-TIME ACUTE CORONARY SYNDROME: A PROSPECTIVE, POPULATION-BASED, COHORT STUDY IN SWEDEN

P. Drivelegka[1], L. T. H. Jacobsson[1], U. Lindström[1], K. Bengtsson[1], M. Dehlin[1].
[1]*Institute of Medicine, The Sahlgrenska Academy at University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*

Background: Gout is associated with an increased risk of cardiovascular disease (CVD), but it is not clear whether this risk is intrinsic to gout itself or to underlying comorbidities. Although the impact of gout on CVD has been studied previously, the results have been conflicting and studies from European countries are scarce.

Objectives: To investigate the risk of first-time acute coronary syndrome (ACS) in patients with incident gout in western Sweden, compared to the general population.

Methods: Using data from the population-based health care database VEGA, we identified all patients with incident gout diagnosis at either primary or specialized health care units in western Sweden, in the period 2007– 2017 (20,287 cases; mean age, 65.6 years; 67.4% males). Cases regarded as incident, if they did not have any recorded diagnosis of gout in the previous seven years. For each case, up to five controls matched on age, sex, and county at the date of first gout diagnosis were identified from the census register (84,240 controls). Cases and controls with prior history of ischemic heart disease were

excluded. The follow-up began at the first diagnosis of gout, and ended at the earliest of an ACS event, emigration, death, or 31 December 2017. To estimate the risk of first-time ACS, we used incident rate (IR) and univariable and multivariable Cox regression analysis with adjustments for the following cardiovascular risk factors: the diagnoses of hypertension, diabetes, hyperlipidemia, obesity, renal disease, heart failure, cardiomyopathy, psoriasis, chronic obstructive pulmonary disease, alcoholism, cancer, cerebrovascular, and atherosclerotic disease, as well as for the dispensed prescriptions of statins, anticoagulants, anti-hypertensive, anti-diabetic, anti-hyperlipidemic, anti-obesity, and vasodilator drugs.

Results: The IR of first-time ACS was 9.0 events per 1,000 person-years in the gout cohort, compared to 6.3 in the control cohort. The IRs were lower for women than men, both in the gout (IR, 8.2 vs 9.4) and in the control cohort (IR, 5.0 vs 7.0). Univariable analysis showed that patients with gout have a higher risk of first-time ACS, as compared to the general population (Figure 1, Table 1), but the increased risk is largely diminished after adjustments for cardiovascular risk factors (Table 1).

Table 1. Risk of first-time ACS in patients with incident gout, as compared to the general population.

	Unadjusted HR	95% CI	p-value	Adjusted HR	95% CI	p-value
ACS						
Overall	1.43	1.32-1.55	<.0001	1.15	1.05-1.24	0.0013
Men	1.35	1.23-1.48	<.0001	1.12	1.02-1.23	0.0230
Women	1.63	1.41-1.89	<.0001	1.21	1.03-1.41	0.0207

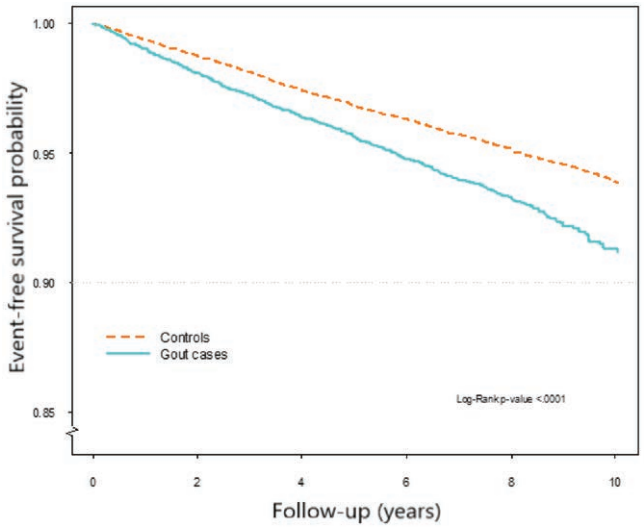


Figure 1. Event-free survival curve for patients with gout and controls during the follow-up, where event is first-time acute coronary syndrome.

Conclusion: Patients with incident gout have a 43% higher risk of first-time ACS, as compared to the general population. This increased risk is largely explained by the increased occurrence of comorbidities in gout, but there is still a modestly increased risk that may be due to gout related factors. Our results underline the importance of cardiovascular risk assessment and the need for appropriate management of the underlying cardiovascular risk factors in patients with gout.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3256

OP0193

EVALUATION OF THE CAUSAL EFFECTS BETWEEN GOUT AND HYPERTENSION: A MENDELIAN RANDOMIZATION STUDY

Y. J. Chang[1], L. C. Wang[2], C. K. Chen[1], C. I. Hsieh[2], C. F. Kuo[1,2]. *[1]Chang Gung Memorial Hospital, Center for Artificial Intelligence in Medicine, Taoyuan, Taiwan, Republic of China*; *[2]Chang Gung Memorial Hospital, Rheumatology, Allergy and Immunology, Taoyuan, Taiwan, Republic of China*

Background: Gout is the most common inflammatory arthritis worldwide associated with comorbidities that may impair well-being and reduce longevity. Epidemiological evidence generally supports that gout patients are at high risk of hypertension. However, the causality between gout and hypertension is uncertain since confounding and other types of bias are difficult to contain in the observational study.

Objectives: To test the causal link between gout and hypertension using a Mendelian Randomization (MR) analysis.

Methods: A mendelian randomization analysis was conducted using individual patient data from the Taiwan Biobank featured 2452 individuals with gout and 66527 controls. We selected 12 SNPs as instrumental variables (IVs) with p-values $< 5 \times 10^{-8}$ and the linkage disequilibrium (LD) R^2 value less than 0.8. We conducted traditional MR analysis using the inversed weighted variance (IVW) and median methods with different settings as the primary analysis. Further IV assumption-free methods, the MR-Egger methods [1], Causal Analysis Using Summary Effect Estimates (CAUSE) model [2], and structural equation modeling (SEM) [3,4] were also performed as a sensitivity analysis.

Results: The prevalence of hypertension was 0.15% (n = 9549) in the cohort. Table 1 shows causal effect estimates between gout and hypertension using different methods. The average causal effect β is estimated at 0.09 and the corresponding odds ratio (OR) at 1.09 using traditional methods across different settings. Similar estimates were observed in the MR-Egger method, SEM model, and the CAUSE model, demonstrating the robustness of the causal association between gout and hypertension considering pleiotropic effects (Table 1). Furthermore, the model fit of the hypothesized SEM model is excellent with a comparative fit index of 0.978 and Tucker-Lewis index of 0.968. The SEM model explains at least 32.70% variance of hypertension and 32.6% variance of gout (Figure 1).

Table 1. Estimate the causal effect of MR analysis and sensitivity analysis

Method	Causal effect estimate β	95% lower bound	95% upper bound	p-value
Primary analysis				
IVW with fixed effect, first order	0.0900	0.0656[a]	0.1145[a]	$<10^{-5}$
IVW with fixed effect, second order	0.0895	0.0647[a]	0.1143[a]	$<10^{-5}$
IVW with random effect, first order	0.0900	0.0656[a]	0.1145[a]	$<10^{-5}$
IVW with random effect, second order	0.0895	0.0647[a]	0.1143[a]	$<10^{-5}$
Median method, simple	0.0989	0.0645[a]	0.1332[a]	$<10^{-5}$
Median method, weighted	0.0902	0.0583[a]	0.1220[a]	$<10^{-5}$
Median method, penalized	0.0902	0.0583[a]	0.1220[a]	$<10^{-5}$
Sensitivity analysis				
MR-Egger	0.0786	0.0132[a]	0.1440[a]	0.0183
SEM	0.0519	0.0481[a]	0.0697[a]	$<10^{-5}$
CAUSE model	0.0764	0.0176[b]	0.1349[b]	$<10^{-5}$

* [a] represents the 95% confidence interval; [b] represents the 95% credible interval.

** For the random effect model, if the estimated residual standard error is less than 1, then the *MendelianRandomization* package will automatically set the value of residual standard error into 1.

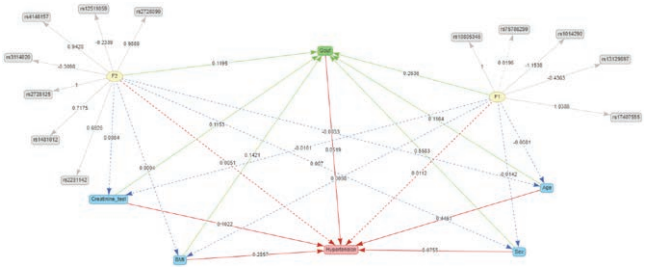


Figure 1. Pathway analysis for SEM study assessing the relationships between gout and hypertension.

Conclusion: These results strongly suggest that the association between gout and hypertension has a causal basis.

REFERENCES:

[1] Bowden J, Davey Smith G, Burgess S. Mendelian randomization with invalid instruments: effect estimation and bias detection through Egger regression. Int J Epidemiol. 2015 Apr; 44(2):512-525.

[2] Morrison J, Knoblauch N, Marcus JH, Stephens M, He X. Mendelian randomization accounting for correlated and uncorrelated pleiotropic effects using genome-wide summary statistics. Nat Genet. 2020 Jul; 52(7):740-747.

[3] Streiner DL. Building a better model: an introduction to structural equation modelling. Can J Psychiatry. 2006 Apr; 51(5):317-324.

[4] Stephen B, Rhian MD, Adam SB, Simon GT, and the EPIC-InterAct. Network Mendelian randomization: using genetic variants as instrumental variables to investigate mediation in causal pathways. Int J Epidemiol. 2015 Apr; 44(2): 484-495.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2061

Immune events with checkpoint inhibitors

OP0194 GENERALIZED IMMUNE ACTIVATION IN STRUCTURES RELATED TO PMR OR GCA ON PET/CT ASSESSMENT DOES NOT OCCUR IN IMMUNE CHECKPOINT INHIBITOR-TREATED PATIENTS WHO DO NOT GO ON TO DEVELOP RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS

D. Liew[1,2,3], A. Poon[4], C. Mcmaster[1,2,3], C. Owen[1,3], J. Leung[1,3], A. Frauman[2,3], J. Cebon[5,6,7], A. Scott[3,4,5], R. Buchanan[1,3]. *[1]Austin Hospital, Rheumatology, Heidelberg, Australia*; *[2]Austin Hospital, Clinical Pharmacology and Therapeutics, Heidelberg, Australia*; *[3]University of Melbourne, Medicine, Parkville, Australia*; *[4]Austin Hospital, Molecular Imaging and Therapy, Heidelberg, Australia*; *[5]Olivia Newton-John Cancer Wellness & Research Centre, Medical Oncology, Heidelberg, Australia*; *[6]La Trobe University, Melbourne Campus, Tumour Immunology Laboratory, Bundoora, Australia*; *[7]La Trobe University, Melbourne Campus, School of Cancer Medicine, Bundoora, Australia*

Background: The pathogenesis of rheumatic immune-related adverse events (irAEs) from checkpoint inhibitor cancer immunotherapy directed against programmed cell death protein 1 (PD-1) and programmed death ligand 1 (PD-L1) remains unknown, even though they are a consequence of pharmacologic inhibition of a specific immune mechanism. Given that some irAEs resemble polymyalgia rheumatica (PMR) or giant cell arteritis (GCA), a disease whose pathogenesis is poorly understood, observations regarding the pathogenesis of PMR-like or GCA-like irAEs are of significant interest. One proposed pathogenic mechanism involves generalized immune activation leading to a spectrum of subclinical disease. Interrogation of this hypothesis may be aided by PET/CT, which is frequently utilized for oncological staging purposes but is also useful in classical PMR or GCA diagnosis. If PMR or GCA irAEs merely represent a spectrum of generalized immune activation, low-grade subclinical PMR or GCA-related changes on PET/CT might be expected to be seen in patients who receive immunotherapy, irrespective of whether they develop clinically evident rheumatic irAEs.
Objectives: This study investigated whether such changes occurred in patients receiving immunotherapy who did not develop clinically evident rheumatic irAEs.
Methods: Consecutive patients exposed to PD-1 or PD-L1 inhibitor immunotherapy at a single center had scintigraphic uptake calculated by a nuclear medicine physician experienced in assessment of vasculitis. Patients were included if they had had 18F-fluorodeoxyglucose (18F-FDG) PET/CT imaging both within the two weeks prior to immunotherapy initiation and after at least eleven weeks of immunotherapy. Patients who went on to develop a rheumatic irAE were excluded, as were patients with scintigraphic evidence of liver metastases owing to their potential influence on scoring of uptake. Quantification of 18F-FDG uptake by maximum standardized uptake values (maximum standard unit value, SUVmax) was performed at sites relevant to PMR or GCA (17 sites relevant to PMR, 17 sites relevant to GCA) in paired scans, and the difference calculated.
Results: Twenty-four patients receiving nivolumab, pembrolizumab or avelumab met the inclusion criteria, primarily for melanoma, non-small cell lung cancer, or lymphoma. The mean age was 67 at the time of the first scan, 71% were male, and 66% had a complete or partial oncological response at best response. No statistically or clinically significant difference in SUVmax was noted at any PMR or GCA-relevant anatomical site interrogated. Latent class analysis did not reveal clusters identifiable by cancer type, best response, or presence of combination therapy.
Conclusion: Patients treated with PD-1/PD-L1 inhibitors without clinically evident rheumatic irAEs do not develop subclinical PMR or GCA-like changes on PET/CT. This supports the proposition that PMR-like and GCA-like irAEs are a distinct entity with stochastic onset, and do not simply represent generalized immune activation induced by immunotherapy.
Acknowledgements: David Liew is the recipient of the Ronald John Gleghorn Bursary from the University of Melbourne.
Disclosure of Interests: David Liew: None declared, Aurora Poon: None declared, Christopher McMaster: None declared, Claire Owen Speakers bureau: Roche, Jessica Leung Speakers bureau: GIlead, Novartis, Albert Frauman: None declared, Jonathan Cebon: None declared, Andrew Scott: None declared, Russell Buchanan: None declared
DOI: 10.1136/annrheumdis-2021-eular.2788

OP0195 PLASMA CHECKPOINT PROTEIN LEVELS AND GALECTIN-9 IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS

E. Sag[1,2], K. Yüksel[1], S. Demir[1], S. Ozdel[3], U. Kaya Akca[1], E. Atalay[1], M. Kasap-Cuceoglu[1], R. Topaloglu[4], Y. Bilginer[1,2], S. Özen[1,2]. *[1]Hacettepe University Faculty of Medicine, Department of Pediatric Rheumatology, Ankara, Turkey*; *[2]Hacettepe University Faculty of Medicine, Translational Medicine Laboratories, Pediatric Rheumatology Unit, Ankara, Turkey*; *[3]Dr Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Department of Pediatric Rheumatology, Ankara, Turkey*; *[4]Hacettepe University Faculty of Medicine, Department of Pediatric Nephrology, Ankara, Turkey*

Background: Systemic Lupus Erythematosus (SLE) is the prototype for a systemic autoimmune disease. SLE is a disease of the adaptive immune system where T lymphocyte dysfunction has an important role as well. Checkpoint proteins have become an important topic in the study of Tcell. The balance of T cell co-stimulatory and co-inhibitory receptors is important for the regulation of the adaptive immune system response.
Objectives: In this study we aimed to assess the checkpoint proteins in childhood SLE patients
Methods: Fourty-nine jSLE patients together with 15 age- and gender-matched controls were included. Clinical features, disease activity scores and laboratory parameters were recorded both retrospectively and at the time of samplimg. Patient samples were collected at their last visit, Plasma CD25 (IL-2Rα), 4-1BB, B7.2 (CD86), TGF-β1, CTLA-4, PD-L1, PD-1, Tim-3, LAG- 3, Galectin-9 levels were studied by the cytometric bead-based multiplex assay panel according to manufacturer's instruction (LEGENDplex HU Immune Checkpoint Panel 1 (10-plex); catalogue number 740962, Biolegend) and analysed by Novocyte 3005 flow cytometer. Two-step cluster analysis procedure was conducted over the chosen 7 symptom status and 3 clusters were chosen for the final analysis
Results: A total of 49 patients (71.4% female) diagnosed with SLE according to the SLICC criteria and 15 healthy controls (73.3% female) were included in the study. The mean age of the patients was 17.7 ± 2.6 years and the controls was 13.3±1.4 years. The median disease duration was 5.7 years. At the time of sampling fifteen of the patients had a SLEDAI score of zero (no activity), 21 of them had between 1-5 (mild activity), 7 of them had between 6-10 (moderate activity), 5 of them had between 11-19 (high activity), 1 of them had >20 (very high activity).
Galectin-9 and PD-L1 were significantly higher in SLE patients. Other checkpoint proteins and IL-2Rα were also higher but did not reach statistical significance. There were significant correlations between SLEDAI and IL-2Rα, Galectin-9 and PDL1. (Figure 1) There were three clinical clusters: Cluster 1 included patients with no major organ involvement, cluster 2 had predominantly haematological involvement (n=16) and cluster 3 (n=11) had predominantly renal involvement. Checkpoint proteins were not different among these three clusters.

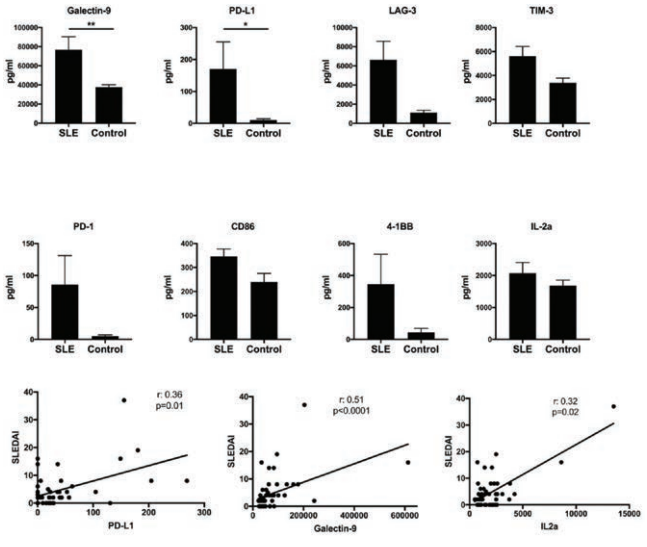


Figure 1.

Table 1. Demographic, Clinical and Laboratory Features of Patients (n=49)

Female gender, n (%)	35 (%71.4)
Mean age at diagnosis, years (mean±SD)	12.5±3.3
Mean age at the time of inclusion, years (mean±SD)	17.7±2.6
Duration of illness, years (median/IQR)	5.7 (3.0-7.0) years
Active system involvement at study,	n (%)
Renal	14 (28.5)
Skin	11 (22.4)
Musculoskeletal	9 (18.3)
Hematologic	9 (18.3)
Neurologic	1 (2.0)
Serositis	1 (2.0)
Laboratory findings (median/minimum-maximum)	
Hemoglobin, gr/dl	12.7 (7.3-18.3)
WBC, /mm^3	6.900 (2.600-26.200)
Platelet, /mm^3	252.000 (39.000-529.000)
Erythrocyte sedimentation rate, mm/hour	10 (1-71)
C-reactive protein, mg/dl	0.1 (0-21.1)
Complement 3, mg/dl	87.6 (25.4-186.0)
Complement 4, mg/dl	15.3 (0-45.8)
Anti-ds DNA, IU/ml	12.8 (0-741.7)
SLEDAI score (mean±SD)	4.69±6.69

Conclusion: Our data supports that Galectin 9 and IL-2Rα are good markers for disease activity in childhood SLE. We need larger series to evaluate differences between disease clusters in SLE. We failed to show a significant correlation with checkpoint proteins and SLEDAI except for PDL1.

REFERENCES:

[1] Sharabi A and Tsokos GC. T cell metabolism: new insights in systemic lupus erythematosus pathogenesis and therapy. *Nature reviews Rheumatology* 2020; 16: 100-112
[2] Nishimura H, Nose M, Hiai H, et al. Development of lupus-like autoimmune diseases by disruption of the PD-1 gene encoding an ITIM motif-carrying immunoreceptor. *Immunity* 1999; 11: 141-151.
[3] McKinney EF, Lee JC, Jayne DR, et al. T-cell exhaustion, co-stimulation and clinical outcome in autoimmunity and infection. *Nature* 2015
[4] Wherry EJ and Kurachi M. Molecular and cellular insights into T cell exhaustion. *Nat Rev Immunol* 2015; 15: 486-499

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1957

The aftermath of metabolic imbalance in OA

OP0196 CIRCULATING LEVEL OF IL-6 IS ASSOCIATED WITH 10.7-YEAR KNEE CARTILAGE VOLUME LOSS AND WORSE PAIN TRAJECTORY

F. Pan[1], J. Tian[1], F. Cicuttini[2], G. Jones[1]. [1]*University of Tasmania, Menzies Institute for Medical Research, Hobart, Australia*; [2]*Monash University Medical School, Department of Epidemiology and Preventive Medicine, Melbourne, Australia*

Background: There is growing evidence that inflammation plays a critical role in osteoarthritis (OA) progression and its symptoms evolution. OA pain is heterogeneous and there are distinct subgroups within OA pain patients. Recently, we identified three homogeneous subgroups following distinct pain trajectories in which metabolic mechanism may be involved. Whether circulating inflammatory markers are associated with long-term knee structural changes on MRI, and whether the association between inflammatory markers and the trajectories we identified differs remain to be clarified.

Objectives: To examine whether inflammatory markers are associated with 10.7-year knee structural changes including knee cartilage volume (CV) and bone marrow lesions (BMLs), and to assess the associations between inflammatory markers and different pain trajectories.

Methods: This study was conducted as part of a population-based older adult (mean age 63 years, 51% of females) cohort study with 1,099, 875, 768 and 563 participants attending at baseline, and 2.6-, 5.1- and 10.7-year follow-ups. Circulating levels of interleukin (IL)-6, tumour necrosis factor alpha (TNF-α) and high sensitivity C-reactive protein (CRP) were measured at baseline in 193 randomly selected participants. T1-weighted or T2-weighted MRI of the right knee was performed to measure CV and BMLs at baseline and 10.7-year. X-ray was performed to assess radiographic knee osteoarthritis (ROA). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain questionnaire was used to measure knee pain at all four visits. Data on demographic, psychological, lifestyle and comorbidities were also collected. Pain trajectories was previously identified using the group-based trajectory modelling. Linear, log-binomial and multi-nominal logistic regression modellings were used for the analyses.

Results: IL-6 was associated with both medial and lateral tibial CV loss (Medial: β=-0.51% per log pg/ml, 95%CI -0.88 to -0.15; Lateral: β=-0.34% per log pg/ml, 95%CI -0.64 to -0.04) after adjusting for age, sex, body mass index, physical activity, comorbidities, and ROA. TNF-α was not associated with either medial or lateral CV loss, but CRP was positively associated with medial tibial CV loss (Medial: β=0.27% per log mg/L, 95%CI 0.04 to 0.49), not lateral CV loss. No inflammatory markers were found to associate with medial and lateral BML size increase. Of 169 participants who had complete data at baseline, 54%, 35% and 11% of participants fell into 'Minimal pain', 'Mild pain' and 'Moderate pain' trajectory group, respectively. In multivariable analysis, IL-6 was associated with an increased risk of being a 'Moderate pain' trajectory (relative risk ratio [RRR]: 4.03, 95%CI 1.34 to 12.13) in comparison with 'Minimal pain' trajectory group. There was no significant association of TNF-α and CRP with trajectory groups.

Conclusion: IL-6 was associated with both medial and lateral tibial CV loss (Medial: β=-0.51% per log ml/pg, 95%CI -0.88 to -0.15; Lateral: β=-0.34% per log ml/pg, 95%CI -0.64 to -0.04) after adjusting for age, sex, body mass index, physical activity, comorbidities, and ROA. TNF-α was not associated with either medial or lateral CV loss, but CRP was positively associated with medial tibial CV loss (Medial: β=0.27% per log ml/pg, 95%CI 0.04 to 0.49), not lateral CV loss. No inflammatory markers were found to associate with medial and lateral BML size increase. Of 169 participants who had complete data at baseline, 54%, 35% and 11% of participants fell into 'Minimal pain', 'Mild pain' and 'Moderate pain' trajectory group, respectively. In multivariable analysis, IL-6 was associated with an increased risk of being a 'Moderate pain' trajectory (relative risk ratio [RRR]: 4.03, 95%CI 1.34 to 12.13) in comparison with 'Minimal pain' trajectory group. There was no significant association of TNF-α and CRP with trajectory groups.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.375

OP0197 EVALUATION OF THE RELATIONSHIP OF LEPTIN WITH THE METABOLIC PHENOTYPE OF KNEE OSTEOARTHRITIS IN THE CONTEXT OF OBESITY THERAPY

E. Strebkova[1], L. Alekseeva[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Osteoarthritis, Moscow, Russian Federation*

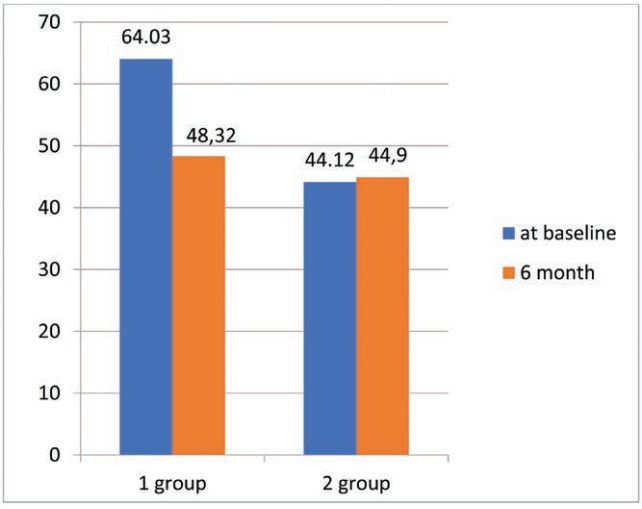
Background: Obesity and components of the metabolic syndrome (MS) play a key role in the pathogenesis of the metabolic phenotype of osteoarthritis (OA). Obesity is a process meta inflammation due to the synthesis of proinflammatory mediators (adipokines and adipocytokines). The severity of OA depends on the presence of obesity, adipokine activity, comorbidity, and the presence of MS. The problem of treatment of metabolic OA and obesity is very relevant, in connection with the obesity pandemic.

Objectives: To evaluate the relationship of leptin with the clinical manifestations of OA and various components of MS in the context of obesity therapy.

Methods: The study included 50 female patients aged 45-65 y.o. with Kellgren-Lawrence stage II-III knee OA and obesity (body mass index (BMI)>30kg/m^2). The average age of the patients was 56.5 ± 5.86 years, the average duration of the disease was 7.43 ± 3.93 years. 62% of patients were diagnosed MS. Patients were randomly divided into 2 groups for the treatment of obesity.

Patients from group 1 (n=25) took orlistat 120mg 3 times a day in combination with a hypocaloric diet and exercise for 6 months. Patients from group 2 (n=25) were on a hypocaloric diet in combination with exercise for 6 months. The groups were comparable in clinical parameters. The clinical course of OA was determined by the WOMAC and VAS. Anthropometric data (height, weight) were determined. All patients underwent a laboratory examination at 2 points (initially and after 6 months): a biochemical blood test, leptin was determined by PCR in peripheral blood.

Results: 8% of patients had 1 MS component, 34% - 2 MS components, 34% - 3 MS components, 22% - 4 MS components, and 2% - 5 MS components at the beginning of the study. High leptin levels (p=0.001) were determined in patients with more than 3 MS components. The correlation analysis showed direct correlations of high leptin levels with the severity of knee WOMAC pain (r=0.36, p=0.02) and VAS pain (r=0.51, p=0.01). A positive correlation was determined between high leptin levels and body weight (r=0.56, p<0.01) and waist circumference (r=0.38, p<0.01). Patients from group 1 had a significant decrease of body weight by 10.07% (p<0.05), the indicators of the WOMAC index improved: pain decreased by 52.5% (p<0.05), stiffness by 47.98% (p<0.05), joint functional failure by 51.55% (p<0.05) after 6 months of drug therapy for obesity. Patients of group 2 had a not significant decrease of body weight by 0.84% (p>0.05), and they were worse indicators of clinical manifestations of OA according to WOMAC compared to group 1 (p<0.05). 24% of patients from group 1 showed a decrease in the number of MS components. 12% of patients from group 2 had a decrease in the number of MS components and 12% patients increase in MS components. Patients from 1 group with a significant decrease in body weight, there was a decrease in the level of leptin (p = 0.05) (graphic 1), in contrast to patients without weight loss on the background of non-drug therapy (p = 0.64). We found direct correlations between a decrease in leptin levels and a decrease in the WOMAC index (pain, stiffness, joint functional failure, total WOMAC) (r=0.5, p=0.01; r=0.4, p=0.04; r=0.4, p=0.03; r=0.5, p=0.01, respectively). Patients with a decrease in the number of MS components had a significantly lower leptin levels (p=0.01).



Graphic 1. Dynamic of leptin.

Conclusion: Leptin is a predictor of a worse course of the metabolic phenotype of OA associated with MS and obesity. High levels of leptin were observed with more MS components, and were associated with the severity of knee pain and body weight. We observed a decrease in the level of leptin, a decrease in the number of MS components, and an improvement in the clinical manifestations of OA against the background of a significant decrease in body weight. Thus, the treatment of obesity in patients with the metabolic phenotype of OA and other interventions aimed at reducing the level of leptin may contribute to reducing the progression of knee OA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3338

Monitoring and restoring health: Should we have a core set for multidisciplinary care in rheumatology_

OP0198-HPR

A STRUCTURED MODEL FOR OA CARE IN PRIMARY HEALTHCARE IS A COST-EFFECTIVE ALTERNATIVE COMPARED TO USUAL CARE FOR PEOPLE WITH HIP AND KNEE OA

N. Østerås[1], E. Aas[2], T. Moseng[1], L. Van Bodegom-Vos[3], K. Dziedzic[4], B. Natvig[5], J. H. Røtterud[6], T. P. M. Vliet Vlieland[7], K. B. Hagen[8].
[1]Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway; *[2]University of Oslo, Department Health Management and Health Economics, Oslo, Norway*; *[3]Leiden University Medical Center, Dep. of Biomedical Data Sciences, Leiden, Netherlands*; *[4]Keele University, Primary Care Centre Versus Arthritis, Keele, United Kingdom*; *[5]University of Oslo, Department General Practice, Oslo, Norway*; *[6]Akershus University Hospital, Department of Orthopaedic Surgery, Lørenskog, Norway*; *[7]Leiden University Medical Center, Department of Orthopaedics, Leiden, Norway*; *[8]Norwegian Institute of Public Health, Health Services, Oslo, Norway*

Background: To improve quality of care for patients with hip and knee osteoarthritis (OA), a structured model for integrated OA care was developed based on international treatment recommendations. A previous analysis of a cluster RCT (cRCT) showed that compared to usual care, the intervention group reported higher quality of care and greater satisfaction with care. Also, more patients were treated according to international guidelines and fulfilled recommendations for physical activity at the 6-month follow-up.

Objectives: To assess the cost-utility of a structured model for hip or knee OA care.

Methods: A cRCT with stepped-wedge cohort design was conducted in 6 Norwegian municipalities (clusters) in 2015-17. The OA care model was implemented in one cluster at the time by switching from "usual care" to the structured model. The implementation of the model was facilitated by interactive workshops for general practitioners (GPs) and physiotherapists (PTs) with an update on OA treatment recommendations. The GPs explained the OA diagnosis and treatment alternatives, provided pharmacological treatment when appropriate, and suggested referral to physiotherapy. The PT-led patient OA education programme was group-based and lasted 3 hours followed by an 8–12-week individually tailored resistance exercise programme with twice weekly 1-hour supervised group sessions (5–10 patients per PT). An optional 10-hours Healthy Eating Program was available. Participants were ≥45 years with symptomatic hip or knee OA.
Costs were measured from the healthcare perspective and collected from several sources. Patients self-reported visits in primary healthcare at 3, 6, 9 and 12 months. Secondary healthcare visits and joint surgery data were extracted from the Norwegian Patient Register. The health outcome, quality-adjusted life-year (QALY), was estimated based on the EQ-5D-5L scores at baseline, 3, 6, 9 and 12 months. The result of the cost-utility analysis was reported using the incremental cost-effectiveness ratio (ICER), defined as the incremental costs relative to incremental QALYs (QALYs gained). Based on Norwegian guidelines, the threshold is €27500. Sensitivity analyses were performed using bootstrapping to assess the robustness of reported results and presented in a cost-effectiveness plane (Figure 1).

Results: The 393 patients' mean age was 63 years (SD 9.6) and 74% were women. 109 patients were recruited during control periods (control group), and 284 patients were recruited during interventions periods (intervention group). Only the intervention group had a significant increase in EQ-5D-5L utility scores from baseline to 12 months follow-up (mean change 0.03; 95% CI 0.01, 0.05) with QALYs gained: 0.02 (95% CI -0.08, 0.12). The structured OA model cost approx. €301 p.p. with an additional €50 for the Healthy Eating Program. Total 12 months healthcare cost p.p. was €1281 in the intervention and €3147 in the control group, resulting in an incremental cost of -€1866 (95% CI -3147, -584) p.p. Costs related to surgical procedures had the largest impact on total healthcare costs in both groups. During the 12-months follow-up period, 5% (n=14) in the intervention compared to 12% (n=13) in the control group underwent joint surgery; resulting in a mean surgical procedure cost of €553 p.p. in the intervention as compared to €1624 p.p. in the control group. The ICER was -€93300, indicating that the OA care model resulted in QALYs gained and cost-savings. At a threshold of €27500, it is 99% likely that the OA care model is a cost-effective alternative.

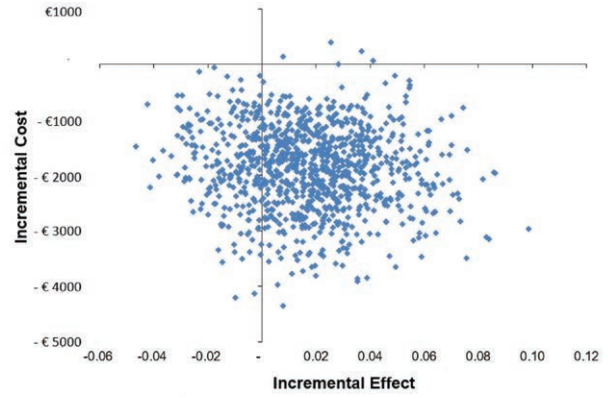


Figure 1 Cost-effectiveness plane for the comparison of implementation of a structured model for OA care (intervention group) and usual care (control group)

Conclusion: The results of the cost-utility analysis show that implementing a structured model for OA care in primary healthcare based on international guidelines is highly likely a cost-effective alternative compared to usual care for people with hip and knee OA. More studies are needed to confirm this finding, but this study results indicate that implementing structured OA care models in primary healthcare may be beneficial for the individual as well as for the society.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.950

Emerging molecular targets in OA

OP0199 EX VIVO BIOMARKER PROFILING IDENTIFIES ONCOSTATIN-M AS SPINE OSTEOARTHRITIS-SPECIFIC OSTEOIMMUNOLOGICAL TARGET

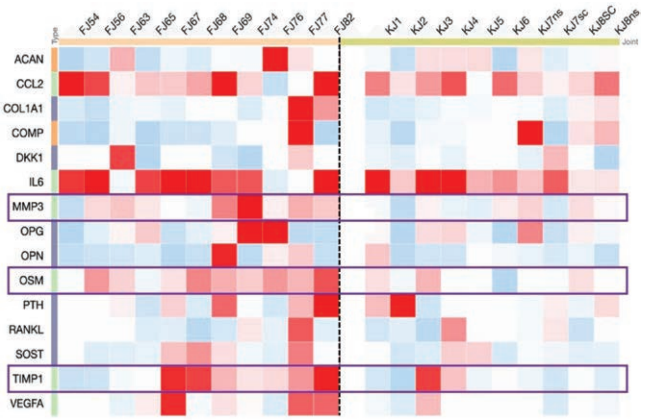
O. Roessinger[1], M. Blanchard[1], M. Briki[1], D. Jurić[2], C. Netzer[3], T. Hügle[1], T. Ecker[4], J. Geurts[1]. [1]*Lausanne University Hospital, Rheumatology, Lausanne, Switzerland*; [2]*University Hospital Basel, Orthopaedics & Traumatology, Basel, Switzerland*; [3]*Lausanne University Hospital, Spine Surgery, Basel, Switzerland*; [4]*Lausanne University Hospital, Spine Surgery, Lausanne, Switzerland*

Background: Disease heterogeneity, both clinically and molecularly, has been a major hurdle in the development of efficacious disease-modifying osteoarthritis drugs (DMOADs). Biomechanical, inflammatory, osteoporotic and metabolic OA have been proposed as clinically relevant subtypes for stratification of knee OA patients, yet this remains to be included in clinical trial design. Disease heterogeneity does not only occur within, but also between joint types. However, robust data on joint-specific pathomechanisms of OA are still lacking.

Objectives: In this study, we performed ex vivo biomarker profiling of human osteochondral tissue of knee and spine OA to identify joint-specific pathomechanisms and DMOAD treatment responses.

Methods: Facet joint and tibial plateaus were obtained from patients undergoing lumbar spinal fusion (n=11, mean age 72.8) and total joint arthroplasty (n=8, mean age 73.0) respectively. Osteochondral specimens were cut in equal-sized samples (100-300 mg wet weight) and randomly assigned to treatment groups: control (DMSO), inflammation (1 µg/mL LPS) or inflammation + DMOAD (TGF-beta type I receptor inhibitor,10 µM SB-505124). Explant culture was conducted for one week and biomarkers of bone metabolism (Pro-Col-Ia, SOST, OPG, SPP1), inflammation (MCP-1, IL-6, MMP3, OSM, TIMP1, VEGFA) and cartilage metabolism (ACAN, COMP) were determined by ELISA. Normalized biomarker secretion was analysed using clusteranalyses and ANOVA. Cartilage proteoglycans were assessed by whole mount Alcian blue staining. Expression of Oncostatin-M (OSM) and its receptors OSMR and LIFR in joint tissues was assessed by RT-PCR and immunohistochemistry.

Results: Clusteranalyses revealed that LPS stimulation increased IL-6 and MCP-1 secretion by both facet joint (FJ) and knee joint (KJ) tissues. Interestingly, Oncostatin-M (OSM) and its downstream mediators MMP3 and TIMP1 were increased in the majority of FJ, but not KJ specimens. Statistical analyses corroborated increased OSM, MMP3 and TIMP1 levels in a spine-specific fashion (Figure).



Whole mount Alcian blue staining revealed heterogeneous effects of LPS treatment on cartilage proteoglycans, which was negatively correlated with OSM (r=-0.54) and TIMP1 levels (r=-0.45) – yet poorly associated with ACAN (r=0.19). Inhibition of TGF-beta type I receptor signalling in osteochondral tissues led to a drastic reduction of Pro-Collagen-Ia and IL-6 secretion in both spine and knee OA specimens. Interestingly, DMOAD treatment significantly reduced OSM, TIMP1 and MMP3 levels in FJ specimens only. Vice versa, KJ tissues revealed a specific upregulation of monocyte chemoattractant protein-1 (MCP-1) and osteopontin (SPP1) upon inhibition of TGF-beta signalling. OSM was exclusively expressed in subchondral bone marrow macrophages. Isolated chondrocytes and osteoblasts expressed both LIFR and OSMR, yet intact cartilage only showed OSMR expression, while OSMR and LIFR was expressed in marrow tissue

Conclusion: Oncostatin-M expression and signalling was uncovered as specific pathomechanism of spine OA. DMOAD treatment effects suggested interplay of OSM and TGF-beta signalling pathways in facet joint osteoarthritis. Known to be predominantly expressed by macrophages and immune cells, OSM may be an important osteoimmunological mediator of tissue damage and remodelling in spine, but not knee OA. This study also highlights the value of *ex vivo* human tissue models for OA phenotyping and preclinical evaluation of DMOADs.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2493

OP0200 BLOCKING ROR2 IMPROVES CARTILAGE INTEGRITY AND PROVIDES PAIN RELIEF IN OSTEOARTHRITIS

A. S. Thorup[1], D. Strachan[1], S. Caxaria[1], B. Poulet[2], B. Thomas[1], S. Eldridge[1], G. Nalesso[3], J. Whiteford[4], C. Pitzalis[1], T. Aigner[5], R. Corder[6], J. Bertrand[7], F. Dell'accio[1]. [1]*William Harvey Research Institute, Experimental Medicine and Rheumatology, London, United Kingdom*; [2]*University of Liverpool, Institute of Ageing and Chronic Disease, Liverpool, United Kingdom*; [3]*School of Veterinary Medicine, Department of Veterinary Pre-Clinical Sciences, Guildford, United Kingdom*; [4]*William Harvey Research Institute, Centre for Microvascular Research, London, United Kingdom*; [5]*Medical Center Coburg, Institute of Pathology, Coburg, Germany*; [6]*William Harvey Research Institute, Translational Medicine and Therapeutics, London, United Kingdom*; [7]*Otto-von-Guericke University, Department of Orthopaedic Surgery, Magdeburg, Germany*

Background: Osteoarthritis (OA) is the leading cause of chronic disability worldwide, affecting 12% of the population, and yet we still do not have a disease-modifying treatment. Cartilage breakdown is the hallmark of OA, and patients suffer from pain and loss of joint function/independence, severely affecting quality of life. Therefore, there is a huge unmet clinical need.

Receptor tyrosine kinase–like orphan receptor 2 (ROR2) is a non-canonical WNT receptor that regulates the planar cell polarity pathway, controlling limb outgrowth during development. During skeletal development, chondrocytes require ROR2 to undergo hypertrophy throughout the process of endochondral bone formation[1]. Loss of function mutations in humans causes Recessive Robinow Syndrome, leading to limb shortening and brachydactyly[2,3].

Although absent from healthy adult articular cartilage, our initial studies identified high expression levels of ROR2 in chondrocytes from patients with OA, suggesting a role in the disease process

Objectives: To test the potential of ROR2 blockade as a disease-modifying treatment for OA.

Methods: Human cartilage organoid model in nude mice, menisco-ligament injury (MLI) model of OA in mice, behavioural studies, *in vitro* studies in cells.

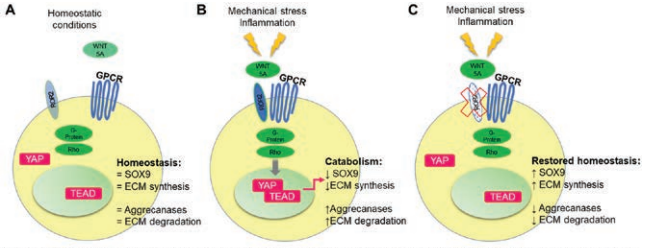
Results: ROR2/WNT5A signaling was increased in osteoarthritic cartilage. Blocking ROR2 was sufficient to induce articular chondrogenesis and suppress expression of aggrecanases in a mesenchymal stem cell line, and to support cartilage formation in a human cartilage organoid model in nude mice using primary chondrocytes from patients with OA.

In the MLI model of OA, blocking ROR2 in therapeutic regime using atelocollagen-conjugated siRNA resulted in reduced cartilage destruction and in rapid and sustained pain relief. Due to the limited expression pattern of ROR2 in adulthood, no systemic or local toxicity were expected, nor were any observed[4].

With the current technology, ROR2 blockade requires intra-articular (IA) injections of siRNA conjugated to atelocollagen every 5 days. Preliminary efficacy data of potentially longer-acting ROR2 blockers are promising.

The mechanism of action of ROR2 blockade was independent of modulation of canonical WNT signaling.

ROR2/WNT5A promoted nuclear localization of YAP, which required both Rho and G-proteins. YAP signaling downstream of ROR2 also required Rho, but not G-proteins. YAP and TEAD inhibition was required, but not sufficient, for the chondrogenic effect of blocking ROR2. Therefore, additional, yet unknown mechanisms must be involved downstream of ROR2.



(**A**) ROR2 and WNT5A are expressed in low amounts in the cartilage in adulthood, under physiological conditions. (**B**) Upon cartilage injury, ROR2 and WNTs, including WNT5A, are upregulated. WNT5A activates ROR2 signaling, and through G-proteins and Rho induces nuclear localization of YAP, and interaction with TEAD transcription factors; and activates catabolic signaling. (**C**) Blocking ROR2 prevents nuclear localization of YAP and restores homeostasis through downregulation of catabolic enzymes and increased proteoglycan production. In the menisco-ligament injury model of osteoarthritis, this ameliorates pain and protects the cartilage from damage.

Conclusion: ROR2 blockade has potential as a disease-modifying treatment for OA, resulting in cartilage protection and rapid and sustained pain relief in a murine model. This will be crucial for clinical success of any treatment for OA and promote patient compliance.

Our current siRNA-atelocollagen based technology requires IA injections too frequently to be acceptable for patients. We are developing ROR2 blockade which can be administered systemically or IA not more often than every 3 months - work funded by FOREUM.

REFERENCES:

[1] DeChiara, T. M. *et al.* Ror2, encoding a receptor-like tyrosine kinase, is required for cartilage and growth plate development. *Nat. Genet.* **24**, 271–4 (2000).

[2] Bokhoven, H. Van, Celli, J. & Kayserili, H. Mutation of the gene encoding the ROR2 tyrosine kinase causes autosomal recessive Robinow syndrome. *Nature* **25**, 423–426 (2000).

[3] Afzal, A., Rajab, A., Fenske, C. & Oldridge, M. Recessive Robinow syndrome, allelic to dominant brachydactyly type B, is caused by mutation of ROR2. *Nature* **25**, 419–422 (2000).

[4] Thorup, A.-S. *et al.* ROR2 blockade as a therapy for osteoarthritis. *Sci. Transl. Med.* **12**, eaax3063 (2020).

Acknowledgements: We gratefully acknowledge funding support of this work by the Medical College of St Bartholomew's Hospital Trust, the William Harvey Research Foundation, FOREUM foundation for research in rheumatology (1016807), the MRC (MR/L022893/1, MR/N010973/1, MR/P026362/1, MR/K013076/1), Versus Arthritis (21515, 20886, 21621, 20859), and the DFG Emmy-Noether program (BE4328/5-1).

Disclosure of Interests: Anne-Sophie Thorup: None declared, Danielle Strachan: None declared, Sara Caxaria: None declared, Blandine Poulet: None declared, Bethan Thomas: None declared, Suzanne Eldridge: None declared, Giovanna Nalesso: None declared, James Whiteford: None declared, Costantino Pitzalis: None declared, Thomas Aigner: None declared, Roger Corder: None declared, Jessica Bertrand: None declared, Francesco Dell'Accio Consultant of: Samumed and UCB

DOI: 10.1136/annrheumdis-2021-eular.2358

Origin and role of myeloid cells during homeostasis and inflammation

OP0201

DYNAMIC CHANGES IN O-GLCNACYLATION REGULATE OSTEOCLAST DIFFERENTIATION AND BONE LOSS IN ARTHRITIS

C. W. Chen[1], Y. N. Li[1], T. Trinh-Minh[1], Z. Honglin[2], A. E. Matei[1], X. Ding[1], C. Tran Manh[1], X. Xu[1], C. Liebel[1], R. Liang[1], M. C. Huang[3], N. Y. Lin[3], A. Ramming[1], G. Schett[1], J. H. W. Distler[1]. [1]*Friedrich Alexander University Erlangen-Nuremberg and Universitaetsklinikum Erlangen, Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany*; [2]*Xiangya Hospital, Central South University, Department of Rheumatology, Changsha, China*; [3]*National Taiwan University College of Medicine, Graduate Institute of Anatomy and Cell Biology, Taipei, Taiwan, Republic of China*

Background: Bone remodeling is a constant process maintained by the balance between osteoclast-triggered bone resorption and osteoblast-mediated bone formation. In inflammatory arthritis, such as rheumatoid arthritis (RA), the pro-inflammatory environment favors osteoclast differentiation and skews the balance towards resorption, leading to progressive bone erosion and bone loss. O-GlcNAcylation is a post-translational modification, which transfers a single N-acetylglucosamine molecule to the serine or threonine of the target protein. The modification is accomplished by a single pair of enzymes, O-GlcNAc transferase (OGT) and O-GlcNAcase (OGA). Unlike other glycosylation, O-GlcNAcylation occurs in multiple cellular compartments, including the nucleus. Although O-GlcNAcylation is one of the most common modifications, its role in bone homeostasis is still poorly understood.

Objectives: We aimed to investigate the role of O-GlcNAcylation in osteoclastogenesis under pro-inflammatory milieus. We also focused on dissecting the signaling pathways affected by O-GlcNAcylation during osteoclast differentiation.

Methods: We examined the levels of O-GlcNAc during in vitro osteoclastogenesis by western blotting. The levels of O-GlcNAc in tissue from RA patients and experimental arthritis were detected by immunofluorescence. Pharmacological inhibition and genetic knockout were used to manipulate O-GlcNAcylaiton during osteoclastogenesis. RNA sequencing was performed to study O-GlcNAc-mediated pathways.

Results: We demonstrate the dynamic changes in O-GlcNAcylation during osteoclastogenesis. The elevated O-GlcNAcylation was found in the early differentiation stages, whereas its downregulation was detected in the maturation process. TNFα elaborates the dynamic changes in O-GlcNAcylation, which further intensifies osteoclast differentiation.

Targeting OGT by selective inhibitor and genetic knockout restrain O-GlcNAcylation and hinder the expression of the early differentiation marker *Nfatc1*. Inhibition of OGA, which forces high levels of O-GlcNAcylation throughout the differentiation, reduces the formation of multinucleated mature osteoclasts. Consistent with our *in vitro* data, suppressing OGT and OGA both ameliorate bone loss in experimental arthritis. We detected a reduced number of TRAP-expressing precursors and mature osteoclasts in the mice subjected to OGT inhibition. While inhibiting OGA only lowers the number of $TRAP^+F4/80^-$ mature osteoclasts without affecting the number of $TRAP^+F4/80^+$ precursors.

Transcriptome profiling reveals that O-GlcNAcylation regulates several biological processes. Increased O-GlcNAcylation promotes cytokine signaling and oxidative phosphorylation. The downregulation of O-GlcNAcylation is essential for cytoskeleton organization and cell fusion.

Conclusion: We demonstrate that the dynamic changes of O-GlcNAcylation are essential for osteoclast differentiation. These findings reveal the therapeutic potential of targeting O-GlcNAcylation in pathologic bone resorption.

Disclosure of Interests: Chih-Wei Chen: None declared, Yi-Nan Li: None declared, Thuong Trinh-Minh: None declared, ZHU Honglin: None declared, Alexandru-Emil Matei: None declared, Xiao Ding: None declared, Cuong Tran Manh: None declared, Xiaohan Xu: None declared, Christoph Liebel: None

declared, Ruifang Liang: None declared, Min-Chuan Huang: None declared, Neng-Yu Lin: None declared, Andreas Ramming Speakers bureau: Boehringer Ingelheim, Roche, Janssen, Consultant of: Boehringer Ingelheim, Novartis, Gilead, Pfizer, Grant/research support from: Pfizer, Novartis, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB, Jörg H.W. Distler Shareholder of: 4D Science, Speakers bureau: Boehringer Ingelheim, Paid instructor for: Boehringer Ingelheim, Consultant of: Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, Grant/research support from: Anamar, Active Biotech, Array Biopharma, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB, Employee of: FibroCure

DOI: 10.1136/annrheumdis-2021-eular.856

Crystal diseases

OP0202 DOES EXCESS WEIGHT AFFECT GOUT RISK DIFFERENTLY AMONG GENETICALLY PREDISPOSED INDIVIDUALS? – SEX-SPECIFIC PROSPECTIVE COHORT FINDINGS OVER >26 YEARS

C. Yokose[1,2], N. McCormick[1,2], L. Lu[3], A. Joshi[4], H. Choi[1,2]. [1]*Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [2]*Massachusetts General Hospital, Clinical Epidemiology Program, Mongan Institute, Department of Medicine, Boston, United States of America*; [3]*Arthritis Research Canada, n/a, Richmond, Canada*; [4]*Massachusetts General Hospital, Clinical and Translational Epidemiology Unit, Boston, United States of America*

Background: Global burden of gout has increased substantially, particularly among women.[1,2] Addressing obesity, a major modifiable risk factor for gout, may alleviate this burden; however, there is also a significant genetic contribution to gout risk according to the genome-wide association studies (GWAS).[3,4] Genetic predisposition may modify the excess weight effect on gout risk.

Objectives: To investigate the potential role of genetic predisposition on the association between excess weight (i.e., BMI ≥ 25 kg/m^2) and gout risk in two US prospective longitudinal cohorts over >26 years, stratified by sex.

Methods: We examined the association between excess weight and risk of incident gout meeting the ACR survey criteria,[5] according to genetic risk, in 18,512 women from the Nurses' Health Study (NHS) over 32 years, and 10,917 men from Health Professionals Follow-Up Study (HPFS) over 26 years. We derived a genetic risk score (GRS) using 114 serum urate single nucleotide polymorphisms from the latest GWAS.[3] We also calculated the population attributable risk (PAR) for excess weight according to GRS stratum.

Results: We ascertained 530 incident gout cases in NHS and 983 in HPFS. While the relative risks (RRs) due to excess weight (overweight or obesity) appeared larger among women above the mean than below the mean, the RRs among men appeared similar according to genetic predisposition (Table 1). The RRs among women for excess weight compared to normal were 1.66 (95% CI, 1.17 to 2.37) and 2.55 (1.95 to 3.34) below and above the mean GRS, respectively (P for multiplicative interaction = 0.06), whereas corresponding RRs among men were 1.68 (95% CI, 1.31 to 2.16) and 1.76 (1.47 to 2.10) (P for multiplicative interaction = 0.8). The risk differences (RD) among women for excess weight were 0.69 and 2.38 with GRS below and above the mean, respectively, resulting in the relative excess risk due to interaction (RERI) of 1.69 (95% CI, 1.03 to 2.35, P for additive interaction = 5.4x10^{-}7); for men, the corresponding RDs were 0.70 and 1.46, with RERI = 0.76 (0.26, 1.25; P for additive interaction = 2.6x10^{-}3). Excess weight accounted for a larger proportion of incident gout cases among women with GRS above the mean (PAR, 48.5% [95% CI, 38.8 to 55.9]) compared to those with GRS below the mean (PAR, 29.0% [95% CI, 10.5 to 42.1]), whereas the PARs among men were similar (31.6% vs 29.7%, respectively).

Conclusion: These large scale longitudinal prospective cohorts suggest maintaining healthy weight is an important gout prevention strategy, regardless of underlying genetic risk. In genetically predisposed individuals, addressing excess weight may prevent a large proportion of gout cases, especially among women.

Table 1. Relative Risk of Gout by Body Mass Index, Stratified by Mean Genetic Score

	HPFS (men)							
		Below Mean				Above Mean		
BMI	Overall	<25	25-30	>30	Overall	<25	25-30	>30
No. Cases	333	88	172	73	650	172	349	129
Person-Years	104055	43314	49253	11488	98634	41994	46096	10544
Age-Adjusted RR	-	1.0 (ref)	1.71 (1.32, 2.22)	3.00 (2.18, 4.12)	-	1.0 (ref)	1.80 (1.50, 2.16)	2.87 (2.27, 3.62)
MV Adjusted* RR	-	1.0 (ref)	1.53 (1.18, 1.99)	2.31 (1.66, 2.21)	-	1.0 (ref)	1.63 (1.35, 1.96)	2.38 (1.87, 3.03)
	NHS (women)							
		Below Mean				Above Mean		
BMI	Overall	<25	25-30	>30	Overall	<25	25-30	>30
No. Cases	173	47	40	86	357	72	120	165
Person-Years	244392	123849	76414	44129	239259	120229	76123	42907
Age-Adjusted RR	-	1.0 (ref)	1.23 (0.81, 1.88)	4.46 (3.10, 6.41)	-	1.0 (ref)	2.41 (1.79, 3.23)	5.68 (4.82, 7.52)
MV Adjusted* RR	-	1.0 (ref)	1.00 (0.65, 1.53)	2.84 (1.92, 4.20)	-	1.0 (ref)	1.97 (1.46, 2.65)	3.61 (2.68, 4.87)

*Adjusted for age (continuous), menopause, use of hormone therapy (never, past or current), history of hypertension, and systolic and diastolic blood pressure, alcohol, total energy intake and intake of meat, seafood and dairy foods (all continuous).

REFERENCES:

[1] Safiri et al., PMID 32755051
[2] Xia et al., PMID 31624843
[3] Tin et al., PMID 31578528
[4] Tai et al., PMID: 32017447
[5] Wallace et al., PMID: 856219

Acknowledgements: The authors thank the participants of the NHS and HPFS. CY is supported by the Rheumatology Research Foundation Scientist Development Award and NIH T32 AR007258. HC is supported by NIH P50AR060772 and R01AR065944.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1296

OP0203 GENE-DIET INTERACTION ON THE RISK OF INCIDENT GOUT AMONG WOMEN – PROSPECTIVE COHORT STUDY OVER 32 YEARS

C. Yokose[1,2], N. McCormick[1,2], L. Lu[3], A. Joshi[4], H. Choi[1,2]. [1]*Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [2]*Massachusetts General Hospital, Clinical Epidemiology Program, Mongan Institute, Department of Medicine, Boston, United States of America*; [3]*Arthritis Research Canada, n/a, Richmond, Canada*; [4]*Massachusetts General Hospital, Clinical and Translational Epidemiology Unit, Boston, United States of America*

Background: Although gout is conventionally known as a male condition, the recent Global Burden of Disease (GBD) Study found disproportionate worsening among women.[1] We have found Dietary Approaches to Stop Hypertension (DASH) diet is independently associated with a lower risk of incident gout, while Western diet is associated with increased risk.[2] Whether these risks vary according to genetic risk remains unknown.

Objectives: To investigate the influence of genetic predisposition on the relation between diets (one protective and another hazardous) and gout risk in a large prospective US cohort of women over 32 years.

Methods: We examined the role of genes on the association between two dietary patterns (DASH and Western) on the risk of incident gout in 18,512 women from the Nurses' Health Study. Using validated food frequency questionnaires, for each participant we derived: 1) DASH score emphasizing fruits, vegetables, nuts, legumes, whole grains, low-fat dairy, and reduced intake of saturated fat and sugar-sweetened beverages (SSBs) and 2) Western diet score characterized by high intake of red and processed meats, SSBs, desserts, French fries, and refined grains. A genetic risk score (GRS) was derived using 114 serum urate single nucleotide polymorphisms from the latest GWAS consortium.[3]

Results: There were 523 incident gout cases meeting ACR survey criteria[4] (170 vs. 353 in GRS below and above the mean, respectively) (Table 1). Among women with GRS below and above the mean, the multivariable relative risks (RRs) of gout were 1.0, 1.56. 1.32, 0.89, and 0.61 (0.34 to 1.09) and 1.0, 1.0, 0.85, 0.51, and 0.68 (0.49 to 0.96), for quintiles (Q) 1 through 5 of DASH score, respectively (p for interaction = 0.69) (Table 1). For the Western diet, RRs for Q1 through 5 were 1, 1.34, 1.07, 1.33, and 1.63 (0.91 to 2.93) for those with GRS below the mean and 1.0, 1.17, 0.93, 1.27, and 1.77 (1.19 to 2.61) among those with GRS above the mean, respectively (p for multiplicative interaction = 0.64).

Conclusion: In this prospective female cohort that ascertained gout with standardized criteria over 32 years, regardless of genetic predisposition, DASH diet was similarly associated with lower risk of incident gout while Western diet was associated with a higher risk. The anticipated absolute impact of diet among

Table 1. Relative Risk of Gout by Quintiles of DASH and Western Diet Score, Stratified by Mean GRS

	DASH										
	Below Mean					Above Mean					
	Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5	P Interaction
No. Cases	27	49	51	21	22	75	89	90	34	65	
Person-Years	39208	47247	57227	34953	58764	39815	45853	55401	34733	56521	
Age-Adjusted RR	1.0 (ref)	1.43 (0.89, 2.29)	1.22 (0.76, 1.96)	0.8 (0.45, 1.42)	0.5 (0.28, 0.88)	1.0 (ref)	0.97 (0.72, 1.33)	0.79 (0.58, 1.07)	0.47 (0.31, 0.70)	0.54 (0.39, 0.76)	0.73
MV-Adjusted* RR	1.0 (ref)	1.56 (0.97, 2.51)	1.32 (0.82, 2.12)	0.89 (0.50, 1.59)	0.61 (0.34, 1.09)	1.0 (ref)	1.0 (0.73, 1.37)	0.85 (0.63, 1.17)	0.51 (0.33, 0.76)	0.68 (0.49, 0.96)	0.69
	Western										
	Below Mean					Above Mean					
	Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5	P Interaction
No. Cases	21	36	28	39	46	52	70	56	76	99	
Person-Years	47397	49348	47837	47589	45283	45529	47913	47357	46	44785	
Age-Adjusted RR	1.0 (ref)	1.49 (0.86, 2.56)	1.26 (0.71, 2.23)	1.71 (1.00, 2.93)	2.22 (1.31, 3.74)	1.0 (ref)	1.21 (0.85, 1.74)	0.98 (0.67, 1.43)	1.35 (0.94, 1.93)	1.88 (1.34, 2.65)	0.72
MV-Adjusted* RR	1.0 (ref)	1.34 (0.78, 2.32)	1.07 (0.60, 1.90)	1.33 (0.76, 2.34)	1.63 (0.91, 2.93)	1.0 (ref)	1.17 (0.81, 1.68)	0.93 (0.63, 1.38)	1.27 (0.87, 1.84)	1.77 (1.19, 2.61)	0.64

*Adjusted for age (continuous), menopause, use of hormone therapy (never, past or current), history of hypertension, systolic and diastolic blood pressure (continuous), alcohol (continuous), total energy intake (continuous), and intake of meat, seafood, and dairy foods (continuous).

genetically predisposed females was larger with greater absolute risk difference. These data agree with the recent GBD Study's recommendation for intensive dietary and anti-obesity measures for gout prevention, especially in females.[1]

REFERENCES:
[1] Xia et al., PMID 31624843
[2] Keller et al., PMID: 28487277
[3] Tin et al., PMID 31578528
[4] Wallace et al., PMID: 856219

Acknowledgements: The authors thank the participants of the NHS.
CY is supported by the Rheumatology Research Foundation Scientist Development Award and NIH T32 AR007258. HC is supported by NIH P50AR060772 and R01AR065944.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3758

OP0204 URATE CRYSTAL DEPOSITIONS ARE ASSOCIATED WITH INFLAMMATORY MARKERS AND CAROTID PLAQUES INDICATING SUBCLINICAL INFLAMMATION IN GOUT; BASELINE RESULTS FROM THE NOR-GOUT STUDY

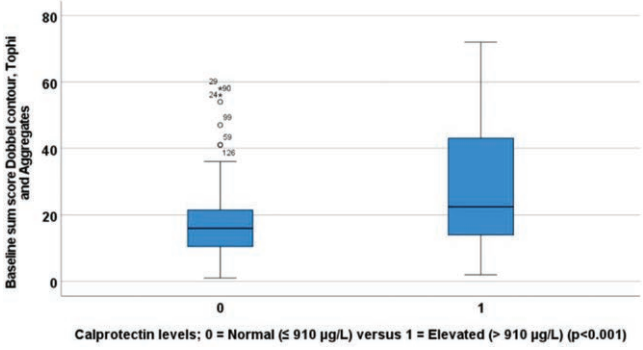
H. B. Hammer[1,2], S. Rollefstad3, G. Jensen3, L. Karoliussen3, L. Terslev[4], E. A. Haavardsholm[2,3], T. K. Kvien[2,3], A. G. Semb3, T. Uhlig[2,3]. [1]*Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway*; [2]*University of Oslo, Faculty of Medicine, Oslo, Norway*; [1]*Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway*; [4]*Rigshospitalet Glostrup, Centre for Rheumatology and Spinal Diseases, Copenhagen, Denmark*

Background: In gout patients the extent of monosodium urate (MSU) crystal depositions can be quantitated by use of ultrasound. Gout may be associated with atherosclerotic disease which might be related to low-grade inflammation. Calprotectin is a major granulocyte protein reflecting the level of systemic inflammation.
Objectives: To explore whether the extent of MSU crystal depositions is associated with low grade systemic inflammation as assessed by calprotectin/C-reactive protein (CRP) and with carotid pathologies in asymptomatic gout patients.
Methods: The baseline data from NOR-GOUT, a prospective study of patients with crystal-proven gout with increased serum urate levels (>360 µmol/L), were used. All patients were assessed by ultrasound (GE Logiq E9 machine) to assess MSU depositions (OMERACT definitions; double contour (DC), tophi and aggregates) with bilateral assessment of wrist, MCP2, knee, ankle, MTP1 and insertions of triceps, quadriceps, proximal/distal patellar and Achilles tendons, all scored semi-quantitatively 0-3. Bilateral B-mode ultrasound assessments of the carotid arteries examined carotid intima-media thickness (cIMT; increased thickness >0.9mm). Atherosclerotic plaques were identified as protrusions of ≥1.5 mm or ≥ 2 times the adjacent IMT. Sum scores of each of the ultrasound elementary lesions for MSU depositions were calculated and the associations with calprotectin (plasma assessed by ELISA (Calpro), normal levels <910 µg/L), CRP (routine assessment, normal levels <4mg/L) as well as cIMT and presence of carotid plaque were explored. Correlations were performed by use of Spearman and differences between group was investigated by Mann-Whitney test.
Results: A total of 202 gout patients without flare were included (95.5% men, mean (SD) age of 56.5 (13.8) years, 7.9 (7.7) years since first flare). The mean (SD) sum sore of DC was 4.4 (3.5), tophi 6.6 (6.6), aggregates 9.3 (5.6), calprotectin 801 (525) µg/L, CRP 7 (14) mg/L and serum urate (SUA) 499 (77) µmol/L. Carotid examinations were performed in 122 (60.4%) of the patients. Significant correlations were found between the MSU depositions and the inflammatory markers as well as cIMT. The 27% patients with increased calprotectin had the highest levels of each of the three elementary lesions (p=0.001) (Figure), and the 39% with elevated CRP levels had the highest levels of tophi and aggregates (p<0.05). The 18% with increased thickness of cIMT and the 53% of patients with carotid plaque had the highest levels of aggregates (p=0.003 and p=0.037, respectively).
Conclusion: In asymptomatic gout patients, higher load of MSU crystal depositions was associated with increased levels of inflammatory markers, cIMT and presence of atherosclerotic plaques in the carotid arteries. This may indicate that crystal depositions cause subclinical inflammation with subsequent systemic implications, but future longitudinal studies are needed to confirm such causal relationships.

	Sum score double contour	Sum score tophi	Sum score aggregates
Calprotectin	0.26**	0.32**	0.28**
CRP	0.20*	0.25**	0.18*
Right IMT	NS	NS	0.18*
Left IMT	NS	NS	0.21*
Sum bilateral IMT	NS	NS	0.22*

Spearman's correlations. NS; Not significant, *p<0.05, **p<0.001

Disclosure of Interests: Hilde Berner Hammer Speakers bureau: AbbVie, Lilly and Novartis, Silvia Rollefstad: None declared, Gro Jensen: None declared, Lars Karoliussen: None declared, Lene Terslev Speakers bureau: Speakers fee from AbbVie, Janssen, Roche, Novartis, Pfizer, MSD, BMS and GE, Espen A Haavardsholm: None declared, Tore K. Kvien Speakers bureau: Tore K Kvien has received fees for speaking and/or consulting and/or research funding to Diakonhjemmet Hospital from AbbVie, Biogen, BMS, Celltrion, Egis, Evapharma, Ewopharma, Eli Lilly, Gilead, Hikma, MSD, Mylan, Novartis, Oktal, Pfizer, Sandoz, Sanofi and UCB., Anne Grete Semb: None declared, Till Uhlig: None declared



DOI: 10.1136/annrheumdis-2021-eular.290

OP0205 ULTRASOUND-DETECTED CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION: WHICH SITES SHOULD BE SCANNED?

E. Cipolletta[1], J. DI Battista[1], W. Grassi[1], E. Filippucci[1]. [1]*Polytechnic University of Marche, Department of Clinical and Molecular Sciences, Ancona, Italy*

Background: In recent years, ultrasonography (US) has emerged as an accurate and reliable tool for the diagnosis of calcium pyrophosphate (CPP) deposition disease (CPPD) in daily practice. Previous studies analyzed the diagnostic value of US findings in different tissues and joints. However, no studies have investigated the optimal US scanning protocol in the diagnosis of CPPD at patient level.
Objectives: To assess the diagnostic value of the combinations of OMERACT-defined US findings of CPPD in the upper and lower limbs and to select the best minimal combination of anatomic structures to be scanned for diagnosing CPPD in inter-critical periods.

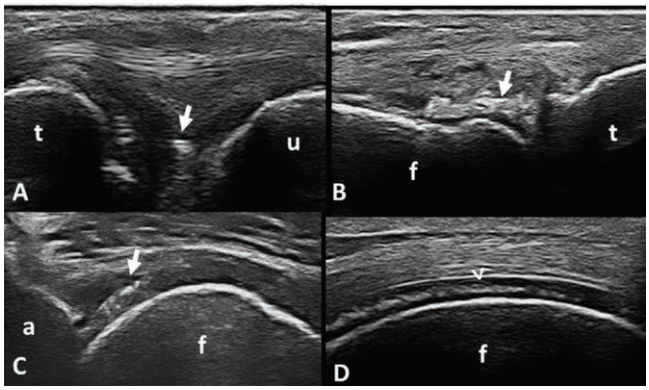
Methods: Patients with a crystal-proven diagnosis of CPPD and age- and sex-matched disease-controls were prospectively enrolled in this cross-sectional, monocentric, case-control study. All subjects underwent a bilateral US examination of 9 hyaline cartilages (HC), 6 fibrocartilages (FC), 5 tendons, 1 joint recess and 1 ligament as follows: shoulder (glenoid FC, humeral HC and acromioclavicular FC), elbow (humeral HC and triceps tendon), wrist (triangular FC, scapho-lunate ligament, volar recess of the radio-lunate joint), hand (HC of the metacarpophalangeal joints from 2nd to 5th finger), hip (acetabular FC and femoral HC), knee (femoral condyles' HC, meniscal FC, patellar and quadriceps tendons), ankle (talar HC, Achilles tendon and plantar fascia). US assessment was carried-out by a rheumatologist blinded to clinical data. CPP deposits were identified as presence/absence, according to the OMERACT definitions [1].
Results: Ninety-five patients were enrolled: 45 CPPD patients (age: 72±10.6 years, disease duration: 5.6±7.8 years, female/male ratio: 1.3) and 50 age- and sex-matched disease-controls (18 with rheumatoid arthritis, 13 with osteoarthritis, 10 with psoriatic arthritis and 9 with gout).
The FC of the medial and lateral meniscus were the most frequently involved targets of CPP deposits in cases (81.8% and 77.3% of patients, respectively), followed by the triangular FC of the wrist (68.2%), the HC of the femoral condyles (54.5%), the scapho-lunate ligament (52.3%) and the acetabular FC (50.0%). In all these anatomical targets, US findings indicative of CPP deposits were detected in a significantly higher percentage of cases than controls ($p<0.01$).
The US scanning protocols that showed the best balance between sensitivity and specificity, the most sensitive and the most specific were shown in Table 1.

Table 1. Diagnostic performances of different US scanning protocols

Anatomical targets	SE	SP	LH+	LH-
Knee meniscal FC and wrist triangular FC	0.86 (0.76-0.96)	0.86 (0.73-0.94)	6.35 (3.17-12.72)	0.13 (0.06-0.30)
Knee meniscal FC, wrist triangular FC and hip acetabular FC	0.93 (0.82-0.99)	0.82 (0.69-0.91)	5.19 (2.85-9.42)	0.08 (0.03-0.24)
Hip acetabular FC, knee femoral condyles' HC and wrist scapho-lunate ligament	0.67 (0.51-0.80)	0.96 (0.86-0.99)	16.67 (4.22-65.82)	0.35 (0.23-0.53)

LH: likelihood ratio, **SE**: sensitivity, **SP**: specificity, **US**: ultrasonography.
In all US scanning protocols, each anatomical target was assessed bilaterally.

Figure 1 includes representative pictures showing CPP crystal deposits in different anatomical targets.



A: Wrist, longitudinal scan of the triangular FC complex.
B: Knee, longitudinal scan of the lateral meniscus.
C: Hip, longitudinal scan of the acetabular labrum FC,
D: Knee, longitudinal scan of the medial femoral condyle's HC.
Arrows: CPP crystal deposits at FC, arrowhead: CPP crystal deposits at HC.
Conclusion: Our results suggest that bilateral US assessment of knee, wrist and hip provided acceptable sensitivity and specificity for diagnosing CPPD.
REFERENCES:
[1] Filippou G, et al. Identification of calcium pyrophosphate deposition disease (CPPD) by ultrasound: reliability of the OMERACT definitions in an extended set of joints-an international multiobserver study by the OMERACT Calcium Pyrophosphate Deposition Disease Ultrasound Subtask Force. Ann Rheum Dis. 2018;77:1194-9.
Disclosure of Interests: Edoardo Cipolletta: None declared, Jacopo Di Battista: None declared, Walter Grassi Speakers bureau: Walter Grassi has received speaking fees from AbbVie, Celgene, Grünenthal, Pfizer and Union Chimique Belge Pharma., Emilio Filippucci Speakers bureau: Emilio Filippucci. has received speaking fees from AbbVie, Bristol-Myers Squibb, Janssen-Cilag, Novartis, Pfizer, Roche and Union Chimique Belge Pharma.
DOI: 10.1136/annrheumdis-2021-eular.496

OP0206 ASSOCIATION BETWEEN FEMALE REPRODUCTIVE FACTORS AND GOUT: NATIONWIDE POPULATION-BASED COHORT STUDY OF 1 MILLION POSTMENOPAUSAL WOMEN

Y. Eun[1], I. Y. Kim[2], K. D. Han[3], K. Lee[3], S. Y. Kang[1], S. Lee[1], H. S. Cha[1], E. M. Koh[1], J. Lee[1], H. Kim[4]. *[1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medicine, Seoul, Korea, c of (South Korea)*; *[2]National Police Hospital, Department of Medicine, Seoul, Korea, Republic of (South Korea)*; *[3]Soongsil University, Department of Statistics and Actuarial Science, Seoul, Korea, Republic of (South Korea)*; *[4]Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medical Humanities, Seoul, Korea, Republic of (South Korea)*

Background: Previous studies have shown that the incidence of gout differs according to gender, and its risk factors also differ according to gender. However, little research has been done on the association between reproductive factors and gout.
Objectives: Our study attempted to determine whether there is an association between reproductive factors and the incidence of gout in a large nationwide population-based cohort of postmenopausal women.
Methods: Postmenopausal women aged 40-69 who participated in national health screenings in 2009 were included in the study. Subjects who had been diagnosed with gout prior to medical examination were excluded from the study, and a total of 1,076,378 women were included in the study. Outcome was the occurrence of gout which was defined as a case of two outpatient visit or one hospitalization for gout using the ICD-10 code of gout (M10) in the claim database. The Cox proportional hazard model was used for the analysis, and stratified analysis according to the body mass index (BMI) and chronic kidney disease (CKD) was performed.
Results: Mean follow-up duration was 8.1 years, and incident cases of gout were 64,052. Later menarche (adjusted HR 1.10, 95% CI 1.02-1.19 in >16 years, compared with ≤12 years), earlier menopause (adjusted HR 1.12 in <40 years, 1.06 in 40-45 years, 1.03 in 45-50 years, compared with 50-55 years), and shorter reproductive span (adjusted HR 1.10 in <30 years, 1.06 in 30-35 years, compared with ≥40 years) were associated with a high risk of gout. No association between parity and gout incidence was observed. Use of oral contraceptives (OC; adjusted HR 1.03 in <1 year, 1.05 ≥1 year, compared with non-user) and hormone replacement therapy (HRT; adjusted HR 1.16 in <2 years, 1.16 in 2-5 years, 1.18 in ≥5 years, compared with non-user) were associated with an increased risk of gout. The association between reproductive factors and gout remained in the trend without statistical significance in the low BMI group, but not in the high BMI group. The effects of use OC and HRT on gout were not significant in the CKD group.
Conclusion: Shorter exposure to endogenous estrogen was associated with a high risk of gout. Conversely, exposure to exogenous estrogen such as OC and HRT was associated with an increase in gout risk. This association was not significant in subjects with high BMI or CKD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4169

OP0207 ASSOCIATION BETWEEN DEMENTIA AND GOUT: A NATIONWIDE POPULATION-BASED STUDY

J. Kim[1], H. M. P. Park[2], D. H. Yim[3], I. A. Choi[4], S. Y. Eom[5]. *[1]Chungbuk National University Hospital, Internal Medicine, Division of Rheumatology, Cheongju-si, Chungcheongbuk-do, Korea, Republic of (South Korea)*; *[2]Chungbuk National University Hospital, Psychiatry, Cheongju, Korea, Republic of (South Korea)*; *[3]Chungbuk National University, Center for Environmental Medicine, Cheongju, Korea, Republic of (South Korea)*; *[4]Chungbuk National University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Cheongju, Korea, Republic of (South Korea)*; *[5]College of Medicine, Chungbuk National University, Department of Preventive Medicine, Cheongju, Korea, Republic of (South Korea)*

Background: Dementia is a common mental illness associated with aging. Alzheimer's disease (AD) and Vascular dementia (VaD) are the most common causes of dementia in the elderly. In previous studies, hyperuricemia was suggested to have anti-oxidant effects and possible neuroprotective effects [1,2].
Objectives: Hyperuricemia is the most important factor in the pathogenesis of gout. This study aims to investigate association between gout and dementia.
Methods: We conducted a nationwide population-based study using the NHIS-NSC database of the Korean populations consisted of 1 million individuals between 2002 and 2013. Gout patients were defined by International Classification of Diseases (ICD)-10 code for gout (M10) and prescriptions for urate lowering therapy including allopurinol, febuxostat and benzbromarone at least 30days. Dementia was also defined by ICD-10 codes for dementia; Alzheimer's disease (AD; F00), vascular dementia (VaD; F01).

Results: Excluded 40 patients with previous diagnosed dementia, total 5,496 gout patients were compared to 27,480 age- and sex-matched control group. The analysis results showed that gout patients had a lower risk of overall dementia [odds ratio (OR): 0.79; 95% confidence interval (CI): 0.63-0.99; p < 0.05] after adjusted for age, sex, household income, comorbidities. The risk of VaD (OR: 0.77; 95% CI: 0.32-1.9; p=0.68) and AD (OR; 0.8; 95% CI: 0.53-1.19; p=0.06) tended to be lower in gout group but these were not significant.

Conclusion: Gout patients had a lower risk of dementia. This result tended to exist for both AD and VaD type of dementia.

REFERENCES:

[1] Hooper DC, Spitsin S, Kean RB, et al. Uric acid, a natural scavenger of peroxynitrite, in experimental allergic encephalomyelitis and multiple sclerosis. Proc Natl Acad Sci USA. 1998; 95: 675–80.

[2] Bowman GL, Shannon J, Frei B, et al. Uric acid as a CNS antioxidant. J Alzheimer's Dis. 2010; 19: 1331–6.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2292

OP0208 INCIDENT GOUT: RISK OF DEATH AND CAUSE-SPECIFIC MORTALITY IN WESTERN SWEDEN – A NESTED CASE CONTROL STUDY

M. Dehlin[1], T. Zverkova Sandström[1], L. T. H. Jacobsson[1]. [1]*Institute of Medicine, Sahlgrenska Academy, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*

Background: Excess mortality in gout has been attributed to it's positive association with many comorbidities. Lately, a negative association with dementia has been suggested in some cohort studies. Data is limited on how this reflects in cause-specific mortality of gout patients.

Objectives: Our aims were to determine the relative risks in incident gout patients compared to general population 1) for overall death 2) for cause-specific mortality.

Methods: All incident cases of gout (definition: 1≥ ICD-10 code for gout (M10/M14.0) in the population based health care database VEGA; no gout diagnosis ≥5 years previously) between 2006-2015 in western Sweden were identified. Five population controls per case matched on age, sex and place of residence were identified. Comorbidities, defined by ICD-10 codes, (alcohol related disorders, hypertension, ischemic heart disease, heart failure, cerebrovascular disease, diabetes, dyslipidemia, obesity, renal disease, dementia, lung diseases and cancer) were identified for 5 years preceding index date for cases and controls in VEGA. Patients were followed until the earliest of death, migration or study end 31 of December 2017. Cause of death was identified through the national cause of death register and grouped as death due to: CVD, renal disease, dementia, infections, diabetes, diseases of the digestive system, lung diseases, cancer and other. COX regression analyses, adjusted for baseline demographics and comorbidities, were used to compare mortality in cases and controls, taking competing cause of death into account by the Fine and Gray method.

Results: From the total adult population of western Sweden between 2006 and 2015 (yearly average of 1264150 individuals), we identified 24320 cases of incident gout and 119781 controls, who were followed on average 5.3 and 5.6 years respectively. At baseline mean age was (SD) 67.3 years (15.3) and 67.6% were men. At baseline, income and level of education was significantly lower in gout cases compared to controls, whereas all comorbidities were significantly more common among gout cases (data not shown) except for dementia which was significantly more common in controls, 4.2% versus 2.5% in cases, p<.0001. The HR for overall death was increased in gout patients (HR: 1.08 (95% CL: 1.05-1.11) (Table 1). Gout cases had significantly increased risk for death by CVD, renal disease, infections, diseases of the digestive system and significantly decreased risk for death by dementia and cancer (Table 1). Point estimates were similar in men and women (data not shown).

Table 1. Causes of death by exposure status and cause-specific mortality overall, gout cases compared to controls, adjusted hazard ratios by the Fine and Gray method, 95% confidence intervals

Causes of death	Cause of death, n (%)		Hazard ratios (95% CI)	
	Gout cases, n = 24320	Controls, n= 119781	Model 1	Model 2
Cardiovascular disease	3527 (14.5)	11369 (9.5)	1.61 (1.55-1.67)	1.20 (1.16-1.26)
Renal disease	140 (0.6)	239 (0.2)	2.79 (2.26-3.44)	1.68 (1.31-2.16)
Dementia	287 (1.2)	2922 (2.4)	0.45 (0.40-0.51)	0.68 (0.60-0.77)
Infections	437 (1.8)	1631 (1.4)	1.27 (1.14-1.41)	1.15 (1.03-1.28)
Diabetes	250 (1.0)	665 (0.6)	1.80 (1.55-2.08)	1.02 (0.87-1.20)
Diseases digestive system	226 (0.9)	725 (0.6)	1.49 (1.29-1.74)	1.36 (1.16-1.59)
Lung diseases	306 (1.3)	1216 (1.0)	1.20 (1.06-1.36)	0.89 (0.78-1.01)
Cancer	1179 (4.9)	6067 (5.1)	0.92 (0.87-0.98)	0.94 (0.88-0.99)
Other	655 (2.7)	2899 (2.4)	1.08 (0.99-1.17)	1.09 (0.99-1.19)
All-cause mortality	7007 (28.8)	27733 (23.2)	1.32 (1.29-1.36)	1.08 (1.05-1.11)

Model 1: adjusted for age and sex

Model 2: adjusted for baseline values for: age, sex, marital status, income, education, born outside of Sweden, alcohol related disorders, hypertension, ischemic heart disease, heart failure, cerebrovascular disease, diabetes, dyslipidemia, obesity, renal disease, dementia, lung diseases and cancer

Conclusion: This study demonstrates a modest increase in overall mortality in gout patients and a decreased risk of death from dementia reflecting it's inverse relation to gout.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.454

OP0209 SONOGRAPHIC ESTIMATION OF MONOSODIUM URATE BURDEN PREDICTS THE FULFILMENT OF THE 2016 REMISSION CRITERIA FOR GOUT: A 12-MONTH STUDY

E. Cipolletta[1], A. DI Matteo[1], W. Grassi[1], E. Filippucci[1]. [1]*Polytechnic University of Marche, Department of Clinical and Molecular Sciences, Ancona, Italy*

Background: Preliminary remission criteria for gout include the following five domains: serum uric acid (SUA) levels <360 µmol/l, absence of subcutaneous tophi, absence of gouty flares, pain (due to gout) <2/10 and patient global assessment of disease activity <2/10 [1]. To achieve remission, all criteria must be fulfilled at least twice in a 12-month period [1]. Although imaging techniques allow to visualise monosodium urate (MSU) deposits and to estimate their burden, an imaging domain was not included.

Objectives: To investigate whether baseline MSU burden estimated by ultrasonography (US) predicts the achievement of remission according to these criteria [1] over 12 months.

Methods: In this 12-month prospective, observational and monocentric study, patients with gout according to the 2015 ACR/EULAR criteria and on urate-lowering therapy for at least the preceding 6 months were consecutively recruited. After the baseline clinical assessment, only patients fulfilling all domains of the remission criteria [1] (and therefore amenable to achieve the remission at 12 months) were followed up at 6-month intervals for one year.

The US findings indicative of MSU deposits were identified according to the OMERACT definitions. The following joints were included in the US scanning protocol: elbows, wrists, 2nd metacarpophalangeal joints, knees, ankles and 1st metatarsophalangeal joints. Sum scores of aggregates, double contour (DC) signs, and tophi were calculated separately, and a total score resulting from the sum of all elementary US findings was recorded.

Results: Seventy patients with gout were recruited; of these, 20 (28.6%) were excluded at baseline because 13 (18.6%) did not satisfy the SUA domain, 11 (15.7%) tophus domain, 7 (10.0%) pain domain and 5 (7.1%) disease activity domain.

In the enrolled patients (Age: 59.9±14.8 years, female/male ratio: 1/49, disease duration: 6.5±6.6 years), remission criteria were fulfilled in 21 (42.0%) of 50 patients over 12 months.

No significant difference was found between patients fulfilling and not fulfilling the remission criteria at 12 months in all clinical and laboratory data except for the gout flare prophylaxis (7, 33.3% vs 20, 69.0%; p=0.02).

The baseline US MSU burden was significantly lower (total score 1.9±1.8) in patients in remission than in those not in remission at 12 months (total score 5.1±3.1) (p<0.01). The fulfilment of the remission criteria at 12 months was recorded in 87.5% of the patients without baseline US evidence of MSU deposits and in only 33.0% of those with at least one US finding indicating MSU deposits (p<0.01).

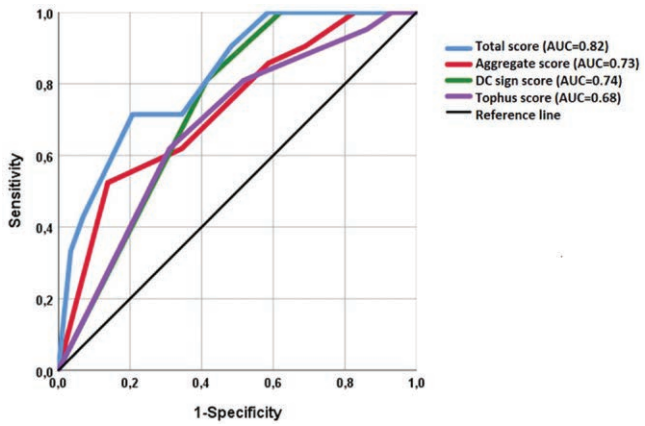
US scores and gout flare prophylaxis were the only significant predictors of remission in the univariate analyses (Table 1).

Table 1. Predictive values of baseline data for the remission at 12 months.

	OR (95%CI)	P value
Ongoing flare prophylaxis	0.23 (0.07-0.75)	**0.02**
Total score=0	10.83 (1.14-102.59)	**0.04**
Aggregate score=0	5.53 (1.34-22.76)	**<0.01**
DC sign score=0	7.33 (1.71-31.44)	**<0.01**
Tophus score=0	3.88 (1.08-13.92)	**0.02**

95%CI: 95% confidence interval; **OR:** odds ratio.

The risk of not fulfilling the remission criteria increased with the US burden of MSU deposits. For each 1-point increase in total score, aggregate score, DC sign score and tophus score, the risk increased by 1.81- (95%CI: 1.27-2.60), 1.73- (95%CI: 1.14-2.64), 4.16- (95%CI: 1.55-11.3) and 1.95-fold (95%CI: 1.07-3.56), respectively (Figure 1).



Conclusion: Baseline US estimation of MSU burden is an independent predictor of gout clinical remission at 12 months. The absence of US MSU deposits was the most significant predictor of remission, whereas the US detection of DC sign in at least one joint of not achieving remission. Thus, performing an US examination in patients amenable to fulfil the remission criteria after 12 months may improve risk-stratification and inform management of these patients.

REFERENCES:

[1] de Lautour H, *et al.* Development of Preliminary Remission Criteria for Gout Using Delphi and 1000Minds Consensus Excersices. *Arthritis Care Res* 2016;**68**:667–72

Disclosure of Interests: Edoardo Cipolletta: None declared, Andrea Di Matteo: None declared, Walter Grassi Speakers bureau: Walter Grassi has received speaking fees from AbbVie, Celgene, Grünenthal, Pfizer and Union Chimique Belge Pharma., Emilio Filippucci Speakers bureau: Emilio Filippucci. has received speaking fees from AbbVie, Bristol-Myers Squibb, Janssen-Cilag, Novartis, Pfizer, Roche and Union Chimique Belge Pharma

DOI: 10.1136/annrheumdis-2021-eular.495

Rheumatoid arthritis - comorbidity and clinical aspects - II

OP0210

PREGNANCY OUTCOMES IN RELATION TO DISEASE ACTIVITY AND ANTI-RHEUMATIC TREATMENT STRATEGIES IN WOMEN WITH RHEUMATOID ARTHRITIS – A MATCHED COHORT STUDY FROM SWEDEN AND DENMARK

K. Hellgren[1,2], A. E. Secher[3], B. Glintborg[3], A. Lilleoere Rom[4], B. Gudbjornsson[5], B. Michelsen[6], F. Granath[1], M. L. Hetland[3]. [1]*Karolinska Institutet, Clinical Epidemiology Division, Department of Medicine Solna, Stockholm, Sweden*; [2]*Karolinska Institutet, Division of Rheumatology, Department of Medicine Solna, Stockkholm, Sweden*; [3]*DANBIO and COPECARE, Center for Rheumatology and Spine Diseases, Centre of Head and Orthopedics, Rigshospitalet, Copenhagen, Denmark*; [4]*Rigshospitalet, Department of Obstetrics and Research Unit Women's and Children's Health, Copenhagen, Denmark*; [5] *Landspitali University Hospital and University of Iceland, Centre for Rheumatology Research and Faculty of Medicine, Reykjavik, Iceland*; [6]*Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway*

Background: Women with rheumatoid arthritis (RA) are at increased risks of adverse pregnancy outcomes, especially preterm birth (PTB) and small for gestational age (SGA). However, the link between RA disease activity, type and timing of anti-rheumatic treatment, and the risk of these outcomes remains unclear.
Objectives: To explore the associations between maternal RA and PTB/SGA in relation to disease activity and use of anti-rheumatic treatment before and during pregnancy.
Methods: By linking national medical birth registers to prospective clinical rheumatology registers (CRRs) in Sweden (SRQ) and Denmark (DANBIO), we identified 1739 RA-pregnancies and 17390 control-pregnancies (matched 1:10 on maternal age, birth year, and parity) with delivery 2006-2018. From CRRs and prescribed drug registers, we collected information on RA disease activity (DAS28, CRP and HAQ-score) and anti-rheumatic drugs (biologics, conventional synthetic (cs)DMARDs and oral steroids) nine months before and during pregnancy. Using logistic regression, we estimated adjusted odds ratios (ORs) with 95% confidence intervals (CI) for PTB and SGA in RA-pregnancies vs. control-pregnancies overall, and stratified by disease activity and type of anti-rheumatic treatment before and during pregnancy. Apart from the matching variables we adjusted for body mass index, smoking, educational level and country.
Results: Overall, RA-pregnancies were associated with increased ORs of PTB (1.92, 95% CI 1.56-2.35) and SGA (1.93, 95% CI 1.45-2.57). High maternal disease activity during pregnancy strengthened the associations with both PTB and SGA, whereas the ORs approached 1 for low disease activity (control-pregnancies constituting the reference), Table 1. Among RA-pregnancies with available information on DAS28-CRP (n=686, 39%), OR was 2.69 (95% CI 1.37-5.26) for PTB, and 3.39 (95% CI 1.43-8.06) for SGA, comparing DAS28-CRP >=3.2 vs.<3.2 during pregnancy. Stratifying on type of anti-rheumatic treatment did not substantially change the results. Combination therapy with biologics together with oral steroids and/or csDMARDs in the nine months before pregnancy was associated with PTB (ORs spanning 2.57-3.45) and SGA (ORs spanning 2.40-3.81).
Conclusion: During pregnancy, disease activity rather than treatment, appears to be the most important risk factor for PTB and SGA in RA. The findings highlight the importance of monitoring RA during pregnancy, especially in women receiving extensive anti-rheumatic treatment or with residual disease activity.

Acknowledgements: The Nordic clinical rheumatology registers for allowing us to use their clinical data. We also would like to acknowledge the NordForsk and FOREUM, especially the patient representatives of the NordForsk collaboration.

Disclosure of Interests: Karin Hellgren Consultant of: UCB, Anne Emilie Secher: None declared, Bente Glintborg Grant/research support from: Pfizer, Biogen and BMS, Ane Lilleoere Rom: None declared, Björn Gudbjornsson Speakers bureau: Amgen and Novartis, Brigitte Michelsen Consultant of: Novartis, Grant/research support from: Novartis, Fredrik Granath: None declared, Merete Lund Hetland Speakers bureau: Biogen, Celltrion, Janssen Biologics B.V, MSD, Pfizer, Samsung Biopis, Consultant of: Biogen, Celltrion, Janssen Biologics B.V, MSD, Pfizer, Samsung Biopis, Grant/research support from: AbbVie, Biogen, BMS, Eli Lilly Danmark A/S, Lundbeck Fonden, Pfizer, Roche, Sandoz, Novartis

DOI: 10.1136/annrheumdis-2021-eular.605

Table 1. Adjusted odds ratios (ORs)1 for PTB and SGA in RA-pregnancies in relation to disease activity and functional status during pregnancy vs. control pregnancies

		Preterm birth			Small for gestational age[1]		
		Pregnancies, n	Events, n (%)	Adjusted OR (95% CI)	Pregnancies, n	Events, n (%)	Adjusted OR (95% CI)
Control-pregnancies[2]		17312	794 (5)	1 (REF)	17184	418 (2)	1(REF)
All RA pregnancies[2]		1734	144 (8)	**1.92 (1.56-2.35)**	1722	75 (4)	**1.93 (1.45-2.57)**
DAS28-CRP[3,4]	<3.2	459	26 (6)	1.05 (0.64-1.72)	456	13 (3)	0.96 (0.49-1.91)
	3.2-5.1	182	17 (9)	**2.40 (1.40-4.11)**	181	13 (7)	**3.13 (1.64-5.97)**
	>5.1	43	5 (12)	2.77 (0.86-8.87)	43	4 (9)	**4.59 (1.59-13.2)**
	No information	1050	96 (9)	**2.18 (1.71-2.78)**	1042	45 (4)	**2.06 (1.46-2.90)**
HAQ-score[3]	<0.5	338	19 (6)	1.31 (0.79-2.16)	335	8 (2)	0.93 (0.41-2.12)
	0.5-0.9	166	15 (9)	**2.37 (1.34-4.19)**	165	5 (3)	1.50 (0.60-3.74)
	≥1	196	19 (10)	**1.85 (1.06-3.24)**	195	18 (9)	**3.70 (2.05-6.67)**
	No information	1034	91 (9)	**2.06 (1.60-2.64)**	1027	44 (4)	**1.98 (1.39-2.82)**
CRP, mg/L[3]	<10	455	21 (5)	0.91 (0.55-1.51)	452	14 (3)	1.09 (0.57-2.07)
	10-29	191	22 (11)	**2.58 (1.52-4.38)**	190	12 (6)	**2.68 (1.38-5.22)**
	≥30	57	9 (16)	**4.59 (2.28-9.22)**	57	5 (9)	**4.12 (1.68-10.1)**
	No information	1031	92 (9)	**2.10 (1.64-2.70)**	1023	44 (4)	**2.05 (1.44-2.90)**

[1]Missingness on small for gestational age in 12 RA-pregnancies and 128 control-pregnancies [2]Only among live births, i.e. stillbirths excluded. [3]Maximum value any time during pregnancy [4]Defined as DAS28-CRP without patient's global health VAS

OP0211

PATERNAL INFLAMMATORY ARTHRITIS IS ASSOCIATED WITH A HIGHER RISK OF MISCARRIAGES: RESULTS OF A LARGE MULTICENTER STUDY (IFAME-FERTILITY)

L. F. Perez-Garcia[1], E. Röder[1], R. Goekoop[2], M. R. Kok[3], P. Kok[4], H. T. Smeele[1], I. Tchetverikov[5], A. Van der Helm - van Mil[1,6], J. H. Van der Kaap[1,7], B. Krijthe[1,8], R. Dolhain[1]. *[1]Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands*; *[2]Haga Hospital (Leyweg), Rheumatology, Den Haag, Netherlands*; *[3]Maasstad Hospital, Rheumatology, Rotterdam, Netherlands*; *[4]Reinier de Graaf Gasthuis, Rheumatology, Delft, Netherlands*; *[5]Albert Schweitzer Hospital, Rheumatology, Dordrecht, Netherlands*; *[6]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[7]Adrz Medical Center, Rheumatology, Goes, Netherlands*; *[8]Franciscus Gasthuis & Vlietland, Rheumatology, Rotterdam, Netherlands*

Background: The effect of inflammatory arthritis (IA) on pregnancy outcomes has been studied mainly in women. Paternal older age, sperm DNA integrity and certain genetic defects have been associated with worse pregnancy outcomes (1). However, pregnancy outcomes of partners of men with IA have never been studied.

Objectives: To describe the pregnancy characteristics and outcomes of partners of men diagnosed with IA.

Methods: We performed a multicenter cross-sectional retrospective study conducted in eight Dutch hospitals. Men with IA (Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA) and Spondyloarthritis (SpA)) who were over 40 years old and indicated that their family size was complete were invited to participate. Participants completed a digital questionnaire that included pregnancy-related questions and questions regarding their demographic and clinical information. To analyze the impact of IA on pregnancy outcomes, pregnancies were classified into two groups; pregnancies that occurred after diagnosis of IA and before the diagnosis of IA.

Results: In total 628 male participants diagnosed with IA were included. 408 men reported 897 singleton pregnancies that resulted in 794 live births. Regarding pregnancy characteristics, pregnancies conceived after diagnosis of IA had a higher mean paternal and maternal age at conception and a lower rate of spontaneous pregnancies (90.91 vs 96.60%, p=<0.005) (See Table 1). With regards to pregnancy outcomes, pregnancies conceived after receiving the diagnosis of IA had a lower rate of live births (86.36% and 89.22%, p=0.053) and a significant higher rate of miscarriages (12.27 vs 7.53%, p=<0.05). After correcting for maternal age and year of pregnancy, pregnancies conceived after the diagnosis of IA had a higher risk of miscarriages (OR 1.71 [CI 1.04-2.81], p<0.05). No statistically significant differences between the two groups were reported for the rates of abortions, preterm births and pregnancy complications.

Table 1. Pregnancy characteristics and outcomes.

	All pregnancies	Pregnancy after diagnosis of IA	Pregnancy before diagnosis of IA	P value
Pregnancy characteristics				
Total number of pregnancies	897	220	677	
Maternal age at conception, mean (SD)	29.00 (5.00)	30.69 (5.16)	28.45 (4.83)	**p<0.005**
Paternal age at conception, mean (SD)	31.31 (5.72)	34.27 (6.08)	30.49 (5.34)	**p<0.005**
Spontaneous pregnancy, n (%)	854 (95.21)	200 (90.91)	654 (96.60)	**p<0.005**
Pregnancy duration-months, median (IQR)	39 (38-40)	39 (38-40)	39 (38-40)	p=0.928
Pregnancy outcomes				
Live births, n (%)	794 (88.52)	190 (86.36)	604 (89.22)	p=0.053
Miscarriage, n (%)	78 (8.70)	27 (12.27)	51 (7.53)	**p<0.05**
Abortion, n (%)	25 (2.78)	3 (1.36)	22 (3.25)	p=0.128
*Medical indication	5 (20.00)	0 (0)	5 (22.73)	
*Personal reasons	20 (80.00)	3 (100.00)	17 (77.27)	
Pre-term birth	149 (16.61)	31 (14.09)	118 (17.43)	p=0.248
Pregnancy complications				
No complications during pregnancy, n (%)	754 (84.34)	184 (83.64)	570 (84.57)	p=0.741
Hypertensive disorders (hypertension, pre/eclampsia), n (%)	41 (4.57)	8 (3.64)	33 (4.87)	p=0.445
Gestational Diabetes Mellitus	11 (1.28)	2 (0.94)	9 (1.38)	p=0.619
Growth restriction	12 (1.34)	1 (0.45)	11 (1.65)	p=0.193

Conclusion: This is the largest study to describe the pregnancy characteristics and outcomes of partners of men diagnosed with IA and the first to demonstrate that paternal IA is associated with a higher risk of miscarriage. Prospective studies are needed to corroborate these findings.

REFERENCES:

[1] Ibrahim Y, Johnstone E. The male contribution to recurrent pregnancy loss. Translational andrology and urology. 2018;7(Suppl 3):S317-S27.

Acknowledgements: The authors would like to acknowledge Ron Buijs, data manager of the Department of Rheumatology of the Erasmus MC, for his technical support with regards to data collection.

Disclosure of Interests: Luis Fernando Perez-Garcia Consultant of: Galapagos, Esther Röder: None declared, Robbert Goekoop: None declared, Marc R Kok Consultant of: Roche, Grant/research support from: Roche, Petra Kok: None declared, Hieronymus TW Smeele: None declared, Ilja Tchetverikov: None declared, Annette van der Helm - van Mil: None declared, J.H. van der Kaap: None declared, Bouwe Krijthe: None declared, Radboud Dolhain Speakers bureau: Abbvie, UCB, Genzyme, Novartis, Consultant of: Galapagos, Grant/research support from: UCB

DOI: 10.1136/annrheumdis-2021-eular.1732

OP0212

MEN DIAGNOSED WITH INFLAMMATORY ARTHRITIS BEFORE THE AGE OF 40 YEARS HAVE A LOWER FERTILITY RATE THAN THOSE DIAGNOSED AFTER THE AGE OF 40 YEARS: RESULTS OF A LARGE MULTICENTER STUDY (IFAME-FERTILITY)

L. F. Perez-Garcia[1], E. Röder[1], R. Goekoop[2], J. Hazes[1], M. R. Kok[3], P. Kok[4], H. T. Smeele[1], I. Tchetverikov[5], J. H. Van der Kaap[1,6], A. Van der Helm - van Mil[1,7], B. Krijthe[1,8], R. Dolhain[1]. *[1]Erasmus University Medical Centrum, Rheumatology, Rotterdam, Netherlands*; *[2]Haga Hospital, Rheumatology, Den Haag, Netherlands*; *[3]Maasstad Hospital, Rheumatology, Rotterdam, Netherlands*; *[4]Reinier de Graaf Gasthuis, Rheumatology, Delft, Netherlands*; *[5]Albert Schweitzer Hospital, Rheumatology, Dordrecht, Netherlands*; *[6]Adrz Medical Center, Rheumatology, Goes, Netherlands*; *[7]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[8]Franciscus Gasthuis & Vlietland, Rheumatology, Rotterdam, Netherlands*

Background: The effect of inflammatory arthritis (IA) on fertility has been mainly studied in women. Multiple factors associated with lower fertility rate in women can also be present in male patients with IA (1). The fertility rate in men with IA, however, has never been studied.

Objectives: To describe the fertility rate (number of biological children per individual) of men with IA.

Methods: We performed a multicenter cross-sectional retrospective study conducted in eight Dutch hospitals. Men with IA (Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA) and Spondyloarthritis (SpA)) who were over 40 years old and indicated that their family size was complete were invited to participate. Men who were still planning on having biological children were excluded. Participants completed a digital questionnaire that included fertility-related questions and questions regarding their demographic and clinical information. To analyze the impact of IA on male fertility rate, patients were divided into groups according to the age at the time of their diagnosis: age<30 years, age 31-40 years and age>41 years.

Results: In total 628 participants diagnosed with IA were included. The response rate 34.87%. Information regarding their age, age at diagnosis, clinical diagnosis and number of children is presented per group in Table 1. Regarding the total number of children per man, there was a statistically significant difference between the three groups (p=<0.005). The mean total number of children was significantly lower in men diagnosed at age<30 years (1.39 {SD 1.41}) and at age 31-40 years (1.60 {SD 1.35}) compared to those diagnosed after at age>41 years (1.88 {SD 1.14}). Compared to men from the general population of the Netherlands, the total number of children of men diagnosed at age>41 years was not statistically different (1.88 vs 1.80, respectively).

Table 1. Participants' basic demographic and clinical characteristics, including the number of biological children per men.

	All patients	IA diagnosed at age <30 years	IA diagnosed at age 31-40 years	IA diagnosed at age >41 years
Total, n (%)	628	137 (21.82)	149 (23.73)	342 (54.46)
Age, mean (SD)	57.17 (9.98)	53.01 (9.96)	52.76 (7.35)	61.06 (9.47)
Diagnosis, n (%)				
• iRA	297 (47.29)	42 (30.66)	67 (44.97)	188 (55.32)
• AJIA	10 (1.59)	10 (6.25)	0 (0)	0 (0)
• ISpA (incl. PsA)	320 (50.96)	90 (65.69)	83 (55.70)	147 (42.98)
Age at diagnosis, mean (SD)	41.29 (13.08)	26.27 (9.15)	36.99 (5.66)	49.98 (9.70)
Disease duration, mean (SD)	15.89 (11.88)	26.48 (12.57)	15.70 (8.52)	11.30 (9.87)
Number of biological children, mean (95% CI)	1.71 (1.60-1.81)	**1.39 (1.15-1.63)**[a,b]	**1.60 (1.38-1.82)**[a]	1.88 (1.75 -2.01)

[a] p< 0.05 compared to those diagnosed age >41 years[b] p< 0.05 compared to those diagnosed age >31-40 years

Conclusion: This is the largest study ever conducted to evaluate the impact of IA on male fertility. We demonstrated that men diagnosed with IA before and during their reproductive years have a lower fertility rate than those men diagnosed with IA after their reproductive years. Multiple mechanisms (biological and non-biological) can be responsible for this association. More research is needed to identify the causes of these lower fertility rates in men with IA.

REFERENCES:

[1] Perez-Garcia LF, Te Winkel B, Carrizales JP, Bramer W, Vorstenbosch S, van Puijenbroek E, et al. Sexual function and reproduction can be impaired in men with rheumatic diseases: A systematic review. Semin Arthritis Rheum. 2020;50(3):557-73.

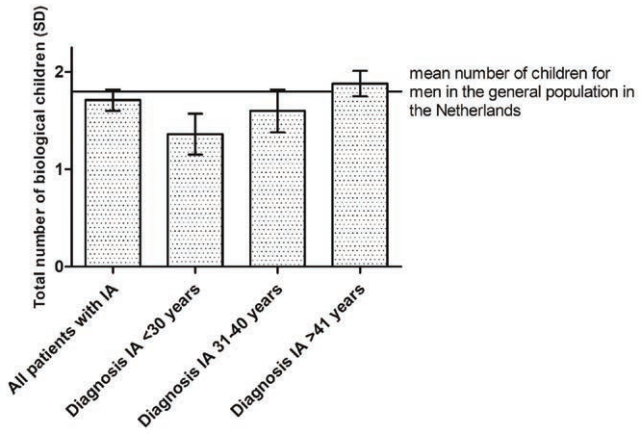


Figure 1. Total number of biological children (mean and SD) per group.

Acknowledgements: The authors would like to acknowledge Ron Buijs, data manager of the Department of Rheumatology of the Erasmus MC, for his technical support with regards to data collection.

Disclosure of Interests: Luis Fernando Perez-Garcia Consultant of: Galapagos, Esther Röder: None declared, Robbert Goekoop: None declared, Johanna Hazes: None declared, Marc R Kok Consultant of: Novartis, Grant/research support from: Novartis, Petra Kok: None declared, Hieronymus TW Smeele: None declared, Ilja Tchetverikov: None declared, J.H. van der Kaap: None declared, Annette van der Helm - van Mil: None declared, Bouwe Krijthe: None declared, Radboud Dolhain Speakers bureau: UCB, Roche, Abbvie, Genzyme, Novartis, Consultant of: Galapagos, Grant/research support from: UCB

DOI: 10.1136/annrheumdis-2021-eular.639

OP0213 SEX DIFFERENCES IN MULTIMORBIDITY BETWEEN PATIENTS WITH RHEUMATOID ARTHRITIS AND COMPARATORS IN A LARGE NATIONWIDE US STUDY

H. J. Dykhoff[1], E. Myasoedova[2,3], M. Peterson[2], J. M. Davis III[2], V. Kronzer[2], C. Coffey[2], T. Gunderson[3], C. S. Crowson[2,3]. *[1]Mayo Clinic, Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, United States of America*; *[2]Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; *[3]Mayo Clinic, Department of Quantitative Health Sciences, Rochester, United States of America*

Background: Patients with rheumatoid arthritis (RA) have an increased burden of multimorbidity. Although many comorbidities vary by sex, sex differences in multimorbidity among individuals with RA have not been examined.

Objectives: We aimed to compare multimorbidity between women and men with RA and comparators without RA.

Methods: We used a large longitudinal, real-world data warehouse with de-identified administrative claims for commercial and Medicare Advantage enrollees, to identify cases of RA and matched controls. Cases were defined as patients aged ≥18 years with ≥2 diagnoses of RA in January 1, 2010 - June 30, 2019 and ≥1 prescription fill for methotrexate in the year after the first RA diagnosis. Controls were persons without RA matched 1:1 to RA cases on age, sex, census region, calendar year of index date (corresponding to the date of second diagnosis code for RA), and length of prior medical/pharmacy coverage. Race was classified as non-Hispanic White (White), non-Hispanic Black (Black), Asian, Hispanic, or other/unknown, based on self-report or derived rule sets. Multimorbidity (2 or more comorbidities) was defined using 25 chronic comorbidities from a combination of the Charlson and Elixhauser Comorbidity Indices assessed during the year prior to index date. Rheumatic comorbidities were not included. Logistic regression models were used to estimate odds ratios (OR) with 95% confidence intervals (CI).

Results: The study included 16,363 cases with RA and 16,363 matched non-RA comparators (mean age 58.2 years, 70.7% female for both cohorts). In both cohorts, women were slightly younger (mean age 57.5 vs. 59.8 years). Among RA patients, women were more racially/ethnically diverse than men, with 72% of women (78% men) being White, 12% (10%) Hispanic, 11% (7%) Black, 3% (3%) Asian, and 3% (3%) other/unknown. Racial/ethnic diversity was similar among non-RA women and men with 74% women (75% men) being White, 9% (9%) Hispanic, 10% (8%) Black, 4% (4%) Asian, and 3% (4%) other/unknown. Patients with RA had more multimorbidity than non-RA subjects (51.3% vs 44.8%). Observed rates of multimorbidity were similar in women and men with RA (51.6% vs 50.5%, p=0.18), but among non-RA patients, women had lower observed rates of multimorbidity than men (43.7% vs 47.4%, p<0.0001). However, following adjustment for age, race/ethnicity, and geographic region, multimorbidity among RA patients was greater in women versus men (OR: 1.19; 95% CI: 1.11-1.28) and similar among non-RA women and men (OR: 0.97 for females; 95% CI: 0.90-1.05). Examination of individual comorbidities showed that women with RA had more depression, hypothyroidism, diabetes mellitus, and chronic pulmonary disease compared to men with RA and women without RA.

Conclusion: This large nationwide study showed increased occurrence of multimorbidity in women with RA compared to men with RA, while women and men without RA had similar levels of multimorbidity following adjustment for age, race/ethnicity, and geographic region. The underlying mechanisms for these sex differences require further investigation.

Disclosure of Interests: Hayley J. Dykhoff: None declared, Elena Myasoedova: None declared, Madeline Peterson: None declared, John M Davis III Grant/research support from: Research grant from Pfizer, Vanessa Kronzer: None declared, Caitrin Coffey: None declared, Tina Gunderson: None declared, Cynthia S. Crowson: None declared

DOI: 10.1136/annrheumdis-2021-eular.1625

OP0214 IMPACT OF A MULTI-MORBIDITY SCREENING AND PREVENTION PROGRAM IN CHRONIC INFLAMMATORY RHEUMATIC DISEASES ON THE ONE-YEAR HOSPITALIZATION RATE BASED ON AN ANALYSIS OF THE FRENCH NATIONAL HEALTH DATABASE

G. Decarriere[1], J. Pastor[2], D. Demoulin[2], G. Mouterde[1], C. Lukas[1], B. Combe[1], G. Mercier[2], J. Morel[1], C. Daien[1]. *[1]CHU, Rheumatology, Montpellier, France*; *[2]CHU, Medical Information, Montpellier, France*

Background: A screening program for multimorbidities started in 2014 at the Montpellier University Hospital for primary prevention in patients with chronic inflammatory rheumatic diseases (IRD).

Objectives: The objective of this work was to assess the impact of this program on morbidity by comparing the hospitalization rate of those patients in the year following the screening to the one of patients with IRD who did not benefit from this program.

Methods: Patients with IRD who benefit from the screening program in 2015, 2016 and 2017 were identified in the French national health database PMSI and matched to 3 controls living in the same area on age, sex, type of IRD, use of intravenous (IV) biologic (b) DMARDs and index date. The exclusion criteria were subjects in secondary prevention identified as history of myocardial infarction in the previous 5 years or use of antiplatelet therapy. The primary outcome was the rate of all-cause hospitalization in the following year. The secondary endpoints were hospitalizations for another reason than IRD ("non-IRD") including those for cardiovascular [CV] events and major fractures. Hospitalization rates were compared between the two groups in the year after screening (or index date) and also between the year preceding screening and the year after for each group. Univariate and multivariate odds ratios (CI95%) were calculated, taking into account the medical history (hypertension, diabetes, heart failure, CV disease, COPD, major fractures in the 5 years preceding the index date) and hospitalizations in the previous year.

Results: 486 patients were identified and matched with 1458 controls. 67.08% had rheumatoid arthritis and 21.81% spondyloarthritis; 7% of them had IV bDMARDs. Unscreened patients had more hypertension (19% vs 10.1%), diabetes (9% vs 4.9%), heart failure (2.3% vs 0.4%) and "non-IRD" hospitalizations (78.5% vs 72.2%) in the 5 years preceding the index date. In the year following the index date, the percentages of "all causes" and "non-IRD" hospitalizations were significantly higher in non-screened than in screened patients (n = 1944, 64.8% versus 51%, Chi2 test, p <0.001; and 47.1% versus 37.9%, p <0.001 respectively). 17 (1.17%) cardiovascular events occurred in non-screened versus 2 (0.41%) in screened patients (n = 1944, Chi2 test, p = 0.14). There was no difference in the occurrence of CV events or major fractures between the 2 groups. In multivariate analysis, screening was associated with a 49% (0.51 [0.41-0.64]) reduction in "all causes" hospitalization and a 27% (0, 73 [0.58-0.91]) decrease in "non-IRD" hospitalization, with no difference for CV or fracture cardiological events. The risk factors associated with "non-IRD" hospitalization were: history of "non-IRD" hospitalization in the previous year (2.26 [1.63-3.13]), IV bDMARDs (1.69 [1, 14-2.53]) and age> 70 years (1.44 [1.02-2.03] vs <50 years). Hospitalization in the previous year for "all causes" or "non-IRD" was associated with

rehospitalization in the following year in the non-screened group (p <0.001), but not in the screened group (p = 0.750 and p = 0.066 respectively).
Conclusion: Our screening and prevention program was associated with a reduction in hospitalizations in the following year and a decrease in the risk of re-hospitalization compared to unscreened patients with IRD. This suggests a positive impact of performing systematic screening for multi-morbidities in IRD patients.
Acknowledgements: We thank Pfizer for their financial support
Disclosure of Interests: guillaume decarriere: None declared, Jenica PASTOR: None declared, David DEMOULIN: None declared, Gael Mouterde Speakers bureau: Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Pfizer, Cédric Lukas Speakers bureau: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Consultant of: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Grant/research support from: Pfizer, Novartis and Roche-Chugai, Bernard Combe Speakers bureau: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Consultant of: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Novartis, Pfizer, and Roche-Chugai, Grégoire Mercier: None declared, Jacques Morel Speakers bureau: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Consultant of: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Novartis, Pfizer, and Roche-Chugai, Claire Daien Speakers bureau: Pfizer, Roche-Chugai, Fresenius, BMS, MSD, Lilly, Novartis, Galapagos, Consultant of: Abivax, Abbbvie, BMS, Roche-Chugai, Grant/research support from: Pfizer, roche-chugai, fresenius, MSD
DOI: 10.1136/annrheumdis-2021-eular.3454

OP0215 MENTAL HEALTH, SLEEP AND COGNITION CHARACTERISTICS IN RHEUMATOID ARTHRITIS AND ASSOCIATIONS WITH RHEUMATOID FACTOR STATUS IN THE UK BIOBANK

I. Stanciu[1], S. Siebert[2], D. Mackay[1], D. Lyall[1]. [1]*University of Glasgow, Public Health, Glasgow, United Kingdom*; [2]*University of Glasgow, Infection Immunity & Inflammation, Glasgow, United Kingdom*

Background: There are significant gaps in the literature regarding sleep, mental health, and cognition for people with rheumatoid arthritis (RA) despite being important aspects of patients' overall quality of life. Similarly, there is a lack of understanding about the role of rheumatoid factor (RF) on these domains.
Objectives: The aim of the current study was to characterize mental health, cognition, and sleep variables in people with RA and to compare these associations in people with positive RF (RF+) and negative RF (RF-) in a large population cohort.
Methods: This cross-sectional study used baseline data from the UK Biobank cohort (n= 502,506) to compare people with and without RA and people that are RF+ versus RF- on a variety of sociodemographic, lifestyle, illness-related factors and depression, neuroticism, performance on cognitive tests and sleep-related factors. Logistic regression analyses were also performed to determine whether RF seropositivity was associated with mental health, cognition, and sleep variables. We adjusted for the covariates of age, sex, ethnicity, deprivation index, smoking status, BMI and alcohol intake.
Results: In this sample 5,907 people self-reported having RA (1.17%), of which 74% were RF- and 26% were RF+. There were significant differences ($p < 0.05$) between people with and without RA for depression, neuroticism, nap during the day, getting up in the morning, insomnia, reaction time, fluid intelligence and prospective memory. There were significant differences ($p < 0.05$) between RF+ and RF- people for depression, neuroticism, sleep duration, nap during the day, getting up in the morning, insomnia, and reaction time. In the unadjusted regression analyses neuroticism (B=-0.06, SE= 0.01, $p < 0.001$), sleep duration (B=0.02, SE= 0.005, $p < 0.001$), nap during the day (OR=1.28, 95% CI: 1.02-1.65, $p < 0.05$) and reaction time (B=4.55, SE=0.53, $p< 0.001$) were significantly associated with RF status. After adjusting for covariates, only sleep duration (B=0.01, SE=0.005, $p< 0.01$) remained significant.
Conclusion: The current study suggests that RA diagnosis and RF status are associated with differences in mental health, sleep, and cognition, highlighting the importance of addressing these aspects in clinical settings and future research.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1767

OP0216 TRENDS IN OCCURRENCE OF DEMENTIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: A POPULATION-BASED COHORT STUDY, 1980-2009

V. Kronzer[1], C. S. Crowson[1], J. M. Davis III[1], M. Vassilaki[2], M. Mielke[2], E. Myasoedova[1]. [1]*Mayo Clinic, Rheumatology, Rochester, United States of America*; [2]*Mayo Clinic, Health Sciences Research, Rochester, United States of America*

Background: Some cross-sectional studies show increased odds of cognitive impairment and dementia in patients with rheumatoid arthritis (RA) compared to the general population, while others show the reverse. Furthermore, existing studies have not evaluated trends in incidence of dementia on a longitudinal basis.
Objectives: We aimed to assess the incidence of dementia over time in patients with incident RA and to compare it to those of population-based comparators.
Methods: This population-based, retrospective cohort study included Olmsted County residents with incident RA and non-RA individuals matched on age, sex, and calendar year. All RA cases met 1987 ACR criteria for RA between 1980 and 2009. Index date was the date of RA criteria fulfillment or a corresponding date for referents. All individuals were followed until death, migration, or 12/31/2019. For sensitivity analyses, follow-up of each decade was truncated at eleven years to make the length of follow-up comparable (e.g., the 1980–89 cohort was truncated at 12/31/1999). Incident dementia was defined as an ICD-9/10 code for dementia. Patients with dementia prior to RA incidence/index date were excluded. Cox proportional hazards models calculated hazard ratios (HR) with 95% confidence intervals (CI) for incident dementia by decade, adjusting for age and sex. The cumulative incidence of dementia was assessed, adjusting for the competing risk of death.
Results: The study included 895 persons with RA (mean age 55.3 years; 69% female) followed up for a median of 15.2 years. The 10-year cumulative incidence of dementia in these individuals during the 1980s was 12.7% (95%CI 7.9-15.7%), 1990s was 7.2% (95%CI 3.7-9.4%), and 2000s was 6.2% (95%CI 3.6-7.8%) Patients with incident RA in 2000-09 had markedly lower cumulative incidence of dementia than patients diagnosed in the 1980s (HR 0.57; 95%CI 0.33-0.98). Patients with incident RA were then compared to population-based comparators without RA (N=880, mean age 55.2 years; 68% female) followed up for a median of 16.4 years. The 10-year cumulative incidence of dementia in these individuals in the 1980s was 9.3% (95%CI 4.6-11.9%), in the 1990s was 5.0% (95%CI 2.2-6.3%) and in the 2000s was 7.1% (95%CI 4.3-8.9%). Overall, the risk of dementia in RA patients was significantly higher than in the non-RA persons (HR 1.38; 95%CI 1.04-1.83). When subdivided by decade, the risk of dementia in patients diagnosed with RA was higher than non-RA comparators in the 1980s and 1990s but not 2000s (Figure 1). Sensitivity analysis with truncated follow-up yielded similar results.

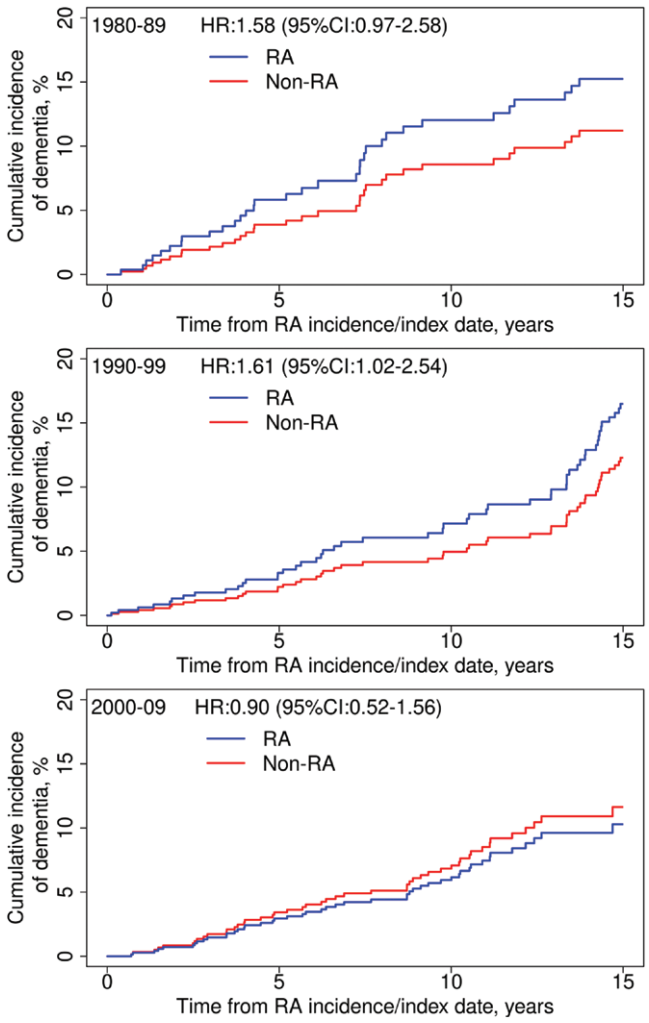


Figure 1. Cumulative incidence of dementia (based on ICD 9/10 codes) versus age-and sex-matched non-RA comparators by decade of RA incidence/index.

Conclusion: Our findings show substantial decline in risk of dementia in patients with RA onset in the 2000s as compared to 1980s, including when compared to the general population comparators. This decline coincides with the advent of novel biologic treatments for RA. Further studies should investigate this association using manual verification rather than billing codes for dementia, and should also elucidate the role of inflammation, autoimmunity, and anti-rheumatic treatments in risk of dementia.

Acknowledgements: This work was funded by grants from the National Institutes of Health, NIAMS (R01 AR46849) and NIA (R01 AG068192, R01 AG034676).

Disclosure of Interests: Vanessa Kronzer: None declared, Cynthia S. Crowson: None declared, John M Davis III Grant/research support from: Pfizer, Maria Vassilaki Shareholder of: Abbott Laboratories, Johnson and Johnson, Medronic and Amgen, Grant/research support from: Roche, Biogen, Michelle Mielke Consultant of: Biogen and Brain Protection Company, Elena Myasoedova: None declared

DOI: 10.1136/annrheumdis-2021-eular.150

OP0217 IS METACARPOPHALANGEAL-JOINT PAIN AS AN EARLY SYMPTOM OF PATIENTS AT RISK FOR PROGRESSION TO INFLAMMATORY ARTHRITIS EXPLAINED BY MRI-DETECTED SUBCLINICAL INFLAMMATION? – A LARGE OBSERVATIONAL STUDY

Q. Dumoulin[1], X. Matthijssen[1], F. Wouters[1], A. Van der Helm - van Mil[1,2], E. Niemantsverdriet[1]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; [2]*Erasmus MC, Rheumatology, Rotterdam, Netherlands*

Background: Pain in metacarpophalangeal (MCP)-joints in patients presenting with clinically suspect arthralgia (CSA) is one of the clinical features by which patients are considered at risk for progression to inflammatory arthritis (IA). As such this symptom is characteristic for CSA and therefore part of a list of clinical parameters determined by an EULAR-taskforce to identify a more homogeneous group of patients within CSA (the EULAR definition of arthralgia suspicious for progression to RA). MRI-detected subclinical inflammation is known to be present in patients with CSA. In general, arthralgia in CSA can be explained by this subclinical inflammation, however to date, the association of subclinical inflammation with pain in MCP-joints specifically is not clear. Subsequently, it is unknown whether this association differs pertinently when investigated with self-reported pain, or with pain in the form of tenderness at physical examination.
Objectives: This study will investigate whether MCP-pain and MCP-joint tenderness are associated with MRI-detected subclinical inflammation in patients with CSA, and more specifically those who have progressed to IA.
Methods: Between April 2012- February 2019, 602 patients were consecutively included in the Leiden clinically suspect arthralgia (CSA)-cohort. Follow-up ended when patients developed clinically apparent IA (determined at physical examination), or else after 2-years (median follow-up time 25 months). MCP-joints were assessed for self-reported joint pain by the patient using a mannequin and subsequently for joint tenderness by physical examination. Baseline unilateral MRIs of the MCP (2-5)-joints were scored by two readers, blinded for clinical data, on subclinical inflammation (synovitis, tenosynovitis, osteitis). Associations between MCP-pain or MCP-joint tenderness and MRI-detected subclinical inflammation were studied at patient level by logistic regression analyses, entering the mentioned MRI-detected features separately (univariable) and together (multivariable).
Results: 33% of 227 patients with self-reported MCP-pain had MRI-detected subclinical inflammation and 38% of 226 patients with MCP-joint tenderness had MRI-detected subclinical inflammation. Self-reported MCP-joint pain was univariable associated with subclinical inflammation and synovitis in particular (OR 2.00, 95% CI: 1.21-3.30, OR 2.87, 95% CI: 1.29-6.39). In multivariable analysis this MCP-pain was associated with synovitis (OR 2.54, 95% CI: 1.12-5.77). MCP-joint tenderness was univariable associated with subclinical inflammation, and synovitis and tenosynovitis in particular (OR 1.84, 95% CI: 1.29-2.63, OR 1.76, 95% CI: 1.10-2.81, OR 1.69, 95% CI: 1.12-2.55, respectively). In multivariable analysis, tenosynovitis remained significant (OR 1.54, 95% CI: 1.00-2.36). Of all patients with self-reported MCP-joint pain who developed IA, 50% had MRI-detected subclinical inflammation. For MCP-joint tenderness this was 61%. Patients with MCP-joint tenderness without subclinical inflammation who developed IA, developed clinical arthritis at a joint that was not scanned (85%), hence they may have had subclinical inflammation that was not imaged. The other 15% did develop arthritis in an MCP-joint, suggesting that subclinical inflammation developed after CSA-onset.
Conclusion: Arthralgia in the MCP-joints is associated with subclinical inflammation in CSA, in particular with synovitis and tenosynovitis. The prevalence of subclinical inflammation is highest for tender joints at physical examination; this can be acknowledged when applying the EULAR definition of arthralgia suspicious for progression to RA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1597

Unrevealing the impact of PsA and comorbidity prevention

OP0218 MORTALITY IN PATIENTS WITH PSORIATIC ARTHRITIS IN SWEDEN

S. Exarchou[1], D. DI Giuseppe[2], G. M. Alenius[3], E. Klingberg[4,5], V. Sigurdardottir[6,7], S. Wedrén[2,8], U. Lindström[5], C. Turesson[1], L. T. H. Jacobsson[5], J. Askling[2], J. K. Wallman[9,10]. [1]*Lund University, Department of Clinical Sciences Malmö, Rheumatology, Lund, Sweden*; [2]*Karolinska Institutet, Department of Medicine Solna, Clinical Epidemiology Division, Stockholm, Sweden*; [3]*Umeå University, Department of Public Health and Clinical Medicine/Rheumatology, Umeå, Sweden*; [4]*Sahlgrenska University Hospital, Department of Rheumatology, Gothenburg, Sweden*; [5]*Sahlgrenska Academy, University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; [6]*Falun Hospital, Department of Rheumatology, Falun, Sweden*; [7]*Uppsala University, Centre for Clinical Research Dalarna, Uppsala, Sweden*; [8]*Karolinska University Hospital, Department of Rheumatology, Stockholm, Sweden*; [9]*Skåne University Hospital, Department of Rheumatology, Lund, Sweden*; [10]*Lund University, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden*

Background: In contrast to the increased mortality reported in other inflammatory diseases such as rheumatoid arthritis and psoriasis, prior mortality studies in psoriatic arthritis (PsA) have shown inconsistent results.
Objectives: To compare all-cause mortality between PsA patients in Sweden and matched general population controls, and to describe cause of death distributions in the two groups.
Methods: All individuals in Sweden with ≥1 main diagnosis of PsA (ICD-10: L40.5/M07.0-M07.3) from outpatient visits to rheumatology or internal medicine clinics at age ≥18 years (y) 2001-2017 were identified from the Swedish National Patient Register. Each case was matched to 5 general population controls based on sex, county and age in the year of the first registered arthritis diagnosis for the case. Cases and controls were followed from 1 Jan, 2007, or from first PsA diagnosis thereafter for index cases, until first occurrence of death (data from the Swedish Cause of Death Register), emigration or 31 Dec, 2018. Mortality was assessed overall, as well as stratified by sex (45% males) and disease duration (PsA diagnosis prior to 2007 [38% of cases] vs. 2007-2017), using matched Cox proportional hazard regression, or – in case the Cox assumption regarding proportionality did not hold – matched Breslow test. To account for potential PsA misclassification (in a previous validation study, 86% of 400 cases fulfilled PsA classification criteria), a sensitivity analysis was performed by randomly replacing 20% of cases with one of their own controls. Moreover, incidence rate ratios (IRR) of death were calculated overall and stratified by sex, disease duration and age. Finally, causes of death (from the Cause of Death Register) were described for PsA cases and controls.
Results: Over the 12y follow-up, 3 121 deaths occurred among 33 036 PsA cases (268 402 person-years at risk) and 12 884 deaths among 161 144 controls (1 302 250 person-years), resulting in an increased mortality among the PsA cases (HR 1.11 [95%CI 1.07-1.16], p<0.001, Figure and Table; sensitivity analysis HR 1.09 [1.05-1.14]). The increased mortality was seen mainly among female PsA cases and among cases with longer disease duration (Figure; Table). IRR:s of death were significantly increased for all ages except <40y, with the numerically highest point-estimates for ages 40-49y and 50-59y (Table). Cause of death frequencies among the PsA cases/controls: cardiovascular disease 29/27%; diabetes mellitus 2.1/2.5%; chronic kidney disease 0.4/0.3%; infection 5.7/4.5%; chronic pulmonary disease 5.1/4.1%; malignancy 29/34%; suicide 2.3/2.0%; other 27/26%.
Conclusion: In this nationwide 12y assessment, the mortality risk among PsA patients in Sweden was increased by around 10% as compared to the general population, mainly driven by increased risks among females and patients with longer disease duration. Cause of death distributions were numerically similar between PsA cases and controls.

References:

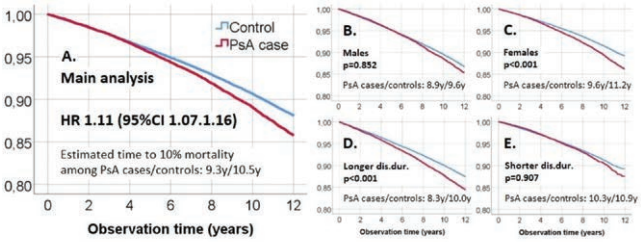


Figure. Kaplan-Meier survival curves displaying all-cause mortality among PsA cases and matched general population controls in Sweden overall (**A**) and in subgroups (**B-E**). Estimated time to 10% mortality are displayed in the respective graphs. **A.** Main analysis. **B.** Males, analysed by Breslow test. **C.** Females, HR 1.23 (95%CI 1.16-1.30). **D.** Longer disease duration, HR 1.18 (95%CI 1.12-1.25). **E.** Shorter disease duration, analysed by Breslow test. Dis.dur, disease duration; PsA, psoriatic arthritis; y, years.

Table 1. Mortality rates and incidence rate ratios

	PsA cases			Population controls			
	Number of deaths	Person-years at risk	Mortality rate*	Number of deaths	Person-years at risk	Mortality rate*	Incidence rate ratio (95%CI)
Overall	3 121	268 402	11.6	12 884	1 302 250	9.9	1.18 (1.13-1.22)
Males	1 459	120 517	12.1	6 468	580 285	11.1	1.09 (1.03-1.15)
Females	1 662	147 886	11.2	6 416	721 966	8.9	1.27 (1.20-1.34)
Longer disease duration	1 943	139 379	13.9	7 459	670 174	11.1	1.25 (1.19-1.32)
Shorter disease duration	1 178	129 023	9.1	5 425	632 077	8.6	1.06 (1.00-1.13)
Age intervals (years)							
<40	18	33 568	0.5	98	163 278	0.6	0.89 (0.54-1.48)
40-49	90	50 552	1.8	322	246 955	1.3	1.37 (1.08-1.73)
50-59	280	65 820	4.3	1 131	321 730	3.5	1.21 (1.06-1.38)
60-69	723	70 224	10.3	3 132	341 587	9.2	1.12 (1.04-1.22)
70-79	960	37 232	25.8	4 160	178 909	23.3	1.11 (1.03-1.19)
≥80	1 050	11 007	95.4	4 041	49 791	81.2	1.18 (1.10-1.26)

* Per 1000 person-years.

Disclosure of Interests: Sofia Exarchou Consultant of: AbbVie, Novartis, Daniela Di Giuseppe: None declared, Gerd-Marie Alenius: None declared, Eva Klingberg Speakers bureau: Eli Lilly, Consultant of: Novartis, Grant/research support from: Roche, Valgerdur Sigurdardottir Consultant of: Novartis, Sanofi, Sara Wedrén: None declared, Ulf Lindström: None declared, Carl Turesson Speakers bureau: AbbVie, BMS, Pfizer, Roche, Consultant of: Roche, Grant/research support from: BMS, Lennart T.H. Jacobsson Consultant of: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, Johan Askling Grant/research support from: For ARTIS: AbbVie, BMS, Eli Lilly, Merck, Pfizer, Roche, Samsung Bioepis, Sanofi, UCB. This study was supported by AbbVie, Amgen, Eli Lilly, Novartis and Pfizer. The sponsors were allowed to comment on the study protocol and were provided with a report of the results, but had no influence on the study design or decision to submit the abstract., Johan K Wallman Consultant of: Celgene, Eli Lilly, Novartis
DOI: 10.1136/annrheumdis-2021-eular.104

OP0219 THE ASSOCIATION OF PSORIATIC ARTHRITIS WITH ALL-CAUSE MORTALITY AND LEADING CAUSES OF DEATH IN PSORIATIC ARTHRITIS

A. Haddad[1], W. Saliba[2,3], I. Lavi[3], A. Batheesh[4], S. Kasem[2,4], T. Gazitt[1], I. Feldhamer[5], A. Cohen[5,6], D. Zisman[1,2]. *[1]Carmel Medical Center, Rheumatology, Haifa, Israel*; *[2]Technion, Ruth and Bruce Rappaport Faculty of Medicine, Haifa, Israel*; *[3]Clalit Health Services, Department of Epidemiology, Haifa, Israel*; *[4]Carmel Medical Center, Internal Medicine, Haifa, Israel*; *[5]Clalit Health Services, Department of Epidemiology, Telaviv, Israel*; *[6]Ben Gurion University of the Negev, Dermatology, Bear-Sheva, Israel*

Background: Data on the association between PsA and mortality remains conflicting as it has been hampered by small sample size with few events and the potential for confounders of selection and severity biases from clinic-based studies.
Objectives: To examine the association between PsA and all-cause mortality in a cohort of PsA patients and matched controls, using data from a population-based large medical record database.
Methods: Patients with newly diagnosis of PsA between January 1st, 2003 and December 31st, 2018 from the Clalit Health database were identified. 4 controls without PsA were selected and matched to cases of PsA by age (within 1 year), sex, ethnicity (Jewish *vs.* non-Jewish), and index date. The two groups were followed from the index date until the first occurrence of death from any cause or end of follow-up (June 30, 2019). Data on mortality and on the immediate cause of death was based on the Notification of Death form legally required by the Israeli Ministry of the Interior for every deceased person in the country. Demographic data including age, sex, ethnicity (Jewish or Arab), and socioeconomic status (SES) at inception were retrieved from the CHS database. Data regarding tobacco use (ever), obesity, body mass index, diabetes mellitus, hyperlipidemia, hypertension, ischemic heart disease, prior cerebrovascular accident, congestive heart failure, chronic renal failure, chronic obstructive pulmonary disease, cirrhosis, prior malignancy, psoriasis, and the concomitant use of glucocorticosteroids, conventional and biologic disease-modifying anti-rheumatic drugs (cDMARDs and bDMARDs, respectively) were extracted from the database.
We estimated the attributable fraction of the various causes of death in PsA patients and compared it to the proportionate mortality rate (PMR) of the leading causes of death in Israel during 2014-2016 based on a recently published report by the Central Bureau of Statistics. Cox proportional hazard regression models were used to estimate the crude and the multivariate adjusted hazard ratio (HR) for the association between PsA and all-cause mortality, as well as for factors associated with mortality within the PsA group.
Results: A total of 5275 PsA patients were identified between 2003 and 2018 and where matched to 21,011 controls based on age, sex, and ethnicity. The mean age was 51.7 ± 15.4 years of whom 53% were females. More individuals in the PsA group were smokers, obese, with diabetes, hypertension, and dyslipidemia, as well as with a history of ischemic heart disease, cerebrovascular disease, congestive heart failure, chronic obstructive pulmonary disease, chronic renal failure and cirrhosis than patients in the control group, and 38.2% of PsA patients were on b-DMARDS. Overall 471 (8.9%) patients died in the PsA group compared to 1,668 (7.9%) in the control group during a mean follow-up of 7.2 ± 4.4 years. The crude HR for the association of PsA and all-cause mortality was 1.16 (95% CI, 1.042-1.29). However, the association was not significant on multivariate analysis with HR of 1.096 (95% CI, 0.977-1.229).
In PsA patients, malignancy was the leading cause of death, constituting 26% of all deaths, followed by ischemic heart disease 15.8%, diabetes 6.2%, cerebrovascular diseases 5.5% and septicemia 5.5%, in keeping with the order of the leading causes of death in the general population of Israel during 2014-2016 as recently reported by the Central Bureau of Statistics.
On multivariate model Cox regression analysis, male sex, increased body mass index, increased Charlson comorbidity index scores and history of hospitalization in a year prior to death were associated with higher mortality, whereas treatment bDMARDs and cDMARDs were associated with a lower relative risk of death.
Conclusion: No clinically relevant increase in mortality rate was observed in PsA patients from the period 2003-2018. The most common causes of specific proportionate mortality rates in our cohort were similar to those in the general population.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1895

OP0220 SECULAR TRENDS IN BASELINE CHARACTERISTICS, TREATMENT RETENTION AND RESPONSE RATES IN 17453 BIONAÏVE PSORIATIC ARTHRITIS PATIENTS INITIATING TNFI – RESULTS FROM THE EUROSPA COLLABORATION

S. N. Christiansen[1], L. Midtbøll Ørnbjerg[1], S. H. Rasmussen[1], A. G. Loft[2,3], J. K. Wallman[4], F. Iannone[5], B. Michelsen[1,6], M. J. Nissen[7], J. Zavada[8], M. J. Santos[9], M. Pombo-Suarez[10], K. Eklund[11], M. Tomsic[12], B. Gudbjornsson[13], İ. Sari[14], C. Codreanu[15], D. DI Giuseppe[16], B. Glintborg[1,3], M. Sebastiani[17], K. M. Fagerli[6], B. Moeller[18], K. Pavelka[8], A. Barcelos[19], C. Sánchez-Piedra[20], H. Relas[11], Z. Rotar[12], T. Love[13], S. Akar[21], R. Ionescu[15], G. Macfarlane[22], M. G. H. Van de Sande[23], M. L. Hetland[1,3], M. Østergaard[1]. *[1]Rigshospitalet Glostrup, Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre for Head and Orthopedics, Glostrup, Denmark*; *[2]Aarhus University Hospital, Department of Rheumatology, Aarhus, Denmark*; *[3]Rigshospitalet Glostrup, DANBIO Registry, Glostrup, Denmark*; *[4]Skåne University Hospital, Lund University, Lund, Sweden*; *[5]University of Bari, Rheumatology Unit, Bari, Italy*; *[6]Diakonhjemmet Hospital, Division of Rheumatology, Oslo, Norway*; *[7]Geneva University Hospital, Department of Rheumatology, Geneva, Switzerland*; *[8]Institute of Rheumatology, Institute of Rheumatology, Prague, Czech Republic*; *[9]Hospital Garcia de Orta, Rheumatology Department, Almada, Portugal*; *[10]Hospital Clinico Universitario, Rheumatology Service, Santiago de Compostela, Spain*; *[11]Helsinki University Hospital, Department of Rheumatology, Helsinki, Finland*; *[12]University Medical Centre Ljubljana, Department of Rheumatology, and Universitiy of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia*; *[13]Centre for Rheumatology Research, University Hospital and Faculty of Medicine, University of Iceland, Reykjavik, Iceland*; *[14]Dokuz Eylul University School of Medicine, Division of Rheumatology, Izmir, Turkey*; *[15]University of Medicine and Pharmacy, Carol Davila, Bucharest, Romania*; *[16]Karolinska Institutet, Department of Medicine Solna, Stockholm, Sweden*; *[17]University of Modena and Reggio Emilia, Rheumatology Unit, Modena, Italy*; *[18]Inselspital, University Hospital Bern, Department Rheumatology & Immunology, Bern, Switzerland*; *[19]Centro Hospitalar do Baixo Vouga, Department of Rheumatology, Aveiro, Portugal*; *[20]Sociedad Española de Reumatologia, Research Unit, Madrid, Spain*; *[21]Katip Celebi University School of Medicine, Division of Rheumatology, Izmir, Turkey*; *[22]University of Aberdeen, Aberdeen Centre for Arthritis and Musculoskeletal Health (Epidemiology Group), School of Medicine, Medical Sciences and Nutrition, Aberdeen, United Kingdom*; *[23]Amsterdam Rheumatology and Immunology Center (ARC), Amsterdam UMC/AMC, University of Amsterdam, Amsterdam, Netherlands*

Table 1. Secular trends in baseline characteristics, treatment retention, remission and response rates in European PsA patients initiating a 1st TNFi

Baseline characteristics	Group A (1999–2008)			Group B (2009–2014)			Group C (2015–2018)		
Age, median (IQR)	62 (54–72)			58 (49–67)			54 (45–62)		
Male, %	51			48			47		
Years since diagnosis, median (IQR)	5 (2–10)			3 (1–9)			3 (1–8)		
Smokers, %	16			17			17		
DAS28, median (IQR)	4.6 (3.7–5.3)			4.3 (3.4–5.1)			4.0 (3.2–4.8)		
DAPSA28, median (IQR)	29.9 (19.3–41.8)			25.7 (17.2–38.1)			24.0 (16.1–35.5)		
CDAI, median (IQR)	21.8 (14.0–31.1)			20.0 (13.0–29.0)			18.6 (12.7–26.1)		
TNFi drug, % (Adalimumab / Etanercept / Infliximab / Certolizumab / Golimumab)	27 / 43 / 30 / 0 / 0			36 / 31 / 14 / 5 / 14			21 / 40 / 21 / 8 / 10		
Follow up	**6 months**			**12 months**			**24 months**		
	Gr A	**Gr B**	**Gr C**	**Gr A**	**Gr B**	**Gr C**	**Gr A**	**Gr B**	**Gr C**
Retention rates, % (95% CI)	88 (87–89)	83 (82–84)	84 (83–85)	79 (78–80)	72 (71–73)	72 (71–73)	68 (67–69)	60 (59–61)	60 (59–62)
DAS28, median (IQR)	2.7 (1.9–3.6)	2.4 (1.7–3.4)	2.3 (1.7–3.2)	2.5 (1.8–3.4)	2.2 (1.6–3.1)	2.1 (1.6–2.9)	2.1 (1.6–3.1)	2.0 (1.6–2.9)	1.9 (1.5–2.6)
DAPSA28, median (IQR)	10.6 (4.8–20.0)	9.5 (3.9–18.3)	8.7 (3.6–15.9)	9.1 (4.1–17.8)	7.7 (3.1–15.4)	7.6 (2.9–14.4)	6.7 (2.7–13.7)	6.6 (2.7–13.5)	5.9 (2.4–11.8)
CDAI, median (IQR)	7.8 (3.0–15.2)	8.0 (3.0–15.0)	6.4 (2.6–12.2)	6.4 (2.5–13.0)	6.2 (2.5–12.1)	5.8 (2.2–11.4)	5.0 (2.0–11.0)	5.5 (2.0–11.2)	5.0 (2.0–9.0)
DAS28 remission, %, c/L	47 / 42	55 / 46	61 / 51	53 / 43	62 / 45	66 / 48	64 / 42	68 / 37	75 / 41
DAPSA28 remission, %, c/L	22 / 19	26 / 22	28 / 23	25 / 20	31 / 22	32 / 23	36 / 23	34 / 19	38 / 21
CDAI remission, %, c/L	23 / 21	23 / 19	26 / 22	27 / 21	27 / 20	29 / 21	34 / 22	31 / 17	35 / 19
ACR50 response, %, c/L	26 / 23	22 / 18	24 / 20	27 / 22	23 / 17	21 / 15	23 / 15	18 / 10	14 / 8

Gr, Group; c/L, crude/LUNDEX.

Background: Knowledge of changes over time in baseline characteristics and tumor necrosis factor inhibitor (TNFi) response in bionaïve psoriatic arthritis (PsA) patients treated in routine care is limited.

Objectives: To investigate secular trends in baseline characteristics and retention, remission and response rates in PsA patients initiating a first TNFi.

Methods: Prospectively collected data on bionaïve PsA patients starting TNFi in routine care from 15 European countries were pooled. According to year of TNFi initiation, three groups were defined a priori based on bDMARD availability: Group A (1999–2008), Group B (2009–2014) and Group C (2015–2018).

Retention rates (Kaplan-Meier), crude and LUNDEX adjusted[1] remission (Disease Activity Score (DAS28) <2.6, 28-joint Disease Activity index for PsA (DAPSA28) ≤4, Clinical Disease Activity Index (CDAI) ≤2.8) and ACR50 response rates were assessed at 6, 12 and 24 months. No statistical comparisons were made.

Results: A total of 17453 PsA patients were included (4069, 7551 and 5833 in groups A, B and C).

Patients in group A were older and had longer disease duration compared to B and C. Retention rates at 6, 12 and 24 months were highest in group A (88%/77%/64%) but differed little between B (83%/69%/55%) and C (84%/70%/56%).

Baseline disease activity was higher in group A than in B and C (DAS28: 4.6/4.3/4.0, DAPSA28: 29.9/25.7/24.0, CDAI: 21.8/20.0/18.6), and this persisted at 6 and 12 months. Crude and LUNDEX adjusted remission rates at 6 and 12 months tended to be lowest in group A, although crude/LUNDEX adjusted ACR50 response rates at all time points were highest in group A. At 24 months, disease activity and remission rates were similar in the three groups (Table).

Conclusion: Over the past 20 years, patient age, disease duration and disease activity level at the start of the first TNFi in PsA patients have decreased. Furthermore, TNFi retention rates have decreased while remission rates have increased, especially remission rates within the first year of treatment. These findings may reflect a greater awareness of early diagnosis in PsA patients, a lowered threshold for initiating TNFi and the possibility for earlier switching in patients with inadequate treatment response.

REFERENCES:

[1] Arthritis Rheum 2006; 54: 600-6.

Acknowledgements: Novartis Pharma AG and IQVIA for supporting the Euro-SpA Research Collaboration Network.

Disclosure of Interests: Sara Nysom Christiansen Speakers bureau: BMS and GE, Grant/research support from: Novartis, Lykke Midtbøll Ørnbjerg Grant/research support from: Novartis, Simon Horskjær Rasmussen: None declared, Anne Gitte Loft Speakers bureau: AbbVie, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: AbbVie, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Grant/research support from: Novartis, Johan K Wallman Consultant of: Celgene, Eli Lilly, Novartis, Florenzo Iannone Speakers bureau: Abbvie, MSD, Novartis, Pfizer and BMS, Brigitte Michelsen Consultant of: Novartis, Grant/research support from: Novartis, Michael J. Nissen Speakers bureau: Novartis, Eli Lilly, Celgene, and Pfizer, Consultant of: Novartis, Eli Lilly, Celgene, and Pfizer, Jakub Zavada: None declared, Maria Jose Santos Speakers bureau: AbbVie, Novartis, Pfizer, Manuel Pombo-Suarez: None declared, Kari Eklund: None declared, Matija Tomsic Speakers bureau: Abbvie, Amgen, Biogen, Medis, MSD, Novartis, Pfizer, Consultant of: Abbvie, Amgen, Biogen, Medis, MSD, Novartis, Pfizer, Björn Gudbjornsson Speakers bureau: Amgen and Novartis, İsmail Sari: None declared, Catalin Codreanu Speakers bureau: AbbVie, Amgen, Egis, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, Egis, Novartis, Pfizer, UCB, Daniela Di Giuseppe: None declared, Bente Glintborg Grant/research support from: Pfizer, Biogen, AbbVie, Marco Sebastiani: None declared, Karen Minde Fagerli: None declared, Burkhard Moeller: None declared, Karel Pavelka Speakers bureau: AbbVie, Roche, MSD, UCB, Pfizer, Novartis, Egis, Gilead, Eli Lilly, Consultant of: AbbVie, Roche, MSD, UCB, Pfizer, Novartis, Egis, Gilead, Eli Lilly, Anabela Barcelos: None declared, Carlos Sánchez-Piedra: None declared, Heikki Relas: None declared, Ziga Rotar Speakers bureau: Abbvie, Amgen, Biogen, Medis, MSD, Novartis, Pfizer, Consultant of: Abbvie, Amgen, Biogen, Medis, MSD, Novartis, Pfizer, Thorvardur Love: None declared, Servet Akar: None declared, Ruxandra Ionescu Speakers bureau: Abbvie, Amgen, Boehringer-Ingelheim Eli-Lilly,Novartis, Pfizer, Sandoz, UCB, Gary Macfarlane Grant/research support from: GlaxoSmithKline, Marleen G.H. van de Sande: None declared, Merete L. Hetland Speakers bureau: Abbvie, Biogen, BMS, Celltrion, Eli Lilly, Janssen Biologics B.V, Lundbeck Fonden, MSD, Pfizer, Roche, Samsung Biopies, Sandoz, Novartis., Mikkel Østergaard Speakers bureau: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB and Wyeth, Consultant of: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB and Wyeth

DOI: 10.1136/annrheumdis-2021-eular.422

OP0221 TARGETED METABOLOMIC PROFILING AND PREDICTION OF CARDIOVASCULAR EVENTS: A PROSPECTIVE STUDY OF PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS

K. Colaco[1,2,3], K. A. Lee[4], S. Akhtari[5], R. Winer[6], P. Welsh[7], N. Sattar[7], I. Mcinnes[8], V. Chandran[9,10], P. Harvey[5,9], R. Cook[4], D. D. Gladman[9,10], V. Piguet[1,9], L. Eder[1,9]. *[1]Women's College Hospital, Women's College Research Institute, Toronto, Canada*; *[2]University Health Network, Krembil Research Institute, Toronto, Canada*; *[3]University of Toronto, Institute of Medical Science, Toronto, Canada*; *[4]University of Waterloo, Statistics and Actuarial Science, Waterloo, Canada*; *[5]Women's College Hospital, Cardiology, Toronto, Canada*; *[6]Rambam Health Care Campus, Neurology, Haifa, Israel*; *[7]University of Glasgow, Institute of Cardiovascular & Medical Sciences, Glasgow, United Kingdom*; *[8]University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; *[9]University of Toronto, Medicine, Toronto, Canada*; *[10]Toronto Western Hospital, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto, Canada*

Background: Psoriatic arthritis and psoriasis, collectively termed psoriatic disease (PsD), are associated with increased cardiovascular (CV) risk. Metabolites comprise biomarkers that may add predictive value over traditional CV risk factors.

Objectives: We aimed to identify metabolites associated with CV events (CVEs) and to determine whether they could improve CV risk prediction beyond traditional CV risk factors.

Methods: Patients from a longitudinal PsD cohort without a prior history of CVEs were included. In the first available serum sample, a targeted nuclear magnetic resonance (NMR) metabolomics platform was used to quantify 64 metabolite measures comprised of lipoprotein subclasses, fatty acids, glycolysis precursors, ketone bodies and amino acids. The study outcome included any of the following CVEs occurring within the first 10 years of biomarker assessment: angina, myocardial infarction, congestive heart failure, transient ischemic attack, cerebrovascular accident, revascularization procedures and CV death. The association of each metabolite with incident CVEs were analyzed separately using Cox proportional hazards regression models first adjusted for age and sex, and subsequently for traditional CV risk factors. Variable selection was performed using penalization with boosting after adjusting for age and sex. The added predictive value of the selected metabolites to improve risk prediction beyond traditional CV risk factors was assessed using the area under the receiver operator characteristic curve (AUC).

Results: A total of 977 patients with PsD, followed between 2002 and 2019, were analyzed (mean age 49.1 ± 12.6 years, 45.1% female). During a mean follow-up of 7.1 years, 70 (7.2%) patients developed incident CVEs. In Cox regression models adjusted for CV risk factors, alanine, tyrosine, total high-density lipoprotein (HDL) cholesterol, medium and large HDL particles, and the degree of unsaturation of fatty acids were significantly associated with decreased CV risk. Glycoprotein acetyls, apolipoprotein B, remnant cholesterol, very low-density lipoprotein (VLDL) cholesterol, and very small VLDL particles were associated with an increased CV risk. In proportional sub-distribution hazards regression models adjusted for age and sex, 13 metabolites were selected (Table 1). The age- and sex-adjusted expanded model (base model + 13 metabolites) significantly improved prediction of CVEs beyond the base model (only age and sex) with an AUC of 79.9 vs. 72.6, respectively (p=0.019) (Figure 1).

Table 1. Regression coefficients of the selected metabolites in a model adjusted for age and sex.

Category	Metabolite	Model adjusted for Age and Sex
Amino Acids	Alanine	-0.1179
	Glycine	-0.0339
	Tyrosine	-0.1010
Fatty acid ratios, relative to total fatty acids	Docosahexaenoic acid	-0.0862
	Unsaturation degree, double bonds per fatty acid	-0.1265
Fluid Balance	Albumin	+0.0685
Glycerides	Triglycerides in IDL cholesterol	+0.1546
Glycolysis precursors	Glucose	+0.1391
Inflammation	Glycoprotein acetyls	+0.1478
Ketone bodies	Acetoacetate	+0.0464
Lipoprotein subclasses	HDL_3 Cholesterol	-0.0211
	Medium HDL	-0.0296
	Large HDL	-0.0309

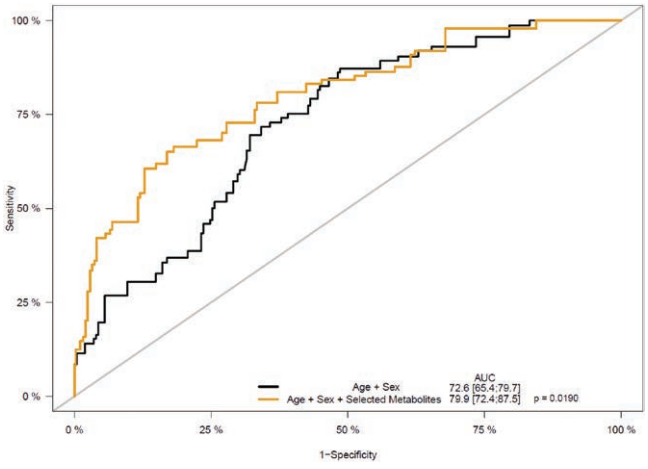


Figure 1. Predictive performance of a model with age and sex alone is compared to a model with age and sex plus selected metabolites.

Conclusion: Using NMR metabolomics profiling, we identified a variety of metabolites associated with a lower and higher risk of developing CVEs in patients with PsD. Further study of their underlying association with CVEs is needed to clarify the clinical utility of these biomarkers to guide CV risk assessment in this population.

REFERENCES:

[1] Eder L, Wu Y, Chandran V, et al. Incidence and predictors for cardiovascular events in patients with psoriatic arthritis. *Ann Rheum Dis* 2016;75(9):1680-6.

[2] Soininen P, Kangas AJ, Wurtz P, et al. Quantitative serum nuclear magnetic resonance metabolomics in cardiovascular epidemiology and genetics. *Circ Cardiovasc Genet* 2015;8(1):192-206.

Acknowledgements: Keith Colaco is supported by the Enid Walker Estate, Women's College Research Institute, Arthritis Society (TGP-19-0446), National Psoriasis Foundation (Early Career Grant) and the Edward Dunlop Foundation. Lihi Eder is supported by a Young Investigator Award from the Arthritis Society and an Early Researcher Award from the Ontario Ministry of Science and Innovation. The study was supported in part by a discovery grant from the National Psoriasis Foundation and an operating grant from the Arthritis Society (YIO-16-394).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1154

OP0222 THE INCIDENCE OF INTERSTITIAL LUNG DISEASE IN PSORIATIC ARTHRITIS COMPARED TO RHEUMATOID ARTHRITIS. DATA FROM OVER 89 000 BDMARD TREATMENT COURSES DERIVED FROM FIVE NORDIC REGISTERS

S. Aarrestad Provan[1], B. Michelsen[1], L. Ljung[2,3], T. Jonmundsson[4], B. Gudbjornsson[4], D. DI Giuseppe[5], M. L. Hetland[6,7], G. B. Reynisdóttir[4], B. Glintborg[6,7], E. Kristianslund[1], H. Relas[8], K. Aaltonen[9], D. Nordström[8], T. K. Kvien[1], J. Askling[5,10]. *[1]Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway*; *[2]Clinical Epidemiology Section, Karolinska Institutet, Medicine Solna, Stockholm, Sweden*; *[3]Stockholm Health Service, Center for Rheumatology, Academic Specialist Center, Stockholm, Sweden*; *[4]University Hospital, Rheumatology, Reykjavik, Iceland*; *[5]Clinical Epidemiology Section, Karolinska Institutet, Medicine Solna, Stockholm, Sweden*; *[6]University of Copenhagen, Department of Clinical Medicine, Faculty of Health and Medical Sciences, Copenhagen, Denmark*; *[7]Copenhagen Center for Arthritis Research, Rigshospitalet Glostrup, Center for Rheumatology and Spine Diseases, Copenhagen, Denmark*; *[8]ROB-FIN, Helsinki University Hospital and Helsinki University, Department of Medicine and Rheumatology, Helsinki, Finland*; *[9]Ministry of Social Affairs and Health, Pharmaceuticals Pricing Board, Helsinki, Finland*; *[10]Karolinska University Hospital, Rheumatology, Theme Inflammation and Infection, Stockholm, Sweden*

Background: Interstitial lung disease (ILD) is an established extra-articular manifestation of rheumatoid arthritis (RA). Few studies have investigated the prevalence of ILD in patients with psoriatic arthritis (PsA). Methotrexate (MTX) is frequently used in the treatment of both RA and PsA and has been suggested to be a risk factor for the development of ILD. It is of interest to understand the interaction between disease and treatment in the development of ILD.

Objectives: To compare the incidence of ILD between patient with PsA and RA treated with biologic disease modifying antirheumatic drugs (bDMARDS), with or without MTX as a co-medication.

Methods: Cohorts of patients with RA and PsA starting bDMARD were identified in Nordic registers (Danish nationwide clinical register for patients with RA (DANBIO), Register on antirheumatic and biological therapy in Finland (ROB-FIN), Icelandic nationwide database of biologic therapy (ICEBIO), Norwegian Antirheumatic Drug Register (*NOR-DMARD*), and the Swedish Rheumatology Quality Register (SRQ)). Linkages to the National Patient Registers and to the Cause of Death Registers were performed in each country to identify cases of ILD. Each individual patient could contribute several treatment courses. ILD was identified as hospital or death certificate ICD10 codes of ILD (J84.1, J84.8, J84.9, J70.2, J70.3, J70.4, J99.0, J99.1, J99.8) given during the follow-up period which was defined as the treatment course duration, plus a 30-day wash-out period added to the end of treatment course period. MTX co-medication was specified as use of MTX at the start of bDMARD. Incidence rates (IR) for any ILD were calculated per 1000 person years at risk (PYR) for each country. The five cohorts were pooled and incidence rate ratios (IRR) for PsA vs. RA were calculated. Hazard ratios (HR) for any ILD in PsA vs. RA were estimated in Cox regression models adjusted for age, gender and repeated observations, and stratified for the use of MTX co-medication.

Results: Overall 47 987 individual patients representing 89 239 bDMARD treatment courses and contributing 201 279 PYR were included in the study (Table 1). Methotrexate was reported as comedication in 29 916 (33.5 %) of the treatment courses (PsA vs. RA, 30.4 % vs 34.5 %). 970 cases of ILD were identified during the follow-up period. The risk of ILD was consistently lower in patients with PsA compared to patients with RA in all countries. In models stratified for co-medication the HR for ILD in PsA vs. RA was 0.34 (0.21-0.57) in patients treated with MTX and 0.26 (0.18-0.36) in patients not treated with MTX.

Table 1. Interstitial lung disease in PsA vs. RA in five Nordic biologic registers

	DENMARK		FINLAND		ICELAND		NORWAY		SWEDEN	
	RA	PsA	RA	PsA	RA	PsA	RA	PsA	RA	PsA
Number of individuals	7829	3386	4946	1091	675	470	1590	999	20596	6393
Number of treatment courses	17 072	6640	8634	1845	1280	859	2379	1427	38 279	10 824
Age baseline (SD)	57.3 (13.1)	49.0 (12.6)	53.8 (13.4)	48.8 (11.4)	53.9 (14.2)	50.1 (13.3)	53.8 (13.7)	48.7 (12.0)	57.1 (13.7)	50.6 (12.8)
Female n (%)	12 963 (76)	3929 (59)	6571 (76)	933 (51)	969 (76)	551 (65)	1815 (77)	818 (57)	29 635 (77)	6162 (57)
Number of PYR	40235	13986	21798	4910	4517	2799	4556	2653	120334	27412
ILD-events within PYR	218	22	132	8	7	2	32	6	680	28
IR pr 1000 PYR	5.4	1.6	6.1	1.6	1.5	0.7	7.0	2.3	5.7	1.0
IRR PsA vs RA crude	0.29 (0.18-0.45)		0.27 (0.11-0.55)		0.46 (0.05-2.42)		0.32 (0.11-0.78)		0.18 (0.12-0.26)	
HR PsA vs RA	0.31 (0.17-0.56)		0.46 (0.22-0.96)		0.62 (0.12-3.14)		0.19 (0.06-0.54)		0.25 (0.17-0.37)	

PYR: Patient years at risk, IR: Incidence rates, IRR: Incidence rate ratios, HR: Hazard Ratios

Conclusion: In these preliminary analyses, the incidence of ILD is lower in bDMARD treated PsA vs. RA patients, irrespective of co-medication with MTX. This indicates that the clinician should consider the rheumatological diagnosis when assessing the risk for future ILD in patients treated with bDMARDs and MTX.

Acknowledgements: Partly funded by NordForsk and FOREUM

Disclosure of Interests: Sella Aarrestad Provan Consultant of: Novartis, Grant/research support from: Boehringer-Ingelheim, Brigitte Michelsen: None declared, Lotta Ljung: None declared, Thorarinn Jonmundsson: None declared, Björn Gudbjornsson Speakers bureau: Amgen and Novartis, Daniela Di Giuseppe: None declared, Merete Lund Hetland Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck and Samsung Bioepis, Consultant of: Eli Lilly, Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen and Pfizer, Guðrún Björk Reynisdóttir: None declared, Bente Glintborg: None declared, Eirik kristianslund: None declared, Heikki Relas: None declared, Kalle Aaltonen: None declared, Dan Nordström Speakers bureau: Abbvie, BMS, Celgene, Eli Lilly, MSD, Novartis, Pfizer, Roche and UCB., Consultant of: Abbvie, BMS, Celgene, Eli Lilly, MSD, Novartis, Pfizer, Roche and UCB., Tore K. Kvien Speakers bureau: Amgen, Celltrion, Egis, Evapharma, Ewopharma, Hikma, Oktal, Sandoz, Sanofi., Consultant of: AbbVie, Amgren, Biogen, Celltrion, Eli Lilly, Gilead, Mylan, Novartis, Pfizer, Roche, Sandoz, Sanofi., Johan Askling Grant/research support from: Abbvie, BMS, Eli Lilly, Merck, Pfizer, Roche, Samsung Bioepis, and Sanofi

DOI: 10.1136/annrheumdis-2021-eular.2955

OP0223

DEVELOPMENT AND PRELIMINARY VALIDATION OF ULTRASONOGRAPHIC DISEASE ACTIVITY AND DAMAGE SCORES IN PSORIATIC ARTHRITIS PATIENTS: RESULTS FROM THE UPSTREAM (ULTRASOUND IN PSORIATIC ARTHRITIS TREATMENT) STUDY

A. Zabotti[1], M. Piga[2], A. Zanetti[3], M. Canzoni[4], N. Boffini[5], V. Picerno[6], G. Zanframundo[7], E. Silvagni[8], I. Giovannini[1], B. Raffeiner[9], P. Scolieri[10], P. Mancini[11], S. Parisi[12], A. Bortoluzzi[8], G. Sakellariou[13], O. De Lucia[14], I. Tinazzi[15], F. Figus[16], L. Idolazzi[17], M. Lorenzin[18], S. Z. Callegher[1], A. Cauli[19], G. Carrara[3], C. A. Scirè[3], A. Iagnocco[16], on behalf of The Musculoskeletal Ultrasound Study Group of the Italian Society of Rheumatology. *[1]University of Udine, Rheumatology Clinic, Santa Maria della Misericordia Hospital, Medical and Biological Sciences Department, Udine, Italy*; *[2]Rheumatology Unit, AOU and University of Cagliari, Department of Medical Sciences and Public Health, Monserrato, Italy*; *[3]Italian Society for Rheumatology, Epidemiology Research Unit, Milano, Italy*; *[4]Local Health Unit (ASL) Rome-1, Rome-4 and Viterbo, Rheumatologist Outpatient Specialist, Rome, Italy*; *[5]IRCCS Ospedale S. Raffaele, UNIRAR Department, Milano, Italy*; *[6]Azienda Ospedaliera San Carlo, Dipartimento internistico, Potenza, Italy*; *[7]Pavia, Department of Internal Medicine and Therapeutics, Pavia, Italy*; *[8]University of Ferrara, Department of Medical Sciences, Cona, Italy*; *[9]Central Hospital of Bolzano, Rheumatology Unit, Bolzano, Italy*; *[10]Ospedale Nuovo Regina Margherita, Dipartimento delle Specialità Mediche, Rome, Italy*; *[11]Ospedale S.Spirito e Nuovo Regina Margherita, U.O.C. Radiologia, Rome, Italy*; *[12]AOU Città della Salute e della Scienza di Torino, Rheumatology Unit, Turin, Italy*; *[13]Scientific Clinical Institutes Maugeri IRCCS, Department of General Medicine, Pavia, Italy*; *[14]ASST Centro Ortopedico Traumatologico G. Pini-CTO, Dipartimento di reumatologia e scienze mediche, Milano, Italy*; *[15]Ospedale Sacro Cuore di Negrar, UOS di Reumatologia, Negrar di Valpolicella, Italy*; *[16]Academic Rheumatology Centre, Dipartimento Scienze Cliniche e Biologiche, Turin, Italy*; *[17]University of Verona, Department of Medicine, Verona, Italy*; *[18]Padua, Department of Medicine DIMED, Padua, Italy*; *[19]Rheumatology Unit, Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy*

Background: The UPSTREAM (NCT03330769) is a 24-month multi-center prospective cohort study that primarily aims to evaluate the additional value of musculoskeletal ultrasound (msk-US) over clinical examination in predicting 6-month minimal disease activity in Psoriatic Arthritis (PsA). (1)

Objectives: To develop and preliminarily validate an activity msk-US score and a damage msk-US score for PsA using the UPSTREAM database.

Methods: Patients classified with PsA according to CASPAR criteria and starting a new course of therapy for clinically active peripheral joint disease were eligible. The information regarding objectives, study design, clinical and US assessment has already been published (1). The msk-US examination was performed in 42 joints, 36 tendons, 12 entheses and 2 bursae defined through a web-based exercise (2). The sonographic elementary lesions were allocated to disease activity [i.e. synovitis (sy), tenosynovitis (ts), peritendinitis (pt), bursitis (bs) all evaluated both in Grey Scale (GS) and Power Doppler (PD) and active enthesitis (en)] and to damage (i.e. joint erosion, bone proliferation, tendon tear, enthesophyte, calcification and irregular enthesis bone profile). Hands and feet X-ray were assessed using the modified Sharp-Van der Heijde (mSVH) score. A principal component (PC) analysis (PCA) was performed for each score and the number of PCs was defined by means of parallel analysis using baseline data. Each PC was normalized (n) taking into account the proportion between the observed value (e.g. sy-GS count) and the maximum expected value (e.g. 42 for sy-GS). Spearman' correlation was used to investigate the construct and discrimination validity of the new scores.

Results: Between February 2017 and May 2020, 312 PsA patients (155 men), with a mean (SD) age of 52.8 13.4, were enrolled from 19 centers; 22 expert sonographers were involved with substantial agreement for US lesions evaluated (k ≥0.7). The median [IQR] disease duration was 1.3 [0.1-6.1] years and the median [IQR] tender joint and swollen joint counts were 6 [3-13] and 2 [1-5], respectively. The weight derived from PCA for each sonographic lesions and the final equation for calculating the scores are reported in Figure 1 (1A activity and 1B damage). The final msk-US activity score **[n(ts-GS + ts-PD)*2.87] + [n(bs-GS + bs-PD)*1.76] + [n(pt-GS + pt-PD)*1.43] + [n(active en)*1.00] + [n(sy-GS)*0.83] + [n(sy-PD)*0.45]** has the best construct and discrimination validities according to a significant correlation with all clinical variables usually related to clinical activity (Table 1). The msk-US damage score correlated with mSVH score, HAQ and other clinical variables (Table 1).

Table 1.

	Msk-US activity score		Msk-US damage score	
Variables	*Spearman correlation*	*P-value*	*Spearman correlation*	*P-value*
ESR	0.196	0.002	0.075	0.235
CRP	0.209	<0.001	0.068	0.254
TJC	0.338	<0.001	0.286	<0.001
SJC	0.338	<0.001	0.072	0.221
Dactylitis count	0.284	<0.001	-0.061	0.306
LEI	0.194	0.001	0.214	<0.001
Physician GA	0.15	0.012	0.016	0.793
Patient GA activity	0.138	0.018	-0.073	0.221
Patient GA pain	0.199	0.001	-0.027	0.648
HAQ	0.238	<0.001	0.146	0.014
BASDAI	0.237	<0.001	0.175	0.003
PSAID-9	0.7	0.004	0.148	0.013
DAPSA	0.392	<0.001	0.228	<0.001
Sharp van Der Heijde score	0.115	0.2	0.266	0.003

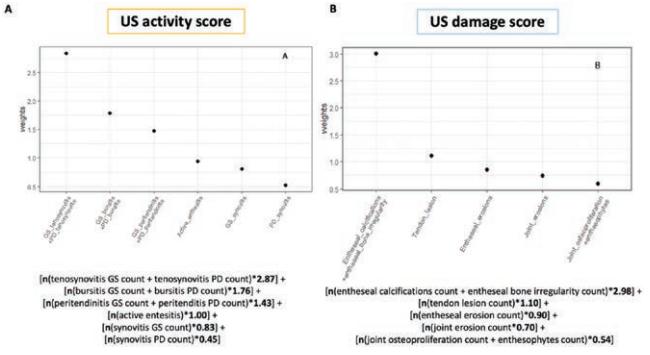


Figure 1.

Conclusion: These newly developed and preliminary validated msk-US activity and damage scores could be used in patients with PsA in the context of observational and controlled trials.

REFERENCES:

[1] Canzoni M et al. BMJ Open. 2018;8:e021942.
[2] Zabotti A et al. Ann Rheum Dis 2018;77:1537–1538.

Acknowledgements: Alberto Batticciotto; Oscar Massimiliano Epis; Luisa Arcarese; Luca Navarini; Marta Caprioli; Mirco Magnani; Roberta Ramonda; Marco Amedeo Cimmino

Disclosure of Interests: Alen Zabotti: None declared, Matteo Piga: None declared, Anna Zanetti: None declared, Marco Canzoni: None declared, nicola boffini: None declared, valentina picerno: None declared, Giovanni Zanframundo: None declared, Ettore Silvagni: None declared, Ivan Giovannini: None declared, BERND RAFFEINER: None declared, Palma Scolieri: None declared, Paola Mancini: None declared, Simone Parisi: None declared, Alessandra Bortoluzzi Grant/research support from: GSK, Garifallia Sakellariou Consultant of: Consultant for Abbvie and Novartis, Orazio De Lucia: None declared, Ilaria Tinazzi: None declared, Fabiana Figus: None declared, Luca Idolazzi Speakers bureau: Received grants as speaker for Eli Lilly, UCB, Celgene, MSD, Abbvie, Novartis, Paid instructor for: Paid instructor for UCB during Product specialist Meeting, Mariagrazia Lorenzin: None declared, Sara Zandonella Callegher: None declared, Alberto Cauli: None declared, Greta Carrara: None declared, Carlo Alberto Scirè: None declared, Annamaria Iagnocco: None declared

DOI: 10.1136/annrheumdis-2021-eular.2609

OP0224 CONTINUOUS COMPOSITE MEASURES FOR ROUTINE CARE IN PSORIATIC ARTHRITIS: THRESHOLDS OF MEANING AND CLINICALLY IMPORTANT DIFFERENCE ESTIMATES FOR THE 3 AND 4 VAS SCALES FROM A UK MULTICENTRE STUDY

W. Tillett[1,2], J. Day[1], N. Mchugh[2], O. Fitzgerald[3], L. C. Coates[4], P. Helliwell[5]. *[1]Royal National Hospital for Rheumatic Diseases, Rheumatology, Bath, United Kingdom*; *[2]University of Bath, Pharmacy and Pharmacology, Bath, United Kingdom*; *[3]University College Dublin, Conway Institute for Biomolecular Research, Dublin, Ireland*; *[4]University of Oxford, Nuffield Department of Orthopaedics, Oxford, United Kingdom*; *[5]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*

Background: There is a recognised need for a continuous composite measure of disease activity for the assessment of Psoriatic Arthritis (PsA) in routine clinical settings to allow objective assessment of response and implementation of treat to target.[1] Longer multidimensional measures are considered less feasible in routine care and a number of shorter measures have been proposed including, the Disease Activity Score for Psoriatic Arthritis (DAPSA), Disease Activity Score 28 (DAS28), the 3 Visual Analogue Scale (VAS) (comprising physician global VAS, patient global VAS and patient skin VAS) or 4 VAS (comprising physician global VAS, patient pain VAS, joint VAS and patient skin VAS). Testing of these measures in clinical trial datasets has been suggested but thresholds of meaning have not been established.[2]

Objectives: To estimate clinically relevant thresholds of disease activity and improvement for composite measures for routine clinical practice in PsA.

Methods: Clinical and patient reported outcome measures were assessed in patients fulfilling CASPAR criteria for PsA at three consecutive follow up visits in a UK multicentre observational study. Participants underwent clinical assessment and completed patient reported measures including health anchor questions. Estimates for Minimal Detectible Change (MDC) were derived using 1.96*2*Standard Error of the Mean (SEM). Minimal Clinically Important Difference (MCID) for improvement were derived using the health anchor method and two distribution methods (Table 1). Thresholds for low, moderate and high disease activity were triangulated from established cut-off values for the patient global VAS, PASDAS and DAPSA.

Table 1. Minimal Clinically Important Difference (MCID) and Minimal detectable change (MDC)

	ANCHOR (MEDIAN)	DISTRIBUTION#1	DISTRIBUTION #2	MDC
CPDAI	0.5	1.49	1.5	4.16
GRACE	0.26	0.6	0.77	2.18
PASDAS	1.22	0.64	0.76	1.58
DAS28	0.2	0.85	0.62	1.46
3VAS	1.13	1.16	0.91	3.12
4VAS	1.11	0.96	0.94	2.45
DAPSA	7.25	9.09	10.40	35.63

Disease Activity Score for Psoriatic Arthritis (DAPSA); Psoriatic Arthritis Disease Activity Score (PASDAS); Composite Psoriatic Arthritis Disease Activity Index (CPDAI); Disease Activity Score 28 (DAS28).Distribution #1: Baseline standard deviation (sd) * √ 1 – Cronbach's alphaDistribution #2: 0.5 * baseline sdMinimal detectable change (MDC): 1.96*2*SEM where SEM = baseline sd √1 - ICC

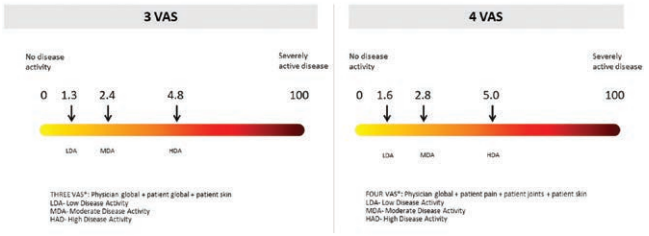
Results: 139 subjects were recruited (59 male, 80 female, mean (range) age (years) 52.7 (19 – 83), mean (range) duration of psoriasis (years) 21.9 (2 – 71), mean (range) duration of psoriatic arthritis (years) 6.1 (0 – 41). Cut-off values for low, moderate and high disease activity were 1.3, 2.4, and 4.8 for the 3 Vas and 1.6, 2.8 and 5.0 for the 4 VAS (Figure 1). Estimates for the MCID and MDC for the continuous composite measures and are reported in Table 1.

Conclusion: We report estimates of clinically relevant improvements for continuous composite measures in PsA and estimates of low, moderate and high disease activity for the 3 and 4 VAS scales. The thresholds of meaning can now be tested in independent observational and clinical trial datasets.

REFERENCES:

[1] Coates et al 2018 A&R Mar;70(3):345-355.
[2] Tillett W et al 2021 J Rheum In Press

Figure 1: Thresholds of Meaning for the 3 and 4 VAS



Acknowledgements Funding: This report is independent research funded by the National Institute for Health Research, Programme Grants for Applied Research [Early detection to improve outcome in patients with undiagnosed PsA ('PROMPT'), RP-PG-1212-20007]. The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

Disclosure of Interests: William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer, and UCB, Consultant of: AbbVie, BMS, Celgene, Lilly, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, BMS, Janssen, Novartis, Pfizer, and UCB., Julia Day: None declared, Neil McHugh: None declared, Oliver FitzGerald Speakers bureau: AbbVie, BMS, Celgene, Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, BMS, Celgene, Lilly, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, BMS, Janssen, Novartis, Pfizer, and UCB., Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Gilead, Eli Lilly, Janssen, Medac, Novartis, Pfizer, and UCB., Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Pfizer, and Novartis, Philip Helliwell: None declared

DOI: 10.1136/annrheumdis-2021-eular.1622

OP0225 DEPRESSIVE SYMPTOMS IN PSA: A CROSS-SECTIONAL ANALYSIS FROM THE NATIONAL GERMAN RABBIT-SPA REGISTRY

A. Regierer[1], A. Weiß[1], M. Bohl-Buehler[2], X. Baraliakos[3], F. Behrens[4], G. Schett[5], A. Strangfeld[1]. *[1]German Rheumatism Research Centre, Epidemiology Unit, Berlin, Germany*; *[2]Rheumatology Practice, Rheumatology, Potsdam, Germany*; *[3]Rheumazentrum Ruhrgebiet Herne, Ruhr-University, Bochum, Germany*; *[4]Goethe University, Rheumatology and Fraunhofer Institute Translational Medicine and Pharmacology ITMP, Frankfurt, Germany*; *[5]Friedrich Alexander University Erlangen-Nuremberg and Universitatsklinikum Erlangen, Department of Internal Medicine 3, Erlangen, Germany*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease affecting the musculoskeletal system as well as skin and nails. The prevalence of depression in psoriasis and PsA is high and ranges from 7-40% [1]. Persistent depressive mood may influence disease activity outcome in PsA, especially patient-reported outcomes.

Objectives: To assess the correlation of depressive symptoms with PsA-specific outcome parameters.

Methods: RABBIT-SpA is a prospective longitudinal cohort study including PsA patients enrolled at start of a new conventional treatment or b/tsDMARD treatment. In regularly provided follow-up questionnaires, physician- and patient-reported information on the disease course including the depression screening tool WHO-5 to assess mental health is collected. For the current analysis, the WHO-5 score was categorised into 4 groups using validated cut-offs: severe depressive symptoms <13, moderate depressive symptoms 13-28, mild depressive symptoms 29-50, well-being >50. Spearman correlation coefficient was calculated to analyse the relationship between the WHO-5 score and various PsA related outcome parameters.

Results: 936 PsA patients were included. Baseline characteristics are shown in Table 1. In 411 patients (43.9%) the WHO-5 score indicated well-being, 249

(26.6%) had mild depressive, 203 (21.7%) moderate depressive and 73 patients (7.8%) severe depressive symptoms. WHO-5 results correlated with patient reported skin involvement (DLQI: -0.25, patient assessment skin: -0.17), and the composite scores DAPSA (-0.33) and DAS28 (-0.28) as well as with patient reported pain (-0.43) and patient global disease assessment (-0.42). The highest correlation was found for physician assessed global health status (-0.51) and PSAID (-0.62). No significant correlation was found with CRP, swollen joint count and physician assessed skin involvement including body surface area (BSA).

Table 1. Baseline characteristics of patients included in the analysis stratified by WHO-5 categories.

Parameter	WHO-5 (<13) severe N=73	WHO-5 (13-28) moderate N=203	WHO-5 (29-50) mild N=249	WHO-5 (>50) well-being N=411	Total N=936
Age, mean (SD)	52.6 (11.4)	51 (11.3)	51.4 (12.5)	52.8 (12.7)	52 (12.2)
Female, n (%)	52 (71.2)	127 (62.6)	157 (63.1)	227 (55.2)	563 (60.1)
Disease duration, years, mean (SD)	8.3 (8.7)	6 (7.9)	6.2 (6.7)	6.4 (7.5)	6.4 (7.5)
Dactylitis, n (%)	14 (19.7)	31 (15.5)	46 (18.5)	77 (18.8)	168 (18.1)
Axial involvement, n (%)	14 (19.7)	54 (26.9)	49 (19.7)	71 (17.3)	188 (20.2)
Nail involvement, n (%)	34 (47.2)	85 (42.3)	106 (42.6)	158 (38.6)	383 (41.1)
BMI>=30, n (%)	37 (51.4)	75 (37.1)	98 (39.5)	125 (30.9)	335 (36.2)
CRP of >=5 mg/L, n (%)	33 (51.6)	84 (45.4)	99 (46.5)	138 (39.1)	354 (43.4)
BSA (0-100), mean (SD)	10.1 (18.3)	9.5 (16.8)	8.5 (14.9)	8.1 (14.6)	8.7 (15.5)
Physician assessed global health (NRS 0-10), mean (SD)	6.3 (1.5)	5.6 (1.8)	5.2 (1.7)	4.9 (1.9)	5.2 (1.9)
TJC68, mean (SD)	9.9 (7.1)	8.6 (7.6)	8.2 (7.6)	7.3 (8.2)	8 (7.8)
SJC66, mean (SD)	6 (5.2)	4.8 (4.9)	4.7 (4.4)	4.3 (3.8)	4.6 (4.4)
DAPSA, mean (SD)	29.3 (11.1)	25.1 (12.9)	23.4 (12.1)	18.9 (12.4)	22.3 (12.8)
DAS28-CRP, mean (SD)	4.1 (1)	3.8 (1.2)	3.7 (1.1)	3.2 (1.1)	3.6 (1.2)
Patient assessed global health (NRS 0-10), mean (SD)	7.9 (2.1)	6.6 (2.1)	5.9 (2)	4.8 (2.3)	5.7 (2.4)
Patient assessed pain (NRS 0-10), mean (SD)	7.8 (1.8)	6.4 (2.1)	5.8 (2)	4.6 (2.4)	5.5 (2.4)
DLQI (0-30), mean (SD)	8.5 (8.2)	7.8 (7.2)	5.4 (5.7)	4.1 (4.9)	5.6 (6.2)
PSAID (0-10), mean (SD)	6.9 (1.8)	5.5 (1.8)	4.4 (1.7)	3 (1.7)	4.2 (2.2)

Conclusion: The impact of depressive symptoms on outcome parameters used in rheumatology is increasingly being recognised. Interestingly, direct measures of inflammatory disease activity of joint and skin disease such as BSA, CRP, and swollen joint count were not correlated with depressive symptoms. The highest correlation was found for broader assessments like global health status and PSAID.

REFERENCES:

[1] Haugeberg et al. Arthritis research & Therapy, 2020, 22:198

Acknowledgements: RABBIT-SpA is supported by a joint, unconditional grant from AbbVie, Amgen, Biogen, Hexal, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, UCB and Viatris.

We thank all participating rheumatologists and patients.

Disclosure of Interests: Anne Regierer Grant/research support from: AbbVie, Amgen, Biogen, Hexal, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, UCB and Viatris., Anja Weiß Grant/research support from: AbbVie, Amgen, Biogen, Hexal, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, UCB and Viatris., Martin Bohl-Buehler: None declared, Xenofon Baraliakos: None declared, Frank Behrens: None declared, Georg Schett: None declared, Anja Strangfeld Grant/research support from: AbbVie, Amgen, Biogen, Hexal, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, UCB and Viatris.

DOI: 10.1136/annrheumdis-2021-eular.2130

Psoriatic arthritis - treatment

OP0226

TOWARDS DEVELOPMENT OF AN ULTRASOUND ENTHESITIS SCORE IN PSORIATIC ARTHRITIS: 24-WEEK RESULTS FROM THE PHASE III RANDOMISED ULTIMATE STUDY

M. A. D'agostino[1], P. G. Conaghan[2], C. Gaillez[3], M. Boers[4], E. Naredo[5], P. Carron[6], P. Hanova[7], T. Cazenave[8], C. Bakewell[9], A. M. Duggan[10], P. Goyanka[11], G. Schett[12]. *[1]Catholic University of Sacred Heart, UOC of Rheumatology, Agostino Gemelli University Polyclinic Foundation IRCCS, Roma, Italy*; *[2]University of Leeds, Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[3]Novartis Pharma AG, Global Medical Affairs, Basel, Switzerland*; *[4]Amsterdam Rheumatology and Immunology Centre, Amsterdam UMC, Vrije Universiteit, Department of Epidemiology and Data Science, Amsterdam, Netherlands*; *[5]Hospital Fundación Jiménez Díaz and Autónoma University, Department of Rheumatology and Joint and Bone Research Unit, Madrid, Spain*; *[6] VIB Inflammation Research Centre, Ghent University Hospital, Department of Rheumatology, Ghent, Belgium*; *[7]Charles University, Institute of Rheumatology and Department of Rheumatology, Prague, Czech Republic*; *[8]Instituto de Rehabilitacion Psicofisica, Rheumatology, Buenos Aires, Argentina*; *[9]Salt lake Clinic, Intermountain Healthcare Medical Group, Salt lake city, United States of America*; *[10]Novartis Ireland Limited, CTS Stats Analysis, Dublin, Iceland*; *[11]Novartis Healthcare Pvt Ltd, Clinical Project Management, Hyderabad, India*; *[12]Friedrich Alexander University of Erlangen-Nuremberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3, Erlangen, Germany*

Background: Enthesitis is a key clinical domain and imaging hallmark of psoriatic arthritis (PsA). Ultrasound (US) is a highly sensitive tool for detecting synovitis and enthesitis in PsA. The Outcome Measures in Rheumatology Initiative (OMERACT) has developed an US definition and scoring system of enthesitis for clinical studies.[1] The ULTIMATE study (NCT02662985) is the first large double-blind (DB), placebo-controlled phase IIIb study designed to demonstrate a rapid and significant benefit of subcutaneous secukinumab vs. placebo on US detected synovitis in patients with PsA.[2]

Objectives: To report the enthesitis response to secukinumab over 24 weeks using two novel US composite enthesitis scores.

Methods: This was a 52-week study consisting of a 12-week DB, a 12-week open-label (OL) and a 6-month extension period.[2] Inclusion criteria required ≥1 clinical enthesitis as per SPARCC enthesitis index, but not US-assessed enthesitis.[2] Patients were randomised (1:1) to either weekly secukinumab (300 or 150 mg according to severity of skin psoriasis) or placebo followed by 4-weekly dosing thereafter. All placebo patients switched to OL secukinumab (placebo-secukinumab) at Week 12. Throughout the study, enthesitis was assessed with SPARCC and US. Six anatomical sites were assessed bilaterally with US: insertions of lateral epicondyle tendons, quadriceps, patellar ligaments (distal and proximal insertions), Achilles tendons and plantar fascia. Two exploratory global OMERACT-US enthesitis scores were tested: Definition 1 combining power Doppler (PD; 0–3) and Grey Scale (0–1) inflammation and Definition 2 rating PD only (0–3) across the six anatomical sites. Data were analysed with mixed-effect model repeated measures (MMRM) up to Week 12 and as observed from Week 12 to 24. The comparison of OMERACT-US enthesitis score within treatment groups was tested with paired and between treatment groups with unpaired t-tests.

Results: Of 166 patients enrolled, 93% completed 24 weeks of treatment (secukinumab, 95%; placebo-secukinumab, 92%). The average clinical enthesitis count at baseline was 4. Since the presence of PD was not a mandatory inclusion criterion, a higher proportion of patients met Global OMERACT-US enthesitis score with Definition 1 vs. Definition 2 (81% vs. 33%) at baseline (Table). Mean reduction from baseline to Week 24 in SPARCC enthesitis index was 3 each for initial secukinumab and placebo-secukinumab groups. Resolution of enthesitis (SPARCC) was 46% for initial secukinumab and 54% for placebo-secukinumab groups at Week 24. A comparable decrease in OMERACT-US enthesitis (Definition 1 and 2) score was observed from baseline to Week 24 for initial secukinumab and placebo-secukinumab groups (Figure).

Table 1. Distribution of US detected enthesitis at baseline according to OMERACT enthesitis score Definition 1 and 2

	Secukinumab		Placebo	
	Def 1 >0	Def 2 >0	Def 1 >0	Def 2 >0
N=	73	34	61	20
Anatomical sites, %				
Achilles tendon	49	12	45	2
Lateral epicondyle	49	21	46	21
Patellar ligament distal insertion	34	8	29	4
Patellar ligament proximal insertion	34	10	18	4
Plantar fascia	36	0	28	0
Quadriceps insertion	55	12	40	2

Proportion of patients is irrespective of the enthesitis site left or right side. N, total number of patients

Conclusion: A consistent clinical and US response on enthesitis was shown through 24 weeks across initial secukinumab and placebo switcher groups. While ULTIMATE has demonstrated the responsiveness of these global OMERACT-US enthesitis scores, further work is required to test these scores in PsA cohorts with inclusion criteria for both clinical and US enthesitis.

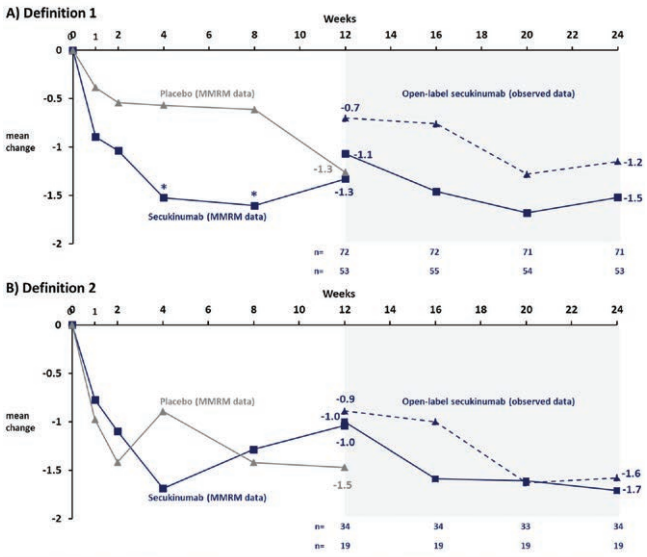
REFERENCES:

[1] Balint PV, et al. *Ann Rheum Dis*. 2018;77:1730-5.

[2] D'Agostino MA, et al. *Arthritis Rheumatol*. 2020;72(suppl 10).

Disclosure of Interests: Maria-Antonietta D'Agostino Speakers bureau: Sanofi, Novartis, BMS, Janssen, Celgene, AbbVie, UCB pharma and Eli Lilly, Consultant of: Sanofi, Novartis, BMS, Janssen, Celgene, AbbVie, UCB pharma and Eli Lilly, Philip G Conaghan Speakers bureau: AbbVie, AstraZeneca, BMS, Eli Lilly, Galapagos, Gilead, Novartis and Pfizer, Consultant of: AbbVie, AstraZeneca, BMS, Eli Lilly, Galapagos, Gilead, Novartis and Pfizer, Corine Gaillez Shareholder of: Novartis and BMS, Employee of: Novartis, Maarten Boers Consultant of: BMS, Novartis, Pfizer, and GSK, Esperanza Naredo Speakers bureau: AbbVie, Roche, BMS, Pfizer, UCB, Eli Lilly, Novartis, Janssen and Celgene, Consultant of: AbbVie, Novartis and BMS, Grant/research support from: Eli Lilly, Philippe Carron Speakers bureau: Pfizer, MSD, Novartis, BMS, AbbVie, UCB, Eli Lilly, Gilead and Celgene, Consultant of: Pfizer, MSD, Novartis, BMS, AbbVie, UCB, Eli Lilly, Gilead and Celgene, Grant/research support from: UCB, MSD and Pfizer, Petra Hanova: None declared, Tomás Cazenave: None declared, Catherine Bakewell Speakers bureau: AbbVie, Novartis, Sanofi Genzyme, and consulting honoraria from Pfizer, UCB, and Janssen, Consultant of: AbbVie, Novartis, Sanofi Genzyme, and consulting honoraria from Pfizer, UCB, and Janssen, Anne-Marie Duggan Employee of: Novartis, Punit Goyanka Employee of: Novartis, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Gilead, Janssen, Eli Lilly, Novartis, Roche and UCB pharma

Figure: Global OMERACT-US enthesitis score change from baseline to Week 12 and from Week 12 to 24



*P < 0.05. **Definition 1:** MMRM difference (SE) at Week 12: -0.1 (0.5); 95% CI: (-1.0, 0.8); *P*=0.44. Within treatment group from Week 12 to 24: NS for both initial secukinumab and placebo-secukinumab groups. Between treatment groups from baseline to Week 24: -0.4; 95% CI: (-1.5, 0.7); *P*=0.50; NS. **Definition 2:** MMRM difference (SE) at Week 12: 0.4 (0.7); 95% CI: (-0.9, 1.8); *P*=0.26. Within treatment group from Week 12 to 24: -0.7; 95% CI: (-1.3, -0.2); *P*=0.02 for initial secukinumab group and NS for placebo-secukinumab group. Between treatment groups from baseline to Week 24: -0.1; 95% CI: (-1.5, 1.2); *P*=0.85; NS. n, number of evaluable patients; NS, non-significant

DOI: 10.1136/annrheumdis-2021-eular.1702

OP0227

EFFICACY OF DEUCRAVACITINIB, AN ORAL, SELECTIVE TYROSINE KINASE 2 INHIBITOR, IN MUSCULOSKELETAL MANIFESTATIONS OF ACTIVE PSORIATIC ARTHRITIS IN A PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

P. J. Mease[1], A. Deodhar[2], D. Van der Heijde[3], F. Behrens[4], A. Kivitz[5], T. Lehman[6], L. Wei[7], M. Nys[8], S. Banerjee[9], M. Nowak[10]. [1]*Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America*; [2]*Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America*; [3]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [4]*CIRI/Rheumatology and Fraunhofer Institute, Goethe University, Translational Medicine and Pharmacology ITMP, Frankfurt, United States of America*; [5]*Altoona Center for Clinical Research, Department of Rheumatology, Duncansville, United States of America*; [6]*Bristol Myers Squibb, Rheumatology, Princeton, United States of America*; [7]*Bristol Myers Squibb, Medical Immunology, Princeton, United States of America*; [8]*Bristol Myers Squibb, GBS Biostatistics, Braine-l'Alleud, Belgium*; [9]*Bristol Myers Squibb, Rheumatology and Dermatology, Princeton, United States of America*; [10]*Bristol Myers Squibb, Clinical R&D, Princeton, United States of America*

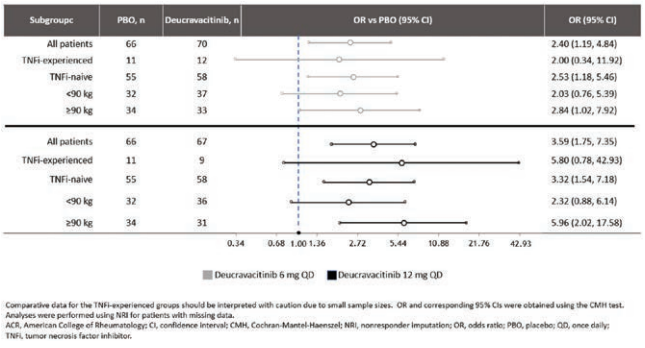
Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates IL-23, IL-12, and IFNα/β signaling. Deucravacitinib is a novel, oral selective inhibitor of TYK2 acting via the TYK2 regulatory domain. Phase 2 results showed deucravacitinib was efficacious and well tolerated versus placebo (PBO) in patients with active psoriatic arthritis (PsA).

Objectives: This analysis further evaluated improvements in musculoskeletal disease manifestations in patients in the Phase 2 PsA trial.

Methods: The ongoing Phase 2 trial (NCT03881059) enrolled patients who had a PsA diagnosis for ≥6 months, met CASPAR criteria, had active disease (≥3 tender joints, ≥3 swollen joints, C-reactive protein [CRP] ≥3 mg/L), and had at least 1 active skin lesion. Patients either failed or were intolerant to at least 1 nonsteroidal anti-inflammatory drug, corticosteroid, conventional synthetic disease-modifying antirheumatic drug, and/or 1 TNF inhibitor (TNFi; ≤30%). Patients were randomized 1:1:1 to deucravacitinib 6 mg QD or 12 mg QD or PBO, and stratified by TNFi status (experienced vs naive) and body weight (<90 vs ≥90 kg). The primary endpoint, ACR20 response at Week 16, was met and significant improvements in enthesitis vs PBO were observed. The current prespecified subgroup analysis assessed the likelihood of achieving ACR20 response at Week 16 based on study stratification factors. A post hoc analysis evaluated mean change from baseline to Week 16 in ACR components (tender joint count, swollen joint count, Physician's Global Assessment of PsA, Patients' Global Assessment of disease activity, Patients' Global Assessment of pain, high-sensitivity CRP [hCRP], and HAQ-DI score). Analyses were descriptive using data as observed.

Results: Patients treated with deucravacitinib were numerically more likely to achieve ACR20 response at Week 16 compared with PBO-treated patients regardless of TNFi experience or body weight, although some of these groups were small (Figure). Improvements for deucravacitinib 6 mg and 12 mg QD versus PBO were observed in all ACR components, with apparent separation occurring as early as Week 4 on, for example, HAQ-DI (mean change from baseline, -0.2 vs -0.2 vs -0.1, respectively) and hCRP (mean change from baseline, -7.4 vs -5.2 vs 0.3, respectively) and maintained through Week 16 (Table).

Figure. ACR20 subgroup analysis at Week 16



Comparative data for the TNFi-experienced groups should be interpreted with caution due to small sample sizes. OR and corresponding 95% CIs were obtained using the CMH test. Analyses were performed using NRI for patients with missing data.
ACR, American College of Rheumatology; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; NRI, nonresponder imputation; OR, odds ratio; PBO, placebo; QD, once daily; TNFi, tumor necrosis factor inhibitor.

Table 1. Mean (SD) change from baseline for ACR components

	TJC	SJC	PtGA	Pain	PGA	HAQ-DI	hCRP
Baseline[a]							
PBO	16.9 (9.8)	10.5 (7.7)	66.2 (15.8)	64.9 (18.2)	63.8 (14.8)	1.3 (0.6)	20.4 (39.1)
DEUC 6	18.1 (10.3)	11.9 (7.0)	68.2 (16.8)	63.6 (21.7)	68.2 (14.7)	1.3 (0.6)	17.6 (23.6)
DEUC12	19.4 (11.8)	11.3 (9.0)	63.6 (15.6)	63.8 (15.9)	63.3 (16.1)	1.3 (0.6)	16.5 (21.7)
Week 16[b]							
PBO	-4.6 (9.7)	-4.3 (8.0)	-13.4 (23.5)	-13.8 (21.5)	-19.9 (21.8)	-0.1 (0.4)	-3.3 (22.6)
DEUC 6	-9.3 (9.7)	-7.7 (5.8)	-28.7 (23.1)	-25.3 (26.1)	-33.6 (23.0)	-0.4 (0.5)	-14.2 (24.5)
DEUC 12	-12.2 (10.2)	-8.5 (9.1)	-27.6 (25.8)	-27.5 (25.0)	-32.2 (25.0)	-0.4 (0.6)	-10.9 (22.8)

PBO, n/N=58/66; DEUC 6, n/N=63/70; DEUC 12, n/N=59/67; n/N = number of patients who completed treatment/number of patients randomized; the number of patients with data available for individual components at each time point may vary.[a]Mean (SD). [b]Mean (SD) change from baseline.ACR, American College of Rheumatology; DEUC 6, deucravacitinib 6 mg QD; DEUC 12, deucravacitinib 12 mg QD; HAQ-DI, Health Assessment Questionnaire-Disability Index total score; hCRP, high-sensitivity C-reactive protein; PBO, placebo; PGA, Physician's Global Assessment of psoriatic arthritis; PtGA, Patients' Global Assessment of disease activity; QD, once daily; SJC, swollen joint count; TJC, tender joint count.

Conclusion: Analyses confirmed the efficacy of deucravacitinib versus PBO across TNFi and body weight subgroups. With deucravacitinib treatment, improvements were displayed in all ACR components.

Acknowledgements: This study was sponsored by Bristol Myers Squibb. Professional medical writing assistance was provided by Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

Disclosure of Interests: Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB, Atul Deodhar Consultant of: AbbVie, Amgen, Boehringer

Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer, UCB, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma. Director of Imaging Rheumatology BV, Frank Behrens Consultant of: Pfizer, AbbVie, Sanofi, Lilly, Novartis, Genzyme, Boehringer, Janssen, MSD, Celgene, Roche, Chugai, Bristol Myers Squibb, UCB Pharma, Grant/research support from: Pfizer, Janssen, Chugai, Celgene, Roche, Alan Kivitz Shareholder of: Pfizer, Sanofi, GlaxoSmithKline, Gilead Sciences, Inc., Novartis; Paid consultant: AbbVie, Boehringer Ingelheim, Flexion, Janssen, Pfizer, Sanofi, Regeneron, SUN Pharma Advanced Research, Gilead Sciences, Inc, Speakers bureau: Amgen, Horizon, Lilly, Novartis, Pfizer, Sanofi, Genzyme, Flexion, AbbVie, Thomas Lehman Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Lan Wei Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Marleen Nys Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Subhashis Banerjee Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Miroslawa Nowak Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.2653

OP0228

EFFICACY AND SAFETY OF RISANKIZUMAB FOR ACTIVE PSORIATIC ARTHRITIS, INCLUDING PATIENTS WITH INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGIC THERAPIES: 24-WEEK RESULTS FROM THE PHASE 3, RANDOMIZED, DOUBLE-BLIND, KEEPSAKE 2 TRIAL

A. Ostor[1], F. Van den Bosch[2], K. Papp[3], C. Asnal[4], R. Blanco[5], J. Aelion[6], G. Alperovich[7], Y. Zhang[8], Z. Wang[8], A. M. Soliman[8], A. Eldred[8], A. Kivitz[9]. *[1]Monash University, Cabrini Hospital, and Emertius Research, Melbourne, Australia*; *[2]Ghent University, Department of Rheumatology, Gent, Belgium*; *[3]Probity Medical Research, K. Papp Clinical Research, Waterloo, Canada*; *[4]Buenos Aires, DOM Centro de Reumatología, Buenos Aires, Argentina*; *[5]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain*; *[6]West Tennessee Research Institute, Not Applicable, Jackson, United States of America*; *[7]AbbVie, Inc, Not Applicable, Madrid, Spain*; *[8]AbbVie, Inc, Not Applicable, North Chicago, United States of America*; *[9]Altoona Center for Clinical Research, Not Applicable, Duncansville, United States of America*

Background: Risankizumab (RZB) is a humanized immunoglobin G1 monoclonal antibody that specifically inhibits interleukin 23 by binding its p19 subunit. RZB is being investigated as a treatment for adults with psoriatic arthritis (PsA).
Objectives: To compare the efficacy and safety of RZB vs placebo (PBO) for the treatment of active PsA in patients who have had inadequate response or intolerance to 1 or 2 biologic therapies (Bio-IR) or to ≥ 1 conventional synthetic disease modifying antirheumatic drug (csDMARD-IR).
Methods: KEEPsAKE 2 (NCT03671148) enrolled adults with active PsA (≥ 5 swollen joints [SJC] and ≥ 5 tender joints [TJC]) who were Bio-IR or csDMARD-IR. Patients were randomized to receive blinded subcutaneous RZB 150 mg or PBO at weeks 0, 4, and 16. The primary endpoint was the proportion of patients achieving ≥ 20% improvement in American College of Rheumatology score (ACR20) at week 24. Ranked secondary endpoints and other secondary endpoints are shown in the Table. Safety was assessed throughout the study. Results reported here are from the 24-week double-blind period; the open-label period with all patients receiving RZB is ongoing.
Results: A total of 443 patients (RZB, N = 224; PBO, N = 219) were included in the analysis. Demographics and baseline disease characteristics were similar across treatment arms (mean SJC: 13.3; mean TJC: 22.6; mean duration of PsA: 8.2 years; mean body surface area involved with psoriasis [BSA] in patients with BSA ≥ 3%: 12.1%); 206 patients (46.5%) were Bio-IR. Significantly greater proportions of RZB-treated patients vs PBO-treated patients achieved the primary endpoint (51.3% vs 26.5%, respectively; $P < .001$) and all ranked secondary endpoints ($P < .001$ for all except for Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-Fatigue; $P < .009$]; Table). Other secondary outcomes also showed improvement for RZB- vs PBO-treated patients (Table). Serious adverse events were reported for 4.0% and 5.5% of RZB- and PBO-treated patients, respectively; serious infections were reported for 0.9% and 2.3%.
Conclusion: RZB resulted in significantly greater improvements in signs and symptoms of PsA compared with PBO and was well tolerated in patients who were Bio-IR or csDMARD-IR.

Table. Efficacy Results

	RZB 150 mg N = 224	PBO N = 219	Difference (95% CI)	*P* value[a]
Primary endpoint				
ACR20, %	51.3	26.5	24.5 (15.9, 33.0)	< .001***
Ranked secondary endpoints				
HAQ-DI score, change	−0.22	−0.05	−0.16 (−0.26, −0.07)	< .001***
PASI 90,[a] %	55.0	10.2	44.3 (33.9, 54.6)	< .001***
ACR20 at week 16, %	48.3	25.3	22.6 (13.9, 31.2)	< .001***
MDA, %	25.6	11.4	14.0 (7.0, 21.0)	< .001***
SF-36 PCS score, change	5.9	2.0	3.9 (2.4, 5.3)	< .001***
FACIT-Fatigue score, change	4.9	2.6	2.2 (0.6, 3.9)	.009**
Other secondary endpoints				
ACR50, %	26.3	9.3	16.6 (9.7, 23.6)	< .001†
ACR70, %	12.0	5.9	6.0 (0.8, 11.3)	.024†
Resolution of enthesitis,[a] %	42.9	30.4	13.8 (3.5, 24.2)	.009†
Resolution of dactylitis,[a] %	72.5	42.1	38.8 (22.9, 54.8)	< .001†

ACR20/ACR50/ACR70, ≥ 20/50/70% improvement in American College of Rheumatology score; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; PASI 90, ≥ 90% reduction in Psoriasis Area Severity Index; PBO, placebo; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary.
All endpoints assessed at week 24 unless otherwise noted. All changes are mean changes from baseline.
***: statistically significant at 0.001 level, multiplicity controlled.
**: Statistically significant at 0.01 level; multiplicity controlled.
†: Nominal *P* value.
[a]For patients with involved body surface area ≥ 3% (PASI 90; RZB N = 123; PBO N = 119), enthesitis (RZB N = 147; PBO N = 158), or dactylitis (RZB N = 40; PBO N = 57) at baseline.

Disclosure of Interests: Andrew Ostor Speakers bureau: AÖ has received speaker or consulting fees and/or research grants from AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB., Consultant of: AÖ has received speaker or consulting fees and/or research grants from AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB., Grant/research support from: AÖ has received speaker or consulting fees and/or research grants from AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB., Filip van den Bosch Speakers bureau: FVdB has received speaker and/or consulting fees from Abbvie, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB., Consultant of: FVdB has received speaker and/or consulting fees from Abbvie, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB., Kim Papp Speakers bureau: KP has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant, as well as grants as principal investigator from AbbVie, Amgen, Astellas, Bausch Health (Valeant), Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO Pharma, Lilly, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB., Consultant of: KP has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant, as well as grants as principal investigator from AbbVie, Amgen, Astellas, Bausch Health (Valeant), Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO Pharma, Lilly, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB., Grant/research support from: KP has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant, as well as grants as principal investigator from AbbVie, Amgen, Astellas, Bausch Health (Valeant), Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO Pharma, Lilly, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB., CECILIA ASNAL Speakers bureau: CA has received honoraria or fees for serving on advisory boards or as a speaker, as well as research support from AbbVie, Genentech, Janssen, Lilly, Pfizer, and Roche., Grant/research support from: CA has received honoraria or fees for serving on advisory boards or as a speaker, as well as research support from AbbVie, Genentech, Janssen, Lilly, Pfizer, and Roche., Ricardo Blanco Speakers bureau: RB has received grants or research support from AbbVie, Merck, and Roche; and has received consultation fees or honoraria for serving as a speaker for AbbVie, Bristol-Myers Squibb, Janssen, Lilly, Merck, Pfizer, and Roche., Consultant of: RB has received grants or research support from AbbVie, Merck, and Roche; and has received consultation fees or honoraria for serving as a speaker for AbbVie, Bristol-Myers Squibb, Janssen, Lilly, Merck, Pfizer, and Roche., Grant/

research support from: RB has received grants or research support from AbbVie, Merck, and Roche; and has received consultation fees or honoraria for serving as a speaker for AbbVie, Bristol-Myers Squibb, Janssen, Lilly, Merck, Pfizer, and Roche., Jacob Aelion Grant/research support from: JA has received grants or research support from AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Galapagos/Gilead, Genentech, GlaxoSmithKline, Lilly, Mallinckrodt, Nektar Therapeutics, Nichi-Iko, Novartis, Pfizer, Regeneron, Roche, Sanofi, Selecta Biosciences, and UCB., Gabriela Alperovich Shareholder of: GA is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Employee of: GA is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Ying Zhang Shareholder of: YZ is a former AbbVie employee, and may hold AbbVie stock or stock options., Employee of: YZ is a former AbbVie employee, and may hold AbbVie stock or stock options., Zailong Wang Shareholder of: ZW is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Employee of: ZW is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Ahmed M. Soliman Shareholder of: AS is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Employee of: AS is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Ann Eldred Shareholder of: AE is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Employee of: AE is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Alan Kivitz Shareholder of: AK is a shareholder of or has received honoraria or fees as a consultant, speaker, or expert witness for AbbVie, Boehringer Ingelheim, Celgene, Flexion, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB., Speakers bureau: AK is a shareholder of or has received honoraria or fees as a consultant, speaker, or expert witness for AbbVie, Boehringer Ingelheim, Celgene, Flexion, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB., Consultant of: AK is a shareholder of or has received honoraria or fees as a consultant, speaker, or expert witness for AbbVie, Boehringer Ingelheim, Celgene, Flexion, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2695

OP0229

THE GROUP FOR RESEARCH AND ASSESSMENT OF PSORIASIS AND PSORIATIC ARTHRITIS (GRAPPA) TREATMENT RECOMMENDATIONS 2021

L. C. Coates[1], E. Soriano[2], N. Corp[3], H. Bertheussen[4], K. Callis-Duffin[5], C. Barbosa Campanholo[6], J. Chau[7], L. Eder[8], D. Fernandez[9], O. Fitzgerald[10], A. Garg[11], D. D. Gladman[12], N. Goel[13,14], S. Grieb[15], P. Helliwell[16], M. E. Husni[17], D. Jadon[18], A. Katz[19], D. Laheru[20], J. Latella[21], Y. Y. Leung[22], C. Lindsay[23], E. Lubrano[24], L. Mazzuoccolo[25], R. Mcdonald[26], P. J. Mease[27,28], D. O'sullivan[29], A. Ogdie[30], W. Olsder[31], L. Schick[15], I. Steinkoenig[32], M. De Wit[33], D. Van der Windt[34], A. Kavanaugh[35]. *[1]University of Oxford, NDORMS, Oxford, United Kingdom*; *[2]Hospital Italiano de Buenos Aires, Rheumatology, Buenos Aires, Argentina*; *[3]Keele University, School of Primary, Community and Social Care, Keele, United Kingdom*; *[4]GRAPPA, Patient Research Partner, Oslo, Norway*; *[5]University of Utah, Dermatology, Salt Lake City, United States of America*; *[6]Santa Casa de Sao Paulo, Rheumatology, Sao Paulo, Brazil*; *[7]GRAPPA, Patient Research Partner, Hong Kong, Hong Kong (SAR)*; *[8]University of Toronto, Rheumatology, Toronto, Canada*; *[9]Hospital Universitario San Ignacio, Rheumatology, Bogota, Colombia*; *[10]University College Dublin, Rheumatology, Dublin, Ireland*; *[11]Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Dermatology, Hempstead, United States of America*; *[12]Toronto Western Hospital, Schroeder Arthritis Institute, Toronto, Canada*; *[13]GRAPPA, Patient Research Partner, Durham, United States of America*; *[14]Duke University, Rheumatology, Durham, United States of America*; *[15]GRAPPA, Patient Research Partner, Seattle, United States of America*; *[16]University of Leeds, Leeds Institute of Rheumatology and Musculoskeletal Medicine, Leeds, United Kingdom*; *[17]Cleveland Clinic Main Campus, Rheumatology, Cleveland, United States of America*; *[18]University of Cambridge, Rheumatology, Cambridge, United Kingdom*; *[19]GRAPPA, Patient Research Partner, Haifa, Israel*; *[20]Churchill Hospital, Dermatology, Oxford, United Kingdom*; *[21]GRAPPA, Patient Research Partner, Connecticut, United States of America*; *[22]Singapore General Hospital, Rheumatology, Singapore, Singapore*; *[23]GRAPPA, Patient Research Partner, Propser, United States of America*; *[24]University of Molise, Rheumatology, Campobasso, Italy*; *[25]Hospital Italiano de Buenos Aires, Dermatology, Buenos Aires, Argentina*; *[26]GRAPPA, Patient Research Partner, Toronto, Canada*; *[27]Swedish Medical Center, Rheumatology, Seattle, United States of America*; *[28]University of Washington, Rheumatology, Seattle, United States of America*; *[29]GRAPPA, Patient Research Partner, Dublin, Ireland*; *[30]University of Pennsylvania, Rheumatology, Philadelphia, United States of America*; *[31]GRAPPA, Patient Research Partner, Eindhoven, Netherlands*; *[32]GRAPPA, Patient Research Partner, Cleveland, United States of America*; *[33]GRAPPA, Patient Research Partner, Amsterdam, Netherlands*; *[34]Keele University, School of Primary Community and Social Care, Keele, United Kingdom*; *[35]University of California San Diego, Rheumatology, La Jolla, United States of America*

Background: Since the 2015 GRAPPA treatment recommendations were published, therapeutic options and management strategies for psoriatic arthritis (PsA) have advanced considerably.

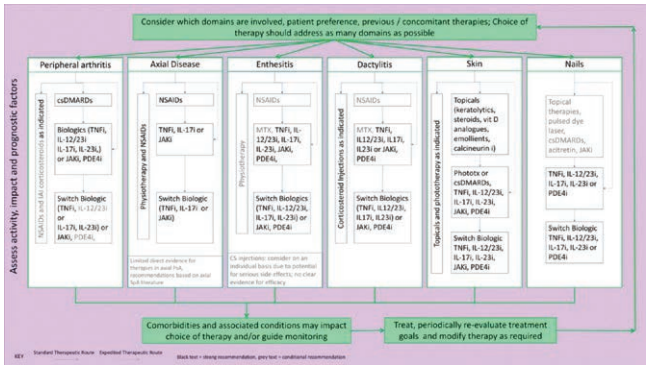
Objectives: The goal of the GRAPPA recommendations update is to develop high quality, evidence-based recommendations for the treatment of PsA, including related conditions and comorbidities.

Methods: GRAPPA rheumatologists, dermatologists and patient research partners (PRPs) updated overarching principles for the management of adults with PsA by consensus. Principles considering use of biosimilars and tapering/discontinuing of therapy were added to this update. Systematic literature searches based on data publicly available from three databases (MEDLINE, EMBASE, and Cochrane CENTRAL) were conducted from the end of the previous recommendations' searches through August 2020. Additional abstract searches were performed for conference presentations in 2017-2020. Searches covered PsA treatments (peripheral arthritis, axial arthritis, enthesitis, dactylitis, skin, and nail disease). Additional searches were performed for related conditions (uveitis and IBD) and comorbidities evaluating their impact on safety and treatment outcomes. Individual groups assessed the risk of bias and applied the GRADE system to generate strong or conditional recommendations for therapies within the domain groups and for the management of comorbidities and related conditions. These recommendations were then incorporated into an overall treatment schema.

Results: Updated, evidence-based treatment recommendations are shown (Table 1). Since 2015, many new medications have been incorporated. Additional results for older medications, such as methotrexate, have been published across PsA domains. Based on the evidence, the treatment recommendations developed by individual groups were incorporated into the overall schema including principles for management of arthritis, spondylitis, enthesitis, dactylitis, skin, and nail disease in PsA, and associated conditions (Figure 1). Choice of therapy for an individual should ideally address all of the domains that impact on that patient, supporting shared decision making with the patient involved. Additional consideration in the recommendations was given to key associated conditions and comorbidities as these often impact on therapy choice.

Conclusion: These GRAPPA treatment recommendations provide up to date, evidence-based guidance to providers who manage and treat adult patients with PsA. These recommendations are based on domain-based strategy for PsA and supplemented by overarching principles developed by consensus of GRAPPA members.

Indication	Strong For	Conditional For	Conditional Against	Strong Against	Insufficient evidence
Peripheral Arthritis DMARD Naïve	csDMARDs, TNFi, PDE4i, IL-12/23i, IL-17i, IL-23i, JAKi	NSAIDs, oral CS, IA CS,	IL-6i,		
Peripheral Arthritis DMARD IR	TNFi, IL-12/23i, IL-17i, IL-23i, JAKi	PDE4i, other csDMARD, NSAIDs, oral CS, IA CS,	IL-6i,		
Peripheral Arthritis bDMARD IR	TNFi, IL-17i, IL-23i, JAKi,	NSAIDs, oral CS, IA CS, IL-12/23i, PDE4i, CTLA-4-Ig	IL-6i,		
Axial arthritis, Biologic Naïve	NSAIDs, Physiotherapy, simple analgesia, TNFi, IL-17i, JAKi	CS SIJ injections, bisphosphonates		cs DMARDs, IL-6i,	IL-12/23i, IL-23i
Axial PsA, Biologic IR	NSAIDs, Physiotherapy, simple analgesia, TNFi, IL-17i, JAKi			csDMARDs, IL-6i,	IL-12/23i, IL-23i
Enthesitis	TNFi, IL-12/23i, IL-17i, PDE4i, IL-23i, JAKi	NSAIDs, physiotherapy, CS injections, MTX		IL-6i,	Other cs DMARDs
Dactylitis	TNFi IL-12/23i, IL-17i, IL-23i, JAKi, PDE4i	NSAIDs, CS injections, MTX	Other csDMARDs		
Psoriasis	Topicals, phototherapy, csDMARDs, TNFi, IL-12/23i, IL-17i, IL-23i, PDE4i, JAKi	Acitretin			
Nail psoriasis	TNFi, IL12/23i, IL17i, IL23i, PDE4i	Topical CS, tacrolimus and calcipotriol combination or individual therapies, Pulsed dye laser, csDMARDs, acitretin, JAKi			Topical Cyclosporine / Tazarotene, Fumarate, Fumaric Acid Esters, UVA and UVB Phototherapy, Alitretinoin
IBD	TNFi (not ETN), IL-12/23i, JAKi			IL-17i	
Uveitis	TNFi (not ETN)				



Disclosure of Interests: Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Gilead, Eli Lilly, Janssen, Medac, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Pfizer, and Novartis, Enrique Soriano Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb,GSK, Genzyme, Janssen, Lilly, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb,GSK, Genzyme, Janssen, Lilly, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Grant/research support from: AbbVie, Janssen, Novartis Pharma, Pfizer, Roche, and UCB, Nadia Corp: None declared, Heidi Bertheussen Consultant of: Pfizer, Kristina Callis-Duffin Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Lilly, Janssen, Novartis, Pfizer, Sienna Biopharmaceuticals, Stiefel Laboratories, UCB, Ortho Dermatologics, Inc, Regeneron Pharmaceuticals, Inc., Anaptys Bio, Boehringer Ingelheim., Cristiano Barbosa Campanholo Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Jeffrey Chau: None declared, Lihi Eder Consultant of: Abbvie, UCB, Janssen, Eli Lily, Pfizer, Novartis, Grant/research support from: Abbvie, UCB, Janssen, Eli Lily, Pfizer, Novartis, Daniel Fernandez Consultant of: Abbvie, UCB, Roche, Janssen, Pfizer, Amgen and Brystol, Grant/research support from: Abbvie, UCB, Roche, Janssen, Pfizer, Amgen and Brystol, Oliver FitzGerald Speakers bureau: AbbVie, Janssen and Pfizer Inc, Consultant of: BMS, Celgene, Eli Lilly, Janssen and Pfizer Inc, Grant/research support from: AbbVie, BMS, Eli Lilly, Novartis and Pfizer Inc, Amit Garg Consultant of: Abbvie, Amgen, Asana Biosciences, Bristol Myers Squibb, Boehringer Ingelheim, Incyte, InflaRx, Janssen, Pfizer, UCB, Viela Biosciences, Grant/research support from: Abbvie, Dafna D Gladman Consultant of: Abbvie, Amgen, BMS, Eli Lilly, Galapagos, Gilead, Jansen, Novartis, Pfizer and UCB, Grant/research support from: Abbvie, Amgen, Eli Lilly, Jansen, Novartis, Pfizer and UCB, Niti Goel: None declared, Suzanne Grieb: None declared, Philip Helliwell Speakers bureau: Janssen, Novartis, Pfizer, Consultant of: Eli Lilly, M Elaine Husni Consultant of: Abbvie, Amgen, Janssen, Novartis, Lilly, UCB, Regeneron, and Pfizer, Deepak Jadon Speakers bureau: AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Healthcare Celltrion, Janssen, MSD, Novartis, Pfizer, Roche, Sandoz, UCB, Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Healthcare Celltrion, Janssen, MSD, Novartis, Pfizer, Roche, Sandoz, UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Healthcare Celltrion, Janssen, MSD, Novartis, Pfizer, Roche, Sandoz, UCB, Arnon Katz: None declared, Dhruvkumar Laheru: None declared, John Latella: None declared, Ying Ying Leung Speakers bureau: Novartis, AbbVie, Eli Lilly, Janssen, Consultant of: Pfizer and Boehringer Ingelheim, Grant/research support from: Pfizer and conference support from AbbVie, Christine Lindsay Shareholder of: Amgen, Employee of: Aurinia pharmaceuticals, Ennio Lubrano Speakers bureau: Alfa-Sigma, Abbvie, Galapagos, Janssen Cilag, Lilly., Consultant of: Alfa-Sigma, Abbvie, Galapagos, Janssen Cilag, Lilly., Luis Mazzuoccolo Speakers bureau: Abbvie, Amgen, Novartis, Elli Lilly, Jansen, Consultant of: Abbvie, Amgen, Novartis, Elli Lilly, Jansen, Roland McDonald: None declared, Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead Sciences, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead Sciences, Janssen, Novartis, Pfizer, SUN and UCB, Denis O'Sullivan: None declared, Alexis Ogdie Consultant of: AbbVie, Amgen, BMS, Celgene, Corrona, Gilead, Janssen, Lilly, Novartis, and Pfizer, Grant/research support from: Novartis and Pfizer and Amgen, Wendy Olsder: None declared, Lori Schick: None declared, Ingrid Steinkoenig: None declared, Maarten de Wit Consultant of: AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Roche, Danielle van der Windt: None declared, Arthur Kavanaugh Speakers bureau: AbbVie, Amgen, BMS, Eli Lilly, Gilead Janssen, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, BMS, Eli Lilly, Gilead Janssen, Novartis, Pfizer, UCB

DOI: 10.1136/annrheumdis-2021-eular.4091

OP0230

EFFICACY AND SAFETY OF GUSELKUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS WHO DEMONSTRATED INADEQUATE RESPONSE TO TUMOR NECROSIS FACTOR INHIBITION: WEEK 24 RESULTS OF A PHASE 3B, RANDOMIZED, CONTROLLED STUDY

L. C. Coates[1], L. Gossec[2], E. Theander[3], P. Bergmans[4], M. Neuhold[5], C. Karyekar[6], M. Shawi[6], W. Noel[5], G. Schett[7], I. Mcinnes[8]. [1]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; [2]*Sorbonne Université, Professor of Rheumatology, Paris, France*; [3]*Janssen Scientific Affairs, LLC, Immunology, Solna, Sweden*; [4]*Janssen, Biostatistics, Breda, Netherlands*; [5]*Janssen Scientific Affairs, LLC, Immunology, Brussels, Belgium*; [6]*Janssen Global Services, LLC, Immunology, Horsham, United States of America*; [7]*University of Erlangen-Nuremberg, Internal Medicine 3, Erlangen, Germany*; [8]*University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*

Background: Guselkumab (GUS), a selective monoclonal antibody targeting the interleukin-23p19 subunit, has demonstrated efficacy in 2 pivotal Ph3 psoriatic arthritis (PsA) studies (DISCOVER-1,[1] DISCOVER-2[2]).

Objectives: Evaluate GUS efficacy and safety in PsA patients (pts) with inadequate response (IR) to tumor-necrosis-factor inhibition (TNFi) through Week24 (W24) of the Ph3b COSMOS study.

Methods: In this randomized, double-blind, placebo (PBO)-controlled trial, 285 pts with active PsA (≥3 swollen & ≥3 tender joints) who demonstrated lack of benefit or intolerance to 1-2 TNFi were randomized 2:1 to subcutaneous GUS 100mg (n=189) or PBO (n=96) at W0, W4, then every 8 weeks (Q8W) through W44 (with PBO crossover to GUS at W24). At W16, pts who met early escape (EE) criteria (<5% improvement in both tender & swollen joint counts) also could switch from PBO to GUS. The primary efficacy endpoint was ACR20 response at W24 among randomized, treated pts. Pts missing ACR20 data at W24 or who met treatment failure criteria (including meeting EE criteria at W16) were considered nonresponders (NRs). Subgroup analyses were performed to assess consistency of primary treatment effect based on demographics, disease characteristics, and medication use at baseline. Prespecified sensitivity analyses included 'Per-Protocol' (PP) (excluded pts with major protocol deviations) and 'EE-Correction' (included pts incorrectly routed to EE) analyses. Adverse events (AEs) were summarized by treatment received.

Results: Baseline characteristics were similar across GUS and PBO pts, though a higher proportion of females and more severe joint symptoms were seen in the GUS group. At W24, 44.4% of GUS vs 19.8% of PBO pts achieved ACR20 (p<0.001) (Figure). GUS was superior to PBO for all major secondary endpoints. Efficacy was consistent across subgroups defined by baseline characteristics, including in pts who discontinued prior TNFi use due to inadequate efficacy (84% GUS vs 81% PBO) and safety (16% GUS vs 19% PBO) (Table). 20 pts (12 GUS, 8 PBO) were incorrectly routed to EE. Results of PP (48.8% vs 23.8%) and EE-correction (48.1% vs 19.8%) sensitivity analyses were consistent with the primary analysis (Figure). AEs were similar between GUS- and PBO-treated pts (Table).

Table 1. Baseline characteristics of, and adverse events reported by, randomized and treated COSMOS pts

	GUS 100 mg Q8W (N=189)	PBO (N=96)
Age, y	49	49
Sex, Female	54%	46%
Duration of PsA, y	8.3	8.7
Body mass index, kg/m^2	29	31[a]
Swollen (0-66) / tender (0-68) joint count	10 / 21	9 / 18
Pt pain / Pt global arthritis / Physician global disease, 0-10 cm VAS	6.5 / 6.5 / 6.9	6.0 / 6.2 / 6.4
Health Assessment Questionnaire-Disability Index, 0-3	1.3[b]	1.2
C-reactive protein, mg/dL	1.2[b]	1.2
Methotrexate use at baseline	56%	53%
Psoriatic body surface area, %	17.9	13.4
Number of prior TNFi: 1 / 2	88% / 12%	89% / 11%
Reason for prior TNFi discontinuation: Efficacy / Safety	84% / 16%*	81% / 19%*
Pts with ≥1 AE / SAE	37% / 3%	48% / 3%
Pts with ≥1 infection / serious infection	18% / 0%	20% / 0%
Pts with ≥1 AE leading to study agent discontinuation	2%	2%
Pts with ≥1 malignancy	0.4%	0
Pts with ≥1 injection-site reaction	2%	1%

Data shown are mean or %. [a]N=95; [b]N=188. *Missing for 1 pt. *SAE – serious adverse events*; *VAS – visual analog scale*

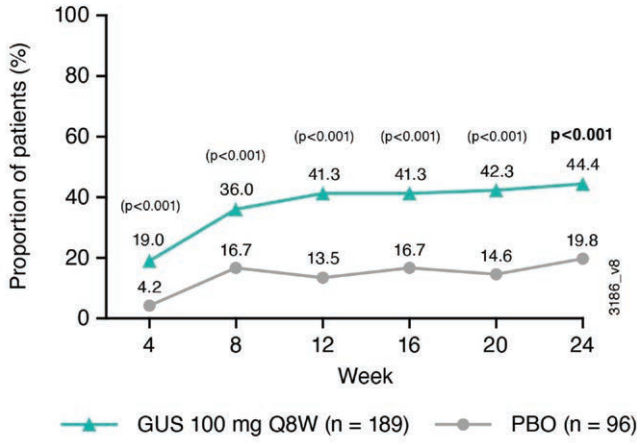
Conclusion: In this Ph3b, placebo-controlled study of PsA pts with IR to 1-2 TNFi, GUS 100 mg Q8W elicited a significantly higher ACR20 response rate vs.

PBO at W24; results of prespecified sensitivity and subgroup analyses were consistent. GUS safety in TNF-IR PsA pts through W24 is consistent with the favorable GUS safety profile in psoriasis and biologic-naïve PsA pts.[3]

REFERENCES:
[1] Deodhar A. *Lancet* 2018;391: 2213–24.
[2] Mease PJ. *Lancet* 2020;395: 1126–36.
[3] Guselkumab Prescribing Information. Janssen Biotech, Inc.

Disclosure of Interests: Laura C Coates Consultant of: AbbVie, Amgen, Biogen, BMS, Boehringer Ingelehim, Celgene, Domain, Eli Lilly, Gilead, Janssen, Medac, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Novartis, Pfizer, Laure Gossec Consultant of: AbbVie, Amgen, BMS, Biogen, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Samsung Bioepis, Sanofi-Aventis, UCB, Grant/research support from: Amgen, Eli Lilly, Galapagos, Janssen, Pfizer, Sandoz, Sanofi, Elke Theander Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Paul Bergmans Shareholder of: Johnson & Johnson, Employee of: Janssen, Marlies Neuhold Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Chetan Karyekar Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Wim Noel Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Georg Schett: None declared, Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and UCB

Figure. ACR 20 Response through Week 24 of COSMOS.



Bolded p values are adjusted for multiplicity of testing; p values shown in parentheses are not adjusted for multiplicity of testing

DOI: 10.1136/annrheumdis-2021-eular.42

OP0231

DIFFERENCES IN REAL-WORLD PATIENT CHARACTERISTICS OF 8921 PSORIASIS PATIENTS WITH AND WITHOUT COMORBID PSORIATIC ARTHRITIS USING THE UK BADBIR DATABASE

W. Tillett[1], A. Ogdie[2], P. Gorecki[3], A. Passey[4]. [1]*Royal National Hospital for Rheumatic Diseases, Rheumatology, Bath, United Kingdom*; [2]*University of Pennsylvania, Perelman School of Medicine, Philadelphia, United States of America*; [3]*Janssen, Medical Affairs, High Wycombe, United Kingdom*; [4]*Janssen Real World Evidence, HEMAR EMEA, High Wycombe, United Kingdom*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis (PsO) and multiple comorbidities.[1] Approximately one-third of PsO patients develop PsA during the course of their disease.[2] As patient cohorts included in randomised clinical trials are not necessarily representative of the real world, registry data can complement any information gained on patient characteristics and disease outcomes.[3] The British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR) is one such registry for patients with plaque PsO, with PsA being one of the recorded comorbidities at time of patient enrolment into the database.

Objectives: The primary objective of this study was to evaluate baseline characteristics and comorbidities in PsO patients with and without a PsA diagnosis using the BADBIR database. The hypothesis was that patients with both diseases show a higher likelihood of being diagnosed with additional comorbid conditions vs. PsO alone.

Methods: This was a retrospective observational study using two cohorts of BADBIR data (i.e. adult PsO patients either receiving ustekinumab [UST] as their biologic treatment or receiving conventional systemic anti-psoriatic medication [conventional systemic]). Comparisons were made between PsA and PsO alone in each cohort at baseline, additionally stratifying by biologic experience in the UST treatment group. Baseline characteristics of interest were evaluated, including body mass index, smoking and employment status, as well as comorbidities (i.e. diabetes, hypertension, myocardial infarction and depression). Effect sizes and 95% confidence intervals were generated via matching with a two-sided Fisher's exact test.

Results: Cohort patient counts were as follows: 2697 UST treated without PsA; 590 UST treated with PsA; 5105 conventional systemic without PsA; 529 conventional systemic with PsA. PsO patients with a PsA diagnosis had a higher prevalence of diabetes, obesity and hypertension across both conventional systemic and UST cohorts vs. PsO alone (Table 1). Similarly, inability to work was notably higher in PsO patients with PsA vs. PsO alone (Figure 1). Patients with PsO and comorbid PsA who were receiving UST were more likely to have a diagnosis of depression than those receiving conventional systemic treatment (Table 1).

Table 1. Prevalence odds ratio of baseline characteristics of patients with PsO treated with either UST or a conventional systemic agent.

Baseline variable	Treatment cohort	Odds ratio	95% CI
Ability to work	UST	0.27	0.21–0.35
	Conventional systemic	0.49	0.37–0.65
Smoking	UST	0.94	0.76–1.17
	Conventional systemic	0.72	0.58–0.89
Depression	UST	1.54	1.25–1.88
	Conventional systemic	1.14	0.91–1.42
Obesity*	UST	1.34	1.11–1.62
	Conventional systemic	1.21	1.01–1.46
Diabetes	UST	1.45	1.10–1.89
	Conventional systemic	1.51	1.11–2.04
Hypertension	UST	1.54	1.26–1.87
	Conventional systemic	1.30	1.03–1.62
Myocardial infarction	UST	1.67	0.98–2.76
	Conventional systemic	1.17	0.56–2.21

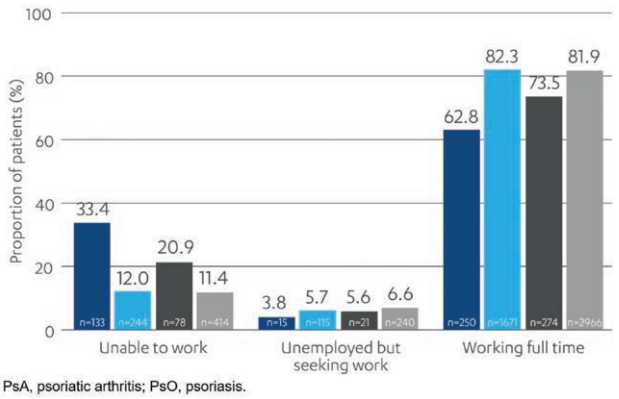
Odds ratios and 95% CIs are shown for the prevalence of each patient baseline characteristic in the PsO with comorbid PsA group vs. the prevalence in the PsO group. *Obesity is defined as a BMI ≥30 kg/m^2. BMI, body mass index; CI, confidence interval; PsA, psoriatic arthritis; PsO, psoriasis; UST, ustekinumab.

Conclusion: These results indicate that PsO patients with PsA had a higher prevalence of obesity, diabetes, hypertension and inability to work vs. PsO alone. Depression also seems to be more prevalent in PsO patients with comorbid PsA receiving biologic treatment vs. those receiving conventional systemics. These results potentially indicate a higher inflammatory and quality-of-life burden in PsO patients with a PsA diagnosis, highlighting the need for adequate patient assessment and follow-up to ensure a best possible holistic patient management approach.

REFERENCES:
[1] Shah et al. *RMD Open* 2017;3:e000588
[2] Coates et al. *Lancet* 2015;386:2489–98
[3] Mason et al. *JAMA Dermatol* 2018;154:581–8

Disclosure of Interests: William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB, Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, MSD, Pfizer and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen and UCB, Alexis Ogdie Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Janssen, Eli Lilly, Novartis and Pfizer, Grant/research support from: Pfizer to Penn, Novartis to Penn, Amgen to Forward/NDB, Patricia Gorecki Employee of: Janssen-Cilag Ltd, Alun Passey Employee of: Janssen-Cilag Ltd

Figure 1: Employment status of patients with PsO by presence of comorbid PsA and treatment type



PsA, psoriatic arthritis; PsO, psoriasis.

DOI: 10.1136/annrheumdis-2021-eular.1018

OP0232

FEMALE VERSUS MALE BURDEN OF PSORIATIC ARTHRITIS IS HIGHER AND TREATMENT PERSISTENCE SHORTER AFTER USTEKINUMAB OR TUMOUR NECROSIS FACTOR INHIBITOR TREATMENT: 1-YEAR DATA FROM THE PSABIO STUDY

I. van der Horst-Bruinsma[1], M. Nurmohamed[2], A. Van Kuijk[2], S. Siebert[3], P. Bergmans[4], K. De Vlam[5], E. Gremese[6], B. Joven-Ibáñez[7], T. Korotaeva[8], W. Noel[9], P. Sfikakis[10], E. Theander[11], J. S. Smolen[12], L. Gossec[13,14].
[1]Amsterdam University Medical Center, Location VUmc, Department of Rheumatology and Immunology, Amsterdam, Netherlands; *[2]Reade and VU University Medical Center, Department of Rheumatology, Amsterdam, Netherlands*; *[3]University of Glasgow, Institute of Infection Immunity and Inflammation, Glasgow, United Kingdom*; *[4]Janssen-Cilag BV, Biostatistics, Breda, Netherlands*; *[5]University Hospitals Leuven, Division of Rheumatology, Leuven, Belgium*; *[6]Catholic University of the Sacred Heart, Fondazione Policlinico A Gemelli IRCCS, Rome, Italy*; *[7]University Hospital 12 de Octubre, Department of Rheumatology, Madrid, Spain*; *[8]VA Nasonova Research Institute of Rheumatology, Department of Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*; *[9]Janssen Pharmaceutica NV, Medical Affairs, Beerse, Belgium*; *[10]National and Kapodistrian University of Athens Medical School, First Department of Propaedeutic and Internal Medicine, Athens, Greece*; *[11]Janssen-Cilag AB, Medical Affairs, Solna, Sweden*; *[12]Medical University of Vienna, Division of Rheumatology, Department of Medicine III, Vienna, Austria*; *[13]Sorbonne University, INSERM, Pierre Louis Institute of Epidemiology and Public Health, Paris, France*; *[14]Pitié-Salpêtrière Hospital, AP-HP, Department of Rheumatology, Paris, France*

Background: Sex-related differences in biologic treatment of psoriatic arthritis (PsA) have been insufficiently studied in a real-world setting.
Objectives: To evaluate impact of sex on PsA, treatment effectiveness and persistence after 1 year of biologic treatment.
Methods: PsABio (NCT02627768) is a multinational, prospective real-world study in PsA with ustekinumab (UST) or TNF inhibitor (TNFi) as 1st/2nd/3rd-line biologic. Males and females were compared for disease activity and patient-reported outcomes. Descriptive statistics including 95% CI at baseline (BL) and 12 (±3) months (LOCF) follow-up are presented. Intra-sex comparisons between UST and TNFi cohorts were done by logistic regression analysis, with propensity score adjustment for imbalanced BL covariates and non-response imputation for stopping/switching biologic drugs.
Results: Among 494 females and 399 males, age and disease duration were similar. However, differences in disease characteristics at BL were considerable:

Table 1. Patient and disease characteristics at BL and 1-year by sex

	BL female	BL male	1-year LOCF female	1-year LOCF male
Biologic line, %				
1st	46	55	N/A	N/A
2nd	34	33		
3rd	20	13		
Co-treatment, %				
MTX	37.4	34.3	N/A	N/A
Corticosteroids	34.6	32.1		
NSAIDs	59.9	64.4		
Antidepressant	**7.9**	**2.5**		
Comorbidities, %			N/A	N/A
Cardiovascular	**69.0**	**59.4**		
metabolic syndrome	40.1	31.7		
Obesity	**35.2**	**23.7**		
Anxiety/depression	12.6	7.5		
Smoking status, %			N/A	N/A
Never	54.9	41.9		
Past	16.8	26.6		
Current	22.7	24.3		
Unknown	5.7	7.3		
Joint counts, n				
Swollen 66	6.1 (5.4; 6.9)	5.6 (4.7; 6.4)	**2.2 (1.7; 2.6)**	**1.3 (1.0; 1.6)**
Tender 68	**13.2 (12.0; 14.4)**	**10.0 (8.9; 11.1)**	**6.0 (5.2; 6.7)**	**3.6 (2.9; 4.3)**
cDAPSA score, mean (95% CI)				
cDAPSA, %	**32.5 (30.5; 34.4)**	**26.9 (24.9; 29.0)**	**15.9 (14.5; 17.2)**	**10.3 (9.0; 11.6)**
Remission	1.0 (0.3; 2.6)	4.0 (2.1; 6.7)	**17.8 (14.1; 22.0)**	**37.7 (32.4; 43.2)**
Low	**6.7 (4.4; 9.7)**	**15.0 (11.3; 19.4)**	33.0 (28.3; 37.9)	36.5 (31.3; 42.0)
Moderate	38.9 (34.0; 44.0)	42.6 (37.2; 48.2)	**34.3 (29.6; 39.2)**	**16.9 (13.0; 21.4)**
High	**53.4 (48.2; 58.4)**	**38.3 (33.0; 43.9)**	14.9 (11.6; 18.9)	8.9 (6.0; 12.5)
MDA	**2.3 (1.0; 4.3)**	**7.7 (5.1; 11.2)**	**27.5 (23.1; 32.1)**	**52.2 (46.6; 57.7)**
VLDA	0.0	0.9 (0.2; 2.6)	**6.2 (4.1; 9.0)**	**19.7 (15.6; 24.3)**
HAQ-DI score	**1.31 (1.25; 1.37)**	**0.93 (0.86; 1.00)**	**0.95 (0.89; 1.02)**	**0.53 (0.47; 0.59)**
PsAID-12 score	**6.1 (5.9; 6.3)**	**5.1 (4.9; 5.3)**	**4.0 (3.8; 4.3)**	**2.7 (2.4; 2.9)**
EQ5D VAS score	**48.6 (46.6; 50.5)**	**53.8 (51.6; 55.9)**	**59.2 (56.9; 61.4)**	**68.0 (65.5; 70.4)**
Enthesitis	50.7 (45.9; 55.5)	48.1 (42.8; 53.3)	**32.6 (28.3; 37.3)**	**18.0 (14.1; 22.3)**
Dactylitis	**15.6 (12.4; 19.3)**	**24.7 (20.4; 29.3)**	5.7 (3.8; 8.3)	4.8 (2.9; 7.4)

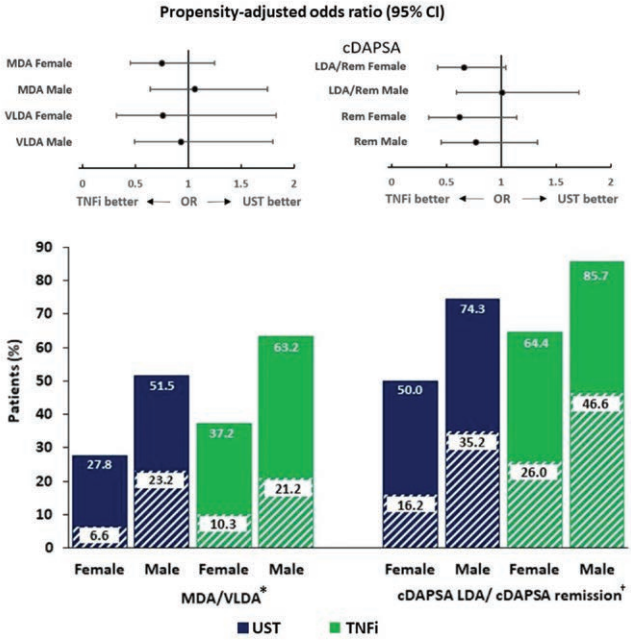
Data are % (95% CI) unless indicated otherwise. Bold data are significantly different (non-overlapping 95% CI).

females had worse scores than males for cDAPSA, HAQ-DI, EQ5D VAS, PsAID-12, pain and comorbidities. At 1 year, similar improvements from BL were observed between sexes, but females remained in a worse health state than males (Table). Achievement of composite endpoints MDA (including VLDA) and cDAPSA LDA (including remission) was high overall (38.6% and 61.5%, respectively), but reached by >2-fold and 3-fold more males than females, respectively. HAQ-DI scores remained worse for females at 1 year (0.95) than for males at BL (0.93). Enthesitis resolution was achieved in 46% of females and 75% of males. No significant differences in effectiveness of UST vs TNFi were detected between sexes (Figure). Kaplan–Meier estimated drug persistence was significantly better in males than females (log-rank p=0.0007). There was no intra-sex difference between UST or TNFi in risk of stopping/switching in males or females.

Conclusion: These real-world data from PsABio on sex differences with biologic treatment suggest that females generally start biologics in a worse PsA state than males. Although treatment improvements were similar between sexes, females remained in worse health at 1 year, and stopped/switched biologic earlier. More comprehensive treatment before severe disease manifestations evolve may improve management in females.

Acknowledgements: This study was funded by Janssen

Proportion of females and males achieving treatment targets at 1 year



*Solid bar represents MDA and hashed bar represents VLDA.
†Solid bar represents cDAPSA LDA/remission (≤13) and hashed bar represents cDAPSA remission (≤4).

BL, baseline; cDAPSA, clinical Disease Activity in Psoriatic Arthritis; CI, confidence interval; EQ5D, EuroQoL 5-dimensional questionnaire; HAQ-DI, Health Assessment Questionnaire-Disability Index; LOCF, last observation carried forward; LDA, low disease activity; MDA, minimal disease activity; MTX, methotrexate; N/A, not available; NSAID, non-steroidal anti-inflammatory drugs; OR, odds ratio; PsAID-12, Psoriatic Arthritis Impact of Disease 12-item questionnaire; Rem, remission; TNFi, tumour necrosis factor inhibitor; UST, ustekinumab; VAS, visual analogue scale; VLDA, very low disease activity

Disclosure of Interests: Irene van der Horst-Bruinsma Consultant of: AbbVie, Lilly, MSD, Novartis, UCB, Grant/research support from: AbbVie, MSD, Pfizer, UCB, Michael Nurmohamed Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi, UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi, UCB, Arno Van Kuijk Consultant of: AbbVie, Janssen, LEO Pharma, Novartis, Grant/research support from: Janssen, Stefan Siebert Speakers bureau: AbbVie, Amgen (previously Celgene), Biogen, Janssen, Novartis, UCB, Consultant of: AbbVie, Janssen, UCB, Grant/research support from: Amgen (previously Celgene), Boehringer Ingelheim, Bristol-Myers Squibb, GSK, Janssen, Novartis, Pfizer, UCB, Paul Bergmans Shareholder of: Johnson & Johnson, Employee of: Janssen, Kurt de Vlam Speakers bureau: AbbVie, Amgen, Eli Lilly, Novartis, UCB, Paid instructor

for: Amgen, Galapagos, UCB, Consultant of: Eli Lilly, Johnson &Johnson, Novartis Galapagos, UCB, Grant/research support from: Celgene, Elisa Gremese: None declared, Beatriz Joven-Ibáñez Speakers bureau: AbbVie, Celgene, Janssen, MSD, Novartis, Pfizer, Tatiana Korotaeva Speakers bureau: AbbVie, Amgen, Biocad, Janssen, Lilly, MSD, Novartis, Novartis-Sandoz, Pfizer, UCB, Consultant of: AbbVie, Amgen, Biocad, Janssen, Lilly, MSD, Novartis, Novartis-Sandoz, Pfizer, UCB, Grant/research support from: Pfizer, Wim Noel Employee of: Janssen, Petros Sfikakis Consultant of: AbbVie, Actelion, Boehringer Ingelheim, Enorasis, Farmaserv-Lilly, Genesis, Gilead, MSD, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Faran, Janssen, Pfizer, Roche, Elke Theander Employee of: Janssen, Josef S. Smolen Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Consultant of: AbbVie, AstraZeneca, Lilly, Novartis, Roche, Laure Gossec Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Biogen, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Samsung Bioepis, Sanofi-Aventis, UCB, Grant/research support from: Amgen, Galapagos, Janssen, Lilly, Pfizer, Sandoz, Sanofi

DOI: 10.1136/annrheumdis-2021-eular.1575

OP0233

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS AND AXIAL INVOLVEMENT

A. Deodhar[1], R. Ranza[2], F. Ganz[3], T. Gao[4], J. Anderson[4], A. Ostor[5].
[1]*Oregon Health & Science University, Rheumatology, Portland, United States of America*; [2]*Universidade Federal de Uberlândia, Rheumatology, Uberlândia, Brazil*; [3]*AbbVie Inc., Rheumatology, Baar, Switzerland*; [4]*AbbVie Inc., Rheumatology, North Chicago, United States of America*; [5]*Cabrini Hospital, Monash University & Emeritus Research, Melbourne, Australia*

Background: Patients (pts) with psoriatic arthritis (PsA) and axial involvment exhibit greater disease activity and quality of life impairments compared with those without axial involvment.
Objectives: To characterize PsA pts with and without axial involvement and compare efficacy of UPA vs placebo (PBO) in PsA pts with axial involvement.
Methods: In SELECT-PsA 1 (NCT03104400; N=1705, non-biologic DMARD IR) and SELECT-PsA 2 (NCT03104374; N=642, biologic DMARD IR), pts with active PsA (≥3 swollen and ≥3 tender joints), active or historical psoriasis, and on ≤2 non-biologic DMARDs were randomized to once daily UPA 15 mg, UPA 30 mg, adalimumab 40 mg every other week (SELECT-PsA 1 only), or PBO. Efficacy was assessed in pts with axial involvement (diagnosed by investigators based on totality of information) pooled from the 2 studies. Assessments included change from BL in BASDAI, BASDAI Q2 (neck/back/hip pain) and Q3 (joint swelling/pain), and the AS Disease Activity Score (ASDAS-CRP), and percentage with BASDAI 50 response, ASDAS inactive disease (ID), ASDAS low disease activity (LDA), ASDAS major improvement (MI), and ASDAS clinically important improvement (CII). Uveitis and inflammatory bowel disease (IBD) adverse events were reviewed. Data on 24-week PBO-controlled period are presented.
Results: Prevalence of axial involvment was 31.3% in SELECT-PsA 1 and 34.2% in SELECT-PsA 2 (Table). Treatment with UPA 15 mg and 30 mg resulted in significantly greater improvements from BL in the BASDAI, BASDAI Q2 (neck/back/hip pain) and Q3 (joint swelling/pain) and ASDAS-CRP at weeks 12 and 24 vs PBO (Figure). Similarly, significantly higher percentages of pts on UPA 15 mg and 30 mg achieved BASDAI 50, ASDAS ID, LDA, MI, and CII at weeks 12 and 24 vs PBO (Figure). One pt on UPA 30 mg had incident uveitis, and no IBD was reported on UPA.
Conclusion: PsA pts with axial involvement had higher BL disease burden compared with those without axial involvement. UPA was efficacious in treating axial symptoms in pts with psoriatic spondylits.

REFERENCES:

[1] van der Heijde D, et al. *Lancet*. 2019;394(10214):2108-2117.

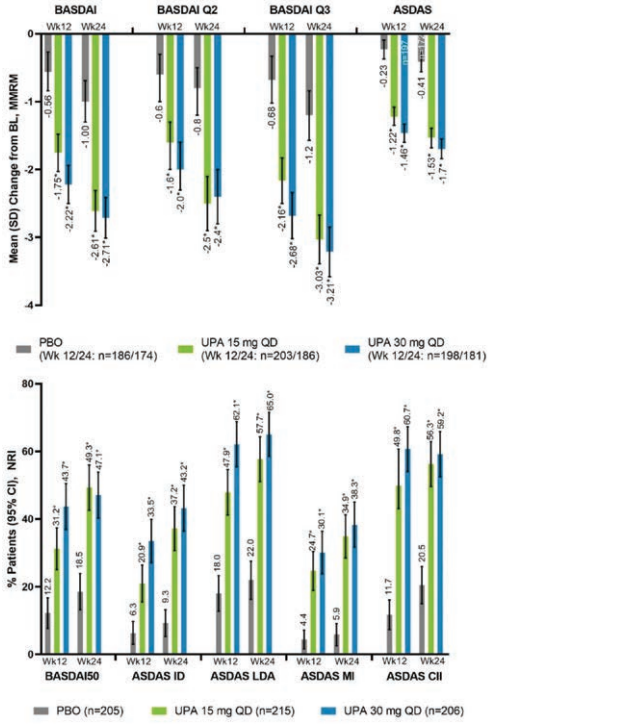
Acknowledgements: Abbvie funded the study. AbbVie participated in study design, research, analysis, data collection, interpretation of the data, reviewing, and approval. All authors had access to the relevant data and participated in the drafting, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by M Mehta, and J Matsuura of ICON plc (North Wales, PA) and was funded by AbbVie.

Table 1. Demographics and Baseline Characteristics

Parameter, mean (SD)	SELECT-PsA 1 With Psoriatic Spondylitis (n=534)	SELECT-PsA 1 Without Psoriatic Spondylitis (n=1170)	SELECT-PsA 1 *P* value*	SELECT-PsA 2 With Psoriatic Spondylitis (n=219)	SELECT-PsA 2 Without Psoriatic Spondylitis (n=421)	SELECT-PsA 2 *P* value*
BMI (kg/m^2)	29.9 (6.5)	30.5 (6.9)	.0810	31.6 (8.0)	31.3 (6.9)	.6226
TJC68	21.6 (15.1)	19.2 (13.5)	**.0022**	27.5 (18.0)	23.3 (16.2)	**.0027**
SJC66	11.7 (9.4)	11.0 (7.9)	.1184	12.9 (9.2)	11.7 (8.7)	.0804
Physician's Global Assessment (NRS 0–10)	6.7 (1.6)	6.5 (1.7)	**.0437**	6.6 (1.8)	6.5 (1.7)	.1897
HAQ-DI	1.2 (0.6) n=531	1.1 (0.6) n=1164	**.0170**	1.2 (0.6) n=218	1.2 (0.7) n=416	.2049
Presence of dactylitis, n (%)†	188 (35.2)	328 (28.0)	**.0028**	69 (31.5)	100 (23.8)	**.0348**
Presence of enthesitis, n(%)‡	432 (80.9)	884 (75.6)	**.0147**	189 (86.3)	337 (80.0)	**.0125**
ASDAS–CRP	3.4 (0.9) n=530	3.1 (1.0) n=1161	**<.0001**	3.3 (1.0) n=217	3.2 (1.1) n=416	.1032
BASDAI	5.8 (2.0) n=530	5.3 (2.2) n=1161	**<.0001**	6.2 (2.2) n=217	5.8 (2.2) n=416	.0673
Morning Stiffness Duration (NRS 0–10; BASDAI Q6)	5.0 (3.0) n=530	4.7 (3.0) n=1161	**.0368**	5.6 (3.2) n=217	5.1 (3.0) n=416	**.0454**
Patient's Assessment of Inflammatory Neck, Back, or Hip Pain (NRS 0–10; BASDAI Q2)	5.8 (2.7) n=530	4.6 (3.2) n=1161	**<.0001**	6.4 (2.8) n=217	5.4 (3.1) n=416	**.0001**

*Calculated by t-test for continuous variables and chi-square test for categorical values. Bolded if <0.05.Defined as †LDI>0 and ‡total enthesitis count >0

Figure. Integrated Analysis of Efficacy in PsA Patients With Axial Involvement



ASDAS, ankylosing spondylitis disease activity score; BL, baseline; CII, clinically important improvement; ID, inactive disease; LDA, low disease activity; MI, major improvement; MMRM, mixed-effects model repeated measurement; NRI, non-responder imputation; QD, once daily; UPA, upadacitinib.
*P<0.0001, UPA vs placebo; nominal P values are presented and were not adjusted for multiple testing.
MMRM analysis with unstructured variance-covariance matrix, including treatment, visit, treatment-by-visit interaction, study, and the stratification factor of current DMARD use (yes/no) as fixed factors and the continuous fixed covariates of baseline measurement.
NRI analysis with nominal P value constructed using the Mantel-Haenszel estimation adjusting for study and the main stratification factor of current DMARD use (yes/no); 95% CI for response rate calculated based on normal approximation to the binomial distribution.

Disclosure of Interests: Atul Deodhar Speakers bureau: Novartis and Pfizer, Consultant of: Novartis, Pfizer, AbbVie, Eli Lilly, UCB Pharma, GlaxoSmithKline, Galapagos, Janssen, Boehringer Ingelheim and Celgene, Grant/research support from: Novartis, Pfizer, AbbVie, Eli Lilly, UCB Pharma, GlaxoSmithKline, R Ranza Speakers bureau: AbbVie, Janssen, Lilly, Novartis, and Pfizer, Consultant of: AbbVie, Janssen, Lilly, Novartis, and Pfizer, Grant/research support from: AbbVie, Janssen, Fabiana Ganz Shareholder of: AbbVie, Employee of: AbbVie, Tianming Gao Shareholder of: AbbVie, Employee of: AbbVie, Jaclyn Anderson Shareholder of: AbbVie, Employee of: AbbVie, Andrew Ostor Consultant of: AbbVie, BMS, Roche, Janssen, Lilly, Novartis, Pfizer, UCB, Gilead, and Paradigm
DOI: 10.1136/annrheumdis-2021-eular.439

Epidemiology and public health

OP0234

RISK OF ACUTE MYOCARDIAL INFARCTION AMONG NEW USERS OF CHONDROITIN SULPHATE: A NESTED CASE-CONTROL STUDY

R. Mazzucchelli[1], S. Rodriguez-Martin[2], A. García-Vadillo[3], M. Gil[4], A. Rodríguez-Miguel[2], D. Barreira-Hernández[5], A. García-Lledó[6], F. De Abajo[7]. *[1]Hospital Universitario Fundación Alcorcón, Rheumatologu Unit, Alcorcón, Spain*; *[2]Hospital Universitario Príncipe de Asturias, Clinical Pharmacology Unit, Alcalá de Henares, Spain*; *[3]Hospital de La Princesa, Rheumatologu Unit, Madrid, Spain*; *[4]Spanish Agency of Medicines and Medical Devices, Division of Pharmacoepidemiology and Pharmacovigilance, Madrid, Spain*; *[5]Hospital Universitario Príncipe de Asturias, Clinical Pharmacology Unit, Meco, Spain*; *[6]Hospital Universitario Príncipe de Asturias, Department of Cardiology, Alcalá de Henares, Spain*; *[7]Hospital Universitario Príncipe de Asturias, 2 Clinical Pharmacology Unit, Alcalá de Henares, Spain*

Background: There is some evidence from epidemiological studies suggesting that CS and glucosamine could play a role in cardiovascular disease (CVD) prevention (1-4).Studies to date have included prevalent users, therefore a bias that overestimates protection cannot be excluded.
Objectives: To test the hypothesis that chondroitin sulphate (CS) or glucosamine reduce the risk of acute myocardial infarction (AMI).
Methods: Case-control study nested in a primary cohort composed of patients aged 40 to 99 years, with at least one year of follow-up in the BIFAP database during the 2002-2015 study period. From this cohort of patients, we identified incident cases of AMI and randomly selected five controls per case, matched by exact age, gender, and index date. Adjusted odds ratios (AOR) and their corresponding 95% confidence interval (CI)) were calculated through a conditional logistic regression. Only new users of CS or glucosamine were considered.
Results: A total of 23,585 incident cases of AMI and 117,405 controls were included. The mean age was 67.0 (SD 13.4) years and 71.75% were male, in both groups. 558 (2.37%) cases and 3,082 (2.62%) controls used or had used CS. The current use of CS was associated with a lower risk of AMI (AOR 0.57; 95%CI: 0.46–0.72) and disappeared after discontinuation (recent and past users). The reduced risk among current users was observed in both short-term (<365 days AOR 0.58; 95%CI: 0.45-0.75) and long-term users (>364 days AOR 0.56; 95%CI 0.36-0.87), in both sexes (men, AOR=0.52; 95%CI:0.38-0.70; women, AOR=0.65; 95%CI: 0.46-0.91), in individuals over or under 70 years of age (AOR=0.54; 95%CI:0.38-0.77, and AOR=0.61; 95%CI:0.45-0.82, respectively) and in individuals at intermediate (AOR=0.65; 95%CI:0.48-0.91) and high cardiovascular risk (AOR=0.48;95%CI:0.27-0.83), but not in those at low risk (AOR=1.11; 95%CI:0.48-2.56). In contrast, the current use of glucosamine was not associated with either increased or decreased risk of AMI (AOR= 0.86; CI95% 0.66-1.08)
Conclusion: Our results support a cardioprotective effect of CS, while no effect was observed with glucosamine. The highest protection was found among subgroups at higher cardiovascular risk.
REFERENCES:
[1] Ma H, Li X, Sun D, Zhou T, Ley SH, Gustat J, et al. Association of habitual glucosamine use with risk of cardiovascular disease: prospective study in UK Biobank. BMJ. 2019;365(Journal Article):l1628.
[2] de Abajo FJ, Gil MJ, Garcia Poza P, Bryant V, Oliva B, Timoner J, et al. Risk of nonfatal acute myocardial infarction associated with non-steroidal antiinflammatory drugs, non-narcotic analgesics and other drugs used in osteoarthritis: a nested case-control study. PharmacoepidemiolDrug Saf. 2014;23(11):1128–38.
[3] Li Z-H, Gao X, Chung VC, Zhong W-F, Fu Q, Lv Y-B, et al. Associations of regular glucosamine use with all-cause and cause-specific mortality: a large prospective cohort study. Ann Rheum Dis. 2020 Apr 6;annrheumdis-2020-217176.
[4] King DE, Xiang J. Glucosamine/Chondroitin and Mortality in a US NHANES Cohort. J Am Board Fam Med. 2020 Dec;33(6):842–7.

Disclosure of Interests: Ramón Mazzucchelli Speakers bureau: UCB, Lilly, Grant/research support from: Pfizer, Roche, Amgen, Sara Rodriguez-Martin: None declared, Alberto García-Vadillo: None declared, Miguel Gil: None declared, Antonio Rodríguez-Miguel: None declared, Diana Barreira-Hernández: None declared, Alberto García-Lledó: None declared, Francisco de Abajo: None declared
DOI: 10.1136/annrheumdis-2021-eular.123

OP0235

PRO-INFLAMMATORY DIET AND RISK OF INCIDENT GOUT: 3 PROSPECTIVE COHORT STUDIES OF US MEN AND WOMEN

N. McCormick[1,2,3,4], C. Yokose[1,2,3], L. Lu[4], A. Joshi[2,3,5], H. Choi[1,2,3,4]. *[1]Massachusetts General Hospital, Clinical Epidemiology Program, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; *[2]Harvard Medical School, Medicine, Boston, United States of America*; *[3]Massachusetts General Hospital, The Mongan Institute, Boston, United States of America*; *[4]Arthritis Research Canada, Richmond, Canada*; *[5]Massachusetts General Hospital, Clinical & Translational Epidemiology Unit, Boston, United States of America*

Background: Emerging evidence suggests inflammation may drive progression from hyperuricemia to clinical gout, but the role of extrinsic, modifiable sources of chronic inflammation, such as diet, on gout risk is unknown. Notably, greater dietary inflammatory potential has been independently associated with increased risk of incident cardiovascular disease (CVD)[1] and type 2 diabetes (T2D).[2]
Objectives: Prospectively examine the relation between dietary inflammatory potential and risk of gout in three large cohorts of US women and men over 30 years.
Methods: Ascertaining the ACR survey criteria for gout for several decades,[3] we studied gout risk among 164,090 women from Nurses Health Study I (1986-2016) and II (1989-2017) and 40,598 men from Health Professionals Follow-up Study (1986-2016), free of gout at baseline. Dietary intake and covariates were assessed by validated questionnaires every 4 years. Inflammatory potential of diet was evaluated using a food-based empirical dietary index of inflammatory potential score (EDIP) pre-defined based on circulating levels of IL-6, C-reactive protein, adiponectin, and TNFαR2.[4]
We assigned an EDIP score for each participant, adjusted for total energy take, and prospectively examined the association between quintiles of EDIP score and incident gout, adjusting for potential confounders. We also stratified by alcohol intake, as alcohol has anti-inflammatory properties,[4] but is associated with a higher gout risk, particularly beer.[5]
Results: We documented 2,874 incident gout cases over 5,124,940 person-years of follow-up. In pooled multivariable-adjusted analyses, those in the highest EDIP quintile had 59% higher gout risk (multivariable RR 1.59; 95% CI 1.41–1.79), compared with the lowest (Table **1**). This remained positive with further adjustment for BMI, a likely causal intermediate (RR 1.27, 1.12 to 1.42), and was stronger among non-drinkers (RR 2.37, 1.58 to 2.56) than drinkers (RR 1.57, 1.38 to 1.78) (Table 1).

Table 1. Risk Ratio (95% CI) of Gout According to Quintiles of Inflammatory Diet Score, Overall and by Alcohol Use

	Q1: lowest	Q2	Q3	Q4	Q5: highest	P for trend
Overall						
N cases	473	493	530	623	755	
Person-years	1,024,571	1,025,618	1,025,284	1,024,779	1,024,688	
Age-adjusted RR	1.00 (Ref)	1.05 (0.92, 1.19)	1.13 (0.99, 1.27)	1.33 (1.18, 1.50)	1.64 (1.46, 1.84)	<0.001
MV-Adjusted* RR	1.00 (Ref)	1.04 (0.92, 1.18)	1.12 (0.98, 1.26)	1.31 (1.16, 1.48)	1.59 (1.41, 1.79)	<0.001
MV-Adjusted** RR (+ BMI)	1.00 (Ref)	1.00 (0.88, 1.13)	1.03 (0.91, 1.17)	1.16 (1.02, 1.31)	1.27 (1.12, 1.42)	<0.001
No Alcohol Use						
N cases	26	58	84	143	251	
Person-years	118,301	189,938	249,389	313,511	396,080	
MV-Adjusted* RR	1.00 (Ref)	1.31 (0.82, 2.08)	1.37 (0.88, 2.13)	1.80 (1.18, 2.74)	2.37 (1.58, 2.56)	<0.001
MV-Adjusted** RR (+ BMI)	1.00 (Ref)	1.28 (0.80, 2.03)	1.32 (0.85, 2.05)	1.61 (1.06, 2.45)	1.85 (1.23, 2.79)	<0.001
Alcohol Use						
N cases	447	435	446	480	504	
Person-years	906,271	835,680	775,895	711,267	628,609	
MV-Adjusted* RR	1.00 (Ref)	1.04 (0.91, 1.19)	1.13 (0.99, 1.29)	1.31 (1.15, 1.50)	1.57 (1.38, 1.78)	<0.001
MV-Adjusted** RR (+ BMI)	1.00 (Ref)	1.00 (0.88, 1.14)	1.05 (0.92, 1.20)	1.17 (1.03, 1.33)	1.28 (1.12, 1.46)	<0.001

*Multivariable (MV) models adjusted for age (month), White race, smoking, menopause (women only), hormone use (women only), physical activity, history of hypertension, and diuretic use. **MV + BMI models additionally adjusted for BMI (a likely causal intermediate)

Conclusion: Habitual pro-inflammatory dietary pattern was independently associated with higher risk of incident gout in these prospective cohorts, even beyond the pathway through adiposity. Our findings support a role for chronic inflammation in development of gout, similar to CVD[1] and T2D.[2] Adhering to a diet with lower inflammatory potential may modulate systemic inflammation, potentially reducing gout risk and these life-threatening comorbidities.

REFERENCES:
[1] Li et al. J Amer Coll Cardiology (2020) PMID 33153576
[2] Lee *et al. Diabetes Care* (2020) PMID 32873589
[3] Wallace *et al.* PMID 856219
[4] Tabung *et al.* PMID 27358416
[5] Choi *et al.* PMID 15094272

Disclosure of Interests: Natalie McCormick: None declared, Chio Yokose: None declared, Leo Lu: None declared, Amit Joshi: None declared, Hyon Choi Consultant of: Ironwood, Selecta, Horizon, Takeda, Kowa, Vaxart, Grant/research support from: Ironwood, Horizon

DOI: 10.1136/annrheumdis-2021-eular.3430

OP0236 THE EFFECT OF UV-B RADIATION EXPOSURE ON THE RISK OF DEVELOPING RHEUMATOID ARTHRITIS

J. Hagman[1], B. Delcoigne[1], L. Klareskog[1], L. Alfredsson[1], J. Askling[1].
[1]*Karolinska Institute, Department of Medicine, Division of Clinical Epidemiology, Stockholm, Sweden*

Background: UV-B radiation has known immunomodulatory properties, but to what extent UV-B radiation exposure might affect the occurrence of rheumatoid arthritis (RA) has been relatively little studied, and with partially contradictory results.

Objectives: To investigate the association between sun- and travel habits, as proxy markers for UV-B radiation exposure, and risk of incident RA, overall and by RA subtype.

Methods: We performed a matched case-control study of 1151 incident cases with new-onset RA and 2374 population controls from the Swedish Epidemiological Investigation of Rheumatoid Arthritis (EIRA) study, recruited between 2006 and 2017. The association between sunbathing frequency, solarium use, and frequency of travels to sunnier countries than Sweden (exposures) and risk of RA (outcome) were assessed as odds ratios (OR) with 95 % confidence intervals (CI) through logistic regression, and adjusted for age, sex, residential region, year of study entry, body mass index, education, income, smoking and alcohol consumption. We further assessed effect modification by self-reported skin type, income and education, and by rheumatoid factor (RF) serostatus.

Results: Overall, the frequency of sunbathing, and solarium use, were similar among RA cases and controls: 'never doing sunbathing' amongst RA cases vs. controls: 22% vs. 21 %, 'sunbathing daily when possible': 10% vs. 12%, and solarium use 13% vs. 12%. The proportion of 'not travelled abroad to a sunnier country than Sweden during the past 5 years' was higher for RA cases than controls: 27% vs. 23%, and 'travelling abroad more than once a year' was less common among RA cases: 15% vs. 20%.

Sunbathing frequency was not linked to risk of RA (OR 0.91, 95% CI 0.69-1.20), nor was solarium use (OR 1.07, 95% CI 0.85-1.35). Stratification by skin type revealed no major effect modification, nor did stratification by RF status. In contrast, frequency of travel to sunnier countries than Sweden was inversely associated with RA risk comparing the most to least frequent travelers (OR 0.68, 95% CI 0.54-0.87). When stratified by educational level, this association was confined to individuals with medium (OR 0.69, 95% CI 0.48-0.98) or high (OR 0.60, 95% CI 0.50-0.91) and absent among subjects with low education (OR 1.10, 95% CI 0.56-1.99). No such interaction was observed between travel habits and income.

Table 1. RA cases and controls with adjusted odds ratios and confidence intervals for overall risk of RA and by RA serostatus.

	N				OR* for RA (95% CI)		
Exposure variable	**RA cases**	**Controls**	**RF+**	**RF-**	**All RA**	**RF+**	**RF-**
Sunbathing[a]							
Never	249	495	161	85	ref	ref	ref
At least once a month	398	844	265	124	1.05 (0.85-1.29)	1.07 (0.84-1.36)	0.98 (0.72-1.34)
At least once a week	376	751	239	130	1.11 (0.90-1.38)	1.07 (0.83-1.37)	1.21 (0.88-1.66)
Daily	120	278	75	43	0.91 (0.69-1.20)	0.86 (0.62-1.20)	0.96 (0.64-1.46)
Travel[b]							
Never	314	537	208	103	ref	ref	Ref
Seldom	294	568	193	97	0.98 (0.79-1.21)	0.98 (0.77-1.25)	0.98 (0.71-1.35)
Once a year	359	805	227	121	0.82 (0.67-1.01)	0.80 (0.63-1.02)	0.83 (0.61-1.13)
More than once a year	176	463	112	61	0.68 (0.54-0.87)	0.68 (0.51-0.91)	0.70 (0.48-1.01)
Solarium[c]							
Never	991	2083	634	336	ref	ref	Ref
Once per year or more	153	290	107	46	1.07 (0.85-1.35)	1.08 (0.83-1.40)	1.11 (0.77-1.59)

OR = adjusted odds ratio, CI = confidence interval, N = number of participants, RA = rheumatoid arthritis, ref = reference, RF= rheumatoid factor. a Frequency of sunbathing if the weather invites to it? b Frequency of travels to a country sunnier than Sweden in the last 5 years? c Frequency of solarium use in the last 5 years? *Adjusting for age, sex, region, index year, BMI, smoking, alcohol consumption, education level and income. <4 % of data was missing for all variables.

Conclusion: Proxy markers for UV-B exposure (sunbathing frequency and solarium use within the past five years) do not seem to be strong risk factors for RA. Frequency of travels abroad was inversely associated to RA risk. The nature behind this association remains unclear.

Disclosure of Interests: Johanna Hagman: None declared, Bénédicte Delcoigne: None declared, Lars Klareskog: None declared, Lars Alfredsson: None declared, Johan Askling Grant/research support from: JA acts or has acted as PI for agreements between Karolinska Institutet and the following entities, mainly in the context of the ARTIS national safety monitoring programme of immunomodulators in rheumatology: Abbvie, BMS, Eli Lilly, Merck, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB Pharma

DOI: 10.1136/annrheumdis-2021-eular.1430

OP0237 EXPOSURE TO ENVIRONMENTAL AIR POLLUTANTS AS A RISK FACTOR FOR PRIMARY SJÖGREN'S SYNDROME: A POPULATION-BASED COHORT STUDY

K. S. K. MA[1], L. T. Wang[2]. [1]*National Taiwan University, Taipei, Taiwan, ROC, Department of Life Science, Taipei, Taiwan, Republic of China*; [2]*National Taiwan University Hospital, Department of Obstetrics & Gynecology, Taipei, Taiwan, Republic of China*

Background: Recent studies suggest that air pollution may play a role in autoimmune diseases. However, few of them report the correlation between air pollution and primary Sjögren's syndrome (pSS).

Objectives: We sought to determine whether people exposed to environmental fine particulate of air pollution have a higher risk of developing pSS.

Methods: We performed a retrospective population-based cohort study from the National Health Insurance Research Database (NHIRD) of Taiwan's population, using the international Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) to categorize each disease diagnosis. Air pollution data on Nitric oxide (NO), methane (CH4), and carbon monoxide (CO) were obtained from the Taiwan Air Quality-Monitoring Database (TAQMD), where daily air pollution data from community-based monitoring sites (78 sites since 1993) was available on a real-time basis. We followed up from January 1st, 1998 to the endpoint of SS diagnosis or to December 31, 2011. The daily average air pollutant concentrations were divided into 4 quartile-based groups (Q1-Q4). The incidence rate, hazard ratios (HRs), as well as 95% confidence intervals for pSS, were stratified by the quartiles of air pollutant concentration, and calculated with a Cox proportional regression model. Finally, Ingenuity Systems Pathway Analysis (IPA) was conducted to identify activated pathways among air way epithelial cells exposed to airborne coarse, fine, and ultrafine particles, and parotid gland tissues from pSS patients using Z-score visualization.

Results: A total of 200 patients were diagnosed with SS. The mean age of patients with pSS was 53.1 years. The incidence of pSS was 0.11%. With the increase in exposure concentrations of nitrogen dioxide, methane, and carbon monoxide (from Q1 to Q4), the incidence rate for pSS of per 1000 person-years increased from 0.7 to 1.19, from 0.93 to 2.14, and from 0.57 to 1.06, respectively. Moreover, compared with Q1, the adjusted HR in Q4 after adjusting for age, gender, monthly income and urbanization levels increased to 1.86, 2.21 and 2.04, respectively. IPA analyses suggested that the underlying cellular mechanisms involved up-regulation of chronic inflammatory pathways including fibrosis signaling pathway.

Conclusion: Exposure to air pollutants, specifically NO, CH4, and CO, was associated with SS development, mostly driven by fibrotic signaling cascades occurred during chronic inflammation.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3983

OP0238 DRUG COST FOR BIOLOGIC AND TARGETED SYNTHETIC DMARDS FOR RHEUMATOID ARTHRITIS PATIENTS IN NORWAY FROM 2010 TO 2019 - A COUNTRY WITH A NATIONAL TENDER SYSTEM FOR DRUG PRESCRIPTION

A. Brkic[1], A. Diamantopoulos[2], G. Haugeberg[3,4], on behalf of BioRheuma research project. [1]*Sørlandet Hospital, Kristiansand, Research Department,*

Kristiansand, Norway; [2]*Martina Hansens Hospital, Department of Rheumatology, Bærum, Norway*; [3]*Sørlandet Hospital Kristiansand, Division of Rheumatology, Department of Medicine, Kristiansand, Norway*; [4]*NTNU, Norwegian University of Science and Technology, Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, Trondheim, Norway*

Background: Biologic and Target Synthetic disease-modifying antirheumatic drugs (BTSs) have caused a paradigm shift in the treatment of patients with inflammatory joint disorders, e.g., rheumatoid arthritis (RA), where remission is now attainable [1]. The high cost of BTSs has caused restrictions on use and prescription, contributing to inequality of care worldwide [2]. An annual tender system was introduced in 2008 in Norway to reduce the costs of these drugs [3].
Objectives: Explore changes in drug costs for BTSs for RA patients treated at Norwegian rheumatology outpatient clinics between 2010 and 2019.
Methods: The project BioRheuma (BIOlogic treatment of patients suffering from inflammatory RHEUMAtic disorders in Norway) aimed to monitor patients treated with BTSs while using a designed computer program. Anonymized data files from the ten participating centers were merged and analyzed (EXCEL and SPSS). For each year in the ten-year period, the annual total cost for BTSs and mean BTS cost for treatment of one patient was calculated for all current BTSs users, for all those who started BTSs, and for patients starting naïve to BTSs. The cost was calculated based on price offers given at the annual tender process for the different years.
Results: The number of registered RA patients in the databases increased from 4909 in 2010 to 9335 in 2019. Simultaneously, the number of patients treated with BTSs increased from 1959 (39.9%) in 2010 to 4209 (45.1%) in 2019. The total treatment expenditure of these BTS treated patients was lowest in 2010 with 226 million Norwegian Kroner (NOK), highest in 2014 (350 million NOK) treating 3448 patients, and second-lowest in 2019 (255 million NOK).
The number of BTSs used for each year (Figure 1) is shown for all current users, all who started new BTSs treatment, and those starting BTSs naïve to BTSs. The same figure also reports the average cost of treating one RA patient with BTSs in these three groups. For the current users of BTSs, when the number of treated patients during follow-up doubled, the mean cost to treat one patient with BTSs was reduced by approximately 50% (decreasing from 115497 NOK in 2010 to 60701 NOK in 2019). The number of patients starting on BTSs approximately doubled, while keeping a steady small increase for the naïve patients to BTSs (382 in 2010 to 405 in 2019). The average starting treatment cost decreased from 114549 NOK in 2010 to 37384 NOK in 2019, and from 114987 NOK in 2010 to 28249 NOK in 2019, for patients starting on BTSs and for patients naïve to BTSs, respectively.

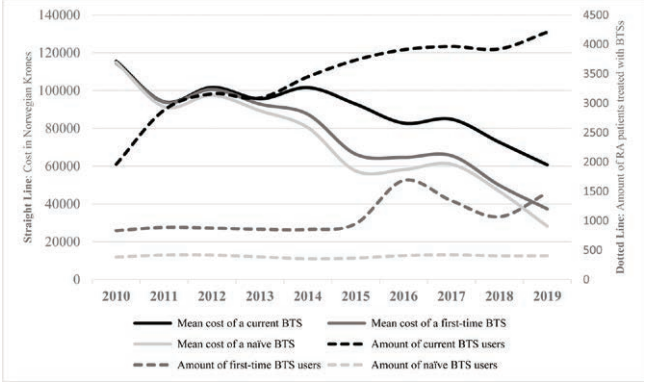


Figure 1. A ten-year overview of treating RA patient with BTSs

Conclusion: Our data shows that the average annual costs of treating a Norwegian RA patient on a current BTS, with a national tender system, were reduced by approximately 50% over the ten years 2010-19. For patients starting on a BTS, the average annual cost was reduced by approximately 75%. The consequence for the payers is that treatment can be offered at a lower price, and thus costly drugs may become more available for patients. We believe that mechanisms like the Norwegian tender system enforced upon the commercial pharmaceutical market improve competition and increase availability and use of costly drugs.

REFERENCES:
[1] Smolen JS, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Ann Rheum Dis 2020;79;685-99.
[2] Bergstra SA, et al. Inequity in access to bDMARD care and how it influences disease outcomes across countries worldwide: results from the METEOR-registry. Ann Rheum Dis 2018;77:1413–20.
[3] Norwegian Hospital Procurement. (Jan 2021). Available from: https://sykehusinnkjop.no.
Acknowledgements: To all members of the BioRheuma project
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2243

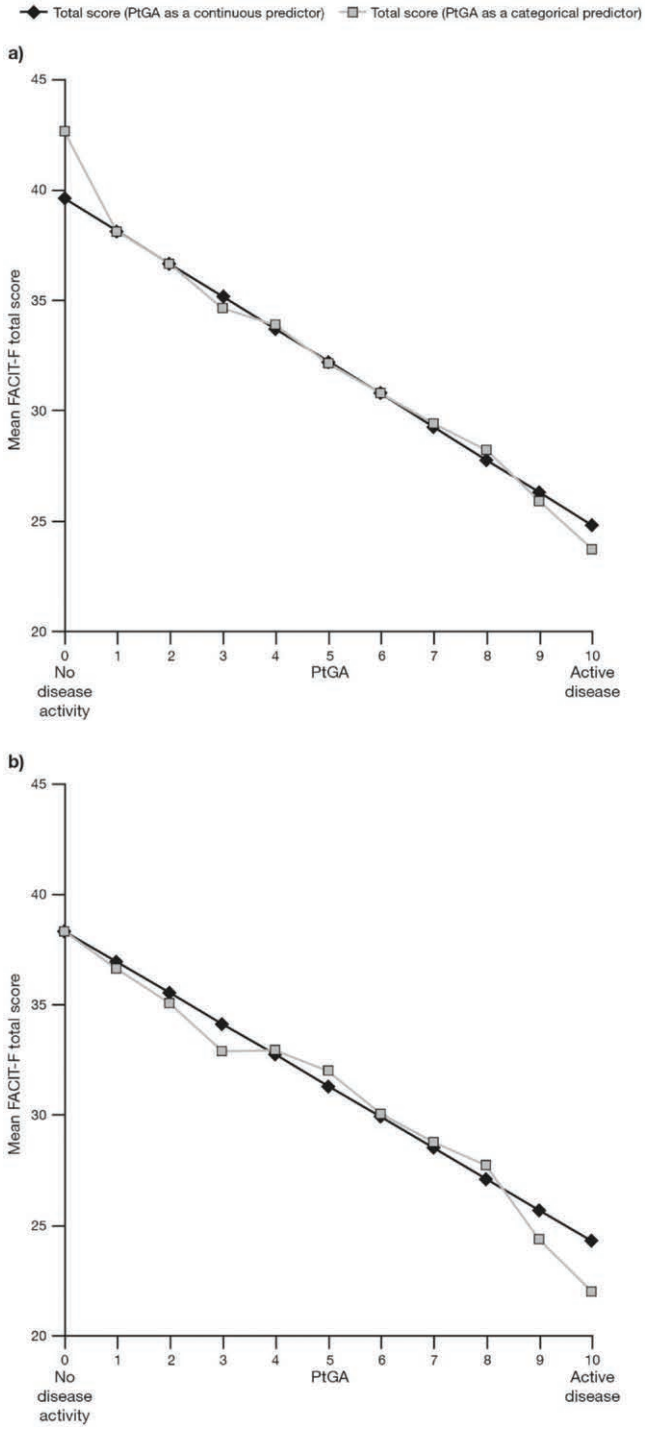
OP0239 PSYCHOMETRIC EVALUATION OF FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY-FATIGUE IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS

D. Cella[1], W. Lenderking[2], P. Chongpinitchai[3], A. G. Bushmakin[4], O. Dina[5], L. Wang[4], J. C. Cappelleri[4], V. Navarro-Compán[6]. [1]*Northwestern University Feinberg School of Medicine, Department of Medical Social Sciences, Chicago, IL, United States of America*; [2]*Evidera, Patient-Centered Research, Waltham, MA, United States of America*; [3]*Evidera, Bethesda, MD, United States of America*; [4]*Pfizer Inc, Inflammation and Immunology, Groton, CT, United States of America*; [5]*Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*; [6]*University Hospital La Paz, Rheumatology Department, Madrid, Spain*

Background: Due to its impact on their health-related quality of life (QoL), fatigue is considered a core domain of disease assessment in patients (pts) with ankylosing spondylitis (AS). Psychometric data analyses in pts with rheumatoid and psoriatic arthritis have previously demonstrated that the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) is a reliable and valid measure in these pt populations,[1,2] but there are limited data supporting the psychometric validity and reliability of the FACIT-F scale in adult pts with active AS.
Objectives: To further evaluate the psychometric properties of the FACIT-F scale in adult pts with active AS.
Methods: This post hoc analysis used data from the Phase (P)2 (NCT01786668, Study 1) and P3 (NCT03502616, Study 2) studies of tofacitinib in pts with active AS. Second-order confirmatory analysis (CFA) evaluated the measurement model of FACIT-F with two domains (Experience and Impact) and the total score at baseline (BL) and the studies' respective primary analysis time points, Week (W)12 (Study 1) or W16 (Study 2). At the same time points, internal consistency reliability was examined by Cronbach's Coefficient alpha (α), and convergent validity was assessed through correlations of FACIT-F domain and total scores with a set of pt-reported outcomes (PROs): Pt Global Assessment of Disease Activity (PtGA), total back pain/nocturnal spinal pain due to AS, Short Form-36 Health Survey (SF-36v2), Bath AS Functional Index, Bath AS Disease Activity Index and ASQoL. Test-retest reliability was assessed by calculating Intraclass Correlation Coefficients (ICCs). The known-groups validity assessment was derived from an anchor-based repeated measures longitudinal model, with PtGA scores as the anchor (PtGA represented pt state from 'no disease activity' to 'very active disease' [PtGA=0 and 10, respectively]), and FACIT-F domain/total scores as the outcome. Estimations of ability to detect change and meaningful within-pt change (MWPC) were derived from anchor-based repeated measures longitudinal models, with change from BL in PtGA scores as the anchor and change from BL in FACIT-F domain/total scores as the outcome.
Results: The CFA model fit the data well (Bentler's Comparative Index ≥0.92 at BL, W12 [Study 1] and W16 [Study 2]), supporting the measurement model of the FACIT-F scale in pts with AS. Across time points in each study, the FACIT-F domain and total scores demonstrated excellent internal consistency (Cronbach's Coefficient α ≥0.88), and correlations between FACIT-F domain/total scores, and all PROs assessed generally exceeded 0.40. Generally, in both studies, the largest correlations (0.62–0.85) were between FACIT-F domain/total scores and the SF-36v2 vitality domain score and ASQoL. Test-retest reliability was acceptable for all FACIT-F domain/total scores (ICC ranged from 0.75–0.89 in both studies). An approximately linear relationship was observed between FACIT-F total scores and PtGA scores in both studies (Figure), as well as for Experience and Impact domain scores. The differences in FACIT-F domain/total scores were large and statistically significant between 'no disease activity' and 'very active disease' pt groups (standardised effect size ≥1.17), supporting known-groups validity. Ability to detect change was evidenced by an approximately linear relationship between changes in PtGA and FACIT-F domain/total scores in both studies; when pts experienced a change in PtGA, values for FACIT-F domain/total scores changed

accordingly. Conservatively, MWPC was estimated as 6.3 for FACIT-F total score, and 2.8 and 3.6 for FACIT-F Experience and Impact domain scores, respectively.

Figure. Relationship between FACIT-F total score and PtGA in a) Study 1 and b) Study 2



Conclusion: This quantitative analysis of data from two clinical studies of tofacitinib demonstrates the validity and reliability of the FACIT-F scale in adult pts with active AS. Therefore, these findings support the use of FACIT-F in AS studies.

REFERENCES:
[1] Cella et al. J Rheumatol 2005; 32: 811-819.
[2] Cella et al. J Patient Rep Outcomes 2019; 3: 30.
Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Kirsten Woollcott, CMC Connect, and funded by Pfizer Inc.
Disclosure of Interests: David Cella Consultant of: AbbVie, Alexion Pharmaceuticals, Astellas Pharma, Bayer, Bristol-Myers Squibb, Clovis Oncology, Evidera, Exelixis, Horizon Therapeutics, Janssen, Merck/Schering-Plough, National Academy of Sciences, Novartis Pharma K.K. (Japan), Pfizer Inc, PledPharma and Regeneron, William Lenderking Shareholder of: Pfizer Inc, Employee of: Evidera, Peter Chongpinitchai Employee of: Evidera, Andrew G Bushmakin Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Oluwaseyi Dina Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lisy Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Joseph C Cappelleri Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Victoria Navarro-Compán Speakers bureau: AbbVie, Janssen, Eli Lilly, MSD, Pfizer Inc, UCB, Consultant of: AbbVie, Janssen, Eli Lilly, MSD, Pfizer Inc, UCB, Grant/research support from: AbbVie, Novartis
DOI: 10.1136/annrheumdis-2021-eular.62

OP0240

EPIDEMIOLOGY, PREDICTORS OF MORTALITY AND ROLE OF PROPHYLAXIS FOR PNEUMOCYSTITIS JIROVECI PNEUMONIA AMONG RHEUMATIC PATIENTS: A TERRITORY-WIDE STUDY

C. W. S. Chan[1], H. Y. Chung[1], W. Y. Yeung[1], C. S. Lau[1], P. H. LI[1]. [1]*The University of Hong Kong, Queen Mary Hospital, Hong Kong, Division of Rheumatology and Clinical Immunology, Department of Medicine, Hong Kong, Hong Kong (SAR)*

Background: *Pneumocystis jiroveci* pneumonia (PJP) is an opportunistic infection affecting immunocompromised individuals. Due to its high mortality, PJP prophylaxis is commonly recommended for many immunocompromising conditions. However, evidence regarding the burden and role of prophylaxis in PJP among rheumatic patients remains limited. There is lack of consensus for when and for whom to initiate prophylaxis. Delineating the epidemiology, predictors of mortality and efficacy of prophylaxis in PJP among rheumatic patients is urgently needed.
Objectives: To delineate the epidemiology of PJP, identify predictors of mortality and evaluate the usefulness of prophylaxis in rheumatology patients.
Methods: We performed a big-data cohort study based on the territory-wide healthcare database of the Hong Kong Hospital Authority. All patients with a diagnosis of anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), immune-mediated myositis (IMM), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), or spondyloarthritis (SpA) between 2015-2019 were included. PJP were identified based on physician diagnosis and/or positive microbiological results from deep respiratory tract specimens. Prophylaxis was defined as prescription of a prophylactic dose of co-trimoxazole for at least 2 weeks and/or inhaled pentamidine. Prevalence of PJP, prophylaxis and mortality among rheumatic patients were calculated. Demographics, blood parameters and immunosuppressants use was also collected for multivariate analysis. Number needed to treat (NNT) analysis was performed based on absolute risk reduction of PJP in patients with and without prior PJP prophylaxis.
Results: A total of 21,587 unique rheumatic patients were analysed (54% RA, 25% SLE, 13% SpA, 5% IMM, 2% AAV and 1% SSc). Between 2015-2019, 1141 (5.3%) patients were prescribed PJP prophylaxis and 48 (0.2%) developed PJP. None of those patients who developed PJP had received prophylaxis prior to infection. The risk of PJP was highest among SSc (1.8%), AAV (1.4%) and IMM (0.7%) patients, with NNT of SSc 36, AAV 48 and IMM 114. Within these disease entities, the majority of PJP occurred at prednisolone dose of 15mg/day (P15) or above (100% in SSc and IIM, 66.7% in AAV). Overall, PJP was associated with a mortality-rate of 39.6%. Glucocorticoid dose (daily prednisolone dose equivalent 29.1±23.5mg vs 11.4±7.2mg, P<0.01) and lymphopenia ($0.44x10^9$/L vs $0.90x10^9$/L, P= 0.04) at PJP diagnosis were associated with PJP mortality in rheumatic patients.
Conclusion: PJP is an uncommon but important infection in rheumatic patients associated with significant mortality. PJP prophylaxis is effective and should be considered in patients with SSc, AAV and IMM, especially in those receiving a steroid dose above P15.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4057

OP0241

SERIOUS INFECTION WITH TOCILIZUMAB COMPARED TO TNF-INHIBITORS AND OTHER BDMARDS IN RHEUMATOID ARTHRITIS PATIENTS: DOES LINE OF THERAPY MATTER?

K. Lauper[1,2,3], L. Kearsley-Fleet[3], R. Davies[3], K. Watson[3], M. Lunt[3], K. Hyrich[3,4]. *[1]Hôpitaux Universitaires de Genève (HUG), Rheumatology, Genève, Switzerland; [2]Faculty of Medicine, University of Geneva, Internal Medicine, Genève, Switzerland; [3]Centre for Musculoskeletal Research, University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom; [4]Manchester University NHS Foundation Trust, National Institute of Health Research Manchester Musculoskeletal Biomedical Research Centre, Manchester, United Kingdom*

Background: In the real-world, tocilizumab is prescribed to a population of patients different from those prescribed TNF-inhibitors, often older with longer disease duration, worse functional status and more previous b- or tsDMARDs.
Objectives: The aim of this study was to evaluate if and how the risk of serious infection on tocilizumab and other bDMARDs differs when stratifying by line of therapy in a real-world population of rheumatoid arthritis patients.
Methods: We included patients registered in the BSRBR-RA treated with tocilizumab, etanercept, adalimumab, infliximab, certolizumab, abatacept or rituximab, including biosimilars. Primary outcome was the occurrence of a serious infection (defined as infection requiring hospitalisation, intravenous antibiotics or resulting in death). Primary covariate of interest was line of therapy (from first to fifth line of therapy). Every change to another b- or tsDMARD was considered a new line of therapy, but not a change between a bio-original and a biosimilar. Hazard ratios (HR) of serious infections were estimated using an inverse probability weighted Cox regression, based on a propensity score including baseline patient and disease characteristics, and adjusting for time in study (see Table). The reference group was etanercept, which included the highest number of patients. Treatment exposure was analysed without and with stratification by line of therapy.

Table.

	N	ETN	TCZ	ADA	IFX	CERT	RTX	ABA
N	33,916	10,655	2,632	7,839	4,430	1,616	5,556	1,188
Patient-years		19,129	4,342	14,504	8,135	2,726	12,009	1,686
Infections		807	192	681	481	74	433	74
Incidence per 100 patient-years (95%CI)		4.2 (3.9-4.5)	4.4 (3.8-5.1)	4.7 (4.4-5.1)	5.9 (5.4-6.6)	2.7 (2.2-3.4)	3.6 (3.3-4.0)	4.0 (3.2-5.1)
Unadjusted HR (95%CI)		Ref.	1.0 (0.9-1.2)	1.1 (1.0-1.2)	1.4 (1.2-1.6)	0.6 (0.5-0.8)	0.9 (0.8-1.0)	0.9 (0.7-1.2)
Adjusted HR* (95% CI)								
All lines of therapy	33,916	Ref.	1.2 (1.0-1.5)	1.1 (1.0-1.3)	1.3 (1.1-1.6)	0.8 (0.6-1.0)	1.0 (0.8-1.1)	1.2 (0.8-1.7)
1st line	16,152	Ref.	0.9 (0.5-1.5)	1.1 (1.0-1.3)	1.3 (1.1-1.6)	0.6 (0.5-0.9)	1.6 (1.2-2.2)	-
2nd line	10,378	Ref.	1.4 (1.0-2.0)	1.1 (0.9-1.4)	1.1 (0.7-1.6)	0.9 (0.4-2.2)	1.0 (0.8-1.2)	0.9 (0.5-1.9)
3rd line	4,676	Ref.	1.4 (0.9-2.3)	1.3 (0.8-2.2)	0.9 (0.4-1.9)	0.9 (0.3-2.9)	0.8 (0.5-1.2)	1.5 (0.7-2.9)
4th line	1,947	Ref.	1.0 (0.5-2.3)	1.3 (0.4-3.7)	1.4 (0.5-4.4)	0.2 (0.0—2.1)	1.0 (0.5.-2.2)	0.9 (0.4-2.3)
5th line	763	Ref.	0.9 (0.2-3.5)	2.5 (0.5-12.4)	0.7 (0.1-7.1)	3.3 (0.6-18.4)	0.9 (0.2-3.5)	0.8 (0.2-3.5)

ABA, abatacept; ADA, adalimumab; CERT, certolizumab; ETN, etanercept; HR, hazard ratio; IFX, infliximab; RTX, rituximab; TCZ, tocilizumab*Adjusted using inverse probably weighting (with age, gender, concomitant steroids, concomitant DMARDs, comorbidities, seropositivity, smoking, disease duration, HAQ and DAS28 at baseline in the model) and time since study entry (categorised from 0 to 4, 0 starting just before or at the moment of entering study, 1 starting during the first year, 2 starting during the second year until 4 for the fourth year and more)

Results: A total of 33,916 treatment courses were included (Table) contributing to 62,532 years of follow-up. Compared to etanercept, participants starting abatacept, tocilizumab and rituximab were older, had more previous bDMARDs, longer disease duration and more comorbidities. The crude HR of serious infections were higher with infliximab and adalimumab, lower with certolizumab and rituximab, and not significantly different for abatacept and tocilizumab compared to etanercept. After adjustment, HR of serious infections were higher with tocilizumab, adalimumab and infliximab. However, when stratified by line of therapy, HR were no longer significantly different compared to etanercept for tocilizumab, adalimumab and infliximab for most lines of therapy.
Conclusion: Whilst initially there appears to be a difference in rates of serious infection between biologic therapies, line of therapy may be a confounding factor when comparing the risk of serious infections between bDMARDs.

Disclosure of Interests: Kim Lauper Consultant of: Gilead-galapagos, Grant/research support from: AbbVie, Lianne Kearsley-Fleet: None declared, Rebecca Davies: None declared, Kath Watson: None declared, Mark Lunt: None declared, Kimme Hyrich Consultant of: AbbVie, Grant/research support from: Pfizer, BMS
DOI: 10.1136/annrheumdis-2021-eular.595

Systemic sclerosis, myositis - etiology, pathogenesis and animal models

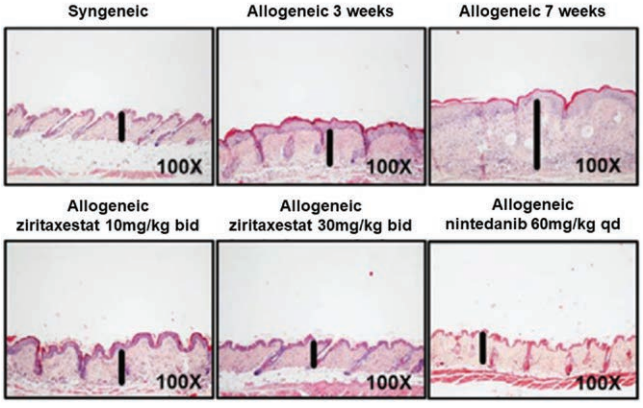
OP0242

EFFECTS OF THE AUTOTAXIN INHIBITOR ZIRITAXESTAT ON SKIN AND LUNG FIBROSIS IN A MURINE GRAFT-VERSUS-HOST DISEASE MODEL OF SYSTEMIC SCLEROSIS

Y. Zhang[1], L. Summa[1], B. Heckmann[2], J. H. W. Distler[1]. *[1]Universitätsklinikum Erlangen, Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany; [2]Galapagos SASU, Drug Innovation, Romainville, France*

Background: There is an unmet medical need for new drugs to treat systemic sclerosis (SSc). Autotaxin (ATX) is a widely expressed enzyme that regulates diverse cellular processes, including proliferation, differentiation and migration, and has been implicated in the pathogenesis of SSc. Targeting ATX is a promising new strategy for treating SSc. The autotaxin inhibitor ziritaxestat (GLPG1690) is a potential first-in-class disease-modifying drug for SSc that has been shown to improve skin score in the Phase 2a NOVESA (NCT03798366) trial in patients with SSc.
Objectives: To investigate the effects of ziritaxestat in a chronic graft-versus-host disease (cGvHD) murine model of SSc.
Methods: Effects of ziritaxestat (10 or 30 mg/kg twice daily [bid]) on disease activity were assessed in a cGvHD murine model of SSc (allogeneic bone marrow transplantation [BMT] with B10.D2 donor and BALB/c recipient; syngeneic mice as controls). Ziritaxestat or nintedanib (60 mg/kg once daily [qd]) as active comparator was administered 21 d after BMT and continued for 35 d. Effects of ziritaxestat were assessed by clinical monitoring, histologic assessment of skin and lungs (dermal thickness, Ashcroft scores and collagen-covered area), immunofluorescence staining with Trichrome and Sirius Red for myofibroblasts, and biochemical analysis of collagen content, as measured by hydroxyproline levels.
Results: Ziritaxestat 30 mg/kg bid for 35 days significantly reduced the clinical cutaneous score in the murine cGvHD model by 57% ($p<0.05$) compared with vehicle, and to a similar extent when compared with nintedanib 60 mg/kg (38%; $p<0.05$). Dermal accumulation of collagen and dermal thickness (Figure) were reduced with ziritaxestat 10 and 30 mg/kg compared with vehicle. At 30 mg/kg, ziritaxestat reversed the increase in the allogeneic model ($p<0.001$), returning dermal thickness to the levels in non-fibrotic control mice. Ziritaxestat also significantly reduced pulmonary fibrosis in the cGvHD model, with reductions in the fibrotic lung area (ziritaxestat 10 and 30 mg/kg; $p<0.001$ for both) and Ashcroft scores (ziritaxestat 30 mg/kg; $p<0.05$). Ziritaxestat was generally well tolerated.
Conclusion: Ziritaxestat improved the histological, biochemical and clinical symptom readouts of dermal and pulmonary fibrosis in a murine model, consistent with a broad and rapid disease-modifying effect in SSc.

Figure. Effect of ziritaxestat on dermal thickness in a murine cGvHD model of SSc



Acknowledgements: This study was funded by Galapagos NV (Mechelen, Belgium). Medical writing/editorial support was provided by Ian Faulkner, PhD (Aspire Scientific, Bollington, UK) funded by Galapagos NV.
Disclosure of Interests: Yun Zhang Employee of: 4D Science, Lena Summa Employee of: 4D Science, Bertrand Heckmann Shareholder of: Galapagos,

Employee of: Galapagos, Jörg H.W. Distler Shareholder of: 4D Science, Consultant of: Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GlaxoSmithKline, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, Grant/research support from: Anamar, Active Biotech, Array Biopharma, ARXX, aTyr, Bristol Myers Squibb, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GlaxoSmithKline, Inventiva, Novartis, Sanofi-Aventis, RedX and UCB

DOI: 10.1136/annrheumdis-2021-eular.1839

OP0243 AN APPROACH COMBINING TRANSCRIPTOMIC AND TOPOGRAPHIC ANALYSIS REVEALS A POTENTIAL ROLE OF PROTEASOME AND AUTOPHAGY DEREGULATION IN THE PATHOPHYSIOLOGY OF DERMATOMYOSITIS

L. Debrut[1], G. Laverny[2], P. Mertz[3], M. Giannini[4], M. Pizzimenti5, A. Charlot5, C. Keime[6], B. Lannes[7], D. Metzger[2], B. Geny[8], J. Sibilia[4], A. Meyer[4]. *[1]Centre de Recherche en Biomédecine de Strasbourg, UR3072, mitochondrie, stress oxydant et protection musculaire, Strasbourg, France*; *[2]IGBMC, IGBMC, Illkirch, France*; *[3]CHU Strasbourg, Immunology, Strasbourg, France*; *[4]CHU Strasbourg, Rhumatologie, Strasbourg, France*; *[1]Centre de Recherche en Biomédecine de Strasbourg, UR3072, mitochondrie, stress oxydant et protection musculaire, Strasbourg, France*; *[6]IGBMC, Genomeast, Illkirch, France*; *[7]CHU Strasbourg, Anatomopathologie, Strasbourg, France*; *[8]CHU Strasbourg, Explorations fonctionnelles, Strasbourg, France*

Background: Dermatomyositis (DM) is a rare autoimmune muscle disease characterized by an atrophy and a type-I interferon signature in perifascicular fibers. We recently showed that muscle mitochondrial dysfunction is also a characteristic of this disease that participates to both decrease exercise capacity and maintenance of inflammation (1). Pathophysiological mechanisms underlying these characteristics are unknown.

Objectives: The objective of this study is to reveal the mechanisms underlying the modifications of perifascicular fibers during DM, taking advantage of a method combining transcriptomic and topographical information.

Methods: Fourteen patients with recent (<6 months) untreated myositis (DM: n=7, other myositis: n=7) who underwent a biopsy of the deltoid muscle for diagnostic purposes were included. Seven other patients with suspected but not confirmed neuromuscular pathology (normal creatine kinase level, electromyogram and deltoid biopsy) were also included (no myopathy: n=7). Under the control of optical microscopy, perifascicular fibers (about 400 fibers) and endofascicular fibers (about 400 fibers) were microdissected by laser. The transcriptome of endofascicular fibers and perifascicular fibers in all three groups of patients were then obtained by massive sequencing of total messenger RNA. The DAVID database (2) (http://david.abcc.ncifcrf.gov) were used to determine the deregulated molecular pathways in the perifascicular fibers during DM.

Results: 482 transcripts were differently expressed in perifascicular fibers of patients with DM compared to perifascicular fibers of the 2 other groups (348 overexpressed and 134 underexpressed). The most overexpressed transcripts were involved in the type I interferon response while the most underexpressed transcripts were involved in mitochondria and in proteasome functioning. The study of the transcripts differentially expressed in perifasicular versus endofascicular fibers revealed that there is a physiological perifascicular signature: in patients without myopathy, 83 genes were overexpressed and 54 were underexpressed in perifascicular fibers compared to endofascicular fibers. This physiological perifascicular signature was abolished in patient with myositis (DM and other myositis). In the group of patients with DM (but not other myositis), a specific perifascicular signature (18 genes overexpressed and 10 genes underexpressed in perifascicular fibers compared to endofascicular fibers) was identified. The most deregulated transcripts in DM perifascicular fibers were involved in autophagy/mitophagy, mitochondria and proteasome pathways.

Conclusion: In the physiological state, perifascicular fibers are characterized by a different transcriptomic profile from endofascicular fibers. During DM, this physiological perifascicular signature is abolished and replaced by a transcriptomic signature that reveal a potential role of proteasome and autophagy deregulation in the pathophysiology of DM.

REFERENCES:

[1] Meyer et al. IFN-β-induced reactive oxygen species and mitochondrial damage contribute to muscle impairment and inflammation maintenance in dermatomyositis Acta Neuropathol. 2017;134:655-666.

[2] Huang, D. W. et al. The DAVID Gene Functional Classification Tool: a novel biological module-centric algorithm to functionally analyze large gene lists. Genome Biol 8, R183 (2007).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2586

OP0244 28 NEW AUTOANTIBODIES AGAINST GPCR, GROWTH FACTORS AND GROWTH FACTOR RECEPTORS ARE ASSOCIATED WITH DISEASE MANIFESTATIONS IN SYSTEMIC SCLEROSIS

K. Sterner[1], C. J. K. Fouodo[2], I. König[2], A. Künstner[3], H. Busch[3], H. Heidecke[4], A. Schumann[5], A. Müller[5], G. Riemekasten[1], S. Schinke[5]. *[1]University of Lübeck, Department of Rheumatology and Clinical Immunology, Lübeck, Germany*; *[2]University of Lübeck, Institute of Medical Biometry and Statistics, Lübeck, Germany*; *[3]University of Lübeck, Lübeck Institute of Experimental Dermatology, Lübeck, Germany*; *[4]CellTrend GmbH, -, Luckenwalde, Germany*; *[5]UKSH Campus Lübeck, Department of Rheumatology and Clinical Immunology, Lübeck, Germany*

Background: The morbidity and mortality of systemic sclerosis (SSc) are largely determined by vascular and fibrotic pathologies. Levels of autoantibodies (ab) against G protein-coupled receptors (GPCR), growth factors (GF) and growth factor receptors (GFR) are altered in SSc compared to healthy controls (HC) [1]. Thus, higher angiotensin II receptor type 1 - (AT1R) and endothelin receptor type A - (ETAR) ab levels are associated with severe disease and SSc-related mortality [2]. CXC motiv chemokine receptor 3 - (CXCR3) and 4 - (CXCR4) ab have predictive value for deterioration of pulmonary fibrosis (PF) [3].

Objectives: We used statistical methods to identify associations between disease manifestations and 28 new ab directed against GPCR, GF and GFR in SSc.

Methods: Ab against the following targets were measured in sera from SSc patients (n = 177) and HC (n = 88): Adrenoceptors alpha-1 (ADRA1), alpha-2 (ADRA2), beta-1 (ADRB1), beta-2 (ADRB2); muscarinoceptors 1-5 (M1R - M5R); AT1R, ETAR, endothelin B receptor (ETBR); CXCR3, CXCR4; complement receptors 3a (C3aR) and 5a (C5aR); protease-activated receptors 1 (PAR1) and 2 (PAR2); vascular endothelial growth factor A (VEGFA) and its receptors 1 (VEGFR1) and 2 (VEGFR2), epithelial growth factor (EGF)/ - receptor (EGFR); hepatocyte growth factor (HGF)/ - receptor (HGFR), platelet-derived growth factor-AA (PDGFAA), placental growth factor (PlGF).

The organ involvement (PF, cardiac involvement, PAH, gastrointestinal tract) and quantitative markers (modified Rodnan skin score, SSc activity score, pulmonary function, cardiac enzymes and echocardiography, routine laboratory, autoimmune diagnostics) as well as demographic data were recorded retrospectively at the time of sample collection. Statistical analysis was performed using the Mann-Whitney U test (MWU), Pearson correlations, ROC analysis, and age-adjusted logistic regression models.

Results: In SSc 20 of 28 measured ab levels are significantly altered compared to HC. According to the Pearson correlation matrix, the ab-levels are highly correlated and build a network that differs between HC and SSc. Furthermore, altered network signatures are formed in the differentiated analysis of several disease manifestations of SSc such as SSc-subtype or PF. Based on ROC analysis, FGF-ab, ADRB1-ab and PlGF-ab are well suited to predict SSc (Figure 1).

In addition, limited cutaneous SSc (lSSc) patients displayed lower levels of most ab than diffuse cutaneous SSc patients, whereas cardiac and pulmonary involvement are associated with higher ab levels. In the logistic regression lSSc is associated with lower levels of ab against M1R, M2R, C5aR, ETAR, AT1R, PAR1, EGFR. Higher levels for ab against M1R, M2R, ETBR, C5aR are associated with PF, higher levels of ab against complement receptors, adrenoreceptors and EGF with NT-proBNP elevation.

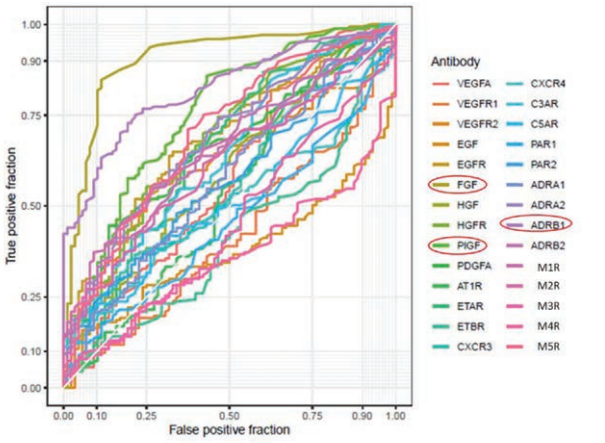


Figure 1: Receiver operating characteristic analyses for 28 new autoantibodies in systemic sclerosis (n =177) compared with healthy controls (n = 88). Ab against FGF, ADRB1 and PlGF may predict SSc.

Conclusion: The newly described antibodies against GPCR, GF and GFR are highly correlated. Associations with morbidity- and mortality-determining organ involvement indicate their possible functional relevance and novel pathophysiological mechanisms. As new biomarkers, some of the ab have prognostic value for SSc; for other manifestations, their value should be evaluated in further studies.

REFERENCES:

[1] Cabral-Marques, O., Marques, A., Giil, L.M. et al. GPCR-specific autoantibody signatures are associated with physiological and pathological immune homeostasis. *Nat Commun* **9,** 5224 (2018). https://doi.org/10.1038/s41467-018-07598-9

[2] Riemekasten G, Philippe A, Näther M, et al. Involvement of functional autoantibodies against vascular receptors in systemic sclerosis Annals of the Rheumatic Diseases 2011;70:530-536.

[3] Weigold, F., Günther, J., Pfeiffenberger, M. et al. Antibodies against chemokine receptors CXCR3 and CXCR4 predict progressive deterioration of lung function in patients with systemic sclerosis. Arthritis Res Ther 20, 52 (2018). https://doi.org/10.1186/s13075-018-1545-8

Disclosure of Interests: Kristina Sterner: None declared, Césaire J. K. Fouodo: None declared, Inke König: None declared, Axel Künstner: None declared, Hauke Busch: None declared, Harald Heidecke Shareholder of: Owner of Cell-Trend, Anja Schumann: None declared, Antje Müller: None declared, Gabriela Riemekasten: None declared, Susanne Schinke Grant/research support from: UCB sponsors EULAR registration fees

DOI: 10.1136/annrheumdis-2021-eular.1504

OP0245 ANTI-S100A4 MONOCLONAL ANTIBODY TREATMENT AMELIORATES SKIN FIBROSIS IN INFLAMMATORY AND NON-INFLAMMATORY PRE-CLINICAL MODELS OF SYSTEMIC SCLEROSIS

M. Tomčík[1], T. Trinh-Minh[2], C. T. Manh[2], H. Štorkánová[1], L. Štorkánová[1], L. Šenolt[1], J. Klingelhöfer[3], R. I. Hussain[3], J. Hallén[3], J. H. W. Distler[2]. [1]*Institute of Rheumatology and First Faculty of Medicine, Charles University, Department of Rheumatology, Prague, Czech Republic*; [2]*Department of Internal Medicine III and Institute for Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Department of Internal Medicine III, Erlangen, Germany*; [3]*Arxx Therapeutics, Arxx Therapeutics, Oslo, Norway*

Background: AX-202 is a monoclonal antibody that inhibits the bioactivity of S100A4. S100A4 is an alarm signal that is released from cells in response to stress or injury and functions as an amplifying mechanism of inflammation and fibrosis in the diseased tissue microenvironment. Previous in vitro studies have found that S100A4 induces fibroblast activation, sensitizes fibroblasts to the effects of TGFβ, drives epithelial-mesenchymal transition, and stimulates monocyte cytokine release (1-3). Moreover, S100A4-/- mice are protected from fibrosis in several animal models (1). In patients with systemic sclerosis (SSc), S100A4 is elevated both in lesional tissue and systemically and correlates with skin involvement, disease activity, and pulmonary function.

Objectives: The aim of this study was to assess the antifibrotic effects of murine AX-202 in two pre-clinical models of SSs reflecting both inflammation-mediated and inflammation non-mediated fibrosis and confirm the in vivo activity of humanized AX-202.

Methods: We first evaluated the effects of murine AX-202 in the bleomycin-induced skin fibrosis model and the tight-skin 1 (Tsk-1) model. In the bleomycin (BLM) model, fibrosis was induced by 3 weeks of BLM s.c. injections followed by 3 weeks of AX-202 treatment in parallel with continued BLM s.c. injections. The control groups included NaCl s.c. injections for 6 weeks, BLM s.c. injections for 6 weeks, or BLM s.c. injections for 3 weeks, followed by NaCl s.c. injections for 3 weeks. Three dosing regimens of AX-202 were tested: 3.75, 7.5, or 12.5 mg/kg i.p. every 3rd day. In the Tsk-1 model, treatment with 7.5 mg/kg i.p. every 3rd day was administered from week 5 until week 10. The control groups included pa mice, Tsk-1 mice, and Tsk-1 mice treated i.p. with isotype IgG. We subsequently evaluated the effects of humanized AX-202 in the model of BLM-induced skin fibrosis in a similar design as used for the murine AX-202 study. Three dosing regimens were tested: 8 mg/kg and 16 mg/kg i.p. every 3rd day and 24 mg/kg i.v. once weekly.

Results: In the BLM model, murine AX-202 (7.5 mg/kg) was effective both in the prevention of progression of pre-established skin fibrosis and in the induction of regression of fibrosis as assessed by the dermal thickness (-55%, p<0.0001 vs BLM for 6 weeks, and -23%, p<0.0001 vs BLM for 3 weeks), myofibroblast count and hydroxyproline content. Murine AX-202 also ameliorated fibrosis in the Tsk-1 model as assessed by the hypodermal thickness (-24%, p=0.01 vs Tsk-1 isotype control), myofibroblast count, and hydroxyproline content. In both models, the antifibrotic effects were associated with a reduction in pSMAD3 expression. Humanized AX-202 was effective in the prevention of progression of pre-established skin fibrosis in all doses tested across all endpoints (dermal thickness, myofibroblast counts, hydroxyproline content). In the two groups treated with 16 mg/kg i.p. and 24 mg/kg i.v., humanized AX-202 also induced regression of fibrosis (-83%, p<0.001, and -61%, p<0.001 vs BLM for 3 weeks, respectively). Both murine and humanized AX-202 were well tolerated in all study groups in both models.

Conclusion: We demonstrate that AX-202 confers potent antifibrotic effects in complementary models of SSc. These results confirm and expand previous data showing that inhibition of S100A4 by AX-202 is a promising potential therapeutic candidate for disease modification in SSc or other fibrotic conditions.

REFERENCES:

[1] Tomcik M et al. S100A4 amplifies TGF-beta-induced fibroblast activation in systemic sclerosis. Ann Rheum Dis. 2015;74(9):1748-55.

[2] Cerezo LA et al. The metastasis-associated protein S100A4 promotes the inflammatory response of mononuclear cells via the TLR4 signalling pathway in rheumatoid arthritis. Rheumatology (Oxford). 2014;53(8):1520-6.

[3] Fei F, et al. Role of metastasis-induced protein S100A4 in human non-tumor pathophysiologies. Cell Biosci. 2017;7:64.

Acknowledgements: The study was supported by Arxx Therapeutics and MHCR 023728.

Disclosure of Interests: Michal Tomčík: None declared, Thuong Trinh-Minh: None declared, Cuong Tran Manh: None declared, Hana Štorkánová: None declared, Lenka Štorkánová: None declared, Ladislav Šenolt: None declared, Jörg Klingelhöfer Employee of: Arxx Therapeutics, Rizwan I Hussain Employee of: Arxx Therapeutics, Jonas Hallén Employee of: Arxx Therapeutics, Jörg H.W. Distler Shareholder of: the stock owner of 4D Science, Consultant of: Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, Grant/research support from: Anamar, Active Biotech, Array Biopharma, ARXX, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB

DOI: 10.1136/annrheumdis-2021-eular.1968

OP0246 PREDICTIVE VALUE OF LABORATORY AND INSTRUMENTAL FINDINGS IN THE VERY EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS. ROLE FOR CXCL4 CHEMOKINE

M. Cadar[1], C. Angelelli[1], G. Pellegrino[1], K. Stefanantoni[1], R. Palazzo[2], R. Lande[2], L. Frasca[2], V. Riccieri[1]. [1]*Sapienza University of Rome, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Roma, Italy*; [2]*Italian National Institute of Health, National Centre for Pre-Clinical and Clinical Drug Research and Evaluation, Pharmacological Research and Experimental Therapy Unit, Roma, Italy*

Background: Systemic sclerosis (SSc) is a rare and progressive autoimmune disease, whose diagnosis is difficult in the early stages because of the lack of specific signs and symptoms. Criteria for a Very Early Diagnosis of SSc (VEDOSS) have been proposed to identify those patients affected by undifferentiated connective tissue disease (UCTD) at risk to develop SSc [1]. For the diagnosis of SSc a strict clinical and laboratory follow up is mandatory [2]. CXCL4 chemokine recently proved to be higher in early SSc [3][4][5].

Objectives: Aim of our study was to evaluate at baseline the main clinical-demographic and laboratory parameters in a group of VEDOSS patients, comparing these features during the follow-up, to detect any difference between progressors (P) and non-progressors (NP) into SSc. Furthermore, we dosed plasma levels of CXCL4.

Methods: We included 27 VEDOSS patients, defined by EUSTAR 2011 Criteria and not fulfilling the 2013 ACR/EULAR classification criteria of SSc, attending the Rheumatology Unit of Policlinico Umberto I in Rome from 2009 to 2020. Demographic, laboratory and instrumental features were analyzed, and, after a mean follow-up of 5.7±1,7 years, we compared the P to NP patients. Having obtained written informed consent, blood samples were taken at baseline to measure plasma levels of CXCL4 chemokine using an ELISA assay.

Results: At baseline the 27 VEDOSS patients (mean age 53.2±13.5 years, all females) had ANA positivity in 25 (93%) cases and Raynaud's phenomenon in 25 (93%) cases. In a mean follow-up time of 43.5 ± 23.1 weeks from the first clinical examination, 15 (55%) patients were classified as P into SSc. These P patients showed a significant association with SSc specific antibodies such as anti-Centromere, anti-Scl70 and anti-RNAPIII (p=0.014) as well as with a specific "*Scleroderma pattern*" at the nailfold capillaroscopy (p=0.022) respect to those NP into SSc. A group of 6 P patients evolved in less than 24 months (mean 19,6 ± 6,8 weeks) and were defined "*Fast Progressor*". They were also significantly associated with those autoantibodies considered as having a worse prognosis such as anti-Scl70 and anti-RNAPIII (p=0.005), and had a shorter duration of RP (88 vs 189.3 months) and a younger mean age (49.5 vs 55.4 years) respect to "*Slow Progressor*" (SSc evolving in >24 months). At baseline we detected significantly higher median plasma levels of CXCL4 in the 27 VEDOSS patients compared to 10 healthy subjects (9024±10559 pg/ml versus 348,5±684,3 pg/ml; p=0.0047). We also noticed a trend for lower CXCL4 levels in the "*Fast Progressor*" than in

the "*Slow Progressor*" (3303 ± 6065 pg/ml vs 13300 ± 10308 pg/ml; p=0.052) without reaching a significant value, due probably to the low number of cases.
Conclusion: Our study confirms that the presence of specific autoantibodies and capillaroscopic abnormalities correlate to an increased risk of developing SSc in patients with UCTD [6]. Beside we found significantly higher levels of CXCL4 in our 27 VEDOSS patients respect to controls, in agreement with other authors showing the association of this chemokine with early stages and specific organ involvement [4][5][7]. The finding of CXCL4 lower levels in "*fast progressor*" cases is consistent with our recent report of anti-CXCL4 antibodies in patients with early SSc, determining lower levels of this antigen [7]. We need deeper investigations to better evaluate the role of CXCL4 in the different stages of SSc.

REFERENCES:

[1] J. Avouac et al., Ann. Rheum. Dis., 2011.
[2] F. van den Hoogen et al., Ann. Rheum. Dis., 2013.
[3] G. Valentini et al., Clin. Exp. Med., 2017.
[4] R. Lande et al., Nat. Commun., 2019.
[5] L. van Bon et al., N. Engl. J. Med., 2014.
[6] M. Vasile et al., Clin. Exp. Rheumatol., 2018.
[7] R. Lande et al., Int. J. Mol. Sci., 2020.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2188

OP0247 IN MYOSITIS MUSCLE FIBRE PLAYS A DIRECT AND CRITICAL ROLE IN THERAPEUTIC RESPONSE TO GLUCOCORTICOIDS

M. Giannini[1], G. Laverny[2], D. Duteil[2], D. Rovito[2], A. L. Charles[3], B. Geny[4], D. Metzger[2], A. Meyer[5]. *[1]University of Strasbourg, Service de Physiologie et d'explorations fonctionnelles, Nouvel Hopital Civil, Centre de Référence des Maladies Autoimmunes Rares, Fédération de Médecine Translationnelle, UR3072, Strasbourg, Strasbourg, France*; *[2]University of Strasbourg, CNRS UMR7104, INSERM U1258, IGBMC, F-67400 Illkirch, Illkirch, France*; *[3]University of Strasbourg, Fédération de Médecine translationnelle, UR3072, Strasbourg, Strasbourg, France*; *[4]University of Strasbourg, Service de Physiologie et d'explorations fonctionnelles, Nouvel Hopital Civil, Fédération de Médecine Translationnelle, UR3072, Strasbourg, Strasbourg, France*; *[5]University of Strasbourg, Service de Physiologie et d'explorations fonctionnelles, Nouvel Hopital Civil, Centre de Référence des Maladies Autoimmunes Rares, Fédération de Médecine Translationnelle, UR3072, Strasbourg, Strasbourg, France*

Background: Myositis are rare autoimmune diseases, affecting more women than men, characterized by chronic inflammation of skeletal muscle causing muscle weakness, decreased quality of life and increased mortality.
Glucocorticoids (GC) are potent anti-inflammatory drugs, and are the first line treatment of myositis. They improve muscle strength of myositis patients (therapeutic effect), yet muscle recovery is generally only partial. Moreover, GC have an iatrogenic effect on skeletal muscle fibre leading to steroid myopathy. Thus myositis care has to be improved. Despite the autoimmune terrain of myositis, our team has recently shown that muscle fibres themselves develop immuno-metabolic modifications that participate to muscle weakness and perpetuation of the disease[1]. GC effects are mediated by the glucocorticoid receptor (GR), which is expressed in various cell types including immune cells and myofibres, but the cells mediating therapeutic responses remain to be determined.
Objectives: Unravel the mechanisms underlying the therapeutic effect of GC in myositis, particularly elucidate the role of skeletal muscle fibres.
Methods: Experimental myositis was induced in eight to ten week-old C57BL/6J female mice by a single intradermal injection of part of skeletal muscle fast-type C protein along with Freund's adjuvant and an intraperitoneal (IP) injection of pertussis toxin, as previously described[2]. Prednisone (PDN) was administered 14 days (D) after the immunization at 1 mg/kg/day for 7 days by gavage. Mice were euthanized 21 days after myositis induction. Muscle strength was assessed by grip test at D 0, before the 1st PDN administration (D 14) and the day before sacrifice (D 20). To investigate whether the PDN effects are mediated by myofibre, we generated transgenic mice carrying two LoxP sites within the GR gene in muscle, expressing the tamoxifen-inducible Cre-ERT2 recombinase selectively in skeletal muscle fibre (HSA-CreERT2/GR L2/L2). Tamoxifen (1 mg/day for 5 days by IP injection) was administered 9 days after immunization to induce GR ablation selectively in skeletal muscle fibres (GR(i)skm-/- mice). Similar treatments were applied to GR L2/L2 that do not express Cre-ER(T2), and served as controls.
We compared 4 groups of myositis mice, GR L2/L2 treated by PDN (n=9) or vehicle (n=9) and GR(i)skm$^{-/-}$ treated by PDN (n=10) or vehicle (n=10), by grip test and at the histological level (hematoxylin-eosin (HE) and Gomori trichrome (GT) staining). Moreover, LC3 expression was studied by RTqPCR and western blot.
Results: Muscle strength was decreased in both GR L2/L2 and GR(i)skm$^{-/-}$ myositis mice from D 14 to D 20. GR L2/L2 myositis mice recovered muscle strength after PDN treatment; no significant difference compared to D 0 was detected. In contrast, PDN did not improve muscle strength in GR(i)skm$^{-/-}$ myositis mice (Figure 1).
HE and GT staining did not reveal quantitative differences in inflammatory infiltrate. Necrotic and degenerative fibres were detected in the 4 groups. At RTqPCR, LC3, an autophagy marker, was upregulated in PDN-treated GR L2/L2 myositis mice compared to untreated GR L2/L2 myositis mice; moreover it was 2-fold more expressed in PDN-treated GR L2/L2 myositis mice compared to PDN-treated GR(i)skm$^{-/-}$ mice.
Conclusion: GR in skeletal muscle fibre is crucial to mediate the therapeutic response to GC in a murine model of myositis. Autophagy is one of the candidate pathways controlled by myofibre GR underlying this effect.

REFERENCES:

[1] Meyer A et al. IFN-β-induced reactive oxygen species and mitochondrial damage contribute to muscle impairment and inflammation maintenance in dermatomyositis. Acta Neuropathol. 2017 Oct;134(4):655-666.
[2] Sugihara T et al. A new murine model to define the critical pathologic and therapeutic mediators of polymyositis. Arthritis Rheum. 2007 Apr;56(4):1304-14.

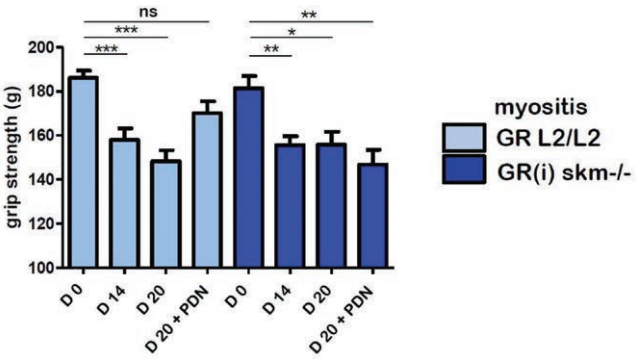


Figure 1. Grip test analysis in GR L2/L2 and GR(i) skm-/- myositis mice. ns, not significant; * p<0.01; ** p<0.001; *** p<0.0001

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2863

OP0248 DEVELOPMENT OF A 3D SKIN MICROTISSUE MODEL FOR FIBROTIC DISEASES

E. Pachera[1], G. Kania[1], A. Juengel[1,2], M. Calcagni[3], O. Distler[1,2]. *[1]Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland*; *[2]Department of Physical Medicine and Rheumatology, Balgrist University Hospital, University of Zurich, Zurich, Switzerland*; *[3]Department of Hand Surgery, Balgrist University Hospital, University of Zurich, Zurich, Switzerland*

Background: Traditional preclinical approaches, such as two-dimensional cell culture and animal models, are often inadequate to mimic the pathophysiological features of complex diseases such as systemic sclerosis (SSc). Human specific targets, such as the recently described pro-fibrotic long non coding RNA (lncRNA) H19X[1], are becoming increasingly relevant in preclinical research, creating the need of new strategies and tools in translational medicine. The employment of novel three-dimensional (3D) culture systems, where multiple cell types are included, is filling an important gap left by the traditional preclinical methods.
Objectives: To develop an easy to produce 3D fibrotic skin microtissues model for translational proof of concept studies.
Methods: Two thousand five hundred dermal fibroblasts isolated from skin of SSc patients were seeded in ultra-low attachment 96-well plates. Fibroblast were let to aggregate into spheres for 48h. Two thousand five hundred primary normal human keratinocytes were added to the culture and let to layer onto the fibroblast spheres for 72h. H19X silencing experiments were used as proof of concept studies. H19X silencing with antisense oligonucleotides or transfections with a scrambled control were performed in fibroblasts prior to the sphere formation for 24h. TGFβ (10 ng/ml) was added to microtissue to exacerbate the fibrotic phenotype. Haematoxylin eosin staining as well as immunohistochemistry staining for vimentin and cytokeratin 10 was performed. Skin microtissues were processed for RNA and protein isolation. Pro-collagen Iα1 and fibronectin were quantified in the supernatants with ELISA.

Results: The microtissues presented a core of SSc fibroblast as revealed by vimentin staining and an external layer of keratinocytes as revealed by cytokeratin 10 staining, mimicking the human skin architecture. Gene expression analysis following TGFβ stimulation displayed induced expression of extracellular matrix gene *COL1A1* (p=0.044) and the myofibroblast marker *ACTA2* (p=0.018), indicating that the microtissues were able to develop a fibrotic response. Microtissues, where H19X was silenced, displayed reduced gene expression of *COL1A1* and *ACTA2* after TGFβ stimulation (*COL1A1* p=0.007, *ACTA2* p=0.045). Additionally, H19X silencing led to lower levels of αSMA protein expression (p=0.009) and pro-collagen1α1 secretion (p=0.039) in the supernatant of the microtissue cultures as revealed by Western Blot and ELISA, respectively. *FN1* expression and fibronectin protein levels were not significantly reduced in the microtissues after H19X silencing.

Conclusion: We were able to produce a 3D microtissue resembling skin architecture that can respond to fibrotic stimuli. Knockdown experiments of pro-fibrotic lncRNA H19X confirmed the potential of the model as screening platform for novel pro-fibrotic effectors. A future aim will be to optimize the model for high-throughput automated screening platforms.

REFERENCES:

[1] Pachera, E., et al. (2020). "Long noncoding RNA H19X is a key mediator of TGF-β–driven fibrosis." The Journal of Clinical Investigation 130(9): 4888-4905.

Disclosure of Interests: Elena Pachera: None declared, Gabriela Kania: None declared, Astrid Juengel: None declared, Maurizio Calcagni Speakers bureau: Arthrex, Consultant of: Medartis, Arthrex, SilkBiomaterials, Grant/research support from: Medartis, Oliver Distler Speakers bureau: Actelion, Bayer, Boehringer Ingelheim, Medscape, Novartis, Roche, Consultant of: Abbvie, Actelion, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Bayer, Baecon Discovery, Blade Therapeutics, Boehringer, CSL Behring, ChemomAb, Corpuspharma, Curzion Pharmaceuticals, Ergonex, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, -Kymera, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Sanofi, UCB, Grant/research support from: Abbvie, Actelion, Bayer, Boehringer Ingelheim, Kymera Therapeutics, Mitsubishi Tanabe

DOI: 10.1136/annrheumdis-2021-eular.3306

OP0249 SERUM PROTEOMIC BIOMARKERS DEFINE PATIENTS WITH SYSTEMIC SCLEROSIS WITH INTERSTITIAL LUNG DISEASE

M. De Santis[1], N. Isailovic[1], A. Ceribelli[1], F. Motta[1,2], M. Vecellio[2,3], C. Selmi[1,2]. *[1]Humanitas Clinical and Research Center - IRCCS, Rheumatology and Clinical Immunology, Rozzano, Italy*; *[2]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy*; *[3]University of Oxford, Botnar Research Center, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*

Background: Systemic sclerosis (SSc) is a systemic condition affecting multiple organs and thus being burdened by high morbidity and mortality; disease management is based largely on the early detection of organ involvement, particularly in the case of interstitial lung disease (ILD), ideally through noninvasive biomarkers. Beside serum autoantibodies associated with diffuse SSc, there is currently no reliable serum marker to predict the onset of SSc organ involvement, monitor its progression, and foresee the response to treatments. Proteomic analysis based on aptamer technology is a powerful method with the potential to address this unmet need in SSc.

Objectives: To identify serum biomarkers associated with ILD in SSc.

Methods: Serum samples from 6 women with SSc (3 with ILD at high-resolution pulmonary CT scan) and 7 age-matched female healthy controls (HC) were analyzed using the SOMAscan platform (SomaLogic, Inc., Boulder, CO, USA) to test more than 1300 proteins even at femtomolar concentration. Subsequent validation of candidate proteins was performed using ELISA in an independent cohort of 88 patients with SSc and 48 HC. Statistical analysis included Student's t-test and was assessed using the SomaSuite software (SomaLogic, Boulder, CO, USA).

Results: The proteomic analysis identified 33 proteins with significantly different serum levels in SSc cases compared to HC and 9 proteins differentiating SSc patients according to ILD (Table 1). Compared to HC, SSc sera manifested an altered expression of proteins involved in extracellular matrix formation and cell-cell adhesion (with higher Calpain, EphA5, IDS, MATN2, MMP-12, TNR4, and lower desmoglein-1, SNP25), angiogenesis (with higher anti-angiogenetic factors as angiopoietin-2 and kininogen high molecular weight) lymphocyte recruitment, activation, and signaling (with higher CXCL-1, LAG3 and lower SH21A) with an overall inhibition of neutrophil function (with lower G-CSF-R, CD177, calgranulin B).

Table 1. Significantly altered proteins at serum proteomic analysis of systemic sclerosis (SSc) with or without interstitial lung disease (ILD) and healthy controls (HC)

SSc versus healthy controls		SSc with ILD versus SSc without ILD and healthy controls	
Increased	Reduced	Increased	Reduced
Aldolase A	Adrenomedullin	FCRL3	BAFF
Angiopoietin-2*	ASGR1	IL-22BP**	DERM
C1QR1	C1s	MCP-3	
Calpain	C5	PDE11	
COLEC12 Eotaxin	Calgranulin B	PGP9.5	
EphA5	CD177	sICAM-5	
Fractalkine/CXCL-1	Desmoglein-1	Stratifin	
Granulins	Flt-3 ligand		
IDS Kininogen, HMV	G-CFS-R		
LAG-3	IL-1Ra		
Lamin-B1	Leptin		
LRP1b	Lypd3		
MATN2	SH21A		
MMP-12	SNP25		
STAT1 TMR4	TPBS2		

*significantly increased also at ELISA** significantly increased at ELISA only in SSc with ILD versus HC

The majority of proteins with higher levels in SSc with ILD compared to SSc without ILD were involved in intracellular signaling and cell cycle (FCRL3, PDE11, Stratifin), along with higher MCP-3, a monocyte chemoattractant, and sICAM-5, ligand for the leukocyte adhesion protein LFA-1. Of note, we found that increased IL-22BP, antagonist of IL-22, and decreased BAFF levels characterized SSc with ILD.

Conclusion: Aptamer proteomic analysis allowed to define serum profiles differentiating SSc patients from healthy controls and SSc with ILD from SSc without ILD; the proteins identified are involved in SSc pathogenic pathways and after further investigation on larger cohorts they can be used as reliable biomarkers.

Characters from table content including title and footnotes: 631

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3099

Imaging in axial spondyloarthritis – what is new?

OP0250 MRI VERTEBRAL CORNER INFLAMMATION AND FAT DEPOSITION ARE ASSOCIATED WITH WHOLE SPINE LOW DOSE CT DETECTED SYNDESMOPHYTES: A MULTILEVEL ANALYSIS

R. Stal[1], X. Baraliakos[2], A. Sepriano[1], F. A. Van Gaalen[1], S. Ramiro[1], R. Van den Berg[1], M. Reijnierse[3], J. Braun[2], R. B. M. Landewé[4], D. Van der Heijde[1]. *[1]Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; *[2]Rheumazentrum Ruhrgebiet, Rheumatology, Herne, Germany*; *[3]Leiden University Medical Center, Radiology, Leiden, Netherlands*; *[4]Amsterdam University Medical Center, Rheumatology, Amsterdam, Netherlands*

Background: A few studies have shown an association between vertebral corner inflammation (VCI) and vertebral corner fat deposition (VCFD) on MRI and syndesmophyte formation on cervical and lumbar conventional radiography.

Objectives: To investigate whether magnetic resonance imaging (MRI) patterns of VCI, VCFD and a combination of both are associated with the development of new or grown syndesmophytes as detected by whole spine low dose computed tomography (ldCT), thereby studying these associations also in the thoracic spine.

Methods: Patients in the Sensitive Imaging in Ankylosing Spondylitis cohort underwent MRI at baseline, 1 year and 2 years, and ldCT at baseline and 2 years. MRI lesions were scored by 3 central readers, using the SPARCC method for VCI and the CanDen method for VCFD, and coded as absent or present per timepoint and per reader. MRI patterns over time (Table) were based on patterns studied by Machado et al.[1] and deemed present if seen by ≥2 out of 3 readers. The patterns reflect hypothetical associations between presence and absence of VCI and VCFD, independently and combined, on ldCT detected new or grown syndesmophytes. Individual reader change scores were used for ldCT images, scored by 2 central readers with the Computed Tomography Syndesmophyte Score. New (CTSS 0 to 1, 2 or 3) and grown (CTSS 1 to 2 or 3; 2 to 3) syndesmophytes were grouped together to represent bone formation. Corners not at risk

for the outcome due to presence of a bridged syndesmophyte at baseline were excluded. Multilevel generalized estimated equations were used, with separate models per MRI pattern, accounting for correlations within patients and between ldCT readers.

Table 1. Effect of vertebral corner inflammation and vertebral corner fat deposition on syndesmophyte formation

Patterns of lesions over time on MRI	Corners with VCI/ VCFD pattern N(%)	OR (95% CI)
1. VCI at any TP, irrespective of VCFD	691 (15.0%)	**2.37 (1.49-3.78)**
2. VCFD at any TP, irrespective of VCI	1080 (23.5%)	**2.58 (1.97-3.39)**
3. VCI on ≥1 TP and absence of VCFD on all TPs	372 (8.1%)	**1.90 (1.15-3.13)**
4. VCFD on ≥1 TP and absence of VCI on all TPs	754 (16.4%)	**1.87 (1.41-2.48)**
5. VCI precedes VCFD	43 (0.9%)	2.20 (0.83-5.86)
6. VCI precedes or coincides with VCFD. VCFD does not precede VCI	198 (4.3%)	**2.33 (1.47-3.69)**
7. Absence of VCI and VCFD on all TPs	3108 (67.6%)	**0.35 (0.25-0.49)**

VCI, vertebral corner inflammation; VCFD, vertebral corner fat deposition; TP, timepoint.

Results: 50 patients were included, contributing a total of 4600 vertebral corners. Their mean age was 49.3 years (SD 9.8), 86% were male and 78% were HLA-B27+. Presence of VCI and VCFD patterns ranged from 43 (0.9%) to 3108 (67.6%) corners (Table), with the lowest frequency being for VCI preceding VCFD. Protection against syndesmophyte development was seen in case of absence of both VCI and VCFD (OR 0.35) and positive associations with ORs ranging from 1.87-2.58 were observed for various VCI/VCFD patterns. Nevertheless, out of all corners with a new or grown syndesmophyte, 47.3% of corners according to reader 1 and 43.9% according to reader 2 had neither VCI nor VCFD preceding the bone formation.

Conclusion: Presence of VCI or VCFD and combinations of the two, measured yearly on MRI, increased odds of bone formation 2 years later, whereas absence of both VCI and VCFD decreased the odds, showing that VCI and VCFD have some role in the development of syndesmophytes. However, almost half of all bone formation occurred in corners without VCI or VCFD, suggesting the presence of these lesions in yearly MRIs does not fully explain the development of syndesmophytes. This study confirmed that there is an association between VCI and VCFD and bone formation also for the thoracic spine and on ldCT compared to conventional radiography.

REFERENCES:

[1] Machado et al ARD 2016

Disclosure of Interests: Rosalinde Stal: None declared, Xenofon Baraliakos: None declared, Alexandre Sepriano: None declared, Floris A. van Gaalen Grant/ research support from: Novartis, Sofia Ramiro: None declared, Rosaline van den Berg: None declared, Monique Reijnierse: None declared, Juergen Braun: None declared, Robert B.M. Landewé: None declared, Désirée van der Heijde: None declared

DOI: 10.1136/annrheumdis-2021-eular.1337

OP0251 DATA-DRIVEN DEFINITIONS BASED ON INFLAMMATORY LESIONS FOR A POSITIVE MRI OF THE SPINE CONSISTENT WITH AXIAL SPONDYLOARTHRITIS

W. P. Maksymowych[1,2], R. G. Lambert[3], X. Baraliakos[4], S. Juhl Pedersen[5,6], U. Weber[7], I. Eshed[8], P. Machado[9], M. De Hooge[10], J. Sieper[11], S. Wichuk[1], D. Poddubnyy[11], M. Rudwaleit[12], D. Van der Heijde[13], R. B. M. Landewé[14], M. Østergaard[5,6], on behalf of ASAS MRImagine. [1]*University of Alberta, Medicine, Edmonton, Canada*; [2]*CARE Arthritis, Rheumatology, Edmonton, Canada*; [3]*University of Alberta, Radiology and Diagnostic Imaging, Edmonton, Canada*; [4]*Rheumazentrum Ruhrgebiet, Rheumatology, Herne, Germany*; [5]*COPECARE, Rheumatology, Copenhagen, Denmark*; [6]*Rigshospitalet, Rheumatology, Glostrup, Denmark*; [7]*Practice Buchsbaum, Rheumatology, Schaffhausen, Switzerland*; [8]*Sheba Medical Center, Radiology and Diagnostic Imaging, Tel Aviv, Israel*; [9]*University College London, Rheumatology, London, United Kingdom*; [10]*Ghent University Hospital, Rheumatology, Ghent, Belgium*; [11]*Charité Universitätsmedizin, Rheumatology, Berlin, Germany*; [12]*Klinikum Bielefeld, Rheumatology, Bielefeld, Germany*; [13]*Leiden University Medical Centre, Rheumatology, Leiden, Netherlands*; [14]*Academic Medical Center, Rheumatology, Amsterdam, Netherlands*

Background: The ASAS definition of a positive MRI for inflammation in the spine (ASAS-MRIspine+) is intended for classification of patients as having axSpA but is often misused for diagnostic purposes. This is problematic because bone marrow edema (BME) in the spine may occur in 20-40% of those with mechanical back disorders. The ASAS MRI group has generated updated consensus lesion definitions which have been validated on MRI spine images from the ASAS Classification Cohort.

Objectives: We aimed to identify quantitative cut-offs based on numbers of vertebral corners that define ASAS-MRIspine+, there being two gold standards: A. majority central reader decision as to the presence of spine MRI findings consistent with axSpA B. rheumatologist expert opinion diagnosis of axSpA.

Methods: Eight ASAS-MRI readers recorded MRI lesions in the spine according to recently updated ASAS definitions from 62 cases in an eCRF that comprises global assessment (MRI consistent with axSpA? (yes/no)), and detailed scoring of lesions for all sites in the spine. We calculated sensitivity and specificity for numbers of vertebral corners with BME where a majority of readers (≥5/8) agreed as to the presence of MRI findings consistent with axSpA. We selected cut-offs with ≥95% specificity. These cut-offs were analyzed for their predictive utility for rheumatologist diagnosis of axSpA by calculating positive and negative predictive values (PPV, NPV) and selecting cut-offs with PPV ≥95%. Both criteria were considered requirements for designation of MRI cut-offs defining ASAS-MRIspine+.

Results: MRI findings consistent with axSpA were observed by majority read in 8 (20%) of 40 cases diagnosed with axSpA, and 0 (0%) of 19 cases without axSpA. Cut-offs achieving specificity of ≥95% for MRI findings consistent with axSpA were 4 vertebral corners (sensitivity 75%) for all cases, 3 vertebral corners (sensitivity 37.5%) for cases with ≥1 additional location with inflammation, 1 vertebral corner (sensitivity 62.5%) in cases with ≥2 vertebral corner fat lesions (Table 1). All of the above cut-offs also had very high PPV (≥95%) for diagnosis of axSpA in cases diagnosed by the rheumatologist (Table 2).

Table 1. Majority readers agree MRI findings consistent with axSpA are present is the gold-standard external reference

MRI cut-offs	Sensitivity (95%CI)	Specificity (95%CI)
BME in ≥2 vertebral corners	87.5 (47.3 - 99.7)	87.0 (75.1 - 94.6)
BME in ≥ 3 vertebral corners	87.5 (47.3 - 99.7)	94.4 (84.6 - 98.8)
BME in ≥4 vertebral corners	**75.0 (34.9 - 96.8)**	**98.2 (90.1 - 100.0)**
Cases with ≥1 additional non-corner site inflammatory lesion		
BME in ≥2 vertebral corners	37.5 (8.5 - 75.5)	94.4 (84.6 - 98.8)
BME in ≥3 vertebral corners	**37.5 (8.5 - 75.5)**	**98.2 (90.1-100.0)**
Cases with ≥2 vertebral corner fat lesions		
BME in ≥1 vertebral corner	**62.5 (24.5 - 91.5)**	**100.0 (93.4-100.0)**
BME in ≥2 vertebral corners	62.5 (24.5 - 91.5)	100.0 (93.4-100.0)

Table 2. Predictive values of cut-offs for number of vertebral corners with BME according to the diagnostic ascertainment of the rheumatologist

MRI cut-offs	Sensitivity (95%CI)	Specificity (95%CI)	PPV	NPV
MRI findings consistent with axSpA ≥any 2 readers	52.5 (36.1 - 68.5)	94.7 (74.0 - 99.9)	95.5 (75.3 - 99.3)	48.6 (40.2 - 57.2)
MRI findings consistent with axSpA ≥majority read	20.0 (9.1 - 35.6)	100.0 (82.4 - 100.0)	100.0	37.3 (33.7 - 40.9)
BME in ≥ 4 vertebral corners	**17.5 (7.3 - 32.8**	**100.0 (82.4 - 100.0)**	**100.0**	**36.5 (33.3 - 39.9)**
Cases with ≥1 additional inflammatory lesion				
BME in ≥ 3 vertebral corners	**10.00 (2.8 - 23.7)**	**100.00 (82.4 - 100.0)**	**100.0**	**34.5 (32.2 - 36.9)**
Cases with ≥2 vertebral corner fat lesions				
BME in ≥1 vertebral corner	**12.50 (4.2 - 26.8)**	**100.00 (82.4 - 100.0)**	**100.0**	**35.2 (32.6 - 37.9)**

Conclusion: A cut-off of BME in ≥4 vertebral corners, or ≥3 corners in the setting of additional inflammatory lesions at other locations or corner fat, are primary candidates for defining ASAS-MRIspine+. These cut-offs apply to typical patients referred to a rheumatologist with a high index of suspicion of axSpA and may not be appropriate in other populations.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3914

OP0252 ARTHRITIS AND ENTHESITIS IN THE HIP AND PELVIS REGION IN SPONDYLOARTHRITIS – VALIDATION OF TWO WHOLE-BODY MRI METHODS

M. Wetterslev[1,2], R. G. Lambert[3,4], W. P. Maksymowych[5,6], I. Eshed[7], S. Juhl Pedersen[1], P. Bird[8], M. Stoenoiu[9], S. Krabbe[1], A. J. Mathew[1,2], V. Foltz[10], F. Gandjbakhch[10], J. Paschke[6], G. De Marco[11,12], H. Marzo-Ortega[11,12], P. Carron[13,14], A. E. F. Poulsen[1], J. L. Jaremko[3], P. G. Conaghan[11,12], M. Østergaard[1,2]on behalf of the OMERACT MRI in Arthritis Working Group. [1]*Rigshospitalet, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Copenahgen, Denmark*; [2]*University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark*; [3]*University of Alberta, Department of Radiology and Diagnostic Imaging,*

Table 1. MRI-WIPE hip/pelvis and HIMRISS interreader reliability for OMERACT exercises 3-4

			MRI-WIPE hip/pelvis				HIMRISS			
			Osteitis		Synovitis/effusion		Osteitis		Synovitis/effusion	
Variables	No. patients (cases)	Type of score	Mean score	ICC	Mean score	ICC	Mean score	ICC	Mean score	ICC
Exercise 3 9 readers	11	Status	2.3 (0-10)	0.69 (0.23-0.93)	1.4 (0-4)	0.58 (-0.06-0.96)	8.2 (1-60)	0.84 (0.56-0.99)	12.8 (3-25)	0.52 (0.00-.91)
	11	Change	-0.2 (-1-1)	NA	-0.2 (-3-1)	0.50 (0.10-0.87)	-0.35 (-3-1)	NA	-1.8 (-17-10)	0.50 (-0.05-0.89)
Exercise 3 3 readers	11	Status	1.8 (0-10)	0.63 (0.46-0.93)	1.7 (0-5)	0.60 (0.34-0.80)	6.6 (0-65)	0.88 (0.77-0.94)	12.8 (2-28)	0.89 (0.87-0.91)
	11	Change	-0.12 (-1-1)	NA	-0.12 (-3-2)	0.60 (0.48-0.83)	-0.7 (-7-0)	NA	-1.6 (-21-8)	0.78 (0.70-0.87)
Exercise 4 9 readers	10 (1-10)	Status	1.2 (0-4)	0.21 (-0.39-0.91)	1.1 (0-2)	0.19 (-0.31-0.69)	1.8 (0-6)	0.07 (-0.17-0.83)	16.4 (9-23)	0.31 (0.00-0.89)
	10 (11-20)	Status	1.6 (0-6)	0.51 (-0.08-0.99)	1 (0-3)	0.40 (-0.17-0.88)	3.5 (1-8)	0,08 (-0.21-0.95)	11.2 (5-24)	0.49 (0.00-0.94)
	10 11-20)	Change	-0.4 (-2-0)	NA	-0.39 (-2-0)	0.22 (-0.68-0.83)	-2.2 (-7-2)	NA	-5.2 (-18-0)	0.57 (0.02-0.92)
	20 (1-20)	Status	1.4 (0-6)	0.41 (-0.35-0.92)	1.0 (0-3)	0.27 (-0.07-0.75)	2.7 (0-9)	0.09 (-0.17-0.85)	13.8 (5-25)	0.45 (0.01-0.90)
Exercise 4 3 readers	10 (1-10)	Status	0.8 (0-4)	0.29 (0.01-0.78)	1.3 (0-2)	-0.02 (-0.29-0.12)	0.4 (0-2)	-0.04 (-0.04-0.04)	15.8 (5-26)	0.73 (0.59-0.89)
	10 (11-20)	Status	1.8 (0-9)	0.65 (0.52-0.76)	1.2 (0-4)	0.72 (0.62-0.81)	1.7 (0-5)	0.06 (-0.17-0.35)	9.2 (2-26)	0.68 (0.53-0.88)
	10 (11-20)	Change	-0.6 (-2-0)	NA	-0.5 (-3-1)	0.52 (0.49-0.55)	-0.2 (-2-1)	NA	-2.8 (-19-6)	0.85 (0.82-0.88)
	20 (1-20)	Status	1.3 (0-9)	0.58 (0.43-0.69)	1.2 (0-4)	0.38 (0.31-0.44)	1.0 (0-5)	0.10 (-0.09-0.33)	12.5 (2-26)	0.73 (0.69-0.77)

Sum scores and ICCs are mean (range). ICC is 2-way mixed, single measure, by absolute agreement.

Edmonton, Alberta, Canada; [4]*Medical Imaging Consultants, Edmonton, Alberta, Canada*; [5]*University of Alberta, Department of Medicine, Edmonton, Alberta, Canada*; [6]*CARE Arthritis, Edmonton, Alberta, Canada*; [7]*Tel-Aviv University, Department of Diagnostic Imaging, Sheba Medical Center, Affiliated to the Sackler School of Medicine, Israel*; [8]*University of New South Wales, Division of Medicine, Sydney, Australia*; [9]*Université catholique de Louvain, Department of Rheumatology, Cliniques Universitaires Saint-Luc, Institut de Recherche Expérimentale et Clinique, Brussels, Belgium*; [10]*Sorbonne University, Department of Rheumatology, APHP, Pitié-Salpêtrière Hospital, Paris, France*; [11]*University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [12]*Leeds Teaching Hospitals NHS Trust, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*; [13]*Ghent University Hospital, Department of Rheumatology, Ghent, Belgium*; [14]*Ghent University, VIB Inflammation Research Centre, Ghent, Belgium*

Background: Whole-body MRI (WB-MRI) allows assessment of the overall inflammation in arthritis patients, including joint and entheses. To enhance the use of WB-MRI in clinical trials, the OMERACT MRI in Arthritis Working Group developed the OMERACT MRI Whole-body score for Inflammation in Peripheral joints and Entheses in inflammatory arthritis (MRI-WIPE) [1]. This has been validated for the entire body, including the hip/pelvis region, but not for each individual region. More detailed scoring systems exist for heels, hands and feet but although hip arthritis is a key cause of functional impairment in spondyloarthritis (SpA), no detailed scoring system has been published for use in SpA. The Hip Inflammation Magnetic Resonance Imaging Scoring System (HIMRISS) was developed and validated in osteoarthritis showing good reliability.

Objectives: To validate reliability, correlation and responsiveness of two WB-MRI scores for the hip/pelvis region in SpA.

Methods: Inflammation in the hip/pelvis region was assessed on coronal WB-MRIs in 4 iterative multi-reader exercises using MRI-WIPE for the hip/pelvis region and HIMRISS (Figure 1). In final exercises, images (axial/peripheral SpA and psoriatic arthritis) were obtained before and after TNF-inhibitor.

Figure 1

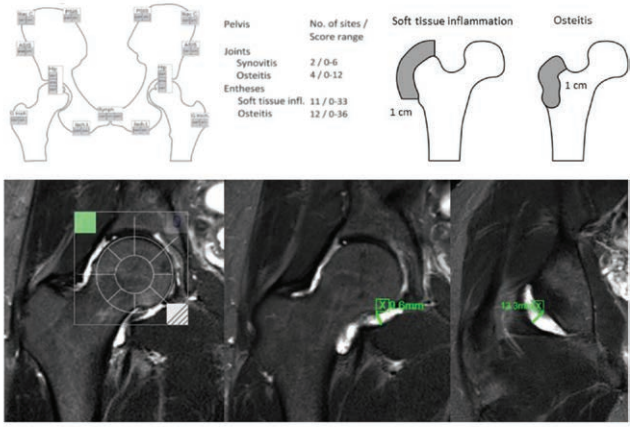


Figure 1. Upper row, left: MRI-WIPE schematic and scoring ranges for the hip and pelvis insertion of the region from Krabbe et al. [1]; Lower row, right: schematic drawing of the principle of scoring osteitis and soft tissue inflammation using MRI-WIPE, illustrated by the greater trochanter.
Lower row: Left coronal STIR whole-body MR image of the hip with the web-based semitransparent overlay used in HIMRISS for osteitis scoring positioned for femoral head and acetabulum; Right two examples of synovitis/effusion measuring according to HIMRISS.

Results: In final exercises reliability was mostly good for the best calibrated readers. Median single-measure intraclass correlation coefficients were 0.58-0.65 (WIPE osteitis), 0.10-0.88 (HIMRISS osteitis), 0.38-0.72/0.52-0.60 (WIPE synovitis/effusion) and 0.68-0.89/0.78-0.85 (HIMRISS synovitis/effusion) (Table 1). The methods correlated significantly for status in osteitis (0.72, p=0.019) and for synovitis/effusion status (0.83, p=0.003) and change (0.73, p=0.017) (Table 1). In exercise 4 Wilcoxon signed-rank test showed significant change in osteitis between timepoints using WIPE hip/pelvis and SRM was large (1.23), while lower for WIPE synovitis/effusion and HIMRISS.

Conclusion: MRI-WIPE and HIMRISS may be useful tools in modular WB-MRI evaluation of hip/pelvis inflammation in clinical trials in SpA.

REFERENCES:

[1] Krabbe S et al. J Rheum. 2019;46(9):1215-21
[2] Jaremko JL et al. J Rheum. 2019;46(9)1239-42

Acknowledgements: We thank CARE Arthritis Limited (carearthritis.com) for help with setting up the web-based scoring interface, scoring exercises, and the web-based meetings. We acknowledge the contribution of SIG (Special Interest Group) participants at the virtual OMERACT meeting October 29, 2020. HMO, GDM and PGC are supported in part by the National Institute for Health Research (NIHR) Leeds Biomedical Research Centre, United Kingdom. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Disclosure of Interests: Marie Wetterslev: None declared, Robert G Lambert Consultant of: Parexel and Pfizer, Walter P Maksymowych Speakers bureau: AbbVie, Janssen, Novartis, Pfizer and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Novartis, Pfizer and UCB, Iris Eshed: None declared, Susanne Juhl Pedersen Speakers bureau: MSD, Pfizer, AbbVie, Novartis and UCB, Consultant of: AbbVie and Novartis, Grant/research support from: AbbVie, MSD, and Novartis, Paul Bird Speakers bureau: Janssen, Abbvie, UCB, Celgene, BMS, Novartis, Pfizer, Gilead, Eli-Lilly, Consultant of: Janssen, Abbvie, UCB, Celgene, BMS, Novartis, Pfizer, Gilead, Eli-Lilly, Maria Stoenoiu: None declared, Simon Krabbe: None declared, Ashish Jacob Mathew: None declared, Violaine Foltz: None declared, Frederique Gandjbakhch: None declared, Joel Paschke: None declared, Gabriele De Marco: None declared, Helena Marzo-Ortega Speakers bureau: AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer, Takeda and UCB, Grant/research support from: Janssen and Novartis, Philippe Carron Speakers bureau: Pfizer, MSD, Novartis, BMS, AbbVie, UCB, Eli Lilly, Gilead and Celgene, Consultant of: Pfizer, MSD, Novartis, BMS, AbbVie, UCB, Eli Lilly, Gilead and Celgene, Grant/research support from: UCB, MSD and Pfizer, Anna Enevold Fløistrup Poulsen: None declared, Jacob L Jaremko: None declared, Philip G Conaghan Speakers bureau: AbbVie, BMS, Eli Lilly, Flexion Therapeutics, Galapagos, Gilead, Novartis, Pfizer, Regeneron, Stryker, Consultant of: AbbVie, BMS, Eli Lilly, Flexion Therapeutics, Galapagos, Gilead, Novartis, Pfizer, Regeneron, Stryker, Mikkel Østergaard Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Consultant of: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB

DOI: 10.1136/annrheumdis-2021-eular.952

OP0253

STRUCTURAL DAMAGE IN AXIAL SPONDYLOARTHRITIS: IS THERE A PREFERRED WAY TO ASSESS PROGRESSION OVER TIME?

X. Baraliakos[1], V. Rios Rodriguez[2], M. Torgutalp[2], A. Dilbaryan[2], H. Haibel[2], M. Verba[2], J. Sieper[2], J. Braun[1], M. Rudwaleit[3], D. Poddubnyy[2,4]. [1]*Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*; [2]*Charité-Universitätsmedizin, Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany*; [3]*Klinikum Rosenhöhe, Universitätsklinikum OWL, Bielefeld, Germany*; [4]*German Rheumatism Research Centre, Epidemiology Unit, Berlin, Germany*

Background: Axial spondyloarthritis (axSpA) is characterized by development of structural damage in the spine, assessed by conventional radiographs (CR). The modified Stokes Ankylosing Spondylitis Scoring System (mSASSS) includes all the SpA-relevant CR findings and is the most frequently used scoring system for quantification of spinal structural damage in patients (pts) with axSpA. Radiographic progression over 2 years using mean mSASSS progression, scored by a blinded 'paired' (sets of CRs of the same patient) approach, is considered as a key treatment outcome reflecting structural progression in clinical trials. However, this approach has been accompanied by questions about the influence of pts showing mSASSS 'improvement', indicating possible disappearance of syndesmophytes over time, something 'naturally unexpected'.

Objectives: To investigate the performance of mSASSS in assessing spinal radiographic damage and progression in axSpA pts using different approaches of CR evaluations.

Methods: Complete sets (cervical and lumbar CRs) from the German SpA Inception Cohort (GESPIC) at baseline and after 2 years were blinded to all clinical and demographic characteristics and then scored using the mSASSS by 5 different experienced readers, 2 blinded and 3 unblinded to the timepoint of CR performance. The final mSASSS score was calculated as a mean of 2 (blinded) or 3 (unblinded) readers. Descriptive statistics, cumulative probability plots and shift analyses *(agreement of 2/2 readers in the blinded and 2/3 readers in the unblinded group)* were performed for each reader group.

Results: A total of 210 pts (mean age 37.3y, 51% male, 79% HLA-B27+) with non-radiographic (n=115) and radiographic (n=95) axSpA at baseline were included. The mean mSASSS at baseline was 4.3±8.3 vs. 3.4±7.9, while the mean progression was 0.7±2.3 vs.1.0±1.9 mSASSS units for the blinded vs. the unblinded group, respectively (Figure). On the patient level, progression of ≥2 mSASSS units was found in 30 (14.3%) vs. 37 (17.6%) pts in the blinded vs. the unblinded group, while agreement between groups was seen in 179 (85.2%) pts, 18 (8.9%) pts for progression and 161 (76.7%) for no progression.

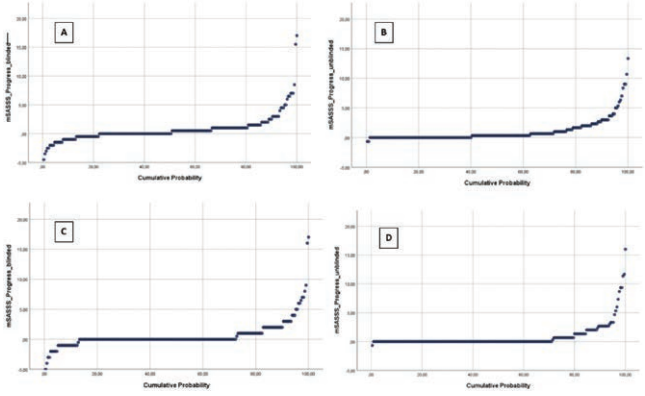


Figure 1. Cumulative probability plot for mean mSASSS scores (all scores) in blinded (A) and unblinded (B) and 'definite' scores in blinded (C) and unblinded (D) scoring approach

In the analysis of 'definite' CR findings (only scores of 2=syndesmophytes or 3=ankylosis), the mean mSASSS score at baseline was 3.3±8.0 vs. 2.6±7.2 and the mean radiographic progression was 0.6±2.4 vs. 0.8±2.1 mSASSS units for the blinded vs. the unblinded group, respectively (Figure). On the patient level, progression was found in 37 (17.6%) vs. 33 (15.7%) pts in the blinded vs. the unblinded group, while agreement between groups was seen in 188 (89.5%) pts, 24 (11.3%) for progression and in 164 (78.1%) pts for no progression.

In the shift analysis, mSASSS worsening was found in 35 (0.8%) and mSASSS 'improvement' in only 4 (0.1%) out of a total of 4.373 vertebral edges (VE) analyzed in the blinded and in 109 (2.2%) and 2 (0.04%), respectively, out of a total of 4.914 VE analyzed in the unblinded group (Table). The majority of progression was found for the development of 'definite' signs of progression in both the blinded (25/35, 71.4%) and the unblinded (61/109, 56%) group, while more VE showing 'minor' (only scores of 1=sclerosis, squaring, erosion) signs of progression were found in the unblinded (48/109, 44%) vs. to the blinded (10/25, 28.6%) group.

Conclusion: Despite lower mean baseline mSASSS, higher mean mSASSS progression was found using the unblinded approach, while in the shift analysis the unblinded approach was also more specific, confirming the absence of 'improvement' of radiographic damage over time. These results were similar in the analysis on the patient's level. The scoring approach and the influence of 'minor' radiographic changes should be taken into account for avoiding the so-called 'background noise' in the evaluation of mSASSS.

Acknowledgements: GESPIC was initially supported by the BMBF. As a consequence of the funding reduction by BMBF according to schedule in 2005 and stopped in 2007, complementary financial support has been obtained also from Abbott, Amgen, Centocor, Schering–Plough, and Wyeth. Starting from 2010, the core GESPIC cohort was supported by AbbVie.

Table 1. Shift analysis of the blinded and unblinded reading approach on the basis of VE.

Blinded reading						
mSASS Scores		2-year follow-up				Total
		0	1	2	3	
Baseline	0	4.166	10	8	9	4.193
	1	0	29	4	0	33
	2	3	1	48	4	56
	3	0	0	0	92	92
Total		4.169	40	60	105	4.374

Unblinded reading						
mSASS Scores		2-year follow-up				Total
		0	1	2	3	
Baseline	0	4.575	48	14	3	4.640
	1	1	75	16	8	100
	2	0	0	69	20	89
	3	0	1	0	84	85
Total		4.576	124	99	115	4.914

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2532

OP0254

AN ARTIFICIAL NEURAL NETWORK FOR THE DETECTION OF DEFINITE RADIOGRAPHIC SACROILIITIS WITH HIGH SPECIFICITY IN THE DIAGNOSTIC SETTING

J. L. Vahldiek[1], K. K. Bressem[1], S. Niehues[1], L. Adams[1], L. Spiller[2], M. Protopopov[2], V. Rios Rodriguez[2], B. Muche[2], J. Rademacher[2], H. Haibel[2], M. Torgutalp[2], F. Proft[2], D. Poddubnyy[2,3]. [1]*Charité – Universitätsmedizin Berlin, Division of Radiology, Berlin, Germany*; [2]*Charité – Universitätsmedizin Berlin, Division of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany*; [3]*Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), ein Institut der Leibniz-Gemeinschaft, Epidemiology Unit, Berlin, Germany*

Background: Radiographs of the sacroiliac joints are commonly used as the first imaging method for the diagnosis of axial spondyloarthritis (axSpA), but the reliability of sacroiliitis detection is usually low. Recently we developed a deep convolutional neural network (CNN) that can detect radiographic sacroiliitis with expert-like accuracy in patients with axSpA, i.e., classification as radiographic or non-radiographic [1]. There is frequent criticism that many artificial intelligence algorithms for diagnostic analysis of medical images lack robust validation in real-world clinical applications.

Objectives: The aim of this study was to evaluate the performance of our deep CNN in detecting definite radiographic sacroiliitis in the diagnostic setting.

Methods: In this study, we included a total of 361 patients with chronic back pain who presented to a rheumatologist in a specialized SpA center with a suspicion of axSpA within the OptiRef project [2]. All patients received a structured rheumatologic diagnostic work-up that resulted in the final diagnosis of axial SpA/no axial SpA. Radiographs of sacroiliac joints were evaluated by a rheumatologist and radiologist according to the modified New York criteria; the consensus judgement of the presence of definite radiographic sacroiliitis (>=grade 2 bilaterally or >=grade 3 unilaterally) was used as a reference. The predictions of the deep CNN's inference (with a balanced cutoff of 0.724 for the predictions of the model that was derived from the training and validation steps [1]) on all available pelvic radiographs was compared to this reference judgement.

Results: Pelvic radiographs of 340 patients (110 with axSpA including 61 patient with radiographic and 49 with non-radiographic axSpA, and 230 without SpA) were available for the CNN evaluation. The deep CNN achieved a sensitivity of 79% for the diagnosis of radiographic axSpA. The specificity of radiographic sacroiliitis detection was 94% (Table 1). The area under the receiver operating characteristics curve for the prediction of the presence of definite radiographic sacroiliitis was 88%. Figure 1 shows an exemplary class activation map of our CNN.

Table 1. Convolutional neural network predictions of the presence of radiographic sacroiliitis in patients with suspected axSpA according to the final diagnosis by rheumatologist in OptiRef (N=340).

Clinical diagnosis	CNN's prediction on the presence of definite radiographic sacroiliitis	
	Present	**Not present**
Radiographic axial SpA	48/61 (78.7%)	13/61 (21.3%)
Non-radiographic axial SpA	4/49 (8.2%)	45/49 (91.8%)
No SpA (other diagnosis)	14/230 (6.1%)	216/230 (93.9%)

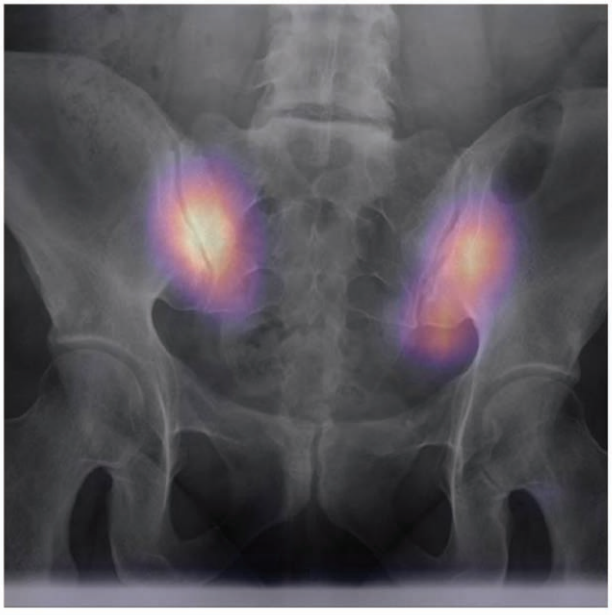
Conclusion: The artificial neural network showed good generalizability and a high specificity with acceptable sensitivity in the detection of radiographic sacroiliitis when applied in the diagnostic setting of patients with chronic back pain and suspicion of axSpA. This algorithm can therefore be used to aid the detection of radiographic sacroiliitis as a part of the diagnostic approach.

REFERENCES:

[1] Bressem KK, et al. medRxiv. 2020:2020.05.19.20105304.
[2] Proft F, et al. Semin Arthritis Rheum. 2020;50:1015-1021.

Acknowledgements: The OptiRef study was supported by a research grant from Novartis.

Figure 1. Inference of the proposed CNN on a randomly chosen pelvic radiograph from the OptiRef study.



This exemplary class activation map shows that our CNN almost exclusively and correctly focusses on the sacroiliac joints to predict whether definite radiographic sacroiliitis is present or not.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3512

OP0255 THE ROLE OF PELVIC MORPHOLOGY IN AXIAL SPONDYLOARTHRITIS

E. Zaccagnino[1], R. Patel[2], L. S. Gensler[3]. [1]*UCSF Medical Center, School of Medicine, San Francisco, United States of America*; [2]*UCSF Medical Center, Radiology & Biomedical Imaging, San Francisco, United States of America*; [3]*UCSF Medical Center, Rheumatology, San Francisco, United States of America*

Background: Axial Spondyloarthritis (axSpA) is a chronic inflammatory disease affecting the axial skeleton. It includes non-radiographic axSpA and radiographic axSpA [Ankylosing Spondylitis (AS)]. Male axSpA patients often have greater damage, while women report a higher disease burden. The role of pelvic morphology in the axSpA phenotype has not been explored. There is anatomic sexual dimorphism between the male and female pelvis. Given the phenotypic gender differences in axSpA, the role of pelvic morphometry is of interest.

Objectives: The purpose of this study is to determine whether an association exists between pelvic dimensions and radiographic damage in patients with axSpA, as well as to compare these measurements in axSpA patients and healthy controls.

Methods: This was a cross-sectional analysis comparing axSpA cases from a prospective cohort and non-axSpA controls from the UCSF radiology databank. Informed consent was obtained from axSpA cohort patients and this study was approved by the institutional IRB. To be included in the analysis, we limited inclusion to age ≤ 50 with an Anterior Posterior (AP) pelvis radiograph in the system. We excluded non-nulliparity, pelvic fracture history, BMI ≥ 30kg/m2, any prosthetic history and avascular necrosis. We measured the pelvic inlet, pelvic outlet, and subpubic angle (based on validated scoring methods) (Figure 1) and assessed its relation to sacroiliac joint (SIJ) damage (average SIJ score, New York criteria) and modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) in cases. AxSpA patients were also compared to age/gender matched controls. Pelvic measurements were performed by 2 blinded independent-trained readers in randomized, blinded image order. Inter-rater reliability was assessed. When examining the relationship between pelvic measurements and damage, linear regression was used to stratify by gender and adjust for potential confounders.

Results: The axSpA cohort included 481 patients, of which 210 men and 89 women were included in this analysis and gender/age matched controls. Rater inter-class correlation was above 0.70 for pelvic outlet and above 0.80 for other measures. Cases and controls were similar (Table 1). The regression analysis showed a significant relationship between the sub-pubic angle and damage in the spine (coeff=-0.342, p=0.003) in men with axSpA. A sensitivity analysis, excluding mSASSS outliers (mSASSS ≥ 16) upheld the relationship (coeff=-1.40, p=0.002).

Conclusion: In men with axSpA, there appears to be a relationship between sub-pubic angle and spinal radiographic damage. This is consistent with our finding that women have larger sub-pubic angles and lower spinal radiographic damage than men. A greater sub-pubic angle may protect against spinal involvement or associate with other protective factors. Further work should be performed to understand the contribution of pelvic anatomy to damage in axSpA.

Disclosure of Interests: Ethan Zaccagnino: None declared, Rina Patel: None declared, Lianne S. Gensler Consultant of: AbbVie, Eli Lilly, Gilead, Novartis, Pfizer and UCB., Grant/research support from: Pfizer and UCB.

DOI: 10.1136/annrheumdis-2021-eular.188

OP0256 CHOOSE WISELY: IMAGING FOR DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS

T. Diekhoff[1], I. Eshed[2], F. Radny[1], K. Ziegeler[1], F. Proft[3], J. Greese[1], D. Deppe[1], R. Biesen[4], K. G. Hermann[1], D. Poddubnyy[3,5]. [1]*Charité Universitaetsmedizin Berlin, Division of Radiology, Berlin, Germany*; [2]*Chaim Sheba Medical Center, Division of Radiology, Tel Aviv, Israel*; [3]*Charité Universitaetsmedizin Berlin, Divison of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany*; [4]*Charité Universitaetsmedizin Berlin, Division of Rheumatology and Clinical Immunology, Berlin, Germany*; [5]*German Rheumatism Research Centre, Epidemiology Unit, Berlin, Germany*

Background: To date, the European Alliance of Associations for Rheumatology (EULAR) guidelines recommend X-ray (XR) as first line imaging in axial Spondyloarthritis (axSpA) and magnetic resonance imaging (MR) if the diagnosis cannot be established by XR and clinical features. However, much knowledge has been gained recently strengthening the applicability of MR for the detection of structural lesions and raising the question, whether XR is still necessary. Also, several publications used low-dose computed tomography (CT) as reference standard and imaging test.

Objectives: In light of this complex diagnostic situation, the aim of this study was to compare the three major modalities, XR, MR and CT of SIJ, in their diagnostic performance of axSpA and differential diagnosis in a cohort of patients with low back pain using the final judgment of the rheumatologist as standard of reference.

Methods: 163 patients (89 with axSpA; 74 with degenerative diseases) underwent XR, CT and MR. Three blinded experts categorized the imaging into axSpA, other diseases or normal in 5 separate reading rounds (XR, CT, MR, XR+MR, CT+MR, respectively). The results were compared to the clinical diagnosis. Sensitivity and specificity values for axSpA and interrater reliability were compared.

Results: XR showed lower sensitivity and specificity (66.3%/67.6% respectively) compared to MR (82.0%/86.5%) and CT (77.5%/97.3%). Sensitivity and specificity of XR+MR was similar to MR alone (77.5% / 87.8%). However, CT+MR was

superior to MR alone (75.6% / 97.3%) (see Figure). CT had the best interrater reliability (kappa = 0.875) followed by MR (0.665) and XR (0.517). CR+MR reliability was similar (0.662) compared to MR alone, while CT+MR reliability (0.732) was superior.

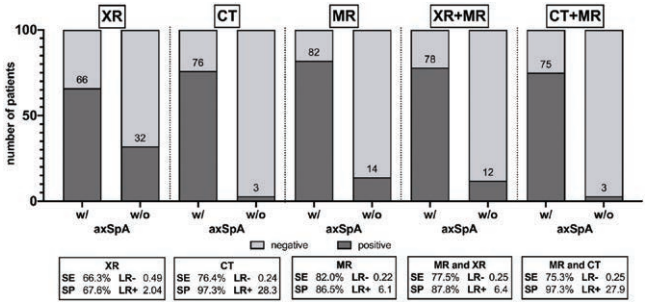


Figure 1. Frequency of positive and negative findings in radiography (XR), computed tomography (CT), magnetic resonance imaging (MR) and combinations and resulting diagnostic accuracy values. SE: Sensitivity, SP: Specificity, LR-/+: negative/positive likelihood ratio.

Conclusion: In conclusion, XR is inferior to cross-sectional imaging and should be replaced by MR or CT for differential diagnosis. While MR is the most sensitive imaging technique, it lacks specificity when compared to CT. CT alone has high diagnostic accuracy, despite being insensitive to bone marrow lesions such as fatty metaplasia or osteitis. Adding CT to MR leads to an increase in specificity at a minor expense of sensitivity.

REFERENCES:

[1] Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. Ann Rheum Dis. 2009;68 Suppl 2:ii1-44.
[2] Mandl P, Navarro-Compán V, Terslev L, et al. EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. Ann Rheum Dis. 2015;74(7):1327-39.
[3] Diekhoff T, Hermann KA, Greese J, et al. Comparison of MRI with radiography for detecting structural lesions of the sacroiliac joint using CT as standard of reference: results from the SIMACT study. Ann Rheum Dis. 2017.
[4] Diekhoff T, Greese J, Sieper J, Poddubnyy D, Hamm B, Hermann KA. Improved detection of erosions in the sacroiliac joints on MRI with volumetric interpolated breath-hold examination (VIBE): results from the SIMACT study. Ann Rheum Dis. 2018;77(11):1585-89.
[5] Baraliakos X, Hoffmann F, Deng X, Wang YY, Huang F, Braun J. Detection of Erosions in Sacroiliac Joints of Patients with Axial Spondyloarthritis Using the Magnetic Resonance Imaging Volumetric Interpolated Breath-hold Examination. The Journal of rheumatology. 2019;46(11):1445-49.
[6] Wu H, Zhang G, Shi L, et al. Axial Spondyloarthritis: Dual-Energy Virtual Noncalcium CT in the Detection of Bone Marrow Edema in the Sacroiliac Joints. Radiology. 2019;290(1):157-64.

Disclosure of Interests: Torsten Diekhoff Speakers bureau: Canon MS, Roche, Novartis, MSD, Grant/research support from: Assessment of Spondyloarthritis International Society, Iris Eshed: None declared, Felix Radny: None declared, Katharina Ziegeler: None declared, Fabian Proft: None declared, Juliane Greese: None declared, Dominik Deppe: None declared, Robert Biesen: None declared, Kay-Geert Hermann: None declared, Denis Poddubnyy: None declared

DOI: 10.1136/annrheumdis-2021-eular.2301

OP0257

VALUE OF COLOR DOPPLER ULTRASOUND ASSESSMENT OF SACROILIAC JOINTS IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS:A COMPARISON WITH ANKYLOSING SPONDYLITIS

N. MA[1], S. Haili[1]. [1]*Lanzhou University Second Hospital, Rheumatology, Lanzhou, China*

Background: Ultrasound (US) is an accessible imaging technique with a possible role to diagnose active sacroiliitis, so this technique is projected as a promising diagnostic tool for the diagnosis of spondyloarthritis(SpA).The diagnostic value of sacroiliac US has been studied in patients with Ankylosing Spondylitis(AS),becoming a useful and practical tool in comparison with MRI.There are scarce data on the utility of US in the evaluation of Non-radiographic Axial Spondyloarthritis (nr-axSpA).

Objectives: The aim of this study is to evaluate the diagnostic utility of color Doppler ultrasound (CDUS) for the detection of sacroiliitis in patients with nr-axSpA and AS.

Methods: Patients with nr-axSpA (n=114) and AS(n=80) were enrolled in the study with standardized clinical criteria.According to the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI),nr-axSpA and AS patients were separately divided into active group(n=47,n=43)and inactive group (n=67,n=37). All patients underwent clinical evaluation,and CDUS of sacroiliac joints (SIJs) within the same week. Vascularization, the resistive index (RI) of the SIJs and the first foraminal ramus of the lateral sacral artery were observed and measured by a sonographer who is blinded to initial clinical and radiological assessments. The associated statistics and graphs was utilized to obtain the relationship,which were reflected by the Co-index receiver operating characteristic(ROC)curve or calculating the area under ROC curve(AUC),between the RI of the SIJs and the RI of the first foraminal ramus of the lateral sacral artery in nr-axSpA and AS by using the Logistic Regressive analysis methods,SPSS24.0 and MedCalc19.6.0 software.With MRI-proven sacroiliitis as the
diagnostic standard,the Kappa test were used to measure the consistency between the RI of the SIJs and MRI.

Results: 1. The RI of the SIJs(AUC=0.855,P<0.001)and Co-index-(AUC=0.886,P<0.001)were similar sufficient (Z=1.331, P=0.183) to distinguish the active and inactive group in nr-axSpA .2.The RI of the SIJs(AUC=0.869,P<0.001)and Co-index(AUC=0.893,P<0.001)were also similar sufficient (Z=1.292, P=0.196) to distinguish the active and inactive group in AS .3.Neither of the RI of the first foraminal ramus of the lateral sacral artery in nr-axSpA(AUC=0.748,P<0.001)and AS(AUC=0.674,P=0.003)was outstanding to distinguish the active and inactive group.4.The RI of the SIJs was similar sufficient (Z=0.267,P=0.790) to detect sacroiliitis in nr-axSpA and AS.5. The Co-index was also similar sufficient (Z=0.146, P=0.884) to detect sacroiliitis in nr-axSpA and AS.6.The RI of the SIJs in nr-axSpA and AS showed moderate consistency with MRI(the Kappa values were 0.534 and 0.609,respectively,P<0.01).

Conclusion: The RI of the SIJs is a possible role to diagnose active sacroiliitis, so CDUS is projected as a promising diagnostic tool for the diagnosis of nr-axSpA and AS in comparison with MRI.

REFERENCES:

[1] Rosa JE, Ruta S, Bravo M, et al. Value of Color Doppler Ultrasound Assessment of Sacroiliac Joints in Patients with Inflammatory Low Back Pain. J Rheumatol. 2019 Jul;46(7):694-700.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3666

HPR Abstract Session (II)

OP0258-HPR

IS THERE A SUBSET OF PATIENTS WITH SJÖGREN'S SYNDROME WHO ARE MORE AT RISK FOR SEXUAL DYSFUNCTION? RESULTS FROM A SCOPING REVIEW

J. McCready[1], M. Hogg[2], V. Deary[3,4], T. Collins[1], K. Hackett[1,4]. [1]*Northumbria University, Department of Social Work, Education and Community Wellbeing, Newcastle upon Tyne, United Kingdom*; [1]*Northumbria University, Department of Social Work, Education and Community Wellbeing, Newcastle upon Tyne, United Kingdom*; [3]*Northumbria University, Department of Psychology, Newcastle upon Tyne, United Kingdom*; [4]*Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom*

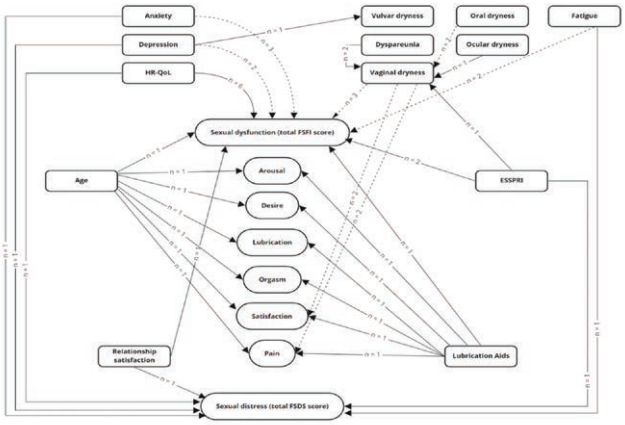
Background: Individuals with Sjögren's syndrome (SS) experience significantly higher levels of sexual dysfunction and sexual distress than healthy controls (van Nimwegen et al., 2015). Identifying associated factors may help to identify a subgroup of patients with SS who may benefit from early intervention to maintain sexual wellbeing and avoid unnecessary sexual disruption.

Objectives: To explore and map the salient symptoms and factors that influence alterations in sexual functioning and intimate relationships for people with SS.

Methods: The protocol for this review was registered with the Open Science Framework prior to commencement of the searches. The peer-reviewed search strings were used to search the following databases from inception to June 2019: Cochrane Library, CINAHL [EBSCO], MEDLINE [ProQuest], PUBMED [MEDLINE], ScienceDirect, Scopus and Web of Science. Grey literature was searched for on academic databases, topic-specific repositories, and Google Scholar. Databases were searched using key terms corresponding to sexual functioning and intimate relationships. Studies were included if their participant sample was comprised of adults aged ≥18 years, with a diagnosis of primary or secondary SS. Studies were not excluded based on source type, methodology or design. To qualify for inclusion, studies needed to have been peer-reviewed and available in English. Retrieved articles were then screened against the inclusion/exclusion criteria by two reviewers. Hand-searching was conducted on the reference lists of included articles, as well as the three most prevalent publishing journals until saturation had been achieved.

Results: The search strategy returned 3527 unique citations. After screening processes were completed, only 19 articles met the inclusion criteria. Studies were predominately conducted in European countries (79%), within the last decade (68%; 2010-2019), and were mainly quantitative (n = 17; 89.5%), case-controlled

(88.3%), and cross-sectional (100%) in nature. In total there were 1281 patients, 47% (n = 605) were patients with primary SS and the remaining 53% (n = 676) were patients with secondary SS. Both patient groups were predominately comprised of females (n = 600; 99% and n = 673; 99.5%, respectively), with a combined mean age of 50.82 years (*M* ranges = 35 – 62.82 years). An amalgamation of results from 17 studies, found that women with SS who score higher on the ESSPRI scale (total score and the subdomains of pain, fatigue and dryness) were more likely to experience significantly greater levels of vaginal dryness, sexual dysfunction and sexual distress. Moreover, women with SS who present with clinical levels of anxiety or depression were also more likely to experience disruptions in their sexual functioning and appraise their sexual life more negatively. Furthermore, patients who report greater severity of oral or ocular dryness, or dyspareunia may experience vaginal dryness, which may have ramifications on sexual functioning. Women of all ages are at risk of experiencing sexual dysfunctions, however, younger women (≤50 years) may experience more burdensome disruptions than older women. Finally, women who do not use lubrication products during sexual activity may be impacted further.



Note. The solid line represents results that were significant across studies. The dotted line represents results where the significance was inconsistent across studies. Relationships that were unanimously non-significant are not shown.

Figure 1. Factors significantly associated with sexual dysfunction and sexual distress for patients with SS.

Conclusion: Younger women (≤50) with SS who present with more severe symptoms of fatigue, pain, and oral or ocular dryness, or with clinical levels of anxiety or depression, may be at increased risk of experiencing sexual dysfunction and sexual distress. Healthcare professionals should be aware of these potential risk factors and initiate conversations around sexuality as and when a potentially 'at risk' individual is identified.

REFERENCES:

[1] van Nimwegen, J. F., Arends, S., van Zuiden, G. S., Vissink, A., Kroese, F. G. M., & Bootsma, H. (2015). The impact of primary Sjögren's syndrome on female sexual function. Rheumatology, 54(7), 1286-1293.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.887

OP0259-HPR THE EFFECT OF OSTEOARTHRITIS ON HEALTHY WORKING LIFE EXPECTANCY AT AGE 50 IN ENGLAND

M. Lynch[1], M. Bucknall[1], C. Jagger[2], R. Wilkie[1]. *[1]Keele University, School of Medicine, Newcastle under Lyme, United Kingdom*; *[2]Newcastle University, Population Health Sciences Institute, Newcastle, United Kingdom*

Background: Retirement ages are rising in many countries due to population ageing and increasing life expectancy. However, poor health, comorbidity and workplace factors are major reasons for work absence and it is unclear if people in later working-age life (age ≥50) are able to work for longer. Osteoarthritis (OA), the most common joint condition in adults, is the fastest increasing major health condition globally and is a leading cause of disability (especially in adults age ≥50).

Objectives: We aimed to estimate healthy working life expectancy (HWLE; defined as the average number of years that adults from age 50 can expect to be healthy and in paid work) for adults with and without osteoarthritis and investigate the role of mental health problems as a comorbidity and the role of workplace factors through examining whether there is a sense of having any control over what happens at work.

Methods: Longitudinal survey data of adults aged ≥50 years were used from six waves (2002-2013) of the English Longitudinal Study of Ageing with linked mortality data from the National Health Service Central Register. HWLE was defined using two self-report variables; health was defined as no long-standing illness or no activity limitation if long-standing illness was present, and work was defined being in employment or self-employment. OA status was identified by self-report of ever receiving a diagnosis from a doctor. Mental health and control of work were measured by self-report. Continuous-time multistate models with three states (healthy and working [state 1], other alive [2], dead [3]) were fitted in R (version 3.6.1) to investigate factors driving transitions out of the healthy and working state. Models included age and combinations of sex, OA, control at work, and mental health problems. Age-adjusted hazards of transitions between states were estimated using the 'msm' R package. HWLE for adults with different factors (OA, control of work, mental health) was estimated with the 'elect' R package using models fitted with 'msm'. Missing data was handled using multiple imputation by predictive mean matching.

Results: There were 11,540 adults with at least two observations (including survey and mortality data) for the study period (5251 males, 6289 females). Life expectancy at age 50 was 29.7 years for men and 33.4 years for women with HWLE being 9.9 years (men) and 8.3 years (women). HWLE at age 50 for adults with osteoarthritis was 7.3 years (men: 8.2, women: 6.8), and for adults without osteoarthritis was higher at 9.9 years (men: 10.6, women: 9.1). After adjusting for age, the instantaneous risk of ceasing to be both healthy and in work (not due to death) for people with OA was 1.5 times that of people without OA (hazard rate ratio 1.5 with 95% CI [1.3, 1.6]). For adults without OA, HWLE at age 50 was 13.2 years if they felt they had control at work and 4.1 years without control at work, whilst for adults with OA, HWLE was 10.4 years if they felt they had control at work and 3.1 years without. The effect of mental health problems as a comorbidity on HWLE was smaller; for adults without OA, HWLE at age 50 was 11.0 years for those without mental health problems and 8.3 years for those with, whilst for adults with OA, HWLE was 8.6 years for those without mental health problems and 6.2 years with.

Conclusion: While the average HWLE for men and women in England is lower than State Pension age, HWLE at age 50 is even lower (by approximately 25%) in adults with OA compared to adults without OA. Poor mental health further reduces HWLE. However, good quality work environments significantly lessen the impact of osteoarthritis (there is a 7.3 year difference in HWLE for those with OA who do and do not experience control at work). These results suggest that interventions and policies that create appropriate job opportunities and supportive workplaces for older workers with health conditions are key to the feasibility and success of extended working life policies.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2349

OP0260-HPR PREDICTORS OF WORK PARTICIPATION IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AFTER 12 MONTHS OF T2T THERAPY INTERVENTION

S. E. Meyer[1,2], J. R. Hoeper[3], T. Witte[1,2], K. Hoeper[1,2], D. Meyer-Olson[1,4]. *[1]Medizinische Hochschule Hannover, Clinic for Rheumatology and Immunology, Hannover, Germany*; *[2]Regionales Kooperatives Rheumazentrum Niedersachsen e.V., Hannover, Germany*; *[3]Leibniz Universität Hannover, Center for Health Economics Research Hannover, Hannover, Germany*; *[4]m&i Fachklinik Bad Pyrmont and Medizinisches Forschungszentrum Weserbergland, Bad Pyrmont, Germany*

Background: Rheumatoid arthritis (RA) is associated with restrictions on work participation (WP) caused mainly by periods of sick leave (absenteeism), reduced productivity at work due to disease (presenteeism) and occupational disability, which account for a significant proportion of indirect costs.

Objectives: We investigate the predictors of WP after 12 months of Treat-to-Target (T2T) intervention.

Methods: Data were analyzed from the multi-center ERFASS study, which included patients with rheumatoid factor and/or APCA positive RA after initiation or escalation of disease modifying anti rheumatic drug (DMARD) therapy following a T2T regimen prospectively over 12 months from 01/2018 to 12/2019. A total of 157 patients of working age (18 to 65 years) were included in this evaluation. Socio-demographic and occupational characteristics (WPAI, self-conducted work questionnaire), clinical parameters including disease activity (DAS28, RADAI), impact of disease (RAID), functional capacity (FFbH), depression (PHQ-9) and fatigue (VAS) were analyzed and logistic regression analysis to detect baseline predictors for unimpaired WP after 12 months was performed.

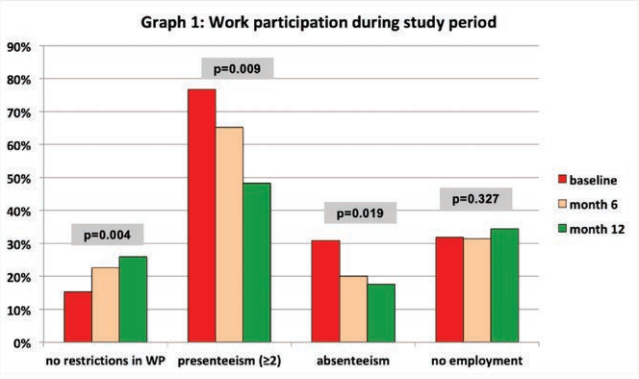
Results: The mean age of the patients was 52.9 years (standard deviation (SD): 8.19) and 117 (74.5%) were female. 51 patients (32.5%) started first line DMARDs and in 106 patients (67.5%) treatment was escalated. T2T resulted in a significant decrease in mean DAS28 from 4.2 (SD 1.10) at baseline to 2.5 (SD 1.11; p<0.001) after 12 months, 64.3% of the patients were in remission (DAS28<2.6) and 12.1% had low disease activity (DAS28 2.6-3.2). The proportion of patients with no impairment of WP increased significantly and presenteeism and absenteeism became significantly less prevalent, but the proportion

of patients with reduced WP at month 12 remained high (74.1%; graph 1). We observed a moderate positive significant correlation between presenteeism and absenteeism (r_{Mo12}=0.446; p<0.001). Patients with no restrictions on WP showed a significantly greater decrease in mean DAS28 from 3.7 (SD 1.15) at baseline to 1.9 (SD 0.61) at month 12 as compared to patients with restrictions (mean DAS28: 4.4 (SD 1.04) at baseline to 2.7 (SD 1.15) at month 12; p<0.001). Results from univariate and logistic regression analyses revealed high functional capacity and low depression score at baseline as major contributing factors for unimpaired WP (Table 1).

Table 1. Baseline predictors of work participation[1] at month 12

Predictors (independent variables)	Univariate analysis[2]: p-values	Multivariate analysis[3]: Odds Ratios, p-values
gender	0.117+	OR: 0.412; p=0.113
age	0.010*+	OR:0.951; p=0.071
school graduation	0.150+	
professional degree	0.739	
duration of complaints	0.127+	
therapy group (starters vs. escalation/ change)	0.004*+	
DAS-28(CRP)	0.001*	
CRP	0.906	
tender joints	0.004*	
swollen joints	0.021*	
disease activity (VAS)	0.003*+	OR: 0.827; p=0.086
subjective disease activity (RADAI)	<0.001*	
disease burden (RAID)	<0.001*	
functional capacity (FFbH)	<0.001*+	OR: 1.477; p=0.031*
fatigue (VAS)	<0.001*+	
depression (PHQ-9)	<0.001*+	OR: 0.876; p=0.035*
working time model (full vs. part-time)	0.498	
physical work load	0.427	

[1] dependant variable: 0=reduced WP (not working/ absenteeism/ presenteeism (≥2)); 1=full WP (working without absenteeism/ presenteeism (≥2))[2] according to applicability chi-square test, t-test for independent variables, Mann-Whitney-U test[3] binary logistic regression analysis, stepwise-backward procedure+ included into logistic regression model* significance level: p<0.05



Conclusion: Despite T2T and high DAS28 remission, we observed persistent limitations in WP. Impaired WP was associated with increased disease activity but logistic regression revealed a significant influence of depression and functional capacity. Our data underscore the multifactorial causes of impaired WP, which should be targeted by vocational rehabilitation.

Disclosure of Interests: Sara Eileen Meyer: None declared, Juliana Rachel Hoeper: None declared, Torsten Witte: None declared, Kirsten Hoeper Speakers bureau: She has received consultancy and speaker honoraria from Abbvie, Chugai, Gilead, Lilly, Novartis, Sandoz Hexal and Sanofi., Dirk Meyer-Olson Speakers bureau: He has received consultancy and speaker honoraria from Abbvie, Amgen, Berlin Chemie, Bristol Myers Squibb, Cellgene, Chugai, Fresenius Kabi, GSK, Jansen Cilag, Lilly, Medac, Merck Sharp & Dome, Mylan, Novartis, Pfizer, Sandoz Hexal, Sanofi and UCB.

DOI: 10.1136/annrheumdis-2021-eular.1250

OP0261-HPR PERCEIVED CHALLENGES AT WORK AND NEED FOR SUPPORT AMONG PEOPLE WITH INFLAMMATORY ARTHRITIS

C. M. T. Madsen[1,2], J. Reffstrup Christensen[3,4], A. Bremander[1,2,5], J. Primdahl[1,2,6]. [1]*Danish Hospital for Rheumatic Diseases, University Hospital of Southern Denmark, Sønderborg, Denmark*; [2]*Department of Regional Health Research, University of Southern Denmark, Odense, Denmark*; [3]*Research Unit of General Practice, Department of Public Health, University of Southern Denmark, Odense, Denmark*; [4]*Research Unit of User Perspectives, Department of Public Health, University of Southern Denmark, Odense, Denmark*; [5]*Section of Rheumatology, Department of Clinical Sciences Lund, Lund University, Lund, Sweden*; [6]*Hospital of Southern Jutland, University Hospital of Southern Denmark, Aabenraa, Denmark*

Background: People with inflammatory arthritis (IA), i.e. rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis, often experience low work ability and up to 38% lose their job during the first years after being diagnosed with IA (1). As a result, people with IA have a higher risk of job loss and permanent exclusion from the labor market than people without IA (1, 2). Work-related rehabilitation is complex and encompass a variety of interventions which aim to reduce barriers to maintain work and improve work ability. Unfortunately, positive results from work-related rehabilitation is scarce (3), why a better understanding of the challenges people at risk for job loss experience is needed to develop relevant interventions.

Objectives: To explore perceived challenges and need for support to remain at work among people with IA who are at risk of job loss.

Methods: A qualitative explorative design based on a hermeneutic approach was applied. Outpatients with IA who considered themselves at risk for long-term job loss, were recruited at the Danish Hospital for Rheumatic Diseases. An interview guide was developed based on earlier results from a systematic review and qualitative studies in close cooperation with three patient research partners. Individual semi-structured interviews were performed from December 2019 to May 2020.

Results: Eleven women and four men with IA (aged 36-68 years) were interviewed. The participants were employed full time, part time or on sick leave. From the analysis, a main theme 'Balancing work as a part of everyday life' and four sub-themes emerged: 1) Working despite challenges, 2) Prioritizing energy for work, 3) Fatigue affects everything and 4) Need for support. To be able to work was very important to all participants. In general, they were stretching their limits, had concerns about maintaining their job and they used different strategies to deal with the challenges they met at work. Flexibility at work in every possible way and support from employers and co-workers were the main needs to be able to remain at work.

Conclusion: Overall, patients with IA prioritized to keep working, but experienced challenges with balancing their work and energy in everyday life. They need support and flexibility at work to be able to remain at work.

REFERENCES:

[1] Sokka T, Kautiainen H, Pincus T, Verstappen SMM, Aggarwal A, Alten R, et al. Work disability remains a major problem in rheumatoid arthritis in the 2000s: Data from 32 countries in the QUEST-RA Study. Arthritis Research and Therapy. 2010;12(2):R42-R.

[2] Hansen SM, Hetland ML, Pedersen J, Ostergaard M, Rubak TS, Bjorner JB. Effect of rheumatoid arthritis on longterm sickness absence in 1994-2011: A danish cohort study. Journal of Rheumatology. 2016;43(4):707-15.

[3] Madsen CMT, Kjaer, S., Primdahl, J., Christensen, J. R., & von Bulow, C. A SYSTEMATIC REVIEW OF JOB LOSS PREVENTION INTERVENTIONS FOR PERSONS WITH INFLAMMATORY ARTHRITIS. Annals of the rheumatic diseases, 79(Suppl 1) 916-917 [FRI0624-HPR]2020.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1549

OP0262-HPR THE NEURO-QOL UPPER EXTREMITY FUNCTION SCALE: NEW OPPORTUNITIES TO MORE RELIABLY AND PRECISELY MEASURE SELF-REPORTED HAND FUNCTION AND SELF-CARE ACTIVITIES IN PEOPLE WITH RA

S. J. Bartlett[1], O. Schieir[2], M. F. Valois[3], G. Boire[4], J. Pope[5], E. Keystone[6], C. Thorne[7], D. Tin[7], C. Hitchon[8], L. Bessette[9], G. Hazlewood[10], V. Bykerk[11]on behalf of CATCH Investigators. [1]*McGill University & McGill University Health Centre, Clinical Epidemiology & Rheumatology, Montreal, Canada*; [2].,., *Montreal, Canada*; [3]*McGill University, Clinical Epidemiology, Montreal, Canada*; [4]*University of Sherbrooke, Rheumatology, Sherbrooke, Canada*; [5]*Western University, Rheumatology, London, Canada*; [6]*University of Toronto, Rheumatology,Toronto, Canada*; [7]*The Arthritis Program, Rheumatology, Newmarket, Canada*; [8]*University of Manitoba, Rheumatology, Winnipeg, Canada*; [9]*Laval University, Rheumatology, Québec, Canada*; [10]*University of Calgary, Rheumatology, Calgary, Canada*; [11]*Hospital for Special Surgery, Rheumatology, New York, Canada*

Background: RA is an inflammatory disease that results in pain and loss of function, especially in the hands and wrists. Brief self-assessment tools that can reliably and precisely quantify hand/wrist function are needed to assess inflammatory activity when a physical exam is not feasible and to capture day-to-day experience of living with RA. Neuro-QoL is part of the PROMIS family of self-report measures created using a patient-centred approach and IRT methodology. The Neuro-Qol Upper Extremity Function (UEF) scale measures ability across fine motor and ADLs involving digital, manual and reach-related function and self-care. Little is known about its performance in RA.

Objectives: To evaluate the validity and responsiveness of the 8-item Neuro-QoL UEF in RA. We hypothesized scores would be strongly (r>.70) associated with MHAQ, MD-HAQ, and PROMIS PF, moderately (r=.4 to .7) to symptoms, disease activity, and QoL indicators, and be responsive to change in disease activity and PF.
Methods: Data were from the 0 and 6-month visits of adults with early RA (sx <1 yr) enrolled in the Canadian Early Arthritis Cohort, a prospective real-world study at 16 sites across Canada. Participants completed the Neuro-QoL UEF, MHAQ, MDHAQ, PROMIS-29, and PT Global at each visit. Rheumatologists recorded joint counts and MD Global. To evaluate content validity, we examined descriptive statistics across CDAI disease activity levels, and Pearson correlations between the Neuro-QOL UEF, legacy measures, CRP & ESR. Responsiveness was assessed by correlating change scores from visits 0-6 between Neuro-QoL UEF, disease activity and legacy PF scores.
Results: The 262 participants were mostly white (83%) women (71%) with a mean (SD) age of 55 (13). Summary statistics at 6-months are shown in Table 1. Neuro-QOL UEF was moderately-strongly correlated with MHAQ, MDHAQ, PROMIS-PF (|r|=.63-.75) and moderately correlated with pain and stiffness, (|r|=.59, -.64), and CDAI, SDAI, PT&MD Global, TJ & SJ (|r|=.39-.58). Neuro-QOL UEF was moderately correlated with PROMIS QoL domains Pain, Fatigue, Anxiety, Depression, Sleep & Participation (|r|=.39-.60).

Table 1. Summary statistics of physical function and RA disease activity indices at 6 months.

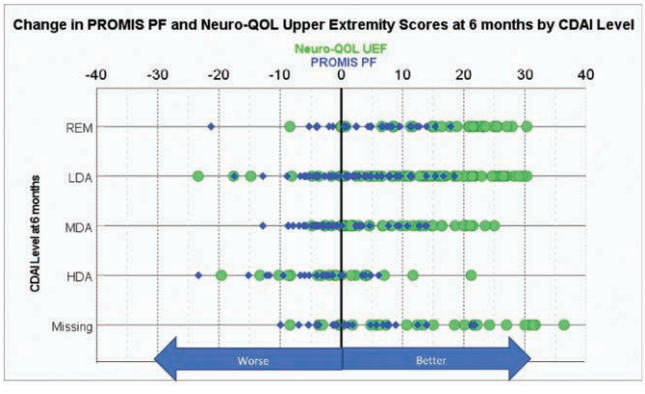
	Mean	SD	Mdn	25%	75%	(Min, Max)
Physical Function						
Neuro-Qol UEF	46.5	9.7	53.8	37.5	53.8	(21.8, 53.8)
MHAQ (0-3)	0.29	0.43	0.13	0.00	0.38	(0.00, 2.25)
MD-HAQ (0-10)	1.39	1.64	0.70	0.00	2.00	(0.00, 8.00)
PROMIS-PF	46.4	8.5	46.2	39.5	56.0	(23.3, 56.0)
RA Disease Activity						
CDAI	9.3	9.9	6.0	3.0	13.0	(0.0, 56.0)
SDAI	10.7	10.9	6.8	3.1	15.2	(0.0, 57.0)
Patient Global	3.0	2.5	3	1	5	(0, 10)
MD Global	1.8	2.2	1	0	3	(0, 9)
Swollen Joints (28)	2.1	3.7	0	0	2	(0, 20)
Tender Joints (28)	2.4	3.9	1	0	3	(0, 24)

Neuro-QOL scores decreased in a dose-response manner across worsening CDAI DA states reflecting increasing impairment (Table 2). Persons with HDA reported the highest disability, scoring nearly 0.5 SD lower on the Neuro-QoL UEF than PROMIS PF. Change from baseline to 6 months in Neuro-QoL UEF was moderately correlated with changes in PROMIS PF, MHAQ, PT Global, and CDAI (|r|=.44-.65). The mean change and range from 0-6 months in Neuro-QoL was significantly larger than in PROMIS (8.9 [95% CI 7.5, 10.4] vs. 5.4 [95% CI 4.4, 6.4])(see Figure).

Table 2. Mean scores (95% CI) at 6 months by CDAI level.

	REM	LDA	MDA	HAD
NeuroQol UEF	52.8 (51.8, 53.7)	48.1 (46.6, 49.7)	42.0 (39.4, 44.6)	33.8 (30.5, 37.1)
MHAQ (0-3)	0.05 (0.02, 0.09)	0.19 (0.14, 0.24)	0.45 (0.34, 0.57)	0.90 (0.63, 1.17)
MD-HAQ (0-10)	0.31 (0.17, 0.46)	1.11 (0.90, 1.32)	2.15 (1.71, 2.59)	3.56 (2.56, 4.56)
PROMIS-PF	52.8 (51.4, 54.2)	46.8 (45.3, 48.2)	42.3 (40.4, 44.2)	38.0 (34.4, 41.6)

Conclusion: Clinicians, researchers, and patients benefit from practical self-report tools that reliably and precisely monitor hand function in RA. Results offer initial evidence of validity and responsiveness and support use of Neuro-QoL UEF to self-assess inflammatory activity in the hands and day-to-day experiences of living with RA.



Acknowledgements: The CATCH study was designed and implemented by the investigators and financially supported through unrestricted research grants from: Amgen and Pfizer Canada - Founding sponsors since January 2007; AbbVie Corporation and Hoffmann-LaRoche since 2011; Medexus Inc. since 2013;, Merck Canada since 2017, Sandoz Canada, Biopharmaceuticals since 2019,Gilead Sciences Canada since 2020 and Fresenius Kabi Canada Ltd. since 2021. Previously funded by Janssen Biotech from 2011-2016, UCB Canada and Bristol-Myers Squibb Canada from 2011-2018, Sanofi Genzyme from 2016-2017, and Eli Lilly Canada from 2016-2020.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3259

OP0263-HPR THE ROLE OF PHYSICAL EXERCISES IN REDUCING CHRONIC FATIGUE IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Aleksandrov[1,2], M. Nikitin[3], V. Aleksandrov[1,2], N. Aleksandrova[1]. *[1]Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», Department of Functional Research Method, Volgograd, Russian Federation*; *[2]Volgograd State Medical University, Department of Hospital Therapy, Volgograd, Russian Federation*; *[3]FSB Institution "National Medical Research Center for Rehabilitation and Balneology" of the Ministry of Health of the Russian Federation, Sanatorium-Resort Complex "Vulan" - Scientific and Clinical Branch, Gelendzhik, Russian Federation*

Background: Physical activity is an important non-pharmacological intervention that has a combination of biological, physical and psycho-social benefits and can positively influence chronic fatigue in patients with rheumatoid arthritis (RA) [1, 2, 3].
Objectives: Evaluation of the effectiveness of the use of aerobic exercise (walking) to reduce fatigue in RA patients.
Methods: The study included 111 women with RA (mean age 54.4 ± 11.03 years old, mean duration of illness - 11.9 ± 9.3 years old). The DAS28-ESR indicator in RA patients was 2.84 [2.32; 3.05] points: low disease activity was diagnosed in 61.3% of patients, and remission in 38.7%. The average level of fatigue according to the VAS screening scale was 71.6 ± 8.93 points. Fatigue was assessed using the Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS V2). To assess the patient's tolerance to physical activity, a 6-minute walking distance (6MWD) test was used. A walking test at 50 meters was used to assess the functional state of patients in dynamics. The rehabilitation program (RP) of patients (for 21 days) included morning hygienic gymnastics, dosed walking (daily, duration 30-60 minutes) and walking in the air up to 3-3.5 hours a day. Vigorous movements "through pain" were contraindicated.
Results: No association was found between the duration of RA and all of the used numerical fatigue scales (p> 0.05), but there was a weak positive relationship between VAS and NRS-overcoming with age (r = 0.21 and r = 0.28). An association between DAS28-ESR and numerical fatigue scales VAS (r = 0.21), NRS effect (r = 0.25) and NRS - overcoming (r = 0.24) was found, despite the fact that this study did not include patients with moderate and high RA activity. There was a significant correlation between the walking time and the number of steps during the 50-meter test (r = 0.6, p <0.001), as well as an association between the fatigue and the walking time (r = 0.33, p = 0.001 for VAS and r = 0.41, p <0.001 for NRS-severity) and the number of steps (r = 0.39, p <0.001 for VAS; r = 0.47, p <0.001 for NRS-severity; r = 0.44, p <0.001 for NRS-bridging).

Table 1. Dynamics of fatigue levels and physical indicators in RA patients

	Before RP	In the end of RP	p
VAS fatigue level	71,2 ± 9,08 (71,5; 64–78)	70,4 ± 9,15 (70; 64–78)	p>0,05
BRAF-NRS: severity	6,83 ± 1,21 (7; 6–8)	6,51 ± 1,18 (7; 6–7)	p<0,01
BRAF-NRS: effect	6,24 ± 1,07 (5; 4–6)	5,95 ± 1,08 (6; 5–7)	p<0,05
BRAF-NRS: overcoming	5,0 ± 1,7 (7; 6–8)	7,76 ± 1,37 (5; 4–5)	p>0,05
50 meter test, number of steps	79,3 ± 8,64 (78; 73–84)	78,91 ± 8,15 (78; 73–83)	p>0,05
50-meter test, walking time, seconds	56,7 ± 8,72 (57; 50–63)	55,9 ± 8,59 (56; 51–60)	p=0,01

* The data are presented as mean ± standard deviation (median; interquartile range)After the completion of RP (Table), RA patients showed a significant reduction in the aspects of fatigue according to the NRS-severity (Z = 2.98, p = 0.003) and NRS-effect (Z = 2.08, p = 0.037) scales. There was also a decrease in the time spent by patients performing the 50 m walking test (t = 2.63, p = 0.01), but the total number of steps did not change (t = 1.44, p = 0.154). Fatigue and pain are important barriers to physical activity, but it is severe fatigue that reduces physical activity in patients with RA [4]. At the same time, physical activity itself can become a factor in reducing fatigue [5], including by reducing the activity of the disease [6].

Conclusion: The severity of fatigue in RA patients can be reduced by actively using non-pharmacological treatment strategies. Walking is a simple and effective solution to increase physical activity and it has a significant effect on fatigue in RA.

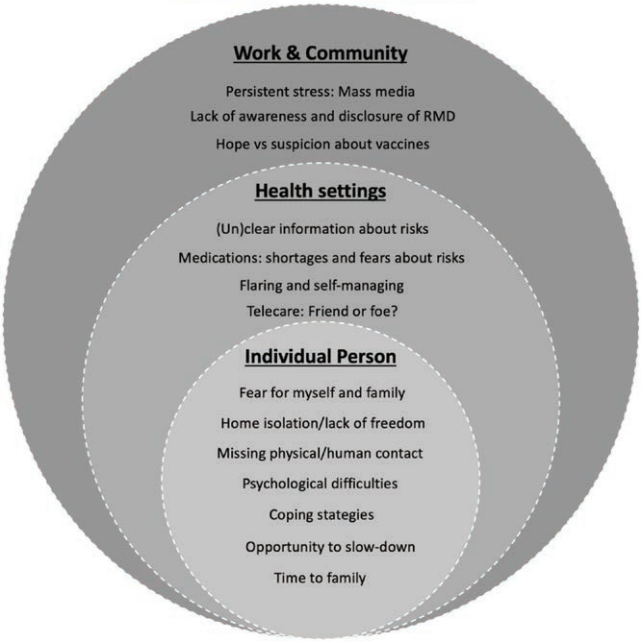
REFERENCES:
[1] Rongen-van Dartel SA et al. *Arthritis Care Res (Hoboken)*. 2015;67:1054–1062.
[2] Brosseau L et al. *PLoS One.* 2014;9(5):e95369.
[3] Cherkashina IV et al. *Vopr Kurortol Fizioter Lech Fiz Kult*. 2016;93(2):13-16.
[4] Loppenthin K et al. *Rheumatol Int.* 2015;35:1655–1664.
[5] Cramp F et al. *Cochrane Database Syst Rev*. 2013;8:CD008322.
[6] Sveaas SH et al. *Br J Sports Med.* 2017;51:1065–1072.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3211

OP0264-HPR "I LITERALLY CONVINCED MYSELF I WAS GOING TO CATCH IT AND DIE": LIVED EXPERIENCES OF THE COVID-19 PANDEMIC BY PEOPLE WITH RHEUMATIC DISEASES FROM FOUR EUROPEAN COUNTRIES

R. J. O. Ferreira[1,2], C. Costa[3], A. Marques[1,2,4], A. J. Barata Cavaleiro[2,4], S. Makri[5], K. Parperis[6], S. Psarelis[7], R. Williams[8], G. E. Fragoulis[9], H. Lempp[8], E. Nikiphorou[8,10]. *[1]Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal*; *[2]Escola Superior de Enfermagem de Coimbra, Health Sciences Research Unit: Nursing (UICISA: E), Coimbra, Portugal*; *[3]Centro Hospitalar e Universitário de Coimbra, Ortophedics, Coimbra, Portugal*; *[4]Escola Superior de Enfermagem de Coimbra, UCP Elderly Nursing, Coimbra, Portugal*; *[5]Cyprus League Against Rheumatism, Board, Nicosia, Cyprus*; *[6]University of Cyprus Medical School, Rheumatology, Nicosia, Cyprus*; *[7]Nicosia General Hospital, Rheumatology, Nicosia, Cyprus*; *[8]King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; *[9]Laiko Hospital, University of Athens, First Department of Internal Medicine, Athens, Greece*; *[10]King's College Hospital, Rheumatology, London, United Kingdom*

Background: The COVID-19 pandemic has resulted in unforeseen challenges for humanity, taking a significant toll, especially the immune-suppressed individuals. In this regard, the health and general well-being of people with rheumatic diseases, the great majority users of immunosuppressives, have been at stake.
Objectives: To explore the impact of the COVID-19 pandemic on people with rheumatic diseases on immunosuppression during the first wave, concerning a) (self-)management of their disease; b) interaction with the health care team; c) emotional well-being and d) overall health.
Methods: A qualitative study was conducted following a phenomenological approach. Adults (>18 years) with a rheumatic disease from four European countries (Cyprus, England, Greece, Portugal). Patients were recruited through patient's associations and social media and were invited to participate in semi-structured, audio-recorded interview or focus groups, between July - August 2020. Following a pilot study the information provided was transcribed verbatim, anonymized and translated into English where necessary. An inductive approach was adopted to carry out a thematic framework analysis with the assistance of ATLAS.ti to identify key themes and subthemes. Data validation strategies were employed, and Ethical approval and informed consent were obtained.
Results: Participants were 24 patients (21 women, age range 33 to 74 years) divided by 7 focus-groups and 1 individual interview. Most frequent diagnoses were rheumatoid arthritis (n=7), lupus (n=4), juvenile idiopathic arthritis (n=3).
Three key themes with 3-7 subthemes were identified within the analytical framework, centred around the impact of the Covid-19 on patients' lives (Figure 1): i) individual person (e.g. fear for myself and family, social isolation and lack of personal freedom, more time with family) ii) health settings (e.g. (un)clear information about risks of contamination, fear or risk of shortages of medication, remote consultations), and iii) work and community (e.g. persistent stress due to mass media exposure, lack of awareness by others about patients' rheumatic disease and its disclosure, hope and suspicion about new vaccine development: "I hear that they will ask vulnerable groups to have the vaccine first (...) Why is that? we will be again the innocent victims"). Findings were similar across countries, except for spirituality (i.e. the pandemic as "the hand of God"), a coping subtheme particular to Portugal. These main themes resonated well with the social ecological model and Walsh's Family Resilience Process [1,2].

Figure 1. **Lived experiences of the Covid-19 pandemic by people with rheumatic diseases**



Conclusion: When experiencing a significant life-event people require some time to process the different lived experiences. This study provides insights on how patients from four countries coped with the new challenges. Such insights are invaluable for health care providers and policy makers, in guiding more meaningful support tailored to individual needs, especially at times of crisis. The study highlights the impact of COVID-19 on the lives of people with rheumatic disease. A follow-up study is currently underway to examine the effect of subsequent waves of the pandemic.
REFERENCES:
[1] Golden SD, Earp JA. Social ecological approaches to individuals and their contexts: twenty years of health education & behavior health promotion interventions. Health Educ Behav. 2012;39(3):364-72. doi: 10.1177/1090198111418634.
[2] Walsh F. Family resilience: a framework for clinical practice. Fam Process. 2003;42(1):1-18. doi: 10.1111/j.1545-5300.2003.00001.
Acknowledgements: We thank the participants of this study.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1586

OP0265-HPR IMPACT OF COVID-19 PANDEMIC ON RHEUMATOLOGY PATIENTS IN NORTHERN IRELAND – A WEB BASED CROSS-SECTIONAL SURVEY

P. McKee[1], A. Irvine[1], C. Riddell[1], E. Ball[1]. *[1]Musgrave Park Hospital, Rheumatology, Belfast, United Kingdom*

Background: Concern for the susceptibility of rheumatology patients to severe COVID-19 illness has been raised since the start of the pandemic. Rheumatic disease and their immunosuppressant therapies placed many patients into the 'clinically extremely vulnerable' group when the UK's shielding guidance commenced on 23 March 2020. The impact of DMARDs/glucocorticoids/biologics on COVID-19 remains under investigation [1]. A recent study suggested caution may be required with rituximab and sulfasalazine in COVID-19 patients [2].

Objectives: The objective of this study is to evaluate the impact of the COVID-19 pandemic on rheumatology patients in Northern Ireland by assessing demographics, rheumatic disease, medications, disease progress, shielding advice, access to primary & tertiary care and incidence of COVID-19 infection.
Methods: A web-based cross-sectional survey was completed in Northern Ireland. The study duration was between 23rd November 2020 and 22nd January 2021. The questionnaire included consent, demographic details, medication history, comorbidities, disease course, patient experience, shielding advice, COVID-19 illness and hospitalisation. The survey was publicised by sending 6,032 Belfast Trust NHS patients a link via SMS, posters were displayed in rheumatology departments, and links made available via NHS/Versus Arthritis social media platforms.
Results: There were 2,615 responses and of these 2,539 had been completed and were analysed. Most respondents were aged 45+ (78.27%) and female (N=1819). Rheumatoid arthritis (41%) and psoriatic arthritis (29%) were the most common diagnoses. Just over one third (35.27%, N=896) of patients were on biological drugs. Most patients were taking methotrexate (28.04%) followed by hydroxychloroquine (15.20%) and adalimumab (12.52%). The majority (79.6%) continued treatment during the pandemic. There was evidence of disease 'flaring' in 30.75% of patients who had stopped treatment. Of the respondents surveyed 7.8% (N=198), tested positive for Covid-19 and of these 77.55% reported that they had received adequate shielding advice, primarily from GP or UK government sources. Only 11.11% (N=22) of those who tested positive for Covid-19 required hospital admission and 2 patients required intensive care support. Both patients requiring ICU were not on immunosuppression. Less than one third of patients testing positive for COVID-19 were on biological drugs (30.3%, N=60). Cardiovascular disease was the most prevalent comorbidity. Of the 22 patients hospitalised with COVID-19, 13.64% (N=3) were on solitary sulphasalazine therapy.
Conclusion: The survey showed low levels of COVID-19 hospitalisation despite most patients continuing DMARD/biologic/glucocorticoid therapy. This has been replicated in other studies [1], however data continues to be gathered on the safety of some biologic drugs particularly rituximab [2]. Most of our patients received clear understandable shielding guidance from a variety of sources. Many patients expressed fear of mortality, isolation and mental health issues. The survey findings indicated that stopping medication can have a negative impact on disease control.
REFERENCES:
[1] Robinson PC, Yazdany J. The COVID-19 Global Rheumatology Alliance: collecting data in a pandemic. Nat Rev Rheumatol. 2020 Jun;16(6):293-294.
[2] Strangfeld A, Schäfer M, Gianfrancesco MA, *et al*. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. Annals of the Rheumatic Diseases Published Online First: 27 January 2021. doi: 10.1136/annrheumdis-2020-219498
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3200

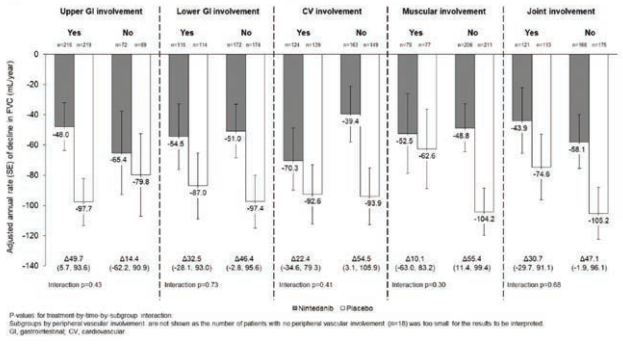
Progress in myositis and scleroderma research - II

OP0266 EFFICACY OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) AND INTERNAL ORGAN INVOLVEMENT: DATA FROM THE SENSCIS TRIAL

Y. Allanore[1], A. M. Hoffmann-Vold[2], M. Mayes[3], M. Vonk[4], C. Miede[5], M. Alves[6], G. Riemekasten[7,8]on behalf of the SENSCIS trial investigators.. [1]*Descartes University,APHP,Cochin Hospital, Department of Rheumatology A, Paris, France*; [2]*Oslo University Hospital, Department of Rheumatology, Oslo, Norway*; [3]*University of Texas McGovern Medical School, Division of Rheumatology and Clinical Immunogenetics, Houston, United States of America*; [4]*Radboud University Medical Center, Department of Rheumatology, Nijmegen, Netherlands*; [5]*Mainanalytics GmbH, Statistics, Sulzbach (Taunus), Germany*; [6]*Boehringer Ingelheim International GmbH,TA Inflammation Med, Ingelheim am Rhein, Germany*; [7]*University Hospital Charité, Rheumatology and Clinical Immunology, Berlin, Germany*; [8]*University Hospital Schleswig-Holstein, Rheumatology, Lübeck, Germany*

Background: SSc is a heterogeneous autoimmune disease characterised by fibrosis of the skin and internal organs. In most patients with SSc-ILD, organs other than the lungs are also affected. In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% versus placebo.
Objectives: We investigated the extent of organ involvement related to SSc at baseline in patients in the SENSCIS trial and the effect of nintedanib versus placebo on the rate of FVC decline in subgroups by internal organ involvement.
Methods: The SENSCIS trial enrolled patients with SSc-ILD with first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD ≥10% on high-resolution computed tomography (HRCT) and FVC ≥40% predicted. Patients with clinically significant pulmonary hypertension were excluded. Patients were randomised to receive nintedanib or placebo until the last patient reached week 52 but for ≤100 weeks. In post-hoc analyses, we analysed the rate of decline in FVC (mL/year) over 52 weeks in subgroups with and without different types of SSc-related internal organ involvement (upper gastrointestinal; lower gastrointestinal; cardiovascular [CV]; peripheral vascular; muscular; joint). These subgroups were defined based on patients' SSc-related medical history as reported in the case report form. A random slope and intercept model was used to assess the rate of decline in FVC (mL/year) and an interaction test applied to assess potential heterogeneity in the treatment effect of nintedanib between the subgroups.
Results: Of 576 patients, 96.9% had peripheral vascular involvement, 75.5% had upper gastrointestinal and 39.8% lower gastrointestinal involvement, 45.7% had CV involvement, 40.6% had joint involvement, and 27.1% had muscular involvement at baseline. In the placebo group, the rate of decline in FVC (mL/year) was numerically greater in patients with than without upper gastrointestinal involvement and in patients without than with joint involvement or muscular involvement (Figure). The exploratory interaction p-values did not indicate heterogeneity in the treatment effect of nintedanib versus placebo on reducing the rate of decline in FVC (mL/year) between the subgroups based on organ involvement (p>0.05 for all treatment-by-time-by-subgroup interactions) (Figure).
Conclusion: Patients in the SENSCIS trial had diverse complications related to SSc. There was no evidence of a differential treatment effect of nintedanib on reducing the rate of decline in FVC based on gastrointestinal, CV, joint, or muscular involvement at baseline.

Figure. Rate of decline in FVC (mL/year) over 52 weeks in subgroups by internal organ involvement at baseline in the SENSCIS trial.



Acknowledgements: The SENSCIS trial was funded by Boehringer Ingelheim. Medical writing support was provided by FleishmanHillard Fishburn, London, UK. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE).
Disclosure of Interests: Yannick Allanore Consultant of: Boehringer Ingelheim, Medsenic, Menarini and Sanofi, Grant/research support from: Alpine Pharmaceuticals, Anna-Maria Hoffmann-Vold Speakers bureau: Actelion, Boehringer Ingelheim, Lilly, MSD and Roche, Consultant of: Actelion, ARXX, Bayer, Boehringer Ingelheim, Lilly, Medscape, MSD and Roche, Grant/research support from: Boehringer Ingelheim, Maureen Mayes Consultant of: Paid consultant or member of Advisory Board/Steering Committee for Boehringer Ingelheim, Eicos, Galapagos and Mitsubishi Tanabe Pharma, Grant/research support from: Clinical trial research support from Boehringer Ingelheim, Corbus, Eicos and Galapagos, Madelon Vonk Speakers bureau: Boehringer Ingelheim, GlaxoSmithKline, Janssen and Roche, Consultant of: Boehringer Ingelheim and Janssen, Grant/research support from: Boehringer Ingelheim, Ferrer, Galapagos and Janssen, Corinna Miede Employee of: Currently an employee of mainanalytics GmbH, contracted by Boehringer Ingelheim, Margarida Alves Employee of: Currently an employee of Boehringer Ingelheim, Gabriela Riemekasten Speakers bureau: Actelion, Boehringer Ingelheim, Cellgene, GlaxoSmithKline, Janssen, Novartis and Roche, Consultant of: Actelion, Boehringer Ingelheim and Janssen, Grant/research support from: Janssen
DOI: 10.1136/annrheumdis-2021-eular.1067

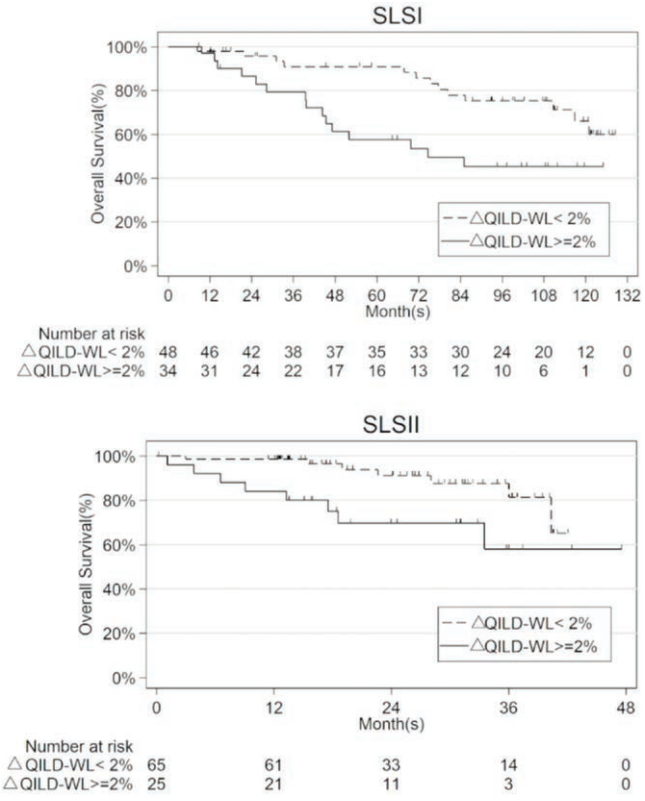
OP0267 SHORT-TERM CHANGES IN THE RADIOGRAPHIC EXTENT OF INTERSTITIAL LUNG DISEASE PREDICT LONG-TERM MORTALITY IN SYSTEMIC SCLEROSIS

E. Volkmann[1], D. Tashkin[1], M. Roth[1], J. Goldin[2], G. Kim[2]. [1]*UCLA, Medicine, Los Angeles, United States of America*; [2]*UCLA, Radiology, Los Angeles, United States of America*

Background: The forced vital capacity (FVC) is often used as the primary endpoint in treatment trials for systemic sclerosis-interstitial lung disease (SSc-ILD), and while trends in FVC have been found to predict mortality in SSc-ILD,[1,2] FVC measurements are also influenced by extra-pulmonary factors, such as cutaneous sclerosis, myopathy, and patient/technician effort. Change in the quantitative extent of ILD (QILD) on HRCT is an emerging endpoint in clinical trials; however, no studies have evaluated whether changes in radiographic extent ILD predict mortality in SSc-ILD.
Objectives: To evaluate the relationship between changes QILD in the whole lung (WL) and long-term survival in patients who participated in the Scleroderma Lung Study (SLS) I[3] and II.[4]

Methods: SLS I randomized 158 SSc-ILD patients to 12 months of cyclophosphamide (CYC) vs. placebo. SLS II randomized 142 SSc-ILD patients to 12 months of CYC, followed by 12 months of placebo vs. 24 months of mycophenolate (MMF). QILD-WL scores were calculated at baseline and 12 months (SLS I) and 24 months (SLS II). Participants were followed for up to 12 (SLS I) and 8 years (SLS II). Using landmark survival analysis, Kaplan Meier curves were generated to compare survival between participants who had worse QILD-WL scores (≥2% increase) and those who had stable/improved QILD-WL scores (<2% increase). Cox proportional hazards models were created to determine whether the change in QILD-WL scores predicted survival after controlling other variables found to affect survival in these cohorts.
Results: Among all the SLS I and II participants, 82 and 90 had follow up HRCT scans, respectively, and were included in these analyses. SLS I participants with an increase in QILD-WL scores of ≥2% at 12 months had significantly worse long-term survival (P= 0.01; Figure). Similarly, SLS II participants with an increase in QILD-WL scores of ≥2% at 24 months had significantly worse long-term survival (P= 0.019; Figure). After adjusting for baseline FVC, age, and modified Rodnan skin score (mRSS), an increase in QILD-WL scores of ≥2% remained associated with worse long-term survival in SLS I (*trend:* P=0.089) and SLS II (P=0.014).
Conclusion: Progression of the radiographic extent of ILD of ≥2% was associated with worse long-term survival in two independent SSc cohorts with extensive long-term follow up. The findings provide compelling evidence that short-term changes in the radiographic extent of ILD may serve as a surrogate endpoint for mortality in patients with SSc.

REFERENCES:
[1] Goh NS, et al. Arthritis Rheum 2017.
[2] Volkmann ER, et al. Ann Rheum Dis 2019.
[3] Tashkin DP, et al. NEJM 2006.
[4] Tashkin DP, et al. Lancet Resp Med 2016.



Disclosure of Interests: Elizabeth Volkmann Consultant of: Boehringer Ingelheim, Grant/research support from: Forbius, Corbus, Donald Tashkin: None declared, Michael Roth Grant/research support from: Genentech/Roche, Jonathan Goldin: None declared, Grace Kim: None declared
DOI: 10.1136/annrheumdis-2021-eular.1134

OP0268 TREATMENT STATUS AFFECTS HOW PULMONARY BIOMARKERS PREDICT PROGRESSION OF SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE

E. Volkmann[1], D. Tashkin[1], M. Leng[1], N. LI[1], G. Kim[2], J. Goldin[2], A. Harui[1], M. Roth[1]. [1]*UCLA, Medicine, Los Angeles, United States of America*; [2]*UCLA, Radiology, Los Angeles, United States of America*

Background: The course of interstitial lung disease (ILD) varies considerably in patients with systemic sclerosis (SSc), and no biomarkers have been found to consistently predict ILD progression in this population. Treatment may affect how a candidate biomarker correlates with improvement/worsening of SSc-ILD. We hypothesized that specific proteins recovered from bronchoalveolar lavage (BAL) would differentially predict progression of SSc-ILD based on whether a patient was receiving ILD therapy.
Objectives: (1) To assess the relationship between 68 unique BAL proteins measured in participants of Scleroderma Lung Study (SLS) I[1] and changes in radiographic extent of SSc-ILD; (2) To determine if treatment affects whether a specific protein predicts improvement or worsening of SSc-ILD.
Methods: Bronchoscopy was performed on 144 of the 158 participants in SLS I (Cyclophosphamide [CYC] vs. placebo) with 103 BAL samples available for analysis. BAL was lyophilized, concentrated 10X and used in a multiplex protein analysis of 68 distinct cytokines, chemokines and growth factors. Quantitative imaging analysis (QIA) was used to calculate the extent of radiographic fibrosis (QLF) in the whole lung using HRCT of the chest at baseline and 12 months. Multivariable linear regression models were created to determine the key BAL proteins associated with change in QLF scores using a backward selection process adjusting for treatment arm and ILD severity. The bootstrap procedure was employed for internal validation.
Results: A number of BAL proteins were significantly associated with change in QLF scores at 12 months; however, the directionality of these associations was often based on the presence/absence of treatment. For example, increased levels of granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin (IL)-1, monocyte chemoattractant protein (MCP)-3, chemokine ligand (CCL)-5, transforming growth factor (TGF)-β, hepatocyte growth factor (HGF), stem cell factor (SCF), IL-4, TGF-α, were associated with worse QLF scores in patients who received placebo; whereas, increased levels of these same proteins were associated with improved QLF scores in patients who received CYC (Figure). Increased levels of Fractalkine were associated with worse in QLF scores, and increased levels of IL-7 were associated with improved QLF scores, regardless of treatment arm. In the multivariable model adjusting for treatment arm and baseline severity of ILD, IL-1, MCP-3, surfactant protein C, IL-7, and CCL-5 were independently associated with change in QLF scores.

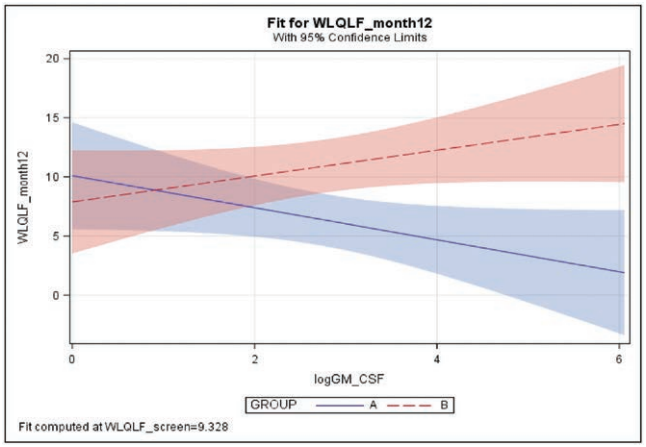


Figure 1. Example of a specific BAL protein (GM-CSF) that predicts worse QLF scores in patients receiving placebo (Group B, Red dotted line) and improved QLF scores in patients receiving CYC (Group A, Blue solid line). Shaded areas represent 95% confidence intervals.

Conclusion: Proteins that mediate both inflammation and fibrosis differentially affected progression of SSc-ILD based on treatment status. Higher levels of certain proteins predicted worsening of ILD in patients receiving placebo, but improvement in patients receiving CYC. Measuring these proteins could help to identify patients who: (1) are at risk for ILD progression, and (2) may preferentially benefit from treatment with immunosuppression.
REFERENCES:
[1] Tashkin DP, et al. NEJM 2006.
Disclosure of Interests: Elizabeth Volkmann Consultant of: Boehringer Ingelheim, Grant/research support from: Corbus, Forbius, Donald Tashkin: None declared, Mei Leng: None declared, Ning Li: None declared, Grace Kim: None declared, Jonathan Goldin: None declared, Airi Harui: None declared, Michael Roth Grant/research support from: Genentech/Roche
DOI: 10.1136/annrheumdis-2021-eular.1136

OP0269 A COMBINED CLINICAL AND BIOMARKER ALGORITHM TO PREDICT FVC DECLINE IN SYSTEMIC SCLEROSIS ASSOCIATED INTERSTITIAL LUNG DISEASE: RESULTS FROM AN INTERNATIONAL MULTICENTRE OBSERVATIONAL COHORT

M. Hutchinson[1], G. Abignano[1], J. Blagojevic[2], S. L. Bosello[3], Y. Allanore[4], C. Denton[5], O. Distler[6], P. Emery[1], M. Matucci-Cerinic[3], F. Del Galdo[1]. [1]*United Kingdom, Institute of Rheumatic and Musculoskeletal Medicine and NIHR Biomedical Research*

Centre, University of Leeds, Leeds, United Kingdom; [2]*Italy, University of FLorence, florence, Italy*; [3]*Universita la Cattolica, Rheumatology, florence, Italy*; [4]*INSERM, Rheumatology, Paris, France*; [5]*University College Lodon, Rheumatology, London, United Kingdom*; [6]*University of Zurich, Rheumatology, Zürich, Switzerland*

Background: Interstitial lung disease (ILD) is the leading cause of mortality in patients with Systemic Sclerosis (SSc). Forced Vital Capacity (FVC) is a major indicator of severity in SSc ILD. The ELF serum test and its constituent biomarkers (HA, PIIINP and TIMP-1) have shown to correlate with FVC in two large, independent multicentre cohorts of 457 patients, but also showed a correlation with age.
Objectives: Here we aimed to investigate the relationship of the ELF biomarkers and age in a large population of healthy controls and to identify a combined clinical and biomarkers model to stratify for risk of ILD progression in a multicentre longitudinal cohort of patients with SSc.
Methods: ELF score was measured in sera from 925 healthy controls in one centre and 869 longitudinal samples from 254 SSc patients from 6 centres across 4 European countries. Clinical data were recorded according to EUSTAR Minimal Essential dataset. FVC% change over time was estimated by Mixed-effects modelling. Patients were then divided in two groups: progressors, with a %FVC drop > 3%/year (according to published MCID) and a group of patients with stable or improving FVC. Lasso penalised regression was carried out with biomarkers and the available clinical and demographic variables at patient's first visit as potential predictors. The resulting linear predictor was used to derive two thresholds, one for optimal sensitivity (rule-out) and one for optimal specificity (rule-in). Patients within thresholds were further selected according to the ratio of TIMP-1: PIIINP (Figure 1).
Results: HA was the only ELF biomarker that correlated significantly with age in the healthy control cohort. Therefore, we defined by linear regression a "residual HA" which accounted for age. TIMP1, PIIINP and residual HA were then considered as distinct biomarkers in the analysis of the SSc cohort. 189 SSc patients with 785 time-points had complete datasets and were included in the analysis. Median follow up was 33 months (IQR 18-48). One-hundred and forty patients (74%) were classified as non progressors, 94 (50%) with no change or improving FVC and 46 (24%) with FVC drop <3% year. 49 patients (26%) were classed as progressors (drop of 3%/year or more in FVC, median slope -4.7%/year). Variable selection via Lasso penalised logistic regression resulted in a model with a c-index of 0.69 (95% CI: 0.60-0.78)) and contained age, disease duration (from first non-Raynaud's symptom), residual HA, anti-centromere antibodies (ACA) status, previous diagnosis of ILD, joint synovitis and history of protein pump inhibitor use. A two-step process was developed using the linear predictor from the model and the ratio of TIMP-1 and PIIINP (Figure 1). The stratification tool increased by nearly two-fold the ability to predict progressors in any 12 months interval (46 to 49% predictive value vs 26% probability) identifying an 82 to 91% negative predictive value for progression.
Conclusion: Building on the face and content validity of the biomarkers included in the ELF score, here we identify an easy to assess combined clinical and biomarker model to stratify patients for their risk of ILD progression. Despite its derivation from a large multicentre cohort, independent validation will determine the clinical value of Scleroscore as a stratification tool for risk of progression of SSc ILD.

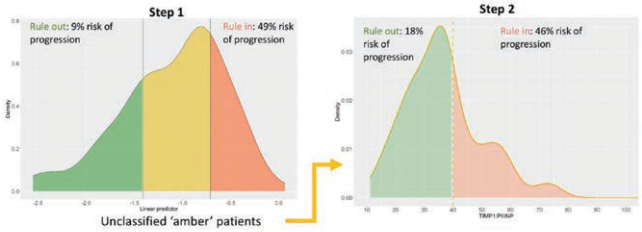


Figure 1: Two-step process to stratify patients for risk of ILD progression
Patients with overall 24% risk of 3% yearly FVC drop are stratified by regression model in patients with 49% (rule in) vs 9% risk (rule out) in (Step 1). Patients in between thresholds of Step 1 are further stratified according to the biomarker ratio (TIMP1/PIIINP) in the same risk categories.

Disclosure of Interests: Michelle Hutchinson: None declared, Giuseppina Abignano: None declared, Jelena Blagojevic: None declared, Silvia Laura Bosello: None declared, Yannick Allanore Grant/research support from: Alpine, Boehringer Ingelheim, Genentech/Roche, Medsenic, and Sanofi, Christopher Denton Consultant of: Corbus, Actelion, GlaxoSmithKline, Bayer, Sanofi, Galapagos, Inventiva, Boehringer Ingelheim, Roche, CSL Behring, Acceleron, Horizon, Arxx Therapeutics, Grant/research support from: Corbus, Actelion, GlaxoSmithKline, Bayer, Sanofi, Galapagos, Inventiva, Boehringer Ingelheim, Roche, CSL Behring, Acceleron, Horizon, Arxx Therapeutics, Oliver Distler Consultant of: Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB, Grant/research support from: Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB, Paul Emery Consultant of: Lilly, Abbvie, Roche, Grant/research support from: Lilly, Marco Matucci-Cerinic Consultant of: Chemomab, Lilly, Abbvie, Actelion, Francesco Del Galdo Speakers bureau: Astra-Zeneca, Boehringer Ingelheim, Actelion, Consultant of: Astra-Zeneca, Mitsubishi-Tanabe, Capella Biosciences, Chemomab, Actelion, Boehringer-Ingelheim, Grant/research support from: Capella Biosciences, Chemomab, Kymab, Mitsubishi-Tanabe
DOI: 10.1136/annrheumdis-2021-eular.1861

OP0270 LONG-TERM EFFICACY AND SAFETY OF BOSENTAN IN PATIENTS WITH DIGITAL ULCERS RELATED TO SYSTEMIC SCLEROSIS

N. Cristina[1], L. Groseanu[1,2], F. Berghea[1,2], A. Balanescu[1,2], V. Bojinca[1,2], D. Mazilu[1,2], S. Daia[1,2], D. Opris-Belinski[1,2], I. Saulescu[1,2], C. L. Constantinescu[1,2], M. Abobului[1,2], A. Borangiu[1,2], M. M. Negru[1,2], C. Cobilinschi[1,2], D. Predeteanu[1,2], M. Duna[1,2], R. Ionescu[1,2]. [1]*St Mary Clinical Hospital, Department of Internal Medicine and Rheumatology, Bucharest, Romania*; [2]*Carol Davila University of Medicine and Pharmacy, Internal Medicine and Rheumatology, Bucharest, Romania*

Background: Two pivotal studies, RAPIDS-1 and RAPIDS-2 revealed that bosentan reduces the development of new digital ulcers (DUs) in patients with systemic sclerosis (SSc). However data regarding the long-term use of this dual endothelin antagonist receptor in the treatment of DUs is scarce.
Objectives: The aim of the present study was to evaluate long term efficacy and safety profile of bosentan in patients with DUs related to SSc.
Methods: A prospective observational case-control study, conducted between 2014 and 2020 enrolled 65 SSc patients with ≥1 active DUs at baseline, who received bosentan therapy. Demographic and clinical features, including DUs incidence and patients subjective perception of DU pain and/or Raynaud's Phenomenon, were collected. Nailfold videocapillaroscopy was performed in all patients.
Results: The study included 51 females and 14 males, with a mean age of 52.6 years, 30 with diffuse subset, most of them with late scleroderma pattern (46/65). Number of DUs at baseline was 4.55 (±2.8), median duration of treatment was 25.95 (±19.4) months. Microangiopathy evolution score (MES) was 5.1 (2.19), visual analog scale (VAS) for DU was 77.9, VAS for Raynaud was 73.4.
Patients receiving bosentan had clinically significant reduction in the mean number of DU ($p<0.001$). The effect was most powerful for the first 6 months of treatment, but the improvement was sustained until 24 months' follow-up, when the mean DU number reached a plateau that was kept until end of study. 6 month and 24 month evaluations also revealed significant decrease in the VAS for DU ($p<0.05$) and in the VAS for Raynaud ($p<0.01$). Statistically significant difference was noted between bosentan-treated and the control group with respect to the decrease in the mean number of digital ulcers. ($p=0.005$).
There was a clear trend towards an improvement in MES score, between baseline and the next follow-up assessments ($p=0.003$). The difference was statistically significant when compared to control group, but only for the first 18 months of treatment ($p<0.001$).
14 patients (28.75%) discontinued bosentan therapy for administrative reasons. The median time among patients who interrupted the treatment was 6.9 months. An accelerated development of new DU was described 6 months after ($p=0.02$). Following recommencement of bosentan, the mean number of DU has rapidly decreased ($p=0.008$). There was no significant difference between patients who temporarily discontinued bosentan for 6 or 12 months.
Bosentan was stopped due to lack of efficacy in 2 cases and due to side effects in 7 cases: 4 elevated liver enzymes, 1 severe trombocytopenia, 1 dyspneea agravation and low blood pressure.
Conclusion: The present data suggest that treatment with endothelin receptor antagonist bosentan was associated with a significant reduction in the mean number of DU in patients with SSc. The beneficial effect of bosentan persisted throughout the study but was most evident in the first 6 months of treatment. Statistical analysis showed a significant improvement of the microangiopathy evolution score from baseline to end of therapy. 14 patients had a high relapse rate due to potential rebound effect, 6 months after bosentan withdrawal.The drug was reintroduced succesfully for 10 (70%) patients with a significant decrease in the number of DU.
REFERENCES:
[1] UK Scleroderma Study Group: digital vasculopathy in systemic sclerosis, Rheumatology, Volume 54, Issue 11, November 2015, Pages 2015
[2] Groseanu L, Berghea F, Bojinca V, et al AB0779 Long term follow-up of a systemic sclerosis group treated with bosentan, Annals of the Rheumatic Diseases 2018;77:1523-1524.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1916

OP0271

JUVENILE LOCALIZED SCLERODERMA: A LARGE RETROSPECTIVE COHORT STUDY FROM A TERTIARY CARE CENTER

B. Egeli[1], J. Dallas[1], E. Anderson[1], M. Min[2], D. Mazori[2], S. Gellis[2], M. B. Son[1], R. Sundel[1], R. Vleugels[2], F. Dedeoglu[1]. *[1]Boston Children's Hospital, Rheumatology, Boston, United States of America*; *[2]Boston Children's Hospital, Dermatology, Boston, United States of America*

Background: Juvenile Localized Scleroderma (jLS) is a rare pediatric inflammatory disease of skin and underlying tissues that may cause significant functional impairment and disfigurement. Management approaches vary and an optimum treatment regimen is lacking. In 2012, a group of jLS researchers of Childhood Arthritis and Rheumatology Research Alliance (CARRA) proposed consensus treatment plans (CTPs), aimed to streamline the approach to care for jLS patients.

Objectives: This study aimed to evaluate a large jLS patient cohort seen over a 21-year period in a single tertiary care pediatric hospital in the USA, in order to examine treatments utilized and determine parameters for systemic therapy initiation.

Methods: This retrospective cohort study included jLS patients with disease onset in childhood (≤18-years of age) who were seen in rheumatology, dermatology, or combined rheumatology-dermatology clinics from 1999-2020, with ≤ 3 years of follow-up. Data on demographics, disease characteristics, therapies prescribed, and treatment trends were analyzed.

Results: Of the 270 jLS patients identified, 101 fulfilled the inclusion criteria. The primary reason for exclusion was <3 years of follow-up. Selected demographic data and disease characteristics of patients are shown in Table 1. There were no statistically significant differences in most patient and disease characteristics between patients who received systemic treatment and those who did not. There were no significant differences in baseline laboratory values. The group treated with systemic therapy did have higher rates of extracutaneous involvement and had a higher proportion of patients with a generalized morphea phenotype.

Table 1. Demographic and Disease Characteristics

	All Patients (n=101)	On Systemic Therapy (n=63)	No Systemic Therapy (n=38)	p value
Age-onset (Y), median (IQR)	7.5 (6.4)	9 (6)	7 (4)	NS
Age-diagnosis(Y), median (IQR)	9 (7.9)	10 (6.7)	9 (3.7)	NS
Diagnostic delay(M), median (IQR)	10 (2.9)	12 (13)	7.5 (17)	NS
Follow-up (M), median (IQR)	74 (69.3)	65 (44.5)	78 (47.7)	NS
Subtype				
Linear	56	39	17	NS
Face	29	20	9	NS
Circumscribed	23	4	19	<0.0001
Mixed	2	2	0	NS
Generalized	20	18	2	0.004
Extracutaneous Involvement	19	18	1	0.001
Clinic type				
Dermatology	29	2	27	<0.0001
Rheumatology	21	19	2	0.003
Combined	51	42	9	<0.0001

The majority of patients who were on systemic immunomodulatory therapy were treated with methotrexate (59/63, 93.6 %) and/or systemic corticosteroids (21/63, 33 %). 5 patients were treated with hydroxychloroquine, 2 of which were also on methotrexate. 6 patients on methotrexate were either switched to or had mycophenolate mofetil added as concomitant therapy. The most common adverse effects observed in methotrexate-treated patients were gastrointestinal complaints (12/61, 19.7%) and fatigue (7/61, 11.5%). The median treatment duration was 50 months (IQR: 33.5). Patients were more likely to receive systemic therapy if they were followed in rheumatology or combined rheumatology-dermatology clinics as compared to dermatology clinics. Finally, 78% of patients with jLS received systemic treatment after 2013 (a year after publication of the CARRA jLS CTP) as compared to 55% of patients prior to 2013 ($p < 0.05$).

Conclusion: This jLS cohort is one of the largest reported from a single center and reflects an increase in the use of systemic therapy since publication of CARRA CTPs in 2012. Further studies on long-term treatment outcomes and therapeutic approaches utilized when first-line treatment failures occur are warranted.

REFERENCES:

[1] Li SC, Torok KS, Pope E, et al. Development of consensus treatment plans for juvenile localized scleroderma: a roadmap toward comparative effectiveness studies in juvenile localized scleroderma. *Arthritis Care Res (Hoboken)*. 2012;64(8):1175-1185.

Disclosure of Interests: Bugra Egeli: None declared, Johnathan Dallas: None declared, Edwin Anderson: None declared, Michelle Min: None declared, Daniel Mazori: None declared, Stephen Gellis: None declared, Mary Beth Son: None declared, Robert Sundel: None declared, Ruth Vleugels: None declared, Fatma Dedeoglu Consultant of: Novartis

DOI: 10.1136/annrheumdis-2021-eular.4066

OP0272

68GA-FAPI-04 PET/CT STUDY EXTENSION FOR THE ASSESSMENT OF FIBROBLAST ACTIVATION AND RISK EVALUATION IN SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE

C. Bergmann[1], J. H. W. Distler[1], C. Treutlein[2], K. Tascilar[1], A. T. Mueller[1], A. Atzinger[3], A. E. Matei[1], J. Knitza[1], A. H. Györfi[1], A. Lueck[1], C. Dees[1], A. Soare[1], A. Ramming[1], V. Schönau[1], O. Distler[4], O. Prante[3], P. Ritt[3], T. I. Goetz[3], M. Koehner[3], M. Cordes[3], T. Baeuerle[2], T. Kuwert[3], G. Schett[1], C. Schmidkonz[3]. *[1]University Hospital Erlangen, Department Internal Medicine 3, Erlangen, Germany*; *[2]University Hospital Erlangen, Department Radiology, Erlangen, Germany*; *[3]University Hospital Erlangen, Department Nuclear Medicine, Erlangen, Germany*; *[4]University Hospital Zuerich, Department Rheumatology, Zuerich, Switzerland*

Background: Interstitial lung disease (ILD) is the most common cause of death in systemic sclerosis (SSc). To date, the progression of SSc-ILD is judged by the accrual of lung damage on computed tomography (CT) and functional decline (forced vital capacity). However, this approach does not directly assess the activity of tissue remodeling. Moreover, prediction of the course of ILD in individual SSc patients remains challenging. Fibroblast Activation Protein (FAP) is a specific, ex vivo validated marker for activated fibroblasts.

Objectives: The aims of this study were: 1. To assess differences in the uptake of ^{68}GA-FAPI 04 in SSc-ILD patients compared to controls, to analyze 2. whether ^{68}GA-FAPI 04 uptake at baseline correlates with other risk factors of disease progression and 3. Whether ^{68}GA-FAPI 04 uptake is associated with the course of SSc-ILD.

Methods: Between September 2018 and April 2020, 21 patients with SSc-ILD confirmed by HRCT and onset of SSc-ILD within ≤ 5 years or signs of progressive ILD and 21 controls without ILD were consecutively enrolled. All participants underwent ^{68}Ga-FAPI-04 PET/CT imaging and standard-of-care procedures including HRCT and lung function testing (PFT) at baseline. Patients with SSc-ILD patients were followed-up for 6 months with HRCT and PFT. Follow-up ^{68}Ga-FAPI-04 PET/CT scans were obtained in a subset of patients treated with nintedanib. We compared baseline ^{68}Ga-FAPI-04 PET/CT uptake to standard diagnostic tools and currently used predictors of ILD progression. The association of ^{68}Ga-FAPI-04 uptake with changes in FVC was analyzed using mixed-effects models.

Results: ^{68}Ga-FAPI-04 accumulated in fibrotic areas of the lungs in SSc-ILD compared to controls with a median (q1-q3 interval) wlSUVmean of 0.8 (0.6 to 2.1) in the SSc-ILD group and 0.5 (0.4 to 0.5) in the control group ($p<0.0001$ with Mann-Whitney test) and a median whole lung maximal standardized uptake value (wlSUVmax) of 4.4 (3.05 to 5.2) in the SSc-ILD group compared to 0.7 (0.65 to 0.7) in the control group ($p<0.0001$). wlFAPI-MAV and wlTL-FAPI were not measurable in control subjects, as no 68Ga-FAPI-04 uptake above background level was observed. In the SSc-ILD group the median wlFAPI-MAV was 254cm^3 (163.4 to 442.3) and the median wlTL-FAPI was 183.6cm^3 (98.04 to 960.7). ^{68}Ga-FAPI-04 uptake was higher in patients with extensive disease, with previous ILD progression or high EUSTAR activity scores. Increased ^{68}Ga-FAPI-04 uptake at baseline was associated with progression of ILD independently of extent of involvement on HRCT scan and the forced vital capacity at baseline. In consecutive ^{68}Ga-FAPI-04-PET/CTs, changes in ^{68}Ga-FAPI-04 uptake was concordant with the observed response to the fibroblast-targeting antifibrotic agent nintedanib.

Conclusion: Our study presents first in human evidence that ^{68}Ga-FAPI-04-fibroblast uptake correlates with fibrotic activity and disease progression in the lungs of SSc-ILD patients and that ^{68}Ga-FAPI-04-PET/CT may be of potential to improve risk assessment of SSc-ILD.

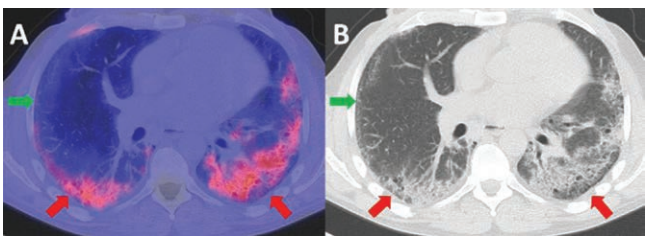


Figure 1. A and B: ^{68}Ga-FAPI-04 PET/CT scan from a patient with SSc-ILD with selective ^{68}Ga-FAPI-04 uptake in fibrotic areas of the left- and right lower lung lobes (red arrows), but not in non-fibrotic areas such as the middle lobe (green arrow). B Corresponding CT component.

Acknowledgements: We gratefully acknowledge Prof. Uwe Haberkorn (University Hospital Heidelberg and DKFZ, Heidelberg, Germany) and iTheranostics Inc. (Dulles, VA, USA) for providing the precursor FAPI-04.
Disclosure of Interests: Christina Bergmann: None declared, Jörg H.W. Distler Speakers bureau: Actelion, Anamar, ARXX, Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, and UCB, Grant/research support from: Anamar, Active Biotech, Array Biopharma, ARXX, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB, Christoph Treutlein: None declared, Koray Tascilar Speakers bureau: Gilead sciences GmbH, Pfizer Turkey, UCB Turkey, Anna-Theresa Mueller: None declared, Armin Atzinger: None declared, Alexandru-Emil Matei: None declared, Johannes Knitza: None declared, Andrea-Hermina Györfi: None declared, Anja Lueck: None declared, Clara Dees: None declared, Alina Soare: None declared, Andreas Ramming: None declared, Verena Schönau: None declared, Oliver Distler Speakers bureau: Arxx Therapeutics, Baecon Discovery, Blade Therapeutics,Bayer, Böhringer Ingelheim, Catenion,Competitive Drug Development International Ltd, Corbuspharma, CSL Behring, ChemomAb, Horizon Pharmaceuticals, Ergonex, Galaapagos NV, Glenmark Pharmaceuticals,GSK, Inventiva, Italfarmaco, IQvia, Kymera, Lilly, Medac, Medscape, MSD, Novartis, Pfizer, Roche, Sanofi, Taget Bio Sciencec, UCB, Grant/research support from: Bayer,Böhringer Ingelheim, Mitsubishi Tanabe Pharma, Olaf Prante: None declared, Philipp Ritt: None declared, Theresa Ida Goetz: None declared, Markus Koehner: None declared, Michael Cordes: None declared, Tobias Baeuerle: None declared, Torsten Kuwert Speakers bureau: Honoraria for occasional lectures by Siemens Healthineers, Grant/research support from: Research grant to the Clinic of Nuclear Medicine by this entity covering projects in the field of SPECT/CT, Georg Schett: None declared, Christian Schmidkonz: None declared
DOI: 10.1136/annrheumdis-2021-eular.114

OP0273 **THE SCLERODERMA CLINICAL TRIALS CONSORTIUM DAMAGE INDEX (SCTC-DI) IN A SYSTEMIC SCLEROSIS COHORT WITH 10-YEARS FOLLOW-UP**

M. G. Lazzaroni[1], M. Breda[1], F. Franceschini[1], P. Airò[1]. [1]*ASST Spedali Civili of Brescia, University of Brescia, Rheumatology and Clinical Immunology Unit, Department of Clinical and Experimental Sciences, Brescia, Italy*

Background: Systemic Sclerosis (SSc) is characterized by increased mortality and organ damage accrual. A composite SSc Damage Index was recently developed by the Scleroderma Clinical Trials Consortium (SCTC-DI) and was demonstrated as a predictor of mortality both in the Australian derivation cohort and in the Canadian validation cohort.
Objectives: To evaluate in a single centre cohort of SSc patients with 10-years follow-up: (1) the evolution of organ damage over time; (2) factors associated with the development and accrual of organ damage.
Methods: A retrospective analysis was performed on patients prospectively followed in our centre from 1989 to 2019. Organ damage was evaluated with SCTC-DI (0-55 scale; moderate damage >5, severe damage>12) and comorbidities with Charlson Comorbidity Index (CCI, which includes the age of the patient). Patients were included when a follow-up of at least 10 years was available together with SCTC-DI at the diagnosis (baseline, T0), 1 year (T1), 5 years (T5) and 10 years (T10) after the diagnosis. Univariable and multivariable analysis (logistic regression) were performed when appropriated.
Results: 253 SSc patients were included (female 93%; Caucasians: 99%; median age at diagnosis: 52 years (IQR: 43-60); diffuse cutaneous subset: 15%; anti-centromere (ACA)+ 55%; anti-Topoisomerase 1+20%; anti-RNA polymerase III+: 4%; ever smokers: 28%). Median interval between the first SSc symptom other than Raynaud's phenomenon and the diagnosis was 1 year. SCTC-DI progressively increased from diagnosis to T10 (p<0.0001; Kruskal-Wallis test).
Moderate damage (score:6-12) was observed in 22 patients at T0 (8.7%), in 30 at T1 (11.9%), in 45 at T5 (17.7%) and in 73 at T10 (28.9%). None of the patients had severe damage (score:13-55) at T0 and T1, while it was present in 6 at T5 (2.4%) and in 13 at T10 (5.1%).
At T0 no difference in SCTC-DI scores was observed when comparing different subgroups according to gender (female vs. male), disease subsets (diffuse vs. limited) and autoantibodies (ACA- vs. ACA+). At T1, SCTC-DI score was higher in patients with diffuse vs. limited cutaneous subset, and ACA- vs ACA+ (p<0.0001 for both).
Multivariable analysis demonstrated that a moderate or severe organ damage (SCTC-DI score >5) at 5 years was positively associated with diffuse cutaneous involvement (p:0.009, OR 4.55, 1.46-14.1), SCTC-DI at T0 (p:0.015, OR 1.34, 1.06-1.70) and at T1 (p:<0.0001, OR 1.65, 1.30-2.07), and negatively associated with ACA+ (p:0.024, OR 0.32, 0.12-0.86), while CCI and male sex showed no association. At 10 years SCTC-DI>5 was associated with diffuse cutaneous involvement (p:0.013, OR 4.30, 1.36-13.7), SCTC-DI at T5 (p:<0.0001, OR 1.67, 1.38-2.01), while SCTC-DI at T0, CCI, male sex and ACA+ had no association.
Among 253 patients, 90 (36%) died after >10 years of follow-up. In non-survivors, as compared to survivors, SCTC-DI score was significantly higher at the baseline (T0) and during the entire follow-up (p<0.0001 for every timepoint).
Conclusion: At the end of 10-years follow-up (T10), 35% of patients in our cohort had moderate or severe organ damage (SCTC-DI score>5). Diffuse cutaneous involvement was associated with higher SCTC-DI scores at different time points (T5 and T10). Organ damage, quantified by SCTC-DI at different time points, was confirmed as a factor associated with mortality in patients who reached more than 10 years of follow-up.
REFERENCES:
[1] Ferdowsi N, et al. Ann Rheum Dis. 2019;78:807-16.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.582

PARE Abstract session

OP0274-PARE **EVALUATION OF PATIENT SATISFACTION FOR TELEHEALTH (PHONE AND VIDEO) IN RHEUMATOLOGY OUTPATIENTS DURING COVID-19 PANDEMIC**

Y. Oh[1,2], A. Hennessey[1,2], L. Young[1,2], D. Yates[1,2], C. Barrett[1,2]. [1]*Redcliffe Hospital, Rheumatology, Redcliffe, Australia*; [2]*The University of Queensland, Medicine, Saint Lucia, Australia*

Background: Telehealth via phone (TPhone) or video conference (TVideo) in rheumatology has been a topic of interest for many years. Its use was rapidly expanded due to the international public health emergency of coronavirus disease-19 (COVID-19) outbreak in 2020. Australian Medicare Benefits Schedule (MBS) swiftly enabled temporary MBS telehealth items on 13 March 2020, currently extended until 31 March 2021[1]. In the early phase of the COVID-19 pandemic, Antony et al. conducted a single-centre public survey to assess patient perception of rheumatology telehealth. Their results showed that 98.4% of patients consider telehealth acceptable during the pandemic[2]. It is unclear, however, whether this positive perception persists after patients experience a telehealth. In addition, a survey data in 2019 suggested more than half of Australian rheumatologists work in private practice[3]. Therefore, inclusion of private patients will better represent patient perception of telehealth.
Objectives: The aim of this study was to evaluate patient satisfaction with telehealth during the COVID-19 pandemic. This would determine its feasibility to be integrated in future rheumatology outpatient model.
Methods: A questionnaire containing 30 questions was sent to rheumatology patients who attended telehealth appointments at a level 2 public hospital and a local private clinic between April and May 2020. The questionnaires aimed to obtain information on baseline demographics (sex, age, public or private patient, employment status, visual or auditory impairment), appointment details (TPhone or TVideo, usual arrangement for face-to-face (F2F) appointment, cost effectiveness) and appointment satisfaction using a 5-point Likert scale. Descriptive statistical analysis was conducted.
Results: The questionnaire was sent to 1452 patients, of which 494 patients responded (34%). Female predominance (77.1%) and a higher proportion of TPhone (79.1%) was seen in the respondents. A majority of patients were existing patients known to the services (90.9%). More than 70% of responses indicated overall satisfaction in specialist care via telehealth, and 88.7% perceived this suitable during a pandemic. Of all respondents, 21.7% were prescribed new medication, and the majority of these patients were confident in taking the new medication after the telehealth appointment. Future acceptability for TPhone was significantly lower in private patients compared to public patients (p= 0.01). Subgroup analysis revealed that higher telehealth satisfaction was associated with needing to take time off work to attend face-to-face appointment (p= 0.02), perception of cost effectiveness (p<0.001) and TVideo (p=0.03).
Conclusion: This is the first study which included both public and private rheumatology patients to evaluate patient satisfaction for telehealth during the COVID-19 pandemic. Overall high level of satisfaction was seen in telehealth most notably associated with its cost effectiveness. A higher percentage of patients who had TVideo compared to TPhone were receptive to future telehealth via TVideo, supportive of the importance of visual cues. This in turn will have significant administrative and technological burdens to coordinate in comparison to a F2F or TPhone review. This qualitative study provides valuable insight of patient perception of telehealth, which has the potential to compliment the traditional rheumatology outpatient model of care following the pandemic.
REFERENCES:
[1] COVID-19 Temporary MBS Telehealth Services 2020 [Available from: http://www.mbsonline.gov.au/internet/mbsonline/publishing.nsf/Content/Factsheet-TempBB.
[2] Antony A, Connelly K, De Silva T, Eades L, Tillett W, Ayoub S, et al. Perspectives of Patients With Rheumatic Diseases in the Early Phase of COVID-19. Arthritis Care & Research. 2020;72(9):1189-95.
[3] Association AR. Workforce Survey Exective Summary 2019 2019 [Available from: https://rheumatology.org.au/members/documents/WorkforceSurveyExecutiveSummary-websiteMay2019.pdf.

Acknowledgements: University of Queensland
Nursing staff at Redcliffe Hospital and Administration officers at Redcliffe & Northside Rheumatology
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2885

OP0275-PARE THE UNACCEPTABLE DELAY TO DIAGNOSIS IN AXIAL SPONDYLOARTHRITIS; DEVELOPING A CALL TO ACTION FOR A GLOBAL HEALTHCARE CHALLENGE

W. Gerhart[1], M. T. Duruöz[2], J. Lowe[3], D. Webb[4], L. Wermskog[5], J. Davies[6], R. Howard[7], M. Mallinson[8], C. L. Koehn[9]. [1]*Canadian Spondylitis Association, Director, Toronto, Canada*; [2]*Marmara University School of Medicine, PMR Department, Istanbul, Turkey*; [3]*Axialspondyloarthritis International Federation, Projects, London, United Kingdom*; [4]*National Axialspondyloarthritis Society, Director, London, United Kingdom*; [5]*Spafo Norge Spondyloartrittforbundet, Director, Oslo, Norway*; [6]*Axialspondyloarthritis International Federation, Executive, London, United Kingdom*; [7]*Spondylitis Association of America, Executive, Los Angeles, United States of America*; [8]*Axialspondyloarthritis International Federation, Volunteering, London, United Kingdom*; [9]*Arthritis Consumer Experts, Director, Vancouver, Canada*

Background: The current delay to diagnosis from symptom onset represents one of the greatest challenges in axial spondyloarthritis (axSpA). Research shows an average global delay of almost 7 years[1] – and as long as 15 years in some cases[2] – during which time the condition can progress considerably and lead to irreversible damage. Data indicates that women wait longer than men for a diagnosis[3], and there has been very limited progress in reducing the time to axSpA diagnosis. The axSpA diagnosis delay has a hugely detrimental impact on an individual's quality of life. Because the disease frequently has early onset[1], individuals are left with untreated or incorrectly-treated symptoms at a formative period in their life course, whilst they await their diagnosis.
Objectives: The Axial Spondyloarthritis International Federation (ASIF) set out to coordinate a comprehensive evidence-based global review of the factors influencing the current axSpA diagnosis delay and to produce a definitive report that shines a light on these barriers, as well as providing a resource that can ultimately empower a range of international stakeholders to reduce this delay.
Methods: A full literature review was carried out to identify relevant available global evidence exploring the axSpA diagnosis delay. In autumn 2020 ASIF held two virtual global forum events, involving patients and patient group representatives, researchers, rheumatologists and other healthcare professionals, to methodically explore key diagnosis challenges across different healthcare systems and the opportunities for addressing these. Break-out discussions were held and participants were asked to identify the personal and societal effects of the diagnostic delay; the reasons it occurs; and initiatives to tackle the challenge. Alongside key stakeholder testimonies, best practices from around the world were also identified. 92 stakeholders participated in the events; they represented patients and healthcare professionals from 23 countries across five continents.
Results: The findings from these activities were incorporated within a new 'Delay to Diagnosis' report, which for the first time definitively sets out the lived realities from a global perspective of the axSpA diagnosis delay. The report identified important commonalities across different countries and healthcare systems contributing to the current average global 7-year diagnosis delay, including:

- Poor awareness of axSpA, particularly in primary care services
- Complexities in diagnosing the disease
- Poorly defined referral pathways
- Insufficient patient access to rheumatologists and appropriate diagnostics

The report also highlights the significant impact this delay has on individuals and wider society, providing a foundation for future advocacy work. A series of recommendations have also been identified, the implementation of which will help to instigate tangible progress in reducing the current delay.
Conclusion: Despite longstanding challenges, there are now clear opportunities for transforming how axSpA is diagnosed around the world. This message needs to be heard and acted upon urgently by all those involved in the management and delivery of axSpA care. The future programme of work for ASIF's Delay to Diagnosis project will respond to these findings and be centred around supporting axSpA patient associations globally to take this call to action forward throughout 2021 and beyond.
REFERENCES:
[1] Zhao et al; Diagnostic delay in axial spondyloarthritis: a systematic review and meta-analysis; *Rheumatology*, 2021
[2] Garrido-Cumbrera, M., Poddubnyy, D., Gossec, L. et al. The European Map of Axial Spondyloarthritis: Capturing the Patient Perspective—an Analysis of 2846 Patients Across 13 Countries. Curr Rheumatol Rep 21, 19 (2019)
[3] Jovani et al; Understanding How the Diagnostic Delay of Spondyloarthritis Differs Between Women and Men: A Systematic Review and Metaanalysis; The Journal of Rheumatology December 2016

Disclosure of Interests: Wendy Gerhart Employee of: I was employed by Janssen Canada from 1992 - 2017, Mehmet Tuncay Duruöz: None declared, Jo Lowe Grant/research support from: No financial grants received individually. However, my role as Project Manager at ASIF is currently funded partially by UCB Global and partially by Novartis Global, Dale Webb Speakers bureau: Janssen and Novartis, Grant/research support from: Individually, no. But NASS receives grants from AbbVie, Biogen, Eli Lilly, Janssen, Novartis and UCB, Lillann Wermskog Grant/research support from: Individually, no. But Spafo Norge receives a small amount of funding for ongoing projects from Novartis., Jo Davies Grant/research support from: Individually, no. However, ASIF are currently funded by UCB, Lilly, Boehringer Ingelheim, Janssen and Novartis; this funding partially covers staff salaries as well as a range of projects, the content and outputs of which are not influenced by the funders., Richard Howard Shareholder of: AbbVie, Amgen, Bristol-Myers Squibb, GSK, Johnson & Johnson, Eli Lilly, Merck, Novartis, Pfizer, and Teva. I own <20 shares of any one stock and these stocks represent <4% of personal investments, Consultant of: Yes, GSK, Novartis - but then donated to Spondylitis Association of America, Grant/research support from: I have not personally received financial grants. SAA has received financial support from AbbVie, Amgen, BI, J&J, Lilly, Novartis, Pfizer, UCB., Michael Mallinson Consultant of: No. But, for full disclosure: I have received honoraria in the past, for participating in patient advisory board activities, from Abbvie, Novartis, Pfizer and UCB., Cheryl L Koehn Grant/research support from: OUR ORGANIZATION, ARTHRITIS CONSUMER EXPERTS, HAS. I HAVE NOT AS AN INDIVIDUAL. HERE IS OUR PUBLICLY AVAILABLE DISCLOSURE ON ALL ONLINE AND PRINT MATERIALS, PRESENTATIONS, MEETINGS, GOVERNMENT CONSULTATIONS:
https://jointhealth.org/about-principles.cfm?locale=en-CA
Over the past 12 months, ACE received grants-in-aid from: Arthritis Research Canada, Amgen Canada, Canadian Institutes of Health Research, Canadian Rheumatology Association, Eli Lilly Canada, Hoffman-La Roche Canada Ltd., Knowledge Translation Canada, Merck Canada, Novartis Canada, Pfizer Canada, Sandoz Canada, Sanofi Canada, St. Paul's Hospital (Vancouver), UCB Canada, and the University of British Columbia.
DOI: 10.1136/annrheumdis-2021-eular.2368

OP0276-PARE CREATING POLITICAL LEVERS TO IMPROVE AXIAL SPONDYLOARTHRITIS CARE

J. Hamilton[1], D. Webb[2], S. Whalley[3]. [1]*National Axial Spondyloarthritis Society, Head of Policy & Health Services, London, United Kingdom*; [2]*National Axial Spondyloarthritis Society, CEO, London, United Kingdom*; [3]*M&F Health, Health Communications, London, United Kingdom*

Background: Research carried out in 2016 by NASS showed that the range and quality of axial spondyloarthritis (axial SpA) services generally offered around the UK were variable [1]. The publication by the regulator, the National Institute for Health and Care Excellence (NICE), of a Guideline for Spondyloarthritis (NG65) in 2017 [2] and the corresponding Quality Standard (QS170) in 2018 [3], for the first time provided national guidance and standards of services that should be available for people with axial SpA. National oversight of the implementation of these however was missing.
Objectives: NASS worked with Parliamentarians to establish the All-Party Parliamentary Group for Axial Spondyloarthritis in January 2019. We gave it a very specific objective - to oversee the implementation of NH65 and QS170. The group seeks to improve axial SpA services in England whilst raising awareness of the condition at a parliamentary level, working closely with NASS.
Methods: The group is a unique forum in the UK, bringing together patients, clinicians, researchers, policy makers, national bodies and parliamentarians. The group has met five times covering a range of topics including the delay to diagnosis, the uptake of NG65 and hydrotherapy.
In 2019 the group carried out a national inquiry into the standards of axial SpA services in the UK, developing a ten-question quality framework, based largely on the NICE Guideline recommendations and Quality Standard. In July 2020 a meeting was convened to discuss the impact of COVID-19 on axial SpA services. The meeting presented research carried out by NASS and M&F Health with patients and clinicians respectively.
Results: The results of the national inquiry for England were published in January 2020 [4]. The inquiry found that large discrepancies remain in the provision of axial SpA services. Only 21% of local commissioning bodies have an inflammatory back pain pathway, and less than half of NHS providers have a specialist axial SpA clinic.
The results of COVID survey shows significant impacts on the health of axial SpA patients and on the availability and modality of rheumatology services. The APPG later published a report with a set of recommendations [5], creating minimum service specifications for axial SpA services during crisis periods such as the recent pandemic, as well as service recovery. Comment on this research was also published in The Lancet Rheumatology [6].

In September 2020 the work of the APPG led to a debate in Parliament on delayed diagnosis in axial SpA.
Discussions on the future of hydrotherapy services has resulted in the mobilisation of stakeholders across condition areas.
Conclusion: All All Party Parliamentary Group is already proving to be an effective political lever to improve axial SpA care. It has shown huge variations in the standard of care and provision of services still remain and has brought this to the attention of Parliamentarians, policy makers and clinicians.
REFERENCES:
[1] Mohammed H Derakhshan, Himanshu Pathak, Debbie Cook, Sally Dickinson, Stefan Siebert, Karl Gaffney, NASS and BRITSpA investigators, *Services for spondyloarthritis: a survey of patients and rheumatologists*, Rheumatology, February 2018
[2] *Spondyloarthritis in over 16s: diagnosis and management (NG65)*, https://www.nice.org.uk/guidance/ng65, February 2017
[3] *Spondyloarthritis (QS170)*, https://www.nice.org.uk/guidance/qs170, June 2018
[4] *Axial Spondyloarthritis Services in England – A national inquiry*, https://nass.co.uk/wp-content/uploads/2020/01/Axial-Spondyloarthritis-Services-in-England-FINAL.pdf, January 2020
[5] COVID-19 & Axial SpA: Government Recommendation Paper, https://nass.co.uk/wp-content/uploads/2020/10/APPG-Recommendation-Paper-COVID-19-Axial-SpA-for-website-1.pdf, October 2020
[6] Helena Marzo Ortega, Simon Whalley, Jill Hamilton, Dale Webb, *COVID-19 in axial spondyloarthritis care provision: helping to straighten the long and winding road*, https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30413-6/fulltext, 1 December 2020
Disclosure of Interests: Jill Hamilton Grant/research support from: Funding was received from Novartis to support APPG 1, 2 and 4, Dale Webb Grant/research support from: Funding was received from Novartis for APPG 1, 2 and 4, Simon Whalley: None declared
DOI: 10.1136/annrheumdis-2021-eular.2612

OP0277-PARE METABERN, THE EUROPEAN REFERENCE NETWORK FOR RARE HEREDITARY DISEASES: STRUCTURE, OBJECTIVES, METABOLIC RMDS AND THE ROLES OF EUROPEAN PATIENT ADVOCACY GROUPS (EPAGS)

L. Wagner[1], S. Sestini[2], C. Brown[3], A. Finglas[4], R. Francisco[5], S. Bond[6], C. Lampe[7], C. Belettato[6], C. Van Lingen[6], M. Scarpa[6], on behalf of MetabERN collaboration group. [1]*Deutschsprachige Selbsthilfegruppe für Alkaptonurie e.V., DSAKU e.V., Stuttgart, Germany*; [2]*Associazione italiana dei malati di alcaptonuria, AimAKU, Siena, Italy*; [3]*Krabbe UK, Krabbe UK, London, United Kingdom*; [4]*MSD Action Foundation, MSD Action Foundation, Dublin, Ireland*; [5]*Portuguese Association for CDG and Other Rare Metabolic Diseases, APCDG-DMR, Almada, Portugal*; [6]*Udine University Hospital, MetabERN, Regional Coordination Center for Rare Diseases, Udine, Italy*; [7]*Center for Rare Diseases Giessen, ZSEGI, Giessen, Germany*

Background: Inborn metabolic disorders (IMDs) currently encompass more than 1,500 diseases with new ones still to be identified[1]. Each of them is characterised by a genetic defect affecting a metabolic pathway. Only few of them have curative treatments, that target the respective metabolic pathway. Commonly, treatment examples include diet, substrate reduction therapies, enzyme replacement therapies, gene therapy and biologicals, enabling IMD-patient now to survive to adulthood. About 30 % of all IMDs involve the musculoskeletal system and are here referred to as rare metabolic RMDs. Generally, IMDs are very heterogenous with respect to symptoms and severity, often being systemic and affecting more children than adults. Thus, challenges include certified advanced training of adult metabolic experts, standardised transition plans, social support and development of therapies for diseases that do not have any cure yet.
Objectives: Introduction of MetabERN, its structure and objectives, highlighting on the unique features and challenges of metabolic RMDs and describing the involvement of patient representation in MetabERN.
Methods: MetabERN is stratified in 7 subnetworks (SNW) according to the respective metabolic pathways and 9 work packages (WP), including administration, dissemination, guidelines, virtual counselling framework, research/clinical trials, continuity of care, education and patient involvement. The patient board involves a steering committee and single point of contacts for each subnetwork and work package, respectively[2]. Projects include identifying the need of implementing social science to assess the psycho-socio-economic burden of IMDs, webinars on IMDs and their transition as well as surveys on the impact of COVID-19[3] on IMD-patients and health care providers (HCPs), social assistance for IMD-patients and analysing the transition landscape within Europe.
Results: The MetabERN structure enables bundling of expertise, capacity building and knowledge transfer for faster diagnosis and better health care. Rare metabolic RMDs are present in all SNWs that require unique treatments according to their metabolic pathways. Implementation of social science to assess the psycho-socio-economic burden of IMDs is still underused. Involvement of patient representatives is essential for a holistic healthcare not only focusing on clinical care, but also on the quality of life for IMD-patients. Surveys identified unmet needs of patient care, patients having little information on national support systems and structural deficits of healthcare systems to ensure HCP can provide adequate clinical care during transition phases. These results are collected by MetabERN and forwarded to the Directorate-General for Health and Food Safety (DG SANTE) of the European Commission (EC) to be addressed further.
Conclusion: MetabERN offers an infrastructure of virtual healthcare for patients with IMDs. Thus, in collaboration with ERN ReCONNET, MetabERN can assist in identifying rare metabolic disorders of RMDs to shorten the odyssey of diagnosis and advise on their respective therapies. On the other hand, MetabERN can benefit from EULAR's longstanding experience regarding issues affecting the quality of life, all RMD patients are facing, such as pain, stiffness, fatigue, rehabilitation, maintaining work and disability claims.
REFERENCES:
[1] IEMbase - Inborn Errors of Metabolism Knowledgebase http://www.iembase.org/ (accessed Jan 29, 2021).
[2] MetabERN: European Refence Network for Hereditary Metabolic Disorders https://metab.ern-net.eu/ (accessed Jan 29, 2021).
[3] Lampe, C.; Dionisi-Vici, C.; Bellettato, C. M.; Paneghetti, L.; van Lingen, C.; Bond, S.; Brown, C.; Finglas, A.; Francisco, R.; Sestini, S.; Heard, J. M.; Scarpa, M.; MetabERN collaboration group. The Impact of COVID-19 on Rare Metabolic Patients and Healthcare Providers: Results from Two MetabERN Surveys. *Orphanet J. Rare Dis.* **2020**, *15* (1), 341. https://doi.org/10.1186/s13023-020-01619-x.

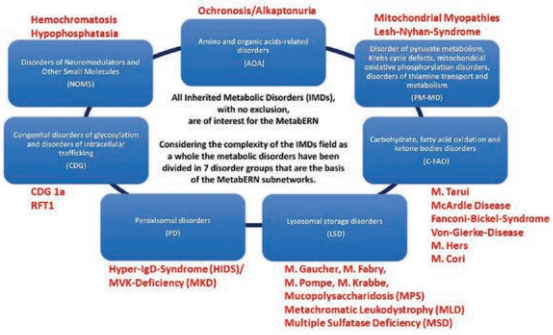


Figure: Examples of inborn metabolic diseases (IMD) with known RMD-symptoms, allocated to the respective subnetworks of MetabERN. However, the list is incomplete.

Acknowledgements: The authors thank the MetabERN collaboration group, the single point of contacts (SPOC) of the MetabERN patient board and the Transition Project Working Group (TPWG)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3372

OP0278-PARE PROVIDING SUPPORT TO FAMILIES OF CHILDREN NEWLY-DIAGNOSED WITH CHILDHOOD ARTHRITIS: A PATIENT AND PARENT-LED PILOT STUDY TO DEVELOP AND ASSESS 'A LITTLE BOX OF HOPE' SUPPORT PACKS

S. Chibnell-Smith[1], A. L. Chibnell-Smith[1], R. Beesley[1]. [1]*Juvenile Arthritis Research, JAR Project, Tonbridge, United Kingdom*

Background: Juvenile Idiopathic Arthritis (JIA) is a heterogenous group of autoimmune disorders characterised by chronic joint inflammation, diagnosed in around 1 in 1,000 children and young people (CYP) under the age of 16. Delays in diagnosis are common [1], awareness is low, and paediatric rheumatological conditions have a considerable impact on young people and their families [2]. A lack of understanding amongst families of newly-diagnosed children leads to uncertainty and anxiety.
Objectives: This patient and parent-led project developed a resource pack for parents of CYP newly-diagnosed with JIA, to provide information and support. Following a pilot, feedback from recipients was collated and analysed to help improve future provision.
Methods: A young person with JIA identified the need for direct family support. Juvenile Arthritis Research (a UK charity) developed a unique pack of support information, containing resources for both children and their families - called *A Little Box Of Hope.* This included information about JIA and support services available for families, as well as Kipo (a children's book about JIA) and accompanying finger puppet. Clinicians at one paediatric rheumatology centre provided information about the packs to newly diagnosed families, who then requested a free box to be posted to them.

Following an initial pilot study, recipients were invited to complete a short online questionnaire and provide feedback to allow refinement of the provision.
Results: Respondents were asked a series of questions, each on a scale of 1-5. Every respondent gave a score of 5 in response to "What do you think of the idea of *A Little Box Of Hope*?"
Every parent of children under ten years old gave a score of 5 for every item when asked "How useful is each item in your *Little Box Of Hope*?"
Respondents also gave free-text comments:
* "It was very well thought out and I felt supported"
* "I know so much more about JIA now than I did before. I cannot thank you enough."
* "It was extremely useful and made me feel supported during a very stressful time and this enabled me to support my son more effectively."
* "It made my daughter feel less alone."
Some parents of older children felt that some information specifically for teens would be useful, and a Teen pack is being developed.
Conclusion: Recipients of *A Little Box Of Hope* have found the information useful and feel supported. Following the pilot study, we have developed *My JIA*, a booklet reviewed by a multi-disciplinary clinical team, with comprehensive information for families affected by JIA. A Teen pack, for children aged around 10 years or older, is being developed to provide targeted support to this group.
The COVID-19 pandemic has adversely affected access to healthcare services, increasing the need for remote parent- and charity-provided support through *A Little Box Of Hope*.
As such, we intend to expedite the roll-out of the project across the country building on the success of the pilot project.
REFERENCES:
[1] McErlane F, Foster HE, Carrasco R, et al. Trends in Paediatric Rheumatology Referral Times and Disease Activity Indices over a Ten-Year Period among Children and Young People with Juvenile Idiopathic Arthritis: Results from the Childhood Arthritis Prospective Study. *Rheumatology (Oxford)* 2016;55(7):1225–34.
[2] Foster HE, Scott C, Tiderius CJ, et al. Improving Musculoskeletal Health for Children and Young People - A "Call to Action". *Best Pract Res Clin Rheumatol* 2020;34(5):101566.
[3] Dejaco C, Alunno A, Bijlsma JWJ, et al. Influence of COVID-19 Pandemic on Decisions for the Management of People with Inflammatory Rheumatic and Musculoskeletal Diseases: A Survey among EULAR Countries. *Ann Rheum Dis* 2020;0:1-9.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2332

OP0279-PARE CHRONIC RHEUMATIC DISEASE (CRD) AND SPORT

P. Lemesle[1], L. Poulain[2], X. Grapton[3], N. Bouhedja[2]on behalf of CREER.
[1]*Hospital of Courbevoie, Clinic Rives de Seine, Courbevoie, France*; [2]*La Garenne-Colombes, Private practice, La Garenne-Colombes, France*; [3]*Neuilly-sur-Seine, Private practice, Neuilly-sur-Seine, France*

Background: In order to study the state of mind of patients with chronic inflammatory rheumatic disease (CRD) regarding physical/sports activity, excluding household activities despite their quantifiable energy value (MET), the CREER group produces this study.
Objectives: Analyze a population in the Ile-de-France region with CRD practicing a physical activity (their motivations, expectations, nature and rhythm). Determine the place of physical activity in the management of an CRD by the rheumatologist (Rh).
Methods: 207 patients, 53 yo average, 56% between 50 and 70 years, 60% are women; 97% of the CRD, Rheumatoid arthritis (RA): 57%) or Ankylosing Spondylitis (AS): 40%, low or moderate activity (66%).
10 years evolution (RA) and 11.5 years (AS), corticosteroids RA/AS as follows (34/5 %), NSAIDs (15/52 %), conventional DMARDS (84/30%) or biotherapies (21/43%).
Co-morbidities are found for RA/AS in 55% vs 44%, includes high blood pressure 20%, overweight 21%, tobacco 13.5%, other 19%.
Results: 7/10 patients are encouraged to engage in physical activity, regardless of gender, age, RA or AS. The most common activity proposed is walking (53%), followed by swimming and/or aquagym (40%) and gym (19%). The practice is regular in 60% more by women, RA=AS, more before 40 yo and after 60 years old (70%).
The activity actually practiced is: 1- walking 46.4%, 2- aquatic activities 37%, 3- cycling 29%, 4- home sports 19%.
Once/week minimum is good for cycling and swimming, insufficient for walking, very good for sport at home.
50% have been practicing for 3 years. 60% adapt the rhythm to rheumatism. Their motivations are: to maintain one's health, to de-stress.
A discordance exists between Rh/General physician that advise sport 8 times/10 vs 4.5/10. Nevertheless 50% ignore whether he or she is getting worse or better, hence the need for information.
Rh needs to communicate more about the interest of physical activity and the absence of deleterious effect on CRD which one patient over two ignores.
If 60% of patients modify their activity with CRD, many do not participate in sports because no time, no need, no desire RA=AS.
If the activity is supervised, adapted, prescribed is well-known, its application is confidential due to lack of coaches, and of qualified centers.
Conclusion: If the main activity practiced by patients and advocated by Rh is walking, the patients go beyond this framework by mobilizing for cycling, walking, swimming and gym. But the reluctance persists and we must, through therapeutic education convince of the benefits of the activity on CRD and its co-morbidities, unknown to 50% of patients. To map lesions, judge the ability and desires are necessary to set goals for duration and frequency of activity. Using connected tools improves compliance. Finally, walking which does not require neither schedule nor equipment (otherwise a cane) should become a first-line prescription.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.866

OP0280-PARE A MINDFULNESS PROGRAM DOSING STUDY TO EVALUATE IMPROVEMENT IN EMOTIONAL DISTRESS AMONG PEOPLE WITH RHEUMATIC DISEASE

J. Thompson[1], N. Parikh[1], K. Gavigan[1], S. Venkatachalam[1], W. B. Nowell[1].
[1]*Global Healthy Living Foundation, Patient Centered Research, Upper Nyack, United States of America*

Background: Mindfulness-based interventions for chronic pain and emotional distress have increased in popularity as complementary therapies among people living with rheumatic and musculoskeletal disease (RMD).[1,2] Despite growing evidence that mindfulness meditation reduces pain and anxiety associated with RMD, more research is needed to specify the optimal duration of mindfulness training necessary to be effective for short- and long-term benefit.
Objectives: To evaluate and compare the effectiveness of full-length versus brief mindfulness training programs for improving anxiety among people living with RMD.
Methods: Adult US participants (pts) within the ArthritisPower registry were invited to participate in the Healthy Mind Healthy You study comparing the effectiveness of two online mindfulness training programs of different lengths accessed via the MoodNetwork platform. The full-length mindfulness based cognitive therapy program lasted 8 weeks, while the brief evidence-based mindfulness program lasted 3 weeks. Pts were randomized to one of the two programs and completed assessments every two weeks during the program and then every four weeks during the 12-week follow-up period. Assessments included World Health Organization-Five Well-Being Index (WHO-5), Five Facet Mindfulness Questionnaire (FFMQ), Perceived Stress Scale (PSS), and two measures of emotional distress, PROMIS Short Forms for Anxiety and Depression. Analyses compared demographic characteristics and assessment scores by program length.
Results: 324 pts completed assessments at baseline and 70 pts completed them at week 8, an attrition rate of 78% in each of the program arms. The majority of pts were female, White, with 67% between the ages of 45-64 years. No statistically significant differences were observed at baseline between participants randomized to each of the two programs, and in their assessment scores at week 8 (Table 1); PROMIS Anxiety and Depression scores improved from baseline to week 8 for pts in both programs (Figure 1). Overall, mean (SD) PROMIS Depression scores improved from 58.4 (7.7) at baseline to 55.4 (7.2) at week 8 (p=0.018), a meaningfully important difference, among the 70 pts reporting scores at both time points.

Table 1. Assessment Scores at Baseline and Week 8, Mean (SD)

	Baseline				Week 8			
	All (n=324)	8-week course (n=163)	3-week course (n=161)	p-value	All (n=70)	8-week course (n=35)	3-week course (n=35)	p-value
WHO-5 [b]	10.6 (4.9)	10.4 (4.8)	10.9 (5.0)	0.378	12.0 (5.1)	12.5 (5.5)	11.6 (4.7)	0.488
FFMQ [c]	42.7 (6.1)	42.7 (6.1)	42.7 (6.1)	0.932	39.2 (5.7)	38.9 (6.1)	39.4 (5.3)	0.741
PSS [d]	18.7 (7.5)	19.2 (6.8)	18.3 (8.2)	0.304	16.6 (7.3)	15.7 (7.8)	17.6 (6.8)	0.291
PROMIS Depression [e]	56.5 (8.3)	57.3 (8.0)	55.7 (8.6)	0.097	55.1 (8.5)	54.8 (9.3)	55.5 (7.8)	0.735
PROMIS Anxiety [f]	58.7 (8.2)	59.0 (8.2)	58.4 (8.1)	0.470	55.4 (7.2)	54.6 (7.4)	56.1 (7.1)	0.404

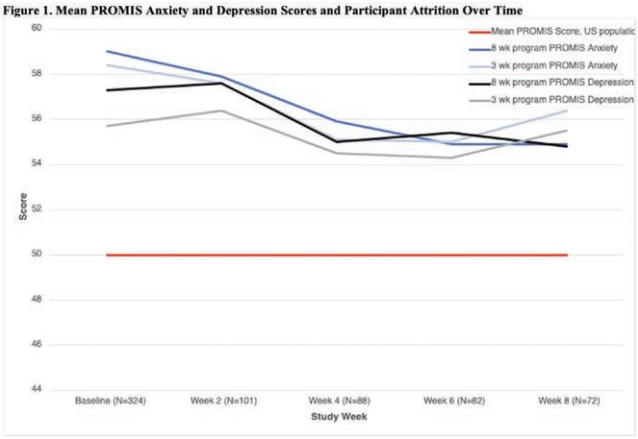
[a] denotes use of Fisher's Exact Test [b] Range 0 (worse) to 25 (better), [c] Range 3 (worse) to 15 (better), [d] Range 0 (better) to 40 (worse), [e] Range 24.7 (better) to 63.5 (worse), [f] Range 25.7 (better) to 62.0 (worse)

Conclusion: People living with RMD who are part of a real-world US registry are willing to participate in an online mindfulness training program study, but may require additional support to remain engaged and adherent throughout the program and to participate to study conclusion. Participation in a mindfulness training program, whether full-length or brief, appears to improve symptoms of emotional distress among people with RMD.

REFERENCES:

[1] Zhou, B. et al. Comp. Ther. in Clin. Prac. 2020; 39:1-7
[2] Reiner, K. et al. Pain Medicine. 2013; 14(2): 230-242

Acknowledgements: The authors would like to thank ArthritisPower members for participating in the study, and the Healthy Mind Healthy You study team at Massachusetts General Hospital (see MoodNetwork.org) for leading it. The study was funded by the Patient-Centered Outcomes Research Institute (XPPRN-1512-33786).



Disclosure of Interests: Julia Thompson: None declared, Nupur Parikh: None declared, Kelly Gavigan: None declared, Shilpa Venkatachalam: None declared, W. Benjamin Nowell Grant/research support from: Full-time employee of Global Healthy Living Foundation, an independent nonprofit organization, which has received funding to conduct research; Principal Investigator for studies with grant support from AbbVie, Amgen and Eli Lilly.

DOI: 10.1136/annrheumdis-2021-eular.2728

New Developments in COVID-Research

OP0281 EXCESS GIANT CELL ARTERITIS CASES ARE ASSOCIATED WITH PEAKS IN COVID-19 PREVALENCE

B. Mulhearn[1,2], J. Ellis[1], S. Skeoch[1], J. Pauling[1,2], S. Tansley[1,2]. [1]*Royal United Hospital, Royal National Hospital For Rheumatic Diseases, Bath, United Kingdom*; [2]*University of Bath, Pharmacy and Pharmacology, Bath, United Kingdom*

Background: Immediately following the first wave of the COVID-19 pandemic, the number of giant cell arteritis (GCA) diagnoses noticeably increased at the Royal National Hospital for Rheumatic Diseases in Bath, UK. Furthermore, there was an increase in the proportion of patients with visual complications [1]. The finding supports the viral hypothesis of GCA aetiopathogenesis as previously described [2]. This not only has ramifications for understanding the underlying disease mechanisms in GCA but also has implications for the provision of local GCA services which may have already be affected by the pandemic.

Objectives: The objective of the study was to estimate the incidence of giant cell arteritis during the COVID-19 pandemic years of 2020 – 2021 and compare it to 2019 data. Given that there have now been two distinct peaks of COVID-19 as reflected by hospital admissions of COVID-19-positive patients this has allowed us to investigate if there is a temporal relationship between the prevalence of COVID-19 and the incidence of GCA.

Methods: The incidence of GCA was calculated by assessing emailed referrals to the GCA service and the hospital electronic medical records to identity positive cases from 2019 to the current date. Local COVID-19 prevalence was estimated by measuring the number of hospital beds taken up by COVID-19 positive patients, available publicly in a UK Government COVID-19 dataset [3].

Results: There were 61 (95% Poisson distribution confidence interval [CI] 47 - 78) probable or definite GCA diagnoses made in 2020 compared to 28 (CI 19 – 40) in 2019 (Figure 1). This is an excess of 33 cases in 2020, or an increase in 118%. Given that 41% of the hospital's catchment population is over 50, this equates to an annual incidence rate of 13.7 per 100,000 in 2019 and 29.8 per 100,000 in 2020. This compares to a previously estimated regional incidence rate of 21.6 per 100,000 for the South West of the UK [4].

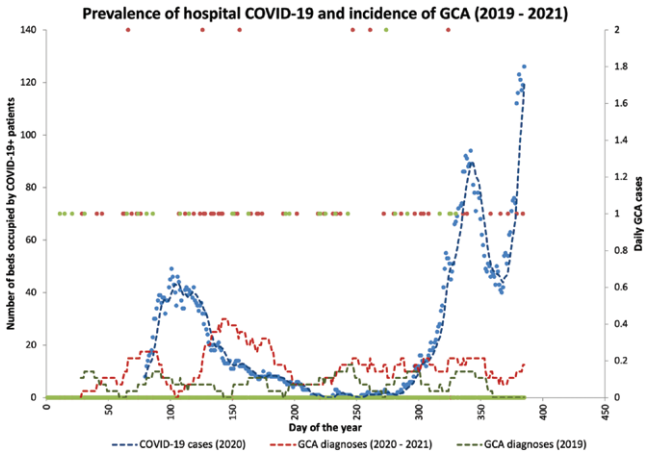


Figure 1. Prevalence of hospital COVID-19 and incidence of GCA (2019 – 2021). Graph showing the number of hospital beds occupied by COVID-19-positive patients in 2020 – 2021 (blue circles), number of daily GCA diagnoses in 2020 – 2021 (red circles), and previous GCA diagnoses in 2019 (green circles). The broken lines represent moving averages with a period of 7 days for COVID-19 cases and 28 days for GCA diagnoses.

A peak in COVID-19-positive inpatients was seen on 10th April 2020 with a corresponding peak of GCA diagnoses on 29th May 2020, giving a lag period of approximately 6 weeks between these peaks (Figure 1).

Conclusion: The incidence of GCA in Bath was significantly increased in 2020 compared to 2019. This may be the result of the widespread infection of the local population with the COVID-19 virus as a precipitating factor. Possible mechanisms include, but are not limited to, endothelial disruption by the virus, immune system priming towards T helper cell type 1 (Th1) cellular immunity and/or activation of the monocyte-macrophage system. More work is currently underway to assess the causal relationship between the two diseases.

There was a lag period of 6 weeks between the peak during the first wave of the pandemic and the rise in GCA cases. We shall be closely monitoring the number of referrals that follow the current wave of the pandemic.

REFERENCES:

[1] Luther R, Skeoch S, Pauling JD, *et al.* Increased number of cases of giant cell arteritis and higher rates of ophthalmic involvement during the era of COVID-19. *Rheumatol Adv Pract* 2020;**4**:1–4. doi:10.1093/rap/rkaa067
[2] Russo MG, Waxman J, Abdoh AA, *et al.* Correlation between infection and the onset of the giant cell (temporal) arteritis syndrome. *Arthritis Rheum* 1995;**38**:374–80. doi:10.1002/art.1780380312
[3] England PH. GOV.UK Coronavirus (COVID-19) in the UK. 2021.https://coronavirus.data.gov.uk/details/download (accessed 25 Jan 2021).
[4] Smeeth L, Cook C, Hall AJ. Incidence of diagnosed polymyalgia rheumatica and temporal arteritis in the United Kingdom, 1990-2001. *Ann Rheum Dis* 2006;**65**:1093–8. doi:10.1136/ard.2005.046912

Disclosure of Interests: Ben Mulhearn Speakers bureau: Novartis UK, 2019, Grant/research support from: Chugai, 2019, Jessica Ellis: None declared, Sarah Skeoch: None declared, John Pauling: None declared, Sarah Tansley: None declared

DOI: 10.1136/annrheumdis-2021-eular.848

OP0282 RITUXIMAB ASSOCIATED WITH SEVERE COVID-19 AMONG PATIENTS WITH INFLAMMATORY ARTHRITIDES: A 1-YEAR MULTICENTER STUDY IN 1116 SUCCESSIVE PATIENTS RECEIVING BIOLOGIC AGENTS

R. Felten[1], P. M. Duret[2], E. Bauer[3], M. Ardizzone[4], H. J. Djossou[5], J. H. Salmon[6], C. Fabre[7], J. Walther[7], I. Chary Valckenaere[3], M. Geoffroy[6], L. Messer[2], F. Berenbaum[5], M. Soubrier[8], J. Sellam[5], J. E. Gottenberg[1]on behalf of BIOCOV Study Group. [1]*Hôpitaux Universitaires de Strasbourg, Service de Rhumatologie, Centre National de Référence des Maladies Auto-immunes Systémiques Rares Est Sud-Ouest (RESO), Strasbourg, France*; [2]*Hospices Civils de Colmar, Hôpital Pasteur, Service Rhumatologie, Colmar, France*; [3]*Hôpitaux Universitaires de Nancy, Service de Rhumatologie, Nancy, France*; [4]*Hôpital Emile MULLER de Mulhouse, Service de Rhumatologie, Mulhouse,*

France; [5]*Hôpital Saint Antoine, APHP, Service de Rhumatologie, Paris, France*; [6] *Hôpitaux Universitaires Reims, Service de Rhumatologie, Reims, France*; [7]*Hôpitaux Universitaires de Strasbourg, Service de Pharmacie-Stérilisation, Strasbourg, France*; [8]*Hôpitaux Universitaires de Clermont-Ferrand, Service de Rhumatologie, Clermont-Ferrand, France*

Background: At a time when vaccines are being prioritized for individuals most at risk, there is currently no clear evidence that risk of SARS-CoV-2 infection is higher for patients with than without inflammatory arthritides (IA). Biologic use was not associated with worse COVID-19 outcomes for yet but the case of rituximab (RTX) remains an issue, given its immunological long term effect, the role of humoral response against SARS-CoV-2 and its indirect effect on T-cell response. A potential association between rituximab and worse COVID-19 outcomes was raised by case reports and retrospective, declarative studies (with few data on the total number of patients exposed).

Objectives: To address differently the issue of the risk of COVID-19 related to RTX and limit biases, we examined the occurrence of severe COVID-19 in all patients receiving intravenous biologic agents at day-hospitals during the pandemic in France.

Methods: From 1st September 2019 to 1st January 2021, we analyzed patients with IA prospectively treated with intravenous biologic agents (RTX, abatacept, infliximab or tocilizumab) in 7 clinical centers in France. We obtained the list of patients receiving intravenous biologic agents in each center from the pharmacist of the hospitals. Therefore, all consecutive patients receiving 1 of the 4 drugs at the time of the study were included in each center. Patients with no follow-up after September 2020 were systematically contacted by phone. The occurrence of a severe COVID -19 (i.e. resulting in death, hospitalization or increase in length of hospitalization related to COVID-19) was the primary outcome criteria.

Results: In total, 1116 patients receiving intravenous biologic agents were included: 449 with infliximab, 392 RTX, 170 tocilizumab and 105 abatacept. From 1st September 2019, the median follow-up time was 15 months (interquartile range 14-16). In total, 10 cases of severe COVID-19 occurred, 9 treated with RTX and 1 with infliximab (supplementary Table 1). Four deaths occurred in our cohort during follow-up but none was related to COVID-19 (1 patient treated by tocilizumab, 1 by RTX and 2 by infliximab). In univariate analysis, the proportion of severe COVID-19 was significantly higher for patients receiving RTX than other biologic agents (9/392 vs 1/724, p=0.0003, OR [95%CI] 17.0 [2.1-134.6]). To take into account potential confounders, we performed multivariate analysis accounting for baseline parameters that differed between RTX and other biologic groups. RTX remained significantly associated with risk of severe COVID-19 (p=0.019) (Table 1).

Patient characteristics	Rituximab (n= 392)	Other bDMARDs (n= 724)	Univariate analysis, p-value	Multivariate analysis, p-value
Median age (years), — [IQR]	64 [56-71]	57.3 [47.0-67.0]	**< 0.0001**	0.51
Female — n (%)	285 (72.7)	426 (58.8)	**< 0.0001**	0.58
IA diagnosis			**< 0.0001**	0.12
Median follow-up from 1st September to last news	14 [13-15]	15 [14-16]	**< 0.0001**	0.86
Confirmed severe COVID-19 cases —n (%)	9 (2.3)	1 (0.1)	**0.0003**	**0.019**
Comorbidities** (history of) — n (%)				
Cardiovascular disease	60 (15.4)	167 (23.1)	**0.0025**	0.77
Chronic lung disease,	92 (23.5)	84 (11.6)	**0.0001**	0.88
Median BMI (kg/m^2) — [IQR]	25.8 [23.2-29.4]	27.3 [23.4-31.2]	**0.015**	0.80
Treatments — n (%)				
Methotrexate	179 (45.8)	322 (44.5)	0.71	
Leflunomide	41 (10.5)	39 (5.4)	**0.0023**	0.43
Hydroxychloroquine	35 (8.9)	24 (3.3)	**0.0001**	0.15
Glucocorticoids	127 (41.8)	100 (19.4)	**< 0.0001**	0.36
Median dose (mg/day) — [IQR]	1 [0-5]	0 [0-0]	**< 0.0001**	

No significant difference in terms of baseline gammaglobulins (p=0.46) or number of previous RTX infusions (p=0.57) was observed among patients receiving RTX with or without a severe COVID-19.

Conclusion: The present results highly indicate increased risk of severe COVID-19 with RTX. Among patients with inflammatory arthritides, those receiving RTX should be prioritized for vaccination against SARS-CoV-2, sufficiently long before infusion/reinfusion and the immunization checked, or an alternative targeted therapy proposed.

Acknowledgements: We thank Dr. Karine Demesmay and all the pharmacists who helped us for this study.

Disclosure of Interests: Renaud FELTEN Speakers bureau: Abbvie, Biogen, BMS, Lilly, Novartis, Pfizer, Pierre-Marie Duret: None declared, Elodie BAUER: None declared, Marc Ardizzone: None declared, H Julien Djossou: None declared, Jean-Hugues Salmon: None declared, Cassandre Fabre: None declared, Julia Walther: None declared, Isabelle CHARY VALCKENAERE: None declared, marion geoffroy: None declared, Laurent Messer: None declared, Francis Berenbaum: None declared, Martin SOUBRIER: None declared, Jérémie SELLAM Speakers bureau: MSD, Pfizer, Abbvie, Roche, BMS, Lilly, Janssen, Novartis, Galapagos, Sandoz, Fresenius Kabi, Grant/research support from: Roche, MSD, Pfizer, Jacques-Eric Gottenberg: None declared

DOI: 10.1136/annrheumdis-2021-eular.1521

OP0283 DOES TNF-INHIBITION DECREASE THE RISK OF SEVERE COVID-19 IN RMD-PATIENTS?

R. Hasseli[1], B. F. Hoyer[2], A. Krause[3], H. M. Lorenz[4], A. Pfeil[5], A. Regierer[6], J. Richter[7], T. Schmeiser[8], A. Strangfeld[6], H. Schulze-Koops[9], R. Voll[10], C. Specker[11], U. Müller-Ladner[1]. [1]*Justus-Liebig-University Giessen, Campus Kerckhoff, Department of Rheumatology and Clinical Immunology, Bad Nauheim, Germany*; [2]*University Hospital Schleswig-Holstein, Campus Kiel, Department of Rheumatology and Clinical Immunology, Clinic for Internal Medicine I, Kiel, Germany*; [3]*Immanuel Hospital, Berlin, Department of Rheumatology, Clinical Immunology and Osteology, Berlin, Germany*; [4]*University Hospital Heidelberg, Division of Rheumatology, Department of Medicine V, Heidelberg, Germany*; [5]*University Hospital Jena, Department of Internal Medicine III, Jena, Germany*; [6]*German Rheumatism Research Centre, Berlin, Epidemiology Unit, Berlin, Germany*; [7]*Heinrich-Heine-University Duesseldorf, Medical Faculty, Duesseldorf, Department of Rheumatology and Hiller Research Unit, Duesseldorf, Germany*; [8]*Private Practice Cologne, Rheumatologie im Veedel, Cologne, Germany*; [9]*University of Munich, Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, Munich, Germany*; [10]*University of Freiburg, Faculty of Medicine, Freiburg, Department of Rheumatology and Clinical Immunology, Freiburg, Germany*; [11]*Kliniken Essen-Mitte, Essen, Department of Rheumatology and Clinical Immunology, Essen, Germany*

Background: Patients with rheumatic and musculoskeletal diseases (RMD) might have an increased risk for infection due to their immunomodulatory treatment, secondary to their disease and comorbidities. Recent studies suggest a decreased risk of severe COVID-19 in RMD-patients treated with biologics.

Objectives: The aim of this study was to assess courses of RMD patients treated with TNF-inhibitors (TNF-I) included in the German COVID-19 registry.

Methods: In the German physician-reported COVID-19-RMD registry, patients with an RMD and confirmed SARS-CoV-2-infection were documented (data entered between March 30, 2020 and January 30, 2021). We analysed TNF-I treated patients, their course and outcome of the infection. Data were compared to RMD-patients treated with other immunomodulatory drugs (OID) than TNF-I.

Results: A total of 269 patients were treated with a TNF-I (57% female) compared to 874 patients who were treated with OID (68% female). Median age was 52 years (range: 19-87) in the TNF-I-group versus 58 years (range: 18-91) in the OID-group. Rheumatoid arthritis was the most common diagnosis (38% in TNF-I-group vs. 52% in the OID-group), followed by ankylosing spondylitis (32% vs. 6%), psoriatic arthritis (22% vs. 11%) and other RMD (9% vs. 31%). Adalimumab (35%) and etanercept (35%) were the most frequently used TNF-I (tab. 1). Glucocorticoids (GC) were used in 22% of TNF-I-treated patients and in 42% of the OID-group.

Under TNF-I, stable disease was reported prior to the SARS-CoV-2-infection in 53% of the patients (OID-group: 47%), followed by low disease activity in 35% (OID: 34%), moderate disease activity in 6% (OID: 12%) and high disease activity in 4% (OID: 3%). Most frequent comorbidities were arterial hypertension (29% under TNF-I vs. 35% under OID), diabetes (8% vs. 11%) and cardiovascular diseases (7% vs. 12%).

The most common reported COVID-19 symptoms were dry cough (57% vs. 55%), fever (53% vs. 61%) and fatigue (50% vs. 49%). Hospitalization due to SARS-CoV infection was required in only 12% of the TNF-I-treated cases vs. in 29% in the OID-group. Oxygen treatment was necessary in 5% of the patients under TNF-I compared to 22% under OID and invasive ventilation in 2% in the TNF-I-group compared to 6% under OID. Most notably, no fatal courses of COVID-19 were reported among the 269 RMD-patients treated with TNF-I versus 49 deaths in the 874 cases (5.6%) treated with OID. Focussing on the hospitalizated TNF-I patients, the rate of concomitant GC use (p<0.001) and higher disease activity (p=0.005) was significant higher (tab.1).

Conclusion: High or moderate RMD-disease activity is an important factor associated with severity of COVID-19 including mortality. In this large cohort RMD patients treated with TNF-I show a low hospitalisation rate and no fatal course. This is reassuring for patients and treating rheumatologists to use TNF-I to control RMD disease activity. The use of glucocorticoids and high disease activity seem to counteract possible protective effects of TNF-I.

Table 1.

	TNF inhibition (269)		Other immunomodulation (874)	
	Total patients	Rate (%)	Total patients	Rate (%)
Disease activity				
stable	141	53	408	47
low	93	35	299	34
Moderate	15	6	108	12
High	10	4	29	3
Comorbidities				
cardiovascular diseases	18	7	104	12
arterial hypertension	77	29	303	35
bronchial asthma	12	4	65	7
COPD/interstitial lung disease	11	4	86	10
chronic renal failure	9	3	77	9
Osteoporosis	13	5	67	8
Diabetes	22	8	92	11
COVID-19 related symptoms				
Fever	142	53	478	55
dry cough	152	57	530	61
Expectoration	31	12	83	9
muscular pain	97	36	280	32
Fatigue	135	50	424	49
Headache	101	38	237	27
shortness of breath	49	18	245	28
no symptoms	23	9	56	6
COVID-19 outcome				
Outpatients	237	88	619	71
Inpatients	32	12	255	29
need of oxygen treatment	18	7	189	22
invasive ventilation	5	2	49	6
fatal course	0	0	49	6
TNF inhibitors				
Adalimumab	95	35		
Infliximab	23	9		
Certolizumab	33	12		
Golimumab	24	9		
Etanercept	94	35		
GC and disease activity in TNF-I treated patients				
TNF-I inpatients treated with GC	18/32	56	p< 0.001	
TNF-I outpatients treated with GC	42/237	18		
TNF-I inpatients with high disease activity	4/32	13		
TNF-I outpatients with high disease activity	6/237	6	p= 0.005	

Acknowledgements: The authors would like to thank all physicians and personnel involved in the documentation of the cases in our registry.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4027

OP0284

OUTCOME OF COVID-19 IN PATIENTS WITH RHEUMATIC AND INFLAMMATORY DISEASES TREATED WITH RITUXIMAB: DATA FROM DE FRENCH RMD COVID-19 COHORT

J. Avouac[1], E. Drumez[2], E. Hachulla[3], R. Seror[4], S. Georgin-Lavialle[5], S. El Mahou[6], E. Pertuiset[7], T. Pham[8], H. Marotte[9], A. Servettaz[10], F. Domont[11], P. Chazerain[12], M. Devaux[13], P. Claudepierre[14], V. Langlois[15], A. Mekinian[16], A. Maria[17], B. Banneville[18], B. Fautrel[18], J. Pouchot[19], T. Thomas[9], R. M. Flipo[20], C. Richez[21]on behalf of FAI2R/SFR/SNFMI/SOFREMIP/CRI/IMIDIATE consortium and contributors. *[1]COCHIN Hospital, Rheumatology, Paris, France*; *[2]CHU Lille, ULR 2694 - METRICS, Lille, France*; *[3]CHU Lille, Internal Medicine, Lille, France*; *[4]Bicêtre Hospital, Rheumatology, Paris, France*; *[5]Tenon Hospital, Internal Medicine, Paris, France*; *[6]CHU Tourcoing, Rheumatology, Paris, France*; *[7]Centre Hospitalier René Dubos, Rheumatology, Pontoise, France*; *[8]Université Aix-Marseille, Rheumatology, Marseille, France*; *[9]CHU Saint Etienne, Rheumatology, Saint Etienne, France*; *[10]CHU Reims, Internal Medicine, Reims, France*; *[11]Pitié-Salpêtrière Hospital, Internal Medicine, Paris, France*; *[12]Groupe Hospitalier Diaconesses-croix St-Simon, Internal Medicine, Paris, France*; *[13]CHI Poissy Saint Germain, Internal Medicine, Poissy, France*; *[14]Henri Mondor Hospital, Rheumatology, Paris, France*; *[15]Le Havre Hospital, Internal Medicine, Le Havre, France*; *[16]Saint Antoine Hospital, Internal Medicine, Paris, France*; *[17]CHU Montpellier, Internal Medicine, Montpellier, France*; *[18]Pitié-Salpêtrière Hospital, Rheumatology, Paris, France*; *[19]Hôpital Européen Georges Pompidou, Internal Medicine, Paris, France*; *[20]CHU Lille, Rheumatology, Lille, France*; *[21]CHU Bordeaux, Rheumatology, Bordeaux, France*

Background: Various observations have suggested that the course of the COVID-19 infection may be less favorable in patients with inflammatory rheumatic and musculoskeletal diseases (iRMD) receiving rituximab (RTX).

Objectives: To investigate whether treatment with RTX is associated with severe infection and death.

Methods: We performed an observational, multicenter, French national cohort study querying the French RMD COVID-19 cohort, including highly suspected/confirmed iRMD-COVID-19 patients. The primary endpoint was to assess the severity rate of COVID-19. Severe disease was defined by hospitalization in intensive care unit or death. The secondary objectives were to analyze death rate and length of hospital stay. Two control groups were considered for comparison with RTX treated patients: a first group including all non-RTX treated iRMD patients and a second consisting on RTX untreated iRMD patients with diseases for which RTX is a recognized therapeutic option. Adjusting on potential confounding factors was performed by using inverse probability of treatment weighting (IPTW) propensity score method.

Results: We collected a total of 1090 records. Patients were mainly females (67.3%, 734/1090) with a mean age of 55.2±16.4 years, and 51.1% (557/1090) were over the age of 55. Almost 70% of the population had at least one comorbidity (756/1090). A total of 63 patients were treated with RTX, mainly for rheumatoid arthritis (RA) (31/63, 49.2%). RTX treated patients were more likely to be males, with older age, higher prevalence of comorbidities and corticosteroid use. The control population consisted on 1027 non-RTX treated iRMD patients, and 495 RTX untreated iRMD patients with diseases for which RTX is a recognized therapeutic option.

Of the 1,090 patients, 137 developed severe disease (12.6%). After adjusting on potential confounding factors (age, sex, arterial hypertension, diabetes, smoking status, body mass index, interstitial lung disease, cardiovascular diseases, cancer, corticosteroid use, chronic renal failure and the underlying disease), severe disease was confirmed to be observed more frequently in patients receiving RTX compared to all RTX untreated iRMD patients (effect size, ES 3.26, 95% confidence interval, CI 1.66 to 6.40, p<0.001) and the subgroup of untreated RTX patients with diseases eligible for RTX therapy (ES 2.62, 95% CI 1.34 to 5.09, p=0.005). Patients who developed a severe disease had a more recent rituximab infusion compared to patients with mild or moderate disease. Indeed, the time between the last infusion of rituximab and the first symptoms of COVID-19 was significantly shorter in patients who developed a severe form of COVID-19 (Figure 1).

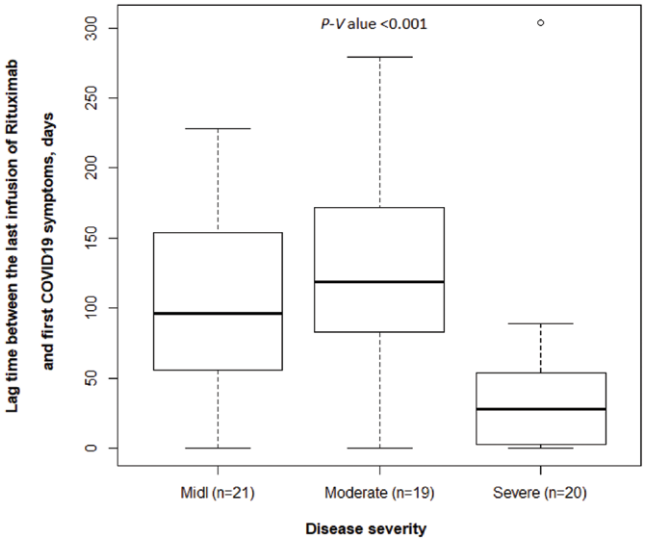


Figure 1. Distribution (Tukey's box plot) of Lag time between last infusion of Rituximab according to disease severity. P-Values for comparison between disease severity with Kruskal Wallis test are reported; P-Value<0.001 for either post-hoc comparison of severe disease group with moderate or mild disease group (calculated using Dunn's test).

Eighty-nine patients in our cohort died, resulting in an overall death rate of 8.2%. Death rate was numerically higher in RTX treated patients (13/63, 20.6%) compared to all RTX untreated iRMDs patients (76/1027, 7.4%) and the subgroup of untreated RTX patients with diseases eligible for RTX therapy (49/495, 9.9%). After considering the previously described confounding factors, the risk of death was not significantly increased in patients treated with RTX compared to all RTX untreated iRMDs patients (ES 1.32, 95% CI 0.55 to 3.19, p=0.53) (Table 2) and the subgroup of untreated RTX patients with diseases eligible for RTX therapy (ES 1.48, 95% CI 0.68 to 3.20, p=0.32). In line with a more severe COVID-19 disease, the length of hospital stay was markedly longer in patients treated with RTX compared to both untreated RTX patient groups.

Conclusion: RTX therapy is associated with a more severe COVID-19 infection. RTX will have to be applied with particular caution in patients with iRMDs.

Acknowledgements: Muriel Herasse played a major role in collecting the missing data of the cohort.
We thank Julien Labreuche (biostatistician, CHU-Lille) for the help in the statistical analysis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1092

OP0285 COVID-19 HOSPITALIZATIONS, ICU ADMISSION, AND DEATH AMONG PATIENTS WITH IMMUNE MEDIATED INFLAMMATORY DISEASES (IMID) – A POPULATION-BASED STUDY

L. Eder[1,2], R. Croxford[3], A. Drucker[2,4], A. Mendel[5], K. Bindee[4,6], Z. Touma[4,7], R. Cook[8], S. Johnson[4,7], S. Bernatsky[5], N. Haroon[1,7], J. Widdifield[9,10].
[1]University of Toronto, Medicine and Institute of Medical Science, Toronto, Canada; *[2]Women's College Research Institute, Medicine, Toronto, Canada*; *[3]ICES, NA, Toronto, Canada*; *[4]University of Toronto, Medicine and Health Policy Management and Evaluation, Toronto, Canada*; *[5]McGill University, Medicine, Montreal, Canada*; *[6]Sinai Health System, Medicine, Toronto, Canada*; *[7]Toronto Western Hospital, Medicine, Toronto, Canada*; *[8]University of Waterloo, Biostatistics, Waterloo, Canada*; *[9]University of Toronto, Institute of Health Policy Management and Evaluation, Toronto, Canada*; *[10]Sunnybrook Research Institute, Medicine, Toronto, Canada*

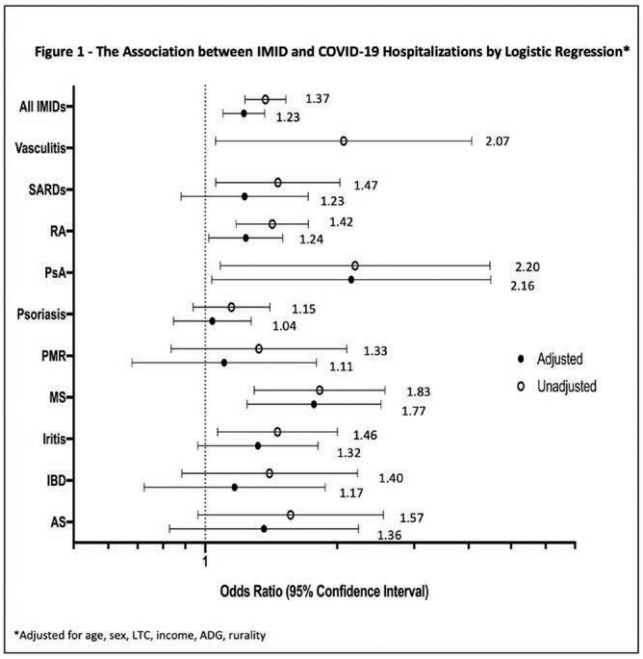
Background: It remains unclear whether patients with IMID are at greater risk for severe COVID-19.
Objectives: To investigate the risk of COVID-19 hospitalizations and their outcomes in patients with IMID compared with matched non-IMID patents from the general population.
Methods: A population-based, matched cohort study was conducted in adults living in Ontario, Canada using health administrative data. Ten cohorts of the following IMID were assembled: rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, systemic autoimmune rheumatic diseases (SARDs, including systemic lupus, systemic sclerosis, Sjogren's, myositis), multiple sclerosis (MS), iritis, inflammatory bowel disease, polymyalgia rheumatica (PMR), and vasculitis (including giant cell arteritis and other types of vasculitidies). Each patient was matched with 5 non-IMID comparators based on age, sex, area of residence and living in long-term care (LTC). Patients who were admitted to hospital from January 1st to July 31th, 2020 and had ICD-10 COVID-19 diagnosis codes (U07.2 or U07.1) were identified. Among those with COVID-19 hospitalizations, we determined those with admissions to intensive care unit or required mechanical ventilation or died in hospital ('complicated hospitalization'). Age-sex-standardized rates were compared between IMID and non-IMID patients and risk factors for hospitalizations were identified by multivariable logistic regression analysis.
Results: In total, 493,499 IMID (417 hospitalized) and 2,466,946 non-IMID patients (1,519 hospitalized) were assessed. The age-sex-standardized rate of COVID-19 hospitalization was higher in IMID (6.4 per 10,000, 95% confidence interval (CI) 5.8, 7.2) versus non-IMID patients (4.8 per 100,000, 95% CI 4.5, 5). The highest rates of hospitalizations were found in vasculitis (18/10,000), MS (16.7/10,000) and PMR (10.1/10,000). IMID diagnosis was associated with 37% higher risk of being hospitalized for COVID-19 (Odds Ratio (OR) 1.37, 95% CI 1.23, 1.53) (Figure 1). This risk was slightly attenuated after adjusting for sociodemographic factors and comorbidities but remained elevated by 23% compared to non-IMID (OR 1.23, 95% CI 1.10, 1.37). The risk for hospitalizations was increased in RA, vasculitis, SARDs, PsA, MS and iritis (Figure 1). Risk factors for COVID-19 hospitalizations included older age, male sex, lower income, multimorbidity and living in long-term care (Table 1). The risk for complicated COVID-19 hospitalizations was higher by 21% in IMID patients (OR 1.21, 95% CI 1.02, 1.43), however, this association was attenuated after adjustment for demographics and comorbidities (OR 1.08).

Table 1. Risk Factors for COVID-19 Hospitalizations in IMIDs vs. non-IMIDs

Variable	OR	95% CI
IMIDs vs. Non-IMID	1.23	1.10, 1.37
Age (10 yrs)	1.49	1.44, 1.54
Sex: Female	0.68	0.62, 0.75
Long term care resident	8.28	7.32, 9.37
ADG: 5-9 vs. 0-4	1.45	1.22, 1.71
10-14 vs. 0-4	2.26	1.92, 2.67
15+ vs. 0-4	3.23	2.73, 3.82
Income (quintile)		
Quintile 2 vs. 1	0.82	0.73, 0.93
Quintile 3 vs. 1	0.76	0.67, 0.86
Quintile 4 vs. 1	0.56	0.48, 0.64
Quintile 5 vs. 1	0.46	0.40, 0.54
Urban vs. rural	4.33	3.32, 5.67

ADG - Aggregated Diagnosis Groups

Conclusion: Patients with IMID were at higher risk of being hospitalized with COVID-19 and for having complicated hospitalizations. Hospitalization risk was partially independent of their comorbid conditions.
Acknowledgements: The study is supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). Parts of this material are based on data and information compiled and provided by MOHLTC and the Canadian Institute for Health Information. The opinions, results and conclusions reported in this paper are those of the authors and are independent of the funding or data sources; no endorsement is intended or should be inferred.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1466

OP0286 CHARACTERISTICS ASSOCIATED WITH SEVERE COVID-19 OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): RESULTS FROM THE COVID-19 GLOBAL RHEUMATOLOGY ALLIANCE (COVID-19 GRA)

M. F. Ugarte-Gil[1,2], G. S. Alarcon[3,4], A. Seet[5], Z. Izadi[5,6], C. Reategui Sokolova[2,7], A. E. Clarke[8], L. Wise[9], G. Pons-Estel[10], M. J. Santos[11], S. Bernatsky[12], L. Mathias[9], N. Lim[9], J. Sparks[13], Z. Wallace[14], K. Hyrich[15], A. Strangfeld[16], L. Gossec[17], L. Carmona[18], E. Mateus[19], S. Lawson-Tovey[20], L. Trupin[5], S. Rush[5], G. Schmajuk[5], P. Katz[5], L. Jacobsohn[5], S. Al Emadi[21], E. Gilbert[22], A. Duarte-Garcia[23], M. Valenzuela-Almada[24], T. Hsu[25], K. D'silva[26], N. Serling-Boyd[27], P. Dieudé[28], E. Nikiphorou[29], V. Kronzer[30], N. Singh[31], B. Wallace[32], A. Akpabio[33], R. Thomas[34], S. Bhana[35], W. Costello[36], R. Grainger[37], J. Hausmann[38], J. Liew[39], E. Sirotich[40], P. Sufka[41], P. Robinson[42], P. Machado[43], M. Gianfrancesco[5], J. Yazdany[44]on behalf of COVID-19 Global Rheumatology Alliance. *[1]Universidad Científica del Sur, School of Medicine, Lima, Peru*; *[2]Hospital Nacional Guillermo Almenara Irigoyen, EsSalud, Rheumatology, Lima, Peru*; *[3]University of Alabama at Birmingham, Department of Medicine, Birmingham, Alabama, United States of America*; *[4]Universidad Peruana Cayetano Heredia, Facultad de Medicina, Lima, Peru*; *[5]University of California, Division of Rheumatology, Department of Medicine, San Francisco, United States of America*; *[6]University of California, Department of Epidemiology and Biostatistics, San Francisco, United States of America*; *[7]Universidad San Ignacio de Loyola, Unidad de Investigación para la Generación y Síntesis de Evidencias en Salud, Lima, Peru*; *[8]Cumming School of Medicine. University of Calgary, Division of Rheumatology Department of Medicine, Calgary, Canada*; *[9]University of Southern California, Division of Rheumatology, Department of Internal Medicine, Los Angeles, CA, United States of America*; *[10]Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina*; *[11] Instituto de Medicina Molecular, Faculdade de Lisboa, Rheumatology Department, Hospital Garcia de Orta, Almada and Rheumatology Research Unit, Lisbon, Portugal*; *[12]McGill University Health Centre, Divisions of Rheumatology and Clinical Epidemiology,*

Quebec, Canada; [13]*Brigham and Women's Hospital and Harvard Medical School, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, United States of America*; [14]*Massachusetts General Hospital, Harvard Medical School, Clinical Epidemiology Program and Rheumatology Unit, Division of Rheumatology, Allergy, and Immunology, Boston, MA, United States of America*; [15]*The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [16]*German Rheumatism Research Center (DRFZ Berlin), Epidemiology and Health Care Research, Berlin, Germany*; [17]*Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France*; [18]*Instituto de Salud Musculoesquelética, Instituto de Salud Musculoesquelética, Madrid, Spain*; [19]*Portuguese League Against Rheumatic Diseases (LPCDR), Portuguese League Against Rheumatic Diseases (LPCDR), Lisbon, Portugal*; [20]*University of Manchester, Centre for Genetics and Genomics Versus Arthritis, Centre for Musculoskeletal Research, Manchester, United Kingdom*; [21]*Hamad Medical Corporation, Rheumatology Department, Doha, Qatar*; [22]*Mayo Clinic, Division of Rheumatology, Jacksonville, Florida, United States of America*; [23]*Mayo Clinic, Division of Rheumatology and Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, Minnesota, United States of America*; [24]*Mayo Clinic, Division of Rheumatology, Rochester, Minnesota, United States of America*; [25]*righam and Women's Hospital and Harvard Medical School, Division of Rheumatology, Inflammation, and Immunity, Boston, United States of America*; [26]*Massachusetts General Hospital, Harvard Medical School, Clinical Epidemiology Program and Rheumatology Unit, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [27]*Massachusetts General Hospital, Harvard Medical School, Rheumatology Unit, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [28]*Hôpital Bichat, Rheumatology, Paris, France*; [29]*Kings College London, Centre for Rheumatic Disease, London, United Kingdom*; [30]*Mayo Clinic, Rheumatology, Rochester, United States of America*; [31]*University of Washington, Division of Rheumatology, Washington, United States of America*; [32]*University of Michigan, Department of Internal Medicine/Rheumatology, Michigan, United States of America*; [33]*University of Uno Teaching Hospital, Rheumatology, Uyo, Nigeria*; [34]*University of Queensland, UQ Diamantina Institute, Brisbane, Australia*; [35]*Crystal Run Health, Crystal Run Health, Middletown, NY, United States of America*; [36]*Irish Children's Arthritis Network (iCAN), Irish Children's Arthritis Network (iCAN), Ireland*; [37]*University of Otago, Department of Medicine, Wellington, New Zealand*; [38]*Beth Israel Deaconess Medical Center, Harvard Medical School, Program in Rheumatology, Boston Children's Hospital; Division of Rheumatology and Clinical Immunology, Boston, MA, United States of America*; [39]*Boston University School of Medicine, Section of Rheumatology, Department of Medicine, Boston, United States of America*; [40]*McMaster University, Department of Health Research Methods, Evidence, and Impact, Hamilton, ON, Canada*; [41]*Healthpartners, St. Paul, MN, United States of America*; [42]*University of Queensland, Faculty of Medicine, Brisbane, United States of America*; [43]*University College London, Centre for Rheumatology & Department of Neuromuscular Diseases, London, United Kingdom*; [44]*University of California, Division of Rheumatology, Department of Medicine, San Francisco, United States of America*

Background: An increased risk of severe COVID-19 outcomes may be seen in patients with autoimmune diseases on moderate to high daily doses of glucocorticoids, as well as in those with comorbidities. However, specific information about COVID-19 outcomes in SLE is scarce.

Objectives: To determine the characteristics associated with severe COVID-19 outcomes in a multi-national cross-sectional registry of COVID-19 patients with SLE.

Methods: SLE adult patients from a physician-reported registry of the COVID-19 GRA were studied. Variables collected at COVID-19 diagnosis included age, sex, race/ethnicity, region, comorbidities, disease activity, time period of COVID-19 diagnosis, glucocorticoid (GC) dose, and immunomodulatory therapy. Immunomodulatory therapy was categorized as: antimalarials only, no SLE therapy, traditional immunosuppressive (IS) drug monotherapy, biologics/targeted synthetic IS drug monotherapy, and biologic and traditional IS drug combination therapy. We used an ordinal COVID-19 severity outcome defined as: not hospitalized/hospitalized without supplementary oxygen; hospitalized with non-invasive ventilation; hospitalized with mechanical ventilation/extracorporeal membrane oxygenation; and death. An ordinal logistic regression model was constructed to assess the association between demographic characteristics, comorbidities, medications, disease activity and COVID-19 severity. This assumed that the relationship between each pair of outcome groups is of the same direction and magnitude.

Results: Of 1069 SLE patients included, 1047 (89.6%) were female, with a mean age of 44.5 (SD: 14.1) years. Patient outcomes included 815 (78.8%) not hospitalized/hospitalized without supplementary oxygen; 116 (11.2) hospitalized with non-invasive ventilation, 25 (2.4%) hospitalized with mechanical ventilation/extracorporeal membrane oxygenation and 78 (7.5%) died. In a multivariate model (n=804), increased age [OR=1.03 (1.01, 1.04)], male sex [OR =1.93 (1.21, 3.08)], COVID-19 diagnosis between June 2020 and January 2021 (OR =1.87 (1.17, 3.00)), no IS drug use [OR =2.29 (1.34, 3.91)], chronic renal disease [OR =2.34 (1.48, 3.70)], cardiovascular disease [OR =1.93 (1.34, 3.91)] and moderate/high disease activity [OR =2.24 (1.46, 3.43)] were associated with more severe COVID-19 outcomes. Compared with no use of GC, patients using GC had a higher odds of poor outcome: 0-5 mg/d, OR =1.98 (1.33, 2.96); 5-10 mg/d, OR =2.88 (1.27, 6.56); >10 mg/d, OR =2.01 (1.26, 3.21) (Table 1).

Table 1. Characteristics associated with more severe COVID-19 outcomes in SLE. (N=804)

	OR (95% CI)
Age, years	1.03 (1.01, 1.04)
Sex, Male	1.93 (1.21, 3.08)
Race/Ethnicity, Non-White vs White	1.47 (0.87, 2.50)
Region	
Europe	Ref.
North America	0.67 (0.29, 1.54)
South America	0.67 (0.29, 1.54)
Other	1.93 (0.85, 4.39)
Season, June 16th 2020-January 8th 2021 vs January-June 15th 2020	1.87 (1.17, 3.00)
Glucocorticoids	
0 mg/day	Ref.
0-5 mg/day	1.98 (1.33, 2.96)
5-10 mg/day	2.88 (1.27, 6.56)
=>10 mg/day	2.01 (1.26, 3.21)
Medication Category	
Antimalarial only	Ref.
No IS drugs	2.29 (1.34, 3.91)
Traditional IS drugs as monotherapy	1.17 (0.77, 1.77)
b/ts IS drugs as monotherapy	1.00 (0.37, 2.71)
Combination of traditional and b/ts IS	1.00 (0.55, 1.82)
Comorbidity Burden	
Number of Comorbidities (excluding renal and cardiovascular disease)	1.39 (0.97, 1.99)
Chronic renal disease	2.34 (1.48, 3.70)
Cardiovascular disease	1.93 (1.34, 3.91)
Disease Activity, Moderate/ high vs Remission/ low	2.24 (1.46, 3.43)

IS: immunosuppressive. b/ts: biologics/targeted synthetics

Conclusion: Increased age, male sex, glucocorticoid use, chronic renal disease, cardiovascular disease and moderate/high disease activity at time of COVID-19 diagnosis were associated with more severe COVID-19 outcomes in SLE. Potential limitations include possible selection bias (physician reporting), the cross-sectional nature of the data, and the assumptions underlying the outcomes modelling.

Acknowledgements: The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance and do not necessarily represent the views of the ACR, EULAR) the UK National Health Service, the National Institute for Health Research (NIHR), or the UK Department of Health, or any other organization.

Disclosure of Interests: Manuel F. Ugarte-Gil Grant/research support from: Pfizer, Janssen, Graciela S Alarcon: None declared, Andrea Seet: None declared, Zara Izadi: None declared, Cristina Reategui Sokolova: None declared, Ann E Clarke Consultant of: AstraZeneca, BristolMyersSquibb, GlaxoSmithKline, Exagen Diagnostics, Leanna Wise: None declared, Guillermo Pons-Estel: None declared, Maria Jose Santos: None declared, Sasha Bernatsky: None declared, Lauren Mathias: None declared, Nathan Lim: None declared, Jeffrey Sparks Consultant of: Bristol-Myers Squibb, Gilead, Inova, Janssen, and Optum unrelated to this work., Grant/research support from: Amgen and Bristol-Myers Squibb, Zachary Wallace Consultant of: Viela Bio and MedPace, Grant/research support from: Bristol-Myers Squibb and Principia/Sanofi, Kimme Hyrich Speakers bureau: Abbvie, Grant/research support from: MS, UCB, and Pfizer, Anja Strangfeld Speakers bureau: AbbVie, MSD, Roche, BMS, Pfizer, Grant/research support from: AbbVie, BMS, Celltrion, Fresenius Kabi, Lilly, Mylan, Hexal, MSD, Pfizer, Roche, Samsung, Sanofi-Aventis, and UCB, Laure Gossec Consultant of: Abbvie, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sanofi-Aventis, UCB, Grant/research support from: Lilly, Mylan, Pfizer, Loreto Carmona: None declared, Elsa Mateus Grant/research support from: Pfizer, Abbvie, Novartis, Janssen-Cilag, Lilly Portugal, Sanofi, Grünenthal S.A., MSD, Celgene, Medac, Pharmakern, GAfPA, Saskia Lawson-Tovey: None declared, Laura Trupin: None declared, Stephanie Rush: None declared, Gabriela Schmajuk: None declared, Patti Katz: None declared, Lindsay Jacobsohn: None declared, Samar Al Emadi: None declared, Emily Gilbert: None declared, Ali Duarte-Garcia: None declared, Maria Valenzuela-Almada: None declared, Tiffany Hsu: None declared, Kristin D'Silva: None declared, Naomi Serling-Boyd: None declared, Philippe Dieudé Consultant of: Boerhinger Ingelheim, Bristol-Myers Squibb, Lilly, Sanofi, Pfizer, Chugai, Roche, Janssen unrelated to this work, Grant/research support from: Bristol-Myers Squibb, Chugaii, Pfizer, unrelated to this work, Elena Nikiphorou: None declared, Vanessa Kronzer: None declared, Namrata Singh: None declared, Beth Wallace: None

declared, Akpabio Akpabio: None declared, Ranjeny Thomas: None declared, Suleman Bhana Consultant of: AbbVie, Horizon, Novartis, and Pfizer (all <$10,000) unrelated to this work, Wendy Costello: None declared, Rebecca Grainger Speakers bureau: Abbvie, Janssen, Novartis, Pfizer, Cornerstones, Jonathan Hausmann Consultant of: Novartis, Sobi, Biogen, all unrelated to this work (<$10,000), Jean Liew Grant/research support from: Pfizer outside the submitted work, Emily Sirotich Grant/research support from: Board Member of the Canadian Arthritis Patient Alliance, a patient run, volunteer based organization whose activities are largely supported by independent grants from pharmaceutical companies, Paul Sufka: None declared, Philip Robinson Speakers bureau: Abbvie, Eli Lilly, Janssen, Novartis, Pfizer and UCB (all < $10,000), Consultant of: Abbvie, Eli Lilly, Janssen, Novartis, Pfizer and UCB (all < $10,000), Pedro Machado Speakers bureau: Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, all unrelated to this study (all < $10,000)., Consultant of: Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, all unrelated to this study (all < $10,000), Milena Gianfrancesco: None declared, Jinoos Yazdany Consultant of: Eli Lilly and AstraZeneca unrelated to this project

DOI: 10.1136/annrheumdis-2021-eular.2984

OP0287 IMMUNOMODULATORY THERAPIES FOR SEVERE FORMS OF COVID-19: A SYSTEMATIC LITERATURE REVIEW TO INFORM EULAR POINTS TO CONSIDER

A. Alunno[1], A. Najm[2], X. Mariette[3], J. Emmel[4], L. Mason[4], G. De Marco[5], D. Mcgonagle[5], P. Machado[6]. [1]*Rheumatology Unit, University of Perugia, Department of Medicine, Perugia, Italy*; [2]*Institute of Infection, Immunity and Inflammation, University of Glasgow, College of Medical Veterinary and Life Sciences, Glasgow, United Kingdom*; [3]*Paris-Saclay University, AP-HP, INSERM, Le Kremlin Bicêtre, France*; [4]*Leeds Teaching Hospitals NHS Trust, Library & Evidence Research Centre, Medical Education, Leeds, United Kingdom*; [5]*University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [6]*University College London, Centre for Rheumatology & Department of Neuromuscular Diseases, London, United Kingdom*

Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) pandemic is a global health problem. Beside the specific pathogenic effect of SARS-CoV-2, a deleterious aberrant non-effective host immune response plays an important role especially in severe forms of COVID-19. There is intense investigation to explore the utility of immunomodulatory drugs commonly used in the Rheumatology arena as agents that may mitigate against COVID-19 to improve disease prognosis. Rheumatologists are used to the utilization of these immune targeted therapies.

Objectives: To summarize the available information on the use of immunomodulatory agents in severe COVID-19.

Methods: As part of a EULAR taskforce, a systematic literature search was conducted from January 2019 up to December 11, 2020. Two reviewers independently identified eligible studies according to the PICO framework P (population): patients with SARS-CoV-2 infection; I (intervention): any immunomodulator agent/strategy; C (comparator): any comparator; O (outcome) any clinical outcome including but not limited to mortality, admission to intensive care unit and clinical improvement. Data on efficacy and safety of immunomodulatory agents utilized therapeutically in SARS-CoV-2 infection at any stage were extracted. The risk of bias was assessed using validated tools.

Results: Of 60372 records, 401 articles were eligible for inclusion. Studies were at variable risk of bias. Randomised controlled trials (RCTs) were available for the following drugs: hydroxychloroquine (N=12), glucocorticoids (N=6), tocilizumab (N= 4), convalescent plasma (N=4), interferon beta (N=2), IVIg (N=2) and N=1 each for anakinra, baricitinib, colchicine, leflunomide, ruxolitinib, interferon kappa, and vilobelimab. For glucocorticoids, dexamethasone reduced mortality only in patients requiring respiratory support; while methylprednisolone reduced mortality in patients aged 60 years or over. Data from RCTs on tocilizumab are conflicting and definite conclusions cannot be drawn at this point in time, but recent studies suggest possible benefit in patients requiring respiratory support. Hydroxychloroquine was not beneficial at any disease stage, one RCT with anakinra was negative, one RCT with baricitinib+remdesivir was positive, and individual trials testing some other compounds provided interesting, albeit preliminary, results.

Conclusion: Although there is emerging evidence about immunomodulatory therapies for the management of COVID-19, conclusive data is scarce with some conflicting data. Since glucocorticoids seem to improve survival in some subsets of patients, RCTs comparing glucocorticoids alone versus glucocorticoids plus anti-cytokine/immunomodulatory treatment are warranted. This SLR informed the initiative to formulate EULAR points to consider on pathophysiology and use of immunomodulatory therapies in COVID-19.

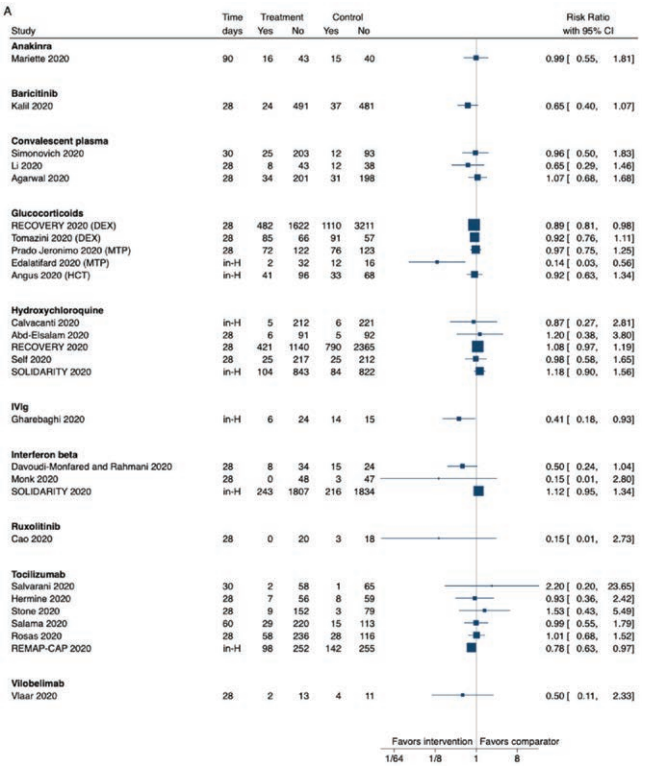


Figure 1. Forest plots showing the risk ratio (RR) and 95% confidence interval for mortality in randomized controlled trials divided by intervention. The latest follow-up available is reported in the timing column.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3367

OP0288 MACHINE LEARNING ALGORITHMS TO PREDICT COVID-19 ACUTE RESPIRATORY DISTRESS SYNDROME IN PATIENTS WITH RHEUMATIC DISEASES: RESULTS FROM THE GLOBAL RHEUMATOLOGY ALLIANCE PROVIDER REGISTRY

Z. Izadi[1,2], M. Gianfrancesco[2], K. Hyrich[3,4], A. Strangfeld[5], L. Gossec[6,7], L. Carmona[8], E. Mateus[9,10], S. Lawson-Tovey[4,11], L. Trupin[2], S. Rush[2], G. Schmajuk[2,12], L. Jacobsohn[2], P. Katz[2], S. Al Emadi[13], L. Wise[14], E. Gilbert[15], M. Valenzuela-Almada[16], A. Duarte-Garcia[15], J. Sparks[17], T. Hsu[17], K. D'silva[18], N. Serling-Boyd[19], S. Bhana[20], W. Costello[21], R. Grainger[22], J. Hausmann[23,24], J. Liew[25], E. Sirotich[26,27], P. Sufka[28], Z. Wallace[18], P. Machado[29,30,31], P. Robinson[32,33], J. Yazdany[2]. [1]*University of California, San Francisco, Department of Epidemiology and Biostatistics, San Francisco, United States of America*; [2]*University of California, San Francisco, Division of Rheumatology, Department of Medicine, San Francisco, United States of America*; [3]*The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [4]*Manchester Academic Health Science Centre, National Institute of Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, Manchester, United Kingdom*; [5]*German Rheumatism Research Center (DRFZ Berlin), Epidemiology and Health Care Research, Berlin, Germany*; [6]*Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France*; [7]*University Hospitals Pitié Salpêtrière - Charles Foix, Rheumatology, Paris, France*; [8]*Instituto de Salud Musculoesquelética (InMusc), Department of Rheumatology, Madrid, Spain*; [9]*Portuguese League Against Rheumatic Diseases (LPCDR), Rheumatology, Lisbon, Portugal*; [10]*European League Against Rheumatism (EULAR) Standing Committee of People with Arthritis/Rheumatism in Europe (PARE), Rheumatology, Kilchberg, Switzerland*; [11]*University of Manchester, Centre for Genetics and Genomics Versus Arthritis, Centre for Musculoskeletal Research, Manchester, United Kingdom*; [12]*San Francisco VA Healthcare System, Department of Rheumatology, San Francisco, United States of America*; [13]*Hamad Medical Corporation, Rheumatology Department, Doha, Qatar*; [14]*University of Southern California, Division of Rheumatology, Department of Internal Medicine, Los Angeles, United States of America*; [15]*Mayo Clinic, Department of Rheumatology, Rochester, United*

States of America; [16]*Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; [17]*Brigham And Women's Hospital, Harvard Medical School, Division of Rheumatology, Inflammation, and Immunity, Boston, United States of America*; [18]*Massachusetts General Hospital, Harvard Medical School, Clinical Epidemiology Program and Rheumatology Unit, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [19]*Massachusetts General Hospital, Harvard Medical School, Rheumatology Unit, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [20]*Crystal Run Health, Department of Rheumatology, Middletown, United States of America*; [21]*Irish Children's Arthritis Network (iCAN), Chairperson of iCAN, Tipperary, Ireland*; [22]*University of Otago, Wellington, Department of Rheumatology, Wellington, New Zealand*; [23]*Boston Children's Hospital, Program in Rheumatology, Boston, United States of America*; [24]*Beth Israel Deaconess Medical Center (BIDMC), Harvard Medical School, Division of Rheumatology and Clinical Immunology, Boston, United States of America*; [25]*Boston University School of Medicine, Section of Rheumatology, Department of Medicine, Boston, United States of America*; [26]*McMaster University, Department of Health Methods, Evidence, and Impact, Hamilton, Canada*; [27]*Canadian Arthritis Patient Alliance, Rheumatology, Toronto, Canada*; [28]*Healthpartners, Department of Rheumatology, St. Paul, United States of America*; [29]*University College London, Centre for Rheumatology & Department of Neuromuscular Diseases, London, United Kingdom*; [30]*University College London Hospitals NHS Foundation Trust, Department of Rheumatology & Queen Square Centre for Neuromuscular Diseases, London, United Kingdom*; [31]*Northwick Park Hospital, London North West University Healthcare NHS Trust, Department of Rheumatology, London, United Kingdom*; [32]*University of Queensland, Faculty of Medicine, Brisbane, Australia*; [33]*Royal Brisbane & Women's Hospital, Metro North Hospital & Health Service, Rheumatology, Queensland, Australia*

Background: Acute Respiratory Distress Syndrome (ARDS) is a life-threatening complication of COVID-19 and has been reported in approximately one-third of hospitalized patients with COVID-19[1]. Risk factors associated with the development of ARDS include older age and diabetes[2]. However, little is known about factors associated with ARDS in the setting of COVID-19, in patients with rheumatic disease or those receiving immunosuppressive medications. Prediction algorithms using traditional regression methods perform poorly with rare outcomes, often yielding high specificity but very low sensitivity. Machine learning algorithms optimized for rare events are an alternative approach with potentially improved sensitivity for rare events, such as ARDS in COVID-19 among patients with rheumatic disease.

Objectives: We aimed to develop a prediction model for ARDS in people with COVID-19 and pre-existing rheumatic disease using a series of machine learning algorithms and to identify risk factors associated with ARDS in this population.

Methods: We used data from the COVID-19 Global Rheumatology Alliance (GRA) Registry from March 24 to Nov 1, 2020. ARDS diagnosis was indicated by the reporting clinician. Five machine learning algorithms optimized for rare events predicted ARDS using 42 variables covering patient demographics, rheumatic disease diagnoses, medications used at the time of COVID-19 diagnosis, and comorbidities. Model performance was assessed using accuracy, area under curve, sensitivity, specificity, positive predictive value, and negative predictive value. Adjusted odds ratios corresponding to the 10 most influential predictors from the best performing model were derived using hierarchical multivariate mixed-effects logistic regression that accounted for within-country correlations.

Results: A total of 5,931 COVID-19 cases from 67 countries were included in the analysis. Mean (SD) age was 54.9 (16.0) years, 4,152 (70.0%) were female, and 2,399 (40.5%) were hospitalized. ARDS was reported in 388 (6.5% of total and 15.6% of hospitalized) cases. Statistically significant differences in the risk of ARDS were observed by demographics, diagnoses, medications, and comorbidities using unadjusted univariate comparisons (data not shown). Gradient boosting machine (GBM) had the highest sensitivity (0.81) and was considered the best performing model (Table 1). Hypertension, interstitial lung disease, kidney disease, diabetes, older age, glucocorticoids, and anti-CD20 monoclonal antibodies were associated with the development of ARDS while tumor necrosis factor inhibitors were associated with a protective effect (Figure 1).

Table 1. Performance of machine learning algorithms.

	GBM	SVM	GLMNET	NNET	RF
Accuracy	0.79	0.68	0.66	0.66	0.67
AUC	0.75	0.70	0.74	0.58	0.74
Sensitivity	0.81	0.68	0.65	0.68	0.67
Specificity	0.49	0.60	0.73	0.48	0.68
PPV	0.96	0.96	0.97	0.95	0.97
NPV	0.16	0.12	0.13	0.09	0.13

GBM: Gradient Boosting Machine, SVM: Support vector machines, GLMNET: Lasso and Elastic-Net Regularized Generalized Linear Models, NNET: Neural Networks, RF: Random Forest. AUC: Area Under Curve; PPV: Positive Predictive Value; NPV: Negative Predictive Value.

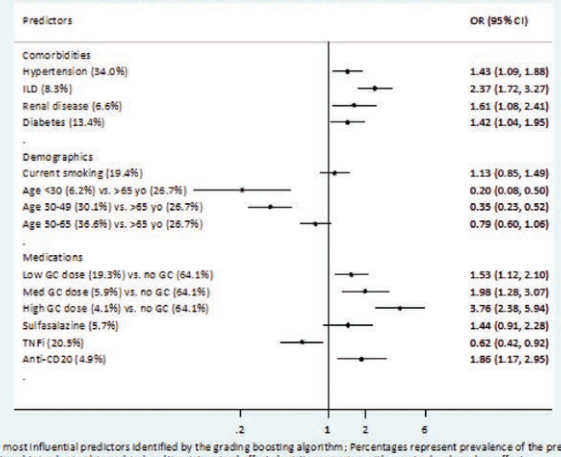
Conclusion: In this global cohort of patients with rheumatic disease, a machine learning model, GBM, predicted the onset of ARDS with 81% sensitivity using baseline information obtained at the time of COVID-19 diagnosis. These results identify patients who may be at higher risk of severe COVID-19 outcomes. Further studies are necessary to validate the proposed prediction model in external cohorts and to evaluate its clinical utility. Disclaimer: The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance, and do not necessarily represent the views of the ACR, NIH, (UK) NHS, NIHR, or the department of Health.

REFERENCES:

[1] Tzotzos SJ, Fischer B, Fischer H, Zeitlinger M. 2020;24(1):516.
[2] Wu C, Chen X, Cai Y, et al. JAMA Intern Med. 2020;180(7):934-943.

Acknowledgements: The COVID-19 Global Rheumatology Alliance.

Figure: Adjusted odds ratios (ORs) corresponding to the most influential predictors



Top 10 most influential predictors identified by the grading boosting algorithm; Percentages represent prevalence of the predictors. Estimates obtained using hierarchical multivariate mixed-effects logistic regression with country-level random effects.
ILD: Interstitial lung disease; Low GC dose: 1-9mg (daily prednisone-equivalent), Medium dose: 10-20mg, High dose: >20mg.
TNFi: Tumor Necrosis Factor inhibitor; Anti-CD20: Anti-CD20 monoclonal antibody.
Number of cases= 5931, Number of countries = 67

Disclosure of Interests: Zara Izadi: None declared, Milena Gianfrancesco: None declared, Kimme Hyrich Speakers bureau: Abbvie and grant income from BMS, UCB, and Pfizer, all unrelated to this study., Anja Strangfeld Speakers bureau: AbbVie, MSD, Roche, BMS, Pfizer, outside the submitted work., Grant/research support from: A consortium of 13 companies (among them AbbVie, BMS, Celltrion, Fresenius Kabi, Lilly, Mylan, Hexal, MSD, Pfizer, Roche, Samsung, Sanofi-Aventis, and UCB) supporting the German RABBIT register., Laure Gossec Consultant of: Abbvie, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sanofi-Aventis, UCB., Grant/research support from: Lilly, Mylan, Pfizer, all unrelated to this study., Loreto Carmona Consultant of: Loreto Carmona's institute works by contract for laboratories among other institutions, such as Abbvie Spain, Eisai, Gebro Pharma, Merck Sharp & Dohme España, S.A., Novartis, Farmaceutica, Pfizer, Roche Farma, Sanofi Aventis, Astellas Pharma, Actelion Pharmaceuticals España, Grünenthal GmbH, and UCB Pharma., Elsa Mateus Grant/research support from: LPCDR received grants from Abbvie, Novartis, Janssen-Cilag, Lilly Portugal, Sanofi, Grünenthal S.A., MSD, Celgene, Medac, Pharmakern, GAfPA and Pfizer., Saskia Lawson-Tovey: None declared, Laura Trupin: None declared, Stephanie Rush: None declared, Gabriela Schmajuk: None declared, Lindsay Jacobsohn: None declared, Patti Katz: None declared, Samar Al Emadi: None declared, Leanna Wise: None declared, Emily Gilbert: None declared, Maria Valenzuela-Almada: None declared, Ali Duarte-Garcia: None declared, Jeffrey Sparks Consultant of: Bristol-Myers Squibb, Gilead, Inova, Janssen, and Optum unrelated to this work., Grant/research support from: Amgen and Bristol-Myers Squibb., Tiffany Hsu: None declared, Kristin D'Silva: None declared, Naomi Serling-Boyd: None declared, Suleman Bhana Employee of: Suleman Bhana reports non-branded marketing campaigns for Novartis (<$10,000)., Wendy Costello: None declared, Rebecca Grainger Speakers bureau: Abbvie, Janssen, Novartis, Pfizer, Cornerstones and travel assistance from Pfizer (all < $10,000)., Jonathan Hausmann Consultant of: Novartis, unrelated to this work (<$10,000)., Jean Liew Grant/research support from: Pfizer, outside the submitted work., Emily Sirotich Grant/research support from: Emily Sirotich is a Board Member of the Canadian Arthritis Patient Alliance, a patient run, volunteer-based organization whose activities are largely supported by independent grants from pharmaceutical companies., Paul Sufka: None declared, Zachary Wallace Consultant of: Viela Bio and MedPace, outside the submitted work., Grant/research support from: Bristol-Myers Squibb and Principia/Sanofi., Pedro Machado Speakers bureau: Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, all unrelated to this study (all < $10,000)., Philip Robinson Consultant of: Abbvie, Eli Lilly, Janssen, Novartis, Pfizer and UCB and travel assistance from Roche (all < $10,000)., Jinoos Yazdany Consultant of: Eli Lilly and Astra Zeneca, unrelated to this project.

DOI: 10.1136/annrheumdis-2021-eular.446

SLE, Sjörgen's and APS - Clinical Aspects

OP0289

LLDAS (LOW LUPUS DISEASE ACTIVITY STATE), LOW DISEASE ACTIVITY (LDA) AND REMISSION (ON- OR OFF-TREATMENT) PREVENT DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS IN A MULTINATIONAL MULTICENTER COHORT

M. F. Ugarte-Gil[1,2], J. Hanly[3], M. B. Urowitz[4], C. Gordon[5], S. C. Bae[6], J. Romero-Diaz[7], J. Sanchez-Guerrero[7], S. Bernatsky[8], A. E. Clarke[9], D. J. Wallace[10], D. Isenberg[11], A. Rahman[11], J. T. Merrill[12], P. Fortin[13], D. D. Gladman[4], I. N. Bruce[14], M. A. Petri[15], E. M. Ginzler[16], M. A. Dooley[17], R. Ramsey-Goldman[18], S. Manzi[19], A. Jonsen[20], R. Van Vollenhoven[21], C. Aranow[22], M. Mackay[22], G. Ruiz-Irastorza[23], S. S. Lim[24], M. Inanc[25], K. C. Kalunian[26], S. Jacobsen[27], C. Peschken[28], D. L. Kamen[29], A. Askanase[30], B. Pons-Estel[31], G. S. Alarcon[32,33]on behalf of The SLICC Group. *[1]Universidad Cientifica del Sur, School of Medicine, Lima, Peru*; *[2]Hospital Nacional Guillermo Almenara Irigoyen, EsSalud, Rheumatology, Lima, Peru*; *[3]Queen Elizabeth II Health Sciences Center and Dalhousie University, Department of Medicine and Department of Pathology, Nova Scotia, Canada*; *[4]Toronto Western Hospital and University of Toronto, Center for Prognosis Studies in the Rheumatic Diseases, Ontario, Canada*; *[5]University of Birmingham, Birmingham, Rheumatology Research Group, Institute of Inflammation and Ageing, College of Medical and Dental Sciences, Birmingham, United Kingdom*; *[6]Hanyang University Hospital for Rheumatic Diseases, Rheumatology, Seoul, Korea, Rep. of (South Korea)*; *[7]Instituto Nacional de Ciencias Médicas y Nutrición, Inmunología y Reumatología, Mexico City, Mexico*; *[8]McGill University, Divisions of Rheumatology and Clinical Epidemiology, Quebec, Canada*; *[9]Cumming School of Medicine, University of Calgary, Rheumatology, Alberta, Canada*; *[10]UCLA, Cedars Sinai/David Geffen School of Medicine, Los Angeles, United States of America*; *[11]University College London, Medicine, London, United Kingdom*; *[12]Oklahoma Medical Research Foundation, Deparment of Clinical Pathology, Oklahoma, United States of America*; *[13]CHU de Québec - Université Laval, Rheumatology, Quebec, Canada*; *[14]University of Manchester, Faculty of Biology Medicine and Health, Manchester Academic Health Sciences Center, Manchester, United Kingdom*; *[15]Johns Hopkins University School of Medicine, Division of Rheumatology, Baltimore, United States of America*; *[16]SUNY Downstate Medical Center, Department of Medicine, New York, United States of America*; *[17]University of North Carolina, Thurston Arthritis Research Center, North Carolina, United States of America*; *[18]Northwestern University and Feinberg School of Medicine, Medicine, Chicago, United States of America*; *[19]Allegheny Health Network, Lupus Center of Excellence, Pennsylvania, United States of America*; *[20]Lund University, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden*; *[21]Amsterdam UMC, Amsterdam University Medical Centers, Amsterdam, Netherlands*; *[22]Feinstein Institute for Medical Research, Feinstein Institute for Medical Research, New York, United States of America*; *[23]BioCruces Bizkaia Health Research Institute, Hospital Universitario Cruces, University of the Basque Country, Autoimmune Diseases Research Unit, Department of Internal Medicine, Barakaldo, Spain*; *[24]Emory University School of Medicine, Division of Rheumatology, Atlanta, United States of America*; *[25]Istanbul Medical Faculty, Istanbul University, Division of Rheumatology, Department of Internal Medicine, Istanbul, Turkey*; *[26]University of California San Diego, School of Medicine, La Jolla, United States of America*; *[27]Copenhagen University Hospital, Department of Rheumatology, Rigshospitalet, Copenhagen, Denmark*; *[28]University of Manitoba, Departments of Medicine and Community Health Sciences, Manitoba, Canada*; *[29]Medical University of South Carolina, Division of Rheumatology, Charleston, South Carolina, United States of America*; *[30]New York University, Hospital for Joint Diseases, New York, United States of America*; *[31]Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina*; *[32]University of Alabama at Birmingham, Department of Medicine, Birmingham, Alabama, United States of America*; *[33]Universidad Peruana Cayetano Heredia, Facultad de Medicina, Lima, Peru*

Background: Remission, LDA and LDAS have been proposed as treatment goals for SLE. However, the independent impact of these states on damage accrual has not been fully evaluated.

Objectives: To determine the independent impact of remission (both off & on treatment), LDA, and LLDAS on damage accrual.

Methods: We studied a long-term longitudinal multinational SLE cohort, including patients completing at least two annual assessments. Remission off-treatment was defined as a SLEDAI (excluding serology) =0, without prednisone and immunosuppressive (IS) drugs. Remission on-treatment was defined as a SLEDAI (excluding serology) =0, prednisone daily dose<=5 mg/d and maintenance IS drugs. LDA was defined as a SLEDAI (excluding serology) <=2, without prednisone or IS drugs. LLDAS was defined as a SLEDAI <=4 with no activity in major organ systems, with no new features of lupus disease activity compared to the previous assessment, prednisone daily dose<=7.5 mg/d and maintenance IS drugs. Antimalarials were allowed in all groups. Damage accrual was ascertained with the SLICC/ACR damage index (SDI). Univariable and multivariable generalized estimated equation (GEE) negative binomial regression models were used. To create mutually exclusive groups, disease activity was divided into five states: remission off-treatment, remission on-treatment (minus remission off treatment), LDA (minus remission), LLDAS (minus remission and LDA) and not-optimally controlled. The proportion of the time that patients were in the specific state at each visit since cohort entry was determined. Possible effect modifiers and confounders adjusted for included sex, age at diagnosis, race/ethnicity, education, baseline disease duration, follow-up time, the highest-ever glucocorticoid dose prior to cohort entry, antimalarials and SDI. Time-dependent covariates were determined at the same annual visit as disease activity state; the outcome was the increase in the SDI and it was assessed at the subsequent visit.

Results: There were 1,652 patients, 1464 (88.6%) were female, mean age at diagnosis was 34.6 (SD 13.4) years and mean baseline disease duration was 5.5 (SD 4.1) months. Patients had a mean follow-up of 6.5 (SD 4.3) years, 11686 visits were included. 763 patients (46.2%) had an increase in SDI score ≥1 during follow-up. 2483 (21.2%) of the visits were classified as remission off-treatment, 2276 (19.5%) as remission on-treatment, 544 (4.7%) as LDA, 657 (5.6%) as LLDAS and 5726 (49.0%) as not-optimally controlled. Being in remission off-treatment, remission on-treatment, LDA and LLDAS were predictive of a lower probability of damage accrual [remission off-treatment IRR=0.403, 95% CI 0.301-0.541); remission on-treatment IRR=0.313 (95% CI 0.218-0.451) LDA: IRR=0.469 (CI 95% CI 0.272-0.809); LLDAS IRR=0.440 (95% CI 0.241-0.803)]. The multivariable model is summarized in Table 1.

Table 1. Multivariable GEE model of the impact of disease activity states on damage accrual.

	Incidence Rate Ratio	95% CI
Disease activity state		
Remission off treatment	0.403	0.301-0.541
Remission on treatment	0.313	0.218-0.451
LDA	0.469	0.272-0.809
LLDAS	0.440	0.241-0.803
Gender, male	1.274	1.086-1.495
Age at diagnosis	1.024	1.020-1.029
Ethnicity		
Caucasian US	Ref.	
Caucasian other	1.017	0.849-1.217
African	1.467	1.211-1.776
Asian	0.863	0.693-1.075
Hispanic	1.266	1.034-1.550
Other	1.121	0.759-1.656
Educational level, years	0.977	0.957-0.996
Disease duration at baseline	0.960	0.801-1.150
Follow-up time	0.942	0.923-0.960
Antimalarial use	0.786	0.681-0.908
Highest prednisone dose before baseline	1.002	1.001-1.007
SDI before	1.100	1.050-1.1152

LLDAS: Low lupus disease activity state LDA: Low disease activity SDI: SLICC/ACR Damage Index

Conclusion: Remission on- and off-treatment, LDA and LLDAS were associated with less damage accrual, even adjusting for possible confounders and effect modifiers. This highlights the importance of treating to target in SLE.

Disclosure of Interests: Manuel F. Ugarte-Gil Grant/research support from: Pfizer, Janssen, John Hanly: None declared, Murray B Urowitz: None declared, Caroline Gordon Speakers bureau: UCB, Consultant of: Center for Disease Control, Astra-Zeneca, MFP, Sanofi, UCB, Sang-Cheol Bae: None declared, Juanita Romero-Diaz: None declared, Jorge Sanchez-Guerrero: None declared, Sasha Bernatsky: None declared, Ann E Clarke Consultant of: AstraZeneca, BristolMyersSquibb, GlaxoSmithKline, and Exagen Diagnostics, Daniel J Wallace Grant/research support from: Exagen, David Isenberg: None declared, Anisur Rahman: None declared, Joan T Merrill: None declared, Paul Fortin: None declared, Dafna D Gladman Consultant of: Abbvie, Janssen, Pfizer, Novartis, Amgen, Grant/research support from: Abbvie, Janssen, Pfizer, Novartis, Amgen, Ian N. Bruce: None declared, Michelle A Petri: None declared, Ellen M Ginzler Grant/research support from: Aurinia pharmaceutical, M.A. Dooley: None declared, Rosalind Ramsey-Goldman: None declared, Susan Manzi: None declared, Andreas Jonsen: None declared, Ronald van Vollenhoven Speakers bureau: AbbVie, Galapagos, GSK, Janssen, Pfizer, UCB, Consultant of: Abbvie, AstraZeneca, Biogen, Biotest, Celgen, Galapagos, Gilead, Janssen, Pfizer, Sanofie, Servier, UCB, Vielabo, Grant/research support from: BMS, GSK, Lilly, UCB, Cynthia Aranow: None declared, Meggan Mackay: None declared, Guillermo Ruiz-Irastorza: None declared, S. Sam Lim: None declared, Murat Inanc: None declared, Kenneth C Kalunian Consultant of: Roche, Biogen, Janssen, AstraZeneca, Eli Lilly, Genetech, Gilead, ILTOO, Nektar, Viela, Equillium, Bristol-Meyers Squibb,

Soren Jacobsen Grant/research support from: BMS, Christine Peschken: None declared, Diane L Kamen: None declared, Anca Askanase Consultant of: Abbvie, Grant/research support from: Glaxo Smith Kline, Astra Zeneca, Janssen, Eli Lilly and Company, Mallinckrodt, Pfizer, Bernardo Pons-Estel Consultant of: GSK, Janssen, Graciela S Alarcon: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1133

OP0290 CLINICAL CHARACTERISTICS AND PROGNOSIS OF ANTIPHOSPHOLIPID SYNDROME PATIENTS BASED ON CLUSTER ANALYSIS: A 10-YEAR COHORT STUDY

W. Qi[1], J. L. Zhao[1], X. Tian[1], M. LI[1], X. Zeng[1]. [1]*Peking Union Medical College Hospital, Department of Rheumatology, Beijing, China*

Background: APS is an autoimmune disease characterized by persistent antiphospholipid antibodies (aPLs) positivity, leading to thrombotic events or pregnancy morbidity. High-risk aPLs profiles included positive lupus anticoagulant (LA) and multiple aPLs positivity[1]. Association was also found between aPLs and a variety of manifestations beyond thrombosis, referred to "non-criteria manifestations" (i.e. thrombocytopenia, hemolytic anemia, heart valve disease and aPL-related nephropathy)[2], of which the role in APS risk stratification is poorly understood. The manifestation spectrum of APS is wide, ranging from asymptomatic aPLs positivity to life-threatening catastrophic APS, and patients other than confirmed APS also need proper management. Therefore, a risk stratification integrating demographic data, aPL-related manifestations, aPLs profiles, coexisting cardiovascular risk factors and SLE is needed for management guidance and prognosis assessment.
Objectives: Using cluster analysis, to identify phenotypes among aPL-positive patients and assess the prognosis of each phenotype.
Methods: This is a single-center, prospective cohort study of aPL-positive patients who presented to Peking Union Medical College Hospital from 2004 to 2020. Demographic characteristics, aPL-related manifestations, cardiovascular risk factors, antibodies profile and follow-up data were recorded. The primary end point was defined as a combination of newly onset arterial thrombosis (AT) or deep venous thrombosis (DVT), major bleeding events, non-criteria manifestations and all-cause death. Hierarchical cluster analysis with the Euclidean distance and the Ward method was applied to identify clusters of patients and variables separately. Multiple comparison and Kaplan-Meier survival analysis were performed among clusters.
Results: Four clusters among 383 patients (70.2% female; mean age 37.7 years) were identified (Figure 1A). Cluster 1 (n=138): female patients with SLE, non-criteria manifestations, triple aPLs positivity, high AT rate and moderate DVT rate. Cluster 2 (n=112): male patients with obesity, smoking history, hypertension, hyperhomocysteinemia, triple aPLs positivity and the highest rate of AT and DVT. Cluster 3 (n=83): female patients with the highest pregnancy morbidity rate and the lowest thrombosis rate. Cluster 4 (n=50): 62% male patients with isolated LA positivity, high AT rate and moderate DVT rate. Four clusters of variables were also identified (Figure 1A). From Kaplan-Meier survival analysis, 1-, 5- and 10-year event-free survival rates were 92.6%, 79.8% and 66.8%, respectively. Cluster 3 showed lowest incidence of primary endpoint (Figure 1B), while Cluster 1 and 2 showed higher newly-onset AT risk compared with other clusters (P=0.028 for 2 vs 3 and P=0.049 for 2 vs 4).

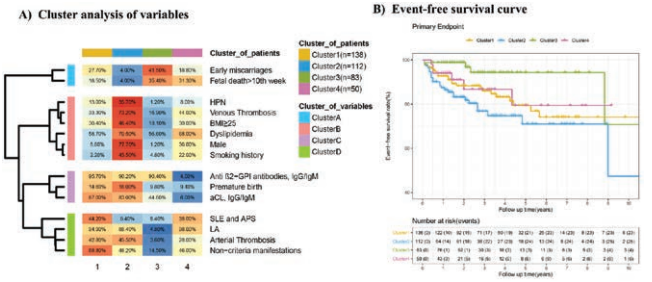


Figure 1.

Conclusion: We identified 4 clinical phenotypes of aPL-positive patients. APS secondary to SLE was always aggregated with non-criteria manifestations. Clinicians should be alert to the possibility of SLE in aPL-positive patients with coexisting non-criteria manifestations, for whom immunosuppressive therapy besides anticoagulation may be necessary. Cluster 4 represented patients with isolated LA positivity and shared similar prognosis with secondary APS and male patients, which confirmed that LA represented a high-risk antibody spectrum. Additionally, cardiovascular risk factors (i.e. male, smoking history and obesity) played an important role in thrombosis events, and led to poor prognosis. Therefore, more attention should be paid to male patients, and the screening and management of cardiovascular risk factors should not be ignored.

REFERENCES:

[1] Tektonidou MG, Andreoli L, Limper M et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. Ann Rheum Dis 2019;78:1296–304.
[2] Miyakis S, Lockshin MD, Atsumi T et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295–306.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1223

OP0291 SEVERITY OF LABIAL MINOR SALIVARY GLAND FOCUS SCORE AND FUTURE LYMPHOMA DEVELOPMENT IN SJÖGREN'S SYNDROME

A. Goules[1], L. Chatzis[1], V. Pezoulas[2], C. Baldini[3], F. Skopouli[4], A. Venetsanopoulou[5], P. Voulgari[5], S. De Vita[6], M. Voulgarelis[1], H. M. Moutsopoulos[7], D. Fotiadis[2], A. Tzioufas[1]. [1]*School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece*; [2]*University of Ioannina, Unit of Medical Technology and Intelligent Information Systems, Athens, Greece*; [3]*University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Athens, Greece*; [4]*Harokopio University of Athens, Department of Nutrition and Clinical Dietetics, Athens, Greece*; [5]*University of Ioannina, Department of Internal Medicine, Athens, Greece*; [6]*University of Udine, Rheumatology Clinic, Department of Medical area, Athens, Greece*; [7]*Academy of Athens, Chair Medical Sciences/Immunology, Greece, Athens, Greece*

Background: The typical histologic picture of focal sialadenitis in the labial minor salivary gland (LMSG) tissues has been incorporated as a parameter in the majority of Sjögren's syndrome (SS) classification criteria, with focus score (FS) being the most widely used (1). In previous studies, higher FS has been associated with the presence of autoantibodies and extra-glandular manifestations including lymphoma, implying that FS can predict severe disease (2,3). However, there are no studies exploring the association of FS with lymphoma development along with the time interval from SS diagnosis to lymphoma diagnosis.
Objectives: To investigate an association of focus score grading with lymphoma development and time to lymphoma occurrence.
Methods: From a total population 1998 consecutive patients fulfilling the 2016 ACR-EULAR criteria for SS who were followed-up in 5 Rheumatology centers from Greece and Italy (Universities of Athens, Pisa, Udine, Harokopio and Ioannina) (UPAHI group), those with positive (LMSG) (FS ≥1) were identified. (1). Patients who had not been subjected to an LMSG biopsy or had a negative biopsy (FS<1) or the biopsy was evaluated using other histologic classifications were excluded from the present study. Lymphoma patients with diagnostic LMSG biopsy performed within a year from lymphoma diagnosis as well as non-lymphoma patients with less than 1 year between SS diagnosis and their last follow up, were also excluded. Cumulative clinical and histologic data attributed to SS as defined by ESSDAI and/or ESSPRI, up to lymphoma diagnosis or last follow up, were recorded. A combined data driven Fast Correlation Based Feature selection (FCBF)/Logistic Regression (LR) model was applied on the unified dataset to identify independent lymphoma associated risk factors. A correlation between FS and time interval until lymphoma diagnosis was performed using the Pearson formula.
Results: A unified dataset of 618 SS patients with FS≥1 and at least one year of disease duration from SS diagnosis to lymphoma diagnosis or last follow up, with 30 clinical, laboratory and histologic features, was constructed. The median age at SS diagnosis was 53 (range: 15 – 80) years old, the female to male ratio was 20:1 and the median disease duration was 6 years (range: 1-35). Half (49%) of the study population had focus score between one and two (1≤FS<2), followed by a declining proportion of patients accounted for every subsequent escalating FS group. No statistically significant difference was found regarding disease duration among the various FS escalating groups (p= 0.1603, Kruskal-Wallis test). Fifty eight patients had lymphoma with no statistically significant difference in disease duration compared to non-lymphoma controls. The data driven FCBF/LR algorithm with lymphoma on the whole dataset revealed that cryoglobulinemia (p=0.021), salivary gland enlargement (p=0.008) and FS (p=0,049) are independent lymphoma associated risk factors. A statistically significant negative correlation was found using a Pearson formula (R=-0.32 and p=0.015) regarding the focus score and the time to lymphoma diagnosis.
Conclusion: This is the largest study of SS patients' histologic analysis exploring the association of LMSG FS grading with lymphoma development and the time interval until its diagnosis. Higher FS values correlate with increased lymphoma risk and early lymphoma occurrence.

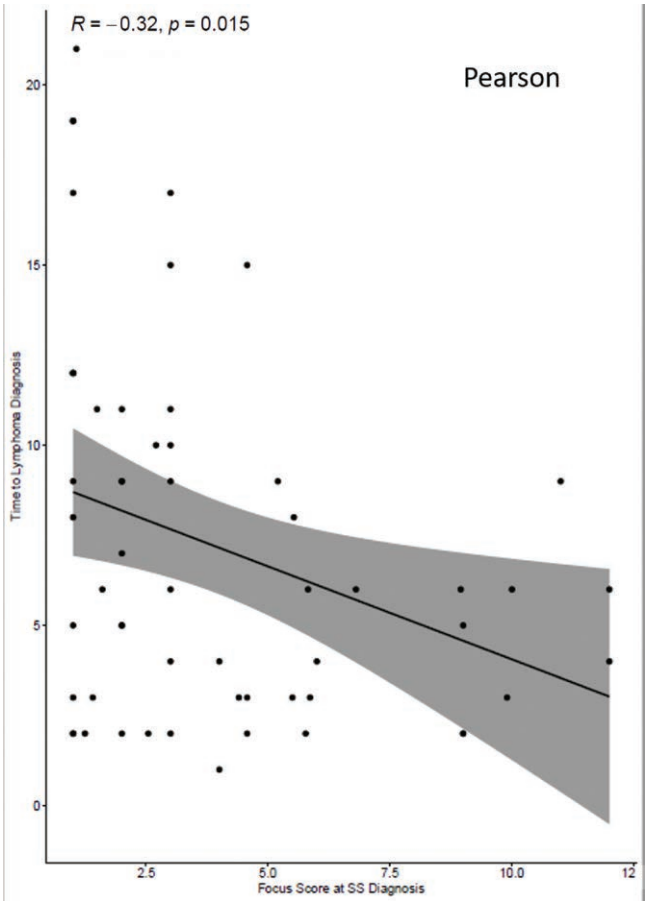


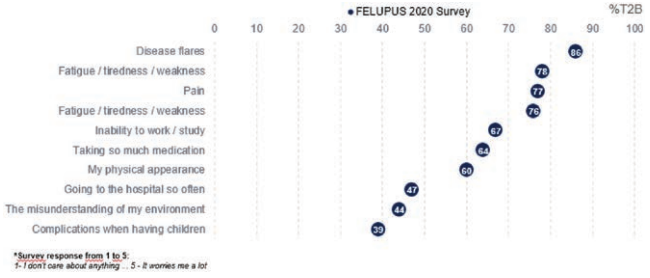
Figure 1. Pearson correlation between FS and time interval until lymphoma diagnosis

REFERENCES:
[1] Shiboski et al. Arhtritis Rheumatol. 2017
[2] Carrubi et al. Lupus 2015
[3] Risselada AP et al. Ann Rheum Dis 2014
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2539

OP0292 SURVEY ON THE PERCEPTIONS AND EXPERIENCES OF SPANISH LUPUS PATIENTS. RESULTS ABOUT KNOWLEDGE OF THE DISEASE AND RELATIONSHIP TO DISEASE-FELUPUS SURVEY

P. Fanlo[1], T. C. Salman Monte[2], J. L. Callejas-Rubio[3], M. Galindo[4], Á. Robles Marhuenda[5], L. Pallares Ferreres[6], M. J. Ángel Torres[7], S. Pérez Ortega[7]on behalf of FELUPUS. *[1]Complejo Hospitalario de Navarra, Internal Medicine, Pamplona, Spain*; *[2]Hospital Universitario del Mar, Rheumatology, Barcelona, Spain*; *[3]Internal Medicine, Hospital Universitario Clínico San Cecilio, Granada, Spain*; *[4]Hospital Universitario 12 de Octubre, Rheumatology, Madrid, Spain*; *[5]Hospital Universitario La Paz, Internal Medicine, Madrid, Spain*; *[6]Hospital Universitario Son Spases, Internal Medicine, Palma de Mallorca, Spain*; *[7]FELUPUS, FELUPUS, Madrid, Spain*

Background: Despite great advances in the diagnosis and treatment of lupus, the scientific community does not know the perception of our patients regarding the knowledge of the disease and the relationship between patients and disease. Fatigue had the greatest impact on activities of daily living, yet the majority reported receiving no support or poor support in managing it[1].
Objectives: Through this initiative, it is intended to investigate about the knowledge of the disease and impact of the disease on quality of life of Lupus patients. Another objective is to give visibility to the current needs of people living with lupus.
Methods: It was performed a national survey with 1,263 interviews with Lupus patients who reside in Spanish territory and belonging to lupus patient associations in Spain. The survey was carried out by the Spanish Lupus Federation (FELUPUS) in collaboration with GSK company.
Online interview lasting approximately 25 minutes. The collection of information was anonymously carried out from May 21 to June 30, 2020.
Results: 1.263 lupus patients were interviewed, 92% diagnosed with SLE and 8% with CLE. Survey sample is representative of the Lupus patient population in Spain [associated sampling error: 2.76%]. Questions about knowledge of the disease showed that 73% of patients considered that there is very little knowledge of the disease by society. Patient awareness of lupus increases as the disease progresses, so at the time of diagnosis, level of knowledge of the patient about Lupus is low in 92% of patients and at the moment of survey, 68% of patient had high knowledge. In terms of the perception of his illness, the affectation of the kidneys and heart (97%), fatigue and skin rashes (97%), are the statements that generate the greatest consensus. The survey about the relationship to disease demonstrated that 3 out of 4 patients have symptoms related to the disease, muscle and joint pain (75%) and fatigue (74%) are the symptoms that cause the greatest discomfort (Graph 1). Remarkable degree of agreement with the fact of not being able to sunbathe (78%), as well as the lack of energy (61%) and weakness in the body (60%). Flare-ups (86%), followed by fatigue (78%) and pain (77%) cause great concern. At diagnosis, 92% of patients have some organic involvement and regarding the diagnosis, at present, a greater number of patients present damage to the CNS (17%) and bones (21%). Many patients do not understand the concept of organ damage, wrongly relating it to fatigue (38%) or joint pain (47%).



Graph 1.

Conclusion: Among the conclusions of the survey, it stands out that society and the general population are unaware of what lupus is, while in the case of lupus patients, knowledge increases as the disease progresses. Citizen awareness campaigns about this disease are necessary, where patient associations together with health authorities have a crucial job. On the other hand, 92% of patients present organ damage at diagnosis. This means that we are arriving late to the diagnosis of many patients, which makes it necessary to promote a close collaboration between Primary Care and Hospitals, to refer patients as soon as they suspect SLE.
REFERENCES:
[1] Sloan M, Harwood R, Sutton S, D'Cruz D, Howard P, Wincup C, Brimicombe J, Gordon C. Medically explained symptoms: a mixed methods study of diagnostic, symptom and support experiences of patients with lupus and related systemic autoimmune diseases. Rheumatol Adv Pract. 2020 Feb 26;4(1):rkaa006.
What worries the most to Lupus patients?
Question P12. Please indicate your level of concern with the following aspects of Lupus. Percentage of patients who have scored a 4 or 5 for each item (% T2B).
Acknowledgements: GSK funded the study presented in the abstract.
Disclosure of Interests: Patricia Fanlo Grant/research support from: GSK funded the study presented in the abstract.
DOI: 10.1136/annrheumdis-2021-eular.509

OP0293 OPTIMIZING A TOOL TO IDENTIFY LUPUS FLARES IN DAILY CLINICAL PRACTICE: SLE-DAS FLARE VERSUS SELENA FLARE INDEX

L. Saraiva[1], A. R. Cunha[2], D. Jesus[3,4], J. A. P. Da Silva[1,5], A. Doria[6], L. Inês[1,4]. *[1]Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal*; *[2]Centro Hospital do Baixo Vouga, Rheumatology, Aveiro, Portugal*; *[3]Centro Hospitalar de Leiria, Rheumatology, Leiria, Portugal*; *[4]Faculty of Health Sciences, University of Beira Interior, Health Sciences, Covilhã, Portugal*; *[5]Faculty of Medicine, University of Coimbra., Coimbra Institute for Clinical and Biomedical Researh (iCBR), Coimbra, Portugal*; *[6]University of Padova, Rheumatology, Padova, Italy*

Background: In the management of patients with Systemic Lupus Erythematosus (SLE), it is of utmost importance to accurately identify lupus flares. There is a conceptual consensus definition of lupus flares [1]; however, the instruments used to identify flares in clinical trials, such as the SELENA Flare Index (SFI) are too cumbersome to apply in daily clinical practice. The SLE disease activity score (SLE-DAS) is a validated continuous measure of disease activity with higher sensitivity to change and validity in predicting damage accrual when compared

to SLEDAI-2K. SLE-DAS is quickly scored with its online calculator. An increase in SLE-DAS ≥1.72 was validated as a clinically meaningful worsening of SLE disease activity. [2]

Objectives: To compare the performance of SLE-DAS, classic SFI (c-SFI), revised SFI (r-SFI) and SLEDAI-2K in the identification of lupus flares in a real-life clinical setting.

Methods: We included patients with SLE fulfilling classification criteria [ACR (1997) and/or SLICC and/or EULAR/ACR], followed at an academic lupus clinic from January 2017 to June 2020, and presenting with lupus low disease activity score (LLDAS) at baseline.

Flares occurring after baseline were identified as fulfillment of the conceptual definition of flare, as assessed by the senior lupus expert at time of each outpatient visit. For each flare event, we evaluated the fulfillment of flare criteria according to c-SFI, r-SFI, SLEDAI-2K (score increase ≥4 points from baseline), and SLE-DAS (score increase ≥1.72 from baseline). As control visits without flare, we considered the first visit after baseline, where we assessed the four tools, excluding those where a flare was identified by the gold-standard expert evaluation. Sensitivity and specificity of the four flare tools were estimated and McNemar's test applied to assess differences with the gold-standard flare definition. The inter-instrument agreement with the gold-standard was assessed through Cohen's Kappa.

Results: We included 297 patients (female: 86.2%; mean age: 48.9±14.6 years, mean disease duration: 12.5±9.0 years). At baseline, all patients were in LLDAS, receiving ongoing antimalarials, immunosuppressants, and/or glucocorticoids in 91.0%, 43.8% and 33.6%, respectively. During follow-up, 22.2% developed flares. The analysis included 92 flares [musculoskeletal (40.2%); renal (23.9%), mucocutaneous (18.5%), haematological (5.9%), serositis (3.3%); multisystemic (8.7%)], with increase or change of treatment in 80.4% of these episodes, and 292 visits without flare considered as control.

There was no statistically significant difference between either SLE-DAS flare or c-SFI and the gold-standard expert flare definition (p=0.41 and p=0.82, respectively), while r-SFI and SLEDAI-2K flare were different from the gold-standard (Table 1). There was a strong agreement between SLE-DAS flare, c-SFI, r-SFI and the expert definition (Cohen's kappa, Table 1).

Table 1. Performance of the flare tools for the gold-standard flare definition.

	Sensitivity (%)	Specificity (%)	McNemar's[§§]	Kappa[§]
SLE-DAS flare	90.1	95.0	n.s.	0.836
c-SFI flare	91.1	96.5	n.s.	0.869
r-SFI flare	93.4	92.9	p<0.01	0.820
SLEDAI-2K flare	51.6	98.6	p<0.0001	0.590

[§§] McNemar's test: significant difference from gold-standard if p<0.05; [§] Cohen's kappa agreement (0-1) with the gold-standard flare definition; n.s.: non-significant

Conclusion: The c-SFI and SLE-DAS showed the best performance in identifying SLE flares. The SLE-DAS flare definition is easier to apply and hence might be considered as an optimal tool to be used in daily clinical practice.

REFERENCES:

[1] Ruperto N, Hanrahan LM, Alarcón GS, et al. International consensus for a definition of disease flare in lupus. *Lupus*. 2011;20(5):453-62.

[2] Jesus D, Matos A, Henriques C, et al. Derivation and validation of the SLE Disease Activity Score (SLE-DAS): a new SLE continuous measure with high sensitivity for changes in disease activity. Ann Rheum Dis 2019; 78:365-71.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.748

OP0294

SJÖGREN'S SYNDROME ASSOCIATED LYMPHOMAS: CLINICAL DESCRIPTION AND 10-YEAR SURVIVAL

L. Chatzis[1], V. Pezoulas[2], A. Goules[1], I. Stergiou[1], C. Mavragani[3], G. Tsourouflis[4], D. Fotiadis[2], H. M. Moutsopoulos[5], M. Voulgarelis[1], A. Tzioufas[1].

[1]School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece; [2]University of Ioannina, Unit of Medical Technology and Intelligent Information Systems, Athens, Greece; [3]School of Medicine, National and Kapodistrian University of Athens, Physiology, Athens, Greece; [4]School of Medicine, National and Kapodistrian University of Athens, Second Department of Propaedeutic Surgery, Athens, Greece; [5]Academy of Athens, Chair Medical Sciences/Immunology, Chair Medical Sciences/Immunology, Greece, Athens, Greece

Background: Sjögren's Syndrome (SS) is a chronic systemic autoimmune disease of unknown etiology, carrying the highest lymphoma risk among autoimmune diseases, with significant impact on mortality and morbidity of patients.

Objectives: To describe: i) the clinical phenotype of SS, ii) the histologic type, stage, treatment options regarding lymphomas and iii) the prognosis of patients with SS related lymphoproliferative disorders.

Methods: Eight hundred and fifteen consecutive SS patients' records from a single center fulfilling the 2016 ACR/EULAR were reviewed retrospectively for the purpose of this study. One hundred twenty-one patients with a diagnosis of non-Hodgkin Lymphoma (NHL) were identified and enrolled in the study population. Cumulative clinical, laboratory and histologic data were recorded and overall survival as well as event free survival curves were constructed using the Kaplan-Meier method. An event was defined as a disease progression, lymphoma relapse, treatment failure, histologic transformation, development of a 2nd lymphoma or death from any cause.

Results: From 121 pSS patients with lymphoma the most common histologic type encountered was MALT lymphoma (92/121, 76,0%) followed by DLBCL (11/121, 9.0%) and NMZL (8/119, 6.6%). The remaining 10 patients had various lymphomas of B (follicular, lymphoplasmacytic, chronic lymphocytic leukemia} and T cell origin (peripheral T cell lymphoma not otherwise specified, primary cutaneous T cell lymphoma, angioimmunoblastic t-cell lymphoma). Permanent salivary gland enlargement (66.1%, 80/121), palpable purpura (34,7% 42/121), peripheral nervous involvement (9,9%, 12/121), interstitial lung disease (8,2%, 10/121) presence of serum cryoglobulins (38,7%, 43/111) and C4 hypocomplementemia (69,8% 81/116) present at least 1 year before the development of lymphoma were the main pSS related features. The median age at lymphoma diagnosis was 58 years old (range 29-82) while MALT lymphomas developed earlier compared to DLBCL from pSS diagnosis (8 vs 3 OR= 3.84, 95%CI: 0.29 to 10.46; p=0.0266). The commonest biopsy proven extranodal sites included the labial minor salivary (43,8% patients) and parotid glands (30,5%) while 11% of patients had more than 1 extranodal sites affected. Bone marrow involvement was evident in 24,3% of patients (29/119) while nodal involvement in 35,5% (42/118). The majority of patients (65%) had limited disease (stage I or II). A watch and wait therapeutic policy was chosen in 40 patients while the rest received rituximab with or without chemotherapy. The 10-year survival and event free rates were 79% and 45,5% for MALT lymphomas, 40,9% and 24,2% for DLBCL and 46% and 31% for NMZL respectively (Figure 1). The Mantel-Cox log-rank comparison of the overall survival curves revealed a statistically significant difference (p=0.0016) among lymphoma subtypes.

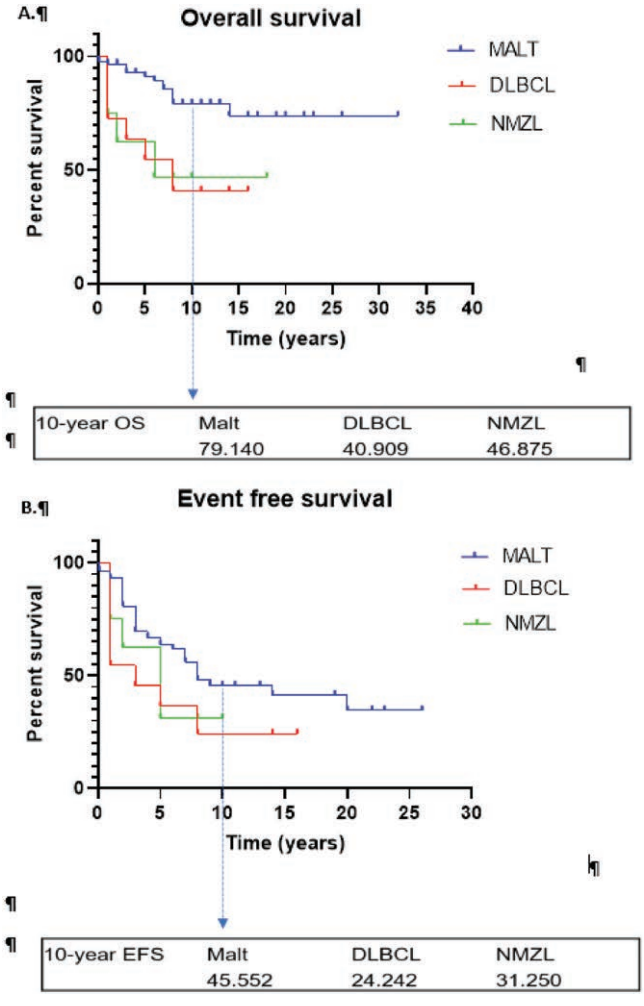


Figure 1. Overall and event free survival of SS-associated lymphoma patients. A. Kaplan-Meier overall survival analysis. B. A Kaplan-Meier event free survival analysis.

Conclusion: This is the largest single center series of SS- associated lymphoma patients, providing a detailed description of SS and lymphoma related features, combined with a 10-year survival and event free curves for the first time in the literature.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2400

OP0295 GR2 MULTICENTRIC PROSPECTIVE FRENCH STUDY'S RESULTS: DAMAGE BUT NOT REMISSION AT FIRST TRIMESTER PREDICTS ADVERSE PREGNANCY OUTCOME IN LUPUS PREGNANCIES

M. Larosa[1,2], V. Le Guern[1], G. Guettrot Imbert[1], E. Lazaro[3], N. Morel[1], N. Abisror Jeannin[4], C. Morati-Hafsaoui[5], P. Orquevaux[6], E. Diot[7], F. Sarrot-Reynauld[8], A. Doria[2], A. Moltó[9], C. Deneux-Tharaux[10], N. Costedoat-Chalumeau[1]on behalf of GR2 Group. *[1]AP-HP, Hôpital Cochin; Centre Référence Maladies Rares, Service de Médecine interne, Paris, France*; *[2]University of Padova, Rheumatology Unit, Department of Medicine-DIMED, Padova, Italy*; *[3]Centre Hospitalier Universitaire de Bordeaux, Service De Médecine Interne et Maladies Infectieuses, Bordeaux, France*; *[4]AP-HP, Hôpital Saint-Antoine, Service de Médecine interne, Paris, France*; *[5]CH Annecy Genevois, Service Infectiologie et médecine interne, Annecy, France*; *[6]CHU de Reims-Robert Debré, Service de Médecine interne, Reims, France*; *[7]CHRU de Tours - Hôpital Bretonneau, Service de Médecine interne, Tours, France*; *[8]CHU Grenoble, Service de Médecine interne, Grenoble, France*; *[9]AP-HP, Hôpital Cochin, Service de Rhumatologie B, Paris, France*; *[10]Epidemiology and Statistics Research Center/CRESS, INSERM, INRA F-75004, Equipe Épope, Paris, France*

Background: Active Systemic Lupus Erythematosus (SLE) during pregnancy is associated with poor obstetrical outcome but it is still not clear if remission, lupus low disease activity state (LLDAS) is the best target to achieve at conception. Besides, the effect of damage on pregnancy outcome has not been studied.

Objectives: Our aim was to determine the 1st trimester risk factors for adverse pregnancy outcome (APO).

Methods: Inclusion criteria were: 1) women≥18 years enrolled in the prospective GR2 study; 2) with SLE (SLICC criteria); 3) and an ongoing singleton pregnancy at 12 weeks (only 1 pregnancy per patient). We used the following definitions: DORIS[1], DORIA[2], clinical SLEDAI-2K=0, LLDAS[3] (for SLE activity), SFI[4] (for flares), and SLICC-damage index[5] (for damage). APO included: foetal death, neonatal death, placental insufficiency with premature delivery<37 weeks, and small for gestational age (SGA:≤3rd percentile).

Results: 238 patients were included. 234 (98.3%) women were on hydroxychloroquine (HCQ) and 206 (86.5%) had a clinical SLEDAI-2K=0. Regarding pregnancy outcome, 230 (96.6%) patients had a live birth (mean term 37.7 weeks). Thirty-four (14.3%) patients developed at least 1 APO: placental insufficiency (n=22), foetal death (n=7), neonatal death (n=1), and SGA (n=5). Two different regression logistic models were assessed, one for DORIA and one for LLDAS. We found that only SLICC-Damage index and lupus anticoagulant (LAC) were associated with APO (p=0.02, OR 1.8, 95% CI: 1.1-2.9; p=0.001, OR 4.2, 95% CI: 1.8-9.7 respectively for DORIA model; p=0.03, OR 1.7, 95% CI:1.1-2.8; p=0.002, OR 3.7, 95% CI: 1.6-8.7 respectively for LLDAS model).

Table 1.

Univariate analysis for APO

Maternal features	Total (N=238)	APO (N=34)	Non-APO (N=204)	P value
Age, mean (SD)	31.6(4.5)	30.7(4.8)	31.7(4.4)	0.22
Secondary APS	34(14.3)	10(29.4)	24(11.8)	**0.01**
Previous renal phenotype	67(28.2)	13(38.2)	54(26.5)	0.16
At least 1 flare during pregnancy	37(15.5)	6(17.4)	31(15.2)	0.80
Positive anti-DNA (N=222)	104(46.8)	21(67.7)	83(43.5)	**0.01**
Hypocomplementemia (N=216)	57(26.4)	13(40.6)	44(23.9)	**0.05**
LAC (N=232)	41(17.7)	15(44.1)	26(13.1)	**<0.001**
Triple aPL (N=232)	17(7.3)	5(14.7)	12(6.1)	0.08
24h-proteinuria>0.5g/day	9(3.8)	3(8.8)	6(2.9)	0.12
Activity/Damage				
SLEDAI-2K, median (IQR) (N=212)	2(0-3)	2(2-4)	2(0-2)	**0.01**
SLICC-DI, median (IQR) (N=236)	0(0-0)	0(0-0)	0(0-0)	**0.007**
PGA, median (IQR)(N=235)	0.1(0-0.2)	0.1(0-0.41)	0.1(0-0.2)	0.06
DORIA remission*	154(64.7)	17(50.0)	137(67.2)	**0.05**
DORIS remission**	147(61.8)	17(50.0)	130(63.4)	0.13
LLDAS (N=219)	157(71.7)	19(57.6)	138(74.2)	**0.05**
Clinical SLEDAI-2K=0	206(86.5)	28(82.4)	178(87.3)	0.44
Treatment				
Prednisone (PDN)	119(50.0)	23(67.7)	96(47.1)	**0.03**
PDN (mg/day) median (IQR)	7(5-10)	0(0-6)	5(0-10)	**0.007**
Immunosuppressants	57(24.0)	13(38.2)	44(21.6)	**0.04**
Hydroxychloroquine	234(98.3)	34(100.0)	200(98.0)	1.00
Low dose aspirin	165(69.3)	29(85.3)	136(66.7)	**0.03**
Low molecular weight heparin	61(25.6)	15(44.1)	46(22.6)	**0.01**

Legend: APS: antiphospholipid syndrome; aPL: antiphospholipid; PGA: Physician global assessment. *: DORIA definition of remission = clinical SLEDAI=0 and prednisone ≤5 mg/day; **: DORIS definition of remission = clinical SLEDAI=0, prednisone ≤5 mg/day, and PGA<0.5.

Conclusion: We confirmed that LAC predicts APO. We found for the first time that chronic damage at 1st trimester also predicted APO. No effect of remission/LLDAS was observed in this cohort of patients on HCQ with a stable and well-controlled SLE.

REFERENCES:

[1] van Vollenhoven R, et al. ARD 2017.
[2] Zen M, et al. ARD. 2015.
[3] Franklyn, K. et al. ARD 2016.
[4] Petri M, et al. NEJM 2005.
[5] Gladman DD, et al. Arthritis Rheum, 1997.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3876

OP0296 THE 2021 DORIS DEFINITION OF REMISSION IN SLE – FINAL RECOMMENDATIONS FROM AN INTERNATIONAL TASK FORCE

R. van Vollenhoven[1,2], G. Bertsias[3], A. Doria[4], D. Isenberg[5], E. F. Morand[6], M. A. Petri[7], B. Pons-Estel[8], A. Rahman[5], M. Ugarte-Gil[9], A. Voskuyl10,11, L. Arnaud[12], I. N. Bruce[13], R. Cervera[14], N. Costedoat-Chalumeau[15], C. Gordon[16], F. Houssiau[17], M. Mosca[18], M. Schneider[19], M. Ward[20], C. Aranow[21]on behalf of The DORIS Task Force. *[1]Amsterdam UMC, Rheumatology and Clinical Immunology, Amsterdam, Netherlands*; *[2]Amsterdam Rheumatology Center, Rheumatology, Amsterdam, Netherlands*; *[3]University of Crete, Rheumatology, Heraklion, Greece*; *[4]University of Padova, Medicine, Padova, Italy*; *[5]University College London, Rheumatology, London, United Kingdom*; *[6]Monash University, School of Clinical Sciences, Melbourne, Australia*; *[7]Johns Hopkins University, Rheumatology, Baltimore, United States of America*; *[8]Grupo Oroño - Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR)., n/a, Rosario, Argentina*; *[9]Universidad Cientifica del Sur, Medicine, Lima, Peru*; *[1]Amsterdam UMC, Rheumatology and Clinical Immunology, Amsterdam, Netherlands*; *[2]Amsterdam Rheumatology Center, Rheumatology, Amsterdam, Netherlands*; *[12]University Hospitals of Strasbourg, Rheumatology, Strasbourg, France*; *[13]University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; *[14]Hospital Clinic, Autoimmune Diseases, Barcelona, Spain*; *[15]AP-HP, Cochin Hospital, Internal Medicine, Paris, France*; *[16]University of Birmnigham, Rheumatology, Birmingham, United Kingdom*; *[17]Cliniques universitaires Saint-Luc, Rheumatology, Brussels, Belgium*; *[18]University of Pisa, Rheumatology, Pisa, Italy*; *[19]Heinrich-Heine University, Rheumatology, Dusseldorf, Germany*; *[20]NIAMS/NIH, Intramural Research Program, Bethesda, United States of America*; *[21]Feinstein Institute for Medical Research, n/a, Manhasset, United States of America*

Background: Remission is the stated goal for both patient and care-giver (1), but consensus on a definition of remission has been lacking. Previously, an international task force consisting of patient representatives and medical specialists published a frame-work for such a definition (2), but without making a final recommendation.

Objectives: To achieve consensus around a definition of remission in SLE (DORIS).

Methods: The DORIS task force met annually from 2015 to 2020 and consisted of patient representatives and specialists in rheumatology, nephrology, dermatology, and clinical immunology. Systemic literature reviews of several key topics were done and specific research questions were examined in suitably chosen datasets. The findings were discussed, reformulated as recommendations, and voted upon. Level of evidence (LoE), strength of recommendation (SoR), and agreement were determined in standard fashion. The final recommendation for the DORIS definition of remission was established by electronic vote after finalization of the minutes of the most recent task force meeting.

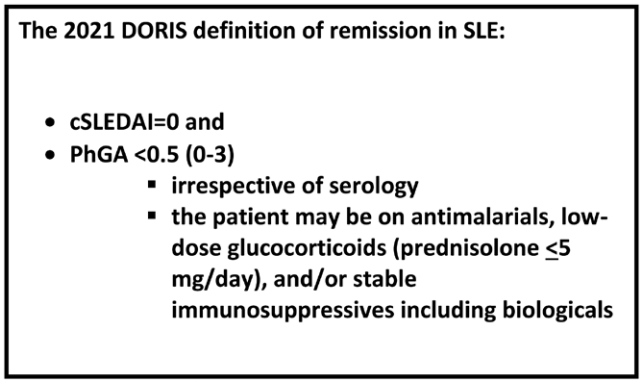
Results: Based on data from the literature and from several SLE-specific data sets, five key recommendations were endorsed (Table 1) that should be seen as additions to those published previously (2). Literature reviews identified strong support for the face-, content-, construct- and criterion validity of the definition based on the clinical SLEDAI (not including anti-DNA and complement) equal to zero plus low physician global assessment and allowing stable medical treatment. Thus, the DORIS Task Force recommended a single definition of remission in SLE, based on clinical SLEDAI = 0, evaluator's global assessment <0.5 (0-3),

prednisone 5 mg/day or less, and stable antimalarials, immunosuppressives and biologics.

Table 1.

	Vote in favor	LoE	SoR	Agreement
1.Inclusion of serology [anti-DNA, complement] in the DORIS definition of remission-on-treatment does not meaningfully alter the construct validity and therefore it is not recommended to include it	90%	2a	B	8.38
2.While the goal of treatment is sustained remission, a definition of remission should be able to be met at any point in time; therefore, duration should not be included in the definition	100%	5	C	9.02
3.To date, the SLEDAI-based definitions of remission have formally been investigated more extensively than BILAG-or ECLAM-based definitions. The SLEDAI-based definitions can therefore more confidently be recommended	91%	2a	B	9.25
4.Remission off treatment, while the ultimate goal for many patients and providers, is achieved very rarely. In clinical research and as an outcome in clinical trials, the definition for remission-on-treatment is recommended	92%	2a	B	9.52
5.In clinical trials, the LLDAS definition for low disease activity and the DORIS definition of remission are both recommended as outcomes	100%	5	C	9.25

The 2021 DORIS definition of remission in SLE:



Conclusion: The 2021 DORIS definition of remission in SLE was established. It is recommended for use as an aspirational treatment target in clinical care, a clear concept in education, and a key outcome in research including clinical trials and observational studies.

REFERENCES:

[1] van Vollenhoven RF, Mosca M, Bertsias G, et al. Treat-to-target in systemic lupus erythematosus: recommendations from an international task force. Ann Rheum Dis 2014;73:958-67.

[2] van Vollenhoven R, Voskuyl A, Bertsias G, et al. A framework for remission in SLE: consensus findings from a large international task force on definitions of remission in SLE (DORIS). Ann Rheum Dis 2016.

Disclosure of Interests: Ronald van Vollenhoven Speakers bureau: AbbVie, Galapagos, GSK, Janssen, Pfizer, UCB, Consultant of: AbbVie, AstraZeneca, Biogen, Biotest, Celgene, Galapagos, Gilead, Janssen, Pfizer, Sanofi, Servier, UCB, Vielabo, Grant/research support from: BMS, GSK, Lilly, UCB, George Bertsias: None declared, Andrea Doria: None declared, David Isenberg: None declared, Eric F. Morand: None declared, Michelle A Petri: None declared, Bernardo Pons-Estel Consultant of: GSK, Janssen, Anisur Rahman: None declared, Manuel Ugarte-Gil Grant/research support from: Janssen, Pfizer, Alexandre Voskuyl: None declared, Laurent Arnaud Consultant of: Alexion, Amgen, AstraZeneca, BMS, GSK, Janssen-Cilag, LFB, Lilly, Menarini France, Medac, Novartis, Pfizer, Roche-Chugaï, UCB., Ian N. Bruce: None declared, Ricard Cervera Consultant of: GSK, Alexion, Eli Lilly, Astra Zeneca, Termo-Fisher, Rubió, Nathalie Costedoat-Chalumeau: None declared, Caroline Gordon Speakers bureau: UCB, Consultant of: Center for Disease Control, Astra-Zeneca, MGP, Sanofi, UCB, Frederic Houssiau: None declared, Marta Mosca: None declared, Matthias Schneider: None declared, Michael Ward: None declared, Cynthia Aranow: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1192

OP0297

THE SLE-DAS ENABLES ACCURATE AND USER-FRIENDLY DEFINITIONS OF REMISSION AND CATEGORIES OF LUPUS DISEASE ACTIVITY: DERIVATION AND VALIDATION STUDY IN 1190 SLE PATIENTS

D. Jesus[1,2], M. Larosa[3], C. Henriques[4,5], A. Matos[4,6], M. Zen[3], P. Tomé[4,6], V. Alves[4,6], N. Costa[4], V. Le Guern[7], L. Iaccarino[3], N. Costedoat-Chalumeau[7], A. Doria[3], L. Inês[2,8]. *[1]Centro Hospitalar de Leiria, Rheumatology Department, Leiria, Portugal*; *[2]University of Beira Interior, Faculty of Health Sciences, Covilhã, Portugal*; *[3]University of Padova, Division of Rheumatology, Padova, Italy*; *[4]Institute of Viseu, Technology and Management, Viseu, Portugal*; *[5]University of Coimbra, Centre for Mathematics, Coimbra, Portugal*; *[6]Research Centre in Digital Services, CISeD, Viseu, Portugal*; *[7]Cochin Hospital, Internal Medicine Department, Paris, France*; *[8]Centro Hospitalar e Universitário de Coimbra, CHUC Lupus Clinic, Rheumatology Department, Coimbra, Portugal*

Background: Treatment of systemic lupus erythematosus (SLE) is tailored according to the intensity of SLE disease activity and aims to achieve remission. Current definitions of remission and disease activity categories are mostly based on the SLE Disease Activity Index (SLEDAI), which has important limitations. The SLE Disease Activity Score (SLE-DAS) is a validated continuous disease activity score with higher accuracy in measuring SLE activity and higher sensitivity-to-change as compared to SLEDAI[1]. SLE-DAS is user-friendly with its online calculator.

Objectives: To derive and validate the SLE-DAS cut-off values for defining SLE disease activity categories and SLE clinical remission state.

Methods: Derivation study was conducted at the Padova Lupus Clinic. Validation was performed prospectively in patients from the Cochin Lupus Clinic and by post-hoc analysis of BLISS-76 (NCT00410384) trial. Gold-standard for clinical remission state was fulfillment of Definition Of Remission In SLE (DORIS). In Padova and Cochin Clinics, at time of inclusion, a senior clinician classified each patient as presenting: (i) remission, (ii) mild, or (iii) moderate/severe disease activity. Derivation of the SLE-DAS cut-offs for disease activity categories was performed using ROC curve analysis against this expert clinical classification. Performance of these SLE-DAS categories of disease activity was assessed as compared with: (i) expert classification (in Cochin cohort); (ii) British Isles Lupus Assessment Group (BILAG) index (in BLISS-76). An index-based and a Boolean definition of remission were tested applying decision trees, using CHAID (chi-square automatic interaction detection) algorithm and their performance estimated.

Results: We included 1190 SLE patients (221 in Padova, 150 in Cochin and 819 from BLISS-76 cohorts). In the derivation cohort, best SLE-DAS cut-off values for disease activity categories were: (i) remission, SLE-DAS≤2.08; (ii) mild activity, 2.08<SLE-DAS≤7.10; (iii) moderate/severe activity, SLE-DAS>7.10. Table 1 shows the performance of these SLE-DAS cut-offs. The SLE-DAS Boolean-based definition of remission (all SLE-DAS clinical items scores = 0 and prednisone ≤5mg/day) showed sensitivity and specificity of 100% in the derivation (Padova) and validation (Cochin) clinical cohorts. The SLE-DAS index-based definition of remission (SLE-DAS ≤2.08 and prednisone ≤5mg/day) presented sensitivity =100% and specificity =97.4% in the derivation and validation clinical cohorts. The SLE-DAS definitions of remission were fully substantiated by CHAID.

Table 1. Performance of SLE-DAS cut-offs for remission and disease activity categories compared to physician's classification and BILAG (n =1190).

	Disease activity category	Sensitivity (%)	Specificity (%)	Accuracy (%)
Derivation Padova Cohort	**Remission** (SLE-DAS≤2.08)	99.3	97.1	98.6
	Mild Disease Activity (2.08<SLE-DAS≤7.10)	74.2	98.9	95.5
	Moderate and Severe Disease Activity (SLE-DAS>7.10)	97.4	96.7	96.8
Validation Cochin Cohort	**Remission** (SLE-DAS≤2.08)	99.1	93.9	98.0
	Mild Disease Activity (2.08<SLE-DAS≤7.10)	82.6	99.2	96.7
	Moderate and Severe Disease Activity (SLE-DAS>7.10)	100.0	98.6	98.7
Validation BLISS-76	**Remission and Mild Disease Activity**§ ***vs.*** **Moderate and Severe Disease Activity**§§ (SLE-DAS≤7.10 *vs.* >7.10)	91.4	84.1	90.8

§ Remission/Mild: No BILAG B or A scores§§ Moderate/severe: ≥1 BILAG B or A scores

Conclusion: The SLE-DAS is an accurate and easy to use tool for defining clinical remission state and SLE disease activity categories, validated with both the expert assessment and BILAG.

REFERENCES:

[1] Jesus D, *et al.* Derivation and validation of the SLE Disease Activity Score (SLE-DAS): a new SLE continuous measure with high sensitivity for changes in disease activity. *Ann Rheum Dis* 2019;78:365-71.

Acknowledgements: The authors would like to thank GlaxoSmithKline (Uxbridge, UK) for granting access to the data from the BLISS-76 trial through the Clinical Study Data Request consortium.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1677

Difficult to treat RA: definitions and mechanisms

OP0298

ARE PATIENTS WITH PSORIATIC ARTHRITIS BEING TREATED OPTIMALLY ACROSS THE WORLD? DISPARITIES IN HEALTH CARE FOR PATIENTS WITH PSORIATIC ARTHRITIS ACROSS COUNTRIES WITH DIFFERENT GDP'S, AN ANALYSIS OF 429 PATIENTS FROM 13 COUNTRIES

F. Lucasson[1], U. Kiltz[2], J. D. D. Cañete[3], A. M. Orbai[4], Y. Y. Leung[5], P. Palominos[6], A. Balanescu[7], S. Meisalu[8], A. Ruyssen-Witrand[9], M. Soubrier[10], L. Eder[11], I. Gaydukova[12], U. Kalyoncu[13], P. Richette[14], M. De Wit[15], E. Lubrano[16], J. S. Smolen[17], L. C. Coates[18], R. Scrivo[19], E. Dernis[20], S. Aydin[21], M. E. Husni[22], L. Gossec[1]. *[1]Sorbonne Université and Hôpital Pitié Salpêtrière, Department of Rheumatology, Paris, France*; *[2]Ruhr University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*; *[3]Hospital Clínic, Barcelona, Department of Rheumatology, Barcelona, Spain*; *[4]Johns Hopkins University School of Medicine, Division of Rheumatology, Baltimore, MD, United States of America*; *[5]Singapore General Hospital, Department of Rheumatology and Immunology, Singapore, Singapore*; *[6]Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Serviço de Reumatologia, Porto Alegra, Brazil*; *[7]Sf Maria Hospital, University of Medicine and Pharmacy Carol Davila, Internal Medicine and Rheumatology, Bucharest, Romania*; *[8]East Tallinn Central Hospital, Department of Rheumatology, Tallinn, Estonia*; *[9] Toulouse University Hospital, UMR 1027, Inserm, Université Paul Sabatier Toulouse III, Rheumatology Unit, Toulouse, France*; *[10]CHU Gabriel Montpied, Service de rhumatologie, Clermont-Ferrand, France*; *[11] University of Toronto, Women's College Hospital and the Department of Medicine, Toronto, Canada*; *[12]North-Western State Medical University, Department of Therapy And Rheumatology, Saint Petersburg, Russian Federation*; *[13]Hacettepe University, Department of Rheumatology, Ankara, Turkey*; *[14]AP-HP Lariboisiere Hospital, Department of Rheumatology, Paris, France*; *[15]Amsterdam Public Health (APH), Amsterdam University Medical Centre, Department of Medical Humanities, Amsterdam, Netherlands*; *[16]Dipartimento di Medicina e Scienze della Salute 'Vincenzo Tiberio', University of Molise, Academic Rheumatology Unit, Campobasso, Italy*; *[17]Medical University of Vienna, Rheumatology, Vienna, Austria*; *[18]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; *[19]Sapienza Università di Roma, Rheumatology Unit, Department of Internal Medicine and Medical Specialties, Roma, Italy*; *[20] Le Mans Central Hospital, Rheumatology Department, Le Mans, France*; *[21]University of Ottawa Faculty of Medicine, Ottawa Hospital Research Institute, Rheumatology, Ottawa, Canada*; *[22]Cleveland Clinic, Department of Rheumatologic and Immunologic Diseases, Cleveland, OH, United States of America*

Background: In psoriatic arthritis (PsA), EULAR recommendations are to aim for remission or low disease activity(1). Many treatments are now available, though some are costly and not widely available in all countries. Country of patient care, and in particular Gross Domestic Product (GDP) may be linked to PsA outcomes(2). Although patients with high disease activity are eligible for targeted therapies such as biologic disease-modifying anti-rheumatic drugs (bDMARDs), they may not be able to get the benefits from these efficacious treatments in all countries equally.

Objectives: The objective was to explore the rate of PsA patients with high to moderate disease activity, not receiving bDMARDs across countries, and to assess the consequences on functional incapacity.

Methods: This was a cross-sectional analysis of an observational study (ReFlap, NCT03119805)(3), which included adult patients with PsA with ≥ 2 years disease duration from 14 countries. One country was excluded from this analysis since only 7 patients were included. We explored the rate of patients with significant disease activity (i.e based on DAPSA > 14) and no ongoing bDMARD prescription. Countries of inclusion were analysed separately, and classified into tertiles by GDP/capita (lowest tertile: Brazil, Turkey, Russia, Romania, Estonia; middle tertile: Spain, Italy, UK, France; highest tertile: Canada, Germany, USA and Singapore). The rate of no bDMARDs - DAPSA > 14 patients was analysed by country and compared between the 3 tertiles of GDP/capita by parametric tests. Functional capacity (HAQ) was compared between no bDMARDs - DAPSA > 14 patients and the other patients (pooling patients with moderate or high disease activity with bDMARD, low disease activity and remission with or without bDMARD). There was no imputation of missing data.

Results: Of the 459 patients, 429 had complete data available and were analysed: mean age 52.3 (SD 12.6) years, mean disease duration 10.2 (SD 8.2) years, 215 (50.1%) males. The rate of no bDMARDs - DAPSA > 14 patients was 18.4% (76/414). The rate ranged from 7.4% (UK and Spain) to 40% (Russia): Figure 1. A link was seen with the country and the tertiles of countries according to GDP/capita, with higher rate of no bDMARDs - DAPSA > 14 patients in the lowest GDP/capita countries (28.8%, 15.3% and 14.3% in the 3 GDP/capita tertiles, respectively, p=0.005; Figure 1). Of note, 40/76 no bDMARDs - DAPSA > 14 patients received a treatment intensification during the visit. Among no bDMARDs - DAPSA > 14 patients, functional incapacity was higher than in the other patients, as expected (mean HAQ 0.96 (SD 0.64) vs 0.57 (SD 0.63), p<0.001).

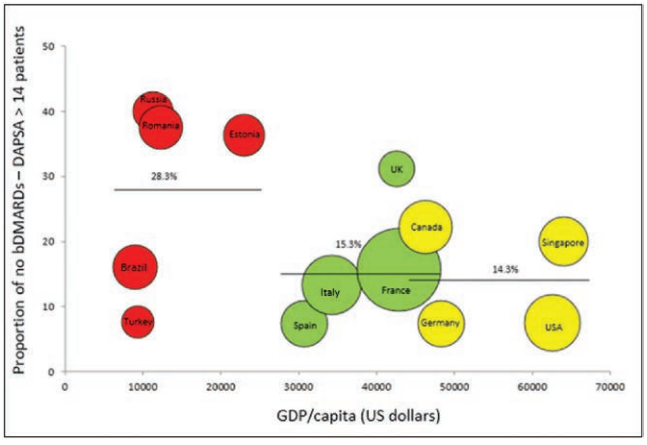


Figure 1. The size of the bubbles represent the number of patients per country (range, 13 to 89).The horizontal lines represent the mean proportion of patients with no bDMARDs – DAPSA > 14 for each tertiles of countries by GDP/capita.

Conclusion: In this exploratory comparison of disease patterns and treatments choices in 13 countries, we observed that more PsA patients with high or moderate disease activity and living in low GDP/capita countries were less likely to be treated with bDMARDs. As a consequence, no bDMARDs – DAPSA > 14 patients had worse functional incapacity. Equitable access to bDMARDs should be aimed for all patients regardless of their country of origin.

REFERENCES:

[1] Gossec L *et al*. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis. 2020 Jun;79(6):700-712.

[2] Gossec L *et al*. Are There Country Differences in Disease Activity and Life Impact of Psoriatic Arthritis? An Analysis of 436 Patients from 14 Countries [abstract]. Arthritis Rheumatol. 2019; 71 (suppl 10).

[3] Gorlier C *et al*. Comparing patient-perceived and physician-perceived remission and low disease activity in psoriatic arthritis: an analysis of 410 patients from 14 countries. Ann Rheum Dis. 2019 Feb;78(2):201-208.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1120

OP0299

IN RHEUMATOID ARTHRITIS PATIENTS HIGHER NUMBER OF COMORBIDITIES PREDICTS 6-MONTH INSUFFICIENT RESPONSE TO FIRST BIOLOGIC THERAPY AND EVENTUAL CATEGORIZATION OF THE DISEASE AS DIFFICULT-TO-TREAT

I. Flouri[1], A. Repa[1], N. Avgustidis[1], N. Kougkas[1], A. Eskitzis[1], A. Molla Ismail Sali[1], S. Pitsigavdaki[1], K. Pateromichelaki[1], E. Kalogiannaki[1], M. Terizaki[1], G. Bertsias[1], P. Sidiropoulos[1]. [1]*University Hospital of Heraklion, Crete, Rheumatology Department, Heraklion, Crete, Greece*

Background: Difficult-to-treat rheumatoid arthritis (D2T RA) was recently defined by a EULAR study group (1) and, as a disease category it is largely complicated and under-researched. Patient comorbidities may play a significant role in the response to therapy with biologic disease-modifying antirheumatic drugs (bDMARDs) and in the disease classification as D2T RA.
Objectives: To evaluate the impact of comorbidities [studied as total Comorbidities Count (CC) and rheumatic disease comorbidity index (RDCI)] on 6-month response to therapy with the first bDMARD in real-world clinical practice and on eventual disease designation as D2T RA.
Methods: Prospective study of all RA patients who start any bDMARD in a tertiary centre University Hospital after their consent. All patient comorbidities [among a list of approximately 100 pre-specified major comorbidities] are registered by treating physicians. Response to therapy was defined as achievement of low disease activity or remission (LDA/Rem) according to simplified disease activity index (SDAI) and health assessment questionnaire (HAQ) improvement of ≥ 0.25.
D2T RA patient group was defined according to the EULAR definition of D2T RA and was compared to: a/ all other patients and b/ to a sub-group of patients designated as "well-controlled RA" (follow-up ≥2 years and ≥2 visits in the last year in LDA/Rem).
Logistic regression models were used to adjust for the potential confounding of age, sex, disease duration, seropositivity, number of previous synthetic DMARDs, type of 1st bDMARD initiated (TNF inhibitor vs. non-TNF inhibitor), co-administered methotrexate and corticosteroids (yes/no), baseline SDAI and HAQ and year of therapy start.
Results: Analysis included 501 RA patients who received a total of 1098 bDMARD treatments. At 1st bDMARD treatment start, patients (women: 81%) had a median (IQR) age: 60 (51-68) years, disease duration: 5.4 (3-11) years, SDAI: 36 (28-46), HAQ: 1.0 (0.5-1.5), CC: 3 (2-6) και RDCI: 2 (0-3).
In adjusted analyses, total comorbidity count (CC) ≤1 (vs ≥ 2) was predicting LDA/Rem at 6 months of therapy [OR (95%CI) = 4.1 (1.5-11), p=0.005], while RDCI=0 (vs. ≥ 1) was predicting HAQ improvement ≥ 0.25 [OR (95% CI) = 2.6 (1.2-6.7), p=0.046].
During 2614 patient-years of follow-up, the disease in 98 patients could be classified as "D2T RA", while 127 patients had "well-controlled RA". Baseline independent predictors for D2T RA compared to all other patients were RDCI ≥ 1 (vs. 0) [OR = 3.3 (1.7-9.4), p = 0.024], female sex [OR =3.1 (1.01-9.5)] and age [OR = 0.97 (0.94-0.99)]. Multivariable analyses for predictors of "D2T" compared to "well-controlled" RA yielded similar results.
Conclusion: In RA patients starting the first bDMARD treatment, a higher number of comorbidities at baseline is an independent predictor of lower 6-month response to therapy and final disease classification as "difficult-to-treat" RA.
REFERENCES:
[1] Nagy G, Roodenrijs NM, Welsing PM, Kedves M, Hamar A, van der Goes MC, et al. EULAR definition of difficult-to-treat rheumatoid arthritis. Ann Rheum Dis. 2021 Jan;80(1):31–5.
Acknowledgements: Pancretan Health Association and Special Account for Research Grants (ELKE) – University of Crete.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4110

Quantitative imaging

OP0300

USE OF THERMOGRAPHY OF HANDS AND MACHINE LEARNING TO QUANTIFY JOINT INFLAMMATION AND ESTIMATE DAS28, CDAI, SDAI IN PATIENTS WITH RHEUMATOID ARTHRITIS

I. Morales-Ivorra[1,2], C. Gómez Vaquero[3], C. Moragues Pastor[3], J. M. Nolla[3], J. Narváez[3], J. A. Narvaez[4], D. Grados Canovas[1], M. A. Marin-López[2]. [1]*Hospital Igualada, Rheumatology, Igualada, Spain*; [2]*Singularity Biomed, R+D, Sant Cugat del Vallès, Spain*; [3]*Hospital Universitari de Bellvitge, Rheumatology, L' Hospitalet de Llobregat, Spain*; [4]*Hospital Universitari de Bellvitge, Radiodiagnosis, L' Hospitalet de Llobregat, Spain*

Background: Disease activity scores such as DAS28, CDAI and SDAI are used in the follow-up of patients with rheumatoid arthritis (RA). These scores include variables obtained on physical examination such as the tender joint count (TJC) and the swollen joint count (SJC). In telematic consultations, it is not possible to determine these variables by physical joint assessment. Therefore, it is necessary to develop new tools that allow detecting joint inflammation in places close to the patient. Thermography is a safe and fast technique that measures heat through infrared imaging. Inflammation of the joints causes an increase in temperature and can therefore be detect by thermography. Machine learning methods are highly accurate in analyzing medical images automatically.
Objectives: To develop an algorithm that, based on thermographic images of hands and machine learning, learn to quantify joint inflammation in patients with RA and estimate the DAS28, CDAI, SDAI by including the patient global health (PGH).
Methods: Multicenter observational study conducted in the rheumatology and radiology service of two hospitals. Patients with RA, psoriatic arthritis (PA), undifferentiated arthritis (UA) and arthritis of hands secondary to other diseases (SA) that attended the follow-up visits were recruited. Companions of patients and healthcare professionals were also recruited as healthy subjects (HS). In all cases, a thermographic image of the hands was taken using a Flir One Pro or a Thermal Expert TE-Q1 camera connected to a smartphone. Ultrasound (US) of both hands was performed in patients with RA, PA, UA and SA. The degree of synovial hypertrophy (SH) and power doppler (PD) was assessed for each joint (score from 0 to 3). Machine learning was used to quantify joint inflammation (SH+PD) from the thermal images using US as ground truth. RA patients whose thermal image was taken with the Thermal Expert TE-Q1 camera were used to evaluate the performance (test dataset). The other participants were used as training dataset. The TJC, SJC, PGH, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were also assessed in the test dataset. A linear regression was used to estimate the DAS28, CDAI and SDAI with the resultant joint inflammation quantification from the thermal images and the PGH. Performance was evaluated by means of Pearson's correlation coefficient. The study was approved by the Clinical Ethics and Research Committee of both centers.
Results: The total number of recruited subjects was 521 (422 for the training and 99 for the testing dataset). In the training dataset, the thermography of 296 patients was taken with the Flir One Pro (163 RA, 17 PA, 22 UA, 12 SA and 82 HS) and 126 with the Thermal Expert TE-Q1 camera (6 RA without clinical data, 20 PA, 7 UA, 23 SA and 70 HS).
We found higher correlations between joint inflammation variables (US and SJC) and thermography (0.48, p<0.01 for US and 0.48, p<0.01 for SJC) than between joint inflammation variables (US and SJC) and the PGH (0.29, p<0.01 for US and 0.35, p<0.01 for SJC). Thermography did not show statistically significant correlation with the PGH (0.14, p=0.164). The linear regression of thermography and the PGH showed strong correlation with the DAS28 (0.73, p<0.01), CDAI (0.84, p<0.01) and SDAI (0.82, p<0.01).
Conclusion: Thermography of hands and machine learning can effectively quantify joint inflammation and can be used in combination with the PGH to estimate disease activity scores. These results open an opportunity to develop tools that facilitate telematic consultations in patients with RA.
REFERENCES:
[1] Brenner M, Braun C, Oster M, Gulko PS. Thermal signature analysis as a novel method for evaluating inflammatory arthritis activity. Ann Rheum Dis. 2006;65(3):306-11
[2] Lynch CJ, Liston C. New machine-learning technologies for computer-aided diagnosis. Nat Med. 2018;24(9):1304-1305
[3] Tan YK, Hong C, Li H, Allen JC Jr, Thumboo J. Thermography in rheumatoid arthritis: a comparison with ultrasonography and clinical joint assessment. Clin Radiol. 2020;75(12):963
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1247

Let's consider Biologic Immunogenicity

OP0301 **RISK FACTORS FOR ANTI-INFLIXIMAB ANTIBODY FORMATION: RESULTS FROM THE RANDOMISED CONTROLLED NOR-DRUM A TRIAL**

M. K. Brun[1,2], G. L. Goll[1], K. K. Jørgensen[3], J. Sexton[1], J. E. Gehin[2,4], Ø. Sandanger[5], I. Olsen[6], R. A. Klaasen[4], D. J. Warren[4], C. Mørk[7], T. K. Kvien[1,2], J. Jahnsen[2,3], N. Bolstad[4], E. A. Haavardsholm[1,2], S. W. Syversen[1] on behalf of the NOR-DRUM Study Group. *[1]Diakonhjemmet Hospital, Division of Rheumatology and Research, Norway, Norway*; *[2]University of Oslo, Institute of Clinical Medicine, Oslo, Norway*; *[3]Akershus University Hospital, Department of Gastroenterology, Lørenskog, Norway*; *[4]Norwegian Radium Hospital, Department of Medical Biochemistry, Oslo, Norway*; *[5]Oslo University hospital, Section of Dermatology, Oslo, Norway*; *[6]Oslo University hospital, Department of Research Support for Clinical Trials, Oslo, Norway*; *[7]Akershus dermatologist center, Department of Dermatology, Lørenskog, Norway*

Background: Immunogenicity is related to loss of efficacy and safety to TNFα inhibitors and is frequently observed early in the treatment course. The highest rate of anti-drug antibody (ADAb) formation has been reported for infliximab (IFX). [1] Knowledge about risk factors for immunogenicity might contribute to better handling of this problem in clinical practice.

Objectives: To identify risk factors for ADAb formation during the early phase of IFX treatment.

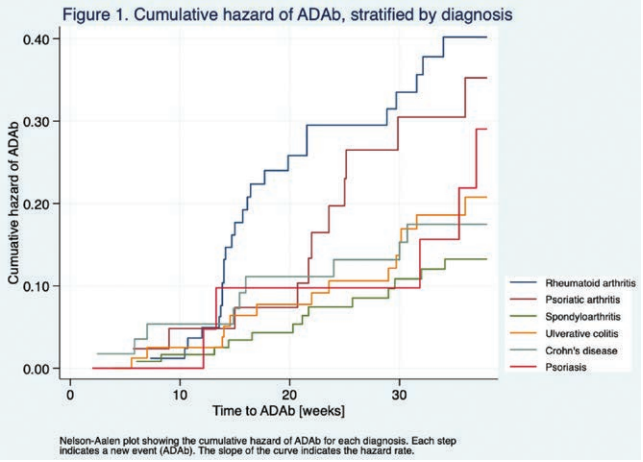
Methods: 411 patients with immune-mediated inflammatory diseases (84 rheumatoid arthritis (RA), 119 spondyloarthritis (SpA), 45 psoriatic arthritis, 83 ulcerative colitis, 58 Crohn's disease and 22 psoriasis) initiating IFX treatment were included in the 38-week NOR-DRUM A trial and randomised 1:1 to therapeutic drug monitoring or standard IFX therapy.[2] The primary endpoint was clinical remission at week 30. Serum (s) IFX levels and ADAb were measured at each infusion by in-house assays; time-resolved fluorometric assay for sIFX and inhibition assay for ADAb.[2] In this sub-study, possible risk factors for ADAb formation including demographic variables, diagnosis, comedication, disease activity, IFX dose, sIFX and drug holidays, were assessed using logistic regression. Variables with a p-value <0.25 in univariate analyses were further examined in multivariate analyses adjusting for potential confounders (diagnosis, disease activity, age and gender).

Results: 410 of 411 patients had at least one measurement of sIFX and were included in the present analyses. 76% of patients were biologic-naive and 45% (18% of RA patients) used IFX as monotherapy. Patients received a mean IFX dose of 3.2-5.9 mg/kg (RA 3.2 mg/kg). ADAb were detected in 78 (19%) patients. The Table 1 shows variables with a significant association to ADAb development. Analyses revealed an increased risk of ADAb development in patients with RA (Odds ratio (OR) 2.1, 95% confidence interval (CI) 1.1-3.9), while SpA had a lower risk (OR 0.5, CI 0.2-0.9) compared to the other diagnoses. These findings were consistent in both univariate- and multivariate analyses (Table 1). Figure 1 shows the cumulative hazard for ADAb development according to diagnosis. Other risk factors for ADAb (Table 1) were smoking (OR 1.8, CI 1.0-3.3) and drug holidays of more than 12 weeks (OR 4.7, CI 1.2-18.3). Additionally, the risk of ADAb increased with higher disease activity (OR 1.5, CI 1.0-2.3) and lower sIFX levels (0.7, 0.6-0.8). Patients co-treated with methotrexate (OR 0.4, CI 0.2-0.9) or thiopurines (OR 0.3, CI 0.1-0.8), or having one or more IFX dose increments (OR 0.4, CI 0.3-0.8), had a reduced risk of immunogenicity.

Table 1. Risk factors for ADAb. Results from logistic regression analyses

	Univariate analyses		Multivariate analyses (Adjusted for diagnosis, disease activity, age and gender)	
	OR	CI	OR	CI
RA	2.2**	[1.3,3.8]	2.1*	[1.1,3.9]
SpA	0.4**	[0.2,0.8]	0.5*	[0.2,0.9]
Methotrexate	1.1	[0.7,1.9]	0.4*	[0.2,0.9]
Thiopurine	0.3*	[0.1,0.9]	0.3*	[0.1,0.8]
Current or former smoking	2.2**	[1.3,3.8]	1.8*	[1.0,3.3]
Mean sIFX	0.7***	[0.6,0.8]	0.7***	[0.6,0.8]
>12 weeks between infusions	4.5*	[1.3,16.0]	4.7*	[1.2,18.3]
IFX dose increment	0.5*	[0.3,0.9]	0.4**	[0.3,0.8]
Mean DAS28 (RA and PsA)	1.5*	[1.0,2.1]	1.5*	[1.0,2.3]
Mean ESR	1.1***	[1.0,1.1]	1.1***	[1.0,1.1]
Mean CRP	1.1**	[1.0,1.1]	1.1**	[1.0,1.1]

* p<0.05, ** p<0.01, *** p<0.001Only variables with a p-value <0.05 are shown. Non-significant variables include other demographic variables and IFX dose.



Conclusion: This study identified smoking, drug holidays, high disease activity, IFX monotherapy and low sIFX levels as risk factors for ADAb development. Of particular interest, we found that RA patients had significantly increased risk of ADAb compared to the other immune-mediated inflammatory diseases. Whether this novel finding reflects different underlying disease mechanisms or the fact that RA patients receive a lower IFX dose, is not known and needs to be further explored.

REFERENCES:

[1] Thomas SS et al. BioDrugs 2015;29(4):241-58 [2] Syversen SW et al. Trials 2020 6;21(1):13

Disclosure of Interests: Marthe Kirksæther Brun: None declared, Guro Løvik Goll Speakers bureau: Pfizer, AbbVie, Boehringer Ingelheim, Roche, Orion pharma, Sandoz and Novartis, Kristin Kaasen Jørgensen Speakers bureau: Celltrion, AOP Orphan Pharmaceuticals and Norgine, Joe Sexton: None declared, Johanna Elin Gehin Speakers bureau: Roche, Øystein Sandanger: None declared, Inge Olsen: None declared, Rolf Anton Klaasen: None declared, David J Warren: None declared, Cato Mørk Speakers bureau: Novartis Norge AS, LEO Pharma AS, ACO Hud Norge AS, Cellgene AS, Abbvie, Galderma Nordic and UCB, Tore K. Kvien Speakers bureau: TAmgen, Celltrion, Egis, Evapharma, Ewopharma, Hikma, Oktal, Sandoz and Sanofi, Consultant of: AbbVie, Amgen, Biogen, Celltrion, Eli Lilly, Gilead, Mylan, Novartis, Pfizer, Sandoz and Sanofi, Grant/research support from: Research funding to Diakonhjemmet Hospital from AbbVie, Amgen, BMS, MSD, Pfizer and UCB, Jørgen Jahnsen: None declared, Nils Bolstad Speakers bureau: Roche Pharmaceuticals and Novartis, Consultant of: Janssen, Espen A Haavardsholm Speakers bureau: Pfizer, AbbVie, Celgene, Novartis, Janssen, Gilead, Eli-Lilly and UCB, Silje Watterdal Syversen Speakers bureau: Thermo Fisher.

DOI: 10.1136/annrheumdis-2021-eular.1380

Context matters: Placebo and nocebo effects for pain management

OP0302-HPR **IDENTIFYING THE CONTEXTUAL FACTORS IN THE PATIENT-PRACTITIONER ENCOUNTER THAT HAVE THERAPEUTIC EFFECT: A SYSTEMATIC REVIEW AND META-ANALYSIS**

A. Ismail[1,2], M. Hall[3,4], K. Yaseen[2,3], M. Doherty[1,4,5], W. Zhang[4,5,6]. *[1]University of Nottingham, Academic Rheumatology Department, Division of Rheumatology, Orthopaedics and Dermatology, School of Medicine, Nottingham, United Kingdom*; *[2]King Abdulaziz University, Faculty of Medical Rehabilitation Sciences, Jeddah, Saudi Arabia*; *[3]University of Nottingham, Division of Physiotherapy School of Health Sciences, Nottingham, United Kingdom*; *[4]University of Nottingham, Arthritis Research UK Pain Centre, Nottingham, United Kingdom*; *[5]National Institute for Health Research, Nottingham Biomedical Research Centre, Nottingham, United Kingdom*; *[6]University of Nottingham, School of Medicine, Division of Rheumatology, Orthopaedics and Dermatology, Nottingham, United Kingdom*

Background: Placebo or contextual effect is an integral part of the treatment effect (1). The factors related to this effect are "contextual factors" (CFs) (2). CFs may be categorised into five groups as factors related to practitioner, patient, practitioner-patient interaction, treatment and therapeutic environment (3). Several CFs have demonstrated their therapeutic effect, whereas others not (4). The majority of musculoskeletal pain relief result from CFs (5). Identifying the key CFs may encourage health practitioners to optimize the contextual aspects of care.

Objectives: To identify the modifiable CFs that can improve clinical outcomes in published randomised controlled trials (RCTs).
Methods: A systematic search was carried out, up until April 18th 2019, on the following databases: MEDLINE via Ovid, EMBASE, AMED, PsycINFO and Cochrane library. RCTs comparing contextual enhanced interventions versus non-enhanced control in adults for any health conditions were searched. The outcomes included both self-reported outcomes and objectively measured outcomes. The effect size and 95%confidence interval were calculated using the standard mean difference. Risk of bias was evaluated using the modified Cochrane tool. The random effects model was used to pool the results.
Results: Of 3900 records generated from the systematic search, 15 trials (4615 participants) met the inclusion criteria, and 13 were included in this meta-analysis (Figure 1). Conditions studied included musculoskeletal [4], cardiovascular [2], irritable bowel syndrome [1], diabetes [1], asthma [1], GP or hospital patients [6]. Three CFs have been identified from these trials, including empathy, patient involvement and positive communication. All were found to be effective for patient experience i.e. satisfaction. Positive communication was also effective for symptoms but not objective outcomes (Table 1).

Table 1. Summary of results.

Outcome	Intervention	Number of studies (Number of participants)	SMD (95% CI)	I^2
Patient experience outcomes, e.g. satisfaction	Empathy	2 (137)	0.45 (0.11, 0.79)	42.2 %
	Patient involvement	4 (1596)	0.31 (0.21, 0.41)	93.0 %
	Positive communication	3 (793)	0.38 (0.24, 0.52)	93.9 %
Symptomatic outcomes, e.g. pain	Empathy	1 (221)	-0.18 (-0.45, 0.08)	0.0 %
	Patient involvement	1 (314)	-0.05 (-0.27, 0.17)	0.0 %
	Positive communication	3 (658)	0.20 (0.05, 0.35)	64.8 %
Objective outcomes, e.g. peak expiratory flow	Positive communication	2 (266)	0.10 (-0.14, 0.34)	66.6 %

Positive SMD favours intervention group. SMD= Standard mean difference, CI= Confidence interval, I^2= heterogeneity.

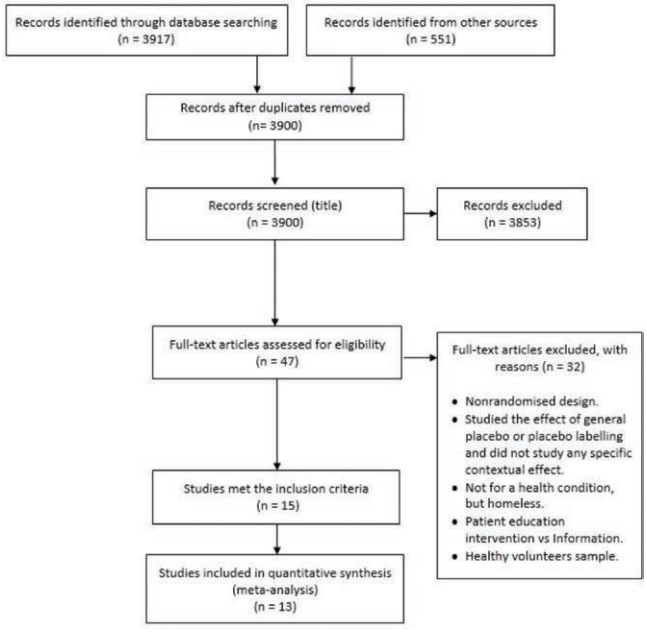


Figure 1. Summary of screening process.

Conclusion: This systematic review has identified three CFs (empathy, patient involvement and positive communication) that have therapeutic effects for different conditions in trials, especially for self-reported outcomes. More research is needed to examine the clinical outcomes of CFs and to understand the influence of health practitioners on disease processes.
REFERENCES:
[1] Zou K, Wong J, Abdullah N, Chen X, Smith T, Doherty M et al. Examination of overall treatment effect and the proportion attributable to contextual effect in osteoarthritis: meta-analysis of randomised controlled trials. Annals of the Rheumatic Diseases. 2016;75(11):1964-1970.
[2] Miller F, Kaptchuk T. The power of context: reconceptualizing the placebo effect. Journal of the Royal Society of Medicine. 2008;101(5):222-225.
[3] Di Blasi Z, Harkness E, Ernst E, Georgiou A, Kleijnen J. Influence of context effects on health outcomes: a systematic review. The Lancet. 2001;357(9258):757-762.
[4] Howick J, Moscrop A, Mebius A, R Fanshawe T, Lewith G, L Bishop F et al. Effects of empathic and positive communication in healthcare consultations: a systematic review and meta-analysis. Journal of the Royal Society of Medicine. 2018;111(7):240–252.
[5] Rossettini G, Carlino E, Testa M. Clinical relevance of contextual factors as triggers of placebo and nocebo effects in musculoskeletal pain. BMC Musculoskeletal Disorders. 2018;19(1).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.125

Myths and taboos around relationships: strategies for a sexy life

OP0303-HPR

IT IS NOT JUST ABOUT THE SEX: VIEWPOINTS OF DUTCH ADULT MEN WITH INFLAMMATORY ARTHRITIS REGARDING THE IMPACT OF THE DISEASE ON THEIR SEXUAL HEALTH

L. F. Perez-Garcia[1], E. Röder[1], H. Pastoor[2], H. Bolt[2], J. Van Exel[3], R. Dolhain[1].
[1]Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands; *[2]Erasmus University Medical Center, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Rotterdam, Netherlands*; *[3]Erasmus University Rotterdam, Erasmus School of Health Policy and Management, Rotterdam, Netherlands*

Background: Sexual health (SH) can be impaired in men with inflammatory arthritis (IA) (1). In addition to biological factors, such as inflammation, subjective factors such as personal beliefs can also impair SH. The Q methodology combines aspects of qualitative and quantitative approaches to systematically study subjectivity, and has been applied successfully in other medical fields.
Objectives: To describe the viewpoints of adult men with IA on the impact of IA on their SH using the Q methodology.
Methods: Men, 18 years and older, diagnosed with RA or JIA were invited by their rheumatologist. Participants ranked 34 opinion statements about potential impacts of IA on their SH on an agreement scale. A by-person factor analysis identified common patterns in the rankings. These patterns represent the different viewpoints among the men. Data from interviews, in which the men explained their ranking, was used to further interpret the viewpoints. A Q-methodology study usually consists of 30-40 participants.
Results: 30 men with IA were included. Their mean age was 43.2 (range 22–77) years. The analysis revealed three viewpoints:
1."I am satisfied with my sex life"
Men with viewpoint 1 experience no significant impact of IA on their SH. However, most men indicated that when their disease was active, IA had a negative impact on their SH.
2."Arthritis has a negative influence on my sex life"
Men with viewpoint 2 experience a dramatic impact, due to pain, fatigue and gloom. Their relationship worsened and they feel guilty towards their partner. Discussing their problems is not difficult.
3."I am keeping up appearances"
Men with viewpoint 3 experience SH impairment mainly as a result of pain. IA impairs them physically, makes them feel less of a man, less attractive and reduces their self-confidence. Due to problems with accepting their disease and communicating their problems, these men tend to hide their problems.
Conclusion: We identified 3 viewpoints on the impact of IA on male SH, 2 of them revealing a negative influence that goes beyond the physical act of sex. IA can also affect relationships, self-confidence and manhood. Future research will focus on identifying men with SH problems in the clinic and the best counseling approach.
REFERENCES:
[1] Perez-Garcia LF, Te Winkel B, Carrizales JP, Bramer W, Vorstenbosch S, van Puijenbroek E, et al. Sexual function and reproduction can be impaired in men with rheumatic diseases: A systematic review. Semin Arthritis Rheum. 2020;50(3):557-73.
Disclosure of Interests: Luis Fernando Perez-Garcia Consultant of: Galapagos, Esther Röder: None declared, Hester Pastoor: None declared, Hanneke Bolt: None declared, Job van Exel: None declared, Radboud Dolhain Speakers bureau: Abbvie, UCB, Genzyme, Consultant of: Galapagos, Grant/research support from: UCB.
DOI: 10.1136/annrheumdis-2021-eular.640

OP0304-PARE **DEVELOPMENT OF INTERACTIVE DECISION AID TOOL FOR MOTHERHOOD AND PARENTHOOD AMONG PATIENTS LIVING WITH AUTOIMMUNE RHEUMATIC DISEASES**

Y. El-Miedany[1,2], M. El Gaafary[3], N. El Aroussy[4], S. Bahlas[5], D. Palmer[6]. *[1]Canterbury Christ Church University, Rheumatology, Canterbury, United Kingdom*; *[2]King's College London, Education, London, United Kingdom*; *[3]Faculty of Medicine, Ain Shams University, Community and Public health, Cairo, Egypt*; *[4]Faculty of Medicine, Ain Shams University, Rheumatology and Rehabilitation, Cairo, Egypt*; *[5]King Abdulaziz University, Rheumatology, Jeddah, Saudi Arabia*; *[6]North Middlesex University Hospital, Rheumatology, London, United Kingdom*

Background: There are clear educational pregnancy-related needs for both women and men living with Autoimmune Rheumatic Diseases (ARDs) who seek specific advice from their health care providers. Most of the time those subjects would seek specific information regarding their chances of pregnancy, impact of the disease, as well as safety of their medications during pregnancy and breast feeding. They also require emotional and physical support as well as advice towards practical coping strategies to manage pain and disease flares particularly during the postnatal period.
Objectives: To evaluate the effectiveness of a new interactive pregnancy decision aid (DA) developed for both men and women living with inflammatory arthritis.
Methods: Driven by the Cochrane review of patient decision aids (DA) and the International Patient Decision Aids framework (IPDAS), which identify shared decision making (SDM) instrument as evidence-based tools designed to help people engage in deliberative management-related decision making by providing information on the options and outcomes relevant to health status. This project involved an overall three-phase SDM aid development. It has been set up for both men and women and included information on pregnancy, contraception and breast feeding. The first phase included the development of the decision tool and review by expert faculty composed of: decision experts, patient representatives, policy makers, and patients living with RA, PsA, AS and SLE. The second phase was a pilot testing of the tool in both online and paper format styles. The third phase involved an evaluation of the decision support tool and its impact on the patients. The DA adopted an interactive style with embedded video recordings (this was converted into text in the paper format). All the patient completed these questionnaires: the ReproKnow, Decisional Conflict Scale (DCS), Hospital Anxiety and Depression Scale (HADS), and Arthritis Self-Efficacy Scale (ASES) pre- and post-intervention. A control group of 92 patients (19 men and 71 women) managed according to the standard protocols was also included. Comprehensibility of the video recordings were also assessed using VAS (0-10).
Results: 126 patients shared in this work (101 women and 25 men). The patients who received the DA had an 81% (women) and 83% (men) increase in ReproKnow scores and a 76 % decrease in scores on the decisional conflict (DCS), compared to the control group (10 % and 11 % respectively); p< 0.001. There were no changes in the scores of depression and anxiety symptoms (p= 0.873) indicating no adverse psychological impact detected. There was no significant difference in terms of self-efficacy assessment p=0.481. The patients rated the comprehensibility of the video recording as high (9.4/10)
Conclusion: The DA which was developed to support pregnancy and breast feeding decision-making for patients with ARDs. The interactive SDM aid was found to be a simple, user-friendly tool which can be implemented in standard clinical practice. The interactive style made it more comprehensible to the patients. It is consistent with the IPDAS criteria. Results revealed its effectiveness in improving relevant knowledge and reducing decisional conflict without causing distress to the patients.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.513

Controversies on phenotypes in PsA

OP0305 **VALIDATION OF THE PSORIASIS EPIDEMIOLOGY SCREENING TOOL (PEST) AND THE NEW EARLY ARTHRITIS FOR PSORIATIC PATIENTS (EARP) IN PEDIATRIC POPULATION - PILOT STUDY**

Y. Butbul[1]. *[1]The Ruth and Bruce Rappaport Faculty of Medicine, Technion - Israel Institute of Technology; PEDIATRIC RHEUMATOLOGY UNIT, Haifa, Israel*

Background: Juvenile Psoriatic Arthritis (JPsA) is an inflammatory arthritis associated with irreversible joint damage among the pediatric population, which is associated with psoriasis in most cases.
While there are few validated screening tools for diagnosis of arthritis for adult patients with psoriasis, those screening tools were never evaluated in children.
Objectives: The aims of this study were to evaluate two screening tools among pediatric patients with psoriasis.
Methods: Thirty-nine patients with the diagnosis of psoriasis were administered two screening questionnaires: the new Early Arthritis for Psoriatic Patients (EARP) questionnaire and the Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire.
All patients were evaluated by a rheumatologist for the diagnosis of JPsA, and the accuracy of the two questionnaires compared.
Results: The 4/39 (10.1%) patients diagnosed with JPsA had a PEST questionnaire score of ≥ 3, compared to a median PEST score of the patients without the diagnosis of JPsA of 0 (0-2). Thus both the sensitivity and specificity of the PEST in diagnosing JPsA were 100%.
For the EARP questionnaire, 8/39 patients had a screening questionnaire score of ≥ 3, suggestive of JPsA, four were true positive, and four false positive. Thus, the sensitivity and specificity of EARP in diagnosing JPsA were 100% and 89%, respectively.
Conclusion: Both the PEST and EARP questionnaires were easy to use and had high sensitivity for pediatric population with psoriasis, however the PEST questionnaire had a higher specificity than the EARP.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4165

OP0306 **ETANERCEPT AND ADALIMUMAB IN THE TREATMENT OF JUVENILE PSORIATIC ARTHRITIS**

K. Aleksanyan[1], S. Chebysheva[1], O. Sukhovyova[1], E. Zholobova[1]. *[1]I.M. Sechenov First Moscow State Medical University, Clinical Institute of Child Health named after N.F. Filatov, Moscow, Russian Federation*

Background: Juvenile psoriatic arthritis (JPsA) accounts for 4 to 9% of children with juvenile arthritis (1). Biologics, particularly TNF-α inhibitors, have proved to be effective and safe for treatment of psoriatic arthritis in adults (2). However, no comprehensive evidence exists on the comparative effectiveness and safety of TNF-α inhibitors in the treatment of JPsA, which challenges a decision of what biologic should be prescribed to children with JPsA.
Objectives: To study the comparative effectiveness of etanercept and adalimumab in patients with JPsA with respect to both the articular and skin manifestations.
Methods: Our observational (2012-2019), parallel-group, open-label, single-centre cohort clinical study involved 34 patients (2-13 y/o) with JPsA who met Vancouver and I/E criteria and received etanercept SC (0.8 mg/kg QW, max 50 mg per week) or adalimumab SC (max 40 mg Q2W), both in combination with methotrexate (10-15 mg/m^2 QW). Intention-to-treat analysis was used to evaluate treatment efficacy at months 6, 12, and 18 after biologic therapy initiation. To assess articular manifestations of JPsA, we applied ACRpedi criteria; to estimate the surface area of involved skin and severity of psoriasis – the PASI score.
Results: We observed 34 patients with JPsA (2 to 13 y/o), who were initiated by biological therapy (etanercept [n=18 - group 1] and adalimumab [n=16 - group 2]) (Table 1, Figure 1).

Table 1. Clinical and demographic characteristics of patients with JPsA before biologic therapy initiation (n=34)

clinical and demographic indicators	Group 1 (Etanercept) M±δ / Me (Q1-Q3)	Group 2 (Adalimumab) M±δ / Me (Q1-Q3)
Girl/Boy Ratio	12:6 (2:1)	10:6 (1,7:1)
Average age, years	7,58 ± 3,7	5,8 ± 3
Duration of the disease, years	3,0 (1,4-6,6)	3,5 ± 2
Uveitis (n, %)	0	5 (31,3%)
ANA positivity (n, %)	2 (11%)	8 (50%)
RF positivity (%)	0	0
No. active joints	8,0 (5-16,5)	5,5 (3-8,5)
No. joints with LOM	9(5,75-18,25)	6 (3,5-10,5)
PGA of disease activity, mm	70 ± 15	65,9 ± 12,7
Parent's global assessment of the child's pain, VAS	71,5 (65-90)	72,5 ± 14
CHAQ	1,34 (1,1-1,68)	1,25 (0,93-1,44)
Psoriasis BSA, %	7,0 (4-13)	8 (3-13)
PASI score	5,7 (3-8,2)	9 (5-19)
ESR, mm/h	28 (20,75-40)	24,5 (21-32)

ANA - antinuclear antibodies, RF - rheumatoid factor, LOM - limitation of motion, PGA - physician's global assessment; VAS - visual analog scale, CHAQ - Childhood Health Assessment Questionnaire; BSA - body surface area; PASI - Psoriasis Area Severity Index, ESR - erythrocyte sedimentation rate; CRP - C-reactive protein.

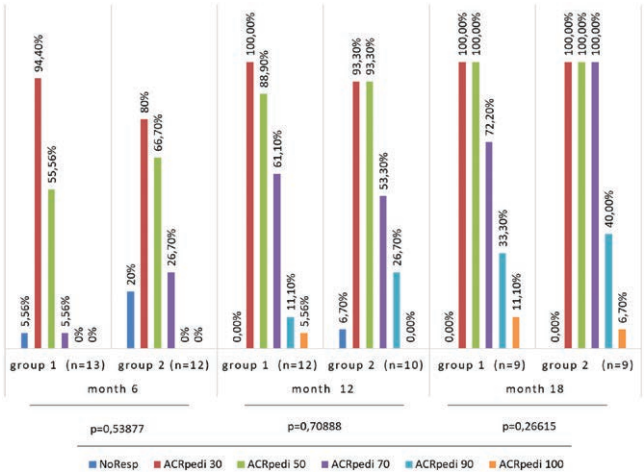


Figure 1. Comparative efficacy of etanercept and adalimumab in children with JPsA, according to the ACRpedi criteria at months 6, 12, and 18 after treatment initiation.No statistically significant difference in the efficacy of etanercept and adalimumab in patients with juvenile psoriatic arthritis was obtained, according to the ACRpedi criteria.The efficacy of biologic treatment on skin manifestations of JPsA was also evaluated (Figure 2).

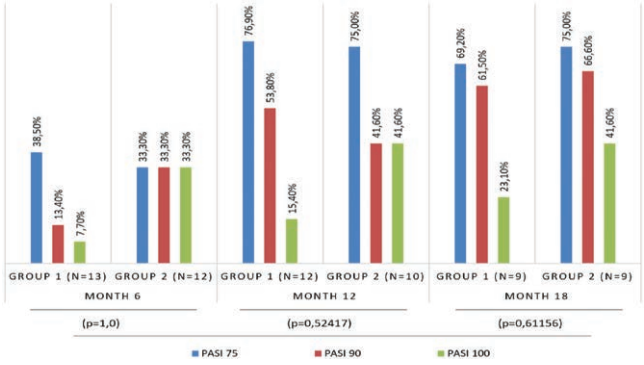


Figure 2. Comparative efficacy of etanercept and adalimumab in children with JPsA by PASI score at months 6, 12, and 18 after treatment initiation.Both TNF-α blockers (etanercept, adalimumab) showed similar efficacy for psoriasis in patients with JPsA, though response rate for psoriasis in adalimumab group was higher than in etanercept group.

Conclusion: Both TNF-α inhibitors (etanercept and adalimumab) proved to be effective in the treatment of arthritis and psoriasis in JPsA. There was no statistically significant difference in the effectiveness of etanercept and adalimumab in the treatment of JPsA in our cohort. Both biological agents can be successfully used to treat JPsA.

REFERENCES:

[1] Beukelman T., et al. The new Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry: design, rationale, and characteristics of patients enrolled in the first 12 months. PediatrRheumatol Online J. 2017;15(1):30

[2] Ruyssen-Witrand A., et al. Efficacy and safety of biologics in psoriatic arthritis: a systematic literature review and network meta-analysis. RMD Open. 2020;6(1):e001117

Disclosure of Interests: Karina Aleksanyan: None declared, Svetlana Chebysheva: None declared, Olga Sukhovyova: None declared, Elena Zholobova Speakers bureau: Pfizer, AbbVie, Novartis, Roche.

DOI: 10.1136/annrheumdis-2021-eular.2827

Pharmacology and Microbiota

OP0307

GUT MICROBIOTA AND ITS RELEVANCE TO PERIPHERAL LYMPHOCYTE SUBPOPULATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

T. Cheng[1], X. Wang[1], S. X. Zhang[1], J. Yang[2], C. Zhao[3], Y. Wang[1], J. An[1], J. Chen[1]. [1]*The Second Hospital of Shanxi Medical University / Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [2]*The Central Hospital of Xinghualing District, Department of Rheumatology, Taiyuan, China*; [3]*Xi'an International Medical Center Hospital, Department of Rheumatology, Taiyuan, China*

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with disturbance of lymphocyte subpopulations[1]. Growing experimental and clinical evidence suggests that chronic inflammatory response induced by gut microbiome critically contribute to the development of SLE[2 3].

Objectives: To investigate the characteristics of gut microbiome and the associations between flora and peripheral lymphocyte subpopulations in SLE patients.

Methods: A total of 19 SLE patients who fulfilled the 2019 American college of Rheumatology (ACR) and European League Against Rheumatism (EULAR) classification criteria and 16 age- and sex- matched healthy controls (HC) were enrolled in this study. The peripheral T lymphocyte subsets of these participants were assessed by flow cytometry and the gut microbiota were investigated via 16s rRNA. Indicators of disease activity such as erythrocyte sedimentation rate (ESR), complement C3 and C4 were recorded at the same time. Mann-Whitney U test was applied to compare T lymphocyte subsets between SLE patients and HC. Spearman analysis was used for calculating correlation between T subsets and highly expressed differential flora as well as their correlation with disease activity indicators. All *P*-values reported herein were two-tailed and *P*-value<0.05 was taken as statistically significant.

Results: SLE patients had higher proportions of Th17 cells (*P*=0.020) and γδT cells (*P*=0.018) but lower levels of Treg cells (*P*=0.001), Tfh cells (*P*=0.018) and Naïve $CD4^+$T cells (*P*=0.004) (Figure 1a-e). The diversity and relative abundance of intestinal flora in patients with SLE were significantly different from those in HCs. Detailly, the α-diversity was decreased in SLE (*P*<0.05) (Figure 2a-c). Compared with HC, 11 species of flora were discovered to be distinctly different(*P*<0.05) (Figure 2d-e). Moreover, there was a significant positive correlation between Treg levels and *Ruminococcus2* (*P*=0.042), Th17 and *Megamonas* (*P*=0.009), γδT and *Streptococcus* (*P*=0.004) as well as *Megamonas* (*P*=0.003), Tfh and *Bacteroides* (*P*=0.040). Whereas Th1 levels and *Bifidobacterium* were negatively correlated in these participants (*P*=0.005). As for clinical disease measures, there were negative correlations not only between ESR and Treg

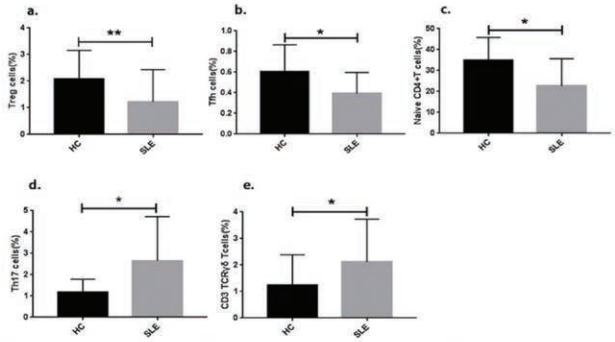


Figure 1(**a-e**) Comparison of T lymphocyte subsets in peripheral blood between healthy controls and SLE patients.

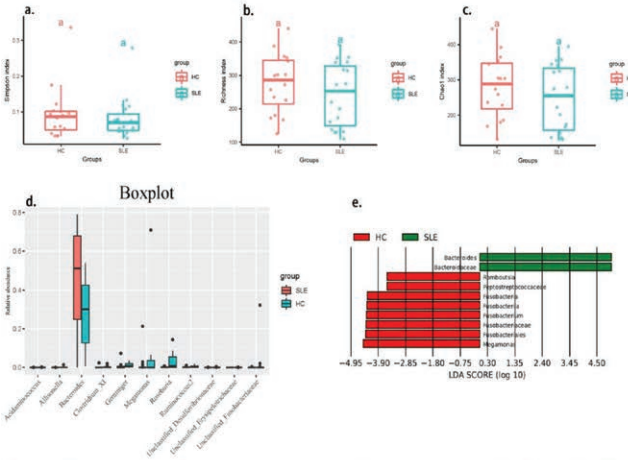


Figure 2(**a-e**) Variation of gut microbiota in SLE patients compared with HC and the LDA score of highly expressed differential flora. *P < 0.05, **P < 0.01, ***P < 0.001.

cells (*P*=0.031) but also C4 and the amount of *Unclassified Ruminococcaceae* (*P*=0.032).

Conclusion: Abnormality of T cell subsets, especially the level of Naïve CD4$^+$T, γδT, Tfh, Treg, and Th17 cells contributes to the occurrence and progression of SLE, which may be related to the disturbance of gut microbiota. Therefore it is necessary to attach importance to the alteration of gut microbiota to prevent the outbreak of inflammation and maybe they can be identified as biomarkers predicting disease activity.

REFERENCES:

[1] Katsuyama T, Tsokos GC, Moulton VR. Aberrant T Cell Signaling and Subsets in Systemic Lupus Erythematosus. *Front Immunol* 2018;9:1088. doi: 10.3389/fimmu.2018.01088 [published Online First: 2018/06/06]

[2] López P, de Paz B, Rodríguez-Carrio J, et al. Th17 responses and natural IgM antibodies are related to gut microbiota composition in systemic lupus erythematosus patients. *Sci Rep* 2016;6:24072. doi: 10.1038/srep24072 [published Online First: 2016/04/06]

[3] Esmaeili SA, Mahmoudi M, Momtazi AA, et al. Tolerogenic probiotics: potential immunoregulators in Systemic Lupus Erythematosus. *J Cell Physiol* 2017;232(8):1994-2007. doi: 10.1002/jcp.25748 [published Online First: 2016/12/21]

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3021

What can we learn from the tissue

OP0308 SENESCENT PROGENITOR CELLS IN THE SKIN OF LUPUS PATIENTS

X. Wang[1], G. Diercks[2], W. Lambers[1], J. Westra[1], H. Bootsma[1], F. G. M. Kroese[1], K. De Leeuw[1], S. A. Pringle[1]. *[1]UMCG, Rheumatology and Clinical Immunology, Groningen, Netherlands*; *[2]UMCG, Department of Pathology, Groningen, Netherlands*

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease, which is characterized by skin lesions, amongst other symptoms. These lesions (chronic discoid lupus erythematosus (CDLE) and subacute cutaneous lupus erythematosus (SCLE)) feature lymphocytic infiltration close to basal layer of the epidermis (i.e. the location of the epidermal progenitor cells), namely the epidermal dermal junction (EDJ) area. Epidermal progenitor cells maintain the homeostasis of the skin through their proliferation and differentiation into keratinocytes. In fast turnover tissues, like the skin, a population of 'transient amplifying cells' (TA cells), additionally facilitates generation of enough daughter cells to maintain skin homeostasis. These cells are located in an upper layer (suprabasal layer) of the epidermis, next to the basal layer. Senescence is an irreversible and locally spreading phenomenon that induces permanent cell cycle arrest.

Objectives: To evaluate expression of senescence markers p16 and p21 in the epidermal progenitor and TA niches in patients with SCLE and CDLE. This was compared to a panel of other dermatological conditions with and without infiltration close to EDJ, as disease controls, and to control skin tissue.

Methods: Age-matched skin lesions from patients with SCLE (n=12), CDLE (n=8), other conditions with EDJ infiltration (e.g. lichen planus, n=22), and dermatoses without EDJ infiltration (e.g. eczema, n=27), and non-lesion control biopsies (n=3) from SLE patients were employed. p16 and p21 expression in the progenitor niche (basal layer) and TA cell niche (suprabasal layer), and the whole epidermis of skin lesions biopsies were examined by immunohistochemistry.

Results: In healthy skin biopsies, 0 ± 0 SEM p16$^+$ cells/mm2 in the progenitor niche and 5 ± 4 SEM p21$^+$ cells/mm2 in TA niche were observed. In skin lesions from patients with CDLE and SCLE, significantly more p16$^+$ cells in the progenitor cell niche (45 ± 14 SEM/mm2) and p21$^+$ cells (182 ± 38 SEM/mm2) in TA niches were detected, compared to control biopsies ($p < 0.05$), and compared to those dermatoses without EDJ infiltration (p16$^+$ 11 ± 3 SEM/mm2, p21$^+$ 86 ± 28 SEM/mm2, $p < 0.05$, Figure 1). p16 and p21 expression in CDLE and SCLE lesions did not significantly differ from other dermatoses with EDJ infiltration ($p>0.05$). Across all dermatoses analyzed, the number of p16$^+$ cells was significantly correlated with the number of p21$^+$ cells, both in the progenitor niche ($r=0.45$, $p<0.0001$) and TA niche ($r=0.47$, $p<0.0001$). p16$^+$ cells however were more frequently found in the progenitor cell niche, and p21$^+$ cells conversely in the TA cell niche ($p<0.0001$).

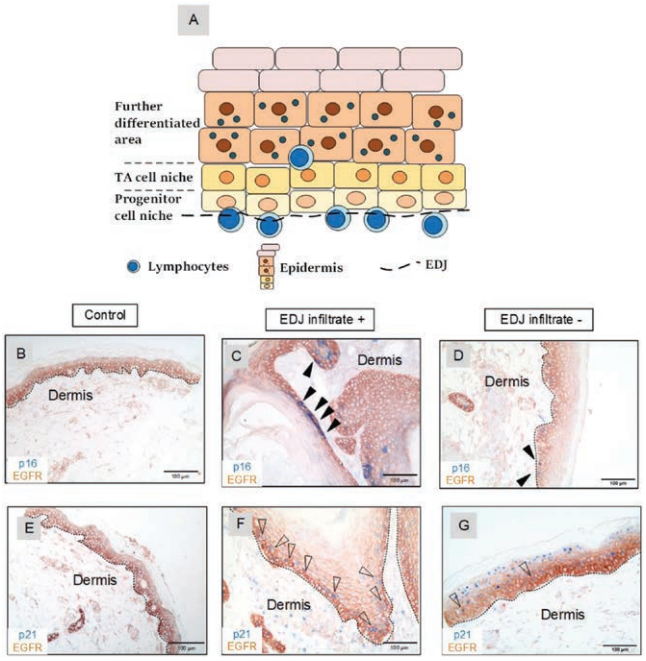


Figure 1. Increased p16$^+$ and p21$^+$ cells in the progenitor and TA niches in dermatoses with EDJ infiltration.A. Graphic illustration for the progenitor cell niche (the basal layer), the transient amplifying (TA, the supra-basal layer) cell niche, and the further differentiated area. B-D. Representative staining of p16 (blue) and epidermal growth factor receptor (EGFR, brown, an epithelial cell marker) in dermatoses with (CDLE) and without (PMLE) epidermal-dermal junction (EDJ) infiltration groups. Black arrowheads point to p16$^+$ progenitor epidermal cells. E-G. Representative staining of p21 (blue) and EGFR (brown) in dermatoses with (CDLE) and without (PMLE) EDJ infiltration groups. Hollow arrowheads point to p21$^+$ TA epidermal cells. The dashed line indicates the EDJ. CDLE: chronic discoid lupus erythematosus, PMLE: polymorphous light eruption.

Conclusion: In CDLE and SCLE, cutaneous manifestations of SLE, more progenitor and TA cells expressing markers of senescence were detected. This was in common with other dermatological conditions where lymphocytic infiltration is in close proximity to the progenitor and TA cell niche, namely in the EDJ. Increased senescence might infer the collapse of homeostasis in target (local) epidermis, which may influence tissue repair in the lesion. Elimination of senescent cells may therefore represent a viable therapeutic option to encourage timely and complete wound healing, in skin lesions of CDLE and SCLE patients.

Acknowledgements: This research was funded by a China Scholarship Council grant (201606220074), Dutch Arthritis Foundation Translational Research Grant (T015-052) and a Dutch Arthritis Foundation Long Term Project Grant (LLP-29).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1105

EULAR Projects in musculoskeletal imaging

OP0309 THE ROLE OF IMAGING TO GUIDE INTERVENTIONAL PROCEDURES IN RHEUMATIC AND MUSCULOSKELETAL DISEASES: A SYSTEMATIC LITERATURE REVIEW TO INFORM EULAR RECOMMENDATIONS

P. Bosch[1], F. Carubbi[2], C. A. Scirè[3], X. Baraliakos[4], L. Falzon[5], C. Dejaco[1,6], P. M. Machado[7]. *[1]Medical University of Graz, Rheumatology and Immunology, Graz, Austria*; *[2]University of L'Aquila, Medicine, Aquila, Italy*; *[3]University of Ferrara, Rheumatology, Ferrara, Italy*; *[4]Ruhr University Bochum, Reumatology, Bochum, Germany*; *[5]Northwell Health, Medical Research, New York, United States of America*; *[6]Hospital of Bruneck, Rheumatology Service, Bruneck, Italy*; *[7]Centre for Rheumatology, University College London, Neuromuscular Diseases, London, United Kingdom*

Background: Imaging guidance gives the opportunity to visualize a needle or other instrument when performing interventions on musculoskeletal sites in patients with rheumatic and musculoskeletal diseases (RMDs). Studies assessing the role of imaging guided procedures have been performed, however, no consensus has been made yet about when and which imaging techniques to use for these interventions.

Objectives: To inform a EULAR taskforce on the current literature on different imaging techniques, procedures and materials to guide interventions on musculoskeletal sites in RMD patients.
Methods: Prospective and retrospective studies published in English and comparing either palpation or imaging guided interventions in patients with RMDs were included. MEDLINE, EMBASE, the Cochrane Library and Epistemonikos were searched through October 2021. Risk of bias (RoB) was assessed using the Cochrane RoB tool for randomized trials version 2 (ROB2), the RoB tool for Non-Randomized Studies of Interventions (ROBINS-I) and the appraisal tool for cross-sectional studies (AXIS).
Results: Sixty-six studies, with moderate to high RoB, consisting of 49 randomized controlled trials, three prospective cohort studies and 14 retrospective studies were included.
Fifty-one studies compared one imaging technique against either another imaging technique, or palpation-guided interventions. Most of the studies were on peripheral joints (47/51), while data on joints of the axial skeleton were scare and heterogeneous (4/51). For peripheral joints, ultrasound (US) was the most studied imaging technique (49/51), followed by fluoroscopy (10/51). Results revealed a higher accuracy and safety (including procedural pain) of US or fluoroscopy compared to palpation- guided interventions. Data on other imaging techniques was scarce (computed tomography: n=3, arthroscopy: n=1) and the results heterogeneous. Results of studies comparing different imaging techniques (12/51) did not favor one imaging method over another.
Three studies comparing different materials used for imaging guided interventions were found (e.g. automatic vs manual syringes), showing little evidence for one material being superior to another one.
Fifteen studies were found comparing different imaging guided procedures (e.g. intraarticular vs periarticular injections). Overall, studies indicated an advantage of targeted vs. not targeted interventions (intraarticular vs periarticular or intraepineurial vs extraepineurial injections) concerning pain levels, while the comparison of different puncture sites to inject (e.g. ulnar vs midline carpal tunnel injection) was inconclusive.
Conclusion: Imaging guidance, especially US, performs favorably for interventions at the peripheral joints compared to palpation-guided interventions, concerning accuracy and safety. Data for the axial skeleton are scarce. Imaging guided targeted interventions may lead to better outcomes than non-targeted interventions.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3801

What's new: Latest advances in treatment and care in vasculitis and fibromyalgia

OP0310 **GENDER AND FIBROMYALGIA SEVERITY: REAL LIFE DATA FROM THE ITALIAN REGISTRY**

A. Batticciotto[1], F. Campanaro[1], F. Atzeni[2], A. Alciati[3], M. Dl Carlo[4], L. Bazzichi[5], M. Govoni[6], G. Biasi[7], M. Dl Franco[8], F. Mozzani[9], E. Gremese[10], L. Dagna[11], F. Fischetti[12], R. Giacomelli[13], S. Guiducci[14], G. Guggino[15], M. Bentivegna[16], R. Gerli[17], C. Salvarani[18], G. Bajocchi[19], M. Ghini[20], F. Iannone[21], V. Giorgi[22], S. Farah[4], S. Bonazza[6], S. Barbagli[7], C. Gioia[8], A. Capacci[10], G. Cavalli[11], F. Carubbi[23], F. Nacci[14], R. Ilenia[17], L. Sinigaglia[24], M. Cutolo[25], A. Cappelli[1], P. Sarzi-Puttini[22], F. Salaffi[4]. *[1]ASST dei Sette Laghi, Rheumatology Unit, Internal Medicine Department, Varese, Italy; [2]University of Messina, Rheumatology Unit, Internal Medicine Department, Messina, Italy; [3]Hermanas Hospitalarias, Villa San Benedetto Menni Hospital, Department of Clinical Neurosciences, Albese con Cassano, Como, Italy; [4]University Polytechnic of Marche, Rheumatological Clinic, Department of Clinical and Molecular Science, Jesi, Italy; [5]AOU Pisana, Rheumatology Unit, Pisa, Italy; [6]University of Ferrara and Azienda Ospedaliera-Universitaria di Ferrara, Rheumatology, Department of Medical Sciences, Ferrara, Italy; [7]University of Siena, Rheumatology Unit, Department of Medical Sciences, Surgery and Neurosciences, Siena, Italy; [8]Policlinico Umberto I, La Sapienza University of Rome, Department of Clinical Internal Medicine, Anesthesiological and Cardiovascular Sciences –Rheumatology Unit, Rome, Italy; [9]Azienda Ospedaliero-Universitaria di Parma, Internal Medicine and Rheumatology Unit, Parma, Italy; [10]Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Division of Rheumatology, Rome, Italy; [11]IRCCS San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), Milan, Italy; [12]University of Trieste, DDF of Rheumatology, ASUGI and Clinical University Department of Medical, Surgery and Health Sciences, Trieste, Italy; [13]University of Rome "Campus Biomedico"- School of Medicine Rome, Division of Rheumatology and Clinical Immunology, Rome, Italy; [14]University of Florence, Florence, Italy, Division of Rheumatology, Department of Experimental and Clinical Medicine, Florence, Italy; [15]University of Palermo, Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties, Palermo, Italy; [16]ASP 7, Scicli Hospital, Integrated Reference Center of Rheumatology, Ragusa, Italy; [17]Department of Medicine & Surgery, University of Perugia, Rheumatology Unit, Perugia, Italy; [18]University of Modena and Reggio Emilia, Azienda USL-IRCCS di Reggio Emilia, Rheumatology Unit, Reggio Emilia, Italy; [19]S. Maria Hospital - USL, IRCCS Institute, Rheumatology Unit, Reggio Emilia, Italy; [20]Azienda USL di Modena, Rheumatology Unit, Modena, Italy; [21]University of Bari, Rheumatology Unit, Department of Emergency Surgery and Organ Transpantations, Bari, Italy; [22]ASST Fatebenefratelli-Sacco, Milan; University School of Medicine, Rheumatology Unit, Internal Medicine Department, Milan, Italy; [23]School of Medicine, University of L'Aquila, Clinical Unit of Rheumatology, L'Aquila, Italy; [24]Italian Society of Rheumatology, Past President, Milan, Italy; [25]Department of Internal Medicine, University of Genoa, IRCCS San Martino, Laboratory of Experimental Rheumatology and Division of Clinical Rheumatology, Genoa, Italy*

Background: Fibromyalgia (FM) patients report chronic widespread pain, fatigue, cognitive difficulties and sleep disturbances, often associated with anxiety and/or depression (1). FM syndrome more frequently affects women and many papers describe gender-related differences in the perception, description and expression of pain (2), but up to now, the impact of gender on the clinical severity of FM is still a controversial topic.
Objectives: The aim of this study was to analyse the data from a web-based registry of FM patients in order to detect a relationship between gender and disease severity.
Methods: Adult patients with FM, diagnosed on the basis of the 2010/2011 American College of Rheumatology (ACR) diagnostic criteria (3), were recruited at 19 Italian rheumatology centres between November 2018 and April 2019. Those affected by other conditions that could interfere with the assessment of FM, e.g. psychiatric disorders, were excluded from the study. The severity of the disease was evaluated by validated FM-specific questionnaires: the revised Fibromyalgia Impact Questionnaire (FIQR) (4), the modified Fibromyalgia Assessment Status (ModFAS) questionnaire (5), and the Polysymptomatic Distress Scale (PDS) (6). The data obtained were collected in the Italian Fibromyalgia Registry, an online registry created with the support of the Italian Society of Rheumatology (SIR).
Results: We analyse data from 2.381 patients affected by FM, 2.184 females (91.7%) and 197 males. No significant differences in mean age, disease duration, or BMI between the two genders were reported. The women expressed greater disease burden as indicated by higher scores for each completed test: higher mean ModFAS score (25.23 ± 8.83 Vs 23.37 ± 9.22; p = 0.005), mean FIQR score (58.62 ± 23.22 Vs 51.68 ± 23.06; p <0.001), and mean PDS score (18.77 ± 7.34 Vs 17.19 ± 7.25; p = 0.004). Figure 1 shows the mean scores of each item of the FIQR divided by gender. Women reported significantly higher values on all the items of FIQR except three (feeling overwhelmed, FIQR-11; depression, FIQR-16; and anxiety, FIQR-18). It is interesting to note that men self-reported higher levels of depression (FIQR-16).

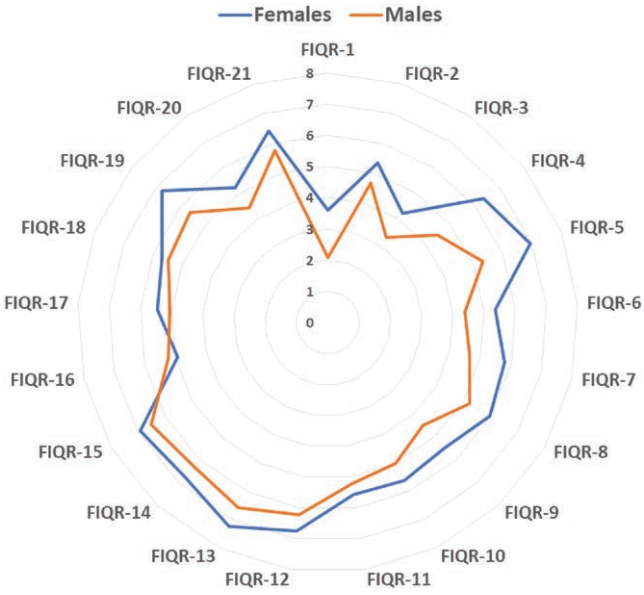


Figure 1. Mean scores for each FIQR item by gender.

Conclusion: Our findings demonstrate that women with FM are globally more impaired than men (even if some psychological aspects of the disease are comparable), thus reinforcing the idea that gender plays a role in symptoms and functional impairments associated with the disease.

REFERENCES:
[1] Clauw DJ. Fibromyalgia: a clinical review. JAMA. 2014;311:1547-55.
[2] Nascimento, et al. Gender role in pain perception and expression: an integrative review. BrJP. 2020; 3: 58-62
[3] Wolfe F, et al. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: A modification of the ACR preliminary diagnostic criteria for fibromyalgia. J Rheumatol 2011;38:1113–22.
[4] Burckhardt CS, et al. The fibromyalgia impact questionnaire: development and validation. J Rheumatol 1991;18:728–33.
[5] Salaffi F, et al. Diagnosis of fibromyalgia: comparison of 2011/2016 ACR and AAPT criteria and validation of the modified Fibromyalgia Assessment Status. Rheumatol 2020; 0:1-8.
[6] Wolfe F, et al. Fibromyalgia prevalence, somatic symptom reporting, and the dimensionality of polysymptomatic distress: results from a survey of the general population. Arthritis Care Res. 2013; 65:777–85
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3482

OP0311 **THE ROLE OF COMORBID PATHOLOGY IN THE PROGRESSIVE COURSE OF ANCA-ASSOCIATED SYSTEMIC VASCULITIS**

A. Chudinov[1], I. Belyaeva[2], V. Mazurov[2], O. Inamova[1]. [1]*Clinical rheumatological hospital #25, rheumatology, Saint-Peterburg, Russian Federation*; [2]*North-West State Medical University named after I.I. Mechnikov, rheumatology, Saint-Peterburg, Russian Federation*

Background: ANCA-associated systemic vasculitis (AAV) is characterized by a high incidence of complications and high damage index. Comorbid pathology at the onset can significantly worsen the prognosis AAV. The most significant comorbid conditions in patients with AAV are coronary artery disease, hypertension and dyslipidemia.
Objectives: The aim of this study was to determine the role of comorbid pathology in the progressive course in patients with AAV.
Methods: Patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) were observed during the first 3 years of the disease and included in this study between 2010 and 2018. At the onset of AAV 75% of patients had significant comorbidities (coronary artery disease, hypertension, dyslipidemia, chronic obstructive pulmonary disease, peptic ulcer, diabetes mellitus, autoimmune thyroiditis and others).
Results: In total 209 (165 [79%] female and mean age 51.8 ± 13.2 years) AAV patients (94 GPA; 46 MPA; and 69 EGPA) were included in the analysis. Formation of chronic kidney disease was significantly more frequent in the group of AAV patients with hypertension at the onset, than in patients without hypertension (respectively 37% and 23.6%, p=0.041). Development of thromboembolic complications was significantly more frequent in the group of AAV patients with coronary artery disease at the onset of AAV, than in patients without coronary artery disease (respectively 34% and 14.8%, p=0.034). Dyslipidemia also was risk factor for cardiovascular complications (OR – 3.81, 95% CI (2.43; 8.2) p=0.009). Presence of diabetes mellitus in the AAV onset was risk factor for infectious complications (OR – 1.77, 95% CI (1.14; 3.45) p=0.038).
Conclusion: Our study has shown that comorbid pathology increase risk of serious complications and can significantly worsen the prognosis AAV. Prevention of development of comorbid conditions and control of lipid levels, hypertension levels are necessary to prevent the formation of irreversible organ damage.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4094

Stress, inflammation & autoimmunity

OP0312 **METABOLIC REPROGRAMMING IN MEMORY CD4+ T CELLS IS ASSOCIATED WITH REACTIVE OXYGEN INDUCED IMMUNE CELL DYSFUNCTION DURING AGING**

Y. Chen[1,2], Y. Ye[3], H. Wu[4], P. L. Krauß[1,2], P. Löwe[1,2], M. Pfeiffenberger[1,2], L. Ehlers[1,2], A. Damerau[1,2], P. Hoff[1], F. Buttgereit[1,2], T. Gaber[1,2]. [1]*Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; [2]*German Rheumatism Research Centre (DRFZ) Berlin, a Leibniz Institute, Berlin, Germany*; [3]*Quanzhou First Hospital Affiliated to Fujian Medical University, Department of Gastroenterology, Quanzhou, China*; [4]*Julius-Maximilians Universität Würzburg, Institut für Systemimmunologie, Würzburg, Germany*

Background: Inflamm-aging is a chronic, sterile, low-grade inflammatory status, characterized by an increase of proinflammatory cytokines which participate in the development of most age-related diseases such as cancer, Alzheimer's disease, type 2 diabetes mellitus, stroke, cardiovascular diseases, and rheumatoid arthritis (RA). As cellular metabolism modulates T cell function, it can be assumed that metabolic changes accompany the differentiation of memory CD4+ T cells into senescent CD4+ T cell and contribute to memory CD4+ T cells dysfunction during aging.
Objectives: Therefore, we hypothesized that metabolic reprograming in memory CD4+ T cells might represent an essential factor promoting immune cell dysfunction during aging, thereby fuelling to the pathogenesis of age-related diseases including RA
Methods: To this end, we analysed memory CD4+ T cells isolated from PBMCs of young donors (20-32 years) and old donors (52-67 years) by using MACS™ technology. *Ex vivo* memory CD4+ T cells were analysed by Seahorse™ Technology to determine proton efflux rate (PER) as a measure of glycolysis (glycPER) and oxygen consumption rate (OCR) as a measure of mitochondrial respiration (mitoOCR). Cytokine expression and secretion was measured by flow cytometry and multiplex assay with and without Mitotempo an inhibitor of reactive oxygen species (ROS). Finally, TCR-stimulated memory CD4+ T cell proliferation was determined using CSFE and Ki-67 after 3 days and 4 days by flow cytometry. ROS and mitochondrial activity were analysed after 24 h using DCF-DA and CellROX Deep Red and Mitotracker by flow cytometry.
Results: In a quiescent state, memory $CD4^+$ T cells from elderly individuals demonstrated a decrease in basal glycolysis and compensatory glycolysis, and an increase in the ratio of basal mitochondrial oxygen consumption rate (mitoOCR) to glycolytic proton efflux rate (glycoPER) while their mitochondrial profile was equivalent to that of young donors while the amount of mitochondria was higher with no increase in steady-state ATP level. In this line and in comparison to the younger reference group, memory $CD4^+$ T cells from aged donors presented a greater spare respiratory capacity after TCR-activation and a marked increase in intracellular ROS production. Interestingly, we did not observe an impact of aging on memory $CD4^+$ T cell proliferation as determined by CFSE and Ki-67. Although the capacity of intracellular cytokine expression did not differ between the compared groups, the levels of secreted IFN-γ, IP-10, IL-6, IL-9, and MCAF were significantly higher in the supernatants of memory $CD4^+$ T cells taken from aged donors but were sensitive to ROS inhibition. .
Conclusion: These findings suggest that metabolic reprogramming in human memory $CD4^+$ T cells during aging results in an increased expression of proinflammatory cytokines as a result of ROS production and mitochondrial dysfunction. This process may culminate in T cell dysfunction and thus contribute to the pathogenesis of inflamm-aging and the development of age-related diseases such as rheumatoid arthritis (RA).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3937

Hyperinflammation and Covid19

OP0313 **PRELIMINARY CRITERIA FOR MACROPHAGE ACTIVATION SYNDROME ASSOCIATED WITH CORONAVIRUS DISEASE-19**

S. Amikishiyev[1], M. G. Gunver[2], M. Bektas[1], S. Aghamuradov[1], B. Ince[1], N. Koca3, E. S. Torun[1], N. Aliyeva[1], S. Sarı[1], C. Cetin[1], B. Ç. Yalçın Dulundu[1], R. Deniz[4], F. Kemik[4], B. F. Agargun[4], U. A. Gulseren[4], B. Besisik[4], O. Alkan[4], C. Bağrıaçık[4], Y. B. Tor[4], Y. Catma[4], G. Durak[5], S. Mese[6], A. Agacfidan[6], M. Kose[4], M. Erelel[7], A. A. Çağatay[8], S. Ş. Yavuz[8], S. K. Besısık[9], F. Esen[10], A. Gül[1]. [1]*Istanbul Faculty of Medicine, Istanbul University, Division of Rheumatology, Istanbul, Turkey*; [2]*Istanbul Faculty of Medicine, Istanbul University, Department of Biostatistics, Istanbul, Turkey*; [1]*Istanbul Faculty of Medicine, Istanbul University, Division of Rheumatology, Istanbul, Turkey*; [4]*Istanbul Faculty of Medicine, Istanbul University, Department of Internal Medicine, Istanbul, Turkey*; [5]*Istanbul Faculty of Medicine, Istanbul University, Department of Radiology, Istanbul, Turkey*; [6]*Istanbul Faculty of Medicine, Istanbul University, Department of Medical Microbiology, Division of Virology and Fundamental Immunology, Istanbul, Turkey*; [7]*Istanbul Faculty of Medicine, Istanbul University, Department of Chest Diseases, Istanbul, Turkey*; [8]*Istanbul Faculty of Medicine, Istanbul University, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey*; [9]*Istanbul Faculty of Medicine, Istanbul University, Division of Hematology and Therapeutic Apheresis Unit, Istanbul, Turkey*; [10]*Istanbul Faculty of Medicine, Istanbul University, Department of Anesthesiology, Istanbul, Turkey*

Background: COVID-19 runs a severe disease associated with acute respiratory distress syndrome in a subset of patients, and a hyperinflammatory response developing in the second week contributes to the worse outcome. Inflammatory

features are mostly compatible with macrophage activation syndrome (MAS) observed in other viral infections despite resulting in milder changes. Early detection and treatment of MAS may be associated with a better outcome. However, available criteria for MAS associated with other causes have not been helpful.
Objectives: To identify distinct features of MAS associated with COVID-19 using a large database enabling to assess of dynamic changes.
Methods: PCR-confirmed hospitalized COVID-19 patients followed between March and September 2020 constituted the discovery set. Patients considered to have findings of MAS by experienced physicians and given anakinra or tocilizumab were classified as the MAS group and the remaining patients as the non-MAS group. The MAS group was then re-grouped as the cases with exact-MAS and borderline-MAS cases by the study group. Clinical and laboratory data including the Ct values of the PCR test were obtained from the database, and dynamic changes were evaluated especially for the first 14 days of the hospitalization. The second set of 162 patients followed between September-December 2020 were used as the replication group to test the preliminary criteria. In the second set, hospitalization rules were changed, and all patients required oxygen support and received dexamethasone 6mg/day or equivalent glucocorticoids. Daily changes were calculated for the laboratory items in MAS, borderline, and non-MAS groups to see the days differentiating the groups, and ROC curves and lower and upper limits (10-90%) of the selected parameters were calculated to determine the cutoff values.
Results: A total of 769 PCR-confirmed hospitalized patients were analysed, and 77 of them were classified as MAS and 83 as borderline MAS patients. There was no statistically significant difference in the baseline viral loads of MAS patients compared to the non-MAS group according to the Ct values. Daily dynamic changes in the MAS group differed from the non-MAS group especially around the 6th day of hospitalization, and more than a twofold increase in ferritin and a 1.5-fold increase in D-dimer levels compared to the baseline values help to define the MAS group. Twelve items selected for the criteria are given in Table 1 below. The total score of 45 provided 79.6% sensitivity for the MAS (including borderline cases) and 81.3% specificity around days 5 and 6 in the discovery set, and a score of 60 increased the specificity to 94.9% despite a decrease in sensitivity to 40.8%. The same set provided a similar sensitivity (80.3%) in the replication, but a lower specificity (47.4-66% on days 6 to 9) due to a group of control patients with findings of MAS possibly masked by glucocorticoids.

Table 1. Preliminary Criteria for Macrophage Activation Syndrome Associated with Coronavirus Disease-19

1.Fever (>37.0 °C)
2.Ferritin concentration > 550 ng/mL
3.More than 2 times increase of ferritin concentration within 7 days of disease onset
4.Neutrophil count > 6000 cell/mm^3
5.Lymphopenia < 1000 cell/mm^3
6.Neutrophil/lymphocyte ratio > 6
7.D-dimer concentration > 1000 ng/ml
8.More than 50% increase of D-dimer concentration within 7 days of disease onset
9.CRP concetration > 50 mg/L
10.LDH concentration > 300 U/L
11.ALT or AST concentration > 50 U/L
12.Procalcitonin concentration < 1.2

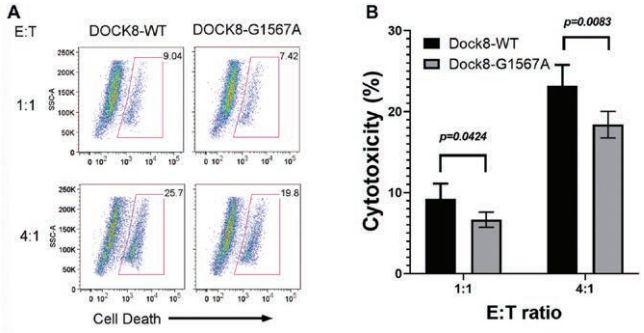
1 point for each positive item assessed on Days 5-7Score calculation: Total points / 12 x 100Possible MAS ≥45 and Definite MAS ≥60

Conclusion: This study defined a set of preliminary criteria using the most relevant items of MAS according to the dynamic changes in the parameters in a group of COVID-19 patients. A score of 45 would be helpful to define a possible MAS group with reasonable sensitivity and specificity to start necessary treatments as early as possible.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3113

OP0314 **DOCK8 MUTATIONS IN COVID-19 AND MIS-C CYTOKINE STORM SYNDROME**

R. Cron[1], M. Zhang[1], D. Absher[2], J. Bridges[1], A. Schnell[3], P. Bhatraju[4], A. Vagrecha[5], S. Lozinsky[6], S. Acharya[7], C. Levy[7], W. Chatham[3]. [1]*University of Alabama at Birmingham, Pediatrics, Birmingham, United States of America*; [2]*HudsonAlpha Institute for Biotechnology, Genomic Health Research, Huntsville, United States of America*; [3]*University of Alabama at Birmingham, Medicine, Birmingham, United States of America*; [4]*University of Washington, Medicine, Seattle, United States of America*; [5]*Hofstra University, Pediatrics, Hempstead, United States of America*; [6]*Hofstra University, Neurosurgery, Hampstead, United States of America*; [7]*Hofstra University, Pediatrics, Hampstead, United States of America*

Background: We recently identified *DOCK8* as a novel gene associated with cytokine storm syndrome (CSS)[1]. Heterozygous missense mutations in *DOCK8* diminish NK cell lytic function and contribute to increased pro-inflammatory cytokine production (CSS). CSS is a potential complication of COVID-19 with severe consequences[2]. Children are at risk of a SARS-CoV-2 post-infectious CSS, multisystem inflammatory syndrome in children (MIS-C)[3]. Host genetic factors associated with COVID-19 CSS and MIS-C CSS are unknown.
Objectives: The goals are to identify and functionally study rare mutations in *DOCK8* in patients with SARS-CoV-2 COVID-19 and MIS-C.
Methods: To date, 16 adult patients enrolled in a COVID-19 CSS clinical trial at UAB had whole genome sequencing. Four (25%) had rare heterozygous *DOCK8* mutations (3 missense, 1 intronic). A COVID-19 CSS adult patient in Seattle also had a *DOCK8* missense mutation. In addition, *DOCK8* missense mutations were identified in five children (UAB & Northwell) hospitalized with MIS-C. *DOCK8* mutations, or wild-type (WT) sequence controls, were introduced into human NK-92 cells by FOAMY virus transduction. WT and mutant DOCK8-expressing NK-92 cells were incubated with K562 target cells and compared for cytolysis and degranulation (CD107a).
Results: One COVID-19 patient *DOCK8* mutation (Gly523Arg) reduced NK cell degranulation by 30% and cytolysis by 23% (n=3) (Figure 1). Similar studies of 3 MIS-C patients with *DOCK8* missense mutations (Arg899Trp, Ala2Thr, Pro687Leu) revealed up to 31% reduced NK cell degranulation and 48% reduction in cytolysis by 3 distinct mutations (n=3). Two-way ANOVA analysis revealed statistically significant ($p<0.05$) differences in NK cell degranulation and lysis for four unique *DOCK8* mutations.



Conclusion: Heterozygous *DOCK8* missense mutations may contribute to severe COVID-19 and MIS-C CSS by partial dominant-negative effects yielding decreased NK cell cytolysis.
REFERENCES:
[1] Schulert GS, Cron RQ. The genetics of macrophage activation syndrome. *Genes Immun* 2020:**21**:169-181.
[2] Cron RQ, Chatham WW. The rheumatologist's role in COVID-19. *J Rheumatol* 2020:**47**:639-642.
[3] Reiff D, Mannion ML, Samuy N, Scalici P, Cron RQ. Distinguishing active pediatric COVID-19 from MIS-C. *Pediatr Rheumatol Online J, in press*.
Disclosure of Interests: Randy Cron Consultant of: SOBI, Novartis, Pfizer, Sironax, Grant/research support from: SOBI, Mingce Zhang: None declared, Remy Cron: None declared, Devin Absher: None declared, John Bridges: None declared, Amanda Schnell: None declared, Pavan Bhatraju: None declared, Anshul Vagrecha: None declared, Shannon Lozinsky: None declared, Suchitra Acharya: None declared, Carolyn Levy: None declared, Winn Chatham Grant/research support from: SOBI.
DOI: 10.1136/annrheumdis-2021-eular.1865

Metabolic pathways during the regulation of inflammation and immunity

OP0315 **EFFECTOR CD4 T CELLS REQUIRE SURVIVIN FOR REGULATION OF GLUCOSE METABOLISM AND IFNG PRODUCTION**

M. Erlandsson[1,2], K. M. Andersson[1], N. Oparina[1], S. Töyrä Silfverswärd[1], M. I. Bokarewa[1,2]. [1]*Gothenburg University, Rheumatology and Inflammation Research, Gothenburg, Sweden*; [2]*Sahlgrenska University Hospital, Rheumatology clinic, Göteborg, Sweden*

Background: Interferon-gamma (IFNg) producing effector T cells play the leading role in triggering and perpetuation of inflammation in rheumatoid arthritis. Inflammation leads to metabolic reprogramming of T cells and high energy consumption supporting proliferation and IFNg production. Being a part of chromosomal passenger complex, oncoprotein survivin is essential for cell proliferation. It has also been identified as a marker of severe therapy-resistant rheumatoid

arthritis. Thus, we aimed to explore the association between survivin and IFNg producing phenotype of CD4 T cells.
Objectives: We study if survivin mediates the glucose dependent mechanism of IFNg production in CD4 T cells.
Methods: CD4 cells were sorted from the peripheral blood of RA patients and healthy controls, activated with aCD3, cultured in presence of survivin inhibitor YM155 and subjected to RNA sequencing (Illumina, Life Science). IFNg levels in supernatants were measured by ELISA. To study glucose uptake in presence of YM155, CD4 cells were treated with IFNg+aCD3 overnight followed by 2NBD-glucose challenge for 30 min. Uptake of fluorescent 2NBD-glucose probe was measured by flow cytometry. Statistical analysis of RNAseq was performed in R-studio using the Bioconductor package DESeq2.
Results: Comparison of the whole-genome transcription profile of CD4 cells different by levels of BIRC5, coding for survivin, demonstrated that the BIRC5hi group expressed significantly higher levels of IFNg (mRNA, $p=10^{-26}$ and protein, $p=10^{-4}$). Also, BIRC5hi CD4 cells had higher expression of glucose transporter GLUT1 (SLC2A1, p=0.0064) and of glycolytic enzymes glucose-6-phosphate dehydrogenase (G6PD, $p=10^{-6}$), pyruvate kinase (PFKP, $p=10^{-6}$), and lactate dehydrogenase (LDHA, $p=10^{-14}$). On the contrary, expression of the key regulator of glycolysis 6-phosphofructo-2-kinase (PFKFB3) was significantly lower in the BIRC5hi group ($p=4.4x10^{-5}$). Notably, expression of glycolytic enzymes G6PD and PFKFB3 correlated strongly to IFNg (r=0.880 and -0.698, respectively), TBX21 (r=0.811 and -0.698) and perforin (r=0.781 and -0.698). To demonstrate functional relevance of the connection between BIRC5 and glucose metabolism, survivin was inhibited in CD4 cell cultures. Survivin inhibition resulted in significant increase of PFKFB3 ($p=7x10^{-6}$) and LDHA (p=0.0089), leading to inhibition of phosphoglycerate mutase PGAM1 and ATF citrate lyase ACLY (p=0.021 and p=0.0074, respectively), which dignify the restoration of aerobic glycolysis. Importantly, inhibition of survivin decreased 2NBD-glucose uptake by CD4 cells (p=0.031) and reduced expression of GLUT1 (p=0.034). These changes in glucose metabolism were followed by decreased IFNg production in supernatants (p=0.037).
Conclusion: The study demonstrates a strong connection between IFNg production and glucose metabolism in CD4 cells. Survivin emerges as an important regulator of glycolysis acting through expression of glycolytic enzymes and glucose transport.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2295

Let's work. Together.

OP0316

ASSOCIATION BETWEEN INDIVIDUAL AND COUNTRY-LEVEL SOCIOECONOMIC FACTORS AND WORK PARTICIPATION IN PERIPHERAL AND AXIAL SPONDYLOARTHRITIS: ANALYSIS OF THE ASAS PERSPA STUDY

S. S. Zhao[1], E. Nikiphorou[2], A. Boonen[3,4], C. López-Medina[5,6], M. Dougados[5,7], S. Ramiro[8,9]. [1]*University of Liverpool, Musculoskeletal Biology, Institute of Life Course and Medical Sciences, Liverpool, United Kingdom*; [2]*King's College London, Department of Rheumatology and Centre for Rheumatic Diseases, London, United Kingdom*; [3]*Maastricht University, Care and Public Health Research Institute (CAPHRI), Maastricht, Netherlands*; [4]*Academic Hospital Maastricht, Department of Internal Medicine, Division of Rheumatology, Maastricht, Netherlands*; [5]*Cochin Hospital, Université de Paris, Rheumatology Department, Paris, France*; [6]*University of Cordoba, Rheumatology Department, Reina Sofia Hospital, IMIBIC, Córdoba, Spain*; [7]*University of Paris, INSERM (U1153): Clinical Epidemiology and Biostatistics, Paris, France*; [8]*Leiden University Medical Center (LUMC), Department of Rheumatology, Leiden, Netherlands*; [9]*Zuyderland MC, Department of Rheumatology, Heerlen, Netherlands*

Background: Work outcomes in spondyloarthritis (SpA) have mostly been studied in axSpA, less in peripheral SpA (pSpA) or PsA. The ASAS-COMOSPA study showed that lower education, female gender and lower healthcare expenditures (HCE) are associated with lower odds of employment in SpA. However, it is unknown whether country-level factors or SpA phenotype (axSpA/pSpA/PsA) modify the effect of individual-level socioeconomic factors.
Objectives: To examine whether associations between socioeconomic factors and work outcomes differ across SpA phenotype and whether associations for individual-level socioeconomic factors are modified by country-level factors.
Methods: Working age patients (18-65 years) from the ASAS-perSpA (peripheral involvement in SpA) study were included. Associations between individual- (age, gender, education, marital status) and country-level socioeconomic factors (Human Development Index (HDI), HCE) with work outcomes (employment status (binary), absenteeism, presenteeism (tertiles)) were assessed using mixed-effects logistic and ordinal logistic models. Models were adjusted for confounders. Separate models for ASDAS, BASFI and BASDAI were created in turn due to collinearity. Effect modification by SpA phenotype and country-level factors was tested using interaction terms.
Results: A total of 3835 patients (mean age 42 years, 61% males) from 23 countries worldwide were included (66% axSpA, 10% pSpA, 23% PsA). Being employed was associated with gender (male vs female OR 2.5; 95%CI 1.9-3.2), education (university vs primary OR 3.7; 2.9-4.7) and being married (vs single OR 1.3; 1.04-1.6) (Table 1). University (vs primary) education was associated with lower odds of absenteeism (OR 0.7; 0.5-0.7) and presenteeism (OR 0.5; 0.3-0.7). Associations were not statistically different across SpA phenotypes. HCE was significantly associated with all work outcomes: employment (OR 2.5; 1.5-4.1), absenteeism (OR 0.6; 0.4-0.9) and presenteeism (OR 0.6; 0.3-0.9). HDI results were similar. Gender discrepancy in odds of employment was greater in countries with lower socioeconomic development; eg, males had 3.5 higher odds of employment than females in countries with low HCE, whereas the difference was 1.8 fold in high HCE countries.

Table 1. Effect of individual socio-economic factors on work outcomes.

		Employment status	Absenteeism	Presenteeism
		OR (95% CI)	OR (95% CI)	OR (95% CI)
N		3780	2218	2127
Age		1.43 (1.36,1.51)	1.00 (0.99,1.01)	1.00 (0.99,1.01)
Age^2		0.996 (0.995, 0.996)	NS - uni	NS - uni
Male (vs female)		2.48 (1.92,3.21)	1.22 (0.96,1.56)	0.97 (0.78,1.20)
Education	Primary	ref	ref	ref
	Secondary	1.86 (1.48,2.35)	0.69 (0.49,0.99)	0.69 (0.49,0.99)
	University	3.68 (2.87,4.72)	0.67 (0.47,0.96)	0.49 (0.34,0.69)
Marital status	Single	ref	ref	ref
	Married	1.27 (1.04,1.56)	0.95 (0.73,1.22)	0.98 (0.78,1.22)
	Divorced or Widowed	1.39 (0.98,1.97)	1.39 (0.88,2.18)	1.16 (0.74,1.82)
ASDAS		0.78 (0.72,0.84)	1.51 (1.33,1.72)	2.31 (2.04,2.61)
Fatigue		NS - multi	1.14 (1.09,1.21)	1.30 (1.24,1.36)
Depression		0.70 (0.59,0.82)	1.45 (1.15,1.82)	1.95 (1.59,2.39)
Fibromyalgia		NS - multi	1.62 (1.11,2.35)	1.58 (1.03,2.41)
BMI		NS - multi	0.99 (0.97,1.02)	NS - multi
Dactylitis		1.41 (1.12,1.76)	NS - uni	NS - uni
Uveitis		NS - multi	0.62 (0.46,0.84)	NS - uni
NSAIDs		NS - multi	1.53 (1.18,1.99)	1.32 (1.07,1.64)
bDMARDs		NS - multi	NS - uni	1.23 (1.01,1.51)

Models used ASDAS rather than BASDAI/BASFI, which are collinear. NS, not significant in the univariable or multivariable model.

Conclusion: Individual- (lower education) and country-level socioeconomic factors (lower healthcare expenditure) were both associated with (lower) work participation, independently of SpA phenotype. The disadvantageous effect of female gender on employment is particularly strong in countries with lower socioeconomic development. This highlights the need for wider societal interventions, such as improving education and healthcare investment, to improve work outcomes.
Disclosure of Interests: Sizheng Steven Zhao: None declared, Elena Nikiphorou Speakers bureau: Pfizer, Lilly, AbbVie, Annelies Boonen Consultant of: Yes, Grant/research support from: Yes, Clementina López-Medina: None declared, Maxime Dougados: None declared, Sofia Ramiro Speakers bureau: Lilly, MSD, Novartis, UCB, Consultant of: AbbVie, Lilly, MSD, Novartis, UCB, Sanofi, Grant/research support from: MSD.
DOI: 10.1136/annrheumdis-2021-eular.486

OP0317-PARE

THE CONTEMPORARY WORK-RELATED BURDEN OF DISEASE FOR PEOPLE WITH RHEUMATIC DISEASES IN GREECE

K. Koutsogianni[1], F. Asimakopoulou[2], E. Repa[3], I. Papadakis[4], M. Chatziioannou[5], A. Verikiou[2], M. Chatzigeorgiou[6], P. Pratsidou-Gertsi[7], I. Chatzikrystallis[8]. [1]*PanHellenic Federation ReuMAzein, PanHellenic Federation ReuMAzein, Heraklion Crete, Greece*; [2]*PanHellenic Federation ReuMAzein, Patients' Association with Rheumatic Diseases of Patra, Patra, Greece*; [3]*PanHellenic Federation ReuMAZein, Parents' and Caregivers' Association of Children With Chronic Rheumatic Diseases,Thessaloniki, Greece*; [4]*PanHellenic Federation ReuMAzein,The arthritis foundation of Crete, Heraklion Crete, Greece*; [5]*PanHellenic Federation ReuMAZein,The arthritis foundation of Crete, Heraklion Crete, Greece*; [6]*PanHellenic Federation ReuMAzein, PanHellenic Society of Patients with Autoimmune Rheumatic Diseases,Thessaloniki, Greece*; [7]*PanHellenic Federation ReuMAZein, Friends Association of Children With Chronic Rheumatic Diseases,Thessaloniki, Greece*; [8]*PanHellenic Federation ReuMAZein, PanHellenic Federation ReuMAZein,Thessaloniki, Greece*

Background: EULAR recommendations emphasize the importance of suitable working conditions for people with Rheumatic diseases (RD). Thus, opportunities and choices at work need to be increased for people with rheumatic diseases. Conversely, the COVID-19 pandemic has challenged the working population and particularly those with chronic conditions, such as those with RD. However, there is still a lack of reliable data.
Objectives: To depict contemporary real-life data regarding the work-related burden of disease among Greek patients with RD. To develop a White Paper with proposals to the State in order to facilitate people with rheumatic diseases to rejoin or be retained in the work force.
Methods: A 24-item quantitative questionnaire was uploaded in the website and social media of REUMAZEIN to capture patients' responses in respect to work life. The questionnaire was online accessible for a 45-day period (15/8-30/9/2020).
Results: The responses of 503 adult people with RD (M/F/NA 94/408/1), were available for analysis. Their age was stratified in decades (18-20 0.6%,21-30 5.99%, 31-40 22.36%, 41-50 38.92%, 51-60 22.16% and over 60 9.58%); totally, 83.44% were in the "work-reproductive" period. The predominant RD types were RA 30.3%, SLE 22.8%, AS 20.2% and PsA 20.2%, respectively. Nearly 90% were on medication, namely 40% on biologics, 33% on methotrexate (as a monotherapy or combined therapy), 16.2% on steroids. A minority were either on alternative therapies (2.8%) or off medication (7.5%), respectively. Most of the people were still employed (72.9%) on a full-time schedule (57.7%) and 4.8% on a part-time one, due to their RD. The rest of them (27.1%) were out of work either due to RD (17%) or retirement (1.7%) or for unrelated to the RD reasons (8.4%). The main source of financial income was personal work (52.4%), followed by a family member support (31.1%), while 11% had either a state pension (8%) or a subsidy (3.2%). In respect to the daily house-keeping, half of them (59.3%) had a varying difficulty (mild 36.3%, severe 23%) and 0.8% considered themselves as "unable". The diagnosis was mostly established (81%) prior to the work onset. Post-diagnosis, RD had not affected their working schedule in 47.2%, 17% continued to work with respective adaptations but 30% had quitted or resigned from their work 1-7 years later. RD was notified to the work environment by 85%. As for a compassionate work management, 46% reported no change, 28% an improved policy but 28% a worse one. The development of relative adaptations in the work setting (as chairs, devices, flexible schedule) were considered as favorite factors easing the work by 85%. 17% reported an employer's knowledge on RD related working legislation, 43% the contrary and another 38.7% wished for a future employer's awareness. Most of the participants (58.9%) had no personal information on this field but were eager to get it. The uneventful impact of RD on finding or keeping a job was registered by 77.4% and 66.9%, respectively. During COVID, most of the participants (53%) have not asked for an RD-related leave and only 24.2% chose to telework, a policy that raised mutual satisfaction in 19%. Of note, the working conditions have not mainly been altered (67%) after the end of the 1st quarantine.
Conclusion: This study highlighted that although RD predominate in females, women are more willing to participate in such projects (F 90%). The financial income was mainly based on a personal or a family member work reimbursement (83%), while 11% depended on a state pension or subsidy. The majority has notified the RD to their work environment (85%) while another 85% considered as favorite factors easing the work, several adaptations in the work setting such as chairs, devices, flexible schedule etc. Interestingly, 60% of the participants were unaware of the beneficial legal work rights and nearly 70% of them believe that RD is an obstacle for employment or working maintenance. COVID has not dramatically impaired their work life although the use of teleworking should be strengthened.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1385

Deconditioning in rheumatic disease, time to recognise and tackle it

OP0318 TREATMENT TAPERING AND WITHDRAWAL IN RHEUMATOID ARTHRITIS WITH STABLE REMISSION - FINAL ANALYSIS OF THE RETRO STUDY

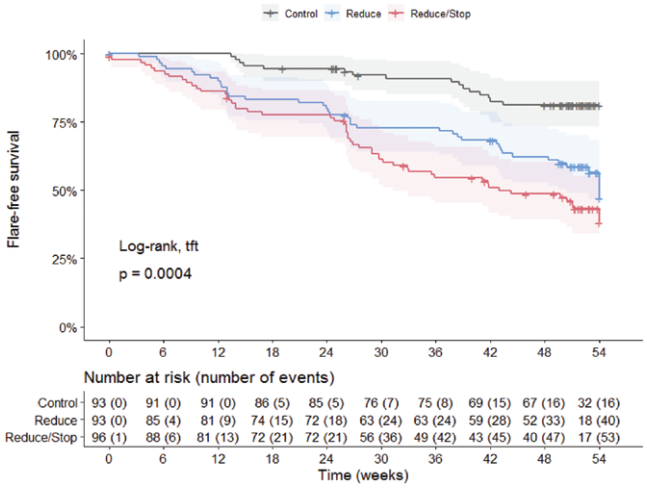
M. Hagen[1], K. Tascilar[1], M. Reiser[1], L. Valor[1], J. Haschka[2], A. Kleyer[1], A. Hueber[3], B. Manger[1], J. Cobra[4], C. Figuereido[4], S. Finzel[5], H. P. Tony[6], J. Wendler[7], S. Kleinert[7], F. Schuch[7], M. Ronneberger[7], M. Feuchtenberger[8], M. Fleck[9], K. Manger[10], W. Ochs[11], M. Schmitt-Haendle[11], H. M. Lorenz[12], R. Alten[13], J. Henes[14], K. Krueger[15], J. Rech[1], G. Schett[1]. *[1]Friedrich-Alexander-University Erlangen-Nuremberg (FAU), Medical Clinic 3, Rheumatology and Immunology, Erlangen, Germany*; *[2]Hanusch Hospital of the WGKK and AUVA Trauma Center, 1st Medical Department at Hanusch Hospital, Ludwig Bolzmann Institute of Osteology, Vienna, Germany*; *[3]Sozialstiftung Bamberg, Section Rheumatology, Bamberg, Germany*; *[4]Institutio de Reumatologia, Sao Paolo, Brasil, Institutio de Reumatologia, Sao Paulo, Brazil*; *[5]University Medical Center Freiburg, Department Innere Medizin, Klinik für Rheumatologie und Klinische Immunologie, Freiburg, Germany*; *[6]Klinikum der Universität Würzburg, Medizinische Klinik 2, Rheumatologie/Klinische Immunologie, Würzburg, Germany*; *[7]Rheumatologische Schwerpunktpraxis, Rheumatologische Schwerpunktpraxis, Erlangen, Germany*; *[8]Kreiskliniken Altötting-Burghausen, Medizinische Klinik II, Sektion Rheumatologie und Klinische Immunologie, Burghausen, Germany*; *[9]Asklepios Klinikum, Rheumatologie und Klinische Immunologie, Bad Abbach, Germany*; *[10]Rheumatology Practice Bamberg, Rheumatology Practice Bamberg, Bamberg, Germany*; *[11]Internistisch-Rheumatologische Schwerpunktpraxis Bayreuth, Internistisch-Rheumatologische Schwerpunktpraxis Bayreuth, Bayreuth, Germany*; *[12] Universität Heidelberg, Medizin 5, Heidelberg, Germany*; *[13]Akademisches Lehrkrankenhaus der Charité - Universitätsmedizin Berlin, Innere Medizin II Rheumatologie, Klinische Immunologie, Osteologie, Berlin, Germany*; *[14]Universitätsklinik Tübingen, Medizinische Abt. II (Onkologie, Hämatologie, Rheumatologie, Immunologie, Pulmonologie), Tübingen, Germany*; *[15]Praxiszentrum St.Bonifatius München, Rheumatologie, Munich, Germany*

Background: Due to better treatment strategies and higher remission rates the management of rheumatoid arthritis (RA) patients in sustained remission is of increasing interest (1). The Rheumatoid Arthritis in Ongoing Remission (RETRO) study investigated the possibility to taper and stop disease modifying anti-rheumatic drugs (DMARDs).
Objectives: To compare one-year remission and relapse rates in rheumatoid arthritis patients randomized to continued treatment, reduced treatment or gradual treatment withdrawal after stable remission under routine care.
Methods: Primary data of the phase III, randomized, controlled RETRO trial in RA patients with stable conventional synthetic and/or biologic DMARD treatment in sustained (>6 months) DAS28-ESR remission (<2.6 units). Patients were randomized 1:1:1 into three strategy arms (continuation of 100% DMARD dose, CONT; tapering to 50% DMARD dose, TAP; 50% tapering followed by withdrawal of DMARDs, STOP). The primary endpoint was the proportion of patients in sustained DAS28-ESR remission after 1 year.
Results: 316 RA patients in sustained remission were included, 303 were randomized (CONT: N=100; TAP: N=102; STOP: N=101) and 282 (93%) had complete data sets after 1 year (CONT:N=93; TAP: N=93; STOP: N=96; Table 1). After 1 year, 81.2%, 58.6%, 43.3% of patients, maintained their remission state over 1 year in the CONT, TAP and STOP arms, respectively (p=0.0004 with log rank test for trend; Figure 1). Hazard ratios for flare were 3.02 (95%CI 1.69 to 5.40) and 4.34 (95%CI 2.48 to 7.60) for the TAP and STOP arms. RA patients who flared were more likely to be female, have longer disease duration, RF/ACPA positivity and higher baseline DAS-28 scores with standardized mean differences >0.2. Serious adverse events were reported in 10.8%, 7.5%, and 13.5% in the CONT, TAP and STOP arms, respectively.

Table 1. Baseline Characteristics

	Group			
	Control	**Reduce**	**Reduce/Stop**	**Overall**
N	93	93	96	282
Age, mean(SD)	55.9 (12.7)	56.9 (13.0)	56.5 (13.3)	56.5 (13.0)
Female, n (%)	53 (57.0)	57 (62.0)	57 (59.4)	167 (59.4)
RF, n (%)	52 (55.9)	58 (62.4)	52 (54.2)	162 (57.4)
ACPA, n (%)	53 (57.0)	50 (54.9)	55 (57.3)	158 (56.4)
Disease duration, years, mean(SD)	7.6 (6.9)	7.8 (6.9)	6.8 (8.1)	7.4 (7.3)
Remission duration, months, mean(SD)	20.6 (18.0)	16.5 (15.9)	22.7 (30.4)	20.0 (22.6)
Biologics, n (%)	39 (41.9)	44 (47.3)	39 (40.6)	122 (43.3)
Methotrexate, n (%)	71 (76.3)	67 (72.0)	75 (78.1)	213 (75.5)
Other DMARDs, n (%)	24 (25.8)	20 (21.5)	16 (16.7)	60 (21.3)
Glucocorticoids, n (%)	27 (29.0)	23 (24.7)	17 (17.7)	67 (23.8)
CRP, mg/L, mean(SD)	0.3 (0.3)	0.5 (0.5)	0.5 (0.6)	0.4 (0.5)
ESR, mm/h, mean(SD)	11.3 (8.4)	12.2 (8.8)	13.0 (10.0)	12.2 (9.1)
Tender joint count, mean(SD)	0.2 (0.6)	0.0 (0.2)	0.1 (0.3)	0.1 (0.4)
Swollen joint count, mean(SD)	0.1 (0.3)	0.1 (0.3)	0.1 (0.4)	0.1 (0.3)
Physician VAS,mm, mean(SD)	1.8 (4.2)	2.6 (4.4)	2.0 (3.9)	2.1 (4.2)
Patient VAS,mm, mean(SD)	6.4 (9.0)	5.5 (8.3)	4.5 (8.4)	5.5 (8.6)
HAQ, standard, mean(SD)	0.2 (0.4)	0.2 (0.3)	0.2 (0.4)	0.2 (0.4)
HAQ, alternative, mean(SD)	0.2 (0.4)	0.1 (0.3)	0.2 (0.3)	0.2 (0.3)
DAS-28, mean(SD)	1.7 (0.7)	1.7 (0.6)	1.7 (0.6)	1.7 (0.6)
SDAI, mean(SD)	1.4 (1.5)	1.4 (1.5)	1.3 (1.3)	1.3 (1.4)
DAS-28 remission, n (%)	91 (97.8)	93 (100.0)	95 (99.0)	279 (98.9)
SDAI remission, n (%)	79 (87.8)	79 (84.9)	88 (92.6)	246 (88.5)
Boolean remission, n (%)	69 (75.8)	71 (76.3)	76 (79.2)	216 (77.1)

Conclusion: This randomized controlled study shows that half of RA patients in sustained remission relapse when tapering/stopping their DMARDs. Presence of autoantibodies, higher baseline DAS28-ESR and female sex are predictors for flares.



REFERENCES:

[1] Schett G et al. Tapering biologic and conventional DMARD therapy in rheumatoid arthritis: current evidence and future directions. Ann Rheum Dis. 2016 Aug;75(8):1428-37.

Disclosure of Interests: Melanie Hagen Speakers bureau: advisory boards, Koray Tascilar Speakers bureau: advisory board, Michaela Reiser: None declared, Larissa Valor: None declared, Judith Haschka Speakers bureau: advisory board, Arnd Kleyer Speakers bureau: advisory board, Axel Hueber Speakers bureau: advisory boards, Bernhard Manger Speakers bureau: advisory boards, Jayme Cobra Speakers bureau: advisory boards, Camille Figuereido Speakers bureau: advisory boards, Stephanie Finzel Speakers bureau: advisory boards, Hans-Peter Tony Speakers bureau: advisory boards, Joerg Wendler Speakers bureau: advisory boards, Stefan Kleinert Speakers bureau: advisory boards, Florian Schuch Speakers bureau: advisory boards, Monika Ronneberger: None declared, Martin Feuchtenberger Speakers bureau: advisory boards, Martin Fleck Speakers bureau: advisory boards, Karin Manger: None declared, Wolfgang Ochs: None declared, Matthias Schmitt-Haendle: None declared, Hanns-Martin Lorenz Speakers bureau: advisory boards, Rieke Alten Speakers bureau: advisory boards, Jörg Henes Speakers bureau: advisory boards, Klaus Krueger Speakers bureau: advisory boards, Jürgen Rech Speakers bureau: advisory boards, Georg Schett Speakers bureau: advisory boards.

DOI: 10.1136/annrheumdis-2021-eular.2174

OP0319 OSTEOSARCOPENIA INCREASES THE RISK OF FALLS IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF A FOUR-YEAR LONGITUDINAL STUDY

M. Tada[1], Y. Yamada[2], K. Mandai[3], N. Hidaka[1]. [1]*Osaka City General Hospital, Orthopaedic Surgery, Osaka, Japan*; [2]*Osaka City University Medical School, Orthopaedic Surgery, Osaka, Japan*; [3]*Osaka Saiseikai Nakatsu Hospital, Orthopaedic Surgery, Osaka, Japan*

Background: Osteosarcopenia is defined as osteoporosis combined with sarcopenia. Both osteoporosis and sarcopenia are risk factors for falls and fractures in healthy individuals[1]. The relationships of falls and fractures to osteosarcopenia in rheumatoid arthritis (RA) patients are unknown.

Objectives: The synergistic effect of osteoporosis and sarcopenia and the impact of osteosarcopenia on falls and fractures in RA patients were investigated using four years of data from a longitudinal study.

Methods: The data from a prospective, observational study (CHIKARA study: UMIN000023744) were examined. The patients were divided into four groups according to their baseline status: no sarcopenia and osteoporosis (SP-OP-); only sarcopenia (SP+OP-); only osteoporosis (SP-OP+); and both sarcopenia and osteoporosis (SP+OP+). Sarcopenia was diagnosed by the criteria of the Asia Working Group on Sarcopenia 2014[2]. Patients with osteoporosis were defined as those having a therapeutic intervention for osteoporosis. The survival rate and Cox hazard ratio were analyzed using falls and fractures as endpoints, adjusted by age, sex, and body mass index.

Results: A total of 100 RA patients (female 78%, mean age 66.1 years) were enrolled. The number of SP-OP-, SP+OP-, SP-OP+, and SP+OP+ patients was 45, 17, 27, and 11, respectively. Their baseline characteristics are shown in Table 1. A total of 35 patients had falls, and 19 patients had fractures during the four-year follow-up. The fall-free survival rate in the SP-OP-, SP+OP-, SP-OP+, and SP+OP+ groups was 75.6%, 64.7%, 51.9%, and 36.4%, respectively; that of the SP+OP+ group was significantly lower than that of the other groups (P=0.021) (Figure 1). The fracture-free survival rate in the SP-OP-, SP+OP-, SP-OP+, and SP+OP+ groups was 86.7%, 82.4%, 81.5%, and 54.5%, respectively. That of the SP+OP+ group was relatively lower than that of the other groups (P=0.121). The hazard ratio of falls was significantly increased in the SP+OP+ group by 3.32-fold (95%CI: 1.01-10.9) compared to that in the SP-OP- group, whereas that in the SP+OP- and SP-OP+ groups was 2.58-fold (95%CI: 0.75-8.8) and 2.29-fold (95%CI: 0.94-5.6) higher, respectively. There were no significant differences compared to the SP-OP- group. The hazard ratio of fractures in the SP+OP+ group was increased 2.73-fold (95%CI: 0.61-12.2) compared to that in the SP-OP- group.

Table 1. Baseline characteristics of the four groups

	SA-OP-	SA+OP-	SA-OP+	SA+OP+	P value*
Female, %	73.3	58.8	88.9	100	0.027
Age, years	63 (49, 72)	69 (60, 79)	73 (64, 75)	73 (65, 81)	0.008
Disease duration, years	4.4 (1.0, 8.4)	4.0 (1.3, 8.9)	7.6 (1.5, 14.5)	10.5 (3.2, 26.5)	0.035
DAS28-ESR	3.14 (2.66, 3.70)	3.55 (3.01, 4.65)	3.93 (3.28, 4.63)	3.53 (2.48, 3.89)	0.01
mHAQ	0.25 (0, 0.375)	0.375 (0.125, 0.875)	0.375 (0.125, 0.875)	0.5 (0.125, 0.875)	0.065
MTX, mg/week, rate (%)	8.4 ± 2.9 (86.7)	8.7 ± 3.5 (70.6)	8.3 ± 2.8 (92.6)	6.8 ± 1.0 (90.9)	0.388
Glucocorticoid, mg/day, rate (%)	3.7 ± 1.9 (20.0)	6.3 ± 1.8 (11.8)	4.0 ± 1.7 (44.4)	3.8 ± 1.8 (18.2)	0.400
Body mass index, kg/m^2	23.4 ± 3.8	19.2 ± 2.3	21.7 ± 2.4	19.2 ± 2.0	<0.001

Data are shown as mean ± standard deviation (SD) or median (25th, 75th percentile).*: compared in four groups by Kruskal-Walls test.

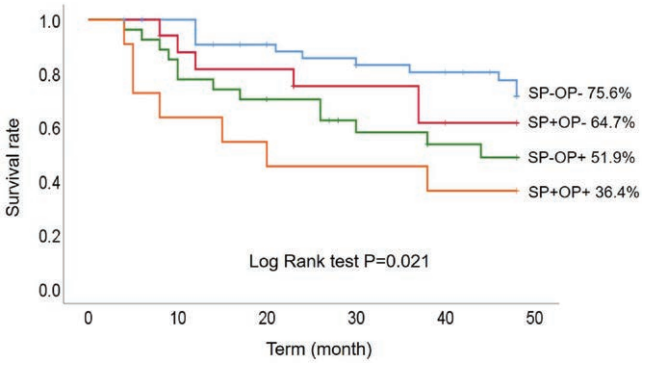


Figure 1. Fall-free survival rates of the four groups.

Conclusion: The survival rates with the endpoints of falls and fractures in RA patients with osteosarcopenia were lower during the four-year follow-up. In particular, the risk of falls increased with the synergistic effect of osteoporosis and sarcopenia in RA patients.

REFERENCES:

[1] Dennison, E. M. *et al.* Fracture risk following intermission of osteoporosis therapy. *Osteoporos Int* **30**, 1733-1743, doi:10.1007/s00198-019-05002-w (2019).

[2] Chen, L. K. *et al.* Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc* **15**, 95-101, doi:10.1016/j.jamda.2013.11.025 (2014).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.942

EFIS session: Emerging concepts how B cells drive systemic autoimmunity: from bench to clinic

OP0320 CHARACTERISTICS OF PERIPHERAL BLOOD B-CELL SUBSETS IN PATIENTS WITH SJOGREN SYNDROME

A. Torgashina[1], E. Sokol[1], J. Khvan[1], B. Chalcev[1], D. Tabakov[2], S. Glukhova[3], O. Golovina4. *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory of intensive care of rheumatic diseases, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Laboratory of immunology and molecular biology, Moscow, Russian Federation*; *[3]V.A. Nasonova Research Institute of Rheumatology, Educational-methodical department, Moscow, Russian Federation*; *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory of intensive care of rheumatic diseases, Moscow, Russian Federation*

Background: B-cells play a pivotal role in primary Sjogren's syndrome (SS) pathogenesis. Recent studies have shown disturbances in the peripheral B cell populations in primary SS.
Objectives: To examine B-cell subsets in peripheral blood of SS patients (pts) and to analyze the association between B-cell subsets and SS activity.
Methods: Twenty active SS pts (19F/1M): median age 42 years (range) (32-54); disease duration 3 (2-10) years; ESSDAI score ≥5 in 6 pts, <5 in 14 pts), were included. SS was diagnosed based on the ACR-EULAR 2016 criteria. Twenty healthy donors composed the control group. CD19+B cells, memory B-cells (CD19+CD27+), non-switched memory B-cells (CD19+IgD+CD27+), switched memory B-cells (CD19+IgD-CD27+), naïve (CD19+IgD+CD27-), double negative (CD19+IgD-CD27-), transitional (CD19+IgD+CD10+CD38+) B-cells, plasmablasts (CD19+CD38+++IgD-CD27+), and plasma cells (CD19+CD38+) were analyzed by multicolor flow cytometry using cytometer Navios (Beckman Coulter, USA).
The nonparametric Mann-Whitney test, the unpaired Student's t test for group comparison, and the Pearson`s x2 criterion were used for statistical analysis. Data were shown as median (Me) with an interquartile range of 25 - 75 percentile. The differences were considered statistically significant when p <0.05. Statistica 10 for Windows (StatSoft Inc., USA) package was used for statistical data processing.
Results: The percentages/absolute numbers of plasmablasts, plasma cells and transitional B-cells in SS were significantly higher than in healthy donors, p<0.01 for all cases (Table 1).

Table 1. B-cell subsets in patients with SS, SS and MALT lymphoma and healthy donors.

B-cell subsets	SS		HD		Pt 1		FN
	%	Abs. cells/μl	%	Abs. cells/μl	%	Abs. cells/μl	
B lymphocyte	12,8 (7,9 – 19,7)	151 (95-112)	8,5 (7,2-11,0)	200 (100-200)	4,5	31	**
plasma cells	6,9 (4,2-10)	12 (6-22)	0,1 (0,05-0,1)	0,1 (0-0,2)	5,7	13	*
plasmablasts	0,88 (0.37-1.8)	2 (1-3)	0,1 (0,1-0,2)	0,2 (0,1-0,4)	26,6	12	*/**
transitional B-cells	5.7 (0.9-17)	8 (4-32)	0,1 (0-0,1)	0,1 (0-0,3)	0	0	*
switched cells	9.1 (5.9-20.7)	18 (11-29)	12,8 (9,3-17,0)	20 (10-40)	52	16	**
non-switched memory B-cells	4.13 (2.7-5.4)	7 (3-15)	7,4 (3,7-11,1)	10 (5-20)	16	5	**

SS Sjogren's patients; HD healthy donors, Pt 1 patient with SS and MALT lymphoma* SS and HD groups compared, p<0.01** Pt 1 and SS group compared

One of the patients (Pt 1) was diagnosed with MALT lymphoma of the parotid salivary gland; she had a distinct B-lymphocyte subpopulations distribution, which was different from the rest of the SS group. She had the lowest percentage / absolute B lymphocyte count of all patients with SS, the highest percentage of switched cells and non-switched memory B-cells, and the highest percentages/ absolute numbers of plasmablasts. For this reason, the patient was excluded from the subsequent analysis (Table 1).
Patients with activity of SS by ESSDAI ≥ 5 had a significantly higher percentage of B cells (p=0.007), and significantly higher absolute B lymphocyte count of naïve cells (p=0.04) and plasmablasts (p=0.048).
Conclusion: Immunophenotyping showed disturbed homeostasis of the B-cells subpopulations in our SS cohort. A significant increase in plasmablasts in SS, as well as a positive correlation of the level of plasmablasts with the SS activity and presence of lymphoma could suggest the important role of these cells in the pathogenesis of SS.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2982

OP0321 DELINEATING THE IMMUNOGENIC DOMAINS OF MDA5 USING PATIENT DERIVED AUTOANTIBODIES

E. Van Gompel[1,2,3], C. Cerqueira[2,3,4], E. Wigren[2,3,5], S. Gräslund[2,3,5], K. Chemin[2,3], B. Horuluoglu[2,3], E. De Langhe[1,6], O. Benveniste[7], I. E. Lundberg[2,3]. *[1]KU Leuven, Department of Development and Regeneration, Leuven, Belgium*; *[2]Karolinska Institutet, CMM, Stockholm, Sweden*; *[3]Karolinska University Hospitals, Karolinska Institutet, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden*; *[4]4D Cell, -, Montreuil, France*; *[5]Structural Genomics Consortium, CMM, Stockholm, Sweden*; *[6]UZ Leuven, Reumatologie, Leuven, Belgium*; *[7]Hôpital Pitié-Salpêtrière, UMR 974, UPMC, Internal Medicine and Clinical Immunology, Paris, France*

Background: The presence of myositis specific anti-melanoma differentiation associated protein 5 (MDA5) autoantibodies is associated with mucocutaneous ulcerations, rapidly progressing interstitial lung disease (RPILD), arthritis and mild muscle involvement in patients. RPILD is the major cause of mortality. At present it is unknown which domain of the MDA5 protein is the main elicitor of an immunogenic response.
Objectives: The aim of this study is to delineate the domains in the MDA5 protein that are the target of autoantibodies.
Methods: Anti-MDA5 IgG were isolated from MDA5(+) patient plasma (7 UPMC, 1 KI and 1 KULeuven) by affinity chromatography using an in-house affinity column as described earlier in *Ossipova et al, 2014*[(1)]. 8 constructs covering different regions of the MDA5 protein were recombinantly produced in *E.coli* (Uniprot ID Q9BYX4, Figure 1). An in-house ELISA was developed to identify the domains with the main epitope(s) by measuring the reactivity of the plasma samples and purified autoantibodies against these MDA5 protein constructs, similar to what was reported by *Fernandes-Cerqueira et al, 2018*[(2)]. The biotinylated MDA5 proteins were immobilized on streptavidin coated plates and subsequently incubated with primary antibodies (purified autoantibodies[(2)] or original plasma) and a HRP-conjugated secondary antibody. The ELISA was developed by the addition of TMB substrate and the optical density (OD) was measured at 450 nm.

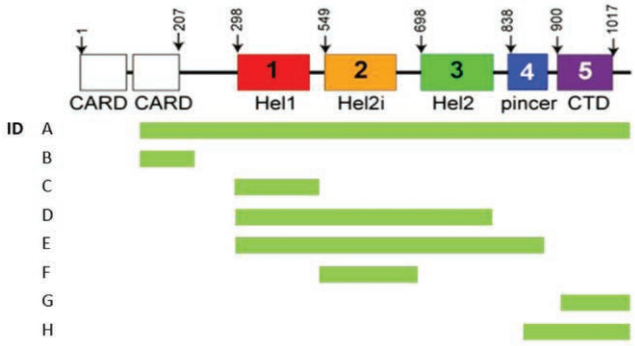


Figure 1. Graphical presentation of the constructs representing different (combinations of) domains of the MDA5 protein.

Results: The preliminary data suggest the main reactivity of the plasma samples and the corresponding purified autoantibodies is directed towards the helicase domains and that there is variability between the patients in the reactivity towards domains located at the end of the protein.

Conclusion: The study aims to resolve the main immunogenic domain of the MDA5 protein, which will lead to more insight in the disease mechanisms. The preliminary results suggest this domain is in the center of the MDA5 protein, but further experiments are necessary. We will use this set up to study differences in reactivity between patients (from different cohorts) and assess if differences in antibody reactivity could be linked to clinical features such as RPILD. Such correlations might be beneficial to predict the disease progression and to apply personal treatment approaches.
REFERENCES:
[1] Ossipova E, Cerqueira CF, Reed E, Kharlamova N, Israelsson L, et al. Affinity purified anti-citrullinated protein/peptide antibodies target antigens expressed in the rheumatoid joint. Arthritis Res Ther. 2014;16(4):R167.
[2] Fernandes-Cerqueira C, Renard N, Notarnicola A, Wigren E, Gräslund S, et al. Patients with anti-Jo1 antibodies display a characteristic IgG Fc-glycan profile which is further enhanced in anti-Jo1 autoantibodies. Scientific reports. 2018;8(1):17958.

Disclosure of Interests: Eveline Van Gompel: None declared, Catia Cerqueira: None declared, Edvard Wigren: None declared, Susanne Gräslund: None declared, Karine Chemin: None declared, Begum Horuluoglu: None declared, Ellen De Langhe: None declared, Olivier Benveniste: None declared, Ingrid E. Lundberg Consultant of: Consulting fees from Corbus Pharmaceuticals, Inc, Grant/research support from: Research grants from Bristol Myers Squibb and AstraZeneca.
DOI: 10.1136/annrheumdis-2021-eular.4264

[Joint session HPR/ PARE/ ARP] Mastering Self-management: State of art in a New Era

OP0322-HPR

EMPOWERMENT AND ASSOCIATIONS TO DISEASE ACTIVITY AND PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

M. Andersson[1,2], A. Bremander[1,2,3,4], I. Larsson[2,5]on behalf of BARFOT study group. [1]*Lund University, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden*; [2]*Spenshult Reserach and Development center,., Halmstad, Sweden*; [3]*University of Southern Denmark, Department of Regional Health Research, Odense, Denmark*; [4]*University Hospital of Southern Denmark, Danish Hospital for Rheumatic Diseases, Sønderborg, Denmark*; [5]*Halmstad University, School of Health and Welfare, Halmstad, Sweden*

Background: The WHO describes empowerment as a process in which patients can take control and make informed decisions about their life and health. Empowerment is important for patients with rheumatoid arthritis (RA) since most of the care is provided by the patients themselves.
Objectives: The aim was to study levels of empowerment and associated variables in individuals with RA and to investigate longitudinal clinical data in patients with low and high empowerment.
Methods: This study involved patients with RA from the BARFOT (Better Anti-Rheumatic PharmacOTherapy) cohort, who were recruited between 1992 and 2006 and included in the study at the time for diagnosis (n = 2,837) [1]. The patients were assessed according to a structured protocol at inclusion and after 3, 6, 12, 24, 60, 96, and 180 months. At each follow-up DAS28-3, HAQ and pain were assessed. In 2017, a postal survey was sent to all still living patients (n=1542), with a response rate of 69% (n = 1,065). The questionnaire included disease characteristics, questions about lifestyle habits and the Swedish Rheumatic Disease Empowerment Scale (SWE-RES-23) [2]. The 844 patients who answered the SWE-RES-23 made up the study cohort. Differences in empowerment between groups (lowest third [LE], SWE-RES-23 ≤3.48 vs. highest third [HE], SWE-RES-23 ≥4.04) were analysed with t-tests. Logistic regression analysis was used to study associations with LE vs. all others. Thirdly, differences between LE and HE were studied with longitudinal data (seven time points) of pain, HAQ and disease activity.

Results: Responders were mean 65 (SD13) years old, disease duration 15.6 (3.9) years, and 74% were women. The LE group (n=282) were older and were more often women, and reported worse overall health compared with the HE group (n=270), Table 1.

Table 1. Descriptives at questionnaire 2017, including all participants and comparisons between highest and lowest third of SWE-RES-23

	All	Low SWERES*	High SWERES*	p-value
	Mean (sd)	Mean (sd)	Mean (sd)	
N	844	282	270	
Sex, women, %	74	78	69	0.015
Age	65 (13)	66 (13)	63 (12)	0.002
Disease duration, year	15.6 (3.9)	15.7 (4.1)	15.6 (3.8)	0.917
TJC28 (0-28)	5 (6)	6 (8)	4 (5)	<0.001
SJC28 (0-28)	3 (5)	3 (4)	3 (4)	0.334
PatGA (0-10)	3 (2)	4 (3)	2 (2)	<0.001
Pain (0-10)	3 (2)	4 (3)	3 (2)	<0.001
Fatigue (0-10)	4 (3)	5 (3)	3 (3)	<0.001
HAQ (0-3)	0.62 (0.61)	0.81 (0.69)	0.42 (0.51)	<0.001
EQ5D (0-1)	0.70 (0.25)	0.62 (0.29)	0.79 (0.19)	<0.001
SWERES	3.8 (0.7)	3.1 (0.3)	4.6 (0.3)	<0.001

*tricotomized data, lowest third vs. highest third

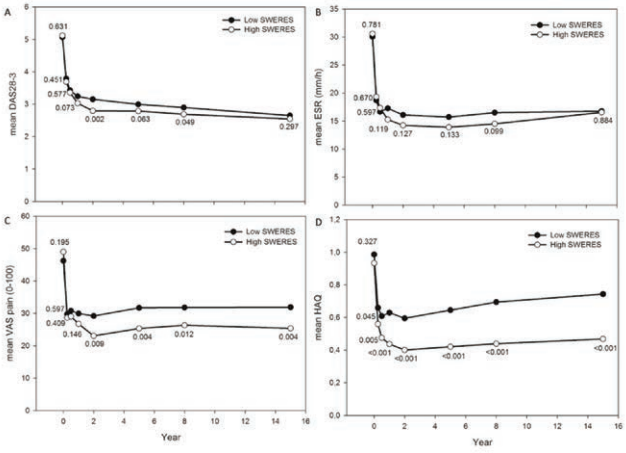


Figure 1. Panel showing mean DAS28-3 (A), ESR (B), VAS pain (C) and HAQ (D) over 15 years in the different groups.

Regarding lifestyle habits, there were no differences between the groups in smoking habits, diets, or drinking habits. Moderate physical activity for ≥150 min/week was reported by 27% in the LE group vs. 41% in the HE group, p<0.001. Vigorous physical activity ≥60 min/week was reported by 22% vs. 37% in the LE and the HE group respectively, p<0.001.
In the logistic regression analysis (n=844), several factors were associated with LE: being a woman (OR 1.40, 95% CI 1.00-1.97), pain-related factors as higher tender joint count (OR 1.04, 95% CI 1.01-1.06), worse patient global assessment (OR 1.19, 95% CI 1.12-1.27), pain (OR 1.14, 95% CI 1.08-1.21), fatigue (OR 1.14, 95% CI 1.09-1.21), HAQ (OR 2.08, 95% CI 1.64-2.64) and EQ-5D (OR 0.16, 95% CI 0.09-0.28). There were also associations between moderate physical activity (<150 min/week) (OR 1.60, 95% CI 1.16-2.19) and vigorous (< 60min/week) (OR 1.50, 95% CI 1.07-2.10) and LE.
Analysing longitudinal data, the LE group reported worse pain and HAQ at all timepoints, a worse DAS28-3 at year 2 and 8, and a worse ESR at 15 years follow-up compared with the HE group (p<0.05).

Conclusion: In patients with RA, low empowerment is associated with worse all over health. Interventions aimed to improve empowerment may include mastering of pain, physical function, and improved physical activity.

REFERENCES:
[1] Hafstrom I et al. Open Access Rheumatol 2019;11:207-17.
[2] Arvidsson S et al. Musculoskeletal Care 2012;10:101-9.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.455

Members and Volunteers – Unknown beings? How to explore their interests, establish contacts and support

OP0323-PARE

"CELEBRATING THE 50TH ANNIVERSARY OF OUR ORGANISATION IN TIMES OF PANDEMIC: HOW WE USED DIGITAL TOOLS TO OVERCOME CHALLENGES AND DIFFICULTIES AND CAME INTO CONTACT WITH MORE PARTICIPANTS AND VIEWERS THAN EVER ENVISAGED!"

C. Elling-Audersch[1]. [1]*Deutsche Rheum-Liga Bundesverband, NRW, Solingen, Germany*

Background: The German League against Arthritis (DRL) with about 300.000 members wanted to celebrate its 50th anniversary in 2020. The original idea to perform a large jubilee gala was crossed by the limitation of contact and the precaution for members our organisation in times of pandemic.
Objectives: It was a big challenge to transfer the celebration into a digital form in the pandemic. Our goal was to reach as many people (with RMDs, their family, colleagues, politicians) as possible, not only members of our organisation. We wanted to generate even more awareness for people with RMDs, their needs and difficulties nationwide.
Methods: We decided to focus on digital formats and produced video clips and podcasts that were presented online. Some of the topics of the videos: Voluntary work,

Young people with RMDs, Participation, Doctors and Patients as Partners. Furthermore, in 17 podcasts our member organisations highlighted their activities for people with RMDs. Volunteers vividly described their inside view in the podcasts. In addition, we created a historical timeline for the website. Special highlight was a radio programme based on our videos, summarising our activities that was broadcast by 19 radio stations.
Results: The video clips attracted more viewers than could have been reached with an event in Berlin. For example we generated 35.000 viewers on our YouTube channel by presenting the birthday speech by our president. Altogether we reached successfully approximately 1.5 million people national wide. I will present the numbers of people our activities reached and feedback we received.
Conclusion: We are convinced going on the right track using digital media as one of our priorities not only in times of pandemic but as a valuable enrichment for all RMD patients on national and international level.
These examples of best practise experiences shall encourage other patient organisations to take on the challenge in pandemic times. By using digital tools and formats patient organisations can succeed in reaching more RMD patients and in staying connected with their members.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3063

OP0324-PARE PATIENT INFORMATION IN TIMES OF CRISIS: LESSONS LEARNED FROM COVID-19 COMMUNICATION IN RHEUMATOLOGY

M. M. Bakker[1,2], T. Luttikhuis[1], I. Jansen[1], J. Rademakers[2,3], M. De Wit[4], A. Boonen[1,2], P. Putrik[1,2]. [1]*Maastricht University Medical Centre, Department of Internal Medicine, Rheumatology Division, Maastricht, Netherlands*; [2]*Maastricht University, CAPHRI - Care and Public Health Research Institute, Maastricht, Netherlands*; [3]*Nivel - Netherlands Institute for Health Services Research, -, Utrecht, Netherlands*; [4]*Tools2Use Patient Association, -, Amsterdam, Netherlands*

Background: The rapid global spread of COVID-19 required swift action to provide people with rheumatic and musculoskeletal diseases (RMDs) with reliable information. Important issues included the risk of infection and severe illness, (continued) use of medication, temporary closure of clinics, and organization of (semi-) virtual care. People with limited health literacy are a particularly vulnerable group that might have difficulty accessing, understanding, and applying health information.

Objectives: To evaluate (a) key aspects of crisis communication and (b) explicit consideration of people's health literacy needs in communication to people with RMDs during the first wave of COVID-19 in the Netherlands.

Methods: We conducted an explorative qualitative study including seven interviews in May and June 2020 with representatives of organisations (a mixed regional/academic hospital, the association for RMD professionals and two patient organisations) responsible for information provision to people with RMDs in the Netherlands. Interviewees were asked about preparedness (1) and strategy (2) for crisis communication, and content (3) and reach (4) of communication, considering principles of good crisis communication and health literacy. In addition, through systematic screening of websites, social media and emails, we identified and analysed 13 written communications provided to people with RMDs by these organisations during the first three months of the COVID-19 pandemic. We assessed comprehensibility and applicability with the Dutch adapted version of the Patient Education Materials Assessment tool (PEMAT), the outcome being a percentage of adherence to 24 criteria. We assessed difficulty level using an online assessment application (Figure 1), with Common European Framework of Reference for Languages (CEFR) level B1 being the highest acceptable level.

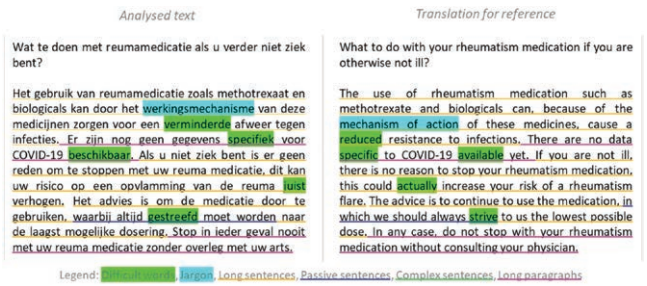


Figure 1. Example of textual assessment using the application. Note: Dutch-language text was used for analysis; the English translation is provided as a reference only and might be of different difficulty.

Results: While admittedly being underprepared, respondents generally perceived their crisis communication as adequate. They quickly adapted to people's needs and changing circumstances and attempted to adapt written and verbal communication to people with limited health literacy. Respondents reported challenges related to the scientific uncertainty, lack of reach, difficulty simplifying information, and being unsure if their communication approach was adequate. Textual assessment showed great variation in applicability (range 60-100%) and comprehensibility (range 58-100%) of these texts, and 69% of communications were more difficult than B1-level. Considering principles of crisis communication and health literacy, we propose several lessons to be learned for future crises (Table 1).

Table 1. Recommendations for improvement of crisis communication

Preparedness:
Use current experience to establish a future crisis communication plan
Train staff and management in crisis communication and health literate communication
Strategy:
Collaborate with relevant organisations to ensure consistency in messages
Inform people early and frequently
Remain transparent about uncertainty
Content:
Adapt information to different people's needs, considering e.g. age, cultural background
Check difficulty level of written information (aim at B1) and adapt accordingly
Ask your audience for feedback
Make sure information is directly applicable in practice
Combat fake news through acknowledgement and counterarguments
Reach:
Use multiple channels
Use diverse outreach strategies to cater to a diverse audience
Overall:
Consider people's health literacy throughout

Conclusion: The rheumatology organisations mostly adhered to principles of crisis communication, and made efforts to adapt information to their audience's needs, including health literacy needs. Nevertheless, important recommendations were drawn which are potentially also relevant for other clinical fields.
Acknowledgements: We thank Mr. Tigran Spaan for providing free access to the online language assessment application.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.348

LB0001 MAVRILIMUMAB IMPROVES OUTCOMES IN PHASE 2 TRIAL IN NON-MECHANICALLY-VENTILATED PATIENTS WITH SEVERE COVID-19 PNEUMONIA AND SYSTEMIC HYPERINFLAMMATION

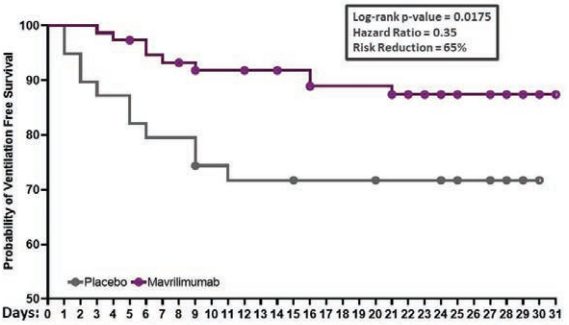
L. Pupim[1], T. S. Wang[2], K. Hudock[3], J. Denson[4], N. Fourie[5], L. Hercilla Vasquez[6], K. Luz[7], M. Madjid[8], K. Mcharry[9], J. F. Saraiva[10], E. Tobar[11], T. Zhou[1], M. Samant[1], J. Pirrello[12], F. Fang[1], J. F. Paolini[1], A. Pano[1], B. C. Trapnell[3]. [1]*Kiniksa Pharmaceuticals Corp., Clinical Development, Lexington, United States of America*; [2]*University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, United States of America*; [3]*University of Cincinnati, Cincinnati Children's Hospital Medical Center, Cincinnati, United States of America*; [4]*Tulane University School of Medicine, Critical Care, New Orleans, United States of America*; [5]*IATROS International, IATROS International, Bloemfontein, South Africa*; [6]*Hospital Nacional Alberto Sabogal Sologuren, Hospital Nacional Alberto Sabogal Sologuren, Callao, Peru*; [7]*Rio Grande do Norte Federal University, Rio Grande do Norte Federal University, Rio Grande do Norte, Brazil*; [8]*University of Texas Medical School at Houston, McGovern Medical School, Houston, United States of America*; [9]*TASK Eden, TASK Eden, George, South Africa*; [10]*Instituto de Pesquisa Clínica de Campinas, Instituto de Pesquisa Clínica de Campinas, São Paulo, Brazil*; [11]*Hospital Clinico Universidad de Chile, Hospital Clinico Universidad de Chile, Santiago, Chile*; [12]*Kiniksa Pharmaceuticals Corp., Business Development, Lexington, United States of America*

Background: Granulocyte/macrophage-colony stimulating factor (GM-CSF) is a cytokine both vital to lung homeostasis and important in regulating inflammation and autoimmunity[1,2,3] that has been implicated in the pathogenesis of respiratory failure and death in patients with severe COVID-19 pneumonia and systemic hyperinflammation.[4-6] Mavrilimumab is a human anti GM-CSF receptor α monoclonal antibody capable of blocking GM-CSF signaling and downregulating the inflammatory process.
Objectives: To evaluate the effect of mavrilimumab on clinical outcomes in patients hospitalized with severe COVID-19 pneumonia and systemic hyperinflammation.
Methods: This on-going, global, randomized, double-blind, placebo-controlled seamless transition Phase 2/3 trial was designed to evaluate the efficacy and safety of mavrilimumab in adults hospitalized with severe COVID-19 pneumonia and hyperinflammation. The Phase 2 portion comprised two groups: Cohort 1 patients requiring supplemental oxygen therapy without mechanical

ventilation (to maintain SpO_2 ≥92%) and Cohort 2 patients requiring mechanical ventilation, initiated ≤48 hours before randomization. Here, we report results for Phase 2, Cohort 1: 116 patients with severe COVID- 19 pneumonia and hyperinflammation from USA, Brazil, Chile, Peru, and South Africa; randomized 1:1:1 to receive a single intravenous administration of mavrilimumab (10 or 6 mg/kg) or placebo. The primary efficacy endpoint was proportion of patients alive and free of mechanical ventilation at Day 29. Secondary endpoints included [1] time to 2-point clinical improvement (National Institute of Allergy and Infectious Diseases COVID-19 ordinal scale), [2] time to return to room air, and [3] mortality, all measured through Day 29. The prespecified evidentiary standard was a 2-sided α of 0.2 (not adjusted for multiplicity).

Results: Baseline demographics were balanced among the intervention groups; patients were racially diverse (43% non-white), had a mean age of 57 years, and 49% were obese (BMI ≥ 30). All patients received the local standard of care: 96% received corticosteroids (including dexamethasone) and 29% received remdesivir. No differences in outcomes were observed between the 10 mg/kg and 6 mg/kg mavrilimumab arms. Results for these groups are presented together. Mavrilimumab recipients had a reduced requirement for mechanical ventilation and improved survival: at day 29, the proportion of patients alive and free of mechanical ventilation was 12.3 percentage points higher with mavrilimumab (86.7% of patients) than placebo (74.4% of patients) (Primary endpoint; p=0.1224). Mavrilimumab recipients experienced a 65% reduction in the risk of mechanical ventilation or death through Day 29 (Hazard Ratio (HR) = 0.35; p=0.0175). Day 29 mortality was 12.5 percentage points lower in mavrilimumab recipients (8%) compared to placebo (20.5%) (p=0.0718). Mavrilimumab recipients had a 61% reduction in the risk of death through Day 29 (HR= 0.39; p=0.0726). Adverse events occurred less frequently in mavrilimumab recipients compared to placebo, including secondary infections and thrombotic events (known complications of COVID-19). Thrombotic events occurred only in the placebo arm (5/40 [12.5%]).

Mavrilimumab Reduced the Risk of Mechanical Ventilation or Death by 65% Versus Placebo



Mavrilimumab Patients at Risk, n	75	75	75	75	74	73	71	69	68	67	65	65	65	64	64	63	63	59	59	59	59	59	55	52	50	49	47	47	45	38	18	3
Placebo Patients at Risk, n	39	39	37	35	34	34	32	31	31	31	28	28	27	27	27	27	26	26	26	26	26	25	25	25	25	24	22	22	17	14	4	

Conclusion: In a global, diverse population of patients with severe COVID-19 pneumonia and hyperinflammation receiving supplemental oxygen therapy, corticosteroids, and remdesivir, a single infusion of mavrilimumab reduced progression to mechanical ventilation and improved survival. Results indicate mavrilimumab, a potent inhibitor of GM-CSF signaling, may have added clinical benefit on top of the current standard therapy for COVID-19. Of potential importance is that this treatment strategy is mechanistically independent of the specific virus or viral variant.

REFERENCES:

[1] Trapnell, Nat Rev Dis Pri, 2019
[2] Wicks, Nat Rev Immunology, 2015
[3] Hamilton, Exp Rev Clin Immunol, 2015
[4] De Luca, Lancet Rheumatol, 2020
[5] Cremer, Lancet Rheumatol, 2021
[6] Zhou, Nature, 2020

Disclosure of Interests: Lara Pupim Employee of: Kiniksa, Shareholder of: Kiniksa, Tisha S. Wang Consultant of: Partner Therapeutics; steering committee for Kinevant BREATHE clinical trial, Kristin Hudock: None declared, Joshua Denson: None declared, Nyda Fourie: None declared, Luis Hercilla Vasquez: None declared, Kleber Luz: None declared, Mohammad Madjid Grant/research support from: Kiniksa, Kirsten McHarry: None declared, José Francisco Saraiva: None declared, Eduardo Tobar: None declared, Teresa Zhou Employee of: Kiniksa, Shareholder of: Kiniksa, Manoj Samant Employee of: Kiniksa, Shareholder of: Kiniksa, Joseph Pirrello Employee of: Kiniksa, Shareholder of: Kiniksa, Fang Fang Employee of: Kiniksa, Shareholder of: Kiniksa, Johnn F. Paolini Employee of: Kiniksa, Shareholder of: Kiniksa, Arian Pano Employee of: Kiniksa, Shareholder of: Kiniksa, Bruce C. Trapnell: None declared

DOI: 10.1136/annrheumdis-2021-eular.5012

LB0002

COVID-19 VACCINE SAFETY IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASE

P. M. Machado[1], S. Lawson-Tovey[2], K. Hyrich[2], L. Carmona[3], L. Gossec[4], E. Mateus[5], A. Strangfeld[6], B. Raffeiner[7], T. Goulenok[8], O. Brocq[9], M. Cornalba[10], J. A. Gómez-Puerta[11], E. Veillard[12], L. Trefond[13], J. E. Gottenberg[14], J. Henry[15], P. Durez[16], G. R. Burmester[17], M. Mosca[18], E. Hachulla[19], H. Bijlsma[20], I. McInnes[21], X. Mariette[22]. *[1]University College London, Centre for Rheumatology and Department of Neuromuscular Diseases, London, United Kingdom*; *[2]The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; *[3]Instituto de Salud Musculoesquelética, INMUSC, Madrid, Spain*; *[4]Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France*; *[5]Portuguese League Against Rheumatic Diseases, LPCDR, Lisbon, Portugal*; *[6]German Rheumatism Research Center (DRFZ Berlin), Epidemiology and Health Care Research, Berlin, Germany*; *[7]Central Hospital of Bolzano, Rheumatology, Bolzano, Italy*; *[8]Bichat -Claude Bernard Hospital, APHP, Department of Internal Medicine, Paris, France*; *[9]CHPG, Department of Rheumatology, Monaco, Monaco*; *[10]ASST Gaetano Pini - CTO Institute, Division of Clinical Rheumatology, Milan, Italy*; *[11]Hospital Clinic, Department of Rheumatology, Barcelona, Spain*; *[12]Cabinet de Rhumatologie des "Marines de Chasles", Department of Rheumatology, Saint Malo, France*; *[13]CHU GABRIEL Montpied, Department of Rheumatology, Clermont Ferrand, France*; *[14] Hopital de Hautepierre, Department of Rheumatology, Strasbourg, France*; *[15]Hopitaux Universitaires Paris Sud, Department of Rheumatology, Paris, France*; *[16]Cliniques Universitaires Saint-Luc, Department of Rheumatology, Brussels, Belgium*; *[17]Charité – Universitätsmedizin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; *[18]University of Pisa, Department of Rheumatology, Pisa, Italy*; *[19]Lille University, Hopital Claude Huriez, Lille, France*; *[20]University of Utrecht, Department of Rheumatology, Utrecht, Netherlands*; *[21]University of Glasgow, Institute for Infection, Immunity and Inflammation, Glasgow, United Kingdom*; *[22]Hôpital Bicêtre, Assistance Publique-Hôpitaux de Paris, Department of Rheumatology, Paris, France*

Background: The consequences of the COVID-19 outbreak are unprecedented and have been felt by everyone around the world, including people with rheumatic and musculoskeletal diseases (RMDs). With the development of vaccines, the future is becoming brighter. Vaccines are a key pillar of public health and have been proven to prevent many serious diseases. However, vaccination also raises questions, especially for patients with inflammatory RMDs and/or treated with drugs that influence their immune system.

Objectives: Our aim was to collect safety data among RMD patients receiving COVID-19 vaccines.

Methods: The EULAR COVID-19 Vaccination (COVAX) Registry is an observational registry launched on 5 February 2021. Data are entered voluntarily by clinicians or associated healthcare staff; patients are eligible for inclusion if they have an RMD and have been vaccinated against SARS-CoV-2. Descriptive statistics are presented.

Results: As of 27 April 2021, 1519 patients were reported to the registry. The majority were female (68%) and above the age of 60 (57%). Mean age was 63 years (SD 16), ranging from 15 to 97 years. A total of 28 countries contributed to the registry, with France (60%) and Italy (13%) as the highest contributors. The majority (91%) had inflammatory RMDs. Inflammatory joint diseases accounted for 51% of cases, connective tissue diseases 19%, vasculitis 16%, other immune mediated inflammatory diseases 4%, and non-inflammatory/mechanical RMDs 9%. The most frequent individual diagnoses were rheumatoid arthritis (30%), axial spondyloarthritis (8%), psoriatic arthritis (8%), systemic lupus erythematosus (SLE, 7%) and polymyalgia rheumatica (6%). At the time of vaccination, 45% were taking conventional synthetic DMARDs, 36% biological DMARDs, 31% systemic glucocorticoids, 6% other immunosuppressants (azathioprine; mycophenolate; cyclosporine; cyclophosphamide; tacrolimus), and 3% targeted synthetic DMARDs. The most frequent individual DMARDs were methotrexate (29%), TNF-inhibitors (18%), antimalarials (10%) and rituximab (6%). The vaccines administered were: 78% Pfizer, 16% AstraZeneca, 5% Moderna and 1% other/unknown; 66% of cases received two doses and 34% one dose. Mean time from 1st and 2nd dose to case report was 41 days (SD 26) and 26 days (SD 23), respectively. COVID-19 diagnosis after vaccination was reported in 1% (18/1519) of cases. Mean time from first vaccination until COVID-19 diagnosis was 24 days (SD 17). Disease flares were reported by 5% (73/1375) of patients with inflammatory RMDs, with 1.2% (17/1375) classified as severe flares. Mean time from closest vaccination date to inflammatory RMD flare was 5 days (SD 5). The most common flare types were arthritis (35/1375=2.5%), arthralgia (29/1375=2.1%), cutaneous flare (11/1375=0.8%) and increase in fatigue (11/1375=0.8%). Potential vaccine side effects were reported by 31% of patients (467/1519). The majority were typical early adverse events within 7 days of vaccination, namely pain at the site of injection (281/1519=19%), fatigue (171/1519=11%) and headache (103/1519=7%). Organ/system adverse events were reported by 2% (33/1519) but only 0.1% (2/1519) reported

severe adverse events, namely a case of hemiparesis in a patient with systemic sclerosis/SLE overlap syndrome (ongoing at the time of reporting), and a case of giant cell arteritis in a patient with osteoarthritis (recovered/resolved without sequelae).

Conclusion: The safety profiles for COVID-19 vaccines in RMD patients was reassuring. Most adverse events were the same as in the general population, they were non-serious and involved short term local and systemic symptoms. The overwhelming majority of patients tolerated their vaccination well with rare reports of inflammatory RMD flare (5%; 1.2% severe) and very rare reports of severe adverse events (0.1%). These initial findings should provide reassurance to rheumatologists and vaccine recipients, and promote confidence in COVID-19 vaccine safety in RMD patients, namely those with inflammatory RMDs and/or taking treatments that influence their immune system.

Acknowledgements: EULAR COVID-19 Task Force; European Reference Network on rare and Complex Connective Tissue and Musculoskeletal Diseases; European Reference Network on Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases Network; all rheumatologists contributing to the EULAR COVAX Registry.

Disclosure of Interests: Pedro M Machado Consultant of: Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript., Grant/research support from: Orphazyme, unrelated to this manuscript., Speakers bureau: Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript., Saskia Lawson-Tovey: None declared, Kimme Hyrich Grant/research support from: BMS, UCB, and Pfizer, all unrelated to this manuscript., Speakers bureau: Abbvie, Loreto Carmona Consultant of: her institute works by contract for laboratories among other institutions, such as Abbvie Spain, Eisai, Gebro Pharma, Merck Sharp & Dohme España, S.A., Novartis Farmaceutica, Pfizer, Roche Farma, Sanofi Aventis, Astellas Pharma, Actelion Pharmaceuticals España, Grünenthal GmbH, and UCB Pharma, all unrelated to this manuscript., Laure Gossec Grant/research support from: AbbVie, Amgen, BMS, Biogen, Celgene, Gilead, Janssen, Lilly, Novartis, Pfizer, Samsung Bioepis, Sanofi-Aventis, UCB, all unrelated to this manuscript., Speakers bureau: Amgen, Lilly, Janssen, Pfizer, Sandoz, Sanofi, Galapagos, all unrelated to this manuscript., Elsa Mateus Grant/research support from: LPCDR received support for specific activities: grants from Abbvie, Novartis, Janssen-Cilag, Lilly Portugal, Sanofi, Grünenthal S.A., MSD, Celgene, Medac, Pharmakern, GAfPA; grants and non-financial support from Pfizer; non-financial support from Grünenthal GmbH, outside the submitted work., Anja Strangfeld Speakers bureau: AbbVie, MSD, Roche, BMS, and Pfizer, all unrelated with this manuscript., BERND RAFFEINER: None declared, Tiphaine Goulenok: None declared, Olilvier Brocq: None declared, Martina Cornalba: None declared, José A Gómez-Puerta Speakers bureau: AbbVie, BMS, GSK, Janssen, Lilly, MSD, Roche and Sanofi., Eric Veillard: None declared, Ludovic Trefond: None declared, Jacques-Eric Gottenberg: None declared, Julien Henry: None declared, Patrick Durez: None declared, Gerd Rüdiger Burmester: None declared, Marta Mosca: None declared, Eric Hachulla: None declared, Hans Bijlsma: None declared, Iain McInnes: None declared, Xavier Mariette Consultant of: BMS, Galapagos, Gilead, Janssen, Novartis, Pfizer, Sanofi-Aventis, UCB, and grant from Ose, all unrelated to this manuscript.

DOI: 10.1136/annrheumdis-2021-eular.5097

LB0003

IMMUNOGENICITY AND SAFETY OF THE BNT162B2 MRNA COVID-19 VACCINE IN ADULT PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES AND GENERAL POPULATION: A MULTICENTER STUDY

V. Furer[1], T. Eviatar[1], D. Zisman[2], H. Peleg[3], D. Paran[1], D. Levartovsky[1], M. Zisapel[1], O. Elalouf[1], I. Kaufman[1], R. Meidan[1], A. Broyde[1], A. Polachek[1], J. Wollman[1], I. Litinsky[1], K. Meridor[1], H. Nochomovitz[1], A. Silberman[1], D. Rosenberg[1], J. Feld[2], A. Haddad[2], T. Gazitt[2], M. Elias[2], N. Higazi[2], F. Kharouf[3], G. Shefer[4], O. Sharon[4], S. Pel[1], S. Nevo[1], O. Elkayam[1]. [1]*Tel Aviv Medical Center, Rheumatology, Tel Aviv, Israel*; [2]*Carmel Medical Center, Rheumatology, Haifa, Israel*; [3]*Hadassah Medical Center, Rheumatology, Jerusalem, Israel*; [4]*Tel Aviv Medical Center, Endocrinology, Tel Aviv, Israel*

Background: Vaccination represents a cornerstone in mastering the COVID-19 pandemic. Data on immunogenicity, efficacy, and safety of the novel BNT162b2 mRNA vaccine in patients with autoimmune inflammatory rheumatic diseases (AIIRD) are limited.

Objectives: To investigate the immunogenicity, efficacy, and safety of the BNT162b2 mRNA vaccine in patients with AIIRD compared to the general population.

Methods: A prospective multicenter study investigated immunogenicity, efficacy, and safety of the two-dose regimen BNT162b2 mRNA vaccine in adult patients with AIIRD including rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthropathy (axSpA), systemic lupus erythematosus (SLE), connective tissues diseases (CTD), systemic vasculitides, and idiopathic inflammatory myositis (IIM), compared to control subjects without rheumatic diseases or immunosuppressive therapies. Serum IgG antibody levels against SARS-CoV-2 spike S1/S2 proteins were measured 2 - 6 weeks after the second vaccine dose. Seropositivity was defined as IgG ≥15 binding antibody units (BAU)/ml. Post-vaccination efficacy defined as post-vaccination COVID-19 infection and safety were assessed. Pre- and post- vaccination disease activity indices were assessed as appropriate for each disease.

Results: A total of 686 AIIRD patients and 121 controls participated into the study. AIIRD patients were significantly older than controls, mean age±SD 56.76±14.88 vs 50.76±14.68, respectively, p<0.0001. A total of 95.2% (n=653) AIIRD patients were treated with immunomodulatory medications.

The seropositivity rate was 86% (n=590) in patients with AIIRD compared to 100% in controls (p <0.0001) The level of the S1/S2 antibodies was significantly reduced in AIIRD patients compared to controls (mean± SD 132.9±91.7 vs 218.6±82.06, P<0.0001). In patients with PsA, AxSpA, SLE, and LVV, the seropositive rate was above 90%. In RA, the seropositive rate was 82.1% and the lowest seropositive rate (<40%) was observed in patients with AAV and IIM.

Anti-CD20 significantly impaired the vaccine's immunogenicity, with the lowest seropositivity rate of 39%. The use of GC, mycophenolate mofetil (MMF), and abatacept was associated with a significantly lower rate of seropositivity (Figure 1). MTX significantly reduced the seropositivity in patients treated with MTX monotherapy and in combinations with other treatments (92% and 84%, respectively), although at a lesser magnitude than anti-CD20, MMF, and abatacept. More than 97% of patients treated with anti-cytokine therapies including TNFi, interleukin-17 and interleukin-6 inhibitors had an appropriate immunogenic response when used as monotherapy. The combination of TNFi with MTX significantly reduced the rate of seropositivity to 93%, p=0.04. Age over 65 years, a diagnosis of RA, IIM, ANCA-associated vascilitis, and treatment with GC, MMF, anti-CD20, and abatacept were associated with a reduced likelihood of seropositivity.

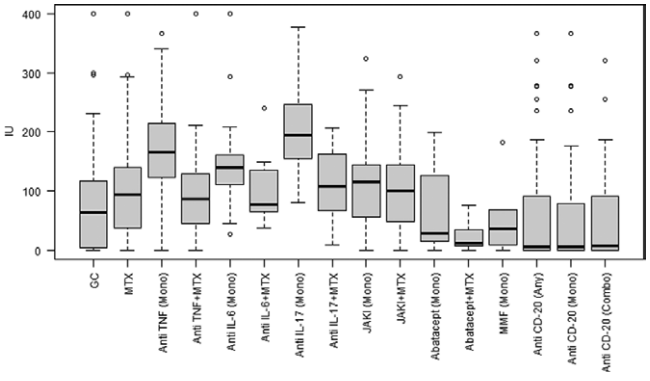


Figure 1. Seropositivity rate by immunosuppressive treatment.

There were no post-vaccination symptomatic cases of COVID-19 among AIIRD patients and one mild case in the control group. Major adverse events in AIIRD patients included death (n=2) several weeks after the second vaccine dose, non-disseminated herpes zoster (n=6), uveitis (n=2), and pericarditis (n=1). Post-vaccination disease activity remained stable in the majority of patients.

Conclusion: Vaccination with the BNTb262 vaccine resulted in an adequate immunogenic response with an acceptable safety profile in the majority of patients with AIIRD. Treatment with GC, rituximab, MMF, and abatacept may impair BNT162b2-induced immunogenicity. Postponing administration

of rituximab, when clinically feasible, seems to be reasonable to improve vaccine-induced immunogenicity. Holding treatment with abatacept and MMF may be considered on an individual basis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.5096

LB0004

EFFICACY AND SAFETY OF SECUKINUMAB IN ENTHESITIS-RELATED ARTHRITIS AND JUVENILE PSORIATIC ARTHRITIS: PRIMARY RESULTS FROM A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, TREATMENT WITHDRAWAL, PHASE 3 STUDY (JUNIPERA)

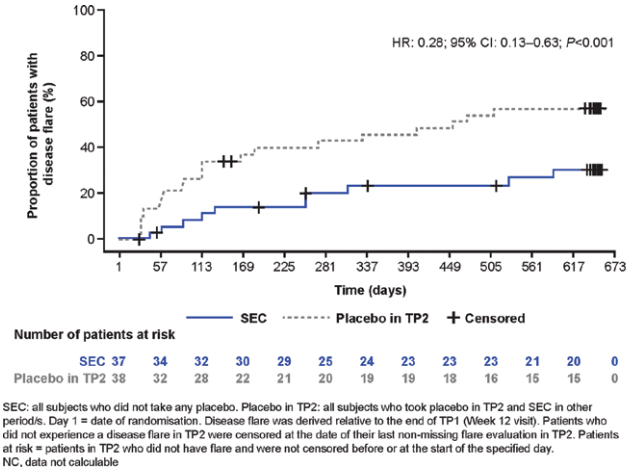
N. Ruperto[1], I. Foeldvari[2], E. Alexeeva[3], N. Aktay Ayaz[4], I. Calvo[5], O. Kasapcopur[6], V. Chasnyk[7], M. Hufnagel[8], Z. Żuber[9], G. Schulert[10], S. Ozen[11], A. Popov[12], A. Ramanan[13], C. Scott[14], B. Sözeri[15], E. Zholobova[16], X. Zhu[17], S. Whelan[18], L. Pricop[19], A. Ravelli[20], A. Martini[21], D. J. Lovell[22], H. Brunner[23]on behalf of PRCSG and PRINTO investigative sites. *[1]IRCCS Istituto G. Gaslini, Università di Genova Pediatria, Pediatrics, Genova, Italy*; *[2]Hamburger Zentrum fuer Kinder und Jugendrheumatologie, Pediatrics, Hamburg, Germany*; *[3]National Scientific and Practical Center of Children's Health, Pediatrics, Moscow, Russian Federation*; *[4]Istanbul University, Pediatric Rheumatology, Istanbul, Turkey*; *[5]Hospital Universitario i Politecnic La Fe Valencia, Pediatrics, Valencia, Spain*; *[6]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Pediatrics, Istanbul, Turkey*; *[7]St. Petersburg State Pediatric Medical Academy, Pediatrics, St. Petersburg, Russian Federation*; *[8]University of Freiburg, Pediatrics and Adolescent Medicine, Freiburg, Germany*; *[9]Wojewodzki Specjalistyczny Szpital Dzieciecy im Sw Ludwika, Pediatrics, Krakow, Poland*; *[10]University of Cincinnati, Pediatrics, Ohio, United States of America*; *[11]Hacettepe University Medical Faculty, Pediatrics, Ankara, Turkey*; *[12]Ural State Medical University, Pediatrics, Yekaterinburg, Russian Federation*; *[13]University Hospitals Bristol NHS Foundation Trust and Bristol Medical School, University of Bristol, Bristol, UK, Pediatrics, Bristol, United Kingdom*; *[14]University of Cape Town, Paediatric Rheumatology, Cape Town, South Africa*; *[15]Health Sciences University, Pediatric Rheumatology, Istanbul, Turkey*; *[16]First Moscow State Medical University, Pediatrics, Moscow, Russian Federation*; *[17]Novartis Pharmaceutical Corporation, Biostatistics, East Hanover, United States of America*; *[18]Novartis Ireland Limited, Clinical Development, Dublin, Ireland*; *[19]Novartis Pharmaceutical Corporation, Clinical Development, East Hanover, United States of America*; *[20]Istituto Giannina Gaslini, and Università degli Studi di Genova, Pediatrics, Genova, Italy*; *[21]IRCCS Istituto G. Gaslini, Università di Genova Pediatria II, Pediatrics, Genova, Italy*; *[22]Cincinnati Children's Hospital Medical Center, University of Cincinnati, Rheumatology, Cincinnati, United States of America*; *[23]University of Cincinnati, Pediatrics, Cincinnati, United States of America*

Background: Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) are two ILAR categories of juvenile idiopathic arthritis (JIA) and represent paediatric correlates of axial spondyloarthritis (axSpA) and adult psoriatic arthritis (PsA), respectively.[1,2] Secukinumab (SEC) has demonstrated efficacy and safety in adult patients (pts) with PsA, ankylosing spondylitis and non-radiographic axSpA.[3-5]

Objectives: Evaluate efficacy and safety of SEC using a flare prevention design in pts with active ERA and JPsA.

Methods: This 2-yr study consisted of an open-label (OL) s.c. SEC (75/150 mg in pts <50/ ≥50 kg) at baseline (BL), and at Weeks (Wk) 1, 2, 3, 4, 8 and 12 in treatment-period (TP) 1. Responder pts who achieved at least JIA ACR 30 response at Wk 12 were randomised into the double-blinded TP2 to continue SEC or placebo (PBO) q4w until a disease flare, or up to Wk 100. Pts (aged 2 to <18 yrs) classified as ERA or JPsA according to ILAR criteria of ≥6 months duration with active disease were included. Primary endpoint was time to flare in TP2 and key secondary endpoints were JIA ACR 30/50/70/90/100, inactive disease, JADAS, enthesitis count and safety. Analysis of time to flare in TP2 included proportion of disease flare, Kaplan-Meier (KM) estimate of median time to flare in days, hazard ratio (95% CI) from Cox model, and *P*-value for the Stratified log-rank test. KM estimates of the probability to disease flare by treatment groups in TP2 were plotted against days. Observed data were used in all analyses. Post-hoc analyses using non-responder imputation (NRI) were performed for JIA ACR 30/50/70/90/100 responses.

Results: 86/97 (89%) pts were enrolled in the OL period TP1 (mean age, 13.1 yrs; female, 33.7%; ERA, n=52; JPsA, n=34). At BL, mean JADAS-27 score was 15.1 and enthesitis count was 2.6. At the end of TP1, 90.4% (75/83) of pts achieved JIA ACR 30 and 69.9% (58/83) achieved JIA ACR 70. There were 21 and 10 flares in TP2, respectively in PBO and SEC treated pts with a significantly longer time to flare and 72% risk of flare reduction in SEC treatment vs PBO (HR: 0.28; 95% CI: 0.13–0.63; *P*<0.001) (Figure 1). JIA ACR responses, disease activity and enthesitis count are reported in Table 1. NRI analyses showed that 87.2%, 83.7%, 67.4%, 38.4% and 24.4% of pts achieved JIA ACR 30/50/70/90/100, respectively. Rates of adverse events (AEs; 91.7% vs 92.1%) and serious AEs (14.6% vs 10.5%) in SEC and PBO groups were comparable in the entire TP. No new safety signals were observed.



SEC: all subjects who did not take any placebo. Placebo in TP2: all subjects who took placebo in TP2 and SEC in other period/s. Day 1 = date of randomisation. Disease flare was derived relative to the end of TP1 (Week 12 visit). Patients who did not experience a disease flare in TP2 were censored at the date of their last non-missing flare evaluation in TP2. Patients at risk = patients in TP2 who did not have flare and were not censored before or at the start of the specified day.
NC, data not calculable

Figure 1. Time to flare in Treatment Period 2 (Primary Endpoint)

Table 1. Efficacy of secukinumab in Treatment Periods 1 and 2 (Key secondary endpoints)

	TP1	TP2[¥]		
Efficacy Outcomes, %	**SEC (N=83)[^]**	**SEC (N=37)**	**PBO (N=37)**	***P*-value**
JIA ACR 30	90.4	89.2	64.9	**0.014**
JIA ACR 50	86.7	78.4	62.2	0.152
JIA ACR 70	69.9	67.6	43.2	**0.042**
JIA ACR 90	39.8	51.4	40.5	0.431
JIA ACR 100	25.3	43.2	37.8	0.745
Inactive disease[#]	36.1	47.2	37.8	0.500
JADAS-27, mean (SD)	15.1 (7.2)	14.6 (8.1)	13.3 (5.8)	NA
Enthesitis count, mean change from BL (SD)	–1.8 (2.3)	–2.1 (2.0)	–1.9 (1.2)	NA

P-values: Cochran-Mantel-Haenszel test, adjusted for analysis factors: JIA category (ERA/JPsA) and MTX use at BL

[¥]The N numbers are values at the end of TP2

[^]Efficacy outcomes (%) in TP1 calculated in patients with evaluable data at Wk 12 (N=83)

[#]Inactive disease: Definition adapted from JIA ACR criteria of Wallace et al., 2011. N=36 for SEC at the end of TP2

JADAS, Juvenile Arthritis Disease Activity Score; N, total number of patients in the treatment group; NA, data not available

Conclusion: In children and adolescents with ERA and JPsA, efficacy of SEC was demonstrated with a significantly longer time to flare vs PBO with sustained improvement of signs and symptoms up to Wk 104 and a favourable safety profile.

REFERENCES:
[1] Colbert RA. *Nat Rev Rheumatol*. 2010;6:477–85.
[2] Martini A, et al. *J Rheumatol*. 2019;46:190–7.
[3] McInnes IB, et al. *Lancet*. 2015;386:1137–46.
[4] Baeten D, et al. *N Engl J Med*. 2015;373:2534–48.
[5] Deodhar A, et al. *Arthritis Rheumatol*. 2021;73:110–20.

Disclosure of Interests: Nicolino Ruperto Consultant of: Ablynx, Astrazeneca-Medimmune, Bayer, Biogen, Boehringer, Bristol Myers and Squibb, Celgene, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sinergie, Sobi and UCB, Grant/research support from: BMS, Eli-Lilly, GlaxoSmith-Kline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi, Speakers bureau: Ablynx, Astrazeneca-Medimmune, Bayer, Biogen, Boehringer, Bristol Myers and Squibb, Celgene, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sinergie, Sobi and UCB, Ivan Foeldvari Consultant of: Novartis, Speakers bureau: Novartis, Ekaterina Alexeeva Grant/research support from: Novartis, Pfizer, Sanofi, MSD, AMGEN, Eli Lilly, Roche, Speakers bureau: Novartis, Pfizer, Sanofi, MSD, AMGEN, Eli Lilly, Roche, NURAY AKTAY AYAZ: None declared, Inmaculada Calvo Consultant of: Sobi, Novartis, Abbvie, GlaxoSmithKline, Pfizer, Amgen, Clementia, Speakers bureau: Sobi, Novartis, Abbvie, GlaxoSmithKline, Pfizer, Amgen, Clementia, Ozgur KASAPCOPUR: None declared, Vyacheslav Chasnyk: None declared, Markus Hufnagel Grant/research support from: Astellas, F. Hoffmann-La Roche, Novartis, Zbigniew Żuber: None declared, Grant Schulert Consultant of: Sobi, Novartis, Seza Ozen: None declared, Artem Popov: None declared, Athimalaipet Ramanan Speakers bureau: Roche, Sobi, Eli Lilly, UCB, Novartis, Christiaan Scott: None declared, Betül Sözeri: None declared, Elena Zholobova Grant/research support from: Pfizer, Novartis, Speakers bureau: Abbvie, Pfizer, Roche, Novartis, Xuan Zhu Employee of: Novartis, sarah whelan Employee of: Novartis, Shareholder of: Novartis, Luminita Pricop Employee of: Novartis, Shareholder of: Novartis, Angelo Ravelli Consultant of: Abbvie, Bristol-Myers Squibb, Pfizer, Hoffmann-LaRoche, Novartis, Centocor, Angelini Holding, Reckitt Benckiser, Speakers bureau: Abbvie, Bristol-Myers Squibb, Pfizer, Hoffmann-LaRoche, Novartis, Centocor, Angelini Holding, Reckitt Benckiser, Alberto Martini Consultant of: Eli Lilly, EMD Serono, Janssen, Novartis, Pfizer, Abbvie, Speakers bureau: Eli Lilly, EMD Serono, Janssen, Novartis, Pfizer, Abbvie, Daniel J Lovell Consultant of: AstraZeneca, Wyeth, Amgen, Abbott, Pfizer, Hoffmann-La Roche, Novartis, UBC, Takeda, Janssen, GlaxoSmithKline, Boehringer Ingelheim, Celgene, Bristol Myers Squibb, AbbVie, Forest Research, Speakers bureau: AstraZeneca, Wyeth, Amgen, Abbott, Pfizer, Hoffmann-La Roche, Novartis, UBC, Takeda, Janssen, GlaxoSmithKline, Boehringer Ingelheim, Celgene, Bristol Myers Squibb, AbbVie, Forest Research, Hermine Brunner Consultant of: Aurina, AbbVie, Astra Zeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Celgene, Eli Lilly, EMD Serono, GlaxoSmithKline, F. Hoffmann-La Roche, Merck, Novartis, R-Pharm, Sanofi, Pfizer, Grant/research support from: Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, F. Hoffmann-La Roche, Janssen, Novartis, and Pfizer, Speakers bureau: Pfizer, Roche and GlaxoSmithKline

DOI: 10.1136/annrheumdis-2021-eular.5038

Poster Tours

Adaptive immunity (T cells and B cells) in rheumatic diseases

POS0001 PHENOTYPE AND FUNCTIONAL CHARACTERISTICS OF ANTIGEN-SPECIFIC, AUTO-REACTIVE B CELL RESPONSES REVEAL DIFFERENTIAL IMMUNOLOGICAL ACTIVITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

C. Wortel[1], N. Van Leeuwen[1], S. Liem[1], M. Boonstra[1], C. Fehres[1], T. Huizinga[1], R. Toes[1], J. De Vries-Bouwstra[1], H. U. Scherer[1]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*

Background: Systemic Sclerosis (SSc) is a systemic autoimmune disease that carries the highest mortality burden among the rheumatic diseases. Disease risk and course are difficult to predict in individual patients, and anti-inflammatory and B-cell depleting therapies show varying results. >95% of SSc patients harbor autoantibodies. Among those, anti-topoisomerase antibodies (ATA) and anti-centromere antibodies (ACA) are most prevalent, mutually exclusive in individual patients and associate with distinct disease phenotypes. Despite these associations, the clinical value of both ATA and ACA for patient stratification within these phenotypes is limited. Here, we hypothesized that phenotypic and functional characteristics of the underlying autoreactive B cell responses could allow insights in differential 'immunological disease activity' in individual patients, thereby providing indications as to potential drivers of these responses as well as granularity as to which patients may benefit from targeted interventions.
Objectives: To assess phenotypic and functional characteristics of anti-topoisomerase and anticentromere specific B cell responses in individual patients with SSc.
Methods: Peripheral blood mononuclear cells (PBMC) from ATA- and ACA-positive SSc patients were cultured without stimulation or in the presence of CD40L-expressing fibroblasts, IL-21 and BAFF. Following culture, ATA- and ACA-IgG and -IgA were measured in culture supernatants by ELISA. In addition, PBMC were depleted of circulating plasmablasts by fluorescence activated cell sorting (FACS), and isolated plasmablasts were cultured separately. Furthermore, the presence of antigen-specific plasmablasts was confirmed by ELISPOT. Finally, the degree of spontaneous ATA secretion was correlated to the presence or absence of interstitial lung disease (ILD; based on high-resolution computed tomography). Healthy donors and patients with rheumatoid arthritis served as controls.
Results: We observed that individual ATA- and ACA-positive SSc patients harbored circulating B cells that secrete either ATA-IgG or ACA-IgG upon stimulation, depending on their serotype. In addition, we noted spontaneous secretion of ATA-IgG and, more remarkably, extensive secretion of ATA-IgA in ATA-positive patients. This degree of spontaneous, antigen-specific IgA secretion was specific for the ATA response, while spontaneous ACA-IgA secretion was undetectable in patients harboring ACA. FACS experiments and ELISPOT showed that the spontaneous ATA-IgA and -IgG secretion was attributable to circulating plasmablasts. Of note, the degree of spontaneous ATA-IgG secretion was remarkably higher in patients with ILD than in those without.
Conclusion: Our findings demonstrate that individual ATA-positive SSc patients harbor activated ATA-IgG and ATA-IgA B cell responses, as indicated by the spontaneous secretion of both ATA isotypes by circulating plasmablasts. Importantly, by taking the presence of plasmablasts as a proxy for recent B cell activation, our data suggest a link between the activity of the antigen-specific B cell response and the presence of ILD. In contrast, the ACA B cell response was far less active and lacked the active IgA component, which suggests a difference in the triggers driving these autoreactive B cell responses in patients. In fact, the remarkable ATA-IgA secretion points towards a potential mucosal trigger of the ATA response, which may be continuously active in individual patients.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4161

POS0002 PI16 REPRESSES FOXP3 EXPRESSION IN T REGULATORY CELLS AND EXACERBATES AUTOIMMUNE ARTHRITIS VIA INHIBITING THE K48-LINKED POLYUBIQUITIN DEGRADATION OF BMI-1

S. Lin[1], X. Gu[1,2], F. Wang[3], W. Tan[1]. [1]*The First Affiliated Hospital of Nanjing Medical University, China, Department of Rheumatology, Nanjing, China;* [2]*The Affiliated Hospital of Jiangnan University, Department of Cardiology, Wuxi, Jiangsu, China;* [3]*The First Affiliated Hospital of Nanjing Medical University, China, Department of Cardiology, Nanjing, China*

Background: Regulatory T cells (Tregs) play an essential role in maintaining self-tolerance and immune homeostasis. Abnormalities in the quantity or function of Treg cells are believed in RA patients, contributing to the inability to suppress autoimmunity and proinflammatory cytokines. Forkhead box P3 (Foxp3) is a crucial transcription factor for the development and differentiation of Tregs. How Tregs lose Foxp3 expression under inflammatory milieu remains largely unknown. Peptidase inhibitor 16 (PI16) is a member of the CAP (Cysteine-rich secretory proteins, Antigen 5, and Pathogenesis-related 1) protein family and its function are largely poor understood. In a genome-wide expression profiling study for identifying human Foxp3 target genes revealed PI16 was expressed on the cell surface of >80% of resting human $CD25^+$ $Foxp3^+$ Tregs. In the inflamed joint of juvenile idiopathic arthritis revealed a low number of $PI16^+$ Tregs but high number of Th17 cells. However, little is known the function role of PI16 on Tregs or on RA development.
Objectives: To investigate the role of peptidase inhibitor 16 (PI16) on the key T regulatory (Tregs) cells transcription factor Foxp3 expression and on the development of autoimmune arthritis.
Methods: The expression of PI16 in blood, synovial fluid, inflamed joints were examined in Rheumatoid arthritis (RA) patients and in arthritic mice. Arthritis symptom, histological features and Foxp3 expression in PI16 transgenic ($PI16^{Tg}$) arthritic mice were examined. Posttranslational mechanisms on PI16-mediated Foxp3 expression were analyzed. The specific role PI16 on Foxp3 expression was validated in conditional knockout (KO) mice.
Results: The expression of PI16 was significantly increased in PBMC, serum, synovial tissue from RA patients or arthritic mice compared with controls. $PI16^{Tg}$ arthritic mice exhibited obvious inflammation, synovial hyperplasia and articular cartilage destruction in the joints compared with those in wild-type mice (WT) arthritic mice.
Foxp3 is downregulated in splenic T cells and synovial tissue from $PI16^{Tg}$ arthritic mice. Naïve T cells derived from $PI16^{Tg}$ arthritic mice showed the decreased capacity to differentiate into Tregs. Polycomb-group (PcG) proteins complex molecule of Bmi-1 was significant increase in Tregs and joint tissue from $PI16^{Tg}$ arthritic mice. A direct interaction between 1-95AA domains of PI16 and 169 and 436 domains of Bmi-1 in Tregs promoter was observed. The binding of PI16 with Bmi-1 in the Foxp3 promoter inhibit the K48-linked polyubiquitin degradation of Bmi-1 at lysine site 72 and 153 region, which prompts the repressive histone modification of H3K27me3 and H2AK119ub, and inhibits the active histone modification of H3K4me3. Furthermore, conditional knockout of PI16 in Tregs retarded Foxp3 loss and blunted disease progression in experimental arthritis.
Conclusion: PI16 represses Foxp3 expression by mediating histone modification via inhibiting K48-linked polyubiquitin degradation of Bmi-1 in Foxp3 promoter, contributing to disease progression in arthritic mice.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2756

POS0003 RITUXIMAB THERAPY IN SYSTEMIC LUPUS ERYTHEMATOSUS – TRANSIENT EFFECTS ON AGE ASSOCIATED B-CELLS

F. Faustini[1,2], N. Sippl[1], R. Stålesen[1], K. Chemin[1], I. Gunnarsson[1,2], V. Malmström[1]. [1]*Karolinska Institutet, Department of Medicine, Solna, Division of Rheumatology, Centre of Molecular Medicine, Stockholm, Sweden;* [2]*Karolinska University Hospital, Rheumatology, Stockholm, Sweden*

Background: Immune system's abnormalities in SLE involve several subsets of the B-cell compartment, including double negative B-cells (DN) and CD11c+CD21- B cells (also referred to as ABC-age associated B cells), which are expanded in the disease. ABC cells are also known to interact with T helper cells, T follicular and peripheral helper cells (1). Rituximab, a chimeric anti- CD20 antibody, depleting B cells, is commonly used off-label as treatment for SLE patients, especially in lupus nephritis. Little is known on the impact of B-cell depletion on such B-cell subsets and on B-T-cell interactions.
Objectives: to investigate the effects of rituximab (RTX) on the frequencies of double negative B-cell subsets and CD11c+CD21- ABC cells and as well as T follicular helper (T_{FH}, CXCR5+ PD-1+) and T peripheral helper (T_{PH}, PD-1^{high}) CD4+ T-cell subsets.
Methods: 15 SLE patients, starting RTX and followed longitudinally up to two years, were analyzed for lymphocyte subsets using multicolor flow cytometry. Cryopreserved PBMC were thawed and stained at the same time together with one buffy coat. Around 1 x 10^6 PBMC for each panel were labeled and further stained with fluorescent antibodies for B and T-cell markers. For the B-cell panel, PBMC were stained with anti-CD3, CD14, CD16, CD19, IgD, CD27, CD38, CD11c, CD21 and in some samples with anti-CXCR5 antibodies. For the T-cell panel, PBMC were labeled with anti-CD16, CD14, CD19 and CD3, CD4, CD8,

PD-1, CCR7, CXCR5, CD45RA antibodies. All patients fulfilled the ACR 1982 classification criteria for SLE. Cellular changes were analyzed in the context of clinical information.

Results: in the present cohort, the SLE patients were mainly female (86.6%) and of median age of 36.7 (29.8-49.4) with a disease duration of 6.1(1.6-11.8) years, and active disease with SLEDAI-2K at baseline 12.0 (8.0-16.0). The frequency of age-associated B cells (ABCs; CD27-IgD-CD11c+ CD21-) decreased by 13% (p=0.03) in the first two to four months after rituximab start, while globally the DN (IgD-CD27-) B cells transiently increased by around 3% (p=0.15) at the first follow-up. This increase could not be attributed to the DN1 (CXCR5+CD11c-) or DN2 (CXCR5-CD11c+) subsets but to the CD11c-CXCR5- DN (DN3) B cells (increase= 6.7%, p=0.03). In parallel, T effector cells (CCR7- CD45RA+) and TEMRA (CD45RA+ CCR7-) frequencies increased after first follow up in both CD4+ and CD8+ T cells. The frequency of T_{FH} (CXCR5+ PD-1+) cells did not change after rituximab, however a decrease of PD-1^{high} CD4+ cells was observed in most patients, although not significant, after 2-4 month of treatment. In most patients the frequency of PD-1^{high} CD4+ cells either reduce or stay the same after RTX treatment (reduction= 0.53, p=0.28). After 11-15 months of RTX treatment the frequency of PD-1^{high} CD4+ T cell reduces by a -0.5% in comparison to 2-4 months (p=0.039). The SLEDAI at baseline did not correlate with the frequency of PD-1^{high} CD4+ T cells (r=0.03, p=0.9).

Conclusion: the importance of T cell - B cell interactions in SLE pathogenesis was recently strengthened by the identification of the lymphocyte subsets T_{FH}/T_{PH} and ABCs respectively. Here, in the context of rituximab treated SLE, we could detect a reduction in the frequencies of both ABCs and PD-1^{high} T cells after treatment with rituximab, while the DN3 and effector memory T cells frequencies increased. Our data suggests that anti-CD20 mediated B-cell depletion affects both B-cell and T-cell subsets frequencies, and that monitoring these specific cell subsets may be clinically relevant.

REFERENCES:

[1] Bocharnikov AV, Keegan J, Wacleche VS, Cao Y, Fonseka CY, Wang G, et al. PD-1hiCXCR5- T peripheral helper cells promote B cell responses in lupus via MAF and IL-21. JCI insight. 2019;4(20)

Disclosure of Interests: Francesca Faustini Speakers bureau: More than two years ago and not in relation to any aspect of the present research, Natalie Sippl: None declared, Ragnhild Stålesen: None declared, Karine Chemin: None declared, Iva Gunnarsson: None declared, Vivianne Malmström: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2366

POS0004 T-CELL REPERTOIRE OF SYNOVIAL FLUID IN SPONDYLOARTHROPATHIES EXHIBITS HALLMARKS OF HLA-DEPENDENT CLONAL EXPANSIONS AND REMAINS STABLE OVER 1.5 YEARS

E. Komech[1], A. Koltakova[2], E. Shmidt[3], A. Barinova[1,4], M. Salnikova[1], A. Minervina[1], T. Korotaeva[2], Y. Lebedev[1], I. Zvyagin[1,4]. *[1]Shemaykin-Ovchinnikov Institute of Bioorganic Chemistry, Laboratory of Comparative and Functional Genomics, Moscow, Russian Federation; [2]Nasonova Research Institute of Rheumatology, Lab of Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation; [3]Pirogov Russian National Research Medical University, City Clinical Hospital #1, Moscow, Russian Federation; [4]Pirogov Russian National Research Medical University, Institute of Translational Medicine, Moscow, Russian Federation*

Background: Different studies show involvement of T-cells in pathogenesis of spondyloarthropathies (SpAs) - a group of rheumatic diseases strongly associated with presence of several MHC-I alleles (HLA-B*27, -B*38, -B*39, etc). Recently we and others identified a specific T-cell receptor motif in blood and synovial fluid of HLA-B*27+ AS patients that reinforces the “arthritogenic peptide” hypothesis of AS pathogenesis [1-2]. However, common characteristics of clonal T-cell repertoire of synovial fluid in SpAs remain poorly investigated.

Objectives: We aimed to investigate synovial fluid T-cell repertoires of SpA patients with different HLA-genotypes and stability of the clonal composition in recurring flares of the disease.

Methods: Mononuclear cells were isolated from paired peripheral blood (PB) and synovial fluid (SF) samples of SpA patients (ankylosing spondylitis and psoriatic arthritis, n=27). For 3 patients additional SF samples were collected during relapse of the synovitis (after 9-15 months). CD4 and CD8 T-cells were isolated by immunomagnetic separation. Deep sequencing of UMI-tagged TCR beta cDNA libraries was used to accurately reconstruct clonal T-cell repertoires. HLA class I and II were typed for each donor using an in-house NGS-based system.

Results: We observed restricted T-cell clonal composition in synovial fluid: on average only 6% of PB T-cell clonotypes were detected in SF of the same donor. T-cell repertoires of both CD4 and CD8 SF subsets compared to PB were highly oligoclonal (index Gini PB vs SF: CD4 0.36±0.10 vs 0.68±0.08, CD8 0.57±0.17 vs 0.81±0.12) in all patients. Number of identical amino acid CDR3 sequences between two repertoires correlated with the number of identical HLA-alleles for the donors. This trend was exhibited more strikingly in SF compared to PB, suggesting that common antigens may play a role in accumulation of identical T-cell clonotypes in the inflamed joint. Using several bioinformatic approaches we identified groups of highly similar SF clonotypes linked to HLA-B*27 and/or HLA-B*38 genotype.

Total SF repertoires of relapsing synovitis of the same donor showed huge clonal overlap, and the most frequent clonotypes remained almost unchanged (Morisita’s overlap index for total SF repertoires 0.69±0.26; for top 1000 clonotypes 0.79±0.19, n=3).

Conclusion: We report HLA-dependent sharing of identical and similar T-cell clonotypes in SF of patients with ankylosing spondylitis and psoriatic arthritis and high stability of SF repertoire during several flares that support antigen-driven accumulation of T-cells in the site of inflammation.

REFERENCES:

[1] Komech EA et al. *Rheumatology (Oxford)*. 2018;57(6):1097-1104.
[2] Faham M et al. *Arthritis Rheumatol*. 2016;11(10):300-308.

Acknowledgements: The work is supported by Russian Science Foundation grant №20-75-00041.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3498

POS0005 THE EFFECT OF LKB1 INHIBITION IN RA PATHOGENESIS

H. R. Lee[1,2], J. Kim[2], S. J. Yoo[2], J. A. Park[2], S. W. Kang[1,2]. *[1]Chungnam National University School of Medicine, Research Institute for Medical Sciences, Daejeon, Korea, Republic of (South Korea); [2]Chungnam National University Hospital, Department of Internal Medicine, Daejeon, Korea, Republic of (South Korea)*

Background: Liver kinase B1 (LKB1) is known as a tumor suppressor gene and also inhibits reactive oxygen species (ROS) levels. Intracellular ROS are catalyzed by the enzyme complex nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX). We previously reported that NOX4 induced the migration and invasion of fibroblast-like synoviocytes (FLS) in rheumatoid arthritis (RA). Although LKB1 is expected to alleviate synovial inflammation through ROS regulation, the role of LKB1 in RA has not been examined.

Objectives: To explore whether LKB1 affects RA inflammation, we transfected LKB1 siRNA and analyzed related gene expressions in RA FLS.

Methods: Synovial tissues were obtained from RA patients who were undergoing synovectomy or joint replacement. The isolated cells were cultured in Dulbecco’s modified Eagle’s medium (DMEM) supplemented with 10% fetal bovine serum, 100 U/ml penicillin and 100 mg/ml streptomycin and maintained in a 5% CO_2 incubator at 37 °C. FLS were used for experiments after four to six passages. Cells were transfected with lipofectamine transfection reagent and LKB1 siRNA duplex targeting constructs. After incubation for 24 h, downregulation of target expression was evaluated by real-time PCR and western blot analysis.

Results: RA FLS was transfected with LKB1 siRNA and 90% of LKB1 mRNA expression was decreased. LKB1 knock-down also caused the decreased expression of mechanistic target of rapamycin (mTOR; 0.38 fold) and serine/threonine kinase (AKT) 2 (0.40 fold), which are downstream targets of LKB1. NOX4 was significantly increased (4.94 fold) by LKB1 inhibition. On the other side, the down regulated NOX4 induced significantly elevated LKB1 mRNA expression in RA FLS. When the expressions of proinflammatory cytokines were examined, IL-1β, IL-6, TNF-α were highly increased by LKB1 deficiency. FLS migration-related chemokines, IL-8 and MMP-3 were also enhanced compared to control.

Conclusion: There was a negative correlation between NOX4 and LKB1 in RA FLS. As LKB1 deficiency induced the expression of proinflammatory cytokines and migration related chemokines, LKB1 could play a critical role in RA pathogenesis.

REFERENCES:

[1] Bartok B, Firestein GS. Fibroblast-like synoviocytes: key effector cells in rheumatoid arthritis. Immunol Rev. 2010;233(1):233–55.
[2] Mateen S, Moin S, Khan AQ, Zafar A, Fatima N. Increased reactive oxygen species formation and oxidative stress in rheumatoid arthritis. PLoS One. 2016;11(4):e0152925.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.946

POS0006 NX-5948, A SELECTIVE DEGRADER OF BTK, SIGNIFICANTLY REDUCES INFLAMMATION IN A MODEL OF AUTOIMMUNE DISEASE

D. Robbins[1], M. Noviski[2], M. Tan[3], C. Guiducci[2], T. Ingallinera[4], D. Karr[4], A. Kelly[2], Z. Konst[1], A. Tenn-Mcclellan[2], J. Mckinnell[4], L. Perez[2], G. Hansen[5], R. Rountree[2]. *[1]Nurix Therapeutics, Medicinal Chemistry, San Francisco, United States of America; [2]Nurix Therapeutics, Discovery Biology, San Francisco, United States of America; [3]Nurix Therapeutics, Translational Medicine, San Francisco, United States of America; [4]Nurix Therapeutics, Preclinical*

Development, San Francisco, United States of America; [5]Nurix Therapeutics, Nurix Therapeutics, San Francisco, United States of America

Background: Aberrant activation of B cells and autoantibody mediated tissue damage are hallmarks of autoimmune diseases such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Therefore, novel treatments that prevent autoantibody generation or antibody-mediated end organ tissue damage are of high interest. Bruton's tyrosine kinase (BTK) transduces signals downstream of the B cell receptor (BCR), toll-like receptors, and Fc receptors in B cells and myeloid cells [1]. Overexpression of BTK in B cells leads to hyperactive BCR signaling, plasma cell generation, autoantibody secretion, and an SLE-like disease in mice [2]. Conversely, reducing BTK expression in B cells can ameliorate disease in Lyn-deficient mice.[3] BTK inhibitors, such as evobrutinib, have entered clinical studies for the treatment of autoimmune diseases.[4]

Objectives: Small molecule-induced protein degradation offers a unique approach to target BTK; this approach simultaneously eliminates both BTK kinase activity and BTK-mediated scaffolding interactions in the signalosome. Chimeric Targeting Molecules (CTMs) are small molecules that catalyze ubiquitylation and proteasomal degradation of target proteins and are comprised of a ubiquitin ligase binding element ("harness"), a linker, and a target binding element ("hook"). NX-5948 is a CTM that contains a BTK hook linked to a cereblon (CRBN) harness. We examined the activity of NX-5948 in a collagen-induced arthritis model as part of an assessment of its potential as a drug candidate for autoimmune disease.

Methods: Cellular degradation of BTK, Aiolos and Ikaros as well as induction of CD69 and CD86 was determined using flow cytometry. Degradation of BTK in CD-1 mice or cynomolgus monkey was determined using flow cytometry analysis. In a collagen-induced arthritis (CIA) model, mice were vaccinated with type II collagen and treated before the onset of symptoms. Serum cytokine and anti-type II collagen antibody levels were determined using Luminex and ELISA, respectively.

Results: In human PBMCs, NX-5948 degrades BTK at sub-nanomolar concentrations and inhibits BCR signaling as measured by CD69 and CD86 induction in anti-IgM-stimulated B cells with similar potency. Oral administration of NX-5948 in mice leads to BTK degradation to <10% of baseline levels in circulating and splenic B cells. NX-5948 also promotes potent BTK degradation in cynomolgus monkeys, and it can suppress BTK levels to <10% of baseline levels after a single oral dose as low as 10 mg/kg.

Unlike IMiD drugs such as lenalidomide, the CRBN harness of NX-5948 was designed to avoid the degradation of known CRBN neo-substrates Aiolos (IKZF3) and Ikaros (IKZF1). In primary human T cells, NX-5948 induces minimal degradation of Aiolos and Ikaros and does not promote IL-2 secretion suggesting that NX-5948 does not convey IMiD activity associated with agents such as lenalidomide.

We examined the activity of NX-5948 in a mouse CIA model compared to that of the BTK inhibitor ibrutinib or dexamethasone as a positive control. In mice treated with NX-5948, symptoms of arthritis were resolved, and a significant reduction in arthritis clinical score was observed. Treatment with NX-5948 resulted in a reduction in anti-type II collagen titer and serum levels of the pro-inflammatory cytokine IL-6. Treatment with NX-5948 yielded superior anti-inflammatory activity relative to ibrutinib and similar activity to dexamethasone. Treatment with NX-5948 was well-tolerated and, unlike dexamethasone, did not promote body weight loss.

Conclusion: Degradation of BTK by NX-5948 shows robust activity in a CIA model compared to existing agents tested as controls. These findings provide support for further investigation of NX-5948 in additional models of autoimmune disease to inform plans for clinical development.

REFERENCES:

[1] Crofford et al. 2016. Expert Rev Clin Immunol 12: 763–773.
[2] Kil et al. 2012. Blood 119: 3744-3756.
[3] Whyburn et al. 2003. J Immunol 171: 1850-1858.
[4] Haselmayer, et. Al. 2019. J Immunol 202: 2888-2906.

Disclosure of Interests: DANIEL ROBBINS Shareholder of: Nurix therapeutics, Employee of: Nurix therapeutics, Mark Noviski Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, May Tan Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, Cristiana Guiducci Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, Timothy Ingallinera Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, Dane Karr Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, Aileen Kelly Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, Zef Konst Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, Austin Tenn-McClellan Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, Jenny McKinnell Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, Luz Perez Employee of: Nurix Therapeutics, Gwenn Hansen Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics, Ryan Rountree Shareholder of: Nurix Therapeutics, Employee of: Nurix Therapeutics

DOI: 10.1136/annrheumdis-2021-eular.1675

POS0007

LOSS OF BALANCE BETWEEN PROTECTIVE AND PRO-INFLAMMATORY SYNOVIAL TISSUE T CELL POLYFUNCTIONALITY PREDATES CLINICAL ONSET OF RHEUMATOID ARTHRITIS

A. Floudas[1], N. Neto[2], M. Canavan[1], T. Mcgarry[1], V. Krishna[3], S. Nagpal[3], M. Monaghan[2], D. Veale[4], U. Fearon[1]. *[1]Trinity Biomedical Sciences Institute, Molecular Rheumatology, Dublin, Ireland; [2]Trinity Biomedical Sciences Institute, Mechanical and Manufacturing Engineering, Dublin, Ireland; [3]Janssen Research & Development, Immunology, Spring House, United States of America; [4]St Vincent's University Hospital, UCD, EULAR Centre of Excellence, Centre for Arthritis and Rheumatic Diseases, Dublin, Ireland*

Background: Effective treatment of Rheumatoid arthritis (RA) patients is achievable within a short window of opportunity following diagnosis. T-cells are early drivers of synovial inflammation of RA, therefore, identification of pathogenic T-cell subsets at the synovial tissue of pre-RA, arthralgia subjects, would greatly improve our understanding of disease pathogenesis. Comparative analysis of healthy control, arthralgia subject and RA-patient derived synovial tissue T-cell responses will lead to the identification of pathogenic as well as protective cytokine milieu, thus enabling the identification of early therapeutic targets to help steer the immune response towards resolution.

Objectives: Characterization of T-cell polyfunctionality in the periphery and synovial tissue of 'at-risk; subjects (Arthralgia) RA-patients and healthy controls (HC).

Identification of specific, pathogenic, synovial tissue T-cell subsets.

Methods: Synovial biopsies from RA, AR and HC were obtained by arthroscopic surgery followed by RNAseq analysis (Guo et al., PLoS One, 2018). Single cell synovial tissue cell suspensions from RA, AR and HC and paired PBMC were stimulated *in vitro* and polyfunctional synovial T-cell subsets examined by flow cytometric analysis, SPICE visualization and FlowSom clustering. Flow-Imaging, was utilised to confirm specific T-cell cluster identification. Fluorescent Lifetime Imaging Microscopy (FLIM) was used to visualise metabolic status of specific T-cell populations.

Results: T-cell associated pro-inflammatory gene pathways were increased in RNAseq analysis of RA-patient and arthralgia subject compared to HC synovial tissue biopsies. Flow cytometric analysis of pro-inflammatory cytokine (TNF-α, IFN-γ, IL-2, GM-CSF, IL-17A, IL-22) production and SPICE analysis of *ex vivo* stimulated T-cells revealed marked polyfunctionality of arthralgia subject synovial T-cells, thus providing evidence for a dysregulated synovial T-cell response that pre-dates clinical onset of disease. Importantly, HC synovial tissue harbours a small, albeit surprisingly polyfunctional, CD4 T-cell population characterised

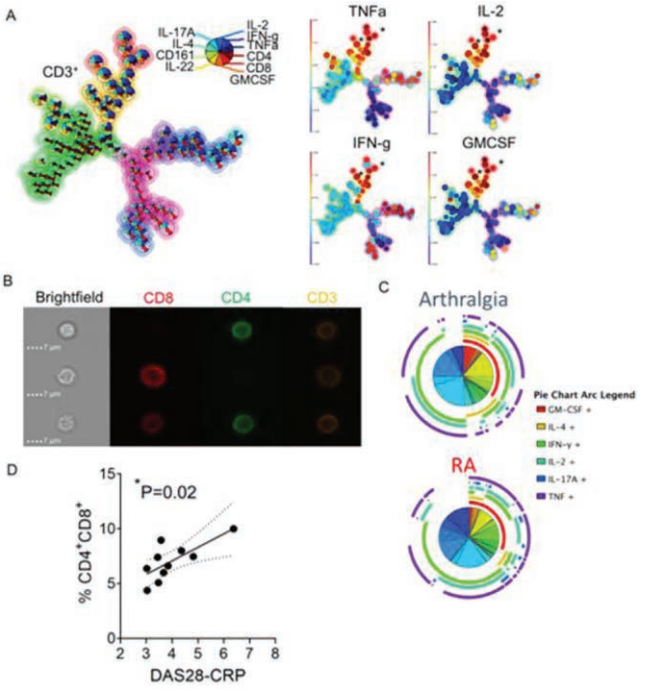


Figure 1. Identification of highly polyfunctional and pro-inflammatory synovial DP T-cells. A. Cluster analysis of RA-patient synovial tissue T-cells (asterisks indicate DP T-cell clusters). B. Flow imaging of $CD4^+$, $CD8^+$ and DP synovial T-cells. C. SPICE flow cytometric data visualization of DP arthralgia subject and RA-patient synovial T-cells. D. Correlation between the frequency of RA-patient synovial DP T-cells and disease severity.

by significantly increased IL-4 and GM-CSF cytokine production compared to arthralgia subject (P<0.001 and P=0.01) and RA-patient (P<0.001 and P=0.004) synovial tissue. However, not all polyfunctional T-cells are equal in their pathogenic potential. Therefore, in order to identify highly pathogenic synovial T-cells, cluster analysis of flow cytometric data using the unsupervised algorithm FlowSom was performed and led to the identification of specific T-cell clusters with unique polyfunctionality characteristics. Specifically a cluster of $CD4^+CD8^+$ double positive (DP) T-cells with high polyfunctionality scores was identified. Hybrid flow cytometry and imaging technique confirmed the co-expression of CD4 and CD8 by a synovial T-cell population. DP T-cells are enriched in RA-patient synovial fluid and synovial tissue and arthralgia subject synovial tissue, but are absent from HC synovial tissue. Importantly, DP T-cell synovial accumulation strongly (P=0.002) correlates with DAS28(CRP) of RA-patients. Initial studies utilising the novel, non-invasive FLIM technique for visualisation of cellular NAD, revealed that DP T-cells have a metabolic profile indicative of activated memory T-cells.

Conclusion: These data highlight a key early loss of balance between protective and pathogenic synovial T-cell polyfunctionality and the emergence of specific, highly polyfunctional and pathogenic T-cell clusters in RA.

Disclosure of Interests: Achilleas Floudas: None declared, Nuno Neto: None declared, Mary Canavan: None declared, Trudy McGarry Employee of: Novartis, Vinod Krishna Employee of: Janssen, Sunil Nagpal Employee of: Janssen, GSK, Michael Monaghan: None declared, Douglas Veale Speakers bureau: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Consultant of: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Grant/research support from: Janssen, Abbvie, Pfizer, UCB, Ursula Fearon Speakers bureau: Abbvie, Grant/research support from: Janssen, Abbvie, Pfizer, UCB.

DOI: 10.1136/annrheumdis-2021-eular.2220

POS0008 IDENTIFICATION AND CHARACTERIZATION OF HISRS+ CD4+ T CELLS PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

B. Horuluoglu[1], A. S. Galindo-Feria[1], K. Chemin[1], G. Kozhukh[1,2], A. Dubnovitsky[1,2], V. Malmström[1], I. E. Lundberg[1]. *[1]Karolinska Insitutet, Division of Rheumatology, Center for Molecular Medicine, Department of Medicine, STOCKHOLM, Sweden; [2]Karolinska Insitutet, Science for Life Laboratory, Department of Medicine, Stockholm, Sweden*

Background: Idiopathic inflammatory myopathies (IIM) also known as myositis, are rare chronic autoimmune disorders which are represented by muscle weakness and extra-muscular features such as skin rash, interstitial lung disease (ILD) and arthritis. One of the most common autoantibodies in myositis, with a prevalence of 25-35%, is the anti Jo-1 autoantibodies, targeting the histidyl-transfer RNA synthetase (HisRS). Although the exact mechanism of how these antibodies are developed is unknown, we have previously shown that upon stimulation of both peripheral blood mononuclear cells (PBMC) and bronchoalveolar lavage fluid cells (BALF) with HisRS protein, $CD4^+$ T cells were activated and produced inflammatory cytokines. Hitherto the presence of antigen specific autoreactive T cells has not been established in myositis, however previous studies by our group showed a strong indication of their presence with a reactivity to a specific HisRS peptide.

Objectives: The main aim of this project is to detect and characterize HisRS specific $CD4^+$T cells using HLA Class II tetramers. HLA Class II tetramers allow the detection of rare antigen specific CD4+ T cells and are widely used in studies of immunity, vaccine development, allergy monitoring and in autoimmunity. These cells are of specific interest to understand autoimmunity and to develop new therapies in autoimmune diseases

Methods: HLA-DRB1*03:01 monomers with selected tetanus and HisRS peptides were in-house in *E.coli* system. The peptides of interest were attached to the N-terminus of the HLA b-chain *via* a flexible peptide linker. HLA-tetramers were assembled using a commercial fluorescently labeled streptavidin. The efficacy of the peptide-HLA tetramers was validated by stimulating PBMCs from HLA-matched healthy controls with tetanus peptide. The drequency of tetanus specific $CD4^+$ T cells were detected at different time points (6,13 and 21 days) from the cultures using tetanus peptides bound HLA-DRB1*0301 tetramers. The presence of tetanus specific T cells was confirmed by the secretion of significantly higher IFNg levels upon re-stimulation of cells with tetanus peptide. The same protocol is applied for the HisRS-peptide tetramers. Peripheral blood cells are analysed from anti-Jo1+ and HLA-DRB1*0301 positive patients with IIM.

Results: Applying this method, our preliminary findings demonstrate the presence of $HisRS^+CD4^+$ T cells in peripheral blood from Jo-1+ patients (n=3) using HisRS tetramers following stimulation with the respective peptide. We are now including more patient samples to confirm our findings, and further characterize their phenotype and functionalities by flow cytometry and ELISA/fluorospot assays

Conclusion: Myositis is a rare and chronic autoimmune disorder, with no currently available cure. Previous studies indicate the importance of T cells in this disease. However, the phenotype, functionality and role of these cells in the disease pathogenesis has not been fully established. Characterization of this autoreactive T-cell population will help us enhance our understanding of the disease pathogenesis and thus to develop better treatment options.

Acknowledgements: This work has been supported by grants from Karolinska Instiutet Resarch Foundation, Professor Nanna Svartz Stiftelse, Hjärt-Lung Fonden and Vetenskapsrådet in Sweden.

Disclosure of Interests: Begum Horuluoglu: None declared, Angeles Shunashy Galindo-Feria: None declared, Karine Chemin: None declared, Genadiy Kozhukh: None declared, Anatoly Dubnovitsky: None declared, Vivianne Malmström: None declared, Ingrid E. Lundberg Consultant of: Consulting fees from Corbus Pharmaceuticals, Ind, Grant/research support from: Research grants from Bristol Myers Squibb and Astra Zeneca.

DOI: 10.1136/annrheumdis-2021-eular.3583

POS0009 THE RELATIONSHIP BETWEEN DIFFERENT IGG AND IGA ANTI-MODIFIED PROTEIN AUTOANTIBODIES IN RHEUMATOID ARTHRITIS

C. Grönwall[1], L. Liljefors[1], H. Bang[2], A. Hensvold[1], M. Hansson[1], L. Mathsson-Alm[3], L. Israelsson[1], A. Svärd[4], C. Clavel[5], E. Svenungsson[1], I. Gunnarsson[1], G. Serre[5], S. Saevarsdottir[6], A. Kastbom[4], L. Alfredsson[7], V. Malmström[1], J. Rönnelid[8], A. Catrina[1], K. Lundberg[1], L. Klareskog[1]. *[1]Karolinska Institutet, Department of Medicine, Division of Rheumatology, Stockholm, Sweden; [2]ORGENTEC Diagnostika GmbH, Mainz, Germany; [3]Thermo Fisher Scientific, Uppsala, Sweden; [4]Linköping University, Department of Biomedical and Clinical Sciences, Linköping, Sweden; [5]INSERM - Université de Toulouse, Unité Différenciation Épithéliale et Autoimmunité Rhumatoïde, Toulouse, France; [6]Karolinska Institutet, Department of Medicine Solna, Division of Clinical Epidemiology, Stockholm, Sweden; [7]Karolinska Institutet, Institute of Environmental Medicine, Stockholm, Sweden; [8]Uppsala University, Department of Immunology, Genetics and Pathology, Uppsala, Sweden*

Background: Seropositive rheumatoid arthritis (RA) is characterized by the presence of rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) with different fine-specificities. Yet, other serum anti-modified protein autoantibodies (AMPA), e.g. anti-carbamylated (Carb), anti-acetylated (KAc), and anti-malondialdehyde acetaldehyde (MAA) modified protein antibodies, have been described. By using RA patient single-cell derived monoclonal antibodies we have previously shown that individual ACPA clones recognize small distinct citrulline-containing epitopes giving them extensive multireactivity when these epitopes are found in many peptides and proteins. Moreover, certain CCP2+ multireactive ACPA clones bind also to cabamylated and acetylated autoantigens [1].

Objectives: To provide a comprehensive evaluation of serum IgG and IgA autoreactivity to different post-translational modifications in RA.

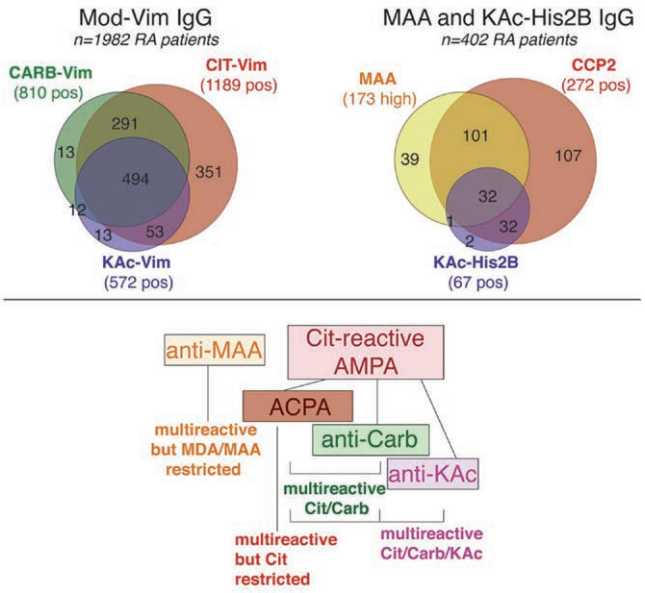
Methods: We analyzed 30 different IgG and IgA AMPA reactivities to modified antigens by ELISA and autoantigen arrays, in N=1985 newly diagnosed RA patients and population controls. The study utilized both previously established (i.e IgG and IgA CCP2; IgG ACPA fine-specificities; IgG anti-Carb fibrinogen and Carb FCS; IgG and IgA Cit/Carb/KAc/Orn(Ac)-vimentin), and novel assays (e.g. IgG anti-MAA and IgG anti-acetylated histones). Association with patient characteristics such as smoking and disease activity were explored. The newly developed assays were also evaluated in SLE disease controls and CCP2+ RA-risk individuals without arthritis.

Results: Carb and KAc reactivities by different assays were primarily seen in patients also positive for citrulline-reactivity. Modified vimentin (mod-Vim) peptides were used for direct comparison of different AMPA reactivities, revealing that IgA AMPA recognizing mod-Vim was mainly detected in subsets of patients with high IgG anti-Cit-Vim levels and a history of smoking. IgG acetylation reactivity was mainly detected in a subset of patients with Cit and Carb reactivity. Anti-acetylated histone 2B reactivity was RA-specific and associated with high anti-CCP2 IgG levels, multiple ACPA fine-specificities, and smoking. This reactivity was also found to be present in CCP2+ RA-risk individuals without arthritis. Our data further demonstrate that IgG autoreactivity to MAA was increased in RA compared to controls with highest levels in CCP2+ RA, but was not RA-specific, and showed low correlation with other AMPA. Anti-MAA was instead associated with disease activity and was not significantly increased in CCP2+ individuals at risk of RA. Notably, RA patients could be subdivided into four different subsets based on their AMPA IgG and IgA reactivity profiles.

Conclusion: We conclude that autoantibodies exhibiting different patterns of ACPA fine-specificities as well as Carb and KAc reactivity are present in RA and may be derived from multireactive B-cell clones. Anti-Carb and anti-KAc could be considered reactivities within the “Cit-umbrella” similar to ACPA fine-specificities, while MAA is distinctly different.

REFERENCES:

[1] Sahlström P, Hansson M, Steen J, Amara K, Titcombe PJ, Forsström B, Stålesen R, Israelsson L, Piccoli L, Lundberg K, Klareskog L, Mueller DL, Catrina AI, Skriner K, Malmström V, Grönwall C. Different Hierarchies



of Anti-Modified Protein Autoantibody Reactivities in Rheumatoid Arthritis. Arthritis Rheumatol. 2020 Oct;72(10):1643-1657. PMID: 32501655

Caroline Grönwall: None declared, Lisa Liljefors: None declared, Holger Bang Employee of: Employee at ORGENTEC Diagnostika GmbH, Aase Hensvold: None declared, Monika Hansson: None declared, Linda Mathsson-Alm Employee of: Employee at Thermo Fisher Scientific, Lena Israelsson: None declared, Anna Svärd: None declared, Cyril CLAVEL: None declared, Elisabet Svenungsson: None declared, Iva Gunnarsson: None declared, Guy Serre: None declared, Saedis Saevarsdottir: None declared, Alf Kastbom: None declared, Lars Alfredsson: None declared, Vivianne Malmström: None declared, Johan Rönnelid: None declared, Anca Catrina: None declared, Karin Lundberg: None declared, Lars Klareskog: None declared

DOI: 10.1136/annrheumdis-2021-eular.3003

POS0010 CD38+ MEMORY T CELLS ARE A FUNCTIONALLY DISTINCT SUBSET THAT IS EXPANDED IN SLE AND ASSOCIATED WITH LUPUS NEPHRITIS

L. Ostendorf[1,2,3], P. Garantziotis[1,2], D. L. Wagner[4,5,6], P. Durek[7], F. Heinrich[7], P. Enghard[3], G. R. Burmester[1], A. Radbruch[8], M. F. Mashreghi[7], F. Hiepe[1,2], T. Alexander[1,2]. *[1]Charité Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany; [2]Deutsches Rheumaforschungszentrum Berlin, Autoimmunology Laboratory, Berlin, Germany; [3]Charité Universitätsmedizin Berlin, Department of Nephrology and Intensive Care Medicine, Berlin, Germany; [4]Charité Universitätsmedizin Berlin, BIH Center for Regenerative Therapies (BCRT), Berlin, Germany; [5]Charité Universitätsmedizin Berlin, Berlin Center for Advanced Therapies (BeCAT), Berlin, Germany; [6]Charité Universitätsmedizin Berlin, Institute of Transfusion Medicine, Berlin, Germany; [7]Deutsches Rheumaforschungszentrum Berlin, Therapeutic Gene Regulation Laboratory, Berlin, Germany; [8]Deutsches Rheumaforschungszentrum Berlin, Cell Biology Laboratory, Berlin, Germany*

Background: We recently reported the beneficial clinical responses of the anti-CD38 monoclonal antibody daratumumab in two patients with systemic lupus erythematosus (SLE) [1]. While the primary rationale for its use was the depletion of autoantibody-producing long-lived plasma cells, daratumumab may promote additional therapeutic effects on CD38-expressing T cells, but their origin, lifestyle and role in lupus pathophysiology remains elusive.

Objectives: To investigate the phenotype, transcriptional program, functional properties and clinical associations of CD4+ and CD8+CD38+ memory T cells in SLE compared to healthy controls (HC).

Methods: CD38-expression on memory T cell subsets was measured by flow cytometry in 65 patients with SLE and 28 healthy controls. We investigated the functional capacity of CD38+ T cells using CFSE staining and intracellular cytokine staining after polyclonal stimulation. Additionally, we performed single-cell transcriptome and T-cell-receptor sequencing of 7 SLE patients and 7 matched healthy controls, including surface protein expression analysis using CITE-seq (RNA-barcoded) antibodies.

Results: Compared to healthy controls, the frequency of CD38-expressing memory T cells in SLE was significantly increased in both CD4+ and CD8+ T cells. SLE patients with a previous or current lupus nephritis had significantly increased levels of CD8+CD38+ memory T cells compared to those without history of renal involvement. CD38+ memory T cells expressed increased levels of Ki-67 and displayed higher proliferative capacity upon polyclonal stimulation than their CD38- counterparts, both in SLE patients and HC, while they showed decreased ability to secrete IFN-γ, IL-2, GM-CSF and TNF-α. Single-cell transcriptome sequencing revealed that CD8+CD38+ memory T cells were enriched within terminally differentiated, cytotoxic CD8 T cells, and had reduced TCR repertoire diversity compared to their CD38- counterparts. CD8+CD38+ memory T cells from SLE patients had significantly higher expression of type I interferon associated genes, both compared to CD38- memory T cells from SLE patients and CD38+ cells from HCs.

Conclusion: CD38+ memory T cells with increased proliferative capacity but altered effector functions are significantly expanded in peripheral blood of SLE and correlate with the lupus nephritis. Although the factors mediating their generation and their precise role in the disease pathophysiology remain to be investigated, CD38-expressing T cells may be useful as a future biomarker for lupus nephritis.

REFERENCES:

[1] Ostendorf L, Burns M, Durek P, Heinz GA, Heinrich F, Garantziotis P, et al. Targeting CD38 with Daratumumab in Refractory Systemic Lupus Erythematosus. N Engl J Med. 2020 Sep 17;383(12):1149–55.

[2] Katsuyama E, Suarez-Fueyo A, Bradley SJ, Mizui M, Marin AV, Mulki L, et al. The CD38/NAD/SIRTUIN1/EZH2 Axis Mitigates Cytotoxic CD8 T Cell Function and Identifies Patients with SLE Prone to Infections. Cell Reports. 2020 Jan;30(1):112-123.e4.

Acknowledgements: We thank our patients and healthy controls for making our research possible.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3104

Epidemiology and treatment of pain in RMDs

POS0011 THE ASSOCIATION BETWEEN BARIATRIC SURGERY AND CARPAL TUNNEL SYNDROME: A COHORT STUDY FROM SWEDISH NATIONWIDE HEALTHCARE REGISTRIES

J. Lane[1], D. Holmberg[2], A. M. Burden[3,4], D. Furniss[1], T. Burkard[3]. *[1]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, Oxford, United Kingdom; [2]Karolinska Institutet and Karolinska University Hospital, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [3]ETH Zurich, Department of Chemistry and Applied Biosciences, Zurich, Switzerland; [4]Maastricht University Medical Center+, Department of Clinical Pharmacy and Toxicology, Maastricht, Netherlands*

Background: Carpal tunnel syndrome (CTS) is a chronic compression neuropathy caused by entrapment of the median nerve in the wrist causing pain and sensory loss. Prior observational research suggested that obesity increased the risk of CTS. However, the impact of weight loss among obese patients on CTS has not been assessed to date.

Objectives: To assess the association between bariatric surgery and CTS in a secondary care setting.

Methods: We performed a propensity score (PS)-matched cohort study using data from Swedish nationwide healthcare registries (patient registry [secondary care], causes of death registry, prescribed drug registry). Patients aged 18-79 years who underwent bariatric surgery between 2006 and 2019 were matched to up to 2 obese bariatric surgery-free patients (called unexposed patients) based on their PS. PS-matching was carried out in risk set sampling to reduce selection bias, within 4 sequential cohort entry blocks to account for time trend biases. The outcome CTS was defined as a diagnosis of CTS in secondary care or carpal tunnel decompression surgery. After a 1-year run-in period, patients were followed in an "as-treated" approach. We applied Cox proportional hazard regression to calculate hazard ratios (HR) with 95% confidence intervals (CIs) of CTS among bariatric surgery patients when compared to obese unexposed patients overall, and in subgroups of age, sex, bariatric surgery type, and by duration of follow-up.

Results: A total of 40 619 bariatric surgery patients were PS-matched to 63 540 obese unexposed patients. A total of 72.3% of bariatric surgery patients were women. Bariatric surgery patients had a mean age of 41.7 years and a mean follow-up of 6.8 years. All patient characteristics in obese unexposed patients were highly similar. We observed 1 356 and 1 938 severe CTS cases among bariatric surgery and obese unexposed patients, respectively. Bariatric surgery was not associated overall with CTS (HR of 0.98, 95% CI 0.91-1.05). However, the risk of CTS seemed to decrease with age at bariatric surgery – the lowest CTS risk was observed among bariatric surgery patients aged 18-34 years (HR of 0.87, 95% CI 0.74-1.01), when compared to obese unexposed patients. Sex did not modify the risk of CTS among bariatric surgery patients compared to obese

unexposed patients. Restrictive bariatric surgery yielded lower risks of CTS (HRs of 0.81, 95% CI 0.69-0.88) than did malabsorptive bariatric surgery (HR of 0.95, 95% CI 0.88-1.02) when compared to obese unexposed patients. The risk of CTS increased with duration of follow-up. The lowest risk was observed 1-3 years after bariatric surgery (HR of 0.77, 95% CI 0.68-0.88) and the highest risk 6-13 years after bariatric surgery (HR of 1.20, 95% CI 1.05-1.36) when compared to obese unexposed patients.

Conclusion: Our results suggest that substantial weight loss is not overall associated with severe CTS in an obese patient population. However, bariatric surgery was associated with an initial decreased risk of CTS after bariatric surgery followed by an increased risk in later follow-up. Furthermore, restrictive bariatric surgery but not malapsorptive bariatric surgery was associated with a decreased risk of CTS.

Acknowledgements: We thank Prof. Dr. Jesper Lagergren (Karolinksa Institutet, Stockholm, Sweden) for hosting Dr. Theresa Burkard for a research stay at the Upper Gastrointestinal Surgery Group and making the data available for use. Furthermore, we thank Dr. Giola Santoni (Karolinksa Institutet, Stockholm, Sweden) for her technical support.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4083

POS0012 EPIDEMIOLOGY OF FIBROMYALGIA HOSPITALIZATIONS IN THE UNITED STATES

K. Mathias[1], A. Mantha[2], L. Mathias[3], D. Arkfeld[3]. *[1]University of Chicago, Internal Medicine, Los Angeles, United States of America; [2]USC Keck School of Medicine, Internal Medicine, Los Angeles, United States of America; [3]USC Keck School of Medicine, Rheumatology, Los Angeles, United States of America*

Background: Fibromyalgia is a chronic pain syndrome that is associated with protean symptoms including musculoskeletal pain, psychiatric symptoms, cognitive dysfunction, memory difficulty, and sleep disturbance. Fibromyalgia can be a primary diagnosis, or it can be associated with other conditions. Fibromyalgia is often seen in conjunction with autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis. In 1990, the American College of Rheumatology released classification criteria for fibromyalgia that included symptoms of diffuse pain and physical exam findings of at least 11 of 18 defined tender points. In 2010, the ACR updated these criteria and eliminated the requirement of tender points. In 2011, these criteria were further modified to that they could be self-administered. A previous study used the national inpatient sample to examine hospitalization data for patients with fibromyalgia from 1999-2007. [1] No studies, however, have examined this data since the new ACR criteria were established in 2010.

Objectives: We aim to characterize the epidemiology of hospitalized patients with diagnosis of fibromyalgia.

Methods: Hospitalized patients with a diagnosis of fibromyalgia were identified in the 2016-2018 National Inpatient Sample (NIS) using the International Classification of Diseases 10 system (ICD-10). The NIS is an all-payer inpatient database that estimates over 37 million annual U.S. hospitalizations and is maintained by the Healthcare Cost and Utilization Project. The primary outcomes were prevalence of fibromyalgia and comorbid rheumatologic conditions among hospitalized patients. Secondary outcomes included cause of admission, mortality, length of stay, and cost of care.

Results: Of 1,351,234 patients with fibromyalgia identified, 437,145 were admitted in 2016 increasing to 461,820 in 2018. On average 59.1 years old, more likely female (1,262,735, 93.5%) and white (1,060,845, 81.3%). Patients were most likely to have Medicare (775,420, 57.5%) and were in the bottom quartile of income (402,945, 30.3%). The most common rheumatologic comorbidities were rheumatoid arthritis (142,195, 10.5%), lupus (69,980, 5.2%), and inflammatory bowel disease (38,165, 2.2%). Notably fibromyalgia was commonly associated with depression (500,420, 37.0%), obesity (379,324, 28.1%), hypothyroidism (334,585 24.7%), and congestive heart failure (213,790, 15.8%).The mortality rate was 13,605 (1.0%) patients, the average length of stay was (4.53 days), and the average cost of hospitalization ($12,522). The most common causes of admission were inflammatory syndromes and joint disorders (13.4%) of which OA (4.2%) was most common complaint, digestive complaints (12.1%) of which IBD (4.4%) was most common.

Conclusion: The yearly number of fibromyalgia hospital discharges were greater than previously described. This may be a result of a more sensitive classification criteria. Further investigation into the etiology of this increase in fibromyalgia hospitalization diagnosis is warranted.

REFERENCES:

[1] Haviland MG, Banta JE, Przekop P. Fibromyalgia: prevalence, course, and co-morbidities in hospitalized patients in the United States, 1999-2007. Clin Exp Rheumatol. 2011 Nov-Dec;29(6 Suppl 69):S79-87. Epub 2012 Jan 3. PMID: 22243553.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3416

POS0013 MUSCULOSKELETAL MANIFESTATIONS IN PATIENTS WITH ENDOCRINE DISEASES IN TERTIARY SERVICE

T. Quereza e Silva Faria[1], S. Ribeiro[1], J. Simão[1], A. Vieira[1], A. P. Narciso Resk Maklouf[1], R. Patrícia Quereza e Silva Faria[1], L. Praciano[1], G. Araújo[1], B. Corrêa[1]on behalf of IMUNOLOGIA DAS DOENÇAS TROPICAIS - IMMUNOLOGY OF TROPICAL DISEASES. *[1]UFAM, Clínca médica, Manaus, Brazil*

Background: Musculoskeletal diseases represent about 50 to 70% of the frequency of chronic diseases according to previous studies (SOUZA, OLIVEIRA, 2015). Chronic pain is often associated with these diseases and is an important cause of care in the health service. Thus, medical professionals are required to adequately manage their patients. Despite the lack of knowledge of some, endocrine diseases are basic diseases linked to musculoskeletal manifestations. Thus, secondary arthropathies of the non-rheumatologic origin or osteoarticular complaints that simulate or show rheumatic diseases can be seen in patients with endocrine diseases during their evolution or in the initial phase along with other systemic symptoms.

Based on this concept, the musculoskeletal manifestations presented by patients with endocrine disorders in tertiary health service were monitored and evaluated.

Objectives: The objective of this study is to characterize the musculoskeletal manifestations in patients with endocrine diseases: type 1 and type 2 diabetes mellitus; hypothyroidism; hyperthyroidism and pituitary diseases and to clinically classify the patients based on physical and imaging findings.

Methods: A cross-sectional and descriptive study, where clinical screening was performed at the endocrinology outpatient clinic, in which patients with musculoskeletal complaints were identified. These patients were referred for evaluation with a rheumatologist with clinical, laboratory and imaging investigation for the diagnosis of rheumatic disease. A questionnaire with epidemiological and clinical data was applied.

Results: In this study, 325 patients with endocrine diseases were interviewed, 53 ± 16.4 years old, 258 (80%) were female and 64 (20%) males. Of the interviewed patients, 236 (72.8%) reported musculoskeletal pain, being that 196 (75.9%) of the women and 33% of the men indicated this type of symptom. Regarding endocrine diseases, the most frequent was Diabetes Mellitus type 2 with 158 patients (48.6%), and 75% of these people have chronic musculoskeletal pain, most 5 to 7 times a week, showing an intrinsic character of this disease with pain complaints from a large part of this population. It was also identified the prevalence of 25% of Hypothyroidism, 12% of Diabetes type 1, 9% of Hyperthyroidism and less expressive amounts of other endocrine diseases such as Acromegaly (2.1%), Gigantism (0.3%) and similar. About 63% of those who have pain are not followed up in the service of rheumatology, 42% of these have already indicated these pains to their endocrinologist, however they have not had their complaint properly flagged. Of these patients, 94 (29%) use Antihypertensives and 25% Oral Antidiabetics. The most notable diagnoses in rheumatology are: Rheumatoid Arthritis (29%); Osteoarthritis (27%); Osteoporosis and Fibromyalgia both with 20.6% of diagnoses and Psoriatic Arthritis and GOUT with 6%. The main regions that are subject to pain are the Hands (52%); Knees (40%); Spine and feet with 30% each.

Conclusion: Although there is a demand of more confirmatory studies, our preliminary results showed the mutuality between endocrine diseases and musculoskeletal manifestations and, therefore, that rheumatological findings are increasingly frequent in this population. The high prevalence of these symptoms secondary to endocrine diseases raises serious questions in order to improve the quality of life of these patients, and also to increase the number of researches in this field, because the pathophysiological mechanisms of this association are not well elucidated and, from this, expand this information to professionals who may not be aware of this relationship.

REFERENCES:

[1] SOUZA, Cesario da Silva; OLIVEIRA, Anamaria Siriani. Prevalência de encaminhamentos às doenças musculoesqueléticas segundo a classificação estatística internacional de doenças (CID-10): reflexões para formação do fisioterapeuta na área de musculoesquelética. Fisioterapia e Pesquisa v. 22, n. 1, p. 48–53, 2015.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1481

POS0014 TIME-TRENDS IN COCAINE AND HALLUCINOGEN USE DISORDER HOSPITALIZATIONS IN RHEUMATIC DISEASES: A NATIONAL TIME-TRENDS STUDY

J. Singh[1]. *[1]University of Alabama at Birmingham, Medicine, Birmingham, United States of America*

Background: Cocaine use disorder is a frequent cause of drug use disorders in the U.S. Although hallucinogen use disorder is less common, both are potentially preventable public health issues. To our knowledge, epidemiological studies

estimating burden of cocaine or hallucinogen use disorders in common Musculoskeletal diseases (MSDs) are lacking.
Objectives: To assess national time-trends in cocaine use and hallucinogen use disorders in people with MSDs
Methods: This study used the U.S. National Inpatient Sample (NIS), a de-identified national all-payer inpatient health care database (https://www.hcup-us.ahrq.gov/nisoverview.jsp) from 1998-2014. The NIS is a 20% stratified sample of hospital discharges in the U.S. It is commonly used to derive national estimates of hospitalization and outcomes. Cocaine or hallucinogen use disorder hospitalization was defined in a validated approach as the presence of the following International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes: cocaine use disorder, 304.2x, or 305.6x; and hallucinogen use disorder, 304.5x or 305.3x; hospitalizations for drug use in remission, drug counseling, rehabilitation or detoxification were excluded, as in previous studies. MSDs were identified based on the respective ICD-9 codes, a validated approach (5-9), in non-primary position: Gout: 274.xx; rheumatoid arthritis (RA): 714.xx; Fibromyalgia: 729.1; osteoarthritis (OA): 715.xx; or low back pain (LBP): 724.
Results: In 1998-2000, the highest frequency of cocaine use hospitalizations was in people with LBP: LBP (n=5,914), followed by OA (n=4,931), gout (n=2,093), RA (n=2,026), and fibromyalgia (n=1,620). In 2013-2014, the order changed slightly with OA (n=22,185), followed by LBP (n=16,810), gout (n=10,570), RA (n=8,975), and fibromyalgia (n=5,680). Respective rates per 1 million U.S. NIS hospitalizations in 2013-2014 and the relative increase from 1998-2000 to 2013-2014 were: Gout, 10.2 (increase, 4.1-fold); OA, 21.4 (3.5-fold); fibromyalgia, 5.48 (2.5-fold); RA, 8.66 (3.4-fold); and LBP, 16.22 (1.8-fold; Figure 1).
In 1998-2000, hallucinogen use disorder hospitalizations were as follows: LBP (n=176), followed by OA (n=63), RA (n=42), fibromyalgia (n=41) and gout (n<10; cells with frequency of 10 of fewer are reported as <10 per NIS guidance). In 2013-2014, the frequency order was the similar, with the highest numbers for LBP (n=525) followed by OA (n=400), RA (n=395), gout (n=135) and fibromyalgia (n=125). Respective rates per 1 million US NIS hospitalizations in 2013-2014 and the relative increase from 1998-2000 to 2013-2014 were: Gout, 0.13 (increase, 25-fold); OA, 0.39 (5.5-fold); fibromyalgia, 0.12 (2-fold); RA, 0.38 (8.5-fold); and LBP, 0.51 (2-fold; Figure 1).
Conclusion: This study confirmed an increasing rate of both, cocaine use and hallucinogen use disorder hospitalizations in people with 5 MSDs over a 17-year period from 1998-2014 in the U.S.

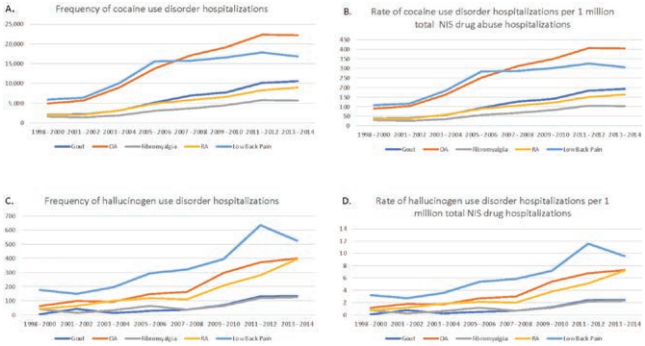


Figure 1. Time-trends in the rates of hospitalization with cocaine use and hallucinogen use disorder (A), non-home discharge (B), and in-hospital mortality (C) per 100,000 NIS hospitalization claims.The x-axis shows rate per 100,000 NIS hospitalization claims and the y-axis the study periods

Acknowledgements: I thank John D. Cleveland, MS of the University of Alabama at Birmingham for performing data analyses according to the protocol.
Disclosure of Interests: Jasvinder Singh Shareholder of: JAS owns stock options in TPT Global Tech, Vaxart pharmaceuticals and Charlotte's Web Holdings, Inc. JAS previously owned stock options in Amarin, Viking and Moderna pharmaceuticals., Consultant of: JAS has received consultant fees from Crealta/Horizon, Medisys, Fidia, UBM LLC, Trio Health, Medscape, WebMD, Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam associates, Focus forward, Navigant consulting, Spherix, Practice Point communications, the National Institutes of Health and the American College of Rheumatology. JAS is on the speaker's bureau of Simply Speaking. JAS is a member of the executive of Outcomes Measures in Rheumatology (OMERACT), an organization that develops outcome measures in rheumatology and receives arms-length funding from 12 companies.
DOI: 10.1136/annrheumdis-2021-eular.610

POS0015 PREVALENCE OF NEUROPATHIES IN RHEUMATIC AND MUSCULOSKELETAL DISEASES

R. Hasseli[1], M. Tschernatsch[2,3], N. Heimann[1], E. Neumann[1], T. Gerriets[2,4], J. Allendörfer[5], T. Ruck[6], A. Schänzer[7], U. Müller-Ladner[1]. [1]*Justus-Liebig-University Giessen, Campus Kerckhoff, Department of Rheumatology and Clinical Immunology, Bad Nauheim, Germany*; [2]*Justus-Liebig-University Giessen, Department of Neurology, Giessen, Germany*; [3]*Gesundheitszentrum Wetterau, Department of Neurology, Bad Nauheim, Germany*; [4]*Gesundheitszentrum Wetterau, Department of Neurology, Friedberg, Germany*; [5]*Asklepios Hospital, Department of Neurology, Bad Salzhausen, Germany*; [6]*Heinrich-Heine-University Duesseldorf, Department of Neurology, Giessen, Germany*; [7]*Justus-Liebig-University Giessen, Institute of Neuropathology, Giessen, Germany*

Background: In rheumatic and musculoskeletal diseases (RMDs), peripheral neurons can be affected, which can result in sensory symptoms like pain, burning, tingling, numbness and motor symptoms like muscle-atrophy or even paresis. More detailed knowledge about the prevalence and the cause of neuropathy (NP) in RMD are urgently needed, especially as RMD patients may develop different subtypes of NP.
Objectives: The aim of this project was to assess the prevalence and the individual types of NP in rheumatoid arthritis (RA), spondyloarthritis (SpA) and systemic sclerosis (SSc) patients, and to elucidate the clinical, neurophysiological and neuropathologic features of associated NP.
Methods: Baseline questionnaires and neurological and physical examination were used to elucidate the presence of neuropathic pain and autonomic dysfunction. Laboratory tests were performed to exclude other causes for NP. Electrophysiological tests were performed to differentiate demyelinating from axonal large fiber (LF)NPs. Additionally, skin biopsies were used to detect an involvement of small fibres (SF).
Results: A total of 31 patients (median age 64 years (range 43-75)) were included. The majority of patients were female (90%). The mean disease duration was 10 years (1-41 years). More than 50% of the patients were diagnosed with RA, 7 with SpA and 6 with SSc. Of 31 patients, 48% (15/31) had clinical signs of NP and of those, neurophysiological examination showed 14 axonal 2, demyelinating and 4 mixed types. A combined LFNP and SFNP was present in 35% (11/31) of the patients. In 4 patients, only a SFNP was detectable, and in only two patients, no NP was detectable.
Conclusion: NP was detectable in 94% (29/31) of the RMD patients, with LFNP predominating. This high proportion of NP in RMD suggests a surprisingly high coincidence of both diseases.

Table 1. Subtypes of NP in RMD

	Number of patients
Axonal NP	14/31 (45%)
Demyelinating NP	2/31 (6%)
Mixed axonal and demyelinating NP	4/31 (12%)
Sensory NP	9/31 (26%)
Sensorimotor NP	5/31 (10%)
Motor NP	1/31 (3%)

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3931

POS0016 THE EVALUATION OF FUNCTIONAL ABILITIES OF PATIENTS WITH OSTEOPOROTIC VERTEBRAL FRACTURES AS A BASIS FOR REHABILITATION PROGRAMS DEVELOPING

L. Marchenkova[1], V. Vasileva[1], M. Eryomushkin[1]. [1]*National Medical Research Center for Rehabilitation and Balneology of Ministry of Health of Russian Federation, Rehabilitation Department for Somatic Patients, Moscow, Russian Federation*

Background: Due to the demand for special rehabilitation programs for patients with osteoporotic vertebral fractures (VFs), it is of interest to study the functional abilities of those patients. The scientific hypothesis suggests that osteoporotic VFs would cause muscle weakness, muscle dysfunction and conditional disturbances.
Objectives: to estimate muscle strength, motor function and coordination disorders in patients with VFs in the setting of systemic osteoporosis as a basis for rehabilitation programs developing.
Methods: 120 patients aged 43–80 with primary osteoporosis were enrolled. Study group comprised of 60 subjects (56 women, 4 men) with at least 1 VF confirmed by X-rays. Control group included 60 subjects (56 women, 4 men) with osteoporosis but without any osteoporotic fracture. The examination program included back muscles tenzodynamometry, balance tests and stabilometry.
Results: Muscle strength deficiency was estimated in study group in trunk flexors (TF) — 40.9% and in trunk extensors (TE) — 18.1% with an adequate function of the left lateral flexors (LLF) and in right lateral flexors (RLF). Patients with VFs had the lower muscle strength vs controls of TE (15.64±9.8 vs 27.73±9.9 kg, p=0.00002), TF (14.61±8.98 vs 21.28±8.38 kg, p=0.0006), LLF (13.10±7.2 vs

24.06±8.9 kg, p=0.005) and RLF 13.44±7.43 vs 24.26±7.65 kg, p=0.0003). Patients with VFs lose their balance faster during one-leg-standing test with open eyes (5.0 [1.0; 10.0] vs 7.5 [5.0; 10.5] sec in control group, p=0.03) and with closed eyes (2.0 [0; 3.0] vs 3.5 [3.0; 5.0] sec, p=0.04). Fukuda-Unterberger test showed greater side dislocation in study group — 40º [25; 45] vs controls 30º [10; 45], (p=0.02). According to stabilometry study group was characterized vs control group by lower balance coefficient with open eyes (77.2±7.6 vs 85.7±9.4%, p=0.002) and with closed eyes (67.1±9.8 vs 73.4±9.9%, p=0.03), greater sagittal displacement (6.8 [2.1; 37.7] vs 4.8 [1.8; 10.7] mm, p=0.025) and deviation in the saggital plane (1.2 [-1.07; 1.5] vs -1.2 [-1.5; 1.2] mm, p=0.01), and also less pressure center velocity (9.51±4.4 vs 7.1±2.7 mm/sec, p=0.009).

Conclusion: Osteoporotic VFs are associated with reduction of trunk muscles strength and negatively affect static and dynamic balance function that should be taken into account when developing rehabilitation programs for these patients.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4260

POS0017 IMC-1, A FIXED DOSE COMBINATION OF FAMCICLOVIR AND CELECOXIB, IMPROVES COMMON SYMPTOMS ASSOCIATED WITH FIBROMYALGIA IN ADDITION TO PAIN: POST HOC ANALYSIS OF A PHASE 2A TRIAL

W. Pridgen[1], C. Duffy[2], J. F. Gendreau[3], R. M. Gendreau[4]. [1]*Tuscaloosa Surgical Associates, P.C., LLC, Tuscaloosa, United States of America*; [2]*University of Alabama, Department of Biological Sciences, Tuscaloosa, United States of America*; [3]*Gendreau Consulting, LLC, Poway, United States of America*; [4]*Virios Therapeutics, Alpharetta, United States of America*

Background: Fibromyalgia is a chronic disease characterized by widespread pain and severe fatigue that may be triggered by reactivation of latent herpes simplex virus type 1 (HSV-1). In a Phase 2a proof of concept trial, IMC-1 (a fixed dose combination of famciclovir and celecoxib) demonstrated greater tolerability and statistically significant reduction in pain compared with placebo, as measured by change from baseline to week 16 in 24-hour recall pain intensity on an 11-point Numerical Rating Scale (NRS) and 7-day recall pain intensity on the 11-point pain item on the Revised Fibromyalgia Impact Questionnaire (FIQ-R).

Objectives: In this post hoc analysis, we evaluated the effects of IMC-1 compared with placebo on other fibromyalgia symptoms, including lack of energy, stiffness, problems with sleep, problems with memory, depression, and anxiety.

Methods: In the double-blind, multi-center, placebo-controlled trial, male or female patients 18–70 years of age who met diagnostic criteria for fibromyalgia and had at baseline a 24-hour recall average pain intensity score between 4 and 9 on the NRS were randomized 1:1 to 16 weeks of treatment with IMC-1 or placebo. Mean changes from baseline to week 16 in FIQ-R symptom scores were analyzed using a Mixed-Effect Model Repeated Measure (MMRM) model with treatment as the main effect, and investigative site and baseline FIQ-R symptom scores as covariates.

Results: A total of 143 patients were enrolled and randomized to treatment with IMC-1 (n=69) or placebo (n=74). Baseline demographic and clinical characteristics were comparable between treatment groups; the majority of patients were Caucasian (95.8%) and female (93.7%) with a mean age of ~49 years. Compared with placebo, treatment with IMC-1 resulted in statistically significant improvements in the FIQ-R symptom scores of stiffness (least squares mean change from baseline -0.96 vs. -1.92, P=0.03), sleep quality (-0.76 vs. -1.76, P=0.039), depression (-0.44 vs. -1.33, P=0.016), and anxiety (-0.30 vs. -1.69, P<0.001), but not in energy level (-0.67 vs. -1.29, P=0.115) or memory problems (-0.71 vs. -1.24, P=0.165).

Conclusion: In addition to alleviation of chronic pain, treatment with IMC-1 appears to be effective in improving many of the other symptoms often associated with fibromyalgia. Further clinical trials are warranted.

REFERENCES:

[1] Pridgen WL, Duffy C, Gendreau JF, Gendreau RM. A famciclovir + celecoxib combination treatment is safe and efficacious in the treatment of fibromyalgia. *J Pain Res*. 2017;10:451-460.

Disclosure of Interests: William Pridgen Consultant of: Virios Therapeutics, Carol Duffy Consultant of: Virios Therapeutics, Grant/research support from: The University of Alabama, Department of Biological Sciences has received financial research support from Innovative Med Concepts (now Virios Therapeutics) in the form of two Sponsored Research Agreements., Judy F. Gendreau Consultant of: Tonix, Dare Bioscience, Virios Therapeutics, R. Michael Gendreau Consultant of: Tonix, Teva, Swing Therapeutics, Dare Bioscience, Employee of: Virios Therapeutics.

DOI: 10.1136/annrheumdis-2021-eular.1424

POS0018 INVESTIGATING VIRTUAL IMMERSIVE EXPERIENCES IN THE MANAGEMENT OF CHRONIC PAIN – THE VIPA STUDY (PRELIMINARY RESULTS)

J. Tsigarides[1], V. Grove[1], D. Sethi[1], J. Chipping[1], S. Miles[1], N. Shenker[2], S. Sami[1], A. Macgregor[1]. [1]*University of East Anglia, Norwich Medical School, Norwich, United Kingdom*; [2]*Addenbrookes University Hospital, Rheumatology, Cambridge, United Kingdom*

Background: Chronic pain is debilitating and prevalent. Current non-pharmacological management of pain conditions such as Fibromyalgia Syndrome (FMS) are labour intensive to implement and poorly available, especially during the pandemic. There is an urgent need to develop widely adoptable, innovative treatment options for pain cohorts.

Virtual reality (VR) provides an innovative therapeutic tool, immersing users within a three-dimensional, interactive virtual environment with use of a head-mounted display (HMD). Beneficial effects of VR have been demonstrated in acute pain[1], with limited studies in chronic pain. Given the variation of available VR technologies, it is vital to investigate the impact of different VR characteristics on acceptability in specific chronic pain cohorts.

Objectives: This feasibility study aims to establish the acceptability of four different VR technologies in patients with FMS whilst undertaking a single interactive VR experience.

Methods: Patients with FMS were recruited through outpatient clinics at the Norfolk and Norwich University Hospital. Baseline questionnaires were used including the McGill pain questionnaire (MPQ-SF), pain visual analogue scale (VAS) and Revised Fibromyalgia Impact Questionnaire (FIQR). Subjective experience questionnaires collected acceptability data with 7-point Likert scale rating questions (strongly disagree to strongly agree). The simulation sickness questionnaire (SSQ) gained side-effect data (total severity score: 0-235). Categorical data were described using frequencies; and continuous data using mean and standard deviation. Likert-scale data were dichotomised (rating ≤3: disagree, rating ≥5: agree).

Four VR systems representing the spectrum of commercially available technologies were used (seen in Figure 1). These possess different characteristics including screen resolution, processor speed, weight, strap and controller type. The VR experience used with each headset was co-developed alongside industry partners (Orbital Global). Participants are immersed within a naturalistic environment, situated on a wooden boat travelling slowly along a calm river surrounded by trees and hills. The interactive element involves the user shooting targets that appear using handheld controllers.

Results: 13 patients with FMS were included (mean age 41.8±15.6, 92.3% female). Most had severe disease (mean FIQR 67.8±14.1) with moderate self-reported pain at baseline (mean MPQ 25.5±8.8, VAS 6.0±1.7). Most had no previous VR exposure (69.2%). 100% of participants agreed that they would be open to using VR for future pain management (mean rating 6.5±0.7) and that they would use VR regularly at home (mean rating 6.5±0.7). VR HMD comfort and enjoyment data are presented in Table 1. Mean ratings of comfort were high across the four HMDs (Gear VR: 4.9±1.7, Oculus Go: 4.5±1.8, Oculus Quest 5.3±1.9, Oculus Rift 6.6±0.5). Mean ratings of enjoyment with each HMD were also high (Gear VR: 5.4±1.6, Oculus Go: 5.4±1.8, Oculus Quest: 5.6±1.9, Oculus Rift S: 6.6±0.5). Low levels of side effects were described with mean SSQ total scores ranging from 20.1±16.8 (Oculus Rift S) to 38.0±23.9 (Gear VR).

Conclusion: Preliminary results indicate that FMS patients find VR acceptable, describing high ratings of comfort and enjoyment across the VR HMD spectrum. Side-effect frequency was low, with most settling after HMD removal. All participants were open to future use of VR for home-based pain management.

REFERENCES:

[1] Dascal J, Reid M, Ishak WW, Spiegel B, Recacho J, Rosen B, Danovitch I. Virtual reality and medical inpatients: A systematic review of randomized, controlled trials. *Innov Clin Neurosci* 2017;14(1-2):14-21

Table 1. Subjective experience results across VR HMDs

	Mean Likert scale ratings (% agreement: rating ≥5)	
VR HMD	*Overall, I found the VR experience using this equipment comfortable*	*Overall, I enjoyed using this VR headset*
Gear VR	4.9±1.7 (62%)	5.4±1.6 (77%)
Oculus Go	4.5±1.8 (54%)	5.4±1.8 (75%)
Oculus Quest	5.3±1.9 (77%)	5.6±1.9 (100%)
Oculus Rift S	6.6±0.5 (100%)	6.6±0.5 (100%)

Figure 1

Spectrum of VR technologies used in this study. From left to right: Oculus Quest, Oculus Go, Gear VR, Oculus Rift S.

Acknowledgements: I would like to acknowledge the contributions of the staff working within the Rheumatology department at the Norfolk and Norwich University Hospital. I would also like to thank and acknowledge our participants for being involved in the study.

Disclosure of Interests: Jordan Tsigarides Grant/research support from: Our digital health industry partners (Orbital Global) provided a small financial contribution to support this study., Vanessa Grove: None declared, Dheeraj Sethi: None declared, Jacqueline Chipping: None declared, Susan Miles: None declared, Nicholas Shenker: None declared, Saber Sami: None declared, Alex MacGregor: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2017

POS0019 PREDICTORS OF SUSTAINED 6 MONTHS REMISSION AND FLARE IN PATIENTS WITH POLYMYALGIA RHEUMATICA

C. Perricone[1], E. Fiumicelli[1], G. Cafaro[1], R. Bursi[1], R. Ilenia[1], E. Bartoloni Bocci[1], R. Gerli[1]. [1]*Rheumatology, Department of Medicine and Surgery, Perugia, Italy*

Background: Polymyalgia rheumatica (PMR) is a typical inflammatory disease of the elderly. The mainstay of treatment is usage of oral glucocorticoids (GC) usually leading to a dramatic response. However, long-term treatment is often required. In some instances, remission cannot be achieved and disease flares can occur. To date, few papers investigated the predictive factors of response to GC therapy suggesting a role for weight, elevated plasma viscosity and C-reactive protein (CRP). Moreover, there are no data on predictor factors of disease flares after 6 months of sustained remission.

Objectives: To evaluate the factors predictive of sustained 6 months remission and of flare in patients with PMR.

Methods: We evaluated clinical data from 137 PMR patients treated with GC for more than 6 months between September 2002 and June 2020. Patients were evaluated at baseline, re-evaluated at 1 month and after 3 months and then at least every 3 months. We analyzed the differences between patients who achieved remission within 6 months of diagnosis, who maintained it for at least 6 months, and patients who did not. Remission was defined as 1) the absence of clinical symptoms, 2) <7.5 mg / day of prednisone equivalents and 3) negativity of ESR and CRP. Patients treated with methylprednisolone were excluded from the analysis.

Results: Among the 137 patients (baseline F68: M69, mean age ± SD 74.5±6.6 years, mean ESR ± SD 49.9±27.7 mm/h, mean CRP ± SD 6.1±11.4 mg/dl), 57 achieved remission at 6 months (41.6%), and after this period, another 47 went into remission for a total of 104 patients (75.9%). The months required to achieve remission averaged 6.4 ± 3. No differences were observed between patients who achieved remission and patients who did not regarding age, sex, CRP, starting dose of GC, anti-CCP and rheumatoid factor. The ESR at baseline was higher in patients who did not achieve remission (58.1±33.4 mm/h) than in patients who achieved it (46±24.8 mm/h, p=0.06). ESR at baseline correlated with the time needed to reach normalization of both ESR and CRP (p=0.01, Figure 1). Thirty-six of 104 patients (34.6%) had a disease flare after a mean of 6.1±2.7 months of remission. The mean GC intake at flare was 2.8±3 mg/day. Only 15/36 (41.6%) patients were able to withhold GCs after flare, compared with 48/68 (70.5%) patients who achieved remission and did not experience flare. There were no significant differences in any analyzed parameters between patients who experienced flares and those who did not, including ESR and CRP values at baseline (50.3±26.7 mm/h and 6.8±12.1 mg/dl, respectively). A higher percentage of patients who did not achieve remission experienced flare than patients who went into remission (p=0.009).

Conclusion: Achieving complete remission at 6 months occurs in a consistent percentage of patients with PMR. Despite this, a significant percentage of patients may need prolonged steroid treatment and may experience flare, even after 12 months of follow-up. Remission at 6 months is likely to be a good predictor of remission at 12 months, as already reported in recent studies (1, 2). Elevated ESR at diagnosis appears to be a negative predictor for remission at 6 months. Patients who achieve complete remission are less likely to develop flare. True remission should coincide with the discontinuation of steroid treatment; in fact, the maintenance of steroid therapy, even at low doses, is predictive of the development of flare.

REFERENCES:

[1] Hattori K, et al. Int J Rheum Dis. 2020

[2] Camellino D, et al. Nat Rev Rheumatol. 2020

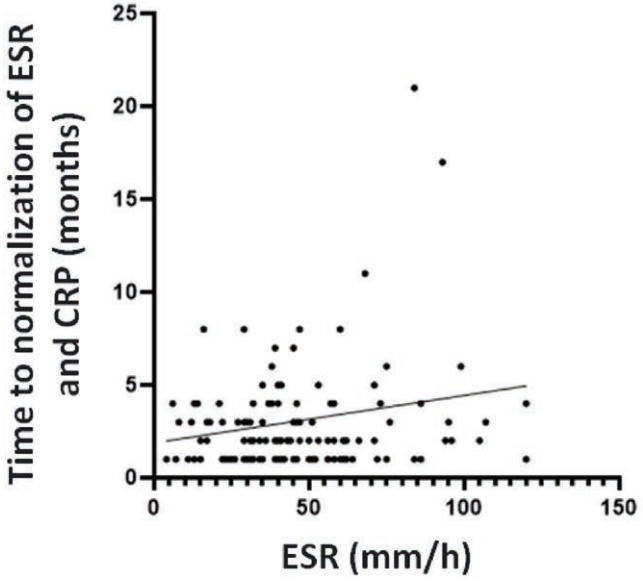


Figure 1.

Disclosure of Interests: Carlo Perricone Speakers bureau: BMS, Lilly, Celgene, UCB, Abbvie, Pfizer, Sanofi, Accord, Novartis, Elena Fiumicelli: None declared, Giacomo Cafaro: None declared, Roberto Bursi: None declared, Ricucci Ilenia: None declared, Elena Bartoloni Bocci: None declared, Roberto Gerli: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3593

POS0020 EFFICACY AND SAFETY OF SECUKINUMAB IN PATIENTS WITH ROTATOR CUFF TENDINOPATHY: A 24-WEEK, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE II PROOF-OF-CONCEPT TRIAL

N. L. Millar[1], I. Mcinnes[1], L. Mindeholm[2], A. Seroutou[3], J. Praestgaard[4], U. Schramm[2], R. Levitch[5], E. Weber[6], D. Laurent[7], J. Rosen[8], G. Schett[9], R. Roubenoff[10], M. Schieker[2]. [1]*Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow, United Kingdom*; [2]*Novartis Institutes for BioMedical Research,TM MSD Bone, Joint and Tendon, Basel, Switzerland*; [3]*Novartis Institutes for BioMedical Research, Biostatistics, Basel, Switzerland*; [4]*Novartis Institutes for BioMedical Research, Data Science, Cambridge, United States of America*; [5]*Novartis Institutes for BioMedical Research, Cardio-renal-metabolic, Basel, Switzerland*; [6]*Novartis Institutes for BioMedical Research, MSD LAB WEBER, Basel, Switzerland*; [7]*Novartis Institutes for BioMedical Research, BMD Clincal &Transplant Imaging, Basel, Switzerland*; [8]*New York Presbyterian Queens, Department of Orthopaedics & Rehabilitation, New York, United States of America*; [9]*University of Erlangen-Nuremberg, Department of Internal Medicine 3, Erlangen, Germany*; [10]*Novartis Institutes for BioMedical Research,Translational Medicine, Basel, Switzerland*

Background: Rotator cuff tendinopathy (RC TP) is a multifactorial condition and one of the most common causes of musculoskeletal burden. Current standard of care (SoC) is limited to pain relief with NSAIDs and physiotherapy. Recent evidence indicates that IL-17A-expressing tendon-resident immune cells are present in human overuse tendinopathy, and IL-17A levels are increased in early human tendinopathic tissue samples [1, 2]. Secukinumab (SEC) is a fully human, monoclonal antibody that binds to and neutralises IL-17A.

Objectives: To evaluate the efficacy and safety of SEC in patients with active overuse RC TP refractory to oral NSAIDs/acetaminophen, physiotherapy or corticosteroid injections.

Methods: 96 patients with symptomatic RC TP with no or <50% rupture were randomly assigned to receive seven subcutaneous injections of SEC 300 mg or placebo (PBO) at baseline and Weeks 1, 2 and 3, followed by every 4 weeks starting at Week 4. The primary endpoint was change from baseline in the Western Ontario Rotator Cuff (WORC) index score at Week 14 for SEC vs PBO (two-sided p<0.1). Secondary endpoints included, visual analogue scale (VAS) pain score, Disability of Arm, Shoulder and Hand Questionnaire (QuickDASH) score,

American Shoulder and Elbow Surgeons Shoulder Evaluation Form (ASES), EQ-5D-5L score and patient global assessment (PGA) score. All endpoints were assessed through 24 weeks.

Results: Clinically relevant improvement in both SEC and PBO groups on top of SoC treatment was observed, with no statistically significant difference demonstrated in the full study population on physical symptoms and function (Table 1). Similar results were observed in the secondary endpoints with marked improvement in both groups over time. Exploratory post-hoc analyses in a subpopulation of 39% of the study subjects with non-acute, moderate to severe disease, SEC provided significant and clinically relevant improvements vs PBO through Week 24 in total WORC score (overall treatment difference: 19.2, p <0.01) and pain (VAS, overall treatment difference: 15, p = 0.02) with early effect observed after two weeks (Figure 1). A favourable treatment effect in the more severe subgroup was demonstrated in other patient-reported outcomes. No serious adverse events were reported.

Conclusion: Although SEC did not demonstrate a significant benefit vs PBO in the overall patient population with active overuse RC TP, SEC did provide benefit in the subpopulation with non-acute, moderate to severe disease. Larger clinical trials of SEC in this area are warranted.

REFERENCES:

[1] Millar NL, et al. *Sci Rep*. 2016;6:27149.
[2] Millar NL, et al. *Nat Rev Rheumatol*.2017;13:110-122.

Table 1. Change from baseline in the SEC versus PBO groups in WORC index and pain (VAS)

Visit	SEC 300 mg	PBO	p-value
Total treated population N=96			
WORC Index percentage score (0 worst -100 best)[a]			
Day 29	22.35	19.49	0.45
Day 99	37.00	37.77	0.87
Day 169	43.41	40.97	0.64
Pain (VAS, 0 best - 100 worst)[b]			
Day 29	−26.04	−23.13	0.57
Day 99	−46.11	−40.56	0.28
Day 169	−52.23	−50.74	0.78
Post-hoc population* N=37			
WORC Index percentage score (0 worst - 100 best)[c]			
Day 29	30.09	10.84	0.002
Day 99	48.26	31.83	0.048
Day 169	55.98	35.24	0.028
Pain (VAS, 0 best - 100 worst)[d]			
Day 29	−29.20	−14.85	0.125
Day 99	−51.48	−35.37	0.045
Day 169	−57.01	−46.64	0.217

[a]Day 1: SEC 42.47, PBO 40.47; [b]SEC 67.04, PBO 64.85; [c]SEC 35.93, PBO 32.90, [d]SEC 71.72, PBO 67.58. Day 1 values are given as absolute values to describe baseline WORC/Pain status*Post-hoc subpopulation: Baseline: (Disease duration 2-6 months) AND (WORC ≤40 OR Tear Thickness (Bauer) ≥1 OR Sein ≥2)PBO, placebo; SEC, secukinumab; SoC, standard of care; WORC, Western Ontario Rotator Cuff Index; VAS, visual analogue scale

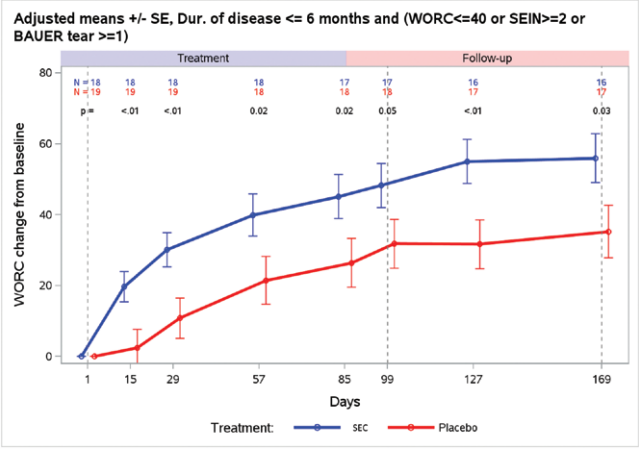


Figure 1. Post-hoc analysis of function (WORC) in the treatment groups in non-acute, moderate to severe subpopulationSECSE, standard error; SEC, secukinumab; WORC, Western Ontario Rotator Cuff Index

Disclosure of Interests: Neal L Millar Grant/research support from: Honoraria or research funding from Novartis and Stryker, Iain McInnes Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB, Linda Mindeholm Employee of: Employee of Novartis, Abdelkader Seroutou Employee of: Employee of Novartis, Jens Praestgaard Employee of: Employee of Novartis, Ursula Schramm Employee of: Employee of Novartis, Rafael Levitch Employee of: Employee of Novartis, Eckhard Weber Employee of: Employee of Novartis, Didier Laurent Employee of: Employee of Novartis, Jeffrey Rosen Consultant of: Research advisor for Novartis, Georg Schett Speakers bureau: Received speakers honoraria from Abbvie, Amgen, BMS, Eli Lilly, Gilead, Janssen, Novartis, UCB, Ronenn Roubenoff Employee of: Employee of Novartis, Matthias Schieker Employee of: Employee of Novartis.
DOI: 10.1136/annrheumdis-2021-eular.45

Epidemiology: Big Questions - Big studies

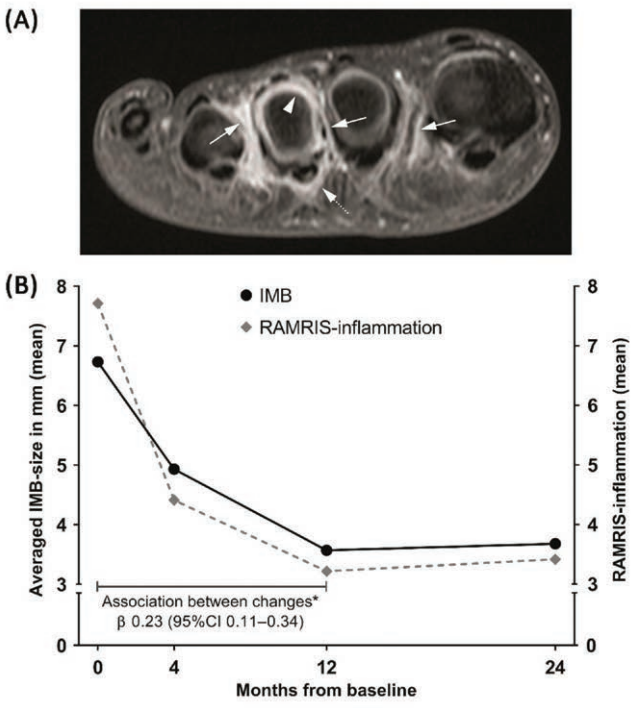
POS0021

INTERMETATARSAL BURSITIS, A NOVEL FEATURE OF JUXTA-ARTICULAR INFLAMMATION IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM A LONGITUDINAL MRI-STUDY

B. Van Dijk[1], Y. Dakkak[1], X. Matthijssen[1], E. Niemantsverdriet[1], M. Reijnierse[2], A. Van der Helm-van Mil[1,3]. [1]*Leiden University Medical Centre (LUMC), Rheumatology, Leiden, Netherlands*; [2]*Leiden University Medical Centre (LUMC), Radiology, Leiden, Netherlands*; [3]*Erasmus Medical Centre (EMC), Rheumatology, Rotterdam, Netherlands*

Background: Rheumatoid arthritis (RA) is characterised by inflammation of the synovial lining. In addition to synovitis, the tendon sheaths of small hand and foot joints are also frequently inflamed. This results in tenosynovitis, which is often missed at clinical evaluation in early RA but visible on imaging, such as MRI. A third anatomical structure surrounded by a synovial lining is formed by the intermetatarsal bursae in the forefeet. Inflammation of these bursae (intermetatarsal bursitis; IMB) was recently identified at MRI-studies and shown to be specific for early RA.[1] This suggests that IMB is also a feature of early RA.

Figure. (**A**) Example MR-image of IMB co-occurring with synovitis and flexor tenosynovitis; (**B**) IMB-size and total RAMRIS-inflammation in the forefoot over time



Legend

(A) Full arrows: IMB; Dotted arrow: tenosynovitis; Arrowhead: synovitis.
(B) * β signifies the association of change in averaged IMB-size with change in total RAMRIS-inflammation between 0–12 months, estimated using GEEs. IMB-decrease was statistically significantly associated with total RAMRIS-inflammation decrease at the 0.05 level.

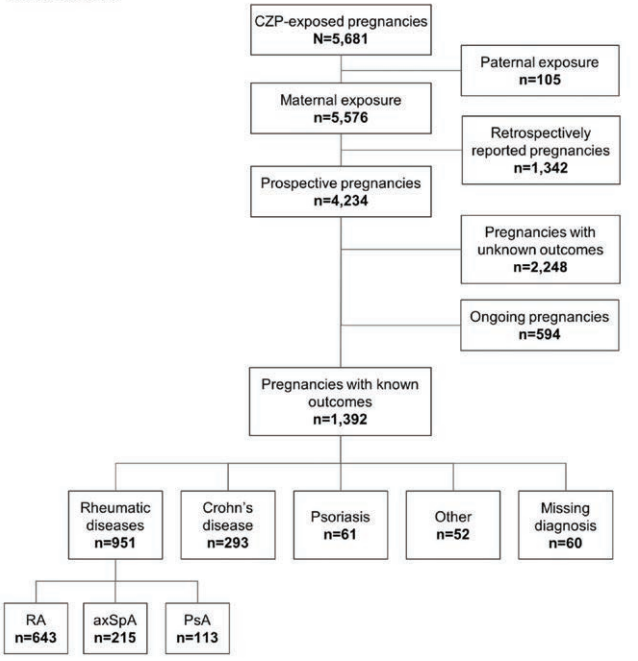
Objectives: We hypothesised that if IMB is indeed an RA-feature, then (1) at diagnosis its presence associates with other measures of local inflammation (synovitis, tenosynovitis and osteitis) and (2) it responds to DMARD therapy similarly as these other local inflammatory measures. These hypotheses were tested in a comprehensive MRI-study.
Methods: 157 consecutive early RA patients underwent unilateral contrast-enhanced 1.5T MRI of the forefoot at diagnosis. MRIs were evaluated for presence of IMB and for synovitis, tenosynovitis and osteitis in line with the RA MRI scoring system (summed as RAMRIS-inflammation). MRIs at 4, 12 and 24 months were evaluated for presence and size of IMB-lesions in patients who had IMB at baseline and received early DMARD-therapy. Logistic regression was used for analyses at patient-level; generalised estimating equations were used for bursa-level analyses. Stratification for ACPA was performed.
Results: 69% of RA patients had ≥1 IMB. In multivariable analyses on bursa-level, presence of IMB was independently associated with local presence of synovitis and tenosynovitis (OR 1.69 (95%CI 1.12–2.57) and 2.83 (1.80–4.44), respectively), but not with osteitis. On patient-level, presence of IMB was most strongly associated with tenosynovitis (OR 2.92 (1.62–5.24)). During treatment with DMARDs, the average size of IMB-lesions decreased (Figure 1). This decrease was associated with decrease in RAMRIS-inflammation scores; most strongly with a decrease in synovitis but not in osteitis. Within ACPA-positive and ACPA-negative RA similar results were obtained.
Conclusion: IMB particularly accompanies inflammation of the synovial lining of joints and tendon-sheaths, both regarding simultaneous occurrence at diagnosis and simultaneous treatment-response. These findings suggest that IMB represents juxta-articular synovial inflammation and indeed is a hallmark of early RA.
REFERENCES:
[1] Dakkak YJ et al. Increased frequency of intermetatarsal and submetatarsal bursitis in early rheumatoid arthritis: a large case-controlled MRI study. Arthritis Res Ther 22, 277 (2020).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.303

POS0022 PHARMACOVIGILANCE PREGNANCY DATA IN A LARGE POPULATION OF PATIENTS WITH CHRONIC INFLAMMATORY DISEASE EXPOSED TO CERTOLIZUMAB PEGOL: PREGNANCY OUTCOMES AND CONFOUNDERS

M. Clowse[1], R. Fischer-Betz[2], C. Nelson-Piercy[3], A. Scheuerle[4], T. Kumke[5], B. Lauwerys[6], R. Kasliwal[7], F. Förger[8]. [1]*Duke University Medical Center, Division of Rheumatology, Durham, United States of America*; [2]*Heinrich Heine University Düsseldorf, Department for Rheumatology, Düsseldorf, Germany*; [3]*Guy's and St Thomas' NHS Foundation Trust, Department of Women and Children's Health, London, United Kingdom*; [4]*UT Southwestern Medical Center, Department of Pediatrics, Division of Genetics and Metabolism, Dallas, United States of America*; [5]*UCB Pharma, N/A, Monheim am Rhein, Germany*; [6]*UCB Pharma, N/A, Brussels, Belgium*; [7]*UCB Pharma, N/A, Slough, United Kingdom*; [8]*Inselspital, University of Bern, University Clinic for Rheumatology, Immunology and Allergology, Bern, Switzerland*

Background: Chronic inflammatory diseases (CID) in women of reproductive age are increasingly being treated with tumour necrosis factor inhibitors (TNFi), in line with recent guidelines.[1] However, data on TNFi-exposed pregnancy outcomes are still limited. Certolizumab pegol (CZP), a PEGylated, Fc-free TNFi, has no/minimal placental transfer from mother to infant during the third trimester.[2]
Objectives: To assess pregnancy outcomes from the UCB Pharmacovigilance safety database from over 1,300 prospectively reported pregnancies with maternal CZP exposure.
Methods: Details of CZP-exposed pregnancies from the UCB Pharmacovigilance safety database were reviewed up to November 1, 2020. Analysis was limited to prospectively reported cases with known pregnancy outcomes to avoid potential reporting bias. Confounders (specific CID, non-biologic medications and maternal infection) were evaluated using a multivariate stepwise regression model; results from the confounders analysis are reported as odds ratios (OR) with 95% confidence intervals (CI). Patients with missing information about presence or absence of confounders were excluded from the model.
Results: 1,392 prospective pregnancies (1,425 fetuses) with maternal CZP exposure and known outcomes were reported (Figure 1). Mean (SD) maternal age was 31.9 (5.1) years. Of these, 1,021/1,392 (73.3%) pregnancies had at least first-trimester CZP exposure and 547/1,392 (39.3%) were exposed during all trimesters. Overall, there were 1,259/1,425 (88.4%) live births, 150/1,425 (10.5%) abortions (miscarriages and terminations), 11/1,425 (0.8%) stillbirths, and 5/1,425 (0.4%) ectopic pregnancies. Congenital malformations were reported in 35/1,425 fetuses (2.5%) and in 30/1,259 live-born infants (2.4%); 26 (2.1%) congenital malformations were major according to the Metropolitan Atlanta Congenital Defects Program criteria. There was no pattern of specific congenital malformations. Preterm births occurred in 124/1,259 (9.8%) live births, and 101/1,259 (8.0%) of infants had low birth weight (<2.5 kg). In the confounders analysis, reported corticosteroid use was independently associated with increased odds of preterm birth (OR [95% CI]: 2.1 [1.3–3.4]; p<0.005) and low birth weight (OR [95% CI]: 1.7 [1.0–2.9]; p<0.05), but decreased odds of abortion (OR [95% CI]: 0.5 [0.3–0.9]; p<0.05). Reported NSAID use was associated with increased odds of abortion (OR [95% CI]: 2.2 [1.2–4.0]; p<0.05), as was methotrexate/leflunomide use (OR [95% CI]: 3.2 [1.7–6.2]; p<0.0005). Maternal infections were associated with increased odds of preterm birth (OR [95% CI]: 1.9 (1.1–3.5; p<0.05). Finally, there was an association between a diagnosis of Crohn's disease and odds of abortion (OR [95% CI]: 2.5 [1.5–4.1]; p=0.0005), and between rheumatoid arthritis and low birth weight (OR [95% CI]: 1.9 [1.1–3.3]; p<0.05).
Conclusion: This prospective analysis, including more than 1,000 pregnancies with CZP exposure in at least the first trimester, represents one of the largest cohorts of pregnancies with known outcomes in patients with CID. Our data confirm the impact of specific CID, concomitant drugs or comorbidities on pregnancy outcomes. In particular, additional use of corticosteroids was highlighted as a risk factor for preterm birth and low birth weight in our cohort of CZP-treated patients. No increase in adverse pregnancy outcomes or specific congenital malformations was observed in CZP-exposed pregnancies, compared to the general population,[3,4] which offers further reassurance for women of childbearing age considering CZP treatment.
REFERENCES:
[1] Sammaritano LR. Arthritis Rheum 2020;72:529–56;
[2] Mariette X. Ann Rheum Dis 2018;77:228–33;
[3] Ventura SJ. Natl Vital Stat Rep 2012;60:1–21;
[4] Lee H. BMC Pregnancy Childbirth 2020;20:33.

Figure. Reports of pregnancies exposed to CZP identified in the UCB Pharmacovigilance safety database



Some patients may have had multiple indications for CZP treatment. axSpA: axial spondyloarthritis; CZP: certolizumab pegol; PsA: psoriatic arthritis; RA: rheumatoid arthritis.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical.
Disclosure of Interests: Megan Clowse Consultant of: UCB Pharma, Grant/research support from: Janssen, Pfizer, Rebecca Fischer-Betz Consultant of: AbbVie, BMS, Celgene, Chugai, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi, UCB Pharma, Catherine Nelson-Piercy Consultant of: Alliance Pharma, UCB Pharma, Angela Scheuerle Consultant of: Antiretroviral Pregnancy Registry, Harmony Biosciences, IQVIA, ICON, NovoNordisk, PPD, Roche, Sanofi-Genzyme, Syneos, UCB Pharma, ViiV, Thomas Kumke Shareholder of: UCB Pharma, Employee of: UCB Pharma, Bernard Lauwerys Employee of: UCB Pharma, Rachna Kasliwal Employee of: UCB Pharma, Frauke Förger Speakers bureau: Mepha, Roche, UCB Pharma, Grant/research support from: UCB Pharma.
DOI: 10.1136/annrheumdis-2021-eular.577

POS0023 RACIAL/ETHNIC AND REGIONAL DIFFERENCES IN MULTIMORBIDITY BETWEEN PATIENTS WITH RHEUMATOID ARTHRITIS AND COMPARATORS IN A LARGE NATIONWIDE US STUDY

H. J. Dykhoff[1], E. Myasoedova[2,3], M. Peterson[2], J. M. Davis III[2], V. Kronzer[2], C. Coffey[2], T. Gunderson[3], C. S. Crowson[2,3]. [1]*Mayo Clinic, Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester,*

United States of America; [2]*Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; [3]*Mayo Clinic, Department of Quantitative Health Sciences, Rochester, United States of America*

Background: Patients with rheumatoid arthritis (RA) have an increased burden of multimorbidity. Racial/ethnic disparities have also been associated with an increased burden of multimorbidity.
Objectives: We aimed to compare multimorbidity among different racial/ethnic groups and geographic regions of the US in patients with RA and comparators without RA.
Methods: We used a large longitudinal, real-world data warehouse with de-identified administrative claims for commercial and Medicare Advantage enrollees, to identify cases of RA and matched controls. Cases were defined as patients aged ≥18 years with ≥2 diagnoses of RA in January 1, 2010 - June 30, 2019 and ≥1 prescription fill for methotrexate in the year after the first RA diagnosis. Controls were persons without RA matched 1:1 to RA cases on age, sex, census region, calendar year of index date (corresponding to the date of second diagnosis code for RA), and length of prior medical/pharmacy coverage. Race was classified as non-Hispanic White (White), non-Hispanic Black (Black), Asian, Hispanic, or other/unknown, based on self-report or derived rule sets. Multimorbidity (2 or more comorbidities) was defined using 25 chronic comorbidities from a combination of the Charlson and Elixhauser Comorbidity Indices assessed during the year prior to index date. Rheumatic comorbidities were not included. Logistic regression models were used to estimate odds ratios (OR) with 95% confidence intervals (CI).
Results: The study included 16,363 cases with RA and 16,363 matched non-RA comparators (mean age 58.2 years, 70.7% female for both cohorts). Geographic regions were the same in both cohorts: 50% South, 26% Midwest, 13% West, and 11% Northeast. Race/ethnicity was not part of the matching criteria and varied slightly between the cohorts: among RA (non-RA) patients, 74% (74%) were White, 11% (9%) Hispanic, 10% (9%) Black, 3% (4%) Asian, and 3% (4%) other/unknown. Patients with RA had more multimorbidity than non-RA subjects (51.3% vs 44.8%). Multimorbidity comparisons across US geographic regions were similar in both cohorts, with comparable multimorbidity levels for patients in the West and Midwest and higher levels for those in the Northeast and South (Figure 1). Among the non-RA patients, 43.5% of Whites experienced multimorbidity, compared to 33.9% of Asians, 46.1% of Hispanics, and 58.4% of Blacks. These associations remained after adjustment for age, sex, and geographic region, with significantly lower multimorbidity among Asians (OR: 0.81; 95%CI: 0.67-0.99) and significantly higher multimorbidity among Hispanics (OR: 1.21; 95%CI: 1.07-1.37) and Blacks (OR: 1.74; 95%CI: 1.54-1.97), compared to Whites in the non-RA cohort. Among the RA patients, racial/ethnic differences were less pronounced; 50.6% of Whites, 42.8% of Asians, 48.8% of Hispanics, and 58.4% of Blacks experienced multimorbidity. Adjusted analyses revealed no significant differences in multimorbidity for Asians (OR: 0.88; 95%CI: 0.70-1.08) and Hispanics (OR: 1.06; 95%CI: 0.95-1.19) and a less pronounced increase in multimorbidity among Blacks (OR: 1.32; 95%CI: 1.17-1.49) compared to Whites in the RA cohort.
Conclusion: This large nationwide study showed increased occurrence of multimorbidity in RA versus non-RA patients and in both cohorts for residents of the Northeast and South regions of the US. Racial/ethnic disparities in multimorbidity were more pronounced among patients without RA compared to RA patients. This indicates the effects of RA and race/ethnicity on multimorbidity do not aggregate. The underlying mechanisms for these associations require further investigation.

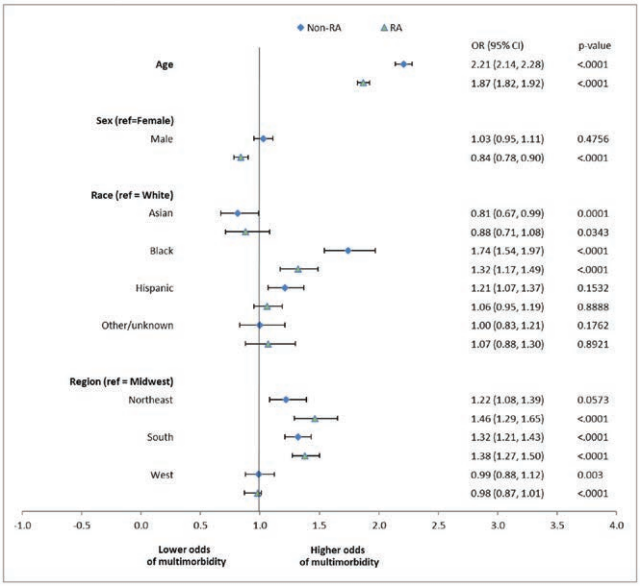


Figure 1. Logistic regression models comparing multimorbidity levels in RA and non-RA cohorts.

Disclosure of Interests: Hayley J. Dykhoff: None declared, Elena Myasoedova: None declared, Madeline Peterson: None declared, John M Davis III Grant/research support from: Research grant from Pfizer, Vanessa Kronzer: None declared, Caitrin Coffey: None declared, Tina Gunderson: None declared, Cynthia S. Crowson: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1610

POS0024

ESTIMATED PREVALENCE, INCIDENCE AND HEALTHCARE COSTS OF SJÖGREN'S SYNDROME IN FRANCE: A NATIONAL CLAIMS-BASED STUDY

R. Seror[1], L. Chiche[2], G. Desjeux[3], J. Zhuo[4], B. Bregman[5], V. Vannier-Moreau[6], V. Devauchelle-Pensec[7]. [1]*Université Paris-Sud, AP-HP, Hôpitaux Universitaires Paris-Sud, N/A, Paris, France*; [2]*Hôpital Européen Marseille, Unité de medicine interne et recherche clinique, Marseille, France*; [3]*Sanoia, eHealth services, Aubagne, France*; [4]*Bristol Myers Squibb, Worldwide Health Economics and Outcomes Research, Princeton, United States of America*; [5]*Bristol Myers Squibb, Health Economics and Public Health, Rueil-Malmaison, France*; [6]*Bristol Myers Squibb, Medical Affairs, France, Rueil-Malmaison, France*; [7]*CHU de Cavale Blanche, Rheumatology Department, Brest, France*

Background: Sjögren's syndrome (SS) is a chronic, systemic autoimmune disorder characterised by oral and ocular dryness related to lymphocytic infiltration of exocrine glands.[1–3] Extra-glandular manifestations may include fatigue, musculoskeletal pain and glomerulonephritis.[1,3] SS can present as primary SS (pSS)

or as SS associated with another autoimmune disorder (SS+AID).[1] Reported prevalence of pSS in the French general population is 1.02–1.52 cases/10,000 people.[3]

Objectives: To estimate prevalence, incidence and healthcare costs of SS in France using national health insurance claims data.

Methods: Claims from 2011–2018 from the Système National des Données de Santé (SNDS), comprised of data from 99% of the French population, were analysed. Patients (pts) with SS were identified using an algorithm.[4] Inclusion criteria: International Classification of Diseases, Tenth Revision code M35.0 (Sicca syndrome [Sjögren]) or M35 (other systemic involvement of connective tissue), and ≥2 drug reimbursements for SS-related treatments. Key exclusion criteria: amyloidosis, sarcoidosis, HIV, and head and neck radiotherapy. Denominators for estimated prevalence rates were derived from French population census data. Healthcare costs were based on Assurance Maladie rates.

Results: 23,152 pts with pSS and 15,462 with SS+AID were identified during the study period. Estimated prevalence of SS (2011–2018) per 100,000 persons ranged from 22–32 (pSS) and 17–22 (SS+AID) and was stable over time; proportion of female pts was 90–91% (pSS) and 92–93% (SS+AID); mean age ranged from 63–66 (pSS) and 58–63 (SS+AID) years. Estimated incidence of SS (2012–2018) per 100,000 persons ranged from 4.1–0.3 (pSS) and 2.1–0.1 (SS+AID); proportion of female pts was 76–87% (pSS) and 74–90% (SS+AID); mean age ranged from 53–64 (pSS) and 50–62 (SS+AID) years. RA was the most frequently associated autoimmune disorder (32%) in pts with SS+AID. In the first year, artificial tears was the most frequently reimbursed drug (66% [pSS], 55% [SS+AID]), followed by hydroxychloroquine (19% [pSS], 35% [SS+AID]). From 2014–2018, ~30% of men and ~22% of women with pSS reported no drug reimbursement; ~20% of men and ~15% of women with SS+AID reported no drug reimbursement during the same time frame. From 2013–2018, ~50% of all pts had consultations with a dentist or an ophthalmologist. Mean healthcare costs increased over the study period: from €5836 to €9618 (pSS) and €8905 to €13,271 (SS+AID). Pt characteristics and healthcare consumption data are presented (Table 1).

Conclusion: Prevalence of pSS in this French claims data study was stable over time and consistent with previous reports.[3] Based on these results, SS may be considered an orphan disease. Overall costs for pts with SS were higher than previously estimated.[5] Results may help inform and optimise specialist care for pts with SS in France.

REFERENCES:

[1] Patel R, Shahane A. *Clin Epidemiol* 2014;6:247–255.
[2] Mariette X, Criswell LA. *N Engl J Med* 2018;378:931–939.
[3] Maldini C, et al. *Arthritis Care Res (Hoboken)* 2014;66:454–463.
[4] Devauchelle Pensec V, et al. *Arthritis Rheumatol* 2019;71(suppl 10):abstract 1101.
[5] l'Assurance Maladie. Améliorer la qualité du système de santé et maîtriser les dépenses. July 2019.

Acknowledgements: This study was sponsored by Bristol Myers Squibb. Professional medical writing assistance was provided by Lindsay Craik at Caudex and was funded by Bristol Myers Squibb.

Disclosure of Interests: Raphaèle Seror Consultant of: Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Fresenius Kabi, GlaxoSmithKline, Janssen, Pfizer, Roche, Laurent Chiche: None declared, Guillaume Desjeux: None declared, Joe Zhuo Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Bruno Bregman Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Virginie Vannier-Moreau Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Valerie Devauchelle-Pensec Consultant of: AbbVie, Bristol Myers Squibb, Novartis, Grant/research support from: Bristol Myers Squibb, Lilly, Roche-Chugai.

DOI: 10.1136/annrheumdis-2021-eular.78

POS0025

INCIDENCE RATES AND POINT PREVALENCE OF SEROPOSITIVE AND SERONEGATIVE RHEUMATOID ARTHRITIS IN DENMARK: A NATIONWIDE REGISTER-BASED STUDY FROM 1998 TO 2018 USING FOUR DIFFERENT CASE CRITERIA

B. G. Soussi[1], R. L. Cordtz[1], S. Kristensen[1,2], C. S. Bork[3], J. Christensen[2,4], E. B. Schmidt[2,3], D. Prieto-Alhambra[5], L. Dreyer[1,2]. *[1]Aalborg University Hospital, Department of Rheumatology, Aalborg, Denmark*; *[2]Aalborg University, Department of Clinical Medicine, Aalborg, Denmark*; *[3]Aalborg University Hospital, Department of Cardiology, Aalborg, Denmark*; *[4]Aalborg University Hospital, Department of Nephrology, Aalborg, Denmark*; *[5]University of Oxford, CSM-NDORMS, Oxford, United Kingdom*

Background: Few previous studies have investigated the incidence rate (IR) and point prevalence (PP) of seropositive and seronegative rheumatoid arthritis (RA), and further, the estimates remain unknown in the Danish population.

Objectives: To investigate the IR and PP of seropositive and seronegative RA in the adult Danish population from 1998 to 2018 using four register-based case definitions of RA.

Methods: Nationwide register-based cohort study. Using the Danish administrative registers, patients with RA between 1998 and end of 2018 were identified. ICD-10 codes for RA were identified in the Danish National Patient Registry and information on DMARD prescriptions were obtained through the Danish National Prescription Registry using ATC codes. The used case definitions were[1]: Criteria A, first time M05/M06 RA diagnosis and redemption of a DMARD in the following year; Criteria B, two RA diagnoses within 90 days of each other, originating from department of rheumatology or general internal medicine, where the latest registered M05/M06 diagnosis defined the serologic status; Criteria C, a M05/M06 diagnosis recorded at any time preceded or followed by redemption of a DMARD prescription within one year, where the M05/M06 diagnosis recorded determined the serologic status; Criteria D, as Criteria A, but with the additional requirements that cases had no registration for other selected inflammatory diseases.

In calculation of IRs the total Danish population from 1998 to 2018 was used as reference population for standardisation. The PP was calculated for years 2000, 2009, 2011 and 2018.

Results: From 1998 to 2018 the overall IR was 18.0 (95%CI 17.7 to 18.3) per 100,000 person years (PY) for seropositive RA and 16.7 (95%CI 16.4 to 16.9) per 100,000 PY for seronegative RA using Criteria A. A higher IR for seropositive RA than for seronegative RA was found regardless of the case criteria used. Figure 1 shows the temporal IRs of seropositive and seronegative RA.

Regardless of case criteria used, the PP increased from 2000 to 2018 for both seropositive and seronegative RA, and the estimates were higher for seropositive RA than for seronegative RA (Table 1).

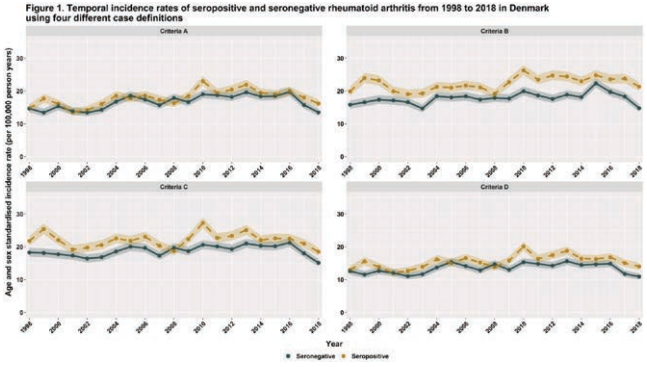


Figure 1. Temporal incidence rates of seropositive and seronegative rheumatoid arthritis from 1998 to 2018 in Denmark using four different case definitions

Table 1. Characteristics and healthcare consumption data for pts with SS in the SNDS (2011–2018)

	pSS			SS+AID		
Age at disease onset, overall and by sex						
	M (n=2515)	**F (n=20,637)**	**All (n=23,152)**	**M (n=1350)**	**F (n=14,112)**	**All (n=15,462)**
Mean (SD)	62 (15)	60 (15)	60 (15)	59 (14)	56 (15)	56 (15)
Age, yrs, n (%)						
<50	480 (19)	4948 (24)	5428 (23)	328 (24)	4507 (32)	4835 (31)
50–74	1471 (59)	11,567 (56)	13,038 (56)	852 (63)	7887 (56)	8739 (57)
≥75	564 (22)	4122 (20)	4686 (20)	170 (13)	1718 (12)	1888 (12)
Healthcare consumption						
Mean (IQR) no. prescriptions for treatment of interest		37 (9–58)			52 (20–78)	
≥1 Schirmer's test, n (%)		2409 (10)			1303 (8)	
Reimbursement for antinuclear antibody test, n (%)		13,312 (58)			9587 (62)	
Mean no. dental reimbursements/yr		2			1	
Mean no. ophthalmologist reimbursements/yr		1			1	

F=female; IQR=interquartile range; M=male; yr=year.

Table 1. Point prevalence of rheumatoid arthritis in Denmark in year 2000, 2009, 2011 and 2018 using four different case definitions

		2000		2009		2011		2018	
		Seropositive	Seronegative	Seropositive	Seronegative	Seropositive	Seronegative	Seropositive	Seronegative
Criteria A	**N**	3029	2741	7474	7127	8712	8121	12437	11662
	Population	3964040		4166298		4202891		4269677	
	PP, % (95%CI)	0.08 (0.08 to 0.08)	0.07 (0.07 to 0.07)	0.18 (0.18 to 0.19)	0.17 (0.17 to 0.18)	0.21 (0.20 to 0.21)	0.19 (0.19 to 0.20)	0.27 (0.27 to 0.28)	0.26 (0.25 to 0.26)
Criteria B	**N**	7507	4893	11565	9033	12710	10011	16334	13340
	PP, % (95%CI)	0.20 (0.19 to 0.20)	0.13 (0.12 to 0.13)	0.28 (0.28 to 0.29)	0.22 (0.21 to 0.22)	0.30 (0.30 to 0.31)	0.24 (0.23 to 0.24)	0.36 (0.35 to 0.36)	0.29 (0.29 to 0.30)
Criteria C	**N**	6701	4570	11174	9125	12417	10149	15881	13712
	PP, % (95%CI)	0.18 (0.17 to 0.18)	0.12 (0.12 to 0.12)	0.27 (0.27 to 0.28)	0.22 (0.22 to 0.23)	0.29 (0.29 to 0.30)	0.24 (0.24 to 0.25)	0.35 (0.34 to 0.35)	0.30 (0.30 to 0.31)
Criteria D	**N**	2724	2390	6612	5984	7695	6759	10830	9452
	PP, % (95%CI)	0.07 (0.07 to 0.07)	0.06 (0.06 to 0.07)	0.16 (0.16 to 0.16)	0.15 (0.14 to 0.15)	0.18 (0.18 to 0.19)	0.16 (0.16 to 0.17)	0.24 (0.23 to 0.24)	0.21 (0.20 to 0.21)

PP = Point prevalence

Conclusion: In Denmark, the IR and PP estimates were higher for seropositive compared to seronegative RA during the study period. However, when applying stricter case criteria for RA (Criteria A and D) the differences in IR and PP estimates were smaller, than when using less strict criteria (Criteria B and C). The findings of such small differences between seropositive and seronegative IRs warrant further investigation.

REFERENCES:

[1] Soussi BG et al. Incidence and prevalence of rheumatoid arthritis in Denmark: a nationwide population based study investigating the effect of four different case definitions [abstract]. Ann Rheum Dis. 2020;79(supplement 1):46

Acknowledgements: The authors will like to thank The Danish Rheumatism Association for supporting this work.

Disclosure of Interests: Bolette Gylden Soussi: None declared, René Lindholm Cordtz: None declared, Salome Kristensen: None declared, Christian Sørensen Bork: None declared, Jeppe Christensen: None declared, Erik Berg Schmidt: None declared, Daniel Prieto-Alhambra Grant/research support from: Grants from AMGEN, UCB Biopharma and Les Laboratoires Servier; and Janssen, on behalf of IMI-funded EHDEN and EMIF consortiums, and Synapse Management Partners have supported training programmes organised by DPA's department and open for external participants, Lene Dreyer Grant/research support from: Grants from BMS, Galderma and Eli Lilly.

DOI: 10.1136/annrheumdis-2021-eular.131

POS0026

ASSOCIATION BETWEEN RA DISEASE ACTIVITY AND TOOTH LOSS: RESULTS OF TWO NATIONAL COHORTS

K. Albrecht[1], P. De Pablo[2], T. Eidner[3], G. Hoese[4], S. Wassenberg[5], A. Zink[1], J. Callhoff[1,6]. [1]*German Rheumatism Research Centre, Epidemiology, Berlin, Germany*; [2]*University of Birmingham, Rheumatology Research Group, Institute of Inflammation & Ageing, College of Medical & Dental Sciences, Birmingham, United Kingdom*; [3]*Jena University Hospital, Department of Internal Medicine III, Division of Rheumatology & Osteology, Jena, Germany*; [4]*Practice of Rheumatology, Stadthagen, Stadthagen, Germany*; [5]*Rheumazentrum Ratingen,, Ratingen, Germany*; [6]*Charité - Universitätsmedizin Berlin, Institute for Social Medicine, Epidemiology and Health Economics, Berlin, Germany*

Background: Cross-sectional studies suggest an association between the presence of tooth loss and/or periodontitis, cytokine levels and disease activity in patients with rheumatoid arthritis (RA) (1).

Objectives: To analyze the association between tooth loss and disease activity/inflammatory activity in patients with early arthritis and established RA.

Methods: Two data sources were used for analysis. Participants of the early arthritis cohort study CAPEA, conducted between 2010 and 2013, reported their number of teeth present at baseline and were followed over 2 years. Tooth loss categories were defined according to the number of teeth present, as follows: 0, 1-19, 19-27, and all 28 teeth. Disease activity/inflammatory activity data, such as disease activity scores (DAS28-ESR) and disease activity parameters, including swollen joint count (SJC) and inflammatory markers, i.e. erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), were collected longitudinally at baseline, 3, 6, 12, 18, and 24 months. We used linear mixed regression models (with negative binomial distribution for SJC) to estimate the association between tooth loss and disease activity scores, SJC and inflammatory markers (ESR, CRP), over time. We also investigated the association between tooth loss and disease activity/inflammatory markers in patients with established RA, using cross-sectional data from the German National database (NDB) collected between 2015 and 2018. All models were adjusted for age, sex, smoking (ever vs. never), rheumatoid factor and education level, defined as years in education. Models with the NDB data were additionally adjusted for disease duration, missing data were imputed using multiple imputation. In all models, number of teeth was entered as a continuous variable.

Results: Of a total of 1,124 CAPEA participants included, those with higher tooth loss were older, more often smokers, had a lower level of education, higher inflammatory markers and higher disease activity scores at baseline (Table 1). Inflammatory markers decreased comparably across all categories of tooth loss over time (Figure 1), in particular CRP. Tooth loss was not significantly associated with CRP or SJC alone. Glucocorticoid use was higher among those with more tooth loss, however dose reduction was similar across tooth loss categories. Among 7,179 NDB participants, adjusted disease activity scores and inflammatory markers were higher across tooth loss categories (DAS28 no teeth: 2.7, all teeth: 2.4; ESR no teeth: 23 mm/h, all teeth: 17 mm/h). SJC was not relevantly associated with tooth loss (no teeth: 1.2, all teeth: 1.2). Mean disease duration in the NDB sample was 13 years.

Table 1. Early arthritis cohort (CAPEA) baseline characteristics, stratified by number of teeth

	Number of teeth present				Total	n
	0	1-19	20-27	All 28		
N	89	315	452	268	1,124	1,124
Female, %	57	65	64	69	65	1,124
Age (years), mean	69	64	54	45	56	1,124
ESR (mm), mean	42	38	28	24	31	1,074
CRP (mg/l), mean	25	24	15	15	19	1,069
SJC, mean	6.1	6.9	5.6	5.2	5.9	1,120
DAS28-ESR, mean	5.5	5.2	4.7	4.5	4.9	983
RF positive, %	63	53	52	54	54	1,124
Education, %						1,020
<=8 years	80	58	35	21	42	
9-10 years	16	30	43	46	38	
11-13 years	4	12	22	33	20	
Smoking (ever), %	73	64	61	56	61	1,102

ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, DAS28: disease activity score, RF: rheumatoid factor, SJC: swollen joint count

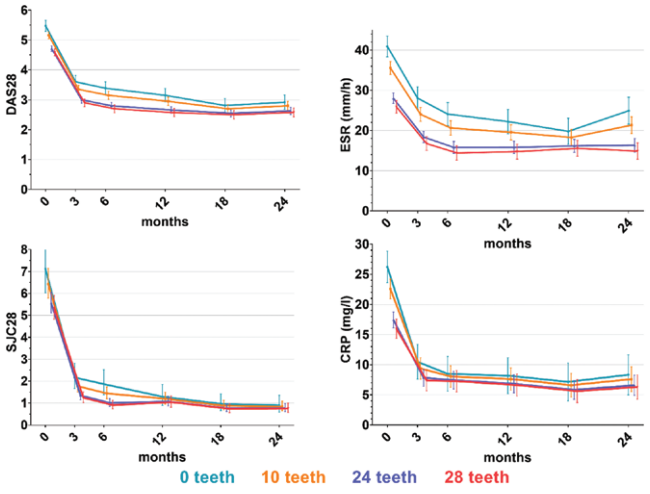


Figure 1. Disease activity parameters during the 24-months follow-up, stratified by the number of teeth at baseline: results from mixed models, adjusted for age, sex, smoking and education level.

Conclusion: While we observed a significant association between tooth loss and disease activity and inflammation markers in both early arthritis and established RA, our longitudinal results suggest that tooth loss has no influence on response to therapy.

REFERENCES:

[1] Rodriguez-Lozano B, Gonzalez-Febles J, Garnier-Rodriguez JL, Dadlani S, Bustabad-Reyes S, Sanz M, et al. Association between severity of periodontitis and clinical activity in rheumatoid arthritis patients: a case-control study. Arthritis Res Ther. 2019;21(1):27.

Acknowledgements: We thank all participating rheumatologists and patients for their valuable contributions.

The CAPEA periodontitis project was funded by the Deutsche Rheuma-Liga Bundesverband e.V.

Capea was funded by an unconditional research grant from Pfizer.

The National Database of the German Collaborative Arthritis centers has been supported since 2007 by the Association of Regional Cooperative Rheumatology Centres and joint contributions to the Rheumatological Training Academy and the DRFZ by the following members of the Working Group of Corporate Members of the German Society for Rheumatology: AbbVie, Actelion, BMS, GSK, Lilly, Medac, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis and UCB. The researchers have full academic freedom.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.658

POS0027

SECULAR TRENDS IN BASELINE CHARACTERISTICS, TREATMENT RETENTION AND RESPONSE RATES IN 27189 BIO-NAÏVE AXIAL SPONDYLOARTHRITIS PATIENTS INITIATING TNFI – RESULTS FROM THE EUROSPA COLLABORATION

L. Midtbøll Ørnbjerg[1], S. N. Christiansen[1], S. H. Rasmussen[1], A. G. Loft[2,3], U. Lindström[4], J. Zavada[5], F. Iannone[6], F. Onen[7], M. J. Nissen[8], B. Michelsen[1,9], M. J. Santos[10], G. Macfarlane[11], D. Nordström[12], M. Pombo-Suarez[13], C. Codreanu[14], M. Tomsic[15], I. Van der Horst-Bruinsma[16], B. Gudbjornsson[17], J. Askling[18], B. Glintborg[1,3], K. Pavelka[5], E. Gremese[19], N. Akkoc[20], A. Ciurea[21], E. Kristianslund[9], A. Barcelos[22], G. T. Jones[23], A. M. Hokkanen[24], C. Sánchez-Piedra[25], R. Ionescu[14], Z. Rotar[15], M. G. H. Van de Sande[26], A. J. Geirsson[27], M. Østergaard[1], M. L. Hetland[1,3]. *[1]Rigshospitalet Glostrup, Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Glostrup, Denmark*; *[2]Aarhus University Hospital, Department of Rheumatology, Aarhus, Denmark*; *[3]Rigshospitalet Glostrup, DANBIO registry, Glostrup, Denmark*; *[4]Gothenburg University, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; *[5]Institute of Rheumatology, Institute of Rheumatology, Prague, Czech Republic*; *[6]University of Bari, Rheumatology Unit, Bari, Italy*; *[7]Dokuz Eylul University School of Medicine, Division of Rheumatology, Izmir, Turkey*; *[8]Geneva University Hospital, Department of Rheumatology, Geneva, Switzerland*; *[9]Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway*; *[10]Hospital Garcia de Orta, Rheumatology Department, Almada, Portugal*; *[11]University of Aberdeen, School of Medicine, Medical Sciences and Nutrition, Aberdeen Centre for Arthritis and Musculoskeletal Health, Aberdeen, United Kingdom*; *[12]Helsinki University and University Hospital, Division of Medicine and Rheumatology, Helsinki, Finland*; *[13]Hospital Clinico Universitario, Rheumatology Service, Santiago de Compostela, Spain*; *[14]University of Medicine and Pharmacy, Carol Davila, Bucharest, Romania*; *[15]University Medical Centre Ljubljana, Department of Rheumatology, and Universitiy of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia*; *[16]Amsterdam UMC, location Vumc, Department of Rheumatology, Amsterdam, Netherlands*; *[17]Centre for Rheumatology Research, University Hospital and Faculty of Medicine, University of Iceland, Reykjavik, Iceland*; *[18]Karolinska Institutet, Clinical Epidemiology Division, Department of Medicine Solna, Stockholm, Sweden*; *[19]Division of Rheumatology, Fondazione Policlinico Universitario A.Gemelli-IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy*; *[20]Celal Bayar University School of Medicine, Division of Rheumatology, Manisa, Turkey*; *[21]University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland*; *[22]Centro Hospitalar do Baixo Vouga, Department of Rheumatology, Aveiro, Portugal*; *[23]University of Aberdeen, Aberdeen Centre for Arthritis and Musculoskeletal Health, Aberdeen, United Kingdom*; *[24]Helsinki University and Päijät Häme Central Hospital, Department of Rheumatology, Lahti, Finland*; *[25]Sociedad Española de Reumatologia, Research Unit, Madrid, Spain*; *[26]Amsterdam Rheumatology and Immunology Center (ARC), Amsterdam UMC/AMC, University of Amsterdam, Amsterdam, Netherlands*; *[27]University Hospital, Department of Rheumatology, Reykjavik, Iceland*

Background: Knowledge of changes over time in baseline characteristics and tumor necrosis factor inhibitor (TNFi) response in bio-naïve axial spondyloarthritis (axSpA) patients treated in routine care is limited.

Objectives: To investigate secular trends in baseline characteristics and retention, remission and response rates in axSpA patients initiating a first TNFi.

Methods: Prospectively collected data on bio-naïve axSpA patients starting TNFi in routine care from 15 European countries were pooled. According to year of TNFi initiation, three groups were defined a priori based on bDMARD availability: Group A (1999–2008), Group B (2009–2014) and Group C (2015–2018). Retention rates (Kaplan-Meier), crude and LUNDEX adjusted[1] remission (Ankylosing Spondylitis Disease Activity Score (ASDAS) <1.3, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) <20) and response (ASDAS Major and Clinically Important Improvement (MI/CII), BASDAI 50) rates were assessed at 6, 12 and 24 months. No statistical comparisons were made.

Results: In total, 27189 axSpA patients were included (5945, 11255 and 9989 in groups A, B and C).

At baseline, patients in group A were older, had longer disease duration and a larger proportion of male and HLA-B27 positive patients compared to B and C, whereas disease activity was similar across groups.

Retention rates at 6, 12 and 24 months were highest in group A (88%/81%/71%) but differed little between B (84%/74%/64%) and C (85%/76%/67%).

In all groups, median ASDAS and BASDAI had decreased markedly at 6 months (Table 1). The ASDAS values at 12 and 24 months and BASDAI at 24 months were higher in group A compared with groups B and C. Similarly, crude remission and response rates were lowest in group A. After adjustments for drug retention (LUNDEX), remission and response rates showed less pronounced between-group differences regarding ASDAS measures and no relevant differences regarding BASDAI measures.

Conclusion: Nowadays, axSpA patients initiating TNFi are younger with shorter disease duration and more frequently female and HLA-B27 negative than previously, while baseline disease activity is unchanged. Drug retention rates have decreased, whereas crude remission and response rates have increased. This may indicate expanded indication but also a stable disease activity threshold for TNFi initiation over time, an increased focus on targeting disease remission and more available treatment options.

Table 1. Secular trends in baseline characteristics, treatment retention, remission and response rates in European axSpA patients initiating a 1st TNFi

Baseline characteristics	**Group A** (1999–2008)			**Group B** (2009–2014)			**Group C** (2015–2018)		
Age, years, median (IQR)	57 (49–66)			51 (42–60)			46 (37–56)		
Male, %	66			60			57		
HLA-B27, %	87			77			72		
Years since diagnosis, median (IQR)	5 (1–12)			2 (0–8)			2 (0–7)		
Smokers, %	23			24			25		
ASDAS, median (IQR)	3.5 (2.8–4.1)			3.4 (2.8–4.1)			3.5 (2.8–4.1)		
BASDAI, median, (IQR)	57 (42–71)			59 (43–72)			57 (41–71)		
TNFi drug, % (Adalimumab / Etanercept / Infliximab / Certolizumab / Golimumab)	22 / 35 / 43 / 0 / 0			37 / 21 / 20 / 4 / 18			27 / 28 / 24 / 8 / 13		
Follow up	**6 months**			**12 months**			**24 months**		
	Gr A	**Gr B**	**Gr C**	**Gr A**	**Gr B**	**Gr C**	**Gr A**	**Gr B**	**Gr C**
Retention rates, %, (95% CI)	88 (88–89)	84 (83–85)	85 (84–86)	81 (80–82)	74 (74–75)	76 (75–76)	71 (70–72)	64 (63–65)	67 (66–68)
ASDAS, median, (IQR)	1.8 (1.2–2.8)	1.9 (1.2–2.8)	1.8 (1.2–2.6)	1.9 (1.3–2.6)	1.7 (1.2–2.5)	1.6 (1.1–2.4)	1.9 (1.4–2.6)	1.7 (1.1–2.4)	1.5 (1.1–2.2)
ASDAS inactive disease, %, c/L	28 / 25	28 / 24	30 / 26	24 / 19	32 / 24	34 / 26	23 / 16	34 / 20	39 / 23
ASDAS CII, %, c/L	57 / 51	59 / 50	63 / 54	61 / 50	63 / 47	67 / 51	59 / 41	68 / 40	74 / 45
ASDAS MI, %, c/L	31 / 27	32 / 27	37 / 32	32 / 26	37 / 27	41 / 31	30 / 20	42 / 25	46 / 28
BASDAI, median, (IQR)	23 (10–40)	26 (11–48)	24 (10–44)	21 (10–38)	23 (10–42)	20 (8–39)	22 (9–40)	20 (8–39)	16 (6–35)
BASDAI remission, %, c/L	44 / 40	40 / 34	43 / 36	45 / 36	45 / 34	50 / 38	44 / 30	48 / 29	56 / 34
BASDAI 50 response, %, c/L	53 / 47	50 / 42	53 / 45	57 / 46	56 / 42	58 / 44	57 / 39	60 / 35	63 / 38

Gr, Group; c/L, crude/LUNDEX adjusted.

REFERENCES:
[1] Arthritis Rheum 2006; 54: 600-6.
Acknowledgements: Novartis Pharma AG and IQVIA for supporting the Euro-SpA Research Collaboration Network.
Disclosure of Interests: Lykke Midtbøll Ørnbjerg Grant/research support from: Novartis, Sara Nysom Christiansen Speakers bureau: BMS and GE, Grant/research support from: Novartis, Simon Horskjær Rasmussen: None declared, Anne Gitte Loft Speakers bureau: AbbVie, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: AbbVie, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Grant/research support from: Novartis, Ulf Lindström: None declared, Jakub Zavada: None declared, Florenzo Iannone: None declared, Fatos Onen: None declared, Michael J. Nissen Speakers bureau: Novartis, Eli Lilly, Celgene, and Pfizer, Consultant of: Novartis, Eli Lilly, Celgene, and Pfizer, Brigitte Michelsen Consultant of: Novartis, Grant/research support from: Novartis, Maria Jose Santos Speakers bureau: AbbVie, Novartis, Pfizer, Gary Macfarlane Grant/research support from: GlaxoSmithKline, Dan Nordström Consultant of: Abbvie, BMS, MSD, Novartis, Pfizer, Roche, UCB, Manuel Pombo-Suarez: None declared, Catalin Codreanu Speakers bureau: AbbVie, Amgen, Egis, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, Egis, Novartis, Pfizer, UCB, Matija Tomsic Speakers bureau: Abbvie, Amgen, Biogen, Medis, MSD, Novartis, Pfizer, Consultant of: Abbvie, Amgen, Biogen, Medis, MSD, Novartis, Pfizer, Irene van der Horst-Bruinsma Speakers bureau: Abbvie, BMS, MSD, Novartis, Pfizer, Lilly, UCB, Björn Gudbjornsson Speakers bureau: Amgen and Novartis, Johan Askling: None declared, Bente Glintborg Grant/research support from: Pfizer, Biogen, AbbVie, Karel Pavelka Speakers bureau: AbbVie, Roche, MSD, UCB, Pfizer, Novartis, Egis, Gilead, Eli Lilly, Consultant of: AbbVie, Roche, MSD, UCB, Pfizer, Novartis, Egis, Gilead, Eli Lilly, Elisa Gremese: None declared, Nurullah Akkoc: None declared, Adrian Ciurea Speakers bureau: Abbvie, Eli-Lilly, MSD, Novartis, Pfizer, Eirik kristianslund: None declared, Anabela Barcelos: None declared, Gareth T. Jones Grant/research support from: Pfizer, AbbVie, UCB, Celgene, Amgen, GSK, Anna-Mari Hokkanen Grant/research support from: MSD, Carlos Sánchez-Piedra: None declared, Ruxandra Ionescu Speakers bureau: Abbvie, Amgen, Boehringer-Ingelheim Eli-Lilly,Novartis, Pfizer, Sandoz, UCB, Ziga Rotar Speakers bureau: Abbvie, Amgen, Biogen, Medis, MSD, Novartis, Pfizer, Consultant of: Abbvie, Amgen, Biogen, Medis, MSD, Novartis, Pfizer, Marleen G.H. van de Sande: None declared, Arni Jon Geirsson: None declared, Mikkel Østergaard Speakers bureau: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB and Wyeth, Consultant of: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB and Wyeth, Merete L. Hetland Speakers bureau: Abbvie, Biogen, BMS, Celltrion, Eli Lilly, Janssen Biologics B.V, Lundbeck Fonden, MSD, Pfizer, Roche, Samsung Biopies, Sandoz, Novartis.
DOI: 10.1136/annrheumdis-2021-eular.589

POS0028 DEFINING THE PREVALENCE OF UNMET NEED IN SLE: DATA FROM A LARGE MULTINATIONAL LONGITUDINAL SLE COHORT

R. Kandane-Rathnayake1, W. Louthrenoo[2], A. Hoi[1], V. Golder[1], Y. H. Chen[3], S. F. Luo[4], Y. J. Jan Wu[5], A. Lateef[6], J. Cho[6], L. Hamijoyo[7], C. S. Lau[8], S. Navarra[9], L. Zamora[9], Z. LI[10], Y. An[10], S. Sockalingam[11], Y. Katsumata[12], M. Harigai[12], Y. Hao[13], Z. Zhang[13], J. Kikuchi[14], T. Takeuchi[14], B. Basnayake[15], F. Goldblatt[16,17], M. Chan[18], K. Ng[19], S. C. Bae[20], S. Oon[21], S. O'neill[22], K. Gibson[22], S. Kumar[23], N. Tugnet[24], Y. Tanaka[25], M. Nikpour[26], E. F. Morand[1]on behalf of The Asia Pacific Lupus Collaboration. *[1]Monash University, School of Clinical Sciences at Monash Health, Clayton, Australia*; *[2]Chiang Mai University Hospital, Department of Internal Medicine, Faculty of Medicine, Chiang Mai, Thailand*; *[3]Taichung Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Taichung, Taiwan, Republic of China*; *[4]Chang Gung Memorial Hospital, Department of Rheumatology, Allergy and Immunology, Taipei, Taiwan, Republic of China*; *[5]Chang Gung Memorial Hospital, Department of Rheumatology, Allergy and Immunology, Keelung, Taiwan, Republic of China*; *[6]National University Hospital, Rheumatology Division, University Medical Cluster, Singapore, Singapore*; *[7]Padjadjaran University/ Hasan Sadikin General Hospital, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Bandung, Indonesia*; *[8]The University of Hong Kong/Queen Mary Hospital, Division of Rheumatology & Clinical Immunology, Department of Medicine, Pok fu lam, Hong Kong (SAR)*; *[9]University of Santo Tomas Hospital, Joint and Bone Center, Manila, Philippines*; *[10]People's Hospital Peking University Health Science Center, Department of Rheumatology and Immunology, Beijing, China*; *[11]University of Malaya, Department of Medicine, Faculty of Medicine, Kuala Lumpur, Malaysia*; *[12]Tokyo Women's Medical University, Institute of Rheumatology, Tokyo, Japan*; *[13]Peking University First Hospital, Rheumatology and Immunology department, Beijing, China*; *[14]Keio University, Division of Rheumatology, Department of Internal Medicine, School of Medicine, Tokyo, Japan*; *[15]Teaching Hospital Kandy, Division of Nephrology, Kandy, Sri Lanka*; *[16]Flinders Medical Centre, Department of Rheumatology, Bedford Park, Australia*; *[17]Royal Adelaide Hospital, Rheumatology Unit, North Terrace, SA, Australia*; *[18]Tan Tock Seng Hospital, Department of Rheumatology, Allergy & Immunology, Tan Tock Seng, Singapore*; *[19]North Shore Hospital, Department of Medicine, Auckland, New Zealand*; *[20]Hanyang University Hospital for Rheumatic Diseases, Department of Rheumatology, Seoul, Korea, Republic of (South Korea)*; *[21]St. Vincent's Hospital, Melbourne, Department of Rheumatology, Melbourne, Australia*; *[22]Liverpool Hospital, Rheumatology department, Sydney, Australia*; *[23]Middlemore Hospital, Department of Rheumatology, Auckland, New Zealand*; *[24]Greenlane Clinical Centre, Department of Rheumatology, Auckland, New Zealand*; *[25]University of Occupational and Environmental Health, The First Department of Internal Medicine, Kitakyushu, Japan*; *[26]St. Vincent's Hospital, Department of Rheumatology, Melbourne*

Background: The recent prospectively validated definition of the lupus low disease activity state (LLDAS) allows characterisation of patients not achieving a treatment goal, providing impetus for an analysis of unmet needs in SLE using formal definitions. Other recently described definitions of high disease burden include disease activity over time, high disease activity status (HDAS) episodes, and the combination of high disease activity, serological activity and glucocorticoid (GC) use (HDAS+SA+GC).
Objectives: To determine the prevalence of formal categories of unmet need, and the association of these with adverse outcomes, in SLE.
Methods: Data from a 13-country longitudinal SLE cohort (ACR/SLICC criteria) were collected between 2013 and 19 using standard templates. Unmet need was defined as (i) patients never attaining LLDAS defined as in Golder *et al.*, 2019 [1], (ii) having persistently active disease (time adjusted mean SLEDAI-2K (AMS) > 4), (iii) ever exhibiting high disease activity status (HDAS; SLEDAI-2K ≥10[2]), or (iv) ever exhibiting all of SLEDAI≥10, serological activity, and glucocorticoid use (HDAS+SA+GC)[3]. Health-related quality of life (HRQoL) was assessed using SF36 (v2) surveys and damage accrual using SLE Damage Index (SDI).
Results: 3,384 SLE patients were followed for 30,313 visits over median [IQR] 2.4 [0.4, 4.3] years. 53% of all visits were not in LLDAS; 813 patients (24%) never achieved LLDAS during observation. Median AMS was 3.0 [1.4, 4.9] and 34% of patients had AMS > 4 throughout the study. 25% of patients had at least one episode of HDAS, representing 8% of visits. 702 patients (21%) had at least one episode of HDAS+SA+GC, representing 8% of visits. Each of never-LLDAS, AMS>4, ever-HDAS, and ever-HDAS+SA+GC were associated with significantly greater number of physician visits, higher mean glucocorticoid dose, lower HRQoL and higher mortality. 31%, 58% and 83% of never-LLDAS, AMS>4, and ever-HDAS patients respectively were also HDAS+SA+GC on at least one occasion.
Conclusion: Data from a multinational longitudinal SLE cohort indicate that unmet need, defined by LLDAS-never, AMS>4, HDAS, or HDAS+SA+GC, is prevalent in SLE, and that these definitions are associated with poor outcomes.
REFERENCES:
[1] Golder, V., et al., Lupus low disease activity state as a treatment endpoint for systemic lupus erythematosus: a prospective validation study. The Lancet Rheumatology, 2019. **1**(2): p. e95-e102.
[2] Koelmeyer, R., et al., High disease activity status suggests more severe disease and damage accrual in systemic lupus erythematosus. Lupus Sci Med, 2020. **7**(1).
[3] van Vollenhoven, R.F., et al., Belimumab in the treatment of systemic lupus erythematosus: high disease activity predictors of response. Annals of the Rheumatic Diseases, 2012. **71**(8): p. 1343-1349.
Acknowledgements: The APLC acknowledges all the Data Collectors and Patients for their valuable contributions to research.
Disclosure of Interests: Rangi Kandane-Rathnayake: None declared, Worawit Louthrenoo: None declared, Alberta Hoi Consultant of: Abbvie and GSK, Grant/research support from: AstraZeneca, GSK, BMS, Janssen, and Merck Serono, Vera Golder: None declared, Yi-Hsing Chen Speakers bureau: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Lilly, AstraZeneca, Sanofi, MSD, Guigai, Astellas, Inova Diagnostics, UCB, Agnitio Science Technology, United Biopharma, Thermo Fisher, Consultant of: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Lilly, AstraZeneca, Sanofi, MSD, Guigai, Astellas, Inova Diagnostics, UCB, Agnitio Science Technology, United Biopharma, Thermo Fisher, Gilead, Grant/research support from: Pfizer, Norvatis, BMS, Abbevie,

Johnson & Johnson, Roche, Sanofi, Guigai, Roche, Boehringer Ingelheim, UCB, MSD, Astra-Zeneca, Astellas, Gilead, Shue Fen Luo: None declared, Yeong-Jian Jan Wu Speakers bureau: Pfizer, Lilly, Novartis, Abbvie, Aisha Lateef: None declared, Jiacai Cho: None declared, Laniyati Hamijoyo Speakers bureau: Pfizer, Novartis, Abbot, Chak Sing Lau Shareholder of: Pfizer, Sanofi, and Janssen, Sandra Navarra Speakers bureau: Pfizer, Johnson & Johnson, Novartis, Astellas, Grant/research support from: Astellas, Johnson & Johnson, Leonid Zamora: None declared, Zhanguo Li Speakers bureau: Eli, Lilly, Novartis, GSK, AbbVie, Paid instructor for: Pfizer, Roche, Johnson., Consultant of: Lilly, Pfizer, Grant/research support from: Pfizer, Yuan An: None declared, Sargunan Sockalingam Speakers bureau: Pfizer, Roche, Novartis, Grant/research support from: Roche and Novartis, Yasuhiro Katsumata Speakers bureau: Chugai Pharmaceutical Co., Ltd., Glaxo-Smithkline K.K., and Sanofi K.K., masayoshi harigai Speakers bureau: AbbVie Japan GK, Ayumi Pharmaceutical Co., Boehringer Ingelheim Japan, Inc.,Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., GlaxoSmithKline K.K., Kissei Pharmaceutical Co., Ltd., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd., Consultant of: AbbVie, Boehringer-ingelheim, Bristol Myers Squibb Co., Kissei Pharmaceutical Co.,Ltd. and Teijin Pharma., Grant/research support from: AbbVie Japan GK, Asahi Kasei Corp., Astellas Pharma Inc., Ayumi Pharmaceutical Co., Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Daiichi-Sankyo, Inc.,Eisai Co., Ltd., Kissei Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Nippon Kayaku Co., Ltd., Sekiui Medical, Shionogi & Co., Ltd., Taisho Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd., Yanjie Hao: None declared, Zhuoli Zhang Speakers bureau: Norvatis, GSK, Pfizer, Jun Kikuchi: None declared, Tsutomu Takeuchi Speakers bureau: AbbVie AYUMI Pharmaceutical Corp. Bristol-Myers Squibb Chugai Pharmaceutical Co, Ltd. Daiichi Sankyo Co., Ltd. Eisai Co., Ltd. Eli Lilly Japan, Gilead Sciences, Inc. Mitsubishi-Tanabe Pharma Corp. Pfizer Japan Inc. Sanofi K.K., Consultant of: Astellas Pharma, Inc. Chugai Pharmaceutical Co, Ltd. Eli Lilly Japan, Mitsubishi-Tanabe Pharma Corp., Grant/research support from: AbbVie, Asahikasei Pharma Corp. Chugai Pharmaceutical Co, Ltd. Mitsubishi-Tanabe Pharma Corp. Sanofi K.K., BMDB Basnayake: None declared, Fiona Goldblatt: None declared, Madelynn Chan Speakers bureau: AbbVie, Novartis, Consultant of: Pfizer, Eli-Lilly, Kristine Ng Speakers bureau: Abbvie, Novartis, Janssen, Sang-Cheol Bae: None declared, Shereen Oon: None declared, Sean O'Neill Consultant of: GSK, Kathryn Gibson Speakers bureau: UCB, Consultant of: Novartis, Janssen, Grant/research support from: Novartis, Sunil Kumar: None declared, Nicola Tugnet: None declared, Yoshiya Tanaka Speakers bureau: Daiichi-Sankyo, Eli Lilly, Novartis, YL Biologics, Bristol-Myers, Eisai, Chugai, Abbvie, Astellas, Pfizer, Sanofi, Asahi-kasei, GSK, Mitsubishi-Tanabe, Gilead, Janssen, Grant/research support from: Abbvie, Mitsubishi-Tanabe, Chugai, Asahi-Kasei, Eisai, Takeda, Daiichi-Sankyo, Mandana Nikpour Speakers bureau: Actelion, GSK, Janssen, Pfizer, UCB, Paid instructor for: UCB, Consultant of: Actelion, Boehringer Ingelheim, Certa Therapeutics, Eli Lilly, GSK, Janssen, Pfizer, UCB, Grant/research support from: Actelion, Astra Zeneca, BMS, GSK, Janssen, UCB, Eric F. Morand Speakers bureau: AstraZeneca, Paid instructor for: Eli Lilly, Consultant of: AstraZeneca, Amgen, Biogen, BristolMyersSquibb, Eli Lilly, EMD Serono, Genentech, Janssen, Grant/research support from: AstraZeneca, BristolMyersSquibb, Eli Lilly, EMD Serono, Janssen.

DOI: 10.1136/annrheumdis-2021-eular.938

POS0029

INCIDENCE AND TREATMENT PENETRATION OF RHEUMATOID ARTHRITIS IN NORWAY – A NATIONWIDE REGISTER LINKAGE STUDY

A. Kerola[1,2], J. Sexton[1], G. Wibetoe[1], S. Rollefstad[1], C. S. Crowson[3], E. Haavardsholm[1], T. K. Kvien[1], A. G. Semb[1]. [1]*Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway*; [2]*Päijät-Häme Joint Authority for Health and Wellbeing, Rheumatology, Lahti, Finland*; [3]*Mayo Clinic, Department of Quantitative Health Sciences, Rochester, Minnesota, United States of America*

Background: Incidence of rheumatoid arthritis (RA) in Norway has not been evaluated in a nationwide setting.

Objectives: To estimate the incidence of RA and real-life penetration of disease-modifying antirheumatic drug (DMARD) use in Norway.

Methods: The Norwegian Cardio-Rheuma register comprises pseudonymized data from nationwide registries including the total Norwegian population ≥18 years during 2008-2017. Demographic and socioeconomic data were retrieved from the National Population Register and Statistics Norway. Data on public or private somatic specialized care episodes were collected from the Norwegian Patient register (NPR) (ICD-10 codes for diagnoses and medical procedure codes for biologic DMARD infusions). Dispensed DMARD prescriptions were captured from the Norwegian Prescription Database. RA cases were defined as persons with NPR records of all of the following: 1) 1st episode with ICD-10 code M05/M06 as main or contributory diagnosis (index date), 2) 2nd episode with code M05/M06 within 2-year period following index date, 3) M05/M06 recorded in an internal medicine or rheumatology department during the 2-year period. Years 2008-2010 served as a look-back period to identify prevalent RA cases. To estimate person-years (pyrs) at risk, we calculated number of persons aged ≥ 18 living in Norway on the 1st of January of each year 2011-2015 and multiplied it by one year (prevalent RA cases excluded). Standardized estimates were calculated with 5-year age groups using Norwegian adult population 1st of January 2015 as the standard.

Results: Between 2011 and 2015, 9,493 persons fulfilled the RA definition (62.4% seropositive based on ICD-10 codes). Incidence rate was 49/100,000 pyrs (32 in men and 65 in women). A sensitivity analysis excluding cases who had dispensed DMARDs >12 months before index date yielded 8,125 RA cases (incidence 42/100,000 pyrs). Whereas absolute number of incident cases was highest among those aged 60-69 in both sexes, incidence was highest among those aged 70-79 (Figure 1). Both crude and age- and sex-standardized incidences were lower among persons with higher education level (crude/standardized incidence per 100,000 pyrs for those below upper secondary education 60/57; upper secondary or post-secondary non-tertiary education 53/52; higher education 36/39). Of incident cases, 94% received any DMARD treatment or glucocorticoids, 78% methotrexate, and 17% biologic DMARDs within 2 years after index date (Table 1).

Conclusion: Contemporary register-based estimate of RA incidence in Norway is comparable to other Nordic countries.[1,2] In line with treatment recommendations, methotrexate is the most commonly used DMARD in the initial treatment strategy in Norway. One in six patients used a biologic DMARD within 2 years from 1st recorded RA diagnosis.

REFERENCES:

[1] Eriksson JK, Neovius M, Ernestam S et al. Incidence of rheumatoid arthritis in Sweden: a nationwide population-based assessment of incidence, its determinants, and treatment penetration. Arthritis Care Res 2013;65:870-878.

[2] Puolakka K, Kautiainen H, Pohjolainen T et al. Rheumatoid arthritis remains a threat to work productivity: a nationwide register-based incidence study from Finland. Scand J Rheumatol 2010;39:436-438.

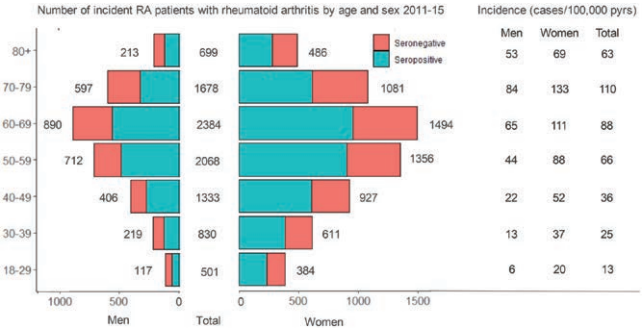


Figure 1.

Table 1. Characteristics and treatment penetration of incident RA patients 2011-2015

	All		Excluding cases with DMARDs >12 months before index date	
N	9493		8125	
Women, n (%)	6339 (66.8)		5379 (66.2)	
Age at index date, median (IQR)	60.5 (48.5 - 70.5)		60.8 (48.8 - 70.9)	
RF positive, n (%)	5927 (62.4)		5193 (63.9)	
Use of DMARDs after index date, n (%)	**12 months**	**24 months**	**12 months**	**24 months**
Any conventional DMARD	7797 (82.1)	8023 (84.5)	6682 (82.2)	6855 (84.4)
Methotrexate	7133 (75.1)	7402 (78.0)	6228 (76.7)	6436 (79.2)
Sulfasalazine	902 (9.5)	1218 (12.8)	745 (9.2)	1034 (12.7)
Any biologic DMARD	1102 (11.6)	1642 (17.3)	754 (9.3)	1219 (15.0)
TNF-inhibitors	1006 (10.6)	1513 (15.9)	690 (8.5)	1130 (13.9)
Oral glucocorticoids	6524 (68.7)	6974 (73.5)	5858 (72.1)	6199 (76.3)
Any DMARD or glucocorticoids	8789 (92.6)	8957 (94.4)	7498 (92.3)	7639 (94.0)

Acknowledgements: This work has been supported by a research grant from FOREUM Foundation for Research in Rheumatology.
Disclosure of Interests: Anne Kerola Speakers bureau: Boehringer-Ingelheim, Consultant of: Pfizer, Gilead, Boehringer-Ingelheim, Joseph Sexton: None declared, Grunde Wibetoe: None declared, Silvia Rollefstad: None declared, Cynthia S. Crowson: None declared, Espen Haavardsholm: None declared, Tore K. Kvien Speakers bureau: Amgen, Celltrion, Egis, Evapharma, Ewopharma, Hikma, Oktal, Sandoz, Sanofimgen, Celltrion, Egis, Evapharma, Ewopharma, Hikma, Oktal, Sandoz, Sanofi, Consultant of: AbbVie, Amgen, Biogen, Celltrion, Eli Lilly, Gilead, Mylan, Novartis, Pfizer, Sandoz, Sanofi, Grant/research support from: research funding to Diakonhjemmet Hospital from AbbVie, Amgen, BMS, MSD, Pfizer and UCB, Anne Grete Semb Speakers bureau: AbbVie, Bayer, Lilly, Novartis, and Sanofi, Consultant of: Sanofi, Grant/research support from: collaborative research support from Lilly, outside the submitted work.
DOI: 10.1136/annrheumdis-2021-eular.975

POS0030 SARCOIDOSIS INCIDENCE IN A NORTHERN SPANISH HEALTH REGION.

C. Álvarez-Reguera[1], R. Fernández-Ramón[2], J. J. Gaitán-Valdizán[2], J. L. Martín-Varillas[3], L. Sanchez-Bilbao[1], D. Martínez-López[3], I. González-Mazón[1], R. Demetrio-Pablo[2], M. Á. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*; [2]*Hospital Universitario Marqués de Valdecilla, Ophthalmology, Santander, Spain*; [3]*Hospital de Sierrallana, Rheumatology,Torrelavega, Spain*

Background: Sarcoidosis is a systemic and potentially severe disease **(1).** Its incidence varies widely worldwide.
Objectives: The aim of this study was to estimate the sarcoidosis incidence in a Northern Spanish population-based cohort.
Methods: All incident cases of sarcoidosis between January 1999 and December 2019 in a tertiary hospital were reviewed. Inclusion criteria were **a)** diagnosis of sarcoidosis according to ATS/ERS/WASOG *(Eur Respir J. 1999; 14:735-7)* and **b)** patients residing in our health region. Incidence between 1999 and 2019 was estimated by sex, age, and year of diagnosis.
Results: From a total of 384 patients diagnosed with sarcoidosis, 234 (129 women/ 105 men) met the inclusion criteria and were finally included in the study. Mean age of the cohort at diagnosis was 48.43±14.83 years (46.95±14.50 in males; 49.63±15.04 in females, p=0.12). Annual incidence during 1999-2019 period was 3.56 per 100,000 population (3.32 per 100,000 in males and 3.72 per 100,000 in females). An upward trend in annual incidence over time was observed with rates ranging from 1.73 per 100,000 inhabitants in 1999 to 6.91 per 100,000 inhabitants in 2016 (Figure 1). Overall, sarcoidosis was predominantly diagnosed during middle adulthood. A bimodal distribution of age-specific incidence rates was observed in both sexes with two peaks in the age groups of 30-39 (4.98 per 100,000) and 60-69 years (5.12 per 100,000) in men, and in 40-49 (6.45 per 100,000) and 60-69 years (5.94 per 100,000) in women.
Comparative studies with other regions are summarize in Table 1.
Conclusion: A progressive increase in incident sarcoidosis is observed. The estimated incidence of sarcoidosis in this study (3.56 per 100,000) was like that of other Mediterranean countries **(2).** No gender predominance was observed. Demographics variations, changes in practice patters or diagnostic test improvements could explain the upward trend in sarcoidosis incidence detected in our study. Consistent with previous studies, male presented an incidence peak 10 years earlier than female **(3-5)**.
REFERENCES:
[1] Riancho-Zarrabeitia L, et al. Clin Exp Rheumatol 2014; 32(2): 275-84. PMID: 24321604
[2] Brito-Zerón P, et al. Clin Exp Rheumatol. 2019;37(6):1052–64.
[3] Arkema E V., et al. Eur Respir J. 2016;48(6):1690-9.
[4] Yoon H, et al. Am J Respir Crit Care Med. 2018;197(MeetingAbstracts):1-8.
[5] Ungprasert P, et. Mayo Clin Proc. 2016 Feb;91(2):183-8.

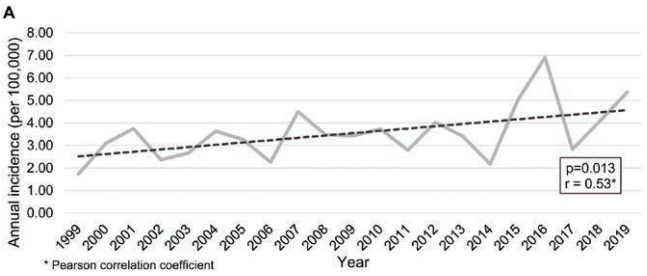


Figure 1. Annual incidence of sarcoidosis in 1999-2019 (A)

Table 1. Sarcoidosis incidence rates reported in the literature.

Study, year	Country, data source	Time period	Incident cases	Incidence per 100,000 persons-year
Pietinalho, 1995	Finland, hospital database	1984	1,378	11.4
Pietinalho, 1995	Japan, Hokkaido, hospital database	1984	288	1.0
Yigla, 2002	Israel, hospital database	1980-1996	120	0.8
Byg, 2003	Denmark, Danish National Patient Registry	1980-1994	5,536	7.2
Gribbin, 2006	UK, Health Improvement Network	1990-2003	1,019	5.0
Gillman, 2007	Australia, Victoria, hospital database	1995-2005	122	4.4-6.3
Haraldsdottir, 2007	Iceland, hospital database	1981-2003	235	3.8
Musellin, 2009	Turkey, healthcare providers	2004-2006	293	4.0
Deubelbeiss, 2010	Switzerland, Swiss Federal Office for Statistics	2002-2005	2,925	7.0
Kowalska, 2014	Poland, Katowice, National Health Fund	2006-2010	1,217	3.8-4.5
Arkema, 2016	Sweden, National Patient Register	2003-2013	10,787	10.4-14.8
Baughman, 2016	USA, Optum Health Care Database	2010-2013	29,372	African American: 17.8; Caucasian: 8.1; Hispanic: 4.3; Asian: 3.2
Duchemann, 2017	France, Seine-Saint-Denise County	2012	361	4.9
Škopljanac, 2017	Croatia, Split- Dalmatia County, hospital database	1986-2015	318	3.1-3.4
Yoon, 2018	Korea, National Health Insurance	2007-2016	4,791	0.85
Fidler, 2019	Canada, Ontario, health administrative data	1996-2015	18,550	6.8-7.9
Fernandez, 2011	Spain, Leon, hospital database	2001-2008	118	4.51
Present study, 2020	Spain, Santander, hospital database	1999-2019	234	3.56

Disclosure of Interests: Carmen Álvarez-Reguera: None declared, Raúl Fernández-Ramón: None declared, Jorge Javier Gaitán-Valdizán: None declared, José Luis Martín-Varillas: None declared, Lara Sanchez-Bilbao: None declared, David Martínez-López: None declared, Iñigo González-Mazón: None declared, Rosalía Demetrio-Pablo: None declared, Miguel Á. González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi and MSD., Grant/research support from: Abbvie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD., Grant/research support from: Abbvie, MSD and Roche.
DOI: 10.1136/annrheumdis-2021-eular.1870

POS0031

THE PREVALENCE OF INFLAMMATORY BACK PAIN AND HLA-B27 IN A LARGE POPULATION-BASED COHORT IN THE NETHERLANDS

S. Kieskamp[1], S. Arends[1], E. Brouwer[1], H. Bootsma[1], I. M. Nolte[2], A. Spoorenberg[1]. [1]University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands; [2]University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands

Background: Although chronic low back pain (≥3 months) before the age of 45 and inflammatory back pain (IBP) are regarded as early presenting and key features of axial spondyloarthritis (axSpA), and Magnetic Resonance Imaging (MRI) can be used to demonstrate sacroiliitis, the substantial delay in the diagnosis of axSpA has not improved.(1) Additionally, knowledge on the prevalence of chronic low back pain before the age of 45 and IBP in combination with the axSpA-related genetic risk factor Human Leukocyte Antigen-B27 (HLA-B27) in the general population is scarce.

Objectives: To estimate the prevalence of chronic low back pain before the age of 45 and IBP in combination with the presence of HLA-B27 in a large Dutch population based cohort.

Methods: Participants of the Lifelines cohort, a large population-based cohort of the northern region of the Netherlands, filled out a questionnaire on chronic low back pain and IBP. Chronic low back pain was defined as an affirmative answer to the question 'Did you suffer from low back pain for ≥3 months?'. IBP was questioned based on the validated European Spondyloarthropathy Study Group (ESSG) IBP criteria and was confirmed if at least 4 out of the following 5 criteria were present: (a) onset before age 45, (b) insidious onset, (c) improvement with exercise, (d) associated with morning stiffness, (e) at least 3 months duration. Participants reporting to have been diagnosed with axSpA were identified using variations of the search terms "Bechterew", "spondyloarthritis" and "ankylosing spondylitis". The Illumina global screening array (GSA) beadchip-24 v1.0 was used to genotype genome-wide SNPs in a subset of Lifelines participants. HLA-B haplotypes were imputed using neighboring SNPs with HIBAG, which is an R-package, using published parameter estimates.(2) The predicted HLA-B haplotype was considered valid if the posterior probability was >80%.

Results: In total 94,277 Lifelines participants answered the chronic low back pain question, of which 93,665 (99.4%) completed the ESSG IBP questions. Of these participants, 56,008 (59.8%) were female, mean age was 45.6 ± 12.8 years and 22,192 (23.7%) reported to have been suffering from chronic low back pain. In this chronic low back pain group, the pain began before the age of 45 in 17,122 (77.2%; 18,3% of entire Lifelines population) participants, and 13,514 (60.9%; 14.4% of entire Lifelines population) participants reported to have IBP according to the ESSG criteria.

Of 32,785 participants genetic data were available and in 29,399 (89.7%) the HLA-B haplotype could be determined with high prediction accuracy, of which 2,279 (7.8%) participants were HLA-B27 positive. Of these HLA-B27 positive participants, 1,610 (70.6%) also had available chronic low back pain data, of which 373 (23.2%) reported chronic low back pain. Of these 373 patients with chronic back pain and HLA-B27 positivity, the pain began before the age of 45 in 296 (79.4%), and 237 (64.2%) fulfilled the ESSG IBP criteria of which only 11 (4.6%) participants reported to be diagnosed with axSpA.

Conclusion: In this large population-based cohort, 18.3% of participants reported chronic low back pain that began before the age of 45. 14.4% of the participants reported IBP, which is relatively high in comparison to previous studies. HLA-B27 prevalence (7.8%) was similar to previously published data from the North-Western European population. The vast majority of participants with both IBP and the presence of HLA-B27 did not report an axSpA diagnosis. A next step in the analyses will be to explore associations with other demographic and clinical factors present including additional SpA features.

REFERENCES:

[1] Zhao SS, et al. Rheumatology (Oxford). 2021; keaa807

[2] Internet: https://zhengxwen.github.io/HIBAG/hibag_index.html (Accessed: 25 November 2020)

Disclosure of Interests: Stan Kieskamp: None declared, Suzanne Arends Grant/research support from: Research support from Pfizer, Elisabeth Brouwer Speakers bureau: Roche, Consultant of: Roche, Hendrika Bootsma Grant/research support from: Roche, Ilja M. Nolte: None declared, Anneke Spoorenberg Consultant of: Abbvie, Pfizer, MSD, UCB, Novartis, Grant/research support from: Abbvie, Pfizer, UCB, Novartis.

DOI: 10.1136/annrheumdis-2021-eular.3988

Imaging in axial spondyloarthritis

POS0032

SCORING MRI STRUCTURAL LESIONS IN SACROILIAC JOINTS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: HOW MANY SLICES ARE OPTIMAL?

W. P. Maksymowych[1,2], U. Weber[3], X. Baraliakos[4], P. Machado[5], S. Juhl Pedersen[6,7], J. Sieper[8], S. Wichuk[1], D. Poddubnyy[8], M. Rudwaleit[9], D. Van der Heijde[10], R. B. M. Landewé[11], J. Paschke[2], M. Østergaard[6,7], R. G. Lambert[12]on behalf of ASAS MRImagine. [1]University of Alberta, Medicine, Edmonton, Canada; [2]CARE Arthritis, Rheumatology, Edmonton, Canada; [3]Practice Buchsbaum, Medicine, Schaffhausen, Switzerland; [4]Rheumazentrum Ruhrgebiet, Rheumatology, Herne, Germany; [5]University College London, Rheumatology, London, United Kingdom; [6]COPECARE, Rheumatology, Copenhagen, Denmark; [7]Rigshospitalet, Clinical Medicine, Glostrup, Denmark; [8]Charité Universitätsmedizin, Rheumatology, Berlin, Germany; [9]Klinikum Bielefeld, Rheumatology, Bielefeld, Germany; [10]Leiden University Medical Centre, Rheumatology, Leiden, Netherlands; [11]Academic Medical Center, Rheumatology, Amsterdam, Netherlands; [12]University of Alberta, Radiology and Diagnostic Imaging, Edmonton, Canada

Background: There is no international consensus on the optimal number of slices for evaluation of MRI structural lesions in the SIJ. An "all slice" method evaluates lesions from the most anterior slice, defined as the first slice with vertical height of ≥1cm of the SIJ joint cavity, up to the most posterior slice, defined as the most posterior slice where ≥1cm vertical height of the cartilaginous portion is still visible. The SPARCC method scores the transitional slice between cartilaginous and ligamentous compartments as the first slice and then an additional 4 slices anterior to the transitional slice.

Objectives: We aimed to investigate inter-reader reliability, the extent of detection of lesions, and frequency of cases with a positive MRI for structural lesions when using an "all slice" approach versus the SPARCC scoring of 5 central slices.

Methods: MRI T1W images with DICOM series were available from 148 cases who had MRI performed in the ASAS-Classification Cohort. Seven central readers recorded MRI lesions in an eCRF that recorded global assessments of presence/absence of changes suggestive of axSpA and structural lesions typical of axSpA. Structural lesions per the ASAS definitions were also recorded in consecutive semicoronal slices using the "all slice" approach, but also recording the transitional slice, according to their presence/absence in SIJ quadrants (erosion, fat lesion, sclerosis) or halves (backfill, ankylosis). Structural lesion frequencies were assessed descriptively according to majority agreement (≥4/7) of central readers and also any 2 central readers. Reliability for detection of MRI lesions was compared between central and local readers using the ICC.

Results: The mean (SD) (range) number of anterior and posterior slices peripheral to the 5 central slices was 1.0 (1.0) (0-4) and 2.2 (1.8) (0-6) per case, respectively. There were 2 cases (1.4%) where ≥2 readers scored structural lesions in peripheral slices but not in the 5 central slices. The mean percentage of the total structural lesion score that was captured by the 5 central slices was >75% for all types of lesions except ankylosis (59%) (Table 1). Inter-reader reliability was greater for all lesions when assessing the 5 central slices and especially for erosion and backfill (Table 1).

Conclusion: The major component of structural lesion data is captured by assessment of 5 slices, which includes the transitional slice and the subsequent 4 anterior slices. Moreover, reliability for detection of structural lesions is substantially worse in peripheral slices.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3427

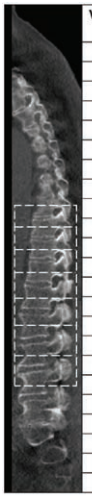
MRI Lesion	"All slice"	Central 5 slices	Peripheral slices	P value central vs peripheral slices	P value "all slice" vs central slices
Mean (SD) Lesion Score Per Case					
Erosion	2.4 (4.5) (0-22.9)	1.8(3.4) (0-17.1)	0.6 (1.4) (0-10.1)	<0.001	< 0.001
Fat lesion	2.5 (5.9) (0-34.0)	1.8 (4.5) (0-25.1)	0.7 (1.8) (0-9.9)	< 0.001	<0.001
Sclerosis	2.0 (4.9) (0-39.0)	1.5 (3.6) (0-26.1)	0.5 (1.5) (0-12.9)	< 0.001	<0.001
Backfill	0.5 (1.5) (0-12)	0.4 (1.2) (0.0-9.3)	0.1 (0.4) (0-2.7)	< 0.001	0.84
Ankylosis	0.5 (3.4) (0-30.7)	0.3 (2.3) (0-20.0)	0.2 (1.2) (0-11.3)	0.10	0.18
Mean (SD) (Range) % of Total Lesion Score in Central vs Peripheral slices					
Erosion	100%	76.4% (28.9%) (0-100%)	23.6% (28.9%) (0-100%)	<0.001	NA
Fat lesion	100%	75.4% (26.5%) (0-100%)	24.6% (26.5%) (0-100%)	<0.001	NA
Sclerosis	100%	79.5% (22.9%) (0-100%)	20.5% (22.9%) (0-100%)	<0.001	NA
Backfill	100%	86.0% (20.2%) (0-100%)	14.0% (20.2%) (0-100%)	<0.001	NA
Ankylosis	100%	59.0% (36.4%) (0-100%)	41.0% (36.4%) (0-100%)	0.56	NA
ICC of 7 readers (Mean (SD) (Range))					
MRI lesion	**All slices**	**Central 5 slices**	**Peripheral slices**		
Erosion	0.54 (0.15) (0.28-0.84)	0.58 (0.13) (0.34-0.85)	0.40 (0.17) (0.10-0.66)		
Fat lesion	0.61 (0.18) (0.30-0.89)	0.63 (0.16) (0.35-0.88)	0.52 (0.20) (0.19-0.82)		
Sclerosis	0.73 (0.18) (0.36-0.94)	0.73 (0.16) (0.36-0.91)	0.67 (0.19) (0.27-0.94)		
Backfill	0.37 (0.21) (0.10-0.85)	0.39 (0.19) (0.14-0.83)	0.18 (0.23) (0.0-0.80)		
Ankylosis	0.97 (0.02) (0.91-0.99)	0.99 (0.01) (0.97-1.0)	0.85 (0.10) (0.62-0.98)		

POS0033

IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS, BRIDGING SYNDESMOPHYTES INCREASE RISK OF FACET JOINT ANKYLOSIS ON THE SAME VERTEBRAL LEVEL WHILE FACET JOINT ANKYLOSIS DOES NOT INCREASE RISK OF SAME LEVEL SYNDESMOPHYTES

R. Stal[1], A. Sepriano[1], F. A. Van Gaalen[1], X. Baraliakos[2], R. Van den Berg[1], M. Reijnierse[3], J. Braun[2], R. B. M. Landewé[4], D. Van der Heijde[1]. [1]Leiden University Medical Center, Rheumatology, Leiden, Netherlands; [2]Rheumazentrum Ruhrgebiet, Rheumatology, Herne, Germany; [3]Leiden University Medical Center, Radiology, Leiden, Netherlands; [4]Amsterdam University Medical Center, Rheumatology, Amsterdam, Netherlands

Background: In radiographic axial spondyloarthritis (r-axSpA), spinal damage manifests as syndesmophytes and facet joint ankylosis (FJA).
Objectives: Explore whether syndesmophytes and FJA seem to have a preferential order of development.
Methods: Data were used from the Sensitive Imaging in Ankylosing Spondylitis cohort from Leiden and Herne. Patients underwent low-dose Computed Tomography (ldCT) at baseline and two-years. LdCT images were scored independently by two trained readers. Vertebrae were scored according to the Computed Tomography Syndesmophyte Score (CTSS) for presence and size of syndesmophytes; facet joints were scored as not-ankylosed and ankylosed. Analyses were performed on the vertebral unit (VU) level and using individual-reader data (Figure 1). Two hypotheses were tested: 1) presence of bridging syndesmophyte(s) is associated with FJA on the same VU two years later, and 2) presence of FJA is associated with syndesmophyte(s) on the same VU two years later. Generalized Estimating Equations (GEE) models were used to take into account the correlations between VUs from the same patient and adjusting for reader to account for individual reader scores. Two models were tested per hypothesis using different outcomes. Model 1 uses the presence of syndesmophytes or FJA as outcome adjusting for the outcome at baseline. Model 2 uses development of new syndesmophytes or FJA at two years plus an increase in the number of syndesmophytes or FJA.**Results:** In total, 50 patients were included (mean age 49, 84% male, 82% HLA-B27+). At baseline, there was a higher percentage of bridging syndesmophytes (range: 10-60%) than FJA (range: 8-36%) considering all VUs and both readers (Figure 1). In both models, presence of bridging syndesmophytes was associated with development of FJA two years later (OR (95%CI) Model 1: 3.35 (2.18-5.14); Model 2: 2.23 (1.19-4.16)) while presence of FJA at baseline did not have a statistically significant association with development of syndesmophytes two years later (Table 1).
Conclusion: The data showed a higher occurrence of bridging syndesmophytes than FJA at baseline and showed significantly increased odds to develop FJA when bridging syndesmophyte(s) are present on the same VU two years prior. This mechanism did not hold true for the other direction. These results cautiously imply that bridging syndesmophytes precede FJA, rather than FJA preceding syndesmophytes.



VU	Segment	≥1 bridging synd at BL reader 1	≥1 bridging synd at BL reader 2	≥1 FJA at BL reader 1	≥1 FJA at BL reader 2
1	Cervical	22%	26%	12%	35%
2		28%	28%	14%	21%
3		26%	30%	23%	20%
4		32%	33%	28%	27%
5		22%	27%	27%	27%
6		26%	21%	32%	30%
7	Thoracic	26%	28%	29%	25%
8		32%	36%	22%	27%
9		50%	48%	26%	31%
10		56%	56%	24%	36%
11		46%	54%	22%	36%
12		48%	46%	24%	26%
13		56%	54%	28%	26%
14		52%	54%	22%	28%
15		52%	56%	22%	32%
16		58%	60%	24%	34%
17		54%	52%	26%	28%
18		47%	47%	27%	33%
19	Lumbar	24%	27%	14%	20%
20		27%	22%	10%	20%
21		20%	20%	10%	12%
22		18%	20%	8%	18%
23		10%	10%	10%	12%

Figure 1. Percentage of occurrence of syndesmophytes and facet joint ankylosis per vertebral unit and per reader at baseline.

Figure 1 displaying percentages of patients with a bridging syndesmophyte and with facet joint ankylosis at baseline, per reader. The image on the left illustrates the vertebral unit level (VU) at which analyses were performed. Seven VUs are illustrated in dashed boxes as example. Synd, syndesmophyte; FJA, facet joint ankylosis; BL, baseline.

Table 1. Associations between facet joint ankylosis and syndesmophytes

	Model 1: development of new FJA/syndesmophytes at FU OR (95% CI)	**Model 2**: development and/or increase FJA/syndesmophytes at FU OR (95% CI)
Hypothesis 1 Presence bridging syndesmophytes at BL on development of FJA at FU	**3.35 (2.18-5.14)**	**2.23 (1.19-4.16)**
Hypothesis 2 Presence FJA at BL on development of syndesmophytes at FU	1.60 (0.88-2.91)	1.12 (0.76-1.66)

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1097

POS0034

RADIOGRAPHIC ENTHESEAL LESIONS AT HIP AND PELVIC REGION ARE ASSOCIATED WITH LONGER DISEASE DURATION, HIGHER BMI AND MORE SEVERE SPINAL AND HIP RADIOGRAPHIC DAMAGE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

F. Wink[1], T. Diemel[2], S. Arends[2], A. Spoorenberg[2]. [1]Medical Center Leeuwarden, Rheumatology, Leeuwarden, Netherlands; [2]University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands

Background: Enthesitis is an important feature of ankylosing spondylitis (AS) and structural and inflammatory entheseal lesions (EL) are frequently present on ultrasound. Plain radiographs also provide good imaging of structural entheseal involvement1. Until now, little is known about the presence of structural EL at the hip and pelvic region and the association with patient characteristics in AS.
Objectives: Our aim was to investigate the prevalence of radiographic EL at the hip and pelvic region in AS patients compared to age and sex matched control subjects and to explore the relation with AS patient characteristics.
Methods: AS patients from the Groningen Leeuwarden Axial SpA (GLAS) cohort, included between November 2004 and December 2010, with available anteroposterior (AP) pelvis radiographs at baseline were included. All patients fulfilled the modified New York criteria for AS. Additionally, 100 randomly selected AP pelvis radiographs from age and sex matched control subjects were obtained from the radiology department of the University Medical Center Groningen. The sacroiliac joints of all radiographs were blinded and radiographs were scored independently by two trained observers unaware of patient characteristics and treatment. The entheseal sites scored were: trochanter major, trochanter minor, os ischium, crista iliaca, both left and right side. The following 3 EL were scored: erosion/cortical irregularity, calcification and enthesophyte. Only lesions with absolute agreement between both observers were used for analyses. Radiographic spinal involvement was scored according to the modified Stoke AS Spine Score (mSASSS; range 0-72) and radiographic hip involvement according to the Bath AS Radiology Index (BASRI)-hip (range 0-4). Independent samples t test, Mann-Whitney U test, Chi-Square test, and Fisher Exact test were used to compare patient characteristics between patients with and without radiographic EL.
Results: Of the 167 included AS patients, 117 (70%) were male, mean age was 43 ± 11 years, 133 (80%) were HLA-B27 positive and median symptom duration was 16 years (range 1-53). 127 (76%) AS patients and 58 (58%) controls showed EL, with 501 lesions in total of which 377 (75%) in AS patients. AS patients showed significantly more lesions than controls at all 5 locations. Os ischii showed the most lesions in both AS patients and controls (66% vs 53%, p<0.05). The most prevalent type of lesion in both groups was erosion/cortical irregularity (72% vs 51%, p<0.005). Enthesophytes were also more often observed in AS patients than in controls (31% vs 21%, p=0.07). Prevalence of calcifications was low in both groups and not significantly different (5% vs 2%, p=0.22). AS patients with EL were significantly older (mean 45.2 vs 35.1 yrs, p<0.005) and had longer symptom duration (median 18 vs 7.5 yrs, p<0.005) than patients without EL. Furthermore, patients with BMI >25 had significantly more often enthesophytes (42% vs 16%, p<0.05) than patients with a normal BMI. Additionally, AS patients with EL had significantly more often radiographic spinal damage than patients without EL with median mSASSS total score 8.7 vs 1.0 (p<0.005) and a trend toward significance for radiographic hip involvement (BASRI-hip score ≥2; p=0.06).
Conclusion: Radiographic EL at hip and pelvic region are significantly more prevalent in AS patients than in age and sex matched controls. AS patients with EL were significantly older, had longer symptom duration and more spinal radiographic damage than patient without EL. Furthermore, BMI >25 was associated with a higher prevalence of enthesophytes. These new findings contribute to the knowledge of entheseal involvement in AS.
REFERENCES:
[1] Voudouris et al. J Musculoskelet Neuronal Interact. 2003;3(1):89-100.
Disclosure of Interests: Freke Wink Consultant of: Abbvie, Thomas Diemel: None declared, Suzanne Arends: None declared, Anneke Spoorenberg Consultant of: Abbvie, Pfizer, MSD, UCB, and Novartis, Grant/research support from: Abbvie, Pfizer, UCB and Novartis.
DOI: 10.1136/annrheumdis-2021-eular.3057

POS0035

ONE IN TWENTY INFLAMMATORY BOWEL DISEASE PATIENTS WHO UNDERWENT ABDOMINOPELVIC COMPUTED TOMOGRAPHY HAVE UNDIAGNOSED AXIAL SPONDYLOARTHRITIS

C. S. E. Lim[1], L. Hamilton[1], S. Low[2], A. Toms[2], A. Macgregor[1], K. Gaffney[1]. [1]Norfolk & Norwich University Hospital, Rheumatology, Norwich, United Kingdom; [2]Norfolk & Norwich University Hospital, Radiology, Norwich, United Kingdom

Background: The diagnosis of axial spondyloarthritis (axSpA) is challenging and hindered by delay. There may be an opportunity to identify sacroiliitis for further rheumatology review in inflammatory bowel disease (IBD) patients who undergo Computed Tomography (CT) for non-musculoskeletal (MSK) indications.
Objectives: To identify what proportion of IBD patients who underwent abdominopelvic CT for non-MSK indications have axSpA and to explore the role of an imaging strategy for identifying axSpA.
Methods: Abdominopelvic CT scans of verified IBD patients were identified retrospectively from eight years of imaging archive. Patients between 18-55 yrs. were selected as having the highest diagnostic yield for axSpA. CT review (using criteria from a validated CT screening tool developed by Chan[1]) was undertaken by a trained radiology team for presence of CT-defined sacroiliitis (CTSI). All CTSI patients were sent a screening questionnaire. Those with self-reported chronic back pain (CBP), duration > 3 months, onset < 45 years were invited for rheumatology review. This included a medical interview, physical examination (joint count, MASES, dactylitis count, BASMI), patient reported outcomes (BASDAI, BASFI, BASGI, Harvey-Bradshaw-Index, Partial-Mayo-Index), relevant laboratory tests (CRP, ESR, HLA-B27), axSpA protocol MRI, and remote review by a panel of experienced rheumatologists with a special interest in axSpA.
Results: CTSI was identified in 60 of 301 patients. Thirty-two (53%) responded to the invitation to participate and 27 (84%) were enrolled. Of these, eight had a pre-existing axSpA diagnosis and five did not report chronic back pain. Fourteen patients underwent rheumatological assessment; three of 14 (21.4% [95% CI: 4.7%, 50.8%]) had undiagnosed axSpA. In total, 11 of 27 (40.7% [95% CI: 22.4%, 61.2%]) patients had a rheumatologist verified diagnosis of axSpA.
Conclusion: One in five patients (60/301) with IBD who underwent abdominopelvic CT for non-MSK indications have CTSI and at least one in five (11/60) have axSpA. Five percent (3/60) were previously undiagnosed. This highlights a hidden disease burden and a potential strategy for identifying new cases.
REFERENCES:
[1] Chan J, Sari I, Salonen D, Inman RD, Haroon N. Development of a Screening Tool for the Identification of Sacroiliitis in Computed Tomography Scans of the Abdomen. J Rheumatol 2016; 43(9); 1687-94.
Acknowledgements: We are indebted to Baljeet Dhillon and Shin Azegami for their assistance in the scoring of the CTSI.
Disclosure of Interests: Chong Seng Edwin Lim Grant/research support from: AbbVie, Louise Hamilton: None declared, Samantha Low: None declared, Andoni Toms: None declared, Alex MacGregor: None declared, Karl Gaffney Speakers bureau: AbbVie, Eli Lilly, Novartis, UCB Pharma, Consultant of: AbbVie, Eli Lilly, Novartis, UCB Pharma, Grant/research support from: AbbVie, Gilead, Eli Lilly, Novartis, UCB Pharma.
DOI: 10.1136/annrheumdis-2021-eular.2047

POS0036

AN ARTIFICIAL INTELLIGENCE MODEL IN RHEUMATOLOGY: INTERPRETATION OF THE SACROILIAC JOINT GRAPHY IN ANKYLOSING SPONDYLITIS

A. C. Genç[1,2], Z. N. Kaya[3], F. Turkoglu Genc[4], L. Genc Kaya[5], Z. Öztürk[6], D. Karatas[6], S. M. Turk[6], E. Gönüllü[6]. [1]Geyve Government Hospital, Internal Medicine, Sakarya, Turkey; [2]Bahcesehir University, Artificial Intelligence, Istanbul, Turkey; [3]Saratoga High School, SHS AI Club, Saratoga, United States of America; [4]Sakarya University, Internal Medicine, Sakarya, Turkey; [5] Data Scientist, Data Scientist, Santa Clara, United States of America; [6]Sakarya University, Rheumatology, Sakarya, Turkey

Background: There is an average of 8 years delay in the diagnosis of ankylosing spondylitis (AS). The most important danger of late diagnosis is that the disease can cause physical and functional disability (2). There is no specific diagnostic biomarker for AS. Sacroiliac joint (SIJ) radiography is frequently used in the diagnosis and follow-up of AS due to its easy accessibility and low cost. It can be classified as grade 0, 1, 2, 3, 4, and these classes may not be sharply separated from each other (3).
Objectives: Interpretation of the SIJ radiography may differ from physician to physician. In fact, the same physician may interpret it differently at different times (3). We wanted to find a solution to the intraobserver disagreement problem with the artificial intelligence model.
Methods: The SIJ radiography of 590 patients who applied to our center were divided into 3 categories as right and left, separately, grade 0, grade 1-2, grade 3-4, and an educational data set was prepared for the object recognition method. 488 images were augmented through noise from 490 images in the training data. 242 articular objects were trained for grade 0, 278 for grade 1-2, and 1426 for grade 2-3. The model was tested with 100 images for 36 joint objects for grade 0, 29 for grade 1-2, and 135 for grade 3-4 to create a computer vision-artificial intelligence model (image 1).
Results: Training performance is 70% for grade 0, %63 for grade 1-2, %90 for grade 3-4 and test performance is %52 for grade 0, %24 for grade 1-2, %86

intersection over union (I/U:Intersection over Union is a form of measurement used to indicate the accuracy of an object detector.) for grade 3-4. The mean average precision (mAP) score of our object detection model is %65.9 for test data set (image 1). The estimation quality of the model can be affected by the distribution and number of each class.

Conclusion: The experience of the x-ray technician, dose adjustment, and position differences due to patient compliance complicate the standardization of SIJ radiography and this may cause interobserver disagreement (3). Artificial intelligence models to be created with a larger and homogeneous data set in order to ensure objective standardization in the interpretation of the SIJ graph can help physicians.

REFERENCES:

[1] Braun J. 'Axial spondyloarthritis including ankylosing spondylitis' Rheumatology (Oxford). 2018 1;57(suppl_6):vi1-vi3

[2] Rudwaleit M, van der Heijde D, Khan MA, Braun J, Sieper J. How to diagnose axial spondyloarthritis early. Ann Rheum Dis 2004; 63:535-543.

[3] van den Berg, R. *et al.* Agreement between clinical practice and trained central reading in reading of sacroiliac joints on plain pelvic radiographs. Results from the DESIR cohort. *Arthritis Rheumatol* 66, 2403–2411 (2014).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3343

POS0037 DOES IMAGING OF THE SACROILIAC JOINT DIFFER IN PATIENTS PRESENTING WITH UNDIAGNOSED BACK PAIN AND PSORIASIS, ACUTE ANTERIOR UVEITIS, AND COLITIS: AN INCEPTION COHORT STUDY

W. P. Maksymowych[1,2], U. Weber[3], J. Chan[4], R. Carmona[5], J. Yeung[6], S. Aydin[7], J. Reis[8], L. Martin[9], A. Masetto[10], O. Ziouzina[9], D. Mosher[9], S. Keeling[1], S. Rohekar[11], R. Dadashova[2], J. Paschke[2], A. Carapellucci[2], R. G. Lambert[2,12]on behalf of Screening for Axial Spondyloarthritis in Psoriasis, Iritis, Colitis. [1]University of Alberta, Medicine, Edmonton, Canada; [2]CARE Arthritis, Rheumatology, Edmonton, Canada; [3]Practice Buchsbaum, Rheumatology, Schaffhausen, Switzerland; [4]Artus Health Clinic, Rheumatology, Vancouver, Canada; [5]St. Joseph's Healthcare, Rheumatology, Hamilton, Canada; [6]James Yeung Rheumatology, Rheumatology, Richmond, Canada; [7]Ottawa Hospital, Rheumatology, Ottawa, Canada; [8]Polmed Research, Rheumatology, Saskatoon, Canada; [9]University of Calgary, Medicine, Calgary, Canada; [10]University of Sherbrooke, Medicine, Sherbrooke, Canada; [11]Lawson Health Research Institute, Medicine, London, Canada; [12]University of Alberta, Radiology and Diagnostic Imaging, Edmonton, Canada

Background: Axial spondyloarthritis (axSpA) presents diagnostic challenges incurring a delay of up to a decade and relies considerably on radiographic and MRI evidence of sacroiliitis which has led to the development of classification criteria which also rely on imaging. However, it has been suggested that such criteria may not be appropriate for axSpA patients presenting with other forms of SpA, especially psoriatic, because imaging features may vary in frequency and/or may be atypical. This hypothesis has never been tested in a prospective inception cohort of patients presenting with undiagnosed back pain.

Objectives: We aimed to compare the spectrum of radiographic and MRI abnormalities in the sacroiliac joint (SIJ) of an inception cohort of patients presenting with undiagnosed back pain and psoriasis, iritis, and colitis.

Methods: We used data from the prospective multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study, which is aimed at early detection of axial SpA in patients referred by the respective specialist after first presenting with these disorders. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, AAU, or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA followed by imaging. In SASPIC I, MRI evaluation of the SIJ was ordered per rheumatologist decision. In SASPIC II, MRI evaluation was ordered for all patients. Radiographs and MRI scans were assessed by two central readers and comparisons of the three groups were based on concordant assessments of imaging features. Evaluation of MRI scans included both global assessment for presence/absence of axSpA with confidence scale (-10 to +10), active and structural lesions typical of axSpA per recent ASAS definitions, and granular assessment of individual lesions according to SIJ quadrants and halves in consecutive semicoronal slices through the SIJ. Groups were compared by ANOVA and the chi-square test.

Results: A total of 240 patients were recruited, 143 from SASPIC I and 97 from SASPIC II, 101 (42.1%) being diagnosed with axSpA (65.3% male, mean age 34.4 years, mean symptom duration 8.7 years, B27 positive 55.4%). Mean age of colitis (N=101), psoriasis (N=61), iritis (N=78) patients were 33.4, 36.6, 34.3 years, respectively, mean symptom duration was 6.8, 7.2, 9.4 years, respectively, and % males were 45.5%, 52.5%, 51.3%, respectively. There were no significant group differences for unilateral versus bilateral radiographic sacroiliitis and no significant differences in the frequencies, type, or distribution of MRI lesions (Table 1).

Conclusion: Data from the SASPIC prospective inception cohort does not support the view that imaging of the SIJ differs in psoriatic axSpA, which appears similar to axSpA associated with iritis or colitis. These data support the umbrella concept of axSpA.

Imaging Feature	Colitis (n=30)	Psoriasis (n=19)	Iritis (n=52)	P value
Unilateral sacroiliitis (grade ≥2), N(%)	1 (3.3%)	0 (0%)	2 (3.8%)	0.69
mNY criteria +, N(%)	5 (16.7%)	6 (31.2%)	15 (28.8%)	0.39
Grade of sacroiliitis, mean(SD)	1.8 (2.2)	2.1 (2.7)	2.2 (2.4)	0.76
MRI indicative of axSpA, N(%)	15 (50.0%)	11 (57.9%)	32 (61.5%)	0.60
MRI indicative of axSpA (confidence ≥5/10), N(%)	14 (46.7%)	10 (52.6%)	30 (57.7%)	0.63
MRI active lesion typical of axSpA, N(%)	6 (20.0%)	6 (31.6%)	18 (34.6%)	0.37
MRI structural lesion typical of axSpA, N(%)	11 (36.7%)	7 (36.8%)	18 (34.6%)	0.98
MRI with unilateral lesion (any)	2 (6.7%)	3 (15.8%)	11 (21.2%)	0.22
MRI with unilateral lesion (BME)	1 (3.3%)	2 (10.5%)	5 (9.6%)	0.54
MRI with unilateral lesion (Erosion)	0 (0%)	0 (0%)	3 (5.8%)	0.23
MRI with unilateral lesion (Sclerosis)	1 (3.3%)	1 (5.3%)	3 (5.8%)	0.89
MRI with unilateral lesion (Fat)	0 (0%)	0 (0%)	0 (0%)	NA
MRI with iliac lesion	17 (56.7%)	12 (63.2%)	32 (61.5%)	0.88
MRI with sacral lesion	12 (40.0%)	11 (57.9%)	31 (59.6%)	0.21

Disclosure of Interests: Walter P Maksymowych Speakers bureau: Abbvie, Janssen, Novartis, Pfizer, UCB, Consultant of: Abbvie, BMS, Boehringer, Galapagos, Gilead, Lilly, Novartis, Pfizer, UCB, Grant/research support from: Abbvie, Novartis, Pfizer, Ulrich Weber: None declared, Jon Chan: None declared, Raj Carmona: None declared, James Yeung: None declared, Sibel Aydin: None declared, Jodie Reis: None declared, Liam Martin: None declared, Ariel Masetto: None declared, Olga Ziouzina: None declared, Dianne Mosher: None declared, Stephanie Keeling: None declared, Sherry Rohekar: None declared, Rana Dadashova: None declared, Joel Paschke: None declared, Amanda Carapellucci: None declared, Robert G Lambert: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3382

POS0038 THE INFLUENCE OF AGE ON THE PREVALENCE OF INFLAMMATORY AND POST-INFLAMMATORY MRI LESIONS IN THE SACROILIAC JOINTS OF PATIENTS WITH AND WITHOUT AXIAL SPONDYLOARTHRITIS

X. Baraliakos[1], S. Tsiami[1], A. Kühn[1], M. Fruth[2], J. Braun[1]. [1]Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany; [2]Radiologie blikk, Rheumazentrum Ruhrgebiet, Herne, Germany

Background: Axial spondyloarthritis (axSpA) is clinically characterized by chronic inflammatory back pain and by inflammatory and structural changes in the sacroiliac joint (SIJ) as assessed by magnetic resonance imaging (MRI). Several studies have reported high rates of bone marrow edema (BME) suggestive of inflammatory SIJ changes in up to 20% of individuals in the general population <45 years. An update of the definition of a positive MRI of the SIJ in axSpA for classification purposes, based on the number of slices or quadrants showing BME or structural changes such as erosions or fat lesions (FL), was recently published by ASAS.

Objectives: To compare the influence of age on the prevalence of inflammatory and structural MRI changes in the SIJ of patients with chronic low back pain diagnosed with axSpA or non-SpA.

Methods: MRIs of the SIJ of patients referred for differential diagnosis of back pain who were finally diagnosed with axSpA or not by experienced rheumatologists, were evaluated using semi-coronal STIR and T1-weighted MRI sequences. All images were scored blinded to, age, sex and diagnosis for the occurrence of BME, FL, erosions and ankylosis on the level of SIJ-quadrants (SIJ-Q). Patient groups were built based on decade of age (until 29, 30-39, 40-49 and ≥50 years).

Results: A total of 309 patients (175 axSpA and 134 non-SpA) with complete MRI sets were included in the analysis. The mean age was 38.5±11.4 and 43.4±13.8, 66.9% and 35.8% were male, the mean CRP was 1.6±2.4 and 1.1±2.1mg/dl and the median back pain symptom duration was 48 and 60 months, respectively. The number of SIJ-Q with BME and erosions was significantly higher in axSpA vs. non-SpA independent of the age group (Table 1). In comparison, with exception of the patients in the oldest population (≥50 years), the number of SIJ-Q with FL and the number of patients with at least one FL was not different between subgroups, while the number of erosions and FL but not BME was higher in both groups with increasing age. In the univariate analysis, only female sex was significantly associated with higher occurrence of FL.

Conclusion: Despite a relatively high prevalence in non-SpA patients, BME and erosions were significantly more frequent in axSpA independent of age, while the presence of FL was not different between groups. FL and erosions are increasingly found in older age groups independent of diagnosis. These data are relevant for the interpretation of MRI findings in the SIJ of patients suspicious of axSpA.

Table 1. Comparison of MRI findings between axSpA and non-SpA patients at different age groups

Age subgroup	Diagnosis	Mean number of SIJ quadrants			Proportion of patients with…		
		BME	FL	Erosion	BME	FL	Erosion
until 29 years	axSpA (n=46)	6.0±3.7	6.8±5.7	4.4±3.8	95.7%	80.4%	89.1%
	non-SpA (n=25)	1.4±1.5	5.4±4.4	0.8±1.5	64,0%	76,0%	48,0%
	p-value	*<0.001*	*0.311*	*<0.001*	*<0.001*	*0.664*	*<0.001*
30-39 years	axSpA (n=50)	5.0±4.1	8.7±5.9	4.6±3.7	92,0%	98,0%	82,0%
	non-SpA (n=26)	1.0±1.3	9.5±6.0	1.1±1.3	46.2%	92.3%	53.8%
	p-value	*<0.001*	*0.485*	*<0.001*	*<0.001*	*0.23*	*0.01*
40-49 years	axSpA (n=47)	4.2±3.7	11.3±6.0	4.6±3.7	85.1%	97.9%	87.2%
	non-SpA (n=35)	1.4±2.9	10.3±5.8	1.6±2.4	34.3%	97.1%	62.9%
	p-value	*<0.001*	*0.413*	*<0.001*	*<0.001*	*0.833*	*0.010*
≥50 years	axSpA (n=32)	5.2±4.9	16.4±5.4	5.5±4.1	87.5%	100,0%	87.5%
	non-SpA (n=48)	1.9±2.1	13.4±4.5	2.0±2.0	66.7%	100%	72.9%
	p-value	*0.001*	*0.006*	*<0.001*	*0.036*	*1,000*	*0.121*

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3154

POS0039

MRI LESIONS IN SPA: A COMPARISON WITH AGE AND SEX MATCHED PARTICIPANTS WITH NON-INFLAMMATORY BACK PAIN

C. W. S. Chan[1], E. T. F. Chui[1], H. H. L. Tsang[1], C. S. Lau[1], H. Y. Chung[1]. [1]The University of Hong Kong, Queen Mary Hospital, Hong Kong, Division of Rheumatology and Clinical Immunology, Department of Medicine, Hong Kong, Hong Kong (SAR)

Background: Magnetic resonance imaging (MRI) is becoming increasingly important in axial spondyloarthritis (SpA) due to its unique role in early diagnosis, classification, and monitoring of disease (1, 2). It is the only disease assessment tool that has been validated with histological inflammatory cellularity in tissue biopsy of the sacroiliac (SI) joint (3). However, many MRI lesions are not exclusive to axial SpA and may occur in other conditions such as infection, degeneration and malignancy. Further characterization of these lesions may guide more targeted therapies.
Objectives: The objective of this study was to describe, investigate associated factors, and to compare individual MRI lesions with age and sex matched controls.
Methods: This was a cross-sectional observational study of MRI lesions of 431 participants with axial SpA compared with 53 age and sex matched participants with non-inflammatory back pain. Individual lesions identified included: discovertebral lesions (DVL), facet joint lesions, costovertebral joint lesions, corner inflammatory lesions (CIL), and fatty corner lesions (FCL). Associated factors of the lesions were determined by regression analyses.
Results: Compared to the control group, participants with axial SpA had more costovertebral lesions (12.5% vs 1.9%; p=0.02), CIL (46.6% vs 15.1%; p=0.03), and FCL (55.5% vs 39.6%; p=0.03). Multivariate regression showed that age (OR=1.02; p=0.03), regular alcohol use (OR=0.40; p=0.04) and radiographic axial SpA (OR=1.89; p=0.01) were associated with DVL; Chinese ethnicity (OR=0.06; p=0.01) and radiographic axial SpA (OR=3.63; p=0.01) were associated with facet joint lesion; radiographic axial SpA (OR=4.26; p<0.001) was associated with costovertebral joint lesion; male gender (ß=1.10; p=0.01), HLA B27 (ß=1.02; p=0.02), and radiographic axial SpA (ß=1.05; p=0.01) were associated with CIL; age (ß=0.10; p<0.01), male gender (ß=1.96; p=0.01), body weight (ß=0.11; p<0.01), HLA B27 (ß=3.23; p<0.001), and radiographic axial SpA (ß=1.77; p=0.02) were associated with FCL.
Conclusion: The individual MRI lesions more specific to axial SpA when compared to non-inflammatory back pain were costovertebral joint lesions, CIL, and FCL.
REFERENCES:
[1] Mandl P, Nacarro-Compan V, Terslev L, Aegerter P, van der Heijde D, D'Agpstino MA, et al. EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. Ann Rheum Dis. 2015;74(7): 1327-39.
[2] Ostergaard M, Lambert RG. Imaging in ankylosing spondylitis. Ther Adv Musculoskeletal Dis. 2012;4(4):301-11.
[3] Bollow M, Fischer T, Reisshauer H, Backhaus M, Sieper J, Hamm B, et al. Quantitative analyses of sacroiliac biopsies in spondyloarthropathies: T cells and macrophages predominate in early and active sacroillitis - cellularity correlates with the degree of enhancement detected by magnetic resonance imaging. Ann Rheum Dis. 2000;59(2):135-40.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4113

Molecular and structural changes of bone turnover during inflammatory disease

POS0040

THE DECREASE IN BONE MINERAL DENSITY DEPENDS ON THE CONCENTRATIONS OF ANGIOPOIETIN-LIKE PROTEIN TYPE 4 IN PATIENTS WITH RHEUMATOID ARTHRITIS

V. Aleksandrov[1,2], L. Shilova[1], A. Aleksandrov[1,2], G. Osmanova[1], N. Aleksandrova[2], I. Zborovskaya[2]. [1]Volgograd State Medical University, Department of Hospital Therapy, Volgograd, Russian Federation; [2]Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», Department of Clinical and Laboratory Diagnostics, Volgograd, Russian Federation

Background: New serological markers that can serve as objective indicators of osteoporotic changes in patients with rheumatoid arthritis (RA) are being currently searched [1, 2, 3, 4, 5].
Objectives: To reveal the connection between the concentrations of serum angiopoietin-like protein type 4 (ANGPTL4) and the decrease in bone mineral density (BMD) in patients with RA.
Methods: 114 patients with reliable RA (90.4% of women, 9.6% of men) aged 21 to 80 years (mean age 55.4 ± 11.2 years old, disease duration - 11.18 ± 9.03 years, positive for rheumatoid factor (RF-IgM) - 63.2%, positive for anti-citrullinated protein antibody (ACPA) - 59.7%) were examined using a bone X-ray densitometer LUNAR DPX (GE, USA). Patients with an advanced clinical stage - 49%, moderate activity according to DAS28 - 58.8%, II-III radiological stage - 85.1% and functional class II - 64.9% prevailed. ANGPTL4 measurement in blood serum was carried out by enzyme immunoassay using a commercial test system "RayBio Human ANGPTL4 ELISA Kit" (RayBiotech, USA). ESR, RF, as well as C-reactive protein (CRP), ACPA, and antibodies to modified vimentin (anti-MCV) in an ELISA test were determined in all RA patients.
Results: ANGPTL4 indices in RA patients correlated with the CRP level (r = 0.34, p = 0.001) and the DAS-28 (r = 0.29, p = 0.002). There was no correlation between the level of ANGPTL4 and the intake of glucocorticoids, both at the time of the study (p = 0.678) and with their long-term (more than 3 months) use (p = 0.097). There was a negative correlation of weak strength between ANGPTL4 and the dose of non-steroidal anti-inflammatory drugs (r = -0.21, p = 0.035). There was no correlation between ACPA, anti-MCV, and ANGPTL4 levels (p> 0.1 and p = 0.084). A direct correlation was found between the level of ANGPTL4 and the presence of osteopenia in RA patients (r = 0.43, p = 0.036), as well as a negative correlation between ANGPTL4 and bone mineral density in the spine (BMD L_{1-4}, r = -0.631, p <0.001), but not in the femur (p> 0.05). Densitometry data also allowed to establish a negative correlation between low values of the T-criterion and increased titers of anti-MCV (r = -0.51, p = 0.029), but not ACPA (p = 0.276). It has previously been noted that anti-MCV are able to activate osteoclasts with a consequent decrease in periarticular BMD.
Conclusion: The absence of a relationship between anti-MCV and the level of ANGPTL4 may indicate different mechanisms of osteoporosis development and localization of osteoporotic changes in groups of anti-MCV or ANGPTL4 positive patients with RA.
REFERENCES:
[1] Ramli FF, Chin KY. A Review of the Potential Application of Osteocyte-Related Biomarkers, Fibroblast Growth Factor-23, Sclerostin, and Dickkopf-1 in Predicting Osteoporosis and Fractures. Diagnostics (Basel). 2020;10(3):145. doi: 10.3390/diagnostics10030145
[2] Aleksandrov V., Aleksandrov A. Angiopoetin-like protein type 3 as an indicator of rheumatoid inflammation and resorption of bone tissue in rheumatoid arthritis. Ann Rheum Dis. 2020;79(s1):1340. doi: 10.1136/annrheumdis-2020-eular.2174
[3] Nagy EE, Nagy-Finna C, Popoviciu H, Kovács B. Soluble Biomarkers of Osteoporosis and Osteoarthritis, from Pathway Mapping to Clinical Trials: An Update. Clin Interv Aging. 2020;15:501-518. doi: 10.2147/CIA.S242288
[4] Aleksandrov A.V., Alekhina I.Y., Aleksandrova N.V., Shilova L.N., Aleksandrov V.A. High antibody titers to cyclic citrullinated vimentin promote the development of periarticular osteoporosis in patients with rheumatoid arthritis. Osteoporosis International. 2019; 30(s2):680.
[5] Donati S, Ciuffi S, Palmini G, Brandi ML. Circulating miRNAs: A New Opportunity in Bone Fragility. Biomolecules. 2020;10(6):927. doi: 10.3390/biom10060927
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2266

POS0041 THE GASOTRANSMITTER HYDROGEN SULFIDE (H2S) IS PROTECTIVE AGAINST CALCIFIC TENDINOPATHY (CT)

I. Bernabei[1], D. Kronenberg[2], R. Stange[2], J. Bertrand[3], T. Hügle[1], A. So[1], N. Busso[1], S. Nasi[1]. [1]Centre Hospitalier Universitaire Vaudois and University of Lausanne, Department of Musculoskeletal Medicine, Service of Rheumatology, Lausanne, Switzerland; [2]Institute of Musculoskeletal Medicine, Westfaelische Wilhelms University Muenster, Department of Regenerative Musculoskeletal Medicine, Münster, Germany; [3]Otto-von-Guericke University, Department of Orthopaedic Surgery, Magdeburg, Germany

Background: Pathological (or heterotopic) calcification is the deposition of calcium-containing crystals in soft tissues that normally do not calcify. The deposition of these crystals in tendons such as the rotator cuff and the Achilles tendon is known as calcific tendinopathy (CT). CT is a painful condition, which increases tendon rupture rate and leads to disability.
Objectives: To understand what inhibits calcification, in order to provide new strategies to treat a condition for which existing therapies are ineffective.
Methods: We investigated the role of the gasotransmitter hydrogen sulfide (H_2S), and in particular of the H_2S-producing enzyme cystathionine γ-lyase (CSE) in CT. *In vitro*, we induced calcification in tenocytes from WT and CSE KO mice or we treated WT tenocytes with different H_2S donors. *In vivo,* calcification was assessed in a surgery-induced murine model of CT (tenotomy of the Achilles tendon) and in a spontaneous model of CT (aging). Samples obtained from patients with rotator cuff or Achilles tendon CT were also analyzed. To investigate the underlying mechanisms of the CSE-H_2S effect, we focused on the bone morphogenic proteins (BMPs) pathway. We additionally explored if altered extracellular matrix (ECM) organization, due to lysyl oxidase (LOX) activity and aberrant collagen-crosslinks, could also be involved in CT. In this context, we studied if H_2S could affect LOX expression and activity.
Results: *In vitro*, tenocyte calcification was inhibited by exogenous H_2S-donors, while it was exacerbated in CSE KO tenocytes. The protective role of CSE-H_2S was confirmed *in vivo.* In aged mice, microtomography analysis revealed exacerbated Achilles tendon calcification in CSE KO mice compared to WT. In the surgery-induced model of CT, an inverse correlation between calcification and CSE expression in operated Achilles tendon was seen over time. Similarly, inversed correlation between calcification and CSE expression was found in human CT samples.
Reduced calcification in tenocytes exposed to H_2S was accompanied by decreased expression of genes coding for BMP2, BMP4 and decreased activation of the BMP signaling pathway (pSMAD1/5/8). On the contrary, BMPs expression and BMPs-pathway activation were exacerbated in CSE KO tenocytes compared to WT tenocytes.
We next investigated whether ECM disorganization could play a role in CT. Tenocytes cultured in calcification media and treated with the pan-inhibitor of lysyl oxidases (LOX, LOXL1-4) β-aminopropionitrile (BAPN) showed decreased calcification. This pointed to a potential beneficial role of LOX inhibition, therefore decreased collagen-crosslinks, in CT. By analysis of LOXs gene expression in WT and CSE KO tenocytes cultured in calcifying condition, we found much higher expression (4-fold) of LOX, LOL2 and LOXL4 in CSE KO tenocytes. Moreover, H_2S-donors inhibited LOX activity. Altogether, these results suggest that decreased H_2S could lead to aberrant LOX expression and activity, excessive collagen cross-links in the ECM, and ultimately calcification. Further experiments are ongoing to prove these hypotheses.
Conclusion: We suggest targeting H_2S production by CSE, or supplying an H_2S-donor, is of therapeutic relevance to pathological calcification in the context of CT and can modify its disease course.
The anti-mineralizing effect of H_2S in tendons could be due to both inhibition of the BMPs pathway and suppression of abnormal LOXs activity.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2419

POS0042 NOTCH 1 INHIBITION INCREASES OSTEOCLAST PROGENITOR ACTIVITY IN THE MOUSE MODEL OF RHEUMATOID ARTHRITIS

M. Filipović[1], A. Šućur[1], D. Flegar[1], Z. Jajić[2], M. Ikić Matijašević[3], N. Lukač[1], N. Kovačić[1], T. Kelava[1], D. Šisl[1], K. Zrinski Petrović[1], V. Katavić[1], D. Grčević[1]. [1]University of Zagreb School of Medicine, Croatian Institute for Brain Research, Laboratory for Molecular Immunology, Zagreb, Croatia; [2]University of Zagreb School of Medicine, Clinical Hospital Center "Sestre Milosrdnice", Department of Rheumatology, Physical Medicine and Rehabilitation, Zagreb, Croatia; [3]University of Zagreb School of Medicine, Clinical Hospital "Sveti Duh", Department of Clinical Immunology and Allergology, Zagreb, Croatia

Background: Osteoclasts mediate periarticular and systemic bone loss in rheumatoid arthritis (RA). Osteoclast progenitor cells (OCPs) derived from the myeloid lineage are susceptible to regulation through Notch signaling. Murine bone marrow and splenic OCPs, identified as $CD45^+Ly6G^-CD3^-B220^-NK1.1^-CD11b^{lo/+}CD115^+CCR2^+$ cells, are specifically increased in arthritis. We previously identified an increased frequency of OCPs expressing Notch receptors in arthritic mice.
Objectives: Several studies suggested that Notch signaling modulation affects the course of experimental arthritis. We aimed to determine the effects of Notch receptor signaling inhibition on OCP activity and arthritis severity in murine collagen-induced arthritis (CIA).
Methods: Male C57/Bl6 and DBA mice were immunized with chicken type II collagen and treated with i.p. injections of anti-Notch 1 neutralizing antibodies (1mg/kg). Notch receptor 1 through 4 expression on OCPs was analyzed by flow cytometry in periarticular bone marrow (PBM) and spleen (SPL). Gene expression of Notch receptors, ligands and transcription targets as well as osteoclast differentiation genes RANK, cFos and cFms was determined by qPCR from tissues and sorted OCPs. FACS sorted OCPs were stimulated by osteoclastogenic factors (M-CSF and RANKL), in control, IgG, Jagged (Jag)1 or Delta-like (DLL)1 coated wells, with or without anti-Notch 1 antibodies. Research was approved by the Ethics Committee.
Results: We confirmed the expression of Notch receptors on OCPs by flow cytometry with Notch 1 and 2 being most abundantly expressed (around 25% and 40% positive OCPs in PBM and 35% and 20% in SPL respectively), with a significant increase of Notch 2 expression in arthritis. Seeding OCPs on DLL1 coated wells significantly increased while seeding on Jag1 coated wells significantly decreased osteoclastogenesis as reflected on the number of TRAP+ osteoclasts and expression of osteoclast differentiation genes. The addition of anti-Notch 1 antibodies to ligand-stimulated OCPs resulted in an increased number of TRAP+ osteoclasts, partially reversing Jag1 inhibition. *In vivo* treatment with anti-Notch 1 antibodies did not affect total OCP frequency, but increased expression of Notch 4 both in PBM and SPL as seen by flow cytometry and qPCR. Additionally, anti-Notch 1 treatment stimulated Notch transcription factors HES and HEY. Both PBM and SPL cultured OCPs from anti-Notch 1 treated mice produced a higher number of large TRAP+ osteoclasts, doubling the area covered with osteoclasts in the latter compared to untreated mice. Increased osteoclastogenesis *in vitro* was further confirmed by an increased expression of osteoclast differentiation genes in the treated group.
Conclusion: Our results confirm that Notch signaling may represent an important therapeutic target for the regulation of osteoclast activity in arthritis. Both *in vitro* and *in vivo* anti-Notch 1 neutralizing antibodies enhanced osteoclastogenesis in CIA model, implying an inhibitory role of Notch 1 signaling in osteoclast differentiation. As Notch 2 expression is increased on OCPs of arthritic mice, we next plan to determine the effects of Notch 2 neutralization on osteoclast activity and arthritis severity.
REFERENCES:
[1] Ikić Matijašević M, Flegar D, Kovačić N, Katavić V, Kelava T, Šućur A, et al. Increased chemotaxis and activity of circulatory myeloid progenitor cells may contribute to enhanced osteoclastogenesis and bone loss in the C57BL/6 mouse model of collagen-induced arthritis. Clin Exp Immunol. 2016;186(3):321–35.
[2] Šućur A, Filipović M, Flegar D, Kelava T, Šisl D, Lukač N, et al. Notch receptors and ligands in inflammatory arthritis – a systematic review. Immunology Letters 2020 Vol. 223, p. 106–14.
Acknowledgements: The work has been supported by Croatian Science Foundation projects IP-2018-01-2414, UIP-2017-05-1965 and DOK-2018-09-4276.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2601

POS0043 PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY IN THE ASSESSMENT OF BONE MINERAL DENSITY IN ANTI-TNF-TREATED RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS PATIENTS

B. Juhász[1], K. Gulyás[2], Á. Horváth[2], E. Végh[2], A. Pusztai[2], A. Szentpetery[3], Z. Pethő[2], N. Bodnár[2], A. Hamar[2], L. Bodoki[2], H. P. Bhattoa[4], É . Szekanecz[1], K. Hodosi[2], A. Domjan[2], S. Szamosi[2], C. Horváth[5], S. Szántó[2], G. Szücs[2], H. Raterman[6], W. Lems[7], O. Fitzgerald[8], Z. Szekanecz[2]. [1]University of Debrecen, Oncology, Debrecen, Hungary; [2]University of Debrecen, Rheumatology, Debrecen, Hungary; [3]Uppsala University Hospital, Rheumatology, Uppsala, Sweden; [4]University of Debrecen, Laboratory Medicine, Debrecen, Hungary; [5]Semmelweis University, Medicine, Budapest, Hungary; [6]Northwest Clinics, Rheumatology, Alkmaar, Netherlands; [7]University of Amsterdam, Rheumatology, Amsterdam, Netherlands; [8]University College Dublin, Conway Institute for Biomolecular Research, Dublin, Ireland

Background: Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) have been associated with osteoporosis. There have been very few data on the use of peripheral quantitative computed tomography (QCT) in anti-TNF-treated patients.

Objectives: We wished to assess volumetric bone mineral density (BMD) by forearm QCT in conjunction with dual-energy X-ray absorptiometry (DXA) and bone biomarkers in RA and AS.
Methods: Forty RA and AS patients treated with etanercept (ETN) or certolizumab pegol (CZP) were included in a 12-month follow-up study. Peripheral QCT and DXA BMD were determined. Bone biomarkers, such as PTH, osteocalcin, RANKL, 25-hydroxyvitamin D (VITD), P1NP, CTX, sclerostin, DKK-1 and cathepsin K (CATHK) were assessed by ELISA.
Results: There was no further bone loss during anti-TNF treatment. Volumetric and areal BMD showed significant correlations with each other ($p<0.05$). Total QCT BMD after 12 months was inversely determined by disease activity at baseline in the full cohort ($p=0.030$). Cortical BMD was negatively determined by baseline disease activity ($p=0.005$) and CATHK ($p=0.025$). In RA, VITD-0 determined QTRABBMD-12 ($p=0.005$). In the full cohort, the one-year change in QTRABBMD was related to TNF inhibition together with higher VITD-0 ($p=0.031$). Therapy and lower CATHK determined QCORTBMD changes ($p=0.006$). In RA, treatment together with VITD-0 ($p<0.01$) or CATHK-0 ($p=0.002$), while in AS, treatment together with RANKL-0 ($p<0.05$) determined QCT BMD changes.
Conclusion: QCT confirmed that biologics may attenuate bone loss. Disease activity, CATHK, RANKL and VITD may predict the effects of anti-TNF treatment on volumetric BMD changes. There may be differences between RA and AS in this respect.
Acknowledgements: This research was supported by Hungarian National Scientific Research Fund (OTKA) grant No. K 105073 (H.P.B. and Z.S.); by the European Union and the State of Hungary and co-financed by the European Social Fund in the framework of TAMOP-4.2.4.A/2-11/1-2012-0001 'National Excellence Program '(Z.S.); by the European Union grant GINOP-2.3.2-15-2016-00050 (Z.S.); and by the Pfizer Investigator Initiated Research Grants no. WS1695414 and WS1695450 (Z.S.).
Disclosure of Interests: Balázs Juhász: None declared, Katalin Gulyás: None declared, Ágnes Horváth: None declared, Edit Végh: None declared, Anita Pusztai: None declared, Agnes Szentpetery: None declared, Zsófia Pethö: None declared, Nóra Bodnár: None declared, Attila Hamar: None declared, Levente Bodoki: None declared, Harjit Pal Bhattoa: None declared, Éva Szekanecz: None declared, Katalin Hodosi: None declared, Andrea Domjan: None declared, Szilvia Szamosi Speakers bureau: Roche, Csaba Horváth: None declared, Sándor Szántó Speakers bureau: Abbvie, MSD, Novartis, Consultant of: Abbvie, Novartis, Gabriella Szücs Speakers bureau: Roche, Boehringer, Actelion, Sager, Consultant of: Actelion, Boehringer, Hennie Raterman: None declared, WIllem Lems Speakers bureau: Pfizer, Amgen, Lilly, UCB, Galapagos, Consultant of: Pfizer, Amgen, Lilly, UCB, Galapagos, Oliver FitzGerald Speakers bureau: AbbVie, Janssen, Pfizer, Consultant of: BMS, Celgene, Eli Lilly, Janssen, Pfizer, Grant/research support from: AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Zoltán Szekanecz Speakers bureau: Pfizer, Roche, Abbvie, Novartis, Lilly, Sanofi, Consultant of: Pfizer, Abbvie, Novartis, Grant/research support from: Pfizer, UCB.
DOI: 10.1136/annrheumdis-2021-eular.1951

POS0044 T315 SUPPRESSES OSTEOGENIC DIFFERENTIATION IN SAOS-2 CELLS BY INHIBITING PHOSPHORYLATION OF AKT

Z. Huang[1], X. Huang[1], Y. Huang[1], Z. Li[1], Q. Huang[1], T. Li[1]. [1]Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China

Background: New bone formation is common in the late stage of various inflammatory arthritis, while osteoblasts play a vital role in this process. Activation of PI3K/ Akt pathway promotes the differentiation and enhances the function of osteoblasts [1]. T315 is a novel small molecule drug, which may induce apoptosis and suppress the expression of cellular markers of chronic lymphocytic leukemia cells by disrupting PI3K/ Akt pathway [2]. However, the lack of study focuses on the influence of T31T on the other cells, except tumor cell lines.
Objectives: We aimed to assess the effect of T315 on human osteoblast-like Saos-2 cells, while its potential mechanism in PI3K/ Akt pathway was evaluated as well.
Methods: (1) Saos-2 was stimulated with an osteogenic reagent which contained L-ascorbic acid, β-glycerophosphoric acid, and dexamethasone. The concentration of T315 was adjusted to 0μg/ml, 1μg/ml, and 2μg/ml in the culture medium. (2) Alizarin red stain and alkaline phosphatase (ALP) stain were performed at d0, d7, d14, and d21 after being treated with T315. (3) Cellular protein was extracted at d0, d3, and d6 after being treated with T315, then ALP activity was tested based on a recommendation from the manufacturer of the kit. (4) Collagen type 1α2 Chain (Col1α2) and osteocalcin (OCN), two osteogenic markers, were measured through western blot, with glyceraldehyde 3-phosphate dehydrogenase (GAPDH) as an endogenous control. (5) Phospho-phosphoinositide 3-kinase (pPI3K), phospho-protein kinase B (pAkt), and runt-related transcription factor 2 (Runx2) was tested through western blot as well. GAPDH or protein kinase (Akt) was chosen as an internal reference as appropriate. (6) Analysis of variance with the least significant difference was used to analyze the data. A $P<0.05$ was considered statistically significant.
Results: (1) The higher concentration of T315 related to the less relative mineralized area and the positive area of ALP, while longer incubation time with T315 decreased these regions as well (Figure 1A-C). (2) T315 reduced the activity of ALP accordingly (Figure 1D). (3) T315 suppressed the protein expression of Col1α2 and OCN in a dose-dependent and time-dependent manner (Figure 1E, F). (4) T315 did not alter pPI3K, but it inhibited the phosphorylation of Akt (Figure 1G, H). (5) Runx2 was reduced because of the greater dose or longer incubation time with T315 (Figure 1).
Conclusion: T315 inhibits the differentiation of osteoblasts through inhibiting the phosphorylation of Akt. Surprisingly, pPI3K seldom changes in this process, so its detail mechanism should be investigated in further.
REFERENCES:
[1] Exp Biol Med (Maywood) 2020;245(6):552-561.
[2] Blood 2015;125(2):284-295.

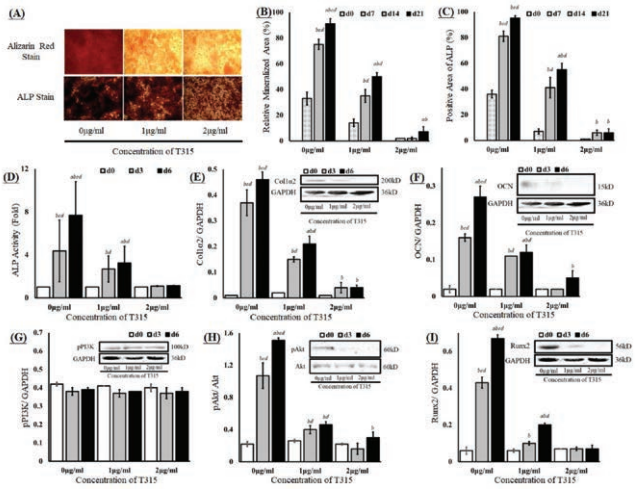


Figure 1. Effect of T315 on Saos-2 cells and PI3K/Akt pathway. (A) Alizarin red stain and ALP stain at d21. (B) Relative mineralized area in Alizarin red stain. (C) Positive area in ALP stain. (D) ALP activity. Western blot analysis and its bands at d6 for Col1α2 (E), OCN (F), pPI3K (G), pAkt (H), and Runx2 (I). Results were normalized by GAPDH or Akt.ALP: Alkaline phosphatase; Col1α2: Collagen type 1α2 Chain; GAPDH: Glyceraldehyde 3-phosphate dehydrogenase; OCN: Osteocalcin; pPI3K: Phospho-phosphoinositide 3-kinase; pAkt: Phospho-protein kinase B; Akt: Protein kinase; Runx2: Runt-related transcription factor 2.[a] Compared with d3 in the same concentration of T315, $P<0.05$.[b] Compared with d0 in the same concentration of T315, $P<0.05$.[c] Compared with 1μg/ml T315 in the same incubation time, $P<0.05$.[d] Compared with 2μg/ml T315 in the same incubation time, $P<0.05$.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2428

POS0045 LEAST SIGNIFICANT CHANGE IN BONE DENSITOMETRY IN PATIENTS WITH OBESITY

D. Claire[1], M. Geoffroy[1], L. Kanagaratnam[2], C. Isabelle[1], A. Hittinger[1], B. Loïs[1], C. Clément[1], J. H. Salmon[1]. [1]Centre Hospitalier Universitaire de Reims, Rheumatology, Reims, France; [2]Centre Hospitalier Universitaire de Reims, Unité d'aide méthologique, Reims, France

Background: Dual energy X-ray absoprtiometry is the reference method to mesure bone mineral density (1). Loss of bone mineral density is significant if it exceeds the least significant change. The threshold value used in general population is 0,03 g/cm^2 (2). Patients with obesity are known for having a higher bone mineral density due to metabolism and physiopathology characteristics (3,4).
Objectives: The aim of our study was to determine the least significant change in bone densitometry in patients with obesity.
Methods: We conducted an interventionnal study in 120 patients with obesity who performed a bone densitometry. We measured twice the bone mineral density at the lumbar spine, the femoral neck and the total hip in the same time (5,6). We determined the least significant change in bone densitometry from each pair of measurements, using the Bland and Altman method. We also determined the least significant change in bone densitometry according to each stage of obesity.
Results: The least significant change in bone densitometry in patients with obesity is 0,046g/cm^2 at the lumbar spine, 0.069 g/cm^2 at the femoral neck and 0.06 g/cm^2 at the total hip.

Conclusion: The least significant change in bone densitometry in patients with obesity is higher than in general population. These results may improve DXA interpretation in this specific population, and may personnalize their medical care.

REFERENCES:

[1] Lees B, Stevenson JC. An evaluation of dual-energy X-ray absorptiometry and comparison with dual-photon absorptiometry. Osteoporos Int. mai 1992;2(3):146-52.
[2] Briot K, Roux C, Thomas T, Blain H, Buchon D, Chapurlat R, et al. Actualisation 2018 des recommandations françaises du traitement de l'ostéoporose post-ménopausique. Rev Rhum. oct 2018;85(5):428-40.
[3] Shapses SA, Pop LC, Wang Y. Obesity is a concern for bone health with aging. Nutr Res N Y N. mars 2017;39:1-13.
[4] Savvidis C, Tournis S, Dede AD. Obesity and bone metabolism. Hormones. juin 2018;17(2):205-17.
[5] Roux C, Garnero P, Thomas T, Sabatier J-P, Orcel P, Audran M, et al. Recommendations for monitoring antiresorptive therapies in postmenopausal osteoporosis. Jt Bone Spine Rev Rhum. janv 2005;72(1):26-31.
[6] Ravaud P, Reny JL, Giraudeau B, Porcher R, Dougados M, Roux C. Individual smallest detectable difference in bone mineral density measurements. J Bone Miner Res. août 1999;14(8):1449-56.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3819

POS0046 MICRO-CT ANALYSIS OF SACROILIAC JOINT AS A NEW TOOL FOR STUDYING TRABECULAR BONE AND OSTEO-ARTICULAR LESIONS IN MURINE MODELS

S. Hilliquin[1,2], V. Zhukouskaya[1,3,4], O. Fogel[2], C. Chaussain[1,4,5], C. Miceli Richard[2], C. Bardet[1]. [1]Université de Paris, Dental School, and Plateforme d'Imagerie du Vivant (PIV), Laboratory Orofacial Pathologies, Imaging and Biotherapies, URP2496 and FHU-DDS-Net, Montrouge, France; [2]Université de Paris, Department of Rheumatology, Cochin Hospital, Paris, France; [3]Université d'Evry, Université Paris-Saclay, Evry, France, INTEGRARE, Genethon, Inserm, Evry, France; [4]Hôpital de Bicêtre, Centre de référence des maladies rares du métabolisme du calcium et du phosphate, Plateforme d'expertise maladies rares Paris Saclay, filière OSCAR, EndoRare and BOND ERN, Le Kremlin-Bicêtre, France; [5]Bretonneau Hospital, GHN, AP-HP Reference Center for Rare Disorders of the Calcium and Phosphate Metabolism, Dental Medicine Department, PARIS, France

Background: Skeletal disorders affect the skeleton in different ways with some bones being very impaired while others less severely. In translational studies using murine models of human disorders, the bone phenotype is mainly evaluated at distal femur or proximal tibia. The sacroiliac joint (SIJ), which connects the spine to the pelvis, is involved in the balanced transfer of mechanical energy from the lumbar spine to the lower extremities. Its role in biomechanical stress makes it of particular interest in various bone diseases. For instance, patients with X-linked hypophosphatemia (XLH), who mainly display osteomalacia, are frequently affected with early osteoarthritis of the SIJ. Interestingly, we recently showed that the *Hyp* mouse, a murine model of XLH that greatly mimics the human disorder, displayed early and severe osteoarticular alterations of the SIJ [1].

Objectives: Here, using the *Hyp* mouse as a model, we show that the SIJ constitutes a highly reliable joint to investigate in murine models of skeletal disorders.

Methods: SIJ and distal femur were evaluated in 3-month-old *Hyp* mice compared to wild-type (WT) mice (n=10 per group). using high-resolution microCT. Measurements of trabecular and cortical bone parameters at sacral and iliac sides and trabecular bone parameters at distal femur were performed with the CTanalyzer software.

Results: *Hyp* mice displayed a significant reduction in parameters of trabecular bone at distal femur, compared to WT mice (Figure 1A). Similarly, a reduction in trabecular bone was shown in *Hyp* SIJ compared to WT at sacral side (Figure 1B). There was a significant positive correlation between trabecular bone parameters of distal femur and sacral side of SIJ in *Hyp* mice (e.g. bone volume to total volume [BV/TV]: r = 0,763 p: 0,01). Bone parameters such as sacral BV/TV were higher in comparison to femoral parameters (Figure 1C). No difference was observed on trabecular bone parameters at iliac side of Hyp and WT mice. However, regarding the cortical bone of SIJ, significant alterations were noticed especially at iliac side of SIJ in *Hyp* mice compared to WT mice. An increase in open cortical porosity, and a decrease in cortical area fraction, as well as in average cortical thickness at iliac side of SIJ in *Hyp* mice were suggestive of osteo-articular lesions, characteristic for XLH.

Conclusion: Trabecular bone parameters at the SIJ, in comparison to the femur, appear to be a relevant alternative to evaluate bone alterations in *Hyp* mice. Our study suggests that the SIJ represents a valuable tool to investigate both bone and local osteo-articular alterations for murine models of skeletal disorders.

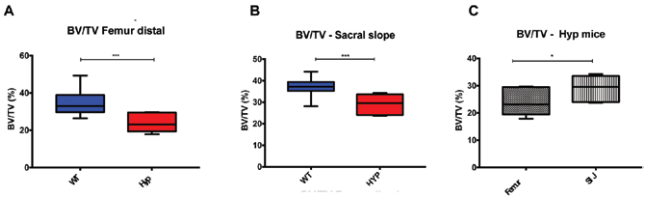


Figure 1. A) Bone to total volume ratio in the trabecular bone of distal femur, expressed in percent. **B)** Bone to total volume ratio in the trabecular bone of sacral slope of the SIJ, expressed in percent. **C)** Bone to total volume ratio in the trabecular bone of distal femur and sacral slope of the SIJ of *Hyp* mice, expressed in percent. *: p < 0,05; **: p < 0,01; ***: p< 0,001; ****: p< 0,0001.

REFERENCES:

[1] Cauliez, Zhukouskaya *et al*. Impact of Early Conventional Treatment on Adult Bone and Joints in a Murine Model of X-Linked Hypophosphatemia. *Front Cell Dev Biol*.:doi: 10.3389/fcell.2020.591417

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3881

New Developments in COVID research

POS0047 OUTCOMES IN INFLAMMATORY ARTHROPATHY PATIENTS HOSPITALIZED FOR COVID-19

T. Collins[1], V. Patel[1], A. Babajanians[2], S. Kubomoto[3]. [1]Riverside Community Hospital, Internal Medicine, Riverside, United States of America; [2]Riverside Medical Clinic, Rheumatology, Riverside, United States of America; [3]Riverside Community Hospital, Graduate Medication Education, Internal Medicine, Riverside, United States of America

Background: Covid 19 is a new and rapidly spreading corona virus which has reached pandemic proportions. As of 5/22/20 there are 5.08 million confirmed cases and 332,000 deaths worldwide. Primary manifestations are respiratory, with a subset developing severe hypoxic respiratory failure. Several risk factors predispose patients to worse outcomes including age, obesity, hypertension, chronic kidney disease, COPD, asthma, CHF, and diabetes. This is a retrospective cohort analysis of patients with Rheumatoid arthritis, Ankylosing spondylitis, or Psoriatic arthritis who were hospitalized for COVID-19 infection across 165 HCA hospitals from 1/1/2020 to 5/30/2020. We compared endpoints and calculated odds of ICU admission, invasive ventilation, mortality compared to control as well as length of stay and discharge location.

Objectives: Our objectives include measuring the outcome of Patients in two arms, the first being those with Rheumatoid arthritis, Ankylosing spondylitis, and Psoriatic arthritis who are infected with COVID 19 to an age matched and comorbidity matched arm (using the Charlson comorbidity index) for the composite endpoint of ICU admission, invasive ventilation, and death. We believe the inflammatory arthropathy arm will have a worse composite endpoint then the control arm. we will also attempt to calculate a hazard ratio of this arm vs the control to the composite endpoint. We will also examine the length of stay as well as inflammatory markers mentioned in between the two arms. We suspect initial inflammatory markers will be lower in the inflammatory arthropathy arm, particularly CRP and LDH, due to chronic immune modulating medication and these markers will not correlate as closely with severe illness represented by the composite endpoint as in the control arm.

Methods: We analyzed 86,217 patients admitted with COVID-19 comparing 751 patients who had inflammatory arthropathy to patients who did not. T tests were used for parametric outcome and chi square tests for non-parametric outcomes. Multivariate analysis included potential confounders such as age, and comorbidities such as diabetes, heart disease, etc.

Results: The odds ratio for mortality in the arthropathy arm was 1.37 with a confidence interval of 1.09 to 1.71 with a p value of 0.006. The odds ratio for ventilation was 1.35 with CI of 1.09 to 1.67 and p value of 0.006. The odds ratio of ICU admission was 1.46 with CI of 1.24 to 1.72 and P value of 0.000. The average length of stay of the arthropathy arm was 8.51 days +/- 10.02 vs 4.59 days +/- 8.26 of the control, p < 0.001. The discharge disposition of the arthropathy arm vs control group is as follows, 13.32% died inpatient vs 5.87% in the control, 56.72% were discharged home vs 77.19%, 6.79% went to hospice care vs 3.10%, 4.79% remained inpatient at the end of the study interval vs 3.45%, 17.18% were discharged to rehab vs 8.43%, and other discharges not included in the above groupings were 1.2% vs 1.96%, p<0.001. 31.29% of the arthropathy

group required ICU admission vs 16.32% and 13.98% required ventilation vs 6.9%, p <0.001. The average age was higher in the arthropathy arm vs control at 66.56 years old vs 51.53, p <0.001. Charlson comorbidity index was also higher in the arthropathy arm at 2.72 vs 0.96, p <0.001.

Conclusion: This is a large analysis of inflammatory arthropathy patients hospitalized with COVID-19. While the arthropathy group was older, and had more co-morbidities, when adjusting for potential confounders, inflammatory arthropathy patients had a higher risk of death and mechanical ventilation, as well as longer length of stay.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.482

POS0048 SEROPREVALENCE OF ANTI-SARS-COV-2 ANTIBODIES IN RHEUMATIC PATIENTS TREATED WITH BIOLOGICAL AND TARGETED THERAPY LIVING IN LOMBARDY, ITALY (MAINSTREAM PROJECT)

E. G. Favalli[1], G. Maioli[1], M. Bombaci[2], M. Biggioggero[1], A. Favalli[2], E. Agape[1], G. Andrea[2], E. Pesce[2], E. Zagato[2], T. Fabbris[2], M. Martinovic[2], E. Marchisio[3], S. Abrignani[2,4], R. Grifantini[2], R. Caporali[1,5]. [1]ASST Gaetano Pini-CTO Institute, Division of Clinical Rheumatology, Milan, Italy; [2]Istituto Nazionale Genetica Molecolare, Padiglione Romeo ed Enrica Invernizzi, Milan, Italy; [3] Dia.Pro, Diagnostic Bioprobes srl, Milan, Italy; [4]Università degli Studi di Milano, Department of Clinical Sciences and Community Health, Milan, Italy; [5]Università degli Studi di Milano, Department of Clinical Sciences and Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Milan, Italy

Background: Emerging observational data have shown that rheumatic patients seem not to be more susceptible to SARS-CoV-2 infection neither to worse outcomes. However, the true prevalence of COVID19 is still unknown due to the high proportion of subclinical infection. In this scenario, measuring the seroprevalence of SARS-CoV-2 may be crucial to improve the knowledge about the impact of COVID19 in rheumatic patients.

Objectives: To estimate in a COVID19 high-endemic area (Lombardy, Italy) the prevalence of anti-SARS-CoV-2 antibodies in a large cohort of patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA) treated with biologic (b-) or targeted synthetic (ts-) disease modifying drugs (DMARDs).

Methods: A seroprevalence cross-sectional study was conducted in the period between 4th May and 16th June 2020, including patients with confirmed RA or SpA treated with b- or tsDMARDs. Patients were tested for anti-SARS-CoV-2 IgG, IgM and IgA antibodies against main viral antigens (nucleoprotein [N], spike 1 [S1], receptor-binding domain [RBD]) using ELISA. These data were compared with those observed in the healthy population in the same period and region. Patients also answered a questionnaire on history of symptoms consistent with COVID19, risk factors and comorbidities. Serological response to RBD was evaluated according to symptom severity (asymptomatic, minor, or major [respiratory and fever >37.5°C] symptoms).

Results: The study population included 300 patients (62% females, mean age 53 years, 20% over 65 years old) diagnosed with RA (56%), psoriatic arthritis (23%), or ankylosing spondylitis (21%), treated with anti-TNF (57%), abatacept (20%), anti-IL6 (11%), or JAK inhibitors (5%). Four patients (1.3%) referred a prior diagnosis of COVID19 defined by nasopharyngeal swab. Immunoglobulin titers were evaluated resulting in 9%, 13.6%, and 13.3% positive patients for IgG, IgM and IgA, respectively (Table 1), with no significant difference to the healthy population. Among seropositive patients, 55.3% were asymptomatic, 16% had minor and 19.6% major symptoms, 7.1% were hospitalized. No deaths or admission to intensive care units occurred. IgM, IgG and IgA titers to RBD were higher in patients with both minor and major symptoms compared with asymptomatic ones (Figure 1). No differences were found between seronegative and seropositive patients in relation to age, sex, rheumatic diagnosis, and treatments with b- or tsDMARDs. A relative lower risk of seropositivity was observed in patients receiving concomitant methotrexate (RR 0.49, 95% CI 0.25-0.94; p 0.04), while an increased risk was associated with obesity (RR 2.33, 95% CI 1.26-3.79; p 0.019) and presence of at least 2 comorbidities (RR 1.94, 95% CI 1.11-3.15; p 0.037). Corticosteroids use was numerically more frequent in seropositive than seronegative patients (18% vs 14%).

Conclusion: This study confirms that, even in a cohort of rheumatic patients, the spread of SARS-CoV-2 infection is much greater than that observed by capturing only swab-diagnosed COVID19 cases. The underlying rheumatic disease and ongoing therapy with b/ts-DMARDs do not seem to impact SARS-CoV-2 antibody positivity, which conversely seems to be proportional to the intensity of COVID19 symptoms and less frequent in patients receiving concomitant methotrexate. The project was co-financed by Lombardy Region 2014-2020 Regional Operational Programme under the European Regional Development Fund.

Table 1. Prevalence of specific anti-SARS-CoV-2 antibodies.

Antibodies	Posivite(n)	Seroprevalence (%)	(95% CI)
IgG	27	9%	(6.2 – 12.7)
IgG anti-N	26	8.6%	(5.9 – 12.3)
IgG anti-RBD	20	6.6%	(4.3 – 10)
IgG anti-S1	18	6%	(3.8 – 9.2)
IgM	41	13.6%	(10.2 – 18)
IgM anti-N	35	11.6%	(8.5 – 15.7)
IgM anti-RBD	25	8.3%	(5.7 – 12)
IgA	40	13.3%	(9.9 – 17.6)
IgA anti-N	37	12.3%	(9.0 – 16.5)
IgA anti-RBD	25	8.3%	(5.7 – 12)
IgG+IgM	23	7.6%	(5.1 – 11.2)
IgG+IgM+IgA	22	7.3%	(4.9 – 10.5)
IgG+IgA	24	8%	(5.4 – 11.6)
IgG/IgM/IgA	56	18.6%	(14.6 – 23.4)

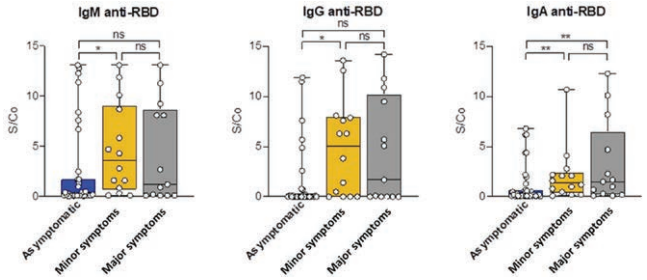


Figure 1. Antibody levels (S/Co) against SARS-CoV-2 RBD.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.594

POS0049 SARS-COV-2 INFECTION IN CHILDREN WITH RHEUMATIC DISEASE: EXPERIENCE OF A TERTIARY REFERRAL CENTER

B. Sözeri[1], F. Demir[1], S. Kalın[2], C. Hasbal Akkuş[3]. [1]İstanbul Health Sciences University, Umraniye Training and Research Hospital, Pediatric Rheumatology, Istanbul, Turkey; [2]İstanbul Health Sciences University, Umraniye Training and Research Hospital, Pediatric Radiology, Istanbul, Turkey; [3]İstanbul Health Sciences University, Umraniye Training and Research Hospital, Pediatrics, Istanbul, Turkey

Background: Patients with rheumatic diseases are considered at risk for serious infections due to their immune-compromised-status set in their primary systemic disease and the usage of immune-modulating therapies. Although various results have been reported on the subject, it is still unknown whether patients with rheumatic disease, many of whom are on immune-suppression, are at higher risk of severe COVID-19.

Objectives: We aim to share our clinical SARS-CoV-2 experience in patient with the childhood rheumatic disease during pandemic.

Methods: We evaluated 4470 patients at our pediatric-rheumatology clinic during the pandemic, from 11-March to 15-October-2020. Demographic and clinical features, treatments, laboratory results, imaging findings, and clinical outcomes of patients diagnosed with COVID-19 and/or multisystem inflammatory syndrome (MIS-C) were review from the medical records. The data of all these patients were compared between groups and presented. A p-value <0.05 was considered statistically significant.

Results: Among 4470 patients, 87 COVID-19 suspected patients were included in the study. Fifty six (64.4%) patients were hospitalized and 31 were followed without hospitalization. The most common rheumatic diseases among them were juvenile idiopathic arthritis and familial Mediterranean fever (35.6% and 34.5%). The primary disease status of these patients were; 78 (89.6%) were in remission, while 9 (10.3%) had active disease at the time of COVID-19 diagnosis. Twenty six of these patients were treated with biologic DMARDs. SARS-CoV-2 infection (RT-PCR and/or antibody test) was found positive in 84 patients (96.5%). Also, fifty one (58.6%) patients had an epidemiologic contact to a person with COVID-19. Fifty six of 87 (64.3%) had a fever and 20 (23%) had a fever for five or more days. Gastrointestinal system involvement was in 11 (12.6%), the respiratory system was in 40 (46%) and fatigue was in 57 (65.5%) patients. Cutaneous involvement was seen in 5 patients including maculopapular rash in two, vasculitic rash in two, and chilblain in one patient. 63.2% of patients had increased C-reactive protein (CRP), 40.2% had lymphocytopenia (<1500/mm3) and 26.4 % had elevated D-dimer

level. SARS-CoV-2 infection was confirmed in 84 patients (96.5%). The diagnosis was confirmed by RT-PCR in 74 patients and by antibody test in 10. 18 patients met the clinical criteria and diagnosed with MIS-C. Nine of them had also hypotension and seven patients admitted the intensive care unit because of shock and severe end-organ illness. COVID-19 outbreak also caused exacerbation of systemic disease in 56 children due to a discontinue of medication, postponed drug switch, or viral infection triggered.

Conclusion: In conclusion, children with rheumatic disease do not appear to present a higher risk of severe COVID-19. Whether these patients receive biological treatment does not affect the severity of the disease, but it is still not true to say that these drugs are protective. The immunosuppressive treatments can be adjusted in case of infection, otherwise it is not recommended interrupt the treatments. Physicians should be cautious about the hyperinflammatory syndrome associated with COVID-19 in rheumatic children, which may be severe in this group of patients and may be confused with primary diseases.

REFERENCES:

[1] Wahezi DM, Lo MS, TB Rubinstein, Ringold S, Ardoin SP, Downes KJ, et al. American College of Rheumatology Guidance for the Management of Children with Pediatric Rheumatic Disease During the COVID-19 Pandemic: Version 1. *Arth & Rheum* 2020;doi:10.1002/art.41455.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1164

POS0050 ARE PATIENTS WITH IMMUNE MEDIATED INFLAMMATORY DISEASES (IMID) MORE LIKELY TO RECEIVE COVID-19 TESTS AND TEST POSITIVE FOR SARS-COV-2? A MATCHED POPULATION-BASED STUDY

L. Eder[1,2], R. Croxford[3], A. Drucker[2,4], A. Mendel[5], K. Bindee[4,6], Z. Touma[4,7], S. Johnson[4,7], R. Cook[8], S. Bernatsky[5], N. Haroon[1,7], J. Widdifield[3,4,9].
[1]University of Toronto - St. George Campus, Medicine and Institute of Medical Science, Toronto, Canada; [2]Women's College Hospital, Medicine, Toronto, Canada; [3]ICES, NA, Toronto, Canada; [4]University of Toronto - St. George Campus, Medicine and Institute of Health Policy Management and Evaluation, Toronto, Canada; [5]McGill University, Medicine, Montréal, Canada; [6]Sinai Health System, Medicine, Toronto, Canada; [7]Toronto Western Hospital, Medicine, Toronto, Canada; [8]University of Waterloo, Biostatistics, Waterloo, Canada; [9]Sunnybrook Health Sciences Centre, Research Institute, Toronto, Canada

Background: Population-based data about the COVID-19 risk in patients with IMID remain scarce.

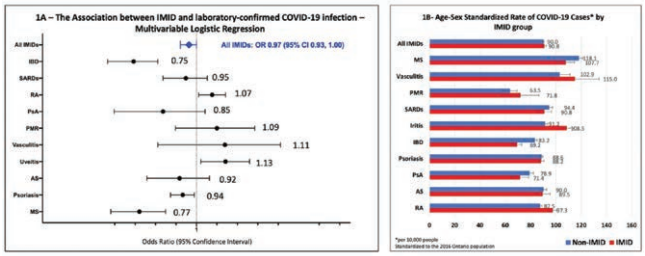
Objectives: To investigate the cumulative incidence and risk factors for laboratory-confirmed COVID-19 infection and SARS-CoV2 testing in patients with IMID compared with matched non-IMID patients from the general population.

Methods: A population-based, matched cohort study was conducted using health administrative data from adults living in Ontario, Canada from January to December 2020. Cohorts for each of the following IMID were assembled: rheumatoid arthritis (RA), psoriasis, psoriatic arthritis, ankylosing spondylitis, systemic autoimmune rheumatic diseases (including lupus, systemic sclerosis, Sjogren's, inflammatory myositis), multiple sclerosis (MS), iritis, inflammatory bowel disease (IBD), polymyalgia rheumatica (PMR) and vasculitis. Each patient was matched with 5 non-IMID comparators based on age, sex, area of residence and living in long term care (LTC). Standardized cumulative rates of testing for SARS-CoV2, and for receiving a positive test between IMID and non-IMID were compared between IMID and non-IMID patients. Multivariable logistic regression analyses assessed sociodemographic factors associated with COVID-19 testing and positivity.

Results: A total of 493,499 IMID patients and 2,466,946 non-IMID comparators were assessed. Significantly more IMID patients versus non-IMID were tested for SARS-CoV2 (27.4% vs. 22.7%), while the proportions of those positive for COVID-19 were identical (0.9% of all patients in both groups). Overall, IMID patients were more likely to undergo SARS-CoV2 testing (odds ratio (OR) 1.28, 95% CI 1.27, 1.29), but their overall risk of laboratory-confirmed COVID-19 was not elevated (OR 0.97 (95% CI 0.93, 1)). However, the risk of laboratory-confirmed COVID-19 infection was lower in IBD (OR 0.75), MS (OR 0.77) and psoriasis (OR 0.94) and marginally higher in RA (OR 1.07) and iritis (OR 1.13) compared with non-IMID comparators (Figure 1A). The highest standardized rates of COVID-19 infection were found in vasculitis (115 per 10,000 patients) and iritis (109 per 10,000 patients) (Figure 1B). Risk factors for COVID-19 infection included younger age, living in LTC, multimorbidity, urban living and lower income (Table 1).

Conclusion: Patients across all IMID were more likely to be tested for COVID-19 versus non-IMID patients. IMID patients were not at higher risk for testing positive for COVID-19 as an overall group, yet risk varied across disease subgroups.

Figure 1 – Laboratory confirmed COVID-19 Risk in IMID vs. Non-IMID by multivariable regression analysis (1A) and standardized cumulative incidence (1B)



AS – ankylosing spondylitis; IBD – inflammatory bowel disease; MS – multiple sclerosis; PsA - Psoriatic Arthritis; PMR – polymyalgia rheumatica; RA- Rheumatoid arthritis; SARDs – systemic autoimmune rheumatic disease;

Table 1. Factors associated with COVID-19 infection in IMID vs. Non-IMID – Multivariable Logistic Regression

Variable	OR	CI 95%
IMID vs. Non-IMID	0.97	0.93, 1.00
Age (10-year increase)	0.89	0.89, 0.90
Sex: Female vs. Males	0.95	0.93, 0.97
LTC	18.64	17.9, 19.42
ADG score:		
•5-9 vs. 0-4	1.40	1.35, 1.45
•10-14 vs. 0-4	1.73	1.67, 1.80
•15+ vs. 0-4	1.18	1.13, 1.23
Urban vs. Rural	3.49	3.26, 3.72
Income quintile		
•Quintile 2 vs. 1	0.92	0.89, 0.96
•Quintile 3 vs. 1	0.90	0.86, 0.93
•Quintile 4 vs. 1	0.73	0.70, 0.76
•Quintile 5 vs. 1	0.60	0.58, 0.63

ADG - Aggregated Diagnosis Groups; IMIDs – Immune medicated inflammatory disease; LTC – long term care

Acknowledgements: The study is supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). Parts of this material are based on data and information compiled and provided by MOHLTC and the Canadian Institute for Health Information. The opinions, results and conclusions reported in this paper are those of the authors and are independent of the funding or data sources; no endorsement is intended or should be inferred.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1647

POS0051 THE IMPACT OF COVID-19 ON RHEUMATOLOGY TRAINING: RESULTS FROM THE COVID-19 GLOBAL RHEUMATOLOGY ALLIANCE TRAINEE SURVEY

K. Young[1], S. A. Yeoh[2], M. Putman[3], E. Graef[4], F. Berenbaum[5,6,7], R. Conway[8], R. Grainger[9], A. Kilian[10], M. Konig[11], J. Liew[12], P. M. Machado[2], S. E. Sattui[13], J. Sparks[14,15], P. Sufka[16], M. Ugarte-Gil[17], L. Upton[18], Z. Wallace[15,19], J. Yazdany[20], A. Jayatilleke[21]on behalf of the COVID-19 Global Rheumatology Alliance. [1]University of Texas Southwest Medical Center, Rheumatology, Dallas, United States of America; [2]University College London, Rheumatology, London, United Kingdom; [3]Medical College of Wisconsin, Rheumatology, Milwaukee, United States of America; [4]Emerson Hospital, Department of Medicine, Concord, United States of America; [5]Sorbonne University, Rheumatology, Paris, France; [6]AP-HP Saint-Antoine Hospital, Rheumatology, Paris, United Kingdom; [7]Inserm, Rheumatology, Paris, France; [8]St. James's Hospital, Rheumatology, Dublin, Ireland; [9]University of Otago Wellington, Department of Medicine, Wellington, New Zealand; [10]George Washington University, School of Medicine and Health Sciences, Washington DC, United States of America; [11]Johns Hopkins University, Rheumatology, Baltimore, United States of America; [12]Boston University School of Medicine, Section of Rheumatology, Boston, United States of America; [13]Hospital for Special Surgery, Department of Medicine, New York, United States of America; [14]Brigham and Women's Hospital, Rheumatology, Boston, United States of America; [15]Harvard Medical School, Rheumatology, Boston, United States of America; [16]HealthPartners & Regions Hospital, Rheumatology, St. Paul, United States of America; [17]Universidad Cientifica del Sur, Rheumatology, Lima, Peru; [18]Georgetown University, School of Medicine, Washington DC, United States of America; [19]Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America; [20]University of California San Francisco, Division of Rheumatology, San Francisco, United States of America; [21]Temple University Lewis Katz School of Medicine, Rheumatology, Philadelphia, United States of America

Background: The COVID-19 pandemic has disrupted healthcare delivery and education of physicians, including rheumatology trainees.
Objectives: To assess the impact of the COVID-19 pandemic on the clinical experiences, research opportunities, and well-being of rheumatology trainees.
Methods: A voluntary, anonymous, web-based survey was administered in English, Spanish, or French from 19/08/2020 to 05/10/2020. Adult and paediatric rheumatology trainees worldwide in training in 2020 were invited to participate via social media and email. Using multiple choice questions, Likert scales, and free text answers, we assessed trainee patient care activities, redeployment, research, and well-being.
Results: The 302 respondents were from 33 countries, with most (83%, 252/302) in adult rheumatology training. Many trainees (45%, 135/300) reported an increase in non-rheumatology clinical work (e.g. care of COVID-19 patients), with 52% of these (70/135) also continuing rheumatology clinical work. COVID-19 redeployment was not optional for 68% (91/134).
Trainees reported a negative impact of the pandemic in their growth in rheumatology (Figure 1). They also reported a substantial impact on several training areas: outpatient clinics (79%, 238/302), inpatient consultations (59%, 177/302), formal teaching (55%, 167/302), procedures (53%, 147/302), teaching opportunities (52%, 157/302), and ultrasonography (36%, 110/302), with 87-96% perceiving a negative impact on these areas. Only 54% (159/294) reported feeling comfortable with their level of clinical supervision during the pandemic (Figure 1). Many trainees (46%, 128/280) reported changes in research experiences during the pandemic; 39% (110/285) reported that COVID-19 negatively affected their ability to continue their pre-pandemic research and 50% (142/285) reported difficulty maintaining research goals (Figure 1).
Some rheumatology trainees reported having health condition(s) putting them at high risk for COVID-19 (10%, 30/302) and 14% of trainees (41/302) reported having had COVID-19 (Table 1). Only 53% (160/302) reported feeling physically safe in the workplace while 25% (76/302) reported not feeling physically safe; reasons included lack of training about COVID-19, lack of comfort in the clinical setting, insufficient personal protective equipment, immunocompromised state, and pregnancy. Half (151/302) reported burnout and 68% (204/302) an increase in stress from work during the pandemic (Figure 1), whilst 25% (75/302) reported that changes to their training programme negatively impacted their physical health.
Conclusion: The COVID-19 pandemic has negatively impacted the experience of rheumatology training as well as the well-being of trainees globally. Our data highlight concerns for rheumatology trainees including research opportunities and clinical care which should be a focus for curriculum planning.

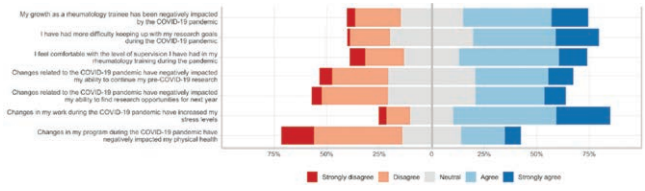


Figure 1. Rheumatology trainee perceptions of pandemic impact and changes in training programme.

Table 1. Rheumatology trainees reporting health vulnerabilities or having acquired COVID-19. Data is presented as n (%). Rest of the world (ROW) data includes the United States (116), Asia (50), Central and South America (23), Canada (12), Australia (8), and Africa (4).

	Europe n = 89	ROW n = 213	Combined n = 302
Disability	1 (1)	9 (4)	10 (3)
High risk	7 (8)	23 (11)	30 (10)
Pregnant	4 (5)	15 (7)	19 (6)
Shielding/Quarantining	12 (13)	70 (33)	82 (27)
Acquired COVID-19	20 (22)	21 (10)	41 (14)

Disclosure of Interests: Kristen Young: None declared, Su-Ann Yeoh: None declared, Michael Putman: None declared, Elizabeth Graef: None declared, Francis Berenbaum: None declared, Richard Conway: None declared, Rebecca Grainger Speakers bureau: Speaker fees from Abbvie, Janssen, Novartis, Pfizer, Cornerstones, all not related to this work, Consultant of: Consultancy fees from Abbvie, Janssen, Novartis, Pfizer, Cornerstones, all not related to this work, Grant/research support from: Travel assistance from Pfizer, not related to this work, Adam Kilian: None declared, Maximilian Konig: None declared, Jean Liew Grant/research support from: Research grant from Pfizer unrelated to this manuscript, Pedro M Machado Speakers bureau: Speaker fees from Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript, Consultant of: Consulting fees from Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript, Sebastian E. Sattui: None declared, Jeffrey Sparks Consultant of: Consultancy for Bristol-Myers Squibb, Gilead, Inova Diagnostics, Optum, and Pfizer unrelated to this manuscript, Grant/research support from: Research support from Bristol-Myers Squibb unrelated to this manuscript, Paul Sufka: None declared, Manuel Ugarte-Gil Grant/research support from: Research grants from Janssen and Pfizer unrelated to this manuscript, Laura Upton: None declared, Zachary Wallace: None declared, Jinoos Yazdany Consultant of: Consultancy for Astra Zeneca, Eli Lilly, and Pfizer, not related to this work, Grant/research support from: Research grants from Gilead and Pfizer, not related to this work, Arundathi Jayatilleke: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2236

POS0052 PATHOPHYSIOLOGY OF ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 INFECTION: A SYSTEMATIC LITERATURE REVIEW TO INFORM EULAR POINTS TO CONSIDER

A. Najm[1], A. Alunno[2], X. Mariette[3], B. Terrier[4], G. De Marco[5], L. Mason[6], J. Emmel[6], D. Mcgonagle[5], P. M. Machado[7]on behalf of EULAR Task Force on pathophysiology and use of immunomodulatory therapies in COVID-19..
[1]Institute of Infection, Immunity and Inflammation, College of Medical Veterinary and Life Sciences, Rheumatology, Glasgow, United Kingdom; [2]University of Perugia, Rheumatology, Perugia, Italy; [3]Paris-Saclay University, Rheumatology, Paris, France; [4]University of Paris, Assistance Publique-Hôpitaux de Paris, Cochin Hospital, INSERM U970, Paris, France; [5]Leeds Institute of Rheumatic and Musculoskeletal Medicine, Rheumatology, Leeds, United Kingdom; [6]Library & Evidence Research Centre, Leeds Teaching Hospitals NHS Trust, Medical Education, Leeds, United Kingdom; [7]Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, Rheumatology, London, UK, United Kingdom

Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is a global health problem. Beside the specific pathogenic effect of SARS-CoV-2, incompletely understood deleterious and aberrant host immune responses play critical roles in severe disease. Rheumatologists have the best experience of studying and treating these complicated hyperinflammatory processes.
Objectives: To summarize the available information on pathophysiology of COVID-19.
Methods: As part of a EULAR taskforce, two systematic literature reviews were performed one on pathophysiology and one on immunomodulatory therapies. Two reviewers independently identified eligible studies according to the following PICO framework: P (population): patients with SARS-CoV-2 infection; I (intervention): any intervention/no intervention; C (comparator): any comparator; O (outcome) any clinical or serological outcome including but not limited to immune cell phenotype and function and serum cytokine concentration. The results pertaining to pathophysiology of COVID-19 are presented here.
Results: Of the 55496 records yielded, 85 articles were eligible for inclusion. Included studies were at variable risk of bias and exploring various aspects of disease pathogenesis from immune to non-immune cells (Table 1). Pro-inflammatory cytokines' expression including IL-6, was increased, especially in severe COVID-19, although not as high as other states with severe systemic inflammation. Innate and adaptative immune cell compartments were differentially affected by SARS-CoV-2 infection: neutrophils displayed an immature differentiation state and also increased neutrophil extracellular traps (NETs) formation. Dendritic cell number was reduced and classical monocytes was increased although displaying a reduced expression of HLA-DR. The lymphoid compartment was also affected: lymphopenia was present with a reduced number of CD4+ and CD8+ T lymphocytes and more frequent PD1+CD8+ T cells corresponding to an exhausted phenotype. Antibody response to SARS-CoV-2 infection showed a high variability across individuals and disease spectrum. Multiparametric algorithms showed variable diagnostic performances in predicting survival, hospitalization, disease progression or severity, and mortality. Differences in SARS-CoV-2 manifestations in adults and children were highlighted.
Conclusion: Overall, SARS-CoV-2 infection affects both innate and adaptative immune responses in a variable way, according to both disease severity and individual parameters. This SLR informs the EULAR points to consider on pathophysiology and use of immunomodulatory therapies in COVID-19.

Table 1. Studies on SARS-CoV-2 infection pathogenesis

Research question	N
Cytokines profile	7
Immune profile	18
Algorithm	17
Children	3
Comorbidities	1
Endothelial dysfunction and platelets	8
Gut and microbiota	3
Genetics and variants	8
Histology	7
Antibodies profiles	8
Viral load and immune response	4
Interferon	3
Immunosenecsnce	3
Total	90*

*Some manuscripts were including in several research questions. Total number of studies included n=85.

Disclosure of Interests: Aurelie Najm Speakers bureau: BMS, Consultant of: BMS, Alessia Alunno: None declared, Xavier Mariette Speakers bureau: BMS, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Novartis, Pfizer, Servier and UCB, Consultant of: BMS, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Novartis, Pfizer, Servier and UCB, Benjamin Terrier Speakers bureau: Roche, Chugai, Vifor Pharma, GSK, AstraZeneca, Terumo BCT, LFB and Grifols, Consultant of: Roche, Chugai, Vifor Pharma, GSK, AstraZeneca, Terumo BCT, LFB and Grifols, Gabriele De Marco: None declared, Laura Mason: None declared, Jenny Emmel: None declared, Dennis McGonagle Speakers bureau: Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Consultant of: Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Pedro M Machado Speakers bureau: Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, Consultant of: Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2851

POS0053

RHEUMATOID ARTHRITIS AND THE RISK OF COVID-19 DIAGNOSIS, HOSPITALISATION AND DEATH: A POPULATION-BASED MULTI-STATE COHORT ANALYSIS INCLUDING 5,586,565 PEOPLE IN CATALONIA, SPAIN

A. Vivekanantham[1,2], E. Burn[1,3], S. Fernandez-Bertolin3, M. Aragon3, T. Duarte-Salles3, D. Prieto-Alhambra[1,4]. *[1]University of Oxford, Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, Oxford, United Kingdom; [2]Nuffield Orthopaedic Centre, Rheumatology, Oxford, United Kingdom; [3]Fundació Institut Universitari per a la recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, (IDIAPJGol), Barcelona, Spain; [4]Erasmus University Medical Center, Health Data Sciences, Rotterdam, Netherlands*

Background: The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is of particular concern for people with rheumatoid arthritis (RA), with concerns that these people may be at higher risk and have poorer outcomes. However, at present the implications of COVID-19 for people with RA remain poorly understood.

Objectives: To investigate the associations between rheumatoid arthritis and the risk of COVID-19 diagnosis, hospitalisation with COVID-19 and COVID-19-related death.

Methods: A population-based cohort study including all individuals registered in the Information System for Research in Primary Care (SIDIAP). SIDIAP includes primary care records covering over 80% of the population of Catalonia, Spain, and was linked to region-wide SARS-CoV-2 PCR testing, hospital and mortality records. Outpatient diagnoses of COVID-19, hospitalisations with COVID-19 and deaths with COVID-19 were identified as study outcomes between 1st March and 6th May 2020. A multi-state model was used, with cause-specific Cox survival models estimated for each transition, adjusted for age and sex.

Results: A total of 5,586,565 individuals were identified in SIDIAP as of the 1st March 2020, of which 16,344 had RA. RA patients were median (IQR) 63 years (52.0, 74.0) and the majority (n=11,727, 71.8%) were female. Having RA was positively associated with being diagnosed with COVID-19 (adjusted HR 1.14 (1.03 to 1.28)), with hospitalisation with COVID-19 (HR 1.66 (1.35 to 2.04)). However, we did not find an association between RA status and the risk of worsening from outpatient diagnosis to hospitalization or death, or from hospitalization to death (see Table 1).

Table 1. Estimated hazard ratios, adjusted for age and gender, for individuals with rheumatoid arthritis

Transition	Study population (RA), n	Total events (RA), n	Hazard Ratios (95% Confidence Intervals)
From general population to diagnosed with COVID-19	5,586,565 (16,344)	88,396 (324)	1.14 (1.03 to 1.28)
From general population to hospitalised with COVID-19	5,586,565 (16,344)	10,143 (90)	1.66 (1.35 to 2.04)
From diagnosed with COVID-19 to hospitalised with COVID-19	88,396 (324)	5,946 (30)	0.95 (0.66 to 1.36)
From diagnosed with COVID-19 to death	88,396 (324)	2,295 (16)	0.96 (0.58 to 1.56)
From hospitalised with COVID-19 to death	16,089 (120)	2,602 (27)	1.13 (0.77 to 1.64)

Conclusion: To our knowledge, this is the largest study performed to date looking at COVID-19 outcomes in RA patients. Individuals with RA were found to have an increased risk of COVID-19 diagnosis and hospitalisation with COVID-19, compared to the general population. Further research is needed to address factors associated with this including the presence of other co-morbidities, underlying RA disease activity and the use of immunosuppressive medications.

Disclosure of Interests: Arani Vivekanantham: None declared, Edward Burn: None declared, Sergio Fernandez-Bertolin: None declared, Maria Aragon: None declared, Talita Duarte-Salles: None declared, Daniel Prieto-Alhambra Grant/research support from: Dr. Prieto-Alhambra reports grants and other from AMGEN, grants, non-financial support and other from UCB Biopharma, grants from Les Laboratoires Servier, outside the submitted work; and Janssen, on behalf of IMI-funded EHDEN and EMIF consortiums, and Synapse Management Partners have supported training programmes organised by DPA's department and open for external participants.

DOI: 10.1136/annrheumdis-2021-eular.3160

POS0054

THE IMPACT AND OUTCOME OF COVID-19 ON SYSTEMIC SCLEROSIS PATIENTS FROM THE EUROPEAN SCLERODERMA TRIAL AND RESEARCH GROUP (EUSTAR)

A. M. Hoffmann-Vold[1], C. Brunborg[2], F. Tirelli[3], P. Carreira[4], N. Del Papa[5], A. Mekinian[6], M. Vonk[7], A. Giollo[8], G. De Luca[9], M. De Santis[10], C. Campochiaro[9], C. Mihai[3], P. Airò[11], M. G. Lazzaroni[11], E. Zanatta[12], R. Foti[13], Y. Allanore[14], D. Furst[15], M. Matucci-Cerinic[16], A. Gabrielli[17], O. Distler[3]. [1]Oslo University Hospital, Rheumatology, Oslo, Norway; [2]Oslo University Hospital, Centre for Biostatistics and Epidemiology, Research Support Services, Oslo, Norway; [3]University Hospital Zurich, University of Zurich, Rheumatology, Zurich, Switzerland; [4]12 de Octubre University Hospital, Rheumatology, Madrid, Spain; [5]ASST G. Pini-CTO, University of Milan, Rheumatology, Milan, Italy; [6]Hôpital Saint Antoine, Internal Medicine, Paris, France; [7]Radboud University Medical Center, Rheumatology, Nijmegen, Netherlands; [8]University of Verona, Rheumatology, Verona, Italy; [9]IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy; [10]IRCCS Humanitas Research Hospital, Rheumatology and Clinical Immunology, Milan, Italy; [11]ASST Spedali Civili of Brescia, Rheumatology and Clinical Immunology, Brescia, Italy; [12]University of Padova, Rheumatology, Padova, Italy; [13]A.O.U. Policlinico S. Marco, Rheumatology, Catania, Italy; [14]Cochin Hospital, Université de Paris, Rheumatology, Paris, France; [15]University of California in Los Angeles, Rheumatology, Los Angeles, United States of America; [16]University of Florence, Rheumatology, Florence, Italy; [17]Università Politecnica delle Marche, Scienze Cliniche e Molecolari, Ancona, Italy

Background: Coronavirus disease-19 (COVID-19) has been a major clinical challenge worldwide. Sex, age and comorbidities have been associated with worse outcome in the general population. Systemic sclerosis (SSc) is a severe, autoimmune disease with frequent multi-organ involvement.

Objectives: To assess the impact of COVID-19 and to determine factors associated with worse outcome in SSc patients from the European Scleroderma Trial and Research (EUSTAR) database.

Methods: SSc patients from the EUSTAR database with COVID-19 were prospectively collected between 15.03.-31.12.2020. Two outcomes were chosen: (1) hospitalization; and (2) severe outcome defined as either non-invasive ventilation, mechanical ventilation/extracorporeal membrane oxygenation (ECMO) or death. General risk factors assessed were sex, age and number

of comorbidities. SSc related risk factors were SSc subtype, autoantibodies, disease duration, SSc associated organ manifestations including interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), cardiac, gastrointestinal (GI), and musculoskeletal involvement; digital ulcers (DU), CRP at last visit, renal disease (scleroderma renal crisis and SSc associated renal insufficiency), modified Rodnan skin score (mRSS) and immunosuppressive treatment. Descriptive statistics and logistic regression models were applied.

Results: In total, 178 European SSc patients with COVID-19 were registered with a median observation time of 5.5 weeks (Table 1). 95 patients (53%) could recall SAR-Cov-2 contact, while 47 (26%) had no contact. 156 (88%) were symptomatic at COVID-19 onset with fever, cough, malaise and dyspnea being most prevalent. Over the disease course, 63 (36%) developed pneumonia. In total, 67/176 (38%) were hospitalized which were in 84% due to COVID-19. 41/170 (24%) had a severe outcome including 21 (12%) deaths. 128 (72%) recovered completely, while 14 (8%) complained of sequela, with 7 (50%) stating respiratory complications. Age, non-SSc comorbidities, presence of ILD, PAH and SSc associated renal or cardiac disease were numerically associated with hospitalization and severe outcome (Table 1). Univariable logistic analyses for hospitalization and severe outcome are shown in Figure 1. In multivariable logistic regression, age (OR 1.03, 95%CI 1.01-1.07, p=0.019), presence of non-SSc comorbidities (OR 2.52, 95%CI 1.16-5.47, p=0.019) and SSc-related renal disease (predicting success perfectly) were associated with hospitalization and for severe outcome age (OR 1.05, 95%CI 1.01-1.08).

Conclusion: SSc patients at older age, with non-SSc comorbidities, SSc related renal disease or ILD are at risk of a more severe outcome and should follow precautions to avoid COVID-19 infections and need careful monitoring in case of COVID-19.

Table 1. SSc disease characteristics of COVID-19 patients

	All (n=172)	Hospitalized (n=67)	Severe outcome (n=41)
Age at COVID-19, yrs (SD)	57 (14.0)	63 (13.8)	65 (12.2)
Male sex, n (%)	38 (21)	18 (27)	12 (29)
≥1 comorbidity, n (%)	63/176 (36)	37 (55)	30 (58)
SSc disease duration at COVID, yrs (SD)	11.5 (8.8)	13.3 (9.7)	12.7 (10.2)
Diffuse cutaneous SSc, n (%)	74 (42)	29 (43)	19 (46)
mRSS, median (IQR)	5 (8)	5 (9)	5 (7)
ILD, n (%)	90/175 (51)	36/65 (55)	26/40 (65)
PAH, n (%)	21/175 (12)	11/65 (17)	8/40 (20)
GI disease, n (%)	112/176 (64)	45 (67)	30 (73)
Cardiac disease, n (%)	37/166 (22)	19/59 (32)	16/36 (44)
Musculoskeletal disease, n (%)	40/175 (23)	15/65 (23)	6/40 (15)
Renal disease, n (%)	8/175 (5)	7/65 (11)	5/40 (13)
Ever DU, n (%)	69/175 (39)	27/65 (42)	14/40 (35)
CRP, ng/ml (SD)	35/177 (20)	14 (21)	9 (22)
Immunosuppressive treatment, n (%)	104/177 (59)	41/66 (62)	26 (63)

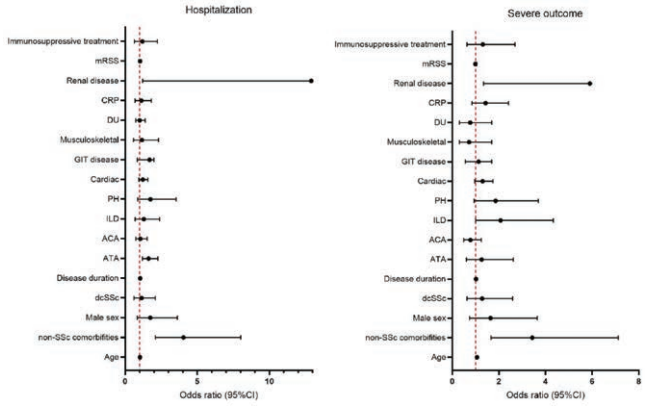


Figure 1. Univariable logistic analyses for hospitalization and severe outcome

Disclosure of Interests: Anna-Maria Hoffmann-Vold Speakers bureau: Actelion, Boehringer Ingelheim, Roche, Merck Sharp & Dohme, ARXX, Lilly and Medscape, Consultant of: Actelion, Boehringer Ingelheim, Bayer, ARXX, and Medscape , Grant/research support from: Boehringer Ingelheim, Cathrine Brunborg: None declared, Francesca Tirelli: None declared, Patricia Carreira: None declared, Nicoletta Del Papa: None declared, Arsene Mekinian: None declared, Madelon Vonk: None declared, Alessandro Giollo: None declared, Giacomo De Luca: None declared, Maria De Santis: None declared, Corrado Campochiaro: None declared, Carina Mihai: None declared, Paolo Airò Speakers bureau: Bristol Myers Squibb, Bohringer Ingelheim, Consultant of: Bristol Myers Squibb, Bohringer Ingelheim, non-financial support from CSL Behring, SOBI, Janssen, Roche, Sanofi, Pfizer, Maria Grazia Lazzaroni: None declared, Elisabetta Zanatta: None declared, Rosario Foti: None declared, Yannick Allanore: None declared, Daniel Furst: None declared, Marco Matucci-Cerinic: None declared, Armando Gabrielli: None declared, Oliver Distler Speakers bureau: Actelion, Kymera Therapeutics, Mitsubishi Tanabe Pharma, Abbvie, Acceleron, Alexion, Amgen, AnaMar, Arxx Therapeutics, Baecon, Discovery, Blade Therapeutics, Corbus Pharmaceuticals, Drug Development International, Ltd, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Kymera Therapeutics, Lilly, Novartis, Pfizer, Topadur and UCB, Consultant of: Actelion, Kymera Therapeutics, Mitsubishi Tanabe Pharma, Abbvie, Acceleron, Alexion, Amgen, AnaMar, Arxx Therapeutics, Baecon, Discovery, Blade Therapeutics, Corbus Pharmaceuticals, Drug Development International, Ltd, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Kymera Therapeutics, Lilly, Novartis, Pfizer, Topadur and UCB, Grant/research support from: Boehringer Ingelheim.

DOI: 10.1136/annrheumdis-2021-eular.3267

POS0055 SARS-COV-2 OUTBREAK IN AUTOIMMUNE DISEASES: THE EURO-COVIMID STUDY

D. Saadoun[1], M. Vieira[1], M. Vautier[1], X. Baraliakos[2], I. Andreica[2], J. A. P. Da Silva[3], M. Sousa[3], M. Luis[3], N. Khmelinskii[4], J. M. Alvaro-Gracia[5], I. Castrejon[5], J. C. Nieto González[5], C. A. Scirè[6], E. Silvagni[6], A. Bortoluzzi[6], H. Penn[7], S. Hamdulay[7], P. Machado[7], B. Fautrel[8,9], P. Cacoub[1], M. Resche-Rigon[10], L. Gossec[8,9]. *[1]University Hospitals Pitié Salpêtrière - Charles Foix, Département de Médecine Interne et Immunologie Clinique, Centre National de Références Maladies Autoimmunes systémiques rares, Centre National de Références Maladies Autoinflammatoires et Amylose Inflammatoire, Paris, France; [2]Ruhr-Universität Bochum, Rheumazentrum Ruhrgebiet, Bochum, Germany; [3]Centro Hospitalar e Universitário de Coimbra, Rheumatology Department, Coimbra, Portugal; [4]Hospital de Santa Maria, Rheumatology Department, Lisboa, Portugal; [5]Gregorio Marañón Hospital, Rheumatology, Madrid, Spain; [6]University of Ferrara, Department of Medical Sciences, Ferrara, Italy; [7]Northwick Park Hospital, Department of Rheumatology, London, United Kingdom; [8]University Hospitals Pitié Salpêtrière - Charles Foix, Rheumatology Department, Paris, France; [9]Pierre Louis Institute of Epidemiology and Public Health, Inserm UMR 1136, PEPITES team, Paris, France; [10]Hospital Saint-Louis, URC Saint-Louis, Paris, France*

Background: Coronavirus disease 2019 (COVID-19), has raised several questions in patients with immune-mediated inflammatory diseases (IMID). Whether the seroprevalence and factors associated with symptomatic COVID-19 are similar in IMID patients and in the general population is still unknown.

Objectives: To assess the serological and clinical prevalence of COVID-19 in European IMID patients, along with the factors associated with its risk and the impacts the pandemic had on the IMID management.

Methods: Prospective multicentre cross-sectional study among patients with five IMID (i.e. systemic lupus erythematous, Sjögren's syndrome, rheumatoid arthritis, axial spondylarthritis or giant cell arteritis) from six tertiary-referral centers from France, Germany, Italy, Portugal, Spain and United Kingdom. Demographics, comorbidities, IMID, treatments, flares and COVID-19 details were collected. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serological tests were systematically performed.

Results: Between June 7 and December 8, 2020, 3028 patients were included (median age 58 years, 73.9% females). SARS-CoV-2 antibodies were detected in 166 (5.5%) patients. Symptomatic COVID-19 was seen in 122 patients (prevalence: 4.0%, 95% CI 3.4-4.8%); 23 (24.2%) of them were hospitalized and four (3.2%) died. In multivariate logistic regression analysis, symptomatic COVID-19 was more likely to be observed in patients with higher levels of C-reactive protein (OR: 1.18; 95% CI 1.05-1.33; p = 0.006), and increased with the number of IMID flares (OR: 1.27; 95% CI 1.02-1.58; p = 0.03). Conversely, it was less likely to occur in patients treated with biological therapy (OR: 0.51; 95% CI 0.32-0.82; p = 0.006). During the pandemic, at least one self-reported disease flare was seen in 654 (21.6%) patients. Also, 519 (20.6%) patients experienced changes in their treatment, with 125 of these (24.1%) being due to COVID-19.

Conclusion: The SARS-CoV-2 prevalence in IMID patients over the study period seems to be similar to that of the general population[1]. The IMID inflammatory status seems to be independently associated with the development of COVID-19.

REFERENCES:

[1] Pollán M, Pérez-Gómez B, Pastor-Barriuso R, Oteo J, Hernán MA, Pérez-Olmeda M, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet Lond Engl. 2020 Aug 22;396(10250):535–44.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3368

POS0056 ANXIETY AND CONCERNS RELATED TO THE WORK SITUATION DURING THE COVID-19 PANDEMIC IN >5,000 PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASE FOLLOWED IN THE DANISH DANBIO REGISTRY, RESULTS FROM A NATIONWIDE QUESTIONNAIRE

B. Glintborg[1], D. V. Jensen[2], S. Engel[1], L. Terslev[1], M. Pfeiffer Jensen[1], O. Hendricks[3], M. Østergaard[1], S. H. Rasmussen[1], T. Adelsten[4], A. Colic[4], K. Danebod[1], M. Kildemand[5], A. G. Loft[6], H. L. Munk[7], J. K. Pedersen[8], R. Østgård[9], C. M. Sørensen[10], N. Steen Krogh[11], J. Nørgaard Agerbo[12], C. Ziegler[12], M. L. Hetland[1]. [1]Centre of Head and Orthopedics, Rigshospitalet, DANBIO and Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Glostrup, Denmark; [2]Gentofte and Herlev Hospital, Department of rheumatology, Center for Rheumatology and Spine Diseases, Gentofte, Denmark; [3]University Hospital of Southern Denmark, Sønderborg, Danish Hospital for Rheumatic Diseases, Sønderborg, Denmark; [4]Zealand University Hospital, Department of Rheumatology, Køge, Denmark; [5]Odense University Hospital, Department of Rheumatology, Odense, Denmark; [6]Aarhus University Hospital, Department of Rheumatology, Aarhus, Denmark; [7]Odense University Hospital, Department of Rheumatology, Odense, Denmark; [8]Odense University Hospital and Svendborg Hospital, Department of Rheumatology, Odense and Svendborg, Denmark; [9]Silkeborg Regional Hospital, Diagnostic Center, Silkeborg, Denmark; [10]Horsens Regional Hospital, Department of Medicine, Horsens, Denmark; [11]ZiteLab Aps, Copenhagen, Denmark; [12]Gigtforeningen/Danish Rheumatism Association, Copenhagen, Denmark

Background: During the COVID-19 pandemic, widespread changes in how we work have been observed. Working from home is not an option for everyone. At work it may be difficult to keep social distance, which may lead to fear and anxiety of being infected with SARS-CoV-19 or of spreading the virus.

Objectives: To explore frequency of anxiety and concerns related to work in patients with inflammatory rheumatic diseases(IRD) during the COVID-19 pandemic and to identify patient and disease characteristics associated with increased anxiety.

Methods: Patients in routine care followed in the nationwide Danish DANBIO registry were invited to answer an on-line questionnaire regarding current rheumatic disease activity, behavior and anxiety including current work-status and -concerns. Responses were linked to patient data previously recorded in DANBIO. Clinical factors associated with work-related concerns (completely/mostly agree versus neither/nor, completely/mostly disagree) were explored with multivariable logistic regression.

Results: Among 14,758 respondents (38% of eligible patients), 5,950 patients (40%) were currently working (60% full time/31% part time/9% self-employed) (61% female, 53% rheumatoid arthritis/19% psoriatic arthritis/20% axial spondyloarthritis/9% other). Although 68% reported that the workplace helped to make necessary interventions, work-related concerns and anxiety were frequent. Thus, 22% found it difficult (completely/mostly agree) to keep physical distance at work and 20% were worried about going to work (Figure 1).

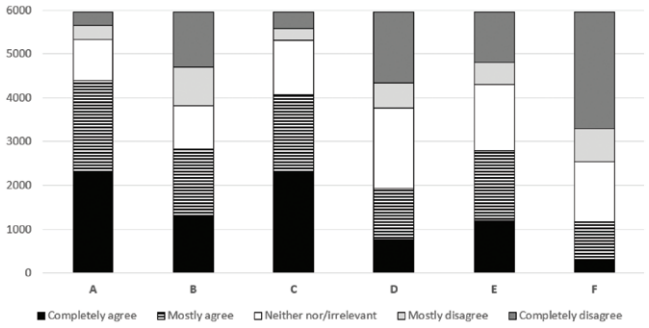
Factors associated with concerns about going to work were female gender, longer education, other chronic conditions, biological therapy, and higher (=poorer) EQ-5D, whereas diagnosis was without significance. Similar patterns were found for other work-related concerns (not shown).

Conclusion: In this cohort of >5,000 patients with inflammatory rheumatic diseases followed in a nationwide registry, during the COVID-19 pandemic anxiety and concerns related to the work situation were frequent, especially in women and patients treated with biologicals, with other chronic diseases and with poor quality of life.

REFERENCES:

[1] Glintborg et al, 2021, https://rmdopen.bmj.com/content/rmdopen/7/1/e001505.full.pdf

Figure. Concerns related to work situation in 5,950 patients with inflammatory arthritis during the COVID-19 pandemic in November 2020



Questions: **A**: It is important for me to keep physical distance at my job, **B**: It is difficult for me to keep physical distance at my job, **C**: My work-place helped to make necessary interventions for me to safely tend my job, **D**: I fear that my arthritis condition increases my risk of COVID-19 infection at work more than others my age, **E**: Due to my arthritis condition I should take more precautions at work to avoid infection compared to others my age, **F**: I am worried to go to work

Table 1. Factors associated with being worried (agree versus disagree) to go to work (Figure 1, panel F). Multivariable logistic regression analyses

		Odds ratio (95% CI)	p
Gender	female	1	
	male	0.45 (0.38;0.54)	<0.001
Age, years	>40	1	
	40-60	1.12 (0.87;1.44)	0.4
	>60	0.89 (0.67;1.20)	0.5
Education	Long	1	
	No/short	0.80 (0.69;0.93)	0.005
Living alone, yes		0.97 (0.79;1.20)	0.8
Other chronic condition, yes		1.37 (1.17;1.59)	<0.001
Biological therapy		1.36 (1.17;1.58)	<0.001
Diagnosis	Rheumatoid arthritis	1	
	Psoriatic arthritis	1.21 (0.99;1.48)	0.06
	Axial spondyloarthritis	1.03 (0.84;1.28)	0.8
	Other	1.17 (0.89;1.54)	0.3
PASS, yes*		1.03 (0.85;1.25)	0.7
Smoking	Current	1	
	Previous	1.17 (0.94;1.47)	0.2
	Never	1.10 (0.90;1.35)	0.4
EQ5D**		0.03 (0.02;0.06)	<0.001

*patient acceptable symptom state, **European Quality of Life, 5 dimensions

Disclosure of Interests: Bente Glintborg Grant/research support from: AbbVie, BMS, Pfizer, Dorte Vendelbo Jensen: None declared, Sara Engel: None declared, Lene Terslev Speakers bureau: AbbVie, Janssen, Roche, Novartis, Pfizer, MSD, BMS and GE, Mogens Pfeiffer Jensen: None declared, Oliver Hendricks: None declared, Mikkel Østergaard Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB., Grant/research support from: Abbvie, BMS, Celgene, Merck, Novartis, Simon Horskjær Rasmussen: None declared, Thomas Adelsten: None declared, Ada Colic: None declared, Kamilla Danebod: None declared, Malene Kildemand: None declared, Anne Gitte Loft Speakers bureau: AbbVie, Eli-Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Heidi Lausten Munk: None declared, Jens Kristian Pedersen: None declared, René Østgård Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Eli-Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi and UCB., Grant/research support from: Abbvie, Christian Møller Sørensen: None declared, Niels Steen Krogh: None declared, Jette Nørgaard Agerbo: None declared, Connie Ziegler: None declared, Merete L. Hetland Grant/research support from: AbbVie, Biogen, BMS, Celtrion, Eli Lilly Denmark A/S, Janssen Biologics B.V, Lundbeck Fonden, MSD, Pfizer, Roche, Samsung Biopis, Sandoz. MLH chairs the steering committee of the Danish Rheumatology Quality Registry (DANBIO), which receives public funding from the hospital owners and funding from pharmaceutical companies. MLH co-chairs the EuroSpA research collaboration, which generates real-world evidence of treatment of psoriatic arthritis and axial spondylorthritis based on secondary data and is partly funded by Novartis.

DOI: 10.1136/annrheumdis-2021-eular.721

PARE Poster Tour

POS0057-PARE SUMMARY OF PATIENT/PARENT ORGANISATION SERVICES PROMOTING SELF- AND SHARED-MANAGEMENT OF JIA IN THE UK AND IRELAND

S. Stones[1], V. Swallow[2], L. Milnes[1]. [1]University of Leeds, School of Healthcare, Leeds, United Kingdom; [2]Sheffield Hallam University, Department of Nursing & Midwifery, Sheffield, United Kingdom

Background: Various patient/parent organisations provide information, education, and support services to children and young people with JIA and their families. Some organisations are JIA/uveitis focused, while others are umbrella rheumatic and musculoskeletal disease (RMD) organisations or have a broader remit to long-term conditions (LTCs). However, there are no summaries of such collective services offered in the UK and Ireland, which can add to confusion for children, young people, and families, while contributing to inconsistent signposting to services from healthcare professionals.
Objectives: To summarise current and recent services promoting self- and shared-management of JIA by patient/parent organisations in the UK and Ireland.
Methods: An electronic search of known patient/parent organisation platforms (website and/or social networking sites) was performed between August 2020 and January 2021. Materials provided at conference exhibitions since October 2016 were also reviewed. Services were identified, including their aims and further details, if available. These were then mapped by format (*e.g.,* educational, telemedicine, art therapy) and element (*e.g.,* informational videos, monitoring through self-report diaries, discussing art and related feelings), according to their mode of delivery (individual or group), adapted from Sattoe et al. (2015) [1].
Results: Twelve patient/parent organisations in the UK and Ireland were identified (11 of which had some form of charity/company registration): seven were JIA-specific, one was uveitis-specific, two were RMD-focused, and two were LTC-focused. In total, 48 services were identified across the twelve organisations. Generally, group mode of delivery was more popular than individual mode of delivery. Of group-based services, educational and/or support sessions and residential/excursion programmes were the most frequently observed. Of individual-based services, educational sessions including written and visual information were predominant. No one organisation provided services across all formats and elements identified. There appeared to be a limited focus on goal setting, individual level skills training, and explicitly improving self-and/or shared-management capacity. Gamification techniques were notably absent, as was the use of psychotherapeutic approaches, such as cognitive behavioural therapy and motivational interviewing.
Conclusion: Various services are offered by multiple patient/parent organisations with an interest in JIA across the UK and Ireland to promote self- and shared-management. However, no single organisation provides a comprehensive package of services to address the entire information, education, and support needs of children and young people with JIA, or their families. Furthermore, clarity of services offered across the sector is poor. Enhanced collaboration between organisations, together with a clearer focus on enhancing self- and shared-management of JIA across the lifecourse, may help to improve the offering to children, young people, and their families, so that they can more competently manage JIA.
REFERENCES:
[1] Sattoe et al. Self-management interventions for young people with chronic conditions: A systematic overview. *Patient Education and Counseling* 2015; 98(6): 704-715.
Acknowledgements: This work formed part of a PhD study funded by the University of Leeds.
Disclosure of Interests: Simon Stones Speakers bureau: Janssen., Consultant of: Envision Pharma Group., Veronica Swallow: None declared, Linda Milnes: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1153

POS0058-PARE INCREASING PREECLAMPSIA KNOWLEDGE IN SLE WITH A SPECIFIC EDUCATIONAL TOOL: PRELIMINARY RESULTS

J. Y. E. Lee[1], A. Mendel[2], I. Malhamé[3], S. Bernatsky[2], E. Vinet[2]. [1]McGill University, Experimental Medicine, Montréal, Canada; [2]McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal, Canada; [3]McGill University Health Centre, Department of Medicine, Division of General Internal Medicine, Montreal, Canada

Background: Pregnant women with systemic lupus erythematosus (SLE) are at high risk of preeclampsia, leading to substantial maternal and fetal morbidity. Aspirin reduces preeclampsia risk but recent studies suggest aspirin is used only in a minority of SLE pregnancies. There is an urgent need to improve preeclampsia counselling and management in this vulnerable population.
Objectives: We are conducting the PREPARE (PREeclamPsia knowledge & Aspirin adheRence in lupus prEgnancies) trial, a randomized controlled trial (RCT) evaluating an educational tool on preeclampsia knowledge and aspirin adherence among pregnant women with SLE. We present preliminary analyses of the effect of this tool on preeclampsia knowledge.
Methods: Consecutive pregnant SLE women are recruited until the 16th gestational week at 5
Canadian Systemic Lupus International Collaborating Clinics centres (i.e. Montreal, Halifax, Quebec, Winnipeg, and Calgary) since 05/2018. Subjects are randomly assigned to receive either the specifically-designed educational tool (intervention group) or standard of care (control group). At baseline (i.e. first trimester) and second trimester visits, the participants complete self-administered preeclampsia knowledge questionnaires (scored out of 30 by the research team blinded to the intervention). We restricted the current analysis to participants enrolled in Montreal (accounting for nearly half of the total planned sample size). We performed a univariate linear regression analysis to assess the effect of the educational tool on preeclampsia knowledge (i.e. mean score difference between the two groups from baseline to second trimester visit).
Results: Thirty-three pregnant SLE women were included in the study, among which 16 were exposed to the intervention and 17 were unexposed. Baseline characteristics were well balanced between the two groups with similar mean maternal age between intervention group (32.2 years, standard deviation, SD, 4.6) and control group (34.1 years, SD 4.2) and identical proportion of subjects with post-secondary education (i.e. 80%). The difference in mean preeclampsia knowledge scores between second trimester and baseline visits in the intervention group was 4.4 points (95% CI -0.1, 9.0) and in the control group was 1.5 points (95% CI -2.7, 5.7). The mean difference in knowledge scores (from baseline to second trimester) for those receiving the educational tool was 2.7 points higher (95% CI -1.5, 6.9) than those receiving standard of care.
Conclusion: Approximately midway into the PREPARE trial, we observed a trend for improvement in preeclampsia knowledge from the baseline to the second trimester visit in pregnant women with SLE who received a specifically-designed educational tool compared to the control group, although the CIs included the null. Our RCT is well-poised to provide a new evidence-based approach to improve preeclampsia knowledge in pregnant women with SLE, which could help to optimize aspirin use and outcomes in this vulnerable population.
REFERENCES:
[1] Schramm AM, Clowse ME. Aspirin for prevention of preeclampsia in lupus pregnancy. *Autoimmune Dis.* 2014;2014:920467. doi:10.1155/2014/920467
[2] Bujold E, Roberge S, Lacasse Y, et al. Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis. *Obstet Gynecol.* 2010;116(2 Pt 1):402-414. doi:10.1097/AOG.0b013e3181e9322a
[3] Andreoli L, Bertsias GK, Agmon-Levin N, et al. EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome. *Ann Rheum Dis.* 2017 Mar;76(3):476–85. doi: 10.1136/annrheumdis-2016-209770.
[4] Mendel A, Bernatsky SB, Hanly JG, et al. Low aspirin use and high prevalence of preeclampsia risk factors among pregnant women in a multinational SLE inception cohort. *Ann Rheum Dis.* 2019;78(7):1010-1012. doi:10.1136/annrheumdis-2018-214434
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1480

POS0059-PARE DELAY TO DIAGNOSIS IN AXIAL SPONDYLOARTHRITIS – TIME FOR A GOLD STANDARD APPROACH

D. Webb[1], K. Gaffney[2], R. Sengupta[3], S. S. Zhao[4], L. Swingler[5]. [1]National Axial Spondyloarthritis Society, CEO, London, United Kingdom; [2]Norfolk & Norwich NHS Foundation Trust, Rheumatology, Norwich, United Kingdom; [3]Royal National Hospital for Rheumatic Disease, Rheumatology, Bath, United Kingdom; [4]University of Liverpool, Rheumatology, Liverpool, United Kingdom; [5]National Axial Spondyloarthritis Society, Service Improvement, London, United Kingdom

Background: In the UK, the average time to diagnosis of axial SpA is 8.5 years (1). There is little evidence this has improved, despite the acceptance of MRI use in diagnosis (2). A recent review identified significant clinical, economic and humanistic burden from delayed diagnosis (3). Urgent action is needed to ensure delayed diagnosis is not normalized.

Objectives: We created a proposal for a Gold Standard time to diagnosis for axial SpA and a national implementation plan (4) through consensus development with patients, healthcare professionals and professional bodies.
Methods: A.A scoping literature review identifying where delays occur, from first symptom onset to diagnosis by a rheumatologist, and potential solutions. From this, a summary report / draft plan was produced for consultation
B.A national consultation survey to elicit views on the proposals from clinicians, healthcare professionals, professional societies and patients
C.Structured feedback to written proposals via e-consultation with clinicians and patients
D.A consensus development workshop to finalise the Gold Standard and implementation plan.
Results: The literature review identified four delays:
1. People do not know axial SpA may be a cause of their chronic back pain
2. Primary care practitioners may not recognise features of axial SpA
3. People may be referred to non-rheumatologists who may not recognise axial SpA promptly
4. Rheumatology and radiology teams may not optimally request or interpret investigations.
202 participants responded to the summary report (74% patients, 21% healthcare professsionals, 5% professional societies). All supported the principles behind the gold standard time to diagnosis. Qualitive analysis confirmed agreement with the proposed solutions, underscoring the importance of education and visibility for axial SpA within primary care and increased public awareness. Additional proposals were suggested, including a tool in primary care to run audits on IT systems.
40 clinicians contributed to the e-consultation and 55 clinicians, policy makers, social marketing experts, health journalists and patients attended the consensus workshop. Consensus was reached on a gold standard time to diagnosis of one year, and the principles, key components and phasing of the implemention plan. This included: public awareness about axial SpA symptoms; a primary care clinical champions programme; creating a referral pathway from primary care direct to rheumatology; a secondary care service educational programme.
Conclusion: There is consensus from UK axial SpA clinicians, patients and professional societies on the need for a Gold Standard time to diagnosis of axial SpA of one year, so that patients can live happy, healthy and productive lives.
REFERENCES:
[1] Hamilton L, Gilbert A, Skerett J, et al. Services for people with ankylosing spondylitis in the UK - a survey of rheumatologists and patients. *Rheumatology* 2011:50:1991
[2] Sykes MP, Doll H, R Sengupta, Gaffney, K. Delay to diagnosis in axial spondyloarthritis: are we improving in the UK? *Rheumatology*, July 2015
[3] Yi E, Ahuja A, Rajput T, et al. Clinical, Economic, and Humanistic Burden Associated With Delayed Diagnosis of Axial Spondyloarthritis: A Systematic Review. *Rheumatol Ther.* 2020 Mar;7(1):65–87.
[4] Webb D, Zhao S, Whalley S, et al. Gold Standard Time to Diagnosis in axial Spondyloarthritis: Consultation Document. 2020, NASS.
Disclosure of Interests: Dale Webb Speakers bureau: Janssen, Novartis, Grant/research support from: NASS receives grants from AbbVie, Biogen, Eli Lilly, Novartis and UCB, Karl Gaffney Speakers bureau: Abbvie, Lilly, Novartis, UCB, Consultant of: Abbvie, Celltrion, Lilly, Grant/research support from: Abbvie, Pfizer, Lilly, UCB, Raj Sengupta Speakers bureau: Abbvie, Biogen, Celgene, Novartis, Roche, UCB, Consultant of: Advisory boards for Abbvie, Biogen, Novartis, UCB, Grant/research support from: Abbvie, Celgene, Novartis, Sizheng Steven Zhao: None declared, Lisa Swingler Grant/research support from: NASS receives grants from AbbVie, Biogen, Eli Lilly, Novartis and UCB.
DOI: 10.1136/annrheumdis-2021-eular.846

POS0060-PARE RHEUMATOID ARTHRITIS IN NORWAY: A SURVEY-BASED PATIENT EXPERIENCE

C. P. Fjellstad[1], M. Hägg[2], M. Kautonen[3], R. Mandla[4]. *[1]Norsk Revmatikerforbund, PAG, Oslo, Norway; [2]Nordic Healthcare Group Oy, Research, Helsinki, Finland; [3]Nordic Healthcare Group Oy, Service Design, Helsinki, Finland; [4]Pfizer, Medical Affairs, Oslo, Norway*

Background: The Norwegian Association of Rheumatologists has established a national procedure for management of rheumatoid arthritis (RA) in Norway.[1] The purpose of the procedure is to support equal and evidence-based diagnosis, care and follow-up of RA patients[1]. It serves as guidance to all responsible of RA patient health care. The procedure includes recognized themes in rheumatic care.[2,3] The impact of the procedure on RA care in Norway is, however, unknown.
Objectives: To understand the patient experience through evaluating how the national procedure for RA is being followed from the patient viewpoint. To identify gaps and areas of improvement to align the national procedure and patient experience.
Methods: Members of patient organization Norwegian Rheumatism Association were invited to answer a survey on demographic and disease-specific variables, perceived health and quality of care. The survey was supported by service design patient interviews (N=14). The invitations for interviews were sent through many initiatives for a representable population.
Results: The observational RA cohort constituted of N=374. The patients were on average satisfied with shared decision-making, care and follow-ups: 71 % felt their illness was under control. Patients in centralized areas were more satisfied with well-being. Diagnosis times have shortened from on average 1.7 to 1.5 year in 10 years. Patients, especially those working, were dissatisfied with rehab support. 30 % of patients felt cooperation of primary and secondary care was not satisfactory and 32 % were worried for future treatment.
Table 1 shows the differences in awareness of comorbidities and regular vaccination need. Where applicable, the table also shows the percentage of patients screened. The results show that patients are aware of risks, but are not being screened for the conditions. Younger patients (< 50 years) with symptoms for less than five years were generally less aware.

Table 1. Awareness of comorbidity and regular vaccination need

	Comorbidities						Regular vaccine need
	Heart disease		Lung disease		Osteoporosis		
	Awareness	Screened	Awareness	Screened	Awareness	Screened	Awareness
Overall (# of patients)	70 % (239/342)	34 % (115/342)	37 % (127/342)	25 % (87/342)	58 % (201/344)	41 % (141/343)	56 % (191/344)
Age							
Under 50 yrs	67 % (42/63)	24 % (15/63)	39 % (24/62)	27 % (17/63)	46 % (29/63)	19 % (12/63)	51 % (32/63)
Over 50 yrs	71 % (197/279)	36 % (100/279)	37 % (103/280)	25 % (70/279)	61 % (172/281)	46 % (129/280)	57 % (159/281)
Disease onset							
Under 5 yrs	56 % (27/48)	19 % (9/48)	29 % (14/48)	20 % (10/49)	51 % (25/49)	21 % (10/48)	59 % (29/49)
Over 5 yrs	72 % (212/294)	36 % (106/294)	38 % (113/294)	26 % (77/293)	59 % (176/295)	44 % (131/295)	55 % (162/295)

The education of patients about regular vaccines (e.g. influenza and pneumonia) could be improved. Only 56 % were aware of the need for these vaccines due to RA. When asked specifically, 73 % of patients had received an influenza vaccine and 48 % pneumonia vaccine.

Conclusion: This survey examines quality of care, shared decision-making, disease awareness and planning and provides a gap analysis of patient experience and national procedure. The results show that national procedure in RA is being followed from the patient viewpoint. Patients are satisfied with care, but information on preventive care (e.g. vaccination and comorbidity awareness and screenings) could be strengthened. This could improve planning of care and the outlook, particularly for young patients.
REFERENCES:
[1] Aga AB, Haavardsholm EA. Revmatoid artritt. Nasjonal veileder i revmatologi. 2020
[2] Barber CEH, Lacaille D, Hall M, Bohm V, Li LC, Barnabe C, Hazlewood GS, Marshall DA, Rankin JA, Tsui K, English K, MacMullan P, Homik J, Mosher D, Then KL. Priorities for High Quality Care in Rheumatoid Arthritis: Results of Patient, Health Professional, and Policymaker Perspectives. J Rheumatol. 2020
[3] Brekke M, Hjortdahl P, Kvien TK. Involvement and satisfaction: a Norwegian study of health care among 1,024 patients with rheumatoid arthritis and 1,509 patients with chronic noninflammatory musculoskeletal pain. Arthritis Rheum. 2001 Feb;45(1):8-
Disclosure of Interests: Christian Pollock Fjellstad: None declared, Milla Hägg Consultant of: Pfizer, Moona Kautonen Consultant of: Pfizer, Randeep Mandla Shareholder of: Pfizer, Consultant of: Pfizer, Employee of: Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.966

POS0061-PARE **HOW DO THE COMPLICATIONS OF SPONDYLOARTHRITIS (SPA*) IMPACT THE QUALITY OF LIFE (QOL) OF PATIENTS LIVING WITH SPA?**

S. Patenaude[1], W. Gerhart[2]. [1]Canadian Spondylitis Association, Intern, Phelpston, Canada; [2]Canadian Spondylitis Association, Executive Director, Phelpston, Canada

Background: SpA describes a group of chronic inflammatory arthritic diseases with common features, including inflammation of the spine, eyes, skin and gastrointestinal tract. These conditions can be painful and debilitating for many. Delayed diagnosis and treatment can lead to irreversible damage to the spine and other joints. Diagnosis of these conditions can take, on average, 7 years or more. We don't know what causes SpA and there is no cure. The onset of symptoms can be in early childhood and expands throughout one's lifespan. It affects children, women and men worldwide.
Objectives: To understand how the complications of living with SpA impacts QOL as well as what is important to patients in order to help the CSA** prioritize advocacy focus and resource development.
Methods: The CSA surveyed the community virtually from 11/19/19 to 01/21/20. The results of 838 respondents were analyzed after the survey closed. 466 participants responded to the questions regarding complications.
Results: In total, participants had an average of 3.3 complications. Those living with ankylosing spondylitis experienced an average of 3.5 while those with psoriatic arthritis reported an average of 3.9.
Sleep issues (65%), chronic pain (63%), and combined depression and anxiety (56%) were the most prevalent conditions reported among participants. In addition, 23% said they live with inflammatory bowel disease. Other complications include uveitis, weight issues, migraine, vertebral disc herniations and hypertension.
Those who reported weight issues (over 44%) consequently had increased anxiety, depression and chronic pain compared to those without weight issues.
Over 65% reported experiencing sleep issues. Many (26%) said that nothing helps with their sleep. Others used cannabis (24%), prescribed sleeping pills (20%) and exercise (19%) to cope.
36% of participants said that they suffer from chronic fatigue syndrome. When asked how they manage their fatigue, the most common answer was exercise. Most participants said they have yet to find something that helps them efficiently manage their fatigue.
Over 400 people said they suffer from either depression or anxiety, or both. When asked how they cope with this, 40% said talking to loved ones. Exercise to cope was reported by 32% and 31% take prescription medication. Those who suffer from Psoriasis experienced a higher prevalence of anxiety and depression.
Conclusion: Overall, the presence of complications is an additional stressor to SpA patients. Many pointed out that the complications are sometimes more burdensome than the actual SpA condition and some patients even prioritize the management of the complications over the actual SpA condition. These complications can lead to increased trips to the physician resulting in more healthcare interventions and medications, causing frustration to patients.
Only 59% of respondents mentioned that their rheumatologist regularly asks them about additional complications such as depression, fatigue and gut issues. Many felt that their rheumatologist seems to be more concerned with pain management and continuing function and do not necessarily address other health concerns and complications, particularly mental health. Although these are often overlooked, it is clear that complications have a significant impact on patient health and overall QOL.
The CSA is committed to developing programs and resources to help patients manage all the complications commonly experienced to improve health outcomes and overall QOL.
It doesn't have to be visible to be real. Together we are stronger!

REFERENCES:

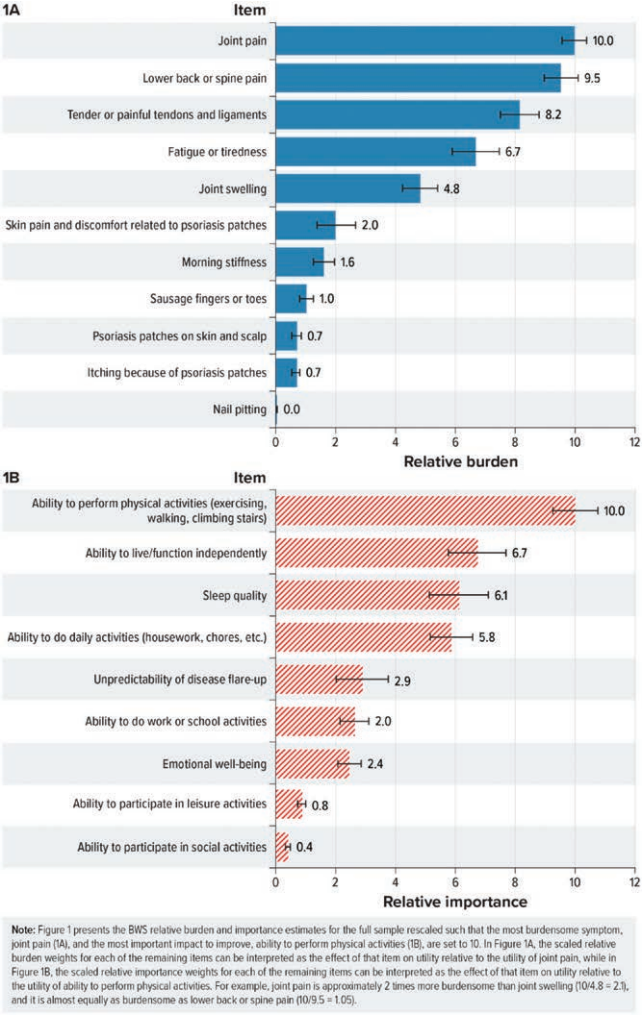
[1] SpA conditions include: Ankylosing Spondylitis, Psoriatic Arthritis, non-radial SpA, Axial SpA, Peripheral Spondyloarthritis, Enteropathic Arthritis, Reactive Arthritis and Juvenile Onset Arthritis
[2] The Canadian Spondylitis Association (CSA) is a national non-profit patient association supporting and advocating for those living with SpA.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1611

POS0062-PARE **REAL-WORLD PATIENT EXPERIENCE AND TREATMENT PREFERENCES IN PATIENTS WITH PSORIATIC ARTHRITIS**

A. Ogdie[1], C. Mansfield[2], K. Myers[2], W. Tillett[3], P. Nash[4], C. Leach[2], W. B. Nowell[5], K. Gavigan[6], P. Zueger[7], E. Mcdearmon-Blondell[8], J. A. Walsh[9,10]. [1]Perelman School of Medicine, University of Pennsylvania, Department of Medicine, Philadelphia, United States of America; [2]RTI Health Solutions, Health Preference Assessment, Research Triangle Park, United States of America; [3]Royal National Hospital for Rheumatic Diseases, Department of Rheumatology, Bath, United Kingdom; [4]Griffith University, Department of Medicine, Brisbane, Australia; [5]Global Healthy Living Foundation, Patient-Centered Research, Upper Nyack, United States of America; [6]Global Healthy Living Foundation, Research and Data Science, Upper Nyack, United States of America; [7]AbbVie, Global Rheumatology, Chicago, United States of America; [8]AbbVie, Global Medical Affairs, Chicago, United States of America; [9]University of Utah School of Medicine, Division of Rheumatology, Salt Lake City, United States of America; [10]George E. Wahlen Veteran Affairs Medical Center, Rheumatology, Salt Lake City, United States of America

Background: Despite recent advances in the treatment of psoriatic arthritis (PsA), many patients experience inadequate response or intolerance to therapy, indicating that unmet treatment-related needs remain. An understanding of patients' experience with PsA and its treatment is needed to bring the patient's perspective into treatment decision-making and development of new therapies.
Objectives: To better understand real-world PsA patients' experience with PsA via evaluation of (1) the burden and importance of common PsA symptoms and disease impacts and (2) treatment preferences.
Methods: A cross-sectional, web-based survey was developed, informed by published literature and treatment guidelines, expert clinical opinion, and cognitive debriefing interviews with PsA patients. Adults with a self-reported diagnosis of PsA were recruited from a US rheumatology patient-centered research registry and other online patient communities. Object case best-worst scaling (BWS) was used to evaluate the relative burden of 11 PsA-related symptoms and the relative importance of improvement in 9 PsA-related disease impacts. BWS data were analyzed using a random parameters logit model. Data on patient demographics and preferences for PsA treatment attributes, including experience with methotrexate and preference for route and frequency of administration, were analyzed descriptively.
Results: The sample of 247 respondents was 79% female, had a mean age of 53.4 years (range 24-79 years), and had a mean time since PsA diagnosis of 9.4 years, with 86% currently being treated by a rheumatologist. The most common PsA symptoms ever experienced were joint pain, morning



Note: Figure 1 presents the BWS relative burden and importance estimates for the full sample rescaled such that the most burdensome symptom, joint pain (1A), and the most important impact to improve, ability to perform physical activities (1B), are set to 10. In Figure 1A, the scaled relative burden weights for each of the remaining items can be interpreted as the effect of that item on utility relative to the utility of joint pain, while in Figure 1B, the scaled relative importance weights for each of the remaining items can be interpreted as the effect of that item on utility relative to the utility of ability to perform physical activities. For example, joint pain is approximately 2 times more burdensome than joint swelling (10/4.8 = 2.1), and it is almost equally as burdensome as lower back or spine pain (10/9.5 = 1.05).

stiffness and fatigue, while the least common symptom was skin pain/discomfort related to psoriasis patches. In the BWS, patients reported pain-related symptoms (i.e., joint pain and lower back or spine pain) as the most bothersome, while the least bothersome symptoms were psoriasis-related (Figure 1). Patients reported ability to perform physical activities as the most important disease impact to improve, followed by ability to live/function independently, sleep quality, and ability to do daily activities. Nearly half the sample (49%) stated they would strongly prefer a treatment for PsA that does not include methotrexate. Among patients who were not satisfied with methotrexate, the top reason was dislike of the short-term side effects after each dose. When asked to choose among four different ways of taking their PsA medication (oral once a day, oral twice a day, injection every 2 weeks, injection once a month), the most preferred method was oral once a day (38%) followed by injection once a month (26%), with 24% indicating no preference. Additionally, 49% of the sample felt that mode of administration was an important factor when deciding to start a new therapy.

Conclusion: Among real-world patients with PsA, the most bothersome PsA symptoms were related to pain while patients most wanted to improve functional impacts of their disease. Patients most preferred an oral once a day treatment option and treatment regimens that do not include methotrexate. These findings can serve to better inform development of new therapies and guide shared patient-provider treatment decision making.

Disclosure of Interests: Alexis Ogdie Consultant of: Abbvie, Amgen, BMS, Celgene, Corrona, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, Grant/research support from: Pfizer to Penn, Novartis to Penn, Amgen to Forward/NDB.
Royalties: Novartis to husband, Carol Mansfield: None declared, Kelley Myers: None declared, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer Inc., and UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer Inc., and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Peter Nash Grant/research support from: Abbvie, Pfizer, Roche, Sanofi, Boerhringer, Lilly, Novartis, BMS, MSD, Janssen, Gilead, and Samsung, Colton Leach: None declared, W. Benjamin Nowell Grant/research support from: AbbVie, Amgen, and Eli Lilly, Kelly Gavigan: None declared, Patrick Zueger Shareholder of: AbbVie, Employee of: AbbVie, Erin McDearmon-Blondell Shareholder of: AbbVie, Employee of: AbbVie, Jessica A. Walsh Consultant of: AbbVie, Amgen, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Merck, Pfizer.

DOI: 10.1136/annrheumdis-2021-eular.852

POS0063-PARE IMPLEMENTING SHARED DECISION MAKING TO ADVANCE PATIENT CENTRED RHEUMATOID ARTHRITIS CARE: A ROLE FOR A PATIENT ORGANISATION

P. Pennings Msc[1], H. Voogdt-Pruis[2,3], B. Maat[4], T. Foekens[4], L. J. Kranenburg - van Koppen[5], A. Pasma[5], J. Hoes[6], I. Schoonen-Nuijten7, M. Van den Dikkenberg, Msc[8], N. Basoski[8], A. Weel[8,9], G. Willemsen- de Mey Msc[1]. [1]National Association ReumaZorg Nederland, Patientparticipation and Communication, Nijmegen, Netherlands; [2]National Association ReumaZorg Nederland, Projectmanager Project Shared Decision Making in RA Care, Nijmegen, Netherlands; [3]University Medical Centre Utrecht (UMCU), Department of Julius Global Health, Utrecht, Netherlands; [4]National Association ReumaZorg Nederland, Patientpartner for the department of Patientparticipation and Communication, Nijmegen, Netherlands; [5]Erasmus Medical Centre, Department of Rheumatology, Rotterdam, Netherlands; [6]Bravis Medical Centre, Department of Rheumatology, Roosendaal, Netherlands; [6]Bravis Medical Centre, Department of Rheumatology, Roosendaal, Netherlands; [8]Maasstad Medical Centre, Department of Rheumatology, Rotterdam, Netherlands; [9]Erasmus University, Department ESHPM (HTA), Rotterdam, Netherlands

Background: In rheumatoid arthritis (RA) care, patients and professionals face treatment decisions regularly due to the high number of treatment options, the chronic character of the disease and challenges around multi-morbidity. Recent studies have underlined the added value of shared decision making (SDM) between patients and professionals in RA care for health outcomes (i.e. disease activity, pain and joint damage) [1-4]. Therefore, effort is needed to facilitate the implementation of SDM in daily clinical practice in order to advance patient centred RA care.

Objectives: The aim of this implementation project was to improve SDM about treatment options for patients with RA. In addition the use of (Patient Reported) Outcome Measures in the process of SDM was taken into account.

Methods: An implementation programme was developed by the National Association ReumaZorg Nederland (RZN) in co-creation with patientpartners and RMD professionals. Three hospital departments of rheumatology in the Netherlands participated in the project between January 2020 and March 2021. The implementation of SDM was supported by a project team of RZN.

Results: The implementation programme started with the recording of RMD consultations in three participating departments of rheumatology. The consultations were then evaluated on the process of SDM (OPTION5) and discussed during the training of professionals that followed. Three observed improvements in SDM in RA care were: a. A more explicit introduction of choice for a patient is needed during the consultation; b. Tasks within the process of SDM should be allocated clearly among RMS specialists and nurses working together, in order to avoid unnecessary repetition of the same - or even inconsistent information; c. Besides the use of (patient reported) outcome measures in the SDM process, it is also important to include patients' values (what matters to them?) when deciding on the best fitting treatment option. After the training, implementation support for SDM was given and aids to support the SDM process (i.e. redesign of health care processes, task allocation, hand card with explanation of the 4 steps of SDM) were developed. The implementation programme was tailored to the needs and stage of change for each hospital. Implementation materials for the hospital teams were developed in co-creation with patientpartners and the professionals. At the end of the project, a second set of consultations was recorded and evaluated on SDM. The hospital teams concluded that a continuous improvement cycle is needed to further enhance SDM.

Conclusion: A continuous implementation programme on shared decision making could stimulate the enhancement of patient centred care in daily practice. Patient organisations could take a significant role in such a programme.

REFERENCES:

[1] Pablos JL et al. Patient. 2020 Feb;13(1):57-69.
[2] Fautrel B et al. Rheumatol Int. 2018 Jun;38(6):935-947. doi: 10.1007/s00296-018-4005-5.
[3] Mathijssen EGE et al. RMD Open. 2020 Jan;6(1):e001121. doi: 10.1136/rmdopen-2019-001121.
[4] Nota, I. 2017. Shared Decision-Making in rheumatology: What matters to patients? Thesis, University of Twente.

Acknowledgements: This project of the National Association ReumaZorg Nederland (RZN) was made possible thanks to the effort of the following patientpartners, RMD specialists and researchers within the field of RMDs:
Helene R Voogdt-Pruis, (AP PhD, RZN projectmanager Shared Decision Making within RMD care), Bertha Maat (RZN patient research partner), Theo Foekens (RZN patient research partner), Laura Kranenburg-van Koppen (MD, Msc, rheumatologist Erasmus and IJsselland Medical Centre), Annelieke Pasma (PhD, researcher Erasmus Medical Centre), Jos Hoes (MD PhD, rheumatologist Bravis Medical Centre), Inge Schoonen-Nuijten (RMD nurse, Bravis Medical Centre), Marijke van den Dikkenberg, (MSc, researcher Maasstad Medical Centre), Natalja Basoski (MD MSc, rheumatologist Maasstad Medical Centre), Angelique Weel-Koenders (Prof. Dr., rheumatologist Maasstad Medical Centre, Erasmus University), Gerardine Willemsen- de Mey (MSc, Chair of RZN).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1085

POS0064-PARE DESIGN OF AN INNOVATIVE MHEALTH SOLUTION FOR FIGHTING STIGMA ASSOCIATED WITH CHRONIC PAIN

Y. Koumpouros[1], K. Antonopoulou[2], A. Pappa[3], K. Tsekoura[3], N. Malliou[4], M. Salamaliki[5], E. Oikonomoula[6], S. Makri[7]. [1]University of West Attica, Department of Public and Community Health, Athens, Greece; [2]Hellenic League Against Rhuematism, Headquarters, Athens, Greece; [2]Hellenic League Against Rhuematism, Headquarters, Athens, Greece; [4]Hellenic League Against Rhuematism, Thessaloniki, Thessaloniki, Greece; [5]Hellenic League Against Rhuematism, Patras, Patras, Greece; [6]Hellenic League Against Rhuematism, Thessaly, Trikala, Greece; [7]Cyrpus League Against Rhuematism, Headquarters, Nicosia, Cyprus

Background: Pain is associated with a plethora of diseases. The statistics reveal that chronic pain affects around 100 million people across Europe and is closely associated with high unemployment rates, depression, substance abuse & social exclusion. Stigma is a significant and persistent problem for those with chronic pain. Lack of public awareness & stigma associated with pain affect not only patients but also society.

Objectives: The present research proposes a holistic solution to combat stigma using the latest technological developments. A mobile health application has been designed in order to serve the various stakeholders (patients, families, community) in the field under study. The objective of the final "StigmApp" solution is 4-fold:(i) to facilitate pain management, (ii) to aware the general public, (iii) to educate all different parties & (iv) to facilitate actions & research to combat stigma. Another innovative feature is that it delivers the required information to each party in a highly automated, personalized & digestible way making the whole experience enjoyable, while ensuring user engagement.

Methods: A multidisciplinary team was formed at the beginning of the project in order to ensure the desired outcome. Two patient organizations from Cyprus & Greece, two behavioral scientists, three physicians, one psychologist, ten

citizens, ten patients, two marketeers and two experts in mobile health applications participated. A participatory design methodology was followed in order to capture & address the whole user experience.

Results: An iterative process was followed bringing & different end-users on board. The different parties evaluated and assessed all modules implemented providing appropriate feedback. It currently runs only on Android operating system and supports: (i) pain management (intense &points of pain, medications used, underlying diseases, life style, etc.),(ii) raise awareness & education (through information nuggets & bite-sized learning), (iii) "Share your story" option to inspire others, (iv) fund raising using crowd-funding techniques, (v) become a volunteer, (vi) organize an inspiring event, (vii) networking, (viii) automatic creation of infographics on how pain affects peoples' lives. It has been awarded the first prize by BMP Innovation Grant.

Conclusion: StigmApp has been designed to support the ecosystem around chronic pain regardless of the underlying disease. Our main concern is to raise awareness in order to fight stigma associated with pain & make life easier for patients & their families. The involvement of all different potential actors in the design guarantees a product/service that could meet their needs & can be applied in real life. In the next months the final solution will be piloted by a number of different end users in order to assess it under real life conditions.

REFERENCES:

[1] Fayaz A, Croft P, Langford RM, Donaldson LJ, Jones GT. Prevalence of chronic pain in the UK: a systematic review & meta-analysis of population studies. BMJ Open 2016 Jun 20;6(6):e010364. DOI:10.1136/bmjopen-2015-010364. PMID:27324708; PMCID: PMC4932255.

[2] Koumpouros Y, Georgoulas A. A systematic review of mhealth funded R&D activities in EU. Trends, technologies and obstacles, Informatics for Health&Social Care. 2020;45(2):168-187. DOI:10.1080/17538157.2019.1656208. Epub2019 Nov 19. PMID:31743060.

[3] Lalloo C, Jibb LA, Rivera J, Agarwal A, Stinson JN. There's a Pain App for That: review of patient-targeted smartphone applications for pain management.Clin J Pain.2015;31(6):557–63. DOI:10.1097/AJP.0000000000000171.

[4] De Ruddere, Liesa, Craig, Kenneth D. Understanding stigma & chronic pain:a-state-of-the-art review,PAIN:August 2016-Volume 157-Issue 8-p1607-1610, doi:10.1097/j.pain.0000000000000512

Acknowledgements: The project is funded by the Brain, Mind, and Pain, Patient-Centred Innovation Grant.

Many thanks to the two patient organizations Hellenic League Against Rheumatism & Cyprus League Against Rheumatism for their valuable contribution in the project.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2398

POS0065-PARE HEALTH IMPACT OF OVERWEIGHT AND OBESITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

M. Garrido-Cumbrera[1], D. Poddubnyy[2], L. Christen[3], C. Bundy[4], R. Mahapatra[5], S. Makri[6], S. Sanz-Gómez[1], J. Correa-Fernández[1], C. J. Delgado-Domínguez[1], V. Navarro-Compán[7] on behalf of IMAS working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain; [2]Charité - Universitätsmedizin Berlin, Rheumatology Department, Berlin, Germany; [3]Novartis Pharma AG, Patient Engagement, Basel, Switzerland; [4]Cardiff University, School of Healthcare Sciences, Cardiff, United Kingdom; [5]Axial Spondyloarthritis International Federation (ASIF), Patient Advocacy, London, United Kingdom; [6]Cyprus League Against Rheumatism (CYPLAR), Patient Advocacy, Nicosia, Cyprus; [7]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*

Background: Growing evidence on the negative role of overweight and obesity on the health outcomes of patients with axial spondyloarthritis (axSpA) exists.

Objectives: The aim of the study is to evaluate the association between Body Mass Index (BMI) categories and sociodemographic, disease-characteristics and patient-reported outcomes (PROs) in a large sample of axSpA patients.

Methods: Data from 2,846 unselected patients of the European Map of Axial Spondyloarthritis (EMAS) through an online survey (2017-2018) across 13 European countries were analyzed. Using self-reported height and weight patients were classified into under and normal weight (<24.9 Kg/m^2), overweight (25.0-29.9Kg/m^2) or obese (>30.0Kg/m^2) following WHO guidelines. The Kruskal-Wallis test was used to compare the means of numerical variables between polytomous variables, the χ^2 test was used to compare the distribution between the categorical variables. Simple and multivariate logistic regression were used to identify possible associated factors.

Results: A total 2,846 axSpA patients participated in the EMAS survey: mean age was 43.9 years, 61.3% female, 48.1% had a university degree and 67.9% were married and 71.3% were HLA-B27 positive. The percentage of patients with obesity was 18.7%, overweight 33.5%, normal weight 44.0% and underweight 3.8% with an accumulate prevalence of overweight/obesity of 52.2% (compared to 51.6 % of the EU's population[1]). Those with obesity engage less frequently in sport (50.1% vs 33.3%; p<0.001) and in intimate relationships since disease onset (36.5% vs 20.4%; p<0.001), have higher functional limitations when tying shoe laces (46.8% vs 33.6%; p<0.001) and higher functional limitations regarding housework (52.2% vs 48.2%; p=0.024). Furthermore, they present greater disease activity (6.1±1.8 vs 5.4±2.0; p<0.001) and spinal stiffness (8.6±2.3 vs 7.4±2.5; p<0.001) compared to under and normal weight. For obese patients, the percentage of depression is higher (34.5% vs 23.7%; p<0.001), presenting a poorer mental health (5.7 ± 4.3 vs 5.0 ±4.2; p<0.001). The factors most strongly associated with obesity were higher functional limitation when tying shoe laces (OR=1.467; p<0.001), the female gender (OR=1.433; p<0.001) and lesser frequency of intimate relation (OR=1.239; p<0.001; see Table 1).

Table 1. Logistic regression analysis to predict presence of obesity (N = 1,194)

	Simple			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.026	1.018, 1.034	**<0.001**	1.026	1.012, 1.040	**<0.001**
Gender (female)	1.336	1.095, 1.629	**0.004**	1.433	1.031, 1.990	**0.032**
Marital status (married)	1.384	1.184, 1.617	**<0.001**	0.982	0.746, 1.292	0.897
Educational level (university)	0.776	0.681, 0.884	**<0.001**	1.046	0.849,1.289	0.674
Employment status (employed)	1.035	0.987, 1.085	0.154	NA	NA	NA
Engage in sports (much less than before)	1.313	1.202, 1.433	**<0.001**	1.143	0.978, 1.336	0.093
Travel/ excursions (much less than before)	1.316	1.186, 1.461	**<0.001**	0.981	0.800, 1.202	0.852
Intimate relations (much less than before)	1.571	1.393, 1.772	**<0.001**	1.239	1.003, 1.530	**0.047**
Tying shoe laces (high)	1.433	1.232, 1.666	**<0.001**	1.467	1.176, 1.830	**0.001**
Housework / cleaning (high)	1.226	1.048, 1.434	**0.011**	0.760	0.596, 0.970	**0.028**
BASDAI (0-10) N:2,584	1.220	1.156, 1.288	**<0.001**	1.127	1.021, 1.244	**0.018**
Spinal Stiffness (3-12) N:2,660	1.184	1.136, 1.234	**<0.001**	1.057	0.987, 1.133	0.115
Sleep disorders diagnosis	1.558	1.284, 1.892	**<0.001**	1.045	0.753, 1.449	0.793
Depression diagnosis	1.648	1.340, 2.027	**<0.001**	1.267	0.892, 1.799	0.186
Psychological distress GHQ-12 (0-12)	1.053	1.029, 1.078	**<0.001**	0.995	0.954, 1.038	0.813

Conclusion: Results from the largest European axSpA survey reveal a similar prevalence of overweight and obesity to the general population. However, compared to normal weight, obese patients present greater disease activity, spinal stiffness and poorer mental health. Additionally, women with axSpA appear to be more vulnerable than men to obesity.

REFERENCES:

[1] EU Eurostat. Overweight and obesity - BMI statistics.

Acknowledgements: This study was supported by Novartis Pharma AG. The authors would like to thank all patients who participated in the study.

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Denis Poddubnyy Speakers bureau: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Abbvie, MSD, Novartis, and Pfizer, Laura Christen Employee of: Novartis Pharma AG, Christine Bundy Speakers bureau: Abbvie, Celgene, Janssen, Lilly, Novartis, and Pfizer, Raj Mahapatra: None declared, Souzi Makri: None declared, Sergio Sanz-Gómez: None declared, José Correa-Fernández: None declared, Carlos Jesús Delgado-Domínguez: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.974

POS0066-PARE REHABILITATION WITH KINESIOTHERAPY IN MUSCLE FUNCTION AND WEIGHT LOSS IMPROVING IN OBESITY PATIENTS

V. Vasileva[1], M. Eryomushkin[1], L. Marchenkova[1]. [1]National Medical Research Center of Rehabilitation and Balneology, National Medical Research Center of Rehabilitation and Balneology, Moscow, Russian Federation

Background: exercise is one of the main factors for the successful treatment of obesity. It is known that with increasing age, muscle strength (sarcopenic obesity) decreases in an obese patient, which can lead to early disability and an increased risk of falls. Regular exercise therapy increases the functional capacity of the cardiovascular system, prevention of obesity among the population, as well as treatment for persons with sarcopenia and obesity. Therefore, it is relevant to study muscle function in obese patients while using kinesiotherapy.
Objectives: was to estimate the affect of complex 3-week treatment with 4 kinesiotherapy methods on body weight loss and muscle function in patients with obesity.
Methods: 80 men and women aged 21-69 years old with alimentary obesity were enrolled in the study (mean age 52.4±11 years, weight 111.3±24.5 kg, BMI 40.3±8.1 kg/m2, waist circumstance WC 113.4±16 cm, hip circumstance HC 124.2±16 cm). The complex kinesiotherapy administered daily for 3 week and included interactive sensorimotor trainings on double unstable platform, kinesiohydrotherapy in a pool, special complex of physical exercises in a gym and ergocycle trainings. Weight, WC, HC, fall number for last 3 weeks were measured at baseline and after the treatment was completed. Muscle strength and walking speed functional tests results assessment (10-meters-walk test, Up-and-go test, 4 special tests for back and abdomen muscle endurance to static and dynamic loading) were performed at baseline and in 3 weeks.
Results: there was a significant reduction in body weight (111.3±24.4 kg at baseline vs 107.9±23.1 kg in 3 weeks; p=0,000), in BMI (40.3±8.1 vs 39.1±7.7 kg/m^2; p=0.000), in WC (113.4±15.9 vs 109.2±15.1 cm; p=0.000) and in HC (124.1±15.5 vs 119.7±14.1 cm; p=0.000) in treated obese patients. 10-meters-walk speed increased from 0.84±0.15 m/sec at baseline to 0.88±0.17 m/sec in 3 weeks (p=0.000). Up-and-go test results improved from 8.4±2.1 to 7.9±2.09 sec (p=0.000). We registered statistically significant elevation of the endurance to static loading in abdomen muscles from 13.1±9.7 to 16.49±12.8 sec (p=0.000) and in back muscles from 14.8±11.9 sec to 18.6±14.9 sec (p=0.000). The endurance to dynamic loading increased in abdomen muscles from 29.9±11.2 to 34.84±11.93 times (p=0.000) and also in back muscles from 9.1±7.4 to 12.2±9.2 times (p=0.000). Fall number markably decreased from 0.14 ±0.34 at baseline to 0.0 (95%CI: 0.02; 0.25) after completion of treatment.
Conclusion: investigated complex treatment with 4 kinesiotherapy methods promotes body weight loss, WC and HC reduction in obesity. 3-week special training of obese patients is associated with increasing in gate speed and lower extremities muscle strength, and it also causes improvement in static and dynamic loading endurance of back and abdomen muscles. Those changes may probably improve balance function and decrease risk of falling in obese patients.
REFERENCES:
[1] O.Lee, DS. Lee, S.Lee, Associations between Physical Activity and Obesity Defined by waist – to-height ratio and body mass index in the Korean Population. // PLOS ONE- 11(7). -2016. P. 1-11.
[2] I.I. Baidovletova, Physiotherapy for obesity. // Psychology and pedagogy: methods and problems. 2015.- S. 177-180.
[3] L. A. Marchenkova, V. A. Vasileva, Motor and balance function disorders and possibilities of their correction in patients with obesity and metabolic syndrome // Lechashchiy vrach. 2019. № 4. S. 68.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3065

Pediatric Rheumatology – Basic and translational science

POS0067 HIGH DEGREE OF INTER-PATIENT HETEROGENEITY IN SYNOVIOCYTE HYPERPLASIA AND IMMUNE CELLS INFILTRATION IN THE SYNOVIUM OF JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

C. Triaille[1,2], C. Boulanger[2,3], T. Sokolova[1], L. Meric de Bellefon[1,4], A. Nzeusseu Toukap[1,4], C. Galant[5], N. Limaye[3], B. Lauwerys[1,4], P. Durez[1,4]. [1]Université catholique de Louvain, Pôle de pathologies rhumatismales systémiques et inflammatoires, Institut de Recherche Expérimentale et Clinique, Brussels, Belgium; [2]Cliniques Universitaires Saint-Luc, Service d'Hématologie, Oncologie et Rhumatologie pédiatrique, Brussels, Belgium; [3]Université catholique de Louvain, Genetics of Autoimmune Diseases and Cancer, de Duve Institute, Brussels, Belgium; [4]Cliniques Universitaires Saint-Luc, Service de Rhumatologie, Brussels, Belgium; [5]Cliniques Universitaires Saint-Luc, Service d'Anatomie Pathologique, Brussels, Belgium

Background: Increasing evidence indicates that synovial tissue analysis can deliver pathophysiological insights but also individual clinically-relevant information in adult-onset inflammatory arthritides. Little is known about synovial pathology in juvenile idiopathic arthritis, especially regarding inter-patient variability of histopathological features.
Objectives: To assess the heterogeneity of main synovial features (synoviocyte hyperplasia and immune cells infiltration) in juvenile idiopathic arthritis (JIA) patients and a cohort of young adults (<30 years old) with early rheumatoid arthritis (RA).
Methods: Synovial biopsies were sampled using needle arthroscopy or ultrasound (US) guided biopsy during intra-articular joint injection. Tissue was embedded in paraffin then sections were stained with hematoxylin and eosin. Synoviocyte hyperplasia (SH) and immune cells infiltration (ICI) was assessed by an experienced pathologist on a 0 – 3 scale where 0 represents the absence of the feature and 3 the highest level.
Results: 34 JIA patients (age (median ±SD): 15.5±6.47 years, oligo-articular JIA n=28/34, polyarticular JIA n=6/34, ANA-RF-ACPA positivity=56%-10%-3%) and 22 RA (age (median ±SD): 24.3±2.6 years, ANA-RF-ACPA positivity=10%-36%-32%) patients were included. Synovial tissue was obtained from knee (n=49/56), wrist (n=4/56) or metacarpophalangeal/intercarpophalangeal joints (n=3/56), using US guided biopsy in 27% of patients and needle arthroscopy in 73%.
Individual scores of SH and ICI were correlated in both JIA (Spearman's r=0.503, p value=0.0024) and RA (Spearman's r=0.636, p value=0.0015). There was no significant difference in SH and ICI scores between the 2 groups (SH score (Q25-Q50-Q75) in JIA= 0.5-1.125-2 and in RA = 0.75-2-2; ICI score (Q25-Q50-Q75) in JIA= 1-2-2 and in RA = 0.75-2-2.25). Intra-group variability of the two assessed features was comparable between the 2 groups (SH coefficient of variation: 72.2% for JIA and 68.2% for RA; ICI coefficient of variation: 52.2% for JIA and 71.2% for RA). Within JIA patients, there was no significant difference in SH/ICI scores between groups based on ANA positivity, oligo or polyarticular involvement nor ongoing treatment.
Conclusion: Studying main histological features of synovitis, we found no difference between JIA and young RA patients. Furthermore, we report a similar degree of inter-patient heterogeneity in synovial pathological features of JIA and RA patients. These variations were not explained by common clinical characteristics. Whether they relate to different molecular signatures as suggested in adult RA will be further investigated using bulk tissue RNA sequencing.
Acknowledgements: This work was funded in part by Cap48 (RTBF). Clément Triaille is funded by the Fonds National de la Recherche Scientifique (FNRS, Communauté française de Belgique) and Fondation Saint-Luc (Cliniques Universitaires Saint-Luc).
Disclosure of Interests: Clément Triaille: None declared, Cécile Boulanger: None declared, Tatiana Sokolova: None declared, Laurent Meric de Bellefon: None declared, Adrien Nzeusseu Toukap: None declared, Christine Galant: None declared, Nisha Limaye: None declared, Bernard Lauwerys Employee of: currently employed at UCB Biopharma, Patrick Durez: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2100

POS0068 HIGH LEVELS OF PORPHYROMONAS GINGIVALIS AND PREVOTELLA INTERMEDIA ANTIBODIES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

F. Zekre[1], R. Cimaz[2], M. Paul[3], J. L. Stephan[4], S. Paul[5], H. Marotte[6]. [1]INSERM U1111-CNRS. INSERM U1059-SAINBIOSE, Campus Santé Innovations Faculté de Médecine Jacques Lisfranc, Saint Priest en Jarez, France; [2]Università degli studi di Milano Statale, Reumatologia pediatrica, Milano, Italy; [3]INSERM U1059, SAINBIOSE, Université de Lyon, Saint Etienne, Saint Priest en Jarez, France; [4]Hôpital Nord, Service pédiatrie, CHU Saint Etienne, Saint Priest en Jarez, France; [5]INSERM U1111-CNRS, Université de Lyon, Saint-Etienne, Saint Priest en Jarez, France; [6]INSERM U1059, SAINBIOSE, Université de Lyon, Saint-Etienne, France, Saint Priest en Jarez, France

Background: Idiopathic juvenile arthritis (JIA) is a heterogeneous group of pathologies whose origin remains unknown at present (1). They are characterised by a systemic inflammatory and joint disease affecting children under 16 years of age. The current classification groups the different forms of JIA into 7 distinct entities (systemic forms, polyarticular forms with or without rheumatoid factors, oligoarticular forms, inflammatory arthritis associated with enthesopathies (ERA), arthritis associated with psoriasis and unclassifiable arthritis). Exact etiology of JIA is still unknown. To date, the various hypotheses put forward on the occurrence of JIAs integrate the genetic and environmental framework.
The link between periodontal disease and rheumatoid arthritis (RA) is largely reported. Recently, *Porphyromonas gingivalis* (*P. gingivalis*) infection explained the occurrence of arthritis in rodent and in RA (2). Several studies mention the beneficial effect of *P. gingivalis* treatment on disease activity.
Currently, there are very few studies on the prevalence of *P. gingivalis* in patients with JIA and the possible involvement of the germ in the development of inflammatory joint diseases in the pediatric population(3)(4).
Objectives: The objective of our study is to determine presence of high IgG antibodies against *P. gingivalis* and *Prevotella Intermedia* in a cohort of patients with JIA compared to a control population and to determine variation of level according to sub-classes of JIA.

Methods: Sera were obtained from 101 patients satisfying the ILAR classification criteria for JIA and in 25 patients with two other dysimmune disorders (type 1 diabetes and juvenile inflammatory bowel disease). Level of IgG antibodies against *P. gingivalis* and *Prevotella Intermedia* were obtained by homemade ELISA already used previously (5).

Results: In the JIA group, major children were oligarthritis (47.5%), polyarthritis represents 31.7% of JIAs, ERA and systemic forms of JIA are respectively 9 and 11%. For the control group, 10 (40%) children had diabetes and 15 (60%) had IBD.

Levels of anti-*P. gingivalis* anti-*Prevotella Intermedia* antibodies were higher in AJI group compared at control groups (P<0.01, P<0.05). Theses difference are mainly related to oligoarthritis and ERA subsets for both *P. gingivalis* and *Prevotella Intermedia*.

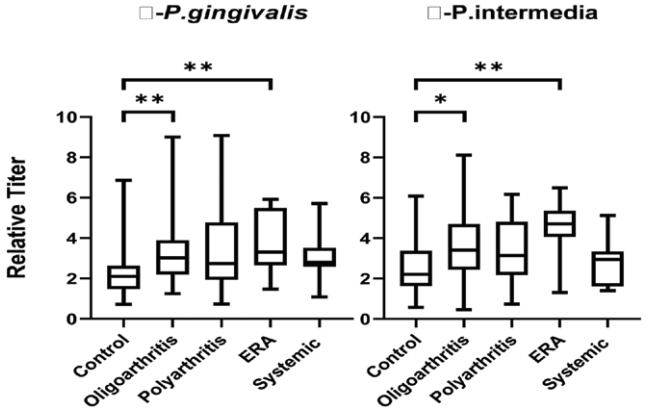


Figure 1. Relative titer of antibodies to P. gingivalis and anti Prevotella intermedia.*: P<0.05; **: P<0.01; ***: P<0.001.P. gingivalis (control vs oligoarthritis p= 0.0032. control vs ERA p= 0.0092).Prevotella intermedia (control vs oligoarthritis p= 0.0194. control vs ERA p= 0.0039).

Conclusion: We confirmed high level of anti-*P. gingivalis* and anti-*Prevotella intermedia* antibodies in JIA compared to other inflammatory disorders. For the first time, we observed that this high level was mainly in oligoarthritis and ERA. Further investigations are required to investigate involvement of oral dysbiosis in AJI pathogenesis. As observed in RA, it could be a new way to integrate in JIA therapy management.

REFERENCES:

[1] Thatayatikom A, De Leucio A. Juvenile Idiopathic Arthritis (JIA). StatPearls Publishing; 2020

[2] Cheng Z, Meade J, Mankia K, Emery P, Devine DA. Periodontal disease and periodontal bacteria as triggers for rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2017;31(1):19–30.

[3] Romero-Sánchez C, Malagón C, Vargas C, Fernanda Torres M, Moreno LC, Rodríguez C, et al. Porphyromonas Gingivalis and IgG1 and IgG2 Subclass Antibodies in Patients with Juvenile Idiopathic Arthritis. J Dent Child Chic Ill. 2017 May 15;84(2):72–9.

[4] Lange L, Thiele GM, McCracken C, Wang G, Ponder LA, Angeles-Han ST, et al. Symptoms of periodontitis and antibody responses to Porphyromonas gingivalis in juvenile idiopathic arthritis. Pediatr Rheumatol Online J. 2016 Feb 9

[5] Rinaudo-Gaujous M, Blasco-Baque V, Miossec P, Gaudin P, Farge P, Roblin X, et al. Infliximab Induced a Dissociated Response of Severe Periodontal Biomarkers in Rheumatoid Arthritis Patients. J Clin Med. 2019 May 26;8(5).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2222

POS0069 INCREASED T CELL RESPONSES, METABOLIC ACTIVITY AND FIBROBLAST INVASIVE CAPACITY IN CHILDREN WITH DOWN'S SYNDROME-ASSOCIATED ARTHRITIS COMPARED TO JUVENILE IDIOPATHIC ARTHRITIS

S. Foo[1,2], A. Floudas[1,2], S. Wade[1,2], A. O' Brien[1,2], S. Ansboro[1], R. Mullan[3], D. Veale[2], E. MacDermott[4], D. Deely[4], C. Foley[4], O. Killeen[4], U. Fearon[1,2]. [1]Trinity College Dublin, Molecular Rheumatology, Dublin, Ireland; [2]University College Dublin, St Vincent's Hospital, Centre for Arthritis and Rheumatic Diseases, Dublin, Ireland; [3]Tallaght University Hospital, Department of Rheumatology, Dublin, Ireland; [4]Children's Health Ireland (CHI) at Crumlin, Department of Rheumatology, Dublin, Ireland

Background: Juvenile idiopathic arthritis (JIA) was thought to be the most common inflammatory arthritis in children (Shih *et al.*, 2019). However an aggressive, erosive arthritis of little-known immunologic mechanism occurs 20 times more frequently in children with Down's syndrome (Foley *et al.*, 2019).

Objectives: This study was undertaken to characterize immune cell responses and synovial fibroblast invasiveness in children with Down's syndrome-associated arthritis (DA).

Methods: Multiparametric flow cytometric analysis was used to examine peripheral blood T cell, B cell and monocyte populations. In addition, T cell cytokine responses and their metabolic profile in children with DA, JIA, Down's Syndrome (trisomy 21 [T21]), and in healthy controls were assessed. The function of DA primary synovial fibroblasts (FLS) was assessed in response to stimulation with pro-inflammatory mediators alone and in combination (TNF-α, IL-17a, IFN-γ, GM-CSF). The two major energy pathways glycolysis (ECAR) and oxidative phosphorylation (OCR) were quantified by the Seahorse XFe96 Analyser. Migration, adhesion, invasion and cytokine/chemokine secretion were quantified by wound repair scratch assays, Transwell collagen invasion chambers, adhesion binding assays, and ELISAs.

Results: T cell frequencies were higher in DA compared to JIA and T21 in contrast to B cell frequencies which were decreased. T cell responses in DA were characterized by increased frequencies of $CD4^+$ and $CD8^+$ TNF- α, IFN- γ and GM-CSF producing T cells. The frequency of T peripheral helper (Tph) cells were elevated in children with DA compared to all other groups. In parallel, an increase in their metabolic profile evident by higher phosphorylation of mTOR pathway components AKT, mTOR and S6. Comparison of DA and JIA FLS demonstrated that DA FLS display a more invasive/migratory capacity and are more metabolically active. Based on the increased cytokine responses in DA T cells, we next examined the effect T cell derived cytokines TNF-α, IL-17A, IFN-γ and GM-CSF alone and in combination on DA FLS function. TNF-α, IL-17a and IFN-γ induced IL-6, RANTES and MCP-1 secretion, with no effect observed for GM-CSF. Furthermore, TNF-α and IL-17A induced DA FLS migration and PBMC adhesion to DA FLS. Finally IL17A and IFN-γ potentiated the effect of TNF-α on IL-6 and MCP-1 secretion compared to stimulations alone.

Conclusion: DA is a more common and aggressive form of arthritis compared to JIA. It is characterized by increased T cell responses and a more invasive FLS phenotype compared to that of JIA, with T cell derived cytokine alone and in combination further inducing DA FLS pathogenic mechanisms. These effects mirror the increased erosive disease observed clinically.

REFERENCES:

[1] Foley, C. *et al.* (2019) 'Increased T cell plasticity with dysregulation of T follicular helper, T peripheral helper and T regulatory cell responses in children with JIA and Down syndrome-associated arthritis', *Arthritis & Rheumatology*, pp. 0–1. doi: 10.1002/art.41150.

[2] Shih, Y. J. *et al.* (2019) 'Enthesitis-related arthritis is the most common category of juvenile idiopathic arthritis in Taiwan and presents persistent active disease', *Pediatric Rheumatology*. Pediatric Rheumatology. doi: 10.1186/s12969-019-0363-0.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2104

POS0070 POPULATION PHARMACOKINETICS OF INFLIXIMAB IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

A. Nassar-Sheikh Rashid[1], D. Schonenberg-Meinema[1], S. Berends[2], J. M. Van den Berg[1], R. Mathot[2]. [1]Amsterdam UMC, Locatie AMC, Department of Pediatric Immunology, Rheumatology and Infectious Diseases, Emma Children's Hospital, Amsterdam, Netherlands; [2]Amsterdam UMC, Locatie AMC, Hospital Pharmacy, Amsterdam, Netherlands

Background: Higher dosage regimes for Infliximab (IFX) have been described to be effective in partial- or non-responding adults and children with rheumatic disease and appear to be safe (1,2). To optimize IFX treatment in juvenile idiopathic arthritis (JIA) patients, therapeutic drug monitoring (TDM) might be beneficial. To support routine TDM of IFX and dose regimen optimization in JIA patients, more in-depth knowledge of the pharmacokinetic (PK) variability of IFX is needed. Ultimately, as soon as the optimal therapeutic drug ranges will be known, PK model-based simulation can be used to individualize drug dosing recommendations. Individual dosages may be adjusted by taking specific patient characteristics into account that explain inter-patient variability in pharmacokinetics (PK). Inter-patient variability can be quantified and investigated by the population approach.

Objectives: Our hypothesis is that optimizing dosage and frequency of IFX administration for individual patients will improve treatment outcome. In this current study, the population PK for IFX are described for JIA patients.

Methods: Data including IFX trough concentrations and anti-IFX antibodies of 27 JIA patients on IFX maintenance treatment were retrieved from electronic charts. Three population pharmacokinetic models from literature were validated for our dataset using nonlinear-mixed effects modeling program NONMEM (3,4,5). A novel population pharmacokinetic model was developed based on our study data.

Results: A total of 65 obtained blood samples after a median of 32 days after the last IFX infusion (IQR 28-42) were analyzed. The three published models underpredicted the observed trough concentrations. A newly developed one compartment model best described the IFX serum concentration over time data in JIA patients (see Figure 1).
Conclusion: Our study shows a novel and the first PK model for IFX in JIA patients. Our main finding was that a one- compartment model best described the IFX serum concentration over time data. Predictive performance of the known models from literature was insufficient for our patient data. Our data also show that different PK models are needed for different age categories (children or adults) and in different diseases.
REFERENCES:
[1] Nozaki Y et al. Infliximab dose adjustment can improve the clinical and radiographic outcomes of rheumatoid arthritis patients: REVIVE study results. Biologics. 2018.
[2] Tambralli A et al. High doses of infliximab in the management of juvenile idiopathic arthritis. J Rheumatol. 2013.
[3] Fasanmade AA et al. Pharmacokinetic properties of infliximab in children and adults with Crohn's disease: a retrospective analysis of data from 2 phase III clinical trials. Clin Ther. 2011.
[4] Xu Z et al. Population pharmacokinetics of infliximab in patients with ankylosing spondylitis. J Clin Pharmacol. 2008.
[5] Ternant D et al. Relationship between inflammation and infliximab pharmacokinetics in rheumatoid arthritis. Br J Clin Pharmacol. 2014.

Table 1. Patient characteristics

	N=27 patients
Weight (kg)	52 [40 – 62]
BSA	1.6 [1.3 – 1.8]
Age (years)	14 [11 – 17]
Male, N (%)	6 (22%)
CRP (mg/L)	0.5 [0.2 – 0.7]
WBC count	6.5 [5.6 –7.5]
Antibodies-to-IFX	1 (4%)
Dose (mg)	300 [200-400]
Dose (mg/kg)	5.4 [4.9 -7.0]
Hemoglobine (mmol/L)	7.9 [7.5 -8.2]
ESR (mm/h)	5 [5-8]
Uveitis	3 (11%)

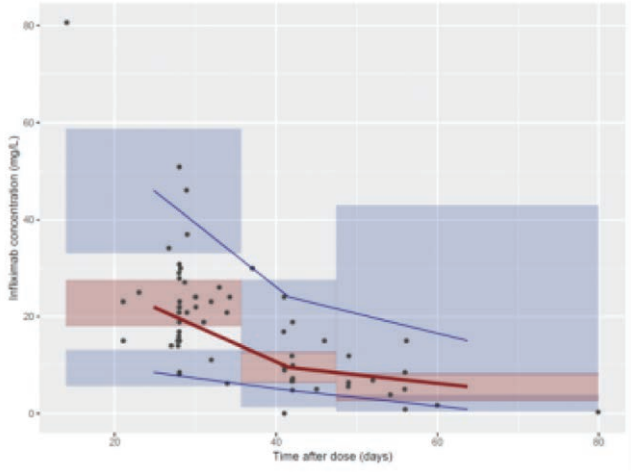


Figure 1: Visual predictive check final model

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4025

POS0071 IS ANTI-NXP2 AUTOANTIBODY A RISK FACTOR FOR CALCINOSIS AND POOR OUTCOME IN JUVENILE DERMATOMYOSITIS PATIENTS?

N. Toplak[1,2], P. P. Chavan[3], S. Rosina[4], T. Dallos[5], R. Semo Oz[6], C. Aguiar[7], R. Khubchandani[8], A. Ravelli[9], A. Patwardhan[10]. [1]University Children's Hospital, University Medical center Ljubljana, Department od Allergology, Rheumatology and Clinical Immunology, Ljubljana, Slovenia; [2]Faculty of Medicine, Pediatrics, Ljubljana, Slovenia; [3]NH SRCC Children's Hospital, Pediatric Rheumatology, Mumbai, India; [4] IRCCS Istituto Giannina Gaslini, Pediatric Rheumatology, Genova, Italy; [5]Comenius University Medical School, National Institute of Children's Diseases, Departmet of Paediatrics, Bratislava, Slovakia (Slovak Republic); [6]University of Chicago, University of Chicago, Chicago, United States of America; [7]EVMS, Children's Hospital of The King's Daughters, Norfolk, VA, USA, Pediatric Rheumatology, Norfolk, United States of America; [8]NH SRCC Childrens Hospital, Pediatric Rheumatology, Mumbai, India; [9]IRCCS Istituto Giannina Gaslini, Pediatric Rheumatology, Genova, Italy; [10]UAMS, Arkansas Children's Hospital, Pediatric rheumatology, Arkansas, United States of America

Background: It has been published that the presence of NXP2 autoantibodies presents a risk for calcinosis in patients with JDM.
Objectives: To investigate the incidence of calcinosis and response to the treatment in NXP2 positive JDM patients with calcinosis.
Methods: The study design is a retrospective, multinational, multicenter study. Data on gender, race, age at disease onset and age at disease diagnosis, age at inclusion in the study, clinical presentation, muscle function tests, laboratory results, imaging, data on treatment and outcome of disease were collected
Results: we collected 26 patients (19 F, 7 M) with JDM and positive NXP2 antibodies. Fourteen patients were white, eight asian, three black and one Hispanic ethnicity. The mean age at disease presentation was 6.5 years (SD 3.7), the median diagnosis delay was 4 months (range 0.5- 27 months). Patients were divided in two groups (A and B) based on the presence of calcinosis.
Eleven patients (42%) developed calcinosis (group A) in the course of the disease, 10 females and 1 male. Four patients already had calcinosis at presentation, 1 developed after 4 months, and 6 developed calcinosis later in disease course (median 2 years, range 0,8- 7,8). Four patients developed lipodystrophy in group A (1 in group B). In group A, 3 patients developed skin ulcerations (1 in group B), 2 patients had polyarthritis (1 in group B), 2 patients had gut involvement (1 in group B) and 1 patient had lung involvement (2 in group B).
The mean age at disease presentation (5.2 / 7.5 y) and mean CK level (1548.6 / 1811.6 U/L) were lower in group A. The platelet count (306.5 / 258 10^9/L), and mean values of AST (111.4 / 103.8 U/L), ALT (72.2 / 50.8 U/L), LDH (1048.3 / 808 IU/L), and IgG (11.8 / 9.9 g/L) were higher in group A. However, the differences were not statistically significant. ANA antibodies were positive in 9/11 in group A and 12/15 in group B. One patient in group A was also positive for anti-MDA5 antibody. The data on muscle strength measurement (MMT/CMAS) were available only in a few patients.
Treatments used for patients with calcinosis includes, methotrexate and glucocorticosteroids (GCS) (all patients), hydroxychloroquine (9), IVIG (7), cyclosporine (4), bisphosphonate (4), MMF (5), rituximab (4), cyclophosphamide (1), abatacept (1) and TNF alpha blocker (1).
Disease outcome (by evaluation of the treating physician) was excellent in 4, good in 2, stable in 2 and poor in 3 patients. None of the patients from group B had a poor disease outcome. Patients with excellent disease outcomes from group A were treated with GCS and methotrexate (4), hydroxychloroquine (3), IVIG (1) and cyclosporine (1). Out of two patients who had good outcomes, one was additionally treated with MMF, bisphosphonates and rituximab and the second was treated with cyclophosphamide and rituximab. One patient with calcinosis at the presentation (age 4 years) was treated also with anti-TNF alpha therapy which not only stopped progression but partially dissolved the calcinosis. However, after 2 years of anti-TNF alpha therapy the calcinosis start to progress and the therapy was changed to MMF and rituximab, which stopped the progression of calcinosis.
Conclusion: Our preliminary results showed that calcinosis occurred in 42% of NXP2 positive JDM patients. Children with calcinosis were treated with several combinations of drugs. In four cases, rituximab and in one case, for limited time of 2 years, anti-TNF alpha agent, were used successfully.
REFERENCES:
[1] Chung MP, Richardson C, Kirakossian D, Orandi AB, Saketkoo LA, et al. Calcinosis biomarkers in adult and juvenile dermatomyositis. Autoimmun Rev 2020; 19(6):102533.
Disclosure of Interests: Natasa Toplak: None declared, Pallavi Pimpale Chavan: None declared, Silvia Rosina: None declared, Tomas Dallos Consultant of: Abbvie, Novartis, Rotem Semo Oz: None declared, Cassyanne Aguiar: None declared, Raju Khubchandani: None declared, Angelo Ravelli: None declared, Anjali Patwardhan: None declared.
DOI: 10.1136/annrheumdis-2021-eular.603

POS0072 COMPREHENSIVE IMMUNE PROFILING OF 20 CHILDREN WITH MULTISYSTEM INFLAMMATORY SYNDROME

M. Zajc Avramovic[1,2], N. Emersic[1], A. N. Kopitar[3], M. Korva[3], T. Avsic-Zupanc[3], A. Ihan[3], T. Avcin[1,2]. [1]University Medical Center Ljubljana, Children's Hospital, Department for Allergology, Rheumatology and Clinical Immunology, Ljubljana, Slovenia; [2]University of Ljubljana, Faculty of Medicine, Pediatrics, Ljubljana, Slovenia; [3]University of Ljubljana, Faculty of Medicine, Institute of Microbiology and Immunology, Ljubljana, Slovenia

Background: Multisystem inflammatory syndrome in children (MIS-C) is a rare complication of SARS-CoV-2 infection in the pediatric population, caused by extensive activation of immune system. The understanding of the distorted immune response is still in the early stages.
Objectives: To analyze comprehensively immune profile in MIS-C patients including detailed serologic response to SARS-CoV-2 in comparison with control groups.
Methods: Blood samples of consecutive MIS-C patients were collected at admission. Flow cytometric analysis of all lymphocyte populations including T and B cell differentiation was performed. Immunophenotyping was performed by six-color panels for the detection of lymphocyte subpopulations. Anti-SARS-CoV-2 specific antibodies were measured in the patients serum. The IgA and IgG antibodies against S protein, the IgG S1 and S2 specific antibodies, antibodies against nucleoprotein and neutralising antibodies were measured. Patients were assessed for a wide range of auto-antibodies, namely ANA, anti-ENA (Jo-1, PL-7, PL-12, SRP, Mi-2, Ku, Pm/Scl 100, Scl-70), myositis specific antibodies (EJ, MDA-5, TIH-Y, Ro52, SAE-1, SAE-2, NXP-2), anti-dsDNA, anti-phopholipid antibodies (aCl IgA, IgG, IgM, antiβ2GPI IgG, IgM) and ANCA. Control groups to compare specific antibody response consisted of 14 healthy children and 19 healthy adults, who had SARS-CoV-2 infection in the last 2 months.
Results: Samples of 20 patients were included (14/20 boys, median age 12.4 years). Patients had higher percentage of double negative T cells and low numbers of of cytokine producing T cells Th1, Th2 and Th17. . Numbers of immune competent and CD21+ transitional B cells were also lowered. All patients had positive antibodies against SARS-CoV-2 including neutralising antibodies. Nine (9/19; 47 %) patients had high titer (≥1:160) of neutralising antibodies. Results were compared with 2 control groups; 14 healthy children (7/14 boys; median age 8 years,) and 19 healthy adults, who all experienced SARS-CoV-2 infection in the last two months. Patients with MIS-C had significantly higher levels of anti-S IgA (p<0.0001), patients with MIS-C and healthy children had significantly higher titers of anti-S1 (p=0.001) and significantly lower titers of anti-S2 (p=0.016) in comparison to adults (Figure 1). No differences were found in the titers of neutralising antibodies and anti-N antibodies. All patients were ANA negative, 19/20 patients were anti-ENA negative, whereas 1 patient had anti-Ro antibodies in low titre. Three patients had aCL IgG in medium titre and 2 patients anti-beta2GPI IgG in low titre. Patients were negative for all other autoantibodies.
Conclusion: The immune response in MIS-C patients is specific with most prominent differences in elevated percentage of double negative T cells and low numbers of Th1, Th2, Th17 and CD21+ transitional B cells. MIS-C patients have distinct serologic response with high anti-S IgA, high anti-S1 and low anti-S2 titres.

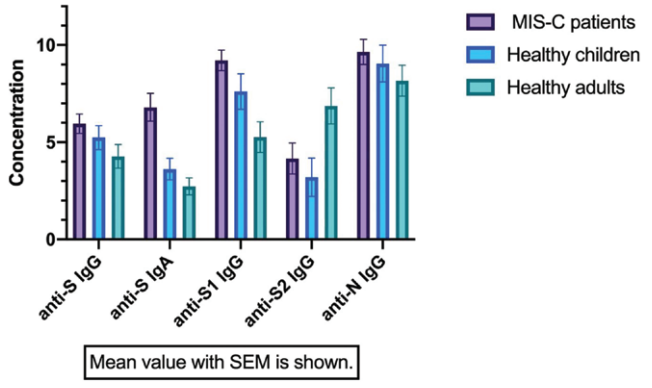


Figure 1. Antibody titres in patient group and control groups. Mean value with SEM s shown.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4109

POS0073 ASSOCIATION OF SAA1 GENE POLYMORPHISM -13T/C (RS12218) WITH CRYOPYRIN ASSOCIATED PERIODIC SYNDROMES (CAPS), BUT NOT FAMILIAL MEDITERRANEAN FEVER (FMF)

I. Guseva[1], E. Fedorov[2], S. Salugina[2], M. Krylov[1], E. Samarkina[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Pediatric Rheumatic Diseases, Moscow, Russian Federation*

Background: Autoinflammatory diseases (AIDs) are a group of rare, genetically determined diseases characterized by a periodic events of inflammation, fever, and clinical symptoms that mimic rheumatic pathology. Laboratory serological markers of AIDs are C reactive protein (CRP) and serum amyloid A (SAA) protein.
Objectives: We investigated whether *SAA1* gene polymorphism -13T/C (rs12218) may affect the susceptibility to pediatric FMF and CAPS patients (pts). We also evaluate whether this polymorphism can affect CRP and SAA protein levels.
Methods: 26 FMF pts - 8 boys, 18 girls; age - M(SD) 7.37(5.32) years and 24 CAPS pts - 12 girls, 12 boys; age – 4.76(5.83) years, and 95 healthy individuals (controls) were included in this study. The diagnosis of FMF was based on Turkish paediatric criteria for the diagnosis of familial Mediterranean fever [1] and was confirmed by the detection of pathogenic mutations of the *MEFV* gene in the homozygous or compound-heterozygous states. The diagnose of CAPS was made on the basis of characteristic clinical signs and was confirmed by the detection of a pathogenic mutation in the *NLRP3* gene. *SAA1* gene polymorphism -13T/C was genotyped using allele-specific RT-PCR assay. SAA protein concentration was measured using nephelometry in FMF and CAPS pts.
Results: Table 1 shows the genotypic and allelic frequencies of *SSA1* gene in FMF, CAPS and controls. There were no significant differences between FMF pts and controls in the genotypic and allelic distributions of -13T/C gene polymorphism. The frequency of -13C allele was significantly higher in CAPS pts compared with controls (OR=2.03 [CI 1.02-4.03], p=0.03). Moreover, a statistically significant difference was revealed in the genotypic and allelic distributions between FMF and CAPS pts groups (p=0.047 and p=0.02 respectively). The CRP levels did not correlate with *SAA1* - 13T/C polymorphism. The SAA protein concentration was associated with *SAA1* gene polymorphism in FMF pts (p=0.036).

Table 1. The distribution of genotypes and alleles of *SAA1* gene polymorphism -13T/C in FMF, CAPS and control groups.

Genotypes/Alleles	FMF n=26 (%)	CAPS n=24 (%)	Controls n=95 (%)
TT	12 (46,2)	4 (16,7)	39 (41,1)
TC	12 (46,2)	14 (58,3)	42 (44,2)
CC	2 (7,7)	6 (25,0)	14 (14,7)
P (pts vs controls)	>0,05	>0,08	
T	24 (63,2)	21 (50,0)	80 (61,5)
C	14 (36,8)	21 (50,0)	50 (38,5)
P (pts vs controls)	>0,05	0.03	

Conclusion: Our preliminary study in small groups of pediatric FMF and CAPS pts revealed that *SAA1* gene polymorphism -13T/C (rs12218) is associated with susceptibility to CAPS, but not FMF. The influence of this polymorphism on SAA protein levels in FMF pts was also shown. Further investigations are required to clarify the role of *SAA1* gene polymorphism -13T/C in susceptibility to FMF and CAPS in large studies in different ethnic and population groups.
REFERENCES:
[1] Yalcinkaya F, Ozen S, Ozcakar ZB, et al. Rheumatology (Oxford). 2009,48(4): 395-8. doi: 10.1093/rheumatology/ken509.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3910

POS0074 CAN WE PREDICT THE DEVELOPMENT OF NEPHRITIS IN PEDIATRIC IGA VASCULITIS PATIENTS?

E. Sag[1,2], S. Demir[1,2], Y. Bilginer[1,2], S. Özen[1,2]. [1]*Hacettepe University Faculty of Medicine, Department of Pediatric Rheumatology, Ankara, Turkey*; [2]*Hacettepe University Faculty of Medicine, Translational Medicine Laboratories, Pediatric Rheumatology Unit, Ankara, Turkey*

Background: IgA vasculitis (IgAV) is the most common systemic vasculitis of childhood, characterized by palpable purpura, arthritis, gastrointestinal and renal involvement [1]. It is a relatively self-limited disease apart from the renal involvement which is associated with the long term morbidity.
Objectives: We aimed to define a marker at disease onset to predict the renal involvement.
Methods: In this pilot study, we analyzed a targeted panel of vascular inflammation markers (sT2, RAGE, TIE-2, sCD40L, TIE-1, sFlt-1, LIGHT, TNF-a, PlGF, IL6, IL18, IL10 and MCP-1) in the plasma samples of eight patients IgAV at the onset of the disease, before any treatment was initiated. At the time of sample collection, none of the patients had renal involvement; four of these patients subsequently developed nephritis and were defined as the IgAVN group. The levels of the markers were studied by a cytometric bead-based multiplex assay panel according to manufacturer's instruction (LEGENDplex HU Vascular Inflammation panel 2 (13-plex); catalogue number 740966, Biolegend) and analyzed by Novocyte 3005 flow cytometer.

Results: There were no significant differences in gender, age, clinical manifestations, and laboratory findings between IgAV and IgAVN patients (Table 1). sCD40L levels were higher (median 1938.1 vs 754.9 pg/mL, p=0.04) whereas sST2 levels were lower (median 862.8 vs 2302.8 pg/mL, p=0.02) in the patients who developed IgAV nephritis (Figure 1). sRAGE levels were higher and IL18 levels were lower in IgAVN patients but did not reach statistical significance, probably due to the low number of patients. The other parameters did not show any specific pattern.

Table 1.

	IgAV (n=4)	IgAVN (n=4)	p value
Gender	2F, 2M	1F, 3M	0.49
Age at disease onset	9.0±5.4	10.3±3.4	0.68
Arthralgia/arthritis	50%	75%	0.49
GIS involvement	75%	50%	0.49
Haemoglobine (gr/dL)	12.4±2.3	12.3±0.6	0.95
White blood cells, x10^9/L	11150±1933	8525±1497	0.08
Platelets x10^9/L	290250±87328	269250±38741	0.68
Erythrocyte sedimentation rate (mm/hr)	10.5±9.1	21.0±14	0.26
C-reactive protein (mg/dL)	0.63±0.03	1.16±0.96	0.39

Data are given as mean±SD

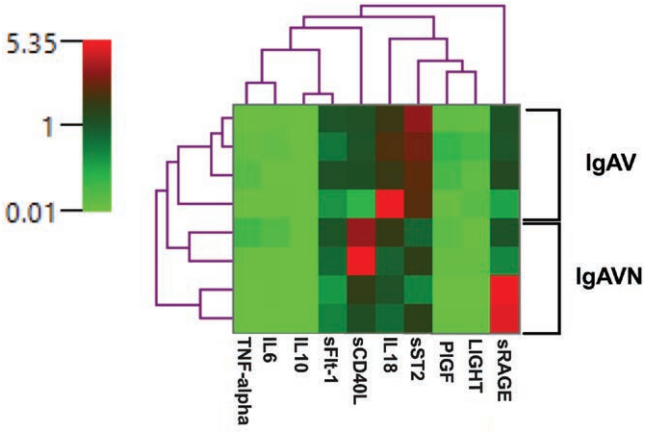


Figure 1.

Soluble CD40 ligand (sCD40L) is expressed on platelets and released on activation. It is proinflammatory for endothelial cells and promotes coagulation by inducing expression of tissue factor on monocytes and endothelial cells [2]. It was investigated in acute coronary syndrome and was suggested as a risk factor for vascular damage. [2]. Furthermore, the levels of sCD40L were shown to be correlated with disease activity in ANCA-associated vasculitis[3]. Thus in IgAV, sCD40L may be associated with the involvement of the kidney vasculature, which represents the more severe form of the disease. Receptor for advanced glycation end-products (RAGE) is another marker for endothelial damage and vasculitis which was higher in IgAVN, as well.

IL33 is expressed by epithelial and endothelial cells and overexpression of IL33 have been shown in large vessel vasculitis [4]. sST2 acts as a decoy receptor and inhibits IL33 signalling[4]. It was interesting to see that the levels of the IL-18 and sST2, which are members of IL-1 family, were lower in IgAVN patients.

Conclusion: Although the number of the patients were limited in this pilot study, we suggest that sCD40L and sRAGE might be used to predict the development of renal disease in IgAV patients. Further studies with larger number of patients are needed to confirm our findings.

REFERENCES:

[1] Sag E, Batu ED, Ozen S. Childhood systemic vasculitis. *Best practice & research Clinical rheumatology* 2017;31(4):558-75.

[2] Heeschen C, Dimmeler S, Hamm CW, et al. Soluble CD40 ligand in acute coronary syndromes. *The New England journal of medicine* 2003;348(12):1104-11.

[3] Tomasson G, Lavalley M, Tanriverdi K, et al. Relationship between markers of platelet activation and inflammation with disease activity in Wegener's granulomatosis. *The Journal of rheumatology* 2011;38(6):1048-54.

[4] Desbois AC, Cacoub P, Leroyer AS, et al. Immunomodulatory role of Interleukin-33 in large vessel vasculitis. *Sci Rep* 2020;10(1):6405.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1306

Pediatric Rheumatology - Clinical

POS0075

SAFETY AND EFFICACY OF GOLIMUMAB FOR THE TREATMENT OF POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS - AN UPDATE FROM THE BIKER REGISTRY

A. Zimmer[1], A. Klein[2], K. Minden[3], T. Hospach[4], F. Weller-Heinemann[5], J. Kuemmerle-Deschner[6], M. Fasshauer[7], N. Hofmann[8], H. Koessel[9], I. Foeldvari[10], S. Mrusek[11], D. Windschall[12], N. Onken[13], M. Hufnagel[14], D. Foell[15], N. Brueck[16], P. T. Oommen[17], F. Dressler[18], A. Helling-Bakki[19], G. Horneff[2]. *[1]Kinderklinik St. Augustin, Paediatric Rheumatology, Sankt Augustin, Germany*; *[2]Kinderklinik St. Augustin, Paediatric Rheumatology, St. Augustin, Germany*; *[3]Charité Universitätsklinik Berlin, Paediatric Rheumatology, Berlin, Germany*; *[4]Klinikum Stuttgart- Olgahospital, Paediatric Rheumatology, Stuttgart, Germany*; *[5]Klinikum Bremen-Mitte, Professor-Hess-Kinderklinik, Paediatric Rheumatology, Bremen, Germany*; *[6]Universitätsklinikum Tübingen, Paediatric Rheumatology, Tübingen, Germany*; *[7]Klinikum St. Georg gGmbH, Paediatric Rheumatology, Leipzig, Germany*; *[8]Klinikum Bamberg, Sozialstiftung Bamberg, Paediatric Rheumatology, Bamberg, Germany*; *[9]Städtisches Klinikum Brandenburg GmbH, Paediatric Rheumatology, Brandenburg, Germany*; *[10]Hamburger Zentrum für Kinder- und Jugendrheumatologie am Klinikum Eilbek, Paediatric Rheumatology, Hamburg, Germany*; *[11]Praxis für Kinder- und Jugendrheumatologie, Paediatric Rheumatology, Baden-Baden, Germany*; *[12]Klinik für Kinder- und Jugendrheumatologie, Paediatric Rheumatology, Sendenhorst, Germany*; *[13]Kinder- und Jugendärztliche Gemeinschaftspraxis, Paediatric Rheumatology, Lüneburg, Germany*; *[14]Universitätsklinikum Freiburg, Paediatric Rheumatology, Freiburg, Germany*; *[15]Universitätsklinikum Münster, Paediatric Rheumatology, Münster, Germany*; *[16]Universitätsklinikum Carl Gustav Carus, Paediatric Rheumatology, Dresden, Germany*; *[17]Universitätskinderklinikum Düsseldorf, Paediatric Rheumatology, Düsseldorf, Germany*; *[18]Medizinische Hochschule Hannover, Paediatric Rheumatology, Hannover, Germany*; *[19]UniversitätsKlinikum Heidelberg, Paediatric Rheumatology, Heidelberg, Germany*

Background: Golimumab (GOL) is approved for treatment of polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years and older. Data on long-term safety of GOL in this indication are limited.

Objectives: To assess long-term safety and efficacy of GOL in pJIA patients.

Methods: In this ongoing non-interventional observational study, clinical characteristics, disease activity and safety parameters were analysed using the German Biologics in Paediatric Rheumatology (BiKeR) registry. 81 pJIA-patients treated with GOL were body weight-matched with 162 patients receiving alt. tumor necrosis factor inhibitors (TNFi) and 81 biologic–naïve patients under methotrexate (MTX)-therapy.

Results: Baseline parameters of GOL patients differed from the alternative TNFi and MTX cohorts. In patients starting with GOL treatment, disease duration was longer, corticosteroid use was less and disease activity, measured by the mean number of active joints and the JADAS10, was lower (Table 1).

The long-term clinical efficacy of GOL in pJIA is highlighted by a decrease of the mean JADAS 10 from 11.6 (baseline) to 5.2 after 24 months. After 2 years, a JADAS 10 minimal disease activity was reached by 44.4 % of patients, whereas 22.2 % of patients were in remission and the JIA ACR 30/50/70/90 response rates were 77.8/72.2/66.7/55.6% respectively.

AE, SAE and infectious AE rates between the three cohorts were comparable (Table 1). In the GOL cohort, 4 SAE (1 uveitis, 1 arthritis flare, 1 fibromyalgia syndrome and 1 abscess) were reported, while in the alt. TNFi group 7 SAEs and in the MTX cohort 1 SAE were noted (Table 1). One serious infectious event (1 abscess) was documented in the GOL cohort, 2 alt. TNFi patients had influenza and no serious infectious events were seen in the MTX control group.

Few autoimmune processes occurred: 2 incident events in the GOL cohort (1 uveitis, 1 psoriasis), 3 cases in the alt. TNFi group (2 uveitis, 1 psoriasis,) and 1 event in MTX-patients (celiac disease) (Table 1). Out of the 20 GOL patients with preexisting uveitis at baseline, 6 had flare events; there were no reported uveitis flares of the 17 patients in the alt. TNFi group and no patients with preexisting uveitis in the MTX-group. No malignancies or deaths were reported.

Conclusion: Our interim results show an acceptable safety profile of GOL therapy, comparable to treatment with alt. TNFi or MTX. No new safety signals occurred. The efficacy outcome data confirm long-term benefits of GOL treatment in pJIA patients.

Acknowledgements: We greatly appreciate the kind support of Z. Huang, S. Calhoun.

Disclosure of Interests: Angela Zimmer: None declared, Ariane Klein: None declared, Kirsten Minden: None declared, Toni Hospach: None declared, Frank Weller-Heinemann: None declared, Jasmin Kuemmerle-Deschner: None declared, Maria Fasshauer: None declared, Nadja Hofmann: None declared, Hans Koessel: None declared, Ivan Foeldvari: None declared, Sonja Mrusek:

Table 1. Baseline parameters and adverse events

	GOL n=81	alt. TNFi n=162	MTX n=81	p-value ∞ GOL vs alt. TNFi	p-value∞ GOL vs MTX
Gender female °	67 (83)	127 (78)	64 (79)	0.5	0.7
Disease duration (yrs)	7.1±4.3	4.3±3.7	1.2±2.1	**<0.0001**	**<0.0001**
RF neg. Polyarthritis °	40 (49)	79 (49)	50 (62)	1.0	0.15
RF pos. Polyarthritis °	8 (10)	22 (14)	16 (20)	0.5	0.1
Extended Oligoarthritis °	30 (37)	54 (33)	13 (16)	0.6	**0.004**
Psoriatic arthritis °	3 (4)	7 (4)	2 (3)	1.0/1.0	1.0
Pretreatment bDMARD °	68 (84.0)	35 (21.6)	0	**<0.0001**	**<0.0001**
Concomitant systemic steroids, n (%)	13 (16)	38 (24)	39 (48)	0.2	**<0.0001**
Active joint count #	4.6±4.8	4.9±5.7	9.6±6.5	0.4	**<0.0001**
CHAQ DI #	0.4±0.5	0.5±0.5	0.6±0.6	0.1	**0.02**
JADAS10 #	11.6±6.2	12.1±6.1	16.8±5.3	0.6	**<0.0001**
AE *	91 (107.4; 88-132)	213 (88.7; 78-101)	113 (119.8; 100-144)	0.1	0.4
SAE *	4 (4.7; 2-13)	7 (2.9; 1-6)	1 (1.1; 0.1-8)	0.4	0.2
Serious infections *	1 (1.2; 0.2-8.4)	2 (0.8; 0.2-3.3)	0	0.7	n.a.
Autoimmune process (%)	2 (2.4)	3 (1.9)	1 (1.2)	1.0	1.0
Patients with uveitis new manifestation after study entry *	1 (1.2; 0.2-8)	2 (0.8; 0.5-3)	0	0.7	n.a.
Patients with uveitis flare events with preexisting uveitis at baseline*	6 (7.1; 3-16)	0	0	n.a.	n.a.

Rheumatoid factor (RF), biologic disease modifying antirheumatic drug (bDMARD), childhood health assessment questionnaire disability index (CHAQ Di), juvenile arthritis disease activity index (JADAS), adverse event (AE), patient year (PY), ° n (%), # mean (SD), * n (rate/100PY; 95%CI), Golimumab (GOL), alternative tumor necrosis factor inhibitor (alt. TNFi), methotrexate (MTX), ∞ by t-test or χ2-test as appropriate.

None declared, Daniel Windschall: None declared, Nils Onken: None declared, Markus Hufnagel: None declared, Dirk Foell: None declared, Normi Brueck: None declared, Prassad Thomas Oommen: None declared, Frank Dressler: None declared, Astrid Helling-Bakki: None declared, Gerd Horneff Speakers bureau: MSD.

DOI: 10.1136/annrheumdis-2021-eular.2145

POS0076

S100A8/A9 AND S100A12 AS POTENTIAL PREDICTIVE BIOMARKERS OF ABATACEPT RESPONSE IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

N. Ruperto[1], G. Schulert[2], A. Sproles[2,3], S. Thornton[2,3], G. Vega Cornejo[4], J. Anton[5], R. Cuttica[6], M. Henrickson[2], I. Foeldvari[7], D. Kingsbury[8], M. Askelson[9], J. Liu[10], S. Mukherjee[11], R. Wong[12], D. J. Lovell[13], A. Martini[14], A. Grom[2], H. Brunner[2]on behalf of Pediatric Rheumatology Collaborative Study Group (PRCSG) and Paediatric Rheumatology International Trials Organisation (PRINTO). [1]*IRCCS Istituto Giannina Gaslini, Clinica Pediatrica e Reumatologia, Genova, Italy*; [2]*Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, United States of America*; [3]*University of Cincinnati College of Medicine, Department of Pediatrics, Cincinnati, United States of America*; [4]*Hospital México Americano, CREA, Guadalajara, Mexico*; [5]*Hospital Sant Joan de Déu, Division of Pediatric Rheumatology, Barcelona, Spain*; [6]*Hospital General de Niños Pedro de Elizalde, Pediatric Rheumatology, Buenos Aires, Argentina*; [7]*Hamburg Centre for Pediatric and Adolescent Rheumatology, Schön Klinik Hamburg Eilbek, N/A, Hamburg, Germany*; [8]*Randall Children's Hospital at Legacy Emanuel, Division of Rheumatology, Portland, United States of America*; [9]*Bristol Myers Squibb, Global Biometric Sciences, Princeton, United States of America*; [10]*Bristol Myers Squibb, Translational Medicine, Princeton, United States of America*; [11]*Bristol Myers Squibb (at the time of analysis), Translational Medicine, Princeton, United States of America*; [12]*Bristol Myers Squibb, Immunology and Fibrosis, Princeton, United States of America*; [13]*Cincinnati Children's Hospital Medical Center, Department of Pediatrics, Division of Rheumatology, Cincinnati, United States of America*; [14]*University of Genoa, N/A, Genoa, Italy*

Background: The calcium-binding proteins S100A8/A9 (calprotectin) and S100A12 (extracellular newly identified receptor for advanced glycation end-products binding protein [EN-RAGE]) are involved in multiple signalling pathways to mediate inflammation, can be secreted by activated monocytes/macrophages and exhibit cytokine-like extracellular functions. Circulating levels of these proteins have been associated with disease and clinical responses in systemic juvenile idiopathic arthritis (sJIA), including treatment response.[1] Studies suggest that serum S100A8/A9 and S100A12, which are released at inflammation sites, are more specific biomarkers of local inflammation (e.g. in the synovium) than systemic biomarkers such as CRP and ESR.[2,3]

Objectives: To investigate if baseline S100A8/A9 and S100A12 predict clinical response to abatacept treatment in polyarticular JIA (pJIA), and to assess whether changes from baseline in S100A8/A9 or S100A12 can be better prognostic markers for response to abatacept treatment than CRP in pJIA.

Methods: Data are from a phase III trial of SC abatacept for the treatment of pJIA (NCT01844518).[4] This 24-month, single-arm, open-label, international, multicentre, two-part study included male and female patients with pJIA aged 2–17 years. This analysis examined the correlation between biomarkers (S100A8/A9, S100A12 and high-sensitivity CRP [hsCRP]) and disease activity (measured using Juvenile Arthritis Disease Activity Score [JADAS]) at baseline, baseline biomarker values as predictors of future treatment response (ACR and JADAS endpoints), and the correlation between change from baseline in biomarker values and treatment response at Day 113.

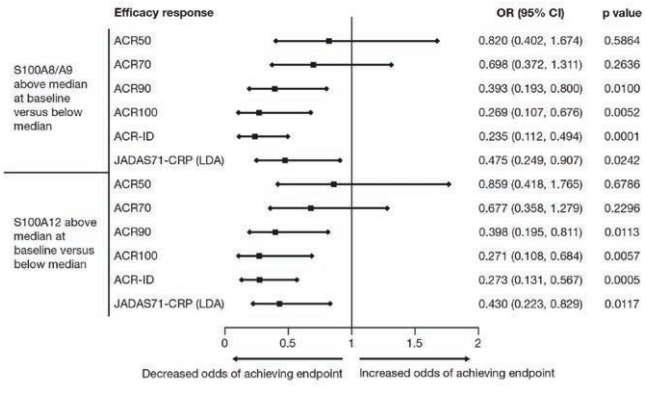
Results: Of 219 total patients, 158 (72%) had S100A8/A9 values and 155 (71%) had S100A12 values at baseline. Median S100A8/A9 and S100A12 values were 3295 ng/mL (normal range, 716–3004 ng/mL) and 176 ng/mL (normal range, 32–385 ng/mL), respectively. S100A8/A9, S100A12 and hsCRP (median 0.20 mg/dL; normal ≤0.6 mg/dL) had a low-to-moderate but significant association with disease activity at baseline; coefficients for associations between JADAS71-CRP low disease activity (LDA) and the biomarkers S100A8/A9, S100A12 and hsCRP were 0.23 (p=0.0038), 0.16 (p=0.0448) and 0.26 (p=0.0001), respectively. Baseline S100A8/A9 level above the median was associated with lower odds of ACR100 at Day 113 (p=0.0052). Figure 1 shows the associations of baseline biomarker values with Day 113 ACR and JADAS scores in the overall population. Baseline S100A8/A9 or S100A12 did not significantly influence ACR50 or ACR70 responses at Day 113, but high baseline values were associated with reduced odds of ACR90 (p=0.01), ACR100 (p=0.005), ACR-inactive disease (ID) (p=0.0001), and JADAS71-CRP (LDA) (p=0.02). By Day 477, elevated baseline S100A12 was still significantly associated with lower odds of ACR100 overall (0.467; p=0.0248) but baseline S100A8/A9 was not; at Day 645, neither was significantly associated with ACR100 response. At Day 113, changes from baseline in S100A8/A9 and S100A12 were correlated with ACR100 (coefficients of 0.22 [p=0.0082] and 0.26 [p=0.0015], respectively) and with ACR-ID (0.22 [p=0.0067] and 0.26 [p=0.0014], respectively); change in hsCRP was not significantly correlated with disease response.

Conclusion: S100A8/A9 and S100A12 may serve as prognostic biomarkers to predict response to abatacept treatment at Day 113. Changes from baseline S100A8/A9 and S100A12 levels were more highly correlated with efficacy outcomes including ACR100 and ACR-ID at Day 113 compared with hsCRP.

REFERENCES:

[1] Aljaberi N, et al. *Pediatr Rheumatol Online J* 2020;18:7.
[2] Hammer H, et al. *Arthritis Res Ther* 2011;13:R178.
[3] Nordal HH, et al. *BMC Musculoskelet Disord* 2014;15:335.
[4] Brunner H, et al. *Arthritis Rheumatol* 2018;70:1144–1154.

Figure 1. Effect of baseline S100A8/A9 or S100A12 level on efficacy response at Day 113 in the overall population



ACR50/70/90/100=50/70/90/100% improvement in ACR criteria; ID=inactive disease; JADAS71-CRP=Juvenile Arthritis Disease Activity Score in 71 joints using CRP; LDA=low disease activity; OR=odds ratio.

Acknowledgements: Professional medical writing and editorial assistance was provided by Rob Coover, MPH, at Caudex and was funded by Bristol Myers Squibb.

Disclosure of Interests: Nicolino Ruperto Speakers bureau: NR has received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, Astrazeneca-Medimmune, Bayer, Biogen, Boehringer, Bristol Myers Squibb, Celgene, Eli Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sinergie, Sobi and UCB, Consultant of: NR has received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, Astrazeneca-Medimmune, Bayer, Biogen, Boehringer, Bristol Myers Squibb, Celgene, Eli Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sinergie, Sobi and UCB, Grant/

research support from: The IRCCS Istituto Giannina Gaslini (IGG), where NR works as full-time public employee has received contributions (>10.000 USD each) from the following industries in the last 3 years: Bristol Myers Squibb, Eli Lilly, F Hoffmann-La Roche, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Grant Schulert Speakers bureau: Novartis, Consultant of: SOBI, Alyssa Sproles: None declared, Sherry Thornton: None declared, Gabriel Vega Cornejo Speakers bureau: AbbVie, Grant/research support from: Bristol Myers Squibb, Eli Lilly, Janssen, Parexel, Sanofi, Jordi Anton Speakers bureau: AbbVie, Gebro, GlaxoSmithKline, Novartis, Pfizer, Roche, Sobi, Consultant of: AbbVie, Gebro, GlaxoSmithKline, Novartis, Pfizer, Roche, Sobi, Grant/research support from: AbbVie, Amgen, Gebro, GlaxoSmithKline, Lilly, Novartis, Novimmune, Pfizer, Roche, Sanofi, Sobi, Ruben Cuttica Speakers bureau: AbbVie, Bristol Myers Squibb, GlaxoSmithKline, Lilly, Novartis, Pfizer, Roche, UCB, Paid instructor for: AbbVie, Novartis, Pfizer, Roche, Consultant of: AbbVie, Bristol Myers Squibb, GlaxoSmithKline, Lilly, Novartis, Pfizer, Roche, UCB, Michael Henrickson: None declared, Ivan Foeldvari Consultant of: Bristol Myers Squibb, Gilead, Hexal, MEDAC, Novartis, Pfizer, Sanofi, Daniel Kingsbury Consultant of: Pfizer, Margarita Askelson Consultant of: Currently working for Syneos Health providing services to Bristol Myers Squibb, Jinqi Liu Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Sumanta Mukherjee Shareholder of: Bristol Myers Squibb, GlaxoSmithKline, Employee of: Bristol Myers Squibb, GlaxoSmithKline, Robert Wong Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Daniel J Lovell Speakers bureau: Genentech, Wyeth Pharm, Consultant of: Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, GlaxoSmithKline, Hoffman-La Roche, Novartis, Pfizer, Regeneron, Takeda, UBC, Wyeth Pharma, Xoma, Alberto Martini Speakers bureau: AbbVie, Novartis, Consultant of: AbbVie, Eli Lilly, EMD Serono, Idorsia, Janssen, Novartis, Pfizer, Alexei Grom Consultant of: AB2Bio, Novartis, Sobi (NovImmune), Grant/research support from: AB2Bio, Novartis, Sobi (NovImmune), Hermine Brunner Speakers bureau: GlaxoSmithKline, Novartis, Pfizer, Roche, Paid instructor for: Novartis, Pfizer (funds go to CCHMC/employer), Consultant of: Boehringer Ingelheim, Bristol Myers Squibb, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Roche, UCB (funds go to CCHMC/employer), Grant/research support from: Bristol Myers Squibb, Pfizer (funds go to CCHMC/employer).

DOI: 10.1136/annrheumdis-2021-eular.1081

POS0077 PHYSICAL ACTIVITY AND SPORT PARTICIPATION: A COMPARISON BETWEEN CHILDREN AND ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) AND THE GERMAN GENERAL POPULATION

F. Milatz[1], M. Niewerth[1], J. Klotsche[1], J. Hörstermann[1], S. Hansmann[2], T. Kallinich[3], C. Rietschel[4], R. Trauzeddel[5], J. Peitz[6], M. Hartmann[7], H. Girschick[8], K. Minden[1,9]. *[1]German Rheumatism Research Centre, Epidemiology and Health Care Research, Berlin, Germany*; *[2]University Children's Hospital Tuebingen, Center for Pediatric Rheumatology, Autoinflammation Reference Centre Tuebingen (arcT), Tuebingen, Germany*; *[3]Charité University Medicine Berlin, Department of Pediatric Pneumology and Immunology, Berlin, Germany*; *[4]Clementine Children's Hospital, Rheumatology for Children and Adolescents, Frankfurt/Main, Germany*; *[5]Helios Klinik Berlin-Buch, Department of Paediatrics, Berlin, Germany*; *[6]Asklepios Clinic, Paediatric Rheumatology Centre, Sankt Augustin, Germany*; *[7]German Center for Paediatric and Adolescent Rheumatology, Motion Analysis, Garmisch-Partenkirchen, Germany*; *[8]Vivantes Hospital im Friedrichshain, Children's Hospital, Berlin, Germany*; *[9]Charité University Medicine Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*

Background: Physical activity (PA), including sport participation is essential for children throughout their growth and maturation. It improves physiological and psychosocial health and limits the risk of developing metabolic disorders. The beneficial effect of PA specifically in patients with JIA has also been linked to its potential regulatory effect on the balance between pro- and anti-inflammatory responses [1].

Objectives: The study aimed i) to quantify the frequency of PA and participation in (organised) sports compared to the general population, ii) to determine self-reported reasons for not practicing sports, and iii) to identify clinical parameters associated with non-participation in sports.

Methods: Data from children and adolescents with JIA recorded in the National Paediatric Rheumatological Database (NPRD) in the year 2019 were considered for the analyses. In accordance with the methodology used in the general population survey (KIGGS) [2], achievement of the WHO recommendations on PA for at least 60 minutes per day as well as sport-related data were determined on the basis of self-reported outcomes in individuals aged 3 to 17 years. In order to compare PA-related data with the general population, a sex- and age-matched sample was drawn. A logistic regression model was used to explore the association between non-participation in sports and patients' clinical outcomes.

Results: Data of 5.333 matched-pairs (mean age 11.0 ± 4.3 years, female 67%, patients' disease duration 4.8 ± 3.8 years, persistent oligoarthritis 43%) were available for evaluation. Almost 38% of patients aged 3 to 17 years met the recommended PA amount (76% aged 3 to 6; 48% aged 7 to 10; 30% aged 11 to 13; 15% aged 14 to 17). In matched controls, 21% fulfilled the WHO recommendations on PA (41% aged 3 to 6; 23% aged 7 to 10; 17% aged 11 to 13; 10% aged 14 to 17). Largest differences across JIA categories were found in persistent oligoarthritis (43%) and enthesitis-related arthritis (22%). 64% of patients and 74% of controls reported participating in sports, of which 72% of patients and 58% of controls stating to participate in a formally organised way. In both groups, boys indicated organised sports participation more often than girls. Among those who declared not participating in sports, "no interest" (patients 27% vs. controls 29%), "no suitable offer nearby" (patients 25% vs. controls 31%), "health restrictions" (patients 22% vs. controls 4%) and "no time" (patients 15% vs. controls 23%) were the most frequently mentioned reasons (multiple responses possible). CJADAS-10 (OR = 1.02, 95% CI = 1.00-1.04), CHAQ (OR = 1.79, 95% CI = 1.50-2.14), DMARD use (OR = 1.32, 95% CI = 1.15-1.53) and disease duration (OR = 0.97, 95% CI = 0.95-0.99) were significantly associated with non-participation in sports.

Conclusion: Based on self-reported data, children and adolescents with JIA meet the WHO recommendation on PA more often than general population controls. Patients are less frequently engaged in sports, but more often involved in formally organised forms. In order to bring joyful, interesting PA opportunities in line with WHO recommendations, further components (e.g. intensity), facilitators and barriers to PA and sports need to be addressed in the future while controlling for JADAS and CHAQ.

REFERENCES:

[1] Rochette E et al. JIA and physical activity: possible inflammatory and immune modulation and tracks for interventions in young populations. Autoimmun Rev 2015;14:726–734.

[2] Finger JD et al. Körperliche Aktivität von Kindern und Jugendlichen in Deutschland - Querschnittergebnisse aus KiGGS Welle 2 und Trends. Journal of Health Monitoring 2018;3:24-31.

Acknowledgements: The National Paediatric Rheumatological Database has been funded by AbbVie, Chugai, Novartis and GSK.

Disclosure of Interests: Florian Milatz: None declared, Martina Niewerth: None declared, Jens Klotsche: None declared, Jana Hörstermann: None declared, Sandra Hansmann: None declared, Tilmann Kallinich: None declared, Christoph Rietschel: None declared, Ralf Trauzeddel: None declared, Joachim Peitz: None declared, Matthias Hartmann: None declared, Hermann Girschick: None declared, Kirsten Minden Speakers bureau: Pfizer, AbbVie, Consultant of: Novartis.

DOI: 10.1136/annrheumdis-2021-eular.2356

POS0078 CROSS-SECTIONAL ANALYSIS OF INTERFERON SIGNATURE IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

R. Raupov[1], E. Suspitsin[2,3], E. Kalashnikova[1], N. Lybimova[4], E. Kuchinskaya[4], R. Mulkidzhan[2], A. Kosmin[2], M. Kostik[1,4]. *[1]Saint-Petersburg State Pediatric Medical University, Department of Hospital Pediatrics, Saint-Petersburg, Russian Federation*; *[2]N.N.Petrov Institute of Oncology, Molecular diagnostics, Saint-Petersburg, Russian Federation*; *[3]Saint-Petersburg State Pediatric Medical University, Department of Medical Genetics, Saint-Petersburg, Russian Federation*; *[4]Almazov National Medical Research Centre, Pediatrics, Saint-Petersburg, Russian Federation*

Background: the role of interferon pathways in the pathogenesis of systemic lupus erythematosus (SLE) has been proven over the past years. Existing data suggest that interferon score (IFN I score) may serve as a useful marker of disease activity and patient clinical characteristics.

Objectives: to compare characteristics of pediatric SLE patients with high and normal IFN I score.

Methods: 40 SLE patients (33 girls, 7 boys) under 18 years old were included in the cross-sectional study. In all cases the diagnosis was made using Systemic Lupus International Collaborating Clinics (SLICC) classification criteria. The data on clinical manifestations, disease activity by SLEDAI and ECLAM, laboratory findings in the onset of the disease and at the moment of interferon signature assessment were evaluated. Interferon signature was assessed by real-time PCR quantitation of 5 IFN I-regulated transcripts; median expression of ≥2 was considered as a threshold. The patients were divided into 2 groups depending on the level of interferon score: high (group1, n=31) and normal (group2, n=9).

Results: The mean age of the disease onset was 12 (9.5; 14.0) years. The most common symptoms were skin lesions (85%), arthritis (67.5%), fever (55%), mucosa (45%), CNS (37.5%) and kidney (30%) involvement. Anemia, leukopenia and thrombocytopenia were observed in 62.5%, 27.5% and 50% of cases,

while 87.5% and 70% of patients had ANA positivity and dsDNA antibodies at the onset. The comparison between the groups with increased and normal IFN I-signature is presented in Table 1.

Table 1.

Parameters	Group 1 (High IFN-s)	Group 2 (Normal IFN-s)	p-value
Girls, n (%)	25 (80.7)	8 (88.9)	0.567
The onset age, years	12.0(10.0; 14.0)	11.0 (9.0; 13.0)	0.353
Time to IFN-signature study, months from onset	18.3 (7.0; 26.5)	0.97 (0.87;1.73)	0.987
Skin involvement, n (%)	12 (38.7)	4 (44.4)	0.837
CNS involvement, n(%)	8 (25.8)	1 (11.1)	0.353
Arthritis, n(%)	11 (35.5)	2 (22.2)	0.455
Anemia, n(%)	9 (29.0)	2 (22.20	0.687
Leucopenia, n(%)	9 (29.0)	1 (11.1)	0.274
ANA-positivity, n (%)	27 (87.1)	5 (55.6)	0.037
anti dsDNA antibodies, n(%)	12 (38.7)	2 (22.2)	0.361
Rheumatoid factor, n (%)	11 (35.5)	0 (0.0)	0.036
Hypocomplementemia, n (%)	18/28 (64.3)	2/6 (33.3)	0.162
Ferritin level, mkg/l	112.0 (39.0; 271.0)	21.0 (5.3; 23.7)	0.0008
Hematuria, n (%)	10 (32.3)	0 (0.0)	0.049
Proteinuria, n (%)	11 (35.5)	0 (0.0)	0.036
SELENA-SLEDAI, points	9 (2;15)	1 (0; 4)	0.073
ECLAM, points	3.0 (1.0; 6.0)	1.0 (0.0; 1.5)	0.048
Treatment with Rituximab or Cyclophosphamide, n (%)	22 (71.0)	3 (33.3)	0.040
GCS dose 0,2 mg/kg achievement for 6 months, n (%)	9/21 (42.9)	5/6 (83.3)	0.080

Conclusion: high IFN I-signature correlated with kidney involvement, ANA and RF-positivity, ferritinemia, proteinuria and hematuria. Patients with high IFN I-signature received more aggressive treatment and needed longer glucocorticosteroid (GCS) treatment. More meticulous dynamic evaluation of IFN-signature is needed to clarify its role as a predictive and prognostic marker.

Acknowledgements: This work was supported by the RSF grant № 20-45-01005.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1956

POS0079 PATIENTS WITH JUVENILE SYSTEMIC SCLEROSIS HAVE A DISTINCT PATTERN OF ORGAN INVOLVEMENT.RESULTS FROM THE JUVENILE SYSTEMIC SCLEROSIS INCEPTION COHORT. WWW.JUVENILE-SCLERODERMA.COM

I. Foeldvari[1], J. Klotsche[2], O. Kasapcopur[3], A. Adrovic[3], K. Torok[3], M. T. Terreri[3], A. P. Sakamoto[3], B. Feldman[3], V. Stanevicha[3], J. Anton[3], F. R. Sztajnbok[3], R. Khubchandani[3], E. Alexeeva[3], M. Katsikas[3], S. Sawhney[3], V. Smith[3], S. Appenzeller[3], T. Avcin[3], M. Kostik[3], T. Lehman[3], E. Marrani[3], D. Schonenberg[3], W. A. Sifuentes-Giraldo[3], N. Vasquez-Canizares[3], M. Janarthanan[3], M. Moll[3], D. Nemcova[3], A. Patwardhan[3], M. J. Santos[3], C. Battagliotti[3], L. Berntson[3], B. Bica[3], J. Brunner[3], R. Cimaz[3], P. Costa Reis[3], D. Eleftheriou[3], L. Harel[3], G. Horneff[3], S. Johnson[3], D. Kaiser[3], T. Kallinich[3], D. Lazarevic[3], K. Minden[2], S. Nielsen[3], F. Nuruzzaman[3], S. Opsahl Hetlevik[3], Y. Uziel[3], N. Helmus[1]. *[1]Hamburg Centre for Pediatric and Adolescent Rheumatology, Schön Klinik Hamburg Eilbek, Hamburg, Germany*; *[2]German Rheumatism Research Center, German Rheumatism Research Center, Berlin, Germany*; *[3]jSSc Collaborative Group, Hamburg Centre for Pediatric and Adolescent Rheumatology, Hamburg, Germany*

Background: Juvenile systemic sclerosis (jSSc) is a rare disease with a prevalence of around 3 in 1,000,000 children. To better capture the clinical manifestations of jSSc the juvenile systemic sclerosis inception cohort (jSScC) has been prospectively enrolling patients with predetermined clinical variables over the past 12 years. One of the goals is to study the demographic, clinical features, and physician and patient reported outcome differences between those with juvenile limited cutaneous (lc) compared to diffuse cutaneous (dc) disease subtypes, to determine if characteristics are similar or different between dc and lc jSSc.

Objectives: Evaluation of the baseline clinical characteristics of jSSc patients in the jSScC. Compare clinical phenotype between diffuse (dcjSSc) and limited cutaneous (lcjSSc) subtypes.

Methods: Demographic, physical examination, organ system evaluation, autoantibody profile, treatment, and patient and physician reported outcome variables were evaluated from the jSSc Inception cohort and summary statistics applied using chi-square test and Mann Whitney U-test comparing lcjSSc and dcjSSc subtypes.

Results: At the time of data extraction, 175 jSSc patients were enrolled in the cohort, 81% were Caucasian and 81% female. Diffuse cutaneous jSSc subtype predominated (73%). Mean disease duration was 3.1 year (±2.7). Mean age at Raynaud´s was 10 years (+3.8) and mean age of first non-Raynaud´s was 10.2 years (±3.8). Significant differences were found between dcjSSc versus lcjSSc, regarding several clinical characteristics. Patients with diffuse cutaneous subtype had significantly higher modified Rodnan skin score (p=0.001), presence of sclerodactyly (p=0.02), presence of Gottron's papules (p=0.003), presence of telangiectasia (p=0.001), history of digital tip ulceration (p=0.01), and frequency of elevated CK value (p=0.04). Cardiac involvement was significantly higher in limited cutaneous jSSc subtype (p=0.02). Diffuse cutaneous jSSc patients had significantly worse scores for Physician Global Assessment of disease activity (38 vs 25; p=0.002) and disease damage (34 vs 19; p=0.008).

Table 1. Comparison of demographic data and significant differences between dcjSSc and lcjSSc at time of inclusion

	Whole Cohort N=175	Diffuse Subtype N=128	Limited Subtype N=47	P value
Female to Male Ratio	4.3:1 (142/33)	4.1:1 (103/25)	4.8:1 (39/8)	0.829
Cutaneous subtype				
Diffuse subtype	73% (128)	128	0	
Limited subtype	27% (47)	0	47	
Mean Disease duration (years)	3.1 (± 2.7)	3.3 (± 2.9)	2.6 (± 2.2)	0.135
Mean age of onset of Raynaud´s (years)	10.0 (± 3.8) 17 non-Raynaud	9.8 (± 3.6) 10 non-Raynaud	10.6 (± 4.3) 7 non-Raynaud	0.219
Mean age of onset of non-Raynaud´s (years)	10.2 (± 3.9)	10.0 (± 3.7)	10.9 (± 4.3)	0.173
Disease modifying drugs	88% (154)	89% (114)	85% (40)	0.446
Cutaneous				
Mean modified Rodnan skin score	14.3 (0-51)	17.4 (0-51)	6.1 (0-24)	0.001
Gottron Papules	27% (46/171)	33% (41/124)	11% (5)	0.003
Sclerodactyly	78% (126/162)	82% (98/119)	65% (28/43)	0.020
Laboratory values	25% (30/122)	30% (26/88)	12% (4/34)	0.041
Elevated CK				
Vascular				
Telangiectasia	36% (56/154)	44% (49/111)	16% (7/43)	0.001
History of ulceration	53% (91/173)	61% (77/127)	30% (14/46)	0.001
Cardiac	6% (10)	2% (3)	15% (7)	0.002
Cardiac Involvement				
Patient Related Outcomes				
Physician global disease activity (0-100) min -max	35 (0-90) n=141	38 (0-90) n=108	25 (0-80) n=33	0.002
Physician global disease damage (0-100) min -max	31 (0-85) n=140	34 (0-85) n=108	19 (0-60) n=32	0.008

Conclusion: Results from this large international cohort of jSSc patients demonstrate significant differences between dcjSSc and lcjSSc patients. According to the general organ involvement and physician global scores, the dcjSSc patients had significantly more severe disease. These observations strengthen our previous findings of the unique organ pattern of pediatric patients.

Supported by the "Joachim Herz Stiftung"

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.799

POS0080 TOFACITINIB TREATMENT IN CHILDREN WITH RHEUMATIC DISEASES: SINGLE-CENTER EXPERIENCE

M. Kostik[1], R. Raupov[1], E. Suspitsin[2], E. Isupova[1], T. Gabrusskaya[3], M. Dubko[1], L. Snegireva[1], V. Masalova[1], T. Ermachenkova[2], L. Sorokina[1], T. Likhacheva[1], M. Kaneva[1], E. Gaidar[1], O. Kalashnikova[1], V. Chasnyk[1]. *[1]Saint-Petersburg State Pediatric Medical University, Hospital Pediatrics, Saint-Petersburg, Russian Federation*; *[2]N.N.Petrov Institute of Oncology, Molecular diagnostics, Saint-Petersburg, Russian Federation*; *[3]Saint-Petersburg State Pediatric Medical University, Gasrtoenterology, Saint-Petersburg, Russian Federation*

Background: While efficacy of tofacitinib (TOF) has been proven in many adult immune-mediated conditions, the information on its' safety and efficacy in the pediatric population is limited.

Objectives: to evaluate the safety and efficacy of TOF in children with immune-mediated diseases.

Methods: from 23 children whom TOF has been initiated, 17 children with treatment duration of > 6 months were extracted including 16 girls and 1 boy with the following diagnosis: JIA (n=10), autoinflammatory diseases (AID) (n=5) and juvenile dermatomyositis (JDM) (n=2) due to impossibility to taper corticosteroids (CS) or previous biologic treatment failed. The treatment outcome was classified according to the opinion of the attending physicians as complete response (CR) i.e., the absence of disease activity, partial response (PR) – a significant

Table 1.

#	Diagnosis	Indication	Previous biologics	Current treat-ment	TOF, dose, mg/kg	Duration of TOF treat-ment, months	Genetic variants detected	Efficacy
1	AID	Severe inflamma-tion, aortitis, colitis	INX, TCZ, ADA	CS, TOF	0.5	7	NOD2 c.2578G>A (p.A860T); NOD2 c.2722G>C (p.G908R) ADA2 c.927G>A (p.M309I)	PR
2	JDM	recurrent skin rash		CS, TOF, MTX	0.5	5		PR
3	JDM	skin involvement, ulceration		CS, MTX, TOF	0.7	7	NLRP12c.154G>A (p.G52S)	CR
4	AID, IFP	skin rash, recurrent inflammation, failure to thrive	CAN, TCZ	CS, TOF, CAN	0.5	32	RNASEH2B c.916dupA (p.I309Nfs*7)	CR
5	JIA, poly	severe arthritis	ETA,TCZ, ADA	TOF,TCZ	0.27	22		PR
6	soJIA	resistant to CS and biologic systemic inflammation, arthritis	TCZ, ABC, CAN	TOF, TCZ	0.4	23		PR
7	JIA, poly (RF+) alopecia	Severe arthritis, lung involvement, alopecia	ETA, ABC, TCZ, ADA	TOF, MTX, CS	0.3	37	IL1RN c.10G>C (p.A4P); NLRP3 c.2113C>A (p.Q705L); MEFV c.1105C>T (p.P369S)	CR
8	IFP, CANDLE-like	recurrent inflammation, digital ischemia, ulcers, CS-dependency	ETA, RTX, CAN	TOF, CS	0.25	43	MDA5 NLRP3	CR
9	AID, IFP	systemic inflammation, ulcers	ETA	TOF, CS	0.5	13		CR
10	JIA, ERA	arthritis	ETA	TOF, MTX	0.2	44		CR
11	JIA, poly	arthritis	ABC, ETA	TOF, MTX	0.25	38		CR
12	JIA, poly	Arthritis, alopecia	ETA	TOF	0.15	31		PR
13	soJIA + MAS	systemic inflammation, arthritis	TCZ, CAN, ETA	TOF, CS	0.5	38		NR
14	JIA, poly	arthritis	INX, ETA, ADA, TCZ	TOF, MTX	0.2	24		PR
15	AID	Systemic inflammation, CS-dependency	TCZ	TOF,CS	0.5	21	STAT3, c1343A>C	PR
16	JIA, ERA	arthritis	ETA	TOF	0.25	21		PR
17	JIA, poly	arthritis	ADA, TCZ, ETA	TOF	0.15	39		CR

improvement of symptoms and disease activity or no response (NR) - no changes in disease activity.

Results: Mean duration of TOF treatment was 25.4±18.9 months. TOF was used as monotherapy in 3 cases, in combination with methotrexate (MTX) in 6, and in combination with other biologics in 3 children: tocilizumab (n=2) and canakinumab (n=1). Nine patients received CS. (Table 1). In two JIA patients with alopecia TOF induced intensive hair growth and controlled joint inflammation. 9 patients had CR: AID (n=3), JIA (n=4) and JDM(n=1): 7 patients had PR and 1 was NR. 13 patients had a previous history of several subsequent failed biologic: 4 biologics (n=1), 3 biologics (n=6), 2 biologics (n=1), 1 biologic (n=5). TOF treatment allowed discontinuation of CS in patient#6 and reducing the CS in 8/10 patients from 0.4 ±0.27 mg/kg to 0.15±0.1 mg/kg in 3.7±3.4 times: in 2 cases the tapering of steroids failed (Figure 1). 4 patients had side effects not requiring treatment discontinuation: liver enzymes elevation (n=2), hypercholesterolemia (n=1), lymphadenitis (n=1). In pt#6 after achievement of the remission the TOF dosage was decreased up to 2 times and tocilizumab intervals were increased up to 6 weeks.

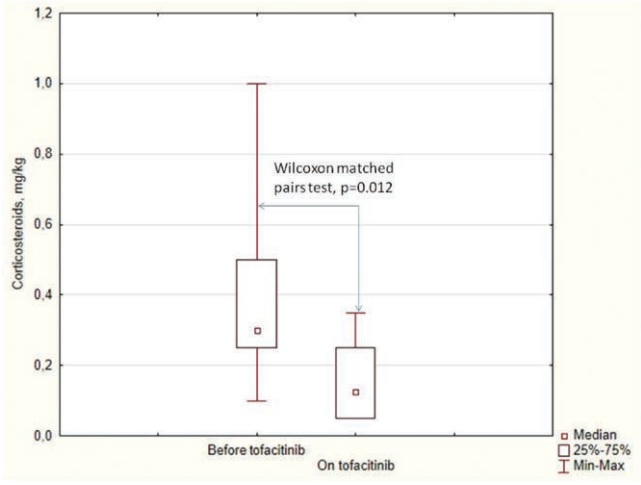


Figure 1.

Conclusion: Tofacitinib is a promising agent in treating pediatric rheumatic diseases. In our study the best results were in AID patients with rare alleles in interferon pathway genes, patients with arthritis and alopecia and in children with JDM. Future studies are needed to identify clear indications for treatment with JAK-inhibitors.

Acknowledgements: This work was supported by the RSF grant №20-45-01005.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1913

POS0081 CLINICAL FEATURES OF PEDIATRIC BEHÇET'S DISEASE IN CHINA

S. Zheng[1], Z. Huang[1], Y. Liu[1], Y. Huang[1], T. W. Li[1]. [1]*Guangdong Second Provincial General Hospital, Rheumatology, Guangzhou, China*

Background: Behçet's disease (BD) is a systemic inflammatory disease involving primarily the oral and genital mucosa, skin and eyes. Some patients exhibit broader involvement with multi-organ system inflammation, causing significant morbidity and mortality. With much of the literature focused on adult-onset BD, the clinical spectrum of BD in children is not well studied. The diagnosis of pediatric BD is difficult to make due to its rarity in childhood, the paucity of experience among pediatricians and the lack of validated diagnostic criteria.

Objectives: We aim to describe the clinical characteristic of children with Behçet's disease in China.

Methods: We performed a cross-sectional cohort analysis of patients with BD recruited between June 2017 and May 2020. We enrolled a total of 848 patients with pediatric BD (onset prior to age 18 years) and 1531 patients with adult-onset BD. Clinical data were collected by retrospective chart review.

Results: From a cohort of 848 patients with pediatric BD (412 males, 436 females), the average age of disease onset was 11.59 ± 4.11 years and the earliest case was appeared the first symptom at 7 months of age. Clinical manifestations in this group included recurrent oral aphtosis (100%), genital ulcers (77.71%), ocular involvement (30.19%), skin involvement (63.56%), neurological involvement (4.60%), gastrointestinal involvement (20.05%), vascular involvement (9.79%), heart valve involvement (3.66%), arthritis / arthralgia (32.43%), fever (0.35%) and positive pathergy test (21.11%; Table 1). The prevalence of these clinical findings was largely similar to that of adult BD patients with the exception of mild differences in the frequency of gastrointestinal, heart valve, joint involvement and fever. However, the time from symptom onset to diagnosis was significantly longer in children with BD compared to adults (13.34±9.13 years vs. 6.73±33.21 years, P<0.001). The most common initial symptom in pediatric BD was recurrent oral aphtosis (91.57% vs. 86.28% in adults, P<0.001).

In the pediatric group, clinical manifestations also differed between males and females. In addition to oral ulcers, the most common clinical manifestations in male patients were ocular involvement (42.23%), vascular involvement (15.53%), heart

valve involvement (5.10%) and epididymitis (9.95%). Among female patients, the frequency of genital ulcers is significantly higher than that of men (86.24% vs. 68.69%, P<0.001).

Conclusion: We described the clinical characteristics of a large cohort of pediatric BD patients in China. While the clinical manifestations are largely similar to adult BD, the time from symptom onset to diagnosis is significantly delayed in pediatric patients. Our study highlights the need to improve awareness of BD among pediatric providers to facilitate rapid diagnosis and treatment in children.

REFERENCES:

[1] Yıldız et al. Pediatric Behçet's disease- clinical aspects and current concepts. Eur J Rheumatol 2020; 7(Suppl 1): S38-S47.

[2] Koné-Paut. Behçet's disease in children, an overview. Pediatric Rheumatology (2016) 14:10.

Table 1. Comparison of clinical features of BD in children and adults

	Children (n=848)	Adult (n=1531)	P
Age of first symptom (y)	11.59±4.11	27.08±7.91	
Sex(M/F)	412/436		
Years of diagnosis (y)	13.34±9.13	6.73±33.21	<0.001
Recurrent oral aphthosis	848 (100%)	1518 (99.15%)	0.007
Genital Ulcers	659 (77.71%)189	1152 (75.24%)379	0.176
Ocular signs	256 (30.19%)592	508 (33.18%)1023	0.134
Cutaneous signs	539 (63.56%)309	1020 (66.62%)511	0.132
Neurological signs	39 (4.60%)809	82 (5.36%)1449	0.421
Gastrointestinal signs	170 (20.05%)678	244 (15.94%)1387	0.001
Vascular signs	83 (9.79%)765	162 (10.58%)1369	0.542
Heart valve signs	31 (3.66%)817	110 (7.18%)1421	<0.001
Joint signs	275 (32.43%)573	612 (39.97%)919	<0.001
Fever	3 (0.35%)845	22 (1.44%)1509	0.013
Positive pathergy test	179 (21.11%)669	347 (22.66%)1184	0.381

Acknowledgements: China Behcet' Disease Patients Assossiation.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3621

POS0082 PERFORMANCES OF THE RISK FACTORS AND PEDIATRIC VASCULITIS ACTIVITY SCORES FOR DISEASE SEVERITY IN CHILDREN WITH MULTISYSTEM INFLAMMATORY SYNDROME

B. Sözeri[1], Ş. Çağlayan[1], A. Akyol[2], K. Ulu[1], T. Coşkuner[1], C. Hasbal Akkuş[2], F. Demir[1]. [1]*Health Sciences University, Umraniye Traning and Research Hospita, Pediatric rheumatology, Istanbul, Turkey*; [2]*Health Sciences University, Umraniye Traning and Research Hospita, Pediatrics, Istanbul, Turkey*

Background: Multisystem Inflammatory Syndrome in Children (MIS-C) is observed by hyperinflammation and cytokine storm. The spectrum of severity ranged from standard hospitalization to pediatric intensive care unit management. There is no specific activity score that predicts whether this hyperinflammatory state will be severe or result in mortality in pediatric patients. There are activity scores used in KD and other vasculitis such as Kobayashi score (KS) and Pediatric Vasculitis Activity Score (PVAS) that determine the severity of the disease in children.

Objectives: Based on the clinical similarity of MIS-C to these disease groups, we wanted to evaluate the performance of these disease activity scores. Also, we aimed to identify the factors associated with the disease severity of patients with MISC

Methods: We retrospectively enrolled a single-center cohort of 45 consecutive pediatric patients with MISC admitted to Umraniye Training and Resrach Hospital, Pediatric Rheumatology Clinic, Istanbul, Turkey, from April 20 to December 31, 2020. Medical information of each patient including demographic data, clinical characteristics, laboratory results, and outcomes was extracted retrospectively through review of electronic medical records. We analyzed all score systems including KS, PVAS, NLR, cHIS, and C-reactive protein/albumin ratio (CAR) as assessment factors for diagnosis for severe disease and evaluation of disease activity in MISC. All scores were compared between two groups and receiver operating characteristic (ROC) curve analysis was performed to evaluate diagnostic utility.

Results: We reported 45 patients (10 female, 35male) with MISC. Their mean age was 9.65±4.93 years (7 months-18 years). All patients had fever (median 4 days), 71 % patients had acute gastrointestinal symptoms, 37.8 % of patient's conjunctivitis and only 5 patients had respiratory findings at admission. Twenty-four (46.7%) patients met criteria for classic KD. Macrophage activation syndrome and myocardial dysfunction with or without cardiogenic shock were seen 14 and 10 patients respectively. All the patients had positive serology for SARS-CoV-2, abnormal complete blood counts and coagulation tests, and elevated inflammatory markers.

We divided the disease severity into a moderate or severe group based on admission on intensive care unit (ICU). There were 15 patients with severe illness (33%). The median age of these patients was significantly older (11.3 years vs 9.16 years, p=0.05). The median hospital stay period was 10 days. The median need for intensive care was on the first day (1-14th days), and the median lasted 5 (1-9) days. The majority of MISC patients were on Intravenous immunoglobulin (IVIG) (89%), and corticosteroid (73.3%). A total of 12 patients received anakinra. In the severe group, all patients had higher values of KD, PVAS, NLR, cHIS, and CAR than the patients in moderate group. For severe MISC, the area under receiver operating characteristic curve (AUC) was 0.864 (95% confidence interval [CI], 0.729–1) for the PVAS, 0.911 (95% CI, 0.827–0.995) for the NLR, and 0.853 (95% CI, 0.744–0.963) for the CAR, with optimal cut-off values of 3.5, 9.05, and 4.86, respectively. Thirty-eight (84.4%) of the 45 patients met two or more cHIS criteria at the time of their hospitalization; 39% of these patients were identified as severe group (OR 1.62, 95% CI 1.27-2.13, p=0.04). At the time of diagnosis, 29 patients with a Kobayashi score greater than 4 were detected, of which 15 required intensive care (OR 2.07, 95% CI 1.42-3.0, p=0.00).

Conclusion: This study demonstrated that both inflammatory scores (CAR and NLR) and disease activity scores (KS, PVAS and cHIS) can be used to aid the assessment for severity of MISC

REFERENCES:

[1] Webb BJ, et al Lancet Rheumatol. 2020 Dec;2(12):e754-e763.

[2] Feldstein LR et al N Engl J Med. 2020;383(4):334-346

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2916

POS0083 USEFUL EXPERIENCE OF RHEUMATOLOGISTS FOR UNDERSTANDING OF THE DISEASE ORIGIN AND APPROACHES TO THERAPY IN FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

I. Nikishina[1], S. Arsenyeva[1], V. Matkava[1], A. Arefieva[1], M. Kaleda[1], T. Pachkoria[1], Z. Kolkhidova[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Paediatric, Moscow, Russian Federation*

Background: Many monogenic genetic conditions, such as auto-inflammatory diseases (AIDs), have similar clinical manifestations and immunopathogenesis to "classic" rheumatic diseases (RD). Such cases may include Fibrodysplasia ossificans progressiva (FOP), an extremely rare genetic disease, which, according to our previous study and data from other authors1, may represent an example of AID with catastrophic heterotopic ossification due to a mutation in the ACVR1 gene. it seems that the experience of rheumatologists, especially children's ones, will be useful in the treatment of FOP.

Objectives: To analyzed the dynamics of clinical manifestations and to therapy approaches including target anti-inflammatory drug Tofacitinib (TOFA) in the one of the world's largest groups of patients (pts) with FOP.

Methods: The study was based on the analysis retrospective and prospective observation of the 35 pts (17 males and 18 females) with a verified diagnosis of FOP for the period from 1998 to 2020. In 9 pts with severe course of FOP TOFA administration were evaluated.

Results: In all 35 pts the diagnosis was verified by "classic" FOP phenotype: malformed great toes in 33 pts (94,3%); short malformed thumbs-8 (22.8%); peripheral osteochondromas-20 (57.1%); abnormalities of the cervical spine-32 (91.4%), multiple heterotopic ossifications-32 (91,4%). Genetic tests were done in 26, it confirmed mutation in the ACVR1 gene in 100%. Long term follow-up detected a lot of spondyloarthritis-like signs similar to the manifestation of RD: ankylosis of the facet joints and vertebral bodies (by the type of syndesmophytes) in most pts, sacroiliitis, confirmed by radiological methods (X-ray, CT, MRI), gradual ankylosis in the peripheral joints in 18 (56.4%), synovitis in large joints in 8 (25%) pts (knee and hip mostly). In 9 pts with the most difficult course with rapid progression of ossification due to continuous flares despite the NSAIDs and steroids intake, we tried to use TOFA after the approval of the local Ethic Committee. We use the similar dose to randomized trial for JIA (up to 5 mg twice a day). The first patient was 16 y.o. at the time of TOFA administration in December 2019, the age of the other pts was from 2 to 12 y.o. By present time duration of TOFA therapy is from 6 to 15 mo. For the previous 6 months before TOFA initiation the number of flares was in average 8 per patient. After 6 months of TOFA treatment the number of new flares decreased to 0-1, except youngest patient of 2 y.o. in whom the number of flares decreased from 10 to 4 per the same period. In all 9 pts we minimize the dose or completely stop the steroids. New nodes formation stopped immediately in most pts and also the significant motion improvement of large (shoulder) joints were established. Drug tolerance was good in all pts, no AE were registered. But despite the good clinical effect without new heterotopic ossification in our first patient, we found continuous intraskeletal ossification between vertebral bodies, facet and sacroiliac joints in MRI.

Conclusion: We are confident that the processes of heterotopic ossification in FOP are very similar to new born formation phenomenon in spondyloarthritis and reliable suppression of inflammation can interrupt the progression of the disease. We used similar justifications to our colleagues for the use of anti-cytokine drugs, but used a JAK-kinase inhibitor, it was extremely important the oral rout of drug administration and possibility to escape any injections in FOP. TOFA demonstrated positive effect

and safety in children with severe course of FOP. It showed their advantages over the use of steroids and possibility to inhibit the rate of progression.

REFERENCES:

[1] R.Haviv et al. Is fibrodysplasia ossificans progressiva aninterleukin-1 driven auto-inflammatory syndrome? Pediatric Rheumatology (2019) 17:84 //doi.org/10.1186/s12969-019-0386-6

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4307

POS0084 SEPTIC ARTHRITIS IN CHILDREN. A LONGITUDINAL POPULATION-BASED STUDY IN WESTERN AUSTRALIA

J. Nossent[1,2], D. Preen[3], H. Keen[1,4], W. Raymond[1], C. Inderjeeth[1,2]. [1]*The University of Western Australia, Medical School, Rheumatology Section, Perth, Australia*; [2]*Sir Charles Gairdner Hospital, Rheumatology, Nedlands, Australia*; [3]*The University of Western Australia, School of Population and Global Health, Bentley, Australia*; [4]*Fiona Stanley Hospital, Rheumatology, Murdoch, Australia*

Background: The incidence of Septic arthritis (SA) in adults is rising, but few data are available for children (1). SA symptomatology in young children is often atypical and delayed diagnosis can cause significant morbidity.

Objectives: To describe the incidence, risk factors and long-term outcomes in children hospitalised with septic arthritis (SA) in Western Australia (WA).

Methods: We extracted population-based longitudinally linked administrative health data for patients under 16 years with a first inpatient primary or secondary code of 711.xx (ICD9-CM) and M00.xx (ICD10-AM) in WA for the study period 1990-2010 (to allow a minimum 5 year followup). We report annual incidence rates per 100.000 (AIR), prior conditions during lookback (median 15 months, IQR 5-45) as well as joint and other comorbidities including Charlson comorbidity index (CCI) and standardised mortality rates (SMR) during a median follow-up of 10 years. Age and gender speficic population and mortality rate data were obtained from the Australian Bureau of Statistics.

Results: A total of 891 patients (62% male, median age 6.4 (IQR 1.9-10.6) years with 34% <3 years of age) had a first admission for SA. AIR was 9.85 (CI 4.79-14.41) overall with higher rates in males (11.9 vs 7, p<0.01) and no apparent period (Figure 1) or seasonal variation. Knees (43.9%), hips (34.6%), and ankles (13.3%) were most frequently affected with Staphylococci (49%) the predominant organism in patients with positive cultures (41.5%). Prior infections (40.4%) and respiratory disease (7 %) were the main preexisting morbidities. Mean hospital stay was 5.78 (± 6.4) days with ICU admission required in 1.9%, while 30-day readmittance rate was 10.4%. During follow-up 25 patients (3%) had recurrent/persistent osteomyelitis, nine patients were diagnosed with osteoarthrosis (1.1%) and five patients (0.6%) underwent joint replacement. More female patients developed new comorbidity (CCI>0, 34.6 vs 27.2%, p=0.02) including diabetes (4.2% vs 0%, p=0.001), cardiovascular events (4.2 vs 1.4%, p=0.002) and chronic arthritis (1% vs 0, p=0.05). While the crude mortality rate was low (0.3%) SMR was significantly increased for female patients (10.52, CI 1.59-41.6).

Conclusion: The statewide incidence of septic arthritis in children in WA is similar to a recent report (1) and did not change over a 20-year period. In this large population based study, subsequent bone/joint disease occured in 4.6 %, while a third of patients developed other comorbidity before the age of 18. Such (subclinical) comorbidity may thus be a contributing factor to SA development and to the increased mortality risk in female SA patients.

REFERENCES:

[1] Cohen E, Katz T, Rahamim E, Bulkowstein S, Weisel Y, Leibovitz R, Fruchtman Y, Leibovitz E. Septic arthritis in children: Updated epidemiologic, microbiologic, clinical and therapeutic correlations. Pediatr Neonatol. 2020 Jun;61(3):325-330. doi: 10.1016/j.pedneo.2020.02.006

Figure 1. Annual incidence of septic arthritis per 100,000 population <16 years in Western Australia over period 1990-2010 by gender.

Acknowledgements: The authors wish to thank the Arthritis Foundation of WA for their support and would like to acknowledge the support of the Western Australian Data Linkage Branch, the Western Australian Department of Health, and the data custodians of, the Hospital and Morbidity Data Collection, the Emergency Department Data Collection the WA Cancer Register and the WA Death Register for their assistance with data collection.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2269

POS0085 EVALUATION OF DURATION OF CLINICAL REMISSION IN CHILDREN WITH NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS AFTER WITHDRAWAL OF ANTI – TUMOR NECROSIS FACTOR - ALPHA THERAPY

I. Tsulukiya[1], E. Alexeeva[1,2], T. Dvoryakovskaya[1,2], K. Isaeva[1], R. Denisova[1], O. Lomakina[1], A. Mamutova[1], A. Chomakhidze[1], A. Fetisova[1], M. Gautier[1], I. Kriulin[1,2], E. Krekhova[1,2]. [1]*National Medical Research Center of Children's Health, Rheumatology, Moscow, Russian Federation*; [2]*Sechenov First Moscow State Medical University, Pediatric, Moscow, Russian Federation*

Background: Juvenile idiopathic arthritis (JIA) is the most common and prevalent rheumatic disease in childhood which is based on a chronic autoimmune inflammation. Inactive disease and remission are now the primary treatment goal in JIA and biologics have been playing an important role to reach this objective. The biologics of the first choice for the treatment of non-systemic JIA are the Tumor Necrosis Factor - alpha (TNFα) inhibitors; on this therapy patients can achieve clinically inactive disease and long-term remission.

Currently, little is known about when or how to stop TNFα inhibitors, when a good clinical response is achieved, and therefore no guidelines are available.

Objectives: To estimate the length of clinical remission after discontinuation of treatment with TNFα inhibitors in patients with non-systemic juvenile idiopathic arthritis.

Methods: A total of 393 patients with JIA who were treated with TNFα inhibitors at the Rheumatology Department of the National Medical Research Center of Children's Health (Moscow, Russia) were screened for inclusion in this retrospective study.

Patients were treated with etanercept 1 times a week, 0.8 mg per kg of body weight per dose, with adalimumab 24 mg/m2 body surface area administered every other week until the end of therapy.Treatment was terminated abruptly. Inactive disease was defined according to the preliminary criteria of Wallace et al.[1]

Results: 77 patients (27—male, 50—female) with a mean age at diagnosis of 4 years (range 1–18 years) were included in the analysis. Of those, 69 of them discontinued TNFα inhibitors due to a long-term remission on treatment, 8 patients as a result of side effects, and there were excluded from our study.:

allergic reaction (n = 5), development of uveitis (n = 1), alopecia (n = 1), recurrent infection (n=11).The clinical subtypes of JIA were RF-negative polyarticular JIA -28 (40,58%) oligoarthritis—38 (55,07%), enthesitis-related arthritis—3 (4,35%). TNFα inhibitors were started after a mean 46,43 (range 1–144) months of disease. The mean duration of therapy with TNFα inhibitors were 46,63 (range 10-113) months, with a mean duration of remission on medication 40,63 (range 6-107) months before withdrawal of TNFα inhibitors.

40/69 (57,97 %) patients did not develop a disease exacerbation and remained in long-term remission off medication—more than 24 months.

Early flares, that is less than 6 months after termination of TNFα inhibitors, were observed in 4/69 (5,8%) patients.

29 (42,03%) patients restarted TNFα inhibitors after exacerbation, due to lack of improvement after no biological DMARDs. All patients in whom TNFα inhibitors were reinitiated responded satisfactorily.

Conclusion: Among patients with JIA in whom TNFα inhibitors were discontinued after inactive disease was achieved, 57,97 % had disease in clinical remission more than 24 months after stopping anti-TNFα therapy. No association was observed between the duration of inactive disease prior to TNFα inhibitors cessation and the time to disease relapse. In addition, we also ob- served no correlation between the risk of flare and the length of anti-TNF α therapy after inactive disease was achieved. In our population, TNFα antagonists were withdrawn a median of 38 (4-107) months after inactive disease was achieved. Data from our experience with anti-TNF α agents in the treatment of JIA suggest that 57,97 % of patients can be successfully withdrawn from TNF α antagonists for at least 24 months.

REFERENCES:

[1] Wallace CA, Giannini EH, Huang B, Itert L, Ruperto N, for the Childhood Arthritis and Rheumatology Research Alliance (CARRA), the Pediatric Rheumatology Collaborative Study Group (PRCSG), and the Paediatric Rheumatology Interna- tional Trials Organisation (PRINTO). American College of Rheumatology provisional criteria for defining clinical in- active disease in select categories of juvenile idiopathic arthritis. Arthritis Care Res (Hoboken) 2011;63:929–36.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2257

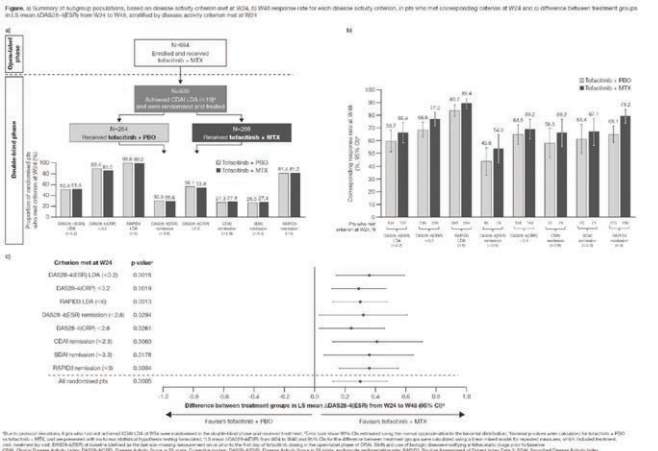
Rheumatoid arthritis - non biologic treatment and small molecules - PART 1

POS0086

ANALYSIS OF DISEASE ACTIVITY MEASURES IN THE CONTEXT OF A METHOTREXATE WITHDRAWAL STUDY AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB 11 MG ONCE DAILY + METHOTREXATE: POST HOC ANALYSIS OF DATA FROM ORAL SHIFT

R. Fleischmann[1], B. Haraoui[2], M. H. Buch[3,4], D. Gold[5], G. Sawyerr[6], H. Shi[7], A. Diehl[7], K. Lee[6]. [1]*Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Department of Medicine, Dallas, TX, United States of America*; [2]*Institut de Rhumatologie de Montréal, Montreal, QC, Canada*; [3]*School of Biological Sciences, Faculty of Biology, Medicine & Health, University of Manchester, Centre for Musculoskeletal Research, Manchester, United Kingdom*; [4]*NIHR Manchester Biomedical Research Centre, Manchester, United Kingdom*; [5]*Pfizer Inc, Inflammation and Immunology, Montreal, QC, Canada*; [6]*Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*; [7]*Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America*

Background: The Phase 3b/4 study ORAL Shift demonstrated sustained efficacy and safety of tofacitinib modified-release (MR) 11 mg once daily (QD) following methotrexate (MTX) withdrawal that was non-inferior to continued tofacitinib + MTX use (per DAS28-4[ESR]), in patients (pts) with rheumatoid arthritis (RA) who achieved CDAI-defined low disease activity (LDA) with tofacitinib + MTX at Week (W)24.[1]
Objectives: To assess the performance of alternative disease activity measures at W24 (randomisation) and W48 (study endpoint) in ORAL Shift.
Methods: ORAL Shift (NCT02831855) enrolled pts aged ≥18 years with moderate to severe RA and an inadequate response to MTX. Pts received open-label tofacitinib MR 11 mg QD + MTX for 24 weeks. Achievement of CDAI LDA (≤10) at W24 was set as the criteria for entry to the 24-week double-blind MTX withdrawal phase, with pts randomised 1:1 to receive tofacitinib MR 11 mg QD + placebo (PBO) (ie blinded MTX withdrawal) or continue tofacitinib + MTX. In this post hoc analysis, efficacy analyses were performed in 8 subgroups defined by achievement of various disease activity criteria at W24: DAS28-4(ESR) remission (<2.6) or LDA (≤3.2); DAS28-4(CRP) <2.6 or ≤3.2; RAPID3 remission (≤3) or LDA (≤6); CDAI remission (≤2.8); and SDAI remission (≤3.3). For each subgroup, the proportion of pts who achieved the corresponding disease activity criterion at W48 was calculated, with a 95% confidence interval (CI) estimated using the normal approximation to the binomial distribution. The change (Δ) from W24 to W48 in least squares (LS) mean DAS28-4(ESR) and DAS28-4(CRP) was also calculated in each subgroup, with a 95% CI for the difference between treatment groups estimated using a mixed model with repeated measures. Nominal p values were calculated and are presented with no formal statistical hypothesis testing formulated.
Results: Overall, 694 pts entered the open-label phase of ORAL Shift, and 530 were randomised and received treatment in the double-blind phase; 264 and 266 pts received tofacitinib + PBO and tofacitinib + MTX, respectively (Figure 1a). Considering those pts who were randomised and treated, the proportion of pts achieving each disease activity criterion at W24 varied, but was similar between treatments within each subgroup (Figure 1a). Among pts who met each disease activity criterion at W24, generally the majority of pts in both treatment groups also met the same criterion at W48 (Figure 1b). Numerically more pts receiving tofacitinib + MTX vs tofacitinib + PBO continued to meet the corresponding criterion at W48. Regardless of the disease activity criterion met at W24, differences between treatment groups in LS mean ΔDAS28-4(ESR) (Figure 1c) and ΔDAS28-4(CRP) (data not shown) from W24 to W48 favoured tofacitinib + MTX vs tofacitinib + PBO.



Conclusion: This post hoc analysis of data from pts randomised and treated in ORAL Shift demonstrated that, regardless of the disease activity state criterion met at W24, generally a majority of pts receiving tofacitinib maintained achievement of the corresponding disease activity criterion at W48, with or without continued MTX. Differences between treatment groups in LS mean ΔDAS28-4(ESR) from W24 to W48, as defined by achievement of LDA or remission with a variety of disease activity measures, were less than a change of 1.2, which is considered to be the threshold for a minimal clinically important improvement.[2]

REFERENCES:

[1] Cohen et al. Lancet Rheumatol 2019; 1: E23-34.
[2] Ward et al. Ann Rheum Dis 2015; 74: 1691-1696.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Gemma Turner, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: Roy Fleischmann Speakers bureau: Pfizer Inc, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celltrion, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celltrion, Eli Lilly, Genentech, GlaxoSmithKline, Janssen, Novartis, Pfizer Inc, Samumed, Sanofi-Aventis, UCB, VORSO, Boulos Haraoui Speakers bureau: Amgen, Pfizer Inc, UCB, Consultant of: AbbVie, Amgen, Eli Lilly, Merck, Pfizer Inc, UCB, Grant/research support from: AbbVie, Maya H Buch Speakers bureau: AbbVie, Consultant of: AbbVie, Eli Lilly, Gilead, MSD, Pfizer Inc, Roche, Sanofi, Grant/research support from: Pfizer Inc, Roche, UCB, David Gold Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Gosford Sawyerr Consultant of: Pfizer Inc, Employee of: Syneos Health Inc, Harry Shi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Annette Diehl Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Kristen Lee Shareholder of: Pfizer Inc, Employee of: Pfizer Inc.

DOI: 10.1136/annrheumdis-2021-eular.56

POS0087

LONG-TERM SAFETY AND EFFICACY OF UPADACITINIB OR ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 3 YEARS FROM THE SELECT-COMPARE STUDY

R. Fleischmann[1], E. Mysler[2], L. Bessette[3], C. Peterfy[4], P. Durez[5], Y. Tanaka[6], J. Swierkot[7], N. Khan[8], X. Bu[8], Y. LI[8], I. H. Song[8]. [1]*Univ of Texas Southwestern Med Center, Metroplex Clinical Research Center, Dallas, United States of America*; [2]*Organización Medica de Investigación, Rheumatology, Buenos Aires, Argentina*; [3]*Laval University, Rheumatology, Quebec, Canada*; [4]*Spire Sciences Inc, Boca Raton, United States of America*; [5]*Institut de Recherche Expérimentale et Clinique, UCL Saint-Luc, Pôle de Recherche en Rhumatologie, Brussels, Belgium*; [6]*University of Occupational and Environmental Health, The First Department of Internal Medicine, Kitakyushu, Japan*; [7]*Wroclaw Medical University, Department of Rheumatology and Internal Medicine, Wroclaw, Poland*; [8]*AbbVie, Immunology, North Chicago, United States of America*

Background: In the SELECT-COMPARE study, the Janus kinase inhibitor, upadacitinib (UPA), demonstrated significant improvements in the signs and symptoms of rheumatoid arthritis (RA) when administered at 15 mg once daily (QD) on background methotrexate (MTX) compared with adalimumab (ADA) plus MTX at Week 12 that were maintained through 72 weeks in patients with prior inadequate response to MTX.[1]
Objectives: To assess the long-term safety and efficacy of UPA vs ADA over 3 years in the ongoing long-term extension (LTE).
Methods: Patients receiving background MTX were randomized 2:2:1 to UPA 15 mg QD, placebo (PBO), or ADA 40 mg every other week. Between Weeks 14-26, rescue was mandated for either lack of response (<20% improvement in tender or swollen joint counts: Weeks 14, 18, 22) or failure to achieve a targeted disease outcome (CDAI low disease activity: Week 26). Patients who completed the 48-week double-blind period could enter an LTE for up to 10 years total. This analysis describes patients through 3 years of treatment. Treatment-emergent adverse events (TEAEs) per 100 patient years (PY), including events of special interest (AESI), were summarized up to 3 years based on exposure to UPA and to ADA. Efficacy was analyzed by original randomized groups. Patients who were rescued or prematurely discontinued study drug were categorized as non-responders for visits after rescue or discontinuation. Descriptive analyses were performed without formal statistical comparisons.
Results: In total, 651, 651, and 327 patients were randomized at baseline to receive UPA, PBO, and ADA, respectively. Between Weeks 14-26, 252 (39%) patients were rescued from UPA to ADA, 159 (49%) were rescued from ADA to UPA, and all PBO patients were switched to UPA by Week 26.[1] A higher proportion of patients randomized to UPA completed 3 years without rescue compared to those randomized to ADA (47% vs 36%, respectively). UPA was generally well-tolerated as assessed by the rates of TEAEs, including serious AEs, AEs leading to discontinuation of study drug, and AESIs, including serious and opportunistic infections, malignancies, adjudicated major adverse cardiac events or venous thromboembolism; Figure 1). Consistent with previous analyses, the event rates of AESIs were generally comparable between the UPA and

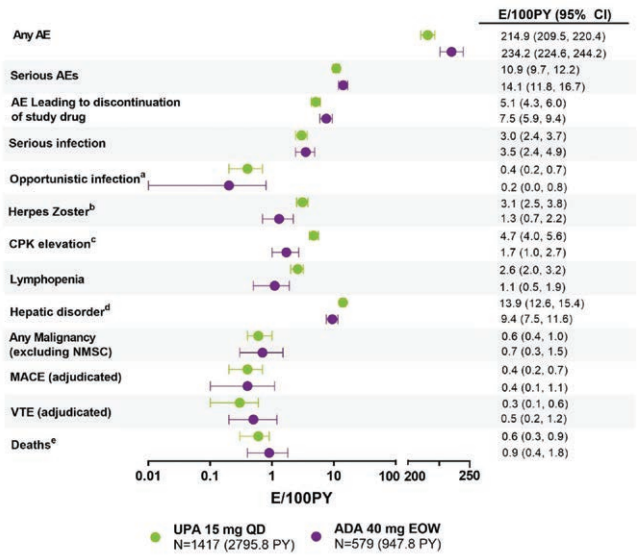
ADA groups, while herpes zoster, lymphopenia, hepatic disorder, and CPK elevation were reported at higher rates with UPA. Consistent with earlier time points, greater proportions of patients randomized to UPA achieved low disease activity and remission at 3 years based on CDAI, as well as DAS28(CRP) ≤3.2 or <2.6, compared with patients randomized to ADA (Table 1).

Conclusion: The safety profile of UPA was consistent with the results reported previously and with the integrated Phase 3 safety analysis.[1,2] Higher levels of clinical response continued to be observed with UPA vs ADA through 3 years of treatment.

REFERENCES:

[1] Fleischmann R, et al. *Ann Rheum Dis* 2020;79:323.
[2] Cohen SB, et al. *Ann Rheum Dis* 2020;doi:10.1136/annrheumdis-2020-218510.

Figure. Exposure-adjusted Event and Incidence Rates of Treatment-emergent AEs Over 3 Years



ADA, adalimumab; AE, adverse event; CI, confidence interval; CPK, creatine phosphokinase; EAER, exposure-adjusted event rates; EOW, every other week; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PY, patient years; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolism.
Exposure adjusted incidence rates (EAIR) are reported for malignancy, MACE, VTE, and deaths; exposure adjusted event rates (EAER) are reported for the remaining events.
[a]Excluded tuberculosis and herpes zoster.
[b]Herpes zoster: majority of cases on UPA were non-serious and involved 1 or 2 dermatomes.
[c]CPK elevation: most were mild or moderate and asymptomatic, with no reports of rhabdomyolysis.
[d]Hepatic disorders: majority were transaminase elevations.
[e]Includes treatment-emergent and non-treatment emergent deaths.

Table 1. Efficacy Endpoints at 3 Years (NRI)

Endpoints, % (95% CI)	UPA 15 mg QD N=651*	ADA 40 mg EOW N=327*
CDAI ≤10	39 (36, 43)	29 (24, 34)
CDAI ≤2.8	24 (21, 28)	17 (12, 21)
DAS28(CRP) ≤3.2	37 (33, 41)	26 (21, 31)
DAS28(CRP) <2.6	32 (29, 36)	22 (17, 26)

ADA, adalimumab; CI, confidence interval; DAS28(CRP), Disease Activity Score for 28-joints C-Reactive Protein; CDAI, clinical disease activity index; EOW, every other week; NRI, non-responder imputation; QD, once daily; UPA, upadacitinib.*Patients who were rescued prior to/at Week 26 were considered non-responders. 252/651 and 159/327 patients were rescued of those randomized to UPA and ADA, respectively.

Acknowledgements: AbbVie and the authors thank the patients, trial sites, and investigators who participated in this clinical trial. AbbVie, Inc was the trial sponsor, contributed to trial design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. No honoraria or payments were made for authorship. The authors thank Dr. Tim Shaw of AbbVie Inc. for his support with the interpretation of the data. Medical writing support was provided by Ramona Vladea, PhD, of AbbVie, Inc.

Disclosure of Interests: Roy Fleischmann Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, GSK, Janssen, Novartis, Pfizer Inc, Sanofi-Aventis, and UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Genentech, Janssen, Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis and UCB, Eduardo Mysler Consultant of: AbbVie, AstraZeneca, Lilly, Pfizer, Roche, BMS, Sandoz, GSK, Janssen, Grant/research support from: AbbVie, AstraZeneca, Lilly, Pfizer, Roche, BMS, Sandoz, GSK, Janssen, Louis Bessette Consultant of: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, Novartis, Gilead, Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, Novartis, Gilead, Charles Peterfy Shareholder of: Spire Sciences, Inc, Speakers bureau: Amgen, Bristol-Myers Squibb, Consultant of: Aclaris, Centrexion, Daiichi Sankyo, EMD, Serono, Five Prime, Flexion Therapeutics, Genentech, Gilead, GlaxoSmithKline, Istresso, Eli Lilly, Myriad Genetics, Novartis, Roche, SetPoint, Sorrento, UCB, Employee of: Spire Sciences, Inc, Patrick Durez Speakers bureau: BMS, Sanofi, Eli Lilly, Celltrion, Yoshiya Tanaka Speakers bureau: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Teijin, Consultant of: Daiichi-Sankyo, Astellas, Chugai, Eli Lilly, Pfizer, AbbVie, YL Biologics, Bristol-Myers, Takeda, Mitsubishi-Tanabe, Novartis, Eisai, Janssen, Teijin, Grant/research support from: Asahi-kasei, Mitsubishi-Tanabe, Chugai, Takeda, Sanofi, Bristol-Myers, UCB, Daiichi-Sankyo, Eisai, Ono, Jerzy Swierkot Speakers bureau: AbbVie, Sandoz, Pfizer, Roche, BMS, UCB, MSD, Accord, Janssen, Consultant of: AbbVie, Sandoz, Pfizer, Roche, BMS, UCB, MSD, Accord, Janssen, Grant/research support from: AbbVie, Sandoz, Pfizer, Roche, BMS, UCB, MSD, Accord, Janssen, Nasser Khan Shareholder of: AbbVie, Employee of: AbbVie, Xianwei Bu Shareholder of: AbbVie, Employee of: AbbVie, Yihan Li Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie, Employee of: AbbVie.

DOI: 10.1136/annrheumdis-2021-eular.535

POS0088

EFFICACY OF JANUS KINASE INHIBITORS FOR DIFFICULT-TO-TREAT RA IN CLINICAL PRACTICE

M. Kamiya[1], D. Togawa[1], S. Mori[1], K. Yamazaki[1]. [1]*Nara Hospital, Kindai University, Orthopaedic Surgery and Rheumatology, Ikoma City, Japan*

Background: In 20-30% of rheumatoid arthritis (RA) patients, the first biologic disease-modifying antirheumatic drugs (bDMARDs) (generally tumour necrosis factor inhibitors (TNFis)) is ineffective, and among the patients who do respond to therapy, 20% is faced with secondary ineffectiveness within the first 2 years of treatment [1]. In practice, when refractory RA is present, of which the definition implies previous use of at least two bDMARDs (generally TNFis), the next treatment choice often made is a bDMARD of another class (non-TNFis) [2]. On the other hand, patients who are inadequately responding to bDMARDs need new treatment options because subsequent bDMARD treatment reduces their response [3]. Janus Kinase inhibitors (JAKis) are the first targeted synthetic DMARDs (tsDMARD) licensed for the treatment of RA with comparable efficacy to bDMARDs. Unlike the single cytokine targeting approach of bDMARDs, JAKis are specifically designed to inhibit intracellular signalling molecules common to the receptors of multiple inflammatory cytokines implicated in RA pathogenesis.
Objectives: Difficult-to-treat (D2T) RA is defined as refractory to two or more b/ts DMARDs with different mechanisms of action, with active and progressive disease, as published by Eular(4). We evaluated real world efficacy of approved JAKis and factors that may help to continue them in patients with D2T RA.
Methods: Patients who had inadequate response to two or more bDMARDs (including both TNFis and non-TNFis) at our hospital by December 2019 were defined as D2T RA, and patients who switched to JAKis were retrospectively investigated. The drug retention rate was determined by Kaplan-Meier method, and the difference was tested by Logrank test. Multiple regression analysis was used as the statistical method to predict continuation of JAKis for more than 1 year, with patient background (age, gender, during the disease, number of bDMARDs used, with or without methotrexate and/or glucocorticoids, disease activity score assessing 28 joints using erythrocyte sedimentation rate' presence of rheumatoid factor/anti-CCP antibody, matrix metalloproteinase 3 value, Health Assessment Questionnaire disability index) at the time of initiation as an explanatory variable.
Results: A total of 915 bDMARDs had been administered to 394 RA patients. The retention rate of bDMARDs and the number of bDMARDs used were 89.3% and 1.48 bDMARDs at 1 year, 67.7% and 2.27 bDMARDs at 5 years, and 52.0% and 3.15 bDMARDs at 10 years, respectively. The retention rate of JAKis at 1 year was 60.2% in 65 patients with tofacitinib (TOF) and 67.2% in 70 patients with baricitinib (BAR) (P=0.38). Among them, the drug retention rate in D2T RA patients was 50.8% in 38 TOF patients and 66.3% in 35 BAR patients with no significant difference (P=0.30). There were no patient background factors that significantly predicted continuation at 1 year for any JAKis.
Conclusion: Despite the limited number of patients and the retrospective nature of the study, TOF and BAR were shown to be effective options for D2T RA, regardless of patient background such as disease activity or number of bDMARDs used. Other JAKis and switches between JAKis need to be investigated in the future.

REFERENCES:

[1] Schaeverbeke T, Truchetet ME, Kostine M et al. Immunogenicity of biologic agents in rheumatoid arthritis patients: lessons for clinical practice. Rheumatology 2016;55:210_20.
[2] Smolen JS, Landewe R, Bijlsma J et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 2017;76:960_77.

[3] Rendas-Baum R, Wallenstein GV, Koncz T et al. Evaluating the efficacy of sequential biologic therapies for rheumatoid arthritis patients with an inadequate response to tumor necrosis factor-α inhibitors. Arthritis Res Ther 2011;13:R25.
[4] Nagy G, et al. EULAR definition of difficult-to-treat rheumatoid arthritis. Ann Rheum Dis 2021;80:31–35. doi:10.1136/annrheumdis-2020-217344.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.542

POS0089

AZD9567 VERSUS PREDNISOLONE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A PHASE 2A, RANDOMISED, DOUBLE-BLIND, PARALLEL-GROUP EFFICACY AND SAFETY STUDY

J. M. Van Laar[1], A. Lei[2], M. Safy-Khan[1], J. Almquist[3], C. Astbury[4], M. Belvisi[5], A. Platt[6], S. Prothon[3], S. Samuelsson[7], P. Svanberg[8], C. Keen[7]on behalf of The SEMRA Study Group. *[1]University Medical Center Utrecht, Division of Internal Medicine and Dermatology, Department of Rheumatology & Clinical Immunology, Utrecht, Netherlands; [2]AstraZeneca, Patient Safety, Respiratory & Immunology, Chief Medical Office, R&D, Barcelona, Spain; [3]AstraZeneca, Clinical Pharmacology and Quantitative Pharmacology, Clinical Pharmacology & Safety Sciences, R&D, Gothenburg, Sweden; [4]AstraZeneca, Research and Early Development, Respiratory & Immunology, BioPharmaceuticals R&D, Cambridge, United Kingdom; [5]AstraZeneca, Research and Early Development, Respiratory & Immunology, BioPharmaceuticals R&D, Gothenburg, Sweden; [6]AstraZeneca, Translational Science and Experimental Medicine, Research and Early Development, Respiratory & Immunology, BioPharmaceuticals R&D, Cambridge, United Kingdom; [7]AstraZeneca, Clinical Development, Research and Early Development, Respiratory & Immunology, BioPharmaceuticals R&D, Gothenburg, Sweden; [8]AstraZeneca, Drug Metabolism and Pharmacokinetics, Research and Early Development, Respiratory & Immunology, BioPharmaceuticals R&D, Gothenburg, Sweden*

Background: Oral corticosteroids such as prednisolone are potent anti-inflammatory drugs but their use is limited by side effects caused by unwanted actions on the glucocorticoid receptor (GR), such as increased insulin resistance, and off-target actions on the mineralocorticoid receptor (MR) that disrupt electrolyte balance and increase water retention. AZD9567 is an oral, selective, non-steroidal glucocorticoid receptor modulator being developed to treat inflammatory diseases. Pre-clinical and phase 1 clinical data indicate that AZD9567 is the first GR modulator with an improved efficacy–dysglycaemic side effect profile versus prednisolone.

Objectives: To compare the efficacy, safety and tolerability of AZD9567 with prednisolone in patients with active rheumatoid arthritis (RA), at doses with predicted equivalent anti-inflammatory activity.

Methods: In this phase 2a, randomised, double-blind, parallel-group, multicentre study in RA patients with DAS28-CRP ≥ 3.2 despite stable treatment with conventional disease-modifying anti-rheumatic therapies (NCT03368235), patients were randomised 1:1 to AZD9567 40 mg or prednisolone 20 mg orally once daily for 14 days. The primary endpoint was change from baseline in DAS28-CRP at day 15. Secondary outcomes included components of DAS28-CRP, TJC68, SJC66, ACR response (ACR20, ACR50, ACR70) and safety outcomes, including serum electrolytes.

Results: All 21 randomised patients (AZD9567, n = 11; prednisolone, n = 10) completed the study. There was a slight imbalance between the treatment groups at baseline, with higher age (mean ± SD: 64.5 ± 8.4 vs 55.5 ± 13.6 years), more women (8 vs 5) and greater disease severity (DAS28-CRP, mean ± SD: 5.26 ±

Table 1. Change from baseline to day 15 in clinical disease activity measures.

	AZD9567 (n = 11)		Prednisolone (n = 10)		Comparison (AZD9567 – prednisolone)		
	LSM CFB (SE)	95% CI	LSM CFB (SE)	95% CI	LSMD (SE)	95% CI	*p* value
DAS28–CRP score	−1.93 (0.35)	−2.66, −1.21	−2.40 (0.34)	−3.11, −1.70	0.47 (0.46)	−0.49, 1.43	0.315
TJC28 score	−6.12 (1.25)	−8.76, −3.49	−6.07 (1.21)	−8.61, −3.52	−0.05 (1.60)	−3.43, 3.32	0.973
SJC28 score	−5.14 (0.65)	−6.51, −3.76	−5.40 (0.63)	−6.73, −4.08	0.26 (0.84)	−1.50, 2.03	0.757
GH score	−27.7 (7.3)	−42.8, −12.5	−37.4 (7.1)	−52.3, −22.6	9.8 (9.7)	−10.5, 30.1	0.325
CRP, mg/L	−10.8 (2.4)	−15.9, −5.8	−15.6 (2.5)	−20.9, −10.3	4.8 (3.5)	−2.5, 12.0	0.187
TJC68 score	−9.02 (2.46)	−14.21, −3.82	−7.90 (2.36)	−12.88, −2.91	−1.12 (3.12)	−7.69, 5.46	0.724
SJC66 score	−6.24 (0.89)	−8.13, −4.36	−6.66 (0.86)	−8.48, −4.85	0.42 (1.14)	−1.98, 2.81	0.717

CFB, change from baseline; CRP, C-reactive protein; DAS28, 28-joint disease activity score; GH, global health; LSM(D), least-squares mean (difference); SJC, swollen joint count; TJC, tender joint count.

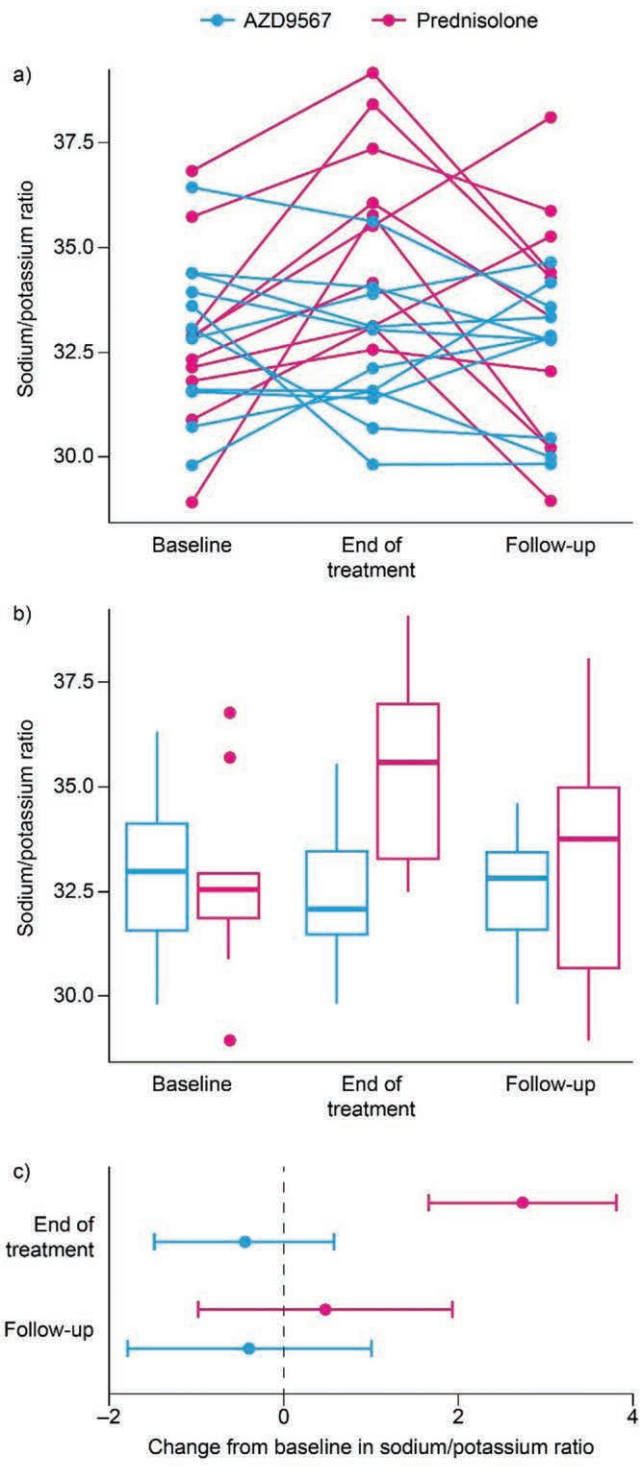


Figure. Morning serum sodium/potassium ratio with AZD9567 or prednisolone, under fasting conditions. a) Individual-level data. b) Box-and-whisker plots showing median, interquartile range and range. c) Change from baseline to day 15 (i.e. end of treatment; adjusted for baseline values) with 95% confidence intervals. Follow-up was approximately 14 days after the last dose.

0.98 vs 4.90 ± 0.74) in the AZD9567 group versus the prednisolone group. There was no statistically significant or clinically meaningful (i.e. > 1.2) difference in change from baseline to day 15 in DAS28-CRP between AZD9567 and prednisolone, although this was numerically lower with AZD9567 (Table 1). Similar results were observed for TJC68, SJC66, CRP and GH (Table 1). The proportions of patients achieving ACR20, 50 and 70 response criteria were similar in both groups, albeit numerically lower with AZD9567. Similar numbers of patients in each group reported treatment-emergent adverse events (AZD9567, n = 10, prednisolone, n = 9); most were mild in severity. One serious adverse event, suicidal depression, was reported after completing AZD9567 treatment. Morning fasting serum sodium/potassium ratio at day 15 was not altered with AZD9567 but was increased from baseline with prednisolone (Figure 1).

Conclusion: AZD9567 40 mg had a similar efficacy profile to prednisolone 20 mg in patients with active RA. Both drugs were well tolerated, with no new safety signals. Unlike prednisolone, AZD9567 had no effect on serum sodium/potassium ratio, suggesting selectivity of AZD9567 for the GR over the MR. These results support further trials of AZD9567 in patients with inflammatory disease.

Acknowledgements: Medical writing support was provided by Richard Claes PhD of PharmaGenesis London, London, UK, funded by AstraZeneca, Gothenburg, Sweden in accordance with Good Publication Practice 3 (GPP3) guidelines (http://www.ismpp.org/gpp3).

This study was funded by AstraZeneca. AZD9567 is an investigational medical product with no approved indication.

Disclosure of Interests: Jacob M. van Laar Consultant of: Honoraria from - Abbvie, Arxx Tx, Galapagos, Gesyntha, Leadiant, Magenta, Roche, Sanofi Genzyme, Grant/research support from: AstraZeneca, Pfizer, Roche, Alejhandra Lei Shareholder of: AstraZeneca., Grant/research support from: Boehringer Ingelheim in 1998, Bristol-Myers Squibb in 1999, Employee of: AstraZeneca. Past employee of Almirall, Grünenthal, Boehringer Ingelheim, CESIF Pharma, Mary Safy-Khan Grant/research support from: Student grant from AstraZeneca 2015-2018., Joachim Almquist Shareholder of: AstraZeneca, Consultant of: AstraZeneca., Employee of: AstraZeneca., Carol Astbury Shareholder of: AstraZeneca., Employee of: AstraZeneca., Maria Belvisi Shareholder of: AstraZeneca., Grant/research support from: AstraZeneca and Chiesi, Employee of: AstraZeneca., Adam Platt Shareholder of: AstraZeneca., Employee of: AstraZeneca., Susanne Prothon Shareholder of: AstraZeneca., Employee of: AstaZeneca., Sara Samuelsson Shareholder of: AstraZeneca, Employee of: AstraZeneca, Petter Svanberg Employee of: AstraZeneca, Christina Keen Shareholder of: AstraZeneca., Employee of: AstraZeneca.

DOI: 10.1136/annrheumdis-2021-eular.632

POS0090

RISK OF QT INTERVAL PROLONGATION ASSOCIATED WITH CHRONIC USE OF HYDROXYCHLOROQUINE IN RHEUMATIC PATIENTS AND THE EFFECT OF COTREATMENTS

M. Antivalle[1], G. La Paglia[1], M. C. Ditto[2], S. Parisi[2], E. Fusaro[2], M. Agosti[3], P. Sarzi Puttini[1]. [1]*L. Sacco University Hospital, Rheumatology, Milano, Italy*; [2]*AOU Città della Salute e della Scienza di Torino; Rheumatology Unit;, Department of Medical Science, Torino, Italy*; [3]*Azienda Socio-Sanitaria Territoriale (ASST) di Vimercate, Department of Medical Science, Vimercate, Italy*

Background: Hydroxychloroquine (HCQ) has been used safely for over 60 years in rheumatic patients. However, following its recent use in covid-19 disease, its safety has been questioned, following controversial reports of cardiac toxicity[1], possibly related to a prolongation of the QT interval[2].

Objectives: To explore the influence of chronic treatment with hydroxychloroquine on QT interval in rheumatic patients, and the possible effects of drug-to-drug interference[3].

Methods: 12-lead electrocardiogram tracings were recorded with standard equipment in 229 ambulatory patients (SLE = 53, RA = 52, SSc = 56, UCTD = 38, Others = 30). The present analysis was performed on corrected QT intervals (QTc) calculated according to Framingham formula (QTc = QT+0.154 (1–RR)), with ULN = 449 ms in males, and 467 ms in females. Estimated glomerular filtrate rate (eGFR) was calculated from serum creatinine with the CKD-EPI equation. The influence on QTc values of demographic variables, chronic (≥3 months) HCQ treatment, and of the use of selected comedications -Statins, Angiotensin Converting Enzyme inhibitors (ACEi), Angiotensin Receptor Blockers (ARBs), Selective Serotonin Reuptake Inhibitors (SSRIs), Proton-Pump Inhibitors (PPI), Calcium Channel Blockers (CCBs) – were evaluated by parametric or non parametric statistical methods, as appropriate. All statistic al analyses were performed with the IBM SPSS statistical package version 25.

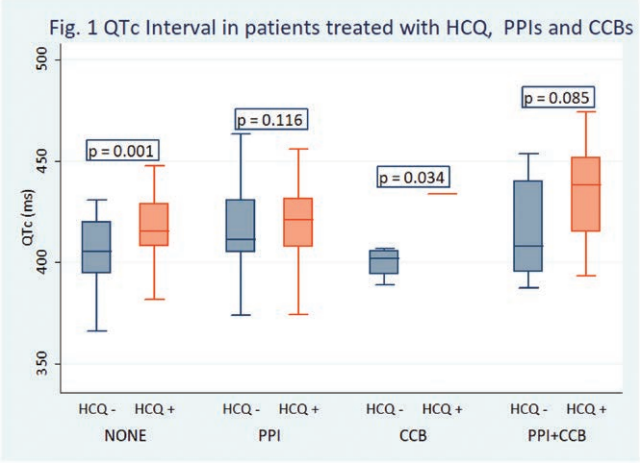
RESULTS:

Table 1. Demographic and clinical variables in patients treated with HCQ (HCQ+) and in controls (HCQ-).

	N	Age	Female	eGFR	Statins	ACEi	ARB	SSRI	PPI	CCB
		Yrs	N	mL/min/1.73m^2	N	N	N	N	N	N
		±SD	%		%	%	%	%	%	%
All	229	58.02	206	87.14	29	48	19	14	138	30
		±14.36	90.0	18.96	12.7	21.8	8.3	6.1	60.3	13.1
HCQ+	132	58.71	122	87.00	18	32	11	9	80	17
		±14.49	92.4	20.04	13.6	24.2	8.3	6.8	60.6	12.9
HCQ-	97	57.51	84	87.32	11	16	8	5	58	13
		±14.30	86.6	17.47	11.3	16.5	8.2	5.2	59.8	13.4
p		0.532	0.183	0.897	0.690	0.189	1.000	0.782	1.000	1.000

Demographic variables, and the use of evaluated comedications were not different in HCQ+ and HCQ- patients (Table 1). In the whole population, the QTc mean duration was 416.72 ± 20.70 ms, and was correlated with age (r = 0.215, p= 0.001), but not with gender (p = 0.548), eGFR (r = -0.93, p = 0.163), or disease (p = 0.092). In only 4 patients (HCQ+: 3 (2.3%) – HCQ-: 1 (1%), p = 0.639) QTc duration was above ULN.

QTc duration was not associated with the use of Statins, ACEi, ARBs, or SSRIs (p = 0.454, 0.276, 0.475, and 0.131 respectively), but was significantly prolonged in patients treated with HCQ (421.26 ± 19.19 vs 410.55 ± 21.18 msec, p < 0.001), PPIs (420.57 ± 21.45 vs 410.89 ± 18.12 ms, p < 0.001), and CCBs (424.22 ± 25.97 vs 415.59 ± 19.62 ms, p < 0.033). Furthermore, as reported in Fig. 1, our data show a trend - albeit not statistically significant - towards an additive effect on QT prolongation of the association of PPIs and CCBs with HCQ, even more evident in the case of association of the 3 drug classes.



Conclusion: In this study, the QTc interval was significantly prolonged in patients treated with hydroxychloroquine as compared to controls, although significant prolongation was extremely infrequent. Furthermore, our data revealed signs of drug-drug interference, suggesting that regular monitoring of the electrocardiogram is advisable in these patients, often undergoing cotreatment with multiple drugs.

REFERENCES:

[1] Imad M. Tleyjeh, et al. The Cardiac Toxicity of Chloroquine or Hydroxychloroquine in COVID-19 Patients: A Systematic Review and Meta-regression Analysis. Mayo Clin Proc Innov Qual Outcomes. 2020 Nov 2 doi: 10.1016/j.mayocpiqo.2020.10.005 [Epub ahead of print].

[2] Teodoro J. Oscanoa, et al. Frequency of Long QT in Patients with SARS-CoV-2 Infection Treated with Hydroxychloroquine: A Meta-analysis. Int J Antimicrob Agents.

[3] Byung Jin Choi, et al. Risk of QT prolongation through Drug-drug Interactions between Hydroxychloroquine and Concomitant Drugs Prescribed in Real-world Practice. Preprint from Research Square, 22 Sep 2020 DOI: 10.21203/rs.3.rs-79572/v1 PPR: PPR217328.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.738

POS0091

OFF-TARGET PROFILING OF JANUS KINASE (JAK) INHIBITORS IN RHEUMATOID ARTHRITIS: A COMPUTER-BASED APPROACH FOR DRUG SAFETY STUDIES AND REPURPOSING

M. L. Faquetti[1], F. Grisoni[1], P. Schneider[2], G. Schneider[2], A. M. Burden[1]. [1]*ETH Zurich, Department of Chemistry and Applied Biosciences, Zürich, Switzerland*; [1]*ETH Zurich, Department of Chemistry and Applied Biosciences, Zürich, Switzerland*

Background: The JAK inhibitors (JAKi's) tofacitinib and baricitinib are new alternatives for treating rheumatoid arthritis. Safety concerns associated with JAKi's, such as the increased risk for thrombosis and viral infections, have emerged worldwide. The underlying explanatory mechanisms remain unknown, suggesting the elevated risk is likely due to underlying confounding or an off-target binding effect. Computational approaches can explore the potential for a small molecule drug to interact with previously unknown biological targets and identify potential safety-related concerns, and open doors for potential drug repurposing.
Objectives: To identify and characterize the off-target binding effects of baricitinib and tofacitinib, with a focus on targets related to thrombosis and viral infection
Methods: Potential targets of baricitinib and tofacitinib were predicted using two neural-network-based systems (TIGER[1] and SPiDER[2]). Targets were considered relevant if they had (1) a SPiDER confidence with p<0.05, or (2) a TIGER score >1. Selected targets related to the outcome of interest were experimentally evaluated at Eurofins Cerep (France-Celle L'Evescault, www.eurofins.com) if commercial available. Compounds were tested at (1) single concentration (30 µM) with technical replicates, using radioligand or enzymatic assays, or (2) multiple concentrations (30 µM highest concentration; dilution factor in a log-scale) with technical replicates, using calcium flux or inhibition of [cAMP] assays. Observed activity of ≥50% inhibition or stimulation on the target was considered active, between 25 to 50% inhibition (or a dissociation constant [Kd] from 1 to 10 µM) was considered as moderate activity, and lower than 25% was considered inactive. Dose-response curve were performed on active and moderate targets for IC_{50} / EC_{50} (half maximal inhibitory / effective concentration) determination.
Results: TIGER and SPiDER suggested a total of 99 off-target binding effects (baricitinib n=41; tofacitinib n=58), of which 17 targets had potential impact on thrombosis or viral infection (baricitinib n=5 and 4, respectively; tofacitinib n=5 and 3, respectively). Commercial testing was available on 11 targets (Adenosine Receptor A2A [AA2AR], Epidermal growth factor receptor, induclible NOS, PI3 Kinase (p110b/p85a), Phosphodiesterase 10A2 [PDE10A2] and Protein Kinase N2 [PKN2] for baricitinib; and Adenosine receptor A3, 15-Lipoxygenase [15-LO], PKN2, Transient receptor potential cation channel [TRPM6] and AA2AR for tofacitinib). Of these, 5 targets showed active or moderately active binding activity (baricitinib n=2; tofacitinib n=3), and were tested for dose-response curves. Test results confirmed ligand-binding activity with IC_{50} on nanomolar (PKN2), and micromolar ranges (PDE10A2 and TRPM6).
Conclusion: The results suggest both baricitinib and tofacitinib are promiscuous binders with effects on several families. Although it may lead to side effects, off-target binding also represents a potential opportunity for drug repurposing. Besides on-target effects, both drugs are under clinical investigation for the treatment of COVID-19 due to off-target interactions. The proposed pharmacological off-target effects of those with active binding include attenuation of pulmonary vascular remodeling, anti-fibrotic and anti-psychotic activities (PDE10A2), modulation of viral response (PKN2), and hypomagnesaemia (TRPM6), which is involved in cardiovascular diseases. This study supports tofacitinib and baricitinib as candidates for drug repurposing (e.g., in COVID-19, Hepatitis C virus, and pulmonary hypertension). We did not identify active off-target interactions linked to thrombosis to explain the elevated risk observed in clinical practice. Further research is required to elucidate the underlying patient-specific factors (confounders) that could explain this safety concern.

REFERENCES:

[1] Schneider P *et al. Angew Chem Int Ed* 2017;56:11520–4.
[2] Reker D *et al. PNAS* 2014;111:4067–72.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.982

POS0092

HERPES ZOSTER IN THE FILGOTINIB RHEUMATOID ARTHRITIS PROGRAM

K. Winthrop[1], M. H. Buch[2], J. Curtis[3], G. R. Burmester[4], D. Aletaha[5], K. Amano[6], A. Pechonkina[7], I. Tiamiyu[8], C. Leatherwood[9], L. Ye[10], Q. Gong[10], R. Besuyen[11], J. Galloway[12]. [1]*Oregon Health and Science University, Division of Infectious Diseases, Portland, United States of America*; [2]*University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; [3] *University of Alabama at Birmingham, Division of Clinical Immunology & Rheumatology, Birmingham, United States of America*; [4]*Charité University Hospital Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; [5]*Medical University of Vienna, Division of Rheumatology, Department of Medicine 3, Vienna, Austria*; [6]*Saitama Medical University, Department of Rheumatology and Clinical Immunology, Saitama, Japan*; [7]*Gilead Sciences, Inc., Inflammation and Respiratory Therapeutic Area, Foster City, United States of America*; [8]*Gilead Sciences, Inc., Clinical Research, Foster City, United States of America*; [9]*Gilead Sciences, Inc., Inflammation & Respiratory Therapeutics, Foster City, United States of America*; [10]*Gilead Sciences, Inc., Biostatistics, Foster City, United States of America*; [11]*Galapagos BV, Clinical Development, Leiden, Netherlands*; [12]*King's College London, Centre for Rheumatic Diseases, School of Immunology and Microbial Sciences, London, United Kingdom*

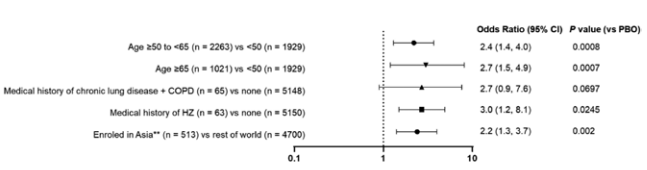
Background: The once daily, oral Janus kinase (JAK)-1 preferential inhibitor filgotinib (FIL) improved signs and symptoms of rheumatoid arthritis (RA) in phase (P)3 trials.[1-3] Patients (pts) with RA have increased herpes zoster (HZ) reactivation risk vs the general population. JAK inhibition is associated with increased infection incidence, including HZ.[4]
Objectives: To assess long-term safety of FIL across the global clinical program with respect to HZ.
Methods: Pts meeting 2010 ACR/EULAR RA criteria in a pooled analysis of P2 DARWIN 1–2 (D1–2), P3 FINCH 1–3 (F1–3), and long-term extension studies (D3, F4) were included. Placebo (PBO)-controlled as-randomised analysis included pts receiving FIL 100 mg (FIL100), FIL 200 mg (FIL200), or PBO up to week (W)12 (D1–2, F1–2); active-controlled as-randomised analysis included pts receiving FIL100, FIL200, adalimumab (ADA), or methotrexate (MTX) up to W52 (F1, F3). Long-term as-treated analysis included pts in all 7 studies receiving FIL100, FIL200, ADA, MTX, or PBO; data after re-randomisation were included and contributed to treatment received. Exposure-adjusted incidence rates (EAIR)/100 patient-years, calculated up to the last follow-up time or day, and differences with 95% confidence intervals (CIs) were calculated from the Poisson model. Logistic regression model was used for treatment-emergent (TE) HZ risk factor analysis and odds ratio (95% CI) and *P* value were provided.
Results: Table 1 shows TE HZ EAIRs in a pooled analysis. Rates of HZ were lower for FIL200 vs PBO during the 12W PBO-controlled period. At 52W, HZ rates were higher for FIL200/100 vs active control. Long-term HZ rates increased for FIL200 vs FIL100.

Table 1. EAIR of treatment-emergent herpes zoster

	N	Patient-years exposure	EAIR (95% CI)	EAIR diff (95% CI vs PBO/active control)
12W PBO-controlled				
FIL200	777	179.8	0.6 (0.1, 3.9)	–0.56 (–2.5, 1.3)
FIL100	788	181.6	1.1 (0.3, 4.4)	–0.02 (–2.2, 2.2)
PBO	781	178.4	1.1 (0.3, 4.5)	
Active-controlled, as-randomised[a]				
FIL200	475	439.7	1.4 (0.6, 3.0)	0.69 (–0.7, 2.1)
FIL100	480	443.4	0.9 (0.3, 2.4)	0.23 (–1.1, 1.5)
ADA	325	297.6	0.7 (0.2, 2.7)	
Active-controlled, as-randomised[a]				
FIL200	626	578.0	1.7 (0.9, 3.2)	0.65 (–0.8, 2.2)
FIL100	207	195.0	1.5 (0.5, 4.8)	0.46 (–1.6, 2.5)
MTX	416	372.2	1.1 (0.4, 2.9)	
Long-term as-treated[b]				
FIL200	2267	4047.7	1.8 (1.4, 2.3)	NC
FIL100	1647	2032.9	1.1 (0.8, 1.7)	NC

[a]up to W52. [b]data cut for LTE FINCH 4, Sept 19, 2019; DARWIN 3, April 26 2019.ADA, adalimumab; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; MTX, methotrexate; NC, not calculated; PBO, placebo; W week.

Figure 1 shows multivariate logistic regression model of TE risk factors.



Of 104 pts with TE HZ in long-term as-treated analysis set, 5 receiving FIL200 had history of HZ; EAIR (95% CI) was 8.7 (3.6–21.0). Of 8 pts with multiple events, 3 had events of differing severity for the same HZ episode.
EAIRs (95% CI) of TE HZ in Asia were: 3.7 (1.7–8.1) FIL200, n=197; 2.8 (1.3–6.3) FIL100, n=158; 0 ADA, n=40; 2.8 (0.4–19.6) MTX, n=43; and 3.4 (0.5–23.8) PBO, n=77 in long-term as-treated population. EAIRs (95% CI) in rest of the world were: 1.6 (1.2–2.1) FIL200, n=2070; 0.9 (0.6–1.5) FIL100, n=1489; 0.8 (0.2–3.1) ADA, n=285; 0.9 (0.3–2.9) MTX, n=373; and 0.7 (0.2–2.9) PBO, n=704 for all pts as-treated.

Most TE HZ infections were mild to moderate and non-serious; 6 were serious; 2 were recurrences. No visceral TE HZ occurred across the FIL RA program; there was 1 case each of genital, disseminated, and ophthalmic HZ. The disseminated HZ occurred in a pt with prior HZ history. Lymphopenia was not associated with HZ during the PBO-controlled W12 period.

Conclusion: HZ was more common in both FIL groups vs ADA or MTX up to 52 weeks but comparable vs PBO during the 12-week placebo-controlled period. In multivariate analyses, prior history of HZ, Asian region, and age ≥50 years were associated with increased HZ risk.

REFERENCES:

[1] Genovese et al. *JAMA.* 2019;322:315–25.
[2] Westhovens et al. *Ann Rheum Dis*. 2021; online first.
[3] Combe et al. *Ann Rheum Dis.* 2021; online first.
[4] Higarashi and Honda. *Drugs*. 2020;80:1183–201.

Disclosure of Interests: Kevin Winthrop Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly and Co., Galapagos NV, Gilead Sciences, GlaxoSmithKline, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, and Pfizer, Maya H Buch Speakers bureau: AbbVie; Eli Lilly and Company; Gilead Sciences, Inc.; Merck-Serono; Pfizer; Roche; Sandoz; Sanofi; and UCB, Consultant of: AbbVie; Eli Lilly and Company; Gilead Sciences, Inc.; Merck-Serono; Pfizer; Roche; Sandoz; Sanofi; and UCB, Grant/research support from: AbbVie; Eli Lilly and Company; Gilead Sciences, Inc.; Merck-Serono; Pfizer; Roche; Sandoz; Sanofi; and UCB, Jeffrey Curtis Grant/research support from: AbbVie, Amgen, BMS, Corrona, Eli Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, Gerd Rüdiger Burmester Speakers bureau: AbbVie; Eli Lilly; Pfizer; and Gilead Sciences, Inc., Consultant of: AbbVie; Eli Lilly; Pfizer; and Gilead Sciences, Inc., Daniel Aletaha Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Medac, Merck, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Sandoz, Sanofi/Genzyme, and UCB, Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Medac, Merck, Novartis, Pfizer, Roche, Sandoz, and Sanofi/Genzyme, Grant/research support from: AbbVie, Merck Sharp & Dohme, Novartis, and Roche, Koichi Amano Speakers bureau: AbbVie GK, Astellas, Chugai Pharmaceutical Co. Ltd., Eli Lilly, GlaxoSmithKline KK, Pfizer Japan, Mitsubishi-Tanabe Pharma, Grant/research support from: Asahi Kasei Pharma, Alena Pechonkina Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Iyabode Tiamiyu Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Cianna Leatherwood Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Lei Ye Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Qi Gong Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Robin Besuyen Shareholder of: Galapagos, BV, Employee of: Galapagos, BV, James Galloway Speakers bureau: Pfizer, Bristol-Myers Squibb, UCB and Celgene

DOI: 10.1136/annrheumdis-2021-eular.1408

Rheumatoid arthritis - prognosis, predictors and outcome

POS0093

HETEROGENEITY IN ADVERSE EVENT ASSESSMENT BETWEEN COUNTRIES PARTICIPATING IN AN INTERNATIONAL COLLABORATION OF REGISTRIES OF RHEUMATOID ARTHRITIS PATIENTS USING JANUS KINASE INHIBITORS (THE JAK-POT STUDY)

K. Lauper[1], D. Mongin[1], S. A. Bergstra[2], D. Choquette[3], C. Codreanu[4], D. De Cock[5], L. Dreyer[6], O. Elkayam[7], K. Hyrich[8], F. Iannone[9], N. Inanc[10], E. Kristianslund[11], T. K. Kvien[11], B. Leeb[12], G. Lukina[13], D. Nordström[14], K. Pavelka[15], M. Pombo-Suarez[16], Z. Rotar[17], M. J. Santos[18,19], A. Strangfeld[20], D. Courvoisier[1], A. Finckh[1]on behalf of Epidemiology and registry working group. *[1]Geneva University Hospital, Rheumatology, Geneva, Switzerland*; *[2]LUMC, Rheumatology, Leiden, Netherlands*; *[3]CHUM, Institut de Recherche en Rhumatologie, Montréal, Canada*; *[4]University of Medicine, Center of Rheumatic Diseases, Bucharest, Romania*; *[5]KU Leuven, Skeletal Biology and Engineering Research Center, Leuven, Belgium*; *[6]Aalborg University Hospital, Rheumatology, DANBIO Aalborg, Aalborg, Denmark*; *[7]Tel Aviv University, Rheumatology, Tel Aviv, Israel*; *[8]University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; *[9]University Hospital of Bari, GISEA, Rheumatology, Bari, Italy*; *[10]Marmara University School of Medicine, Rheumatology, Istanbul, Turkey*; *[11]Diakonhjemmet Hospital, Rheumatology, Oslo, Norway*; *[12]University Hospital St. Poelten, Rheumatology, St. Poelten, Austria*; *[13]V.A.Nasonova Research Institute, Rheumatology, Moscow, Russian Federation*; *[14]Helsinki University, ROB-FIN, Helsinki, Finland*; *[15]Institute of Rheumatology, Rheumatology, Prague, Czech Republic*; *[16]Hospital Clinico Universitario, Rheumatology, Santiago de Compostela, Spain*; *[17]University Medical Centre Ljubljana & Universitiy of Ljubljana, Rheumatology, Ljubljana, Slovenia*; *[18]Rheuma.pt, RA, Lisbon, Portugal*; *[19]Faculdade de Medicina de Lisboa, Rheumatology Research Unit, Instituto de Medicina Molecular, Lisbon, Portugal*; *[20]DRFZ, Programme Area Epidemiology, Berlin, Germany*

Background: Industry, regulators, and the rheumatology community have recognized the need for observational studies to monitor the safety of new anti-rheumatic agents. Registries provide a unique opportunity to understand the safety of newer therapies, but pharmacovigilance studies require large number of patients to evaluate rare drug-related adverse-events (AEs). Because JAK-inhibitors (JAKi) have only recently been approved for the treatment of rheumatoid arthritis, it makes sense to combine data from several registries in order to obtain a sufficiently large sample size to promote earlier detection of adverse events.

Objectives: The purpose of this analysis was to evaluate how AEs are assessed in the various registries in preparation for a collaborative pharmacovigilance analysis, and present preliminary results.

Methods: The "JAK-pot" collaboration includes 19 RA registries. The principal investigators of the participating registries were sent a structured questionnaire on AE assessment and 18 (94%) provided complete responses on the AE assessment procedures of their registries. We present simple descriptive statistics of the AE assessment procedures employed by the participating registries.

Results: The 19 registries represent 7186 patients initiating a JAKi (Table 1), who are on average 57 years old, with a mean disease duration 11 years, seropositive (83%), female (82%) and with moderate disease activity at treatment initiation.

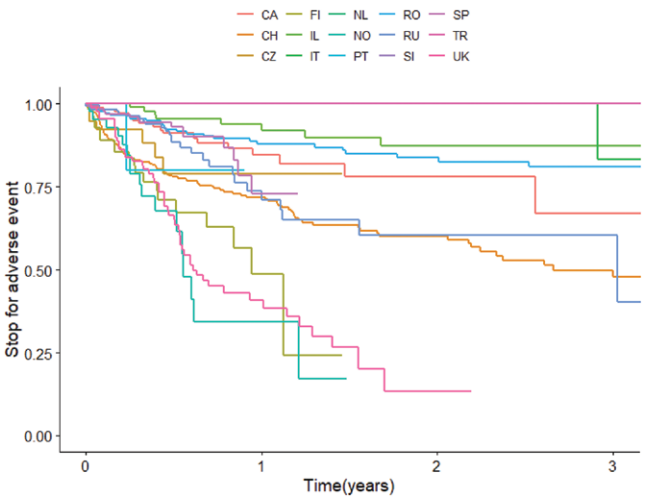
Table 1.

Country, registry	N° of patients on JAKi included
Austria, BIOREG	87
Belgium, TARDIS	2113
Canada, RHUMADATA	363
Czech Republic, ATTRA	197
Denmark, DANBIO	506
Finland, ROB-FIN	229
Germany, RABBIT	620
Italy, GISEA	244
Israel, I-RECORD	96
Netherlands, METEOR	4
Norway, NOR-DMARD	97
Portugal, REUMA.PT	44
Romania, RRBR	252
Russia, ARBITER	428
Slovenia, biorx.si	141
Spain, BIOBADASER	139
Switzerland, SCQM	738
Turkey, TURKBIO	404
UK, BSRBR	484

After ineffectiveness, AEs was the second most common reason for JAKi discontinuation (25.5%), with large differences between registries (Figure 1).

Of the participating registries, 2 registries do not collect AEs, while 16 (89%) assess incident AEs, by means of a pre-specified extraction form (3 registries), by free text (5 registries), by a combination of both (6 registries) and/or the use of linkage to external electronic records (3registries). AEs are coded using a predefined coding system by 11 registries (MeDRA (8), other (3)), but nearly all are recording the severity of the AE (15, 94%), AE related-death (15, 94%), or AE-related hospitalisation (15, 94%). AEs of special interest, such as serious infections (15, 94%), thromboembolic events (15, 94%), or shingles (9, 56%), are recorded by most registries. Incident AEs are linked by the treating physician to specific therapies in 11 registries (69%), while the other 5 registries extrapolate potential causal associations based on therapy start and stop dates. A pre-specified adjudication process for AEs is made only by 5 registries (31%).

Figure 1: Treatment discontinuation of JAKi for AEs in registries with individual patient-level information



Conclusion: Substantial heterogeneity exists among registries regarding AE assessment within the JAK-pot collaboration. These differences must be taken into account when analysing the safety of JAKi across different countries in collaborative studies. For comparative analyses, stratified analyses by country are required to account for differential AE assessment and varying degrees of potential under-reporting.

Disclosure of Interests: Kim Lauper: None declared, Denis Mongin: None declared, Sytske Anne Bergstra: None declared, Denis Choquette: None declared, Catalin Codreanu: None declared, Diederik De Cock: None declared, Lene Dreyer: None declared, Ori Elkayam: None declared, Kimme Hyrich: None declared, Florenzo Iannone: None declared, Nevsun Inanc: None declared, Eirik kristianslund: None declared, Tore K. Kvien: None declared, Burkhard Leeb: None declared, Galina Lukina: None declared, Dan Nordström: None declared, Karel Pavelka: None declared, Manuel Pombo-Suarez: None declared, Ziga Rotar: None declared, Maria Jose Santos: None declared, Anja Strangfeld: None declared, Delphine Courvoisier: None declared, Axel Finckh Speakers bureau: Eli-Lilly, Pfizer, Consultant of: Eli-Lilly, Pfizer, Grant/research support from: BMS, Pfizer.

DOI: 10.1136/annrheumdis-2021-eular.2216

POS0094 EFFECTS OF RANKL INHIBITION ON PROMOTING HEALING OF BONE EROSION IN RHEUMATOID ARTHRITIS USING HR-pQCT: A 2-YEAR, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

H. So[1], I. T. Cheng[1], S. L. Lau[1], E. Chow[1], T. Lam[1], V. W. Hung[2], E. Li[1], J. F. Griffith[3], V. W. Lee[4], L. Shi[3], J. Huang[3], Y. K. Kwok[5], I. C. Yim[6], T. K. LI[1], V. Lo[1], J. M. Lee[7], J. J. W. Lee[8], L. Qin[2], L. S. Tam[1]. *[1]The Chinese University of Hong Kong, Medicine and Therapeutics, Hong Kong, Hong Kong (SAR)*; *[2]The Chinese University of Hong Kong, Orthopedics & Traumatology, Hong Kong, Hong Kong (SAR)*; *[3]The Chinese University of Hong Kong, Imaging & Interventional Radiology, Hong Kong, Hong Kong (SAR)*; *[4]The Chinese University of Hong Kong, School of Pharmacy, Hong Kong, Hong Kong (SAR)*; *[5]Queen Elizabeth Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[6]Tseung Kwan O Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[7]Tai Po Hospital, Medicine and Geriatrics, Hong Kong, Hong Kong (SAR)*; *[8]The Chinese University of Hong Kong, The Jockey Club School of Public Health & Primary Care, Hong Kong, Hong Kong (SAR)*

Background: Partial repair of bone erosions in rheumatoid arthritis (RA) is known from high-resolution peripheral quantitative computer tomography (HR-pQCT) studies in patients with moderate to high disease activity using biologics [1]. Whether RANKL inhibition by denosumab is efficacious in healing existing erosions in RA patients with low disease activity or in remission on conventional synthetic DMARDs is uncertain.

Objectives: To evaluate the effects of denosumab on erosion healing at 2-4 metacarpophalangeal head as determined by HR-pQCT in patients with RA with stable disease.

Methods: This was a randomized, placebo-controlled, double-blind study. RA patients with disease activity score 28 joints (DAS28) ≤5.1 were randomized (1:1) to subcutaneous denosumab 60 mg or placebo once every six months for 24 months. The primary outcome was erosion healing at MCP 2-4 on HR-pQCT at 12 months. The effects of denosumab on erosion and joint space parameters on HR-pQCT and radiographs, disease activity and health assessment questionnaire-disability index (HAQ-DI) were also examined.

Results: At 24 months, HR-pQCT images were analyzed in 98 patients. Baseline demographic, clinical characteristics and imaging parameters were comparable between the two treatment groups (table 1). Seventeen patients in each group (placebo group: 17/52, 32.6%; denosumab group: 17/50, 34.0%) achieved sustained low disease activity (DAS28 ≤ 3.2) throughout the 24 months. At 12 months, changes in erosion parameters on HR-pQCT were similar between the two groups. At 24 months, new erosions (19% vs 9%, p=0.009) and erosion progression (34% vs 16%, p<0.001) were more common in the placebo group than the denosumab group. Erosion healing was seen in a significantly higher proportion of patients in the denosumab group (20% vs 6%, p=0.045) at 24 months. The details of the changes in HR-pQCT erosion parameters are shown in figure 1. No significant differences in the changes in joint space parameters on HR-pQCT, van der Heijde-Sharp erosion score, DAS28 and HAQ-DI were observed between the two groups at 12 and 24 months.

Conclusion: Although no differences in erosion parameters were observed at 12 months, denosumab was more efficacious than placebo in erosion repair on HR-pQCT after 24 months.

REFERENCES:

[1] Finzel S, Rech J, Schmidt S, et al. Interleukin-6 receptor blockade induces limited repair of bone erosions in rheumatoid arthritis: a micro CT study. Ann Rheum Dis 2013;72:396-400.

Table 1. Baseline clinical, demographic, disease activity parameters and medications

	Placebo (n=55)	Denosumab (n=55)	Total (n=110)
Age	56.5 ± 7.1	57.2 ± 8.5	56.8 ± 7.8
Gender (Female)	47 (86)	41 (75)	88 (80)
Disease duration (years)	8.5 ± 6.8	7.3 ± 6.9	7.9 ± 6.8
Rheumatoid factor positive	40 (72)	38 (69)	78 (71)
ACPA positive	43 (78)	44 (80)	87 (79)
DAS28-CRP	2.43 ± 0.83	2.6 ± 0.92	2.51 ± 0.88
DAS28-CRP>3.2	8 (15)	13 (24)	21 (19)
HAQ-DI (0-3)	0.31 ± 0.38	0.46 ± 0.47	0.39 ± 0.43
csDMARDs	49 (89)	52 (95)	101 (92)
Combination csDMARDs	26 (47)	33 (60)	59 (54)
Glucocorticoids	5 (10)	5 (9)	10 (9)
vdH- Sharp erosion score	10.4 ± 18.4	8.9 ± 13.8	9.6 ± 16.2
vdH- Sharp JSN score	12.4 ± 17.7	11.5 ± 17.2	11.9 ± 17.4
Lumbar spine aBMD, g/cm^2	0.914 ± 0.147	0.930 ± 0.143	0.922 ± 0.145
Total hip aBMD, g/cm^2	0.837 ± 0.102	0.847 ± 0.146	0.841 ± 0.125
Femoral neck aBMD, g/cm^2	0.681 ± 0.099	0.695 ± 0.128	0.687 ± 0.114

Data are reported as mean ± SD or number (%). ACPA: Anti-cyclic citrullinated peptide antibody; DAS28: disease activity score 28; csDMARDs: conventional synthetic disease modifying anti-rheumatic drug. HAQ-DI: health assessment questionnaire disability index; vdH- Sharp score: Van der Heijde- Sharp score; aBMD: areal bone mineral density

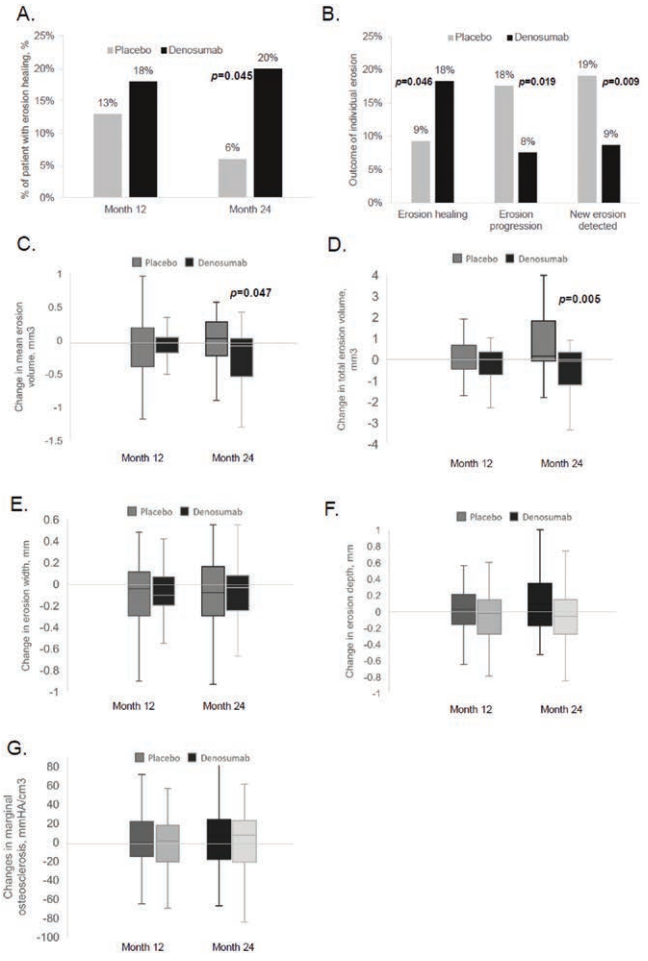


Figure 1. Changes in erosion parameters by HR-pQCT. (A) Percentage of patients with overall erosion healing; (B) Outcome of individual erosion with healing, progression and new erosion detected across study period; change in (C) mean erosion volume; (D) total erosion volume; (E) erosion width; (F) erosion depth and (G) marginal osteosclerosis per patient.

Disclosure of Interests: Ho SO: None declared, Isaac T. Cheng: None declared, Sze-Lok Lau: None declared, Evelyn Chow: None declared, Tommy Lam: None declared, Vivian W Hung: None declared, Edmund Li: None declared, James F Griffith: None declared, Vivian WY Lee: None declared, Lin Shi: None declared, Junbin Huang: None declared, Yan Kitty Kwok: None declared, Isaac C Yim: None declared, Tena K. Li: None declared, Vincent Lo: None declared, Jolly M Lee: None declared, Jack Jock Wai Lee: None declared, Ling Qin: None declared, Lai-Shan Tam Grant/research support from: Grants from Novartis and Pfizer

DOI: 10.1136/annrheumdis-2021-eular.2752

POS0095

DEVELOPPING A SCORE TO PREDICT PRECLINICAL INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS – A CROSS-SECTIONAL STUDY FROM THE ESPOIR COHORT

P. A. Juge[1], B. Granger[2], M. P. Debray[3], E. Ebstein[1], F. Louis Sidney[4], J. Kedra[2], R. Borie[5], A. Constantin[6], B. Combe[7], R. M. Flipo[8], X. Mariette[9], O. Vittecoq[10], A. Saraux[11], G. Carvajal Alegria[11], J. Sibilia[12], F. Berenbaum[13], C. Kannengiesser[14], C. Boileau[14], B. Crestani[5], B. Fautrel[2], P. Dieudé[1]. *[1]Bichat-Claude Bernard Hospital, Rheumatology, Paris, France*; *[2]University Hospitals Pitié Salpêtrière - Charles Foix, Rheumatology, Paris, France*; *[3]Bichat-Claude Bernard Hospital, Radiology, Paris, France*; *[4]Hospital Pierre Zobda-Quitman, Rheumatology, Fort-de-France, Martinique*; *[5]Bichat-Claude Bernard Hospital, Pulmonology, Paris, France*; *[6]Hospital Pierre Paul Riquet Toulouse, Rheumatology, Toulouse, France*; *[7]Chu Montpellier, Rheumatology, Montpellier, France*; *[8]Chu De Lille, Rheumatology, Lille, France*; *[9]CHU du Kremlin-Bicêtre, Rheumatology, Le Kremlin-Bicêtre, France*; *[10]CHU Hôpitaux de Rouen, Rheumatology, Rouen, France*; *[11]Hospital De Carhaix, Rheumatology, Carhaix-Plouguer, France*; *[12]Chu Strasbourg, Rheumatology, Strasbourg, France*; *[13]Hospital Saint-Antoine Ap-Hp, Rheumatology, Paris, France*; *[14]Bichat-Claude Bernard Hospital, Genetic, Paris, France*

Background: Interstitial lung disease (ILD) is an extra-articular manifestation of rheumatoid arthritis (RA) detected in 20% to 60% of patients with RA on high-resolution computed-tomography (HRCT) chest scan and is clinically significant in near 10%. Despite a high morbi-mortality rate, a definite strategy for preclinical ILD screening in patients with RA remains to be determined. To date, several factors have been reported to increase the risk of RA-ILD occurrence (*i.e.* older age at RA onset, ACPA positivity, male sex, RA disease activity, the *MUC5B* rs35705950 promoter variant...). However, none of these risk factors has been validated in a prospective cohort of patients with RA. The ESPOIR prospective cohort includes patients aged 18 to 70 years with recent arthritis (less than 6 months) and a definite or probable diagnosis of RA.

Objectives: To identify in the ESPOIR cohort factors associated with ILD after at least 10 years of RA duration in order to develop a predictive score to identify patients with preclinical RA-ILD.

Methods: An ILD detection by chest HRCT scan was systematically offered to every patient with definite RA after at least 10 years-follow-up. Chest HRCT scans were centrally reviewed by an experienced radiologist. Potential predictors of ILD were prospectively collected from baseline to the date of the HRCT scan, and all included patients were genotyped for *MUC5B* rs35705950. To take into account repeated measures, trajectories were determined for disease activity, C reactive protein, smoking, treatment exposure (*i.e.* prednisone, methotrexate [MTX] and biological disease modifying anti-rheumatic drugs [bDMARDs]). A logistic model was used to identify independent predictors for the occurrence of ILD on HRCT scans. Confidence intervals were estimated using sampling methods. A predictive score for preclinical ILD occurrence was developed based on the identified predictors.

Results: 163 RA patients according to 2010 ACR/EULAR classification criteria, none of whom had pulmonary symptoms, were investigated with a chest HRCT scan (128 women (78.5%), mean RA duration 13.7 ± 1.1 years, age at inclusion 47.6 y/o ± 10.4, mean disease activity score [DAS]-28 during follow up was 3.1 ± 1.0). ILD was detected in 31 patients (19.0%). The *MUC5B* rs35705950 minor allele frequency (MAF) was 22.2% and 10.0% in the RA-ILD and RA-noILD populations, respectively (OR univariate=2.6 $CI_{95\%}$ [1.2-5.5], P=0.01). After logistic regression, independent predictors for preclinical RA-ILD were male sex (OR=3.9 $CI_{95\%}$ [1.4-11.4]), older age at RA onset (OR=1.1 per year $CI_{95\%}$ [1.0-1.2]), mean DAS-28 score during the follow-up (OR=2.0 $CI_{95\%}$ [1.2-3.4]) and *MUC5B* rs35705950 T risk allele (OR=3.7 $CI_{95\%}$ [1.4-10.4]) (Figure 1). No influence of the use of RA-related drugs (prednisone, MTX or bDMARDs) was identified as risk factor. The logistic model could predict preclinical ILD occurrence after 13 years of RA duration with an AUC=0.82 $CI_{95\%}$ (0.72-0.91). A predictive score for preclinical RA-ILD based on the 4 identified predictive risk factors was developed (Sensitivity 80%, Specificity 56%).

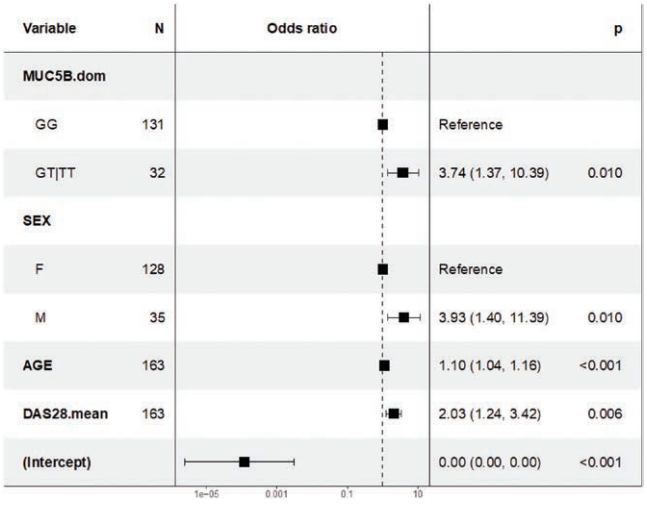


Figure 1. Factors independently associated with preclinical ILD after 13 years of RA duration

Conclusion: In this cross-sectional study of the prospective ESPOIR cohort, we identified clinical and genetic predictors for ILD after 13 years of RA duration. We developed a predictive score that could improve risk stratification for preclinical RA-ILD and help physicians identify patients with RA in whom a HRCT scan should be performed.

Disclosure of Interests: Pierre-Antoine Juge Consultant of: BMS, Benjamin Granger: None declared, Marie-Pierre Debray: None declared, Esther Ebstein: None declared, Fabienne Louis Sidney: None declared, Joanna KEDRA: None declared, Raphael Borie: None declared, Arnaud Constantin Consultant of: Bristol-Meyers Squibb, Chugai, Roche, Abbvie, MSD, Pfizer, and UCB, Bernard Combe Consultant of: Abbvie, Bristol-Meyers Squibb, Lilly, MSD, Janssen, Pfizer, Roche, Chigai, and Sanofi, Grant/research support from: Abbvie, Bristol-Meyers Squibb, Lilly, MSD, Janssen, Pfizer, Roche, Chugai, and Sanofi, René-Marc Flipo Consultant of: Bristol-Meyers Squibb, Roche, Chugai, Abbvie, and Pfizer, Grant/research support from: Roche, Chugai, Abbvie, and Pfizer, Xavier Mariette Consultant of: Bristol-Meyers Squibb, GSK, Janssen, Pfizer, and UCB, Olivier VITTECOQ Consultant of: Bristol Myers Squibb, Roche, Chugai, MSD, Novartis, Pfizer, Abbvie, and Lilly, Alain Saraux Consultant of: Roche, Chugai, and Bristol-Meyers Squibb, Grant/research support from: Roche, Chugai, and Bristol-Meyers Squibb, Guillermo CARVAJAL ALEGRIA: None declared, Jean Sibilia Consultant of: Roche, Chugai, Bristol-Meyers Squibb, UCB, GSK, LFB, Actelion, Pfizer, MSD, Novartis, Amgen, Hospira, AbbVie, Sandoz, Gilead, Lilly, Sanofi, Janssen, and Mylan, Francis Berenbaum Consultant of: Boehringer, Bone Therapeutics, Expanscience, Galapagos, Gilead, GSK, Elli Lilly, Merck Sereno, MSD, Nordic, Novartis, Pfizer, Regulaxis, Roche, Sandoz, Sanofi, Servier, UCB, Peptinov, TRB Chemedica, 4P Pharma, Caroline Kannengiesser: None declared, Catherine Boileau: None declared, Bruno Crestani Consultant of: Boehringer Ingelheim, Roche, Sanofi, Apellis, Astra-Zeneca, Grant/research support from: MedImmune, Boehringer Ingelheim, Bruno Fautrel Consultant of: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, Sanofi-Aventis, SOBI, UCB, Grant/research support from: AbbVie, MSD, Pfizer, Philippe Dieudé: None declared

DOI: 10.1136/annrheumdis-2021-eular.2817

POS0096

SPLENIC METABOLIC UPTAKE IN FDG-PET/CT PREDICTS RISK OF FUTURE CARDIOVASCULAR THROMBOSIS EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. J. Lee[1], C. M. Hong[2], Y. M. Kang[1]. *[1]School of Medicine, Kyungpook National University, Internal Medicine, Daegu, Korea, Rep. of (South Korea)*; *[2]School of*

Medicine, Kyungpook National University, Nuclear Medicine, Daegu, Korea, Rep. of (South Korea)

Background: Patients with the rheumatoid arthritis (RA) have an increased risk of cardiovascular disease (CVD) compared to general population. However there are insufficient modality to predict future CVD risk in RA.
Objectives: This study assessed whether splenic and arterial activity measured by positron emission tomography/ computed tomography (PET/CT) predict the risk of CVD thrombosis events beyond conventional risk factors in patients with RA.
Methods: We enrolled 84 patients with active RA who underwent fluorine-18-fluorodeoxyglucose (FDG) PET/CT and disease activity evaluation at the same time. CVD thrombosis events were independently evaluated, while blinded to activity of PET/CT, during follow up periods. FDG uptake by nuclear medicine physician was examined in the spleen and ascending aorta and blood pool activity of superior vena cava as SUV (standardized uptake values) and target-to-background-ratio (TBR) while blinded to CVD events.
Results: During follow-up periods, 19 patients developed CVD thrombosis events. Both splenic and arterial TBR were significantly increased in patients with subsequent CVD events compared to in patients without (2.19 ± 0.60 vs 1.80 ± 0.34, p < 0.013, 1.72 ± 0.22 vs 1.57 ± 0.22, p< 0.012). Splenic TBR was associated with an increased risk of CVD events after adjustment for conventional CVD risk factors [hazard ratio (HR): 3.15; 95% confidence interval (CI): 1.46 to 6.79; p = 0.003]. Moreover, the association between splenic TBR and CVD events remained significant after adjustment for disease activity (HR: 3.00; CI: 1.36 to 6.63; p = 0.007) and after adjustment for arterial TBR (HR: 3.00; CI: 1.36 to 6.63; p = 0.007).
Conclusion: Our results show splenic metabolic uptake in FDG-PET/CT in patients with RA provide information for subsequent CVD events beyond conventional risk factors.
REFERENCES:
[1] Lee SJ, Jeong JH, Lee CH, et al. Development and validation of an (18) F-fluorodeoxyglucose-positron emission tomography with computed tomography-based tool for the evaluation of joint counts and disease activity in patients with rheumatoid arthritis. *Arthritis Rheumatol*. 2019;71:1232-1240.
Disclosure of Interests: : None declared
DOI: 10.1136/annrheumdis-2021-eular.3574

POS0097 JOINT INFLAMMATION TENDS TO RECUR IN THE SAME JOINTS DURING THE RHEUMATOID ARTHRITIS DISEASE COURSE

S. Heckert[1], S. A. Bergstra[1], X. Matthijssen[1], Y. Goekoop-Ruiterman[2], F. Fodili[3], C. Allaart[1], T. Huizinga[1]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; [2]*Hagaziekenhuis, Rheumatology, Den Haag, Netherlands*; [3]*Reumazrg Z.-W. Eng., Roosendaal, Rheumatology, Roosendaal, Netherlands*

Background: It is unknown whether in the disease course of rheumatoid arthritis (RA), inflammation recurs in the same joints over time or is more variable in joint locations. Joint involvement patterns over time might provide clues about the underlying mechanisms causing local joint inflammation.
Objectives: The aim of this study is to assess if local joint inflammation at presentation of RA tends to recur or persist in the same joints.
Methods: Data from the BeSt study were used, a treat-to-target (DAS≤2.4) trial in newly diagnosed RA (ACR 1987 criteria) patients. During 10 years, for each patient 68 joints were assessed three-monthly (41 visits) by trained nurses for swelling (yes/no) and tenderness.
We analyzed the association between local joint swelling at baseline and later swelling of the same joint using a multilevel mixed-effects logistic regression model. Models were adjusted for joint location and for timepoint, with joints clustered within patients. A sensitivity analysis was done for the 25% most affected joints (MCP 1-3, PIP 2-3, wrists and MTP 2-4).
To investigate whether later swelling of a joint is predicted by baseline swelling of that same joint specifically, rather than by baseline swelling in general, a permutation test with 1000 permutations was performed. A p-value <0.05 indicates that joint swelling is better predicted by its baseline swelling than by baseline swelling of randomly selected other joints.
In a separate model, with an interaction term between baseline swelling and previous visit swelling (yes/no), we evaluated if the association between baseline swelling and later local swelling was influenced by whether later swelling was persistent (swelling at both the current and previous visit) or recurrent (swelling at current visit but not at the previous visit).
Results: The 508 patients had a median (IQR) follow-up duration of 10 (6-10) years. At baseline, 8,137/34,423 (24%) assessed joints were scored as swollen. Baseline swelling was subsequently persistent in 21% of the joints with a median (IQR) duration of 1 (1-2) visit (± 3 months after baseline). In addition, after resolution of initial swelling, swelling recurred at least once in 46% of the joints with baseline swelling.
Baseline swelling was significantly associated with swelling in the same joint during follow-up (OR 2.37, 95% CI 2.30-2.43). A sensitivity analysis of the most affected joints showed similar results (OR 2.10 [95% CI 2.03-2.19]).
The permutation test showed a significant result with p<0.001, indicating that joint swelling is better predicted by baseline swelling of that same joint than by baseline swelling of other joints.
The association between baseline swelling and later local swelling was weaker in case of persistent swelling than in case of recurrent swelling (interaction term baseline swelling * swelling at previous timepoint 'yes': OR 0.80 [95% CI 0.75-0.85]).
Conclusion: In newly diagnosed RA, over median 10 years of treatment to target DAS≤2.4, baseline swelling persisted in 21% of the joints, for median 3 months after baseline. Local recurrence after initial resolution occurred in 46% of the joints. Baseline joint swelling was significantly associated with local joint swelling during follow-up, even when taking into account the higher a priori chance of swelling in the joints that are most often affected, and joint swelling during follow-up was better predicted by baseline swelling of that particular joint than by baseline swelling of other joints. Local persistence and recurrence of joint swelling despite DAS≤2.4 steered treatment adjustments suggest that local joint conditions or even joint memory play a role in mechanisms of joint inflammation.
Acknowledgements: We would like to thank all patients for their contribution as well as the rheumatologists who participated in the BeSt study group. We would also like to thank all other rheumatologists and trainee rheumatologists who enrolled patients in these studies, and all research nurses for their contributions.
Disclosure of Interests: Sascha Heckert: None declared, Sytske Anne Bergstra: None declared, Xanthe Matthijssen: None declared, Yvonne Goekoop-Ruiterman: None declared, F. Fodili: None declared, Cornelia Allaart Grant/research support from: The original BeSt study was supported by a government grant from the Dutch insurance companies, with additional funding from Schering-Plough B.V. and Janssen B.V., Thomas Huizinga: None declared
DOI: 10.1136/annrheumdis-2021-eular.280

POS0098 THE INFLUENCE OF THE ACTIVITY OF RHEUMATOID ARTHRITIS TO INFECTIOUS AND WOUND COMPLICATIONS AFTER TOTAL HIP AND KNEE ARTHROPLASTY

A. Khramov[1], M. Makarov[1], S. Makarov[1], S. Maglevaniy[1], E. Naryshkin[1], A. Dubinin[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Orthopaedic, Moscow, Russian Federation*

Background: Surgical treatment of patients with rheumatoid arthritis (RA) is associated with an increased risk of complications. This is due to the presence of inflammation, many variants of the disease, reduced physical activity, severity of functional disorders, prolonged therapy with glucocorticoids, disease-modifying antirheumatic drugs (DMARDs) and biological DMARDs, osteoporosis, as well as activity of the underlying disease.
Objectives: to conduct a comparative analysis of the influence of RA activity levels on infectious complications (periprosthetic infection) and wound complications (poor healing, divergence, necrosis of the wound edges) after hip and knee arthroplasty in RA patients.
Methods: 1113 arthroplasties were analyzed in patients with RA, which were performed between 2002 and 2019. Of these, 649 total knee arthroplasties and 464 total hip arthroplasties were performed.
Results: Infectious complications after total hip and knee arthroplasty did not occur at 0 grade of disease activity (remission). At the I grade of activity, periprosthetic infections were detected with a frequency of 0.31%, at the II grade – 0.89%, and at the III level in 3.06% of cases.
Complications from the operative wound occurred in 0.91% of cases with I grade of activity, at II grade with a frequency of 5.68%, and at III – 6.98%. There were no cases of complications from the wound in patients with remission of RA.
Statistical analysis of the obtained data revealed a significantly higher number of complications in the group of RA patients (p<0.005). During analyzing each type of complication, significant differences were also obtained (p<0.005).
Conclusion: Risk of periprosthetic infection and complications from the wound is several times higher in patients with a high grade of RA activity. This means that performing arthroplasty, as well as other operations, in patients with high RA activity correlates to a high risk of complications.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.626

POS0099 CLINICAL REMISSION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB IS ASSOCIATED WITH LOW BASELINE EXPRESSION OF GENES RELATED TO ENERGY METABOLISM AND WITH CELLULAR CAPACITY OF THEIR UPREGULATION DURING FOLLOW-UP

E. Tchetina[1], A. Satybaldyev[2], G. Markova[1]. [1]*Nasonova Research Institute of Rheumatology, Immunology and Molecular Biology, Moscow, Russian Federation*; [2]*Nasonova Research Institute of Rheumatology, Early Arthritis, Moscow, Russian Federation*

Background: Rheumatoid arthritis (RA) is an autoimmune disease of unknown etiology, which is characterized by erosive arthritis (synovitis) and systemic inflammation. Tofacitinib (TFCN) is a small molecule Janus kinase (JAK) inhibitor that targets JAK1/JAK3. Identification of patients sensitive to TFCN before treatment could significantly improve therapy outcome. Presently it is not possible to predict TFCN efficacy in every patient while some patients are non-responsive to the drug that may produce adverse effects. TFCN function in RA patients has been recently associated with alterations in bioenergetics, mitochondrial function, and ATP production [1]. Therefore, we hypothesized that baseline metabolic status of RA patients prior to drug administration can predict the therapeutic outcome.

Objectives: To investigate the importance of baseline expression of genes involved in energy generation in RA patients, which could serve prognostic biomarkers for treatment response to tofacitinib.

Methods: Peripheral blood of 28 RA patients aged 52.2±15.6 years old, average disease duration 3.5 years (range 0.6-19) treated with TFCN (5-10 mg twice a day) during three months and 26 healthy age-matched control subjects were examined. Clinical response was assessed by disease activity score (DAS28-ESR), serum levels of ACPA antibodies, rheumatoid factor (RF), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Clinical remission was assessed according to ACR criteria and DAS28 (DAS28 <2.6). Protein concentrations were measured using ELISA. Total RNA was isolated and used in gene expression studies performed with quantitative real-time RT-PCR.

Results: All of the patients were Steinbrocker's radiographic stage II-III at baseline. The majority of patients demonstrated erosive arthritis (23 out of 28), they were ACPA- (25 out of 28) and RF- (24 out of 28) positive. TFCN treatment significantly decreased the disease activity according to DAS28. At the end of the study the majority of patients demonstrated moderate disease activity (3.2< DAS28 <5.1), four patients retained high disease activity while 8, attained remission (DAS28 <2.6). This was accompanied by significant decrease in CRP and the number of swollen and tender joints. ESR values were not changed significantly. Gene and protein expression analysis revealed that RA patients, which attained clinical remission after TFCN treatment demonstrated significantly lower baseline expression of genes associated with glycolysis (pyruvate kinase), oxidative phosphorylation (succinate dehydrogenase and uncoupling protein (UCP) 2) compared to other examined RA patients and control subjects. Moreover, these gene expressions increased in RA patients who attained clinical remission in the course of follow-up while in refractory for TFCN treatment patients these gene expressions were tending to downregulate.

Conclusion: Clinical remission attainment in RA patients treated with tofacitinib is associated with lower baseline expression of genes associated with energy generation pathways (pyruvate kinase, succinate dehydrogenase, and UCP2) compared to other examined subjects. Non-responsiveness to tofacitinib is accompanied by high baseline expression of genes related to glycolysis and oxidative phosphorylation compared to controls.

REFERENCES:

[1] McGarry et al. JAK/STAT Blockade Alters Synovial Bioenergetics, Mitochondrial Function, and Proinflammatory Mediators in Rheumatoid Arthritis. Arthritis Rheumatol, 2018; 70:1959.

Acknowledgements: Russian Ministry of Education and Science (Project No. AAAA-A19-11-9021190145-2 to EVT).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.837

POS0100 VITAMIN D LEVEL IN RHEUMATOID ARTHRITIS PATIENTS STARTING A BIOLOGIC DISEASE-MODIFYING DRUG AND ITS CORRELATION WITH DISEASE ACTIVITY AND RESPONSE TO TREATMENT

S. Garcia[1], B. M. Fernandes[1], F. Oliveira Pinheiro[1], M. Rato[1], D. Fonseca[2], A. Martins[1], D. Santos Oliveira[1,3], F. R. Martins[4], G. Terroso[1], M. Bernardes[1,5], L. Costa[1]. [1]*São João Universitary Hospital Center, Rheumatology, Porto, Portugal*; [2]*Centro Hospitalar Vila Nova de Gaia / Espinho - Unit 1, Rheumatology, Vila Nova de Gaia, Portugal*; [3]*Faculdade de Medicina da Universidade do Porto - FMUP, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; [4]*University Hospital Center of Algarve, Faro, Rheumatology, Faro, Portugal*; [5]*Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal*

Background: Vitamin D, a fat soluble vitamin that is mainly involved in the regulation of calcium/phosphate metabolism, has a increasingly understood role in immunomodulatory activity, both in innate and adaptive immune system. In rheumatoid arthritis (RA), vitamin D showed to suppress the proliferation of synoviocytes and to reduce the production of proinfammatory cytokines, in vitro. (1) Recently the hypothesis has been raised that vitamin D has a negative association with RA activity. (2)

Objectives: This study aimed to evaluate the relationship between the 25-hydroxyvitamin D (25(OH) vitD) level, RA activity and response to a first biologic disease-modifying drug (bDMARD).

Methods: This is a longitudinal, retrospective study including consecutive patients with the diagnosis of RA followed at our rheumatology department. Demographic, clinical, and laboratorial data were collected from our national database at baseline, 6 and 12 months after initiation of a first bDMARD. Statistical analysis was performed using SPSS 23.0. Correlations between variables were studied using Spearman correlation analysis and comparison between groups was performed using Wilcoxon and Kruskal-Wallis tests; p<0.05 was considered statistically significant.

Results: Mean age of patients (n=236) was 51.5± 11.2 years old, 192 (81.4%) were females with a median disease duration of 10.1 [4.7, 16.7] years. Seropositivity for anti-citrullinated protein antibodies was present in 192 (81.4%) patients and for rheumatoid factor in 175 (74.2%). The majority exhibited a very high or high disease activity at baseline (median DAS28 5.75 [4.99 – 6.63]) and 90% (n=212) of them were concomitantly using corticosteroids and/or other disease-modifying anti-rheumatic drugs (117 with methotrexate (MTX), 62 with leflunomide and 32 with sulfasalazine). Regarding bDMARD, 56.8% (n=134) initiated an TNF alpha inhibitor.

After 6 and 12 months from a bDMARD initiation there was a significant reduction of ESR, CRP levels, TJCs, SJCs and DAS28 (all p-values < 0.001), as expected. Median baseline serum 25(OH) vitD concentrations was 25.5 [16.5, 30.0] ng/ml; notably, 34.2% of our sample was affected by hypovitaminosis D at baseline (25(OH) vitD< 20 ng/mL).

Among our study population 42.5% patients were responders to first bDMARD (23.8% good and 18.7% moderate responders) according to the EULAR response criteria. Disease remission (DAS28 < 2.6) was achieved by 17.6% of patients.

The percentage of good responders was significantly lower in the subgroup of patients with hypovitaminosis D compared to subjects with normal 25(OH) vitamin D levels at baseline (p=0.002), as it was for the percentage of disease remission (p=0.015).

The bivariate correlation analyses showed that 25(OH) vit D levels at baseline correlated with CRP levels and good response to RA treatment after 12 months (Spearman's coefficient -0.201, p = 0.028; Spearman's coefficient 0.255, p < 0.019, respectively). 25(OH) vit D levels at baseline, 6 and 12 months after bDMARD initiation did not correlate with age, BMI, ESV, number of tender or swollen joints, DAS28, HAQ or with SDAI or CDAI at 6 or 12 months of treatment.

Conclusion: In patients with RA, basal 25(OH) vit D levels correlated with response to a bDMARD. These results suggest a role of basal vitamin D status in the prediction of disease evolution and support the hypothesis that vitamin D has an immunomodulatory potential.

REFERENCES:

[1] Huhtakangas JA, Veijola J, Turunen S et al. 1,25(OH)2D3 and calcipotriol, its hypocalcemic analog, exert a long-lasting anti-infammatory and anti-proliferative effect in synoviocytes cultured from patients with rheumatoid arthritis and osteoarthritis. J Steroid Biochem Mol Biol 2017; 173: 13- 22.

[2] Lee YH, Bae SC. Vitamin D level in rheumatoid arthritis and its correlation with the disease activity: a meta-analysis. Clin Exp Rheumatol. 2016 Sep-Oct;34(5):827-833. Epub 2016 Apr 6. PMID: 27049238.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1172

SLE, Sjögren's and APS - clinical

POS0101 ADVERSE HEALTH-RELATED QUALITY OF LIFE OUTCOME DESPITE ADEQUATE CLINICAL RESPONSE TO TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

A. Gomez[1,2], J. Lindblom[1,2], V. Qiu[1,2], A. Cederlund[1,2], A. Borg[1,2], S. Emamikia[1,2], Y. Enman[1,2], J. Lampa[1,2], I. Parodis[1,2]. [1]*Karolinska Institutet, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden*; [2]*Karolinska University Hospital, Department of Gastroenterology, Dermatology and Rheumatology, Stockholm, Sweden*

Background: Despite improvements in medical care that have contributed to prolonged life expectancy for people living with systemic lupus erythematosus (SLE) over the past decades, they still suffer from substantial diminutions of health-related quality of life (HRQoL) compared with the general population and with other chronic diseases.

Some studies have demonstrated that conventional synthetic and biological disease-modifying agents contribute to improvements in SLE patients' HRQoL, and responders to treatment have been shown to report greater improvements than non-responders. Although these observations are clinically relevant,

improvement following a therapeutic intervention does not necessarily signify that the individual has achieved a satisfactory health state perception. In rheumatoid arthritis, significant pain and severe fatigue persist in a substantial proportion of patients who achieve a good clinical response to treatment or remission. This paradoxical observation has not been thoroughly explored in SLE.

Objectives: To determine the prevalence of adverse HRQoL outcomes in patients with SLE who achieved an adequate clinical response after a 52-week long period on standard therapy plus belimumab or placebo, within the frame of two phase III clinical trials. We further aimed to compare frequencies of adverse HRQoL outcomes across different age categories and ethnic groups, and sought to identify contributing factors.

Methods: We included patients who met the primary endpoint of the BLISS-52 (NCT00424476) and BLISS-76 (NCT00410384) trials (N=760/1684), i.e. attainment of the SLE Responder Index 4 at week 52. Accordingly, evaluation of adverse HRQoL outcomes was based on patient reports at week 52 from treatment initiation, using the Medical Outcomes Study Short Form 36 (SF-36) health survey and the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-Fatigue) scale. Adverse HRQoL outcomes were defined as (i) SF-36 scale scores ≤ the 5th percentile derived from age- and sex-matched US population-based norms from the SF-36 health survey user manual; and (ii) FACIT-Fatigue scores <30.

Pearson's chi-square or Fisher's exact tests were used to investigate associations between dichotomous variables. Comparisons of continuous data between SLE patients and age- and sex-matched norms were performed using the Wilcoxon signed-rank test. Multivariable logistic regression models were created in order to assess independence and priority of potential factors associated with adverse HRQoL outcomes.

Results: We found clinically important diminutions of HRQoL in SLE patients compared with matched norms and high frequencies of adverse HRQoL outcomes, the highest in SF-36 general health (29.1%), followed by FACIT-Fatigue (25.8%) and SF-36 physical functioning (25.4%). Overall, frequencies were higher with increasing age. Black/African American and White/Caucasian patients reported higher frequencies than Asians and Indigenous Americans, while Hispanics experienced adverse HRQoL less frequently than non-Hispanics. Increasing organ damage was associated with adverse physical but not mental HRQoL outcomes; disease activity showed no impact. In multivariable logistic regression analysis, addition of belimumab to standard therapy was associated with lower frequencies of adverse SF-36 physical functioning (OR: 0.59; 95% CI: 0.39–0.91; P=0.016) and FACIT-F (OR: 0.53; 95% CI: 0.34–0.81; P=0.004).

Conclusion: Substantial proportions of SLE patients reported adverse HRQoL outcomes despite adequate clinical response to treatment, especially in physical aspects. Particularly high proportions were seen within Black/African American and White/Caucasian patients. Add-on belimumab may be protective against adverse physical functioning and severe fatigue. Our results corroborate that HRQoL diminutions constitute a substantial burden in patients with SLE, and highlight the limitations of current therapeutic strategies.

Acknowledgements: The authors would like to thank GlaxoSmithKline (Uxbridge, UK) for sharing the data from the BLISS-52 (NCT00424476) and BLISS-76 (NCT00410384) trials with the Clinical Study Data Request (CSDR) consortium, Dimitris Ladakis, Joaquin Matilla and Martin Pehr for contributing to the management of data, as well as all participating patients.

Disclosure of Interests: Alvaro Gomez: None declared, Julius Lindblom: None declared, Victor Qiu: None declared, Arvid Cederlund: None declared, Alexander Borg: None declared, Sharzad Emamikia: None declared, Yvonne Enman: None declared, Jon Lampa: None declared, Ioannis Parodis Grant/research support from: Research funding and/or honoraria from Amgen, Elli Lilly and Company, Gilead Sciences, GlaxoSmithKline and Novartis.

DOI: 10.1136/annrheumdis-2021-eular.1472

POS0102 GO ASK YOUR PATIENTS! PSS-QoL REPORTED PERCEPTION OF DRYNESS CORRELATES WITH LACRIMAL AND SALIVARY FLOW IN PRIMARY SJÖGREN'S SYNDROME

A. Lackner[1], P. Bosch[1], S. Zenz[1], J. Hermann[1], J. Horwath-Winter[2], D. Rabensteiner[2], M. Stradner[1]. *[1]Medical University of Graz, Department of Rheumatology, Graz, Austria*; *[2]Medical University of Graz, Department of Ophtalmology, Graz, Austria*

Background: The patient perspective is an essential outcome parameter in the quest for effective therapy in primary Sjögren's Syndrome (PSS). The EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) is recommended by EULAR to quantify patient's symptom burden and has been used in several clinical trials. Surprisingly, the patient's perception of dryness quantified with ESSPRI does not correlate with objective measures of salivary or lacrimal flow.

Objectives: Thus, we evaluated a newly developed assessment tool-the Primary Sjögren's Syndrome Quality of Life Questionnaire (PSS-QoL) - for quantifying symptoms of dryness in comparison with the ESSPRI and objective measurements of salivary and lacrimal flow.

Methods: Data of patients from the PSS registry of the Medical University of Graz fulfilling the 2016 ACR/EULAR classification criteria for PSS were analysed. The patient perspective was analyzed by PSS-QoL, ESSPRI, Xerostomia Inventory (XI) and Ocular Surface Disease Index (OSDI). Sicca signs were measured with Schirmer's test, unstimulated salivary flow test (USF) and stimulated salivary flow test (SSF). Patients were categorized into groups based on the presence of subjective and/or objective dryness: 1) objective dryness only, 2) subjective dryness only, and 3) both, subjective and objective dryness. ESSDAI (EULAR Sjögren's Syndrome Disease Activity Index) and EGA (Evaluator Global Assessment, numeric rating scale from 0 to 10) were obtained. In addition, free light chains (FLC) κ and λ, rheumatoid factor (RF) IgM and IgA were determined.

Results: Data from 123 PSS patients were analyzed; 91.9% (n=113) were female, with a mean disease duration of 6.2 (±5.3) years and mean age of 60.1 (±12.4) years. PSS-QoL-dryness revealed significant negative correlations with Schirmer's test (r=-0.31, p<0.05) and SSF-test (r=-0.39, p<0.01). In contrast, we found no significant correlation between ESSPRI-dryness and any objective dryness test. Lower perceived dryness was associated with higher immunological activity determined by increased levels of IgG, FLC and RF-IgA. Patients with objective signs and subjective symptoms of dryness had higher clinical and immunological disease activity compared to patients with subjective symptoms only (table 1).

Conclusion: Patients' perception of dryness assessed by PSS-QoL correlates with objective measurements of salivary gland function while ESSPRI-dryness did not. Based on the PSS-QoL and objective measures of dryness two distinct groups of PSS patients could be distinguished, which may have implications in daily practice and future clinical studies.

Table 1. Comparison of perceived dryness-groups with clinical parameters

	PSS-QoL Mouth		p	PSS-QoL Eyes		p
	subj	obj/subj		subj	obj/subj	
EGA	1.0 [0-5]	2.0 [0-7]	<0.05	1.0 [0-3]	2.0 [0-7]	<0.05
ESSDAI	1.0 [0-14	4.0 [0-15	<0.05	3.0 [0-7	4.0 [0-15	ns
ESSPRI-pain	3.0 [0-9]	3.0 [0-10]	ns	4.0 [1-8]	3.0 [0-10]	<0.05
RF-IgM	19.0 [5-524]	31.0 [7-417]	ns	10.0[5-33]	26.0[7-524]	<0.01
FLC-λ	15.1 [7.0-68.3]	20.1 [2.6-124.0]	<0.01	13.4 [7.0-54.5]	18.7[2.6-124.0]	<0.01
IgG	11.9 [6.5-37.2]	16.1 [7.4-33.8]	ns	12.8 [6.5-20.6]	14.8[7.4-37.2]	ns
C4	0.2 [0.01-0.41]	0.17 [0.00-0.43]	<0.01	0.2 [0.09-0.41]	0.18 [0.00-0.43]	ns
RF-IgA	11.0 [1-500]	103 [0-500]	<0.01	4.5 [1-465]	63 [0-500]	<0.01

C4=Complementfactor 4; EGA=Evaluators Global Assessment; ESSDAI=EULAR Sjögren Syndrome Disease Activity Index; ESSPRI=EULAR Sjögren Syndrome Patient Reported Index; FLC-λ=Free light chain Lambda; IgG=Immunoglobulin G; obj/subj=objective and subjective dryness-group; PSS-QoL=Primary Sjögren Syndrome Quality of Life Questionnaire; RF-IgA=rheumatoid factor Immunoglobulin A; RF-IgM=rheumatoid factor Immunoglobulin M; subj=subjective dryness-group.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2319

POS0103 C3 AND C4 VARIATIONS IN SLE PREGNANCIES: PRELIMINARY RESULTS FROM THE GR2 STUDY

M. Larosa[1,2], V. Le Guern[1], G. Guettrot Imbert[1], E. Diot[3], C. Morati-Hafsaoui[4], N. Abisror Jeannin[5], N. Morel[1], O. Souchaud-Debouverie[6], F. Sarrot-Reynauld[7], P. Orquevaux[8], V. Queyrel[9], T. Goulenok[10], N. Limal[11], A. Doria[2], A. Moltó[12], E. Lazaro[13], N. Costedoat-Chalumeau[1]on behalf of GR2 Group. *[1]AP-HP, Hôpital Cochin; Centre Référence Maladies Rares, Service de médecine interne, Paris, France*; *[2]University of Padova, Rheumatology Unit, Department of Medicine-DIMED, Padova, Italy*; *[3]CHRU de Tours - Hôpital Bretonneau, Service de médecine interne, Tours, France*; *[4]CH Annecy Genevois, Service Infectiologie et médecine interne, Annecy, France*; *[5]AP-HP, Hôpital Saint-Antoine, Service de Médecine interne, Paris, France*; *[6]CHU de Poitiers – Milétrie, Service de Médecine interne, Poitiers, France*; *[7]CHU Grenoble, Service de médecine interne, Grenoble, France*; *[8]CHU de Reims-Robert Debré, Service de Médecine interne, Reims, France*; *[9]Hôpital de l'Archet, CHU de Nice, Service de Médecine interne, Nice, France*; *[10]AP-HP, Hôpital Bichat, Service de Médecine interne, Paris, France*; *[11]Hôpital Henri Mondor, Service de Médecine interne, Creteil, France*; *[12]AP-HP, Hôpital Cochin, Service de Rhumatologie B, Paris, France*; *[13]CHU-Hôpital Haut-Lévêque, Service de Médecine interne et maladies infectieuses, Bordeaux, France*

Background: Serum complement levels have been reported, as other proteins, to increase during pregnancy including in patients with systemic lupus erythematosus (SLE). Low C3/C4 levels are taken into account in disease activity scores such as the SLE-Pregnancy Disease Activity (SLEPDAI) (1) and several others. Nonetheless, their exact variations during pregnancy, especially in SLE, remain unknown, and no cut-off values per trimester of gestation have been identified.

Objectives: Our aim was to describe variations of C3 and C4 serum levels in a prospective cohort of SLE pregnancies implemented in 2014.

Methods: Inclusion criteria required that women: 1) were at least 18 years and enrolled in the French prospective observational GR2 study of pregnancies and rare autoimmune diseases; 2) diagnosed with SLE (SLICC criteria); 3) and had a pregnancy which ended before the 25th December 2020. The GR2 study is part of the European network of pregnancies registers in Rheumatology (EuNeP) supported by FOREUM (Foundation for Research in Rheumatology) (2) and follow EULAR recommendations regarding core data set for pregnancy registries in rheumatology (3).

For women with more than 1 pregnancy included in the GR2 study, only the 1st pregnancy meeting the inclusion criteria was analysed. In case of multiple C3 and C4 measures per patient, only the first measure for each trimester was considered when comparing the mean values of serum C3 and C4 levels at each trimester.

Results: This study included 290 pregnant women with SLE (mean age 32.2 years). 669 values of C3 and 648 values of C4 were available and figure 1 represents the variations in serum C3 and C4 levels during pregnancy.

Overall, mean serum C3 value increased from 0.97 g/L in the 1st trimester to 1.24 g/L in the 3rd trimester which corresponded to a 28% increase (Table 1 and figure 2). Mean C4 increased from 0.18 g/L in the 1st trimester to 0.20 g/L in the 3rd trimester which corresponded to a 11% increase (Table 1 and figure 3).

When analysing only the patients with at least one available value of serum C3 and C4 levels at each trimester (n=96 and n=101, respectively), we found very similar results (Table 1). This remained true when patients with flares were excluded (data not shown).

Conclusion: Mean C3 at third trimester increased by 28% compared to first trimester whereas mean C4 levels increased by 11% compared to first trimester. These preliminary results will lead to more precisely define which lowest cut-off value should be used to count low complement during pregnancy in SLE scores.

REFERENCES:

[1] Buyon JP, et al. Assessing disease activity in SLE patients during pregnancy. Lupus 1999.

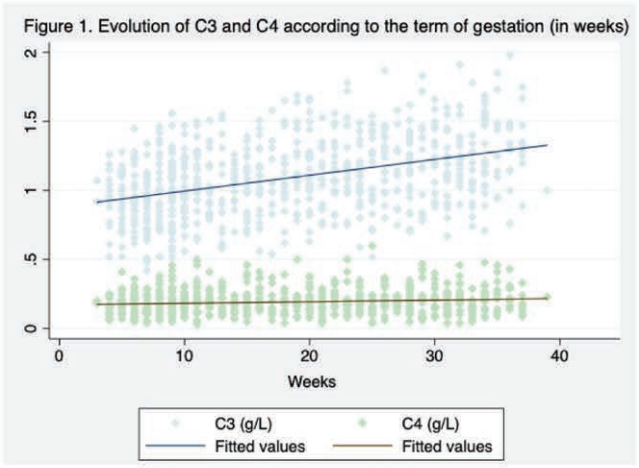
[2] Meissner Y, et al. European Network of Pregnancy Registers in Rheumatology (EuNeP)-an overview of procedures and data collection. *Arthritis Res. Ther.* 2019.

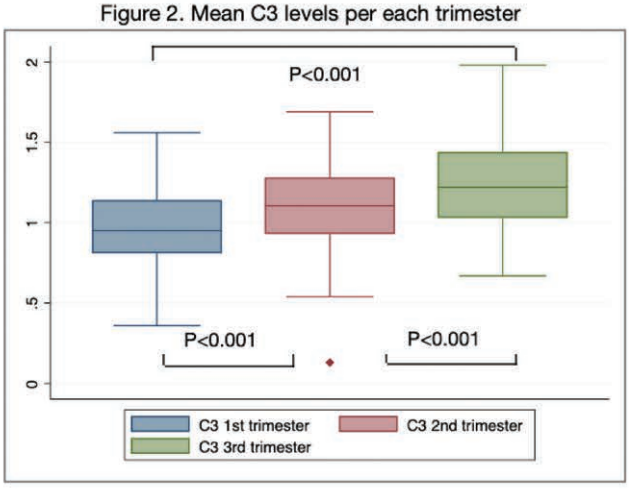
[3] Meissner Y, et al. EULAR recommendations for a core data set for pregnancy registries in rheumatology. *Ann. Rheum. Dis.* 2020.

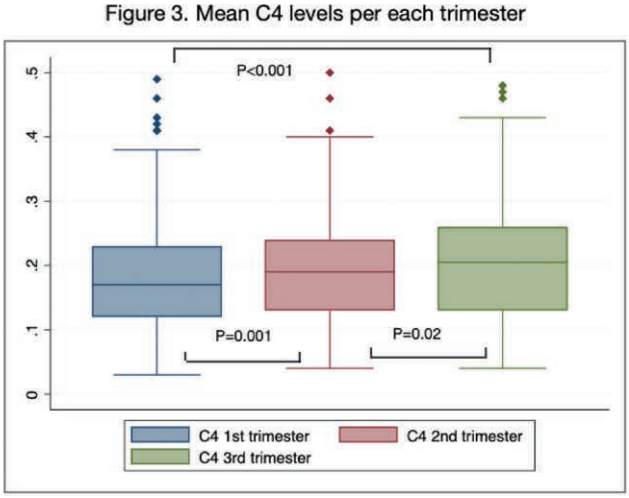
Table 1. Mean C3 and C4 levels (g/L) assessed during pregnancy

	First trimester	Second trimester	Third trimester
Mean C3 (SD), g/L	0.97 (0.24) (n=245)	1.10 (0.26) (n=158)	1.24 (0.28) (n=125)
Mean C3 (SD), g/L (in women with at least 1 available measure per each trimester)	0.99 (0.24) (n=96)	1.11 (0.28) (n=96)	1.23 (0.29) (n=96)
Mean C4 (SD), g/L	0.18 (0.08) (n=245)	0.20 (0.09) (n=159)	0.20 (0.10) (n=126)
Mean C4 (SD), g/L (in women with at least 1 available measure per each trimester)	0.18 (0.08) (n=101)	0.20 (0.09) (n=101)	0.20 (0.09) (n=101)

Legend to Table 1. SD: Standard deviation; g: grams; L: Litre.







Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3786

POS0104

ESSDAI AND ITS ASSOCIATION WITH PATIENT OUTCOMES IN SJÖGREN'S SYNDROME: A REAL-WORLD SURVEY IN THE US

B. Ndife[1], B. Hoskin[2], N. Booth[2]. [1]*Novartis Pharmaceuticals Corp., Novartis, East Hanover, United States of America*; [2]*Adelphi Real World, Adelphi Real World, Bollington, United Kingdom*

Background: The EULAR Sjögren's syndrome disease activity index (ESSDAI) is considered the gold standard for measuring Sjögren's syndrome disease activity in clinical trials, but there is limited evidence of its application in the real-world.
Objectives: To describe the distribution of ESSDAI scores in the real-world and it's association with patient outcomes.
Methods: Data were drawn from the Adelphi Primary Sjögren's syndrome (pSS) Disease Specific Programme™, a real-world point-in-time survey of rheumatologists and their consulting pSS patients in the United States. Proxy ESSDAI scores were calculated for each patient by assigning a score to the rheumatologists' perception of "not present", "mild", "moderate" or "severe" for each of the twelve domains of the ESSDAI. ESSDAI scores were then grouped according to the definitions of mild (ESSDAI 0-4), moderate (ESSDAI 5-13) and severe (ESSDAI ≥14). Rheumatologists provided data about patient demographics and clinical characteristics. Patients self-completed patient reported outcome (PRO) tools including the EuroQol 5-dimension 5-level utility score (EQ-5D), Work Productivity and Activity Impairment questionnaire (WPAI) and The Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F). Differences in clinical characteristics and patient-reported outcomes were examined according to ESSDAI severity score. Spearman's Rho association was used to assess the correlation of ESSDAI severity with PROs.
Results: Rheumatologists (n=84) provided data for 511 pSS patients, mean age 53.3 years, 88.5% female, 79.8% white/Caucasian and mean time since diagnoses 4.6 years. Of the 511 patients, 44.2% were considered to be mild, 30.9% moderate and 24.9% severe in terms of their calculated ESSDAI score. Demographic characteristics of the three ESSDAI groups were similar, Table 1. Patients with severe ESSDAI scores have been diagnosed with pSS for longer than those with mild or moderate ESSDAI scores.
Increasing ESSDAI severity was associated with worse EQ-5D utility scores (rho=-0.346, p<0.0001), worse FACIT-F scores (rho=-0.277, p<0.0001) and worse overall work impairment (rho=0.462, p<0.0001).

Table 1. Demographic characteristics of pSS patients in the US, by ESSDAI severity

	Total (n=511)	Mild ESSDAI (n=226)	Moderate ESSDAI (n=158)	Severe ESSDAI (n=127)
Patient age, mean (SD) years	53.3 (14.2)	52.6 (15.0)	53.6 (14.0)	54.2 (12.9)
% (n) female	88.5 (452)	89.4 (226)	88.6 (158)	86.6 (127)
Ethnicity, % (n)				
White/Caucasian	79.8 (408)	86.3 (195)	74.7 (118)	74.8 (95)
African-American	9.2 (47)	6.2 (14)	10.1 (16)	13.4 (17)
Hispanic/Latino	6.1 (31)	5.3 (12)	8.2 (13)	4.7 (6)
Other	4.9 (25)	2.2 (5)	7.0 (11)	7.1 (9)
Time since diagnosis, mean (SD) years [n]	4.6 (5.4) [379]	4.0 (4.9) [162]	4.9 (5.6) [118]	5.1 (5.8) [99]
Insurance type, % (n)				
Commercial (including employer provided)	59.9 (306)	62.4 (141)	56.3 (89)	59.8 (76)
Medicare	20.5 (105)	18.1 (41)	23.4 (37)	21.3 (27)
Health insurance exchange plan	9.6 (49)	10.2 (23)	10.1 (16)	7.9 (10)
Other	9.6 (49)	8.8 (20)	9.5 (15)	11.0 (14)
None	- (2)	- (1)	- (1)	- (0)
Employment status, % (n)				
Working full or part time	58.9 (301)	61.9 (140)	53.2 (84)	60.6 (77)
Long-term sick/unemployed/ retired	24.5 (125)	20.8 (47)	27.2 (43)	27.6 (35)
Homemaker	12.7 (65)	10.2 (23)	17.1 (27)	11.8 (15)
Other/unknown	3.9 (20)	7.1 (16)	2.5 (4)	- (0)
Smoking status, % (n) current smoker	6.8 (35)	3.5 (8)	5.7 (9)	14.2 (18)

Conclusion: A worsening severity on the ESSDAI scale is associated with worse outcomes for patients in the real-world. Treating systemic disease beyond symptomatic treatments is important to improve patient outcomes.

Disclosure of Interests: Briana Ndife Shareholder of: Novartis Pharmaceuticals Corp, Employee of: Novartis Pharmaceuticals Corp, Ben Hoskin: None declared, Nicola Booth: None declared

DOI: 10.1136/annrheumdis-2021-eular.3807

POS0105

PREDICTORS OF FLARE IN SLE PATIENTS ATTAINING LUPUS LOW DISEASE ACTIVITY STATE: A REAL-LIFE COHORT STUDY OF 292 PATIENTS WITH 36-MONTH FOLLOW-UP

A. R. Cunha[1], L. Saraiva[2], J. A. P. Da Silva[2,3], L. Inês[4,5]. [1]*Centro Hospitalar do Baixo Vouga, Rheumatology, Aveiro, Portugal*; [2]*Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal*; [3]*Coimbra Institute for Clinical and Biomedical Research(i.CIBR), Faculty of Medicine, Coimbra, Portugal*; [2]*Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal*; [5]*University of Beira Interior, Faculty of Health Sciences, Covilhã, Portugal*

Background: Lupus Low Disease Activity State (LLDAS) is a target for management of patients with SLE, that should be maintained in the long-term by preventing flares. Stratification of flare risk would be useful to optimize management.
Objectives: To identify predictors of flare in SLE patients attaining LLDAS.
Methods: Patients with SLE fulfilling classification criteria [ACR (1997) and/or SLICC and/or EULAR/ACR], followed at an academic lupus clinic from January 2017 to March 2020 were eligible. Baseline for each patient was the first visit with LLDAS within the study period. Patients never fulfilling LLDAS were excluded. Flares were identified as change from baseline by 3 instruments: revised SELENA flare index (r-SFI); SLEDAI-2K; Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS). Time to first flare up to 36 months was identified separately for each instrument. Predictors of flare were sought through survival analysis, with distinct models for each of the three definitions of flare. Univariate analysis was performed using Kaplan-Meir curves and Log-Rank tests. Tested variables at baseline were: gender; age at time of SLE diagnosis; disease duration; cumulative SLE organ involvement (arthritis; mucocutaneous; renal; neurologic; haematological; anti-phospholipid syndrome); cumulative immunological features (anti-dsDNA; anti-Sm; anti-RNP, anti-phospholipid antibodies; hypocomplementemia); ongoing treatment (hydroxychloroquine; prednisone; immunosuppressants). Variables with p<0.1 were further tested in multivariate Cox regression models. Hazard ratios (HR) were determined with 95% confidence intervals (95%CI).
Results: From 322 patients in this SLE cohort, 292 (90.7%) fulfilled LLDAS and were included in the analyses (female: 87.3%; mean age: 46.2±14.5 years; previous lupus nephritis: 36.0%; receiving ongoing antimalarials, immunosuppressants, glucocorticoids: 92.8%, 34.6% and 29.8%, respectively. Over follow-up, the proportion of patients with flares according to each definition were: 28.4% (r-SFI), 24.7% (SLE-DAS) and 13.4% (SLEDAI-2K). The r-SFI flares were moderate in 28.9% and severe in 9.6% of the cases. From all patients, 54.1% maintained stable glucocorticoid-free control of the disease, without flares during follow-up. In the multivariate models, the following parameters were independent predictors of flare, as defined by any of the definitions (Table 1): anti-RNP+; oral glucocorticoids; immunosuppressants.
Conclusion: Patients attaining LLDAS but requiring ongoing treatment with immunosuppressants and/or glucocorticoids present a higher risk of flare and thus might need a tighter clinical monitoring. Anti-RNP+ was newly identified as a potential biomarker for higher risk of flares. Glucocorticoid-free, stable low disease activity is an achievable target.

REFERENCES:

[1] Mathian A, Pha M, Haroche J, Cohen-Aubart F, Hié M, Pineton de Chambrun M, et al. Withdrawal of low-dose prednisone in SLE patients with a clinically quiescent disease for more than 1 year: a randomised clinical trial. Ann Rheum Dis. 2020;79(3):339-46.
[2] Inês L, Duarte C, Silva RS, Teixeira AS, Fonseca FP, da Silva JA. Identification of clinical predictors of flare in systemic lupus erythematosus patients: a 24-month prospective cohort study. Rheumatology (Oxford). 2014;53(1):85-9.

Table 1. Predictors of flare in multivariate Cox regression according to each of the flare definitions (r-SFI; SLE-DAS; SLEDAI-2K)

	r-SFI	SLE-DAS	SLEDAI-2K
Anti-RNP+	2.11 (1.30-3.42)	2.39 (1.44-3.95)	2.22 (1.11-4.42)
Immunosuppressants	1.96 (1.22-3.15)	2.32 (1.38-3.88)	2.26 (1.12-4.54)
Prednisone*	1.93 (1.19-3.14)	1.99 (1.18-3.35)	2.17 (1.07-4.38)
Blood cytopenias§	2.08 (1.03-4.17)	n.s.	n.s.
Arthritis§	n.s.	n.s.	2.23 (1.12-4.44)

* Prednisone ≤7.5 mg/day as required by LLDAS. § Blood cytopenias; arthritis: cumulative SLE features up to baseline. Risk for each predictor reported as Hazard Ratio (95% Confidence Interval); n.s.: non-significant

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.478

POS0106 BILAG-2004 LDA AND BST LDA ARE VALID TREAT TO TARGET IN SLE

C. S. Yee[1], C. Gordon[2], M. Akil[3], P. Lanyon[4], C. J. Edwards[5], D. Isenberg[6], A. Rahman[6], L. S. Teh[7], S. Tosounidou[8], R. Stevens[1], A. Prabu[2], B. Griffiths[9], N. Mchugh[10], I. N. Bruce[11], Y. Ahmad[12], M. Khamashta[13], V. Farewell[14]on behalf of British Isle Lupus Assessment Group (BILAG). *[1]Doncaster & Bassetlaw Teaching Hospitals NHS Foundation Trust, Department of Rheumatology, Doncaster, United Kingdom*; *[2]University of Birmingham, Rheumatology Research Group, Birmingham, United Kingdom*; *[3]Sheffield Teaching Hospitals NHS Foundation Trust, Department of Rheumatology, Sheffield, United Kingdom*; *[4]Nottingham University Hospitals NHS Trust, Department of Rheumatology, Nottingham, United Kingdom*; *[5]University Hospital Southampton NHS Foundation Trust, Department of Rheumatology, Southampton, United Kingdom*; *[6]University College London, Centre for Rheumatology Research, London, United Kingdom*; *[7]Royal Blackburn Hospital, Department of Rheumatology, Blackburn, United Kingdom*; *[8]Sandwell and West Birmingham Hospitals NHS Trust, Department of Rheumatology, Birmingham, United Kingdom*; *[9]Newcastle upon Tyne Hospitals NHS Foundation Trust, Department of Rheumatology, Newcastle, United Kingdom*; *[10]Royal National Hospital for Rheumatic Diseases NHS Trust, Department of Rheumatology, Bath, United Kingdom*; *[11]The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; *[12]Betsi Cadwaldr University Health Board, Department of Rheumatology, Wales, United Kingdom*; *[13]Guy's and St Thomas' NHS Foundation Trust, Department of Rheumatology, London, United Kingdom*; *[14]University of Cambridge, MRC Biostatistics Unit, Cambridge, United Kingdom*

Background: Low disease activity state has been defined using SLEDAI and used as treatment target in SLE. However, there has not been any such definition using BILAG-2004 index (BILAG-2004).

Objectives: This study was to determine if low disease activity state according to BILAG-2004 is valid for use as treatment target in SLE. We also assessed disease activity longitudinally using BILAG-2004 systems tally (BST). BST is an alternative way of representing BILAG-2004 scores that combines the flexibility and simplification of numerical scoring of BILAG-2004 with the clinical intuitiveness of BILAG-2004 structure.

Methods: This was a prospective multi-centre longitudinal study in the UK of an inception cohort of SLE patients (recruited within 12 months of achieving 1997 ACR revised criteria for SLE). Data were collected on disease activity (BILAG-2004 and BILAG2004-Pregnancy Index during pregnancy), SLICC/ACR DI (SDI), cumulative drug exposure and death at every visit. This study ran from 1st January 2005 to 31st December 2017. Four low disease activity states (LDA) were defined using BILAG-2004: 1) BILAG-2004 LDA when all 9 systems had scores of C, D or E on assessment (no Grade A or B), 2) BST LDA when there was persistent score of C, D or E in all 9 systems between 2 consecutive visits (equivalent to 2 consecutive visits with BILAG-2004 LDA), 3) BILAG-2004 Remission when all 9 systems had scores of D or E on assessment and 4) Persistent Remission when there was persistent score of D or E in all 9 systems between 2 consecutive visits. Longitudinal analysis using Poisson regression with random effects model was used with development of new damage as the outcome of interest. Gender, cardiovascular risk factors, antiphospholipid syndrome status and most drugs (except hydroxychloroquine, glucocorticoids, mycophenolate and cyclophosphamide) were excluded from the model as they were not associated with development of damage in univariate analysis.

Results: 273 patients were recruited (91.2% female, 59.3% Caucasian, 17.2% African/Caribbean, 17.2% South Asian) with mean age at recruitment of 38.5 years (SD 14.8). 97.8% had no damage at recruitment (2.2% had SDI score of 1). Median follow-up was 73.4 months (range: 1.8, 153.8) with total follow-up of 1767 patient-years. There were 13 deaths and 114 new damage items occurred during follow-up. There were 6674 assessments with disease activity score: 319 assessments with Grade A activity in 95 patients (84.6% had only 1 system with grade A, range: 1 - 4) and 1704 assessments with Grade A or B activity in 239 patients (78.7% had only 1 system with Grade A or B, range: 1 - 5).

BILAG-2004 LDA was achieved in 74.5% of assessments (from 271 patients). BILAG-2004 Remission occurred in 28.2% of assessments (from 234 patients). 6401 observations with BST were available (1 observation derived from change in activity between 2 consecutive assessments) and 63.7% were in BST LDA. There was no observation with Persistent Remission between consecutive visits. Table 1 summarises multivariate analysis which showed BILAG-2004 LDA to be inversely associated with damage. Similar results were obtained with BILAG-2004 Remission (RR 0.60 with 95% CI 0.38, 0.96) and BST LDA (RR 0.65 with 95% CI 0.43, 0.99). Cumulative drug exposure since recruitment for mycophenolate was protective against new damage (RR 0.99 with 95% CI 0.99, 0.99).

Table 1.

Variable	Relative Risk (95% CI) for New Damage
Ethnicity	
Afro-Caribbean	1.22 (0.68, 2.18)
South Asian	1.81 (0.97, 3.38)
Others	2.22 (0.63, 7.85)
Age at diagnosis	**1.06 (1.04, 1.08)**
Prior SDI score	0.68 (0.43, 1.06)
BILAG-2004 LDA	**0.60 (0.39, 0.94)**
Hydroxychloroquine since last visit (per g)	**0.99 (0.98, 0.99)**
Steroids since last visit (per 100mg)	**1.02 (1.01, 1.03)**
Cyclophosphamide since last visit (per g)	**1.67 (1.15, 2.41)**

Conclusion: BILAG-2004 LDA and BST LDA are valid treatment targets in SLE. BILAG-2004 Remission and Persistent Remission are uncommon, which make them unrealistic as a treatment target.

REFERENCES:

[1] Yee C. S., et al. The BILAG-2004 systems tally – a novel way of representing the BILAG-2004 index scores longitudinally. Rheumatology (Oxford) 2012; 51[11]: 2099-2105.

Acknowledgements : Versus Arthritis, Vifor Pharma

Disclosure of Interests: Chee-Seng Yee Consultant of: Bristol Myers Squibb, ImmuPharma, Grant/research support from: Vifor Pharma, Caroline Gordon Speakers bureau: UCB, Consultant of: Center for Disease Control, Astra-Zeneca, MGP, Sanofi and UCB, Mohammed Akil: None declared, Peter Lanyon: None declared, Christopher John Edwards Consultant of: Glaxo Smith Kline, Roche, Grant/research support from: Glaxo Smith Kline, Roche, David Isenberg: None declared, Anisur Rahman: None declared, Lee-Suan Teh: None declared, Sofia Tosounidou: None declared, Robert Stevens: None declared, Ahtiveer Prabu: None declared, Bridget Griffiths: None declared, Neil McHugh: None declared, Ian N. Bruce: None declared, Yasmeen Ahmad: None declared, Munther Khamashta: None declared, Vernon Farewell: None declared

DOI: 10.1136/annrheumdis-2021-eular.10

POS0107 TAPERING BELIMUMAB IN PATIENTS WITH SLE: A SINGLE CENTER EXPERIENCE

M. Fredi[1], T. Vojinovic[2], F. Regola[1], G. Babaglioni[3], D. Bettoni[3], I. Cavazzana[2], F. Franceschini[1]. *[1]UO Reumatologia e Immunologia Clinica ASST Spedali Civili e Università degli Studi di Brescia, ASST Spedali Civili, Brescia, Italy*; *[2]UO Reumatologia e Immunologia Clinica, ASST Spedali Civili, Brescia, Italy*; *[3]Farmacia Aziendale, ASST Spedali Civili, Brescia, Italy*

Background: In Italy, the use of belimumab has been authorized since 2013, in patients with active systemic lupus erythematosus (SLE) with positive anti–double-stranded DNA and low C3 or C4 levels, despite standard therapy. Belimumab is effective in reducing disease activity and number of flares and in blocking damage progression. To our knowledge, no data are available on dose tapering of belimumab in SLE patients chronically treated with it.

Objectives: The aim of this retrospective study was to analyse prevalence of tapering in a single cohort and to evaluate disease activity after tapering.

Methods: Patients, who received intravenous belimumab (10mg/kg) for at least 12 months between June 2013 and December 2020 were enrolled. The Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC-SDI), Physician Global Assessment (PGA), C3 and C4 levels, and prednisone daily dose were recorded at baseline and every six-months. Follow-up was stopped when patients switched to subcutaneous belimumab or when it was discontinued for more than 6 months (interrupted). Dose tapering was defined as the prolongation of the regular dose interval, after initial treatment based on the registered dosage.

Results: Between June 2013 and December 2020, 48 patients received intravenous belimumab for at least 12 months (100% Caucasians, 94% females). All patients received standard belimumab dosage of 10mg/Kg every 4 weeks. Fourteen (29.1%) of 48 patients lengthened the dosing interval to 5 weeks; a subsequent lengthening of the interval occurred in 7 patients every 6 weeks and in 1 patient belimumab was gradually tapered to every 13 weeks.

Twelve months (T12) after belimumab introduction, 3 patients (6.2%) were receiving a tapered dosage; at T24, 9 out of the 37 (24.3%), at T36 9 out of 21 (42.8%), and at T48 8 out of 18 (44.4%). Differences in disease activity, damage, concomitant medications, disease duration at belimumab introduction (baseline) were evaluated among patients that maintained the standard interval versus the group that received a tapered dose. Notably, no differences were found among the two groups (standard dose vs tapering) concerning median age at baseline (41, IQR 31-47.5 vs 38, IQR 32.2-51.5), disease duration (median 11, IQR 7.2-16

vs 9, IQR 5.5-14.5), median prednisone daily dosage (7.1mg, IQR 5-11.9 versus 11mg, IQR 7.6-17.5) and median SLEDAI-2K (8, IQR 6-9.75 vs 8, IQR 5-10). Differences in concomitant medications or clinical manifestations are reported in Figure 1A.

Among the group that received the standard dose, 7 patients discontinued the treatment (20.6%), specifically 2 renal flares and one adverse event occurred. Whereas, in the reduced dose group, 2 discontinuations occurred (14.3%) due to a pregnancy and a renal flare. Noteworthy, the patient with the renal flare resumed subcutaneous belimumab 12 months after the flare. Finally, the disease activity was analysed in the 12 months after the first drug reduction (Figure 1B-E), with no sign of worsening of evaluated parameters (Figure 1B-1E), but with a significant reduction of steroids and SLEDAI-2K, 6 months after tapering.

Conclusion: In our single retrospective cohort, we have demonstrated that belimumab tapering seems to be safe and not associated with a worsening disease activity over the following months. However, further studies are required to identify eligibility criteria and to determine the optimal dose-tapering strategy both for the intravenous and the subcutaneous formulations.

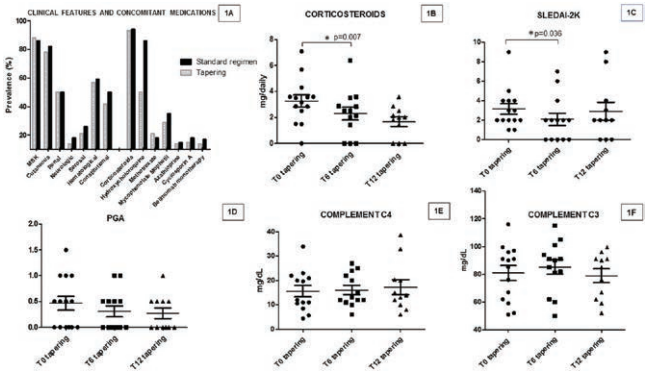


Figure 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.744

POS0108

PLASMA MITOCHONDRIAL DNA AS A BIOMARKER IN DIAGNOSIS AND FOLLOW-UP OF SYSTEMIC LUPUS ERYTHEMATOSUS

S. Giaglis[1,2], D. Daoudlarian[1,2], D. Kyburz[1,2], N. Venhoff[3], U. Walker[1,2].
[1]University of Basel, Department of Biomedicine, Laboratory for Experimental Rheumatology, Basel, Switzerland; *[2]University Hospital Basel, Department of Rheumatology, Basel, Switzerland*; *[3]University Medical Center Freiburg, Department of Rheumatology and Clinical Immunology, Freiburg, Germany*

Background: A fundamental role of mitochondria in systemic lupus erythematosus (SLE) was recently demonstrated (1). In brief, mitochondrial ROS participate in the formation of neutrophil extracellular traps (NETs) (2), while extrusion of cell-free mitochondria and highly oxidized interferogenic mtDNA causes disease in an animal model of SLE (3-5).

Objectives: The diagnostic and prognostic value of cell-free DNA in SLE is still unknown. The aim of the present study was therefore to examine the clinical utility of cell-free DNA quantification as a non-invasive biomarker in SLE.

Methods: Total DNA was isolated from platelet-free plasma samples of healthy individuals (HC) and consecutive SLE patients. Plasma and clinical data were collected at baseline and follow-up. Copy numbers were quantified by qPCR for mitochondrial (mt) DNA (ATP-6 gene) and nuclear (n) DNA (GAPDH gene).

Results: Fifty-six HC (median age 48.3 ± 13.5, 64% female) and 103 SLE patients (median age 46.8 ± 15.8, 99% female, mean SLEDAI: 3 ± 4) were available for analysis.

mtDNA levels were significantly elevated in SLE plasma ($1.3x10^8$ copies/ml plasma, 95% CI: $7.3x10^7$ to 1.7 $x10^{8)}$), compared to HC plasma ($8.6x10^6$ copies/ml plasma, 95% CI: $6.9x10^6$ to $1.0x10^7$, p<0.0001). nDNA levels in contrast did not differ between SLE ($8.3x10^6$ copies/ml plasma, 95%CI: $5.9x10^6$ to 1.4 $x10^7$) and HC ($1.0x10^7$ copies/ml plasma, 95%CI: $2.0x10^6$ to 1.5 $x10^7$, p=0.61). Receiver *operating characteristic* curve analysis showed that a cut-off value of $1.9x10^7$ mtDNA copy numbers differentiated between SLE and HC with 87.4% sensitivity, 94.6% specificity and an AUC of 0.95 (Figure 1a).

mtDNA levels correlated with the SLE Disease Activity Index 2000 (SLEDAI-2K) (r=0.29, p=0.0026), less so also nDNA copy numbers (r=0.24, p=0.014). There was no association of mtDNA elevation with any particular type of SLE organ involvement and no correlation between mtDNA copy numbers in SLE plasma and dsDNA antibody levels.

Follow-up data were available for 32 SLE patients (median follow-up 4.0 months, IQR: 4.0). delta mtDNA-levels robustly correlated with changes in SLEDAI-2K (r=0.51, p=0.0012, Figure 1b).

Conclusion: The quantification of cell free mtDNA, but not nDNA copy numbers allows a sensitive and specific distinction between healthy individuals and patients with SLE. mtDNA levels correlate cross sectionally with disease activity in SLE patients and within individual SLE patients longitudinally with the SLEDAI. Plasma mtDNA quantification may therefore aid in the diagnosis of SLE and in monitoring SLE activity.

REFERENCES:

[1] Riley JS, Tait SW. Mitochondrial DNA in inflammation and immunity. EMBO Rep. 2020;21(4):e49799.
[2] West AP, Shadel GS. Mitochondrial DNA in innate immune responses and inflammatory pathology. Nat Rev Immunol. 2017;17(6):363-75.
[3] Crow MK, Olferiev M, Kirou KA. Type I Interferons in Autoimmune Disease. Annu Rev Pathol. 2019;14:369-93.
[4] Kim J, Gupta R, Blanco LP, Yang S, Shteinfer-Kuzmine A, Wang K, et al. VDAC oligomers form mitochondrial pores to release mtDNA fragments and promote lupus-like disease. Science. 2019;366(6472):1531-6.
[5] Lood C, Blanco LP, Purmalek MM, Carmona-Rivera C, De Ravin SS, Smith CK, et al. Neutrophil extracellular traps enriched in oxidized mitochondrial DNA are interferogenic and contribute to lupus-like disease. Nat Med. 2016;22(2):146-53.

Declaration of conflict of interest: UW is coinventor of patents owned by Freiburg University; NV is coinventor of patents owned by Freiburg University.

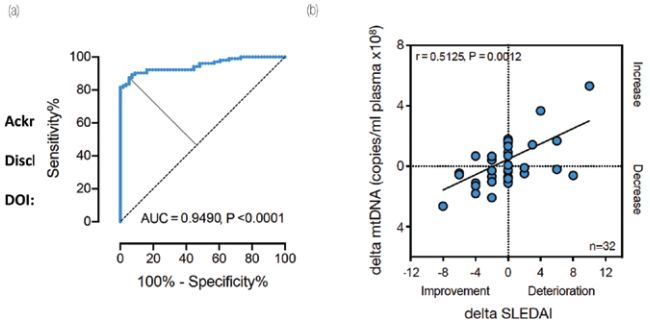


Figure 1. (a) Receiver operating characteristic curve for mtDNA plasma concentrations to discriminate between HC and SLE patients. AUC: area under the curve. (b) Changes in plasma mtDNA levels in SLE patients correlate with the evolution of disease activity at follow-up.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1833

POS0109

IDENTIFICATION OF PRIMARY SJOGREN'S SYNDROME SUBTYPES BY MACHINE LEARNING

M. T. Qiu[1,2,3], S. X. Zhang[1,2,3], J. Qiao[1,2,3], J. Q. Zhang[1,2,3], S. Song[1,2,3], R. Zhao[1,2,3], M. J. Chang[1,2,3], Y. Zhang[1,2,3], G. Y. Liu[1], P. F. He[4], X. Li[1,2,3]. *[1]The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; *[2]Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; *[3]Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; *[4]Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Sjogren's syndrome(pSS) is a chronic, progressive, and systematic autoimmune disease characterized by lymphocytic infiltration of exocrine glands [1 2]. Sicca symptoms and abnormal fatigue are the main clinical presentation, but those symptoms are non-specific to patients, which lead to delayed diagnosis [1 3]. The heterogeneous of clinical manifestation raise challenges regarding diagnosis and therapy in pSS, thus it's necessary for us to sub-classify pSS.

Objectives: To explore new biomarkers for diagnosis and subtypes of pSS based on Machine Learning Primary.

Methods: All microarray raw datas (CEL files) were screened and downloaded from Gene Expression Omnibus (GEO). Meta-analysis to identify the consistent DEGs by MetaOmics. Weighted gene co-expression network analysis (WGCNA) was used to the modules related to SS for further analysis. Subclasses were computed using a consensus Non-negative Matrix Factorization (NMF) clustering method. Immune cell infiltration was used to evaluate the expression of immune cells and obtain various immune cell proportions from samples. *P* value < 0.05 were considered statistically significant. All the analyses were conducted under R environment (version 4.03).

Results: A total of 3715 consistent DEGs were identified from the four datasets, including 1748 up-regulated and 1967 down-regulated genes. Tour

meaningful modules, including yellow, turquoise, grey60 and bule, were identified (Figure 1A,1B). And 183 overlapping gene were screened from the DEGs and the Hub genes in the four modles for further analysis. We final divided pSS patients into three subtypes, of which yellow and turquoise in Sub1, grey60 in Sub2 and blue in Sub3. Sub1 and Sub3 were related to cell metabolism, while Sub2 had connection with virus infection (Figure 1C,1D). Infiltrated immune cells were also different among these three types (Figure 1E,1F).

Conclusion: Patients with pSS could be classified into 3 subtypes, this classification might help for assessing prognosis and guiding precise treatment.

REFERENCES:

[1] Ramos-Casals M, Brito-Zerón P, Sisó-Almirall A, et al. Primary Sjogren syndrome. BMJ (Clinical research ed) 2012;344:e3821. doi: 10.1136/bmj.e3821 [published Online First: 2012/06/16].

[2] Brito-Zeron P, Baldini C, Bootsma H, et al. Sjogren syndrome. Nat Rev Dis Primers 2016;2:16047. doi: 10.1038/nrdp.2016.47 [published Online First: 2016/07/08].

[3] Segal B, Bowman SJ, Fox PC, et al. Primary Sjogren's Syndrome: health experiences and predictors of health quality among patients in the United States. Health Qual Life Outcomes 2009;7:46. doi: 10.1186/1477-7525-7-46 [published Online First: 2009/05/29].

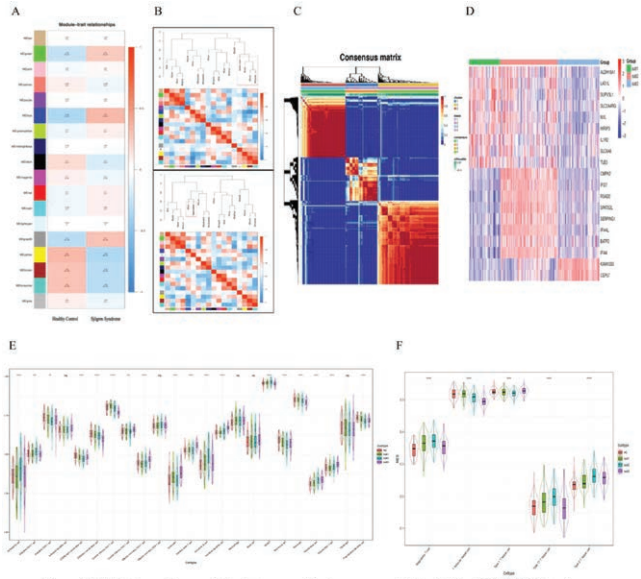


Figure: (A,B) Heatmap of the correlation between module eigengenes and clinical traits of SS. (C,D) Molecular typing of patients with SS based on ferroptosis-related gene expression profiles consensus clustering of GEO samples by NMF, a heatmap displaying the expression pattern of subtypes is shown. (Figure E,F) The scores of 23 immune cells are displayed in boxplots. Adjusted P values were showed as: ns, not significant. ns P> 0.05; *P< 0.05; **P< 0.01; ***P< 0.001.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2402

POS0110 ASSOCIATION OF MIR-155 AND MIR-34A EXPRESSION IN LUPUS NEPHRITIS RENAL TISSUE WITH DISEASE ONSET AND OUTCOMES

C. Di Mario[1], L. Petricca[2], M. R. Gigante[2], S. Costanzi[3], G. Vischini[4], A. Paglionico[2], V. Varriano[1], L. Bui[5], G. Tanti[1], L. Lanzo[1], F. Federico[5], G. Grandaliano[3,6], M. A. D'agostino[1,2], S. Alivernini[2], B. Tolusso[2], E. Gremese[1,2]. *[1]Division of Rheumatology, Università Cattolica del Sacro Cuore, Rome, Italy*; *[2]Division of Rheumatology, Fondazione Policlinico Universitario A. Gemelli-IRCCS, Rome, Italy*; *[3]Division of Nephrology, Fondazione Policlinico Universitario A. Gemelli-IRCCS, Rome, Italy*; *[4]Division of Nephrology, S.Orsola Malpighi Hospital, Bologna, Italy*; *[5]Division of Histopathology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy*; *[6]Division of Nephrology, Università Cattolica del Sacro Cuore, Rome, Italy*

Background: Epigenetic factors such as non-coding RNA (miRNA) have been shown to be deregulated in Systemic Lupus Erythematosus (SLE). In mouse models, different miRNAs have been associated with lupus nephritis (LN), one of the most severe manifestations of the disease[1].

Objectives: To evaluate the expression of miR-155 and miR-34a in renal tissues as biomarkers of organ involvement and inflammatory tissue activity in patients with LN.

Methods: Thirty-two SLE patients with LN (age: 32.2 ± 9.2 years) with active renal involvement undergoing ultrasound-guided renal biopsy were enrolled between 2010 and 2019. The nephritic manifestation was present in 13 (41%) patients at disease onset (early-LN SLE), while 19 (59%) patients showed a renal involvement after disease onset (long-LN SLE, mean disease duration at LN onset: 7.3 ± 5.7 years). Twelve age-matched patients with IgA nephropathy were enrolled as control group. Clinical, laboratory and demographic data were collected for each patient. Disease activity was recorded using SLEDAI-2K and renal activity, using the total SLEDAI-2K fraction including the items related to the renal involvement. MiR-155 and miR-34a expression in renal tissues was carried out by extraction of total RNA from paraffin-preserved biopsies and was evaluated, after a retrotrascription protocol, using real-time PCR by relative quantification considering the ΔCt (Ct miRNA- Ct housekeeping gene)[2].

Results: MiR-155 and miR-34a expression in renal tissues was higher in LN-SLE patients as compared to IgA nephropathy patients (ΔCt miR-155: 9.4 ± 10.1 vs 21.9 ± 3.6, p<0.01; ΔCt miR-34a: 10.1 ± 9.8 vs 19.2 ± 3.1, p=0.02). MiR-155 and miR-34a expression in LN-SLE patients renal tissues was comparable in the different histological classes. Furthermore, a direct correlation was observed between the expression of miR-155 and miR-34a (r = 0.91, p <0.001). Dividing patients based on nephritic onset, SLE patients with long-LN showed higher expression of miR-155 (ΔCt 6.1 ± 8.7) and miR-34a (ΔCt 7.1 ± 9.0) as compared to patients with early-LN (miR-155: ΔCt 13.4 ± 10.6 p = 0.08; miR-34a: ΔCt 15.1 ± 9.5 p = 0.02) or patients with IgA nephropathy (miR-155 p<0.01 and miR-34a p<0.01). Moreover, in early-LN SLE it was observed an inverse correlation between miR-34a expression and C3 and C4 complement components (r=-0.7.2; p=0.05 and r=-0.86; p=0.01, respectively) and a direct correlation between miR-155 and 24h-UP (r=0,67; p=0.03). Considering SLE patients with early-LN, the expression of miR-34a was slightly significant in patients who had relapsed (ΔCt 8.2 ± 11.4 vs ΔCt 18.4 ± 7.9 p = 0.08), although no correlation emerged between the expression of miR-155 and miR-34a at the time of the biopsy and with disease activity indices.

Conclusion: MiR-155 and miR-34a may represent tissue biomarkers of inflammatory activation in SLE patients with LN; in particular, the higher expression of these miRNA in long-LN and the correlation between miR-155 expression with p24h-UP in early-LN could indicate a possible role of these biomarkers in renal involvement in patients with SLE with later renal onset. The increased expression of miR-34a could give indications of a disease recurrence suggesting a closer monitoring of patients.

REFERENCES:

[1] Leiss H et al. Plosone 2017.

[2] Alivernini S et al. Nat Commun 2018.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3761

POS0111 DEVELOPMENT OF DAMAGE AND MORTALITY IN AN INCEPTION COHORT OF SLE PATIENTS

C. S. Yee[1], V. Farewell[2], M. Akil[3], P. Lanyon[4], C. J. Edwards[5], D. Isenberg[6], A. Rahman[6], L. S. Teh[7], S. Tosounidou[8], R. Stevens[1], A. Prabu[9], B. Griffiths[10], N. Mchugh[11], I. N. Bruce[12], Y. Ahmad[13], M. Khamashta[14], C. Gordon[9]on behalf of British Isles Lupus Assessment Group (BILAG). *[1]Doncaster & Bassetlaw Teaching Hospitals NHS Foundation Trust, Department of Rheumatology, Doncaster, United Kingdom*; *[2]University of Cambridge, MRC Biostatistics Unit, Cambridge, United Kingdom*; *[3]Sheffield Teaching Hospitals NHS Foundation Trust, Department of Rheumatology, Sheffield, United Kingdom*; *[4] Nottingham University Hospitals NHS Trust, Department of Rheumatology, Nottingham, United Kingdom*; *[5]University Hospital Southampton NHS Foundation Trust, Department of Rheumatology, Southampton, United Kingdom*; *[6]University College London, Centre for Rheumatology Research, London, United Kingdom*; *[7]Royal Blackburn Hospital, Department of Rheumatology, Blackburn, United Kingdom*; *[8]Sandwell and West Birmingham Hospitals NHS Trust, Department of Rheumatology, Birmingham, United Kingdom*; *[9]University of Birmingham, Rheumatology Research Group, Birmingham, United Kingdom*; *[10]Newcastle upon Tyne Hospitals NHS Foundation Trust, Department of Rheumatology, Newcastle, United Kingdom*; *[11]Royal National Hospital for Rheumatic Diseases NHS Trust, Department of Rheumatology, Bath, United Kingdom*; *[12]The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; *[13]Betsi Cadwaldr University Health Board, Department of Rheumatology, Wales, United Kingdom*; *[14]Guy's and St Thomas' NHS Foundation Trust, Department of Rheumatology, London, United Kingdom*

Background: There had been very limited data on the development of damage and mortality in an inception cohort of SLE patients who were recruited very soon after diagnosis.

Objectives: This study aimed to analyse the development of damage and death in an inception cohort of SLE patients recruited within 1 year of diagnosis with up to 13 years of follow-up.
Methods: This was a prospective multi-centre longitudinal study in the UK of SLE patients recruited within 12 months of achieving 1997 ACR revised criteria for SLE. Data were collected on BILAG-2004, BILAG2004-Pregnancy Index (during pregnancy), SLICC/ACR DI (SDI), cumulative drug exposure and death at every visit. Information on cardiovascular risk factors and antiphospholipid syndrome status were also collected. This study ran from 1st January 2005 to 31st December 2017. Mortality and development of damage were analysed.
Results: There were 273 patients recruited (91.2% female, 59.3% Caucasian, 17.2% African/Caribbean, 17.2% South Asian) with mean age at recruitment of 38.5 years (SD 14.8). 97.8% had no damage at recruitment (2.2% had SDI score of 1). Median follow-up was 73.4 months (range: 1.8, 153.8) with total follow-up of 1767 patient-years.
There were 13 deaths (4.8%): 76.9% female, 84.6% Caucasian, 15.4% South Asian, mean age 62.6 years (± SD 15.8) and mean disease duration 3 years (± SD 1.8). Causes of death were cancer in 5 (38.5%), infection in 3 (23.1%), ischaemic heart disease in 1 (7.7%) and unknown in 4 (30.8%).
114 new damage items in 83 patients occurred during follow-up. The distribution of damage was musculoskeletal (21, 18.4%), ophthalmic (18, 15.8%), neuropsychiatric (18, 15.8%), renal (14, 12.3%), malignancy (12, 10.5%), cutaneous (7, 6.1%), GIT (7, 6.1%), cardiac (6, 5.3%), pulmonary (4, 3.5%), diabetes mellitus (4, 3.5%) and vascular (3, 2.6%). The rate of development of damage appears to be higher in the first 3 years which subsequently stabilised (Table 1).

Table 1. Incidence rate of development of damage over period of follow-up at 3 yearly intervals

Period of follow-up (year)	Person-years at risk	Number of new items of damage	Incidence rate, per 1000 person-years (95% CI)
0 – 3	753.4	60	79.6 (61.8, 102.6)
3 – 6	534.0	31	58.1 (40.8, 82.6)
6 – 9	321.2	12	37.4 (21.2, 35.8)
9 – 12	152.5	5	32.8 (13.6, 78.7)
> 12	5.9	0	-

Conclusion: Mortality is uncommon during the first 12 years of follow-up for newly diagnosed SLE patients. However, development of damage appears to be higher in the first 3 years before stabilizing to a lower rate subsequently.
Acknowledgements: Versus Arthritis, VIfor Pharma
Disclosure of Interests: Chee-Seng Yee Consultant of: Bristol Myer Squibb, ImmuPharma, Grant/research support from: Vifor Pharma, Vernon Farewell: None declared, Mohammed Akil: None declared, Peter Lanyon: None declared, Christopher John Edwards Consultant of: Glaxo Smith Kline, Roche, Grant/research support from: Glaxo Smith Kline, Roche, David Isenberg: None declared, Anisur Rahman: None declared, Lee-Suan Teh: None declared, Sofia Tosounidou: None declared, Robert Stevens: None declared, Ahtiveer Prabu: None declared, Bridget Griffiths: None declared, Neil McHugh: None declared, Ian N. Bruce: None declared, Yasmeen Ahmad: None declared, Munther Khamashta: None declared, Caroline Gordon Speakers bureau: UCB, Consultant of: Center for Disease Control, Astra-Zeneca, MGP, Sanofi and UCB
DOI: 10.1136/annrheumdis-2021-eular.8

Translating vasculitis

POS0112 CD8+ T-CELL INFILTRATION IS ASSOCIATED WITH LESIONAL GM-CSF OVEREXPRESSION IN GCA

W. F. Jiemy[1], R. Reitsema[2], A. Kwant[2], W. Abdulahad[1,2], A. Boots[2], P. Heeringa[1], E. Brouwer[2]. [1]*University of Groningen, University Medical Center Groningen, Department of Pathology and Medical Biology, Groningen, Netherlands*; [2]*University of Groningen, University Medical Center Groningen, Department of Rheumatology and Clinical Immunology, Groningen, Netherlands*

Background: Giant cell arteritis (GCA) is a large-vessel vasculitis characterized by granulomatous T cell- and macrophage infiltration. Granulocyte-macrophage colony stimulating factor (GM-CSF) is present in GCA-affected vessels where it may be involved in skewing of tissue destructive macrophages (1). Furthermore, a recent phase 2 clinical trial demonstrated that GM-CSF receptor blockade was superior to placebo at 26 weeks in GCA. However, the cellular source of GM-CSF in GCA is still unclear.
Objectives: As T cells have been identified as a major source of GM-CSF in other immune-mediated diseases such as multiple sclerosis, we investigated whether T cells are GM-CSF producers in GCA patients, both systemically and locally.
Methods: GM-CSF production capacity by PMA-stimulated PBMCs from newly diagnosed, untreated GCA patients and HCs (N=10 each) was assessed using flow cytometry. Temporal artery biopsies (TABs, N=5) were immunohistochemically stained for CD3, CD8 and GM-CSF. Colocalization of these markers was assessed with immunofluorescence.
Results: Proportions of CD4+ (median GCA=3.1%; HCs=2.76%) and CD8+ (median GCA=5.8%; HCs=5.8%) T cells produced GM-CSF after *in vitro* stimulation, but no significant differences were found between the groups. Immunofluorescence staining confirmed that CD3+ T cells (both CD8+ and CD8-) were positive for GM-CSF in TABs. Interestingly, GM-CSF positivity in TABs correlated strongly with the extent of CD8+ T-cell infiltration ($r=0.74$, $p<0.01$), but not with CD3+ T-cell infiltration ($r=0.38$, $p=0.16$).
Conclusion: Our data imply that T cells are an important source of GM-CSF in GCA lesions. The correlation of the extent of CD8+ T-cell infiltration with GM-CSF positivity suggests that CD8+ T cells are the major source of local GM-CSF overexpression in tissue.
REFERENCES:
[1] W.F. Jiemy, Y. Sleen, K.S. Geest, H.A. Berge, W.H. Abdulahad, M. Sandovici, A.M. Boots, P. Heeringa, E. Brouwer, Distinct macrophage phenotypes skewed by local granulocyte macrophage colony stimulating factor (GM-CSF) and macrophage colony stimulating factor (M-CSF) are associated with tissue destruction and intimal hyperplasia in giant cell arteritis, Clin. Transl. Immunol. 9 (2020).
Disclosure of Interests: William Febry Jiemy: None declared, Rosanne Reitsema: None declared, Ayla Kwant: None declared, Wayel Abdulahad: None declared, Annemieke Boots Consultant of: Grünenthal Gmbh until 2017, Peter Heeringa: None declared, Elisabeth Brouwer Speakers bureau: Roche, paid to the UMCG
DOI: 10.1136/annrheumdis-2021-eular.1899

POS0113 BAFF-APRIL-BAFFR PATHWAY ON THE PATHOGENESIS OF IMMUNOGLOBULIN-A VASCULITIS

D. Prieto-Peña[1], S. Remuzgo Martinez[1], F. Genre[1], V. Pulito-Cueto[1], B. Atienza-Mateo[1,2], B. Sevilla[3], J. Llorca[4], N. Ortego[5], L. Lera-Gómez[1], M. Leonardo[6], A. Peñalba[6], J. Narváez[7], L. Martín-Penagos[8], J. A. Miranda-Filloy[9], L. Caminal Montero[10], P. Collado[11], J. Sanchez Perez[12], D. De Argila[12], E. Rubio-Romero[13], M. Leon Luque[13], J. M. Blanco-Madrigal[14], E. Galindez[14], J. Martin Ibanez[15], S. Castañeda[16], R. Blanco[1], M. A. González-Gay[1,17,18], R. López-Mejías[1]. [1]*Research Group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain*; [2]*López Albo´ Post-Residency Programme, Hospital Universitario Marqués de Valdecilla, Santander, Spain*; [3]*Hospital Universitario San Cecilio, Division of Pediatrics, Granada, Spain*; [4]*Department of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Santander, Spain*; [5]*Hospital Universitario San Cecilio, Systemic Autoimmune Diseases Unit, Granada, Spain*; [6]*Hospital Universitario Marqués de Valdecilla, Division of Pediatrics, Santander, Spain*; [7]*Hospital Universitario de Bellvitge, Division of Rheumatology, Barcelona, Spain*; [8]*Hospital Universitario Marqués de Valdecilla, Division of Nephrology, Santander, Spain*; [9]*Hospital Universitario Lucus Augusti, Division of Rheumatology, Lugo, Spain*; [10]*Hospital Universitario Central de Asturias, Division of Rheumatology, Oviedo, Spain*; [11]*Hospital Universitario Severo Ochoa, Division of Rheumatology, Madrid, Spain*; [12]*Hospital Universitario de La Princesa, Dermatology Department, Madrid, Spain*; [13]*Hospital Universitario Virgen del Rocío, Division of Rheumatology, Sevilla, Spain*; [14]*Hospital Universitario de Basurto, Division of Rheumatology, Bilbao, Spain*; [15]*Instituto de Parasitología y Biomedicina 'López-Neyra', CSIC, PTS Granada, Granada, Spain*; [16]*Hospital Universitario la Princesa, IIS-IP, Division of Rheumatology, Madrid, Spain*; [17]*University of Cantabria, School of Medicine, Santander, Spain*; [18]*University of the Witwatersrand, Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, Johannesburg, South Africa*

Background: *BAFF, APRIL* and *BAFFR* are genes that encode cytokines with a key role in the development and survival of B-lymphocytes [1-4]: The B cell-activating factor (BAFF, also known as BLyS), a proliferation-inducing ligand (APRIL) and BAFF receptor (BAFF-R), respectively. Previous genetic studies have revealed that the *BAFF-APRIL-BAFFR* pathway is implicated in the genetic predisposition to several immune-mediated diseases [5].
Objectives: To determine whether the *BAFF-APRIL-BAFFR* pathway represents a novel genetic risk factor for the pathogenesis of Immunoglobulin-A vasculitis (IgAV), an inflammatory disease in which IgA deposits and B-lymphocytes are crucial [6, 7].
Methods: A functional *BAFF* polymorphism (rs374039502) and two tag variants within *APRIL* (rs11552708 and rs6608) and *BAFFR* (rs7290134 and rs77874543)

were genotyped in 386 Caucasian IgAV patients (the largest series of Caucasian patients with IgAV ever assessed for genetic studies) and 806 sex and ethnically matched healthy controls by TaqMan assays.

Results: No statistically significant differences in the genotype and allele frequencies between patients with IgAV and healthy controls were observed when each genetic variant of *BAFF APRIL* and *BAFFR* was analyzed independently (Table 1). Likewise, no statistically significant differences in genotype and allele frequencies of *BAFF APRIL* or *BAFFR* were found when patients with IgAV were stratified according to the age at disease onset or to the presence/absence of gastrointestinal or renal manifestations. Similar results were disclosed when haplotype frequencies of *APRIL* and *BAFFR* were compared between patients with IgAV and healthy controls as well as patients with IgAV stratified according to the age at disease onset or to the presence/absence of gastrointestinal or renal manifestations.

Conclusion: Our results suggest that the *BAFF-APRIL-BAFFR* pathway does not contribute to the genetic network underlying IgAV.

REFERENCES:

[1] J Exp Med 1999;190:1697-710; [2] Science 1999;285:260-3; [3] Nat Genet 2005;37:829-34; [4] Nat Immunol 2002;3:822-9; [5] N Engl J Med 2017;376:1615-26; [6] N Engl J Med 2013;368:2402-14; [7] Autoimmun Rev 2018;17:301-315.

Table 1. Genotype and allele frequencies of *BAFF, APRIL* and *BAFFR* genes in patients with IgA vasculitis and healthy controls.

Polymorphism	Locus	1/2	Data set	1/1	1/2	2/2	1	2
rs374039502	BAFF	T/A	Patients	91.9 (353)	8.1 (31)	0	95.9 (737)	4.1 (31)
			Controls	91.5 (733)	8.1 (65)	0.4 (3)	95.6 (1531)	4.4 (71)
rs11552708	APRIL	G/A	Patients	78.1 (299)	20.6 (79)	1.3 (5)	88.4 (677)	11.6 (89)
			Controls	77.9 (625)	20.4 (164	1.6 (13)	88.1 (1414)	11.9 (190)
rs6608	APRIL	C/T	Patients	71.9 (277)	26.0 (100)	2.1 (8)	84.9 (654)	15.1 (116)
			Controls	70.0 (561)	27.6 (221)	2.5 (20)	83.7 (1343)	16.3 (261)
rs7290134	BAFFR	A/G	Patients	58.0 (224)	36.3 (140)	5.7 (22)	76.2 (588)	23.8 (184)
			Controls	57.2 (459)	36.4 (292)	6.5 (52)	75.3 (1210)	24.6 (396)
rs77874543	BAFFR	G/C	Patients	82.7 (316)	16.0 (61)	1.3 (5)	90.7 (693)	9.3 (71)
			Controls	83.0 (666)	16.6 (133)	0.4 (3)	91.3 (1465)	8.7 (139)

Acknowledgements: This study was supported by European Union FEDER funds and “Fondo de Investigaciones Sanitarias” (grant PI18/00042) from ‘Instituto de Salud Carlos III’ (ISCIII, Health Ministry, Spain). DP-P is a recipient of a Río Hortega programme fellowship from the ISCIII, co-funded by the European Social Fund (ESF, `Investing in your future´) [grant number CM20/00006]; SR-M is supported by funds of the RETICS Program co-funded by the European Regional Development Fund (ERDF) [grant number RD16/0012/0009]; VP-C is supported by a pre-doctoral grant from IDIVAL [grant number PREVAL 18/01]; BA-M is a recipient of a `López Albo´ Post-Residency Programme funded by Servicio Cántabro de Salud; LL-G is supported by funds of IDIVAL [grant number INNVAL20/06]; RL-M is a recipient of a Miguel Servet type I programme fellowship from the ISCIII, co-funded by the European Social Fund (ESF, `Investing in your future´) [grant number CP16/00033].

Disclosure of Interests: Diana Prieto-Peña Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD and Roche, Sara Remuzgo Martinez: None declared, Fernanda Genre: None declared, Verónica Pulito-Cueto: None declared, Belén Atienza-Mateo: None declared, Belén Sevilla: None declared, Javier Llorca: None declared, Norberto Ortego: None declared, Leticia Lera-Gómez: None declared, Maite Leonardo: None declared, Ana Peñalba: None declared, J. Narváez: None declared, Luis Martín-Penagos: None declared, Jose Alberto Miranda-Filloy: None declared, LUIS CAMINAL MONTERO: None declared, PAZ COLLADO: None declared, Javier Sanchez Perez: None declared, Diego de Argila: None declared, Esteban Rubio-Romero: None declared, MANUEL LEON LUQUE: None declared, Juan María Blanco-Madrigal: None declared, E. Galindez: None declared, Javier Martin Ibanez: None declared, Santos Castañeda: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD and Roche, Miguel A González-Gay Speakers bureau: Pfizer, Abbvie, MSD, Grant/research support from: Pfizer, Abbvie, MSD, Raquel López-Mejías: None declared

DOI: 10.1136/annrheumdis-2021-eular.707

POS0114 ABERRANT MONOCYTE SUBSETS IN PATIENTS WITH BEHÇET’S DISEASE

C. Li[1,2], J. Liu[1], H. Chen[1], W. Zheng[1]. [1]*Peking Union Medical College Hospital, Rheumatology and Clinical Immunology, Beijing, China*; [2]*Peking University Shougang Hospital, Rheumatology, Beijing, China*

Background: Behçet’s Disease (BD) is a systemic vasculitis of unknown etiology[1]. Monocytes closely related to inflammation potentially contribute to BD’s pathogenesis. They are classified into three subsets: classical monocytes (CM), intermediate monocytes (IM) and non-classical monocytes (NCM). Abnormalities of monocyte subsets have been reported in many infectious, inflammatory and autoimmune diseases[2-6], but their implication in BD remains elusive.

Objectives: To investigate the distribution, phenotypes and functions of monocyte subsets in BD and explore their roles in BD pathogenesis.

Methods: The frequencies and phenotypes of monocyte subsets in BD and healthy controls (HC) were determined by flow cytometry, and their correlation with clinical parameters was analyzed. Intracellular cytokines and phosphorylated signal proteins [phosphorylated p65(p-p65) and phosphorylated p38(p-p38)] were determined in LPS-activated monocyte subsets by flow cytometry. Monocyte subsets of BD and HC were sorted and co-cultured with naïve CD4 + T cells, and Th1 cell frequencies were measured on day 5.

Results: A higher IM (9.0±3.6 % vs. 4.5±2.0%, p<0.01) and lower NCM (2.6±1.2% vs. 4.2±2.0%, p<0.01) population in BD patients were noted. BD IM were positively correlated with CRP (r=0.5456, $p<0.05$), ESR (r=0.4683, p=0.05), and the serum level of TNF-a (r=0.7372, $p<0.001$) and IL-6(r=0.5013, $p<0.05$). BD NCM were negatively correlated with CRP (r=0.4822, $p<0.05$) and the serum level of IgM (r=-0.7830, $p<0.001$). Moreover, BD IM decreased (12.3±3.8% vs. 5.7±3.6%, $p<0.05$), while BD NCM increased (2.6±1.3% vs. 3.5±1.5%, $p<0.01$) after BD patients achieved remission. CD11b and CD64 expression on CM, IM and NCM in BD were enhanced. BD CM promoted TNF-a (61.0±11.4% vs 48.3±9.9%, $p<0.05$) and IL-6 (7.2±5.4% vs1.9±1.7%, $p<0.05$) production and facilitated Th1 differentiation. BD IM promoted IL-6 production (6.2±3.8% vs 2.6±1.6%, $p<0.05$). Furthermore, we demonstrated a higher level of p-p65 (12.8±2.9% vs 3.3±1.1%, $p<0.01$) in BD CM and increased p-p65 (3.2±0.6% vs 0.01±0.01%, $p<0.01$) and p-p38 (1.1±0.6% vs 0.03±0.01%, $p<0.01$) in BD IM.

Conclusion: To our knowledge, our study is the first study on monocyte subsets in BD. Our data highlighted the aberrant populations of IM and CM in BD, potentially implicated in BD pathogenesis.

REFERENCES:

[1] Ahmet, Gül, Pathogenesis of Behçet’s disease: autoinflammatory features and beyond, Semin. Immunopathol. 37 (2015) 413-418.
[2] G.Fingerle, A.Pforte, B.Passlick, et al.The novel subset of CD14+/CD16+ blood monocytes is expanded in sepsis patients, Blood. 82 (1993) 3170-3176.
[3] M.Moniuszko, A. Bodzenta-Lukaszyk, K. Kowal, et al. Enhanced frequencies of CD14++CD16+, but not CD14+CD16+, peripheral blood monocytes in severe asthmatic patients, Clin. Immunol. 130 (2009) 338-346.
[4] M.D.Sanchez, Y.Garcia, C.Montes,et al.Functional and phenotypic changes in monocytes from patients with tuberculosis are reversed with treatment, Microbes. Infec. 8 (2006) 2492-2500.
[5] S.Koch, T.Kucharzik, J.Heidemann,et al. Investigating the role of proinflammatory CD16+ monocytes in the pathogenesis of inflammatory bowel disease, Clin. Exp. Immunol. 161 (2010) 332-341.
[6] H. Zhu, F. Hu, X. Sun,et al.CD16(+) Monocyte Subset Was Enriched and Functionally Exacerbated in Driving T-Cell Activation and B-Cell Response in Systemic Lupus Erythematosus, Front. immunol. 7 (2016) 512.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1157

POS0115 RISK FACTORS FOR CORONARY HEART DISEASE AND ATHEROSCLEROSIS IN PATIENTS WITH BECHET’S DISEASE

R. Goloeva[1], Z. Alekberova[1], T. Popkova[1], S. Glukhova[1]. [1]*V A Nasonova Research Institute of Rheumatology, systemic rheumatic diseases, Moscow, Russian Federation*

Background:

Objectives: To evaluate traditional risk factors for clinically manifest and asymptomatic atherosclerosis in pts with BD.

Methods: Traditional risk factors for atherosclerosis were evaluated in 95 pts with Bechet’s disease (BD) and 40 healthy age and gender matched controls. The male-to-female ratio was 3,7:1, pts’ mean age was 29.7 (23-35) y, the mean age at the disease onset - 19,9 (14-25) y, and mean disease duration - 9,6 (4-15) y. The common carotid artery intima-media thickness (IMT) was evaluated by high resolution B-mode ultrasonography. A plaque was defined as a local intima-media thickening ≥1,2 mm, with reference IMT thickness <0,9 mm. Serum concentration of high-sensitivity C-reactive protein (hs CRP) was measured by immunonephelometric assay (BN-100 Analyzer; Dade Behring). Lipid profile evaluation included total cholesterol, TGs, HDL, LDL and atherogenic index.

Results: Traditional risk factors for atherosclerosis (one or more) were found in 85,3% of BD pts, dyslipidemia was the most common risk factor and was present in 76,84% of pts, mostly due to increased total cholesterol (TC) and

low-density lipoprotein cholesterol (LDL-C) levels. 22,1% had arterial hypertension (AH), 29,5% were current smokers, 27,4% had excess body weight, 3,1% had family history of cardiovascular diseases (CVD). Traditional risk factors for atherosclerosis were found in 80% out of 40 gender and age matching subjects from the control group, i.e., showing practically the same prevalence as in BD pts.

Table 1. The incidence-rate of traditional risk factors in BD patients and controls

Variables	BD pts (n=95)	Controls (n=40)	p
Age, years	29,0 [23,0;35,0]	29,0 [25,0;32,0]	NS
BMI, kg/m^2	23,1 [21,1;25,5]	23,8 [22,0;26,0]	NS
BMI ≥ 25 kg/m^2, n (%)	26 (27,4)	15 (37,5)	NS
Arterial hypertension, n (%)	21 (22,1)	4 (10)	NS
Family history of CVD	3 (3,1)	5 (12,5)	0,05
Cigarette smoking, n (%)	28 (29,5)	12 (30,0)	NS
Dyslipidemia, n (%)	73 (76,8)	27 (67,5)	NS
Total cholesterol, mml/l	5,0 [4,3;6,1]	5,1 [4,5;5,7]	NS
Cholesterol > 5,0 mml/l, n (%)	47 (49,5)	25 (62,5)	NS
TGs, mml/l	0,92 [0,7;1,3]	0,89 [0,60;1,08]	NS
TGs > 1,7 mml/l, n (%)	8 (8,4)	3 (7,5)	NS
LDL, mml/l	3,36 (2,8;4,0)	3,3 [2,7;3,7]	NS
LDL > 3 mml/l, n (%)	63 (66,3)	25 (62,5)	NS
HDL, mml/l	1,19 [1,0;1,5]	1,35 [1,2;1,6]	0,06
HDL ≤1 mml/l (male), ≤ 1,2 mml/l (female) n (%)	30 (31,6)	5 (12,5)	0,03

Reduced HDL levels were more common in BD pts vs the controls - 30 (31,6%) vs 5 (12,5), p=0,03 as shown in table 1. Other traditional risk factors were similarly present in both groups with no significant difference between BD pts and the controls.

Analysis showed similar incidence of CV events (nonfatal myocardial infarction, angina pectoris and stroke) in both groups. There were no differences between BD pts and healthy people in terms of lifetime risk for CVD. High lifetime risk ≥ 20% was found in 4 BD pts vs 0 in the control group; moderate lifetime risk >10% < 20% - in 6,3% of BD pts vs 2,5% in the control group, and low lifetime risk < 10% -was found in 89,5% of BD pts vs 97,5% of the controls.

Average IMT values were significantly higher in BD pts - 0.68 [0.60;0.73] vs 0.63 [0.56;0.65], p=0.008, but at the same time, IMT thinning (up to < 0.5 mm) was significantly more common in BD pts - 32.6% vs 12.5% in the control group (p=0.01). HsCRP serum levels were significantly higher in BD pts (2.42 [0.5;8.8] mg / l) than in the control group (0.37 [0.15;0.75]), p=0.001. There was a correlation between hs-CRP and BMI in BD pts (r=0.2, p<0.05), but no correlation was found between hsCRP and BD activity/BD clinical manifestations.

Conclusion: Decreased HDL cholesterol levels were more common in BD patients than in the control group, just as thinning of IMT, most likely because of vasculitis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3431

POS0116 HEART RATE VARIABILITY IN PATIENTS WITH BEHCETS DISEASE

R. Goloeva[1], Z. Alekberova[1], T. Popkova[1], S. Glukhova[1], D. Novikova[1]. [1]*V A Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases, Moscow, Russian Federation*

Background: Behcet's disease (BD) is a systemic vasculitis affecting all types and sizes of blood vessels. Heart rate variability (HRV) reflects sympathetic -parasympathetic imbalance in the autonomic NS regulation. Low HRV values are known as independent risk factor of death and non-fatal cardiovascular events in both - survivors of a myocardial infarction and in asymptomatic population.

Objectives: The aim of this study is to evaluate HRV in BD pts vs healthy controls.

Methods: The study group included 74 BD pts (53males/21females) with disease duration of 9,0 (5,0;15,0)/9,0 (7;20) years, and the control group - 32/15 age-matched healthy m/f. The following HRV parameters from 24h ECG ambulatory recording were assessed: MeanNN and time-domain variables, adjusted by MeanNN (SDNNn%, SDNNin%, RMSSDn%). Additionally, all traditional cardiovascular risk factors such as systolic blood pressure (SPB), smoking status, BMI values, dyslipidemia profile, ultrasonographic values of carotid intima-media thickness (IMT), and levels high sensitive CRP (hsCRP) as a marker of inflammation were evaluated.

Results: In BD patients HRV values (RMSSDn%) were significantly lower compared to healthy controls (table 1).

Table 1. HRV parameters in BD patients and control group

Parameters	Males		Females	
	BD (n=53)	Control (n=32)	BD (n=21)	Control (n=15)
Age, years	30 (24; 36)	30 (26; 35)	32 (26; 37)	28 (24; 31)
MeanNN, ms	810 (732; 849)	782 (732; 835)	776 (708; 830)	764 (694; 832)
SDNN n (%)	16,9 (13,6; 19,4)	17,2 (16,3; 21,1)	13,1 (11,3; 5,3)	12,2 (10,7; 14,6)
SDNNi n (%)	6,8 (5,1; 8,1)	6,8 (5,0; 8,3)	7,1 (6,1; 7,7)	5,2 (4,9; 5,7)
RMSSD n (%)	2,1 (1,5; 2,3)**	4,1 (2,7; 5,2)**	1,7 (1,4; 3,7)*	2,8 (2,2; 3,9)*

Data are presented in median values and interquartile range, *p<0,05, **p<0,005 vs controls.

There was a significant negative correlation in BD patients between HRV (SDNNin%) and age (r= -0,4; p=0,00), disease duration (r= -0,3; p=0,00), BMI (r= -0,2; p<0,01), cholesterol levels (r= -0,3; p=0,00), LDLP (r= -0,3; p=0,00) and increased IMT (r= -0,2; p=0,04), and also between HRV (RMSSD%) and age (r= -0,2; p=0,04), disease duration (r= -0,2; p=0,01), cholesterol levels (r= -0,3; p=0,00), HDLP (r= -0,2; p=0,04); a positive correlation was established between HRV (SNNN%) and smoking (r= -0,2; p=0,04). The control group showed positive correlation between HRV (SNNN%) and increased IMT (r= 0,4; p=0,01).

Conclusion: HRV reduction reflects impaired sympathetic -parasympathetic regulation in BD pts, associated with pts' age, disease duration and presence of traditional cardiovascular risk factors: BMI, increased cholesterol levels, LDLP, and such asymptomatic manifestation of atherosclerosis as increased IMT.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3682

POS0117 RENAL AND OVERALL OUTCOMES OF DOUBLE-POSITIVE (ANCA AND ANTI-GBM ANTIBODIES) PATIENTS COMPARED TO ANCA-ASSOCIATED VASCULITIS PATIENTS WITH SEVERE RENAL INVOLVEMENT: A MULTICENTER RETROSPECTIVE STUDY WITH SYSTEMATIC RENAL PATHOLOGY ANALYSIS

M. Clerte[1], R. Philip[2], C. Levi[1], E. Cornec-Legall[3], V. Audard[4], A. Huart[5], X. Puéchal[6], M. Touzot[7], N. Rabot[8], E. Thervet[1], A. Aouba[2], A. Karras[1]. [1]*Division of Nephrology, University Paris Descartes, Georges Pompidou European Hospital, APHP, 75, Paris, France*; [2]*Division of Clinical Immunology and Internal Medicine, Normandie University, UNICAEN, CHU of Caen Normandie, 14, Caen, France*; [3]*Division of Nephrology, Hospital of the Cavale Blanche, CHRU of Brest, 29, Brest, France*; [4]*Department of Nephrology and Renal Transplantation, Reference Center-Idiopathic Nephrotic Syndrome, Henri-Mondor Hospital, APHP F-94000 Créteil, INSERM U955, Paris East Créteil University F-94000, 94, Créteil, France*; [5]*Division of Nephrology and Transplantation, Reference Center of Rare Renal Diseases, University Paul Sabatier - Toulouse III, Hôpital Rangueil, 31, Toulouse, France*; [6]*Division of Clinical Immunology and Internal Medecine, University Paris Descartes, Cochin Hospital, APHP, 75014, 75, Paris, France*; [7]*Division of Dialysis and Therapeutic Apheresis, Health Center of Aura Paris Plaisance, 75, Paris, France*; [8]*Division of Immunology and Nephrology, University François Rabelais, CHRU of Tours, 37, Tours, France*

Background: Among small vessel vasculitis, double-positive patients (DPP), combining serum and/or histologic findings for glomerular basement membrane (GBM) disease, and anti-neutrophil cytoplasmic antibodies (ANCA), is a rare, newly and poorly described condition.

Objectives: We aimed to compare characteristics between DPP and ANCA-associated vasculitis patients (AAVP) with severe-renal-involvement.

Methods: Retrospective multicenter study comparing 33 DPP and 45 severe-renal-involvement (serum creatinine >300 µmol/L) AAVP, all with biopsy-proven nephropathy.

Results: Except for 2 patients (6%) who had pure renal presentation during their entire follow-up period, others exhibited at least one extrarenal manifestation: pulmonary involvement (64%), weight loss (39%), gastrointestinal involvement (33%), ENT manifestations (21%), musculoskeletal symptoms (21%), fever (18%), neurological (12%), cutaneous (6%) and/or cardiac (6%) signs. All DPP (including up to 18% exhibiting negative serum anti-GBM antibodies) presented severe acute kidney failure with histologic GBM involvement. Compared to our AAVP, they had higher serum creatinine (719 versus 501 µmol/L; p=0.006) and a higher of patients requiring initial renal replacement therapy (82% vs 36%; p<0.001). Berden classification significantly differed (p=0.003), with more crescentic glomerulonephritis and fewer sclerotic lesions in DPP. One-year renal survival was significantly lower in DPP than in AAVP (27% versus 64%; p<0.0002). With comparable proportions of ANCA subtypes (2/3 with anti-MPO autoantibodies),

numbers of extrarenal manifestations, remission-inducing immunosuppressants and median follow-ups (three years) between groups, relapse rates were similar: 9.1% of DPP and 10% of AAVP. Please, see the table 1 for more detailed data.
Conclusion: Although DPP have features of both kinds of eponymous vasculitis, the anti-GBM component is the dominant phenotype, with more severe renal presentation and prognosis compared to AAVP with severe renal failure. Simultaneous testing of both antibodies and a systematically performed renal biopsy should be recommended in all rapidly progressive glomerulonephritis patients to recognize this difficult-to-treat, rare disease.

Table 1. Comparison of clinical characteristics and outcomes between the cohorts of DPP and AAVP

	DPP n = 33	AAVP n = 45	p
Age (year)	71,5 [14 - 89]	63 [45 - 93]	0.14
Male	16 (48)	19 (42)	0.65
Birmingham Vasculitis Activity Score	18,1 ± 4,8	20,4 ± 5,4	0.07
Organ involvement (except kidney)	1,7 ± 0,8	1,9 ± 1,1	0.31
Serum creatinine (µmol/L)	719 [238 - 2412]	501 [310 - 1683]	0.006
ANCA (MPO/PR3)	22/11	34/11	0.45
Berden classification	n = 31	n = 44	0.003
s (sclerotic) / c (crescentic)	6 (19) / 22 (71)	12 (27) / 16 (37)	
f (focal) / m (mixed)	0 / 3 (10)	11 (25) / 5 (11)	
Brix renal risk score	n = 27	n = 44	0.000014
Low / Medium / High	0 (0) / 4 (15) / 23 (85)	1 (2) / 29 (66) / 14 (32)	
Initial immunosuppressive therapy			
IV Cyclophosphamide	25 (76)	40 (82)	0.14
Rituximab	1 (3)	3 (7)	0.64
Plasma exchanges	25 (76)	19 (42)	0.005
Maintenance treatment	17 (48)	40 (89)	0.046
Initial RRT requirement	27 (82)	16 (36)	0.00007
Renal recovery (% initial RRT requirement)	4 (12)	6 (38)	0.9
1 year renal survival	9 (27)	29 (64)	0.0002

Values are displayed as absolute number (%) or as median [range]. DPP: double positive patients; AAVP: ANCA associated vasculitis patients; MPO: myeloperoxidase; PR3: proteinase 3; RRT: renal replacement therapy; IV: intravenous.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3089

POS0118 A WORLDWIDE PHARMACOEPIDEMIOLOGICAL UPDATE OF DRUG-ASSOCIATED ANCA-ASSOCIATED VASCULITIS AT THE TIME OF TARGETED THERAPIES

S. Deshayes[1], C. Dolladille[2], A. Dumont[1], N. M. Silva[1], B. Chretien[2], H. De Boysson[1], J. Alexandre[2], A. Aouba[1]. [1]*CHU de Caen Normandie, Internal Medicine, Caen, France*; [2]*CHU de Caen Normandie, Pharmacology, Caen, France*

Background: Several pharmacological classes are involved in drug-associated anti-neutrophil cytoplasmic antibody-associated vasculitis (DA-AAV). However, the literature data supporting the role a drug in the onset of DA-AAVs mainly rely on case reports or short series and implicate old treatments. Moreover, the advent of new treatments, including targeted therapies, may have modified the epidemiology of these adverse drug reactions (ADRs).
Objectives: To update this list by using a pharmacovigilance-based data mining approach.
Methods: We collected data on ADRs reported with the MedDRA preferred term "Anti-neutrophil cytoplasmic antibody positive vasculitis" up to November 2020, from the World Health Organization pharmacovigilance database. For each retrieved drug, a case/noncase analysis was performed, and disproportionate reporting was calculated by using the information component (IC). A positive IC025 value, which is the lower end of the 95% credibility interval, was considered significant.
Results: A total of 483 deduplicated individual case safety reports of DA-AAV involving 15 drugs with an IC025>0 were retrieved. DA-AAV occurred in 264 (71.2%, n=371) women, the median age at onset was 62 years [45-72], and the median time to onset between the introduction of the suspected drug and DA-AAV was 9 months [1-36]. DA-AAV occurrence was considered serious in 472 (97.7%, n=481) cases and fatal in 43 (8.9%) cases. The drugs associated with the highest disproportionate reporting were hydralazine, propylthiouracil, thiamazole, sofosbuvir, minocycline, carbimazole, mirabegron, and nintedanib (Table 1).

Table 1. List of the 15 drugs associated with ANCA-associated vasculitis in the World Health Organization pharmacovigilance database with significant disproportional reporting, sorted by decreasing IC_{025}.

Drug	$N_{observed}$	N_{fatal} (%)	IC_{025} / IC	ROR [95%CI]	Delay (in days) between the introduction of the drug and AAV, median [Q1-Q3] (n available)
Hydralazine	208	19 (9%)	8.2 / 8.4	2683.5 [2269.3-3173.3]	1277 (n=1)
Propylthiouracil	108	4 (4%)	7.2 / 7.5	1201.5 [974.8-1480.9]	1003 [425-1959] (n=19)
Thiamazole	40	5 (13%)	5.2 / 5.6	138.7 [100.7-191.1]	411 [58-966] (n=6)
Sofosbuvir	46	0	4.9 / 5.3	74.6 [55.3-100.8]	(n=0)
Minocycline	17	0	3.8 / 4.6	72.4 [44.7-117.3]	(n=0)
Carbimazole	6	0	2.0 / 3.4	44.9 [20.1-100.4]	92 (n=1)
Mirabegron	7	2 (29%)	1.5 / 2.7	11.1 [5.3-23.3]	291 [289-415] (n=3)
Nintedanib	6	2 (33%)	1.4 / 2.8	14.2 [6.3-31.7]	56 [36-132] (n=4)
Penicillamine	4	1 (25%)	1.4 / 3.1	170.3 [63.5-456.3]	(n=0)
Influenza vaccine	29	2 (7%)	1.3 / 1.9	4.1 [2.8-6.0]	24 [20-26] (n=7)
Allopurinol	7	2 (29%)	1.2 / 2.4	8.0 [3.8-16.8]	(n=0)
Rifampicin	7	2 (29%)	0.6 / 1.9	4.7 [2.2-9.8]	(n=0)
Peginterferon alfa-2b	4	0	0.3 / 2.1	7.0 [2.6-18.6]	98 (n=1)
Montelukast	4	4 (100%)	0.2 / 1.9	5.8 [2.2-15.5]	(n=0)
Rosuvastatin	6	0	0.1 / 1.5	3.4 [1.5-7.5]	(n=0)

IC: information component; ROR: reporting odds ratio; CI: confidence interval; AAV: ANCA-associated vasculitis

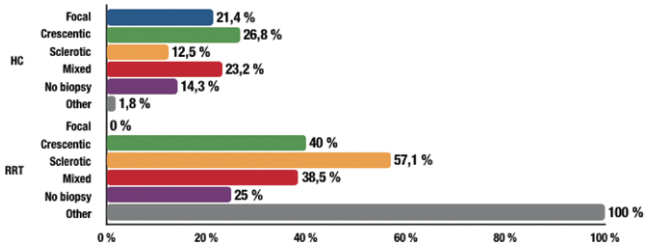
Conclusion: This study strengthens the previously suspected association but also identifies 3 new drugs that may cause DA-AAV. Particular attention should be given to these drugs by prescribers and in experimental studies.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1465

POS0119 RENAL INVOLVEMENT AND NEED OF RENAL REPLACEMENT THERAPY IN ANCA ASSOCIATED VASCULITIS IN A SPANISH SINGLE-CENTER STUDY

J. Álvarez Troncoso[1], J. C. Santacruz Mancheno[2], A. Díez Vidal[1], S. Afonso Ramos[3], A. Noblejas Mozo[1], T. Olea Tejero[3], J. J. Rios[1], B. Rivas[3], Á. Robles Marhuenda[1], M. C. Vega Cabrera[3], E. Martínez Robles[1], C. Soto Abánades[1], F. Arnalich Fernández[1]. [1]*Hospital Universitario La Paz, Internal Medicine, Madrid, Spain*; [2]*Clínica de los Riñones Menydial, Nephrology, Quito, Ecuador*; [3]*Hospital Universitario La Paz, Nephrology, Madrid, Spain*

Background: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EPGA). Renal involvement is frequent in AAV and is an important factor for morbidity and mortality.
Objectives: The main objective of this study was to analyze the demographic, clinical, histological and therapeutic characteristics of renal involvement in patients with AAV and the risk of renal replacement therapy (RRT) or death.
Methods: Retrospective observational study of 56 patients with AAV fulfilling classificatory criteria and renal involvement diagnosed between 1995 and 2020 from a Spanish tertiary centre. We studied the histological involvement (according to the 2010 classification in focal, crescentic, mixed or sclerotic), immunofluorescence (IF) and the treatment received with the risk of RRT or death.
Results: We included 56 patients diagnosed with AAV and renal involvement. The mean age was 61.08±4.05 years; 58.9% were women. The mean follow-up

time of these patients was 16.14± 8.80 years. Only 57.1% of patients presented systemic involvement.
Most frequent non-renal AAV manifestations were lung involvement (39.3%), central nervous system (30.4%), otorhinolaryngology (ORL) (14.3%), skin (8.9%) and cardiac involvement (8.9%). Main immunological findings were ANCA-MPO+ (69.6%), ANCA-PR3+ (23.2%), ANCA-negative (5.4%). Low C3 was found in 19.6% patients. Histologic classification (HC) and need of RRT is described in table 1. Main HC in renal AAV was crescentic, mixed, focal and sclerotic respectively. Eight patients had not biopsy performed. IF was positive for C3 deposits in 20 patients (35.7%). Half of the patients presented <50% normal glomeruli.



The treatment of renal involvement in AAV in our cohort was as follows: 83.9% (47) corticosteroids (CS) and cyclophosphamide (of which 40 received intravenous and 7 oral cyclophosphamide; and 12 patients associated plasma exchange (PE) with this treatment), 5.36% CS alone, 2 patients received CS and mycophenolate; 1 CS and rituximab, 1 CS and PE, and 2 patients received no treatment. A total of 13 patients received PE and 18 RRT. The mean time to RRT was 65.44±32.72 months. Relapses were not uncommon, 33.93% of the patients presented ≥1 relapse and 10.71% presented ≥2. Infections were very frequent since they were present in 91.07% of the patients. Other frequent non-immunological complications observed in the follow-up of these patients were thrombosis in 31.14%, cardiovascular events in 28.57% and cancer in 19.64%. Patients with ANCA-PR3+ were younger at diagnosis (p<0.001), were more likely to present cardiac (p=0.045) and ORL involvement (p<0.001). However, neither ANCA-PR3+ nor ANCA-MPO+ were specifically associated with the need of RRT or higher risk of death in our cohort. Use of CS alone for the treatment of renal AAV was associated with higher mortality (p=0.006) but CS and cyclophosphamide with lower mortality (p=0.044). ANCA-negative patients were more likely to receive no treatment. Having <50% normal glomeruli and C3 deposits on IF were associated with an increased need for RRT. Presenting focal disease on HC was protective for the need of RRT. Older age at diagnosis, systemic involvement of AAV and need of RRT was associated with higher mortality.
Conclusion: AAVs are complex vasculitides with frequent renal involvement. Increased C3 deposition, non-focal histological forms, and <50% normal glomeruli were related to the need for RRT. In turn, the need for RRT, a later age at diagnosis, and systemic involvement were associated with higher mortality. Holistic and multidisciplinary early management of AAVs in experience centers can help improve renal prognosis and decrease mortality.

		OR	IC (95%)	p
RRT	Number of glomeruli <50% normal	9.66	2.56-36.39	p < 0,001
	IF: C3 deposits	6	1.69-21.26	p = 0,009
Death	Age>70	6.53	1.84-23.15	p < 0,001
	Systemic disease	1.89	0.95-3.73	p = 0,029
	RRT	5.54	1.60-19.13	p = 0,005

REFERENCES:
[1] Binda et al. ANCA-associated vasculitis with renal involvement. J Nephrol. 2018 Apr;31(2):197-208.
[2] Kronbichler et al. Clinical associations of renal involvement in ANCA-associated vasculitis. Autoimmun Rev. 2020 Apr;19(4):102495.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.345

POS0120 INCIDENCE OF MALIGNANCIES IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS AND MICROSCOPIC POLYANGIITIS DIAGNOSED BETWEEN 1988 AND 2020

A. Masiak[1], M. Ziętkiewicz[1], A. Dębska-Ślizień[2], Z. Zdrojewski[1]. [1]*Medical University of Gdańsk, Department of Internal Medicine, Connective Tissue Diseases and Geriatrics, Gdańsk, Poland*; [2]*Medical University of Gdańsk, Department of Nephrology, Transplantology and Internal Diseases, Gdańsk, Poland*

Background: Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) is a group of systemic necrotizing small vessel vasculitides. Microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) are two most common types of AAV affecting mainly middle-aged and elderly people. Previous data indicated an increased occurrence of cancer in AAV patients [1], which has been mainly attributed to exposure to cyclophosphamide [2].
Objectives: The purpose of this paper was to analyze cancer incidence in unselected patients with GPA and MPA treated in one academic center since 1988 with follow-up until 2020.
Methods: With case record review, the baseline characteristics, outcomes and malignancy development in a cohort of 251 patients were assessed. Patients were followed up from time of diagnosis to their death or most recent hospital or outpatient's assessment.
Results: Twenty-eight of 251 patients with AAV (65 % cANCA, 26% pANCA, 9.0 % ANCA-negative) developed a total of 32 malignancies during a mean follow-up of 8.6 years. Patients characteristic is presented in table 1. Mean time since AAV onset to cancer diagnosis was 5.86±6.78 years. Of these malignancies, 2 melanoma, 6 were non-melanoma skin cancers, 4 gastrointestinal tract cancer (2 colon, 1 stomach, 1 liver), 3 bladder cancer, 2 breast cancer, 2 uterine cancer, 1 ovarian cancer, 2 prostate cancer, 1 testis cancer, 2 lung cancer, 6 haematological malignancies (1 lymphoma, 1 chronic myeloid leukemia, 4 monoclonal gammopathy of unknown significance), additionally 1 benign salivary gland tumor was found. Four of the 16 patients with renal transplants developed a total of 6 malignancies. There were no differences in the incidence of cancer by gender, age, severity and activity of the disease, ANCA status, smoking status, number of relapses and treatment. There was no association between cancer and cumulative dose of cyclophosphamide.
Conclusion: In the AAV group, 11% of patients developed different type of cancer. The most common was non-melanoma skin cancer. The risk of developing malignancy increased with follow-up time. We found no association of tumor development and cumulative cyclophosphamide dose.
REFERENCES:
[1] Rahmattulla et al. Incidence of malignancies in patients with antineutrophil cytoplasmic antibody-associated vasculitis diagnosed between 1991 and 2013. Arthritis Rheum. 2015;67(12):3270–3278.
[2] Faurschou M et al. Prolonged risk of specific malignancies following cyclophosphamide therapy among patients with granulomatosis with polyangiitis. Rheumatology (Oxford) 2015; 54:1345–1350.

Table 1. Characteristics of the AAV patients included in the study.

	Total sample (n=251)	No malignancy occurrence (n=223)	Malignancy occurrence (n=28)	P value
Age at diagnosis, mean ± SD years	53.0±15.9	52.4±16.4	57.9±9.45	NS
Female, n (%)	115 (45.8%)	106 (47.5 %)	9 (32.1 %)	NS
Mean observation time (years)	5.72±5.17	5.35±4.93	8.61±6.17	0.002
BVASv3	18.9±8.49	18.9±8.46	18.6±8.90	NS
DEI	7.03±2.86	7.04±2.90	6.96±2.62	NS
Organ involvement, n (%)				
Upper respiratory tract	170 (67.7 %)	151 (67.7 %)	19 (67.9 %)	NS
Lungs	163 (64.9 %)	142 (63.7 %)	21 (75.0 %)	NS
Kidney	171 (68.1 %)	151 (67.7 %)	20 (71.4 %)	NS
Skin	62 (24.7 %)54 (21.5 %)	55 (24.7 %)49 (22.0 %)	7 (25.0 %)	NS
Eyes	11 (4.4 %)	11 (4.9 %)	5 (17.9 %)	NS
Heart	30 (12.0 %)	24 (10.8 %)	0 (0.0 %)	NS
Gastrointestinal tract	34 (13.5 %)	32 (14.3 %)	6 (21.4 %)	NS
Follow-up				
0–5 years	145 (57.8 %)	136 (61.0 %)	9 (32.1 %)	0.004
> 5–10 years	62 (24.7 %)	52 (23.3 %)	10 (35.7 %)	NS
> 10 years	44 (17.5 %)	35 (15.7 %)	9 (32.1 %)	0.031
Deaths, n(%)	56 (23.0 %)	45 (20.8 %)	11 (39.3 %)	0.029
Renal transplantation, n(%)	16 (6.4 %)	12 (5.4 %)	4 (14.3 %)	NS
Cumulative Cyclophosphamide dose (g)	14.7±30.0	14.5±30.8	16.6±23.6	NS

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3840

POS0121

RESPONSE OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS TO MEPOLIZUMAB ACCORDING TO DISEASE MANIFESTATIONS. A SINGLE CENTRE EXPERIENCE

R. Ríos-Garcés[1], S. Prieto-González[1], J. Hernández-Rodríguez[1], M. C. Cid[1], G. Espígol-Frigolé[1]. [1]*Hospital Clínic de Barcelona, Systemic Autoimmune Diseases, Barcelona, Spain*

Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a relapsing disease with frequent glucocorticoid (GC) dependence. Mepolizumab (MEPO) has been demonstrated to reduce flares and spare GC. However, EGPA is a heterogeneous disease and the effects of MEPO on specific disease manifestations has not been completely delimitated.

Objectives: To analyze the impact of MEPO on manifestations derived from small-vessel vasculitis, ENT symptoms, asthma, eosinophilic tissue infiltration and ANCA status in a single-centre cohort of EGPA patients.

Methods: Medical chart of EGPA patients treated with MEPO were reviewed to describe demographics, clinical characteristics, steroid dose at the initiation of MEPO and during follow-up, flares, disease activity, damage accrual and laboratory results.

Results: Among 52 EGPA patients regularly controlled in our department, 11 patients were treated with MEPO. MEPO was prescribed when a) patients required prednisone (PDN) at ≥ 7.5 mg/d to maintain stability, or b) when maintained with < 7.5mg/d, presented at least 4 exacerbations/year requiring an increase in PDN dose. 6 were males and 5 females, with a mean age of 54 years at MEPO initiation. Baseline characteristics of the patients and course under treatment are presented in Table 1. ENT involvement, followed by asthma and eosinophil-related tissue-infiltration (ETI) were the most common symptoms when prescribing MEPO. Regarding treatment, patients received MEPO at 100-300mg SC monthly. The definition of flare was the same used in the MIRRA trial[1]. The mean time of treatment with MEPO was 34 months. All patients achieved a BVAS score of 0 points at 12 months or earlier. In general, patients reduced the number of flares, which tended to be milder, and all related to asthma or ENT manifestations. All improved their asthma control, but 3 of them persisted with recurrent ENT symptoms in spite of treatment with MEPO. None of them had vasculitic manifestations (cutaneous, neurological, gastrointestinal, renal) manifestations during treatment. All patients were able to tapper their PDN dose to ≤5 mg/day or less, except 3 patients. Of the 3 patients who required ≥5mg/d, 1 had severe asthma, but diminished the previous PDN dose (22.5 mg/d pre-MEPO, 10 mg/d currently) and the yearly rate of flares (8.2 pre-MEPO, 0.64 under-MEPO). The other one notably improved his asthma, but had ENT symptoms that responded unsatisfactorily to MEPO and required a maintenance PDN dose of 7.5 mg/d. The last one, improved her asthma control and was able to begin PDN tapering, but persisted with ENT symptoms. Regarding damage accrual, 6 patients remained stable during treatment, and 5 worsened. Two of three ANCA positive patients remained positive in spite of treatment.

Table 1.

	Baseline characteristics at diagnosis	At mepolizumab initiation	After mepolizumab (last follow-up)
Age, median (range) years	49 (23-67)	54 (35-69)	-
Male/Female, n (%)	6/5 (54.5%/45.5%)	-	-
BVAS, median (range)	11 (2-20)	2 (0-6)	0
FFS, value (n, %)	1 (1, 9.1%)	-	-
VDI, mean (range)	-	1.7 (0-5)	2.3 (0-5)
Asthma, n (%)	11 (100%)	3 (27.3%)	0 (0%)
ENT, n (%)	10 (90%)	4 (36.4%)	3 (27.3%)
SVV, n (%)	4 (36.4%)	0 (0%)	0 (0%)
ETI signs/symptoms, n (%)	7 (63.6%)	2 (18.2%)	0 (0%)
Constitutional symptoms, n (%)	4 (36.4%)	0 (0%)	0 (0%)
Eosinophils, mean (range) cells x10^9	5500 (600-8850)	240 (0-600)	55 (0-200)
ANCA positivity (IIF)	7 (77.8%)	3	2
Anti-MPO titers, mean (range)	286 (93-740)	88 (3-739)	7 (3-37)
Yearly rate of flares	-	1,75	0.51
Immunosuppressants, n	-	3	1
Prednisone dose, mg/d (range)	8 (7.5-25)	11.4 (5-22.5)	5.125 (0-10)

Conclusion: MEPO was effective for the treatment of patients with EGPA, with a reduction in the number and severity of flares and a decrease in PDN doses. A worse response of ENT involvement was observed. No vasculitic flares were observed in spite of GC reduction. Mepolizumab did not prevent damage accrual during the treatment period.

REFERENCES:

[1] Wechsler ME et al. MEPO or Placebo for Eosinophilic Granulomatosis with Polyangiitis. N Engl J Med. 2017.

Acknowledgements: Funding: Plan Estatal de Investigación Científica y Técnica y de Innovación 2013-2016 (PI18/00461), co-funded by Instituto de Salud Carlos III (ISCIII) and Fondo Europeo de Desarrollo Regional (FEDER) and by Río Hortega program (ISCIII, CM19/00032).

Disclosure of Interests: Roberto Ríos-Garcés: None declared, Sergio Prieto-González: None declared, José Hernández-Rodríguez: None declared, Maria C. Cid Paid instructor for: GSK and Vifor, Consultant of: GSK, Abbvie and Janssen, Grant/research support from: Kiniksa and Roche, Georgina Espígol-Frigolé Consultant of: Janssen, Grant/research support from: Roche

DOI: 10.1136/annrheumdis-2021-eular.2852

Central pain and other extra-articular associations to KOA

POS0122

THE ASSOCIATIONS BETWEEN DISEASE MODIFYING ANTI-RHEUMATIC DRUGS AND INCIDENT, AND PROGRESSION OF, RADIOGRAPHIC HAND OSTEOARTHRITIS IN RHEUMATOID ARTHRITIS PATIENTS

T. Burkard[1], C. Lechtenboehmer[2], S. Reichenbach[3], M. Hebeisen[4], U. Walker[5], A. M. Burden[1,6], T. Hügle[7]. [1]*ETH Zurich, Department of Chemistry and Applied Biosciences, Zurich, Switzerland*; [2]*University Hospital of Basel, Department of Radiology, Basel, Switzerland*; [3]*University of Bern, Institute for Social and Preventive Medicine, Bern, Switzerland*; [4]*SCQM Foundation, SCQM Foundation, Zurich, Switzerland*; [5]*University Hospital of Basel, Department of Rheumatology, Basel, Switzerland*; [6]*Maastricht University Medical Center+, Department of Clinical Pharmacy and Toxicology, Maastricht, Switzerland*; [7]*Lausanne University Hospital (CHUV) and University Lausanne, Department of Rheumatology, Lausanne, Switzerland*

Background: Hand osteoarthritis (OA) is characterized by bone erosions, joint space remodeling, and new bone formation mainly in distal interphalangeal (DIP) joints and thereby differs from hand manifestations in rheumatoid arthritis (RA). There are conflicting data about the benefit of treatment with conventional synthetic (cs) and biologic (b) disease modifying anti-rheumatic treatment (DMARD) on DIP OA.

Objectives: To assess the associations between DMARDs and incident, and progression of, radiographic DIP OA in RA patients.

Methods: We performed two observational cohort studies in the longitudinal Swiss Clinical Quality Management in Rheumatic Diseases registry (SCQM) between 1997 and 2014. RA patients who had ≥2 eligible hand radiographs were included at their first eligible radiograph (baseline) and were followed until the outcome or their last eligible radiograph. Radiographs were eligible if all 8 DIP joints could be scored. Modified Kellgren-Lawrence scores (KLS) were obtained by evaluating DIP joints for severity of osteophytes, joint space narrowing, subchondral sclerosis, and erosions. Incident/existing DIP OA was defined as KLS ≥2 in ≥1 DIP joint. Progression of existing DIP OA was defined as an increase of ≥1 in KLS in ≥1 DIP joint. We divided the study population into two cohorts based on whether DIP OA was present or absent at cohort entry (cohorts 1 and 2, respectively). Exposure status was defined time-dependently into mutually exclusive exposure groups: csDMARD monotherapy, bDMARD monotherapy, bDMARD/csDMARD combination therapy, past bDMARD/csDMARD therapy, or never DMARD use. Cox time-varying proportional hazard regression analyses were used to estimate hazard ratios (HRs) with 95% confidence intervals (CI) of DIP OA progression (cohort 1) or DIP OA incidence (cohort 2) associated with DMARD exposure categories (csDMARD monotherapy was the reference group because it was the largest group). Exposure and covariate information were extracted at every radiograph and other visit date. Missing covariate information was imputed using multiple imputation by chained equations. In sensitivity analyses, we repeated all analyses using generalised estimation equations (GEE).

Results: Among 2234 RA patients with 5928 eligible radiographs, 1340 patients had radiographic DIP OA at cohort entry (cohort 1) and 894 were DIP OA naïve (cohort 2). In cohort 1, radiographic progression of existing DIP OA was characterized by new osteophyte formation (666, 52.4%), followed by joint space narrowing (379, 27.5%), subchondral sclerosis (238, 17.8%), and erosion (62, 4.3%). bDMARD monotherapy was associated with an increased risk of radiographic DIP OA progression compared to csDMARD monotherapy (adjusted HR 1.34, 95% CI 1.07–1.69). The risk of DIP OA progression was not significant in csDMARD/bDMARD combination therapy users (adjusted HR 1.12, 95% CI 0.96–1.31), absent in past DMARD users (adjusted HR 0.96, 95% CI 0.66–1.41), and significantly lower among never DMARD users (adjusted HR 0.54, 95% CI 0.33–0.90), compared to csDMARD monotherapy users. In cohort 2, the risk of incident OA did not differ materially between treatment groups. Results from GEE analyses corroborated all findings.

Conclusion: Our results from this real-world RA cohort suggest that monotherapy with bDMARDs is not associated with incident DIP OA but may increase the risk of radiographic progression of existing DIP OA when compared to csDMARDs.

Acknowledgements: We thank all patients and rheumatologists involved for their contribution to the SCQM RA cohort. A list of rheumatology offices and hospitals that contribute to the SCQM registry can be found at http://www.scqm.ch/institutions. The SCQM is financially supported by pharmaceutical industries and donors. A list of financial supporters can be found at http://www.scqm.ch/sponsors.

Disclosure of Interests: Theresa Burkard: None declared, Christian Lechtenboehmer: None declared, Stephan Reichenbach: None declared, Monika Hebeisen: None declared, Ulrich Walker: None declared, Andrea Michelle Burden: None declared, Thomas Hügle Consultant of: Pfizer, Abbvie, Novartis, Grant/research support from: GSK, Jansen, Pfizer, Abbvie, Novartis, Roche, MSD, Sanofi, BMS, Eli Lilly, UCB

DOI: 10.1136/annrheumdis-2021-eular.3927

POS0123 NEUROPATHIC PAIN SYMPTOMS IN INFLAMMATORY HAND OSTEOARTHRITIS(OA) LOWERS HEALTH RELATED PHYSICAL QUALITY OF LIFE AND MAY REQUIRE ANOTHER APPROACH THAN ANTI-INFLAMMATORY TREATMENT

C. Van der Meulen[1], L. Van de Stadt[1], F. Kroon[1,2], M. Kortekaas[1], A. Boonen[3], S. Böhringer[4], M. Niesters[5], M. Reijnierse[6], F. Rosendaal[7], N. Riyazi[8], M. Starmans[2], F. Turkstra[9], J. Van Zeben[10], C. Allaart[1], M. Kloppenburg[1].
[1]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands; *[2]Zuyderland Medical Center, Rheumatology, Heerlen, Netherlands*; *[3]Maastricht University Medical Center and Care and Public Health Research Institute, Rheumatology, Maastricht, Netherlands*; *[4]Leiden University Medical Center (LUMC), Department of Biomedical Data Sciences, Leiden, Netherlands*; *[5]Leiden University Medical Center (LUMC), Anaesthesiology, Leiden, Netherlands*; *[6]Leiden University Medical Center (LUMC), Radiology, Leiden, Netherlands*; *[7]Leiden University Medical Center (LUMC), Clinical Epidemiology, Leiden, Netherlands*; *[8]Haga Hospital, Rheumatology, The Hague, Netherlands*; *[9]Amsterdam Rheumatology and Immunology Center Reade, Rheumatology, Amsterdam, Netherlands*; *[10]Sint Franciscus Vlietland Groep, Rheumatology, Rotterdam, Netherlands*

Background: Pain is a common, difficult to manage symptom in hand osteoarthritis (OA). Multiple pain mechanisms may play a role in hand OA.

Objectives: To investigate presence of neuropathic pain symptoms in patients with inflammatory hand OA, characteristics of those patients, their impact on health related quality of life (HR-QoL), and the influence of anti-inflammatory treatment on neuropathic pain symptoms.

Methods: Data from a randomised, double-blind, placebo-controlled trial of prednisolone including 92 patients with hand OA fulfilling ACR criteria were used. At baseline patients had signs of synovial inflammation, a VAS finger pain of ≥30 mm and who flared ≥20 mm upon NSAID washout. The primary endpoint was VAS finger pain (0-100) at week 6.

Neuropathic pain symptoms were measured at baseline and week 6 using the validated painDETECT questionnaire, consisting of questions on pain quality, pain intensity over time and radiating pain. Scores range -1 to 38 and patients are classified as having unlikely (<13), indeterminate (13-18) and likely (>18) neuropathic pain. HR-QoL was measured with physical component scale (PCS) of Short-Form 36 (SF36; 0-100), comorbidities with the Self-administered Comorbidities Questionnaire (SCQ; 0-45), radiographic severity with Kellgren-Lawrence (KL) sum score (0-120), and treatment response with OMERACT-OARSI responder criteria.

Association of patient characteristics with neuropathic pain symptoms was analysed with univariate and multivariate ordinal logistic regression, with painDETECT as dependent variable. Association of neuropathic pain symptoms with HR-QoL was analysed with multivariate linear regression, adjusted for age, sex, BMI, VAS finger pain, SCQ score and KL sum score, with PCS as dependent variable. Response of neuropathic pain symptoms and VAS pain to prednisolone was analysed with generalised estimating equations. Association of neuropathic pain symptoms at baseline with response to treatment was analysed using χ^2-tests and GEE.

Results: 91 patients had complete painDETECT data at baseline (mean painDETECT score 12.8 [SD 5.9]). Scores were <13 in 53%, 13-18 in 31% and >18 in 16%. Higher painDETECT score categories were associated with less radiographic damage, more comorbidities, female sex and higher VAS finger pain in multivariate analysis. (table 1)

Patients with painDETECT scores >18 had a lower HR-QoL (PCS -6.5 [95%CI -10.4 to -2.6]) than those with painDETECT scores <13.

PainDETECT scores remained unchanged throughout the trial in both prednisolone-treated and placebo-treated patients, and there was no between-group difference at week 6. VAS pain improved more in the prednisolone group than in the placebo group (mean between-group difference -16.5 [95%CI -26.1 to -6.9]) (figure 1). No association between the presence of neuropathic pain symptoms at baseline and OMERACT-OARSI response to treatment was found.

Conclusion: Patients with inflammatory hand OA and additional neuropathic pain symptoms are more often female and have more comorbidities, and report a lower QoL, than those without. Neuropathic pain symptoms seem unresponsive to anti-inflammatory therapy. Clinicians should be aware of neuropathic pain symptoms in their patients as they might benefit from additional, specific treatment.

Table 1. Ordinal logistic regression with painDETECT categories as dependent variable

Variables	Mean (SD) N=91 (100%)	Odds ratio (95% CI)
Age	64 (9)	0.96 (0.90 to 1.02)
Female sex; N (%)	72 (79%)	3.84 (1.19 to 12.39)*
BMI; median (SD)	27 (24 to 29)	0.97 (0.89 to 1.06)
SCQ score; median (SD)	2 (1 to 5)	1.04 (1.04 to 1.36)*
VAS finger pain	53.8 (2.1)	1.02 (1.00 to 1.04)*
KL sum score	37 (16)	0.96 (0.93 to 1.00)*

***p<0.05. BMI = body mass index. SCQ = Self-administered comorbidities questionnaire. VAS = visual analog scale. KL= Kellgren-Lawrence.**

Acknowledgements: The authors thank all patients for their participation in the HOPE study, and participating rheumatologists for inclusion of patients in the HOPE study. We also thank research nurses B.A.M.J. van Schie-Geyer and S. Wongsodihardjo, and technicians J.C. Kwekkeboom and E.I.H. van der Voort, for their contributions.

Figure 1

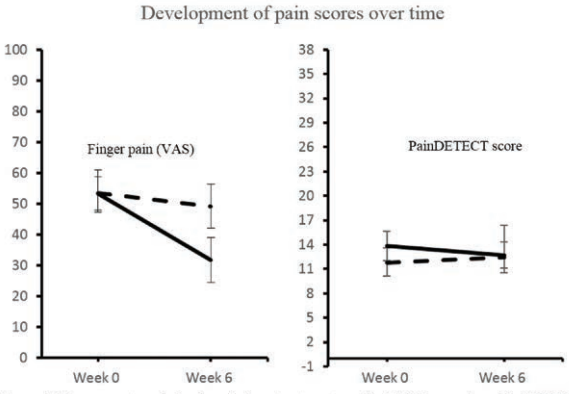


Figure 1. Mean score at week 0 and week 6, per treatment arm, for VAS finger pain and PainDETECT. Placebo shown in dashed line, prednisolone 10 mg daily in solid line. Whiskers indicate 95% CI.

Disclosure of Interests: Coen van der Meulen: None declared, Lotte van de Stadt: None declared, Féline Kroon: None declared, Marion Kortekaas: None declared, Annelies Boonen Speakers bureau: Lecture for UCB; paid to department., Consultant of: Yes. Advisory board meetings at Galapagos, Eli Lilly and Abvvie; paid to department., Grant/research support from: Yes. Grants by Celgene and Abbvie; paid to department., Stefan Böhringer: None declared, Marieke Niesters: None declared, Monique Reijnierse: None declared, Frits Rosendaal: None declared, Naghmeh Riyazi: None declared, M. Starmans: None declared, Franktien Turkstra: None declared, Jende van Zeben: None declared, Cornelia Allaart: None declared, Margreet Kloppenburg Consultant of: For Abbvie, Pfizer, Levicept, GlaxoSmithKline, Merck-Serono, Kiniksa, Flexìon, Galapagos, Jansen, CHDR and local investigator of industry-driven trial (Abbvie). All fees were paid to the institution., Grant/research support from: Grant by the Dutch Arthritis Society

DOI: 10.1136/annrheumdis-2021-eular.692

POS0124 QUALITY OF LIFE FOR PATIENTS WITH KNEE OSTEOARTHRITIS WITH OR WITHOUT PAIN SENSITIZATION

W. R. Goh[1], W. J. Ong[2], D. Chan[3], Y. Y. Leung[1]. *[1]Singapore General Hospital, Rheumatology & Immunology, Singapore, Singapore*; *[2]Duke-NUS Medical School, Singapore, Singapore*; *[3]Singapore General Hospital, Pain Medicine, Singapore, Singapore*

Background: Patients with central sensitization (CS) may have poorer quality of life (QOL).

Objectives: We aim to evaluate whether different ways of classifying CS have an impact on a patient's QOL among patients with knee osteoarthritis (KOA).
Methods: We use the baseline pre-operative data from a cohort of consecutive KOA patients enlisted for knee replacement surgery (1). We collected demographics, number and position of painful sites of body. Quality of life was assessed by the Medical Outcome Survey Short-Form 36 (SF-36). Pain pressure threshold was measured at volar side of right forearm. We classify CS using three sets of criteria: 1). widespread pain (pain involving both upper/ lower trunk, and both side of body), 2). lowest 10th percentile of pressure pain threshold (PPT) measured at the forearm and 3) the painDETECT questionnaire >=13/38.
Results: Of 233 patients (79.8% women) with complete data set for analysis, mean (standard deviation, SD) age was 66.0 (8.3) years. 15.5%, 25.8%, and 4.7% of patients were classified as having CS by widespread pain, low PPT and painDETECT criteria. KOA patients with CS have poorer QoL compared with those without. Low PPT identified patients with poorer general health, while widespread pain and PainDETECT criteria identified patients with poorer QoL in more domains including vitality mental health (Table 1).
Conclusion: KOA patients who have CS have poorer QoL compared to those without. Different criteria defined patients with different pattern of QoL impacts. In general, KOA patients who have CS have poorer QoL compared to those without. This highlight the importance of additional impact of CS to QoL

Table 1. Quality of life comparing patients with or without CS

	Widespread pain		lowest 10th percentile of forearm PPT		PainDETECT >=13/38	
	No (n = 197)	Yes (n= 36)	No (n= 206)	Yes (n= 27)	No (n= 222)	Yes (n= 11)
SF-Physical functioning	39.0 (21.8)	32.6 (19.0)	38.7 (21.8)	32.8 (17.8)	38.8 (21.3)	22.3 (19.2)*
SF-Role physical	21.6 (33.3)	8.3 (22.4)*	20.3 (32.2)	13.9 (32.0)	19.7 (32.6)	15.9 (23.1)
SF-Bodily pain	36.3 (19.5)	28.1 (14.0)*	35.1 (19.5)	34.0 (14.7)	35.5 (19.1)	24.2 (13.3)
SF-General health	68.9 (21.1)	64.6 (20.3)	69.4 (20.6)	59.3 (22.4)*	68.7 (20.7)	58.4 (25.7)
SF-Vitality score	69.7 (22.4)	59.3 (20.4)**	68.8 (22.5)	63.1 (21.1)	69.0 (21.8)	51.8 (29.2)*
SF-Social functioning	57.7 (37.2)	48.3 (39.2)	57.3 (38.0)	48.1 (33.7)	56.7 (37.7)	47.7 (42.1)
SF-Role emotion	86.1 (34.4)	86.1 (33.2)	86.7 (33.5)	79.0 (38.3)	86.9 (32.9)	63.6 (50.5)
SF-Mental health	82.4 (16.2)	77.4 (19.2)	82.2 (16.8)	77.8 (15.8)	82.2 (16.3)	70.2 (22.2)*
Physical component score	32.5 (10.1)	30.3 (8.0)	32.4 (9.8)	30.6 (9.7)	32.4 (9.9)	28.8 (8.7)
Mental component score	53.0 (10.5)	48.3 (10.0)*	52.7 (10.6)	48.5 (9.2)	52.6 (10.2)	44.2 (13.7)**

* p<0.05; **p<0.01

REFERENCES:

[1] Leung YY, Lim Z, Fan Q, et al. Pre-operative pressure pain thresholds do not meaningfully explain satisfaction or improvement in pain after knee replacement: a cohort study. Osteoarthritis and cartilage 2019;27(1):49-58.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1698

POS0125

CALCULATING RISK OF HAND OSTEOARTHRITIS PROGRESSION AT TEN YEARS THROUGH A PREDICTION MODEL

K. Shah[1], G. Bullock[1,2], A. Silman[1], D. Furniss[1], N. Arden[1,2], G. Collins[3,4].
[1]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, Oxford, United Kingdom; [2]University of Oxford, Centre for Sport, Exercise and Osteoarthritis Research, Versus Arthritis, Oxford, United Kingdom; [3]University of Oxford, Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, Oxford, United Kingdom; [4]Oxford University Hospitals NHS Foundation Trust, NIHR Oxford Biomedical Research Centre, Oxford, United Kingdom

Background: Hand osteoarthritis (OA) is a chronic, progressive disease, commonly affecting middle aged women. OA at the interphalangeal joints (IPJs) or the thumb base are considered different disease subsets (1). Few studies have investigated individual risk factors for IPJ OA progression (2). Prediction models can be used to calculate overall disease risk from multiple risk factors. This can guide prevention and treatment options.
Objectives: Develop and internally validate a prediction model for IPJ OA progression.
Methods: Data from the Chingford 1000 Women Study (Chingford Study), the largest population-based cohort worldwide assessing hand OA, was used. It is representative of the middle-aged female population in the United Kingdom (3). At baseline, 1,003 women aged 45 to 64 years' old were recruited, and 693 measurements taken. Hand radiographs were taken at baseline and after ten years, read using the Kellgren-Lawrence (KL) atlas (inter-observer correlation: ≥0.7 (4)). For the current study, participants must have had OA (KL ≥2 in ≥1 IPJ) on baseline hand radiographs. Participants with KL 4 in all 16 IPJs at baseline were excluded. Risk factors from the Chingford Study at baseline were selected by biological plausibility, literature evidence (2), and hand surgeons' consensus (5): age (years), occupation (manual versus non manual), OA in ≥1 thumb base (KL ≥2 versus KL<2), body mass index (BMI) (kg/m^2), family history of hand OA (yes versus no). The outcome was defined on an ordinal scale for the number of IPJs (up to >5 IPJs) with OA progression (increase by KL ≥1), at ten years'.
The prediction model was developed using a penalized proportional odds logistic regression. Odds ratios (95% confidence intervals) were reported for each risk factor. The model was internally validated using 2,000 bootstrap iterations. Model performance was assessed for discrimination (C-statistic), and calibration (C-slope). 3.5% of data was missing, and complete case analysis was used.
Results: 699 women had baseline hand radiographs: 38 were unreadable, 459 had no IPJ OA. Seven participants had missing data (occupation: 5, BMI: 1, family history: 1) and were excluded. 195 participants were included this study. Median age at baseline was 59 (interquartile range: 8) years.
181 (92.8%) participants had OA progression at 10 years (Figure 1). Thumb base OA (odds ratio: 1.32 (0.93 to 1.88)) was most strongly associated with IPJ OA progression (Table 1). C-statistic was 0.57, and calibration slope was 1.38 for the optimism-corrected model.
Conclusion: More stringent cut-offs for OA progression would be clinically useful. It was only weakly possible to predict which participants with IPJ OA would progress. This suggests that other risk factors, such as gender, ethnicity and genetics, may be predominant.

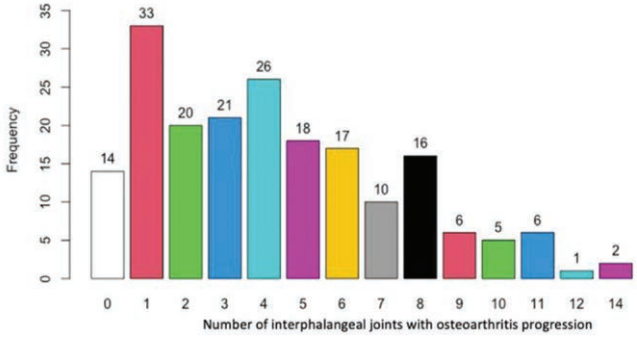


Figure 1. Hand interphalangeal joints with osteoarthritis progression (Kellgren-Lawrence grade ≥1) at 10 years' follow up

Table 1. Odds ratios for risk factors

Risk factor	Odds ratio (95% confidence interval)
Age (years)	1.02 (0.99 to 1.06)
Occupation (manual versus non manual)	0.88 (0.60 to 1.29)
Thumb base OA (Kellgren-Lawrence grade ≥2 versus <2)	1.32 (0.93 to 1.88)
Family history of hand OA (yes versus no)	1.03 (0.72 to 1.45)
Body mass index (kg/m^2)	1.04 (0.99 to 1.09)

OA: Osteoarthritis

REFERENCES:

[1] Kloppenburg M, et al. Research in hand osteoarthritis: time for reappraisal and demand for new strategies. Ann Rheum Dis. 2007;66(9):1157-61.
[2] Shah K, et al. Risk factors for the progression of finger interphalangeal joint osteoarthritis: a systematic review. Rheumatol Int. 2020;40(11):1781-1792.
[3] Hart DJ, Spector TD. The relationship of obesity, fat distribution and osteoarthritis in women in the general population: the Chingford Study. J Rheumatol. 1993;20:331-335.
[4] Hart DJ, et al. Reliability and reproducibility of grading radiographs for osteoarthritis of the hand. Br J Rheum. 1993;32:S1.
[5] Shah K, et al. Delphi consensus of risk factors for development and progression of finger interphalangeal joint osteoarthritis. J Hand Surg Eur Vol. 2019;44(10):1089-1090.

Acknowledgements: We would like to thank all of the participants of The Chingford 1000 Women Study, Professor Tim Spector, Dr Deborah Hart, Dr Alan Hakim, Maxine Daniels, Alison Turner, James van Santen and Julie Damnjanovic for their time and dedication.

Disclosure of Interests: Karishma Shah: None declared, Garrett Bullock: None declared, Alan Silman: None declared, Dominic Furniss: None declared, Nigel Arden Consultant of: Receives personal fees from Pfizer/Lily for consultancy outside the scope of this work, Grant/research support from: Receives grant from Merck outside the scope of this work, Gary Collins: None declared
DOI: 10.1136/annrheumdis-2021-eular.1126

POS0126 EARLY STAGE HAND OSTEOARTHRITIS IN PATIENTS WITH THE EHLERS-DANLOS SYNDROME: AN EXPLORATIVE STUDY

L. Rombaut[1], K. De Baere[2], E. Debacker[2], L. Decavele[2], F. Malfait[1,3], R. Wittoek[4,5]. *[1]Ghent University Hospital, Center for Medical Genetics, Gent, Belgium*; *[2]Ghent University, Rehabilitation Sciences, Ghent, Belgium*; *[3]Ghent University, Department of Biomolecular Medicine, Ghent, Belgium*; *[4]Ghent University, Internal Medicine and Pediatrics, Ghent, Belgium*; *[5]Ghent University Hospital, Department of Rheumatology, Gent, Belgium*

Background: The Ehlers-Danlos Syndromes (EDS) are a group of rare heritable connective tissue disorders caused by various defects in the biosynthesis or secretion of fibrillar collagens. The three main clinical features of EDS are joint hypermobility, skin fragility and general soft tissue fragility. 13 clinical subtypes of EDS are recognized, of which the hypermobile type (hEDS) and classical type (cEDS) are the most prevalent. It has been hypothesized that the (micro-)trauma in the joint due to typical subluxations and dislocations, make EDS patients prone to developing osteoarthritis (OA) in early stage. Conversely, it has been mentioned that joint hypermobility provides a larger joint surface area and prevents OA. Abnormal biomechanical loading has been identified as a risk factor for the development of OA in the wrist and hand. However, no studies have yet been performed in EDS patients.
Objectives: The primary aim was to investigate the presence of any degenerative features for hand OA, and if this differs between cEDS and hEDS patients. The second aim was to evaluate hand function and pain related to OA signs in EDS patients.
Methods: cEDS and hEDS patients between 35 and 50 years old were invited to participate. cEDS diagnosis was genetically confirmed and hEDS diagnosis was performed according the clinical 2017 hEDS criteria. Exclusion criteria were a body mass index ≥35, not being able to stand straight up for five minutes, suffering from an auto-immune disease or rheumatological condition, or pregnancy. Conventional X-rays of both hands were performed and scored independently by three assessors according to Kallman[1]. Presence of osteophytes (0-3), joint space narrowing (0-3), malalignment (>15°)(0/1), erosions (0/1), subchondral sclerosis (0/1), and subchondral cysts (0/1) were scored in all interphalangeal (distal and proximal), metacarpophalangeal and thumb base joints of both hands[1]. We defined early hand OA as minimally three features (≥1) were present. Several clinical assessments were made, e.g. tenderness, bony swelling and soft tissue swelling. The Michigan Hand Outcomes Questionnaire (MHOQ) and Australian/Canadian Osteoarthritis Hand Index (AUSCAN) questionnaires were completed.
Results: In total, 31 patients (mean age 41 ± 5.6 years, 13 men and 18 women) diagnosed with EDS participated, of whom 19 with cEDS and with 12 hEDS. In total, 927 joints were assessed. Level of agreement of radiographic assessments was very high (>98%). Early hand OA was found in more than 40% of the EDS patients, with a significant higher frequency in cEDS patients compared to hEDS patients (58% vs. 17%) (p=0.032). Joint space narrowing was most frequently present and significantly more in the cEDS patients compared to hEDS patients (79% vs. 21%) (p=0.003). However, radiographic changes were found in only 10% of all finger joints. Of all fingers, thumb joints were most affected. Regarding the clinical features of hand OA, all patients showed deformity in one or more finger joints, most frequently at the thumb, especially the IP joint (both hyperflexion and hyperextension). Tenderness and bony swelling was present in 36% and 45% of all patients, respectively, whereas soft tissue swelling was less frequently observed (10% of all patients). Here, no significant differences were found between cEDS and hEDS patients. Moderate disability was present (mean (SD) AUSCAN= 45.47 (27.10) and MHQ = 65.97 (14.21). cEDS showed significant less hand pain (p=0.03), a better hand function (p=0.03) and less disability (p=0.026) than hEDS.
Conclusion: This explorative study demonstrates that a high number of EDS patients present with minimal degenerative features of hand OA, but in a minority of joints. Patients with cEDS were significantly more affected, but showed a better function compared to hEDS. Possibly, cEDS patients are more susceptible to develop hand OA.
REFERENCES:
[1] Altman R, Gold G. Atlas of individual radiographic features in osteoarthritis, revised. OARSI. 2007;15:A1-A56.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1351

POS0127 ASSOCIATION BETWEEN HYPERURICEMIA AND OSTEOARTHRITIS

E. Taskina[1], E. Strebkova[1], L. Alekseeva[1,2], N. Kashevarova[1], K. Telyshev[1], E. Sharapova[1], S. Anikin[1], F. Bibulatova[1], A. Lila[2,3]. *[1]V.A. Nasonova Research Institute of Rheumatology, Osteoarthritis, Moscow, Russian Federation*; *[2]Russian Medical Academy of Continuous Professional Education, Rheumatology, Moscow, Russian Federation*; *[3]V.A. Nasonova Research Institute of Rheumatology, Director, Moscow, Russian Federation*

Background:
Objectives: To evaluate the relationship of hyperuricemia (GU) with the course of knee osteoarthritis (OA) and the components of metabolic syndrome (MS).
Methods: The prospective study included 107 women aged 40-75 y.o, with a reliable diagnosis of I-III Kellgren J. - Lawrence J. stage of knee OA (ACR), who signed an informed consent. The average age of patients was 59.1 ± 8.9 y.o. (from 38 to 74), the duration of the disease was 9 (4-12) years. The average values of the body mass index (BMI) corresponded to obesity (30.6 ± 5.7 kg / m2), waist circumference (WC) - 93.9 ± 12.1 cm. An individual card was filled out for each patient, including anthropometric parameters, anamnesis and clinical examination data, an assessment of knee joint pain according to VAS, and concomitant diseases. All patients underwent standard X-ray of the knee joints, DEXA scan of the lumbar spine and total hip, and laboratory examination.
Results: Hyperuricemia was diagnosed in 26.2% of patients. Patients with GU had a higher BMI and WC (p<0.05). X-ray examination revealed significantly larger sizes of osteophytes (p = 0.02) and smaller sizes of the medial space of the knee joint (p = 0.02), while the patients of both groups were comparable in age and duration of OA (Table 1). Patients with GU had a statistically significantly higher bone mineral density (BMD) values were observed in L1-L4 and total hip (p<0.05). MS was almost 2 times more often diagnosed in patients with GU (83.3% vs. 49.2%, RR=1.71, 95%CI 1.21-2.36, p=0.01). Higher levels of CRP, COMP, leptin, triglycerides (TG), creatinine, ALT and AST were determined in patients with GU (Table 1). Spearman rank ordered correlation coefficients between GU and BMI (r=0.22, p=0.03), WC (r=0.26, p=0.02), MS (r=0.29, p=0.01), and CHD (r=0.21, p=0.04). There were a correlation between GU and the stage of knee OA (X-ray) (r=0.34, p=0.02), the size of medial osteophytes in the femur (mm) (r=0.37, p=0.01) and the medial space of the knee joint (mm) (r=-0.27, p=0.01), BMD L1-L4 (r=0.37, p=0.03) and the total hip (r=0.37, p=0.04). There were also significant positive associations with the following laboratory parameters: CRP (r=0.27, p=0.007), COMP (r=0.25, p=0.05), leptin (r=0.29, p=0.03), creatinine (r=0.45, p<0.0001), TG (r=0.44, p=0.0001), ALT (r=0.32, p=0.002), AST (r=0.25, p=0.02).

Table 1. Comparative characteristics of OA patients with and without GU

Parameter	OA Patients with GU (n = 28)	OA Patients without GU (n = 79)	p
Age, y.o.	61 (53-68)	60 (54-66)	0.33
Duration OA, years	10 (6-14)	7.5 (3-12)	0.06
WC, cm	99.3 ± 12.8	92.2 ± 11.4	0.02
BMI, kg/m^2	33.5 ± 5.6	30 ± 5.6	0.04
The size of the medial space of joint according to X-ray, mm	2.3 (1.2-3.3)	3.2 (2.0-4.3)	0.02
The size of the osteophytes of the femur, mm	5.8 (3.7-6.3)	2.9 (1.7-4.5)	0.02
BMI L1-L4, g/cm^2	1.18 (1.12-1.24)	1.0 (0.86-1.15)	0.04
BMI total hip, g/cm^2	1.05 (1.0-1.13)	0.9 (0.82-0.98)	0.04
CRP, mg/l	2.8 (1.9-6.2)	1.9 (1.2-3.6)	0.007
COMP, ng/ml	31.9 (27.6-45)	24.2 (18.9-38.7)	0.05
Leptin, ng/ml	46.2 (36.5-72)	30.5 (19.5-45.6)	0.03
TG, mmol/l	1.97 (1.61-2.41)	1.26 (0.87-1.63)	0.002
Creatinine, mmol/l	79 (74.9-86)	68 (62-74)	0.0001
ALT, mmol/l	26.5 (17.2-32.9)	17.9 (13.2-21.7)	0.003
AST, mmol/l	22.5 (18.5-27.8)	18.9 (16.8-21.9)	0.02

Conclusion: GU may be an aggravating predictor of not only MS-associated diseases such as obesity, dyslipidemia, but also OA. Thus, at high levels of uric acid, more advanced radiological stages of OA, high values of the BMD of the axial skeleton and increased values of CRP, COMP are noted. In this connection, therapeutic interventions of OA in patients with GU should also be aimed at reducing the concentration of uric acid, which may provide a slowdown in the progression of the disease. Further study of this issue is needed.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3364

POS0128 PHYSICIAN AND PATIENT PERCEPTIONS OF SURGICAL PROCEDURES FOR KNEE OA ACROSS JAPAN, THE US AND 5 EU COUNTRIES: RESULTS OF A REAL-WORLD STUDY

N. Fukui[1], P. G. Conaghan[2], K. Togo[3], N. Ebata[3], L. Abraham[4], J. Jackson[5], J. Jackson[5], M. Berry[5], H. Pandit[2]. *[1]The University of Tokyo Komaba Campus,*

Graduate School of Arts and Sciences, Meguro City, Japan; [2]*University of Leeds, Musculoskeletal Medicine, Leeds, United Kingdom*; [3]*Pfizer, Inc., HEOR, Shibuya City, Japan*; [4]*Pfizer Ltd, HEOR, Surrey, United Kingdom*; [5]*Adelphi Real World, Real World Research, Bollington, United Kingdom*

Background: Patients with knee osteoarthritis (OA) who do not achieve adequate pain relief and functional improvement with a combination of non-pharmacologic and pharmacologic therapies are recommended an arthroplasty as an effective option to relieve severe pain and functional limitations. However, some patients are reluctant to undergo surgical interventions, and clinicians may choose to avoid or delay surgery due to safety risks and/or the financial cost. It is of interest to understand if the use and perception of surgery differs between countries, however, few published data exist.
Objectives: To demonstrate how surgery and the use of surgical procedures differs across Japan, United States of America (US) and 5 major European countries (EU5) and to evaluate patient perception towards surgery.
Methods: Data were drawn from the Adelphi OA Disease Specific Programme (2017-18), a point-in-time survey of primary care physicians (PCP), rheumatologists (rheums), orthopaedic surgeons (orthos) and their OA patients. Patients with physician-diagnosed knee OA were included and segmented into two categories: had previous surgery (PS) and never had surgery (NS). A Fisher's exact test was performed on the two groups. Physicians reported on patient demographics; whether patients had undergone surgery; type of surgery; success of surgery; how success was defined; and reasons for wanting to delay surgery. Patients reported their willingness to undergo surgery; reasons for not wanting surgery; how successful their surgery was; and how they defined this success.
Results: Physician/patient reported data were available for 302,230 (Japan), 527,283 (US) and 1487,726 (EU5) patients with diagnosed knee OA. Patients were categorised by their physicians as mild (40% Japan; 34% US; 24% EU5), moderate (49% Japan; 49% US; 56% EU5) or severe (9% Japan; 17% US; 19% EU5). Patients in Japan were more likely to be female (78% vs 54% US; 58% EU5), older (73 vs 65 US; 66 EU5) and have a lower BMI than patients in the US and EU5. Obesity and diabetes were much less prevalent among patients in Japan. One in ten patients in Japan had undergone a surgery (10%), far fewer than in the US (22%) or EU5 (17%). When surgery was performed, this was more likely to be a total joint replacement (TJR) in Japan, whereas in the EU and US, arthroscopic washout was more commonly performed.
For over half of Japanese patients (56%), successful surgery was more likely to be defined as having no more pain (vs. 35% US; 14% EU5). Improved mobility and a reduction in pain were also commonly reported reasons. Physicians (in each region) were more likely to suggest pain reduction, rather than no pain, and improved mobility as markers of success. Patients in Japan were much more likely to say they would not agree to surgery if recommended by their doctor, or were unsure (84% vs. 68% US; 62% EU5). The main reason for patient reluctance in Japan was fear of surgery, whereas in the US and EU5 the main reason given was that surgery was not needed. This finding was also evident among physicians in Japan, who frequently reported that patient reluctance was a key reason for delaying surgery. Physicians in Japan, do however, report that patient request was one of their main triggers for recommending surgery (45% vs 20% US; 16% EU5).
Conclusion: Although surgery can be an effective option for those with OA who have exhausted other treatment options, some patients are reluctant to undergo surgery out of fear, especially in Japan, possibly due to the higher patient age. Physicians aiming to delay surgery were driven by patient reluctance in Japan, whereas cost to patient was a bigger factor in the US and EU5. The higher level of TJR vs. other surgery options among patients in Japan may suggest physicians are looking for higher levels of efficacy.
Disclosure of Interests: Naoshi Fukui Speakers bureau: Pfizer, Consultant of: Pfizer, Philip G Conaghan Speakers bureau: Abbvie, Novartis, Consultant of: AstraZeneca, BMS, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, Gilead, Novartis, Pfizer, Kanae Togo Shareholder of: Pfizer, Employee of: Pfizer, Nozomi Ebata Shareholder of: Pfizer, Employee of: Pfizer, Lucy Abraham Shareholder of: Pfizer, Employee of: Pfizer, James Jackson: None declared, Jessica Jackson: None declared, Mia Berry: None declared, Hemant Pandit Paid instructor for: Bristol Myers Squibb, Consultant of: Johnson and Johnson, Grant/research support from: GSK
DOI: 10.1136/annrheumdis-2021-eular.2510

POS0129 ASSOCIATION BETWEEN OSTEOARTHRITIS-RELATED SERUM BIOCHEMICAL MARKERS OVER 11 YEARS AND KNEE MRI-BASED IMAGING BIOMARKERS IN MIDDLE-AGED ADULTS

B. Antony[1], A. Singh[1], L. Blizzard[1], A. Venn[1], G. Jones[1], J. Burgess[1], V. Parameswaran[2], F. Cicuttini[3], L. March[4], C. Ding[1]. [1]*University of Tasmania, Menzies Institute for Medical Research, Hobart, Australia*; [2]*Royal Hobart Hospital, Department of Endocrinology, Hobart, Australia*; [3]*Monash University, Department of Epidemiology and Preventive Medicine, Melbourne, Australia*; [4]*University of Sydney, Institute of Bone and Joint Research, Kolling Institute of Medical Research, Sydney, Australia*

Background: Serum levels of osteoarthritis (OA)-related cartilage and joint-specific biochemical markers – cartilage oligomeric matrix protein (COMP), matrix metalloproteinase (MMP)-3, and hyaluronan (HA) –are shown to be associated with cartilage degradation, joint tissue degradation, and synovitis in patients with OA. Although these OA-related biochemical markers may initially precede the MRI biomarkers of joint structural changes, such changes detected in MRI can lead to biochemical marker changes later as the condition progresses. However, there is a lack of data on OA-related biochemical markers' association with MRI-based biomarkers in the middle-aged general population.
Objectives: We aimed to describe the associations between OA-related biochemical markers and MRI-based imaging biomarkers in middle-aged adults followed up over 10-13 years.
Methods: Blood samples were collected during the Childhood Determinants of Adult Health (CDAH)-1 study at baseline (year: 2004-06, age: 26–36 years) and 10-13 year follow-up (CDAH-3; year: 2014–2019, age: 36–49 years). Serum samples from baseline (n=156) and follow-up (n= 167) were analyzed for three OA-related biomarkers – namely COMP, MMP-3, and HA– using non isotopic ELISA assay methodology. Knee MRI scans were obtained during the CDAH-knee study (year: 2008-10, age: 30-40 years, n=313), and MRIs were assessed for cartilage volume, cartilage thickness, subchondral bone area, cartilage defects, and bone marrow lesions (BML). Univariable and multivariable (adjusted for age, sex, and body mass index (BMI)) linear regression and logistic regression were used to describe the association of biochemical marker at CDAH-1 and MRI-based imaging biomarkers at CDAH-knee, and Tobit regression was used to describe the association of MRI-based imaging biomarkers at CDAH-knee and biochemical markers at CDAH-3.
Results: In the multivariable model for the association of biochemical marker with MRI-based imaging biomarkers (assessed after 4 years), we found a significant negative association of COMP with medial femorotibial compartment cartilage thickness (-0.010 (-0.019, -0.000) p=0.045), and MMP-3 with patellar cartilage thickness (-9.075 (-16.344, -1.807) p=0.015) and total bone area (-0.047 (-0.086, -0.007) p=0.020). No significant association was observed between HA and MRI markers.
In the multivariable model for association of MRI-based imaging biomarkers with biochemical markers (assessed after 6-9 years), a significant negative association of total cartilage volume (-0.0005 (-0.0008, -0.0002) p=0.001) and total cartilage thickness (-0.628 (-1.143, -0.114) p=0.017) with MMP-3, and total bone area with COMP (0.270 (-0.474, -0.006) p=0.010) was observed. No significant association was observed between MRI-based imaging biomarkers and HA.
Conclusion: COMP and MMP-3 levels were negatively associated with knee cartilage thickness assessed 4-years later. Similarly, knee cartilage thickness and volume were negatively associated with COMP and MMP-3 levels assessed 6-9 years later in population-based middle-aged adults, indicating an interdependent negative association of OA-related biochemical markers and MRI-based imaging biomarkers. These results suggest that OA-related biochemical markers may predict future MRI-based imaging biomarkers in middle-aged adults and thus represent possible at-risk populations to target for structure modification interventions.
Acknowledgements: This project was funded by the National Health and Medical Research Council of Australia Project Grant and Royal Hobart Hospital Research Foundation Project Grant.
Disclosure of Interests: Benny Antony Grant/research support from: Investigator-Initiated Clinical Trial support from Nat Rem Ltd., Ambrish Singh: None declared, Leigh Blizzard: None declared, Alison Venn: None declared, Graeme Jones Speakers bureau: Speaker for various pharma, Grant/research support from: Investigator-Initiated Clinical Trial support, John Burgess: None declared, Venkat Parameswaran: None declared, Flavia Cicuttini: None declared, Lyn March: None declared, Changhai Ding: None declared
DOI: 10.1136/annrheumdis-2021-eular.3418

POS0130 ASSOCIATION BETWEEN HYPERTENSION AND OSTEOARTHRITIS

E. Taskina[1], E. Strebkova[1], L. Alekseeva[1,2], N. Kashevarova[1], K. Telyshev[1], S. Anikin[1], E. Sharapova[1], D. Kudinsky[1], A. Lila[2,3]. [1]*V.A. Nasonova Research Institute of Rheumatology, Osteoarthritis, Moscow, Russian Federation*; [2]*Russian Medical Academy of Continuous Professional Education, Rheumatology, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Director, Moscow, Russian Federation*

Background:
Objectives: To evaluate the relationship between arterial hypertension (AH) and the course of knee osteoarthritis (OA).

Methods: The prospective study included 109 women aged 38-75 y.o., of I-III Kellgren J. - Lawrence J. stage of knee OA (ACR), who signed an informed consent. The average age was 59.3 ± 8.7 y.o. (from 38 to 74), the average duration of the OA was 7 (4-12) years. The average values of the body mass index (BMI) corresponded to obesity (30.9 ± 5.4 kg / m^2), waist circumference (WC) – 94.4 ± 11.7 cm. An individual card was filled in for each patient, including anthropometric parameters, anamnesis and clinical examination data, assessment of knee joint pain according to VAS, WOMAC, KOOS and DN4 indices, and concomitant diseases. All patients underwent standard X-ray of the knee joints, laboratory examination.

Results: AH was diagnosed in 69.7 % patients with OA. Patients were divided into 2 groups, according to the presence or absence of AH (Table 1). Patients with AH were older, had a higher BMI, WC, a longer duration of menopause and significantly earlier its onset (p<0.05). Patients with OA and AH had a more severe course of OA: higher values of pain in VAS, total WOMAC and all its components, DN4, worse indicators of total KOOS (p<0.05). X-ray examination showed a tendency to a more significant narrowing of the medial space of the knee joints (p = 0.07). Laboratory examination showed higher values of CRP, ESR, IL-6, and leptin (p < 0.05).

Table 1. Comparative characteristics of OA patients with and without AH

Parameters	Patients with AH (n=76)	Patients without AH (n=33)	p
Age, y.o.	61 (57-68)	55.5 (49-58)	<0.01
WC, cm	92 (90-105)	86.5 (84-90)	<0.01
Age of menopause, y.o.	50 (47-52)	55.5 (49-58)	0.02
Duration of menopause, years	14 (7.5-19)	7 (4-8)	<0.01
Duration of OA, years	10 (5-15)	4 (1-6)	0.001
VAS pain score, mm	49 (40-57)	42 (24-50)	0.02
WOMAC pain, mm	189.5 (140-250)	140 (108-162)	0.001
WOMAC stiffness, mm	77.5 (42-100)	56 (33.5-71.5)	0.01
WOMAC functional impairment (FI), mm	651 (547-902)	546.5 (320-663.5)	0.002
Total WOMAC, mm	899 (728-1280)	734 (526.5-882)	0.001
KOOS, points	0.47 (0.36-0.57)	0.6 (0.53-0.75)	<0.01
DN4, points	2 (1-3)	1 (0-2)	0.01
Overall health status, mm	45 (35-55)	36.5 (28.5-48.5)	0.02
The size of the medial space of joint according to X-ray, mm	2.45 (1.35-4.35)	3.6 (2.8-4.3)	0.07
CRP, mg/l	2.38 (1.47-4.85)	1.21 (0.69-2.53)	<0.01
Leptin, ng/ml	37.4 (26.5-53.3)	23.6 (15.1-40.2)	0.01
IL-6, pg/ml	0.7 (0.4-1.2)	0.45 (0.3-0.7)	0.03
ESR, mm/h	14 (7-18)	7 (6-12)	0.02

We founded positive (p <0.05) associations between AH and a more severe, prolonged course of OA (r=-0.39, p<0.01) in the the Spearman rank-order correlation coefficient analysis. Thus, patients with AH had higher values of VAS pain (r=0.31, p<0.01), total WOMAC (r=0.31, p<0.01) and all its components (pain (r=0.33, p<0.01), FI (r=0.3, p<0.01) and stiffness (r=0.24, p<0.01), DN4 (r=0.24, p=0.01), worse indicators of total KOOS (r=-0.42, p<0.01) and overall health status (r=0.23, p=0.02), more often detected more advanced stage of OA (r=0.24, p=0.03) and synovitis (r=0.23, p=0.01). In addition, positive relationships were found with CRP (r=0.31, p<0.01), IL - 6 (r=0.3, p=0.03), ESR (r=0.3, p=0.02). Positive relationships were confirmed between AH and age (r=0.39, p<0.01), menopause duration (r=0.39, p<0.01), WC (r=0.37, p<0.01), leptin (r=0.35, p=0.01), the presence of hypertriglyceridemia (r=0.35, p=0.01) and cardiovascular risks according to SCORE (r=0.26, p=0.02), considering traditional risk factors for cardiovascular diseases (CVD).

Conclusion: Thus, we found that AH in patients with knee OA is affected by a variety of variables, both related to traditional CVD factors and to OA itself, and the correlations found are approximately equal in strength. The results obtained require further study, and it is possible that preventive measures aimed at reducing the traditional risk factors of diseases of the circulatory system, or correcting existing CVD, will contribute to a more favorable course of OA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3859

POS0131 10-YEAR PROBABILITY OF A MAJOR OSTEOPOROTIC FRACTURES IN WOMEN WITH OSTEOARTHRITIS OF THE KNEE JOINT

E. Usova[1], O. Malyshenko[1], M. Letaeva[1], J. Averkieva[1], M. Koroleva[1], T. Raskina[1]. [1]*State Educational Institution of Higher Education "Kemerovo State Medical University", Kemerovo, Russian Federation, Department of Internal Diseases, Kemerovo, Russian Federation*

Background: The relationship between osteoporosis and osteoarthritis (OA) is complex and contradictory. Some studies suggest a protective effect of OA in osteoporosis [1-2]. However, other studies show that increased bone mineral density (BMD) in OA not only does not reduce the risk of fractures, but can also increase it [3-4].

Objectives: To assess the 10-year probability of osteoporotic fractures using the FRAX calculator in women with OA of the knee joint.

Methods: The study included 22 women (average age 63.7±1.01 years) diagnosed with ACP of the knee joint according to the ACR criteria (1991). The Control Group included 24 conditionally healthy women without OA knee joint, with an average age of 63.6±1.37 years.

The BMD (g/cm2) and the T-criterion (standard deviation, SD) of the neck of the femur and lumbar spine (LI-LIV) were evaluated by the method of two-power X-ray absorption (DXA) (apparatus «Lunar Prodigy Primo», USA). 10-year probability of major osteoporotic fractures (clinically significant fracture of the spine, distal fracture of the forearm, fracture of the proximal femur, or fracture of the shoulder) and fracture of the proximal thigh with the FRAX calculator (version 3.5 for Russian population).

Results: An osteopenic syndrome in the cohort under investigation was found in 42 (91.3%) patients, of whom osteopenia in 24 (52.2%) women and osteoporosis in 18 (39.1%). A normal BMD is registered in 4 (8.7%) patients.

In the group of patients with knee joint OA, only 2 (9.1%) of women had a normal BMD, 11 (50.0%) of osteoporosis, and 9 (40.9%). Osteopenic syndrome is generally found in 20 (90,9%) patients.

In the control group, osteopenic syndrome has been diagnosed in 22 (91,7%) of whom: osteopenia in 13 (54.2%), osteoporosis in 9 (37.5%) patients. Two (8.3%) women had a normal BMD. There were no statistically significant differences in the structure of the osteopenic syndrome among the studied groups (p=0.961).

An analysis of the 10-year probability of major osteoporotic fractures found that women with OA knee joint had the above probability of 12.3±0.91, and in the control group 14.2±1.06 (p=0.085).

The 10-year probability of fracture of the proximal femur in women with OA was statistically less significant than in the control group: 1.55 (0.70;1.98) and 2.10 (1.20;2.95), (p=0.031), respectively.

Conclusion: The total incidence of the osteopenic syndrome in the cohort under investigation was 91.3% (90.9% in women with OA, 91.7% in the control group). The frequency of registration of osteopenia and osteoporosis in women with OA did not differ statistically significantly from the control group. The probability of major osteoporotic fractures within 10 years was comparable in these groups. The probability of a proximal femur fracture in women with OA was statistically significant, but not clinically significant, compared to the control group.

REFERENCES:

[1] Yamamoto Y, Turkiewicz A, Wingstrand H, et al. Fragility Fractures in Patients with Rheumatoid Arthritis and Osteoarthritis Compared with the General Population. J Rheumatol. 2015 Nov;42(11):2055-8.

[2] Vala CH, Kärrholm J, Kanis JA, et al. Risk for hip fracture before and after total knee replacement in Sweden. Osteoporos Int. 2020 May;31(5):887-895.

[3] Kim BY, Kim HA, Jung JY, et al. Clinical Impact of the Fracture Risk Assessment Tool on the Treatment Decision for Osteoporosis in Patients with Knee Osteoarthritis: A Multicenter Comparative Study of the Fracture Risk Assessment Tool and World Health Organization Criteria. J Clin Med. 2019 Jun 26;8(7):918.

[4] Soh SE, Barker AL, Morello RT, et al. Applying the International Classification of Functioning, Disability and Health framework to determine the predictors of falls and fractures in people with osteoarthritis or at high risk of developing osteoarthritis: data from the Osteoarthritis Initiative. BMC Musculoskelet Disord. 2020 Feb 29;21(1):138.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3446

Crystal arthritis

POS0132 IS THE INTERCRITICAL GOUT REALLY ASYMPTOMATIC? THE INFLAMMATORY ROLE OF THE SILENT URATE CRYSTAL DEPOSITION

C. Diaz-Torne[1], M. A. Ortiz[2], S. Jeria Navarro[1], A. Garcia-Gullien[1], L. Sainz[1], H. Corominas[1], S. Vidal[2]. [1]*Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*; [2]*Institut de Recerca Hospital de la Santa Creu i Sant Pau, Immunology, Barcelona, Spain*

Background: Gout is the most prevalent inflammatory arthritis. Gout is chronic inflammatory deposition disease related to an increase of cardiovascular (CV) events and mortality. Subclinical chronic inflammation has been demonstrated in this patients but not its relation with the monosodium urate (MSU) crystal deposit size and the number of CV risk factors.

Objectives: To study the subclinical inflammation in intercritical gout patients and its possible relation to the estimated size of the crystal deposition and the number of CV risk factors.
Methods: To analyze subclinical inflammation we performed a secretome analysis and a cytokine and adiponektine plasma levels quantification (IL-1β, IL-18, IL-6, sIL-6R, TNFα, CXCL-5, RANTES, leptin, resistin and adiponectin) in a cohort of gout patients. As nowadays it is not feasible to determinate the whole body deposit of MSU crystals we created three different MSU crystal deposit size patient groups using an indirect clinical and analytical classification to estimate it. Then we compared cytokine levels between healthy donors and gout patients. We also compared cytokine levels between the different crystal size deposition groups and studied its association to the number of CV risk factors.
Results: Ninety consecutive patients attending a Crystal Arthritis Unit were studied. Mean age was 68.27 (28-101) years. 81.1% were male. Clinical gout evolution was of 10.1±9.8 years. 77.5% were on urate lowering treatment. 24% had tophaceous gout. Mean uric acid was 6.3±2.1 mg/dl with 47.1% of them being on target. Hypertension was present in 68.9%, diabetes mellitus in 18.9%, dislipemia in 48.9%, BMI>30 in 32.9%, abdominal obesity in 50% and 16.1% suffered from ischemic heart disease. From the 102 molecules studied in the secretome analysis in 56 there was at least a 20% difference between donors group and any of the deposition groups. In 74% of them gout patients secreted lower levels. IL-18, sIL-6R, RANTES, leptin and adiponectin were higher in patients than in healthy donors. IL-18, sIL6-R, RANTES and CXCL5 levels were associated to the size of the crystal deposits. IL-18, sIL-6R, RANTES and leptin were higher in gout groups with CV risk factors. IL-18, sIL6-R, RANTES and leptin were higher in gout patients with no risk factors when compared to healthy donors with no risk factors. We found no differences when comparing urate lowering treated and non-treated patients.
Conclusion: Our results demonstrate that some proinflammatory cytokines and metabolic proteins are raised in intercritical gout patients. Some of them are different from the flare/inflammasome expected ones. In some cytokines this elevation is related to the size of the monosodium urate crystal deposit and/or to the number of cardiovascular risk factors. This cytokine changes could help to explain the increase of the cardiovascular events in gout patients.
Disclosure of Interests: Cesar Diaz-Torne Grant/research support from: Received a grant from Grünenthal, Maria Angels Ortiz: None declared, Sicylle Jeria Navarro: None declared, Andrea Garcia-Gullien: None declared, Lluis Sainz: None declared, Hector Corominas: None declared, Silvia Vidal: None declared
DOI: 10.1136/annrheumdis-2021-eular.1478

POS0133 MONOSODIUM URATE CRYSTALS REDUCE HUMAN LIGAMENT CELLS VIABILITY THROUGH INCREASE OF ROS PRODUCTION

Y. Huang[1], Y. Liu[1], Q. Huang[1], W. Deng[1], T. W. Li[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*

Background: Ligament destruction is a frequent complication of gout and is strongly associated with tophi. Ligament fibroblasts are important cellular mediators of ligament remodeling. None of study has paid attention to the effects of monosodium urate (MSU) crystals on ligament fibroblasts.
Objectives: The study aims to investigate the effects and mechanism of MSU crystals on ligament fibroblasts.
Methods: MSU crystals were added to human ligament fibroblasts(HLFs) cultures or primary ligament cells cultures. Cell counting kit-8 (CCK-8) assay, cell migration assay, Annexin V-FITC/PI assay were conducted. Reactive Oxygen Species(ROS) was tested by ROS Assay Kit.
Results: The higher concentrations of MSU crystals (0.5-1mg/mL) reduced the viability of HLFs or primary ligament cells after 24 h as assessed by CCK8 assays, with a further reduction in viability observed at the 48 h time point. When observed under light microscopy, HLFs cultured with MSU crystals (0.5mg/mL) appeared unhealthy with fewer cells present. The cell migration ability of HLFs was decreased significantly on MSU crystals (0.5mg/mL). According to the result of Annexin V-FITC/PI assay, the survival rate of HLFs on MSU crystals (0.5mg/mL) was lower than that of 0.25mg/ml and 0 mg/ml at 72h. ROS assay results showed that the production of ROS increased as the concentrations of MSU crystals increased.
Conclusion: MSU crystals inhibit human ligament cells viability through the increase of ROS production. It may contribute to disordered ligament remodeling in gout patients with ligament destruction.
REFERENCES:
[1] Ashika Chhana, et al. Monosodium urate crystals reduce osteocyte viability and indirectly promote a shift in osteocyte function towards a proinflammatory and proresorptive state. Arthritis Res Ther. 2018, 20(1): 208.

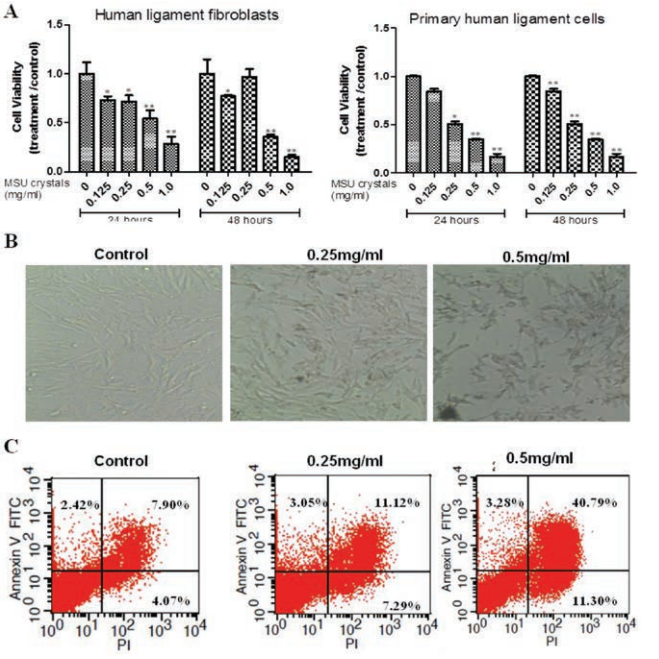


Figure 1. MSU crystals reduce human ligament fibroblasts and primary human ligament cells viability over time. A: CCK-8 assay; B: Observation of HLFs morphology; C: Annexin V-FITC/PI assay.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2316

POS0134 INCREASED PREVALENCE OF LUMBAR SPINE MONOSODIUM URATE DEPOSITION AMONG GOUT PATIENTS ON DUAL-ENERGY CT

M. Toprover[1,2], M. Mechlin[3], A. Slobodnick[1], V. C. Pike[1], C. Oh[4], C. Davis[5], T. Fields[6], F. Becce[7], M. H. Pillinger[1,2]. [1]*New York University Grossman School of Medicine, Medicine/Rheumatology, New York, United States of America*; [2]*New York Harbor Health Care System, US Department of Veterans Affairs, Medicine/Rheumatology, New York, United States of America*; [3]*New York University Grossman School of Medicine, Musculoskeletal Radiology, New York, United States of America*; [4]*NYU Grossman School of Medicine, Biostatistics, New York, United States of America*; [5]*NYU Grossman School of Medicine, Medicine/Rheumatology, New York, United States of America*; [6]*The Hospital for Special Surgery, Rheumatology, New York, United States of America*; [7]*Lausanne University Hospital, Radiology and Interventional Radiology, Lausanne, United States of America*

Background: Gout affecting the spine is reported as a rare event presenting with neuropathy, spinal compression and acute back pain (1). Cases are often diagnosed by tissue confirmation of monosodium urate (MSU) deposition. The frequency of gout involving the spine asymptomatically or with milder, non-specific symptoms is likely higher than reported.
Objectives: Using dual-energy CT (DECT), we are determining prevalence/extent of MSU deposition in the lumbosacral spines of patients with gout and tophaceous gout, compared to non-gout controls.

Methods: We are recruiting 25 controls, 25 non-tophaceous and 25 tophaceous gout patients, 45-80 years old. Exclusion criteria include CPPD disease, RA, spondyloarthropathy or spinal malignancy. All gout subjects meet ACR gout classification criteria with entry serum urate (sU) of >6.8 mg/dL, or sU >6.0 mg/dL on ULT for <6 months. Demographics, gout history, Aberdeen back pain scale, sU, ESR, and CRP are collected. DECT of the lumbosacral spine is used to assess MSU deposition and osteoarthritic changes.

Results: 63 subjects are enrolled and analyzed to date (25 control, 23 non-tophaceous and 15 tophaceous gout). Control, non-tophaceous gout, and tophaceous gout subjects have similar mean age in years (controls 61.8±3.8, non-tophaceous 64.0±6.2, tophaceous 63.5±9.2, p=0.45), but differ in BMI (controls 28.3±6.5 kg/m2, non-tophaceous 32.1±6.7 kg/m^2, tophaceous 29.1±4.3 kg/m^2, p=0.01) and creatinine (controls 1.0±0.2 mg/dL, non-tophaceous 1.4±0.6 mg/dL, tophaceous 1.7±0.9 mg/dL, p=0.048). Mean sU and ESR are higher in gout subjects (sU-controls 5.3±1 mg/dL, non-tophaceous 8.3±1.4 mg/dL, tophaceous 8.4±2.0 mg/dL, p<0.05; ESR-controls 13.7±13.8 mm/h, non-tophaceous 25.2±18.7 mm/h, tophaceous 22.5±15.1 mm/h, p<0.05). Using default threshold settings for MSU visualization, greater MSU deposition is observed in the spine of gout patients (controls 2.2±1.2 cm^3, non-tophaceous 4.5±4.3 cm^3, tophaceous 8.5±12.5 cm^3, p<0.05; Table 1). Reanalysis of several scans using narrower threshold settings to limit possible artifact confirms increased MSU signal among gout patients. Although many subjects in each group do not have excessive MSU deposition, deposition is more common in both gout groups. No subject demonstrated a frank spinal tophus.

Conclusion: Based on preliminary results, gout patients have higher inflammatory markers and greater spinal MSU deposition than controls. Preliminary analyes with more stringent DECT threshold settings suggests these differences are not artifact, but analysis is ongoing. These data suggest that MSU deposition in the spine occurs in a subset of gout patients.

REFERENCES:

[1] Toprover M, Krasnokutsky S, Pillinger MH. Gout in the Spine: Imaging, Diagnosis, and Outcomes. Curr Rheumatol Rep. 2015;17(12):70.

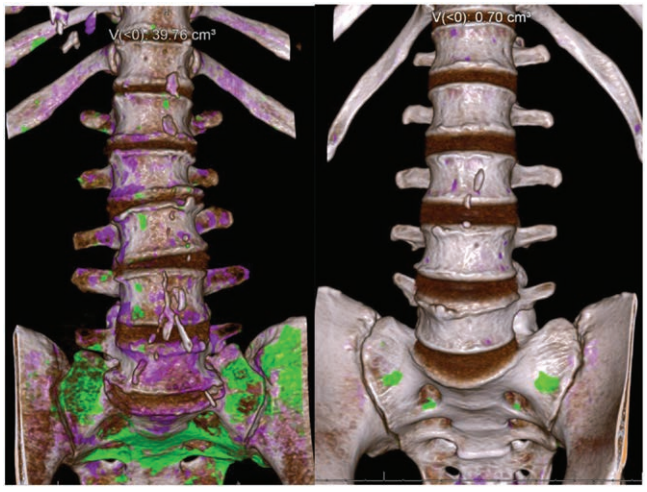


Figure 1. DECT of the spine. (A) Patient with tophaceous gout (SU 8.9mg/dL, DECT volume 39.76cm3). (B) Control patient (SU 4.5mg/dL, DECT volume 0.70cm3).

Table 1. Baseline characteristics and mean DECT deposition volumes. Bold font indicates statistical significance.

Characteristic	Control	Non-tophaceous Gout	Tophaceous Gout	P-value
Number of subjects	25	23	15	
Age in years, mean ± SD	61.8 ± 3.8	64.0 ± 6.2	63.5 ± 9.2	0.45
Male sex, n (%)	23 (92.0)	23 (100.0)	13 (86.7)	0.23
Race:				0.52
-White, n (%)	18 (72.0)	14 (60.9)	7 (46.7)	
-Black, n (%)	6(24.0)	6 (26.1)	6 (40.0)	
-Hispanic, n (%)	1 (4.0)	3 (13.0)	2 (13.3)	
BMI, mean ± SD	28.3 ± 6.5	32.1 ± 6.7	29.1 ± 4.3	0.01
Chronic kidney disease, n (%)	0 (0.0)	6 (26.1)	3 (20.0)	0.03
Diabetes mellitus type II, n (%)	3 (12.0)	5 (21.7)	2 (13.3)	0.62
Hyperlipidemia, n (%)	14 (56.0)	15 (65.2)	7 (46.7)	0.52
History of myocardial infarction, n (%)	1 (4.0)	2 (8.7)	1 (6.7)	0.80
Mean sU, mg/dL ± SD	5.31 ± 0.98	8.25 ± 1.4	8.42 ± 2.0	<0.001
Mean ESR, mm/hr ± SD (normal 0-10)	13.7 ± 13.8	25.2 ± 18.7	22.53 ± 15.1	0.04
Mean CRP, mg/L ± SD (normal 0-5)	2.7 ± 4.7	7.6 ± 12.5	4.1 ± 5.0	0.13
Mean serum creatinine, mg/dL ± SD	0.97 ± 0.18	1.36 ± 0.58	1.70 ± 0.88	0.048
Mean DECT volume, cm^3	2.2 ± 1.2	4.5 ± 4.3	8.5 ± 12.5	p<0.05

Acknowledgements: Supported by an investigator-initiated grant from Horizon Therapeutics

Disclosure of Interests: Michael Toprover Consultant of: Horizon Pharmaceuticals, Michael Mechlin: None declared, Anastasia Slobodnick: None declared, Virginia C. Pike: None declared, Cheongeun Oh: None declared, Claudine Davis: None declared, Theodore Fields Consultant of: Horizon Pharmaceuticals, Avion Pharmaceuticals, Fabio Becce Consultant of: Horizon Therapeutics, Michael H. Pillinger Consultant of: Horizon Pharmaceuticals, Grant/research support from: Horizon Pharmaceuticals

DOI: 10.1136/annrheumdis-2021-eular.2733

POS0135

REDUCING IMMUNOGENICITY OF PEGLOTICASE (RECIPE) WITH CONCOMITANT USE OF MYCOPHENOLATE MOFETIL IN PATIENTS WITH REFRACTORY GOUT: A PHASE II RANDOMIZED CONTROLLED TRIAL

P. Khanna[1], D. Khanna[1], G. Cutter[2], J. Foster[3], J. Melnick[3], S. Jaafar[1], S. Biggers[3], F. Rahman[2], H. C. Kuo[2], M. Feese[2], K. Saag[3]. *[1]University of Michigan, Medicine, Ann Arbor, United States of America*; *[2]University of Alabama at Birmingham, Biostatistics, Birmingham, United States of America*; *[3]University of Alabama at Birmingham, Medicine, Birmingham, United States of America*

Background: Pegloticase is a recombinant, pegylated uricase, used for treatment of gout patients who fail oral urate lowering therapy (ULT). Its use has been limited due to immunogenicity leading to infusion reactions.[1]

Objectives: We evaluated if co-administration of an immunomodulatory agent could prolong the efficacy of pegloticase.

Methods: Participants were recruited in a Phase II, double-blind, placebo-controlled trial over 18 months and randomized in a 3:1 ratio by site. Inclusion criteria were: a) Age ≥ 18 years who met 2015 ACR/EULAR gout classification criteria and b) chronic refractory gout defined as symptoms inadequately controlled with ULT or contraindications. After a 2-week run-in of mycophenolate mofetil (MMF) 1000 mg twice daily or matching placebo (PBO), they received a combination of pegloticase

8 mg biweekly with MMF or PBO for 12 weeks. Subsequent to this MMF or PBO were discontinued but pegloticase was continued for another 12 weeks. The primary endpoint was proportion of patients who sustained a serum urate (SU) level of ≤ 6 mg/dl at 12 weeks. Secondary endpoints included 24-week durability of SU ≤ 6 mg/dl and rate of adverse events (AEs). Fisher's exact test and Wilcoxon two-sample test were used for analyses along with Kaplan-Meier estimates and log-rank tests to compare survival curves between groups. Hypothesis tests were two-tailed and p-value (p) < 0.05 indicated statistical significance.

Results: Of 42 subjects screened, 35 were randomized, and 32 who received at least one dose of pegloticase were included in modified intention to treat analyses. Subjects were predominantly men (88%), mean age of 55.2 years (SD=9.7). Mean duration of gout was 13.4 years (SD=9.0), mean baseline sUA was 9.2 mg/dL (SD=1.6). Tophi were present in 88% and majority were on optimized ULT - 59% on allopurinol and 16% on febuxostat, with 63% reporting > 1 flare in the past year. At baseline both arms (MMF vs. PBO) had similar comorbidities – (82% vs 70%), diabetes mellitus/metabolic syndrome (14% vs 20%), coronary artery disease/peripheral vascular disease (41% vs.70%), BMI>30 (86% vs. 90%) and renal insufficiency (defined as eGFR < 90 mL/min; 73% vs. 70%). At 12 weeks, 19 of 22 (86%) in the MMF arm achieved SU ≤ 6 mg/dl compared to 4 of 10 (40%) in PBO arm (p-value = 0.01). At 24 weeks, the SU was ≤ 6 mg/dl in 68% of MMF arm vs. 30% in PBO (p-value = 0.06), and rates of AEs per month were similar between groups with the PBO arm having more infusion reactions (30% vs. 0%). The MMF arm had higher AEs compared to placebo: musculoskeletal (41% vs. 10%), gastrointestinal (18% vs. 10%), and infections (9% vs. 0%). Figure 1 shows that the percentage of subjects maintaining a sUA < 6 mg/dL at 12 weeks was significantly higher (p=0.02) in the MMF arm, and a significant difference (p=0.03) at 24 weeks indicates sustained benefit from MMF.

Conclusion: To our knowledge this is the first randomized-controlled proof of concept trial to demonstrate the ability of an immunomodulatory agent in prolonging the efficacy of pegloticase. Short-term concomitant use of MMF therapy with pegloticase was well tolerated and showed a clinically meaningful improvement in the targeted SU ≤6 mg/dL at 12 and 24 weeks. This study suggests an innovative approach to utilize pegloticase therapy in patients with chronic gout.

REFERENCES:

[1] Sundy et al. Efficacy and tolerability of pegloticase for the treatment of chronic gout in patients refractory to conventional treatment: two randomized controlled trials. JAMA. 2011;306(7):711-20.

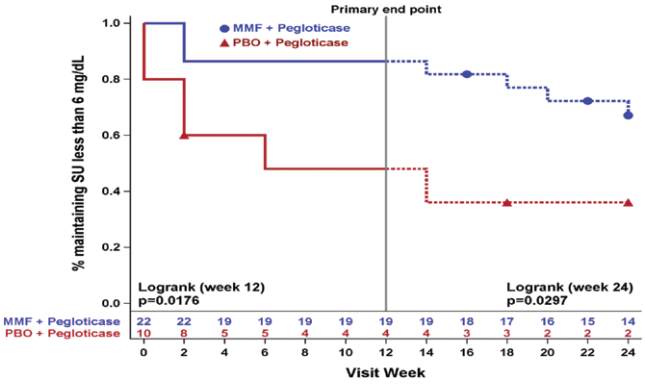


Figure 1. Proportion of subjects maintaining serum urate (SU) ≤ 6 mg/dL over 24 week studyperiod in mycophenolate mofetil + pegloticase vs. placebo + pegloticase

Disclosure of Interests: Puja Khanna Consultant of: Horizon Pharmaceuticals, Swedish Orphan Biovitrum A, Grant/research support from: Selecta, 2)DYVE, Dinesh Khanna Consultant of: Horizon Pharmaceuticals, Gary Cutter: None declared, Jeff Foster: None declared, Josh Melnick: None declared, Sara Jaafar: None declared, Stephanie Biggers: None declared, Fazlur Rahman: None declared, Hui-Chen Kuo: None declared, Michelle Feese: None declared, Kenneth Saag Consultant of: AbbVie, Inc., Bayer, Daiichi Sankyo Company LTD, Gilead Services, Inc., Horizon Pharma plc, Mallinkrodt, Radius Health, Inc., Roche/Genentech, Shanton Pharma Co., LTD, Teijin, Dyve Bioscience, LG Chem, Regeneron Pharmaceuticals., Swedish Orphan Biovitrum AB, Takeda Pharmaceuticals America, Inc.,

DOI: 10.1136/annrheumdis-2021-eular.3111

POS0136 ROLES OF AUTOPHAGY IN THE PATHOGENESIS OF PRIMARY GOUTY ARTHRITIS

Y. Q. Huang[1], Q. B. Zhang2, J. X. Zheng[3], G. L. Jian2, T. H. Liu2, X. He2, F. N. Xiao2, Q. Xiong2, Y. F. Qing[4]. *[1]The Affiliated Hospital of North Sichuan Medical College, Geriatrics, Nanchong, Sichuan, China*; *[1]The Affiliated Hospital of North Sichuan Medical College, Geriatrics, Nanchong, Sichuan, China*; *[3]The Affiliated Hospital of North Sichuan Medical College, Institute of Rheumatology and Immunology, Nanchong, Sichuan, China*; *[4]The Affiliated Hospital of North Sichuan Medical College, Rheumatology and Immunology, Nanchong, Sichuan, China*

Background: Gout is a chronic autoinflammatory disease caused by monosodium urate (MSU) crystal deposition [1].Acute gout is characterized by an acute inflammatory reaction that resolves spontaneously within a few days[2], which is one of the distinguishing features of gout compared to other arthropathies or self-inflammatory diseases. Autophagy is a lysosomal degradation pathway that is essential for cellular growth, survival, differentiation, development and homeostasis [3]. Studies have demonstrated that autophagy might play a key role in the pathogenesis of primary gouty arthritis (GA) [4-7]. However, the roles of autophagy in the development of gout have not yet been elucidated.

Objectives: The aim of our study was to investigate the changes in autophagy-related gene (ATG) mRNA and protein in patients and the clinical importance of these genes in primary gouty arthritis (GA) and to explore the roles of autophagy in the pathogenesis of GA.

Methods: The mRNA and protein expression levels of ATGs (ATG3, ATG7, ATG10, ATG5, ATG12, ATG16L1, ATG4B and LC3-2) were measured in peripheral blood mononuclear cells (PBMCs) from 196 subjects, including 57 acute gout patients (AG group), 57 intercritical gout patients (IG group) and 82 healthy control subjects (HC group). The relationship between ATG expression levels and laboratory features was analyzed in GA patients.

Results: The expression levels of ATG4B, ATG5, ATG12, ATG16L1, ATG10 and LC3-2 mRNA were much lower in the AG group than in the IG and HC groups ($p<0.05$), while the ATG7 mRNA level was much higher in the AG group than in the IG and HC groups ($p<0.05$). The protein expression levels of LC3-2, ATG3, ATG7 and ATG10 were much higher in the AG group than in the other groups, while those of ATG5, ATG12, ATG16L1 and ATG4B were far lower in the AG group than in the other groups ($p<0.05$). In GA patients, the levels of ATG mRNA and protein correlated with laboratory inflammatory and metabolic indexes.

Conclusion: Altered ATG expression suggests that autophagy is involved in the pathogenesis of GA and participates in regulating inflammation and metabolism.

REFERENCES:

[1] Dalbeth N, Choi HK, Joosten LAB, Khanna PP, Matsuo H, Perez-Ruiz F, et al. Gout. Nat Rev Dis Primers. 2019;5: 69.doi:10.1038/s41572-019-0115-y.

[2] Schauer C, Janko C, Munoz LE, Zhao Y, Kienhöfer D, Frey B, et al. Aggregated neutrophil extracellular traps limit inflammation by degrading cytokines and chemokines. Nat Med. 2014;20: 511-517.doi:10.1038/nm.3547.

[3] Han Y, Zhang L, Xing Y, Zhang L, Chen X, Tang P, et al. Autophagy relieves the function inhibition and apoptosis-promoting effects on osteoblast induced by glucocorticoid. Int J Mol Med. 2018;41: 800-808. doi:10.3892/ijmm.2017.3270.

[4] Yang QB, He YL, Zhong XW, Xie WG, Zhou JG. Resveratrol ameliorates gouty inflammation via upregulation of sirtuin 1 to promote autophagy in gout patients. Inflammopharmacology. 2019;27: 47-56.doi:10.1007/s10787-018-00555-4.

[5] Mitroulis I, Kambas K, Chrysanthopoulou A, Skendros P, Apostolidou E, Kourtzelis I, et al. Neutrophil extracellular trap formation is associated with IL-1β and autophagy-related signaling in gout. PLoS One. 2011;6: e29318. doi: 10.1371/journal.pone.0029318.

[6] Crişan TO, Cleophas MCP, Novakovic B, Erler K, van de Veerdonk FL, Stunnenberg HG, et al. Uric acid priming in human monocytes is driven by the AKT-PRAS40 autophagy pathway. Proc Natl Acad Sci U S A. 2017;114: 5485-5490.doi:10.1073/pnas.1620910114.

[7] Lee SS, Lee SW, Oh DH, Kim HS, Chae SC, Kim SK. Genetic analysis for rs2241880(T > C) in ATG16L1 polymorphism for the susceptibility of Gout. J Clin Rheumatol. 2019;25: e113-e115.doi:10.1097/rhu.0000000000000685.

Disclosure of Interests: Yu-Qin Huang: None declared, Quan-Bo Zhang Grant/research support from: National Natural Science Foundation of China(General Program) (no.81974250) and Science and Technology Plan Project of Sichuan Province (no.2018JY0257), Jian-Xiong Zheng: None declared, gui-lin jian: None declared, tao-hong liu: None declared, Xin He: None declared, fan-ni xiao: None declared, qin xiong: None declared, Yu-Feng Qing Grant/research support from: Science and Technology Project of Nanchong City (no.18SXHZ0522)

DOI: 10.1136/annrheumdis-2021-eular.3592

POS0137 CARDIOVASCULAR RISK ASSOCIATED WITH TREATMENT OF ALLOPURINOL AND BENZBROMARONE IN PATIENTS WITH GOUT

Y. Eun[1], S. Y. Kang[1], S. Lee[1], H. Kim[2], J. Lee[1], E. M. Koh[1], H. S. Cha[1]. *[1]Samsung Medical Center, Sungkyunkwan University School of Medicine,*

Department of Medicine, Seoul, Korea, Republic of (South Korea); [2]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medical Humanities, Seoul, Korea, Republic of (South Korea)*

Background: Previous studies have shown that cardiovascular risk is increased in patients with gout. There are many studies on the effect of uric acid lowering therapy on CV risk in gout patients, but few studies have compared allopurinol and benzbromarone.
Objectives: A nationwide population-based cohort study is designed to compare cardiovascular risk according to the treatment of allopurinol and benzbromarone in Korean gout patients.
Methods: We used South Korea's database of the Health Insurance Review and Assessment service (HIRA) to identify gout patients 18 years of age or older who newly started allopurinol or benzbromarone between 2009 and 2015. The start date of allopurinol or benzbromarone is defined as the index date. We excluded patients who have been prescribed uric acid lowering agents or have been on dialysis for one year prior to the index date. During the study period, patients who used uric acid lowering agents other than allopurinol and benzbromarone or who used both drugs in combination were also excluded from the study. The primary outcome of the study was the occurrence of a composite cardiovascular endpoint, which included coronary revascularization, hospitalization due to MI, ischemic stroke, and transient ischemic attack (TIA). Cox proportional hazard regression analysis and Kaplan-Meier curves were used for the analysis.
Results: 257,097 allopurinol initiators and 7,868 benzbromarone initiators were included in the study. The mean age was 54.4 years, 86% were male. The mean adherence of drug administration was 68.2% for allopurinol initiators and 75.5% for benzbromarone initiators. In baseline, the benzbromarone initiator had more cardiovascular comorbidities and related drug administration than the allopurinol initiator. In allopurinol and benzbromarone initiators, the adjusted hazard ratio (aHR) of the composite CV endpoint was 1.01 (95% CI 0.83-1.21), which was not significantly different. No significant difference was found between the two groups in each of the items of the composite CV endpoint and hospitalization for heart failure. The results did not change even when 1:3 propensity score matching was performed for baseline characteristics. In subgroup analysis of high risk patients with cardiovascular disease, there was no significant difference between allopurinol and benzbromarone initiators. However, when the analysis was limited to the group taking allopurinol ≥200mg and benzbromarone ≥50mg, there was no difference in primary outcome and other outcomes, but the risk of coronary revascularization was higher in benzbromarone initiator (aHR 1.58, 95% CI 1.16-2.14).
Conclusion: In our study, there was no significant difference in cardiovascular risk between allopurinol initiator and benzbromarone initiator. In the high risk group of cardiovascular disease, there was no difference in risk between the two drugs.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3952

POS0138 ALTERED RISK OF GOUT ACCORDING TO CHANGE OF METABOLIC PARAMETERS IN YOUNG ADULTS

Y. Eun[1], I. Y. Kim[2], K. D. Han[3], S. Y. Kang[1], S. Lee[1], H. S. Cha[1], E. M. Koh[1], H. Kim[4], J. Lee[1]. [1]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medicine, Seoul, Korea, Rep. of (South Korea)*; [2]*National Police Hospital, Department of Medicine, Seoul, Korea, Rep. of (South Korea)*; [3]*Soongsil University, Department of Statistics and Actuarial Science, Seoul, Korea, Rep. of (South Korea)*; [4]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medical Humanities, Seoul, Korea, Rep. of (South Korea)*

Background: Many studies have shown a link between gout and metabolic syndrome (MetS). It is well known that lifestyle modifications such as weight reduction and abstinence from alcohol are effective in the treatment of gout, but data are lacking on how exactly the change of metabolic parameters affects gout.
Objectives: The purpose of this study was to investigate the relationship between gout risk and metabolic parameters in a nationwide population based young adult cohort, and to determine whether changes in metabolic parameters affect gout risk changes.
Methods: Among adults aged 20-39 years who participated in national health check-up programs from 2009 to 2012, a total of 6,290,914 subjects were included in the study, excluding subjects who were previously diagnosed with gout. To determine the effect of changes in metabolic parameters on gout incidence, 2,701,138 subjects who participated in the health examination once more 2 years later were used for the analysis. Outcome was defined as the occurrence of gout, when the ICD-10 code (M10) was registered twice in the claim database. The Cox proportional hazard model and Kaplan Meier curve were used for the analysis.
Results: The incidence rate of gout was higher in those with MetS compared to those without (10.1 vs. 3.6 per 1,000 person-years). The risk of gout in people with MetS was 85% higher (adjusted HR 1.85, 95% CI 1.83-1.87) and was more significant in men than in women (adjusted HR 1.88 in male and 1.56 in female). Each component of MetS was also associated with increased gout risk, and hypertriglyceridemia showed the highest adjusted HR. The greater the number of MetS components, the higher the gout risk. The risk of gout was 70% higher in those who had MetS consistently (adjusted HR 1.71, 95% CI 1.67-1.75) and 44% higher in those with newly developed MetS (adjusted HR 1.47, 95% CI 1.40-1.48) than those who did not have MetS at the two health examinations. Similar risk patterns were observed according to the change of each metabolic parameter. Among the metabolic parameters, the change in hypertriglyceridemia was associated with the greatest difference in the change in gout risk.
Conclusion: In young adults, MetS was associated with a higher risk of gout, especially with more components, the higher the risk. Since the occurrence of MetS is associated with an increased risk of gout, prevention of MetS would be important to reduce gout incidence.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4032

POS0139 TWO-YEAR REDUCTION OF URATE LOAD IN DUAL-ENERGY CT DURING A TREAT-TO-TARGET APPROACH IN GOUT PATIENTS: RESULTS FROM A LONGITUDINAL STUDY (NOR-GOUT)

T. Uhlig[1], T. Eskild[2], L. F. Karoliussen[1], T. K. Kvien[1], E. A. Haavardsholm[1], N. Dalbeth[3], H. B. Hammer[1]. [1]*Diakonhjemmet Hospital, Rheumatology, Oslo, Norway*; [2]*Diakonhjemmet Hospital, Clinical Service Radiology, Oslo, Norway*; [3]*University of Auckland, Medicine, Auckland, New Zealand*

Background: Dual-energy computed tomography (DECT) detects urate depositions, and is included in the ACR/EULAR classification criteria for gout. There is lack of longitudinal studies in large patient populations for changes in urate deposition measured by DECT during urate lowering therapy (ULT).
Objectives: To explore by DECT the longitudinal changes urate depositions during a treat-to-target approach in gout with ULT.
Methods: In a prospective observational study, patients with crystal-proven gout were included if they presented after a recent gout flare and with increased serum urate levels (>360 µmol/L/>6 mg/dl). In a treat-to-target approach they received ULT with escalating drug doses with monthly follow-up during the first year until the treatment target was met with serum urate <360 µmol/L or 360 µmol/L if tophi.
A DECT scanner (General Electric Discovery CT750 HD) acquired data from bilateral forefeet and ankles at 80 KW and 140 KV, processed with a software with a 2-material decomposition algorithm which colour codes urate. Follow-up DECT was performed after one and two years.
Images were scored with a semiquantitative method (Bayat et al. 2015) by one experienced radiologist in known order and blinded to serum urate and clinical data. Each scan assessed four regions: the first metatarsophalangeal (MTP1) joint, the other joints of the toes, the ankles and midfeet, and all visible tendons in the feet and ankles. Each region was then scored according to the maximum amount of urate deposition observed on visual inspection (0=no deposits, 1=dots, 2=single deposit, 3=more than one deposit). A total DECT sum score was derived by adding all values from the four regions, with a maximum score of 12.
Results: DECT was at baseline measured in 187 of 211 patients. 95.2% were males, mean (SD) age was 56.7 (13.7) years, disease duration 8.1 (7.9) years), and 17% had clinical tophi.
The total DECT scores and all subscores decreased from baseline to 2 years ($p<0.001$ for all comparisons versus baseline), table 1.
The mean (SD) serum urate level (µmol/L) decreased from 501 (80) at baseline to 311 (48) at 12 months and 322 (67) at 24 months. Reaching the treatment target <360 µmol/L after year 1 or 2 was only numerically but not statistically related to reductions in DECT scores. Patients with clinical tophi at baseline had larger reductions in total DECT scores after 1 (3.4 vs. 1.5, $p<0.01$) and 2 years (6.5 vs. 2.3, $p<0.001$) than patients without tophi.
Conclusion: During a treat-to-target approach urate deposition visualised by DECT were clearly reduced in ankles and feet after 1 year with further reduction after 2 years.

Table 1.

	Baseline (n=187) Mean (SD)	1 year (n=157) Mean (SD)	2 years (n=166) Mean (SD)
MTP1 (0-3)	1.4 (2.0)	1.0 (1.7)	0.6 (1.3)
Toes (0-3)	1.0 (1.8)	0.6 (1.4)	0.3 (1.0)
Ankle/Midfoot (0-3)	1.2 (2.1)	0.7 (1.6	0.3 (1.0)
Tendons (0-3)	1.0 (1.7)	0.5 (1.2)	0.3 (0.8)
Sum score (0-12)	4.6 (6.4)	2.8 (4.7)	1.5 (3.2)

Disclosure of Interests: Till Uhlig Speakers bureau: Grünenthal, Novartis, Consultant of: Grünenthal, Novartis, Tron Eskild: None declared, Lars Fridtjof Karoliussen: None declared, Tore K. Kvien Consultant of: AbbVie, MSD, UCB, Hospira/Pfizer, Eli-Lilly, Roche, Hikma, Orion, Sanofi, Celltrion, Sandoz, Biogen, Amgen, Egis, Ewopharma, Mylan, Grant/research support from: BMS, AbbVie, MSD, UCB, Hospira/Pfizer, Eli-Lilly, Espen A Haavardsholm Consultant of: Pfizer, UCB, Eli Lilly, Celgene, Janssen-Cilag, AbbVie and Gilead, Nicola Dalbeth Speakers bureau: Menarini, AstraZeneca, Takeda, S. Nicolaou, Consultant of: AstraZeneca, Fonterra, Takeda, Pfizer, Cymabay, Crealta, Grant/research support from: AstraZeneca, Siemens Healthcare, Hilde Berner Hammer Consultant of: AbbVie, Lilly and Novartis
DOI: 10.1136/annrheumdis-2021-eular.751

POS0140 **URATE-LOWERING THERAPY REDUCES NON-EPISODIC FOOT PAIN IN PATIENTS WHO FAIL TO MEET ACR/EULAR 2015 GOUT CLASSIFICATION CRITERIA: AN EFFECT PREDICTED BY ULTRASOUND**

R. Flood[1], C. Kirby[2], Y. Alammari[2], D. Kane[2], R. Mullan[2]. [1]*Tallaght University Hospital, Rheumatology, Dublin, Ireland*; [1]*Tallaght University Hospital, Rheumatology, Dublin, Ireland*

Background: Emerging evidence that the joints of asymptomatic hyperuricaemic individuals contain monosodium urate (MSU) deposits and that alternative presentations of foot pain occur in hyperuricaemia suggests that preclinical phases may occur prior to a first episodic gout attack. (1) This case–control study evaluates urate deposition in hyperuricaemic individuals not fulfilling the current gout classification criteria, as well as a potential therapeutic role for urate lowering therapy (ULT).
Objectives: To investigate whether ULT reduces non-episodic foot pain in patients who fail to meet ACR/EULAR 2015 gout classification criteria.
Methods: Following informed consent, hyperuricaemic individuals with persistent, non-episodic foot pain (n=53) not fulfilling ACR/EULAR 2015 gout classification criteria, were compared with asymptomatic hyperuricaemic controls (n=18). Ultrasound (US) of bilateral first metatarsophalangeal (MTP) joints and features of MSU deposition including double contour (DC) sign, tophus and juxta-articular erosion were recorded. Cases only were treated with febuxostat or allopurinol daily for 6 months. Serum urate, 24-hour and 7-day visual analogue score (VAS) 0–100 mm pain scales and the Manchester Foot Pain and Disability Index (MFPDI) were recorded before treatment and after 3 and 6 months. MTP Ultrasound was repeated after a minimum of 6 months on treatment.
Results: 53 hyperuricaemic individuals with persistent, non-episodic foot pain not meeting the ACR/EULAR 2015 gout classification criteria were recruited. At baseline MTP US DC sign, erosion and tophus occurred in 62.5%, 20.8% and 49% of cases, respectively. No US features of gout occurred in controls. No significant difference was seen in baseline serum urate between cases (481±14 mg/dL) versus controls (437±14; p=NS). Serum urate in cases fell at 3 months (325±25; p<0.01) and 6 months (248±19; p<0.01). For cases, baseline 24-hour pain VAS (46±3.9) reduced at 3 months (32±4.1; p<0.05) and 6 months (21±5.2; p<0.05) of ULT. The 7-day pain VAS (59±3.9) decreased at 3 months (35±4.5; p<0.05) and 6 months (30±5.3; P<0.05). MFPDI (17±1.4) decreased at 3 month (13±1.8; p=<0.05) and 6 months (11±2.2; p=<0.05). When cases were grouped according to the presence (N=33) or absence (N=18) of DC sign on baseline US, no differences were observed for baseline pain scores. Following ULT however, 24-hour pain VAS were significantly lower in DC positive patients at 3 months (22±4.48 DC positive vs 42±6.14 DC negative; p<0.05) and 6 months (12.±5.4 vs 33±8.4; p<0.05). The 7-day pain VAS were significantly lower in DC positive patients at 3 months (23±4.6 vs 47±6.6; p<0.05) and MFDPI were significantly lower in DC positive patients at 3 months (10±1.9 DC positive vs 19±2.9 DC negative; p<0.05).
Conclusion: These findings indicate that persistent, non-episodic foot pain in hyperuricaemia is both associated with US features of MSU deposition and is responsive to ULT. Symptomatic hyperuricaemia occurring prior to episodic gout therefore represents an earlier or alternative disease presentation. Changes to the ACR/ EULAR classification criteria to include non-episodic foot pain in the presence of US features of gout may increase the sensitivity of disease classification at an early stage, leading to improved future treatment strategies and long-term outcomes.
REFERENCES:
[1] Stewart S, Dalbeth N, Vandal AC, Rome K. Characteristics of the first metatarsophalangeal joint in gout and asymptomatic hyperuricaemia: A cross-sectional observational study. J Foot Ankle Res. 2015;8(1):1–8.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1571

POS0141 **ACTIVE SCREENING FOR GOUT IDENTIFIES A LARGER CARDIOVASCULAR POPULATION AT HIGH MORTALITY RISK**

S. Ruiz-Simón[1], I. Calabuig[2], M. Gomez-Garberi[3], M. Andrés[1,2]. [1]*Miguel Hernandez University, Clinical Medicine, San Juan de Alicante, Spain*; [2]*Alicante General University Hospital-ISABIAL, Rheumatology, Alicante, Spain*; [3]*San Juan de Alicante University Hospital, Urology, San Juan de Alicante, Spain*

Background: We have recently revealed by active screening that about a third of gout cases in the cardiovascular population is not registered in records [1], highlighting the value of field studies.
Objectives: To assess whether gout screening in patients hospitalized for cardiovascular events may also help identify patients at higher risk of mortality after discharge.
Methods: A retrospective cohort field study, carried out in 266 patients admitted for cardiovascular events in the Cardiology, Neurology and Vascular Surgery units of a tertiary centre in Spain. The presence of gout was established by records review and face-to-face interview, according to the 2015 ACR/EULAR criteria. The occurrence of mortality during follow-up and its causes were obtained from electronic medical records. The association between gout and subsequent mortality was tested using Cox regression models. Whether covariates affect the gout-associated mortality was also studied.
Results: Of 266 patients recruited at baseline, 17 were excluded due to loss to follow-up (>6mo), leaving a final sample of 249 patients (93.6%). Thirty-six cases (14.5% of the sample) were classified as having gout: twenty-three (63.9%) had a previously registered diagnosis, while 13 (36.1%) had not and was established by the interview.
After discharge, the mean follow-up was 19.9 months (SD ±8.6), with a mortality incidence of 21.6 deaths per 100 patient-years, 34.2% by cardiovascular causes. Gout significantly increased the risk of subsequent all-cause mortality, with a hazard ratio (HR) of 2.01 (95%CI 1.13 to 3.58). When the analysis was restricted to gout patients with registered diagnosis, the association remained significant (HR 2.89; 95%CI 1.54 to 5.41).
The adjusted HR for all-cause mortality associated with gout was 1.86 (95% CI 1.01-3.40). Regarding the causes of death, both cardiovascular and non-cardiovascular were numerically increased.
Secondary variables rising the mortality risk in those with gout were age (HR 1.07; 1.01 to 1.13) and coexistent renal disease (HR 4.70; 1.31 to 16.84), while gender, gout characteristics and traditional risk factors showed no impact.
Conclusion: Gout was confirmed an independent predictor of subsequent all-cause mortality in patients admitted for cardiovascular events. Active screening for gout allowed identifying a larger population at high mortality risk, which may help tailor optimal management to minimize the cardiovascular impact.
REFERENCES:
[1] Calabuig I, et al. Front Med (Lausanne). 2020 Sep 29;7:560.
Disclosure of Interests: Silvia Ruiz-Simón: None declared, Irene Calabuig: None declared, Miguel Gomez-Garberi: None declared, Mariano Andrés Speakers bureau: Grunenthal, Menarini, Consultant of: Grunenthal, Grant/research support from: Grunenthal
DOI: 10.1136/annrheumdis-2021-eular.1872

Fine-tuning strategies (beyond treatments) to reduce the impact of PsA

POS0142 **MINIMAL DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS AND ASSOCIATED FACTORS: REAL LIFE DATA FROM A SINGLE CENTER**

M. Bektaş[1], B. Çelik[2], B. Ince[1], Y. Yalçınkaya[1], B. Artim-Esen[1], A. Gül[1], M. L. Ocal[1], M. Inanc[1]. [1]*Istanbul Faculty of Medicine, Internal Medicine, Rheumatology Division, Istanbul, Turkey*; [2]*Istanbul Faculty of Medicine, Istanbul Faculty of Medicine, Istanbul, Turkey*

Background: Psoriatic arthritis (PsA) is a heterogeneous disease and GRAPPA have proposed Minimal disease activity (MDA) as a composite outcome measure and has been validated in PsA.
Objectives: In this study, we aimed to evaluate the characteristics, MDA frequencies, first biological disease modifying antirheumatic drugs (b-DMARD) continuation rate and associated factors in our PsA cohort.
Methods: PsA patients who fulfilled the CASPAR classification criteria and had at least six months of follow-up data were evaluated cross-sectionally for MDA.Clinical data were collected from patient charts with standard forms.b-DMARD treatment was initiated in patients who did not respond to at least one conventional synthetic (cs)

DMARD for at least three months. Only anti-TNFs were used as a first line b-DMARD therefore secukinumab (Secu) was used after first line b-DMARD treatment. Adalimumab, certolizumab, etanercept, golimumab were grouped as subcutaneous (s.c) anti-TNFs. MDA was defined as meeting five out of seven criteria during follow-up [1].
Results: One hundred seventy-two patients (61% female) were included into the analysis. The mean follow-up time was 105.4±76 (6-444) months and the mean age was 50.2±13.3 (16-81) years. Mean age of onset for PsA was 38±11.9 (11-79) years; mean PsA and PsO duration were 140±90.7 (7.9-528) and 253±138 (0-756) months, respectively. Methotrexate was the most commonly used (88 %) cs-DMARD and biological DMARDs were used in 74 patients (43.3%)
Overall, 95 patients (55.2 %) were observed at MDA which was significantly lower in b-DMARD users compared to only cs-DMARD users (45.9 % vs 61.9 %; p=0.038, OR: 4.3). MDA did not differ according to PsA subtypes. The addition of cs-DMARD treatment to b-DMARDs did not affect MDA frequency In univariate analysis; higher MDA frequency was associated with older age (p=0.002), longer PsO duration (p=0.036), late onset of PsA (p=0.007) and continuation of first b-DMARD (OR:13.9 p<0.001). In multivariate analysis, older age (OR:1.3;95 % CI:1.02-1.68), late onset PsA (OR:1.03; 95 % CI:1.01-1.067) and continuation of first b-DMARD (OR:46.8; 95 % CI:1.6-1371) were associated with MDA.
Conclusion: Although frequency of MDA in our cohort was consistent with previous reports, a significant number of patients could not achieve MDA. Frequency of MDA was found to be lower in b-DMARD users compared to cs-DMARD users, possibly resulted from initiation of b-DMARD in patients with higher disease activity. Higher MDA rate was associated with higher continuation rate at first line b-DMARD treatment (TNF-inhibitor) and decreased gradually after b-DMARD switches. Although combined use of cs-DMARD with b-DMARDs did not increase the frequency of MDA, it was associated with higher b-DMARD retention. MDA is a useful outcome measure in daily follow-up of PsA patients and the importance of reaching sustained MDA for prognosis should be investigated further.
REFERENCES:
[1] Coates, L.C., J. Fransen, and P.S. Helliwell, Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis, 2010. **69**(1): p. 48-53.

Table 1. b-DMARD responses, continuation rate and frequency of achieving MDA in patients with PsA

b-DMARD treatment	Mean (median) duration (month)	Continuation rate n, (%)	Primary inefficacy n, (%)	Secondary inefficacy n, (%)	MDA n, (%)
First line b-DMARD (n=74)	50.4 (36)	37 (50)	9 (24.3)	17 (46)	34 (45.9)
*s.c TNF inhibitors (n=62; 83.8 %)	50.8 (35.5)	32 (51.7)	8 (26.7)	9 (30)	31 (50)
Infliximab (n=12; 16.2 %)	13.8 (11)	3 (25)	1 (11.1)	7 (77.8)	3 (25)
Second line b-DMARD (n=29)	28.4 (13.5)	15 (51.7)	5 (35.7)	3 (21.4)	8 (27.6)
*s.c TNF inhibitors (n=22; 75.9 %)	28.6 (15)	11 (50)	4 (36.4)	2 (18.2)	5 (22.7)
Infliximab (n=5; 17.2 %)	35.2 (36)	3 (60)	-	-	2 (40)
Secukinumab (n=2; 6.9 %)	9 (9)	1 (50)	1 (50)	-	1 (50)

s.c:subcutaneous

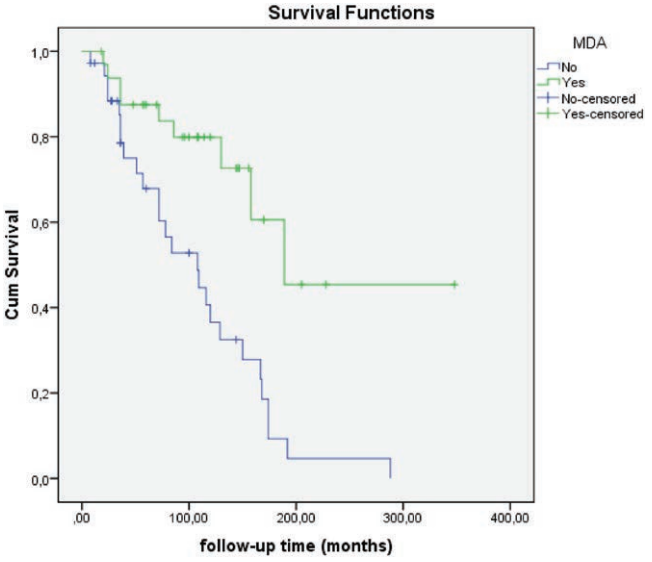


Figure 1. Comparison of b-DMARD retention according to MDA status in patients with ongoing first line b-DMARD treatmentLog rank: p=0.001

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.714

POS0143 POST-STRESS ULTRASOUND ASSESSMENT OF THE ACHILLES TENDON IS USEFUL TO DIFFERENCIATE PSORIATIC ARTHRITIS FROM THE PHYSIOLOGICAL ADAPTATION TO EXERCISE

C. Guillén-Astete[1], V. García García2, N. García-Montes[1], Á. Andreu-Suárez[1]. *[1]Hospital Ramón y Cajal, Rheumatology, Madrid, Spain*; *[1]Hospital Ramón y Cajal, Rheumatology, Madrid, Spain*

Background: Achilles enthesitis is the most accessible psoriatic arthritis hallmark to assess through ultrasound scan. Recently it has been demonstrated that continuous mechanical stress such as experimented by runners can drive to the development of physiological morphological changes that resembles those observed in psoriatic arthritis. In a subject with the suspicious diagnostic of psoriatic arthritis who practice any sports associated to continuous impact over the heels, the challenge to determine in what extent the morphological changes are linked to the exercise or to the disease, is remarkable.
Objectives: To determine morphological differences between patients with psoriatic arthritis, trained runners and sedentary volunteers through ultrasound scan of the Achilles tendon.
Methods: An ultrasound scan of the Achilles tendon was performed to the following subjects: Patients with diagnosis of psoriatic arthritis with a DAPSA score of low activity in at least six months and with history of heel pain in the past, volunteers runners with not less of 3-year sport activity at least three times a week and sedentary volunteers. In the group of patients, ultrasound scan was performed over the feet with history of heel pain. In the case of volunteers, the ultrasound scan was performed in the dominant feet. The selection of volunteers was not randomly-based in order to match their age and sex to the patients as much as possible. Besides demographic features, a comparison between tendon thickness at the level of the calcaneus bone border and the height of the retrocalcaneus bursae in the longitudinal axis were performed through ANOVA test. Power Doppler signal was scaned in all subjects before and after a controlled mechanical stress of the Achilles tendon by climbing stairs (100 steps, two times).
Results: Female/male distribution of the group of patients, runners and sedentary people were: 12/10, 18/18 and 20/18, respectively. Achilles tendon mean thickness ± standard deviation was 6.61 ± 1.05, 5.91 ± 1.44 and 4.61 ± 2.1mm, respectively (*P*=0.01). Retrocalcaneus bursae height was 3.42 ± 0.21, 3.22 ± 0.27 and 2.21 ± 0.31 (*P*=0.01). Basal PD signal was present into the enthesis of 2/22, 1/36 and 0/38, respectively (P not significant). After exercise, PD signal was present in 8/22, 5/36 and 0/38, respectively (P<0.001).
Conclusion: Power Doppler signal after exercise was identified as the most relevant ultrasound hallmark to distinguish a patient with psoriatic arthritis from a trained runner, even when psoriatic arthritis were considered as low activity. Post exercise ultrasound scan should be considered as a diagnosis tool in sportsmen with suspicious of psoriatic arthritis, until further studies confirm our findings.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3897

POS0144 NOVEL APPLICATION OF OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY AND NAILFOLD CAPILLAROSCOPY IN PSORIATIC ARTHRITIS - DIAGNOSTIC AND PROGNOSTIC ACCURACY IN RELATION TO PSORIASIS AND HAND OSTEOARTHRITIS

J. Guldberg-Møller[1,2], T. Schjødt Jørgensen[1], M. Henriksen[1], K. Ellegaard[1], M. Mogensen[3], L. E. Kristensen[1]. *[1]The Parker Institute, University Hospitals of Copenhagen, Bispebjerg and Frederiksberg, Copenhagen F, Denmark*; *[2]Slagelse Sygehus, Zealand University Hospitals, Slagelse, Denmark*; *[3]University Hospitals of Copenhagen, Bispebjerg and Frederiksberg, Department of Dermatology, Copenhagen F, Denmark*

Background: Nailfold video capillaroscopy (NVC) and angiographic optical coherence tomography (OCTA) have potential in diagnosing psoriatic arthritis (PsA) and differentiating it from psoriasis vulgaris (PsO) and hand osteoarthritis (OA).
Objectives: To assess the diagnostic properties of NVC and OCTA in patients with PsA compared to patients with PsO and hand OA based on nailfold capillary patterns.
Methods: Patients with distal interphalangeal-joint PsA and nail involvement (n=50), PsO with nail involvement (n=12); and OA (n=13) were included in this cross-sectional study. Capillaries were evaluated semi-quantitatively and qualitatively. Differences in capillary findings between groups were assessed using

mixed linear models. Binary logistic regression analyses were performed to determine the probability for PsA diagnosis based on capillaroscopy findings.

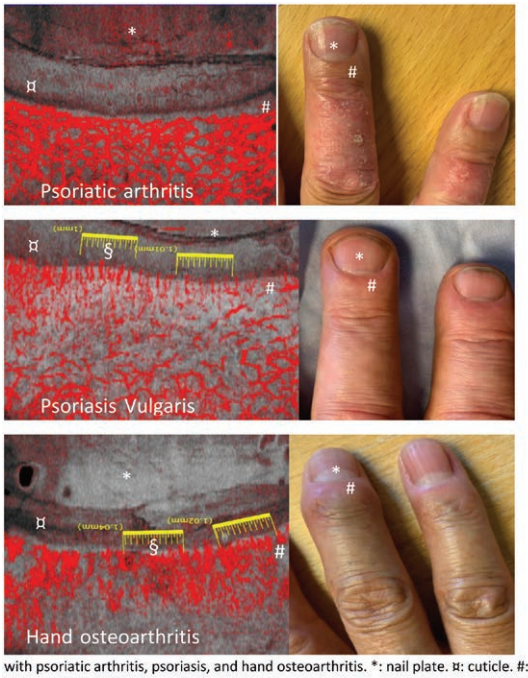
Results: Reduced capillary density and reduced nailfold blood flow in OCTA images distinguished PsA from both PsO (p=0.004 and p=0.052) and OA (p=0.024 and p<0.001). Qualitative analysis revealed that glomerular capillaries were found in only 3% of PsA patients but in 13% of PsO patients (P=0.003). Furthermore, coiled vessels were only seen in 55% of PsA patients and 71% in PsO patients (P=0.043). NVC microhaemorrhage was dominant in PsA patients (13 % and 17 %) and significantly different to OA patients (p=0.05). No capillary pattern was associated with an increased probability of the PsA diagnosis.

Conclusion: A pathognomic pattern for PsA diagnosis was not identified, however we demonstrated characteristics significant capillaroscopy findings for PsA such as decreased capillary density, reduced blood flow, and less coiled vessels in OCTA and presence of NVC microhemorrhages.

Table 1.

	NVC-rating	PsA (n=188)	PsO (n=42)	OA (n=48)	PsA vs PsO	PsA vs OA
NVC ad modum Cutolo	Reduced capillary density	51 %	31 %	51 %	P=0.107	0.770
	Irregularly enlarged capillaries	22 %	33 %	25 %	P=0.082	P=0.988
	Giant capillary	2 %	0	0	P=0.400	P=0.375
	Microhaemorrhages	13 %	7 %	2 %	P=0.327	P=0.05
	Capillary ramifications	14 %	24 %	29 %	P=0.054	P=0.307
	Capillary disorganisation	45 %	57 %	48 %	P=0.170	P=0.685
	OCTA-rating	PsA n=193	PsO n=48	OA n=52	PsA vs PsO	PsA vs OA
OCTA ad modum Cutolo	Reduced capillary density	53 %	21 %	33 %	P=0.004	P=0.024
	Irregularly enlarged capillaries	34 %	56 %	19 %	p=0.015	P=0.178
	Giant capillary	0	0	0	-	-
	Microhaemorrhages	0	0	0	-	-
	Capillary ramifications	0	0	0	-	-
	Capillary disorganisation	55 %	46 %	49 %	P=0.209	0.723
OCT	Nail thickness*, mm., mean (SD)	0.62 (0.13)	0.73 (0.39)	0.59 (0.08)	p=0.876	P=0.020
	OCTA blood flow percentage, mean (SD)	6.00 (2.94)	6.94 (3.08)	7.88 (3.30)	P=0.052	P<0.001
	Capillary morphology	PsA n=192	PsO n=48	OA n=52	PsA vs PsO	PsA vs OA
Qualitative evaluation of NVC morphology	Tortuous/Coiled capillaries	55 %	71 %	56 %	P=0.043	P=0.890
	Enlarged capillary diameter	17 %	21 %	17 %	P=0.557	P=0.984
	Ramified capillaries	13 %	15 %	19 %	P=0.701	P=0.215
	Microhaemorrhages	17 %	6 %	8 %	P=0.068	P=0.106
	Elongated capillaries	6 %	4 %	4 %	P=0.669	P=0.592
	Different capillary shapes, glomerular	3 %	13 %	2 %	P=0.003	P=0.779

The distribution of NVC and OCTA capillary morphology between PsA, PsO and OA, and qualitative evaluation of NVC morphology. Data are presented as percentage of capillary findings within the group. Differences between PsA and the other groups are presented as p-values. PsA: psoriatic arthritis, PsO: psoriasis vulgaris, OA: hand osteoarthritis, NVC nailfold video capillaroscopy, OCTA: angiographic optical coherence tomography. *: 1 patient (PsO group) was excluded from the analysis because of nail thickness>2.0 mm exceeding the maximum penetration depth of the OCT laser, representing an outlier.



with psoriatic arthritis, psoriasis, and hand osteoarthritis. *: nail plate. ¤: cuticle. #: proximal nailfold. §: one-millimetre field.

Figure 1. Optical coherence tomography angiography of the nail and nailbed blood vessels in patients with psoriatic arthritis, psoriasis, and hand osteoarthritis. *: nail plate. ¤: cuticle. #: proximal nailfold. §: one-millimetre field.

Acknowledgements: The data-analysis of blood flow in angiographic OCT images was kindly performed as a batch analysis by CEO Jon Holmes, Michelson Diagnostics Ltd., Kent.

Disclosure of Interests: Jørgen Guldberg-Møller Speakers bureau: AbbVie, NOVARTIS, Eli-Lilly and BK Ultrasound outside the present work., Tanja Schjødt Jørgensen Speakers bureau: AbbVie, Pfizer, Roche, Novartis, UCB, Biogen and Eli Lilly., Consultant of: AbbVie, Pfizer, Roche, Novartis, UCB, Biogen and Eli Lilly., Marius Henriksen Consultant of: Advisory Board member of Thuasne Group, France, Karen Ellegaard: None declared, Mette Mogensen: None declared, Lars Erik Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals., Consultant of: Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals.

DOI: 10.1136/annrheumdis-2021-eular.1394

POS0145

PREDICTORS OF PSORIATIC ARTHRITIS DEVELOPMENT IN PSORIASIS PATIENTS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

A. Zabotti[1], O. De Lucia[2], G. Sakellariou[3], A. Batticciotto[4], G. Cincinelli[2], I. Giovannini[1], L. Idolazzi[5], G. Maioli[2], I. Tinazzi[6], D. Aletaha[7], S. De Vita[1],

A. Marchesoni[2], J. S. Smolen[7], A. Iagnocco[8], D. Mcgonagle[9], R. Caporali[2]. *[1]Rheumatology Clinic, Department of Medical and Biological Science, Udine, Italy; [2]ASST Centro Traumatologico Ortopedico G. Pini-CTO, Department of Rheumatology and Medical Sciences, Milan, Italy; [3]Division of Rheumatology, University of Pavia, Istituti Clinici Scientifici Maugeri, Pavia, Italy; [4]Rheumatology Unit, Department of Internal Medicine, ASST-Settelaghi. "Ospedale di Circolo-Fondazione Macchi", Varese, Italy; [5]Rheumatology Unit, University of Verona, Ospedale Civile Maggiore, Verona, Italy; [6]Unit of Rheumatology, IRCSS Ospedale Sacro Cuore Don Calabria, Negrar, Italy; [7]Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Wien, Austria; [8]Rheumatology Unit, Dipartimento di Scienze Mediche, Universita degli Studi di Torino, Torino, Italy; [9]Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, United Kingdom*

Background: Up to 30% of Psoriasis (PsO) patients are prone to develop Psoriatic Arthritis (PsA). Agreement on how to identify PsO patients at risk of developing PsA is still lacking (1).

Objectives: To identify predictors of PsA development in PsO patients through a systematic literature review (SLR) and meta-analyses (MA).

Methods: MEDLINE, EMBASE and COCHRANE databases were searched (up to February 22nd, 2020). The PICO framework (population = PsO patients; intervention = clinical, environmental, imaging and genetic features; comparator = not applicable; outcome = PsA development) was used to design searches and define the eligibility of studies for inclusion. The MA focuses on 3 major features as possible predictors: i) PsO skin and nail involvement; ii) musculoskeletal (MSK) complaints; iii) inflammation and structural damage detected by imaging (Table 1). The sample estimates of the relative risk were pooled only when the studies were homogeneous in terms of cohort of patients, follow-up, study design and metrics.

Results: 4698 articles were screened for eligibility, 110 underwent a full reading and 29 were finally included. Figure 1 shows the study flow-chart for article selection. Though pooling was judge not appropriate, 5/7 prospective studies significantly support a predictive value of PsA development in patients with severe PsO (n=174635). While the predictive value of nail involvement is not well defined (n=2202), the pooled estimate from two cohort studies (n=474) supports nail pitting as predictor of PsA (RR=2.14 [1.32; 3.46]). Moving to the MSK complaints, the risk of developing PsA is about two times greater in PsO with than without arthralgia (pooled RR: 2.15 [1.16, 3.99]) within 2 years. Lastly, PsO patients with inflammation or structural damage detected by imaging are nearly four times more likely to develop PsA within 1-2 years (pooled RR from 4 cohort studies (n=247): 3.72 [2.12; 6.51]) (Table 1). The incidence rate of PsA varies from 1.34 to 5.9/100 p-ys in PsO and from 10.9 to 12.5/100 p-ys in PsOAr.

Conclusion: Arthralgia and inflammation and/or structural damage detected by imaging are predictive features, likely prodromal, of PsA development. PsO severity and nail pitting are clinical manifestations related to PsA development.

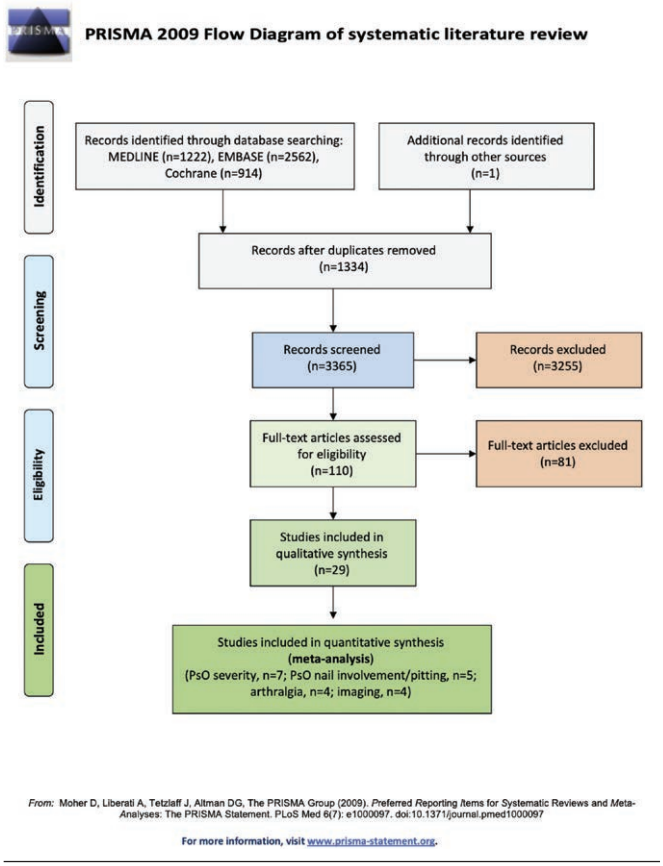


Figure 1.

REFERENCES:

[1] Zabotti A, et al. Curr Rheumatol Rep. 2020 May 16;22(6):24. doi: 10.1007/s11926-020-00891-x.

Table 1. Studies reporting the major features as possible predictors of PsA development.

PsO skin – severity PsO nail involvement PsO nail lesions	Variables	Relative Risk [95%CI]	Follow-up
Wilson, 2009	PsO nail involvement	$HR_{adjusted}$: 2.24 [1.26; 3.98]	13.1±8.8 ys
Faustini, 2015	PASI score +	/○= -0.18[-0.84; 0.48]	1.2±0.2 ys
	PsO nail involvement	RR: 0.95 [0.37; 2.47]	
Eder, 2016	PASI score	HR (>20vs<10): 5.39 [1.64; 17.7]	4.1±2.1 ys
	PsO nail involvement	$HR_{unadjusted}$: 1.36 [0.76; 2.45]	
	Type of PsO nail lesions	$HR_{unadjusted}$: 2.21 [1.24; 3.92]	
Eder, 2017	PASI score +	$HR_{unadjusted}$: 1.05 [1.01; 1.09]	3.8±2.1 ys
	Type of PsO nail lesions	$HR_{unadjusted}$: 1.98 [0.83; 4.74]	
Lewinson, 2017	PsO severity defined from medications	$HR_{adjusted}$ (moderate/severe vs mild): 5.02 [4.18; 6.04]	5.1 ys
Egeberg, 2018	PsO severity defined from medications	RR (severe vs mild): 1.31 [1.18; 1.46]	18 ys
Elnady, 2019	PASI score +	/○= 0.79[-0.37; 1.95]	2 ys
	PsO nail Involvement	RR: 1.43 [0.38; 5.31]	
Green, 2020	PsO severity defined from medication	RR (severe vs mild): 2.79 [2.49; 3.13]	5.8 ys
MSK-complaints	Variables	Incident-PsA cases	Follow-up
Faustini, 2015	Arthralgia	RR: 1.98 [0.75; 5.19]	1.2±0.2 ys
Eder, 2017	Arthralgia	$HR_{adjusted}$: 2.59 [1.15; 5.88]	3.8±2.1 ys
Zabotti, 2019	Arthralgia	RR: 4.44 [0.54; 36.72]	1.6±0.5 ys
Simon D, 2020	Arthralgia	RR: 2.04 [0.86; 4.86]	2.4±1.5 ys
Sub-clinical inflammation or structural damage detected by imaging	Variables	Incident-PsA cases	Follow-up
Faustini, 2015	MRI	RR: 2.10 [0.75; 5.90]	1.2±0.2 ys
Elnady, 2019	MSK-US	RR: 5.38 [1.17; 24.63]	2 ys
Zabotti, 2019	MSK-US	RR: 6.86 [0.83; 56.63]	1.6±0.5 ys
Simon D, 2020	HR-pQCT	RR: 4.32 [1.96; 9.55]	2.3±1.4 ys

Disclosure of Interests: Alen Zabotti Speakers bureau: UCB, Novartis, Janssen, Paid instructor for: Amgen, Consultant of: Janssen, Orazio De Lucia Speakers bureau: Not relevant for this type of study, Consultant of: Not relevant for this type of study, Grant/research support from: Not relevant for this type of study, Garifallia Sakellariou Consultant of: AbbVie, Novartis, Alberto Batticciotto Speakers bureau: Not relevant for this type of study, Consultant of: Not relevant for this type of study, Grant/research support from: Not relevant for this type of study, Gilberto Cincinelli: None declared, Ivan Giovannini: None declared, Luca Idolazzi Speakers bureau: Eli Lilly, UCB, Celgene, MSD, Abbvie, Novartis, Paid instructor for: UCB, Gabriella Maioli Speakers bureau: Not relevant for this type of study, Consultant of: Not relevant for this type of study, Grant/research support from: Not relevant for this type of study, Ilaria Tinazzi Speakers bureau: Not relevant for this type of study, Consultant of: Not relevant for this type of study, Grant/research support from: Not relevant for this type of study, Daniel Aletaha Speakers bureau: not relevant for this type of study, Consultant of: not relevant for this type of study, Grant/research support from: not relevant for this type of study, Salvatore De Vita Consultant of: GSK, Roche, Grant/research support from: Not relevant for this type of study, Antonio Marchesoni Speakers bureau: not relevant for this type of study, Consultant of: not relevant for this type of study, Grant/research support from: not relevant for this type of study, Josef S. Smolen Speakers bureau: Not relevant for this type of study, Consultant of: Not relevant for this type of study, Grant/research support from: Not relevant for this type of study, Annamaria Iagnocco Speakers bureau: not relevant for this type of study, Paid instructor for: not relevant for this type of study, Consultant of: not relevant for this type of study, Grant/research support from: not relevant for this type of study, Dennis McGonagle Speakers bureau: ABBVIE, CELGENE, PFIZER, MSD, NOVARTIS, JANSSEN, UCB, GILEAD, BMS, LILLY, Grant/research support from: ABBVIE, CELGENE, PFIZER, MSD, NOVARTIS, JANSSEN, UCB, GILEAD, BMS, LILLY, Roberto Caporali Speakers bureau: Abbvie, Amgen, BMS, Celltrion, Galapagos, Gilead, Lilly, Pfizer, Roche, UCB, Sanofi, Fresenius Kabi, Samsung bioepis, MSD, Consultant of: Galapagos, Gilead, Lilly, Janssen, MSD
DOI: 10.1136/annrheumdis-2021-eular.1513

POS0146 PERIPHERAL NEUROPATHY IN PSORIASIS AND PSORIATIC ARTHRITIS: A SINGLE BLIND, CONTROLLED, ELECTROPHYSIOLOGICAL STUDY

M. Izci[1], S. Kanyılmaz Turgut[1], O. Akan[2], I. Topal[3], O. Kuru[1]. *[1]Prof Dr Cemil Tascioglu City Hospital, Physical Medicine and Rehabilitation Clinic, İstanbul, Turkey*; *[2]Prof Dr Cemil Tascioglu City Hospital, Neurology Clinic, İstanbul,Turkey*; *[3]Prof Dr Cemil Tascioglu City Hospital, Dermatology Clinic, İstanbul,Turkey*

Background: It is well known that both psoriasis (PsO) and psoriatic arthritis (PsA) causes morbidity and disability in patients' lives. Additional pathologies such as peripheral neuropathy (PN) may interfere with disease specific symptoms and may increase the burden of disease. Neuropathic complaints of patients with PsO and PsA are observed during patients' follow-up (1,2). However, the presence of PN in PsO and PsA is not well defined in clinical studies and clinicians might be neglecting this issue.
Objectives: Our aim was to investigate the presence of PN by electrophysiological methods and to examine its relationship with neuropathic pain and with treatments in patients with PsO and PsA.
Methods: 38 patients with PsA, 36 patients with PsO and 37 age&sex-matched healthy volunteers were enrolled into this prospective, single-blind study. Disease activity was assessed with Psoriasis Area Severity Index (PASI) for patients with PsO and with Disease Activity in Psoriatic Arthritis (DAPSA) score for patients with PsA. Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) score was used to evaluate neuropathic pain. All participants were electrophysiologically examined in Electromyography (EMG) Laboratory by an experienced neurologist blinded for study groups.
Results: There were no significant differences on patients age, sex and body mass index among 3 study groups (p>0.05). However, disease duration was significantly longer in PsO group compared to PsA group (median 19.1[1-43] years in PsO vs median 7.5[2-29] years in PsA; p<0.01). PN was detected in 7 patients (19.44%) in the PsO group, 14 patients (34.21%) in the PsA group, and in 1 volunteer (2.7%) in the control group (PsO vs control: p<0.05; PsA vs control: p<0.001, PsO vs PsA: p>0.05) (Table 1). Among patients with PsA, 1 patient had ulnar neuropathy and 1 patient had both carpal tunnel syndrome (CTS) and sensory polyneuropathy. All other PNs detected electrophysiologically were CTS. Neuropathic pain was present in 11 patients (30.56%), 20 patients (52.63%) and in 2 volunteers (5.41%) in PsO, PsA and control groups consecutively (PsO vs control: p<0.05; PsA vs control: p<0.001, PsO vs PsA: p>0.05). PN did not show any significant correlation with disease activity or treatments including biological agents.
Conclusion: To our knowledge, this is the first study to investigate simultaneously the presence of neuropathic pain and PN by electrophysiological methods in patients with PsO and PsA. We observed PN and neuropathic pain high in patients with PsO&PsA and among them CTS appears as the most prominent neuropathy. Clinicians should keep this in mind during routine care of patients with PsO and PsA, which may improve patient-centred care. Large, prospective studies are needed to understand the characteristics of these neuropathies and its prognosis.
REFERENCES:
[1] Rifbjerg-Madsen S, Christensen AW, Christensen R, Hetland ML, Bliddal H, Kristensen LE, Danneskiold-Samsøe B, Amris K (2017) Pain and pain mechanisms in patients with inflammatory arthritis: a Danish nationwide cross-sectional DANBIO registry survey. PLoS One 12(7):e0180014.
[2] Ljosaa TM, Mork C, Stubhaug A, et al. Skin pain and skin discomfort is associated with quality of life in patients with psoriasis. J Eur Acad Dermatol Venereol. 2012;26:29-35.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1258

POS0147 ANALYSIS OF VENOUS THROMBOEMBOLIC RISK AMONG PSORIATIC ARTHRITIS PATIENTS

T. Gazitt[1], J. Pesachov[2], I. Lavi[3], M. Elias[1], A. Haddad[1], I. Feldhamer[4], A. Cohen[4], W. Saliba[3], D. Zisman[1,5]. *[1]Carmel Hospital, Rheumatology, Haifa, Israel*; *[2]Technion - Israel Institute of Technology, Ruth and Bruce Rappaport Faculty of Medicine, Haifa, Israel*; *[3]Carmel Hospital, Community Medicine and Epidemiology, Haifa, Israel*; *[4]Clalit Health Organization, Chief Physician's Office, Central Headquarters,Tel Aviv, Israel*; *[2]Technion - Israel Institute of Technology, Ruth and Bruce Rappaport Faculty of Medicine, Haifa, Israel*

Background: Psoriatic arthritis (PsA) is a chronic, immune-mediated, systemic inflammatory arthritis associated with comorbidities including metabolic syndrome, cardiovascular risk factors and cardiovascular disease (CVD).
Objectives: To evaluate the prevalence of venous thromboembolism (VTE) in a PsA patient cohort using a large health care provider database.
Methods: A large health care provider database serving 4.7 million healthcare subscribers was interrogated for an adult patient cohort who were newly diagnosed with PsA between January 2005 (start date) and 31 December 2018 with date of diagnosis considered the index date. A risk set was employed to randomly select 4 controls without PsA as a comparator group to the PsA cohort matched by age, sex, ethnic group, and index date. Both groups were followed from the index date until the first occurrence of VTE event, death, or end of follow-up 31 December 2019, whichever came first. Marginal model with robust covariant estimate counting for the matching was used to estimate the crude and adjusted hazard ratio (HR) for the association between PsA and VTE. Within the group of PSA patients, Cox proportional hazard regression models was used to calculate the risk of having VTE given demographic variables, SES, smoking, selected comorbidities, and conventional vs biologic disease modifying anti-rheumatic drugs (c/bDMARD). Continuous variables were summarized with mean ± standard deviation, and categorical variables were presented as numbers and proportions. All tests were 2-sided; p values of < = 0.05 were considered statistically significant. All data were analyzed using SPSS, 24 (IBM SPSS Statistics for Windows, version 24.0, 2016, Armonk, NY) and SAS, 9.4 (SAS institute Inc, Cary, NC).

Table 1. Results of peripheral neuropathy and neuropathic pain in control group and patients with PsO and PsA

	Control Group (n=37)	PsO Group (n=36)	PsA Group (n=38)	p^	p+	p&
CTS	1 (%2.70)	7 (%19.44)	13* (%34.21)	0.028[a]	<0.001[a]	0.153[a]
Ulnar Neuropathy	0	0	1 (%2.63)			
Polyneuropathy	0	0	1* (%2.63)			
Total PN	1 (%2.70)	7 (%19.44)	14 (%36.64)	0.028[a]	<0.001[a]	0.097[a]
LANSS Score	5 (0:13)	6.50 (0:16)	13 (3:19)	0.170[b]	<0.001[b]	0.004[b]
According to LANSS likely neuropathic pain	2 (%5.41)	11 (%30.56)	20 (%52.63)	0.005[a]	<0.001[a]	0.054[a]

*: Both polyneuropathy and CTS were detected in one patient in the PsA group; Data are given as n (%) and median (minimum: maximum); a: Chi-Square Test, b: Kruskal Wallis Test; p^ value: control vs PsO, p+ value: control vs PsA, p& value: PsO vs PsA

Results: The PsA cohort consisted of 5,275 patients, 53.2% females with mean age of 51.66 ±15.41. The control group consisted of 21,011 subjects matched for age and sex. In relation to the control group, the PsA cohort had a higher SES (25.1% vs 23.4%, p<0.0001), higher tobacco use (42.2% vs.39.6% p<0.0001) and obesity (33.5% vs 25.8%, p<0.0001). The study group had a statistically significant higher incidence of diabetes (33.8% vs 26.2%, p<0.0001), IHD (10.3% vs 8.6%, p<0.0001), CHF (2.2% vs 1.6%, p=0.004), hypertension (30.1% vs 26.2%, p<0.0001), CVA/TIA (4.6% vs 3.9%, p=0.024) and vascular disease (3.7% vs 3.0%, p=0.005). There were 62 patients (1.2%) diagnosed with VTE in the PsA group as opposed to 176 patients (0.8%) in the control group (p=0.023, HR=1.397, CI 1.05-1.87). The mean age of patients diagnosed with VTE was higher in the PsA group relative to controls (64.90± 13.20 vs 51.54 ± 15.41, respectively, p<0.0001), with higher age, BMI>30, cancer, IHD, vascular disease, and previous VTE found to be associated with VTE in the PsA group relative to controls in both univariate and multivariate analyses. The higher prevalence of VTE in PsA patients relative to controls did not remain statistically significant in multivariate analysis following adjustment for risk factors. Within the PsA group, patients with VTE were more often of older age and with past history of VTE. Both cDMARD and bDMARD were not associated with increased risk of VTE among PsA patients.

Conclusion: The prevalence of VTE was higher in PsA group compared to the general population, but after adjustment for comorbidities and risk factors, it no longer remained statistically significant. Among PsA patients, age and previous history of VTE were associated with increased risk of VTE. Addressing VTE risk in the management of patients with PsA is recommended especially in the era of Janus kinase inhibitors.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1811

POS0148 MATERNAL AND NEONATAL OUTCOMES IN PREGNANT WOMEN WITH PSORIASIS AND PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

W. Xie[1], H. Huang[1], Z. Zhang[1]. [1]*Peking University First Hospital, Department of Rheumatology and Clinical Immunology, Beijing, China*

Background: Psoriasis and psoriatic arthritis (PsA) are inflammatory diseases that affect women in their reproductive years. The evidence regarding the pregnancy outcomes in psoriasis and PsA is more limited and conflicting, to a large extent, confusing our knowledge on this topic.

Objectives: We aim to investigate whether maternal psoriasis and PsA are associated with adverse pregnancy outcomes.

Methods: We searched multiple electronic databases from inception to 3 August 2020, and reference lists of selected articles. Observational studies reporting at least one pregnancy outcomes in women with psoriasis or PsA with a comparator of general population or healthy subjects were included. Data were pooled by random-effects models (DerSimonian and Laird method) and expressed as odds ratio (OR) and 95% confidence interval (CI).

Results: Overall, 16 studies were included in the meta-analysis. The pooled analyses showed pregnant women with psoriatic diseases have significantly higher risk of adverse maternal outcomes compared with general population (caesarean delivery: 1.33 (1.17-1.52); preterm birth: 1.32 (1.15-1.52); (pre)eclampsia: 1.28 (1.14-1.43); gestational diabetes: 1.19 (1.10-1.30); gestational hypertension: 1.30 (1.18-1.44) (Figure 1). However, no statistically increased risks of fetal complications were observed in women with psoriatic diseases (small for gestational age: 1.02 (0.93-1.11); low birth weight: 1.15 (0.93-1.42); congenital malformations: 1.03 (0.93-1.14); Apgar score <7: 1.07 (0.81-1.39); neonatal mortality: 1.13 (0.90-1.43); stillbirth: 1.19 (0.95-1.50)). Subgroup analysis found similar results in women with either psoriasis or PsA regarding maternal outcomes, but the magnitude of risk estimates seems to be greater in PsA.

Conclusion: Pregnant women with psoriasis and PsA have excess risk of adverse maternal events, with seemingly higher risk in women with PsA, but not adverse neonatal events. Close monitoring of the mothers' clinical status before and during pregnancy are decidedly required in daily practice.

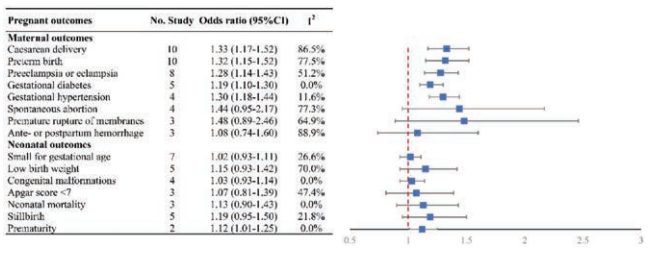


Figure 1. Forest plots of the odds ratio for the risk of adverse pregnancy outcomes in patients with psoriatic diseases.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2283

POS0149 MUSCULOSKELETAL PAIN IN PATIENTS WITH PSORIASIS AND THE INFLUENCE ON HEALTH-RELATED QUALITY OF LIFE: RESULTS FROM A DANISH POPULATION-BASED SURVEY

S. Kamp Felbo[1,2], L. Terslev[1,2], I. J. Sørensen[3], L. Skov[2,4], C. Zachariae[2,4], M. Østergaard[1,2]. [1]*Rigshospitalet, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Glostrup, Denmark*; [2]*University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark*; [3]*Rigshospitalet, Center for Rheumatology and Spine Diseases, Copenhagen, Denmark*; [4]*Herlev and Gentofte Hospitals, Department of Dermatology and Allergy, Gentofte, Denmark*

Background: Psoriasis (PsO) impacts health-related quality of life (HRQoL). The impact of musculoskeletal (MSK) pain in patients without diagnosed psoriatic arthritis (PsA) (1) is poorly understood.

Objectives: To assess the pattern of MSK pain in patients with PsO, and its influence on important patient-reported outcomes.

Methods: A nationwide survey of patients with PsO and PsA, covering skin and MSK symptoms, healthcare contacts, self-assessed disease severity, treatment satisfaction, HRQoL (including Dermatology Life Quality Index (DLQI) and European Quality of life-5 Dimensions (EQ5D)) and disability. Respondents were grouped according to MSK pain as shown in Table 1. 'PsO previous pain' was combined with 'PsO no pain ever' (labeled 'PsO no pain now') for some analyses and with 'PsO pain now' (labeled 'PsO pain ever') for others.

Results: 561 respondents with PsO completed the questionnaire. Population and subgroup demographics, clinical PsA/PsO features and HRQoL measures are shown in Table 1. Patients in 'PsO pain now' had poorer HRQoL (higher DLQI, lower EQ5D) compared to 'PsO no pain now', and similar to patients with PsA. Patients with PsA assessed their PsO severity higher than patients with 'PsO pain ever' and 'PsO no pain ever' (median (interquartile range) 2 (2-3), 2 (1-3) and 2 (1-2) on a five-level scale, respectively). PsO treatment satisfaction (five-level scale) was lower for 'PsO pain ever' (3 (3-4)) than for 'PsO no pain ever' (4 (3-4), p=0.03). Figure 1 shows contacts to dermatologists and rheumatologists, where 72% of patients in 'PsO pain ever' had never been examined by a rheumatologist. Time from symptom debut to diagnosis was 1.5 (1-3) years for PsO and 7.5 (1.5-12.5) for PsA.

Table 1. Population and subgroup characteristics

DEMOGRAPHICS	All	PsO no pain ever	PsO previous pain	PsO pain now	PsA	p-value*		
N	561	178	104	130	108			
Male	212 (38%)	79 (44%)	34 (33%)	36 (28%)	40 (37%)	0.02		
Age (years)	58 (43-68)	58 (43-68)	56 (42-63)	53 (43-63)	58 (48-68)	0.05		
Body Mass Index	27 (24-32)	26 (23-30)	28 (24-32)	29 (25-33)	28 (24-33)	0.01		
No current occupation[1]	119 (21%)	20 (11%)	23 (22%)	34 (26%)	35 (32%)	<0.001		
PsO/PsA FEATURES	All	1. PsO no pain ever	2. PsO pain ever		3. PsA	1 vs. 2	1 vs. 3	2 vs. 3
N	561	178	234		108			
BSA (%)	1 (1-2)	1(1-2)	1 (1-2)		2 (1-2)	0.10	<0.001	0.01
Nail psoriasis	134 (24%)	27 (15%)	50 (21%)		46 (48%)	0.13	<0.001	<0.001
'Dactylitis'[2a]	80 (14%)	2 (1%)	34 (15%)		40 (42%)	<0.001	<0.001	<0.001
'Enthesitis'[2b]	74 (13%)	4 (2%)	30 (13%)		39 (41%)	<0.001	<0.001	<0.001
QUALITY OF LIFE AND DISABILITY	All	1. PsO no pain now	2. PsO pain now		3. PsA	1 vs. 2	1 vs. 3	2 vs. 3
N	561	282	130		108			
DLQI score (0-30)	2 (1-5)	1 (1-4)	2 (1-5)		2 (1-6)	0.001	0.04	0.52
EQ5D index (0-1)	0.797 (0.691-0.859)	0.859 (0.768-1)	0.732 (0.679-0.859)		0.702 (0.598-0.802)	<0.001	<0.001	0.53
HAQ score (0-3)	0.63 (0-1.25)		0.50 (0-0.88)		0.88 (0.13-1.38)			0.03

Numbers are numbers (%) (binary data), median (interquartile range) (continuous data).BSA: Body Surface Area (palm-size areas of the body with psoriasis). DLQI: Dermatology life quality index (higher scores = higher impact of disease). EQ5D: European Quality of life-5 Dimensions -5 Domain (higher scores = better health state). HAQ: Health assessment questionnaire. PsA: Psoriatic arthritis. PsO: Psoriasis.* Multiple groups: Chi-square test/ Kruskal-Wallis test. Pairwise: Fishers exact test/Mann-Whitney U test1. I.e. work/studies/retirement 2. a. "Swollen entire finger or toe" b. "Tender or swollen tendon".

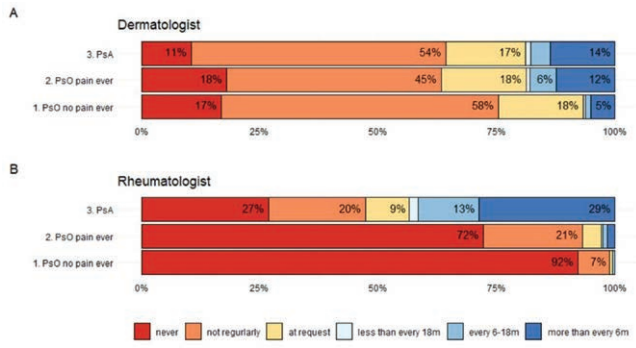


Figure 1. Contacts to specialists by subgroup

Conclusion: Patients with PsO and MSK pain have decreased HRQoL compared to patients with PsO without MSK pain, to a similar degree as patients with PsA. Many have never been examined by a rheumatologist, demonstrating an unmet need for adequate evaluation of these patients.

REFERENCES:

[1] Lebwohl MG et al. Patient perspectives in the management of psoriasis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey. *J Am Acad Dermatol*. 2014.

Acknowledgements: The authors acknowledge the participants who contributed to this study. The study was financially supported by Amgen/Celgene. The Danish Rheumatism Association, The Danish Psoriasis Research Foundation and The Capital Region of Denmark have supported the work of SKF. The sponsors had no influence on study design, data analysis or manuscript preparation.

Disclosure of Interests: Sara Kamp Felbo Grant/research support from: Celgene, Lene Terslev Speakers bureau: AbbVie, Janssen, Roche, Novartis, Pfizer, MSD, BMS, Inge Juul Sørensen: None declared, Lone Skov Speakers bureau: AbbVie, Eli Lilly, Novartis, and LEO Pharma, Consultant of: AbbVie, Janssen Cilag, Novartis, Eli Lilly, LEO Pharma, UCB, Almirall, Bristol-Myers Squibb, and Sanofi., Grant/research support from: Novartis, Sanofi, Bristol-Myers Squibb, Janssen Cilag, and LEO Pharma., Claus Zachariae Speakers bureau: Eli Lilly, Jansen Cilag, Novartis, Abbvie, Takeda, Amgen, Almirall, CSL, UCB, Regeneron, MSD, and Leo Pharma, Consultant of: Eli Lilly, Jansen Cilag, Novartis, Abbvie, Takeda, Amgen, Almirall, CSL, UCB, Regeneron, MSD, and Leo Pharma, Mikkel Østergaard Speakers bureau: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Consultant of: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB

DOI: 10.1136/annrheumdis-2021-eular.1053

POS0150 BEING OVERWEIGHT IS ASSOCIATED WITH NOT REACHING LOW DISEASE ACTIVITY IN WOMEN BUT NOT MEN WITH PSORIATIC ARTHRITIS

M. Mulder[1], M. Wenink[1], J. Vriezekolk[1]. [1]*Sint Maartenskliniek, Rheumatology, Nijmegen, Netherlands*

Background: Disease manifestations and outcomes of psoriatic arthritis (PsA) seem to differ between sexes. Gaining knowledge about the underlying mechanisms of these differences between men and women is important to optimize treatment strategies, especially given that women seem to less often reach low disease activity (LDA) treatment targets[1,2].

Objectives: To assess sex differences in disease activity parameters and health-related quality of life in PsA, and to assess whether determinants associated with *not* reaching treatment target differed between men and women.

Methods: A cross-sectional study was conducted, using data from a routine practice cohort of 855 patients with PsA, that were all tightly monitored and treated. Gender differences with respect to Psoriatic Arthritis Disease Activity Score (PASDAS), skin/nail disease, SF12-PCS, SF12-MCS, inflammatory backpain (IBP), and demographics were assessed. Multivariate analyses were used to examine determinants associated with *not* reaching PASDAS ≤3.2 (LDA) in men and women.

Results: Women had worse scores for - among others- swollen and tender joints, CRP, enthesitis, and function (all P<0.001). Higher PASDAS scores in women were found than in men, mean 3.5 (SD=1.5) vs 2.7 (SD=1.5), p<0.001. Likewise, women were more often not at PASDAS treatment target (OR = 2.03, P<0.001). Besides being female, also the presence of nail disease and IBP, a higher number of DMARDs used in the past or current number of DMARDs used, and a higher Body Mass Index (BMI) were associated with not reaching the treatment target in the overall sample. No differences in current medication use was found between the sexes. Table 1 shows that for women, but not men, BMI was associated with not reaching PASDAS ≤3.2 (BMI 25-30: OR =3.6, P<0.001; BMI 30-35: OR=2.41, P=0.023; BMI >35: OR=2.45, P=0.002).

Conclusion: Women with PsA in a tightly monitored and treated setting have more severe disease than men. This is demonstrated by worse scores for women in both subjective and objective disease activity measures, in addition to women less often reaching the treatment target. Notably, being overweight is associated with not reaching the treatment target in women, but not men.

REFERENCES:

[1] Theander E, Husmark T, Alenius GM, Larsson PT, Teleman A, Geijer M, et al. Early psoriatic arthritis: short symptom duration, male gender and preserved physical functioning at presentation predict favourable outcome at 5-year follow-up. Results from the Swedish Early Psoriatic Arthritis Register (SwePsA). Ann Rheum Dis. 2014;73(2):407-13.

[2] Orbai AM, Perin J, Gorlier C, Coates LC, Kiltz U, Leung YY, et al. Determinants of Patient-Reported Psoriatic Arthritis Impact of Disease: An Analysis of the Association with Gender in 458 Patients from 14 Countries. Arthritis Care Res (Hoboken). 2019.

Table 1. Final multivariate logistic regression model of determinants associated with *not* reaching PASDAS target stratified for gender

	Men (N = 465)		Women (N = 390)	
Variable	OR (95% CI)	P-value	OR (95% CI)	P-value
BMI 25-30 kg/m^2 (ref: <25)			3.6 (1.86-6.99)	<0.001
BMI 30-35 kg/m^2 (ref: <25)			2.41 (1.12-5.14)	0.023
BMI >35 kg/m^2 (ref: <25)			2.45 (1.40-4.28)	0.002
Presence of nail disease			1.57 (0.97-2.55)	0.066
Presence of IBP	2.75 (1.13-6.70)	0.026	3.22 (1.52-6.85)	0.002
MCS (SF12)	0.93 (0.90-0.95)	<0.001	0.96 (0.94-0.98)	0.001
cDMARD use (ref: no DMARD)	1.16 (0.58-2.31)	0.671		
bDMARD use (ref: no DMARD)	0.49 (0.23-1.02)	0.057		
Number of DMARDs history	1.36 (1.17-1.59)	<0.001	1.13 (1.02-1.25)	0.015
Number of DMARDs current	1.90 (1.11-3.24)	0.018		

* A P-value of <0.05 is considered significant. PASDAS = psoriatic arthritis disease activity score; BMI = body mass index; IBP = inflammatory backpain; SF12-MCS = short form-12 mental component scale; cDMARD = conventional DMARD; bDMARD = biological disease-modifying antirheumatic drug.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1530

POS0151

A PRACTICAL GUIDE FOR THE ASSESSMENT OF PSORIASIS BURDEN IN PATIENTS WITH PSORIATIC ARTHRITIS

F. R. Kasiem[1], A. Pasma[1], I. Tchetverikov[2], J. Luime[1], J. Hazes[1], M. Van Doorn[3], M. R. Kok[4], M. Vis[1]on behalf of CICERO. [1]*Erasmus MC, Rheumatology, Rotterdam, Netherlands*; [2]*Albert Schweitzer Hospital, Rheumatology, Dordrecht, Netherlands*; [3]*Erasmus MC, Dermatology, Rotterdam, Netherlands*; [4]*Maasstad Hospital, Rheumatology & Clinical Immunology, Rotterdam, Netherlands*

Background: Rheumatologists play an important role in the management of patients with Psoriatic Arthritis (PsA). With PsA being a multifaceted disease, it can be challenging to assess the impact of psoriatic skin symptoms, next to the musculoskeletal complaints. We have previously shown that a dermatology-specific Health-related Quality of Life (HRQoL) questionnaire provides insight into the burden of skin symptoms, in contrast to a general HRQoL questionnaire.[1] When treating PsA patients, specific questions on skin symptoms are necessary in order to assess the burden of psoriasis.

Objectives: To create a set of questions that can easily identify PsA patients with a high psoriasis burden in daily rheumatology clinical practice.

Methods: Data from patients receiving usual care were used from the Dutch south west Psoriatic Arthritis (DEPAR) cohort, consisting of newly diagnosed PsA patients included between July 2013 and March 2020. The two dermatology-specific HRQoL questionnaires used were the Skindex-17 and Dermatology Life Quality Index (DLQI), both with a one-week recall period.

First, an exploratory principal component analysis (PCA) with varimax rotation was performed on both questionnaires combined, to identify underlying latent traits. Subsequently, items were dichotomized on their median frequencies. And a 2-parameter logistic (2PL) model was fitted for each latent trait. Item characteristic curves were plotted for each latent trait. Item selection took place based on the discrimination and difficulty of the items. Per latent trait, we selected 2 to 3 items distributed far apart across the latent trait. A flowchart was made with the selected questions.

Results: In total, 413 patients with completed Skindex-17 and DLQI questionnaires at baseline were included. Mean (sd) age was 50.3 (13.4) years and median (IQR) Psoriasis Area and Severity Index (PASI) score 2 (0.5-4.2). The PCA gave the best fit with two underlying clusters of questions, namely psychosocial (n=20) questions and questions regarding physical symptoms (n=7). Three questions were selected to assess psychosocial impact and two for impact of physical symptoms (Figure 1). Questions should be asked in chronological order.

Cluster 1: Psychosocial

The first question is if the patient was embarrassed by their skin condition. If answered with "never", the patient experienced the lowest burden. When answered with "rarely/sometimes" or "often/always", continue to the second question. Ask the patient if they tended to stay at home because of their skin condition. If answered with "never", they experienced a higher burden. If answered with "rarely/sometimes" or "often/always", continue to the last question. Ask the patient if their skin condition has prevented them from working or studying. If not, the patient experienced a higher burden and if answered with "yes", they experienced the highest burden in this domain.

Cluster 2: Physical symptoms

First ask the patient how itchy, sore, painful or stinging their skin was. If they answer with "not at all", they experienced the lowest burden. If answered with "a little/a lot/very much", continue to the second question. Ask if their skin was irritated. If answered with "never/rarely/sometimes", they experienced a higher burden. If answered with "often/always", the patient experienced the highest burden in this domain.

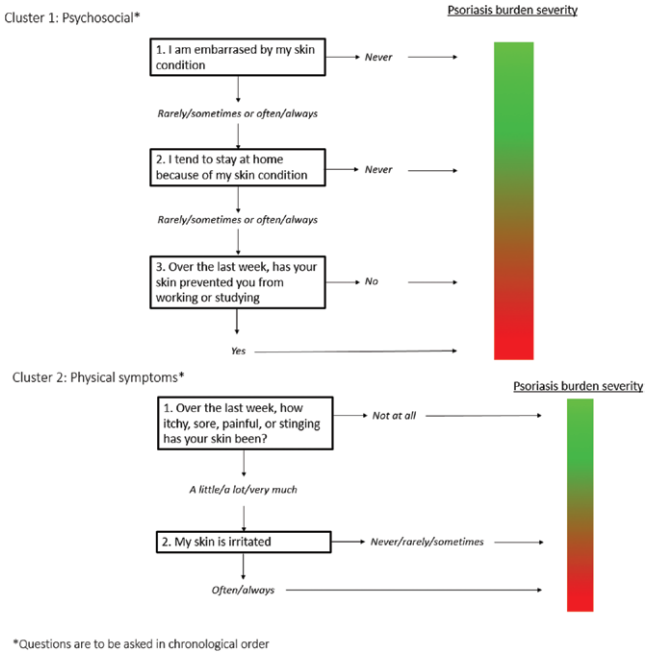


Figure 1. Flowchart of questions assessing psoriasis burden.

Conclusion: We have created a practical guide for rheumatologists to distinguish PsA patients with a high psoriasis burden from those with a lower burden. With a minimum of two and a maximum of five questions, both psychosocial burden of psoriasis and burden of physical symptoms can be easily identified in daily clinical practice.

REFERENCES:

[1] Kasiem FR, Kok MR, Tchetverikov I, Wervers K, Hazes J, Luime J, et al. AB0786 Impact of psoriasis severity on Health-Related Quality of Life in early psoriatic arthritis: results from real world data, the DEPAR study. Annals of the Rheumatic Diseases. 2020;79:1691-2.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2477

HPR - Adapting and individualising care

POS0152-HPR

REMOTE CLINICAL MANAGEMENT: INCORPORATING ELECTRONIC ASSESSMENT OF PATIENTS WITH RHEUMATIC DISEASES INTO STANDARD CLINICAL PATHWAYS DURING THE COVID-19 PANDEMIC: A PILOT STUDY

T. Malley[1], J. Jackman[1], S. Manderson[1], L. Saldana Pena[1], E. Evans[1], J. Barrett[2], A. Soni[2], R. Luqmani[2]. [1]*Nuffield Orthopaedic Centre, Rheumatology, Oxford, United Kingdom*; [2]*The Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Rheumatology, Oxford, United Kingdom*

Background: Many patients with rheumatic disease require immunosuppressive medication putting them at high risk of COVID-19 infection. Reduced staffing in rheumatology due to redeployment to COVID-19 work, limited out patient capacity and patient vulnerability have had a major impact on our ability to review our patients to assess their condition and treatment (by face-to-face, video or telephone consultations). Novel strategies are essential to safely and effectively treat patients with rheumatic disease whilst minimising their risk of exposure to COVID-19 infection.

Objectives: The objective was to develop a digital solution to help deliver safe, efficient and effective care for patients with rheumatic diseases. The aim was to produce a system that allowed us to integrate data recorded directly by patients with information held in our electronic health records to provide a virtual review of care.

Methods: An online questionnaire was used to collect clinical information, including validated disease activity measures, to conduct a remote assessment in 175 patients awaiting follow-up appointments. This assessment was integrated within our electronic health records (EHR). The questionnaire contained measures of disease activity (DAS28 or BASDAI); patient reported outcomes; patient preferences regarding the urgency and type of appointment; any recent problems or changes in medication. This information was imported into a database for clinician review, together with previous clinical records and results of relevant investigations, to inform clinical decisions and to decide on the safest and most appropriate timing for follow-up. Report letters were sent to the patient and their primary care providers.

Results: Of the 175 patients (149 with RA and 26 with AS), 108 patients (89/149 [60%] with RA [mean age=64; female=65%] and 19/26 [73%] with AS [mean age=45; female=54%]) submitted responses over a 6-week period based on which clinical decisions were made. The mean questionnaire completion time was 19 minutes for RA responders and 16 minutes for AS responders. Non responders (67/175 [mean age=61; female=63%]) remained on our list of patients awaiting follow-up arrangements to be made. Sixty-nine responders (64%) had stable disease therefore did not require any changes to their treatment and were offered an appointment within the next 6 months, of whom 12 (11%) requested face-to-face follow-up. Of the remaining 39 – with less stable disease – requiring more rapid follow-up assessment, 22 patients (56%) required a face-to-face consultation to consider treatment change. So far 9 of these patients have had follow-up, of whom 6 necessitated treatment escalation (Methotrexate increase n=2; anti-inflammatory increase n=2; intramuscular steroid n=1; anti-TNF escalation n=1). Thirty-nine patients (36%) provided feedback on the process of completing the questionnaire, 85% of whom used a mobile phone and the remainder used a computer or tablet. The majority (70%) found it "extremely easy" or "somewhat

easy" to complete; remaining responses: "neutral" 20%, "somewhat difficult" 10%, "extremely difficult" 0%.

Conclusion: We have created and tested a system of remote clinical management for patients with RA and AS. Amongst the 108 responders, just 31% required a face-to-face appointment, with treatment changes made accordingly. With a backlog of 3,800 awaiting allocation to follow-up appointments, remote clinical management will allow us to safely and efficiently prioritise patients requiring urgent follow-up for treatment optimisation. We will integrate this system into our standard care pathway beyond the COVID-19 pandemic to streamline our service, deliver effective care and provide evidence to support the use of costly biologic drugs.[1] We plan to investigate the barriers for non-responders.

REFERENCES:

[1] Holroyd CR, Seth R, Bukhari M, et al. The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis. Rheumatology. 2019; 58 (2): e3–e42.

Disclosure of Interests: Tamir Malley: None declared, John Jackman: None declared, Sarah Manderson: None declared, Larissa Saldana Pena Grant/research support from: Pfizer's Global Medical Grants program, Ellie Evans: None declared, Joe Barrett Grant/research support from: Pfizer's Global Medical Grants program, Anushka Soni Grant/research support from: Pfizer's Global Medical Grants program, Raashid Luqmani Grant/research support from: Pfizer's Global Medical Grants program

DOI: 10.1136/annrheumdis-2021-eular.309

POS0153-HPR IDENTIFYING TARGETS FOR BEHAVIOURAL INTERVENTIONS IN FIBROMYALGIA: PHYSICAL ACTIVITY BEHAVIOUR

K. Mayana[1], Y. Prior[2]. [1]*University of Salford, School of Health and Society, Manchester, United Kingdom*; [2]*University of Salford, School of Health and Society, Salford, United Kingdom*

Background: There has been much interest in the efficacy of exercise and physical activity interventions in people with Fibromyalgia. This has resulted in guidelines recommending exercise as the first line of management (Macfarlane et al., 2017). Notwithstanding the efficacy of exercises, adherence to structured exercise and interventions aiming to increase physical activities remains a considerable challenge in this population. Exploring behavioural factors that may hinder exercise and physical activity participation in people with Fibromyalgia may help to identify targets for interventions to improve adherence and engagement with physical activities and support self-management.

Objectives: To explore people with Fibromyalgia's perspectives on the personal, social and contextual factors impacting their physical activity behaviour and pain perception.

Methods: Twelve participants with Fibromyalgia were recruited from Social Media, Fibromyalgia charities, organisations and associations across the UK. Semi-structured, one-to-one in-depth telephone interviews were conducted with each participant. Interviews were audio-recorded and transcribed verbatim. Qualitative data analysis was conducted by two researchers independently, using Thematic Analysis. Critical Realism framework was employed to inform the interpretation of the findings.

Results: Four main themes emerged from the data: (i) Lack of guidance on physical activity: most participants expressed increased pain intensity following a vigorous physical activity which, have led to spending more time on sedentary behaviour to recover from pain. (ii) Participants expressed fear of fatigue as a barrier to physical activity participation: This also led to increased sedentary and protective behaviours. (iii) Impact of treatments on physical activity: Participants who received multimodal therapies and patient education reported better coping strategies e.g., pacing physical activities and less pain. (iv): Impact of social support on physical activity participation: Participants felt that a lack of understanding from employers, their family and friends and the wider society has negatively impacted their physical activity behaviours, access to workplace support and psychological wellbeing.

Conclusion: A multimodal approach, incorporating patient education with behavioural components is essential to increase adherence to and engagement with exercise and physical activity interventions to support self-management of Fibromyalgia. There is a need to improve the public perception of this syndrome to increase social and workplace support.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3239

POS0154-HPR FACTORS FACILITATING THE SELF- AND SHARED-MANAGEMENT OF JIA BY CHILDREN, YOUNG PEOPLE, THEIR FAMILIES, AND PROFESSIONALS INVOLVED IN THEIR CARE: A REALIST EVALUATION

S. Stones[1], V. Swallow[2], L. Milnes[1]. [1]*University of Leeds, School of Healthcare, Leeds, United Kingdom*; [2]*Sheffield Hallam University, Department of Nursing & Midwifery, Sheffield, United Kingdom*

Background: Juvenile idiopathic arthritis (JIA) is a long-term condition, often requiring some element of lifelong management. Therefore, it is logical that children and young people are empowered to become competent at self-managing their health and wellbeing, while families are supported in their shared-management role during childhood, relinquishing control at age- and developmentally appropriate periods in their child's development. However, there are limited theoretical foundations underpinning optimal self- and shared-management support for children, young people and families living with JIA.

Objectives: To explain the factors facilitating the self- and shared-management of JIA by children, young people, and their families, with professional support from healthcare professionals, third sector organisations, and education professionals.

Methods: Guided by the Individual and Family Self-management Theory and the Shared Management Model, a three-stage realist evaluation was undertaken: 1) initial JIA self- and shared-management question theories were elicited from a document review, integrative review, and stakeholder insights [1]; 2) seven initial question theories were tested using qualitative research methods with 20 participants (young people, families, healthcare professionals, education professionals, and third sector representatives); 3) analysis of findings using a theory-driven approach to thematic analysis, in order to identify demi-regularities to extend or refute the initial question theories. The analysis drew on deductive, inductive, and retroductive reasoning.

Results: There were six refined JIA self- and shared-management question theories: 1) meaningful and bespoke self-management support across the life course for children and young people with JIA; 2) recognised and valued shared-management support for the families of children and young people with JIA, with autonomy in mind; 3) individual healthcare plans as a shared management communication tool to facilitate optimal management of JIA; 4) consistent recognition, value, and encourage of self- and shared-management support from the paediatric rheumatology multi-disciplinary team and associated professionals; 5) child, young-person, and family-focused paediatric rheumatology care and support services across the lifecourse; and 6) bespoke and inclusive approaches by education providers to enable children and young people with JIA to feel safe, supported, and able to fulfil their potential.

Conclusion: There is an increasing recognition of the importance of self- and shared-management of JIA. However, there is a lack of an overall, cohesive approach to self- and shared-management between healthcare providers, education providers, and the third sector. Findings from this study illuminate the factors facilitating JIA self- and shared-management at individual, interpersonal, institutional and infrastructural levels. Further work is required to empirically test these refined question theories with interventions designed to enhance JIA care, education, and support.

REFERENCES:

[1] Stones et al. (2020). A realist approach to eliciting the initial programme theories for the self- and shared-management of juvenile idiopathic arthritis by children, young people, families and professionals involved in their care. Pediatric Rheumatology 18(Suppl 2): O062.

Acknowledgements: The authors thank all of the participants who helped to shape the findings of this study. This work formed part of a PhD study funded by the University of Leeds.

Disclosure of Interests: Simon Stones Speakers bureau: Janssen, Consultant of: Parexel, Envision Pharma Group, 67 Health, On The Pulse Consultancy, Veronica Swallow: None declared, Linda Milnes: None declared

DOI: 10.1136/annrheumdis-2021-eular.1286

POS0155-HPR DIAPHRAGMATIC BREATHING RELAXATION TECHNIQUE TO DECREASE ANXIETY DURING JOINT INFILTRATION: A RANDOMIZED CONTROLLED TRIAL

R. Ben Aissa[1,1], S. Boussaid[2], H. Tbini[2], H. Sahli[1], S. Jemmali[1], S. Rekik[1], M. El Euch[2]. [1]*Rabta Hospital, Department of Rheumatology, Tunis, Tunisia*; [1]*Rabta Hospital, Department of Rheumatology, Tunis, Tunisia*

Background: Joint infiltration is the injection of therapeutic substances directly into a joint. It may be a stressful experience for patients as imagined different from other usual injections. Several techniques are used to manage anxiety and pain during such a procedure.

Objectives: To evaluate the effectiveness of diaphragmatic breathing relaxation on reducing anxiety and pain during joint infiltration.

Methods: Patients scheduled for a joint infiltration at the rheumatology department's daycare unit were recruited. All infiltrations were performed using steroids without anesthetic therapy except for the hip. Patients were randomized into two groups (cases=38, controls=34). Cases learned from a trained health agent diaphragmatic breathing relaxation technique to perform it immediately before and during the procedure while controls received the usual procedure. We used the Visual Analogue Scale (VAS) to assess self-estimated both anxiety (VAS-Anx) and pain (VAS-Pain) as evaluated on pre and post-joint infiltration. VAS-Pain was evaluated as expected then as experienced respectively on pre and

post-infiltration. We also assessed heart rate and blood pressure on pre and post-procedure.
Results: Seventy-two participants were included with a mean age of 55.48 ± 12.39 years (39-78), treated for an inflammatory rheumatic or degenerative disease (21, 51 respectively), and receiving joint infiltration for the first time among 37. Sites of infiltrations were: wrist=7, elbow=10, shoulder=17, hip=1, knee=22, epidural=6, plantar heel=9. There were no significant differences in pre-procedural
VAS-Anx, VAS-pain, or physiological parameters between cases and controls. Cases had a significant decrease in VAS-Anx from pre to post-infiltration (Mean post-VAS-Anx=23.33/100, p=0,017) but not significant compared with controls (p=0.297). Patients who have performed the breathing technique had no significant decrease in VAS-Pain from pre- to post-infiltration (p=0.083) and compared with controls (p=0.662). Physiological parameters showed a significant decrease in heart rate of cases from pre to post-infiltration (p<0,0001) and compared with controls (p=0,036), but no significant decrease in systolic or diastolic blood pressure from pre to post-infiltration and compared with controls. There were no correlations between all participants' VAS-Anx/VAS-Pain and age, gender, infiltration site or history and joint pain causes.
Conclusion: This study suggests that diaphragmatic breathing relaxation is an effective nonpharmacological intervention that could be used in controlling anxiety and experienced pain during joint infiltration.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2861

POS0156-HPR 'THE RIGHT ADVICE, IN THE RIGHT WAY AND AT THE RIGHT TIME': AN INNOVATIVE MULTIDISCIPLINARY APPROACH TO ADDRESS CLIENT-IDENTIFIED PARTICIPATION NEEDS IN EARLY INFLAMMATORY ARTHRITIS

Y. Codd[1,2], R. Mullan[2], D. Kane[2], A. Coe[2], T. Stapleton[1]. *[1]Trinity College Dublin, Discipline of Occupational Therapy, School of Medicine, Dublin, Ireland*; *[2]Naas General & Tallaght University Hospitals, Rheumatology, Dublin, Ireland*

Background: Inflammatory arthritis (IA) is a complex life-long disease with negative consequences on occupational performance and significant impact on meaningful life roles. International guidelines for the clinical management of IA consistently recommend early intervention and a multidisciplinary (MDT) approach as the optimum method to address the medical, symptom and broader life impacts, however, barriers to timely access to the MDT is a common issue in clinical practice. Limited research has explored how clinical services support broader life impacts and participation restrictions associated with early disease as part of routine healthcare. Four rheumatology services in Ireland have recently reconfigured to provide an MDT-led early arthritis service which operates in parallel to traditional medical clinics. Staffed by nurses, occupational therapists, and physiotherapists this service provides assessment and management to clients with a new diagnosis of IA along a model of care within four to six weeks of diagnosis with mechanisms to follow the client over their first year of diagnosis.
Objectives: To explore how a novel MDT-led early arthritis service addresses client-identified participation restrictions associated with early IA.
Methods: A qualitative description (QD) study was used to explore the perspectives of service providers and service users of this MDT-led early arthritis service. Data were gathered using one-off focus groups with service providers, and individual interviews with service users.
Results: All staff (n=15) currently working in these services participated in the focus groups. Forty-three service users with IA participated in individual interviews (males n=12: females n=31); diagnosis duration ranged from 5 to 24 months. QD principles and thematic analysis were used in data analysis.
Extensive limitations in everyday activity and restriction in participation in meaningful, age-appropriate life roles in early IA were outlined by service users and service providers. Participants described how the MDT-led model provided automatic and immediate access to services focussed on identification and management of occupation-based participation restrictions early in the disease. Participants described how the model used a flexible approach that ensured; ease of early access to a full MDT, prolonged support from the MDT, and a person-centred approach incorporating social prescribing and self-management principles. Service users emphasised the strength of the MDT approach of providing 'the right advice, in the right way and at the right time' as the most influential feature that assisted them to address participation restrictions and support positive health outcomes. This was accomplished by the service providers acting in a coordinated and interdisciplinary manner with a clear remit to address participation restrictions alongside the traditional symptom management approach. Findings highlight the feasibility of the MDT-led early arthritis model as an approach to address participation-based restrictions as part of routine healthcare that delivers on the rheumatology guidelines and was positively regarded by both service users and service providers.
Conclusion: Findings provide important insights into the role of an innovative early MDT intervention approach in addressing client-identified participation needs in early IA. This model maps onto the Irish rheumatology model of care (HSE, 2018), 'right place, right time' approach but importantly includes a 'right way' approach which is identified as influential in the effective delivery of client-focussed and client-centred care.
REFERENCES:
[1] HSE. (2018). Model of care for rheumatology in Ireland. Retrieved 15/09/2019, https://www.hse.ie/eng/about/who/cspd/ncps/rheumatology/achievements/model-of-care-for-rheumatology-in-ireland.pdf
Acknowledgements: The authors, thank you to the research sites who facilitated this study & the service providers and service users who partook in the research. Thank you to Kildare Branch of Arthritis Ireland who provided funding support for the research
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.583

POS0157-HPR CONSTRUCT VALIDITY OF THE OCTOPUS STRATIFICATION ALGORITHM FOR ALLOCATING PATIENTS WITH KNEE OSTEOARTHRITIS INTO CLINICALLY RELEVANT SUBGROUPS

J. Knoop[1], R. Ostelo[1], M. Van der Esch[2], A. De Zwart[2], K. Bennell[3], M. Van der Leeden[2,4], J. Dekker[4]. *[1]Vrije Universiteit Amsterdam, Health Sciences, Amsterdam, Netherlands*; *[2]Reade, Centre for Rehabilitation and Rheumatology, Amsterdam, Netherlands*; *[3]University of Melbourne, School of Health Sciences, Department of Physiotherapy, Melbourne, Australia*; *[4]Amsterdam UMC (VUmc), Department of Rehabilitation, Amsterdam, Netherlands*

Background: We recently developed a model of stratified exercise therapy [1], consisting of (i) a stratification algorithm allocating patients with knee osteoarthritis (OA) into clinically relevant subgroups, and (ii) subgroup-specific exercise therapy. More specifically, in our model we distinguish the following subgroups with proposed underlying phenotypes: 'high muscle strength subgroup' representing a post-traumatic phenotype, 'low muscle strength subgroup' representing an age-induced phenotype and 'obesity subgroup' representing a metabolic phenotype.
Objectives: In the present study, we aimed to validate the construct of this algorithm, focusing on 3 research questions: (i) are the proportions of patients in each subgroup similar across cohorts?; (ii) are the characteristics of each of the subgroups in line with their proposed underlying phenotypes?; (iii) are the effects of usual exercise therapy in the 3 subgroups in line with the proposed effect sizes?
Methods: Data from five studies (four trials and one cross-sectional cohort) were used to validate the construct of our algorithm by 63 a priori formulated hypotheses regarding the research questions.
Results: Baseline data from a total of 1,211 patients with knee OA were analyzed for the first and second research question, and follow-up data from 584 patients who were part of an exercise arm within a trial for the third research question. In total, the vast majority (73%) of the hypotheses were confirmed. Regarding our first research question, we found similar proportions in each of the three subgroups across cohorts, especially for three cohorts. Regarding our second research question, subgroup characteristics were almost completely in line with the proposed underlying phenotypes. Regarding our third research question, unexpectedly, usual exercise therapy resulted in similar, moderate to large effect sizes for knee pain and physical function for all three subgroups.
Conclusion: This study suggests that our algorithm might be a valid instrument to allocate patients with knee OA into clinically relevant subgroups, as most of our a priori hypotheses could be confirmed. On the other hand, subgroups did not differ substantially in effects of usual exercise therapy, contrary to our expectation. An ongoing trial [1] will assess whether this algorithm accompanied by subgroup-specific exercise therapy improves clinical and economic outcomes.
REFERENCES:
[1] Knoop J, Dekker J, van der Leeden M, de Rooij M, Peter WFH, van Bodegom-Vos L, van Dongen JM, Lopuhäa N, Bennell KL, Lems WF, van der Esch M, Vliet Vlieland TPM, Ostelo RWJG. Stratified exercise therapy compared with usual care by physical therapists in patients with knee osteoarthritis: A randomized controlled trial protocol (OCTOPuS study). Physiother Res Int. 2020 Apr;25(2):e1819. doi: 10.1002/pri.1819. Epub 2019 Nov 28.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1515

POS0158-HPR UNDERSTANDING NURSE-LED CARE IN EARLY RA: INTERVIEW STUDY WITH RHEUMATOLOGY NURSE SPECIALISTS

A. M. T. Sweeney[1], J. Robson[1], C. Flurey[1], P. Richards[1], C. Mccabe[1], M. Ndosi[1]. *[1]University of the West of England, Faculty of Health and Applied Sciences, Bristol, United Kingdom*

Background: Nurse-led care in early RA is not well defined in the literature and the current recommendations.
Objectives: This study aimed to develop an understanding of what comprises nurse-led care in early RA from the perspective of rheumatology nurse specialists.
Methods: This was a qualitative study using semi-structured telephone interviews with rheumatology nurse specialists in England (Summer 2020). Interviews were audio-recorded, transcribed verbatim and analysed using inductive thematic analysis.[1]
Results: Sixteen nurses were recruited and interviews lasted between 30 to 60 minutes. Seven themes were identified.
Early disease management
Care was characterised by evidence-based RA management provided by experienced nurse specialists with a high degree of autonomy, in the context of a rheumatology multidisciplinary team. The aims of care were to: start treatment, keep in treatment, educate and support.
'So treat to target...escalating treatment as necessary, and addressing any concerns that the patients might have' (CNS14)
Addressing psychosocial needs
Patients with early RA experience shock, fear, anger, grief and denial while feeling unwell with pain and fatigue. Nurses use a holistic, person-centred and empathetic approach to address psychosocial needs, building a working relationship, listening and creating trust.
'Because it all relates, and if they're stressed because they're not coping at work, then their arthritis isn't going to be so good. So everything relates to one another really' (CNS06)
Monitoring treatment, disease impact and patient outcomes
Nurses monitor disease activity and disease impact using validated outcome measures and by asking questions during the consultation. Good outcomes are disease control, managing disease impact, medication and side effects, wellbeing and keeping in work.
'When you get them stable, when you get them into remission, when they're happy, when they're feeling well, I think there's lots of ways you can measure that'… (CNS13)
Coordinating care, referring and signposting
Nurses coordinate care, refer to other health professionals and signpost patients to relevant services and charities. Lack of access to psychology expertise was highlighted.
'And whilst most of us have got some degree of understanding of…self management, or psychology…we're not psychologists' (CNS02)
Providing a 'lifeline'
Nurse-led telephone advice services provide a 'lifeline' for patients. If patients struggle, they can call and speak with a specialist who knows them and their RA well.
'The advice line has been a lifeline to them, to be able to speak to someone, to be able to get a response quickly to their questions, they feel very well supported, they know that they can always call us' (CNS16)
Service evaluation and auditing
The individual clinics are reviewed regularly. Patients are asked for feedback on their experience of appointments, if their needs were met and about changes to the service.
...'It's really important to ask them initially what they expect to have from the consultation...We've always had really good feedback in general'… (CNS02)
COVID-19 challenges and opportunities
The pandemic caused major disruptions to the services, prohibiting most face-to-face consultations which was an essential aspect of clinical assessments. Despite the challenges imposed by the pandemic, the services adapted fast, using telephone, video clinics and digital solutions, which streamlined procedures and improved documentation and communication.
'I do have to rely on them telling me what's going on, because I can't see it at the moment' (CNS14)
'With Covid we're doing it over the telephone, and we're getting them to watch the video [injection tutorial] before we have the appointment with them' (CNS04)
Conclusion: Nurse-led care in early arthritis is a specialist service, addressing complex needs of patients, using evidence based and person-centred approaches. Innovation and service improvement are seen as part of the role.
REFERENCES:
[1] Braun V, Clarke V. *Successful Qualitative Research*. First edition. London: SAGE 2013.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.555

POS0159-HPR IMPACT OF SLEEP DISTURBANCES ON ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

M. Sellami[1], O. Hamdi[1], S. Miladi[2], A. Fazaa[2], L. Souabni[2], K. Ouenniche[2], S. Kassab[2], S. Chekili[2], K. Ben Abdelghani[2], A. Laatar[2]. [1]*Mongi Slim Hospital, Rheumatology, Tunisia, Tunisia*; [1]*Mongi Slim Hospital, Rheumatology, Tunisia, Tunisia*

Background: Sleep disturbances have been reported in various rheumatic diseases especially in the elderly. It may be caused by pain and depressive mood. However, reports on the impact of sleep problems in rheumatoid arthritis (RA) activity and functional status were limited.
Objectives: To assess sleep quality in elderly patients with RA and its impact on disease activity and functional status.
Methods: This cross-sectional study included 70 RA patients aged ≥ 65 years fulfilling the ACR/EULAR criteria. Sociodemographic data were collected. RA activity was assessed with the Disease Activity Score (DAS_{28}) and functional status with the Health Assessment Questionnaire (HAQ). Sleep quality was assessed using Arabic translated versions of two indexes: the Insomnia Severity Index (ISI) and the Pittsburg Sleep Quality Index (PSQI). An ISI score of [8-14], [15-21], and [22-28] determined respectively mild, moderate, and severe insomnia. A PSQI score > 5 determined poor sleep quality. ANOVA test was used to assess the relationship between DAS_{28} erythrocyte sedimentation rate (ESR), HAQ, and sleep quality indexes.
Results: This study included 52 females and 18 males with a mean age of 68.3 ± 25 years [65-81]. Seventy percent of patients were married, 27% were widowed and 2% were divorced. Seventy-one percent of patients were illiterate, 18% had primary education and 11% had secondary education. Eighteen percent of patients were employed whereas 34.7% were retired. A history of depression was noted in 16.5% of patients. The mean duration of RA was 17.4 ± 5.2 years. Eighty-five percent of patients were on conventional synthetic DMARD whereas 15% were treated with biologic treatment. The mean patient's global assessment of disease activity was 5.2 ± 1.3. The mean tender joint count and mean swollen joint count were 8 ±1.5 and 5 ±1 respectively. The mean DAS_{28} ESR was 4.7 ±0.9. The mean HAQ was 2.4 ± 0.45. Poor sleep quality was detected in 84% of cases according to the PSQI score. Mild insomnia was detected in 46% of cases, moderate insomnia in 34% of cases, and severe insomnia in 12% of cases. RA activity was higher in patients with poor sleep quality: the mean DAS_{28} ESR was 5.2 in patients with severe insomnia, 4.82 in moderate insomnia, and 4.13 in mild insomnia; p= 0.00 respectively. The mean ESR was 31.5 mm in patients with severe insomnia, 22.1 mm in moderate insomnia, and 10.6 mm in mild insomnia; p= 0.01 respectively. Furthermore, the higher the PSQI was, the higher DAS_{28} ESR is (p =0.01). However, no association was found between poor sleep quality and joint count, swollen joint count, CRP, and HAQ.
Conclusion: Disease activity was a major contributor to poor sleep quality in elderly patients with RA. Functional status however wasn't associated with insomnia. Physicians should include sleep in the clinical assessment of RA patients to improve their quality of life.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.408

POS0160-HPR THE CARE PROCESS OF HIP AND KNEE OSTEOARTHRITIS: GIVING AN ACCOUNT OF PATIENTS' EXPERIENCE

S. Battista[1,2], M. Manoni[1], A. Dell'isola[2], M. Englund[2], A. Palese[3], M. Testa[1]. [1]*University of Genova, Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, Savona, Italy*; [2]*Lund University, Clinical Epidemiology Unit, Orthopedics, Department of Clinical Sciences, Lund, Sweden*; [3]*University of Udine, School of Nursing, Department of Medical Sciences, Udine, Italy*

Background: The care process is often a complex and intimate process experienced by patients. Osteoarthritis (OA) care is usually characterised by multimodal interventions that consider the broader array of symptoms and functional limitations and often require a high level of patients' compliance. Despite efforts to improve the quality of care of patients suffering from OA, and the publication of state-of-the-art clinical practice guidelines [1], the quality of the care process, as experienced by patients, seems to be suboptimal [2]. Hence, it is essential to investigate how patients experience this process to highlight potential elements that can enhance or spoil it to optimise the care quality.
Objectives: To explore the patients' experience of the received OA care process.
Methods: Qualitative study, 10 semi-structured interviews were performed. The interview guide was created by a pool of healthcare professionals (physiotherapists, psychologists, nurses) and expert patients. It investigated the emotional experience, beliefs, expectations, perceived barriers and facilitators towards conservative treatments perceived by patients suffering from OA. The interviews lasted approximately one hour, were transcribed verbatim and analysed independently by two authors, who labelled their core parts to find categories and subcategories. A theme-based analysis was performed following an ecological paradigm, naturalistic epistemology, philosophy of phenomenological research.
Results: Our analysis revealed 7 main categories with several subcategories (Fig. 1). 1) *Uncertainty* as some patients perceived treatment choice not to be

based on medical evidence "there is an almost religious way of thinking on how to deal with the pathology. It is not an exact science when you choose the physicians you choose the treatment". 2) *Relationship with the self and the others* as some patients did not feel understood or even shameful and hopeless about their condition. 3) *Patients' and Health Professionals' beliefs about the pathology management* where common thoughts were the perceived (ab)use of passive therapies, the movement as something dangerous and that OA is "something that you try to resist to, but (surgery) is your destiny". 4) *facilitators and 5) barriers of the adherence to therapeutic exercise* that revolve around the cost of the therapy, the time needed and the willingness to change life habits. 6) *Patients' attitudes towards pathology* in which the oldest patients perceive OA as "something I have to accept since I am getting old" and the youngest as "Something I have to fight". 7) *Relationship with food* in which diet is seen as something that "you force yourself to follow" which is useful only to lose weight and not to preserve a high health status and where overeating is used "to eat your feelings".

Conclusion: Patients suffering from hip and knee OA seem to experience an uncertain care process. The lack of clear explanations and the attitude towards conservative treatment, which is considered as "a pastime while waiting for surgery," fosters the importance of providing patients with adequate information about the treatment, to shift their beliefs and improve their awareness. This will enhance a patient-centred and shared decision-making treatments.

REFERENCES:

[1] Fernandes L, Hagen KB, Bijlsma JWJ, *et al.* EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Ann. Rheum. Dis. 2013;**72**:1125–35.

[2] Basedow M, Esterman A. Assessing appropriateness of osteoarthritis care using quality indicators: a systematic review. *J Eval Clin Pract* 2015;**21**:782–9.

Figure 1. Categories and Subcategories stemmed from the analysis of the patients' interviews

Acknowledgements: This work is part of the project funded by EULAR Health Professionals Research Grant 2020.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.843

POS0161-HPR BARRIERS AND FACILITATORS RELATED TO SELF-MANAGEMENT OF SHOULDER PAIN: A SYSTEMATIC REVIEW AND QUALITATIVE SYNTHESIS

A. O'shea[1], J. Drennan[2], C. Littlewood[3], H. Slater[4], J. Sim[5], J. Mcveigh[1].
[1]*University College Cork, Discipline of Physiotherapy, College of Medicine and Health, Cork, Ireland*; [2]*University College Cork, School of Nursing and Midwifery, College of Medicine and Health, Cork, Ireland*; [3]*Manchester Metropolitan University, Department of Health Professions, Faculty of Health, Psychology & Social Care, Manchester, United Kingdom*; [4]*Curtin University, School of Physiotherapy and Exercise Science, Perth, Australia*; [5]*Keele University, School of Medicine, Faculty of Medicine and Health Sciences, Keele, United Kingdom*

Background: Shoulder pain is a significant cause of pain and disability in the general population.[1] Current research suggests that shoulder pain can be resistant to treatment and is often recurrent.[2] Systematic review-level evidence shows modest short-term benefits for most current treatments.[3] Effective self-management strategies that equip patients with the necessary tools to self-manage their condition are urgently required. However, engagement with self-management is poor, potentially compromising treatment outcomes and contributing to ongoing disability.[4]

Objectives: The objectives of this review were to:

• Systematically identify and appraise relevant qualitative evidence on barriers and facilitators relating to self-management from the perspectives of people with shoulder pain and healthcare professionals.

• Collate and synthesise this evidence, to gain an understanding of factors that influence self-management of shoulder pain.

• Develop evidence-based recommendations to inform the implementation and delivery of self-management programmes for shoulder pain.

Methods: A meta-aggregative approach to the synthesis of qualitative evidence was used. Twelve databases were searched, from inception to 13 July 2020, to identify studies exploring barriers and facilitators related to self-management of shoulder pain from the perspectives of people with shoulder pain and clinicians involved in the care of such patients. Two independent reviewers identified eligible articles, extracted the data and conducted critical appraisal. Two reviewers independently identified and developed categories, with validation by two further researchers. Categories were discussed among the wider research team and a comprehensive set of synthesized findings was derived.

Results: Sixteen studies were included in the review, exploring several shoulder conditions: shoulder instability; rotator cuff-related pain; dysfunction post rotator cuff surgery; and degenerative rotator cuff tears. From the perspective of patients, three synthesized findings were identified that influenced self-management: (1) support for self-management, including subthemes related to patient-centred support, knowledge, time, access to equipment, and patient digital literacy; (2) personal factors, including patient beliefs, patient expectations, patient motivation, pain, and therapeutic response; and (3) external factors, including influence of the clinician and therapeutic approach. From the perspective of clinicians, two synthesized findings were identified that influenced adherence to self-management: (1) support for self-management, including education, patient-centred support, patient empowerment, time, and clinician digital literacy; and (2) preferred management approach, including clinician beliefs, expectations, motivation, therapeutic approach, and therapeutic response.

Conclusion: Patients and clinicians identified several barriers and facilitators that influenced self-management of shoulder pain. Clinicians' awareness of these factors could positively influence patient management, enhance patients' ability to self-manage, and improve treatment outcomes.

REFERENCES:

[1] Walker-Bone K, Palmer KT, Reading I, Coggon D, Cooper C. Prevalence and impact of musculoskeletal disorders of the upper limb in the general population. *Arthritis and Rheumatism.* 2004;51(4): 642-651.

[2] Croft P, Pope D, Silman A. The clinical course of shoulder pain: prospective cohort study in primary care. Primary Care Rheumatology Society Shoulder Study Group. *British Medical Journal.* 1996;313(7057): 601-602.

[3] Littlewood C, May S, Walters S. A review of systematic reviews of the effectiveness of conservative interventions for rotator cuff tendinopathy. *Shoulder & Elbow.* 2013;5(3): 151-167.

[4] Littlewood C, Malliaras P, Mawson S, May S, Walters S. Patients with rotator cuff tendinopathy can successfully self-manage, but with certain caveats: a qualitative study. *Physiotherapy.* 2014;100(1): 80-85.

Disclosure of Interests: Aidan O'Shea: None declared, Jonathan Drennan: None declared, Chris Littlewood: None declared, Helen Slater Speakers bureau: AbbVie PTY LTD 2018, Julius Sim: None declared, Joseph McVeigh: None declared

DOI: 10.1136/annrheumdis-2021-eular.1279

Metabolic bone disease / Osteoporosis

POS0162 PREDICTIVE FACTORS OF A NEW FRAGILITY FRACTURE AFTER WRIST FRAGILITY FRACTURE

S. Azevedo[1], H. Parente[1], D. Esperança Almeida[2], F. Guimarães[1], J. Rodrigues[1], D. Faria[1], D. Peixoto[1], J. Tavares-Costa[1], C. Afonso[1], F. Teixeira[1].
[1]*Unidade Local de Saúde do Alto Minho, Rheumatology Department, Ponte de Lima, Portugal*; [2]*Hospital de Braga, Rheumatology Department, Braga, Portugal*

Background: Fragility fractures (FF) are fractures that result from mechanical forces that would not ordinarily result in fracture, known as low-level (or 'low energy') trauma.[1] Studies have shown that history of wrist fracture increases the risk for subsequent FF.[2]

Objectives: To assess predictive factors of FF occurring after a wrist fracture.

Methods: Retrospective monocentric study that included patients with a wrist FF observed at the emergency department (ED) in a tertiary center, between 1st January 2017 and 31st December 2018. Wrist fractures were identified through the 10th International Classification of Diseases and FF were identified after revision of the clinical record. Patients with relevant missing data were excluded. Seven hundred thirty-three wrist FF were identified. After calculating a representative sample (90% confidence interval), 188 patients were included. Their clinical records until 31th December 2020 (2 to 3 years after FF) were reviewed. SPSS was used for statistical analysis and significance level was defined as 2-sided $p<0.05$. In multivariate analysis we included variables with a significant association in univariate analysis and those with clinical relevance (reported in others studies).

Results: Wrist fractures represented 44.3% of the FF observed at the ED.

Most patients were woman (83.5%) with a mean age of 70.7 (SD=11.2) years-old at the time of their wrist fracture. A previous FF was seen in 22.9% of patients and 13.3% had a new FF during the follow-up period.
We found an association between the occurrence of a new FF and the number of comorbidities (p=0.012), number of visits to the ED due to falls (p<0.001), previous diagnosis of chronic pulmonary disease (p=0.029) and hematologic pathologies (p=0.047), and the need for hospitalization at time of the wrist FF (p=0.018). No associations were found between the age at the wrist fracture time, number of drugs taken daily nor its type (anxiolytics, antiepileptics, corticoids), previous fractures (and localization), overweight/obesity and other cardiovascular risk factors, endocrinopathies, psychiatric or neurologic disease or other comorbidities.
After adjustment for age, gender, anti-osteoporotic treatment and comorbidities, the main predictors of a new FF were visits to the ED for falls (p=0.005), chronic pulmonary disease (p=0.040), hematologic pathologies (p=0.004) and need for hospitalization (p=0.040) (table 1).

Table 1. Multivariate analyses: linear multiple regression for predictive factors of new fragility fracture.

Determinants	Unstandardized Coefficients B	Standardized Coefficients Beta	95.0% CI	p-value
Age	-0.025	0.975	0.924 – 1.030	NS
Gender	2.065	7.889	0.757 – 82.165	NS
Number of comorbidities	0.186	1.204	0.846 – 1.713	NS
Visits to the emergency service for falls	-2.136	0.118	0.026 – 0.529	0.005
Chronic pulmonary disease	-1.326	0.266	0.075 – 0.940	0.040
Hematologic pathologies	-4.296	0.014	0.001 – 0.255	0.004
Need for hospitalization	-2.764	0.063	0.004 – 0.887	0.040
Anti-osteoporotic treatment	0.157	1.170	0.227 – 6.017	NS

CI: Confidence Interval; NS: non-significant;

Conclusion: Certain comorbidities seem to be associated with new FF. Patients with visits to the emergency service after falls and those who needed hospitalization due to the wrist fracture were more prone to have a new FF. There might be a substantial missed opportunity for intervention in these patients.
REFERENCES:
[1] Osteoporosis: assessing the risk of fragility fracture. London: National Institute for Health and Care Excellence (UK); 2017 Feb. PMID: 32186835.
[2] Crandall CJ, Hovey KM, Cauley JA, Andrews CA, Curtis JR, Wactawski-Wende J, Wright NC, Li W, LeBoff MS. Wrist Fracture and Risk of Subsequent Fracture: Findings from the Women's Health Initiative Study. Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research. 2015;30(11):2086–2095. doi: 10.1002/jbmr.2559.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3298

POS0163 INCIDENT FRACTURE RISK PREDICTION USING THE FRAGILITY SCORE CALCULATED BY LUMBAR SPINE RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS) SCANS

D. Ciardo[1], P. Pisani[2], F. A. Lombardi[2], R. Franchini[2], F. Conversano[2], S. Casciaro[2]. *[1]National Research Council, Institute of Clinical Physiology, Lecce, Italy*; *[1]National Research Council, Institute of Clinical Physiology, Lecce, Italy*

Background: The main consequence of osteoporosis is the occurrence of fractures due to bone fragility, with important sequelae in terms of disability and mortality. It has been already demonstrated that the information about bone mass density (BMD) alone is not sufficient to predict the risk of fragility fractures, since several fractures occur in patients with normal BMD [1].
The Fragility Score is a parameter that allows to estimate skeletal fragility thanks to a trans-abdominal ultrasound scan performed with Radiofrequency Echographic Multi Spectrometry (REMS) technology. It is calculated by comparing the results of the spectral analysis of the patient's raw ultrasound signals with reference models representative of fragile and non-fragile bones [2]. It is a dimensionless parameter, which can vary from 0 to 100, in proportion to the degree of fragility, independently from BMD.
Objectives: This study aims to evaluate the effectiveness of Fragility Score, measured during a bone densitometry exam performed with REMS technology at lumbar spine, in identifying patients at risk of incident osteoporotic fractures at a follow-up period of 5 years.
Methods: Caucasian women with age between 30 and 90 were scanned with spinal REMS and DXA. The incidence of osteoporotic fractures was assessed during a follow-up period of 5 years. The ability of the Fragility Score to discriminate between patients with and without incident fragility fractures was subsequently evaluated and compared with the discriminatory ability of the T-score calculated with DXA and with REMS.
Results: Overall, 533 women (median age: 60 years; interquartile range [IQR]: 54-66 years) completed the follow-up (median 42 months; IQR: 35-56 months), during which 73 patients had sustained an incident fracture.
Both median REMS and DXA measured T-score values were significantly lower in fractured patients than for non-fractured ones, conversely, REMS Fragility Score was significantly higher (Table 1).

Table 1. Analysis of T-score values calculated with REMS and DXA and Fragility Score calculated with REMS. Median values and interquartile ranges (IQR) are reported. The p-value is derived from the Mann-Whitney test.

	Patients without incident fragility fracture	Patients with incident fragility fracture	p-value
T-score DXA [median (IQR)]	-1.9 (-2.7 to -1.0)	-2.6 (-3.3 to -1.7)	0.0001
T-score REMS [median (IQR)]	-2.0 (-2.8 to -1.1)	-2.7 (-3.5 to -1.9)	<0.0001
Fragility Score [median (IQR)]	29.9 (25.7 to 36.2)	53.0 (34.2 to 62.5)	<0.0001

By evaluating the capability to discriminate patients with/without fragility fractures, the Fragility Score obtained a value of the ROC area under the curve (AUC) of 0.80, higher than the AUC of the REMS T-score (0.66) and of the T-score DXA (0.64), and the difference was statistically significant (Figure 1).

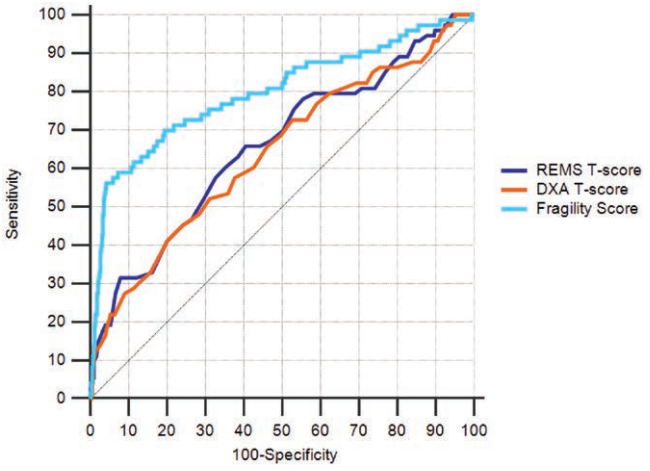


Figure 1. ROC curve comparison of Fragility Score, REMS and DXA T-score values in the classification of patients with incident fragility fractures.

Furthermore, the correlation between the Fragility Score and the T-score values was low, with Pearson correlation coefficient *r*=-0.19 between Fragility Score and DXA T-score and -0.18 between the Fragility Score and the REMS T-score.
Conclusion: The Fragility Score was found to be an effective tool for the prediction of fracture risk in a population of Caucasian women, with performances superior to those of the T-score values. Therefore, this tool presents a high potential as an effective diagnostic tool for the early identification and subsequent early treatment of bone fragility.
REFERENCES:
[1] Diez Perez A et al. *Aging Clin Exp Res* 2019; 31(10):1375-1389.
[2] Pisani P et al. *Measurement* 2017; 101:243–249.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2311

POS0164 THE NEED FOR ANTI-OSTEOPOROTIC INTERVENTION IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS BASED ON THE FRACTURE RISK ASSESSMENT

O. Dobrovolskaya[1], A. Feklistov[1], O. Nikitinskaya[1], A. Efremova[1], N. Toroptsova[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Department of Osteoporosis, Moscow, Russian Federation*

Background: Rheumatoid arthritis (RA) is a chronic disabling disease that is associated with bone loss. Previous studies estimated that approximately

one-third of the RA patients had osteoporosis (OP). However, most fragility fractures occur in patients not suffering from OP, that can be partly explained by impaired quality of bone, which is not measured with DXA. Therefore, only the measurement of bone mineral density is not sufficient to determine the indication for OP treatment. Another tool for assessing the need for anti-osteoporotic therapy is to calculate the 10-year probability of a major fracture using the fracture risk assessment tool (FRAX).

Objectives: To assess the need for anti-osteoporotic therapy in women with rheumatoid arthritis (RA) based on the identification of individuals with fragility fractures and high risk of fracture according to FRAX.

Methods: 295 postmenopausal women with RA were included in the study. The average age was 63±7 years, the duration of RA was 11 [4;16] years, the duration of postmenopausal period was 13 [6; 20] years. 121 (41%) patients took glucocorticoids (cumulative dose 9025 [3650; 20720] mg in prednisolone equivalent). A survey was conducted to identify patients with risk factors and a history of fragility fractures. The 10-year probability of a major osteoporotic fracture was assessed using the FRAX tool. In patients treated with glucocorticoids at a dose >7.5 mg in prednisolone equivalent the estimates of probabilities of a major osteoporotic fracture were adjusted in accordance with the recommendations [1]. Dual-energy X-ray absorptiometry (DXA) of the proximal femur was performed in patients with a moderate risk (probabilities between the upper and lower assessment age-dependent intervention threshold) and the risk of fracture was recalculated with including femoral neck BMD.

Results: 83 (28.1%) patients had a prior fragility fracture: 44 (14,9%) – 1, 20 (6,8%) – 2 and 19 (6.4%) – 3 or more. Vertebral fractures were the most common, they accounted for 62,1% of all fractures, distal forearm was the second frequent fractures localization (18.2%). Only 2 (0.7%) women had hip fracture. The average 10-year probability of a major osteoporotic fracture was 17 % [11; 28] in RA women. 92 (31.2%) persons were at high risk, 28 (9.5%) patients - at low risk, and 175 (59.3%) - at moderate risk. After recalculation of fracture risk with including femoral neck BMD in people at moderate risk 48 (16.3 %) patients became at high risk, 9 (3.1%) – at very high risk, and 118 (40.0%) - at low risk.

Thus, 149 (50.5%) RA patients were at very high or high risk and 146 (49,5%) – at low risk of major osteoporotic fracture according to FRAX, among the last – only 3 persons had a history of fragility fracture after age of 40 years.

Conclusion: Our study demonstrated that a half of postmenopausal women with RA had indications for anti-osteoporotic treatment based on the results of a 10-year probability of major fragility fractures using FRAX tool.

REFERENCES:

[1] Kanis JA, Johansson H, Oden A, McCloskey EV. Guidance for the adjustment of FRAX according to the dose of glucocorticoids. Osteoporos Int. 2011;22(3):809-816. doi:10.1007/s00198-010-1524-7.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1332

POS0165 STUDY OF VERTEBRAL AND FEMUR FRACTURE PREVALENCE AND SCANOGRAPHIC BONE ATTENUATION COEFFICIENT OF THE FIRST LUMBAR VERTEBRA IN AN ACADEMIC HOSPITAL SETTING

Z. Vaghaiwalla[1], P. Wasserman[2], G. Kaeley[1]. [1]*University of Florida College of Medicine- Jacksonville, Rheumatology, Jacksonville, United States of America*; [2]*University of Florida College of Medicine- Jacksonville, Radiology, Jacksonville, United States of America*

Background: Patients with osteoporosis are prone to suffer fragility fractures leading to an increased risk of future fractures. Detection of osteoporosis has been led by dual energy-ray absorptiometry (DEXA) as the gold standard. However, in acute fracture incidents, DEXA imaging is typically unavailable, and treatment is often delayed. In recent years scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1) on incidental computed tomography (CT) scans of the lumbar spine has been utilized as an alternative assessment of bone density. In particular, SBAC-L1 ≤ 145 HU correlates with osteoporotic bone density on DEXA imaging.[2]

Objectives: This study aims to assess the SBAC-L1 in HU of incidental CT scans in patients presenting with vertebra or femur fragility fractures in an academic hospital as it relates to osteoporosis.

Methods: We conducted a retrospective chart review of patients aged ≥ 45 admitted to an academic hospital for active vertebral or femur fracture between 1/1/2017- 1/31/2019, excluding traumatic and pathological fractures. Measurement of SBAC-L1 in HU was obtained on incidental CT scan imaging.

Sex, race, prior and post diagnoses of osteoporosis, prior and post DEXA scan orders, use of calcium, vitamin D, and steroids were abstracted.

Results: There were 297 patients with vertebral or femur fractures from 1/1/2017-1/31/2019. Of 297 patients, 85 deemed appropriate after excluding pathological, traumatic fractures, and lack of CT scan on the admission for fracture.

Average SBAC-L1 for all patients was 100.4 ± standard deviation (SD) of 46.5 HU. 82% of all patients had SBAC-L1 ≤ 145 HU. Caucasian patients had a lower average SBAC-L1 [99.4 HU] than African American (AA) patients [122.1 HU]. More Caucasian [n=15] had prior diagnoses of osteoporosis than AA [n=2]. Caucasian patients were prescribed Calcium and Vitamin D more often [n=39] than AA [n=3]. DEXA scan orders were placed more often in Caucasian patients [n=4] than AA patients [n=1]. Osteoporosis medications were prescribed more often in Caucasian patients [n=8] than AA patients [n=0].

Male average SBAC-L1 was 97.4 HU compared to females at 106.3 HU. Females were prescribed calcium and vitamin D more often [n=38] than males [n=8]. DEXA scan orders were placed more frequently in females [n=5] than males [n=2]. Osteoporosis medications were prescribed more often in females [n=9] than male patients [n=0].

Table 1. Study Characteristics

	Total Patients [n=85]	Caucasian Patients [n=67]	AA Patients [n=16]	Male Patients [n=31]	Female Patients [n=54]
SBAC- L1 Average ± SD (HU)	100.4 ± 46.5	99.4 ± 44.1	122.1 ± 49.9	97.4 ± 44.3	106.3 ± 47.2
Patients with SBAC- L1 ≤ 145 HU	70	58	10	26	44
Patients with SBAC- L1 > 145 HU	15	9	6	5	10
Vertebral Fractures	57	47	8	19	38
Femur Fractures	28	20	8	12	16
Age Average	71.7	72	70.9	74	70.4
Prior diagnosis of osteoporosis	16	15	1	2	14
Post diagnosis of osteoporosis	6	2	2	2	4
Calcium	20	16	2	2	18
Vitamin D	26	23	1	6	20
Osteoporosis medication	9	8	0	0	9
Steroid use	5	4	1	2	3
DEXA prior	13	12	1	0	13
DEXA after	7	4	1	2	5

Conclusion: 70 of 85 patients with incidental fragility fractures exhibited SBAC-L1 ≤ 145 HU. This is consistent with osteoporotic bone density on DEXA imaging supporting the use of SBAC-L1 measurement to corroborate the diagnosis osteoporosis. SBAC-L1 ≤ 145 HU can be utilized to increase inpatient diagnostic confidence of osteoporosis in the setting of acute fragility fractures to allow initiation of treatment prior to awaiting outpatient DEXA imaging.

The results here also highlight health disparities present among African Americans and males of all races when considering bone health.

REFERENCES:

[1] Lewiecki, E. Michael, et al. "Healthcare policy changes in osteoporosis can improve outcomes and reduce costs in the United States." *JBMR plus* 3.9 (2019): e10192.

[2] Fauny, Marine, et al. "Study of vertebral fracture and Scanographic Bone Attenuation Coefficient in rheumatoid arthritis and ankylosing spondylitis vs. controls." *Scientific reports* 9.1 (2019): 1-9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1475

POS0166 ASSOCIATION OF TRABECULAR BONE SCORE AND FAT DISTRIBUTION IN MOROCCAN RHEUMATOID ARTHRITIS PATIENTS

H. Azzouzi[1], O. Lamkhanat[1], I. Linda[1]. [1]*Mohammed VI University Hospital, Mohammed I University, Faculty of Medicine, Rheumatology, Oujda, Morocco*

Background: The association between body composition and bone microarchitecture reflected by trabecular bone score (TBS) has been studied lately (1). In rheumatoid arthritis (RA), this association, especially with fat mass, needs further confirmation.

Objectives: The purpose of the present work was to study the association of TBS with fat distribution in RA.

Methods: We designed a cross-sectional study of patients with RA diagnosis according to ACR-EULAR 2010 classification recruited from first January 2021. Those with prior cancer, hyperparathyroidism, hyperthyroidism, diabetes, chronic kidney disease, cirrhosis, and a body mass index (BMI) of more than 36kg/m^2 were excluded. TBS, total body fat mass (BFM), and its distribution (gynoid (GFM), android (AFM), visceral (VFM), limbs (LFM), trunk (TFM)) were measured with Dual-energy X-ray absorptiometry (Hologic). Clinical data and laboratory tests of the same day of the DXA scan were analyzed. The associations between TBS, BFM, and its distribution were studied by correlations and multiple linear regressions using SPSS 20.

Results: Sixty-nine patients were included. Their mean age was 49.86 ± 14.33 years, mean DAS28CRP was 2.56 ± 1.27, and mean disease duration was 14.84 ± 10.99 years. Sixty-two (89.9%) were women, with 30 (48.4%) had menopause. The mean BMI was 26.46 ± 5.26 kg/m^2, and 41 patients were obese (59.4%).

In the Pearson correlation analysis, TBS was associated with BFM (p = 0.04), AFM (p = 0.001), TFM (p = 0.007), and VFM (p < 0.0001). However, there was no correlation with LFM (p = 0.262), and GFM (p = 0.469). At multivariate analysis, only VFM (p = 0.005, β = - 0.355, 95%IC [- 0.0002; - 0.00004]), and AFM (p = 0.02, β = - 0.395, 95%IC [- 0.00007; - 0.000006]) were associated with TBS, when adjusted on age, menopause, disease duration, disease duration under treatment, lumbar BMD, BMI, HAQ, CRP, and triglycerides level.

Conclusion: In RA patients, TBS was negatively associated with visceral and android fat mass. This result may explain the intriguing coexistence of high BMD and vertebral fractures in RA obese patients.

REFERENCES:

[1] Lv S, Zhang A, Di W, et al. Assessment of Fat distribution and Bone quality with Trabecular Bone Score (TBS) in Healthy Chinese Men. *Sci Rep*. 2016; 6:24935. Published 2016 Apr 26. doi: 10.1038/srep24935.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3352

POS0167 SECONDARY PREVENTION OF VERTEBRAL FRACTURES IN REAL PRACTICE

J. E. Oller Rodríguez[1], E. Grau García[1], S. Leal Rodriguez[1], M. E. Acosta[2], C. Riesco Barcena[1], A. V. Huaylla Quispe[1], C. Pávez Perales[1], M. De la Rubia Navarro[1], I. Martínez Cordellat[1], C. Nájera Herranz[1], R. Negueroles Albuixech[1], F. M. Ortiz Sanjuan[1], E. Vicens Bernabeu[1], C. Alcañiz Escandell[1], I. Cánovas Olmos[1], I. Chalmeta Verdejo[1], J. J. Fragío Gil[1], L. Gonzalez Puig[1], J. Ivorra Cortés[1], J. A. Román Ivorra[1]. *[1]HUP La Fe, Rheumatology Department, Valencia, Spain*; *[2]Complejo Asistencial Universitario de Salamanca, Rheumatology Department, Salamanca, Spain*

Background: Vertebral fractures increases the risk of new fractures and deaths. There are different antiresorptive medications to prevent a secondary fracture, as bisphosphonates, teriparatide or denosumab, but little is known about the effects of secondary fracture appearance in real life.

Objectives: To evaluate the appearance of new vertebral fractures depending on the treatment used for secondary prevention.

Methods: We conducted a prospective descriptive study of patients with a first diagnosis of vertebral fracture from 2010 to 2017 and assessed the subsequent finding of new fractures. We selected patients with at least 3 years of secondary prevention with antiresorptive drugs or with sequential treatment (anabolic followed by, at least, 1 year with antiresorptive drugs), and excluded those who experienced new fractures within the first 6 months of treatment.

Results: A total of 400 patients were selected from an initial base of 1018 patients. The average age of onset of the first fracture was 69.7 years, 84% of female patients and 16% of female patients. 38.5% suffered dorsal fractures, 33.75% lumbar fractures and 27.75% dorsolumbar fractures. We classified the secondary prevention strategies according to the different therapeutic options, as we can see in Table 1.

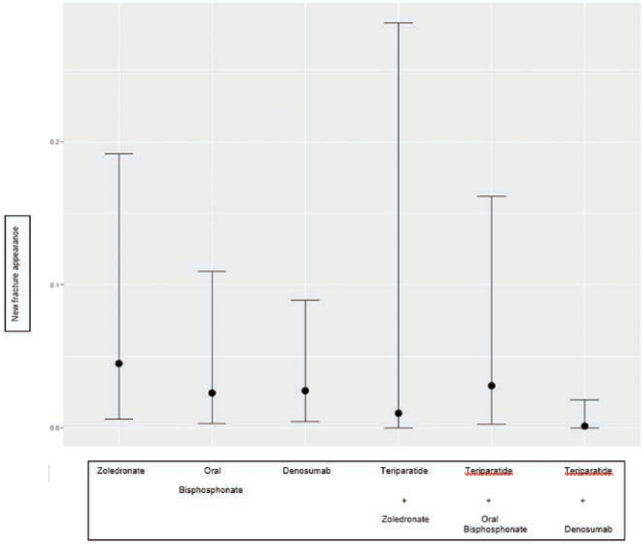
We analysed the association between the appearance of new vertebral fracture corrected by sex with the age of the initial fracture its location. No association was found.

We also performed a multivariate Bayesian model of logistic regression, in order to analyze the association between the appearance of new vertebral fracture and factors as the age of the initial fracture, its sex and the pharmacologic option used as secondary prevention. No statistically significant differences were observed between the different antiresorptive treatments and their efficacy as a secondary prevention of vertebral fractures. However, there was a tendency for a smaller occurrence of new fractures in patients undergoing sequential treatment. On the other hand, similar results were observed between denosumab and oral bisphosphonates, observing somewhat worse data with zoledronate (figure 1), probably due to patients under zoledronate treatment showed high osteoporotic risk and worse prognosis.

Pharmacologic option	Patients (%)	New fractures (%)
Denosumab	192 (48%)	10 (5.21%)
Teriparatide (up to 2 years) + Denosumab (at least 1 year)	86 (21.5%)	0 (0%)
Oral bisphosphonate (alendronate, risedronate or ibandronate)	58 (14.5%)	3 (5.17%)
Zoledronate	33 (8.25%)	4 (12.12%)
Teriparatide (up to 2 years) + oral bisphosphonate (at least 1 year)	28 (7%)	2 (7.14%)
Teriparatide (up to 2 years) + Zoledronate (at least 1 year)	3 (0,75%)	0 (0%).

Conclusion: No differences between the different secondary prevention options in terms of the appearance of new fractures were observed.

Disclosure of Interests: None declared



DOI: 10.1136/annrheumdis-2021-eular.3108

POS0168 BONE MINERAL DENSITY IN PATIENTS WITH MULTIPLE SCLEROSIS. A DESCRIPTIVE STUDY FROM A UNIQUE CENTER FROM THE EAST OF SPAIN

E. Flores-Fernández[1], C. Valera-Ribera[1], I. Vázquez-Gómez[1], A. V. Orenes Vera[1], À. Martínez-Ferrer[1], L. Landete[2], E. Valls-Pascual[1], D. Ybáñez-García[1], J. J. Alegre-Sancho[1]. *[1]Doctor Peset University Hospital, Rheumatology, València, Spain*; *[2]Doctor Peset University Hospital, Neurology, València, Spain*

Background: Several studies have suggested that multiple sclerosis (MS) patients have low bone mineral density (LBMD) compared to healthy adults of same age. This fact, combined with the functional impairment of the disease, increases the risk of fractures. However, information about the prevalence and the risk factors of LBMD in Spanish patients with MS is still quite limited[1–3].

Objectives: To evaluate the prevalence of LBMD and low vitamin D in patients with MS from a unique center from the east of Spain, describing the clinical features of these patients.

Methods: Type of study: observational, cross-sectional, descriptive. Patients with MS from a local cohort have been consecutively recruited for this study since Apr-2020. A cross-sectional visit which included a clinical interview, analytic test (blood and urine) and a dual-energy X-ray absorptiometry (DXA) was performed. We defined LBMD as T score ≤-1SD in postmenopausal women and men over 50 years and a Z score ≤-2SD in premenopausal women and men under 50 years. Low levels of vitamin D were defined as < 20ng/mL. A descriptive and associative analysis of these data was carried out using the SPSS software.

Results: From a cohort of 288 MS patients, due to the COVID-19 pandemia, we have only been able to assess 60 patients, and only 48 out of them have undergone all the tests required. These were 30 women and 18 men, with a mean age of 49 (SD 11,6) years. The main type of MS was relapsing-remiting (77,1%) and 25% of them were not taking any maintenance treatment. Some of the classical factors related to a LBMD are shown in table a1. A 43,8% of the patients had a LBMD and 40,5% had low levels of vitamin D. Despite these results, as far as 89% of patients had never received any specific treatment, not even calcium and/or vitamin D supplementation. Furthermore, 13 patients (27,1%) must have received specific treatment, according to latest guidelines[4], and only 4 of them (8,5%) were being adequately treated.

Table 1.

Women/Men (n)	30/18
Mean age; SD (years)	49; 11,6
Non smokers/Smokers (%)	58,4/41,7
Alcohol abuse (%)	8,3
Personal history of fracture (%)	10,4
Personal history of nephrolithiasis (%)	14,6
Normal/Reduced mobility (%)	77,1/22,9
Sedentary lifestyle (%)	66,7

Conclusion: These preliminary results show that almost half of the MS patients have LBMD and a low vitamin D, most of them without taking any specific treatment. Taking this in mind, it is necessary to integrate the early diagnosis of LBMD

in MS patients, working together with neurologists, to prevent the appearance of fractures and protect the quality of life of these patients. An analysis of our whole cohort of MS patients will help us in correctly assessing the magnitude of this problem.

REFERENCES:

[1] López Méndez P, Sosa Henríquez M. Vitamin D and multiple sclerosis. Prevalence of hypovitaminosis D. *Rev Osteoporos y Metab Miner*. 2015;7(2):71-78.
[2] Gupta S, Ahsan I, Mahfooz N, Abdelhamid N, Ramanathan M, Weinstock-Guttman B. Osteoporosis and multiple sclerosis: Risk factors, pathophysiology, and therapeutic interventions. *CNS Drugs*. 2014;28(8):731-742.
[3] Moen S, E.Celius, L S, L N, E E, T H. Low bone mass in newly diagnosed multiple sclerosis and clinically isolated syndrome. *Neurology*. 2011;77(2):151-157.
[4] Lems WF, Dreinhöfer KE, Bischoff-Ferrari H, et al. EULAR/EFORT recommendations for management of patients older than 50 years with a fragility fracture and prevention of subsequent fractures. *Ann Rheum Dis*. 2017;76(5):802-810.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3214

POS0169 FETUIN-A AS A MARKER OF OSTEOPOROSIS AND OSTEOPOROTIC FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS

Y. Akhverdyan[1], E. Papichev[1], B. Zavodovsky[1], L. Seewordova[1], J. Polyakova[1]. [1]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology Named After A.B. Zborovsky», Joint Diseases Treatment and Prevention Laboratory, Volgograd, Russian Federation*

Background: The main mechanism of the effect of fetuin-A (FeA) on bone metabolism is its ability to bind calcium and proteins of the TGF-β family. It has been proven that the optimal concentration of TGF-β is necessary for the differentiation of bone tissue, and a high concentration inhibits bone mineralization. Thus, adequate osteogenesis is based on a complex balance between FeA and TGF-β levels. It can be assumed that the determination of the FeA level in the blood of patients with rheumatoid arthritis (RA) will help to optimize the diagnosis and predict the severity of osteoporosis (OP).

Objectives: to study the possibility of predicting the development of osteoporosis and osteoporetic fractures in patients with RA, depending on the level of FeA in blood serum.

Methods: We examined two groups of patients (52 patients with RA complicated by OP, 58 patients with RA without OP) and 30 apparently healthy individuals. The age of the surveyed ranged from 18 to 72 years, the average duration of the disease was 7.53±0.89 years. In both groups, the FeA level was determined by an indirect enzyme-linked immunosorbent assay using a commercial test. Bone mineral density (BMD) was also measured in both groups (Lunar DPX-NT GE).

Results: The average FeA level in the group of RA patients was lower than in the group of conventionally healthy individuals (731.21±109.9 μg/ml and 812.9±76.2 μg/ml, respectively; F=13.34; p=0,0004). The normal FeA level was calculated using the formula M±2σ in the group of apparently healthy individuals and ranged from 653.55 μg/ml to 972.19 μg/ml.

A decreased level of FeA was found in 20 patients (86.96%) in the group of patients with OP and only in 3 (13.04%) patients with RA who did not suffer from OP (p<0.001). It can be concluded that patients with RA and a low concentration of FeA in the blood serum have a higher risk of developing OP.

In the group of patients with normal FeA level, osteoporetic fractures were observed in 12 (13.79%) patients and were absent in 75 (86.21%) patients (p<0.001). Thus, RA patients with normal serum FeA levels have a lower risk of osteoporetic fractures.

We also found a positive significant correlation between the level of FeA and BMD in the femoral neck area. In the group of patients with a reduced FeA level (23 people), the mean BMD values were 0.732±0.022 g/cm2, and in the group of patients with a normal FeA level (87 patients) - 0.890±0.014 g/cm2 (p<0.001, F=27.663). The obtained values are in agreement with the literature data on the effect of the serum FeA concentration on the BMD values.

Conclusion: We consider it expedient to determine the serum FeA concentration in patients with RA. At a FeA level of 653.55 μg/ml and below, a higher risk of developing OP and osteoporetic fractures can be predicted. In this case, the patient is shown a standard examination for osteoporosis. At values of 653.55 μg/ml and above, a more expectant management of the patient is allowed. Thus, by determining the serum concentration of FeA, it is possible to implement an integrated approach to the patient and to optimize the schemes for the diagnosis of OP in patients with RA.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.753

POS0170 IMPROVING MANAGEMENT OF GLUCOCORTICOID INDUCED OSTEOPOROSIS IN RHEUMATOLOGY

A. Bankole[1], S. Pachigolla[2]. [1]*Virginia Tech Carilion School of Medicine, Medicine, Roanoke, United States of America*; [2]*Carilion Roanoke Memorial Hospital, Internal Medicine, Roanoke, United States of America*

Background: Glucocorticoids (GC) are used in the treatment of various inflammatory conditions and it is estimated that about 1% of US population is treated with long term steroids. High doses of GC particularly those used by rheumatologists have adverse effects on bone health and is associated with rapid bone loss resulting in Glucocorticoid induced Osteoporosis(GIO) and an increased risk of fractures. The risk of bone loss relates to high daily dose and the high cumulative dose of the GC.

Despite the availability of effective preventative and treatment options, GIO is often under treated with many patients treated only after a fracture has occurred.

Objectives: The purpose of this study was to examine if providing education to care providers lead to an improvement in the identification, evaluation, and treatment of GIO.

Methods: This is a single center, prospective study that was performed at a university based tertiary referral center. Patients over 40 years, receiving a total cumulative dose of GC of >5 grams and/or a single dose of >30 mg of prednisone or equivalent was enrolled. A patient list was generated by our technology group. All providers received intervention in the form of an academic Journal Club, at which the current ACR guidelines regarding GIO was reviewed. Monthly reminders were shared with all providers within our monthly communications.

All the pre and post interventional data was analyzed. The continuous variables were analyzed using T-test or Mann-Whitney U test. Categorical variables were analyzed using Chi-square Tests or Fisher's exact tests. Statistical analysis was performed using SAS9.4, and p value <0.05 was considered statistically significant.

Results: Post education, there was a statistically significant increase in vitamin D replacement and the use of bisphosphonates as well as a reduction in the use of bone mineral density (BMD) tests within the at risk group while on GC.

Table 1. Glucocorticoid induced Osteoporosis (GIO)

	Pre-treatment (N=72)	Post-treatment (N=54)	p-value
Demographics			
Age (years)	58.9 ± 19.2	64.2 ± 16.7	0.11
Body Mass Index	29.0 ± 6.7	29.4 ± 8.4	0.77
Gender (Female)	73.6%	74.1%	0.95
Race			
White	83.3%	77.8%	0.43
Hispanic	1.4%	5.6%	0.31
Insurance			
ANTHEM BCBS	16.9%	26.9%	
Commercial	11.3%	11.5%	
Medicaid	12.7%	9.6%	
Medicare	59.2%	51.9%	
			0.58
Medical History			
Osteoporosis	68.1%	64.8%	0.70
Osteoporotic Fracture	15.3%	11.1%	0.50
Vasculitis	26.4%	22.2%	0.59
Systemic Lupus Erythematosus	18.1%	13.0%	0.44
Rheumatoid Arthritis	12.5%	25.9%	0.05
Polymyalgia Rheumatica	6.9%	11.1%	0.41
Inflammatory Muscle Disease	18.1%	20.4%	0.74
Spondyloarthritis	1.4%	1.9%	0.99
Lab Results			
Serum Vitamin D (Normal)	41.3% (19/46)	52.8% (19/36)	0.3
GIO Prevention Measures			
Calcium	2.8%	13.0%	0.04
Vitamin D	18.1%	61.1%	<0.01
Bisphosphonates	9.7%	35.2%	<0.01
RANKL inhibitors	4.2%	11.1%	0.17
Bone Mineral Density	43.5% (10/23)	10.5% (2/19)	0.02

Conclusion: There was a significant improvement between the GIO pre and post-educational data, with increasing use of GIO preventive measures. Importantly, there was also a reduction in BMD testing of patients while still on GC. This research show the importance of provider education as a means of disseminating information and improving the quality of patient care.

REFERENCES:

[1] Compston J. Glucocorticoid-induced osteoporosis: an update. Endocrine. 2018 Jul;61(1):7-16. doi: 10.1007/s12020-018-1588-2.

[2] 2017 American college of rheumatology guideline for the prevention and treatment of Glucocorticoid-induced Osteoporosis. Arthritis & Rheumatology Vol. 69, No. 8, august 2017, pp 1521-1537. DOI 10.1002/art.40137.

[3] Fardet L, Petersen I, Nazareth I. Monitoring of patients on long-term glucocorticoid therapy: a population-based cohort study. Medicine (Baltimore). 2015 Apr;94(15):e647. doi: 10.1097/MD.0000000000000647.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.127

POS0171 UNDERESTIMATION OF THE FRACTURE RISK BY THE FRAX FORMULA IN CHRONIC GLUCOCORTICOID USERS: A 10-YEAR LONGITUDINAL VALIDATION STUDY

C. C. Mok[1], L. Y. Ho[1], S. M. Tse[1], K. L. Chan[1]. [1]*Tuen Mun Hospital, Medicine, Hong Kong, Hong Kong (SAR)*

Background:

Objectives: To compare the actual fracture incidence over 10 years in a longitudinal cohort of patients using glucocorticoids (GCs) with the risk prediction from FRAX (fracture risk assessment tool).

Methods: Patients who attended our out-patient rheumatology clinics were included according to the following criteria: (1) adult patients ≥18 years; (2) underlying rheumatic diseases requiring prednisolone treatment (≥5mg/day); and (3) have had a DXA scan (baseline) performed between years 2007-2009. The predicted rates of major osteoporotic and hip fractures were estimated using FRAX (China database) based on the clinical data at the time of DXA, with adjustment when daily dose of prednisolone ≥7.5mg (multiply by 1.15 for major osteoporotic and 1.20 for hip fracture). The actual observed incidence of symptomatic vertebral and non-vertebral fractures at 10 years (in years 2017-2019) follow-up was retrieved by medical record review and compared with the estimated rates by FRAX. Factors associated with symptomatic clinical fractures at 10 years were studied by logistic regression.

Results: 89 patients were studied (age 49.3±8.8 years at DXA examination; 98% women). The underlying rheumatic diseases were systemic lupus erythematosus (69%), rheumatoid arthritis (17%) and others (14%). The mean daily dose of prednisolone at baseline was 7.7±6.5mg (38% patients had daily dose ≥7.5mg). History of personal fracture was present in 4(4.5%) patients and 22% of female patients had menopause before the age of 45 years. The mean body mass index (BMI) was 23.5±3.3kg/m^2 (4.5% ≤18kg/m^2). Osteoporosis (bone mineral density [BMD] T score ≤-2.5) of the hip, femoral neck and lumbar spine occurred at a frequency of 11.2%, 13.5% and 25.8%, respectively at baseline (32% at any of the 3 sites). 30(34%) patients received anti-osteoporotic treatment (oral bisphosphonates in 25, raloxifene in 3 and denosumab in 2 patients). The estimated mean 10-year risk of major osteoporotic and hip fractures using the BMD data and other risk factors in the FRAX formula, adjusted for prednisolone dose, was 4.3% and 1.0%, respectively. After a follow-up of 10 years, one patient had a hip fracture, 3 patients had humerus fractures and 9 patients had symptomatic vertebral fractures. The actual observed major osteoporotic and hip fracture incidence was 14.6% and 1.1%, respectively (0.146 and 0.011 per 10 patient-years). The observed major clinical fracture rate was significantly higher than that estimated by FRAX (14.6% vs 4.3%; p=0.04). Logistic regression revealed that the only factor independently associated with major clinical fracture at 10 years was BMD T score ≤-2.5 at spine, hip or femoral neck at baseline (OR7.11[1.73-29.2]; p=0.007). Age, prednisolone daily dose, BMI, history of fracture, chronic smoking, having underlying SLE vs not and early menopause were not significantly associated with new clinical fractures.

Conclusion: Despite adjustment for prednisolone dosage, the FRAX formula underestimates the major clinical fracture risk in patients using long-term GCs. The deleterious effect of GCs on bone quality, high proportion of SLE patients, disease activity and use of additional doses of GCs and other immunosuppressive drugs during follow-up are among the contributing factors for this underestimation.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3400

Molecular profiles in connective tissue disease outcome

POS0172 THROMBIN GENERATION ASSAY AND LUPUS ANTICOAGULANT IDENTIFY DIFFERENT POPULATIONS OF PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES

M. Radin[1], A. Barinotti[1], I. Cecchi[1], S. G. Foddai[1], E. Rubini[1], D. Roccatello[1], E. Menegatti[1], S. Sciascia[1]. [1]*University of Turin, Clinical and Biological Sciences, Turin, Italy*

Background: Risk stratification in patients with antiphospholipid antibodies (aPL) remains a clinical challenge [1].

Objectives: We aimed to evaluate the role of Thrombin Generation Assay (TGA) in distinguishing various populations of aPL positive patients (with and without lupus anticoagulant - LA) and its association with β2GPI-dependent and anti-phosphatidyl-serine/prothrombin(aPS/PT) antibodies.

Methods: One-hundred-and-eight patients were tested with TGA and divided as follows: 21 patients with aPS/PT IgG/IgM (**Group 1**), 29 with aβ2GPI IgG/IgM (**Group 2**), 31 with aPS/PT and aβ2GPI IgG/IgM (**Group 3**), 27 with aPS/PT and/or aβ2GPI IgM low-titers (**Group 4**). Table 1 resumes the clinical characteristics of the APS patients (excluding aPL asymptomatic). Thirty-one healthy donors (HDs) and 24 controls treated with VKA were also included.

Results: The most deranged TGA and LA profile was observed in patients with both aPS/PT and aβ2GPI when compared to those with an isolated positivity for aPS/PT or aβ2GPI and patients with aPS/PT and/or aβ2GPI IgM at low titres (Figure 1). Similarly, patients with aPS/PT and/or aβ2GPI at medium/high titres presented with the higher rate of clinical manifestations.

When comparing the TGA curves of APS patients, asymptomatic aPL positive (aPL+) subjects, HDs and controls treated with VKA, we observed that aPL+ patients (particularly those with a confirmed diagnosis of APS) showed a characteristic profile.

Differences among groups were confirmed also when comparing APS clinical manifestations. When comparing Group 1 and Group 4 we found significant differences with respect to the number of thrombotic events (21vs.15,p<0.05), the number of venous events (9vs.3,p<0.05), the recurrence of thrombosis (19%vs.0%,p<0.05). Group 2 and Group 4 showed differences in the occurrence of venous thromboses (50vs.20,p<0.05), and in the occurrence of DVT (8vs.2,p<0.05). Group 3 and Group 4, had higher number of thrombotic events (36vs15, p<0.05), the occurrence and the number of venous events (46%-15vs20%-3,p<0.05), the occurrence of TIA and DVT (4-11vs0-2,p<0.05).

When analysing the cumulative frequency of extra-criteria APS manifestations, Group 1,2 and 3 were comparable, while comparing Group 3 and those positive for aβ2GPI and/or aPS/PT IgM at low titres (Group 4) we found a statistically significant difference (71%vs13%,p<0.05).

Conclusion: TGA seems a valuable approach to stratify aPL+ patients according to their risk profile. The differences among groups and different populations of autoantibodies specificities obtained from this test can be considered a translational validation of the increased thrombotic risk of patients with triple or tetra aPL positivity.

REFERENCES:

[1] Miyakis S et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J. Thromb. Haemost. 2006;4(2):295–306.

Table 1. "Classical" and "Extra-criteria" APS clinical manifestations of each group (considering solely patients with a confirmed diagnosis of APS).

	Group 1: isolated aPS/PT+ IgG/IgM (16)	Group 2: isolated aβ2GPI+ IgG/IgM(20)	Group 3: aPS/PT+ and aβ2GPI+ IgG/IgM (24)	Group 4: aPS/PT+ and/or aβ2GPI+ IgM low titres (15)
APS clinical manifestations				
Thrombosis (Y/N), n (%)	14 (87,5%)	16 (80%)	21 (87,5%)	13 (86,6%)
N of thrombotic events	21	23	36	15
Arterial thrombosis (Y/N), n (%)	10 (62,5%)	9 (45%)	14 (58,3%)	11 (73,3%)
Arterial events, n	13	10	21	12
Venous thrombosis (Y/N), n (%)	6 (37,5%)	10 (50%)	11 (45,8%)	3 (20%)
Venous events, n	9	13	15	3
Pregnancy morbidity, n (%)	3 (18,8%)	4 (20%)	3 (12,5%)	2 (13,3%)
Recurrent thrombosis (Y/N), n (%)	3 (18,8%)	3 (15%)	7 (29,1%)	0
Livedo reticularis, n (%)	1 (6,2%)	1 (5%)	4 (16,6%)	0
Thrombocytopenia, n (%)	4 (25%)	4 (20%)	6 (25%)	2 (13,3%)
Valvular, n (%)	1 (6,2%)	0	2 (8,3%)	0
Peripheral artery disease, n (%)	0	3 (15%)	4 (16,6%)	0
Diffuse alveolar hemorrhage, n (%)	0	0	1 (4,1%)	0

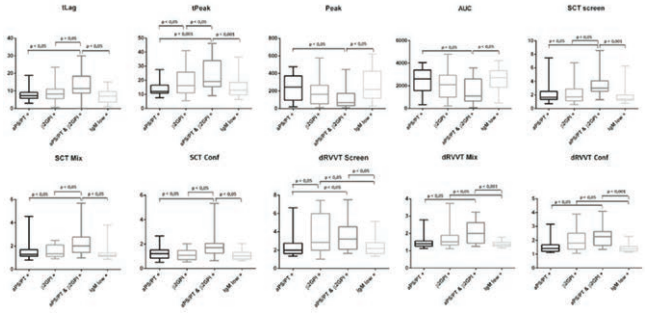


Figure 1. Graphical representation of the differences between TGA and LA profiles between groups.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2341

POS0173 **METABOLOMIC PROFILING AND SYMPTOM BURDEN IN BLACK WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

L. P. Kimble[1], A. Khosroshahi[2], R. C. Eldridge[1], G. S. Brewster[1], N. S. Carlson[1], E. J. Corwin[3]. [1]*Emory University, School of Nursing, Atlanta, United States of America*; [2]*Emory University, School of Medicine, Rheumatology Division, Atlanta, United States of America*; [3]*Columbia University, School of Nursing, New York, United States of America*

Background: Black individuals with systemic lupus erythematosus (SLE), who are predominantly women, have disproportionately poorer health outcomes across the trajectory of their disease including increased mortality, higher symptom burden, and poor quality of life than non-Hispanic Whites. The heterogeneity of immunopathology and biochemical complexity of SLE create major knowledge gaps around the mechanisms of disease and differences in SLE symptom expression. Metabolomics may reveal biochemical dysregulation that underlies SLE symptoms and provide novel metabolic targets for precision symptom interventions.

Objectives: We conducted untargeted metabolomic plasma profiling of Black females with SLE and Black female non-SLE controls to gain insight into metabolic disturbances associated with SLE.

Methods: We analyzed blood specimens collected from 23 Black female patients with diagnosis of SLE during a routine outpatient rheumatology visit and from 21 Black female non-SLE controls whose data were collected as part of another study of obese caregivers. Data collection for both cases and controls was completed with harmonized protocols. Clinical data for cases were obtained via chart review and both cases and controls completed identical, reliable and valid measures of fatigue, depression, anxiety, and sleep disturbance. A commercial metabolomics analysis company within the US conducted untargeted metabolomics on the 44 plasma samples using ultrahigh performance liquid chromatography/tandem mass spectrometry along with metabolite identification and quantification to examine differences between SLE/non-SLE groups.

Results: All SLE subjects met 2019 EULAR/ACR criteria (Aringer et al., 2019). SLE subjects were significantly ($p < .05$) younger (42.5 ± 12.2 vs. 63.2 ± 6.4), had a lower BMI (30.3 ± 9.4 vs. 34.9 ± 4.1), and greater co-morbidities (2.3 ± 1.3 vs. 1.1 ± 1.3) than non-SLE controls. SLE subjects reported higher symptoms than controls across all measures, but differences were not statistically significant. Metabolomics analysis revealed 290 biochemicals that were statistically significant ($p \leq .05$) between SLE and non-SLE groups. Random Forest analysis had a predictive accuracy of 91% in differing between the two groups using out-of-bag sampling. Significant metabolic differences between groups were noted in biochemicals associated with glycolysis, the TCA cycle (see Table 1), fatty acid metabolism, branched chain amino acids, sterol levels, heme catabolism, and potential markers of renal impairment. Overall, the differences would suggest reduced energy production among SLE patients compared to controls.

Table 1- Comparison SLE (n= 23)and No SLE Subjects (n=21) on Biochemicals in the TCA Cycle

Pathway	Metabolite	SLE/ No SLE log_2 fold change	p-value	FDR q-value
TCA Cycle	citrate	0.82	0.0005	0.008
	aconitate [cis or trans]	0.65	< 0.0001	0.001
	alpha-ketoglutarate	0.74	0.0017	0.017
	succinylcarnitine (C4-DC)	0.94	0.3558	0.362
	succinate	0.75	0.0001	0.003
	fumarate	0.64	0.0002	0.004
	malate	0.73	0.0149	0.057
	citraconate/glutaconate	1.46	0.6843	0.507

Note: SLE= systemic lupus erythematosus. Welch's Two sample t-test used to compare groups. FDR= False discovery rate. Green color indicates value for SLE group significantly lower than non-SLE controls.

Conclusion: Black women with SLE had biochemical profiles consistent with reduced energy production which has implications for the high burden of fatigue and other symptoms in this population. Future work with larger sample sizes should involve integrating symptom and metabolomics data to identify potential biomarkers of symptom burden.

References: Aringer, M., Costenbader, K., Daikh, D. et al. (2019). 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Ann Rheum Dis, 78*,1151-1159.

Acknowledgements: This work was supported by a research re-entry supplement to L. Kimble under the parent award 1P30NR018090-02S1 Center for the Study of Symptom Science, Metabolomics, and Multiple Chronic Conditions

(Song, PI) funded by the National Institute of Nursing Research, National Institutes of Health, USA.
Disclosure of Interests: Laura P. Kimble: None declared, Arezou Khosroshahi Consultant of: Have received honorarium for advisory board but has no relationship with this work., Grant/research support from: Have received a research grant from Pfizer; but has no relationship with this work., Ronald C. Eldridge: None declared, Glenna S. Brewster: None declared, Nicole S. Carlson: None declared, Elizabeth J. Corwin: None declared
DOI: 10.1136/annrheumdis-2021-eular.491

POS0174 IMMUNOPHENOTYPE OF SJÖGREN´S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IDENTIFIED TWO ENDOTYPES WITH POTENTIAL THERAPEUTIC IMPLICATIONS

L. Martin-Gutierrez[1,2], J. Peng[1,2], G. Robinson[1,2], M. Naja[2,3], H. Peckham[2], W. Wu[2], D. Isenberg[1,3], E. Jury[1], C. Ciurtin[2,3]. [1]*Centre for Rheumatology Research, Department of Medicine, London, United Kingdom*; [2]*Centre for Adolescent Rheumatology Versus Arthritis, Department of Medicine, London, United Kingdom*; [3]*University College London Hospitals, Department of Rheumatology, London, United Kingdom*

Background: Primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE) are chronic autoimmune rheumatic diseases (ARDs) that share a strong female gender bias, as well as genetic, clinical and serological characteristics.Although significant progress has been made in improving treatment and patient related outcomes in pSS and SLE, there is a need for improved early diagnosis, adequate therapy monitoring, treatment of refractory manifestations and strategies to address co-morbidities. However, the results of many clinical trials are disappointing, and nobiologic treatments are licensedin pSS, while few are available for SLE patients with refractory disease.
Objectives: Identifying shared immunological features between patients with pSS and SLE that could lead to better treatment selection using a stratification approach.
Methods: Immune-phenotyping of 29 immune-cell subsets in peripheral blood from patients with pSS (n=45), SLE (n=29) and secondary SS associated with SLE (SLE/SS) (n=14) with low disease activity or in clinical remission, and sex-matched healthy controls (n=31), was performed using flow cytometry. Data were analysed using logistic regression and multiple t-tests andsupervised machine learning (balanced random forest-BRF, sparse partial least squares discriminant analysis-sPLS-DA). Patients were stratified by k-means clustering. Clinical trajectories were analysed over 5 year follow-up.
Results: Comparing the immune profile of pSS and SLE patients using a variety of statistical and machine learning (ML) approaches, identified very few statistically significant differences between the two cohorts despite patients having a different clinical presentation and diagnosis. Thus, we hypothesised that immune-based subtypes could be shared between pSS, SLE and SLE/SS patients. Unsupervised k-means clustering was applied to the immunological features of the combined patient cohorts and two distinct patient endotypes, were identified: Group-1 (n=49; pSS=24, SLE=19, SLE/SS=6) and Group-2 (n=39; pSS=21, SLE=10, SLE/SS=8). Significant differences in immune-cell phenotypes across B-cell and T-cell subsets were identified by logistic regression, BRF (AUC=0.9942, assessed by 10-fold cross-validation) and sPLS-DA analysis. Comparison of the multiple analysis approaches identified eight common immune-cell subsets, including total and memory CD4+ and CD8+ T-cell subsets but no B-cell subsets. Using this common immune-signature the stratification between the groups was maintained and slightly improved (AUC=0.9979 and accuracy 96.16%). Interestingly, patients in Group-2 had elevated disease activity measures at baseline and over a 5-year trajectory compared to Group-1. Finally, correlation analysis identifed correlations between disease activity markers and the top ranked immune features from the ML models.
Conclusion: The identified immune-cell signatures could reflect the underlying disease pathogenesis that spans diagnositc criteria and could be used to select patients for targeted therapeutic approaches.
Acknowledgements: LM-G is supported by a project grant from The Dunhill Medical Trust (RPGF1902\117); JP is supported by Versus Arthritis (21226). GAR is supported by Lupus UK, The Rosetrees Trust (M409) and Versus Arthritis (21593). MN is supported by NIHR UCLH Biomedical Research Centre (BRC525/III/CC/191350). HP has a Versus Arthritis PhD studentship (22203). This work was performed within the Centre for Adolescent Rheumatology Versus Arthritis at UCL UCLH and GOSH supported by grants from Versus Arthritis (21593 and 20164), GOSCC, and the NIHR-Biomedical Research Centres at both GOSH and UCLH.
We would like to thank Mr Jamie Evans for expert support with flow cytometry analysis and Ms Eve McLoughlin for support with patient recruitment.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2434

POS0175 ASSOCIATION BETWEEN BIOMARKERS AND THERAPEUTIC PATHWAY IN PATIENTS WITH SLE

S. U. Hassan[1,2], K. Mahmoud[1,2], Z. Wigston[1], A. Burska[1], M. Y. MD Yusof[1,2], E. Vital[1,2]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine, Rheumatology, Leeds, United Kingdom*; [2]*NIHR Leeds Musculoskeletal Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: SLE is heterogeneous in clinical presentation, underlying immunology, and response to therapy. Patients with severe or resistant disease receive cyclophosphamide or rituximab. Although effective, late use of these therapies entails cumulative damage.
Emerging predictors of response to rituximab include demographics, IFN-Scores and autoantibodies. For such predictors to change treatment strategy we need to understand their association with the effectiveness of other therapeutic options at earlier decision points.
Prospective studies of treatment pathways are difficult to perform, requiring large populations followed for many years. We therefore investigated this question by analysing retrospective treatment pathways since diagnosis in patients whose biomarker status is subsequently known.
Objectives: To use interferon scores and other markers to;

[1] identify SLE patients more likely to need escalation of therapy to either rituximab or cyclophosphamide, and
[2] determine if this occurred sooner than in others.

Methods: In patients with established SLE, attending Leeds SLE clinic, we collected demographics, clinical characteristics and blood at a single timepoint. Two previously validated IFN-Scores[1,2] (IFN-Score A and IFN-Score B) were measured using Taqman. Autoantibodies were measured using immunoprecipitation. Treatment history covering all antimalarials, oral and intravenous immunosuppressants (agent, start and stop dates and reasons) since diagnosis was collected. Univariable and multivariable Cox proportional hazards models were used to test variables as predictors of the primary endpoint: time to cyclophosphamide/rituximab.
Results: 124 patients were included. Follow up since diagnosis was Median (IQR) 37.5 (27.4-52.3) years, total therapies per patient was 3 (1-4), therapies per year was 0.2 (0.1-0.3). 54/124 (44%) patients required cyclophosphamide/rituximab.
Results of Cox regression are shown in the table 1. There was a significant association between high expression of IFN-Score B and requirement for cyclophosphamide/rituximab as well as trends for age in the first quartile (<28 years), IFN-Score A and anti-Sm/U1RNP antibodies. Both age <28 and IFN-Score B retained trends as independent predictors in a multivariable model.

Table 1.

Characteristic	CYC/ RTX=Yes n(%)	CYC/ RTX = No n(%)	Univariable Hazard ratio (95% CI)	Univariable p value	Multivariable Hazard Ratio (95% CI)	Multivariable p value
Age						
-Q1: under 28	22 (71%)	9 (29%)	2.25 (0.99,5.12)	0.054	1.74 (0.95,3.18)	0.074
-Q2: 28 – 38	12 (39%)	19 (61%)	1.03 (0.41,2.56)	0.949	Not included	Not included
-Q3: 38 – 52	12 (39%)	19 (61%)	1.52 (0.62,3.72)	0.360	Not included	Not included
-Q4: over 52	8 (26%)	23 (74%)	reference	reference	Not included	Not included
Ethnicity						
-Caucasian	42 (48%)	46 (52%)	1.17 (0.58,2.35)	0.660	Not included	Not included
-AfroCaribbean, South Asian, East Asian, Other	10 (36%)	18 (64%)	reference	reference		
IFN Score A, mean (SD)	−2.59 (−2.67)	−3.84 (−2.71)	1.10 (0.98,1.24)	0.113	Not included	Not included
IFN Score B, mean (SD)	−2.61 (−1.16)	−3.53 (−1.76)	1.31 (1.05,1.64)	0.017	1.23 (0.98,1.55)	0.079
Anti-Sm/U1RNP Ab positive	17 (61%)	11 (39%)	1.50 (0.84,2.67)	0.171	Not included	Not included
Anti-Ro(60) Ab positive	14 (45%)	17 (55%)	0.88 (0.47,1.65)	0.686	Not included	Not included

Conclusion: Patients developing SLE before age 28 with raised interferon scores may be forecast to develop severe disease, fail oral therapies, and require rituximab. While this retrospective analysis may be confounded by a survivorship bias, our findings are consistent with other literature on these variables as predictors of severe disease. Future work will analyse more biomarkers in a larger and more varied patient population.

REFERENCES:

[1] Md Yusof et al. Ann Rheum Dis 2018
[2] El-Sherbiny et al. Sci Rep 2018

Disclosure of Interests: Sabih-Ul Hassan: None declared, Khaled Mahmoud: None declared, Zoe Wigston: None declared, Agata Burska: None declared, Md Yuzaiful Md Yusof: None declared, Edward Vital Grant/research support from: Honoraria and research grant support from Roche, GSK and AstraZeneca.

DOI: 10.1136/annrheumdis-2021-eular.2467

POS0176 COMBINING CXCL5 WITH CONVENTIONAL THERAPY PROVIDES DURABLE IMMUNOSUPPRESSION IN MURINE LUPUS NEPHRITIS

X. Fan[1,2], D. Guo[1], F. Lim[1], J. Thumboo[3], W. Hwang[4,5], C. T. Ng[3], A. Low[3]. *[1]Singapore General Hospital, Department of Clinical Translational Research, Singapore, Singapore*; *[2]Duke-NUS Medical School, SingHealth Duke-NUS Medicine Academic Clinical Programme, Singapore, Singapore*; *[3]Singapore General Hospital, Department of Rheumatology and Immunology, Singapore, Singapore*; *[4]National Cancer Centre, -, Singapore, Singapore*; *[5]Singapore General Hospital, Department of Haematology, Singapore, Singapore*

Background: Lupus nephritis (LN) is a condition arising from abnormal immune responses to internal organs. Patients with LN suffer from severe morbidity and mortality[1, 2]. Despite the aggressive regimen, 20-40% of patients do not respond to current conventional therapy. CXCL5, as a potent chemoattractant and activator of neutrophils[3], demonstrates strong immunosuppression in the pre-clinical mouse model of graft versus host disease (GvHD)[4] and lupus nephritis (LN) by intravenous administration.

Objectives: In this study, we aim to evaluate whether the therapeutic effect of conventional therapy could be further improved by combination therapy with CXCL5.

Methods: Ten doses of exogenous CXCL5 (3ug/kg, biweekly) together with conventional therapy (methylprednisolone (MP, intravenous (IV) injection with 8.3mg/kg/day at day-1, day-2 and day-3) + cyclophosphamide (CP, IV injection with 0.5g/BSA at day-4, monthly for 5 doses)) were administered to 8-week-old Fas^{lpr} mice by IV injection. Mice were monitored for 64 weeks. Splenic immune profile at 3 weeks post treatment (PT) was measured by flow cytometry. Circulating cytokine profile were detected by Luminex technology. Renal function was evaluated by urinary spot albumin creatinine ratio. In situ renal immune cell infiltration and complement 3 deposition were detected by Haematoxylin and Eosin (H&E) and immunohistochemistry staining.

Results: Comparing to control mice (dPBS: 0% at 28 weeks PT), mice survival was improved to 100% at 40 weeks PT and 55.6% at 64 weeks PT by combination therapy of CXCL5 and conventional therapy (MP + CP) (p<0.0001). The accumulation of autoantibody (anti-dsDNA) and proteinuria were reduced 61.2-fold at 32 weeks PT (p=0.004) and 83.5-fold at 28 weeks PT (p=0.03) respectively. Both autoantibody and proteinuria were maintained at low level for 64 weeks. The classification of LN was significantly reduced at 10 weeks PT and equivalent to the classes we observed in pre-onset mice (p=0.004). Although combination therapy was not able to promote Tregs, it reduced both innate (neutrophils and macrophages) and adaptive (T_H1, T_H2 and T_H17 cells and B cells) immunities significantly. Concomitantly, the serum level of endogenous CXCL5 was boosted up by exogenous administration from 74.2 +/- 53.9 pg/ml to 254.1 +/- 147.1 pg/ml at 8 weeks PT (p=0.05) and this relative high concentration was maintained for 48 weeks.

Conclusion: Combining CXCL5 with conventional therapy provides effective and durable immunosuppression in murine LN and it may provide a new option for LN therapy.

REFERENCES:

[1] Almaani S, Meara A, Rovin BH. Update on Lupus Nephritis. *Clin J Am Soc Nephrol*. May 8 2017;12(5):825-835. doi:10.2215/cjn.05780616.
[2] Touma Z, Gladman DD. Current and future therapies for SLE: obstacles and recommendations for the development of novel treatments. *Lupus Sci Med*. 2017;4(1):e000239. doi:10.1136/lupus-2017-000239.
[3] Koltsova EK, Ley K. The mysterious ways of the chemokine CXCL5. *Immunity*. Jul 23 2010;33(1):7-9. doi:10.1016/j.immuni.2010.07.012.
[4] Fan X, Guo D, Cheung AMS, et al. Mesenchymal Stromal Cell (MSC)-Derived Combination of CXCL5 and Anti-CCL24 Is Synergistic and Superior to MSC and Cyclosporine for the Treatment of Graft-versus-Host Disease. *Biol Blood Marrow Transplant*. Jun 5 2018;doi:10.1016/j.bbmt.2018.05.029.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2766

POS0177 POTENTIAL INVOLVEMENT OF IL-40 AND IL-40-PRODUCING CELLS IN PRIMARY SJOGREN'S SYNDROME (PSS) AND PSS-ASSOCIATED LYMPHOMA

C. Rizzo[1], M. Lo Pizzo[2], L. Mohammadnezhad[2], V. L. Lentini[3], D. Di Liberto[2], G. Grasso[1], P. Ruscitti[4], R. Giacomelli[5], F. Ciccia[6], G. Guggino[1]. *[1]"P. Giaccone" University Hospital, University of Palermo, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, Rheumatology Unit, Palermo, Italy*; *[2]"P. Giaccone" University Hospital, University of Palermo, Biomedicine, Neuroscience and Advanced Diagnostic, Palermo, Italy*; *[3]Azienda Ospedaliera Ospedali Riuniti Villa Sofia Cervello, Pathology Unit, Palermo, Italy*; *[4]"San Salvatore" University Hospital, Department of Biotechnological and Applied Clinical Science, L'Aquila, Italy*; *[5]University "Campus Bio-Medico", Unit of Allergology, Immunology, Rheumatology, Department of Medicine, Rome, Italy*; *[6]University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Napoli, Italy*

Background: The pathogenesis of pSS relies on a complex interplay between both innate and adaptive immune responses in which B cells play a pivotal role. Their chronic aberrant hyperactivation may drive clonal escape and consequent lymphomagenesis [1]. In the last few years, B cells have emerged as potential effector cells, able to release a wide range of cytokines that actively contribute to shape the microenvironment they act in. Recently, IL-40, a novel B cell associated cytokine encoded by an uncharacterized gene (C17orf99; chromosome 17 open reading frame 99) was described. Naïve B cells can express IL-40 at both tissue and peripheral level and the stimulation of B cells with IL-4 and TGF-β significantly increases IL-40 release. In addition, human B cells lymphomas are able to constitutively produce IL-40 [2]. Taking into account this emerging evidence and considering the well-known role of IL-4 and TGF-β in pSS pathogenesis, as well as the association with lymphomas, we decided to focus our attention on IL-40 in pSS patients.

Objectives: The aim of the present study was to investigate IL-40 expression in the salivary glands of patients affected by pSS and pSS-associated non-Hodgkin's lymphoma (NHL).

Methods: Minor salivary gland biopsies were obtained from 22 patients with pSS and 12 patients with non-specific chronic sialoadenitis (nSCS), included as controls. Paraffine-embedded samples of parotid glands from patients with a previous diagnosis of pSS-associated NHL (n=10) were selected from the biopsy bank of the Pathology Unit of the Ospedale Cervello (Palermo, Italy). Quantitative gene expression analysis by TaqMan real-time PCR and immunohistochemistry (IHC) for IL-40, IL-4, TGF-β1 was performed on salivary glands from patients and controls. The cellular sources of IL-40 among infiltrating inflammatory cells were determined by fluorescence-activated cell sorting (FACS) analysis and immunofluorescence (IF). Serum IL-40 levels were measured by ELISA in both patients (n=10) and controls (n=9).

Results: IL-40 was significantly increased at both protein and mRNA level in the inflamed salivary glands of patients with pSS where a positive strong correlation between the IL-40 mRNA levels and the focus score (FS) was evidenced. The expression of IL-40 in parotid glands of pSS-associated NHL was also markedly increased (Figure 1). IL-40 expression correlated with the presence of IL-4 and TGF-β; both cytokines were significantly increased in pSS at mRNA and protein level. Among infiltrating immune cells, $CD19^+$ B cells resulted the major source of IL-40. However, we identified $CD4^+$, $CD8^+$ T cells and $CD68^+$ macrophages as additional producers of IL-40 in both FACS and IF analysis. The ELISA test also showed a significant increase of serum IL-40 concentration in pSS patients (p value = 0.0190), compared to controls.

Conclusion: Our preliminary results suggest that IL-40 may play a role in the pathogenesis of pSS and pSS-associated NHL. To the best of our knowledge, this is the first demonstration of the overexpression of this cytokine in salivary gland tissue and sera in pSS. Moreover, we demonstrated that IL-40 is produced by several cellular types, such as T cells and macrophages, and is not exclusively released by B cells. Further studies are necessary to clarify IL-40 pathways and functions in order to unravel IL-40 possible role in pSS development.

REFERENCES:
[1] Mariette X, Criswell LA. Primary Sjogren's Syndrome. N Engl J Med. 2018;379(1):97.
[2] Catalan-Dibene J, Vazquez MI, Luu VP, Nuccio SP, Karimzadeh A, Kastenschmidt JM, et al. Identification of IL-40, a Novel B Cell-Associated Cytokine. J Immunol. 2017;199(9):3326-35.

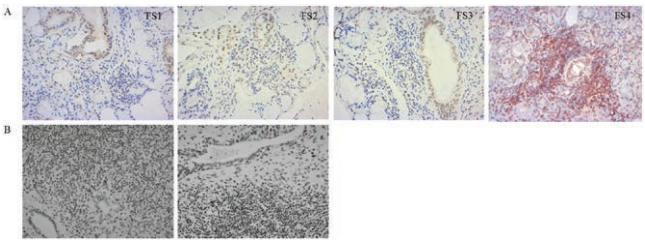


Figure 1. IL-40 overexpression in pSS and pSS-associated lymphoma **A**, Salivary gland biopsies stained for IL-40 showing a marked increase in IL-40 expression in presence of higher focus score. **B**, Parotid gland specimens of pSS-associated lymphoma showing intense staining for IL-40.

Disclosure of Interests: Chiara Rizzo: None declared, Marianna Lo Pizzo: None declared, Leila Mohammadnezhad: None declared, Vincenzo Luca Lentini: None declared, Diana Di Liberto: None declared, Giulia Grasso: None declared, Piero Ruscitti Consultant of: Pfizer, Novartis, Celgene, Abbvie, Roche, Lilly, Rorberto Giacomelli Consultant of: Pfizer, Novartis, Celgene, Abbvie, Roche, Lilly, francesco ciccia Consultant of: Pfizer, Novartis, Celgene, Abbvie, Roche, Lilly, Giuliana Guggino Consultant of: Pfizer, Novartis, Celgene, Abbvie, Roche, Lilly
DOI: 10.1136/annrheumdis-2021-eular.3792

POS0178 GENE SIGNATURE FINGERPRINTS DIVIDE SLE PATIENTS IN SUBGROUPS WITH COMPARABLE BIOLOGICAL DISEASE PROFILES: A MULTICENTRE LONGITUDINAL STUDY

M. J. Wahadat[1,2], C. G. Van Helden-Meeuwsen[1], S. Van Tilburg[1], E. Schatorjé[3,4], E. Hoppenreijs[3,4], P. C. E. Hissink Muller[5], J. M. Van den Berg[6], D. Schonenberg-Meinema[6], S. Kamphuis[2], M. Versnel[1]. [1]*Erasmus University Medical Center, Department of Immunology, Rotterdam, Netherlands*; [2]*Sophia Children's Hospital, Erasmus University Medical Center, Department of Pediatric Rheumatology, Rotterdam, Netherlands*; [3]*Amalia Children's Hospital, Radboudumc, Paediatric Rheumatology, Nijmegen, Netherlands*; [4]*St. Maartenskliniek, Paediatric Rheumatology, Nijmegen, Netherlands*; [5]*Leiden University Medical Center, Department of Paediatrics/Paediatric Rheumatology, Leiden, Netherlands*; [6]*Emma Children's Hospital AMC, University of Amsterdam, Department of Paediatric Immunology, Rheumatology and Infectious Diseases, Amsterdam, Netherlands*

Background: Even in the hands of experienced clinicians, clinical phenotyping and predicting treatment responses in Systemic Lupus Erythematosus (SLE) patients remains challenging. Therefore, the identification of biomarkers that can help physicians to divide patients into subgroups based upon aberrantly activated pathways is relevant and might guide future treatment strategies. Extensive blood transcriptional profiling has identified various gene modules that seem promising for stratification of SLE patients into subgroups (1). However, the feasibility to implement these complicated and expensive tests for use in the daily practice of routine clinical laboratories is challenging if not impossible.
Objectives: The aim of this study was to develop gene signatures that stratify patients into groups with comparable disease profiles and are feasible to perform in routine clinical laboratories.
Methods: To identify coordinated expression of a set of genes and reduce data complexity, genes from 4 previously described modules (Interferon M1.2, Interferon M5.12, Neutrophil- and Plasmablast (PB)(1)) were measured using real-time quantitative PCR expression on whole blood RNA samples. Subsequently, a principle component analysis was used to select 2-5 indicator genes, that represent a specific signature. Expression levels of these genes were measured in healthy donors (n=42) and samples from two independent childhood-onset SLE cohorts (n=51 and n=20). Scores higher than the mean + 2 S.D. score of healthy controls were defined as high gene signature scores. Based on their expression levels, gene signatures were divided over 14 clusters. Associated clusters were subsequently grouped into three gene fingerprints termed 1) all-signatures-low, 2) only high IFN (M1.2 and/or M5.12) and 3) high PB and/or Neutrophil. Disease activity was measured by the SELENA-SLEDAI score.
Results: All four gene signatures were higher expressed in patients compared to healthy controls and showed a significant correlation with the SLEDAI. The PB signature showed the highest association with disease activity (r= 0.6512, P<0.0001). In longitudinally collected samples, the PB signature was reduced in patients who were on treatment and showed a significant trend with the SLEDAI. When patients were divided into the described gene fingerprints, the highest SLEDAI scores (median score=8) were observed in the high PB-Neutrophil group. The lowest disease activity (median score =2) was observed in the all-signatures-low group. The same distribution was seen when samples from a second time point were divided based on this stratification method and this was also reproduced in samples from an independent SLE cohort (figure 1).
Conclusion: Various gene signatures are associated with disease activity, which underlines the involvement of different pathophysiological mechanisms in SLE. Combining these signatures into gene fingerprints can help to stratify patients into comparable groups and guide individualized treatment choices for patients in the future.
REFERENCES:
[1] Banchereau R, Hong S, Cantarel B, Baldwin N, Baisch J, Edens M, et al. Personalized Immunomonitoring Uncovers Molecular Networks that Stratify Lupus Patients. Cell. 2016;165(6):1548-50.

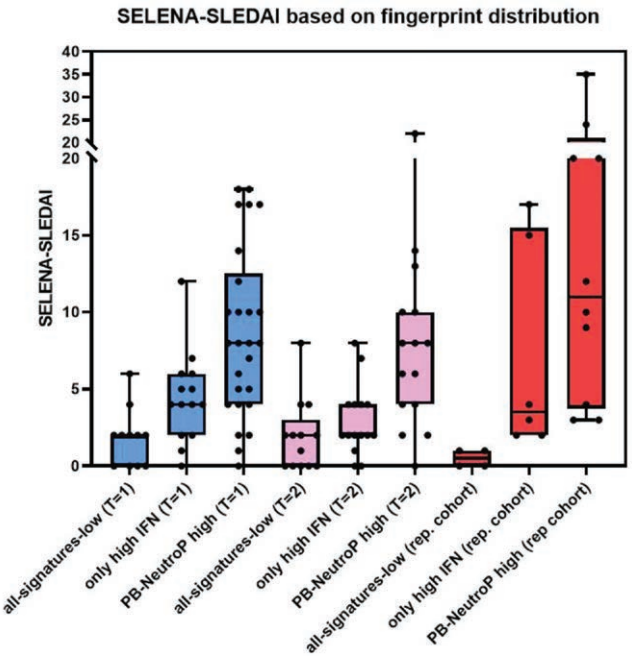


Figure 1. SELENA-SLEDAI scores based on gene fingerprint distribution. Blue indicates time point one of cohort 1 (n=51); pink indicates time point two of cohort 1 (n=45); red indicates time point one of the replication cohort (n=20)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4011

POS0179 EXPLORING THE EFFECTS OF A TWO-SCORE INTERFERON SIGNATURE AND RESPONSES TO INTERFERON STIMULUS

Z. Wigston[1], A. Burska[1], M. Wittmann[1], E. Vital[1,2]. [1]*University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [2]*NIHR, Leeds Biomedical Research Centre, Leeds, United Kingdom*

Background: IFN Scores are increasingly important as biomarkers to stratify RMDs and select patients for interferon targeted therapies. Several studies have previously demonstrated that different sets of interferon stimulated genes (ISGs) have different clinical associations. We validated a 2-score system of ISGs expression consisting of Score A (a set of ISGs included in most interferon signature assays) and Score B (a set of less commonly

measured ISGs). Score B consistently demonstrated stronger clinical associations in studies of diagnosis, prediction of progression to SLE in At-Risk individuals, response to rituximab and imaging-proven synovitis. Previous literature suggested that subsets of ISGs were explained by different interferon subtypes.

Objectives: To understand the determinants of IFN Score A and IFN Score B.

Methods: PBMCs and whole blood Tempus from 4 different healthy donors were stimulated with various cytokines and IFNs at 6- and 24-hour time points. RNA from both sample types were extracted and the expression of 26 interferon stimulated genes were measured using TaqMan and normalised to house-keeping gene PPIA. IFN Scores A and B were calculated as previously described [1]. To compare relative increase in expression with each condition, we calculated delta Ct fold change relative to non-stimulated. To represent greater expression as numerically higher positive values, relative expression was calculated as (fold change*-100) +100. Independent T-test calculated the significant differences between each condition compared to IFN α stimulation.

Results: Table 1 shows differences between each condition compared with IFN α at the 6-hour time point. In both sample types, all conditions excluding IFN β stimulation were shown to induce significantly lower expression of both scores compared to IFN α ($p < 0.01$). At 6 and 24 hours, IFN α and IFN β showed a strong induction of IFN score A and B. At 6 hours, IFN γ, κ, and λ induced IFN score A and B but weaker than IFN α and β which was shown in both sample types. We did not observe a difference between the expression of these two scores according to interferon subtype. Other cytokines (TNF, IL-1 and IL-6) weakly induced expression of Score A and B. For IL-10 there was a possible discordant effect with increase in expression of Score B, but decreased expression of Score A, however these changes were small in magnitude.

Table 1.

Condition	IFN Score A		IFN Score B	
	Mean relative expression vs. non-stimulated	P value (vs IFN α)	Mean relative expression vs. non-stimulated	P value (vs IFN α)
PBMC				
IFN α	103.4	-	71.8	-
IFN β	97.1	0.373	64.7	0.352
IFN γ	37.5	<0.001	29.5	0.002
IFN κ	16.6	<0.001	3.1	<0.001
IFN λ	24.8	<0.001	11.1	<0.001
IL-1	9.7	<0.001	4.4	<0.001
IL-6	4.5	<0.001	4.1	<0.001
IL-10	-15.2	<0.001	8.0	<0.001
TNF α	9.6	<0.001	1.2	<0.001
Whole Blood				
IFN α	116.7	-	74.1	-
IFN β	116.6	0.997	73.2	0.894
IFN κ	23.0	0.001	7.9	0.003
IFN λ	23.0	0.001	7.6	<0.001

Conclusion: We found a difference in the induction of ISG expression between subtypes of Type I interferon, as well as other interferons and cytokines. However, the relative expression of IFN Score A and IFN Score B is not easily explained by the subtypes of interferon. We have also previously shown that these scores are both similarly expressed comparing different cell subsets. The explanation for the coordinated expression of these ISGs is therefore unclear and future work will explore the scores with a combination of conditions.

REFERENCES:

[1] El-Sherbiny, Y.M., et al. Scientific Reports, 2018. **8**(1): p. 5793.

Disclosure of Interests: Zoe Wigston: None declared, Agata Burska: None declared, Miriam Wittmann Consultant of: Abbvie, Celgene, Janssen, L'Oreal, Novartis and Pfizer, Edward Vital Speakers bureau: Becton Dickinson and GSK, Consultant of: AstraZeneca, GSK, Roche/Genentech, and Sandoz, Grant/research support from: AstraZeneca, Roche/Genentech

DOI: 10.1136/annrheumdis-2021-eular.1100

POS0180

TYPE I INTERFERON DEPENDENT HSA-MIR-145-5P DOWNREGULATION MODULATES MUC1 AND TLR4 OVEREXPRESSION IN SALIVARY GLANDS FROM PRIMARY SJÖGREN'S SYNDROME PATIENTS

D. Jara[1], S. Aguilera[2], P. Carvajal[1], I. Castro[3], M. J. Barrera[4], S. González[5], C. Molina[4], M. J. González[1]. [1]*Instituto de Ciencias Biomédicas, Facultad de Medicina, Universidad de Chile, Programa de Biología Celular y Molecular, Santiago, Chile*; [2]*Clínica INDISA, Rheumatology, Santiago, Chile*; [3]*Facultad de Medicina, Universidad de Chile, Departamento de Tecnología Médica, Santiago, Chile*; [4]*Universidad San Sebastián, Facultad de Odontología, Santiago, Chile*; [5]*Facultad de Ciencias, Universidad Mayor, Escuela de Odontología, Santiago, Chile*

Background: Primary Sjögren's syndrome (pSS) is an autoimmune and inflammatory disease that mainly affects the salivary glands (SG) and is characterized by an overactivation of the type I interferon pathway (IFNs I). IFNs I are known to regulate the levels of microRNAs (miRNAs), non-coding RNAs whose levels are altered in pSS. IFNs I can decrease the levels of miR-145-5p, a miRNA with anti-inflammatory roles that has been reported downregulated in SG of from pSS patients [1]. This miRNA has TLR4 and MUC1 transcripts as predicted targets. MUC1 and TLR4 are two proteins overexpressed in SG of pSS patients that contribute, through various mechanisms, to the inflammatory state and glandular dysfunction [2-3]. Thus, we propose that IFNs I may contribute to a self-perpetuating inflammation loop through a hsa-miR-145-5p dependent MUC1 and TLR4 overexpression in the SG of pSS patients.

Objectives: to evaluate whether mRNA levels of MUC1 and TLR4 are modulated by hsa-miR-145-5p in a IFNs I dependent manner.

Methods: 13 pSS patients and 9 controls SG biopsies were analyzed. hsa-miR-145-5p levels were determined by TaqMan assays and MUC1, TLR4, IFN-α and IFN-β mRNA levels by RT-qPCR. Additionally, in vitro assays using type I IFNs and chemically synthesized hsa-miR-145-5p mimics and inhibitors were performed to study its effect on MUC1 and TLR4 expression. JAK1 and STAT1 mRNA levels were also measured.

Results: By Taqman assays we validated the decreased hsa-miR-145-5p levels ($p=0.0001$) in SG of pSS patients compared to controls. The decreased hsa-miR-145-5p levels correlated inversely with the increased mRNA levels of IFN-β ($p=0.0192$) in SG of pSS-patients. The hsa-miR-145-5p downregulation also correlated inversely with the overexpression of its predicted targets MUC1 ($p=0.010$) and TLR4 ($p=0.0004$). In vitro assays showed that IFN-β induces the overexpression of JAK1 ($<p=0.0001$) and STAT1 ($p=<0.0001$) leading to the downregulation of hsa-mir-145-5p ($p=<0.0001$) and increased MUC1 ($p=<0.0001$) and TLR4 mRNA levels ($p=<0.0001$). Functional assays suggest a regulation of hsa-miR-145-5p on MUC1 and TLR4 expression as MUC1 and TLR4 mRNA levels were decreased in HSG cells transfected with hsa-miR-513c-3p mimic and increased in HSG cells transfected with the miRNA inhibitor.

Conclusion: Our findings suggest that IFNs I could induce the downregulation of hsa-miR-145-5p leading to the overexpression of MUC1 and TLR4 in SG from pSS patients. TLR4 is activated by ectopic mucins in the SG extracellular matrix from pSS patients which induces pro-inflammatory cytokines secretion [3]. Furthermore, the high levels of the MUC1-SEC and MUC1-Y isoforms observed in SG from pSS patients may favor cytokine synthesis through the immuno-enhancing peptide of MUC1-SEC or through the formation of a MUC1-SEC/MUC1-Y complex [4]. Therefore, IFNs I may contribute to the development of SS through amplification and perpetuation of inflammation due to a hsa-miR-145-5p dependent MUC1 and TLR4 overexpression.

REFERENCES:

[1] I. Alevizos, et al,. Arthritis Rheum, 2011;63:535-44.
[2] HH. Sung, et al,. Oral Dis. 2015;21(6):730-8.
[3] MJ. Barrera, et al,. Rheumatology (Oxford). 2015;54(8):1518-27
[4] LM. Herbert, et al,. Cancer Res. 2004;64(21):8077-84.

Acknowledgements: Fondecyt 1210055, Fondecyt 1160015, Fondecyt Iniciación 11170049, Fondecyt Iniciación 11201058, CONICYT fellowship (DJ, PC)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2651

PROMs and markers

POS0181 HOW FIT ARE THE SOCIAL SUPPORT INSTRUMENTS USED IN RMDS: A SYSTEMATIC REVIEW OF VALIDATION STUDIES

D. De Cock[1], D. Benavent[2], L. Falzon[3], S. Ramiro[4,5], L. Carmona[6]. [1]*KU Leuven, Skeletal Biology and Engineering Research Centre, Leuven, Belgium*; [2]*Hospital Universitario la Paz-IdiPaz, Rheumatology Service, Madrid, Spain*; [3]*Northwell Health, Center for Personalized Health, New York, United States of America*; [4]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [5]*Zuyderland Medical Center, Rheumatology, Heerlen, Netherlands*; [6]*Instituto de Salud Musculoesquelética (InMusc), Rheumatology, Madrid, Spain*

Background: Rheumatic and musculoskeletal diseases (RMDs) diminish psychosocial well-being. Social support (SS) is considered to improve this psychosocial wellbeing. Therefore, SS is an important construct to measure in RMDs.
Objectives: To systematically review and summarize the psychometric properties of SS instruments developed or validated in RMDs.
Methods: A comprehensive search in Medline, Embase, PsycINFO, CINAHL and Epistemonikos was performed from inception to June 8, 2020, with the aid of an experienced librarian (LF). Two researchers (DDC and DB) independently screened articles on title+abstract and next on full text. Reference lists of included studies were reviewed for additional references. Articles were included if covering psychometric properties (detailed in the Table 1) of SS instruments used in RMDs. Studies on questionnaires lacking an English version, unpublished material, case reports, editorials, letters, or reviews were excluded. Risk of bias of studies and instruments was assessed via the COSMIN checklist.
Results: From 4986 articles captured, 30 met the predefined inclusion criteria. These articles included 21 SS instruments used in 8 RMDs, mainly rheumatoid arthritis and osteoarthritis.
Table 1 shows the psychometric properties per instrument. Construct validity, structural validity, and internal consistency were assessed for most instruments, while measurement invariance, measurement error, criterion validity and responsiveness in ≤3 instruments each. Development and content validity of the instruments gave consistently high risk of bias by the COSMIN checklist.
The most widely validated instruments were the Arthritis Impact Measurement Scales (AIMS) and the Osteoarthritis Knee and Hip Quality of Life (OAKHQOL), with their respective derived instruments (AIMS2, AIMS2-SF, mini-OAKHQOL and e-OAKHQOL). For the AIMS SS scale, internal consistency ranged between 0.33-0.69 (Cronbach's α) and test-retest reliability was estimated 0.92 (Guttman reproducibility coefficient). For the OAKHQOL SS scale, internal consistency ranged between 0.78-0.81 (Cronbach's α) and test-retest reliability ranged between 0.5-0.85 (ICC). Responsiveness was only investigated in AIMS and the Sickness Impact Profile (SIP) instrument. Relative efficiency for SS for the SIP was considerably higher than for AIMS (0.74 vs 0.18).
Conclusion: This review gives a summary of the psychometric properties of SS instruments in RMDs. Most instruments show sufficient structural validity internal consistency and reliability, but some psychometric properties such as criterion validity, measurement error and invariance, need to be investigated before choosing an optimal SS instruments.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2020

POS0182 MINIMAL CLINICALLY IMPORTANT IMPROVEMENT (MCII) AND PATIENT ACCEPTABLE SYMPTOM STATE (PASS) FOR PAIN AND FUNCTION INSTRUMENTS IN HAND OSTEOARTHRITIS (OA)

F. Kroon[1,2], L. Van de Stadt[1], D. Van der Heijde[1], M. Kloppenburg[1,3]. [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [2]*Zuyderland Medical Center, Rheumatology, Heerlen, Netherlands*; [3]*Leiden University Medical Center, Clinical Epidemiology, Leiden, Netherlands*

Background: Australian/Canadian Hand OA Index (AUSCAN), Michigan Hand Outcomes Questionnaire (MHQ), Functional Index of Hand OA (FIHOA) and visual analogue scale (VAS) are frequently used instruments to measure pain and function in hand OA research. MCII and PASS are useful to interpret results of patient reported outcomes.
Objectives: To estimate MCII and PASS for these instruments using anchor-based methods.
Methods: Hand OA patients participating in a six-week randomised placebo-controlled trial with prednisolone (RCT; NTR5263) and those attending the two-year follow-up visit of the observational Hand OSTeoArthritiS cohort completed AUSCAN subscales pain and function, MHQ subscales pain, activities of daily living (ADL) and overall function, FIHOA and 100mm VAS pain. RCT participants were asked to indicate whether they changed compared to baseline (improved/no change/worse) and to rate the importance of improvement (very much/moderately/slightly/not at all). MCII was defined as the minimal improvement in symptoms achieved by 75% of participants who stated a slight/moderate improvement during the RCT, calculated as the 75th percentile of the distribution of change scores from baseline in this group. Absolute and relative percentage change were evaluated. For MCII direction of effect was unified, so positive values indicate worse symptoms and vice versa. Participants from both studies rated satisfaction with their state of health (acceptable/unacceptable). PASS was defined as the minimal score considered acceptable for 75% of participants, calculated as the 75th percentile of the distribution of scores in participants who rated their health 'acceptable'.
Results: Demographics of the RCT (n=92, mean age 63.9, 79% women) and cohort (n=383, 60.9 years, 84% women) participants were typical for hand OA. RCT participants were more symptomatic (e.g. mean [SD] VAS pain 54.0 [20.5] versus 35.2 [19.1]). Of the function instruments, only AUSCAN had a credible MCII (relative percentage improvement 9.8%), while the (positive) MCII values for FIHOA and MHQ subscales would indicate that worsening was rated as functional improvement (table 1). MCII was negative (corresponding to improvement) for all pain instruments, with relative percentage change around 25% for VAS and MHQ, compared to only 2% for AUSCAN. PASS values of all instruments were comparable in the two populations. Most instruments had a PASS around 50% of the possible maximum score, except for MHQ ADL, in which higher is better and a relatively high PASS is thus indicative of a floor effect (table 1).

Table 1. psychometric properties per social support instrument

Instrument	Face validity	Content Validity	Structural validity	Criterion validity	Internal consistency	Reliability	Measurement error	Hypothesis testing for construct validity	Cross-cultural validity/ Measurement invariance	Responsiveness
AIMS			●		●	●		●		●
AIMS2	●	●	●		●	●		●		
AIMS2-SF			●		●			●		
Brief Screening Questions	●			●				●		
Dyadic Efficacy Scale	●	●	●		●					
EIS			●		●	●		●		
Flanagan QOL			●		●	●		●		
FS	●	●	●		●	●		●	●	
IRGL			●	●	●	●		●		
ISSI					●	●		●		
LISRES					●	●		●		
MEPS	●	●	●			●	●	●		
MWA			●			●		●		
OAKHQOL	●	●	●		●	●	●	●		
e-OAKHQOL			●		●			●		
Mini-OAKHQOL	●	●	●		●	●		●		
PFSSADI			●	●	●	●				
RASP			●		●	●		●		
SIP								●		●
SPQ			●		●	●		●		
SSQT			●		●	●		●	●	

Arthritis Impact Measurement Scales (AIMS); Short Form (SF); Emotional Intimacy Scale (EIS); Quality of Life (QOL); Friendship Scale (FS); Impact on Rheumatic diseases and General health and Lifestyle (IRGL); Interview Schedule for Social Interactions (ISSI); Life Stressors and Social Resources Inventory (LISRES); Medical Issues, Exercise, Pain, and Social Support (MEPS); Modified Work APGAR (MWA); Osteoarthritis Knee and Hip Quality of Life (OAKHQOL); preferences for formal social support of autonomy and dependence in pain inventory (PFFSADI); Responses and Attitudes to Support during Pain questionnaire (RASP); Sickness Impact Profile (SIP); Social support and Pain Questionnaire (SPQ); Social Support Questionnaire for Transactions (SSQT).

Table 1. MCII and PASS of pain and function instruments in hand OA patients in two settings.

	MCII (95% CI) in RCT†			PASS (95% CI)	
Instrument	Absolute units	Percentage	[n]	RCT (n=68)	Cohort (n=126)
MHQ					
Overall function, 0-100*	3.4 (-2.7;9.5)	3.6 (-9.1;16.3)	[23]	55.6 (52.6;58.5)	48.1 (45.7;50.4)
ADL, 0-100*	1.6 (-4.4;7.6)	2.8 (-9.6;15.3)	[23]	71.7 (68.2;75.1)	62.9 (59.8;66.0)
Pain, 0-100	-12.2 (-17.2;-7.1)	-23.1 (-35.4;-10.8)	[16]	47.0 (40.5;53.5)	55.7 (52.0;59.5)
AUSCAN					
Function, 0-36	-3.3 (-5.7;-0.9)	-9.8 (-23.9;4.2)	[23]	17.1 (15.3;19.0)	20.9 (19.4;22.3)
Pain, 0-20	-1.1 (-2.6;0.4)	-1.8 (-18.5;14.9)	[27]	9.0 (8.2;9.9)	11.1 (10.3;11.8)
FIHOA, 0-30	0.1 (-1.6;1.7)	22.7 (-0.7;46.0)	[23]	12.4 (11.1;13.7)	13.9 (12.8;15.0)
VAS pain, 0-100	-11.5 (-18.2;-4.7)	-24.4 (-36.1;-12.8)	[27]	47.7 (42.2;53.3)	48.8 (44.6;53.0)

Direction of effect of all instruments is higher is worse, except those with *.†For all MCII direction of effect was unified, so positive values indicate worse symptoms and negative values values indicate improved symptoms.

Conclusion: The only function instrument with an acceptable threshold for MCII was AUSCAN function, while for pain MHQ and VAS performed better than AUSCAN. PASS values show a relatively high level of tolerance of 50% of the maximum of the scale.
Disclosure of Interests: Féline Kroon: None declared, Lotte van de Stadt Grant/research support from: The HOSTAS and HOPE studies were sponsored by the Dutch Arthritis Society., Désirée van der Heijde: None declared, Margreet Kloppenburg Grant/research support from: The HOSTAS and HOPE studies were sponsored by the Dutch Arthritis Society.
DOI: 10.1136/annrheumdis-2021-eular.400

POS0183 SIGLEC1 AS A TYPE I INTERFERON BIOMARKER IN IDIOPATHIC INFLAMMATORY MYOPATHIES

M. Graf[1], A. S. L. Von Stuckrad[2], A. Uruha[3,4], J. Klotsche[5], L. Zorn-Pauly[1], N. Unterwalder[6], T. Buttgereit[7], M. Krusche[1], C. Meisel[6], G. R. Burmester[1], F. Hiepe[1], R. Biesen[1], T. Kallinich[2], W. Stenzel[4], U. Schneider[1], T. Rose[1].
[1]Charité – Universitätsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany; *[2]Charité – Universitätsmedizin Berlin, Pediatric Pneumology, Immunology and Critical Care Medicine and SPZ (Center for Chronically Sick Children), Berlin, Germany*; *[3]Tokyo Metropolitan Neurological Hospital, Neurology, Tokyo, Japan*; *[4]Charité – Universitätsmedizin Berlin, Neuropathology, Berlin, Germany*; *[5]Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), DRFZ, Berlin, Germany*; *[6]Labor Berlin - Charité Vivantes GmbH, Immunology, Berlin, Germany*; *[7]Charité – Universitätsmedizin Berlin, Dermatology and Allergy, Dermatological Allergology, Berlin, Germany*

Background: Idiopathic inflammatory myopathies (IIM) are autoimmune diseases that mainly affect skeletal muscle, lung, skin and joints. IIM can be separated into dermatomyositis (DM), inclusion body myositis (IBM), antisynthetase syndrome (AS) and immune-mediated necrotizing myopathy (IMNM). Type I interferons (IFN) are known to play a crucial role in the etiopathogenesis of some of these entities such as DM.[1] Sialic acid binding Ig-like lectin 1 (SIGLEC1, CD169) is part of the type I IFN signature found in SLE and DM and is expressed on the cell surface of monocytes. Thus, analysis of SIGLEC1 expression by flow cytometry enables a straightforward assessment of the type I IFN signature. Its utility has been shown for juvenile and adult SLE and other rheumatic diseases but not in IIM.[2,3] The assessment of the type I IFN system in clinical practice is an unmet need and, in this context, SIGLEC1 might be useful.
Objectives: To assess SIGLEC1 expression on monocytes by flow cytometry as a type I IFN biomarker in IIM
Methods: Pediatric and adult patients with a clinical diagnosis of DM, AS, IMNM and IBM and at least one measurement of SIGLEC1 who have been treated at the Department of Rheumatology, Charité - Universitätsmedizin Berlin between 2015 and 2020 were included in this retrospective study. Control groups of healthy individuals (n=19) and SLE patients (n=30) were included. Disease activity was assessed by Physician Global Assessment (PGA) and Childhood Myositis Assessment Scale (CMAS). SIGLEC1 expression on monocytes was analyzed by flow cytometry. Cross-sectional analyses (n=74) were performed using Mann Whitney-U test (MWU) and two-level mixed-effects linear regression model was used for longitudinal analyses (n=26, 110 visits). This study was approved by the local ethics committee of the Charité - Universitätsmedizin Berlin.
Results: 74 patients (adult/juvenile DM: n=21/n=17; AS: n=19; IMNM: n=8; IBM: n=9) were included. In cross-sectional analysis, SIGLEC1 expression was significantly upregulated in adult and juvenile DM patients with moderate to severe disease activity (PGA≥5) compared with adult/juvenile DM patients with no to moderate disease activity (PGA<5) (both p<0.001). In longitudinal analyses, SIGLEC1 correlated with disease activity in juvenile DM (SIGLEC1 vs. CMAS: betaST=-0.65; p<0.001) and adult DM (SIGLEC1 vs. PGA: betaST=0.52; p<0.001), better than Creatine Kinase (CK) (juvenile DM, CK vs. CMAS: betaST=-0.50; p<0.001; adult DM, CK vs PGA: betaST=0.17; p=0.149). In AS 42,1% of the patients showed elevated SIGLEC1 expression, while it was not upregulated in IMNM and only in two patients with IBM, who were concurrently positive for autoantibodies that affect the type I IFN system (see Figure 1).
Conclusion: SIGLEC1 is a useful biomarker to identify an activated type I IFN system in IIM. Flow cytometry is used widely in laboratory medicine, which could facilitate the implementation of SIGLEC1 into clinical routine.

REFERENCES:

[1] Gallay L, Mouchiroud G, Chazaud B. Interferon-signature in idiopathic inflammatory myopathies: *Current Opinion in Rheumatology* 2019;**31**:634–42. doi:10.1097/BOR.0000000000000653
[2] Rose T, Grutzkau A, Hirseland H, *et al.* IFNalpha and its response proteins, IP-10 and SIGLEC-1, are biomarkers of disease activity in systemic lupus erythematosus. *Ann Rheum Dis* 2013;**72**:1639–45. doi:10.1136/annrheumdis-2012-201586
[3] Stuckrad SL von, Klotsche J, Biesen R, *et al.* SIGLEC1 (CD169) is a sensitive biomarker for the deterioration of the clinical course in childhood systemic lupus erythematosus. *Lupus* 2020;:961203320965699. doi:10.1177/0961203320965699

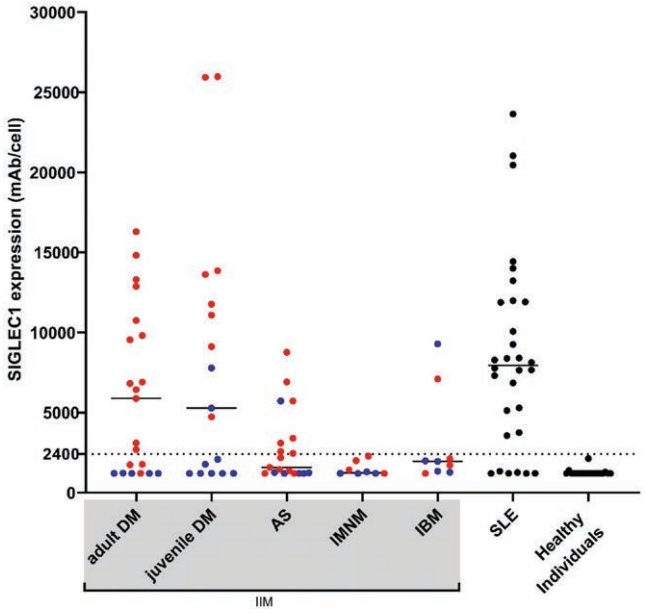


Figure 1. SIGLEC1 expression on monocytes in IIM subgroups and control groups; in IIM subgroups, patients with low disease activity (PGA<5) are marked in blue, patients with high disease activity (PGA≥5) are marked in red; mAb/cell, monoclonal antibodies bound per cell

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2816

POS0184 URINE-GALECTINE 3 BINDING PROTEIN (U-GAL3BP) IS A SENSITIVE MARKER OF KIDNEY INFLAMMATION AND RESPONSE TO TREATMENT IN LUPUS

F. Faustini[1,2], H. Idborg[2], E. Svenungsson[1,2], S. Poetzsch[3], S. Okitsu[4], A. Larsson[5], I. Gunnarsson[1,2]. *[1]Karolinska University Hospital, Rheumatology, Stockholm, Sweden*; *[2]Karolinska Institutet, Department of Medicine, Division of Rheumatology, Stockholm, Sweden*; *[3]Merck Healthcare KGaA, Merck Healthcare KGaA, Darmstadt, Germany*; *[4]EMD Serono Research and Development Institute, EMD Serono Research and Development Institute, Billerica, MA, United States of America*; *[5]Uppsala University, Department of Medical Sciences/Clinical Chemistry, Uppsala, Sweden*

Background: Lupus nephritis (LN) represents a serious manifestation of systemic lupus erythematosus (SLE) which requires timely diagnosis, treatment and monitoring. Kidney biopsy is the gold standard of diagnosis and is instrumental to treatment decisions, however it is not generally performed for monitoring and evaluation of response to treatment. To such purposes, accessible biomarkers, for instance urinary, might be highly advantageous.
Objectives: To evaluate urine-Galectin 3 binding protein (uGAL3BP) as a novel biomarker in biopsy-proven active lupus nephritis (A-LN) in comparison to active non-renal SLE (ANR-SLE), inactive SLE (I-SLE), and in population-based controls (HC). Furthermore, we compared uGAL3BP with known markers of renal pathology including neutrophil gelatinase-associated lipocalin (NGAL), osteopontin (OPN), kidney injury molecule 1 (KIM-1), and galectin 3 (GAL3).
Methods: Urine samples from A-LN (n=86), ANR-SLE (n=63), I-SLE (n=73) and HC (n=48) were included. uGAL3BP was measured using a commercial ELISA kit and values, adjusted for u-creatinine levels, were expressed as ng/mmol. Other markers analyzed according to clinical routine at the Department of Clinical Chemistry at Uppsala University Hospital were also adjusted for u-creatinine levels. Renal biopsies were graded according to the ISN/RPS classification(1) and evaluated for activity and chronicity index. Ten A-LN patients were evaluated before and after induction treatment.
Results: In the A-LN group, median (IQR) levels of u-GAL3BP were 15.8 (6.8-24.6) ng/mmol, while in ANR-SLE, I-SLE, HC were significantly lower 4.4 (2.0-9.0), 2.8 (1.7-4.7), 2.0 (0.9-4.8) respectively (Kruskal-Wallis p<0.0001). Similarly, u-NGAL was found at higher levels in A-LN patients, 3.3 (2.0-5.7) µg/mmol, with respect to the ANR-SLE 2.0 (0.9-4.5), I-SLE 1.6 (0.8-3.2), and HC 2.4 (1.2-5.3), (p=0.008). The highest levels of OPN were found in the group of I-SLE (190.6 (85.1-299.9) µg/mmol, compared to A-LN 72.98 (37.6-118.1), ANR-SLE 92.3 (58.5-129.7) and HC 76.5 (58.2-120.3), (p<0.0001). KIM-1 levels differed among groups with higher levels in the A-LN group (188.9 (113.7-309.7) ng/mmol), in comparison to ANR-SLE 131.4 (92.2-186.1), I-SLE 123.8 (70.3-200.2), and HC 78.2 (68.8-115.1), (p<0.0001). GAL3 showed comparable levels across groups.
When exploring the biomarkers across histologic subgroups of LN, u-GAL3BP could discriminate between proliferative and mesangial forms (17.7(9.6-32.5) vs 6.7(5.1-16.1) ng/mmol, p=0.027), while it did not discriminate against membranous LN. U-NGAL was higher in proliferative LN 3.7(2.4-5.8) µg/mmol with respect to membranous 2.4 (1.1-3.8) (p=0.01), while mesangial LN showed comparable levels. OPN, KIM-1 and GAL3 were comparable across groups.
In the ten patients with available samples after induction therapy (mycophenolate mofetil (MMF) in 4, rituximab (RTX) in one, cyclophosphamide in 5 (one combined with MMF and one with RTX), u-GAL3BP showed a significant decrease of median levels from 218.8 to 41.5 ng/mmol (Wilcoxon p=0.03). u-GAL3BP associated with renal activity in class III/IV LN (R=0.42, p=0.004).
Conclusion: Among the tested markers, high uGal3BP adjusted for creatinine was found to be a promising marker of renal involvement in SLE patients and associated with renal activity in patients with proliferative forms (class III/IV) of LN. A decrease was further seen following therapy, suggesting that u GAL3-BP could be used to monitor renal activity.
REFERENCES:
[1] Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. J Am Soc Nephrol. 2004;15(2):241-50.
[2] Houssiau FA, Vasconcelos C, D'Cruz D, Sebastiani GD, Garrido Ed Ede R, Danieli MG, et al. Immunosuppressive therapy in lupus nephritis: the Euro-Lupus Nephritis Trial, a randomized trial of low-dose versus high-dose intravenous cyclophosphamide. Arthritis Rheum. 2002;46(8):2121-31.
Disclosure of Interests: Francesca Faustini Speakers bureau: I have received speaking fees, last time more than two years ago, Helena Idborg: None declared, Elisabet Svenungsson: None declared, Sven Poetzsch Employee of: Merck Serono, Shinji Okitsu Employee of: Merck Serono, Anders Larsson: None declared, Iva Gunnarsson: None declared
DOI: 10.1136/annrheumdis-2021-eular.3477

POS0185

IDENTIFICATION AND VALIDATION OF TWO NOVEL SERUM BIOMARKERS ASSOCIATED WITH THE SEROLOGICAL STATUS OF RHEUMATOID ARTHRITIS PATIENTS.

V. Calamia[1], L. Lourido[1], P. Fernández Puente[1,2], A. Illiano[3], R. Paz González[1], B. Rocha Loureda[1], L. Collado Rodríguez[1], E. Perez-Pampín[4], C. Ruiz-Romero[1], A. Gonzalez[4], F. J. Blanco[1]. *[1]Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas, Universidade da Coruña (UDC), Unidad de Proteómica, Grupo de Investigación de Reumatología (GIR), A Coruña, Spain*; *[2]Universidad de A Coruña (UDC), Centro de Investigaciones Científicas Avanzadas (CICA), A Coruña, Spain*; *[3]University of Naples Federico II, Department of Chemical Sciences, Naples, Italy*; *[4]Instituto de Investigación Sanitaria (IDIS). Hospital Clínico Universitario de Santiago (CHUS), Experimental and Observational Rheumatology and Rheumatology Unit, Santiago de Compostela, Spain*

Background: Despite the diagnostic value of Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibodies (ACPA), more serological markers are needed in order to improve early diagnosis and treatment response of the Rheumatoid Arthritis (RA) patients. Increased knowledge about how these two major autoreactivities arise is crucial for understanding how RA develops and what mechanisms drive pathogenesis.
Objectives: We aimed to investigate, using a proteomic strategy, novel protein biomarkers associated with RF and/or ACPA that might be useful to stratify seropositive and seronegative RA patients.
Methods: A shotgun proteomic analysis was performed on 80 sera from the RA cohort of the Rheumatology Unit of the University Hospital of Santiago de Compostela (CHUS). Sera were classified as seropositive or seronegative according to their RF and ACPA values, and were then analyzed employing the iTRAQ labelling technique (Sciex) followed by LC-MALDI-MS/MS analysis (MALDI-TOF). A Multiple Reaction Monitoring (MRM) method was subsequently developed using the Skyline Software for the simultaneous quantification of 26 peptides belonging to ten putative protein biomarkers. The quantitative targeted analysis was performed using peptides with isotope labelled amino acids as internal standards. Serum levels of orosomucoid 1 (ORM1) and haptoglobin (HPT) were measured using commercially available ELISA Kits in the whole RA cohort (n=260) from the Rheumatology Unit of the University Hospital of A Coruña (HUAC).
Results: For the initial screening, eighty sera were grouped according to the ACPA/RF status in 4 pools (20 patients/pool). Using an iTRAQ technology-based quantitative proteomic approach, the abundance of eleven proteins was altered in the sera from $ACPA^{pos}/RF^{pos}$, 13 proteins in $ACPA^{neg}/RF^{pos}$ and 12 proteins in $ACPA^{pos}/RF^{neg}$, compared to $ACPA^{neg}/RF^{neg}$. Vitamin D binding protein (VTDB) was the unique protein that resulted increased in all the comparisons. For the biomarker verification phase, all the samples from the CHUS cohort were analyzed individually (n=80). Using the MRM technology, 26 peptides belonging to ten putative protein biomarkers associated with double positivity were simultaneously quantified. The statistical analysis showed a significant modulation of 9 peptides (belonging to 4 different proteins) in $ACPA^{pos}/RF^{pos}$, 7 peptides (5 proteins) in $ACPA^{neg}/RF^{pos}$, and 9 peptides (6 proteins) in $ACPA^{pos}/RF^{neg}$ compared to $ACPA^{neg}/RF^{neg}$ ($p<0.05$). Two acute phase reactants (ORM1 and HPT) displayed the same modulation in both screening and verification phases, thus confirming their association with the double positivity. Finally, in the biomarker validation phase, a total of 260 patients from CHUAC were included (Table 1). RA patients were classified as follows: (1) 112 patients (43.1%) were $ACPA^{pos}/RF^{pos}$; (2) 73 patients (28.1%) were $ACPA^{neg}/RF^{neg}$; (3) 51 patients (19.6%) were $ACPA^{neg}/RF^{pos}$; and (4) 24 patients (9.2%) were $ACPA^{pos}/RF^{neg}$. Serum levels of ORM1 and HPT (Figure 1), measured by commercial immunoassays, confirmed their increased values in double seropositive patients (p=0,0053 ORM1; p=0,0026 HPT). Finally, the increased level of ORM1 resulted associated with RF rather than ACPA status (p=0,0008 $ACPA^{neg}/RF^{pos}$); whereas HPT was associated with ACPA rather than RF status (p=0,0112 $ACPA^{pos}/RF^{neg}$).

Table 1. The different phases of RA biomarker development followed in this study.

	DISCOVERY PHASE		VERIFICATION PHASE		VALIDATION PHASE	
Source center	CHUS		CHUS		CHUAC	
Nº of samples	*n*= 4		*n*= 80		*n*= 260	
	ACPA+RF+	Pool 1	ACPA+RF+	20	ACPA+RF+	112
	ACPA-RF-	Pool 2	ACPA-RF-	20	ACPA-RF-	73
	ACPA-RF+	Pool 3	ACPA-RF+	20	ACPA-RF+	51
	ACPA+RF-	Pool 4	ACPA+RF-	20	ACPA+RF-	24
Nº of biomarkers	ORM1, ORM2, HPT, A2GL, AACT, RBP4, PLMN, IC1, VDBP, APOB		ORM1, HPT, A2GL, AACT		ORM1, HPT	

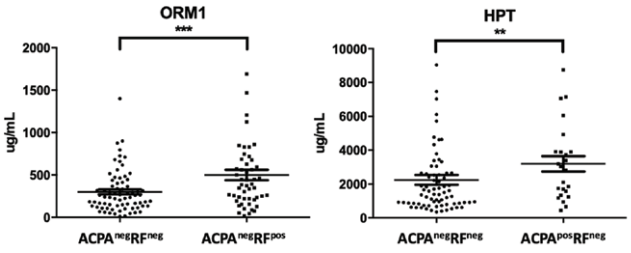


Figure 1: ORM1 levels are increased in RA patients seropositive for RF (499±437 ug/mL in $ACPA^{neg}RF^{pos}$ vs 300±248 ug/mL in $ACPA^{neg}RF^{neg}$). HPT levels are statistically significant increased in RA patients seropositive for ACPA (3193±2233 ug/mL in $ACPA^{pos}RF^{neg}$ vs 2046±1795 ug/mL in $ACPA^{neg}RF^{neg}$).

Figure 1.

Conclusion: The determination of ORM1 and HPT in sera provides novel information useful for patient stratification, which might improve diagnostic and prognostic approaches and facilitate the development of personalized medicine strategies in RA.

Acknowledgements: This work is supported by grants from Fondo de Investigación Sanitaria (RD16/0012/0002, PT17/0019/0014) integrated in the National Plan for Scientific Program, Development and Technological Innovation 2013–2016 and funded by the ISCIII-General Subdirection of Assessment and Promotion of Research-European Regional Development Fund (FEDER) "A way of making Europe".

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2533

POS0186 METABOLOMIC SIGNATURES FOR KNEE CARTILAGE VOLUME LOSS OVER 10 YEARS

Z. Xie[1,2], D. Aitken[3], M. Liu[1], G. Lei[2], G. Jones[3], G. Zhai[1]. [1]*Memorial University of Newfoundland, Division of Biomedical Sciences (Genetics), Faculty of Medicine, St. John's, Canada*; [2]*Central South University, Xiangya Hospital, Changsha, China*; [3]*University of Tasmania, Menzies Institute for Medical Research, Hobart, Australia*

Background: Osteoarthritis (OA) is the most common form of arthritis, and its impact is increasing year by year due to an aging population and lack of effective treatments. One of the main structural pathological changes of OA is the loss of articular cartilage. Tools that can predict cartilage loss would help identify people at high risk, thus preventing OA development.

Objectives: Using a metabolomics approach, the current study aimed to identify serum metabolomic signatures for predicting the loss of knee cartilage volume over 10 years in a well-established community-based cohort - the Tasmania Older Adult Cohort (TASOAC).

Methods: TASOAC is an on-going, prospective, population-based study of older adults who were randomly selected from the roll of electors in Southern Tasmania, Australia. Participants had a right knee magnetic resonance imaging (MRI) scan at baseline and a 10-year follow-up. Cartilage volume was measured in the medial, lateral, and patellar compartments and change in cartilage volume over 10 years was calculated as percentage change per year. Fasting serum samples collected at 2.6-year follow-up were metabolomically profiled using the TMIC Prime Metabolomics Profiling Assay which measures a total of 143 metabolites. 129 metabolite concentrations passed the quality control and the pairwise ratios of them as the proxies of enzymatic reaction were calculated. Linear regression models were used to test the association between each of the metabolite ratios and change in cartilage volume in each of the knee compartments with adjustment for age, sex, and body mass index (BMI). The significance was defined at $a=3.0\times10^{-6}$ to control multiple testing of 16,512 ratios with Bonferroni method.

Results: A total of 344 participants (51% females) were included. The mean baseline age was 62.83±6.13 years and the mean BMI was 27.48±4.41 kg/m^2. The average follow-up time was 10.84±0.66 years. Cartilage volume reduced by 1.34±0.72%, 1.06±0.58%, and 0.98±0.46% per year in the medial, lateral, and patellar compartments, respectively. Our data showed that an increased ratio of hexadecenoylcarnitine (C16:1) to tetradecanoylcarnitine (C14) was associated with a 0.12±0.02% per year reduction in patellar cartilage volume ($p = 8.80\times10^{-7}$). An increased ratio of hexadecenoylcarnitine (C16:1) to dodecanoylcarnitine (C12) was also associated with a 0.12±0.02% per year reduction in patellar cartilage volume ($p = 2.66\times10^{-6}$). While there were several metabolite ratios associated with cartilage volume loss in the medial and lateral compartments, none of them reached the predefined significance level.

Conclusion: Our data suggested that alteration of fatty acid β-oxidation is involved in knee cartilage loss, especially in the patellar compartment, and the serum ratio of C16:1 to C14 and to C12 could be used to predict long-term patellar cartilage loss.

Acknowledgements: We thank all the study participants who made the study possible. The original TASOAC study was supported by the National Health and Medical Research Council (NHMRC) and the current study was supported by the Canadian Institutes of Health Research (CIHR).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2735

POS0187 THE PROGNOSTIC FACTORS IN PREDICTING RELAPSE FOR IGG4-RELATED DISEASE: A LONG-TERM STUDY BASED ON THE CLINICAL AND PATHOLOGICAL CHARACTERISTICS OF THE PATIENTS

Z. Ji[1], L. Chen[2], L. Ma[1], L. Zhang[1], H. Chen[1], L. Ma[1], L. Jiang[1]. [1]*Shanghai Zhongshan hospital, Fudan University, Rheumatology, Shanghai, China*; [2]*Shanghai Zhongshan hospital, Fudan University, Pathology, Shanghai, China*

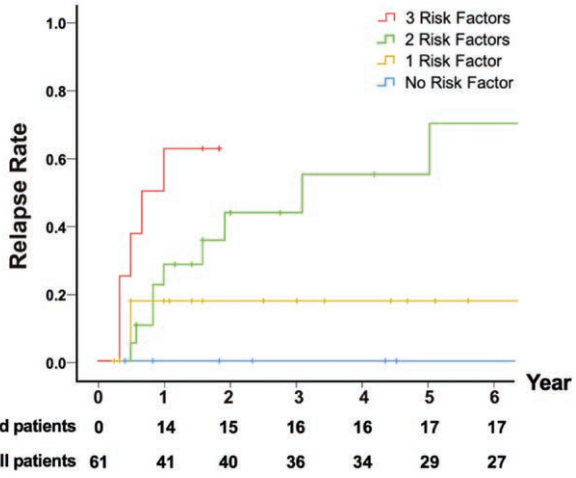
Background: The relationship between the pathological findings and disease relapse has not been well established.

Objectives: We aim to investigate the clinical and pathological manifestations in relation with disease relapse in IgG4-RD, as well as identify prognostic factors in predicting relapsed disease.

Methods: This study enrolled 71 patients newly diagnosed with IgG4-RD between Jan 2011 and April 2020, all of whom had received pathological examinations. Their pathological manifestations and clinical data were collected. Multivariate Cox regression and AUC (area under curve) were used to identify predictors for relapsed disease and assess the predictive value of these predictors, respectively.

Results: During a follow-up period of 26 (range, 6-123) months, 4.2% (3/71) patients died. The remaining 68 patients were all treated with glucocorticoids with or without immunosuppressor continuously. By the end of follow-up, 47 (69.1%) patients sustained clinical remission, and 21 (30.9%) patients suffered relapsed disease with a median relapse time at 10 (6-30) months. We found that IgG4 ≥ 6.5g/L (OR 1.52-11.06), IgG ≥ 20.8g/L (OR 1.11-7.23), IgG4-RD responder index (RI) ≥ 9 (OR 1.28-11.37), and more $IgG4^+$ plasma cell infiltration (≥ 60 / HPF in visceral organs, or ≥ 200 / HPF in head and neck organs) (OR 1.79-22.41) were all independent predictive factors for disease relapse. A prognostic score was explored for predicting recurrence in IgG4-RD, including three predictive factors (IgG ≥ 20.8g/L, IgG4-RD RI ≥9, and more $IgG4^+$ plasma cell infiltration). The three-year relapse rate for the patients with no, one, two, and three risk factors were 0%, 27.3%, 66.7%, and 100%, respectively.

Conclusion: Patients' earlier IgG4 ≥ 6.5g/L, IgG ≥ 20.8g/L, IgG4-RD RI ≥9, and more $IgG4^+$ plasma cell infiltration independently predicted disease relapse. We explored a prognostic score for predicting recurrence in IgG4-RD include three predictive factors (IgG ≥ 20.8g/L, IgG4-RD RI ≥9, and more $IgG4^+$ plasma cell infiltration), which might be used to evaluate the risk of recurrence in IgG4-RD.



REFERENCES:

[1] DESHPANDE V, ZEN Y, CHAN J K, et al. Consensus statement on the pathology of IgG4-related disease[J]. Mod Pathol,2012,25(9): 1181-1192.
[2] JENNETTE J C, FALK R J, BACON P A, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides[J]. Arthritis Rheum,2013,65(1): 1-11.
[3] OKAZAKI K, UMEHARA H. Are Classification Criteria for IgG4-RD Now Possible? The Concept of IgG4-Related Disease and Proposal of Comprehensive Diagnostic Criteria in Japan[J]. Int J Rheumatol,2012,2012: 357071.
[4] SHIMOSEGAWA T, CHARI S T, FRULLONI L, et al. International consensus diagnostic criteria for autoimmune pancreatitis: guidelines of the International Association of Pancreatology[J]. Pancreas,2011,40(3): 352-358.
[5] OHARA H, OKAZAKI K, TSUBOUCHI H, et al. Clinical diagnostic criteria of IgG4-related sclerosing cholangitis 2012[J]. J Hepatobiliary Pancreat Sci,2012,19(5): 536-542.
[6] KAWANO M, SAEKI T, NAKASHIMA H, et al. Proposal for diagnostic criteria for IgG4-related kidney disease[J]. Clin Exp Nephrol,2011,15(5): 615-626.
[7] GOTO H, TAKAHIRA M, AZUMI A. Diagnostic criteria for IgG4-related ophthalmic disease[J]. Jpn J Ophthalmol,2015,59(1): 1-7.
[8] MATSUI S, YAMAMOTO H, MINAMOTO S, et al. Proposed diagnostic criteria for IgG4-related respiratory disease[J]. Respir Investig,2016,54(2): 130-132.
[9] WEN ZHANG J H S. Management of IgG4-related disease[J]. Lancet Rheumatol,2019,1: e55-e65.
[10] EBBO M, DANIEL L, PAVIC M, et al. IgG4-related systemic disease: features and treatment response in a French cohort: results of a multicenter registry[J]. Medicine (Baltimore),2012,91(1): 49-56.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3391

POS0188 DISEASE ACTIVITY OUTCOME MEASURES ARE ONLY AVAILABLE IN HALF OF THE ELECTRONIC MEDICAL FILES OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS FOLLOWED IN AN OUTPATIENT CLINIC: THE RESULTS OF AN AUDIT OF A TERTIARY-CARE RHEUMATOLOGY DEPARTMENT.

E. Portier[1], M. Dougados[1], C. Roux[1], A. Moltó[1]. [1]*Cochin Hospital, Rheumatology, Paris, France*

Background: Current recommendations for management of patients with axial Spondylarthritis (axSpA) include regular collection of validated disease activity outcomes.

Objectives: This study aimed at evaluating the proportion of patients for whom the elements allowing the calculation of the validated outcome measures were available on the visits reported on the electronic medical records (EMR) and the factors associated with the presence of such information on the EMR.

Methods: This was a cross-sectional and monocentric observational study conducted in a tertiary-care rheumatology department, EULAR center of excellence and ASAS center. We performed a systematic electronic search among all patients with a SpA diagnosis code who attended an outpatient visit between February 1st, 2018 and February 28th, 2019. Thereafter, a manual search was performed in order to check whether disease activity outcome measures (or the elements allowing its calculation): BASDAI individual questions, Disease activity Global, CRP, BASDAI and ASDAS) were reported on EMR. Patient's and physician's demographics disease characteristics (including treatment) and whether the patient had participated in a systematic review were also collected. A descriptive analysis of the percentage of EMR with available outcomes was performed, and the characteristics of patients in whom these measures were available/were not available evaluated by univariable and multivariable analysis (including only variables with p < 0,10 on the univariate)

Results: 320 EMR of axSpA patients seen in the outpatient clinic were screened and selected. Among them, 178 (55.6%) had at least one disease activity outcome measure reported, while 144(45%) and 123 (38.4%) had a BASDAI and an ASDAS reported, respectively. The most frequently reported disease activity items were duration of morning stiffness (n=230, 72%) and CRP (n=224, 70%). Only previous participation on an educational program for self-assessment was found to be independently associated with a reported disease activity outcome: among the patients participating in such program, 93.1% (n=27/29) had a disease activity measure available, compared to 51.9% (n=151/291) in those who did not participate in such program (p<0.001) (Table 1)

Conclusion: Implementation of recommendations with regard to regularly collecting disease activity outcome measures is not optimal. The participation in educational programs including self-assessment educational programs might be one of the keys to improve such implementation.

REFERENCES:

[1] Smolen JS, Braun J, Dougados M, Emery P, Fitzgerald O, Helliwell P, et al. Treating spondyloarthritis, including ankylosing spondylitis and psoriatic arthritis, to target: recommendations of an international task force. Ann Rheum Dis 2014;73:6–16. https://doi.org/10.1136/annrheumdis-2013-203419.

[2] van der Heijde D, Ramiro S, Landewé R, Baraliakos X, Van den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis 2017;76:978–91. https://doi.org/10.1136/annrheumdis-2016-210770.

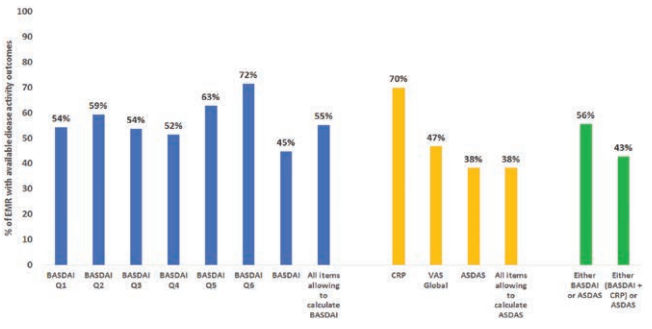


Figure 1. Frequency of disease activity measures reporting in the Electronic Medical Record of patients with axial Spondyloarthritis, followed in a tertiary care rheumatology department outpatient clinic

Disclosure of Interests: Elodie Portier: None declared, Maxime Dougados: None declared, Christian Roux: None declared, Anna Moltó Consultant of: Abbvie, BMS, MSD, Pfizer, Lilly, UCB Novartis, Grant/research support from: Pfizer

Table 1. Factors associated with the presence of a reported disease activity measures on the electronic medical file of patients with axial SpA

	Total (n=320)	At least one disease activity measure available (n=178)	No disease activity measure available (n=142)	Univariable p-value	Multivariable analysis p value
Age (years)	46.2 (14.0)	46.8 (14.2)	45.5 (13.8)	0.404	-
Disease duration (years)	13.3 (11.8)	13.8 (12.4)	12.4 (11.0)	0.339	-
Male gender	186 (58.1%)	96 (53.9%)	90 (63.4%)	0.112	-
University studies (n=276)	149 (46.6%)	87 (48.9%)	62 (43.7%)	0.637	-
Radiographic sacroiliitis (n=257)	171 (66.5%)	101 (56.7%)	70 (49.3%)	0.993	-
MRI sacroiliitis (n=214)	169 (52.8%)	97 (54.5%)	72 (50.7%)	0.34	-
HLA B27 positive (n=267)	196 (61.2%)	118 (66.3%)	78 (54.9%)	0.826	-
Current bDMARD	199 (62.2%)	116 (65.2%)	83 (58.5%)	0.265	-
Age of Rheumatologist	**45.5 (8.85)**	**44.4 (8.47)**	**47.0 (9.15)**	**0.011**	-
Participation in a holistic systematic review	**29 (9.1%)**	**27 (15.2%)**	**2 (1.5%)**	**<0.001**	**0.001**

DOI: 10.1136/annrheumdis-2021-eular.2120

POS0189 SERUM IFNA CONCENTRATIONS MEASURED WITH SINGLE-MOLECULE ARRAY TECHNOLOGY IN SJÖGREN'S SYNDROME REFLECT BLOOD INTERFERON-STIMULATED GENE EXPRESSION

E. Huijser[1], J. Göpfert[2], Z. Brkic[3], C. G. Van Helden-Meeuwsen[1], S. Jansen[1], T. Mandl[4], P. Olsson[4], B. Schrijver[1], M. W. Schreurs[1], P. L. Van Daele[1,3], W. A. Dik[1], M. Versnel[1]. [1]*Erasmus MC, University Medical Center Rotterdam, Immunology, Rotterdam, Netherlands*; [2]*NMI Natural and Medical Sciences Institute at the University of Tübingen, Biochemistry, Reutlingen, Germany*; [3]*Erasmus MC, University Medical Center Rotterdam, Internal Medicine, Division of Clinical Immunology, Rotterdam, Netherlands*; [4]*Lund University, Internal Medicine - Epidemiology, Lund, Sweden*

Background: Type I interferon (IFN-I) activation is a prominent feature of several Rheumatic and Musculoskeletal Diseases (RMDs) including primary Sjögren's syndrome (pSS), systemic lupus erythematosus (SLE) and systemic sclerosis (SSc). Ultrasensitive single-molecule array (SiMoA) technology has facilitated the measurement of subfemtomolar concentrations of IFNs [1-3].

Objectives: Here, we tested the performance of a commercially available SiMoA kit for detection of IFNα in serum from pSS, SLE, and SSc and correlated serum IFNα to whole blood IFN-stimulated gene (ISG) expression.

Methods: Serum IFNα2 was measured in healthy controls (HC; n=68) and patients with pSS (n=85, n=110), SLE (n=24) and SSc (n=23) using a ready-to-use IFNα SiMoA kit on a HD-X Analyzer. IFN-I activation was additionally determined from paired samples of whole blood IFN-stimulated gene (ISG) expression of IFI44, IFI44L, IFIT1, IFIT3, and MxA by RT-PCR or MxA-ELISA.

Results: Serum IFNα2 levels were elevated in pSS (median = 61.3 fg/mL) compared to HC (median < 5fg/mL) and SSc (median = 11.6 fg/mL), lower compared to SLE (median = 313.5 fg/mL), and positively correlated to whole blood ISG expression (rs=0.71-0.76, p<0.001). Comparable to MxA-ELISA (AUC=0.93), IFNα2 SiMoA identified pSS with high ISG expression (AUC=0.90) with 80-93% specificity and 71-84% sensitivity. Blinded validation in an independent pSS cohort yielded a comparable accuracy of 89%. Multiple linear regression indicated independent associations of autoantibodies, IgG, and use of hydroxychloroquine with serum IFNα2 concentrations in pSS. Confirming the literature [4], serum IFNα2 levels were lower in SLE patients in remission (DORIS classification) compared to patients not in remission.

Conclusion: Thus, SiMoA serum IFNα2 reflects blood ISG expression in pSS, SLE and SSc. In light of IFN-targeting treatments, SiMoA could potentially be applied for patient stratification or high-throughput retrospective analysis of stored clinical trial material.

REFERENCES:

[1] Rissin, D.M.; Kan, C.W.; Campbell, T.G.; Howes, S.C.; Fournier, D.R.; Song, L.; Piech, T.; Patel, P.P.; Chang, L.; Rivnak, A.J., et al. Single-molecule enzyme-linked immunosorbent assay detects serum proteins at subfemtomolar concentrations. Nat. Biotechnol. 2010, 28, 595-599.

[2] Wilson, D.H.; Rissin, D.M.; Kan, C.W.; Fournier, D.R.; Piech, T.; Campbell, T.G.; Meyer, R.E.; Fishburn, M.W.; Cabrera, C.; Patel, P.P., et al. The Simoa HD-1 Analyzer: A Novel Fully Automated Digital Immunoassay Analyzer with Single-Molecule Sensitivity and Multiplexing. Journal of Laboratory Automation 2015, 21, 533-547. DOI: 10.1177/2211068215589580.

[3] Rodero, M.P.; Decalf, J.; Bondet, V.; Hunt, D.; Rice, G.I.; Werneke, S.; McGlasson, S.L.; Alyanakian, M.A.; Bader-Meunier, B.; Barnerias, C., et al. Detection of interferon alpha protein reveals differential levels and cellular sources in disease. J. Exp. Med. 2017, 214, 1547-1555. DOI: 10.1084/jem.20161451.
[4] Mathian, A.; Mouries-Martin, S.; Dorgham, K.; Devilliers, H.; Yssel, H.; Garrido Castillo, L.; Cohen-Aubart, F.; Haroche, J.; Hie, M.; Pineton de Chambrun, M., et al. Ultrasensitive serum interferon-alpha quantification during SLE remission identifies patients at risk for relapse. Ann. Rheum. Dis. 2019, 78, 1669-1676. DOI: 10.1136/annrheumdis-2019-215571.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2056

POS0190 ASSOCIATION BETWEEN OSTEOARTHRITIS-RELATED SERUM BIOCHEMICAL MARKERS OVER 11 YEARS AND KNEE SYMPTOMS IN MIDDLE-AGED ADULTS

A. Singh[1], L. Blizzard[2], A. Venn[1], G. Jones[1], J. Burgess[1,3], V. Parameswaran[1,3], C. Ding[1,4,5], B. Antony[1]. [1]*Menzies Institute for Medical Research, Musculoskeletal Health and Disease, Hobart, Australia*; [2]*Menzies Institute for Medical Research, Statistics, Hobart, Australia*; [3]*Royal Hobart Hospital, Department of Endocrinology, Hobart, Australia*; [4]*Monash University, Department of Epidemiology and Preventive Medicine, Clayton, Australia*; [5]*Southern Medical University, Clinical Research Centre, Zhujiang Hospital, Guangzhou Shi, China*

Background: Serum levels of cartilage and joint-specific biochemical markers such as cartilage oligomeric matrix protein (COMP), matrix metalloproteinase (MMP)-3, and hyaluronan (HA) are associated with cartilage degradation, joint tissue degradation, and synovitis in patients with OA. Change in these biomarkers may precede the morphological and clinical manifestations of OA and therefore have been explored as predictive markers in OA. However, few studies have evaluated the association of OA-related biomarkers with knee symptoms in general population-based middle-aged adults
Objectives: To describe the associations between OA-related biomarkers and knee symptoms in middle-aged adults followed up over 10-13 years
Methods: Blood samples were collected during the Childhood Determinants of Adult Health (CDAH)-1 study at baseline (year: 2004-06, age: 26–36 years) and 10-13 year follow-up (CDAH-3; year: 2014–2019, age: 36–49 years). Serum samples from baseline (n=156) and follow-up (n= 167) were analyzed for three OA-related biomarkers – namely COMP, MMP-3, and HA– using ELISA. Knee symptoms (pain, stiffness, and dysfunction) were assessed using the WOMAC scale during the CDAH-3 phase. Univariable and multivariable (adjusted for age, sex, and body mass index (BMI)) zero-inflated Poisson regression models with random effects were used to describe the above associations
Results: The prevalence of knee pain was 46%. In the multivariable model, adjusted for age, sex, and BMI, there was a significant positive association between COMP (ɞ=1.156, 95%CI: 0.989,1.324; p=0.04), MMP-3 (ɞ=1.013, 95%CI: 1.001,1.025; p=0.02), and HA (ɞ=1.008, 95%CI: 1.002,1.015, p=0.01) with knee pain and WOMAC-total score (Table 1) in middle-aged adults. The increase in knee pain per ng/ml increase in COMP, MMP-3, and HA was 15.7%, 1.3%, and 0.8%, respectively. The overall mean biomarker levels decreased over 10-13 years; however, the mean WOMAC-total scores were higher in participants whose COMP and HA levels increased (COMP: 24 (27.31), HA: 14.20 (22.60)) compared to those in whom it decreased or remained stable (COMP: 9.84 (16.83), and HA: 8.28 (13.22)) during this period. There was a significant positive association between COMP (ɞ=1.026, 95%CI: 1.002,1.050, p=0.03) and MMP-3 (ɞ=1.020, 95%CI: 1.009,1.030, p<0.01) measured at baseline and knee pain assessed after 10-13 year in the middle-aged adults (Table 1)
Conclusion: OA-related biochemical markers such as COMP and MMP-3 were positively associated with knee pain in population-based middle-aged adults. These results suggest biochemical markers measured in middle-aged adults may be used as a marker of joint pain
Acknowledgements: AS is supported by International Graduate Research Scholarship, University of Tasmania.
Disclosure of Interests: Ambrish Singh Employee of: Has worked in the past for Abbott and Eli Lilly and Company, Leigh Blizzard: None declared, Alison Venn: None declared, Graeme Jones: None declared, John Burgess: None declared, Venkat Parameswaran: None declared, Changhai Ding: None declared, Benny Antony: None declared
DOI: 10.1136/annrheumdis-2021-eular.98

Table 1. Cross-sectional and longitudinal association between WOMAC symptoms and OA-related biomarkers

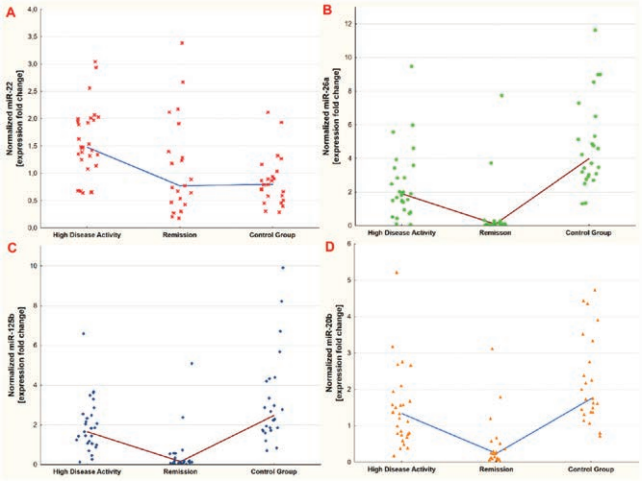
Variables	Longitudinal *Biomarker at CDAH-1, knee symptom at CDAH-3*	Cross-sectional *Biomarker at CDAH-3, knee symptom at CDAH-3*
	Adjusted[‡] Coef. (95%CI) p-value	*Adjusted[‡] Coef. (95%CI)* p-value
COMP (Predictor)		
WOMAC-total	**1.047 (1.035, 1.060) p<0.01**	**1.088 (1.017, 1.159) p=0.01**
Pain	**1.026 (1.002, 1.050) p=0.03**	**1.156 (0.989, 1.324) p=0.04**
Stiffness	1.019 (0.988, 1.051) p=0.23	0.877 (0.708, 1.057) p=0.12
Dysfunction	**1.045 (1.030, 1.061) p<0.01**	1.040 (0.949, 1.130) p=0.38
MMP3 (Predictor)		
WOMAC-total	**1.026 (1.020, 1.031) p<0.01**	**1.017 (1.010, 1.023) p<0.01**
Pain	**1.020 (1.009, 1.030) p<0.01**	**1.013 (1.001, 1.025) p=0.03**
Stiffness	**1.020 (1.004, 1.035) p=0.01**	1.004 (.987, 1.021) p=0.66
Dysfunction	**1.029 (1.022, 1.037) p<0.01**	**1.019 (1.010, 1.026) p<0.01**
HA (Predictor)		
WOMAC-total	**0.995 (0.991, 0.999) p=0.01**	**1.007 (1.003, 1.010) p<0.01**
Pain	0.999 (0.991, 1.006) p=0.75	**1.008 (1.002, 1.015) p=0.01**
Stiffness	**0.989 (0.980, 0.998) p=0.03**	0.997 (0.989, 1.007) p=0.65
Dysfunction	1.003 (0.998, 1.009) p= 0.22	**1.015 (1.010, 1.020) p<0.01**

Bold denotes statistically significant[‡]Model adjusted for age, sex, and BMI

POS0191 THE VALUE OF MIR-20B, MIR-22, MIR-26A, MIR-125B AND MIR-221 IN RHEUMATOID ARTHRITIS

M. Ciesla[1], B. Kolarz[1], M. Majdan[2], M. Dryglewska[2]. [1]*University of Rzeszow, College of Medical Sciences, Rzeszow, Poland*; [2]*Medical University of Lublin, Department of Rheumatology and Connective Tissue Diseases, Lublin, Poland*

Background: Micro-RNAs (miRNAs) are an endogenous small, single-stranded, non-coding RNAs with a 18-25 nucleotide long and have been reported as a potential extracellular biomarkers of various diseases. They mainly decrease the gene expression by inhibiting the translation or cause mRNA destabilization.
Objectives: The aim of the study was to identify miRNAs whose plasma expression level is associated with RA prevalence and/or activity.
Methods: A total of 74 unrelated individuals, 50 with RA and 24 in a control group were enrolled to the study. Real-time PCR was used to evaluate the plasma expression levels of 5 miRNAs: miR-20b, miR-22 miR-26a, miR-125b, miR-221.
Results: We found the differences in four out of five evaluated miRs between RA and HC group – miR-26a, $p<0.0001$; miR-125b, $p<0.0001$; miR-20b $p<0.0001$; miR-22, p=0.005. Graphical presentation of the results is shown in Figure 1. The logistic regression results showed that miR-22 (p=0.0003) and miR-26a (p=0.049) are the most important molecules distinguishing RA patients and healthy controls in the study. MiR-22 was positively correlated with ESR (r_s=0.41), CRP (r_s=0.49) and DAS28 (r_s=0.33) and miR-26a was positively correlated with ESR (r_s=0.49), CRP (r_s=0.41), number of swelling joints (r_s=0.43), number of painful joints (r_s=0.74) and DAS28 (r_s=0.63). Moreover, miR-22 expression was different between rheumatoid factor (RF) positive and RF negative patients (p=0.04).
Conclusion: The results showed that miR-22 (p=0.0003) and miR-26a (p=0.049) may be the most useful in evaluated panel of miRs distinguishing RA



patients and HCs. In this study we demonstrated for the first time that plasma concentration of miR-22 may be considered as a potential molecular marker of RA exacerbation.

REFERENCES:

[1] Ouboussad, L., Hunt, L., Hensor, E.M.A. *et al.* Profiling microRNAs in individuals at risk of progression to rheumatoid arthritis. *Arthritis Res Ther* 2017 **19,** 288.

[2] Churov AV, Oleinik EK, Knip M. MicroRNAs in rheumatoid arthritis: altered expression and diagnostic potential. *Autoimmun Rev.* 2015 14(11):1029-37.**Figure 1.** Diagrams from A to D show the expression levels of miR-22, miR-26a, miR-125b and miR-20b, respectively. The median values of expression have been connected by a line.

Table 1. Spearman's rank correlation between micro-RNA-22 and micro-RNA-26 and the clinical variables.

miRs \ clinical variable	Age	Disease duration	ESR	CRP	SJC	TJC	DAS-28	ACPA	RF
miR-22	0.09	-0.27	**0.41**	**0.49**	0.26	0.21	**0.33**	0.24	0.16
miR-26a	0.2	0.14	**0.49**	**0.41**	**0.43**	**0.74**	**0.63**	0.26	0.16

The significant correlations were bolded and indicated by red. Abbreviations: ACPA, anti-citrullinated protein antibodies; CRP, C-reactive protein; SJC, swollen joint count; TJC, tender joint count; DAS-28, disease activity score 28; ESR, erythrocyte sedimentation rate; RF, rheumatoid factor.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.443

PsA treatment: what is new?

POS0192

PROGNOSTIC FACTORS ASSOCIATED WITH ACHIEVING MINIMAL DISEASE ACTIVITY IN EARLY PSORIATIC ARTHRITIS PATIENTS

E. Loginova[1], T. Korotaeva[1], E. Gubar[1], S. Glukhova[2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Spondyloarthritis and psoriatic arthritis, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Medical and Social Problems in Rheumatology, Moscow, Russian Federation*

Background: The goal of treat to target strategy (T2T) in psoriatic arthritis (PsA) is attaining remission or minimal disease activity (MDA). The benefits of T2T have been seen recently [1]. But prognostic factors for MDA achievement in PsA patients (pts) at an early-stage hasn't been studied yet.

Objectives: to determine the prognostic factors associated with MDA achievement within 12 months (mos.) of treatment according to T2T strategy in early PsA pts.

Methods: 77 pts (M/F=36/41) with early active PsA fulfilling the CASPAR criteria were included. Mean age 36.9±10.45 years (yrs.), PsA duration 11.1±10.0 mos., Psoriasis (PsO) duration 82.8±92.1 mos. At baseline (BL) and at 12 mos. of therapy PsA activity by tender joint count (TJC)/68, swelling joint count (SJC)/66, Pain (VAS), Patient global assessment disease activity (PtGA, VAS), CRP mg/l, dactylitis, enthesitis by LEI and plantar fascia, BSA (%), HAQ and fatigue by FACIT (Functional Assessment of Chronic Illness Therapy) Fatigue Scale (Version 4) were evaluated. A score FACIT <30 indicates severe fatigue and > 30 – less fatigue. All pts was given therapy with Methotrexate (MTX) s/c. After 3-9 mos. of ineffectiveness of MTX treatment 29 pts were given biologic DMARDs. By 12 mos. of therapy, the proportion of pts who had reached MDA (5/7) were calculated. Pts were split into 2 groups: MDA + (n=45) and MDA - (n=32). The one-factor model of logistic regression was used to identify a group of features that are associated with MDA achievement. M±SD, Me [Q25; Q75], Min-Max, %, t-test, Pierson-χ2, Manna-Whitney tests, ORs with 95% CI were performed. All p<0.05, were considered to indicate statistical significance.

Results: Comparative analysis in both groups and one-factor model of logistic regression showed the following features at BL were associated with MDA achievement: TJC/SJC < 3 (p<0.001), PGA ≤ 20 mm (p<0.001), Pain (VAS) ≤ 15 mm (p<0.001), CRP ≤ 5 mg/l (p< 0.03), HAQ ≤ 0.5 (p< 0.001), FACIT > 30 (p< 0.021), absent of entesitis (p< 0.003), dactylitis (p< 0.029) and nail damage (p< 0.012). Early PsA pts with combination of these features at first visit have more chance to achieve MDA within 12 mos in comparison to PsA pts without them, OR=9.684 [CI 95% 4.6-20.4]. (Figure 1).

Conclusion: It is a combination of features at first visit to clinic – TJC, SJC < 3, PGA ≤ 20 mm, pain ≤ 15 mm, CRP ≤ 5 mg/l, HAQ ≤ 0.5, FACIT > 30 points, absent of entesitis, dactylitis and nail PsO - that constitutes a clinical prognostic factors for MDA achievement within 12 mos of T2T strategy in early PsA pts.

REFERENCES:

[1] Coates LC, et al. Lancet. 2015 Dec 19;386(10012):2489-98. doi: 10.1016/S0140-6736(15)00347-5

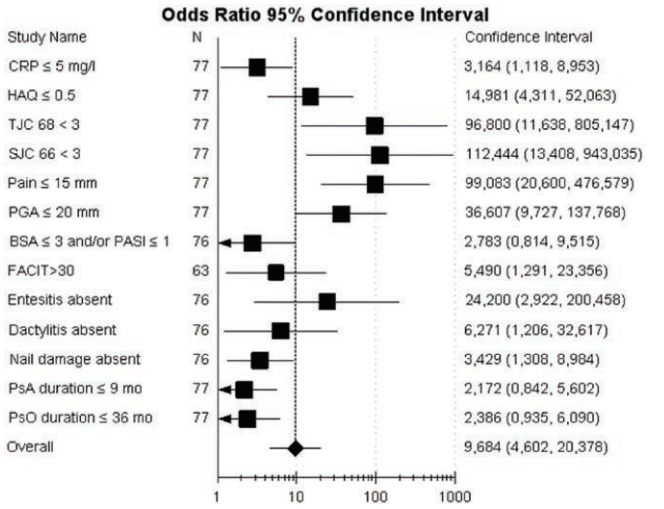


Figure 1. The prognostic factors associated with achievement MDA within 12 months in early PsA pts

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1704

POS0193

DAS28-CRP GUIDED TREAT-TO-TARGET TAPERING OF TUMOR NECROSIS FACTOR INHIBITORS IN PSORIATIC ARTHRITIS: A RETROSPECTIVE COHORT STUDY.

C. Michielsens[1,2], N. Den Broeder[1,2], M. Mulder[1,2], M. Wenink[1], F. Van den Hoogen[1,2], L. M. Verhoef[1], A. Den Broeder[1,2]. [1]*Sint Maartenskliniek, Rheumatology, Nijmegen, Netherlands*; [2]*Radboud university medical center, Radboud Institute for Health Sciences, Nijmegen, Netherlands*

Background: Tumor Necrosis Factor inhibitors (TNFi) have proven to be safe and effective in the treatment of psoriatic arthritis (PsA) [1]. However, they carry disadvantages, such as adverse effects, patient burden, and costs, which could be reduced by treat-to-target (T2T) tapering. Although there is lack of high level evidence, guidelines suggest that T2T tapering and discontinuation might be considered, but no studies comparing this strategy to continuation in PsA were published [2].

Objectives: To assess the effect of T2T TNFi tapering on disease activity and TNFi dosage in PsA patients with low disease activity (LDA).

Methods: PsA patients using TNFi who visited the clinic between April 2012 and October 2018 were included if eligible for tapering, according to local protocol: ≥ 6 months of TNFi treatment and ≥ 6 months of at least LDA (DAS28-CRP < 2.4 (or 2.9 in patients with disease duration > 3 years) or by judgement of physician and patient). Patients with concomitant inflammatory disease preventing tapering were excluded. Three different time periods were defined: i) full-dose TNFi continuation; ii) TNFi tapering; iii) stable TNFi dosage after tapering. A mixed-model analysis was used to estimate mean DAS28-CRP during these three time periods. This model included: age, gender, disease duration, and the following time-varying components: current dose reduction status (three time periods mentioned above), time since eligibility for tapering and use of concomitant conventional synthetic Disease-Modifying Antirheumatic Drugs (csDMARDs), and a random intercept to account for inter-patient variability. Furthermore, a mean percentage of the Daily Defined Dose (%DDD) was calculated as secondary outcome.

Results: 152 patients were included, with a mean of 6.5 DAS28-CRP measurements, of whom 125 attempted dose reduction during follow-up. Median follow-up duration was 41 months (Inter Quartile Range (IQR) 24-59) for patients who never attempted dose reduction and 43 months (IQR 28-58) for those who did (table 1). The mixed model showed no significant difference in DAS28-CRP between the three time periods. Adjusted for gender, age, disease duration at baseline, time since follow-up and csDMARD use, the mean DAS28-CRP was 1.91 in the continuation period (95% Confidence Interval (CI) [1.76-2.05]) and 2.0 in both the TNFi tapering (95%CI [1.90-2.12], difference with continuation: 0.11, p=0.19) and stable TNFi dosage after tapering (95%CI 1.88-2.11], difference with continuation: 0.09, p=0.31) period. The mean percentage of the DDD for the three time periods was 107% for the continuation period; 62% in the TNFi tapering period and 79% in the stable TNFi dosage period.

Conclusion: T2T tapering of TNFi appears to have no negative effects on disease activity in PsA patients compared with full dose continuation, and reduces

drug exposure. DAS28-CRP might however not capture the full disease spectrum in PsA. Trials using PsA specific endpoints are needed to investigate tapering in a prospective and randomized manner.

REFERENCES:

[1] Gossec L. et al. Ann Rheum Dis. 2016;75(3):499-510.
[2] Verhoef LM. et al. Cochrane Database Syst Rev. 2019;5:CD010455.

Table 1. Baseline characteristics of PsA patients

Characteristic	PsA (N=152)
Female, n (%)	60(39%)
Age in years at inclusion, mean (SD)	52(11)
Disease duration at inclusion, years, median	9(3-14)
(IQR)	
Rheumatoid factor negative, n (%)*	132 (87%)
Anti-CCP negative, n (%)**	136 (89%)
Erosions on radiographic imaging, n (%)	34(22%)
Number of previous bDMARD, n (%)	
-0	102(67%)
-1	39(26%)
-2 or 3	11(7%)
Number of previous csDMARD, n (%)	
-0	21(14%)
-1	50(33%)
-≥ 2	81(53%)
Current bDMARD use, n (%)	
-Adalimumab	49(32%)
-Etanercept	81(53%)
-Golimumab	3(2%)
-Infliximab	19(13%)
Current csDMARD use, n (%)	
-None	71(46%)
-Methotrexate	65(43%)
-Leflunomide	12(8%)
-Hydroxychloroquine	1(1%)
-Sulfasalazine	3 (2%)
Duration of current bDMARD use at inclusion, years, median (IQR)	3(1-5)
Duration of follow-up, months, median (IQR)	43(28-58)

*Available for 144 of 152 patients** Available for 145 of 152 patients

Disclosure of Interests: Celia Michielsens: None declared, Nathan den Broeder: None declared, Michelle Mulder: None declared, Mark Wenink: None declared, Frank van den Hoogen Consultant of: Advisor board Abbvie and Galapagos, L.M. Verhoef: None declared, Alfons den Broeder Consultant of: received consultancy honoraria from Abbvie, Amgen, Cellgene, Roche, Biogen, Lilly, Novartis, Celltrion Sanofi, Gilead., Grant/research support from: received research grants (to the institution) from Abbvie, Amgen, Cellgene, Roche, Biogen, Lilly, Novartis, Celltrion Sanofi, Gilead.
DOI: 10.1136/annrheumdis-2021-eular.2080

POS0194

ENTHESITIS IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB OR ADALIMUMAB: A POST HOC ANALYSIS OF EXCEED

G. S. Kaeley[1], G. Schett[2], P. G. Conaghan[3,4], D. Mcgonagle[3,4], F. Behrens[5], P. Goupille[6], C. Gaillez[7], B. Parikh[8], X. Meng[9], C. Bakewell[10]. [1]*University of Florida, Department of Medicine, Division of Rheumatology and Clinical Immunology, Jacksonville, United States of America*; [2]*Friedrich Alexander University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3 and Institute for Clinical Immunology, Erlangen, Germany*; [3]*University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [4]*Leeds Teaching Hospitals NHS Trust, National Institute for Health Research Leeds Biomedical Research Centre, Leeds, United Kingdom*; [5]*Goethe University, Rheumatology and Fraunhofer ITMP - Translational Medicine and Pharmacology, Frankfurt, Germany*; [6]*University Hospital of Tours, University of Tours, Department of Rheumatology, Tours, France*; [7]*Novartis Pharma AG, Global Medical Affairs, Rheumatology, Basel, Switzerland*; [8]*Novartis Pharmaceuticals Corporation, Rheumatology, East Hanover, United States of America*; [9]*Novartis Pharmaceuticals Corporation, Biostatistics, East Hanover, United States of America*; [10]*Intermountain Healthcare Medical Group, Rheumatology, Salt Lake City, United States of America*

Background: Enthesitis is a key musculoskeletal manifestation of psoriatic arthritis (PsA). EULAR guidelines recommend biologics for patients with enthesitis and an inadequate response to or intolerance of nonsteroidal anti-inflammatory drugs, although no guidance on specific biologics is offered. In the EXCEED head-to-head, double-blind study (NCT02745080), secukinumab (SEC) and adalimumab (ADA) showed a similar efficacy in joints and in resolution of enthesitis at Week 52 for patients with PsA,[1] although a detailed analysis of enthesitis was not conducted.

Objectives: To explore detailed enthesitis treatment response, including temporal and additional enthesitis assessment data, in patients with PsA treated with SEC or ADA over 52 weeks.

Methods: In this post hoc analysis, patient data from EXCEED were grouped by presence or absence of baseline enthesitis based on the Leeds Enthesitis Index (LEI) and the Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC). Baseline characteristics of these groups were summarized. Median time to resolution of LEI/SPARCC enthesitis score in patients receiving SEC or ADA was assessed using Kaplan-Meier analysis. Efficacy was further assessed among the enthesitis subset by LEI and SPARCC change from baseline, resolution of enthesitis (LEI/SPARCC) at Weeks 24 and 52, and resolution of enthesitis at Week 52 by baseline enthesitis severity. Relapse of enthesitis after a first resolution was evaluated at Weeks 24 and 52. Missing data were imputed by nonresponder imputation.

Results: Baseline demographics were well balanced in the LEI/SPARCC enthesitis subsets, although a higher proportion of all patients with enthesitis were women vs those with no enthesitis (LEI: 54.6% vs 40.5%; SPARCC: 53.2% vs 36.2%). Patients with baseline enthesitis had higher disease activity vs patients without enthesitis (LEI/SPARCC enthesitis vs no LEI/SPARCC enthesitis: tender joint count of 78 joints [22.8/22.1 vs 15.8/13.8], Health Assessment Questionnaire-Disability Index [1.3/1.3 vs 1.1/1.1], and mean Psoriasis Area and Severity Index [6.4/6.1 vs 5.1/5.3]). Median time to resolution of LEI and SPARCC enthesitis was similar between patients receiving either SEC or ADA (Table 1). Both treatment groups experienced a similar mean change from baseline in LEI and SPARCC enthesitis counts and a similar resolution of LEI and SPARCC at Weeks 24 and 52 (Table 1). Achievement of enthesitis resolution was similar between treatment groups irrespective of disease severity (Figure 1). The proportion of patients who experienced relapse after achieving resolution was low across both treatments (Table 1).

Conclusion: In EXCEED, patients with baseline enthesitis presented with higher disease burden, consistent with the FUTURE trials.[2] SEC and ADA showed similar kinetics of response and efficacy on enthesitis, irrespective of baseline enthesitis severity.

REFERENCES:

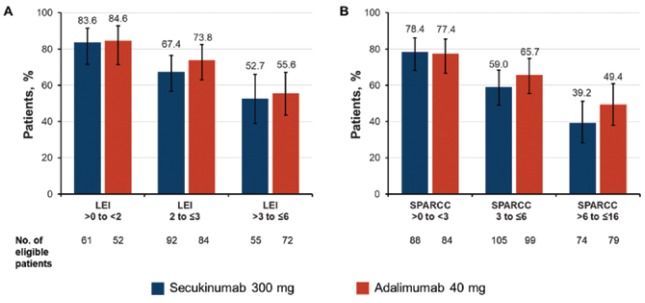
[1] McInnes IB, et al. *Lancet*. 2020;395(10235):1496-1505.
[2] Coates LC, et al. *Arthritis Res Ther.* 2019;21(1):266.

Table 1. Clinical Improvements Among Patients With Baseline LEI or SPARCC Enthesitis Treated with Secukinumab or Adalimumab (nonresponder imputation)

	Secukinumab 300 mg		Adalimumab 40 mg	
Outcomes[a]	**LEI (n=234)**	**SPARCC (n=301)**	**LEI (n=264)**	**SPARCC (n=331)**
Baseline enthesitis count, mean (SD)	2.6 (1.5)	5.0 (3.8)	2.8 (1.6)	5.4 (4.0)
Median time to enthesitis resolution, days (95% CI)	85 (57–113)	113 (85–169)	85 (57–86)	88 (85–114)
Enthesitis count, mean improvement from baseline (SD)				
Week 24	–1.6 (1.6)	–3.3 (3.5)	–1.6 (1.6)	–3.1 (3.5)
Week 52	–1.8 (1.6)	–3.6 (3.2)	–2.1 (1.7)	–3.9 (3.8)
Resolution of enthesitis, n (%)				
Week 24	116 (49.6)	138 (45.8)	115 (43.6)	144 (43.5)
Week 52	142 (60.7)	160 (53.2)	146 (55.3)	170 (51.4)
Enthesitis relapse, n/M (%)				
Week 24	37/210 (17.6)	38/274 (13.9)	49/232 (21.1)	47/293 (16.0)
Week 52	40/208 (19.2)	56/267 (21.0)	32/208 (15.4)	41/263 (15.6)

LEI, Leeds Enthesitis Index; M, number of evaluable patients; SPARCC; Spondyloarthritis Research Consortium of Canada Enthesitis Index.[a] Based on respective enthesitis measures.

Figure. Proportion of Patients Achieving Resolution of Enthesitis at Week 52 by Baseline **(A)** LEI and **(B)** SPARCC Enthesitis Severity[a]



LEI, Leeds Enthesitis Index; SPARCC; Spondyloarthritis Research Consortium of Canada Enthesitis Index.
[a] Error bars represent 95% confidence intervals.

Figure 1.

Acknowledgements: This study was funded by Novartis Pharma AG. The authors thank Richard Karpowicz, PhD, of Health Interactions, Inc, for providing medical writing support/editorial support, which was funded by Novartis Pharmaceuticals Corporation, East Hanover, NJ, in accordance with Good Publication Practice (GPP3) guidelines (http://www.ismpp.org/gpp3).

Disclosure of Interests: Gurjit S. Kaeley Consultant of: Novartis Pharmaceuticals Corporation, Georg Schett Speakers bureau: AbbVie, Bristol Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, and Pfizer, Consultant of: AbbVie, Bristol Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, and UCB, Grant/research support from: Bristol Myers Squibb, Celgene, GSK, Eli Lilly, and Novartis, Philip G Conaghan Consultant of: or Speakers bureau: AbbVie, AstraZeneca, Bristol Myers Squibb, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, Gilead, Novartis, and Pfizer, Grant/research support from: UK National Institute for Health Research (NIHR) Leeds Biomedical Research Centre, Dennis McGonagle Speakers bureau: Roche, Sobi, and Novartis, Grant/research support from: Novartis, Frank Behrens Consultant of: Pfizer, AbbVie, Sanofi, Lilly, Novartis, Genzyme, Boehringer, Janssen, Merck Sharp & Dohme, Celgene, Roche, and Chugai, Grant/research support from: Pfizer, Janssen, Chugai, Celgene, and Roche, and has received investigator fees from Eli Lilly, Philippe Goupille Grant/research support from: and/or Consultant of/Speakers bureau: AbbVie, Amgen, Biogen, Bristol Myers Squibb, Celgene, Chugai, Janssen, Lilly, Medac, Merck Sharp & Dohme, Nordic Pharma, Novartis, Pfizer, Sanofi, and UCB, Corine Gaillez Employee of: Novartis Pharma AG, Bhumik Parikh Employee of: Novartis Pharmaceuticals Corporation, Xiangyi Meng Employee of: Novartis Pharmaceuticals Corporation, Catherine Bakewell Consultant of: and/or Speakers bureau: AbbVie, Novartis, Pfizer, Janssen, UCB, and Sanofi Genzyme/Regeneron

DOI: 10.1136/annrheumdis-2021-eular.463

POS0195 GUSELKUMAB TREATMENT MODULATES CORE PSORIATIC ARTHRITIS GENE EXPRESSION IN TWO PHASE 3 CLINICAL TRIALS (DISCOVER-1 AND -2)

S. Siebert[1], K. Sweet[2], C. T. Ritchlin[3], E. C. Hsia[2,4], A. Kollmeier[5], X. L. Xu[5], Q. Song[2], M. Miron[2]. *[1]University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; *[2]Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; *[3]University of Rochester Medical Center, Department of Medicine, Allergy/Immunology and Rheumatology (SMD), Rochester, United States of America*; *[4]University of Pennsylvania Medical Center, Rheumatology, Philadelphia, United States of America*; *[5]Janssen Research & Development, LLC, Immunology, San Diego, United States of America*

Background: Guselkumab (GUS), an interleukin-23 p19-subunit monoclonal antibody, demonstrated efficacy compared with placebo (PBO) in reducing signs and symptoms of psoriatic arthritis (PsA) in the phase 3 DISCOVER-1 & 2 studies.[1,2]

Objectives: To evaluate gene expression in the blood of PsA patients (pts) in the DISCOVER-1 & -2 studies and the impact of GUS on the expression of these genes.

Methods: Pts were treated with GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or matching PBO. Whole transcriptome profiling by RNA-sequencing was performed using the Novaseq platform on blood samples obtained from a subset of 673 pts with PsA at baseline across the 2 DISCOVER studies, as well as from 21 demographically (age, sex, and ethnicity) matched healthy controls procured independently of the clinical program. A subgroup (N=227) also had serial blood samples (W0/W4/W24) evaluated; the subgroup pts were selected based on having baseline characteristics (demographics, disease activity, medication use) representative of the overall cross-study PsA population. Significance of differentially expressed genes (DEGs) between PsA and healthy controls was defined by a false discovery rate (FDR) <0.05 based on a log-linear model using edgeR. Top genes were defined by significance and |logFC| >1. For cell type analysis, genes that changed with GUS treatment were tested for enrichment using Cibersort. Gene enrichment scores were calculated using Gene Set Variation Analysis (GSVA).

Results: To define disease genes, we compared genes at baseline in pts with active PsA vs. healthy control whole blood transcriptomes and detected 355 upregulated and 314 downregulated (top genes shown in Table 1), defined here as core disease genes. Upregulated genes were largely related to neutrophils, monocytes, macrophages, and extracellular matrix, whereas downregulated genes were related to T cells. The upregulated disease genes were significantly decreased and the downregulated disease genes were significantly increased by GUS treatment vs. PBO at W4 and W24 (Fig 1). Upon stratification by Psoriasis Area and Severity Index 75% response and American College of Rheumatology 20% response, changes in core disease gene expression from W0 were statistically significant among responders, but not in non-responders, at W4 and W24 (data not shown). We then performed the second differential expression analysis comparing baseline to W4 and W24 for both PBO and GUS treatment arms to define genes that change with treatment arm over time. At W4 and W24 we found many DEGs from baseline with GUS treatment and none with PBO. These included genes related to B-, T-, NK-, and plasma cells (increased by GUS) and neutrophils, monocytes, eosinophils, and macrophages (decreased by GUS), suggestive of a partial normalization of immune cell composition in whole blood.

Conclusion: Using whole transcriptome profiling, we detected DEGs in blood samples obtained from PsA pts vs. healthy controls, suggesting a dysregulation of immune cell profiles in PsA. The majority of these disease-associated genes were modulated by GUS, with directionality toward a normalization of whole blood transcriptomic signatures.

REFERENCES:

[1] Deodhar A et al. Lancet. 2020;395:1115.
[2] Mease P et al. Lancet. 2020;395:1126.

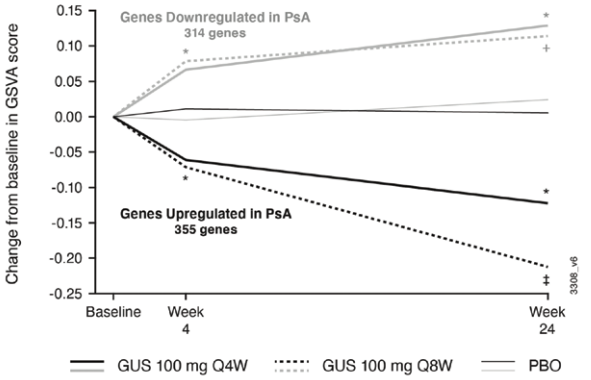
Table 1. Top DEGs derived from PsA vs. healthy whole blood transcriptomes.

Upregulated in PsA				Downregulated in PsA			
Gene	logFC	logCPM	FDR	Gene	logFC	logCPM	FDR
ADGRG7	**5.92**	-0.90	0.02101	AK8	-1.36	-1.06	1.61E-07
ADAMTS2	**4.06**	0.82	0.006466	FTCD	-1.48	-1.74	1.67E-05
PGF	**3.21**	-0.68	0.006466	GPR15	-1.54	1.81	1.67E-05
PCSK9	**3.21**	-2.96	0.023872	CHRM3	-1.54	-2.62	9.6E-08
OLAH	**2.76**	0.75	0.004539	RFPL4AL1	-1.69	-3.34	0.009738
MAOA	**2.55**	-0.26	0.005463	SPACA3	-1.85	-3.23	0.000216
SLC2A14	**2.30**	0.59	0.022594	VANGL2	-1.95	-1.79	9.6E-08
MMP1	**2.25**	-1.16	0.004745	RFPL4A	-2.04	-1.28	0.004539
DAAM2	**2.12**	4.31	0.024628	GLYATL2	-2.77	-2.78	1.93E-15
				BCAR1	-3.13	-2.58	6.24E-26

Bold indicates positive change. CPM = counts per million.

Disclosure of Interests: Stefan Siebert Consultant of: AbbVie, Janssen, Novartis, UCB, Grant/research support from: AbbVie, Amgen (previously Celgene), Bristol Myers Squibb, Boehringer Ingelheim, GSK, Janssen, Novartis, UCB, Kristen Sweet Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development LLC, Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Gilead, Janssen, Eli Lilly, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, and UCB, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development LLC, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development LLC, Qingxuan Song Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development LLC, Michelle Miron Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development LLC

Figure. Change from baseline in median GSVA scores for upregulated and downregulated genes in PsA for GUS and PBO treatment arms from DISCOVER-1 and 2.



*, +, ‡ p ≤ 0.05, 0.01, 0.001, respectively. Wilcox test performed between GUS (Q4W, dashed line; Q8W, solid line) and PBO.

DOI: 10.1136/annrheumdis-2021-eular.479

POS0196 UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS REFRACTORY TO BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: 56-WEEK DATA FROM THE PHASE 3 SELECT-PSA 2 STUDY

P. J. Mease[1], A. Lertratanakul[2], K. Papp[3], F. Van den Bosch[4], S. Tsuji[5], E. Dokoupilova[6], M. Keiserman[7], X. Bu[2], L. Chen[2], R. Mccaskill[2], P. Zueger[2], E. Mcdearmon-Blondell[2], A. Pangan[2], W. Tillett[8]. *[1]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology,*

Seattle, United States of America; [2]*AbbVie Inc, Immunology, North Chicago, United States of America*; [3]*Papp Clinical Research and Probity Medical Research, Dermatology, Waterloo, Canada*; [4]*Ghent University, VIB Center for Inflammation Research, Internal Medicine and Pediatrics, Ghent, Belgium*; [5]*National Hospital Organization, Osaka Minami Medical Center, Orthopaedics/ Rheumatology, Osaka, Japan*; [6]*Medical Plus, s.r.o., Uherske Hradiste, Masaryk University, Pharmaceutical Technology, Brno, Czech Republic*; [7]*Pontificial Catholic University, School of Medicine, Porto Alegre, Brazil*; [8]*Royal National Hospital For Rheumatic Diseases, Rheumatology, Bath, United Kingdom*

Background: Upadacitinib (UPA) is an oral Janus kinase inhibitor currently under evaluation for the treatment of psoriatic arthritis (PsA). Previous 24-week results from the SELECT-PsA 2 study in patients with PsA and prior inadequate response to ≥1 biologic disease-modifying antirheumatic drug (bDMARD) demonstrated UPA efficacy with a safety profile consistent with that observed in rheumatoid arthritis.[1]

Objectives: To evaluate the 56-week efficacy and safety of UPA in the SELECT-PsA 2 study.

Methods: Patients were randomized to 56 weeks of blinded treatment with UPA 15 or 30 mg once daily (QD), or placebo (PBO) switched to UPA 15 or 30 mg QD at Week 24. Efficacy endpoints included proportions of patients achieving 20/50/70% improvement in American College of Rheumatology (ACR) criteria (ACR20/50/70), 75/90/100% improvement in the Psoriasis Area and Severity Index (PASI75/90/100), resolution of dactylitis and enthesitis, and minimal disease activity (MDA). Non-responder imputation was used for missing data. Treatment-emergent adverse events (TEAEs) were summarized for events occurring while on UPA and ≤30 days after last dose (for those who discontinued).

Results: Of 641 patients who received ≥1 dose of study drug, 74.7% completed 56 weeks of treatment. Clinical improvements based on the proportion of patients achieving ACR20/50/70 and MDA (Figure 1), PASI75/90/100, and resolution of dactylitis and enthesitis were generally maintained through 56 weeks of UPA treatment. Week 56 results for patients who switched from PBO to UPA at Week 24 had a similar trajectory to those for patients originally randomized to UPA. Overall, improvements observed with UPA 15 mg were similar to or approached those with UPA 30 mg over 56 weeks. Dose-dependent increases were observed for exposure-adjusted event rates (EAERs) of serious infections, herpes zoster (HZ), hepatic disorders, hematologic lab-related adverse events, and creatine phosphokinase (CPK) elevations, but not for exposure-adjusted incidence rates (EAIRs) of major adverse cardiovascular events (MACE), venous thromboembolic events (VTEs), or malignancies (Table 1). Generally, rates of TEAEs were lower with UPA 15 mg versus 30 mg.

Conclusion: In patients with PsA and prior inadequate response to ≥1 bDMARD, UPA efficacy was maintained over 56 weeks with no new safety signals.

REFERENCES:

[1] Mease PJ, et al. Ann Rheum Dis 2020. Epub ahead of print.

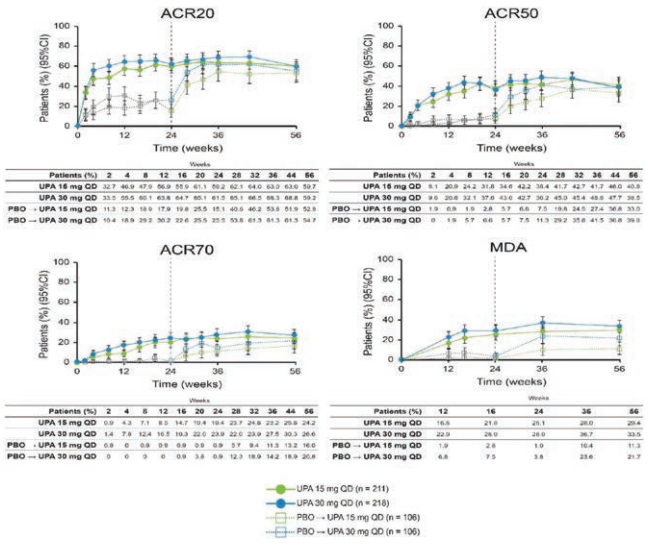
Table 1. Safety through Week 56

Event	UPA 15 mg QD (n=290; PY=419.4)	UPA 30 mg QD (n=308; PY=423.5)
EAER, events/100 PY (95% CI)		
Infection	89.7 (81.0–99.2)	113.6 (103.9–124.2)
Serious infection	2.6 (1.5–4.7)	6.1 (4.2–9.0)
Opportunistic infection[a]	0.7 (0.2–2.2)	0.9 (0.4–2.5)
HZ	3.8 (2.3–6.2)	8.5 (6.1–11.8)
Active TB	0	0
Gastrointestinal perforation (adjudicated)	0	0
Hepatic disorder	4.8 (3.1–7.4)	17.7 (14.1–22.2)
Anemia	2.1 (1.1–4.1)	5.4 (3.6–8.2)
Neutropenia	1.0 (0.4–2.5)	3.1 (1.8–5.3)
Lymphopenia	0.7 (0.2–2.2)	2.4 (1.3–4.4)
CPK elevation	5.2 (3.5–8.0)	8.7 (6.3–12.1)
Renal dysfunction	0.5 (0.1–1.9)	0.2 (0.0–1.7)
EAIR, n/100 PY (95% CI)		
NMSC[b]	1.2 (0.5–2.9)	1.0 (0.4–2.5)
Malignancy other than NMSC[c]	1.2 (0.5–2.9)	1.2 (0.5–2.9)
Lymphoma[d]	0.5 (0.1–1.9)	0
MACE (adjudicated)	0.2 (0–1.7)	0.2 (0–1.7)
VTE (adjudicated)	0.2 (0–1.7)	0.2 (0–1.7)

[a]Excludes TB and HZ. [b]UPA 15 mg: 4 cases of BCC and 1 case of SCC of the skin; UPA 30 mg: 3 cases of BCC and 3 cases of SCC of the skin. [c]UPA 15 mg: 2 cases of prostate cancer, and single cases of malignant melanoma, ovarian cancer, and rectal cancer; UPA 30 mg: single cases of basosquamous carcinoma (considered NMSC after medical review), malignant melanoma, oropharyngeal SCC, and rectal adenocarcinoma, as well as endometrial cancer and ovarian cancer (in the same patient). [d]UPA 15 mg: 2 events of treatment-emergent abnormal lymphocyte morphology; abnormal lymphocytes were not reported in subsequent laboratory testingBCC, basal cell carcinoma; CI, confidence interval; NMSC, non-melanoma skin cancer; PY, patient-years; SCC, squamous cell carcinoma; TB, tuberculosis

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Russell Craddock, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Figure Efficacy through Week 56 (non-responder imputation)



Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squib, Celgene, Eli Lilly, Galapagos, Genentech, Gilead, GSK, Janssen, Novartis, Pfizer, Sun Pharma, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squib, Celgene, Eli Lilly, Galapagos, Genentech, Gilead, GSK, Janssen, Novartis, Pfizer, Sun Pharma, and UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squib, Celgene, Eli Lilly, Galapagos, Genentech, Gilead, GSK, Janssen, Novartis, Pfizer, Sun Pharma, and UCB, Apinya Lertratanakul Shareholder of: May own stock/shares in AbbVie, Employee of: Currently employed by AbbVie, Kim Papp Speakers bureau: AbbVie, Akros, Allergan, Almirall, Amgen, Bausch Health, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, Genentech/Roche, Janssen, Kyowa Kirin, LEO, Meiji, MSD, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, Takeda, UCB, and Valeant, Consultant of: AbbVie, Akros, Allergan, Almirall, Amgen, Arcutis, Avillion, Bausch Health, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, Genentech/Roche, GSK, Janssen, Kyowa Kirin, LEO, Meiji, MSD, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, Takeda, UCB, and Valeant, Grant/research support from: AbbVie, Akros, Allergan, Almirall, Amgen, Arcutis, Avillion, Bausch Health, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, Genentech/Roche, GSK, Janssen, Kyowa Kirin, LEO, Meiji, MSD, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, Takeda, UCB, and Valeant, Filip van den Bosch Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, and UCB, Shigeyoshi Tsuji Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, and UCB., Consultant of: AbbVie, Eli Lilly, Janssen, Novartis, and UCB., Grant/research support from: AbbVie, Eli Lilly, Janssen, Novartis, and UCB., Eva Dokoupilova Grant/ research support from: AbbVie, Affibody AB, Eli Lilly, Galapagos, Gilead, GSK, Hexal AG, MSD, Novartis, Pfizer, R-Pharm, Sanofi-Aventis, and UCB, MAURO KEISERMAN Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/ research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Xianwei Bu Shareholder of: May own stock/shares in AbbVie, Employee of: Currently employed by AbbVie, Liang Chen Shareholder of: May own stock/shares in AbbVie, Employee of: Currently employed by AbbVie, Reva McCaskill Shareholder of: May own stock/shares in AbbVie, Employee of: Currently employed by AbbVie, Patrick Zueger Shareholder of: May own stock/shares in AbbVie, Employee of: Currently employed by AbbVie, Erin McDearmon-Blondell Shareholder of: May own stock/shares

in AbbVie, Employee of: Currently employed by AbbVie, Aileen Pangan Shareholder of: May own stock/shares in AbbVie, Employee of: Currently employed by AbbVie, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, MSD, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, and Janssen

DOI: 10.1136/annrheumdis-2021-eular.1066

POS0197 RESPONSIVENESS OF ULTRASOUND SYNOVITIS AND CLINICAL OUTCOMES IN PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB: DATA FROM THE ULTIMATE TRIAL

M. Boers[1], P. G. Conaghan[2], G. Schett[3], P. Mandl[4], E. Naredo[5], F. Van den Bosch[6], R. Burgos-Vargas[7], A. M. Duggan[8], P. Goyanka[9], C. Gaillez[10], M. A. D'agostino[11]. *[1]Amsterdam UMC, Vrije Universiteit, Department of Epidemiology and Data Science, and Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands*; *[2]University of Leeds, Rheumatology, Leeds, United Kingdom*; *[3]Friedrich Alexander University of Erlangen-Nuremberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3, Erlangen, Germany*; *[4]Medical University of Vienna, Division of Rheumatology, Vienna, Austria*; *[5]Hospital Fundación Jiménez Díaz and Autónoma University, Department of Rheumatology and Joint and Bone Research Unit, Madrid, Spain*; *[6]Ghent University and Ghent University Hospital, Rheumatology, Ghent, Belgium*; *[7]Hospital General de Mexico, Department of Rheumatology, Mexico City, Mexico*; *[8]Novartis Ireland Limited, Immunology, Hepatology and Dermatology, Dublin, Ireland*; *[9]Novartis Healthcare Private Limited, Immunology, Hepatology and Dermatology, Hyderabad, India*; *[10]Novartis Pharma AG, Immunology, Hepatology and Dermatology, Basel, Switzerland*; *[11]Catholic University of Sacred Heart, Rheumatology, Roma, Italy*

Background: Power Doppler ultrasonography is a sensitive imaging tool to assess synovitis in psoriatic arthritis (PsA).[1,2] ULTIMATE (NCT02662985) is the first large, randomised, double-blind placebo-controlled phase IIIb study in PsA, using ultrasound to evaluate early response to secukinumab on synovitis. The use of the standardised and reliable global EULAR-OMERACT composite ultrasound synovitis score at patient level (GLOESS) as the primary endpoint showed the early and significant benefit of secukinumab vs. placebo on synovitis at week 12.[3]

Objectives: To investigate the responsiveness and discriminative validity of GLOESS compared to clinical outcomes on joints at week 12 and report ultrasound and clinical efficacy data up to week 24.

Methods: This is a 52-week study with a 12-week double-blind, placebo-controlled period followed by 12-week open-label (OL) and 6-month OL extension. All placebo patients were switched to secukinumab (300 or 150 mg) at week 12.[3] Discriminative validity of GLOESS was analysed post-hoc: within-group responsiveness was assessed by comparing its standardised response mean (SRM) to that of core set of ACR response in the initial secukinumab group over 12 and 24 weeks. Mean change from baseline up to week 12 of GLOESS was determined with mixed-effect model repeated measures analysis (MMRM) and from week 12-24 as observed. 24 week efficacy outcomes included ACR responses, HAQ-DI, PASI response and resolution of dactylitis. These outcomes were exploratory and reported either according to non-responder imputation (ACR response), or as observed (HAQ-DI, PASI response and resolution of dactylitis).

Results: Of 166 patients enrolled, a total of 155 patients (93%) completed 24 weeks of treatment (secukinumab, 79 patients 95%; placebo, 76 patients 92%). Mean change from baseline to week 24 in GLOESS was similar in the initial secukinumab and placebo-secukinumab groups. A continued improvement in GLOESS was observed in the secukinumab group, with catch-up improvement in the placebo group after switch to active therapy (Figure 1). Both SRM of GLOESS and ACR core components over 12 and 24 weeks were high (Table 1). Similar clinical response rates were reported for clinical joint count, skin, dactylitis and function at week 24 in secukinumab and placebo switchers groups (Table 1).

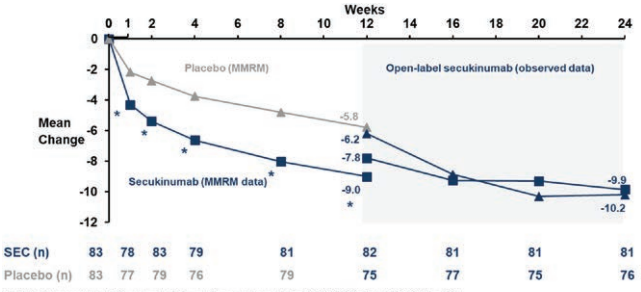


Figure 1. Mean change from baseline in GLOESS by treatment through Week 24

Conclusion: These analyses highlight the responsiveness and high discriminative validity of GLOESS in PsA, resembling that of key clinical PsA manifestations and physical function.

REFERENCES:

[1] D'Agostino MA and Coates LC. *J Rheumatol.* 2019;46:337–9.
[2] Uson J, et al. *Rheumatol Clin.* 2018;14:27–35.
[3] D'Agostino MA, et al. *Arthritis Rheumatol.* 2020;72 (suppl 10).

Table 1. Responsiveness of GLOESS - analysed by standardised response mean and efficacy outcomes at week 24

Standardised response mean (Initial secukinumab)			Efficacy of secukinumab		
	Week 0–12 (N = 83)	Week 0–24 (N = 83)	Responders (%)	Secukinumab week 0–24 (N = 83)	Placebo switchers week 12–24 (N = 83)
GLOESS	1.05	1.06	ACR20	87	74
Tender joint count	1.03	1.35	ACR50	64	49
Swollen joint count	0.91	1.18	ACR70	34	23
Patient global assessment of disease activity	1.37	1.55	HAQ-DI*	80	63
Physician global assessment of disease activity	1.59	2.39	PASI 75†	72	59
Pain	1.32	1.53	PASI 90†	62	45
HAQ-DI score	1.32	1.32	Resolution of dactylitis (LDI=0)	67	59

*HAQ-DI response is defined as an improvement of at least 0.35 score points compared to baseline (change ≤ –0.35)†N value for PASI response in secukinumab and placebo groups are 36 and 33; respectively. PASI response was calculated for patients with BSA ≥ 3 %.BSA, Body Surface Area; LDI, Leeds Dactylitis Index

Disclosure of Interests: Maarten Boers Consultant of: BMS, Novartis, Pfizer, GSK, Philip G Conaghan Speakers bureau: AbbVie, AstraZeneca, BMS, Eli Lilly, Galapagos, Gilead, Novartis and Pfizer, Consultant of: AbbVie, AstraZeneca, BMS, Eli Lilly, Galapagos, Gilead, Novartis and Pfizer, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB, Peter Mandl Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Roche and UCB, Grant/research support from: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Roche and UCB, Esperanza Naredo Speakers bureau: AbbVie, Roche, BMS, Pfizer, UCB, Eli Lilly, Novartis, Janssen, and Celgene, Consultant of: AbbVie, Novartis and BMS, Grant/research support from: Eli Lilly, Filip van den Bosch Speakers bureau: AbbVie, Celgene, Janssen, Eli Lilly, Galapagos, Merck, Novartis, Pfizer, and UCB Pharma, Consultant of: AbbVie, Celgene, Janssen, Eli Lilly, Galapagos, Merck, Novartis, Pfizer, and UCB Pharma, Ruben Burgos-Vargas: None declared, Anne-Marie Duggan Employee of: Novartis, Punit Goyanka Employee of: Novartis, Corine Gaillez Shareholder of: Novartis and BMS, Employee of: Novartis, Maria-Antonietta D'Agostino Speakers bureau: Sanofi, Novartis, BMS, Janssen, Celgene, Roche, AbbVie, UCB, and Eli Lilly, Consultant of: Sanofi, Novartis, BMS, Janssen, Celgene, Roche, AbbVie, UCB, and Eli Lilly

DOI: 10.1136/annrheumdis-2021-eular.1720

POS0198 EFFICACY AND SAFETY OF DEUCRAVACITINIB, AN ORAL, SELECTIVE TYROSINE KINASE 2 INHIBITOR, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

P. J. Mease[1], A. Deodhar[2], D. Van der Heijde[3], F. Behrens[4], A. Kivitz[5], J. Kim[6], S. Singhal[7], M. Nowak[8], S. Banerjee[9]. *[1]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America*; *[2]Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America*; *[3]Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; *[4]CIRI/Rheumatology and Fraunhofer Institute, Goethe University, Translational Medicine and Pharmacology ITMP, Frankfurt, Germany*; *[5]Altoona Center for Clinical Research, Department of Rheumatology, Duncansville, United States of America*; *[6]Bristol Myers Squibb, Global Biometrics Data Sciences, Princeton, United States of America*; *[7]Bristol Myers Squibb, Rheumatology, Princeton, United States of America*; *[8]Bristol Myers Squibb, Clinical R&D,*

Princeton, United States of America; [9]*Bristol Myers Squibb, Rheumatology and Dermatology, Princeton, United States of America*

Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates signaling by key cytokines involved in psoriatic arthritis (PsA) and plaque psoriasis (PsO) pathogenesis. Deucravacitinib is a novel oral agent that selectively inhibits TYK2 via an allosteric mechanism by binding to the nonconserved regulatory domain of the kinase. A previous Phase 2 trial in PsO had demonstrated that deucravacitinib was efficacious and well tolerated, with no laboratory abnormalities observed.

Objectives: To evaluate the efficacy and safety of deucravacitinib in active PsA.

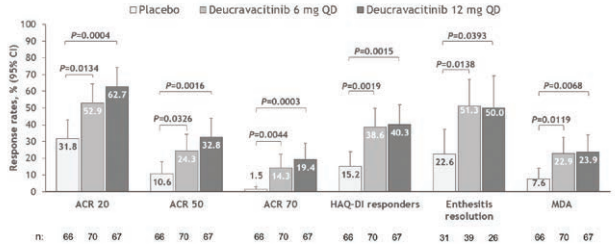
Methods: This is an ongoing, 1-year, randomized, double-blind, placebo (PBO)-controlled (initial 16 weeks), multiregional, Phase 2 trial (NCT03881059). Eligible patients had a PsA diagnosis for ≥6 months, met CASPAR criteria, and had active disease with ≥3 tender and ≥3 swollen joints, C-reactive protein ≥3 mg/L (ULN, 5 mg/L), and ≥1 psoriatic lesion (≥2 cm). Patients had failed or were intolerant to ≥1 nonsteroidal anti-inflammatory drug, corticosteroid, conventional synthetic disease-modifying antirheumatic drug (csDMARD), and/or 1 TNF inhibitor (TNFi; ≤30%). Patients were randomized 1:1:1 to deucravacitinib 6 mg once daily (QD) or 12 mg QD, or PBO. The primary endpoint was achievement of ACR 20 response at Week 16. Additional endpoints included the proportion of patients achieving ACR 50/70 response, Health Assessment Questionnaire-Disability Index (HAQ-DI) response (≥0.35 improvement from baseline), enthesitis resolution (Leeds Index score of 0), minimal disease activity, change from baseline in SF-36 physical component score (SF-36 PCS) and mental component score (SF-36 MCS), Psoriasis Area and Severity Index (PASI) 75 response, adverse events (AEs), and laboratory parameters.

Results: Of 203 patients randomized, 180 (89%) completed 16 weeks of treatment (deucravacitinib 6 mg QD, 63/70 [90%]; deucravacitinib 12 mg QD, 59/67 [88%]; PBO, 58/66 [88%]). Demographic and baseline disease characteristics were similar across groups. Mean age was 49.8 years, 51% of patients were female, median PsA duration was 4.5 years, 66% of patients used csDMARDs at baseline and throughout the study, and 15% had used a TNFi. This study met its primary endpoint, with deucravacitinib 6 mg and 12 mg QD demonstrating significantly higher ACR 20 responses versus PBO at Week 16 (Figure 1). Additional endpoints were also met with deucravacitinib versus PBO (Figure 1). Adjusted mean changes from baseline in SF-36 PCS and SF-36 MCS at Week 16, respectively, were significantly higher in the deucravacitinib 6 mg QD group (5.6 vs 2.3, P=0.0062; 3.6 vs 0.7, P=0.0211) and 12 mg QD group (5.8 vs 2.3, P=0.0042; 3.5 vs 0.7, P=0.0263) compared with PBO. PASI 75 responses were also significantly higher in the deucravacitinib groups (P≤0.0136 vs PBO). The most common AEs in the deucravacitinib 6 mg/12 mg/PBO groups, respectively, during the 16-week treatment period were nasopharyngitis (5.7%/17.9%/7.6%), sinusitis (0%/7.5%/0%), headache (7.1%/1.5%/4.5%), and rash (4.3%/6.0%/0%). No serious AEs, herpes zoster infections, opportunistic infections, or thrombotic events were reported in deucravacitinib-treated patients during this period. Additionally, no significant changes from baseline in hematologic parameters (lymphocytes, neutrophils, platelets, and hemoglobin) or serum lipids were observed with deucravacitinib treatment.

Conclusion: Deucravacitinib was efficacious versus PBO over 16 weeks in patients with active PsA. Treatment was generally well tolerated and the safety and laboratory parameter profile of deucravacitinib was consistent with that observed in an earlier Phase 2 PsO trial.

Acknowledgements: This study was sponsored by Bristol Myers Squibb. Professional medical writing assistance was provided by Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

Figure. Response Endpoints at Week 16



Nominal P values for pairwise comparisons vs placebo. Response endpoints were evaluated using a Cochran-Mantel-Haenszel test with stratification factors (body weight and prior TNFi use), with nonresponder imputation for missing values.
ACR, American College of Rheumatology; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; QD, once daily.

Disclosure of Interests: Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB, Atul Deodhar Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Eli Lilly, Glaxo Smith & Kline, Novartis, Pfizer, UCB, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma, Frank Behrens Consultant of: Pfizer, AbbVie, Sanofi, Lilly, Novartis, Genzyme, Boehringer, Janssen, MSD, Celgene, Roche, Chugai, Bristol Myers Squibb, UCB Pharma, Grant/research support from: Pfizer, Janssen, Chugai, Celgene, Roche, Alan Kivitz Shareholder of: Pfizer, Sanofi, GlaxoSmithKline, Gilead Sciences, Inc., Novartis, Paid Consultant: AbbVie, Boehringer Ingelheim, Flexion, Janssen, Pfizer, Sanofi, Regeneron, SUN Pharma Advanced Research, Gilead Sciences, Inc., Speakers bureau: Celgene, Merck, Lilly, Novartis, Pfizer, Sanofi, Genzyme, Flexion, AbbVie, Jonghyeon Kim Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Shalabh Singhal Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Miroslawa Nowak Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Subhashis Banerjee Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb
DOI: 10.1136/annrheumdis-2021-eular.2603

POS0199 TIME-SERIES ANALYSIS IN MODERATE TO SEVERE PLAQUE PSORIASIS UNDER DIFFERENT BIOLOGICS TREATMENTS

Y. Zhang[1,2,3], S. X. Zhang[1,2,3], J. Qiao[1,2,3], R. Zhao[1,2,3], S. Song[1,2,3], Y. Li[1,2,3], M. J. Chang[1,2,3], G. Y. Liu[1], P. F. He[4], X. Li[1,2,3]. [1]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [2]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [3]*Ministry of Education, Key laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [4]*Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Moderate to Severe Plaque Psoriasis is an inflammatory skin disease that is associated with multiple comorbidities and substantially diminishes patients' quality of life. As one of the most significant therapeutic advancements in the field of dermatology, Biologics such as TNF inhibitors, IL-12/23 inhibitor, IL-17 inhibitors, and IL-23 inhibitors, have higher efficacy compared with oral medications or phototherapy[1]. However, the previous studies did not focus on the simultaneous comparison of molecular changes in different classes of biologics. The identification of time-series genes (TSGs) could help to uncover the mechanisms underlying transcriptional regulation[2].

Objectives: In this study, we aimed to compare the differences in expression patterns and functions of time-series genes in Moderate to Severe Plaque Psoriasis under different biologics treatments.

Methods: The transcription profile of GSE117239 and GSE51440 were obtained from the Gene Expression Omnibus database (GEO). The GSE117239 included 19 samples treated with Etanercept (TNF inhibitors) and 16 samples treated with Ustekinumab (IL-12/23 inhibitor). The GSE51440 included 4 samples treated with Guselkumab (IL-23 inhibitors). Skin biopsy samples (LS: lesion, NL: non-lesion) were collected at baseline, weeks 1 and 12, respectively. After background adjustment and other pre-procession, differentially expressed genes (DEGs) were extracted from LS skin biopsy and untreated NL skin biopsy at different times after three different biologics treatments, respectively. The Short Time-series Expression Miner (STEM) software was used to cluster and compare average DEGs with coherent changes. Afterward, the different expression patterns of TSGs under the three treatment groups were compared. GO analysis and KEGG pathway enrichment analysis of TSGs were performed by Metascape.

Results: Different DEGs varied in LS skin compared with those of NL skin biopsy: 976 genes in Ustekinumab group, 996 genes in Etanercept group, and 601 genes in Guselkumab group detailly (P < 0.05 and [log FC] > 1). Gene landscapes suggested the signatures of LS gradually changed during the treatment process, and gradually converge to NL signatures (Fig.1a, 2a,3a). Time-series genes in the three treatment groups had different expression patterns and functions. In the Ustekinumab group, a total of 448 TSGs in profile 3 showed a stable-stable-decreasing expression trend and significantly

associated with mitotic nuclear division and defense response to other organism, whereas in profile 4 represented a stable-stable-increasing expression trend and significantly associated with positive regulation of cellular response to organic 9 compound (Fig.1). With the treatment of Etanercept, 22 TSGs had a stable-increasing-increasing expression tendency and closely associated with fatty acid metabolism and steroid metabolic process (Fig.2). After Guselkumab treatment, 13 TSGs also represented a stable-increasing-increasing expression tendency that mainly characterized by defense response to other organism and epidermis development (Fig.3). Interestingly, both Ustekinumab and Guselkumab treatment dramatically influenced defense response to other organism-related genes, while Etanercept mainly affected genes involved in fatty acid metabolism and steroid metabolic process.

Conclusion: Biologics effectively reconstituted the gene signatures of psoriasis in different aspects. TSG features could be one of indicator for precise intervention for psoriasis.

REFERENCES:

[1] Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. *Jama* 2020;323(19):1945-60. doi: 10.1001/jama.2020.4006 [published Online First: 2020/05/20]

[2] Ernst J, Bar-Joseph Z. STEM: a tool for the analysis of short time series gene expression data. *BMC Bioinformatics* 2006;7:191. doi: 10.1186/1471-2105-7-191 [published Online First: 2006/04/07]

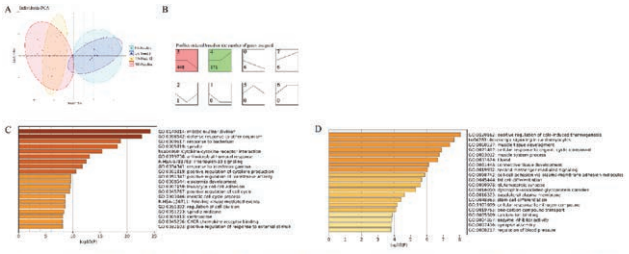


Figure 1 **(A)** PCA result showed a clear separation of the genotypes in Ustekinumab group. **(B)** Expression patterns of time-series genes in Ustekinumab group. The colored profiles represent significant profiles. Colored in red and blue represented statistically significant (P<0.05). **(C)** KEGG pathway and GO enrichment results of the significant stable-stable-decreasing expression trend TSGs. **(D)** KEGG pathway and GO enrichment results of the significant stable-stable-increasing expression trend TSGs.

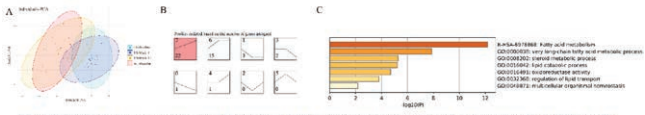


Figure 2 **(A)** PCA result showed a clear separation of the genotypes in Etanercept group. **(B)** Expression patterns of time-series genes in Etanercept group. The colored profiles represent significant profiles. Colored in red represented statistically significant (P<0.05). **(C)** KEGG pathway and GO enrichment results of the significant stable-increasing-increasing expression trend TSGs.

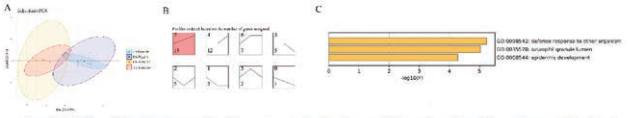


Figure 3 **(A)** PCA result showed a clear separation of the genotypes in Guselkumab group. **(B)** Expression patterns of time-series genes in Guselkumab group. The colored profiles represent significant profiles. Colored in red represented statistically significant (P<0.05). **(C)** KEGG pathway and GO enrichment results of the significant stable-increasing-increasing expression trend TSGs.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2669

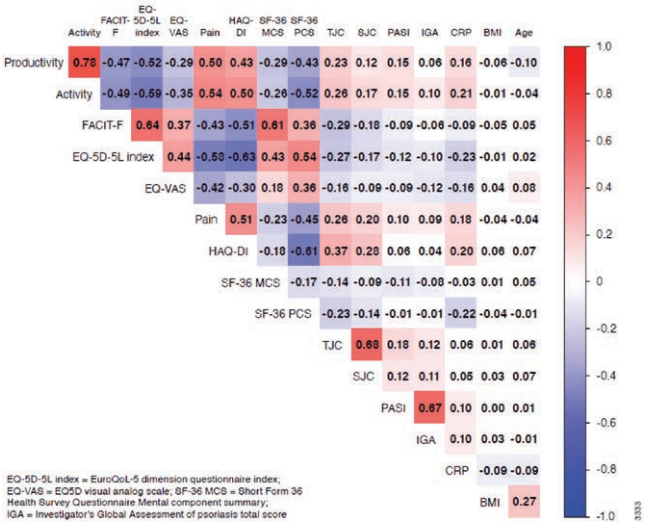
POS0200

CLINICAL CHARACTERISTICS & OUTCOMES ASSOCIATE WITH WORK PRODUCTIVITY IN BIO-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS THROUGH WEEK 24 OF THE DISCOVER-2 STUDY

J. Curtis[1], I. Mcinnes[2], D. D. Gladman[3], F. Yang[4], S. Peterson[4], P. Agarwal[5], A. Kollmeier[6], E. C. Hsia[7,8], C. Han[7], M. Shawi[4], W. Tillett[9], P. J. Mease[10], P. Rahman[11]. [1]*University of Alabama at Birmingham, Department of Medicine, Immunology and Rheumatology, Birmingham, United States of America*; [2]*University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; [3]*Toronto Western Hospital, Centre for Prognosis in the Rheumatic Diseases, Toronto, Canada*; [4]*Janssen Global Services, LLC, Immunology, Horsham, United States of America*; [5]*Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; [6]*Janssen Research & Development, LLC, Immunology, San Diego, United States of America*; [7]*Janssen Research & Development, Immunology, Spring House, United States of America*; [8]*University of Pennsylvania School of Medicine, Rheumatology, Philadelphia, United States of America*; [9]*Royal National Hospital for Rheumatic Diseases, Department of Pharmacy & Pharmacology, Centre for Therapeutic Innovation, Bath, United Kingdom*; [10]*Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America*; [11]*Memorial University of Newfoundland, Craig L Dobbin Genetics Research Centre, St. John's, Canada*

Background: Psoriatic arthritis (PsA), a chronic inflammatory disease characterized by peripheral arthritis, axial inflammation, dactylitis, enthesitis & skin/nail psoriasis, causes impaired physical function, disability & loss of work productivity.
Objectives: Evaluate associations between PsA clinical characteristics & outcomes including fatigue & work productivity using Work Productivity & Activity Impairment Questionnaire: PsA (WPAI-PsA).
Methods: The Phase 3 DISCOVER-2 trial assessed guselkumab (GUS), an anti-IL-23p19 subunit monoclonal antibody, in bio-naïve adults with active PsA (swollen joint count [SJC] ≥5 & tender joint count [TJC] ≥5, C-reactive protein [CRP] ≥0.6 mg/dL) despite standard therapies.[1] Patients (Pts) were randomized 1:1:1 to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or placebo (PBO). WPAI-PsA assesses PsA-related work time missed (absenteeism), impairment while working (presenteeism), productivity loss (absenteeism+presenteeism), & daily activity during the previous week. Spearman correlation testing evaluated relationships between pt demographics & disease characteristics of PsA & WPAI domain scores based on observed values at baseline. Univariate linear regression assessed associations between WPAI & these variables based on observed data at W0 & at W24. Variables with p<0.10 were included in a multivariate analysis employing a mixed-effects model for repeated measures, controlling for all other variables; resulting p-values <0.05 were considered statistically significant.
Results: As reported elsewhere,[2] least-squares mean % changes from baseline at W24 were -3.8/-19.5/-20.0/-20.5 for GUS Q4W, -3.1/-19.4/-19.7/-21.5 for GUS Q8W, & -3.5/-10.2/-10.9/-10.3 for PBO for absenteeism, presenteeism, absenteeism+presenteeism, & daily activity impairment, respectively. Among 738 pts, WPAI domain scores were moderately to strongly correlated (ie, ≥0.4) with pt-reported pain (0-10 visual analog scale), physical function (Health Assessment Questionnaire Disability Index [HAQ-DI]), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F] scale) & 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) score, but weakly correlated with other variables (Figure 1). Based on univariate analyses & evaluation of collinearity between variables, attributes included in multivariate models were age, body mass index (BMI), gender, CRP, FACIT-F, pain, Psoriasis Area Severity Index (PASI), TJC, SJC, enthesitis & dactylitis. In final model, CRP, FACIT-F, & pain were statistically significantly associated with all WPAI domains (Table 1). Presence of enthesitis & higher PASI score were significantly associated with higher loss of work productivity & activity outside work.
Conclusion: In PsA pts, extra-articular symptoms, fatigue, pain & elevated CRP were significantly associated with WPAI-assessed work & activity impairment. Treating all major clinical manifestations of PsA is needed to help pts improve work & activity impairment. GUS effectively treats all major clinical manifestations[1] & improves work & activity impairment in PsA.[2]

Figure. Spearman correlations between pt/disease characteristics & WPAI domains at W0



REFERENCES:

[1] Mease P. Lancet 2020;395:1126-36.

[2] Curtis J. ACR 2020; Poster 0332.

Table 1. Multivariate analysis of clinical characteristics/outcomes & WPAI domains at W0 & W24

Parameter	Absenteeism[a]		Presenteeism[a]		Productivity Loss[a]		Activity Impairment[b]	
	Estimate	p-value	Estimate	p-value	Estimate	p-value	Estimate	p-value
Age	-0.05	0.42	-0.27	**<0.001**	-0.28	**<0.001**	-0.06	0.17
Female	0.91	0.46	-1.54	0.22	-1.74	0.20	2.38	**0.02**
CRP	0.73	**0.04**	0.97	**0.01**	1.01	**0.01**	0.89	**<0.001**
FACIT-F	-0.31	**<0.001**	-0.67	**<0.001**	-0.73	**<0.001**	-0.75	**<0.001**
Pain	1.03	**<0.001**	4.15	**<0.001**	4.25	**<0.001**	4.02	**<0.001**
PASI	0.06	0.36	0.16	**0.02**	0.14	**0.05**	0.15	**0.003**
SJC	0.08	0.48	-0.05	0.61	-0.05	0.66	0.03	0.75
TJC	-0.10	0.13	0.11	0.09	0.09	0.19	0.10	**0.04**
Dactylitis (Y/N)	-1.10	0.39	2.47	**0.05**	2.58	**0.05**	0.54	0.57
Enthesitis (Y/N)	1.52	0.20	2.38	**0.04**	2.99	**0.01**	2.40	**0.01**

[a]Pts working at baseline[b]All pts in study

Disclosure of Interests: Jeffrey Curtis Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Eli Lilly, Myriad, Pfizer, Regeneron, Roche, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Eli Lilly, Myriad, Pfizer, Regeneron, Roche, and UCB, Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, and UCB, Dafna D Gladman Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer and UCB, Feifei Yang Shareholder of: Janssen, Employee of: Janssen, Steve Peterson Shareholder of: Janssen, Employee of: Janssen, Prasheen Agarwal Shareholder of: Janssen, Employee of: Janssen, Alexa Kollmeier Shareholder of: Janssen, Employee of: Janssen, Elizabeth C Hsia Shareholder of: Janssen, Employee of: Janssen, Chenglong Han Shareholder of: Janssen, Employee of: Janssen, May Shawi Shareholder of: Janssen, Employee of: Janssen, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, MSD, Pfizer, and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen, and Novartis, Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB, Proton Rahman Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis
DOI: 10.1136/annrheumdis-2021-eular.274

POS0201

RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN PATIENTS INITIATING BIOLOGICS/APREMILAST FOR PSORIATIC ARTHRITIS: A NATIONWIDE POPULATION-BASED STUDY USING THE FRENCH HEALTH INSURANCE DATABASE

L. Pina Vegas[1,2], P. Le Corvoisier[3,4], L. Penso[1,5], M. Paul[1,6], E. Sbidian[1,4,7], P. Claudepierre[1,2]. [1]*Université Paris Est-Créteil, EpiDermE, Créteil, France*; [2]*Hôpital Henri Mondor, Rhumatologie, Créteil, France*; [3]*Inserm, Université Paris Est-Créteil, Ecole Nationale Vétérinaire d'Alfort, U955-IMRB, Équipe 03, Créteil, France*; [4]*Inserm, Hôpital Henri Mondor, Centre D'investigation Clinique 1430, Créteil, France*; [5]*French National Agency for the Safety of Medicines and Health Products and French National Health Insurance, EPI-PHARE Scientific Interest Group in Epidemiology of Health Products, Saint-Denis, France*; [6]*Hôpital Henri Mondor, Pharmacie, Créteil, France*; [7]*Hôpital Henri Mondor, Dermatologie, Créteil, France*

Background: Psoriatic arthritis (PsA) is associated with other diseases of the spectrum of spondyloarthritis but also appears to be linked to an increased prevalence of numerous comorbidities and more specifically cardiovascular risk factors and events. Several biological disease-modifying anti-rheumatic drugs (bDMARDs) have demonstrated anti-inflammatory effects in PsA. However, their comparative cardiovascular safety profiles remain unknown.
Objectives: Our objective was to assess the relative comparative risk of major adverse cardiovascular events (MACEs) of different classes of bDMARDs or apremilast for PsA.
Methods: This nationwide cohort study involved the administrative healthcare database of the French health insurance scheme covering approximately 67 million individuals linked to the hospital discharge database. All adults with PsA who were new users of bDMARDs/apremilast (neither in the year before the index date) during 2015-2019 were included. Patients with previous cardiovascular diseases were excluded. End of follow-up was December 31, 2019. The primary end point was an occurrence of MACE (acute myocardial infarction and ischaemic stroke) in a time-to-event analysis with propensity score-weighted Cox and Fine-Gray models (including age, sex, inflammatory diseases associated, cardiovascular risk biomarkers and other comorbidities). To assess the sensitivity of the estimated weighted hazard ratio (HRw) with respect to several possible models, we performed a per-protocol analysis, a conventional multivariate Cox model, an analysis using a larger definition of MACE, an analysis modifying the new-user definition (as those who had not filled a prescription for a bDMARDs or apremilast for 5 years before the index date) and an analysis modifying the treatment discontinuation definition.
Results: Between 2015 and 2019, we included 9,510 bDMARD new users (mean age 48.5±12.7 years; 42% men), including 7,289 starting a TNF inhibitor, 1,058 an IL12/23 inhibitor and 1,163 an IL17 inhibitor, with 1,885 apremilast new users (mean age 54.0±12.5 years; 44% men). MACEs occurred in 51 (0.4%) patients (Figure 1). After propensity score weighting, the risk of MACEs was significantly greater with IL12/23 (HRw 2.0, 95%CI 1.3-3.0) and IL17 (HRw 1.9, 95%CI 1.2-3.0) inhibitors than TNF inhibitors, with no significant increased risk with apremilast (HRw 1.3, 95%CI 0.8-2.2). Similar results were observed with the Fine-Gray competing-risks survival model. The sensitivity analyses results were consistent with those of the main analysis.
Conclusion: Analysis of a large national database revealed an overall small number of MACEs. Using robust methodology from the causal inference field, the risk of MACEs was greater for PsA new users of IL12/23 and IL17 versus TNF inhibitors. The risk of MACEs did not significantly differ between new users of apremilast and new users of TNF inhibitors.

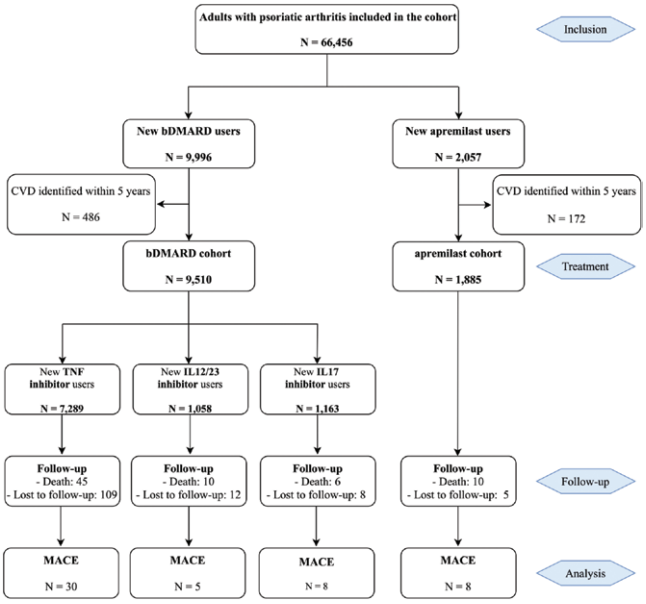


Figure 1. Flowchart for analytic approachData are n. bDMARD: biological disease-modifying antirheumatic drugs; CVD: cardiovascular disease; TNF: tumor necrosis factor; IL: interleukin; MACE: major adverse cardiac events.

Acknowledgements: L Pina Vegas received a Master 2 grant from the French Society of Rheumatology (Bourse Master 2ème Année 2019)
Disclosure of Interests: Laura Pina Vegas: None declared, Philippe Le Corvoisier: None declared, Laetitia Penso: None declared, Muriel Paul: None declared, Emilie Sbidian: None declared, Pascal Claudepierre Speakers bureau: AbbVie, Janssen, Lilly, MSD, Novartis, Pfizer, Consultant of: Abbvie, Pfizer, Roche-Chugai, Bristol-Myers Squibb, MSD, UCB, Novartis, Janssen, Lilly, Celgene (consulting fees, less than 10,000 $ each)., Employee of: Roche Chugai, Sanofi Aventis, Celgene, Pfizer, MSD, Novartis and BMS (investigator).
DOI: 10.1136/annrheumdis-2021-eular.287

Rheumatoid arthritis - biological DMARDs

POS0202

ANALYZING CORD BLOOD LEVELS OF TNF INHIBITORS TO VALIDATE THE EULAR POINTS-TO-CONSIDER FOR TNF INHIBITOR USE DURING PREGNANCY

E. Kemper[1,2], N. Ghalandari[1,2], H. J. M. J. Crijns[2], H. T. Smeele[1], R. Dolhain[1]. [1]*Erasmus MC, Department of Rheumatology, Rotterdam, Netherlands*; [2]*Medicines Evaluation Board, FT group 1, Utrecht, Netherlands*

Table 1. TNF inhibitor use during pregnancy and TNF inhibitor concentrations in mother's blood and cord blood.

	Certolizumab pegol (n = 68)	Etanercept (n = 28)	Adalimumab (n = 24)	Infliximab (n = 13)
Stop time point as recommended by EULAR	N/A	GA 30-32	GA 20	GA 20
Gestational age at time of stopping TNFi, median±IQR	37.29 (32.79 – 38.29)	25.43 (18.71 – 28.36)	18.79 (8.93 – 19.86)	18.86 (14.57 – 20.00)
Measurable TNFi in cord blood, n (%)	4 (5.9%)	0 (0%)	12 (50.0%)	8 (61.5%)
Maternal concentration of TNFi in the 1st trimester, median±IQR (µg/ml)	24.55 (19 – 31)	2.1 (0.8 – 2.5)	8.2 (1.5 – 10)	14 (7.98 – 21)
Maternal concentration of TNFi in the 2nd trimester, median±IQR (µg/ml)	22.52 (13 – 30.72)	1.4 (0.89 – 2.7)	6 (4.5 – 7.5)	6.37 (4.2 – 20)
Maternal concentration of TNFi in the 3rd trimester, median±IQR (µg/ml)	20.5 (13 – 29.58)	0.2 (0.2 – 0.67)	0.85 (0.1 – 1.4)	1.4 (0.09 – 1.9)
Concentration of TNFi in the cord blood if measurable, median±IQR (µg/ml)	0.25 (0.15 – 1.3)	-	0.45 (0.15 – 0.65)	0.4 (0.12 – 1.15)

Background: Increasing evidence suggests that TNF inhibitors (TNFi) are safe to use during pregnancy[1]. A drawback of TNFi use during pregnancy is active transport across the placenta, which is affected by the structure of the TNFi[1]. The European League Against Rheumatism (EULAR) defined points to consider (PtC) on the use of TNFi during pregnancy[2]: to prevent placental transfer, etanercept should be discontinued at gestational age (GA) 30-32 weeks, and both adalimumab and infliximab should be discontinued at GA 20 weeks. Certolizumab pegol can be conditionally continued throughout pregnancy.

Objectives: The aim of this research is to validate the EULAR PtC by measuring the level of TNFi in cord blood.

Methods: Patients were derived from the PreCARA study, an ongoing prospective cohort study on inflammatory rheumatic diseases and pregnancy in the Netherlands. Patients were treated according to a treat-to-target approach, which included the use of TNFi. TNFi were, if possible, discontinued at recommended stop time points. Maternal blood samples were collected in each trimester. Cord blood was analyzed for the presence of certolizumab pegol, etanercept, adalimumab and infliximab. Levels of TNFi in the cord blood were compared between patients that stopped at the advised GA and patients who did not.

Results: Data from 111 patients with inflammatory rheumatic diseases were used for the current analysis. Most patients stopped treatment before the recommended GA (table 1). Certolizumab pegol (n = 68) was measured in a low number of cord blood samples (5.9%) and in low concentrations (median, (IQR): 0.25 µg/ml (0.15 – 1.3)). Etanercept was not detected in any cord blood samples (n = 28). Adalimumab (n = 24) and infliximab (n = 13) were measured more often in cord blood (in 50.0% and 61.5% of patients, respectively), this also was observed in patients that stopped before the recommended GA (in 47.7% for adalimumab and 60.0% for infliximab). However, the observed concentrations were low: the maximum observed concentrations in cord blood were 2.1 µg/ml (stopped at GA 19.4 weeks) for adalimumab and 4.5 µg/ml (stopped at GA 21.1 weeks) for infliximab.

Conclusion: Stopping TNFi around the GA recommended by the EULAR PtC resulted in no measurable levels or low concentrations of TNF inhibitor in the cord blood in a majority of patients.

REFERENCES:

[1] Smeele HTW, Dolhain RJEM. Current perspectives on fertility, pregnancy and childbirth in patients with Rheumatoid Arthritis. *Semin Arthritis Rheum.* 2019;49(3S):S32-S35. doi:10.1016/j.semarthrit.2019.09.010

[2] Götestam Skorpen C, Hoeltzenbein M, Tincani A, et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. *Ann Rheum Dis*. 2016;75(5):795-810. doi:10.1136/annrheumdis-2015-208840

Disclosure of Interests: Erik Kemper: None declared, Nafise Ghalandari: None declared, Hubertina Johanna Maria Josephina Crijns: None declared, Hieronymus TW Smeele: None declared, Radboud Dolhain Speakers bureau: UCB, Roche, Abbvie, Genzyme, Novartis, Consultant of: Galapagos, Grant/research support from: UCB

DOI: 10.1136/annrheumdis-2021-eular.2452

POS0204 AUTOANTIBODIES AND SYSTEMIC LUPUS ERYTHEMATOSUS INDUCED BY ANTI-TUMOUR NECROSIS FACTOR ALPHA THERAPY IN RHEUMATOID ARTHRITIS

D. Santos Oliveira[1,2], A. Martins[1], F. R. Martins[3], F. Oliveira Pinheiro[1], M. Rato[1], D. Fonseca[4], B. M. Fernandes[1], S. Garcia[1], C. Vaz[1,2,5], M. Bernardes[1,5], L. Costa[1]. [1]*Centro Hospitalar Universitário de São João, Rheumatology Department, Porto, Portugal*; [2]*Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; [3]*Centro Hospitalar Universitário do Algarve, Rheumatology Department, Faro, Portugal*; [4]*Centro Hospitalar Vila Nova de Gaia / Espinho, Rheumatology Department, Vila Nova de Gaia, Portugal*; [5]*Faculty of Medicine, University of Porto, Department of Medicine, Porto, Portugal*

Background: Anti-tumour necrosis factor alpha (anti-TNF-α) therapy is commonly used to treat inflammatory conditions such as rheumatoid arthritis (RA). Autoantibodies namely antinuclear antibodies (ANA) induced by these treatments are well established. However, anti-TNF-α-induced systemic lupus erythematosus (SLE) is rarely described and its incidence is yet unknown.

Objectives: This study aimed to determine the prevalence of ANA seroconversion and to characterize the development of SLE induced by anti-TNF-α therapy in patients with RA over time.

Methods: An observational retrospective cohort study was conducted with at least one year of follow-up. Patients with diagnosis of RA, according to American College of Rheumatology criteria (ACR), and registered on Rheumatic Diseases Portuguese Register (Reuma.pt) who started their first anti-TNFα between 2003 and 2019 were included. Patients with positive ANA (titer ≥100) and/or positive double-strand DNA (dsDNA) antibodies and/or with a diagnosis of SLE at their first visit were excluded. Demographic, clinical and laboratory data were obtained by consulting Reuma.pt. As there are no recognized criteria for drug-induced SLE, the diagnosis of SLE induced by anti-TNF-α was considered if there is a temporal relationship between clinical manifestations and anti-TNF-α-therapy, the presence of at least 1 serologic ACR criteria (ANA or anti-dsDNA) and at least 1 nonserologic ACR criteria (arthritis, serositis, hematologic disorder or malar rash) [1]. Continuous variables are presented with mean, standard deviation, median, quartile 1 and quartile 3. Categorical variables are presented with absolute and relative frequencies.

Results: A total of 211 patients (mean age of 49.9±10.9 years old; 84.4% female) were included with a median follow-up time of 6 [3-14] years. We found a seroconversion rate for ANA of 75.4% (n=159) with median treatment duration of 31 [8.5-70.5] months. The most common titre was 1/100 with diffuse and speckled patterns. ANA seroconversion was higher for etanercept (47.8%, n=76) than with adalimumab (23.9%, n=38), infliximab (13.8%, n=22), golimumab (12.6%, n=20) or certolizumab (1.9%, n=3). SLE induced by anti-TNF-α occurred in two patients (0.9%) with erosive and seropositive (rheumatoid factor and anti-citrullinated protein antibodies) RA previously treated with two conventional synthetic disease-modifying antirheumatic drugs, including methotrexate. The first patient, a female with 66 years old and 17 years of disease duration, developed SLE after 16 months of infliximab, with constitutional symptoms, abrupt worsening of polyarthritis, ANA titer of 1/320 diffuse pattern and positive dsDNA (248 UI/mL) antibodies. The second patient, a woman with 43 years old and 11 years of disease duration, developed SLE after 41 months of adalimumab with malar rash and ANA titer of 1/320 diffuse pattern, positive dsDNA (285 UI/mL), positive anti-histone antibodies and hypocomplementemia. In these two cases, anti-TNF-α therapy was stopped and recovery was spontaneous without treatment. The first patient switched to adalimumab and the second switched to golimumab without recurrence of SLE for more than ten years.

Conclusion: We found a high rate of ANA seroconversion induced by anti-TNFα therapy in patients with RA. However, similar to previous literature, only 0.9% of patients developed SLE with mild manifestations without major organ involvement. Although the drug with the highest ANA seroconversion rate was etanercept, those responsible for induced SLE were infliximab and adalimumab. Patients improved after discontinuation of therapy and tolerated an alternative anti-TNF-α drug without recurrence of induced SLE over time. Therefore, ANA and SLE induced by anti-TNF-α should be considered and reported in the follow-up of RA patients. Further research is needed to explore the impact of this adverse event on the outcomes of treatment over time.

REFERENCES:

[1] Hochberg MC. Arthritis Rheum. 1997;40(9):1725.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3255

POS0205 AMELIORATION OF ENDOTHELIAL DYSFUNCTION WITH JAK INHIBITION IN RHEUMATOID ARTHRITIS: JAK CV-RISK REDUCTION STUDY

A. Syngle[1], N. Garg[2], K. Chauhan[3]. [1]*Healing Touch City Clinic, Chandigarh & Fortis Multispecialty Hospital, Mohali, Cardio-Rheuma Division; Internal Medicine & Rheumatology, Chandigarh, India*; [2]*Chitkara College of Pharmacy,*

Chitkara University, Department of Pharmacy Practice, Patiala, India; [3]*Healing Touch City Clinic, Department of Rheumatology, Chandigarh, India*

Background: Cardiovascular (CV) disease is the leading cause of premature mortality and sudden death in Rheumatoid Arthritis (RA). Conventional CV risk factors and disease specific risk factors are responsible for endothelial dysfunction (ED) in RA. ED is the barometer of CV health and key initial event in atherosclerosis. Tofacitinib, a JAK inhibitor, is in clinical use since 2012 and has had the most extensive development program in RA, but its impact on ED has not yet been explored in humans.

Objectives: To investigate the impact of tofacitinib on endothelial dysfunction in RA

Methods: 40 RA patients fulfilling the 2010 Rheumatoid Arthritis classification criteria with active disease (DAS28>3.2) were randomized to receive 24 weeks of treatment with Tofacitinib (5mg bd, n=20) and placebo (n=20) as an adjunct to existing stable antirheumatic drugs. Primary endpoints included endothelial dysfunction assessed by FMD using Angiodefender and lipids were estimated at baseline and after 12 weeks of treatment. The secondary end points included: DAS28, ESR, CRP, HAQ-DI and cardiovascular risk using SCORE chart assessed at week 0 and 12.

Results: At baseline, endothelial function was impaired and levels of inflammatory measures were elevated in both groups. CV risk SCORE was high and HAQ-DI was impaired at baseline. After treatment, FMD improved significantly in the tofacitinib group from (8.16±1.38% to 10.98±2.33%, p≤0.05) as compared to placebo (7.12±0.25% to 8.04±0.30%, p=0.35) (Fig. 1A). DAS28 (Fig. 1B), ESR and CRP (Fig. 1C) levels improved significantly in tofacitinib group as compared to placebo (p≤0.05). Tofacitinib significantly decreased HAQ-DI and SCORE (Fig. 1D) values as compared to placebo. There was significant increase in HDL (p≤0.05) after treatment with tofacitinib as compared to placebo. After 12 weeks of treatment, FMD and HDL increased by 34.55% and 13.58% respectively where as DAS28, ESR and CRP decreased by 37.40%, 36.10% and 76.59% respectively in the tofacitinib group. Significant negative correlation was observed between FMD and DAS28 (r= -0.50, p≤0.05) and CRP (r= -52, p≤0.05) after treatment with tofacitinib where as no such correlation was found in placebo group.

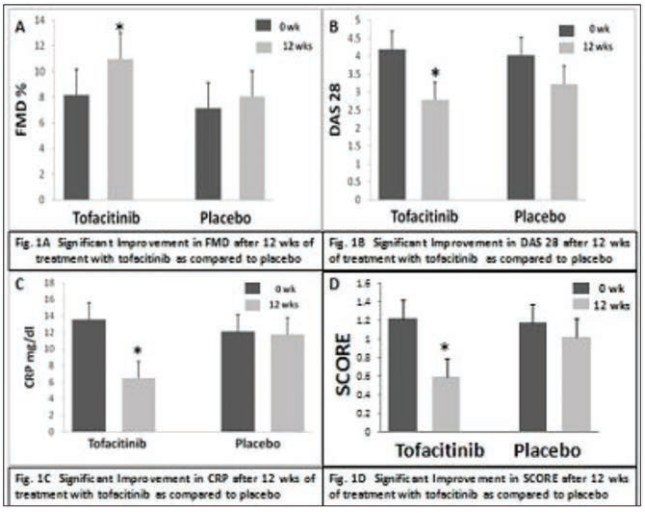


Figure 1. Impact of Tofacitinib on FMD, DAS 28, CRP & SCORE

Conclusion: First study to show that tofacitinib, apart from its anti inflammatory activity, improves endothelial dysfunction and cardiovascular risk in RA. Thus, JAK inhibition with tofacitinib has vasculoprotective and cardioprotective effect mediated through anti-inflammatory and probably other mechanisms. This study would stimulate further research in exploring the vasculoprotective and cardioprotective potential of tofacitinib in RA.

REFERENCES:

[1] Tofacitinib reversed endothelial dysfunction in rheumatoid arthritis: mechanistic insights from the rat adjuvant-induced arthritis model. http://dx.doi.org/10.1136/annrheumdis-2020-eular.2747

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3753

POS0206

DESIGN AND CHARACTERISATION OF A THERAPEUTIC BISPECIFIC TANDEM SCFV-FC FUSION PROTEIN WITH ANTI-TNF AND SYNOVIUM-TARGETING SPECIFICITY FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

S. Pagani[1], F. Colombo[1], C. Pitzalis[1]. [1]*William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, Centre for Experimental Medicine & Rheumatology, London, United Kingdom*

Background: Rheumatoid Arthritis (RA) is a systemic autoimmune disease with a prevalence of 0.5-1% worldwide[1]. Anti-cytokine antibodies, especially anti-Tumor Necrosis Factor (TNF) antibodies are considered the gold standard for RA therapy. However, there are some concerns regarding their lack of therapeutic efficacy in a significant proportion of patients[2] and their potential systemic implications such as the risk of serious infections[3]. Developing novel agents with synovial targeting specificity might help to increase the therapeutic index while reducing systemic side effects of RA therapeutics.

Objectives: Our work aims to develop a novel bispecific tandem single-chain variable fragment (scFv)-Fc fusion protein combining synovium specificity with anti-TNFα activity. The potential advantage of this construct is a reduced systemic TNF-binding activity and increase delivery and activation of the TNF-neutralising capacity at the inflamed joints.

Methods: The therapeutic tandem scFv-Fc fusion protein comprises two external arms with synovium specific targeting ability linked through a metalloproteinase (MMP) cleavable linker to the anti-TNFα variable fragments of Adalimumab fused to the CH2 and CH3 domains of IgG1 (Figure 1). The external scFv regions with synovium specificity were previously identified by *in vivo* phage display using a SCID mouse model transplanted with human synovium[4]. The construct was tested for its ability to bind and neutralize *in vitro* and *ex vivo* targets.

Results: The fusion protein was tested by immunohistochemistry staining on RA synovium biopsies and an array of non-inflamed human tissues showing specific targeting of synovial microvasculature without no reactivity to the non-inflamed tissues. The TNFα binding and blocking capacity of the fusion protein was measured respectively by ELISA and cell assays measuring NF-κB activation, and it showed a two-fold decreased activity compared to the control antibody Adalimumab prior to detachment of the cleavable targeting fragment shielding the active anti-TNF fragment. Human synovial fluid and recombinant human MMP-1 efficiently cleaved the external arms of the antibody, releasing the anti-TNF scFv-Fc. The cleaved construct, detached from the synovium targeting arms, showed the same binding and anti-TNF inhibitory capacity/potency as Adalimumab.

Conclusion: The novel bispecific tandem scFv-Fc demonstrated specific synovium targeting ability and intended reduced anti-TNF activity in its intact form prior to reaching the joint. Following MMPs-induced cleavage present in RA synovial fluid the therapeutic activity was restored to the same level as Adalimumab. Overall, this construct has the potential of decreasing the anti-TNF off-site activity and consequently, reduce systemic toxicity while maintaining high on-site activity. Also, the presence of a synovium targeting domain has the advantage of increasing the delivery and retention within the inflamed synovium and possibly increase the therapeutic index of this anti-TNF therapeutics.

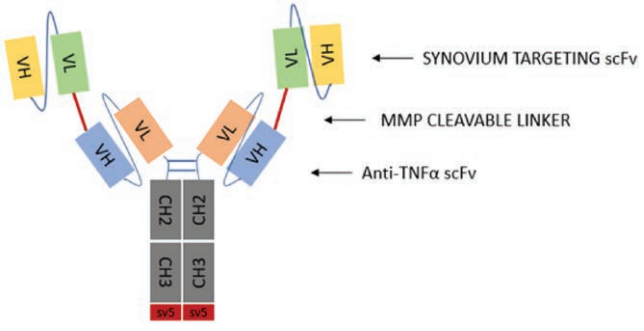


Figure 1. Schematic diagram of the bispecific tandem scFv-Fc fusion protein.

REFERENCES:
[1] Silman, A. J. & Pearson, J. E. Epidemiology and genetics of rheumatoid arthritis. 265–272 (2002).
[2] Balogh, E. *et al.* Comparison of remission criteria in a tumour necrosis factor inhibitor treated rheumatoid arthritis longitudinal cohort: patient global health is a confounder. *Arthritis Res.Ther.* **15**, R221 (2013).
[3] Galloway, J. B. *et al.* Anti-TNF therapy is associated with an increased risk of serious infections in patients with rheumatoid arthritis especially in the first 6 months of treatment: updated results from the British Society for Rheumatology Biologics Register with special emp. *Rheumatology (Oxford).* **50**, 124–131 (2011).
[4] Kamperidis, P. *et al.* Development of a novel recombinant biotherapeutic with applications in targeted therapy of human arthritis. *Arthritis Rheum.* **63**, 3758–3767 (2011).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3917

POS0207 REAL-WORLD RETENTION OF JAK INHIBITORS IS LONGER THAN BDMARDS IN RHEUMATOID ARTHRITIS

K. Machlab[1], S. M. Iskandar[1], T. Nevskaya[1], L. Vanderhoek[1], J. Bylsma[1], S. Hewitt[1], J. Pope[1]. [1]*University of Western Ontario, Schulich School of Medicine & Dentistry, London, Canada*

Background: Biological disease modifying anti-rheumatic drugs (bDMARDs) and Janus Kinase inhibitors (JAKi) are both recommended post conventional synthetic disease modifying anti-rheumatic drug (csDMARD) therapy failure in active rheumatoid arthritis (RA), but the data on long-term durability are limited.
Objectives: The objective of this study is to analyze a database of patients at the Western University, Rheumatology Center who initiated a bDMARD or JAKi and compare the proportion and characteristics of patients associated with retention of a drug class.
Methods: This was a single-center study of 215 adult RA patients (82.76 % females, age 59.8 ± 12.0 years, disease duration 15.5 ± 10.0 years; table 1) failing multiple csDMARDs prior to initiating either bDMARDs (TNF inhibitors, abatacept, rituximab, tocilizumab) or JAKi, between June 2014 (when tofacitinib was approved in Canada) and April 2020. All patients enrolled had failed traditional DMARDs, including methotrexate, hydroxychloroquine, sulfasalazine and/or leflunomide. Durability and predictors of discontinuation were analyzed by Kaplan-Meier and Cox regression analyses for all treatment trials, and for patients receiving bDMARDs/JAKi as a first line after csDMARDs failure.
Results: In 215 patients, there were 320 treatment events (148 bDMARDs, 172 JAKi) and 142 discontinuations (53.5% bDMARDs, 46.5% JAKi). Figure 1 represents the Kaplan-Meier survival curve for time to therapy discontinuation in 215 patients receiving bDMARDs vs JAKi. The Cox proportional hazards model was significant with better retention for JAKi, with a hazard ratio (HR) for treatment discontinuation of JAKi compared with bDMARDs of 0.676 (95% CI 0.47-0.97, p=0.034), adjusted for gender, age, disease duration, and line of therapy (Table 1). Moreover, the analysis revealed better retention for both groups as first line advanced therapy compared to later lines of therapy; 57.6% of JAKi and 31.1% of bDMARDs were used as first line advanced therapy. HR for treatment discontinuation for first line vs later lines of therapy was 0.593 (95% CI 0.40-0.88, p=0.01), adjusted for drug class, gender, age, and disease duration (Table 1). The most common reasons for discontinuations were inefficacy (60%), side effects (22%), or other reasons (18%). Inefficacy (58% vs 62%, p=0.8) and side-effects (16% vs 27%, p=0.4) were equally common for bDMARDs and JAKi. Sex, age at treatment onset, and RA duration did not predict discontinuation by Cox regression analyses, and after sub-grouping into bDMARDs and JAKi.
Conclusion: EULAR guidelines have placed bDMARDs equal to JAKi as post csDMARD failure therapy in active RA. However, this study demonstrates that JAKi has a greater durability than biologics regardless of gender, age, disease duration, and line of therapy. Therefore, JAKi may be considered as a preferable method of treatment post csDMARD failure in active RA.

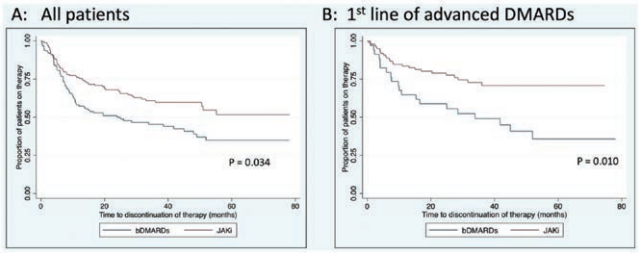


Figure 1. Kaplan-Meier survival curves for (A) time to discontinuation of therapy in all RA patients receiving bDMARDs versus JAKi; P-value represents Cox regression adjusted for gender, age, disease duration, and line of therapy (B) time to discontinuation of therapy in patients using bDMARDs/JAKi as first line of advanced therapy; P-value represents Cox regression adjusted for drug class, gender, age, and disease duration

Table 1. Patient demographics and hazard ratios for discontinuation of bDMARDs versus JAKi by Cox regression model

Characteristic	JAKi (N=172)	bDMARD (N=148)	Mean
Age (years)	60.9	58.5	59.8
Sex (% F)	77.8	88.5	82.8
Disease duration (years)	15.3	15.8	15.5
Line of advanced therapy (% first line)	57.6	31.1	45.3
Drug used (%)	Tofacitinib: 93.5	Rituximab: 26.4 Etanercept: 19.6 Adalimumab: 17.6	
Predictors of Drug Discontinuation		**HR (95% CIs)**	**P values**
Crude Model	JAKi vs bDMARDs	0.60 (0.43, 0.84)	0.003
Adjusted model	JAKi vs bDMARDs	0.68 (0.47, 0.97)	0.034
	Male vs female	0.77 (0.46, 1.31)	0.342
	Age	1.01 (0.99, 1.03)	0.123
	RA duration	0.99 (0.97, 1.01)	0.500
	Treatment line 1 vs >1	0.59 (0.40, 0.88)	0.010

Disclosure of Interests: Karla Machlab: None declared, Samir M. Iskandar: None declared, Tatiana Nevskaya: None declared, Louise Vanderhoek: None declared, Jillian Bylsma: None declared, Sara Hewitt: None declared, Janet Pope Speakers bureau: AbbVie, Amgen, BMS, BI, Gilead, Galapagos, Janssen, Lilly, Medexus, Merck, Novartis, Pfizer, Sanofi, Sandoz, Consultant of: AbbVie, Amgen, BMS, BI, Celltrion, Gilead, Galapagos, Janssen, Lilly, Medexus, Merck, Novartis, Pfizer, Roche, Samsung, Sanofi, Sandoz, Teva, UCB, Grant/research support from: AbbVie, BMS, Merck, Pfizer, Roche, Seattle Genetics

DOI: 10.1136/annrheumdis-2021-eular.705

POS0208 GENDER DIFFERENCES IN RESPONSE TO BIOLOGICALS. WOMEN FARE WORSE ACROSS INFLAMMATORY ARTHRITIS DISEASES - DATA FROM THE BIOREG

E. Loibner[1], V. Ritschl[2], B. Leeb[3,4], P. Spellitz[5,6], G. Eichbauer-Sturm[5], J. Zwerina[5,7,8], M. Herold[5,9], M. Stetter[5], R. Puchner[5], F. Singer[5], R. Fritsch-Stork[1,7,8]. [1]*Sigmund Freud Private University, Medical Faculty, Vienna, Austria*; [2]*Medical University of Vienna, Center for Medical Statistics, Informatics and Intelligent Systems; Section for Outcomes Research, Vienna, Austria*; [3]*BioReg, BioReg, Vienna, Austria*; [4]*Karl Landsteiner Private University of Health Science, Rheumatology, Krems, Austria*; [5]*BioReg, BioReg, Vienna, Austria*; [6]*Rheumazentrum Wien Oberlaa, rheumatology, Vienna, Austria*; [7]*Ludwig Boltzmann Institute of Osteology, Hanusch Hospital of Oesterreichische Gesundheitskassa and Allgemeine Unfallversicherungsanstalt, Vienna, Austria*; [8]*Hanusch Hospital, 1st Internal Medicine, wien, Austria*; [9]*Medical University- Innsbruck, Autoimmune Laboratory, Innsbruck, Austria*

Background: Gender differences in prevalence and disease course are known in various rheumatic diseases; however, investigations of gender difference concerning therapeutical response have yielded variable results.

Objectives: The aim of this retrospective study was to investigate, whether a gender difference in response rate to biological disease-modifying antirheumatic drugs (bDMARDs) and apremilast in bDMARD-naïve patients could be observed across the three most prevalent inflammatory arthritis diseases: rheumatoid arthritis (RA), spondylarthritis (SpA) and psoriatic arthritis (PsA). Additionally, a response to individual TNF blockers was investigated in this respect.

Methods: Data from bDMARD-naïve RA-, SpA- and PsA-patients from Bioreg, the Austrian registry for biological DMARDs in rheumatic diseases, were used. Patients with a baseline (Visit 1=V1) and follow-up visits at 6 months (Visit 2=V2) and 12 months (Visit 3=V3) were included and response to therapy with TNF-inhibitors (TNFi), furthermore to therapy with rituximab, tocilizumab and apremilast was analyzed according to gender. The remaining bDMARDs were not analyzed due to small numbers. Key response-parameter for RA was disease activity score (DAS28), whereas for PsoA the Stockerau Activity Score for Psoriatic Arthritis (SASPA) and for SpA the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) were employed; in addition, the Health assessment Questionnaire

(HAQ) was used. Data were analyzed in R Statistic stratified by gender using Kruskal-Wallis and Wilcoxon tests.

Results: 354 women and 123 men with RA (n=477), 81 women and 69 men with PsA (n=150), 121 women and 191 men with SpA (n=312) were included. No significant differences in biometrics was seen between female and male patients at baseline in all diseases.

In RA patients overall DAS28 decreased from baseline (V1) to V2 and V3 (DAS28: V1: male: 4.38 [3.66, 5.11], female: 4.30 [3.68, 5.03], p(m/f) = 0.905; V2: male: 2.66 [1.73, 3.63], female: 3.10 [2.17, 3.98], p(m/f) = 0.015; V3: male: 2.25 [1.39, 3.36], female: 3.01 [1.87, 3.87], p(m/f) = 0.002). For TNF inhibitors (n=311), there was a significant difference between genders at V2 (Fig.1a). Patients receiving Rituximab (n=41) displayed a significantly higher DAS28 at baseline in females, which diminished in the follow up: V1: (p(m/f) p=0.002; V2: p=0.019; V3: p=0.13); response to tocilizumab (n=63) did not show any gender differences.
In PsA patients overall SASPA decreased from baseline (V1) to V2 and V3 (SASPA: V1: male: 4.00 [2.80, 5.20], female: 4.40 [2.80, 5.80], p(m/f) = 0.399; V2: male: 2.20 [1.20, 3.50], female: 3.40 [2.00, 5.00], p(m/f) = 0.071; V3: male: 1.80 [0.80, 2.70], female: 3.01 [2.35, 4.80], p(m/f) = 0.001). For TNF inhibitors (n=79), there was a significant difference between genders at V3 (Fig 1a). For Apremilast (n=39), there was a significant difference between genders at V2 (Fig.1c).
In SpA patients overall BASDAI decreased from baseline (V1) to V2 and V3 (BASDAI: V1: male: 4.70 [2.88, 6.18], female: 4.80 [3.30, 6.20], p(m/f) = 0.463; V2: male: 3.05 [2.00, 4.60], female: 3.64 [2.62, 5.41], p(m/f) = 0.039; V3: male: 3.02 [1.67, 4.20], female: 3.65 [2.18, 5.47], p(m/f) = 0.016). In V3 a differential BASDAI in response to TNFi (n=299) was observed (Fig.1a).
Possible differences of response to individual TNFi (etanercept, infliximab, other TNFi) measured by HAQ were investigated in all diseases together. The difference between male and females was significant at baseline for all 3 TNFi; whereas with the use of ETA the significant difference was carried through to V2 and V3, it was lost with the use of IFX and was variable with the other TNFi (Fig.1b)

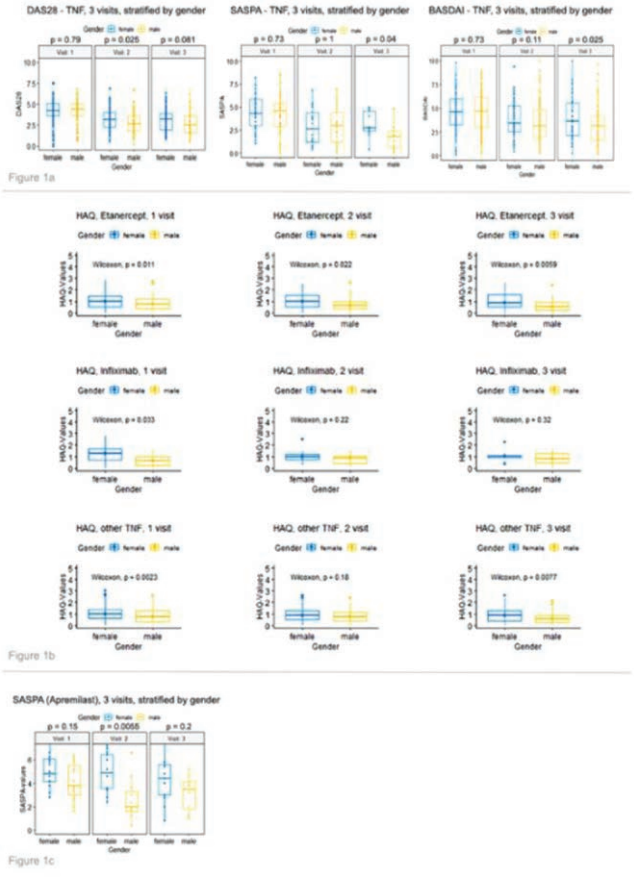


Figure 1.

Conclusion: Female patients showed a statistically lower response to TNFi in all three disease entities (RA, SpA and PsoA) to a variable degree in our homogenous central european population. Interestingly, the difference was not uniform across individual TNFi when measured by HAQ. Gender differences were also seen in response to Apremilast.

Disclosure of Interests: Elisabeth Loibner: None declared, Valentin Ritschl: None declared, Burkhard Leeb Speakers bureau: AbbVie, Roche, MSD, Pfizer, Actiopharm, Boehringer-Ingelheim, Kwizda, Celgene, Sandoz, Grünenthal, Eli-Lilly, Grant/research support from: TRB, Roche, Consultancies: AbbVie, Amgen, Roche, MSD, Pfizer, Celgene, Grünenthal, Kwizda, Eli-Lilly, Novartis, Sandoz;, Peter Spellitz: None declared, Gabriela Eichbauer-Sturm: None declared, Jochen Zwerina: None declared, Manfred Herold: None declared, Miriam Stetter: None declared, Rudolf Puchner Speakers bureau: AbbVie, BMS, Janssen, Kwizda, MSD, Pfizer, Celgene, Grünenthal, Eli-Lilly, Consultant of: AbbVie, Amgen, Pfizer, Celgene, Grünenthal, Eli-Lilly, Franz Singer: None declared, Ruth Fritsch-Stork: None declared

DOI: 10.1136/annrheumdis-2021-eular.3596

POS0209

ASSOCIATION OF FIRST, SECOND, AND THIRD-LINE BDMARDS AND TSDMARD WITH DRUG SURVIVAL AMONG RHEUMATOID ARTHRITIS PATIENTS: A COHORT STUDY

B. Ghang[1], S. Choi[2], E. Y. Lee[3]. *[1]1Division of Rheumatology, Department of Internal Medicine, Jeju National University School of Medicine, Jeju National University Hospital, Rheumatology, Seoul, Korea, Rep. of (South Korea)*; *[2]Seoul National University Graduate School, Biomedical Science, Seoul, Korea, Rep. of (South Korea)*; *[3]Seoul National University College of Medicine, Rheumatology, Seoul, Korea, Rep. of (South Korea)*

Background: Since tofacitnib is a tsDMARD with a different mechanism of action compared to bDMARDs, along with the fact that recent releases of bDMARDs or tsDMARDs have led to numerous possible switching patterns, there is a need for comparative studies of bDMARDs and tofacitinib with subsequent drug survival among RA patients.

Objectives: To determine the association of first, second, and third-line biologic disease- modifying antirheumatic drugs (bDMARDs) and tofacitinib with drug survival among rheumatoid arthritis (RA) patients.

Methods: The study population was composed of 8,018 seropositive RA patients who were prescribed bDMARDs or tofacitinib between January 2014 and January 2019 from the Korean Health Insurance Review and Assessment Service database. First, second, and third-line choice of tumor necrosis factor inhibitors (TNFi) including etanercept, infliximab, adalimumab, and golimumab, as well as non-TNFi including tocilizumab, rituximab, tofacitinib, and abatacept were assessed. Multivariate Cox proportional hazards regression was used to determine the adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for drug failure according to bDMARD or tofacitinib choice starting from the initial prescription date.

Results: Compared to first etanercept users, patients with first tocilizumab (aHR 0.56, 95% CI 0.46-0.68), tofacitinib (aHR 0.27, 95% CI 0.18-0.42), or abatacept (aHR 0.83, 95% CI 0.69- 0.99) had lower risk of drug failure. Second choice of tocilizumab (aHR 0.38, 95% CI 0.25- 0.55), tofacitinib (aHR 0.23, 95% CI 0.15-0.37), or abatacept (aHR 0.54, 95% CI 0.35-0.84) was associated with lower drug failure risk compared to second etanercept users. Finally, third choice of tocilizumab (aHR 0.32, 95% CI 0.16-0.62) or tofacitinib (aHR 0.35, 95% CI 0.19- 0.63) was associated with lower drug failure risk compared to third TNFi users.

Conclusion: First and second-line tocilizumab, tofacitinib, or abatacept may lead to improved drug survival. Third choices of tocilizumab or tofacitinib may be beneficiary in reducing drug failure risk among RA patients.

REFERENCES:

[1] .Neovius M, Arkema EV, Olsson H, et al. Drug survival on TNF inhibitors in patients with rheumatoid arthritis comparison of adalimumab, etanercept and infliximab. Ann Rheum Dis 2015;74(2):354-60.

Table 1. Risk of drug failure on rheumatoid arthritis patients according to first, second, and third choice of bDMARD or tofacitinib.

	Events	Person-years	Incidence	aHR	95% CI
First-line choice (n=8,018)					
Etanercept	290	2,396	121	1.00	reference
Infliximab	236	1,417	167	1.36	1.14-1.62
Adalimumab	449	2,718	165	1.28	1.10-1.48
Golimumab	258	1,955	132	1.06	0.90-1.26
Tocilizumab	171	2,623	65	0.56	0.46-0.68
Rituximab	1	29	34	0.29	0.04-2.08
Tofacatinib	24	502	48	0.27	0.18-0.42
Abatacept	216	2,207	98	0.83	0.69-0.99
Second-line choice (n=1,645)					
Etanercept	41	151	272	1.00	reference
Infliximab	16	51	314	1.04	0.58-1.88
Adalimumab	85	275	309	1.07	0.72-1.60
Golimumab	41	204	201	0.79	0.51-1.23
Tocilizumab	85	918	93	0.38	0.25-0.55
Rituximab	4	31	129	0.52	0.18-1.46
Tofacatinib	35	484	72	0.23	0.15-0.37
Abatacept	46	299	154	0.54	0.35-0.84
Third-line choice (n=353)					
Etanercept	3	19	158	1.00	reference
Infliximab	5	10	500	1.27	0.27-5.91
Adalimumab	5	17	294	0.99	0.22-4.38
Golimumab	13	22	591	2.23	0.60-8.25
Tocilizumab	17	127	134	0.47	0.13-1.68
Rituximab	3	22	136	0.60	0.12-3.09
Tofacatinib	23	162	142	0.50	0.14-1.77
Abatacept	17	59	288	1.11	0.31-3.96

Adjusted hazard ratios calculated by multivariate Cox proportional hazards regression after adjustments for age, sex, hospital type, number of csDMARDs, first bDMARDs or tofacitinib for second and third-line choice analysis, Charlson comorbidity index, and enrollment year.Incidence calculated as the number of events per 1,000 person-years.Acronyms: aHR, adjusted hazard ratio; CI, confidence interval.

Disclosure of Interests: Byeongzu Ghang: None declared, Seulggie Choi: None declared, Eun Young Lee Grant/research support from: This work was supported by grants from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute, funded by the Ministry of Health and Welfare, Republic of Korea [HI14C1277] and Britol-Myers Squibb [IM101-735].
DOI: 10.1136/annrheumdis-2021-eular.546

Rheumatoid Arthritis - comorbidity and clinical aspects - Part 1

POS0210 **THE INCIDENCE AND RISK FACTORS OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE**

B. Samhouri[1], R. Vassallo[1], S. Achenbach[2], V. Kronzer[3], J. M. Davis III[3], E. Myasoedova[3], C. S. Crowson[2]. [1]*Mayo Clinic, Division of Pulmonary and Critical Care Medicine, Rochester, MN, United States of America*; [2]*Mayo Clinic, Department of Quantitative Health Sciences, Rochester, MN, United States of America*; [3]*Mayo Clinic, Division of Rheumatology, Rochester, MN, United States of America*

Background: Rheumatoid arthritis (RA) is a systemic inflammatory disease of the joints and other organs, including the lungs.[1] Interstitial lung disease (ILD) is a lung injury pattern associated with significant symptom burden and poor outcomes in RA.[2] Better understanding of its risk factors could help with disease prevention and treatment.

Objectives: Using a population-based cohort, we sought to ascertain the incidence and risk factors of RA-associated ILD (RA-ILD) in recent years.

Methods: The study included adult residents of Olmsted County, Minnesota with incident RA between 1999 and 2014 based on the 1987 ACR classification criteria.[3] Study subjects were followed until death, migration, or 4/30/2019. ILD was defined by the presence of bilateral interstitial fibrotic changes (excluding biapical scarring) on chest computed tomography (CT). In the absence of chest CT imaging, a physician's diagnosis of ILD in conjunction with chest X-ray findings suggestive of ILD and a restrictive pattern on pulmonary function testing (defined as a total lung capacity less than the lower limit of normal) was considered diagnostic of ILD. Evaluated risk factors included age, sex, calendar year, smoking status, body mass index (BMI) and presence/absence of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA). Cumulative incidence of ILD was adjusted for the competing risk of death. Cox models were used to assess the association between potential risk factors and the development of RA-ILD.

Results: In Olmsted County, 645 residents were diagnosed with RA between 1999 and 2014. Seventy percent of patients were females, and 30% were males; median age at RA diagnosis was 55.3 [IQR 44.1-66.6] years, and most patients (89%) were white. Fifty-three percent of patients were never-smokers, and 64% had seropositive RA. Forty percent were obese (i.e., BMI ≥30 kg/m^2); median BMI was 28.3 [IQR 24.3-33.0] kg/m^2.

In the cohort, ILD was identified in 73 patients. The ILD diagnosis predated RA diagnosis in 22 patients (3.4%) who were excluded from subsequent analyses. Final analyses included the remaining 623 patients with no ILD preceding, or at the time of RA diagnosis. Over a median follow-up interval of 10.2 [IQR 6.5-14.3] years, 51 patients developed ILD. Cumulative incidence of ILD, adjusted for the competing risk of death, was 4.3% at 5 years; 7.8% at 10 years; 9.4% at 15 years; and 12.3% at 20 years after RA diagnosis (Figure 1).

Age, and history of smoking at RA diagnosis correlated with the incidence of ILD; adjusted hazard ratios (HRs) were 1.89 per 10-year increase in age (95% confidence interval 1.52-2.34) and 1.94 (95% confidence interval 1.10-3.42), respectively. On the other hand, sex (HR: 1.21; 95% CI: 0.68-2.17), BMI (HR: 0.99; 95% CI: 0.95-1.04), obesity (HR: 0.89; 95% CI: 0.50-1.58), and seropositivity (HR: 1.15; 95% CI: 0.65-2.03) did not demonstrate significant associations with ILD.

Conclusion: This study provides a contemporary estimate of the occurrence of ILD in a well-characterized population-based cohort of patients with RA. Our findings of a lack of association between sex, obesity and seropositivity with ILD may indicate a change in established risk factors for ILD and warrant further investigation.

REFERENCES:

[1] Shaw M, Collins BF, Ho LA, Raghu G. Rheumatoid arthritis-associated lung disease. *Eur Respir Rev*. 2015;24(135):1-16. doi:10.1183/09059180.00008014

[2] Bongartz T, Nannini C, Medina-Velasquez YF, et al. Incidence and mortality of interstitial lung disease in rheumatoid arthritis - A population-based study. *Arthritis Rheum*. 2010;62(6):1583-1591. doi:10.1002/art.27405

[3] Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*. 2010;62(9):2569-2581. doi:10.1002/art.27584

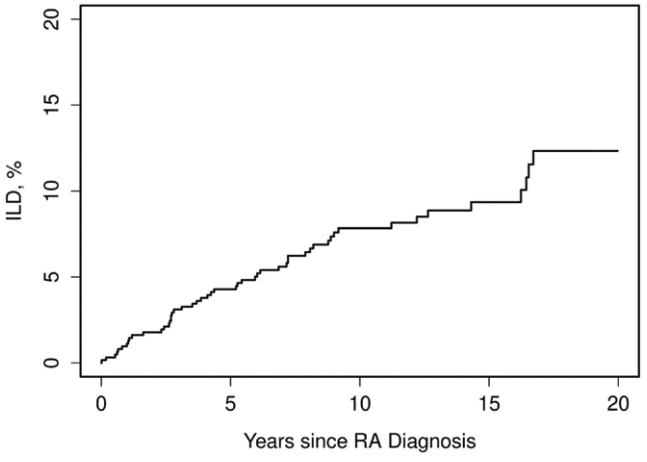


Figure 1. Cumulative incidence of ILD in patients diagnosed with RA between 1999 and 2014, adjusted for the competing risk of death. **Abbreviations.** ILD: interstitial lung disease; RA: rheumatoid arthritis.

Disclosure of Interests: Bilal Samhouri: None declared, Robert Vassallo Grant/research support from: Research grants from Pfizer, Sun Pharmaceuticals and Bristol Myers Squibb, Sara Achenbach: None declared, Vanessa Kronzer: None declared, John M Davis III Grant/research support from: Research grant from Pfizer., Elena Myasoedova: None declared, Cynthia S. Crowson: None declared
DOI: 10.1136/annrheumdis-2021-eular.2183

POS0211 PREDICTORS OF PROGRESSION AND MORTALITY IN PATIENTS WITH PREVALENT RHEUMATOID ARTHRITIS AND INTERSTITIAL LUNG DISEASE: A PROSPECTIVE COHORT STUDY

N. Mena-Vázquez[1], M. Rojas-Giménez[2], C. M. Romero-Barco[3], S. Manrique Arija[1], F. Espildora[4], M. C. Aguilar-Hurtado[5], R. Ortega Castro[6], I. Añón Oñate[7], L. Pérez Albaladejo[8], F. Godoy-Navarrete[1], I. Ureña[1], M. Velloso Feijoo[9], R. Redondo[1], F. G. Jiménez-Núñez[1], B. Panero Lamothe[10], M. I. Padin-Martín[5], A. Fernandez-Nebro[1]. [1]*Instituto de Investigación Biomédica de Málaga (IBIMA), Hospital Regional Universitario de Málaga (HRUM), Reumatología, Málaga, Spain*; [2]*Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC, UGC de Reumatología, Hospital Universitario Reina Sofía de Córdoba, Reumatología, 14004, Spain*; [3]*Instituto de Investigación Biomédica de Málaga (IBIMA), Hospital Clínico Universitario Virgen de la Victoria, Reumatología, Málaga, Spain*; [4]*Hospital Regional Universitario de Málaga (HRUM), Neumología, Málaga, Spain*; [5]*Hospital Regional Universitario de Málaga (HRUM), Radiología, Málaga, Spain*; [6]*Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC). UGC de Reumatología, Hospital Universitario Reina Sofía de Córdoba., Reumatología, Córdoba, Spain*; [7]*Hospital Universitario de Jaén, Reumatología, Jaén, Spain*; [8]*Hospital Universitario Virgen de las Nieves, Reumatología, Granada, Spain*; [9]*Hospital Universitario Virgen de Valme, Reumatología, Málaga, Spain*; [10]*Hospital Clínico Universitario Virgen de la Victoria, Reumatología, Málaga, Spain*

Objectives: To analyze the effect of disease-modifying antirheumatic drugs (DMARDs) and identify risk factors associated with disease progression and mortality in patients with rheumatoid arthritis associated with interstitial lung disease (RA-ILD).
Methods: We performed a multicenter, prospective, observational study of patients with RA-ILD receiving DMARDs between 2015 and 2020. The patients were assessed using high-resolution computed tomography and pulmonary function tests at baseline and at 60 months. The main outcome measure at 60 months was worsening of FVC >10% or DLCO >15% and radiological progression or death. We recorded demographic and clinical characteristics, lung function, and the incidence of adverse events. A Cox regression analysis was performed to identify factors associated with worsening of ILD.
Results: After 60 months, lung disease had stabilized in 66 patients (56.9%), improved in 9 (7.8%), and worsened in 23 (19.8%). Eighteen patients (15.5%) died, with a mean survival of 71.8 (1.9) months. Baseline characteristics of 116 with RA-ILD treated with DMARDs is in table 1.The Cox multivariate analysis revealed the independent predictors of worsening of RA-ILD to be usual interstitial pneumonia (HR, 2.6 [95%CI, 1.0-6.7]), forced vital capacity (%) (HR, 3.8 [95%CI, 1.5-6.7]), anticitrullinated protein antibody titers (HR, 2.8 [95%CI, 1.1-6.8]), smoking (HR, 2.5 [95%CI, 1.1-6.2]), and treatment with abatacept, tocilizumab, or rituximab (HR, 0.4 [95%CI, 0.2-0.8]). During follow-up, 79 patients (68%) experienced an adverse event, mostly infection (61%).
Conclusion: Lung function is stable in most patients with RA-ILD receiving treatment with DMARDs, although one third of patients die. Identifying factors of worsening in RA-ILD is important for clinical management.

Table 1. Baseline characteristics of 116 with RA-ILD treated with DMARDs

Variable	Total=116
Epidemiological characteristics	
Female sex, n (%)	63 (54.3)
Age, years, mean (SD)	68.3 (9.9)
Clinical and analytical characteristics	
Current smoker	
Nonsmoker, n (%)	57 (49.1)
Smoker, n (%)	23 (19.8)
Exsmoker, n (%)	36 (31.0)
Time since diagnosis of RA, months, median (p25-p75)	148.5 (71.5-217.8)
Diagnostic delay, months, median (p25-p75)	8.5 (4.9-16.8)
Time since diagnosis of ILD, months, median (p25-p75)	27.5 (9.8-60.0)
Positive rheumatoid factor (>10), n (%)	111 (95.7)
Positive ACPA titer (>20), n (%)	100 (86.2)
Erosive disease, n (%)	76 (65.5)
Treatment Synthetic DMARD	100 (86.2)
Methotrexate, n (%)	51 (44.0)
Leflunomide, n (%)	30 (25.9)
Sulfasalazine, n (%)	9 (7.8)
Hydroxychloroquine, n (%)	21 (18.1)
Biologic DMARD	50 (43.1)
Infliximab, n (%)	1 (0.9)
Etanercept, n (%)	6 (5.2)
Adalimumab, n (%)	3 (2.6)
Golimumab, n (%)	3 (2.6)
Certolizumab, n (%)	3 (2.6)
Tocilizumab, n (%)	6 (5.2)
Abatacept, n (%)	15 (12.9)
Rituximab, n (%)	13 (11.2)
Immunosuppressants	11 (9.5)
Mycophenolate, n (%)	7 (6.0)
Azathioprine, n (%)	4 (3.4)
Antifibrotic agents, nintedanib, n (%)	1 (0.9)
Baseline corticosteroids, n (%)	69 (60.0)
Dose of baseline corticosteroids, median (p25-p75)	5.0 (0.0-7.5)

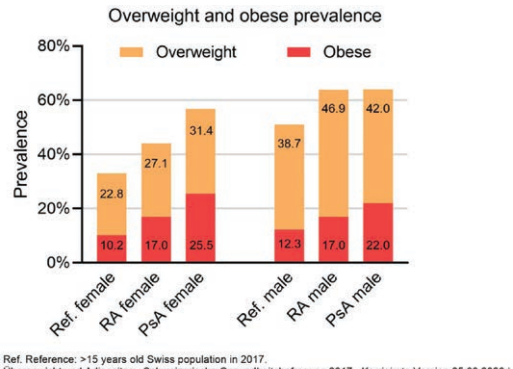
Abbreviations. RA: rheumatoid arthritis; ILD: interstitial lung disease; ACPA: anticyclic citrullinated protein antibody; DMARD: disease-modifying antirheumatic drug; SD: standard deviation.

Acknowledgements: Grant for Medical Researchers of the "Fundación Española de Reumatología" 2019. declare.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1090

POS0212 COMPARISON OF PATIENT CHARACTERISTICS AND TREATMENT PATTERNS ACROSS BODY MASS INDEX CATEGORIES IN PATIENTS WITH PSORIATIC ARTHRITIS AND RHEUMATOID ARTHRITIS

E. Vallejo-Yagüe[1], T. Burkard[1], B. Moeller[2], A. Finckh[3], A. M. Burden[1]. [1]*ETH Zurich, Department of Chemistry and Applied Biosciences, Institute of Pharmaceutical Sciences, Zurich, Switzerland*; [2]*Inselspital, University Hospital of Bern, Rheumatology, Immunology and Allergy, Bern, Switzerland*; [3]*University Hospitals Geneva, Division of Rheumatology, Geneva, Switzerland*

Background: Higher prevalence of obesity has been observed in psoriatic arthritis (PsA) and rheumatoid arthritis (RA) versus the general population, and abnormal body mass index has been associated with worse rheumatic markers.
Objectives: To describe PsA and RA patients in Switzerland, stratified by body mass index (BMI) category.
Methods: We performed a descriptive cohort study in PsA and RA patients registered in the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) database. Two distinct cohorts were generated based on patient diagnosis (PsA or RA) and analysed separately but using similar approaches. In both cohorts, we included patients treated for the first time with biologics or targeted synthetic disease-modifying anti-rheumatic drugs (tsDMARDs), and considered the treatment start as index date. Patients without baseline BMI were excluded. Patients were stratified by BMI category at the start of biologic/tsDMARD treatment, defined as underweight (BMI<18.5), normal weight (BMI 18.5-24.9), overweight (BMI 25.0-29.9), and obese (BMI≥30). In the PsA cohort, underweight and normal weight groups were merged due to low numbers. The proportion of patients categorized as overweight or underweight were compared to national statistics from the Swiss Federal Statistical Office. Information on patient demographics (e.g., age, sex, BMI, life-habits), disease-specific characteristics (e.g., disease activity scores, health questionnaires, biomarkers), co-medications and comorbidities were summarized at the start of the first biologic/tsDMARD treatment. Patient characteristics across BMI categories were compared, using the normal weight category as reference group. Additionally, we summarized the frequency and reasons for recorded treatment stop/switch at ≤6 months, 6 to 12 months, and >12months from treatment start, and illustrated the prescription patterns for first and second biologic/tsDMARD treatment, stratifying by BMI.
Results: We identified 819 PsA [39.7% normal weight, 36.5% overweight, 23.8% obese] and 3217 RA patients [4.4% underweight, 46.8% normal weight, 31.8% overweight, 17.0% obese]. Figure 1 illustrates the prevalence of overweight and obesity in each cohort stratified by sex, compared to the national average. When comparing obese patients to those with normal weight, both PsA and RA obese patients had significantly higher C-reactive protein, worse disease activity score, lower quality of life (QoL) measures, and more frequent cardiovascular disease and diabetes. Among PsA patients, the overweight and obese had worse physician-assessed skin manifestation and patient-reported pain compared to the normal weight group. While in RA, the obese patients had higher erythrocyte sedimentation rate, smaller prevalence of seropositive patients, lower frequency of fractures/surgeries, and higher tender joint counts, but similar swollen joint counts, when compared to the normal weight group. Adalimumab and etanercept, were the most commonly prescribed drugs as first biologic/tsDMARD treatment in both PsA and RA cohorts and among every BMI category. Overall, 55% PsA and 56% RA patients had recorded treatment stop/switch. Among RA patients, significantly fewer obese patients reported treatment stop/switch at >12 months from treatment start, compared to the normal weight group. Adalimumab and etanercept were also the most commonly prescribed second biologic/tsDMARD treatment, but for the obese group among PsA patients (adalimumab, golimumab) and the obese group in the RA cohort (adalimumab, rituximab).
Conclusion: In this national wide study, we observed that the prevalence of obesity in RA and PsA was higher than that of the general Swiss population. Obese PsA/RA patients starting first biologic/tsDMARD treatment presented worse disease activity and poorer QoL than normal weight patients. Results suggest to take BMI into consideration when treating PsA and RA patients.



Ref. Reference: >15 years old Swiss population in 2017.
Übergewicht und Adipositas - Schweizerische Gesundheitsbefragung 2017 - Korrigierte Version 25.09.2020 | Publikation. Bundesamt für Statistik 2020. Accessed January 21, 2021. Available at: https://www.bfs.admin.ch/bfs/de/home/statistiken/gesundheit/erhebungen/sgb.assetdetail.14147705.html

RA rheumatoid arthritis. Study data.

PsA psoriatic arthritis. Study data.

Acknowledgements: We would like to thank all patients and rheumatologists contributing to the SCQM registry, as well as the entire SCQM staff. A list of rheumatology offices and hospitals which contribute to the SCQM registry can be found at http://www.scqm.ch/institutions. The SCQM is financially supported by pharmaceutical industries and donors. A list of financial supporters can be found at http://www.scqm.ch/sponsors.
Disclosure of Interests: Enriqueta Vallejo-Yagüe: None declared, Theresa Burkard: None declared, Burkhard Moeller Speakers bureau: AbbVie, Bristol Myers, Eli Lilly, Janssen, Pfizer, Roche, Novartis, Merck, Axel Finckh Speakers bureau: Pfizer, Eli-Lilly, Paid instructor for: Pfizer, Eli-Lilly, Consultant of: AbbVie, AB2Bio, BMS, Gilead, Pfizer, Viatris, Grant/research support from: Pfizer, BMS, Novartis, Andrea Michelle Burden: None declared
DOI: 10.1136/annrheumdis-2021-eular.1348

POS0213 20 YEAR FOLLOW-UP OF CARDIOVASCULAR EVENT RISK IN RHEUMATOID ARTHRITIS COMPARED TO DIABETES

R. Raadsen[1], R. Agca[1,2], A. Voskuyl[2], M. Boers[3], W. Lems[1,2], M. Nurmohamed[1,2]. [1]*Amsterdam Rheumatology and Immunology Center, location Reade, Rheumatology, Amsterdam, Netherlands*; [2]*Amsterdam Rheumatology and Immunology Center, location VU University Medical Center, Rheumatology, Amsterdam, Netherlands*; [3]*Amsterdam University Medical Center, Location VU University Medical Center, Biostatistics and Epidemiology, Amsterdam, Netherlands*

Background: Patients with rheumatoid arthritis have an increased risk for developing cardiovascular diseases (CVD) compared to the general population, similar to the CVD risk in patients with diabetes mellitus. However, there are no controlled studies investigating the incidence of cardiovascular (CV) events in RA patients with follow up of more than 20 years.
Objectives: The objectives of the current study were to investigate the incidence rates of CV events in a long-term follow up cohort of RA patients, and to compare these to a similar cohort representing the general population, ie. The Hoorn study.
Methods: The CARRÉ study is an ongoing prospective cohort study, which started in 2001, investigating CV mortality and morbidity in 353 randomly selected patients with RA. Primary endpoints, i.e. verified medical history of coronary, cerebral or peripheral arterial disease, were determined at baseline, and after three, ten, fifteen and twenty years of follow up. Patients were censored at the date of an experienced CV event or their death. Incidence density rates per 100 patient years were calculated. Data were compared to results from the Hoorn study, a Dutch cohort study of glucose metabolism and other CV risk factors that began in 1989. All 2,484 participants were subject to an extensive and repeated CV screening program similar to that used in the CARRÉ study.
Results: After 20 years of follow up 118 patients (33%) developed at least one CV event in the Carré group. Mean (SD) follow up time was 11 (6) years with a total of 3,500 years at risk and an incidence rate of 3.4 per 100 patient-years; this is slightly up from the figure reported at 15 years, i.e. 3.2 per 100 patient-years. A CV event-free survival curve is shown in figure 1. After 30 years of follow up, 295 participants of the Hoorn study had developed a CV event, during a mean follow up time 20 (8) years. Total time at risk was 50,000 years, with an incidence rate of 0.6 CV events per 100 patient years.
Conclusion: In our cohort the incidence rate of CV events in RA patients has remained consistently high when compared with the general population, despite better control of RA inflammation in recent years. This again confirms the need for timely CVD-risk screening and management.
REFERENCES:
[1] Agca R, Hopman L, Laan KJC, van Halm VP, Peters MJL, Smulders YM, et al. Cardiovascular Event Risk in Rheumatoid Arthritis Compared with Type 2 Diabetes: A 15-year Longitudinal Study. *J Rheumatol.* 2020;47(3):316-24.

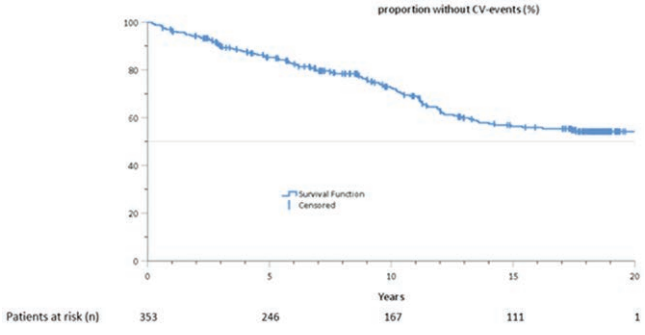


Figure 1. Survival curve of participants with rheumatoid arthritis. RA = rheumatoid arthritis

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1744

POS0214 ASSOCIATION BETWEEN C-REACTIVE PROTEIN AND 10-YEAR RISK OF CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS USING THE ERS-RA SCORE: A CROSS-SECTIONAL ANALYSIS OF THE CORDIS COHORT

G. L. Erre[1], F. Cacciapaglia[2], G. Sakellariou[3], A. Manfredi[4], E. Bartoloni Bocci[5], O. Viapiana[6], M. Fornaro[2], M. Dessì[7], A. A. Mangoni[8], B. L. Palermo[9], E. Gremese[10], G. Cafaro[5], V. Nucera[11], C. Vacchi[12], F. R. Spinelli[13], F. Atzeni[11], M. Piga[14]on behalf of "Cardiovascular Obesity and Rheumatic Disease Study (CORDIS)" Group of the Italian Society of Rheumatology (SIR).. [1]*University and AOU of Sassari, Department of Medical, Surgical and Experimental Sciences, Sassari, Italy*; [2]*University and AOU, Policlinico of Bari, Department of Emergency and Organs Transplantation, Bari, Italy*; [3]*University of Pavia, Istituti Clinici Scientifici Maugeri IRCCS Pavia, Pavia, Italy*; [4]*Azienda Ospedaliera Universitaria Policlinico di Modena, Unit of Rheumatology, Modena, Italy*; [5]*University of Perugia, Department of Medicine and Surgery, Perugia, Italy*; [6]*University of Verona, Dipartimento di Medicina, Verona, Italy*; [7]*University of Cagliari, Department of Medical Sciences and Public Health, Cagliari, Italy*; [8]*Flinders University, College of Medicine and Public Health, Adelaide, Australia*; [9]*University of Pavia, IRCSS San Matteo, Pavia, Italy*; [10]*Policlinico Gemelli, Università Cattolica del Sacro Cuore, Dipartimento di Scienze Mediche e Chirurgiche, Roma, Italy*; [11]*University of Messina, Dipartimento di Medicina Clinica e Sperimentale, Messina, Italy*; [12]*University of Modena and Reggio Emilia, Clinical and Experimental Medicine PhD Program, Modena, Italy*; [13]*Università La Sapienza, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Roma, Italy*; [14]*University of Cagliari, Department of Medical Sciences and Public Health, Monserrato, Italy*

Background: Rheumatoid arthritis (RA) is associated with an increased risk of atherosclerotic cardiovascular disease (CVD). The Expanded Cardiovascular Risk Prediction Score for Rheumatoid Arthritis (ERS-RA) estimates the 10-year risk of myocardial infarction, stroke or CVD-related death based on conventional and RA-specific (clinical disease activity index, CDAI, disease duration, glucocorticoid use) risk factors (1).
Objectives: We evaluated the associations between ERS-RA 10-year risk of CVD, high-sensitivity C-reactive protein (hs-CRP) concentrations, and pharmacological treatment in 1,251 RA patients collected by the "Cardiovascular Obesity and Rheumatic Disease Study (CORDIS)" group of the Italian Society of Rheumatology (SIR).
Methods: We assessed independent associations between ERS-RA risk score and each relevant variable using multivariate regression (ENTER approach; listwise deletion analysis). Given the relatively high number of missing hs-CRP data (n=385), regression analysis was also performed using multiple imputation (10 sets, Stata 16.1). Regression models were not adjusted for independent variables included in the ERS-RA score.
Results: Among 1,251 RA patients [mean (SD) age 60.4(9.3), range (40-80) years; 78% female; mean (SD) disease duration, 11.6(8) years; mean (SD) CDAI, 9(9); mean (SD) HAQ, 0.77(0.7); mean (SD) hs-CRP, 6.8(12) mg/L] the estimated 10-year CVD risk was 11.6(0.9) % [mean (SD)]. Regarding treatment, 539(43%) received glucocorticoids, 676(54%) a biological or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) (n missing=1), and 885(81%) at least one conventional synthetic DMARD (csDMARD). Ninety-three (7.4%) patients did not receive any treatment. After adjusting for the use of b/tsDMARD and csDMARD, hs-CRP concentrations were significantly associated with 10-year risk of CVD both in standard multiple regression (n=865; coefficient=0.005 for each 10 mg/L hs-CRP increment, 95% confidence interval (0.000-0.100), p=0.043) and after multiple imputation (n=1,251; coefficient=0.005 for each 10 mg/L hs-CRP increment, 95% confidence interval (0.000-0.114), p=0.035) (Table 1). This corresponds to an increase of 10-year CV risk of 1% for every 20 mg/L increase in hs-CRP concentrations.
Conclusion: In a large cohort of RA patients, we observed a significant, positive, and independent association between hs-CRP concentrations and 10-year CV risk estimated by ERS-RA. The cross-sectional design of the study did not allow to establish a cause-effect relationship between hs-CRP and CV risk. Given that conventional CV risk factors and inflammation-related variables are accounted for in the ERS-RA risk score, other, unexplored, mechanisms may underlie the observed association between hs-CRP and CV risk.
REFERENCES:
[1] Solomon, D. H., et al. "Derivation and internal validation of an expanded cardiovascular risk prediction score for rheumatoid arthritis: a Consortium of Rheumatology Researchers of North America Registry Study." *Arthritis & rheumatology* 67.8 (2015): 1995-2003.

Table 1. Multiple regression models

	Model 1 n= 865		Model 2 n= 1, 251	
ERS-RA score	Coefficient	95% CI, *p*	Coefficient	95% CI, *p*
hs-CRP, every 10 mg/L increment	0.005	0.000 to 0.100, 0.043	0.005	0.000 to 0.011, 0.035
b/tsDMARD use	-0.002	-0.005 to 0.001, 0.199	-0.000	-0.002 to 0.002, 0.963
csDMARD use	0.002	-0.003 to 0.007, 0.394	0.002	-0.002 to 0.006, 0.371
Prob >F, model with only CRP	0.03		0.03	
Prob >F, full model	0.07		0.08	

A multiple linear regression (ENTER method) was performed for the dependent variable ERS-RA score using a listwise deletion analysis (Model 1) and a multiple imputation analysis (Model 2).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2643

POS0215

DIRECT AND CONDITIONAL EFFECTS OF EPICARDIAL ADIPOSE TISSUE VOLUME ON CORONARY PLAQUE PROGRESSION IN RHEUMATOID ARTHRITIS

G. Karpouzas[1], S. Ormseth[1], E. Hernandez[1], M. Budoff[2]. [1]*The Lundquist Institute, Rheumatology, Torrance, United States of America*; [2]*The Lundquist Institute, Cardiology, Torrance, United States of America*

Background: Epicardial adipose tissue volume (EATv) predicts coronary atherosclerosis presence, progression and cardiovascular event risk in general patients[1,2]. Our group recently reported that EATv associated with greater subclinical coronary plaque burden, non-calcified plaque presence and vulnerable plaque characteristics in patients with rheumatoid arthritis (RA). The relationship was stronger in RA patients with lower disease duration, no traditional cardiac risk factors, and who were not obese.
Objectives: To evaluate the predictive value of EATv on long-term coronary atherosclerosis development, and moderators of the association between EATv and plaque formation.
Methods: This single-center observational cohort study included 100 patients without symptoms or diagnosis of cardiovascular disease who underwent computed tomography angiography for evaluation of EATv and coronary atherosclerosis at baseline and repeat assessments 6.9±0.3 years later to evaluate plaque progression. New plaque formation in segments without plaque at baseline was the main outcome. Robust multivariable logistic regression evaluated the effect of high versus low EATv (based on median) on likelihood of new plaque formation, accounting for clustering of segments within patients. Potential moderator effects of prespecified predictors were also assessed.
Results: High EATv (>107 cm^3) predicted new plaque formation in segments without baseline plaque (OR 2.77 [95% CI 1.43-5.37], p= 0.003); however, significance was lost in the multivariable model. Importantly, high EATv associated with formation of higher-risk non- and partially calcified plaque after adjusting for Framingham D'Agostino risk score, obesity, segment location, time-averaged CRP, duration of bDMARD and statin treatment and cumulative prednisone dose (adjusted OR 2.57 [95% CI 1.02-6.48], p= 0.045). RA duration (<10 versus >10 years), cardiac risk factor burden (≤1 versus >1), presence of mixed/calcified plaque in other coronary segments at baseline, and statin exposure (≤1 versus >1 year, based on median) moderated the effect of EATv on all new plaque formation (all p for interaction ≤ 0.021). Specifically, high EATv predicted new plaque formation in patients with RA duration <10 years (adjusted OR 5.75 [95% CI 1.77-18.67]), those with ≤1 cardiac risk factors (adjusted OR 3.40 [95% CI 1.46-7.90]), those without calcification at baseline (adjusted OR 2.65 [95% CI 1.11-6.31]) and those with statin treatment <1 year (adjusted OR 3.33 [95% CI 1.13-9.77]). This was not the case for patients with RA >10 years, ≥ 2 cardiac risk factors, calcification at baseline and statin treatment >1 year (figure 1).
Conclusion: High baseline EATv independently predicted future higher-risk non-calcified and mixed coronary plaque in RA. Moreover, it conditionally promoted new plaque formation overall in patients with earlier disease, low cardiac risk factor burden, who had little or no atherosclerosis at baseline and who had limited exposure to statin therapy. These findings indicate the need for a larger prospective evaluation of the role of EATv as a biomarker of coronary atherosclerosis development in RA.
REFERENCES:
[1] Hwang I-C et al. *J Atheroscler Thromb* 2017;24:262–74. 2. Ding J et al. *Am J Clin Nutr* 2009;90:499–504.

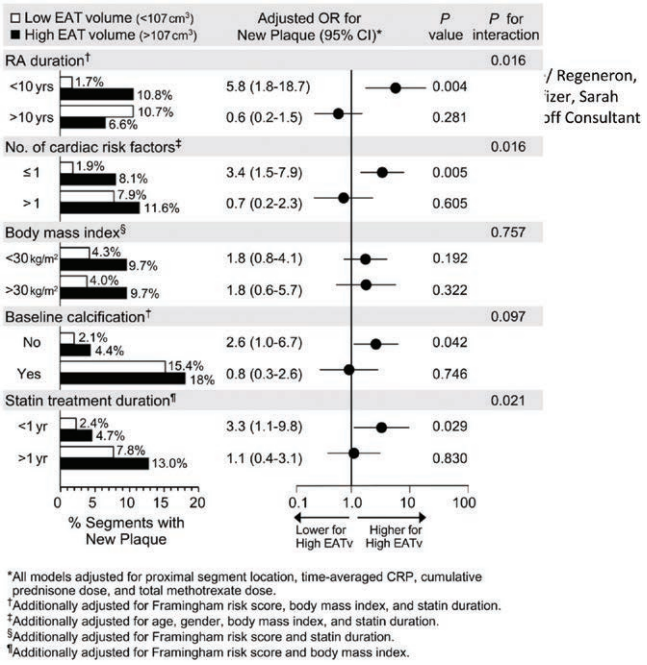


Figure 1. Moderators of influence of EATv on new coronary plaque formation

Disclosure of Interests: George Karpouzas Speakers bureau: Sanofi/ Genzyme/ Regeneron, Consultant of: Sanofi/ Genzyme/ Regeneron, Grant/research support from: Pfizer, Sarah Ormseth: None declared, Elizabeth Hernandez: None declared, Matthew Budoff Consultant of: Pfizer
DOI: 10.1136/annrheumdis-2021-eular.3347

POS0216

GREATER HIGH-DENSITY LIPOPROTEIN LEVELS OVER TIME ARE LINKED TO DECREASED CORONARY PLAQUE FORMATION AND REGRESSION AND STABILIZATION OF HIGH-RISK LESIONS IN RHEUMATOID ARTHRITIS

G. Karpouzas[1,2], S. Ormseth[1], E. Hernandez[1], M. Budoff[3]. [1]*The Lundquist Institute, Rheumatology, Torrance, United States of America*; [2]*Harbor-UCLA Medical Center, Rheumatology, Torrance, United States of America*; [3]*The Lundquist Institute, Cardiology, Torrance, United States of America*

Background: The relationship between serum lipoproteins and cardiovascular disease risk in rheumatoid arthritis (RA) is complex[1]. Their levels and function may vary based on disease activity and medication use. Beneficial effects on high-density lipoprotein (HDL-C) levels, structure and behavior, in response to treatment have been described. However, the impact of HDL-C levels over time on coronary atherosclerosis progression in RA is unknown.
Objectives: We here evaluated the influence of HDL-C levels over time on long-term coronary plaque formation and progression in patients with RA.
Methods: One hundred one RA patients without symptoms or history of cardiovascular disease who participated in a computed tomography angiography study of coronary atherosclerosis had repeat assessments after 6.9±0.3 years to evaluate plaque progression. Clinical, laboratory and medication data were recorded at baseline and regular outpatient follow-up visits thereafter. Time-averaged HDL-C was calculated for each patient using available consecutive HDL measurements between baseline and follow-up. Robust logistic regression assessed the association between time-averaged HDL-C and likelihood of new plaque formation in segments without plaque at baseline, and transition of prevalent mixed plaque to calcified plaque. Robust multinomial logistic regression evaluated the effect of time-averaged HDL-C on likelihood of new non-calcified, mixed or calcified plaque formation in segments without plaque (compared to remaining without plaque), and non-calcified plaque regression or transition to mixed or calcified plaque at follow-up (compared to remaining non-calcified). All models accounted for clustering of coronary segments within patients and adjusted for Framingham D'Agostino risk score, proximal segment location, time-averaged CRP, cumulative prednisone dose, bDMARD duration, statin duration, waist-to-height ratio, and time-averaged triglycerides.
Results: Participants were mostly female (n=87, 86.1%), with a mean ± standard deviation (SD) age of 51.5±10.3 years and time-averaged HDL-C of 51.7±13.9. Ninety-seven new plaques formed in segments without plaque at baseline; 20 were noncalcified, 21 were mixed, and 56 were calcified. Time-averaged HDL-C

had no effect on new total plaque formation (adjusted odds ratio-OR 0.88 [95% CI 0.64-1.21]). However, each 1-SD increase in time-averaged HDL-C associated with a 44% reduced likelihood of new non-calcified plaque formation at follow-up (adjusted OR 0.56 [95% CI 0.35-0.92], Figure 1). In contrast, there was no effect of time-averaged HDL-C on new mixed or calcified plaque formation. Of 98 non-calcified plaques at baseline, 42 did not change at follow-up, 32 regressed (disappeared), 16 transitioned to mixed and 8 to calcified plaques. Each SD increase in time-averaged HDL-C yielded a 2.2-fold greater likelihood of non-calcified plaque regression (adjusted OR 2.21 [95% CI 1.02-4.83]). Sixteen of 52 mixed plaques present at baseline transitioned to more stable calcified lesions, and time-averaged HDL-C (per 1-SD increment) predicted a 3.5-fold increased likelihood of transition of mixed to fully calcified plaque (adjusted OR 3.56 [95% CI 1.25-10.17]).

Conclusion: Higher HDL-C over time predicted regression of existing and decreased formation of new higher-risk non-calcified plaque. It also associated with transition of vulnerable mixed plaque to more stable fully calcified plaque. These effects were independent of RA treatment duration, prednisone dose and statin exposure.

REFERENCES:

[1] Toms TE et al. Curr Vasc Pharmacol. 2010;8:301–326.

Outcome	No. of coronary segments (%)	Adjusted OR (95% CI) per 1-SD increment in time-averaged HDL*	*P* value
New plaque formation			
None to none	1331 (93.2)	1.00 (reference)	—
None to non-calcified	20 (1.4)	0.56 (0.35-0.92)	0.021
None to mixed	21 (1.5)	0.93 (0.65-1.33)	0.678
None to calcified	56 (3.9)	0.91 (0.59-1.41)	0.673
Non-calcified plaque transition			
Non-calcified to non-calcified	42 (42.9)	1.00 (reference)	—
Non-calcified to none	32 (32.7)	2.21 (1.02-4.83)	0.045
Non-calcified to mixed	16 (16.3)	1.02 (0.37-2.87)	0.961
Non-calcified to calcified	8 (8.2)	0.81 (0.26-2.51)	0.712
Mixed plaque progression			
Mixed to mixed	36 (69.2)	1.00 (reference)	—
Mixed to calcified	16 (30.8)	3.56 (1.25-10.17)	0.018

*Adjusted for Framingham D'Agostino cardiac risk score, proximal segment location, time-averaged CRP, biologic DMARD treatment duration, statin treatment duration, cumulative prednisone dose, waist-to-height ratio, and time-averaged triglycerides.

Figure 1. Impact of HDL-C over time on coronary plaque progression in RA

Disclosure of Interests: George Karpouzas Speakers bureau: Sanofi/Genzyme/Regeneron, Consultant of: Sanofi/Genzyme/Regeneron, Grant/research support from: Pfizer, Sarah Ormseth: None declared, Elizabeth Hernandez: None declared, Matthew Budoff: None declared

DOI: 10.1136/annrheumdis-2021-eular.3383

POS0217 PULSE WAVE VELOCITY ELEVATION ABOVE INDIVIDUAL REFERENCE VALUES AND AORTIC-BRACHIAL STIFFNESS MISMATCH AS EARLY MARKERS OF ARTERIAL STIFFNESS INCREASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Troitskaya[1], S. Velmakin[1], R. Osipyants[1], A. Arbuzova[1], V. R. Espinoza[2], Z. Kobalava[1]. *[1]Peoples' Friendship University of Russia (RUDN University), Internal diseases, Moscow, Russian Federation*; *[2]Peoples' Friendship University of Russia (RUDN University), Int, Moscow, Russian Federation*

Background: Arterial stiffness (AS) is a known predictor of cardiovascular (CV) disease. The measurement of pulse wave velocity (PWV) is considered to be a gold standard of AS assessment but the recommended threshold of 10 m/s[1] may not take into account multiple factors influencing PWV. Use of the proposed individual reference values may help to identify patients with AS increase despite PWV level below this threshold[2]. The impact of AS on CV outcomes may be mediated by the reversal of the aortic-brachial stiffness (AS gradient)[3]. One small study in patients with type 2 diabetes has shown that the aortic-brachial stiffness mismatch (hereafter AS mismatch) was an earlier marker of AS than PWV elevation[4]. Patients with rheumatoid arthritis (RA) have high CV risk and may benefit from early detection of AS increase. Both approaches have not been studied in RA previously

Objectives: To evaluate the incidence of PWV elevation above individual reference values and the frequency of AS mismatch in RA

Methods: Study group included 85 patients (pts) with RA (females 77.6%, aged 59.7±14.3 years, HTN 65%, mean DAS-28(CRP) 3.7±1.1) and control group (40 pts matched by gender, age and risk factors). Parameters of AS were measured by applanation tonometry. Individual PWV reference values were assessed[2]. The AS gradient was calculated as carotid-femoral (cf)PWV/carotid-radial (cr)PWV ratio and its elevation ≥1 was considered as AS mismatch. p<0,05 was considered significant

Results: In pts with RA with and without history of HTN mean cfPWV was 10.3±3.1 and 7.3±1.5 m/s, respectively, mean AS gradient – 1.4±0.4 and 1.1±0.1 (p<0.001 for trend); in controls – 9.6±1.9 and 6.7±1.4 m/s and 1.3±0.3 and 0.99±0.2, respectively (p<0.001 for trend). cfPWV elevation ≥10 m/s was observed in 34.1% pts with RA and 32.5% of controls: 6.7 and 6.3% of normotensives and 49.1 and 50% of hypertensives, respectively (p>0.05). cfPWV elevation above individual reference values was observed in 41.2% RA pts and 27.5% of controls (p=0.03): in 40% and 6.3% of normotensives (p=0.02) and 41.8% and 41.7% of hypertensives, respectively. After adjustment by age, gender and systolic BP cfPWV elevation above individual reference values in normotensive RA pts was independently associated with BMI (beta=0.39, p=0.02) and dyslipidemia (beta=0.48, p=0.01). The frequency of AS mismatch in RA was significantly higher compared to the controls in both normotensive and hypertensive subgroups: 76.7% vs 43.8% (p=0.03) and 94.5% vs 79.2% (p=0.04), respectively. The same trend was observed in a subgroup with normal cfPWV: AS mismatch was present in RA and controls in 82.1% vs 51.9% (p=0.004) in pts with PWV ≤ 10 m/s and in 82% and 51.7% (p=0.04), respectively in pts with PWV below individual reference values.

Conclusion: Patients with RA are characterized by higher frequency of cfPWV elevation above individual reference values compared to controls irrespectively of history of HTN. This method may be more appropriate for AS evaluation than use of standard criteria in this population. AS mismatch in RA pts is highly prevalent and may be considered as an earlier marker of AS than cfPWV elevation. These findings may be used for early detection of vascular ageing in patients with RA.

REFERENCES:

[1] Williams B, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. J Hypertens 2018;36(10):1953-2041

[2] Reference Values for Arterial Stiffness' Collaboration. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: 'establishing normal and reference values'. Eur Heart J. 2010;31(19):2338-50

[3] Yu S, et al. Central Versus Peripheral Artery Stiffening and Cardiovascular Risk. Arterioscler Thromb Vasc Biol. 2020;40(5):1028-1033

[4] Troitskaya, E., et al. Aortic-brachial stiffness mismatch in patients with arterial hypertension and type 2 diabetes mellitus, J Hypertens 2018;36:e191

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3889

POS0218 TUMOR-NECROSIS FACTOR INHIBITORS IMPROVE AORTIC STIFFNESS IN PATIENTS WITH LONGSTANDING RHEUMATOID ARTHRITIS

A. Giollo[1], G. Cioffi[1], G. Orsolini[1], F. Ognibeni[1], A. Dalbeni[2], R. Bixio[1], G. Adami[1], A. Fassio[1], L. Idolazzi[1], D. Gatti[1], M. Rossini[1], O. Viapiana[1]. *[1]University of Verona, Rheumatology Section, Department of Medicine, Verona, Italy*; *[2]University of Verona, Internal Medicine and Hypertension Unit, Department of Medicine, Verona, Italy*

Background: Major cardiovascular disease (CVD) benefits of disease-modifying anti-rheumatic drugs (DMARDs) therapy occur in early RA patients with treat-to-target strategy. However, it is unknown whether long-term DMARDs treatment in established RA could be useful to improve CVD risk profile.

Objectives: The aim of this study was to comparatively describe aortic stiffness progression in patients with longstanding and established RA treated with tumor necrosis factor inhibitors (TNFi) or conventional synthetic DMARDs (csDMARDs).

Methods: Ultrasound aortic stiffness index (AoSI) has to be considered a proxy outcome measure in established RA patients. We measured AoSI in a group of RA patients on long-term treatment with TNFi or csDMARDs. Eligible participants were assessed at baseline and after 12 months; changes in serum lipids, glucose and arterial blood pressure were assessed. All patients were on stable medications during the entire follow-up.

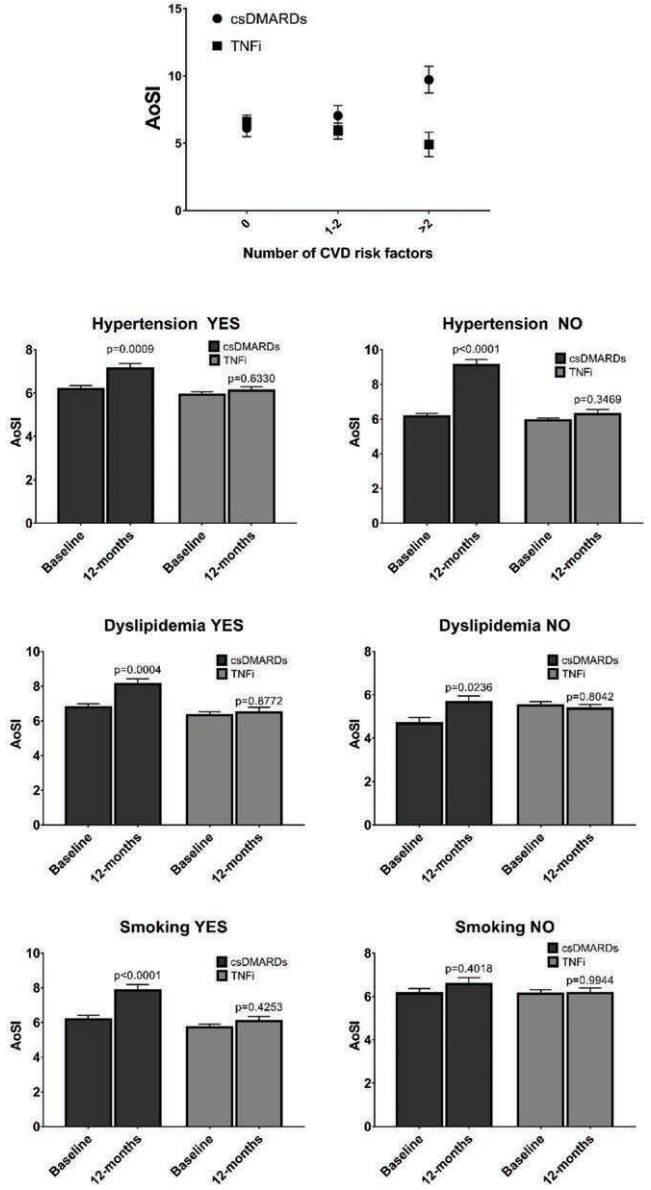
Results: We included 107 (64 TNFi and 43 csDMARDs) RA patients. Most patients (74%) were in remission or low disease activity and had some CVD risk factors (45.8% hypertension, 59.8% dyslipidemia, 45.3% smoking; table 1). The two groups did not differ significantly for baseline AoSI (5.95±3.73% vs 6.08±4.20%, p=0.867). Follow-up AoSI was significantly increased from baseline in the csDMARDs group (+1.00%; p<0.0001) but not in the TNFi group (+0.15%, p=0.477). Patients on TNFi had significantly lower follow-up AoSI from baseline than the csDMARDs group (-1.02%, p<0.001; ANCOVA corrected for baseline AoSI, age and systolic blood pressure). Furthermore, follow-up AoSI was significantly lower in TNFi users with 1-2 or >2 CVD risk factors than in those without (figure 1).

Conclusion: Long-term treatment with TNFi was associated with reduced aortic stiffness in patients with established RA and several CVD risk factors.

Baseline characteristics of the study population.	csDMARDs (n=43)	TNFi (n=64)	P value
Age, median years (IQR)	58.6 (53.0, 66.0)	58.1 (49.3, 67.0)	0.839
Female sex	33 (76.7)	54 (84.4)	0.321
Obesity	5 (11.6)	7 (10.9)	0.999
Hypertension	19 (44.2)	30 (46.9)	0.784
Anti-hypertensive drug	17 (39.5)	28 (43.8)	0.784
Smoking status, ever	18 (42.9)	30 (46.9)	0.684
Dyslipidemia	30 (40.2)	34 (59.8)	0.085
Current statin use	13 (34.2)	10 (15.9)	0.033
Diabetes mellitus	3 (7.0)	3 (4.7)	0.676
Anti-diabetic medication	1 (2.3)	1 (1.5)	0.999
CVD risk factors, median (IQR)	2 (1, 3)	2 (1, 3)	0.199
RF and/or ACPA positive	28 (65.1)	33 (51.6)	0.165
Disease duration, median years (IQR)	14.1 (11.5)	15.4 (10.5)	0.538
Methotrexate	38 (88.4)	52 (81.3)	0.192
Leflunomide	5 (17.9)	12 (19.0)	0.999
Hydroxychloroquine	9 (31.0)	5 (7.8)	0.009
Prednisone > 5 mg daily	7 (7.7)	5 (5.5)	0.823
NSAIDs	6 (20.7)	22 (34.4)	0.227

ACPA, anti-citrullinated peptides antibodies; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; IQR, interquartile range; NSAIDs, non-steroidal anti-inflammatory drugs; RF, rheumatoid factor; TNFi, tumor necrosis factor inhibitors. All data reported as absolute numbers (percentage) otherwise specified. P-value refers to Chi-squared or Fisher test for categorical variables or ANOVA for continuous variables.

Disclosure of Interests: None declared



DOI: 10.1136/annrheumdis-2021-eular.404

POS0219

EFFECT OF LOW-DOSE METHOTREXATE ON ESTIMATED GLOMERULAR FILTRATION RATE AND KIDNEY ADVERSE EVENTS IN THE CARDIOVASCULAR INFLAMMATION REDUCTION TRIAL

J. Sparks[1], K. Vanni[1], M. Sparks[2], C. Xu[1], L. Santacroce[1], R. Glynn[3], P. Ridker[4], D. Solomon[1]. *[1]Brigham and Women's Hospital, Division of Rheumatology, Boston, United States of America; [2]Duke University School of Medicine, Division of Nephrology, Durham, United States of America; [3]Brigham and Women's Hospital, Divisions of Cardiovascular and Preventative Medicine, Boston, United States of America; [4]Brigham and Women's Hospital, Division of Preventative Medicine, Boston, United States of America*

Background: Low-dose methotrexate (LD-MTX) is a common first-line treatment for systemic rheumatic diseases, and its use is contraindicated in advanced chronic kidney disease (CKD) because it is primarily excreted by the kidneys. Among patients with preserved kidney function, the safety of LD-MTX on estimated glomerular filtration rate (eGFR) and kidney adverse events (AEs) has not been established.

Objectives: To investigate the effect of LD-MTX on eGFR and kidney AEs using data from a randomized clinical trial.

Methods: We performed a secondary analysis for eGFR and kidney AEs using the randomized double-blind, placebo-controlled Cardiovascular Inflammation Reduction Trial. Adults with known cardiovascular disease and diabetes and/or metabolic syndrome were randomly allocated to oral LD-MTX (target dose 15-20 mg/week) or placebo. All participants took folic acid 1 mg six days/week. Exclusion criteria included systemic inflammatory disease and creatinine clearance <40 mL/min (by Cockcroft-Gault). eGFR was calculated using the CKD-EPI formula. Clinical kidney AEs were blindly adjudicated. The least-squares mean change of eGFR from baseline was calculated at each study visit; the difference in eGFR slopes between LD-MTX and placebo was compared using a modified intention-to-treat approach. We also compared rates of kidney AEs for LD-MTX versus placebo using Cox proportional hazards models.

Results: A total of 2,391 subjects were randomized to LD-MTX and 2,395 to placebo. At baseline, mean age was 66 years, 19% were female, mean eGFR was 80.0 mL/min/1.73m^2, and 18% had stage 3 CKD or worse. Median follow-up duration was 23 months, and median LD-MTX dose was 16 mg/week. Those randomized to LD-MTX had less decline in eGFR over the entire follow-up compared to placebo (slope difference 1.12, 95%CI 0.59-1.65, p<0.001, Figure 1). Those with CKD stage 3 or worse on LD-MTX saw less eGFR decline than those with CKD stage 2 or better (slope difference among CKD stage 3 or worse: 2.46, 95%CI 1.10-3.82, p<0.001; p for interaction 0.02). The LD-MTX group had higher eGFR than placebo over the first 24 months of study follow-up (p<0.05 at each visit). On safety laboratory monitoring, there were 159 acute kidney injury AEs in the LD-MTX group and 187 in the placebo group (HR 0.83, 95%CI 0.67-1.02, Table 1). There were 37 clinical kidney AEs in the LD-MTX group and 42 in the placebo group (0.87, 95%CI 0.56-1.36). One subject began dialysis in the LD-MTX group compared to 3 in the placebo group.

Conclusion: These results demonstrate the kidney safety of LD-MTX among patients without advanced CKD at baseline. We observed a possible beneficial effect of LD-MTX on preserving kidney function, suggesting that inflammation may be involved in the pathogenesis of CKD in this population.

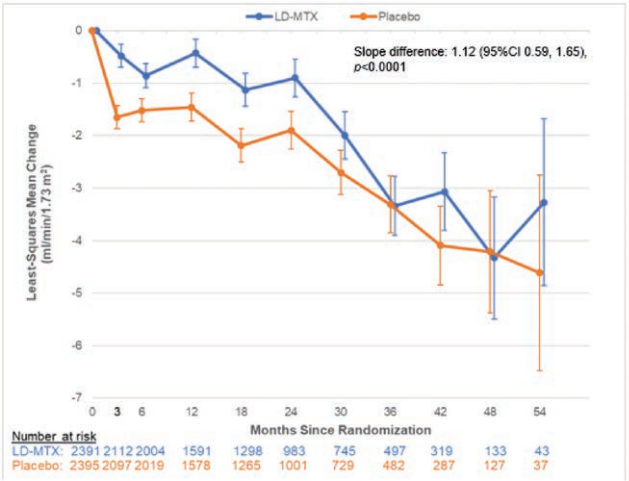


Figure. Least-squares mean change of estimated glomerular filtration rate (eGFR) from baseline to each follow-up visit according to random assignment of low-dose methotrexate (LD-MTX) or placebo in the Cardiovascular Inflammatory Reduction Trial (n=4,786). eGFR was calculated using the CKD-EPI equation. A slope difference significantly above 0 denotes less decline in eGFR for the LD-MTX group.

Table 1. Rates and hazard ratios for kidney adverse events per random assignment of low-dose methotrexate or placebo in the Cardiovascular Inflammation Reduction Trial (n=4,786).

	Low-dose methotrexate (n=2,391)		Placebo (n=2,395) (reference)		
	Events	Rate per 100 person-years (95%CI)	Events	Rate per 100 person-years (95%CI)	HR (95%CI)
SCr collected at safety visits					
Any event*	159	3.42 (2.93, 3.98)	187	4.06 (3.53, 4.67)	0.83 (0.67, 1.02)
Mild (SCr 1.5-1.9x baseline)	154	3.47 (2.97, 4.06)	177	4.06 (3.51, 4.69)	0.85 (0.68, 1.06)
Moderate (SCr 2-2.9x baseline)	19	0.41 (0.26, 0.64)	24	0.52 (0.35, 0.78)	0.78 (0.43, 1.43)
Severe (SCr ≥3x baseline)	2	0.04 (0.01, 0.17)	5	0.11 (0.05, 0.26)	0.40 (0.08, 2.04)
Adjudicated clinical kidney adverse events					
Any event*	37	0.80 (0.58, 1.11)	42	0.92 (0.68, 1.24)	0.87 (0.56, 1.36)
Mild	24	0.52 (0.35, 0.77)	25	0.55 (0.37, 0.81)	0.95 (0.55, 1.67)
Moderate	11	0.24 (0.13, 0.43)	11	0.24 (0.13, 0.43)	1.00 (0.43, 2.29)
Severe	4	0.09 (0.03, 0.23)	8	0.17 (0.09, 0.35)	0.50 (0.15, 1.64)
New dialysis	1	0.02 (0.00, 0.15)	3	0.17 (0.09, 0.35)	0.34 (0.04, 3.17)

*Acute kidney injury presence and severity was defined by KDIGO (Kidney Disease: Improving Global Outcomes) classification.

CI, confidence interval; HR, hazard ratio; SCr, serum creatinine.

Disclosure of Interests: Jeffrey Sparks Consultant of: Dr. J Sparks has performed consultancy for Bristol-Myers Squibb, Gilead, Inova Diagnostics, Optum, and Pfizer unrelated to this work., Grant/research support from: Dr. J Sparks has received research support from Bristol-Myers Squibb., Kathleen Vanni: None declared, Matthew Sparks: None declared, Chang Xu: None declared, Leah Santacroce: None declared, Robert Glynn Grant/research support from: Dr. Glynn has received grant support unrelated to the present research from AstraZeneca, Kowa, Pfizer, and Novartis., Paul Ridker Consultant of: Dr. Ridker has served as a consultant to Corvidia, Inflazome, and CiviBioPharm., Grant/research support from: Dr. Ridker receives research support unrelated to the present study from Kowa, Novartis, and Amarin., Daniel Solomon Grant/research support from: Dr. Solomon receives research support unrelated to the present study from Abbvie, Amgen, Corrona, Genentech, Janssen, and Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.1627

Rheumatoid arthritis - non biologic treatment and small molecules - PART 2

POS0220

INTEGRATED SAFETY PROFILE OF UPADACITINIB WITH UP TO 4.5 YEARS OF EXPOSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. B. Cohen[1], R. Van Vollenhoven[2], J. R. Curtis[3], L. Calabrese[4], C. Zerbini[5], Y. Tanaka[6], L. Bessette[7], C. Richez[8], I. Lagunes-Galindo[9], J. Liu[9], H. Camp[9], Y. Song[9], S. Anyanwu[9], G. R. Burmester[10]. [1]*Metroplex Clinical Research Center, Rheumatology, Dallas, Texas, United States of America*; [2]*Amsterdam Rheumatology and Immunology Center, Rheumatology and Immunology, Amsterdam, Netherlands*; [3]*University of Alabama at Birmingham, Rheumatology, Birmingham, Alabama, United States of America*; [4]*Cleveland Clinic, Rheumatology, Cleveland, Ohio, United States of America*; [5]*Centro Paulista de Investigaçao Clínica, Rheumatology, São Paulo, Brazil*; [6]*University of Occupational and Environmental Health, Rheumatology, Kitakyushu, Japan*; [7]*Laval University, Rheumatology, Quebec City, Quebec, Canada*; [8]*Université de Bordeaux, Rheumatology, Bordeaux, France*; [9]*AbbVie Inc., Immunology, North Chicago, United States of America*; [10]*Charité University Medicine, Rheumatology, Berlin, Germany*

Background: The safety and efficacy of the oral Janus kinase inhibitor upadacitinib (UPA) has been evaluated across a spectrum of patients with rheumatoid arthritis (RA) in the phase 3 SELECT clinical program.[1–6]
Objectives: To describe the long-term integrated safety profile of UPA relative to active comparators (cutoff date: June 30, 2020) in patients with RA treated in the SELECT clinical program.
Methods: This analysis included updated data from 6 randomized controlled UPA RA trials.[1–6] Treatment-emergent adverse events (TEAEs; onset after first dose and ≤30 days after last dose of study drug or ≤70 days for adalimumab [ADA]) including AEs of special interest were summarized as follows: pooled UPA 15 mg once daily (QD; UPA15, 6 trials); pooled UPA 30 mg QD (UPA30, 4 trials); methotrexate (MTX, 1 trial), and ADA (1 trial). TEAEs were reported as exposure-adjusted adverse event rates (EAERs; events/100 patient-years [E/100 PY]), which included both incident and recurrent events.
Results: 4413 patients (UPA15, n=3209; UPA30, n=1204) received ≥1 dose of UPA, providing 10,115.4 PY of exposure. EAERs for AEs, serious AEs (SAEs), and AEs leading to discontinuation were similar for UPA15, MTX, and ADA; rates for UPA30 were numerically higher than UPA15 (Table 1). The most common AEs were upper respiratory tract infection, nasopharyngitis, and urinary tract infection for both UPA doses, and for UPA30 only, increased creatine phosphokinase (CPK). Pneumonia was the most common SAE for both UPA15 and UPA30. Serious infection rates were similar for UPA15, MTX, and ADA but higher for UPA30 (Figure 1). Rates of herpes zoster (HZ) were higher for both UPA groups (dose-dependent) vs MTX and ADA. Most HZ cases with UPA were non-serious (94%) and involved a single dermatome (74%). CPK elevations, which were mostly asymptomatic, were more common for both UPA groups (dose-dependent) vs MTX and ADA. EAERs of adjudicated gastrointestinal perforations were <0.1 and 0.2 E/100 PY for UPA15 and UPA30, respectively. Rates of non-melanoma skin cancer (due in part to more recurrent events with UPA30), anemia, and neutropenia were higher with UPA30 vs other treatment groups. Events of anemia and neutropenia were generally mild/moderate and treatment discontinuation due to these events was uncommon (<0.4%). Rates of other AEs of special interest, including major adverse cardiovascular and venous thromboembolic events, were broadly similar across treatment groups. The rate of deaths in UPA-treated patients with RA was not higher than expected for the general population (standardized mortality ratio [95% confidence interval (CI)]: UPA15, 0.43 [0.29, 0.63]; UPA30, 0.68 [0.40, 1.08]).
Conclusion: The updated safety profile of UPA with up to 4.5 years of exposure in patients with RA was comparable to previous analyses,[7] with no new safety signals reported. With the exception of HZ and elevated CPK, the safety profile of UPA15, the approved dose for RA, was similar to that observed for ADA.

REFERENCES:

[1] Burmester GR, et al. Lancet 2018;391:2503–12;
[2] Smolen JS, et al. Lancet 2019;393:2303–11;
[3] Fleischmann R, et al. Arthritis Rheumatol 2019;71:1788–800;
[4] Genovese MC, et al. Lancet 2018;391:2513–24;
[5] van Vollenhoven R, et al. Arthritis Rheumatol 2020;72:1607–20;
[6] Rubbert-Roth A, et al. N Engl J Med 2020;383:1511–21;
[7] Cohen SB, et al. Ann Rheum Dis 2020;79(Suppl 1):319–20.

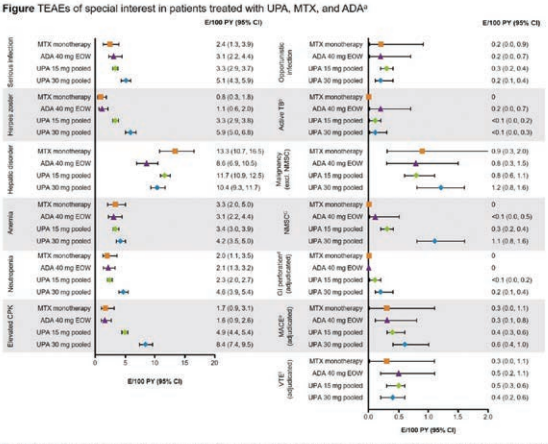
Table 1. TEAEs in patients treated with UPA, MTX, and ADA

	UPA 15 mg QD	UPA 30 mg QD	ADA 40 mg EOW	MTX
n	3209	1204	579	314
Exposure				
Total, PY	7023.8	3091.6	1051.8	637.4
Mean (SD), weeks	114 (64)	134 (66)	95 (70)	106 (67)
Median (range), weeks	136 (0, 232)	160 (0, 231)	118 (2, 231)	144 (1, 221)
E/100 PY (95% CI)				
Any AE	230.7 (227.2, 234.3)	283.6 (277.7, 289.6)	216.6 (207.8, 225.7)	227.8 (216.2, 239.8)
Any SAE	13.0 (12.2, 13.9)	18.8 (17.3, 20.4)	13.3 (11.2, 15.7)	10.4 (8.0, 13.2)
Any AE leading to discontinuation of study drug	5.6 (5.0, 6.1)	8.5 (7.5, 9.6)	6.8 (5.3, 8.5)	6.3 (4.5, 8.5)
Deaths[a]	0.4 (0.3, 0.6)	0.6 (0.3, 0.9)	0.9 (0.4, 1.6)	0.5 (0.1, 1.4)

[a]Both treatment and non-treatment-emergent deathsEOW, every other week

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Hilary Wong, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Figure TEAEs of special interest in patients treated with UPA, MTX, and ADA[a]



MTX: n=314, PY=637.4; ADA 40 mg EOW: n=579, PY=1051.8; UPA 15 mg pooled: n=3209, PY=7023.8; UPA 30 mg pooled: n=1204, PY=3091.6

AEs are defined using standardized MedDRA query or company MedDRA query search criteria

[a]Patients who switched from placebo, ADA, or MTX to UPA were included in the UPA analysis set from the start of UPA, while those who switched from UPA to ADA were included in the ADA analysis set from the start of ADA, and were censored at the time of switch. MTX monotherapy was censored at time of rescue to combination therapy (addition of UPA). [b]ADA, 2 events; UPA 15 mg, 6 events; UPA 30 mg, 3 events. [c]UPA 15 mg, 20 events reported in 20 patients (no recurrent events); UPA 30 mg, 35 events reported in 23 patients. [d]UPA 15 mg, 5 events; UPA 30 mg, 8 events. [e]MACE defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke. [f]VTE defined as deep vein thrombosis and pulmonary embolism

ADA, adalimumab; CI, confidence interval; CPK, creatine phosphokinase; E/100 PY, events per 100 patient-years; EOW, every other week; GI, gastrointestinal; MACE, major adverse cardiovascular event; MedDRA, Medical Dictionary for Regulatory Activities; MTX, methotrexate; NMSC, non-melanoma skin cancer; PY, patient-years; TB, tuberculosis; TEAE, treatment-emergent adverse event; UPA, upadacitinib; VTE, venous thromboembolic event

Disclosure of Interests: Stanley B. Cohen Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Gilead, Pfizer, Roche, and Sandoz, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Gilead, Pfizer, Roche, and Sandoz, Ronald van Vollenhoven Consultant of: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, Eli Lilly, GSK, Janssen, Medac, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Arthrogen, Bristol-Myers Squibb, Eli Lilly, GSK, Pfizer, and UCB, Jeffrey R. Curtis Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Crescendo, Janssen, Pfizer, Sanofi/Regeneron, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Crescendo, Janssen, Pfizer, Sanofi/Regeneron, and UCB, Leonard Calabrese Speakers bureau: AbbVie, Crescendo, Genentech, Horizon, Janssen, Novartis, and Sanofi, Consultant of: AbbVie, Bristol-Myers Squibb, Crescendo, Genentech, Gilead, GSK, Horizon, Janssen, Novartis, and Sanofi, Cristiano Zerbini Speakers bureau: MSD, Pfizer, and Sanofi, Consultant of: MSD, Pfizer, and Sanofi, Grant/research support from: Amgen, Eli Lilly, GSK, MSD, Novartis, Pfizer, Roche, Sanofi, and Servier, Yoshiya Tanaka Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, Gilead, GSK, Janssen, Mitsubishi Tanabe, Novartis, Pfizer, Sanofi, and YL Biologics, Grant/research support from: Asahi Kasei, Chugai, Daiichi Sankyo, Eisai, Mitsubishi Tanabe, Takeda, and UCB, Louis Bessette Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Christophe Richez Speakers bureau: AbbVie, Amgen, AstraZeneca, Biogen, Bristol-Myers Squibb, Eli Lilly, GSK, MSD, and Pfizer, Consultant of: AbbVie, Amgen, AstraZeneca, Biogen, Bristol-Myers Squibb, Eli Lilly, GSK, MSD, and Pfizer, Ivan Lagunes-Galindo Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Jianzhong Liu Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Heidi Camp Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Samuel Anyanwu Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Eli Lilly, Gilead, Janssen, MSD, Pfizer, Roche, and UCB, Consultant of: AbbVie, Eli Lilly, Gilead, Janssen, MSD, Pfizer, Roche, and UCB

DOI: 10.1136/annrheumdis-2021-eular.1856

POS0221 COMPARISON OF TOFACITINIB AND BARICITINIB BY INVERSE PROBABILITY OF TREATMENT WEIGHTING ANALYSES BASED ON PROPENSITY SCORE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL CLINICAL PRACTICE

Y. Miyazaki[1], S. Nakayamada[1], K. Nakano[1], S. Kubo[1], Y. Inoue[1], Y. Fujino[2], Y. Tanaka[1]. *[1]Hospital of University of Occupational and Environmental Health, The First Department of Internal Medicine, Kitakyushu, Japan*; *[2]Hospital of University of Occupational and Environmental Health, Department of Environmental Epidemiology, Institute of Industrial Ecological Sciences, Kitakyushu, Japan*

Background: Tofacitinib (TOFA) and baricitinib (BARI) have been widely used in many regions for treatment of rheumatoid arthritis (RA). The selection of JAK inhibitor for RA treatment based on patient type remains a major concern.
Objectives: The differences of efficacy between each Janus kinase (JAK) inhibitors have not been clarified in the patients with RA in clinical practice. Here, we compared the efficacy between TOFA and BARI in clinical practice.
Methods: A retrospective observational study. The efficacy of TOFA (n=156) in patients with RA was compared with BARI (n=138). Selection bias was reduced to a minimum using propensity score-based inverse probability of treatment weighting (IPTW). We analyzed the trajectories of changes in disease activity in patients receiving TOFA or BARI using growth mixture modeling (GMM). Multivariable logistic regression analysis was performed to identify factors contributing to belonging to treatment-resistance group defined by GMM. The observation period of the study was 24 weeks.
Results: No significant difference was observed in patient characteristics between the TOFA and BARI groups in after adjustment by propensity score-based IPTW. The retention rates over 24 weeks did not differ between the TOFA and BARI groups. No difference was observed in the incidence of adverse events in the TOFA and BARI groups. Clinical disease activity index (CDAI) at week 24 after the introduction of JAK inhibitors was 8.0 ± 8.9 and 6.2 ± 7.2 in the TOFA and BARI group, respectively. The rates of CDAI-remission at week 24 in the TOFA and BARI groups were 43/153 (28.3%) and 57/141 (40.4%), respectively. Compared to the TOFA group, the BARI group showed a significantly lower CDAI (⊿CDAI=-1.9, 95% confidence interval: -3.7 to -0.3, p=0.02) and a significantly higher rate of CDAI-remission (odds ratio: 1.7, 95% CI: 1.1–2.7, p=0.04) at week 24. Similarly, at week 24, SDAI was significantly lower in the BARI group (TOFA vs. BARI = 10.1 ± 9.9 vs. 7.3 ± 7.5, ⊿SDAI=-2.2, 95% CI: -4.2 to -0.2, p=0.04), and the rates of SDAI-remission (OR: 1.6, 95% CI: 1.0–2.6, p=0.04).
The patients were divided into two groups: patients with MDA to HDA at baseline (Group 1) and patients with HDA at baseline than Group 1 (Groups 2 and 3) based on the analysis of the trajectories of CDAI using GMM, In Groups 1 and 2, disease activity was improved immediately after the introduction of JAK inhibitors. In Group 3, disease activity was partially improved, and LDA was not achieved at week 24 after the introduction of JAK inhibitors. The patients in Group 3 were resistant to treatment (Group 3: treatment-resistance group).
When multivariable logistic regression analysis was performed for all patients receiving JAK inhibitors, the factors contributing to belonging to treatment-resistance group were: high baseline HAQ-DI score (OR: 1.76, 95% CI: 1.09–2.84, p=0.02) and high number of biological disease-modifying anti-rheumatic drugs (bDMARDs) used before JAK inhibitors (OR: 1.51, 95% CI: 1.16–1.95, p=0.002) and TOFA use (OR: 2.13, 95% CI: 1.05–4.30, p=0.03).
Next, multivariable logistic regression analysis was separately performed for each treatment group. The patients receiving more bDMARDs before the JAK inhibitor were more likely to belong to treatment-resistance group in the TOFA group (OR: 1.76, 95% CI: 1.24–4.06). Among patients with RA who received TOFA, those who had received ≥4 bDMARDs before the introduction of TOFA were more likely to be classified into the treatment-resistant group.
In the BARI group, multivariable logistic regression analysis did not identify any factors associated with belonging to treatment-resistance group.
Conclusion: TOFA may be partially effective in patients resistant to many bDMARDs. Consequently, efficacy may differ between TOFA and BARI. Because TOFA was less effective in RA patients resistant to ≥4 bDMARDs, the present study suggests that BARI may be more appropriate for RA patients resistant to many bDMARDs.

Disclosure of Interests: Yusuke Miyazaki Speakers bureau: Eli Lilly, Shingo Nakayamada Speakers bureau: Bristol-Myers, UCB, Astellas, Abbvie, Eisai, Pfizer, Takeda, Kazuhisa Nakano Speakers bureau: Bristol-Myers, Sanofi, AbbVie, Eisai, Eli Lilly, Chugai, Pfizer, Takeda, and Mitsubishi-Tanabe, Satoshi Kubo Speakers bureau: Bristol-Myers, Yoshino Inoue: None declared, Yoshihisa Fujino: None declared, Yoshiya Tanaka Speakers bureau: Abbvie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD, and Santen

DOI: 10.1136/annrheumdis-2021-eular.2012

POS0222 PREDICTORS OF RESPONSE: BASELINE CHARACTERISTICS AND EARLY TREATMENT RESPONSES ASSOCIATED WITH ACHIEVEMENT OF REMISSION AND LOW DISEASE ACTIVITY AMONG UPADACITINIB-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS

A. Kavanaugh[1], Z. Szekanecz[2], E. C. Keystone[3], A. Rubbert-Roth[4], S. Hall[5], R. Xavier[6], J. Polido-Pereira[7], I. H. Song[8], N. Martin[9], Y. Song[8], S. Anyanwu[8], P. Nash[10]. *[1]University of California San Diego, Division of Rheumatology, Allergy and Immunology, Department of Medicine, San Diego, California, United States of America*; *[2]University of Debrecen, Division of Rheumatology, Faculty of Medicine, Debrecen, Hungary*; *[3]MaRS Center, Rheumatology, Toronto, Ontario, Canada*; *[4]Kantonsspital St. Gallen, Rheumatology, St. Gallen, Switzerland*; *[5]Emeritus Research and Monash University, Rheumatology, Melbourne, Victoria, Australia*; *[6]Hospital de Clínicas de Porto Alegre, Serviço de Reumatologia, Porto Alegre, Brazil*; *[7]Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte and Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisbon Academic Medical Centre, Lisbon, Portugal*; *[8]AbbVie Inc., Immunology, North Chicago, Illinois, United States of America*; *[9]AbbVie Inc., Immunology, Saint Laurent, Quebec, Canada*; *[10]University of Queensland, Rheumatology, Brisbane, Queensland, Australia*

Background: Upadacitinib (UPA) 15 mg once daily (QD) has demonstrated efficacy in phase 3 studies of patients with rheumatoid arthritis (RA).1–4 Early prediction of response to treatment with UPA could help to optimize therapy.
Objectives: To identify baseline (BL) characteristics or Week (Wk) 12 disease activity measures that may predict the achievement of remission (REM) or low disease activity (LDA) at 6 months in patients with RA receiving UPA 15 mg.
Methods: This ad hoc analysis included patients who were randomized to UPA 15 mg QD, as monotherapy in methotrexate (MTX)-naïve patients (SELECT-EARLY) or in combination with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), in patients with an inadequate response (IR) to MTX (SELECT-COMPARE) or ≥1 tumor necrosis factor inhibitors (TNFis) (SELECT-BEYOND and SELECT-CHOICE). The association of BL characteristics (including age, disease duration, prior/concomitant treatments, C-reactive protein [CRP], seropositivity, and disease activity) and Wk 12 disease activity parameters with the achievement of Clinical Disease Activity Index (CDAI) REM (≤2.8) or LDA (≤10) at Wk 24 (or Wk 26 in SELECT-COMPARE) was assessed by concordance statistics (C-statistics), or area under the

receiver operator characteristic curve. C-index values and 95% confidence intervals were calculated by fitting a univariate logistic regression model for: demographic and BL characteristics, Wk 12 disease activity measures, and change from BL at Wk 12 in disease activity measures. A multivariate logistic regression with stepwise model selection was also performed. The proportion of patients achieving Wk 24/26 CDAI REM/LDA was stratified by ≥50% improvement from BL in swollen and/or tender joint count in 66/68 joints (SJC66/TJC68).

Results: A total of 1377 patients were included in the analysis. Across the 4 studies, CDAI REM and LDA were achieved in 11.0–28.4% and 50.0–58.6% of patients, respectively (Table 1). BL demographics and disease characteristics were weakly predictive (C-index <0.70) of Wk 24/26 CDAI REM (C-index 0.49–0.69) or LDA (C-index 0.47–0.65), with the exception of BL Health Assessment Questionnaire-Disability Index in SELECT-BEYOND, which was moderately predictive of CDAI REM (C-index 0.73). Changes from BL in disease activity measures at Wk 12 were weakly or moderately predictive of Wk 24/26 CDAI REM (Figure 1) or LDA. CDAI value at Wk 12 was strongly predictive (C-index >0.80) of Wk 24/26 CDAI REM or LDA. Disease Activity Score in 28 joints using CRP and pain at Wk 12 were strongly predictive of Wk 24/26 CDAI REM (except in SELECT-CHOICE). Physician's global assessment at Wk 12 was the only common predictor in the multivariate regression models for CDAI REM/LDA at Wk 24/26 across the 4 studies. A greater proportion of patients achieving ≥50% improvement in SJC66 and TJC68 at Wk 12 achieved CDAI REM (16.5–37.8% vs 0–9.4%) or LDA (66.0–72.8% vs 20.9–35.7%) at Wk 24/26 than those who did not.

Conclusion: BL characteristics did not strongly predict response to UPA, but composite disease activity scores at Wk 12 predicted Wk 24/26 REM/LDA with UPA 15 mg QD across MTX-naïve, MTX-IR, and TNFi-IR patients. ≥50% improvement in SJC/TJC at Wk 12 was also associated with Wk 24/26 REM/LDA.

REFERENCES:

[1] van Vollenhoven R, et al. Arthritis Rheumatol 2020;72:1607–20; 2. Genovese MC, et al. Lancet 2018;391:2513–24; 3. Fleischmann R, et al. Arthritis Rheumatol 2019;71:1788–800; 4. Rubbert-Roth A, et al. N Engl J Med 2020;383:1511–21.

Table 1. Achievement of CDAI LDA and REM at Wk 24/26[a]

	SELECT-EARLY	SELECT-COMPARE	SELECT-BEYOND	SELECT-CHOICE
Patient population	MTX-naïve	MTX-IR	TNFi-IR	TNFi-IR
Treatment	UPA 15 mg mono-therapy (n=317)	UPA 15 mg + MTX (n=651)	UPA 15 mg + csDMARD (n=146)	UPA 15 mg + csDMARD (n=263)
Efficacy at Wk 24/26[a], n (%)				
CDAI REM (≤2.8)	90 (28.4)	150 (23.0)	16 (11.0)	60 (22.8)
CDAI LDA (≤10)	178 (56.2)	343 (52.7)	73 (50.0)	154 (58.6)

[a] Wk 26 for SELECT-COMPARE only

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Laura Chalmers, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

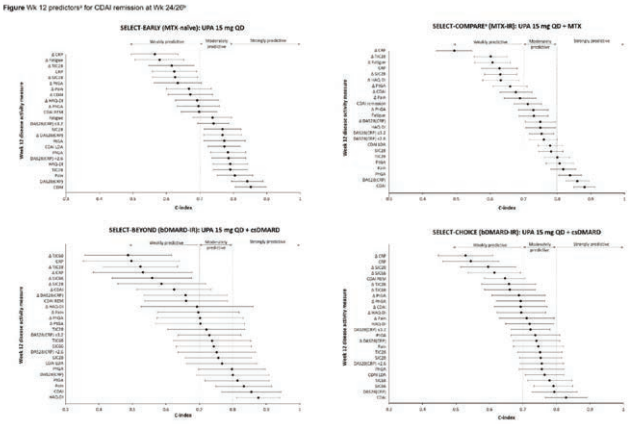


Figure Wk 12 predictors* for CDAI remission at Wk 24/26†

*Determined by a univariate logistic regression model. C-statistics provide a C-index value from 0.5 (chance prediction) to 1 (perfect prediction). Error bars indicate 95% CI. † Wk 26 for SELECT-COMPARE only.

CRP, C-reactive protein; DAS28(CRP), Disease Activity Score in 28 joints using C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; PhGA, Physician Global Assessment; PtGA, Patients Global Assessment; SJC28/66, swollen joint count in 28/66 joints; TJC28/68, tender joint count in 28/68 joints

Disclosure of Interests: Arthur Kavanaugh Consultant of: Janssen, Grant/research support from: Janssen, Zoltán Szekanecz: None declared, Edward C. Keystone Speakers bureau: Abbott, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Eli Lilly, Genentech, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Consultant of: Abbott, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Eli Lilly, Genentech, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Grant/research support from: Abbott, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Eli Lilly, Genentech, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Andrea Rubbert-Roth Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Chugai, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and Sanofi, Stephen Hall Grant/research support from: Pfizer, Ricardo Xavier: None declared, Joaquim Polido-Pereira: None declared, In-Ho Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Naomi Martin Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Samuel Anyanwu Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2137

POS0223 PATTERNS OF JANUS KINASE INHIBITOR CYCLING FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS IN REAL-WORLD CLINICAL PRACTICE: AN ANALYSIS OF THE OPAL DATASET

S. Ciciriello[1,2], T. Smith[1], C. Osullivan[1], K. Tymms[1,3], P. Youssef[1,4], D. Mathers[1,5], C. Deakin[1], H. Griffiths[1,6], G. Littlejohn[1,7]. [1]*OPAL Rheumatology, Ltd., Sydney, Australia*; [2]*Dept. Rheumatology, Royal Melbourne Hospital, Melbourne, Australia*; [3]*Canberra Rheumatology, Canberra, Australia*; [4]*Dept. Rheumatology, Royal Prince Alfred Hospital, Camperdown, Australia*; [5]*Georgetown Arthritis, Georgetown, Australia*; [6]*Barwon Rheumatology, Services, Geelong, Australia*; [7]*Dept. of Medicine, Monash University, Clayton, Australia*

Background: There are currently eleven biologic and targeted synthetic (b/ts) DMARDs acting via five different modes of action available for the treatment of RA in Australia. The cost of b/tsDMARDs is subsidized by government for patients that have active RA despite six months of combination csDMARD therapy. Once a patient is eligible, the clinician can prescribe the b/tsDMARD they deem to be the most clinically appropriate for the patient. In Oct 2015 the first JAK inhibitor (JAKi) became available in Australia (tofacitinib, TOF), baricitinib (BARI) became available in Sept 2018, and upadacitinib (UPA) in May 2020. Each of these oral tsDMARDs possess different selectivity profiles towards different members of the JAK family (JAK1–3 and Tyk2).

Objectives: The aim of this analysis was to determine the patterns of JAKi cycling in real-world practice in Australia.

Methods: Deidentified clinical data were sourced from the OPAL dataset, which is collected in a custom-built electronic medical record during the routine consultation[1]. Data from patients >18 years with RA who commenced a b/tsDMARD between Jan-2007 and Dec-2020 were included in the analysis. A visual analytics software program was used to display data on medication initiation and cessation dates, and reasons for stopping tsDMARDs, which is recorded in the medical record at the time of the decision.

Results: At Dec 2020, 28% of the 52,190 patients with RA in the OPAL dataset were prescribed b/tsDMARDs. Of these patients, 3,850 (26.3%) were currently prescribed a JAKi with 51.4% receiving TOF, 29.2% BARI and 19.4% UPA. In 2020, JAKi initiations accounted for 48.8% of all initiations and 30.7% of 1st line initiations; an increase of 6.1% and 3.5% from 2019, respectively. The percentage of patients switching from a first line JAKi to a second line JAKi rather than an agent with another mode of action increased from 33.1% in 2019 to 42.6% in 2020. This is despite 26.2% in 2019 and 45.8% in 2020 of the patients switching to another JAKi citing lack of efficacy as the reason for JAKi discontinuation. In the period between May 2020, when a third JAKi (UPA) become available, and Dec 2020, the majority of patients switching from first line TOF or BARI to another JAKI switched to UPA (69.4% and 83.9%, respectively), whilst 30.6% of first line TOF patients switched to BARI (30.6%), and 16.1% of first line BARI patients switched to TOF in second line. The majority of patients switching from second line TOF or BARI to a third line JAKi switched to UPA (73% and 96%, respectively), with 27% of second line TOF patients switching to BARI and a very low number moving from second line BARI to TOF (4%). JAKi choice after a third line TOF or BARI was almost exclusively UPA (86.2% and 95.5%, respectively).

Conclusion: There has been significant and sustained uptake of JAKi for the management of RA in Australia and JAKi cycling is increasingly common in routine clinical care. Clinical outcomes and persistence following JAKi cycling requires further investigation.

REFERENCES:

[1] Littlejohn GO, Tymms KE, Smith T, Griffiths HT. Using big data from real-world Australian rheumatology encounters to enhance clinical care and research. Clin Exp Rheumatol. Sep-Oct 2020;38(5):874-880.

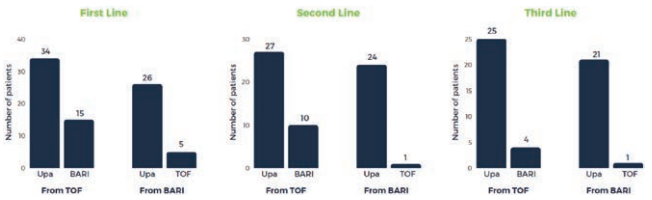


Figure 1. Patterns of JAKi cycling for the management of rheumatoid arthritis in first, second and third line switching.

Acknowledgements: The authors acknowledge the members of OPAL Rheumatology Ltd and their patients for providing clinical data for this study, and Software4Specialists Pty Ltd for providing the Audit4 platform
Disclosure of Interests: Sabina Ciciriello: None declared, Tegan Smith: None declared, Catherine OSullivan: None declared, Kathleen Tymms: None declared, Peter Youssef: None declared, David Mathers: None declared, Claire Deakin: None declared, Hedley Griffiths Consultant of: AbbVie, Gilead, Novartis and Lilly., Geoff Littlejohn Speakers bureau: Over the last 5 years Geoffrey Littlejohn has received educational grants and consulting fees from AbbVie, Bristol Myers Squibb, Eli Lilly, Gilead, Novartis, Pfizer, Janssen, Sandoz, Sanofi and Seqirus.
DOI: 10.1136/annrheumdis-2021-eular.2256

POS0224 SELECTIVITY OF CLINICAL JAK INHIBITORS AND THE IMPACT ON NATURAL KILLER (NK) CELL FUNCTIONAL RESPONSES

P. Gonzalez-Traves[1], L. Simpson[1], B. Murray[2], A. Meng[3], J. A. Di Paolo[4], E. Grant[1], G. Min-Oo[1]. *[1]Gilead Sciences, Inflammation Biology, Foster City, United States of America*; *[2]Gilead Sciences, Drug Metabolism, Foster City, United States of America*; *[3]Gilead Sciences, Clinical Pharmacology, Foster City, United States of America*; *[4]Gilead Sciences, External Innovation, Foster City, United States of America*

Background: Janus kinase (JAK) inhibitors (JAKinibs) show similar efficacy in rheumatoid arthritis (RA). However, in vitro studies have shown differences in JAK selectivity profiles for baricitinib (BARI), tofacitinib (TOFA), upadacitinib (UPA) and filgotinib (FIL).[1,2] These lead to distinct pharmacologic profiles in cellular signaling assays that may impact clinical efficacy or safety[1]. NK cells are innate lymphocytes important in anti-pathogen responses and immune surveillance, which function via production of cytokines and cell killing[3]. NK cell proliferation and IFNγ production are JAK-dependent pathways and may be modulated by JAKinibs. Clinical findings show transient decreases in NK cell numbers in patients treated with JAKinibs, but the link to safety is unclear[4]
Objectives: To extend upon findings in proximal cell signaling assays, we compared the selectivity and potency of clinical JAKinibs on NK cell function by assessing proliferation mediated by IL-15 (JAK1/3) and IFN-γ production driven by IL-12 (JAK2/TYK2)+IL-18.
Methods: NK cells were isolated from healthy donor PBMC, incubated in vitro with 8 concentrations of each evaluated JAKinib (TOFA, BARI, FIL, FIL metabolite, UPA) and stimulated with IL-15 for proliferation or IL-12/18 for IFNγ production. Proliferation was assessed by Cell Trace dye dilution after 6 days and IFNγ production by intracellular flow cytometry 4hrs post-stimulation. Half maximal inhibitory concentration (IC_{50}) values were calculated for $CD56^{bright}$, $CD56^{dim}$, and total NK cells. Steady-state pharmacologic profile over a clinical dosing interval was modeled using concentration-time profiles from JAKinib population pharmacokinetic data in RA subjects under the therapeutic dose[5-7]. For each JAKinib, the time above IC_{50} and average daily inhibition of IFNγ or proliferation were calculated for each NK cell population in each donor.
Results: Cellular assays in purified NK cells showed dose-dependent inhibition of IL-15-induced proliferation by all JAKinibs with TOFA showing the highest average inhibition and time above IC_{50} (35-60% inhibition for 8-15 hrs; TOFA>UPA>BARI≈FIL). The differences between JAKinibs are in line with differences in pSTAT inhibition downstream of IL-15[1]. Interestingly, IL-12/18-induced production of IFNγ, which is mediated via JAK2/TYK2 (IL-12) and non-JAK dependent pathways (IL-18), showed weaker inhibition for all compounds. Moreover, all JAKinibs showed <25% average inhibition of IFNγ production over 24hrs and did not show any time above IC_{50} for IFNγ production or pSTAT4 inhibition at clinical doses. $CD56^{dim}$ and $CD56^{bright}$ sub-populations of NK cells are proposed to have distinct functions and unique expression of surface receptors. Analysis of the IC_{50} for pSTAT4 and IFNγ production showed ~2-10-fold weaker inhibition by JAKinibs in $CD56^{bright}$ NK cells, suggesting less dependence on JAK-dependent signals in $CD56^{bright}$ NK cells than $CD56^{dim}$ NK cells.
Conclusion: NK cell proliferation depends on JAK1 and JAK3-mediated signaling and is differentially inhibited at clinical doses of distinct JAKinibs. In contrast, functional responses downstream of JAK2/TYK2-dependent IL-12/18 were not substantially inhibited by any of the JAKinibs studied. Inhibition of functional and proliferative responses in purified NK cells aligned well with proximal pSTAT inhibition. JAKinib modulation of NK cell proliferation, but not response to IL-12, reflects unique pharmacologic profiles of the drugs studied and could be one component underlying clinical safety observations, including increased risk of viral infections or malignancy[4].
REFERENCES:
[1] Traves PG et al. *Ann Rheum Dis* 2021 (in press)
[2] McInnes IB, et al. *Arthritis Res Ther* 2019;21:183.
[3] Cooper MA, Fehniger TA, Caligiuri MA. *Trends Immunol* 2001 Nov;22(11):633-40.
[4] Winthrop KL. *Nat Rev Rheumatol* 2017; 13(4):234-243
[5] Zhang X, et al. *CPT Pharmacometrics Syst Pharmacol* 2017;6(12):804-13.
[6] CDER. Application Number: 203214Orig1s000. NDA 203214: Tofacitinib.
[7] Klunder B et al. *Clin Pharmacokinet* 2019;58(8):1045-58.
Disclosure of Interests: Paqui Gonzalez-Traves Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Laura Simpson Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Bernard Murray Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Amy Meng Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Julie A. Di Paolo Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Ethan Grant Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Gundula Min-Oo Shareholder of: Gilead Sciences, Employee of: Gilead Sciences
DOI: 10.1136/annrheumdis-2021-eular.2741

POS0225 RISK OF MAJOR CARDIOVASCULAR EVENT ACROSS JAK INHIBITOR TREATED PATIENTS: ANALYSIS OF A NATIONAL CLAIM DATABASE

A. Gouverneur[1,2], J. Avouac[3], C. Prati[4], J. L. Cracowski[5], T. Schaeverbeke[6], A. Pariente[1,2], M. E. Truchetet[6]. *[1]University of Bordeaux, Inserm, Bordeaux Population Health Research Center, Pharmacoepidemiology Team, UMR 1219, Bordeaux, France*; *[2]CHU of Bordeaux, Pôle de Santé Publique, Service de Pharmacologie, Bordeaux, France*; *[3]Université de Paris, Service de Rhumatologie, Hôpital Cochin, AP-HP.CUP, Paris, France*; *[4]University Hospital - CHU Minjoz, Rheumatology Unit, Besancon, France*; *[5]Université Grenoble Alpes, INSERM, HP2, Grenoble, France*; *[6]CHU de Bordeaux, Hôpital Pellegrin, Department of Rheumatology, National Reference Center for Systemic Autoimmune Rare Diseases, Bordeaux, France*

Background: Inhibiting a specific JAK may impede more than one pathway, explaining both the efficacy and adverse effects observed with JAK inhibitors (JAKi). Among those, there have been recent concerns about potential thromboembolic risks with these drugs. As patients enrolled are not representative of all patients who may receive JAKi, data from trials are unlikely to provide definitive answers. Real impact of JAKi in real life on major cardiovascular events is not known.
Objectives: To evaluate the risk of venous and arterial thromboembolic events with the use of JAKi in a real-world setting.
Methods: A self-controlled case series analysis (method in which individuals act as their own control) was performed using data from the French national healthcare insurance system SNDS ("Système National des Données de Santé"), which included all anonymized individual level data about sociodemographic data, outpatient healthcare dispensed, hospital discharge summaries, and registration status for a list of 30 long term diseases. All patients treated by JAKi (baricitinib or tofacitinib) for rheumatoid arthritis, psoriasis arthritis and/or inflammatory bowel disease, and with at least one thromboembolic event (venous (VTE): deep vein thrombosis (DVT), pulmonary embolism (PE), arterial (ATE): acute coronary syndrome (ACS), myocardial infarction (MI), transient ischemic attack (TIA) and stroke) between 2017/11/01 and 2019/06/30 were included in the study. Associations were evaluated by incidence rate ratios (IRR), which compare the rate of events during exposed periods with rate of event during all other observed time periods. Exposed periods were defined as i) exposure to JAKi, ii) the month following exposure (post-exposure 1-30 days), and iii) long-term post-exposure (31 to 60 days). A pre-exposure period of 7 days was individualized to identify event-dependent probabilities of exposure and potential reverse causality bias, and all other periods were considered as non-exposed periods.
Results: Among the 5,870 patients treated with JAKi between 2017/11/01 and 2019/06/30, 94 presented an incident thromboembolic event and were included. Almost two thirds were female (n=61, 64.9%), and median age was 65.4 [IQR: 55.5; 75.8] years. Most of patients have a rheumatoid arthritis (n=91, 96.8%), 62 (66.0%) were treated by baricitinib, and 32 (34.0%) by tofacitinib. Almost half (n=42, 44.7%) presented a venous thromboembolism, mainly DVT (n=31, 33.0%), and 52 (55.3%) presented an arterial thromboembolism, mainly MI (n=16, 17.0%) and stroke (n=14, 14.9%). Eleven patients (11.7%) died during the study period. The median time of occurrence of VTE was 4.3 [IQR: 2.5; 8.9] months, and 6.1 [IQR: 3.3; 9.2] months for ATE.

The median duration of exposure was 6.0 [IQR: 3.3; 10.1] months for VTE, and 12.0 [IQR: 4.8; 15.3] months for ATE. The IRR for VTE and ATE were increased during exposure, and during the 30 days following exposure (Table 1). The IRR for VTE was only increased during exposure and in the early post-exposure phase contrary to the IRR for ATE that was also increased in the pre-exposure 7-Day period. Analysis conducted on survival patients confirmed results.

Conclusion: The present study found an increased risk of VTE and ATE for baricitinib and tofacitinib. The risk persists in the month following the discontinuation of treatment but disappears after day 30 post-exposure.

Table 1.

	N	Patient-years	IRR	95%CI
Venous thromboembolic events				
Non-exposure (reference)	8	3975.0	1	-
Pre-exposure to JAK-i	1	135.2	4.7	0.6-38.0
Exposure to JAK-i	27	2090.5	9.8	4.1-23.3
Post-exposure 1-30 d	5	369.0	6.2	1.9-19.9
Post-exposure 31-60 d	1	139.0	1.5	0.2-12.6
Arterial thromboembolic events				
Non-exposure (reference)	7	4076.8	1	-
Pre-exposure to JAK-i	3	344.1	11.5	2.8-46.8
Exposure to JAK-i	32	6363.8	7.4	2.9-18.7
Post-exposure 1-30 d	8	659.2	11.5	3.8-34.6
Post-exposure 31-60 d	2	132.2	4.3	0.8-22.0

Disclosure of Interests: Amandine Gouverneur: None declared, Jérôme Avouac Consultant of: JA has/had consultancy relationship and/or has received research funding in the area of potential treatments for rheumatoid arthritis from (last three years): Abbvie, Galapagos, Pfizer, Bristol Myers Squibb, Sanofi, Nordic Pharma, Chugai and MSD., Grant/research support from: JA has/had consultancy relationship and/or has received research funding in the area of potential treatments for rheumatoid arthritis from (last three years): Abbvie, Galapagos, Pfizer, Bristol Myers Squibb, Sanofi, Nordic Pharma, Chugai and MSD., Clément Prati: None declared, Jean-Luc Cracowski: None declared, Thierry Schaeverbeke Consultant of: TS consultancy and/or research fundings: Abbvie, Lilly, Pfizer, Galapagos, Novartis, BMS, Medac, NordicPharma, Biogen, Mylan, Janssen., Grant/research support from: TS consultancy and/or research fundings: Abbvie, Lilly, Pfizer, Galapagos, Novartis, BMS, Medac, NordicPharma, Biogen, Mylan, Janssen., Antoine Pariente Grant/research support from: AP reports acting as an independant expert towards the French Medicines Agency (Agence Nationale de Securité du Médicament et des Produits de Santé, ANSM) and the European Medicines Agency (EMA). AP coordinates the DRUGS Systematised Assessment in real-liFe EnviRonment (DRUGS-SAFER) programme funded by the Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM)., Marie-Elise Truchetet Consultant of: has/had consultancy relationship and/or has received research funding in the area of potential treatments for rheumatoid arthritis and spondyloarthritis and their complications from (last three years): Abbvie, Galapagos, Lilly, Medac, Novartis, Pfizer, and Roche., Grant/research support from: has/had consultancy relationship and/or has received research funding in the area of potential treatments for rheumatoid arthritis and spondyloarthritis and their complications from (last three years): Abbvie, Galapagos, Lilly, Medac, Novartis, Pfizer, and Roche.

DOI: 10.1136/annrheumdis-2021-eular.2976

Spondyloarthritis - treatment

POS0226

BIMEKIZUMAB LONG-TERM SAFETY AND EFFICACY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: 3-YEAR RESULTS FROM A PHASE 2B STUDY

D. Van der Heijde[1], A. Deodhar[2], L. S. Gensler[3], D. Poddubnyy[4], A. Kivitz[5], M. Dougados[6], N. De Peyrecave[7], M. Oortgiesen[8], T. Vaux[9], C. Fleurinck[7], X. Baraliakos[10]. *[1]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; *[2]Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America*; *[3]University of California San Francisco, Department of Rheumatology, San Francisco, United States of America*; *[4]Charité – Universitätsmedizin Berlin, Department of Rheumatology, Berlin, Germany*; *[5]Altoona Center for Clinical Research, Altoona Arthritis & Osteoporosis Center, Duncansville, United States of America*; *[6]Hôpital Cochin, Department of Rheumatology, Paris, France*; *[7]UCB Pharma, N/A, Brussels, Belgium*; *[8]UCB Pharma, N/A, Raleigh, United States of America*; *[9]UCB Pharma, N/A, Slough, United Kingdom*; *[10]Ruhr-University Bochum, Rheumazentrum Ruhrgebiet Herne, Herne, Germany*

Background: Bimekizumab (BKZ), a monoclonal antibody that selectively inhibits interleukin (IL)-17A and IL-17F, has demonstrated clinical efficacy and safety in patients with ankylosing spondylitis (AS) treated over a period up to 96 weeks.[1,2]

Objectives: To report 3-year interim safety and efficacy of BKZ in patients with active AS from a phase 2b dose-ranging study (BE AGILE; NCT02963506) and its ongoing open-label extension (OLE; NCT03355573).

Methods: BE AGILE study design has been described previously.[1] Patients treated with BKZ 160 mg or 320 mg every 4 weeks (Q4W) at Week 48 in BE AGILE were eligible for OLE entry. All OLE patients received BKZ 160 mg Q4W. Treatment-emergent adverse events (TEAEs) are reported for the BE AGILE safety set (patients who received ≥1 dose of BKZ on study entry) for total exposure to BKZ across BE AGILE and the OLE. Efficacy outcomes are reported for the OLE full analysis set (patients who entered the OLE and had ≥1 dose of BKZ and ≥1 valid efficacy variable measurement in the OLE), and include: ASAS40, ASAS20, ASAS PR, ASDAS, ASDAS-CII, ASDAS-MI, ASDAS-ID (<1.3) and ASDAS <2.1. Data are reported as imputed (multiple imputation [MI] based on the missing at random assumption, or non-responder imputation [NRI]) and as observed case (OC).

Results: 262/303 (86%) patients randomised at BE AGILE study baseline completed Week 48 on BKZ 160 mg or 320 mg. At Week 48, 255/262 (97%) patients entered the OLE (full analysis set: 254); 219 patients had an efficacy assessment at Week 156. Over the 156 weeks, the exposure-adjusted incidence rate (EAIR) per 100 patient-years (PY) of TEAEs was 143.5, with an EAIR of 5.8 for serious TEAEs, 1.3 for serious infections, and 3.8 for *Candida* infections (Table 1). All *Candida* infections were mild or moderate; none were systemic or led to study discontinuation. Over 156 weeks, the EAIR of inflammatory bowel disease (1.2), anterior uveitis (0.8), and injection site reactions (0.5) remained low. Efficacy demonstrated at Week 48 in BE AGILE was maintained or improved up to Week 156 (Figure 1). Mean ASDAS improved from 3.9 at BE AGILE baseline to 2.0 and 1.8 at Weeks 48 and 156 respectively (by MI). At Week 156 in the NRI analyses, ASAS40 and ASAS PR were achieved by 62.6% (OC: 72.6%) and 32.7% (OC: 37.9%) patients respectively. ASDAS-ID and ASDAS <2.1 responder rates (NRI) were maintained or continued to increase from Week 48, and by Week 156, responses were achieved by 28.0% (OC: 33.0%) and 57.1% (OC: 67.4%) patients respectively. ASDAS-MI responder rates (NRI) continued to increase from 44.9% at Week 48 to 46.5% at Week 156 (OC: 52.9%).

Conclusion: The safety profile of BKZ in patients with AS was in line with previous observations.[1,2] Patients treated with BKZ demonstrated sustained and consistent efficacy over 156 weeks.

REFERENCES:

[1] van der Heijde D. Ann Rheum Dis 2020;79:595–604; **2.** Baraliakos X. Arthritis Rheumatol 2020;72 (suppl 10).

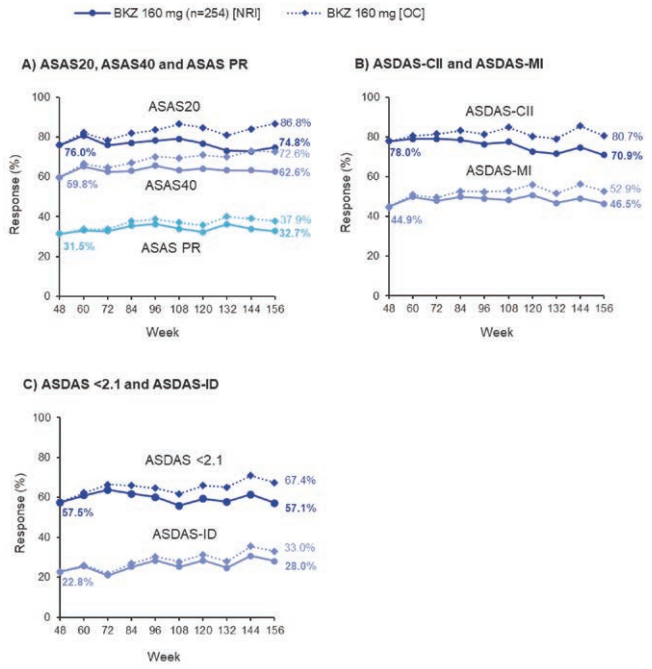
Table 1. Safety for total exposure to BKZ across BE AGILE and the OLE

	BE AGILE Weeks 0–48			BE AGILE + OLE Weeks 0–156
n (%) [EAIR/100 PY]	BKZ 160 mg (n=149; 114.2 PY)	BKZ 320 mg (n=150; 119.6 PY)	All BKZ (N=303; 261.3 PY)	All BKZ (N=303; 781.0 PY)
Any TEAE	103 (69.1) [168.7]	122 (81.3) [221.1]	235 (77.6) [186.2]	280 (92.4) [143.5]
Serious TEAEs	5 (3.4) [4.4]	6 (4.0) [5.1]	13 (4.3) [5.1]	43 (14.2) [5.8]
Key TEAEs of special monitoring				
Serious infections	3 (2.0) [2.7]	1 (0.7) [0.8]	4 (1.3) [1.5]	10 (3.3) [1.3]
Candida infections	10 (6.7) [9.1]	9 (6.0) [7.9]	19 (6.3) [7.5]	28 (9.2) [3.8]
Inflammatory bowel disease	1 (0.7) [0.9]	2 (1.3) [1.7]	4 (1.3) [1.5]	9 (3.0) [1.2]
Anterior uveitis	1 (0.7) [0.9]	1 (0.7) [0.8]	2 (0.7) [0.8]	6 (2.0) [0.8]
Study discontinuations due to TEAEs	7 (4.7)	10 (6.7)	20 (6.6)	38 (12.5)
Drug-related TEAEs	48 (32.2)	54 (36.0)	110 (36.3)	149 (49.2)
Deaths	1 (0.7)	0	1 (0.3)	2 (0.7)

TEAEs are reported for the BE AGILE safety set for total exposure to BKZ across BE AGILE and the OLE. There was one death in BE AGILE (cardiac arrest) and one in the OLE (road traffic accident); neither was considered treatment-related.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical.

Figure. Efficacy responses from Week 48 to Week 156 (NRI and OC)



Full analysis set (N=254). Patients received BKZ 160 mg or 320 mg during the BE AGILE dose-ranging study. Missing data were imputed using NRI. ASAS: Assessment of SpondyloArthritis international Society; ASAS20/40: ASAS 20%/40% response; ASAS PR: ASAS partial remission; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-CII: ASDAS clinically important improvement (≥1.1 decrease from baseline ASDAS score); ASDAS-ID: ASDAS inactive disease (ASDAS<1.3); ASDAS-MI: ASDAS major improvement (≥2.0 decrease from baseline ASDAS score or achievement of lowest possible ASDAS score [0.6]); BKZ: bimekizumab; NRI: non-responder imputation; OC: observed case; OLE: open-label extension.

Disclosure of Interests: Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma, Employee of: Director of Imaging Rheumatology, Atul Deodhar Speakers bureau: Janssen, Novartis, Pfizer, Consultant of: AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Gilead, GSK, Janssen, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB Pharma, Lianne S. Gensler Consultant of: AbbVie, Eli Lilly, Gilead, GSK, Novartis, Pfizer, UCB Pharma, Grant/research support from: Pfizer, Denis Poddubnyy Speakers bureau: AbbVie, BMS, Eli Lilly, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Biocad, Eli Lilly, Gilead, GSK, MSD, Novartis, Pfizer, Samsung Bioepis, UCB Pharma, Grant/research support from: AbbVie, MSD, Novartis, Pfizer, Alan Kivitz Shareholder of: Pfizer, Novartis, Speakers bureau: Amgen, Eli Lilly, Pfizer, Novartis, Consultant of: Novartis, UCB Pharma, Maxime Dougados Consultant of: AbbVie, Eli Lilly, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Eli Lilly, Novartis, Pfizer, UCB Pharma, Natasha de Peyrecave Employee of: UCB Pharma, Marga Oortgiesen Employee of: UCB Pharma, Thomas Vaux Employee of: UCB Pharma, Carmen Fleurinck Employee of: UCB Pharma, Xenofon Baraliakos Speakers bureau: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma, Paid instructor for: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma

DOI: 10.1136/annrheumdis-2021-eular.156

POS0227 SHOULD ALL PATIENTS TRIAL SUBCUTANEOUS METHOTREXATE PRIOR TO COMMENCING BIOLOGIC THERAPY – A REAL WORLD STUDY

A. Mirza[1], M. K. Nisar[1]. [1]*Luton and Dunstable University Hospital, Rheumatology, Luton, United Kingdom*

Background: Methotrexate (MTX) is the bed rock of inflammatory arthritis management. However intolerance is a major limiting factor for drug optimisation and retention. There is data to suggest that subcutaneous (SC) MTX is tolerated better and is now being recommended in several guidelines including ACR's. It is less clear though whether this strategy is effective in those where oral preparation is inefficacious and its potential to avoid escalation to biologic therapy.

Objectives: Our aim was to analyse the reasons for switching to SC formulation in a real world setting, clinical outcomes achieved and proportion requiring biologic prescription.

Methods: We undertook a retrospective survey of all patients prescribed SC MTX in a large university teaching hospital between 1983 and Apr 2019. We had access to full patient records including details on co-morbidities, drugs and disease management. We analysed demographics, reasons for SC MTX initiation, clinical outcomes and impact on biologic prescription.

Results: 352 patients were identified during the study period. The mean age of the cohort was 54 yrs (3-87). 192 (70%) were women. 260 (74%) were Caucasian, 64 (18%) Asian, 21 (6%) Afro-Caribbean and remaining of other ethnicity. Two most common diagnoses were RA [n=243 (69%)] and pSpA [n=66 (18%)]. Average disease duration was 74 months (11-324) with mean of three comorbidities (0-11).

284 (80%) had switched from oral to SC MTX. 137 (49%) stopped oral MTX due to side effects. Mean duration of oral MTX prior to switching was 26 months (0.25-167). Follow up period for SC MTX ranged from two to 132 months (mean 29) until the data cut-off date of Apr 2019. 103 (29%) patients progressed to biologic therapy.

Amongst RA patients, DAS28 improved from mean 4.16 (0.63-8.06) to 2.83 (0.14-7.32) following the switch. pSpA cohort's mean TJC and SJC improved from mean seven (0-42) and two (0-26) to two (0-25) and one (0-6) respectively.

Conclusion: Our study confirms that SC MTX is an effective solution irrespective of whether oral MTX is inefficacious or intolerable. This applies to people with both RA and pSpA. In accordance with prior published data, our findings support the utility of SC MTX for those intolerant of enteral option. Additionally, it shows that even in instances where oral MTX was ineffective, a switch to SC formulation achieved low disease activity despite multi-morbidity, long disease course and protracted oral MTX exposure. This intervention also prevented over two-thirds of patients progressing to biologic therapy with significant financial savings. SC MTX therefore remains a durable strategy with excellent disease outcomes and confers substantial economic benefits to healthcare.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1116

POS0228 BASELINE CHARACTERISTICS AND TREATMENT RESPONSE TO IXEKIZUMAB CATEGORISED BY SEX IN RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLARTHRITIS PATIENTS THROUGH 52 WEEKS: DATA FROM 3 PHASE III, RANDOMIZED, CONTROLLED TRIALS

I. Van der Horst-Bruinsma[1], R. Bolce[2], T. Hunter[2], D. Sandoval[2], D. Zhu[2], V. J. Geneus[2], J. Lisse[2], S. Liu Leage[2], M. Magrey[3]. [1]*Amsterdam UMC, locatie VUmc, Department of Rheumatology, Amsterdam, Netherlands*; [2]*Eli Lilly and Company, Lilly Corporate Center, Indianapolis, United States of America*; [3]*MetroHealth, Rhematology Department, Cleveland, United States of America*

Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease of the axial skeleton comprising two subtypes within the same spectrum: radiographic (r-axSpA) and non-radiographic (nr-axSpA). Previous studies have shown that clinical presentation and treatment response of males and females may differ[1] despite similar disease burden.[2] Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets interleukin-17A, has demonstrated superior efficacy to placebo in the treatment of patients with r-axSpA (COAST-V/W [bDMARD- naïve/TNFi-experienced]) and nr-axSpA (COAST-X [bDMARD-naïve]).[3]

Objectives: Assess baseline characteristics and treatment response to IXE categorised by sex in patients with r-axSpA and nr-axSpA for up to 52 weeks.

Methods: Patients fulfilled the ASAS classification criteria for r-axSpA or nr-axSpA. Patients were randomized to receive 80 mg subcutaneous IXE every 2 weeks (Q2W) or 4 weeks (Q4W), or to placebo (PBO) [16 weeks COAST-V/W; 52 weeks COAST-X]. Baseline characteristics and treatment outcomes were assessed. Patients were categorised by sex, missing data was controlled for using non-responder imputation (NRI) and modified baseline observation carried forward (mBOCF) analysis was conducted on continuous efficacy variables.

Results: At baseline, females were older, with significantly higher pain and fatigue scores and peripheral joint symptoms (table 1). ASAS40 response rate with IXEQ4W was achieved in 39% of males with r-axSpA by week 16, and 44% by week 52. Females achieved 16.7% at week 16, and 33.3% at week 52. In nr-axSpA, 46% of IXEQ4W males achieved ASAS40 at week 16 and 30% at week 52. 23.9% of females achieved ASAS40 at week 16, increasing to 30.4% at week 52.

Conclusion: This analysis demonstrates that for the axSpA disease spectrum, females present with higher disease burden as reflected by higher scores in fatigue/tiredness, and spinal pain at night. Our findings indicate that males and females respond to IXE; however, females experience this benefit later in their treatment course, with a more prolonged attainment of peak response.

REFERENCES:
[1] van der Horst-Bruinsma IE, et al. Ann Rheum Dis. 2019;78:1550-1558.
[2] Zhao SS, et al. Rheumatology. 2019;58:2025-2030.
[3] Deodhar A, et al. Lancet. 2020;395:53-64.

Table 1. Baseline Characteristics of Patients Categorised by Sex

	Patients with r-axSpA (COAST-V/W) (n=376)			Patients with nr-axSpA (COAST-X) (n=198)		
Characteristic	**Male (n=298)**	**Female (n=78)**	**p value**	**Male (n=99)**	**Female (n=99)**	**p value**
Age at onset (yrs), mean (SD)	26.5 (8.7)	30.1 (10.1)	**0.002***	27.9 (7.7)	32.0 (10.7)	**0.002***
Symptom duration (yrs), mean (SD)	16.7 (10.5)	17.8 (12.2)	0.420	9.5 (9.2)	12.3 (11.3)	0.057
ASDAS, mean (SD)	4.0 (0.8)	3.9 (0.7)	0.304	3.7 (0.8)	3.9 (0.8)	0.143
BASDAI, mean (SD)	7.10 (1.4)	7.4 (1.5)	0.179	6.9 (1.4)	7.4 1.4)	**0.013***
Fatigue/tiredness (BASDAI Q1), mean (SD)	7.4 (1.6)	7.8 (1.5)	**0.036***	7.0 (1.6)	7.9 (1.5)	**<0.001***
Spinal pain (BASDAI Q2), mean (SD)	7.9 (1.5)	8.0 (1.5)	0.682	7.5 (1.4)	7.9 (1.5)	**0.029***
Pain/swelling in other joints (BASDAI Q3), mean (SD)	6.5 (2.1)	6.9 (2.2)	0.129	6.6 (2.3)	7.2 (1.9)	**0.039***
Tenderness to touch/pressure (BASDAI Q4), mean (SD)	6.8 (1.8)	7.0 (1.9)	0.339	6.6 (1.9)	6.8 (1.8)	0.404
Morning stiffness (BASDAI Q5), mean (SD)	7.5 (1.6)	7.7 (1.8)	0.504	7.3 (1.7)	7.7 (1.9)	0.137
Morning stiffness duration (BASDAI Q6), mean (SD)	6.5 (2.3)	6.5 (2.8)	0.944	6.3 (2.3)	6.6 (2.5)	0.392
Spinal pain at night NRS, mean (SD)	7.4 (1.5)	7.8 (1.7)	**0.033***	7.0 (1.8)	7.6 (1.8)	**0.027***
BASFI, mean (SD)	6.8 (1.8)	7.0 (2.0)	0.466	6.2 (1.8)	6.7 (2.1)	0.108
SF-36 PCS, mean (SD)	30.9 (8.3)	28.9 (8.2)	0.075	33.1 (7.7)	32.1 (7.2)	0.348

p-value from Fisher's exact test analysis of variance (ANOVA) with sex as a factor for continuous data. Data includes pooled IXEQ2W and IXEQ4W.

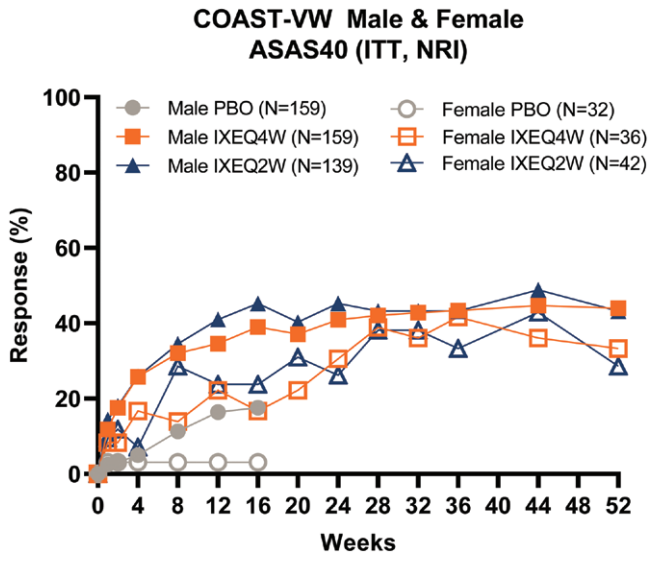


Figure 1. COAST-V/W ASAS40 (ITT, NRI) Patients initially randomized to PBO in COAST-V/W switched to IXEQ2W or Q4W at week 16 by study design; PBO data are summarised up to week 16.

Acknowledgements: Writing support was provided by Dr Geraldine Fahy, an employee of Eli Lilly and Company
Disclosure of Interests: Irene van der Horst-Bruinsma Speakers bureau: BMS, AbbVie, Pfizer, UCB, MSD, Consultant of: Abbvie, UCB, MSD, Lilly, Novartis, Grant/research support from: MSD, Pfizer, AbbVie, Rebecca Bolce Shareholder of: Eli Lilly, Employee of: Eli Lilly, Theresa Hunter Shareholder of: Eli Lilly, Employee of: Eli Lilly, David Sandoval Shareholder of: Eli Lilly, Employee of: Eli Lilly, Danting Zhu Employee of: Eli Lilly, Vladimir J. Geneus Employee of: Eli Lilly, Jeffrey Lisse Shareholder of: Eli Lilly, Employee of: Eli Lilly, Soyi Liu Leage Shareholder of: Eli Lilly, Employee of: Eli Lilly, Marina Magrey Consultant of: Novartis, Eli Lilly, Pfizer, Abbvie, UCB and Jansen, Grant/research support from: Amgen, AbbVie, and UCB Pharma
DOI: 10.1136/annrheumdis-2021-eular.684

POS0229

DISEASE ACTIVITY AND INFLAMMATION FOLLOWING WITHDRAWAL OF CERTOLIZUMAB PEGOL TREATMENT IN AXIAL SPONDYLOARTHRITIS PATIENTS WHO DID NOT EXPERIENCE FLARES DURING THE C-OPTIMISE STUDY

L. S. Gensler[1], X. Baraliakos[2], L. Bauer[3], B. Hoepken[3], T. Kumke[3], M. Kim[4], R. B. M. Landewé[5,6]. [1]*University of California San Francisco, Department of Rheumatology, San Francisco, United States of America*; [2]*Ruhr-University Bochum, Rheumazentrum Ruhrgebiet Herne, Herne, Germany*; [3]*UCB Pharma, N/A, Monheim am Rhein, Germany*; [4]*UCB Pharma, N/A, Smyrna, United States of America*; [5]*Amsterdam University Medical Center, Department of Rheumatology & Clinical Immunology, Amsterdam, Netherlands*; [6]*Zuyderland Medical Center, Department of Rheumatology, Heerlen, Netherlands*

Background: C-OPTIMISE was a phase 3b clinical trial investigating certolizumab pegol (CZP) maintenance dose continuation, reduction or withdrawal following achievement of sustained remission in patients with axial spondyloarthritis (axSpA). During the C-OPTIMISE maintenance period, the majority of patients randomised to CZP, either the full or reduced maintenance dose, did not experience disease flares. Conversely, in those who had CZP withdrawn, only a minority of patients remained flare-free.[1]
Objectives: This post-hoc analysis evaluates disease activity and clinical markers of inflammation in patients who did not experience a disease flare following randomisation to CZP full maintenance dose, CZP reduced maintenance dose or placebo (PBO) during the maintenance period (Weeks 48–96) of C-OPTIMISE.
Methods: C-OPTIMISE (NCT02505542) was a multicentre, double-blind, parallel-group, randomised phase 3b study with a 48-week open-label run-in period.[1] Adult patients with early (<5 years' symptom duration) active axSpA received open-label CZP 200 mg every 2 weeks (Q2W) for the first 48 weeks; from Week 48, patients who achieved sustained remission (Ankylosing Spondylitis Disease Activity Score [ASDAS] <1.3 at Week 32 or 36 and Week 48) were randomised 1:1:1 to double-blind CZP 200 mg Q2W (full maintenance dose), CZP 200 mg Q4W (reduced maintenance dose) or PBO for a further 48 weeks (maintenance period). A flare was defined as ASDAS ≥2.1 at two consecutive visits or ASDAS >3.5 at any visit. We report ASDAS, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and C-reactive protein (CRP) and fecal calprotectin levels during Weeks 48–96 in CZP- and PBO-randomised patients who did not experience a flare (i.e. completed Week 96 on randomised treatment). Missing data were imputed using last observation carried forward.
Results: Of 313 patients entering the maintenance period at Week 48, 197 (62.9%) completed Week 96 on randomised treatment without experiencing a flare; of these, 89 (85.6%) and 84 (80.0%) patients were in the CZP 200 mg Q2W and CZP 200 mg Q4W arm, respectively, with only 24 (23.1%) patients randomised to PBO not experiencing a flare. Baseline characteristics of these patients are shown in the Table 1. During Weeks 48–96, disease activity (ASDAS, BASDAI) and CRP levels were comparable between the CZP full and reduced maintenance dose group, and lower in both CZP arms than in PBO (Figure 1 A–C). From Week 60 up to Week 96, PBO patients who did not flare had consistently higher mean ASDAS, BASDAI and CRP levels compared with CZP-randomised patients (Figure 1 A–C). Similarly, there was a greater increase in fecal calprotectin levels between Weeks 48 and 96 in the PBO arm compared with both CZP arms (Figure 1 D).
Conclusion: Despite not meeting the threshold for a flare, consistently higher disease activity and increases in serologic and inflammatory biomarkers were observed in PBO-randomised patients who did not experience a flare during the C-OPTIMISE study compared to those who remained on CZP. These findings confirm that patients with axSpA who achieve sustained remission benefit from continued CZP treatment, either with the full or reduced maintenance dose, over treatment withdrawal.
REFERENCES:
[1] Landewé R. Ann Rheum Dis 2020;79:920–8.

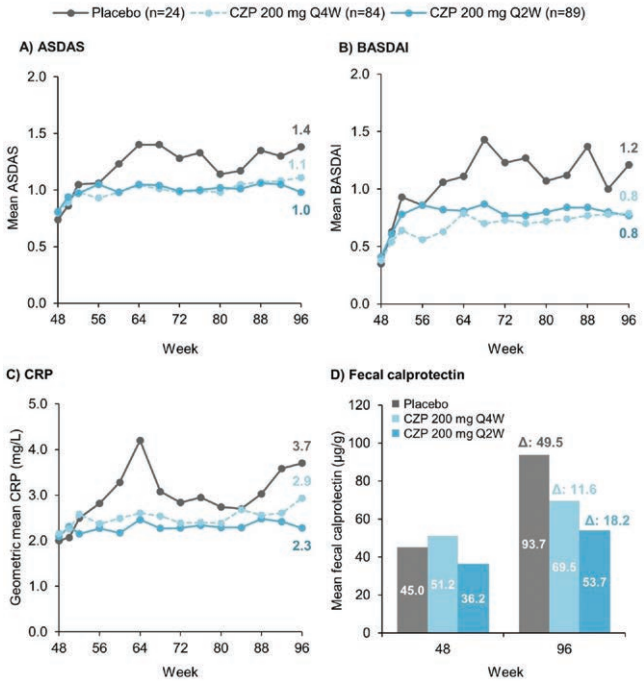
Table 1. Baseline (Week 0) characteristics of patients who did not experience flares during the C-OPTIMISE maintenance period

	Placebo (n=24)	CZP 200 mg Q4W (n=84)	CZP 200 mg Q2W (n=89)
Age (years), mean (SD)	29.8 (7.4)	32.9 (6.7)	32.4 (7.2)
Male, n (%)	19 (79.2)	69 (82.1)	69 (77.5)
Time since diagnosis (years)			
Mean (SD)	2.0 (1.8)	2.0 (1.7)	2.5 (1.6)
Median	1.2	1.2	2.7
Symptom duration (years)			
Mean (SD)	2.7 (1.7)	3.4 (1.9)	3.9 (2.9)
Median	2.8	3.5	3.9
ASDAS, mean (SD)	3.4 (0.8)	3.7 (0.8)	3.7 (0.7)
BASDAI, mean (SD)	6.3 (1.1)	6.6 (1.5)	6.4 (1.4)
CRP (mg/L), geometric mean	6.28	7.88	7.35
Fecal calprotectin (µg/g), mean (SD)	71.8 (111.4)	87.1 (110.5)	81.0 (120.0)

SD: standard deviation.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical.

Figure. (A) ASDAS, (B) BASDAI, (C) CRP and (D) fecal calprotectin in patients who did not experience a flare during the C-OPTIMISE maintenance period (Weeks 48–96)



Missing data were imputed using last observation carried forward. Δ values for fecal calprotectin show change from Week 48. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; CZP: certolizumab pegol; Q2W/Q4W: every 2/4 weeks.

Disclosure of Interests: Lianne S. Gensler Consultant of: AbbVie, Eli Lilly, Gilead, GSK, Novartis, Pfizer, UCB Pharma, Grant/research support from: Pfizer, Xenofon Baraliakos Speakers bureau: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, Novartis, Merck, Pfizer, UCB Pharma, Paid instructor for: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, Novartis, Merck, Pfizer, UCB Pharma, Consultant of: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, Novartis, Merck, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Merck, Novartis, Lars Bauer Shareholder of: UCB Pharma, Employee of: UCB Pharma, Bengt Hoepken Shareholder of: UCB Pharma, Employee of: UCB Pharma, Thomas Kumke Shareholder of: UCB Pharma, Employee of: UCB Pharma, Mindy Kim Shareholder of: UCB Pharma, Employee of: UCB Pharma, Robert B.M. Landewé Speakers bureau: Abbott, Amgen, BMS, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, Consultant of: Abbott, Ablynx, Amgen, AstraZeneca, BMS, Centocor, GSK, Merck, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth

DOI: 10.1136/annrheumdis-2021-eular.1547

POS0230 INTESTINAL MICROBIOTA CHANGES TNF-INHIBITORS INDUCED IN IBD-RELATED SPONDYLOARTHRITIS

M. C. Ditto[1], S. Parisi[1], G. Landolfi[2], R. Borrelli[1], G. Caviglia[3], D. G. Ribaldone[4], M. Astegiano[4], A. Zanetti[2], G. Carrara[2], C. A. Scirè[2], M. Antivalle[5], P. Sarzi-Puttini[5], E. Fusaro[1]. [1]*AOU Città della Salute e della Scienza di Torino, Rheumatology Unit, Turin, Italy*; [2]*Italian Society for Rheumatology, Epidemiology Research Unit, Milan, Italy*; [3]*University of Turin, Medical Sciences, Turin, Italy*; [4]*AOU Città della Salute e della Scienza di Torino, Gastroenterology Unit, Turin, Italy*; [5]*ASST Fatebenefratelli-Sacco, Rheumatology Unit, Milan, Italy*

Background: the close relationship between joints and gut inflammation has long been known and several data suggest that the dysbiosis could represents the link between Spondyloarthritis (SpA) and Inflammatory Bowel Diseases (IBD). To date, the manipulation of the intestinal microbiota is considered the key to the cure or control of the natural history of several pathologies sustained or favored by dysbiosis. The introduction of biologic drugs, in particular Tumor Necrosis Factor inhibitors (TNFi), revolutionized the management of both these diseases, thanks to the strong inhibition of inflammation and partially indirectly with mechanisms not yet fully clarified. While the impact of conventional drugs on gut microbiota is well known poor data are available about TNFi.
Objectives: to investigate the impact of TNFi on gut microbiota.
Methods: we included CD or UC patients fulfilling criteria for axial or peripheral SpA (ASAS 2009) on a typical Mediterranean diet, naïve to biologics needing TNFi. Clinical history, physical examination, instrumental examinations, biochemical examination including C-reactive protein (CRP), erhytrocyte sedimentation rate (ESR), HLA-B27 and fecal calprotectin at the baseline and after 6 months were performed. TNFi included infliximab and adalimumab. Fecal samples were collected by patients themselves by 24 hours before the start of the therapy. The processing was performed through metagenomic NGS (next generation sequencing) including the amplification of the V3 and V4 regions of the 16S (V3 and V4) and sequencing on the Illumina MiSeq platform. All patients received the treatment at least until week 24. Clinical disease indices included Visual Analogue Scale (VAS)-pain and Visual Analgue Scale(VAS)-disease activity for all patients, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for axial involvement, clinical disease activity index (CDAI) and Health Assessment Questionnaire-Disability Index (HAQ-DI) for peripheral involvement, Harvey-Bradshaw Index for CD (HBI), or partial Mayo (pMAYO) score for UC, were assessed at baseline and at the end of the study. The study was approved by the ethics committee (approval code 0056924).
Results: we evaluated 20 patients affected by enteropatic arthritis, naïve for biologic drugs, treated with TNFi. After six months of therapy we observed a significant increase in Lachnospiracae family (Δ +10.3, p 0.04) and in Coprococcus genus (Δ +2.8, p 0.003). We also observed a decrease trend in Proteobacteria (Δ -8.0 p 0.095) and Gammaproteobacteria (Δ -9, p 0.093) and an increase trend in Clostridia (Δ +8.2 p 0.083). We didn't find differences between TNFi responders (SpA improvement or IBD remission achieved) and not responders in terms of alpha and beta-diversity.
Conclusion: the decrease of Proteobacteria and the increase of Lachnospiraceae and Coprococcus is consistent with the hypothesis that TNFi therapy, by decreasing inflammation, tends to restore the intestinal eubiosis. However further studies on larger cohort incuding the evaluation of gut virota and micobiota will be necessary to definitively clarify the effects of TNFi on the composition and function of the gut microbiota.

REFERENCES:

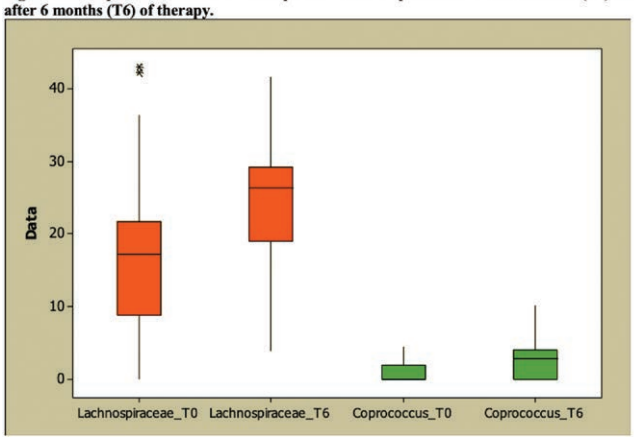
[1] Bazin T et al. *Sci Rep*. 2018;8(1):5446.
[2] Aden K et al. *Gastroenterology*. 2019;157(5):1279-1292.e11.

Table 1. Comparison between clinical variables between baseline and T6 (six months)

Clinical variables	T0	T6	P_value
Fecal Calprotectin(µg/g)- median (IQR)	207.5(125.5-446.2)	81(50-197.2)	0.004
CRP(mg/L)- median(IQR)	8.2(4.8-20.8)	2.9(1-4)	0.001
ESR(mm/h)- median(IQR)	21.5(10.8-34)	11(7.8-21)	0.003
VAS_pain- median(IQR)	50(38.8-60)	35(10-42.5)	0.001
VAS_disease- median(IQR)	50(38.8-50)	37.5(25-42.5)	0.006
HAQ- mediana(IQR)	0.6(0.1-0.8)	0.2(0.1-0.6)	0.004
BASDAI_score- median(IQR)	5.2(4.1-5.6)	2.8(2.5-4.3)	0.013
CDAI_activity- median(IQR)	13(10.5-16)	7(5.2-11)	0.004
IBD activity n(%) - 0	11 (55%)	20 (100%)	0.174
IBD activity n(%) - 1	6 (30%)	0 (0%)	
IBD activity n(%) - 2	2 (10%)	0 (0%)	
IBD activity n(%) - 3	1 (5%)	0 (0%)	

Disclosure of Interests: None declared.

Figure 1. Comparison between Lachnospiraceae and Coprococcus at the baseline (T0) and after 6 months (T6) of therapy.



DOI: 10.1136/annrheumdis-2021-eular.1589

POS0231 IMPACT OF GENDER AND COMORBIDITIES IN ENTEROPHATIC SPONDYLOARTHRITIS: A CROSS-SECTIONAL STUDY

A. D'antonio[1], M. S. Chimenti[1], P. Conigliaro[1], P. Triggianese[1], S. Ferrigno[1], M. Ferraioli[1], B. Neri[2], L. Biancone[2], R. Perricone[1]. [1]*University of Rome Tor Vergata, Rheumatology, Allergology and Clinical Immunology, Rome, Italy*; [2]*University of Rome Tor Vergata, GI Unit, Rome, Italy*

Background: Enteropathic Spondyloarthritis (ESpA) belongs to the group of Spondyloarthritis (SpA) typically associated with inflammatory bowel disease (IBD). SpA are divided into axial (ax) or peripheral disease. Ax-SpA are classified as

ankylosing spondylitis (AS) and non-radiographic (nr-) axSpA based on the presence or absence of definite structural changes in conventional radiographs (CR).
Objectives: Aim of this study was to determine whether comorbidities and gender could lead to a different response rate to TNF-inhibitors (TNFi) in ESpA patients.
Methods: ESpA patients treated with TNFi [adalimumab (ADA) or infliximab (IFX)] were retrospectively evaluated between November 2018 and October 2020 and divided in two cohort according to gender. In addition, TNFi treatments line/s, effectiveness and reasons of discontinuations, as inefficacy, intolerance, acute adverse reaction, development of infections and other causes, were evaluated at baseline (T0), at 6 (T6), 12 (T12), and 24 (T24) months of therapy. Patients who were failure to at least two TNFi were considered as "multifailure". Statistical analyses were performed using chi square/Fisher tests and variance analysis (SPSS software).
Results: 120 ESpA patients (M 40.52%; F 40.18%) treated with TNFi were evaluated. Clinical and laboratory baseline (T0) characteristics are summarized in Table 1. AS subtype was more common in men (39.5%) than in woman (14.3%) (p=0.03). Concerning comorbidities, hypertension and anemia were more prevalent in men than women (25% vs 9%, p=0.01; 11.6% vs 1.3%, p=0.02, respectively), while thyreopathy and psychiatric disorders were more common in female than male (11.7% vs 0%, p=0.02; 16.9% vs 4.6%, p=0.04, respectively). No difference was observed between genders in distribution of BMI, smokers, disease duration, HLAB27 positivity and presence of extra-articular manifestations. 202 TNFi treatments (50.9% ADA and 24.3% IFX) were evaluated in 120 patients [74 treatments (36.6%) in 43 men; 128 treatments (63.4%) in 77 women]. Considering treatment effectiveness, higher prevalence of failure was observed in woman that in men (67.2% vs 39.2%, p=0.0005). Moreover, women with psychiatric disorders undergone more lines treatment that men (16.8% vs 4.6%, p=0.01, OR=4). On the other hand, men with hypertension, were more multifailure compared with women (25.6% vs 16.3%, p=0.001, OR=3). No other differences according to gender were found.
At T6, 7.5% of patients (n=9) had acute adverse reaction (n=1 with ADA; n=8 with IFX); at T12, 14.2% of patients (n=17) had IBD inefficacy. At T24, secondary inefficacy on IBD and/or SpA was the main cause of TNFi discontinuation compared with other causes (58.4% vs 41.6%; p=0.04), mostly in female cohort (40% *vs* 20% in woman; p=0.04). Analyzing TNFi effectiveness, CRP and HAQ improvement was noted at T6 (p=0.024 and 0.036, respectively), as ASDAS-CRP and BASDAI (p=0.02 and p=0.013, respectively) and maintained in the following evaluations at T12 and T24. At T24, men shown higher PCR and BASDAI improvement compared with women (p=0.036 and p=0.04, respectively).
Conclusion: Data suggest that gender and comorbidities could influenced TNFi response in ESpA patients, advising differences among woman and men. Knowledge of these variable represents a major challenge for a personalized treatment management.

Table 1. Clinical and laboratory baseline (T0) characteristics of ESpA patients treated with TNFi.

	Women N= 77	Men N=43
Age (years)	44.5±14.5	42.9±11.9
Duration of ESpA (months)	81±75.13	85.46±77.09
IBD duration (months)	187.35±112.9	219.35±123.5
Diagnostic delay of EspA (months)	43±65.4	75.71±122
Peripheral ESpA	42/54.5	17/39.5
Axial ESpA	35/45.5	26/60.5
CD (n / %)	48/62.3	33/76.4
UC (n / %)	29/37.7	10/23.6
Family history (n/%)	17/22	7/16.3
Appendectomy (n/%)	25/32.5	10/23.3
Smokers (n/%)	19/24.7	12/27.9
BMI	23.7±3.9	24.8±3.7
HLAB27 positivity (n/%)	8/10.4	4/9.3
Extra-articular manifestations (n/%)	34/44.2	17/39.5
Comorbidities (n/%)	32/41.6	21/48.8
TNFi treatments: biologic-naïve	50/64.9 *	16/37.2
ADA treatments: biologic-naïve second/third line	68/53.1 32/74.1 25/36.9	35/47.3 17/48.6 18/51.4
IFX treatments: biologic-naïve second line	46/35.9 35/76.1 11/23.9	32/43.2 26/21.3 6/18.7
ESR (mm/h)	26.3±25.1	28.1±23.1
CRP (mg/dL)	0.7±1.1	1.12±1.4
VAS pain (0-10)	5±2.53	4±3
(PG)-VAS (0-10)	5±2.4	4.6±2.4
ASDAS-CRP	2.6±0.9	3.7±6.5
BASDAI	5.28±2.2	3.85±2.34
BASFI	3.8±8.5	1.9±2.1
HAQ-S	1.9±8.2	0.5±0.5

Data are expressed as mean ± SD. * Women versus men ESpA: Enteropathic Spondyloarthritis; IBD: inflammatory bowel disease; CD: Crohn's disease; UC: Ulcerative colitis; BMI: body mass index; TNFi: tumor necrosis factor inhibitor; ADA: Adalimumab; IFX: Infliximab; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; VAS: Visual Analog Scale; PG: patient global; ASDAS: ankylosing spondylitis disease activity score; BADSAI: bath ankylosing spondylitis disease activity index; BASFI: bath ankylosing spondylitis functional index; HAQ-S: health assessment questionnaire for SpA.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2563

POS0232

CLINICAL EFFECTIVENESS OF ADALIMUMAB VERSUS NON-BIOLOGIC THERAPY IN THE MANAGEMENT OF EXTRA-ARTICULAR MANIFESTATIONS IN ANKYLOSING SPONDYLITIS PATIENTS OVER 24 MONTHS – RESULTS OF THE COMPLETE-AS CANADIAN OBSERVATIONAL STUDY

L. Bessette[1], B. Haraoui[2], B. Florica[3], M. C. Laliberté[4], M. Khraishi[5].
[1]Laval University, Centre Hospitalier de l'Université Laval, Laval University, Centre Hospitalier de l'Université Laval, Quebec City, Canada; *[2]Institut de rhumatologie de Montréal, Institut de rhumatologie de Montréal, Montreal, Canada*; *[3]University of Toronto, Toronto, University of Toronto, Toronto, Toronto, Canada*; *[4]AbbVie Corporation, AbbVie Corporation, Montreal, Canada*; *[5]Memorial University of Newfoundland, Memorial University of Newfoundland, St. John's, Canada*

Background: COMPLETE-AS was a Canadian observational study among biologic-naïve adults with active ankylosing spondylitis (AS) initiated on either adalimumab (ADA) or subsequent non-biologic disease-modifying anti-rheumatic drugs and/or non-steroidal anti-inflammatory drugs (nbDMARD/NSAID) after a switch from initial treatment due to inadequate response or intolerance, as per the judgement of the treating physician.
Objectives: The aim of this analysis was to assess the 24-month effectiveness of ADA compared to nbDMARD/NSAID in the management of heel enthesitis and extra-articular manifestations (EAMs).
Methods: Patients were enrolled between July 2011 and December 2017, and followed for up to 24 months. Patients were treated as per routine care and all analyses were performed using the intent-to-treat (ITT) approach. The disease outcomes assessed in this study included enthesitis (of the heel) and EAMs [inflammatory bowel disease (IBD), uveitis, and psoriasis (PsO)]. The rate ratio (RR) for first occurrence or flare-up/exacerbation of disease outcomes was ascertained with multivariate models. The time to first occurrence of EAMs and enthesitis was ascertained with Cox proportional hazard models, generating a hazard ratio (HR).
Results: A total of 452 patients treated with ADA and 187 patients receiving a subsequent nbDMARD/NSAID were enrolled in the study. Baseline characteristics were overall comparable between treatment groups: patients had a mean (SD) age of 42.7 (13.4) years, 55.6% were male, and 85.8% were Caucasian. The mean (SD) duration of AS since diagnosis was 5.6 (9.3) years. A total of 17.7%, 12.4%, 18.5%, and 16.3% of patients had experienced enthesitis, IBD, uveitis, and PsO, respectively at baseline. Disease severity (mean [SD] BASDAI) was however higher among ADA- vs. nbDMARD/NSAID-treated patients (6.4 [1.8] vs. 5.0 [1.8]; p<0.001).
In terms of the rates of first occurrence or flare-up/exacerbation of enthesitis and EAMs, statistically significant between-group differences were found, whereby ADA-treated patients had a 60% reduced rate of both uveitis [RR (95% CI): 0.4 (0.2-0.6)] and enthesitis [0.4 (0.3-0.7)] compared to nbDMARD/NSAID-treated patients. The rates of first occurrence or flare-up/exacerbation for IBD [1.1 (0.7-1.7)] and PsO [3.3 (0.9-12.7)]were statistically comparable between treatment groups.
The time to first occurrence of both enthesitis and uveitis was also statistically significant (p<0.05) between groups. ADA-treated patients had a 50% lower risk of enthesitis as a first occurrence compared to nbDMARD/NSAID-treated patients [HR (95% CI): 0.5 (0.3-0.9)], and an 80% lower risk of uveitis [0.2 (0.0-0.8)]. The time to first occurrence of IBD [0.7 (0.2-2.1)] and PsO [1.9 (0.8-4.6)], were statistically comparable between treatment groups.
Conclusion: Despite a comparable proportion of patients reporting baseline EAMs and enthesitis, patients treated with ADA were less likely to experience a first occurrence or flare-up/exacerbation, of both enthesitis and uveitis compared to patients treated with nbDMARD/NSAID. The results of this real-world Canadian study suggest that treatment with ADA among AS patients is more effective at preventing the first occurrence / exacerbation of select EAMs and heel enthesitis.
Acknowledgements: The authors wish to acknowledge JSS Medical Research for their contribution to the statistical analysis, medical writing, and editorial support during the preparation of this abstract. AbbVie provided funding to JSS Medical Research for this work.
Disclosure of Interests: Louis Bessette Speakers bureau: Speaker for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Gilead, Sandoz, Fresenius Kabi, Consultant of: Consultant for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, Gilead, Sandoz, Samsung Bioepis, Fresenius Kabi, Grant/research support from: Investigator for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Gilead, Boulos Haraoui Speakers bureau: Speakers for AbbVie, Amgen, BMS, Gilead, Lilly, Merck, Pfizer, Sandoz, and UCB, Consultant of: Advisor for AbbVie, Amgen, BMS, Gilead,

Lilly, Merck, Pfizer, Sandoz, and UCB, Grant/research support from: Research grants from AbbVie, Amgen, BMS, Gilead, Lilly, Merck, Pfizer, Sandoz, and UCB, Brandusa Florica Speakers bureau: Speaker for Merck, AbbVie, Roche, BMS, and Novartis, Consultant of: Consultant for Roche, AbbVie, Pfizer, Janssen, Celgene, and UCB, Grant/research support from: Investigator for AbbVie, Pfizer, and BMS, Marie-Claude Laliberté Employee of: Employee of AbbVie, Majed Khraishi Speakers bureau: Speaker for AbbVie, Consultant of: Consultant for AbbVie, Grant/research support from: Principal Investigator for AbbVie.
DOI: 10.1136/annrheumdis-2021-eular.2627

POS0233 THE EFFICIENCY OF TREATMENT OF COXITIS IN AXIAL SPONDYLOARTHRITIS: EXPERIENCE OF REAL CLINICAL PRACTICE

E. Agafonova[1], S. Erdes[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*

Background: Standard therapy for axial spondyloarthritis (axSpA) is effective in inflammatory lesions of the axial skeleton and peripheral arthritis, but its effect on coxitis has not been studied.
Objectives: To assess the effectiveness of anti-TNF therapy for coxitis in patients with axSpA.
Methods: An open observational study was conducted. There were 56 patients with axSPA and coxitis for 2 years who received NSAIDs or NSAIDs+anti-TNF therapy in real clinical practice. The study included only those patients who completed a 2-year follow-up period. All patients regardless of complaints underwent X-ray examination of the pelvis, ultrasound and magnetic resonance imaging (MRI) of the hip joints. An increase in the cervical-capsular distance (CCD) of more than 7 mm and the presence of asymmetry between the joints of more than 1.5 mm were taken for coxitis on ultrasound of the hip joint. The presence of synovitis and/or osteitis was taken for coxitis on MRI. The average age was 31.1±7.0 years, with an average duration of the disease 74.5±100.1 months. HLA-B27 positive were 52 (92%) patients.
Results: A comparative analysis of clinical, laboratory and other parameters of the disease was carried out against the background of 2-year follow-up of patients who were constantly taking only NSAIDs or their combination with anti-TNF therapies (Table 1).

Table 1.

Parametrs	Group NSAIDs+ anti-TNF n=27 baseline	Group NSAIDs+ anti-TNF n=27 after 2 y	p	Group NSAIDs n=29 baseline	Group NSAIDs n=29 after 2 y	p
BASRI hip ≥2; n %	10 (37%)	18 (67%)	>0,05	6 (21%)	14 (48%)	<0,05
MRI coxitis; n %	27 (100%)	19 (70%)	<0,05	28 (97%)	24 (83%)	>0,05
CCDmm;Me, [25 ‰;75‰]	7,9 [7,0;8,2]	7,2 [6,1;8,3]	<0,05	7,2 [6,2;7,8]	6,2[5,6;7,8]	>0,05
CRP,mg/L; Me, [25 ‰; 75‰]	23,7[8,4;56]	6,0 [1,0;17,3]	<0,05	10,3 [2,9;18,6]	8,4[2,9;18,5]	>0,05
ESR; Me, [25 ‰; 75‰]	25 [15;38]	15,0 [5;35,2]	<0,05	13 [7,8;25,5]	13 [6;26,3]	>0,05
ASDAS CRP; Me, [25 ‰; 75‰]	3,5 [2,4;4,7]	2,0 [1,0;2,4]	<0,05	2,6 [1,3;3,6]	2,0[1,1;2,3]	>0,05
BASDAI; Me, [25‰; 75‰]	4,7[4,2;6,9]	2,2 [2,0;3,7]	<0,05	4,2 [2,4;5,8]	2,2[1,4;4,2]	>0,05
BASFI; Me,[25‰;75‰]	4,0 [2,0;6,5]	1,9 [0,9;2,9]	<0,05	1,2 [0,3;2,5]	0,9[0,4;2,8]	>0,05

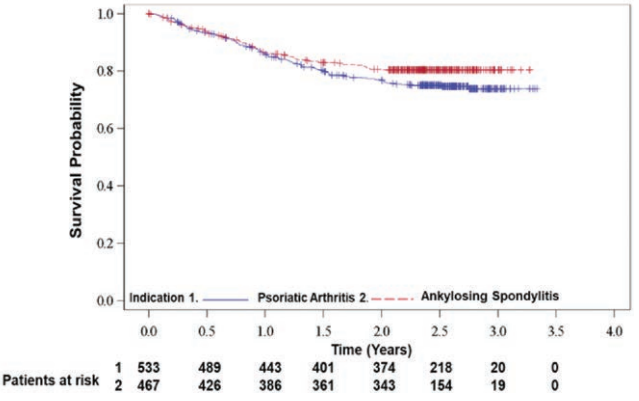
Conclusion:
1. Anti-TNF+NSAIDs therapy with 2 years of use effectively controls the activity of axSpA.
2. Two-year therapy with NSAIDs in combination with anti-TNF, reduces the inflammation of hip joints in some patients according to ultrasound and MRI data.
3. The present study did not conclusively confirm that 2-year anti-TNF therapy with NSAIDs effectively prevents the progression of X-ray bursitis in axSpA.
4. Further studies are needed to improve the effectiveness of treatment of coxitis in axSpA.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2865

POS0234 SECUKINUMAB RETENTION AND SAFETY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS OR ANKYLOSING SPONDYLITIS: 2 YEAR INTERIM RESULTS OF THE OBSERVATIONAL SERENA STUDY

U. Kiltz[1,2], P. Sfikakis[3], N. Gullick[4], A. Theodoridou[5], J. Brandt-Juergens[6], E. Lespessailles[7], R. Rashkov[8], J. Fang[9], E. Pournara[10], B. Schulz[10], P. Jagiello[10], K. Gaffney[11]on behalf of The study was sponsored by Novartis Pharma AG, Basel, Switzerland.. *[1]Rheumazentrum Ruhrgebiet, Claudiusstraße, Herne, Germany*; *[2]Ruhr-Universität Bochum, Universitätsstraße, Bochum, Germany*; *[3]National and Kapodistrian University of Athens, Medical School, Athens, Greece*; *[4]University Hospital Coventry & Warwickshire, Clifford Bridge Road, Coventry, United Kingdom*; *[5]Euromedica Geniki Kliniki, General Hospital, Thessaloniki, Greece*; *[6]Rheumatologische Schwerpunktpraxis, Seelbergstraße, Stuttgart, Germany*; *[7]Regional Hospital and, University of Orleans, Orléans, France*; *[8]Medical University - Sofia, булевард,"Академик Иван Евстратиев Гешов", София, Bulgaria*; *[9]Novartis Pharmaceuticals Corp., Immunology, Hepatology and Dermatology, East Hanover, United States of America*; *[10]Novartis Pharma AG, Immunology, Hepatology and Dermatology, Basel, Switzerland*; *[11]Norfolk and Norwich University Hospital, NHS Foundation Trust, Norfolk, United Kingdom*

Background: SERENA is an ongoing, prospective, non-interventional study evaluating retention, effectiveness, safety/tolerability and quality of life in more than 2900 patients (pts) with moderate to severe plaque psoriasis, active psoriatic arthritis (PsA) or active ankylosing spondylitis (AS) treated with secukinumab (SEC) at 438 sites across Europe for a period of up to 5 years[1].
Objectives: We present interim results reporting SEC treatment retention and safety data through 2 years in the PsA and AS pts enrolled in the study.
Methods: This interim analysis presents data from 534 PsA and 470 AS pts who were enrolled (target population fulfilling all eligibility criteria) in the study and were followed up for at least 2 years. Pts (aged ≥18 years) with active PsA or AS should have received at least 16 weeks SEC treatment before enrolment in the study[1]. Retention rate was defined as the percentage of pts who have not discontinued SEC treatment. A treatment break was defined as interruption of therapy for at least 3 months after last injection.
Results: The mean treatment duration prior to enrolment in the study was 1.0 year and 0.91 year for PsA and AS, respectively. The retention rates for SEC after 1 year since enrolment and since initiation of treatment were: PsA, 85.2% [n=519, CI: 82.01–88.32] and 96.8% [n=528, CI: 95.18–98.38]; AS, 85.8% [n=452, CI: 82.52–89.17] and 94.2% [n=464, CI: 91.94–96.42], respectively. After 2 years since enrolment and since initiation of treatment, the retention rates were: PsA, 74.9% [n=498, CI: 70.99–78.81] and 87.0% [n=515, CI: 83.99–89.99]; AS, 78.9% [n=437, CI: 75.01–82.88] and 84.8% [n=454, CI: 81.39–88.21], respectively. Survival probabilities for individual indications are presented in Figure 1. At baseline, the majority of PsA (79.5%; n/N=423/532) pts were receiving SEC 300 mg, while 97.0% (n/N=456/470) of AS pts were receiving SEC 150 mg. The majority of pts continued their initial SEC dose; "no dose change" in SEC treatment was reported after 1 and 2 years in the study (Year 1: PsA, 93.4% [n=499] and AS, 92.6% [n=435]; Year 2: PsA, 89.7% [n=479] and AS, 87.9% [n=413]). SEC treatment break was recorded for 31 PsA pts [median (min, max) treatment break duration in days: 125.0 (61, 461)] and for 42 AS [118.0 (61, 813)] pts mainly due to adverse events reported in 58.1% (n=18) and 45.2% (n=19) of pts, respectively. The retreatment started with monthly dosing in most of the cases: PsA, 80.6% (n/N=25/31) and AS, 76.2% (n/N=32/42). No new or unexpected safety signals were reported (Table 1).
Conclusion: Secukinumab retention rates in a real world setting after more than 2 years since initiation of treatment and after 2 years since enrolment in the study indicate high persistence rates. Safety data collected prospectively for up to 2 years confirm the favorable safety profile of secukinumab.

Figure: Time to treatment discontinuation of secukinumab by individual indications



REFERENCES:
[1] Kiltz, U et al. Adv Ther 2020; 37:2865–83.

Table 1. Safety profile of treatment-emergent adverse events within the study period

	PsA N=575		AS N=499	
AE summary, n (%)	**Year 1**	**Year 2**	**Year 1**	**Year 2**
Subject with any AE	239 (41.6)	289 (50.3)	203 (40.7)	247 (49.5)
Subject with any serious AE	29 (5.0)	45 (7.8)	29 (5.8)	44 (8.8)
Subject with AE leading to discontinuation	55 (9.6)	84 (14.6)	47 (9.4)	62 (12.4)
Death	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
AEs of special interest, n (IR per 100 subject-years)				
Serious infections and infestations	5 (0.96)	9 (0.95)	8 (1.78)	11 (1.33)
Candida infections	1 (0.19)	2 (0.21)	2 (0.44)	2 (0.24)
Malignancy	5 (0.96)	7 (0.74)	N/R	3 (0.36)
Major adverse cardiovascular events	N/R	1 (0.11)	2 (0.44)	3 (0.36)
Inflammatory bowel disease	N/R	N/R	1 (0.22)	1 (0.12)

N, total number of patients in the safety set; n, number of patients with event; AE, adverse events; IR, incidence rate; N/R, not reported.

Disclosure of Interests: Uta Kiltz Consultant of: AbbVie, Biocad, Biogen, Chugai, Eli Lilly, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: AbbVie, Biocad, Biogen, Chugai, Eli Lilly, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Petros Sfikakis Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli-Lilly, Janssen, Novartis and Pfizer, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli-Lilly, Janssen, Novartis and Pfizer, Nicola Gullick Speakers bureau: AbbVie, Celgene, Eli Lilly, Izana, Janssen, Novartis, UCB., Consultant of: AbbVie, Celgene, Eli Lilly, Izana, Janssen, Novartis, UCB., Grant/research support from: AbbVie, Celgene, Eli Lilly, Izana, Janssen, Novartis, UCB., Athina Theodoridou Consultant of: UCB, Amgen, Novartis, Jan Brandt-Juergens Speakers bureau: AbbVie, Pfizer, Roche, Sanofi-Aventis, Novartis, Lilly, MSD, UCB, BMS, Janssen, and Medac, Consultant of: AbbVie, Pfizer, Roche, Sanofi-Aventis, Novartis, Lilly, MSD, UCB, BMS, Janssen, and Medac, Eric Lespessailles Speakers bureau: Amgen, Expanscience, Lilly and MSD, Consultant of: Amgen, Expanscience, Lilly and MSD, Grant/research support from: Abbvie, Amgen, Lilly, MSD and UCB, Rasho Rashkov Speakers bureau: AbbVie, Amgen, Pfizer, Novartis, MSD, UCB, Roche and Janssen, Consultant of: AbbVie, Amgen, Pfizer, Novartis, MSD, UCB, Roche and Janssen, Jenny Fang Employee of: Novartis, Effie Pournara Shareholder of: Novartis, Employee of: Novartis, Barbara Schulz Employee of: Novartis, Piotr Jagiello Employee of: Novartis, Karl Gaffney Speakers bureau: AbbVie, Celgene, Lilly, Pfizer, Gilead, MSD, Novartis and UCB, Consultant of: AbbVie, Celgene, Lilly, Pfizer, Gilead, MSD, Novartis and UCB, Grant/research support from: AbbVie, Celgene, Lilly, Pfizer, Gilead, MSD, Novartis and UCB.
DOI: 10.1136/annrheumdis-2021-eular.2263

POS0235

COMPARISON OF AXIAL AND PERIPHERAL MANIFESTATIONS IN PATIENTS WITH PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS IN UPADACITINIB CLINICAL TRIALS

X. Baraliakos[1], A. Deodhar[2], R. Ranza[3], S. Rednic[4,5], F. Ciccia[6], F. Ganz[7], T. Gao[7], A. Lertratanakul[7], I. H. Song[7], A. Ostor[8], L. C. Coates[9].
[1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Rheumatology, Bochum, Germany; *[2]Oregon Health & Science University, Rheumatology, Portland, Oregon, United States of America*; *[3]Universidade Federal de Uberlândia, Serviço de Reumatologia, Uberlândia, Minas Gerais, Brazil*; *[4]Emergency Clinical County Hospital, Rheumatology, Cluj-Napoca, Romania*; *[5]Iuliu Hatieganu University of Medicine and Pharmacy, Rheumatology, Cluj-Napoca, Romania*; *[6]University of Campania Luigi Vanvitelli, Rheumatology, Caserta, Italy*; *[7]AbbVie Inc., Immunology, North Chicago, Illinois, United States of America*; *[8]Monash University, Cabrini Hospital & Emeritus Research, Rheumatology, Melbourne, Victoria, Australia*; *[9]University of Oxford, Rheumatology, Oxford, United Kingdom*

Background: Axial, peripheral, and other disease manifestations often overlap between psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Upadacitinib (UPA) is an oral Janus kinase inhibitor under evaluation for the treatment of PsA and AS.
Objectives: To describe and compare baseline characteristics and UPA efficacy across 4 subgroups of patients (pts) from clinical trials: active PsA (with/without axial involvement) and active AS (with/without peripheral involvement).
Methods: Baseline characteristics and efficacy of UPA in reducing axial and peripheral signs and symptoms were assessed via an integrated analysis across the 4 pt subgroups from the SELECT-PsA 1,[1] SELECT-PsA 2,[2] and SELECT-AXIS[3] studies. Analyses of baseline characteristics included pts in the UPA 15 mg once daily (QD), UPA 30 mg QD, and placebo (PBO) groups; efficacy analyses included pts in the UPA 15 mg QD group only. Axial involvement in PsA (axial PsA) was determined by investigator assessment. Peripheral involvement in AS was defined based on presence of tender or swollen joints (TJC68 >0 or SJC66 >0), or presence of enthesitis at baseline (Maastricht Ankylosing Spondylitis Enthesitis Score >0).
Results: 2102 pts (UPA 15 mg; UPA 30 mg; PBO) were evaluated across the 4 subgroups (PsA [with/without axial involvement]: 626/1289; AS [with/without peripheral involvement]: 135/52). 33% of pts with PsA had axial PsA; 72% of pts with AS had peripheral symptoms. Pts with axial PsA had higher peripheral joint (TJC68 and SJC66) and skin (psoriasis) burden than pts with AS with peripheral involvement (p<0.0001). Pts with AS with peripheral involvement had significantly greater overall pain (pt's assessment of pain; p=0.0002) and back pain (BASDAI Q2; p<0.0001) scores, and higher total BASDAI (p=0.0076) and ASDAS (p=0.0351) scores than pts with axial PsA; physician's global assessment of disease activity, and peripheral pain and tenderness (BASDAI Q3 and Q4) were numerically similar for these 2 subgroups (Table 1). The efficacy of UPA 15 mg (measured using ASDAS and BASDAI) was generally consistent across the 4 pt subgroups regardless of peripheral or axial involvement (Figure 1).
Conclusion: Pts with PsA with axial involvement and pts with active AS showed some differences in baseline characteristics but similar improvements versus placebo with UPA 15 mg QD.

REFERENCES:

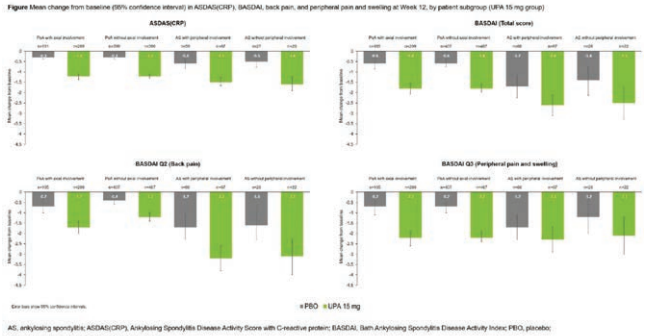
[1] McInnes I, et al. Ann Rheum Dis 2020;79(Suppl 1):16–17; 2. Genovese MC, et al. Ann Rheum Dis 2020;79(Suppl 1):139; 3. van der Heijde D, et al. Lancet 2019;394:2108–17.

Table 1. Baseline demographics, medical history, and disease characteristics

Mean (SD), unless otherwise specified	PsA with axial involvement n=626	PsA without axial involvement n=1289	AS with peripheral involvement n=135	AS without peripheral involvement n=52	p-value (PsA with axial involvement versus AS with peripheral involvement)
Male, n (%)	300 (47.9)	583 (45.2)	88 (65.2)	44 (84.6)	0.0003
Age, years	50.7 (12.6)	52.0 (12.0)	46.6 (12.7)	42.2 (11.4)	0.0008
Body mass index, kg/m^2	30.3 (7.1)	30.7 (6.8)[a]	26.7 (4.9)	26.8 (5.2)	*
Duration of disease symptoms, years	11.2 (9.3)[b]	10.4 (9.5)[a]	14.6 (10.9)	14.0 (10.6)	0.0009
Duration of disease since diagnosis, years	7.7 (8.0)	7.3 (8.0)	7.0 (9.2)	6.8 (8.4)	0.3738
TJC68	23.6 (16.4)	20.6 (14.6)	5.3 (8.2)	0	*
SJC66	11.9 (9.0)	11.2 (8.2)	1.5 (3.2)	0	*
Psoriasis, n (%)	616 (98.4)	1269 (98.4)	7 (5.2)	0	*
Uveitis, n (%)	1 (0.2)	5 (0.4)	3 (2.2)	1 (1.9)	0.0191
Inflammatory bowel disease, n (%)	10 (1.6)	13 (1.0)	2 (1.5)	2 (3.8)	1.0000
PhGA	6.7 (1.7)	6.5 (1.7)	6.7 (1.5)[c]	6.9 (1.7)[b]	0.6960
Pain, VAS 0–10	6.3 (2.0)[b]	6.1 (2.2)[d]	6.9 (1.6)[a]	6.8 (1.7)[a]	0.0002
ASDAS(CRP)	3.4 (1.0)[e]	3.1 (1.0)[f]	3.5 (0.7)[a]	3.7 (0.8)[a]	0.0351
BASDAI (Total score)	6.0 (2.1)[e]	5.5 (2.2)[f]	6.4 (1.6)	6.3 (1.8)[a]	0.0076
BASDAI Q2 (Back pain)	6.1 (2.7)[e]	4.8 (3.2)[f]	7.2 (1.7)	7.2 (1.6)[a]	*
BASDAI Q3 (Peripheral pain/ swelling)	6.3 (2.4)[e]	6.0 (2.6)[f]	5.9 (2.4)	5.5 (2.4)[a]	0.0747
BASDAI Q4 (Tenderness)	5.8 (2.6)[e]	5.6 (2.7)[f]	6.1 (2.5)	5.7 (2.4)[a]	0.3196

*p<0.0001 Data missing for [a]n=1, [b]n=3, [c]n=6, [d]n=11, [e]n=4, [f]n=14

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Grant Thomas Kirkpatrick, MSc, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.



Disclosure of Interests: Xenofon Baraliakos Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, and UCB, Atul

Deodhar Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, and UCB, R Ranza Speakers bureau: AbbVie, Janssen, Novartis, and Pfizer, Consultant of: AbbVie, Janssen, Novartis, and Pfizer, Simona Rednic: None declared, francesco ciccia Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Novartis, Pfizer, UCB, and Werfen, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, MSD, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Celgene, Chugai, Pfizer, and UCB, Fabiana Ganz Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Tianming Gao Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Apinya Lertratanakul Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Andrew Ostor Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Gilead, MSD, Novartis, Pfizer, and Roche, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Gilead, MSD, Novartis, Pfizer, and Roche, Laura C Coates: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2105

Clinical aspects of spondyloarthritis

POS0236 COMPARISON OF WORK PRODUCTIVITY OUTCOMES BETWEEN CHRONIC BACK PAIN PATIENTS WITH AND WITHOUT A DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS AFTER 2-YEAR PROTOCOLISED FOLLOW-UP: DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY COHORT

A. Boel[1], M. Van Lunteren[1], K. M. Fagerli[2], R. Ramonda[3], S. Exarchou[4], M. Van de Sande[5], F. A. Van Gaalen[1], D. Van der Heijde[1]. [1]*Leiden University Medical Centre, Rheumatology, Leiden, Netherlands*; [2]*Diakonhjemmet Hospital, Rheumatology, Oslo, Norway*; [3]*University of Padova, Rheumatology Unit, Padova, Italy*; [4]*Lund University, Clinical Sciences, Section of Rheumatology, Malmö, Sweden*; [5]*Amsterdam University Medical Center, Rheumatology and Clinical Immunology, Amsterdam, Netherlands*

Background:

Objectives: To compare work-productivity and activity impairment outcomes between chronic back pain (CBP) patients with and without an axSpA diagnosis after two years of protocollised follow-up.

Methods: Work productivity was assessed using the Work Productivity and Activity Impairment (WPAI) general health version 1.0 questionnaire. Presenteeism was defined as a reduction in performance due to disease while at work; absenteeism was time missed from work due to disease; work productivity loss (WPL) was a combined measure of presenteeism and absenteeism; and activity impairment was impairment due to disease in all non-work related activities. All WPAI outcomes were presented as percentages; higher scores implying greater impairment. Additionally, the proportion of patients with any (>0%) absenteeism, presenteeism, WPL and activity impairment were given.

This study used data from the SPACE cohort, which consists of patients with CBP (≥ 3 months <2 years) suspected of axSpA. Analyses were restricted to patients with a diagnosis axSpA or no axSpA (CBP group) with a level of confidence ≥7 (on a 0-10 scale) after locally read imaging. Additionally, data had to be available on the WPAI questionnaire at both timepoints. Assessment of presenteeism, absenteeism and WPL was restricted to the working population, defined as having paid work at baseline and 2-year follow-up. Activity impairment was assessed for the entire study population.

Regression models were used to test the difference between groups at two-year follow-up for all WPAI variables. Baseline WPAI values and NSAID-use over time were tested as confounders.

Results: Patients with a diagnosis of axSpA were more frequently male (56% vs 30%) and HLA-B27 positive (73% vs 31%) and had more SpA features at baseline compared to the patients with CBP [mean (SD) 5(2) vs 3(1)]. Age, symptom duration, NSAID-use and the percentage of patients with paid work at baseline were similar between groups.

The population having paid work at baseline and 2 years consisted of 124 patients (69%) in the axSpA group and 52 patients (70%) in the CBP group. In both groups the proportion of patients with any as well as the mean WPL reduces. This reduction was apparent in both presenteeism and absenteeism. Nevertheless, presenteeism, WPL and activity impairment were significantly higher at two-year follow-up in the group with CBP (Table 1). In these regression models with baseline values and NSAID-use over time as covariates, axSpA was an independent predictor of lower presenteeism, WPL and activity impairment at two-year follow-up.

Table 1. Work-productivity outcomes at baseline and two-year follow-up for the group with a diagnosis of axSpA and the group without a diagnosis.

	Diagnosis axSpA		CBP		p-values
	Baseline	2 years	Baseline	2 years	between groups at 2yrs
Working population	N=124		N=52		
Presenteeism, mean (SD) %	31 (28)	18 (24)†	40 (29)	30 (30)†	p=0.003*
Presenteeism present, %	73	52	87	67	
Absenteeism, mean (SD) %	7 (18)	4 (14)†	12 (25)	6 (21)†	p=0.334
Absenteeism present, %	22	7	27	12	
Overall work impairment, mean (SD) %	33 (29)	22 (27)†	43 (30)	35 (33)	p=0.005*
Overall work impairment present, %	72	46	87	65	
Total population	N=181		N=74		
Activity impairment, mean (SD) %	38 (28)	22 (24)†	50 (29)	33 (29)†	p=0.001*
Activity impairment, n(%)	86	64	93	70	

* Significant difference between groups at two years; after correction for baseline values and NSAID use over time† Significant improvement within group over time

Conclusion: Despite significant improvements in both groups, patients with axSpA have significantly better work-related outcomes after two years of protocolised follow-up compared to those without axSpA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.351

POS0237 GUT DYSBIOSIS LINKED TO WORSE DISEASE STATUS IN AXIAL SPONDYLOARTHRITIS

J. Sagard[1,2], T. Olofsson[1,2], E. Mogard[1,2], J. Marsal[3,4], K. Andréasson[1,2], M. Geijer[5,6,7], L. E. Kristensen[1,8], E. Lindqvist[1,2], J. K. Wallman[1,2]. [1]*Lund University, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden*; [2]*Skåne University Hospital, Department of Rheumatology, Lund, Sweden*; [3]*Lund University, Department of Immunology, EMV, Lund, Sweden*; [4]*Skåne University Hospital, Department of Gastroenterology, Lund, Sweden*; [5]*University of Gothenburg, Sahlgrenska Academy, Institute of Clinical Sciences, Department of Radiology, Gothenburg, Sweden*; [6]*Sahlgrenska University Hospital, Department of Radiology, Gothenburg, Sweden*; [7]*Lund University, Department of Clinical Sciences, Lund, Sweden*; [8]*Copenhagen University Hospital, Frederiksberg and Bispebjerg, Parker Institute, Department of Rheumatology, Copenhagen, Denmark*

Background: Based on clinical and genetic associations, axial spondyloarthritis (axSpA) and inflammatory bowel disease (IBD) are suspected to have a linked pathogenesis. Gut dysbiosis, intrinsic to IBD, has also been observed in axSpA. It is, however, not established to what degree gut dysbiosis is associated with axSpA disease severity.

Objectives: To compare presence and degree of gut dysbiosis between axSpA patients and controls, and to explore whether gut dysbiosis is associated with axSpA disease activity, function and pain.

Methods: The GA-map Dysbiosis Test (Genetic Analysis, Oslo, Norway) was used to identify and grade gut dysbiosis based on faecal samples from 44 non-radiographic axSpA (nr-axSpA; ASAS criteria) and 88 ankylosing spondylitis (AS; modified New York criteria) patients without IBD, consecutively enrolled in a population-based cohort study, and from 46 controls without rheumatic disease or IBD (frequency-matched to the patients for age/sex). The GA-map Dysbiosis Test is a validated method grading microbiota aberration on a 1-5 scale (Dysbiosis Index, DI), where ≥3 denotes dysbiosis. Analysis of covariance (ANCOVA) was used to compare DI between axSpA patients (nr-axSpA and AS combined) and controls, adjusted for age, sex, body mass index (BMI) and smoking. Within the axSpA group, disease activity (ASDAS-CRP; BASDAI), function (BASFI) and pain (VAS pain) were compared between patients with various DI levels by One-way analysis of variance (ANOVA) or Kruskal-Wallis test, as appropriate. Finally, axSpA patients were subdivided by presence of dysbiosis (DI ≥3 vs. <3) followed by comparison of ASDAS-CRP, BASDAI, BASFI, VAS pain and Evaluator´s global assessment of disease activity (EvalGlobal; 0-4: remission-maximal) by ANCOVA. Analyses were conducted unadjusted and adjusted for age, sex, BMI, smoking, axSpA subtype, gut inflammation (faecal calprotectin ≥50 mg/kg), irritable bowel syndrome symptoms (ROME III criteria), ASAS 3-month NSAID score and cs/bDMARD treatment.

Results: Characteristics of the patients/controls are shown in the Table 1. Gut dysbiosis (DI≥3) was observed in 33% of axSpA patients and 17% of controls. DI was significantly higher among the patients (β-estimate [bootstrapped 95%CI] for the between-group difference: 0.34 [0.04-0.65]; p=0.027). In the axSpA group, higher DI was associated with worse scores in all assessed outcomes (Figure 1, panel A). Moreover, presence of dysbiosis (DI≥3) was associated with worse ASDAS-CRP, BASDAI, BASFI, VAS pain and EvalGlobal (Figure 1, panel B; EvalGlobal not shown in the Figure: unadjusted β [bootstrapped 95%CI]: 0.32 [0.09-0.55], adjusted: 0.28 [0.03-0.52] for patients with DI ≥3 vs. <3), with between-group differences remaining significant after adjustment, except for ASDAS-CRP (p=0.079) and VAS pain (p=0.064).

Conclusion: Gut dysbiosis, present to a higher degree in axSpA patients than controls, is associated with worse axSpA disease activity and function. These

associations appear independent of gut inflammation and both NSAID and immunomodulatory treatment. This provides further evidence for an important link between disturbances in gastrointestinal homeostasis and axSpA manifestations, and implies that gut dysbiosis may be a novel biomarker for severe disease.

Table 1.

	All patients n=132	Nr-axSpA n=44	AS n=88	Controls n=46
Male sex, n (%)	72 (55)	17 (39)	55 (63)	23 (50)
Age, y	53 (13)	48 (12)	55 (13)	51 (14)
Symptom duration, y	26 (14)	21 (11)	28 (14)	
Body mass index, kg/m^2	27 (4.3)	27 (4.2)	27 (4.3)	25 (3.3)
Smoking ever, n (%)	43 (33)	9 (20)	34 (39)	13 (28)
CRP, mg/L	3.7 (5.3)	2.3 (2.4)	4.3 (6.1)	
F-Calprotectin ≥50 mg/kg, n (%)	46 (35)	12 (27)	34 (39)	
Evaluator´s global, 0-4, median (IQR)	1 (0-1)	1 (0-1)	1 (0-1)	
ASDAS-CRP	1.8 (0.9)	1.9 (0.9)	1.8 (0.9)	
BASDAI	3.1 (2.2)	3.3 (1.9)	3.0 (2.4)	
BASFI	2.0 (2.1)	2.0 (1.7)	2.1 (2.2)	
VAS pain, cm	3.3 (2.5)	3.4 (2.2)	3.2 (2.7)	
IBS symptoms, n (%)	43 (33)	15 (34)	28 (32)	
ASAS 3-month NSAID score	37 (44)	36 (44)	37 (44)	
Ongoing csDMARD, n (%)	24 (18)	9 (20)	15 (17)	
Ongoing bDMARD, n (%)	56 (42)	19 (43)	37 (42)	

Mean (SD) unless otherwise specified. y, years; IBS, irritable bowel syndrome

Disclosure of Interests: Jonas Sagard: None declared, Tor Olofsson Consultant of: Eli Lilly, Merck Sharp & Dohme, Elisabeth Mogard: None declared, Jan Marsal Consultant of: AbbVie, Bristol-Myers Squibb, EuroDiagnostica, Ferring, Hospira, Janssen-Cilag, Merck, Sharp & Dohme (MSD), Otsuka, Pfizer, Sandoz, Takeda, Tillotts, UCB Pharma, Grant/research support from: AbbVie, Ferring, and Pfizer, Kristofer Andréasson: None declared, Mats Geijer Speakers bureau: UCB Pharma, AbbVie, Novartis, Pfizer, Lars Erik Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Celegene, BMS, MSD, Novartis, Eli Lilly, Janssen pharmaceuticals, Consultant of: Pfizer, AbbVie, Amgen, UCB, Celegene, BMS, MSD, Novartis, Eli Lilly, Janssen pharmaceuticals, Elisabet Lindqvist: None declared, Johan K Wallman Consultant of: Celgene, Eli Lilly, Novartis

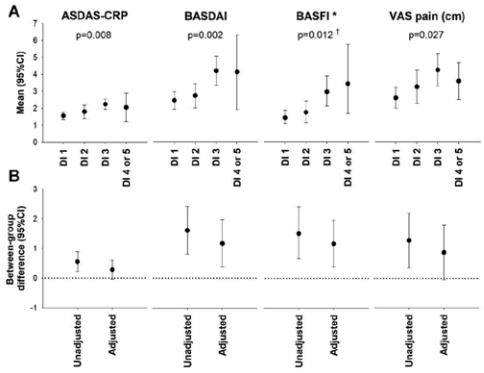


***Figure – A:** AxSpA outcomes in relation to Dysbiosis Index (DI, a measure of gut microbiota aberration, with ≥3 denoting dysbiosis). P-values for overall between-group differences (One-way ANOVA; † Kruskal-Wallis test). **B:** Between-group differences (unadjusted and adjusted) in axSpA outcomes between patients with gut dysbiosis (DI≥3) vs. those without. * Bootstrapped 95%CI:s.*

DOI: 10.1136/annrheumdis-2021-eular.472

POS0238 SICK LEAVE AND ITS PREDICTORS IN EARLY AXIAL SPONDYLOARTHRITIS: THE ROLE OF CLINICAL AND SOCIOECONOMIC FACTORS. FIVE-YEAR DATA FROM THE DESIR COHORT

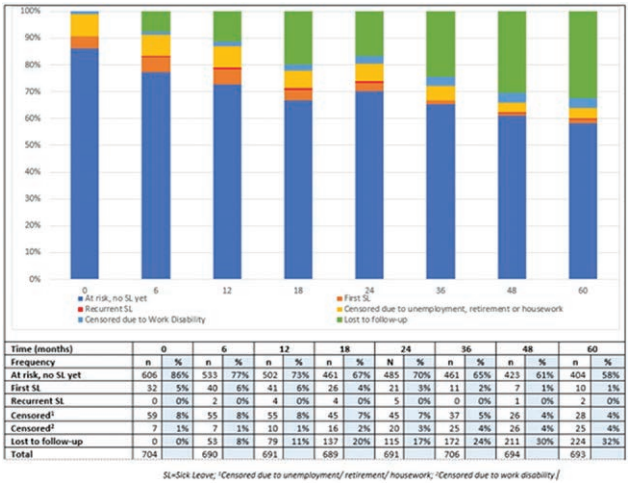
E. Nikiphorou[1,2], P. Carvalho[3,4,5], A. Boonen[6,7], B. Fautrel[8], P. Richette[9], P. M. Machado[10], D. Van der Heijde[11], R. B. M. Landewé[12,13], S. Ramiro[11,12]. [1]*King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; [2]*King's College Hospital NHS Trust, Rheumatology, London, United Kingdom*; [3]*Centro Hospitalar Universitário do Algarve, Rheumatology, Faro, Portugal*; [4]*Centro Académico Médico de Lisboa, Rheumatology, Lisboa, Portugal*; [5]*Algarve Biomedical Center, Rheumatology, Faro, Portugal*; [6]*Maastricht University Medical Center and Care and Public Health Research Institute (CAPHRI), Rheumatology, Maastricht, Netherlands*; [7]*Academic Hospital Maastricht, Internal Medicine, Div. of Rheumatology, Maastricht, Netherlands*; [8]*Sorbonne University – Assistance Publique Hopitaux de Paris, Pitie Salpetriere Hospital, Pierre Louis Institute for Epidemiology and Public Health, INSERM UMRS 1136, PEPITES Teams, Rheumatology, Paris, France*; [9]*Université de Paris, Hopital Lariboisière, Rheumatology, Paris, France*; [10]*University College London, Centre for Rheumatology, London, United Kingdom*; [11]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; [12]*Zuyderland MC, Rheumatology, Heerlen, Netherlands*; [13]*Amsterdam University Medical Center, Rheumatology, Amsterdam, Netherlands*

Background: Sick leave (SL) represents an often poorly studied adverse work outcome especially in early axSpA, with speculation around the potential role of clinical and socioeconomic (SE) factors.

Objectives: To investigate the occurrence of SL and the impact of clinical and SE factors on SL in early axSpA.

Methods: Patients with a clinical diagnosis of axSpA from the DESIR cohort up to 5 years of follow-up (6-month visits in the first 2 years, followed by annual visits) were studied. Time to SL and potential baseline and time-varying predictors were explored, with a focus on SE variables: age, gender, smoking status since last visit, ethnicity (Caucasian vs other), job type based on 'collar' (blue vs white), educational status (low vs high -university), marital status (married vs not) and parental status (number of children); and clinical factors including disease activity (ASDAS/BASDAI), function (BASFI), mobility (BASMI), at each time point. The incidence of SL was calculated as the number of SL events over the total number of person-days under observation. Univariable analyses, followed by collinearity and interaction tests, guided subsequent multivariable Cox survival model building.

Results: In total, 704 axSpA patients with work-related data were included in this study: mean (SD) age 33.8 (8.6); 46% male. At baseline, 80% of patients were employed; of these, 5.7% reported being on SL, with people shifting in and out of different work states over time. The distribution of first and recurrent SL episodes over time is shown in the figure 1. The incidence of SL amongst those at risk (n=620, 88%) and across the five years of DESIR was 0.05 (95% CI 0.03, 0.06) per 1000 days calculated in a total of 913,559 observed person-days. In survival analyses, 7% (n=43) of those at risk developed SL at some point. Mean (SD) time to SL was 806 (595) days (min 175, max 2021 days). In people who developed SL, 25% did so at 364 days; 50% and 75% at 545 and 1172 days, respectively. Significant differences were seen between baseline socio-demographic, clinical variables and treatment in patients who developed SL at any point, compared to those who did not. In multivariable models (Table 1) older age, higher disease activity, smoking and use of TNFi, the latter likely a proxy to worse disease, were all significantly associated with more SL. Male gender and higher education were associated with less SL. There were no relevant interactions between SE factors and clinical variables.



Time (months)	0		6		12		18		24		36		48		60	
Frequency	n	%	n	%	n	%	n	%	N	%	n	%	n	%	n	%
At risk, no SL yet	606	86%	533	77%	502	73%	461	67%	485	70%	461	65%	423	61%	404	58%
First SL	32	5%	40	6%	41	6%	26	4%	21	3%	11	2%	7	1%	10	1%
Recurrent SL	0	0%	2	0%	4	0%	4	0%	5	0%	0	0%	1	0%	2	0%
Censored[1]	59	8%	55	8%	55	8%	45	7%	45	7%	37	5%	26	4%	28	4%
Censored[2]	7	1%	7	1%	10	1%	16	2%	20	3%	25	4%	26	4%	25	4%
Lost to follow-up	0	0%	53	8%	79	11%	137	20%	115	17%	172	24%	211	30%	224	32%
Total	704		690		691		689		691		706		694		693	

SL=Sick Leave; [1]Censored due to unemployment/ retirement/ housework; [2]Censored due to work disability.

Figure 1. Distribution of first and recurrent sick leave episodes over time in the study population at risk.

Table 1. Univariable and multivariable model analyses with Sick Leave as outcome.

Type of analysis	Univariable analysis HR (95% CI)	Multivariable model HR (95% CI) (N = 614)
Explanatory variables		
Age	1.04 (1.01, 1.08)	1.05 (1.01, 1.09)
Male gender	0.37 (0.19, 0.74)	0.41 (0.20, 0.86)
High education	0.33 (0.17, 0.61)	0.48 (0.24, 0.95)
Marital status	2.44 (1.12, 5.27)	NS
ASDAS (CRP)	1.83 (1.34, 2.50)	1.49 (1.04, 2.13)
BASFI, 0-10	1.24 (1.09, 1.40)	*
BASMI, 0-10	1.76 (1.31, 2.38)	*
Comorbidity count	1.77 (1.22, 2.57)	NS
HLA-B27 positive	0.51 (0.28, 0.93)	NS
Smoking (current vs not)	2.40 (1.31, 4.37)	2.55 (1.32, 4.91)
NSAID score last week, 0-400	1.01 (1.00, 1.01)	NS
Oral Corticosteroid use (vs no)	3.90 (1.80, 8.46)	NS
TNF use	2.86 (1.55, 5.28)	2.41 (1.27, 4.58)

*Variables tested in models separate from ASDAS. NS=Not significant in multivariable model.

Conclusion: In this early axSpA cohort of young, working-age individuals, older age and worse disease activity were associated with more SL, whereas male gender and higher education were associated with less SL. The findings suggest a role of SE factors such as gender and level of education in adverse work outcomes, alongside active disease.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.723

POS0239 ROOT JOINT INVOLVEMENT IN SPONDYLOARTHRITIS: A POST-HOC ANALYSIS FROM THE INTERNATIONAL ASAS-PERSPA STUDY

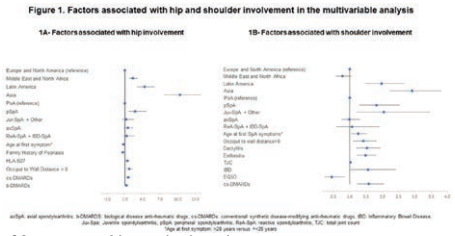
N. Ziade[1], J. El-Hajj[2], J. Rassi[3,4], S. Hlais[5,6], C. López-Medina[7,8], S. Gamal[9], B. Zorkany[9,10], M. Dougados[7], X. Baraliakos[11]. [1]*Saint-Joseph University, Rheumatology, Beirut, Lebanon*; [2]*Saint-Joseph University, Medicine, Beirut, Lebanon*; [3]*Saint-Joseph University, Surgery, Beirut, Lebanon*; [4]*Hotel-Dieu de France, Orthopedic Surgery, Beirut, Lebanon*; [5]*Saint-Joseph University, Family Medicine, Beirut, Lebanon*;

[6]*American University of Beirut, Family Medicine, Beirut, Lebanon*; [7]*Cochin Hospital, Rheumatology, Paris, France*; [8]*Reina Sofia University Hospital / IMIBIC/ University of Cordoba, Rheumatology, Cordoba, Spain*; [9]*Cairo University, Rheumatology, Cairo, Egypt*; [10]*Kasr Alaini Hospital, Rheumatology, Cairo, Egypt*; [11]*Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Rheumatology, Herne, Germany*

Background: In patients with spondyloarthritis (SpA), root joint diseases (RJD), i.e. hip or shoulder involvement, may be associated with a distinct disease phenotype compared to those with other affected joints. The ASAS-PerSpA study (PERipheral involvement in SPondyloArthritis) [1], offers a unique opportunity to study the phenotypes of patients with RJD in a global cohort.
Objectives: Primary objective was to compare the clinical characteristics of SpA patients with and without RJD. Secondary objectives were to compare the prevalence of RJD across the different SpA subtypes and the different regions of the world, compare the severity of axial disease as well as the disease burden in SpA patients with and without RJD.
Methods: This is a post-hoc analysis of the ASAS-PerSpA study, which included 4,465 patients with any subtype of SpA (axial SpA (axSpA), peripheral SpA (pSpA), psoriatic arthritis (PsA), inflammatory bowel disease associated SpA (IBD-SpA), reactive arthritis (ReA) and Juvenile SpA (Juv-SpA)) according to the rheumatologist's diagnosis. RJD was defined as a positive answer by the investigator to the following question: "Do you consider that the patient has ever suffered from RJD (e.g. hip, shoulder) related to SpA?" In case of a positive answer, a potential specific treatment (e.g. Total Articular Replacement) was investigated. The patient's characteristics were compared between those with and without RJD involvement, using Chi-2 or Fisher exact test for the categorical variables and t-test for the continuous variables. Two separate multivariable stepwise binary logistic regression analyses were conducted to identify factors associated with the dependent variables "hip involvement" and "shoulder involvement".
Results: RJD occurred in 1,503 patients (33.7%), with more prevalent hip (24.2%) than shoulder (13.2%) involvement. The prevalence of RJD as a group was the highest in Juv-SpA (52.7%), followed by pSpA (44.3%) and axSpA (33.9%). The highest prevalence of RJD was found in Asia and the lowest in Europe and North America. Among patients with hip involvement, 6.0% had a history of hip replacement (highest in the Middle East and North Africa and Latin America); among patients with shoulder involvement, 0.8% had a history of shoulder replacement. Hip had a distinct pattern of associations compared to shoulder involvement (Figure 1). Hip involvement was significantly associated with the SpA main diagnosis (highest in pSpA, lowest in PsA), younger age at first SpA symptom, lower prevalence of family history of psoriasis, positive HLA-B27, occiput-to-wall distance>0, and treatment with cs-DMARDs and b-DMARDs. Shoulder involvement was associated with the SpA main diagnosis (highest in Juv-SpA and pSpA, lowest in axSpA), older age at first SpA symptom, higher prevalence of enthesitis, dactylitis, tender joints count, IBD, occiput-to-wall distance>0, EQ5D score and treatment with cs-DMARDs.
Conclusion: Hip involvement was more prevalent than shoulder involvement in patients with SpA, and had a distinct phenotype resembling axial disease whereas shoulder involvement was mostly associated with features of peripheral disease. Hip and shoulder involvement should be analyzed separately in future studies rather than under the RJD entity.

REFERENCES:

[1] Lopez-medina, C. et al. Prevalence and Distribution of Peripheral Musculoskeletal Manifestations in Axial Spondyloarthritis, Peripheral Spondyloarthritis and Psoriatic Arthritis: Results of the International, Cross-sectional ASAS-PerSpA Study. RMD Open; 2021;7:e001450.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.651

POS0240

GEOGRAPHICAL PREVALENCE OF A FAMILY HISTORY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND ITS ASSOCIATION WITH HLA-B27: DATA FROM THE WORLDWIDE ASAS-PERSPA STUDY

M. Van Lunteren[1], A. Boel[1], C. López-Medina[2], J. Sieper[3,4], D. Van der Heijde[1], F. A. Van Gaalen[1]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; [2]*Cochin Hospital, Rheumatology, Paris, France*; [3]*Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Rheumatology, Berlin, Germany*; [4]*German Rheumatism Research Centre, Rheumatology, Berlin, Germany*

Background: Research has shown that in axial spondyloarthritis (axSpA) patients, the most common form of spondyloarthritis (SpA) in a family history is axSpA. Moreover, the association between a positive family history of spondyloarthritis (PFH) and HLA-B27 carriership is driven by a PFH of axSpA and possibly acute anterior uveitis (AAU), but not by other forms of SpA. However, this research was limited to mostly Western European patients.
Objectives: To investigate the impact of geographical region on family history and its association between HLA-B27 carriership in patients with axSpA around the world.
Methods: Data from the Assessment in SpondyloArthritis international Society (ASAS) peripheral involvement in Spondyloarthritis (ASAS-perSpA) study was used. Analyses were restricted to patients with an axSpA diagnosis who had information available on HLA-B27 status and family history. The frequencies of any PFH, as well as a PFH for axSpA, psoriasis, AAU, inflammatory bowel disease (IBD) and reactive arthritis (ReA), were determined per geographical region. Logistic regression models were built to assess the effect of HLA-B27 status on the occurrence of any PFH and each disease in a PFH in the total population and also stratified per geographical region.
Results: In total, 2,048 patients were included from 4 regions: Asia (n=545), Europe & North America (n=840), Latin America (n=202), and Middle East & North Africa (n=461). Patients had a median age (IQR) of 40 (31-50) years, 31% were female, and had a disease duration of 11 (5-20) years.
A PFH of axSpA was the most common in all geographical regions, regardless of HLA-B27 carriership. A PFH of psoriasis and IBD appeared to be more common in HLA-B27 negative patients, and a PFH of ReA was rare in all patients (figure 1). Univariable logistic regression models showed an association between a PFH and HLA-B27 carriership in the Asian population, but this association does not seem apparent in the other geographical regions (table 1). Contrary, a PFH of axSpA was associated with HLA-B27 carriership in all geographical regions except the Middle East & North Africa (table 1). An association between HLA-B27 carriership and a PFH of psoriasis was solely present in Middle East & North Africa (OR=0.4, 95% CI 0.2-0.7), and an association with a PFH of IBD was solely present in Europe & North America (OR=0.5, 95% CI 0.3-0.9). No associations were found for HLA-B27 carriership and a PFH of AAU and ReA in any geographical region. There was also no effect modification of geographical region (p=0.43) on the association between HLA-B27 status and a PFH.

Table 1. Univariable associations between HLA-B27 carriership and a positive family history of axSpA patients in the perSpA cohort stratified per geographical region

	HLA-B27+ n=1,609	HLA-B27-n=439	OR (95% CI)	p-value
Any positive family history				
Total population				
Yes	**631**	**149**	**1.26 (1.01-1.57)**	**0.044**
No	978	290	Ref.	
Per geographical region				
Asia	**157/487**	**11/58**	**4.23 (2.26-7.91)**	**<0.001**
Europe & North America	270/658	67/182	1.19 (0.89-1.61)	0.241
Latin America	50/164	9/38	1.65 (0.80-3.39)	0.175
Middle East & North Africa	154/300	62/161	0.74 (0.53-1.02)	0.063
Positive family history for axSpA				
Total population				
Yes	**518**	**90**	**1.84 (1.43-2.38)**	**<0.001**
No	1,087	348	Ref.	
Per geographical region				
Asia	**144/487**	**11/58**	**4.19 (2.24-7.83)**	**<0.001**
Europe & North America	**196/658**	**30/182**	**2.09 (1.40-3.13)**	**<0.001**
Latin America	**37/164**	**3/38**	**3.95 (1.21-12.89)**	**0.023**
Middle East & North Africa	141/300	46/161	0.98 (0.69-1.40)	0.917

axSpA, axial spondyloarthritis; **CI,** confidence interval; **HLA-B27,** human leucocyte antigen B27; **OR,** odds ratio

Conclusion: Throughout the world, axSpA was the most common form of SpA in a family history. In all regions except Middle East & North Africa, a PFH of axSpA was associated with HLA-B27 carriership in axSpA patients. These results suggest that the current expert definition of a PFH of SpA should be revaluated.

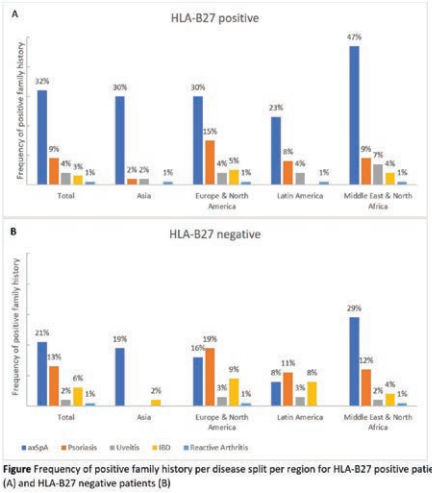


Figure Frequency of positive family history per disease split per region for HLA-B27 positive patients (A) and HLA-B27 negative patients (B)

Acknowledgements: We would like to thank all ASAS-perSpA investigators and members of the scientific committee.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.841

POS0241

VALIDATION OF THE ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE WITH A QUICK QUANTITATIVE C-REACTIVE PROTEIN ASSAY (ASDAS-QCRP) IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS (AXSPA): A PROSPECTIVE, NATIONAL, MULTICENTER STUDY

F. Proft[1], J. Schally[1], H. C. Brandt[2], J. Brandt-Juergens[3], G. R. Burmester[4], H. Haibel[1], H. Käding[1], K. Karberg[2], S. Lüders[1], B. Muche[1], M. Protopopov[1], J. Rademacher[1], V. Rios Rodriguez[1], M. Torgutalp[1], M. Verba[1], S. Zinke[5], D. Poddubnyy[1]. [1]*Charité - Universitätsmedizin Berlin, Division of Gastroenterology, Infectiology and Rheumatology, Campus Benjamin Franklin, Berlin, Germany*; [2]*Praxis für Rheumatologie und Innere Medizin, Praxis für Rheumatologie und Innere Medizin, Berlin, Germany*; [3]*Rheumatologische Schwerpunktpraxis, Rheumatologische Schwerpunktpraxis, Berlin, Germany*; [4]*Charité - Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; [5]*Rheumapraxis Berlin, Rheumapraxis Berlin, Berlin, Germany*

Background: According to international recommendations, the Ankylosing Spondylitis Disease Activity Score (ASDAS) is the preferred score for assessing disease activity in axial spondyloarthritis (axSpA) [1]. However, routine determination of C-reactive protein (CRP) to calculate ASDAS values takes hours to days. This limits the use of ASDAS in clinical routine and clinical trials and hinders the implementation of treat-to-target approaches in axSpA. Whereas quick quantitative CRP (qCRP) tests allow CRP assessment within a few minutes. In a pilot project the performance of qCRP-based ASDAS assessment (ASDAS-qCRP) was already investigated in a single center study of 50 newly diagnosed, bDMARD-naïve axSpA patients with promising results [2].
Objectives: To validate the ASDAS-qCRP in a prospective, multicenter study of axSpA patients in a typical axSpA cohort with an appropriate sample size.
Methods: The study was conducted in five centers in Germany. Consecutive adult (≥ 18 years) axSpA patients were included. In addition to a rheumatological assessment, including patient reported outcomes (PROs), routine CRP and erythrocyte sedimentation rate (ESR) were measured in the local labs. Additionally, a qCRP testing with the „QuikRead go instrument" (Aidian Oy, Finland) was performed at the study center (measurement range 0.5 - 200 mg/l for hematocrit concentrations of 40 – 45%). Statistical analysis included descriptive statistics, cross tabulation and weighted Cohen´s kappa comparing disease activity categories, Bland-Altman plots and intraclass correlation coefficient (ICC) for ASDAS-CRP and ASDAS-qCRP.
Results: In this study 251 axSpA patients were included between January and September 2020 (mean age: 38.4 years; mean disease duration: 6.2 years, 159 patients (63.3%) were male, 211 (84.1%) HLA-B27 positive and 195 (77.7%) were classified as radiographic axSpA). 143 patients (57.0%) were treated with bDMARDs. CRP and qCRP showed mean values of 2.12 and 2.17 mg/l, respectively. With the ASDAS-qCRP, 242 patients (96.4%) were assigned to the same disease activity category as compared to the ASDAS based on the conventional lab CRP measurement (Table 1). Weighted Cohen´s kappa was 0.966 (95%CI: 0.943; 0.988). ICC for ASDAS-CRP- and ASDAS-qCRP-values was 0.997 (95%CI: 0.994; 0.999). The agreement of ASDAS-qCRP and ASDAS-CRP is shown in a Bland-Altman plot (Figure 1).
Conclusion: The ASDAS-qCRP and ASDAS-CRP showed an almost perfect agreement on the assignment to disease activity categories (96%) with the important advantage of time. With ASDAS-qCRP, rheumatologists could base their clinical decision-making on a disease activity measurement by using a composite score immediately. ASDAS-qCRP, therefore, can be integrated in clinical routine and clinical trials in the future and may facilitate implementation of the treat-to-target concept in axial SpA.

REFERENCES:

[1] Smolen JS, et al. Ann Rheum Dis. 2018 Jan; 77(1):3-17.
[2] Proft F, et al. Joint Bone Spine. 2019 Jul 29.

Table 1. Disease activity categories by ASDAS-qCRP vs. ASDAS-CRP

		ASDAS-qCRP (n = 251)			
		Inactive Disease (< 1.3)	Low Disease Activity (1.3 - < 2.1)	High Disease Activity (2.1 - 3.5)	Very high Disease Activity (> 3.5)
ASDAS-CRP	Inactive Disease (< 1.3)	56 (22.3%)	2 (0.8%)		
	Low Disease Activity (1.3 - < 2.1)		62 (24.7%)	7 (2.8%)	
	High Disease Activity (2.1 - 3.5)			97 (38.6%)	
	Very high Disease Activity (> 3.5)				27 (10.8%)

The fields highlighted in red indicate that disease activity categories do not match.ASDAS = Ankylosing Spondylitis Disease Activity Score, CRP = C-reactive protein, qCRP = quick quantitative CRP

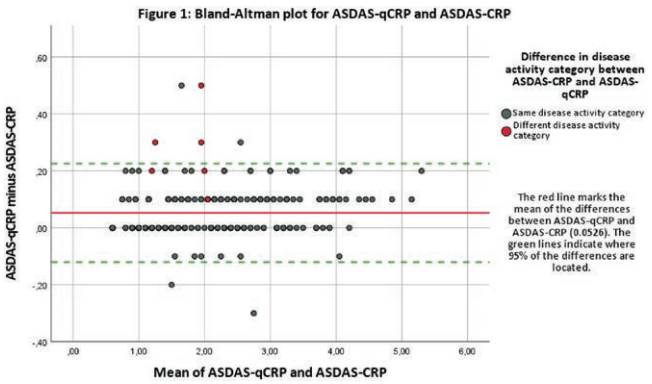


Figure 1. Bland-Altman plot for ASDAS-qCRP and ASDAS-CRP

Acknowledgements: The authors would like to deeply thank Braun T, Doerwald C, Deter N, Höppner C, Lackinger J, Lorenz C, Lunkwitz K, Mandt B, Sron S and Zernicke J for their practical support and coordinating the study.
Funding statement: The AQUA study was supported by an unrestricted research grant from Novartis. Testing kits were provided free of charge from Aidian Oy, Finland.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2352

POS0242

ROLE OF HLA-B27 CARRIERSHIP IN PERIPHERAL SPONDYLOARTHRITIS: DATA FROM ASAS PERSPA STUDY

M. Arévalo[1], C. López-Medina[2], V. Navarro-Compán[3], M. Moreno[1], M. Llop Vilaltella[1], J. Calvet[1], J. Gratacos-Masmitja[1], M. Dougados[4]on behalf of ASAS group. [1]*Hospital Parc Taulí I3PT, Rheumatology, Sabadell, Spain*; [2]*Hospital Universitario Reina Sofía/IMIBIC/Universidad de Córdoba, Rheumatology, Cordoba, Spain*; [3]*Hospital Universitario la Paz, IdiPaz, Rheumatology, Madrid, Spain*; [4]*Hôpital Cochin, Rheumatology, Paris, France*

Background: HLA-B27 is well known for its role in conferring susceptibility to spondyloarthritis (SpA), and several studies evaluating its association to axial SpA phenotype have been published. However, there is few evidence about its influence in patients affected with peripheral SpA (pSpA). In this sense we find ASAS perSpA registry suitable for this purpose.
Objectives: To identify phenotypical differences in pSpA patients regarding HLA-B27 status.
Methods: Data from all patients fulfilling ASAS pSpA criteria with HLA-B27-testing result available included in the ASAS perSpA study were used for this analysis. Socio-demographic and disease characteristics were collected. A descriptive and comparative analysis was performed between HLA-B27 positive and negative patients, using a simple logistic regression for all variables to assess their association to HLA-B27 positivity. Results were considered significant when $p < 0.05$. A multivariate model was also performed including significant ($p < 0.1$) and the most relevant clinical variables in agreement of medical criteria.
Results: Among the 4465 patients included in the registry, 555 fulfilled ASAS pSpA criteria and of them 286 had the HLA-B27 typing available. HLA-B27 was positive in 118 (41.3%) and negative in 168 (58.7%). Results are listed in Table 1. No differences were observed for gender distribution (males 55.1% in HLA-B27 positive vs 49.4% in HLA-B27 negatives). HLA-B27 positive patients were significantly younger, presented a younger disease onset, had significantly higher prior axial involvement, radiographic sacroiliitis and higher root joint involvement. On the other hand, HLA-B27 negative patients showed longer disease duration with a higher diagnosis delay. Around half of the patients in both groups showed a mono or oligoarticular pattern without differences regarding HLA-B27 status, however, psoriatic arthritis (PsA) and peripheral joint damage was significantly higher in HLA-B27 negative patients. Also psoriasis and inflammatory bowel disease (IBD) were more frequent in HLA-B27 negative patients compared to positive ones, and acute anterior uveitis (AAU) was significantly more frequent in HLA-B27 positive patients without differences in number of AAU episodes lifelong. Finally, obesity and concomitant fibromyalgia were both more common in HLA-B27 negatives. No significant differences were found for the rest of variables evaluated.
In the multivariate analysis, age at disease onset (OR 0.96, CI95% 0.94-0.98), disease duration (OR 0.96, CI95% 0.92-0.99), PsA (OR 0.28, CI95% 0.09-0.85), presence of psoriasis (OR 0.22, CI95% 0.07-0.64), IBD related arthritis (OR 0.03, CI95% 0.01-0.19), AAU (OR 3.63, CI95% 1.22-11.9) and tarsitis (OR 2.61, CI95% 1.01-6.98) were the most important variables independently associated to HLA-B27 status.

Conclusion: Presence of HLA-B27 in pSpA patients was associated to a higher axial and root joint involvement, an earlier disease onset and presence of AAU, but not to PsA, psoriasis and IBD that were higher in HLA-B27 negative patients.

Table 1.

	HLA-B27+ (N = 118)		HLA-B27- (N = 168)		
	N/mean	%/SD	N/mean	%/SD	p
Obesity (BMI >30)	14	11,9%	44	26,3%	0,003
Men	65	55,1%	83	49,4%	0,344
Family history	44	37,3%	52	31,0%	0,265
Axial involvement	62	52,5%	42	25,0%	<0.001
Radiographic sacroilitis	30	28,3%	25	16,8%	0,029
Psoriathic arthritis	23	19,5%	112	72,6%	<0.001
Reactive arthritis	5	4,2%	3	1,8%	0,229
IBD arthritis	1	0,9%	8	4,8%	0,098
Mono/oligoarticular pattern	59	54,6%	76	51,0%	0,566
Root joint involvement	52	44,1%	54	32,1%	0,04
Tarsitis	22	18,6%	16	9,5%	0,028
Enthesitis	62	52,5%	69	41,1%	0,056
Dactylitis	31	26,3%	51	30,4%	0,452
Peripheral structural damage	9	7,6%	41	24,4%	<0.001
Psoriasis	21	17,8%	125	74,4%	<0.001
AAU	21	17,8%	7	4,2%	<0.001
IBD	2	1,7%	13	7,7%	0,039
Fibromyalgia	15	13,2%	43	26,7%	0,008
Age (y)	42,7	14,8	52,2	13,4	<0.001
Age onset (y)	33,9	13,7	38,3	14,5	0,013
Dx delay (m)	4,7	8,2	7,7	9,8	0,009
Disease duration (y)	9,06	10,2	14,2	11,6	<0.001
BASDAI	3,9	2,2	4,4	2,4	0,06
CRP	16,9	25,1	12	27,3	0,148
ASDAS-CRP	2,7	1,2	2,7	1,1	0,876
AAU number of episodes	6,8	8,4	2,1	1,7	0,265

Disclosure of Interests: Marta Arévalo Speakers bureau: Abbvie, Nordic Pharma, Clementina López-Medina: None declared, Victoria Navarro-Compán: None declared, Mireia Moreno Speakers bureau: Abbvie, Novartis, UCB, Bristol and AMGEN, María LLop Vilaltella Speakers bureau: Novartis, Joan Calvet: None declared, Jordi Gratacos-Masmitja Speakers bureau: During the course of the year, I have received funding for courses and conferences or as an advisor and speaker from MSD, Pfizer, AbbVie, Janssen Cilag, Novartis, Celgene, and Lilly., Maxime Dougados: None declared

DOI: 10.1136/annrheumdis-2021-eular.965

POS0243

WHAT DOES REMISSION IN AXIAL SPONDYLOARTHRITIS MEAN FOR CLINICIANS? AN EXPLORATORY STUDY OF 200 FRENCH RHEUMATOLOGISTS BASED ON A VIGNETTE EXERCISE INCLUDING 36 CASES AND PRIORITY RATINGS

K. Aouad[1], D. Wendling[2], A. Baglin[3], M. Breban[4], S. Dadoun[5,6], C. Hudry7, A. Moltó[8,9], E. Pertuiset[10], L. Gossec[1]. [1]*Sorbonne University; AP-HP, Pitié Salpêtrière Hospital, Rheumatology Department, Paris, France*; [2]*Besançon University Hospital, Rheumatology Department, Besançon, France*; [3]*Novartis, Pharmaceutical, Ile de France, France*; [4]*APHP, Ambroise Paré Hospital, Rheumatology Department, Boulogne, France*; [5]*Private practice, Rheumatology, Paris, France*; [6]*CeSOA, MGEN action sociale, Rheumatology, Paris, France*; [6]*CeSOA, MGEN action sociale, Rheumatology, Paris, France*; [8]*Cochin Hospital, APHP, Rheumatology Department, Paris, France*; [9]*INSERM U-1153 (ECAMO), CRESS, Université de Paris, Rheumatology, Paris, France*; [10]*Rene Dubos Hospital, Rheumatology Department, Pontoise, France*

Background: Treat-to-target in axial spondyloarthritis (axSpA) aims to achieve and maintain clinical remission/inactive disease or alternatively, low disease activity [1]. However, there is no consensual definition of remission in axSpA: the T2T international task force has proposed Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease, but this definition is not widely accepted [1, 2].

Objectives: To explore rheumatologists' perception of remission in axSpA, using vignette cases and a priority exercise.

Methods: A steering group of 7 rheumatologists designed a national cross-sectional survey during two face-to-face meetings in 2019-2020. The survey comprised 36 vignette cases: fixed elements included the clinical picture (34 year-old-male with confirmed axSpA, normal C-reactive protein (CRP), without synovitis, enthesitis, dactylitis or extra-articular manifestations) and there were 3 varying parameters (axial pain (0-10) [ranging 2 to 5], fatigue (0-10) [2 to 8], and morning stiffness [<15 minutes, 30 minutes or 1 hour]. For each vignette, the rheumatologist answered binarily: "do you consider this patient in remission: yes/no". The second part of the survey comprised a priority rating (0-10 priority and 4 top items) of elements important to consider for remission, from a list of 12 items (BASDAI, ASDAS, elements of BASDAI and ASDAS including CRP, NSAIDs use, extra-articular manifestations, and other explanations for the symptoms e.g., fibromyalgia). The analysis was descriptive.

Results: Overall, 200 French rheumatologists participated between June and September 2020. Out of 2,400 vignette evaluations (mean of 66 evaluations per vignette), 463 (19%) were classified as remission by rheumatologists. Six vignette cases constituted 56% of all remission cases (Figure 1): these comprised a short duration of morning stiffness (<15 minutes), a low VAS axial pain (2 or 3) but with varying levels of VAS fatigue. When the duration of morning stiffness increased from 15 to 30 minutes and VAS axial pain increased from 2-3 to 4-5 independently, classification as remission decreased from 42% to 12% and from 28-33% to 5-11%, respectively. However, when VAS fatigue increased, it impacted less remission.

In priority ratings, 4 items were selected as important by 68-75% of rheumatologists: morning stiffness and axial pain (both included in the vignettes), as well as extra-articular manifestations and NSAID use, whereas only 18% selected fatigue. BASDAI was cited as the 1st priority criteria by 24% of rheumatologists and ASDAS as the 2nd by 16% of rheumatologists.

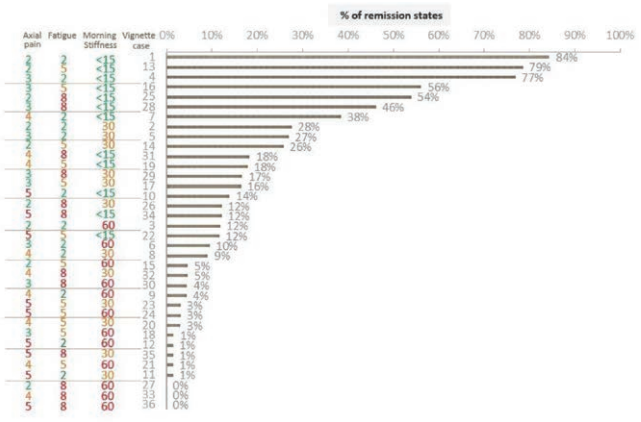


Figure 1. Frequencies of the declared remission states by rheumatologists for each of the 36 vignette cases

Conclusion: Morning stiffness, axial pain, NSAIDs use, and extra-articular manifestations seem to impact the physicians' perception of remission in axSpA, whereas fatigue has less impact on remission for rheumatologists. Consensus is needed on remission in axSpA.

References: [1Smolen JS *et al.* Treating axial spondyloarthritis and peripheral spondyloarthritis, especially psoriatic arthritis, to target: 2017 update of recommendations by an international task force. *Ann Rheum Dis* 2018;**77**:3–17.

[2] Wendling D *et al.* 2018 update of French Society for Rheumatology (SFR) recommendations about the everyday management of patients with spondyloarthritis. *Joint Bone Spine* 2018;**85**:275–84.

Funding: This study was funded and organized by Novartis France

Disclosure of Interests: Krystel Aouad: None declared, Daniel Wendling: None declared, Anne BAGLIN Employee of: Novartis, Maxime Breban: None declared, sabrina DADOUN: None declared, Christophe Hudry: None declared, Anna Moltó: None declared, Edouard Pertuiset: None declared, Laure Gossec: None declared

DOI: 10.1136/annrheumdis-2021-eular.1019

POS0244

PATIENT JOURNEY WITH AXIAL SPONDYLOARTHRITIS: CRITICAL ISSUES FROM THE PATIENT PERSPECTIVE. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

M. Garrido-Cumbrera[1], D. Poddubnyy[2], C. Bundy[3], L. Christen[4], R. Mahapatra[5], S. Makri[6], C. J. Delgado-Domínguez[1], S. Sanz-Gómez[1], P. Plazuelo-Ramos[7], V. Navarro-Compán[8]on behalf of IMAS working group. [1]*Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; [2]*Charité - Universitätsmedizin Berlin, Rheumatology Department, Berlin, Germany*; [3]*Cardiff University, School of Healthcare Sciences, Cardiff, United Kingdom*; [4]*Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; [5]*Axial Spondyloarthritis International Federation (ASIF), Patient Advocacy, London, United Kingdom*; [6]*Cyprus League Against Rheumatism (CYPLAR), Patient Advocacy, Nicosia, Cyprus*; [7]*Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; [8]*Hospital Universitario La Paz, IdiPaz, Madrid, Spain*

Background: The journey of axial spondyloarthritis (axSpA) for most patients is slow and arduous.
Objectives: The goal of this analysis is to describe the journey to diagnosis and further management in axSpA patients.
Methods: 2,846 unselected patients participated in EMAS, a cross-sectional study (2017-2018) across 13 European countries. Descriptive analysis of socio-demographic factors, insurance scheme, diagnostic journey and post diagnosis healthcare utilization was performed. Mann-Whitey test was used to analyse possible differences between BASDAI (>4 v ≤4) and the number of visits to healthcare professionals and follow-up tests undertaken.
Results: Mean age was 43.9 years, 61.3% were female, 48.1% university educated, 67.9% married, 53.9% employed and 81.7% had public health insurance. Mean age at symptoms onset was 26.6 (11.1), while mean age at diagnosis was 33.7 (11.5) and mean diagnostic delay was 7.4 years. Over 50% had a diagnostic delay of ≥4 years. Prior to receiving a diagnosis, patients visited on average 2.6 specialists. The most commonly performed diagnostic tests were x-rays (72.3%), HLA B27 tests (65.4%) and MRIs (64.3%). 78.4% were diagnosed by a rheumatologist while 14.9% received their diagnosis by a GP. Patients who experienced a diagnostic delay of more than a year (n= 2,208) undertook a considerable number of visits to specialists and medical tests in the year prior to participating in EMAS, which increased with disease activity. Patients with active disease (BASDAI >4) reported a higher number of visits to rheumatologists (3.7±3.5 vs 2.9±2.6), general practitioners (6.6±10.0 vs 3.5±4.1), physiotherapists (19.3±25.0 vs 11.7±17.0), and psychologists/psychiatrists (3.4±10.7 vs 1.9±7.7). Patients with active disease also undertook more x-rays (1.8±2.8 vs. 1.3±1.9), MRI scans (0.9±1.2 vs. 0.6±1.1), and blood tests (4.7±4.4 vs 3.6±3.2). However, one in five patients visited the rheumatologist only once in the year prior to EMAS (21.1%).
Conclusion: Diagnostic delay continues to be a key challenge in the axSpA patient journey, with patients waiting an average of 7.4 years and visiting multiple doctors prior to diagnosis. Once diagnosed, disease management presents a further challenge, as patients with higher disease activity reported more healthcare professional visits as well as medical tests. Safeguarding health and controlling healthcare utilization requires effective disease management, greater education for non-specialists, rapid referral routes for diagnosis and collaborative care between specialists and non-specialists.

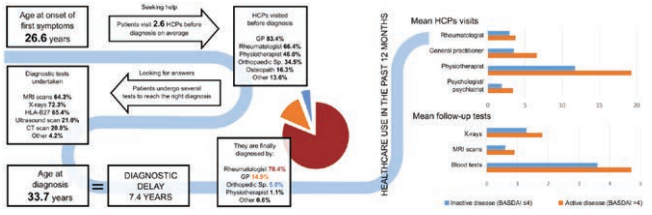


Figure 1. axSpA Patient journey according to EMAS

Acknowledgements: This study was supported by Novartis Pharma AG. The authors would like to thank all participants who participated in this study.
Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Denis Poddubnyy Consultant of: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Abbvie, MSD, Novartis and Pfizer, Christine Bundy Consultant of: Abbvie, Celgene, Janssen, Lilly, Novartis, and Pfizer, Laura Christen Employee of: Novartis Pharma AG, Raj Mahapatra: None declared, Souzi Makri: None declared, Carlos Jesús Delgado-Domínguez: None declared, Sergio Sanz-Gómez: None declared, Pedro Plazuelo-Ramos: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB
DOI: 10.1136/annrheumdis-2021-eular.2426

POS0245 PERFORMANCE OF STANDARDIZED SCORES FOR DISEASE ASSESSMENT AND PAIN IN PATIENTS WITH SPONDYLOARTHRITIS AND FIBROMYALGIA

X. Baraliakos[1], S. Tsiami[1], P. Dukatz[1], M. C. Gkelaki[1], U. Kiltz[1], J. Braun[1]. [1]*Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*

Background: The pathogenesis of spondyloarthritis (SpA) including axial SpA (axSpA) and psoriatic arthritis (PsA) differs from fibromyalgia (FM). However, symptoms partially overlap and both patient groups suffer from pain and stiffness. In addition, SpA patients may also develop a secondary form of FM. Classification criteria for SpA and diagnostic criteria for FM are used to differentiate between these subsets. Patient reported outcomes (PRO) often generated by questionnaires are used to assess severity and other disease features.
Objectives: To study whether PROs developed for axSpA, PsA, and related physician-based information behave in a similar way in patients diagnosed with FM without an additional chronic inflammatory rheumatic disease (CIRD) as in patients with a primary diagnosis of SpA without or with secondary FM.
Methods: Patients were consecutively recruited. The main inclusion criterion was a clinical diagnosis of FM (without CIRD), axSpA or PsA (without or with secondary FM) and the indication for a treatment adaptation (escalation or change within the same class) for any reason, based on the judgement of experienced rheumatologists. Standardized assessment tools and lab parameters (BASDAI, ASDAS-CRP, DAPSA, patient´s and global assessment (NRS), CRP, BASFI, Fibromyalgia Impact questionnaire (FIQ), Leeds Enthesitis Index (LEI), Maastricht Ankylosing Spondylitis (MASES) and SpA Research Consortium of Canada (SPARCC) Enthesitis Score were assessed and compared between subgroups.
Results: The baseline demographics of 300 recruited patients (100 FM. 100 axSpA and 100 PsA) are shown in Table 1. All patients with FM (primary or secondary to SpA) showed the highest scores in almost all assessments, and this was independent of the main diagnosis (Table 2). In comparison, patients with axSpA or PsA without secondary FM showed significantly lower scores in all PROs as compared to those with primary and secondary FM, with exception of (i) scores of ASDAS-CRP and (ii) duration of morning stiffness (Question 6 of BASDAI), which were not affected by the presence of secondary FM (Table 2).
Conclusion: Secondary FM is leading to significantly higher levels of SpA-specific scores. ASDAS-CRP was the only score that was not influenced by the presence of secondary FM in patients with axSpA even though it was also increased in patients with primary FM, while similar results were found for the duration but not the level of morning stiffness. On the other hand, FM-specific questionnaires also showed high scores in patients with axSpA and PsA with concomitant FM but not in those without.

Table 1. Baseline characteristics of all diagnosis subtypes and comparison (*p-values*) to primary FM diagnosis. '+': diagnosis with concomitant FM, '-': diagnosis without concomitant FM

Table 1	FM	axSpA-	*p-value*	axSpA+	*p-value*	PsA-	*p-value*	PsA+	*p-value*
Age	56.4±10.2	53.5±14.2	*0.086*	48.7±13.5	*0.026*	56.0±13.2	*<0.001*	58.5±10.4	*0.962*
Male	2%	67%	*<0.001*	0%	---	38%	*<0.001*	6%	*0.322*
HLAB27 pos.	0%	84%	---	71%	---	16%	---	50%	---
CRP (mg/dl)	0.3±0.5	1.1±2.1	*0.001*	0.5±0.3	*0.035*	1.4±3.0	*0.001*	0.5±0.5	*0.031*
NRS pain	7.5±1.6	6.1±2.4	*<0.001*	7.7±1.8	*0.768*	6.4±2.2	*<0.001*	7.3±1.1	*0.223*

Table 2. Mean values (±standard deviation) of the assessed disease-specific indices and comparison (p-values) to primary FM diagnosis.

Table 2	FM	axSpA-	*p-value*	axSpA+	*p-value*	PsA-	*p-value*	PsA+	*p-value*
BASDAI	6.9±1.4	5.2±2.0	*<0.001*	6.9±1.4	*0.858*	---	---	---	---
BASDAI Q1: Fatigue	7.4±1.9	5.7±2.6	*<0.001*	7.8±1.2	*0.667*	---	---	---	---
ASDAS-CRP	3.3±0.6	3.1±1.0	*0.086*	3.7±1.2	*0.208*	---	---	---	---
BASFI	6.4±2.1	5.4±2.5	*0.005*	7.1±1.8	*0.41*	---	---	---	---
DAPSA	43.0±17.8	---	---	---	---	32.0±18.6	*<0.001*	46.5±19.7	*0.37*
FIQ	68.5±13.5	53.9±21.2	*<0.001*	72.3±13.7	*0.352*	57.2±18.3	*<0.001*	68.5±11.6	*0.978*
LEI	4.0±1.6	1.5±1.7	*<0.001*	3.3±1.4	*0.179*	2.4±2.0	*<0.001*	3.6±2.0	*0.625*
MASES	8.6±3.0	3.4±3.3	*<0.001*	8.2±2.9	*0.642*	4.2±3.6	*<0.001*	7.1±3.6	*0.101*
SPARCC	9.4±3.4	3.5±3.4	*<0.001*	7.7±3.8	*0.139*	5.1±3.7	*<0.001*	8.1±3.9	*0.412*

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3139

Clinical vasculitis

POS0246 THE WORLDWIDE INCIDENCE AND PREVALENCE OF ANCA VASCULITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF EPIDEMIOLOGICAL STUDIES

R. Redondo Rodriguez[1], N. Mena-Vázquez[1], A. M. Cabezas-Lucena[1], F. Godoy-Navarrete[1], M. Morales-Águila[1], S. Manrique Arija[1]. [1]*Instituto de Investigación*

Biomédica de Málaga. Hospital Regional Universitario de Málaga, Reumatología, Málaga, Spain

Objectives: To evaluate the worldwide incidence and prevalence of ANCA vasculitis through a systematic review of the literature and meta-analysis.
Methods: A systematic search of MEDLINE and EMBASE search engines was carried out for studies that analyzed the incidence and prevalence of ANCA vasculitis in different geographical areas. Inclusion criteria: patients diagnosed with ANCA vasculitis according to ACR criteria/ Chapel Hill Consensus and adult patients (> 16 years). All ANCA vasculitis (microscopic polyangiitis, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis) were considered. Exclusion criteria: editorials, conference abstracts, case or cases series reports and narrative reviews; insufficient description of the methods; lack of data to compute incidence or prevalence; and duplicate studies.Variables: Main variable: the pooled prevalence measured by the number of prevalent cases per million / person-year (95% CI) and the pooled incidence measured as the number of incident cases per million / person-year (95% CI). Secondary variables: the prevalence and incidence of each vasculitis ANCA and according geographic area. A meta-analysis was undertaken to estimate the pooled incidence and the pooled prevalence per million / person-years. The 95% CI and I2 for heterogeneity were calculated.
Results: Twenty four studies were included. The pooled incidence (95% CI) was 12.2 per million / person-year (8.4-16.5) and the pooled prevalence (95% CI) was 130 per million / person-year (67.5-213). The individual incidence for each vasculitis was: GPA (6.7), MPA (5.9) and EGPA (1.6). The individual prevalence for each vasculitis was: GPA (69.3), MPA (21.9) and EGPA (13.5).
In the analysis by continents, the pooled incidence for GPA vasculitis was higher in Europe (7.5), while the pooled incidence for MPA vasculitis was higher in America (6.9) and for EGPA vasculitis it was higher in Asia (1.8). The pooled prevalence for GPA and MPA vasculitis was higher in Europe (83.9,24.4 respectively) than in America (14.2, 12.8 respectively).
Conclusion: The pooled incidence and the pooled prevalence are higher in the case of GPA vasculitis compared to the rest of ANCA vasculitis. In general there is a predominance of incidence and prevalence of all ANCA vasculitis in the northern hemisphere compared to the south.

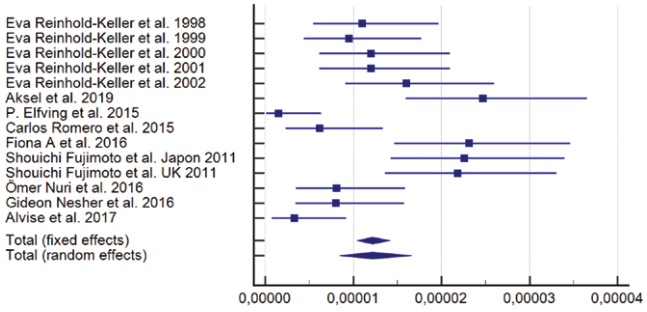


Figure 1. The pooled incidence ANCA vasculitis.

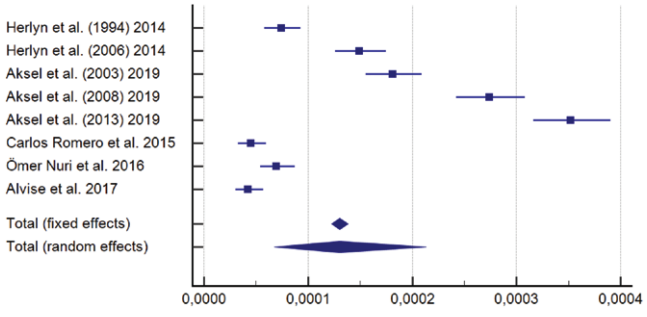


Figure 2. The pooled prevalence ANCA vasculitis

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1630

POS0247 INTERSTITIAL ANCA-ASSOCIATED VASCULITIS ASSOCIATES WITH SEVERE KIDNEY INJURY INDEPENDENT OF GLOMERULONEPHRITIS

S. Hakroush[1], B. Tampe[2]. [1]*University Medical Center Göttingen, Institute of Pathology, Göttingen, Germany*; [2]*University Medical Center Göttingen, Department of Nephrology and Rheumatology, Göttingen, Germany*

Background: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a small vessel vasculitis affecting multiple organ systems, including the kidney. Small vessels in the kidney include small-sized arteries (interlobular artery, afferent and efferent arteriole), capillaries (glomerular and peritubular capillary) and venules.
Objectives: Although crescentic ANCA glomerulonephritis (GN) is a common histological finding reflecting glomerular small vessel vasculitis, it is reasonable that manifestation of AAV could also contribute to interstitial small vessel vasculitis. Therefore, we here aimed to expand our current knowledge focusing on interstitial vasculitis in ANCA GN by systematic histological scoring of vascular lesions analogous to Banff.
Methods: A total number of 49 kidney biopsies with confirmed renal involvement of AAV at the University Medical Center Göttingen were retrospectively included between 2015 till 2020. A renal pathologist (SH) evaluated all biopsies and was blinded to clinical data collection and analysis. A detailed methological section is provided in the Supplementary material and methods section.
Results: Since previous studies established that crescentic ANCA GN associates with severe kidney injury and acute deterioration of kidney function in AAV, we first systematically scored interstitial vasculitis in association with requirement of renal replacement therapy (RRT). Among all active and chronic tubulointerstitial lesions analogous to the Banff scoring system, the only association between severe kidney injury requiring RRT was observed for interstitial vasculitis in AAV reflected by peritubular capillaritis (ptc, p=0.0002) and arteritis (v, p=0.0069), affecting 5/49 (10.2%) and 11/49 (22.4%) of renal biopsies, respectively. Since it is known that severe deterioration of kidney function also correlates with crescentic ANCA GN, we next directly compared glomerular and tubulointerstitial lesions. The fraction of normal glomeruli was inversely associated with interstitial fibrosis (ci), total (ti) and inflammation in IFTA (i-IFTA), whereas glomerular crescents were associated with interstitial inflammation (i), tubulitis (t) and total inflammation (ti). In contrast, global glomerular sclerosis associated with less interstitial inflammation (i) but correlated with interstitial fibrosis (ci) and tubular atrophy (ct), confirming established mechansim that chronic glomerular injury leads to tubular atrophy and interstitial fibrosis. Interestingly, no association between interstitial vasculitis (ptc and v correlating with severe kidney injury) and any glomerular lesion in ANCA GN (also correlating with severe kidney injury) was observed, thereby confirming that interstitial vasculitis contributes to severe kidney injury independent of ANCA GN. By contrast, short-term renal recovery from RRT was equal in both groups, suggesting a distinct association with acute decline of kidney function at disease onset.
Conclusion: Taken together, by using the Banff scoring system we here expand our current knowledge of renal interstitial lesions in AAV revealing peritubular capillaritis and arteritis as important histological alterations associated with severe kidney injury in a considerable subset of AAV. Furthermore, our findings that interstitial vasculitis did not correlate with crescentic ANCA GN implicate that the characteristics of each vasculitis manifestation are independent and could further improve our understanding of mechanisms contributing to renal injury. These observations suggest that interstitial vasculitis in AAV may also affect long-term prognosis requiring further investigation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4296

POS0248 PSYCHOMETRIC PROPERTIES OF OUTCOME MEASUREMENT INSTRUMENTS FOR ANCA-ASSOCIATED VASCULITIS: A SYSTEMATIC LITERATURE REVIEW

A. Berti[1,2], G. Boleto[3], P. A. Merkel[4], G. Tomasson[5], S. Monti[6], K. A. Quinn[7], L. Carmona[8], S. Ramiro[9,10]on behalf of OMERACT Vasculitis Working Group. [1]*Hospital of Trento, University of Trento, Rheumatology, Trento, Italy*; [2]*Mayo Clinic, Thoracic Disease Research Unit, Rochester, United States of America*; [3]*Cochin Hospital, Rheumatology, Paris, France*; [4]*Penn Medicine, University of Pennsylvania Health System, Rheumatology, Philadelphia, United States of America*; [5]*Landspítali The National University Hospital of Iceland, Rheumatology, Reykjavik, Iceland*; [6]*University of Pavia, Rheumatology, Pavia, Italy*; [7]*National institute of arthritis and musculoskeletal and skin diseases, Rheumatology, Bethesda, United States of America*; [8]*Instituto de Salud Musculoesquelética (INMUSC), Rheumatology, Madrid, Spain*; [9]*Department of Rheumatology, Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [10]*Department of Rheumatology, Zuyderland Medical Center, Rheumatology, Heerlen, Netherlands*

Background: The OMERACT Vasculitis Working Group has defined a Core Domain Set of outcome measures for ANCA-associated vasculitis (AAV). However, the psychometric properties of available outcome measurement instruments in AAV, an essential consideration when choosing among instruments, have not been summarized.
Objectives: To systematically review and summarize the psychometric properties of outcome measurement instruments used in AAV.

Methods: A comprehensive search of several databases (Medline, EMBASE, Cochrane, Scopus, among others) from inception to July 14, 2020 and without language limitations was conducted. Articles were included if they covered psychometric properties of instruments used in AAV (granulomatosis with polyangiitis, GPA; microscopic polyangiitis, MPA; eosinophilic granulomatosis with polyangiitis, EGPA); articles encompassing other systemic vasculitides and not presenting the data for AAV separately were excluded. Following the COSMIN and OMERACT frameworks, different psychometric properties (validity, inter- and intra-observer reliability, sensitivity to change, and feasibility) of outcome measurement instruments used in AAV were assessed. Risk of bias was assessed according to the COSMIN checklist.

Results: From 2505 articles identified, 20 met the predefined criteria. Three were identified as development studies, 14 were validation studies, and 3 pursued both objectives.

These studies provided information on 16 instruments: 8 assessing disease activity, 1 assessing disease damage, 3 assessing patient-reported outcome, 4 assessing function (Figure 1). Overall, a few psychometric properties have been considered in each study, ranging from one to five. Most of the instruments were tested in GPA only (n=7), followed by AAV as a group (GPA, MPA and EGPA; n=5), MPA and GPA (n=3), and EGPA only (n=1). Sample sizes of the studies ranged between 27 and 626 patients. The studies with a higher risk of bias, according to COSMIN definitions, were those assessing RAPID3, MVIA, ENT/GPA DAS, and ODSS.

There was a wide heterogeneity of the psychometric proprieties assessed for each instrument. Validity was the most frequently assessed domain in 88% of the instruments, and few properties other than construct validity were reported (Figure 1).

Within each domain, BVAS/WG for activity, VDI for damage, AAV-PRO for patient-reported outcomes, and ODSS for function were the instruments with more psychometric features assessed. For the disease activity domain, BVAS/WG showed a good validity having the highest correlation with physician global assessment (r=0.90), a good reliability (intra-observer ICC=0.62; inter-observer ICC=0.97), and good feasibility and responsiveness. For disease damage, VDI showed moderate validity (correlations with BVAS/WG at 5-year with r=0.20 and BVAS/WG at 1-year with r=0.40) and good feasibility. Among patient-reported outcomes, AAV-PRO had the best performance in terms of validity (construct validity: correlations of the 6 disease domains and EQ-5D-5L, with r ranging between -0.78 and -0.55; discriminating validity between active disease versus remission of the 6 disease domains, p<0.0001 for all comparisons). The performance of instruments assessing function domain was low-to-moderate.

Psychometric properties of outcome measures used in the study of ANCA-associated vasculitis

DOMAIN	INSTRUMENTS	VALIDITY				RELIABILITY				
		FACE	CONTENT	CONSTRUCT	CRITERION	INTERNAL CONSISTENCY	INTRA-OBSERVER	INTER-OBSERVER	FEASIBILITY	RESPONSIVENESS
Disease activity	BVAS.v3			✓					✓	✓
	BVAS/WG	✓		✓	✓		✓	✓	✓	✓
	ENT/GPA DAS	✓		✓	✓				✓	✓
	ENTAS						✓	✓		✓
	ENTAS 2						✓	✓		✓
	DEI	✓		✓			✓	✓	✓	✓
	PtGA			✓					✓	
	MVIA			✓						
Disease damage	VDI			✓	✓				✓	
Patient-reported outcome	AAV-PRO	✓	✓	✓		✓	✓		✓	
	SF-36			✓					✓	
	MFI-20 (physical)			✓					✓	
Function	RAPID3			✓					✓	
	HAQ			✓		✓			✓	
	ODSS			✓	✓			✓		✓
	COMPASS31			✓						

Abbreviations: ENT=Ear nose and throat: GPA=granulomatosis with polyangiitis, BVAS=Birmingham Vasculitis Activity Score; VDI=Vasculitis Damage Index; DAS= disease activity score; ENTAS=ENT assessment score; DEI=Disease Extent Index; RAPID3=Routine assessment of patient index data 3; SF-36=Medical Outcomes Study Short-Form 36; MVIA= multivariable index for AAV; AAV-PRO=ANCA-associated vasculitis -Patient reported outcome; PtGA: Patient Global assessment; HAQ=Health Assessment Questionnaire; ODSS=Overall Disability Sum Score; COMPASS31=Composite Autonomic Symptom Score 31. MFI-20=Multidimensional Fatigue Inventory-20

* Only the physical fatigue domain of the score was assessed (not the overall score)

Conclusion: Sixteen instruments covering the OMERACT domains of disease activity, damage, patient-reported outcome, and function had their psychometric properties assessed in the study of AAV. The majority were developed or validated for GPA only or AAV as a group. Overall, validity was the domain most frequently assessed. BVAS/WG, VDI, AAV-PRO, and ODSS were the instruments with more psychometric features assessed. More rigorous studies aimed at estimating a wider range of psychometric properties in larger numbers of patients with AAV are warranted.

REFERENCES:
[1] Castrejon I, et al. Clin Exp Rheumatol. 2015
[2] Merkel PA, Journal of Rheumatology, July 2011
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1451

POS0249 THE EFFECT OF NASAL STAPHYLOCOCCUS AUREUS COLONIZATION ON DISEASE ACTIVITY AND THE EFFECT OF ANTIBIOTIC TREATMENT IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS; A RETROSPECTIVE COHORT STUDY

C. Schaap[1], R. Krol[1,2], H. H. F. Remmelts[2], R. Klaasen[3], E. Hagen[2], J. Spierings[1], M. W. Heijstek[1]. [1]*University Medical Center Utrecht, Department of Rheumatology and Clinical Immunology, Utrecht, Netherlands*; [2]*Meander Medical Center, Department of Internal Medicine, Amersfoort, Netherlands*; [3]*Meander Medical Center, Department of Rheumatology, Amersfoort, Netherlands*

Background: Antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) is a necrotizing vasculitis, predominantly affecting small or medium vessels with few or no immune deposits. Ear, nose and throat (ENT) involvement in AAV is frequently present. AAV has a relapsing-remitting disease course. A factor that has been associated with induction of relapses is nasal Staphylococcus aureus (S. aureus) colonization. This alleged association between nasal colonization and induction of relapses has resulted in the use of antibiotics. However, the effect of antibiotic treatment on disease activity remains controversial. Some studies showed a beneficial effect of antibiotic treatment whereas other studies found no effect of antibiotic treatment on disease activity.

Objectives: The aim of this study was to identify the role of nasal S. aureus colonization and the effect of systemic or local antibiotic treatment on disease activity in patients with AAV.

Methods: Clinical, laboratory and histological data from all AAV patients with ENT involvement, diagnosed in two medical centers between 1981 and 2020, were retrospectively collected. Nasal S. aureus colonization was defined as at least one positive nasal swab during follow-up. Data on systemic (cotrimoxazole and azithromycin) and local antibiotics (mupirocin) use was collected. Disease activity was divided into systemic and local disease activity. Systemic disease activity consisted of history of relapses, relapse number per patient years and Birmingham vasculitis activity score version 3 (BVAS3) at last visit. Local disease activity included history of ENT relapses, development of saddle nose deformity or subglottic stenosis during follow-up.

Results: Two-hundred and thirteen patients were included in the analysis. Median follow-up time was 8 (IQR 3 -17) years. S. aureus colonization was tested in 100 (46.9%) cases of which 44 patients tested positive. Only one patient developed a subglottic stenosis, and 13 patients developed a saddle nose deformity during follow-up. Systemic and local disease activity at baseline and at last visit were comparable between patients with and without and S. aureus colonization. Regression analysis showed no difference in relapse number per patient year between AAV patients colonized with S. aureus versus non-colonized patients (RR 2.03; 95%CI, 0.97 – 4.26, p=0.06). This also accounted for local ENT relapses (OR 0.134; 95%CI 0.06-1.47, p=0.14) and saddle nose deformity (OR 0.61; 95%CI 0.04-10.68, p=0.74). Twenty-eight (13.1%) S. aureus positive patients received antibiotics aimed at eradication of S. aureus. Twenty-two (10.3%) received cotrimoxazole, 2 (0.9%) received azithromycin and 17 (8.0%) patients received mupirocin ointment. No significant difference was found between the treated versus non-treated group with regard to systemic and local disease activity.

Conclusion: Nasal S. aureus colonization does not influence systemic or local disease activity. Antibiotic eradication treatment did not modify disease activity in this study.

Table 1. Effect of AB treatment on disease activity of 40 AAV patients with ENT involvement and S. aureus colonization

Disease activity	Antibiotic treatment		
	Yes (n=28)	No (n=12)	P-value
Systemic symptoms			
History of one or more relapses, n (%)	18 (47.4%)	4 (10.5%)	0.635
Relapse number per patient years, median (IQR) *	0.11 (0-0.18)	0.17 (0.02 – 0.26)	0.346
BVAS3 last visit, median (IQR)	1 (0-4)	1 (0-4)	0.932
Local symptoms			
History of one or more ENT relapses, n(%) *	9 (33.3%)	3 (11.1%)	0.438
Development of saddle nose deformity during follow-up, n (%) *	4 (12.1%)	0 (0%)	0.367

*Values are median (interquartile range IQR) or n (%). BVAS3: Birmingham Vasculitis Activity Score version 3; ANCA: Anti-Neutrophilic Cytoplasmic Autoantibody; AAV: ANCA associated vasculitis; ENT: ear, nose and throat. * More than 10% missings in analysis. For an overview of the number of included patients per analysis, see supplementary table B.*

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3659

POS0250 SIGNIFICANT DAMAGE OCCURS EARLY IN THE COURSE OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS AND IS MAINLY DUE TO DISEASE-RELATED SEQUELAE

P. Delvino[1,2], A. Milanesi[1], F. Brandolino[1], S. Monti[1,2], C. Montecucco[1]. [1]*IRCCS Policlinico S. Matteo Foundation, University of Pavia, Rheumatology, Pavia, Italy*; [2]*University of Pavia, PhD in Experimental Medicine, Pavia, Italy*

Background: Following the introduction of effective immunosuppressive treatments, ANCA-associated vasculitides (AAV) have become chronic diseases with a remitting-relapsing course. Therefore, preventing chronic damage accrual during follow-up is critical, as relapses, treatment-related side effects, and comorbidities may significantly affect the long-term outcomes of AAV patients. At present, no study specifically evaluated the burden of damage in patients with eosinophilic granulomatosis with polyangiitis (EGPA).
Objectives: To describe short-term (6 months) and long-term (5 years) damage accrual in patients with newly diagnosed EGPA.
Methods: Patients diagnosed with EGPA, according to ACR criteria and/or Chapel Hill definitions and regularly followed-up in our vasculitis center for ≥5 years were included. Damage accrual was assessed with the Vasculitis Damage Index (VDI). Short-term and long-term damage accrual was defined by VDI at 6 months and at 5 years, respectively, and categorized as related to vasculitis or its treatment.
Results: VDI data at 6 months were available for 45 EGPA patients: 24 (53.3%) female, mean age at diagnosis 51.6±13.0 years. ANCA were positive in 17 patients (37.8%), with MPO being the only detected enzyme immunoassay (EIA)-specificity. At 6 months mean VDI was 2.8±1.3; 25/45 (55.6%) and 6/45 patients (13.3%) presented ≥3 and ≥5 items, respectively, whilst only 1 patient (2.2%) showed no items of damage. VDI data at 5 years were available for 32/45 EGPA patients (71.1%): 16 (50%) female, mean age at diagnosis 51.5±13.1 years. MPO-ANCA were positive in 13 patients (40.6%). At 5 years mean VDI was 3.5±1.3, with 26/32 (81.3%) and 7/32 patients (21.9%) presenting ≥3 and ≥5 items, respectively; notably, no patients presented a VDI=0 at 5 years.
The most frequent disease-related VDI items at 6 months and at 5 years were asthma, chronic sinusitis, peripheral neuropathy, cardiomyopathy, pulmonary function tests abnormalities and nasal blockage (Figure 1). Osteoporotic fractures, diabetes and systemic hypertension were the most commonly reported treatment-related items at 6 months and at 5 years (Figure 1). Damage accrual progressively rose during the 5-year follow-up (P=0.023), mainly due to disease-related items rather than treatment-related items both at 6 months (disease related VDI 2.6±1.2, treatment-related VDI 0.3±0.6) and at 5 years (disease related VDI 2.9±1.2, treatment-related VDI 0.6±0,7). No significant difference in terms of damage accrual was observed between ANCA-positive and ANCA-negative patients (P >0.5).
Conclusion: In our cohort of EGPA patients damage accrual occurs early, with more than half of the patients displaying ≥3 VDI items already at 6 months. Poor control of previous disease activity, particularly ENT and respiratory manifestations, contributes to progressive damage accrual more than treatment side effects.

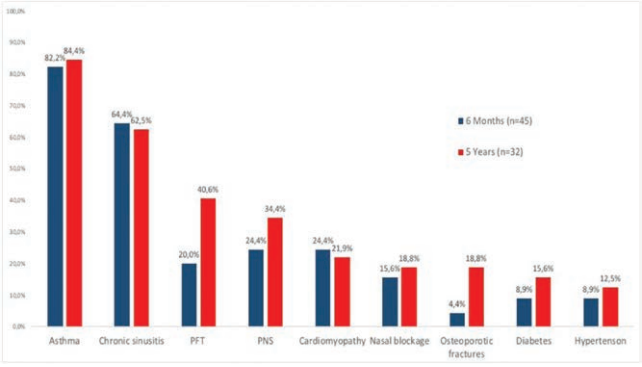


Figure 1. Disease-related and treatment-related VDI items at 6 months and at 5 years in patients with EGPA.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2683

POS0251 ARE CLINICAL FEATURES AND OUTCOMES OF ANCA (+) EGPA PATIENTS DIFFERENT FROM ANCA NEGATIVE ONES?

E. Duran[1], E. Bilgin[1], E. Erkantarcı Levent[2], Ö. Can Bostan[3], L. Kılıç[1], E. Damadoğlu[3], S. Kiraz[1], O. Karadag[1,4]. [1]*Hacettepe University School of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; [2]*Hacettepe University School of Medicine, Department of Internal Medicine, Ankara, Turkey*; [3]*Hacettepe University School of Medicine, Department of Chest Disease, Division of Allergy and Clinical Immunology, Ankara, Turkey*; [4]*Hacettepe University School of Medicine, Vasculitis Research Centre, Ankara, Turkey*

Background: Recent reports describe EGPA as having two subgroups as ANCA positive and ANCA negative. Furthermore, there could be differences in terms of clinical features and outcomes (1).
Objectives: The aim of this study was to compare the clinical characteristics and outcomes of ANCA positive EGPA patients with those of ANCA negative ones.
Methods: This retrospective, descriptive study included 50 EGPA patients (male/female:13/27) from our prospective vasculitis database from October 2014 (2). The patients had fulfilled the ACR 1990 or DCVAS criteria for EGPA. In addition to clinical features (activity index) and treatment regimens, outcomes of patients (relapse and damage) were also reviewed. For relapse-free survival analysis, time to first relapse was compared according to ANCA phenotype by Kaplan-Meier survival analysis.
Results: Of the patients, 17 (34%) were in ANCA (+) group, 33 (66%) were in ANCA (-) group. Renal involvement and peripheral neuropathy were more frequent in ANCA (+) patients whereas ANCA (-) patients were significantly younger at the time of diagnosis and they had more nasal polyposis. The median BVAS at the EGPA diagnosis was significantly high in ANCA (+) group. All 3 of patients with cardiac involvement were in the ANCA (-) group but difference was found in terms of FFS and VDI between ANA (+) and (-) groups. However, pulse steroid and cyclophosphamide treatments were more commonly used in ANCA (+) group while mepolizumab were used in ¼ of ANCA (-) patients (Table 1). During median 47 (IQR 69.9) months follow up, about 40% of patients had at least one relapse but there was no difference for relapse-free survival rate according to the ANCA status (Figure 1).
Conclusion: Not only clinical features and disease activity but also treatments received were significantly different between ANCA (+) and (-) patients. These results could partially define two distinct subgroups of EGPA. However, these groups were similar regarding damage and relapse.

REFERENCES:

[1] Comarmond C, Pagnoux C, Khellaf M, Cordier JF, Hamidou M, Viallard JF, et al. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss): Clinical characteristics and long-term followup of the 383 patients enrolled in the French Vasculitis Study Group cohort. Arthritis and rheumatism. 2013;65(1):270-81.
[2] Karadağ Ö, Bilgen SA, Armagan B, Sari A, Erden A, Batu E D et al. Two-year Results of a Prospective Vasculitis Cohort from Eastern Mediterranean: Demographic Characteristics and Distribution of the Vasculitides Frequencies. Rheumatology, 2017; 56(suppl_3), iii88-iii95.

Table 1. Demographics and clinical characteristics of the patients with EGPA during disease course

Characteristics*	ANCA (+) (n=17)	ANCA (-) (n=33)	P
Age at the diagnosis (years)	53.8 ± 16.3	37.9 ± 14.3	0.001
Sex, female	10 (58.8)	17 (51.5)	0.62
Asthma	12 (70.6)	29 (87.9)	0.13
Nazal polyp	2 (11.8)	15 (45.5)	0.017
Eosinophilia (>1000/μL)	11 (64.7)	27 (81.8)	0.18
Disease duration (years)	4.1 (5.9)	3.7 (5.9)	0.69
Organ specific involvement, %			
- Pulmonary	76.5	78.8	0.85
- ENT	82.4	87.9	0.59
- Renal	52.9	3	<0.001
- PNS	47.1	9.1	0.002
- Cardiac	0	9.1	N/A
BVAS at the diagnosis	17 (13)	9 (4)	0.002
Revized FFS			
- 0	11 (64.7)	26 (78.8)	0.28
- ≥ 1	6 (35.3)	7 (78.8)	
VDI	1 (1)	1 (1)	0.41
Treatment regimens for induction, %			
- Pulse steroid	64.7	11.2	0.002
- Cyclophosphamide	58.8	18.2	0.004
- Rituximab	11.8	3	0.21
- Mepolizumab	0	12.1	N/A
Treatment regimens for maintenance, %			
- Rituximab	11.8	3	0.21
- Mycophenolate mofetil	35.3	3	0.002
- Mepolizumab	0	24.2	N/A
- Azathioprine or methotrexate	47.1	42.4	0.75
Relapse, n (%)	7 (41.2)	12 (42.9)	0.66
Exitus, n (%)	2 (11.8)	1 (3)	0.26

* Med (IQR) for numerical data excluding age; mean ± SD for ageANCA: Antineutrophil cytoplasmic antibody, BVAS: Birmingham Vasculitis Activity Score, ENT: Ear, nose, and throat, IQR: Interquartile range, med: median, N/A: Not applicable, PNS: Peripheral nervous system, VDI: Vasculit damage index

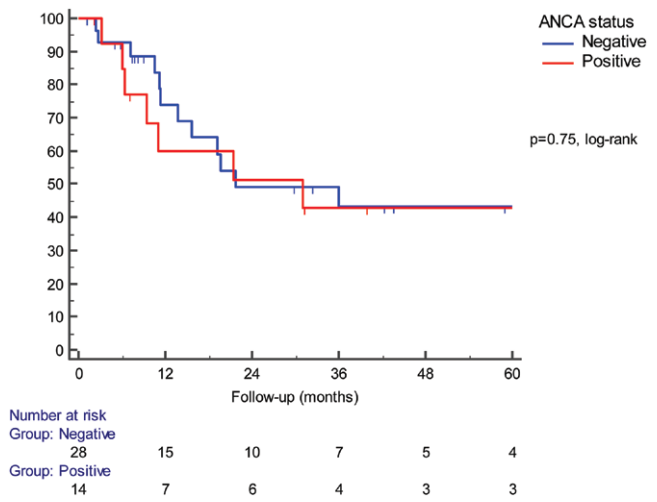


Figure 1. Kaplan-Meier relapse-free survival curve according to the ANCA status

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3261

POS0252 IMPACT OF ANCA-ASSOCIATED VASCULITIS ON CLINICAL OUTCOMES AND RESOURCE UTILIZATION IN ELECTIVE PCI

K. Mathias[1], L. Mathias[2], A. Mantha[3], D. Arkfeld[2]. [1]*University of Chicago, Internal Medicine, Chicago, United States of America*; [2]*USC Keck School of Medicine, Rheumatology, Los Angeles, United States of America*; [3]*USC Keck School of Medicine, Internal Medicine, Los Angeles, United States of America*

Background: Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitides (AV) can increase risk of atherosclerosis. [1] Patients with autoimmune disease have increased rates of coronary events that are not fully explained by classic risk factors. [2] A prior study has shown that autoimmune vasculitides –including polyarteritis nodosa, hypersensitivity granulomatosis with polyangiitis, giant cell arteritis, thrombotic angiitis, Takayasu arteritis, Goodpasture syndrome, and Kawasaki disease –are associated with increased cost of care and increased 30-day readmission after percutaneous coronary intervention (PCI). [3] It is important to distinguish the cardiovascular outcomes of small–vessel ANCA-associated vasculitides from the other vasculitides included in this prior study because coronary arteritis is typically a complication of medium to large vessel vasculitis.
Objectives: To investigate the impact of comorbid ANCA-associated small vessel vasculitis (AV) on outcomes of PCI in a nationally representative cohort.
Methods: Patients undergoing PCI in the 2016-2018 National Inpatient Sample were selected and those with ANCA-associated vasculitis were identified using the ICD-10 classification system. The NIS is an all-payer, survey-weighted, inpatient database estimating 37 million annual U.S. hospitalizations managed by the Healthcare Cost and Utilization Project (HCUP). Primary study outcomes were prevalence of comorbid vasculitis, mortality, complications, and cost of care.
Results: Of 1,351,670 patients undergoing PCI were identified, 410 (0.03%) had diagnosis of ANCA-vasculitis. AV patients were similar to non-AV patients in distribution of gender, race, and median household income. AV patients were older (70.9 vs 65.2 years, P<0.001) and more likely to utilize Medicare (78% vs 53%, P<0.005). AV patients were more likely to present with non-ST segment myocardial infarction (NSTEMI) (57.3% vs 41.5%, P<0.005) and less likely to present with ST-elevation myocardial infarction (NSTEMI) (18.3% vs 31.3%, P<0.05). AV patients had similar adjusted mortality (6.1% vs 2.6%, aOR: 2.1, P=0.8), cost of care ($32,985 vs $25,767, β = 0.02, P=0.7), and length of hospitalization (6.0 vs 3.9, IRR: 1.2, P=0.13).
Conclusion: The presence of ANCA-associated vasculitis did not appear to negatively impact inpatient clinical outcomes or utilization of care among patients undergoing PCI in the United States. Cost of care was not increased, in contrast to an increase cost of care when small, medium, and large vasculitides are grouped together. The greater proportion of NSTEMI patients among those with AAV corresponds with a growing body of literature implicating inflammatory processes in the pathogenesis of certain forms of myocardial infarction meriting further investigation.
REFERENCES:

[1] Misra DP, Shenoy SN. Cardiac involvement in primary systemic vasculitis and potential drug therapies to reduce cardiovascular risk. *Rheumatol Int*. 2017;37(1):151-167. doi:10.1007/s00296-016-3435-1.
[2] Amaya-Amaya J, Sarmiento-Monroy JC, Rojas-Villarraga A. *Cardiovascular Involvement in Autoimmune Diseases*. El Rosario University Press; 2013. Accessed February 1, 2021. https://www.ncbi.nlm.nih.gov/books/NBK459468/.
[3] Bailey KL, Mantha A, Sanaiha Y, Mathias L, Benharash P, Ebrahimi R. Short-Term Outcomes After Percutaneous Coronary Intervention in Patients With Autoimmune Vasculitides. *J Am Coll Cardiol*. 2019;74(1):159-160. doi:10.1016/j.jacc.2019.04.051.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3369

POS0253 RITUXIMAB-BIOSIMILAR FOR ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES-ASSOCIATED VASCULITIS: EXPERIENCE OF A SINGLE ITALIAN CENTER

S. Sartorelli[1], A. Cariddi[1], L. Moroni[1,2], E. Baldissera[1], E. Bozzolo[1], L. Dagna[1,2]. [1]*IRCCS San Raffaele Hospital, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy*; [2]*Vita-Salute San Raffaele University, School of Medicine, Milan, Italy*

Background: Rituximab (RTX), an anti-CD20 monoclonal antibody, represents a valuable treatment for anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV). RTX biosimilar CT-P10 (RTX-B) has been approved in Europe in all indications held by RTX originator (RTX-O). As stated by recent international consensus-based recommendations, [1] there is evidence regarding safety and efficacy of biosimilars in the context of rheumatic diseases, but it is encouraged to gather additional data. [2,3]
Objectives: To report the experience of a single Italian center with RTX-B in AAV in terms of safety and efficacy.
Methods: We retrospectively reviewed the charts of all AAV patients followed up in our Small Vessel Vasculitis Clinic and we selected those who received RTX-B between October 2017 and May 2020, both naïve to RTX (RTX-Bn) or already treated with ≥1 course of RTX-O and switched to RTX-B (RTX-Bs). Baseline features, disease outcome, concomitant therapy and adverse events 6 (T6), 12 (T12) and 24 (T24) months after RTX-B introduction, when available, were collected. Non-parametric statistic tests were used.
Results: Fifty-six AAV patients (44 [78.6%] granulomatosis with polyangiitis (GPA), 12 [21.4%)] microscopic polyangiitis (MPA)) received RTX-B with a median follow up of 20 (IQR 10-24) months. ANCA were positive in 49 (87.5%) patients. Ten (17.9%) patients were newly diagnosed with AAV, while 23 (41.1%) had refractory disease and another 23 had relapsing disease.
Thirty-three (58.9%) patients were RTX-Bs, whereas 23 (41.1%) RTX-Bn. In 29 (51.8%) patients RTX was decided because of remission induction, while in 27 (48.2%) as maintenance regimen. Median cumulative RTX-B dose was 2.5 (2-3.875) grams with 3 (IQR 2-4) median courses. AAV activity, adverse events and concomitant therapy at T6, T12 and T24 are shown in Table 1. One GPA patient died of severe infection 3 months after a single infusion of RTX-B 500 mg as maintenance therapy.
Considering the 52 (92.6%) patients who reached a 6 months-follow up, we marked a significant decrease of number of patients on steroid therapy (39 [75%] vs 27 [51.9%]; p=0.003), of median prednisone daily dose (5 [IQR 5-25] vs 2.5 [IQR 1.25-5 mg; p=0.001) and of number of patient on concomitant bDMARDs (10 [19.2%] vs 5 [9.6%]; p=0.003).
Analysing the 40 (71.4%) patients who reached a 12 months-follow up, we confirmed the tendency with a decrease of number of patients on steroid therapy (29 [72.5%] vs 13 [32.5%]; p=0.007), of median prednisone daily dose (5 [IQR 5-12.5] vs 3.75 [IQR 2.75-7.5]; p=0.008) and of number of patient on concomitant bDMARDs (9 [22.5%] vs 3 [7.5%]; p=0.009).
No statistically significant difference was found for the same variables comparing T0 versus T24.

Table 1. AAV activity, concomitant therapy and adverse events at T0, T6, T12 and T24.

	T0	T6	T12	T24
n (%)	56 (100)	52 (92.6)	40 (71.4)	18 (32.1)
Dose RTX-B, median (IQR) grams	1.75 (0.5-2)	0.5 (0.5-1)	0.5 (0.5-1)	0.5 (0.5-1)
Concomitant prednisone therapy, n (%)	42 (75)	27 (48.2)	13 (32.5)	4 (22.2)
Dose prednisone, median (IQR) milligrams/day	5 (5-15.625)	2.5 (2.5-5)	3.75 (2.75-7.5)	2.75 (1.56-4.5)
Concomitant bDMARDs, n (%)	10 (17.9)	5 (9.6)	3 (7.5)	1 (5.6)
Refractoriness	NA	4 (7.7)	2 (5)	1 (5.6)
Relapse	NA	0 (0)	3 (7.5)	2 (11.1)
Remission	NA	48 (92.3)	35 (87.5)	15 (83.3)
Suspension	NA	10 (19.2)	9 (22.5)	4 (22.2)
Infusion reaction, n (%)	1 (1.8)	1 (1.9)	0 (0)	0 (0)
Infectious adverse events, n (%)	NA	10 (19.2)	6 (15)	3 (16.7)
Severe infectious adverse events, n (%)	NA	2 (3.8)	1 (2.5)	0 (0)

Conclusion: Our experience with RTX-B is limited; however, it represents an extensive report about the use of RTX-B in AAV patients and confirmed that it may be a well-tolerated and effective therapy in AAV setting, in agreement with previous evidence on RTX-O. Prospective and larger studies are needed to confirm this preliminary evidence.

REFERENCES:

[1] Kay J, et al. Ann Rheum Dis 2018;77:165–74.
[2] Kwon HC, et al. Yonsei Med J 2020;61:712-9.
[3] Mittal S, et al. Clin Rheumatol 2021;40:645-51.

Disclosure of Interests: Silvia Sartorelli: None declared, adriana cariddi: None declared, Luca Moroni: None declared, Elena Baldissera Speakers bureau: Pfizer, Roche, Sanofi-Genzyme, Consultant of: Novartis, Enrica Bozzolo: None declared, Lorenzo Dagna Consultant of: Abbvie, Amgen, Biogen, BristolMyers Squibb, Celltrion, Galapagos, GlaxoSmithKline, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI., Grant/research support from: The Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR) received unrestricted research/educational grants from Abbvie, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Merk Sharp & Dohme, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI.
DOI: 10.1136/annrheumdis-2021-eular.1672

POS0254 EFFICACY OF APREMILAST IN THE TREATMENT OF ORAL ULCERS OF BEHÇET'S SYNDROME: RESULTS FROM THE EUROPEAN SUBGROUP OF RELIEF

A. Mahr[1], G. Hatemi[2], M. Takeno[3], D. Kim[4], M. Melikoglu[1], D. Saadoun[5], C. C. Zouboulis[6], S. Cheng[7], S. Richter[8], S. Jardon[8], M. Paris[8], M. Chen[8], Y. Yazici[9]. *[1]Cantonal Hospital St. Gallen, Department of Rheumatology, St. Gallen, Switzerland*; *[2]Istanbul University - Cerrahpasa, Department of Internal Medicine, Istanbul, Turkey*; *[3]Nippon Medical School, Musashi Kosugi Hospital, Department of Allergy and Rheumatology, Kawasaki, Japan*; *[4]Yonsei University College of Medicine and Severance Hospital, Associate Professor, Hepotolgy, Seoul, Korea, Rep. of (South Korea)*; *[5]Pitié-Salpêtrière Hospital, Department of Internal Medicine and Clinical Immunology, Paris, France*; *[6]6Dessau Medical Center, Brandenburg Medical School Theodor Fontane, Director of the Departments of Dermatology, Venereology, Allergology and Immunology, Dessau, Germany*; *[7]Amgen, Inc., Global Medical Affairs, Director Biostats, Thousand Oaks, CA, United States of America*; *[8]Amgen, Inc., Global Medical Affairs, Thousand Oaks, CA, United States of America*; *[9]New York University School of Medicine, Department of Rheumatology, New York, NY, United States of America*

Background: Behçet's syndrome, a chronic, multi-system variable vessel vasculitis, is often characterized by painful oral ulcers (OU) affecting quality of life (QoL). Apremilast (APR), an oral PDE4 inhibitor, demonstrated efficacy in OU treatment in the phase 3 multinational RELIEF study.

Objectives: To evaluate APR efficacy in OU treatment in patients with active Behçet's syndrome in a prespecified subgroup of patients enrolled in 13 European RELIEF sites (France, Germany, Greece, and Italy).

Methods: patients were adults with active Behçet's syndrome and ≥3 OU at randomization or ≥2 OU at screening and randomization, without active major organ involvement. Patients were randomized (1:1) to APR 30 mg BID or PBO during a 12-week double-blind phase. The primary endpoint was area under the curve for the number of OU through Week 12 (AUC_{Wk0-12}). Other outcomes were OU pain visual analog scale (VAS); achievement of OU complete response (ie, OU-free) and maintenance of OU complete response (ie, complete response at Week 6 and remaining OU-free for ≥6 additional weeks); OU partial response (ie, OU reduction ≥50%); disease activity (Behçet's Syndrome Activity Score [BSAS]; Behçet's Disease Current Activity Form [BDCAF], including Behçet's Disease Current Activity Index [BDCAI], and Patient's and Clinician's Perception of Disease Activity); and QoL (BDQoL; Short Form Health Survey version 2 [SF-36v2], including Physical Functioning [PF] scale and Physical and Mental Component Summary [PCS, MCS]).

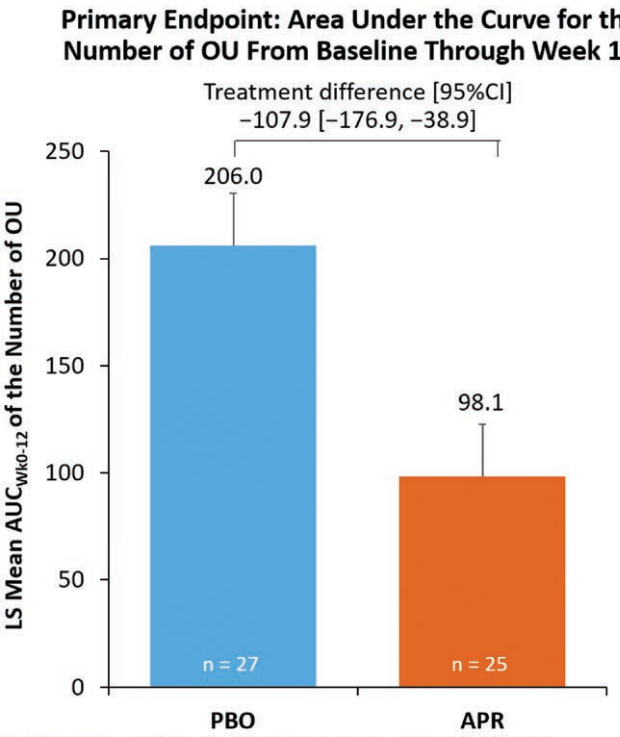
Results: Of 207 patients randomized and treated in RELIEF, 52 were in the European subgroup. Mean (±SD) age in the subgroup was 39 (±12) years; 54% were women. Baseline disease characteristics were similar between treatment groups (Table 1). Patients receiving APR achieved lower AUC_{Wk0-12} for OU vs PBO (Figure 1) and greater reduction in pain. A greater proportion of patients receiving APR achieved complete, maintained, or partial OU responses at Week 12 vs those receiving PBO (Table 1). Consistent treatment effects favoring APR vs PBO were observed in disease activity, as shown by BSAS and BDCAF component scores at Week 12 (Table 1). Greater improvement in SF-36v2 MCS was observed favoring APR vs PBO at Week 12, and moderate treatment differences were seen for other QoL measures (BDQoL, SF-36v2 PF, and SF-36v2 PCS).

Conclusion: In the European subgroup of patients with Behçet's syndrome and OU in RELIEF, APR resulted in greater reduction in OU count, OU pain, and disease activity as well as favorable treatment effect on QoL measures than PBO. These results are consistent with the efficacy of APR treatment in the overall RELIEF population.

Baseline Disease Characteristics, Mean*	PBO (n = 27)	APR (n = 25)	
Duration of BD, years	9.0	8.2	
OU count	3.8	4.0	
OU pain (VAS 0-100)	60.6	64.2	
BSAS (0-100)	38.7	41.4	
BDCAI (0-12)	3.5	3.6	
BDQoL (0-30)	10.5	9.0	
Efficacy Outcomes at 12 Weeks*	PBO (n = 27)	APR (n = 25)	Treatment Difference [95% CI]
OU pain (VAS 0-100), mean†	–17.7	–48.7	–31.0 [–44.7, –17.3]
OU complete response, n (%)‡	4 (14.8)	16 (64.0)	51.5 [29.8, 73.3]
OU maintained response, n (%)‡	1 (3.7)	8 (32.0)	26.7 [7.4, 46.0]
OU partial response, n (%)‡	11 (40.7)	21 (84.0)	46.0 [23.9, 68.0]
BSAS (0-100)†,§	–5.23	–20.68	–15.5 [–22.6, –8.3]
BDCAI (0-12)†,§	–0.0	–1.4	–1.4 [–2.2, –0.6]
Patient's Perception of Disease Activity†,§	–0.4	–1.6	–1.2 [–2.1, –0.4]
Clinician's Overall Perception of Disease Activity†,§	–0.6	–1.7	–1.0 [–1.7, –0.4]
BDQoL (0-30)†,§	–1.25	–2.37	–1.12 [–3.8, 1.5]
SF-36v2 MCS (0-100)†,§	–2.1	4.2	6.3 [2.2, 10.4]

***ITT population. †LS mean of the change from baseline at Week 12. ‡Non-responder imputation for missing data. §LOCF approach. All efficacy endpoints (except BDQoL) were significant at the level of *P*<0.05.**

Acknowledgements : This study was funded by Celgene. Additional analyses were funded by Amgen Inc. Writing support was funded by Amgen Inc. and provided by Kristin Carlin, RPh, MBA, of Peloton Advantage, LLC, an OPEN Health company.



P<0.05; ITT population; error bars represent standard error.
Multiple imputation used for imputing missing data.

Disclosure of Interests: Alfred Mahr Speakers bureau: Chugai; Roche, Consultant of: Celgene; Chugai, Gulen Hatemi Speakers bureau: AbbVie, Novartis, and UCB, Grant/research support from: Celgene, Mitsuhiro Takeno Speakers bureau: AbbVie, Esai, and Mitsubishi-Tanabe, Consultant of: Celgene, Grant/research support from: Novartis, Doyoung Kim: None declared, Melike Melikoglu: None declared, david Saadoun Consultant of: AbbVie, Celgene, Janssen, and Roche, Grant/research support from: AbbVie and Roche, Christos C. Zouboulis Speakers bureau: Amgen, Galderma, Pierre Fabre, PPM and Sobi, Consultant of: AbbVie, AccureAcne, Almirall, Bayer Healthcare, GSK/Stiefel, Incyte, Inflarx, Janssen, Novartis, PPM, Regeneron, and UCB, Grant/research support from: Celgene, NAOS-BIODERMA, and Relaxera, Sue Cheng Employee of: Amgen Inc, Sven Richter Employee of: Amgen Inc, Shauna Jardon Employee of: Amgen Inc, Maria

Paris Employee of: Amgen Inc, Mindy Chen Employee of: Amgen Inc, Yusuf Yazici Consultant of: Bristol-Myers Squibb, Celgene, Genentech, and Sanofi
DOI: 10.1136/annrheumdis-2021-eular.2591

POS0255

IMPACT OF PLASMA EXCHANGE (PLEX) IN SEVERE ANCA-ASSOCIATED VASCULITIS (AAV): A REAL-LIFE DATA FROM A PROSPECTIVE COHORT

E. Bilgin[1], E. Duran[1], E. Erkantarcı Levent[2], T. Yıldırım[3], M. Arıcı[3], A. İ. Ertenli[1], O. Karadag[1]. *[1]Hacettepe University, Internal Medicine, Rheumatology, Ankara, Turkey*; *[2]Hacettepe University, Internal Medicine, Ankara, Turkey*; *[3]Hacettepe University, Internal Medicine, Nephrology, Ankara, Turkey*

Background: PEXIVAS was the largest clinical trial conducted on severe AAV patients and failed to demonstrate the contribution of PLEX on the prognosis of severe AAV. This data needs to be tested with real life experiences.
Objectives: The aim of this study was to explore the effects of PLEX on the prognosis of severe AAV in a real-life cohort.
Methods: Hacettepe University Vasculitis Research Center (HUVAC) prospective database was established in October 2014 by registering past and newly diagnosed patients. Baseline disease characteristics, treatments and survival status were recorded. For this study, patients with granulomatosis polyangiitis (GPA) and microscopic polyangiitis (MPA) who met the inclusion criteria of PEXIVAS trial [briefly; ANCA positive MPA or GPA patients with either severe renal involvement (necrotizing glomerulonephritis or active urinary sediment, and eGFR <50 ml/min) and/or severe pulmonary involvement (pulmonary hemorrhage due to active vasculitis)] at the disease onset were included. Patients were grouped whether they had PLEX or not. Demographic and disease-specific data and immunosuppressive agents used in induction phase were compared. Primary outcome was accepted as composite index of mortality or end-stage renal disease (ESRD) at the first year and at the final visit.
Results: Of 145 GPA and MPA patients, 49 patients had inclusion criteria and distribution of patients were as GPA (n=38), MPA (n=8) or renal-limited (n=3). 16 (32.6%) patients had PLEX. Median number of plasma exchange cycles was 6.5 (min-max; 2-12). Although severe pulmonary [10 (62.5%) vs. 5 (15.2%), p=0.001] and combined severe renal+pulmonary involvements were more prevalent [9 (56.3%) vs. 4 (12.1%), p=0.001] and baseline creatinine levels were higher in PLEX (+) group, BVAS and FFS scores were similar (Table 1). Induction immunosuppressive regimens were comparable.
At first year evaluation, primary composite outcome was observed in 11 patients (3 deceased, 8 ESRD) of PLEX (+) group whereas in 12 patients (2 deceased, 10 ESRD) of PLEX (-) group (p = 0.03, log-rank). In multivariate analysis: **combined renal+pulmonary involvements** (aOR: 6.5 [1.1-37.9]) and **serum creatinine** (for 1 mg/dl increment) (aOR: 1.3 [1.1-1.7]) were associated with primary outcome. In this model, having plasma exchange was not associated with a favorable outcome.
At the end of median follow-up [40.7 (1.2-170.3) months], outcome was observed in 12 patients (9 deceased, 3 ESRD) of PLEX (+) group and in 13 patients (6 deceased, 7 ESRD) of PLEX (-) group (p < 0.001, log-rank). In multivariate analysis: **having plasma exchange** (HR: 3.5 [1.4-8.5]) and **combined renal+pulmonary involvements** (HR: 2.4 [1.05-5.8]) were found as the predictors of primary composite outcome. In the figure 1, comparison of primary outcome according to FFS and plasma exchange status was given.
Conclusion: In real-life plasma exchange did not have a positive impact on the composite index of mortality and ESRD, similar to PEXIVAS trial. Presence of combined severe renal and pulmonary involvement was the predictor of worse outcome at 1-year and overall follow-up.

Table 1. Comparison of disease characteristics and composite indexes of patients

	PLEX (+) (n=16)	PLEX (-) (n=33)
GPA/MPA/Renal-limited (n)	12/3/1	26/5/2
Female, n(%)	8 (50.0)	13 (39.4)
Age at diagnosis, months (med,min-max)	54.5 (18.8-77.8)	55.6 (18.1-86.3)
MPO-ANCA / PR3-ANCA (n)	5 / 11	16 / 17
Follow-up duration, months (med, min-max)	16.6 (1.2-116.5)	50.5 (2.2-170.0)
BVAS at diagnosis, (med, min-max)	23 (14-37)	23 (8-33)
FFS ≥ 2 (n,%) (N=45)	23 (85.7)	26 (83.9)
Creatinine (mg/dl) at diagnosis† (med,min-max)	8.1 (4.1-8.9)	3.1 (1.8-6.2)
CRP (mg/dl) at diagnosis (med,min-max)	21.8 (15.0-29.0)	11.5 (3.6-20.0)
Immunosuppressive (induction) (n,%)		
-Pulse steroid	14 (87.5)	29 (87.9)
-Rituximab	1 (6.3)	3 (9.1)
-Cyclophosphamide	12 (75.0)	28 (84.8)

†p = 0.005

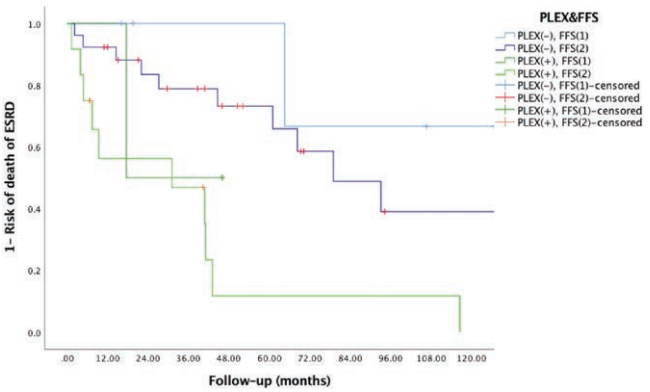


Figure 1. Comparison of primary outcome according to FFS and plasma exchange status

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3169

Diagnostics and imaging procedures

POS0256

AUTOMATED CAPILLARY DETECTION AND IMAGE ANALYSIS SOFTWARE IN CAPILLAROSCOPY: CAPILLARY.IO

B. Gracia Tello[1,2], E. Ramos[3], C. P. Simeón-Aznar[4], V. Fonollosa Pla[4], A. Guillén-Del-Castillo[4], A. Selva-O'callaghan[4], L. Sáez-Comet[5], E. Martínez Robles[6], J. J. Rios[6], G. Espinosa[7], J. A. Todolí Parra[8], J. L. Callejas-Rubio[9], N. Ortego[9], B. Marí-Alfonso[10], M. Freire[11], P. Fanlo[12]. *[1]Hospital Clinico Universitario Lozano Blesa, Department of Internal Medicine, Zaragoza, Spain*; *[2]Zaragoza, Instituto de investigación Sanitaria de Aragón (ISSA), Zaragoza, Spain*; *[3]Zaragoza, Computer Science Graduate by University of Zaragoza, Zaragoza, Spain*; *[4]Hospital Universitario Vall d'Hebron, Unit of Autoimmune Diseases, Department of Internal Medicine, Barcelona, Spain*; *[5]Hospital Universitario Miguel Servet, Zaragoza, Spain, Department of Internal Medicine, Zaragoza, Spain*; *[6]Hospital General Universitario La Paz, Department of Internal Medicine, Madrid, Spain*; *[7]Hospital Clínic, Department of Internal Medicine, Unit of Autoimmune Diseases, Barcelona, Spain*; *[8]Hospital La Fe, Valencia, Spain, Department of Internal Medicine, Valencia, Spain*; *[9]Hospital Universitario Virgen de las Nieves, Granada, Spain, Unit of Autoimmune Diseases, Department of Internal Medicine, Granada, Spain*; *[10]Hospital Universitario Parc Taulí, Sabadell (Barcelona), Spain, Department of Internal Medicine, Barcelona, Spain*; *[11]Complejo Hospitalario Universitario de Santiago, Department of Internal Medicine, Santiago de Compostela, Spain*; *[12]Complejo Hospitalario de Navarra, Department of Internal Medicine, Pamplona, Spain*

Background: A nailfold capillaroscopy procedure is a non-invasive, low-cost, and well-established examination that can be used to diagnose several rheumatic autoimmune diseases and support the necessary follow-up of patients. There are two main elements to nailfold capillaroscopy: image acquisition and image interpretation. Both of these can present challenges: we need to ensure that the best possible images are captured, and we need to define the enlarged capillaries, capillary loss and pericapillary hemorrhages objectively. We introduce Capillary.io, an automatic image reading system able to recognize capillaries in images obtained with any microscope, generate automatic measurements of each capillary and take advantage of this information to report capillary morphology. Together it allows a comprehensive analysis that is capable of producing detailed reports for each patient.
Objectives: The primary outcome was general sensitivity and specificity, using images assessed by expert capillaroscopists as the gold standard.
Methods: 6500 images previously analyzed by capillaroscopists from GREC were compared with Capillary.io. Capillary morphology (enlarged capillaries, tortuosities, ramifications, megacapillaries, hemorrhages) of each of the capillaries contained in each of the images was analyzed manually by at least one expert capillaroscopist. Subsequently, the automatic image interpretation system was used to fully automatically analyze each of the capillaries contained in each image and the results obtained were compared.
Results: Overall, a total of 78.347 capillaries were compared, of which 47.734 were normal capillaries, 21.991 enlarged capillaries, 2672 megacapillaries, 8512 tortuosities, 1322 ramifications and 5149 hemorrhages. Capillary.io was able to detect 38.101 normal capillaries, 19.126 enlarged capillaries, 2389 megacapillaries, 5698 tortuosities, 718 ramifications and 3706 hemorraghes.

Capillary.io presented a sensitivity (S) of 79.82% and a specificity (E) of 82% in the recognition of normal capillaries. The automatized system was able to recognize enlarged capillaries with a sensitivity of 86.97% and a specificity of 81.38%. Megacapillaries were detected with 89.41% sensitivity and 78.75% specificity. Similarly, the system was able to detect tortuosities (S 66.94%; E 67.71%), ramifications (S 54.34%; E 58.61%) and hemorrhages (S 71.36; E 73.97%).

Conclusion: Capillary.io is a simple, easy-learning web-based system to get interpretation of nailfold capillaroscopic images. It may be a very useful tool to standardize the interpretation of capillaroscopic pictures and could provide great research in that field.

REFERENCES:

[1] Bernardino V, Rodrigues A, Lladó A, Fernandes M, Panarra A. The Impact of Nailfold Capil- laroscopy in the Approach of Microcirculation. In: Vascular Biology - Selection of Mechanisms and Clinical Applications IntechOpen; 2020.

[2] Boulon C, Devos S, Mangin M, Chevoir JDL, Senet P, Lazareth I, et al. Reproducibility of capillaro- scopic classifications of systemic sclerosis: results from the SCLEROCAP study. Rheumatology 2017 jul;56(10):1713–1720.

[3] Capillary io, Capillaroscopy made quick, simple and objective; 2020. Available at https:// capillary.io.

[4] Chen K, Wang J, Pang J, Cao Y, Xiong Y, Li X, et al. MMDetection: Open MMLab Detection Toolbox and Benchmark. arXiv preprint arXiv:190607155 2019;.

[5] Cutolo M, Pizzorni C, Sulli A. Nailfold videocapillaroscopy assessment of microvascular damage in systemic sclerosis - Reply. The Journal of Rheumatology 2000 11;27:2722–2723.

[6] Cutolo M, Trombetta AC, Melsens K, Pizzorni C, Sulli A, Ruaro B, et al. Automated assessment of absolute nailfold capillary number on videocapillaroscopic images: Proof of principle and validation in systemic sclerosis. Microcirculation 2018 May;25(4):e12447.

Disclosure of Interests: Borja Gracia Tello Shareholder of: Co-founder and shareholder of Capillary.io., Eduardo Ramos Shareholder of: co-founder and shareholder of Capillary.io., Carmen Pilar Simeón-Aznar: None declared, Vicent Fonollosa Pla: None declared, Alfredo Guillén-Del-Castillo: None declared, Albert Selva-O'Callaghan: None declared, Luis Sáez-Comet: None declared, Elena Martínez Robles: None declared, Juan José Rios: None declared, Gerard Espinosa: None declared, Jose Antonio Todolí Parra: None declared, Jose Luis Callejas-Rubio: None declared, Norberto Ortego: None declared, Begoña Marí-Alfonso: None declared, Mayka Freire: None declared, Patricia Fanlo: None declared

DOI: 10.1136/annrheumdis-2021-eular.4022

POS0257 TOWARDS A SIMPLIFIED FLUID-SENSITIVE MRI-PROTOCOL IN SMALL JOINTS OF THE HAND IN EARLY ARTHRITIS PATIENTS: RELIABILITY BETWEEN MDIXON AND REGULAR FSE FAT SATURATION MRI-SEQUENCES

E. Niemantsverdriet[1], M. Verstappen[1], F. Wouters[1], M. Reijnierse[2], H. Bloem[2], A. Van der Helm - van Mil[1]. *[1]Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; *[2]Leiden University Medical Center, Radiology, Leiden, Netherlands*

Background: MRI facilitates early recognition of rheumatoid arthritis (RA) by depicting inflammation. Contrast-enhanced T1-weighted and T2-weighted fat-suppressed sequences have been sensitive and thus recommended, but are hampered by invasiveness, costs and long scan time. Therefore we introduced a modified Dixon-sequence (mDixon) which is more patient-friendly, reduces cost, and scan times by 83%. However, it is not known if this mDixon-sequence is reliable in relation to regular MRI-sequences with and without contrast (T1- and T2-weighted, respectively).

Objectives: We determined the reliability between regular MRI-sequences with and without contrast (T1- and T2-weighted, respectively) and mDixon-MRI in early arthritis patients.

Methods: 29 early arthritis patients underwent regular fat-suppressed-MRI (T1- and T2-weighted) and mDixon-sequences, of metacarpophalangeal-2-5 and wrist-joints. Two readers scored erosions, osteitis, synovitis and tenosynovitis. Intraclass correlation coefficients (ICCs) between readers, and comparing the two sequences, were studied. Spearman correlations were determined.

Results: Performance between the two readers with the regular-MRI sequences, was good to excellent (ICCs all ≥0.88). The between reader ICC was also good to excellent for the mDixon-MRI (ICCs all ≥0.76). Next, ICCs between the two sequences was investigated to determine the reliability of mDixon. ICCs were good to excellent for total RAMRIS score 0.87 (95%CI 0.74-0.94), for erosions 0.88 (95%CI 0.69-0.95), and total inflammation score 0.84 (95%CI 0.69-0.82). The individual MRI-inflammation scores, had ICCs for osteitis 0.97 (95%CI 0.93-0.98), for tenosynovitis 0.78 (95%CI 0.58-0.89), and for synovitis 0.57 (95%CI 0.26-0.77). In addition, scores were highly correlated for total RAMRIS, erosions, and total MRI-inflammation score (ρ=0.82, ρ=0.81, ρ=0.80, respectively).

Conclusion: Regular-MRI sequences and mDixon-MRI perform equally well, this suggests that mDixon-sequence is reliable to detect joint inflammation. Thus, this is the first step towards an simplified and abridged MRI-protocol in small hand-joints in early arthritis patients. The ultimate goal will be implementation of this mDixon-MRI sequence. Validation in larger studies is warranted.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1333

POS0258 REAL-TIME VERSUS STATIC SCORING IN MUSCULOSKELETAL ULTRASONOGRAPHY IN PATIENTS WITH INFLAMMATORY HAND OSTEOARTHRITIS

L. Van de Stadt[1], F. Kroon[1], M. Reijnierse[2], D. Van der Heijde[1], F. Rosendaal[3], N. Riyazi[4], R. De Slegte[5], J. Van Zeben[6], C. Allaart[1], M. Kloppenburg[1], M. Kortekaas[1]. *[1]Leiden University Medical Center (LUMC), Reumatology, Leiden, Netherlands*; *[2]Leiden University Medical Center (LUMC), Radiology, Leiden, Netherlands*; *[3]Leiden University Medical Center (LUMC), Clinical Epidemiology, Leiden, Netherlands*; *[4]Haga Hospital, Reumatology, The Hague, Netherlands*; *[5]Reade, Radiology, Amsterdam, Netherlands*; *[6]Sint Franciscus Vlietland Groep, Reumatology, Rotterdam, Netherlands*

Background: Ultrasound (US) is used in rheumatic musculoskeletal diseases (RMDs) such as hand osteoarthritis (OA) as outcome measure. Traditionally scoring is performed real-time, but central reading of static US images could avoid issues of inter-rater reliability. However, agreement between real-time and static assessment has not been studied

Objectives: To study the agreement between real-time and static scoring of US in inflammatory hand OA.

Methods: Ultrasound was performed of 30 joints obtained in 75 patients with hand osteoarthritis, treated with prednisolone or placebo in a randomized double-blind trial. Hand joints were assessed for synovial thickening, effusion, Doppler signal and osteophytes by ultrasound (score 0-3 per joint) at baseline and after treatment. Two ultrasonographers blinded for clinical data scored the live images together (simultaneously) in real-time. A consensus score for each joint was recorded. Representative images stored during scanning were scored by one ultrasonographer minimally 6 months after real-time scoring. For each patient, images of each visit were scored paired, with known chronological order. Agreement between scoring methods was studied at joint level with quadratic weighted kappa. At patient level, intra-class correlations (ICC; mixed effect model, absolute agreement, with clustering taken into account) were calculated at both timepoints. ICCs were also calculated for the delta of sum scores. Responsiveness of scoring methods was analyzed with generalized estimating equations (GEE) with treatment as independent and ultrasonography findings as dependent variable.

Results: Thirty-nine patients (52%) were treated with prednisolone and 36 (48%) were treated with placebo. Patient characteristics were well-balanced between treatment groups.

All patients had signs of synovial thickening and osteophytes as assessed by real-time ultrasonography, and almost all signs of effusion (99%) or a positive Doppler signal (95%) in at least one joint. Total ultrasonography sum score for osteophytes was high (mean 45 ±SD 12), whereas sum score was low for positive Doppler signal (mean 5.9 ±SD 4.4), with intermediate sum scores for synovial thickening and effusion (mean 16 ±SD 6.3 and 11 ±SD 6.0 respectively). Static sum scores were overall slightly higher (osteophytes mean 48 ±SD 10; Doppler mean 6.9 S±D 5.0; synovial thickening mean 20 ±SD 7.0 and effusion 13 ±SD 6.5)

Agreement at baseline was good to excellent at joint level (kappa 0.72-0.88) and moderate to excellent at patient level (ICC 0.59-0.86). Agreement for delta sum scores was poor to fair for synovial thickening and effusion (ICC 0.18 and 0.34 respectively), but excellent for Doppler signal (ICC 0.80) (Table 1).

Real-time ultrasonography showed responsiveness to prednisolone with a mean between-group difference of synovial thickening sum score of -2.5 (CI:-4.7 to-0.3). Static ultrasonography did not show a decrease in synovial thickening (Figure 1). No difference in ultrasonography scores was seen for the other ultrasonography features, neither with real-time nor static scoring.

Conclusion: While cross-sectional agreement between real-time and static ultrasonography was good, agreement of delta sum scores was not and paired static ultrasonography measurement of synovial thickening did not show responsiveness to prednisone therapy where real-time ultrasonography did. Therefore, when using ultrasonography in clinical trials, real-time dynamic scoring should remain the standard.

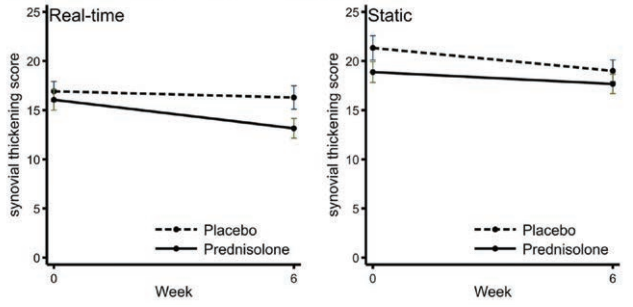
Table 1. Agreement on patient level

	Baseline	Week 6	Delta W6-BL
	ICC (95% CI)	ICC (95% CI)	ICC (95% CI)
Synovitis	0.59 (0.26-0.76)	0.58 (0.24-0.77)	0.18 (0 - 0.40)
Effusion	0.84 (0.66-0.92)	0.84 (0.75-0.89)	0.34 (0.12-0.53)
Osteophytes	0.82 (0.50-0.92)	0.78 (0.56-0.88)	ND
Doppler	0.86 (0.75-0.92)	0.91 (0.85-0.94)	0.80 (0.70 -0.87)

ICC: intra-class correlation coefficient linear mixed model (random patient, fixed rating), absolute agreement. ND: Not Dertermined

Disclosure of Interests: Lotte van de Stadt: None declared, Féline Kroon: None declared, Monique Reijnierse Grant/research support from: Dutch Arthritis Foundation, Désirée van der Heijde Consultant of: bbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma, Frits Rosendaal: None declared, Naghmeh Riyazi: None declared, R. de Slegte: None declared, Jende van Zeben: None declared, Cornelia Allaart: None declared, Margreet Kloppenburg Consultant of: Abbvie, Pfizer, Levicept, GlaxoSmithKline, Merck-Serono, Kiniksa, Flexion, Galapagos, Jansen, CHDR, Grant/research support from: MI-APPROACH, Marion Kortekaas: None declared

Figure 1 Ultrasonography synovial thickening score of patients treated with prednisolone versus placebo.



DOI: 10.1136/annrheumdis-2021-eular.3007

POS0259 ULTRASOUND AS AN IMAGING BIOMARKER OF EARLY RESPONSE TO TOCILIZUMAB AND METHOTREXATE IN VERY EARLY RHEUMATOID ARTHRITIS, TOVERA – A LONGITUDINAL STUDY

M. Stoenoiu[1,2], M. Maruseac[1], M. Messaoudi[1], A. Nzeusseu Toukap[1,2], E. Naredo[3]. *[1]Cliniques Universitaires Saint-Luc, Department of Rheumatology, Brussels, Belgium*; *[2]Institut de recherche expérimentale et cliniques (IREC), Department of Rheumatology, Brussels, Belgium*; *[3]Joint and Bone Research Unit. Hospital Universitario Fundación Jiménez Díaz, IIS Fundación Jiménez Díaz and Universidad Autónoma de Madrid., Department of Rheumatology, Madrid, Spain*

Background: The combination of methotrexate (MTX) and tocilizumab (TCZ) has been proven to be superior to MTX alone in early rheumatoid arthritis (RA)[1] and was able to prevent radiographic progression. Ultrasound (US) has become a valid imaging modality in managing RA. Together with clinical examination, US may allow a comprehensive monitoring of response to therapy. So far, few data are available concerning the early response to TCZ plus MTX in very early RA (VERA).

Objectives: In this study we aimed to assess the early US response to TCZ plus MTX in VERA, DMARD-naïve patients.

Methods: In this open-label, single-arm study, VERA patients received TCZ (162 mg/week, subcutaneously) and MTX (15-20 mg/week, *per os*) for 24 weeks as induction therapy, followed by MTX as maintenance therapy. RA was diagnosed according to the 2010 ACR/European league against rheumatism (EULAR) criteria. All patients who fulfilled the inclusion criteria (ClinicalTrials.gov: NCT02837146) underwent blood tests, clinical and ultrasound examinations at the predefined time-points: 0,2,4,8,12,24,32,48,54 weeks (w). Ultrasound examination of 34 joints (elbows, wrists, MCP [1-5, bilateral], PIP ([2-5, bilateral], knees, ankles and MTP [2-5, bilateral]) was performed blindly to clinical data. Gray-scale (GS), power-Doppler (PD) scores, and the global *OMERACT*-EULAR synovitis score (*GLOESS*) were assessed in each joint. The sum of individual scores was calculated for 17-joint score (JS) (whole joint set), 10-JS (wrists, MCP, ankles and MTP joints), 12-JS[2], and 7-JS[3].

Results: Forty-four patients (77% women), aged 46.7 ± 12.4 years, completed the 24-week period. Two-thirds (72.7%) were positive for anti-citrullinated protein antibody (ACPA) and 18.2% had bone erosions. At baseline, the mean 28 swollen joints count (28-SJC) was 7.55± 4.5, mean disease activity score (DAS28)-CRP score was 5.2 ± 0.15, mean simplified clinical activity score (SDAI) was 31.4 ± 1.9, mean clinical activity score (CDAI) was 29.1 ± 1.8 and mean health assessments questionnaire (HAQ) score was 1.3 ± 0.1. The C-reactive protein (CRP) decreased significantly at 2w ($p<0.05$) and, accordingly DAS28-CRP score decreased significantly at 4w ($p<0.05$). The 28-SJC and CDAI scores decreased significantly at 8w ($p<0.05$). The HAQ and visual analogue scale (VAS) disease activity reported by patients decreased significantly at 8w ($p<0.05$) and VAS fatigue at 12w ($p<0.05$).

The GLOESS and GS scores allowed us detecting the earliest significant treatment response at 2w and PD scores at 4w ($p<0.05$). Among US joint subsets, 17-JS ($p<0.01$), 12-JS ($p<0.05$) and 10-JS ($p<0.05$) were able to detect the earliest treatment response at 2w. The 7-joint score detected the earliest response at 4w, both in GS and PD ($p<0.05$).

Conclusion: US scores were able to detect therapeutic response to TCZ plus MTX earlier than clinical scores and may therefore be a promising imaging biomarker.

REFERENCES:

[1] Burmester GR *et al.* Ann Rheum Dis 2017; 76; 1279-1284.
[2] Naredo E *et al.* Arthritis Rheum 2008; 59(4): 515-522.
[3] Backhaus M *et al.* Arthritis Rheum 2009; 61: 1194-1201.

Disclosure of Interests: Maria Stoenoiu Grant/research support from: UCB, Roche, Abbvie, MSD, Sanofi, Celgene, Mihaela Maruseac: None declared, Mouna Messaoudi: None declared, Adrien Nzeusseu Toukap Grant/research support from: AbbVie, Eli Lilly, Janssen, UCB, Novartis, Celgene Corporation, Pfizer, Esperanza Naredo Grant/research support from: AbbVie, Roche, BMS, Pfizer, UCB, Eli Lilly, Novartis, Janssen, Celgene

DOI: 10.1136/annrheumdis-2021-eular.3625

POS0260 ULTRASOUND ASSESSMENT OF HANDS AND FEET FOR SYNOVITIS PRIOR TO FIRST CLINICAL VISIT MARKEDLY REDUCES TIME TO DIAGNOSIS - EXPERIENCE FROM ROUTINE CARE

M. Ammitzbøll Danielsen[1], U. Møller Døhn[1], V. Fana[1], T. Møller[1], S. N. Ng[1,2], A. E. Secher[1], J. J. Lykkegaard[1], L. Terslev[1]. *[1]Rigshospitalet, Center for Rheumatology and Spine Diseases, Glostrup, Denmark*; *[2]Private Practise, Rheumatology, Hong Kong, China*

Background: All patients referred to our Rheumatology department suspected of having arthritis are scheduled for a visit in the out-patient fast track clinic (FTC) for arthritis. Routine blood samples including C-reactive protein (CRP), anti-CCP, IgM RF, and x-ray of hands and feet are available at the first clinical visit where the medical history and clinical examination is obtained by rheumatologists or rheumatologists-in-training under supervision. The role of ultrasound (US) in routine care for diagnosing arthritis is not fully elucidated but US is more sensitive than clinical joint examination for detecting synovitis. Therefore, US may facilitate diagnosis of arthritis.

Objectives: To assess whether US examinations of hands and feet in relation to the first clinical visit impact the time to diagnosis and number of clinical visits needed.

Methods: From Oct. 2017 to June 2018, US examination of hands and feet (wrist, metacarpophalangeal and proximal interphalangeal joints, ankle, and metatarsophalangeal joints) were performed prior to the first clinical visit by ultrasound-experienced rheumatologists. Using the OMERACT scoring system for grey-scale (GS) and Doppler, synovitis was defined as GS score >1 with or without Doppler score ≥1. Examination time was 20 minutes.

Time from the first clinical visit to the final clinical diagnosis and the number of clinical visits needed in the FTC was assessed and compared to a similar patient cohort the previous year (Nov. 2016 to June 2017) where ultrasound was performed ad hoc. Number of revised diagnoses and the number of patients re-referred after 12 months was noted. Local ethics committee ruled that approval was not needed.

Results: From 2017- 2018, 163 referred patients had US prior to first clinical visit. 76(47%) were diagnosed with inflammatory arthritis (IA), 12(7%) with crystal-related arthritis, 39(24%) with other Rheumatic Diseases (RMDs) and 36(22%) with no RMD diagnosis. The comparative cohort comprised of 109 patients of whom 29(27%) were diagnosed with IA, 16 (15%) with crystal-related arthritis, 31(28%) with other RMDs and 33 (30%) with no RMD diagnosis. Adding US to the first clinical visit reduced the time to diagnosis from mean 31 (standard deviation(SD) ±32.2) days to mean 12 (±17.3) days. The number of clinical visits needed was reduced from mean 2.8(±1.1) to 2.1 (±1.3) corresponding to a reduction of 114 visits in the period from 2017–2018. The mean number of all US examinations in the FTC was 1.1 (±0.3) in the US cohort versus 0.8(±0.7) in the comparative cohort. In the US cohort vs. comparative cohort 8 (4.9%) vs. 17

(15.7%) patients had a revised diagnosis at 1 year-follow-up, and 7 (4%) vs. 12 (11%) were re-referred, respectively. For demographics, clinical, US, and laboratory characteristics see Table 1 where median values and inter-quartile range (IQR) for all parameters.

Conclusion: Adding routine US examination to the first clinical visit reduces time to diagnosis markedly, lowers the number of clinical visits needed thereby reducing the time patients spent away from work, and freeing time for visits in the FTC to be used for other patients

Table 1.

		Comparative cohort		US cohort		P
		(n=109)		(n=163)		
Age	Median [IQR]	55.5	[42;69]	53	[40;67]	0.44
	Mean ±SD	54.7	±16.1	53.2	±17.2	
Time to diagnosis days	Median [IQR]	12.4	[10;42]	0	[0;25]	<0.01
	Mean ±SD	30.6	±32.2	12.4	±17.3	
Visits in FTC	Median [IQR]	3	[2;3]	2	[1;2]	<0.01
	Mean ± SD	2.8	±1.1	2.1	±1.3	
US assessments in the FTC	Median [IQR]	1	[0;1]	1	[1;1]	<0.01
	Mean ±SD	0.8	±0.7	1.1	±0.27	
Swollen joint count (0-28)	Median [IQR]	0	[0;1]	0	[0;2]	0.19
	Mean ±SD	1.1	±2.1	1.8	±3.1	
Tender joint count (0-28)	Median [IQR]	1	[0;5]	1	[0;5]	0.06
	Mean ±SD	3.1	±3.7	3.1	±5.2	
Grey-scale US sum score (0-72)*	Median [IQR]	1	[0;3]	4	[1;8]	<0.01.
	Mean ± SD	2.8	±5.9	6.3	±7.9	
Colour Doppler US sum score (0-36)*	Median [IQR]	0	[0;0]	0	[0;2]	<0.01
	Mean ±SD	1.2	±4.0	2.8	±5.9	
CRP (mg/l)	Median [IQR]	4	[1;16.5]	3	[1.75;12]	0.42
	Mean ± SD	13.4	±23.1	9.6	±14.6	

P, p-value for Mann-Whitney U test for comparing independent data.* US sum score for both hands and feet.

Disclosure of Interests: Mads Ammitzbøll_Danielsen: None declared, Uffe Møller Døhn Speakers bureau: Roche, Lilly, Novartis, Viktoria Fana: None declared, Torsten Møller: None declared, Sin Ngai Ng: None declared, Anne Emilie Secher: None declared, Jens Jørgen Lykkegaard: None declared, Lene Terslev Speakers bureau: Novartis, Pfizer, Roche,

DOI: 10.1136/annrheumdis-2021-eular.713

POS0261 DIAGNOSTIC PERFORMANCE AND CLINICAL UTILITY OF TWO REFERRAL RULES FOR INFLAMMATORY ARTHRITIS

E. Van Delft[1], D. Lopes Barreto[1], A. Van der Helm - van Mil[2,3], C. Alves[4], J. Hazes[3], M. Kuijper[1], A. Weel[1,5]. *[1]Maasstad Hospital, Rheumatology, Rotterdam, Netherlands*; *[2]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[3]Erasmus MC, Rheumatology, Rotterdam, Netherlands*; *[4]ZGT Almelo, Rheumatology, Almelo, Netherlands*; *[5]Erasmus University Rotterdam, Health Technology Assessment, Rotterdam, Netherlands*

Background: The Rotterdam Early Arthritis Cohort (REACH) rule [1] and Clinical Arthritis RulE (CARE) [2] are both evidence-based and easy-to-use methods developed to identify the presence of inflammatory arthritis (IA) in patients suspected by their general practitioner (GP). However, the clinical utility of both models in daily clinical practice in an independent primary care setting has not yet been established. While developed for recognizing IA, we believe that it is also important that the broader spectrum of inflammatory rheumatic diseases (IRDs) is correctly classified from primary care, to facilitate appropriate referral towards outpatient rheumatology clinics.

Objectives: The primary objective was to determine the diagnostic performance and clinical utility of the REACH and CARE referral rules in identifying IA in an independent population of unselected suspected patients from primary care. Secondly we will assess the diagnostic performance and clinical utility of both models in identifying IRDs.

Methods: This prospective observational diagnostic study consisted of adults newly suspected by their GP for the need of referral to the rheumatology outpatient clinic of the Maasstad Hospital in Rotterdam. Primary outcome was IA, consisting of rheumatoid arthritis, axial spondylitis and psoriatic arthritis. Secondary outcome was IRD, defined as IA plus arthritis in systemic disorders such as systemic lupus erythematosus, systemic sclerosis and morbus sjögren. Rheumatologist diagnosis was used as gold standard. To evaluate the clinical performance of the REACH and CARE referral rules in this population, diagnostic accuracy measures were investigated using the Youden index (J) [3]. Moreover, a net benefit approach [4] was used to determine clinical utility of both rules when compared to usual care.

Results: This study consisted of 250 patients (22.8% male) with a mean age of 50.8 years (SD 13.9 years). In total 42 (17%) patients were diagnosed with IA and 55 (22%) with an IRD. Figure 1 presents the diagnostic performance in IA (Figure 1A) and in IRD (Figure 1B). For the primary outcome, the REACH model shows an AUC of 0.72 (95% CI 0.64-0.80) and the optimal cut-off point is indicated (J). The CARE model shows an AUC of 0.82 (95% CI 0.75-0.88) and at J there is a somewhat higher sensitivity and specificity. When taking the broader spectrum of IRDs as outcome, the AUC was 0.66 (95% CI 0.58-0.74) for the REACH and 0.76 (95% CI 0.69-0.83) for the CARE model. The net benefit analysis with either IA or IRD as outcome showed that the CARE was of the highest clinical value when compared to usual care.

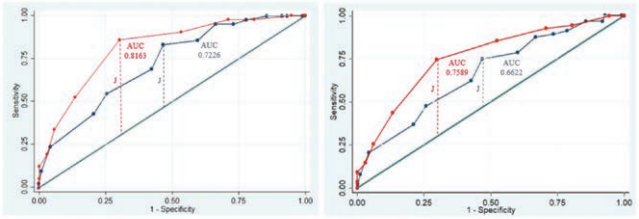


Figure 1: ROC curves; blue lines indicating the REACH model and red lines indicating the CARE model

Conclusion: Both the REACH and CARE model showed a good diagnostic performance for detecting IA in an independent population of unselected suspected patients from primary care. Although not specifically developed to recognize the entire spectrum of IRDs, the CARE shows a good performance in doing so. When evaluating clinical utility, we see that both rules have a net benefit in recognizing IA as well as IRDs compared to usual care, however the CARE shows superiority over the REACH. By using the CARE, over half of all suspected patients can be withheld from expensive outpatient rheumatology care, implied by the high specificity of 70%. These results support the idea that incorporating these easy-to-use methods into primary care could lead to providing patients the right care at the right place and improving value based health care.

REFERENCES:

[1] ten Brinck RM, van Dijk BT, van Steenbergen HW, le Cessie S, Numans ME. Development and validation of a clinical rule for recognition of early inflammatory arthritis. BMJ Open; 2018: 8

[2] Alves, C. Improving early referral of inflammatory arthritis. In *Early detection of patients at risk for rheumatoid arthritis – a challenge for primary and secondary care;* 2015: 27-38 Ridderkerk, the Netherlands.

[3] Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its associated cutoff point. Biom J; 2005: 47(4): 458-472

[4] Vickers AJ, Elkin EB. Decision curve analysis: a novel method for evaluating prediction models. Med Decis Making; 2006: 26(6): 565-574

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1043

POS0262 IDENTIFYING EROSIVE DISEASE FROM RADIOLOGY REPORTS OF VETERANS WITH INFLAMMATORY ARTHRITIS USING NATURAL LANGUAGE PROCESSING

G. Penmetsa[1], S. Pei[1], B. Sauer[1,1], J. A. Walsh[1], B. Feng[2], J. Walker[3], K. Douglas[3], J. Clewell[3]. *[1]1Salt Lake City Veterans Affairs & University of Utah Health., Internal Medicine, Salt Lake City, United States of America*; *[2]University of utah, Dermatology, Salt Lake City, United States of America*; *[3]Abbvie, pharmacy, Salt Lake City, United States of America*

Background: The presence of erosive disease influences diagnosis, management, and prognosis in inflammatory arthritis (IA).Research of IA in large datasets is limited by a lack of methods for identifying erosions.

Objectives: To develop methods for identifying articular erosions in radiology reports from veterans with IA.

Methods: Included veterans had ≥2 ICD codes for ankylosing spondylitis (AS), psoriatic arthritis (PsA), or rheumatoid arthritis (RA) between 2005- 2019, in Veterans Affairs Corporate Data Warehouse. Chart review & annotation of radiology notes produced the reference standard, & identified erosion terms that informed classification rule development. A rule-based natural language processing (NLP) model was created & revised in training snippets. The NLP method was validated in an independent reference sample of IA patients at the snippet & patient levels

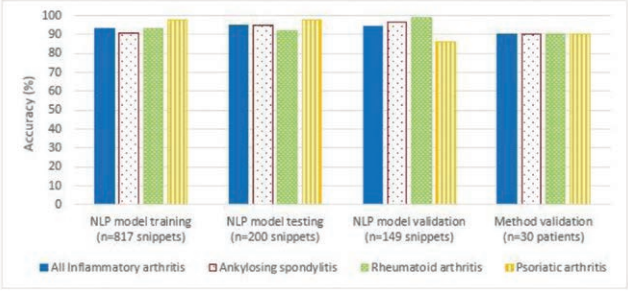
Method development

Step	Description	Number & example
1 Radiology notes		
	a.Select note titles potentially relevant to IA	a. 35,141 notes titles
	b.Extract notes with titles potentially related to IA	b. 2,926,113 radiology notes
2 Possible meaningful terms		
	a.Compile list of root terms that may indicate erosion	a. 11 root terms (i.e. ero*, pencil*cup, irreg*)
	b.Query radiology notes for root term variations	b. 1178 variations (i.e. erosion, erotic, erode)
	c.Select possible meaningful terms	c. 179 possible terms (i.e. erosion, erode)
3 Annotation		
	a.Extract snippets^ containing possible meaningful terms	a.5000 snippets from radiology notes
	b.Classify snippets according to: 1) Meaningful term, 2) Relevance to joint, 3) Attribution to IA, 4) Affirmation	b.4068 classifications with 1017 snippets (in rounds of 50-417 snippets for NLP training & testing)
4 Rule development		
	a.Identify meaningful terms representing erosion	a. 6 terms (pencil * cup, erosion, erosive, etc.)
	b.Exclude erosive processes irrelevant to joint(s)	b. 28 irrelevant processes (i.e. gastric erosion)
	c. Exclude articular erosive processes not attributed to IA	c. 5 non-IA processes IA (i.e. infection)
	d. Classify as affirmed/negated (erosion present/absent)	d. 83 affirmation/negation rules
5 NLP training	Design & revise NLP model until accuracy ≥90%	6 rounds, 817 snippets (AS 417, RA 200, PsA 200)
6 NLP testing	Test NLP model	200 snippets (AS 100, RA 50, PsA 50)
7 Pt classification		
	a. Develop rules for classifying pts with discordant snippets	a. 5 rules developed in 368 pts
	b. Build reference sample (pts classified as erosive or non-erosive via chart review)	b. 30 IA pts (10 AS, 10 RA, 10 PsA)
8 NLP validation	Validate NLP model in reference sample at snippet level	149 snippets (29 AS, 76 RA, 44 PsA)
9 Method validation	Validate methods (NLP+pt classification) at pt level	30 IA pts (reference sample)

pt= patient. ^Snippets include text containing 30 words before & after meaningful terms

Results: In 168,667 veterans with IA, the mean age was 63.1 & 90.3% were male. Method development involved radiology note & erosion term selection, rule development, NLP model building, & method validation. The NLP model accuracy was 94.6% at the snippet level & 90.0% at the patient level, for all IA patients.

Accuracy of methods.



Conclusion: The methods accurately identify erosions from radiology reports of veterans with IA. They may facilitate a broad range of research involving cohort identification & disease severity stratification

REFERENCES:

[1] Walsh JA, et al. J Rheumatol. 2020;47(1):42-49

Disclosure of Interests: Gopi Penmetsa: None declared, Shaobo Pei: None declared, Brian Sauer Grant/research support from: I have been an investigator on research contracts supported by Abbvie., Jessica A. Walsh Consultant of: AbbVie, Amgen, Janssen, Lilly, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Merck, Pfizer, Bingjian Feng Grant/research support from: Bing-Jian Feng reports funding and sponsorship to his institution on his behalf from Pfizer Inc., Regeneron Genetics Center LLC, and Astra Zeneca (UK). The PERCH software, for which Bing-Jian Feng is the inventor, has been non-exclusively licensed to Ambry Genetics for clinical genetic testing services and research., Jodi Walker Shareholder of: Abbvie and mutual funds containing various pharmaceutical companies, Employee of: Abbvie, Kevin Douglas Shareholder of: employed by Abbvie, Employee of: employed by Abbvie, Jerry Clewell Shareholder of: Own Abbvie Shares and mutual funds that hold pharmaceutical and other health care stocks, Employee of: I am current Abbvie Inc employee and past employee of Eli Lilly co

DOI: 10.1136/annrheumdis-2021-eular.1794

POS0263 CLINICAL RELEVANCE OF DFS70 ANTIBODIES – A MULTICENTRE STUDY

A. S. Pinto[1], J. P. Vilas[2], F. Cunha Santos[1,3], M. Cunha[4], B. Samões[5], A. Eduarda Porto Raposo[6], P. Abreu[7], E. Costa[8], N. Madeira[9], J. F. Ferreira[1,10], C. Vaz[1,10]. *[1]Unidade Local de Saúde da Guarda, Serviço de Reumatologia, Guarda, Portugal*; *[2]Baixo Vouga Hospital Centre, Rheumatology Department, Aveiro, Portugal*; *[3]University Hospital Centre of Coimbra, Rheumatology Department, Coimbra, Portugal*; *[4]Garcia de Orta Hospital, Rheumatology Department, Almada, Portugal*; *[5]Vila Nova de Gaia/Espinho Hospital Centre, Rheumatology Department, Vila Nova de Gaia, Portugal*; *[6]Trás-Os-Montes e Alto Douro Hospital Centre, Rheumatology Department, Vila Real, Portugal*; *[7]Local Health Unit of Castelo Branco, Rheumatology Department, Castelo Branco, Portugal*; *[8]Hospital of Braga, Rheumatology Department, Braga, Portugal*; *[9]Portuguese Institute of Rheumatology, Rheumatology Department, Lisboa, Portugal*; *[10]Beira Interior University, Faculty of Health Sciences, Covilhã, Portugal*

Background: Anti-Dense Fine Speckled 70 (DFS70), also known as lens epithelium-derived growth factor (LEDGF) is a common finding when ANA are positive (1.7% in the whole population and 4.6% in the ANA-positive samples). DFS70 antibodies are rare in SARD, especially in the absence of clinical evidence or concomitant anti-extractable nuclear antigen (ENA) antibodies.

Objectives: Our study aimed to understand the meaning of anti-DFS70 antibodies and characterize the clinical and serological features of patients with anti-DFS70 positivity.

Methods: We performed a retrospective observational study of consecutive patients followed up at 9 Portuguese Rheumatology Centres observed from January 2018 until April of 2020 with anti-DFS70 antibodies positivity. Descriptive statistics were presented as mean ± standard deviation if normally distributed or as median and interquartile range if non-normally distributed (continuous variables) or as absolute and relative frequencies (categorical variables). Sensibility and specificity were calculated. Positive and negative predictive values were calculated between patients with and without SARD-specific autoantibodies. Associations between DFS70 with other disease-specific antibody and clinical manifestations were tested using Chi-Square or Fischer's Exact Test, as appropriate.

Results: 120 patients were included, 99 (82.5%) were female with a mean age of 47.8 ± 18.2 years. 96.7% of the patients had ANA titers ≥1:160 (32.5% 1:160; 38.3% 1:320; 16.7% 1:640; 7.5% 1:1280 and 1.7% 1:2560) and 3.3% ANA <1:160.

The main clinical reasons for ANA determination was arthralgia (44.2%), arthritis (11.6%) and Raynaud Phenomenon (RP) (10%). The main analytical reason (7.5%) was an elevation of inflammatory parameters (C-Reactive Protein (CRP) or Erythrocyte Sedimentation Rate (ESR), leukopenia (3.3%) and anaemia (2.5%). Concerning the immunology: 58.3% of patients didn´t have an associated antibody, 9.2% had a positive rheumatoid factor, 5.8% positive ds-DNA, 4.2% histone and 3.3% SS-A. 26 patients had more than one associated antibody.

30 (25%) patients were healthy; 43 (35.8%) patients had Systemic Autoimmune Rheumatic Diseases (SARD) and 47 patients (39.2%) had other diseases (non-SARD). Among patients with a SARD, 16 patients presented an isolated positive anti-DFS70 and 27 patients had other antibodies associated. There was found a positive association with non-SARD and arthralgia (p=0.001) and SARD with arthritis (p<0.001). There was an association with SARD and raised inflammatory parameters (p=0.045), but no association was found with anaemia (p=1.000) or leukopenia (p=0.131). Comparative analysis is described in Table 1, with chi-square or Fischer tests, as appropriated.

The sensitivity of isolated DFS70 was 70.1% and specificity was 62.8%. The positive predictive value was 77.1% and the negative predictive value was 54.0%.

Table 1. Comparative analysis using chi-square or Fischer test

	SARD	Non-SARD	p-value
Arthralgia, n	10	43	0.001
Arthritis, n	14	0	<0.001
Raynaud Phenomenon, n	7	5	0.114
Raised Inflammation parameters, n	6	3	0.045
Anaemia, n	1	2	1.000
Leukopenia, n	3	1	0.131

Conclusion: We concluded that 64.2% of patients with positive DFS70 did not present a SARD and if we only consider patients with isolated anti-DFS70, 77.1% didn´t present a SARD. Therefore, in our study, 22.9% of the patients presented a SARD, which was associated with some clinical features like arthritis or raised inflammatory parameters (p<0.05). Although isolated anti-DFS70 are not specific of a particular condition, our study supports that it can be used as a negative predictor of SARD, if a correlation with clinical and laboratory features is made.

REFERENCES:

[1] Leuchten, N. et al. Performance of Antinuclear Antibodies for Classifying Systemic Lupus Erythematosus: A systematic literature review and meta-regression of diagnostic data. Arthritis Care Res. 70, 428–438 (2018).

[2] Carter JB, Carter S, Saschenbrecker S, Goeckeritz BE (2018) Recognition and relevance of anti-DFS70 autoantibodies in routine antinuclear autoantibodies testing at a community hospital.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1201

POS0264 THE EMERGING ROLE OF MAGNETIC RESONANCE IMAGING IN INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS: EVIDENCE FOR ULTRA SHORT TE AND COMPRESSED SENSING VIBE ACQUISITIONS AS PROMISING TOOLS FOR THE EVALUATION OF PARENCHYMAL ALTERATIONS

N. Landini[1], M. Orlandi[2], M. Occhipinti[3], C. Nardi[3], L. Tofani[2], S. Bellando-Randone[2], C. Bruni[2], M. Matucci-Cerinic[2], G. Morana[1], S. Colagrande[3]. *[1]Ca' Foncello General Hospital, Department of Radiology, Treviso, Italy*; *[2]University of Florence, Department of Experimental and Clinical Medicine, Florence, Italy*; *[3]University of Florence-Azienda Ospedaliero-Universitaria Careggi, Department of Experimental and Clinical Biomedical Sciences, Florence, Italy*

Background: Interstitial lung disease (ILD) is a frequent complication and the major cause of death in Systemic sclerosis (SSc). Computed tomography (CT) is the gold standard imaging technique to assess ILD but is burdened by exposure to ionizing radiations that limits its use for the follow-up. MRI sequences with Ultra Short Echo Time (UTE) are promising for ILD.

Objectives: We tested two MRI sequences, UTE Spiral VIBE and Compressing Sensing (CS) VIBE, in SSc-ILD, in comparison to chest CT.

Methods: SSc patients with suspected-ascertained ILD were evaluated for undergoing CT-MRI examinations in the same day. Two radiologists visually scored the extent of ground glass opacities (GGO), reticulations, honeycombing and consolidations on CT-MRI. The sum of alteration was assumed as ILD extent. A quantitative texture analysis (qCT) was also performed on CT. Cohen's k was adopted for interreader concordance in ILD detection. MRI sensitivity and specificity in ILD detection were evaluated. Lin's concordance was adopted to compare extent analysis between readers and between CT (visual and qCT analysis) and MRI sequences.

Results: 54 patients performed both CT and MRI. MRI interreader concordance was moderate in ILD detection, while ILD and GGO extent analysis showed good or very good concordance. UTE Spiral VIBE had a sensitivity and specificity in ILD detection of 95.8% and 77.8%, while alterations extent analysis obtained a very good concordance with CT for ILD and GGO. CS VIBE showed a sensitivity and specificity in ILD detection of 46.7% and 95.0%, but a slight or fair concordance with CT in all alterations' extent analysis.

Conclusion: MRI UTE Spiral VIBE sequences are helpful in the evaluation of SSc-ILD. Larger cohorts of patients will be needed to confirm that MRI may be useful in clinical practice, reducing the radiological load of chest CT

REFERENCES:

[1] Romei C, Turturici L, Tavanti L, et al. The use of chest magnetic resonance imaging in interstitial lung disease: a systematic review. Eur Respir Rev. 2018;27(150):180062. Doi:10.1183/16000617.0062-2018

[2] Miller GW, Mugler JP, Sá RC, Altes TA, Prisk GK, Hopkins SR. Advances in functional and structural imaging of the human lung using proton MRI. NMR Biomed. 2014;27(12):1542-1556. doi:10.1002/nbm.3156

[3] Pinal-Fernandez I, Pineda-Sanchez V, Pallisa-Nuñez E, et al. Fast 1.5 T chest MRI for the assessment of interstitial lung disease extent secondary to systemic sclerosis. Clin Rheumatol. 2016;35(9):2339-2345. doi:10.1007/s10067-016-3267-0

[4] Ohno Y, Koyama H, Yoshikawa T, et al. Pulmonary high-resolution ultrashort TE MR imaging: Comparison with thin-section standard- and low-dose computed tomography for the assessment of pulmonary parenchyma diseases: Pulmonary MRI with UTE in Pulmonary Disease. J Magn Reson Imaging. 2016;43(2):512-532. doi:10.1002/jmri.25008

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3253

POS0265 CLINICAL AND ULTRASONOGRAPHIC ENTHESITIS IN INFLAMMATORY BOWEL DISEASE WITH AND WITHOUT PSORIASIS

G. Citriniti[1], A. Soriano[2], E. Bertolini[2], G. Sandri[3], A. Bertani[4], I. Tinazzi[5], F. Martinis[1], N. Girolimetto[1], C. Salvarani[1,3], M. Beltrami[2], P. Macchioni[1]. *[1]AUSL-IRCCS Reggio Emilia, Rheumatology Department, Reggio Emilia, Italy*; *[2]AUSL-IRCCS Reggio Emilia, Medicine department, IBD Unit, Reggio Emilia, Italy*; *[3]Rheumatology Unit, University of Modena & Reggio Emilia, Rheumatology Department, Modena, Italy*; *[4]University of Modena & Reggio Emilia, Gastroenterology Department, IBD Unit, Modena, Italy*; *[5]Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy, Rheumatology Unit, Negrar, Italy*

Background: Previous studies have reported an association between psoriasis (PsO) and inflammatory bowel disease (IBD). Coexistence of IBD and PsO has been associated with significant higher prevalence of enthesitis and dactylitis[1].

Objectives: To compare the prevalence of clinical and ultrasonographic peripheral enthesis abnormalities in a consecutive series of patients with IBD and psoriasis (PsO) as compared to a group of IBD patients without psoriasis (IBD).

Methods: One-hundred seventy-four IBD consecutive patients [36 PsO and 138 IBD, M/F 91/83, mean age 42.6±14.7 years, mean disease duration 110 ±12.3 months] entered the study. A complete clinical examination, including rheumatological history, 66/68 peripheral joint count, MASES and LEI scores, BASDAI, and dactylitis count, was performed at study entry. Laboratory test (ESR, CRP, Hb, fecal calprotectin) were collected. Axial or peripheral SpA diagnosis was made using ASAS criteria [2].

US examination was executed by a rheumatologist blind to clinical data, using an Esaote MyLabClass, 18-6MHz linear multifrequence transducer both in B-mode and PD-mode. The following sites were examined bilaterally: lateral epicondyle of the humerus, distal quadriceps femoris insertion into the patella, inferior pole of the patella, tibial distal insertion of the patellar tendon, calcaneal insertion of the Achilles tendon, and plantar aponeurosis insertion. Knee and ankle joints were evaluated for synovial hypertrophy, PD signal and fluid effusion. Enthesitis was defined according to OMERACT [3] and scored as 0-36 for GUESS and 0-136 for MASEI.

Results: PsO patients had later IBD onset (mean age 39±14.7 vs 33 ± 13.2 in IBD group, p=0.02). There weren't observed any significant differences in IBD duration and Crohn/UC prevalence.

No significant difference between the two groups in rheumatological history and clinical examination was detected, except for familiar history of psoriasis (PsO 44% vs IBD 16%, p <0.001). Prevalence of SpA was 33,3% in PsO group and 37% in IBD group (p = 0.687).

146 patients (83.4%) showed structural damage at ≥ 1 enthesis, 44 patients (25%) had at least 1 active enthesitis, with no significant difference between the two groups. PsO group showcased a significantly increased prevalence of patients having ≥ 1 thickened enthesis (86.1% vs 63.9%, p=0.009) and of PD signal at knee examination (11.1% vs 2.2%, p= 0.034). Higher values of GUESS score were observed in PsO (8.1±5.1 vs 5.8±3.9, p=0.017). Enthesis hypoechogenicity was more prevalent in IBD group (27.5% vs 11.1%, p=0.049).

Enthesis thickness was significantly increased in PsO, in every examined site. Enthesophyte length was significantly increased in PsO group at quadriceps tendon, patellar distal insertion and Achilles tendon.

Conclusion: No differences in clinical manifestation and rheumatological history between IBD and PsO patients were observed. Subclinical (US) abnormalities were significantly increased in IBD patients with associated PsO, as compared to patients affected by IBD.

REFERENCES:

[1] Cantini, F. *et al. J. Rheumatol.* **44**, 1341–1346 (2017).

[2] Rudwaleit, M. *et al. Ann. Rheum. Dis.* **68**, 777–783 (2009).

[3] Balint, P. V. *et al. Ann. Rheum. Dis.* **77**, 1730–1735 (2018).

Acknowledgements: Abbvie provided funding for medical writing

Disclosure of Interests: Giorgia Citriniti: None declared, Alessandra Soriano: None declared, Elena Bertolini: None declared, Gilda Sandri: None declared, Angela Bertani: None declared, Ilaria Tinazzi: None declared, Federica Martinis: None declared, Nicolò Girolimetto: None declared, Carlo Salvarani: None declared, Marina Beltrami Grant/research support from: Abbvie provided funding for medical writing, Pierluigi Macchioni: None declared

DOI: 10.1136/annrheumdis-2021-eular.4162

HPR - Understanding and measuring: expanding the toolbox

POS0266-HPR PATIENT-PERCEIVED ASPECTS OF RA FLARE EVOLVE OVER TIME, AS REFLECTED BY THE FLARE-RA QUESTIONNAIRE: POST-HOC ANALYSIS OF TAPERA

M. Doumen[1,2], S. Pazmino[1], D. Bertrand[1], D. De Cock[1], J. Joly[2], R. Westhovens[1,2], P. Verschueren[1,2]on behalf of the TapERA study group. *[1]KU Leuven, Skeletal Biology and Engineering Research Center, Leuven, Belgium*; *[2]University Hospital Leuven, Rheumatology, Leuven, Belgium*

Background: Flares are common in rheumatoid arthritis (RA). While flares negatively impact clinical and patient-reported outcomes, different aspects of disease activity may constitute a flare to patients. Flare Assessment in RA (FLARE-RA) is a patient-reported questionnaire aiming to detect active or recent RA flares (1). During its validation, arthritis and general health subscales were identified and the instrument was adapted from 13 questions (1-6 Likert scale) to 11 questions (0-10).

Objectives: To investigate which patient-perceived aspects of flare are assessed by FLARE-RA in the context of a TNFi-tapering trial, using exploratory factor analysis (EFA).

Methods: Patients with RA in DAS28CRP/ESR-remission (≥6 months) and treated with etanercept 50 mg weekly (≥1 year) were included in the 12-month TapERA (Tapering Etanercept in Rheumatoid Arthritis) trial between 2012 and 2014. Participants completed 3-monthly FLARE-RA questionnaires.

The first and final follow-up visits (M3 & M12) were analyzed. Missing data were imputed with multiple imputation (n = 10). Sampling adequacy was assessed by Kaiser-Meyer-Olkin (KMO) and correlations between variables were evaluated with Bartlett's sphericity test. Spearman correlation matrices were constructed in each of the 10 imputed datasets. The pooled matrix was then analyzed by EFA with principal component extraction and promax-rotation. EFA aims to identify clusters of questions that elicit similar responses because of association with the same underlying latent (not observable) constructs/factors.

Results: Sixty-six patients (68% female) with a mean age of 55 years (SD 13) and a mean disease duration of 14.8 years (SD 9) completed a total of 330 FLARE-RA questionnaires. Sampling adequacy was acceptable (KMO = 0.94) and correlation between items was sufficient for factor analysis ($p < 0.001$).

Table 1 shows the results of EFA in TapERA compared to the validation study (1). Factor loadings indicate how strongly each item correlates with its underlying factor. EFA of the full 13-item FLARE-RA at M3 revealed 3 factors: Arthritis, General health and a Medication factor relating to management of flare. The Arthritis factor explained the largest proportion of variance (31%). EFA at M12 showed the same underlying factors, but a less robust factor structure (cross-loadings >0.3) and a larger proportion of variance explained by the General health factor (33%).

Conclusion: FLARE-RA assessed similar patient-perceived aspects of RA flare within the context of a TNFi-tapering trial when compared to the validation study, including a Medication factor reflecting use of both glucocorticoids and analgesics. This underlines the usefulness of FLARE-RA in providing a multi-faceted view of patients' conceptions of RA flare. However, these aspects and their relative importance do seem to evolve over time. Further research is needed to assess if this is due to the influence of time or specific to the studied population/tapering setting.

REFERENCES:

[1] Fautrel B, et al. Validation of FLARE-RA, a Self-Administered Tool to Detect Recent or Current Rheumatoid Arthritis Flare. Arthritis Rheumatol. 2017;69(2):309–19

Table 1. Factor loadings (>0.3) from exploratory factor analysis of the 13-question FLARE-RA collected in TapERA, compared to results from the FLARE-RA validation study (1). Factors presented in descending order of % variance explained. Q5 & Q7 were removed in the final FLARE-RA.

ITEM	FLARE-RA Validation		TapERA M3			TapERA M12		
	GF	AF	AF	GF	MF	GF	AF	MF
Q1: stiffness	0.33	0.75	0.93				0.73	
Q2: pain	0.47	0.65	0.91				1.00	
Q3: swelling	0.35	0.80	0.92				0.93	
Q4: nocturnal pain	0.39	0.82	0.67				0.76	
Q5: overall	0.39	0.84	0.86				0.86	
Q6: analgesics	0.36	0.81			0.68	0.47		0.51
Q7: glucocorticoids					0.91			0.96
Q8: fatigue	0.68	0.51		0.70		0.87		
Q9: limitation	0.73	0.48	0.30	0.75		0.74		
Q10: irritability	0.85	0.39		0.77		0.69		
Q11: mood	0.83	0.44		0.97		0.79		
Q12: withdrawal	0.90			0.89		1.06		
Q13: needing help	0.81	0.38		0.72		0.60	0.30	
Variance explained (%)	66	10	31	31	12	33	31	10

AF = arthritis factor, GF = general health factor, MF = medication factor

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2003

POS0267-HPR IDENTIFYING MEANINGFUL AND DETECTABLE CHANGE FROM THE PATIENT PERSPECTIVE ACROSS COMMON FATIGUE MEASURES IN RHEUMATOID ARTHRITIS

S. J. Bartlett[1,2], U. Haque3, V. Bykerk[4], J. R. Curtis[5], M. Jones[3], C. Bingham[3]. *[1]McGill University, Clinical Epidemiology & Rheumatology, Montreal, Canada*; *[2]Johns Hopkins Medicine, Rheumatology, Baltimore, United States of America*; *[2]Johns Hopkins Medicine, Rheumatology, Baltimore, United States of America*; *[4]Hospital for Special Surgery, Rheumatology, New York, United States of America*; *[5]University of Alabama at Birmingham, Rheumatology, Birmingham, United States of America*

Background: Different tools are commonly used to assess fatigue in RA including single items (visual analogue (VAS), numeric rating (NRS), and Likert scales), SF-36 Vitality, and PROMIS. Evidence is needed to identify scores that reflect meaningful change to patients to interpret fatigue results in trials and for clinical care.

Objectives: To use symptom-specific and RA change anchors to estimate meaningful and detectable change scores from the patient perspective across several fatigue measures.

Methods: Stable RA patients (ACR/EULAR 2010 criteria) were recruited from 3 academic clinical practices across the Southern, Mid-Atlantic, and Northeastern United States. Scales were administered at 2 consecutive visits to capture PROs including fatigue. We also asked a fatigue-specific change question (*How would*

you rate your fatigue since the last visit?). Response options were a lot better, *a little better, the same, a little worse, and a lot worse*. An RA disease activity change question followed a similar format. We compared mean change between visits across fatigue and RA change categories for the Fatigue NRS, Fatigue 5-point Likert (none to very severe), SF36 Vitality, and PROMIS Fatigue 4a, 7a, and 8a.

Results: The sample included 282 patients with stable RA who completed questionnaires 4.6 (SD 2.4) months apart. Patients were mostly white (78%) women (82%) with RA duration of 13 (11) years. At V1, most were in CDAI LDA (57%) or MDA (30%) with 5% in REM and 8% in HDA states. Using the Fatigue change anchor, 6% were *a lot better*, with mean change ranging from |1-11|points across scales (Table 1); among 13% *a little better*, smaller changes |0.4 to 5|were reported. Across all measures score changes for meaningful and minimal improvement were numerically larger for improvement than worsening.

	Fatigue Change Categories														
	Lot Better 6%			Little Better 13%			Same 49%			Little Worse 22%			Lot Worse 10%		
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD
Fatigue 11 point NRS	19	-2.2	2.4	37	-0.7	2.3	137	-0.5	1.9	61	0.4	1.9	26	1.3	2.1
Fatigue 5-point Likert	19	-0.8	1.2	36	-0.4	1.2	137	0.0	0.9	60	0.2	0.9	27	0.6	1.2
SF36 Vitality (0-100)	19	11.2	16.1	36	4.9	13.7	137	0.3	10.6	59	-3.2	15.3	26	-11.4	16.6
PROMIS Fatigue 7a	19	-5.9	8.5	37	-2.6	7.5	138	0.0	6.4	62	-0.3	6.5	27	4.3	8.3
PROMIS Fatigue 8a	19	-6.1	10.2	37	-2.7	7.1	138	-0.3	7.1	62	1.3	6.9	27	5.6	11.0
PROMIS Fatigue 4a	19	-6.8	9.9	37	-3.3	8.2	138	-0.4	7.4	60	1.2	7.2	27	5.2	11.5

Using the RA change categories, more people rated their RA as at least *a little better* compared with fatigue (28% vs. 19%, respectively) at the second visit (Table 2). Similar patterns were evident across RA change categories, though score changes associated with improvement and worsening were about half those observed using fatigue change anchors.

	RA Disease Activity Change Categories														
	Lot Better 13%			Little Better 15%			Same 42%			Little Worse 21%			Lot Worse 9%		
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD
Fatigue 11 point NRS	36	-0.8	2.3	43	-0.6	2.7	117	-0.2	1.9	58	-0.2	1.9	26	0.7	2.2
Fatigue 5-point Likert	35	-0.3	1.2	42	-0.3	1.1	118	0.1	1.0	58	0.1	0.8	26	0.3	1.3
SF36 Vitality (0-100)	35	6.4	17.4	43	3.8	13.0	117	-0.6	12.9	57	-3.7	11.3	25	-6.0	17.0
PROMIS Fatigue 7a	37	-1.6	9.5	43	-1.5	7.4	118	-0.3	7.0	59	0.5	5.6	26	1.3	7.5
PROMIS Fatigue 8a	37	-2.1	9.5	43	-1.7	9.0	118	0.1	7.6	59	0.7	4.8	26	3.0	11.4
PROMIS Fatigue 4a	36	-2.7	9.6	43	-2.3	9.0	118	0.1	8.1	59	0.4	5.6	25	2.6	12.0

Conclusion: The score change associated with meaningful improvement and worsening between visits on commonly used fatigue scales was much larger with fatigue vs. RA change categories. More people rated their RA improved as compared with fatigue at the 2nd visit. Symptom-specific anchors are likely to offer more relevant change scores associated with meaningful improvement and worsening than RA change anchors. These estimates offer new information about meaningful and detectable improvement and worsening on common measures for trialists, researchers, and clinicians monitoring fatigue in people with RA.

Acknowledgements: The primary research data included within this report were acquired through funding in part from a PCORI Methods Award (SC14-1402-10818). This work was also supported by the NIH through the Rheumatic Diseases Resource-based Core Center (P30-AR053503 Core D, and P30-AR070254, Core B), the Camille Julia Morgan Arthritis Research and Education Fund, and the Rheumatoid Arthritis Discovery Fund.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3999

POS0268-HPR PATIENT-REPORTED ACTIVITY LIMITATIONS IN HIP AND KNEE OSTEOARTHRITIS IN PRIMARY CARE

T. Moseng[1], H. Solveig Dagfinrud[1], B. Natvig[2], N. Osteras[1]. [1]*Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Department of Rheumatology, Oslo, Norway*; [2]*University of Oslo, Institute of Health and Society, Department of General Practice, Oslo, Norway*

Background: To ensure delivery of high-quality osteoarthritis (OA) care, structured care models incorporating patient education and exercise are increasingly implemented in primary care [1]. A goal is to improve patients' physical function and coping with daily life demands and activities. Yet, there is limited knowledge regarding the type and severity of activity limitations experienced by people with hip and knee OA.

Objectives: 1) To map activity limitations reported by patients with hip and knee OA participating in a research study implementing an OA care model in primary care. 2) To investigate potential changes in self-reported difficulty performing these activities from baseline to 12-weeks follow-up.

Methods: A structured OA care model was implemented in six Norwegian municipalities between January 2015 and October 2017, using a stepped-wedge cluster-randomized controlled design. Implementation was facilitated by interactive workshops for general practitioners and physiotherapists (PTs). The PTs provided a 3-hour, group-based patient education program followed by individually tailored 8-12 weeks exercise with twice weekly 1-hour supervised group sessions. Patients with clinically or radiologically verified symptomatic hip or knee OA ≥45 years were eligible. Patients who received the new model of care completed the Patient-Specific Functional Scale (PSFS) at baseline by identifying between one and three "important activities that you are unable to do or are having difficulty with because of your hip or knee OA". The patients rated their performance of the reported activities on an 11-point numeric rating scale (NRS) ranging from 0 (unable to perform activity) to 10 (perform activity with no problems). After 12 weeks the patients re-rated their previously identified activities. The reported activities were linked to the International Classification of Functioning, Disability and Health (ICF) at Chapter and Domain (second and third) level. Absolute change in scores from baseline to follow-up was calculated as the mean score of the reported activities. Change from baseline to follow-up was investigated using paired samples t-test. P-value was set to <0.05. Clinically important change was regarded 2 points on the 0-10 scale.

Results: A total of 284 patients received the new model of care. The mean age was 63 (SD 10) years, and 211 (74%) were female. The main affected OA joint was the knee for 174 (61%), the hip for 100 (35%) and other joints (e.g. hand) for 9 (3%). The PSFS was completed by 152 (53%) patients, of which 13 reported one, 42 reported two and 97 reported three activities. A total of 382 activities were linked with ICF. Of these, 362 (95%) were linked to the Activities and Participation chapter (D). On second-level, 318 (83%) activities were linked to the Mobility domain (D4). On the third-level, the majority of activities were linked to the domains Changing body positions (d410) (26%), Walking (d450) (23%) and Moving around (d455) (25%). The patients reported significantly less difficulty performing their self-reported activities at 12 week follow-up (4.1 (SD 1.7) versus 6.3 (SD 1.8), mean change 2.1 (95% CI 1.8, 2.5), p<0.001).

Conclusion: The majority of activity limitations reported by patients receiving a structured OA care model in primary care were within the ICF Mobility domain. The most common third-level ICF domains were Changing body positions, Walking and Moving around. After participating in OA patient education and structured 8-12 weeks of exercise, the patients reported a statistically significant and clinically important improvement in the difficulty of performing their individual activities.

REFERENCES:

[1] Allen KD, Choong PF, Davis AM, et al. Osteoarthritis: Models for appropriate care across the disease continuum. *Best practice & research. Clinical rheumatology.* 2016;30(3):503-535.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2023

POS0269-HPR CONTENT VALIDITY OF A MULTIPLE LANGUAGES QUESTIONNAIRE FOR MEASURING FLARE IN KNEE AND HIP OA: DEVELOPMENT OF THE FLARE-OA

F. Guillemin[1], A. Barcenilla-Wong[2], M. Vitaloni[3], L. Adarmouch[4], M. T. Duruöz[5], J. Epstein[6], M. Sebbani[4], Y. Traore[6], C. Rutherford[7], M. Cross[2], B. Fautrel[8], T. Buttel[9], G. A. Hawker[10], L. March[2], D. Hunter[2], E. Spitz[1]on behalf of OMERACT Flares in OA. *[1]Université de lorraine, EA 4360 APEMAC, Metz, France*; *[2]North Shore Private Hospital, Rheumatology, St Leonards, Australia*; *[3]OAFI Foundation (Osteoarthritis Foundation International), General, Barcelona, Spain*; *[4]Université de Marrakech, Public Health, Marrakech, Morocco*; *[5]Marmara University, Rheumatology, Istambul, Turkey*; *[6]Université de Lorraine, School of Public Health, Nancy, France*; *[7]University of Sydney, Faculty of Science, School of Psychology, Sydney, Australia*; *[8]Assistance Publique – Hôpitaux de Paris, Rheumatology, Paris, France*; *[9]OMERACT, Rheumatology, Sydney, Australia*; *[10]University of Toronto - St. George Campus, Rheumatology, Toronto, Canada*

Background: Flare in osteoarthritis (OA) of the knee and hip (KHOA) is an important outcome for patients' daily life and clinical research. A definition of a flare was set, and a core set of domains was recently endorsed by OMERACT/OARSI. No patient reported outcome (PRO) yet focusses on flare in OA specifically.

Objectives: To develop a self-reporting instrument measuring flare in 5 languages, using qualitative methods and international Delphi consensus.

Methods: We generated items using a dual-language (English and French) approach involving patients with OA from Australia, France and the United States and health care professionals (HCP) from international societies (OARSI, SFR, OMERACT). Item generation relied on semi-structured individual interviews conducted with OA patients and HCP and one focus group with patients. Content analysis allowed for identifying verbatim statements that were meaningful for patients and HCP. A Delphi consensus method was used to select the most relevant items, according to core domains set (OMERACT). A cross-cultural approach using current guidelines (1) was applied to produce Spanish (in Spain), Turkish and classical Arabic (in Morocco) versions using independent translation and expert committee to preserve its content validity.

Results: From semi-structured interviews with 29 patients and 16 HCPs and one focus group with 10 patients, 180 statements in French (106) and English (77) were generated. Based on similarity or redundancy, 50 items with equivalent meaning in both languages were retained by an expert committee. After two Delphi rounds involving 50 patients and 116 HCPs from 17 countries on four continents, it was reduced to 33 items (response 0=not at all, to 10=absolutely) in five domains (pain, swelling, stiffness, consequences of symptoms and psychological aspects). This questionnaire was cross-culturally adapted into Spanish, Turkish and classical Arabic. The Spanish version uncovered one inappropriate item in the original questionnaire that was amended accordingly in all 5 languages.

Conclusion: Flare is more than just an exacerbation of pain. The Flare-OA questionnaire includes all OMERACT recommended core domains. High content validity was seen in 2 original and 3 cross-culturally adapted languages. The Flare-OA should be considered as fit for purpose and evaluation of responsiveness in clinical studies in 5 languages.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3870

POS0270-HPR FLARE-OA QUESTIONNAIRE TO MEASURE FLARES IN OSTEOARTHRITIS OF THE KNEE AND HIP: ASSESSMENT OF ITS PSYCHOMETRIC PROPERTIES

Y. Traore[1], J. Epstein[1,2], E. Spitz[2], L. March[3,4], J. F. Maillefert[5], C. Rutherford[6,7], C. Ricatte[2], C. Alleyrat[1], M. Cross[3,4], L. King[8], L. Callahan[9], B. Fautrel[10,11], T. Buttel[3], G. A. Hawker[8], D. Hunter[3,4], F. Guillemin[1,2]. *[1]CHRU Nancy, CIC 1433 EC, Nancy, France*; *[2]Université de Lorraine, EA 4360 APEMAC, Nancy, France*; *[3]University of Sydney, Institute of Bone and Joint Research, Kolling Institute, Sydney, Australia*; *[4]Royal North Shore Hospital, Rheumatology Department, Sydney, Australia*; *[5]Dijon University Hospital, Department of Rheumatology, Dijon, France*; *[6]University of Sydney, Faculty of Science, School of Psychology, Sydney, Australia*; *[7]University of Sydney, Faculty of Medicine and Health, Sydney Nursing School, Sydney, Australia*; *[8]University of Toronto, Department of Medicine, Toronto, Canada*; *[9]University of North Carolina, Thurston Arthritis Research Center, Chapel Hill, United States of America*; *[10]Sorbonne Université – Assistance Publique Hôpitaux de Paris, Rheumatology Department Pitié-Salpêtrière Hospital, Paris, France*; *[11]Institut Pierre Louis d'Epidémiologie et Santé Publique, INSERM UMR-S 1136, Paris, France*

Background: Hip and knee OA is characterised by disease flares – understanding the determinants and consequences of OA flares has been hampered by lack of a standardized flare measure beyond the pain aspect. The patients point of view on the different aspect of their flares is essential.

Objectives: The objective was to assess the psychometric properties of a new questionnaire for measuring the multidimensional aspect of flares in OA.

Methods: Using a bilingual version of the questionnaire (33 items, response on a numeric scale, from 0 to 10), a multicentre survey (Australia, France and United States) was conducted on line with patients diagnosed with OA of the hip and/or the knee. Based on an international OMERACT/OARSI endorsed definition of the five core domains (pain, swelling, stiffness, consequences of symptoms and psychological aspects) composing a flare in OA [1], a confirmatory factorial analysis linked to the content analysis has been used to reduce the number of items and to determine the validity of the structure. The Flare-OA questionnaire (score from 0 to 100) has been tested in French and English for its internal consistency, its convergent validity with HOOS/KOOS and Mini-OAKHQOL questionnaires, and its discriminant validity.

Results: Out of 398 patients (mean age 64 years old) who completed the questionnaire, 70.4% were female and 86.7% had knee OA. The confirmatory factorial analysis retained a model with 19 items (RMSEA =0.06; SRMR =0.04; CFI =0.96 and TLI = 0.94). The Cronbach Alpha was > 0.9 for the 5 domains and for the whole questionnaire. The correlations between the Flare-OA and the other instruments were in line with that hypothesis flare is related but different from other concepts usually measured. The discriminant validity was evidenced by a significant score difference (31.8; p<0,0001) between patients with and without flare, i.e. over twice the standard measurement error.

Conclusion: The optimized Flare-OA questionnaire (19 items) is a reliable and valid instrument freely available from the authors for measuring the frequency and severity of flare in knee and hip OA in clinical research.

REFERENCES:

[1] King LK, Epstein J, Cross M, et al. Establishing the Domains of Knee and Hip Osteoarthritis (OA) Flare: A Report from the OMERACT 2020 Inaugural Virtual Consensus Vote from the Flares in OA Working Group. (Submitted)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3799

POS0271-HPR

PATIENT PERSPECTIVE ON A DRUG SAFETY MONITORING SYSTEM FOR IMMUNE-MEDIATED INFLAMMATORY DISEASES BASED ON PATIENT-REPORTED OUTCOMES

L. Kosse[1], G. Weits[1], H. Vonkeman[2,3], S. Tas[4], F. Hoentjen[5], M. Van Doorn[6], P. Spuls[7], G. D'haens[8], M. Nurmohamed[9], E. Van Puijenbroek[10,11], B. Van den Bemt[12,13], N. Jessurun[1]. *[1]Netherlands Pharmacovigilance Centre Lareb, Monitoring, 's-Hertogenbosch, Netherlands*; *[2]Medisch Spectrum Twente, Rheumatology, Enschede, Netherlands*; *[3]University of Twente, Psychology, Health & Technology, Enschede, Netherlands*; *[4]Amsterdam UMC, location Academic Medical Center, University of Amsterdam, Amsterdam Infection & Immunity Institute and Amsterdam Rheumatology & Immunology Center (ARC), Rheumatology & Clinical Immunology, Amsterdam, Netherlands*; *[5]Radboudumc, Gastroenterology, Nijmegen, Netherlands*; *[6]Erasmus MC, Dermatology, Rotterdam, Netherlands*; *[7]Amsterdam UMC, Amsterdam Public Health, Immunity and Infections, University of Amsterdam, Dermatology, Amsterdam, Netherlands*; *[8]Amsterdam UMC, location Academic Medical Center, University of Amsterdam, Gastroenterology, Amsterdam, Netherlands*; *[9]Reade and Amsterdam Rheumatology & Immunology Center (ARC), Rheumatology, Amsterdam, Netherlands*; *[10]Netherlands Pharmacovigilance Centre Lareb, Signal detection, 's-Hertogenbosch, Netherlands*; *[11]University of Groningen, Groningen Research Institute of Pharmacy, PharmacoTherapy, Epidemiology & Pharmacoeconomics, Groningen, Netherlands*; *[12]Radboudumc, Pharmacy, Nijmegen, Netherlands*; *[13]Sint Maartenskliniek, Pharmacy, Ubbergen, Netherlands*

Background: Patient-reported outcomes (PROs) on adverse drug reactions (ADRs) are increasingly used in cohort event monitoring (CEM) to obtain a better understanding of patient's real-world experience with drugs. Despite the leading role for patients, little is known about their perspectives on these monitoring systems.

Objectives: To obtain more insight in patients' perspectives on the perceived usefulness, ease of use and attitude toward using the Dutch Biologic Monitor (DBM), and their preferred design for a national drug safety monitoring system for immune-mediated inflammatory diseases (IMIDs).

Methods: We developed a cross-sectional open survey following the rationale of the Technology Acceptance Model to obtain insight in patients' perspectives on the DBM. The DBM is a pilot for a PRO-based drug safety monitoring system focused on ADRs attributed to biologics that are prescribed for IMIDs. This survey consisted of 20 categorical and 1 open-ended question. Seven categorical questions contained a text field for additional comments. Five-point Likert-type scales or multiple-choice questions were used to identify patients' preferences and perspectives. Patients were eligible for the survey if they were still enrolled in the DBM at the time of the survey opening and if they had completed at least one questionnaire of the DBM. Categorical questions were descriptively analyzed, whereas text fields were analyzed using theoretical thematic analysis.

Results: At the start of the survey a total of 1,225 patients had participated in the DBM. Approximately 70% had an inflammatory rheumatic disease. The survey was completed by 292 eligible respondents (response rate 44.8%). The respondents generally agreed that it was useful to participate in the DBM and would recommend it to their peers (Figure 1). The response burden of the bimonthly questionnaires was scored as 'low', irrespective of the presence of ADRs or education level (Table 1). A number of respondents suggested that the questionnaire frequency should be synchronized with the regular hospital visits or the administration schedule of the biologic. Moreover, questionnaires should be offered less frequent and preferably shortened in case of an unaltered situation or absence of ADRs. Half (49.0%) of the respondents was interested in sharing their questionnaires with a medical specialist, whereas a third (34.2%) advocated sharing the questionnaires with their pharmacist (Figure 1).

Table 1. Perceived response burden of the Dutch Biologic Monitor questionnaires. The average burden is calculated using a five-point Likert-type scale. Data is represented as the number of respondents (n).

			ADRs reported						Education level[a]			
	Overall (n = 292)		Yes (n = 225)		No (n = 54)		Do not know (n = 13)		Lower (n = 149)		Higher (n = 139)	
Burden	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
1: No burden	224	(76.7)	169	(75.1)	46	(85.2)	9	(69.2)	106	(71.1)	115	(82.7)
2: Low burden	58	(19.9)	48	(21.3)	7	(13.0)	3	(23.1)	36	(24.2)	22	(15.8)
3: Moderate burden	6	(2.1)	6	(2.7)	0	(0.0)	0	(0.0)	4	(2.7)	2	(1.4)
4: High burden	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
5: Very high burden	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
No opinion	4	(1.4)	2	(0.9)	1	(1.9)	1	(0.0)	3	(2.0)	0	(0.0)
Average burden	1.2		1.3		1.1		1.2		1.3		1.2	

[a]Missing: 4 respondents.

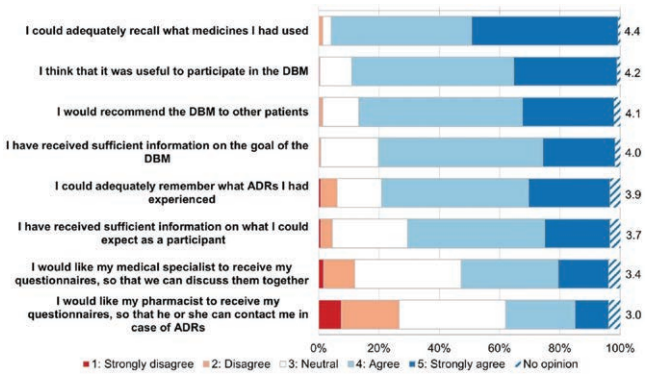


Figure 1. Stacked bar graph of user perspectives. Agreement scores were measured using a five-point Likert-type scale. The average agreement score per statement is indicated on the far right. The percentages represent the share of respondents. DBM: Dutch Biologic Monitor; ADRs: adverse drug reactions.

Conclusion: This study provides valuable insights in the patient perspective on a PRO-based drug safety monitoring system for inflammatory rheumatic diseases and other IMIDs, and provides several useful starting points to further stimulate and improve PRO-based CEM systems. Altogether, it appears feasible to establish a PRO-based drug safety monitoring system that monitors IMID patients' real-world experience with ADRs that has a low burden for the participants.

Disclosure of Interests: Leanne Kosse: None declared, Gerda Weits: None declared, Harald Vonkeman Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Celltrion, Galapagos, Gilead, GSK, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi-Genzyme, all outside the submitted work., Sander Tas Grant/research support from: AbbVie, Arthrogen, AstraZeneca, BMS, Celgene, Galapagos, GSK, MSD, Pfizer, Roche, Sanofi-Genzyme, all outside the submitted work., Frank Hoentjen Speakers bureau: Abbvie, Janssen-Cilag, MSD, Takeda, Celltrion, Teva, Sandoz and Dr Falk, all outside the submitted work, Consultant of: Celgene, Janssen-Cilag, all outside the submitted work, Grant/research support from: Dr Falk, Janssen-Cilag, Abbvie, Takeda, all outside the submitted work, Martijn van Doorn Grant/research support from: Leopharma, Novartis, Abbvie, BMS, Celgene, Lilly, MSD, Pfizer, Sanofi-Genzyme, Janssen Cilag, outside the submitted work., Phyllis Spuls Grant/research support from: Departmental independent research grant for TREAT NL registry from different companies, is involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of e.g. psoriasis and atopic dermatitis, for which financial compensation is paid to the department/hospital and, is Chief Investigator (CI) of the systemic and phototherapy atopic eczema registry (TREAT NL) for adults and children and one of the main investigators of the SECURE-AD registry, all outside the submitted work., Geert D'Haens Consultant of: Abbvie, Ablynx, Active Biotech AB, Agomab Therapeutics, Allergan, Alphabiomics, Amakem, Amgen, AM Pharma, Applied Molecular Therapeutics, Arena Pharmaceuticals, AstraZeneca, Avaxia, Biogen, Bristol Meiers Squibb/Celgene, Boehringer Ingelheim, Celltrion, Cosmo, DSM Pharma, Echo Pharmaceuticals, Eli Lilly, Engene, Exeliom Biosciences, Ferring, DrFALK Pharma, Galapagos, Genentech/Roche, Gilead, Glaxo Smith Kline, Gossamerbio, Pfizer, Immunic, Johnson and Johnson, Kintai Therapeutics, Lycera, Medimetrics, Takeda, Medtronic, Mitsubishi Pharma, Merck Sharp Dome, Mundipharma, Nextbiotics, Novonordisk, Otsuka, Photopill, ProciseDx, Prodigest, Prometheus laboratories/Nestle, Progenity, Protagonist, RedHill, Robarts Clinical Trials, Salix, Samsung Bioepis, Sandoz, Seres/Nestec/Nestle, Setpoint, Shire, Teva, Tigenix, Tillotts, Topivert, Versant and Vifor, all outside the submitted work, Michael Nurmohamed Speakers bureau: AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, Sanofi, all outside the submitted work, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Roche, Sanofi, all outside the submitted work, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Mundipharma, Novartis, Pfizer, Roche, Sanofi, all outside the submitted work, Eugène van Puijenbroek: None declared, Bart van den Bemt: None declared, Naomi Jessurun: None declared

DOI: 10.1136/annrheumdis-2021-eular.635

POS0272-HPR

POOR RESPONSE TO TKA: THE PERSPECTIVE OF PATIENTS AND KNEE SPECIALISTS

M. Te Molder[1], J. Vriezekolk2, J. M. H. Smolders[3], S. Van Onsem[4,5], P. Heesterbeek[2], C. Van den Ende[2]. *[1]Sint Maartenskliniek, Research Department, Nijmegen, Netherlands*; *[1]Sint Maartenskliniek, Research Department, Nijmegen, Netherlands*; *[3]Sint Maartenskliniek, Department of Orthopedics, Nijmegen, Netherlands*; *[4]AZ Alma, Department of Orthopaedics*

and Traumatology, Eeklo, Belgium; [5]*Ghent University, Department of Human Structure and Repair, Ghent, Belgium*

Background: Although most of the patients after total knee replacement (TKA) report very satisfied outcome scores, there is still a significant proportion of patients that experience persistent knee pain, functional disability or dissatisfaction after TKA because of osteoarthritis (OA). It is difficult to quantify the proportion of patients with poor response to TKA, as different definitions on failure are being used (1). Additionally, patients and surgeons only agree in 36% on failure of total joint replacement (TJR) (2). This may be caused by different perceptions about concepts underlying poor response to TKA.
Objectives: To explore if patients and knee specialists have different views about relevant concepts reflecting poor response to primary TKA.
Methods: A qualitative, multicentre study was performed using semi-structured interviews in Belgium and in the Netherlands. Purposive sampling was used to enrich data variation. Twenty-five patients with knee OA without surgical indications (N=2), pre- and postoperative patients (N=11 and N=12, respectively) and fifteen knee specialists (orthopedic surgeons (N=9), physician assistants (N=1), nurse practitioners (N=1) and specialized physiotherapists (N=4)) were interviewed individually. Conversations were audiotaped, transcribed verbatim, and analysed using a thematic analysis.
Results: Concepts underlying poor response to TKA were: persistent pain, limited knee function, limitations in physical functioning, complications, unmet expectations, unexpected sequelae and dissatisfaction (Figure 1). The concepts persistent pain, limited knee functioning, complications and limited physical functioning were found to underly expectations and/or unexpected sequelae after TKA. Dissatisfaction was considered a overarching concept resulting from unmet expectations and/or unexpected sequelae after TKA (e.g. long-term use of pain medication, continuous awareness of the prosthesis). All seven concepts were identified by both patients and knee specialists although poor knee function was more often described by patients in terms of prosthesis awareness, whereas knee specialists described poor knee function in terms of instability.
Conclusion: Patients and knee specialists identified similar concepts as relevant concepts reflecting poor response to TKA. These results will be used to formulate a uniform definition of poor response to TKA.
REFERENCES:

[1] Te Molder MEM, Smolders JMH, Heesterbeek PJC, Van Den Ende CHM. Definitions of poor outcome after total knee arthroplasty: An inventory review. BMC Musculoskelet Disord. 2020;21(1):1–6.
[2] Singh J, Mehta B, Mirza S, Figgie M, Sculco P, Parks M, et al. When has a knee or hip replacement failed? A patient perspective. J Rheumatol. 2019;47(9):1–18.

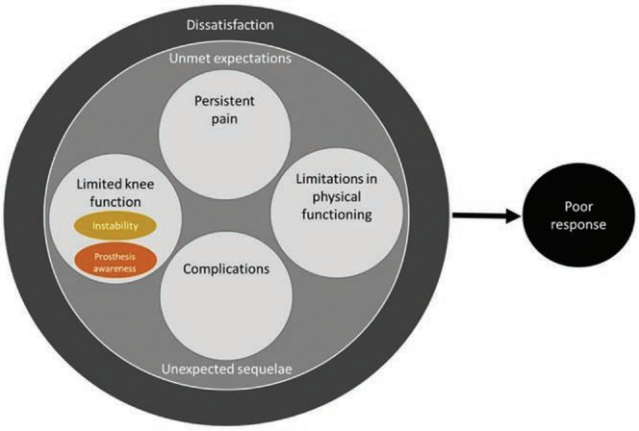


Figure 1. Relevant concepts reflecting poor response to TKA according to the patients' and knee specialists perspectives. Concepts in solid gray were relevant to both, prosthesis awareness was relevant to patients and instability was identified as important outcome by knee specialists.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2572

POS0273-HPR PHARMACIST'S IMPACT ON SELF-MANAGEMENT FOR PATIENTS WITH CHRONIC INFLAMMATORY ARTHRITIS TREATED WITH BIOLOGICAL DMARDS

C. Bottois[1], C. López-Medina[2], S. Dumas[1], H. Julien[1], B. Sephora[1], C. Roux[2], A. Moltó[2], O. Conort[1], M. Dougados[2]. [1]*Hôpitaux Universitaire Paris Centre - Site Cochin, Clinical Pharmacy, Paris, France*; [2]*Hôpitaux Universitaire Paris Centre - Site Cochin, Rheumatology, Paris, France*

Background: Knowledge about chronic inflammatory rheumatisc diseases and skills to administer and manage subcutaneous (subcut) biological DMARDs (bDMARDs) are key aspects to optimize patient's self-management. Intervention of several successive health professionals (e.g comprehensive multidisciplinary team) has proven to be an effective method to improve patient's self-management of their disease and treatment.
Objectives: To assess the pharmacist's impact on patient's knowledge and skills during a multidisciplinary annual review. The secondary objectives were to assess this impact on therapeutic adherence and patient's satisfaction as well as to determine the factors associated with the level of knowledge at baseline.
Methods: Study type: prospective, monocentric, 6 months-follow-up, non-controlled study approved by Local Ethical Committee. Inclusion criteria: patient with either rheumatoid arthritis (RA) or spondyloarthritis (SpA), and treated with subcut bDMARDs. Intervention: The visit with a pharmacist evaluating and discussing patient's knowledge and treatment adherence. At baseline (M0): date of the visit and, 3 (M3) and 6 months (M6) later, knowledge and adherence were assessed using self-administered questionnaires: Biosecure and CQR-5 respectively. A questionnaire was sent at M3 in order to evaluate the patient satisfaction. Endpoints: Primary: Changes in Biosecure score Secondary: Percentage of patients with high level of knowledge (score > 84) and percentage of patients with high adherence at M3 and M6; patient's satisfaction; identification of patient's factors (socio-demographics, rheumatisc disease treatments) associated with different levels of knowledge at baseline.
Statistical analysis: repeated measures ANOVA, Bonferroni and Generalized Estimating Equation, univariate and multivariate linear regression.
Results: The study was conducted from October 2019 to July 2020; 79 patients were included (age (years) = 50±15; sex ratio = 1.1; RA=25, SpA=54). The Biosecure scores changed from 71±18 to 82±15 (M3) and to 84±14 (M6) ($p<0.001$). At M0, M3 and M6, the rate of patients with a high level of knowledge was 24.1%, 59.5% and 63.3% respectively ($p<0.001$). No difference was observed for the change in the 92% of patients considered as high adherent (92% versus 95% at M0 and M6 respectively; $p=0.077$). Patient's satisfaction regarding the pharmaceutical intervention was 25±3 (max = 28).
Factors associated with a better Biosecure score in the multivariate analysis were the following, lifestyle as a couple ($p<0.001$), information given by a nurse ($p=0.033$), information searched for on patient associations ($p=0.013$) and a low Charlson score ($p=0.001$)
Conclusion: Pharmacist's intervention in the comprehensive multidisciplinary annual review resulted in a beneficial impact on patients' knowledge and skills to manage their bDMARDs with a high level of satisfaction from a patient perspective.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2135

POS0274-HPR BARRIERS TO PHYSICAL ACTIVITY COLLECTED BY THE IFAB QUESTIONNAIRE CORRELATE WITH LEVELS OF PHYSICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS OR SPONDYLOARTHRITIS: A CROSS-SECTIONAL STUDY OF 150 PATIENTS

T. Davergne[1], R. Tekaya[2], C. Deprouw[3], J. Sellam[3], A. Tournadre[4], S. Mitrovic[5], A. Ruyssen-Witrand[6], C. Hudry[7], S. Dadoun[8], J. Avouac[9], B. Fautrel[10], L. Gossec[10]. [1]*Sorbonne Université, INSERM, Institut Pierre Louis d'Épidémiologie et de Santé Publique, PEPITES, Paris, France*; [2]*Hôpital Charles Nicolle, University of Tunis El Manar, Rheumatology Department, Tunis, Tunisia*; [3]*Saint-Antoine hospital, Rheumatology Department, Paris, France*; [4]*Clermont Ferrand hospital, University of Clermont, Rheumatology Department, Clermont Ferrand, France*; [5]*Institut Mutualiste Montsouris, Internal Medicine Department, Paris, France*; [6]*Purpan hospital, Rheumatology Department, Toulouse, France*; [7]*CeSOA, MGEN, Paris, France*; [8]*Clinique Geoffroy Saint Hilaire, Ramsay, Paris, France*; [9]*Université de Paris, Cochin hospital, Rheumatology Department, Paris, France*; [10]*Pitié Salpêtrière hospital, APHP, Rheumatology Department, Paris, France*

Background: Physical activity is important for patients with inflammatory arthritis (IA), such as spondyloarthritis (axSpA), rheumatoid arthritis (RA) or psoriatic arthritis (PsA). They are more prone to physical inactivity but derive specific benefits from regular physical activity (1,2). It is not easy to modify physical activity level (3). Barriers and facilitators to physical activity can be assessed through questionnaires (4), however, it is important to demonstrate a link between these explanatory elements and physical activity levels.
Objectives: To measure the correlation between barriers and facilitators to physical activity, assessed through a simple questionnaire, and self-reported physical activity levels.

Methods: This was an international, multicentric, cross-sectional study performed between October 2019 and June 2020 (ClinicalTrial NCT04426747). Consecutive patients were included if they had definite axSpA, RA or PsA, were aged above 18 and able to walk. Barriers and facilitators to physical activity were measured using the 10-item Inflammatory arthritis Facilitators and barriers questionnaire (IFAB) (5). The IFAB ranges -70 to 70 with lower scores indicating more barriers; scores below -5 correspond to significant barriers. Physical activity was measured by the IPAQ-S questionnaire (6). Exploratory analyses used steps per day collected by smartphone, and psychological readiness to change by stages of behavior change. Statistical analysis used Spearman correlation (rho, p<0.05), Student T test or multivariate analysis using R version 3.5.1. There was no imputation of missing data.
Results: Of 245 patients included, 150 had analysable data (69 (46%) axSpA, 63 (42%) RA, 18 (12%) PsA). Mean age was 48.6 years (SD 17.1), mean disease duration 11.7 (10.1) years and 60% were women. The mean score of barriers and facilitators to physical activity was 6.0 (SD 19.2, median 4) (Figure 1). A total of 39 (26%) patients scored less than -5, which could justify a targeted intervention. The mean physical activity was 2837 (SD 2668, median 1784) Metabolic Equivalent of Task min per week. Physical activity was correlated with score of barriers and facilitators to physical activity in linear regression (rho 0.28, p<0.001), as well as the stage of behavior change regarding active lifestyle (rho 0.35, p<0.001). No correlation was observed with steps per day (Table 1)
Conclusion: Perceived barriers and facilitators to physical activity are correlated with physical activity. Targeting patients with high barriers and low facilitators to physical activity could be an effective option to improve physical activity levels.
REFERENCES:
[1] O'DWYER T., et al. *Rheumatology* 2014. Vol. 53, n° 10, pp. 1812-1817.
[2] OSTHOFF, A et al. 2018. Vol. 77, n° 9, pp. 1251-1260. DOI 10.1136/annrheumdis-2018-213585.
[3] MARLEY, J, et al: *BMC Musculoskeletal Disorders*. 2017. Vol. 18, pp. 482. DOI 10.1186/s12891-017-1836-2.
[4] COSTE, N., et al. 2019. DOI 10.1016/j.rehab.2019.07.009.
[5] DAVERGNE, T, et al. *Rheumatology International* 2020. DOI 10.1007/s00296-020-04692-4.
[6] LEE, PH, et al. 2011. Vol. 8, pp. 115. DOI 10.1186/1479-5868-8-115.

Table 1 for abstract: correlation between IFAB questionnaire, each items and level of physical activity with or without extreme values

Item	Correlation with IPAQ-S min/met/week, rho	Correlation with stage of behavior change, rho	Correlation with mean steps per day, rho
Total IFAB score	0.28 ***	0.35 ***	0.08
Item 1	0.29 ***	0.16 *	0.16 *
Item 2	0.06	0.02	0.05
Item 3	0.08	0.16 *	0.01
Item 4	0.13	0.09	-0.07
Item 5	-0.09	0.10	0.07
Item 6	0.22 **	0.25 ***	-0.05
Item 7	0.22 **	0.20 **	0.12
Item 8	0.16 *	0.26 ***	0.11
Item 9	0.15	0.33 ***	0.11
Item 10	0.09	0.17 *	0.02
Social support questions	0.14	0.27 ***	-0.03
Psychological and knowledge status questions	0.22 **	0.16 *	0.09

*=P<0.05, **=p<0.01, ***=p<0.001

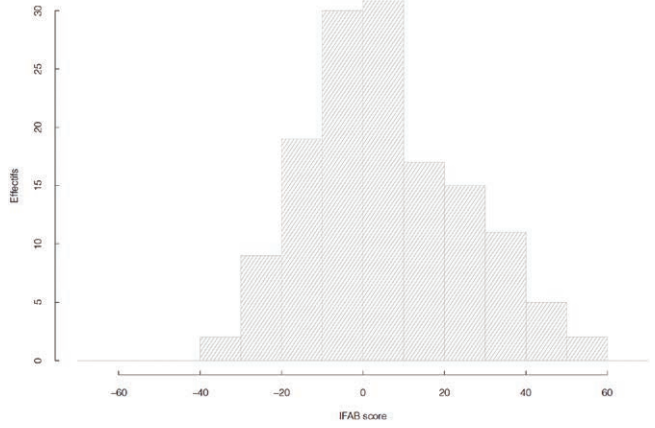


Figure 1. Distribution of the IFAB scoreFootnote: Y axis: effectifs, X axis: IFAB score (possibles values from -70 to 70)

Acknowledgements: I have no acknowledgements to declare.We thank the following coinvestigators: Sylvie Rozenberg, Beatrice Banneville, Rachida Inaoui, Emmanuelle Dernis, Athan Baillet and Catherine Beauvais, and we thank Hervé Servy for expert CRO advice
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1759

POS0275-HPR CONCORDANCE BETWEEN THE PHYSICIAN'S AND THE NURSE'S ASSESSMENT OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS USING DAS-28, CDAI AND SDAI IN SEVEN MIDDLE EASTERN ARAB COUNTRIES

N. Ziade[1,2], B. Zorkany[3], S. Al Emadi[4], M. Abu Jbara[5], H. Halabi[6], S. Saad[7,8], L. Kibbi[9], M. Mashaleh[10], H. Badsha[11], G. Harifi[11], A. Ayko[12], E. Alam[13], A. Daher[14], B. Masri[15], G. Merheb[16,17], J. Messaykeh[18], K. Mroue'[19], N. Salloum[20], T. Arayssi[21]. *[1]Saint-Joseph University, Rheumatology, Beirut, Lebanon*; *[2]Hotel-Dieu de France, Rheumatology, Beirut, Lebanon*; *[3]Cairo University, Rheumatology, Cairo, Egypt*; *[4]Hamad Medical Corporation, Rheumatology, Doha, Qatar*; *[5]Al-Bashir hospital, Rheumatology, Amman, Jordan*; *[6]King Faisal Specialist Hospital, Rheumatology, Jeddah, Saudi Arabia*; *[7]Assiut University, Rheumatology, Assiut, Egypt*; *[8]King Hamad University Hospital, Rheumatology, Bahrain, Bahrain*; *[9]Specialized Medical Center, Rheumatology, Riyadh, Saudi Arabia*; *[10]King Hussein Medical Center, Rheumatology, Amman, Jordan*; *[11]Dr Humeira Badsha Medical Center, Rheumatology, Dubai, United Arab Emirates*; *[12]Heartbeat clinic, Rheumatology, Beirut, Lebanon*; *[13]Levant Hospital, Rheumatology, Beirut, Lebanon*; *[14]Saint-Joseph University, Family Medicine, Beirut, Lebanon*; *[15]Jordan Hospital, Rheumatology, Amman, Jordan*; *[16]Holy-Spirit University, Rheumatology, Kaslik, Lebanon*; *[17]Notre-Dame des Secours, Rheumatology, Jbeil, Lebanon*; *[18]Al Monla Hospital, Rheumatology, Tripoli, Lebanon*; *[19]AL Zahraa Hospital, Rheumatology, Beirut, Lebanon*; *[20]ZClinic, Rheumatology, Beirut, Lebanon*; *[21]Weill Cornell Medicine, Rheumatology, Doha, Qatar*

Background: Managing patients with chronic rheumatic diseases is increasingly relying on the collaboration of a multidisciplinary team, including the rheumatology nurse who can aid assessment of disease activity among other healthcare tasks.
However, this practice, although common in Europe and North America, is still poorly implemented in the Middle eastern Arab countries (MEAC).
Objectives: To evaluate the concordance between the physician's and the nurse's assessment of disease activity in patients with rheumatoid arthritis (RA) in the MEAC.
Methods: During a routine patient visit to one of 9 rheumatology clinics located in 7 Middle Eastern Arab countries, the physician and the rheumatology nurse (who was already working in the clinic) performed the disease activity score 28 (DAS), Clinical Disease Activity Index (CDAI) and Simple Disease Activity Index (SDAI) in a blinded manner. The concordance regarding the 3 continuous scores was calculated using paired t-test. The agreement between physician- and nurse-DAS categories (remission, low, moderate and high disease activity) was calculated using weighted kappa for category comparison. Predictive factors of positive concordance between physician- and nurse-DAS were identified using binary logistic regression.
Results: The study included 373 patients' measurements over a period of two years (2018 to 2019). The mean age of the patients was 49.6 years (±28.2), 82.6% were females, and the mean disease duration was 11.3 years (±7.5).
The mean physician-DAS was slightly higher (3.97 (±1.52)) than the nurse-DAS (3.90 (±1.54)) (p=0.002), with a mean difference of +0.08 [95%CI 0.03; 0.12] (Table 1). The difference in the DAS individual items, the CDAI and the SDAI were not statistically significant.
When analyzing DAS as a categorical 4-items variable, the agreement between the physician and the nurse was present in 79.36% of the cases (weighted kappa was 0.77 [95%CI 0.73;0.83] which is considered as excellent, and was higher in patients with high disease activity (Figure 1).
A positive concordance between the physician- and the nurse-DAS was associated with the country (higher in Egypt, p<0.001) and the status of higher disease activity (p<0.001).
Conclusion: The agreement between the DAS-28 performed by the physician and by the nurse was excellent and was associated with the country and a higher disease activity. The present study confirms that the support of a trained nurse for evaluating disease activity in RA is feasible in the Arab countries and may save some valuable time in the clinic, whilst maintaining the quality of care for patients with RA.

Table 1. Comparison of the disease activity measures reported by the physician and by the nurse.

	Physician	Nurse	p-value
Total Joint Count	4.87 (2.26)	5.02 (6.20)	0.152
Swollen Joint Count	2.13 (3.88)	2.15 (3.83)	0.790
Global Assessment	3.30 (2.41)	3.32 (2.43)	0.702
DAS-28	3.97 (1.52)	3.90 (1.54)	0.002
CDAI	14.26 (12.53)	14.38 (12.59)	0.515
SDAI	21.51 (23.57)	21.61 (21.66)	0.527

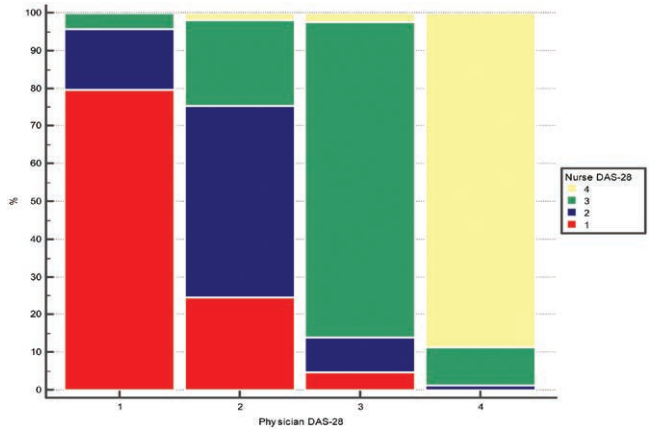


Figure 1. Agreement between physician- and nurse-DAS categories

Acknowledgements: The authors would like to acknowledge the patients for participating in the study and the assistants/ students/ nurses who assisted in the data collection: Dr. Fatima Abdul Majeed Al Hawaj, M. Atef Ahmed, M. Mohammad Alhusamiah, Ms Raquel De Guzman, Ms Lina Razzouk.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.650

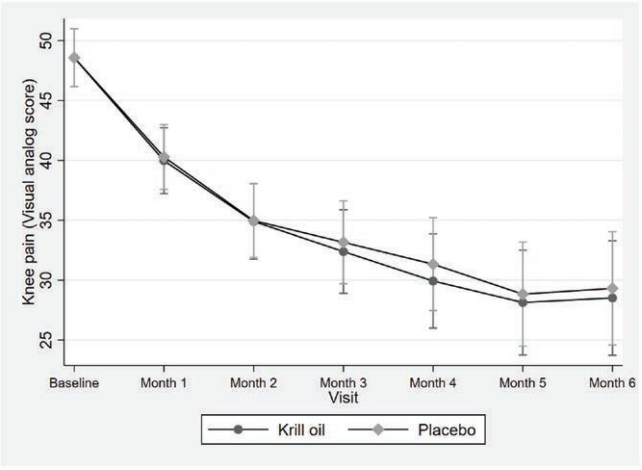
New drugs and therapies

POS0276

EFFICACY OF KRILL OIL IN THE TREATMENT OF KNEE OSTEOARTHRITIS: A 24-WEEK MULTICENTRE RANDOMISED DOUBLE-BLIND CONTROLLED TRIAL

L. Laslett[1], L. Scheepers[1], B. Antony[1], A. Wluka[2], C. Hill[3,4], L. March[5,6], H. Keen[7], P. Otahal[1], F. Cicuttini[2], G. Jones[1]. [1]*University of Tasmania, Menzies Institute for Medical Research, Hobart, Australia*; [2]*Monash University, Department of Epidemiology and Preventive Medicine, Melbourne, Australia*; [3]*Rheumatology Unit, The Queen Elizabeth Hospital, Adelaide, Adelaide, Australia*; [4]*The University of Adelaide, -, Adelaide, Australia*; [5]*Royal North Shore Hospital, Department of Rheumatology, Sydney, Australia*; [6]*University of Sydney, Kolling Inst., Inst. of Bone and Joint Res., Sydney, Australia*; [7]*Fiona Stanley Hospital, School of Medicine and Pharmacology, Perth, Australia*

Background: Elevated levels of systemic inflammation are common in people with osteoarthritis and predict both pain and structural outcomes. Krill oil has anti-inflammatory properties and reduces severity of inflammatory arthritis in mice by 50% compared to controls.[1] In humans, krill oil reduced knee pain and function in two short, moderate quality randomised controlled trials (RCTs) in people with osteoarthritis. However, evidence from longer trials with imaging data is lacking.
Objectives: The aim of this study was to compare the efficacy of krill oil (2g / day) vs. placebo for treating knee pain in patient with clinical knee osteoarthritis who have significant knee pain and effusion-synovitis.
Methods: KARAOKE was a 24-week multicentre, randomised, double-blind, placebo-controlled trial conducted at five Australian sites. Participants aged ≥40 years with symptomatic knee OA (according to ACR criteria), significant knee pain (pain score ≥40mm on a 100mm visual analogue scale [VAS]), and effusion-synovitis present on MRI (grade ≥1 according to modified Whole-Organ Magnetic Resonance Imaging Score (WORMS) scoring) were eligible. The study protocol has been published previously.[2]
Participants were randomised to receive 2g/day of krill oil, (350 mg/g omega-3 content, 12 mg/g total omega-6 content) or inert placebo (vegetable oil, no EPA or DHA, <5 mg/g (0.05%) other omega-3s).
The primary outcome was absolute change in knee pain assessed using a VAS [0-100mm] after 24 weeks. Secondary outcomes were: change in knee pain and function assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score [0-500mm]), change in back and hand pain assessed using a VAS [0-100mm], change in lower limb leg strength assessed using a dynamometer, and change in blood parameters (including CRP, triglycerides, fasting glucose and total, HDL, LDL cholesterol), after 24 weeks.
Linear mixed-models were used, using patient identification as random intercepts and trial centre and treatment month as random effect to adjust for correlated data within trial centres and repeated measures and to allow different treatment effects among patients over time, respectively.
Results: 262 participants were randomised (mean age 61.5 years, 53% females) to receive krill oil (n=130) or placebo (n=132). A total of 85% completed the trial. Knee pain improved in both groups over 24 weeks, but with no between-group difference (krill oil, -20.1mm; placebo, -19.3mm, p=0.81). Secondary outcomes: knee pain and function score improved in both groups, but with no between-group difference (WOMAC pain: krill oil, -86.7; placebo, -82.5mm, p=0.81; WOMAC function: krill oil, -245.3; placebo, -184.3, p=0.14 at 24 weeks). The same applies for hand pain and back pain. No significant changes were seen in leg strength or any of the blood parameters at 24 weeks). Incidence of one or more adverse events was 50% in the krill oil group (n=66) and 55% in the placebo group (n=71). There were 8 serious adverse events in the krill oil group 6 in the placebo group, all considered unrelated to treatment.
Conclusion: Krill oil was safe and well tolerated, but did not significantly reduce knee pain in patients with clinical knee osteoarthritis, significant knee pain and effusion-synovitis after 24 weeks compared to placebo. These findings do not support use of krill oil for alleviating knee pain in clinical knee osteoarthritis.



REFERENCES:
[1] Ierna M, et al. BMC Musculoskelet Disord 2010;11:136.
[2] Laslett L, et al. Trials 2020;21:79

Outcomes	Absolute between group difference at 24 weeks	*P* value
Primary		
Knee pain	0.8 (-5.6 to 7.2)	0.81
Secondary		
Knee pain (WOMAC)	4.2 (-29.1 to 37.5)	0.81
Knee function (WOMAC)	61 (-19.2 to 141.3)	0.14
Hand pain	2.8 (-2.6 to 8.3)	0.31
Back pain	1.9 (-3.9 to 7.8)	0.46
Leg strength	-2.59 (-9.41 to 4.23)	0.52
Metabolic factors		
Total Cholesterol	0.09 (-0.1 to 0.29)	0.34
HDL Cholesterol	-0.03 (-0.1 to 0.03)	0.35
LDL Cholesterol	0.05 (-0.12 to 0.22)	0.57
Triglycerides	0.12 (-0.09 to 0.33)	0.27
Fasting glucose	0.01 (-0.26 to 0.29)	0.93
hsCRP	0.64 (-0.56 to 1.84)	0.30

Disclosure of Interests: Laura Laslett Speakers bureau: once, several years ago, and unrelated to this topic, Grant/research support from: Yes, received funding from Aker Biomarine to conduct this trial, Lieke Scheepers Shareholder of: AstraZeneca, Grant/research support from: Pfizer, unrelated to this topic, Employee of: Previously employed by AstraZeneca, Benny Antony Speakers bureau: Zydus, Grant/research support from: Grant support for investigator-initiated trial from NR Ltd for unrelated research, Anita Wluka: None declared,

Catherine Hill: None declared, Lyn March Speakers bureau: Speaker fees from Pfizer Australia Ltd, Bristol Myer Squibb Australia, Abbvie Australia, Grant/research support from: Grant support for my institution from Janssen for unrelated research, Helen Keen: None declared, Petr Otahal: None declared, Flavia Cicuttini: None declared, Graeme Jones: None declared

DOI: 10.1136/annrheumdis-2021-eular.4242

POS0277 ANABOLIC EFFECT OF LNA043, A NOVEL DISEASE-MODIFYING OSTEOARTHRITIS DRUG CANDIDATE: RESULTS FROM AN IMAGING-BASED PROOF-OF-CONCEPT TRIAL IN PATIENTS WITH FOCAL ARTICULAR CARTILAGE LESIONS

S. Trattnig[1], C. Scotti[2], D. Laurent[2], V. Juras[1], S. Hacker[3], B. Cole[4], L. Pasa[5], R. Lehovec[6], P. Szomolanyi[1], E. Raithel[7], F. Saxer[2], J. Praestgaard[8], F. La Gamba[9], J. L. Jiménez[9], D. S. Ramos[2], R. Roubenoff[2], M. Schieker[2]. [1]*High Field MR Centre, Medical University of Vienna, Department of Biomedical Imaging and Image-Guided Therapy, Vienna, Austria*; [2]*Novartis Institutes for Biomedical Research, Translational Medicine, Basel, Switzerland*; [3]*Horizon Clinical Research, Grossmont Orthopedic Medical Group, San Diego, United States of America*; [4]*Rush University Medical Center, Department of Orthopedics, Chicago, United States of America*; [5]*Trauma Hospital, Trauma Department, Brno, Czech Republic*; [6]*Dr. Pirek's clinic, Orthopaedic surgery, Mladá Boleslav, Czech Republic*; [7]*Siemens Healthcare GmbH, SHS DI MR DL, Erlangen, Germany*; [8]*Novartis Institutes for Biomedical Research, Early Development Biostatistics, East Hanover, United States of America*; [9]*Novartis Institutes for Biomedical Research, Early Development Analytics, Basel, Switzerland*

Background: LNA043 is a modified, recombinant version of the human angiopoietin-like 3 (ANGPTL3) protein acting directly on cartilage-resident cells to transmit its cartilage anabolic effect. A first-in-human study previously demonstrated the favourable safety profile and the modulation of several pathways involved in cartilage homeostasis and osteoarthritis (OA)[1]. A previous proof-of-mechanism imaging study used high field (7 Tesla) magnetic resonance imaging (MRI) to show formation of hyaline-like tissue after a single injection of 20 mg LNA043 (unpublished data).

Objectives: To evaluate non-invasively the chondro-regenerative capacity of multiple intra-articular (i.a.) injections of LNA043 in patients with articular cartilage lesions in the knee (NCT03275064).

Methods: This was a randomised, double-blind, placebo (PBO)-controlled, proof-of-concept study in patients with a partial thickness cartilage lesion. In total, 58 patients (43 [20 mg LNA043]; 15 [PBO]), stratified by lesion type (condylar or patellar) were treated with 4 weekly i.a. injections. The primary endpoint was T2 relaxation time measurement as a marker of collagen fiber network, and cartilage lesion-volume was a secondary endpoint, both using 3-Tesla MRI. Assessments were performed at baseline, weeks (wks) 8, 16, 28 and 52 (the latter in 23/58 patients). While lesion-volume for the secondary endpoint was determined from manually segmented images, the cartilage volume of 21 sub-regions spanning the entire knee was also measured from 3D isotropic MR images employing an automated segmentation prototype software (MR Chondral Health 2.1 [MRCH], Siemens Healthcare)[2]. An exploratory analysis evaluated the treatment effect for the additive volume of the 3 subregions in the weight-bearing area of the medial femur.

Results: No change in T2 relaxation time was detected between treatment and PBO groups. Manual segmentation showed continuous filling of the cartilage lesions up to wk 28 in LNA043-treated patients with femoral lesions (p=0.08, vs PBO) while no effect was detected for patients with patellar lesions. Given the limitations of measuring small, irregularly shaped lesions with manual image-analysis, the MRCH approach was used (Figure 1). In the medial femoral weight-bearing region, refilling was detected over time (Δ=123 mm^3 at wk 28, N= 37, p= 0.05). No overgrowth was detected in the lateral femoral condyles without cartilage damage. The overall safety profile was favourable; only mild/moderate local reactions were reported, including a higher incidence of joint swelling (9.3% vs 0%) and arthralgia (11.6% vs 6.7%) for LNA043 vs PBO resolving spontaneously or with paracetamol/NSAIDs. No anti-drug antibodies were detected.

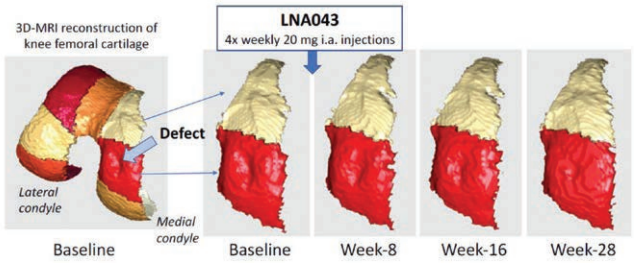
Conclusion: Treatment with 4 weekly i.a. injections of 20 mg LNA043 resulted in regeneration of damaged cartilage in patients with femoral articular cartilage lesions. Automated measurement of cartilage volume in the femoral index region was able to detect a relevant treatment effect and was found to be more sensitive than the manual segmentation method. No sign of cartilage overgrowth was observed in healthy femoral regions. A Phase 2b study in patients with mild to moderate knee OA is in preparation.

REFERENCES:

[1] Scotti et al. *ACR Convergence* 2020; Abstract #1483

[2] Juras et al. *Cartilage* 2020; Sep 29:1-12

Figure 1. Example of successful lesion filling from 3D reconstruction of cartilage MRI in an LNA043-treated patient with damage in the medial femur. Note the complex nature of the lesion which turns out to be deep in its center but shallower in the periphery. No scan is available for this patient at Week 52.



Disclosure of Interests: Siegfried Trattnig: None declared, Celeste Scotti Shareholder of: Novartis, Employee of: Novartis, Didier Laurent Shareholder of: Novartis, Employee of: Novartis, Vladimir Juras: None declared, Scott Hacker Grant/research support from: Novartis, Brian Cole: None declared, Libor Pasa: None declared, Roman Lehovec: None declared, Pavol Szomolanyi: None declared, Esther Raithel Employee of: Siemens Healthcare GmbH, Franziska Saxer Shareholder of: Novartis, Employee of: Novartis, Jens Praestgaard Shareholder of: Novartis, Employee of: Novartis, Fabiola La Gamba Shareholder of: Novartis, Employee of: Novartis, José L. Jiménez Employee of: Novartis, David Sanchez Ramos Shareholder of: Novartis, Employee of: Novartis, Ronenn Roubenoff Shareholder of: Novartis, Employee of: Novartis, Matthias Schieker Shareholder of: Novartis, Employee of: Novartis

DOI: 10.1136/annrheumdis-2021-eular.447

POS0278 A MULTICENTER, OBSERVATIONAL, EXTENSION STUDY EVALUATING THE SAFETY, TOLERABILITY, AND EFFICACY OF A SINGLE LORECIVIVINT INJECTION IN KNEE OA SUBJECTS

I. Simsek[1], C. Swearingen[2], H. Ghandehari[2], S. Kennedy[3], J. Tambiah[3], Y. Yazici[4], N. Skrepnik[5]. [1]*Samumed, LLC, Clinical Development, San Diego, United States of America*; [2]*Samumed, LLC, Biostatistics, San Diego, United States of America*; [3]*Samumed, LLC, Medical Affairs, San Diego, United States of America*; [4]*Samumed, LLC, Chief Medical Officer, San Diego, United States of America*; [5]*Tucson Orthopaedic Institute, Research, Tucson, United States of America*

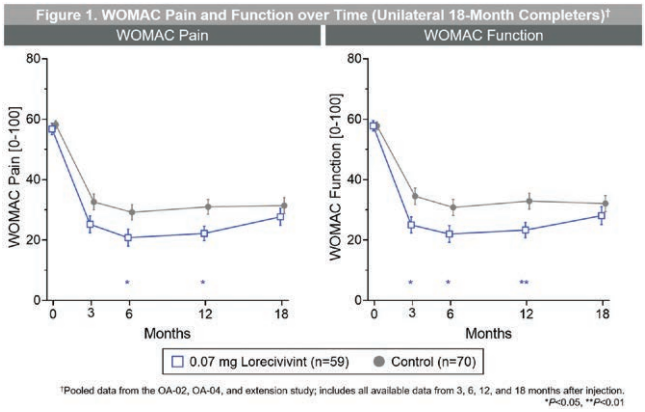
Background: Lorecivivint (LOR), a novel intra-articular (IA) CLK2/DYRK1A inhibitor that modulates the Wnt pathway, is in development as a knee osteoarthritis (OA) treatment.

Objectives: Subjects from two consecutive Phase 2 trials were followed up in a 5-year, pooled, observational study that evaluated the safety and exploratory efficacy of a single LOR injection that was previously administered into the target knee joint of subjects with moderate to severe knee OA. The study was terminated in its third year, as relevant long-term safety information became limited in the absence of repeated LOR administration. The primary objective evaluated the incidence of serious adverse events (SAEs). Safety data for all doses and a post hoc efficacy analysis for the pivotal dose (0.07 mg LOR) are reported.

Methods: This was a Phase 3, multicenter, observational, extension study of completer subjects (OA-05; NCT02951026) from two Phase 2 trials of LOR: a 12-month Phase 2a trial (OA-02; NCT02536833)[1] and a 6-month Phase 2b trial (OA-04; NCT03122860)[2]. Subjects received a single LOR or control (placebo or vehicle) injection at their parent-study baseline visit (OA-02 or OA-04 Visit 0 in this analysis). Pooled data from clinic visits at 6, 12, 24, and 36 months contributed to the extension-study (OA-05) analysis. SAEs, knee-related adverse events (AEs), and AEs of newly diagnosed conditions requiring treatment were collected as safety outcomes. Efficacy was assessed by target knee WOMAC Pain and Function subscores and radiographic medial joint space width (mJSW). A post hoc analysis was performed for 0.07 mg LOR versus control to assess responses in a subject subgroup (unilateral symptoms, no widespread pain, 18-month post-injection radiograph at study termination). Baseline-adjusted ANCOVA was performed using data from both the current and parent studies at 0, 3, 6, 12, and 18 months.

Results: Of 703 subjects, 119 (17%) subjects discontinued prior to study termination. Subjects had a mean age of 60.7 years and mean BMI of 29.1 kg/m2, and 61% were female. The majority of subjects had KL 3 (61.2%) OA. The safety analysis set included 495 LOR-treated subjects and 208 control subjects.

There were 169 AEs reported by 110 [15.6%] subjects. Four AEs were considered to be related to study drug and were reported by 3 (0.6%) subjects across LOR groups; no subjects withdrew from the study due to a treatment-related AE. The most common AEs were osteoarthritis (28 [4.0%] subjects) and arthralgia (25 [3.6%] subjects); incidence was similar between LOR and control groups. During the study, 68 SAEs were reported by 38 (5.4%) subjects, and no SAEs were considered to be related to treatment by investigator. One death occurred in the control group. Post hoc efficacy analyses demonstrated that subjects in the 0.07 mg LOR group (n=59) showed greater improvements from baseline in both WOMAC Pain and Function at 6 and 12 months versus subjects in the control group (n=70) (Figure 1; Day 0):
6 months:Pain: -8.16, 95% CI [-15.60, -0.71], *P*=0.032
Function: -9.47, 95% CI [-17.09, -1.84], *P*=0.015
12 months:Pain: -8.51, 95% CI [-15.17, -1.85], *P*=0.013
Function: -9.62, 95% CI [-16.83, -2.42], *P*=0.009
No mJSW progression was observed in any group over 18 months.
Limitations to this analysis include 1) subjects from LOR and control groups were "completers," therefore, more likely to be responders, and 2) subjects could have been on any medication or treatment in the extension study.
Conclusion: From these data, LOR appeared to be safe and well tolerated. A post hoc-analyzed subset of completer subjects treated with a single 0.07 mg LOR injection reported durable symptom improvements in WOMAC Pain and Function for up to at least 12 months versus control subjects.



REFERENCES:
[1] Yazici Y, et al. *Arthritis Rheumatol*. 2020.
[2] Yazici Y, et al. *ACR meeting*. 2019. Abstract L03.
Disclosure of Interests: Ismail Simsek Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Christopher Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Heli Ghandehari Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Sarah Kennedy Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Jeyanesh Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Yusuf Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Nebojsa Skrepnik Consultant of: Pfizer, Regeneron, Orthofix, Grant/research support from: Samumed, LLC
DOI: 10.1136/annrheumdis-2021-eular.2240

POS0279

WEARABLE TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION DEMONSTRATED BETTER EFFICACY AND SAFETY THAN WEAK OPIOIDS IN THE TREATMENT OF MODERATE TO SEVERE, CHRONIC NOCICEPTIVE PAIN IN KNEE OSTEOARTHRITIS. A RANDOMIZED, CONTROLLED, NON-INFERIORITY TRIAL

E. Maheu[1], S. Soriot-Thomas[2], E. Noel[3], E. Lespessailles[4], B. Cortet[5]on behalf of arthroTENS. [1]*Hospital Saint-Antoine Ap-Hp, Rheumatology, Paris, France*; [2]*Chu D'amiens-Picardie Site Sud, Clinical Research Center,Amiens, France*; [3]*Santy Orthopedic Center, Rheumatology, Lyon, France*; [4]*Hospital Center Régional D'orléans Hospital La Source, Rheumatology, Orléans, France*; [5]*Chu lille, Rheumatology, Lille, France*

Background: In knee osteoarthritis (KOA) recommendations, the first pharmacological analgesic line is paracetamol. However, its low efficacy, frequently leads to the use of weak opioids (WO) despite their poor tolerance, especially in elderly patients.
Objectives: The primary objective was to compare analgesic efficacy and safety of a new wearable transcutaneous electrical nerve stimulation (W-TENS) to those of WO in the treatment of moderate to severe, nociceptive, chronic pain in KOA patients.
Methods: ArthroTENS study was a phase 3, non-inferiority, multicentric, prospective, randomized, single-blinded for primary efficacy outcome, controlled, in 2-parallel groups, clinical study comparing W-TENS versus WO on two periods: a 3-month controlled period and an additional, optional, non-controlled, 3-month follow-up for patients in W-TENS group.
Eligible participants were KOA patients, ≥55 years old, at Kellgren-Lawrence radiographic grade ≥2, with moderate to severe nociceptive chronic (≥3 months) mean 8-day pain ≥4 on a 11-point numerical rating scale, and in treatment failure with non-opioid analgesics, including NSAIDs. Patients with neuropathic pain were excluded.
Co-primary endpoints were, for efficacy, mean pain intensity (PI), assessed at M3 and, for safety, the number of adverse events (AE) during the 3-month follow-up period.
In W-TENS group, an advanced, mobile app enabled, wearable TENS was used. High (100 Hz) and low (2 Hz) frequency stimulations were delivered via electrodes with standardized positioning (Figure 1).

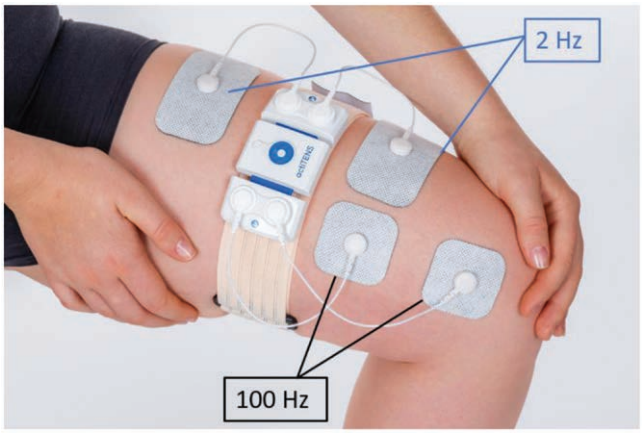


Figure 1. Electrode's positioning

In WO group, investigators chose, for each patient, the best suitable WO and its daily dose, and could switch to another WO, and/or adapt its daily dose if necessary.
A non-inferiority analysis was performed on the primary efficacy endpoint using a pre-defined non-inferiority margin (0.825 point) on PI, below the minimal clinically significant improvement.
Results: Demographic and baseline characteristics were balanced across both groups.
110 patients (55/group) were randomized and 48/55 (87.3%) and 44/55 (80.0%) patients completed the 3-month follow-up in W-TENS and WO groups, respectively. WO's prescriptions were balanced between codeine, opium-powder, tramadol and WO-paracetamol combinations.
Non-inferiority of W-TENS was demonstrated in the PP and ITT populations (Table 1). Since the 95% confidence interval (CI) of the between-treatments difference was below 0 in the ITT population, a planned superiority analysis was performed showing that W-TENS was significantly superior to WO at M3 (p=0.0124) on PI. Additionally, the number of AEs was significantly lower (p<0.001) in W-TENS (n=7) group than in WO (n=36) group. In WO group, AEs were systemic AEs usually reported with WO while AEs in W-TENS group were local, related to the technique used, such as local cutaneous reaction (erythema).

Table 1. Non-inferiority analyses on pain intensity at M3. ITT and PP populations. Least squares means for each study group and study group difference estimate and corresponding 95% CI

Group Population	Within-group change				Between-group difference	
	W-TENS		WO		W-TENS - WO	
ITT Population (n)	55		55			
Non inferiority						
Mean (SD)	3.83 (0.28)	<0.001	4.74 (0.28)	<0.001	-0.92 (0.40)	Non inferiority‡
95% CI	[3.27, 4.40]		[4.18, 5.30]		[-1.71, -0.12]	demonstrated
PP Population (n)	52		47			
Mean (SD)	3.87 (0.30)	<0.001	4.66 (0.32)	<0.001	-0.79 (0.44)	Non inferiority‡
95% CI	[3.28, 4.46]		[4.03, 5.28]		[-1.65, 0.08]	demonstrated

‡ Noninferiority was demonstrated when 95% CI < 0.825

Thirty-nine (70.9%) patients wished to extend W-TENS treatment for 3 additional months. Only one patient discontinued this additional period and results obtained at M3 remained stable at M6.

Conclusion: In this study, W-TENS was more effective and better tolerated than WO in the treatment of nociceptive KOA chronic pain and should represent an interesting non-pharmacological alternative to WO.

Acknowledgements: We gratefully thank P. Fardellone (Amiens), E. Coudeyre (Clermont-Ferrand), Y. Donazzolo (Gieres), A. Amouzougan (Saint-Etienne), L. Grange (Grenoble), T. Conrozier (Belfort), E. Senbel (Marseille), J.P. Sanchez (Billere), R. Forestier (Aix-les-Bains), H. Bard (Paris) and E. Gibert (Ivry-sur-Seine) for their active contribution throughout arthroTENS study

Disclosure of Interests: Emmanuel Maheu Speakers bureau: TRB chemedica, Consultant of: SUBLIMED, Moirans, FRANCE; Sandrine Soriot-Thomas Speakers bureau: Grunenthal, Consultant of: SUBLIMED, Moirans, FRANCE;
Grunenthal
Kyowa Kirin pharma, Grant/research support from: Grunenthal
Sanofi
Teva
Mylan
Therable, Eric Noel Consultant of: SUBLIMED, Moirans, FRANCE; Eric Lespessailles Consultant of: SUBLIMED, Moirans, FRANCE; Bernard Cortet Consultant of: SUBLIMED, Moirans, FRANCE;

DOI: 10.1136/annrheumdis-2021-eular.2086

POS0280 ASSOCIATION OF COMPLEMENTARY AND ALTERNATIVE MEDICINE USE WITH KNEE SYMPTOMS AND KNEE STRUCTURAL CHANGES OVER 2.6 YEARS: A POPULATION-BASED COHORT STUDY OF TASMANIAN OLDER ADULTS

Z. Wang[1], G. Jones[1], D. Aitken[1], S. Balogun[2], Z. Zhou[1], L. Blizzard[1], F. Cicuttini[3], B. Antony[1]on behalf of Musculoskeletal group. *[1]Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia*; *[2]College of Health & Medicine, Australian National University, Canberra, Australia*; *[3]Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia*

Background: There is increasing use of complementary and alternative medicines (CAMs) alone or as an adjuvant therapy to conventional palliative medicines.[1] However, there remains clinical uncertainty about the benefit of CAMs in the management of osteoarthritis in older population.

Objectives: To describe the association between CAM use (alone or in combination with conventional analgesics) with knee symptoms and structural changes amongst a representative sample of Tasmanian older adults.

Methods: A total of 1,099 participants were selected from the Tasmania Older Adult Cohort Study (TASOAC), an ongoing prospective population-based study. Exposure to CAM and conventional medications was classified into four categories according to the national drug code directory: [2] CAM only, conventional analgesics only, both CAM and conventional analgesics, and neither CAMs nor conventional analgesics. Knee pain was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and a 1.5-T MRI of the right knee was performed at baseline and follow-up (around 2.6 years). Longitudinal associations were assessed using mixed effect linear models.

Results: At baseline, participants‘ mean age was 63, 86.5% (n=951) reported any medication use. The prevalence of CAM use was 35.0% and of conventional analgesics was 58.6%. Over follow-up, the analgesic only group had a significant increase in WOMAC pain, function, and stiffness scores compared to those who took neither CAMs nor conventional analgesics. There was a statistically significant femoral cartilage volume loss across all four groups, and no statistical difference was found between participants who takes both CAMs and analgesics group and the reference group, but participant in the CAM only or the analgesics only groups loss statistically significant more femoral cartilage volume than the reference group (Table 1).

Conclusion: CAM use alone or in combination with conventional analgesics may associate with slower progression of knee pain. Conclusive evidence on the longitudinal benefits of CAM in the management of osteoarthritis among older adults warrants more studies.

REFERENCES:

[1] **Steel A,** McIntyre E, Harnett J, *et al*. Complementary medicine use in the Australian population: Results of a nationally-representative cross-sectional survey. *Sci Rep* 2018;**8**:17325.

[2] **National Center for Health Statistics**. Long-term Care Drug Database System: Drugs by NDC Class Code, Drug Code and Name 2007 Available from: https://www.cdc.gov/nchs/data/nnhsd/DrugsbyNDCClass3.pdf [accessed date: 2020 23 December].

Table 1. Association of change in clinical knee symptoms and knee structural changes over 2.6 years with different medications groups.

		Change for each category, coefficient (95% confident intervals)			
	Mean change for reference group*	CAMs	Both	Analgesics	Reference group*
No. of participants	327	128	257	387	327
WOMAC pain (5-50)	-0.95 (-1.42, -0.48)	0.04 (-0.85, 0.93)	0.32 (-0.4, 1.04)	0.78 (0.13, 1.43)	Ref
WOMAC function (17-170)	-3.09 (-4.52, -1.67)	1.02 (-1.7, 3.73)	1.39 (-0.81, 3.59)	2.32 (0.33, 4.31)	Ref
WOMAC stiffness (2-20)	-0.39 (-0.62, -0.17)	0.15 (-0.28, 0.58)	0.35 (0, 0.7)	0.40 (0.09, 0.72)	Ref
Femoral cartilage volume (mL)	-187.98 (-228.79, -147.18)	-113.81 (-192.60, -35.03)	-1.92 (-65.00, 61.17)	-127.19 (-186.31, -68.06)	Ref

*Reference group=participants taken neither CAMs nor conventional analgesics

The data were fitted using mixed effect linear models, which were constructed by entering baseline medication group, phase, the interaction between medication group and phase, covariates (baseline age, sex, body mass index [BMI], baseline value of outcome), the interaction between the covariates and phase, random intercept, and random slope on phase (time).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2762

POS0281 RUBUS IDAEUS LEAF EXTRACT IMPROVES SYMPTOMS IN KNEE OSTEOARTHRITIS PATIENTS: RESULTS FROM A DOUBLE BLIND RANDOMIZED CLINICAL STUDY

Y. Henrotin[1], R. Le Cozannet[2], P. Franca-Berthon[2], R. Truillet[3], M. Cohen Solal[4]. *[1]University of Liège, Musculoskeletal Innovative Research Lab, Liège, Belgium*; *[2]Naturex SA, Taste & Wellbeing, Avignon, France*; *[3]Atlanstat, Biostatistics, Rezé, France*; *[4]Université de Paris, Rheumatology, Paris, France*

Background: Osteoarthritis (OA) is the most common cause of disability in older adults. Currently, the aim of the patient management is to reduce symptoms and to improve quality of life using therapeutic modalities with no adverse effects (1). Unfortunately, the first line treatments of OA symptoms remain nonsteroidal anti-inflammatory drugs (NSAIDS) and paracetamol which if long-term administration are associated with severe adverse effects. Therefore, we need of save alternative to manage chronic OA symptoms. One candidate is Rubus idaeus (raspberry) leaf extract rich in flavonoids and phenols known to inhibit inflammatory responses.

Objectives: The aim of this study was to investigate the effects of a 12-weeks intervention with an ethanolic extract from Rubus idaeus leaf on symptoms of knee OA.

Methods: The study was a randomized, double-blind, placebo-controlled, monocentric trial of 198 subjects with femoro-tibial OA. Subjects were randomized equally to receive one daily treatment during 3 months either of 1 cap of Rubus idaeus leaf extract 400 mg, or 200 mg or placebo (maltodextrine). The main objective of this first exploratory study was to assess pain reduction over time. Pain was measured using different scales from the Western Ontario McMaster osteoarthritis index (WOMAC) to the knee pain VAS.

Results: In the ITT population, Rubus idaeus leaf extract 400 mg and 200 mg after 12 weeks of treatment reduced pain measured by the VAS respectively of -10.93 (1.95) mm and -8.51 (1.92) mm compared to baseline, while placebo group had a -3.84 (1.89) mm reduction. The mean pain decrease induced by Rubus ideaus leaf extract was over – 7 mm which is clinically relevant, and reached clinically statistical difference compared to placebo with the highest dose (p=0.017; 95% CI, -13.11 to -1.07). Interestingly, subgroup analysis on the participants with a BMI>25, highlighted clinically relevant pain reduction for the 400 and 200 mg doses compared to baseline of respectively -13.36 (2.26) mm and -11.25 (2.14) mm (placebo = -0.37

(2.16) mm). The reduction was statistically different versus placebo for both doses (400 mg p<0.0001; 95% CI, (-19.95 to -6.04) and 200 mg p=0.0008; 95% CI, (-17.64 to -4.12). There was no effect on the WOMAC subscale of pain.

Conclusion: Rubus idaeus leaf extract, even at the low dose of 200 mg, was effective to relieve pain at short-term in-patient with knee OA. As Rubus idaeus leaf extract is well tolerated, it could be an alternative to nonsteroidal anti-inflammatory drugs and paracetamol to relieve knee joint pain in OA patients.

REFERENCES:

[1]Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, Kraus VB, Lohmander LS, Abbott JH, Bhandari M, Blanco FJ, Espinosa R, Haugen IK, Lin J, Mandl LA, Moilanen E, Nakamura N, Snyder-Mackler L, Trojian T, Underwood M, McAlindon TE. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage. 2019 Nov;27(11):1578-1589.

Disclosure of Interests: Yves Henrotin Speakers bureau: Expanscience, Nestlé, Tilman, Consultant of: Naturex SA, Artialis SA, Tilman SA, Seigakaku, Stemmatters, Expanscience, Romain Le Cozannet Employee of: Naturex SA, Pascale Franca-Berthon Employee of: Naturex SA, Romain Truillet Employee of: Atlanstat, Martine Cohen Solal: None declared

DOI: 10.1136/annrheumdis-2021-eular.1493

POS0282 EVALUATION OF A NEW HYALURONATE FORMULATION ONE YEAR AFTER SINGLE INJECTION TO PATIENTS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS (SOYA STUDY)

C. Gavín[1], F. Moreno[1], F. J. Blanco[2], J. L. Pablos[3], M. A. Caracuel-Ruiz[4], J. Rosas[5], P. Hernández-Esteban[6], F. Navarro[7], P. Coronel[8], M. Gimeno[9]on behalf of SOYA study group. *[1]H.U. Fundación Alcorcón,Traumatology, Alcorcón (Madrid), Spain*; *[2]C.H.U. a Coruña, Rheumatology, A Coruña, Spain*; *[3]H.U. 12 de Octubre, Rheumatology, Madrid, Spain*; *[4]H.U. Reina Sofía, Rheumatology, Córdoba, Spain*; *[5]H. Marina Baixa, Rheumatology, Villajoyosa (Alicante), Spain*; *[6]H.U. La Paz, Traumatology, Madrid, Spain*; *[7]H.G.U. de Elche, Rheumatology, Elche (Alicante), Spain*; *[8]Meiji Pharma Spain, S.A., D. International, Alcalá de Henares (Madrid), Spain*; *[9]Meiji Pharma Spain, Clinical Development, Alcala de Henares, Spain*

Background: Osteoarthritis (OA) is a leading cause of chronic pain and disability, and its prevalence is expected to increase worldwide (1) being the knee the most affected joint, especially in older adults. Intra-articular hyaluronic acid (HA) could be of particular benefit in OA patients with co-morbidities, and in case of inadequate response to other pharmacological treatments (2). HA has been generally administered in cycles of 3-5 injections, however, due to the pressure on public health systems, the trend is to reduce the number of injections maintaining the duration of effects as longer as possible.

Objectives: To assess the effectiveness and safety of a new formulation of HA, up to one year after one single injection to patients in the SOYA (Symptomatic Osteoarthritis one Year Assessment) study.

Methods: Patients with Kellgren-Lawrence (KL) grade 2-3 and Visual Analogue Scale (VAS) pain >=40-<80mm were prospectively included to receive a single injection of MPS-HA2%. At 6m a second injection could be offered to selected patients. Primary outcome was reduction of VAS pain in the target knee. VAS for joint pain and WOMAC were recorded at 6 and 12m; Minimally Clinical Important Improvement MCII (>=20% relative change for VAS pain) and patient and investigator assessments (PGA, IGA) (Likert scale 0-4 points) were also estimated. Adverse events were recorded for safety assessment.

Results: One hundred and one patients (mean age 68 years, 74% female and 78% with overweight) were included. Mean pain at baseline in the target knee was 63.57mm and 57% were grade 3 KL with a mean evolution of 7.5 years. Table 1 shows the improvement in VAS and WOMAC scores at 6 and 12 months in the mITT population. Similar results were obtained in PP population.

Table 1. Changes in VAS and WOMAC scores, expressed as mean values

SCORE	Baseline	6 months		12 months	
	value	value	% variation (95% CI)	value	% variation (95% CI)
VAS pain	63.57	37.59	-39.74* (-49.23; -30.25)	38.37	-37.67* (-47.82; -27.52)
WOMAC					
total	50.19	31.88	-37.96* (-46.83; -29.09)	31.65	-36.47* (-46.20; -26.73)
pain	49.37	32.01	-32.92* (-43.37; -22.46)	31.08	-32.07* (-43.19; -20.95)
stiffness	49.12	28.35	-35.24** (-53.22; -17.23)	28.71	-34.08* (-49.30; 18.86)
function	52.07	35.30	-33.95* (-43.49; -24.40)	35.15	-32.71* (-42.80; -22.62)

*p-value: 0.0001; **p-value: 0.0002. Student test

The MCII was achieved by 66.3% of patients at 6m and 62.2% at 12m. Regarding PGA mean score was 2.44 at baseline, 1.35 at 6m and 1.46 at 12m (Wilcoxon, p-value <0.05). As for the IGA mean score was 2.29 at baseline, 1.06 at 6m and 1.48 at 12m (Wilcoxon, p-value <0.05).

Fourteen patients received a second injection at 6m and 50% of them achieved at 12m a significant and clinically relevant improvement compared to baseline, above the 20% established for the MCII.

In total, 12 adverse events (8 patients) were reported, all of them local, non-serious, and of mild-moderate intensity.

Conclusion: Viscosupplementation with a single intra-articular injection of MPS-HA2% has proven to be effective and well tolerated up to 12 months after treatment. The re-infiltration of the joint in appropriate cases has proven to be effective in a significant number of patients. The acceptability of the treatment by the patient was optimal.

REFERENCES:

[1] Sebbag E, Felten R, Sagez F, et al. The world-wide burden of musculoskeletal diseases: a systematic analysis of the World Health Organization Burden of Diseases Database. Ann Rheum Dis. 2019 Jun;78(6): 844-848.

[2] Bruyère O, Cooper C, Pelletier JP, et al. An algorithm recommendation for the management of knee osteoarthritis in Europe and internationally: a report from a task force of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Semin Arthritis Rheum. 2014 Dec;44(3):253-63.

Disclosure of Interests: Carlos Gavín: None declared, Francisco Moreno: None declared, Francisco J. Blanco: None declared, José Luis Pablos: None declared, Miguel A. Caracuel-Ruiz: None declared, Jose Rosas: None declared, Pablo Hernández-Esteban: None declared, Francisco Navarro: None declared, PILAR CORONEL Employee of: Meiji Pharma Spain, S.A., Mercedes Gimeno Employee of: Employee of Meiji Pharma Spain, S.A.

DOI: 10.1136/annrheumdis-2021-eular.1037

POS0283 TREATMENT PATTERNS AND CLINICAL CHARACTERISTICS OF PATIENTS WITH OSTEOARTHRITIS OF THE HIP AND/OR KNEE TREATED WITH TRADITIONAL NSAIDS VS COX-2S: A REAL-WORLD STUDY OF COMMERCIALLY-INSURED PATIENTS

S. Silverman[1,2], P. Schepman[3], J. B. Rice[4], C. Beck[3], A. White[4], S. Thakkar[3], M. Johnson[4], R. Robinson[5], B. Emir[3]. *[1]Cedars Sinai Medical Center, Los Angeles, United States of America*; *[2]David Geffen School of Medicine at UCLA, Los Angeles, United States of America*; *[3]Pfizer, New York, United States of America*; *[4]Analysis Group, HEOR, Boston, United States of America*; *[5]Eli Lilly and Company, Indianapolis, United States of America*

Background: The 2019 American College of Rheumatology (ACR) guidelines strongly recommend oral nonsteroidal anti-inflammatory drugs (NSAIDs) for management of hip and knee osteoarthritis (OA) and strongly recommend topical NSAIDs for knee OA. There are, however, important safety considerations with NSAIDs in terms of increased rates of gastrointestinal, cardiovascular, and renal events. Given these risks, it is important to understand the characteristics and drug utilization of the patients who start treatment on these different treatments (i.e., traditional NSAIDs [tNSAIDs] and cyclooxygenase-2 inhibitors [COX-2s]).

Objectives: The goal of this research was to describe and compare baseline characteristics of commercially-insured patients diagnosed with OA of the hip and/or knee who started treatment on different types of NSAIDs (i.e., oral tNSAIDs, topical tNSAIDs, and COX-2s).

Methods: The Optum Healthcare Solutions, Inc. claims database (1/2012-3/2017) was used to identify patients ≥18 years old, with ≥2 diagnoses of hip and/or knee OA, and ≥90 days supply of oral tNSAIDs, topical tNSAIDs, or COX-2s during the one-year follow up period. The index date was defined as the first prescription after the first OA diagnosis. Patients were assigned to cohorts based on the type of NSAID prescribed on index date. Patients were required to be continuously-enrolled six months before (baseline period) and 36 months after (follow-up period) the index date. Demographic and clinical characteristics including age, sex, comorbidities, and healthcare resource use (HRU) were summarized during baseline. Drug utilization characteristics including days supply and number of prescriptions for the different NSAIDs types were summarized during follow-up period.

Results: Data for 23,796 patients were analyzed: 18,100 patients received oral tNSAIDs, 4,825 received COX-2s, and 871 topical tNSAIDs. Patients who initiated treatment on oral tNSAIDs were the youngest (mean age of 60.6 vs. 64.6 for COX-2s and 65.0 for topical tNSAIDs) and topical tNSAIDs had the highest proportion of female patients (71% vs. 62% for oral tNSAIDs and 63% for COX-2s). The topical tNSAIDs cohort had the highest presence of chronic kidney disease (2.6% vs. 1.0% and 1.5% for oral tNSAIDs and COX-2s, respectively) and congestive heart failure (2.5% vs. 0.8% and 1.7% for oral tNSAIDs and COX-2s, respectively) at baseline. In terms of HRU during baseline, topical

tNSAIDs had the most patients with emergency department visits (20.8% vs. 16.7% in both COX-2s and oral tNSAIDs), and COX-2 had the most patients with inpatient visits (18.1% vs. 15.4% for topical tNSAIDs and 11.8% for oral tNSAIDs). Oral tNSAIDs had the lowest total all-cause cost ($6,504), and the topical tNSAIDs cohort had the highest costs ($8,455), but fairly comparable with COX-2s ($8,289). During follow-up, oral tNSAIDs patients stayed mostly on oral tNSAIDs as less than 15% of oral tNSAIDs patients later had a prescription for COX-2s or topical tNSAIDs. 37% of COX-2 patients and 56% of topical tNSAIDs patients later took oral tNSAIDs. Topical tNSAIDs patients had an average of 184.4 days of supply for topical tNSAIDs yet also extensively used oral NSAIDs during follow-up (average days of supply for oral tNSAIDs was 315.5 days and for COX-2s was 383.5 days).

Conclusion: This study suggests that patients with more complex comorbidity profiles, including higher rates of adverse effects, often start pharmacological treatment with topical tNSAIDs. However, patients who start treatment with topical tNSAIDs switch to other types of NSAIDs; oral tNSAIDs were the most frequently prescribed treatment across the cohorts. Thus, despite the safety concerns with oral tNSAIDs and COX-2s, patients are still placed on these treatments to manage their OA pain. There is a need for new innovative treatments as there is currently a lack of other options.

Disclosure of Interests: Stuart Silverman Consultant of: Stuart Silverman is a paid consultant to Pfizer and Eli Lilly and Company in connection with this study, Patricia Schepman Shareholder of: Patricia Schepman is an employee of Pfizer with stock and/or stock options, Employee of: Pfizer, James B Rice Consultant of: Brad Rice is an employee of Analysis Group, who were paid consultants to Pfizer and Eli Lilly and Company for this study, Craig Beck Shareholder of: Craig Beck is an employee of Pfizer with stock and/or stock options, Employee of: Pfizer, Alan White Consultant of: Alan White is an employee of Analysis Group, who were paid consultants to Pfizer and Eli Lilly and Company for this study, Sheena Thakkar Shareholder of: Sheena Thakkar is an employee of Pfizer with stock and/or stock options, Employee of: Pfizer, Michaela Johnson Consultant of: Michaela Johnson is an employee of Analysis Group, who were paid consultants to Pfizer and Eli Lilly and Company for this study, Rebecca Robinson Shareholder of: Rebecca Robinson is an employee and minor stockholder of Eli Lilly and Company, Employee of: Eli Lilly and Company, Birol Emir Shareholder of: Birol Emir is an employee of Pfizer with stock and/or stock options, Employee of: Pfizer

DOI: 10.1136/annrheumdis-2021-eular.2175

POS0284 CLINICAL AND MRI COMPARISON OF ECCENTRIC VERSUS CONCENTRIC REHABILITATION IN SYMPTOMATIC KNEE OSTEOARTHRITIS: A PROSPECTIVE RANDOMIZED STUDY

M. C. Trojani[1], D. Bendahan[2], F. Chorin[3], P. Gerus[4], V. Breuil[5], S. Guis[6], C. Roux[7]. [1]*Université cote d'azur, Rheumatology, Nice, France*; [2]*Aix Marseille University, CNRS, Centre de Résonance Magnétique Biologique et Médicale (CRMBM), UMR 7339, Marseille, France*; [3]*Université Cote d'Azur, LAMHESS laboratory, NICE, France*; [4]*Université Cote d'Azur, LAMHESS laboratory, Nice, France*; [5]*Université Cote d'Azur, Rheumatology, Nice, France*; [6] *Aix-Marseille University, 13009, Marseille, France, CRMBM UMR CNRS 7339, Marseille, France*; [7]*Université cote d'azur, Rheumatology, Nice, France*

Background: Rehabilitation is at the center of the non-medical management of knee osteoarthritis. Concentric muscle strengthening is often preferred, while eccentric contractions play an important role in controlling knee flexion and knee stability and allow the development of a high level of strength with a low energy cost. But few studies have focused on these two technique

Objectives: To explore the effect of a 6-week-exercise program on function, pain and performance level in symptomatic knee osteoarthritis patients

Methods: An analysis was performed of the data from 60 individuals with symptomatic knee osteoarthritis who were included in the EXART study. The EXART study was a prospective, randomized controlled trial which included patients aged 40 to 85 with KL 2 or 3 responding to the American College of Rheumatology criteria. The first group benefitted from a 6 week eccentric rehabilitation program and the second group from a standard 6 week concentric rehabilitation program. The endpoints were the changes from baseline to week 6 in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), pain, and performance measured with quadriceps power (PMax) and contraction strength (MMax). MRI muscle analysis was performed before and after physical activity.

Results: Among 80 patients screened, 60 were included in the study and randomized. 25/30 subjects finished the program in the concentric group and 28/30 in the eccentric group. The mean population age was 74 (+/-8), mean IMC 27.2 (+/-4). The baseline total WOMAC mean was 49.2 (+/-19), VAS pain 5.3 (+/-2). At 6 weeks, both groups showed a significant improvement compared to baseline for the WOMAC without any difference between the two groups (mean difference evolution concentric = 7.5 ± 11.9 (p= p<0.0001); mean difference evolution eccentric = 4.5 ± 1.9 (p<0.0001); intergroup analysis p=0.7). Similar significant results were found in the WOMAC function subscale. No difference between the groups appeared in VAS pain evolution (p= 0.7). The eccentric group showed a significant improvement in PMax and high speed MMax evolution (p=0.001 and p=0.002). This improvement was not found for the concentric group (p= 0.52 and p=0.27). MRI showed a vastus medialis hypertrophy only in the eccentric group (p=0.002). We did not observe any change in the fatty infiltration of the quadriceps on MRI.

Conclusion: Rehabilitation, whether eccentric or concentric, has a beneficial action on function and pain in symptomatic knee osteoarthritis whatever the methods. A gain in muscle performance and vastus medialis volume was found only with the eccentric rehabilitation. This study confirms the importance of any type of rehabilitation in knee osteoarthritis and raises the question of the relation between muscle gain/performance and function or pain

Acknowledgements: We would like to thank all the patients who took part in the study as well as all the members of the Fragile Platform of the Nice University Hospital.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3164

POS0285 ARE RACIAL DISPARITIES IN REVISION TKA OUTCOMES ASSOCIATED WITH HOSPITAL OR SURGEON VOLUME?

S. Mirza[1], S. Goodman[2,3], Y. Zhang[2], H. Do[2], B. Mehta[2,3], S. Lyman[2], L. A. Mandl[2,3], M. Figgie[4], M. Parks[4], L. Russell[2,3], A. Bass[2,3]. [1]*Touro College of Osteopathic Medicine, Medical School, New York, United States of America*; [2]*Hospital for Special Surgery, Medicine, New York, United States of America*; [3]*Weill Cornell Medical Center, Medicine, New York, United States of America*; [4]*Hospital for Special Surgery, Orthopedic Surgery, New York, United States of America*

Background: Total knee arthroplasty (TKA) outcomes are linked to surgical volume,[1] despite the increase in TKA utilization, racial disparities in TKA outcomes persist. Blacks in the US are at a higher risk of aseptic revision of TKA (R-TKA) when compared to Whites, yet the reasons for this are not understood.

Objectives: The objective of this study is to examine the relationship between hospital and surgeon annual TKA volume and R-TKA outcomes by race.

Methods: This is an observational cohort study. New York Statewide Planning and Research Cooperative System data for 2004 – 2013 was used to identify patients who underwent primary TKA. Data through 2015 was used to identify R-TKA within 2 years of the index TKA. Hospital characteristics were obtained from the AHA Annual Survey. Surgeon data was collected from New York State Education Department and New York State Physician Profile. Surgeon annual TKA volume was categorized based on cutoffs established by Wilson et al[1] as </=12, 13-59, 60-145 or >/= 146, and hospital TKA volume as </=89, 90-235, 236-644 and >/=645. We calculated the odds of R-TKA in Whites and Blacks separately and generated crude odds ratios (OR) comparing Blacks to Whites to examine trends across volume categories. A multivariable logistic regression model adjusted for known R-TKA risk factors was also performed.

Results: A total of 163,576 patients were included. Mean (SD) age was 66.4 (10.4) years, 107,233 (65.6%) were female, 124,277 (76.6%) were White and 15,990 (9.8%) were Black. 2925 patients underwent aseptic R-TKA. In logistic regression analysis, Blacks had a higher risk of R-TKA (OR 1.42, 95%CI 1.26-1.6) (**Table 1).** Risk of R-TKA was also higher when surgeon annual volume was </=12 (OR 1.5, 95%CI 1.25-1.8) or 13-59 (OR 1.16, 95%CI 1.04-1.29) TKA compared to the highest volume surgeons (>/=146). Patients who had surgery at a hospital with annual volume of 236-634 TKA were less likely to undergo R-TKA compared to the highest volume hospitals (>/=645) (OR 0.88, 95%CI 0.79-0.98). Other risk factors for R-TKA were younger age and worker's compensation, while patients with inflammatory arthritis had a lower risk. Figures 1A and 1B show the odds of R-TKA in Whites and Blacks, respectively, by hospital and surgeon volume. Figure 1C shows the crude OR for Blacks to Whites for each category pair. The OR ranged from 0.9 to 2.5, with the largest disparity found in patients who have TKA performed by surgeons with 60-145 annual TKA volume at the highest volume hospitals (>/=645).

Conclusion: Patients having TKA by a surgeon performing <60 TKA per year have higher risk of R-TKA. Racial disparities in R-TKA risk are highest for TKA by surgeons performing 60-145 TKA per year at hospitals performing >/=645 TKA per year. Future studies should examine factors, such as whether trainees are involved the surgery, that may vary based on social determines of health, such as patient race and payor.

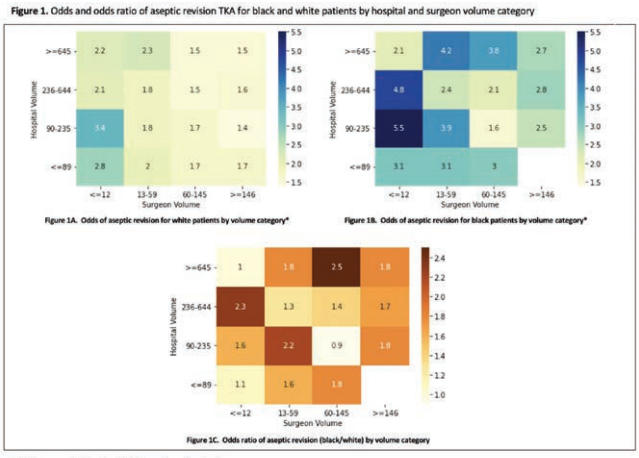
REFERENCES:

[1] Wilson S. et al Meaningful thresholds for the volume-outcome relationship in total knee arthroplasty. *Journal of bone and joint surgery.* 2016; 98:1683

Table 1. Logistic regression of risk for R-TKA

Variable (reference)	Level	Odds ratio	95% CI	p-value
Age	--	0.95	0.94-0.95	<.001
Sex (female)	Male	1.07	0.99-1.15	0.108
Race (white	Asian	0.65	0.42-0.96	0.031
	Black	1.42	1.26-1.6	<.001
	Unknown	0.81	0.64-1.02	0.07
	Other	1.05	0.92-1.21	0.446
Insurance (Medicare)	Medicaid	0.89	0.75-1.06	0.193
	Other	0.89	0.7-1.13	0.331
	Private	0.82	0.74-0.91	<.001
	Work compensation	1.56	1.35-1.8	<.001
Surgeon volume (>/=146)	</=12	1.5	1.25-1.8	<.001
	13-59	1.16	1.04-1.29	0.006
	60-145	1.0	0.91-1.11	0.957
Hospital volume (>/=645)	</= 89	0.98	0.84-1.15	0.848
	90-235	0.99	0.88-1.12	0.869
	236-644	0.88	0.79-0.98	0.018
Hospital bed size (>400 beds)	6-199	1.13	1.02-1.25	0.024
	200-399	1.06	0.96-1.17	0.262

Other variables in model: diabetes, obesity, renal disease, COPD, osteoarthritis, osteonecrosis, dislocation, inflammatory arthritis, surgical complication, infection, no college, poverty >20%, years since residency, US/Canada medical school, orthopedic board certified, AHA control, teaching, rural hospital



Disclosure of Interests: Serene Mirza: None declared, Susan Goodman: None declared, Yi Zhang: None declared, Huong Do: None declared, Bella Mehta: None declared, Stephen Lyman: None declared, Lisa A. Mandl: None declared, Mark Figgie: None declared, Michael Parks Consultant of: Zimmer biomet, Grant/ research support from: Zimmer biomet, Linda Russell: None declared, Anne Bass: None declared
DOI: 10.1136/annrheumdis-2021-eular.664

Oncorheumatology

POS0286

INCIDENCE OF MALIGNANCIES IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM A LARGE JAPANESE NATIONAL REGISTRY

T. Matsui[1], N. Sugiyama[2], S. Toyoizumi[3], F. Matsuyama[4], T. Murata[4], Y. Urata[5], K. Kawahata[6], S. Tohma[7]. [1]*National Hospital Organization Sagamihara National Hospital, Department of Rheumatology, Clinical Research Center for Allergy and Rheumatology, Kanagawa, Japan*; [2]*Pfizer Japan Inc, Inflammation and Immunology, Tokyo, Japan*; [3]*Pfizer R&D Japan, Biometrics and Data Management, Tokyo, Japan*; [4]*CRECON Medical Assessment Inc, Tokyo, Japan*; [5]*Tsugaru General Hospital, Department of Rheumatology, Aomori, Japan*; [6]*St. Marianna University School of Medicine, Division of Rheumatology and Allergology, Department of Internal Medicine, Kanagawa, Japan*; [7]*National Hospital Organization Tokyo National Hospital, Department of Rheumatology, Tokyo, Japan*

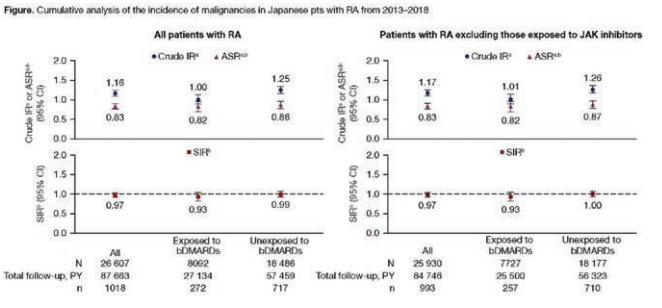
Background: Patients (pts) with rheumatoid arthritis (RA) have an increased risk of some malignancies vs the general population, and this can vary by region/ race.[1,2] Data on the epidemiology and impact of biological (b)DMARDs and targeted synthetic (ts)DMARDs, such as Janus kinase (JAK) inhibitors, on the incidence of malignancies in Japanese pts with RA are limited. The National Database of Rheumatic Diseases in Japan (NinJa) is one of the largest RA registries in Japan.
Objectives: To evaluate the incidence of malignancies in Japanese pts with RA using NinJa registry data.
Methods: This retrospective observational study analysed NinJa registry data for Japanese pts with RA aged ≥18 years with ≥1 data entry between 2013 (first JAK inhibitor approval for RA in Japan) and 2018. The overall cohort included all pts with RA, and two sub-cohorts were analysed: pts exposed and unexposed to bDMARDs (exposure defined as ≥1 bDMARD reported in database). Crude incidence rates (IRs) for malignancies (including non-melanoma skin cancer) were calculated as the number of events per 100 pt-years of follow-up (time between start of follow-up or the date of first bDMARD exposure [for bDMARD-exposed pts] and end of observation period, or withdrawal from database). The most recent data for incidence of malignancy in the Japanese general population (2013–2017 data from the National Cancer Center, Japan) were used to calculate standardised incidence ratios (SIRs) and age- and sex-adjusted standardised rates (ASRs) for malignancies. Cross-sectional (per calendar year) and cumulative analyses were performed for the overall cohort. Cumulative rates were calculated for sub-cohorts, and all cumulative analyses were repeated excluding pts exposed to JAK inhibitors (ie ≥1 JAK inhibitor reported in database).
Results: Data were collected for 26 607 Japanese pts with RA from 2013–2018. In the cross-sectional analysis (Table 1), the SIR and ASR for malignancies in all pts with RA were generally consistent from 2013–2018. In the cumulative analysis, the SIR (95% CI) for malignancies from 2013–2018 was 0.97 (0.91, 1.03) in all pts with RA, and 0.93 (0.82, 1.04) and 0.99 (0.92, 1.07) in pts exposed and unexposed to bDMARDs, respectively (Figure 1). Adjusting for age/sex, the cumulative ASR (95% CI) for malignancies from 2013–2018 was 0.83 (0.76, 0.90) in all pts with RA, and 0.82 (0.69, 0.95) and 0.86 (0.77, 0.96) in pts exposed and unexposed to bDMARDs, respectively (Figure 1). In all cohorts, the cumulative SIR and ASR were similar when pts exposed to JAK inhibitors were excluded (Figure 1).

Table 1. Cross-sectional analysis of the incidence of malignancies in Japanese pts with RA from 2013–2018

	All RA					
	2013 (N=13 423)	2014 (N=15 584)	2015 (N=15 751)	2016 (N=16 107)	2017 (N=15 994)	2018 (N=15 003)
Total follow-up, PY	13 353	14 866	14 829	14 970	14 748	14 898
Pts with events, n	140	164	174	168	161	211
Crude IR[a]	1.05	1.10	1.17	1.12	1.09	1.42
(95% CI)	(0.89, 1.24)	(0.95, 1.29)	(1.01, 1.36)	(0.97, 1.31)	(0.94, 1.27)	(1.24, 1.62)
ASR[a,b]	0.76	0.76	0.90	0.88	0.80	0.88
(95% CI)	(0.60, 0.93)	(0.62, 0.90)	(0.68, 1.11)	(0.68, 1.07)	(0.62, 0.98)	(0.74, 1.01)
SIR[b]	0.97	1.01	1.02	0.88	0.86	1.10
(95% CI)	(0.82, 1.14)	(0.86, 1.17)	(0.87, 1.18)	(0.75, 1.02)	(0.73, 1.00)	(0.95, 1.25)

[a]IR/ASR were calculated as number of events per 100 PY of follow-up[b]Data from a Japanese general population database of malignancy incidence from 2013–2017, provided by the Center for Cancer Control and Information Services, National Cancer Center, JapanPY, pt-years

Conclusion: The incidence of malignancies in Japanese pts with RA, registered in the NinJa database from 2013–2018, was similar to that in the Japanese general population. The SIR and ASR for malignancies were comparable in pts exposed and unexposed to bDMARDs. In all cohorts, rates did not increase when pts exposed to JAK inhibitors were included.



REFERENCES:

[1] Dougados et al. Ann Rheum Dis 2014; 73: 62-68.

[2] Parikh-Patel et al. Cancer Causes Control 2009; 20: 1001-1010.
Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Christina Viegelmann, CMC Connect, and funded by Pfizer Inc.
Disclosure of Interests: Toshihiro Matsui Speakers bureau: Astellas, Ayumi, Chugai, Daiichi-Sankyo, Eli Lilly, Ono, Pfizer Inc, Takeda, Tanabe-Mitsubishi, Consultant of: Pfizer Inc, Grant/research support from: Chugai, Naonobu Sugiyama Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Shigeyuki Toyoizumi Employee of: Pfizer R&D Japan, Fujio Matsuyama Consultant of: Pfizer Inc, Employee of: CRECON Medical Assessment Inc, Tatsunori Murata Consultant of: Pfizer Inc, Employee of: CRECON Medical Assessment Inc, Yukitomo Urata Speakers bureau: Asahi Kasei, Chugai, Eli Lilly, Pfizer Inc, Consultant of: AbbVie, Asahi Kasei, Chugai, Pfizer Inc, Kimito Kawahata Speakers bureau: Pfizer Inc, Consultant of: Pfizer Inc, Grant/research support from: Pfizer Inc, Shigeto Tohma Speakers bureau: Astellas, Ayumi, Chugai, Ono, Pfizer Inc, Takeda, Consultant of: Pfizer Inc
DOI: 10.1136/annrheumdis-2021-eular.365

POS0287 USE OF BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN RELATION TO THE RISK OF LYMPHOMA: A COHORT STUDY OF US VETERANS WITH RHEUMATOID ARTHRITIS

N. Singh[1], A. Peterson[2], A. Baraff[2], A. Korpak[2], M. Vaughan-Sarrazin[3], N. Smith[2], J. Curtis[4], N. Weiss[5]. *[1]1959 NE Pacific St, Internal Medicine, Seattle, United States of America*; *[2]1660 S Columbian Way, Epidemiologic Research and Information Center, Seattle, United States of America*; *[3]UI Hospitals and Clinics, 200 Hawkins Dr, Internal Medicine, Iowa City, United States of America*; *[4]University of Alabama at Birmingham, Internal Medicine, Birmingham, United States of America*; *[5]University of Washington School of Public Health, Epidemiology, Seattle, United States of America*

Background: Epidemiologic studies suggest that disease duration and degree of inflammatory activity of rheumatoid arthritis (RA) contribute to lymphoma development. However, the association of the use of biologic disease modifying anti-rheumatic drugs (bDMARDs) in patients with RA on lymphoma risk needs further evaluation.
Objectives: Examine the effect of administration of bDMARDS on the incidence of lymphoma in an inception cohort of RA.
Methods: We identified patients diagnosed with RA in any US Veterans Affairs (VA) facility from 1/1/2002 and 12/31/2018 using the Veteran's Health Administration (VHA) databases. To be included, each patient was required to meet the following criteria: 1) 2+ RA diagnostic codes at least 7 days apart but no more than 365 days apart 2) a prescription for a conventional synthetic DMARD (csDMARD) within 90 days of the first RA diagnosis 3) One inpatient or outpatient visit 30 days to 2 years preceding first RA diagnosis (indicating they are a regular user of the VHA). We excluded patients for any of the following if they preceded the first RA diagnosis: 1) a prior single RA diagnostic code 2) a prescription for any DMARD medication 3) a concomitant diagnosis of another inflammatory arthritis (e.g. psoriatic arthropathy) 4) a diagnosis of lymphoma. Index date for the study is the date of the first qualifying RA diagnosis. Lymphoma diagnoses were identified through VHA records using the International Classification of Diseases-Oncology codes.
Results: We identified 27,536 veterans with RA in the study period meeting the inclusion and exclusion criteria. Of these, 53% (n=14,705) were in the age range 60 to 80 years. The cohort was 89% male, 75.5% White, 13.7% African American. Over the study period, 1.2% (n=332) of the study population developed a lymphoma.
Conclusion: Using the nationwide VHA we have identified a large inception cohort of patients with RA of whom 1.2% developed lymphoma over study follow-up. This data will be used in future analyses to produce estimates of the effect of biologic medications on lymphoma risk, adjusting for confounding by indication and other variables.

Table 1. Baseline characteristics of the cohort based on bDMARD exposure status

Characteristic	bDMARD-naive (n= 19,095)	bDMARD-exposed (n=8,441)
Overall Lymphomas		
Age (years)	171	161
18-40	4	6
40-60	63	78
60-80	100	74
>80	4	3
Males	17,206 (90%)	7,270 (86%)
Race		
White	14,150 (74%)	6,627 (76%)
Black	2,674 (14%)	1,090 (13%)
Asian	96 (0.5%)	46 (0.5%)
Native American or Pacific Islander	371 (2%)	187 (2.2%)
Missing	1,804 (9%)	491 (6%)

Acknowledgements: The work in this abstract is supported by Investigator Award from the Rheumatology Research Foundation to Dr Singh.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3395

POS0288 A KEY TIF1Γ EPITOPE MAY FACILITATE THE IDENTIFICATION OF PATIENTS AT HIGHEST RISK OF CANCER ASSOCIATED MYOSITIS

V. Riddell[1], F. Mcmorrow[2], A. Oldroyd[3], C. Deakin[4], J. Lamb[3], H. Chinoy[3,5], L. Wedderburn[4,6], S. Bagby[1], N. Mchugh[2], S. Tansley[2,7]. *[1]University of Bath, Biology and Biochemistry, Bath, United Kingdom*; *[2]University of Bath, Pharmacy and Pharmacology, Bath, United Kingdom*; *[3]University of Manchester, NIHR Manchester Musculoskeletal Biomedical Research Centre, Manchester, United Kingdom*; *[4]University College London, GOS Institute of Child Health, London, United Kingdom*; *[5]Salford Royal NHS Foundation Trust, Rheumatology, Manchester, United Kingdom*; *[6]Great Ormond Street Hospital, Rheumatology, London, United Kingdom*; *[7]Royal United Hospitals Bath NHS Foundation Trust, Rheumatology, Bath, United Kingdom*

Background: The myositis specific autoantibody anti-TIF1γ targets TRIM33, a TRIM family proetin with a PHDBromo domain at the C terminal end. Anti-TIF1γ is strongly associated with malignancy in adult patients with idiopathic inflammatory myopathies (IIM). Intriguingly, anti-TIF1γ is also the most common autoantibody in juvenile-onset IIM but younger patients with anti-TIF1γ do not have an increased risk of cancer (1-3). Genetic studies have consistently shown human leukocyte antigen (HLA) to be the strongest risk factor for IIM. Adult and juvenile-onset patients with anti-TIF1γ have recently been shown to have different associations at the *HLA-DQB1* locus (4). This could be due to differences in the key TIF1γ epitopes and may relate to differences in aetiology, such as malignancy in adults versus other environmental factors in juvenile onset disease.
Objectives: To identify key epitopes targeted by anti-TIF1γ antibody in patients with IIM and establish if different TIF1γ epitopes are targeted in patients with and without malignancy.
Methods: Patient plasma/serum samples were obtained from UK Juvenile Dermatomyositis Cohort and Biomarker and UKMyoNet studies. Autoantibody status had previously been determined by immunoprecipitation. Cancer data was collated from the UK Health and Social Care Information Centre and cancer associated IIM (CAM) defined as that occurring within 3 years of IIM diagnosis. An in house ELISA was developed using a purified TIF1γ fragment comprising residues 882-1090, produced in *E.coli,* corresponding to the PHDBromo protein domain. An ELISA cut-off of 5SD above the mean of 38 healthy control samples was used.
Results: 38 healthy controls, and 117 anti-TIF1γ IIM patient sera (60 juvenile onset) were analysed for reactivity to the TIF1γ PHDbromo domain.
No healthy controls were positive. Anti-TIF1γPHDbromo was more common in JDM: 18 (30%) juvenile patients and 6 (10.5%) adult patients were positive, p=0.01. Additional data was available for 39 adult patients (82% female, median age 52 (IQR 38-64)). Anti-TIF1γPHDbromo was only found in CAM patients plus one young adult non-CAM patient aged 27 years at disease onset, p =0.07 (p=0.02 for patients >30 years at disease onset), see Table 1. No juvenile patients had a history of malignancy.

Table 1. Anti-TIF1γPHDbromo in 39 adult patients with cancer data available

	anti-TIF1γPHDbromo positive	anti-TIF1γPHDbromo negative
Cancer associated myositis n(%)	5[a] (83)	12(36)
Myositis not associated with cancer n(%)	1[b](17)	21(64)
Total	6	33

a. Median age 64 yearsb. Age 27 years

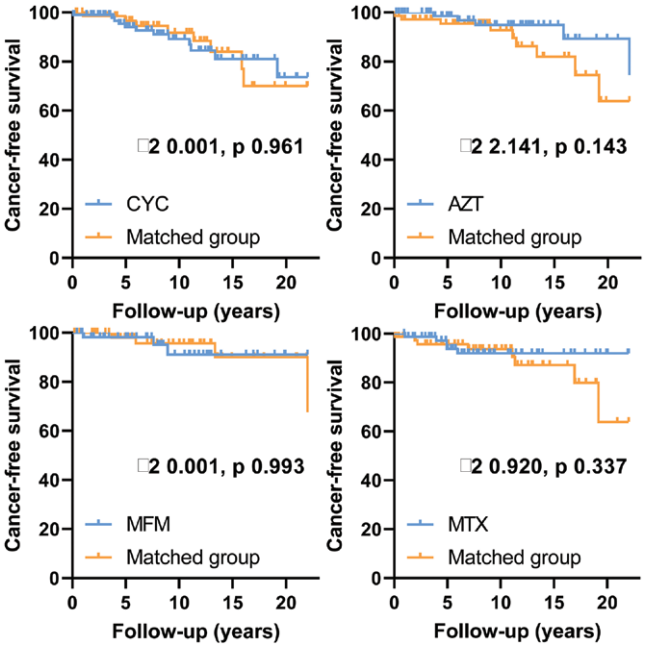
Conclusion: The TIF1γ PHDBromo domain is an important epitope and autoantibody reactivity is more common in patients with juvenile-onset disease and adults with CAM. The distinction between adult and juvenile-onset IIM is arbitrary and it is relevant that the only adult with anti-TIF1γPHDbromo not to have malignancy was just 27 years old. Our numbers are small and further work is needed to establish if anti-TIF1γPHDbromo, and indeed other TIF1γ epitopes, could help identify patients at highest risk of malignancy, and how this relates to our understanding of IIM aetiopathogenesis. Our findings may add weight to the theory that the development of IIM in younger patients occurs after immune-mediated resolution of a pre-cancer event.
REFERENCES:
[1] Oldroyd A, Sergeant JC, New P et al. The temporal relationship between cancer and adult onset anti-transcriptional intermediary factor 1 antibody-positive dermatomyositis. Rheumatology. 2019;58(4):650-655
[2] Tansley SL, Simou S, Shaddick G et al. Autoantibodies in juvenile-onset myositis: Their diagnostic value and associated clinical phenotype in a large UK cohort. J Autoimmun. 2017;84:55-64

[3] Fujimoto M, Hamaguchi Y, Kaji K et al. Myositis-specific anti-155/140 autoantibodies target transcription intermediary factor 1 family proteins. Arthritis Rheum. 2012;64(2):513-22.
[4] Rothwell S, Chinoy H, Lamb JA et al. Focused HLA analysis in Caucasians with myositis identifies significant associations with autoantibody subgroups. Ann Rheum Dis. 2019;78(7):996-1002.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.964

POS0289 CANCER RISK IN IMMUNOSUPPRESSED SCLERODERMA PATIENTS: A PROPENSITY SCORE MATCHING ANALYSIS

L. Verardi[1], E. De Lorenzis[1], G. Natalello[1], L. Gigante[1], M. A. D'agostino[1], S. L. Bosello[1]. [1]*Fondazione Policlinico Universitario A. Gemelli IRCCS - Catholic University of the Sacred Heart, Rheumatology Unit, Rome, Italy*

Background: An increased incidence of cancer in patients with systemic sclerosis (SSc) is well-established[1]. Current knowledge about the onco-transforming power of immunosuppressive treatments in both non-rheumatological and rheumatological pathologies, suggests an increased incidence of hematological and solid neoplasms[2]. Evidences on the possible role of the immunosuppressants in the onset of cancer during SSc are lacking.
Objectives: To evaluate the incidence of malignancies in SSc patients exposed to immunosuppressive therapy.
Methods: The incidence of neoplasia in a cohort of 600 patients with SSc was evaluated retrospectively. Patients diagnosed with malignancy within 36 months from SSc onset were excluded from the analysis since suspected for paraneoplastic form. Patients exposed to methotrexate, cyclophosphamide, azathioprine and mycophenolate were confronted with a group comparable for age at onset, sex, disease variant, autoantibodies and exposure to other disease-specific therapies, using propensity score matching analysis. The considered follow-up was between the clinical onset and the diagnosis of cancer or the last available visit or the twenty-fifth year of illness.
Results: The analysis was carried out on 526 patients observed for an average period of 12.1 ± 6.0 years (males 9.5%, age at onset 49.0 ± 15.3 years); 24.9% had diffuse cutaneous variant of the disease and 39.0% and 34.8% were respectively positive for anti-centromere and anti-Scl70 antibodies. During the follow-up, 19.0% of patients were exposed to cyclophosphamide, 15.3% to azathioprine, 14.4% to methotrexate and 11.6% to mycophenolate mofetil. Sixty-five cancer diagnoses were made after the 36th month from onset (incidence 1.02: 100 patients/year), comprising 16 mammary cancers, 12 cancers of the gastro-intestinal tract, 11 cancers of the head-neck area, 10 cancers of the lungs, 9 cases of skin-cancer, 5 haematological malignancies and 1 brain tumour. The incidence of cancers did not differ in relation to treatment with cyclophosphamide (X^2 = 0.001, p = 0.961), azathioprine (X^2 = 2.141, p = 0.143), mycophenolate mofetil (X^2 = 0.001, p = 0.993) or methotrexate (X^2 = 0.920, p = 0.337) (Figure 1).
Conclusion: Our data are consistent with an increased incidence of neoplasms in the course of SSc, with a rate that appears almost doubled compared to the general Italian population with similar sex and age distribution (0.55: 100 patients/year; Italian Association of Tumor Registries data[3]). In our SSc cohort this risk is independent of exposure to immunosuppressive drugs commonly used for the treatment of scleroderma disease.



REFERENCES:
[1] Akira O et al. Cancer Incidence in Systemic Sclerosis: Meta-Analysis of Population-Based Cohort Studies. Arthritis & Rheumatism. 2013
[2] Zitvogel L et al. Cancer despite immunosurveillance: immunoselection and immunosubversion. Nat Rev Immunol. 2006
[3] Registri Tumori di popolazione in Italia: la Banca Dati AIRTUM (Associazione Italiana Registri Tumori). 2020
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2701

POS0290 PREDICTING RISK FACTORS OF MALT LYMPHOMA IN SJÖGREN'S SYNDROME

L. Chatzis[1], V. Pezoulas[2], A. Goules[1], I. Stergiou[1], C. Mavragani[3], H. M. Moutsopoulos[4], M. Voulgarelis[1], D. Fotiadis[2], A. Tzioufas[1]. [1]*School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Ag thoma 15, Greece*; [2]*University of Ioannina, Unit of Medical Technology and Intelligent Information Systems, Ioannina, Greece*; [3]*School of Medicine, National and Kapodistrian University of Athens, Physiology, Athens, Greece*; [4]*Academy of Athens, Chair Medical Sciences/Immunology, Greece, Athens, Greece*

Background: Primary Sjögren Syndrome (SS) is a slowly progressive systemic autoimmune disease complicated by lymphoma, with mucosa associated lymphoid tissue (MALT) type being the most common lymphoma form. Several predictors related to pSS associated lymphomas have been described, but there are no studies focusing on specific risk factors for the MALT histologic subtype.
Objectives: To identify predictors at SS diagnosis for MALT lymphoma development in pSS patients using simple clinical features.
Methods: From 815 SS patients of a single center fulfilling the 2016 ACR/EULAR criteria, those with subsequent development of MALT lymphoma according to the 2016 WHO classification were identified and matched in 1:2 ratio, with non-lymphoma SS control patients according to age, disease duration from SS diagnosis and gender. Lymphoma patients diagnosed within a year from SS diagnosis were excluded from the current study. Clinical, laboratory, histologic data as well as the ESSDAI scores at the time of SS diagnosis were recorded and compared between lymphoma and non-lymphoma patients. Independent lymphoma predictors were identified by a data driven Fast Correlation Based Feature selection (FCBF)/Logistic Regression (LR) algorithm.
Results: A unified dataset of 57 MALT lymphoma patients and 114 non lymphoma controls along with 39 features/variables was generated. The median age of SS diagnosis and the disease duration from SS diagnosis to lymphoma diagnosis (lymphoma group) or last follow up (control group) was 50,5 years old (range 25-77) and 7 years (range 0- 30) for the control group and 50 years old (range 24-70) and 8 years (range 1 -30) for the lymphoma group, respectively. MALT lymphoma patients presented more frequently with palpable purpura (23,2% vs 5,3% p=0,001), cryoglobulinemia (30,2% vs 1,6% p<0,0001), low C4 serum levels (62,9% vs 32,1% p=0,0003), rheumatoid factor (76,9% vs 56,1% p=0,01), anti La/SSB antibodies (33,9% vs 50,8% p=0,049) and higher median ESSDAI score (5 vs 2, p<0,0001). In contrast, autoimmune thyroiditis was more prevalent in controls (48,2% vs 18,6%, p=0,004). The FCBF/LR model revealed cryoglobulinemia (p=0,03) and ESSDAI at SS Diagnosis (p<0,001) as the only independent lymphoma predictors.
Conclusion: MALT is the predominant pSS related lymphoproliferative histologic type, associated with systemic disease activity and vasculitic manifestations at SS diagnosis. Cryoglobulinemia and ESSDAI score were proven independent risk factors for MALT lymphoma development.

Table 1. An FCBF-based multivariable logistic regression analysis results for investigating risk factors for MALT lymphoma development

Prominent feature	Regression coefficient	Odds ratio	p-value	CI low	CI upper
Cryoglobulinemia	1.67	5.342	0.033*	1.18	24.327
Total ESSDAI at diagnosis	0.28	1.318	<0.001*	1.208	1.439
Kidney involvement	0.07	1.069	0.5	0.101	0.351

•< 0.05 (95% confidence interval). The rest of the features that participated in the analysis include the following: Palpable purpura, Low C4, Salivary gland enlargement, Lacrimal gland enlargement, ANA Titers, RF, Focus score at Sjögren diagnosis, PNS involvement, Anti-La, Disease duration from SS onset to SS diagnosis, Neutrophils<1500, Autoimmune thyroiditis, Lung involvement – interstitial disease Type, Lymphocytes<1000, Lymphadenopathy fixed, Arthralgias, Dry eyes, Raynaud, Gender, Age at Sjögren diagnosis, Dry mouth, Aca, Hb<12.5 g/dL, ANA, Disease duration from SS Diagnosis to Lymphoma diagnosis or last follow up, Anti-Ro, Arthritis, WBC<4000/μL, Lung involvement bronchocentric disease, Interstitial renal disease, PLTs<100.000/μL, Liver involvement-PBC, Liver involvement–autoimmune hepatitis, CNS involvement.•AUC=0.78

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2260

POS0291 THE IMPACT OF DRUG INDUCED AND OTHER RHEUMATIC MUSCULOSKELETAL DISORDERS (MD) ON THE QUALITY OF LIFE (QOL) OF CANCER PATIENTS RECEIVED ANTICANCER DRUG TREATMENT

A. Koltakova[1], A. Lila[2], L. P. Ananyeva[1], A. Fedenko[3]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Adminisrtation, Moscow, Russian Federation*; [3]*National Medical Research Radiological Centre of the Ministry of Health of the Russian Federation, Department of Drug Treatment of Cancer, Moscow, Russian Federation*

Background: Pts with cancer may have MD that can be caused by neoplastic/ paraneoplastic disease, rheumatic diseases or be induced by anticancer drug treatment. There is no data about MD influence on the QoL of cancer patients. The EORTC QoL questionnaire (QLQ)-C30 is a valid questionnaire designed to assess different aspects (Global health (GH), Functional (FS) and symptoms (SS) scales) that define the QoL of cancer patients [1].
Objectives: The objective of the study was to assess the impact of drug induced and other types of MD on the QoL of cancer patients that received anticancer drug treatment by using of EORTC QLQ-C30 v3.0.
Methods: The sampling of 123 pts (M/F – 40/83; mean age 54.4±12.8) with breast (32,5%), gastrointestinal (17%), ovary (8%), lung (7%) and other cancer was observed by rheumatologist in the oncology outpatient clinic. All pts received anticancer drug treatment: chemotherapy (104 pts), target therapy (16 pts) checkpoint-inhibitors (14 pts), hormone therapy (13 pts) in different combinations. 102(82.9%) of 123pts had MD include arthritis (12 pts), synovitis (5 pts), arthralgia (66 pts), periarthritis (34 pts), osteodynia (13 pts). There were 58 pts (group 1; M/F – 14/44; mean age 52.5±12.2) with anticancer drug treatment induced MD and 44 pts (group 2; M/F – 16/27; mean age 57.6±13.5) with other type of MD include 26 pts with skeletal metastasis. The were 21 pts (group 3; M/F – 10/11; mean age 52.9±11.1) without MD. All pts fulfilled EORTC QLQ-C30 v3.0 (tab.1).

Table 1. The median [Q1;Q3] of results of GH, SS and SS of EORTC QLQ-C30

Scale	Subscale	Group1	Group2	Group3
GH		58.3[50;58]	58.3[41.7;83.3]	50[50;66.7]
FS*	Physical functioning	73.3[60;86.7]	73.3[66.7;86.7]	86.7[80;93]
	Role functioning	66.7[66.7;100]	83.3[50;100]	100[83;100]
	Emotional functioning	83.3[66.7;100]	75[66.7;91.7]	91.6[83.3;100]
	Social functioning	83.3[66.7;100]	83.3[50;100]	100[83.3;100]
SS*	Pain	33.3[0;50]	16.7[0;33.3]	0[0;16.7]

*There are only the scores that had got a statistical difference between the groups.

Kruskal-Wallis H and post-hoc (Dwass-Steel-Critchlow-Fligner (DSCF) pairwise comparisons) tests for data analysis were performed.
Results: A Kruskal-Wallis H test has shown a statistically significant difference in physical ($\chi2(2)=7.54$; p=0.023), role ($\chi2(2)=9.87$; p=0.007), emotion ($\chi2(2)=7.69$; p=0.021) functioning and pain ($\chi2(2)=8.44$; p=0.015) scores between the different groups. A post-hoc test with DSCF pairwise comparisons of median has shown a statistically significant difference between 1 and 3 groups (W=3.904; p=0.016) for physical functioning, between 2 and 3 groups (W=3.35; p=0.004) for role functioning, between 2 and 3 groups (W=4.03; p=0.012) for emotional functioning, between 1 and 3 groups (W=-3.97; p=0.014) for pain scale.
Conclusion: The study has shown that MD associated with anticancer drug treatment adversely affected the QoL of cancer patients received anticancer drug treatment by reducing a physical functioning and by increasing pain scores. Presence of other types of MD adversely affect the QoL by reducing emotional and role functioning.
REFERENCES:
[1] Aaronson NK,et al.The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst.1993;85(5):365-376. doi:10.1093/jnci/85.5.365
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2286

POS0292 OSTEOPOROSIS IN BREAST CANCER PATIENTS ON AROMATASE INHIBITORS THERAPY: ABOUT 200 CASES

R. Assadi[1], K. Nassar[1], S. Janani[1]. [1]*CHU ibn rochd, Rheumatology, Casablanca, Morocco*

Background: Breast cancer is the most common cancer affecting women both before and after the menopause. Aromatase inhibitors (AIs) used as adjuvant therapy cause bone loss and increase the risk of osteoporosis (OP) (1).
Objectives: To assess the bone status and the frequency of OP in breast cancer patients using AIs.
Methods: We conducted a retrospective study in the rheumatology department, over 5 years (2016-2020).
Inclusion criteria: patients followed for breast neoplasm in oncology department on AIs therapy and referred to rheumatology department for bone evaluation.
All of these patients underwent an evaluation of bone mineral density (BMD) and phosphocalcic assessment.
Exclusion criteria: patients treated by another type of hormone therapy and having other risk factors for OP.
Results: 200 breast cancer women were enrolled for the study, 92 patients (46%) were treated with AIs, the average age was 58.22 years (41 - 75 years) with an average age of discovery of the breast cancer of 46.75 years and the average time between the start of AIs therapy and the diagnosis of OP was 21.6 months. the characteristics of the patients are summed up in Table 1.
97% of patients were postmenopausal and 38% of them had menopause secondary to treatment.
In AIs users, 85 patients (92.3%) were osteoporotic, and 11% had bone fractures. In regard to osteodensitometry measurement, lumbar spine was the most affected site (88%) with mean T score of -2.98 and mean BMD of 0.854, followed by femoral neck (17%) with mean T score of - 2.8 and mean BMD of 0.740 and total hip (14%) with mean T score of -3.10 and mean BMD of 0.497.
The cancer was metastatic in 15.18% patients, 75% of the group had bone metastasis and 25% had visceral metastasis.
The phosphocalcic status of the osteoporotic patients was: mean calcemia: 92.83 mg / l, mean calciuria: 131.8 mg / 24h, mean phosphatemia: 48.09 mg / l, mean 25 OH Vit D level: 19.78 ng / ml, mean PTH: 79 pg / ml.
Osteoporotic patients were treated with bisphosphonates, 60% women had received Alendronate, 17% Risedronate and 12% Zoledronate in addition to dietary measures and correction of calcium and vitamin D deficiency.
Conclusion: AIs are correlated with a high risk of OP and fractures in 30% of patients (2), the frequency of OP in our series is estimated at 42.5%.
Assessment of bone status and OP clinical risk factors should be systematic in all breast cancer patients receiving adjuvant AIs therapy.
Bisphosphonates appear to be beneficial in treating secondary OP, in preventing bone fractures, and in reducing the incidence of breast cancer bone metastases.
REFERENCES:
[1] Aromatase Inhibitor-Associated Bone Loss Clinical Considerations P Shubham, L. Shapiro Drugs 2008; 68 (18): 2591-2600
[2] Aromatase inhibitor-associated bone loss and its management with bisphosphonates in patients with breast cancer M.Bauer, J. Bryce, P.Hadji Breast Cancer. 2012; 4: 91–101

Table 1. Characteristics of osteoporotic patients using AIs therapy

	Results
Total of patients	92 (46%)
Mean age	58.22 years
Mean age of breast cancer diagnosis	46.75 years
Delay between AIs therapy and OP	21.6 months
Post menopausal patients	97%
Menopausis due to AIs	38%
Osteoporotic patients	85 (92.3%)
Fractures	11%
Sites of OP in osteodensitometry	
lumbar spine	88%
femoral neck	17%
total hip	14%
Cancer metastasis	15.18%
Bone	75%
Visceral	25%
Phosphocalcic status (mean values)	
calcemia	92.83 mg / l
calciuria	131.8 mg / 24h
phosphatémie	48.09 mg / l
25 OH vitaminD	19.78 ng / ml
PTH	79 pg / ml
Biphosphanates therapy	
Alendronate	60%
Risedronate	17%
Zoledronate	12%

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2886

POS0293

TRHEUMA REGISTRY PROVIDES FIRST EVIDENCE OF DIFFERENT COURSE OF RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS AND TUMOUR RESPONSE RATES DEPENDING ON THE TUMOUR ENTITY

L. Diekmann[1], L. Daniello[2], J. Kunz[2], J. Leipe[3], H. M. Lorenz[1], J. Hassel[4], K. Jordan[1], P. Christopoulos[2], K. Benesova[1]. [1]*University Hospital Heidelberg, Department of Medicine V, Hematology, Oncology and Rheumatology, Heidelberg, Germany*; [2]*Thoraxklinik Heidelberg, Department of Thoracic Oncology, Heidelberg, Germany*; [3]*University Hospital Mannheim, Division of Rheumatology, Department of Medicine V, Mannheim, Germany*; [4]*University Hospital Heidelberg, Department of Dermatology and National Center for Tumor Diseases, Heidelberg, Germany*

Background: Rheumatic immune-related adverse events (irAE) are associated with a better tumour response to immune checkpoint inhibitors (ICI). In contrast to other irAEs, their potentially chronic course may require long-term immunosuppressive treatment.
Objectives: Our registry-based study analyses real-world data on the characteristics and outcome of rheumatic irAEs and underlying malignancy. Herein, we present first evidence that these parameters and the optimal clinical management may differ depending on the tumour entity.
Methods: The TRheuMa registry is a prospective long-term observational study of a patient cohort suffering from rheumatic side effects of cancer therapies with focus on ICI. It is part of the MalheuR project initiated in July 2018 at the University Hospital Heidelberg to explore interrelations of malignancies and RMDs.
Results: 64 patients were recruited due to a rheumatic irAE under ICI treatment (nivolumab n=30, pembrolizumab n=33, ipilimumab n=12, PD-L1i n=5, ipi/nivo n=10) with a follow-up of up to 30 months. Of these, 47% had NSCLC and 41% melanoma. In local cohorts of patients receiving ICI, 4% of NSCLC (n total=888) and 13% of melanoma (n total=195) developed a rheumatic irAE. 7% of NSCLC and 23% of melanoma patients experienced a flare of a pre-existing RMD. De novo irAE mostly resembled phenotypes of spondyloarthritis both in NSCLC (43%) as well as in melanoma patients (33%). CRP levels were increased in 83% of NSCLC and 71% of melanoma patients. Almost all irAE patients showed autoantibody negativity and signs of inflammation in ultrasound examination (96%). Comparison of best responses to treatment in patients with and without rheumatic irAE in melanoma and without any irAE in NSCLC patients were as following: Complete remission (CR) in 48% vs. 4% of melanoma patients and partial remission (PR) in 68% vs. 41% of NSCLC patients. In accordance with our severity-based treatment algorithm, 25% of the melanoma patients in CR and 16% of the NSCLC patients in PR needed add-on DMARDs for sufficient irAE-treatment. ICI-treatment was discontinued in 7 cases (17% NSCLC, 8% melanoma)
Conclusion: Prospective real-world data from the TRheuMa-registry provide first evidence that rheumatic irAE have distinct characteristics depending on the underlying malignancy. Oncological outcome was better with rheumatic irAE than in their absence and this effect was more pronounced in melanoma patients despite a larger use of immunosuppressants for irAE-treatment.
Disclosure of Interests: Leonore Diekmann: None declared, Lea Daniello: None declared, Julia Kunz: None declared, Jan Leipe Consultant of: Pfizer; Novartis; Honoraria (self), Abbvie; Astra Zeneca; BMS; Celgene; Hospira; Janssen-Cilag; Gilead; LEO Pharma; Lilly; MSD; Roche; Sanofi; UCB., Grant/research support from: Research grant/Funding (self): Pfizer; Novartis; Honoraria (self), Hanns-Martin Lorenz Consultant of: Abbvie; BMS; MSD; Pfizer; Celgene; Roche; Chugai; Medac; GSK; Honoraria (self), Novartis; UCB; Janssen-Cilag; Astra Zeneca; Lilly, Grant/research support from: Research grant/Funding (institution): Abbvie; BMS; MSD; Pfizer; Celgene; Roche; Chugai; Medac; GSK; Honoraria (self), Research grant/Funding (institution), Novartis; UCB; Janssen-Cilag; Astra Zeneca; Lilly; Research grant/Funding (institution): Baxter; SOBI; Biogen; Actelion; Mundipharma; Bayer Vital; Octapharm; Sanofi; Hexal; Thermo Fischer; Shire., Jessica Hassel Consultant of: MDS; Honoraria (self): Roche; Novartis; Pierre Fabre., Grant/research support from: BMS; Honoraria (self), Karin Jordan Consultant of: Advisory/Consultancy: Amgen; Merck; MSD; Riemser; Helsinn; Tesaro; Kreussler; Voluntis; Pfizer; Pomme-med; Hexal., Petros Christopoulos Consultant of: advisory board/lecture fees from AstraZeneca, Boehringer Ingelheim, Chugai, Novartis, Pfizer, Roche, Takeda., Grant/research support from: research funding from AstraZeneca, Novartis, Roche, Takeda, Karolina Benesova Grant/research support from: Foundations and Awards" commission of the University of Heidelberg: University of Heidelberg; AbbVie; Novartis; Rheumaliga Baden-Württemberg e.V
DOI: 10.1136/annrheumdis-2021-eular.591

POS0294

PROFILE OF SPINAL TUMORS IN RHEUMATOLOGY DEPARTMENTS

B. A. Hiba[1], H. Sahli[2], S. Boussaid[3], S. Nouicer[3], S. Jemmali[3], S. Rekik[2], M. Eleuch[1]. [1]*La Rabta, Rheumatology, Tunis, Tunisia*; [2]*La Rabta, Rheumatology, Tunis, Tunisia*; [3]*La Rabta, Rheumatology, Tunis, Tunisia*

Background: Spine tumors remain a hot topic because of their associated morbidity by affecting motor and sensory function. Contrary to metastatic spine disease (MSD), extremely prevalent, rise within or surrounding the spinal cord and/or vertebral column, primary spinal tumors are rare, 5% of all primary skeletal tumors and frequently benign (20%). The diagnostic delay of these tumors, even when benign, is associated with a poor prognosis. Establishing the correct diagnosis is heavily reliant on magnetic resonance imaging and histological confirmation.
Objectives: to provide an overview of the epidemiology, radiological and histopathological of spinal tumors diagnosed in a rheumatology department.
Methods: A retrospective study consisting of clinical characteristics analysis, laboratory and x-ray examinations, was performed on 40 patients who were hospitalised for a spinal tumor, in a rheumatology department, over 5-year period from 2015 to 2020.
Results: A total of 40 patients with a mean age of 66 ± 13.5 years [18-93] and a sex-ratio of 1.1, were included. The most common initial complaints were inflammatory back pain (67.5%) and fatigue (52.5%), with a median duration of 5 months. Physical examination abnormalities included lumbar stiffness (32.5%), radicular signs (18.7%), hepatomegaly (12.5%), and lymphadenopathy (17.5%). Neurological deficit was found in only 3 patients (7.5%). Hypercalcemia (corrected serum calcium > 105 mg/l), and anemia (hemoglobin (Hb) < 100 g/l in female, Hb <110g/l in male) were present initially in respectively 47.5% and 46.3% patients, while biological inflammatory syndrome was present in 89.7% patients (median C-reactive protein of 44.7). Tumor markers were performed in 12 patients and they were positive in 9 of them.
Plain radiographs findings were vertebral compression fractures (43.6%), osteolytic lesions (30.8%) and osteoblastic lesions (12.5%). Lumbar spine was the most affected (57.5%), followed by the dorsal spine (45%). Magnetic resonance imaging (MRI) was performed in 55%, and the most common lesion was low signal intensity on T1-weighted sequences and high signal intensity on T2-weighted sequences (68.1%).
In our study, only one patient was diagnosed for a myxopapillary ependymoma, a benign primary spinal tumor characterised by a metastatic dissemination risk. For the rest (39 patients), the diagnosis of bone metastasis, multiple myeloma (57.7%), and of solid tumor cancers (40%), were established. Primary cancers were mainly prostate cancer (37.5%), lung cancer (18.7%) and kidney cancer (18.7%). By a median follow-up time of 25 months, overall survival rate was 30%.
Conclusion: Extradural lesions are the most common, and are typically metastatic. Special attention should be pain to the patient's medical history and laboratory abnormalities. In fact, an early diagnosis requires a high index of clinical suspicion.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3905

POS0295

NO CAUSAL EFFECTS OF GENETICALLY DETERMINED SERUM URATE LEVELS ON THE RISK OF ALL-CAUSE AND SITE-SPECIFIC CANCER: A MENDELIAN RANDOMIZATION STUDY

T. Fatima[1], Y. Borné[2], M. Dehlin[3], S. Burgess[4], A. Mason[5], L. T. H. Jacobsson[6], M. C. Kapetanovic[7]. [1]*University of Gothenburg, Department of Rheumatology and Inflammation Research, Göteborg, Sweden*; [2]*University of Lund, Department of Clinical Sciences, Malmö, Sweden*; [3]*University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; [4]*University of Cambridge, MRC Biostatistics Unit, School of Clinical Medicine, Cambridge, United Kingdom*; [5]*University of Cambridge, Cardiovascular Epidemiology Unit, School of Clinical Medicine, Cambridge, United Kingdom*; [3]*University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; [7]*University of Lund, Department of Clinical Sciences, Lund, Sweden*

Background: Positive associations between urate levels and gout and the risk of some cancer types (urogenital, prostate, gastrointestinal and lung) have been reported in a number of observational studies; however, whether the relationship is causal remains uncertain.
Objectives: The study aim was to evaluate a causal effect of genetically determined serum urate (SU) concentrations on cancer risks (overall and major cancer types) in individuals with European ancestry using Mendelian randomization (MR) analyses design.
Methods: We used the individual-level data from two population-based Swedish cohorts including middle-aged subjects (mean follow-up = 21.2 years), Malmö Diet Cancer and Malmö Preventive Project (MDC/MPP), for one-sample MR setting. Data from a total of 17,597 individuals (n = 17,597 for SU at baseline, diagnoses during follow-up: 5659 for all-cause, 516 for bladder, 545 for lung, 791 for bowel, 1521 for prostate and 729 for breast cancer) was included. For two-sample MR, summary-statistic data for SU was obtained from Global Urate Genetic Consortium (GUGC: n = 110,347), while UK-Biobank data was employed for several major cancer outcomes (n = 36,815 for all-cause, 2,245 for

bladder, 2,590 for lung, 4,488 for bowel, 6,474 for prostate and 10,274 for breast cancer). The definitions for cancer endpoints were matched for ICD9 and 10 codes between MDC/MPP and UK-Biobank cohorts. For both MR settings, a set of 26 urate-associated single nucleotide variants was selected to build-up the SU instrument (*SU-instr*) to test for a causal effect of SU on cancer outcomes. Statistical analysis, adjusted for age and sex, was done using multiple conventional MR methodologies and MR package in R (v4.0.2). A $p < 0.05$ was designated as statistically significant.

Results: We found no causal effect of our *SU-instr* on neither all-cause nor site-specific cancer across all MR analyses (all $p > 0.05$). In MDC/MPP, *SU-instr* did not show a causal effect on the risk of all-cause [OR = 1.06, $p = 0.32$], bladder [OR = 0.96, $p = 0.84$], lung [OR = 1.26, $p = 0.17$], bowel [OR = 0.96, $p = 0.81$], prostate [OR = 1.05, $p = 0.62$], and breast [OR = 0.99, $p = 0.98$] cancer. Similar findings were made in the two-sample settings. Detailed results are provided in Table 1.

Conclusion: Our MR study, using a series of causal inference approaches, does not support a causal effect of genetically determined SU for major cancer outcomes. There is no evidence to support changing SU levels by lifestyle or pharmacological intervention to attenuate the risk of major cancer types.

Table 1. Results from a range of MR analyses for causal effect of SU on cancer risk in MDC/MPP (one-sample MR) and GUGC and UK-Biobank (two-sample MR) cohorts

One-sample MR

	IVW			2SLS		GRS	
Cancer type	OR (95% CI)	*p*-causal	*p*-Het	OR (95% CI)	*p*-causal	OR (95% CI)	*p*-causal
Bladder	0.96 (0.68; 1.36)	0.84	0.55	0.99 (0.70; 1.42)	0.99	0.94 (0.67; 1.34)	0.76
Lung	1.26 (0.90; 1.77)	0.17	0.89	1.29 (0.91; 1.82)	0.14	1.26 (0.90; 1.77)	0.17
Bowel	0.96 (0.72; 1.28)	0.81	0.44	0.95 (0.72; 1.27)	0.77	0.97 (0.73; 1.28)	0.83
Prostate	1.05 (0.84; 1.31)	0.62	0.84	1.04 (0.83; 1.30)	0.72	1.04 (0.83; 1.30)	0.69
Breast	0.99 (0.74; 1.33)	0.98	0.11	0.98 (0.73; 1.32)	0.92	0.98 (0.73; 1.32)	0.94
All-cause	1.06 (0.93; 1.21)	0.32	0.6	1.07 (0.94; 1.21)	0.28	1.07 (0.94; 1.21)	0.29

Two-sample MR

	IVW			Weighted median		MR-Egger	
Cancer type	OR (95% CI)	*p*-causal	*p*-Het	OR (95% CI)	*p*-causal	OR (95% CI)	*p*-causal
Bladder	1.02 (0.88; 2.16)	0.77	0.36	1.03 (0.86; 2.10)	0.7	1.03 (0.83; 2.13)	0.75
Lung	0.86 (0.73; 1.08)	0.07	0.04	0.86 (0.73; 1.09)	0.09	0.84 (0.66; 1.16)	0.15
Bowel	0.82 (0.69; 1.02)	0.03	< 0.0001	0.89 (0.78; 1.06)	0.06	0.92 (0.72;1.67)	0.52
Prostate	1.00 (0.91; 2.64)	0.97	0.72	0.98 (0.88; 2.17)	0.77	0.94 (0.83; 1.45)	0.37
Breast	0.97 (0.88; 1.95)	0.67	0.0002	1.00 (0.91; 2.70)	0.99	0.95 (0.81; 1.59)	0.46
All-cause	0.96 (0.90; 1.20)	0.18	< 0.0001	0.97 (0.92; 1.23)	0.21	0.93 (0.86; 1.12)	0.11

OR; odds ratio, 95% CI; 95% confidence interval, IVW; Inverse variance weighted method, 2SLS; two-stage least square, GRS; genetic risk score, *p*-Het; *p*-value for heterogeneity.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2416

Public Health, Health Services and Health Economics

POS0296 DOSING OF BDMARDS IN AXSPA AND PSA IN A REAL WORLD SETTING

A. Regierer[1], A. Weiß[1], D. Poddubnyy[1,2], H. Kellner[3], F. Behrens[4], G. Schett[5], J. Braun[6], J. Sieper[2], A. Strangfeld[1]. [1]*German Rheumatism Research Centre, Epidemiology Unit, Berlin, Germany*; [2]*Charité University Medicine Berlin, Rheumatology, CBF, Berlin, Germany*; [3]*Rheumatology Practice, Rheumatology, Munich, Germany*; [4]*Goethe University, Rheumatology and Fraunhofer Project Group Translational Medicine and Pharmacology, Frankfurt, Germany*; [5]*Friedrich Alexander University Erlangen-Nuremberg and Universitatsklinikum Erlangen, Department of Internal Medicine 3, Erlangen, Germany*; [6]*Ruhr-University, Rheumazentrum Ruhrgebiet Herne, Bochum, Germany*

Background: The treatment of patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) has been revolutionised by the introduction of biologic DMARDs targeting TNF, IL17, and IL23 inhibitors (i). In Germany, about 30-50% of axSpA and PsA patients receive treatment with bDMARDs. Although many patients benefit from these drugs, in some patients effectiveness of the standard dose may be insufficient and higher doses are used.

Objectives: To describe dosing of TNFi and non-TNFi bDMARDs over a 2 year period in a real world cohort of patients with axSpA and PsA managed by rheumatologists.

Methods: RABBIT-SpA is a prospective longitudinal cohort study including axSpA and PsA patients enrolled at the start of a new conventional treatment (including NSAID) or b/tsDMARD treatment. Description of dosing of TNFi (adalimumab bio-original (bo), adalimumab bio-similar (bs), etanercept bo, etanercept bs, golimumab, certolizumab) in comparison to nonTNFi-bDMARDs (secukinumab, ustekinumab, ixekizumab, guselkumab) in axSpA and PsA. Standard dosing was defined according to the current labels for axSpA and PsA.

Results: 1628 patients (axSpA: n=903, PsA: n=725) were included in this analysis. At inclusion mean age was 44 years in axSpA and 51 years in PsA. 44% of patients with axSpA and 58% of those with PsA were female. The mean disease duration of axSpA was 7.6 years, of PsA 6.4 years.

Standard doses of TNFi were used during a 2 year period in > 90% of patients with axSpA and PsA (Figure 1). In contrast, standard doses of non-TNFi-bDMARDs were only used in 70-80% of patients. The percentage of documented higher doses in patients with axSpA ranged from 20-30% at different time points. In PsA, this percentage increased from 27% at baseline to 44% at 2 years. On the other hand, TNFi were used in lower doses than the label in up to 9% and 7 % of patients with axSpA and PsA, respectively, after 2 years.

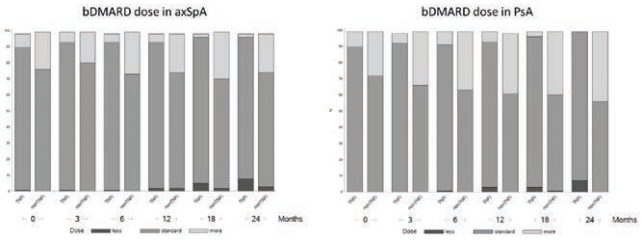


Figure 1. Percentages of patients with axSpA or PsA who received less than, equal to, or more than the approved doses of bDMARDs at baseline and at 5 follow-up visits.

Conclusion: While TNFi are used in licensed doses in most patients, non-TNFi-bDMARDs were often used in higher doses, which corresponds to higher doses approved in other indications like psoriasis. The effectiveness of this treatment strategy in axSpA and PsA needs to be analysed further.

Acknowledgements: RABBIT-SpA is supported by a joint, unconditional grant from AbbVie, Amgen, Biogen, Hexal, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, UCB, and Viatris.

We thank all participating patients and rheumatologists.

Disclosure of Interests: Anne Regierer Grant/research support from: AbbVie, Amgen, Biogen, Hexal, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, UCB, and Viatris., Anja Weiß Grant/research support from: AbbVie, Amgen, Biogen, Hexal, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, UCB, and Viatris., Denis Poddubnyy: None declared, Herbert Kellner: None declared, Frank Behrens: None declared, Georg Schett: None declared, Juergen Braun: None declared, Joachim Sieper: None declared, Anja Strangfeld Grant/research support from: AbbVie, Amgen, Biogen, Hexal, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, UCB, and Viatris

DOI: 10.1136/annrheumdis-2021-eular.2155

POS0297 HOSPITAL ADMISSIONS FOR PATIENTS WITH RHEUMATOID ARTHRITIS IN WESTERN AUSTRALIA HOSPITALS HAVE DECLINED OVER TIME

K. Almutairi[1], J. Nossent[1], D. Preen[2], H. Keen[1], C. Inderjeeth[1]. [1]*The University of Western Australia, School of Medicine, Perth, Australia*; [2]*The University of Western Australia, School of Population and Global Health, Perth, Australia*

Background: Rheumatoid arthritis (RA) represents a substantial burden on patients and society in terms of morbidity, enduring disability, and medical expenses (1). RA prevalence is poorly described in Australia, and linked health datasets can provide a more meaningful picture for RA epidemiology in the Australian population.

Objectives: To describe the period prevalence rate of RA patients per 1000 hospital separations coded as RA primary or secondary diagnosis in Western Australia (WA) hospitals between 1995 and 2014.

Methods: We extracted data on all patients identified in the WA Hospital Morbidity Data Collection between 1995 and 2014, with the International Classification of Diseases (ICD) codes for RA (ICD 10 M05.00–M06.99, and the corresponding ICD 9 codes). We estimated period prevalence rates per 1000 hospital separations and annual average percentage changes, with the total number of hospital separations each year.

Results: A total of 17,125 patients were admitted to WA hospitals with a diagnostic code for RA over the study period (1995-2014). The total number of hospital separations for RA patients was 50,353, indicating an average of three hospital separations per patient over twenty years. The RA prevalence was 3.4 per 1000 separations over the study period, with a -2.89% annual average decrease since 1995.

Conclusion: These data demonstrate that hospitalisation for RA has decreased considerably in WA over the last two decades. As this decrease roughly coincides with the introduction of biological drug treatment for RA, the reduced need for hospital admission is likely due to improvements in RA management.

REFERENCES:

[1] Uhlig T, Moe RH, Kvien TK (2014) The burden of disease in rheumatoid arthritis. Pharmacoeconomics 32:841-851. doi:10.1007/s40273-014-0174-6

Table1: Hospitalisation for rheumatoid arthritis (RA) in Western Australia (WA) (1995-2014).

Year	Total RA hospital Separations	WA hospital separations	RA per 1000 separations	Average annual change per annum (RA hospital Separations)	Average annual change per annum (WA hospital separations)
1995	3,518	451,195	7.8	0%	0%
1996	3,751	473,677	7.9	7%	5%
1997	3,994	506,721	7.9	6%	7%
1998	3,927	544,566	7.2	-2%	7%
1999	2,785	575,489	4.8	-29%	6%
2000	1,755	612,774	2.9	-37%	6%
2001	1,577	617,891	2.6	-10%	1%
2002	1,685	648,423	2.6	7%	5%
2003	1,908	657,439	2.9	13%	1%
2004	1,836	691,975	2.7	-4%	5%
2005	2,045	714,353	2.9	11%	3%
2006	2,215	740,059	3.0	8%	4%
2007	2,282	783,620	2.9	3%	6%
2008	2,184	829,595	2.6	-4%	6%
2009	2,682	887,209	3.0	23%	7%
2010	2,627	966,033	2.7	-2%	9%
2011	2,597	1,024,462	2.5	-1%	6%
2012	2,689	1,058,751	2.5	4%	3%
2013	2,281	1,070,399	2.1	-15%	1%
2014	2,015	1,081,463	1.9	-12%	1%
Total RA hospital separations	50,353				
Total WA hospital separations		14,936,094			
RA Period prevalence per 1000 separations (1995-2014)		3.4			
Average annual change since 1995				-2.89%	4.71%

Acknowledgements: Khalid Almutairi was supported by an Australian Government Research Training Program PhD Scholarship at the University of Western Australia.

Disclosure of Interests: Khalid Almutairi: None declared, Johannes Nossent Speakers bureau: Janssen, David Preen: None declared, Helen Keen Speakers bureau: Pfizer Australia, Abbvie Australia, Charles Inderjeeth Speakers bureau: Eli Lilly

DOI: 10.1136/annrheumdis-2021-eular.339

POS0298 UNDERSERVED POPULATIONS IDENTIFY BARRIERS AND PROPOSE SOLUTIONS FOR SELF-MANAGING ARTHRITIS AND CHRONIC CONDITIONS

S. Mills[1], K. Khehra[2], P. Ghuman[2], D. Au[3], C. L. Koehn[4], R. Maynard[5], N. Clark[6,7], C. Davis[8], A. Cui[9], C. B. Hamilton[2,10], D. Lacaille[2,10]. *[1]University of British Columbia, Deparment of Medicine, School of Population and Public Health, Vancouver, Canada*; *[2]University of British Columbia, Department of Medicine, Faculty of Medicine, Vancouver, Canada*; *[3]MOSAIC (Multi-lingual Orientation Service Association for Immigrant Communities), Vancouver, Canada*; *[4]Arthritis Consumer Experts, Vancouver, Canada*; *[5]Portland Hotel Society Community Services Society, Vancouver, Canada*; *[6]University of Victoria, School of Nursing, Victoria, Canada*; *[7]University of British Columbia, Centre for Migration Studies, Vancouver, Canada*; *[8]Centre for Collaboration, Motivation and Innovation, Vernon, Canada*; *[9]University of British Columbia, Vancouver, Canada*; *[10]Arthritis Research Canada, Vancouver, Canada*

Background: Underserved populations, such as ethnic minorities, low-income adults, and Indigenous people living with arthritis are more likely to have lower health literacy, higher rates of multi-morbidity, and face challenges in accessing care[1-3]. Self-management support (SMS) can help to mitigate the impacts of living with arthritis[4]. However, we require a more in-depth understanding of the daily barriers underserved communities face in living with arthritis in order to develop effective SMS that can meaningfully improve well-being and quality of life.

Objectives: The study objective was to bring together underserved people living with arthritis to identify common barriers they face in taking care of their conditions in daily life, and to identify their solutions to the identified challenges.

Methods: A team of researchers from several universities, nurse practitioners, physicians, policy makers, an arthritis consumer-patient leader and our community partners (Multi-lingual Orientation Service Association for Immigrant Communities and the Portland Hotel Society Community Services Society) engaged in a Community-based Participatory and Concept Mapping (CM) study[5-7] where participants from underserved communities identified major barriers they face in managing arthritis, agreed on key themes that emerged, and determined priorities for actions. This involved three key CM activities: 1) brainstorming ideas; 2) sorting and rating ideas; and 3) analyzing and interpreting concept maps[8]. Data was collected through face-to-face interviews and prioritized and interpreted in workshop settings.

Results: Sixty-three individuals who were ethnic minorities, immigrants, refugees, low-income, over 65, and/or housing insecure and living with arthritis identified 35 common barriers and made recommendations in the areas of financial difficulties, social services, access to health services, quality of health services, lack of knowledge, and mental health. Additional funding has been sought through Community-University Engagement Support Funding to enable our community partners to prioritize the recommendations in their communities, and to develop mechanisms for implementation using already existing community structures, processes, and services.

Conclusion: Persons living with arthritis in diverse underserved communities face significant health and social inequities, including lack of access to basic life necessities such as food, housing, employment, and safety, which creates barriers to self-managing arthritis and other chronic conditions in daily life. SMS for these communities needs to address these social and environmental barriers shaping capacity for self-management, and ultimately, quality of life and well-being.

REFERENCES:

[1] Ackerman I, Busija L. Access to self-management education, conservative treatment and surgery for arthritis according to socioeconomic status. Best Pr Res Clin Rheumatol. 2012;26(5):561–83.
[2] Shadmi E. Multimorbidity and equity in health. Int J Equity Heal. 2013;12(59):59.
[3] Foster M, Kendall E, Dickson P, Chaboyer W, Hunter B, Gee T. Participation and chronic disease self-management: are we risking inequitable resource allocation? Aust J Prim Health. 2003;9(3):132–40.
[4] Brady T, Anderson L, Kobau R. Chronic disease self-management support: public health perspectives. Front Public Heal. 2015;2(234).
[5] Trochim W. An introduction to concept mapping for planning and evaluation. Eval Progr Plann. 1989;12(1):1–16.
[6] Anderson L, Day K, Vandenberg A. Using a concept map as a tool for strategic planning: the healthy brain initiative. Prev Chronic Dis. 2011;8(5):A117.
[7] Petrucci C, Quinlan K. Bridging the research practice gap: concept mapping as a mixed methods strategy in practice-based research and evaluation. J Soc Serv Res. 2007;34(2):25–42.
[8] Kane M, Trochim W. Concept mapping for planning and evaluation. Thousand Oaks (CA): SAGE Publications; 2007.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2211

POS0299 SOCIOECONOMIC BACKGROUND IS ASSOCIATED WITH DISCORDANCE BETWEEN HEALTH LITERACY OF PEOPLE WITH RMDS AND ASSESSMENT OF HEALTH LITERACY BY THEIR TREATING HEALTH PROFESSIONAL

M. M. Bakker[1,2], C. Dikovec[1], P. Putrik[1,2], J. Rademakers[2,3], M. Van de Laar[4], H. Vonkeman[4,5], M. R. Kok[6], H. Voorneveld[6], S. Ramiro[7,8], M. De Wit[9], R. Buchbinder[10,11], R. Batterham[12,13], R. Osborne[12], A. Boonen[1,2]. *[1]Maastricht University Medical Centre, Internal Medicine, Rheumatology Division, Maastricht, Netherlands*; *[2]Maastricht University, CAPHRI - Care and Public Health Research Institute, Maastricht, Netherlands*; *[3]Nivel - Netherlands Institute for Health Services Research, -, Utrecht, Netherlands*; *[4]University of Twente, Psychology, Health and Technology, Enschede, Netherlands*; *[5]Medisch Spectrum Twente, Arthritis Center Twente - Rheumatology and Clinical Immunology, Enschede, Netherlands*; *[6]Maasstad Hospital, Rheumatology and Clinical Immunology, Rotterdam, Netherlands*; *[7]Leiden University Medical Centre, Rheumatology, Leiden, Netherlands*; *[8]Zuyderland Medical Centre, Rheumatology, Heerlen, Netherlands*; *[9]Tools2Use Patient Association, -, Amsterdam, Netherlands*; *[10]Monash University, School of Public Health and Preventive Medicine, Melbourne, Australia*; *[11]Cabrini Institute, Monash Clinical Epidemiology, Melbourne, Australia*; *[12]Swinburne University of Technology, Centre for Global Health and Equity, Melbourne, Australia*; *[13]Thammasat University, Faculty of Public Health, Bankok, Thailand*

Background: Health literacy is increasingly recognised as a critical determinant of health. While care should be tailored to the health literacy needs of each patient [1], research in primary care shows that physicians often under- or overestimate their patients' health literacy, with socioeconomic factors playing a role [2]. Evidence in a rheumatology setting is scarce.

Objectives: -To investigate discordance between health literacy of patients with rheumatic and musculoskeletal diseases (RMDs) and assessment by their treating health professional, across the nine domains of the Health Literacy Questionnaire (HLQ).
-To explore whether discordance is associated with the patient's socioeconomic background.
Methods: Patients with rheumatoid arthritis (RA), spondyloarthritis (SpA), or gout from three Dutch outpatient rheumatology clinics completed the HLQ [3]. The treating health professional (rheumatologist, physician assistant, nurse (practitioner) or resident) assessed their patient's level for each HLQ domain, or answered "I don't know". Discordance per domain was calculated as the patient's score subtracted from the professional's score (both on a 0-10 scale). Discordance was defined as a ≥2-point difference in either direction. Adjusted multilevel multinomial regression models (ref. = no discordance) with patients clustered by health professionals were computed to test the role of socioeconomic factors (age, gender, education level, immigration background, living alone and employment status) in negative (i.e. professional scored lower) and positive (i.e. professional scored higher) discordance.
Results: Of 778 patients included, 41% had RA, 34% had SpA, and 25% had gout. We observed considerable discordance across all HLQ domains (Table 1). Professionals answered "I don't know" most often for "Having social support for health" (19.4%, domain 4). Most discordance occurred for "Critically appraising information" (42.1%, domain 5). For all HLQ domains except "Having social support for health" (domain 4), discordance was associated with socioeconomic factors. In patients with a non-Western immigration background, professionals were likely to assign lower scores than patients' HLQ scores in six domains. Education level was an important driver of discordance in seven domains, with the direction of the association being domain-dependent. Other factors associated with discordance in multiple domains were type of rheumatic disease, comorbidities, mastery, how well the professional knew the patient, type of professional, and disease impact.

Table 1. Discordance per HLQ domain (n=778)

HLQ domain	Professional scored lower	No discordance	Professional scored higher	Professional did not know
	n (%)			
1. Healthcare provider support	128 (16)	514 (66)	126 (16)	10 (1)
2. Having sufficient information	100 (13)	528 (68)	143 (18)	7 (1)
3. Actively managing health	95 (12)	461 (59)	208 (27)	14 (2)
4. Having social support for health	55 (7)	397 (51)	175 (22)	151 (19)
5. Critically appraising information	78 (10)	448 (58)	250 (32)	2 (0)
6. Actively engaging with providers	205 (26)	500 (64)	70 (9)	3 (0)
7. Navigating the health system	115 (15)	544 (70)	107 (14)	12 (2)
8. Finding health information	163 (21)	492 (63)	98 (13)	25 (3)
9. Understanding health information	145 (19)	511 (66)	110 (14)	12 (2)

Conclusion: Considerable discordance between patients' health literacy and their treating health professionals' assessment exists across health literacy domains. In eight out of nine domains, discordance was associated with the patient's socioeconomic background, particularly education and immigration background. Understanding and addressing the reasons for discordance between patient-reported and professional-perceived health literacy has potential to improve responsiveness to patients' needs, promote better communication and ultimately improve care outcomes.
REFERENCES:
[1] Bakker et al., Arthrit Care Res (2021)
[2] Storms et al., BMJ Open (2019)
[3] Osborne et al., BMC Public Health (2013)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2344

POS0300 DOES COGNITIVE BEHAVIORAL THERAPY IMPROVE PSYCHOSOCIAL OUTCOME IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

A. Van Breda[1], D. De Cock[1], C. Vervloesem[1], M. Doumen[1,2], D. Bertrand[1], S. Pazmino[1], R. Westhovens[1,2], P. Verschueren[1,2]. *[1]KU Leuven, Skeletal Biology and Engineering Research Centre, Leuven, Belgium*; *[2]University Hospitals Leuven, Rheumatology, Leuven, Belgium*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory auto-immune disease impacting both physical and mental wellbeing of patients. Cognitive behavioral therapy (CBT), a psycho-social intervention aiming to revert maladaptive thinking and dysfunctional behavior, could improve psychosocial wellbeing in patients with RA. However, it is unclear which CBT components are most successful in improving wellbeing and if certain subpopulations might be more sensitive to CBT therapy.
Objectives: To summarize in a systematic literature review, the effect of CBT on psychosocial outcomes in RA, focussing on most successful components and which patient subgroups benefit most from CBT.
Methods: A search was conducted with the support of a health sciences librarian at the KU Leuven Biomedical Library from inception until 28.06.2020 in 5 electronic databases: PubMed, EMBASE, Web of Science Core Collection, Cochrane Library and Cumulated Index to Nursing and Allied Health Literature (CINAHL). We included studies in English and Dutch involving patients >18 years old with RA, using cognitive behavioral approaches as intervention, with outcomes related to psychosocial variables. Two reviewers (CV&AVB) independently screened first the titles and abstracts of the studies, and later the full texts for eligibility. A third reviewer (DDC) was consulted if no consensus was found. Quality was assessed by the Critical Appraisals Skills Programme (CASP) RCT checklist.
Results: In total, 18 of 1114 retrieved articles could be included (Table 1). Mean age of the participants ranged between 48-63 years with a mean disease duration between 13-16 years. The most used CBT techniques included relaxation training, attention diversion strategies, problem solving skills, goal setting, communication, and social skills training. CBT resulted in ameliorated psychosocial wellbeing related to more active coping styles, improved self-efficacy and reduced perception of disease stressors. Six/18 studies focused on a Ra patient subgroup with an increased psychosocial risk profile, such as high levels of depression. There was limited evidence for an improved treatment effect in these patients because of the elevated levels of psychological distress, but internal motivation seemed key for success.

Table 1. Included studies

First Author	Year	Country	Population	Mean age	Outcomes assessed
O`Leary	1988	USA	N=30	49y	Self-efficacy, Depression, Loneliness, perceived stress
Radojevic	1992	USA	N=59	54y	Depression, Anxiety, Pain coping
Germond	1993	SA	N=24	49y	Coping, Health Control, Stress, Mood, Impact
Parker	1995	USA	N=141	60y	Life stress, Daily stressors, helplessness, depression, anxiety, self-efficacy, impact
Kraaimaat	1995	NL	N=43	57y	Anxiety, Depression, Social Support, Pain Coping
Sharpe	2001	UK	N=55	56y	Anxiety, Depression, Coping
Evers	2002	NL	N=64	54y	Anxiety, Negative mood, Social functioning, Illness cognitions, coping, pain, compliance
Parker	2003	USA	N=54	56y	Depression, Stressors, Stress, Anxiety, Helplessness, Self-efficacy
Van Lankveld	2004	NL	N=58	50y	Depression, Anxiety, Stressors, Coping, Social Support
Zautra	2008	USA	N=142	52y	Affect, Depression, Coping, Pain, Catastrophizing
Hammond	2008	UK	N=167	55y	Self-efficacy, distress, Control, Self-Management
Barsky	2010	USA	N=168	53y	Distress
Hewlett	2011	UK	N=117	60y	Anxiety, Depression, Fatigue
Sharpe	2012	AU	N=104	56y	Anxiety, Depression
Garnefski	2013	NL, BE	N=82	48y	Depression, Anxiety, Self-efficacy
Lumley	2014	USA	N=266	55y	Anxiety, Depression
Vermaak	2015	AU	N=113	54y	Depression, Anxiety, Self-Efficacy, Distress, QoL
Hewlett	2019	UK	N=319	63y	Fatigue, Mood, QoL, Self-Efficacy, Helplessness

Conclusion: Adding CBT to standard care induces modest improvements in psychosocial outcomes for patients with RA. CBT seems more successful if patients are motivated to reflect on their cognitions and behaviours. However, more research with large-scale studies, focusing also on the critical early disease phase, is needed to investigate the long-term benefits of CBT.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4090

POS0301 NO MAJOR DIFFERENCES BETWEEN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASE WHO UNDERWENT MONO- OR MULTISWITCHING OF BIOSIMILARS IN ROUTINE CARE (PERCEPTION STUDY)

S. Gall[1], U. Kiltz[1], T. Kobylinski[1], I. Andreica[1], K. Vaupel[1], X. Baraliakos[1], J. Braun[1]. [1]*Rheumazentrum Ruhrgebiet at Ruhr-University Bochum, Rheumatology, Herne, Germany*

Background: The increasing availability of biosimilars (bsDMARDs) has created a financial incentive to encourage switching to cheaper products ("non-medical switch") leading to different switching scenarios. While the clinical efficacy and safety of multiswitching seems to be established (1), limited data on patients' knowledge about bsDMARDs and satisfaction with care are available.

Objectives: The aim of our study was to learn more about the outcome of mono- and multiswitching scenarios in routine care with respect to patients' attitudes towards bsDMARDs in chronic inflammatory rheumatic diseases (CIRD) such as rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA).

Methods: Consecutive patients with CIRD who were planned to switch treatment of one adalimumab biosimilar (ADA-bsDMARD) to another ADA-bsDMARD were recruited. The number of previous ADA-bsDMARD categorized the patients into: monoswitch = 1 and multiswitch = >1. Demographics and standard assessments using validated outcome parameters for disease activity, physical function, and patient satisfaction with care (Leeds Satisfaction Questionnaire (LSQ) were documented. LSQ contains items on five subscales (provision of information; empathy with the patient; attitude to the patient; access to and continuity with the care giver; and technical competence) and a general satisfaction scale. Knowledge about bsDMARDs was recorded using a structured questionnaire.

Results: Out of 90 patients in total, there were 42 with a monoswitch and 48 with a multiswitch scenario (Table 1). Patients were satisfied with care irrespective of the switching scenario. However, the knowledge about bsDMARDs was generally rather low (Figure 1). Less than one third of patients was able to identify correct answers about manufacturing, efficacy/safety issues, approval status and costs of bsDMARDs. However, when comparing the two switch scenarios, no differences in disease characteristics nor in satisfaction with care were found. Also the number of switches had not increased the knowledge about bsDMARDs.

Conclusion: This study shows that multiswitching did not lead to reduced satisfaction with care in patients on treatment with bsDMARDs. Especially, the number of switches did have no negative impact on patients satisfaction. The observation that patients who underwent multiple switches had no more knowledge about bsDMARDs than patients who just had one switch may just be explained by the positive experience most patients had with switching.

REFERENCES:

[1] Kiltz U et al. Ann Rheum Dis 2020;79 (supplement 1):1872

Table 1. Patients and disease characteristics stratified by switch scenario

Variables*	Monoswitch (n=42)	Multiswitch (n=48)	P-Wert
Sex, male, n (%)	23 (54.7)	26 (54.2)	
Age, years	44 (14)	51 (11)	
Rheumatoid Arthritis, n (%)	14 (33.3)	7 (14.6)	
Axial Spondyloarthritis, n (%)	23 (54.8)	31 (64.6)	
Psoriatic arthritis, n (%)	5 (11.9)	10 (20.8)	
Disease duration, years	9.2 (2.5)	10.6 (6.7)	0.48
DAS28	2.2 (1.2)	2.9 (0.7)	0.13
HAQ	1.2 (0.6)	1.2 (0.5)	0.91
ASDAS	2.1 (1.2)	1.6 (1)	0.70
BASFI	4.6 (2.9)	3.7 (2.9)	0.87
Patient satisfaction			
LSQ-General (1-5) #	3.7 (0.7)	3.9 (0.6)	0.58
LSQ-Information (1-5)	3.7 (0.6)	3.6 (0.4)	0.20
LSQ-Empathy (1-5)	3.6 (0.6)	3.5 (0.5)	0.57
LSQ-Technical (1-5)	4.1 (0.5)	4.1 (0.5)	0.51
LSQ-Attitude (1-5)	3.8 (0.7)	3.9 (0.5)	0.62
LSQ-Access (1-5)	3.7 (0.6)	3.8 (0.6)	0.70

*values in mean (SD)# values of 1 indicate dissatisfaction

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1742

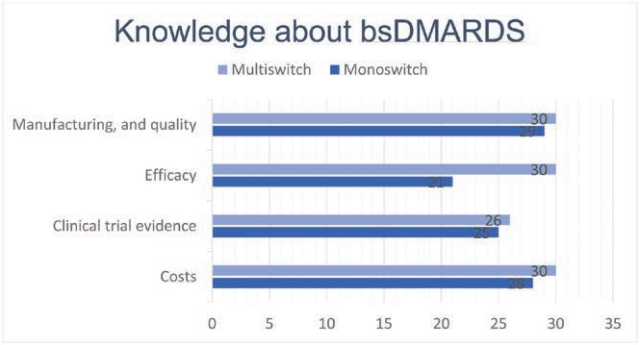


Figure 1. Knowledge about biosimilarsbsDMARDs: biosimilar disease-modifying anti-rheumatic drugs

POS0302 BURNOUT IN RHEUMATOLOGISTS IN LATIN AMERICA

M. Intriago[1], G. Maldonado[2], R. Guerrero[1], E. Soriano[3], L. Moreno[4], C. Rios[1,4]. [1]*Universidad Espiritu Santo, Rheumatology, Samborondon, Ecuador*; [2]*Loyola MacNeal Hospital, Internal Medicine, Berwyn, United States of America*; [3]*Hospital Italiano, Rheumatology, Buenos Aires, Argentina*; [4]*Centro de Reumatología y Rehabilitación, Rheumatology, Guayaquil, Ecuador*

Background: Rheumatology is considered a low-risk specialty, but studies have shown a prevalence of burnout between 42% to 51%[1,2]. Factors associated with it include the use of electronic medical records, administrative tasks and prolonged working hours. This has several repercussions such as higher prevalence of depression/anxiety and less productivity.

Objectives: To determine the prevalence of burnout in rheumatologists in Latin America and the factors associated with it.

Methods: Cross-sectional study based on a survey completed through Google Forms platform that was sent by the national rheumatology associations of Latin America. Burnout was assessed with the Maslach Burnout Inventory (MBI) with cut off values of ≥27 for emotional exhaustion (EE), ≥10 for depersonalization (DP), and ≤33 for personal accomplishment (PA). Other variables were studied such as demographics, working conditions, satisfaction, comorbidities, depression using PHQ-9 and happiness using the Subjective Happiness Scale. Data was analyzed using the statistical program SPSS v.22.

Results: 297 rheumatologists from 15 countries were included, mainly Argentina (28.3%), Brazil (26.3%) and Mexico (12.8%). The majority were women 62%, 42.4% worked in public hospitals with an average of 40.1 ± 14.2 hours per week. 31.3% did research, 13.1% clinical trials, 56.6% teaching, and 42.8% administrative work. 36% received an annual income less than 25K.

56.6% had burnout in at least 1 dimension. According to the dimensions, 35.7% had burnout in EE, 25.6% in PA and 26.6% in DP. 32.3% had burnout in only 1 dimension, 17.2% in two and 7.1% in all three dimensions. Only 20.2% thought they had burnout, 9.1% were currently with professional help and 15.8% had sought help in the past. 72.1% said they were willing to participate in a program to reduce burnout.

The rheumatologists with burnout were younger than those without burnout (46.5 vs 49.9 years, p = 0.015), mentioned more frequently that they would like to decrease the number of working hours (56.5% vs 36.4%, p = 0.002) and had lower practice satisfaction (5.2 vs 6.2, p <0.001) and income satisfaction (3.4 vs 4.6, p <0.001). Those with burnout were less happy than those without burnout (5.1 vs 5.9, p <0.001) and had higher PHQ-9 (7.7 vs 2.5, p <0.001). In the burnout group, there was a higher percentage with an income less than $ 25K/year (45.7% vs 25.4%, p=0.008), presence of comorbidities (53.6% vs 40.3%, p=0.023), anxiety (11.9 % vs. 2.3%, p=0.002), use of SSRIs/SNRIs (19% vs 8.5%, p=0.011), suicidal thoughts (13.6% vs 1.6%, p <0.001) and low self-esteem (12.5% vs 3.1%, p <0.001). There was a higher percentage of rheumatologists involved in teaching in the group without burnout (66.7% vs 48.8%, p = 0.002). No statistically significant associations were found between burnout and sex, exercise, alcohol consumption, duration of career, main workplace, type of clinical practice, duration of vacation, clinical research, clinical trials and administrative work.

Conclusion: Burnout affects near half of rheumatologists in Latin America and was associated to younger age, long working hours, low satisfaction, less happiness, higher PHQ-9, suicidal thoughts, anxiety, income, presence of comorbidities and low self-esteem. Most of the rheumatologists were willing to participate in programs to reduce burnout which represents an opportunity for interventions to reduce this syndrome.

REFERENCES:
[1] Martin K. Medscape Rheumatologist Lifestyle, Happiness & Burnout Report 2020. 2020; Available at: https://www.medscape.com/slideshow/2020-lifestyle-rheumatologist-6012480#4. Accessed July 10, 2020.
[2] Tiwari V, Kavanaugh A, Martin G, Bergman M. High impact of burnout on rheumatology practitioners. Journal of rheumatology 2020:jrheum.191110.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4078

POS0303 PREVENTION OF CHRONIC DISEASES DUE TO INFLAMMATION IN INFLAMMATORY ARTHRITIS: RESULTS OF A DELPHI PROCESS TO SELECT CARE RECOMMENDATIONS FOR AN ELECTRONIC MEDICAL RECORD (EMR) INTERVENTION

I. Sheriff[1], A. Lima[2], O. Tseng[3], A. Aviña[2,4], M. Dawes5, C. E. H. Barber[6], J. Esdaile[2,7], K. Shojania[2,7], C. L. Koehn[8], A. Hoens[2,9], S. Mcquitty[10], S. Singh5, J. Yap[3,11], D. Page[12], J. Kur7, B. Hobson[3,13], M. Price[3], D. Lacaille[2,7]. *[1]Arthritis Research Canada, Summer Student Research, Vancouver, Canada*; *[2]Arthritis Research Canada, Research, Vancouver, Canada*; *[3]The University of British Columbia, Department of Family Practice, Vancouver, Canada*; *[4]The University of British Columbia, Department of Medicine, Division of Rheumatology, Vancouver, Canada*; *[3]The University of British Columbia, Department of Family Practice, Vancouver, Canada*; *[6]University of Calgary, Departments of Medicine and Community Health Sciences, Calgary, Canada*; *[4]The University of British Columbia, Department of Medicine, Division of Rheumatology, Vancouver, Canada*; *[8]Arthritis Consumer Experts, President, Vancouver, Canada*; *[9]The University of British Columbia, Department of Physical Therapy, Vancouver, Canada*; *[10]Arthritis Research Canada, Arthritis Patient Advisory Board, Vancouver, Canada*; *[11]New Westminster Family Practice, Family Physician, New Westminster, Canada*; *[12]The University of British Columbia, UBC Family Practice Residency Program, Vancouver, Canada*; *[13] Doctors of BC (previously BC Medical Association) Shared Care Committee and Practice Support Program for Family Physicians, Family Physician, Vancouver, Canada*

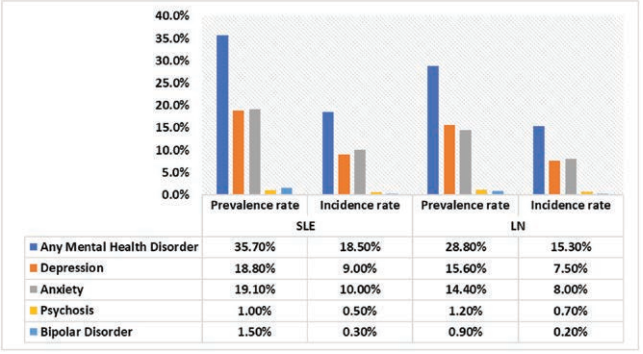
Background: Inflammatory arthritis (IA) predisposes patients to several chronic conditions including cardiovascular diseases (CVD), diabetes (DM), osteoporosis (OP) and infections, likely due to systemic effects of inflammation. Studies have found that patients with IA often receive suboptimal care for screening and managing these conditions.
Objectives: This is the first phase of a study which will develop and pilot test automated EMR reminders for family physicians. The reminders will prompt family physicians to screen for and address risk factors for these conditions. We conducted a Delphi process to select care recommendations to be addressed by the EMR reminders.
Methods: We conducted a review of current BC, Canadian and international guidelines for screening and addressing risk factors for CVD, DM, OP and infection. A list of 22 care recommendations, including their level of evidence and risks/benefits of implementation, was reviewed by a panel of six family physicians, three rheumatologists and three IA patients, in a three-round online modified Delphi process. Panelists rated each care recommendation, using 9-point scales, on 1) their clinical importance, 2) their likelihood of improving outcomes, and 3) implementation feasibility. Results were discussed in an online forum. Panelists then rated slightly revised care recommendations, modified based on feedback from the discussion. Care recommendations were retained if the median rating was ≥7 with no disagreement as defined by the RAND/UCLA Method handbook.
Results: A list of 15 care recommendations was selected by the Delphi process for EMR integration, including recommendations that address CVD risk assessment (1), hypertension screening (1), DM screening (2), fracture risk assessment (1), BMD testing (1), osteoporosis prevention (1) and treatment (1) with bisphosphonates, preventing infections through immunization (2), minimizing steroids (1) and hepatitis screening (1), screening for hydroxychloroquine retinal toxicity (1), and counselling for lifestyle modifications (2). We excluded 7 recommendations which addressed lipid testing (1), BMD testing in steroid users (1), immunizations (2), weight management (1), and DMARD laboratory test monitoring (2). Recommendations were excluded on the basis of importance (1) or feasibility (6).
Conclusion: The results of the Delphi process will inform the development of reminders, integrated in EMRs, that will support family physicians in their efforts to engage IA patients in addressing risk factors for chronic diseases related to inflammation. We hope to improve the prevention of these diseases, which represent an important cause of morbidity and mortality for people with inflammatory arthritis.

Acknowledgements: Iman Sheriff's work on this project was funded by the CRA summer studentship programme. Dr. Lacaille is supported by the Mary Pack Chair in Arthritis Research from UBC and The Arthritis Society of Canada. Thank you to all who participated in the Delphi survey.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2093

POS0304 EPIDEMIOLOGY AND ECONOMIC BURDEN ASSOCIATED WITH MENTAL HEALTH COMORBIDITIES IN SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS PATIENTS

M. A. Petri[1], D. Naessens[2], A. Ogbomo[3], A. Ratiu[3], C. Gutierrez[3], C. Karyekar[4]. *[1]John Hopkins University School of Medicine, Division of Rheumatology, Baltimore, United States of America*; *[2]Janssen Pharmaceutica NV, Director Global Market Access Immunology, Beerse, Belgium*; *[3]STATinMED Research, HEOR, Ann Arbor, United States of America*; *[4]Janssen Global Commercial Strategic Organization, Compound Development Team, Horsham, United States of America*

Background: Systemic lupus erythematosus (SLE), a multisystem autoimmune disease, is associated with mental health (MH) disorders. There is scarce information on the epidemiology and economic burden associated with MH comorbidities and the impact on SLE as well as the subpopulation with lupus nephritis (LN).
Objectives: Examined the incidence and prevalence rate of MH, healthcare resource utilization (HCRU), and costs associated with MH comorbidities in SLE/LN patients.
Methods: Adult SLE and LN patients with ≥1 inpatient or ≥2 outpatient diagnosis claims for SLE/LN (ICD-9 code: 710.0; and ICD-10 codes M32.10-19, M32.8, M32.9) were identified between 01JAN2013-30JUN2019 from two large US commercial databases. Inclusion required continuous enrollment benefits 12 months pre-/post-index date. Patients were divided into two groups: those with (WMH) vs. those without (NMH). WMH was defined as a MH diagnosis of depression, anxiety, bipolar disorder, or psychosis. Index date for the WMH group was first MH diagnosis claim. For the NMH group, a random index date was assigned between 01JAN2014-30JUN2018. The groups were then matched with a 1:1 ratio based on age, sex, and region within their respective databases. Incidence and prevalence rate of MH in the SLE/LN population were determined. All-cause healthcare costs and HCRU per patients per year (PPPY) were examined with generalized linear models.
Results: A total of 7,760 SLE and 336 LN patients were identified. The majority of patients were female (SLE=93.5%; LN=95.2%) with a mean age of 55.1 years (SLE) and 44.5 years (LN). The prevalence rate of MH was 35.7% for SLE and 28.8% for LN patients and the incidence rate was 18.5% and 15.3%, respectively. Anxiety and depression were the most common MH comorbidities (Figure 1). WMH inpatient stays averaged an additional 2.6 and 7.2 days longer than NMH for SLE and LN, respectively. In addition, WMH patients averaged 10.4 (SLE) and 18.4 (LN) significantly more outpatient visits PPPY than NMH. Overall healthcare cost PPPY was significantly higher for WMH patient in both SLE ($49,553 vs $26,064), and LN ($112,169 vs $39,529). Inpatient costs were approximately 3 – 5 times greater in the WMH group (Table 1).
Conclusion: This real-world study shows that MH comorbidities have a high incidence and prevalence rate in SLE and LN patients. Health care costs and utilization for SLE and LN patients with MH comorbidities were significantly higher than patients without MH comorbidities. This study highlights not just the high prevalence of MH comorbidity but its large contribution to SLE healthcare costs.



	SLE		LN	
	Prevalence rate	Incidence rate	Prevalence rate	Incidence rate
Any Mental Health Disorder	35.70%	18.50%	28.80%	15.30%
Depression	18.80%	9.00%	15.60%	7.50%
Anxiety	19.10%	10.00%	14.40%	8.00%
Psychosis	1.00%	0.50%	1.20%	0.70%
Bipolar Disorder	1.50%	0.30%	0.90%	0.20%

Figure 1. Incidence and Prevalence Rate of Mental Health Comorbidities in the SLE and LN PopulationsLN: Lupus nephritis; SLE: Systemic lupus erythematosus

Table 1. Follow-up Healthcare Cost and Utilization for SLE/LN Case and Control Population

	SLE with MH Comorbidities N=3,880 (WMH)	SLE without MH comorbidities N=3,880 (NMH)	P-value	LN with MH Comorbidities N=168 (WMH)	LN without MH comorbidities N=168 (NMH)	P-value
All-cause health care utilization PPPY	Mean	Mean		Mean	Mean	
Mean # inpatient visits	1.36	0.50	<0.0001	1.86	0.86	<0.0001
Mean # outpatient visits	32.11	21.67	<0.0001	47.85	29.45	<0.0001
Mean # office visits	13.49	9.74	<0.0001	14.94	10.29	<0.0001
Mean # ER visits	1.27	0.66	<0.0001	1.40	0.63	0.0005
Mean # other outpatient visits	25.55	17.08	<0.0001	41.48	24.19	<0.0001
Mean # pharmacy Rx	33.33	20.82	<0.0001	36.96	23.81	<0.0001
Length of inpatient stay (mean, days)	3.69	1.09	<0.0001	9.53	2.37	<0.0001
All-cause health care costs PPPY						
Outpatient costs (ER+ office +other)	$19,271	$12,847	<0.0001	$34,956	$19,530	<0.0001
Pharmacy costs	$7,222	$4,707	<0.0001	$7,874	$4,254	<0.0001
Inpatient costs	$22,605	$8,191	<0.0001	$68,216	$14,680	<0.0001
Total costs	$49,553	$26,064	<0.0001	$112,169	$39,529	<0.0001

PPPY: Per patient per year; ER: Emergency room; LN: Lupus nephritis; SLE: Systemic lupus erythematosus

Disclosure of Interests: Michelle A Petri Consultant of: Yes, Grant/research support from: Yes, Dominik Naessens Shareholder of: Yes (Johnson and Johnson), Employee of: Employee of Janssen Pharmaceuticals., Adesuwa Ogbomo: None declared, Anna Ratiu: None declared, Cynthia Gutierrez: None declared, Chetan Karyekar Shareholder of: Own Stock Options as part of being a company employee., Employee of: Current employee of Janssen Pharmaceuticals

DOI: 10.1136/annrheumdis-2021-eular.2638

Rheumatoid Arthritis - comorbidity and clinical aspects - Part 2

POS0305

PHYSICIAN AND PATIENT ATTITUDES TOWARDS TREAT-TO-TARGET, ITS IMPLEMENTATION AND STATED TREATMENT GOALS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A REAL-WORLD SETTING ACROSS EUROPE

B. Fautrel[1], R. Caporali[2,3], E. Holdsworth[4], B. Donaghy[4], M. Khalid[5], M. Moore[6], K. Van Beneden[7], Y. Piette[8], S. Romero-Yuste[9], J. Broen[10], P. C. Taylor[11]. *[1]Sorbonne University – APHP, Pitie-Salpetriere University Hospital, Rheumatology Department, Paris, France*; *[2]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy*; *[3]Gaetano Pini Hospital, Clinical Rheumatology Unit, Milan, Italy*; *[4]Adelphi Real World, Rheumatology, Bollington, United Kingdom*; *[5]Galapagos NV, Evidence Generation & Epidemiology, Mechelen, Belgium*; *[6]Gilead Sciences Europe Ltd, Global Medical Affairs, Uxbridge, United Kingdom*; *[7]Galapagos NV, Medical Affairs, Mechelen, Belgium*; *[8]AZ Sint-Jan Brugge - Oostende AV, Department of Rheumatology, Bruges, Belgium*; *[9]Complexo Hospitalario Universitario de Pontevedra, Rheumatology, Pontevedra, Spain*; *[10]Maxima Medical Center, Regional Rheumatology Center, Eindhoven, Netherlands*; *[11]University of Oxford, Botnar Research Centre, Oxford, United Kingdom*

Background: The principles of treat to target (T2T) include defining an appropriate treatment target, assessed at pre-defined intervals, with a commitment to changing therapeutic approach if the target is not met (1). T2T is recommended as a key strategy for the treatment of rheumatoid arthritis (RA).

Objectives: To explore attitudes towards T2T, its implementation and stated treatment goals among physicians and their patients with RA.

Methods: The Adelphi RA Disease Specific Programme™ was a large, quantitative, point-in-time survey conducted amongst rheumatologists (n=296) and their consulting patients with RA (n=3042) in Europe (France, Germany, Italy, Spain, UK) between Q4 2019–Q3 2020. Physicians were recruited via publicly available lists, completing an online survey and medical record extraction for their next 10–12 consecutive patients. The same patients were invited to voluntarily complete a self-report questionnaire (n=1098, 36% response), collecting data on attitudes towards T2T and treatment goals.

Results: Physicians reported that 76% of patients were in remission (DAS28: <2.6) or had low disease activity (DAS28: 2.6 – 3.2), and 24% had moderate-high disease activity (DAS28: >3.2). Patient mean age was 53.0 years (SD 14.0), mean time since diagnosis was 7.2 years (SD 7.2). The proportion of patients currently receiving an advanced therapy (AT; defined as biologic or targeted synthetic DMARD) was 68%, of whom 70% were on a first line AT. No difference was observed between disease activity groups.

In the physician survey, 86% of physicians stated they followed T2T principals in at least some of their RA patients, and would utilize a T2T approach in RA patients with moderate-high disease activity (61%), the most uncontrolled patients (37%) and those who do not respond well to initial therapy (34%). In this sample of real-world RA patients, 66% were reported by physicians to be on a T2T plan at the time of data collection. The most common physician-reported targets were remission (DAS28: <2.6) (75%), improvement of quality of life (QoL) (41%) and reduction of pain (31%), with 85% of physicians perceiving these treatment goals were fully or partially met. The most stated reasons for not implementing T2T was physician preference not to adjust current treatment (34%), patient preference not to adjust current treatment (23%), and there are no achievable goals for this patient (16%).

Overall, 29% of patients reported they were involved in setting their T2T goals, while 34% stated their T2T goals were set by their physicians only, and 29% perceived no T2T goal had been set (n=620). The most common overall T2T goals from the patient perspective were remission (61%), controlling symptoms (41%), and reducing impact on QoL (34%). Of those patients who acknowledged a T2T goal had been set (n=407), 77% reported their T2T goal was fully or partially achieved.

Of 719 patients who had moderate-high disease activity, 57% were on a T2T plan, with 46% of physicians perceiving these treatment goals were fully or partially met. The most common physician-stated reason for not implementing T2T was a lack of achievable targets (29%).

Conclusion: Rheumatologists in this study reported a strong belief in T2T. The most common physician-set T2T goals were remission, improvement of QoL and reduction of pain, corresponding with T2T goals as reported by patients. However, a third of patients in this cohort were not aware of a defined T2T objective in their management, which may be a result of a perceived lack of achievable goals by physicians. It may be desirable to promote more patient involvement in defining achievable targets amongst those with moderate-high disease activity who despite best efforts may not reach a clinical state of remission. Further research is needed to identify and understand goals important to RA patients.

REFERENCES:

[1] van Vollenhoven R. Treat-to-target in rheumatoid arthritis - are we there yet? Nat Rev Rheumatol. 2019;15(3):180-6.

Acknowledgements: This study was funded by Galapagos NV, Belgium.

Medical writing support was provided by Gary Sidgwick, PhD (Adelphi Real World, Bollington, UK) and editorial support was provided by Debbie Sherwood, BSc, CMPP (Aspire Scientific, Bollington, UK), both funded by Galapagos NV.

Disclosure of Interests: Bruno Fautrel Consultant of: AbbVie, Amgen, Biogen, BMS, Celgene, Celltrion, Fresenius Kabi, Gilead, Janssen, Lilly, Medac, MSD, Mylan, NORDIC Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi-Genzyme, SOBI, UCB, Grant/research support from: AbbVie, Lilly, MSD, Pfizer, Roberto Caporali Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Galapagos, Gilead, Lilly, Pfizer, Roche, UCB, Sanofi, Fresenius Kabi, Samsung Bioepis, MSD, Consultant of: Galapagos, Gilead, Lilly, Janssen, MSD, Elizabeth Holdsworth Employee of: Adelphi Real World, Bethany Donaghy Employee of: Adelphi Real World, Mona Khalid Shareholder of: Galapagos, Employee of: Galapagos, Mark Moore Shareholder of: Gilead Sciences, Speakers bureau: Gilead Sciences (only as employee), Paid instructor for: Gilead Sciences (only as employee), Consultant of: Gilead Sciences (only as employee), Grant/research support from: Gilead Sciences (only as employee), Employee of: Gilead Sciences, and previously Sanofi and AstraZeneca, Katrien Van Beneden Shareholder of: Galapagos, Employee of: Galapagos, Yves Piette Consultant of: AbbVie, Amgen, Galapagos, Grünenthal and Sandoz, Grant/research support from: Amgen, Mylan and UCB, Susana Romero-Yuste Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Grunenthal, Kern Pharma, Lilly, Roche, Sandoz, Sanofi, UCB, Janssen, Consultant of: AbbVie, Biogen, Fresenius, Galapagos, Gebro, Janssen, Lilly, Grant/research support from: Bristol Myers Squibb, MSD, Novartis, Pfizer, Jasper Broen Shareholder of: Pharming Group, Consultant of: Galapagos, Gilead, Novartis, Peter C. Taylor Consultant of: AbbVie, Biogen, Galapagos, Gilead, GlaxoSmithKline, Janssen, Lilly, Pfizer, Roche, Sanofi, Nordic

Pharma, Fresenius, UCB, Grant/research support from: Celgene, Galapagos, Gilead, Lilly
DOI: 10.1136/annrheumdis-2021-eular.893

POS0306 IMPACT OF MULTIMORBIDITY ON DISEASE MODIFYING ANTI-RHEUMATIC DRUG THERAPY IN EARLY RHEUMATOID ARTHRITIS: DATA FROM THE ESPOIR COHORT

A. Beltai[1], B. Combe[1], A. Coffy[2], C. Gaujoux-Viala[3], C. Lukas[1], A. Saraux[4], M. Dougados[5], J. P. Daures[2], C. Hua[3]. [1]*CHU Montpellier, Rheumatology, Montpellier, France*; [2]*University Institute of Clinical Research, AESIO santé, Statistiques, Montpellier, France*; [3]*CHU Nîmes, Rheumatology, Nîmes, France*; [4]*CHU Brest, Rheumatology, Brest, France*; [5]*CHU Cochin, Rheumatology, Paris, France*

Background: Multimorbidity is frequent in rheumatoid arthritis (RA) and could interfere with the therapeutic response.
Objectives: The aim of this study was to evaluate multimorbidity in the French cohort of early arthritis (ESPOIR cohort) and its possible impact on the therapeutic response.
Methods: We included patients fulfilling 2010 ACR/EULAR criteria for RA. An adapted MultiMorbidity Index (aMMI) was developed [1]. Each patient was assigned scores of binary aMMI (0= no comorbidity, 1= at least 1 comorbidity) and counted and weighted aMMI. The primary endpoint was achievement of Clinical Disease Activity Index (CDAI) low disease activity after initiation of a first disease-modifying anti-rheumatic drug (DMARD) according to the aMMI. Secondary endpoints were other disease activity scores and response criteria. We collected data from the visit preceding the first DMARD initiation (baseline visit) and the visit after at least 3 months of treatment (follow-up visit). The impact of aMMI on therapeutic maintenance at 1, 3, 5 and 10 years was evaluated.
Results: Analyses involved 472 patients: 302 (64%) had at least 1 comorbidity. Overall, 45.3% and 44.7% with binary aMMI= 0 or 1, respectively (p= 0.9), achieved CDAI low disease activity (Table 1). Similar results were found with counted and weighted aMMI. Use of other disease activity scores or response criteria did not show a significant impact of multimorbidity on the therapeutic response. Therapeutic maintenance was significantly better with binary aMMI = 1 than binary aMMI = 0. Increased counted aMMI was associated with increased probability of still being on the first initiated DMARD at each time point (Table 2).
Conclusion: In the ESPOIR cohort, therapeutic response to a first DMARD was not affected by multimorbidity but therapeutic maintenance was better in multimorbid patients.
REFERENCES:
[1] Radner H, Yoshida K, Mjaavatten MD, *et al.* Development of a multimorbidity index: Impact on quality of life using a rheumatoid arthritis cohort. *Semin Arthritis Rheum* 2015;**45**:167–73.

Table 1. Impact of aMMIs on CDAI, DAS28 and SDAI low disease activity (LDA) achievement at follow-up visit (univariate analyses)

	LDA achievement								
	CDAI			DAS28			SDAI		
	Yes	No	p	Yes	No	p	Yes	No	p
Binary aMMI, n (%)									
0	77 (45.3)	93 (54.7)	0.9*	85 (50.0)	85 (50.0)	0.2*	80 (47.1)	90 (52.9)	0.9*
1	135 (44.7)	167 (55.3)		131 (43.4)	171 (56.6)		141 (46.7)	161 (53.3)	
Counted aMMI, mean (SD)	1.0 (1.1)	1.1 (1.1)	0.7	1.0 (1.1)	1.1 (1.1)	0.2	1.1 (1.1)	1.1 (1.1)	1.0
Weighted aMMI, mean (SD)	4.1 (5.2)	4.0 (4.7)	0.9	4.0 (5.2)	4.1 (4.7)	0.3	4.0 (5.0)	4.0 (4.9)	1.0

aMMI= adapted MultiMorbidity Index; CDAI= Clinical Disease Activity Index; SDAI= Simplified Disease Activity Index* Proportion of patients achieving LDA between patients with binary aMMI= 0 and binary aMMI= 1. Because of no statistically significant results, no multivariate analysis was performed.

Table 2. Probability of first DMARD maintenance at 1, 3, 5 and 10 years (multivariate analysis)

Time point	First DMARD maintained or stopped	Binary aMMI# 0	Binary aMMI# 1	Counted aMMI§
1 year	Maintenance (n= 300)	2	298	1.71 (0.93)
	OR [95% CI]*	> 999		221.3
(n= 530)		[286.2->999]		[84.0-583.0]
	Withdrawal (n= 230)	205	25	0.12 (0.37)
3 years	Maintenance (n= 285)	10	275	1.66 (0.94)
	OR [95% CI]*	153.9		26.1
(n= 493)		[73.0-324.5]		[15.1-45.3]
	Withdrawal (n= 208)	175	33	0.22 (0.64)
5 years	Maintenance (n= 116)	9	107	1.72 (1.05)
	OR [95% CI]*	10.9		2.2
(n= 459)		[5.1-23.3]		[1.8-2.7]
	Withdrawal (n= 343)	163	180	0.82 (1.0)
10 years	Maintenance (n= 40)	2	38	1.58 (0.84)
	OR [95% CI]*	14.0		1.6
(n= 415)		[3.3-59.1]		[1.2-2.0]
	Withdrawal (n= 375)	158	217	0.99 (1.12)

#data are number of patients§ data are mean (standard error)* data are odds ratios (ORs) and 95% confidence intervals (95% CI) of still being on the first initiated DMARD at 1, 3, 5 and 10 years between patients with binary aMMI = 1 and binary aMMI = 0 and according to counted aMMI, per additional point.

The variables included in multivariate analyses were sex, rheumatoid factor and/or anti-citrunillated peptide antibody positivity, age, CDAI at baseline visit, number of treatments at baseline visit.
Acknowledgements: We are grateful to Nathalie Rincheval (Montpellier) for expert monitoring and data management and all the investigators who recruited and followed the patients (F. Berenbaum, Paris-Saint Antoine; MC. Boissier, Paris-Bobigny; A. Cantagrel, Toulouse; B. Combe, Montpellier; M. Dougados, Paris-Cochin; P. Fardellone and P. Boumier, Amiens; B. Fautrel, Paris-La Pitié; RM. Flipo, Lille; Ph. Goupille, Tours; F. Liote, Paris- Lariboisière; O. Vittecoq, Rouen; X. Mariette, Paris-Bicêtre; P. Dieude, Paris Bichat; A. Saraux, Brest; T. Schaeverbeke, Bordeaux; and J. Sibilia, Strasbourg).
Disclosure of Interests: Aurélie BELTAI: None declared, Bernard Combe Speakers bureau: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Consultant of: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Novartis, Pfizer, and Roche, Amandine Coffy: None declared, Cécile Gaujoux-Viala: None declared, Cédric Lukas Speakers bureau: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai and UCB, Consultant of: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai and UCB, Grant/research support from: Pfizer, Novartis and Roche-Chugai, Alain Saraux Speakers bureau: AbbVie; Bristol-Myers Squibb; Lilly; Nordic; Novartis; Pfizer; Roche-Chugai; Sanofi and UCB, Consultant of: AbbVie; Bristol-Myers Squibb; Lilly; Nordic; Novartis; Pfizer; Roche-Chugai; Sanofi and UCB, Grant/research support from: AbbVie; Bristol-Myers Squibb; Lilly; Nordic; Novartis; Pfizer; Roche-Chugai; Sanofi and UCB, Maxime Dougados Speakers bureau: Pfizer, Abbvie, Lilly, UCB, Merck, BMS, Roche, Biogen, Sanofi, Novartis, Sandoz, Consultant of: Pfizer, Abbvie, Lilly, UCB, Merck, BMS, Roche, Biogen, Sanofi, Novartis, Sandoz, Grant/research support from: Pfizer, Abbvie, Lilly, UCB, Merck, BMS, Roche, Biogen, Sanofi, Novartis, Sandoz, Jean-Pierre DAURES: None declared, Charlotte Hua: None declared
DOI: 10.1136/annrheumdis-2021-eular.2868

POS0307 FATIGUE IN RHEUMATOID ARTHRITIS PATIENTS IS ASSOCIATED TO SUBJECTIVE BUT NOT OBJECTIVE ASSESSMENTS OF DISEASE ACTIVITY DURING TREATMENT WITH TOCILIZUMAB

H. B. Hammer[1], B. Agular[2], L. Terslev[3]. [1]*Diakonhjemmet Hospital, Rheumatology, Oslo, Norway*; [2]*Roche, Rheumatology, Copenhagen, Denmark*; [3]*Rigshospitalet Glostrup, Rheumatology, Copenhagen, Denmark*

Background: Fatigue is common in patients with rheumatoid arthritis (RA), and its association with inflammatory activity is not fully understood.
Objectives: To explore the associations between fatigue and inflammation by clinical, laboratory and ultrasound examinations during follow-up of RA patients on biological treatment.

Methods: A Nordic (Denmark, Finland, Norway, Sweden) open-label, single-arm study (part of the umbrella program – TOZURA (1)), enrolled patients with inadequate response to conventional synthetic (cs) DMARDs. Patients received tocilizumab 162 mg sc weekly for 24 weeks as monotherapy or in combination with a csDMARD. Stable oral NSAIDs and corticosteroids (≤10 mg/day prednisone or equivalent), were allowed. Patients were assessed at baseline, 4, 12 and 24 weeks for fatigue (FACIT-F questionnaire (total sum scores)), patient reported outcome measures ((PROMs) including joint pain and patient's global visual analogue scale (VAS) as well as HAQ-DI), clinical assessments (tender and swollen joints, assessor's global VAS), laboratory examinations (ESR, CRP) and ultrasound assessments (36 joints and 4 tendons, scored according to the Norwegian US atlas (2)). Spearman correlations, performed both at baseline and for changes from baseline of variables during follow-up, explored associations between fatigue and PROMs, clinical, laboratory as well as ultrasound variables. Predictive value of fatigue was investigated by linear regression.
Results: 110 patients were included (83% female, mean (SD) age 55.6 (12.1) years and RA duration 8.7 (9.5) years, 81% anti-CCP positive). All PROMs, clinical, laboratory and ultrasound variables decreased significantly, already after 4 weeks (p<0.001). Both for baseline assessments as well as for changes during follow-up, fatigue was associated with PROMs (Table 1 (baseline) and Table 2 (follow-up)). However, there were no or low associations between fatigue and clinical, laboratory and ultrasound assessments at baseline or during follow-up. In addition, baseline fatigue was predictive of joint pain, patient's global VAS and HAQ-DI during follow-up (p<0.05-0.001), but not for the clinical, laboratory or ultrasound assessments.
Conclusion: Fatigue assessed by an established questionnaire did not show any associations with several assessments of inflammatory activity in RA patients, neither at baseline nor during effective treatment. Thus, the present study adds to the increasing number of papers finding fatigue to reflect other aspects of RA disease activity than inflammation.

REFERENCES:
[1] Choy E et al. Rheumatology 2018; 2. Hammer HB et al, ARD 2011

Table 1. Spearman correlations between FACIT-F total score and patient reported outcomes, clinical, laboratory and ultrasound assessments. *p<0.05. **p<0.001

	Baseline	4 weeks	12 weeks	24 weeks
Patient's global VAS	-0.46**	-0.41**	-0.50**	-0.48**
Joint pain VAS	-0.43**	-0.50**	-0.54**	-0.41**
HAQ-DI	-0.59**	-0.59**	-0.60**	-0.62**
28 tender joint count	-0.07	-0.19	-0.12	-0.22*
28 swollen joint count	0.14	0.12	0.20*	0.19
Examiner's global VAS	0.05	0.05	-0.03	-0.15
ESR (mm/h)	-0.02	-0.01	0.07	-0.04
CRP (mg/L)	-0.11	-0.02	0.06	0.07
Sum score GS	0.09	0.20*	0.24*	0.13
Sum score Doppler	0.06	0.01	0.13	0.02

Table 2. Spearman correlations between changes in FACIT-F total score from baseline to 4, 12 and 24 weeks and changes in patient reported outcomes, clinical, laboratory and ultrasound assessments. *p<0.05. **p<0.001

	4 weeks	12 weeks	24 weeks
Patient's global VAS	-0.59**	-0.56**	-0.59**
Joint pain VAS	-0.60**	-0.50**	-0.52**
HAQ-DI	-0.43**	-0.44**	-0.61**
28 tender joint count	-0.29*	-0.30*	-0.24*
28 swollen joint count	-0.15	-0.17	-0.06
Examiner's global VAS	-0.14	-0.27*	-0.15
CRP (mg/L)	-0.19	-0.21*	-0.25*
ESR (mm/h)	-0.13	-0.18	-0.21
Sum score GS	-0.10	-0.17	-0.12
Sum score Doppler	-0.21*	-0.14	-0.10

Disclosure of Interests: Hilde Berner Hammer Speakers bureau: AbbVie, Pfizer, Roche, Lilly and Novartis, Consultant of: Novartis, Birte Agular Employee of: Roche, Lene Terslev Speakers bureau: Roche, MSD, BMS, Pfizer, AbbVie, Novartis and Janssen
DOI: 10.1136/annrheumdis-2021-eular.152

POS0308 TRAJECTORIES OF FATIGUE IN EARLY RA OVER 10 YEARS: RESULTS FROM THE ESPOIR COHORT

S. Rodriguez-Muguruza[1], B. Combe[2], F. Guillemin[3], A. Olive[4], O. Valero[5], R. Fontova Garrofe[6], S. Marsal[7], F. Bruno[8], C. Lukas[2]. [1]*Hospital Joan XXIII, Rheumatology Department,Tarragona, Spain*; [2]*Hospital Lapeyronie, Rheumatology Department, Montpellier, France*; [3]*Université de Lorraine, Nancy, France, INSERM CIC 1433, CHRU, Nancy, France*; [4]*Hospital Germans Trias i Pujol, Rheumatology Department, Barcelona, Spain*; [5]*Autonomous University of Barcelona, Department of Statistics, Barcelona, Spain*; [6]*Hospital Joan XXIII, Rheumatology Department,Tarragona, Spain*; [7]*Vall d'Hebrón University Hospital, Department of Rheumatology, Barcelona, Spain*; [8]*Pitié-Salpêtrière Hospital, Department of Rheumatology, Paris, France*

Background: Fatigue is one of the most prevalent symptom reported by persons with RA. RA-related fatigue is a complex concept with biological, psychological and social interactions.
Objectives: In a cohort of early RA patients, to determine and characterize fatigue trajectories over 10 years of follow-up and identify predictors of trajectory membership.
Methods: Patients fulfilling the 2010 ACR/EULAR criteria for RA included in the ESPOIR cohort. We used a cluster analysis to obtain fatigue (assessed by fatigue visual analogue scale) trajectories over the course of 10 years from enrolment. Chi-square tests or ANOVA were performed to evaluate differences of baseline variables between fatigue trajectories. Using a multinomial logistic regression we could identify predictors of trajectory membership.
Results: We analysed 598 patients with mean disease duration at enrolment of 26.2 ± 40.9 days. Cluster analysis revealed 3 trajectories: high (18%), moderate (52%) and low fatigue (30%). Compared to patients with moderate or low fatigue trajectory, patients with high fatigue trajectory were predominantly women and reported significantly higher duration and intensity of morning stiffness, HAQ score, number of tender joints, levels of pain, number of awakenings due to arthritis, levels of physician and patient global assessment and more frequent sleep problems, and increased psychological distress. Female patients with pain, psychological distress and presence of sicca symptoms had higher risk of being in high trajectory group.
Conclusion: These findings suggest that levels of fatigue are rather stable over time in each trajectory. Baseline clinical measures and baseline patient-reported measures of functional status better distinguished the three fatigue trajectories. We did not find differences between trajectories in baseline laboratory measures. Inflammatory activity was not a predictor of being in high trajectory fatigue group.
REFERENCES:
[1] Pollard LC, Choy EH, Gonzalez J, Khoshaba B, Scott DL. Fatigue in rheumatoid arthritis reflects pain, not disease activity. Rheumatology (Oxford) 2006;45:885–9
[2] Repping-Wuts H, van Riel P, van Achterberg T. Fatigue in patients with rheumatoid arthritis: what is known and what is needed. Rheumatology (Oxford) 2009;48:207–9.
[3] Pilgaard T, hagelund L, Stallknecht SE, jensen HH, Esbensen BA. Severity of fatigue in people with rheumatoid arthritis, psoritic artrhitis and spondyoarthritis- Results of cross-sectional study. Plos One. 2019;14:e0211831
[4] Feldthusen C, Grimby-Ekman A, Forsblad-d'Elia H, Jacobsson L, Mannerkorpi K. Explanatory factors and predictors of fatigue in persons with rheumatoid arthritis: a longitudinal study. J Rehabil Med 2016 28;48:469–76.
[5] Madsen SG, Danneskiold-Samsøe B, Stockmarr A, Bartels EM. Correlations between fatigue and disease duration, disease activity, and pain in patients with rheumatoid arthritis: a systematic review. Scand J Rheumatol. 2016;45:255-61.
[6] Olsen CL, Lie E, Kvien TK, Zangi HA. Predictors of fatigue in rheumatoid arthritis patients in remission or in a low disease activity state. Arthritis Care Res (Hoboken) 2016;68:1043–8.
[7] Druce K, Jones GT, Macfarlane GJ, Verstappen SMM, Basu N. The longitudinal course of fatigue in rheumatoid arthritis: results from the Norfolk Arthritis Register. J Rheumatol 2015;42:2059–65.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.214

POS0309 SEROPOSITIVITY INCREASES RISK OF INCIDENT DEMENTIA IN INDIVIDUALS WITH RHEUMATOID ARTHRITIS: A POPULATION-BASED COHORT STUDY

V. Kronzer[1], T. Gunderson[2], C. S. Crowson[2], J. M. Davis III[1], M. Vassilaki[2], M. Mielke[2], E. Myasoedova[1]. [1]*Mayo Clinic, Rheumatology, Rochester, United*

States of America; [2]*Mayo Clinic, Health Sciences Research, Rochester, United States of America*

Background: Several studies show increased risk of dementia among individuals with rheumatoid arthritis (RA), while others show no association. One reason for this discrepancy might be differential association by serostatus. No prior studies have investigated the association between RA and dementia by serostatus.
Objectives: We aimed to evaluate the risk of incident dementia among individuals with RA, stratified by serostatus.
Methods: This population-based cohort study included all cases of incident RA within Olmsted County, Minnesota with index date of RA onset between 1 January 1999 and 31 December 2013. We matched RA cases to non-RA comparators 1:1 on age and sex. All RA cases met 1987 ACR criteria for RA. We defined seropositivity as positive rheumatoid factor or anti-cyclic citrullinated peptide antibodies. We defined incident dementia as having two ICD-9/10 codes for dementia at least 30 days apart, with the date of the second code representing the time of dementia onset. We **e**xcluded individuals with dementia prior to index date. We estimated the cumulative incidence of dementia adjusting for the competing risk of death. For the main analysis, cox proportional hazard models estimated adjusted hazard ratios (aHR) with 95% confidence intervals (CI) for incident dementia, adjusting for age, sex, index year, body mass index, and smoking status (never, former, current). These models compared the incidence of dementia for RA versus non-RA, seropositive and seronegative RA versus their matches, and seropositive versus seronegative RA. To validate these results, we also performed sensitivity analyses using groups matched via inverse probability weighting on age, sex, index year, obesity, smoking status, and race.
Results: We identified 597 RA cases (mean age 56, 70% female), and 594 non-RA comparators. Of the RA cases, 388 (65%) were seropositive, and 209 (35%) were seronegative. The ten-year cumulative incidence of dementia in patients with RA was 3.3 (95%CI 2.0,5.5) per 100,000 compared to 2.4 (95%CI 1.3,4.2) in non-RA comparators, for aHR of 1.26 (95%CI 0.7,2.3). When stratifying by serostatus, the ten-year incidence of dementia for seropositive RA cases was 3.6 (95%CI 2.0,6.5), corresponding to aHR of 1.45 (95%CI 0.73,2.9) compared to matched non-RA cases. In contrast, the incidence of dementia in seronegative RA cases was 2.6 (95%CI 1.0,7.0), for an aHR of 1.0 (95%CI 0.29,3.5). Overall, the incidence of dementia in seropositive RA cases was significantly higher than seronegative cases (aHR 3.2, 95%CI 1.2,8.5). Indeed, sensitivity analysis using inverse probability weighting confirmed that among participants aged 50 and older, dementia incidence was higher for seropositive than seronegative RA (aHR 2.9, 95%CI1.1,7.8) (Figure 1).
Conclusion: Individuals with seropositive RA have an increased risk for incident dementia than those with seronegative RA. Future studies should replicate these findings and investigate the mechanism for this association.

Figure 1. Cumulative incidence of dementia for individuals with seropositive versus seronegative RA aged 50 and older, balanced by inverse probability weighting

Acknowledgements: This work was funded by grants from the National Institutes of Health, NIAMS (R01 AR46849) and NIA (R01 AG068192, R01 AG034676).
Disclosure of Interests: Vanessa Kronzer: None declared, Tina Gunderson: None declared, Cynthia S. Crowson: None declared, John M Davis III Grant/research support from: Pfizer, Maria Vassilaki Shareholder of: equity ownership in Abbott Laboratories, Johnson and Johnson, Medronic and Amgen;, Grant/research support from: Roche and Biogen, Michelle Mielke Consultant of: Biogen and Brain Protection Company, Elena Myasoedova: None declared
DOI: 10.1136/annrheumdis-2021-eular.2172

POS0310

EXPOSURE TO MAJOR PSYCHOLOGICAL TRAUMA OR STRESS IN THE PRECEDING ONE YEAR SIGNIFICANTLY CONTRIBUTES TO POOR DISEASE CONTROL IN PATIENTS WITH RHEUMATOID ARTHRITIS: SINGLE CENTRE RESULTS FROM THE PRIME REGISTRY COHORT

M. Haroon[1], S. Asif[1], S. Batool[1], F. Hashmi[1], S. Ullah[1], A. Ashraf[2], H. J. Shaheen[1]. [1]*Fatima Memorial Hospital & FMH College of Medicine and Dentistry, Department of Rheumatology, Lahore, Pakistan*; [2]*CMH Lahore Medical College & Institute of Dentistry, Medicine, Lahore, Pakistan*

Background: Stress response is considered to involve the activation of both the hypothalamus-pituitary-adrenal axis and the autonomic nervous system, along with its communication with the immune system. Because many rheumatic diseases are characterized by immune-mediated joint inflammation, stressful events might contribute to the aetiology, maintenance and exacerbation of rheumatic diseases.
Objectives: We aimed to examine whether real-life major stressful events lead to poor disease control among patients with Rheumatoid arthritis (RA). We addressed this question using real-world data from the PRIME registry.
Methods: This was a cross-sectional study conducted using data collected at the time of patient enrolment in the PRIME registry. The PRIME Registry is a large, independent, prospective, observational cohort initiated in October 2019 that comprises patients diagnosed with RA, SLE, PsA or AS by a rheumatologist, and is being actively followed up. IRB approval and informed consent was obtained. We assessed the registry data for RA patients. The clinical variables studied were gender, age, smoking habits, body mass index, education status, marital status, disease duration, comorbidities (using Charlson Comorbidity Index). Education status was stratified by whether participants completed secondary (high) school education. Evaluation of disease activity and severity was made as per internationally agreed definitions, such as: swollen joint counts (SJC), tender joint counts (TJC), deformed joint counts, and DAS-28. Major psychological trauma or stress was defined if the patient has experienced any of the following in the past year: a) major personal injury or illness; b) death/major illness of a close relative; c) marital separation/divorce; d) loss of job; e) major financial loss; f) mass casualty incident loss.
Results: The data of consecutive 507 RA patients (mean age 42.3±12.6 years, 73.6% female, disease duration of 80±22 months) was reviewed. Thirty-six percent of the cohort reported to have major psychological stress and trauma in the preceding one year. No statistical association of age, gender, and marital status was noted, but statistical association of low education status (p=0.042), longer disease duration (p=0.044), higher DAS-28 values (p<0.001) and other markers of RA disease activity (SJC, TJC, ESR, patient global health) was found. On multiple logistic regression analysis, a significant association of major psychological stress and trauma in the preceding one year was noted with active disease (DAS-28; OR 1.67, CI 1.17-2.4, p=0.005). Following variables were included in the full regression model, disease duration, gender, age, marital status, education status, and DAS-28 value (also used models with SJC, TJC, deformed joint counts, ESR, patient global health, but the results remained unchanged).
Conclusion: Major psychological stress and trauma in the preceding one year is associated with high disease activity among patients with RA. Therapies that focus on stress management may be important adjuncts to traditional pharmacotherapy in the treatment of inflammatory rheumatic diseases.
Disclosure of Interests: Muhammad Haroon Speakers bureau: Roche, Novartis, Grant/research support from: Abbvie, Pfizer, Sadia Asif: None declared, Shabnam Batool: None declared, Farzana Hashmi: None declared, Saadat Ullah: None declared, Arfa Ashraf: None declared, Hafiza Javeria Shaheen: None declared
DOI: 10.1136/annrheumdis-2021-eular.2101

POS0311

NEUROIMAGING BIOMARKERS IN INDIVIDUALS WITH AND WITHOUT RHEUMATOID ARTHRITIS: RESULTS FROM THE MAYO CLINIC STUDY OF AGING

M. Vassilaki[1], C. S. Crowson[1], J. M. Davis III[2], S. Duong[1], D. Jones[3], M. Mielke[1,4], P. Vemuri[3], E. Myasoedova[1,2]. [1]*Mayo Clinic, Department of Quantitative Health Sciences, Rochester, United States of America*; [2]*Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; [3]*Mayo Clinic, Department of Radiology, Rochester, United States of America*; [4]*Mayo Clinic, Department of Neurology, Rochester, United States of America*

Background: Age-related increase in the burden of systemic inflammation is an established key player and potential treatment target in Alzheimer's disease (AD) and other age-related dementias. (Dregan, Chowienczyk et al. 2015) Although rheumatoid arthritis (RA) is an autoimmune hyper-inflammatory disease, studies on RA and dementia or vascular neuroimaging biomarkers are lacking.
Objectives: To examine the associations between RA and dementia/vascular neuroimaging biomarkers in the Mayo Clinic Study of Aging (MCSA).

Methods: The study consisted of 35 RA cases in MCSA and 104 MCSA participants without RA matched 1:3 for age, sex, education, cognitive status (≥50 years old) at baseline and the availability of at least one magnetic resonance imaging (MRI). The primary outcome measures were well established dementia-related neuroimaging biomarkers, including global beta-amyloid (Aβ) using PiB-positron-emission tomography (PET; n=47); neurodegeneration (hypometabolism via FDG-PET (n=45), hippocampal volume (n=139), and cortical thickness via structural MRI [n=138], and cerebrovascular pathology via FLAIR-MRI (white matter hyperintensity [WMH; n=49] burden, subcortical, and cortical infarctions (n=55)). Elevated ^{11}C-PiB-PET was defined as standardized uptake value ratio ≥1.48 in an Alzheimer's disease (AD)-related region of interest and reduced AD signature cortical thickness as ≤2.68mm (neurodegeneration; N+). Kruskal-Wallis rank sum and Pearson's chi-squared tests were used to compare the neuroimaging measures between participants with and without RA.

Results: Participants with vs. without-RA did not differ in age, sex, years of education, major comorbidities, Aβ burden, hippocampal volume, and neurodegeneration measures (Table 1). Although the sample size was small, we observed that RA participants (vs. without-RA) had greater mean WMH volume (relative to the total intracranial volume (TIV) (mean (SD) %: 1.12 (0.57) % vs 0.76 (0.69) % of TIV, p=0.011), were more likely to have cortical infarctions (4 vs.1; p=0.013) and had a higher mean number of cortical infarctions (mean (SD): 0.24 (0.44) vs. 0.05 (0.32), p=0.017).

Conclusion: Our preliminary data suggest significant differences in cerebrovascular biomarker measures by RA status. Further studies would add valuable information to our understanding and insight into the development of interventions for the prevention of cerebrovascular pathology in RA patients.

REFERENCES:

[1] Dregan, A., P. Chowienczyk and M. C. Gulliford (2015). "Are Inflammation and Related Therapy Associated with All-Cause Dementia in a Primary Care Population?" J Alzheimers Dis 46(4): 1039-1047.

Table 1. Participants' baseline characteristics.

	With RA	Without RA	Total	p value*
Age, mean (SD)	76.3 (7.9)	75.9 (7.9)	139	0.82
Male	13 (37%)	37 (36%)	139	0.87
Education (years), mean (SD)	14.5 (2.5)	14.3 (2.4)	139	0.75
Apolipoprotein E ε4 carrier	6 (17%)	28 (27%)	139	0.24
Cognitively unimpaired	27 (77%)	83 (80%)	110	0.94
Mild cognitive impairment	7 (20%)	18 (17%)	25	
Dementia	1 (3%)	3 (3%)	4	
Reduced AD signature cortical thickness	20 (57%)	60 (58%)	138	0.91
Elevated β-amyloid	4 (33%)	11 (31%)	47	0.90
FDG PET SUVR	1.52 (0.16)	1.59 (0.18)	45	0.46
White matter hyperintensity volume % of TIV	1.12 (0.57)	0.76 (0.69)	49	0.011
With cortical infarctions	4 (24%)	1 (3%)	55	0.013

N (%) unless otherwise stated; * Kruskal-Wallis rank sum or Pearson's Chi-squared test.SD=-standard deviation; AD= Alzheimer's disease; SUVR=standardized uptake value ratio; TIV= Total intracranial volume.

Acknowledgements: The study was supported by the NIH AG068192. The Mayo Clinic Study of Aging was supported by the NIH (U01 AG006786, P50 AG016574, R01AG057708, R01 AG011378, R01 AG021927, R01 AG041851, R01 NS097495), the Alexander Family Alzheimer's Disease Research Professorship of the Mayo Clinic, Mayo Foundation for Medical Education and Research, the Liston Award, the Schuler Foundation and was made possible by the Rochester Epidemiology Project (R01 AG034676).

Disclosure of Interests: Maria Vassilaki Shareholder of: M. Vassilaki has equity ownership in Abbott Laboratories, Johnson and Johnson, Medronic and Amgen., Grant/research support from: M. Vassilaki has received research funding from Roche and Biogen in the past., Cynthia S. Crowson: None declared, John M Davis III Grant/research support from: JM. Davis III receives research funding from Pfizer., Stephanie Duong: None declared, David Jones: None declared, Michelle Mielke Consultant of: M. Mielke has consulted for Biogen and Brain Protection Company, Prashanthi Vemuri: None declared, Elena Myasoedova: None declared

DOI: 10.1136/annrheumdis-2021-eular.1137

POS0312 HOW DOES THE PRESENCE OF DEPRESSION IMPACT ON DISEASE ACTIVITY SCORES IN PATIENTS WITH RHEUMATOID ARTHRITIS?

C. A. Isnardi[1], E. E. Schneeberger[1], D. Capelusnik[1], M. Bazzarelli[2], L. Barloco[3], E. S. Blanco[4], A. Benitez[4], F. Benavidez[4], S. Scarafia[5], M. A. Lazaro[5], R. Perez Alamino[6], F. Colombres[6], M. P. Kohan[7], J. Sosa[7], L. Gonzalez Lucero[8], A. L. Barbaglia[8], H. Maldonado Ficco[9], G. Citera[1]. *[1]Psychophysical Rehabilitation Institute, Rheumatology, DQG, Argentina*; *[2]Hospital Provincial Petrona V. de Cordero, Rheumatology, San Fernando, Argentina*; *[3]Hospital Provincial Petrona V. de Cordero, Terapia ocupacional, San Fernando, Argentina*; *[4]General Hospital Dr. Cosme Argerich Treble, Rheumatology, AHD, Argentina*; *[5]IARI-Instituto de Asistencia Reumatológica Integral, Rheumatology, San Fernando, Argentina*; *[6]Hospital de Clínicas Nicolás Avellaneda, Rheumatology, San Miguel de Tucumán, Argentina*; *[7]Dr. Enrique Tornú Hospital, Rheumatology, Ciudad de Buenos Aires, Argentina*; *[8]Hospital Ángel C. Padilla, Rheumatology, San Miguel de Tucumán, Argentina*; *[9]Nuevo Hospital Río Cuarto "San Antonio de Padua", Rheumatology, Río Cuarto, Argentina*

Background: Depression is present in up to half of patients with Rheumatoid Arthritis (RA). The association between this mood disorder and disease activity scores, including DAS28, SDAI and CDAI, has previously been described by various authors.

Objectives: The aim of our study was assessed the effect of depression on the components of different disease activity scores.

Methods: We performed a cross-sectional study of consecutive adults with RA, according to ACR/EULAR 2010 criteria. Sociodemographic data, comorbidities and current treatment were recorded. Disease activity was evaluated using DAS28-ESR, DAS28-CRP, SDAI and CDAI. Depression was assessed using PHQ-9 questionnaire. The PHQ-9 values were categorized in 4 groups as follows: 5 to 9, 10 to 14, 15 to 19, 20 or greater, represents mild, moderate, moderate/severe, and severe depression, respectively. A cutoff value of 10 or greater was set to define major depression. *Statistical analysis:* Student´s T, ANOVA and Chi^2 tests. Multiple logistic regression.

Results: Two hundred fifty eight patients were included, with a median (*m*) disease duration of 9 years (IQR 3.6-16.7). The *m* PHQ-9 score was 6 (IQR 2-12.3) and the prevalence of major depression was 33.7%. Patients with major depression had more tender and swollen joint count (TJC and SJC) (mean 4.9±4.3 vs 2.3±3.7, p<0.0001 and 2.9±3.3 vs 1.7±3.4, p=0.009), more pain (VAS [cm] mean 5.6±2.7 vs 3.3±2.6, p<0.0001), higher patient and physician global assessment (PGA and PhGA) (VAS [cm] mean 5.4±2.9 vs 3.1±2.5, p<0.0001 and 4.4±2.7 vs 2.4±2.4, p<0.0001) and CRP (mean 1.7±3.3 vs 0.7±1.1 mg/dl, p=0.01). ESR values were higher in the group with major depression, but the difference did not reach significance. Disease activity was higher in the depression group by all scores: DAS28-ESR (mean 4.3±1.4 vs 3.3±1.3, p<0.0001), DAS28-CRP (mean 3.9±1.4 vs 2.8±1.7, p<0.0001), SDAI (mean 19.2±12.7 vs 10.3±10.1, p<0.0001) and CDAI (mean 17.6±10.9 vs 9.6±9.9, p<0.0001). While 41 (15.9%) patients had high disease activity according to DAS28-ESR, only 34 (13.2%) had SDAI>26.

In the multivariate analysis, evaluating the association of major depression with the different components of DAS28-ESR, DAS28-CRP, SDAI and CDAI, we observed that the presence of this mood disorder remained significantly associated with higher PGA in all the scores. In addition, a significant association was seen with higher TJC in both DAS28 scores.

Conclusion: Patients with major depression had higher disease activity. It´s presence has a significantly association with the subjective items of the disease activity scores, particularly PGA. CRP value was the only objective component associated with depression.

Disclosure of Interests: Carolina Ayelen Isnardi Speakers bureau: Bristol Myers Squibb, Janssen, Grant/research support from: Pfizer, Emilce Edith Schneeberger Speakers bureau: Abbvie, Amgen, Bristol Myers Squibb, Janssen, Eli Lilly, Boehringer Ingelheim, Pfizer, Genzyme, Grant/research support from: Pfizer, Dafne Capelusnik Speakers bureau: Bristol Myers Squibb, Grant/research support from: Pfizer, Marcela Bazzarelli: None declared, Laura Barloco: None declared, Eliana Soledad Blanco: None declared, Alejandro Benitez Speakers bureau: Abbvie, Novartis, Amgen, Federico Benavidez: None declared, SANTIAGO SCARAFIA: None declared, María Alicia Lazaro Speakers bureau: Abbvie, Rodolfo Perez Alamino Speakers bureau: Pfizer, Abbvie, Amgen, Bristol-Myers-Squibb, Lilly, Janssen, Novartis, Federico Colombres: None declared, María Paula Kohan: None declared, Julia Sosa: None declared, Luciana Gonzalez Lucero: None declared, Ana Lucía Barbaglia: None declared, Hernan Maldonado Ficco Speakers bureau: Pfizer, Abbvie, Jansen, Novartis, Bago, Bristol, Eli Lilly., Consultant of: Pfizer, Abbvie, Novartis, Jansen, Bago, Eli Lilly., Gustavo Citera Speakers bureau: Abbvie, Bristol-Myers-Squibb, Lilly, Jansen, Gema, Pfizer, Roche, Grant/research support from: Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1374

POS0313 INCIDENCE AND PREVALENCE OF POLYAUTOIMMUNITY IN SEROPOSITIVE COMPARED WITH SERONEGATIVE PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE COHORT STUDY

A. Hagelskjær[1], R. Cordtz[1], S. Bliddal[2], A. S. Mortensen[1], S. Kristensen[1,3], C. H. Nielsen[4], U. Feldt-Rasmussen[2,5], C. Torp-Pedersen[6], L. Dreyer[1,3,7]. *[1]Aalborg University Hospital, Department of Rheumatology, Aalborg, Denmark*; *[2]Copenhagen University Hospital, Rigshospitalet, Department of Medical Endocrinology and Metabolism, København, Denmark*; *[3]Aalborg University, Department of Clinical Medicine, Aalborg, Denmark*; *[4]Copenhagen University Hospital, Rigshospitalet, Institute of Inflammation Research, København, Denmark*; *[5]University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark*; *[6]North Zealand Hospital - Hillerød, Department of Cardiology, Hillerød, Denmark*; *[7]DANBIO, Denmark, Nationwide, Denmark*

Background: Rheumatoid arthritis (RA) is categorized as seropositive or seronegative referring to the presence or absence of IgM rheumatoid factor (IgM-RF) and/ or anti-citrullinated protein antibodies (ACPA).
Patients with an autoimmune disease are more likely to develop additional autoimmune conditions than individuals without pre-existing autoimmune disease.
Objectives: The aims of this study were to examine patterns of polyautoimmunity in seropositive compared with seronegative patients with recent-onset RA.
Methods: The study was register-based and used the nationwide DANBIO register (identification of recent-onset (<1 year) seropositive, ICD-10 M05, and seronegative, M06, RA patients) linked to the Danish National Patient Registry and the Danish National Prescription Registry to obtain information on additional autoimmune diseases (see Table 1 for autoimmune conditions). Using age and sex adjusted logistic regression analysis, the odds ratio (OR) of prevalent polyautoimmunity in seropositive compared with seronegative patients at the time of RA diagnosis was calculated.
To estimate the hazard ratio (HR) for developing yet another autoimmune disease in the 5 years after RA diagnosis, adjusted cause-specific Cox regression models were performed. Several sensitivity analyses were carried out including alternative exposure and outcome definitions.
Results: In total, 12,517 patients with recent-onset RA were included. The groups were similar in terms of disease characteristics and DMARD treatment, but seropositive patients were younger and included more women, see Table 1. Patients with seropositive RA had an OR of 0.79 (95% CI 0.71-0.89) for baseline presence of polyautoimmunity compared with seronegative patients, whereas the 5-year HR was 0.86 (95% CI 0.71-1.05) for incident polyautoimmunity. The results remained similar in all sensitivity analyses.
Conclusion: Patients with seropositive RA had a slightly lower prevalence and incidence of polyautoimmunity compared to seropositive patients. The results were somewhat surprising, yet very robust, and thus raises the question if seronegative RA is in fact "more autoimmune" despite the absence of (identified) autoantibodies.

Table 1. Characteristics, prevalence, and incidence of polyautoimmunity in incident RA patients.

	Seropositive	Seronegative
N	7983	4534
Age in years	59.4 (48.6 to 69.1)	63.0 (51.5 to 72.3)
Women	5476 (69 %)	2856 (63 %)
HAQ-DI	0.857 (0.375 to 1.375)	0.875 (0.375 to 1.375)
DAS28-CRP	4.3 (3.3 to 5.2)	4.6 (3.6 to 5.5)
CRP, mg/mL	10 (4 to 23)	10 (3 to 26)
VAS physician, 0-100mm	27 (15 to 45)	30 (16 to 47)
Treated with methotrexate	86 %	84 %
-other csDMARD, %	24 %	24 %
-Biological DMARD, %	5 %	6 %
Smoking status: Current / previous / never / unknown, %	13 / 11 / 17 / 59 %	9 / 9 / 23 / 59 %
Prevalence of polyautoimmunity / diabetes mellitus type 1 / autoimmune thyroid disease / inflammatory bowel disease	549 (10.6 %) / 1.4 % / 6.7 % / 1.4 %	349 (12.8 %) / 1.5 % / 7.8 % / 1.5 %
Age and sex adjusted odds ratio	0.79 (0.71 to 0.89)	1 (ref.)
Incident cases of polyautoimmunity	373 (4.7 %)	242 (5.3 %)
Adjusted hazard ratio	0.86 (0.71 to 1.05)	1 (ref.)

Continuous variables shown as median with interquartile ranges. Autoimmune conditions included:autoimmune thyroid disease (redeemed prescriptions of ATC=H03A); diabetes mellitus type 1 (ICD-10 diagnosis E10 combined with redeemed prescriptions of insulin, ATC=A10A); pernicious anaemia (D51.0); autoimmune haemolytic anaemia (D59.1); idiopathic thrombocytopenic purpura (D69.3); Autoimmune adrenalitis (E27.1B); multiple sclerosis (G35); neuromyelitis optica (G36.0); Guillain-Barré syndrome (G61.0); myasthenia gravis (G70); inflammatory bowel disease (K50-1); primary biliary cirrhosis (K74.3); primary sclerosing cholangitis (K83.0); autoimmune hepatitis (K75.4); celiac disease (K90.0); pemphigus vulgaris (L10.0); bullous pemphigoid (L12.0); dermatitis herpetiformis (L13.0); alopecia areata (L63); vitiligo (L80); lichen sclerosis (L90.0); chronic interstitial cystitis (N30.1).

Acknowledgements: We acknowledge all patients and all Danish departments of rheumatology contributing to the DANBIO registry.
Disclosure of Interests: Amalie Hagelskjær: None declared, René Cordtz: None declared, Sofie Bliddal: None declared, Anders Sandermann Mortensen: None declared, Salome Kristensen: None declared, Claus Henrik Nielsen: None declared, Ulla Feldt-Rasmussen: None declared, Christian Torp-Pedersen: None declared, Lene Dreyer Grant/research support from: Grants from BMS, Galderma, and Eli Lilly
DOI: 10.1136/annrheumdis-2021-eular.668

POS0314

PROSPECTIVE EVALUATION OF A DEDICATED, SERIAL OCCUPATIONAL THERAPY EXERCISE PROGRAM ON HAND FUNCTION IN RHEUMATOID ARTHRITIS (RA)

W. Pietrowski[1], K. Richter-Bastian[2], K. Storck-Müller[2], U. Müller-Ladner[1], U. Lange[1], I. Tarner[1]. [1]*Campus Kerckhoff, Justus-Liebig-University Gießen, Department of Rheumatology, Clinical Immunology, Osteology and Physical Medicine, Bad Nauheim, Germany*; [2]*Rheumazentrum Mittelhessen, Department of Rheumatology, Bad Endbach, Germany*

Background: Rheumatoid arthritis (RA) frequently affects the joints of the hands causing severe pain and significant functional impairment affecting all activities of daily living. At early stages, functional impairment is primarily caused by reversible joint and tendon sheath effusions while at later stages synovial thickening, muscular atrophy and irreversible damage to cartilge, bone, tendons and ligaments cause a reduced range of motion and deformities. Occupational therapy aims to maintain and improve joint mobility and function. However, there is limited data on the effectiveness of serial exercise programs specifically aiming at maintaining and improving hand function in RA.
Objectives: To prospectively evaluate the effects of a dedicated exercise program on hand function, grip strength, joint mobility and pain compared with conventional outpatient physiotherapy not specifically targeting hand function.
Methods: A total of 51 RA patients receiving outpatient physiotherapy once a week were enrolled and randomized to either continue their usual therapy (control group) or to participate in a dedicated hand function training (HFT) twice a week in addition to their usual therapy (HFT group). The HFT program was supervised by an occupational therapist who conducted once weekly HFT sessions and instructed the participants to perform an additional self-administered HFT session at home once a week. Study duration was six months with an option to continue HFT for additional 6 months. Study participants were evaluated at baseline and every 3 months.
The primary outcomes hand function and grip strength were assessed using standardized questionnaires (Cochin hand function scale (CHFS), Australian/ Canadian Osteoarthritis Hand Index (AUSCAN), Michigan Hand Outcomes Questionnaire (MHOQ)) and dynamometer/pinch gauge readings for different types of grip (cylindrical grasp, spherical grasp, hook grasp, tip to tip pinch and key pinch), respectively. The secondary outcomes joint mobility and pain were assessed using a digital goniometer and visual analogue scales (VAS), respectively. Statistical analysis used the Wilcoxon test for evaluating changes of parameters over time within the groups and the Kruskal Wallis test for group comparisons and Bonferroni-Holm correction.
Results: 41 of the 51 patients (HFT group: n = 20, mean age 60.3 ± 8.4 years; control group: n = 21, mean age 60.5 ± 11.5 years) completed the 6-month study period, 14 patients extended their HFT to 12 months. Within the 6-month study period there were no significant improvements of the primary outcome parameters and of pain within the groups vs. baseline and no significant differences between the groups. Only the CHFS improved significantly in the HFT group as of month 9. A significant improvement of the range of motion vs. baseline was achieved by HFT as early as 3 months after baseline which persisted up to month 12. As some improvement was also seen in the control group, there was no significant difference between the groups. Hand mobility improved particularly in the subgroup of patients >60 years of age. There was no influence by pain intensity at baseline (VAS ≤50 mm vs. VAS >50 mm).
Conclusion: Serial dedicated HFT for 6 months resulted in improved joint mobility but did not improve global hand function, grip strength and pain in RA patients. A longer treatment duration (≥12 months), a higher treatment frequency (>2 times/week) and a larger cohort of patients may be required.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3806

Scleroderma, myositis and related syndromes

POS0315

LONG-TERM SAFETY AND EFFICACY OF LENABASUM DURING 3 YEARS IN AN OPEN-LABEL EXTENSION (OLE) OF A PHASE 2 STUDY OF LENABASUM IN REFRACTORY SKIN DISEASE IN DERMATOMYOSITIS (DM)

V Werth.[1], J. Concha[1], J. Burroughs[1], J. Okawa[1], R. Feng[1], A. Jobanputra[1], R. Borucki[1], K. Hally[2], E. Hejazi[1], M. Tillinger[2], S. Constantine[2], N. Dgetluck[2], B. White[2]. [1]*University of Pennsylvania, Dermatology, Philadelphia, United States of America*; [2]*Corbus Pharmaceuticals, Clinical, Norwood, United States of America*

Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of inflammation. Lenabasum had acceptable safety and tolerability and improved efficacy outcomes in the initial 16-week double-blinded, randomized, placebo-controlled Part A of Phase 2 trial JBT101-DM-001 (NCT02466243) in DM subjects with refractory skin involvement. In that study, lenabasum or placebo was added to stable background treatment, with immunosuppressive therapies allowed.
Objectives: To assess long-term safety and efficacy in DM subjects in this study.
Methods: Subjects who completed Part A of the Phase 2 study (n = 22) were eligible to receive oral lenabasum 20 mg BID in an open-label extension (OLE) that assessed safety and efficacy at 4 weeks, then every 8 weeks.

Results: 20/22 (91%) eligible subjects enrolled in the OLE, following a mean interval of 31 weeks from the end of Part A, during which they continued to receive standard-of care treatments, to the start of the OLE during which lenabasum 20mg BID was added. 17/20 (85%) subjects were on stable baseline immunosuppressive drugs. At the time of this data cut-off, 17 subjects were still enrolled, 17 had completed 140 months (2.7 years), and 15 had completed 156 months (3 years) of OLE dosing.

All OLE subjects experienced at least 1 adverse event (AE), with 118 AEs during the OLE through Dec 2020. Most AEs were mild (n = 111, 94%), with 2 severe AEs (fatigue and metastatic prostate cancer) considered unrelated to lenabasum. AEs occurring in ≥ 3/20 OLE subjects were: URI (n = 5); fatigue (n = 4); nausea (n = 3); common cold (n = 3); UTI (n = 3); and DM flare (n = 3). No serious AEs related to lenabasum have been reported in this OLE to date. No subject discontinued the OLE because of an AE related to lenabasum.

Improvement was seen in multiple physician- and patient-reported efficacy outcomes. CDASI activity score improved through the first 15 months of lenabasum treatment in the OLE and remained stable thereafter, with an improvement of ~20 points from the beginning of the study maintained from Month 15 through Year 3 in the OLE. CDASI damage score increased through the first year of the OLE, even though skin activity was decreasing, but lessened thereafter, returning after 3 years to about the same level it was at the beginning of the OLE. Other outcomes shown in Figure 1 followed the same general pattern as CDASI activity score, with improvement through the first 12-16 months of the OLE, then stability thereafter. Of note, 2 subjects had disease flares shortly after stopping lenabasum for conclusion of the OLE.

Conclusion: Lenabasum continues to have a favorable safety and tolerability profile in the OLE of the Phase 2 trial JBT101-DM-001 with no serious AEs or study discontinuations related to lenabasum. The CDASI activity score and multiple other physician and patient-reported outcomes improved and have remained stable, showing durability of improvement in these patients with refractory skin disease. Skin damage was reversible and began to improve once skin activity stabilized. The limitations of attributing this improvement to lenabasum in the setting of open-label dosing is acknowledged. These data support further testing of lenabasum for the treatment of DM, and a Phase 3 study of lenabasum in DM is ongoing.

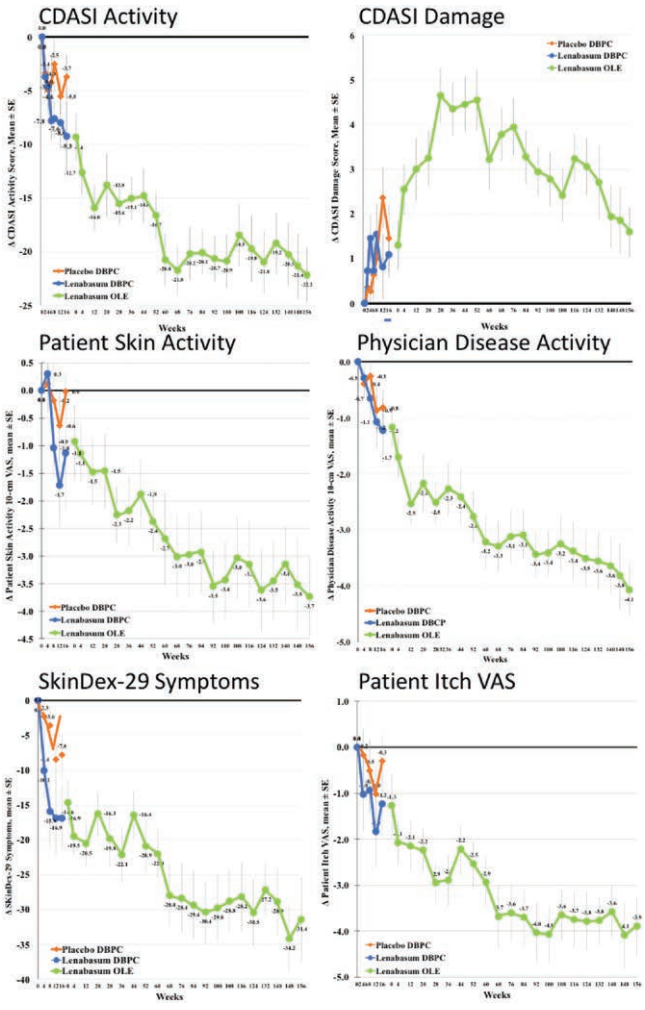


Figure 1. Change from Baseline in Selected Efficacy Outcomes in OLE of Phase 2 Trial JBT101-DM-001

Disclosure of Interests: Victoria Werth Grant/research support from: Investigator for Corbus Pharmaceuticals and received funding to conduct trials, Josef Concha: None declared, Julie Burroughs: None declared, Joyce Okawa: None declared, Rui Feng: None declared, Anisha Jobanputra: None declared, Robert Borucki: None declared, Kathleen Hally Employee of: Employee of Corbus Pharmaceuticals, Emily Hejazi: None declared, Michael Tillinger Employee of: Employee of Corbus Pharmaceuticals, Scott Constantine Employee of: Employee of Corbus Pharmaceuticals, Nancy Dgetluck Employee of: Employee of Corbus Pharmaceuticals, Barbara White Employee of: Employee and stockholder of Corbus Pharmaceuticals

DOI: 10.1136/annrheumdis-2021-eular.2048

POS0316

MODELLING SHORT-TERM FVC CHANGES FROM SENSCIS TO LONG-TERM FVC COURSE IN SSC-ILD DEMONSTRATES CLINICALLY MEANINGFUL REDUCTION OF FVC DECLINE AND SURVIVAL BENEFITS

A. M. Hoffmann-Vold[1], D. Huscher[2], P. Airò[3], E. Zanatta[4], P. Carreira[5], Y. Allanore[6], U. Müller-Ladner[7], A. Giollo[8], M. R. Pozzi[9], C. Souza Muller[10], R. Bečvář[11], M. Iudici[12], D. Majewski[13], A. Gabrielli[14], M. Alves[15], N. Schoof[15], O. Distler[16]. [1]*Oslo University Hospital, Deptartment of Rheumatology, Oslo, Norway*; [2]*Charité-Universitaetsmedizin, Institute of Biometry and Clinical Epidemiology, and Berlin Institute of Health, Berlin, Germany*; [3]*ASST Spedali Civili of Brescia, University of Brescia, Rheumatology and Clinical Immunology, Brescia, Italy*; [4]*University of Padova, Rheumatology Unit, Department of Medicine, Padova, Italy*; [5]*12 de Octubre University Hospital, Department of Rheumatology, Madrid, Spain*; [6]*Cochin Hospital, Department of Rheumatology, Paris, France*; [7]*Justus Liebig University Giessen, Campus Kerckhoff, Department of Rheumatology and Clinical Immunology, Bad Nauheim, Germany*; [8]*University of Verona, Rheumatology Section, Department of Medicine, Verona, Italy*; [9]*University of Milan-Bicocca, Respiratory Unit, San Gerardo Hospital, Department of Medicine and Surgery, Monza, Italy*; [10]*Universidade Federal do Parana, Division of Rheumatology, Department of Medicine, Curitiba, Brazil*; [11]*Charles University, Department of Rheumatology, Praha, Czech Republic*; [12]*Geneva University Hospitals and University of Geneva, Rheumatology Unit, Geneva, Switzerland*; [13]*Poznan University of Medical Sciences, Department of Rheumatology, Rehabilitation and Internal Medicine, Poznan, Poland*; [14]*Università Politecnica delle Marche, Dipartimento di Scienze Climiche e Molecolari, Ancona, Italy*; [15]*Boehringer Ingelheim International GmbH, TA Inflammation Med, Ingelheim am Rhein, Germany*; [16]*University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland*

Background: Nintedanib has shown to slow FVC decline by 41ml over 52 weeks in systemic sclerosis-associated interstitial lung disease (SSc-ILD). However, the long-term effect of nintedanib treatment on ILD progression and mortality in SSc patients is so far unknown.

Objectives: Here, the 52-week treatment efficacy of nintedanib was modeled and extrapolated on the long-term FVC course and survival in SSc-ILD patients from the European Scleroderma Trial and Research (EUSTAR) database.

Methods: SSc patients from the EUSTAR database fulfilling the inclusion criteria of the SENSCIS trial (SSc classification criteria, ILD confirmed by imaging, disease duration of <7 years, FVC≥40%pred, diffusion capacity of the lung for carbon monoxide (DLCO) 30-89%pred); and matched for baseline characteristics as well as matched for the 52-week FVC change of SENSCIS patients were included (n=236). Linear mixed models including time, risk factors at baseline (sex, age, dyspnea class, DLCO%, CRP, modified Rodnan skin score, SSc subtype, SSc auto-antibodies, disease duration, synovitis and muscle weakness) were used to estimate the natural FVC course over time. On this natural course of FVC, the observed effect from the SENSCIS trial representing the absolute 52-week difference of FVC decline between the nintedanib and the placebo group was applied as continuous annual effect (SENSCIS effect model). Survival was estimated for both the natural course as well as the SENSCIS effect model using Cox regression.

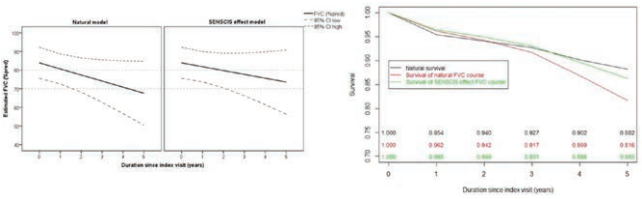
Results: Of the 236 included patients, 75% were females, 65% had diffuse cutaneous SSc. Mean age was 50.6 years, mean FVC 78.2%pred and DLCO 56.3%pred at time of inclusion. Mean FVC change after 12±3 months was -2.3 ±6.9%pred. These parameters were largely similar to the characteristics of the SENSCIS population.

In the longitudinal follow up of this population, the natural course of FVC showed a total FVC decline of -16.3%pred over 5 years. With assumed SENSCIS effects (effects of nintedanib treatment reported in SENSCIS), the 5-year FVC decline was reduced to -10.3%pred (Figure 1).

The reduced FVC progression translated into an improved survival. The natural 5-year survival of this SSc-ILD population was 88.2%. When extrapolating also a severe FVC decline early in the course, frequently terminated by early mortality of SSc patients excluding them from long-term outcome assessment, the estimated 5-year survival was reduced to 81.6%. When the SENSCIS effects on

FVC were considered, the 5-year extrapolated survival was increased to 86.3% (Figure 2).

Conclusion: Long-term experience of nintedanib treatment in SSc-ILD patients is lacking so far, therefore we modeled and extrapolated the 52-week treatment efficacy of nintedanib on the long-term FVC course and survival in SSc-ILD patients from the EUSTAR database. We could demonstrate a significant reduction of FVC decline by extrapolating the annual treatment effects of nintedanib from the SENSCIS trial from 1 to 5 years in EUSTAR. Translating these reductions of FVC decline into survival, the 5-year mortality rate was reduced from 18% to 13%.



Disclosure of Interests: Anna-Maria Hoffmann-Vold Speakers bureau: Boehringer Ingelheim, Actelion, Roche, Merck Sharp & Dohme, Lilly, Consultant of: Actelion, Boehringer Ingelheim, Roche, Bayer, Merck Sharp & Dohme, ARXX, Lilly and Medscape, Grant/research support from: Boehringer Ingelheim, Dörte Huscher: None declared, Paolo Airò Speakers bureau: Boehringer Ingelheim, Consultant of: Bristol-Myers-Squibb, Novartis, Elisabetta Zanatta Speakers bureau: Boehringer Ingelheim, Actelion, GSK, Paid instructor for: GSK, Consultant of: Boehringer Ingelheim, GSK, Patricia Carreira Speakers bureau: Actelion, Boehringer Ingellheim, Janssen, GSK, Paid instructor for: Boehringer Ingelheim, Consultant of: AbbVie, Boehringer Ingelheim, VivaCell, Emerald Health Pharmaceuticals, Gesynta Pharma, Sanofi Genzyme, Grant/research support from: Roche, GSK, Yannick Allanore Consultant of: Honorarium received from Boehringer, Medsenic
Sanofi, Menarini, Grant/research support from: Grants received from Alpine, Ose Immunogenetics, Ulf Müller-Ladner Speakers bureau: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim, Alessandro Giollo: None declared, Maria Rosa Pozzi: None declared, CAROLINA SOUZA MULLER Speakers bureau: Boehinger Ingelheim, Janssen, Roche, LIBBS, Bristol-Myers-Squib, Radim Bečvář Consultant of: Actelion, Boehringer Ingelheim, Michele Iudici: None declared, Dominik Majewski Speakers bureau: Boehringer Ingelheim - 2 x paid as a speaker, Armando Gabrielli Grant/research support from: Pfizer, CSL Behring, Margarida Alves Employee of: Boehringer Ingelheim, Nils Schoof Employee of: Boehringer Ingelheim International GmbH, Oliver Distler Speakers bureau: Boehringer Ingelheim, Medscape, IQone, Roche, Consultant of: Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, Kymera Therapeutics, Lilly, Medac, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB, Grant/research support from: Kymera Therapeutics, Mitsubishi Tanabe
DOI: 10.1136/annrheumdis-2021-eular.2522

POS0317

THE PERFORMANCE OF DIFFUSING CAPACITY FOR MONOXIDE CARBON (DLCO) AND FORCED VITAL CAPACITY (FVC) IN PREDICTING THE ONSET OF SYSTEMIC SCLEROSIS (SSC)-INTERSTITIAL LUNG DISEASE (ILD) IN THE EUROPEAN SCLERODERMA TRIALS AND RESEARCH (EUSTAR) DATABASE

G. Lepri[1], C. Bruni[1], L. Tofani[1], A. Moggi Pignone[2], M. Orlandi[1], T. Sara[3], M. Hughes[4], F. Del Galdo[5], R. Irace[6], O. Distler[7], V. Riccieri[8], Y. Allanore[9], A. M. Gheorghiu[10], E. Siegert[11], J. De Vries-Bouwstra[12], E. Hachulla[13], M. Tikly[14], N. Damjanov[15], F. Spertini[16], L. Mouthon[17], A. M. Hoffmann-Vold[18], A. Gabrielli[19], S. Guiducci[1], M. Matucci-Cerinic[1], D. Furst[1,20], S. Bellando Randone[1]on behalf of EUSTAR. *[1]AOU Careggi, University of Florence, Division of Rheumatology, Florence, Italy*; *[2]AOU Careggi, University of Florence, Division of Internal Medicine, Florence, Italy*; *[3]AOU Careggi, University of Florence, Interventional Pulmonology Unit, Florence, Italy*; *[4]Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Department of Rheumatology, Sheffield, United Kingdom*; *[5]NIHR Biomedical Research Centre and Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Raynaud's and Scleroderma Programme, Leeds, United Kingdom*; *[6]University of Campania "Luigi Vanvitelli", Rheumatology Unit, Department of Precision Medicine, Naples, Italy*; *[7]Univ Hospital Zurich, University of Zurich, Department of Rheumatology, Zurich, Switzerland*; *[8]Rheumatology Unit,"Sapienza" University, Rome, Italy*; *[9]Hopital Cochin, University of Paris, Rheumatology Department, Paris, France*; *[10]Cantacuzino Hospital, Carol Davila University of Medicine and Pharmacy, Internal Medicine & Rheumatology Department, Bucharest, Romania*; *[11]Charite University Hospital, Rheumatology, Berlin, Germany*; *[12]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; *[13]Centre Hospitalier Universitaire, Service de Médecine Interne, Lille, France*; *[14]Chris Hani Baragwanath Academic Hospital University of the Witwatersrand, Division of Rheumatology, Department of Internal Medicine, Johannesburg, South Africa*; *[15]University Belgrade Medical School, Institute of Rheumatology, Belgrade, Serbia*; *[16]CHUV, 16. Service Immunologie et Allergie, Lausanne, Switzerland*; *[17]National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, University Paris Descartes, Paris, France*; *[18]Oslo University Hospital, Department of Rheumatology, Oslo, Norway*; *[19]Università Politecninca delle Marche, Department of Clinical and Molecular Science, Ancona, Italy*; *[20]University Califonia Los Angeles, Division Rheumatology, Los Angeles, United States of America*

Background: In SSc, ILD is a major cause of morbidity and mortality. High resolution computed tomography (HRCT) is the gold standard for the diagnosis. Predictors of ILD onset are eagerly awaited to improve SSc-ILD management. Pulmonary function test (PFTs) are routinely performed to measure lung function changes.

Objectives: Our aim was to investigate the performance of DLCO (diffusing capacity of lung carbon monoxide) and FVC (forced vital capacity) in predicting the development of SSc-ILD.

Methods: The longitudinal data of DLCO, FVC and ILD on HRCT of SSc patients from the EUSTAR database were evaluated at baseline (t_0), after 12 (±4) (t_1) and 24 (±4) (t_2) months. Patients with negative HRCT for any sign of ILD both at t_0 and t_1 were included. Patients who presented or developed pulmonary hypertension during the study period were excluded. At baseline, demographic data, disease duration from Raynaud's onset, disease subsets, autoantibodies and other laboratory and instrumental data were recorded.

Results: 474/17805 patients were eligible for the study (403 females, 71 males): 26.0% dcSSc, 58.3% lcSSc, 220 (48.0%) patients with positive anticentromere antibodies (ACA) and 117 (25.4%) with positive antitopoisomerase I antibodies (Topo-I abs). Among all enrolled patients, 46 (9.7%) developed HRCT signs of ILD at t_2. Patients with Topo-I abs showed an association with ILD development at t_2 (16.7% vs 7.8%, p=0.0031), contrarily ACA positive patients were negatively associated with ILD appearance after 2 years of follow-up (4.4% vs 14.4%, p=0.0001). Positive t_2 HRCT patients had a significant lower value of DLCO and FVC at all three assessments when compared to patients with a negative HRCT at t_2 (Table 1) and both t_0 DLCO and FVC values negatively correlated with ILD development (Table 1). The mean t_0 to t_1 change (Δ) of DLCO in patients with negative t_2 HRTC and positive t_2 HRCT were -0.5 (±12.6) and -1.0 (±15.1), respectively. The mean t_0 to t_1 ΔFVC in patients with negative t_2 HRTC and positive t_2 HRCT were -0.2 (±10.6) and 0.1 (±11.5), respectively. None of them predicted the appearance of ILD at t_2 (ΔDLCO: OR (IC) 0.997 (0.97-1.02), p=0.8024; ΔFVC OR (IC) 1.002 (0.97-1.03), p=0.8664). The data showed an association between t_0 DLCO value<80% and ILD appearance after 2 years of follow-up [OR(IC): 3.09(1.49-6.40), p=0.0023]. Such association was not observed for t_0 FVC value<80% [OR(IC): 1.95(0.81-4.68), p=0.1329]. The predictive capability of t_0 DLCO<80% was moderate but stronger than FVC<80% [AU ROC: 0.62 (0.56-0.69), 0.53 (0.48-0.59) respectively, p=0.0205].

Conclusion: Our data suggest that an impaired baseline DLCO (<80%) may have a predictive value for the development of ILD on HRCT after 2 years of follow-up. Further rigorous prospective studies are warranted to understand the role of DLCO evaluation in the course of SSc.

Table 1. DLCO and FVC values at t_0, t_1 and t_2 values in patients with positive or negative HRCT for ILD at t_2 and their statistical differences.

	Patients without ILD at t2 (mean±SD)	Patients with ILD at t2 (mean±SD)	OR (95%CL)	p-value
DLCO at t_0	79.0 ± 16.6	69.9 ± 17.4	0.97 (0.95 - 0.99)	0.0006
DLCO at t_1	78.4 ± 16.8	68.9 ± 18.6	0.97 (0.95 - 0.98)	0.0005
DLCO at t_2	78.0 ± 17.0	65.1 ± 19.1	0.95 (0.93 - 0.97)	<0.0001
FVC at t_0	102.2 ± 17.3	94.6 ± 16.2	0.97 (0.96 - 0.99)	0.0052
FVC at t_1	101.9 ± 17.9	94.7 ± 16.5	0.98 (0.96 - 0.99)	0.0092
FVC at t_2	101.6 ± 17.6	94.5 ± 20.0	0.98 (0.96 - 1)	0.0126

Disclosure of Interests: Gemma Lepri: None declared, Cosimo Bruni Speakers bureau: CB reports personal fees from Actelion, personal fees from Eli Lilly, Grant/research support from: CB reports personal fees from Actelion, personal fees from Eli Lilly, grants from European Scleroderma Trial and Research (EUSTAR) group, grants from New Horizon Fellowship, grants from Foundation for Research in Rheumatology (FOREUM), grants from Fondazione Italiana per la Ricerca sull'Artrite (FIRA), outside the submitted work, Lorenzo Tofani: None declared, Alberto Moggi Pignone: None declared, Martina Orlandi: None declared, Tomasetti Sara Speakers bureau: Speaker's fees for Roche and Boehringer Ingelheim,

Mike Hughes: None declared, Francesco Del Galdo: None declared, Rosaria Irace: None declared, Oliver Distler Grant/research support from: OD (last three years) has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Valeria Riccieri: None declared, Yannick Allanore Speakers bureau: YA received personal fees from Boehringer, Sanofi, Menarini and Medsenic and grants from Alpine with regards to the management of systemic sclerosis, Grant/research support from: YA received personal fees from Boehringer, Sanofi, Menarini and Medsenic and grants from Alpine with regards to the management of systemic sclerosis, Ana Maria Gheorghiu: None declared, Elise Siegert: None declared, Jeska de Vries-Bouwstra: None declared, Eric Hachulla: None declared, Mohammed Tikly: None declared, Nemanja Damjanov: None declared, Francois Spertini: None declared, Luc Mouthon: None declared, Anna-Maria Hoffmann-Vold Speakers bureau: AMHV: received consulting fees from Actelion, ARXX, Bayer, Boehringer Ingelheim, Lilly, Medscape, Merck Sharp & Dohme and Roche; and grants from Boehringer Ingelheim., Consultant of: AMHV: received consulting fees from Actelion, ARXX, Bayer, Boehringer Ingelheim, Lilly, Medscape, Merck Sharp & Dohme and Roche; and grants from Boehringer Ingelheim., Grant/research support from: AMHV: received consulting fees from Actelion, ARXX, Bayer, Boehringer Ingelheim, Lilly, Medscape, Merck Sharp & Dohme and Roche; and grants from Boehringer Ingelheim., Armando Gabrielli: None declared, Serena Guiducci: None declared, Marco Matucci-Cerinic Speakers bureau: has received consulting fees or honorarium from Actelion, Janssen, Inventiva, Bayer, Biogen, Boehringer, CSL Behring, Corbus, Galapagos, Mitsubishi, Samsung, Regeneron, Acceleron, MSD, Chemomab, Lilly, Pfizer, Roche, Grant/research support from: has received consulting fees or honorarium from Actelion, Janssen, Inventiva, Bayer, Biogen, Boehringer, CSL Behring, Corbus, Galapagos, Mitsubishi, Samsung, Regeneron, Acceleron, MSD, Chemomab, Lilly, Pfizer, Roche, Daniel Furst: None declared, Silvia Bellando Randone: None declared

DOI: 10.1136/annrheumdis-2021-eular.3027

POS0318

CLINICAL PHENOTYPE IN SCLERODERMA PATIENTS WITH ANTI-TOPOISOMERASE I POSITIVITY AND LIMITED CUTANEOUS FORM: DATA FROM THE EUSTAR DATABASE

E. Zanatta[1], D. Huscher[2], P. Airò[3], A. Balbir-Gurman[4], E. Siegert[5], A. Ortolan[1], M. Matucci-Cerinic[6], F. Cozzi[7], G. Riemekasten[8], A. M. Hoffmann-Vold[9], O. Distler[10], A. Gabrielli[11], S. Heitmann[12], N. Hunzelmann[13], C. Montecucco[14], J. Morovic-Vergles[15], C. Ribi[16], A. Doria[1], Y. Allanore[17]on behalf of on behalf of EUSTAR collaborators. [1]*University Hospital of Padova, Department of Medicine, Rheumatology Unit, Padova, Italy*; [2]*Charité-Universitaetsmedizin, Institute of Biometry and Clinical Epidemiology and Berlin Institute of Health, Berlin, Germany*; [3]*Spedali Civili, Rheumatology and Clinical Immunology, Brescia, Italy*; [4]*Rappaport Faculty of Medicine, B. Shine Rheumatology Institute Rambam Health Care Campus, Technion, Haifa, Israel*; [5]*Charité-Universitatsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; [6]*University of Florence, Department of Experimental and Clinical Medicine, Division of Rheumatology, Florence, Italy*; [7]*Ospedale Classificato Villa Salus, Internal Medicine Unit, Venice, Italy*; [8]*Universitatsklinikum Schleswig Holstein-Campus Lubeck, Department of Rheumatology, Lubeck, Germany*; [9]*Oslo University Hospital, Department of Rheumatology, Oslo, Norway*; [10]*University Hospital Zurich, University of Zurich, Department of Rheumatology, Zurich, Switzerland*; [11]*Università Politecnica delle marche, Dipartimento di Scienze Cliniche e molecolari, Ancona, Italy*; [12]*Marienhospital Stuttgart Böheimstrasse, Department of Rheumatology, Stuttgart, Germany*; [13]*University of Cologne, Department of Dermatology, Koln, Nordrhein-Westfalen, Germany*; [14]*IRCCS Policlinico San Matteo Foundation, Department of Rheumatology, Pavia, Italy*; [15]*Dubrava University Hospital, Department of Internal Medicine, Division of Clinical Immunology, Allergology and Rheumatology, Zagreb, Croatia*; [16]*Lausanne University Hospital and University of Lausanne, Department of Rheumatology, Clinical Immunology and Allergy, Lausanne, Switzerland*; [17]*Cochin Hospital, University of Paris Descartes, Department of Rheumatology, Paris, France*

Background: There is renewed interest in the role of autoantibodies to predict outcomes in systemic sclerosis (SSc). Among the newly identified subsets, patients with limited cutaneous form (lcSSc) but anti-topoisomerase I antibodies (Scl70) positivity draw particular attention, and namely, assessing the risk of developing interstitial lung disease (ILD) —the main cause of death in SSc—to improve the management of Scl70-lcSSc patients.

Objectives: We aimed to characterize patients with Scl70-lcSSc in the large multicenter European Scleroderma Trial and Research (EUSTAR) cohort.

Methods: The EUSTAR database was locked in July 2019. We included all patients fulfilling 1980 ACR and/or 2013 ACR/EULAR criteria for SSc, with disease duration at database entry ≤3 yrs and known and stable skin form during the first 3 yrs. Patients with lcSSc were compared: Scl70-lcSSc (target group) vs. ACA-lcSSc and ANA-lcSSc (Step 1); and Scl70-lcSSc vs. Scl70-dcSSc (Step 2). In the ANA subgroup we included ANA+ patients with negative SSc-specific antibodies (Scl70, ACA, RNA polymerase III). In each step, we performed 5 generalized mixed models (GMM) for the risk of the new onset of ILD (defined by imaging), primary myocardial involvement (PMI), pulmonary hypertension (PH), "any severe" (ILD+PMI+PH+scleroderma renal crisis) and all-cause-mortality. An additional GMM assessed the risk of forced vital capacity (FVC) decline ≥10% vs. FVC value at ILD onset. Each GMM was adjusted for age, sex and confounders.

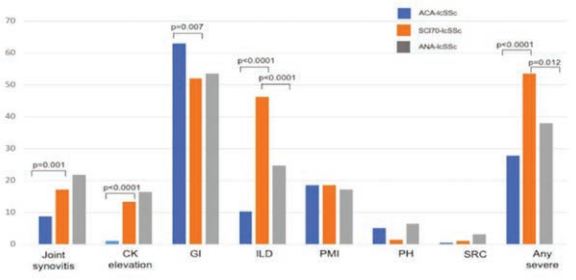
Results: Overall, 1285 SSc patients were included: 1068 (83%) females, 860 (67%) lcSSc and 425 (33%) dcSSc. Among patients with lcSSc, 537 (62%) had ACA+, 194 (23%) Scl70+ and 129 (15%) ANA+; 425 patients had dcSSc and Scl70+. Median follow-up was similar in all 4 groups: 7.2 to 8.1 yrs.

Step 1: At baseline, Scl70-lcSSc patients had significantly shorter time from Raynaud's phenomenon (RP) to SSc onset, higher mRSS (5.8±4.8 vs. 4.3±4, p=0.001), and higher rate of articular and muscular involvement vs. ACA-lcSSc patients (Figure 1). No differences were found between Scl70-lcSSc and ANA-lcSSc comparing the aforementioned variables. ILD was more frequent in Scl70-lcSSc (46%) than in ACA-lcSSc (10%) and ANA-lcSSc (25%), as well as restrictive lung disease. GMM showed that Scl70-lcSSc carries a higher risk of ILD than both ACA-lcSSc (HR 4.55, 95%CI 3.23-6.67) and ANA-lcSSc (HR 2.17, 95%CI 1.39-3.45), with a rate of FVC decline ≥10% over time similar to the other limited forms. In Scl70-lcSSc patients the risk of "any severe" organ involvement was similar to ANA-lcSSc and higher than ACA-lcSSc (HR 1.89, 95%CI 1.40-2.50). In particular, Scl70-lcSSc shows a risk of PMI similar to ANA-lcSSc and lower than ACA-lcSSc; no differences regarding PH risk. The mortality risk in patients with Scl70-lcSSc was similar to the other limited forms'.

Step 2: At baseline, time from RP to SSc onset was longer in patients with Scl70-lcSSc, with less frequent joint synovitis and tendon friction rubs vs. patients with Scl70-dcSSc. Conversely, the frequency of muscular, cardiac and pulmonary involvement was similar. The risk of ILD in Scl70-lcSSc patients was similar to Scl70-dcSSc, with a lower risk of FVC decline ≥10% over time. The risk of "any severe" involvement (HR 0.66, 95%CI 0.49-0.83), PMI and PH was lower and the mortality risk tended to be lower (HR 0.57, 95%CI 0.33-1.01, p=0.053) vs. Scl70-dcSSc.

Conclusion: In our large multicenter EUSTAR cohort one quarter of lcSSc patients were Scl70+. We show a ranking for major organ involvement within lcSSc: Scl70 the most severe, ANA+ intermediate and ACA the milder form. Scl70-dcSSc patients present the most severe phenotype, and Scl70 positivity, more than the cutaneous subset, is strongly predictive of ILD, whereas other variables may influence progression. These results may provide new insight to improve the management of Scl70-lcSSc patients.

Figure 1. Baseline clinical features and organ involvement in the 3 groups of patients with limited cutaneous systemic sclerosis (lcSSc) (step 1)



ACA, anticentromere antibodies; ANA, antinuclear antibodies; CK, creatine kinase; GI, gastrointestinal involvement; ILD, interstitial lung disease; PMI, primary myocardial involvement; PH, pulmonary hypertension; Scl70, anti-topoisomerase I; SRC, scleroderma renal crisis.

Disclosure of Interests: Elisabetta Zanatta: None declared, Dörte Huscher: None declared, Paolo Airò: None declared, Alexandra Balbir-Gurman: None declared, Elise Siegert: None declared, Augusta Ortolan: None declared, Marco Matucci-Cerinic: None declared, Franco Cozzi: None declared, Gabriela Riemekasten: None declared, Anna-Maria Hoffmann-Vold: None declared, Oliver Distler Speakers bureau: has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac,

Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Consultant of: has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Grant/research support from: Kymera Therapeutics, Mitsubishi Tanabe, Armando Gabrielli: None declared, Stefan Heitmann: None declared, Nicolas Hunzelmann: None declared, Carlomaurizio Montecucco: None declared, Jadranka Morovic-Vergles: None declared, Camillo Ribi: None declared, Andrea Doria: None declared, Yannick Allanore: None declared
DOI: 10.1136/annrheumdis-2021-eular.3048

POS0319 PERFORMANCE OF PATIENT REPORTED OUTCOMES (PROS) IN SCLERODERMA PATIENTS WITH REDUCED LUNG FUNCTION IN AN OBSERVATIONAL COHORT

M. G. Lazzaroni[1], G. Abignano[2,3], M. Wilson[2], V. Kakkar[2], F. Del Galdo[2]. *[1]ASST Spedali Civili of Brescia, University of Brescia, Rheumatology and Clinical Immunology, Brescia, Italy*; *[2]University of Leeds, Institute of Rheumatic and Musculoskeletal Medicine and NIHR Biomedical Research Centre, Leeds, United Kingdom*; *[3]Azienda Ospedaliera San Carlo, Rheumatology, Potenza, Italy*

Background: Patient Reported Outcomes (PROs) are used to capture disease impact on patients' Health Related Quality of Life (HRQoL) and they have been increasingly used as endpoints in clinical trials for Systemic Sclerosis (SSc). The DeSScipher project within the EUSTAR group highlighted dyspnea as one of the factors more strongly related with the highest SHAQ scores (1). Nevertheless, the SENSCIS trial in SSc-ILD (2) showed the efficacy of Nintedanib in reducing the annual rate of FVC loss, as compared to placebo, without significant changes in the PROs used as secondary endpoints (St. George's Respiratory Questionnaire and the FACIT-Dyspnoea questionnaire). Since patient's perspective is a crucial determinant to define the overall relevance of an intervention, the performance of PROs in reflecting different lung functional stages is a relevant issue in SSc.
Objectives: To analyse in a prospective SSc cohort the inference of reduced lung function as measured by FVC on median PRO scores and the correlation among distinct commonly used PROs.
Methods: A cross-sectional study was performed on data exported from the STRIKE database regarding SSc patients followed in Leeds Scleroderma Programme for SSc. Data included records of periodical visits with scores of different PROs commonly used in SSc (Scleroderma-Health Assessment Questionnaire (SHAQ), Cochin Hand Function Scale (CHFS) and Borg dyspnoea scale) and FVC%-predicted (%pFVC) and DLCO%-predicted (%pDLCO). SHAQ score was calculated as the mean value of HAQ (0-3) with the average of the 7-VAS scores divided by 3.33. The 7-VAS (score 1-10) were 1: pain, 2: general function, 3: arthritis, 4: gastro-intestinal, 5: dyspnoea, 6: Raynaud Phenomena; 7: digital ulcers. The correlation of FVC with distinct PROs, and the inter-PRO correlation, were analysed through the non-parametric Spearman test.
Results: Complete data were available from 182 visits of 87 SSc patients (41 with diffuse and 46 with limited cutaneous involvement). Mean %pFVC was 95.16 ±24.93 (median 95) and mean %pDLCO was 59.31±16.51 (median 59). Overall, FVC and DLCO showed a moderate correlation with SHAQ (r=-0.36, p<0.001 and r=-0.24, p:0.001 respectively), while Borg score showed a stronger negative correlation with FVC and DLCO (r:-0.42 and r-0.38, p<0.001 for both). In a sub-analysis of patients grouped by FVC, patients with FVC 50-70% showed a significant correlation of FVC with SHAQ (r =-0.47, p:0.012), which was not present in patients with FVC 70-90% (r:-0.23, p:0.13). VAS-5 dyspnoea and Borg were not associated with FVC in these two subgroups of patients.
Inter PROs analysis showed that CHFS score had a stronger correlation with SHAQ than Borg dyspnoea score in the overall population (r:0.86 vs. r:0.57, both p<0.001).
Conclusion: The analysis of a single centre prospective cohort of SSc patients, suggests a small inference of lung function in the overall SHAQ. The stronger correlation of SHAQ with CHFS, than with Borg score, suggests a higher weight of hand function on SHAQ in this population with relatively conserved lung function. In patients with %pFVC <70%, the correlation with SHAQ was stronger than in patients with %pFVC >70%, suggesting that mild reductions in FVC might not be perceived by the patients, or at least they might not modify HrQoL as measured by SHAQ.
REFERENCES:
[1] Jaeger VK, et al. Rheumatology 2017;57(3):441-50.
[2] Distler O, et al. N Engl J Med 2019; 380:2518-2528.
Disclosure of Interests: Maria Grazia Lazzaroni Grant/research support from: Boehringer-Ingelheim, Giuseppina Abignano: None declared, Michelle Wilson: None declared, Vishal Kakkar: None declared, Francesco Del Galdo Consultant of: Astra-Zeneca, Boehringer-Ingelheim, Mitsubishi-Tanabe, Capella Biosciences, Kymab, Actelion, Grant/research support from: Astra-Zeneca, Boehringer-Ingelheim, Mitsubishi-Tanabe, Capella Biosciences, Kymab, Actelion
DOI: 10.1136/annrheumdis-2021-eular.3505

POS0320 POOR PROGNOSIS PREDICTION IN ANTI-MDA5 POSITIVE DERMATOMYOSITIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE: THE CROSS-CAR DECISION TREE MODEL

L. Wang[1], C. Lv[1], F. Yuan[2], J. Li[3], M. Wu[4], Z. Da[5], H. Wei[6], L. Zhou[7], S. Yin[8], J. Wu[9], W. Tan[1]. *[1]The First Affiliated Hospital of Nanjing Medical University, Department of Rheumatology, Nanjing, China*; *[2]The Affiliated Wuxi People's Hospital of Nanjing Medical University, Department of Rheumatology, Wuxi, China*; *[3]Huai'an First People's Hospital, Department of Rheumatology, Huai'an, China*; *[4]The Third Affiliated Hospital of Soochow University, Department of Rheumatology, Changzhou, China*; *[5]Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*; *[6]Northern Jiangsu People's Hospital, Department of Rheumatology, Yangzhou, China*; *[7]Changzhou Second People's Hospital Affiliated to Nanjing Medical University, Department of Rheumatology, Changzhou, China*; *[8]Affiliated Hospital of Xuzhou Medical University, Department of Rheumatology, Xuzhou, China*; *[9]The First Affiliated Hospital of Soochow University, Department of Rheumatology, Suzhou, China*

Background: The prognosis of anti-melanoma differentiation-associated gene 5 positive dermatomyositis (anti-MDA5+ DM) – associated interstitial lung disease (ILD) is poor and heterogeneity.
Objectives: The aim of this study was to evaluate prognostic factors and to develop a simple and generally applicable bedside decision tree model for predicting outcomes in patients with anti-MDA5+ DM and to guide treatment.
Methods: We analyzed data for 246 anti-MDA5+ DM patients from Myositis Study Group-Jiangsu, a multicenter cohort across eighteen tertiary hospitals in Jiangsu province, from March 2019 to October 2020. The primary end point was all-cause death, and the secondary end point was occurring of rapidly progressive-ILD (rp-ILD). We used a multivariable Cox proportional hazards model to identify the independent prognostic risk factors of death and rp-ILD respectively. A decision-tree prediction model was developed by using data from 10 hospital of southern region (n=163), with validation by using contemporaneous data from northern region (n=83).
Results: To assess the risk of rp-ILD, we developed a combined risk score, the CROSS score, that included the following values and scores: C-reactive protein (≤8mg/L, 0; >8mg/L, 3), anti-Ro52 antibody (negative, 0; positive, 4), Sex (Female, 0; Male, 2) and Short course of disease (More than 3 months, 0; Less than 3 months, 2). The mortality risk was identified by the CAR score, including C-reactive protein (≤8mg/L, 0; >8mg/L, 1), Alanine Transaminase (≤50units/L, 0; >50units/L, 1) and rp-ILD (non-rpILD, 0; rp-ILD, 3). We divided patients into three risk groups according to the CROSS score: low, 0 to 3; medium, 4 to 7; and high 8-11. And then Use of a simple decision tree prediction model permitted stratification into three different outcome prediction groups. High-risk patients had significantly higher mortality rates than low- and medium-risk patients in both discovery and validation cohorts (p < 0.0001).
Conclusion: The CROSS-CAR decision tree model is easy to evaluate the poor prognostic risk in MDA5+ DM patients during any follow-up period. Unnecessary lung examination, such as chest CT scan and arterial blood gas analysis was avoided in low- and medium- rpILD risk patients. The special ambulance, with red cross sign tagged on car in China, may help to screen the high risk patients and to guide further treatment.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3514

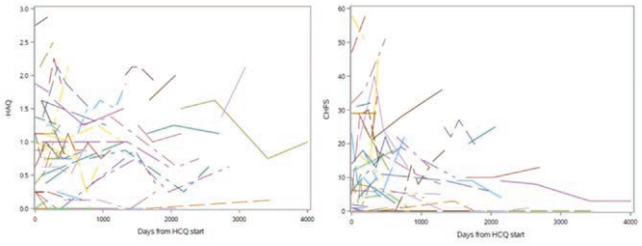
POS0321 USE OF HYDROXYCHLOROQUINE AND SYSTEMIC SCLEROSIS: RESULTS FROM A PROSPECTIVE OBSERVATIONAL STUDY ON THE EUSTAR COHORT

S. Bellando Randone[1], H. Wilhalme[2], C. Bruni[1], E. Siegert[3], P. Airò[4], R. Irace[5], O. Distler[6], A. Doria[7], L. P. Ananieva[8], L. Czirják[9], C. Denton[10], Y. Allanore[11], V. Riccieri[12], A. Vacca[13], I. Foeldvari[14], A. M. Hoffmann-Vold[15], A. Gabrielli[16], M. Matucci-Cerinic[1], D. Furst[1,2]on behalf of EUSTAR. *[1]AOU Careggi University of Florence, Division of Rheumatology, Florence, Italy*; *[2]University of California at Los Angeles, Department of Medicine, Division of Rheumatology, Los Angeles, United States of America*; *[3]Charité University Hospital, Rheumatology, Berlin, Germany*; *[4]Spedali Civili di Brescia, Servizio di Reumatologia Allergologia e Immunologia Clinica, Brescia, Italy*; *[5]II University of Naples,*

Division of Rheumatology, Naples, Italy; [6]*University Hospital Zurich, University of Zurich, Department of Rheumatology, Zurich, Switzerland*; [7]*University of Padova, Rheumatology Unit, Department of Medicine (DIMED), Padova, Italy*; [8]*VA Nasonova Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*; [9]*University of Pecs, Department of Rheumatology and Immunology, Pecs, Hungary*; [10]*University College London, Royal Free Hospital, Department of Rheumatology, London, United Kingdom*; [11]*Hopital Cochin Paris, Division of Rheumatology, Paris, France*; [12]*"La Sapienza" University, 11Department of Internal Medicine and Clinical Specialties, Rheumatology Unit, Rome, Italy*; [13]*University of Cagliari-Policlinico Universitario, II Chair of Rheumatology, Monserrato, Italy*; [14]*Hamburg Centre for Pediatric Rheumatology, Centre for Paediatric and Adolescent Rheumatology, Hamburg, Germany*; [15]*Oslo University Hospital, Department of Rheumatology, Oslo, Norway*; [16]*Università Politecnica delle Marche and Ospedali Riuniti, Department of Medical Science and Surgery, Section of Clinical Medicine, Ancona, Italy*

Background: Hydroxychloroquine (HCQ) is a well-tolerated drug that contributes to downregulating the immune response against autoantigens and it has been used in several autoimmune diseases. In systemic sclerosis (SSc) it is used to treat inflammatory arthritis without proof of efficacy.
Objectives: Our aim was to evaluate the use of HCQ and its impact on Health Assessment Questionnaire disability index (HAQ-DI) and the Cochin Hand Function Status (CHFS). in a large SSc cohort compared to a propensity matched group of SSc patients not using HCQ.
Methods: SSc patients from the European Scleroderma Trials and Research (EUSTAR) data base treated with HCQ for at least 6 months were evaluated. Demographic and clinical data, concomitant drugs, duration of HCQ treatment and reasons for its discontinuation, HAQ-DI and CHFS (at least 2 evaluation) were recorded and were the outcome variables of interest. Statistical analysis was performed using propensity score matching for age, gender, disease duration, corticosteroids, immunosuppressives, vasoactive drugs, DMARDs in a 3:1 control:HCQ ratio. Standard descriptive statistics and Student's t-test and Chi-square test were used to assess the propensity-matched groups.
Results: 1,636 of 17,805 SSc patients (9.2%) were treated with HCQ for at least 6 months; out of these 3% (50/1636). had at least a baseline and follow-up HAQ-DI evaluation, (and 44/1636 (2.7%) had at least a baseline and follow-up CHFS evaluation. Propensity matching assured that pts were matched for demographic variables such as gender (mean on HCQ vs no HCQ:femals:92.0 vs 85.3), age(49.8 vs 49.97yrs) disease duration(8.3 vs 9.1 yrs), limited disease(55.3 vs 62.6%) as well as background medications (P>0.1-0.9). We did not find any significant changes in HAQ or CHFS (difference in slope) over 365 days of treatment, comparing the HCQ-treated group to the non-HCQ treated patients (p=0.240 for both (Figure 1).
Conclusion: Results from the EUSTAR registry showed that HCQ was used by 9.2% of SSc patients. HCQ use did not improve the HAQ or CHFS, comparing HCQ users to non-HCQ users.

Figure 1. HAQ trend and CHFS trend over the time



Disclosure of Interests: Silvia Bellando Randone: None declared, Holly Wilhalme: None declared, Cosimo Bruni: None declared, Elise Siegert: None declared, Paolo Airò: None declared, Rosaria Irace: None declared, Oliver Distler: None declared, Andrea Doria: None declared, Lidia P. Ananieva: None declared, László Czirják: None declared, Christopher Denton: None declared, Yannick Allanore: None declared, Valeria Riccieri: None declared, ALESSANDRA VACCA: None declared, Ivan Foeldvari Consultant of: Gilead, Novartis, Pfizer, Hexal, BMS, Sanofi, MEDAC, Anna-Maria Hoffmann-Vold Speakers bureau: Actelion, Boehringer Ingelheim, Roche, Merck Sharp & Dohme, Lilly and Medscape, Consultant of: Actelion, Boehringer Ingelheim, Roche, Bayer, ARXX, and Medscape, Grant/research support from: Boehringer Ingelheim, Armando Gabrielli: None declared, Marco Matucci-Cerinic: None declared, Daniel Furst: None declared
DOI: 10.1136/annrheumdis-2021-eular.3725

POS0322 CORRELATION BETWEEN QUANTITATIVE COMPUTED TOMOGRAPHY AND DISEASE ACTIVITY IN SYSTEMIC SCLEROSIS

D. Sambataro[1,2], M. Orlandi[3], M. Colaci[1,1], L. Malatino[1], G. Sambataro[1,2], A. Ariani[4]. [1]*University of Catania, Department of Clinical and Experimental Medicine, Catania, Italy*; [2]*Artroreuma srl, Outpatient of Rheumatology associated to Italian National Health System, Mascalucia, Italy*; [3]*University of Florence, Department of Experimental and Clinical Medicine, Florence, Italy*; [4]*Azienda Ospedaliero Universitaria di Parma, Department of Medicine, Parma, Italy*

Background: High Resolution Computed Tomography (HRCT) is the gold standard to evaluate Interstitial Lung Diseases (ILDs) extent and severity. Quantitative Computed Tomography (QCT) is a promising tool as it provides an operator-independent assessment of ILD extent. Even if there are emerging data on QCT in Systemic Sclerosis (SSc), its correlation with disease activity (DA) has not been yet studied.
Objectives: To evaluate the correlation between QCT score and DA in an Italian cohort of SSc patients.
Methods: A multicentric, observational study was conducted in three Italian rheumatological centers.
Adult SSc patients classified according to the ACR/EULAR 2013 criteria [1] were assessed with pulmonary function tests, HRCT and for DA. CT images were analyzed quantitatively with the densitometric radiomic data obtained through a free open software – Mean lung attenuation (MLA), Standard Deviation (SD), Kurtosis, Skewness and Lung volume. DA assessment was conducted according to EUSTAR index [2]: a score ≥2.5 was considered indicative of high disease activity.
Age below 18 and pregnancy were considered exclusion criteria. We used Student's T test to evaluate the means of the parameters, Pearson's r test for correlations, receiver operating characteristics curve to define the cutoff values of the significant details, and linear regression with collinearity test to define the role of the details. P value <0.05 was considered statistically significant.
Results: Sixty patients were enrolled (male 8, female 52), with mean age 53.2 years (SD 15.6) and mean disease duration 5.3 years (SD 4.2). QCT indexes distribution was different in high DA vs low DA SSc patients. In particular mean lung attenuation (MLA, -834.7 vs -812.1, p =0.03), standard deviation (95.9 vs 102, p =0.03), skewness (2.2 vs 1.7, P =0.006) and kurtosis (5.5 vs 3.3, p =0.009) of the parenchymal lung and skewness (3.1 vs 2.8, p =0.03) of the whole lung were statistically different. DA correlates with MLA (r =0.28, p =0.003), standard deviation (r =0.21, p =0.02), skewness (r =-0.32, p =0.001) and kurtosis (r =-0.29, p =0.001) of the parenchymal lung and MLA (r =0.25, p =0.006), skewness (R =-0.27, p =0.003), kurtosis (r =-0.21, P =0.02) of the whole lung. The skewness of the parenchymal lung was the QCT index with the best performance in identifying high DA SSc patients (cutoff value ≤1.85; area under the curve 0.74, p =0.005; sensitivity 79.5%, specificity 68.7% accuracy 76.6%).
Conclusion: To our knowledge, this is the first study which correlate the QCT score with DA in SSc patients. Our results suggest that QCT can identify SSc patients with high DA score. This could open a scenario of new applications as an operator-independent contribution in DA scores with a potential role in clinical practice. Further studies are needed to confirm the data and to better identify the most suitable parameters for the purpose.
REFERENCES:
[1] Van den Hoogen F, et al. 2013 classification criteria for Systemic Sclerosis: and American college of rheumatology / European league against rheumatism collaborative initiative. Ann Rheum Dis 2013;72:1747-1755.
[2] Valentini G, et al. The European Scleroderma Trials and Research group (EUSTAR) task force for the development of revised activity criteria for systemic sclerosis: derivation and validation of a preliminarily revised EUSTAR activity index. Ann Rheum Dis 2017;76:270-276.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4261

POS0323 ANTI PM-SCL ASSOCIATED AUTO IMMUNE DISEASES: MULTICENTRIC COHORT OF 128 PATIENTS

P. Breillat[1], K. Mariampillai[2], P. Martins[1], P. Legendre[1], B. Dunogue[1], J. L. Charuel[3], M. Miyara[3], H. Vanquaethem[4], F. Ackermann[5], O. Benveniste[6], L. Mouthon[1], H. Nunes[7], Y. Allenbach[6], Y. Uzunhan[7]. [1]*Assistance Publique-Hôpitaux de Paris, Hôpital Cochin, Centre de Référence pour les Maladies Auto-immunes Rares, Université de Paris, Médecine Interne, Paris, France*; [2]*Groupe Hospitalier Pitié-Salpêtrière, Centre de Recherche en Myologie, Unité Mixte de Recherche Scientifique 974, Sorbonne Université, Institut National de la Santé et de la Recherche Médicale, Institut de Myologie, Plateforme d'essais cliniques adultes I-Motion, Paris, France*; [3]*Assistance Publique-Hôpitaux de Paris, Groupe Hospitalier Pitié-Salpêtrière, Laboratoire Immunochimie, Paris, France*; [4]*hôpital d'instruction des armées de Bégin,*

Clinique médicale, St-Mandé, France; [5] *Hôpital Foch, Service de Médecine Interne, Suresnes, France*; [6]*Centre de Référence Maladies Neuro-Musculaires, Assistance Publique-Hôpitaux de Paris, Groupe Hospitalier Pitié-Salpêtrière, DHUi2B, Paris, France, Médecine Interne et Immunologie Clinique, Paris, France*; [7]*Assistance Publique-Hôpitaux de Paris, Hôpital Avicenne, INSERM U1272, Université Sorbonne Paris Nord, Service de Pneumologie, Bobigny, France*

Background: Autoantibodies permit to classify and subgroup connective tissue diseases (CTD) in homogeneous groups of patients in terms of phenotype and prognosis. Anti PM-Scl antibodies have been associated with different CTD categories such as: idiopathic inflammatory myositis (IIM), systemic sclerosis (SSc), Sjögren's syndrome (SjS), systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD) or undifferentiated connective tissue disease (UCTD).
Objectives: To determine clinical spectrum of anti-PM-Scl associated disease and if it an homogenous condition.
Methods: This multicentric (four hospitals) observational and retrospective study included all consecutive patients with positive testing for anti PM-Scl antibodies on immunoblot assay and connective tissue disease (2011 -2020). Epidemiological, biological, clinical and radiological data were collected in standard form as well as patient's outcome.
Results: One hundred twenty height patients (female n=96;75%) were included. Median [quartiles] age at diagnosis was 50 [18;84] (IQR) and follow-up duration of 7 [3.75-12] years. Seventy-six (59.3%) patients were simple anti-Pm-Scl positive, and 40.7% were associated with other antibodies: anti-SSA/Ro52 (n=13; 10.92%), SSc associated antibodies (n=21; 16.4%), anti-dsDNA for (n=9; 7%), anti-RNP (n=6; 4.7%) and anti-CCP antibodies (n=6; 4.7%). Most patients had cutaneous involvement (n=106; 83%) with skin thickening (n=47; 36%), mechanics hands (n= 28; 22%), calcinosis (n=26; 20.3%) and subcutaneous edema (n=20; 15.62%). Vascular involvement was frequent with Raynaud phenomenon (n= 89; 69%), telangiectasia (n=36; 28%), skin ulcers (n=27; 21%), pulmonary hypertension (n=8/120; 6.7%) and scleroderma renal crisis (n=2; 1.5%). A majority of patients also displayed an interstitial lung disease (ILD) (n=83; 65.8%); nonspecific interstitial pneumonia (92.7%) and/or organizing pneumonia (25.3%). ILD was characterized by a subacute onset in 37/81 (45.7%); median [quartiles] forced vital capacity (FVC) and total lung capacity (TLC) at diagnosis of 88% [73-105] and 79.5% [68.5-101] respectively. Sixty patients (47%) had muscular sign including myalgia (47%), elevated CPK (n=51; 40%) and muscular weakness (Medical Research Council score <4) (n=19/124;15%). Finally, fifty-three (41.7%) had gastroesophageal reflux. Thirty-nine patients (30.4%) experienced at least one muscular or ILD relapse and 6 (4.84%) died during follow-up (2 breast cancer, 1 pneumonia, 3 unknown etiology). Concerning patients' prognosis, relapses were associated with skeletal (n=29, 74.4% vs n=32, 35.96%, p < 0.001) or cardiac muscle involvement (n=7, 18.4% vs n=2, 2.5%, p=0.007), and subacute ILD (n=19, 65.5% vs n=18, 34.62%, p= 0.05) with organized pneumonia pattern (n=11, 32.3% vs n=10, 13.9%, p=0.05). Strikingly, ILD occurred mainly in men (90.6% vs 57.2%, p < 0.001) and was associated with anti-Scl-70 positivity (n=14, 16.67% vs 0%, p= 0.01). Muscle involvement was associated arthralgia (n=46, 76.67% vs n=34, 50.75%, p=0.005), respiratory signs at diagnosis: dyspnea NYHA ≥3 (n=46, 75.41% vs n=30, 44.78%, p < 0.001), sub-acute ILD (n=24, 61.54% vs n=13, 30.95%, p=0.0111) with lower FVC (73% [64;88] vs 98 [76;105], p < 0.001). Ulcers were associated with Anti-Scl70 positivity (n=9, 33.33% vs n=5, 4.95%, p < 0.001), Raynaud phenomenon (n=27, 100% vs n=62, 61.39%, p < 0.001), digestive involvement (n=20, 74.07% vs n=34, 33.66%, p < 0.001), ILD with chronic onset (n=15, 78.95% vs n=29, 46.77%, p=0.027) and increased incidence of deaths (n=4, 16% vs n=2, 2.02%, p= 0.01).
Conclusion: Conducted on the largest cohort of Anti-PM-Scl patients, this study highlights two main phenotypes that determine different outcome and prognosis. One was associated with muscular disease and subacute onset ILD with more frequent relapses. The second with a vascular phenotype associated with chronic ILD, digestive involvement, chronic evolution and increased incidence of death. This could lead to a reclassification of PM-Scl associated auto immune diseases.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.223

POS0324 SMOKING HISTORY AND SCLERODERMA CLINICAL TRIALS CONSORTIUM DAMAGE INDEX (SCTC-DI) AS INDEPENDENT PREDICTORS OF MORTALITY IN SYSTEMIC SCLEROSIS IN A SINGLE-CENTRE ITALIAN COHORT

M. Breda[1], M. G. Lazzaroni[1], F. Franceschini[1], P. Airò[1]. [1]*ASST Spedali Civili of Brescia, University of Brescia, Rheumatology and Clinical Immunology, Department of Clinical and Experimental Sciences, Brescia, Italy*

Background: Systemic Sclerosis (SSc) is characterized by increased mortality and organ damage accrual. A composite SSc Damage Index was recently developed by the Scleroderma Clinical Trials Consortium (SCTC-DI) and was demonstrated as a predictor of mortality both in the Australian derivation cohort and in the Canadian validation cohort (1). Several independent predictors of mortality in SSc have been reported, but only limited data are available on the role of smoking.
Objectives: To evaluate smoking history and SCTC-DI as independent predictors of mortality in SSc in a single centre Italian cohort.
Methods: A retrospective analysis was performed on patients prospectively followed in our centre from 1989 to 2019, with at least 2 evaluations and/or cause of death available. Organ damage was evaluated through the SCTC-DI (0-55 scale; severe damage>12), while comorbidities through the Charlson Comorbidity Index (CCI). Survival analysis was performed with Kaplan-Meier curves and with Log-rank test to compare different subsets. Cox-regression analysis was performed to identify baseline independent predictors of mortality.
Results: 648 SSc patients were 99% Caucasian, 90% female and had a median age at diagnosis of 55.5 years (IQR: 45.0-65.6); 19% had diffuse cutaneous involvement. ACA was positive in 52%; anti-TopoI in 22% and anti-RNA Polymerase III in 5%.
Median SCTC-DI at diagnosis was 2 (0-4) (n=560); ever smokers were 27%. During the follow-up 240 patients died after a median period of 10.2 years (4.9-16.8). The cause of death was related to SSc in 41% (n=65; most frequent causes pulmonary arterial hypertension (n=35) and interstitial lung disease (n=30)) and to other diseases in 40% (n=95; most frequent cause cancer (n=40)), while was indeterminate in 19%.
Overall survival at 5, 10, 15, 20 years was 87.8% (SE 1.3%), 75.6% (1.9), 63.8% (2.3), 47.7% (2.8), respectively and was higher in females vs. males (p<0.0001) and in ACA+ vs ACA- (p=0.005), but did not differ between cutaneous subsets. 111 patients were lost at follow-up (17%).
In the Cox-regression analysis smoking history and severe organ damage at diagnosis (score>12) were identified as independent predictors of death, while age at diagnosis, female gender, diffuse cutaneous subsets, ACA positivity and CCI were not (Table 1).
Conclusion: Smoking history and severe organ damage were independent predictors of death in a large Italian single centre SSc cohort. SCTC-DI was confirmed as a useful tool to predict mortality at every timepoint
REFERENCES:
[1] Ferdowsi N, et al. Ann Rheum Dis. 2019;78:807-16.

Characteristics	*P-value*	*Hazard ratio*	*Confidence interval 95%*
Female gender	0.9726	0.992	0.619-1.590
Diffuse cutaneous subset	0.7407	1.036	0.729-1.366
Ever smoker	0.0005	1.545	1.211-1.972
SCTC-DI at diagnosis >12 (severe damage)	0.0353	3.450	1.089-10.929
ACA positivity	0.7407	1.046	0.801-1.366
Age at diagnosis	0.4961	1.005	0.991-1.018
Charlson Comorbidity Index (age excluded)	0.1555	1.094	0.966-1.238

Table 1. Cox-regression analysis for any cause of death.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.585

POS0325 RADIOMIC BIOMARKER OF PULMONARY VASCULAR RELATED STRUCTURES PREDICTS MORTALITY IN SYSTEMIC SCLEROSIS

A. Hinze[1], Y. Radwan[1,2], M. Elnagar[1], R. Kurmann[3,4], S. Amin[1], R. Vassallo[5], C. S. Crowson[1,6], B. Bartholmai[7]. [1]*Mayo Clinic, Department of Medicine, Division of Rheumatology, Rochester, United States of America*; [2]*Michigan State University, Department of Medicine, East Lansing, United States of America*; [3]*Mayo Clinic, Department of Cardiology, Rochester, United States of America*; [4]*Heart Center Kantonsspital Luzern, Department of Cardiology, Lucerne, Switzerland*; [5]*Mayo Clinic, Department of Medicine, Division of Pulmonary and Critical Care Medicine, Rochester, United States of America*; [6]*Mayo Clinic, Department of Quantitative Health Sciences, Rochester, United States of America*; [7]*Mayo Clinic, Department of Radiology, Rochester, United States of America*

Background: Quantitative computed tomography (QCT) extracts features from high-resolution CT scans and quantifies lung parenchymal and vascular abnormalities which may not be discernable by qualitative review. The threshold values

of individual parenchymal abnormalities and vascular features measured by QCT methods which associate with mortality in systemic sclerosis (SSc) are currently unknown.

Objectives: To determine whether QCT measures, specifically pulmonary parenchymal abnormalities and pulmonary vascular related structures (PVRS), can predict mortality in SSc and to determine the optimal quantitative thresholds for those parameters.

Methods: A total of 133 subjects (76% women) meeting 2013 ACR/EULAR classification criteria for SSc with a baseline CT within 3 years of diagnosis were retrospectively identified for inclusion. CALIPER (Computer-Aided Lung Informatics for Pathology Evaluation and Rating) was used to quantitatively measure volume of ground glass opacities (GGO), reticular densities, and honeycombing (HC). Total interstitial lung disease (ILD) was the summation of these features. PVRS was also quantified using CALIPER. Values for each feature were expressed as a percentage of total lung volume. Cox models evaluated the hazard ratio (HR) for mortality for each parameter adjusting for age at SSc diagnosis, sex, diffuse SSc subtype, and history of smoking. The optimal thresholds for mortality prediction for each parameter were determined using consensus between 4 methods: Contal and O'Quigley Method, Cox Model Hazard Ratio, Cox Model Wald P-value, and False Discovery Rate. The c-statistic was used to assess each models' ability to predict mortality.

Results: Mean ±SD for age at SSc diagnosis was 61 ± 13 years and length of follow-up was 4.7 ± 3.0 years. There were 32 deaths (24%). A Cox model including age (HR 1.05, 95% CI: 1.01-1.09), female sex (HR 0.49, 95% CI: 0.22-1.08), diffuse SSc subtype (HR 1.50, 95% CI: 0.69-3.30), and history of smoking (HR 2.09, 95% CI: 0.97-4.53) (Model 1) significantly predicted mortality (C-statistic 0.72, 95% CI: 0.63-0.81). Adjusting for Model 1, reticular densities% (HR 1.19, 95% CI: 1.05-1.35), total ILD% (HR 1.02, 95% CI: 1.00-1.03), and PVRS% (HR 1.19, 95% CI: 1.05-1.35) were associated with mortality on univariable analyses; GGO% (HR 1.01, 95% CI: 0.98-1.04) was not significantly associated with mortality. The optimal thresholds for mortality prediction were then determined and were as follows: GGO=20%, reticular densities=8%, total ILD=20%, and PVRS=5%. While the risk of mortality was significantly increased in subjects with GGO ≥20% (HR 2.70, 95% CI: 1.21-6.05), reticular densities ≥8% (HR 4.64, 95% CI: 1.68-12.81), and total ILD ≥20% (2.59, 95% CI: 1.12-5.99), these baseline thresholds did not improve upon mortality prediction when added individually to Model 1 (C-statistic 0.73 for each). PVRS ≥5%, which had an over six-fold increase in mortality (HR 6.42, 95% CI: 2.60-15.88), did improve mortality prediction when added to Model 1 (C-statistic 0.78, 95% CI: 0.70-0.86).

Conclusion: PVRS strongly associates with early mortality in patients with SSc and represents a novel radiomic biomarker that provides prognostic information on mortality beyond pulmonary parenchymal abnormalities. CALIPER derived PVRS quantifies CT data through a function that defines connected tubular branching structures. This extracts pulmonary arteries and veins from the adjacent parenchyma but could potentially also include regions of adjoining of fibrosis.[1] Larger studies examining the association between PVRS and progression of cardiopulmonary disease are warranted.

REFERENCES:

[1] Jacob J, Bartholmai BJ, Rajagopalan S, et al. Predicting Outcomes in Idiopathic Pulmonary Fibrosis Using Automated Computed Tomographic Analysis. Am J Respir Crit Care Med 2018;198:767-76.

Acknowledgements: This project was supported by the Mayo Clinic Margaret Harvey Schering Clinician Career Development Award.

Disclosure of Interests: Alicia Hinze: None declared, Yasser Radwan: None declared, Mamoun Elnagar: None declared, Reto Kurmann: None declared, Shreyasee Amin: None declared, Robert Vassallo Grant/research support from: Pfizer, Bristol Myers Squibb, Sun Pharma, Cynthia S. Crowson: None declared, Brian Bartholmai Consultant of: AstraZenica, Boehringer Ingelheim, Promedior LLC (all <$5,000 annually)

DOI: 10.1136/annrheumdis-2021-eular.745

Systemic sclerosis, myositis - etiology, pathogenesis and animal models

POS0326

ROLE OF THE IL-25 / IL-17RB AXIS IN TH9 POLARIZATION IN PATIENTS WITH PROGRESSIVE SYSTEMIC SCLEROSIS

L. La Barbera[1], M. Lo Pizzo[2], D. DI Liberto[2], C. Schinocca[1], P. Ruscitti[3], R. Giacomelli[4], F. Dieli[2], F. Ciccia[5], G. Guggino[1]. [1]*P. Giaccone University Hospital, University of Palermo, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, Rheumatology Unit, Palermo, Italy*; [2]*University of Palermo, Biomedicine, Neuroscience and Advanced Diagnostic, Palermo, Italy*; [3]*San Salvatore University Hospital, University of L'Aquila, Department of Biotechnological and Applied Clinical Science, Coppito (AQ), Italy*; [4]*University "Campus Bio-Medico", Unit of Allergology, Immunology, Rheumatology, Department of Medicine, Rome, Italy*; [5]*University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Napoli, Italy*

Background: Systemic sclerosis (SSc) is an inflammatory connective tissue disease leading to chronic and progressive fibrosis, typically affecting the skin and internal organs. The alteration of both innate and adaptive immune responses plays a pivotal role in SSc pathophysiology, although it has not yet been fully elucidated [1].

Recent findings have demonstrated interleukin (IL)-9 overexpression and significant group 2 innate lymphoid cells (ILC2) expansion in patients with SSc. Th9-ILC2-mast cells axis seems to be involved in SSc tissue damage and in the induction of fibrosis [2]. Activation and production of IL-9 by Th9 cells are promoted by transforming growth factor (TGF)-β, thymic stromal lymphopoietin (TSLP), IL-25 and IL-33. Thus, the IL-25 / IL-17RB pathway would act as a key player in SSc.

Objectives: The purpose of this study was to evaluate the role of the IL-25 / IL-17RB axis as a driver in Th9 polarization and ILC2 expansion and polarization in SSc patients.

Methods: 26 patients were enrolled in this study. Peripheral blood and skin biopsy specimens were obtained from SSc patients. PBMCs were isolated and incubated with and without recombinant (r)IL-25 for 24-48-72 hours and the frequencies of Th9 cells, Th17 cells and ILC2 were assessed by flow cytometry analysis. Moreover, the *ex vivo* expression of IL-17RB in ILC2 was also assessed. Immunofluorescence analysis was performed on biopsy skin samples to evaluate IL-17RB expression in ILC2.

Results: In SSc samples, Th9 cells frequency progressively increased after stimulation with rIL-25, compared to healthy controls in which IL-9 frequency decreased over time regardless of rIL-25.

Simultaneously, we evaluated the role of the IL-25 / IL-17RB axis in Th17 cells.

In the SSc pool, the initially low rate of IL-17 increased at 72 hours after stimulation with rIL-25. In unstimulated SSc samples, the initially higher IL-17 rate decreased at 72 hours; conversely, it was consistently low in healthy controls, at both baseline and stimulated conditions.

Our results confirmed the presence of IL-25-dependent clonal ILC2 expansion, suggesting a greater and progressive expansion over time in patients with SSc, compared to controls.

Interestingly, increased IL-17RB expression was found in circulating ILC2 from SSc patients supporting the characterization of ILC2 inflammatory phenotype.

Consistently, immunofluorescence on the skin of SSc patients showed a marked infiltrate of $CD3^{-}GATA3^{+}$ $IL\text{-}17RB^{+}$ cells, confirming the presence of the activated inflammatory phenotype ILC2, absent in skin biopsies of healthy controls (Figure 1).

Conclusion: These preliminary data suggest an active role of the IL-25/IL-17RB axis in SSc. It results in Th9 polarization and Th17 clonal expansion, inducing the production of IL-9 and, to a lesser extent, IL-17. Moreover, in addition to promoting Th9-mediated ILC2 differentiation, IL-25 directs the polarization of ILC2 towards the inflammatory phenotype.

REFERENCES:

[1] Denton CP, & Khanna D. (2017). Systemic sclerosis. Lancet (London, England), 390(10103), 1685–1699.

[2] Guggino G, Ciccia F, Di Liberto D, Lo Pizzo M, Ruscitti P, Cipriani P, Ferrante A, Sireci G, Dieli F, Fourniè JJ, Giacomelli R, Triolo G. s.l. Interleukin-9 over-expression and T helper 9 polarization in systemic sclerosis patients. Clin Exp Immunol, 2016 Dec.

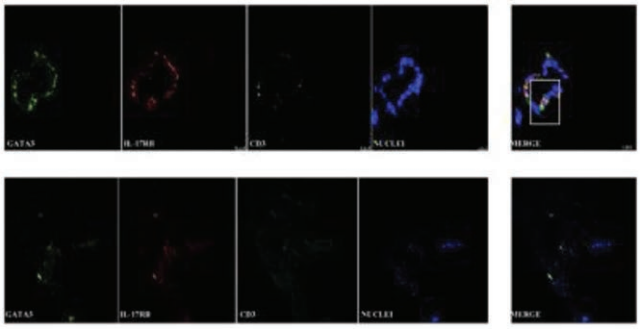


Figure 1. Immunofluorescence on biopsy skin samples of SSc patients (top) and healthy control (bottom).

Disclosure of Interests: Lidia La Barbera: None declared, Marianna Lo Pizzo: None declared, Diana Di Liberto: None declared, Claudia Schinocca: None declared, Piero Ruscitti Consultant of: Pfizer, Novartis, Roche, Lilly, Celgene,

Abbvie, Rorberto Giacomelli Consultant of: Pfizer, Novartis, Roche, Lilly, Celgene, Abbvie, Francesco Dieli: None declared, francesco ciccia Consultant of: Pfizer, Novartis, Roche, Lilly, Celgene, Abbvie, Giuliana Guggino Consultant of: Pfizer, Novartis, Roche, Lilly, Celgene, Abbvie
DOI: 10.1136/annrheumdis-2021-eular.3814

POS0327 INACTIVATION OF ALDEHYDE DEHYDROGENASE 3A2 INHIBITS FIBROBLAST ACTIVATION AND TISSUE FIBROSIS

X. Xu[1], Y. N. Li[1], C. W. Chen[1], T. Trinh-Minh[1], G. Schett[1], J. H. W. Distler[1].
[1]Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and Universitätsklinikum Erlangen, Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany

Background: The aldehyde dehydrogenase (ALDH) superfamily composes a group of 20 enzymes that catalyze aldehyde oxidation. Within this enzyme family, ALDH3A2 stands out for its central role in the oxidation of long-chain aldehydes. Of particular interest, the substrates of ALDH3A2 include also profibrotic lipid mediators such as sphingosine 1-phosphate or leukotrienes, which have been reported to be deregulated in the context of SSc.
Objectives: We aimed to investigate the role of ALDH3A2 in fibrotic tissue remodeling in SSc.
Methods: Fibroblast-to-myofibroblast transition was analyzed by quantification of *ACTA2*/αSMA, by assessment of stress fiber formation and mRNA and protein levels of type I collagens. *ALDH3A2*/*Aldh3a2* siRNAs were employed to specifically knockdown ALDH3A2 in dermal fibroblasts both *in vitro* and *in vivo*. Overexpression of ALDH3A2 was achieved by *ALDH3A2*-pcDNA transfection. The role of ALDH3A2 was investigated in three different mouse models: Bleomycin- and cGvHD-induced dermal fibrosis as well as fibrosis induced by overexpression of a constitutively active TGFβ receptor I (TBRI^{CA}). Target genes of *ALDH3A2* in fibroblasts were identified by RNA sequencing.
Results: The expression of ALDH3A2 was modestly reduced in dermal fibroblasts of SSc skin as compared to matched healthy controls. This reduction in ALDH3A2 expression was phenocopied by activation of TGFβ signaling, whereas selective inhibition of TGFβ signaling prevented the downregulation of ALDH3A2 in experimental fibrosis. ALDH3A2 overexpression promoted fibroblast-to-myofibroblast transition with increased levels of αSMA, enhanced formation of stress fibers and reduced collagen release. In contrast, knockdown of ALDH3A2 in dermal fibroblasts inhibited fibroblast activation and collagen release. Moreover, in vivo knockdown of ALDH3A2 in the skin of mice ameliorated dermal thickening, myofibroblast differentiation and collagen deposition in three different murine models of skin fibrosis: Bleomycin-induced skin fibrosis and scleroderma-tous GvHD-as models of inflammatory stages of SSc and TBRI^{CA}-induced fibrosis as an inflammation-independent model of SSc. RNA sequencing of ALDH3A2-knockdown fibroblasts demonstrated that ALDH3A2 regulates the activity of a network of profibrotic developmental pathways including TGFβ, Wnt, Notch, and Hedgehog signaling.
Conclusion: We demonstrate that ALDH3A2 regulates a network of profibrotic pathways to control fibroblast activation and tissue fibrosis. ALDH3A2 is modestly downregulated in SSc fibroblasts as result of an endogenous, TGFβ-driven feedback loop. Although this modest downregulation is not sufficient to counterbalance the aberrant fibroblast activation in SSc, augmentation of this endogenous regulation by knockdown of ALDH3A2 demonstrates potent antifibrotic potential in experimental dermal fibrosis, thereby providing first evidence for ALDH3A2 as a target for antifibrotic therapies.
Disclosure of Interests: Xiaohan Xu: None declared, Yi-Nan Li: None declared, Chih-Wei Chen: None declared, Thuong Trinh-Minh: None declared, Georg Schett: None declared, Jörg H.W. Distler Consultant of: Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, Grant/research support from: Anamar, Active Biotech, Array Biopharma, ARXX, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB
DOI: 10.1136/annrheumdis-2021-eular.1115

POS0328 ENGRAILED 1 COORDINATES CYTOSKELETAL ORGANIZATION TO PROMOTE MYOFIBROBLAST DIFFERENTIATION AND FIBROTIC TISSUE REMODELING

A. H. Györfi[1,2], A. E. Matei[1,2], M. Fuchs[3], A. Rius Rigau[1], X. Hong[1], Z. Honglin[4], M. Luber[1], C. Bergmann[1,2], C. Dees[1], I. Ludolph[5], R. Horch[5], O. Distler[6], G. Schett[1,2], M. Kunz[3], J. H. W. Distler[1,2]. *[1]Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany*; *[2]FAU Erlangen-Nürnberg and University Hospital Erlangen, Deutsches Zentrum für Immuntherapie (DZI), Erlangen, Germany*; *[3]Friedrich-Alexander University (FAU) of Erlangen-Nürnberg, Chair of Medical Informatics, Erlangen, Germany*; *[4]Xiangya Hospital, Central South University, Department of Rheumatology, Changsha, Hunan, China*; *[5]Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Department of Plastic and Hand Surgery, Erlangen, Germany*; *[6]Center of Experimental Rheumatology, University Hospital of Zurich, Department of Rheumatology, Zurich, Germany*

Background: Engrailed 1 (EN1) is a homeodomain-containing transcription factor with essential roles in embryonic development. In most cell types, the expression of EN1 is restricted to embryonic development. However, under pathological conditions, EN1 can be re-expressed to promote phenotypical adaptation. En1 is transiently expressed in the developing dermis of murine embryos in a distinct fibroblast lineage and silenced before birth (1). Former EN1-expressing cells give rise to a subpopulation of fibroblasts that has a high capacity for extracellular matrix production in adult murine skin. The role of EN1 in systemic sclerosis (SSc) was previously not explored.
Objectives: To study the role of EN1 in the pathological activation of fibroblasts in tissue fibrosis.
Methods: Bulk RNA-Seq and EN1 or SP1 ChIP-Seq were performed from cultured human dermal fibroblasts. The expression of EN1 was inhibited by siRNA. Cytoskeletal drugs paclitaxel, vinblastin and ROCK inhibitor (Y27632) were used to modulate the cytoskeleton in EN1 knockdown or overexpressing dermal fibroblasts. The role of EN1 in fibroblast activation was evaluated by functional experiments with EN1 knockdown or overexpression in standard 2D culture systems as well as in 3D skin equivalent models. The role of EN1 in skin fibrosis was further studied in En1$^{fl/fl}$ X Col6Cre mice, with fibroblast-specific knockout of En1 in three complementary mouse models: overexpression of a constitutively active TGFß-receptor I (TBRI^{CA}), bleomycin-induced skin fibrosis and TSK1 mice.
Results: Pathologically activated dermal fibroblasts from SSc patients express higher levels of EN1 compared with age and sex matched healthy individuals in the skin and *in vitro*. TGFβ induces EN1 expression in fibroblasts in a SMAD3-dependent manner both in cultured fibroblasts and in murine skin. Knockdown of EN1 prevents TGFβ-induced fibroblast activation, whereas overexpression of EN1 fosters the pro-fibrotic effects of TGFβ with increased expression of αSMA, stress fibers and collagen. RNA sequencing demonstrates that EN1 induces a pro-fibrotic gene expression profile functionally related to cytoskeleton organization and ROCK activation. *In silico* analyses of the promoters of En1 target genes coupled with siRNA-mediated knockdown demonstrated that EN1 regulates these pro-fibrotic target genes by modulating the activity of regulatory modules that contain transcription factors of the specificity protein (SP) family. Functional experiments with selective modulators of ROCK and of microtubule polymerization confirm the coordinating role of EN1 on ROCK activity and the re-organization of cytoskeleton during myofibroblast differentiation in both conventional culture systems and 3D skin equivalents. Consistently, mice with fibroblast-specific knockout of En1 demonstrate impaired fibroblast-to-myofibroblast transition, reduced dermal thickening and impaired collagen deposition in the TBRI^{CA}, bleomycin-induced and TSK1 models.
Conclusion: We characterize the homeodomain transcription factor EN1 as a molecular amplifier of TGFβ signaling in myofibroblast differentiation that coordinates cytoskeletal organization in a SP-dependent manner. EN1 might thus be a novel candidate for molecular targeted therapies to interfere with myofibroblast differentiation in fibrotic diseases.
REFERENCES:
[1] Rinkevich Y, Walmsley GG, Hu MS, Maan ZN, Newman AM, Drukker M, et al. Skin fibrosis. Identification and isolation of a dermal lineage with intrinsic fibrogenic potential. Science. 2015;348(6232):aaa2151.
Disclosure of Interests: Andrea-Hermina Györfi: None declared, Alexandru-Emil Matei: None declared, Maximilian Fuchs: None declared, Aleix Rius Rigau: None declared, Xuezhi Hong: None declared, ZHU Honglin: None declared, Markus Luber: None declared, Christina Bergmann: None declared, Clara Dees: None declared, Ingo Ludolph: None declared, Raymund Horch: None declared, Oliver Distler Consultant of: Actellion, AbbVie, Acceleron Pharma, Anamar, Amgen, Blade Therapeutics, CSL Behring, ChemomAb, Ergonex, Glenmark Pharma, GSK, Inventiva, Italfarmaco, iQvia, Medac, Medscape, Lilly, Sanofi, Target BioScience, UCB, Bayer, Boehringer Ingelheim, Catenion, iQone, Menarini, Mepha, Novartis, Mitsubishi, MSD, Roche, Pfizer, Georg Schett: None declared, Meik Kunz: None declared, Jörg H.W. Distler Consultant of: Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB., Grant/research support from: Anamar, Active Biotech, Array Biopharma, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB
DOI: 10.1136/annrheumdis-2021-eular.1428

POS0329

GASTROINTESTINAL INVOLVEMENT IN SYSTEMIC SCLEROSIS: PATHOGENETIC ROLE OF GUT MICROBIOME, CYTOKINES AND ADIPOKINES

E. Pigatto[1], M. Schiesaro2, M. Caputo[3], M. Beggio[3], P. Galozzi[4], F. Cozzi2, P. Sfriso[4]. [1]*Fondazione Villa Salus, Medicine Unit, Venice, Italy*; [1]*Fondazione Villa Salus, Medicine Unit, Venice, Italy*; [3]*Fondazione Villa Salus, Laboratory Unit of clinical chemistry and microbiology, Venice, Italy*; [4]*Azienda Ospedaliera di Padova, Rheumatology Unit, Padua, Italy*

Background: Gastrointestinal (GI) involvement is very common in patients with Systemic Sclerosis (SSc). The pathophysiology of GI manifestations has not yet been defined. Cell-mediated immunological reactions appear to lead to endothelial damage resulting in fibrosis. The risk of developing malnutrition reinforces the need to better understand GI pathophysiology in these patients.
Objectives: The study aimed to evaluate GI symptoms (GIT 2.0) and malnutrition status (MUST) and to determine specific bacterial changes in gut microbiome by investigating the possible presence of positive hot spots in bacterial species in SSc patients and their potential role in the disease progression. We also evaluated serum levels of adipokines and cytokines involved in the pathogenesis of SSc and their role, in addition to gut microbiome, in predicting the onset of GI involvement and malnutrition in SSc patients.
Methods: We enrolled 25 scleroderma patients (EULAR/ACR 2013 criteria). UCLA-SCTC GIT 2.0 questionnaire to evaluate GI symptoms and MUST to investigate the risk of malnutrition were used. Gut microbiome was analyzed and the samples were subjected to extraction for the 16S rRNA gene (Earth Microbiome Project and the NIH-Human Microbiome Project). The microbiome was investigated at phenotypic and genotypic level. Serum levels of cytokines and adipokines (adiponectin and leptin) were evaluated by ELISA.
Results: 79.9% of patients had GERD and 63.5% abdominal distension at GIT 2.0 questionnaires. 48% of patients had moderate risk of malnutrition (MUST=2) and 12% had high risk (MUST=3). Gut microbioma: 19 patients (76%) had low similarity and 11 (44%) low diversity compared to the healthy population. The prevailing enterotypes of gut microbiome was Bacteroides (80%) and Prevotella (20%). The genotypic evaluation showed a reduced concentration of: gluten-digesting (Lactobacillus); lactose-digesting (Faecalibacterium); vitamin K-producing (Enterococcus, Desulfovibrio and Veillonella); acetaldehyde-degrading bacteria. 24 patients (96%) showed a reduction in bacteria devoted to maintaining weight control (Bifidobacterium and Ruminococcus). The patients had an altered intestinal permeability with less mucolytic bacteria (Bacteroides) and reduced production of LPS (Enterobacter and Escherichia). Low levels of butyrate (Eubacterium and Clostridium), acetate and propionate were found for SCFA-producing bacteria. Potentially pathogenic bacteria were also investigated: Salmonella was found in 14 (56%), Klebsiella in 9 (36%) and Enterococcus Faecalis in 3 (12%) patients. 11 (44%) patients had elevated serum levels of IL10 and IL12; 4 (16%) had high value of leptin. Correlation was found in patients who had a reduced concentration of gluten-digesting bacteria and MUST. Elevated MUST was correlated with serological increase in IL17A and IFN-α. Serum levels of IL12 and IL10 were found to correlate with specific bacteria alterations: high concentration of acetaldehyde-producing bacteria and low levels of acetaldehyde-degrade bacteria (also correlated with high serum levels of IL6), mucolytic bacteria and producers of hydrogen sulphide, acetate and propionate. Finally, reduced levels of mucolytic bacteria and acetate producing bacteria correlated with high serum leptin levels.
Conclusion: The relationship between the gut microbiome and SSc seems to be multifactorial. In our study genotypic changes of gut microbioma might play a role in damaging the permeability of the mucosa and increasing risk of malnutrition. The evaluation of gut microbiome and cytokine profile is probably going to be of value in the follow-up of SSc. However, further studies are needed to clarify the impact of GI dysbiosis on the immune system in SSc.
REFERENCES:
[1] Patrone V. et al. Gut microbiota profile in systemic sclerosis patients with and without clinical evidence of gastrointestinal involvement, Sci Rep. 2017; 7: 14874
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1904

POS0330

NINTEDANIB (TYROSINE KINASE INHIBITOR) DOWNREGULATES THE TRANSITION OF CULTURED SYSTEMIC SCLEROSIS FIBROCYTES INTO MYOFIBROBLASTS AND THEIR PRO-FIBROTIC ACTIVITY

S. Soldano[1], P. Montagna[1], E. Gotelli[1], S. Tardito[1], S. Paolino[1], C. Corallo[2], C. Pizzorni[1], A. Sulli[1], C. Schenone[1], G. Pacini[1], V. Smith[3,4,5], M. Cutolo[1]. [1]*University of Genova, IRCCS San Martino Polyclinic Hospital, 1Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Dept. Internal Medicine, Genoa, Italy*; [2]*University of Siena, 2Scleroderma Unit, Department of Medicine, Surgery and Neurosciences, Siena, Italy*; [3]*Ghent University Hospital, Ghent, Department of Rheumatology, Ghent, Belgium*; [4]*Ghent University, Department of Internal Medicine, Ghent, Belgium*; [5]*VIB Inflammation Research Center (IRC), Unit for Molecular Immunology and Inflammation, Ghent, Belgium*

Background: Fibroblast-to-myofibroblast transition is one of the fundamental steps involved in the fibrotic process that characterise systemic sclerosis (SSc) [1]. Myofibroblasts are α-smooth muscle actin (αSMA) positive cells that contribute to fibrosis through the excessive synthesis and deposition of extracellular matrix (ECM) proteins, primarily fibronectin (FN) and type I collagen (COL1) [2]. Among the cells involved in the fibrotic process of SSc, circulating fibrocytes seem to have an emerging role as an important source of fibroblasts and myofibroblasts [3].
Nintedanib is a tyrosine kinase inhibitor approved for the treatment of idiopathic pulmonary fibrosis that interferes with the signalling pathways involved in the pathogenesis of fibrosis (4). Nintedanib was recently demonstrated to have a beneficial effect in patients with interstitial lung disease (ILD) associated with SSc (5).
Objectives: To investigate nintedanib effect in inhibiting the *in vitro* transition of circulating SSc fibrocytes into myofibroblasts and their pro-fibrotic activity.
Methods: Circulating fibrocytes were obtained from 14 SSc patients (mean age 64±14 years), who fulfilled the 2013 ACR/EULAR criteria for SSc and that underwent complete disease staging in a day-hospital setting at the Rheumatology Division of Genoa University. Five age-matched healthy subjects (HSs) were also analysed. All SSc patients and HSs signed the informed consent and the local EC approved the study. Peripheral blood mononuclear cells were isolated by density gradient centrifugation and plated on FN-coated dishes. After overnight culture, non-adherent cells were removed, and adherent cells were maintained in growth medium for 8 days (T8) to obtain fibrocytes [6]. T8-cultured SSc fibrocytes were maintained in growth medium (untreated cells) or treated with nintedanib 0.1μM and 1μM for 3 and 24 hours. Fibroblast specific protein-1 (S100A4) and αSMA, as markers of fibroblast/myofibroblast phenotype, together with COL1 and FN, were investigated by qRT-PCR and Western blotting. Non-parametric Mann-Whitney and Wilcoxon tests were used for the statistical analysis.
Results: Significantly elevated gene and protein expressions of αSMA, S100A4, COL1 and FN were observed in SSc fibrocytes compared to HS fibrocytes (gene: αSMA $p<0.001$; others $p<0.0001$; protein: all $p<0.05$). In accordance with the antibody positivity for Scl70 and the presence or absence of ILD at CT scan, SSc patients were grouped as either Scl70 positive patients with ILD ($Scl70^+ILD^+$) or Scl70 negative patients without ILD ($Scl70^-ILD^-$). Significant αSMA, S100A4, COL1 and FN gene expressions were found in fibrocytes from $Scl70^+ILD^+$ compared to HS fibrocytes (αSMA $p<0.001$; others $p<0.0001$). Moreover, fibrocytes from $Scl70^+ILD^+$patients showed a more significant gene expression of fibroblasts/myofibroblasts markers compared to $Scl70^-ILD^-$patients ($p<0.01$ for S100A4), whereas no differences were observed for ECM gene expression.
Nintedanib reduced the gene and protein expression of αSMA, COL1 and FN in SSc fibrocytes compared to untreated ones with different statistical significance. Noteworthy, nintedanib significantly downregulated αSMA, S100A4, COL1 and FN gene expression (all $p<0.05$) in $Scl70^+ILD^+$fibrocytes, whereas only that of S100A4 and FN was significantly downregulated ($p<0.05$) in $Scl70^-ILD^-$ fibrocytes compared to untreated cells.
Conclusion: Nintedanib seems to downregulate *in vitro* the transition of fibrocytes into myofibroblasts and their pro-fibrotic activity, particularly in cells isolated from $Scl70^+ILD^+$SSc patients.
REFERENCES:
[1] Cutolo M et al. Exp Rev Clin Immunol. 2019;15:753-64.
[2] Van Caam A et al. Front. Immunol. 2018;9:2452.doi:10.3389/fimmu.2018.02452.
[3] Distler JH et al. Arthritis Rheumatol. 2017;69:257-67.
[4] Distler O et al. New Eng J Med. 2019; 380:2518-28.
[5] Maher TB et al. Arthritis Rheumatol.2020.doi:10.1002/art.41576.
[6] Cutolo M et al. Arthritis Res Ther. 2018;20:157.doi:10.1186/s13075-018-1652-6.
Acknowledgements: We thank Stefano-Lutz Willing for the scientific support through the study.
Disclosure of Interests: Stefano Soldano: None declared, Paola Montagna: None declared, Emanuele Gotelli: None declared, Samuele Tardito: None declared, Sabrina Paolino: None declared, Claudio Corallo: None declared, Carmen Pizzorni: None declared, Alberto Sulli: None declared, Carlotta Schenone: None declared, Greta Pacini: None declared, Vanessa Smith: None declared, Maurizio Cutolo Grant/research support from: I received grant/research support from Bristol-Myers Squibb, Boehringer, Celgene
DOI: 10.1136/annrheumdis-2021-eular.2411

POS0331

LUNG TARGETED DELIVERY OF EVEROLIMUS AS A NEW TREATMENT OF SCLERODERMA-RELATED INTERSTITIAL LUNG DISEASE (SSC-ILD) DEVELOPED BY PSGL-1 KO MICE

E. González Sánchez[1], J. Gómez-Román[2], A. Muñoz-Callejas[3], A. Marengo[4], N. Tsapis[4], K. Bohne-Japiassu[4], M. Á. González-Gay[5], E. F. Vicente-Rabaneda[3], E. Fattal[4], S. Castañeda[3], A. Urzainqui[1]. [1]*Fundación de Investigación Biomédica, Instituto de Investigación Sanitaria-Princesa, Hospital de La Princesa, Servicio de Inmunología, Madrid, Spain*; [2]*Universidad de Cantabria. Hospital Universitario Marqués de Valdecilla, IDIVAL, Servicio de Anatomía Patológica, Santander, Spain*; [3]*Fundación de Investigación Biomédica, Instituto de Investigación Sanitaria-Princesa, Hospital de La Princesa, Servicio de Reumatología, Madrid, Spain*; [4]*Institut Galien Paris Sud, School of Pharmacy at University Paris-Saclay, Paris, France*; [5]*Universidad de Cantabria. Hospital Universitario Marqués de Valdecilla, IDIVAL, Servicio de Reumatología, Santander, Spain*

Background: Interstitial lung disease (ILD), the main cause of mortality in scleroderma (SSc) patients (1), has no treatment (2). P-selectin glycoprotein ligand 1 (PSGL-1), the main ligand for P-Selectin, is expressed on leukocytes and responsible for the initial steps of extravasation (3). The absence of PSGL-1 in mice spontaneously develops an autoimmune syndrome similar to human SSc with fibrosis, vascular damage, autoantibodies and pulmonary arterial hypertension in females, and almost 60% of animals older than 12 months develop ILD with aging (4). In this work, the therapeutic action of everolimus-loaded nanomedicine given by local administration as a treatment for ILD was evaluated. The intratracheal administration of everolimus loaded into in liposomes decorated with hyaluronic acid (HA) is studied as an administration strategy to reach the inflammatory and fibrotic cells, targeting these cells and avoiding systemic effects and possible toxicity on epithelial cells

Objectives: 1) To study the effect of everolimus on bronchoalveolar lavage (BAL) cell populations and in lung pathology in SSc-ILD PSGL-1 KO mice

2) To analyze the intratracheal application of everolimus included in empty liposomes (Lip+Ev) *vs*. liposomes decorated with hyaluronic acid (Lip-HA+Ev) as an administration strategy to decrease drug toxicity and increase drug effectivity

Methods: In an observational study, *PSGL-1*$^{-/-}$ C57BL/6 males older than 12 months (n=4) were treated intratracheally with 4 doses of Lip or Lip-HA (with or without everolimus included), once a week (Lip+Ev 295.67µg/mL; Lip+Ev 82.73µg/mL; Lip-HA+Ev 82.73µg/mL). Then, animals were euthanatized and BAL and lungs were obtained. BAL cells were stained for flow cytometry analysis. Lungs were embedded in paraffin blocks for blind histological analysis by a pathologist and evaluated for interstitial inflammation and fibrosis degree. Lip-HA was selected as the treatment of choice for a second experiment (n=8) following the same experimental design (86.22µg/mL)

Results: The observational study showed an increase in CD45$^+$, alveolar macrophages (AM), eosinophils (Eos), granulocytes (Gr1$^+$) and T cells in the BAL of untreated *PSGL-1*$^{-/-}$ mice compared with WT mice. Everolimus reduced these populations to WT levels in all cases

Lip-HA+Ev administration was chosen for further experiments because a lower dose of the drug gave a better result than the high dose in undecorated liposomes. Reduction of CD45$^+$, AM, eosinophils, and CD45$^-$ cells populations by Lip-HA+Ev was confirmed. Lip-HA treatment increased the number of neutrophils and T cells, but this effect is controlled by the everolimus administration

Histological lung analysis showed an increase in interstitial inflammation and fibrosis in untreated PSGL-1$^{-/-}$ and empty Lip-HA experimental groups. Treatment with everolimus included in Lip-HA reduced the fibrotic and inflammatory interstitial lung lesions, reaching values similar to those observed in WT mice

Conclusion: PSGL-1 KO mice present ILD associated with scleroderma (SSc-ILD) with an increase of CD45$^+$, Gr1$^+$, Eos, T cells and AM populations in the BAL. Intratracheal treatment with everolimus included in liposomes decorated with hyaluronic acid reduces immune cell infiltration and fibrosis once SSc-ILD is established

REFERENCES:

[1] Solomon JJ, Olson AL, Fischer A, Bull T, Brown KK, Raghu G (2013). Scleroderma lung disease

[2] Singh D, Parihar AK, Patel S, Srivastava S, Diwan P, Singh MR (2019). Scleroderma: An insight into causes, pathogenesis and treatment strategies. Pathophysiology, 26(2)

[3] Zarbock A, McEver RP, Hidalgo A (2011). Leukocyte Ligands for Endothelial Selectins: Specialized Glycoconjugates That Mediate Rolling and Signaling Under Flow. *BLOOD*

[4] Pérez-Frías A, Núñez-Andrade N, et al. (2014). Development of an autoimmune syndrome affecting the skin and internal organs in P-selectin glycoprotein ligand 1 leukocyte receptor-deficient mice. *Arthritis Rheumatol*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2498

POS0332

ENDOTHELIAL ACTIVATION IN SYSTEMIC SCLEROSIS VASCULOPATHY: ROLE OF LONG NON-CODING RNA H19X

F. Tirelli[1,2], E. Pachera[1], R. Lafyatis[3], M. Huang[2], F. Zulian[2], G. Kania[1], O. Distler[1]. [1]*Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland*; [2]*Rheumatology Unit, Department of Woman's and Child's Health, University of Padova, Padova, Italy*; [3]*Division of Rheumatology and Clinical Immunology, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America*

Background: Long non-coding RNAs (lncRNA) are a class of non-coding transcripts which modulate many biological processes. Our previous studies showed that lncRNA H19X is pivotal in the regulation of TGFβ driven fibrosis in systemic sclerosis (SSc)[1].

Objectives: We aimed to investigate whether H19X plays a functional role in the regulation of endothelial cell (EC) activation, which is crucial in SSc vasculopathy[2].

Methods: Single-cell RNA sequencing (scRNA-seq) data from 27 dcSSc and 10 healthy control (HC) skin biopsies, following 10X Genomics partitioning and cDNA preparation, were analyzed for H19X expression in skin ECs, using Seurat package in R. A total of 4,981 ECs, of which 1,583 cells originated from HC and 3,398 cells originated from SSc patients, ranging from 59 to 342 ECs per subject, characterized by enrichment of EC markers of *CLDN5*, *VWF* and *PECAM1*.

Expression of H19X in Human Dermal Microvascular ECs (HDMEC) was analyzed by qPCR. HDMEC were stimulated with different proinflammatory cytokines including IFNα, IFNβ, IFNγ, TGFβ, TNFα, IL-6, IL-1β and IL-4 at biologically relevant concentrations. In order to ascertain its effect in ECs, H19X was silenced in HDMECs using locked nucleic acid antisense oligonucleotides (LNA GapmeRs). qPCR and Western Blot (WB) were used to analyze the effects of H19X down-regulation on EC activation biomarkers.

Results: scRNA-seq data showed that H19X was significantly upregulated in SSc compared to healthy ECs (p=0.0095). Based on the differentially expressed gene profiles among subclusters, EC were further annotated as arterial (*SEMA3G, HEY1*), capillary (*CA4, RGCC*), venous (*ACKR1, VCAM1*), lymphatic (*PROX1, LYVE1*) ECs, as well as two aberrant clusters, proliferating (*TOP2A*, *MKI67)* and injured (*HSGP2,APLNR)* ECs, which were dominated by the SSc ECs. Specifically, the highest expression of H19X was found in injured SSc ECs and capillary SSc ECs. Overall, 1.5% SSc EC, about 51 cells, expressed detectable levels of H19X.

In HDMEC (n=3), H19X was consistently induced by IFNα, IFNβ and IFNγ. Time curve analysis demonstrated that the strongest induction was observed at 48H (1.5±0.2, 1.6±0.4 and 2.1±0.3 – fold increase respectively). The combination of different IFNs determined stronger H19X induction after 48H stimulation, with a 2.4±0.1 increase with the combination of all IFNs and a 2.4±0.1 increase after the combination of IFNα+γ.

Importantly, H19X knockdown lead to consistent and significant decrease of mRNAs of several adhesion molecules, including VCAM1, E- Selectin and P-Selectin, both in untreated HDMEC and after IFN stimulation. A decrease of VCAM and P-Selectin could be also demonstrated with WB analysis. No change was seen in other EC activation markers, including endothelin-1 and angiogenesis markers including VEGF, VEGFRA, Tie2 and thrombospondin.

Conclusion: This is the first report analyzing a potential role of lncRNA H19X in SSc vasculopathy. Our results suggest that lncRNA H19X could act as a regulator of adhesion molecules expression in EC, possibly mediated by IFNs, and be therefore involved in EC activation.

REFERENCES:

[1] Pachera E, et al. Long noncoding RNA H19X is a key mediator of TGF-β-driven fibrosis. J Clin Invest. 2020 Sep 1;130(9):4888-4905.

[2] Mostmans Y, et al. The role of endothelial cells in the vasculopathy of systemic sclerosis: A systematic review. Autoimmun Rev. 2017 Aug;16(8):774-786.

Acknowledgements: I have no acknowledgements to declare

Disclosure of Interests: Francesca Tirelli: None declared, Elena Pachera: None declared, Robert Lafyatis Consultant of: RL served as a consultant with Bristol Meyers Squibb, Formation, Sanofi, Boehringer-Ingelheim, Merck, and Genentech/Roche, Acceleron, Grant/research support from: RL received grants form Bristol Meyer Squib, Corbus, Formation, Moderna, Regeneron, Pfizer, and Kiniksa, Menqi Huang: None declared, Francesco Zulian: None declared, Gabriela Kania: None declared, Oliver Distler Speakers bureau: Speaker fee on Scleroderma and related complications and on other rheumatology topics: Actelion, Bayer, Boehringer Ingelheim, Medscape, Novartis, Roche, Menarini, Mepha, MSD, iQone, Pfizer, Consultant of: Has consultancy relationship in the area of potential treatments for systemic sclerosis and its complications (last three years):Abbvie, Actelion, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Bayer, Baecon Discovery, Blade Therapeutics, Boehringer, CSL Behring, ChemomAb, Corpuspharma, Curzion Pharmaceuticals, Ergonex, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, -Kymera, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Sanofi, UCB, Lilly, Target BioScience, Pfizer. Consultancy relationship for rheumatology topic other than Scleroderma:

Abbvie, Amgen, Lilly, Target BioScience, Pfizer. In addition, he holds a patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Grant/research support from: Has received grants/research support in the are of potential treatments for systemic sclerosis from Actelion, Bayer, Boehringer Ingelheim, Kymera Therapeutics, Mitsubishi Tanabe Pharma
DOI: 10.1136/annrheumdis-2021-eular.3028

POS0333 ALTERED MACROPHAGE POLARIZATION PHENOTYPES IN SYSTEMIC SCLEROSIS

A. Hukara[1], M. Rudnik[1], C. B. Rufer[1], O. Distler[1], P. Blyszczuk[1], G. Kania[1].
[1]*University Hospital Zurich, University of Zurich, Department of Rheumatology, Center of Experimental Rheumatology, Zurich, Switzerland*

Background: Fos-like 2 (Fosl-2) is a transcription factor of the AP-1 family and has a broad range in inducing cellular changes affecting fibrosis and inflammatory responses. Pathological effects of Fosl-2 have been associated with systemic sclerosis (SSc). In addition, increased expression of Fosl-2 has been detected in human SSc monocyte-derived macrophages [1]. Monocytes and macrophages play a central role in activating and propagating acute inflammation followed by pathological fibrosis and organ dysfunction. The classification of the macrophage polarization phenotype can be assigned based on the stimulus, for example into classically-activated M(LPS), and alternatively-activated M(IL-4) macrophages [2]. However, the role of the Fosl-2 transcription factor in macrophage polarization remains elusive.
Objectives: To investigate the role of Fosl-2 in macrophage polarization in SSc using Fosl-2 overexpressing transgenic (Fosl-2 tg) mice and human blood-derived macrophages from SSc patients.
Methods: Thiogylcolate-elicited peritoneal macrophages were isolated from wild-type (wt) and Fosl-2 tg mice. Human peripheral $CD14^+$ blood-derived monocytes were isolated and differentiated to macrophages (hMDM) from healthy controls and SSc patients. Murine and human macrophages were polarized with LPS (10ng/ml), LPS + recombinant mouse IFN-γ (10ng/ml), recombinant mouse, resp. human IL-4 (10ng/ml) or remained untreated. Macrophage surface marker expression was assessed by flow cytometry using a mouse (F4/80, CD11b, CD86, CD80, CD38, MHCII, CD206, PD-L1, PD-L2, CD36) or human (CD38, CD40, CD86, PD-L2, PD-L1, CD163, CD206) designed polarization panel. Phagocytic activity was detected with pHrodo Red *E.coli* particles by flow cytometry. Gene expression and secretion of pro- and anti-inflammatory markers were measured by RT-qPCR, standard ELISAs and Griess Assay for nitric oxide production.
Results: After LPS stimulation, mRNA levels of IL-1β ($p<0.01$, n=11-12), TNF-α ($p=0.05$, n=11-12) and IFN-γ ($p<0.05$, n=7) were reduced, whereas expression of IL-10 ($p<0.05$, n=11-12) was enhanced in Fosl-2 tg peritoneal macrophages in comparison to wt cells. Secretion of TNF-α ($p<0.01$, n=9-11) and nitric oxide ($p<0.01$, n=9) was impaired in Fosl-2 tg peritoneal macrophages compared to wt cells after LPS stimulation. Peritoneal macrophages were analyzed directly after isolation for macrophage polarization cell surface marker expression. Fosl-2 tg peritoneal macrophages showed an increase in the $F4/80^+CD11b^+PD\text{-}L2^+CD36^+$ cell population ($p<0.01$, n=3-6) compared to peritoneal macrophages from wt mice. The expression of cell surface markers of non-polarized and IL-4 stimulated SSc hMDM (n=17) showed an increased percentage of $CD40^+CD86^+CD206^+PD\text{-}L2^+CD163^+$ cells ($p<0.05$) compared to healthy control hMDM (n=7). Phagocytic activity was enhanced in SSc hMDM (n=7) compared to healthy untreated ($p<0.05$), LPS ($p=0.05$) and IL-4 ($p<0.05$) hMDM (n=5).
Conclusion: Our animal data indicates a role of Fosl-2 in regulating macrophage polarization with a shift from a classically-activated to an alternatively-activated phenotype. Similarly, SSc hMDM resemble a functional M(IL-4) alternative macrophage phenotype. Thus, maintaining a balanced proportion of classically- and alternatively-activated macrophage phenotypes may be an effective tool to control macrophage function in SSc.
REFERENCES:
[1] Moreno-Moral, A., et al., *Changes in macrophage transcriptome associate with systemic sclerosis and mediate GSDMA contribution to disease risk.* Ann Rheum Dis, 2018. **77**(4): p. 596-601.
[2] Kania, G., M. Rudnik, and O. Distler, *Involvement of the myeloid cell compartment in fibrogenesis and systemic sclerosis.* Nat Rev Rheumatol, 2019. **15**(5): p. 288-302.
Disclosure of Interests: Amela Hukara: None declared, Michal Rudnik: None declared, Chantal Brigitta Rufer: None declared, Oliver Distler Speakers bureau: Actelion, Bayer, Boehringer Ingelheim, Medscape, Novartis, Roche, Menarini, Mepha, MSD, iQone, Pfizer, Consultant of: Abbvie, Actelion, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Bayer, Baecon Discovery, Blade Therapeutics, Boehringer, CSL Behring, ChemomAb, Corpuspharma, Curzion Pharmaceuticals, Ergonex, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, Kymera, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Sanofi, UCB, Lilly, Target BioScience, Pfizer, Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Kymera Therapeutics, Mitsubishi Tanabe, Przemyslaw Blyszczuk: None declared, Gabriela Kania: None declared
DOI: 10.1136/annrheumdis-2021-eular.3124

POS0334 INTERSTITIAL LUNG INFLAMMATION WITH ALVEOLAR HEMORRHAGE IN AUTOIMMUNE MRL/MP-LPR/LPR MICE

S. Sato[1]. [1]*Saitama Children's Medical Center, Division of Infectious Diseases and Immunology and Allergy, Saitama, Japan*

Background: Anti-melanoma differentiation-associated gene 5 (MDA5) antibody is associated with interstitial lung disease (ILD) in patients with juvenile dermatomyositis (JDM). Although the mechanisms leading to pulmonary involvements remain uncertain, both inflammatory cytokines and autoimmune response between MDA5 and anti-MDA5 antibody could been inferred. The present study examined the roles of MDA5 in an inducible form of lung involvement that develops in autoimmune mice treated with the pristane.
Objectives: MRL/Mp-lpr/lpr mice and wild type controls (+/+) at 5 weeks of age. They received 0.5ml of pristane or an equal volume of PBS IP at the age 7 week (day 1). And 1.2μg of recombinant human MDA5 protein (rMDA5) was instilled IP or PBS at day2 and Day9. The mice were sacrificed on 8 weeks after the intraperitoneal injection. Lung tissue was harvested for histological assessment.
Methods: MRL/Mp-lpr/lpr mice and wild type controls (+/+) at 5 weeks of age. They received 0.5ml of pristane or an equal volume of PBS IP at the age 7 week (day 1). And 1.2μg of recombinant human MDA5 protein (rMDA5) was instilled IP or PBS at day2 and Day9. The mice were sacrificed on 8 weeks after the intraperitoneal injection. Lung tissue was harvested for histological assessment.
Results: Lung involvements did not develop in PBS-treated MRL/*lpr* mice and WT mice. And Lung involvements did not develop in rMDA5 protein-treated WT mice. H&E staining of lung tissue from MRL/*lpr* mice and WT mouse with pristane that showed induced bland alveolar hemorrhage. H&E staining of lung from WT mouse compared with lung from a MRL/*lpr* mouse treated with pristane + rMDA5 protein showing mild thickening of the alveolar septa despite the alveolar hemorrhage. And perivascular lymphocytes infiltrate in a MRL/*lpr* mouse rather than a WT mouse treated with pristane + rMDA5 protein. CD163 staining of alveolar macrophages were present in the alveolar spaces was more intense in mouse treated with pristane + rMDA5 protein than in mouuse treated with only pristane. The Lymphocyte infiltrations around alveolar macrophages was more prominent in MRL/*lpr* mouse treated with pristane + rMDA5 protein than other mouse.
Conclusion: These results suggest that lung involvements such as the alveolar hemorrhage, are caused by pristeine and rMDA5 prtotein in the pathogenesis of interstitial pneumonia. MRL/*lpr* mouse treated with pristane + rMDA5 protein showed more alveolar macrophages that had lymphocyte infiltrations. After the alveolar hemorrhage by pritane, the antigen exposure of MDA5 might induce continuously inflammatory response to lymphocytes and macrophages in the alveolar lesions.
REFERENCES:
[1] Sunderrajan VE, McKenzie NW, Lieske RT, et al. Pulmonary inflammation in autoimmune MRL/Mp-lpr/lpr mice. Histopathology and bronchoalveolar lavage evaluation. Am J Pathol. 1986;124: 353–362.
[2] Tolga Barker T, Lee YP, Scumpia KK, et al. Pathogenic role of B-cells in the development of diffuse alveolar hemorrhage induced by pristane. Lab Invest. 2011; 91: 1540–1550.

Figure

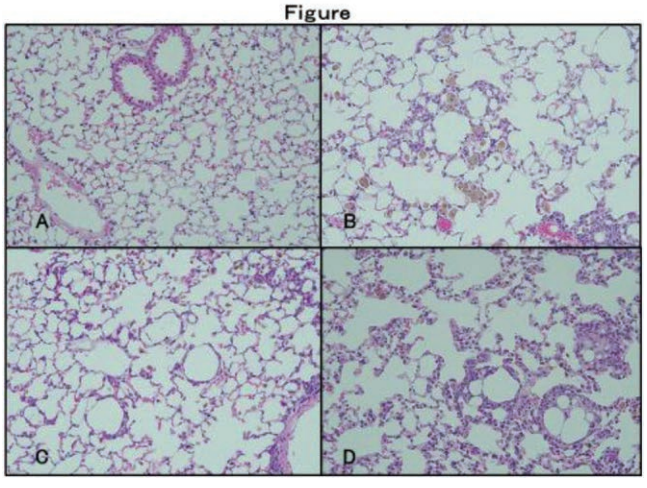


Figure 1. Lung disease (A-D).Light microscopy. Lung tissue from mice 8 weeks after treatment were stained with H&E. (A) Pristeine -treated WT mice with almost no alveolar lesions. (B) Pristane + rMDA5 protein -treated WT mice with alveolar hemorrhage and slight lymphocyte infiltrations. (C) Pristeine -treated MRL/*lpr* mouse with almost no alveolar lesions and slight lymphocyte infiltrations. (D) Pristeine -treated MRL/*lpr* mouse with alveolar hemorrhage and lymphocyte infiltrations, thickening of the alveolar septa.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3411

POS0335 **THE POTENTIAL ROLE OF IL13 IN VASCULOPATHY IN SYSTEMIC SCLEROSIS PATIENTS**

A. Schumann[1], H. Grasshoff[1], S. Comduehr[1], G. Riemekasten[1]. *[1]University Hospital Schleswig-Holstein, Rheumatology and Clinical Immunology, Lübeck, Germany*

Background: Systemic sclerosis (SSc) is a heterogeneous disease characterized by fibrosis, vasculopathy and autoimmunity. Dysfunctions causing disease pathology are characterized by the activation and recruitment of immune cells, as well as the formation of autoantibodies and cytokines. Profibrotic cytokines, such as interleukin-(IL)13, IL4 or IL6 play a crucial role in collagen production and fibrosis development [1]. Preliminary data reveal IL13 as a main driver for obliterative vasculopathy characterized by severe Raynaud phenomenon, acral ulcers and pulmonary arterial hypertension (PAH). Particularly acral ulcerations lead to a severe impairment in functional capacity in everyday life. In addition, pulmonary arterial hypertension is one of the main causes of the high mortality rate in SSc [2].
Objectives: To prove the impact of IL13 in the pathogenesis of systemic sclerosis and thus provide the rationale for the identification of a potential new therapeutic target, we investigated IL13 expression in CD4 and CD8 T cells in patients suffering from systemic sclerosis compared to healthy controls.
Methods: Peripheral blood mononuclear cells (PBMC) obtained from systemic sclerosis (SSc, n=31) patients and healthy controls (HC, n=13) were cultured without or in the presence of phorbol myristate acetate and ionomycin to activate T cells for cytokine production. Brefeldin A was used as an inhibitor of cytokine secretion. The intracellular IL13 and IL4 expression of CD4 and CD8 positive T cells were measured by flow cytometry and were compared between the investigated subgroups.
To identify a disease phenotype mediated by IL13, the expression levels in the SSc group were correlated to clinical, laboratory and apparative parameters assessing organ dysfunction.
Results: While there were no significant differences in IL4 expression between healthy and diseased individuals, analyses of IL13 positive CD4 and CD8 T cells showed significant differences compared to HC (CD8+IL13 p=0.048; CD4+IL13 p=0.0046) revealing the functional differences though high structural homology of the two interleukins. The increased expression of IL13 in T cells from patients with systemic sclerosis further supports the assumption of an interleukin mediated pathomechanism. Considering the IL13-mediated clinical phenotype, high levels were detected in patients showing signs for vasculopathy, correlation with sPAP (CD8+IL13 p=0.0392), NTproBNP (CD4+IL13 p=0.0461), creatinine (CD4+IL13 p=0.0227), angiotensin II receptor type I and endothelin receptor type A antibodies (CD4+IL13 p=0.0105, p=0.0042) was demonstrated. In addition, patients in the fourth quartile of CD4+IL13 expression showed a higher incidence of acral ulcers and pits than patients with low interleukin levels. Moreover, this group of patients had an increased cardiovascular comorbidity including atherosclerosis, coronary heart disease and arterial hypertension.
Conclusion: Increased IL13 levels could be detected in patients with SSc, especially in patients with the phenotype of an obliterative vasculopathy. This indicates preliminary evidence for the use of IL13 blockers as a new therapeutic approach in systemic sclerosis.
REFERENCES:

[1] Furue M, Mitoma C, Mitoma H, Tsuji G, Chiba T, Nakahara T, Uchi H, Kadono T. Pathogenesis of systemic sclerosis-current concept and emerging treatments. Immunol Res. 2017 Aug;65(4):790-797. doi: 10.1007/s12026-017-8926-y.
[2] Tyndall AJ, Bannert B, Vonk M, et alCauses and risk factors for death in systemic sclerosis: a study from the EULAR Scleroderma Trials and Research (EUSTAR) database Annals of the Rheumatic Diseases 2010;69:1809-1815. doi: 10.1136/ard.2009.114264

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3534

Vasculitis - Large vessel vasculitis

POS0336 **PATTERNS OF LARGE-VESSEL LESIONS AND POOR TREATMENT OUTCOMES IN PATIENTS WITH LARGE-VESSEL GIANT CELL ARTERITIS**

T. Sugihara[1,2,3], H. A. Uchida[4], H. Yoshifuji[5], Y. Maejima[6], T. Naniwa[7,8], Y. Katsumata[9], T. Okazaki[1,10], J. Ishizaki[11], Y. Murakawa[12], N. Ogawa[13], H. Dobashi[14], T. Horita[15], Y. Tanaka[16], S. Furuta[17], T. Takeuchi[18], Y. Komagata[19], Y. Nakaoka[20,21], M. Harigai[9]. *[1]St. Marianna University School of Medicine, Division of Rheumatology & Allergology, Department of Internal Medicine, Kawasaki, Japan; [2]Tokyo Metropolitan Geriatric Hospital, Department of Medicine and Rheumatology, Tokyo, Japan; [3]Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Department of Rheumatology, Tokyo, Japan; [4]Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Department of Chronic Kidney Disease and Cardiovascular Disease, Okayama, Japan; [5]Graduate School of Medicine, Kyoto University, Department of Rheumatology and Clinical Immunology, Kyoto, Japan; [6]Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Department of Cardiovascular Medicine, Tokyo, Japan; [7]Nagoya City University Graduate School of Medical Sciences, Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya, Japan; [8]Nagoya City University Hospital, Division of Rheumatology, Department of Internal Medicine, Nagoya, Japan; [9]Tokyo Women's Medical University School of Medicine, Department of Rheumatology, Tokyo, Japan; [10]National Hospital Organization, Shizuoka Medical Center, National Hospital Organization, Shizuoka Medical Center, Shimizu, Japan; [11]Ehime University Graduate School of Medicine, Department of Hematology, Clinical Immunology and Infectious Diseases, Ehime, Japan; [12]Shimane University Faculty of Medicine, Department of Rheumatology, Izumo, Japan; [13]Hamamatsu University School of Medicine, Department of Internal Medicine 3, Hamamatsu, Japan; [14]Faculty of Medicine, Kagawa University, Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Kagawa, Japan; [15]Hokkaido University Graduate School of Medicine, Division of Rheumatology, Endocrinology and Nephrology, Sapporo, Japan; [16]University of Occupational and Environmental Health, Japan, The First Department of Internal Medicine, Kitakyushu, Japan; [17]Chiba University Hospital, Department of Allergy and Clinical Immunology, Chiba, Japan; [18]Keio University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan; [19]Kyorin University School of Medicine, First Department of Internal Medicine, Tokyo, Japan; [20]National Cerebral and Cardiovascular Center Research Institute, Department of Vascular Physiology, Suita, Japan; [21]Osaka University Graduate School of Medicine, Department of Cardiovascular Medicine, Suita, Japan*

Background: Giant cell arteritis (GCA) is characterized by cranial symptoms and large-vessel lesions (LVL) in the aorta or its branches. We retrospectively analyzed the Japanese patients newly diagnosed as GCA between 2007 and 2014, and subsequently treated with glucocorticoid (GC). The imaging studies revealed that LVLs were observed in approximately half of the GCA patients, and the LVLs were significantly associated with the increased probability of poor treatment outcomes (1).
Objectives: The objective of this study is to evaluate whether the distribution of LVLs of GCA was associated with poor treatment response.
Methods: In a retrospective, multi-centric, nationwide registry of GCA patients treated with GCs between 2007 and 2014, 68 newly-diagnosed GCA with LVLs by imaging were detected. All investigators were members of Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis (JPVAS). Poor treatment outcomes (non-achievement of clinical remission by week 24 or relapse during 104 weeks) were primarily evaluated. Cumulative rates and median time to the first event were analyzed by the Kaplan-Meier method and the log-rank test. Associated factors with the outcomes were analyzed by using the Cox proportional hazard model.
Results: The mean age was 70.5 years, and 70.6% were women. Twenty-seven (39.7%) of the 68 patients were diagnosed as having GCA by both positive temporal artery biopsy and positive imaging, and 41 (60.3%) by positive imaging. Aortic lesions were detected in 72.1% (group 2, n=49) of the 68 GCA patients with LVLs. Patients without aortic lesions were categorized into two phenotypes: large-vessel GCA with subclavian lesions (group 1, n=9) and atypical large-vessel GCA without subclavian lesions (group 3, n=10). Cranial lesions were observed in 66.7%, 55.1%, and 80.0% in the group 1, 2, and 3, respectively. The initial mean dose (SD) of prednisolone was 0.74 (0.26) mg/kg/day, and 20.6 % received methotrexate for remission induction therapy. Baseline dose of GCs and mean time to achievement of low-dose GCs (prednisolone ≤ 5 mg/day) was not significantly different among the three groups.
Overall, 35 (51.5%) of the 68 patients had the event of poor treatment outcomes. Eleven patients were not able to achieve clinical remission by week 24. Relapse after achievement of clinical remission was reported in total of 24 patients; 9 between week 0 and 24, 12 between week 24 and 52, 3 between week 52 and 104. The cumulative rate of events of poor treatment outcomes over the two years was 11.1% in patients with group 1, 55.3% in those with group 2, and 88.0% in those with group 3. Mean time to events was significantly different among the three groups. Multivariable analysis showed the risk of poor treatment outcomes was likely to decrease in the group 1 (hazard ratio 0.14 [95% CI 0.02-1.03], p=0.054), while it increased in the group 3 (hazard ratio 2.22 [95% CI 1.06-4.68], p=0.035).
Conclusion: The distribution of LVLs were associated with poorer treatment outcomes. A half of the patients with aortic lesions had poor treatment outcomes while subclavian arteritis without aortic lesions had better clinical outcomes. Atypical large vessel-GCA without the aortic and subclavian artery involvement

was the worst prognostic phenotype of LV-GCA. Extent of LVLs by imaging should be considered when determining the treatment strategy for GCA.

REFERENCES:

[1] Sugihara T, et al. Arthritis Res Ther. 2020;22(1):72

Acknowledgements: The authors would like to acknowledge Mitsuaki Isobe (Sakakibara Heart Institute), Yoshihiro Arimura (Kichijoji Asahi Hospital), and all the investigators in the Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis (JPVAS). In addition to the authors, the following investigators and institutions participated in this study: Department of Internal Medicine, Juntendo University Koshigaya Hospital (Shigeto Kobayashi); Niigata Rheumatic Center (Satoshi Ito); Niigata Prefectural Shibata Hospital (Noriyuki Homma).

Disclosure of Interests: takahiko sugihara Speakers bureau: TS has received honoraria from Abbvie Japan Co., Ltd., AsahiKASEI Co., Ltd., Astellas Pharma Inc., Ayumi Pharmaceutical, Bristol Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd., Eli Lilly Japan K.K., Mitsubishi-Tanabe Pharma Co., Ono Pharmaceutical, Pfizer Japan Inc., Takeda Pharmaceutical Co. Ltd., and UCB Japan Co. Ltd., Grant/research support from: TS has received research grants from AsahiKASEI Co., Ltd., Daiichi Sankyo., and Ono Pharmaceutical., Haruhito A. Uchida Grant/research support from: HAU belongs to the Department of Chronic Kidney Disease and Cardiovascular Disease which is endowed by Chugai Pharmaceutical, MSD, Boehringer Ingelheim, and Kawanishi Holdings., Hajime Yoshifuji Speakers bureau: HY has received lecture fees from Chugai Pharmaceutical Co., Ltd. and Nihon Medi-Physics Co., Ltd., Yasuhiro Maejima Speakers bureau: YM have received honoraria from Chugai Pharmaceutical Co., Ltd.., Taio Naniwa Speakers bureau: TN has received lecture fees from Chugai Pharmaceutical Co., Ltd.., Grant/research support from: TN has received research grants from Chugai Pharmaceutical Co., Ltd.., Yasuhiro Katsumata Speakers bureau: YK has received honoraria from Chugai Pharmaceutical Co., Ltd., Glaxo-Smithkline K.K., Sanofi K.K., Pfizer Japan Inc., and Asahi Kasei Pharma Corp., Takahiro Okazaki Grant/research support from: TO has received research grants from Chugai Pharmaceutical Co., Ltd., Eisai Pharmaceutical., and Actelion, Jun Ishizaki: None declared, Yohko Murakawa Speakers bureau: YM has received honoraria from Abbvie, Astellas, Ayumi Pharmaceutical, Bristol Myers Squibb, Chugai Pharmaceutical, Eisai Pharmaceutical, Janssen Pharmaceutical, Kissei Pharmaceutical, Nippon Kayaku, Pfizer Pharmaceutical, Takeda Pharmaceutical, UCB Pharmaceutical, Grant/research support from: YM has received research grant support from Asahi Kasei Pharma, AbbVie Japan, Chugai Pharmaceutical, Daiichi Sankyo, Eisai Pharmaceutical, Mitsubishi Tanabe Pharma, Nippon Kayaku, Gilead Sciences Inc, Janssen Pharmaceutical, and Teijin Pharma., Noriyoshi Ogawa: None declared, Hiroaki Dobashi: None declared, Tetsuya Horita: None declared, Yoshiya Tanaka Speakers bureau: YT has received consulting fees, speaking fees, and/or honoraria from Daiichi-Sankyo, Astellas, Pfizer, Mitsubishi-Tanabe, Bristol-Myers, Chugai, YL Biologics, Eli Lilly, Sanofi, Janssen, UCB, Grant/research support from: YT has received research grants from Mitsubishi-Tanabe, Takeda, Bristol-Myers, Chugai, Astellas, Abbvie, MSD, Daiichi-Sankyo, Pfizer, Kyowa-Kirin, Eisai, Ono., Shunsuke Furuta: None declared, Tsutomu Takeuchi Speakers bureau: TT has served on speakers' fees for AbbVie, Bristol-Myers Squibb, Chugai, Mitsubishi Tanabe, Pfizer, Astellas, Daiichi Sankyo, Eisai, Sanofi, Teijin, Takeda, and Novartis., Consultant of: TT has received consulting fees from Astra Zeneca, Eli Lilly, Novartis, Mitsubishi Tanabe, AbbVie, Nippon Kayaku, Janssen, Astellas, Taiho, Chugai, Taisho Toyama, GlaxoSmithKline, and UCB., Grant/research support from: TT has received research grants from Astellas, Chugai, Daiichi Sankyo, Takeda, AbbVie, Asahi Kasei, Mitsubishi Tanabe, Pfizer, Eisai, AYUMI, Nippon Kayaku, and Novartis., Yoshinori Komagata Speakers bureau: YK has received speakers' fees from Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Daiichi Sankyo, AbbVie, Nippon Shinyaku, Towa., Consultant of: YK has received consulting fees from Chugai, Kyowa Hakko Kirin, Asahi Kasei, UCB, Yoshikazu Nakaoka Speakers bureau: YN has received lecture fees from Astellas, Takeda, Daiichi Sankyo, Actelion, and Japan Blood Products Organization (JB)., Consultant of: YN has received consulting fees and/or lecture fees from AbbVie and Chugai, Grant/research support from: YN has received research grants from Chugai and Bayer Yakuhin, Ltd, masayoshi harigai Speakers bureau: MH has received speaker's fee from AbbVie Japan GK, Ayumi Pharmaceutical Co., Boehringer Ingelheim Japan, Inc.,Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., GlaxoSmithKline K.K., Kissei Pharmaceutical Co., Ltd., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd., Consultant of: MH is a consultant for AbbVie, Boehringer-ingelheim, Bristol Myers Squibb Co., Kissei Pharmaceutical Co.,Ltd. and Teijin Pharma., Grant/research support from: MH has received research grants from AbbVie Japan GK, Asahi Kasei Corp., Astellas Pharma Inc., Ayumi Pharmaceutical Co., Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Daiichi-Sankyo, Inc.,Eisai Co., Ltd., Kissei Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Nippon Kayaku Co., Ltd., Sekiui Medical, Shionogi & Co., Ltd., Taisho Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd.

DOI: 10.1136/annrheumdis-2021-eular.824

POS0337

SOUTHEND PRE-TEST PROBABILITY SCORE AND HALO SCORE AS MARKERS FOR DIAGNOSIS AND MONITORING OF GCA: EARLY RESULTS FROM THE PROSPECTIVE HAS-GCA STUDY

A. Sebastian[1,2], A. Tomelleri[3], A. Kayani[1], M. Tariq[1], D. Prieto-Peña[4], S. Inness[2], J. Jackson[2], K. Van der Geest[5], B. Dasgupta[1,2]. *[1]Mid and South Essex University Hospital Groups, Southend University Hospital, Rheumatology, Westcliff-on-sea, United Kingdom*; *[2]University of Essex, School of Sport, Rehabilitation and Exercise science, Colchester, United Kingdom*; *[3]IRCCS San Raffaele Hospital, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy*; *[4]Marques de Valdecilla University Hospital, Rheumatology, Santander, Spain*; *[5]University of Groningen, University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*

Background: EULAR recommends doppler ultrasound (US) as the first line imaging in patients with Giant Cell Arteritis (GCA) suspect. Traditionally, US non-compressive halo sign has been used for diagnosis but prospective studies on response and disease monitoring are lacking

Objectives: The HAS GCA study has the objective of prospectively assessing role of US in diagnosis, prognosis and monitoring in newly diagnosed GCA. We report early baseline and up to month 3 data on our current recruitment in a study that has suffered disruption from the pandemic

Methods: HAS GCA (IRAS#264294) is an ongoing, prospective, multicentre study recruiting from referrals of suspected GCA to fast track clinics. The objective is to recruit 270 patients, including 68 GCA patients. Based on the Southend GCA clinical pre-test probability score (SPTPS)[1], patients were stratified in to low, intermediate and high risk categories[2]. Temporal and axillary US Halo Scores were calculated from the halo thickness and extent in bilateral temporal arteries, parietal and frontal branches and axillary arteries. These individual scores were summed (TA Halo Score x1 plus; AA Halo Score x3) to generate a Total Halo Score (THS)[3].

Mann Whitney U test and Fisher's exact test were used to compare baseline features between GCA and controls. Wilcoxon signed rank test was used to evaluate disease features at baseline and at 3 months in GCA patients. Sensitivity (Sn) and Specificity (Sp) were calculated, where applicable. P value <0.05 is statistically significant

Results: Ninety-three patients (29 GCA, 64 controls) have been recruited thus far: 18 completed 3-month follow up assessment; 4 were lost to follow up (2 died, 2 withdrew consent due to pandemic). Demographics, clinical features, and US results are shown (Table 1).

Table 1. Baseline features of GCA patients and controls.

	GCA (n=29)	Controls (n=64)	P-value
Age, median (IQR)	75 (71-80)	67 (61.25 – 75.0)	0.001
Female, n (%)	15 (42)	50 (78)	0.01
SPTPS category, n (%)			
Low risk	0 (0)	31 (48)	<0.001
Intermediate risk	7 (24)	25 (39)	0.24
High risk	22 (76)	8 (13)	<0.001
Halo score (HS), median (range)			
Temporal artery HS	10 (1-21)	1 (0-9)	<0.001
Axillary artery HS	12 (0-18)	6 (0-18)	<0.001
Total HS	21 (2-38)	6 (0-19)	<0.001
Clinical features, n (%)			
Temporal headache	21 (72)	40 (63)	0.48
Scalp tenderness	17 (59)	31 (48)	0.38
Jaw claudication	19 (66)	4 (6)	<0.001
PMR symptoms	16 (55)	6 (9)	<0.001
Constitutional symptoms	17 (59)	18 (28)	0.006
Visual disturbance	18 (62)	38 (59)	1
Vision loss	7 (24)	4 (6)	0.03

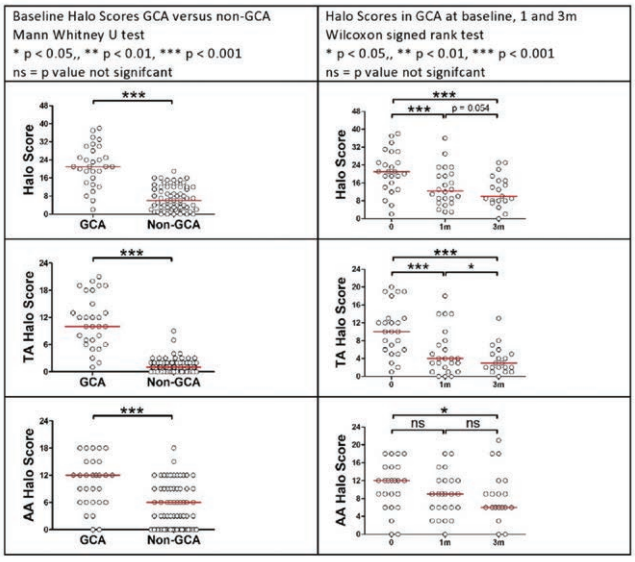
Among GCA patients, 23 had cranial, 2 large-vessel and 4 mixed phenotypes (cranial plus large vessel) disease.

Jaw claudication (66%) and polymyalgic symptoms (55%) were the dominant features in GCA patients. Median age 75 years in GCA (42% females) and 67 years in controls (78% females). GCA and controls were stratified by SPTPS to Low risk (0% vs 48%; Sn-undefined, Sp-97), Intermediate risk (24% vs 39%; Sn-100, Sp-100) and High risk (76% vs 13%; Sn-95, Sp-88). Optimal SPTPS cut-off point was ≥12 (Sn-93, Sp-86); ≥10 (Sn-100 & Sp-69).

Median THS was 21 in GCA and 6 in controls. Optimal cut-off Halo Score in diagnosis was TAHS ≥5 (Sn-90, Sp-98), AAHS ≥11 (Sn-55, Sp-80), THS ≥18 (Sn-72%, Sp-98%). Among the 18 patients who completed 3-months follow up,

median TAHS, AAHS and THS reduced from 10 to 2.5, 12 to 6 and 21 to 10, respectively (Figure 1).

Figure: HS comparing GCA vs non GCA and baseline Halo Score vs 1 and 3 months follow up



AA, Axillary artery; GCA, Giant cell arteritis; TA, Temporal artery

Conclusion: Along with SPTPS, Halo Score successfully discriminates GCA from non GCA mimics. HS is effective in showing 3-month response and may be a useful marker to monitor GCA disease activity.

REFERENCES:

[1] Laskou F et al. A probability score to aid the diagnosis of suspected giant cell arteritis. Clin Exp Rheumatol. 2019

[2] Sebastian A et al. Probability-based algorithm using ultrasound and additional tests for suspected GCA in a fast-track clinic. RMD Open. 2020

[3] Sebastian A et al. Halo score (temporal artery, its branches and axillary artery) as a diagnostic, prognostic and disease monitoring tool for Giant Cell Arteritis (GCA). BMC Rheumatol. 2020

Disclosure of Interests: Alwin Sebastian: None declared, Alessandro Tomelleri: None declared, Abdul Kayani: None declared, Mohammad Tariq: None declared, Diana Prieto-Peña: None declared, Sue Inness: None declared, Jo Jackson: None declared, Kornelis van der Geest Speakers bureau: Roche, Bhaskar Dasgupta Speakers bureau: Roche, GSK, BMS, Sanofi, Abbie, Grant/research support from: Roche

DOI: 10.1136/annrheumdis-2021-eular.1038

POS0338 STEROID-SPARING EFFECT OF ANAKINRA IN GIANT-CELL ARTERITIS: A CASE SERIES WITH CLINICAL, BIOLOGICAL AND ICONOGRAPHIC LONG-TERM ASSESSMENTS

S. Deshayes[1], K. Ly[2], V. Rieu[3], G. Maigné[1], N. M. Silva[1], A. Manrique[4], J. Monteil[5], H. De Boysson[1], A. Aouba[4]on behalf of the French Study Group for Large Vessel Vasculitis (GEFA). [1]*CHU de Caen Normandie, Internal Medicine, Caen, France*; [2]*CHU Dupuytren, Internal Medicine, Limoges, France*; [3]*CHU Estaing, Internal Medicine, Clermont-Ferrand, France*; [4]*CHU de Caen Normandie, Nuclear Medicine, Caen, France*; [5]*CHU Dupuytren, Nuclear Medicine, Limoges, France*

Background: The treatment of giant cell arteritis (GCA) relies on corticosteroids but is burdened by a high rate of relapses and adverse effects. Anti-interleukin-6 treatments show a clear benefit with a significant steroid-sparing effect, but late relapses occur after treatment discontinuation. In addition to interleukin-6, interleukin-1 also appears to play a significant role in GCA pathophysiology.

Objectives: We report herein the efficacy of anakinra, an interleukin-1 receptor antagonist, in 6 GCA patients exhibiting corticosteroid dependence or resistance, specifically analyzing the outcome of aortitis in 4 of them, and including the long-term follow-up of 2 previously described patients (1).

Methods: This retrospective study analyzed the cases of all GCA patients treated with anakinra from the French Study Group for Large Vessel Vasculitis. Patients had to satisfy the following two criteria to be enrolled in this retrospective study. First, their diagnosis of GCA should be based on the fulfillment of at least 3 criteria of the American College of Rheumatology (ACR) for GCA or on the satisfaction of 2 of these criteria along with the demonstration of LVI on imaging. Second, patients should have received anakinra because of corticosteroid dependence or resistance. Corticosteroid dependence was defined as ≥2 relapses or the combination of 2 of the following criteria: a daily dose of oral prednisone >20 mg/day (or 0.3 mg/kg) at 6 months; a daily dose of oral prednisone >10 mg/day (or 0.2 mg/kg) at 12 months; and/or a treatment maintained >24 months because of a relapsing disease course. Corticosteroid resistance was defined as persistent increased inflammatory parameters at month 3 despite a steroid dosage over 0.5 mg/kg.

Results: After a median duration of anakinra therapy of 19 [18–32] months, all 6 patients exhibited complete clinical and biological remission. Among the 4 patients with large-vessel involvement, 2 had a disappearance of aortitis under anakinra, and 2 showed a decrease in vascular uptake. After a median follow-up of 56 [48–63] months, corticosteroids were discontinued in 4 patients, and corticosteroid dosage could be decreased to 5 mg/day in 2 patients. One patient relapsed 13 months after anakinra introduction in the context of increasing the daily anakinra injection interval to every 48 hours. Three patients experienced transient injection-site reactions, and 1 patient had pneumonia.

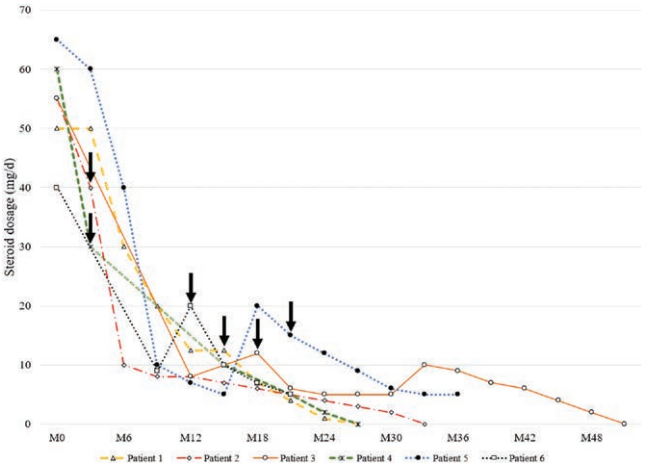


Figure 1. Steroid dosages before and after the introduction of anakinra in 6 patients with giant-cell arteritis and corticosteroid dependence or resistance. The black arrow indicates the time of anakinra introduction.

Conclusion: In this short series, anakinra appears to be an efficient and safe steroid-sparing agent in refractory GCA, with a possible beneficial effect on large-vessel involvement.

REFERENCES:

[1] Ly K-H, Stirnemann J, Liozon E, Michel M, Fain O, Fauchais A-L. Interleukin-1 blockade in refractory giant cell arteritis. Joint Bone Spine 2014;81:76–8.

Disclosure of Interests: Samuel Deshayes: None declared, Kim LY: None declared, Virginie Rieu: None declared, Gwénola Maigné: None declared, Nicolas Martin Silva: None declared, Alain Manrique: None declared, Jacques Monteil: None declared, Hubert de Boysson Speakers bureau: Roche-Chugai, Grant/research support from: Roche-Chugai, Achille Aouba Grant/research support from: SOBI

DOI: 10.1136/annrheumdis-2021-eular.1623

POS0339 PREDICTORS OF DEATH IN PATIENTS DIAGNOSED WITH GIANT CELL ARTERITIS IN WESTERN NORWAY 1972-2012

L. K. Brekke[1], B. T. Svanes Fevang[2], J. Assmus[3]. [1]*Hospital for Rheumatic Diseases, Rheumatology, Haugesund, Norway*; [2]*Haukeland University Hospital, Rheumatology, Bergen, Norway*; [3]*Haukeland University Hospital, Centre for Clinical Research, Bergen, Norway*

Background: Giant cell arteritis (GCA) is the most common systemic vasculitis in adults, and the number of incident cases worldwide is projected to increase [1]. Evidence as to whether or not GCA confers a mortality risk is conflicting, and many studies have been limited by inadequate or lacking adjustment for confounders.

Objectives: To investigate possible predictors of death in a large and well characterized Norwegian cohort of GCA-patients.

Methods: This is a hospital-based retrospective cohort study including patients diagnosed with GCA during 1972-2012. Patients were identified through computerized hospital records using the International Classification of Diseases coding system. Clinical information was extracted from patients' medical journals. Further details about the inclusion process have been published previously [2]. Information on time of death was obtained from the Norwegian Cause of Death Registry. We investigated predicting factors using Cox regression. Selected variables were first analyzed in univariate and block regression models (block 1:

clinical features including histology, block 2: laboratory and treatment factors, block 3: demographic and traditional risk factors). Variables included in the final multivariate model were selected on the following basis: P-value <0.1 in univariate or block regression or otherwise deemed clinically significant.

Results: 881 patients were included of which 626 (71.1%) were females. Mean age was 73 years (SD 9). 490 patients (55.6%) died during the study period (1 January 1972 – 31 December 2012). Characteristics and mortality for the GCA-cohort compared to matched controls have been published previously [3]. Within the GCA-cohort we found that presenting with visual disturbance (any) or scalp necrosis was associated with increased risk of death in univariate analysis (Figure 1). However, in multivariate analysis the traditional risk factors (age, smoking, hypertension and previous cardiovascular disease) were more strongly associated with risk of death. Among laboratory parameters only Hemoglobin (Hb) levels were significantly associated with risk of death with increasing Hb-levels indicating decreased risk. Neither temporal artery biopsy result nor initial or maximal (before first tapering) Prednisolone dose were found to be associated with risk of death. Results from univariate and the final multivariate models are presented in Figure 1.

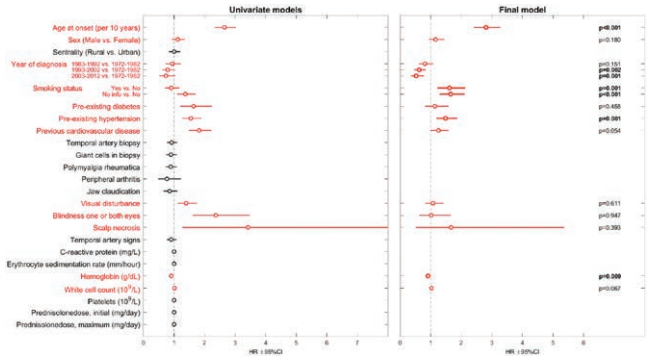


Figure 1.

Conclusion: In our large cohort of GCA-patients the risk of death was found to be predominantly predicted by age (HR 2.81) and traditional risk factors (smoking (HR 1.61), hypertension (HR 1.48) and previous cardiovascular disease (HR 1.26)). Visual disturbance (HR 1.40), visual loss in particular (HR 2.37), and scalp necrosis (HR 3.42) were found to be the clinical features most associated with risk of death. However, we note that our material lacked information about extra-cranial (large vessel) vasculitis, which may also carry increased risk of death.

REFERENCES:

[1] De Smit E, Palmer AJ, Hewitt AW. Projected worldwide disease burden from giant cell arteritis by 2050. J Rheumatol 2015;42:119-25.
[2] Brekke LK, Diamantopoulos AP, Fevang BTS, Assmus J, Esperø E, Gjesdal CG. Incidence of giant cell arteritis in Western Norway 1972-2012: a retrospective cohort study. Arthritis Res Ther. 2017;19(1):278.
[3] Brekke LK, Fevang BTS, Diamantopoulos AP, Assmus J, Esperø E, Gjesdal CG. Survival and death causes of patients with giant cell arteritis in Western Norway 1972-2012: a retrospective cohort study. Arthritis Res Ther. 2019;21(1):154.

Disclosure of Interests: Lene Kristin Brekke Grant/research support from: Unrestricted research grant from MSD, Bjørg Tilde Svanes Fevang Consultant of: Been part of advisory board for Lilly, Jörg Assmus: None declared
DOI: 10.1136/annrheumdis-2021-eular.1988

POS0340 VASCULAR IMAGING IN PATIENTS WITH REFRACTORY TAKAYASU ARTERITIS TREATED WITH TOCILIZUMAB: ANALYSIS FROM A RANDOMIZED CONTROLLED TRIAL

Y. Nakaoka[1,2], M. Yanagawa[3], A. Hata[4], K. Yamashita[5], N. Okada[6], S. Yamakido[7], H. Hayashi[8], D. Jayne[9]. *[1]National Cerebral and Cardiovascular Center Research Institute, Department of Vascular Physiology, Suita, Japan*; *[2]Osaka University Graduate School of Medicine, Department of Cardiovascular Medicine, Osaka, Japan*; *[3]Osaka University Graduate School of Medicine, Department of Diagnostic and Interventional Radiology, Osaka, Japan*; *[4]Osaka University Graduate School of Medicine, Department of Future Diagnostic Radiology, Osaka, Japan*; *[5]Chugai Pharmaceutical Co., Ltd., Medical Science Department, Medical Affairs Division, Tokyo, Japan*; *[6]Chugai Pharmaceutical Co., Ltd., Biometrics Department, Clinical Development Division, Tokyo, Japan*; *[7]Chugai Pharmaceutical Co., Ltd., Primary Clinical Development, Clinical Development Division, Tokyo, Japan*; *[8]Nippon Medical School, Department of Radiology, Tokyo, Japan*; *[9]University of Cambridge, Department of Medicine, Cambridge, United Kingdom*

Background: In the TAKT study, a randomized controlled trial of tocilizumab (TCZ) in patients with refractory Takayasu arteritis (TAK) in Japan, the primary end point of time to relapse after induction of remission with glucocorticoid (GC) treatment showed a trend favoring TCZ over placebo (hazard ratio 0.41 [95.41% confidence interval, 0.15-1.10; p=0.0596]),[1] but the double-blind period was too short for imaging evaluation.

Objectives: To independently evaluate vascular imaging in a post hoc analysis of radiographs from the TAKT study.

Methods: Computed tomography images from patients in the TAKT study were evaluated by three independent radiologists who were not involved in the original trial. Patients who received TCZ and had computed tomography images available (n=28) were included. Assessments were made in 22 arteries for the change from baseline in wall thickness (primary end point), dilatation/aneurysm, stenosis/occlusion, or wall enhancement for at least 96 weeks after the start of tocilizumab treatment. Patient-level assessments were also conducted.

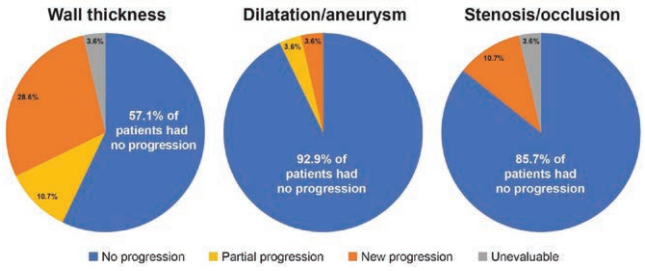
Results: Among 28 patients who received at least one dose of TCZ and for whom images were available, 86.7% of 22 arteries had improved/stable (no progression) wall thickness at week 96. The proportions of patients with no progressed, partially progressed, or newly progressed lesions were 57.1%, 10.7%, and 28.6% for wall thickness, and the proportions without progressed lesions were 92.9% for dilatation/aneurysm and 85.7% for stenosis/occlusion (Figure 1). Patients with newly progressed lesions, reflecting more refractory disease, were receiving glucocorticoid doses that could not be reduced below 0.1 mg/kg/day at week 96.

Conclusion: Approximately 60% of patients with TAK treated with tocilizumab did not experience progression in wall thickness. Few patients experienced progressive dilatation/aneurysm or stenosis/occlusion. Wall thickness progression likely resulted from refractory TAK. Patients who experience this should be monitored regularly by imaging, and additional glucocorticoid or immunosuppressive treatment should be considered to avoid vascular progression.

REFERENCES:

[1] Nakaoka Y et al. *Ann Rheum Dis.* 2018;77:348-354.

Figure. Evaluation of arteries per patient (n=28)



Disclosure of Interests: Yoshikazu Nakaoka Consultant of: Roche/Genentech, Grant/research support from: Roche/Genentech, Masahiro Yanagawa Consultant of: Roche/Genentech, Akinori Hata Consultant of: Roche/Genentech, Katsuhisa Yamashita Employee of: Chugai Pharmaceutical Co., Ltd., Norihiro Okada Employee of: Chugai Pharmaceutical Co., Ltd., Shinji Yamakido Employee of: Chugai Pharmaceutical Co., Ltd., Hiromitsu Hayashi Consultant of: Roche/Genentech, David Jayne Consultant of: Roche/Genentech, Grant/research support from: Roche/Genentech
DOI: 10.1136/annrheumdis-2021-eular.2768

POS0341 SVCAM-1 EXPRESSION IN TAKAYASU ARTERITIS TREATED WITH TOCILIZUMAB: A PROSPECTIVE PILOT STUDY

S. Ackermann[1], P. Villiger[2], A. Gloor[3], K. K. Eriksson[2], M. Seidel[1]. *[1]Hospital Biel, Rhumatology, Biel, Switzerland*; *[2]Inselspital, Rhumatology, Bern, Switzerland*; *[3]Stanford University, Immunoloy and Rhumatology, Stanford, United States of America*

Background: Takayasu arteritis (TA) is a rare disease, its diagnosis is often delayed by years. Biomarkers might be helpful for earlier diagnosis and for monitoring treatment. We have described serum soluble vascular cell adhesion molecule-1 (sVCAM-1) as a marker of inflammation in a variety of rheumatic diseases, including vasculitis (1). Tocilizumab (TCZ) is a monoclonal antibody against the interleukin-6 receptor with established benefits in TA (2). It may spare oral glucocorticoids (GC) and Disease-Modifying Agents (DMARDs). So far, sVCAM-1 has never been examined as diagnostic marker or to monitor disease activity in TA patients treated with TCZ.

Objectives: To analyze sVCAM-1 in TA patients treated with TCZ in a prospective clinical trial and compare these results to age-matched healthy controls (HC) as well as DMARDs. In addition, MRI analyses of aortic wall thickening and enhancement might serve as a morphologic correlate of serologic disease activity.
Methods: 29 TA patients were prospectively followed between 2016 and 2019 (27 females, mean ± SD: 39.2±13.9 years) at the Department of Rheumatology of the University Hospital of Bern, Switzerland. At baseline, patients were without treatment (n=8) or treated with TCZ (n=13), GC (n=4), GC + methotrexate (MTX) (n=1), infliximab (IFX) + MTX (n=1), GC + IFX (n=1), MTX (n=1). Three follow-ups were performed after an average of 12, 24, 34 ± 3 months. sVCAM-1 was measured in serum using a commercially available ELISA kit (R&D Systems, Germany). Results were compared to 29 sera of matched HC (27 females, 40.8±15.1 years). MRI of aortic changes were scored on a scale of 0 (no thickening and vessel wall enhancement) to 3 (maximal thickening and vessel wall enhancement). Cumulated sVCAM-1 concentrations from each MRI scoring group (0-3) were compared to HC in order to determine if sVCAM-1 from high aortic MRI inflammation was significantly elevated.
Results: At baseline, significantly increased serum concentrations of sVCAM-1 (ng/ml) were observed in TA patients without treatment (n=8, 537.3±130.1, p=0.002) vs. HC (336.0±76.1). A smaller difference was found between patients under treatment and HC (n=21, 468.2±105.3 vs. 405.1±82.5, p=0.04). Follow-ups in the TCZ group showed 518.9±138.9 vs. 417.5±46, p=0.12 (n=6) after 12 months, 436.6±77.3 vs. 399.6±113.1, p=0.46 (n=8) after 24 months and 407.1±27.1 vs. 381.8±60.4, p=0.47 (n=4) after 36 months. In contrast, patients under DMARD therapy showed values of 505.8±126.4 vs. 395.6±60.2 p=0.04 (n=8) after 12 months, 437.8±76.2 vs. 396.4±91.9, p=0.24 (n=12) after 24 months and 440±43.3 vs. 323±50 p=0.03 (n=8) after 36 months. MRI analyses showed that group 0 (no inflammation, n=7) had significant increased values compared to HC (474.7±106.8 vs. 356.9±48.8, p=0.02), and group 3 (maximal inflammation, n=11) was also elevated (461.8±98.4 vs. 379.3±88.9, p=0.05).
Conclusion: The results suggest that sVCAM-1 is a biomarker of disease activity in patients with TA. The results at follow-up show that sVCAM-1 decreased more rapidly under treatment with TCZ compared to treatment with DMARDs. Remarkably, sVCAM-1 concentrations did not correlate with disease activity as assessed with MRI.
REFERENCES:
[1] Oleszowsky M, Seidel MF. Serum Soluble Vascular Cell Adhesion Molecule-1 Overexpression Is a Disease Marker in Patients with First-Time Diagnosed Antinuclear Antibodies: A Prospective, Observational Pilot Study. BioMed Res Int. 2018;8286067.
[2] Hellmich B, Agueda A, Monti S, Buttgereit F, Boysson H de, Brouwer E, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis. 2020 Jan 1;79(1):19–30.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3344

POS0342 DISCRIMINANT VALUE OF ULTRASOUND OF THE WALL OF LARGE VESSELS IN THE DIAGNOSIS OF GIANT CELL ARTERITIS

I. González-Mazón[1], E. Fernández-Fernández[2], I. Monjo[3], E. De Miguel[3].
[1]Marqués de Valdecilla University Hospital, Rheumatology, Santander, Spain; *[2]La Paz University Hospital, Rheumatology, Madrid, Spain*; *[2]La Paz University Hospital, Rheumatology, Madrid, Spain*

Background: The EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice suggest the performance of diagnostic imaging tests in all patients with suspected GCA and ultrasound is the recommended first-line test in patients with suspected cranial GCA (c-GCA)[1]. However, a priority imaging modality has not been established in cases of suspected GCA involving large vessels (LV-GCA). Since patients with LV-GCA often undergo extensive screening programs for suspected infection or malignancy before the diagnosis of GCA is established, our knowledge in this field needs to be improved.
Objectives: The aim of this study is to investigate the wall affectation of vasculitis of the proximal arm and neck arteries in patients with suspected GCA, polymyalgia rheumatica (PMR), atherosclerosis and non-GCA patients.
Methods: Retrospective available ultrasound examination from all the patients referred to our GCA fast-track clinic in the last three years were collected. All patients had ultrasound of cranial and large vessel examination (axillary, subclavian and carotid arteries). GCA diagnosis was confirmed by the doctor after a follow-up between six months to three years. Every patient had videos and pictures of every referred vessel. Examination was performed by two rheumatologists with long experience in GCA ultrasound from the same Rheumatology Department with a Esaote Mylab Twice with probe of 13 MHz (2017-2019) and a Esaote Mylab X8plus with a probe of 15 MHz (2019-2020). IMT and hypoechoic halo measures were taken.
Results: We analyzed 300 examinations and selected 196 baseline cases of four different pathologies (29 PMR, 40 atherosclerosis, 71 GCA of which 14 LV-GCA without cranial involvement and 56 non-GCA non-PMR controls). Intima-media thickness (IMT) with the statistical significance between different diseases and controls are showed in the Table 1.

Table 1. Ultrasound IMT and halo measures in large vessels of different diseases and controls

	Non-GCA n=56	GCA n=71	Atherosclerosis n=40	PMR n=29	LV-GCA n=14
Axillary right # *	0.67±.19	0.95±0.30	0.70±0.18	0.65±0.13	1.03±0.33
Axillary left # **	0.61±0.12	0.92±0.29	0.72±0.19	0.66±0.13	0.99±0.25
Subclavian right # *	0.70±0.15	1.00±0.31	0.86±0.29	0.70±0.20	1.09±0.36
Subclavian left # *	0.62±0.14	0.95±0.27	0.70±0.14	0.64±0.18	1.05±0.25
CCD right #	0.79±0.22	0.97±0.26	1.01±0.30	0.81±0.10	0.91±0.29
CCD left #	0.81±0.16	0.99±0.22	0.98±0.32	0.82±0.20	0.97±0.17

GCA= Giant cell arteritis (cranial, large vessel and mixed forms); Non-GCA = Patients suspected but not confirmed as GCA; Atherosclerosis = patients with high arteriosclerosis risk without suspected GCA; PMR = Patients with polymyalgia rheumatica without GCA; LV-GCA= Large vessel vasculitis GCA without cranial involvement.# p<0.01 GCA vs non-GCA and GCA vs PMR* p<0.01 GCA vs Atherosclerosis; ** p<0.05 GCA vs Atherosclerosis

Conclusion: GCA ultrasound of large vessels shows significant differences with other diseases. The differences seem to support the use of ultrasound in the fast-track clinic of GCA not only in c-GCA but also in LV-GCA.
REFERENCES:
[1] Dejaco C et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheum Dis. 2018 May;77(5):636-643. doi: 10.1136/annrheumdis-2017-212649. Epub 2018 Jan 22. PMID: 29358285.
Disclosure of Interests: Iñigo González-Mazón: None declared, Elisa Fernández-Fernández: None declared, Irene Monjo Speakers bureau: Roche, Novartis, UCB, Gedeon Richter, Consultant of: Roche, Eugenio de Miguel Speakers bureau: AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi., Paid instructor for: Janssen, Novartis, Roche, Consultant of: AbbVie, Novartis, Pfizer, Galapagos, Grant/research support from: Abbvie, Novartis, Pfizer
DOI: 10.1136/annrheumdis-2021-eular.3925

POS0343 RITUXIMAB IS SUPERIOR TO PLACEBO IN POLYMYALGIA RHEUMATICA

D. Marsman[1], N. Den Broeder[2], F. Van den Hoogen[3], A. Den Broeder[3], A. Van der Maas[3]. *[1]Sint Maartenskliniek, Rheumatology, Nijmegen, Netherlands*; *[2]Sint Maartenskliniek, Rheumatology, Ubbergen, Netherlands*; *[1]Sint Maartenskliniek, Rheumatology, Nijmegen, Netherlands*

Background: Corticosteroids remain the cornerstone of polymyalgia rheumatica treatment, but their use has several disadvantages such as long treatment duration and glucocorticoid-related adverse events.[1,2] Data on evidence based effective glucocorticoid-sparing agents are negative or absent.[2]
Objectives: Because B-cells may be involved in the pathogenesis of polymyalgia rheumatica, we evaluated the efficacy of rituximab in polymyalgia rheumatica.
Methods: In a 21-week double-blind placebo controlled exploratory study, 47 polymyalgia rheumatica patients (recently diagnosed n=38 / relapsing on prednisolone ≥7.5mg/day n=9) fulfilling the 2012 EULAR/ACR criteria, were randomized 1:1 to intravenous rituximab 1 x 1000 mg (n=23) or placebo (n=24), with a 17-week long glucocorticoid co-treatment. Primary outcome was glucocorticoid-free remission at week 21. Secondary outcomes were glucocorticoid ≤5mg/day and adverse events. Several post-hoc analyses were done for robustness of results.
Results: Glucocorticoid-free remission was achieved in 48% (rituximab) versus 21% (placebo), one-sided 95%-CI 4% to 100%; p=0.049, and glucocorticoid ≤5mg/day in 100% versus 54% (one sided 95%-CI 20% to 100%; p=0.005). Post-hoc analysis showed efficacy mainly in recently diagnosed patients: glucocorticoid-free remission in 58% versus 21% (one-sided 95%-CI 10% to 100%; p=0.02); glucocorticoid ≤5mg/day in 100% versus 47% (one-sided 95%-CI 29 to 100%; p<0.001). No significant differences were observed regarding other outcomes (Table 1), except for less morning stiffness after rituximab.

Table 1. ***Outcomes at week 21****

	Rituximab (n=23)	Placebo (n=24)	Difference, one sided 95%-CI	One sided p-value
Cumulative glucocorticoid dose in mg	*1356* (*151*)	*1406* (*189*)	- ∞ to 34	0.16
Median CRP in mg/l (median, IQR) ‡	3 (1 to 5) - 1.5 (-9 to 2)	2 (1 to 12) [21]	-	0.16
Change from baseline (median, IQR)	[22]	- 5 (-13 to 0)[21]		
Mean ESR in mm/hour	19 (11) [21]	16 (13) [22]	- ∞ to 17	0.79
Change from baseline	-7 (25) [21]	-12 (19) [21]		
Relapsing patients during follow-up – no (%)†	7 (30)	8 (33)	- 100 to 20	0.54
Morning stiffness in minutes (median, IQR)	5 (0 to 30) -60 (-120 to -5)	30 (9 to 90) -20 (-60 to 0)	-	0.02
Change from baseline (median, IQR)				
			Rate ratio rituximab versus placebo (95% CI)	
Any adverse event §	136	148	0.9 (0.8 to ∞)	
Serious adverse event(s) ††	1	0		
Infections ‡ ‡	17	14	1.2 (0.7 to ∞)	
Infusion related complaints ¶	10	3	3.3 (1.2 to ∞)	

*Values are means, SD, unless specified otherwise. Numbers of observations is indicated between brackets []. No correction for type I error.

† Judged by research physician.

‡Wilcoxon rank sum (Mann-Whitney) test

§ All adverse events that occurred during the study period were included in the analyses. Adverse events numbers are number of events, not number of patients with events. Safety outcomes were compared by chi-squared test (cumulative incidences). No correction for type I error was performed. All adverse events were graded according to Common Terminology Criteria for Adverse Events version 5.0, grade range 0–5;higher scores indicate worse events.

†† was A pulmonary embolism occurred in one patient

‡ ‡ Labelled by the research physician. No serious infections ≥ grade 3 occurred.

¶ Labelled by research physician. No serious infusion related complaints ≥ grade 3 occurred.CRP denotes C-reactive protein, IQR interquartile range, ESR erythrocyte sedimentation rate, CI confidence interval

Conclusion: Rituximab is superior to placebo in combination with 17-week glucocorticoid-treatment to achieve glucocorticoid free remission in polymyalgia rheumatica. The largest effect was seen in recently diagnosed polymyalgia rheumatica patients (funding: Sint Maartenskliniek; Dutch trial number NL7414).

REFERENCES:

[1] González-Gay MA et al. Polymyalgia rheumatica. Lancet 2017;390 (10103):1700–12.

[2] Dejaco C et al. 2015 recommendations for the management of polymyalgia rheumatica. Ann Rheum Dis. 2015 Oct 1;74(10):1799–807.

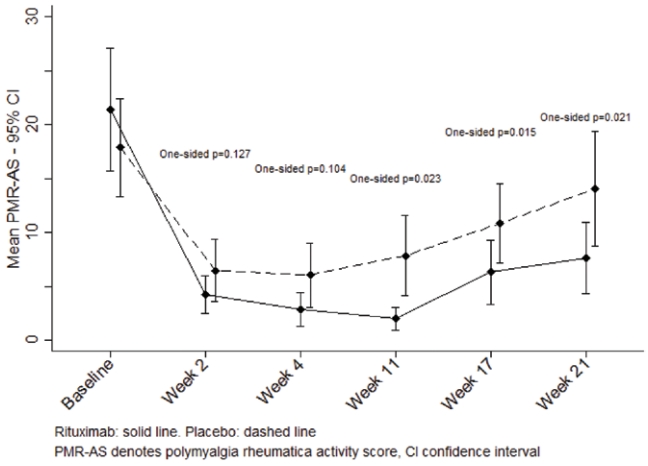


Figure 1. *Mean Polymyalgia Rheumatica Activity Score at each visit.*

Disclosure of Interests: Diane Marsman: None declared, Nathan den Broeder: None declared, Frank van den Hoogen: None declared, Alfons den Broeder Consultant of: Expert witness fee adalimumab biosimilar litigation for Boehringer/Fresenius, Amgen, Merck. Editorial work education for Abbvie,Novartis., Grant/research support from: Research Grants to employer SMK from Abbvie/Sanofi/Pfizer/Novartis or Lilly, Aatke van der Maas: None declared

DOI: 10.1136/annrheumdis-2021-eular.899

POSTERS only

Genomics, genetic basis of disease and functional genomics

POS0344 RISK OF ACPA POSITIVITY BY MOTIF-BASED CLASSIFICATION OF HLA-DRB1 SHARED EPITOPE ALLELES IN RA

K. Wipfler[1], X. Han[2], S. S. H. Park[2], K. Wittstock[2], K. Michaud[1,3]. [1]*FORWARD, The National Databank for Rheumatic Diseases, Wichita, KS, United States of America*; [2]*Bristol Myers Squibb, Health Economics & Outcomes Research, Princeton, NJ, United States of America*; [3]*University of Nebraska Medical Center, Division of Rheumatology and Immunology, Omaha, NE, United States of America*

Background: The shared epitope (SE) is the strongest known genetic risk factor for rheumatoid arthritis (RA) and is associated with an amino acid motif at positions 70-74 in HLA-DRB1. It is linked to anti-citrullinated protein antibody (ACPA) positivity, a specific serological marker for RA. In 2005, a new classification of HLA-DRB1 alleles was proposed, in which each allele is sorted into one of five classes (S1, S2, S3P, S3D, or X).[1] The method was subsequently validated for predicting risk of developing RA[2] and was described as "a major advance and a template for future studies."[3] However, there have been relatively few studies utilizing this classification.

Objectives: To characterize the prevalence of each SE genotype from the 2005 classification and their association with ACPA positivity in a cohort of individuals with RA.

Methods: Participants in FORWARD, The National Databank for Rheumatic Diseases, with RA and donated serum (collected 2010-2019) were analyzed to obtain ACPA status and high-resolution HLA-DRB1 type. Alleles were classified based on the presence (S2, S3P) or absence (S1, S3D, X; collectively L) of the SE motif, and individuals were classified by allele pair. Logistic regression models (adjusted for age, sex, and race/ethnicity) to determine risk of ACPA positivity by class were generated using L/L as the reference.

Results: Characteristics of the 855 participants at the time of sample collection are presented in Table 1. Overall, 67% of participants were SE positive and 51% were ACPA positive. Of the 1,710 total alleles, X was the most common (29%) followed by S3P (24%), S1 (18%), S2 (18%), and S3D (9%). Adjusted models showed that the risk of ACPA positivity was highest among those with the genotype S2/S3P, followed by S2/S2, S2/S3D, S2/X, S3P/S3D, S1/S2, S3P/S3P, S3P/X, and S1/S3P (Figure 1).

Table 1. Characteristics of study population by SE status and allele count (mean [SD] or n [%]). Significance was assessed by Student's t-test or X^2 test, as appropriate.

	SE negative	SE positive			
	0 alleles	All	1 allele	2 alleles	P (SE- vs SE+)
	n=286	n=569	n=407	n=162	
Age, years	57.4 (12.3)	58.1 (11.8)	58.0 (11.9)	58.5 (11.5)	0.42
RA duration, years	15.2 (12.8)	17.0 (13.9)	16.8 (14.1)	17.6 (13.4)	0.07
Female	259 (90.6)	500 (87.9)	359 (88.2)	141 (87.0)	0.24
White	260 (90.9)	525 (92.3)	372 (91.4)	153 (94.4)	0.49
History of smoking	117 (40.9)	223 (39.2)	166 (40.8)	57 (35.2)	0.63
RDCI, 0-9	2.4 (1.8)	2.0 (1.7)	2.1 (1.7)	1.9 (1.7)	<0.01
ACPA positive	74 (25.9)	365 (64.1)	241 (59.2)	124 (76.5)	<0.001
RF positive	84 (29.4)	333 (58.5)	219 (53.8)	114 (70.4)	<0.001
Pain VAS, 0-10	4.2 (2.7)	3.6 (2.7)	3.7 (2.6)	3.5 (2.9)	<0.01
Patient global severity, 0-10	4.0 (2.5)	3.3 (2.5)	3.4 (2.4)	3.1 (2.6)	<0.001
HAQ-II, 0-3	1.0 (0.7)	0.8 (0.6)	0.8 (0.6)	0.8 (0.6)	<0.001
csDMARD use	204 (71.3)	433 (76.1)	302 (74.2)	131 (80.9)	0.13
bDMARD use	165 (57.7)	351 (61.7)	244 (59.95)	107 (66.0)	0.26
Corticosteroid use	98 (34.3)	165 (29.0)	121 (29.7)	44 (27.2)	0.12

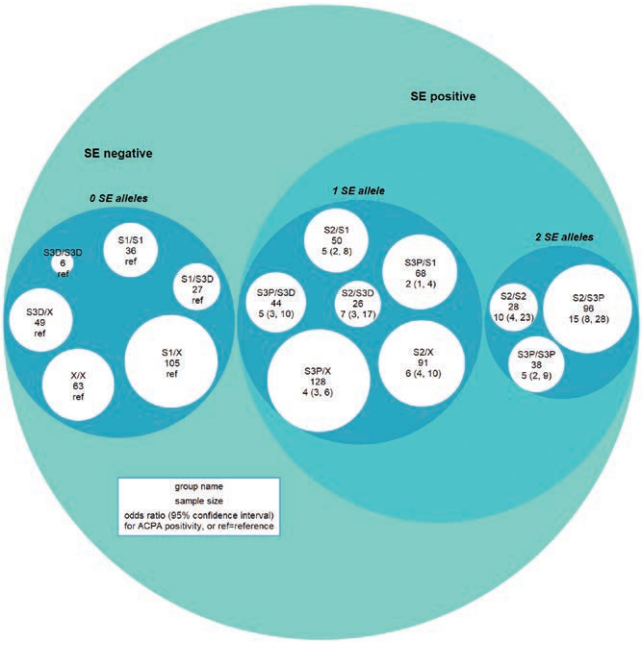


Figure 1. Risk of ACPA positivity by the motif-based classification and prevalence of SE by binary status, allele count, and class. The area within each circle is proportionate to the sample size of that group.

Conclusion: The ranking by risk of ACPA positivity among this RA cohort is similar to the order of risk for developing RA, as determined in the 2006 validation paper for this classification method. A notable trend among the classes with one SE positive allele is the consistent ranking of S3D as higher risk, X in the middle, and S1 as the lowest, suggesting a potential protective effect from S1 alleles. Future work should examine clinical associations with these allele classes, including disease progression and treatment effects.

REFERENCES:

[1] du Montcel, ST *et al.* New classification of HLA-DRB1 alleles supports the shared epitope hypothesis of rheumatoid arthritis susceptibility. *Arthritis Rheum* **52**, 1063–1068 (2005).

[2] Michou, L *et al.* Validation of the reshaped shared epitope HLA-DRB1 classification in rheumatoid arthritis. *Arthritis Res Ther* **8**, R79 (2006).

[3] Winchester, R. Reshaping Cinderella's slipper: the shared epitope hypothesis. *Arthritis Res Ther* **8**, 109 (2006).

Acknowledgements: This study was sponsored by Bristol Myers Squibb.

Disclosure of Interests: Kristin Wipfler: None declared, Xue Han Employee of: Bristol Myers Squibb, Sarah (Sang Hee) Park Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Keith Wittstock Employee of: Bristol Myers Squibb, Kaleb Michaud: None declared

DOI: 10.1136/annrheumdis-2021-eular.153

POS0345 CLINICOGENETIC STUDY OF FIVE NOVEL SUSCEPTIBILITY LOCI FOR TAKAYASU ARTERITIS: SUSCEPTIBILITY LOCI IN THE IL12B AND PTK2B REGION, BUT NOT THE LILRA3, DUSP22, KLHL33 REGIONS, ARE ASSOCIATED WITH VASCULAR DAMAGE IN TAKAYASU ARTERITIS

K. Kadoba[1], R. Watanabe[2], T. Iwasaki[1,3], K. Kitagori[1], S. Akizuki[1], K. Murakami[1], R. Nakashima[1], M. Hashimoto[2], M. Tanaka[2], K. Ohmura[1], A. Morinobu[1], C. Terao[1,4,5,6], H. Yoshifuji[1]. [1]*Graduate School of Medicine, Kyoto University, Department of Clinical Immunology and Rheumatology, Kyoto, Japan*;

[2]*Graduate School of Medicine, Kyoto University, Department of Advanced Medicine for Rheumatic Diseases, Kyoto, Japan*; [3]*Graduate School of Medicine, Kyoto University, Center for Genomic Medicine, Kyoto, Japan*; [4]*Center for Integrative Medical Sciences, RIKEN, Laboratory for Statistical and Translational Genetics, Yokohama, Japan*; [5]*Shizuoka General Hospital, Clinical Research Center, Shizuoka, Japan*; [6]*The School of Pharmaceutical Sciences, University of Shizuoka, The Department of Applied Genetics, Shizuoka, Japan*

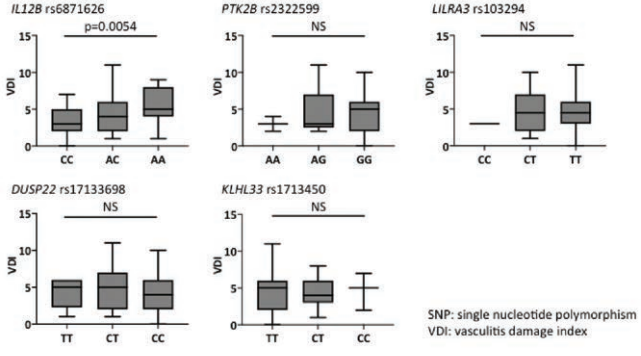
Background: We have previously identified single nucleotide polymorphism (SNP) rs6871626 in *IL12B*, rs103294 in *LILRA3*, rs17133698 in *DUSP22*, rs2322599 in *PTK2B*, and rs1713450 in *KLHL33* as non-HLA susceptibility loci in Takayasu arteritis (TAK) [1, 2]. However, the association of these SNPs with clinical features has scarcely investigated.
Objectives: In this study, we aimed to examine how these SNPs contribute to clinical features and vascular damage in TAK.
Methods: We enrolled 99 TAK patients who were enrolled in our previous genome-wide association study (GWAS) [2]. To assess vascular damage, Takayasu Arteritis Damage Score (TADS) and Vasculitis Damage Index (VDI) were measured at the last visit before November 2020. As for organ damages, the presence or absence of aortic regurgitation (AR), hypertension, ischemic heart disease, cerebrovascular event, visual loss, end-stage renal failure, and inflammatory bowel disease were evaluated. Treatment profiles including immunosuppressive drugs and vascular interventions were also reviewed.
Results: The incidence of AR was positively associated with the risk allele of *IL12B* rs6871626 (p=0.0052; odds ratio (OR) 2.45, 95% confidence interval (CI) 1.27-4.73), and so was the proportion of patients who underwent aortic valve replacement (p=0.023; OR 3.64, 95% CI 1.08-12.24) (table 1). The incidence of hypertension was associated with the risk allele of *IL12B* rs6871626 (p=0.049; OR 1.82, 95% CI 0.99-3.36) and *PTK2B* rs2322599 (p=0.044; OR 2.52, 95% CI 0.97-6.54) (table 1). The proportion of biologic users tended to be higher in the risk genotypes of *IL12B* rs6871626 (p=0.15; OR1.80, 95% CI 0.79-3.99). Regarding vascular damage, there was positive correlation between TADS and the risk allele of *IL12B* rs6871626 (p=0.0035; β= 1.35) (Figure 1). Moreover, VDI was also positively correlated with the allele (p=0.0054; β= 0.96) (Figure 1). No other clinicogenetic associations were observed between five SNPs and vasculitis-associated damages.

Table 1. The association of the five SNPs with aortic regurgitation and hypertension

	Aortic regurgitation		Hypertension	
	OR (95% CI)	p value	OR (95% CI)	p value
IL12B rs6871626	2.45 (1.27-4.73)	0.0052*	1.82 (0.99-3.36)	0.049*
PTK2B rs2322599	1.21 (0.51-2.86)	0.67	2.51 (0.97-6.54)	0.044*
LILRA3 rs103294	1.16 (0.52-2.61)	0.71	1.20 (0.55-1.64)	0.64
DUSP22 rs17133698	0.56 (0.28-1.13)	0.090	0.87 (0.46-1.63)	0.66
KLHL33 rs1713450	0.89 (0.42-1.91)	0.77	1.48 (0.68-3.22)	0.31

SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval

Figure. The association of the five SNPs with VDI



Conclusion: In the present study, *IL12B* rs6871626 was closely correlated with vascular damage. We also found association between *PTK2B* rs2322599 and hypertension. There was no significant relevance between vascular damage and *LILRA3* rs103294, *DUSP22* rs17133698, or *KLHL33* rs1713450.
REFERENCES:
[1] Terao C et al. Am J Hum Genet. 2013;93(2):289-97.
[2] Terao C et al. Proc Natl Acad Sci U S A. 2018;115(51):13045-50.
Disclosure of Interests: Keiichiro Kadoba: None declared, Ryu Watanabe Speakers bureau: I have received speaker's fee from Mitsubishi Tanabe Pharma, Pfizer, Sanofi, AbbVie, Asahi Kasei, Eisai, Eli Lilly, Bristol-Myers Squibb, and Janssen., Takeshi Iwasaki: None declared, Koji Kitagori Grant/research support from: KK has received research grants from GlaxoSmithKline., Syuji Akizuki: None declared, Kosaku Murakami Speakers bureau: I have received speaking fees from Eisai Co. Ltd, Chugai Pharmaceutical Co. Ltd., Pfizer Inc., Bristol-Myers Squibb, Mitsubishi Tanabe Pharma Corporation, UCB Japan Co. Ltd, Daiichi Sankyo Co. Ltd. and Astellas Pharma Inc., Ran Nakashima: None declared, Motomu Hashimoto Speakers bureau: I have received a research grant and/or speaker fee from Bristol-Myers, Eisai, Ely Lilly, Mitsubishi Tanabe Pharma., Grant/research support from: I have received a research grant and/or speaker fee from Bristol-Myers, Eisai, Ely Lilly, Mitsubishi Tanabe Pharma., Masao Tanaka Speakers bureau: I have received research grants and/or speaker fees from AbbVie GK, Asahi Kasei Pharma Corporation, Astellas Pharma Inc., Bristol-Myers Squibb, Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly and Company, Pfizer Inc., UCB Japan Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Corporation, Novartis Pharma K.K., Taisho Pharma Co., Ltd, and Takeda Pharmaceutical Company Limited., Koichiro Ohmura Speakers bureau: I have received speaker's fee from Abbvie, Actelion, Asahikasei Pharma, Astellas, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, GSK, Janssen, JB, Mitsubishi Tanabe, Nippon Kayaku, Nippon Shinyaku, Novartis, Sanofi and Takeda., Grant/research support from: I have received research grants from GlaxoSmithKline., Akio Morinobu Speakers bureau: I have received speaking fees from Chugai Pharmaceutical Co. Ltd., Grant/research support from: I have received research grants from Chugai Pharmaceutical Co. Ltd., Chikashi Terao: None declared, Hajime Yoshifuji Speakers bureau: I have received lecture fees from Chugai., Consultant of: I have been an advisory board for a clinical trial conducted by Janssen.
DOI: 10.1136/annrheumdis-2021-eular.289

POS0346 THE THERAPEUTIC EFFECTS OF OMEGA-6 PUFA (PINOLENIC ACID) ON THE TRANSCRIPTOMIC PROFILE OF ACTIVATED PERIPHERAL BLOOD MONONUCLEAR CELLS ISOLATED FROM HEALTHY CONTROLS AND RHEUMATOID ARTHRITIS PATIENTS

R. Takala[1,2], D. Ramji[2], R. Andrews[1], Y. Zhou[1], J. Burston[1], E. Choy[1,3]. [1]*Cardiff University, Division of Infection and Immunity, School of Medicine, Cardiff, United Kingdom*; [2]*Cardiff University, School of Biosciences, Sir Martin Evans Building, Cardiff, United Kingdom*; [3]*Cardiff University, CREATE Centre, Section of Rheumatology, School of Medicine, Cardiff, United Kingdom*

Background: Globally, Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis. EULAR recommends patient education and disease modifying anti-rheumatic drugs including advanced targeted therapies for management[1 2]. Many patients seek advice on a dietary intervention that may improve symptoms. Foods high in omega-3 polyunsaturated fatty acids (PUFAs) is one of the most common recommended based on their anti-inflammatory properties[3 4]. Previously we showed pinolenic acid (PNLA), an omega-6 (PUFAs) found in pine nuts, reduced lipid uptake, endocytosis and migration of monocyte *in vitro*. PNLA also reduced IL-6, TNF-α, IL-1β and PGE2 produced by lipopolysaccharide (LPS) activated PBMCs from patients with RA and healthy controls (HCs).
Objectives: We hypothesis that PNLA inhibits key inflammatory processes in synovities as in diagram.1. We investigated the transcriptomic profile of PNLA treatment on LPS activated PBMCs isolated from HCs and RA patients.
Methods: Adult RA patients (n=6) were recruited from the Rheumatology Department of University Hospital of Wales together with 6 HCs. Blood was collected after taking signed informed consent. PBMCs were isolated by Ficoll gradient centrifugation and pre-treated with 25 μM PNLA or vehicle and then activated with 100 ng/ml LPS. RNA was extracted followed by library construction and sequencing for whole genomic transcriptome. DEGs were analysed using DESeq2 and pathway analysis was performed using Ingenuity pathway analysis. The study was approved by the Research Ethics Committee for Wales (reference no. 12/WA/0045).
Results: DEGs were selected with at least differential genes using at least 1.2* fold changes and adjusted p-value of <0.05. PNLA significantly upregulates the expression of PDK4, PAI-1 (SERPINE1), FBP1, and NDRG2. These genes have important roles in metabolic pathways. Pathway analysis predicted upstream activation of nuclear receptors peroxisome proliferator-activated receptor (PPARs) involved in the anti-inflammatory process, and inhibition of NF-κB and STAT1, the major transcription factors of the pro-inflammatory cytokines TNF-α, IL-1, IL-6 and IFN-γ.
Conclusion: PNLA has significant effects on the regulation of metabolic and inflammatory pathways in PBMCs from RA patients and HCs. Based on these results we demonstrate that PNLA may have beneficial anti-inflammatory effects in patients with RA
REFERENCES:
[1] Agca R, Heslinga SC, Rollefstad S, Heslinga M, McInnes. IB, Peters MJL, Kvien, TK., Dougados, M, Radner, H, Atzeni, F. and Primdahl, J. 2017. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. *Annals of the rheumatic diseases*, **76**(1), pp.17-28.
[2] Smolen JS, Landewé RBM, Bijlsma JWJ, et al. 2019. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: *updateAnnals of the Rheumatic Diseases* 2020; 79:685-699.

[3] Chehade L, Jaafar ZA, El Masri D, Zmerly H, Kreidieh D, Tannir H, Itani L, and El Ghoch, M. 2019. Lifestyle Modification in Rheumatoid Arthritis: Dietary and Physical Activity Recommendations Based on Evidence. *Current rheumatology reviews*, ***15***(3), pp.209-214.

[4] Marchand NE, Chiu Y-H, Yoshida K, Malspeis S, Sparks JA, Costenbader K, et al. Threshold Level for Long-term Healthy Diet Adherence to Reduce the Risk of Rheumatoid Arthritis Among Women in a *Prospective Cohort Using a Marginal Structural Model Approach*.:**25**.

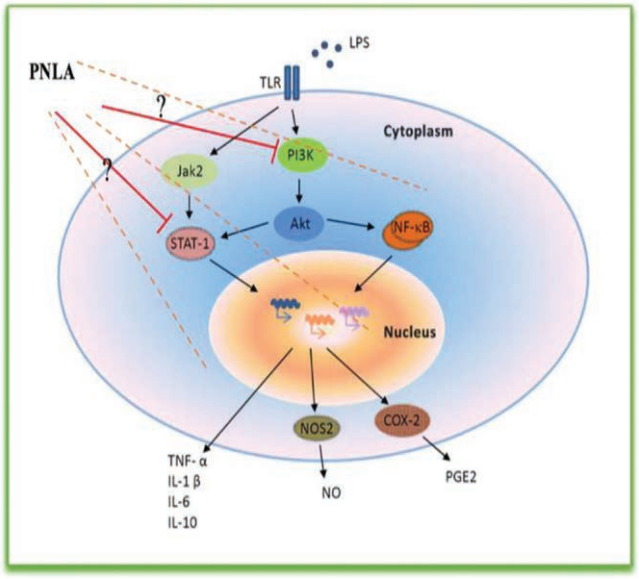


Diagram 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.747

POS0347

SPECIFIC MITO-NUCLEAR INTERACTIONS AND MT16519C VARIANT AS PREDICTIVE BIOMARKERS FOR THE RAPIDLY PROGRESSIVE OSTEOARTHRITIS OF THE KNEE. DATA FROM THE OSTEOARTHRITIS INITIATIVE

A. Durán-Sotuela[1], M. Fernandez-Moreno[1], M. E. Vazquez Mosquera[1], P. Ramos-Louro[1], A. Dalmao-Fernandez[1], S. Relaño-Fernandez[1], V. Suárez-Ulloa[2], V. Balboa-Barreiro[3], N. Oreiro[1], J. Vázquez García[1], F. J. Blanco[1], I. Rego-Perez[1]on behalf of Grupo de investigación en Reumatología (GIR). [1]*Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña., Servicio de Reumatología, A Coruña, Spain*; [2]*Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña., Plataforma de Bioinformática, A Coruña, Spain*; [3]*Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña., Unidad de apoyo a la investigación, A Coruña, Spain*

Background: The early identification of patients with rapid progressive osteoarthritis (RPOA) could allow the implementation of prevention strategies and their inclusion in clinical trials. Polymorphisms in nuclear and mitochondrial DNA (mtDNA) have been associated with OA. Preliminary analyses by our group showed nuclear single nucleotide polymorphism (nSNP) rs12107036 of TP63 as a potential risk factor for RPOA of the knee.

Objectives: i) To analyze interactions between mtDNA haplogroups and rs12107036 ii) To apply Next Generation Sequencing (NGS) to discover novel mitochondrial variants to construct predictive models of RPOA of the knee.

Methods: 1102 Caucasian subjects from the OAI were classified as follows: i) Rapid progressors (N=255), baseline KL grade 0-1 or 2 in at least one knee, that increases up to KL≥ 3 or 4 respectively during 48-month follow-up. ii) Non-rapid progressors (N=847), with the same baseline characteristics as rapid progressors, but with slower or no evolution over time.

mtDNA haplogroups and rs12107036 were assigned by mini-sequencing techniques. Novel mtDNA variants were studied by NGS. Statistical analyses included chi-square tests and generalized estimating equations. Relative excess risk due to interaction (RERI) and attributable proportion (AP) were evaluated for the additive interaction between mtDNA clusters and nSNP rs12107036. A nomogram for the estimation of the risk of RPOA was also developed. Analyses were performed using SPSS Statistics v24 and epi.R package included in R software v3.6.3.

Results: Chi-square analyses revealed an increased risk of RPOA in patients with the allele G of rs12107036 and mtDNA cluster UK (OR 2,013; p=0,001). An excess of 70,3% of RERI between nSNP rs12107036 and mtDNA clusters was detected, indicating that 47,1% (AP) of the risk is attributable to this interaction, therefore harboring both genetic factors increase the risk of RPOA up to 4,7 times compared to harboring just one. mtDNA sequencing revealed the variant mt16519 overrepresented in rapid-progressors (OR 1,620; p=0,002).

Table 1 shows the predictive model for the risk of RPOA. The interaction between the allele G of rs12107036 and mtDNA cluster KU (OR 1,727; p=0,036), in addition to the variant mt16519C (OR 1,690; p=0,003), showed a significant association with the RPOA phenotype regardless of age, BMI, contralateral knee OA, previous injury and WOMAC pain. Image 1 displays the nomogram for predicting risk of RPOA; as an example, a 70 year old male, with a BMI of 28, WOMAC pain score of 10, contralateral OA and presence of both mito-nuclear interaction and mt16519C, has a risk of RPOA of 0,7.

Conclusion: mtDNA genetic variants are useful, not only as modulators of the influence of specific nuclear polymorphisms on the risk of developing RPOA, but also as candidate genetic biomarkers of this phenotype.

Table 1. Predictive model for the risk of RPOA phenotype

Variable	p-value	OR	min 95% CI	MAX 95% CI
Clinical and genetic variables				
Age	**<0,001**#	1,056	1,038	1,074
Female	0,143	1,260	0,925	1,718
BMI	**<0,001**#	1,065	1,030	1,101
Contralateral OA	**<0,001**#	1,927	1,413	2,626
Previous Injury	**<0,001**#	1,770	1,293	2,422
WOMAC pain	**0,001**#	1,097	1,039	1,159
rs12107036 G	0,172	1,226	0,915	1,643
mt16519 C	**0,003**#	1,690	1,202	2,375
mtDNA Clusters$				
Others	0,803	0,921	0,482	1,760
TJ	0,482	1,209	0,712	2,052
UK	0,136	0,698	0,435	1,120
HV				Reference
rs12107036 G*mtDNA Cluster				
G * Others	0,502	0,789	0,395	1,576
G * TJ	0,158	0,647	0,353	1,185
G * UK	**0,036**#	1,727	1,036	2,881
G * HV			Reference	

$mtDNA Clusters: haplogroups with a common phylogenetic origin BMI: Body Mass Index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; OR: Odds Ratio; CI: confidence interval; #: statistical significance declared at P ≤ 0.05, in bold.

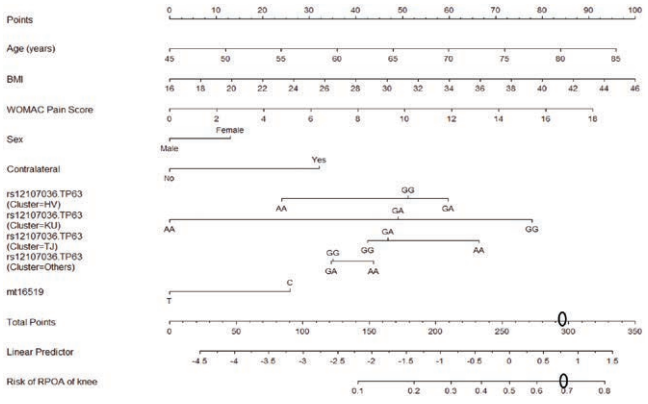


Image 1. Nomogran for the estimation of the risk of RPOA phenotype. Circles represent the values for the example. Clusters: haplogroups with a common phylogenetic origin BMI: Body Mass Index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.750

POS0348

GENETIC SUSCEPTIBILITY VARIANTS FOR RHEUMATOID ARTHRITIS ARE NOT ASSOCIATED WITH EARLY REMISSION; A MULTI-COHORT STUDY

S. Jurado Zapata[1], M. Maurits[1], Y. Abraham[2], E. Van den Akker[3], A. Barton[4], P. Brown[5], A. Cope[6], I. González-Álvaro[7], C. Goodyear[8], A. van der Helm - van Mil[1], X. Hu[9], T. Huizinga[1], M. Johannesson[10], L. Klareskog[10], D. Lendrem[11], I. McInnes[12], F. Morton[12], C. Paterson[12], D. Porter[12], A. Pratt[11], L. Rodriguez Rodriguez[13], D. Sieghart[14], P. Studenic[14], S. Verstappen[4], L. Padyukov[10], A. Winkler[9], J. D. Isaacs[5],

R. Knevel[1]. [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [2]*Janssen Pharmaceutical Companies of Johnson & Johnson, Discovery Science/ Computational Biology, Beerse, Belgium*; [3]*Leiden University Medical Center, Leiden Computational Biology Center, Leiden, United Kingdom*; [4]*University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; [5]*Newcastle University, Institute of Cellular Medicine, Newcastle, United Kingdom*; [6]*King's College London Centre for Rheumatic Diseases, Department of Inflammation Biology, London, United Kingdom*; [7]*Hospital Universitario de la Princesa (IIS-IP), Rheumatology, Madrid, Spain*; [8]*University of Glasgow, Immunology, Glasgow, United Kingdom*; [9]*Pfizer, Inflammation & Immunology Research Unit, Cambridge, United States of America*; [10]*Karolinska Institutet and Karolinska University Hospital, Rheumatology, Stockholm, Sweden*; [11]*Newcastle upon Tyne Hospitals NHS Foundation Trust, Health and Bioinformatics, Newcastle upon Tyne, United Kingdom*; [12]*University of Glasgow, Infection Immunity & Inflammation, Glasgow, United Kingdom*; [13]*Hospital Clínico San Carlos, Rheumatology, Madrid, Spain*; [14]*Medical University of Vienna, Rheumatology, Vienna, Austria*

Background: Patients who achieve remission promptly could have a specific genetic risk profile that supports regaining immune tolerance. The identification of these genes could provide novel drug targets.
Objectives: To test the association between RA genetic risk variants with achieving remission at 6 months.
Methods: We computed genetic risk scores (GRS) comprising of the RA susceptibility variants[1] and HLA-SE status separately in 4425 patients across eight datasets from inception cohorts. Remission was defined as DAS28CRP<2.6 at 6 months. Missing DAS28CRP values in patients were imputed using predictive mean matching by MICE. We first tested whether baseline DAS28CRP changed with increasing GRS using linear regression. Next, we calculated odds ratios for GRS and HLA-SE on remission using logistic regression. Heterogeneity of the outcome between datasets was mitigated by running inverse variance meta-analysis.
Results: Evaluation of the complete dataset, baseline clinical variables did not differ between patients achieving remission and those who did not (Table 1). Distribution of GRS was consistent between datasets. Neither GRS nor HLA-SE was associated with baseline DAS2DAS (OR1.01; 95% CI 0.99-1.04). A fixed effect meta-analysis (Figure 1.) showed no significant effect of the GRS (OR 0.99; 95% CI 0.94-1.03) or HLA-SE (OR 0.8CRP87; 95% CI 0.75-1.01) on remission at 6 months.

Table 1. Summary of the data separated by disease activity after 6 months.

	all	Remission at 6 months	No remission at 6 months
N	4425*	1558	2430
Age, *mean (sd)*	55.38 (13.87)	5517 (14.09)	55.62 (13.59)
Female %	68.98%	65.43%	70.73%
ACPA+ %	61.94%	63.53%	61.67%
Baseline DAS28, *mean (sd)*	4.76 (1.22)	4.47 (1.23)	5.1 (1.15)

**not all patients had 6 months data*

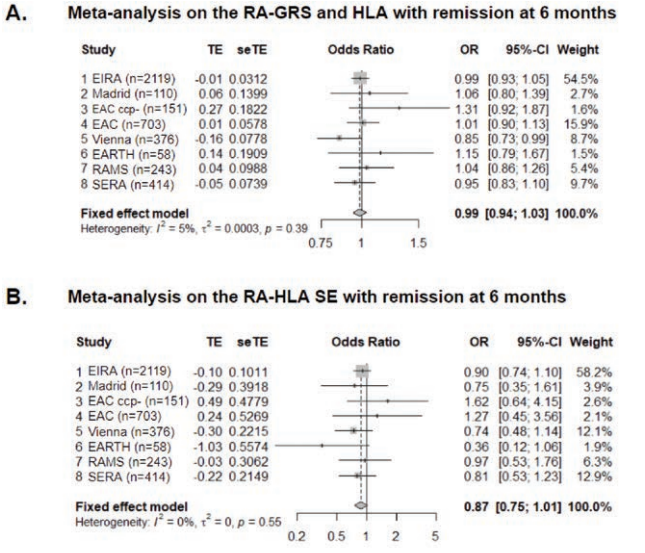


Figure 1. A. Inverse weighted meta-analysis of (**A**) the GRS + HLA and (**B**) the HLA SE. Includes the dataset name (Study), test estimate (TE), the standard error of treatment estimate (seTE), odds ratio (OR), 95% confidence intervals (95%-CI) and the weights of the fixed effect model. I^2 percentage of variation across studies due to heterogeneity. τ^2 states the variance of the true effect size.

Conclusion: In these combined cohorts, RA genetics risk variants are not associated with early disease remission. At baseline there was no difference in genetic risk between patients achieving remission or not. Studies encompassing other genetic variants are needed to elucidate the genetics of RA remission.

REFERENCES:

[1] Knevel R et al. *Sci Transl Med*. 2020;12(545):eaay1548.

Acknowledgements: This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777357, RTCure. This project has received funding from Pfizer Inc.

Disclosure of Interests: Samantha Jurado Zapata: None declared, Marc Maurits: None declared, Yann Abraham Employee of: Pfizer, Erik van den Akker: None declared, Anne Barton: None declared, Philip Brown: None declared, Andrew Cope: None declared, Isidoro González-Álvaro: None declared, Carl Goodyear: None declared, Annette van der Helm - van Mil: None declared, Xinli Hu Employee of: Pfizer, Thomas Huizinga: None declared, Martina Johannesson: None declared, Lars Klareskog: None declared, Dennis Lendrem: None declared, Iain McInnes: None declared, Fraser Morton: None declared, Caron Paterson: None declared, Duncan Porter: None declared, Arthur Pratt: None declared, Luis Rodriguez Rodriguez: None declared, Daniela Sieghart: None declared, Paul Studenic: None declared, Suzanne Verstappen: None declared, Leonid Padyukov: None declared, Aaron Winkler Employee of: Pfizer, John D Isaacs: None declared, Rachel Knevel Grant/ research support from: Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1042

POS0349 SEQUENCE COMPLEMENTARITY BETWEEN SARS-CoV-2 GENOME AND HUMAN NONCODING RNAS ASSOCIATED WITH IMMUNOLOGICAL DISORDERS: AN IN SILICO PIVOTAL STUDY

R. Talotta[1], S. Bahrami[2], M. J. Laska[2]. [1]*University of Messina, Clinical and Experimental Medicine, Messina, Italy*; [2]*Aarhus University, Clinical Medicine, Aarhus, Denmark*

Background: Recent evidence shows that human cells may produce several noncoding (nc)RNAs in response to viral infections. Among them, a central role has been attributed to long noncoding (lnc)RNAs, more than 200 nucleotides in length, which are also crucially involved in cancer and autoimmunity. LncRNAs epigenetically control the transcription of genes presiding over cell proliferation, differentiation, migration and apoptosis, by directly or indirectly binding cellular or foreign nucleic acids, including viral genomes.
Objectives: The objectives of this study were to evaluate *in silico* the presence of a nucleotide sequence complementarity between the RNA genome of Severe Acute Respiratory Syndrome CoronaVirus-2 (SARS-CoV-2) and human ncRNA genes and to analyze any associations between SARS-CoV-2 gene-matching ncRNAs and human diseases.
Methods: The FASTA sequence of each of the 11 SARS-CoV-2 isolate Wuhan-Hu-1 genes (ORF1ab, ORF3a, ORF6, ORF7a, ORF7b, ORF8, ORF10, S, E, M, N) was retrieved from NCBI.nlm.nih.gov/gene (reference sequence NC_045512.2). The ensembl.org library for human ncRNA genes was interrogated for any base-pair match and detected human ncRNAs analyzed for their functional activity. Finally, the associations between ncRNAs and human diseases were searched on GWAS databases (https://www.ebi.ac.uk/gwas and https://www.genecards.org).
Results: A total of 252 matches between SARS-CoV-2 genes and human ncRNAs were recorded (ORF1ab: 28; ORF3a: 9; ORF6: 50; ORF7a: 31; ORF7b: 16; ORF8: 23; ORF10: 5; S: 24; E: 17; M: 32; N: 17). With the exception of two small nuclear RNAs (RNVU1-4 and RNU4-74P corresponding to ORF6 and ORF10, respectively), all of them were lncRNAs, mostly expressed in testis and central nervous system under physiological conditions. Percentage of alignment ranged from 91.30% to 100%, with a mean nucleotide alignment length of 17.5±2.4. Polymorphic variants of these transcripts have mostly been reported in patients with neuropsychiatric disorders, cancer and dysmetabolism. Of note, we found 13 and 15 complementarities with lncRNAs associated with immune-mediated diseases Table 1. and immunological pathways (IL-2, IL-6, IL-12, IL-12R, IL-13, IL-17, M-CSF, CXCL-10, TRAIL-R2 and IgG glycosylation), respectively.
Conclusion: This pivotal study shows that SARS-CoV-2 genes contain complementary sequences to human ncRNAs in turn associated with several diseases, including autoimmunity. The biological effects of this interaction remain to be elucidated.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1077

Table 1. SARS-CoV-2 complementary ncRNAs and associated immunological disorders

SARS-CoV-2 gene	LncRNA	Genomic location	Nucleotide alignment length	Alignment percentage	Associated immunological disorder
S	XACT	X:113705866-113705883	18	100%	Crohn's disease
N	LINC01358	1:59082428-59082574	17	100%	Acute Graft-versus-Host Disease
E	COX10-AS1	17:14029229-14029245	17	100%	Systemic lupus erythematosus
ORF8	AC093765.3	4:116752764-116752784	21	95.24%	Ulcerative colitis
ORF6	CDKN2B-AS1	9:22033529-22033546	18	100%	Multiple sclerosis
	CHROMR	2:178433948-178433968	21	95.24%	Multiple sclerosis Psoriasis Atopic eczema
	WAKMAR2	6:137857643-137857657	15	100%	Atopic eczema Hay fever Allergic rhinitis Multiple sclerosis Psoriasis Systemic sclerosis Systemic lupus erythematosus Rheumatoid arthritis
	AC008691.1	5:159362809-159362828 (promoter flank)	20	95%	Sarcoidosis Psoriasis Psoriatic arthritis Sclerosing cholangitis Celiac disease Type I diabetes mellitus Systemic lupus erythematosus Juvenile idiopathic arthritis Ulcerative colitis Crohn's disease Takayasu arteritis Multiple sclerosis
	LMCD1-AS1	3:7953602-7953616 (enhancer)	15	100%	Systemic sclerosis
M	LINC01934	2:181403969-181403984	16	100%	Multiple sclerosis Ankylosing spondylitis Celiac disease Rheumatoid arthritis
ORF7b	XACT	X:113959816-113959831	16	100%	Crohn's disease
	LINC02621	10:62289643-62302335	15	100%	Rheumatoid arthritis
	LINC01991	3:187966255-187966269	15	100%	IgA deficit Atopic asthma Allergic rhinitis

POS0350

EPIONE APPLICATION: AN INTEGRATED GENOTYPE ANALYSIS WEB SERVER FOR CLINICAL GENOMICS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

L. Papageorgiou[1], H. Alkenaris[1], M. Zervou[2], D. Vlachakis[1], G. Goulielmos[2], E. Eliopoulos[1]. [1]*Agricultural University of Athens, Laboratory of Genetics, Department of Biotechnology, Athens, Greece*; [2]*University of Crete, Section of Molecular Pathology and Human Genetics, Department of Internal Medicine, School of Medicine, Heraklion, Greece*

Background: Genome wide association studies (GWAS) have successfully identified novel autoimmune disease-associated loci, with many of them shared by multiple disease-associated pathways but much of the genetics and pathophysiological mechanisms remain still obscure [1-3]. SLE is a chronic, highly heterogeneous autoimmune disease, characterized by differences in autoantibody profile, serum cytokines, and a multi-system involvement [4]. Epione Application is an integrated bioinformatics web-tool designed to assist medical experts and researchers in the process of diagnosing SLE [5].

Objectives: To identify the most credible gene variants and single nucleotide polymorphisms (SNPs), causing SLE using the genomic data provided for the patient and aid the medical expert in SLE diagnosis [5].

Methods: In the present study, we have analyzed more than 70.000 SLE-related publications using data mining and semantic techniques towards extracting the SLE -related genes and SNPs [6]. The extracted knowledge has been filtered, evaluated, annotated, classified, and stored in the Epione Application Database (EAD) (Figure 1). Moreover, an updated gene regulatory network with the genes implements in SLE has been estimated [7]. This was followed by the design and development of the Epione application, in which the generated datasets and results were included. The application has been tested and presented here with WES data from several related patients with SLE [8].

Results: SLE-related SNPs and variants identified in genome-wide association studies (GWAS), whole-genome (WGS), whole-exome (WES), or targeted sequencing information are classified, annotated, and analyzed in an integrated patient profile with clinical significance information. Probable genes associated with the patient's genomic profile are visualized with several graphs, including chromosome ideograms, statistic bars, and regulatory networks through data mining studies with relative publications, to obtain a representative number of the most credible candidate genes and biological pathways associated with the SLE. An evaluation study was performed on 7 patients from a three-generation family with SLE [9]. All the recognized gene variants that were previously considered SLE-associated were properly identified in the output profile per patient, and by comparing the results, new findings have emerged.

Conclusion: The Epione application was designed to assist medical doctor diagnosis from the early stages by using the patients' genomic data [5, 8, 10]. Its diagnosis-oriented output presents the patient profile through which the user is provided with a structured set of results in various categories, which are generated based on the list of the most predictable candidate gene variants related to SLE. This novel and accessible webserver tool of SLE to assist medical experts in the clinical genomics and precision medicine procedure is available at http://143.233.188.162/epione/.

REFERENCES:

[1] Molineros JE *et al.* (2017). Hum Mol Genet 26:1205-1216.
[2] Sciascia S *et al.* (2018). F1000 Res, 2018:1-17.
[3] Gonzalez-Serna D *et al.* (2020). Sci Rep 10:1862.
[4] Harley JB *et al.* (2006). Springer Semin Immun 28:119–130.
[5] Goulielmos GN *et al.* (2018). Gene 668:59-72.
[6] Zhao Y *et al.* (2020). Front Genet 11:400.
[7] Song YL and Chen S (2009). Interdiscip Sci 1:179-186.
[8] Koile D *et al.* (2018). BMC Bioinformatics 19:25.
[9] Albertsen HM *et al.* (2019). Mol Med Rep 19:1716-1720.
[10] Ebrahimiyan H *et al.* (2018). Meta Gene 16:241-247.

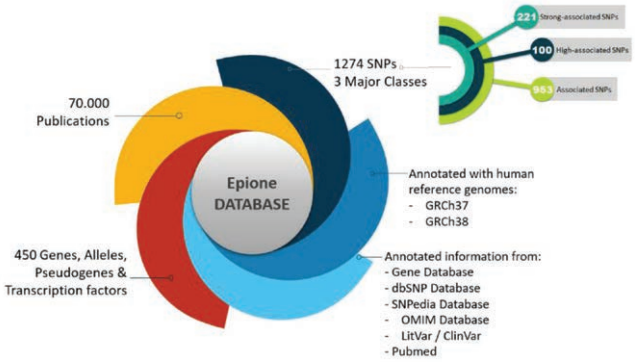


Figure 1. The Epione application database (EAD) for SLE.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1496

POS0351 A DEEP LEARNING METHOD UNCOVERS NOVEL PATHWAY ASSOCIATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

E. F. Morand[1], T. Dörner[2], B. Jia[3], Y. Liu[3], S. de Bono[3], D. Fantini[3], M. Silk[3], N. Bello Vega[3], P. Fischer[3], M. A. Petri[4]. [1]*Centre for Inflammatory Diseases, School of Clinical Sciences at Monash Health, Melbourne, Australia*; [2]*DRFZ Berlin and Department of Rheumatology and Clinical Immunology, Charité University Hospital Berlin, Berlin, Germany*; [3]*Eli Lilly and Company, Lilly Corporate Center, Indianapolis, United States of America*; [4]*Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, United States of America*

Background: While there have been recent improvements in therapy for systemic lupus erythematosus (SLE), unmet need remains for novel, efficacious treatments. Artificial intelligence can facilitate drug discovery by identifying potential target molecules and pathways.
Objectives: To devise a Deep Learning method that ranks genes and pathways differentially expressed in SLE by an integrated metric of expression and interactivity.
Methods: HT2A array expression data (17,799 transcripts) were obtained from whole blood samples taken at baseline (N=1,760) from patients with SLE enrolled in two phase 3 trials (NCT01196091 and NCT01205438). We applied a Deep learning algorithm[1] to create a disease-specific gene network for SLE from the Decagon and MetaCore molecular interaction databases[2,3]. A meta-analysis was conducted for each candidate gene by calculating its distance from other genes in the disease-specific network (interactivity analyses). The distance was then multiplied by each gene's utility score, a measure of the gene's relevance to SLE disease activity derived from public datasets[4,5]. The final output was the fractional rank (0–1) of utilities[5] for each gene against prespecified outcomes of SLEDAI-2K and IFN gene signatures, analyzed as a continuous variable combining 34 IFN-related genes. Selected JAK-STAT, cytokine, and IFN genes are presented. Pathways enriched in the top 250 genes from the input data and Deep Learning output were analyzed by hypergeometric tests.
Results: The highest-ranked gene for SLEDAI-2K and IFN signature status was IFNγ, followed, as expected, by the IFNα gene family (Table 1). Application of the Deep Learning method markedly affected pathway analysis outcomes, revealing strong associations in pathways including those related to CD4+ T cell differentiation as well as macrophage and dendritic cells, which were not apparent in conventional analysis (Figure 1).

Table 1.

Gene	SLEDAI-2K fractional rank	IFN signature fractional rank
IFNγ	0.9999	0.9999
IFNα†	0.999*	0.999*
STAT1	0.9991	0.9991
IL10	0.9990	0.9987
IFNB1	0.9990	0.9989
STAT6	0.9981	0.9966
IL6	0.9974	0.9973
STAT4	0.9959	0.9944
IL12A	0.9952	0.9932
IL12B	0.9950	0.9938
STAT5A	0.9929	0.9940
STAT3	0.9915	0.9930
IFNγR2	0.9829	0.9770
IFNγR1	0.9812	0.9840
IL23A	0.9806	0.9895
IL10RA	0.9805	0.9816
IL6ST	0.9791	0.9695
STAT2	0.9772	0.9914

†IFNα genes were similarly ranked.*Range: 0.9988–0.9999."0.9991" denotes that the SLEDAI-2K rank for STAT1 is higher than 99.91% of the whole genome.

Conclusion: Deep learning algorithms incorporating interactivity analyses revealed disease associations in SLE that were not apparent when using conventional bioinformatic approaches.

REFERENCES:

[1] Kong Y and Yu T. Bioinformatics. 2018;34(21):3727–37.
[2] http://snap.stanford.edu/decagon/.
[3] https://portal.genego.com/.
[4] Valdeolivas A et al. Bioinformatics. 2019;35(3):497–505.
[5] https://cran.r-project.org/web/packages/MetaIntegrator/index.html.

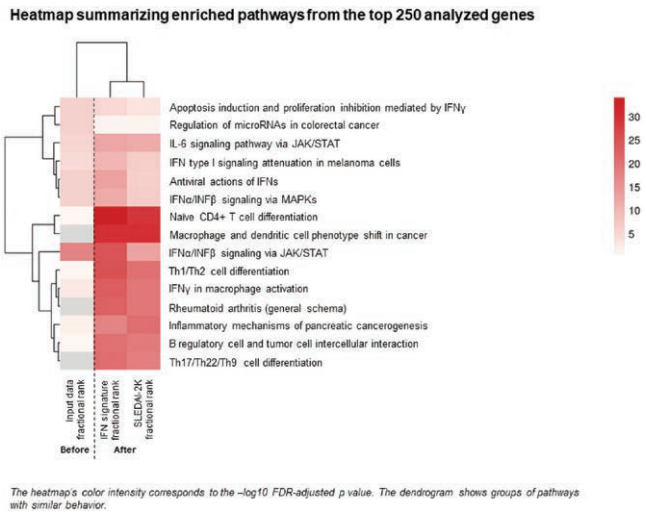


Figure 1.

Disclosure of Interests: Eric F. Morand Speakers bureau: AstraZeneca, Paid instructor for: Eli Lilly, Consultant of: Amgen, AstraZeneca, Biogen, BristolMyersSquibb, Eli Lilly, EMD Serono, Genentech, GlaxoSmithKline, Janssen, Grant/research support from: AstraZeneca, BristolMyersSquibb, Eli Lilly, EMD Serono, GlaxoSmithKline, Janssen, Thomas Dörner Speakers bureau: Eli Lilly, Samsung, Roche, Consultant of: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Roche, Samsung, UCB, Grant/research support from: Janssen, Novartis, Roche, UCB, Sanofi, Bochao Jia Shareholder of: Eli Lilly, Employee of: Eli Lilly, Yushi Liu Shareholder of: Eli Lilly, Employee of: Eli Lilly, Stephanie de Bono Shareholder of: Eli Lilly, Employee of: Eli Lilly, Damiano Fantini Shareholder of: Eli Lilly, Employee of: Eli Lilly, Maria Silk Shareholder of: Eli Lilly, Employee of: Eli Lilly, Natalia Bello Vega Shareholder of: Eli Lilly, Employee of: Eli Lilly, Peter Fischer Shareholder of: Eli Lilly, Employee of: Eli Lilly, Michelle A Petri Consultant of: Eli Lilly, Grant/research support from: Eli Lilly
DOI: 10.1136/annrheumdis-2021-eular.1624

POS0352 ALLELIC VARIANTS IN THE ABCG2 GENE CAN LEAD TO HYPERURICEMIA AND GOUT

K. Pavelcova[1,2], J. Bohata[1,2], B. Stiburkova[1,3]. [1]*Institute of Rheumatology, Prague, Czech Republic*; [2]*First Faculty of Medicine, Charles University, Department of Rheumatology, Prague, Czech Republic*; [3]*First Faculty of Medicine, Charles University and General University Hospital in Prague, Department of Pediatrics and Inherited Metabolic Disorders, Prague, Czech Republic*

Background: The level of uric acid is largely determined by the functions of urate transporters, which are located in the kidney and intestine. The ABCG2 protein is the major excretor of uric acid and its dysfunction may lead to the development of hyperuricemia and gout.
Objectives: The aim of our study was to detect the occurrence and frequency of allelic variants in the ABCG2 gene that can lead to impaired function of the ABCG2 protein and to the development of hyperuricemia and gout.
Methods: We examined allelic variants of *ABCG2* using PCR amplification and Sanger sequencing of all coding regions and exon-intron boundaries in 359 patients with primary hyperuricemia and gout.
Results: We found a rare in-frame deletion p.K360del and 15 missense variants, two of which were common (p.V12M, p.Q141K) and 13 were very rare (p.M71V, p.G74D, p.M131I, p.R147W, p.T153M, p.I242T, p.R236X, p.F373C, p.T421A, p.T434M, p.S476P, p.S572R, p.D620N). The p.R236X variant leads to a premature stop codon. The p.V12M variant probably has a protective effect against gout (minor allele frequency – MAF – in our cohort = 0,025 / MAF in the European population = 0,061), while the p.Q141K variant increases the risk of gout (MAF in our cohort = 0,213 / MAF in the European population = 0,094) (1). As for the rare variants, the p.R147W, p.T153M, p.F373C, p.T434M, p.S476P and p.S572R

according to functional analyzes reduce the function of the ABCG2 protein (2). Based on *in silico* prediction, the impact on reduced function is expected for variants p.M71V, p.G74D, p.M131I, p.R147W, p.I242T, p.F373C, p.T434M, p.S476P and p.S572R.

Conclusion: Our data suggest that the common variant p.Q141K and most of the rare variants in the *ABCG2* gene affect the function of the ABCG2 urate transporter and are a genetic risk factor for hyperuricemia and gout.

REFERENCES:

[1] Stiburkova B, et al. Functional non-synonymous variants of ABCG2 and gout risk. Rheumatology (Oxford). 2017 Nov 1; 56(11):1982-1992.

[2] Toyoda Y, et al. Functional characterization of clinically-relevant rare variants in *ABCG2* identified in a gout and hyperuricemia cohort. Cells. 2019 Apr 18;8(4).

Acknowledgements: This study was supported by the project for conceptual development of research organization 00023728 (Institute of Rheumatology) and RVO VFN64165.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1799

POS0353 DEEP PHENOTYPING OF PSORIASIS BASED ON LIPID METABOLISM RELATED GENES BY INTEGRATIVE SYSTEMS ANALYSIS

J. Shi[1,2,3], S. X. Zhang[1,2,3], J. Qiao[1,2,3], S. Song[1,2,3], R. Zhao[1,2,3], P. Zhao[4], G. Y. Liu[1,2,3], J. Luo[1,2,3], P. F. He[5], X. Li[1,2,3]. [1]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [2]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [3]*Key Laboratory of Cellular Physiology at Shanxi Medical University, Ministry of Education, Taiyuan, China*; [4]*Shanxi Provincial People's Hospital, Department of Dermatology, Taiyuan, China*; [5]*Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Psoriasis is an immune-mediated inflammatory, genetic disease with numerous concomitant metabolic disorders[1]. Patients with psoriasis experience substantial morbidity and increased rates of cardiometabolic diseases[2]. Among the metabolic disorders, lipid disturbances are recognized as a very important part in the pathogenesis of psoriasis and psoriasis-associated cardiometabolic diseases[3 4].

Objectives: To characterize the molecular features of psoriasis by the development of a classification system that was based on the gene expression profile of lipid metabolism related genes.

Methods: We performed molecular subtyping and association analysis of psoriasis from Gene Expression Omnibus (GEO). The training sets includes GSE13355 cohort (N = 58), GSE14905 (N = 28) cohort and GSE30999 cohort (N = 81), while the GSE54456 (N = 92) was selected as the validation set. Energy metabolism-related genes were collected from MSigDB (version 7.0; http://software.broadinstitute.org/gsea/msigdb/). Based on these psoriasis lipid metabolism-related genes, we conducted consensus molecular subtyping with nonnegative matrix factorization (NMF). Finally, Gene set variation analysis (GSVA) was used to score individual subtypes against the metabolism-related gene sets, and each group got a GSVA index.

Results: Total 104 lipid metabolism-related genes were clustered into three subgroups (Figure 1A). GSVA revealed the lipid metabolism with the correlation in subtypes. There was no statistical difference was identified between the subtype 1 and subtype 2($P > 0.05$, Figure 1B), so we merged the two types as a new Sub1, another subtype was named as the new Sub2 (Figure 1C). We finally identified 2 distinct subtypes of psoriasis in GEO cohort that were characterized by significantly different lipid metabolic gene score. Sub1 was featured by higher metabolic gene score compared with that of Sub2($P < 0.001$; Figure 1D). The lipid metabolic subtype classification was successfully validated in another independent patient cohorts (GSE54456).

Conclusion: This study established a new classification based on the gene expression profiles of lipid metabolic genes, thereby furthering the understanding of the pathogenesis and psoriasis-associated diseases.

REFERENCES:

[1] Boehncke WH, Schon MP. Psoriasis. Lancet 2015;386(9997):983-94. doi: 10.1016/S0140-6736(14)61909-7 [published Online First: 2015/05/31].

[2] Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. JAMA 2020;323(19):1945-60. doi: 10.1001/jama.2020.4006 [published Online First: 2020/05/20].

[3] Goolam Mahyoodeen N, Crowther NJ, Pillay L, et al. Relationship of Visceral Fat and Adipokines with Cardiometabolic Diseases in Psoriasis. Acta Derm Venereol 2019;99(13):1218-23. doi: 10.2340/00015555-3327 [published Online First: 2019/10/04].

[4] Pietrzak A, Michalak-Stoma A, Chodorowska G, et al. Lipid disturbances in psoriasis: an update. Mediators Inflamm 2010;2010 doi: 10.1155/2010/535612 [published Online First: 2010/08/14].

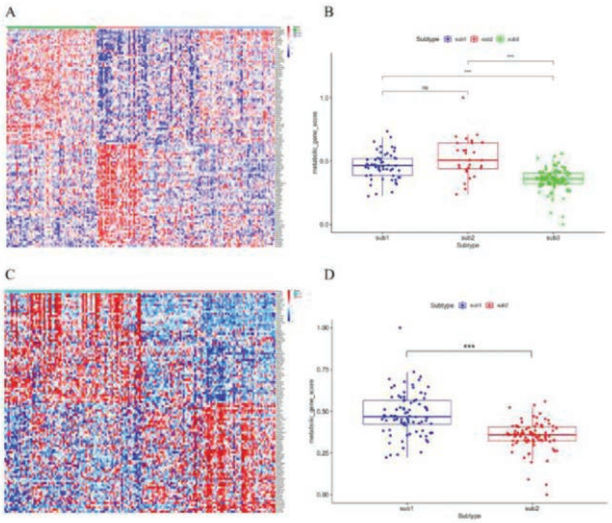


Figure 1: Molecular typing of patients with psoriasis based on lipid metabolism-related gene expression profiles. **(A, C)** consensus clustering of 167 GEO samples by NMF, a heatmap displaying the expression pattern of the lipid metabolism related subtypes is shown. **(B)** comparison of lipid metabolic score levels among three subgroups. **(D)** comparison of lipid metabolic score levels between the final two subgroups. ns $P > 0.05$; ***$P < 0.001$.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2073

POS0354 DETECTION OF ABCG2 VARIANTS IN ENCODING OF URATE TRANSPORTERS ASSOCIATED WITH THE HYPERURICEMIA IN HAEMODIALYSIS PATIENTS

H. Ciferska[1,2], K. Pavelcova[1,2], J. Vachek[3,4], B. Stiburkova[5,6]. [1]*Institute of Rheumatology, Institute of Rheumatology, Prague, Czech Republic*; [2]*First Faculty of Medicine, Charles University, Department of Rheumatology, Prague, Czech Republic*; [3]*General University Hospital, Prague and the First Medical Faculty, Charles University, Department of Nephrology, Prague, Czech Republic*; [4]*Klatovska Hospital, Dialysis Ward, Klatovy, Czech Republic*; [1]*Institute of Rheumatology, Institute of Rheumatology, Prague, Czech Republic*; [6]*First Faculty of Medicine, Charles University and General University Hospital in Prague, Department of Pediatrics and Adolescent Medicine, Prague, Czech Republic*

Background: Hyperuricemia is associated with gout, hypertension, cardiovascular diseases and renal disease. The presence of chronic kidney disease (CKD) is associated with low excretion of the uric acid as the homeostasis in maintaining of serum levels of uric acid is impaired. Progression of CKD is connected to hyperuricemia and lowering levels of the uric acid is one of the most important goals in clinical treatment. Dysfunctional variants of ATP-binding cassette transporter subfamily G member 2 (ABCG2), a major urate transporter in the kidney and intestine, are the major causes of hyperuricemia and gout.

A recent studies found that ABCG2 is also a major transporter of uremic toxins and ABCG2 dysfunctional variants are risk genetics factors for mortality in hemodialysis patients.

Objectives: The aim of the present study was to investigate the frequencies of ABCG2 variants in cohort of hemodialysis patients.

Methods: In this retrospective one centre study 167 patients (age=79,8±11,03;female=74) with end-stage CKD (pre-dialysis n=86; dialysis n=79) were collected. Peak urate levels were 456,3±113,6 µmol/l in pre-dialysis and 572,93±114,56 µmol/l in dialysis. ABCG2 coding regions were analyzed from genomic DNA, as we described previously (1). The reference sequence was defined as version ENST00000237612.7, the reference protein sequence was defined as Q9UNQ0. The chi-square goodness-of-fit test was used to compare minor allele frequencies (MAF), and the log-rank test was used to compare empirical distribution functions.

Results: In the CKD cohort, 15 intronic and seven non-synonymous allelic exonic variants were detected: two common (rs2231137/p.V12M; rs2231142/p.Q141K), five ultra rare and/or rare (rs142634180/p.R45Q, rs759726272/p.M131I, rs140207606/p.R236X, rs138606116/p.G354R, rs138892154/p.A607V), and one novel (p.E344D). Common variant p.V12M, previously reported as protective

allele, was detected in 12 heterozygous patients with. The p.Q141K variant, detected in the homozygous stage in three patients and in 31 patients as heterozygous variant. Heterozygous rare variants p.R45Q, p. G354R, p.A607V, and novel variant p.E344D were detected in one heterozygous patient each; heterozygous p.M131I and p.R236X in two patients.

Conclusion: In this study, significantly higher frequency of dysfunctional ABCG2 variants, common and rare, in comparison with common European population, were identified. On the other hand, the frequency of probably protective allele variant p.V12M was significantly lower in CKD cohort (MAF in our cohort = 0,036/ MAF in the European population = 0,061). Further analysis of ABCG2 association with CKD events *via* ABCG2 inflammation role is necessary. In conclusions, our finding of one novel, five rare and two common non-synonymous ABCG2 allelic variants in a sample of 167 CKD patients suggests that the ABCG2 variants should be considered a risk factor for CKD.

REFERENCES:

[1] Toyoda Y, et al. Functional Characterization of Clinically-Relevant Rare Variants in ABCG2 Identified in a Gout and Hyperuricemia Cohort. *Cells*. 2019;18;8(4).

Acknowledgements: This study was supported by the grant from the Czech Republic Ministry of Health RVO 00023728.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2084

POS0355 ASSOCIATIONS BETWEEN HLA-DRB1 SHARED EPITOPES ALLELES AND ANTI-RA33 ANTIBODIES IN DIFFERENT SUBSETS OF RHEUMATOID ARTHRITIS IN MALAYSIAN POPULATION

A. F. Nurul-Aain[1], S. S. Ch'ng[2], H. Baharuddin[2,3], M. Mohd Zain[2], I. S. Lau[2], H. Mohd Yusoof[2], A. Ahmad[2], A. Rosman[2], A. A. Siti-Aisyah[1], L. Padyukov[4], L. Alfredsson[5], L. Klareskog[4], J. Rönnelid[6], C. L. Too[1,4]on behalf of the MyEIRA Study Group. [1]*Allergy and Immunology Research Centre, Institute for Medical Research, Ministry of Health Malaysia, Selangor, Malaysia*; [2]*Rheumatology Unit, Department of Internal Medicine, Selayang Hospital, Ministry of Health Malaysia, Selangor, Malaysia*; [3]*Medical Faculty, Hospital Selayang Campus, University Institute Technology Mara (UiTM), Selangor, Malaysia*; [4]*Division of Rheumatology, Department of Medicine, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden*; [5]*Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden*; [6]*Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden*

Background: The mechanisms affecting anti-RA33 antibody's involvement in RA pathogenesis is still unclear. Refining our understanding of anti-RA33's role in RA in relation to known RA-associated genes and serological elements is needed.

Objectives: We investigated the relationship between RA-associated HLA-DRB1 epitope (SE) allele and presence of anti-RA33 antibodies in different serological subsets of rheumatoid arthritis in a Malaysian population.

Methods: Serum samples from 550 RA cases comprising seronegative (negative for anti-CCP2, IgG and IgM, n=250), seropositive (triple-autoantibody positive, n=150), singular anti-CCP2 positive (n=100), and double RF positive RA (n=50) were chosen from the Malaysian Epidemiological Investigations of RA (MyEIRA) case-control study. Three hundred MyEIRA population controls were used for comparison. All serum samples were assayed using a commercial anti-RA33 ELISA kit. All genetic samples were genotyped for four-digit HLA-DRB1 alleles using the PCR-SSO method on Luminex platform.

Results: The proportions of anti-RA33 positive was 20.9% in all RA cases (i.e. 34% in RF only positive RA; 25% in seropositive RA; 18% in seronegative RA and 18% in anti-CCP2 only positive RA). The HLA-DRB1 shared epitope alleles were significantly associated with anti-RA33 positive in the seropositive RA subgroup (OR=6.9, 95% CI 1.4-34.8; p=0.02). We observed significant association between anti-RA33 negative and HLA-DRB1 SE alleles among the seropositive RA patients (OR=4.5, 95% CI 2.8-7.2; p<0.001) and among CCP only positive RA (OR=4.4; 95% CI 2.6-7.4; p<0.01). No association was observed between anti-RA33 status and HLA-DRB1 SE alleles in seronegative RA and RF only positive RA.

Conclusion: The HLA-DRB1 SE alleles increased the risk of seropositive and CCP only positive RA independent of anti-RA33 positivity.

REFERENCES:

[1] Boeters, Debbie M et al. "The 2010 ACR/EULAR criteria are not sufficiently accurate in the early identification of autoantibody-negative rheumatoid arthritis: Results from the Leiden-EAC and ESPOIR cohorts." Seminars in arthritis and rheumatism vol. 47,2 (2017): 170-174.

[2] de Brito Rocha, Sara et al. "Clinical and pathophysiologic relevance of autoantibodies in rheumatoid arthritis." Advances in rheumatology (London, England) vol. 59,1 2. 17 Jan. 2019.

Acknowledgements: The authors would like to thank the Director General of Health, Ministry of Health Malaysia for supporting this study. The authors are also indebted to participants for their kind participation. This study was financially supported by the Ministry of Health, Malaysia (JPP-IMR 08-012).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2298

POS0356 THE RELATIONSHIP OF GENETICS AND CLINICALLY SUSPECT ARTHRALGIA IN RA DEVELOPMENT ASSESSED USING HC, CSA AND RA PATIENTS

M. Maurits[1], F. Wouters[1], E. Niemantsverdriet[1], T. Huizinga[1], A. van der Helm - van Mil[1], R. Knevel[1]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*

Background: The identification of a pre-RA stage of patients with clinically suspect arthralgia (CSA) has proven to be beneficial in the early detection of Rheumatoid disease. Similarly, genetic susceptibility studies have identified important genetic risk factors for the development of (CCP positive) RA.[1] The question that arises is whether these findings represent independent etiological pathways and could therefore be complimentary in the early diagnosis of RA.

Objectives: To corroborate the knowledge of genetic differences between HC and RA patients and extend it to include the CSA stage of disease.

Methods: We used three datasets sampled from the same region in the Netherlands: 1,085 healthy controls (HC), 530 CSA and 1,277 RA patients. CSA patients were monitored for a median of 2 years for conversion into clinically apparent inflammatory arthritis (CSAc) or not (CSAnc).[2] We assessed the association between HLA SE and disease stage using logistic regression. The analysis was repeated in the CCP positive and CCP negative strata of both the CSA and the RA populations.

Results: Consistent with previous studies, HLA SE was significantly enriched in RA patients compared to HC (OR 2.28) (Figure 1). HLA SE also differentiated HC vs CSAc (OR 1.69), CSAnc vs CSAc (OR 1.74), and CSAnc vs RA (0R 2.35). No difference was found in HC vs CSAnc and CSAc vs RA.

Conclusion: HLA SE is more prevalent in patients who developed (rheumatoid) arthritis than in both healthy controls and CSA patients who do not progress to arthritis. The results presented here seem to indicate a clear distinction between CSA patients who develop arthritis and those who do not. We therefore believe that known RA genetics play a role in the development of arthritis rather than the CSA symptoms. While this relationship varies by CCP status, an independent effect remains. Studies into the broader role of genetics beyond HLA SE are currently underway.

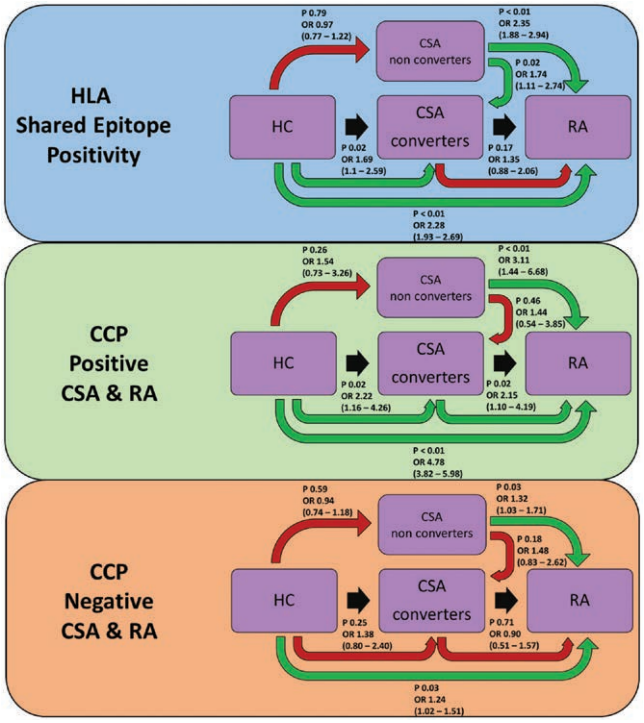


Figure 1. Distinguishing ability of HLA SE across HC, CSAc, CSAnc and RA in the full populations as well as in the CCP positive and negative stratifications. The arrowhead indicates the "case" status in each logistic regression. OR's (95% CI) derived from regression coefficients indicate the change in odds ratio attributable to HLA SE positivity.

REFERENCES:
[1] van der Helm-van Mil, A. H., et al. Arthritis and rheumatism, 2006. 54(4): p. 1117–1121.
[2] van Steenbergen, H.W., et al. Ann Rheum Dis, 2017. 76(3): p. 491-496.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2554

POS0357 MiRNAs CORRELATE WITH IMPROVEMENT IN DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS ON TUMOUR NECROSIS FACTOR INHIBITORS

T. David[1,2], N. Nair[3], J. Oliver[3,4], E. Schordan[5], H. Firat[6], K. Hyrich[1,2,7], A. Morgan[8,9], A. G. Wilson[10], J. D. Isaacs[11,12], D. Plant[3], A. Barton[1,2,3]. *[1]Manchester Royal Infirmary, Manchester University NHS Foundation Trust,The Kellgren Centre for Rheumatology, Manchester, United Kingdom*; *[2]The University of Manchester, NIHR Manchester Musculoskeletal Biomedical Research Unit, Manchester, United Kingdom*; *[3]The University of Manchester, Centre for Musculoskeletal Research, Manchester, United Kingdom*; *[4]Leeds Teaching Hospitals NHS Trust,Yorkshire and North East Genomic Laboratory Hub, Leeds, United Kingdom*; *[5]FIRALIS S.A., CSO (Molecular Diagnostics), Huningue, France*; *[6]FIRALIS S.A., CEO and CSO (Management Team), Huningue, France*; *[7]The University of Manchester,Arthritis Research UK, Centre for Epidemiology, Centre for Musculoskeletal Research, Manchester Academic Health Sciences Centre, Manchester, United Kingdom*; *[8]University of Leeds, Leeds Institute of Cardiovascular and Metabolic Medicine, Leeds, United Kingdom*; *[9]Leeds Teaching Hospitals NHS Trust, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*; *[10]University College Dublin, UCD School of Medicine and Medical Science, Conway Institute, Dublin, Ireland*; *[11]Newcastle University, Translational and Clinical Research Institute, Faculty of Medical Sciences, Newcastle upon Tyne, United Kingdom*; *[12]Newcastle upon Tyne Hospitals NHS Foundation Trust, Musculoskeletal Unit, Newcastle upon Tyne, United Kingdom*

Background: Tumour necrosis factor inhibitors (TNFi) although effective in the treatment of rheumatoid arthritis (RA), show a variable response rate. Therefore, there is a need to identify treatment response predictors to inform therapy selection in order to practise precision medicine. MicroRNAs (miRNAs) are endogenous, single-stranded, non-coding RNAs that can alter gene expression by regulating messenger RNA translation. There is evidence for miRNA involvement in RA pathogenesis and they may serve as a useful biomarker of treatment response.
Objectives: To identify miRNAs associated with response to TNFi in RA.
Methods: Biologic naïve patients were selected from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS), a prospective multi-center UK study investigating treatment response biomarkers to TNFi with a primary outcome measure of change in DAS28 scores. Patients were stratified into European League Against Rheumatism (EULAR) good or non-responders based on their 3 or 6-month DAS28-CRP score.
Pre-treatment and 3-month post-treatment serum samples were substrates for miRNA profiling, which was conducted by FIRALIS using the HTG EdgeSeq miRNA whole transcriptome V2 targeted sequencing assay. Linear modelling using R package limma compared miRNA expression at (i) pre-treatment and at three-months, in EULAR good-responders and non-responders (ii) longitudinal change in expression from pre-treatment to three-months in EULAR good and non-responders.
A literature search was conducted to identify miRNAs associated with RA as a diagnostic and/or treatment response predictor. Data on these miRNAs were extracted from the miRNAs identified in the serum samples. A correction for multiple testing was applied to statistical tests.
Results: A total of 54 patients were analysed; of these, 35 (65%) were female, median disease duration [inter-quartile range] was 6 years [2 – 14] (n=51), and 44/51 (86%) patients were on a concomitant disease modifying anti-rheumatic drug. Of the 54 patients, 39 (72%) were classified as EULAR good-responders and 15 (28%) as non-responders. 1880 miRNAs were detected in the serum samples. 64 miRNAs were identified to be associated with RA from the literature, of which, 26 were identified in the serum samples tested.
No difference in pre-treatment or three-month miRNA levels was seen comparing EULAR good-responders and non-responders **(FDR p<0.05)**. There was a significant differential expression of four miRNAs at 3-months in good-responders compared with pre-treatment levels; miR-125a-3p (downregulated, p-value 0.002), miR-149-3p (upregulated, p-value 0.004), miR-766-3p (downregulated, p-value 0.008), miR-146b-5p (upregulated, p-value 0.006). No significant differences were observed between 3-months and baseline in non-responders.
Conclusion: Although no pre-treatment miRNAs were associated with TNFi response, changes in the levels of four miRNAs were detected at 3-months compared to baseline in EULAR good-responders. Future work involves validation of these samples in a larger patient cohort and analysing miRNA levels at 6 and 12 months. Replication and validation of these results in larger studies are required to analyse the role of miRNAs in stratifying EULAR good-responders from non-responders at three-months, and as treatment response predictors to TNFi in RA.
Acknowledgements: Joint last-author: Dr. Darren Plant
Disclosure of Interests: Trixy David: None declared, Nisha Nair: None declared, James Oliver: None declared, Eric Schordan: None declared, Hüseyin Firat: None declared, Kimme Hyrich Consultant of: consultancy/honoraria from AbbVie, Grant/research support from: Pfizer, UCB, BMS, Ann Morgan: None declared, Anthony G Wilson: None declared, John D Isaacs Speakers bureau: consultancy/speaker fees from AbbVie, Gilead, Roche, UCB, Consultant of: consultancy/speaker fees from AbbVie, Gilead, Roche, UCB, Grant/research support from: Pfizer, Darren Plant: None declared, Anne Barton: None declared
DOI: 10.1136/annrheumdis-2021-eular.2841

POS0358 EVALUATION OF THE EFFECT OF mTOR EXPRESSION ON THE CLINICAL MANIFESTATIONS OF KNEE OSTEOARTHRITIS IN OBESE AND NORMAL WEIGHT PATIENTS

E. Strebkova[1], E. Tchetina[2], L. Alekseeva[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Osteoarthritis, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*

Background: Currently, a large number of molecular biological and genetic markers are known to be involved in the development of osteoarthritis (OA). The mammalian target of rapamycin (mTOR) signaling pathway is responsible for chondrocyte proliferation, cartilage matrix production, and cell growth. OA is characterized by increased mTOR synthesis, which is accompanied by an increase in proliferative activity and destruction of chondrocytes. Obesity is an important factor in the progression of knee OA. The study of mTOR expression in patients with OA and obesity is an urgent task in the development of personalized OA therapy.
Objectives: To determine the expression of mTOR in patients with knee OA in combination with obesity and normal body weight. To evaluate the effect of mTOR on the clinical manifestations of OA in patients with different body mass index (BMI).
Methods: The study included 73 female patients aged 45-65 y.o. with Kellgren-Lawrence stage II-III knee OA. The patients were divided into 2 groups: group 1 (n=50) with obesity (BMI > 30 kg / cm2) and group 2 (n=23) with normal or increased body weight (BMI < 30 kg/cm2). The average age of patients with obesity is 56.5 ± 5.87 years, without obesity - 58.7 ± 5.43 years. Clinical manifestations were evaluated by a WOMAC. RNA was isolated from the patients ' blood samples, which was used to determine the expression of mTOR.
Results: Patients with knee OA with and without obesity did not differ in age. OA develops at an earlier age in obese patients, than in non-obese patients (p < 0.001). Patients from 1 group had a high BMI > 30 kg/m2 at the onset of OA. Obese patients had more severe knee OA is significantly more often detected: Kellgren-Lawrence stage III was determined in 10% of obese patients and in 4.35% - without obesity (p < 0.001). Significantly higher values of the WOMAC index pain, stiffness, joint functional failure, and total WOMAC were observed in obese patients (p = 0.006, p = 0.039, p = 0.037, and p = 0.014, respectively). Obese patients had higher VAS pain scores (p < 0.05) compared to patients with a lower BMI. Obese patients had a higher mTOR expression (p < 0.05) of 8.02±8.62, compared to non-obese patients. High mTOR expression was associated with VAS knee pain (r=0.78; p < 0.05) and WOMAC pain (r=0.89; p<0.05) in obese patients (Table 1).

Table 1. Correlation of m-TOR

Parameters	mTOR (1 group, n=50)	mTOR (2 group, n=23)
Body weight	p > 0,05	p > 0,05
Pain (VAS)	r=0,78; p<0,05	p = 0,07; r = 0,45
Pain (WOMAC)	r=0,89; p<0,05	p > 0,05
Total WOMAC	p > 0,05	p > 0,05

Conclusion: Our study showed that patients with obesity and knee OA have higher rates of mTOR expression, compared to patients with normal body weight. High mTOR expression correlates with the severity of knee pain in obese patients. Thus, the evaluation of mTOR expression in obese patients and knee OA plays an important role in predicting the severity of clinical manifestations of OA, and may influence the choice of personalized therapy tactics for such patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3287

POS0359 MOLECULAR PROFILING OF RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS PATIENTS REVEALS AN ASSOCIATION BETWEEN INNATE AND ADAPTIVE CELL POPULATIONS AND THERAPEUTIC RESPONSE TO ADALIMUMAB

D. Sobral[1], A. F. Fernandes[2], A. Mashayekhi Sardoo[3], M. Bernardes[4], P. Pinto[5], H. Santos[6], J. L. Gomes[7], J. Tavares-Costa[8], J. Silva[9], J. Madruga Dias[10], A. Bernardo[5], J. Gaillard[11], J. Armengaud[11], V. Benes[12], R. Pinheiro Torres[7,13], L. Domingues[13], S. Maia[13], J. Branco[7,13,14], A. V. Coelho[2], F. Pimentel dos Santos[7,13,14]. *[1]Faculdade de Ciências e Tecnologia, Ciências e Tecnologia, Caparica, Portugal*; *[2]ITQB NOVA, Instituto de Tecnologia Química e Biológica, Oeiras, Portugal*; *[3]University of Trás-os-Montes and Alto Douro, Ciências e Tecnologia, Vila Real, Portugal*; *[4]São João Universitary Hospital Center, Rheumatology, Porto, Portugal*; *[5]Centro Hospitalar Vila Nova de Gaia / Espinho - Unit 1, Rheumatology, Vila Nova de Gaia, Portugal*; *[6]Rheumatology Institute (IPR), Rheumatology, Lisboa, Portugal*; *[7]Hospital Egas Moniz, Rheumatology, Lisboa, Portugal*; *[8]Unidade Local de Saúde do Alto Minho, Rheumatology, Ponte de Lima, Portugal*; *[9]Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal*; *[10]Centro Hospital Médio Tejo, Rheumatology, Tomar, Portugal*; *[11]Service de Pharmacologie et Immunoanalyse (SPI), Laboratoire Innovations technologiques pour la Détection et le Diagnostic, Avignon, France*; *[12]Genomics Core Facility, Genomics Core Facility, Heidelberg, Germany*; *[13]CEDOC, Rheumatology, Lisboa, Portugal*; *[14]Nova Medical School, Rheumatology, Lisboa, Portugal*

Background: The response to treatment in spondylarthropaties is heterogeneous, due to factors yet to be better described. For that reason, it is important to find tools that might help clinicians to decide what is the best available therapeutic option for each patient.
Objectives: The goal of this study is to use comprehensive molecular profiling to characterize clinical response to therapy in a real-world setting. Specifically, to identify molecular biomarkers differentiating good responders and non-responders to TNF inhibitors (TNFi) treatment, using adalimumab, in radiographic axial spondyloarthritis | ankylosing spondylitis (r-axSpA|AS) patients context.
Methods: Whole-blood mRNA and plasma proteins were measured in a cohort of biologic naïve r-axSpA|AS patients (n = 35) from the Bioefficacy study (Biomarkers identification of anti-TNF alpha agent efficacy in AS patients using RNA sequencing and mass spectrometry), pre and post (14 weeks) TNFi treatment using adalimumab. Response to treatment was categorized according to ASAS20. Results of differential expression analysis were used to identify the most enriched pathways and in predictive models to distinguish responses to TNFi.
Results: A treatment-related signature, independent of the type of response, suggests a reduction in inflammatory disease activity. We found genes and proteins robustly differentially expressed between baseline and week 14 in responders, including the GWAS AS-associated genes *TNFRSF1A, FCGR2A, TYK2, TBKBP1, IL1R1, IL6R, ICOSLG, IL7R, HHAT and LTBR*. Moreover, CRP and HP proteins showed strong and early decrease in the plasma of AS patients, while a cluster of apolipoproteins (APO1, APO2, APO3) showed an increased expression at week 14. Good responders to TNFi treatment tend to have higher expression of innate immunity genes at baseline, and lower expression of markers associated with adaptive immunity, particularly B-cells. A logistic regression model incorporating ASDAS-CRP, gender and *Gene x*, the top differentially expressed gene at baseline between responders and non-responders, enabled an accurate prediction of response to adalimumab in our cohort (AUC=0.97).
Conclusion: Differences in disease activity and/or innate/adaptive immune cell type composition at baseline may be a major contributor to response to adalimumab in r-axSpA|AS. Alternatively, a model including clinical and gene expression variables could be considered, particularly in patients with mild disease activity.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3683

POS0360 COMPLEX LANDSCAPE OF BIRC5/SURVIVIN GENOME BINDING IN HUMAN CD4+ T CELLS

N. Oparina[1], M. Erlandsson[1], V. Chandrasekaran[1], K. M. Andersson[2], A. Damdimopoulos[3], S. Töyrä Silfverswärd[4], G. Katona[5], M. I. Bokarewa[1]. *[1]University of Gothenburg, Department of Rheumatology and Inflammation Research, Institute of Medicine, Gothenburg, Sweden*; *[1]University of Gothenburg, Department of Rheumatology and Inflammation Research, Institute of Medicine, Gothenburg, Sweden*; *[3]Karolinska Institutet, Department of Bioscience and Nutrition, Huddinge, Sweden*; *[4]Sahlgrenska University Hospital, Rheumatology Clinic, Gothenburg, Sweden*; *[5]University of Gothenburg, Department of Chemistry and Molecular Biology, Gothenburg, Sweden*

Background: Survivin, coded by BIRC5 gene, is a multitasking protein essential for cell renewal and homeostasis. In autoimmune conditions as rheumatoid and psoriasis arthritis, survivin was associated with inflammation severity and joint damage. Importantly, inhibition of survivin alleviated experimental arthritis in mice. We have recently shown survivin to be essential for T cell differentiation and microRNA processing. The known anti-apoptotic and proliferation facilitating functions of survivin does not explain the nuclear localization of survivin in interphase.
Objectives: We aimed to uncover nuclear functions of BIRC5/survivin in CD4 cell of RA patients and healthy.
Methods: CD4 T cells were isolated from the peripheral blood using positive selection on magnetic beads (EasySep) and activated for 48h with ConA+LPS. Chromatin immunoprecipitation (ChIP) with polyclonal anti-survivin antibodies was done in four independent samples of healthy donors (n=5), healthy smokers (n=3), rheumatoid arthritis (n=3) and breast cancer (n=2). Pooled libraries were constructed for each group and ChIPseq was carried out (Illumina). For comparative RNAseq analysis, activated CD4 T cells were incubated with or without survivin inhibitor (YM155) for 24h. State-of-the-art bioinformatics pipelines were applied for NGS data and the survivin-binding peaks were used for comparison with genes, chromatin state annotation and functional gene- and regulatory regions-based functional analysis. Co-localization of peaks in the whole genome and in vicinity of the differentially expressed genes (DEG) was done using ReMap integrated ChIPseq datasets for all human cells and tissues.
Results: We identified 13 thousands non-overlapping survivin ChIP-peaks (>3000 peaks were present in at least 3 samples). Survivin-bound regions were enriched near the genes and promoters (p=e-30 and p=e-8), which implied that survivin role in transcription could be mediated by known transcription factors. Thus, we analyzed survivin peaks vs binding regions of 1135 transcription regulators (TR) available in ReMap. Potential partner proteins of survivin were selected based on the enrichment of the overlapping peaks in the whole genome and in CD4-active regulatory areas. Both, strict overlaps and location within 10 and 100kb survivin peak vicinity were analyzed. This approach allowed us to select >150 TRs enriched in all tests. The enriched TRs were involved in immunity and RA-relevant pathways including cytokine response and production, JAK-STAT signaling, etc. Among the TRs co-localized with survivin were CHD8, MAX, EP300, BRD2, CTCF and RAD21, all responsible for chromatin architecture. Several TRs were massively enriched in the vicinity of DEGs after survivin depletion including MAX, AR, CTCF, MYC and IRF1. Search for TR binding motifs in survivin peaks supported over-representation of binding sites for IRFs (p=e-5) and several proteins of the bZIP-family (p=e-5).
Conclusion: Analysis of the survivin bound DNA in CD4 cells demonstrated the nonrandom distribution with specific enrichment within the regulatory elements of the genes and co-localizeation with protein partners to regulate their transcription.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3708

POS0361 DNA METHYLATION SIGNATURES CHARACTERIZE PSORIASIS AND PSORIATIC ARTHRITIS IN MONOZYGOTIC TWINS DISCORDANT FOR THE DISEASE

M. Vecellio[1,2], A. Ceribelli[2], E. Paraboschi[3], N. Isailovic[2], F. Motta[2], M. De Santis[2], R. Asselta[3], S. Duga[3], C. Selmi[2]. *[1]University of Oxford, NDORMS, Oxford, United Kingdom*; *[2]Humanitas Research Hospital, Rheumatology and Clinical Immunology, Rozzano, Italy*; *[3]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy*

Background: Psoriatic disease is a chronic inflammatory disorder spanning from skin disease (psoriasis) to psoriatic arthritis (PsA). The genetic background is insufficient to explain disease onset as illustrated by not very informative Genome Wide Association Studies and monozygotic (MZ) twin studies recently performed. It is strongly assumed that epigenetics may contribute to disease susceptibility modulating gene expression. DNA methylation has been found involved in several autoimmune inflammatory rheumatic diseases. Here we have analysed the DNA methylation profile of a selected cohort of MZ twins discordant for psoriasis/PsA.
Objectives: To identify the methylome associated with psoriasis and PsA in the peripheral blood of MZ twins discordant for these conditions.
Methods: Peripheral blood from 7 couples of MZ twins discordant for psoriatic disease was collected and DNA extracted for a genome-wide evaluation of the DNA methylation profile, with the Infinium MethylationEPIC BeadChip. *Minfi* and the packages of the Bioconductor were used to analyse the data obtained. Quality control and exclusion criteria were applied to the raw data having a final number of 762.451 probes, which accounts for 88% of the total.
Results: The approach first identified 2564 differentially methylated positions (DMPs; *p<0.005) with 19 genes potentially affected (with at least two DMPs within 1 kb of distance), including SMAD3 and SMARCA4/BRG1 involved in the Interferon and TGFβ pathways. Gene Ontology (GO) analysis of DMP-associated genes showed a significative enrichment (*p<0.005) in transcription factor binding, transcription corepressor and transcription coactivator activity, SMAD binding and histone -lysine-N-methyltransferase activity. To further validate the results, 5'-methylcytosine immunoprecipitation (MedIP) followed by Real Time PCR was performed to assess the methylation level of SMAD3 and SMARCA4/BRG1 promoters in the same cohort of MZ twins. We found significantly DNA methylation enrichment in SMARCA4/BRG1 promoter in psoriatic disease twins (p<0.05). SMAD3 and SMARCA4/BRG1 mRNA expression was also assessed to evaluate any inverse correlation with promoter methylation level, on the MZ cohort used for the EPIC array (n=4) and on a cohort of PsA/Ps patients (n=8) and appropriate healthy controls (n=3). Reduced mRNA expression (p<0.05) was demonstrated for SMARCA4/BRG1 (n=4). Conversely, no changes were found for SMAD3.
Conclusion: We report the first DNA methylation approach in MZ twins discordant for psoriatic disease. We believe that the observed changes in SMAD3

and SMARCA/BRG1 genes may suggest an epigenetic imbalance of chromatin remodelling factors involved in inflammation pathways with a potential role in PsA/psoriasis immunopathogenesis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3948

POS0362 **INVESTIGATING THE ANKYLOSING SPONDYLITIS-ASSOCIATED REGULATORY SNPS AT THE RUNX3 LOCUS WITH A FUNCTIONAL GENOMICS APPROACH**

M. Vecellio[1], P. B. Wordsworth[1], C. J. Cohen[1]. [1]*University of Oxford, NDORMS, Oxford, United Kingdom*

Background: Of the >100 genetic associations with ankylosing spondylitis (AS), RUNX3 transcription factor (TF) involved in diverse immunological processes, is robustly (10^{-15}) associated.[1] The biggest challenge is to understand the mechanism behind this association. We demonstrated the association between AS and the single nucleotide polymorphism (SNP) *rs4648889* located in a 2kb regulatory locus upstream of the *RUNX3* promoter can be explained by allele-specific effects on TF recruitment that alter gene expression, specifically in CD8+ T-cells.[2] We recently dissected the full plethora of TFs affected by *rs4648889* AS-associated allele showing the NuRD complex and IRF5 differentially bound and having a crucial role in CD8+ T-cells function[3]. Nevertheless, other post-GWAS approaches are needed to elucidate the function of *RUNX3* AS-associated SNPs (i.e. the lead SNP *rs6600247*).
Objectives: The purpose of this work is to define the functional effect of *rs6622047* in CD8+ T-cells and monocytes. In specific, we expect to define the impact of AS-associated allele to TF binding and to evaluate chromosome looping between *rs6600247* and the RUNX3 promoter.
Methods: The epigenetic landscape of SNP *rs6600247* was defined using Roadmap database. *In vitro* functional studies were performed to characterize the effects of this SNP on TFs binding. Chromosome conformation capture (3C) provided critical functional evidence for looping among AS-associated SNPs and the *RUNX3* promoter.
Results: (1) *In silico* data revealed a c-MYC ChIP-seq peak in GM12878 lymphoblastoid cells overlapping *rs6600247*; (2) Mobility shift assays (EMSAs) and WB-EMSAs showed reduced DNA/protein binding in the presence of the AS-risk allele in CD14+ monocytes. C-MYC binding-site is disrupted and binding abolished in the presence of the AS-risk allele; (3) 3C experiments indicate low interaction frequency between SNP *rs6600247* and RUNX3 promoter.
Conclusion: The enhancer upstream the *RUNX3* gene has a plausible functional role in AS, probably by regulating gene transcription and DNA looping. These observations are critically important in defining dysregulated pathways and potential therapeutic drug targets.
REFERENCES:
[1] IGAS et al. *Nat Genet*. 2013 Jul;45(7):730-8.
[2] Vecellio M. et al, *Ann Rheum Dis.* 2016 Aug;75(8):1534-40.
[3] Vecellio et al *Arthritis Rheumatol 2020.* doi: 10.1002/art.41628.
Acknowledgements: We thank Professor Julian Knight for his constructive advices and comments to the present work.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4098

Adaptive immunity (T cells and B cells) in rheumatic diseases

POS0363 **IDENTIFICATION OF MOLECULAR PHENOTYPES AND IMMUNE CELL INFILTRATION IN PSORIATIC ARTHRITIS PATIENTS' SKIN TISSUES BY INTEGRATED BIOINFORMATICS ANALYSIS**

T. Cheng[1,2,3], S. X. Zhang[1,2,3], J. Qiao[1,2,3], R. Zhao[1,2,3], S. Song[1,2,3], Y. Zhang[1,2,3], P. Zhao[4], G. Y. Liu[1], P. F. He[5], X. Li[1,2,3]. [1]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [2]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [3]*Ministry of Education, Key laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [4]*Shanxi Provincial People's Hospital, Department of Rheumatology, Taiyuan, China*; [5]*Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease associated with cutaneous psoriasis[1]. Heterogeneity of clinical manifestation often makes differential diagnosis difficult [2]. Thus, the underlying molecular pathogenesis of PsA need to be further studied to diagnose early and ensure optimal management of arthritis and key comorbidities.
Objectives: This research was conducted to identify molecular phenotypes and immune infiltration in the skin tissues of psoriatic arthritis patients according to bioinformatics analysis.
Methods: The mRNA expression profiles of GSE13355 (116 samples), GSE14905 (56 samples) and GSE30999 (162 samples) were obtained from the publicly GEO databases. Non-negative matrix factorization (NMF), functional enrichment and cibersort algorithm were applied to illustrate the conditions of PsA patients' skin tissues for classification after screening the differentially expressed genes (DEGs) between lesion biopsy and non-lesion biopsy.
Results: Two subsets (Sub1 and Sub2) were identified and validated by NMF typing of 612 detected DEGs (Figure 1a). A total of 54 signature genes (18 in Sub1 and 36 in Sub2) were obtained (Figure 1b). GO and KEGG enrichment analysis showed the signature genes in Sub1 were mainly involved in proliferation and differentiation of immune cells, whereas genes in Sub2 were related to humoral immune response mediated by antimicrobial peptide (Figure 1c.1d). Further, immune cell infiltration results revealed Sub2 had higher levels of resting NK cells (P<0.001), macrophages M1(P<0.001), resting mast cells (P<0.001) and regulatory T cells (P<0.001) but lower concentrations of activated $CD4^+$ memory T cells (P<0.001), activated NK cells (P<0.05), activated dendritic cells(P<0.001), eosinophils (P<0.05) and neutrophil (P<0.001) (Figure 1e).
Conclusion: The pathogenesis of psoriatic arthritis is related to both cellular immunity and humoral immunity. It is indispensable to adjust the treatment strategies according to patient's immune status.
REFERENCES:
[1] Ritchlin CT, Colbert RA, Gladman DD. Psoriatic Arthritis. The New England journal of medicine 2017;376(10):957-70. doi: 10.1056/NEJMra1505557 [published Online First: 2017/03/09].
[2]Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. Lancet (London, England) 2018;391(10136):2273-84. doi: 10.1016/s0140-6736(18)30830-4 [published Online First: 2018/06/13].

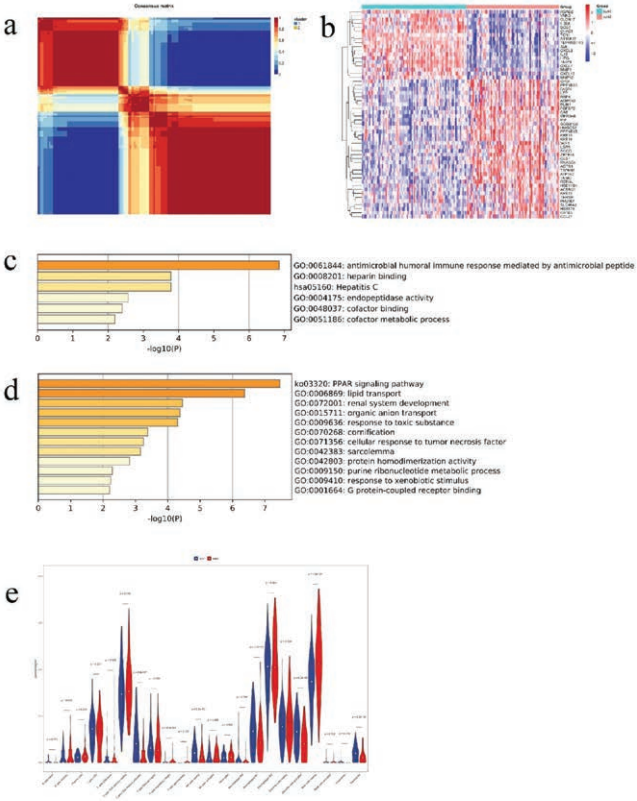


Figure **(a)** NMF consensus clustering of 334 PsA patients based on 612 DEGs. **(b)** Heat map of differentially expressed genes: Each small square represents a gene; the color indicates the expression of the gene. Each column indicates the expression level of genes in a sample; the right side is the gene name. **(c.d)** Visualization GO enrichment analysis and KEGG pathway enrichment. **(e)** Violin plot show the fraction of 22 immune cells subpopulations in two subtypes based on CIBERSORT algorithm.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2171

Innate immunity in rheumatic diseases

POS0364

EFFECT OF BIOLOGIC DMARDS TREATMENT ON GENE EXPRESSION AND ACTIVITY OF NATURAL KILLER CELLS IN RHEUMATOID ARTHRITIS

N. M. Elemam[1], M. Hachim[2], S. Hannawi[3], A. A. Maghazachi[1]on behalf of Immuno-Oncology Group. [1]*Sharjah Institute for Medical Research, University of Sharjah, College of Medicine, Sharjah, United Arab Emirates*; [2]*Mohammed Bin Rashid University of Medicine and Health Sciences, College of Medicine, Dubai, United Arab Emirates*; [3]*Ministry of Health and Prevention, Department of Rheumatology, Dubai, United Arab Emirates*

Background: Rheumatoid arthritis (RA) is the most common inflammatory type of arthritis, with various immune players implicated in its pathogenesis. Natural killer (NK) cells are innate lymphocytes that showed controversial roles in RA, whether pathogenic or protective (Shegarfi, H. et al. 2012, Yap, H.-Y. et al. 2018). Previously, we were able to identify a gene signature in NK cells of RA patients that can aid in understanding the state of NK cells in RA disease and identify RA patients from healthy controls (Elemam, N.M. et al. 2019, Elemam, N.M. et al. 2020). Furthermore, this signature might facilitate the selection of biomarkers that can be used for early detection of RA and prediction of effectiveness of RA treatment.

Objectives: In this study we aimed at exploring the effect of several RA therapeutic agents such as tocilizumab, rituximab and anti-TNFα (adalimumab, etanercept and golimumab) on the previously identified gene signature in NK cells of RA patients.

Methods: Whole blood transcriptomic data from publicly available dataset (GSE93272) was used to predict the percentage of activated NK cells in the blood of RA patients using the software CIBERSORT. Then, a correlation analysis was done between the percentage of NK cells and number of days of receiving tocilizumab treatment. Whole blood samples were collected from the recruited 17 RA patients (satisfying the 2010 ACR/EULAR classification criteria for RA). NK cells were isolated using RosetteSep negative selection method and RNA was extracted and gene expression was assessed using qRT-PCR. RA patients taking tocilizumab, rituximab, or anti-TNFα (adalimumab, etanercept or golimumab but none of the patients received infliximab) were compared to those not receiving any biological DMARDs. Statistical analysis was done using Student's t-test.

Results: In silico analysis has shown that the percentage of activated NK cells is positively correlated with the number of days of tocilizumab therapy in RA patients, suggesting a direct enhancing effect of tocilizumab on NK cell activity. Then, it was crucial to investigate the effect of different biological DMARDs on NK gene expression in RA patients. All the investigated chemokines (CCL2, CXCL10, CXCL16, CXCR1, CXCR2, CXCR6 and CCR4) in the identified gene signature showed a significant change in RA patients receiving tocilizumab, rituximab, or anti-TNFα therapies. Furthermore, the other genes including RELA, ICAM, IL1RN, TLR3 and TLR10 were significantly changed in NK cells of RA patients receiving biological DMARDs in comparison to patients not receiving the treatments. However, some of the genes including CD56, BTK, IBTK, ITGB7, IL1B, PECAM-1, IL12RB2, IFNG and CKLF did not show a significant change upon receipt of biological DMARDs.

Conclusion: In conclusion, NK cell activity and gene expression could be affected by the type of biological DMARDs received by RA patients. Therefore, this identified gene signature of NK cells could be used as a diagnostic tool to identify RA patients and a target for biological DMARDs in RA.

REFERENCES:

[1] Elemam, N. M., M. Y. Hachim, S. Hannawi and A. A. Maghazachi (2019). "Natural Killer Cells Gene Expression Can Differentiate Rheumatoid Arthritis Patients from Healthy Controls [abstract]." ACR/ARP Annual Meeting, supplement of Arthritis & Rheumatology **71**(suppl 10).

[2] Elemam, N. M., M. Y. Hachim, S. Hannawi and A. A. Maghazachi (2020). "Differentially Expressed Genes of Natural Killer Cells Can Distinguish Rheumatoid Arthritis Patients from Healthy Controls." Genes (Basel) **11**(5).

[3] Shegarfi, H., F. Naddafi and A. Mirshafiey (2012). "Natural killer cells and their role in rheumatoid arthritis: friend or foe?" TheScientificWorldJournal **2012**: 491974-491974.

[4] Yap, H.-Y., S. Z.-Y. Tee, M. M.-T. Wong, S.-K. Chow, S.-C. Peh and S.-Y. Teow (2018). "Pathogenic Role of Immune Cells in Rheumatoid Arthritis: Implications in Clinical Treatment and Biomarker Development." Cells **7**(10): 161.

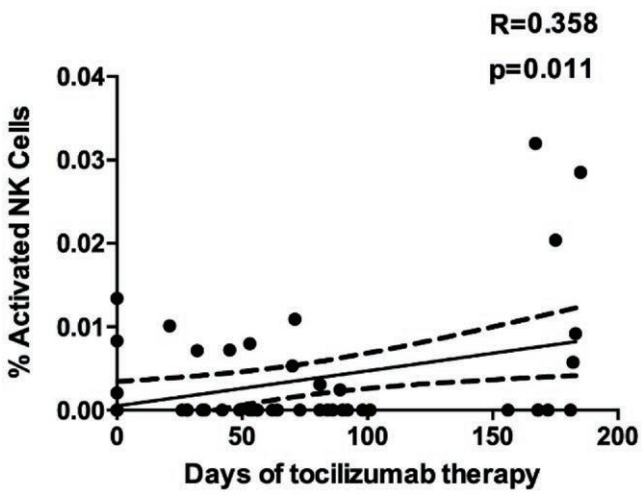


Figure 1. In silico analysis and correlation of NK cell activity with the number of days of Tocilizumab therapy in RA patients.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2075

POS0365

ANTI-TNF GLUCOCORTICOID RECEPTOR MODULATOR ANTIBODY DRUG CONJUGATE FOR THE TREATMENT OF AUTOIMMUNE DISEASES

B. Stoffel[1], M. McPherson[2], A. Hernandez[2], C. Goess[1], S. Mathieu[1], W. Waegell[1], S. Bryant[1], A. Hobson[2], M. Ruzek[1], Y. Pang[3], H. Kupper[4], R. D'Cunha[3], J. Parmentier[5], T. Radstake[6]. [1]*AbbVie Bioresearch Center, Immunology Discovery, Worcester, United States of America*; [2]*AbbVie Bioresearch Center, Biologics Discovery, Worcester, United States of America*; [3]*AbbVie, Clinical Pharmacology, North Chicago, United States of America*; [4]*AbbVie, Clinical Development, Ludwigshafen, Germany*; [5]*AbbVie Bioresearch Center, Precision Medicine, Worcester, United States of America*; [6]*AbbVie, Clinical Development, North Chicago, United States of America*

Background: Glucocorticoids (GC) are potent drugs used for treating many inflammatory diseases. While GCs are effective in many immune diseases, dose and duration of administration is limited due to significant side effects. Resting immune cells have very little TNF expression on the cell surface and it is only in an activated state that TNF expression is upregulated. Upon immune cell stimulation, TNF is upregulated and although a significant amount of TNF is cleaved from an activated cell, a portion remains on the cell surface. We have observed that anti-TNF antibodies bind to transmembrane TNF (tmTNF) and undergo endocytosis to the lysosome (1). We have developed a stable antibody drug conjugate (ADC), ABBV-3373, that has a proprietary, highly potent, glucocorticoid receptor modulator (GRM) payload linked to an anti-TNF monoclonal antibody (mAb) that is able to deliver the GC payload to activated immune cells.

Objectives: We hypothesized that a TNF ADC with a GRM payload would be able to deliver increased efficacy through both TNF inhibition and targeted GRM payload delivery to activated immune cells while sparing systemic glucocorticoid side effects.

Methods: A mouse surrogate TNF GRM ADC was characterized in an acute *in vivo* contact hypersensitivity model of inflammation (CHS) and in a mouse model of collagen induced arthritis (mCIA). Additionally, the human anti-TNF GRM ADC, ABBV-3373 has been characterized in healthy volunteers.

Results: In the CHS model the anti-TNF GRM ADC significantly inhibited the inflammatory response with minimal effect on systemic GC biomarkers. In mCIA a single dose of an anti-TNF GRM ADC, administered at disease onset, was able to completely inhibit arthritis for greater than 30 days while an anti-TNF mAb only partially inhibited disease. ABBV-3373, a human anti-TNF GRM ADC with a GC payload, was evaluated in a Phase 1 study in healthy volunteers. ABBV-3373 demonstrated antibody-like PK profile and ABBV-3373 did not impact cortisol levels at predicted efficacious doses while control subjects that received a single oral dose of 10 mg prednisone demonstrated expected decreases in cortisol levels.

Conclusion: These data suggest that an anti-TNF ADC delivering a GRM payload into activated immune cells may provide improved efficacy in immune mediated diseases, while minimizing systemic side effects associated with standard GC treatment.

REFERENCES:

[1] Deora, A. et al. *MAB*s. 2017;9(4):680-695.

Disclosure of Interests: Bob Stoffel Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Michael McPherson Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Axel Hernandez Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Christian Goess Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Suzanne Mathieu Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Wendy Waegell Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Shaughn Bryant Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Adrian Hobson Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Melanie Ruzek Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Yinuo Pang Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Hartmut Kupper Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Ronilda D'Cunha Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Julie Parmentier Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie, Timothy Radstake Shareholder of: AbbVie, Grant/research support from: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2021-eular.2213

POS0366 PRO-INFLAMMATORY EFFECTS OF HUMAN APATITE CRYSTALS EXTRACTED FROM PATIENTS SUFFERING FROM CALCIFIC TENDINOPATHY

J. Herman[1,2], B. Le Goff[1,2], J. De Lima[2], R. Brion[2], C. Chevalier[2], F. Blanchard[2], C. Darrieutort-Laffite[1,2]. [1]*Nantes University Hospital, Rheumatology, NANTES, France*; [2]*INSERM-UMR1238, Phy-Os Laboratory, Nantes, France*

Background: Calcific tendonitis of the rotator cuff is due to carbonated apatite deposits in the shoulder tendons. During the evolution of the disease, an acute inflammatory episode may occur leading to the disappearance of the calcification. Although hydroxyapatite crystals-induced inflammation has been previously studied with synthetic crystals, no data are available with calcifications extracted from patients suffering from calcific tendinopathy. The objective of the study was to explore the inflammatory properties of human calcifications and the pathways involved.
Objectives: The objective of the study was to explore the inflammatory properties of human calcifications and the pathways involved.
Methods: Human calcifications were obtained from patients treated for their shoulder pain related to a calcific tendinopathy of the rotator cuff. Calcifications were extracted by ultrasound-guided lavage and aspiration as previously described [1]. Human calcifications and synthetic hydroxyapatite (sHA) were used *in vitro* to stimulate human monocytes and macrophages, the human myeloid cell line THP-1 and human tenocytes. The release of IL-1β, IL-6 and IL-8 by cells was quantified by ELISA. Gene expression of pro- and anti-inflammatory cytokines was evaluated by quantitative PCR. NF-kB activation and NLRP3 involvement was assessed in THP-1 cells using a NF-kB inhibitor and a Caspase 1 inhibitor. The inflammatory properties were then assessed *in vivo* using a mouse air pouch model. The membrane thickness and infiltrate were assessed 6 and 24 hours after the injection of human calcifications or synthetic hydroxyapatite using hematoxylin and eosin staining. Macrophages, neutrophils and lymphocytes infiltrates were assessed by immunohistochemistry. Total RNA was extracted from the membranes and expression of IL-1β, IL-6 and TNFβ was quantified by PCR.
Results: Human calcifications were able to induce a significant release of IL-1β when incubated with monocytes, macrophages and THP-1 only if they were first primed with LPS (lipopolysaccharide) for monocytes and macrophages or PMA (Phorbol 12-myristate 13-acetate) for THP-1. No IL-1β was detected in tenocytes' supernatants. Stimulation of THP-1 by human calcifications led to similar levels of IL-1β when compared to synthetic hydroxyapatite although these levels were significantly inferior in monocytes and macrophages. IL-6 and IL-8 levels were not increased in the supernatants after crystal stimulation. Patient's crystals enhanced mRNA expression of pro-IL-1β, as well as IL-18, NF-kB and TGFβ when IL-6 and TNFα expression were not. IL-1β production was reduced by the inhibition NF-kB as well as Caspase 1 indicating the role of NLRP3 inflammasome. In vivo, injection of human calcifications or synthetic hydroxyapatite in air pouch led to significant increase in membrane thickness with an infiltrate mainly composed of macrophages. Significant overexpression of IL-1β was only observed in the synthetic hydroxyapatite group.
Conclusion: As synthetic hydroxyapatite, human calcifications were able to induce an inflammatory response resulting in the production of IL-1β after NF-kB activation and through NLRP3 inflammasome. In some experiments, IL-1β induction was lower with human calcifications compared to synthetic apatite. Differences in size, shape and protein content may explain this observation.
REFERENCES:
[1] Darrieutort-Laffite C, Arnolfo P, Garraud T, Adrait A, Couté Y, Louarn G, et al. Rotator Cuff Tenocytes Differentiate into Hypertrophic Chondrocyte-Like Cells to Produce Calcium Deposits in an Alkaline Phosphatase-Dependent Manner. J Clin Med. 2019 Sep 26;8(10):1544. doi: 10.3390/jcm8101544.
Acknowledgements: Fondation Arthritis, Recherche et Rhumatismes and French Society for Rheumatology for their financial support
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2624

POS0367 NLRC4 AND FC-Γ-R CROSSTALK ON CD1C+ DENDRITIC CELLS DIFFERENTIALLY CONTRIBUTES TO RHEUMATOID ARTHRITIS IMMUNOPATHOLOGY

C. Delgado-Arévalo[1], M. Calvet-Mirabent[1], A. Triguero-Martinez[2], E. Vazquez de Luis[3], A. Benguría-Filippini[3], D. Calzada[1], I. Sánchez-Cerrillo[1], R. Moreno-Vellisca[4], H. De la Fuente[1], A. Ramiro[5], F. Sánchez-Madrid[1,5], S. Castañeda[2], A. Dopazo[3], I. González-Álvaro[2], E. Martin-Gayo[1]. [1]*Hospital de La Princesa, Immunology Unit, Madrid, Spain*; [2]*Hospital de La Princesa, Rheumatology Unit, Madrid, Spain*; [3]*Centro Nacional de Investigaciones Cardiovasculares (CNIC), Genomics Facility, Madrid, Spain*; [4]*Centro Nacional de Investigaciones Cardiovasculares (CNIC), B Lymphocyte Biology Lab, Madrid, Spain*; [5]*Centro Nacional de Investigaciones Cardiovasculares (CNIC), Intercellular Communication in the Inflammatory Response Lab, Madrid, Spain*

Background: Rheumatoid arthritis (RA) is an autoimmune disorder in which Th17 cells, B cells and inflammatory cytokines (1-3) contribute to joint tissue damage, however the role of specific myeloid populations to immunopathogenesis of RA remains unclear.
Objectives: To address this question, we studied transcriptional, phenotypical and functional characteristics of monocytes (Mo), CD1c$^+$ and CD141$^+$ conventional dendritic cells (cDC) from RA patients.
Methods: Frequencies and maturation patterns of Lin-CD14-HLADR+ plasmacytoid (CD11c-), CD1c+ and CD141+ cDC (CD11c+) subsets and CD14+ Mo from n=25 RA patients at baseline were analyzed by multicolor flow cytometry. In addition, longitudinal studies on the evolution of these populations after treatment initiation were conducted on a smaller group of RA patients. Moreover, CD1c+ and CD141+ cDC subsets and total Mo were sorted from the peripheral blood from n=4 untreated RA and healthy individuals and the synovial fluid from n=3 RA and chondrocalcinosis patients. Differential transcriptional patterns within each population were analyzed by RNAseq. Functional validation of targets were performed in vitro with cDC subsets isolated form the synoviual fluid of RA patients. Finally, silencing of expression of NLRC4 and NLRP3 on CD1c+cDCs was performed with specific siRNAs.
Results: Both CD1c$^+$ (p=0.0001) and CD141$^+$ (p=0.0008) cDCs were significantly depleted from the blood and enriched in the synovial fluid from untreated RA patients, but proportions of CD1c+ cDCs were more significantly recovered after treatment initiation and associated with improved clinical parameters. In addition, specific increased expression levels of the IgG-Fc receptor CD64 on CD1c$^+$ cDC was associated with higher DAS28 (p=0.0002). Moreover, differential transcriptional patterns of circulating CD1c$^+$cDCs from RA patients were characterized by genes linked to toll-like receptor, Fc-receptor, inflammasome pathways and elevated CCR2 expression (p=0.016), while CD141$^+$cDCs transcribed interferon-related genes. Importantly, CCR2$^+$ CD64^{Hi} CD1c$^+$cDCs from the synovial fluid from RA patients transcribed proinflammatory cytokines such as IL1-β, CCL3 and IL-8, actively expressed the inflammasome mediator caspase 1 and were more effective activating pathogenic IFNγ$^+$IL-17$^+$ CD4$^+$ T cells *in vitro* than CD141$^+$ cDC (p=0.0019). These functional profiles could be artificially induced stimulating CD1c$^+$ cDCs with dsDNA in the presence of IgGs and was dependent on caspase 1 and the NLRC4 inflammasome.
Conclusion: Our data provides novel insights about specific activation and functional patterns on CD1c$^+$cDC contributing to RA pathogenesis and identifies new sensors that could represent novel therapeutic target to treat RA.
REFERENCES:
[1] Alvandpur N, Tabatabaei R, Tahamoli-Roudsari A, Basiri Z, Behzad M, Rezaeepoor M, et al. Circulating IFN-gamma producing CD4+ T cells and IL-17A producing CD4+ T cells, HLA-shared epitope and ACPA may characterize the clinical response to therapy in rheumatoid arthritis patients. Human immunology. 2020.
[2] Nistala K, Adams S, Cambrook H, Ursu S, Olivito B, de Jager W, et al. Th17 plasticity in human autoimmune arthritis is driven by the inflammatory environment. Proceedings of the National Academy of Sciences of the United States of America. 2010;107(33):14751-6.
[3] Chapuy-Regaud S, Nogueira L, Clavel C, Sebbag M, Vincent C, Serre G. IgG subclass distribution of the rheumatoid arthritis-specific autoantibodies to citrullinated fibrin. Clinical and experimental immunology. 2005;139(3):542-50.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3192

POS0368 CITRULLINATION INDUCES EPIGENETIC MEMORY OF THE INNATE IMMUNE SYSTEM

K. Laskari[1], S. Sabu[1], O. Distler[1], M. Neidhart[1], E. Karouzakis[1,2]. [1]*University Hospital Zurich, University of Zurich, Department of Rheumatology, Center of Experimental Rheumatology, Zurich, Switzerland*; [2]*Galapagos, Translational Medicine, Basel, Switzerland*

Background: During trained immunity, monocytes and macrophages undergo a functional and transcriptional reprogramming toward activation, which is induced by a priming stimulus and results in enhanced responsiveness to subsequent triggers. Monocytes from patients with rheumatoid arthritis (RA) display features consistent with a trained immunity phenotype. Citrullinated proteins as citrullinated vimentin (c-vimentin), which function as damage-associated patterns in RA, may be implicated in the process of trained immunity.
Objectives: We aimed to investigate if c-vimentin induces trained immunity in vitro in healthy individuals.
Methods: Monocytes were isolated from the peripheral blood (EDTA blood, n=22; buffy coats, n=6) from healthy donors by Ficoll-paque centrifugation and negative selection using CD3/CD19/CD56 magnetic beads. The cells were stimulated with c-vimentin (0.1 µg/ml) for 24h and re-stimulated 5 days later with the lipopolysaccharide of *E.coli* (LPS) (10 ng/ml). Protein as well as lactate release were estimated in cell culture supernatants at day 6 by ELISA. RT-PCR and/or Western Blotting were applied to measure mRNA and/or protein expression. The Ligand-receptor glycocapture technology LRC-TRiCEPS was used to identify candidate cell surface targets of c-vimentin. The methylation of histone H3 at lysine 4 (H3K4) was examined by chromatin immunoprecipitation.
Results: Priming with citrullinated vimentin induced training in human monocytes, as suggested by the significantly increased levels of secreted interleukin-6 (IL-6), upon restimulation with LPS (1.29-fold increase, n=22, p<0.001). Likewise, the release of chemokines CXCL1 and CCL20/Macrophage Inflammatory Protein 3a was significantly increased (1.81-fold and 2.32-fold increase, respectively, n=14, both p<0.001). LRC-TRiCEPS enabled the identification of STING cell surface receptor for the ligand c-vimentin. Indeed, c-vimentin induced activation of TBK1, which is implicated in the STING signaling pathway, by phosphorylation, while STING inhibition with the covalent small molecule H151 (2µM) abolished this effect. Besides, H151 inhibited trained immunity by decreasing IL-6 release and expression (1.61-fold and 1.93-fold decrease, respectively, n=5). Trained monocytes also displayed high lactate production (primed vs. unprimed cells, n=9, p=0.004), reflecting a shift in metabolism with an increase in glycolysis. By inhibiting the metabolic pathway of glycolysis by 2-deoxyglucose (11mM), the induction of trained immunity could be counteracted (5.32-fold decrease in IL-6 release, n=7, p=0.016). Finally, c-vimentin induced H3K4 methylation with increased levels of this mark in the promoter of the IL-6 gene. By modulating the function of epigenetic enzymes with methylthioadenosine (1mM), which specifically inhibits histone methyltransferase, trained immunity was reversed (8.43-fold decrease in IL-6 release, n=6, p=0.031).
Conclusion: Citrullinated vimentin induces epigenetic modifications and metabolic changes in monocytes, probably through a STING and TBK1-dependent activation, resulting in enhanced cytokine and chemokine production upon restimulation. Inhibition of the STING signaling pathway may be a novel therapeutic target for myeloid activation in RA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3302

POS0369 ELEVATED EXPRESSION OF TIM-3 ON NEUTROPHILS CORRELATES WITH DISEASE ACTIVITY AND SEVERITY OF ANKYLOSING SPONDYLITIS

X. Huang[1], T. W. Li[1], J. Chen[1], Z. Huang[1], S. Chen[1], X. Guo[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*

Background: Ankylosing spondylitis (AS) is a type of common, chronic inflammatory disease that compromises the axial skeleton and sacroiliac joints, causing inflammatory low back pain and progressive spinal stiffness, over time some patients develop spinal immobility and ankylosis which can lead to a decrease in quality of life. The last few decades, evidence has clearly indicated that neutrophil also plays key roles in the progression of AS. However, the immunomodulatory roles and mechanisms of neutrophils in AS are poorly understood. T-cell immunoglobulin and mucin domain-containing protein 3 (Tim-3) has been reported as an important regulatory molecule, expressed and regulated on different innate immune cells, plays a pivotal role in several autoimmunity diseases. Recent study indicates that Tim3 is also expressed on neutrophils. However, the frequency and roles of Tim3-expressing neutrophils in AS was not clear.
Objectives: In this study, we investigated the expression of Tim3 on neutrophils in AS patients and explored the correlation between the level of Tim3-expressing neutrophils and the disease activity and severity of AS.
Methods: Patients with AS were recruited from Guangdong Second Provincial General Hospital (n=62). Age/sex-matched volunteers as Healthy controls (HC) (n=39). The medical history, clinical manifestations, physical examination, laboratory measurements were recorded. The expression of costimulatory molecules including programmed death 1 (PD-1), Tim-3 on neutrophils were determined by flow cytometry. The mRNA expression of PD-1 and Tim-3 was determined by real-time PCR. The levels of Tim3-expressing neutrophils in AS patients were further analyzed for their correlation with the markers of inflammation such as ESR,CRP,WBC and neutrophil count(NE), as well as disease activity and severity of AS. The expression of Tim3 on neutrophils was monitored during the course of treatment (4 weeks).
Results: The expression of Tim3 on neutrophils in patients with AS was increased compared to the HC (Figure 1A). However, significant difference was observed in the frequency of PD-1-expressing neutrophils between AS patients and HC (Figure 1B). The expression analysis of Tim-3 mRNA, but not PD-1, confirmed the results obtained from flow cytometry (Figure 1C). The level of Tim3-expressing neutrophils in patients with AS showed an positive correlation with ESR, CRP and ASAS-endorsed disease activity score (ASDAS) (Figure 1D). Moreover, the frequency of Tim3-expressing neutrophils in active patients(ASDAS≥1.3) was increased as compare with the inactive patients (ASDAS<1.3) (Figure 1E). As shown in Figure 1F, the frequency of Tim3-expressing neutrophils decreased after the treatment.

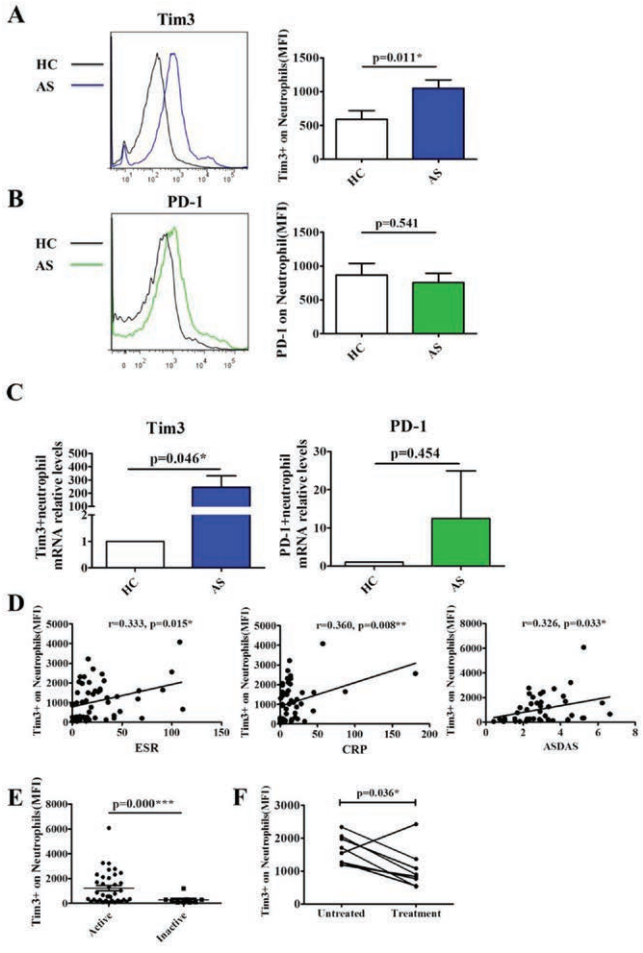


Figure 1. (A,B) The expression of Tim3 and PD-1 on neutrophils in AS and HC were determined by flow cytometry.**(C)** The expression of Tim3 and PD-1 on neutrophils in AS and HC were determined by RT-PCR.**(D)**The correction between Tim3-expressing neutrophils and ESR,CRP,ASDAS.**(E)** The expression of Tim3 on neutrophils in active and inactive patients.**(F)** Influence of treatment on the frequency of Tim3-expressing neutrophils.

Conclusion: Increased Tim-3 expression on neutrophils may be a novel indicator to assess disease activity and severity in AS, which may serves as a negative feedback mechanism preventing potential tissue damage caused by excessive inflammatory responses in AS patients.

REFERENCES:

[1] Han, G., Chen, G., Shen, B. & Li, Y., Tim-3: an activation marker and activation limiter of innate immune cells. FRONT IMMUNOL 4 449 (2013).

[2] Vega-Carrascal, I. et al., Galectin-9 signaling through TIM-3 is involved in neutrophil-mediated Gram-negative bacterial killing: an effect abrogated within the cystic fibrosis lung. J IMMUNOL 192 2418 (2014).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3516

POS0370

TYPE I INTERFERON PATHWAY ASSAYS IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES - SYSTEMATIC LITERATURE REVIEW (SLR) AND DEVELOPMENT OF CONSENSUS TERMINOLOGY FROM A EULAR TASKFORCE

A. Burska[1], J. Rodriguez Carrio[2], P. G. Conaghan[1], W. A. Dik[3], R. Biesen[4], M. L. Eloranta[5], G. Cavalli[6], M. Visser[7], D. Boumpas[8], G. Bertsias[9], M. Wahren-Herlenius[10], J. Rehwinkel[11], M. L. Frémond[12], M. K. Crow[13], L. Ronnblom[5], E. Vital[1], M. Versnel[14]. [1]*University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [2]*University of Oviedo, Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Spain*; [3]*Erasmus MC, Department of Medical Immunology, Rotterdam, Netherlands*; [4]*Charité University Medicine Berlin, Department of Rheumatology, Berlin, Germany*; [5]*Uppsala University, Department of Medical Sciences, Rheumatology, Uppsala, Sweden*; [6]*Vita-Salute San Raffaele University, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy*; [7]*EULAR, PARE Patient Research Partners, Amsterdam, Netherlands*; [8]*University of Crete, Medical School, Department of Internal Medicine, Heraklion, Greece*; [9]*University of Crete, Medical School, Department of Internal Medicine, Heraklion, Greece*; [10]*Karolinska Institutet, Division of Rheumatology, Stockholm, Sweden*; [11]*University of Oxford, MRC Human Immunology Unit, Oxford, United Kingdom*; [12]*Hôpital Necker-Enfants Malades, Immuno-Hématologie et Rhumatologie pédiatriques, Paris, France*; [13]*Hospital for Special Surgery, Weill Cornell Medical College, Mary Kirkland Center for Lupus Research, New York, United States of America*; [14]*Erasmus MC, Department of Immunology, Rotterdam, Netherlands*

Background: The interferon (IFN) pathway is a complex system with multiple proteins and diverse downstream effects on gene and protein expression. IFNs have been implicated in multiple RMDs. Despite significant potential, IFN assays have not progressed into clinical practice.

Objectives: To perform a SLR on IFN assays in RMDs and propose a consensus terminology.

Methods: OvidMedline, Embase and Web of Science were searched for reports of IFN and RMDs up to October 2019. Information about the properties of assays measuring type I IFN and measures of truth were extracted and summarised. Terminology was agreed through an interactive consensus process with reference to the existing evidence.

Results: 10037 abstracts were identified. 275 fulfilled eligibility criteria, and were used for data extraction. Some used more than one technique to measure IFN-I pathway activation. Hence, 275 papers generated data on 393 methods. There was great heterogeneity in the methods used and presentation of results. IFN-I pathway activation was measured using: qPCR (n=121), immunoassays (n=101), microarray (n=69), reporter cell assay (n=38), DNA methylation (n=14), flow cytometry (n=14), cytopathic effect assay (n=11), RNA sequencing (n=9), Plaque reduction assay (n=8), Nanostring (n=5), bisulphite sequencing (n=3). All papers fulfilled Face Validity. Due to lack of gold standard for IFN-I pathway activation, evidence of criterion validity was variable. Concurrent validity was presented for n=150 assays. The terminology used to describe aspects of type I IFN pathway activation was not consistent, so a consensus terminology for IFN research (Table 1) was proposed by the taskforce.

Table 1. Consensus terminology

Term	Abbreviation	Definition
Interferon	IFN	Proteins with anti-viral activity; IFNs are mediators of an anti-viral response. They belong to the Type I, Type II and Type III IFN families.
Type I interferon	IFN-I	The IFNs alpha, beta, omega, kappa, epsilon, secreted by any nucleated cell, and binding to the IFNAR, which is expressed on any nucleated cell.
Type II interferon	IFN-II	IFN gamma, mostly secreted by T cells, binding to the IFNGR, which is expressed on most leucocytes.
Type III interferon	IFN-III	IFN lambda, which are structurally more similar to IL-10 but share downstream signalling and gene expression with IFN-I.
Interferon-stimulated genes	ISGs	Genes whose expression is known to be upregulated by any kind of IFN. Individual ISGs may not exclusively represent Type I IFN pathway activation.
Type I Interferon pathway activation		Any evidence for function of the components of the Type I IFN pathway. This includes: secretion of a Type I IFN protein, binding to the IFNAR, initiation of JAK/STAT signalling pathways, expression of IFN-stimulated genes, expression of IFN-stimulated proteins.
Type I interferon pathway assay		An assay measuring one or more components of the Type I IFN pathway at a molecular or functional level.
Interferon stimulated gene expression signature		A qualitative description of coordinated expression of a set of ISGs that is indicative of Type I IFN pathway activation.
Interferon stimulated gene expression score		A quantitative variable derived from expression of a defined set of ISGs that is indicative of Type I IFN pathway activation.
Interferon stimulated protein score		A variable derived from expression of a defined set of soluble biomarkers known to be upregulated by IFN, although not specific for Type I IFN.
Interferonopathy		Monogenic diseases in which there is constitutive Type I IFN pathway activation with a causal role in pathology. The clinical picture may resemble rheumatic musculoskeletal diseases. However, most diseases with IFN pathway activation are not Interferonopathies.

Conclusion: Diverse methods have been reported as IFN assays and these differ in what elements of type IFN-I pathway activation they measure. The taskforce consensus terminology on type I IFN reporting should be considered for research and clinical applications.

Disclosure of Interests: Agata Burska: None declared, Javier Rodriguez Carrio: None declared, Philip G Conaghan: None declared, Willem A Dik: None declared, Robert Biesen: None declared, Maija-leena Eloranta: None declared, Giulio Cavalli: None declared, Marianne Visser: None declared, Dimitrios Boumpas: None declared, George Bertsias: None declared, Marie Wahren-Herlenius: None declared, Jan Rehwinkel: None declared, Marie-Louise Frémond: None declared, Mary K. Crow Consultant of: AstraZeneca, Bristol Meyers Squibb, Lilly, Shannon Pharmaceuticals, Grant/research support from: Gilead, Lars Ronnblom Consultant of: AstraZeneca, Edward Vital Speakers bureau: GSK, Consultant of: AURINIA, SANDOZ, GSK, AstraZeneca, Roche, Modus, Grant/research support from: AstraZeneca, Marjan Versnel: None declared

DOI: 10.1136/annrheumdis-2021-eular.3788

Osteo arthritis, aetiology, pathology and animal models

POS0371 BIOLOGICAL REPRODUCIBILITY OF TARGETED LIPIDOME ANALYSES IN PLASMA AND ERYTHROCYTES OVER A 6-WEEK PERIOD

M. Loef[1], J. von Hegedus[1], M. Ghorasaini[2], F. Kroon[1], M. Giera[2], A. Ioan-Facsinay[1], M. Kloppenburg[1,3]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; [2]*Leiden University Medical Center, Center for Proteomics and Metabolomics, Leiden, Netherlands*; [3]*Leiden University Medical Center, Clinical Epidemiology, Leiden, Netherlands*

Background: Lipidomics analysis has become a valuable technology for understanding patho-physiological mechanisms and the identification of candidate biomarkers in rheumatic musculoskeletal disorders. Variability in within-subject repeated measurements may lead to bias towards the null when estimating the association between biomarkers and a disease or treatment. Hence, information regarding the stability of the metabolite levels over time is essential.
Objectives: We aimed to assess the lipid composition and biological reproducibility of lipid measurements in plasma and erythrocytes.
Methods: Plasma and erythrocyte samples from 42 osteoarthritis patients (77% women, mean age 65 years, mean BMI 27 kg/m2), obtained non-fasted at baseline and six weeks, were used for the quantitative measurement of up to 1000 lipid species across 13 lipid classes with the LipidyzerTM platform in nmol/mL. Data was processed based on the relative standard deviation of quality controls, taking batch effects into account. Intraclass correlation coefficients (ICCs) and corresponding 95% confidence intervals (CI) were calculated to investigate the variability of the lipid concentrations between timepoints. The ICC distribution of lipid metabolites in plasma and erythrocytes were compared using two-sided paired Wilcoxon tests.
Results: We measured 778 lipids in plasma, compared to 916 lipids in erythrocytes. After data processing, the analyses included 630 lipids in plasma, and 286 in erythrocytes. From these, 243 lipids overlapped between sample types. Major differences were observed between the sample types in the number of lipids per lipid class and the total concentration of the lipids within a class. Triacylglycerols (TAG) and cholesteryl esters (CE) were more abundant in plasma. Conversely, phosphatidylethanolamines (PE), sphingomyelins (SM) and ceramides (CER) were less abundant in plasma compared to erythrocytes (table 1). In plasma 78% of lipid measurements were good to excellently reproduced, with an overall median ICC 0.69. Compared to plasma, a considerably lower amount (35%) of lipids were well reproduced in erythrocytes. Median reproducibility of lipids in erythrocytes was 0.51. Figure 1 shows the ICC score distribution in plasma with erythrocytes, with a significantly better reproducibility in plasma (p-value<0.001). However, while overall reproducibility was better in plasma, this was not observed for all lipid classes. At class-level, reproducibility in plasma was superior for TAGs and CEs, while CERs, DAGs, (L)PEs and SMs showed better reproducibility in erythrocytes.
Conclusion: In plasma biological reproducibility was good for most lipid measurements. Although overall reproducibility was better in plasma compared to erythrocytes, notable differences were observed at individual- and lipid class-level that may favour the use of a particular sample type.

Table 1. Number of individual lipids per class and class concentrations in plasma and erythrocytes

	Plasma		Erythrocytes	
	Number of lipid species	Class concentration (nmol/mL)	Number of lipid species	Class concentration (nmol/mL)
Triacylglycerols	482	1579.4 (1064.9-3195.2)	134	6.5 (5.6-9.4)
Diacylglycerols	9	13.3 (8.4-22.2)	10	5.8 (4.7-6.2)
Free fatty acids	20	745.3 (552.0-1202.9)	20	486.9 (379.2-669.2)
Cholesteryl esters	24	4571.6 (4065.1-5521.3)	5	1.2 (0.9-1.7)
Phosphatidylcholines	31	4013.7 (3203.1-4661.6)	42	3899.2 (3723.0-4296.6)
Phosphatidylethanolamines	26	156.2 (120.9-180.3)	42	3954.6 (3721.9-4323.3)
Lysophosphatidylcholines	9	385.9 (335.6-442.9)	7	119.8 (109.7-168.9)
Lysophosphatidylethanolamines	2	4.2 (3.5-4.9)	4	8.6 (6.8-9.7)
Sphingomyelins	12	1204.6 (1037.0-1351.9)	8	2695.8 (2434.8-2815.6)
Ceramides	6	14.1 (11.9-17.4)	7	163.0 (133.3-186.4)
Dihydroceramides	2	1.0 (0.8-1.3)	1	1.8 (1.4-2.1)
Hexosylceramides	5	5.1 (4.7-5.9)	4	5.6 (5.0-7.4)
Lactosylceramides	2	3.4 (2.7-3.8)	2	23.8 (20.6-33.5)

Numbers represent median (interquartile range) unless otherwise specified. Data represents baseline measurements.

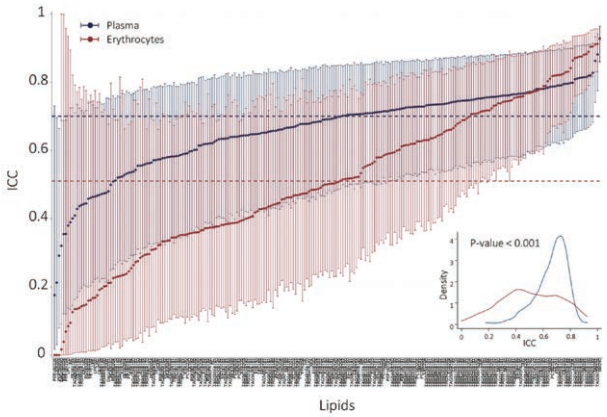


Figure 1. The ICC score distribution of lipids measured in plasma and erythrocytes.
Lipids are ranked ascending by plasma samples. A density plot of the ICC score distributions from plasma and erythrocyte samples is inserted in the lower right corner; the p-value represents the result from the Wilcoxon signed-rank test used to compare the distributions. The dashed lines correspond to the median ICC scores of lipids in plasma (blue) and erythrocytes (red).

Disclosure of Interests: Marieke Loef: None declared, Johannes von Hegedus: None declared, Mohan Ghorasaini: None declared, Féline Kroon: None declared, Martin Giera Shareholder of: Pfizer, Consultant of: Boehringer Ingelheim Pharma, Andreea Ioan-Facsinay: None declared, Margreet Kloppenburg: None declared
DOI: 10.1136/annrheumdis-2021-eular.20

POS0372 LORECIVIVINT (SM04690), AN INTRA-ARTICULAR, SMALL-MOLECULE CLK2/DYRK1A INHIBITOR THAT MODULATES THE WNT PATHWAY, AS A POTENTIAL TREATMENT FOR MENISCAL INJURIES

T. Seo[1], V. Deshmukh[1], Y. Yazici[2]. [1]*Samumed, LLC, Biology, San Diego, United States of America*; [2]*Samumed, LLC, Chief Medical Officer, San Diego, United States of America*

Background: Meniscal injuries are the most common pathology of the knee and are associated with pain, stiffness, and localized swelling. Meniscal damage is a frequent finding on MRI images of knee osteoarthritis (OA).[1] Efforts to repair meniscal damage have been largely unsuccessful and do not prevent the progression of degenerative changes that lead to knee OA.[2] The Wnt signaling pathway has been shown to be regulated during meniscal development,[3] suggesting that manipulation of this pathway may influence the regenerative capacity of the meniscus. Lorecivivint (LOR; SM04690) is an intra-articular (IA), small-molecule CLK2/DYRK1A inhibitor that modulates the Wnt pathway.[4]
Objectives: LOR was evaluated in preclinical studies to determine its protective and anabolic effects in ex vivo explants and in a rat model of chemically induced inflammatory meniscal degeneration.
Methods: Effects of LOR (30 nM) on matrix metalloproteinase (MMP) expression in cultured rat menisci treated with IL-1B were measured by qRT-PCR. In vivo, LOR activity was evaluated in a rat model of monosodium iodoacetate (MIA) injection-induced inflammatory meniscal degeneration. A single IA injection of MIA was immediately followed by a single IA injection of LOR (0.3 ug) or vehicle. Knees were harvested on Days 1, 4, and 11 and menisci were isolated. Anti-inflammatory effects were evaluated by qRT-PCR for *TNFA* and *IL6* expression. Meniscal protection was evaluated by qRT-PCR for MMPs and aggrecanase. Anabolic effects were evaluated by qRT-PCR for collagens.
Results: In ex vivo meniscal explants, LOR inhibited expression of *MMP1*, *MMP3*, and *MMP13* compared with DMSO (P<0.01). In vivo, LOR significantly decreased expression of MMPs and aggrecanase (P<0.05) and reduced expression of inflammatory cytokines *TNFA* and *IL6* compared with vehicle in the rat model of inflammatory meniscal degeneration at Day 4 after MIA injection. Additionally, LOR increased expression of collagen types I, II, and III at Day 11 after MIA injection (Figure 1).
Conclusion: LOR exhibited protective effects in the meniscus ex vivo and in vivo by reducing catabolic enzyme expression compared with control. Anti-inflammatory effects of LOR were demonstrated by inhibition of inflammatory cytokine expression. Compared with vehicle, LOR increased collagen expression in vivo, indicating potential meniscal anabolic effects. These data support further investigation of LOR as a potential structure-modifying treatment for meniscal injuries.

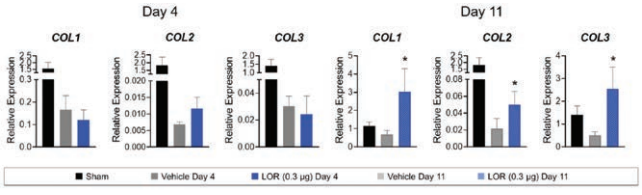


Figure 1. LOR increased collagen gene expression in vivo. A single IA injection of monosodium iodoacetate (MIA; 3 mg) was immediately followed by a single IA injection of LOR (0.3 µg) or vehicle at 10 weeks of age. Knees were harvested on Days 1, 4, and 11 after injection and menisci were isolated. Gene expression was measured by qRT-PCR. N=3, Mean ± SEM, *P<0.05, one-way ANOVA

REFERENCES:
[1] Englund M, et al. *Rheum Dis Clin North Am*. 2009.
[2] Collins JE, et al. *Arthritis Care Res (Hoboken)*. 2019.
[3] Pazin DE, et al. *Dev Dyn*. 2012.
[4] Deshmukh V, et al. *Osteoarthr Cartil.* 2019.
Disclosure of Interests: Tim Seo Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Vishal Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Yusuf Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC
DOI: 10.1136/annrheumdis-2021-eular.611

POS0373 LIRAGLUTIDE HAS POTENT ANTI-INFLAMMATORY AND ANTI-CATABOLIC IN VITRO ACTIVITIES IN OSTEOARTHRITIS

F. Berenbaum[1], C. Meurot[2], L. Sudre[2], K. Bismuth[2], R. Rattenbach[2], P. Denefle[2], C. Martin[2], C. Jacques[3]. [1]*APHP, Sorbonne University, INSERM UMRS_938, CDR St-Antoine, Rheumatology Department, Paris, France*; [2]*4P-Pharma, R&D, Lille, France*; [3]*Sorbonne University, INSERM UMRS_938, CDR St-Antoine, Paris, France*

Background: Osteoarthritis (OA) is an age-related joint disease which provokes chronic pain and limits mobility. The disease progression is associated with inflammatory responses and cartilage degradation. Both chondrocytes, the only cell type present in cartilage, and macrophages from the synovium, play a major role in OA pathophysiology. Liraglutide is a Glucagon-Like Peptide-1 Receptor (GLP-1R) agonist widely prescribed for the treatment of type 2 diabetes. Interestingly, anti-inflammatory properties of the GLP-1 pathway have been reported in various diseases outside diabetes.
Objectives: We evaluated the anti-inflammatory and anti-catabolic effects of Liraglutide in two *in vitro* models relevant to OA by evaluating surrogate markers of inflammation, cartilage matrix proteolysis and differentiation.
Methods: Lipopolysaccharide (LPS)-stimulated murine Raw 264.7 macrophages were treated with 10 concentrations (6.6nM-3.4µM) of Liraglutide for 24h. Anti-inflammatory activity was evaluated by the production of nitric oxide (NO) and prostaglandin E_2 (PGE_2) using Griess reaction and ELISA, respectively. Interleukin 1β (IL-1β)-stimulated mouse articular chondrocytes were treated with Liraglutide (6.6nM-3.4µM) for 24h. Production of IL-6, matrix metalloproteinase-3 (MMP-3) and glycosaminoglycans (GAG) was measured by ELISA and GAG assay, respectively. RTqPCR analyses were performed with three selected concentrations of Liraglutide (13.3nM, 53.1nM and 1.7µM) on both cell types to assess the expression of a panel of genes related to inflammation (IL-6, TNF, iNOS), M1/M2 macrophage phenotype (MCP-1, CD38, ERG-2), catabolism (MMP-13, ADAMTS-5) and differentiation (Sox9, Col2a1, Acan).
Results: Liraglutide induced a dose-dependent inhibition of the LPS-induced production of NO (IC_{50}=45nM) and PGE_2 (IC_{50}=54nM) in macrophages. Moreover, IL-6 and TNF gene expressions were significantly and dose-dependently decreased in Raw 264.7 cells treated with Liraglutide compared to LPS alone. Interestingly, there was a significant dose-dependent reduction of MCP-1 and CD38 (M1 marker) gene expression in cells treated with the 3 doses of Liraglutide compared to LPS alone while we observed a dose-dependent increase of ERG-2 (M2 marker) gene expression induced by Liraglutide. Liraglutide significantly dose-dependently reduced the IL-1β-induced release of IL-6 (IC_{50}=38nM), MMP-3 (IC_{50}=56nM) and GAG (IC_{50}=47nM) in chondrocytes. Additionally, Liraglutide treatment dose-dependently decreased the IL-1β-induced gene expression of iNOS, MMP-13 and ADAMTS-5. Finally, IL-1β decreased gene expression of Sox9, Col2a1 and Acan differentiation markers, which was rescued in a dose-dependent manner by Liraglutide (Table 1).
Conclusion: A shift in M1/M2 macrophage phenotype and the inhibition of chondrocyte expression of several mediators involved in inflammation and cartilage degradation explain, at least in part, our previous results from rodent osteoarthritis models that showed an analgesic, anti-inflammatory and anti-degradative effect of Liraglutide. The fact that Liraglutide is already safely prescribed in another indication allows us to foresee a first trial in humans in the short term.

Table 1. Gene expression results (fold change) in Raw 264.7 murine macrophages or mouse primary articular chondrocytes

Cell type	Markers	Vehicle	Vehicle	Liraglutide (nM)		
				13.3	53.1	1700
Macrophages		**- LPS**		**+ LPS**		
	IL6	1.0±0.2*	63.6±7.1	58.8±6.5	36.3±8.4*	30.8±2.6*
	TNFα	1.0±0.2*	26.8±4.9	17.5±2.6*	9.5±1.8*	4.1±2.1*
	MCP1	1.1±0.6*	91.7±11.2	67.8±4.3*	47.3±6.1*	25.1±5.5*
	CD38	1.1±0.6*	103.5±22.3	73.2±12.3*	44.6±8.9*	17.4±3.3*
	ERG2	1.0±0.3*	0.3±0.1	1.1±0.5*	2.1±0.6*	3.1±0.2*
Chondrocytes		**- IL1β**		**+ IL1β**		
	iNOS	1.0±0.2*	47.8±17.6	34.2±15.5	18.9±8.2*	11.8±2.9*
	MMP13	1.0±0.2*	9.8±2.0	7.6±1.0	4.6±0.7*	2.5±0.4*
	ADAMTS5	1.2±0.8	2.7±0.6	2.0±0.6	1.6±0.3	1.1±0.2
	Sox9	1.0±0.1*	0.4±0.2	0.4±0.2	0.6±0.0	0.7±0.2
	Col2a1	1.0±0.2*	0.3±0.1	0.3±0.1	0.5±0.3	0.8±0.3*
	Acan	1.2±0.8*	0.2±0.1	0.1±0.0	0.5±0.1*	0.7±0.2*

* p<0.05 vs LPS or IL1β alone, n=4

Acknowledgements: All the people who contributed to the InOsteo project: the members of 4P-Pharma, INSERM UMRS_938 research team, SATT Lutech and Sorbonne University
Disclosure of Interests: Francis Berenbaum Consultant of: Boehringer, Bone Therapeutics, CellProthera, Expanscience, Galapagos, Gilead, GSK, Merck Sereno, MSD, Nordic, Novartis, Pfizer, Regulaxis, Roche, Sandoz, Sanofi, Servier, UCB, Peptinov, 4P Pharma, 4Moving Biotech, Grant/research support from: TRB Chemedica, Coralie Meurot Employee of: 4P-Pharma, Laure Sudre Employee of: 4P-Pharma, Keren Bismuth Employee of: 4P-Pharma, Revital Rattenbach Shareholder of: 4P-Pharma, Employee of: 4P-Pharma, Patrice Denefle Speakers bureau: 4P-Pharma, Consultant of: 4P-Pharma, Pierre Fabre, Mimetas, Employee of: 4P-Pharma, Celine Martin Employee of: 4P-Pharma, Claire Jacques: None declared
DOI: 10.1136/annrheumdis-2021-eular.1849

POS0374 SENESCENCE DID NOT ALTER THE CHONDROPROTECTIVE EFFECT OF EXTRACELLULAR VESICLES FROM MESENCHYMAL STROMAL CELLS

J. Boulestreau[1], M. Maumus[1], P. Rozier[1], C. Jorgensen[1], D. Noel[1]. [1]*Inserm, u1183, Montpellier, France*

Background: Age is the most important risk factor in degenerative osteoarthritis (OA) and is associated with the accumulation of senescent cells that contribute to functional decline of joint. We previously demonstrated that extracellular vesicles (EVs) from mesenchymal stromal cells (MSCs) largely mediate the therapeutic effect of parental cells in OA.
Objectives: Here, we assessed the impact of senescence on the characteristics of EVs from adipose tissue-derived MSCs (ASC-EVs) and their properties in an in vitro model of OA
Methods: ASCs were induced to senescence using 25µM etoposide for 24 hours. Senescence was assessed by quantifying proliferation rate, SA-βGal activity, nuclear γH2AX foci number, phalloidin staining and expression of cyclin dependent kinase inhibitors (CDKI) (RT-qPCR). ASC-EVs were isolated by differential ultracentrifugation and characterized by size, concentration, total protein content, structure (cryo-TEM) and immunophenotype. In vitro OA model used chondrocytes isolated from OA patients, which were stimulated with IL1β for 48h before culture with ASCs or ASC-EVs for 7 days. Expression of chondrocytic and inflammatory markers was quantified by RT-qPCR and SASP factors were quantified by ELISA in supernatants.
Results: Senescence-induced ASCs experienced growth arrest and increase of SA-βGal staining, of p21 CDKI expression, of nuclear γH2AX foci, of stress fibers and of several SASP factors (IL6, IL8, MMP3) confirming the expression of main senescence features. Senescent ASCs produced 4-fold more EVs than healthy ASCs and senescent ASC-EVs were larger. In vitro, both healthy and senescent ASCs decreased fibrotic markers (*type III COLLAGEN*), catabolic and hypertrophic markers (*MMP3, MMP13, AP*) and increased *COX2* expression in OA chondrocytes. By contrast, healthy ASCs decreased the expression of *IL6* while senescent ASCs highly increased *IL6*. Looking at the role of ASC-EVs on OA chondrocytes, we found out that both healthy and senescent ASC-EVs were able to increase the expression of *AGG* and *type II COLLAGEN* while they decreased the expression of *MMP13, AP, type X COLLAGEN, HMOX1* and *IL6*. Finally, healthy and senescent ASC-EVs decreased the number of SA-βGal positive chondrocytes but did not impact the expression of p21 in IL1β-induced chondrocytes.
Conclusion: Our results indicated a chondroprotective effect of ASC-EVs, independently of the senescent state of parental cells and suggested that EVs might act through different mechanisms than ASCs, which warrants further investigation

Disclosure of Interests: Jérémy Boulestreau: None declared, Marie Maumus Employee of: Bauerfeind France, Pauline Rozier: None declared, Christian Jorgensen Shareholder of: Medxcell sciences, Consultant of: Medxcell sciences, Daniele Noel Shareholder of: Medxcell sciences, Consultant of: Medxcell sciences
DOI: 10.1136/annrheumdis-2021-eular.2401

POS0375 CHAPERONE-MEDIATED AUTOPHAGY IS A HALLMARK OF JOINT DISEASE IN OSTEOARTHRITIC PATIENTS

I. Lorenzo[1], U. Nogueira-Recalde[1], N. Oreiro[2], J. A. Pinto Tasende[2], M. Lotz[3], F. J. Blanco[1,2], B. Carames[1]. [1]*Instituto de Investigación Biomédica de A Coruña (INIBIC), Unidad de Biología del Cartílago, Grupo de Investigación en Reumatología, A Coruña, Spain*; [2]*Complejo Hospitalario Universitario A Coruña, Grupo de Reumatología Clínica, A Coruña, Spain*; [3]*Scripps Research, Department of Molecular Medicine, La Jolla, United States of America*

Background: In Osteoarthritis (OA), defects in macroautophagy (autophagy) are evident and precede joint damage. Indeed, pharmacological activation of autophagy protects against joint damage.
Objectives: Therefore, identifying hallmarks associated with specific autophagy subtypes could shed light to fundamental mechanisms of joint disease.
Methods: A comparative analysis of 35 autophagy genes was performed from blood from the Prospective OA Cohort of A Coruña (PROCOAC). Non-OA subjects (Age:61,44±1,16 years; BMI:25,25±0,52; Females, n=18) and Knee OA subjects (Age:65,50±1,05 years; BMI:29,55±0,67; Females, n=18, OA grade III-IV) were profiled using an autophagy gene expression array by SYBR green qPCR. Confirmatory studies were performed in blood from Non-OA subjects (Age:60,13±1,12 years; BMI:24,85±0,59; Females; n=30) and Knee-OA subjects (Age:68,4±1,11 years; BMI:29,65±0,55; Females; n=30, OA grade III-IV) by Taqman qPCR. The candidate gene was evaluated in human knee joint tissues (cartilage, meniscus, ligaments, synovium) with different KL grades (Age: KL0=28,3±4,50; KL2=77±6,08; KL4=62,3±3,05, n=3) and in both spontaneous aging (2, 6, 12, 18, and 30 months old, n=3) and surgically-induced OA (10 weeks after surgery, n=4) in mice by IHC. The functional consequences were studied in T/C28a2 and primary human OA chondrocytes. Autophagy, FOXO, Chaperone-mediated autophagy (CMA), inflammation, and cellular senescence were analyzing by gene and protein expression. Moreover, oxidative stress and cell death were evaluated by FACS. The contribution of CMA to chondrocyte homeostasis was evaluated by studying the capacity of CMA to restore proteostasis upon autophagy deficiency by siATG5.
Results: 15 autophagy-related genes were significantly downregulated in blood from knee OA patients compared to non-OA patients. No significant upregulation was found for any studied gene, although a trend towards upregulation was found in genes involved in the mTOR pathway. Four key autophagy-related genes, including ATG16L2, ATG12, ATG4B and MAP1LC3B were found downregulated in knee OA patients. Interestingly, HSP90AA1 and HSPA8, CMA markers involved in stress response and protein folding, were downregulated. Confirmatory studies showed a significant downregulation of MAP1LC3B and HSP90AA1 in blood from knee OA patients. Remarkably, HSP90A was found reduced in femoral cartilage (medial and lateral), meniscus and ACL. Moreover, this reduction was higher in medial cartilage compared to lateral cartilage and meniscus, while in synovial membrane, HSP90A expression was found increased. This expression signature was dependent on OA grade severity. In addition, we observed a decrease of HSP90A with aging and OA in mice. The functional consequences of HSP90AA1 gene silencing are related to an increase in NFκB, MMP13, and p16 expression. Interestingly, LAMP2A, a key CMA mediator, HSPA8, MAP1LC3B and FoxO1 expression were upregulated in chondrocytes with HSP90AA1 deficiency, which might indicate an early response to maintain homeostasis. On the other hand, LAMP2A protein is decreased upon HSP90AA1 deficiency, while LC3II and p62 were increased, indicating a failure in the autophagy flux that leads to impaired lysosomal degradation.
Moreover, p21, p16 and prbS6 were increased upon HSP90AA1 deficiency, besides increasing mitochondrial ROS production and apoptosis. ATG5 silencing blocks autophagy by reducing LC3II and increasing prbs6, p62, p16 and p21. Interestingly, LAMP2A and HSP90A were found increased, indicating a possible compensative activation of CMA in response to autophagy defects. These results support that HSP90A has an important role in chondrocyte homeostasis by participating in the cross-talk between CMA and autophagy.
Conclusion: Taking together, we identified HSP90A, a CMA regulator, as critical in chondrocyte homeostasis. These disease mechanisms are relevant in OA and constitute hallmarks potentially useful to prevent OA progression.
REFERENCES:
[1] Caramés B, et al. Arthritis Rheum. 2010, 2015;
[2] Caramés B, et al. Ann Rheum Dis. 2012.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2639

POS0376 MONOMERIC C REACTIVE PROTEIN (mCRP) REGULATES INFLAMMATORY RESPONSES IN HUMAN AND MOUSE CHONDROCYTES

C. Ruiz-Fernández[1], M. González-Rodríguez[1], V. Francisco[1], I. M. Rajab[2], R. Gómez Bahamonde[3], J. Conde Aranda[1], F. Lago[4], J. Pino[1], A. Mobasheri[5], M. A. González-Gay[6], A. Mera Varela[7], L. A. Potempa[2], O. Gualillo[1]. [1]*Health Research Institute of Santiago de Compostela (IDIS), NeuroEndocrine Interactions in Rheumatic and Inflammatory Diseases Group, Santiago de Compostela, Spain*; [2]*Roosevelt University, College of Pharmacy, Schaumburg, United States of America*; [3]*Health Research Institute of Santiago de Compostela (IDIS), Musculoskeletal Pathology Laboratory, Santiago de Compostela, Spain*; [4]*Health Research Institute of Santiago de Compostela (IDIS), Molecular and Cellular Cardiology Group, Santiago de Compostela, Spain*; [5]*University of Oulu, Research Unit of Medical Imaging, Physics, and Technology, Faculty of Medicine, Oulu, Finland*; [6]*Hospital Universitario Marqués de Valdecilla, IDIVAL, University of Cantabria, Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Santander, Spain*; [7]*Santiago University Clinical Hospital, Division of Rheumatology, Santiago de Compostela, Spain*

Background: C-reactive protein (CRP) is an acute-phase protein that is used as an established biomarker to follow disease severity and progression in a plethora of inflammatory diseases. However, its pathophysiologic mechanisms of action are still poorly defined and remain elusive. CRP, in its pentameric form, exhibits weak anti-inflammatory activity. On the contrary, the monomeric isoform (mCRP) exhibits potent pro-inflammatory properties in endothelial cells, leukocytes, and platelets. So far, no data exists regarding mCRP effects in human or mouse chondrocytes
Objectives: This work aimed to verify the pathophysiological relevance of mCRP in the etiology and/or progression of osteoarthritis (OA)
Methods: We investigated the effects of mCRP in cultured human primary chondrocytes and in the chondrogenic ATDC5 mouse cell line. We determined mRNA and protein levels of relevant factors involved in inflammatory responses and the modulation of nitric oxide synthase type II (NOS2), an early inflammatory molecular target.
Results: We demonstrate, for the first time, that monomeric C reactive protein increases NOS2, COX2, MMP13, VCAM1, IL-6, IL-8, and LCN2 expression in human and murine chondrocytes. We also demonstrated that NF-kB is a key factor in the intracellular signaling of mCRP-driven induction of pro-inflammatory and catabolic mediators in chondrocytes.
Conclusion: mCRP exerts a sustained catabolic effect on human and murine chondrocytes, increasing the expression of inflammatory mediators and proteolytic enzymes, which can promote extracellular matrix (ECM) breakdown in healthy and OA cartilage. In addition, our results implicate the NF-kB signaling pathway in catabolic effects mediated by mCRP.
REFERENCES:
[1] Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Front Immunol. 2018;9(APR). doi:10.3389/fimmu.2018.00754
[2] Francisco V, Pérez T, Pino J, et al. Biomechanics, obesity, and osteoarthritis. The role of adipokines: When the levee breaks. J Orthop Res. 2018;36(2):594-604. doi:10.1002/jor.23788
[3] Kozijn AE, Tartjiono MT, Ravipati S, et al. Human C-reactive protein aggravates osteoarthritis development in mice on a high-fat diet. Osteoarthr Cartil. 2019;27(1):118-128. doi:10.1016/j.joca.2018.09.007
[4] Rajab IM, Majerczyk D, Olson ME, et al. C-reactive protein in gallbladder diseases: diagnostic and therapeutic insights. Biophys Reports. 2020;6(2-3):49-67. doi:10.1007/s41048-020-00108-9
[5] Wu Y, Potempa LA, El Kebir D, Filep JG. C-reactive protein and inflammation: conformational changes affect function. Biol Chem. 2015;396(11):1181-1197. doi:10.1515/hsz-2015-0149
[6] Thiele JR, Zeller J, Bannasch H, Stark GB, Peter K, Eisenhardt SU. Targeting C-Reactive Protein in Inflammatory Disease by Preventing Conformational Changes. Mediators Inflamm. 2015;2015(372432):9. doi:10.1155/2015/372432
[7] Khreiss T, József L, Hossain S, Chan JSD, Potempa LA, Filep JG. Loss of pentameric symmetry of C-reactive protein is associated with delayed apoptosis of human neutrophils. J Biol Chem. 2002;277(43):40775-40781. doi:10.1074/jbc.M205378200
[8] Jia ZK, Li HY, Liang YL, Potempa LA, Ji SR, Wu Y. Monomeric C-reactive protein binds and neutralizes receptor activator of NF-κB ligand-induced osteoclast differentiation. Front Immunol. 2018;9(FEB). doi:10.3389/fimmu.2018.00234
[9] Francisco V, Ruiz-Fernández C, Pino J, et al. Adipokines: Linking metabolic syndrome, the immune system, and arthritic diseases. Biochem Pharmacol. 2019;165:196-206. doi:10.1016/j.bcp.2019.03.030
[10] Ullah N, Ma FR, Han J, et al. Monomeric C-reactive protein regulates fibronectin mediated monocyte adhesion. Mol Immunol. 2020;117:122-130. doi:10.1016/j.molimm.2019.10.013
[11] Boras E, Slevin M, Alexander MY, et al. Monomeric C-reactive protein and Notch-3 co-operatively increase angiogenesis through PI3K signalling pathway. Cytokine. 2014;69(2):165-179. doi:10.1016/j.cyto.2014.05.027
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4290

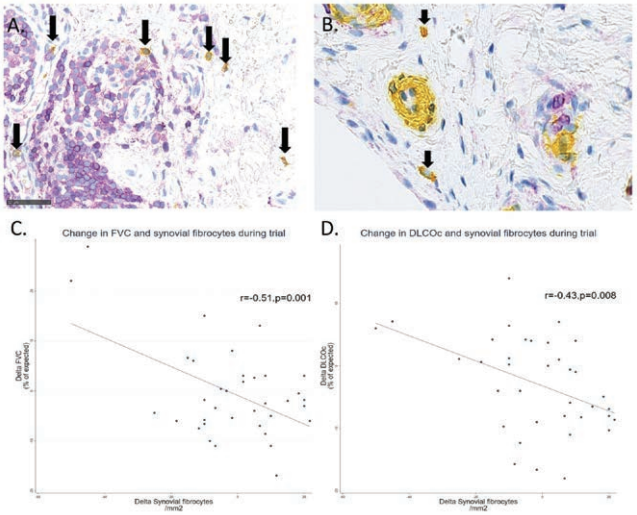
Rheumatoid arthritis - aetiology, pathogenesis and animal models

POS0377

FIBROCYTES IN EARLY AND LONGSTANDING RHEUMATOID ARTHRITIS: A 6-MONTH TRIAL WITH REPEATED SYNOVIAL BIOPSY, IMAGING, AND LUNG FUNCTION TEST

S. A. Just[1,2], C. Nielsen[3], J. Werlinrud[4], P. V. Larsen[5], E. K. Hejbøl[6], H. Tenstad[1], H. D. Schrøder[6], T. Barington[3], T. Torfing[7], F. Humby[8], H. M. Lindegaard[2]. *[1]Svendborg Hospital - Odense University Hospital, Department of Medicine, Svendborg, Denmark; [2]Odense University Hospital, Department of Rheumatology, Odense, Denmark; [3]Odense University Hospital, Department of Clinical Immunology, Odense, Denmark; [4]Odense University Hospital, Department of Orthopaedics, Odense, Denmark; [5]Region of Southern Denmark, Mental Health Services, Odense, Denmark; [6]Odense University Hospital, Department of Pathology, Odense, Denmark; [7]Odense University Hospital, Department of Radiology, Odense, Denmark; [8]Experimental Medicine and Rheumatology, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom*

Background: Fibrocytes are bone marrow-derived cells, that express both hematopoietic and stromal markers. In murine collagen-induced arthritis models circulating fibrocytes have been found to home to inflamed joints and enhance arthritis activity. The cell has, therefore, been proposed to be precursor cells for the fibroblast-like synoviocytes (FLS), which are central in the Rheumatoid Arthritis (RA) pathogenesis. Fibrocytes levels are further correlated with disease progression and mortality in interstitial lung disease (ILD) and identified as a new treatment target. ILD is also an extra-articular manifestation of RA (RA-ILD), leading to a reduced lung diffusion capacity and increased mortality.
Objectives: To correlate the level of fibrocytes in peripheral blood, synovial tissue, and *in vitro* culture in RA to changes in disease activity, imaging, and pulmonary function.
Methods: Twenty patients with early RA (ERA) and 20 patients with longstanding RA (LRA) were enrolled in a six months prospective study. Sixteen patients undergoing wrist arthroscopy were healthy controls. RA patients underwent pulmonary function tests, ultrasound, and synovial ultrasound-guided needle biopsy of the same wrist, at baseline and six months. Wrist magnetic resonance imaging was performed at baseline (all) and six months (ERA). Circulating fibrocytes were measured by flow cytometry, *in vitro* by the number of monocytes that were differentiated to fibrocytes, and in synovial biopsies by counting in histological sections.
Results: Fibrocyte levels did not decline during the trial despite effective RA treatment. Fibrocytes were primarily located around vessels and in the subintimal area in the synovium (Figure 1A and 1B, fibrocytes marked with arrows). In the ERA group, increased synovitis assessed by ultrasound was moderate and strongly correlated to respectively increase in circulating and synovial fibrocyte levels. Increased synovitis assessed by MRI during the trial in the ERA group, was moderately correlated to both increased numbers of circulating and cultured fibrocytes. Absolute diffusion capacity level was overall weakly negatively correlated to the level of circulating and synovial fibrocytes. The decline in forced ventilatory capacity and diffusion capacity during the trial was moderately correlated to increased levels of synovial fibrocytes (Figure 1C and 1D).
Conclusion: Our findings point to fibrocytes as key mediators of RA pathogenesis, and as a possible pathogenic link between the disease process in the synovium and RA lung affection. Studies are needed to investigate if the new therapies targeting fibrocyte differentiation/migration could be a path forward in RA/RA-ILD treatment.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.64

POS0378

CCN1: AN ANGIOGENIC ACTOR IMPLICATED IN THE STRUCTURAL DAMAGES OF RHEUMATOID ARTHRITIS

J. Avouac[1], A. Steelandt[2], O. Amiar[2], A. Leblond[2], A. Cauvet[2], V. Gonzalez[2], Y. Allanore[1]. *[1]Cochin Hospital, Rheumatology, Paris, France; [2]Cochin Institute, INSERM U1016, Paris, France*

Background: We have previously shown that decreased expression of the deacetylase sirtuin-1 (SIRT1) contributes to the proliferative, activated and proangiogenic profile of endothelial cells (EC) in rheumatoid arthritis (RA) (1). The matricellular protein CCN1, characterized by proangiogenic and immunomodulatory properties, may be directly implicated in these processes, since its expression is negatively regulated by SIRT1 (1).
Objectives: To study the implication of CCN1 in RA pathogenesis.
Methods: CCN1 expression was assessed in ECs (25 RA and 10 controls) by quantitative RT-PCR, western blot and ELISA, in the synovial tissue (5 RA and 5 controls) by immunohistochemistry and immunofluorescence, and in the serum (205 RA and 20 controls) by ELISA. Invalidation of CCN1 in RA ECs was achieved through the use of shRNA and neutralizing monoclonal antibodies. The functional consequences of CCN1 invalidation in RA ECs were studied i) *in vitro* by the analysis of proliferation (cell impedance), tube formation in Matrigel and migration in Boyden chambers; and ii) *in vivo* in the murine model of tumor neoangiogenesis.
Results: CCN1 mRNA and protein expression were increased by 1.72- ($p = 0.012$) and 7.2-fold ($p=0.008$) in RA ECs compared to controls, respectively. CCN1 concentrations were significantly increased in RA EC culture supernatants (930±153 vs. 359±199 pg/mL, $p=0.007$). CCN1 was overexpressed in the synovial tissue of RA patients (Figure 1A) and confocal microscopy analyses revealed a prominent CCN1 expression in the vascular endothelium (CD31 +) and T cells (CD3 +) (Figure 1B).
In vitro, recombinant TNF-α and IL-17 induced the mRNA and protein expression of CCN1 in RA ECs. CCN1 invalidation was associated with reduced proliferative capacities, delayed capillary tube formation and decreased migration of RA ECs (Figure 1E). *In vivo*, subcutaneous transplantation of CT26 tumor cells combined with RA ECs transfected with CCN1 shRNA to CB17 SCID mice was associated with a 51% reduction in tumor volume ($p=0.008$) and a 27% reduction in tumoral vascular density ($p=0.032$) compared with mice transplanted with MOCK transfected RA-ECs (Figure 1F).
Serum concentrations of CCN1 were significantly reduced in the serum of RA patients compared to controls (233±118 vs. 279±75 pg/mL, $p=0.045$) (Figure 1C). However, serum CCN1 concentrations were significantly higher in the presence of bone erosions (253±139 vs. 202±7 pg/mL, $p=0.002$) (Figure 1D) and correlated with radiographic Larsen score ($r=0.3$, $p=0.001$) and HAQ ($r=0.25$, $p=0.012$).
Conclusion: CCN1 is overexpressed in ECs and the synovial tissue of patients with RA. CCN1 also regulate the functional properties of RA ECs and their angiogenic potential *in vivo*. CCN1 could represent a new therapeutic target, which is being evaluated in experimental models of erosive arthritis.
CCN1 may be a reliable biomarker of structural damages given the association between its serum concentrations and the extent of radiographic lesions. The performance of CCN1 serum levels to predict structural progression is under investigation.
REFERENCES:
[1] Leblond et a, Ann Rheum Dis 2020.

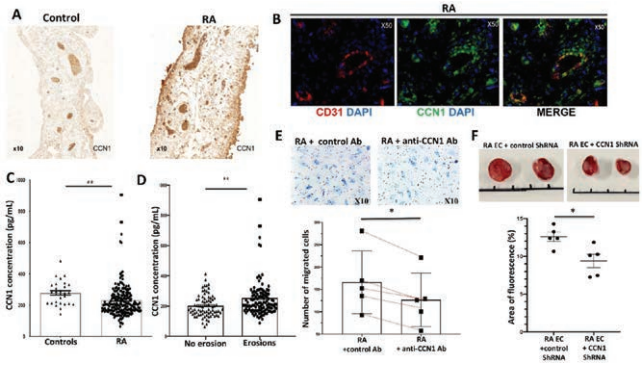


Figure 1. Implication of CCN1 in the pathogenesis of rheumatoid arthritis (RA). **A,** Representative immunohistochemistry staining for CCN1. **B,** Representative confocal microscopy analyses. **C-D**, CCN1 serum concentrations; statistical test: Student t test, ** $p<0.01$. **E,** Representative images of RA endothelial cell (EC) migration; Y-axis shows the number of migrated cells, statistical test: Wilcoxon test, * $p<0.05$. **F,** Representative subcutaneous tumors, Y-axis shows the fluorescence area in %, statistical test: Wilcoxon test, * $p<0.05$.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.979

POS0379

DETERMINING IN WHICH PRECLINICAL STAGE HLA-SHARED EPITOPE ALLELES AND SMOKING EXERT THEIR EFFECT IN THE DEVELOPMENT OF RHEUMATOID ARTHRITIS

F. Wouters[1], M. Maurits[2], L. van Boheemen[3], M. Verstappen[2], X. Matthijssen[2], E. Niemantsverdriet[2], R. Knevel[2], D. van Schaardenburg[3], R. Toes[2], A. van der Helm - van Mil[2,4]. *[1]Leiden University Medical Centre, Department of Rheumatology, Leiden, Netherlands*; *[1]Leiden University Medical Centre, Department of Rheumatology, Leiden, Netherlands*; *[3]Amsterdam Rheumatology and Immunology Centre, Reade, Department of Rheumatology, Amsterdam, Netherlands*; *[4]Erasmus University Medical Centre, Department of Rheumatology, Rotterdam, Netherlands*

Background: The HLA shared epitope (SE) and smoking are the best known genetic and environmental risk factors for rheumatoid arthritis (RA) development; however, at which pre-RA stage they exert their effect is unknown. The following stages are discerned: an asymptomatic stage in which autoimmune responses can develop, a symptomatic stage (clinically suspect arthralgia (CSA)), and development of clinically apparent inflammatory arthritis (IA). Studies in the general asymptomatic population revealed contrasting results on the associations between SE-alleles and smoking and the presence of anti-citrullinated protein antibodies (ACPA). Furthermore, studies on these risk factors in the symptomatic pre-RA phase are scarce and these data might teach us whether SE-alleles and smoking are involved in symptom development and/or progression to clinical arthritis.
Objectives: We aimed to determine at which pre-RA stage SE and smoking exert their effect. In this respect, the analyses were focused on the presence of ACPA, but associations for other anti-modified protein antibodies (anti-carbamylated and anti-acetylated protein antibodies (anti-CarP and AAPA, respectively)) were also studied.
Methods: Results from the literature on the association of SE and smoking with ACPA in the asymptomatic population were summarized in inverse-variance weighted meta-analyses. In addition 577 CSA-patients were studied. Associations of SE and smoking with IgG ACPA were studied at baseline (CSA-onset), to assess an effect on symptom development. Additionally, patients were monitored for the development of clinically apparent inflammatory arthritis (IA) for median 2 years and associations of SE, smoking and auto-antibodies with progression to IA were determined. Analyses were stratified for ACPA-status and associations in ACPA-positive patients were validated in meta-analyses with other arthralgia-cohorts. Finally analyses were repeated for anti-CarP and AAPA.
Results: Meta-analyses showed that SE is not associated with ACPA-positivity in the asymptomatic population (OR 1.06 (95%CI 0.69-1.64)), whereas smoking was associated (OR 1.37 (1.15-1.63)). At CSA-onset, both SE and smoking associated with ACPA-positivity (OR 2.08 (1.24-3.49) and OR 2.41 (1.31-4.43), respectively). During follow-up of CSA-patients SE associated with IA-development (HR 1.86 (1.23-2.82)), in contrast to smoking. SE conferred risk for IA-development in ACPA-negative CSA-patients (HR 1.71 (0.99-2.96)) and in ACPA-positive patients (CSA-cohort HR 1.29 (0.67-2.47); meta-analysis three arthralgia-cohorts HR 1.52 (1.08-2.15)). Investigating the other autoantibodies revealed that SE and smoking were not associated with anti-CarP or AAPA-positivity at CSA-onset; longitudinally AAPA associated with progression to IA independent from ACPA and RF (HR 1.79 (1.02-3.16)), whilst anti-Carp did not.
Conclusion: SE and smoking act in partly different pre-RA stages. Although SE does not associate with ACPA in the general population, it does mediate symptom-development and further progression to clinical arthritis. Smoking confers risk to development of ACPA and/or joint symptoms, but is not further involved in IA-development. The time-specific biologic pathways that are underlying need further exploration. These data enhance the understanding of the timing of key genetic and environmental risk factors in the trajectory of RA development.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1342

POS0380

HORMONES OF ADIPOSE TISSUE IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAVE REDUCED BODY WEIGHT

L. Arefeva[1], G. Kravtsov[2], V. Polyakov[2], V. Kravtsov3, L. Seewordova[4]. *[1]Volgograd State Medical University, Cardiology of University Clinical, Volgograd, Russian Federation*; *[2]Volgograd State Medical University, University Clinical, Volgograd, Russian Federation*; *[1]Volgograd State Medical University, Cardiology of University Clinical, Volgograd, Russian Federation*; *[4]Federal State Budgetary Institution «Zborovsky Research Institute of Clinical and Experimental Rheumatology», Laboratory Methods of Treatment and Prevention of Joint Diseases, Volgograd, Russian Federation*

Background: Overweight in patients with rheumatic diseases is a condition that prolongs chronic inflammation and promotes synthesis and secretion of pro-inflammatory factors by adipose tissue, such as classical cytokines, tumor necrosis factor-α (TNF-α), adipokines (leptin, adiponektin, resistin) and other newly identified proinflammatory factors (fetuin A, nesfatin, hemerin, lipokain, serum amyloid protein 3) [1,2,3,4].
Objectives: We investigated the relationship the effect of weight loss over 5 kg on the clinical manifestations of arthritis and hormones of adipose tissue serum levels in patients with rheumatoid arthritis (RA).
Methods: We observed 80 female patients with RA (EULAR/ARA 2010 criteria) ranged in age from 39 to 69 years (mean age 51,72 ± 5,83 years) and the control group (60 healthy persons) with no complaints of pain in the joints over a lifetime, and without clinical signs of RA. Fetuin A, nesfatin, hemerin, leptin, adiponektin, resistin, visfatin level in serum was determined by ELISA-test using a commercial test systems.
Results: As overweight patients were recruited in the study, hypocaloric diet low in animal fats and physiotherapy has been recommended to all participants. The positive dynamics in body weight loss over 5kg within 3 months has been achieved by 34 patients (27,2%). In RA patients with weight loss, a significant decrease in the serum level of pro-inflammatory cytokines (fetuin A, nesfatin, hemerin, leptin, adiponektin, resistin, visfatin ($p<0.01$)) and an increase in the quality of life according to the EQ-5D-5L ($p<0.001$) index were observed. This fact is probably explained by the decreased activity of inflammatory process after RA therapy and weight reduction.
Conclusion: Thus, as a result of our study patients with RA with weight loss of more than 5 kg had more obvious pain relief than patients with the original weight. These findings suggest that there is a possible role of tissue pro-inflammatory cytokines in the pathogenesis of rheumatoid arthritis. All patients with RA with a BMI over 25 kg / m ^{2} are recommended to lower their weight to decrease the mechanical stress on the joints, and also to reduce the severity of inflammation and metabolic disorders.
REFERENCES:
[1] Akhverdyan, Y. et al. The nicotinamide-phosphoribosiltransferase as a marker of systemic inflammation under osteoarthrosis // Klin Lab Diagn. 2017; 62(10):606-610.
[2] Kravtcov, V. et al. High level of adipokines and overweight as factors contributing to osteoarthritis progression // Osteoporosis International, 2019. V.30 (2). S. 408.
[3] Papichev, E. V. et al. Parameters of mineral-bone metabolism and fetuin-A level in patients with rheumatoid arthritis // Osteoporosis International, 2019. V.30 (2), S.381.
[4] Polyakova J. et al. Tissue cytokines and their role in the pathogenesis of rheumatic diseases // Annal.Rheum.Diseases, 2019. T. 30 (2), № S.387.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1432

POS0381

PATIENTS AT RISK FOR RA SHOW THE SAME AMOUNT OF ACUTE SOLUBLE CARTILAGE DEGRADATION MARKERS AFTER PHYSICAL ACTIVITY COMPARED TO PATIENTS WITH ESTABLISHED RA

L. Bleckwedel-Rolack[1], K. Tascilar[1], V. Nees[1], J. Hühne[1], A. Hueber[2], J. Rech[1], G. Schett[1], A. Kleyer[1], A. M. Liphardt[1]. *[1]Friedrich-Alexander-University Erlangen-Nürnberg & University Hospital Erlangen, Internal Medicine 3 - Rheumatology & Immunology, Erlangen, Germany*; *[2]Sozialstiftung Bamberg - Klinikum am Bruderwald, Rheumatology, Bamberg, Germany*

Background: Serum concentration of cartilage oligomeric matrix protein (COMP) is related to the degree of cartilage destruction in patients with rheumatoid arthritis (RA) and shows a mechanosensitive response to ambulatory loads. We showed previously, that individuals with positive for anti-citrullinated protein antibody (ACPA+) status already show bone loss. It is unclear if these individuals experience cartilage deterioration and how this is related to physical activity.
Objectives: To test whether soluble COMP levels in ACPA+ display the same response as RA patients after a walking exercise and explore the association between overall serum COMP levels and physical activity.
Methods: RA patients and ACPA+ individuals (IRACE cohort: Individuals at Risk for Arthritis Cohort Erlangen; Ethics approval 334_16B) were enrolled in the study after written informed consent. Inclusion criteria were age between 18 and 69 years, RA (by 2010 ACR/EULAR criteria) or ACPA+ (without clinical manifestation of RA and prior treatment with glucocorticoids, DMARDs and biologics). The study comprised three visits (baseline (Visit 1), 6 (Visit 2), and 12 months (Visit 3). During each visit, serum samples were collected after 30 minutes rest (pre) and at 0, 30, 60, and 120 minutes after a 30-minute walking exercise. Serum COMP concentration was analyzed by commercial ELISA. Physical activity duration (hours) was measured using an activity monitor for 7 consecutive days, and physical activity level (metabolic equivalent of the task (MET)) was quantified using the International Physical Activity Questionnaire (IPAQ). The reponse of COMP levels to the walking exercise was modelled using linear mixed-effects regression models. The association between physical activity and overall serum

COMP concentrations was analyzed using a mixed-effects regression model (Random effects: individuals, visits and COMP measurement time points).

Results: 28 RA and 22 ACPA+ patients participated in this prospective study. Table 1 summarizes patient demographics and outcome measures. Serum COMP levels increased in response to the walking exercise in both groups but the acute response was not different in RA patients compared to ACPA+ individuals. Higher physical activity level by IPAQ was associated with higher overall COMP concentration. Doubling of total physical activity is associated with an increase in serum concentration of 0.32 U/L (95%CI 0.09 to 0.54, p=0.006). ACPA+ individuals but not RA patients show an association between serum COMP concentration and physical activity duration (Figure 1).

Table 1. Summary of subject characteristics and outcome measures.

Descriptives						
Measure	**ACPA+**	**RA**				
individuals, number (%)	22 (44.0)	28 (56.0)				
Age, years (mean (SD))	47.6 (12.8)	57.0 (9.1)				
Female, number (%)	14 (28.0)	19 (38.0)				
BMI, kg/m^2, mean (SD)	25.1 (5.6)	27.2 (5.8)				
Anti-CCP positive (N)	17	14				
DAS28-score, mean (SD)	2.5 (1.2)	2.7 (1.4)				
Cartilage Oligomeric Matrix Protein (U/l)						
	Visit 1		**Visit 2**		**Visit 3**	
	ACPA+	**RA**	**ACPA+**	**RA**	**ACPA+**	**RA**
pre-walking exercise	9.4 (2.8)	9.7 (3.8)	10.8 (2.2)	11.3 (4.5)	10.2 (2.5)	10.5 (3.9)
0	9.5 (2.6)	10.4 (3.9)	11.8 (1.8)	12.2 (4.0)	10.1 (2.0)	11.1 (4.6)
30	9.2 (2.2)	9.9 (3.6)	10.8 (1.9)	11.4 (4.4)	9.2 (2.2)	10.6 (4.2)
60	9.2 (2.0)	9.4 (4.0)	10.4 (2.1)	10.9 (4.5)	8.6 (2.9)	10.0 (4.0)
120	9.2 (2.1)	9.5 (4.0)	9.6 (1.8)	10.9 (4.4)	8.0 (2.4)	9.9 (3.9)

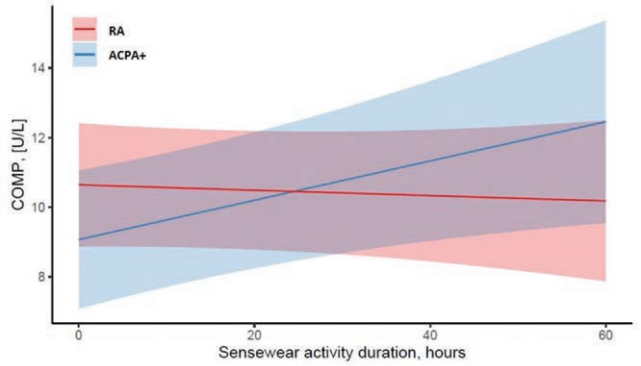


Figure 1. Estimated marginal mean COMP by physical activity duration for RA and ACPA+.

Conclusion: Pre-exercise serum COMP concentration is similar in ACPA+ and RA and shows a similar increase in response to walking in both groups. Physical activity duration appears to influence serum COMP concentration in ACPA+. Given that acute COMP release was not different between ACPA+ and RA while overall COMP values are associated with physical activity level, the discrepancy between ACPA+ and RA for this association can be explained by reduced vigor or qualitative differences in physical activity.

Disclosure of Interests: Lisa Bleckwedel-Rolack: None declared, Koray Tascilar: None declared, Veronika Nees: None declared, Julia Hühne: None declared, Axel Hueber: None declared, Jürgen Rech Speakers bureau: Abbvie, Biogen, BMS, Chugai, GSK, Lilly, MSD; Mylan, Novartis, Roche, Sanofi, Sobi, UCB, Consultant of: Abbvie, Biogen, BMS, Chugai, GSK, Lilly, MSD; Mylan, Novartis, Roche, Sanofi, Sobi, UCB, Grant/research support from: Novartis, Sobi, Georg Schett Speakers bureau: Lilly, Novartis, Consultant of: Lilly, Novartis, Gilead, BMS, Abbvie, Grant/research support from: Lilly, Novartis, Arnd Kleyer Speakers bureau: Lilly, Novartis, Consultant of: Lilly, Novartis, Gilead, BMS, Abbvie, Grant/research support from: Lilly, Novartis, Anna-Maria Liphardt Speakers bureau: Mylan, Paid instructor for: Abbvie, Consultant of: MEDA Pharma, Grant/research support from: Novartis

DOI: 10.1136/annrheumdis-2021-eular.1527

POS0382 EXPANSION OF CD4+/CD8+ DOUBLE-POSITIVE T CELLS IS ASSOCIATED WITH A SEVERE DISEASE COURSE IN RHEUMATOID ARTHRITIS

P. Nguyen[1], K. Rothe[1], M. Melzer[1], M. Krasselt[1], M. Pierer[1], U. Wagner[1].
[1]Leipzig University Hospital, Rheumatology, Leipzig, Germany

Background: CD4$^+$/CD8$^+$ double-positive T (dpT) cells are a set of pathologic T cells, representing about 1% of peripheral blood T cells and increasing with age in healthy individuals. Patients with rheumatoid arthritis (RA) more frequently have expanded dpT cells compared to age-matched controls, up to a frequency of 8% [1]. However, whether dpT cell expansion harbors clinical significance in RA is not known.

Objectives: The goal of the study was to assess possible associations of DPT expansion with clinical features of patients with RA.

Methods: In this cross-sectional study, dpT cells were measured in RA patients (n=70) via fluorescence-activated flow cytometry. Clinical data including age, sex, disease duration, treatment history, disease activity parameters, and radiographic structural damage was collected. Radiographs of hands and feet were used to determine the modified Sharp/van der Heijde (SvdH) score. Expansion of dpT cells was defined as a frequency of >2% of the total T cell pool, based on reference ranges determined in a large cohort of healthy individuals [2]. Mann-Whitney-U test was used to compare groups and X^2 test was used for contingency tables. Statistical analyses were conducted using GraphPad Prism v8 (GraphPad Software, San Diego, USA).

Results: DpT cells were expanded in more than a quarter of our cohort (n=19, 27.1%). Patients with expanded dpT cells more often used biologics or targeted synthetic DMARDs than patients with low dpT cells (68.4% vs. 38%, p=0.02). Radiographic damage was also significantly worse in patients with DPT expansion, as shown in their higher SvdH score (median 24.5 vs. 6, p=0.008) and its component scores for erosion (median 19 vs. 0, p=0.004) and joint space narrowing (median 8 vs. 2, p=0.017) (figure 1A). There was no difference regarding sex, age, disease duration, seropositivity and disease activity between the groups (figure 1B).

Conclusion: DpT cell expansion is associated with higher scores of radiographic structural damage despite more frequent use of highly effective therapeutics. An expansion of dpT cells is not uncommon in RA, and affected patients represent a subset at high risk for a more severe disease course.

REFERENCES:

[1] Quandt D, Rothe K, Scholz R, *et al.* Peripheral CD4CD8 Double Positive T Cells with a Distinct Helper Cytokine Profile Are Increased in Rheumatoid Arthritis. *PLoS ONE* 2014;**9**:e93293. doi:10.1371/journal.pone.0093293

[2] Apoil PA, Puissant-Lubrano B, Congy-Jolivet N, *et al.* Reference values for T, B and NK human lymphocyte subpopulations in adults. *Data Brief* 2017;**12**:400–4. doi:10.1016/j.dib.2017.04.019

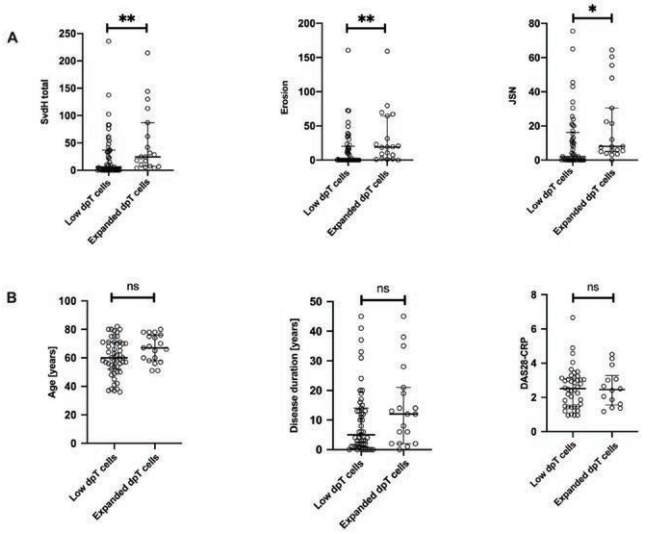


Figure 1. DpT cell expansion is associated with radiographic progression. SvdH, modified Sharp/van der Heijde Score; DpT, CD4$^+$/CD8$^+$ double-positive T cells.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1533

POS0383 EFFECTS OF TOFACITINIB THERAPY ON ARGININE AND METHIONINE METABOLITES IN ASSOCIATION WITH VASCULAR PATHOPHYSIOLOGY IN RHEUMATOID ARTHRITIS: A METABOLOMIC APPROACH

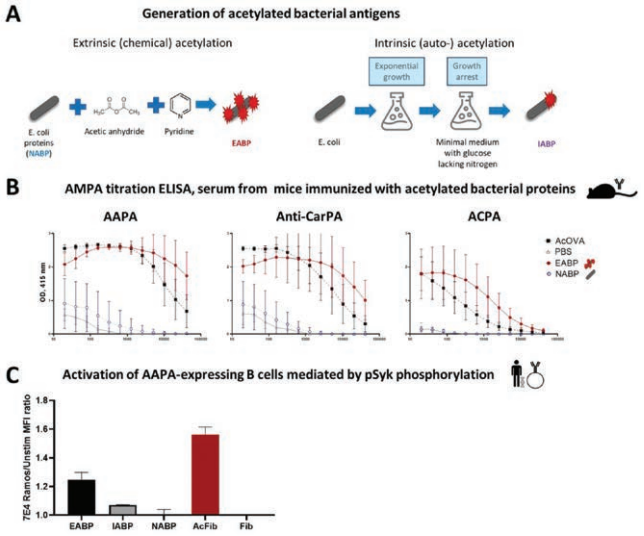
B. Soós[1], A. Hamar[1], A. Pusztai[1], M. Czókolyová[1], E. Végh[1], S. Szamosi[1], Z. Pethő[1], K. Gulyás[1], G. Kerekes[2], É. Szekanecz[3], S. Szántó[1], G. Szücs[1], U. Christians[4], J. Klawitter[4], T. Seres[4], Z. Szekanecz[1]. *[1]University of Debrecen, Rheumatology, Debrecen, Hungary*; *[2]University of Debrecen, Medicine, Debrecen, Hungary*; *[3]University of Debrecen, Oncology, Debrecen, Hungary*; *[4]University of Colorado Anschutz Medical Campus, Anesthesiology, Aurora, CO, United States of America*

Background: Rheumatoid arthritis (RA) has been associated with increased cardiovascular (CV) risk and metabolic changes.
Objectives: We wished to determine how the Janus kinase (JAK) inhibitor tofacitinib influences vascular pathophysiology and metabolites of the arginine and methionine-homocysteine pathways.
Methods: Thirty RA patients with active disease were treated with either 5 mg bid or 10 mg bid tofacitinib and evaluated at baseline and after 6 and 12 months. We determined DAS28, CRP, IgM rheumatoid factor (RF) and anti-cyclic citrullinated peptide (aCCP) levels. We assessed brachial artery flow-mediated vasodilation (FMD), carotid intima-media thickness (IMT) and pulse-wave velocity (PWV) by ultrasound. We also determined plasma L-arginine, L-citrulline, L-ornithine, inducible nitric oxide synthase (iNOS), asymmetric (ADMA) and symmetric dimethylarginine (SDMA), L-N-monomethyl-arginine (L-NMMA), cysteine, homocysteine, and methionine levels.
Results: Twenty-six patients completed the study. Tofacitinib treatment maintained FMD and PWV. Ten mg bid tofacitinib significantly increased L-arginine, L-ornithine, iNOS and methionine levels after 12 months. Tofacitinib transiently increased L-citrulline and L-NMMA and decreased homocysteine levels after 12 months. Based on L-citrulline, L-ornithine, ADMA and SDMA levels, L-arginine remained highly available for endothelial NO production. Multivariate analysis indicated variable correlations of L-arginine, L-citrulline, ADMA, L-NMMA, homocysteine and methionine with DAS28, CRP, ESR and RF but not with aCCP. Regarding vascular pathophysiology, only PWV and methionine correlated with each other after 12 months.
Conclusion: Tofacitinib suppressed systemic inflammation in RA yielding stabilization of vascular function. It may exert CV protective effects in RA, at least in part, by shifting L-arginine metabolism to high arginine availability and decreasing homocysteine levels.
Acknowledgements: This research was supported by the European Union and the State of Hungary and co-financed by the European Social Fund in the framework of TAMOP-4.2.4.A/2-11/1-2012-0001 'National Excellence Program '(Z.S.); by the European Union grant GINOP-2.3.2-15-2016-00015 (Z.S.) and by the WI188341 investigator-initiated research (IIR) grant obtained from Pfizer US (Z.S.).
Disclosure of Interests: Boglárka Soós: None declared, Attila Hamar: None declared, Anita Pusztai: None declared, Monika Czókolyová: None declared, Edit Végh: None declared, Szilvia Szamosi Speakers bureau: Roche, Zsófia Pethö: None declared, Katalin Gulyás: None declared, György Kerekes: None declared, Éva Szekanecz: None declared, Sándor Szántó Speakers bureau: Abbvie, MSD, Novartis, Consultant of: Abbvie, Novartis, Gabriella Szücs Speakers bureau: Actelion, Roche, Sager, Boehringer, Consultant of: Boehringer, Actelion, Sager, Uwe Christians: None declared, Jelena Klawitter: None declared, Tamas Seres: None declared, Zoltán Szekanecz Speakers bureau: Pfizer, Abbvie, Roche, Lilly, Novartis, Boehringer, Consultant of: Pfizer, Abbvie, Novartis, Grant/research support from: Pfizer
DOI: 10.1136/annrheumdis-2021-eular.1697

POS0384 A NOVEL MECHANISM LINKING MUCOSAL BACTERIA WITH AUTOANTIBODY RESPONSES IN RA: ACETYLATED BACTERIAL LYSATE AS A MODEL ANTIGEN

M. Volkov[1], A. S. B. Kampstra[1], K. van Schie[1], J. Kwekkeboom[2], T. Huizinga[2], R. Toes[1], D. van der Woude[1]. [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [2]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*

Background: Rheumatoid arthritis (RA) is characterized by autoantibodies against post-translationally modified proteins (AMPA) such as citrullinated, carbamylated and acetylated proteins. Importantly, these antibodies are highly multireactive, as they often recognize more than one of these post-translational modifications. Despite extensive research, the antigens inducing the breach of tolerance remain unknown, although microbial antigens are often suspected. Various bacteria are known to be capable of acetylation, therefore, it is intriguing to know what mechanisms can underlie the breach of tolerance towards acetylated proteins and development of anti-acetylated protein antibodies (AAPA).
Objectives: To investigate whether acetylated proteins of bacterial origin (1) are recognized by human derived AMPA and AMPA expressing B cells; and (2) can induce AMPA development when used to immunize mice.
Methods: Acetylated E. coli proteins were acquired with two separate methods (Figure 1A): by culturing E. coli in a condition promoting auto-acetylation (intrinsically acetylated bacterial proteins, IABP), or by directly acetylating lysate-derived proteins via a chemical reaction (extrinsically acetylated BP, EABP). Acetylated ovalbumin (AcOVA) served as positive control for AAPA induction in mice, non-acetylated BP (NABP) and phosphate buffer saline (PBS) served as negative control. Mice were immunized with these proteins and the resulting antibody response was studied by ELISA. Furthermore, EABP/IABP/NABP were investigated for recognition by human-derived AAPA with ELISA and AAPA-expressing B cells with spleen tyrosine kinase (Syk) phosphorylation assay; acetylated human fibrinogen and native fibrinogen served as positive and negative control.
Results: Repetitive immunization of mice with EABP resulted in an AMPA response recognizing acetylated, carbamylated and citrullinated proteins. AMPA titers in these mice exceeded the titers in the positive control mice immunized with AcOVA and were substantially higher than in the NABP-immunized mice (Figure 1B). Human-derived monoclonal AAPA recognized EABP and IABP (not shown). B cell activation (measured by Syk phosphorylation) assay indicated that AAPA expressing B cells recognized EABP and (to a lesser extent) IABP, but not NABP (Figure 1C).
Conclusion: Acetylated bacterial proteins are potent antigens that can induce cross-reactive AMPA responses in mice and they are recognized by human AAPA. This suggests that acetylated bacterial proteins could possibly be involved in the breach of tolerance in RA.



Acknowledgements: We thank Dr. Can Araman and Prof. Chunaram Choudhary for their advice regarding optimization of bacterial auto-acetylation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1709

POS0385 DURING DEVELOPMENT OF RHEUMATOID ARTHRITIS, INTERMETATARSAL BURSITIS MAY OCCUR BEFORE CLINICAL JOINT SWELLING: A LARGE MRI STUDY IN PATIENTS WITH CLINICALLY SUSPECT ARTHRALGIA

B. van Dijk[1], F. Wouters[1], E. van Mulligen[1,2], M. Reijnierse[1], A. van der Helm - van Mil[1,2]. [1]*Leiden University Medical Centre (LUMC), Rheumatology, Leiden, Netherlands*; [2]*Erasmus Medical Centre (EMC), Rheumatology, Rotterdam, Netherlands*

Background: Inflammation of the synovial lining is a hallmark of rheumatoid arthritis (RA). A synovial lining is not only present at synovial joints and tendon sheaths but also at bursae. Inflammation of the synovium-lined intermetatarsal bursae in the forefoot, intermetatarsal bursitis (IMB), was recently identified with MRI. It is specific for early RA and present in the majority of RA patients at diagnosis. During development of RA, MRI-detectable subclinical synovitis and tenosynovitis often occur before clinical arthritis presents. Whether IMB is also present in a pre-arthritis stage is unknown.
Objectives: To assess the occurrence of IMB in patients with clinically suspect arthralgia (CSA) and its association with progression to clinical arthritis in a large MRI-study.
Methods: We studied 524 consecutive patients presenting with CSA. CSA was defined as recent-onset arthralgia of small joints that is likely to progress to RA based on the clinical expertise of the rheumatologist. Participants underwent unilateral contrast-enhanced 1.5T MRI of the forefoot, metacarpophalangeal (MCP) joints and wrist at baseline. Thereafter patients were followed for detection of clinical arthritis, as identified at physical joint examination by the rheumatologist. Baseline MRIs were evaluated for IMB at all 4 intermetatarsal spaces. Also synovitis, tenosynovitis and osteitis were

assessed in line with the RA MRI scoring system (summed as RAMRIS-inflammation). Both IMB and RAMRIS-inflammation were dichotomised into positive/negative using data from age-matched symptom-free controls as a reference. Cox regression analysed the association of IMB with progression to clinical arthritis; multivariable analyses were used to adjust for RAMRIS-inflammation which is known to associate with progression to clinical arthritis. Analyses were repeated stratified for ACPA-status, since ACPA-positive and ACPA-negative RA are considered separate entities with differences in pathophysiology.

Results: The baseline MRIs showed ≥1 IMB in 35% of CSA-patients. Patients with IMB were more likely to also have synovitis (OR 2.5 (95%CI 1.2–4.9)) and tenosynovitis (8.9 (3.4–22.9)) on forefoot MRI, but not osteitis (0.9 (0.5–1.8)). Patients were followed for median 25 months (IQR 19–27). IMB-positive patients developed clinical arthritis more often than IMB-negative patients (HR 3.0 (1.9-4.8)). This association was independent of RAMRIS-inflammation (adjusted HR 2.2 (1.4–3.6)). In stratified analyses, IMB was more frequent in ACPA-positive than in ACPA-negative CSA (68% vs. 30%, p<0.001). Moreover IMB predicted clinical arthritis development in ACPA-positive CSA (HR 2.5 (1.1–5.7)) but not in ACPA-negative CSA patients (1.0 (0.5–2.2)).

Conclusion: One-third of CSA patients have IMB. IMB is frequently present in conjunction with subclinical synovitis and tenosynovitis. It precedes the development of clinical arthritis, and in particular the development of ACPA-positive RA. These results reinforce the notion that not only intra- but also juxta-articular synovial inflammation is involved in the development of RA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1710

POS0386 EVOLUTION OF ANTI-MODIFIED PROTEIN ANTIBODY RESPONSES CAN BE DRIVEN BY CONSECUTIVE EXPOSURE TO DIFFERENT POST-TRANSLATIONAL MODIFICATIONS

M. Volkov[1], A. S. B. Kampstra[1], K. van Schie[1], A. Kawakami[2], M. Tamai[2], S. Y. Kawashiri[3], T. Maeda[4], T. Huizinga[1], R. Toes[1], D. van der Woude[1]. *[1]Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; *[2]Nagasaki University Graduate School of Biomedical Sciences, Immunology and Rheumatology, Nagasaki, Japan*; *[3]Nagasaki University Graduate School of Biomedical Sciences, Community Medicine, Nagasaki, Japan*; *[4]Nagasaki University Graduate School of Biomedical Sciences, General Medicine, Nagasaki, Japan*

Background: Besides anti-citrullinated protein antibodies (ACPA), rheumatoid arthritis patients (RA) often display autoantibody reactivities against other post-translationally modified (PTM) proteins, more specifically carbamylated and acetylated proteins. Immunizing mice with one PTM results in an anti-modified protein antibody (AMPA) response recognizing multiple PTMs. Furthermore, human AMPA, isolated based on their reactivity to one PTM, cross-react with other PTMs at the monoclonal and polyclonal level. However, it is unclear whether the AMPA reactivity profile is "fixed" in time, or whether consecutive exposure to different PTMs can shape the evolving AMPA-response.

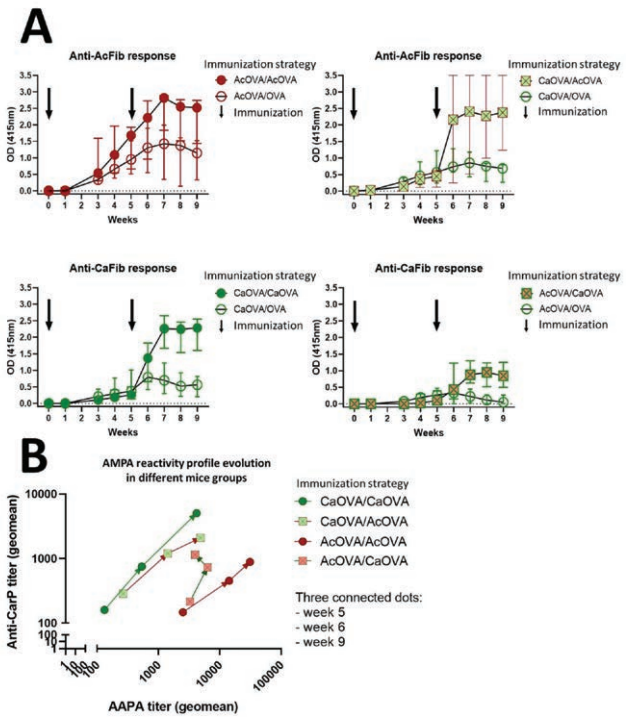
Objectives: To investigate the evolution of the AMPA response in mice with controlled exposure to PTMs as well as in AMPA-positive humans.

Methods: Mice were immunized with acetylated (or carbamylated) protein (ovalbumin) twice or cross-immunized with an acetylated and then a carbamylated protein (or vice versa) and their serum was analyzed for AMPA responses with ELISA using a different backbone protein (fibrinogen) bearing the same modifications. Longitudinally collected serum samples of human individuals at risk of RA and with early RA were tested to investigate the evolution of the AMPA responses in humans.

Results: Mice immunized twice with either solely acetylated or solely carbamylated ovalbumin (AcOVA or CaOVA) developed reactivity against both acetylated and carbamylated antigens. Irrespective of the PTM used for the first immunization, a booster immunization with the other PTM resulted in increased titers to the second/booster PTM (Figure 1A), suggesting that immunization with a defined PTM-antigen leads to the generation of anti-PTM memory B cells able to cross-recognize other PTMs. Furthermore, immunizing with CaOVA and boosting with AcOVA (or vice versa) skewed the overall AMPA-response profile towards a relatively higher reactivity against the "booster" PTM (Figure 1B). Human data also illustrated dynamic changes in AMPA reactivity profiles in both individuals at risk of RA and in early RA patients (not shown).

Conclusion: The relationship between different reactivities within the AMPA response is dynamic. The initial exposure to a PTM antigen induces cross-reactive response that can be boosted by the same or other PTMs. The overall reactivity pattern can be skewed by subsequent exposure to other PTMs. These data might explain temporal changes in the reactivity profile of the AMPA response and point to the possibility that the PTM responsible for the initiation of the AMPA response may differ from the PTM predominantly recognized later in time.

Cross-boosting and skewing of AMPA responses in immunized mice



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1743

POS0387 ACPA STATUS CORRELATES WITH DIFFERENTIAL IMMUNE PROFILE OF RHEUMATOID ARTHRITIS PATIENTS

A. Floudas[1], M. Canavan[1], T. McGarry[1], V. Krishna[2], S. Nagpal[2], D. Veale[3], U. Fearon[1]. *[1]Trinity Biomedical Sciences Institute, Molecular Rheumatology, DUBLIN, IRELAND, Ireland*; *[2]Janssen Research & Development, Immunology, Spring House, United States of America*; *[3] St Vincent's University Hospital, UCD, EULAR Centre of Excellence, Centre for Arthritis and Rheumatic Diseases, Dublin, Ireland*

Background: Rheumatoid arthritis (RA) is a progressive erosive autoimmune disease that affects 1% of the world population. Anti-citrullinated protein autoantibodies (ACPA) are routinely used for the diagnosis of RA, however 20-30% of patients are ACPA negative. ACPA status is a delineator of RA disease endotypes with similar clinical manifestation but potentially different pathophysiology. Elucidating the underlying mechanisms of disease pathogenesis could inform a treat to target approach for both ACPA-positive and ACPA-negative RA patients.

Objectives: To identify peripheral blood and synovial tissue immune population differences that associate with RA disease endotype.

To identify unique RA patient synovial tissue gene signatures and enriched pathways that correlate with ACPA status.

Methods: Detailed high dimensionality flow cytometric analysis with supervised and unsupervised algorithm analysis of ACPApos and ACPAneg RA patient peripheral blood and synovial tissue single cell suspensions. *Ex vivo* peripheral blood and synovial tissue T cell stimulation and cytokine production characterisation. RNAseq analysis with specific pathway enrichment analysis of APCApos and ACPAneg RA patient synovial tissue biopsies.

Results: Detailed profiling based on high dimensionality flow cytometric analysis of key peripheral blood and synovial tissue immune populations including B cells, T follicular helper (Tfh) cells, T peripheral helper cells (Tph) and CD4 T cell proinflammatory cytokine responses with supervised and unsupervised algorithm analysis revealed unique RA patient peripheral blood B cell and Tfh cell profiles. ACPApos RA patients were characterised by significantly (*P=0.03) increased frequency of Tfh ($CXCR5^+CD4^+$) cells and distinct clustering influenced by increased switched (IgD^-CD27^+) and DN (IgD^-CD27^-) memory B cells compared to APCAneg RA patients. Surprisingly synovial tissue B cell subpopulation distribution was similar between ACPAneg and ACPApos RA patients, with significant accumulation of switched and double negative memory B cells, highlighting a key role for specific B cell subsets in both disease endotypes. Interestingly, synovial tissue CD4 T cell

proinflammatory cytokine (TNF-α, IFN-γ, IL-2, GM-CSF, IL-17A, IL-22, IL-4) production was markedly different between ACPAneg and APCApos RA patients with hierarchical clustering and PCA analysis revealing endotype specific cytokine profiles with ACPAneg RA patient synovial T cells showing increased TNF-α (P=0.01) expression. RNAseq analysis of RA patient synovial tissue revealed significant disease endotype specific gene signatures with specific enrichment for B cell receptor signalling and T cell specific pathways in ACPApos compared to ACPAneg RA patients. Additionally, significantly different chemokine receptor expression based on RA patient ACPA status was observed with increased CXCR3 (P<0.001), CCR7 (P=0.002), and CCR2 (P=0.004) but decreased CXCR7 (P=0.007) expression in APCApos compared to ACPAneg RA patient synovial biopsies.

Conclusion: ACPA status associates with unique synovial tissue immune cell and gene profile signatures highlighting differences in the underlying immunological mechanisms involved, therefore reinforcing the need for a treat to target approach for both endotypes of RA.

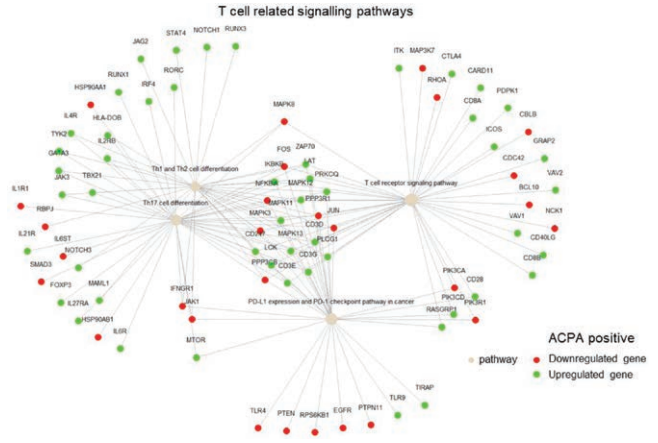


Figure 1. RNAseq analysis of synovial tissue biopsies revealed specific T cell related pathway enrichment in ACPA positive compared to ACPA negative RA patients (n=50, analysis performed with the *DESq2* and *pathfindeR* pipelines in *R*).

Disclosure of Interests: Achilleas Floudas: None declared, Mary Canavan: None declared, Trudy McGarry Employee of: Novartis, Vinod Krishna Employee of: Janssen, Sunil Nagpal Employee of: Janssen, GSK, Douglas Veale Speakers bureau: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Consultant of: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Grant/research support from: Janssen, Abbvie, Pfizer, UCB, Ursula Fearon Speakers bureau: Abbvie, Grant/research support from: Janssen, Abbvie, Pfizer, UCB

DOI: 10.1136/annrheumdis-2021-eular.1885

POS0388 INTERLEUKIN 40 (IL-40) IS UP-REGULATED IN RHEUMATOID ARTHRITIS (RA) AND ASSOCIATED WITH DISEASE ACTIVITY, LEVELS OF AUTOANTIBODIES AND CHEMOKINES

A. Navrátilová[1,2], L. Andres Cerezo[1,2], H. Hulejova[1], V. Becvar[1], D. Tegzová[1,2], M. Olejárova[1,2], D. Veigl[3], K. Pavelka[1,2], J. Vencovský[1,2], L. Šenolt[1,2]. [1]*Institute of Rheumatology, Department of Experimental Rheumatology, Prague, Czech Republic*; [2]*First Faculty of Medicine Charles University, Department of Rheumatology, Prague, Czech Republic*; [3]*First Faculty of Medicine Charles University, First Orthopaedic Clinic, Prague, Czech Republic*

Background: Interleukin 40 (IL-40) is newly identified B cell - associated cytokine implicated in humoral immune responses and in B cell development. As B cells play a pivotal role in autoimmunity, we aimed to investigate the function of IL-40 in rheumatoid arthritis (RA).

Objectives: The aim of our study was to determine the function of IL-40 in RA.

Methods: IL-40 expression in the synovial tissue was determined by immunohistochemistry and immunofluorescence (n=4-5). IL-40 was analysed in the serum/synovial fluid of patients with RA (n=69), systemic lupus erythematosus (SLE; n=69), osteoarthritis (OA; n=44), and in healthy controls (HC; n=25). Given the association of IL-40 with B cells, we analysed the effect of rituximab therapy on the serum IL-40 in 19 patients with RA after 16 and 24 weeks of the therapy. The clinical activity of patients with RA was assessed according to the 28 joint count Disease Activity Score (DAS28). Levels of C-reactive protein (CRP) and autoantibodies were measured by routine laboratory techniques. *In vitro* experiments were performed in RA synovial fibroblasts (n=9). Levels of cytokines and inflammatory mediators were determined in serum, synovial fluid and supernatants using ELISA or multiplex immunoassay.

Results: IL-40 was overexpressed in RA synovial tissue compared to OA, particularly by synovial fibroblasts and immune cells such as B and T lymphocytes, macrophages and neutrophils. The levels of IL-40 were significantly higher in the synovial fluid of RA patients compared to OA (33.2 (6.6-68.9) vs. 0.7 (0.1-2.4) ng/ml; p<0.0001). In addition, IL-40 was increased in the serum of RA patients compared to SLE, OA or HC (4.8 (1.7-24.9) vs. 1.4 (1.0-1.9), 1.6 (0.6-3.1) or 1.5 (0.7-2.7) ng/ml; p<0.0001 for all) and decreased after 16 (p<0.01) and 24 weeks (p<0.001) in a subgroup of rituximab treated patients with RA. IL-40 levels in RA patients correlated with autoantibodies rheumatoid factor (IgM) and anti-citrullinated protein antibody (ACPA) in the serum (p<0.0001 and p<0.01) as well as in the synovial fluid (p<0.0001 and p<0.001). IL-40 in RA synovial fluid was also significantly associated with DAS28 (p<0.05), synovial fluid leukocyte count (p<0.01), number of swollen joints (p<0.05) and neutrophil attractants IL-8 (p<0.01) and MIP-1α (p<0.01). RA synovial fibroblasts exposed to recombinant IL-40 increased secretion of IL-8 (p<0.01), MCP-1 (p<0.05) and MMP-13 (p<0.01) compared to unstimulated cells in *in vitro* conditions.

Conclusion: Our results show for the first time that IL-40 is elevated in RA and decreases following B-cell depletion therapy. The association of IL-40 with autoantibodies and chemokines may imply its potential involvement in RA development. Moreover, IL-40 up-regulates the secretion of chemokines and MMP-13 by synovial fibroblasts, indicating its role in the regulation of inflammation and tissue destruction in RA.

Acknowledgements: Supported by MHCR 023728 a SVV 260 523

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2339

POS0389 NEUTROPHIL AND MONOCYTE EXTRACELLULAR TRAPS IN RHEUMATOID ARTHRITIS: POTENTIAL SOURCE OF DIAGNOSTIC BIOMARKERS

A. Trofimenko[1], S. Bedina[1], M. Mamus[1], E. Mozgovaya[1], S. Spitsina[1]. [1]*Research Institute of Clinical and Experimental Rheumatology Named After A.B. Zborovsky, Clinical Biochemistry Lab, Volgograd, Russian Federation*

Background: Up-to date quite high rheumatoid arthritis (RA) prevalence has also a trend towards steady increase for several decades. Earliest possible diagnosis and personalized treatment of RA are commonly believed to be principal way to prevent or diminish joint destruction. Emerging biomarkers retrieval has therefore critical importance for improvement of RA treatment outcomes, especially for its biological treatment. One of upcoming sources of new biomarkers is newly discovered phenomenon of neutrophil extracellular traps (NET) and monocyte extracellular traps (MET) formation, specifically in RA.

Objectives: Evaluation of peripheral blood neutrophils and monocytes ability to generate NET and MET spontaneously and after induction in vitro in RA.

Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles. 30 patients with verified RA according to the ACR/EULAR 2010 criteria were included in the study. 30 healthy volunteers were enrolled as a reference group. RA disease activity was assessed using DAS28 score did not exceeded 2.6 in every patient at the inclusion timepoint. Neutrophils and monocytes were isolated with one-step centrifugation procedure using three-layer ficoll-amidotrizoate density gradient with density of upper, intermediate and lower layers 1068 kg/m^3, 1080 kg/m^3, and 1090 kg/m^3, respectively. The cell types in the resulting fractions were identified histochemically, and the extent of cell activation was assessed using common nitro-blue tetrazolium test. Generation of NETs was stimulated by phorbol-12-myristate-13-acetate (PMA). Generation of METs was stimulated using bacterial LPS. The shape and size of NETs and ETs were assessed using fluorescence microscopy with SYBR green.

Results: Mean contamination fraction of neutrophils and monocytes in the reference group did not exceeded 3% and 2%, respectively. Mean purity of neutrophil fraction in RA group was 93.1±6.1%, and cell viability in every sample was above 95.4±5.1%. Mean purity of monocyte fraction in RA group was 98.4±6.4%, cell viability in every sample was above 93.4±4.8%. Spontaneous NET and MET formation was observed in neutrophils and monocytes isolated from both RA patients and, significantly less, in healthy controls. Neutrophils from ACPA-positive RA patients were found to reveal increased spontaneous and induced NETs formation compared to ACPA- negative RA patients. Monocytes did not demonstrate any difference between these subgroups.

Conclusion: NETs could probably be considered as a candidate source of citrulline autoantigen participating in autoantibody production, whereas METs may play less important role in this phenomenon. NETs and ETs can be considered as potential diagnostic biomarkers of RA. Further studies of NETosis and ETosis in RA patients can promote emerging researches for targeted therapy of RA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2408

POS0390 SIMULTANEOUS ASSESSMENT OF JOINT AND VASCULAR INFLAMMATION BY PET-CT IN TOFACITINIB-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY

A. Hamar[1], Z. Hascsi[2], A. Pusztai[1], M. Czókolyová[1], E. Végh[1], Z. Pethö[1], K. Gulyás[1], B. Soós[1], G. Kerekes[3], É. Szekanecz[4], K. Hodosi[1], S. Szántó[1], G. Szücs[1], T. Seres[5], Z. Szekanecz[1], S. Szamosi[1]. *[1]University of Debrecen, Rheumatology, Debrecen, Hungary*; *[2]Scanomed Ltd., PET/CT, Debrecen, Hungary*; *[3]University of Debrecen, Medicine, Debrecen, Hungary*; *[4]University of Debrecen, Oncology, Debrecen, Hungary*; *[5]University of Colorado Anschutz Medical Campus, Anesthesiology, Aurora, Co, United States of America*

Background: Rheumatoid arthritis (RA) has bene associated with atherosclerosis and cardiovascular (CV) disease. 18F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}FDG-PET/CT) is suitable to detect synovial and vascular inflammation. Tofacitinib has been used to effectively treat RA.
Objectives: We wished to assess the effects of tofacitinib treatment on synovitis and vascular inflammation simultaneously by ^{18}FDG-PET/CT.
Methods: Thirty RA patients with active disease were treated with either 5 mg bid or 10 mg bid tofacitinib and evaluated at baseline and after 6 and 12 months. We determined DAS28, CRP, IgM rheumatoid factor (RF) and anti-cyclic citrullinated peptide (aCCP) levels. All patients underwent 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) in order to determine vascular and synovial inflammation in five aortic segments and five articular regions, respectively. In the joints, mean (SUV_{mean}) and maximum standard uptake values (SUV_{max}), while in the aorta, mean (TBR_{mean}) and maximum target-to-background ratios (TBR_{max}) were determined. Carotid intima-media thickness (IMT), arterial stiffness (PWV) and endothelial dysfunction (FMD) were determined by ultrasound.
Results: One-year tofacitinib treatment significantly attenuated vascular and synovial inflammation as visualized by PET/CT. Articular SUV_{mean} (p=0.010), SUV_{max} (p=0.001), as well as aorta TBR_{max} (p<0.001) significantly decreased over time. Synovial inflammation as determined by PET/CT variably and positively associated with aCCP, RF, CRP, ApoB, lipoprotein A (LpA), IMT and PWV. Vascular inflammation (TBR_{max}) inversely correlated with HAQ and positively with ESR, ApoA, and PWV. Uni- and multivariable analyses suggested that articular SUV values were independently associated with CRP, ApoB, LpA, IMT and PWV, while aortic TBR_{max} was determined by HAQ and PWV.
Conclusion: ^{18}F-PET/CT is suitable to simultaneously assess synovial and vascular inflammation in RA. One-year tofacitinib treatment dampened inflammation. PET/CT changes were associated with markers of systemic inflammation, atherogenic lipids, carotid atherosclerosis and arterial stiffness.
REFERENCES:
[1] Gotthardt M, Bleeker-Rovers CP, Boerman OC, Oyen WJ. Imaging of inflammation by PET, conventional scintigraphy, and other imaging techniques. J Nucl Med. 2010;51(12):1937-49.
[2] Bucerius J, Hyafil F, Verberne HJ, Slart RH, Lindner O, Sciagra R, et al. Position paper of the Cardiovascular Committee of the European Association of Nuclear Medicine (EANM) on PET imaging of atherosclerosis. Eur J Nucl Med Mol Imaging. 2016;43(4):780-92.
Acknowledgements: This research was supported by the European Union and the State of Hungary and co-financed by the European Social Fund in the framework of TAMOP-4.2.4.A/2-11/1-2012-0001 'National Excellence Program' (Z.S.); by the European Union grant GINOP-2.3.2-15-2016-00015 (G.P., G.T. and Z.S.) and by the Pfizer Investigator Initiated Research Grant no. WI188341 (Z.S.).
Disclosure of Interests: Attila Hamar: None declared, Zsolt Hascsi: None declared, Anita Pusztai: None declared, Monika Czókolyová: None declared, Edit Végh: None declared, Zsófia Pethö: None declared, Katalin Gulyás: None declared, Boglárka Soós: None declared, György Kerekes: None declared, Éva Szekanecz: None declared, Katalin Hodosi: None declared, Sándor Szántó Speakers bureau: Abbvie, MSD, Novartis, Consultant of: Abbvie, MSD, Novartis, Gabriella Szücs Speakers bureau: Boehringer, Actelion, Roche, Consultant of: Boehringer, Actelion, Roche, Tamas Seres: None declared, Zoltán Szekanecz Speakers bureau: Abbvie, Pfizer, Roche, Novartis, Lilly, Sager, Janssen, Consultant of: Pfizer, Abbvie, Roche, Novartis, Grant/research support from: Pfizer, Szilvia Szamosi Speakers bureau: Roche
DOI: 10.1136/annrheumdis-2021-eular.2473

POS0391 ASSESSING SENESCENT HUMAN LYMPH NODE STROMAL CELLS DURING RHEUMATOID ARTHRITIS DEVELOPMENT

T. de Jong[1,2], J. W. Bolt[1,2], J. F. Semmelink[1,2], L. van Baarsen[1,2]. *[1]Amsterdam UMC, University of Amsterdam, Department of Rheumatology & Clinical Immunology and Department of Experimental Immunology, Amsterdam, Netherlands*; *[2]Amsterdam UMC, Amsterdam Rheumatology & Immunology Center (ARC), Amsterdam, Netherlands*

Background: Cellular senescence is a state of proliferation arrest of cells. The persistence and accumulation of senescent cells has been implicated in the pathogenesis of age-related diseases like rheumatoid arthritis (RA). Clinical disease is preceded by loss of immune tolerance and autoimmunity. Lymph node stromal cells (LNSC) are important regulators of this tolerance. Therefore, senescent LNSC may affect tolerance and the development of systemic autoimmunity.
Objectives: To determine the extent of cellular senescence of LNSC during early phases of systemic autoimmunity.
Methods: We included individuals with arthralgia without any evidence of arthritis who were positive for IgM rheumatoid factor (IgM-RF) and/or anti-citrullinated protein antibodies (ACPA; RA-risk group), early arthritis patients (ACR/EULAR 2010 criteria; disease duration < 1 year) and seronegative healthy controls. All study subjects underwent ultrasound-guided inguinal lymph node biopsy. LNSC were isolated and cultured from freshly collected lymph node needle biopsies and passages 0-9 were used for experiments. Cellular senescence was assessed by measuring cell size, granularity, autofluorescence, senescence-associated gene expression levels, DNA damage and senescence-associated β-galactosidase (SA β-gal) activity.
Results: Preliminary flow cytometry data shows that the cell size and autofluorescence of LNSC from RA patients (n=11) and RA-risk individuals (n=7) is increased compared with healthy LNSC (n=7), while granularity was specifically increased in LNSC from RA patients (n=9). Initial stainings indicate higher SA β-gal activity and more DNA damage in LNSC from RA-risk (n=3) and RA patients (n=4) compared with healthy controls (n=3). Expression levels of senescence-associated genes such as p21 and p53 were significantly higher in LNSC from RA patients compared with healthy controls (n=6 per group).
Conclusion: These preliminary findings suggest senescence already in early RA and provide a rationale for investigating the consequence of senescent LNSC on immune cell responses
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2501

POS0392 PRESENCE OF FOUR SERUM AUTOANTIBODIES ASSOCIATES WITH THE ACPA STATUS IN EARLY RHEUMATOID ARTHRITIS

L. Lourido[1], C. Ruiz-Romero[1,2], L. Collado[1], M. Hansson[3], L. Klareskog[3], R. Sjöberg[4], E. Pin[4], P. Nilsson[4], F. J. Blanco[1,5]. *[1]Unidad de Proteómica. Grupo de Investigación de Reumatología (GIR)., Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC)., A Coruña, Spain*; *[2]Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina, (CIBER-BBN), Madrid, Spain*; *[3]Karolinska Institutet, Karolinska University Hospital, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden*; *[4]KTH Royal Institute of Technology & SciLifeLab, Division of Affinity Proteomics, Department of Protein Science, Stockholm, Sweden*; *[5]Universidade da Coruña (UDC), Grupo de Investigación de Reumatología y Salud (GIR-S)., Departamento de Fisioterapia, Medicina y Ciencias Biomédicas, Facultad de Fisioterapia, A Coruña, Spain*

Background: The presence of anti-citrullinated protein antibodies (ACPAs) is a hallmark of rheumatoid arthritis (RA) that precede the development of the disease by years and is used for its clinical diagnosis. However, there are RA subjects that test negative for ACPA and thus the early diagnosis on these patients may be delayed. Furthermore, the presence or absence of ACPA in RA supports the hypothesis that on these two subsets of patients underlie different pathogenesis and clinical outcomes.
Objectives: In this work, we searched for serum autoantibodies useful to assist the early diagnosis of ACPA-seronegative RA and its management.
Methods: We profiled the serum autoantibody repertoire of 80 ACPA-seronegative and 80 ACPA-seropositive RA subjects from the Swedish population-based Epidemiological Investigation of RA (EIRA) cohort. A suspension bead array platform built on protein fragments within Human Protein Atlas and selected from an initial untargeted screening using arrays containing 2660 total antigens was employed to identify IgG and IgA serum autoantibodies. A validation phase on antigen suspension bead arrays was carried out on another set of samples from EIRA containing 386 ACPA-seropositive, 358 ACPA-seronegative and 372 randomly selected control subjects of the same age and sex. A sample-specific threshold based on 20 times the median absolute deviation plus the median of all signals was selected to determine the reactivity of samples. The Wilcoxon rank sum test and Fisher's test were applied for the comparison of autoantibody levels and reactivity frequencies between the groups.
Results: Our data revealed four antigens associated with the ACPA status (Table 1). Testis-specific Y-encoded-like protein 4 (TSPYL4) showed significantly higher IgG reactivity frequency in ACPA-seronegative subjects compared to ACPA-seropositive (8% vs. 3%; P<0.05). Significant differences at IgG autoantibody levels (P<0.05) were also observed between ACPA-seronegative subjects and controls for this specific antigen. Significantly higher

IgG autoantibody levels (P<0.05) towards another antigen, dual specificity mitogen-activated protein kinase kinase 6 (MAP2K6), were also observed in ACPA-seronegative subjects compared to ACPA-seropositive and controls. In contrast, we found significantly higher IgG autoantibody levels (P<0.05) in ACPA-seropositive individuals compared to ACPA-seronegative and controls towards two antigens, anosmin-1 (ANOS-1) and muscle related coiled-coil protein (MURC). ANOS-1 shows also significantly higher IgG reactivity frequency in ACPA-seropositive individuals compared to ACPA-seronegative and controls (22%, 9% and 6% respectively; P<0.05). Interestingly, three out of the four antigens discovered to be associated with the ACPA status in early RA are highly expressed in lungs and heart, two of the main extraarticular sites affected in RA. No significant differences were observed at IgA levels for any of the antigens analyzed.

Table 1. Scheme of the different phases of the study, the features within each phase and the results. The reactivity to four antigens allows to distinguish ACPA-seronegative (ACPA-), ACPA seropositive (ACPA+) and controls.

Phases	Untargeted discovery	Targeted discovery	Targeted validation
Number of samples	80 ACPA- 80 ACPA+	80 ACPA- 80 ACPA+	358 ACPA-372 Controls 386 ACPA+
Antigen array platform	Planar arrays	Suspension bead array 1	Suspension bead array 2
Number of antigens	2660	62	27
Number of candidate biomarkers	62	27	4 (TSPYL4,MAP2K6, ANOS1,MURC)

Conclusion: Upon further validation in other early RA sample cohorts, our data suggest the measurement of these four autoantibodies may be useful for the early diagnosis of ACPA-seronegative RA and give insight into the pathogenesis of the different RA subsets.

Characters from table content including title and footnotes:

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2514

POS0393 FIBRIN DEPOSITION IS AN ACTIVE TRIGGER OF CARTILAGE DEGENERATION IN RHEUMATOID ARTHRITIS

T. Hügle[1], S. Nasi[1], D. Ehirchiou[1], P. Omoumi[2], A. So[1], N. Busso[1]. [1]*Lausanne University Hospital, CHUV, Department of Rheumatology, Lausanne, Switzerland*; [2]*Lausanne University Hospital, CHUV, Radiology, Lausanne, Switzerland*

Background: Fibrin(ogen) maintains inflammation in various disorders but has never been linked to cartilage damage in rheumatoid arthritis (RA) or other forms of inflammatory arthritis.
Objectives: To investigate the role of fibrin deposition on cartilage integrity in arthritis.
Methods: Fibrin deposition on knee cartilage was analyzed by immunohistochemistry in RA patients and in murine adjuvant-induced arthritis (AIA). In chondrocytes, fibrinogen expression (*Fgα, Fgβ, Fgγ*) and procoagulant activity were evaluated by qRT-PCR and turbidimetry respectively. Fibrin-induced catabolic genes were assessed by qRT-PCR in chondrocytes. Fibrin-mediated chondro-synovial adhesion (CSA) with subsequent cartilage tears was studied in co-cultures of human RA cartilage with autologous synoviocytes, in the AIA model, and by MRI. The link between fibrin and calcification was examined in human RA cartilage stained for calcific deposits and *in vitro* in fibrinogen-stimulated chondrocytes.
Results: Fibrin deposition on cartilage correlated with the severity of cartilage damage in human RA explants and in AIA wildtype (WT) mice, while fibrinogen deficient ($Fg^{-/-}$) mice were protected. Accordingly, fibrin upregulated catabolic enzymes (*Adamts5* and *Mmp13*) in chondrocytes. Secondly, CSA was present in fibrin-rich and damaged cartilage in AIA WT but not in $Fg^{-/-}$ mice. In line, autologous human synoviocytes, cultured on RA cartilage explants, adhered exclusively to fibrin-positive degraded areas. Gadolinium-enhanced MRI of human joints showed contrast-enhancement along cartilage surface in RA patients but not in controls. Finally, fibrin co-localized with calcification in human RA cartilage and triggered chondrocyte mineralization inducing pro-calcification genes (*Anx5, Pit1, Pc1*) and cytokine (IL-6). Although at a much lesser extent, we observed similar fibrin-mediated mechanisms in osteoarthritis (OA).
Conclusion: Fibrin deposition directly impacts on cartilage integrity via induction of catabolism, mechanical stress, and calcification. Potentially, fibrin is a key factor of cartilage damage occurring in RA as a secondary consequence of inflammation.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2521

POS0394 NAD+ BOOSTERS REESTABLISH THE ALTERED NAD+ METABOLISM OF LEUKOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS IMPROVING THEIR OXIDATIVE, APOPTOTIC AND INFLAMMATORY STATUS

C. Perez-Sanchez[1], L. M. Sánchez-Mendoza[2], M. D. C. Abalos-Aguilera[1], N. Barbarroja Puerto[1], M. Luque-Tévar[1], A. M. Patiño-Trives[1], I. Arias de la Rosa[1], J. A. Moreno[2], M. I. Burón[2], J. A. González-Reyes[2], E. Collantes Estevez[1], A. Escudero Contreras[3], C. Lopez-Pedrera[1], J. M. Villalba[2]. [1]*IMIBIC, Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, Córdoba, Spain*; [2]*IMIBIC, Department of Cell Biology, Physiology and Immunology, University of Cordoba, Campus de Excelencia Internacional Agroalimentario, ceiA3, Córdoba, Spain, Córdoba, Spain*; [3]*IMIBIC, Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, Cordoba, Spain*

Background: NAD^+ is an important cofactor and second messenger for multiple cellular processes that exhibits antioxidant, anti-apoptotic and anti-inflammatory properties. Pre-clinical studies in animal models of Rheumatoid Arthritis (RA) have demonstrated the therapeutic potential of NAD^+ boosters in the control of the disease activity. However, to date no studies have been set up to evaluate the NAD+ metabolism and the therapeutic effects of NAD^+ boosters in RA patients.
Objectives: 1- To study the NAD^+ metabolism in RA patients and its association with key clinical features. 2- To evaluate the effect of anti-TNF therapy in the NAD+ metabolism.
3- To analyze the beneficial effects of NAD^+ boosters in leukocytes from active RA patients.
Methods: Plasma and PBMCs were purified from 100 RA patients and 50 healthy donors (HDs). Moreover, an additional cohort of 50 RA patients treated with Anti-TNF therapy was analyzed before and after 6 months of treatment. NAD^+ levels were determined by using the NAD/NADH-Glo Assay. NAD^+-consuming genes expression were analyzed by RT-PCR. In parallel, PBMCs from eight HDs and eight active RA patients were treated *ex vivo* with 1 mM of NAD^+ boosters including nicotinamide (NAM), nicotinamide riboside (NR), and nicotinamide mononucleotide (NMN). After 24 hours, intracellular reactive oxygen species (ROS) levels (DFCHDA) and the percentage of apoptotic PBMCs (annnexin V/PI) were assessed by flow cytometry. Lastly, a panel of key pro-inflammatory genes were evaluated by RT-PCR.
Results: NAD^+ and NADH levels were significantly reduced in plasma and PBMCs of RA patients compared with HDs and directly related to disease activity (DAS28, CDAI, SDAI). Accordingly, the expression levels of genes involved in the consumption of NAD^+ such as SIRT-1, CD38 and PARP-1 were found up-regulated in PBMCs from RA patients. Anti-TNF therapy for 6 months restored the altered NAD+ levels towards those showed by HDs. Furthermore, the clinical response promoted by Anti-TNF therapy (changes in DAS28) correlated with changes in NAD+ levels. The *in vitro* treatments of PBMCs isolated from active RA patients with NAD^+ boosters significantly increased the NAD^+ levels and promoted a deep reduction of intracellular ROS levels, the percentage of apoptotic cells and the expression levels of key inflammatory mediators, such as IL-6, IL-8, IL-1ß, TNF-α, CCL2, IL-23, and STAT-3.
Conclusion: 1. NAD^+ metabolism is altered and associated with the disease activity of RA patients, involving both, reduced NAD^+ levels and increased expression of NAD^+-consuming genes. 2. Anti-TNF therapy restored NAD+ levels, which were directly linked to the clinical effectiveness. 3. NAD^+ boosters reduced the oxidative, apoptotic and inflammatory profiles of RA leukocytes through the parallel increase of intracellular NAD^+ levels. Thus, NAD^+ boosters might be considered novel therapeutic tools for RA patients.
Acknowledgements: Supported by PI18/00837, RIER RD16/0012/0015, RTI2018-100695-B-I00, P18-RT-4264 and CVI276, co-funded with FEDER.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2580

POS0395 ANTI-ACETYLATED PROTEIN ANTIBODIES IN RHEUMATOID ARTHRITIS (RA): CLUES FOR THE STARTING POINT OF AUTOANTIBODY RESPONSES IN RA

T. J. van Wesemael[1], A. L. Dorjée[1], T. Huizinga[1], A. van der Helm - van Mil[1], R. Toes[1], D. van der Woude[1]. [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*

Background: Rheumatoid arthritis (RA) is characterized by autoantibodies such as rheumatoid factor (RF) and anti-modified protein autoantibodies (AMPAs) like anti-citrullinated protein antibodies (ACPA) and anti-carbamylated protein

antibodies (anti-CarP). Recently, another AMPA: anti-acetylated protein antibodies (AAPA) have been found in RA patients [1]. The prevalence of AAPA antibodies and their isotypes have yet to be determined. Since isotype profiles reflect the breadth of an immune response, the prevalence of AAPA isotypes in arthritis patients with and without RA can help to understand the relevance of this autoantibody response in RA.

Objectives: To describe the prevalence of AAPA isotypes in arthritis patients with and without RA.

Methods: In 650 RA patients fulfilling the 1987 RA criteria and 555 non-RA arthritis patients from the Leiden Early Arthritis Cohort, baseline serum samples were screened by ELISA for IgG, IgM and IgA to an acetylated- and control peptide that was based upon the CCP-2 backbone. The cutoff for positivity was based on 80 controls (mean + 2SD). A sample was considered positive if it was above the cutoff and was 0.1 optical density higher on the acetylated peptide than on the control peptide.

Results: AAPA IgG was found in 36% of RA patients versus 6.7% of non-RA arthritis patients (figure 1a). Within RA patients, AAPA IgG antibodies were mostly present in the ACPA-(CCP-2) positive group (64% in ACPA-positive, compared to 5% in ACPA-negative). Levels of AAPA IgG and IgA were higher in RA patients than in healthy controls and non-RA arthritis patients (figure 1b), however, surprisingly, no difference in levels was found for IgM.

When isotype profiles in AAPA- positive arthritis patients were compared, patients with RA were more often positive for two or more isotypes then patients without RA, and thus displayed considerably more overlap in AAPA isotypes compared to non-RA patients (table 1). Intriguingly, IgM AAPA was the most prevalent isotype in non-RA patients, versus IgG in RA patients.

Table 1. Anti-acetylated protein antibody (AAPA) isotype overlap in AAPA positive patients.

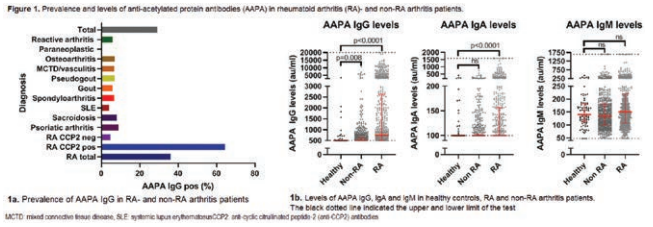
AAPA isotype	RA patients (=310) n (%)	Non-RA arthritis patients (n=106) n (%)
IgG+IgM-IgA-	115 (37.1)	28 (5.1)
IgG-IgM+IgA-	52 (16.8)	48 (8.7)
IgG-IgM-IgA+	14 (4.5)	13 (2.3)
IgG+IgM+IgA-	24 (7.7)	3 (0.5)
IgG+IgM-IgA+	37 (11.9)	4 (0.7)
IgG-IgM+IgA+	9 (2.9)	8 (1.4)
IgG+IgM+IgA+	59 (19.0)	2 (0.4)

AAPA: anti-acetylated protein antibodies, RA: rheumatoid arthritis

Conclusion: AAPA are detected in one third of RA patients, and mainly in the ACPA-positive subgroup. The predominance of IgM AAPA in non-RA arthritis patients and healthy controls suggests that healthy persons can develop AAPA IgM without the development of RA. These results also suggest that in healthy individuals, AAPA responses can occur, but do not mature past the IgM-stage, while in RA patients, the AAPA-response does mature and might form a "starting point" for development of other AMPA leading to the concurrent present of several AMPA in disease.

REFERENCES:

[1] Juarez, M., et al., Identification of novel antiacetylated vimentin antibodies in patients with early inflammatory arthritis. Ann Rheum Dis, 2016. **75**(6): p. 1099-107.



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2777

POS0396

THE LEVEL OF PERIPHERAL REGULATORY T CELLS IS ASSOCIATED WITH THE CHANGES OF INTESTINAL MICROBIOTA IN PATIENTS WITH RHEUMATOID ARTHRITIS

R. Wu[1], J. An[1], T. Ding[1], H. Xue[1], X. F. Li[1], C. Wang[1]. [1]*The Second Hospital of Shanxi Medical University,The Department of Rheumatology,Taiyuan, China*

Background: Rheumatoid arthritis (RA) is a systemic autoimmunity inflammation disease characterized with chronic aggressive arthritis and the presence of abnormal antibodies. Several observations showed that the breakdown of immune tolerance caused by many complex interactions was involved in the development of RA[1]. However, the pathogenesis of RA remained unclear. It has been confirmed that the imbalance of Th17 and Treg cells play a crucial role in destroying immune tolerance [2]. Besides, researches showed that intestinal microbiota can influence host immunity by acting on the immune cells to play pro-inflammatory or anti-inflammatory effect, and in turn immune system can also regulate the microbiota[3, 4]. Thus, a frontier point of view in the field of rheumatism, immune microecology, was proposed, which is a novel concept for the breakdown of immune tolerance. Studies have confirmed that there was an imbalance of intestinal microbiota in patients with RA [4]. But the relationship between the CD4+T subsets cells and intestinal microbiota in RA is unknown.

Objectives: We detected and compared the absolute number of CD4+T cells subsets in the peripheral blood and the proportion or abundance of intestinal microbiota in patients with RA and healthy adults, and then analyzed the relationship between them to explore the role of CD4+T cells subsets and intestinal microbiota in the pathogenesis of RA.

Methods: We collected the sample of stool and blood from 15 patients with RA hospitalized at the Second Hospital of Shanxi Medical University and 8 age and gender-matched healthy controls(HC). The absolute number of CD4+T cells subsets including Th1, Th2, Th17 and Treg cells were detected by flow cytometry. The 16S rRNA in the stool specimens were sequenced by the Roche/45 high-throughput sequencing platform. We analyzed whether there was correlarion between CD4+T subsets cells and intestinal microbiota.

Results: Patients with RA had a higher level of *Christensenellaceae* and a lower level of *Pseudomonadaceae* as compared with those of HCs at the family level ($p<0.05$). And at the genus level, the patients with RA had higher levels of *Ruminococcus torques*, *Christensenellaceae R-7*, *Ruminiclostridium 9* and *Ruminococcus 1* compared with those of HCs ($p<0.05$) (Figure 1).And the *Ruminococcus torques* at the genus level was negative correlated with the absolute number of Treg cells ($p<0.001$) (Figure 2).

Conclusion: The results here suggested that there were different proportion or abundance of intestinal microbiota between the patients with RA andHCs. And the changes of intestinal microbiota such as *Ruminococcus torques* were associated with Treg cells, further indicating that the imbalance of intestinal microbiota in RA can destory the immune tolerance. The above results uncovered that the intestinal microbiota had immunomodulatory function, which may be the upstream mechanism participated in the pathogenesis of RA.

REFERENCES:

[1] Weyand CM, Goronzy JJ. The immunology of rheumatoid arthritis. Nat Immunol 2021, **22**(1): 10-18.

[2] Weyand CM, Goronzy JJ. Immunometabolism in the development of rheumatoid arthritis. Immunol Rev 2020, **294**(1): 177-187.

[3] Brown EM, Kenny DJ, Xavier RJ. Gut Microbiota Regulation of T Cells During Inflammation and Autoimmunity. Annu Rev Immunol 2019, **37:** 599-624.

[4] du Teil Espina M, Gabarrini G, Harmsen HJM, Westra J, van Winkelhoff AJ, van Dijl JM. Talk to your gut: the oral-gut microbiome axis and its immunomodulatory role in the etiology of rheumatoid arthritis. FEMS Microbiol Rev 2019, **43**(1).

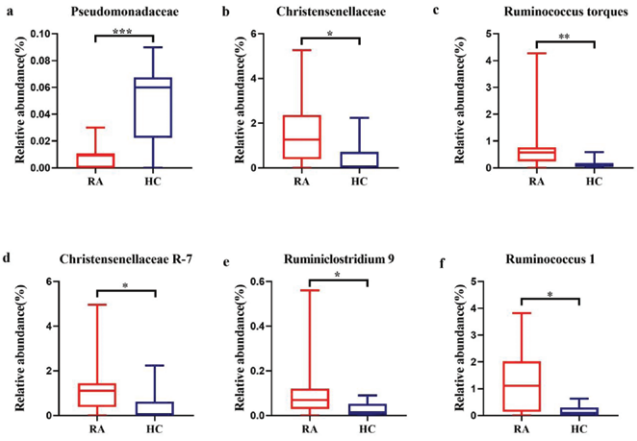


Figure 1. At the family level (a-b) and the genus level(c-f), the relative abundance of intestinal microbiota in patients with RA and HCs were different. Data were expressed as median (Q1, Q3) and analyzed by Wilcoxon test. (*** P < 0.001, **P < 0.01 and *P < 0.05).

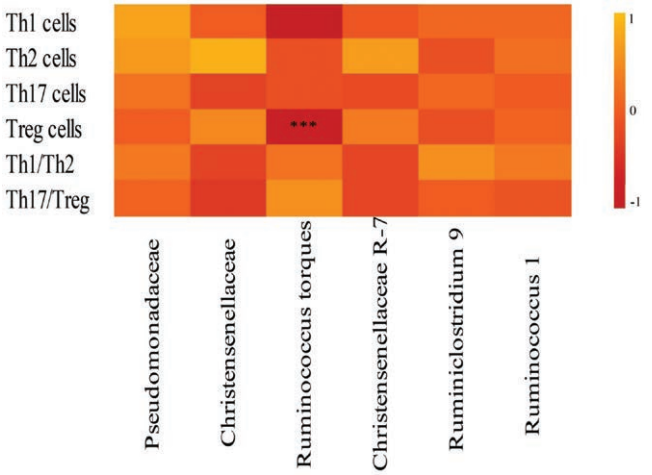


Figure 2. A heatmap shows the correlation between the intestinal microbiota and CD4+T cells in patients with RA, and *Ruminococcus torques* at the genus level was negative related with Treg cells. (Colors indicate the Spearman rank correlation, *** P < 0.001).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2783

POS0397 AGGREGATED SURVIVIN BINDING AROUND HISTONE H3 EPIGENETIC MODIFICATIONS IN RISK LOCI ASSOCIATED WITH RHEUMATOID ARTHRITIS

V. Chandrasekaran[1], G. Katona[2], M. I. Bokarewa[1], K. M. Andersson[1], M. C. Erlandsson[1], M. Jensen[2], N. Oparina[1], A. Damdimopoulos[3]. [1]*Gothenburg University, Department of Rheumatology, Gothenburg, Sweden*; [2]*Gothenburg University, Department of Chemistry and Molecular Biology, Gothenburg, Sweden*; [3]*Karolinska Institute, Department of Bioscience and Nutrition, Huddinge, Sweden*

Background: Survivin is an integral part of the Chromosomal Passenger Complex (CPC) which plays a vital role in mitosis. Experiments have demonstrated that survivin can physically bind to DNA. Crystallographic studies show that survivin binds to Threonine-3 of histone H3. In patients with autoimmune diseases, increased survivin expression contributes to an aggravated disease phenotype. Thus, functional, and mechanistic data point to a potential chromatin regulatory role for survivin, possibly in combination with the established gene regulatory function carried out by histone epigenetic modifications (EM).
Objectives: The objective of the study was to analyse the co-localization of chromatin bound survivin with three histone H3 epigenetic modifications – acetylated lysine 27 (K27ac) and trimethylated lysine 4 (K4me3) and lysine-27 (K27me3). The second objective was to analyse if survivin-bound DNA sequences overlapped with sequences in the vicinity of 106 GWAS SNPs that are associated with a risk of developing rheumatoid arthritis (RA).
Methods: Chromatin from CD4 T cells of 14 female subjects was immunoprecipitated with survivin antibodies and each of the histone H3 antibodies, and coupled with sequencing (ChIPseq, Hiseq2000, Illumina). After mapping the annotations of sequenced regions to the human reference genome hg38, enriched peaks were identified through Homer software. The identified survivin ChIP peaks were analysed for colocalization with peaks of the three histone H3 EMs and with RA risk loci, using the Bioconductor package 'ChIPPeakAnno' through RStudio.
Results: Among the total of ~13,000 individual survivin ChIP-peaks, 33% colocalized with histone H3 EM peaks. The overlapping peaks show a linear increase in average peak size compared with the peaks showing no colocalization with any H3 EM peak. A maximum of 5.5-fold increase in average peak size was observed when survivin bound peaks overlap with peaks of all three H3 EMs. A major proportion (86%) of top RA risk SNPs was associated with either binding of survivin or H3 EMs. In this subset, 63% of RA risk SNPs were found within an area of 100 kilobases from survivin ChIP-peaks, with preferential enrichment of high-scoring peaks when survivin colocalizes with all 3 H3 EMs. Survivin was bound to risk SNPs annotated to, among others, the major immunological genes CD83, IRF4, CD28, ICOS and IL2RA
Conclusion: This study presents experimental evidence that survivin binding to DNA preferentially occurred in regions with high density of histone EMs. The increased aggregation of survivin around histone H3 EMs point to its potential regulatory function in gene transcription. Since regions around RA risk SNPs overlap with survivin peaks, survivin's nuclear function could have immunologically important effects in mechanisms of autoimmune diseases.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3212

POS0398 ADIPONECTIN INDUCES SYNOVIAL ANGIOGENESIS IN RHEUMATOID ARTHRITIS THROUGH METABOLIC REMODELING

L. Wang[1], W. Tan[1], F. Wang[2], M. Zhang[1]. [1]*The First Affiliated Hospital of Nanjing Medical University, Department of Rheumatology, Nanjing, China*; [2]*The First Affiliated Hospital of Nanjing Medical University, Department of Cardiology, Nanjing, China*

Background: Our team have previously reported that Adiponectin correlates well with synovial inflammation and progressive bone erosion in rheumatoid arthritis (RA). Angiogenesis is another important part, which plays a critical role in the pathogenesis of RA.
Objectives: We hypothesized that adiponectin induces synovial angiogenesis in RA.
Methods: Single-cell RNA sequencing (scRNA-Seq) was used to screen cellular changes in local knee joint of collagen-induced arthritis (CIA) after intraarticularly injected of adiponectin. Chimera models of synovium-cartilage-NOD/SCID mice, matrigel plug assay and rat aortic ring assay were performed to demonstrate the pro-angiogenesis role of adiponectin. Cellular experiment, including proliferation, migration, apoptosis, tube formation and angiogenesis related gene expression profile, were detected with Human Umbilical Vein Endothelial Cells (HUVEC) and Mice Lung Microvessel Endothelial Cell (MLMEC) after adiponectin stimulation. Seahorse was performed to clear the influence of adiponectin to cell metabolism.
Results: The synovium and pannus hyperplasia worse in CIA model after intraarticularly injected of adiponectin, along with more serious synovitis and bone erosion. ScRNA-Seq of synovial tissues separated from CIA reminded that endothelial cell barbarically grows via metabolic remodeling after stimulated with adiponectin. Synovial chimera, matrigel plug and rat aortic ring shows adiponectin accelerates angiogenesis significantly in different background conditions. In vitro, endothelial cell proliferation detecting by RCTA and CCK8, migration by wound healing and transwell, apoptosis by FACS, tube formation and angiogenesis related gene expression profile by PCR-ARRAY were promoted by adiponectin in both HUVEC and MLMEC. Seahorse showed HUVEC made more use of glycolysis after co-cultured with adiponectin, a method of cell energy supply that tumor cells possess called warburg effect, that drives endothelial cell hyperplasia in severe environment.
Conclusion: As a classic metabolic regulator, adiponectin exacerbates CIA by promoting angiogenesis through metabolic remodeling. The findings not only provide a novel insight into the pathogenic role of adiponectin, but also reveals a potential therapeutical strategy to attenuate revascularization in RA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3585

POS0399 TMT-BASED QUANTITATIVE PROTEOMICS ANALYSIS OF SYNOVIAL FLUID-DERIVED EXOSOMES IN RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS, GOUT AND OSTEOARTHRITIS

Y. Liu[1,2], Y. Huang[1], Q. Huang[1], Z. Huang[1], Z. Li[1], T. W. Li[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*; [2]*University of South China, Guangdong Second Provincial General Hospital, Guangzhou, China*

Background: The pathogeneses of the joint diseases rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), gout, and osteoarthritis (OA) are still not fully elucidated. Exosomes in synovial fluid (SF) has a critical role in the pathogenesis of arthritis. None of study has compared the proteomics of SF-derived exosomes in RA, axSpA, gout and OA.

Objectives: To compare the proteomics of SF-derived exosomes in RA, axSpA, gout and OA based on tandem mass tags (TMT) labeled quantitative proteomics technique.
Methods: SF-derived exosomes was isolated from RA, axSpA, gout and OA patients by the Exoquick kit combined ultracentrifugation method. TMT labeled quantitative proteomics technique was used to compare the proteomics of SF-derived exosomes. Volcano plot, hierarchical cluster, Gene Ontologies (GO), Encyclopedia of Genes and Genomes (KEGG) pathway analysis were conducted.
Results: A total of 1678 credible proteins were detected. With the cut off criteria of |log2 (fold-change)| ≥1.2 and p-value <0.05, 267 (140 up-regulated and 127 down-regulated)differential proteins were found in OA vs gout, 291 (179 and 112) in axSpA vs OA, 515 (109 and 406) in RA vs axSpA, 298 (191 and 107) in axSpA vs gout, 462 (160 and 302) in RA vs gout, 536 (170 and 366) in RA vs OA. GO analysis showed that the biological progress of differential proteins were mainly enriched in the "immune response". Regarding the molecular function, the differential proteins mainly mediated "antigen binding". GO analysis of the cellular components indicated that most proteins were annotated as "extracellular exosomes". KEGG pathway analysis demonstrated differential proteins were significantly enriched in "complement and coagulation cascades". The hierarchical cluster analysis of the differential proteins in the four groups showed that Lysozyme C and Keratin were more abundant in gout, Hemoglobin and Actin-related protein 2/3 complex subunit 3 in OA, Sodium/potassium-transporting ATPase subunit alpha-1 and Immunoglobulin heavy constant delta in axSpA, Pregnancy zone protein and Stromelysin-1 in RA.
Conclusion: The protein profiles of SF-derived exosomes in RA, axSpA, gout and OA patients were different. The differential proteins were the potential biomarkers of RA, axSpA, gout and OA.
REFERENCES:
[1] Cretu D, Diamandis E P, Chandran V. Delineating the synovial fluid proteome: recent advancements and ongoing challenges in biomarker research.[J]. Critical reviews in clinical laboratory sciences, 2013,50(2):51-63.
[2] McArdle A J, Menikou S. What is proteomics?[J]. Archives of disease in childhood. Education and practice edition, 2020.

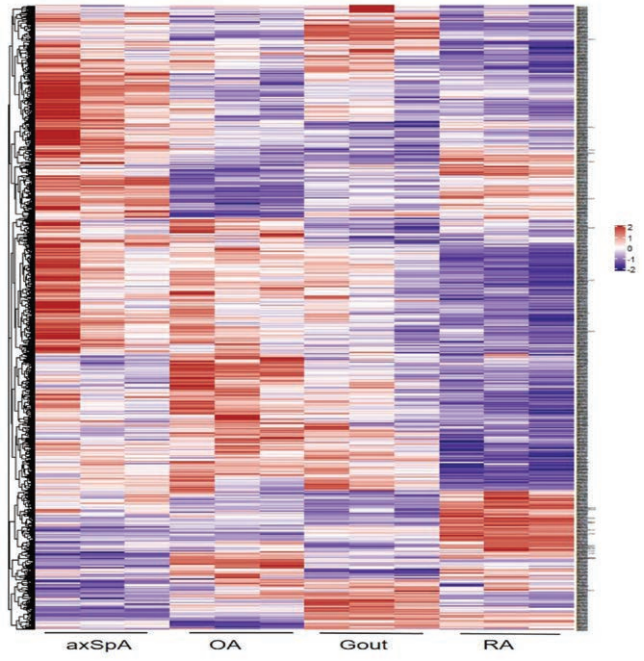


Figure 1. The hierarchical cluster analysis of differential proteins in axSpA, OA, Gout and RA.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3607

POS0400 **METABOLIC CHANGES INDUCED BY ANTI-MALONDIALDEHYDE/MALINDIALDEHYDE-ACETALDEHYDE ANTIBODIES PROMOTE OSTEOCLAST DEVELOPMENT**

K. Sakuraba[1], A. Krishnamurthy[2], A. Circiumaru[2], V. Joshua[2], H. Wähämaa[2], M. Engström[2], M. Sun[2], X. Zheng[3], C. Xu[3], K. Amara[2], V. Malmström[2], S. B. Catrina[3], C. Grönwall[2], B. Réthi[2], A. Catrina[2]. [1]*National Hospital Organization Kyushu Medical Center, Department of Rheumatology, Fukuoka, Japan*; [2]*Karolinska Institutet & Karolinska University Hospital, Department of Medicine, Solna, Stockholm, Sweden*; [3]*Karolinska Institutet & Karolinska University Hospital, Molecular Medicine and Surgery, Stockholm, Sweden*

Background: Malondialdehyde (MDA) is a highly reactive compound generated during lipid-peroxidation in conditions associated with oxidative stress. MDA can irreversibly modify proteins (e.g. lysine, arginine and histidine residues). In addition, acetaldehyde can further react with MDA adducts to form malondialdehyde-acetaldehyde (MAA) modification. Such protein modifications can lead to immunogenic neo-epitopes that are recognized by autoantibodies. In fact, anti-MDA/MAA IgG antibodies are significantly increased in the serum of patients with autoimmune diseases, such as rheumatoid arthritis (RA) (1). Interestingly, anti-MDA/MAA antibodies have been shown to promote osteoclast (OC) differentiation *in vitro* suggesting a potential role for these autoantibodies in bone damage associated with RA (1).
Objectives: Little is known about the molecular mechanisms activated by autoantibodies in RA. Here, we elucidate the pathways specifically triggered by anti-MDA/MAA autoantibodies in developing osteoclasts.
Methods: Recombinant human monoclonal anti-MDA/MAA antibodies, which were previously cloned from single synovial B cells of RA patients, were added to different OC assays. OCs were generated from monocyte-derived macrophages in the presence of the cytokines RANK-L and M-CSF. OC development was monitored by light microscopy following tartrate-resistant acid phosphatase staining and by erosion assays using calcium phosphate-coated plates. Bone morphometrics were studied in anti-MDA/MAA-injected mice using X-ray microscopy. Cellular metabolism was analyzed by mass spectrometry, Seahorse XF Analyzer and a colorimetric L-Lactate assay.
Results: Anti-MDA/MAA antibodies induced a robust OC differentiation *in vitro* and bone loss *in vivo*. The anti-MDA/MAA antibodies acted on developing OCs by increasing glycolysis via an Fcγ receptor I-mediated pathway and the upregulation of the transcription factors HIF-1α, Myc and CHREBP. Such regulation of cellular metabolism was exclusively observed in the presence of the osteoclastogenic anti-MDA/MAA clones, whereas other RA-associated autoantibodies (anti-MDA/MAA or anti-citrullinated protein antibodies) had no effect on metabolism. The anti-MDA/MAA treatment induced a shift in the tricarboxylic acid (TCA) cycle activity in developing OCs, leading to the accumulation of citrate and aconitate.
Conclusion: We described a novel type of autoantibody-induced pathway in RA, which might contribute to increased OC activation and a consequent bone loss. Anti-MDA/MAA antibodies promoted osteoclast development by increasing glycolysis and by modulating the TCA cycle through a signaling pathway that included Fcγ receptor I and a network of transcription factors acting on glycolysis. A TCA cycle bias towards citrate production suggests that the anti-MDA/MAA antibodies might stimulate OCs via increasing lipid biosynthesis in the cells.
REFERENCES:
[1] Grönwall C. et al. J. Autoimmunity 84 (2017): 29-45.
Acknowledgements: This Project has received funding from FOREUM, Foundation for Research in Rheumatology, from the European Research Council (ERC) grant agreement CoG 2017 - 7722209_PREVENT RA, the EU/EFPIA Innovative Medicine Initiative grant agreement 777357_RTCure, the Konung Gustaf V:s och Drottning Victorias Frimurarestiftelse and Knut and Alice Wallenberg Foundation.
Disclosure of Interests: Koji Sakuraba: None declared, Akilan Krishnamurthy: None declared, Alexandra Circiumaru: None declared, Vijay Joshua: None declared, Heidi Wähämaa: None declared, Marianne Engström: None declared, Meng Sun: None declared, Xiaowei Zheng: None declared, Cheng Xu: None declared, Khaled Amara: None declared, Vivianne Malmström Grant/research support from: collaboration with Pfizer, unrelated to the abstract, Sergiu-Bogdan Catrina: None declared, Caroline Grönwall: None declared, Bence Réthi: None declared, Anca Catrina Grant/research support from: collaboration with BMS and Pfizer, unrelated to the present abstract
DOI: 10.1136/annrheumdis-2021-eular.3678

POS0401

THE APPLICATION OF MTX-LOADING DNA TETRAHEDRON IN TREATING COLLAGEN-INDUCED ARTHRITIS MICE VIA REGULATING MACROPHAGE

X. Ge[1], Y. Jin[1], Z. Mao[2], Y. Guo[2], Z. Gu[1]. [1]*Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*; [2]*Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China*

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease which mainly affect joints. [1]. Macrophages often infiltrate in the inflammatory joints. Activated macrophages release TNF-α, IL-1β to accelerate tissue damage, is one of the most important targets for RA intervention. The traditional drugs currently used commonly have some disadvantages cannot be bypassed[2], while DNA nanostructure is a new type of drugs have precise design, and likewise takes biological effect together[3]. We synthesized a DNA tetrahedron loaded with MTX and conjugated with HA which targeted to macrophage.

Objectives: To verify whether MTX-loading DNA tetrahedron can regulate the apoptosis and polarization of macrophage and finally improve the condition of CIA model mice by while decrease the side effect of MTX.

Methods: DNA TET was synthesized by mixing signal strand DNA in TM buffer and heated to 95 °C for 10 min, then cooling to 4 °C. Electrophoresis was applied to confirm the formation of TET. The absorbance of MTX solution was detected by microplate reader to analyze the loading efficiency of MTX into TET. Fluorescence microscope was used to observe the intake of TET into cells. CCK8 experiment was applied to measure the vitality of cells. Flow cytometry was used to detect the apoptosis and polarization. CIA model was established based on DBA/1 mice. Mice were randomly divided into five groups: normal group injected with NS; after established CIA model, CIA group injected with NS, MTX group injected with MTX solution, MTX-TET group injected with MTX-TET NP.

Results: We synthesized DNA tetrahedron(A) and used 8% PAGE electrophoresis to confirmed the successfully synthesis(B). Then We found that when TET concentration fixed, the loading MTX concentration gradually increased and saturated at 190μM(C). While completely loading needed at least 4 hours(D). Fluorescence showed that single DNA strand cannot be taken by RAW, while TET can be easily taken by RAW(E). CCK8 showed that empty TET had no obvious effect on cells, while MTX and MTX-TET with equivalent concentration can obviously suppress the vitality(F). Similarly, the apoptosis trial showed that TET can slightly decrease the apoptosis of RAW, MTX and MTX-TET can significantly promote the apoptosis(G). Flow cytometry showed that the MTX-TET can decrease the expression of M1 marker CD80 (H).

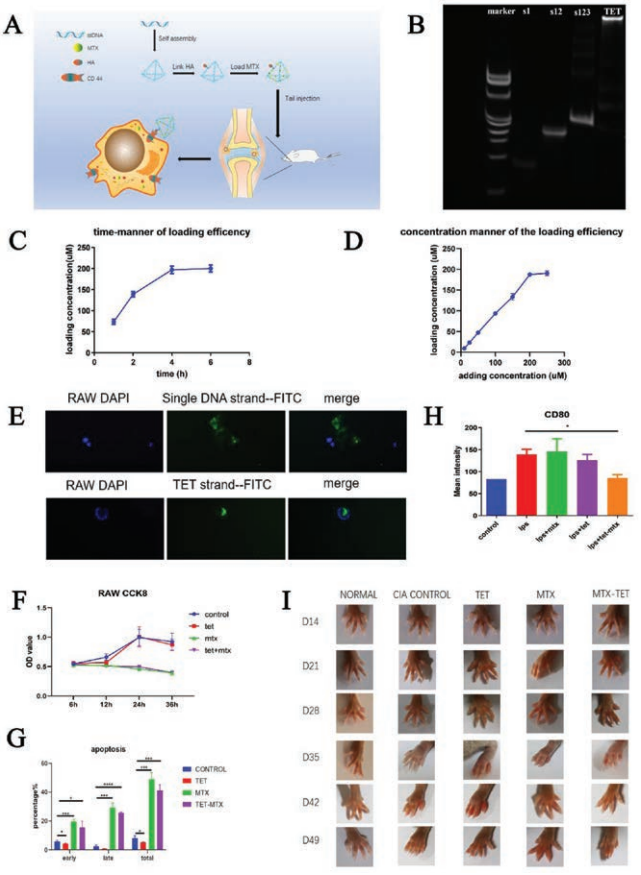


Figure 1.

At last, we treat mice with NS, TET, MTX and MTX-TET once a week after CIA model established, and found that TET have no significantly effect on mice, while MTX and MTX-TET can alleviate the inflammation symptom of paws(I).

Conclusion: Conclusions: We synthesized MTX-loading DNA tetrahedron conjugated with HA, and found that the MTX-TET NP have the excellent ability of promote RAW apoptosis and relieve proinflammatory M1 polarization. while also can alleviate the symptom of CIA mice.

REFERENCES:

[1] Aletaha D, Smolen JS: Diagnosis and Management of Rheumatoid Arthritis: A Review. *JAMA* 2018, 320(13):1360-1372.

[2] Smolen JS, Aletaha D, McInnes IB: Rheumatoid arthritis. *Lancet* 2016, 388(10055):2023-2038.

[3] Hu Q, Li H, Wang L, Gu H, Fan C: DNA Nanotechnology-Enabled Drug Delivery Systems. *Chem Rev* 2019, 119(10):6459-6506.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3690

POS0402

IDENTIFYING MECHANISMS UNDERLYING THE ASSOCIATION BETWEEN RHEUMATOID ARTHRITIS AND PERIODONTITIS USING IN SILICO ANALYSIS OF CANONICAL PATHWAYS

K. S. K. Ma[1], L. T. Wang[2]. [1]*National Taiwan University, Taipei, Taiwan, ROC, Department of Life Science, Taipei, Taiwan, Republic of China*; [2] *National Taiwan University Hospital, Department of Obstetrics & Gynecology, Taipei, Taiwan, Republic of China*

Background: Periodontal pathogens such as *Porphyromonas gingivalis (P.g.)* has been proposed too involve in rheumatoid arthritis (RA) progression via citrullinating and producing exogenously citrullinated human and bacterial epitopes.

Objectives: We identified pathways downstream to periodontitis onset that involved in RA progression with RNA-sequencing data.

Methods: Canonical pathway analysis was conducted by comparing mRNA expression data from whole-transcriptome expression profiling using z-score and p-value visualization to identify underlying mechanisms among patients with RA (n=7) and periodontitis (n=9). Collected biopsies included human blood samples for RA and human gingival tissues for periodontitis. RNA-seq data with -$\log_{10}$(P) values larger than 1.3 were considered significant, and positive z-scores indicated up-regulation. The statistical software was Ingenuity Pathway Analysis (QIAGEN).

Results: Among all significantly enriched (-log10(P) > 1.3) periodontitis-associated pathways underlying RA progression identified from the recruited cases, the production of nitric oxide and reactive oxygen species in macrophages, B cell receptor signaling, osteoarthritis pathway, HOTAIR regulatory pathway, IL-8 signaling, LPS/IL-1 mediated inhibition of RXR function, leukocyte extravasation signaling, and neuroinflammation signaling pathway, were up-regulated in RA patients and patients with periodontitis, when compared with patients without either disease. The z-scores of production of nitric oxide and reactive oxygen species in macrophages were 2.45 for RA (-log10(P) = 1.41), 3.89 for periodontitis (-log10(P) = 4.25); the z-scores of B cell receptor signaling were 2.44 for RA (-log10(P) = 1.93), 2.65 for periodontitis (-log10(P) = 6.97); the z-scores of osteoarthritis pathway were 1.89 for RA (-log10(P) = 3.28), 2.33 for periodontitis (-log10(P) = 4.31); the z-scores of HOTAIR regulatory pathway were 1.63 for RA (-log10(P) = 1.71), 3.40 for periodontitis (-log10(P) = 3.68); the z-scores of IL-8 signaling were 1.34 for RA (-log10(P) = 1.30), 4.43 for periodontitis (-log10(P) = 6.05); the z-scores of LPS/IL-1 mediated inhibition of RXR function were 1.33 for RA (-log10(P) = 2.00), 1.27 for periodontitis (-log10(P) = 3.44); and the z-scores of leukocyte extravasation signaling were 1.13 for RA (-log10(P) = 1.80), 3.68 for periodontitis (-log10(P) = 18.14).

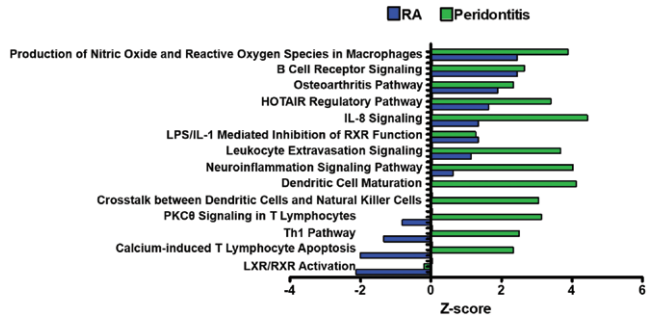


Figure 1. Canonical pathway analysis on transcriptome of blood samples for patients with RA and gingival tissues for periodontitis.

Conclusion: Our findings suggest that infection-driven activation of macrophages and B cells is involved in RA pathogenesis. This occurs primarily

through upregulating cellular activities involving iNOS-presenting macrophages and B cell receptor signaling, which may be associated with the pathogenesis of *P.g.*-triggered RA.

REFERENCES:

[1] Jenning M, Marklein B, Ytterberg J, et al. Bacterial citrullinated epitopes generated by Porphyromonas gingivalis infection-a missing link for ACPA production. Ann Rheum Dis 2020;79:1194–202.doi:10.1136/annrheumdis-2019-216919

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3998

POS0403 **RISK FACTORS FOR PROGRESSION OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: REASSURING IMPACT OF METHOTREXATE**

C. Lucas[1], A. Tremblay[1], S. Jouneau[2], A. Perdriger[1]. [1]*CHU, Rheumatology, Rennes, France*; [2]*CHU, Pneumology, Rennes, France*

Background: Factors associated with rheumatoid arthritis-associated interstitial lung disease (RA-ILD) progression and prognosis are not well identified, especially the impact of methotrexate.

Objectives: Identify risk factors of ILD progression in RA-ILD patients in a longitudinal study.

Methods: RA patients with ILD confirmed in 2 high resolution computed tomography (HRCT) chest scans spaced at least 6 months apart (T0: date of the first HRCT chest scan describing ILD; Tx: date of the last HRCT chest scan available) were consecutively included in this retrospective multi-centric study from 2010 to 2020. HRCT chest scans were analyzed for each patient at T0 and Tx by 2 independent radiologists to determinate ILD pattern (definite UIP, probable UIP, indeterminate UIP, non-UIP) and progression during the follow-up including variation of the fibrosis score (aggravated or non-aggravated). Characteristics of patients (demographic-clinical-biological findings, respiratory function tests, and treatments exposure) at ILD diagnosis and during the follow-up (T0-Tx) were analyzed as potential determinants of ILD progression through multivariable logistic regression analysis. Overall survival was analyzed using Kaplan-Meier method.

Results: 74 RA-ILD patients were included. During a mean duration between T0-Tx of 2.8 years ± 2.4, 26 patients (35%) had ILD progression. Thirty-three patients (45%) were treated by methotrexate at ILD diagnosis (T0) and 29 of them (39%) continued methotrexate during T0-Tx. Logistic regression in multivariate analysis revealed that a treatment by methotrexate at ILD diagnosis was protective against ILD progression (OR=0.14 [0.04-0.52]; p=0.0031). Non-UIP pattern at ILD diagnosis was also protective against ILD progression (OR=0.09 [0.02-0.36]; p=0.0005). The follow-up for survival analysis was 5.1 years ± 2.9. Thirty-three patients (31%) died, and the 3-year survival rate was 80%. Survival was better for non-aggravated ILD patients (HR=3.5 [1.46-8.4]; p=0.004) and for patients treated by methotrexate during T0-Tx (HR= 0.36 [0.15-0.84]; p=0.018) and worse for definite UIP patterns (HR=2.570 [1.078-6.128]; p=0.0332).

Conclusion: In RA-ILD patients, non-UIP pattern and methotrexate treatment are associated with better ILD evolution and prognosis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4157

Spondyloarthritis - aetiology, pathogenesis and animal models

POS0404 **VOLUNTARY WHEEL RUNNING MODEL IN MICE TO MECHANICALLY STIMULATE THE ENTHESIS OF THE ACHILLES TENDON**

A. Briolay[1], S. Delplace[2], F. Duboeuf[3], O. Peyruchaud[3], D. Magne[1], L. Brizuela[1], C. Bougault[1]. [1]*Université Claude Bernard Lyon 1, CNRS UMR 5246, Lyon, France*; [2]*Université du Littoral-Côte d'Opale, ULR 4490, Boulogne/Mer, France*; [3]*Faculté de Médecine Lyon Est, INSERM U1033, Lyon, France*

Background: Excessive bone formation in the entheses is one of the features of peripheral spondyloarthritis. Biomechanical stress is proposed to occupy a central place in spondyloarthritis pathophysiology, but the precise molecular and cellular mechanisms underlying the pathological response of the enthesis are still largely unknown [1]. Besides, physical therapy and exercise are recommended as non-pharmacologic therapies for patients. We focused on the effect of exercising on enthesis ossification.

Objectives: We aimed to develop and characterize an *in vivo* model in mice to study the impact of mechanical stimulation on the enthesis of the Achilles tendon.

Methods: DBA/1 mice were subjected to voluntary running exercise by the use of activity wheels for two weeks, and compared to mice housed in standard conditions (n=17 per group). The running performances were recorded.

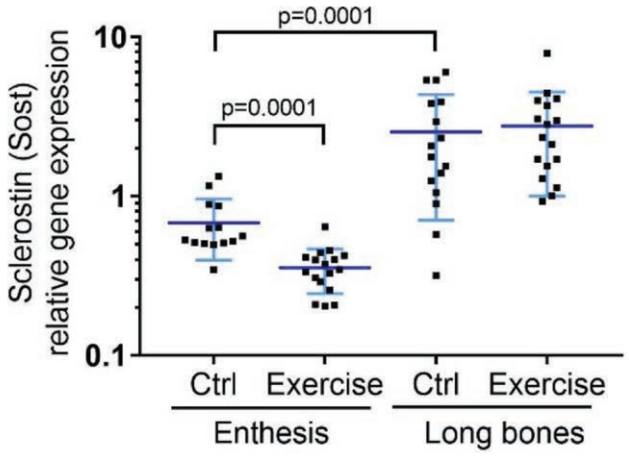


Figure 1. Expression level of the mechanosensitive gene Sclerostin (Sost). It dropped in response to exercise in entheseal tissues, but not in long bones, revealing a tissue-specific response to mechanical stimulation.

mRNAs were extracted from the long bones (flushed tibia and femur) and the ankles' entheses for real-time PCR analysis. µCT was performed on the femurs. Alkaline phosphatase activity was detected by histology on the anchorage of the Achilles tendon to the calcaneum, and by enzymatic assay in serum samples. Luminex analysis was also conducted on serum samples for Il-6 and Il-8/Kc detection.

Results: Free access to the activity wheel resulted in a running exercise of 5.5±0.8 km/day (approximately 80 km in total) at 14.5±0.5 m/min. No effect was detected on the femur architecture by µCT. Sclerostin (*Sost*) gene expression was monitored as a mechanosensitive marker. Its expression was expectedly reduced by half in entheseal tissues, but no modulation was observed in long bones (Figure 1). Similarly, exercise-induced regulation of *Osterix* and *Runx2* expressions was observed only in enthesis samples. This tissue-specific pattern was also verified for key genes of the sphingosine-1 phosphate metabolic pathway, which we recently implicated in spondyloarthritis pathophysiology [2]. The *in situ* staining of alkaline phosphatase activity suggested the presence of more positive cells in the anchorage of Achilles tendon of running mice, compared to control ones. However, alkaline phosphatase activity in serum samples and its gene expression in rough tissue extracts were unchanged. No inflammatory response was detected as Il-8/Kc serum levels were similar in the control and the exercising group (59±14 vs 57±14 pg/mL). In addition, Il-6 was not detected in the serum and its expression was very faint and constant in the tissue extracts.

Conclusion: This work is still in progress for a more complete characterization of the model. We believe that this experimental design will be useful to study the role of mechanical stimulation specifically in the enthesis and that it can help to better understand the spondyloarthritis pathophysiology.

REFERENCES:

[1] Cambré, et al. *Nat Commun*, 2018; [2] El Jamal, et al. *J Bone Miner Res*, 2019

Acknowledgements: Société Arthritis R&D (2020)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.833

POS0405 **GENETIC VARIANTS WITHIN PSORIATIC ARTHRITIS (PsA)-WEIGHTED GENES FBXL19 AND HLA-B*39 MAY SERVE AS A POTENTIAL LINK BETWEEN PsA AND OBESITY**

C. Welsh[1], T. Burry[1], Q. Li[1], A. Dohey[1], D. Codner[1], V. Chandran[2,3,4], D. D. Gladman[3,4], D. O'Rielly[1], P. Rahman[2]. [1]*Memorial University, Genetics, St. John's, Canada*; [2]*Memorial University, Medicine, St. John's, Canada*; [3]*Krembil Research Institute, UHN, Toronto, Canada*; [4]*University of Toronto, Rheumatology, Toronto, Canada*

Background: PsA patients have been observed to have a higher body mass index (BMI) compared to individuals with a similar disease (e.g., rheumatoid arthritis) or healthy controls[1]. Approximately 45% of PsA patients are considered obese with BMI's exceeding 30 kg/m^2, and these patients have more severe articular disease and lower response to therapy[2]. A recent mendelian randomization study noted that higher BMI leads to higher risk of psoriasis when using genetic variants as instrumental variables for BMI[3].

Objectives: To determine if known PsA-weighted genetic variants are overrepresented in an obese population.

Methods: 696 samples were identified from a previous genetic study in obesity where each patient was systematically examined with BMI and other related anthropometric measures were recorded. No patients had psoriasis, inflammatory arthritis or any extra-articular manifestations of spondyloarthritis. Samples were genotyped using a PsA-weighted single nucleotide polymorphism (SNP) panel, representing genetic variants associated with PsA. The cohort consisted of 73% female with an average age of 49 years ± 15. The average BMI of the group was 35± 8 kg/m^2, ranging from 17 to 67 kg/m^2. The PsA SNP panel consists of 42 SNPs associated with PsA including *IL23R, 5q31, PTPN22, TNFAIP3, HLA-C, TNFRSF9, LCE3A, ADAMTS9-MAGI1, HLA-B, IL13, MICA, IL12B, ZNF8816A, TRAF3IP2, KIR2DS2, FBXL19, REL, IL23R, IL23A, TNIP1,* and *TYK2.* DNA (10ng/uL) was used to prepare a PCR, followed by SAP, and extension reaction with Agena iPLEX Pro kit using Agena MassARRAY. Quantitative trait analysis was performed to obtain the association between BMI and genotype of the 42 SNPs using a linear regression model. Bonferroni correction was used to adjust for multiple comparisons. The factors of age, gender, smoking and height also have been adjusted in the analysis (Table 1).

Table 1. Regression analysis between BMI and 2 significant SNPs

SNP	CHR	Allele 1	Allele 2	BETA	SE	T	P (Genotype Only)	P (adjusted with factors)*
rs3131382	6	T	C	2.227	0.7207	3.17	0.001596	5.40E-05
rs10782001	16	G	A	1.584	0.4347	3.644	0.00029	0.0007524
Genotypes of *FBXL19* and *HLA-B*3905* SNPs with mean BMI								
SNP	rs3131382					rs10782001		
Genotypes	TT	TC		CC		GG	GA	AA
Sample Counts	6	99		575		75	324	246
Genotype Frequency	0.0088	0.15		0.84		0.11	0.50	0.38
Mean BMI	47.17	36.73		35.46		37.29	36.36	34.43
SD	16.07	6.64		7.12		7.68	7.40	6.83

*Adjusted for age, sex, height, and smoking

Results: Linear regression analysis with and without clinical factors for the two significant SNPs are presented in Table 1. Genotypes of two SNPs (rs10782001 and rs3131382) showed a difference with BMI (Table 1). The rs10782001 variant is within *FBXL19* and the average BMI in the presence of GG genotype was 37.2 vs 34.3 for the AA genotype (p=0.0007). The rs3131382 variant is within *HLA-B*39:05* and the average BMI with TT genotype was 47.1 vs 35.4 for the CC genotype (p=0.00005). Both SNPs maintained significance after correction for multiple testing (p<0.001).

Conclusion: Homozygotes for the minor allele of SNPs within *HLA-B*39* and *FBXL19* have shown to have an increased BMI, suggesting a potential genetic link between these genes and PsA and obesity. Interestingly, it has been recently noted that miR-26 suppresses adipocyte progenitor differentiation and fat production by targeting FBXL19, leading to possible biologic possibility regarding the link between PsA-weighted genetic variants and obesity[4].

REFERENCES:

[1] Bhole VM et al., *Rheumatology (Oxford).* 2012 Mar;51(3):552-6.
[2] Klingberg E et al., *Arthritis Res Ther*. 2019;21(1):17.
[3] Budu-Aggrey A et al., PLoS Med. 2019 Jan 31;16(1):e1002739.
[4] Acharya A et al., *Fbxl19*. *Genes Dev*. 2019;33(19-20):1367-1380. doi:10.1101/gad.328955.119

Disclosure of Interests: Cassidy Welsh: None declared, Tanya Burry: None declared, Quan Li: None declared, Amanda Dohey: None declared, Dianne Codner: None declared, Vinod Chandran Speakers bureau: AbbVie, Amgen, BMS, Eli Lily, Janssen, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, BMS, Eli Lily, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, Eli Lily, Employee of: Spousal Employment Eli Lilly, Dafna D Gladman Speakers bureau: AbbVie, Amgen, BMS, Eli Lily, Galapagos, Gilead, Janssen, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, BMS, Eli Lily, Galapagos, Gilead, Janssen, Novartis, Pfizer, UC, Grant/research support from: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Darren O'Rielly: None declared, Proton Rahman Speakers bureau: Amgen, Abbott, AbbVie, BMS, Celgene, Eli Lily, Janssen, Novartis, Pfizer, Merck, UCB, Consultant of: Amgen, Abbott, AbbVie, BMS, Celgene, Eli Lily, Janssen, Novartis, Pfizer, Merck, UCB, Grant/research support from: Janssen, Novartis
DOI: 10.1136/annrheumdis-2021-eular.1390

POS0406

miRNAs DEREGULATED IN RESPONSE TO IL17A INHIBITORS IN PSORIATIC ARTHRITIS REGULATE GENE PRODUCTS IN Rho-GTPase PATHWAYS

P. Rahman[1], Q. Li[2], D. Codner[2], D. O'Rielly[2], A. Dohey[2], K. Jenkins[1], D. D. Gladman[3], V. Chandran[1,3,4], I. Jurisica[5]. [1]*Memorial University, Medicine, St. John's, Canada*; [2]*Memorial University, Genetics, St. John's, Canada*; [3]*University of Toronto, Rheumatology, Toronto, Canada*; [4]*Krembil Research Institute, UHN, Toronto, Canada*; [5]*Krembil Research Institute, Medical Biophysics, Toronto, Canada*

Background: Using transcriptomic data at initiation of therapy, we recently identified differentially expressed genes (DEGs) that separated IL-17Ai response from non-response[1]. Integration of cell-type-specific DEGs with protein-protein interactions (PPIs) and further comprehensive pathway enrichment analysis revealed Rho GTPase signaling pathway exhibited a strong signal specific to IL-17Ai response and particularly the genes, *RAC1* and *ROCK*s.

Objectives: To characterize microRNA (miR) profiles among IL-17Ai responders and non-responders, as it relates to RHO GTPase pathway.

Methods: We interrogated 20 psoriatic arthritis (PsA) patients initiating IL-17Ai. Patients achieving at least low disease activity according to the Disease Activity Index for PsA (DAPSA) at three months were classified as responders. There were seven responders (35%) and thirteen non-responders (65%) in the IL-17Ai group, with biologic treatment naïve (bio-naïve) and previously-exposed (bio-exposed) patients exhibiting a 50% (4/8) and a 25% (3/12) response rate, respectively. For the miR analysis, CD4 positive T cells were isolated from peripheral blood mononuclear cells using Dynabeads^{TM} CD4 beads (ThermoFisher). Total RNA was extracted from the CD4$^+$ T cells using Lexogen's Split RNA Extraction Kit (D-Mark Biosciences). Libraries were prepared from 200ng total RNA with the NEXTFLEX Small RNA-Seq Kit v3 with UDIs (Bioo Scientific) and sequenced on the Illumina NovaSeq 6000. Raw sequencing fastq data assessed the quality using FastQC. The miRDeep2 was used to trim the adapter, align and quantify human mature miRs from miRbase (Release 22). The abundance of miRs was converted to read counts per million, normalized and limma R package was used to identify pre- and post-differentially expressed miRs.

Results: We obtained 2,889 miRs. After removing miRs with low reads in >90% of samples, 1902 high quality miRs remained for further analysis. Using mirDIP v4.1 we identified gene targets for differential miRs, and focused on recently identified DEGs related to RHO GTPase pathway. The miRs on the left of the figure 1 are those deregulated in pre-treatment, and the miRs on the right of the figure 1

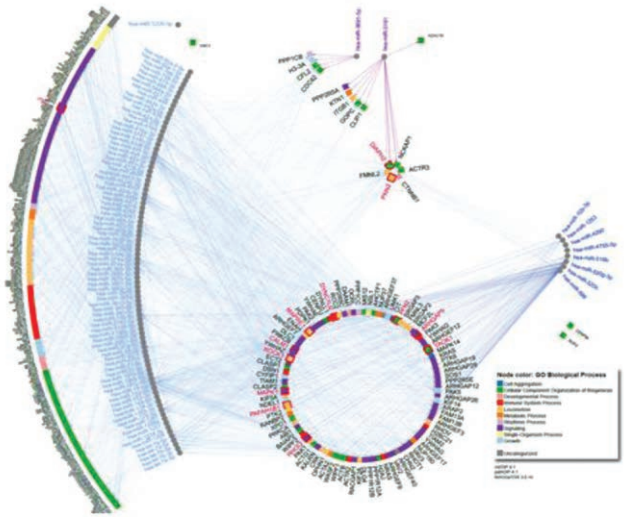


Figure 1.

show the post-treatment deregulated miRs. hsa-miR-3691-5p and hsa-miR-3161 represent the miRs that were deregulated in both conditions. The red highlighted nodes represent the most connected miRs and genes; thus, representing miRs that are the most RHO-pathway centric regulators (hsa-miR-495-3p, 16-5p, 129-5p, 520h, 520g-3p), and genes representing the most strongly regulated RHO-pathway gene products (ROCK1, RHOQ, PFN2, TAOK1, DYNC1L12, MAPRE1, PAFAH1B1, ARHGAP5, MAPK1, CALM1, DIAPH2, PKN2, ITSN1).

Conclusion: Pre- and post-treatment differential miRs related to IL-17Ai response regulate multiple genes from RHO GTPase pathway.

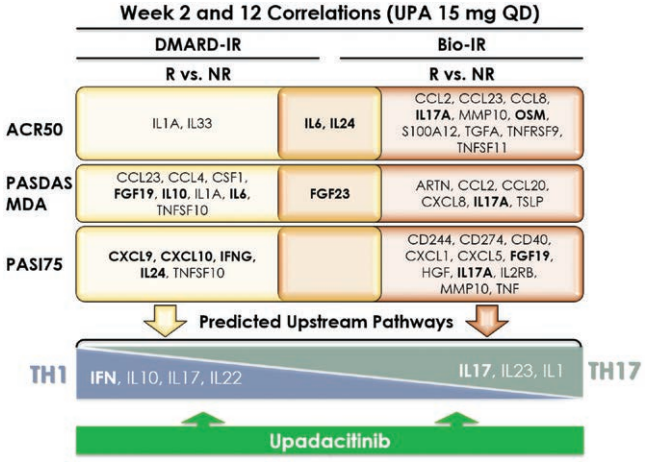
REFERENCES:
[1] Rahmati S, O'Rielly DD, Li Q, Codner D, Dohey A, Jenkins K, Jurisica I, Gladman DD, Chandran V, Rahman P. Rho-GTPase pathways may differentiate treatment response to TNF-alpha and IL-17A inhibitors in psoriatic arthritis. Sci Rep. 2020 Dec 10;10(1):21703.

Disclosure of Interests: Proton Rahman Speakers bureau: AbbVie, Amgen, BMS, Celgene, Eli Lily, Janssen, Merck, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, BMS, Celgene, Eli Lily, Janssen, Merck, Novartis, Pfizer, UCB, Grant/research support from: Janssen, Novartis, Quan Li: None declared, Dianne Codner: None declared, Darren O'Rielly: None declared, Amanda Dohey: None declared, Kari Jenkins: None declared, Dafna D Gladman Speakers bureau: AbbVie, Amgen, BMS, Eli Lily, Galapagos, Gilead, Janssen, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, BMS, Eli Lily, Galapagos, Gilead, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, Eli Lily, Janssen, Novartis, Pfizer, UCB, Vinod Chandran Speakers bureau: AbbVie, Amgen, BMS, Eli Lily, Janssen, Novartis, Pfizer, UCB, Paid instructor for: AbbVie, Amgen, BMS, Eli Lily, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, Eli Lily, Employee of: Spousal Employment Eli Lilly, Igor Jurisica: None declared
DOI: 10.1136/annrheumdis-2021-eular.1434

POS0407 PROTEOMICS ANALYSIS COMPARING THE MODE OF ACTION OF UPADACITINIB BETWEEN NON-BIOLOGIC-DMARD-IR AND BIOLOGIC-DMARD-IR PsA PATIENTS IDENTIFIES DISTINCT PATHOGENIC PATHWAYS IN THE SELECT-PsA 1 AND SELECT-PsA 2 PHASE 3 STUDIES

T. Sornasse[1], J. Anderson[2], K. Kato[2], A. Lertratanakul[2], I. McInnes[3], C. T. Ritchlin[4]. [1]*AbbVie, Precision Medicine Immunology, Redwood City, United States of America*; [2]*AbbVie, Immunology Clinical Development, North Chicago, United States of America*; [3]*University of Glasgow, College of Medical, Veterinary and Life Sciences, Glasgow, United Kingdom*; [4]*University of Rochester, Allergy/Immunology and Rheumatology, Rochester, United States of America*

Background: Treatment of non-biologic-DMARD-IR[1] (DMARD-IR) and biologic-DMARD-IR[2] (bio-IR) PsA patients with upadacitinib (UPA) at 15 mg QD, an oral JAK1 selective inhibitor, resulted in significant improvement in signs and symptoms compared to placebo.
Objectives: Using a pre-defined set of inflammation-related plasma protein biomarkers (pBM), to explore immunological pathway modulation by UPA 15 mg QD in PsA patients with active disease despite treatment with non-biologic or biologic DMARDs in the context of clinical response vs. non-response to treatment.
Methods: Patients from the SELECT-PsA 1 (DMARD-IR) and the SELECT-PsA 2 (bio-IR) studies were randomly selected (PBO, n=100; UPA 15 mg QD, n=100 for each study). The levels of 92 inflammation related protein biomarkers (pBM) were analyzed using a multiplexed Proximity Extension Assay platform in plasma samples collected at baseline, week 2, and 12; change from baseline in protein levels was expressed as Log_2 Fold Change; a Repeated Measure Mixed Linear Model was used to identify pBM modulated by UPA compared to Baseline, and those differentially modulated between responders (R) and non-responders (NR) according to ACR50, PASDAS Minimal Disease Activity, and PASI75 at week 12. Correlation of disease activity measures with relative levels of pBM were derived using Pearson's correlation; PASI score was transformed as Log_{10} (x+1) prior to the analysis. Functional pathway prediction was performed in silico with a commercial distributed software.



Results: At baseline, the relative levels of 37 pBM correlated with at least one baseline disease activity measure, with a marked positive correlation of IL6 with musculoskeletal end points (PASDAS and DAS28CRP), and a strong positive correlation of IL20, IL17A, IL17C, and TGFA with baseline PASI.
At the single pBM-level, treatment with UPA 15 mg QD resulted in a down modulation of pBM associated with T cells, myeloid cells, and IFN-, IL6-, and TNF-related pathways in both DMARD-IR and bio-IR PsA patients. Overall effects of UPA on single pBMs were broadly similar between DMARD-IR and bio-IR patients. However, analysis of pBMs differentially modulated by UPA in R vs NR indicated that favorable clinical response (achievement of ACR50, PASDAS MDA, and PASI75) in DMARD-IR patients was associated with the down modulation of pBMs predicted to be linked to IFN, IL10, IL17, IL22, and IL27 pathways; while favorable clinical response in bio-IR patients was associated with the down modulation of multiple pBM predicted to be linked to the IL17, IL23, and IL1 pathways.
Conclusion: UPA effects in both DMARD-IR and bio-IR PsA patients likely stem from the direct and indirect inhibition of multiple biological pathways belonging to the adaptive and innate immune systems. Responder/Non-Responder analysis suggests a possible shift from a TH1 biased biology in DMARD-IR PsA patients to a more TH17 biased biology in bio-IR PsA patients. This apparent change in the disease biology of PsA patients after inadequate response to prior therapy could be attributed to the actual alteration of the disease biology, treatment outcome-based patient selection, or both. Considering the clinical efficacy of UPA in both DMARD-IR and bio-IR PsA patients, this observation highlights the importance of targeting multiple pathways with drugs such as UPA for the treatment of a broad range of PsA patients.

REFERENCES:
[1] McInnes, I. et al. **Annals of the Rheumatic Diseases 79**, 16-17 (2020).
[2] Mease, P.J. *et al.* ***Annals of the Rheumatic Diseases***, annrheumdis-2020-218870 (2020).

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship.
Disclosure of Interests: Thierry Sornasse Shareholder of: AbbVie, Employee of: AbbVie, Jaclyn Anderson Shareholder of: AbbVie, Employee of: AbbVie, Koji Kato Shareholder of: AbbVie, Employee of: AbbVie, Apinya Lertratanakul Shareholder of: AbbVie, Employee of: AbbVie, Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sanofi Regeneron, UCB Pharma, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sanofi Regeneron, UCB Pharma, Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB Pharma, Grant/research support from: AbbVie, Amgen, UCB
DOI: 10.1136/annrheumdis-2021-eular.1652

POS0408 INVESTIGATING THE ANTI-INFLAMMATORY POTENTIAL OF A NOVEL MK2 INHIBITOR IN A VITRO MODEL OF ENTHESITIS

C. Bridgewood[1], C. Wong[1], R. Gaur[2], F. Ramirez-Valle[2], D. McGonagle[1]. [1]*University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), Leeds, United Kingdom*; [2]*Bristol Myers Squibb, Immunology, Cardiovascular and Fibrosis Thematic Research Center, Cambridge, United States of America*

Background: Enthesitis or inflammation of tendon/ligament anchorage points is the cardinal lesion in spondyloarthritis (SpA). Through the use of cytokine targeting biologics and also murine models, several key mediators have been shown to have a role in enthesitis, such as IL-23/17 axis and TNF[1]. We have previously shown that the human enthesis contains myeloid cells capable of IL-23 and TNF production and range of T-cells capable of IL-17A/F secretion[2,3]. Attempted inhibition of p38 MAPK for inflammatory disease in the past has yielded toxicity issues. The MAPK-associated protein kinase 2 (MK2) is situated downstream of p38 MAPK, relaying the phosphorylation signal to the nucleus, and is thus a promising target.
Objectives: To determine if a novel MK2 inhibitor (MK2i) could supress innate and adaptive immune responses in an in vitro human enthesis model.
Methods: Normal spinous process enthesis was obtained from patients undergoing spinal decompression or surgery for scoliosis correction. Following enzymatic digestion, entheseal cells (n=5) were harvested and stimulated either with LPS/IFNγ (Entheseal myeloid cell activator) or anti-CD3 (Entheseal T-cell activator) with and without MK2i (1, 0.1 and 0.01μM) for 24 hr. Supernatant was harvested and protein detected using multiplexing for panels relating to inflammation (IL-1β, IFN-α2, IFN-γ, TNF, CCL2, IL-6, IL-8, IL-10, IL-12p70, IL-17A, IL-18, IL-23, and IL-33) or T-cell activation (IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-13, IL-17A, IL-17F, IL-22, IFN-γ and TNF).
Results: Following LPS/IFNγ stimulation of entheseal cells, 1μM MK2i significantly attenuated secretion of TNF, IFNα, IL-6, IL-10, IL-8 and CCL2.

Several other targets did not reach statistical significance, but trended downwards with inhibition such as IL-1β, IL-12 IL-18 and IL-33. Following Entheseal T-cell activation by anti-CD3 stimulation, 1μM MK2i supressed TNF and IL-17A.

Conclusion: MK2i suppressed LPS driven production of several disease relevant mediators such as TNF. MK2i also supressed anti-CD3 induced T-cell derived mediators such as TNF and IL-17A. MK2 inhibition is a promising novel therapeutic target in the treatment of Spondyloarthritis.

REFERENCES:

[1] Bridgewood, C., et al., *Spondyloarthritis: new insights into clinical aspects, translational immunology and therapeutics*. Current opinion in rheumatology, 2018. **30**(5): p. 526-532.

[2] Bridgewood, C., et al., *Identification of myeloid cells in the human enthesis as the main source of local IL-23 production*. Annals of the rheumatic diseases, 2019. **78**(7): p. 929-933.

[3] Cuthbert, R.J., et al., *Evidence that tissue resident human enthesis γδT-cells can produce IL-17A independently of IL-23R transcript expression*. Annals of the rheumatic diseases, 2019. **78**(11): p. 1559-1565.

Disclosure of Interests: Charlie Bridgewood: None declared, Chi Wong: None declared, Rajula Gaur: None declared, Francisco Ramirez-Valle: None declared, Dennis McGonagle Speakers bureau: AbbVie, Celgene, Janssen, Merck, Novartis, Pfizer, UCB, Consultant of: AbbVie, Celgene, Janssen, Merck, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Celgene, Janssen, Merck, Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1906

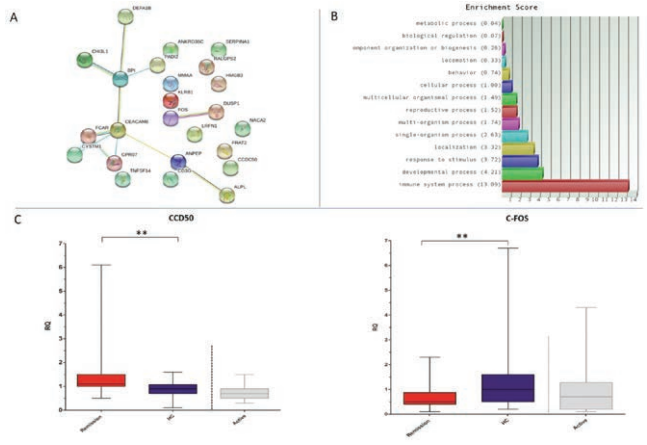
POS0409 MOLECULAR PROFILING OF THE REMISSION STATE IN PSORIATIC ARTHRITIS: IS THE FIRE EXTINGUISHED?

M. M. Angioni[1], I. Cangemi[1], A. Floris[1], M. Congia[1], E. Chessa[1], M. Piga[1], A. Cauli[1]. *[1] AOU and University of Cagliari, Rheumatology Unit, Department of Medical Sciences and Public Health, Monserrato, Italy*

Background: The most important goal of therapy in psoriatic arthritis (PsA) is to reach the remission state of disease. Nowadays, data on molecular players of clinical remission and effective disease inactivation are scarce: gene expression analysis could highlight markers characteristic of PsA remission state.

Objectives: Our aim was to analyze the gene expression profile of patients with clinically inactive (drug-induced remission) PsA versus healthy controls and PsA active state.

Methods: From a cohort of 300 patients affected by PsA according to CASPAR criteria, we selected 40 patients (peripheral arthritis subset) with >1-year remission by TNFα antagonism assessed by DAPSA ≤ 4 (R) and 40 PsA with active disease state by DAPSA > 14 score (no bDMARDs ongoing) (A), and 40 healthy controls (HC) matching for mean age and gender ratio. Both PsA groups were not on corticosteroid treatment. Each condition has been profiled first using pooled RNAs from peripheral blood (biological duplicates) by Affymetrix Human GeneChip HTA 2.0. To identify a transcript as differentially expressed in both duplicates, a fold change (FC) 1.5 and *p-value* 0.05 has been set. Then, from the comparative list of differential expressed genes (DEGs) in R vs HC state, coding mRNAs were selected and interactions analyzed by STRING software, biological functions and annotations by Gene Onthology (GO). From these analysis, 12 genes were validated in the whole PsA cohort (R+A) and HCs, by quantitative real-time PCR (RT-qPCR) in triplicate (TaqMan chemistry, GAPDH housekeeping, $2^{-\Delta\Delta Ct}$ for relative quantification, FC cutoff ±1.5 for differential analysis).



Results: The transcriptomic analysis generated 3 comparative lists of mRNAs (R vs HC= 125; R vs A= 1184; A vs HC= 378 transcripts). Then, we focused on remission state analyzing the mRNAs list R vs HC. Filtering data for coding DEGs, was made a list of 24 genes further analyzed for functions and interactions: STRING analysis created one interactions network and GO highlighted in which biological processes these DEGs are involved (Fig panels 1A, 1B). Validation analysis by rt-qPCR in the PsA cohort (R+A) and HCs confirmed the downregulation of c-FOS and the upregulation of CCDC50 (alias YMER) genes in the R vs HC conditions (*pvalue*= 0.004). The dysregulation of further genes in other comparisons was measured, as shown in Tab and Fig panel 1C.

Conclusion: Observing the amount of DEGs, is evident that the drug-induced remission state is more similar to healthy condition, however this trend of "similarity" does not mean "identical". The bioinformatic analysis showed that DEGs in the R vs HC conditions are primarily involved in biological processes related to immune system as well as correlates in an interactions network. Our molecular characterization of clinical remission revealed that effective disease inactivation appears to be molecularly-driven by two key genes, c-FOS and CCD50 (YMER), both involved in the NF-κB signalling pathway modulation.

Coding DEGs mis-regulated in the remission state. Differentially expressed genes (DEGs) in the Remission (R) state vs Healthy Controls (HC) analyzed for multiple-proteins interaction by STRING software V10.5 (panel A) and biological functions by Gene Set Enrichment Analysis (panel B). DEGs validations by RT-qPCR, confirmed the CCD50 and c-FOS dysregulation in the R state (panel C, RQ= Relative Quantification, t test RvsHC *pvalue*=0,004).

GENE SYMBOL	Gene chip Array R vs HC	Remission vs HC	Active vs HC	Remission vs Active
ALPL	-1.7	-1.1	1.3	-1.25
ANPEP	-1.68	1.0	1.1	-1.1
BPI	-1.57	-1.1	1.27	-1.5
CCDC50	1.5	1.5	-1.25	1.8
CEACAM8	-2.3	-1.2	1.2	-1.5
CHI3L1	-1.59	-1.1	-1.0	-1.0
DEFA1B	-2.3	-1.4	1.9	-2.7
FCAR	-1.56	-1.1	1.1	-1.3
FOS	-1.51	-2.0	-1.5	-1.4
KLRB1	1.52	-1	-1.6	1.6
PADI2	-1.54	-1.1	1.0	-1.1
TNFSF14	-1.51	1.1	1.2	-1.1

DEGs by RT-qPCR. Validated differentially expressed genes (DEGs) in the remission (R) state vs healthy controls (HC) selected from the microarray analysis comparative list (FC cutoff ±1.5). Differential analysis (40 R vs 40 HC vs 40 Active) was made by FoldChange (FC) cutoff ±1.5 (overexpressed ≥ 1.5; - 1.5 ≥ downregulated).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2068

POS0410 BIOMARKERS REFLECTING DISTURBED GUT BARRIER DIFFER IN PATIENTS WITH SPONDYLOARTHRITIS, CROHN'S DISEASE AND ACUTE ANTERIOR UVEITIS

J. Rademacher[1,2], C. Hempel[1], V. Rios Rodriguez[1], F. Proft[1], M. Protopopov[1], M. Torgutalp[1], H. Haibel[1], U. Pleyer[3], B. Siegmund[1], D. Poddubnyy[1]. *[1]Charité Universitätsmedizin Berlin, Campus Benjamin Franklin, Department of Gastroenterology, Infectiology and Rheumatology, Berlin, Germany*; *[2]Berlin Institute of Health, BIH, Berlin, Germany*; *[3]Charité Universitätsmedizin Berlin, Ophthalmology, Berlin, Germany*

Background: Spondyloarthritides (SpA) are characterized by frequent extra-musculoskeletal manifestations (EMM) among them acute anterior uveitis (AAU) and Crohn's disease (CD). Vice versa, about 50% of AAU and 20% of CD patients have concomitant SpA. SpA patients show gut dysbiosis together with frequent subclinical gut inflammation. Biomarkers reflecting disturbed gut barrier (intestinal-fatty acid binding protein (iFABP), lipopolysaccharide binding protein (LBP) and zonulin) were previously found to be elevated in patients with radiographic axial SpA (r-axSpA) (1).

Objectives: To evaluate whether biomarkers reflecting leaky gut are altered in patients with AAU, CD and SpA compared to healthy controls and whether they differ between patients with EMM with and without concomitant SpA.

Methods: A total of 100 patients from the German Spondyloarthritis Inception Cohort (GESPIC) were included – among them 20 patients with r-axSpA without EMM, 40 patients with CD and 40 patients with non-infectious AAU – out of which 19 and 20 patients, respectively, had concomitant SpA (11/8 and 20/0 axial/peripheral SpA, respectively). The GESPIC patients were compared to 20 age- and

sex-matched healthy donors (HD). The following five serum biomarkers were analyzed with ELISA: calprotectin, iFABP, LBP, soluble CD14 (sCD14) and zonulin.
Results: Patient characteristics are shown in Table 1. Serum levels of calprotectin, LBP, sCD14 and zonulin differed significantly between patients with r-axSpA, AAU and CD with and without concomitant SpA and HD (Figure 1). When comparing patients with EMM with and without underlying SpA, calprotectin serum levels were significantly elevated in CD patients with SpA (8.6µg/ml (SD 5.5µg/ml)) compared to CD patients without SpA (5.7µg/ml (SD 4.1µg/ml); Mann-Whitney U Test, p=0.031). Serum levels of the analyzed biomarkers did not differ between AAU patients with and without axSpA. Spearman rank correlation revealed a significant association between CRP and calprotectin (correlation coefficient r=0.230; p=0.012), LBP (r=0.596; p<0.0001), sCD14 (r=0.428; p<0.0001) and zonulin (r=0.221; p=0.016), respectively. Furthermore, LBP and zonulin serum levels correlated positively (r=0.208; p=0.023); as well as LBP and sCD14 levels (r=0.418; p<0.0001).

Table 1. Patient characteristics. Mean values (standard deviation) or absolute numbers are shown.

	CD + SpA	CD	r-axSpA	AAU + axSpA	AAU	HD
N	19	21	20	20	20	20
Age	39.1 (11.3)	38.7 (14.4)	38.4 (10.3)	39.6 (12.0)	39.2 (12.5)	38.6 (12.9)
Male (%)	9 (47%)	9 (43%)	9 (45%)	9 (45%)	9 (45%)	9 (45%)
HLA-B27 positive (%)	5 (26%)	3 (14%)	17 (85%)	17 (85%)	13 (65%)	2 (10%)
CRP in mg/l	14.3 (25.6)	18.0 (41.8)	9.1 (11.3)	6.7 (9.9)	2.3 (3.4)	0.6 (0.7)
ASDAS	2.8 (1.1)		3.2 (0.6)	2.2 (1.0)		
BASDAI	4.1 (2.2)		5.4 (1.2)	3.2 (2.4)		

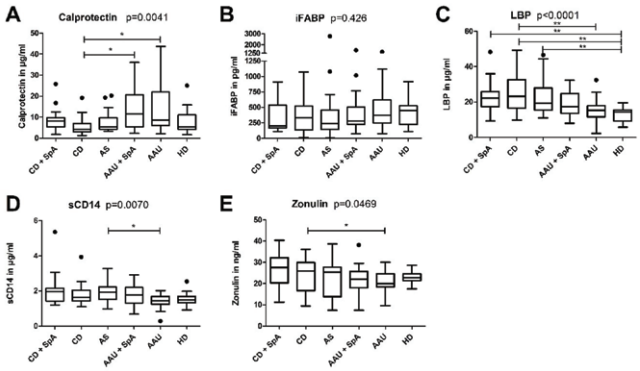


Figure 1. Biomarkers reflecting disturbed gut barrier show distinct signatures in patients with acute anterior uveitis, Crohn's disease and axial Spondyloarthritis. Kruskal Wallis Test; p values shown. Dunn-Bonferroni Post-Hoc analyses, significant pairwise differences are marked; * p<0.05; **p<0.01; ***p<0.0001Conclusion:

We found substantial differences in biomarkers reflecting disturbed gut barrier between with SpA, CD, AAU and healthy controls. The presence of SpA was associated with higher calprotectin serum levels in CD as compared to CD without SpA.
REFERENCES:
[1] Ciccia F, et al. Dysbiosis and zonulin upregulation alter gut epithelial and vascular barriers in patients with ankylosing spondylitis. 2017.
Acknowledgements: Dr. Judith Rademacher is participant in the BIH-Charité Clinician Scientist Program funded by the Charité –Universitätsmedizin Berlin and the Berlin Institute of Health.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2325

POS0411 TARGETING JAK-STAT SIGNALLING ALTERS THE PHENOTYPIC CHARACTERISTICS OF PsA SYNOVIAL FIBROBLASTS IN RESPONSE TO THE JAK/STAT ACTIVATOR ONCOSTATIN M

A. O' Brien[1], M. Hanlon[1], V. Marzaioli[1], K. Flynn[2], S. Wade[1], D. Veale[2], U. Fearon[1]. [1]*Trinity College Dublin, Molecular Rheumatology, Dublin, Ireland*; [2]*Centre for Arthritis and Rheumatic Diseases, St Vincent's Hospital, Dublin, Ireland*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis. The JAK/STAT pathway has been linked to the pathogenesis of PsA. Recently, JAK/STAT inhibitors (JAKi) have emerged as an encouraging class of drugs for the treatment of PsA. Only a few of these inhibitors have been approved for use in PsA patients with others currently in clinical trials.
Objectives: The aim of this study was to examine the effect of JAKi on primary PsA synovial fibroblasts (FLS) function.
Methods: Primary PsA FLS were isolated and cultured with JAKi (Peficitinib, Filgotinib, Baricitinib and Upadacitinib) in the presence of the pro-inflammatory JAK/STAT activator - Oncostatin M (OSM). The effect of JAKi on these cells was determined by Migration and Invasion Assays, ELISA and rtPCR. PsA FLS bioenergetics was assessed using an XF24 analyser, which simultaneously quantifies two energetic pathways- glycolysis (ECAR) and Oxidative phosphorylation (OCR).
Results: OSM-induced Migration and Invasion was supressed by all JAKi with Peficitinib, Filgotinib and Baracitinib showing the greatest effect. Analysis by ELISA and rtPCR showed reduction in MCP-1 and IL-6 expression in response to JAKi, in contrast, an increase in IL-8 was observed. These functional effects were accompanied by a change in the cellular bioenergetic profile of PsA FLS, where OSM significantly increased the ECAR:OCR ratio in favour of glycolysis where PsA FLS displayed a hypermetabolic phenotype. This effect was reversed in the presence of JAKi, which specifically targeted the glycolytic pathway with PsA FLS returning to a more quiescent phenotype.
Conclusion: This study demonstrates that JAK/STAT signalling mediates the complex interplay between inflammation and cellular metabolism in PsA pathogenesis, inhibition of which shows effective suppression of the pathogenic phenotype of PsA FLS that drives joint destruction.
REFERENCES:
[1] Chen M, Dai SM. A novel treatment for psoriatic arthritis: Janus kinase inhibitors. *Chin Med J (Engl)*. 2020;133(8):959-967.
Disclosure of Interests: Aisling O' Brien: None declared, Megan Hanlon: None declared, Viviana Marzaioli: None declared, Keelin Flynn: None declared, Siobhan Wade: None declared, Douglas Veale Speakers bureau: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Consultant of: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Grant/research support from: Janssen, Abbvie, Pfizer, UCB, Ursula Fearon Speakers bureau: Abbvie, Grant/research support from: Janssen, Abbvie, Pfizer, UCB
DOI: 10.1136/annrheumdis-2021-eular.2528

POS0412 CD21-/LOW B-CELLS ARE INCREASED IN PATIENTS WITH ANKYLOSING SPONDYLITIS

R. Wilbrink[1], A. Spoorenberg[1], S. Arends[1], F. G. M. Kroese[1], G. M. Verstappen[1]. [1]*University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*

Background: Ankylosing spondylitis (AS) is a chronic immune mediated inflammatory rheumatic disease, in which primarily the sacroiliac joints and the spine are affected. Extra-skeletal manifestations (ESM) include uveitis, psoriasis, inflammatory bowel disease and peripheral arthritis. In studies into the pathogenesis of AS, B-cells have received little attention most likely due to the lack of auto-antibodies[1]. A B-cell subset that has been particularly associated with autoreactivity is characterized by low expression of CD21. These CD21$^{-/low}$ B-cells are increased in systemic autoimmune diseases, including rheumatoid arthritis, systemic lupus erythematosus and primary Sjögren syndrome (pSS)[2]. At least part of the CD21$^{-/low}$ B-cells are considered to represent anergic, autoreactive B-cells, that fail to become activated through conventional B-cell receptor and CD40 signaling[2].
Objectives: To phenotypically study the peripheral B-cell compartment in in the blood of AS patients compared to pSS patients, a typical B-cell-associated autoimmune disease, and healthy controls (HC). Special emphasis was given to the CD21$^{-/low}$ compartment.
Methods: The proportions and phenotype of peripheral B-cells were assessed in cryopreserved peripheral blood mononuclear cells of 45 AS patients (62% male, mean age 49.2±13.2 years, mean ASDAS 2.5±1.0), 20 age-matched patients with pSS (20% male, mean age 50.6±12.0, median (IQR) ESSDAI 3±6.25) and 30 age- and sex-matched HCs, using 15-color flow-cytometry analysis. Differences between groups were tested using the Independent Samples t-test or Mann-Whitney U test depending on the distribution of variables. Associations between CD21$^{-/low}$ B-cells and clinical parameters were explored using the Pearson or Spearman correlation coefficient.
Results: The percentage of total B-cells in AS patients did not differ from pSS patients and HCs. In AS patients, percentages of CD27^{+} memory B-cells and CD27^{-}IgD^{+} naïve B-cells were also similar to HCs, whereas CD27^{+}IgD^{-} memory B-cells were significantly reduced in pSS patients, as expected. The proportions of CD27^{-}CD38^{low}CD21$^{-/low}$ B-cells among total B-cells were significantly increased in both AS (median 6.4%, p<0.0001) and pSS patients (median 7.8%, p<0.0001) compared to HCs (median 4.9%). Interestingly, only in AS patients, expression of chemokine receptors CXCR3 and CXCR5 was significantly elevated on CD27^{-}CD38^{low}CD21$^{-/low}$ B-cells compared to HCs (p<0.001 and p<0.01, respectively). In comparison to HCs the expression of the immune markers T-bet and CD11c by CD27^{-}CD38^{low}CD21$^{-/low}$ B-cells was significantly lower in AS patients (p<0.01 and p<0.01, respectively). The distribution of IgM and IgD expression within the CD27^{-}CD38^{low}CD21$^{-/low}$ B-cell population was similar between all three study groups. Regarding the association between CD27^{-}CD38^{low}CD21$^{-/low}$ B-cells and clinical parameters in AS patients, we observed a positive correlation with age (r=0.347, p=0.02) and erythrocyte sedimentation rate (ρ=0.386, p=0.01). Furthermore, AS patients with ESM showed increased proportions of CD27^{-}CD38^{low}CD21$^{-/low}$ B-cells compared to patients without ESM (p<0.05).
Conclusion: In this cross-sectional study, we observed an increased proportion of circulating CD27^{-}CD38^{low}CD21$^{-/low}$ B-cells in AS patients, similar as in patients

with pSS, a typical B-cell-mediated autoimmune disease. The elevated expression of CXCR3 on $CD27^{-}CD38^{low}CD21^{-/low}$ B-cells in AS patients is suggestive for active involvement in the inflammatory response. These findings are indicative of B-cell involvement in the pathogenesis of AS, against current dogma.

REFERENCES:
[1] Ranganathan V et al. *Nat Rev Rheumatol*. 2017;13(6):359-367.
[2] Thorarinsdottir K et al. *Scand J Immunol*. 2015;82(3):254-261.

Disclosure of Interests: Rick Wilbrink: None declared, Anneke Spoorenberg: None declared, Suzanne Arends: None declared, Frans G.M. Kroese Speakers bureau: BMS, Roche, Janssen-Cilag, Consultant of: BMS, Grant/research support from: BMS, Gwenny M. Verstappen: None declared
DOI: 10.1136/annrheumdis-2021-eular.2957

POS0413 COMPREHENSIVE IMMUNE PROFILING OF PERIPHERAL BLOOD IN PSORIATIC ARTHRITIS (PsA) PATIENTS: EXPANSION OF INTERMEDIATE MONOCYTES AND DECREASED T REG AND CD8 T CELLS

A. Grivas[1], M. Grigoriou[1], P. Katsimpri[2], P. Verginis[3,4], D. Boumpas[1,2]. *[1]Biomedical Research Foundation of the Academy of Athens (BRFAA), Laboratory of Immune Regulation and Tolerance Autoimmunity and Inflammation, Athens, Greece*; *[2]National and Kapodistrian University of Athens, 4th Department of Internal Medicine, Athens, Greece*; *[3]Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology, Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology, Heraklion, Greece*; *[4]University of Crete Medical School, Laboratory of Immune Regulation and Tolerance, Division of Basic Sciences, Heraklion, Greece*

Background: Psoriatic arthritis (PsA) is a heterogeneous inflammatory arthritis that develops in a subset of patients with psoriasis. According to the current paradigm, cells of the innate and adaptive immunity interact with resident tissue fibroblasts mounting an inflammatory response via complex cytokine networks in the skin and joints in which type 1 and type 17 T cells play a dominant role. The abundance and relative contribution of other peripheral blood immune cells to disease pathogenesis as well the molecular signature of peripheral blood mononuclear cells and tissue fibroblasts remain ill defined.
Objectives: To comprehensively characterize immune cell subsets driving inflammation in the peripheral blood of patients with active PsA and their impact on psoriatic skin fibroblasts.
Methods: Peripheral blood was collected from PsA patients (n=31) and age-/sex-matched healthy individuals (HI) (n=9), after informed consent. Psoriatic skin biopsies were acquired from a subset of 5 patients and 3 HI. All patients fulfilled the CASPAR criteria for the diagnosis and displayed peripheral polyarthritis of moderate- to high-disease activity. Patients' demographic and clinical data were recorded at time of sampling. Disease activity was assessed using the Disease Activity Index for Psoriatic arthritis (DAPSA) score. Skin psoriasis activity indices, enthesitis and dactylitis were also recorded. Peripheral blood mononuclear cells (PBMCs) were isolated by ficoll density gradient centrifugation. Flow cytometry was performed using a BD FACS-Aria-III and analyzed using FlowJo software. The antibody staining panel utilized aimed at the identification of the following immune cell subsets: Monocyte subsets (HLA-DR+ CD14+/- CD16+/-), Plasmacytoid dendritic cells (HLA- DR+ CD123+), T helper (CD4+), cytotoxic T (CD8+), regulatory T (CD4+ CD25+ CD127-) and B cells (CD19+). Statistical analyses were performed using GraphPad Prism software. Differences between groups were compared using unpaired T test for parametric data; Mann-Whitney and Kruskal Wallis tests for non-parametric data. The level of significance was set at $P<0.05$.
Results: 9 males and 22 females PsA patients are included (mean age 50 years and the mean disease duration 19.2 years for skin disease and 5.9 years for arthritis). The mean DAPSA score was 43.4, suggestive of high disease activity, while 8 (26%) patients displayed clinical enthesitis at time of sampling. Flow cytometry analysis revealed aberrancies in peripheral blood immune cell populations. More specifically, PsA patients displayed a significant increase in intermediate monocyte subset (HLA-DR+ CD14+ CD16+) compared to HI with patients with clinical enthesitis demonstrating a more exaggerated expansion of intermediate monocytes compared to patients without enthesitis. A trend towards increased patrolling monocytes (HLA-DR+ CD14- CD16+) was also noted although this did not reach statistical significance. In contrast, both regulatory T cells and cytotoxic CD8+ T cells were significantly decreased probably due to their selective migration at the sites of inflammation. RNA-seq from whole blood and skin fibroblasts from affected skin are in progress.
Conclusion: These data demonstrate significant expansion of intermediate monocytes -more pronounced in the enthesitis affected individuals- and decrease in T regulatory cells and T cytotoxic cells in PsA peripheral blood. Increased antigen presentation and co-stimulation mediated via intermediate monocytes in combination with their proangiogenic properties may contribute to disease pathogenesis

REFERENCES:
[1] Veale, D. J. & Fearon, U. The pathogenesis of psoriatic arthritis. *The Lancet* (2018) doi:10.1016/S0140-6736(18)30830-4.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3540

POS0414 INCREASED BDNF LEVELS AS A PREDICTOR OF CENTRAL SENSITIZATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

I. Shapoval[1], K. Zaichko[1], M. Stanislavchuk[1]. *[1]National Pirogov Memorial Medical University, Vinnytsya, Ukraine, Chair of Internal Medicine #1, Vinnytsya, Ukraine*

Background: Ankylosing spondylitis (AS) is a chronic rheumatic disease that manifests itself in a range of inflammatory changes, severe pain and rapid progression with the development of osteoproliferation and the formation of ankylosis. Prerequisites are created for the emergence of signs of central sensitization. Scientists are growing interested in the role of the phenomenon of central sensitization. Central sensitization is present in almost half of patients with chronic pain (45% SpA, 41% RA, 62% OA and 94% of FM patients) [1]. Brain neurotrophic factor (BDNF) is involved in pain regulation mechanisms and the occurrence of central sensitization, but its role in patients with AS is poorly understood.
Objectives: Our study aimed to determine levels of plasma BDNF in patients with AS and evaluate their role as central sensitization predictors in patients with ankylosing spondylitis.
Methods: We examined 143 patients with AS according to modified New York criteria (26 women and 117 men) with mean age 42.1±11.3 years (M±σ) and 35 persons of the control group, representative by age, sex. The content of plasma BDNF was determined at 8:00 and 20:00 by ELISA and calculated the daily average and morning/evening ratio - 8:00/20:00 BDNF index. All patients completed self-administered questionnaire Fibromyalgia Rapid Screening Tool (FiRST) to detect FM. FM was defined by a score = > 5/6 by the FiRST. The study was conducted in compliance with bioethical standards. All data were analyzed using IBM Statistics SPSS 22.
Results: Among 143 patients with AS, there were 51 persons with FiRST ≥ 5, indicating central sensitization and probable FM. In the group with AS mean scores (M±σ) of plasma BDNF levels were 962.5±357.2 pg/ml at 8:00 and 834.7±510.0 pg/ml at 20:00 compared to control group (785.2±109.7 pg/ml and 450.6±358.9 pg/ml; $p< 0.001$). 36% AS patients were with + FiRST and had higher daily average and evening BDNF levels and a decreased 8:00/20:00 BDNF index. According to 8:00/20:00 BDNF index, we divide AS patients into 4 groups: 1st quartile (Q1) included people with BDNF index <0.83; 2nd quartile (Q2) - 0.83 - 1.15; 3rd quartile (Q3) - 1.16 - 2.49; 4th quartile (Q4) - > 2.49. Table 1 shows detailed information about FM's quantitative characteristics in patients with AS (n = 143) depending on the 8:00/20:00 BDNF index.
In patients with AS and + FiRST was registered an inadequate decrease in plasma BDNF levels in the evening, as evidenced by a decrease in the 8:00/20:00 BDNF index, which was combined with increased disease activity and poorer of the functional status.
The ROC analysis results showed that the 8:00/20:00 BDNF index at the cut-off point of 0.95 confirms the presence of central sensitization in patients with AS with a sensitivity of 86.2% and a specificity of 79.6%. The AUC is 0.878, which indicates a good quality of the model. Patients with the 8:00/20:00 BDNF index <0.95 are many times more likely to detect features of central sensitization (OR = 20.9; 95% CI: 8.66-50.39, $p < 0.001$).
Conclusion: Our results showed high diagnostic value to determine plasma levels of BDNF and to calculate 8:00/20:00 BDNF index as central sensitization marker in patients with AS with a sensitivity of 86.2% and a specificity of 79.6%.

Table 1. Quantitative characteristics of FM in patients with AS (n = 143) depending on the 8:00/20:00 BDNF index.

Parameters	BDNF «8:00 / 20:00»			
	< 0.83	0,83 – 1.15	1,16 – 2.49	> 2.49
	Q1 (n=37)	Q2 (n=35)	Q3 (n=35)	Q4 (n=36)
FiRST (M±σ)	4.49±1,46	4.23±1.42	3.03±1.44 ***#	2.81±1.04 ***#
FiRST≥ 5, n (%)	24 (64,9 %)	17 (48.6 %)	9 (25.7 %) ***#	1 (2.78 %) ***#

Notes: 1. * - statistically significant differences relative to Q1 (* - p <0.05;** - p <0.01; *** - p <0.001); 2. # - statistically significant differences relative to Q2 (# - p <0.05).

REFERENCES:
[1] Guler, M. A., Celik, O. F., & Ayhan, F. F. (2020). The important role of central sensitization in chronic musculoskeletal pain seen in different rheumatic diseases. *Clinical rheumatology*, *39*(1), 269-274.

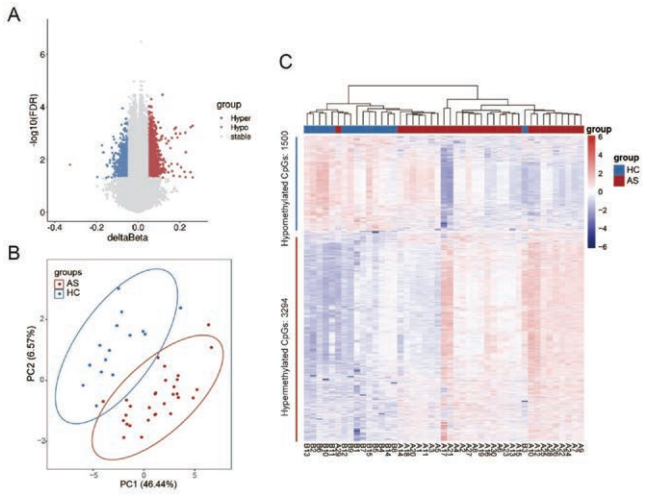
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3908

POS0415

BLOOD-DERIVED DNA METHYLATION EPI-SIGNATURES ASSOCIATED WITH ANKYLOSING SPONDYLITIS

M. Xiao[1], J. Gu[1]. [1]*Third Affiliated Hospital of Sun Yat-sen University, Department of Rheumatology and Immunology, Guangzhou, China*

Background: Most (~90%) of the ankylosing spondylitis (AS) susceptibility loci are undefined and located in non-coding regions. Epigenetic changes may alter the expression of genes involved in AS and explain part of the missing heritability. [1]
Objectives: To identify novel DNA methylation sites significant for AS and comprehensively understand the underlying pathological mechanism.
Methods: Genome-wide DNA methylation of blood samples from 30 AS patients and 15 health controls was measured on the Infinium® MethylationEPIC BeadChip microarray. Methylome data were analyzed with ChAMP package in R.
Results: The epigenome-wide association analysis identified 4,794 differentially methylated positions (DMPs) (FDR <0.05 and delta β >0.05), including 3,294 (68.7%) hypermethylated and 1,500 (31.3%) hypomethylated positions in AS patients (Figure 1A). The identified DMPs allowed clear distinction of most AS cases from controls in the PCA (Figure 1B) and unsupervised hierarchical clustering (Figure 1C). KEGG pathway analysis of AS associated DMPs enriched in T cell receptor signaling pathway, Th1 and Th2 cell differentiation. Besides, a total of 1,048 differentially variable positions (DVPs) were identified, the majority of which (974, 92.9%) were hypervariable in AS, while only 74 DVPs were hypovariable. The increased DNA methylation variability in disease were in line with the previous observation in other diseases, indicating the intrinsic heterogeneity in AS patients, which might be influenced by diverse factors, such as disease activity and treatment.
Figure 1.



Conclusion: Peripheral blood mononuclear cells from AS patients display aberrant DNA methylome and increased DNA methylation variability. The results enhanced our understanding of the important role of DNA methylation in pathology of AS and offered the possibility of identifying new targets for intervention.

REFERENCES:

[1] Whyte JM, Ellis JJ, Brown MA, et al. Best practices in DNA methylation: lessons from inflammatory bowel disease, psoriasis and ankylosing spondylitis. *Arthritis Res Ther* 2019; 21:133.

Acknowledgements: We appreciate all the staff members of the department of rheumatology of the Third Affiliated Hospital of Sun Yat-sen University for assistance and support in the patient's recruitment and sample collection.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4257

SLE, Sjögren's and APS - aetiology, pathogenesis and animal models

POS0416

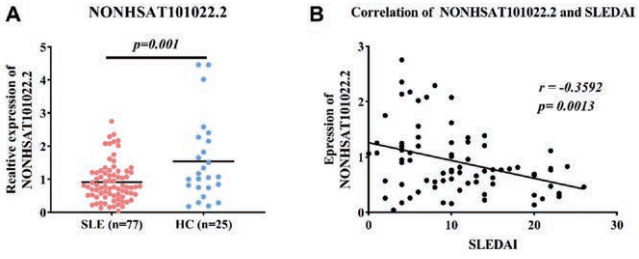
NOVEL LONG NON-CODING RNA EXPRESSION PROFILE OF PERIPHERAL BLOOD MONOUCLEAR CELL REVEALED POTENTIAL BIOMARKERS AND REGULATORY MECHANISM IN SYSTEMIC LUPUS ERYTHEMATOSUS

Q. Cheng[1], M. Chen[1], X. Chen[1], X. Chen[1], H. Wu[1], Y. Du[1]. [1]*the Second Affiliated Hospital of Zhejiang University School of Medicine, Rheumatology, Hangzhou, China*

Background: Systemic lupus erythematosus (SLE) is a complex and heterogeneous autoimmune disease, usually involving multiple systems of the whole body (1). A variety of factors can affect SLE, such as genetic, environmental, immunoregulatory, hormonal and epigenetic (2). Long non-coding RNA is a type of RNA greater than 200 nucleotides that does not encode proteins. With the development of research, lncRNA gradually becomes the key regulator of gene expression in the immune system (3). Studies have shown that several lncRNAs, such as NEAT1 and GAS5 are dysregulated in SLE and are involved in the pathogenesis of SLE (4,5). These results suggest that lncRNA can be used as a potential biomarker for disease diagnosis and treatment. However, our current understanding of SLE related lncRNAS is still limited.
Objectives: The purpose of this study was to find new lncRNAs in peripheral blood monouclear cells of SLE patients by transcriptome sequencing and explore their potential as biomarkers and their correlation with clinical features.
Methods: Transcriptome sequencing was used to screen differentially expressed lncRNAs (DELs) and mRNAs (DEMs). DAVID and WebGestalt were used to perform enrichment analysis. Cytoscape was used to constructed protein-protein network, co-expression network and competitive endogenous RNA network to reveal the regulatory mechanism of lncRNAs in transcriptome level. The expression of these selected lncRNAs in SLE patients and healthy controls were verified by qPCR.
Results: A toal of 1737 DELs and 4078 DEMs were identified between 5 SLE patients and 5 healthy controls. Most of upregulated genes were enriched in defense and immune response, while downregulated genes were mainly enriched in SLE related pathways. Topology network analysis reveal the regulatory mechanism of lncRNAs in transcriptome level including directly acting on mRNA or indirectly affecting gene expression after acting on miRNA. Ten lncRNAs and eight genes was verified by qPCR in bigger samples including 77 SLE patients and 25 healthy controls. LncRNA NONHSAT101022.2 was significantly downregulated in SLE patients (*p=0.001*) and the expression of NONHSAT101022.2 showed a significant negative correlation with SLE disease activity index (SLEDAI, *r=-0.3592, p=0.0013*).
Conclusion: In this work, we identified a large number of mRNAs and novel lncRNAs by transcriptome sequence. The function and regulatory mechanism of these lncRNAs were analyzed by bioinformatics methods. LncRNA NONHSAT101022.2 is significantly downregulated in SLE patients and significantly related to the activity and severity of disease. Additionally, we put forward that NONHSAT101022.2 may enhance the signal transduction of β2-AR by cis-regulating its target gene, LMBRD2, which induces NK cells to produce high levels of IFN-γ, thereby exacerbating SLE.

REFERENCES:

[1] Carter EE, Barr SG, Clarke AE. The global burden of SLE: prevalence, health disparities and socioeconomic impact. Nat Rev Rheumatol. 2016;12(10):605-20.
[2] Han EC. Systemic lupus erythematosus. N Engl J Med. 2012;366(6):573-4; author reply.
[3] Chen YG, Satpathy AT, Chang HY. Gene regulation in the immune system by long noncoding RNAs. Nat Immunol. 2017;18(9):962-72.
[4] Zhang F, Wu L, Qian J, Qu B, Xia S, La T, et al. Identification of the long noncoding RNA NEAT1 as a novel inflammatory regulator acting through MAPK pathway in human lupus. Journal of autoimmunity. 2016;75:96-104.
[5] Liu Q, Deng Y, Li C, Xie H, Liu Q, Ming S, et al. LncRNA GAS5 suppresses CD4(+) T cell activation by upregulating E4BP4 via inhibiting miR-92a-3p in systemic lupus erythematosus. Immunol Lett. 2020;227:41-7.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.129

POS0417

EXOGENOUS CXCL5 RESTORES ENDOGENOUS BLOOD-TISSUE CHEMOKINE GRADIENT TO IMPROVE SURVIVAL IN MURINE LUPUS

F. Lim[1], D. Guo[1], J. Chen[2], A. Law[3], Z. Y. Poon[4,5], A. Cheung[4,6], J. C. Tan[2], S. L. Kong[7], A. H. L. Loh[8], M. G. K. Tan[1], S. Li[9], K. H. Lim[8], J. Thumboo[3,6], C. T. Ng[3,6], W. Hwang[4,10], A. Low[3,6], X. Fan[1,6]. [1]*Singapore General Hospital, Clinical Translational Research, Singapore, Singapore*; [2]*Singapore Immunology Network, Single-cell Computational Immunology, Singapore, Singapore*; [3]*Singapore General Hospital, Rheumatology and Immunology, Singapore, Singapore*; [4]*Singapore General Hospital, Hematology, Singapore, Singapore*; [5]*Singapore-MIT Alliance for Research and Technology, Critical Analytics for Manufacturing Personalized-Medicine (CAMP), Singapore, Singapore*;

[6]Duke-NUS Medical School, SingHealth Duke-NUS Medicine Academic Clinical Programme, Singapore, Singapore; [7]Genome Institute of Singapore (GIS), Genome Institute of Singapore, Singapore, Singapore; [8]Singapore General Hospital, Pathology, Singapore, Singapore; [9]Duke-NUS Medical School, Cancer & Stem Cell Biology, Singapore, Singapore; [10]National Cancer Centre Singapore, National Cancer Centre Singapore, Singapore, Singapore

Background: Systemic lupus erythematosus (SLE) is a multi-organ autoimmune disease that is potentially fatal. There is an unmet need to improve current therapies. In patients with SLE, we observed that serum CXCL5 levels were significantly lower than healthy control subjects and negatively correlated with disease activity[1-9].
Objectives: The aim of this study is to elucidate the effect of supplemental serum CXCL5 in abrogating the pathological processes of SLE.
Methods: Ten doses of exogenous CXCL5 (3μg/kg) was administered to 16-week-old Fas^{lpr} mice weekly by intravenous injection. Mice were monitored for 10 weeks. Splenic immune profile was measured by flow cytometry. Circulating cytokine and immunoglobulin profile were detected by Luminex technology. Renal function was evaluated by urinary spot albumin creatinine ratio. In situ renal immune cell infiltration and complement 3 deposition were detected by Haematoxylin and Eosin (H&E) and immunohistochemistry staining. The molecular pathways involved were examined by RNA sequencing.
Results: In Fas^{lpr} mice, intravenous administration of exogenous CXCL5 significantly improved mouse survival with concomitant reduction of autoantibody secretion, proteinuria, complement 3 deposition, neutrophil infiltration and lupus nephritis classes. Through evaluating the changes of immune profile, cytokine profile and molecular pathways, we found that intravenous CXCL5 reduced inflammation via an orchestral effect of regulating neutrophil trafficking and modulating helper T cell-mediated immune response. Pharmacokinetic and real-time Polymerase Chain Reaction studies further demonstrated that this orchestration was triggered by a cascade reaction - restoring vascular under-expressed CXCL5 by an exogenous stimulation, re-establishing the normal serum levels of endogenous CXCL5 and reverting the CXCL5 chemokine gradient between inflamed tissues and blood circulation.
Conclusion: Managing the dysregulation of CXCL5 by exogenous supplement may provide a new option for SLE therapy.
REFERENCES:

[1] Dufies M, Grytsai O, Ronco C, et al. New CXCR1/CXCR2 inhibitors represent an effective treatment for kidney or head and neck cancers sensitive or refractory to reference treatments. Theranostics. 2019;9(18):5332-5346. doi:10.7150/thno.34681
[2] Yildirim K, Colak E, Aktimur R, et al. Clinical Value of CXCL5 for Determining of Colorectal Cancer. Asian Pac J Cancer Prev. Sep 26 2018;19(9):2481-2484. doi:10.22034/apjcp.2018.19.9.2481
[3] Wu K, Yu S, Liu Q, Bai X, Zheng X. The clinical significance of CXCL5 in non-small cell lung cancer. Onco Targets Ther. 2017;10:5561-5573. doi:10.2147/ott.s148772
[4] Zhao J, Ou B, Han D, et al. Tumor-derived CXCL5 promotes human colorectal cancer metastasis through activation of the ERK/Elk-1/Snail and AKT/GSK3beta/beta-catenin pathways. Mol Cancer. Mar 29 2017;16(1):70. doi:10.1186/s12943-017-0629-4
[5] Han KQ, Han H, He XQ, et al. Chemokine CXCL1 may serve as a potential molecular target for hepatocellular carcinoma. Cancer Med. Oct 2016;5(10):2861-2871. doi:10.1002/cam4.843
[6] Pappa CA, Tsirakis G, Kanellou P, et al. Monitoring serum levels ELR+ CXC chemokines and the relationship between microvessel density and angiogenic growth factors in multiple myeloma. Cytokine. Dec 2011;56(3):616-20. doi:10.1016/j.cyto.2011.08.034
[7] Zhang L, Li H, Ge C, et al. CXCL3 contributes to CD133(+) CSCs maintenance and forms a positive feedback regulation loop with CD133 in HCC via Erk1/2 phosphorylation. Sci Rep. Jun 3 2016;6:27426. doi:10.1038/srep27426
[8] Matsubara J, Honda K, Ono M, et al. Reduced plasma level of CXC chemokine ligand 7 in patients with pancreatic cancer. Cancer Epidemiol Biomarkers Prev. Jan 2011;20(1):160-71. doi:10.1158/1055- 9965.epi-10-0397
[9] Ma Y, Ren Y, Dai ZJ, Wu CJ, Ji YH, Xu J. IL-6, IL-8 and TNF-alpha levels correlate with disease stage in breast cancer patients. Adv Clin Exp Med. May-Jun 2017;26(3):421-426. doi:10.17219/acem/62120

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2262

POS0418 SPLENIC EXTRAMEDULLARY HEMATOPOIESIS IS OMNIPRESENT AND CORRELATES WITH DISEASE SEVERITY IN THE LUPUS NZB/W F1 MURINE MODEL

S. Doumas[1,2], M. Grigoriou[1], A. Banos[1,3], C. Giakopoulou[4], I. Mitroulis[5], P. Verginis[6], D. Boumpas[1,2,7]. [1]Biomedical Research Foundation of the Academy of Athens, Laboratory of Inflammation and Autoimmunity, Athens, Greece; [2]Attikon University Hospital and Joint Rheumatology Program, National and Kapodistrian University of Athens, 4th Department of Internal Medicine, Athens, Greece; [3]Hippokration General Hospital, 2nd Department of Internal Medicine, Athens, Greece; [4]Medical School, National and Kapodistrian University of Athens, 1st Department of Pathology, Athens, Greece; [5]Democritus University of Thrace, Department of Hematology and Laboratory of Molecular Hematology, Department of Medicine, Alexandroupoli, Greece; [6]University of Crete Medical School, Laboratory of Immune Regulation and Tolerance, Heraklion, Greece; [7]Medical School, University of Cyprus, Rheumatology-Clinical Immunology Unit, Nicosia, Greece

Background: Extramedullary hematopoiesis (EMH) is increasingly recognized as an integral component of systemic inflammatory diseases; compared to their bone marrow counterparts, hematopoietic progenitors of EMH have an enhanced role in target organ damage[1,2]. We have found that β-glucan -a non-specific inducer of reprograming of innate immunity- results in dramatic EMH with marked increase in Long-Term (LT)-HSCs, massive splenomegaly and worsening of nephritis in the NZB/W F1 lupus murine model (unpublished data).
Objectives: To investigate EMH's time course and contribution to inflammatory target-organ damage (kidney) in the NZB/W F1 lupus murine model.
Methods: Spleens and kidneys were isolated from female NZB/W F1, at pre-nephritic stage (3-month-old) and nephritic stage (>6-month-old), and age/sex matched C57BL/6 (WT controls). Single-cell suspensions of spleens were analyzed by flow cytometry for Hematopoietic Stem and progenitor cells (HSPCs) phenotyping. Formalin-fixed and paraffin-embedded sections of spleens and kidneys were stained with conventional histological stains (H&E, Silver, Trichrome Masson). Spleens were histologically assessed for the presence of EMH and kidneys were assessed for activity and chronicity through the NIH Lupus nephritis scoring system.
Results: Histological analysis revealed that NZW/B F1 mice at the nephritic stage display massive splenomegaly with concomitant expansion of the red pulp, increased presence of megakaryocytes and disorganized splenic architecture. This is further corroborated by the flow cytometry analysis which demonstrated a significant increase of all HSPCs subsets (Long-term/Short-term Hematopoietic Stem Cells and Multipotent progenitors) compared to the C57BL/6 WT controls at nephritic stage. The degree of HSPC expansion and splenic architecture disorganization correlates strongly with the activity of lupus nephritis as quantified by the NIH scoring system. Of note, evidence of splenic EMH were present even in 3-month-old animals before overt nephritis ensues.
Conclusion: Extramedullary hematopoiesis is present before overt nephritis and is dramatically expanded at the nephritic stage of the NZW/B F1 mouse model. The degree of EMH positively correlates with the severity of lupus nephritis. These data support a pathogenic role of EMH, and spleen derived HSPCs, in driving lupus nephritis.
REFERENCES:

[1] Regan-Komito, D., Swann, J.W., Demetriou, P., Cohen, E.S., Horwood, N.J., Sansom, S.N., Griseri, T., 2020. GM-CSF drives dysregulated hematopoietic stem cell activity and pathogenic extramedullary myelopoiesis in experimental spondyloarthritis. Nature Communications 11, 155.
[2] Griseri, T., McKenzie, B.S., Schiering, C., Powrie, F., 2012. Dysregulated Hematopoietic Stem and Progenitor Cell Activity Promotes Interleukin-23-Driven Chronic Intestinal Inflammation. Immunity 37, 1116–1129.

Acknowledgements: This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 742390)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2490

POS0419 ABERRANT SPLICEOSOME AND ALTERED EXPRESSION OF IFN-RESPONSE RELATED GENES ARE HALLMARKS OF MONOCYTES FROM LUPUS PATIENTS WITH RENAL DISEASE

A. M. Patiño-Trives[1], C. Perez-Sanchez[1], A. Ibañez-Costa[2], M. Luque-Tévar[1], M. D. C. Abalos-Aguilera[1], I. Arias de la Rosa[1], D. Ruiz[1], P. Seguí Azpilcueta[1], M. Espinosa[1], N. Barbarroja Puerto[1], J. P. Castaño[2], R. M. Luque Huertas[2], M. A. Aguirre[1], C. Lopez-Pedrera[3]. [1]IMIBIC, Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, Córdoba, Spain; [2]IMIBIC, Department of Cell Biology, Physiology and Immunology, University of Cordoba, Spain, Córdoba, Spain; [3]IMIBIC, Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, Cordoba, Spain

Background: To date, novel mechanisms such as the involvement of splicing machinery components in lupus nephropathy and its interplay with the transcriptome in innate immune cells have not been evaluated.
Objectives: 1- To identify altered transcriptomic signatures associated with the immune response of monocytes from SLE patients and its association with clinical features. 2- To evaluate the role of the spliceosome linked to the transcriptomic profile of SLE monocytes. 3- To analyze mechanistically the impact of

anti-dsDNA antibodies (Ab) and the modulation of the spliceosome in the SLE monocytes activity.

Methods: Sixty SLE patients and forty healthy donors (HD) were included in the study. Infiltration rate of myeloid cells and its association with clinical features were analyzed in kidney biopsies by Immunohistochemistry. In parallel, circulating monocytes were purified from peripheral blood by immune-magnetic selection. The expression of a set of 770 genes related to autoimmune/inflammatory diseases was evaluated using NanoString Technologies. The levels of the main 45 components of the splicing machinery were further analyzed in these samples using a microfluidic qPCR array (Fluidigm). An extensive clinical/serological evaluation was also performed, comprising disease activity, renal involvement parameters, autoAb profile, and the systemic inflammatory status (27-plex Assay). Finally, *in vitro* studies involving anti-dsDNA-IgG Ab treatment and over/down-expression of splicing machinery components were carried out to analyze their effects in the monocyte activity.

Results: Infiltration of CD68 expressing cells was confirmed in kidney biopsies and associated with parameters of kidney failure (C3/C4, chronic index), highlighting the key role of the myeloid compartment in lupus nephropathy. Gene expression profiling recognized 156 genes differentially expressed in SLE monocytes compared with HDs, including 87 genes up-regulated and 69 down-regulated. Functional analysis showed that most dysregulated genes were associated with the IFN response (i.e. IFIT1, IFI44, IFI44L, RSAD2). In parallel, the altered expression of 27 spliceosome components was demonstrated in SLE monocytes compared with HD, including 3 up-regulated and 24 down-regulated. Correlation studies demonstrated that the aberrant expression of splicing machinery components was linked to the altered interferon signature and the plasma inflammatory profile. This aberrant profile at molecular level was associated with the disease activity status, anti-dsDNA positivity and C3/C4 levels. Interestingly, SLE patients with renal disease displayed a simultaneous alteration of both, the IFN and the spliceosome signatures in monocytes, along with an enlarged pro-inflammatory profile in plasma. Logistic regression models that integrated the concomitant alteration of some splicing machinery components and IFNs genes identified lupus nephritis patients with high accuracy. Mechanistic studies showed that *in vitro* treatment of monocytes from HDs with anti-dsDNA promoted a concomitant deregulation of the IFN signature and the expression of several spliceosome components (i.e. PTB, RBM17, RNU6ATAC). Finally, the over/down-expression of selected spliceosome components (PTB and RBM17) in monocytes from SLE patients reduced the active release of inflammatory cytokines and their adhesion capacity.

Conclusion: 1) Monocytes from SLE patients with renal involvement exhibit a remarkable alteration of genes associated with the IFN response, further linked with the aberrant expression of several splicing machinery components. 2) Anti-dsDNA promoted the dysregulation in monocytes of both the IFN and spliceosome signatures, along with an active release of pro-inflammatory mediators. 3) The modulation of key splicing components in monocytes from SLE patients reduce their pro-inflammatory status and migration capacity. Ongoing studies may provide novel biomarkers and therapeutic tools to treat lupus nephropathy.

Acknowledgements: Funded by ISCIII, PI18/00837 and RIER RD16/0012/0015 co-funded with FEDER

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2534

POS0420 DYSREGULATED CD38 EXPRESSION ON PERIPHERAL BLOOD IMMUNE CELL SUBSETS IN SLE

M. Burns[1], L. Ostendorf[2,3], A. Grützkau[1], F. Hiepe[2,3], T. Alexander[2,3], H. Mei[1]. *[1]Deutsches Rheuma-Forschungszentrum (DRFZ Berlin) – a Leibniz Institute, Immune Monitoring & Mass Cytometry, Berlin, Germany*; *[2]Charité – Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; *[3]Deutsches Rheuma-Forschungszentrum (DRFZ Berlin) – a Leibniz Institute, Autoimmunology, Berlin, Germany*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by pathogenic antinuclear autoantibodies, which are secreted by autoreactive plasma cells. Among novel plasma cell-depleting strategies, CD38 has been identified as promising target. The monoclonal anti-CD38 antibody daratumumab is approved for treatment of multiple myeloma and provided a therapeutically relevant depletion of plasma cells in patients with SLE[1].

Objectives: Beyond plasma cells, CD38 is widely expressed across innate and adaptive immune cells and additional cellular targets of anti-CD38 treatment, especially in patients with SLE, are largely unknown. Therefore, this study aimed to systematically characterize the expression of CD38 in peripheral blood leukocytes to identify potential target cells of CD38-directed therapies that may contribute to or limit therapeutic benefits in SLE.

Methods: We analyzed the expression of CD38 on peripheral blood leukocytes in two different cohorts, comprising a total of 56 SLE patients and 39 healthy controls, by flow and mass cytometry. CD38 expression levels across major immune cells were analyzed for changes between controls and SLE, as well as for correlation across immune cell lineages, and with clinical and serological disease parameters.

Results: We detected increased CD38 expression levels on circulating NK cells, plasmacytoid dendritic cells, $CD4^+$ and $CD8^+$ memory T cells, as well as IgD^-CD27^- and marginal zone-like B cells in SLE compared to healthy controls. In myeloid and NK cells, CD38 expression was associated with an activated cellular phenotype, reflected by co-expression of molecules such as HLA-DR, CD11c or Syk. In the B cell compartment, IgA^- plasmablasts and plasma cells expressed more CD38 than their IgA^+ counterparts. Also, HLA-DR^{high} plasmablasts showed higher CD38 expression compared to HLA-DR^{low} plasma cells. The strongest differences in CD38 expression between controls and SLE were found in $CD8^+$ central and effector memory T cells. Additionally, we detected an expansion in $CD38^{high}$ and $CD38^{int}$ cells in the T cell memory compartment, with some patients showing distinctly increased expression values. We observed a high intra-individual correlation of CD38 expression across immune cell lineages, yet without correlation of CD38 expression levels with clinical activity (SLEDAI-2K), serological markers of SLE or the type I interferon surrogate marker CD169 (SIGLEC-1).

Conclusion: Our data indicate that not only pathogenic plasma cells are potential target cells of CD38-targeting antibodies. The highly dysregulated CD38 expression across innate and adaptive immune cells in SLE could be of pathophysiological importance with respect to the potential efficacy and side effects of such therapies. Since CD38 expression did not correlate with disease activity, it may be assumed that it is not a response protein solely induced and modulated by type I interferons. Nevertheless, our comprehensive characterization of CD38 expression in the immune system might have important implications for personalized approaches with emerging CD38-directed therapeutics.

REFERENCES:

[1] Ostendorf, L. *et al.* Targeting CD38 with Daratumumab in Refractory Systemic Lupus Erythematosus. *N. Engl. J. Med.* 383, 1149–1155 (2020).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3883

POS0421 COMBINED ANALYSIS OF METABOLIC AND TRANSCRIPTOMIC KIDNEY PROFILES OF NZW/B-F1 MURINE LUPUS UNCOVERS BIOLOGICAL MECHANISMS PRECEDING THE ONSET OF NEPHRITIS

T. Manolakou[1], I. Tsiara[2], D. Nikolopoulos[1,3], P. Garantziotis[1,4], D. Benaki[2], E. Gikas[2], E. Frangou[1,5], E. Mikroa[2], D. Boumpas[1,3]. *[1]Biomedical Research Foundation of the Academy of Athens, Center of Translational Research, Athens, Greece*; *[2]National and Kapodistrian University of Athens, Department of Pharmacy, Section of Pharmaceutical Chemistry, Athens, Greece*; *[3]National and Kapodistrian University of Athens, Rheumatology and Clinical Immunology Unit, 4th Department of Internal Medicine, Athens, Greece*; *[4]Hannover Medical University, Division of Immunology and Rheumatology, Hannover, Germany*; *[5]Limassol General Hospital, Department of Nephrology, Limassol, Cyprus*

Background: Metabolic pathways are important regulators of immune differentiation and activation in kidneys. Kidneys directly impact systemic metabolism, circulating metabolite levels, and express intrinsic metabolic activity. The integration of renal metabolomic and transcriptomic profiles may unravel unique gene-metabolite pairs of biological significance in lupus nephritis (LN).

Objectives: To decipher gene-metabolite signatures at both pre-nephritic and nephritic stages of lupus.

Methods: Kidneys were isolated and snap-frozen after perfusion from female NZB/NZW-F1 lupus mice at the pre-nephritic (3-month-old) and nephritic (6-month-old exhibiting ≥100 ng/dL of urine protein) stage of lupus (n=6/group). Age-matched female C57BL/6 mice were used as healthy controls. Sample extracts were used for RNA sequencing and ^{1}H-NMR spectroscopy metabolic profiling. DESeq2 was used to identify differentially expressed genes. Univariate analysis was used to reveal metabolic differences characteristic for nephritis.

Results: Comparative transcriptomic analyses uncovered multiple transcripts related to metabolic pathways: In pre-nephritic kidneys, lipid metabolism, cellular respiration, TCA cycle, amino acid metabolism processes were overrepresented in the upregulated genes while in nephritic kidneys, amino acid metabolism processes were overrepresented among the downregulated genes (Figure 1). ^{1}H-NMR analysis revealed a total of 49 metabolites. Comparison of the metabolic levels of nephritic and pre-nephritic animals revealed that ADP, ATP, NAD+, Taurine and Myo-inositol decreased, while Thr increased significantly. The comparison to corresponding control animals, demonstrated that only myo-inositol increased significantly. Integration of kidney metabolomics and transcriptomics indicated the involvement of processes related to glutathione metabolism, leukocyte trans-endothelial migration and antigen presentation during the established renal disease stage.

Conclusion: The combined transcriptomics and metabolomics analysis revealed metabolic derangements in lupus-affected kidneys both during subclinical and overt LN. Deregulated tissue-levels of taurine and myo-inositol at the subclinical stage of the disease suggest aberrant renal biochemistry preceding the development of overt LN that may directly impact systemic metabolism and circulating metabolite levels.

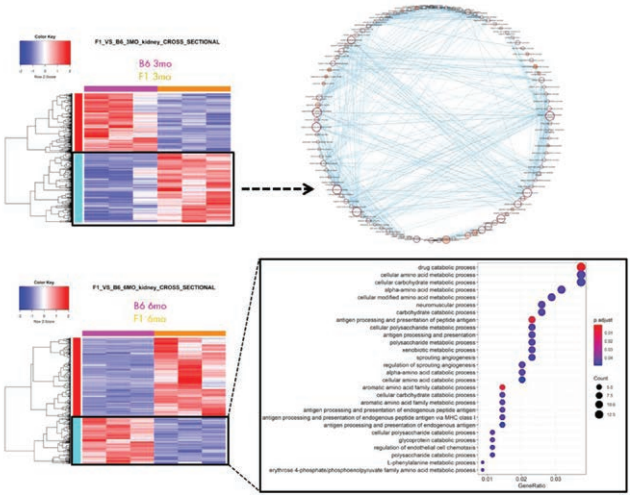


Figure 1. Pathways linked to cell metabolism were overrepresented among 3-month upregulated and 6-month lupus mice (F1) downregulated DEGS (*differentially expressed genes*) compared to controls (C57BL/6).

Acknowledgements: This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 742390).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4115

Systemic sclerosis, myositis and related syndromes - aetiology, pathogenesis and animal models

POS0422 PANNICULITIS AS A MANIFESTATION OF AN AUTOIMMUNE/AUTOINFLAMMATORY DISEASE

O. Egorova[1], A. Datsina[2], A. Potapova[3]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Drug Therapy, Moscow, Russian Federation*; [2]*Pirogov Russian National Research Medical University, Ministry of Health of Russia, Pirogov Russian National Research Medical University, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: ASIA syndrome or Schonfeld syndrome is an autoimmune/inflammatory condition induced by adjuvants in genetically susceptible individuals with the development of rheumatic diseases (RD), multiple sclerosis, sarcoidosis, and others.
Objectives: to characterize the symptoms of panniculitis (Pn) associated with ASIA-syndrome
Methods: Within 7 years, ASIA syndrome was diagnosed in 12 women, average age 37.2±7.4, with a referral diagnosis of "Erythema Nodosum" or "Panniculitis". The duration of the disease was 16.7±3.9 months. In addition to general clinical study, the serum concentration of α-1 antitrypsin, amylase, lipase, ferritin, creatine phosphokinase (CPK), immunological parameters (ANP-Hep2, dsDNA, C3 and C4, CRP, ANCA, Scl-70, antibodies to cardiolipins G and M), computed tomography of the chest organs, pathomorphological and immunohistochemical examination of a biopsy specimen of skin with subcutaneous fat tissue (SFA) from the affected areas.
Results: The development of ASIA syndrome was preceded by gluteoplasty using propantriol-1,2,3 (in 4 patients), liposuction (2), biorevitalization with hyaluronic acid (2) and endoprosthetics with breast implants (2), bone metal construction (1) and mesh hernioplasty (1). The clinical picture of Pn was characterized by generalized red-purple painful (VAS pain 55.8±17.3 mm) subcutaneous indurations on the upper limbs and trunk (in 100% of cases), face (16.6%) and lower limbs (33.3%), with ulceration and oily fluid leakage (58.6%). The saucer symptom was recorded in 83.3% of the observed patients. In 66.6% of cases, fever and articular syndrome were observed, in 41.6% – myasthenic syndrome and lymphadenopathy, in 8.3% – xerophthalmia, keratoconjunctivitis dry, xerostomia and recurrent parotitis. In blood tests, leukopenia (up to 2.0x109/l) was identified in 33.3% of patients, a significant increase in the level of creatinine phosphakinase – in 16,6%, a two or more times increase in ESR and CRP – in 100%. All patients demonstrated immunological changes. The morphological picture of the skin and SFA in 75% of cases resembled lobular Pn, in 8.3% – tumor lymphocytes with the immunophenotype of cytotoxic T-lymphocytes: CD3+, CD8+ were detected. The results obtained allowed confirming RD in 8 patients: systemic lupus erythematosus and idiopathic lobular panniculitis in 2 patients (respectively) and 1 in dermatomyositis, systemic scleroderma of Sjogren's disease, mixed connective tissue disease. One case was diagnosed with sarcoidosis and T-cell lymphoma. In 2 patients after the liposuction procedure the course of Pn was reversible.
Conclusion: Diagnosis of Pn associated with ASIA syndrome is a complex task that requires a multidisciplinary approach to verify the diagnosis and treatment tactics.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.860

POS0423 NCOA3 AMPLIFIES PROFIBROTIC TRANSCRIPTIONAL PROGRAMS IN SYSTEMIC SCLEROSIS

C. Dees[1], S. Poetter[1], M. Fuchs[2], C. Bergmann[1], A. E. Matei[1], A. H. Györfi[1], A. Soare[1], A. Ramming[1], P. Ceppi[3], G. Schett[1], M. Kunz[2], J. H. W. Distler[1]. [1]*Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and Universitätsklinikum Erlangen, Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany*; [2]*Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Chair of Medical Informatics, Erlangen, Germany*; [3]*Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and Universitätsklinikum Erlangen, Interdisciplinary Center for Clinical Research - Junior Research Group 1, Erlangen, Germany*

Background: Excessive activation of fibroblasts with a TGFβ-biased gene signature and deposition of extracellular matrix are key features of fibrotic diseases. The mechanisms underlying these transcriptional changes remain poorly understood. Deregulation, mutations and malfunctions of transcriptional co-regulators, which can interact with multiple transcription factors and enable a broad-spectrum regulation of transcriptional networks, have been implicated as driving factors in a large number of diseases and pathologies.
Objectives: In the present study, we aimed to analyze the role of the co-regulator Nuclear Receptor Co-Activator 3 (NCOA3) in fibroblast activation and tissue fibrosis, and to evaluate a potential interaction of NCOA3 with fibrosis-relevant transcription factors.
Methods: NCOA3 was inhibited genetically by siRNA transfection and pharmacologically by the SRC3 inhibitor-2 (SI-2). We performed bulk RNASeq of human dermal fibroblasts and *in silico* transcription factor binding site screening of differentially expressed genes (DEGs). The interaction of NCOA3 and TGFβ-SMAD signaling was analyzed by reporter and CoIP assays.
Results: The expression of NCOA3 in skin biopsies of SSc patients compared to normal controls demonstrated that SSc fibroblasts express modestly, but significantly reduced levels of NCOA3, which persisted in cultured SSc fibroblasts. Stimulation of normal fibroblasts with chronically high levels of TGFβ as they also occur in fibrotic tissue remodeling strongly decreased NCOA3 expression to a similar extent as in SSc fibroblasts. Furthermore, NCOA3 expression is also deregulated in different murine models of skin fibrosis. To investigate the functional effects of decreased NCOA3 levels, we targeted the expression of NCOA3 in normal fibroblasts. SiRNA-mediated knockdown of NCOA3 ameliorated TGFβ-induced gene expression, collagen release, myofibroblast differentiation and cell proliferation. In contrast, knockdown of NCOA3 had no effects on collagen release, expression of contractile proteins or gene expression in unstimulated fibroblasts, suggesting that NCOA3 is not required for cellular homeostasis. To characterize the molecular mechanisms, we performed RNASeq upon NCOA3 knockdown. We identified 343 significant differentially expressed genes (220 downregulated and 123 upregulated with a Benjamini-Hochberg false discovery rate FDR < 0.25 and fold change > 1.5) between TGFβ-stimulated fibroblasts with and without NCOA3 knockdown (NCOA3-DEGs) including the fibrosis-relevant genes *EDNRB, COL5A3, HES1, IL11* or *IL33*. Functional analysis of the NCOA3-DEGs showed enrichment of pathway terms such as collagen binding and extracellular matrix organization. *In silico* screening of the promoters of the NCOA3-DEGs for potential transcription factor binding motifs revealed binding motifs of core transcription factors of fibroblast activation and tissue fibrosis such as SMAD2/3/4, RBPJ, ZEB1, TCF4, REL, and SNAIL2 amongst the downregulated NCOA3-DEGs. Experimental validation of our biostatistical results using SMAD3 as example demonstrated a higher percentage of NCOA3-pSMAD3 double-positive fibroblasts in skin sections of SSc patients compared to healthy controls. In addition, knockdown of NCOA3 reduced TGFβ-induced SMAD-reporter activity. Furthermore, stimulation with TGFβ increased the interaction of NCOA3 with SMAD3 as analyzed by co-immunoprecipitation. Simultaneous knockdown of NCOA3 and SMAD3 showed no additional reductions compared to the single knockdowns, suggesting that NCOA3 controls SMAD3-dependent gene transcription under fibrotic conditions. Finally, inhibition of NCOA3 showed anti-fibrotic effects in different murine models of experimental skin and lung fibrosis.
Conclusion: Our findings characterize NCOA3 as regulator of multiple pro-fibrotic transcription programs. Pharmaceutical inhibition of NCOA3 might be a strategy to interfere simultaneously with several core pro-fibrotic mediators in fibrotic diseases such as SSc.
Acknowledgements: We thank Lena Summa, Vladyslav Fedorchenko, Wolfgang Espach and Regina Kleinlein for excellent technical assistance.
The study was funded by grants DI 1537/7-1, DI 1537/8-1, DI 1537/9-1 and -2, DI 1537/11-1, DI 1537/12-1, DI 1537/13-1, DI 1537/14-1, DI 1537/17-1, DE 2414/2-1, DE 2414/4-1, and RA 2506/3-1 of the German Research Foundation,

SFB CRC1181 (project C01) and SFB TR221/ project number 324392634 (B04) of the German Research Foundation, grants J39, J40 and A64 of the IZKF in Erlangen, grant 2013.056.1 of the Wilhelm-Sander-Foundation, grants 2014_A47, 2014_A248 and 2014_A184 of the Else-Kröner-Fresenius-Foundation, grant 14-12-17-1-Bergmann of the ELAN-Foundation Erlangen, BMBF (Era-Net grant 01KT1801), MASCARA program, TP 2 and a Career Support Award of Medicine of the Ernst Jung Foundation.

Disclosure of Interests: Clara Dees: None declared, Sebastian Poetter: None declared, Maximilian Fuchs: None declared, Christina Bergmann: None declared, Alexandru-Emil Matei: None declared, Andrea-Hermina Györfi: None declared, Alina Soare: None declared, Andreas Ramming: None declared, Paolo Ceppi: None declared, Georg Schett: None declared, Meik Kunz: None declared, Jörg H.W. Distler Consultant of: Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, Grant/research support from: Anamar, Active Biotech, Array Biopharma, ARXX, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB

DOI: 10.1136/annrheumdis-2021-eular.1106

POS0424 DETERMINING CIRCULATING ENDOTHELIAL CELLS USING CELLSEARCH SYSTEM IN SYSTEMIC SCLEROSIS PATIENTS

F. Pignataro[1], L. Zorzino[2], W. Maglione[1], A. Minniti[1], G. Clericuzio[2], M. Picozzi[2], C. Simonelli[3], F. Picardo[3], R. Caporali[1,4], N. Del Papa[1]. [1]*ASST Gaetano Pini-CTO, Clinical Rheumatology, Milan, Italy*; [2]*IEO, Division of Laboratory Medicine, Milan, Italy*; [3]*Menarini Silicon Biosystems, Medical Affairs, Bologna, Italy*; [4]*University of Milan, Clinical Science and Community Health, Milano, Italy*

Background: Endothelial damage and fibroproliferative vasculopathy of small vessels are pathological hallmarks of Systemic Sclerosis (SSc). Detection and analysis of circulating endothelial cells (CECs) detached from affected blood vessels may be an informative tool to study vascular dysfunction and could be considered a novel biomarker of scleroderma vasculopathy. Our group first showed the presence of CECs in SSc by fluorescence-activated cell sorting (FACS), demonstrating that a raised counts of active CECs may represent direct evidence of active vascular disease in SSc. Despite these interesting data, issues related to difficulties in CEC counting through FACS analysis, due their very low concentration in peripheral blood, prevented further investigations in this field. Recently, a specific kit for the detection of CECs has been developed through the CellSearch System (CS), a semi-automated device for the standardized analysis of rare cells, such as CECs, in peripheral blood.
Objectives: To assess the counts of CECs determined by the CS in SSc patients and to evaluate their clinical implication and potential as vascular biomarker in SSc.
Methods: 10mL of blood samples were collected from 29 subjects (19 SSc patients and 10 healthy donors - HDs) and stored in tubes containing a specific preservative, to allow the analysis of 4mL of blood within 72 hours, according to manufacturer instructions. Out of 19 SSc patients, 18 were female, 10 had the limited form and 9 the diffuse cutaneous variant of SSc. CS uses a proprietary kit containing a ferrofluid-based reagent, that target CD146 to magnetically capture CECs, and the immunofluorescent reagents to stain the CECs, defined as CD146+, CD105-PE+, DAPI+ and CD45-APC-. Clinical, laboratoristic and demographic data were also collected.
Results: The mean number of CECs in patients with SSc was significantly higher in comparison to HDs (554/4mL vs. 53.5/4 mL, p=0.0042). When analyzed according to disease subset, both lcSSc and dcSSc showed significantly increased levels of CECs in comparison with HDs (p=0.003 and p=0.005, respectively). No statistical difference was observed in the mean number of CECs in patients with lcSSc compared to those with dcSSc. Regarding vascular involvement, the CECs counts strictly correlated with the presence of digital ulcers (DUs) (p=0.0001) showing a median of 863cells/4mL for the SSc patients with DUs versus a median of 276.2/4mL for the SSc patients without DUs. No statistical correlation was found between CECs and serological autoantibody pattern, skin parameters, or joint and muscle involvement. Patients with active disease, according to the EUSTAR Activity Index, showed a higher CECs value than those with inactive disease (p=0.0012).
Conclusion: The amount of CECs detectable in peripheral blood has been recently proposed as a marker of endothelial damage in different vascular diseases, including SSc. However, currently no standardized method is available to determine CEC counts, which makes reported data on CECs reliable and suitable. The CS system is a commercially available semi-automated system that enables standardized determination of CECs. Thus, we examined clinical utility of CECs count by this system in SSc patients. Our results confirm that baseline CEC counts, evaluated by a new standardized method, may represent direct evidence of endothelial damage in SSc and could be a promising tool for monitoring active disease and evaluating therapeutic responses to vascular and immunosuppressive treatments.
REFERENCES:
[1] Del Papa N, Pignataro F. Front Immunol. 2018 Jun 18;9:1383
[2] De Simone C et al. J Eur Acad Dermatol Venereol. 2014 May;28(5):590-6
[3] Del Papa N et al. Arthritis Rheum. 2004 Apr;50(4):1296-304

Disclosure of Interests: Francesca Pignataro: None declared, Laura Zorzino: None declared, Wanda Maglione: None declared, Antonina Minniti: None declared, Giulia Clericuzio: None declared, Marco Picozzi: None declared, Cecilia Simonelli Employee of: Menarini Silicon Biosystems, Francesco Picardo Employee of: Menarini Silicon Biosystems, Roberto Caporali: None declared, Nicoletta Del Papa: None declared

DOI: 10.1136/annrheumdis-2021-eular.2150

POS0425 INCREASED KERATIN 9 EXPRESSION IN SYSTEMIC SCLEROSIS SKIN IS DRIVEN BY THE LNCRNA HOTAIR FROM FIBROBLAST DERIVED EXOSOMES

C. Wasson[1], R. Ross[1], J. Bryon[1], F. Del Galdo[1]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine, School of Medicine, Leeds, United Kingdom*

Background: Skin fibrosis is the hallmark fibrotic manifestation of systemic sclerosis (SSc). Despite a key role of tissue fibroblasts, skin changes extend to the keratinocyte layer, which contribute to the loss of skin function. RNA seq. analysis of SSc patient forearm skin showed that palmoplantar specific Keratin 9 (CK9) was highly expressed (1). SSc affected skin shares several features with palmoplantar skin including increased keratinocyte layer thickness and lack of hair. Seminal work of last decade has shown that long noncoding RNA in the HOX loci play a crucial role in skin keratinocyte differentiation (2), with the lncRNA HOTAIR being one of the HOX lncRNA mostly expressed in the palmoplantar region.
Objectives: Following recent data suggesting a role of HOTAIR in the profibrotic phenotype of dermal fibroblasts in SSc (3), here we set out to determine if HOTAIR expressed in SSc dermal fibroblasts was a contributing factor to the high levels of CK9 found in SSc patient skin
Methods: Full-thickness skin biopsies were surgically obtained from the forearms of patients with SSc of recent onset. Fibroblasts were isolated and cultured in monolayers. HOX transcript antisense RNA (HOTAIR) was expressed in healthy dermal fibroblasts by lentiviral induction employing a vector containing the specific sequence. Exosomes were isolated from dermal fibroblast media using the Total exosome isolation reagent (Thermo Fisher). Enhancer of zeste 2 (EZH2) was blocked with GSK126 inhibitor. Skin equivalents were created using scramble and HOTAIR expressing fibroblasts with primary keratinocytes
Results: Media from both SSc patient fibroblasts and HOTAIR expressing fibroblasts induced CK9 expression in healthy keratinocytes *in vitro*. In addition, HOTAIR expressing fibroblasts induces CK9 expression in keratinocytes in 3D skin equivalent models. Media fractionation studies indicated that HOTAIR was present in fibroblasts exosomes and found at a higher concentration (2.7 fold p=0.01) in exosomes from SSc fibroblasts. Importantly, transfection of Exosomal RNAs from SSc fibroblasts could reproduce the increase in CK9 in keratinocytes. Mechanistically, CK9 induction was mediated by changes to the histone methylation profile in the keratinocytes through EZH2.
Conclusion: Pro-fibrotic dermal fibroblasts in systemic sclerosis contribute to the overall skin loss of function by inducing CK9 in adjacent keratinocytes through transfer of the long non-coding RNA HOTAIR. Unraveling the crosstalk of activated fibroblasts with adjacent cells may lead to identify therapeutic targets to re-establish tissue homeostasis and function during fibrosis.
REFERENCES:
[1] Assassi S et.al Arthritis and Rheumatology 2015
[2] Rinn JL et.al Cell 2007
[3] Wasson CW et.al Annals of Rheumatic Disease 2020
Disclosure of Interests: Chris Wasson: None declared, rebecca ross: None declared, Jessica Bryon: None declared, Francesco Del Galdo Speakers bureau: Speakers bureau: Astra-Zeneca, Boehringer Ingelheim, Actelion, Consultant of: Astra-Zeneca, Mitsubishi-Tanabe, Capella Biosciences, Chemomab, Actelion, Boehringer-Ingelheim, Grant/research support from: Grant/research support from: Capella Biosciences, Chemomab, Kymab, Mitsubishi-Tanabe

DOI: 10.1136/annrheumdis-2021-eular.2278

POS0426 CIRCULATING MICRORNA PROFILING IN PATIENTS WITH ANTI-SYNTHETASE SYNDROME AND INTERSTITIAL LUNG DISEASE

G. Zanframundo[1,2], S. Bozzini[3], V. Codullo[2], V. Frangipane[3], L. Pandolfi[3], B. Atienza-Mateo[4], S. Remuzgo Martinez[4], C. Montecucco[1,2], M. A. González-Gay[4], F. Meloni[1,3], L. Cavagna[1,2]. [1]*University of Pavia, Department of Internal Medicine and Therapeutics, Pavia, Italy*; [2]*IRCCS Policlinico San Matteo Foundation, Department of Rheumatology, Pavia, Italy*; [3]*IRCCS Policlinico San Matteo Foundation, Department of Respiratory Diseases, Pavia, Italy*; [4]*Hospital Universitario Marqués de Valdecilla, IDIVAL, Rheumatology Division, Santander, Spain*

Background: Anti-synthetase syndrome (ASSD) is an autoimmune disease characterized by autoantibodies against one of many aminoacyl transfer RNA (tRNA) synthetases. Interstitial Lung Disease (ILD) in ASSD patients is frequent, often severe and rapidly progressive, causing much of the increased morbidity and mortality associated with ASSD as compared to other idiopathic inflammatory myopathies [1].

Objectives: In this study, we hypothesized that immune-related miRNAs may be associated with presence/absence of lung involvement in patients with ASSD and help predict disease course.
Methods: A total of 15 ASSD patients were enrolled: 11 with ILD and 4 without ILD. Differentially expressed miRNAs were identified in plasma derived-exosome, using miRNA PCR array (MIHS-111ZG, Qiagen) including 84 miRNAs involved in activation and differentiation of T and B cells.
Results: Among all miRNAs analyzed we found that miR-15b-5p, miR-23a-3p, miR-25-3p, miR-30a-5p and miR29c-3p were up-regulated in ASSD-ILD patients ($p<0.05$) as compared to patients without lung involvement (Figure 1). To evaluate the effectiveness of the five miRNAs for predicting ILD among ASSD patients, ROC curves were constructed. The AUCs of miR-15b-5p, miR-25-3p, miR-30a-5p and miR29c-3p were 0.83, 0.87, 0.86 and 0.89, respectively ($p= 0.05$ for miR-25-3p and $p<0.05$ for all other curves). The prediction of the biologic targets and pathways as well as cellular processes by DIANA-mirPath analysis showed that all miRNAs associated with ILD presence are involved in PI3K-Akt signaling pathway.
Conclusion: Our study shows that, in ASSD patients with ILD, miR-15b-5p, miR-23a-3p, miR-25-3p, miR-30a-5p and miR29c-3p were up-regulated compared to patients without evidence of ILD. A clear involvement in immune and inflammatory diseases was documented for the miRNAs identified [2] and, for many of these, studies in the literature indicate a possible role in pulmonary fibrosis [3]. It is notable that these miRNAs were related to PI3K-Akt signaling pathway that regulate cell proliferation, differentiation and apoptosis [4]. It has also been demonstrated that in lung fibroblast the PI3K–Akt signals can be aberrantly activated [5]. The identification of markers could be important in the early identification of the disease and for its treatment.

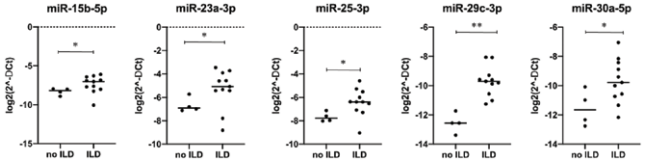


Figure 1. Comparison of relative levels of five miRNAs among patients with and without lung involvement were expressed as $\log_2$ transformed values. $^{*}p<0.05$; $^{**}p<0.01$

REFERENCES:
[1] Kalluri M, Oddis CV. Pulmonary manifestations of the idiopathic inflammatory myopathies. Clinics in chest medicine. 2010; 31:501–512.
[2] Prabahar A, Natarajan J, ImmunemiR-a database of prioritized immune miRNA disease associations and its interactome. MicroRNA, 2017; 6: 71–78.
[3] Sessa R, Hata A. Role of microRNAs in lung development and pulmonary diseases. Pulm Circ. 2013; 3:315-28.
[4] Ersahin T, Tuncbag N, Cetin-Atalay R. The PI3K/AKT/mTOR interactive pathway. Mol Biosyst. 2015;11:1946-54.
[5] Zhang XL, Xing RG, Chen L, Liu CR, Miao ZG. PI3K/Akt signaling is involved in the pathogenesis of bleomycin-induced pulmonary fibrosis via regulation of epithelial-mesenchymal transition. Mol Med Rep. 2016;14:5699-5706.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2433

POS0427 CLINICAL CHARACTERISTICS OF PATIENTS WITH SYSTEMIC SCLEROSIS AND GASTRIC ANTRAL VASCULAR ECTASIA (GAVE)

C. Codina[1], A. Guillén-del-Castillo[1], E. Callejas-Moraga[2], J. Perurena-Prieto[3], M. Roca-Herrera[2], I. Sanz-Pérez[1], A. Gil-Vila[1], A. Selva-O'Callaghan[1], V. Fonollosa-Pla[1], C. P. Simeón-Aznar[1]. [1]*Hospital Universitari Vall d'Hebron, Systemic Autoimmune Diseases Unit, Internal Medicine Service., Barcelona, Spain*; [2]*Hospital de Sabadell, Systemic Autoimmune Diseases Unit, Internal Medicine Service., Sabadell, Spain*; [3]*Hospital Universitari Vall d'Hebron, Immunology, Barcelona, Spain*

Background: Gastric antral vascular ectasia (GAVE) is one of the gastrointestinal (GI) manifestations related to systemic sclerosis (SSc). It can be presented as iron deficiency anemia or even upper gastrointestinal bleeding. GAVE is diagnosed by endoscopy observing an image of confluent vascular ectasias that is oriented longitudinally on the folds of the antrum in the appearance of "watermelon". The definitive treatment for this manifestation consists in endoscopy guided fulguration when the clinical situation allows it.
Objectives: The objective was to study a cohort of SSc patients at their first endoscopy. The clinical characteristics, laboratory tests and treatments received from SSc patients with GAVE were compared to those without this GI manifestation.
Methods: From the cohort of patients with SSc in Hospital Universitari Vall d'Hebron, a total of 269 patients who had undergone at least one endoscopy during follow-up were selected. Twenty seven were diagnosed with GAVE. We compared the clinical, analytical and treatment characteristics of these patients with the remaining 242 who did not present GAVE. The statistical study was carried out using the SPSS 20.0 package (Chicago, IL), a $p<0.05$ was considered as statistical significance.
Results: The prevalence of GAVE in SSc patients was 10.0%. Patients with GAVE had a higher median age SSc onset taking into account the first non-Raynaud's phenomenon (RP) symptom attributable to the disease (56.6 vs 48.0 years, $p = 0.001$). The median age at first endoscopy was 56.5 years in GAVE group compared with 61.7 in the group without GAVE.
Compared with SSc patients without GAVE, patients with GAVE had a higher prevalence of Barrett's esophagus (14.8% vs. 3.7%, $p = 0.011$), intestinal involvement (37% vs. 18.6%, $p = 0.024$) and a trend towards a lower prevalence of interstitial lung disease (25.9% vs 45.0%, $p = 0.057$).
No difference was identified in the prevalence of scleroderma renal crisis. Patients with GAVE presented a higher frequency of early or active Cutolo capillaroscopy pattern with a predominance of enlarged capillaries or megacapillaries (84.6% vs 62.4%, $p = 0.025$), greater frequency of anti-centromere antibodies (63.0% vs. 42.1%, $p = 0.039$) and a trend towards a lower proportion of anti-topoisomerase I (3.7% vs. 18.6%, $p = 0.052$). No difference was found in prevalence of anti-RNA polymerase III antibodies between groups. Patients with GAVE were treated less frequently with non-glucocorticoid immunosuppressants prior to diagnostic endoscopy (0% vs 20.2%, $p = 0.010$). The 33.3% of patients with GAVE were treated with endoscopic fulguration, and 66.7% of them received supplementary treatment with oral iron.
Conclusion: SSc patients with GAVE had higher age at SSc onset, more frequency of Barrett's esophagus and intestinal involvement, prevalence of anti-centromere antibodies, early or active Cutolo scleroderma pattern and lower prior non-glucocorticoids treatment.
REFERENCES:
[1] Ghrénassia E, Avouac J, Khanna D, T.Derk C, Distler O, Suliman Y, et al. Prevalence, Correlates and Outcomes of Gastric Antral Vascular Ectasia in Systemic Sclerosis: A EUSTAR Case-control Study. The Journal of Rheumatology. 2014; 41:1.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2847

POS0428 REGULATION OF IFN SIGNATURE BY HDAC CLASS IIA-CD52 AXIS IN SYSTEMIC SCLEROSIS

M. Rudnik[1], A. Hukara[1], P. Blyszczuk[1], O. Distler[1], G. Kania[1]. [1]*University Hospital Zurich, University of Zurich, Department of Rheumatology, Center of Experimental Rheumatology, Zurich, Switzerland*

Background: Systemic sclerosis (SSc) is associated with an interferon (IFN) signature, which is defined by a higher expression of IFN-stimulated genes (mainly in response to IFNα). Histone deacetylases (HDACs) are a family of epigenetic modifiers mediating immune function. HDACs function via diverse molecular mechanisms, including direct inhibition of gene transcription or indirectly through modulation of nuclear transcription factors such as NF-κB and STATs. CD52 protein regulates T cell receptor and NF-κB signalling. Previously, we showed downregulation of CD52 in SSc monocytes, however, the influence of CD52 on IFN signalling has not been studied yet.
Objectives: We investigated the role of CD52 in the regulation of IFN response in monocytes. Moreover, we explored the regulatory mechanisms of CD52 expression to identify the involvement of HDACs in that process.
Methods: RNAseq of $CD14^+$ monocytes isolated from peripheral blood of lcSSc (n=5, age=54.4±6.7), dcSSc patients (n=5, age=51.8±7.2) and age- and sex-matched healthy controls (HC) (n=5, age=50.8±9.7) was performed using Illumina HiSeq 4000 platform. Differentially expressed genes were computed using DeSEQ2 algorithm. Gene ontology and pathway analysis were performed using Metacore software and ShinyApp. CD52 activity in monocytes was blocked by monoclonal antibody Alemtuzumab [10ug/ml] and IFN signature genes expression was assessed upon IFNα stimulation [1ng/ml] by qPCR and ELISA. HDAC-dependent regulation of CD52 expression in $CD14^+$ monocytes from HC was analysed on mRNA and protein levels after treatment with pan-HDAC inhibitor valproic acid and HDAC class IIa inhibitor TMP269 [both 2.5μM].
Results: Pathway analysis revealed significant alterations in interferon signalling in SSc monocytes. Monocytes treated with Alemtuzumab and IFNα showed induced expression of *STAT1* (p=0.023, N=4), *CXCL9* (p=0.062, N=4) and *CXCL10* (p=0.005, N=4). RNAseq revealed a specific HDAC expression pattern in SSc monocytes with induced expression of HDAC4, 6, 10, 11 ($p<0.05$) and reduced HDAC1, 3 and 8 ($p<0.05$). *CD52* mRNA was significantly decreased after IFNα stimulation (p=0.001, N=3). Treatment with valproic acid and HDAC class IIa inhibitor TMP269 resulted in decreased phosphorylation of STAT1 ($p<0.01$, N=4) followed by a declined level of CXCL10 ($p<0.01$, N=4) and restored level of *CD52* mRNA ($p<0.001$, N=4).
Conclusion: Our findings demonstrated a new aspect of pro-inflammatory type I IFN signalling in SSc. We described a novel regulation feedback loop in monocytes, in which CD52 suppresses IFN signature, while its expression is inhibited by IFN-induced HDAC activity (mainly HDAC class IIa). Therefore, targeting the CD52-IFN-HDAC axis might serve as a novel therapeutic strategy in SSc.

Disclosure of Interests: Michal Rudnik: None declared, Amela Hukara: None declared, Przemyslaw Blyszczuk: None declared, Oliver Distler Speakers bureau: Actelion, Bayer, Boehringer Ingelheim, Medscape, Novartis, Roche, Menarini, Mepha, MSD, iQone, Novartis, Pfizer, Consultant of: Abbvie, Actelion, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Bayer, Baecon Discovery, Blade Therapeutics, Boehringer, CSL Behring, ChemomAb, Corpuspharma, Curzion Pharmaceuticals, Ergonex, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, Kymera, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Sanofi, UCB, Lilly, Target BioScience, Pfizer, Grant/ research support from: Actelion, Bayer, Boehringer Ingelheim, Kymera Therapeutics, Mitsubishi Tanabe, Gabriela Kania: None declared
DOI: 10.1136/annrheumdis-2021-eular.2869

POS0429 INTERLEUKIN-4 ACTIVATES EOSINOPHILS AND CCR3-POSITIVE T HELPER CELLS MIGRATION TO FASCIA AND PROMOTES FIBROSIS IN EOSINOPHILIC FASCIITIS

M. Hosonuma[1,2,3,4], T. Isozaki[2], H. Furuya[2], Y. Yamazaki[5], Y. Ikari[2], S. Nishimi[2], A. Maeoka[2], S. Ishii[2], T. Tokunaga[2], K. Wakabayashi[2], N. Konishi[2], S. Fukuse[2], K. Ishikawa[6], N. Sakai[7], K. Inagaki[6], T. Kasama[2]. *[1]Clinical Research Institute for Clinical Pharmacology & Therapeutics, Showa University, Department of Clinical Immuno Oncology, Tokyo, Japan*; *[2]Showa University, Division of Rheumatology, Department of Medicine, Tokyo, Japan*; *[3]Showa University, Division of Medical Oncology, Department of Medicine, Tokyo, Japan*; *[4]Showa University, Department of Pharmacology, School of Medicine, Tokyo, Japan*; *[5]Showa University School of Pharmacy, Division of Toxicology, Department of Pharmacology, Toxicology and Therapeutics, Tokyo, Japan*; *[6]Showa University School of Medicine, Department of Orthopaedic Surgery, Tokyo, Japan*; *[7]Showa University School of Dentistry, Department of Pharmacology, Tokyo, Japan*

Background: Eosinophilic fasciitis (EF) is a rare disease that causes inflammation and fibrosis mainly in the fascia of the extremities with eosinophilia. It has been reported that the hypertrophied fascia in EF shows inflammatory cell infiltration by the lymphocytes and eosinophils and increased expression of fibrosis-related cytokines genes in fibroblast [1]. However, its pathophysiology in the fascia remains unresolved.
Objectives: Therefore, we focused on fascial fibroblasts and aimed to determine the role of interleukin-4 (IL-4) in eosinophil and helper T cell infiltration and fibrosis in fascial fibroblast in EF.
Methods: Fascial fibroblasts were obtained from fascia biopsy of a patient with EF, and were stimulated with pre- and post-treatment serum of a patient with EF and healthy control, followed by microarray to analyze gene expression. Fascial fibroblasts were stimulated with IL-4 10 ng/mL, and gene expression of IL-4 receptor and CCR3 ligands, CCL7 and CCL11 were measured by qPCR. Transforming growth factor (TGF) -β and periostin in the pre- and post-treatment serum of a patient with EF and conditioned medium of fascial fibroblasts stimulated with IL-4 were measured by ELISA. To examine the role of IL-4 in proliferation, we performed in proliferation assays using fascial fibroblasts treated with IL-4. CCR3-positive T cells in the fascial tissue of EF, dermatomyositis, and polymyositis patients were evaluated by immunostaining.
Results: By microarray analysis, CCL7 and CCL11 expression of fascial fibroblasts stimulated with pre-treatment EF serum was higher than that in post-treatment EF serum and control serum. CCL7 and CCL11 mRNA in IL-4 stimulated facial fibroblasts were increased by 5.1-fold and 7.3-fold, respectively. TGF-β and periostin in IL-4 stimulated facial fibroblast conditioned medium were also increased. In addition, TGF-β and periostin in EF serum were gradually decreased by treatment for 4 and 10 weeks, compared to before treatment. Finally, fascial fibroblast proliferation was significantly increased by stimulation with IL-4. Furthermore, infiltration of CCR3-positive T cells was specific to the fascial tissue of EF.
Conclusion: In EF, IL-4 enhances the production of CCR3 ligands, TGF-β, and periostin from fascial fibroblasts. As a result, it promotes the migration of eosinophils and CCR3-positive T helper cells to the fascia and fibrosis. These results suggest that inhibition of IL-4 pathway could be a novel strategy for eosinophilic fasciitis.
REFERENCES:
[1] Igarashi A, Nashiro K, Kikuchi K, et al. Connective tissue growth factor gene expression in tissue sections from localized scleroderma, keloid, and other fibrotic skin disorders. J Invest Dermatol. 1996 Apr;106(4):729-33.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3542

POS0430 EXPRESSION AND CLINICAL SIGNIFICANCE OF AUTOPHAGY-RELATED GENES IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF SYSTEMIC SCLEROSIS

Y. F. Qing[1], J. Zheng[1], S. B. Wang[1], F. Dai[1], Y. Jiang[1], Y. X. He[1], Q. B. Zhang[2]. *[1]Institute of Rheumatology and Immunology, Department of Rheumatology and Immunology, Nanchong, China*; *[2]Institute of Rheumatology and Immunology, Department of Geriatrics, Affiliated Hospital of North Sichuan Medical College, Nanchong, China*

Background: Growing evidences have demonstrated that autophagy is a powerful regulators in the pathogenesis of fibrosis and autoimmune diseases. Autophagy abnormalities in SSc involve abnormal autophagy-related protein and autophagy-related gene polymorphism[1-2], however there is a few reports on the expression and clinical significance of autophagy-related genes.
Objectives: To investigate the expression and clinical significance of autophagy-related genes LC-3 mRNA, Becline-1 mRNA, Agt-3 mRNA, Agt-5 mRNA, Agt-12 mRNA and Agt-16L1 mRNA in peripheral blood mononuclear cells (PBMC) of systemic sclerosis (SSc).
Methods: 51 cases of SSc and 60 cases of normal control were received from the Affiliated Hospital of North Sichuan Medical College, and autophagy-related genes were detected by RT-PCR. SPSS19.0 statistical software was used to compare the expression of autophagy-related genes between groups and analyze the relationship between autophagy-related genes and clinical data, $P<0.05$ was considered statistically significant
Results: LC-3, Becline-1, and Agt-3 were highly expressed in SSc compared with normal control [LC-3: 0.78(0.60) $\times10^{-3}$ vs. 0.52(0.54) $\times10^{-3}$; Beclin-1: 6.68(3.56)$\times10^{-3}$ vs. 5.22(3.54)$\times10^{-3}$; Agt-3: 17.58(12.33)$\times10^{-3}$ vs. 11.00(4.56)$\times10^{-3}$, $P<0.05$], however Agt-5, Agt-12 and Agt-16L1 of autophagy-related genes were not statistically significant [AGT-5: 6.67(3.58) $\times10^{-3}$ vs. 6.67(2.64) $\times10^{-3}$; AGT-12: 8.64(5.56)$\times10^{-3}$ vs. 8.57(4.66)$\times10^{-3}$; Agt-16L1: 2.69(2.19)$\times10^{-3}$ vs. 2.52(2.26)$\times10^{-3}$] (Figure 1). Beclin-1 and Agt-5 high expressed in SSc with the positive of anti-SSA/Ro antibody. LC-3 was positively correlated with Age($r=0.662$) and ESR($r=0.355$) (all $P<0.05$).
Conclusion: Autophagy-related genes were increased in PBMC of SSc, and were correlated with Age, ESR and autoantibody, suggested that autophagy is a key feature in the pathogenesis of systemic sclerosis.

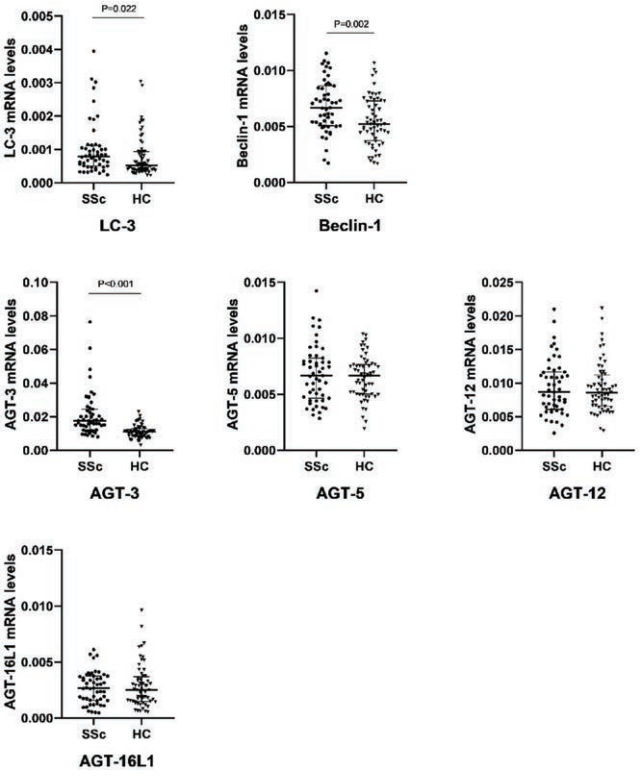


Figure 1. The relative expression of autophagy-related genes

REFERENCES:
[1] LIU C, ZHOU X, LU J, et al. Autophagy mediates 2-methoxyestradiol-inhibited scleroderma collagen synthesis and endothelial-to-mesenchymal transition induced by hypoxia[J]. Rheumatology, 2019;58(11): 1966–1975.
[2] Mayes M D, Bossini-Castillo L, Gorlova O, et al. Immunochip Analysis Identifies Multiple Susceptibility Loci for Systemic Sclerosis[J]. The American Journal of Human Genetics, 2014,94(1):47-61.DOI:10.1016/j.ajhg.2013.12.002.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3562

POS0431

FIBROBLASTS ARE NOT JUST FIBROBLASTS - CLEAR DIFFERENCES IN ECM PRODUCTION BETWEEN DERMAL AND LUNG FIBROBLASTS IN RESPONSE TO GROWTH FACTORS

S. F. Madsen[1,2], A. S. Siebuhr[2], H. Jessen[3], J. M. B. Sand[3], M. Karsdal[4], A. C. Bay-Jensen[2]. [1]*University of Copenhagen, Department of Biomedical Sciences, Copenhagen, Denmark*; [2]*Nordic Bioscience, ImmunoScience, Biomarkers and Research, Herlev, Denmark*; [3]*Nordic Bioscience, Respiratory Research, Biomarkers and Research, Herlev, Denmark*; [4]*Nordic Bioscience, Biomarkers and Research, Herlev, Denmark*

Background: Many systemic sclerosis (SSc) patients develop lung fibrosis, which contribute significantly to increased mortality[1]. Activated and proliferating fibroblasts are responsible for the excessive extracellular matrix (ECM) formation and stiffening of the connective tissue leading to skin and lung fibrosis. There is currently no effective treatment for the fibrosis in SSc and there is therefore a medical need for further understanding the pathogenesis of fibrosis. Fibrosis is associated with different growth factors, including tumor growth factor beta 1 (TGF-β1) and platelet derived growth factor-ab (PDGF-ab)[2].

Objectives: We investigated how stimulation with TGF-β1 and PDGF-ab affected the migration capacity and the ECM production using translational biomarkers of type I, III and VI collagens in healthy human dermal and lung fibroblasts.

Methods: The fibroblasts were grown in DMEM media containing 0.4% fetal calf serum, ficoll (to produce a crowded environment) and ascorbic acid for up to 12 days. The cells were stimulated with TGF-β1 [0.04-1 nM] or PDGF-ab [3 nM] at treatment initiation and changed twice a week. Non-stimulated fibroblasts (w/o) were used as control. A wound was induced by scratching the cells at day 1 after treatment initiation and the migration was followed for 2 days. Type I, III and VI collagen formation (PRO-C1, PRO-C3 and PRO-C6, respectively) were evaluated by validated ELISAs (Nordic Bioscience) in supernatant from day 0, 4, 8 and 12. Statistical analysis included 2-way ANOVA and Dunnett's test.

Results: The PDGF-ab stimulated dermal fibroblasts migrated significantly more than the non-stimulated ($p<0.0001$) and TGF-β1 stimulated ($p<0.001$) dermal fibroblasts 48 hours after the scratch (migration app. 70%, 30% and 30% respectively). There was no difference between the migration of the non-stimulated, TGF-β1 and PDGF-ab stimulated lung fibroblasts after 48 hours, as all migrated to approximately 70%.

TGF-β1 stimulation led to a significant increase in type I collagen formation (PRO-C1) in both dermal and lung fibroblasts from day 4 and onwards compared to w/o ($p<0.0001$). TGF-β1 also lead to a significant increase in type III collagen formation (PRO-C3) from day 8 in lung fibroblasts compared to w/o ($p<0.0001$). PDGF-ab stimulation led to a significant increase in type III collagen formation in dermal fibroblasts from day 8 compared to w/o ($p<0.0001$). PDGF-ab stimulation led to a significant increase in type VI collagen formation (PRO-C6) in both dermal and lung fibroblasts from day 4 and onwards compared to w/o ($p<0.0001$).

Conclusion: PDGF-ab increased the migration activity of the dermal fibroblasts, where the lung fibroblasts had a general high migration activity. The dermal and lung fibroblasts showcase the same ECM production within both type I and type VI collagen formation. The two fibroblasts types did however react opposite each other regarding the type III collagen formation: the dermal fibroblasts responded to PDGF-ab stimulation, where the lung fibroblasts responded to the TGF-β1 stimulation. The clear differences in the ECM production between the dermal and lung fibroblasts can be important in the search for an effective treatment for fibrosis in SSc and related lung fibrosis.

REFERENCES:

[1] McNearney, T. A. *et al.* Pulmonary involvement in systemic sclerosis: Associations with genetic, serologic, sociodemographic, and behavioral factors. *Arthritis Care Res.* **57**, 318–326 (2007).

[2] Wynn, T. A. Common and unique mechanisms regulate fibrosis in various fibroproliferative diseases. *J. Clin. Invest.* **117**, 524–529 (2007).

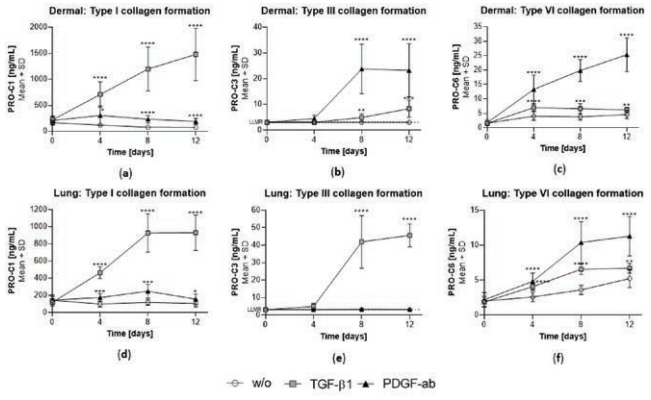


Figure 1. TGF-β1 and PDGF-ab can stimulate ECM production in both dermal and lung fibroblasts. Synthesis of type I (**a**), III (**b**), VI (**c**) collagen in dermal fibroblasts and type I (**d**), III (**e**), VI (**f**) collagen in lung fibroblasts. Data are shown as mean ± SD of 3 separate experiments with 4 replicates each. Data were analyzed by two-way ANOVA with Dunnett's multiple comparisons test against the control (w/o).

Disclosure of Interests: Sofie Falkenløve Madsen Employee of: Nordic Bioscience and University of Copenhagen, Anne Sofie Siebuhr Employee of: Nordic Bioscience A/S, Henrik Jessen: None declared, Jannie Marie Bülow Sand Employee of: Nordic Bioscience A/S, Morten Karsdal Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S

DOI: 10.1136/annrheumdis-2021-eular.3643

POS0432

POST-IMMUNIZATION WITH COLLAGEN V CONFERS A DISADVANTAGEOUS IMMUNE MATRICES MICROENVIRONMENT FOR EARLY LUNG FIBROSIS IN A SSc MOUSE MODEL

V. Elias[1], Z. Queiroz[1], S. Catanozi[2], A. Santos Filho[1], S. Fernezlian[3], A. P. Velosa[1], P. D. Sampaio-Barros[1], V. Capelozzi[3], W. Teodoro[1]. [1]*University of São Paulo, Division of Rheumatology, São Paulo, Brazil*; [2]*University of São Paulo, Division of Endocrinology, São Paulo, Brazil*; [3]*University of São Paulo, Department of Pathology, São Paulo, Brazil*

Background: The autoimmunity and inflammation phenomena observed in systemic sclerosis (SSc) lead to the dysregulation of type V collagen (Col V) and extracellular matrix (ECM) deposition of Col V, collagen I (Col I) and collagen III (Col III) fibers, characteristic of pulmonary fibroproliferative disease. T cells are the predominant inflammatory infiltrate in the lungs and are believed to produce cytokines that drive the synthesis of matrix proteins by fibroblasts, resulting in excessive fibrosis. Although most studies to date have focused on CD4+ T and CD20+ B immune cells in some SSc subsets, cytotoxic CD8+ T cells are also involved in the pathogenesis of SSc. We previously reported that reactivity to the ColV-self antigen predicts late SSc lung fibrosis in mice immunized with Col V after 120 days; however, the profile of underlying immune matrices in early SSc lung fibrosis remains unclear.

Objectives: To quantify T and B-cells and collagen fibers in the days following immunization with Col V in a mouse model mimicking human lung involvement in SSc.

Methods: Female C57BL/6 mice (n=18) were immunized subcutaneously with human Col V (150 µg) in complete Freund´s adjuvant, followed by two intramuscular boosters (IM-COLV). The control group (n=18) did not receive Col V. Three groups of animals (n=6 each) were euthanized on days 15, 30 and 45 after immunization. The lung sections were fixed in 10% buffered formalin, embedded in paraffin, and sectioned at 4 µm. Immunohistochemistry, immunofluorescence and histomorphometry were performed to phenotype and quantify CD4 and CD8 T-cells, CD20 B-cells, and Col I, III and V, respectively.

Results: We found that T-cells ($CD4^+$), cytotoxic T cells ($CD8^+$), and B-cells ($CD20^+$) were present in high densities in the lungs of IM-COLV mice, with variation in the absolute abundance of each of these immune cell lineages at 15, 30 and 45 days after immunization with Col V. In fact, a significantly higher density of $CD4^+$, $CD8^+$, and $CD20^+$ was detected early along the connective matrix of alveolar septa at 15 days after Col V immunization. In addition, higher density of Col I, III and V fibers were also observed early (Table 1). Although early SSc-lung fibrosis is generally considered to be linked to inflammatory cytokines, we also infer that cytotoxic T-cells may induce alveolar cells apoptosis by triggering kinases on macrophages and then accelerate fibrotic scar.

Conclusion: Our study quantitatively establishes that the densities of CD4+ CD8+ and CD20+, as well as Col I, Col III and Col V can be characterized as markers of early lung fibrosis in SSc. These findings suggest that cytotoxic T cells may induce apoptosis and secrete profibrotic cytokines to induce the deposition of collagen fibers in the lungs, inferring that early B cell depletion may improve early lung fibrosis in SSc.

	Post-Col V Immunization (Days)					
	15		30		45	
	Control	IM-COLV	Control	IM-COLV	Control	IM-COLV
Immune Cells						
CD4+ cells/ mm^2 (%)	13.85 ± 0.46	34.14 ± 1.55*	12.63 ± 0.56	23.38 ± 0.83	14.32 ± 0.52	23.62 ± 0.40
CD8+ cells/ mm^2 (%)	13.84 ± 0.60	39.40 ± 0.99**	12.42 ± 0.52	22.87 ± 0.85	12.93 ± 0.57	23.07± 1.00
CD20+ cells/ mm^2 (%)	12.12 ± 1.01	33.84± 1.43#	11.70 ± 1.14	15.23 ± 6.70	12.46 ± 0.50	28.24 ± 0.67
Collagen Fibers						
Col V (area fraction)	0.05 ± 0.003	0.12± 0.01	0.08 ± 0.003	0.14± 0.01††	0.07 ± 0.003	0.11± 0,003
Col I (area fraction)	0.16 ± 0,01	0.38± 0.05##	0.14 ± 0.01	0.25± 0.03	0.15 ± 0.02	0.24± 0.01
Col III (area fraction)	0,16 ± 0,003	0.28± 0.01†	0.14 ± 0.004	0.25± 0.05	0.13± 0,007	0.16± 0.02
Total Col µg/mg	2.7 ± 0.29	3.99 ± 0.58	3.15 ± 0.19	3.77 ± 0.27	2.87 ± 0.30	4.99 ± 0.60

Data are shown as mean ± SD. Comparisons were done using ANOVA/Dunn´s Multiple comparison test$P<0.05$). *15 vs 30 and 45 days; **15 vs 30 and 45 days; #15 vs 30 and 45 days; ## 15 vs 30 and 45 days; † 15 vs 45 days; †† 30 vs 45 days. Col I, collagen type I; Col III, collagen type III; Col V, collagen type V.

Disclosure of Interests: Vitoria Elias: None declared, Zelita Queiroz: None declared, Sergio Catanozi: None declared, Antonio Santos Filho: None declared, Sandra Fernezlian: None declared, Ana Paula Velosa: None declared, Percival D. Sampaio-Barros Speakers bureau: Actelion, Boehringer Ingelheim, Abbvie, Lilly, Novartis, Consultant of: Abbvie, Bayer, Boehringer Ingelheim, Lilly, Novartis, Pfizer, Vera Capelozzi: None declared, Walcy Teodoro: None declared
DOI: 10.1136/annrheumdis-2021-eular.3663

POS0433

CAN INTERLEUKIN 33 (IL-33) BE CONSIDERED A VALUABLE BIOMARKER IN THE EARLY STAGES OF SYSTEMIC SCLEROSIS? ANALYSIS OF A MONOCENTRIC COHORT

C. Angelelli[1], K. Stefanantoni[1], M. Cadar[1], G. Pellegrino[1], F. Conti[1], V. Riccieri[1]. [1]*Sapienza University of Rome, Scienze cliniche internistiche, anestesiologiche e cardiovascolari, Roma, Italy*

Background: The ScS approach has changed considerably in recent years especially concerning the very early diagnosis of the disease (VEDOSS) at the time when the patient is still in an undifferentiated form (UCTD) at risk of developing SSc (1, 2). Of great value are different clinical, instrumental and laboratory findings, such as specific autoantibodies and Nailfold VideoCapillaroscopy (NVC), able to identify those cases progressing into overt SSc. IL-33 cytokine is known to exert pro-fibrotic effects through its membrane receptor ST2 on immune cells and myofibroblasts and recent studies suggest that it can be released following endothelial cell activation at the onset of SSc (3, 4).
Objectives: Our aim has been to evaluate IL-33 serum levels in a monocentric cohort of VEDOSS patients, looking for the possible association with clinical phenotype and disease progression, focusing on the microvascular capillaroscopic changes.
Methods: Fourty-seven VEDOSS patients underwent a complete clinical, instrumental and laboratory evaluation, including NVC and specific SSc autoantibodies. At baseline serum IL-33 levels were measured using an ELISA assay. In 32 of them we also had a second serum sample at a follow-up time of at least 24 months (range 24 to 96 months).
Results: During the follow-up time, 17 patients were subsequently reclassified as having ScS whereas 30 remained VEDOSS. The "progressor" subjects positively correlated with the presence of anti-Topoisomerase I antibodies (p>0,004). IL-33 concentrations had a median value of 427.2 pg/ml (IQR 967.9 pg/ml) at baseline and of 130.4 pg/ml (IQR 399 pg/ml) at the follow up, showing a statistically significant difference independently from the progression of the disease (p=0.03). Besides significantly higher levels were detected in those patients with more severe NVC changes, defined as "active" pattern (p<0.05). Among the 47 VEDOSS patients, 12 started some kind of vascular therapy. In these patients serum IL-33 concentrations significantly lowered during the follow-up respect to those without any treatment (p<0.03)
Conclusion: The analysis of our data confirms previous report (5) on higher IL-33 serum levels in the very early stages of UCTD patients at risk for SSc, regardless of their progression in established SSc, although related to more severe microvascular NVC involvement. The lowering of IL-33 serum levels that we detected in the follow up of our patients, may be linked to the well-known endothelial changes during the progression of the SSc and seems also to be partially affected by treatments. Investigation on a greater number of patients are needed to better understand our findings.
REFERENCES:

[1] J. Avouac et al. Ann Rheum Dis 2011
[2] G Valentini et al. Clin Exp Med 2017
[3] Manetti M, et al. Ann Rheum Dis 2010
[4] Terras S et al. Ann Rheum Dis 2013
[5] Vettori S, et al. J Clin Immunol 2014

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4196

Basic and translational pain science

POS0434

CLINICAL UTILITY OF SCREENING TOOLS IN REFERRAL OF PATIENTS WITH HAND ARTHRALGIA TO RHEUMATOLOGISTS

G. Figueroa-Parra[1], D. Vega-Morales[1], P. Herrera-Sandate[1], J. A. Esquivel Valerio[1], B. R. Vázquez Fuentes[1], M. A. Garza Elizondo[1], Y. G. Ordoñez Azuara[2], R. F. Gutierrez-Herrera[2], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Rheumatology Service, Monterrey, Mexico;* [2]*Hospital Universitario Dr. José Eleuterio González, Family Medicine Department, Monterrey, Mexico*

Background: Clinically Suspect Arthralgia (CSA) was defined by European League Against Rheumatism to identify a combination of clinical features that best characterise patients with arthralgia who are at risk of progression to rheumatoid arthritis (RA) (1). A specificity >90% is obtained with the presence of ≥4 parameters. Another clinical feature useful to identify patients at risk is the squeeze test (ST). Recently, we have identified the necessary strength to screen the patient with arthralgia through ST, with a median squeeze force of 3 kg and 2.78 kg to evoke pain in the right and left hand of the RA patient, respectively (2). Primary care physicians (PCP), the first contact of patients at risk, could benefit from these screening tools, prompting early referral, diagnosis, and treatment of these individuals.
Objectives: To identify the clinical utility of CSA and ST in the referral of patients with hand arthralgia from PCP to rheumatologists.
Methods: We conducted a cohort study from October 2018 to December 2020 in 110 patients who attended a Family Medicine clinic at University Hospital "Dr. Jose Eleuterio Gonzalez" in Monterrey, Mexico. We recruited patients with hand arthralgia with no history of previous trauma or autoimmune rheumatic diseases. A questionnaire assessing CSA criteria was employed, and an ST maneuver was performed through an automated compressor with quantitative measures of applied force. Patients were grouped based on referral to Rheumatology consultation and variables categorized according to clinically relevant thresholds. Chi square test was performed in categorical variables, t-student test was performed in normal, continuous variables and Spearman's rho correlation was utilized between CSA number of criteria and quantitative ST force using SPSS v25.
Results: Out of 110 patients, 49 (44.5%) were referred to a rheumatologist. A non-significant association was found across assessed variables in referred and non-referred patients as seen in Table 1. Spearman's rho found a moderate correlation between the number of CSA criteria and quantitative force in right (r=-.445) and left (r=-.382) hand as seen in Figure 1. Evaluation of CSA cutoffs other than ≥4 did not yield a significant association in referral of patients to the rheumatologist (data not shown).
Conclusion: The clinical utility of CSA criteria and ST in referral of patients with hand arthralgia from PCP to rheumatologists is currently limited. More research is needed to elucidate the clinical utility of these screening tools.
REFERENCES:

[1] van Steenbergen HW, et al. EULAR definition of arthralgia suspicious for progression to rheumatoid arthritis. Ann Rheum Dis. 2017;76(3):491-496.
[2] Vega-Morales D, et al. Automated squeeze test (Gaenslen's manoeuvre) to identify patients with arthralgia suspicious for progression to RA: improving time delay to rheumatology consultation. Ann Rheum Dis. 2017;76(10):e40.

Table 1. Demographic characteristics and clinical performance of CSA and ST in referral of patients with hand arthralgia from PCP to rheumatologists.

	Referred patients, n = 49	Non-referred patients, n = 61	*p*
Female, n (%)	40 (81.6)	50 (82.0)	0.964
Age in years, mean ± SD	46.76 ± 14.43	52.05 ± 15.00	0.064
Patients with ≥4 CSA criteria, n (%)	23 (46.9)	19 (31.1)	0.090
Right hand positive ST patients, n (%)	21 (42.9)	22 (36.1)	0.468
Left hand positive ST patients, n (%)	26 (53.1)	28 (45.9)	0.455
Force in right hand ST, mean kg ± SD	4.19 ± 2.92	3.86 ± 3.07	0.571
Force in left hand ST, mean kg ± SD	4.25 ± 3.04	3.54 ± 2.74	0.198

CSA, Clinically Suspect Arthralgia; ST, Squeeze Test; SD, Standard Deviation.

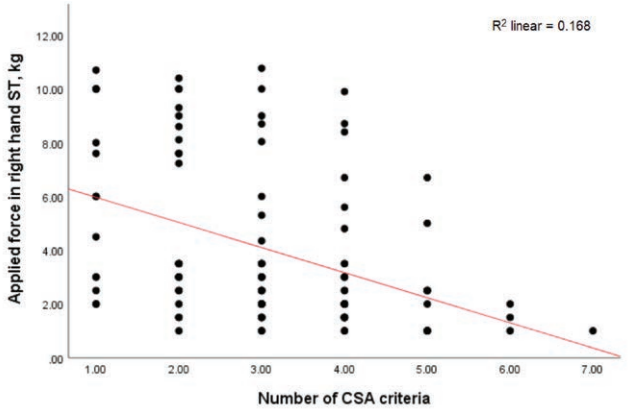


Figure 1. Scatter plot showing a moderate correlation between the number of CSA criteria and applied force in the right hand ST in kg, Spearman's rho = -.445.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3754

Rheumatoid arthritis - prognosis, predictors and outcome

POS0435 CHARACTERISTICS AND 6-MONTH OUTCOMES AMONG REAL-WORLD PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING UPADACITINIB: ANALYSIS FROM THE CORRONA REGISTRY

J. M. Kremer[1,2], N. Tundia[3], R. McLean[1], T. Blachley[1], A. Maniccia[3], D. A. Pappas[1,4]. [1]*Corrona, LLC, Waltham, United States of America*; [2]*Albany Medical College,The Center for Rheumatology,Albany, United States of America*; [3]*AbbVie Inc., North Chicago, United States of America*; [4]*Columbia University, New York, United States of America*

Background: Upadacitinib (UPA) has demonstrated efficacy in randomized controlled trials[1-3]; however, few data are available from patients with rheumatoid arthritis (RA) who have been treated with UPA in real-world clinical practice.
Objectives: Describe the characteristics and 6-month outcomes in patients with RA initiating UPA in a real-world setting.
Methods: We identified adults with RA enrolled in the Corrona RA Registry through October 31, 2020 who initiated UPA during or after August 2019 and had a follow-up visit 6 (±3) months after initiation of UPA. Descriptive statistics were used to summarize characteristics in all patients initiating UPA who had a 6-month follow-up visit. Outcomes (CDAI, modified HAQ-DI, pain, and fatigue) were described at the 6-month visit for all UPA initiators regardless of UPA use at 6 months and for the subset of patients who continued UPA through the 6-month visit. Patients who discontinued UPA before the 6-month visit were considered non-responders for dichotomous variables and were assigned the value at the time of discontinuation for continuous variables. Mean change from baseline in continuous variables was analyzed with one-sample *t* tests or one-sample Wilcoxon rank sum tests. Minimum clinically important difference (MCID) in HAQ-DI is defined as an improvement of 0.22 units or more. MCID in CDAI is an improvement of at least 2, 7, and 13 units for patients in low, moderate and severe disease at initiation, respectively. MCID for 100-point VAS is an improvement of ≥10 points. Percentages of patients achieving MCID thresholds were calculated.
Results: We identified 181 patients who initiated UPA and had a 6-month follow-up visit. Mean±SD age was 58.6±12.1 years, 81% were female. Patients had RA for a mean of 11.5±9.8 years. At UPA initiation, 45% of patients were on monotherapy. Prior use of one or more TNFi and JAKi was 79% and 52%, respectively. Seventy-two percent of patients (n=130) initiated UPA as the third or higher line of therapy. Mean CDAI was 18.7±11.6 and mean HAQ-DI was 1.1±0.8 at initiation. Based on CDAI (n=155), 29%, 52%, and 15% of patients had high, moderate, and low disease activity, respectively; 4.5% were in remission at initiation. At 6 months (n=158), 22%, 39%, and 28% had high, moderate, and low disease activity, respectively; 11% were in remission. Among 138 initiators with valid CDAI measures at initiation and 6 months, mean change in CDAI was –4.8±11.8, $P<0.01$. At 6 months, 46% (63/138) maintained and 39% (54/138) achieved improvement in any CDAI category. Improvements in other outcomes were significantly different from zero. Improvements >=MCID in CDAI, HAQ-DI, pain, and fatigue were achieved in 36–44% of UPA initiators. Improvements were similar, but larger in the subset of patients (n=122) who continued UPA through the 6-month visit (Table 1).
Conclusion: Among patients in the Corrona RA Registry, UPA is frequently started in those who failed multiple previous therapies. UPA initiators responded to therapy in the first 6 months with improvements in several disease activity measures including CDAI and HAQ-DI, as well as patient-reported pain and fatigue.

REFERENCES:

[1] Fleischmann R. *Arthritis Rheumatol*. 2019;71:1788–800.
[2] Smolen JS. *Lancet*. 2019;393:2303–11.
[3] Burmester GR. *Lancet*. 2018;382:2505–12.

Acknowledgements: This study was sponsored by Corrona, LLC. Corrona has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Crescendo, Eli Lilly and Company, Genentech, Gilead, GSK, Janssen, Merck, Momenta Pharmaceuticals, Novartis, Pfizer, Regeneron, Roche, Sun, UCB, and Valeant. The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract. No honoraria or payments were made for authorship.
Medical writing services were provided by Joann Hettasch of Fishawack Facilitate Ltd., part of Fishawack Health, and funded by AbbVie.

Disclosure of Interests: Joel M Kremer Shareholder of: Corrona, Consultant of: AbbVie, Grant/research support from: AbbVie, Employee of: Corrona, Namita Tundia Shareholder of: AbbVie, Employee of: AbbVie, Robert McLean Employee of: Corrona, Taylor Blachley Employee of: Corrona, anna maniccia Shareholder of: AbbVie, Employee of: AbbVie, Dimitrios A Pappas Shareholder of: Corrona, Consultant of: AbbVie, Genentech, Novartis, Regeneron, and Roche Hellas, Employee of: Corrona

Table 1.

Outcomes at 6-month follow-up	All initiators (n=181)		Subset remaining on UPA (n=122)	
	n	Value[a]	n	Value[a]
Remission (CDAI <2.8)	158	18 (11)	105	12 (11)
Low (CDAI >=2.8 and <10)	158	44 (28)	105	38 (36)
Moderate (CDAI >=10 and <22)	158	62 (39)	105	36 (34)
High (CDAI >=22)	158	34 (22)	105	19 (18)
Improvement in any CDAI category	138	54 (39)	89	40 (45)
Maintenance of CDAI category	138	63 (46)	105	39 (44)
Mean change in				
CDAI	138	–4.8±11.8*	89	–7.1±12.0*
HAQ-DI	154	–0.1±0.5*	101	–0.2±0.5*
Pain	154	–9.3±25.1*	101	–13.5±25.8*
Fatigue	153	–7.6±27.3*	100	–12.5±27.5*
MCID achievement in				
CDAI	138	57 (41)	89	43 (48)
HAQ-DI	154	55 (36)	101	39 (39)
Pain	154	68 (44)	101	53 (52)
Fatigue	153	65 (42)	100	49 (49)

[a]Mean±SD or n (%).*$P<0.01$ for improvement significantly different from zero.

DOI: 10.1136/annrheumdis-2021-eular.170

POS0436 PATIENT CHARACTERISTICS AND OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH UPADACITINIB: THE OM1 RA REGISTRY

M. Bergman[1], N. Tundia[2], A. Bryant[3], I. Topuria[3], T. Brecht[3], K. Dunlap[2], A. Gibofsky[4]. [1]*Drexel University College of Medicine, Philadelphia, United States of America*; [2]*AbbVie Inc, North Chicago, United States of America*; [3]*OM1, Boston, United States of America*; [4]*Weill Cornell Medicine, Hospital for Special Surgery, New York, United States of America*

Background: Upadacitinib (UPA) has demonstrated efficacy in the treatment of rheumatoid arthritis (RA) in randomized controlled trials,[1-6] but there are limited data available on its real-world use and effectiveness in patients with RA.
Objectives: To describe the characteristics and clinical outcomes at 3 months among real-world patients with RA initiating UPA.
Methods: The data source for this study was the OM1 RA Registry, a subset of the OM1 Real-World Data Cloud (OM1, Inc, Boston, MA, US), a large, linked clinical and administrative dataset derived from medical and pharmacy claims, electronic medical record data, and death data. This analysis includes data collected in patients who initiated UPA during or after August 2019. Patients had ≥1 prescription for UPA (index date was first UPA prescription), were ≥18 years of age at index date, had ≥6 months of available data in the OM1 RA Registry prior to index date (ie, baseline period), ≥1 baseline disease activity measure, and ≥1 follow-up disease activity measure (3 or 6 months post-index). Disease activity was based on RAPID3 or CDAI. Multivariate analyses were conducted using a mixed-effects linear model adjusting for age, sex, and baseline scores. Outcomes were also assessed by therapy status (monotherapy or combination therapy) and targeted immunomodulator (TIM) use (naïve vs experienced).
Results: Inclusion criteria were met by 1,102 patients, of whom 620 were on monotherapy and 482 were on combination therapy at index. Mean age was 57.7 years, 83% were female, 75% had prior treatment with a biologic, and 47% had prior treatment with a Janus kinase inhibitor. Of 651 patients with known disease activity category, 113 (17%) were in low disease activity (LDA)/remission. At baseline, overall mean±SD scores were 19.9±12.3 for CDAI, 4.5±2.4 for RAPID3, 5.7±2.8 for pain, 5.2±3.0 for fatigue, 3.1±2.7 for MDHAQ Physician Global Assessment (PGA), 5.2±2.8 for MDHAQ Patient Global Assessment (PtGA), and 3.1±2.3 for MDHAQ Functional Index. At 3 months post-UPA initiation, mean (95% CI) change in CDAI was –5.1 (–7.5

to –2.7) in the monotherapy group and –5.9 (–8.7 to –3.0) in the combination group. At 3 months, 29% (109/374) of patients were in LDA/remission and 32% (120/374) of patients showed improvement in disease activity. Of 94 patients with moderate disease at baseline, 34 (36%) were in LDA/remission at 3 months. Of 215 patients with high disease at baseline, 30 (14%) were in LDA/remission and 49 (23%) had moderate disease at 3 months. RAPID3 and other outcomes also improved at 3 months in the monotherapy and combination therapy groups (Figure 1). Improvements in disease activity were observed at 3 months and maintained at 6 months post-UPA initiation. Of 1,102 patients, 16% were TIM naïve and 84% TIM experienced. Both TIM-naïve and TIM-experienced patients achieved significant mean changes in CDAI (–5.7 [–10.8 to –0.6] and–5.0 [–7.0 to –3.0], respectively) and RAPID3 (–1.0 [–1.6 to –0.4] and –0.5 [–0.8 to –0.1]) at 3 months (Table 1). Improvements in clinical outcomes were maintained at 6 months in both TIM-naïve and TIM-experienced patients.

Conclusion: Significant improvements in disease activity were consistently observed at 3 months and maintained at 6 months post-UPA initiation regardless of monotherapy, combination therapy, or prior TIM use.

REFERENCES:

[1] Fleischmann R. *Arthritis Rheumatol*. 2019;71:1788–800.
[2] Smolen JS. *Lancet*. 2019;393:2303–11.
[3] Burmester GR. *Lancet.* 2018;382:2505–12.
[4] Genovese MC. *Lancet*. 2018;391:2513–24.
[5] van Vollenhoven R. *Arthritis Rheumatol*. 2020;72:1607–20.
[6] Rubbert-Roth A. *N Engl J Med*. 2020;383:1511–21.

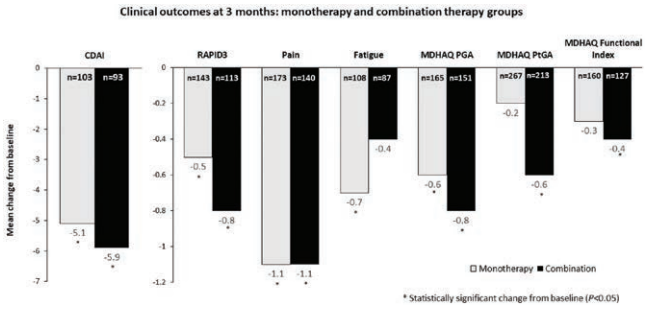


Table 1. Change in clinical outcomes from baseline at 3 months: TIM-naïve and TIM-experienced groups

	TIM naïve (N=179)		TIM experienced (N=923)	
	n	Mean change	n	Mean change
CDAI	36	–5.7*	160	–5.0*
RAPID3	67	–1.0*	189	–0.5*
Pain (VAS)	76	–1.5*	237	–0.9*
Fatigue	46	–0.7	149	–0.5
MDHAQ PGA	65	–0.7*	251	–0.7*
MDHAQ PtGA	97	–0.6*	383	–0.3
MDHAQ Functional Index	72	–0.7*	215	–0.2

*Statistically significant change from baseline (P<0.05).

Acknowledgements: Funding statement: Financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract. All authors contributed to the development of the publication and maintained control over the final content.
Acknowledgment:
Medical writing services were provided by Joann Hettasch of Fishawack Facilitate Ltd, part of Fishawack Health, and funded by AbbVie.

Disclosure of Interests: Martin Bergman Shareholder of: JNJ (parent of Janssen), Speakers bureau: AbbVie, Amgen, BMS, Genentech, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sandoz, Consultant of: AbbVie, Amgen, BMS, Genentech, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sandoz, Namita Tundia Shareholder of: AbbVie, Employee of: AbbVie, Allison Bryant: None declared, Ia Topuria: None declared, Tom Brecht: None declared, Kendall Dunlap Shareholder of: AbbVie, Employee of: AbbVie, Allan Gibofsky Shareholder of: AbbVie, Amgen, Horizon, J&J, Pfizer, Regeneron, Speakers bureau: AbbVie, Acquist, Amgen, Lilly, Merck, Pfizer, Sandoz, Samumed, Consultant of: AbbVie, Acquist, Amgen, Lilly, Merck, Pfizer, Sandoz, Samumed

DOI: 10.1136/annrheumdis-2021-eular.172

POS0437

IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH GOLIMUMAB: SUB-ANALYSIS OF ASIAN PATIENTS ENROLLED IN PHASE-3 CLINICAL TRIALS

W. C. Tsai[1], R. Mu[2], C. H. Suh[3], D. Furtner[4], K. H. Lo[5], Y. Zhou[5], E. C. Hsia[6,7].
[1]Kaohsiung Medical University, Division of Allergy, Immunology, and Rheumatology, Kaohsiung, Taiwan, Republic of China; *[2]Peking University People's Hospital, Department of Rheumatology and Immunology, Beijing, China*; *[3]Ajou University School of Medicine, Department of Rheumatology, Suwon, Korea, Rep. of (South Korea)*; *[4]Janssen, a division of Jonson & Johnson Pte Ltd., Regional Medical Affairs, Singapore, Singapore*; *[5]Janssen Research & Development, LLC, Clinical Biostats, Spring House, Pennsylvania, United States of America*; *[6]Janssen Research & Development, LLC, Immunology, Spring House, Pennsylvania, United States of America*; *[7]University of Pennsylvania Medical Center, Perelman Center for Advanced Medicine, Pennsylvania, United States of America*

Background: Clinical efficacy and safety of Tumour Necrosis Factor-alpha inhibitor golimumab (GLM) for patients with rheumatoid arthritis (RA) and inadequate response to methotrexate (MTX) were studied in phase-3 clinical trials. A greater proportion of patients treated with GLM 50 mg every 4 weeks (q4w) achieved improvement in clinical signs and symptoms, measured by American College of Rheumatology 20% improvement (ACR20) response and patient-reported outcomes (PROs) when compared with placebo (PBO) at Weeks 14 and 24.

Objectives: To assess PROs in RA patients from Asia treated with GLM in phase-3 trials.

Methods: Post-hoc PRO (Health Assessment Questionnaire [HAQ], Short-Form 36 [SF-36] physical component score [PCS] and mental component score [MCS], pain, and work productivity) sub-analysis of RA patients from China (including Taiwan region) and South Korea with inadequate response to MTX randomized to subcutaneous GLM 50 mg + MTX or PBO + MTX from 2 clinical trials (GO-FORWARD, NCT01248780).

Clinically meaningful improvement was defined as improvement of ≥0.25 point in HAQ or ≥5 points in SF-36 PCS and MCS. Nominal p-values were used for descriptive and exploratory purposes.

Results: At Week 24, MTX-experienced patients from Asia treated with GLM + MTX demonstrated improvements versus PBO + MTX in all PROs analyzed. Pooled patients from Asia on GLM + MTX had greater improvements at Week 24 in all measures of PROs than patients with PBO + MTX, and the improvements are comparable to all other regions (Table 1). Greater proportions of RA patients from Asia in GLM group than PBO achieved clinically meaningful improvement in HAQ, SF-36 PCS, and SF-36 MCS (Figure 1).

Conclusion: MTX-experienced RA patients from Asia treated with GLM demonstrated improved PROs after 24 weeks. The pooled results were comparable with patients enrolled from all other regions and demonstrated clinical meaningful improvements in HAQ, SF-36 PCS, and SF-36 MCS.

Table 1. Summary of Improvement from Baseline in HAQ-DI, HRQoL, Pain, and Work Productivity at Week 24: Randomized Patients in RA Studies Pooled for Regions Outside Asia and Randomized Patients from Asia

	MTX experienced from Asia				Pooled RA in All Other Regions			
	Placebo + MTX (N=152)	GLM 50 mg + MTX (N=146)	Difference		Placebo + MTX (N=107)	GLM 50 mg + MTX (N=74)	Difference	
	Mean (SD)	Mean (SD)	Mean (SE)	Nominal p-value	Mean (SD)	Mean (SD)	Mean (SE)	Nominal p-value
HAQ-DI	-0.13 (0.670)	0.28 (0.575)	0.41 (0.072)	<.001	0.18 (0.596)	0.48 (0.540)	0.30 (0.087)	<.001
SF-36 PCS	-0.57 (7.011)	4.73 (7.034)	5.30 (0.814)	<.001	4.77 (8.343)*	8.67 (8.862)	3.90 (1.299)	0.003
SF-36 MCS	-1.89 (11.866)	1.87 (10.833)	3.76 (1.318)	0.005	1.31 (9.440)*	3.80 (10.969)	2.50 (1.533)	0.105
Pain VAS	-0.00 (2.437)	1.46 (2.940)	1.46 (0.312)	<.001	0.76 (2.776)	2.72 (2.586)	1.96 (0.408)	<.001
Productivity VAS	0.17 (2.601)	1.74 (2.599)	1.57 (0.301)	<.001	1.09 (2.976)	2.38 (2.889)	1.28 (0.445)	0.004

GLM, golimumab; HAQ-DI, health assessment questionnaire disability index; HRQoL, health-related quality of life; MTX, methotrexate; RA, rheumatoid arthritis; SD, standard deviation; SE, standard error; SF-36 MCS, short-form 36 mental component score; SF-36 PCS, short-form 36 physical component score; VAS, visual analogue scale*N=105

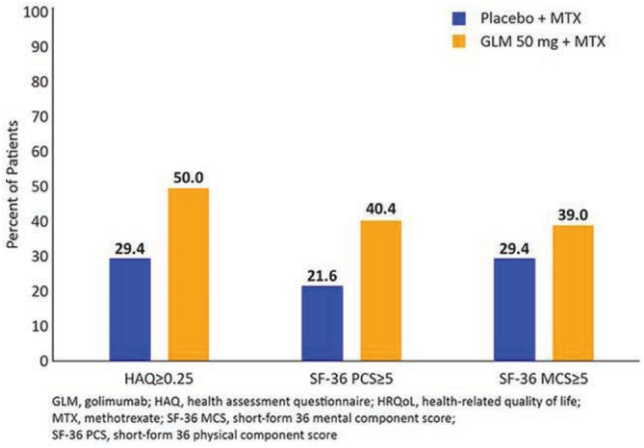


Figure 1. Proportion of Patients with Clinical Meaningful Improvements in HAQ and HRQoL: Randomised Subjects from China, Taiwan and Korea

Disclosure of Interests: Wen-Chan Tsai Consultant of: Pfizer, AbbVie, Roche, and Eli Lilly, Rong Mu: None declared, Chang-Hee Suh: None declared, Daniel Furtner Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson Pte. Ltd., Kim Hung Lo Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Yiying Zhou Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC
DOI: 10.1136/annrheumdis-2021-eular.205

POS0438 IS IMAGING DETECTED JOINT INFLAMMATION HELPFUL IN EXPLAINING FATIGUE IN RHEUMATOID ARTHRITIS AT DIAGNOSIS AND DURING THE DISEASE COURSE? – A LARGE MRI STUDY

X. Matthijssen[1], F. Wouters[1], N. Sidhu[1], A. van der Helm - van Mil[1,2]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; [2]*Erasmus MC, Rheumatology, Rotterdam, Netherlands*

Background: Fatigue in rheumatoid arthritis (RA) is hypothesized to be caused by inflammation. Still ~50% of fatigue in RA cannot be explained by the disease activity score (DAS), nor by generic or psychological factors.
Objectives: Since MRI can detect joint inflammation more sensitively than DAS, we hypothesized that residual inflammation detected by MRI could aid in explaining fatigue in RA at diagnosis and during follow-up.
Methods: 526 consecutive RA-patients were followed longitudinally. Fatigue was assessed yearly on a numerical rating scale. Hand and foot MRIs were performed at inclusion, after 12 and 24-months in 199 patients and were scored for inflammation (synovitis, tenosynovitis and osteitis combined). We studied whether RA-patients with more MRI-inflammation were more fatigued at diagnosis (linear regression), whether the 2-year course of MRI-inflammation associated with the course of fatigue (linear mixed models) and whether decrease in MRI-inflammation in year-1 associated with subsequent improvement in fatigue in year-2 (cross-lagged models). Similar analyses were done with DAS as inflammation measure.
Results: At diagnosis, higher DAS-scores were associated with more severe fatigue (p<0.001). However, patients with more MRI-inflammation were not more fatigued (p=0.94). During 2-year follow-up, DAS decrease associated with improvement in fatigue (p<0.001), but MRI-inflammation decrease did not (p=0.96). DAS decrease in year-1 associated with fatigue improvement in year-2 (p=0.012), as did MRI-inflammation decrease (p=0.039), with similar effect strength.
Conclusion: Sensitive measurements of joint inflammation did not aid in explaining fatigue in RA at diagnosis and follow-up. This supports the concept that fatigue in RA is partly uncoupled from inflammation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.258

POS0439 THE INFLUENCE OF ESCALATED PGA SCORE ON DISEASE ACTIVITY, DAILY ACTIVITY, AND QUALITY OF LIFE, AND SOLUTION FOR OPTIMAL PGA LEVEL THAT DESERVES CLINICAL REMISSION IN PATIENT WITH RHEUMATOID ARTHRITIS

I. Yoshii[1]. [1]*Yoshii Hospital, Rheumatology and Musculoskeletal Medicine, Shimanto City, Japan*

Background: Patient's global assessment (PGA) is one most difficult component as a part of disease activity index for treatment of rheumatoid arthritis (RA), that often causes an obstacle to attaining clinical remission. Moreover, PGA level affects activities in daily living.
Objectives: The influence of escalated PGA score on disease activity, daily activity, and quality of life for patient with RA was investigated., and the optimal PGA level for both disease activity and daily activities was investigated from real world data.
Methods: A total of 24,075 times of monitoring for RA was performed in the institute. Monitored items included TJC, SJC, PGA, EGA, CRP, and calculated values of DAS28, CDAI, SDAI, composite index of Boolean evaluation (Boolean), pain score with visual analog scale (PS-VAS), Health Assessment Questionnaire Disability Index (HAQ-DI), and quality of life score (QOLS) calculated from Euro-QOL questionnaire with 5th dimensions. Each measured item was calculated as mean value according to the PGA score, which was measured at the same time. The PGA score was classified by one increment from zero to ten. The mean values of DAS28, CDAI, SDAI, remission rate of these indices and Boolean remission rate, and mean values of PS-VAS, HAQ-DI, and QOLS were statistically evaluated.
HAQ-DI below 0.5 was determined as remission (HAQ remission). Sensitivity and specificity regarding attaining HAQ remission according to each level of PGA score were calculated, and cutoff index (COI) was determined with receiver operating characteristic (ROC) curve. For PS-VAS, sensitivity and specificity of Boolean remission regarding each level of PS-VAS after classification divided by one increment was calculated, and comparable level (PS-VAS remission) was determined with reference of the curve. ROC was performed according to PGA level, and COI was determined with a same manner.
Results: Number of measures counted 10428, 3099, 3110, 2346, 998, 1773, 751, 703, 655, 139, and 73 for each PGA level. PGA level from 3 to 5, and 5 to 10 were put together for number adjusting.
Mean DAS28, CDAI, and SDAI demonstrated significant increase as PGA level increased, and remission rate of the all indices including Boolean demonstrated significant decrease as PGA level increases (p<0.01%). Boolean remission rate demonstrated zero percent from two, and CDAI and SDAI remission rate demonstrated zero from five, whereas DAS remission rate showed gradual decrease then zero percent was not shown in any level. Mean value of PS-VAS and HAQ-DI score demonstrated also significant decrease as PGA level increases, and QOLS demonstrated significant decrease as PGA level increases (p<0.01%). Increase of HAQ-DI score and decline of QOLS demonstrated more steep from PGA level 3, whereas no significant difference demonstrated from zero to one.
HAQ remission counted 15,703, whereas no HAQ remission counted 8,335. Using ROC, COI of the PGA level was 2.0, whereas sensitivity and specificity were 63.4% and 66.3%, respectively. The estimated PS-VAS remission level was 10mm. Optimal PGA level for PS-VAS remission was set as 1.0, and sensitivity and specificity regarding PS-VAS remission were 87.1% and 71.3%, respectively.
Conclusion: Increase of PGA affects daily activities and quality of life. The evident level that increases deterioration risk significantly was supposed to be from 3. Optimal level of PGA score for attaining the PS-VAS remission was 1.0, whereas the optimal PGA level for HAQ-DI remission is 1.0, despite sensitivity and specificity for the HAQ remission were lower than these for the PS-VAS remission.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.285

POS0440 REDUCTION IN MONOCYTE COUNT PREDICTS SUSTAINED REMISSION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ANTI-TNF THERAPY

R. Amarnani[1], M. Mainuddin[2], M. Shipa[3], S. A. Yeoh[3], M. Ehrenstein[1,3]. [1]*University College Hospital, Rheumatology, London, United Kingdom*; [2]*North Middlesex University Hospital, Rheumatology, London, United Kingdom*; [3]*University College London, Centre for Rheumatology, Division of Medicine, London, United Kingdom*

Background: Sustained remission is the ultimate goal in the management of rheumatoid arthritis (RA) but is infrequently achieved. After conventional therapy, TNFi (tumour necrosis factor inhibitor) has a strong track record for achieving remission. Existing studies suggest variable effect of RA and TNFi on various cellular components of the full blood count (FBC), but their relationship with loss of remission (LOR) is unclear.
Objectives: To investigate whether cellular changes in the FBC can predict LOR (remission defined as DAS28-ESR≤2.6) in patients with RA receiving TNFi, adjusted using key clinical factors.
Methods: Real-world clinical and routine laboratory data were analysed from two independent cohorts of adult RA patients, who were started on their first TNFi (from 2009 to December 2019), and went into remission. Data was extracted in October 2020. A linear mixed model was used to investigate longitudinal changes of different components of FBC and CRP, stratified by LOR, and grouped by

years of follow-up. Pairwise post-hoc comparisons were performed by Bonferroni correction. Area Under the Receiver Operating Characteristics (AUROC) of cellular changes in FBC components to predict LOR at different time points were calculated. Latent class mixed models were used to investigate trajectories of change in cellular components of the FBC from baseline to one year. Further survival analysis to predict LOR of TNFi was done by using the latent class model and adjusted by clinical parameters, demographics and concomitant treatment.

Results: 92 and 43 biologic-naïve RA patients who attained remission were included from cohorts 1 and 2 respectively. 73 (54%) were treated with adalimumab and 62 (46%) with etanercept. 87 (64%) of patients lost remission over a 10-year period with median time to LOR of 3.3 years (95% CI 2.6-3.7).

Among the cellular components of FBC, monocyte count changes in the first year after initiation of TNFi fell significantly in those who maintained remission over the five years of follow-up, compared to those who lost remission [p<0.001 for all years evaluated] (Figure 1). AUROC of monocyte count change at 6 months and 12 months, to predict LOR from year 1 to year 5 (after TNFi initiation) and after 5 years, ranged between 0.70-0.90. Three latent classes were identified based on monocyte count changes over time: 1-decrease (N=41), 2-increase (N=7) and 3- no change (N=87). Among these latent classes, patients in class 1, sustained remission for longer (unadjusted log-rank *p*=0.001) compared to the other 2 classes. Monocyte latent classes as a predictor of LOR was further tested by cox-regression, where variables (anti-citrullinated protein antibody/ACPA, concomitant methotrexate, baseline DAS28-ESR) were selected by elastic net regularisation and further adjusted by use of steroid, age and gender. Class 2 and Class 3 monocyte latent classes showed a hazard ratio (HR) of 3.15 (95% CI 1.02-9.74, *p* = 0.046, n. of event = 6/7) and 5.48 (95% CI 2.6-11.57, *p* <0.001, n. of event = 73/87) respectively compared to Class 1. ACPA positivity also increased the risk of LOR with HR of 2.13 and 95% CI 1.04-4.37, *p* = 0.04 (n. of event = 78/117) compared to seronegative patients (n. of event = 9/18).

Conclusion: In seropositive RA patients treated with TNFi, a reduction of total monocyte count in the first year was associated with maintenance of remission in subsequent years. Further studies are required to determine whether these effects are specific to TNFi or reflect sustained remission in RA irrespective of therapy.

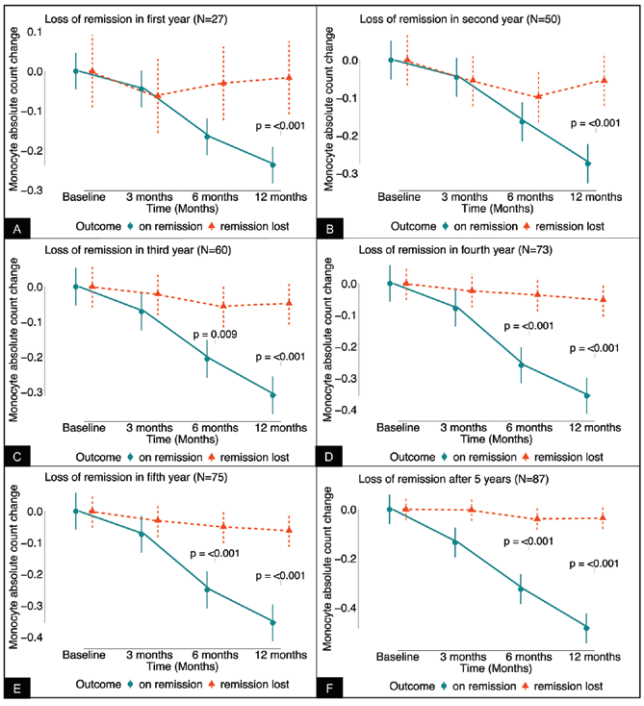


Figure 1 (A-F). Mean change (with 95% confidence interval) in absolute count of monocyte after initiation of tumour necrosis factor inhibitor grouped by years of follow-up and stratified by loss of remission. N = number indicate cumulative number of patients who lost remission by the end of each year.

Acknowledgements: Muhammad Shipa is funded by Versus Arthritis. Su-Ann Yeoh is funded by the Royal College of Physicians, Rosetrees Trust, NIHR University College London Hospitals Biomedical Research Centre, UCLH Charities, and Versus Arthritis. Michael Ehrenstein is supported (in part) by the University College London Hospital Biomedical Research Centre. None of the funding bodies have been involved in preparation of this manuscript.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.312

POS0441 DEVELOPMENT OF RHEUMATOID ARTHRITIS AMONG ANTI-CITRULLINATED PROTEIN ANTIBODIES POSITIVE ASYMPTOMATIC INDIVIDUALS: A PROSPECTIVE OBSERVATIONAL STUDY

S. Mizuki[1], K. Horie[1], K. Imabayashi[1], K. Mishima[2], K. Oryoji[1]. [1]*Matsuyama Red Cross Hospital,The Center for Rheumatic Diseases, Matsuyama, Japan*; [1]*Matsuyama Red Cross Hospital,The Center for Rheumatic Diseases, Matsuyama, Japan*

Background: In the idividuals with genetic and enviromental risk factors, immune events at mucosal surfaces occur and may precede systemic autoimmunity. Anti-citrullinated protein antibodies (ACPA) are present in the serum for an average of 3-5 years prior to the onset of rheumatoid arthritis (RA) during an asymptomatic period. In ACPA-positivite individuals, the additional presence of RA-related risk factors appears to add significant power for the development of RA. To date, there have been few reports in which clinical courses of ACPA-positive asymptomatic individuals were investigated prospectively.

Objectives: To observe the clinical time course of ACPA-positive healthy population for the development of RA.

Methods: Healthy volunteers without joint pain or stiffness, who attended the comprehensive health screening of our hospital, were enrolled in this prospective observational study. The serum ACPA levels were quantified by Ig-G anti-cyclic citrullinated peptide enzyme-linked immunosorbent assay with levels > 4.4 U/mL considered positive. ACPA-positive subjects were followed by rheumatologists of our department clinically or a questionnaire sent by mail for screening to detect arthritis.

Results: 5,971 healthy individuals without joint symptons were included. Ninty-two (1.5%) were positive for ACPA. Of these, 19 (20.7%) developed RA and two were suspected as RA by mail questionnaire. Their average age were 58-years, and women were 68%. The average duration between the date of serum sampling and diagnosis was 10.7 months. ACPA-positive individuals who developed to RA had higher serum ACPA and Ig-M rheumatoid factor levels than ACPA-positive individuals who did not (P value by Mann-Whitney U test: 0.002, 0.005, respectively).

Conclusion: Among ACPA-positive asymptomatic individuals, 20% developed RA. The higher titer of ACPA and Ig-M rheumatoid factor levels are risk factors for devoloping RA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.344

POS0442 RELATIONSHIP BETWEEN PARAOXONASE-1 GENOTYPE, ACTIVITY AND MAJOR ADVERSE CARDIOVASCULAR EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOFACITINIB

C. Charles-Schoeman[1], C. Hyde[2], S. Guan[3], N. Parikh[1], J. Wang[1], A. Shahbazian[1], L. Stockert[4], J. Andrews[4]. [1]*University of California, Department of Medicine, Los Angeles, CA, United States of America*; [2]*Pfizer Inc, Inflammation and Immunology, Groton, CT, United States of America*; [3]*Pfizer Inc, Inflammation and Immunology, Cambridge, MA, United States of America*; [4]*Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America*

Background: Paraoxonase-1 (PON1) is a high-density lipoprotein (HDL)-associated enzyme with paraoxonase, lactonase and arylesterase activities.[1] PON1 contributes to the antioxidant properties of HDL, and is being investigated for its atheroprotective properties.[1] Patients (pts) with rheumatoid arthritis (RA) who are homozygous for the RR genotype of the Q192R gene polymorphism on PON1 (rs662) have increased paraoxonase activity, and lower risk of carotid plaques, vs those with QQ or QR genotypes.[2] Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA.

Objectives: To investigate the relationship between PON1 genotype/activity and risk of major adverse cardiovascular events (MACE) in the tofacitinib RA clinical programme.

Methods: In this post hoc analysis, data were pooled from pts enrolled in nine Phase 2/3 studies of tofacitinib in RA. Enzyme activities in pt plasma samples were measured at individual study baseline (BL) and at follow-up visits using three substrates: paraoxon (paraoxonase activity), dihydrocoumarin (lactonase activity) and phenylacetate (arylesterase activity). The effect of the PON1 Q192R genotype (QQ, QR or RR) on BL paraoxonase/lactonase/arylesterase activity was assessed using linear regression for each study, with age and sex as covariates, and then fixed-effect meta-analysis assessed effects across studies. The risk of MACE by enzyme activity was determined using Cox proportional hazards regression stratified by clinical studies. Univariate regression against BL enzyme activity and other risk factors, as well as both minimally and fully adjusted multivariable regressions against time-varying enzyme activity, are presented.

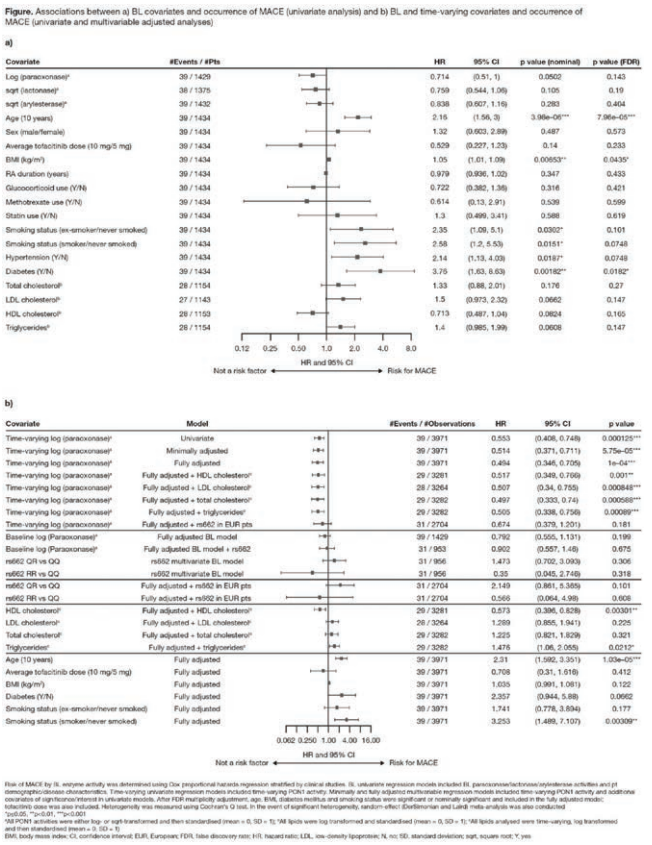
Results: The analysis included 1969 pts with RA who received ≥1 dose of tofacitinib and had PON1 activity measures available at BL; 39 pts had ≥1

MACE event. Compared with the QQ genotype, the RR genotype had a highly significant positive association with BL paraoxonase activity, and a highly significant negative association with BL lactonase and arylesterase activity (Table 1). A univariate analysis identified several BL covariates significantly associated with risk of MACE (Figure 1a). Time-varying models found a highly significant association of increased paraoxonase activity over time with lower risk of future MACE, even after controlling for low-density lipoprotein or HDL cholesterol levels, and other traditional cardiovascular (CV) risk factors identified in univariate analysis (Figure 1b), with similar findings for lactonase and arylesterase (data not shown).

Table 1. Effect of PON1 genotype (RR vs QQ) on BL enzyme activity

	n	Estimate	95% CI	p value	Cochran's Q test
Paraoxonase	1229	1.035	0.93, 1.141	<0.0001	0.209
Lactonase	1188	-0.375	-0.505, -0.246	<0.0001	0.025
Arylesterase	1231	-1.016	-1.382, -0.649	<0.0001	0.251

Fixed-effects model; estimate >0 favours RR genotype and <0 favours QQ genotypeBL, baseline; CI, confidence interval



Conclusion: Higher activity of the HDL-associated protein PON1 over time was associated with a significantly reduced risk of future MACE in pts with RA receiving tofacitinib, after controlling for traditional CV risk factors and cholesterol levels. Further investigation of PON1 as a novel functional lipid biomarker to assess CV risk in pts with RA is warranted.

REFERENCES:

[1] Mackness & Mackness. Gene 2015; 567: 12-21.
[2] Charles-Schoeman et al. Arthritis Rheum 2013; 65: 2765-2772.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Jennifer Higginson, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: Christina Charles-Schoeman Consultant of: AbbVie, Gilead, Pfizer Inc, Regeneron-Sanofi, Grant/research support from: AbbVie, Bristol-Myers Squibb, Pfizer Inc, Craig Hyde Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Shunjie Guan Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Neil Parikh: None declared, Jennifer Wang: None declared, Ani Shahbazian: None declared, Lori Stockert Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, John Andrews Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2021-eular.363

POS0443 EXPLORING NOVEL TENOSYNOVITIS AND COMBINED INFLAMMATION IMAGING OUTCOMES: RESULTS FROM A RANDOMISED CONTROLLED TRIAL IN EARLY RHEUMATOID ARTHRITIS

P. G. Conaghan[1,2], M. Østergaard[3,4], O. Troum[5], Z. Xie[6], A. Brett[7], M. Snyder[8], A. Ebrahim[8], D. Chapman[9], G. Sawyerr[9], J. Andrews[8]. *[1]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[2]National Institute for Health Research Leeds Biomedical Research Centre, Leeds, United Kingdom*; *[3]Rigshospitalet, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Glostrup, Denmark*; *[4]University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark*; *[5]University of Southern California Keck School of Medicine, Division of Rheumatology, Santa Monica, CA, United States of America*; *[6]Pfizer Inc, Inflammation and Immunology, Groton, CT, United States of America*; *[7]Imorphics Ltd, Clinical Trials Group, Manchester, United Kingdom*; *[8]Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America*; *[9]Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*

Background: Magnetic resonance imaging (MRI) trial outcomes have largely focused on synovitis, bone marrow oedema (BME) and erosions. Tenosynovitis is a common manifestation of rheumatoid arthritis (RA), but is relatively understudied; a combined inflammation score (CIS) summing synovitis, BME and tenosynovitis may be a highly responsive measure. We previously showed the responsiveness of the Outcome Measures in Rheumatology (OMERACT) RA MRI scoring system (RAMRIS) and a machine-learning derived automated tool (RAMRIQ) in a randomised controlled trial (RCT) of tofacitinib and methotrexate (MTX) in MTX-naïve patients (pts) with early RA.[1]

Objectives: This post hoc analysis assessed the impact of tofacitinib ± MTX on MRI tenosynovitis and CIS in pts with early RA using semiquantitative and quantitative MRI outcomes.

Methods: Study A3921068 (NCT01164579), a 1-year, exploratory, Phase 2, RCT, compared tofacitinib 10 mg twice daily (BID) ± MTX, and MTX monotherapy, in MTX-naïve pts with early RA.[1] MRI of unilateral wrist and metacarpophalangeal joints was performed at screening/baseline (BL) and Months (M)1/3/6/12. MRI tenosynovitis and CIS were assessed using RAMRIS and RAMRIQ. Changes from BL (Δ) in RAMRIS and RAMRIQ tenosynovitis and CIS were evaluated at M1/3/6/12. Data were assessed using a mixed-effect model for repeated measures, with treatment arms as factors and BL values as covariates. Using data pooled across treatment arms, Spearman's rank correlation coefficients were calculated for associations between BL RAMRIS and BL RAMRIQ tenosynovitis and CIS vs BL Disease Activity Score in 28 joints, C-reactive protein (DAS28-4[CRP]), and ΔRAMRIS and ΔRAMRIQ tenosynovitis and CIS at M12 vs ΔDAS28-4(CRP) at M12.

Results: In total, 109 pts were randomised and treated. ΔRAMRIS and ΔRAMRIQ tenosynovitis and CIS were generally significantly greater at M3/6/12 in pts receiving tofacitinib ± MTX vs MTX, while ΔRAMRIQ CIS was also significantly greater at M1 (Figure 1). Compared with RAMRIS, RAMRIQ outcomes were generally more responsive to treatment with tofacitinib ± MTX. Significant correlations were seen between BL RAMRIS and BL RAMRIQ tenosynovitis and BL RAMRIS CIS vs BL DAS28-4(CRP), and between ΔRAMRIS and ΔRAMRIQ tenosynovitis and CIS at M12 vs ΔDAS28-4(CRP) at M12 (Table 1). In general, stronger correlations were seen between BL DAS28-4(CRP) and BL RAMRIS vs BL RAMRIQ parameters, while correlations were similar between ΔDAS28-4(CRP) at M12 and ΔRAMRIS and ΔRAMRIQ parameters at M12.

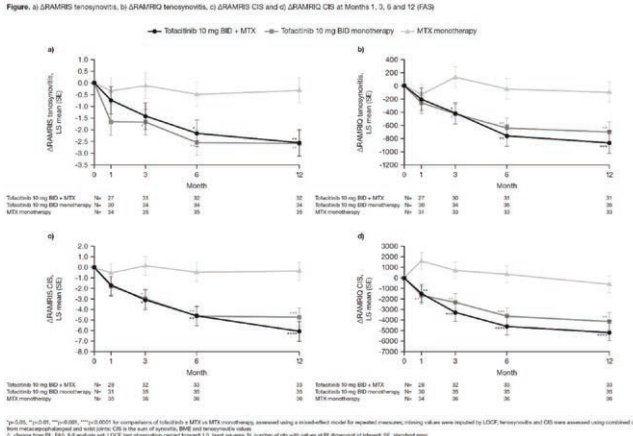


Table 1. Correlations between a) BL RAMRIS and BL RAMRIQ tenosynovitis and CIS vs BL DAS28-4(CRP) (N=109) and b) ΔRAMRIS and ΔRAMRIQ tenosynovitis and CIS at M12 vs ΔDAS28-4(CRP) at M12 (N=73) across treatment arms[a]

a)	BL DAS28-4(CRP)		b)	ΔDAS28-4(CRP)	
BL imaging feature	Correlation	p value	ΔImaging feature	Correlation	p value
RAMRIS tenosynovitis	0.366	0.0001	RAMRIS tenosynovitis	0.531	<0.0001
RAMRIS CIS	0.399	<0.0001	RAMRIS CIS	0.554	<0.0001
RAMRIQ tenosynovitis	0.205	0.037	RAMRIQ tenosynovitis	0.543	<0.0001
RAMRIQ CIS	0.180	0.062	RAMRIQ CIS	0.564	<0.0001

[a]Data were pooled across the tofacitinib 10 mg BID ± MTX and MTX monotherapy armsSpearman's rank correlation coefficients and p values were calculated for associations between RAMRIS and RAMRIQ parameters and DAS28-4(CRP); tenosynovitis and CIS were assessed using combined data from metacarpophalangeal and wrist joints; CIS is the sum of synovitis, BME and tenosynovitis valuesΔ, change from BL; N, number of pts with values at BL/timepoint of interest

Conclusion: Responsiveness of RAMRIS and RAMRIQ tenosynovitis and CIS was demonstrated with significant improvements through M12 in pts receiving tofacitinib 10 mg BID ± MTX vs MTX. Construct validity for RAMRIS and RAMRIQ tenosynovitis and CIS was evident from correlations with DAS28-4(CRP). Further work is needed to validate these novel imaging biomarkers in terms of relative responsiveness and prediction of later structural progression.

REFERENCES:

[1] Conaghan et al. Ann Rheum Dis 2016; 75: 1024-1033.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Jennifer Arnold, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: Philip G Conaghan Speakers bureau: AbbVie, Novartis, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Flexion, Galapagos, Gilead Sciences, GlaxoSmithKline, Janssen, Novartis, Pfizer Inc, Regeneron, Mikkel Østergaard Speakers bureau: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Eli Lilly, GlaxoSmithKline, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer Inc, Regeneron, Roche, Schering-Plough, Takeda, UCB, Wyeth, Consultant of: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Eli Lilly, GlaxoSmithKline, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer Inc, Regeneron, Roche, Schering-Plough, Takeda, UCB, Wyeth, Grant/research support from: AbbVie, Centocor, Merck, Orrin Troum Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Horizon, Novartis, Pfizer Inc, Sanofi-Genzyme, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Horizon, Pfizer Inc, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Centocor, Corrona, Novartis, Pfizer Inc, Zhiyong Xie Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Alan Brett Shareholder of: Stryker Corp, Employee of: Stryker Corp, Mark Snyder Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Abbas Ebrahim Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Douglass Chapman Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Gosford Sawyerr Consultant of: Pfizer Inc, Employee of: Syneos Health, John Andrews Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2021-eular.364

POS0444

DIAGNOSTIC VALUE OF HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY COMPARED TO CONVENTIONAL RADIOGRAPHY FOR DETECTING EROSIVE DISEASE IN RHEUMATOID ARTHRITIS

R. Klose-Jensen[1,2], J. Therkildsen[1,2], A. B. Blavnsfeldt[1], B. Langdahl[3], K. K. Keller[2], E. M. Hauge[1,2]. [1]*Aarhus University Hospital, Department of Rheumatology, Aarhus N, Denmark*; [2]*Aarhus University, Department of Clinical Medicine, Aarhus N, Denmark*; [3]*Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus N, Denmark*

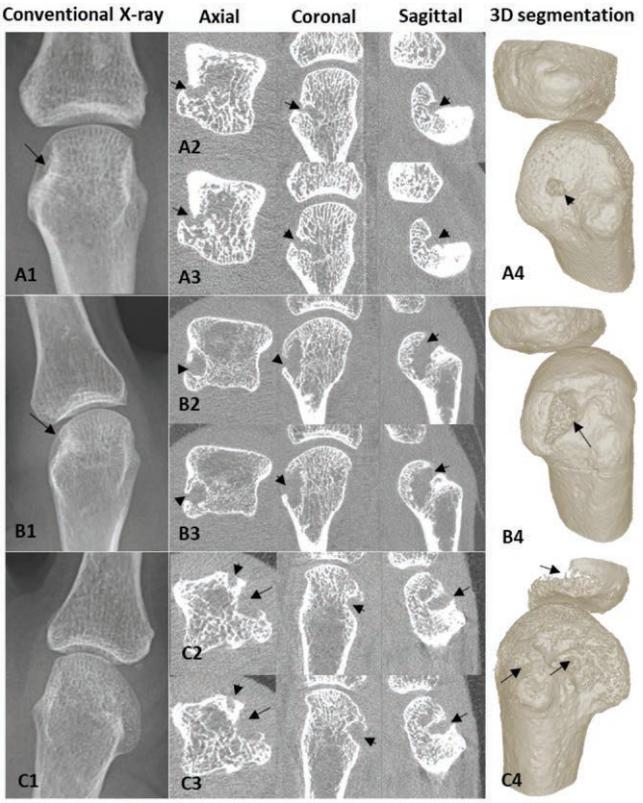
Background: Conventional radiography (CR) of the hands, wrists and feet is currently the gold standard for assessing erosive damage in patients with rheumatoid arthritis (RA). However, CR is prone to relatively low resolution and projection superimposition due to 2-dimensional imaging. Therefore, CR might not detect erosive disease in RA patients. High-resolution peripheral quantitative computed tomography (HR-pQCT) is an imaging modality with superior resolution (82µm^3) to all other imaging modalities in vivo. However, HR-pQCT imaging is limited by a smaller field of view. Therefore, it needs to be illuminated, whether the higher resolution of HR-pQCT imaging is sufficient for diagnosing erosive disease in patients with RA despite the limited field of view.

Objectives: The objective was to investigate whether High-Resolution peripheral Quantitative Computed Tomography (HR-pQCT) of just two metacarpophalangeal (MCP) joints can diagnose more patients having erosive RA than conventional radiography (CR) of 44 joints in the hands, wrist and feet.

Methods: In this single-centre cross-sectional study. Patients with established RA (disease duration ≥ 5 years) were investigated by HR-pQCT and CR. The second and third MCP joints of the dominant hand were assessed for erosions by HR-pQCT. CR in the hands, wrist and feet were scored according to the Sharp/van der Heijde (SHS) method.

Results: Three hundred fifty-four patients were included. By CR, 67 (18.9%) patients were classified with non-erosive RA, and 287 (81.1%) with erosive RA. In the 67 patients with non-erosive RA, 47 patients (70.1%) had erosions in the second and third MCP joints by HR-pQCT (Figure 1). We found an agreement between CR and HR-pQCT for 274 (77.4%) of the patients. The sensitivity and specificity (95%CI) of HR-pQCT for diagnosing erosive RA when CR of hands, wrist and feet were used as the reference was 89% (84 – 92) % and 30% (19 – 42) %, respectively. Using HR-pQCT for two MCP joints as the reference, the sensitivity and specificity of CR of hands, wrist and feet for diagnosing erosive RA were 84% (80 – 88) % and 38% (25 – 52) %, respectively. The McNemar's χ^2 test for diagnosing patients having erosive RA between the two modalities was 2.45, p = 0.146.

Conclusion: HR-pQCT imaging identifies erosions which are not seen by CR. Using HR-pQCT at of the second and third MCP joint reclassified a substantial number of patients as having erosive RA compared to their non-erosive state determined by CR. The sensitivity and specificity of diagnosing patients having erosive RA using HR-pQCT from only two fingers were not statistically different from CR of 44 joints, in the hands, wrist and feet.



Acknowledgements: The authors, we want to acknowledge Aarhus University, The Danish Rheumatism Association, Novo Nordic Foundation and A.P. Møller Fonden who have financially supported the study. The funding sources did not have any role in the collection, analysis and interpretation of data. The authors are grateful for the excellent assistance in recruiting and scheduling the patients by Mia Marie Remmer, Lone Thomasen and Else Sloth Rousing.

Disclosure of Interests: Rasmus Klose-Jensen: None declared, Josephine Therkildsen: None declared, Anne-Birgitte Blavnsfeldt: None declared, Bente

Langdahl Speakers bureau: Eli Lilly, Amgen, UCB, Gilead, and Gideon-Richter, Grant/research support from: Novo Nordisk and Amgen, Kresten Krarup Keller: None declared, Ellen-Margrethe Hauge Speakers bureau: MSD, Pfizer, UCB, and Sobi., Grant/research support from: Roche, Novartis and Novo Nordic Foundation.

DOI: 10.1136/annrheumdis-2021-eular.519

POS0445 PHYSICIAN AND PATIENT REPORTED EFFECTIVENESS OUTCOMES ARE SIMILAR IN TOFACITINIB AND TNF INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS: DATA FROM A RHEUMATOID ARTHRITIS REGISTRY IN CANADA

M. Movahedi[1], A. Cesta[1], X. Li[1], E. Keystone[2], C. Bombardier[1]on behalf of OBRI investigators. *[1] UHN, Toronto General Hospital Research Institute, Toronto, Canada*; *[2]University of Toronto, Medicine, Toronto, Canada*

Background: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment as an alternative option to biologic disease modifying antirheumatic drugs (bDMARDs) including tumor necrosis factor inhibitors (TNFi).

Objectives: We aimed to evaluate physician and patient reported effectivness outcomes in TNFi compared to TOFA, using real-world data from the Ontario Best Practices Research Initiative (OBRI).

Methods: RA patients enrolled in the OBRI initiating their TOFA or TNFi (Adalimumab, Certolizumab, Etanercept, Golimumab, Infliximab, and Biosimilars) between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Patients were required to have physician and patient reported effectivness outcomes data available at treatment initiation and 6-month (± 2 months) follow-up. These included clinical disease activity index (CDAI), rheumatoid arthritis disease activity index (RADAI), HAQ-DI, sleep problem, and anxiety/depression scores. Multiple imputation (Imputation Chained Equation, N=20) was used to deal with missing data for covaraites at treatment initiation. To deal with confounding by indication, we estimated propensity scores for covariates with an absolute standard difference greater than 0.1 between the two treatment groups.

Results: A total of 419 patients were included. Of those, 226 were initiating a TNFi and 193 TOFA, and had a mean (SD) disease duration of 8.0 (8.7) and 12.6 (9.6) years, respectively. In the TNFi group, 81.9% were female and mean age (SD) at treatment initiation was 56.6 (13.4) years. In the TOFA group, 85% were female and mean (SD) age at treatment initiation was 60.3 (11.2) years. The TNFi group was less likely to have prior biologic use (21.7%) compared to the TOFA group (67.9%). At treatment initiation, physical function measured by HAQ-DI was significantly lower in TNFi compared to the TOFA group (1.2 vs.1.4).

The rate of CDAI LDA/remission at 6 months was 36.7% and 33.2% in TNFi and TOFA group, respectively. The generalized linear mixed models (GLMM) adjusting for propensity score quantile, showed that there was no significant difference in CDAI LDA/remission (ORs: 0.85, 95% CI: 0.51, 1.43), RADAI (coefficient: 0.48, 95% CI: -0.18, 1.14), HAQ-DI (coefficient: -0.01, 95% CI: -0.18, 0.16), sleep problems (coefficient: -0.25, 95% CI: -0.95, 0.45), and anxiety/depression scores (coefficient: 0.12, 95% CI: -0.35, 0.58) between the two treatment groups (TOFA used as reference).

Conclusion: In this real-world data study, we found that, physician and patient reported effectivness outcomes are similar in the TNFi and TOFA groups 6 months after treatment initiation in patients with RA.

Disclosure of Interests: Mohammad Movahedi: None declared, Angela Cesta: None declared, Xiuying Li: None declared, Edward Keystone Grant/research support from: Amgen, Merck, Pfizer Pharmaceuticals, PuraPharm. Speaker Honoraria Agreements: AbbVie, Amgen, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis. Consulting Agreements/Advisory Board Membership: AbbVie, Amgen, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis, Claire Bombardier Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Aurora, Bristol-Meyers Squibb, Celgene, Hospira, Janssen, Lilly, Medexus, Merck, Novartis, Pfizer, Roche, Sanofi, & UCB. Dr. Bombardier held a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology

DOI: 10.1136/annrheumdis-2021-eular.787

POS0446 FILGOTINIB-TREATED RHEUMATOID ARTHRITIS PATIENTS WITH HIGH BASELINE NEUTROPHIL-TO-LYMPHOCYTE RATIO SHOW BETTER CLINICAL RESPONSE RATES AND PATIENT-REPORTED OUTCOMES

P. C. Taylor[1], B. Downie[2], S. Kim[2], R. Hawtin[2], R. Moots[3], T. Takeuchi[4]. *[1]University of Oxford, Botnar Research Centre, Nuffield Dept Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; *[2]Gilead Sciences, Inc., Foster City, United States of America*; *[3]Edge Hill University, Faculty of Health, Social Care and Medicine, Ormskirk, United Kingdom*; *[4]Keio University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan*

Background: Rheumatoid arthritis (RA) is a systemic inflammatory disease which includes increased innate and myeloid immune cell activation. Filgotinib (FIL), an oral JAK1 inhibitor, has shown safety and efficacy in three phase 3 studies (FINCH1-3) in adults with moderately-to-severely active RA. The baseline (BL) neutrophil-to-lymphocyte ratio (NLR) in RA has been associated with a positive response to anti-tumor necrosis factor (TNF) therapy[1] and a negative response to DMARD triple therapy[2]. We previously reported a BL signature of clinical response in the FINCH2 (bDMARD-IR) population which included a neutrophil component[3].

Objectives: We conducted a post-hoc analysis to explore whether the BL NLR was associated with response to treatment in the FINCH studies.

Methods: Clinical data of 3273 RA patients (pts) enrolled in the FINCH clinical trials (FINCH3, methotrexate (MTX)-naïve: NCT02886728; FINCH1, MTX-Inadequate Responder (IR): NCT02889796; FINCH2, bDMARD-IR: NCT02873936) were retrospectively analyzed for a relationship between the BL NLR and composite clinical endpoints (ACR-N, DAS28CRP, or CDAI) or PROs (Pain VAS, FACIT Fatigue, HAQ-DI) through week 24. Pts were classified as High or Low BL NLR using a cutpoint (2.7) identified as an independent predictor of treatment failure in a published RA study[2]. Adjusted clinical outcomes were estimated based on mixed effects linear regression models including geographic region and demographics covariates.

Results: 57% of pts enrolled in the FINCH trials were classified as BL NLR-High (Table 1) and FINCH3 NLR-High pts showed higher BL DAS28(CRP). FINCH1 and FINCH3 FIL+MTX-arm NLR-High pts demonstrated significantly better DAS28(CRP) response compared to NLR-Low pts (Figure 1). DAS28(CRP) differences between NLR-High and NLR-Low were detectable as early as Week 2 for FIL200mg + MTX and were sustained through Week 24. FINCH1 and FINCH3 FIL200mg + MTX NLR-High pts also demonstrated sustained clinical and PRO improvements over NLR-Low, including CDAI, ACR-N, Pain VAS, FACIT Fatigue, and HAQ-DI. The strength of these associations was dose-dependent; pts that received FIL100mg + MTX demonstrated weaker but directionally consistent trends in both populations. No significant association between NLR subgroup and clinical efficacy was observed in FINCH2 FIL+MTX-arm pts, FIL-monotherapy (FINCH3) pts, or adalimumab+MTX (FINCH1) pts.

Conclusion: In FINCH1 (MTX-IR) and FINCH3 (MTX-naïve), FIL200mg + MTX -arm NLR-High pts demonstrate better sustained clinical response and PRO scores compared to NLR-Low pts. These data are the first to report an association between the BL NLR and therapeutic response in large randomized RA clinical trials. Future studies on pathobiologies reflected by the NLR biomarker may clarify its potential to guide RA disease management.

REFERENCES:

[1] Farutin V. Arthritis Res Ther. 2019.
[2] Boulos D. Semin Arthritis Rheum. 2019.
[3] Taylor P. Arthritis Rheumatol. 2019; 71 (suppl 10).

Table 1. Demographics of patients enrolled in FINCH clinical trials by baseline NLR category.

	NLR-Low (NLR < 2.7) (N=1407, 43%)	NLR-High (NLR > 2.7) (N=1866, 57%)	Total (N=3273, 100%)	P-value
Age at enrollment				0.668[2]
Mean (SD)	53.00 (12.74)	53.19 (13.24)	53.11 (13.02)	
Female	1,157 (82.2%)	1,448 (77.6%)	2,605 (79.6%)	0.001[1]
Seropositivity	1,073 (76.3%)	1,575 (84.4%)	2,648 (80.9%)	< 0.001[1]
Prior bDMARD #				
Mean (SD)	0.23 (0.73)	0.28 (0.82)	0.26 (0.78)	0.037[2]
Duration of RA				
Mean (SD)	5.93 (7.39)	6.61 (8.07)	6.32 (7.79)	0.013[2]
Baseline oral corticosteroid	537 (38.2%)	895 (48.0%)	1,432 (43.8%)	< 0.001[1]
Baseline DAS28(CRP)	5.55 (0.90)	5.89 (0.97)	5.74 (0.95)	0.001[2]
Baseline HAQ-DI	1.53 (0.60)	1.62 (0.65)	1.58 (0.63)	0.001[2]

[1]Pearson's Chi-squared test. [2]Linear Model ANOVA.

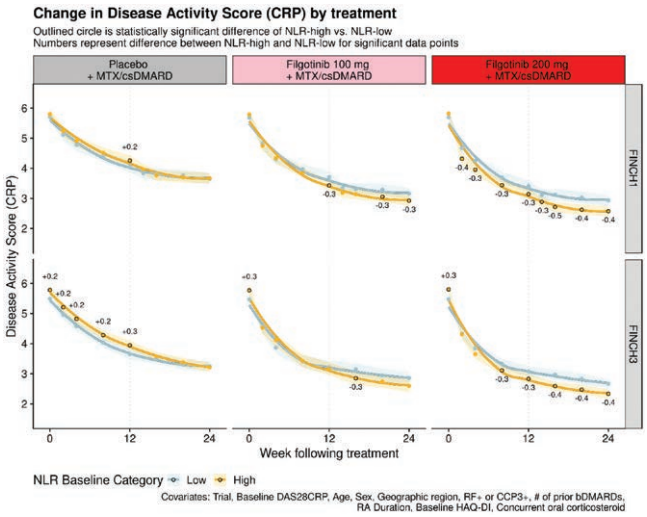


Figure 1. Association of BL NLR with DAS28(CRP). Dots represent DAS28(CRP) estimate from a fully adjusted mixed-effects model, shaded area shows the 95% confidence interval. Outlined circles and proximal text show significantly different values between NLR-High and NLR-Low.

Disclosure of Interests: Peter C. Taylor Consultant of: AbbVie, Biogen, Galapagos, Gilead, GlaxoSmithKline, Janssen, Lilly, BMS, Pfizer, Roche, Celltrion, Sanofi, Nordic Pharma, Fresenius and UCB, Grant/research support from: Celgene, Galapagos, Gilead, Lilly., Bryan Downie Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Sam Kim Shareholder of: Gilead Science, Employee of: Gilead Sciences, Rachael Hawtin Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Robert Moots Speakers bureau: Amgen, Chugai, Gilead, Libbs, Pfizer, Roche, Consultant of: Amgen, Chugai, Novartis, Pfizer, Roche, Grant/research support from: AKL, Novartis, UCB Pharma, Tsutomu Takeuchi Speakers bureau: AbbVie, Eisai Co. Gilead Sciences, Sanofi K.K. Mitsubishi-Tanabe Pharma Corp. Chugai Pharmaceutical Co, Ltd., Eli Lilly Japan,Novartis., Bristol-Myers Squibb., Janssen Pharmaceutical K.K., Consultant of: Astellas Pharma, Inc. AbbVie, Gilead Sciences, Eli Lilly Japan, Novartis, Mitsubishi-Tanabe Pharma Corp. Chugai Pharmaceutical Co, Ltd. Pfizer Japan Inc. Janssen Pharmaceutical K.K., Grant/research support from: Asahikasei Pharma Corp.AbbVie, AYUMI Pharmaceutical Co. Eisai Co., ONO Pharmaceutical Co,LTD.,Sanofi K.K. Mitsubishi-Tanabe, Daiichi Sankyo Co., Chugai Pharmaceutical Co, Ltd. Eli Lilly Japan, Nippon Boehringer Ingelheim Co., Ltd.,UCB JAPAN, DNA Chip Research Inc.

DOI: 10.1136/annrheumdis-2021-eular.850

POS0447

PHYSICAL FUNCTION IN PATIENTS WITH RA, STRATIFIED BY SEROSTATUS AND TREATMENT LINE, FOLLOWING SC ABATACEPT: POST HOC ANALYSIS OF AN OBSERVATIONAL, 2-YEAR STUDY CONDUCTED IN ROUTINE CLINICAL PRACTICE (ASCORE)

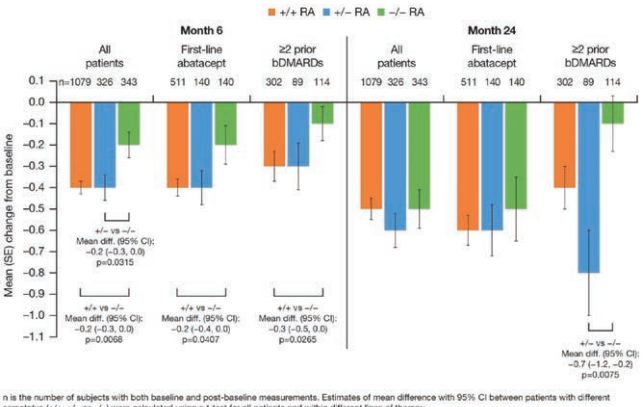
R. Alten[1], X. Mariette[2], R. M. Flipo[3], R. Caporali[4,5], M. H. Buch[6,7], Y. Patel[8], S. Marsal[9], M. T. Nurmohamed[10], H. Griffiths[11], P. Peichl[12], B. Bannert[13], A. Forster[14], M. Chartier[15], Y. Elbez[16], C. Rauch[17], K. Lozenski[18], V. Khaychuk[19].
[1]Schlosspark-Klinik University, Department of Internal Medicine, Rheumatology, Berlin, Germany; *[2]Université Paris-Saclay, AP-HP, Hospital Bicêtre, Department of Rheumatology, Paris, France*; *[3]Centre Hospitalier Universitaire de France, Department of Rheumatology, Lille, France*; *[4]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy*; *[5]G. Pini Hospital, Clinical Rheumatology Unit, Milan, Italy*; *[6]University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[7]University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; *[8]Hull Royal Infirmary, Department of Rheumatology, Hull, United Kingdom*; *[9]Hospital Universitari Vall d'Hebron, Rheumatology, Barcelona, Spain*; *[10]ARC Amsterdam University Hospitals – VU University Medical & Reade, Department of Rheumatology, Amsterdam, Netherlands*; *[11]University Hospital Geelong, Barwon Rheumatology Service, Geelong, Australia*; *[12]Evangelical Hospital, Department of Internal Medicine, Vienna, Austria*; *[13]Universitätsspital Basel, Rheumatologische Universitätsklinik, Basel, Switzerland*; *[14]Schulthess Klinik, Department of Rheumatology, Zürich, Switzerland*; *[15]Bristol Myers Squibb, Non-Registrational Data Generation, Rueil-Malmaison, France*; *[16]Deepscover, Biostatistics, Puteaux, France*; *[17]Bristol Myers Squibb, Medical Immunology & Fibrosis, Munich, Germany*; *[18]Bristol Myers Squibb, Immunology and Fibrosis, Princeton, United States of America*; *[19]Bristol Myers Squibb, US Medical Immunology and Fibrosis, Princeton, United States of America*

Background: RA is characterised by the production of autoantibodies, including RF and anti-citrullinated protein antibodies (ACPAs).[1] Seropositive disease is associated with poorer prognosis in patients with RA,[2] and response to different treatments has been shown to vary based on ACPA status.[3] ASCORE (Abatacept SubCutaneOus in Routine Clinical PracticE; NCT02090556) was a 2-year, observational, prospective, multicentre study of SC abatacept for the treatment of RA.[4]
Objectives: This *post hoc* analysis of the ASCORE study evaluated patient-reported outcomes, assessed using HAQ-DI, by RF/ACPA serostatus and treatment line over 24 months of treatment with abatacept.
Methods: Eligible patients, aged ≥18 years, with active moderate-to-severe RA (ACR/EULAR 2010 criteria) who were IV abatacept-naive and initiated SC abatacept 125 mg once weekly, were enrolled into two cohorts: biologic (b)DMARD-naive patients and those with ≥1 prior bDMARD treatment failure. This *post hoc* analysis assessed mean change from baseline in HAQ-DI score at 6, 12, 18 and 24 months in response to treatment with abatacept stratified by baseline serostatus (RF/ACPA double positive [+/+]; RF/ACPA single positive [+/–; RF+/ACPA– or RF–/ACPA+] or RF/ACPA double negative [–/–]) and by line of therapy (all patients, patients receiving abatacept as a first-line bDMARD or as a ≥ second-line bDMARD [data not shown], and those receiving abatacept following 1 [data not shown] or ≥2 prior bDMARDs). Estimates of mean difference with 95% CIs between patients with different serostatus were calculated using a *t*-test for all patients and within different lines of therapy.
Results: Among 2892 eligible patients in ASCORE, 1748 patients with RF/ACPA status available at baseline were included in this analysis (1079 +/+, 326 +/– and 343 –/–). Of these, 791 patients received abatacept as a first-line bDMARD therapy and 957 as a ≥ second-line bDMARD therapy (505 patients had received ≥2 prior bDMARDs). Among all patients, mean change from baseline in HAQ-DI score at 6 months was greater for patients with +/+ RA (mean difference [95% CI]: –0.2 [–0.3, –0.0]; p=0.0068) or +/– RA (mean difference [95% CI]: –0.2 [–0.3, –0.0]; p=0.0315) versus those with –/– RA at baseline (Figure 1). Similarly, mean change (95% CI) in HAQ-DI score at 6 months was greater for patients with +/+ RA versus –/– RA among those receiving abatacept as first-line therapy (–0.2 [–0.4, –0.0]; p=0.0407) or following treatment with ≥2 bDMARDs (–0.3 [–0.5, –0.0]; p=0.0265) (Figure 1). Among patients treated with abatacept following ≥2 prior bDMARDs, mean change in HAQ-DI score was higher among patients with +/– RA versus –/– RA at 18 months (data not shown) and 24 months (Figure 1). No other significant differences were observed by serostatus or line of therapy at any other time points.
Conclusion: Patients with RA who were RF+/ACPA+ at baseline showed an enhanced initial response to abatacept compared with those who were RF–/ACPA–. Over 24 months of treatment in this real-world setting, abatacept was equally effective as a first- or ≥ second-line therapy.

REFERENCES:

[1] Scott DL, et al. *Lancet* 2010;376:1094–1108.
[2] Hecht C, et al. *Ann Rheum Dis* 2015;74:2151–2156.
[3] Harrold LR, et al. *J Rheumatol* 2018;45:32–39.
[4] Alten R, et al. *Ann Rheum Dis* 2019;78(suppl 2):A1639.

Figure 1. Mean change from baseline in HAQ-DI score over 6 and 24 months by baseline RF and ACPA serostatus in all patients with RA receiving SC abatacept and by line of therapy



n is the number of subjects with both baseline and post-baseline measurements. Estimates of mean difference with 95% CI between patients with different serostatus (+/+, +/– or –/–) were calculated using a *t*-test for all patients and within different lines of therapy.
+/+=RF/ACPA double positive; +/–=RF/ACPA single positive (RF+/ACPA– or RF–/ACPA+); –/–=RF/ACPA double negative; ACPA=anti-citrullinated protein antibody; bDMARD=biologic DMARD.

Acknowledgements: Professional medical writing and editorial assistance was provided by Fiona Boswell, PhD, at Caudex and was funded by Bristol Myers Squibb. This study was funded by Bristol Myers Squibb.
Disclosure of Interests: Rieke Alten Speakers bureau: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Consultant of: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Grant/research support from: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Xavier Mariette Consultant of: Bristol Myers Squibb, Galapagos, Gilead, GlaxoSmithKline, Janssen, Pfizer, UCB, Rene-Marc Flipo Speakers bureau: AbbVie, Bristol Myers Squibb, Janssen, Lilly, Medac, Merck Sharp & Dohme, Novartis, Pfizer, Roche-Chugai, Grant/research support from: Amgen, Janssen, Novartis, Pfizer, Roberto Caporali Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Fresenius Kabi, Galapagos, Gilead, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Samsung Bioepis, Sanofi, UCB, Consultant of: Galapagos, Gilead, Janssen, Lilly, Merck Sharp & Dohme, Maya H Buch Speakers bureau: AbbVie, Consultant of: AbbVie, Eli Lilly, Gilead, Merck Serono, Pfizer, Roche, Sanofi, Grant/research support from: Gilead, Pfizer, Roche, UCB, Yusuf Patel: None declared, Sara Marsal Speakers bureau: Bristol Myers Squibb, Celgene, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol Myers Squibb, Celgene, Galapagos, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, UCB, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Sanofi, UCB, M.T. Nurmohamed Speakers bureau: AbbVie, Bristol Myers Squibb, Eli Lilly, Roche, Sanofi, Consultant of: AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Mundipharma, Novartis, Pfizer, Roche, Sanofi, Hedley Griffiths Consultant of: AbbVie, Gilead, Janssen, Novartis, Peter Peichl: None declared, Bettina Bannert: None declared, Adrian Forster: None declared, Melanie Chartier Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Yedid Elbez Consultant of: Bristol Myers Squibb, Christiane Rauch Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Karissa Lozenski Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Vadim Khaychuk Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb
DOI: 10.1136/annrheumdis-2021-eular.903

POS0448 DISCONTINUATION RATE OF TOFACITINIB AS MONOTHERAPY IS SIMILAR COMPARED TO COMBINATION THERAPY WITH METHOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS: POOLED DATA FROM TWO RHEUMATOID ARTHRITIS REGISTRIES IN CANADA

M. Movahedi[1], D. Choquette[2], L. Coupal[2], A. Cesta[1], X. Li[1], E. Keystone[3], C. Bombardier[1]on behalf of OBRI and RHUMADATA Investigators. [1]*UHN, Toronto General Hospital Research Institute,Toronto, Canada*; [2]*Institut de Rhumatologie de Montréal, RHUMADATA, Montreal, Canada*; [3]*University of Toronto, Medicine,Toronto, Canada*

Background: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). We previously reported the similarity in retention between TOFA monotherapy and TOFA with MTX using data from two different registries separately; the Ontario Best Practices Research Initiative (OBRI) and the Quebec registry RHUMADATA.
Objectives: To increase the study power, we propose to evaluate the discontinuation rate (due to any reason) of TOFA with and without MTX, using pooled data from these two registries.
Methods: RA patients enrolled in the OBRI and RHUMADATA initiating their TOFA between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Concurrent MTX use was defined as MTX use for more than 75% of the time while using TOFA. Multiple imputation (Imputation Chained Equation method, N=20) was used to deal with missing data for covariates at treatment initiation.
Time to discontinuation was assessed using Cox regression models. To deal with confounding by indication, we estimated propensity scores for selected covariates with an absolute standard difference greater than 0.1. We then adjusted Cox regression models for propensity quantile to compare the discontinuation of TOFA with MTX versus TOFA without MTX.
Results: A total of 493 patients were included. Of those, 244 (49.5%) and 249 (51.5%) were treated with MTX and without MTX, respectively. Compared to TOFA monotherapy, the TOFA with MTX group had a significantly lower mean HAQ-DI, fatigue score, and the number of prior biologic use at the time of TOFA initiation. A lower proportion of positive ACPA (59% vs. 66%), prevalence of hypertension (31% vs 37%), and concomitant use of Leflunomide (11% vs. 23%) were also observed for patients using TOFA with MTX.
Over a mean follow-up of 19.0 months, discontinuation was reported in 182 (36.9%) of all TOFA patients. After adjusting for propensity score quantile across 20 imputed datasets, there was no significant difference in discontinuation between treatment groups (adjusted HRs: 1.12, 95% CI: 0.83-1.51; p=0.49).
Conclusion: In this pooled real-world data study, we found that in patients with RA, the retention of TOFA is similar if it is used as monotherapy or in combination with MTX.
Disclosure of Interests: Movahedi: None declared, Denis Choquette Grant/research support from: Rhumadata is supported by unrestricted grants from Abbvie Canada, Amgen Canada, Eli Lilly Canada, Novartis Canada, Pfizer Canada, Sandoz Canada and Sanofi Canada., Louis Coupal: None declared, Angela Cesta: None declared, Xiuying Li: None declared, Edward Keystone Grant/research support from: Amgen, Merck, Pfizer Pharmaceuticals, PuraPharm. Speaker Honoraria Agreements: AbbVie, Amgen, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis. Consulting Agreements/Advisory Board Membership: AbbVie, Amgen, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis, Claire Bombardier Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Aurora, Bristol-Meyers Squibb, Celgene, Hospira, Janssen, Lilly, Medexus, Merck, Novartis, Pfizer, Roche, Sanofi, & UCB.
Acknowledgment: : Dr. Bombardier held a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology
DOI: 10.1136/annrheumdis-2021-eular.920

POS0449 BIOLOGICS INITIATION IN MODERATE VS SEVERE RHEUMATOID ARTHRITIS PATIENTS: PROSPECTIVE OBSERVATIONAL STUDY FROM A CANADIAN REGISTRY

N. Guo[1], X. Li[2], M. Movahedi[2], A. Cesta[2], C. Bombardier[2]on behalf of OBRI Investigators. [1]*Kingstone Health Sciences Centre, Health Science, Kingstone, Canada*; [2]*UHN,Toronto General Hospital Research Institute,Toronto, Canada*

Background: Prior studies have shown that in the real-world setting, rheumatoid arthritis (RA) patients have lower disease activity than those studied in clinical trials. However, randomized controlled trials for biologics continue to mainly recruit patients with severe disease.
Objectives: To assess the implications of this practice, our study investigates the proportion of patients achieving remission (DAS28-ESR ≤ 2.6), in RA patients with moderate disease activity and severe disease activity, at 12 months post starting their first biologic, and identifies baseline predictors of biologic response.
Methods: This study included RA patients who have never been treated with a biologic and initiated their first biologic while enrolled in the Ontario Best Practices Research Initiative (OBRI) registry, between 2008 and 2019. Patients selected had either moderate RA (DAS28 ≥ 3.2 to ≤ 5.1) or severe RA (DAS28 > 5.1). Comparisons were made between the moderate and severe disease groups using the student's t-test for continuous variables, and the chi-square test for categorical variables. Multivariable logistic regression was used to test potential predictors of remission. Backward stepwise model selection was applied to select variables with *p*-value ≤0.10. Multiple imputation (MCMC method; n=20) was used to impute missing data.
Results: Overall, 641 patients initiated their first biologic, 483 had follow up data at 12 months (moderate disease activity=264; severe disease activity=219). In the moderate group, the mean age (SD) was 55.7 (13.1) and 80% were female. In the severe group, mean age (SD) was 58.4 (12.3) and 81% were female. At time of biologic initiation, the mean DAS28 for the moderate group was 4.1 (0.5), and 6.0 (0.6) for the severe group. After 12 months of starting a biologic, the proportion of patients achieving remission was 50% in the moderate group, and 23% in the severe group ($p<0.0001$). In contrast, the proportion of patients achieving significant clinical change from baseline (improvement in DAS28 ≥ 1.2) was 78% in the severe group, compared to 66% in the moderate group ($p=0.0049$). More specifically, the absolute improvement in DAS28 after 12 months was higher in the severe group at 2.2 (1.5), compared to a change of 1.4 (1.3) in the moderate group ($p<0.0001$). Negative predictors of remission include female gender (odds ratio (OR), 0.57, 95% confidence interval (CI), 0.33-0.97; $p=0.039$), and higher HAQ-DI score (OR 0.49, 95% CI 0.36-0.68; $p<0.001$). In turn, moderate disease at time of biologic initiation (OR 2.38, 95% CI 1.50-3.79; $p=0.0390$) was identified as a positive predictor of remission.
Conclusion: This prospective cohort study found RA patients with moderate disease activity are more likely to reach targeted states (remission and low disease activity), whereas severe patients have greater absolute improvements in DAS28 and HAQ-DI but are less likely to achieve remission. Moderate disease is a positive predictor for remission, whereas female gender and a higher HAQ-DI score are negative predictors.

Table 1. Outcomes at 12 months among patients with RA who initiated the first biologic

	Moderate-RA (n=264)	Severe-RA (n=219)	*P*-Value
Remission, *n* (%)	111 (50)	45 (23)	<0.0001
Low disease activity, *n* (%)	151 (59)	74 (35)	<0.0001
Change in DAS from baseline ≥ 1.2, *n* (%)	168 (66)	164 (78)	0.0049
HAQ-DI change >0.22, *n* (%)	98 (53)	83 (52)	0.7974
Change in DAS28 from baseline, mean (SD)	-1.4 (1.3)	-2.2 (1.5)	<0.0001
Change in HAQ-DI from baseline, mean (SD)	-0.29 (0.57)	-0.30 (0.66)	<0.0001
Change in fatigue from baseline, mean (SD)	-0.98 (3.2)	-1.11 (3.2)	<0.0001
Change in sleep from baseline, mean (SD)	-0.85 (3.6)	-1.05 (3.9)	0.0004

Disclosure of Interests: Nancy Guo: None declared, Xiuying Li: None declared, Mohammad Movahedi: None declared, Angela Cesta: None declared, Claire Bombardier Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Aurora, Bristol-Meyers Squibb, Celgene, Hospira, Janssen, Lilly, Medexus, Merck, Novartis, Pfizer, Roche, Sanofi, & UCB.
Acknowledgment: : Dr. Bombardier held a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology
DOI: 10.1136/annrheumdis-2021-eular.1125

POS0450 INCIDENCE RATES OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS IN REAL-WORLD CLINICAL PRACTICE

Y. Hirano[1], J. Hasegawa[1], H. Kosugiyama[2], D. Kihira[2], K. Hattori[2]. [1]*Toyohashi Municipal Hospital, Rheumatology, Toyohashi, Japan*; [2]*Nagoya University Graduate School of Medicine, Orthopaedic Surgery and Rheumatology, Nagoya, Japan*

Background: A definition of difficult-to-treat rheumatoid arthritis (D2T RA) was recently proposed by the European League Against Rheumatism (EULAR) [1]. However, information on the incidence rates of D2T RA in real-world clinical practice is lacking.
Objectives: The aim of this retrospective cross-sectional study was to evaluate the incidence rates of D2T RA in clinical practice in Japan.
Methods: Data from the Toyohashi RA database (TRAD) was used. The TRAD is a collection of single-center retrospective data. Patients with RA who fulfilled the following three requirements were included in this study: (1) had been treated with >1 biological or targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD); (2) >1 year had passed since b/tsDMARD treatment was initiated; and (3) regularly visited our institute at the time of investigation. The number of targeted patients was 363. The criteria of D2T RA used in this study were modified from the EULAR definition for simplification of the investigation as follows: (a) ≥2 b/t DMARDs with different mechanisms of action had been administered; (b) at least moderate disease activity (DAS28-ESR > 3.2 or clinical disease activity index [CDAI] > 10) at the time of investigation; and (c) 7.5-mg/day of prednisolone (PSL) or more was administered at the time of investigation. In this study, D2T RA was defined as criteria (a) + (b) or (a) + (c) or (a) + (b) + (c). The 363 patients were categorized into four groups as follows: group A, DT2 RA; group B, patients with RA who had been treated with ≥2 b/tsDMARDs and did not fulfill the D2T RA definition; group C, RA patients who had been treated with one kind of b/tsDMARD with the same mechanism of action (e.g., two kinds of tumor necrosis factor inhibitors) and fulfilled either or both criteria (b) and (c); and group D, patients with RA who had been treated with one kind of b/tsDMARD with the same mechanism of action (e.g., a tumor necrosis factor inhibitors or two interleukin 6 inhibitors) and did not fulfill either or both criteria (b) and (c). The incidence rates of D2T RA were calculated, and the patients' characteristics at the time of initiation of the b/tsDMARD treatment were compared between the groups.
Results: The number of patients in groups A, B, C, and D were 34, 53, 94, and 182, respectively. Of all the patients included in this study, 9.4% were categorized into group A, those with D2T RA, and 39.1% were treated with ≥2 b/tsDMARDs and categorized into group A (Fig 1). The patients' characteristics were as follows (group A/B/C/D): mean age (57.1/54.3/61.4/56.2 years), RA duration (10.0/6.7/13.8/8.2 years), %Steinbrocker stage III+IV (%; 84.0/60.0/77.3/54.3), %Steinbrocker class 3+4 (%; 68.0/33.3/43.4/23.0), methotrexate (MTX) concomitant rate (%; 79.4/92.5/74.5/91.8), PSL concomitant rate (%; 91.2/52.8/55.3/43.4), DAS28-ESR score (5.5/5.0/5.5/4.7), and CDAI score (12.3/13.7/22.7/16.9). There were statistically significant differences in RA duration, %stage III+IV, %class 3+4 and PSL concomitant rate between group A and B.
Conclusion: D2T RA occurred in 9.4% of patients treated with b/tsDMARDs. Incidence rate was increased to 39.1% after the treatment with ≥2 b/tsDMARDs. The patients with D2T RA tended to be older, have a long RA duration, be treated without concomitant MTX, be treated with concomitant PSL, and have higher disease activity at the time of starting the b/tsDMARD treatment. The baseline patient characteristics in group C were similar to those in group A. In the future, we suggest that patients with D2T RA be included in group C.
REFERENCES:
[1] Nagy et al. Ann Rheum Dis 2021; 80: 31-35.

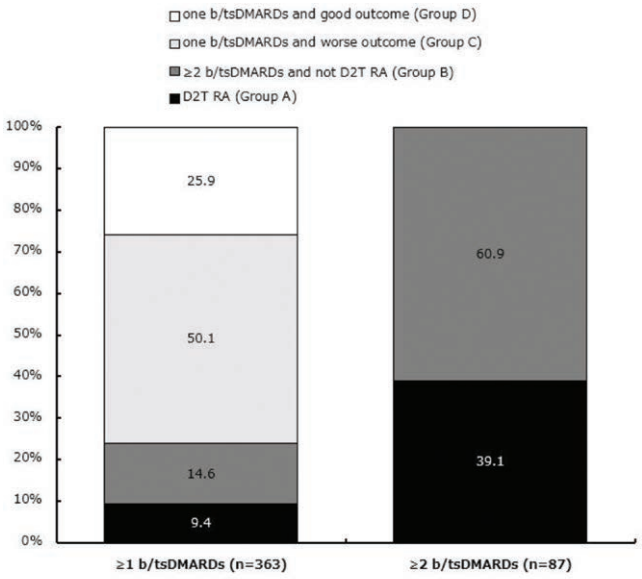


Figure1. Incidence rate of difficult-to-treat rheumatoid arthritis

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1221

POS0451 SERUM FETUIN-A AND VISFATIN LEVELS IN WOMEN WITH RHEUMATOID ARTHRITIS DEPENDING ON DISEASE ACTIVITY

Y. Akhverdyan[1], B. Zavodovsky[1], E. Papichev[1], J. Polyakova[1], L. Seewordova[1]. [1]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», Joint Diseases Treatment and Prevention Laboratory, Volgograd, Russian Federation*

Background: In recent years, the systemic effects of a number of cytokines have been actively studied, in particular, fetuin-A is considered a negative protein of the acute phase response, and visfatin, on the contrary, affects the activation of the cytokine cascade and has a pro-inflammatory effect. Taking into account that women suffer from rheumatoid arthritis (RA) more often, we investigated the levels of fetuin-A and visfatin in the blood serum of females in comparison with a group of healthy individuals and depending on the activity of the disease.
Objectives: to study the levels of fetuin-A and visfatin in the blood serum of women suffering from RA, depending on the activity of the disease
Methods: The study included 110 women with RA and 30 apparently healthy individuals. The inclusion criteria were: a diagnosis of RA verified based on the criteria of the American College of Rheumatology/European Anti-Rheumatic League (ACR/EULAR) 2010. The patients' age ranged from 18 to 90 years. The control group included 30 conventionally healthy individuals. Serum fetuin-A and visfatin levels were determined by indirect enzyme-linked immunosorbent assay using commercial kits. RA activity was determined by the DAS28-CRP index. Activity 0-I was in 33 (30%) patients, grade II in 67 (60.9%), grade III in 10 (9.09%) patients.
Results: The normal level of fetuin-A was calculated using the formula M±2σ in the group of conventionally healthy individuals and ranged from 653.55 to 972.19 μg/ml. In patients with grade 0-I RA activity according to DAS28, the mean serum fetuin-A level was 843.92±130.73 μg/ml, in patients with grade II activity - 742.37±98.85 μg / ml, with III the degree of activity - 663.9±123.7 μg/ml ($p<0.001$).
The average level of visfatin in the blood serum in healthy individuals was 2.43±0.17 ng/ml. The level of normal values of visfatin in healthy individuals, defined as M±2σ, ranged from 0 to 5.07 ng/ml. The average level of visfatin in patients with RA was 6.27±0.18 ng/ml, which is significantly higher than in healthy individuals ($p<0.001$).
In patients with 0-I degree of RA activity according to DAS28, the average level of visfatin in blood serum was 4.94±0.02 ng/ml, in patients with degree II activity - 5.08±0.02 ng/ml, with III degree of activity - 6.82±0.23 ng/ml ($p<0.001$).

Conclusion: Thus, the level of fetuin-A in the blood serum of patients with RA is significantly lower in the case of a high degree of disease activity. The level of visfatin in the blood serum in women with RA is significantly higher in patients with a higher degree of disease activity. Therefore, the concentration values of fetuin-A and visfatin in the blood serum of patients with RA can be used in an integrated assessment of the prognosis of disease activity.

REFERENCES:

[1] Inoue K, Ikeda Y, Yamanaka S, et al. Serum fetuinA levels in patients with rheumatoid arthritis [abstract]. Atherosclerosis. 2002;9(Suppl 1):233. doi: 10-1016/s1567-5688(08)70930-9

[2] Janssens K, ten Dijke P, Janssens S, et al. Transforming growth factor-beta1 to the bone. Endocrine Reviews. 2005;26(6):743-74. doi:10.1210/er.2004-0001

[3] Polyakova J, Korolik O, Papichev E, et al. The role of «new» cytokines in the pathogenesis rheumatoid arthritis. Ann Rheum Dis. 2018; 78(2): 1497

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1244

POS0452 SYNOVIAL MYELOID-STROMAL PATHOTYPE PREDICTS ONE-YEAR RADIOGRAPHIC PROGRESSION IN ACTIVE RHEUMATOID ARTHRITIS

X. Zhang[1], J. D. Ma[1], D. H. Zheng[1], C. Chen[1], T. Wu[1], J. Lin[1], J. Jing[1], Y. Mo[1], Y. Y. Zou[1], L. Dai[1]. *[1]Sun Yat-Sen University Sun Yat-Sen Memorial Hospital, Rheumatology, GuangZhou, China*

Background: Rheumatoid arthritis (RA) is a heterogeneous disease with variable prognosis. The cellular composition in synovium is the driving force of joint destruction in RA, and the predictive values of histopathological assessments on the clinical outcomes of RA have been identified. However, current synovial histopathological assessments mainly focus on the infiltrated immunocytes to distinguish RA synovium into different synovial pathotypes. Whether addition of stromal cells improve the accuracy of histopathological assessments remains unknow.

Objectives: To distinguish synovial pathotypes of RA based on intercellular connection and explore their predictive value on one-year radiographic progression.

Methods: Active RA patients who underwent needle synovial biopsy at baseline were recruited from a real-world prospective cohort. Clinical data were evaluated at baseline and 1, 3, 6, 12 months. Histopathologic assessments included Krenn synovitis score and semiquantitative score of immunohistochemical staining for CD20, CD38, CD4, CD8, CD68, CD31 and CD90. Cluster analysis was used to distinguish synovial pathotypes. The primary outcome was one-year radiographic progression defined as a change in total Sharp/van der Heijde modified score≥0.5 units.

Results: 1. Among 134 RA patients who received synovial biopsy at baseline and finished one-year follow-up, 105 had qualified synovial tissue. The mean age was 50.2±13.3 years with 77.1% female. The median disease duration was 24 (9-120) months. All patients were active RA, and 64.8%, 26.7% and 8.6% patients in high, moderate and low disease activity, respectively. There were 41 (39%) patients who have never been treated with corticosteroids or disease-modifying anti-rheumatic drugs.

2. During one-year follow-up, there were 48.6%, 63.8%, 71.4%, and 69.5% patients achieved CDAI LDA target, and 12.4%, 30.5%, 34.3%, and 32.4% patients achieved CDAI remission after 1, 3, 6, and 12 months, respectively. A total of 33 (31.4%) patients had radiographic progression.

3. All patients were divided into three clusters using cluster analysis based on the seven synovial cellular scores. Patients in cluster 1 (*n*=50, 47.6%) had higher scores of sublining CD68+ macrophages, CD31+ endothelial cells and CD90+ fibroblasts, thus named as myeloid-stromal pathotype. Patients in cluster 2 (*n*=26, 24.8%) had higher scores of CD20+ B cells, CD38+ plasma cells, CD4+ T cells and CD8+ T cells, thus named as lymphoid pathotype. Patients in cluster 3 (*n*=29, 27.6%) had lower scores of all seven cell types, thus named as pauci-cellular pathotype (Figure 1).

4. RA patients with baseline synovial myeloid-stromal pathotype showed higher rate of one-year radiographic progression versus lymphoid and pauci-cellular pathotypes (48% vs. 16.4%, *P*<0.001), whereas there was no difference between lymphoid and pauci-cellular pathotypes (11.5% vs. 20.7, *P*=0.475). Adjusted for confounding factors including age, sex, smoking, disease duration, RF status, ACPA status, CDAI, HAQ-DI and mTSS at baseline, multivariate logistic regression analysis showed that baseline synovial myeloid-stromal pathotype independently predicted one-year radiographic progression (*AOR*=3.602, 95%CI:1.257-10.324, *P*=0.017, Table 1).

Conclusion: Baseline synovial myeloid-stromal pathotype in RA can predict one-year radiographic progression.

Funding: This work was supported by National Natural Science Foundation of China (no. 81971527, 81801606 and 81801605), Guangdong Natural Science Foundation (no. 2018A030313541 and 2018A030313690), Guangdong Medical Scientific Research Foundation (no. A2018062), Guangdong Basic and Applied Basic Research Foundation (no. 2019A1515011928 and 2020A1515110061), and Science and Technology Program of Guangzhou (no. 201904010088).

Acknowledgements: We thank all subjects and medical staff who generously contributed to this study.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1292

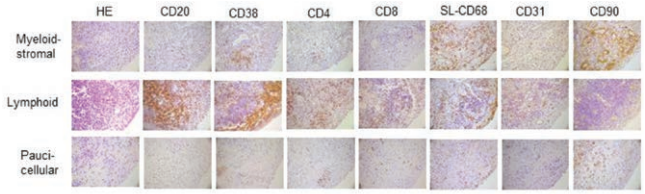


Figure 1 Representative HE staining and immunohistochemistry of three synovial pathotypes

POS0453 VALIDATION OF THE SIMPLIFIED DISEASE ACTIVITY INDEX (SDAI) WITH A QUICK QUANTITATIVE C-REACTIVE PROTEIN ASSAY (SDAI-Q) IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONAL, MULTICENTER STUDY

J. Schally[1], H. C. Brandt[2], J. Brandt-Juergens[3], G. R. Burmester[4], H. Haibel[1], H. Käding[1], K. Karberg[2], S. Lüders[1], B. Muche[1], M. Protopopov[1], V. Rios Rodriguez[1], M. Torgutalp[1], M. Verba[1], S. Zinke[5], D. Poddubnyy[1], F. Proft[1]. *[1]Charité – Universitätsmedizin Berlin, Division of Gastroenterology, Infectiology and Rheumatology, Campus Benjamin Franklin, Berlin, Germany*; *[2]Praxis für Rheumatologie und Innere Medizin, Praxis für Rheumatologie und Innere Medizin, Berlin, Germany*; *[3]Rheumatologische Schwerpunktpraxis, Rheumatologische Schwerpunktpraxis, Berlin, Germany*; *[4]Charité – Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; *[5]Rheumapraxis Berlin, Rheumapraxis Berlin, Berlin, Germany*

Background: Therapeutic decisions in RA patients should be based on regular disease activity assessment using scores like the Simplified Disease Activity Index (SDAI) or the Clinical Disease Activity Index (CDAI) [1]. The CDAI has the benefit of being immediately available, while the SDAI encompasses with the C-reactive protein (CRP) an acute phase reactant and therefore is the recommended score for the use in clinical trials. However, CRP determination takes hours to days, thus hindering the treat-to-target concept using the SDAI. Quick quantitative CRP (qCRP) tests allow CRP measurement within a few minutes. Therefore, qCRP based SDAI (SDAI-Q) could combine the advantages of both scores.

Objectives: To validate the SDAI-Q in a prospective, multicenter study of RA patients.

Methods: The study was conducted in five centers in Berlin, Germany. Consecutive adult (≥ 18 years) RA patients were included. In addition to a rheumatological assessment, including patient reported outcomes, routine CRP was measured in the local labs. Additionally, a qCRP testing with the „QuikRead go instrument" (Aidian Oy, Finland) was performed locally (measurement range 0.5 - 200 mg/l). Statistical analysis included descriptive statistics, cross tabulation and weighted Cohen´s kappa comparing disease activity categories, Bland-Altman plots and intraclass correlation coefficient (ICC) for CRP, qCRP, SDAI, SDAI-Q and CDAI.

Results: In this study 100 RA patients were included (mean age: 60.9 years, mean disease duration: 11.4 years, 73.0% were female, 63.0% RF positive, 57.0% ACPA positive, 49.0% positive and 29% negative for both parameters). 75.0% were treated with csDMARD, 15% with tsDMARDs, 39.0% with bDMARDs and 40% with glucocorticoids (mean prednisolone equivalent: 5.4 mg prednisolone/d). Mean CRP and qCRP-levels were 6.97 and 7.89 mg/l, respectively (ICC 0.992; 95%CI: 0.987; 0.995). Comparing SDAI-Q and SDAI, all patients (100%) achieved the same disease activity status (Table 1A); weighted Cohen´s kappa was 1.000 (95%CI: 1.000; 1.000). ICC for SDAI-Q- and SDAI-values was 1.000 (95%CI: 1.000; 1.000). The agreement of SDAI-Q and SDAI is shown in a Bland-Altman plot (Figure 1). When comparing the CDAI with the SDAI-Q 93 patients (93%) were assigned to the same disease activity category (Table 1B); weighted Cohen´s kappa was 0.929 (95%CI: 0.878; 0.981). ICC for numerical values of SDAI-Q and CDAI was 0.989 (95%CI: 0.978; 0.994).

Conclusion: SDAI-Q showed an absolute agreement with SDAI on the assignment to disease activity categories with the important advantage of time. With SDAI-Q, rheumatologists could base their clinical decision-making immediately on an index-based disease activity measurement by using a composite score considering acute phase reactants. Consequently, SDAI-Q can be integrated in clinical routine and clinical trials and could be implemented into the treat-to-target concept in RA patients.

REFERENCES:

[1] Smolen JS, et al. Ann Rheum Dis. 2016 Jan; 75(1):3-15.

Table 1. A) Disease activity categories by SDAI-Q vs. SDAI; B) Disease activity categories by SDAI-Q vs. CDAI

A		SDAI-Q (n = 100)			
		Remission (≤ 3.3)	**Low Disease Activity** (> 3.3 and ≤ 11)	**Moderate Disease Activity** (> 11 and ≤ 26)	**High Disease Activity** (> 26)
SDAI	**Remission** (≤ 3.3)	**28 (28.0%)**			
	Low Disease Activity (> 3.3 and ≤ 11)		**31 (31.0%)**		
	Moderate Disease Activity (> 11 and ≤ 26)			**35 (35.0%)**	
	High Disease Activity (> 26)				**6 (6.0%)**
B		SDAI-Q (n = 100)			
		Remission (≤ 3.3)	**Low Disease Activity** (> 3.3 and ≤ 11)	**Moderate Disease Activity** (> 11 and ≤ 26)	**High Disease Activity** (> 26)
CDAI	**Remission** (≤ 2.8)	**26 (26.0%)**			
	Low Disease Activity (> 2.8 and ≤ 10)	**2 (2.0%)**	**28 (28.0%)**	**2 (2.0%)**	
	Moderate Disease Activity (> 10 and ≤ 22)		**3 (3.0%)**	**33 (33.0%)**	
	High Disease Activity (> 22)				**6 (6.0%)**

Fields highlighted in red indicate that disease activity categories do not match.SDAI = Simplified Disease Activity Index;SDAI-Q = SDAI calculated with a quick quantitative CRP assay; CDAI = Clinical Disease Activity Index.

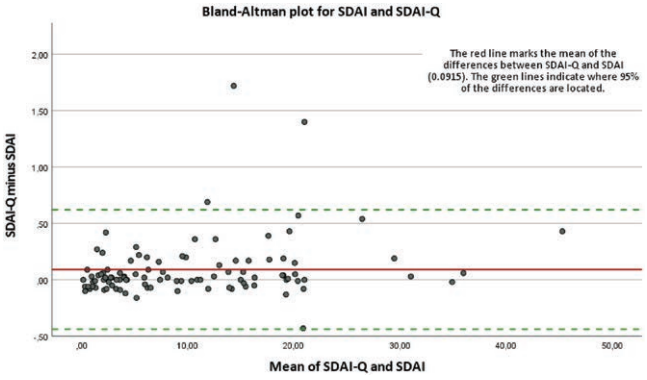


Figure 1. Bland-Altman plot for SDAI and SDAI-Q Acknowledgements

The authors would like to deeply thank Braun T, Doerwald C, Deter N, Höppner C, Lackinger J, Lorenz C, Lunkwitz K, Mandt B, Sron S and Zernicke J for their practical support and coordinating the study.
Funding statement:
The AQUA study was supported by an unrestricted research grant from Novartis. Testing kits were provided free of charge from Aidian Oy, Finland.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1366

POS0454

COMPARISON OF MBDA SCORE, PATIENT GLOBAL ASSESSMENT AND EVALUATOR GLOBAL ASSESSMENT FOR PREDICTING RISK OF RADIOGRAPHIC PROGRESSION

L. Calabrese[1], M. E. Weinblatt[2], N. Shadick[2], C. Heegaard Brahe[3], M. Østergaard[3], M. L. Hetland[3], M. Horton[4], D. Flake[4], E. Sasso[5]. [1]*Cleveland Clinic, Clinical Immunology, Cleveland, United States of America*; [2]*Brigham and Women's Hospital, Rheumatology, Boston, United States of America*; [3]*University of Copenhagen, Center for Rheumatology and Spine Diseases, Copenhagen, Denmark*; [4]*Myriad Genetics, Inc., MMM Informatics, Salt Lake City, United States of America*; [5]*Myriad Autoimmune, R&D Medical, South San Francisco, United States of America*

Background: Busy rheumatologists may assess disease activity and risk for radiographic progression (RP) in RA with informal, qualitative versions of evaluator and/or patient global assessments (EGA and PGA). RA patient care may be improved by having a convenient, objective disease activity measure that predicts risk for RP more accurately than EGA or PGA.

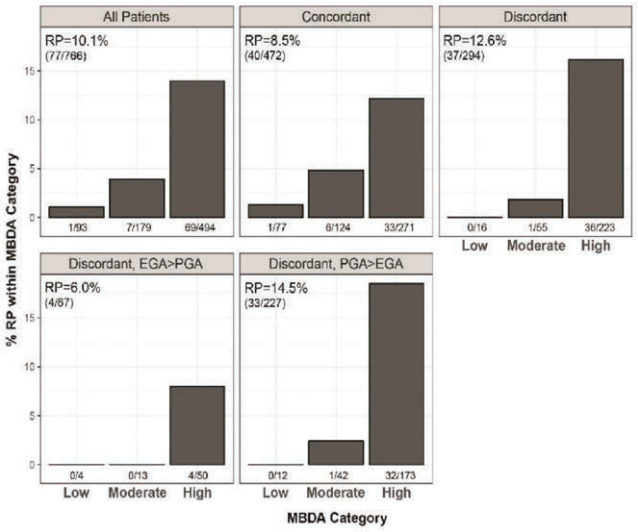
Objectives: To compare the abilities of MBDA score, patient global assessment and evaluator global assessment to assess risk for radiographic progression (RP), and to assess the ability of MBDA score to predict RP among patients with concordant or discordant PGA and EGA.

Methods: Patients were pooled from two RCTs of patients with recent onset RA treated with conventional and biologic DMARDs (OPERA and SWEFOT, N=386) and from a registry of patients with predominantly established RA and diverse treatments (BRASS, N=380). Pearson correlations were determined between MBDA scores (adjusted for the effects of age, sex and adiposity) (scale 1-100), PGA and EGA (each on a scale of 1-10) at baseline. PGA and EGA were considered discordant when they differed by >2.5. Univariable logistic regression assessed ability to predict RP (change in TSS >5 over 1 year) for MBDA score, PGA and EGA as continuous variables; and for discordance of PGA and EGA as 2-level (concordant vs. discordant) or 3-level (PGA>EGA, concordant, EGA>PGA) categorical variables. Multivariable regression considered the main effect and interaction terms of the MBDA score, as a continuous variable, paired with each other variable, to test the ability of each pair to assess risk of RP. All models included a random effect on cohort. Odds ratios were reported for every 10-unit increase in MBDA score. Frequency of RP was determined in subgroups with MBDA score low (<30), moderate (30-44) or high (>44) for patient groups based on PGA/EGA concordance or discordance.

Results: The 766 patients studied were 76% female, 76% positive for RF and/or anti-CCP Ab, with mean age 55 years, DAS28-CRP 4.7, CRP 22 mg/L, CDAI 26, SJC 9.1, PGA 4.4, EGA 3.4, MBDA score 53. No interaction was seen between MBDA score and type of cohort (early vs established RA). PGA and EGA were discordant in 294 of 766 (38%) patients and were weakly to moderately correlated (r=0.38). Among discordant patients, PGA was >EGA in 227 cases and EGA was >PGA in 67 cases. Correlations between MBDA score and PGA or EGA were r=0.41 and r=0.34, respectively. In univariable analyses, MBDA score was a statistically significant predictor of radiographic progression (OR=1.53, $p=6.3x10^{-8}$) whereas PGA, EGA, 2-level discordance and 3-level discordance were not (p=0.38, 0.47, 0.74, 0.83, respectively). In multivariable analyses, significant interactions were observed between MBDA score and discordance (2-level, p=0.0029; 3-level, p=0.0087). The interaction analysis demonstrated, in PGA/EGA-concordant patients, low risk of radiographic progression when MBDA score was low and elevated risk when it was high (OR=1.33 [1.1, 1.59]). A relationship between MBDA score and RP risk was also demonstrated, with heightened trend, among discordant patients with PGA >EGA (OR=2.04 [1.53, 2.81]) and EGA >PGA (OR=3.43 [1.37, 13.8]) (Figure 1).

Conclusion: MBDA score was a significant predictor of radiographic progression, whereas PGA and EGA were not. MBDA score predicted progression whether PGA and EGA were concordant or discordant. These results suggest that MBDA score detects joint-damaging disease activity more accurately than PGA and EGA and it does so whether or not PGA and EGA are in agreement.

Figure 1. Rate of radiographic progression (RP) by MBDA category for patient groups based on concordance or discordance of Patient Global Assessment (PGA) and Evaluator Global Assessment (EGA).



Disclosure of Interests: Leonard Calabrese Grant/research support from: AbbVie, Bristol-Myers Squibb, Cresecendo, Genentech, Gilead, GlaxoSmith-Kline, Horizon, Janssen, Novartis, and Sanofi., Michael E. Weinblatt Shareholder of: Canfite, Inmedix, Scipher, and Vorso, Consultant of: AbbVie, Aclaris, Amgen, Bayer, Bristol-Myers Squibb, Crescendo Bioscience, Corrona, EqRX, GSK,Genosco, Gilead, Lilly, Novartis, Pfizer, Roche, Set Point, Grant/research support from: Bristol-Myers Squibb, Myriad Genetics, Inc.,Eli Lilly and Sanofi, Nancy Shadick Consultant of: BMS, Grant/research support from: Lilly, mallinckrodt, BMS, Amgen and Sanofi, Cecilie Heegaard Brahe: None declared, Mikkel Østergaard Consultant of: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Novartis, Orion, Pfizer, Regeneron, Roche, Takeda, and UCB, Grant/research support from: AbbVie, BMS, Celgene, Myriad Genetics, Inc., Janssen, and Merck, Merete L. Hetland Speakers bureau: Orion, Grant/research support from: AbbVie, Biogen, BMS, CelltrionRoche, Myriad Genetics, Inc., Eli Lily, MSD, Pfizer, and UCB, Megan Horton Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Darl Flake Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Eric Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Autoimmune
DOI: 10.1136/annrheumdis-2021-eular.1467

POS0455 EFFECT OF ANTI-Ro/SSA ANTIBODIES FOR TREATMENT RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

R. Yokochi[1], H. Tamai[2], T. Kido[3], Y. Yagyu[4], D. Waki[5], R. Yanai[6], K. E. Sada[7]. *[1]Teikyo University Chiba Medical Center, Division of Hematology and Rheumatology, Ichihara, Japan*; *[2]Keio University School of Medicine, Division of Rheumatology Department of Internal Medicine, Tokyo, Japan*; *[3]Toyama University Hospital, The First Department of Internal Medicine, Toyama, Japan*; *[4]Tokyo Kyōsai Hospital, Department of Internal Medicine, Tokyo, Japan*; *[5]Kurashiki Central Hospital, Department of Endocrinology and Rheumatology, Kurashiki, Japan*; *[6]Showa University Hospital, Division of Rheumatology, Tokyo, Japan*; *[7]Kochi Medical School, Kochi University, Department of Clinical Epidemiology, Kochi, Japan*

Background: Several previous observational studies have suggested that patients with anti-Ro/SSA antibody-positive rheumatoid arthritis (RA) may respond poorly to treatment, including tumor necrosis factor inhibitors[1]. However, its influence on methotrexate (MTX) treatment, which is the anchor drug of treat-to-target strategy in RA treatment, remains unclear.
Objectives: We compared the clinical response to MTX in both anti-Ro/SSA antibody-positive and -negative patients with MTX-naiive RA and investigated the reasons for the difference in response.
Methods: We recruited 210 consecutive patients with RA who were newly started on MTX in this retrospective cohort study. The effect of the presence of anti-Ro/SSA antibodies on achieving low disease activity (LDA) of DAS28-CRP at six months after initiating MTX was investigated by using logistic regression analysis. CDAI, SDAI, concomitant using DMARDs and painkillers, patient's and evaluator's VAS, tender joint counts, and swollen joint counts at six months were also compared between the anti-Ro/SSA-positive patients and -negative patients. Missing data were imputed by using multiple imputations before multivariate analysis.
Results: 32 anti-Ro/SSA antibody-positive patients and 178 anti-Ro/SSA antibody-negative patients were included. The rate of achieving DAS28-LDA at six months was significantly lower in the anti-Ro/SSA antibody-positive patients than those in the anti-Ro/SSA antibody-negative patients (56.2% versus 75.8%, *P*=0.03). in the logistic regression analysis, the presence of anti-Ro/SSA antibodies was an independent negative predictor for achieving DAS-28-LDA at six months (OR:0.431, 95%CI: 0.190-0.978, *P*=0.044) (Table1). Anti-Ro/SSA antibody-positive patients had significantly higher patient's VAS at six months (median [IQR]: 22 [15-41] vs 19 [5-30], *P*=0.038), and prescribed NSAIDs (37.5% vs 18.0%, *P*=0.018). CDAI and SDAI after six months were not significantly different between the group.
Conclusion: The presence of anti-Ro/SSA antibodies might be one of the predictive factors for the insufficient response to treat to target strategy in RA treatment. Residual pain was suspected as one of the mechanisms contributing to the lesser clinical response of MTX in anti-Ro antibody-positive RA.
REFERENCES:
[1] Ran Matsudaira wt al. J Rheumatol 2011;38(11):2346-54

Table 1. Logistic regression analysis for the rate of achieving DAS28 low disease activity at six months.

Risk factor	Odds ratio	95%CI	*P* value
Age at onset	0.993	0.968-1.018	0.586
Sex (woman)	0.643	0.300-1.384	0.258
RF-positive	1.962	0.853-4.511	0.112
ACPA-positive	0.552	0.225-1.351	0.192
Anti-Ro/SSA antibody-positive	0.431	0.190-0.978	0.044

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1485

POS0456 EXTERNAL VALIDATION OF A MULTI-BIOMARKER-BASED CARDIOVASCULAR DISEASE RISK PREDICTION SCORE FOR RHEUMATOID ARTHRITIS PATIENTS

J. Curtis[1], E. Sasso[2], E. Hitraya[2], C. Chin[2], R. Bamford[2], R. Ben-Shachar[3], A. Gutin[4], D. Flake[4], B. Mabey[4], J. Lanchbury[4]. *[1]University of Alabama at Birmingham, Immunology & Rheumatology, Birmingham, United States of America*; *[2]Myriad Autoimmune, R&D Medical, South San Francisco, United States of America*; *[3]Myriad Genetics, Inc., Clinical Development, Salt Lake City, United States of America*; *[4]Myriad Genetics, Inc., MMM Informatics, Salt Lake City, United States of America*

Background: A novel score for predicting 3-year risk for CVD events in RA patients combines age, four traditional CVD risk factors (diabetes, hypertension, smoking, history of high-risk CVD event), a personalized assessment of RA-related inflammation based on the multi-biomarker disease activity (MBDA) score and, individually, 3 of its 12 biomarkers, TNF-R1, MMP-3 and leptin (log-transformed). This score was developed and internally validated using patient data from the Medicare database.
Objectives: The purpose of this analysis was to externally validate the MBDA-based CVD risk prediction score in a younger cohort from the Symphony claims database.
Methods: A cohort of patients greater than or equal to 18 years old with RA diagnosis from a rheumatologist and evidence of an RA-specific treatment, excluding patients with malignancy, past myocardial infarction (MI) or stroke, was created by a third party (Symphony) by matching medical and pharmaceutical claims and linking them to MBDA scores from a database of tests done for routine care. Medicare patients were excluded to avoid overlap with the internal validation cohort. Only the first MBDA test was used for each patient. The study endpoint was time from MBDA testing to first CVD event within a 3-year time horizon. CVD event was defined as MI or stroke, based on ICD-9 or ICD-10 diagnosis codes in hospital claims. Analyses focused on relative risk, not absolute risk, because CVD event data in Symphony may be incomplete. A univariate Cox proportional hazards regression model was fit with the MBDA-based CVD risk score as the sole predictor of time to CVD event to obtain a hazard ratio (HR) estimate (95% CI) and p-values from a likelihood ratio test (LRT). Sensitivity analyses determined HR for patient subgroups, with p-values determined for the interaction between subgroups and the MBDA-based CVD risk score. Using a multivariate Cox proportional hazard regression model, the MBDA-based CVD risk score was compared to a simpler model that included only age, sex, diabetes, hypertension, history of other CVD, smoking and CRP (log-transformed) for ability to predict time to a CVD event.
Results: 48,868 patients with 337 CVD events met eligibility criteria and had linked biomarker data. Mean age was 54.4 years. 81.7% were female (Table 1).

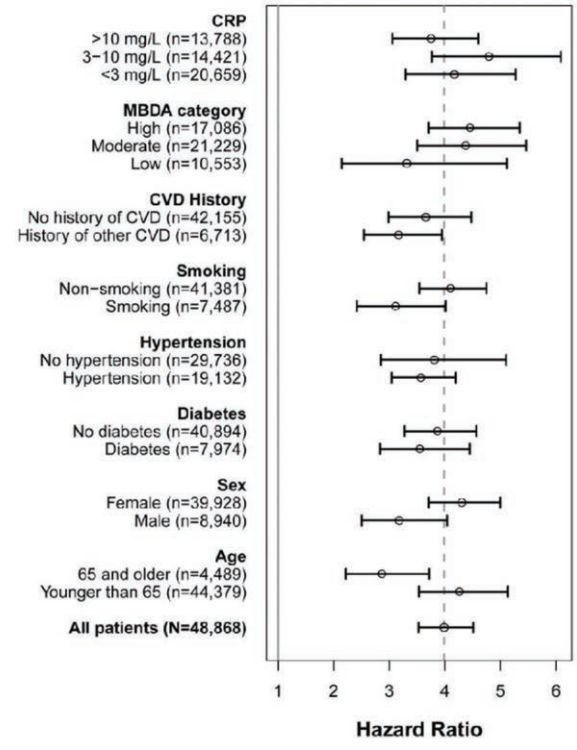
Mean follow-up was 24.4 months. The MBDA-based CVD risk score (mean 3.3, IQR 2.8–3.8) was highly significant in univariate analysis, with HR = 3.99 (95% CI: 3.52-4.51, p = 4.4×10^{-95}); i.e., for every 1-unit increase in risk score, the CVD event rate in this cohort was ~4 times as high. Similar results were seen in the subset of 44,379 patients <65 years old, with HR=4.26 (95% CI: 3.53-5.14, p = 1.2×10^{-47}). In sensitivity analyses, after adjusting for multiple comparisons, there were no significant differences between HR of complementary subgroups (Figure 1). The MBDA-based CVD risk score added significant prognostic information to a simpler, clinical model (HR=2.28 [95% CI: 1.69-3.08, p = 1.6×10^{-7}] after accounting for all other factors).

Conclusion: The MBDA-based CVD risk prediction score has been externally validated in a cohort that is younger than and independent of the Medicare cohort used previously for test development and internal validation.

Table 1. Cohort characteristics of RA patients with linked biomarker data and at risk for CVD events.

Variable	Median (IQR) or N (%)
Total patients	48,868()
Age, years	54 (46-60)
Sex, male	8,940 (18.3%)
Diabetes	7,974 (16.3%)
Hypertension	19,132 (39.2%)
History of high-risk CVD event	6,713 (13.7%)
Smoking	7,487 (15.3%)
CRP, mg/L	4.1 (1.4-11.5)
Leptin, ng/mL	24.3 (10.6-47.1)
MMP-3, ng/mL	21.1 (14.3-36.2)
TNF-RI, ng/mL	1.4 (1.1-1.7)
MBDA score	40 (31-48)
MBDA-based CVD risk score	3.3 (2.8-3.8)

Figure 1. Hazard ratios for CVD event over 3 years in the external validation dataset (N=48,868). Vertical dashed line indicates the hazard ratio for all patients.



Disclosure of Interests: Jeffrey Curtis Grant/research support from: Abbvie, Amgen, BMS, Corrona, Eli Lilly, Jannsen, Myriad Genetics, Inc., Pfizer, Regeneron, Roche, and UCB., Eric Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Autoimmune, Elena Hitraya Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Autoimmune, Cheryl Chin Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Autoimmune, Richard Bamford Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Autoimmune, Rotem Ben-Shachar Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Alexander Gutin Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Darl Flake Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Brent Mabey Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Jerry Lanchbury Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc.

DOI: 10.1136/annrheumdis-2021-eular.1657

POS0457 CHANGES OF RF ISOTYPE PROFILE IN PATIENTS WITH RHEUSMATOID ARTHRITIS: DATA FROM 10 YEARS FOLLOW-UP STUDY

M. R. Nur Aida Sabrina[1], C. L. Too[1,2], A. Haziqah Itqan[1], A. A. Siti-Aisyah[1], A. F. Nurul-Aain[1], L. K. Tan[1], I. S. Lau[3], M. Mohd Zain[3], H. Baharuddin[3], D. L. M. Ang[4], A. R. Amnahliza[4], P. S. Ong[5], N. Mat Husin[5], S. C. Gun[6], N. Mohd Noor[6], M. Z. Taib[7], L. Padyukov[2], L. Alfredsson[8], L. Klareskog[2], J. Rönnelid[9], N. S. Shahril[4]. *[1]Allergy and Immunology Research Center, Institute for Medical Research, Ministry of Health Malaysia, Selangor, Malaysia*; *[2] Department of Medicine, Division of Rheumatology, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden*; *[3]Department of Medicine, Selayang Hospital, Selangor, Malaysia*; *[4]Department of Medicine, Putrajaya Hospital, Putrajaya, Malaysia*; *[5]Department of Medicine, Raja Permaisuri Bainun Hospital, Perak, Malaysia*; *[6]Department of Medicine, Tuanku Ja'afar Hospital, Negeri Sembilan, Malaysia*; *[7]Medical Resource Research Centre, Institute for Medical Research, Ministry of Health Malaysia, Selangor, Malaysia*; *[8]Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden*; *[9]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden*

Background: Presence of autoantibodies such as anti-cyclic citrullinated peptide (anti-CCP2) and rheumatoid factor (RF) is of considerable diagnostic and prognostic value in patients with rheumatoid arthritis (RA). Limited data are available for autoantibody profile changes over time in patients with RA.

Objectives: Thus, we compared the presence of anti-CCP2 and different RF isotypes in individual RA patients at baseline and during 10 years follow-up.

Methods: A total of 320 RA patients from the Malaysian Epidemiological Investigation of Rheumatoid Arthritis (MyEIRA) case-control study was included in this study. The presence of anti-CCP2, IgM RF, IgG RF, and IgA RF at baseline and at later time point (±10 years) were determined using enzyme-linked immunosorbent assays, with identical techniques in paired samples. Seropositive RA is defined by the presence of at least one autoantibody, whilst seronegative RA is defined by the absence of all investigated autoantibodies.

Results: The proportion of seropositive RA were higher for the follow-up samples (n=263, 82.2%) as compared to the baseline samples (n=251, 78.4%). Among the baseline samples, 105 (41.8%) were positive for anti-CCP2 and all RF isotypes. Of these individuals, 85 (81.0%) remained positive for all antibodies at the follow-up, while 20 (19.0%) lost one or more RF isotypes (4 IgM RF, 19 IgG RF and 13 IgA RF). Interestingly, 14 (5.6%) RA patients who were seropositive at baseline became totally seronegative after follow-up. Among the 69 patients seronegative at baseline, 26 (37.7%) acquired one or more autoantibodies at follow-up (14 IgM RF, 2 IgG RF, 9 IgA RF and 8 anti-CCP2) (Figure 1).

Conclusion: Anti-CCP2 present at baseline usually remained at follow-up. Among Malaysian RA patients, changes in status were mainly found for RF of all isotypes.

REFERENCES:

[1] Barra, Lillian et al. "Lack of seroconversion of rheumatoid factor and anti-cyclic citrullinated peptide in patients with early inflammatory arthritis: a systematic literature review." Rheumatology (Oxford, England) vol. 50,2 (2011): 311-6.

[2] van Delft, Myrthe A M, and Tom W J Huizinga. "An overview of autoantibodies in rheumatoid arthritis." Journal of autoimmunity vol. 110 (2020): 102392.

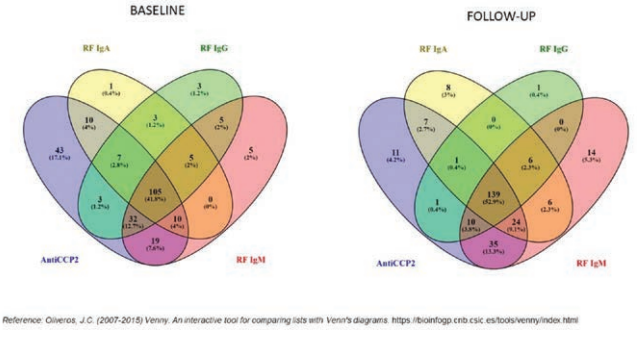


Figure 1. Comparison of serum autoantibody profile in rheumatoid arthritis patients during baseline enrolment and 10 years follow-up.

Acknowledgements: The authors would like to thank the Director General of Health, Ministry of Health Malaysia for supporting this study. The authors are also indebted to participants for their kind participation. This study was financially supported by the Ministry of Health, Malaysia (JPP-IMR 08-012; 18-051).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1714

POS0458 IDENTIFICATION OF HUB GENES AND MOLECULAR PATHWAYS IN PATIENTS WITH RHEUMATOID ARTHRITIS BY BIOINFORMATICS ANALYSIS

L. Cheng[1], S. X. Zhang[2,3,4], S. Song[2,3,4], C. Zheng[1], X. Sun[1], S. Feng[1], T. Kong[1], G. Shi[5], X. Li[2,3], P. F. He[6], Q. Yu[1,6]. [1]*Shanxi Medical University, School of Management, Taiyuan, China*; [2]*Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [3]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [4]*Ministry of Education, Key laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [5]*Shanxi Medical University, Basic Medical College, Taiyuan, China*; [6]*Shanxi Medical University, Institute of Medical Data Sciences, Taiyuan, China*

Background: Rheumatoid arthritis (RA) is a chronic, inflammatory synovitis based systemic disease of unknown etiology[1]. The genes and pathways in the inflamed synovium of RA patients are poorly understood.
Objectives: This study aims to identify differentially expressed genes (DEGs) associated with the progression of synovitis in RA using bioinformatics analysis and explore its pathogenesis[2].
Methods: RA expression profile microarray data GSE89408 were acquired from the public gene chip database (GEO), including 152 synovial tissue samples from RA and 28 healthy synovial tissue samples. The DEGs of RA synovial tissues were screened by adopting the R software. The Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were performed. Protein-protein interaction (PPI) networks were assembled with Cytoscape software.
Results: A total of 654 DEGs (268 up-regulated genes and 386 down-regulated genes) were obtained by the differential analysis. The GO enrichment results showed that the up-regulated genes were significantly enriched in the biological processes of myeloid leukocyte activation, cellular response to interferon-gamma and immune response-regulating signaling pathway, and the down-regulated genes were significantly enriched in the biological processes of extracellular matrix, retinoid metabolic process and regulation of lipid metabolic process. The KEGG annotation showed the up-regulated genes mainly participated in the staphylococcus aureus infection, chemokine signaling pathway, lysosome signaling pathway and the down-regulated genes mainly participated in the PPAR signaling pathway, AMPK signaling pathway, ECM-receptor interaction and so on. The 9 hub genes (PTPRC, TLR2, tyrobp, CTSS, CCL2, CCR5, B2M, fcgr1a and PPBP) were obtained based on the String database model by using the Cytoscape software and cytoHubba plugin[3].
Conclusion: The findings identified the molecular mechanisms and the key hub genes of pathogenesis and progression of RA.

REFERENCES:

[1] Xiong Y, Mi BB, Liu MF, et al. Bioinformatics Analysis and Identification of Genes and Molecular Pathways Involved in Synovial Inflammation in Rheumatoid Arthritis. Med Sci Monit 2019;25:2246-56. doi: 10.12659/MSM.915451 [published Online First: 2019/03/28]
[2] Mun S, Lee J, Park A, et al. Proteomics Approach for the Discovery of Rheumatoid Arthritis Biomarkers Using Mass Spectrometry. Int J Mol Sci 2019;20(18) doi: 10.3390/ijms20184368 [published Online First: 2019/09/08]
[3] Zhu N, Hou J, Wu Y, et al. Identification of key genes in rheumatoid arthritis and osteoarthritis based on bioinformatics analysis. Medicine (Baltimore) 2018;97(22):e10997. doi: 10.1097/MD.0000000000010997 [published Online First: 2018/06/01]

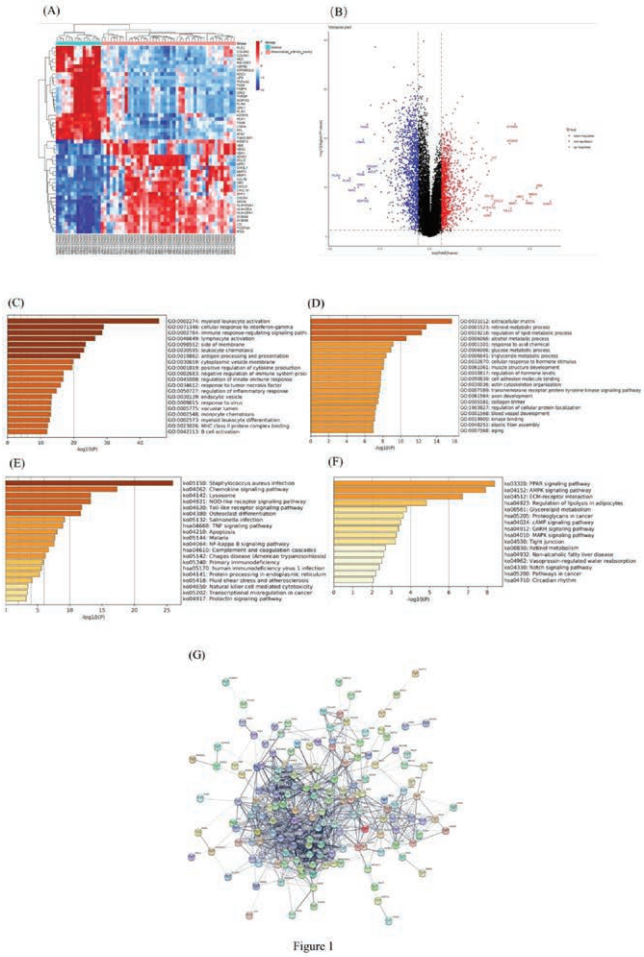


Figure 1

(A) Heat map of the top 50 up-regulated differentially expressed genes: Heatmaps of the differentially expressed genes (DEGs) including the 25 most upregulated and 25 most down-regulated genes. **(B)**Volcano map of gene expression: The horizontal axis is log2 FC and the vertical axis is log10 adj.p.val. Each dot represents a gene, blue represents down-regulated gene, red represents up-regulated gene, and black represents an in differentially expressed gene. **(C,D)**Visualization GO enrichment analysis: Go analysis showed that the function of up-regulated genes was mainly reflected in 20 aspects, and B cell activation had the lowest p value. The function of down regulated genes is mainly reflected in 20 aspects, and aging is the lowest in P value. **(E,F)**KEGG pathway enrichment analysis: Among the signaling pathways of up-regulated genes, the largest P value was Staphylococcus aureus. PPAR signaling pathway has the highest p value among the signaling pathways of down regulated genes. **(G)**Protein-protein interaction network of differentially expressed genes: The 9 hub genes were selected, they were PTPRC, TLR2, tyrobp, CTSS, CCL2, CCR5, B2M, FCGR1A and PPBP.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1938

POS0459 UNSUPERVISED CLUSTERING IDENTIFIES UNIQUE SUBSETS OF PATIENTS IN A RACIALLY AND ETHNICALLY DIVERSE RHEUMATOID ARTHRITIS COHORT

G. Lui[1], E. Noss[2], N. Singh[2], J. Andrews[2], J. Graf[3], K. Wysham[2,4]. [1]*University of Washington, Bioengineering, Seattle, United States of America*; [2]*University of Washington, Rheumatology/Medicine, Seattle, United States of America*; [3]*University of California San Francisco Parnassus Campus, Rheumatology/Medicine, San Francisco, United States of America*; [4]*VA Puget Sound Health Care System, Rheumatology/Medicine, Seattle, United States of America*

Background: Single biomarkers have limited utility to date in guiding RA clinical care. Machine learning algorithms may better identify and stratify RA patients with differential outcomes.
Objectives: To determine if unsupervised machine learning methods can be employed in a racially and ethnically diverse RA cohort to identify clusters of patients with different disease activity trajectories, as measured by DAS28ESR.
Methods: Data are derived from the longitudinal, observational University of California, San Francisco RA Cohort. Along with routine labs, medications and disease activity assessments, a multiple biomarker of disease activity (MBDA)

Table 1. Demographics and clinical characteristics of the RA cohort. Biomarkers significantly associated with DAS28ESR were determined by Lasso regression Values listed are per standard deviation of each biomarker.

		Overall (N=373)	Cluster 1 (N=116)	Cluster 2 (N=70)	Cluster 3 (N=14)	Cluster 4 (N=173)
Demographics:	Age	54.8 ± 3.6	63.6 ± 9.7	50.8 ± 14.9	58.2 ± 15.8	50.3 ± 12.1
	Female Sex	316 (85%)	101 (87%)	57 (81%)	11 (79%)	149 (86%)
	Race: Hispanic/Latino	181 (49%)	22 (19%)	47 (67%)	5 (36%)	107 (62%)
	Asian	123 (33%)	73 (63%)	8 (11%)	6 (43%)	36 (21%)
	Black	35 (9%)	12 (10%)	8 (11%)	2 (14%)	13 (8%)
	White & Other	34 (9%)	9 (7%)	7 (10%)	1 (7%)	17 (10%)
Clinical Characteristics:	Rheumatoid Factor	315 (85%)	104 (90%)	56 (80%)	13 (93%)	142 (82%)
	ACPA	297 (80%)	98 (85%)	54 (77%)	12 (86%)	133 (77%)
	Disease Duration	7.8 ± 7.6	13.7 ± 9.7	5.4 ± 4.6	6.7 ± 5.7	4.9 ± 3.8
	csDMARD	344 (92%)	108 (93%)	63 (90%)	13 (93%)	160 (93%)
	Biologic DMARD	185 (50%)	45 (39%)	30 (43%)	4 (29%)	106 (61%)
	Prednisone Dose	6.7 ± 3.8	6.0 ± 4.0	8.6 ± 4.9	5.8 ± 1.4	6.3 ± 2.8
	Body Mass Index	28.2 ± 4.5	26.6 ± 3.8	28.7 ± 3.8	28.0 ± 6.2	29.1 ± 4.7
	DAS28ESR	4.2 ± 1.1	4.2 ± 1.0	5.5 ± 0.8	3.9 ± 0.8	3.7 ± 0.9
Lasso Results:	EGF	-0.16*	-0.41***	--	--	-0.20**
	Leptin	0.15**	--	0.21*	--	0.21**
	c-reactive protein	0.34**	0.51***	--	--	--
	VCAM1	--	--	--	-0.73*	--
	YKL40	--	0.26*	--	--	--

-EGF: epidermal growth factor; VCAM1: Vascular cell adhesion protein 1; YKL40: Chitinase-3-like protein 1.-*p<0.05, **p<0.01, ***p<0.001

panel was obtained at each visit. The MBDA measures 12 serum biomarkers. Four patient clusters were identified by unsupervised K-prototype clustering after collapsing all observations into a cross sectional dataset. Plots were created to display longitudinal disease activity trajectories for each cluster. Lasso regression was applied to identify biomarkers associated with DAS28ESR.

Results: We identified 4 distinct clusters in our cohort (Table 1) with visually different disease activity trajectories (Fig. 1). Cluster 1 (n=116) was older (63.6±9.7), had the highest proportion of Asian participants (n=73, 63%) with the most study visits and longest disease duration. Cluster 2 (n=70) had the highest mean DAS28ESR (5.5±0.7), and the highest mean dose of prednisone (8.6±4.9mg/day). Cluster 3 had the lowest number of participants (n=14), study visits and lowest biologic use (28.6%). Cluster 4 was the largest cluster (n=173) with the shortest disease duration (4.9±3.8 years) and highest biologic use (61.3%). In the Lasso regressions, leptin was found to have significant positive associations with DAS28ESR in the whole group as well as Clusters 2 and 4. EGF had negative associations with DAS28ESR in the whole group, Cluster 1 and 4. CRP had positive associations with DAS28ESR in the whole group and Cluster 1. YKL40 and VCAM1 were found to have significant associations in Clusters 1 and 3, respectively.

Conclusion: We identified 4 unique clusters of RA patients in a racially and ethnically diverse longitudinal cohort with different disease activity trajectories and biomarkers associated with disease activity. Although additional work is needed to explore longitudinal outcomes in each cluster, the application of machine learning methods may identify unique combinations of patient and disease characteristics influencing RA clinical outcomes.

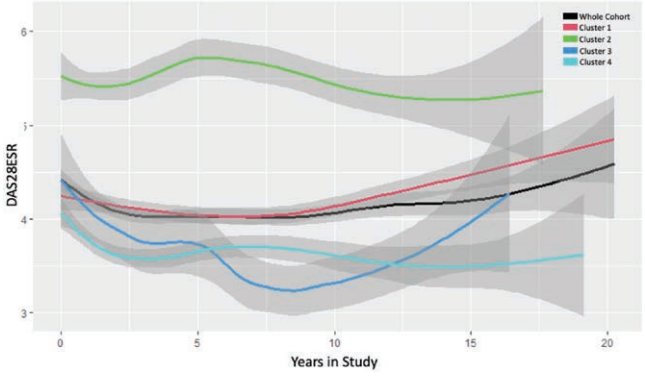


Figure 1. DAS28ESR trajectory plots with 95%CIs for the whole cohort and by cluster.

Acknowledgements: This work was supported by the Rheumatology Research Foundation Scientist Development Award.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1946

POS0460

ASSOCIATION OF ANTI-CITRULLINATED PROTEIN ANTIBODIES OF IgA SUBCLASSES WITH SUSTAINED REMISSION AND FLARE IN RHEUMATOID ARTHRITIS

M. V. Sokolova[1,2], J. Rech[1,2], M. Hagen[1,2], G. Schett[1,2], U. Steffen (née Harre)[1,2].
[1]*Friedrich-Alexander-University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany*; [2]*Friedrich-Alexander-University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Deutsches Zentrum für Immuntherapie, Erlangen, Germany*

Background: Understanding key mechanisms of flare development and sustained remission is one of the acute goals in modern rheumatology. Anti-citrullinated protein antibodies (ACPA) are the most abundant and specific autoantibodies in rheumatoid arthritis (RA) patients. However, the impact of ACPA of IgA isotype is poorly defined. IgA ACPA were previously shown to have a higher percentage of IgA2 in comparison to total IgA; and a correlation between IgA2% ACPA with the DAS28 score was observed in a previous study [1]. Of note, IgA1 and IgA2 were shown to exhibit different effector functions, with IgA2 being pro-inflammatory, which might be the background for its role in RA [1].

Objectives: We aimed to investigate, whether IgA ACPA could be used as a predictive factor for flare development in RA; and to look further into the changes in IgA ACPA levels in patients remaining in stable remission versus patients developing flare.

Methods: We analysed serum of 111 patients from a multicentre randomized controlled trial 'RETRO'. The study observational period was 12 months. Patients in the trial had to be in stable remission (DAS28-ESR<2.6) for a minimum of 6 months and were randomized into 3 different treatment arms: continuation of treatment, tapering by 50% or a gradual tapering until discontinuation [2]. IgA ACPA concentrations were measured with an enzyme-linked immunosorbent assay on CCP2-pre-coated plates.

Results: 60% of patients had IgG-ACPA. IgA ACPA levels were higher among the IgG-ACPA-positive patients (median 4.7 versus 2.24 µg/ml, p<0.0001). Baseline IgA1 and 2 ACPA levels were not different between patients who had a flare later on in the study period and those remaining in remission, showing no predictive value for flare development. However, the percentage of IgA2 in ACPA was correlating with the first registered DAS28 after flare (r=0.36, p=0.046). After the 12 months study period, IgA2 ACPA as well as IgA2% ACPA decreased significantly in patients who remained in stable remission by 17.5% (median, p<0.0001) and 13.6% (p=0.0006), respectively. By contrast, there was no significant change in IgA2 ACPA levels over time in patients who developed a flare. IgA1 ACPA levels remained stable over time. Disease management strategies did not seem to influence IgA ACPA levels in a specific way, as baseline levels were similar between patients on biological and conventional DMARDs and changes in levels after 12 months did not depend on the assignment to either of the study arms.

Conclusion: Neither IgA1 nor IgA2 ACPA levels were predictive of flare development or associated with treatment strategies (though rituximab, JAK-inhibitors and abatacept were not amongst treatment options). However, in patients remaining in sustained remission after 1 year a decrease in IgA2 and IgA2% ACPA was observed and IgA2% ACPA was associated with DAS28 score registered after flare. This could be an indication towards ACPA of IgA2 isotype contributing to the severity of flare, alongside other factors, and its reduction being associated with a prolonged state of remission.

REFERENCES:

[1] Steffen U, Koeleman CA, Sokolova MV, et al. IgA subclasses have different effector functions associated with distinct glycosylation profiles. Nat Commun 11, 120 (2020).
[2] Haschka J, Englbrecht M, Hueber AJ, et al. Relapse rates in patients with rheumatoid arthritis in stable remission tapering or stopping antirheumatic therapy: interim results from the prospective randomised controlled RETRO study. Ann Rheum Dis. 75:45-51 (2016).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2004

POS0461 RESPONSE TO BIOLOGIC THERAPY IN RHEUMATOID ARTHRITIS: RETHINKING OUR CLASSIFICATION

E. Vallejo-Yagüe[1], S. Kandhasamy[1], E. Keystone[2], A. Finckh[3], R. Micheroli[4], A. M. Burden[1]. [1]*ETH Zurich, Department of Chemistry and Applied Biosciences, Institute of Pharmaceutical Sciences, Zurich, Switzerland*; [2]*University of Toronto, Medicine, Toronto, ON, Canada*; [3]*University Hospitals Geneva, Division of Rheumatology, Geneva, Switzerland*; [4]*University Hospital of Zurich, Department of Rheumatology, Zurich, Switzerland*

Background: In rheumatoid arthritis (RA), primary failure with biologic treatment may be understood as lack of initial clinical response, while secondary failure would be loss of effectiveness after an initial response. Despite these clinical concepts, there is no unifying operational definition of primary and secondary non-response to RA treatment in observational studies using real-world data. On top of data-driven challenges, when conceptualizing secondary non-responders, it is unclear if the mechanism behind loss of effectiveness after a brief initial response is similar to loss of effectiveness after previous benefit sustained over time.

Objectives: This viewpoint aims to motivate discussion on how to define primary and secondary non-response in observational studies. Ultimately, we aim to trigger expert committees to develop standard terminology for these concepts.

Methods: We discuss different methodologies for defining primary and secondary non-response in observational studies. To do so, we shortly overview challenges characteristic of performing observational studies in real-world data, and subsequently, we conceptualize whether treatment response should be a dichotomous classification (Primary response/non-response; Secondary response/non-response), or whether one should consider three response categories (Primary response/non-response; Primary sustained/non-sustained response; Secondary response/non-response).

Results: RA or biologic registries are a common data source for studying treatment response in real-world data. While registries include disease-specific variables to assess disease progression, missing data, loss of follow-up, and visits restricted to the year or mid-year visit may present a challenge. We believe there is a general agreement to assess primary response within the first 6 month of treatment. However, conceptualizing secondary non-response, one could wonder if a patient with brief initial response and immediate loss of it should belong to the same response category as a patient who relapses after a period of prior benefit that was sustained over time. Until this concern is clarified, we recommend considering a period of sustained response as a pre-requisite for secondary failure. This would result in the following three categories: a) Primary non-response: Lack of response within the first 6 months of treatment; b) Primary sustained response: Maintenance of a positive effectiveness outcome for at least the first 12 months since treatment start; c) Secondary non-response: Loss of effectiveness after achieved primary sustained response. Figure 1 illustrates this classification through a decision tree. Since the underlying mechanisms for treatment failure may differ among the above-mentioned categories, we recommend to use the three-category classification. However, since this may pose additional methodological challenges in real-world data, optionally, a dichotomous 12-month time-point may be used to assess secondary non-response (unfavourable outcome after 12-months) in comparison to primary non-response or non-sustained response (unfavourable outcome within the first 12-months). Similarly, to study primary response, the solely 6-month timepoint may be used.

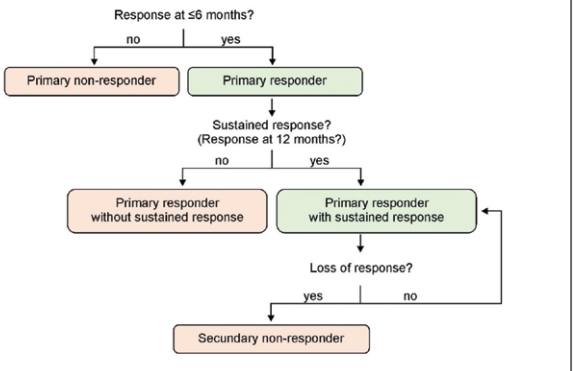


Figure 1. Decision tree to classify treatment response to biologics in rheumatoid arthritis (RA) based on evidence of an initial response, assuming a sustained benefit as pre-requisite prior secondary non-response. Patients discontinuing treatment due to remission or safety reasons are not reflected in the decision tree.

Conclusion: A unified operational definition of treatment response will minimize heterogeneity among observational studies and help improve the ability to draw cross-study comparisons, which we believe would be of particular interest when identifying predictors of treatment failure. Thus, we hope to open the room for discussion and encourage expert committees to work towards a common approach to assess treatment primary and secondary non-response in RA in observational studies.

Disclosure of Interests: Enriqueta Vallejo-Yagüe: None declared, Sreemanjari Kandhasamy: None declared, Edward Keystone Speakers bureau: Amgen, AbbVie, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Novartis, Pfizer Pharmaceuticals, Sanofi Genzyme, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis, Grant/research support from: Amgen, Merck, Pfizer Pharmaceuticals, PuraPharm, Axel Finckh Speakers bureau: Pfizer, Eli-Lilly, Paid instructor for: Pfizer, Eli-Lilly, Consultant of: AbbVie, AB2Bio, BMS, Gilead, Pfizer, Viatris, Grant/research support from: Pfizer, BMS, Novartis, Raphael Micheroli Consultant of: Gilead, Eli-Lilly, Pfizer and Abbvie, Andrea Michelle Burden: None declared
DOI: 10.1136/annrheumdis-2021-eular.2065

POS0462 ALCOHOL AND INFLAMMATORY ARTHRITIS DISEASE ACTIVITY: PERSPECTIVES FROM A 979-PATIENT COHORT WITH SYSTEMATIC REVIEW AND META-ANALYSIS

M. Turk[1], A. Gorman[1], K. Murray[1], Y. Alammari[1], F. Young[1], J. Turk[2], E. Zahavi[2], P. Gallagher[1], L. Freeman[1], U. Fearon[3], D. Veale[1]. [1]*St. Vincent's University Hospital, Rheumatology, Dublin, Ireland*; [2]*Queen's University, Life Sciences, Kingston, Canada*; [3]*Trinity College Dublin, Rheumatology, Dublin, Ireland*

Background: The effect of alcohol on disease activity in inflammatory arthritis remains poorly understood. Studies of alcohol and the incidence or risk of inflammatory arthritis are conflicting [1,2]. Alcohol does downregulate pro-inflammatory cytokines and may therefore reduce immune-mediated disease activity.

Objectives: This study investigates the relationship between alcohol consumption and disease activity in our inflammatory arthritis patient cohort and performs a systematic review with meta-analysis.

Methods: *Cohort Study Design and data analysis*

Patients attending a rheumatology clinic between 2010-2020 were prospectively followed. Information on demographics, alcohol use, smoking habits, and disease outcome measures were collected. Statistical analysis included univariate and multivariate linear and binary logistic regressions, Mann Whitney-U tests, and one-way ANOVA with Tukey's HSD.

Meta-analysis

EMBASE, Pubmed, the Cochrane library, and Web of Science were searched. Studies reporting on alcohol consumption and disease activity in a cohort of RA patients were included for further investigation. Forest plots were generated from 95% confidence intervals of extracted data using mean differences. Linear regression was used to determine correlations between alcohol and antibody status, gender, and smoking status.

Results: *Cohort Study*

Of the 979 analysed patients, 62% had RA, 26.7% had PsA, and 11.2% had AS. Mean DAS28-CRP in RA and PsA at one year was 2.96 ± 1.39, and 64.2% of patients were in remission (DAS28-CRP ≤ 2.6 or BASDAI ≤ 4). Both male gender and risky drinking (>15 units of weekly alcohol) were both significantly associated with remission. Compared to women, men had an odds ratio of 1.78 [1.04, 2.52] (p=0.034) for any alcohol consumption and 6.9 [4.7, 9.1] (p=0.001) for drinking at least 15 weekly drinks. when adjusted for gender, there was no significant association between alcohol and disease activity. Yet, when adjusted for alcohol consumption, gender still influenced disease activity.

Meta-analysis

The search identified 4126 citations of which 14 were included. The pooled mean difference in DAS28 (95% CI) was 0.34 (0.24,0.44) (p<10-5) between non-drinkers and drinkers, 0.33 (0.05,0.62) (p=0.02) between non-drinkers and heavy drinkers, and 0 (-0.3,0.3) (p=0.98). between low- and high-risk drinkers. There was a significant difference in the mean difference of HAQ assessments between those who drink alcohol compared to those who do not (0.3 (0.18,0.41), p<10-5). There was no significant correlation between drinking and gender, smoking status, or antibody positivity.

Conclusion: While it appears that alcohol is linked to remission in inflammatory arthritis, this association is lost when adjusted for gender. Men with inflammatory arthritis drink significantly more than women and men generally have less severe disease activity. However, the meta-analysis suggests alcohol consumption is associated with lower disease activity and self-reported health assessment in rheumatoid arthritis.

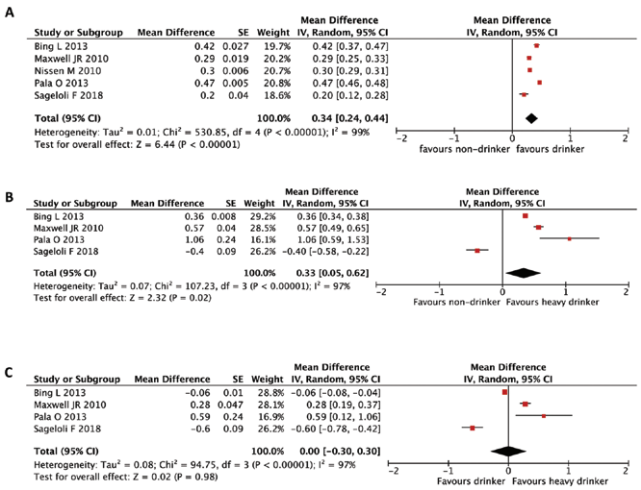


Figure 1. Mean differences in DAS28 between drinking groups. A between non-drinkers and drinkers. B between non-drinkers and high-risk drinkers. C between low-risk and high-risk drinkers.

REFERENCES:

[1] Bae S-C, Lee YH. Alcohol intake and risk of rheumatoid arthritis: a Mendelian randomization study. *Z Rheumatol* 2019;**78**:791–6. doi:10.1007/s00393-018-0537-z

[2] Scott IC, Tan R, Stahl D, *et al*. The protective effect of alcohol on developing rheumatoid arthritis: a systematic review and meta-analysis. *Rheumatology (Oxford)* 2013;**52**:856–67. doi:10.1093/rheumatology/kes376

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2099

POS0463 BEST CARDIOVASCULAR RISK CALCULATOR TO PREDICT ABNORMALITIES IN LEFT VENTRICULAR GEOMETRY IN RHEUMATOID ARTHRITIS

S. Lugo-Perez[1], J. R. Azpiri-López[1], D. Á. Galarza-Delgado[2], I. J. Colunga-Pedraza[2], N. Guajardo-Jauregui[2], A. B. Rodriguez-Romero[2], A. Cárdenas[2], J. A. Davila-Jimenez[2], H. Azpiri-Diaz[1], O. A. Cepeda-Ayala[1], A. Garcia-Heredia[1]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico*; *[2]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*

Background: A relationship between rheumatoid arthritis (RA) and the presence of abnormalities in left ventricular (LV) geometry such as eccentric remodeling has recently been determined, even in the absence of cardiovascular risk factors and before clinical manifestations (1). The 2016 European League Against Rheumatism (EULAR) recommendations that cardiovascular (CV) risk prediction models should be adapted by a 1.5 multiplication factor in RA patients. Risk prediction algorithms based on the CV risk factors (CVRF) have been an important tool for adopting preventive measures and intensifying therapies based on the estimated risk but their application in predicting cardiac structural abnormalities has never been studied.

Objectives: The aim of the study is to determine the CV risk calculator that best predicts alterations in ventricular geometry in RA.

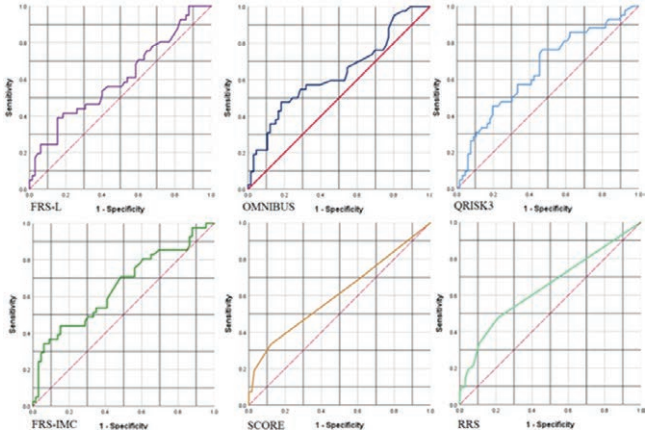
Methods: A cross-sectional, observational study of 108 RA patients between 40-75 years (ACR / EULAR 2010 classification criteria). The QRISK3, OMNIBUS, Framingham Risk Score Lipids (FRSL), Framingham Risk Score BMI (FRS-BMI) and Reynolds Risk Score (RRS) calculators were compared. The diagnostic performance was determined by ROC curves, and the discriminative capacity by the Area Under the Curve (AUC) 95% CI. The echocardiogram was the diagnostic gold standard. A *p* value <0.05 was considered statistically significant.

Results: The prevalence of abnormalities in ventricular geometry was 38.9%. QRISK3 reported AUC of 0.656, 95% CI (0.550-0.762, *p*=0.006), cut-off point ≥4.6, sensitivity of 73.8% and specificity of 54.5%, and likelihood ratio of +1.62. FRS-BMI showed AUC of 0.653, 95% CI (0.543-0.762, *p*=0.008), cut-off point ≥11.02, sensitivity and specificity of 61.9% and 57.6% respectively, and likelihood ratio of +1.46. OMNIBUS showed AUC of 0.635, CI 95% (0.525-0.746, *p*=0.018), cut-off point ≥3.8, sensitivity and specificity of 57.1% and 68.2%. While RRS had AUC 0.644, 95% CI (0.534-0.755, p=0.012), cut-off point of 2.25, sensitivity of 47.6% and specificity 78.8%, and likelihood ratio of +2.24 (Figure 1 and Table 1).

Table 1. Discriminatory capacity of the different cardiovascular risk calculators.

Calculators (cut-off point).	AUC	CI 95%		*p*	Sensitivity	Specificity
		Inferior	Superior			
QRISK (≥4.60)	0.646	0.537	0.754	**0.012**	73.8%	54.5%
SCORE	0.591	0.475	0.706	NS	-	-
OMNIBUS (≥3.80)	0.621	0.509	0.734	**0.038**	57.1%	68.2%
FRSL	0.594	0.480	0.707	NS	-	-
FRS-BMI (≥11.02)	0.642	0.530	0.754	**0.015**	61.9%	57.6%
RRS (≥2.25)	0.627	0.514	0.741	**0.029**	47.6%	78.8%

Figure 1. ROC curves of the different cardiovascular risk calculators.



Conclusion: The QRISK3 calculator showed the highest discriminative ability and sensitivity to predict abnormalities in LV geometry. However, all calculators demonstrated the need for a lower cut-off point to predict alterations in ventricular geometry. Our findings require adequate reproducibility in other population groups to determine the applicability of CV risk algorithms as predictors of structural alteration of LV.

REFERENCES:

[1] Pascale V, Finelli R, Giannotti R, et al. Cardiac eccentric remodeling in patients with rheumatoid arthritis. Sci Rep 2018;8(1):5867. doi: 10.1038/s41598-018-24323-0

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2118

POS0464 IS IT POSSIBLE TO IDENTIFY INDIVIDUALS AT IMMINENT-RISK OF SUB-CLINICAL JOINT INVOLVEMENT?

A. Di Matteo[1], K. Mankia[1], L. Duquenne[1], E. Cipolletta[2], J. Nam[1], L. Garcia-Montoya[1], R. Wakefield[1], M. Mahler[3], P. Emery[1]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom., National Institute for Health Research Leeds Biomedical Research Centre, Leeds, United Kingdom*; *[2]Polytechnic University of Marche, Rheumatology Unit,"Carlo Urbani" Hospital, Jesi, Ancona, Italy., Department of Clinical and Molecular Sciences, Jesi, Italy*; *[3]United States, Inova Diagnostics, INC, San Diego, California, USA, San Diego, United States of America*

Background: In anti-CCP antibody (Ab) positive at-risk individuals with MSK symptoms but without clinical synovitis, the detection of ultrasound (US) subclinical inflammation is associated with an increased risk of progression to inflammatory arthritis (IA) [1]. Studies suggest that in these at-risk individuals, MSK symptoms develop before subclinical joint inflammation occurs on US. As such, anti-CCP Ab positive individuals with MSK symptoms in the absence of clinical or sub-clinical inflammation may be at the critical time-point for preventive treatments, before joint inflammation occurs and eventually becomes established (i.e., before the 'second-hit' in RA pathogenesis); however, identifying these individuals is challenging.

Objectives: To identify, in second generation anti-CCP Ab (CCP2+) at-risk individuals with MSK symptoms, but without clinical or sub-clinical synovitis, predictors of US sub-clinical synovitis.

Methods: In 186 CCP2+ at-risk individuals with normal baseline US scan (i.e., no synovitis or bone erosions), and a complete dataset, US data were analyzed at 6, 12 months, then annually until occurrence of IA. US synovitis was identified according to the EULAR/OMERACT definitions[2]. Relevant demographic (age and gender), clinical [early morning stiffness (EMS), tenderness in the small joints of the hands] and serological [anti-CCP2 Ab level, third generation anti-CCP Ab

(CCP3) and rheumatoid factor (RF)] data were collected at baseline. Regression analyses, Kaplan-Meier analysis and Log-Rank test were performed.
Results: US synovitis was detected in ≥1 longitudinal US scan in 69/186 (37.1%) at-risk individuals (median time to first developing US synovitis: 53 weeks, IQR 27.0-105.8; median number of joints with US synovitis: 2.0, IQR 1.0-2.0). As shown in Table 1, only anti-CCP3 Ab were significantly associated with development of US sub-clinical synovitis in the multi-variable analysis while borderline results were observed with age.

Table 1. Regression analyses for the development of US synovitis.

	Univariable analysis		Multivariable	analysis
	OR (95% CI)	p-value	OR (95% CI)	p-value
Gender (male)	1.02 (0.52-2.02)	0.95	/	/
Age	**1.03 (1.01-1.06)**	**<0.01**	*1.03 (1.00-1.06)*	***0.03***
Tenderness in the hands	0.86 (0.46-1.61)	0.64	/	/
EMS	1.60 (0.87-2.95)	0.13	/	/
Anti-CCP2 Ab (high titre)	**2.79 (1.37-5.67)**	**<0.01**	1.20 (0.50-2.89)	0.69
Anti-CCP3+	**4.44 (2.28-8.66)**	**<0.01**	**3.30 (1.39-7.89)**	**<0.01**
RF+	**2.96 (0.46-1.61)**	**0.01**	1.45 (0.68-3.11)	0.33

CCP2+ individuals with positive anti-CCP3 Ab show a significantly reduced sub-clinical synovitis-free survival rate compared with individuals with negative anti-CCP3 Ab (Figure 1). At 1- and 2-year follow-up, respectively 23.3% and 38.3% of individuals with dual CCP2/CCP3 positivity developed sub-clinical synovitis on longitudinal scans, compared with 8.4% and 13.3% of CCP2+ individuals with negative anti-CCP3 Ab (p=0.01) (Figure 1a).

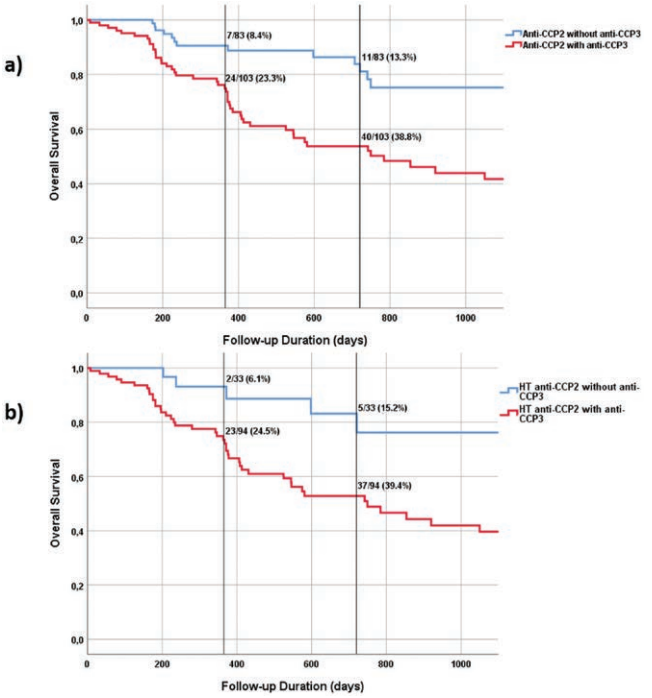


Figure 1. Kaplan-Meier analysis shows US sub-clinical synovitis free survival time in CCP2+ at-risk individuals.

Similar results were observed in the subgroup of high level CCP2+ individuals. At 1- and 2-year follow-up, respectively 24.5% and 39.4% of high level CPP2/anti-CCP3+, but only 6.1% and 15.2% of CCP2+ individuals with negative anti-CCP3 developed sub-clinical synovitis on longitudinal scans (p<0.01) (Figure 1b).
Conclusion: In anti-CCP2+ at-risk individuals with MSK symptoms, anti-CCP3 antibodies improve prediction of imminent development of subclinical joint inflammation. This may represent the critical time-point for interventions to prevent the onset of joint disease. This is also a unique population for investigating the drivers of joint involvement in the development of RA.
REFERENCES:
[1] Duquenne L, et al. The Role of Ultrasound Across the Inflammatory Arthritis Continuum: Focus on "At-Risk" Individuals. 2020.
[2] D'Agostino MA, et al. Scoring ultrasound synovitis in rheumatoid arthritis: a EULAR-OMERACT ultrasound taskforce — Part 1: definition and development of a standardised, consensus-based scoring system. 2017.
Disclosure of Interests: Andrea Di Matteo Grant/research support from: This study was conducted while Andrea Di Matteo was an ARTICULUM Fellow., Kulveer Mankia Speakers bureau: KM reports personal fees from Abbvie, UCB and Eli Lilly (all <$10.000), outside the submitted work., Grant/research support from: Research grants from BMS, Eli Lilly (all <$10.000), Laurence Duquenne: None declared, Edoardo Cipolletta: None declared, Jacqueline Nam: None declared, Leticia Garcia-Montoya: None declared, Richard Wakefield Speakers bureau: RJW has received honoraria from Abbvie, Novartis and GE for ultrasound related educational activities (all <$10.000)., Michael Mahler Employee of: MM is employee of Inova Diagnostics, commercializing CCP3, Paul Emery Speakers bureau: PE reports consultant fees from BMS, AbbVie, Gilead, Galapagos, Lilly, MSD, Pfizer, Novartis, Roche, and Samsung outside the submitted work (all <$10.000)., Grant/research support from: He also reports research grants from UCB, AbbVie, Lilly, Novartis, BMS, Pfizer, MSD and Roche, outside the submitted work. PE is National Institute for Health Research (NIHR) Biomedical Research Centre (BRC) director and BRC funds supported this work. Leticia Garcia-Montoya and Laurence Duquenne are NIHR BRC fellows.
DOI: 10.1136/annrheumdis-2021-eular.2290

POS0465 DIFFERENT CLINICAL RELEVANCE OF ANTI-CITRULLINATED PROTEINS ANTIBODIES IN RA PATIENTS

A. Avdeeva[1], M. Cherkasova[2], E. Nasonov[2]. *[1]V.A. Nasonova Research Institute of Rheumatology, Early Arthritis Laboratory, Moscow, Russian Federation; [2]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology Rheumatic Diseases, Moscow, Russian Federation*

Background: Anti-citrullinated proteins antibodies (ACPA) are a broad group of antibodies, including antibodies to citrullinated fibrinogen, antibodies to cyclic citrullinated peptide (anti-CCP), antibodies to modified citrullinated vimentin (anti-MCV), antibodies to citrullinated α-enolase.
Objectives: To find a potential relationship between ACPA and disease activity, bone destruction, and ACPAs responses to various therapeutic regimens.
Methods: The study included 232 patients (pts) with rheumatoid arthritis (RA); 90 pts (74 women, Me;IQR age 53.0 (38.0–58.5) years had early RA, with mean disease duration 5.0 (4.0–9.0) months, DAS 28 5.3 (4.4–6.1)); 142 pts had advanced stage of the disease (123 women, median age 51.0 (43.0–60.0) years, disease duration 56.0 (24.0–96.0) months, DAS 28 6.2 (5.5–6.8)). Pts with early RA received methotrexate (MTX) subcutaneously at average 17.5 mg dose once weekly. Pts with advanced RA received the following anti-B-cell therapy: 34 pts - rituximab (RTX); 20 pts - RTX biosimilar; 43 pts - tocilizumab (TCZ) in combination with conventional DMARDs. Serum anti-CCP and anti-MCV concentrations were measured using ELISA.
Results: 77 (85.6%) pts with early RA were high positive for anti-CCP, and 29 (70.7%) pts - high positive for anti-MCV. A positive correlation was found between anti-MCV and DAS 28 (r=0.4, *p*=0.04). As for advanced RA, 78 (80.4%) pts were high positive for anti-CCP, and 70 (79.5%) - for anti-MCV. There was a positive correlation between anti-MCV concentration and SDAI (r=0.4, *p*=0.02), as well as CDAI (r=0.4, *p*=0.02). No significant correlations were found between the anti-CCP levels and activity indices, anti-CCP and acute-phase parameters in both early and advanced RA groups. Higher total Sharp scores (96.5 (65.0-122.0)) were found in pts high positive for anti-MCV (n=79), compared to low-positive/negative (57.0 (31.0–88.0), respectively, (n=27, *p*<0.05). anti-MCV levels dropped significantly in pts on RTX and TCZ therapy at weeks 12 and 24 after initiation of treatment, while high anti-CCP concentration persisted throughout the treatment (Table 1)

Table 1.

Indicators	Anti-CCP, U/ml	Anti-MCV, U/ml
RTX group, *n*=34		
- baseline	100,0 (37,9–100,0)	559,4 (139,2–1000,0)
- 12 weeks	100,0 (26,1–100,0)	295,9 (74,0–962,7) [1]
- 24 weeks	100,0 (29,0–100,0)	194,7 (58,3–844,8) [1]
RTX biosimilar group, *n*=20		
- baseline	112,7 (18,3–264,8)	392,6 (75,7–1000,0)
- 12 weeks	71,7 (12,4–161,6)	210,5 (40,3–940,6) [1]
- 24 weeks	61,3 (13,12–129,4)	153,8 (43,1–702,8)
TCZ group, *n*=43		
- baseline	354,8 (67,9–500,0)	762,3 (106,9–2393,1)
- 8 weeks	500,0 (84,4–500,0) [1]	266,6 (85,8–927,0) [1]
- 24 weeks	355,8 (39,8–500,0)	135,7 (27,0–662,1) [1]

Note: [1] *p*<0,05 vs baseline

Conclusion: anti-MCV levels correlated with inflammatory activity and development of bone destruction, and were decreasing in pts on treatment. Anti-CCP was less responsive, showed minor changes during treatment, therefore its' thorough monitoring was not feasible.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2320

POS0466 RHEUMATOID ARTHRITIS PER SE IS NOT RISK FACTOR FOR CLINICAL FRACTURES: NINE-YEAR FINDINGS OF THE TOMORROW STUDY

K. Mamoto[1], T. Koike[2,3], Y. Yamada[1], T. Okano[1], Y. Sugioka[2], M. Tada[4], K. Inui[5], H. Nakamura[1]. *[1]Osaka City University Graduate School of Medicine, Department of Orthopaedic Surgery, Osaka, Japan*; *[2]Osaka City University Medical School, Center for Senile Degenerative Disorders (CSDD), Osaka, Japan*; *[3]Shirahama Foundation for Health and Welfare, Search Institute for Bone and Arthritis Disease (SINBAD), Wakayama, Japan*; *[4]Osaka City General Hospital, Department of Orthopaedic Surgery, Osaka, Japan*; *[5]Osaka Saiseikai Nakatsu Hospital, Department of Orthopaedic Surgery, Osaka, Japan*

Background: Patients with rheumatoid arthritis (RA) who have sarcopenia and stiff or painful joints might be at increased risk of falls and fractures.
Objectives: The present study aimed to prospectively identify the incidence of clinical fractures and associated risk factors in patients with RA in a cohort study named the TOMORROW (UMIN000003876) that started in 2010.
Methods: We evaluated anthropometric parameters, bone mineral density (BMD), disease activity, RA medication at baseline and observed the incidence of clinical fractures during nine years in 202 patients with RA (mean age, 58.6 y; medication with biological agents, 54.9%) and 202 age- and sex-matched non-RA volunteers (mean age, 57.4 y). We compared the incidence of clinical fractures between patients with RA and controls for nine years, and analyzed the risk factors for fractures using Cox proportional hazard model.
Results: The incidence of clinical fractures in RA patients was significantly higher compared to controls (27.5 vs 18.3%, p=0.04). However, Cox proportional hazard model, adjusted by age, sex, smoking and body mass index, revealed that low BMD at thoracic vertebrae (< 0.7 g/cm^2) significantly associated to the incidence of clinical fractures (hazard ratio [HR], 1.86, p=0.02), but not RA morbidity (HR 1.47, p=0.10) (Table 1). Among patients with RA, low BMD at the thoracic vertebrae (< 0.7 g/cm^2) was the most prominent risk factor for clinical fractures (HR, 2.66, p=0.02) (Table 1). Although the use of glucocorticoid (GC) at baseline (HR, 1.68, p=0.09) was not a significant risk factor for fractures, a mean GC dose (≥ 2 mg/day) at entry increased risk for clinical fractures in the patients (HR, 1.91, p=0.04) (Table 1).

Table 1. Cox proportional hazard model (adjusted for fracture risk factors including age, sex, smoking, and body mass) of risk factors for clinical fractures.

		hazard ratio	95% CI	*p*
All participants	History of fractures	0.24	0.77-1.98	0.38
N=404	Morbidity of RA	1.47	0.92-2.34	0.10
	Low BMD at thoracic vertebrae (< 0.7 g/cm^2)	1.86	1.09-3.17	0.02
RA patients	History of fractures	1.27	0.70-2.29	0.43
N=202	GC medication	1.68	0.92-3.06	0.09
	A mean GC dose ≥ 2 mg/day at entry	1.91	1.05-3.49	0.04
	Low BMD at thoracic vertebrae (< 0.7 g/cm^2)	2.66	1.20-5.89	0.02

CI, confidence interval; RA, rheumatoid arthritis; GC, glucocorticoid; BMD, bone mineral density.

Conclusion: RA per se was not a risk factor for clinical fractures in this cohort. Low BMD at the thoracic vertebrae and the use of GC with even low dose at entry were apparently significant risk factors for the incidence of clinical fractures among patients with RA.
Disclosure of Interests: Kenji Mamoto: None declared, Tatsuya Koike Grant/ research support from: Takeda Pharmaceutical, Mitsubishi Tanabe Pharma Corporation,
Chugai Pharmaceutical, Eisai, Abbott Japan, Teijin Pharma, Banyu Pharmaceutical and Ono Pharmaceutical, Yutaro Yamada: None declared, Tadashi Okano: None declared, Yuko Sugioka: None declared, Masahiro Tada: None declared, Kentaro Inui Speakers bureau: Daiichi Sankyo Co. Ltd., Mitsubishi Tanabe Pharma, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Takeda Pharmaceutical Co. Ltd., Ono Pharmaceutical Co. Ltd., Abbvie GK, Pfizer Inc., Eisai Co.,Ltd., Chugai Pharmaceutical Co., Ltd., Grant/research support from: Janssen Pharmaceutical K.K., Astellas Pharma Inc., Sanofi K.K., Abbvie GK, Takeda Pharmaceutical Co. Ltd., QOL RD Co. Ltd., Mitsubishi Tanabe Pharma, Ono Pharmaceutical Co. Ltd., Eisai Co.,Ltd., Hiroaki Nakamura: None declared
DOI: 10.1136/annrheumdis-2021-eular.2331

POS0467 STUDY OF METHOTREXATE METABOLITES CONCENTRATIONS IN RED BLOOD CELLS AND MONONUCLEAR CELLS IN RHEUMATOID ARTHRITIS

V. Sygyrta[1], G. Gridneva[1], A. Lila[1], E. Samarkina[1], N. Baymeeva[2], Y. Muraviev[1], E. Aronova[1], A. Kudryavtseva[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Antirheumatic Drugs Safety Monitoring Laboratories, Moscow, Russian Federation*; *[2]Mental Health Research Center, Mental Health Research Center, Moscow, Russian Federation*

Background: Studying the dynamics of the methotrexate metabolites concentration in cells will help to predict the therapeutic effect and assess patient compliance. We suggest that studying the dynamics of changes in the concentration of methotrexate metabolites in mononuclear cells (MO) may be a more accurate method than measuring in red blood cells (RBC).
Objectives: To study the dynamics of changes in the concentration of MTX and its metabolites in RBC and MO in methotrexate-naive patients with RA.
Methods: 33 patients (26 women, 7 men) aged 53.2 ± 11.7 years with a diagnosis of rheumatoid arthritis, according to the ACR / EULAR 2010 criteria, were included. All patients had GFR >60 ml/min. Patients were monitored after 4, 12, 24 and 36 weeks from the start of MTX. Mean Cell Volume (MCV) of RBC was measured by standard methods. Samples of RBC and MO were collected separately to determine the concentrations of MTX (basic monoglutamate form), total concentration of MTPG2, MTPG3 and MTPG4 (MTPG2-4), 7- hydroxymethotrexate (7-OH-MTX) by tandem mass spectrometry.
RESULTS:
A pairwise comparison of MTX, MTPG2-4 and 7-OH-MTX concentrations, according to the Wilcoxon method did not reveal statistically significant differences at weeks 4, 12 and 24. The concentration of the studied substances did not correlate with the value of the body mass index, taking statins, glucocorticoids, a cumulative dose of MTX, and the frequency of adverse reactions. At the week 4, of therapy, the level of MTPG4 in MO was inversely correlated with the duration of the disease (correlation coefficient - 0.58, p 0.05) The concentration of MTX and its metabolites in MO was lower in smokers (MTX 11.2 [2.6;21.9], 7-OH-MTX 2.1 [0.5; 10.4], MTPG2 0.5 [0.1;1.3]) than in non-smokers (MTX 46.5 [25.3;97.5], 7-OH-MTX 28.2 [7.1; 64.7], MTPG2 8.2 [4.1;32.9]), p = 0.02, 0.01 and 0.003, respectively. At week 24 of therapy, a negative correlation was found between age and MTPG4 level (correlation coefficient 0.51, p <0.05).

Table 1. Total concentration of MTPG2, MTPG3 and MTPG4 (MTPG2-4), nmol/l

		Me	[25;75]	Min	Max
Week 4	RBC	42.8	19.0;155.0	3	987.7
	MO	6.2	5.3;11.9	1.6	147.2
Week 12	RBC	48.1	17.1;89.0	0.1	519.9
	MO	10.9	3.9;31.0	0.9	147.6
Week 24	RBC	39.4	17.2;70.6	2.7	191.8
	MO	8.3	2.7;14.0	0.4	72.4

Conclusion: The inadequate response to MT therapy in smokers, described in many previous studies,
may be associated with a low concentration of the MTX metabolites in mononuclear cells.
The level of MTPG4 in mononuclear cells increases more slowly in patients with a longer duration of the disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2351

POS0468 PREDICTION OF RHEUMATOID ARTHRITIS DISEASE ACTIVITY BY AN ADAPTIVE DEEP NEURAL NETWORK: BETTER RESULTS IN SEROPOSITIVE PATIENTS WITH LONGER DISEASE DURATION

M. Hügle[1], G. Kalweit[1], J. Boedecker[1], R. Muller[2], A. Finckh[3], A. Scherer[4], U. Walker[5], T. Hügle[6]. *[1]University of Freiburg, Department of Computer Science, Freiburg, Germany*; *[2]Kantonsspital Aarau, Department of Rheumatology, Aarau, Switzerland*; *[3] University Hospital Genev, Division of Rheumatology, Geneva, Switzerland*; *[4]SCQM Foundation, Rheumatology, Zürich, Switzerland*; *[5]University Hospital Basel, Department of Rheumatology, Basel, Switzerland*; *[6]Lausanne University Hospital, CHUV, Department of Rheumatology, Lausanne, Switzerland*

Background: Deep neural networks learn from former experiences on a large scale and can be used to predict future disease activity as potential clinical decision support. AdaptiveNet is a novel adaptive recurrent neural network optimized to deal with missing clinical data. In rheumatoid arthritis (RA) it is unknown how disease characteristics influence the predictability by deep learning in terms of classification (e.g. active disease yes/no) or regression (numeric values such as DAS28).
Objectives: To investigate in which clinical RA subtypes AdaptiveNet achieves the best results for the prediction of individual disease activity
Methods: Demographic and disease characteristics from over 9500 patients and 65.000 visits from the Swiss Quality Management (SCQM) database were used to train and evaluate the network. Patient characteristics, clinical and patient reported outcomes, laboratory values and medication were used as input features. DAS28-BSR served as a target to predict active RA and future numeric individual disease activity by classification and regression. Feature importance

was determined by a Random Forest to define the relative importance of variables for disease prediction.
Results: AdaptiveNet predicted active disease defined as DAS28-BSR >2.6 at the next visit with an overall accuracy of 75.6% (SD +- 0.7%) and a sensitivity and specificity of 84.2% (SD +- 1.6%) and 61.5% (SD +- 3.6%), respectively. The performance of the prediction for correct disease status was significantly higher in patients with a disease duration >3 years and positive rheumatoid factor. Regression allowed forecasting individual DAS28-BSR values with a Mean Squared Error (MSE) of 0.9 (SD +- 0.05). Compared to Linear Regression, Random Forests and Support Vector Machines, AdaptiveNet showed an increased performance of 7% in MSE. MSE was significantly lower in patients with disease duration > 3 years and with positive anti-CCP antibodies. Feature importance identified number of painful joints, longer disease duration and age as most relevant factors for prediction of remission, whereas medication played a smaller role.
Conclusion: Predictability of disease activity in RA by this deep neural network was stronger in patients with a longer disease history and a positive auto-antibody status, potentially due to a more stable disease course. Generally, AdaptiveNet had a superior capacity to predict numeric RA disease activity compared to classical machine learning architectures, however all investigated models had limitations in low specificity.
REFERENCES:
[1] Hügle M, Kalweit G, Hügle T, Boedecker J. Dynamic Deep Neural Network For Multimodal Clinical Data Analysis. Stud Comput Intell: Springer Verl. 2020.
Acknowledgements: We thank all rheumatologists and their patients for participation to SCQM.The entire SCQM staff was instrumental for data management and support.
A list of rheumatology practices and hospitals that are contributing to the SCQM registries can be found on http://www.scqm.ch/institutions.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2370

POS0469 FALL RISK ASSESSMENT IN RHEUMATOID ARTHRITIS PATIENTS

O. Jomaa[1], H. Migaw[2], I. Loubiri[2], M. Slama[2], S. Zrour[1], I. Bejia[1], M. Touzi[1], J. Mahbouba[1], N. Bergaoui[1]. *[1]University Hospital Fattouma Bourguiba Monastir, TUNISIA, Rheumatology Department, Monastir,Tunisia*; *[2]University Hospital Fattouma Bourguiba Monastir,TUNISIA, Physical Medicine and Functional Rehabilitation Department, Monastir,Tunisia*

Background: Rheumatoid arthritis patients may have an increased risk of falls due to changes caused by the disease such as muscle weakness, joint impairment, reduced mobility and postural instability.
Objectives: The aim of this study was to analyze the occurrence of falls in RA patients and its risk factors.
Methods: Between January2020 and July 2020, 51 patients with RA were included in the study. fall history, and the number of falls within the past 12 month were questioned. All participants were assessed with Timed Up and Go Test (TUGT), One-Leg Stand Test (OLST), Walking and Talking Test (WTT), Sternal Push Test (SPT), Tinetti Test (TT), Four Test Balance Scale (FTBS), The Short Falls Efficacy Scale-International (FES-I), Pain Severity and Patient Global Assessment (PGA) by Visual Analog Scale (VAS), disability by the Health Assessment Questionnaire (HAQ), and disease activity by Disease Activity Score in 28 joints (DAS28) were evaluated in for for each patient. The Kolmogorov-Smirnov, Mann-Whitney and chi-square tests were performed with a significance level of $P \leq 0.05$.
Results: 22 patients had at least one or more falls. The average age was 54.9±11.5 years with a female predominance (sex ratio = 0.13). Comparing the two groups of patients: those with a history of falls and those without, patients with previous falls were mainly married women (p=0.57), with a low intellectual level (p=0.63). The body mass index in this group was higher (p=0.01) with respectively a higher number of painful and swollen joints (p=0.16, p=0.07); the mean HAQ was higher (p=0.03), and the mean VAS was more important (p=0.05). 12/22 patients had co-morbidities and were poly-medicated.20/22 had joint feet deformities (hallux valgus was the most common deformity). 21/22 were on low dosage corticosteroid therapy. The mean TUGT was 18.5 seconds (>14 seconds). The OLST was less than 5 seconds in 12/22, the sternal push test was positive in 9/22, WTT was positive in 6/22 and the mean tinetti test was 22.4±5.4 suggesting a high risk of falls. The average Short FES-I was 14.6 ±4.4 reflecting a high fear of falls in this group of patients.
Conclusion: Knowledge about risk factors can help to identify high-risk patients in order to decrease their risk of falling, thus preventing fall-related injuries.
DOI: 10.12659/MSM.921862
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2395

POS0470 GLUCOCORTICOID DISCONTINUATION IN EARLY RHEUMATOID AND UNDIFFERENTIATED ARTHRITIS PATIENTS. A SUB-ANALYSIS OF THE BeSt AND IMPROVED STUDIES

J. M. Maassen[1], R. Dos-Santos[2], S. A. Bergstra[1], R. Goekoop[3], T. Huizinga[1], C. Allaart[1]. *[1]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[2]Clinical University Hospital, Rheumatology, Santiago de Compostela, Spain*; *[3]Haga Hospital, Rheumatology,The Hague, Netherlands*

Background: Discontinuation of glucocorticoids (GC) as bridging therapy in rheumatoid arthritis (RA) treatment is recommended as rapidly as clinically feasible. Little is known about the rate of, and possible characteristics associated with successful GC discontinuation.
Objectives: To evaluate the success rate of GC discontinuation, and to study which factors are associated with successful GC discontinuation.
Methods: Data from two treat-to-target studies; BeSt (target DAS ≤2.4, LDA), and IMPROVED (target DAS <1.6, remission) were evaluated for all patients initially treated with a tapered high-dose of oral GC with conventional DMARD(s). GCs were discontinued when DAS ≤2.4 was maintained for 28 weeks in BeSt, and as soon as DAS was <1.6 in IMPROVED. GC discontinuation could be attempted twice: first attempt called 'primary', second attempt after GC restart called 'secondary'. Discontinuation was considered successful if the treatment target was maintained at the next visit. Univariable, and exploratory forward and backward multivariable logistic regression analyses were performed to identify potential characteristics associated with successful discontinuation (p-value <0.2 included in final model).
Results: From the 131 patients initiating combination therapy with prednisone in the BeSt study, 93 attempted discontinuation. Primary discontinuation was successful in 60% (56/93) and secondary discontinuation in 54% (19/35). A lower DAS at the visit prior to GC discontinuation and ACPA negativity were associated with successful discontinuation (table 1). Of the 610 patients in the IMPROVED, 400 attempted discontinuation. Primary discontinuation was successful in 61% (242/400), and secondary in 51% (71/139). A lower DAS both at baseline and at the visit prior to GC discontinuation were associated with successful discontinuation (table 1).
Conclusion: Primary GCs discontinuation was successful in approximately 60% and secondary in 50% of patients, independent of the treatment target and associated threshold for GC discontinuation. Most baseline characteristics were not predictive of successful GC discontinuation, but ACPA negativity (only in BeSt), baseline DAS (only in IMPROVED) and in both studies DAS prior to GC discontinuation were predictive for successful discontinuation. Based on this data it seems that 'standard' baseline characteristics are insufficient to 'personalize' the duration of temporary GC bridging but the DAS at the moment of GC discontinuation might give guidance.

Table 1. Results logistic regression analyses

	Univariable		**Multivariable [a]** $R^2 = 0.173$	
BeSt	OR (95% CI)	p-value	OR (95% CI)	p-value
Age, year	1.00 (0.98; 1.03)	0.98		
Gender, female	0.51 (0.24; 1.09)	0.08		
Symptom duration BL, weeks	1.00 (0.99; 1.01)	0.61		
DAS at BL	0.92 (0.61; 1.40)	0.70		
DAS prior to discontinuation	**0.13 (0.05; 0.33)**	**<0.01**	**0.11 (0.04; 0.30)**	**<0.01**
RF, positive	1.28 (0.62; 2.69)	0.50	2.24 (0.81; 6,17)	0.12
ACPA, positive	0.70 (0.34; 1.43)	0.32	**0.32 (0.12; 0.86)**	**0.02**
Erosions, present at BL	0.65 (0.28; 1.49)	0.31		
	Univariable		**Multivariable [a]** $R^2 = 0.065$	
IMPROVED	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Age, year	1.00 (0.99; 1.02)	0.64		
Gender, female	**0.62 (0.43; 0.89)**	**0.01**	0.75 (0.51; 1.11)	0.15
Symptom duration BL, weeks	1.00 (0.99; 1.00)	0.43	0.99 (0.99; 1.00)	0.08
DAS at BL	**0.80 (0.65; 0.98)**	**0.03**	**0.78 (0.62; 0.98)**	**0.03**
DAS prior to discontinuation	**0.24 (0.15; 0.38)**	**<0.01**	**0.24 (0.14; 0.40)**	**<0.01**
RF, positive	0.82 (0.57; 1.17)	0.27		
ACPA, positive	0.95 (0.66; 1.35)	0.76		
Erosions, present at BL	0.80 (0.49; 1.29)	0.35		

ACPA: anti-citrullinated protein antibodies; BL: baseline; DAS: disease activity score; RF: rheumatoid factor. [a] The final multivariable logistic regression model was based on stepwise forward and backward selection of predictors, both resulting in the same final model.

Acknowledgements: We would like to thank all patients for their contribution as well as the rheumatologists who participated in the BeSt study group and in the IMPROVED-study group. We would also like to thank all other rheumatologists

and trainee rheumatologists who enrolled patients in these studies, and all research nurses for their contributions.

Disclosure of Interests: Johanna M. Maassen: None declared, Raquel Dos-Santos: None declared, Sytske Anne Bergstra: None declared, Robbert Goekoop: None declared, Thomas Huizinga: None declared, Cornelia Allaart Grant/research support from: The original BeSt study was realized with a government grant from the Dutch College of Health Insurance Companies, with additional funding from Schering-Plough and Janssen. the IMPROVED study was financially supported by AbbVie in the first year.

DOI: 10.1136/annrheumdis-2021-eular.2442

POS0471 ASSOCIATION OF HLA-DRB1 HAPLOTYPES WITH CARDIOVASCULAR MORTALITY IN INFLAMMATORY POLYARTHRITIS: RESULTS FROM THE NORFOLK ARTHRITIS REGISTER

S. Sharma[1], D. Plant[1], J. Bowes[1], A. MacGregor[2,3], S. Verstappen[1,4], A. Barton[1,4], S. Viatte[1,5]. *[1]Centre for Genetics and Genomics Versus Arthritis, Centre for Musculoskeletal Research, Manchester, United Kingdom*; *[2]Norwich Medical School, University of East Anglia Faculty of Medicine and Health Sciences, Norwich, United Kingdom*; *[3]Rheumatology Department, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom*; *[4]NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, Manchester, United Kingdom*; *[5]Lydia Becker Institute of Immunology and Inflammation, Faculty of Biology, Medicine and Health; The University of Manchester, Manchester, United Kingdom*

Background: Haplotypes defined by amino acids at HLA-DRB1 positions 11, 71 and 74 associated with susceptibility to rheumatoid arthritis (RA), are associated with radiological outcome, anti-TNF response and all cause-mortality in RA.(*1, 2*) RA is associated with cardiovascular (CV) morbidity and mortality, but the increased prevalence of risk factors of CV disease in RA only partially explains this association.

Objectives: The aim was to investigate whether haplotypes associated with RA disease susceptibility and disease severity are also associated with CV mortality.

Methods: The Norfolk Arthritis register (NOAR) is a primary care-based inception cohort of patients with inflammatory polyarthritis (IP).(*1, 2*) NOAR patients with at least 2 years of follow-up and available mortality and genetic data were included in this study. Mortality data was provided by the Office for National Statistics.

Univariate Cox proportional hazard models were applied using STATA/IC 14.0. Models for CV mortality were adjusted for CV risk factors selected using stepwise regression: namely obesity, gender and hypertension. Hazard models were applied to the entire cohort of patients with inflammatory polyarthritis (IP). When calculating differences between highest and lowest risk genetic factors, bivariate analysis was used.

Results: HLA-DRB1 amino acids, haplotypes or haplotype groups associated with RA susceptibility are also associated with CV mortality as shown in the table 1. HLA-DRB1 polymorphisms encoding amino-acid haplotypes associated with an increased or decreased susceptibility to RA consistently show the same magnitude and direction of association for overall and CV mortality in IP. For example, the SEA-haplotype, associated with the lowest susceptibility to RA, and the best radiographic outcome, was found to be associated with decreased CV mortality (HR 0.67, 95% CI 0.47, 0.91, p=0.023). The relative difference in CV mortality between carriers of the high susceptibility VKA haplotype and carriers of the SEA haplotype was significant (HR 1.67, 95% CI 1.13, 2.48, p=0.01).

Table 1. ***Hazard ratios for CV mortality by genetic factors among patients with IP. Total number (n) of deaths are also displayed alongside the total number (n) of patients included in each analysis.***

Amino acid / Haplotype /Group	Hazard Ratio (95% CI)	N
valine 11	1.10 (0.93, 1.30)	343 (2514)
serine 11	0.82 (0.70, 0.96)*	343 (2514)
Difference	*1.23 (1.01, 1.49)**	
VKA haplotype	1.16 (0.94, 1.43)	310 (2328)
SEA haplotype	0.67 (0.47, 0.94) *	310 (2328)
Difference	*1.67 (1.13, 2.48)**	
Group 1 †	1.10 (0.93, 1.31)	319 (2328)
Group 4 †	0.73 (0.60, 0.89)*	319 (2328)
Difference	*1.37 (1.09, 1.72)**	

** p<0.05† Haplotype groups as defined previously (2)*

HLA-DRB1 haplotypes can be ranked according to the magnitude of their association with RA susceptibility and this hierarchy is conserved for various measures of disease outcome and overall mortality.(*2, 3*) The figure 1 shows that this risk hierarchy is also conserved for CV mortality: HLA-DRB1 haplotypes that predispose to RA also predispose to increased CV mortality, independent of known CV risk factors.

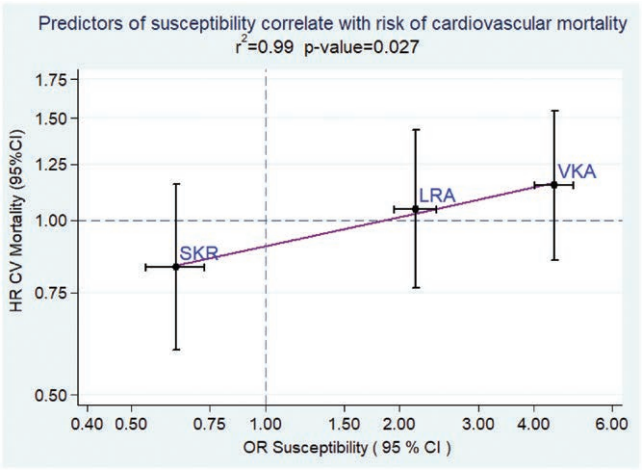


Figure 1. Haplotypes with frequency >12% in NOAR are shown. X axis: susceptibility to ACPA-positive RA as ORs.(2) Y axis: CV mortality risk in IP as HRs, derived from multi-variate cox-proportional hazard models adjusted for CV risk factors. Values are on a logarithmic scale. A one-tailed p value was calculated using linear regression to determine the association between β coefficients of susceptibility and CV mortality.

Conclusion: The originally reported genetic associations between HLA-DRB1 polymorphisms and overall mortality were likely driven by associations with CV mortality.

REFERENCES:

[1] S. Viatte *et al.*, *JAMA* **313**, 1645-1656 (2015).
[2] S. Raychaudhuri *et al.*, *Nat Genet* **44**, 291-296 (2012).
[3] D. P. Symmons, A. J. Silman, *Clin Exp Rheumatol* **21**, S94-99 (2003).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2481

POS0472 COMPARATIVE METABOLOMIC ANALYSIS OF SERUM SAMPLES FROM PATIENTS WITH COINCIDENTAL RHEUMATOLOGICAL AND MALIGNANT DISEASES

D. Marx[1], L. Diekmann[1], K. Klika[2], H. M. Lorenz[1], K. Benesova[1], M. Souto-Carneiro[1]. *[1]Heidelberg University Hospital, Medicine 5 - Rheumatology, Heidelberg, Germany*; *[2]DKFZ Heidelberg, Molecular Structure Analysis, Heidelberg, Germany*

Background: Rheumatic and musculoskeletal diseases (RMDs) and malignancies are both caused by a dysfunctional immune system and the probability of their coincidence in one individual is rising due to advances in cancer treatment and demographic changes. However, the lack of understanding of the complex interrelationship of both conditions often leads to undertreatment and high level of suffering in affected patients. Herein, the MalheuR project breaks new ground by systematic analysis of concomitant malignant and rheumatic diseases and closes the knowledge gaps on the clinical and molecular level.

Objectives: To enable early diagnosis of concomitant malignancy and/or identification of patients at risk in the future, changes in serum metabolome were explored in order to create a diagnostic classification model.

Methods: Serum samples from patients with concomitant RMD and cancer or obligate precancerous lesions (n=78, breast cancer (23), melanoma (14), MGUS (12), prostate cancer (8) and others (21)) were collected as a pilot study within the MalheuR project, a registry-based study initiated in 2018 at the university hospital Heidelberg, Germany. The following groups were defined by the underlying RMD: rheumatoid arthritis (n=42), psoriasis arthritis (n=23), spondylarthritis (n=9) and systemic lupus erythematosus (n=4). RMD patients without any malignancies were used as controls (n=280: 122 RA, 81 PsA, 46 SpA, 31 SLE).

Samples were analyzed by 1H NMR spectroscopy. For all samples, regular 1H acquisition with presaturation and Carr-Purcell-Meiboom-Gill (CPMG) spectra were acquired using a 600 MHz Bruker NMR spectrometer. Spectra were processed with TopSpin using 0.2 Hz of line broadening and manual phasing. Molar concentrations of 26 metabolites were acquired by integration of NMR spectra. With GraphPad Prism, univariate and ANOVA statistical analysis was performed to find significant differences between each malignant group and their control group as well as between all four malignant groups.

Results: Mean disease duration was 11.8 ±10.5 years for cancer and 12.8±10.8 years for RMDs since diagnosis. 1.4% received cancer treatment (6.4% of malignancy group), 69.3% csDMARDs, 42.3% b/tsDMARDs and 46.4% glucocorticoids at the time of sample collection.
Most metabolites tested were significantly lower in the malignancy groups versus associated controls: Concentrations of amino acids V and L were significantly reduced in all malignancy samples. Additionally, T, D, N, Q, E, A, I were altered in RA, SpA and PsA, changes in G were seen in RA, PsA and SLE and P was altered in RA and PsA only. Furthermore, lower concentrations of short chain fatty acids and tricarboxylic acid cycle intermediates were present in the malignancy groups. In no case was a metabolite concentration significantly higher in the malignancy group than in the associated control. When comparing the metabolome within the four malignancy groups, only the concentrations of creatine, threonine and isoleucine were found higher in RA patients with malignancy.
Conclusion: Significant differences between the metabolomic fingerprints of RMD patients with and without malignancies could be observed. These changes might be characteristic for cancer burden, as in most cases the underlying RMD was not relevant when comparing the concentrations between the malignancy groups. Our results may promote understanding of the interrelationships of both disease entities as well as prove useful as biomarkers for diagnostic and therapeutic purposes.
Acknowledgements: Grant/research support from medical faculty (Olympia Morata Programme) and foundations commission (Herbert Daus estate) of University of Heidelberg
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2484

POS0473 AUTOIMMUNITY AGAINST COLLAGEN IN RHEUMATOID ARTHRITIS (RA): SERUM LEVELS OF IgG AGAINST DENATURED TYPE II COLLAGEN SIGNIFICANTLY ELEVATED IN RA

P. Drobinski[1], E. Aighobahi[2], A. C. Bay-Jensen[3], M. Karsdal[3]. [1]*University of Copenhagen/Nordic Bioscience, Department of Biomedical Sciences, Copenhagen, Denmark*; [2]*Technical University of Denmark, Department of Biotechnology and Biomedicine, Copenhagen, Denmark*; [3]*Nordic Bioscience, ImmunoScience, Herlev, Denmark*

Background: The presence of autoantibodies in Rheumatoid Arthritis (RA) is a hallmark of the disease and one of main criteria for diagnosis and clinical classification. Identification of anti-citrullinated protein antibodies (ACPA) and RF-Factors in circulation of RA patients remains the most characteristic and established criteria for diagnosis. However, due to diagnostic limitation of these biomarkers, only approximately 70% of patients with RA can be identified. As a consequence, there is a lack of diagnostic biomarkers for large number of patients. Diagnosis of these patients relies mainly on assessment of their clinical symptoms such as swollen and tender joints. This problem leaves a need for diagnostic improvement and development of more sensitive biomarkers.
Objectives: In this study, we aimed to develop a sensitive biomarker assay capable to identify and quantify presence of autoantibodies against denatured type II collagen in circulation of patients with RA.
Methods: The presence and levels of autoantibodies was measured in serum samples from 50 patients with moderate to severe RA who had inadequate response to Methotrexate (average age 51.2, 86% of female, 78% of white race patients). Control cohort involved serum from 42 healthy age matched patients (average age 48.6, 50% of female, 60% of white race patients). Denaturation of the type II collagen was performed by heat treatment for 15 min at 72 °C. Improvement of assay sensitivity was investigated by measurements of autoimmunity levels against denatured and native type II collagen. Assay specificity was assessed by comparison of presence of autoantibodies against type II collagen versus albumin (non-sense control). The normality of data distribution was checked with Shapiro-Wilk test, significance between cohorts with Mann-Whitney nonparametric test and correlations with Spearman's correlation coefficient (rho).
Results: Serum levels of autoantibodies against denatured type II collagen were significantly higher in RA patients than in healthy controls ($P < 0.0001$) (Figure 1). We observed nearly 4-fold difference between both cohorts. Denaturation of type II collagen showed high improvement of assay sensitivity and increased accessibility of collagen for binding of autoantibodies. Developed assay showed specificity for detection of type II collagen autoantibodies by displaying no levels of autoimmunity against other control proteins (albumin). The levels of serum autoantibodies correlated significantly ($P < 0.03$) with patient disease activity (DAS28) at baseline, displaying rho = 0.3. Our assay showed good technical performance with acceptable inter- and intra- assay variations (18% and 5% respectively).

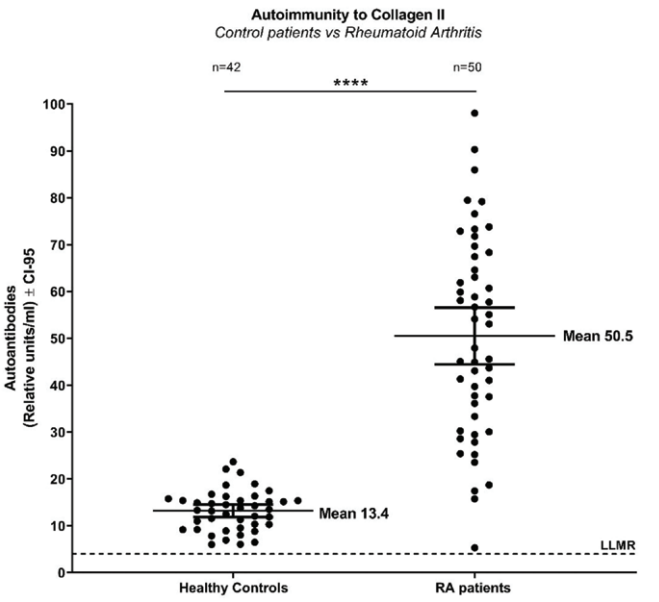


Figure 1. Differences in serum levels of autoantibodies against denatured type II collagen between healthy controls and patients with Rheumatoid Arthritis.

Conclusion: Present findings show that patients with RA carry upregulated levels of circulating autoantibodies directed against type II collagen. Heat-treatment of type II collagen increased exposure of immunogenic epitopes of collagen and enabled for more sensitive detection of autoantibodies directly in patient serum. Developed assay demonstrated potential for specific detection of autoantibodies and may provide additional diagnostic value in RA patients.
Disclosure of Interests: Patryk Drobinski: None declared, Elijah Aighobahi: None declared, Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, Morten Karsdal Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S
DOI: 10.1136/annrheumdis-2021-eular.2488

POS0474 SUBSTANTIAL IMPACT OF AUTOANTIBODY ENRICHMENT ON OUTCOMES IN EARLY RHEUMATOID ARTHRITIS TREATED WITH ABATACEPT: DATA FROM A LARGE POOLED ANALYSIS OF 4 RCTS

K. Michaud[1,2], S. S. H. Park[3], K. Lozenski[4], J. Vaile[5], V. Khaychuk[6], J. Pope[7], P. G. Conaghan[8,9]. [1]*University of Nebraska Medical Center, Internal Medicine Division of Rheumatology, Omaha, NE, United States of America*; [2]*FORWARD, The National Data Bank for Rheumatic Diseases, Wichita, KS, United States of America*; [3]*Bristol-Myers Squibb, US HEOR, Princeton, NJ, United States of America*; [4]*Bristol-Myers Squibb, Medical Data Generation, Princeton, NJ, United States of America*; [5]*Bristol-Myers Squibb, Worldwide Medical, Princeton, NJ, United States of America*; [6]*Bristol-Myers Squibb, US Medical Immunology and Fibrosis, Princeton, NJ, United States of America*; [7]*Western University, Schulich School of Medicine, Division of Rheumatology, London, Ontario, Canada*; [8]*University of Leeds, Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [9]*Leeds Teaching Hospitals NHS Trust, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*

Background: Biomarkers are commonly used as prognostic tools in rheumatoid arthritis (RA) and have additional potential to guide treatment decisions. Previous clinical trials of abatacept (ABA) such as the Early AMPLE trial (eAMPLE) and real-world data suggest differential treatment effects of ABA based on the presence of biomarkers and disease stage.[1-4]
Objectives: To supplement evidence of enhanced efficacy of ABA among patients with enriched autoantibody biomarkers and early disease stage by applying key inclusion criteria from the eAMPLE trial retrospectively to historic ABA RCTs.
Methods: Individual patient data (IPD) from four early-RA ABA trials (AGREE [NCT00122382], AMPLE [NCT00929864], AVERT [NCT01142726], AVERT-2 [NCT02504268]) were pooled. Patients were defined as enriched at baseline if they had: 1) RA disease duration ≤ 12 months, 2) DAS28-CRP ≥ 3.2, 3) ≥ 3 times the upper limit of normal on an anti-cyclic citrullinated peptide (anti-CCP) test, and 4) were rheumatoid factor positive (RF+). Patients were grouped according to treatment status (ABA [monotherapy or with methotrexate (MTX)] or non-ABA [MTX or adalimumab (ADA) plus MTX]). Outcomes included DAS28-CRP mean

change from baseline to week 24, DAS28-CRP remission and ACR 20/50/70 at week 24. IPD mixed-effects meta-regressions were estimated with trial fixed effects, main effects and interaction of enrichment status and treatment type, trial-level random effects on the interaction, and baseline DAS28-CRP score for DAS28-CRP outcomes. These regressions were conducted in the full population and among ABA patients only. Sensitivity analyses defining enrichment using only criteria 3 and 4 were also conducted.

Results: 2,087 patients [1,328 (64%) enriched, 759 (36%) non-enriched] were included (AGREE 492 [24%], AMPLE 509 [24%], AVERT 339 [16%], AVERT-2 747 [36%]). Disease duration, RF+, and anti-CCP values differed as expected between the two groups, while DAS28-CRP was high regardless of enrichment status (Table 1). Among ABA-treated patients, outcomes were more favorable for enriched patients compared to non-enriched patients across all outcomes, either statistically or directionally (Figure 1, ABA treatment arm only analysis). The differences in outcomes between enriched vs. non-enriched patients were larger for ABA than for comparators across all outcomes with the exception of ACR 50, where the difference was directionally consistent (Figure 1, ABA vs. comparator analysis). The relative odds of improved efficacy of ABA vs. comparators ranged from 37% to 87% for remission and ACR responses. The results were consistent in the sensitivity analysis using only anti-CCP and RF seropositivity to define enrichment.

Table 1. Baseline characteristics

	All patients	Non-enriched patients		Enriched patients	
		Abatacept	Comparators	Abatacept	Comparators
	N = 2,087	N = 385	N = 374	N = 784	N = 544
Demographics					
Age (years)	49.3 ± 12.9	49.4 ± 12.6	50.6 ± 12.9	48.6 ± 12.5	49.2 ± 13.5
Female	79.3%	81.3%	83.4%	77.2%	77.9%
Disease characteristics					
Disease duration (months)	8.5 ± 12.5	19.9 ± 15.9	18.3 ± 15.1	2.4 ± 2.8	2.4 ± 2.9
RF Positive	91.0%	74.2%	76.1%	100%	100%
Anti-CCP Positive	81.8%	52.2%	47.3%	100%	100%
DAS28-CRP Score	5.71 ± 1.13	5.72 ± 1.19	5.66 ± 1.20	5.68 ± 1.09	5.76 ± 1.08

Comparators included MTX and MTX+ADA.

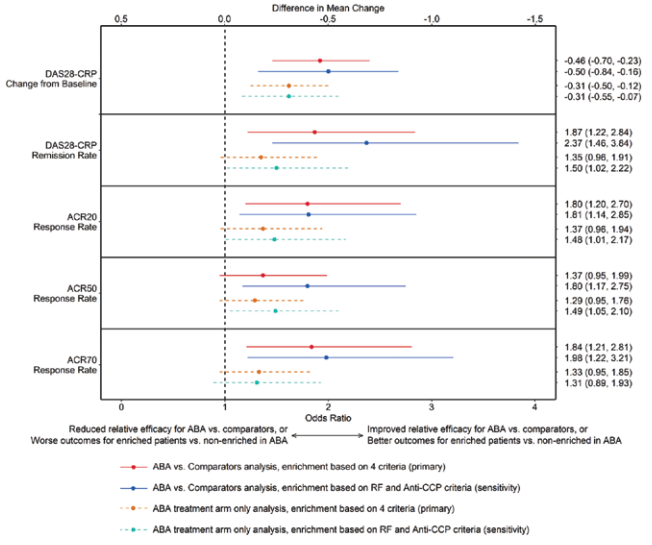


Figure 1. Analysis results

Conclusion: This post-hoc study corroborates previous evidence of improved outcomes among ABA-treated, seropositive early RA patients by applying eAMPLE inclusion criteria retrospectively to ABA RCTs. The findings support a differential treatment effect for costimulation blockade using ABA among enriched and double antibody positive early RA patients, suggesting a potential for patient-tailored RA treatment approaches.

REFERENCES:

[1] Buckner J, et al. Arthritis Rheumatol. 2019; 71 (suppl 10).
[2] Huizinga T, et al Annals of the Rheumatic Diseases 2015;74:234-235.
[3] Harrold L, et al, Rheumatol Ther. 2019 Jun;6(2):217-230.
[4] Sokolove J, et al. Ann Rheum Dis 2016 Apr;75:709–714.

Acknowledgements: This study was sponsored by Bristol Myers Squibb.

Disclosure of Interests: Kaleb Michaud Grant/research support from: Pfizer Aspire grant, Sarah (Sang Hee) Park Employee of: Bristol Myers Squibb, Karissa Lozenski Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, John Vaile Shareholder of: Amgen, Novartis, Bristol Myers Squibb, Regeneron, Employee of: Bristol Myers Squibb, Vadim Khaychuk Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Janet Pope Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, BI, Gilead, Galapagos, Janssen, Lilly, Medexus, Merck, Novartis, Pfizer, Sanofi, Sandoz, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, BI, Celltrion, Gilead, Galapagos, Janssen, Lilly, Medexus, Merck, Novartis, Pfizer, Roche, Samsung, Sanofi, Sandoz, Teva, UCB, Grant/research support from: AbbVie, BMS, Merck, Pfizer, Roche, Seattle Genetics, Philip G Conaghan Speakers bureau: AbbVie, Novartis, Consultant of: Bristol Myers Squibb, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, Gilead, Novartis, Pfizer

DOI: 10.1136/annrheumdis-2021-eular.2513

POS0475

INTEGRATIVE CLINICAL, MOLECULAR AND COMPUTATIONAL ANALYSES ALLOW THE IDENTIFICATION OF DISTINCTIVE PHENOTYPES OF RHEUMATOID ARTHRITIS PATIENTS RELATED TO THE CLINICAL INVOLVEMENT AND THE RESPONSE TO TNF INHIBITORS

M. Luque-Tévar[1], C. Perez-Sanchez[1], N. Barbarroja Puerto[1], A. M. Patiño-Trives[1], I. Arias de la Rosa[1], M. D. C. Abalos-Aguilera[1], J. A. Marín-Sanz[1], D. Ruiz[1], R. Ortega Castro[1], C. López-Medina[1], F. U. Pilar[1], M. Romero-Gómez[1], C. Rodríguez-Escalera[2], J. J. Pérez Venegas[3], D. Ruiz-Montesinos[3], C. Dominguez[3], C. M. Romero-Barco[4], A. Fernandez-Nebro[5], N. Mena-Vázquez[5], J. L. Marenco[6], J. Uceda[6], M. D. Toledo-Coello[7], M. Á. Aguirre-Zamorano[1], A. Escudero Contreras[1], E. Collantes Estevez[1], C. Lopez-Pedrera[1]. *[1]IMIBIC/Hospital Reina Sofia/Universidad de Cordoba (UCO), IMIBIC/Hospital Reina Sofia/Universidad de Cordoba (UCO), Cordoba, Spain*; *[2]Hospital Universitario de Jaen, Hospital Universitario de Jaen, Jaen, Spain*; *[3]Hospital Universitario Virgen Macarena, Hospital Universitario Virgen Macarena, Sevilla, Spain*; *[4]Hospital Clínico Universitario, Hospital Clínico Universitario, Malaga, Spain*; *[5]Hospital Regional Universitario de Malaga, Hospital Regional Universitario de Malaga, Malaga, Spain*; *[6]Hospital Universitario Virgen de Valme, Hospital Universitario Virgen de Valme, Sevilla, Spain*; *[7]Hospital Universitario de Jerez de la Frontera, Hospital Universitario de Jerez de la Frontera, Cadiz, Spain*

Background: TNF inhibitors (TNFi) represent an extraordinary advance in the management of Rheumatoid Arthritis (RA). Despite their benefits, there is a percentage of patients (20–40%) that do not achieve clinical improvement. Therefore, it is necessary to search for new and easily accessible biomarkers predictive of therapeutic response that might guide precision medicine.

Objectives: 1. To explore changes in the molecular profile of RA patients following TNFi therapy in serum samples. 2. To search for new and reliable biomarkers predictive of TNFi response, based on clinical and molecular profiles of RA patients, by using machine learning algorithms.

Methods: In a prospective multicenter study, 79 RA patients undergoing TNFi and 29 healthy donors (HD) were enrolled. Twenty-two RA patients were further included as a validation cohort. Serum samples were obtained before and after 6 months of treatment, and therapeutic efficacy was evaluated. Patients' response was determined following EULAR response criteria. Serum inflammatory profile was analyzed by a multiplex immunoassay, along with oxidative and NETotic profiles, evaluated by commercial kits. A circulating miRNA array was also performed by next-generation sequencing. Clustering analysis was carried out to identify groups of patients with distinctive molecular signatures. Then, clinical and molecular changes induced by TNFi were delineated after 6 months of therapy. Finally, integrative clinical and molecular signatures as predictors of response were assessed at baseline by supervised machine learning methods, using regularized logistic regressions.

Results: Inflammatory, oxidative stress and NETosis-derived biomolecules were found altered in RA patients versus HD, closely interconnected and associated with several deregulated miRNAs. This altered molecular profile at baseline allowed the unsupervised division of three clusters of RA patients with distinctive clinical phenotypes, further linked to TNFi effectiveness. Cluster 1 included RA patients with low levels of pro-inflammatory cytokines, associated with a medium-low disease activity score and good clinical response. Clusters 2-3 comprised patients with high levels of pro-inflammatory cytokines, associated with a high disease activity and a non-response rate of 30%.

After 6 months of therapy the molecular profile found altered in RA patients was reversed in responder patients, who achieved a molecular phenotype similar to HDs. However, non-responder patients' molecular profile remained significantly deregulated, including alterations in inflammatory mediators (IL-6, L-8, TNFα, VEGF, IL-1RA, IL-5, IL-15, GMCSF, GCSF, FGFb), oxidative stress markers (LPO) and NETosis-derived products (Elastase), along with specific miRNAs (miR-199a-5p). These molecular changes further correlated with changes in disease activity score. Machine-learning algorithms identified clinical (Creatinine, IgM, Vitamin D, Swollen Joints, C4, Disease Duration and Tryglicerides) and molecular (Nucleosomes, IL-10, miR-106a-5p, IL-13, IL-12p70, IL-15 and

LPO) signatures as potential predictors of response to TNFi treatment with high accuracy. Furthermore, the integration of both features in a combined model increased the predictive value of these signatures (AUC: 0.91). These results were further confirmed in an independent validation cohort.
Conclusion: 1. RA patients display distinctive altered molecular profiles directly linked to their clinical status and associated with TNFi effectiveness. 2. Clinical response was associated with a specific modulation of the inflammatory profile, the reestablishment of the altered oxidative status, the reduction of NETosis and the reversion of related altered miRNAs. 3. The integrative analysis of the clinical and molecular profiles using machine learning allows the identification of novel signatures as potential predictors of therapeutic response to TNFi therapy.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2549

POS0476 CAN LOW-DOSE ASPIRIN DURING PREGNANCY PREVENT THE DEVELOPMENT OF ADVERSE PREGNANCY OUTCOMES IN WOMEN WITH ARTHRITIS? DATA FROM THE P-RHEUM.IT STUDY

D. Lini[1], M. C. Gerardi[1], A. Zanetti[2], G. Carrara[2], A. Bortoluzzi[2,3], F. Crisafulli[1], M. Filippini[4], M. Fredi[1], R. Gorla[4], M. G. Lazzaroni[1], C. Nalli[4], M. Taglietti[4], A. Lojacono[5], S. Zatti[5], C. A. Scirè[2,3], L. Andreoli[1], F. Franceschini[1], A. Tincani[1]on behalf of P-RHEUM.it. *[1]ASST Spedacli Civili and University of Brescia, Rheumatology Unit, Brescia, Italy*; *[2]Italian Society for Rheumatology (Sir), Epidemiology Unit, Milan, Italy*; *[3]University of Ferrara, SectionoOf Rheumatology, Ferrara, Italy*; *[4]ASST Spedali Civili, Rheumatology Unit, Brescia, Italy*; *[5]ASST Spedacli Civili and University of Brescia, Obstetrics and Gynaecology, Brescia, Italy*

Background: In rheumatic diseases, specifically in chronic inflammatory arthritis (IA), there are no data about the effectiveness of LDA in preventing pregnancy complications.
Objectives: To assess the potential benefit of LDA administration during pregnancy to prevent adverse pregnancy outcomes (APO) in IA.
To compare pregnancy outcomes in IA pregnancies treated during pregnancy with LDA with those untreated.
Methods: Italian P-RHEUM.it register is designed as a nationwide, web-based longitudinal observational cohort study collecting data on pregnancies in inflammatory rheumatic diseases. At baseline, socio-demographic parameters, obstetric history, comorbidities and clinical/laboratoristic characteristics are registered. During pregnancy, the course of maternal disease, medications, development of fetus and complications are collected for each trimester.
Results: From May 2018 to May 2020, 349 patients were enrolled. Forty-five patients with IA had completed their pregnancy with known outcome (20 Rheumatoid Arthritis, 10 Psoriatic Arthritis, 6 Ankylosing spondylitis, 5 Juvenile Idiopathic Arthritis, 4 Undifferentiated Arthritis): 13 (28.89%) treated with LDA during pregnancy and 32 (71.11%) without LDA prophylaxis. LDA was used with a higher frequency in women with previous APO, anti-phospholipid positivity and on biological DMARDs even if it's not statistically significant (Table 1). All the LDA-treated women had a live-birth rate of 100%, whereas among women not treated with LDA the live birth rate was of 84.4% with 27 live-birth pregnancies, 3 early miscarriages, 1 fetal loss and 1 stillbirth observed. There were no significant differences between the LDA and the not LDA groups regarding pregnancy/peripartum obstetric complications (p=0.14), although less adverse pregnancy/peripartum outcomes were registered in LDA patients' group (Table 1).

Table 1. Comparison between inflammatory arthritis pregnancies treated with low-dose aspirin and those untreated.

	LDA (n 19)	Not LDA (n 39)	p
Maternal age at conception, median (IQR)	33 (30.5 - 36.5)	33 (28.2 - 35)	
BMI, median (IQR)	25.4 (22.9 - 28.5)	22.5 (20.4 - 24.5)	
Smoking, n (%)	3 (15.8%)	4/36 (11.1%)	0.68
Previous APO, n (%)	7/11 (63.7%)	7/13 (56.1%)	0.34
aPL+, n (%)	3 (15.8%)	1/36 (2.8%)	0.1
CRP+, n (%)	5/15 (33.3%)	11/27 (40.7%)	0.75
GC at baseline, n (%)	9 (47.4%)	15/34 (44.1%)	0.82
cDMARDs at baseline, n (%)	1 (5.3%)	3/34 (8.8%)	1
bDMARDs at baseline, n (%)	6 (31.6%)	11 (28.2%)	0.79
Live-birth pregnancy, n (%)	18 (94.7%)	32 (82.1%)	0.25
Pregnancy loss, n (%)	1 (5.3%)	7 (17,9%)	0.25
Hypertensive disorders, n (%)	2/18 (11.1%)	6/38 (15,8%)	1
HELLP syndrome, n (%)	0 (0%)	0 (0%)	1
PROM, n (%)	0 (0%)	3/38 (7.9%)	0.54
Preterm delivery, 34-37 GW, n (%)	2 (10.5%)	2 (5.2%)	0.59
Preterm delivery, <34 GW, n (%)	1 (5.3%)	1 (2.6%)	1
IUGR, n (%)	0 (0%)	3 (7.8%)	0.54
SGA, n (%)	0 (0%)	0 (0%)	1
Pregnancy/Peripartum complications, n (%)	3 (15.8%)	11 (28.9%)	0.35

Legend: aPL, Antiphospholipid syndrome; bDMARDs, biological disease-modifying antirheumatic drugs; BMI, Body mass index; cDMARDs, Conventional disease-modifying antirheumatic drugs; CRP, C-reactive protein; GC, Glucocorticoids; GW, gestational week; HELLP, haemolysis, elevated liver enzymes, and low platelets; Hypertensive disorder defined as gestational hypertension, preeclampsia and eclampsia; IQR, Interquartile range; IUGR, intrauterine growth restriction; LDA, Low-dose Aspirin; Pregnancy loss defined as early fetal-loss, miscarriage and still-birth; PROM, Premature rupture of membranes; SGA, Small for gestational age.

Conclusion: The preliminary data of this prospective cohort study show that LDA improve pregnancy outcome in IA even if women treated with LDA had more risk factors for APO. The extension of this cohort will allow us to further investigate these important results.
REFERENCES:
[1] Roberge S, et al. *AmJObstetGynecol.*2017;216:110-120.e6.
[2] Andreoli L et al. *Annals of the Rheumatic Diseases* 2017;76: 476–85.
[3] Sammaritano L et al. *Arthritis & Rheumatology* 2020; 72: 529–56.
Acknowledgements: I would like to acknowledge the Epidemiology Unit of the Italian Society for Rheumatology and the Investigators of the Italian Registry.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2567

POS0477 HIGH DISEASE ACTIVITY AT BASELINE AND SEROPOSITIVITY ARE ASSOCIATED WITH TREATMENT RESPONSE AT ONE YEAR POST SYNOVIAL BIOPSY IN RHEUMATOID ARTHRITIS PATIENTS

K. Murray[1], C. Low[1], F. Young[1], M. Bienicka[1], E. Mylod[2], U. Fearon[2], D. Veale[1]. *[1]Saint Vincent's University Hospital, Rheumatology, Dublin, Ireland*; *[2]Trinity College,Trinity Biomedical Sciences Institute, Dublin, Ireland*

Background: Despite recent therapeutic advances, our ability to predict prognosis and therapeutic response in RA remains imprecise.
Objectives: To determine biomarkers predictive of outcome at one year following arthroscopy.
Methods: RA patients were prospectively recruited and underwent knee arthroscopy performed under local anaesthetic. Each patient underwent a careful systematic assessment of demographic, clinical, and serologic factors on the day of arthroscopy and were reviewed at 2 weeks, 3, 6 and 12 months post arthroscopy. Erosive disease was defined based on plain-film radiographs of hands and feet. Disease activity at one year was used to define treatment response into responders (moderate/good EULAR Response) and non-responders.
Clinical characteristics, synovial tissue cell profiles and immunohistochemistry were analysed for T Cells (CD3), B Cells (CD20, CD138), macrophages (CD68) and vascularity (Factor VIII) to establish predictors of treatment response. All areas of each biopsy section were examined and the sub-lining layer independently scored by 2 observers using a well-validated semiquantitative scoring method, ranging from 0 to 4 (0=no staining, 1=<25%, 2=25–49%, 3=50–74%, and 4=75–100% staining). Factor 8 was scored by calculating the mean count of stained blood vessels per high-power field (at 20X magnification).
Results: There were no significant differences between responders and non-responders regarding gender, age, disease duration, medications, erosive status, ESR, CRP or synovitis or vascularity at arthroscopy (Table 1). Interestingly, rates of RF and ACPA positivity, tender and swollen joint counts, DAS28 and DAS28CRP were all higher amongst treatment responders. Immunohistochemistry was a very poor predictor of treatment response. There were no significant differences between the two groups in CD3, CD20, CD138, CD68 or Factor 8 score.

Table 1. Baseline Characteristics

	Responder (n=30)	Non-responder (n=18)	p value
Female	20 (66.7%)	14 (77.8%)	NS
Age	51.5 (11.2)	54.2 (10.9)	NS
Disease duration	0.5 (0-16)	0.5 (0-10)	NS
RF positive	22 (73.3%)	5 (27.8%)	0.003
ACPA positive	22 (73.3%)	8 (44.4%)	0.045
Erosions	8 (26.7%)	5 (27.8%)	NS
Medications			
No DMARD	23 (76.7%)	10 (55.6%)	NS
csDMARD only	4 (13.3%)	3 (16.7%)	NS
TNFi	2 (6.7%)	3 (16.7%)	NS
Other bDMARD	1 (3.3%)	2 (11.1%)	NS
Patient global health, VAS (mm)	54.2 (10-100)	51.5 (0-90)	NS
SJC (28 Joints)	4.5 (0-16)	1 (0-18)	0.001
TJC (28 Joints)	7 (1-25)	1 (0-15)	0.001
ESR, mm/hr	23 (2-120)	24 (2-81)	NS
CRP, mg/L	5 (1-95)	6.5 (1-64)	NS
DAS28	5.01 (1.95-7.36)	3.93 (1.40-6.62)	0.003
DAS28CRP	4.78 (2.82-7.13)	3.39 (1.21-6.26)	0.002
Synovitis, VAS	65 (10-100)	70 (30-100)	NS
Vascularity, VAS	60 (10-90)	70 (30-100)	NS

Conclusion: In this small study, seropositivity and disease activity were higher in responders. Baseline immunohistochemical staining was not a good discriminator of treatment respons

Disclosure of Interests: Kieran Murray Grant/research support from: Bresnihan Molloy and Newman fellowships, Candice Low: None declared, Francis Young: None declared, Monika Bienicka: None declared, EImear Mylod: None declared, Ursula Fearon: None declared, Douglas Veale: None declared

DOI: 10.1136/annrheumdis-2021-eular.2593

POS0478 ASSOCIATION BETWEEN BODY SHAPES AND BODY SHAPE TRAJECTORIES, AND THE RISK OF RHEUMATOID ARTHRITIS IN THE FRENCH E3N COHORT

C. Salliot[1,2,3], Y. Nguyen[4,5], X. Mariette[3,6], M. C. Boutron-Ruault[2,7], R. Seror[3,8]. *[1]Centre Hospitalier d'Orleans, Rheumatology, Orleans, France*; *[2]Center for Research in Epidemiology and Population Health (CESP), Université Paris-Saclay, Institut pour la Santé et la Recherche Médicale (INSERM) U1018, Villejuif, France*; *[3]Center of Immunology of Viral Infections and Auto-immune Diseases (IMVA), Université Paris-Saclay, Institut pour la Santé et la Recherche Médicale (INSERM) U1184, Le Kremlin Bicetre, France*; *[4]Hôpital Beaujon, Université de Paris, Internal Medicine, Clichy, France*; *[5]Center for Research in Epidemiology and Population Health (CESP), Paris-Saclay, Institut pour la Santé et la Recherche Médicale (INSERM) U1018, Villejuif, France*; *[6]Assistance Publique-Hôpitaux de Paris (AP-HP), AP-HP. Université Paris-Saclay – Hôpital Bicêtre, Rheumatology, Kremlin Bicêtre, France*; *[7]Institut Gustave Roussy, Universite Paris Saclay, Villejuif, France*; *[8]Assistance Publique-Hôpitaux de Paris (AP-HP), AP-HP. Université Paris-Saclay – Hôpital Bicêtre, Rheumatology, Le Kremlin Bicetre, France*

Background: Several cohort and case-control studies have suggested that overweight or obesity is associated with the risk of Rheumatoid Arthritis (RA). Associations were based on Body Mass Index (BMI), although this measurement does not reflect the fat distribution [1].

Objectives: To study the relationships between anthropometric measurements and the risk of RA in women involved in the E3N cohort.

Methods: E3N is an ongoing French prospective cohort that enrolled 98,995 women aged 40-65 years in 1990. Women completed mailed questionnaires every 2-3 years on lifestyle and health-related information. A total of 698 incident RA cases have been validated among 78,452 women [2]. Available anthropometric measurements include birth height and weight, height and weight (collected at baseline and regularly updated during follow-up), and age-related body shapes (BS). Women had to identify the silhouette among 8 BS that best described their BS at 8 years, puberty, 20-25 years, 30-35 years, and study baseline. BS trajectories (from 8 to 30-35 years) were constructed using Nagin's approach to group-based trajectory modeling that identifies 6 different trajectories [3]. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of incident RA were estimated using Cox proportional hazards regression models with age as the time scale. Models were first adjusted for known risk factors of RA (model 1), and then multi-adjusted (model 2).

Results: Taking lean BS as reference, medium BS at puberty was associated with an increased risk of RA [HR=1.23 (95% CI 1.0-1.5)], in the fully adjusted model (table 1), as was large BS at baseline [HR =1.32 (95% CI 1.1-1.6)] (in model 1). Obesity (BMI>30 kg/m^2) was marginally associated with RA in model 1 [HR=1.30 (95% CI 1.0-1.7)], but the association was no longer statistically significant in the multi-adjusted model, taking normal BMI [18-25 kg/m^2[as the reference.

Birth weight and height, BS (at 8, 20-25 and 30-35 years), and BS trajectories were not significantly associated with RA in any model.

Table 1. Cox proportional-hazards analysis of anthropometric factors associated with RA

	RA	Non-cases	MODEL 1		MODEL 2	
			HRs (95%CI)	*ptrend*	**HRs (95%CI)**	*ptrend*
Baseline Body mass index (kg/m^2)						
<18	10	1,797	0.75 (0.4-1.4)	***0.0532***	0.85 (0.4-1.6)	*0.6165*
[18-25[	462	50,330	Ref		Ref	
[25-30]	171	19,716	1.10 (0.9-1.3)		1.00 (0.8-1.2)	
> 30	55	5,911	**1.30 (1.0-1.7)**		1.13 (0.8-1.6)	
Body shape at puberty						
Lean	332	40,485	Ref	*0.0937*	Ref	*0.1490*
Medium	179	17,903	**1.24 (1.0-1.5)**		**1.23 (1.0-1.5)**	
Large	147	15,984	1.14 (0.9-1.4)		1.12 (0.9-1.4)	
Body shape at baseline						
Lean	359	44,718	Ref	***0.0055***	Ref	*0.1743*
Medium	200	20,041	1.20 (1.0-1.4)		1.16 (0.9-1.4)	
Large	110	9,838	**1.32 (1.1-1.6)**		1.20 (0.9-1.6)	

ptrend: p for trend. Ref: reference.

Model 1 adjusted for age, smoking (past/current/never), passive smoking during childhood and/or adulthood (ever/never), educational level (<high–school, up to 2 years of university, ≥ 3 years of university).

Multi-adjusted model 2 included model 1 + body mass index (<18, 18–25, 25–30, >30 kg/m^2), body shape at puberty, body shape at baseline adjusted for age, baseline physical activity (in quartiles), age at menarche (<13, 13–15, ≥15 years), age at menopause (≤45, 45–53, ≥53 years), age at the first pregnancy (<22, 22–27, ≥27 years), number of full-term pregnancies (≤1, 2, ≥3), and duration of premenopausal use of progestogen (0, 0–24, >24 months).

Conclusion: In E3N cohort, medium body shape at puberty was associated with an increased risk of RA independently of the BMI and smoking exposure.

REFERENCES:

[1] Crowson CS, Matteson EL, Davis JM 3rd, Gabriel SE. Contribution of obesity to the rise in incidence of rheumatoid arthritis. Arthritis Care Res (Hoboken). 2013;65:71-7.

[2] Nguyen Y, Salliot C, Gusto G, et al. Improving accuracy of self-reported diagnoses of rheumatoid arthritis in the French prospective E3N-EPIC cohort: a validation study. BMJ Open. 2019;9:e033536.

[3] Nagin D. Analyzing developmental trajectories: a semiparametric, group based approach. Psychol Methods 1999;4:139e57.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2655

POS0479 THE IMPACT OF FLARES ON PATIENT REPORTED OUTCOMES IN RHEUMATOID AND UNDIFFERENTIATED ARTHRITIS PATIENTS – A SUB-ANALYSIS OF THE IMPROVED STUDY

J. M. Maassen[1], S. A. Bergstra[1], P. D. de Buck[2], M. van Oosterhout[3], T. Huizinga[1], C. Allaart[1]. *[1]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[2]Haaglanden Medical Center, Rheumatology,The Hague, Netherlands*; *[3]Groene Hart Hospital, Rheumatology, Gouda, Netherlands*

Background: In rheumatoid arthritis (RA) patients in low disease activity, flares are associated with symptom deterioration. Patients in clinical remission may flare but still have low disease activity. How does this affect patient reported outcomes?

Objectives: To evaluate the prevalence of disease flares in patients treated to target drug free remission, and to study the impact of disease flares on patient-reported outcomes (PROs) for flares with different impact on disease activity.

Methods: In the IMPROVED study 610 patients with rheumatoid arthritis (RA) or undifferentiated arthritis (UA) were treated to target drug free remission (DAS <1.6) for 5 years. As soon as DAS was <1.6, treatment was tapered to discontinuation. Patients with at least 8 months follow-up were selected. A flare was defined according to three definitions; **A)** DAS ≥1.6 and ≥0.6 increase from the previous visit regardless of the previous DAS; **B)** minor flare from remission; a DAS ≥1.6 with <0.6 increase and previous DAS <1.6; **C)** major flare from remission; a DAS ≥1.6 with ≥0.6 increase and previous DAS <1.6. Linear mixed models were used to compare functional ability, measured by the health assessment questionnaire (HAQ), at visits where a flare occurred versus visits without a flare. Fisher's exact test were used to compare percentages with ≥0.22 HAQ increases between groups with and without LDA at the moment of flare. A generalized linear mixed model was used to calculate the odds ratio for a deterioration of ≥20 mm in VAS of PROs global health (GH), disease activity, pain and morning stiffness (from the preceding visit) during a flare.

Results: Of the 585 patients with sufficient follow-up, 75% experienced a flare **A**, 26% a flare **B**, and 68% a flare **C**, at least once. Most flares were observed after t=8 and t=12 months. In 55%, 100%, and 69% of visits with a flare A, B or C, the patients were still in LDA (DAS=<2.4). In 55% of the visits where a flare was associated with a DAS increase ≥0.6 (flare A & C) there was also clinically relevant increase in HAQ of ≥0.22. The mean difference in HAQ was 0.27 with flare **A** (p<0.01), 0.03 with flare **B** (p=0.72) and 0.18 with flare **C** (p<0.01). If was DAS >2.4 (LDA) at the moment of flare, HAQ increased ≥0.22 in 68% of all flares A, and 77% of all flares C (p-values <0.01, compared to flares where patients were still in LDA, DAS=<2.4). The odds ratios of a >20 mm deterioration in VAS global health, VAS disease activity, VAS pain and VAS morning stiffness was significant ≥1 for flares with a ≥0.6 increase in DAS (flares A and C), and ≤1 for minor flares (B) (table 1).

Conclusion: In early arthritis patients, during 5 years treated to target drug free DAS-remission, disease flares with loss of DAS-remission were common. Although the majority of patients who flared were still in LDA, most reported more pain, morning stiffness, increased disease activity and a diminished global health. On average, deterioration in HAQ only exceeded the minimum clinically important difference (delta HAQ >=0.22) in case of a ≥0.6 increase in DAS, independent of the previous DAS. Depending on the definition of flare, up to 45% of patients lost DAS LDA, and in this group the functional deterioration significantly more often exceeded the MCID as compared to the patients that flared but were still in LDA. More research is needed to find out which patients are most at risk for clinically relevant flares, and to evaluate the impact of flares in patients with remission on long term outcomes.

Table 1. Odds Ratios and 95% confidence intervals for > 20 mm increase in PROs on 100mm visual analogue scales

	Flare A		Flare B (minor)		Flare C (major)	
	Prevalence ≥20 mm[a]	OR (95% CI)	Prevalence ≥20 mm[a]	OR (95% CI)	Prevalence ≥20 mm[a]	OR (95% CI)
Global health	62%	2.1 (1.5; 2.8)	45%	0.5 (0.4; 0.7)	62%	1.4 (1.1; 1.8)
Disease activity	62%	2.5 (1.7; 3.8)	45%	0.4 (0.3; 0.6)	62%	2.1 (1.4; 3.0)
Pain	87%	2.0 (1.3; 3.1)	78%	0.5 (0.3; 0.8)	87%	1.8 (1.2; 2.5)
Morning stiffness	84%	1.7 (1.1; 2.6)	77%	0.6 (0.4; 0.9)	86%	2.1 (1.5; 2.9)

[a] The prevalence of >20 mm deterioration in VAS PRO's during a visit with a flare.

Acknowledgements: We would like to thank all patients for their contribution as well as the rheumatologists who participated in the IMPROVED-study group. We would also like to thank all other rheumatologists and trainee rheumatologists who enrolled patients in these studies, and all research nurses for their contributions.

Disclosure of Interests: Johanna M. Maassen: None declared, Sytske Anne Bergstra: None declared, Petronella DM de Buck: None declared, M. van Oosterhout: None declared, Thomas Huizinga: None declared, Cornelia Allaart Grant/ research support from: the IMPROVED study was designed by the investigators and financially supported by AbbVie in the first year.

DOI: 10.1136/annrheumdis-2021-eular.2656

POS0480 ASSOCIATION OF NEUTROPHIL LYMPHOCYTE AND PLATELET LYMPHOCYTE RATIOS WITH JOINT INFLAMMATION IN RHEUMATOID ARTHRITIS

D. Pearce-Fisher[1], D. Orange[1,2], B. Mehta[1,3], D. Jannat-Khah[1,3], S. Goodman[1,3]. [1]*Hospital for Special Surgery, Medicine, New York, United States of America*; [2]*The Rockefeller University, Clinical Investigation, New York, United States of America*; [3]*Weill Cornell Medicine, Medicine, New York, United States of America*

Background: Some patients with rheumatoid arthritis (RA) have high disease activity scores (DAS) and low synovial inflammation, and others have high synovial inflammation and low DAS (subclinical synovitis)[1]. It would be clinically useful to identify blood biomarkers of synovial inflammation. Neutrophil-lymphocyte (NLR) and platelet-lymphocyte ratios (PLR) have been reported to distinguish RA patients with moderate/high DAS28 scores from low DAS28 [2]. However, it is not known if these inexpensive, accessible tests are associated with inflammation in synovial tissue at the histological level.

Objectives: The objective of this study was to evaluate the relationship of pre-operative NLR and PLR with synovial inflammation of the operative joint in RA patients undergoing arthroplasty.

Methods: 230 patients meeting ACR/EULAR 1987 and/or 2010 criteria were recruited prior to elective total hip, knee, shoulder, and elbow replacement. Demographics, RA characteristics, medications, disease activity, and routine tests including complete blood tests (CBC) were collected pre-operatively. Hematoxylin and eosin (H&E) stains were prepared from the synovium of the operative joint and systematically scored by a pathologist as described previously [3]. Synovial lymphocytic inflammation was graded as none, mild, moderate, marked, or band-like. Linear regression was performed to distinguish differences in the NLR, PLR, and CRP in patients with synovial lymphocytic inflammation (SLI).

Results: As expected, patients on glucocorticoids (GCs) had higher NLR (mean 5.52 (SD 7.68) vs mean 2.82 (SD 1.66) (p<0.001) and higher PLR (mean 233.73 (SD 237.21) vs (mean 162.93 (SD 65.35)) (p-value=0.04)) and those patients (N=92) were therefore excluded from down-stream analyses. On the remaining 138 patients, we tested for associations of PLR, NLR and CRP with SLI using linear regression. In all the models the highest category for synovial lymphocytic inflammation was found to be statistically significantly associated with NLR, PLR and CRP, separately (Table 1).

Table 1. Results from linear regressions evaluating the association of NLR, PLR, and CRP with synovial lymphocytic inflammation.

Linear regression Results	NLR	PLR	CRP
Synovial Lymphocytic Inflammation	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
None	Reference	reference	reference
Mild	0.31 (-0.51, 1.13)	26.54 (-8.83, 61.90)	-1.00 (-2.37, 0.36)
Moderate	0.73 (-0.18, 1.64)	28.66 (-10.22, 67.53)	0.46 (-1.09, 2.01)
Marked	0.21 (-0.80, 1.22)	24.62 (-22.80, 72.05)	0.81 (-0.87, 2.49)
Band-like	**1.92 (0.81, 3.02)**	**80.42 (31.46, 129.38)**	**2.32 (0.49, 4.16)**

OR= Odds ratio, Coef = Coefficient, NLR= neutrophil lymphocyte, PLR= platelet lymphocyte ratio, CRP= C-reactive proteinAll significant associations are bolded.

Conclusion: NLR, PLR and CRP are associated with high synovial lymphocytic inflammation of the operative joint. This suggests that these inexpensive, routinely performed blood tests may be a useful blood biomarker of synovial inflammation.

REFERENCES:

[1] Orange, D.E. *et al.* Histologic and Transcriptional Evidence of Subclinical Synovial Inflammation in Patients With Rheumatoid Arthritis in Clinical Remission. *Arthritis Rheumatol.* 71(7): 1034-1041 (2019).

[2] Lee, Y.H. Association between the Neutrophil-to-lymphocyte Ratio, and Platelet-to-lymphocyte Ratio and Rheumatoid Arthritis and their Correlations with the Disease Activity: A Meta-analysis. *J Rheum Dis.* 25(3):169-178 (2018).

[3] Orange, D. E. *et al.* Identification of Three Rheumatoid Arthritis Disease Subtypes by Machine Learning Integration of Synovial Histologic Features and RNA Sequencing Data. *Arthritis Rheumatol. Hoboken NJ* 70: 690–701 (2018).

Disclosure of Interests: Diyu Pearce-Fisher: None declared, Dana Orange Consultant of: Astra Zeneca/MedImmune and Pfizer, Bella Mehta Consultant of: Novartis, Deanna Jannat-Khah: None declared, Susan Goodman Consultant of: UCB, Grant/research support from: Novartis, Horizon Pharmaceuticals

DOI: 10.1136/annrheumdis-2021-eular.2729

POS0481 DOES OLDER REALLY MEAN WISER?

D. Khalifa[1], S. Belghali[1], M. Limam[2], N. El Amri[1], K. Baccouche[1], H. Zeglaoui[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*; [2]*Farhat Hached Hospital, Preventive Medicine, Sousse, Tunisia*

Background: One of the main challenges in Rheumatoid arthritis (RA) is to maintain remission or low disease activity by adhering to the prescribed treatments. However, it is believed that adherence to long term treatments is inadequate in chronic diseases. Does this apply to older people too?

Objectives: To assess treatment adherence among an elderly RA population and to study determining factors of non-adherence

Methods: A cross-sectional study over a period of 4 months was conducted in a rheumatology clinic (September 2020-December 2020). Consenting elderly over the age of 65 presenting with RA were included. Exclusion criteria involved associated connective tissue diseases and troubles communicating. During clinical visits, sociodemographic information, clinical, radiological and therapeutic data were collected. Treatment adherence was assessed by the 5-item compliance questionnaire of rheumatology (CQR-5). Patients were also asked about the degree of satisfaction vis-à-vis the therapeutic effect detected. Univariate and multivariate analysis were conducted using the statistical tool SPSS.20.

Results: Forty patients consented to join the study, 82.5% of them were women. The median of age was 66.5 years old with a minimum of 65 and a maximum of 83. Comorbidities were noted in 55% of the patients. 75% of the patients had health insurance. The mean pain score was 5 out of 10 on a visual analog scale (VAS). The mean DAS 28 was 4.65±1.77 with 72.5%

of the patients having an active disease. Deformities were reported in 60% of the cases and bone destruction on radiographs in 87.2% of the cases. Methotrexate was the most prescribed treatment in 95% of the cases and biologics in 12.5% of the cases. The median number of pills taken (on the day of MTX) was 12.5 (min=6; max=23). Up to 35.5% of the patients were not satisfied with treatment results. 90% of the patients took their medication because they had fewer problems afterwards. 72.5% of them did not dare to miss their RA treatment. 95% of them had their pills stored in the same place to not forget them, 97.5% took their medication because they had complete confidence in their rheumatologist and 92.5% of them hung on to what the doctor told them. The overall results of the CQR-5 revealed that 72.5% of the patients were adherent to their RA medication and 27.5% of them were non-adherent. The study of factors associated to non-adherence showed that being younger (p=0.01), not having a health insurance (p=0.014), having comorbidities (0.03), and not being satisfied with treatments' results (p=0.014) were associated to non-adherence. Multivariate analysis showed that risk factors associated to non-adherence were elevated pain scores (odds ratio=4.11, p=0.042), not having health insurance (odd ratio=7.54, p=0.006) and having to take many pills at once (odds ratio=4.48, p=0.034). Being older was a protector factor of non-adherence (odds ratio=0.81, p=0.034).

Conclusion: Adherence among RA elderly patients is optimal and they have good trust in their medication and confidence in their rheumatologist. Older seems wiser when it comes to treatment taking behaviors in RA.

REFERENCES:

[1] Hughes LD, Done J, Young A. A 5 item version of the Compliance Questionnaire for Rheumatology (CQR5) successfully identifies low adherence to DMARDs. *BMC Musculoskelet Disord* 2013; 14: 286.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2738

POS0482 WOOD SMOKE EXPOSURE IS ASSOCIATED WITH HIGHER ANTI-CCP ANTIBODY TITERS IN HISPANIC PATIENTS WITH RHEUMATOID ARTHRITIS

A. B. Rodriguez-Romero[1], D. Á. Galarza-Delgado[1], J. R. Azpiri-López[2], I. J. Colunga-Pedraza[1], N. Guajardo-Jauregui[1], S. Lugo-Perez[2], A. Cárdenas[1]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology Service, Monterrey, Mexico*; *[2]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology Service, Monterrey, Mexico*

Background: Wood smoke exposure is a risk factor for the development of chronic obstructive pulmonary disease (COPD), lung cancer and cardiovascular disease and it has also been linked to higher anti-CCP antibodies in patients with rheumatoid arthritis (RA) and COPD (1).

Objectives: The objective of the present study is to report the correlation between anti-CCP, IgG, IgM and IgA rheumatoid factor (RF) to wood smoke exposure in patients with RA. Additionally, evaluate the impact of disease activity, biomass exposure, and disease duration on anti-CCP antibody levels.

Methods: A cross-sectional, observational study was designed based on a cohort of Hispanic RA patients. All fulfilled the 2010 ACR/EULAR classification criteria for RA. Biomass smoke exposure was expressed using the biomass exposure index (BEI) calculated from the mean of exposed hours per day multiplied by the number of years exposed. Subjects were divided into two groups: those exposed to wood smoke with BEI ≥1 and subjects not exposed to wood smoke. They were matched by age, gender, and comorbidities. Anti-CCP antibodies and RF were measured by ELISA with cutoff points of <5 U/mL and <20 U/mL respectively.

Results: A total of 318 subjects were included, 159 (50%) of them had a history of exposure to wood smoke. Anti-CCP antibody positivity was present in 102 (64.2%) with a median titer of 97.1 U/mL (1.7-198) in the RA exposed group, and in 89 (56%) with a median titer of 8.5 U/mL (1.1-145) in the RA non-exposed group. A significant difference was found in anti-CCP antibody titers between groups (p=0.003). (Table 1). Spearman's rho showed a small but statistically significant correlation between BEI and anti-CCP antibody titers (rho= 0.170, p=0.002). Biomass exposure was independently related to higher anti-CCP antibody titers (B=35.4, p<0.001).

Conclusion: RA patients who were exposed to wood smoke had higher titers of anti-CCP antibodies than non-exposed RA patients. Furthermore, biomass exposure was shown to be independently related to higher titers of anti-CCP antibodies.

Table 1. Comparison of demographic, seropositivity and clinical characteristic between patients with RA exposed and matched non-exposed RA patients.

Characteristics	RA exposed (n=159)	RA not exposed (n=159)	p
Age years, ± SD	56.7 ± 8.7	55.4 ± 8.1	NS
Female, n (%)	148 (93.1)	148 (93.1)	NS
BEI years, median (p25-p75)	35 (15-90)	0	
Disease duration years, median (p25-p75)	9 (3.5-15.1)	6.8 (2.8-14.6)	NS
DAS 28-CRP, median (p25-p75)	3.37 (2.11-4.4)	3.17 (2.09-4.2)	NS
Dyslipidemia, n (%)	50 (31.4)	43 (27)	NS
Hypertension, n (%)	55 (34.6)	48 (30.2)	NS
Diabetes Mellitus, n (%)	24 (15.1)	23 (14.5)	NS
Active smoking, n (%)	8 (5)	8 (5)	NS
Seropositivity			
Anti-CCP antibody positivity, n (%)	102 (64.2)	89 (56)	0.137
Anti-CCP antibody titers, median (p25-p75)	97.1 (1.7-198)	8.5 (1.1-145)	**0.003**
IgG RF positivity, n (%)	31 (19.5)	24 (15.1)	0.299
IgG RF titers, median (p25-p75)	5 (2-13)	4.9 (2-13)	0.529
IgM RF positivity, n (%)	136 (85.5)	126 (79.2)	0.141
IgM RF titers, median (p25-p75)	198 (41-200)	177 (28-200)	0.067
IgA RF positivity, n (%)	98 (61.6)	92 (57.9)	0.493
IgA RF titers, median (p25-p75)	52.9 (9.3-193)	33(5-159)	0.060

NS, non-significant; RA, rheumatoid arthritis; BMI, body mass index; BEI, biomass exposure index; DAS28-CRP, disease activity score using 28 joints-C-reactive protein; anti-CCP, anti-cyclic citrullinated peptide; RF, rheumatoid factor

REFERENCES:

[1] Fullerton DG, Bruce N, Gordon SB. Indoor air pollution from biomass fuel smoke is a major health concern in the developing world. Trans R Soc Trop Med Hyg. 2008;102(9):843-51.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2778

POS0483 SUBCLINICAL ATHEROSCLEROSIS IN THE FIRST FIVE YEARS OF RHEUMATOID ARTHRITIS DIAGNOSIS

N. Guajardo-Jauregui[1], I. J. Colunga-Pedraza[1], J. R. Azpiri-López[2], D. Á. Galarza-Delgado[1], A. B. Rodriguez-Romero[1], S. Lugo-Perez[2], A. Cárdenas[1], A. C. Garza Acosta[3]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*; *[2]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico*; *[3]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Radiology, Monterrey, Mexico*

Background: Patients with rheumatoid arthritis (RA) have a higher risk of developing a cardiovascular (CV) event than the general population, due to an accelerated process of atherosclerosis (1), which has been documented to begin in early stages of the disease and is directly associated with systemic inflammation (2).

Objectives: The aim of this study was to compare the prevalence of subclinical atherosclerosis detected by carotid ultrasound (US) in patients with RA in the first five years of diagnosis and healthy controls.

Methods: This was a cross-sectional, observational, and comparative study. A total of 53 patients aged 40-75 years old, with RA diagnosis, in the previous five years, according to the 2010 ACR/EULAR classification criteria, and 53 controls matched by age (±5 years), gender and comorbidities were included in this study. Subjects with a previous CV event, such as myocardial infarction, cerebrovascular event and peripheral arterial disease, another connective tissue disease and pregnant women were excluded from this study. A high-resolution B-mode carotid US was performed in all study subjects. Subclinical atherosclerosis was evaluated as the presence of carotid plaque (CP) or an increased carotid intima media thickness (cIMT). CP was defined as a cIMT ≥1.2mm or a focal narrowing ≥0.5mm of the surrounding lumen, and an increased cIMT was defined as a value ≥0.8mm. Distribution was evaluated with the Kolmogorov-Smirnov test. Comparisons were done with χ^2 test and Fisher's exact test for qualitative variables, and Student's t test and Mann-Whitney's U test for quantitative variables. A *p*-value <0.05 was considered statistically significant.

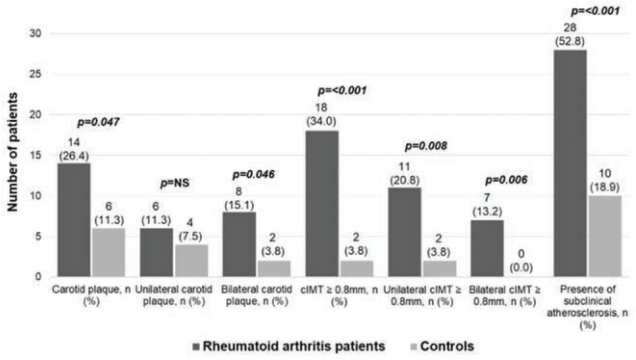
Results: Comparisons of demographic characteristics showed no differences between the RA group and the control group (Table 1). When comparing carotid US findings there was a difference in the presence of CP, being more prevalent in RA patients (26.4% vs 11.3%, *p*=0.047), in the presence of an increased cIMT, being more prevalent in RA patients (34.0% vs 3.8%, *p*=<0.001), in the cIMT as a quantitative variable, being higher in RA patients (0.70mm vs 0.59mm, *p*=<0.001 in the right carotid artery, and 0.75mm vs

Table 1. Demographic and clinical characteristics.

	RA (n=53)	Controls (n=53)	*p*
Age years, mean ± SD	54.48 ± 9.09	54.86 ± 6.83	NS
Women, n (%)	49 (92.5)	49 (92.5)	NS
T2DM, n (%)	8 (15.1)	7 (13.2)	NS
HTN, n (%)	17 (32.1)	17 (32.1)	NS
Dyslipidemia, n (%)	19 (35.8)	19 (35.8)	NS
Obesity, n (%)	21 (39.6)	20 (37.7)	NS
Active smoking, n (%)	3 (5.7)	4 (7.5)	NS
BMI kg/m^2, median (p25-p75)	28.78 (25.92-33.21)	27.59 (24.55-33.34)	NS
Disease duration, mean ± SD	2.48 ± 1.31	-	-
DAS28-CRP, median (p25-p75)	3.21 (1.89-4.12)	-	-
MTX, n (%)	39 (73.6)	-	-
Glucocorticoids, n (%)	29 (54.7)	-	-

NS, not significant; T2DM, type 2 diabetes mellitus; HTN, hypertension; BMI, body mass index; DAS28, disease activity score using 28 joints; CPR, C-reactive protein; MTX, methotrexate.

Figure 1. Carotid ultrasound findings.



0.60mm, *p*=0.001 in the left carotid artery), and in the presence of subclinical atherosclerosis overall, being more prevalent in RA patients (52.8% vs 18.9%, *p*=<0.001) (Figure 1).

Conclusion: Patients with RA in the first five years of diagnosis have a higher prevalence of subclinical atherosclerosis than the general population. CV evaluation including a carotid US should be done at the time of diagnosis of RA patients, and subsequently it must be individualized according to the CV risk of each patient, with a maximum of five years to identify those patients who would benefit from an opportune treatment.

REFERENCES:

[1] Geraldino-Pardilla L, Russo C, Sokolove J, et al. Association of anti-citrullinated protein or peptide antibodies with left ventricular structure and function in rheumatoid arthritis. Rheumatology (Oxford) 2017;56(4):534-40. doi: 10.1093/rheumatology/kew436

[2] Ahmad S, Garg S, Dhar M, et al. Predictors of atherosclerosis in rheumatoid arthritis. Vasa 2012;41(5):353-9. doi: 10.1024/0301-1526/a000221

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2780

POS0484

THE ASSOCIATION BETWEEN SOCIAL STRESSORS AND DISEASE REMISSION AMONG MEN AND WOMEN WITH EARLY RHEUMATOID ARTHRITIS

L. Hedenstierna[1,2,3], A. K. Hedström[4], L. Klareskog[1,2], L. Alfredsson[3,5], J. Askling[6,7], S. Ernestam[2], S. Saevarsdottir[8], L. Ljung[2,6,9]. *[1]Karolinska Institutet, Department of medicine, Solna, Stockholm, Sweden*; *[2]Stockholm Health Services, Academic Specialist Center, Stockholm, Sweden*; *[3]Karolinska Institutet, Institute of Environmental Medicine, Stockholm, Sweden*; *[4]Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden*; *[5]Karolinska Institutet, Center for Occupational and Environmental Medicine, Stockholm, Sweden*; *[6]Karolinska Institutet, Department of Medicine, Solna, Division of Clinical Epidemiology, Stockholm, Sweden*; *[7]Karolinska University hospital, Unit of Rheumatology, Stockholm, Sweden*; *[8]School of Health Sciences, University of Iceland, Faculty of Medicine, Reykjavik, Iceland*; *[9]Umeå Univeristy, Department for Public Health and Clinical Medicine/Rheumatology, Umeå, Sweden*

Background: The role of psychosocial conditions on the disease course of rheumatoid arthritis (RA) is getting increased attention. In our previous study, low social support and low decision latitude at work were associated with known modifiable risk factors for RA disease development, such as smoking and low educational level (1). Further, smoking and low educational level have previously been shown to be associated with worse RA disease outcome (2-4). Whether psychosocial characteristics are related to RA disease outcome needs further investigation.

Objectives: To investigate the relationship between two psychosocial characteristics: low social support and low decision latitude at work, and achievement of remission in patients with RA.

Methods: At inclusion in the Swedish EIRA study, incident RA cases (N=3724) and controls (N=5937), matched for age, sex and residential area, responded to a questionnaire including questions on social support and decision latitude at work. The answers were recoded into separate scores and the distribution of the scores among controls were used to define the exposures. Low social support and low decision latitude at work, respectively, among patients, were set as the level corresponding to the lowest quartile among controls, and were compared with scores corresponding to the remaining three quartiles.

The outcome, disease activity score 28-joint count (DAS28) remission, defined as DAS28<2.6, was captured through linkage with the Swedish Rheumatology Quality Register (SRQ) with data available from diagnosis for 2693 out of 3700 cases for social support and for 847 out of 1248 cases for decision latitude at work.

Logistic regression was used to evaluate the association between low social support or low decision latitude at work, respectively, and the chance of remission at the time-points 3 months, 12 months and 60 months after inclusion. All results were adjusted for age, sex and residential area and the fully adjusted models were also adjusted for smoking, obesity, physical activity and educational level.

Results: Low social support (n=655) was associated with a reduced chance for remission at all three time points in the model adjusted for age, sex and residential area; OR 3 months 0.77 (95% CI 0.61-0.97), OR 12 months 0.78 (95% CI 0.64-0.95) OR 60 months 0.77 (95% CI 0.59-0.99). This association was diminished after further adjustment. After stratifying for sex, this association was enhanced in women but inverse among men (Figure 1).

No association between low decision latitude at work (n=166) and chance for remission was observed neither in the analyses stratified for matching variables, nor in the full model. This result was only marginally changed after stratifying for sex (Figure 1).

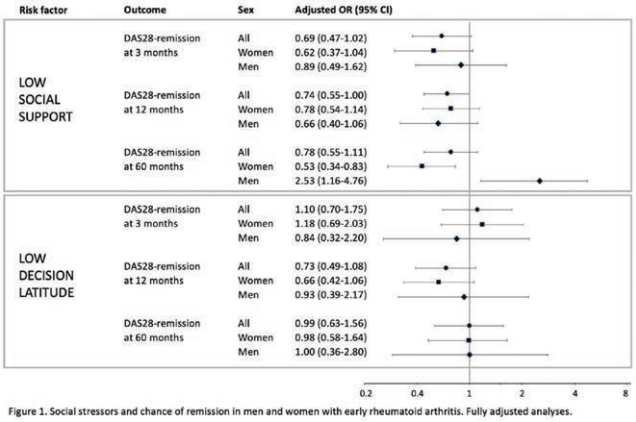


Figure 1. Social stressors and chance of remission in men and women with early rheumatoid arthritis. Fully adjusted analyses.

Figure 1. Odds ratios for assiciation between social stressors and DAS 28 remission

Conclusion: Low social support was associated with lower chance of remission in early RA, but the association was not independent of other risk factors for worse outcome (smoking, physical activity, obesity and low educational level). The interrelationship between social stressors and previously known risk factors for worse outcome highlights the importance of supportive actions at many levels to increase the possibility for the individual to make healthy decisions.

REFERENCES:

[1] Hedenstierna. et al. Scand J Rheumatol. 2021:1-5.

[2] Saevarsdottir, et al. Ann Rheum Dis. 2011;70(3):469-75.

[3] Saevarsdottir, et al. Arthritis Rheum. 2011;63(1):26-36.

[4] Jiang, et al. Arthritis Res Ther. 2015;17:317.

Acknowledgements: We want to thank all the participants of the EIRA study and the clinical collaborators for their valuable contribution. We also want to thank the staff for their dedicated work with the data collection.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2937

POS0485 TRAJECTORY CLUSTERS OF RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS: ASSOCIATIONS WITH CLINICAL VARIABLES

S. Blüml[1], A. Platzer[1], F. Alasti[1], D. Aletaha[1], J. S. Smolen[1], H. Radner[1].
[1]*Medical University Vienna, Rheumatology, Wien, Austria*

Background: Joint damage is a defining feature of rheumatoid arthritis (RA), a major driver of functional impairment and of reduction of quality of life. Many factors are associated with damage accrual however, the course of structural damage of individual patients over time and factors associated with such trajectories have not been investigated.
Objectives: Identification of trajectories of radiographic damage in RA by clustering patients according to the shape of their curve of Sharp-van der Heijde scores (SHS) over time. Developing models to predict their progression cluster from baseline characteristics.
Methods: Patient-level data over a two-year period from 5 large randomized controlled trials on TNF-inhibitors in RA (ERA, PREMIER, TEMPO, GO-BEFORE and GO-FORWARD) were used. SHSs were clustered in a shape-respecting manner to identify distinct clusters of radiographic progression. Characteristics of patients within different progression clusters were compared at baseline and over time. Logistic regression models were developed to predict trajectory of radiographic progression using information at baseline.
Results: In total 1887 patients with 7738 x-rays were used for cluster analyses. We identified 4 distinct clusters with characteristic shapes of radiographic progression: one with a stable SHS over the whole 2-year period (C0/lowChange; 86%); one with relentless progression (C1/rise; 5.8%); one with decreasing SHS (C2/improvement; 6.9%); and one going up and down (C3/bothWays; 1.4%) of the SHS. Robustness of clusters and shapes of progression over time were confirmed using different clustering methods and cut-offs to define radiographic progression (Figure 1). Regression models identified disease duration, baseline CRP and SHS and treatment status as predictors for cluster assignment (Table 1), showing good performance (PCC 87.5%; Nagelkerke r^2 0.36*)*.
Conclusion: We were able to identify 4 different clusters of radiographic progression over time in patients with RA, most remarkably one with relentless progression and another one with amelioration of joint damage over time, suggesting the existence of distinct patterns of joint damage accrual in RA. The nature of the identified trajectories is mostly explained by inflammatory load, disease duration and especially type of treatment.

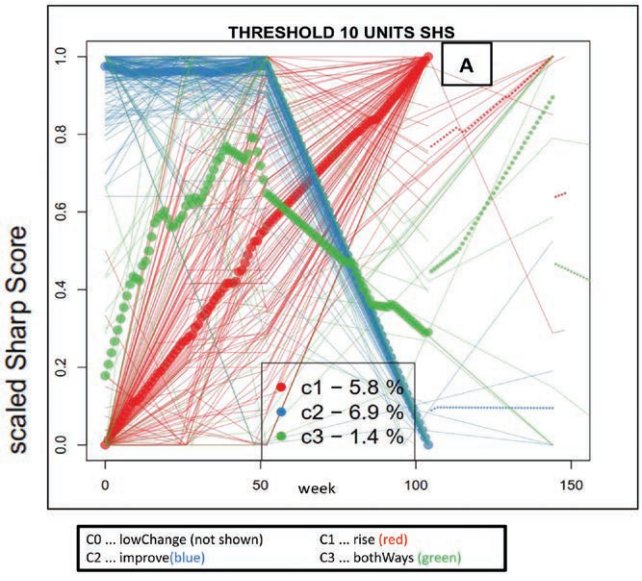


Figure 1. Representations of the major three clusters of radiologic progression curves.*(A) shows the curves of all patients with a SHS-range >= 10, colored by their cluster. Values between visits were linearly interpolated. Big dotted line is the median of particular cluster, thinner lines represent single patient values. Cluster C0 /lowChange are patients without enough variation in SHS to be seen as a curve, therefor not shown in the diagrams.*

Table 1. ***Simple logistic regression models to predict assignment to clusters of radiologic progression using information at baseline. Variables entered but not selected by a stepwise approach were: rheumatoid factor, age, gender, tender joint count*;**

c0/low change vs:	C1/rise Cluster		C2/improve Cluster	
parameters	**OR**	**95%CI**	**OR**	**95%CI**
X-ray Score	1.02	1.01-1.03	1.03	1.02-1.03
CRP (mg/dl)	1.12	1.07-1.16	0.98	0.90-1.07
Duration (years)	0.87	0.80-0.95	1.09	1.05-1.12
Treatment				
Combination	REF	REF	REF	REF
csDMARD	4.98	2.88-8.63	0.05	0.01-0.23
bDMARD Mono	2.28	1.29-4.04	0.64	0.38-1.08

Disclosure of Interests: Stephan Blüml Speakers bureau: Novartis, MSD, Abvie, Pfizer, Consultant of: MSD, Lilly, Novartis, Alexander Platzer: None declared, Farideh Alasti: None declared, Daniel Aletaha Speakers bureau: Abbvie, Amgen, Lilly, Merck, Novartis, Pfizer, Roche, Sandoz, Consultant of: Abbvie, Amgen, Lilly, Merck, Novartis, Pfizer, Roche, Sandoz, Grant/research support from: Abbvie, Amgen, Lilly, Novartis, Roche, SoBi, Sanofi, Josef S. Smolen Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO Pharma, Janssen, Lilly, Merck Sharp & Dohme, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, and UCB., Consultant of: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO Pharma, Janssen, Lilly, Merck Sharp & Dohme, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, and UCB., Grant/research support from: Dr Smolen received grants to his institution from Abbvie, AstraZeneca, Janssen, Lilly, Merck Sharpe & Dohme, Pfizer, and Roche, Helga Radner: None declared
DOI: 10.1136/annrheumdis-2021-eular.2991

POS0486 FACTORS ASSOCIATED WITH CHRONOTROPIC RESPONSE IN PEOPLE WITH RHEUMATOID ARTHRITIS

A. Osailan[1]on behalf of Physical activity in Rheumatoid arthritis research team and Research department in Dudley Hospital. [1]*Prince Sattam Bin Abdulaziz University, Health and Rehabilitation Sciences, Alkharj, Saudi Arabia*

Background: People with rheumatoid arthritis (RA) are at high risk for cardiovascular diseases (CVD) and CVD mortality. Reduced Chronotropic response (CR), which produces exercise intolerance, is known as a contributing factor to CVD and mortality. Studies have shown that people with RA have reduced CR. However, knowledge about the factors associated with CR in people with RA is limited.
Objectives: To explore the factors associated with CR including CVD risk factors, inflammatory markers and cardiorespiratory fitness (VO_2 peak).
Methods: 106 people with RA completed a treadmill exercise tolerance test while heart rate (HR) was monitored via 12 leads ECG. CR was defined as the percentage of [(achieved peak HR minus resting HR) divided by (age-predicted maximum HR minus resting HR)]. Serological CVD risk factors and inflammatory markers including lipids profile, markers of insulin resistance and sensitivity (HOMA, QUICKi), high sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), fibrinogen and white blood cells (WBC) were examined via a fasted blood sample. VO_2 peak was assessed via breath-by-breath gas analysis.
Results: 34% had reduced CR based on the cut-off value (≤ 80%) and the average CR was 86.2 ± 21%. Body mass index (r=-0.33, p=.001), HOMA (r=-0.26, p=.009), hsCRP (r=-0.23, p=.02), ESR (r=-0.21, p=.04), fibrinogen (r=-0.2, p=.05), WBC (r=-0.21, p=.04) were inversely associated with CR, whereas, high density lipoprotein (HDL) (r=0.43, p<.001), QUICKi (r=0.31, p=.002), and VO_2 peak (r=0.4, p<.001) were positively associated with CR. When all the variables were entered into a stepwise linear regression, HDL (p<.001) and VO_2 peak (p=.009) were independently associated with CR.
Conclusion: The current findings suggest that CR in RA was associated with many CVD risk factors, inflammatory markers, and cardiorespiratory fitness. Among all the varibales, HDL and cardiorespiratory fitness were moderately and independently associated with CR. Future studies should investigate the effect of improving these associated variables on CR in people with RA via exercise training programes.
Acknowledgements: Thanks to physical activity in Rheumatoid arthritis research team and Research department in Dudley Hospital. Sincere appreciation and gratitude to Dr Jet Veldhuizen van Zanten, Prof. Joan Duda, and Prof.

George Kitas from the University of Birmingham and Prof. George Metsios from the University of Wolverhampton.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3050

POS0487 ASSOCIATION OF RHEUMATOID ARTHRITIS WITH MORTALITY IN A COHORT OF CHRONIC KIDNEY DISEASE PATIENTS

M. Ezeanuna[1], D. Prince[2], S. A. Alexander[3], J. S. Richards[4], G. Kerr[5], D. Jala[6], N. Bansal[7], J. Liew[8], N. Singh[9]. *[1]Skagit Regional Health, Internal Medicine, Mount Vernon, Washington, United States of America*; *[2]University of Washington, Kidney Research Institute, Seattle, WA, United States of America*; *[3]University of Connecticut, Internal Medicine, Hartford, CT, United States of America*; *[4]UPMC Presbyterian Shadyside, Rheumatology, Pittsburgh, PA, United States of America*; *[5] Howard University Hospital, Rheumatology, Washington, DC, United States of America*; *[6]University of Iowa, Department of Medicine- Nephrology, Iowa, United States of America*; *[7]Kidney research institute, University of Washington, Nephrology, Seattle, WA, United States of America*; *[8]University of Washington, Division of Rheumatology, Seattle, United States of America*; *[9]University of Washington, Division of Rheumatology, Seattle, WA, United States of America*

Background: Rheumatoid Arthritis (RA) is associated with an increased risk of cardiovascular disease. RA is also associated with increased risk of chronic kidney disease (CKD) (1, 2), which is a known cardiovascular risk factor (3). We hypothesized that RA (compared with no RA) would be associated with increased risk of mortality among a cohort of patients with CKD.
Objectives: To determine the risk of mortality in RA patients with CKD.
Methods: This study was conducted using participants from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) prospective Chronic Renal Insufficiency Cohort (CRIC) study. Approximately 3600 participants were enrolled from seven US clinical centers. Patients aged 21 – 74 years with mild to moderate CKD were eligible for enrollment. The primary outcome of interest was all-cause mortality. Secondary outcomes of interest included: kidney event defined as end stage renal disease (ESRD) or 50% decline in estimated glomerular filtration rate (eGFR), myocardial infarction (MI), cerebrovascular accident (CVA), heart failure and a composite cardiovascular endpoint. The association of RA mortality over time was examined using Cox multivariate proportional hazards regression, adjusting for potential covariates (age, sex, race/ethnicity, BMI, current smoker, education).
Results: The study cohort included 492 participants with self-reported RA with a mean follow up of 9.5 years. Compared to the non-RA group, RA patients tended to be older, female, Black. Hypertension, diabetes, use of prednisone was more prevalent among the RA cohort. The unadjusted hazards ratio (HR) for mortality based on RA status was 1.45 (1.26, 1.67) but this association was attenuated after adjusting for the confounding factors [aHR 1.09 (0.94, 1.27)] (Table 1). Participants with RA had a significantly higher risk for heart failure than those without RA [aHR 1.17 (1.02, 1.34)]. We did not observe a statistically significant association between RA status and other secondary outcomes.

Table 1. Estimated hazard ratios (HR) for various outcomes from Cox proportional hazards regression for RA status

	Unadjusted	Model 1	Model 2
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Death	1.45 (1.26, 1.67)	1.09 (0.94, 1.27)	1.13 (0.97, 1.32)
MI or death	1.43 (1.25, 1.63)	1.09 (0.95, 1.26)	1.15 (0.99, 1.33)
CVA or death	1.42 (1.24, 1.63)	1.07 (0.92, 1.24)	1.11 (0.95, 1.29)
CHF or death	1.54 (1.35, 1.75)	**1.17 (1.02, 1.34)**	**1.22 (1.06, 1.40)**
Composite	1.49 (1.31, 1.69)	1.13 (0.99, 1.30)	**1.18 (1.03, 1.35)**
Kidney event	1.09 (0.94, 1.27)	0.91 (0.78, 1.07)	1.01 (0.85, 1.20)

Model 1 adjusted for: age, sex, race/ethnicity, BMI, current smoker, educationModel 2 adjusted for: model 1 + cardiovascular risk factors (urine albumin creatinine ratio, systolic blood pressure, estimated glomerular filtration rate)

Conclusion: RA was not associated with higher mortality among participants with CKD. However, RA was associated with higher rates of heart failure. Further studies evaluating the mechanisms behind this association are needed.
REFERENCES:
[1] Kochi M, Kohagura K, Shiohira Y, Iseki K, Ohya Y. Chronic kidney disease, inflammation, and cardiovascular disease risk in rheumatoid arthritis. J Cardiol. 2018;71(3):277-83.
[2] Sumida K, Molnar MZ, Potukuchi PK, Hassan F, Thomas F, Yamagata K, et al. Treatment of rheumatoid arthritis with biologic agents lowers the risk of incident chronic kidney disease. Kidney Int. 2018;93(5):1207-16.
[3] Chiu HY, Huang HL, Li CH, Chen HA, Yeh CL, Chiu SH, et al. Increased Risk of Chronic Kidney Disease in Rheumatoid Arthritis Associated with Cardiovascular Complications - A National Population-Based Cohort Study. PLoS One. 2015;10(9):e0136508.
[4] Muthukumar P, Dhanapriya J, Gopalakrishnan N, Dineshkumar T, Sakthirajan R, Balasubramaniyan T. Evaluation of renal lesions and clinicopathologic correlation in rheumatoid arthritis. Saudi J Kidney Dis Transpl. 2017;28(1):44-50.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3222

POS0488 THE IMPACT OF ANTINUCLEAR ANTIBODIES INDUCED BY ANTI-TUMOUR NECROSIS FACTOR ALPHA AGENTS ON THE LONG-TERM TREATMENT OUTCOMES IN RHEUMATOID ARTHRITIS PATIENTS

D. Santos Oliveira[1,2], A. Martins[1], F. R. Martins[3], M. Rato[1], F. Oliveira Pinheiro[1], D. Fonseca[4], S. Garcia[1], B. M. Fernandes[1], C. Vaz[1,2,5], M. Bernardes[1,5], L. Costa[1]. *[1]Centro Hospitalar Universitário de São João, Rheumatology Department, Porto, Portugal*; *[2]Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; *[3]Centro Hospitalar Universitário do Algarve, Rheumatology Department, Faro, Portugal*; *[4]Centro Hospitalar Vila Nova de Gaia / Espinho, Rheumatology Department, Vila Nova de Gaia, Portugal*; *[5]Faculty of Medicine, University of Porto, Department of Medicine, Porto, Portugal*

Background: The seroconversion of antinuclear antibodies (ANA) induced by anti-tumour necrosis factor alpha (anti-TNF-α) therapy remains a matter of concern in various inflammatory conditions namely rheumatoid arthritis. However, evidence is still scarce regarding the impact of these autoantibodies on the clinical response to treatment in these patients.

Objectives: This study aimed to explore the impact of ANA induced by anti-TNF-α therapy on the outcomes of treatment in patients with rheumatoid arthritis over two years of follow-up.

Methods: An observational retrospective cohort study was conducted with two years of follow-up. Patients diagnosed with rheumatoid arthritis, according to the American College of Rheumatology (ACR) criteria, and registered on the Rheumatic Diseases Portuguese Register (Reuma.pt) who started their first anti-TNFα agent as first biologic between 2003 and 2018 were included. Patients with positive ANA (titer ≥100) and/or positive anti-double stranded DNA (anti-dsDNA) antibodies and/or with a diagnosis of SLE at their first visit were excluded. Demographic, clinical and laboratory data were obtained by consulting Reuma.pt. Disease Activity Score for 28 joints (DAS28), DAS28 delta, Health Assessment Questionnaire (HAQ), HAQ delta were assessed at baseline, 6, 12, 18 and 24 months. Clinical response was evaluated by EULAR criteria and three response categories were defined: good, mild and no response. The rate of switch of biological treatment was assessed over 24 months. To examine the differences between groups with and without ANA seroconversion independent samples t test for normally distributed continuous data, Mann-Whitney U-tests for non-normally distributed continuous data and Chi-square tests for categorical data were used. Logistic regression models were used to assess the effects of ANA seroconversion on clinical response to treatment

over 6, 12, 18 and 24 months.

Results: A total of 185 patients (mean age of 49.3±10.9 years old; 85.4% female) with a median follow-up of 7 [4-14] years were included. We found an ANA seroconversion rate (titer ≥100) of 77.3% (n=143) with median time of 36 [15-72.3] months. There were no differences among groups regarding age, gender, disease duration, be seropositivity or not (for rheumatoid factor and/or anti-citrullinated protein antibodies) and have an erosive disease or not. DAS28 delta was significantly different (p=0.035) between group with positive ANA (2.01±1.29) and negative ANA (1.15±1.51) at 6 months. DAS28 was significantly different (p=0.014) between group with positive ANA (5.06±3.39) and negative ANA (3.99±1.43) at 12 months. No statistically significant differences were found in the DAS28, DAS28 delta, HAQ, HAQ delta at 18 and 24 months and in the EULAR response at any time. Switch rate was significantly different between patients with ANA seroconversion (median 1[0-1]) versus absence of seroconversion (median 0[0-1]), p=0.025. In the regression model ANA seroconversion did not predict switch rate and EULAR response over time.
Conclusion: This study showed that the majority of patients with rheumatoid arthritis treated with an anti-TNF-α agent developed ANA and that their presence may be associated with worse clinical results (DAS28) at 6 and 12 months. In fact, previous research suggested that a decrease in anti-TNF-α drug concentration due to the production of autoantibodies may lead to worse outcomes of treatment. Moreover, our data demonstrated that patients with ANA seroconversion

had a higher switch rate. Despite these results, there are no differences in the EULAR response between the two groups and ANA seroconversion did not predict this response over time. Therefore, ANA induced by anti-TNF-α agents should be monitored in patients with rheumatoid arthritis and its impact on treatment must be considered. Further research is needed to explore these results through large-scale prospective studies.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3265

POS0489 DOES TIME TO REMISSION DIFFER DEPENDING ON ROUTE OF ADMINISTRATION OF METHOTREXATE IN AN EARLY ARTHRITIS TREAT TO TARGET (T2T) COHORT?

I. Ali[1]. [1]*Our Lady's Hospital Manorhamilton, Rheumatology, Manorhamilton, Ireland*

Background: Rheumatoid arthritis (RA) is a multisystem inflammatory disorder that affects the joints and other body tissues. Approximately 1% of the worldwide population is living with RA 1. Methotrexate is the first line DMARD used for treatment of RA 2.

Objectives: The aim of this study was to analyse MTX use in achieving remission in early arthritis patients and to compare the route of administration to see whether it affects the time interval to remission.

Methods: An observational, prospective study was performed on patients' data available from our Early Arthritis Cohort. Newly diagnosed patients with RA meeting the American College of Rheumatology (ACR) criteria were enrolled in T2T programme led by Advanced Nurse Practitioner (ANP) with consultant supervision. To assess their response to treatment, we used the Clinical Disease Activity Index (CDAI). SPSS was used to analyse the data.

Results: A total of 353 have completed the programme and of these, 341were commenced on MTX. 208 patients (61%) were female. The MTX starting dose was 15mg for 88.4% (305/341) of patients. The median time to first increment in MTX dose was 7 weeks and the figure 1 was identical for the second increment. Of the 238 patients who started oral MTX, 18.48% (44) discontinued. 21.4% (22) of the 103 who started on SC-MTX discontinued (The p-value for discontinuation was 0.538). P-value for likelihood of achieving remission based on oral versus SC MTX was 0.248 and the p-value for time to achieve remission was 0.671 for oral versus SC MTX groups, see figure 1 attached.

Conclusion: Patients in this cohort are being started promptly on an appropriate dose of MTX and are escalated in a timely manner in-line with guidelines. Analysis showed no statistically significant difference in terms of time to remission, likelihood of achieving remission or discontinuation of MTX between oral and SC-MTX groups.

REFERENCES:

[1] Carmona L, Villaverde V, Hernández-García C, Ballina J, Gabriel R, Laffon A, et al. The prevalence of rheumatoid arthritis in the general population of Spain. Rheumatology. 2002;41(1):88-95.
[2] Rachapalli SM, Williams R, Walsh DA, Young A, Kiely PDW, Choy EH, et al. First-line DMARD choice in early rheumatoid arthritis—do prognostic factors play a role? Rheumatology. 2010;49(7):1267-71.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3293

POS0490 SERUM MATRIX METALOPROTINASE 3 AS A MARKER TO DISCRIMINATE SUBCLINICAL DISEASE ACTIVITY FROM ULTRASOUND DEFINED REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

F. Hamdy[1], A. F. Enein[2], N. Morad[1], S. Tharwat[2], A. M. Abd el-Khalek[3], E. E. Eltoraby[4]. [1]*Mansoura University, Rheumatology and Immunology Unit, Mansoura, Egypt*; [1]*Mansoura University, Rheumatology and Immunology Unit, Mansoura, Egypt*; [3]*Mansoura University, Dignostic Radiology, Mansoura, Egypt*; [1]*Mansoura University, Rheumatology and Immunology Unit, Mansoura, Egypt*

Background: Rheumatoid arthritis (RA) is a systemic disease which results in chronic inflammation that primarily involves synovial joints resulting in progressive joint destruction [1]. Detection of subclinical disease activity is important as radiographic progression was observed during remission course in some cases [2]. Ultrasound can detect subclinical activity and synovial inflammation, which predict relapse and radiographic progression [3].

Matrix Metaloprotinase 3 (MMP-3) is an enzyme, which is involved in joint destruction in RA patients. MMP-3 was found to correlate with disease activity, joint erosions, radiographic progression, drug responsiveness and disease outcome in patients with active RA [4]. However no data about its role in detection of subclinical activity in patients with clinical remission.

Objectives: To assess the role of MMP-3 as a marker to discriminate subclinical activity from ultrasound remission in rheumatoid arthritis patients with remission.

Methods: This study was conducted on 45 RA patients fulfilling remission or low disease activity criteria according to DAS 28 AND 45 healthy controls. Ultrasound evaluation was done for all patients using modified German US7 score. According to US7 score patients were classified into two groups: group with sonographic remission in which GS is 0±1 and the other group with subclinical disease activity with higher GS. Both groups underwent clinical and laboratory evaluation including MMP-3.

Results: Sonographic remission was achieved in 44% of patients (20 patients). There was no statistically significant difference as regard age, gender, smoking, disease duration, morning stiffness duration, CDAI, treatment and laboratory data apart from hemoglobin level between patients with subclinical disease activity and patients with remission. However, there is statistically significant difference between the two groups as regard joint deformity, extra articular manifestations, DAS 28, SDAI and hemoglobin level.
There was statistically significant difference in serum MMP-3 between RA patients and healthy control group. Serum MMP-3 was higher in RA patients with subclinical activity than patients with sonographic remission but the difference was not statistically significant (figure 1). Serum MMP-3 was positively correlated with ESR and synovitis score.

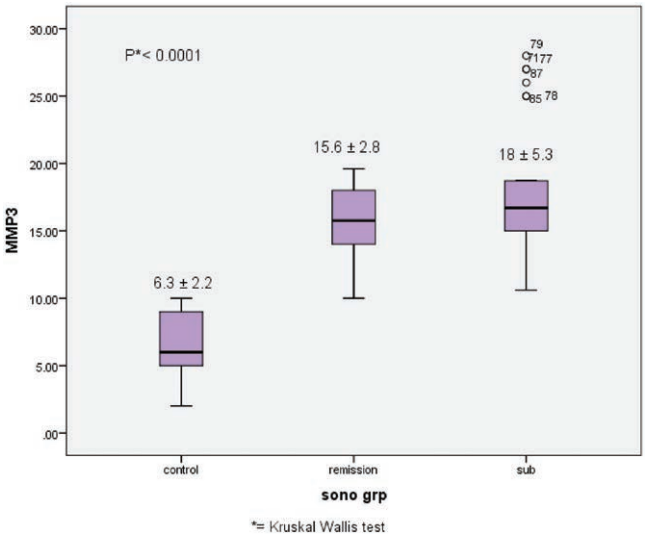


Figure 1.

Conclusion: Serum MMP-3 has correlation with US synovitis score. However, serum MMP-3 was not able to differentiate patients with sonographic remission from patients with subclinical disease activity. Ultrasound is still the gold standard for detection of subclinical disease activity.

REFERENCES:

[1] Ergin, S. (2000). "Romatoid Artrit ve Sjögren Sendromu." Fiziksel Tıp ve Rehabilitasyon, Güneş Kitapevi: 1549-1576.
[2] Ogishima, H., H. Tsuboi, N. Umeda, M. Horikoshi, Y. Kondo, M. Sugihara, T. Suzuki, I. Matsumoto and T. Sumida (2014). "Analysis of subclinical synovitis detected by ultrasonography and low-field magnetic resonance imaging in patients with rheumatoid arthritis." Modern rheumatology **24**(1): 60-68.
[3] Filippucci, E., E. Cipolletta, R. M. Mirza, M. Carotti, A. Giovagnoni, F. Salaffi, M. Tardella, A. Di Matteo and M. Di Carlo (2019). "Ultrasound imaging in rheumatoid arthritis." La radiologia medica **124**(11): 1087-1100.
[4] Lerner, A., S. Neidhöfer, S. Reuter and T. Matthias (2018). "MMP3 is a reliable marker for disease activity, radiological monitoring, disease outcome predictability, and therapeutic response in rheumatoid arthritis." Best Practice & Research Clinical Rheumatology **32**(4): 550-562.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3314

POS0491

LEFT VENTRICULAR GEOMETRIC ABNORMALITIES ASSOCIATED WITH HIGHER TITERS OF RHEUMATOID FACTOR AND ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODIES IN RHEUMATOID ARTHRITIS PATIENTS

N. Guajardo-Jauregui[1], J. R. Azpiri-López[2], D. Á. Galarza-Delgado[1], I. J. Colunga-Pedraza[1], S. Lugo-Perez[2], A. B. Rodriguez-Romero[1], A. Cárdenas[1], O. A. Cepeda-Ayala[2], H. Azpiri-Diaz[2]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*; *[2]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico*

Background: Rheumatoid arthritis (RA) patients have a higher risk of developing left ventricular (LV) geometric abnormalities which can result in the development of heart failure and cardiac death (1). High titers of rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies are associated with a worse cardiovascular (CV) prognosis in RA patients (2).
Objectives: The aim of this study was to assess the association between RF and anti-CCP antibody titers, and the LV geometric abnormalities detected by a transthoracic echocardiogram.
Methods: This was a cross-sectional, observational, and comparative study. Patients aged 40-75 years who fulfilled the 2010 ACR/EULAR classification criteria for RA underwent a transthoracic echocardiogram. Patients with RA and an alteration of LV geometry were matched to RA patients with normal LV geometry, by age, gender, comorbidities, and disease characteristics to eliminate confounders. LV geometry was evaluated with LV mass index and relative wall thickness. A blood sample was taken to measure RF and anti-CCP antibody titers. Distribution was evaluated with the Kolmogorov-Smirnov test. Comparisons were done with Chi square test for qualitative variables and Student's t test and Mann-Whitney's U test for quantitative variables. A p-value <0.05 was considered statistically significant.
Results: A total of 82 RA patients were included in this study, 41 patients with altered LV geometry and 41 patients with normal LV geometry. Of the 41 patients with LV geometric abnormalities, 37 (90.2%) presented LV concentric remodeling and 4 (9.8%) presented LV concentric hypertrophy. We found no significant differences in the demographic and clinical characteristics between both groups (Table 1). Patients with altered LV geometry showed higher titers of IgA-RF (102.11 U/ml vs 21.70 U/ml, p=0.011) and anti-CCP antibodies (193.04 U/ml vs 18.29 U/ml, p=0.005) (Figure 1).

Table 1. Demographic and disease characteristics.

	RA patients with altered LV geometry (n=41)	RA patients with normal LV geometry (n=41)	p
Age years, mean ± SD	53.12 ± 7.62	52.34 ± 7.74	NS
Women, n (%)	39 (95.1)	39 (95.1)	NS
T2DM, n (%)	7 (17.1)	4 (9.8)	NS
HTN, n (%)	13 (31.7)	10 (24.4)	NS
Dyslipidemia, n (%)	9 (22.0)	11 (26.8)	NS
Active smoking, n (%)	4 (9.8)	3 (7.3)	NS
Obesity, n (%)	11 (26.8)	14 (34.1)	NS
BMI kg/m^2, median (p25-p75)	27.95 (25.33-31.45)	28.42 (25.84-32.00)	NS
Disease duration years, median (p25-p75)	10.37 (2.72-17.80)	6.40 (3.43-13.29)	NS
CDAI, median (p25-p75)	14.00 (2.00-22.00)	10.00 (3.00-16.50)	NS
DAS28-CRP, mean ± SD	3.52 ± 1.42	3.09 ± 1.11	NS
Treatment			
MTX, n (%)	33 (80.5)	34 (82.9)	NS
Glucocorticoids, n (%)	25 (61.0)	23 (56.1)	NS
Antihypertensive, n (%)	13 (31.7)	8 (19.5)	NS
Statins, n (%)	6 (14.6)	4 (9.8)	NS

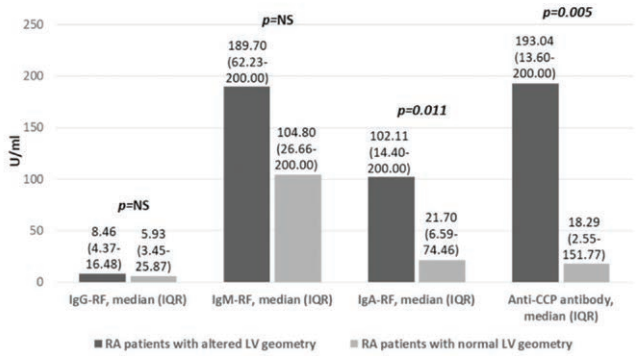
RA, rheumatoid arthritis; LV, left ventricular; NS, not significant; T2DM, type 2 diabetes mellitus; HTN, hypertension; BMI, body mass index; CDAI, clinical disease activity index; DAS28, disease activity score using 28 joints; CPR, C-reactive protein; MTX, methotrexate.

Conclusion: RA patients with altered LV geometry had higher titers of IgA-RF and anti-CCP antibodies. This suggests an association between antibody titers and CV prognosis in RA patients. Rheumatologists should take these data into account when evaluating CV risk in RA patients, assessing the possibility of performing an echocardiogram for early detection of CV abnormalities and an opportune treatment in this group of patients.

REFERENCES:

[1] Myasoedova E, Davis JM, 3rd, Crowson CS, et al. Brief report: rheumatoid arthritis is associated with left ventricular concentric remodeling: results of a population-based cross-sectional study. *Arthritis Rheum* 2013;65(7):1713-8. doi: 10.1002/art.37949
[2] Geraldino-Pardilla L, Russo C, Sokolove J, et al. Association of anti-citrullinated protein or peptide antibodies with left ventricular structure and function in rheumatoid arthritis. *Rheumatology (Oxford)* 2017;56(4):534-40. doi: 10.1093/rheumatology/kew436

Figure 1. Antibody titers.



Acknowledgements: We have no acknowledgements to declare.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3375

POS0492

A MOLECULAR SIGNATURE RESPONSE CLASSIFIER PREDICTS THE LIKELIHOOD OF EULAR NON-RESPONSE TO TNF INHIBITOR THERAPIES IN RA: RESULTS FROM A RETROSPECTIVE COHORT ANALYSIS

L. Zhang[1], C. van der Tog[2], A. den Broeder[2], T. Mellors[1], E. Connolly-Strong[1], J. Withers[1], A. Jones[1], V. Akmaev[1]. *[1]Scipher Medicine Corporation, Science and Technology, Waltham, United States of America*; *[2] Sint Maartenskliniek, Department of Rheumatology, Ubbergen, Netherlands*

Background: Following RA treatment recommendations, most people with rheumatoid arthritis (RA) begin targeted therapy with TNF inhibitors (TNFi), even though inadequate response to TNFi therapies is widespread. Treatment changes from one medication to the next are currently fueled by disease-activity measures and eventually result in disease control for most patients; however, this "trial-and-error" approach wastes precious time on ineffective treatments. A delay in reaching treat-to-target goals has a negative effect on patient burden and, possibly, disease progression.[1] Useful predictors for TNFi response have been challenging to identify but a specific molecular signature response classifier (MSRC) test was shown to be predictive for inadequate response to TNFi therapies.[2] The impact of such identification has the potential to result in improved patient outcomes, but further validation would be welcome, especially for response criteria other than ACR50, and in a stringent treat-to-target setting with lower baseline disease activity.
Objectives: To validate the predictive value of the MSRC test in identifying those patients who do not meet EULAR good response criteria after 6 months of TNFi treatment.
Methods: Data from a prospective cohort study conducted in the Sint Maartenskliniek (Nijmegen, the Netherlands) of RA patients who started adalimumab or etanercept TNFi as their first biologic were included.[3] Baseline RNA samples and clinical assessments were used to identify patients who had a molecular signature[1] of non-response to TNFi therapy. Outcomes were calculated at six months using DAS28-CRP-based EULAR good response, and high and low confidence responders and non-responders were identified using Monte Carlo simulation with 2,000 repeats and 70% precision cut off. Outcome measurements were blinded for test results. Treatment switch before 6 months was imputed as non-response. Odds ratios and area under the ROC curve (AUC) assessments were used to evaluate the ability of the MSRC test to predict inadequate response at 6 months against EULAR good response criteria.
Results: A total of 68 out of 88 RA patients were identified to have a high-confidence response status and were included in analyses (Table 1). EULAR good response was observed in 45.5% (31/68) of patients. Patients were stratified according to detection of a molecular signature of non-response with an AUC of 0.61. The odds that a patient with the molecular signature of non-response at baseline failed to achieve a EULAR good response at 6 months was four times greater than that of a patient lacking the molecular signature (odds ratio 4.0, 95% confidence interval 1.2-13.3).

Table 1. Patient demographics

Characteristic	RA patients (N = 68)
Age, median (SD)	57 (11)
Female, n (%)	43 (63.2)
CCP positive, n (%)	34 (50.0)
RF positive, n (%)	38 (55.9)
Prescribed adalimumab at baseline, n (%)	11 (16.2)
Prescribed etanercept at baseline, n (%)	57 (83.8)

Conclusion: In this validation study, the molecular signature of non-response identified patients who did not fulfill the EULAR good response criteria to TNFi therapies. The patient selection process for this study had limitations; additional analysis in an alternative cohort would further verify the performance of the MSRC test. Nevertheless, the test, previously validated for ACR50, now has been validated using EULAR good response in a treat-to-target setting.

REFERENCES:

[1] Schipper LG et al, Time to achieve remission determines time to be in remission. *Arthritis Res Ther* 201

[2] Mellors T, et al. Clinical Validation of a Blood-Based Predictive Test for Stratification of Response to Tumor Necrosis Factor Inhibitor Therapies in Rheumatoid Arthritis Patients. *Network and Systems Medicine* 2020

[3] Tweehuysen L et al. Predictive value of ex-vivo drug-inhibited cytokine production for clinical response to biologic DMARD therapy in rheumatoid arthritis. *Clin Exp Rheumatol* 2019

Disclosure of Interests: Lixia Zhang Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Celeste van der Tog: None declared, Alfons den Broeder Consultant of: Abbvie, Amgen, Cellgene, Roche, Biogen, Lilly, Novartis, Celltrion Sanofi, Gilead., Grant/research support from: Abbvie, Amgen, Cellgene, Roche, Biogen, Lilly, Novartis, Celltrion Sanofi, Gilead., Ted Mellors Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Erin Connolly-Strong Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Johanna Withers Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Alex Jones Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Viatcheslav Akmaev Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation

DOI: 10.1136/annrheumdis-2021-eular.3396

POS0493 TRIPLE-POSITIVITY AND ANTINUCLEAR ANTIBODIES, INSIGHTS ON DISEASE ACTIVITY: A RETROSPECTIVE COHORT STUDY OF COLOMBIAN RA PATIENTS

K. Maldonado-Cañón[1,2], D. V. Verano Castillo[1], H. F. Arenas Torrado[1], P. Coral Alvarado[2,3], P. A. Mendez Patarroyo[2,3], G. Quintana Lopez[2,3,4]on behalf of Reumavance Research Group. *[1]School of Medicine - National University of Colombia, Reumavance Research Group, Bogota, Colombia*; *[2]Fundacion Santa Fe de Bogota University Hospital, Reumavance Research Group. Internal Medicine Department., Bogotá, Colombia*; *[3] School of Medicine - Universidad de Los Andes, Reumavance research group. Internal Medicine Department., Bogota, Colombia*; *[4]School of Medicine - National University of Colombia, Reumavance research group. Internal Medicine Department., Bogota, Colombia*

Background: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by cartilage and bone destruction, which can lead to joint dysfunction and disability. Antibodies' role as biomarkers in RA has been recently increasing: Anti-citrullinated protein antibodies (ACPAs) are the most specific one (60–70% of cases); whereas rheumatoid factor (RF) is seen in nearly 70% of cases, however, it is less specific than ACPA for RA diagnosis[i]. ACPA/RF positivity is related to a more severe phenotype and a rapid progression to clinically apparent RA[ii]. Other biomarkers are Antinuclear Antibodies (ANAs), which have been related to a worse response to bDMARD treatment[iii].

iNishimura K, Sugiyama D, Kogata Y, Tsuji G, Nakazawa T, Kawano S, et al. Meta-analysis: Diagnostic accuracy of anti-cyclic citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis. Vol. 146, Annals of Internal Medicine. American College of Physicians; 2007. p. 797–808.

iiLingampalli N, Sokolove J, Lahey LJ, et al. Combination of anti-citrullinated protein antibodies and rheumatoid factor is associated with increased systemic inflammatory mediators and more rapid progression from preclinical to clinical rheumatoid arthritis. Clin Immunol. 2018;195:119-126.

iiiIshikawa Y, Hashimoto M, Ito H, Tanaka M, Yukawa N, Fujii T, et al. Anti-nuclear antibody development is associated with poor treatment response to biological disease-modifying anti-rheumatic drugs in patients with rheumatoid arthritis. Semin Arthritis Rheum. 2019;49(2):204–10.

Objectives: Our aim was to compare in terms of mean differences the disease activity according to the presence of RF, ACPA, and ANA in an outpatient clinic-based cohort of Colombian RA patients.

Methods: We conducted a retrospective cohort study with clinical-epidemiological data obtained from May 2013 to Feb. 2020 of patients with RA diagnosis based on the 2010 ACR/EULAR classification criteria. The patients were stratified into eight subgroups according to their autoantibody status. Disease activity, assessed by the DAS28-ESR, was recorded at baseline and after 3, ≈ 12, ≈ 24, and ≈ 36 (+/- 3) months. Mean DAS28-ESR differences were calculated by applying the Wilcoxon non-parametric rank test for two independent samples.

Results: Data of 384 patients who all completed 36 months of follow-up, from an ongoing cohort of ≈1100 patients, were included in the analysis. On our primarily female (n=294, 76,8%) population, RF$^+$ / ACPA$^+$ / ANA$^+$ subgroup was the most prevalent (n=183; 47,8%); interestingly, it was the one with the highest disease activity at baseline. After three months, all showed disease activity reduction; however, when completing follow-up, triple-positive, triple-negative and ANA-positive patients did not reach remission. Statistically significant mean differences were displayed when comparing overall and baseline mean DAS28-ESR scores for ANA$^+$ vs ANA$^-$ patients, as shown in table 1.

Table 1. Disease activity mean differences when comparing ANA$^+$ vs ANA$^-$ patients

	ANA$^+$ (n = 218)	ANA$^-$ (n = 165)	Mean difference	p value
Baseline	**4,05**	**3,62**	**0,43**	**0,014**
3	3,32	3,14	0,18	0,396
12	3,13	2,89	0,24	0,059
24	2,80	2,68	0,11	0,563
36	2,80	2,58	0,22	0,098
Overall	**3,22**	**2,98**	**0,24**	**0,002**

Conclusion: In our study population, triple-positive and ACPA$^+$/ANA$^+$ patients showed higher disease activity at baseline and on average during the follow-up period; furthermore, ANA positivity was shown to be conditional on a significant difference for higher disease activity. RF and ACPA positive have long since been described as determinants for disease activity; nonetheless, our research provides insights for the consideration of ANA titers as a novel addition that enables the preamble of *triple-positivity* as something to be acknowledged. Caution must be applied when interpreting these results, understanding the need for this matter to be subject of future research with greater sample size, and taking into account other potentially confounder variables.

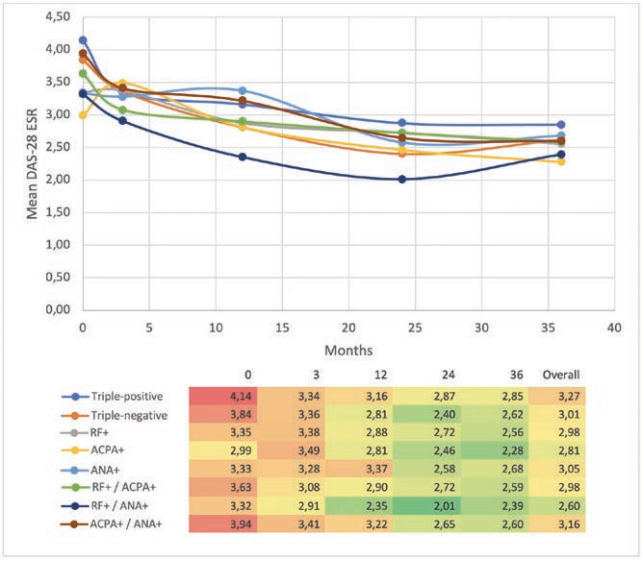


Figure 1. Mean disease activity for each stratum

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3443

POS0494 AN INVESTIGATION OF JOINT INFLAMMATION DEFINED BY COMPREHENSIVE ULTRASOUND ASSESSMENT AND PAIN SENSITISATION IN PATIENTS WITH ACTIVE RA

K. Chaabo[1], E. Chan[2], T. Garrood[2], Z. Rutter-Locher[2], A. Vincent[2], J. Galloway[3,4], S. Norton[5], B. Kirkham[2]. *[1]St George's Hospital, Rheumatology Department, London, United Kingdom*; *[2]Guy's Hospital, Rheumatology Department, London, United Kingdom*; *[3]King's College Hospital, Rheumatology Department, London, United Kingdom*; *[4]King's College London, Rheumatology, London, United Kingdom*; *[5]King's College London, Psychology and Inflammation Biology, London, United Kingdom*

Background: Treat-to-target strategies have improved outcomes in patients with RA. Targets based on clinical assessments of tender (TJC) and swollen joints (SJC) were developed when most patients had active inflammatory disease. It is now recognised some patients have pain sensitisation often termed fibromyalgia (FM), making clinical assessment of inflammatory disease more complex. An indicator of pain sensitisation is the difference between TJC and SJC, an observation we described in a pilot study (1).

Objectives: To study patients with RA to describe the relationships between enhanced clinical and patient-reported outcome measures (PROMS) and active inflammatory joint disease detected by comprehensive PDUS.
Methods: 158 sequential patients with RA with a DAS28ESR score >¬3.2 were enrolled from GSTT Rheumatology after informed consent. They were assessed by a rheumatologist for 66SJC, 68TJC, fibromyalgia tender points & physician global. Recorded PROMS were: patient global, widespread pain index (WPI), symptom severity score (somatic & fatigue), FACIT fatigue, HAQ, EQ5D QoL, GAD7, PHQ9 and PHQ15. All patients had a 44 joint US scored for PD and grey scale by the EULAR scale blind to all patient data. Data were recorded on MedSciNet and statistical analysis used STATA.
Results: Patients meeting the ACR 2010 criteria for FM2(n=72) vs those that did not(n=86) had similar demographics. SJC and US doppler scores were higher in the non-FM group, whereas rheumatoid factor, DAS28 and PROMs were higher in the FM group. Analysis of group differences using multinomial logistic regression and subsequent regularised (lasso) logistic regression, showed the FM group related to higher 28TJC, FACIT-F and PHQ15, with the non-FM group related to higher 28SJC, logESR, and lower Differences in 28S/TJC, Physician Global and FACIT-F. Patients were divided into four groups based on presence or absence of at least one PDUS+ joint and FM criteria; -FM-PD, -FM+PD, +FM-PD and +FM+PD, data summarised Table 1. The -FM-PD and -FM+PD groups related to Physician Global and negatively related to FACIT-F, Difference in 28S/TJC, and PHQ15 (-FM-PD). The +FM-PD group related positively to FACIT-F, Difference 28S/TJC, PHQ15, and negatively to Physician Global with +FM+PD related to PHQ9, FACIT-F and DAS28ESR.

TABLE 1. -FM -PD -FM +PD +FM -PD +FM +PD p-value

Female	34 (79%)	33 (77%)	35 (83%)	22 (73%)	0.77
Total power doppler score	0.0 (0.0-1.0)	16.0 (10.0-25.0)	0.0 (0.0-0.0)	9.0 (8.0-20.0)	<0.001
Total gray scale score	40.0(34.0-48.0)	57.5(45.0-82.0)	34.5(20.0-43.0)	60.0(46.0-84.0)	<0.001
Total Swollen JC	3.0 (1.0-5.0)	6.0 (3.0-9.0)	2.0 (0.0-5.0)	5.5 (2.0-10.5)	<0.001
Total Tender	5.5 (3.0-12.0)	8.0 (4.0-11.0)	13.0 (8.0-20.0)	15.0 (8.0-20.0)	<0.001
Tender-Swollen JC Difference	4.0 (0.0-8.0)	2.0 (0.0-4.0)	8.0 (4.0-18.0)	5.5 (2.5-13.5)	<0.001
ESR mm/hour	10.0 (8.0-16.0)	14.0 (10.0-30.0)	12.0 (7.0-23.0)	19.5 (11.5-42.5)	0.021
Pain VAS	50.0 (40.0-65.0)	50.0 (30.0-60.0)	60.0 (47.5-77.5)	67.5 (55.0-80.0)	<0.001
Patient VAS	50.0 (30.0-70.0)	40.0 (30.0-70.0)	60.0 (40.0-80.0)	65.0 (50.0-80.0)	0.006
Physician VAS	30.0 (20.0-50.0)	50.0 (40.0-60.0)	30.0 (20.0-40.0)	50.0 (32.5-70.0)	<0.001
DAS28 (ESR)	4.2 (3.7-4.9)	4.7 (4.1-5.2)	4.7 (3.9-5.8)	5.6 (4.9-6.6)	<0.001

Conclusion: These data using comprehensive US assessment to detect inflammatory joint disease, demonstrate that active inflammation defined as at least 1PDUS+ joint, may account for disease activity in slightly less than half of unselected patients with RA with a DAS28ESR score >3.2. This study shows how frequently pain sensitisation accounts for symptoms and signs in RA. We suggest in addition to central sensitisation, often called FM, another group identified here as -FM-PD, may have pain from joint damage or peripheral pain sensitisation of joints, likely due to different mechanisms than central pain sensitisation.
REFERENCES:
[1] Mian A et al, BMC Musculoskelet Disord. 2016;17: 404
[2] Wolfe F et al, Arth Care & Res 2010; 62:600
Disclosure of Interests: Khaldoun Chaabo: None declared, Estee Chan: None declared, Toby Garrood: None declared, Zoe Rutter-Locher: None declared, Alexandra Vincent: None declared, James Galloway Speakers bureau: Dr Galloway has received speaker fees / honoraria from Abbvie, BMS, Celgene, Chugai, Gilead, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi, Sobi and UCB, Sam Norton: None declared, Bruce Kirkham Speakers bureau: Professor Bruce Kirkham has received speaker fees / honoraria from Abbvie, Gilead, Janssen, Lilly, Novartis, Pfizer,and UCB., Grant/research support from: Professor Bruce Kirkham has received research support from Lilly, Novartis and UCB.
Professor Bruce Kirkham has received speaker fees / honoraria from Abbvie, Gilead, Janssen, Lilly, Novartis, Pfizer and UCB.
DOI: 10.1136/annrheumdis-2021-eular.3509

POS0495

LARGE JOINT DISEASE IN RHEUMATOID ARTHRITIS AND THE ROLE OF RHEUMATOID FACTOR. RESULTS FROM THE EARLY RHEUMATOID ARTHRITIS STUDY

S. S. Zhao[1], E. Nikiphorou[2], A. Young[3], P. Kiely[4,5]. [1]*University of Liverpool, Institute of Life Course and Medical Sciences, Liverpool, United Kingdom*; [2]*King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; [3]*University of Hertfordshire, Center for Health Services and Clinical Research and Post Graduate Medicine, Hatfield, United Kingdom*; [4]*St George's, University of London, Institute of Medical and Biomedical Education, London, United Kingdom*; [5]*St George's University Hospitals NHS Foundation Trust, Rheumatology, London, United Kingdom*

Background: Rheumatoid arthritis (RA) is classically described as a symmetric small joint polyarthritis with additional involvement of large joints. There is a paucity of information concerning the time course of damage in large joints, such as shoulder, elbow, hip, knee and ankle, from early to established RA, or of the influence of Rheumatoid Factor (RF) status. There is a historic perception that patients who do not have RF follow a milder less destructive course, which might promote less aggressive treatment strategies in RF-negative patients. The historic nature of the Ealy Rheumatoid Arthritis Study (ERAS) provides a unique opportunity to study RA in the context of less aggressive treatment strategies.
Objectives: To examine the progression of large joint involvement from early to established RA in terms of range of movement (ROM) and time to joint surgery, according to the presence of RF.
Methods: ERAS was a multi-centre inception cohort of newly diagnosed RA patients (<2 years disease duration, csDMARD naive), recruited from 1985-2001 with yearly follow-up for up to 25 (median 10) years. First line treatment was csDMARD monotherapy with/without steroids, favouring sulphasalazine for the majority. Outcome data was recorded at baseline, at 12 months and then once yearly. Patients were deemed RF negative if all repeated assessments were negative. ROM of individual shoulder, elbow, wrist, hip, knee, ankle and hindfeet joints was collected at 3, 5, 9 and 12-15 years. The rate of progression from normal to any loss of ROM, from years 3 to 14 was modelled using GEE, adjusting for confounders. Radiographs of wrists taken at years 0, 1, 2, 3, 5, 7, 9 were scored according to the Larsen method. Change in the Larsen wrist damage score was modelled using GEE as a continuous variable, while the erosion score was dichotomised into present/absent. Surgical procedure data were obtained by linking to Hospital Episodes Statistics and the National Joint Registry. Time to joint surgery was analysed using multivariable Cox models.
Results: A total of 1458 patients from the ERAS cohort were included (66% female, mean age 55 years) and 74% were RF-positive. The prevalence of any loss of ROM, from year 3 through to 14 was highest in the wrist followed by ankle, knee, elbow and hip. The proportion of patients at year 9 with greater than 25% loss of ROM was: wrist 30%, ankle 12%, elbow 7%, knee 7% and hip 5%. Odds of loss of ROM increased over time in all joint regions, at around 7 to 13% per year from year 3 to 14. There was no significant difference between RF-positive and RF-negative patients (see Figure 1). Larsen erosion and damage scores at the wrists progressed in all patients; annual odds of developing any erosions were higher in RF-positives OR 1.28 (95%CI 1.24-1.32) than RF-negatives OR 1.17 (95%CI 1.09-1.26), p 0.013. Time to surgery was similar according to RF-status for the wrist and ankle, but RF-positive cases had a lower hazard of surgery at the elbow (HR 0.37, 0.15-0.90), hip (HR 0.69, 0.48-0.99) and after 10 years at the knee (HR 0.41, 0.25-0.68). Adjustment of the models for Lawrence assessed osteoarthritis of hand and feet radiographs did not influence these results.

Figure 1. Odds of progression to any loss of ROM (from no loss of ROM) per year in the overall population and stratified by RF status.

Conclusion: Large joints become progressively involved in RA, most frequently affecting the wrist followed by ankle, which is overlooked in some composite disease activity indices. We confirm a higher burden of erosions and damage at the wrists in RF-positive patients, but have not found RF-negative patients to have a better prognosis over time with respect to involvement of other large joints. In contrast RF-negative patients had more joint surgery at the elbow, hip, and knee after 10 years. There is no justification to adopt a less aggressive treatment strategy for RF-negative RA. High vigilance and treat-to-target approaches should be followed irrespective of RF status.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3626

POS0496

YOUNG VERSUS LATE-ONSET RHEUMATOID ARTHRITIS: A PROSPECTIVE 12 MONTH-FOLLOW-UP COHORT STUDY IN AN EARLY ARTHRITIS COHORT

A. R. Prata[1], M. Sousa[1], H. Assunção[1], L. Saraiva[1], L. Brites[1], M. Luis[1,2], P. Freitas[1], F. Campos Costa[1], T. Santiago[1,2], J. A. P. da Silva[1,2], C. Duarte[1,2]. *[1]Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal*; *[2]University of Coimbra, Faculty of Medicine, Coimbra, Portugal*

Background: Rheumatoid Arthritis (RA) is a chronic inflammatory arthropathy that can present at any age. Data regarding differences in the clinical course and outcome in Late-Onset Rheumatoid Arthritis (LORA) comparing to Young-Onset RA (YORA) are conflicting. Some studies suggested that LORA may represent a more benign form of RA (1), while others have shown a poorer prognosis in these patients (2,3). Only a few publications have included patients with early disease (3).
Objectives: To compare demographic and clinical features between LORA and YORA patients, and clinical activity at baseline and after 12 months of initial therapy, in patients with early disease.
Methods: We conducted a prospective cohort study of 12 months of follow-up based on an early arthritis clinic. Consecutive patients with early RA – less than 12 months duration – fulfilling ACR/EULAR 2010 and/or ACR 1987 RA classification criteria, were included and classified in LORA (disease onset ≥60 years) and YORA groups. Variables were collected from patients' registries at first appointment after symptoms onset and after 12 months of treatment, according to a treat-to-target strategy. Independent t-test and chi-square test were performed to compare variables between groups.
Results: We included 72 patients (40 (55.6%) YORA; 32 (44.4%) LORA), mean age at diagnosis 44.9±1.78 and 72.5± 1.34 years, respectively. In LORA group, the symptoms duration at first observation was shorter (17.0±2.26 vs. 23.8±2.45 weeks; p=0.046) and rheumatoid factor (RF)/ anti-citrullinated protein antibodies (ACPA) positivity was lower (28.1% vs 65.0%; p= 0.002; 31.3% vs 72.5%; p<0.001). At baseline, LORA had higher mean number of tender joints (9.76±1.29 vs 6.50±0.67; p=0.021), erythrocyte sedimentation rate (ESR) (45.7±4.98 vs. 29.3±3.74; p=0.011), C-reactive protein (CRP) (4.63±0.91 vs 2.22±0.46; p=0.022) and disease activity using DAS28-3V (5.11±0.28 vs 4.42±0.19; p=0.046), CDAI (33.7±3.39 vs 23.6±2.18; p=0.015) and SDAI (37.4±3.43 vs 26.3±2.57; p=0.015). At the end of follow-up, there were no statistically significant differences between LORA and YORA groups regarding treatment, disease activity and patient-reported outcomes at 12 months (Table 1).

Table 1. Clinical variables assessment at 12 months of follow-up.

	EORA	YORA	*p*-value
Treatment, % users			
Corticosteroids	93.3	97.4	p= 0.576
Methotrexate	76.7	74.4	p=0.825
Hydroxychloroquine	43.3	46.2	p= 0.815
Sulfasalazine	10.0	15.4	p=0.722
Leflunomide	3.30	5.10	p=1.000
TNF blockers	3.30	5.10	p=0.717
DAS28-3V, mean (SD)	1.99±0.15	2.22±0.15	p=0.286
SDAI, mean (SD)	4.64±1.35	7.68±1.39	p=0.128
CDAI, mean (SD)	4.15±1.17	6.56±1.32	p=0.180
Swollen joints, mean (SD)	1.29±0.49	1.03±0.25	p=0.613
Tender joints, mean (SD)	0.32±0.13	1.28±0.53	p=0.084
ESR, mean (SD)	10.6±1.79	9.43±1.14	p=0.585
CRP, mean (SD)	0.44±0.09	0.50±0.15	p=0.730
PtGA, mean (SD)	21.8±5.90	29.2±6.11	p=0.387
PhGA, mean (SD)	10.6±3.26	13.1±3.11	p= 0.593
Pain intensity (VAS), mean (SD)	20.7±5.82	32.7±6.30	p=0.169
HAQ, mean (SD)	0.23±0.089	0.54±0.13	p=0.060

Legend: DMARD- disease-modifying anti-rheumatic drug; TNF- tumoral necrosis factor; SDAI-simplified disease activity score; CDAI- clinical disease activity score; PtGA/ PhGA – patient's/ physician's global assessment of general health; VAS- visual analogic scale; HAQ- health assessment questionnaire.

Conclusion: LORA patients presented with higher disease activity manifested by higher joint counts and laboratory inflammatory markers but lower RF and ACPA positivity proportion. Despite the more aggressive clinical presentation, the clinical and functional outcomes at 12 months were similar between LORA and YORA patients.
REFERENCES:
[1] Deal et al. Arthritis Rheum 1985;28(9):987-94.
[2] Arnold et al. Rheumatology (Oxford) 2014; 53:10751086.
[3] Romão et al. Semin Arthritis Rheum 2020;0(4):735-743.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3631

POS0497

A RELIABILITY EXERCISE USING CONSENSUAL DEFINITIONS FOR THE ULTRASONOGRAPHY OF THE SHOULDER IN RHEUMATOID ARTHRITIS

K. Ben Abdelghani[1], S. Miladi[1], I. Mahmoud[2], H. Ajlani[3], E. Haddouche[4], A. Maghraoui[5], S. Slimani[6], A. Fazaa[1], A. Ben Tekaya[2], L. Abdelmoula[2], A. Laatar[1], R. Bahiri[7]. *[1]Université de Tunis El Manar, Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*; *[2]Université de Tunis El Manar, Chrles Nicolle Hospital, Rheumatology, Tunis, Tunisia*; *[3]El Yasminet Hospital, Ben Arous, Rheumatology, Tunis, Tunisia*; *[4]Department of Rheumatology, Ben Aknoun Specialized Hospital in the Musculoskeletal System, Rheumatology, Algers, Algeria*; *[5]Rheumatology Private Office, Rheumatology, Rabat, Morocco*; *[6]Atlas Clinic of Rheumatology, Rheumatology, Batna, Algeria*; *[7]El Ayachi Hospital, CHU Rabat-Salé, Rheumatology, Rabat, Morocco*

Background: Although numerous clinical tests for the diagnosis of painful shoulder are available, differentiating articular from periarticular lesions may be difficult in daily practice. Fortunately, the precise diagnosis of shoulder pain in RA benefited from a reliable imaging modality to detect its exact origin as ultrasonography (US).
Objectives: This study aimed to assess the intraobserver and interobserver reliabilities of the ultrasonographic findings for patients with established RA having shoulder pain in a patient-based exercise among maghrebian rheumatologists experts on US.
Methods: A total of 7 operators examined 10 patients in 2 rounds independently and blindly of each other.
Each patient underwent a US scanning of the painful shoulder in four sites based on US technical guidelines of the European society of musculoskeletal radiology: long head of Biceps (LHB), subscapularis recess, posterior recess and axillary recess. The presence of a subdeltoid or subcoracoid bursitis or the presence of transfixiant tear of the suprasupinatus were notified if present. Intra and inter-observer reliabilities were calculated.
Results: Intraobserver reliability was excellent for GS synovitis in subscapularis and posterior recesses (k=0.91 for both) and for subcoracoid bursitis (k=0.81). It was good in case of presence of a subdeltoid bursitis (k=0.79), transfixiant tear of the suprasupinatus (k=0.65), GS synovitis and effusion in LHB (k=0.67 and 0.6 respectively) and subdeltoid bursitis (k= 0.79). Interobserver reliability was good for PD for LHB signals searched longitudinally (k=0.78) and transversally (k=0.78). It was moderate for GS for LHB synovitis (k=0.55). Interobserver agreement was poor for effusion and GS synovitis for subscapularis, posterior and axillary recesses. It was very poor and/or absent for PD signals in these recesses.
Conclusion: US is a reliable imaging tool for shoulder in RA especially with regard to LHB effusion, GS and PD synovitis. Interobserver reliability of subscapularis, posterior and axillary recesses could be optimized by standardization of sites to assess.
REFERENCES:
[1] Bruyn G a. W, Naredo E, Möller I, Moragues C, Garrido J, de Bock GH, et al. Reliability of ultrasonography in detecting shoulder disease in patients with rheumatoid arthritis. Ann Rheum Dis 2009;68:357–61.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3736

POS0498

RELATIONSHIP BETWEEN IMPAIRED MELATONIN SECRETION AND DURATION, RADIOLOGICAL STAGE AND PHYSICAL ACTIVITY OF RHEUMATOID ARTHRITIS

Y. Sikalo[1], L. Zhuravlyova[1], M. Oliinyk[1], V. Fedorov[1]. *[1]Kharkiv National Medical University, Internal Medicine No.3 and Endocrinology, Kharkiv, Ukraine*

Background: There is a close relationship between the development of severe autoimmune diseases and disorders of the neuroendocrine immune regulation of the body [1]. The role of melatonin as the main mediator of neuroendocrino-immune interactions in rheumatoid arthritis (RA) remains poorly understood [2].
Objectives: The aim of the study was to determine the daily serum melatonin profile of RA patients with different duration of the disease, radiological stage and physical activity.
Methods: The daily serum melatonin profile of patients with active RA (n=105, mean age 49.8±12.6 years, 75.5% of women) was compared with that of healthy subjects from the general population (n=30). In addition, we investigated daily serum melatonin secretion in relation to duration of the disease, radiological progression and physical activity (HAQ). Patients were divided into 4 groups depending on the RA duration (mean 8.4±6.6 years): 1st group - up to 2 years (n=12), 2nd group - 2-5 years (n=37), 3rd group - 6-10 years (n=26), 4th group - more than 10 years (n=30). Depending on the radiological progression, patients were divided into stages: 1st stage (n=16), 2nd stage (n=64), 3d stage (n=25). Melatonin serum levels was determined by the enzyme immunoassay at 8 and 20 o`clock. For statistical analysis were used the Man - Whitney test and the Spearman rank correlation method.

Results: The melatonin serum levels in RA patients were in 2 and 3 times higher in the morning and evening time than those of healthy individuals in the control group (p=0.001). We noticed significant correlations between melatonin level and disease duration (r_S =-0.5, p <0.01). Significant differences in melatonin levels were revealed in RA patients in 1st and 3rd groups (p=0.049), in 1st and 4th groups (p = 0.012), in 2nd and 3rd groups (p=0.001), in 2nd and 4th groups (p=0.001). Also we determined significant differences in melatonin levels between 1st and 2nd radiological stages (p =0,001) of RA patients. However, melatonin levels were not related to physical activity (HAQ).
Conclusion: We found a close relationship between serum melatonin levels, duration of the disease and radiological progression in RA patients. The most significant changes in melatonin metabolism occur in patients with the duration of the disease up to 5 years and with lower radiological stages. Our data indicate the important role of neurotransmitter in the pathogenesis of RA, especially at the initial stage of the disease.
REFERENCES:
[1] Sternberg EM. Neuroendocrine regulation of autoimmune/inflammatory disease. J Endocrinol. 2001 Jun;169(3):429-35. doi: 10.1677/joe.0.1690429. PMID: 11375112.
[2]Mańka S, Majewska E. Immunoregulatory action of melatonin. The mechanism of action and the effect on inflammatory cells. Postepy Hig Med Dosw (Online). 2016 Oct 4;70(0):1059-1067. doi: 10.5604/17322693.1221001. PMID: 27708210.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3752

POS0499 WORK ABSENCE DUE TO MUSCULOSKELETAL SYMPTOMS IN PATIENTS AT-RISK OF RHEUMATOID ARTHRITIS IS COMPARABLE TO THOSE WITH ESTABLISHED DISEASE

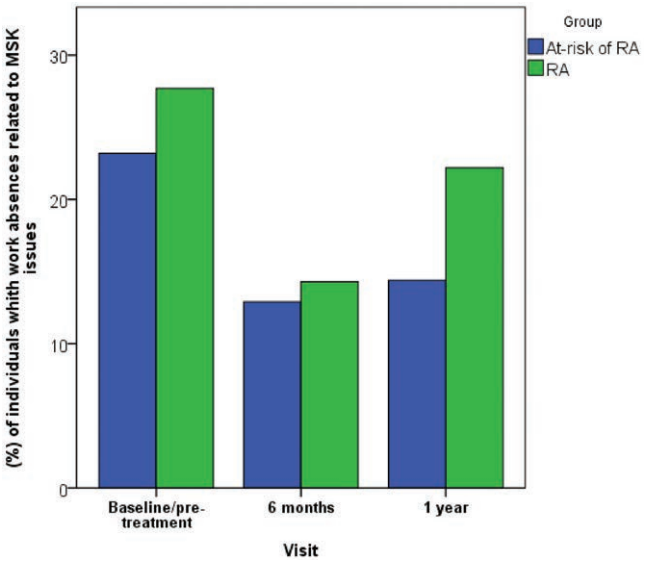
L. Garcia-Montoya[1,2], K. Mankia[1,2], L. Duquenne[1,2], J. Nam[1,2], A. Di Matteo[1,2], J. Peill[1,2], E. Mumba[1,2], P. Emery[1,2]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*; [2]*Leeds Biomedical Research Centre, NIHR, Leeds, United Kingdom*

Background: Rheumatoid arthritis (RA) is an established cause of disability and work absence; however, little is known about the impact of musculoskeletal (MSK) symptoms on sick leave in patients at-risk of developing the disease.
Objectives: To describe the sick leave of individuals at-risk of RA, compared to patients who had recently been diagnosed with RA, over a 12-month period. Additionally, to investigate baseline predictors for sick leave within the first 12 months.
Methods: A prospective observational cohort for individuals at-risk of RA was conducted. A total of 591 consecutive anti-citrullinated protein antibodie positive (ACPA+) individuals, with no clinical synovitis were recruited. A MSK ultrasound scan and a blood test were performed at baseline, and information about employment regime (retired, not in a paid job, part time and full time), days of sick leave and reasons for absences within the previous months were collected every 3 months and analysed at baseline, 6 months, 12 months and at the moment of diagnosis of an inflammatory arthritis (IA) (if the patient had progressed). Subjects who had retired (n=80) were excluded from the analysis.
A comparison was made with 114 RA patients from an observational study. Employment information was collected at pre-treatment, 6 months and 1 year after diagnosis. Univariable and logistic regression analyses were performed to assess predictors of work absence due to MSK reasons in the next 12 months from baseline for at-risk individuals.
Results: Even though the reasons for unemployment were not available, there were no statistically significant differences between employment rates across the timepoints of the study for the at-risk individuals' group (p=0.778). A similar pattern was observed in the RA patient group; which also maintained the same employment rates throughout the study (p=0.311) and these were comparable to the at-risk individuals' (p=0.480).
Over 35% of at-risk individuals in paid employment had work absences in the 3 months prior to the baseline visit. Of these 65.5% were due to MSK related issues, meaning 23.2% of the total absences were MSK related. The other reasons for work absence can be seen in table 1. This fell to 12.9% of the total absences at 6 months (which probably reflects clinical intervention) and increased to 38% if the patient progressed to an IA (graph 1).

Table 1. REASONS FOR SICK LEAVE AT BASELINE IN INDIVIDUALS AT-RISK OF RA (%)

MSK related issues	65.5
Flu-like symptoms	20.1
Gastrointestinal issues	19.4
Stress/anxiety	14.4
Headaches	11.5
Infection	3.6
Fatigue	1.4
Other	3.6

The percentage of individuals who took absence from work due to MSK related issues, was similar in both the at risk and RA group, including an initial reduction possibly due to drug intervention (graph 1). However, the median number of days off work 3 months prior baseline, 6 months and 1 year in RA patients tended to be higher than those in the at-risk group (10, 2 and 6 versus 5, 4 and 3 respectively).
Several factors were assessed to predict sick leave within 12 months in at-risk individuals: age, gender, smoking status, ACPA, rheumatoid factor (RF), anti-nuclear antibodies (ANA), C-reactive protein (CRP), early morning stiffness, shared epitope, joint pain, joint tenderness and abnormal findings in the ultrasound scan (erosions or power doppler); however, only RF [OR 0.18; p=0.018; 95% CI (0.04-0.84)] and CRP [OR 1.3; p=0.021; 95%CI (1.04-1.60)] were statistically significant in the multivariable analysis.
Conclusion: Even though being at-risk of RA is not considered a potential cause of disability, results show that the burden on the workplace, due to MSK related absences, was comparable to subjects diagnosed with RA. Although further investigation is required, initial data suggests that clinical intervention may reduce this burden; which tends to be higher in at-risk individuals with a negative RF and a high CRP.



Graph 1. Percentage of individuals who had work absences related to MSK issues 3 months prior to each timepoint.

Acknowledgements: H. Singh
T. Hulland
G. John
- Leeds Cares -
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3765

POS0500 NUMBER AND CO-EXPRESSION OF TNF RECEPTORS TYPE 1 AND 2 ON IMMUNOCOMPETENT CELLS ARE ASSOCIATED WITH STABILITY OF REMISSION IN RHEUMATOID ARTHRITIS PATIENTS

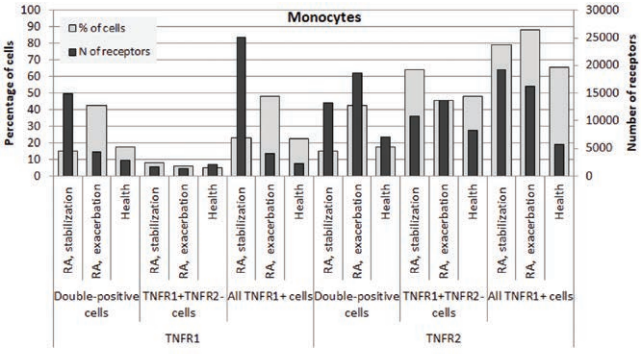
A. Alshevskaya[1], J. Lopatnikova[1], J. Zhukova[1], O. Chumasova[2], N. Shkaruba[2], A. Sizikov[2], S. Sennikov[1,3]. [1]*RIFCI, Laboratory of Molecular Immunology, Novosibirsk, Russian Federation*; [2]*RIFCI, Rheumatology Department, Novosibirsk, Russian Federation*; [3]*Novosibirsk State University, Institute of Medicine and Psychology, Novosibirsk, Russian Federation*

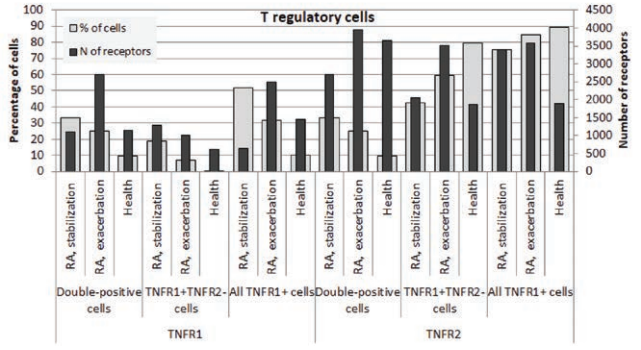
Background: The balance of TNFα receptors expression on cells which are actively involved in immunopathological processes affects both the density of distribution of receptors on cells and co-expression in subsets. Previously it was shown that basic effective RA therapy with methotrexate and glucocorticoids leads to equalization of the expression profile either in the percentage of cells or in the number of receptors, approaching those of healthy donors, but not simultaneously. However, questions about the relationship between the effectiveness of biological therapy and receptors co-expression remain unknown.
Objectives: To assess the differences in co-expression and quantitative expression of TNF receptors type 1 and 2 in subsets of cells associated with the severity of the disease, depending on the response to rituximab therapy.
Methods: Subanalysis of patients with high disease activity level successfully treated with rituximab (alone or in combination treatment scheme) during

hospitalization was performed (n = 14). The first group included 6 patients who retained low disease activity during 1 month follow-up (RA, stabilization). The second group consisted of 8 patients who had exacerbation during follow-up period. As a control group, we used data from 43 comparable healthy donors. Subsets of T regulatory cells and monocytes were studied. A comparison was made among the indicators of receptors number and proportion of cells expressing the corresponding receptor.

Results: For T regulatory cells, the key differences for patients who did not retain low disease activity were significantly higher number of TNF type 1 and type 2 receptors on double-positive cells with a lower percentage of these cells compared to stable patients. At the same time, higher differences between proportions of double-positive cells in comparison with control values of healthy donors were associated with higher probability of maintaining in remission.

For monocytes, the key differences in stable patients were the very high quantitative expression of type 1 receptors on double-positive cells, with a lower percentage of these cells compared to patients with exacerbation. At the same time, lower differences between proportions of double-positive cells in comparison with control values of healthy donors were associated with higher probability of maintaining in remission.





Conclusion: Obtained data confirm the previously proposed hypothesis about the essential role of balance in quantitative expression of TNF receptors type 1 and 2 on double-positive cells to determine the intensity and type of cell response to the mediator and its association with the level of disease activity and response to therapy.

Acknowledgements: This study is supported by grant of the President of the Russian Federation for state support of young Russian PhD scientists №МК-2433.2020.4

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3873

POS0501 SUSTAINED 2-YEAR REMISSION OF THE DISEASE IN A CLINIC OF EXCELLENCE IN RHEUMATOID ARTHRITIS. EXPERIENCE OF THE CLINICAL REGISTRY IN COLOMBIA

J. M. Bello-Gualtero[1,2], E. Peña[3], P. I. Santos Moreno[4], J. Vesga Gualdrón[3], G. Saavedra[5], C. Perez[6]on behalf of Grupo Inmunología Clínica Aplicada de la Universidad Militar Nueva Granada. *[1]Hospital Militar Central, Rheumatology and Immunology, Bogotá, Colombia*; *[2]Universidad Militar Nueva Granada, Grupo Inmunología Clínica Aplicada, Bogotá, Colombia*; *[3]Pontificia Universidad Javeriana, Health Economics, Bogotá, Colombia*; *[4]BIOMAB IPS, Rheumatology, Bogotá, Colombia*; *[5]Hospital Militar Central, Epidemiology, Bogotá, Colombia*; *[6]Hospital Militar Central, Cuenta de alto costo, Bogotá, Colombia*

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease with no cure, characterized by episodes of exacerbation and remission, which requires permanent use of medications. Clinics of excellence are multidisciplinary and centralized programs that improve adherence to treatments. Information on the benefits of these models of care has been published but is not definitive. In Colombia, the clinical registry of patients with RA is kept in the Cuenta de Alto Costo (CAC).

Objectives: To demonstrate the difference in the percentages of sustained remission at 2 years, between an institution with non-centralized management or standard of care (Hospital Militar Central-HMC) compared to another institution with centralized management or clinic of excellence (BIOMAB-IPS) and determine if the results are determined by any of the intervention variables or by the program.

Methods: The 2-year clinical records for the CAC were compared between an institution with non-centralized management (HMC) in comparison with another institution with centralized management (BIOMAB-IPS), performing a sociodemographic description, measuring control of the disease DAS28 clinimetry, Fisher's test non-parametric bivariate analysis, multiple regression model, and population matching with Propensity score Matching (PSM).

Results: Complete information was obtained from 2 years of follow-up, in centralized management 3457 patients and for the non-centralized unit 114 patients. Most of them corresponded to 2962 women (82%), with time of illness of 9.5 years and 10.2 years, respectively, without statistically significant differences. A difference was observed in the 2 programs to maintain remission at 2 years, in favor of the centralized program 54.7% vs 28.6.2% (p <0.00). With the binomial generalized linear regression model, it was confirmed that this difference was not explained by variables such as the use of biological therapy (RR = 0.77; 95% CI 0.69-0.86), use of DMARDs (RR = 0.71; 95% CI 0.62-0.82) and number of rheumatology consultations (RR = 0.97; 95% CI 0.92-1.02) in comparison with the centralized care model (RR = 2.32; 95% CI 1.58-3.35). Due to the biases between the groups due to the non-probability sampling, a PSM was performed, with a 1: 1 match, caliper of 0.065, obtaining a pseudo population with well-balanced covariates (see table 1). In the common support area, statistically significant differences were documented in sustained remission over 2 years, in favor of the centralized care group 45 vs 17.9% (p = 0.001).

Conclusion: With the information from the clinical records, statistical strategies can be used to evaluate important differences in centralized care programs, observing favorable results of these types of care that are not related to isolated elements of the program, but to the overall effect of the program.

REFERENCES:

[1] Austin PC. Double propensity-score adjustment: A solution to design bias or bias due to incomplete matching. Stat Methods Med Res. 2017;26(1):201–22.33333

Disclosure of Interests: Juan Manuel Bello-Gualtero: None declared, Esperanza Peña: None declared, Pedro Iván Santos Moreno: None declared, Jasmin Vesga Gualdrón Employee of: Baxter, Ginna Saavedra: None declared, Clara Perez: None declared

DOI: 10.1136/annrheumdis-2021-eular.3886

POS0502 WHAT IS THE ROLE OF VITAMIN D STATUS IN DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH bDMARDs? – DATA FROM A RHEUMATOLOGY CENTER

D. Fonseca[1], M. Rato[2], F. Oliveira Pinheiro[2], B. M. Fernandes[2], S. Garcia[2], A. Martins[2], D. Santos Oliveira[2,3], F. R. Martins[4], M. Bernardes[2,5], L. Costa[2]. *[1]Centro Hospitalar de Vila Nova de Gaia / Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; *[2]Centro Hospitalar Universitário de São João, Rheumatology, Porto, Portugal*; *[3]Center for Health Technology and Services Research (CINTESIS), University of Porto, Faculty of Medicine, Porto, Portugal*; *[4]Centro Hospitalar Universitário do Algarve, Rheumatology, Faro, Portugal*; *[5]Faculdade de Medicina da Universidade do Porto (FMUP), Rheumatology, Porto, Portugal*

Background: Vitamin D is a fat-soluble vitamin, mainly involved in the regulation of calcium metabolism, and it has gained increasing interest in recent years because of its potential role in immunomodulatory activity. Recent data suggest that it is negatively associated with disease activity in rheumatoid arthritis (RA), however this is not yet fully understood.

Objectives: This study's aim was to investigate if there is any correlation between vitamin D serum levels at baseline, before taking the first biological disease-modifying antirheumatic drug (bDMARD), and at 6 months after, with disease activity in a cohort of RA patients.

Methods: This is a cross-sectional study, including all the rheumatoid arthritis patients taking the first bDMARD with evaluation of the vitamin D status at baseline and 6 months after biologic therapy at our Rheumatology Department and registered in the national database (Reuma.pt).

Demographic, clinical and laboratorial characteristics and disease activity measures were collected from the baseline visit and the visit after 6 months of treatment with the first biologic. For the statistical analysis, two groups were defined, based on the serum levels of 25(OH) vitamin D, considering the most common cut-off of 30 ng/mL. For comparison analyses between groups, chi-square test was used for categorical variables and Mann-Whitney U and T-tests were applied for continuous variables.

Results: Seventy-seven patients were included, 58 (75.3%) were females; the mean age was 54.24 ±11.0 years and seropositivity was founded in 65 (84.4%) for anti-citrullinated protein antibodies and in 58 (75.3%) for rheumatoid factor. The first bDMARD most commonly prescribed were etanercept (28.6%) and rituximab (26%). Regarding the vitamin D status at baseline, the mean serum level for 25(OH)vitamin D was 28.35 ± 18.21 ng/mL, with the majority of patients having vitamin D insufficiency (25(OH)vitamin D < 30 ng/mL) (63.6%). After 6 months of treatment with the first bDMARD, disease activity measures showed that remission or low activity were achieved in 29.9% of the patients, using DAS28 criteria; in 42.9% and 46.8%, according CDAI and SDAI criteria, respectively. Vitamin D serum levels at 6 months were 26.81 ±11.72, with the majority of patients still with vitamin D insufficiency (62.3%).

At baseline, patients with vitamin D insufficiency had greater patient VAS (79.00 ± 19,14 vs 71.71 ± 21.95), greater erythrocyte sedimentation rate (ESR) (40.67 ± 23.17 vs 32.46 ± 26.09) and greater Health Assessment Questionnaire (HAQ) score (1.75 ± 0.609 VS 1.61 ± 0.659) with neither of them having statistical significance. However, when comparing CRP levels at 6 months, it achieved statistical significance with the Mann-Whitney U-test (1.05 ± 1.79 VS 1.41 ± 5.22; p=0.026). The same tendency was confirmed when analyzing vitamin D levels at 6 months. Patients with vitamin D insufficiency presented greater patient VAS (55.33 ± 28.82 vs 42.86 ± 28.28), greater ESR (26.19 ± 21.57 vs 21.00 ± 20.38) and greater HAQ score (1.35 ± 0.662 VS 1.34 ± 0.705), although without statistical significance. However, it did achieve statistical significance when comparing baseline DAS28 and HAQ (5.60 ± 0.91 VS 5.38 ± 1.31; p=0.013 and 1.76 ± 0.53 VS 1.59 ± 0.75; p=0.007, respectively).

Conclusion: Our data failed to demonstrate a statistically significant association between vitamin D serum levels at baseline and at 6 months with disease activity in our RA sample. However, it revealed a positive trend of vitamin D insufficiency related to higher activity disease. Interestingly, it showed that vitamin D insufficiency after 6 months of bDMARD treatment is related to higher DAS28 and HAQ at baseline. Nonetheless, we insist it is of paramount importance to conduct larger studies to confirm these findings.

REFERENCES:

[1] Bellan M, Sainaghi PP, Pirisi M. Role of Vitamin D in Rheumatoid Arthritis. Adv Exp Med Biol. 2017;996:155-168.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4061

POS0503 THE DISCORDANCE BETWEEN PATIENT-REPORTED AND CLINICAL/BIOLOGICAL OUTCOMES COULD HELP IN PREDICTING FUTURE DISEASE IMPACT IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Pazmino[1], A. Lovik[2], A. Boonen[3,4], D. De Cock[1], V. Stouten[1], D. Bertrand[1], M. Doumen[1], J. Joly[5], R. Westhovens[1,5], P. Verschueren[1,5]on behalf of CareRA study group. [1]*Katholieke Universiteit Leuven, Skeletal Biology and Engineering Research Centre, Department of Development and Regeneration, Leuven, Belgium*; [2]*Katholieke Universiteit Leuven, I-Biostat, Leuven, Belgium*; [3]*Academic Hospital Maastricht, Department of Internal Medicine, Division of Rheumatology, Maastricht, Netherlands*; [4]*Maastricht University, Care and Public Health Research Institute (CAPHRI), Maastricht, Netherlands*; [5]*UZ Gasthuisberg Campus, Department of Rheumatology, Leuven, Belgium*

Background: Treatment of Rheumatoid Arthritis (RA) has improved significantly based on early treat-to-target (T2T) strategies. Still, decreased health related quality of life (QoL), restricted ability to work and other unmet needs are reported by RA patients even in the absence of disease activity. We previously identified 3 factors representing the broader impact of RA using exploratory factor analysis: a patient-reported factor (patients global health, pain, fatigue and HAQ), a clinical factor (physician's global health, tender and swollen joint count), and a laboratory factor (ESR and CRP)[1].

Objectives: To test whether the discordance between patient-reported (PRF) and clinical(CF)/laboratory(LF) measures can predict QoL, or has a mediating effect in predicting future disease burden based on disease activity (DAS28CRP).

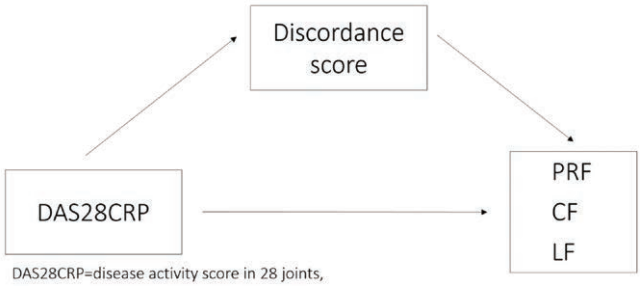
Methods: This is a post-hoc analysis of the 2-year CareRA trial. PRF, CF and LF scores were calculated as weighted (by factor loading) sum of their components at week 16, 52 and 104 after treatment initiation. A discordance score (DS) between PRF and the mean of the other two scores was also computed.

Mediation analyses were fitted to test the hypothesis (Figure 1) that DS could be a mediator for predicting PRF, CF and LF at a future time point (week 16, 52 and 104) using DAS28CRP at a previous time point (baseline and week 16). Confidence intervals were estimated via 10 000 bootstraps. Finally, a linear regression was fitted for DS to predict future QoL (RAQoL questionnaire; range 0-30; higher values indicating worse QoL).

Results: Patients with early RA (n=379) were included with a mean (SD) age of 53.9 (13.0), 77% seropositive and 69% women.

The DS was shown to be mediating the effect of DAS28CRP on any future PRF (Table1). On the other hand, there was no mediation effect of the DS in the prediction of the CF and an inconsistent mediation effect when predicting the LF. Moreover, the DS at week 16 significantly predicted (p<0.0001) RAQoL scores at year 1 with an effect of β 19.05 (SE 1.58) and an R^2 of 0.30 (CI 0.22-0.38). Similarly, it predicted RAQoL (p<0.0001) at year 2 with a β 19.74 (SE 1.56) and R^2 of 0.32 (CI 0.24-0.40).

Figure 1: Postulated mediational path model



DAS28CRP=disease activity score in 28 joints,

PRF= Patient reported factor, CF= Clinical factor, LF=Laboratory factor

Table 1. Results of mediation analyses for prediction of future burden based on previous DAS28CRP and mediated by discordance.

Timepoint	Predictor variables	Direct Effect	95% CIs	R^2	Mediation effect
Patient-reported factor					
W16	DAS28CRP at BL	-0.0091	-0.0240, 0.0058	0.1450	Present
	DS at BL	0.0246*	0.0169, 0.0331	0.1784	
W52	DAS28CRP at W16	0.0215*	0.0010, 0.0419	0.3394	Partial
	DS at W16	0.0580*	0.0442, 0.0739	0.2749	
W104	DAS28CRP at W16	0.0101	-0.0102, 0.0305	0.2798	Present
	DS at W16	0.0528*	0.0396, 0.0686	0.2749	
Clinical factor					
W16	DAS28CRP at BL	0.0153*	0.0074, 0.0232	0.0599	Absent
	DS at BL	0.0019	-0.0010, 0.0048	0.1784	
W52	DAS28CRP at W16	0.0365*	0.0267, 0.0463	0.1944	Absent
	DS at W16	0.0034	-0.0031, 0.0095	0.2749	
W104	DAS28CRP at W16	0.0115*	0.0024, 0.0207	0.0409	Absent
	DS at W16	0.0033	-0.0019, 0.0089	0.2749	
Laboratory factor					
W16	DAS28CRP at BL	0.0063*	0.0015, 0.0111	0.0634	Partial
	DS at BL	0.0030*	0.0012, 0.0050	0.1784	
W52	DAS28CRP at W16	0.0003	-0.0063, 0.0068	0.0305	Present
	DS at W16	0.0051*	0.0012, 0.0096	0.2749	
W104	DAS28CRP at W16	-0.0007	-0.0079, 0.0064	0.0014	Absent
	DS at W16	0.0013	-0.0019, 0.0046	0.2749	

W: week BL: baseline DS: discordance scoreDAS28CRP: disease activity score in 28 joints with C-reactive protein*p<0.01

Conclusion: Early discordance between patient-reported and biological/clinical factors mediates the effect of disease activity on future patient-reported outcomes, but also predicts QoL. Paying attention to this early discordance might provide opportunities to prevent patient's unmet needs by additional non-pharmacological interventions, hence broadening the scope of T2T.

REFERENCES:

[1] Pazmino S, et al. Does Including Pain, Fatigue, and Physical Function When Assessing Patients with Early Rheumatoid Arthritis Provide a Comprehensive Picture of Disease Burden? J Rheumatol. 2020 Nov 15:jrheum.200758. doi: 10.3899/jrheum.200758. Ahead of print.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4099

POS0504 IS BIOELECTRICAL PHASE ANGLE ASSOCIATED WITH FUNCTIONAL STATUS AND DISEASE IMPACT IN PATIENTS WITH RHEUMATOID ARTHRITIS?

M. Ferro[1], S. Charneca[1], J. Vasques[1], E. Dourado[2,3], C. Sousa Guerreiro[1,4], J. E. Fonseca[2,3]. [1]*Laboratório de Nutrição, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal*; [2]*Serviço de Reumatologia e Doenças Ósseas Metabólicas, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Centro Académico de Medicina de Lisboa (CAML), Lisbon, Portugal*; [3]*Unidade de Investigação em Reumatologia, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, CAML, Lisbon, Portugal*; [4]*Instituto de Saúde Ambiental, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease in which an abnormal body composition was reported to be highly prevalent. (1) Bioelectrical phase angle (PhA) is a measure of the relationship between electric resistance and reactance obtained via bioelectrical impedance analysis (BIA). (2) As an indicator of cellular health, PhA has been described as a predictor of worse clinical outcome and higher mortality in various conditions. (3) Since there is evidence that PhA is related to disease progression and prognosis when considering chronic inflammatory conditions, a lower PhA may also be considered an indicator of a worse prognosis in RA. (1)
Objectives: To study the association between PhA, functional status and impact of disease in RA patients.
Methods: Observational and cross-sectional study, including 53 patients with RA diagnosis according to the ACR/EULAR 2010 criteria. Each patient demographic data was recorded, and body composition, including PhA by BIA, was obtained. BIA was performed using Bodystat QuadScan 4000 equipment. Functional status and impact of disease were assessed using the Health Assessment Questionnaire (HAQ) and the Rheumatoid Arthritis Impact of Disease (RAID) scores, respectively. PhA was stratified by tertiles (lowest, middle and highest) to create groups of patients. Statistical analysis was performed using student's t-test (IBM SPSS version 26) for comparisons between groups.
Results: A total of 53 patients with RA (81.1% women) with an average age of 62.2 ± 10.2 years were assessed. Mean PhA was 5.8 ± 1.7 º. A PhA lower than 5.2 º (lowest tertile) was recorded in 17 patients; A PhA ranging from 5.2 º to 6.0 º (middle tertile) was observed in 18 patients; A PhA greater than 6.0 º (highest tertile) was seen in 18 patients. Mean HAQ score was 1.43 ± 0.61 in the lowest tertile, 0.85 ± 0.57 in the middle tertile and 0.67 ± 0.57 in the highest tertile. Mean RAID score was 5.86 ± 1.69 in the lowest tertile, 4.73 ± 2.05 in the middle tertile and 3.00 ± 1.94 in the highest tertile. The statistical analysis showed significant differences in both HAQ and RAID scores between the lowest and the highest tertiles (p=0.001 and p <0.001, respectively). Significant differences were also found between the lowest and the middle tertile for HAQ score (p=0.007) and between the middle and the highest tertile for RAID score (p=0.017).
Conclusion: In our cohort a lower PhA was significantly associated with higher HAQ and RAID scores, indicating higher disease impact and higher disability in RA patients with lower PhA. These results support the hypothesis that PhA may be investigated as a possible indicator of disease prognosis in RA.
REFERENCES:
[1] Pineda-Juárez JA, Lozada-Mellado M, Ogata-Medel M, Hinojosa-Azaola A, Santillán-Díaz C, Llorente L, et al. Body composition evaluated by body mass index and bioelectrical impedance vector analysis in women with rheumatoid arthritis. Nutrition. 2018;53:49–53.
[2] Rinaldi S, Gilliland J, O'Connor C, Chesworth B, Madill J. Is phase angle an appropriate indicator of malnutrition in different disease states? A systematic review. Clin Nutr ESPEN. 2019;29:1–14.
[3] Norman K, Stobäus N, Pirlich M, Bosy-Westphal A. Bioelectrical phase angle and impedance vector analysis - Clinical relevance and applicability of impedance parameters. Clin Nutr. 2012;31(6):854–61.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4119

Rheumatoid arthritis - comorbidity and clinical aspects

POS0505

DEPRESSION, ANXIETY AND STRESS AMONG OUTPATIENTS WITH RHEUMATOID ARTHRITIS FOLLOWED UP AT A TERTIARY CARE HOSPITAL IN SRI LANKA; A CROSS-SECTIONAL STUDY

T. Wijewardena[1], S. Wijewantha[1], N. Wijethunga[1], N. L. de Silva[2], D. Fernando[3]. *[1]Faculty of Medicine, University Of Colombo, Medical Student, Colombo, Sri Lanka*; *[2]General Sir John Kotelawala Defence University, Department of Clinical Sciences, Ratmalana, Sri Lanka*; *[3]Faculty of Medicine, University Of Colombo, Department of Parasitology, Colombo, Sri Lanka*

Background: Increased prevalence of depression, anxiety and stress have been shown among patients with rheumatoid arthritis. Patient and disease characteristics and psychosocial factors associated with these mental health issues are shown to vary among different populations. South Asian studies comprehensively assessing the prevalence and associations of these factors are lacking.
Objectives: To determine the prevalence of depression, anxiety and stress among patients with rheumatoid arthritis and to identify associated patient and disease factors.
Methods: A cross-sectional study was carried out among outpatients at three specialized rheumatology clinics at the National Hospital of Sri Lanka. Individuals with a diagnosis of rheumatoid arthritis were recruited consecutively. An interviewer-administered questionnaire was used to record sociodemographic and clinical data including the Clinical Disease Activity Index. A score 10.1-22.0 was taken as moderate and more than 22.1 was taken as high disease activity. The self-administered Depression, Anxiety, Stress Scale-21 (DASS-21) tool which has been validated for the Sri Lankan population was used. Statistical analysis was done using descriptive analysis and Chi-Square.
Results: A total of 118 participants were recruited in this study. Majority of the participants (n=105) were female and had received a secondary school education (70%). Based on the CDAI assessment most were in the moderate (39%) and high disease activity groups (36%). Prevalence of Depression, Anxiety and Stress were found to be higher than the baseline level of 1% in the general population. A breakdown of the prevalence is shown in Figure 1. Further analysis of each arm, depression anxiety and stress were carried out independently excluding the non-responders. A higher level of prevalence of all three parameters was observed with the deterioration of functional status evidenced by the inability to walk and grip a ball firmly in the palm without it falling. Prevalence of depression was associated with age > 60 years (p=0.035), increased disease activity (p=0.004) and the loss of their job due to poor health (p=0.01). Higher prevalence of anxiety was associated with increased disease activity (p=0.023). A marked increase in stress level was associated with loss of the job (p=0.009) and morning stiffness > 60 minutes (p=0.001). Several Pre-existing co-morbidities were associated with depression and anxiety (Table 1). No association was observed between stress and pre-existing comorbidities.

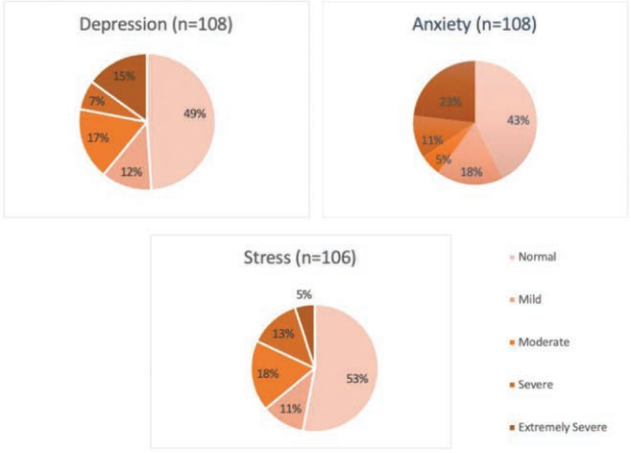


Figure 1. Prevalence of depression, anxiety and stress among patients with rheumatoid arthritis

Table 1. Correlation of comorbidities with depression and anxiety.

		Depression		Anxiety	
Associated Factors		Yes	No	Yes	No
Diabetes Mellitus (%)	Identified	18(72)	07(28)	16(66)	08(34)
	Not Identified	37(45)	46(55)	46(55)	38(45)
P-value		0.016		0.298	
Ischaemic heart disease (%)	Identified	14(82)	03(18)	14(78)	04(22)
	Not Identified	41(45)	50(55)	48(53)	42(47)
P-value		0.005		0.056	
Dyslipidaemia (%)	Identified	20(67)	10(33)	25(78)	07(22)
	Not Identified	35(45)	43(55)	37(49)	39(51)
P-value		0.042		0.005	

Conclusion: Prevalence of depression, anxiety and stress among patients with rheumatoid arthritis is higher than the general population. Functional deterioration, disease activity and presence of co-morbidities are associated with these mental health issues. These can guide clinicians to screen high risk individuals for the mental health issues so that measures to relieve them would potentially improve quality of life and disease outcome.
Acknowledgements: the authors thank the consultants in charge of the Rheumatology Clinics of the National Hospital, Drs. Jeewani Rubasingha, Monica De Silva and Gunendrika Kasthurirathna. We greatly appreciate the assistance given by the staff of the Department of Community Medicine, Faculty of Medicine, University of Colombo.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.121

POS0506

TENOSYNOVITIS HAS A HIGH SENSITIVITY FOR EARLY ACPA-POSITIVE AND ACPA-NEGATIVE RA: A LARGE CROSS-SECTIONAL MRI STUDY

X. Matthijssen[1], F. Wouters[1], N. Sidhu[1], E. Niemantsverdriet[1], A. van der Helm - van Mil[1,2]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; [2]*Erasmus MC, Rheumatology, Rotterdam, Netherlands*

Background: Clinically evident tenosynovitis can be seen in established Rheumatoid arthritis (RA). Imaging research has recently shown that tenosynovitis at small joints occurs in early RA, contributes to typical RA symptoms (including joint swelling) and is infrequent in healthy controls. Imaging-detectable tenosynovitis is often not recognizable at joint examination, hence its prevalence can therefore be underestimated.
Objectives: We hypothesized that if MRI-detectable tenosynovitis is a true RA-feature, the sensitivity for RA is high, in both ACPA-positive and -negative RA, and lower in other diseases that are associated with enthesitis (such as Spondyloarthritis (SpA) and Psoriatic Arthritis (PsA)). So far, no large MRI-study addressed these questions.
Methods: Consecutive early arthritis patients (n=1211) from one health-care region underwent contrast-enhanced 1.5T MRI of hand and foot at diagnosis. MRIs were scored for synovitis and tenosynovitis by two readers blinded for clinical data. All included patients with ACPA-positive RA (n=250), ACPA-negative RA (n=282), PsA (n=88), SpA with peripheral arthritis (n=24), reactive arthritis (n=30) and self-limiting undifferentiated arthritis (UA;n=76) were studied. Sensitivity was calculated.
Results: The sensitivity of tenosynovitis in RA was 85%; 88% for ACPA-positive RA and 82% for and ACPA-negative RA (p=0.19). The sensitivity for RA was significantly higher than for PsA (65%;p=0.001), SpA (53%;p<0.001), reactive arthritis (36%;p<0.001) and self-limiting UA (42%;p<0.001). The observed sensitivity of MRI-synovitis was 91% in RA and ranged 83-54% in the other groups.
Conclusion: MRI-detected tenosynovitis has a high sensitivity for early ACPA-positive and ACPA-negative RA. This supports both juxta-articular (tenosynovitis) and intra-articular synovial involvement is characteristic for RA.

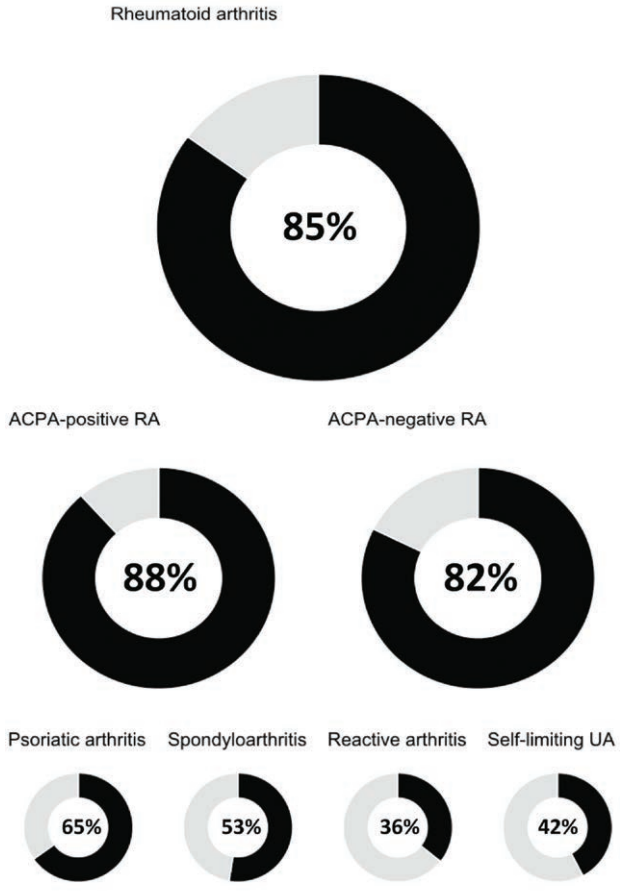


Figure 1. Presence of tenosynovitis (in black) in wrist MCPs and MTPs, in rheumatoid arthritis, stratified for ACPA-status and compared to other diseases**Legend:** RA: Rheumatoïd arthritis; ACPA: anti-citrullinated protein antibodies; UA: undifferentiated arthritis

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.180

POS0507

UNUSUALLY HIGH PREVALENCE OF ATRIAL FIBRILLATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

B. Mukerji[1], F. Wang[1], R. Markert[2], V. Mukerji[3]. [1]*Dayton Veteran Administration Medical Center, Rheumatology, Dayton, United States of America*; [2]*Wright State University, Medicine, Dayton, United States of America*; [3]*Dayton Veteran Administration Medical Center, Cardiology, Dayton, United States of America*

Background: In rheumatoid arthritis, circulating autoantibodies like anticyclic citrullinated peptides and rheumatoid factor may be present for years prior to symptom onset. In RA, there are high levels of circulating tumor necrosis factors, interleukins, matrix metalloproteinases, growth factors, and adhesion molecules that cause tissue damage[1,2]. This can affect different organs in different ways. It is possible that in the heart, they cause inflammation of cardiac tissue [3,4].
Objectives: This study was conducted to determine if patients with RA, an inflammatory arthritis, and osteoarthritis (OA), a degenerative arthritis, differ in the prevalence of cardiac arrhythmias.
Methods: This was a retrospective study. We enrolled 300 consecutive patients, 150 with RA and 150 with OA. Patients were assessed for age, race, gender, body mass index (BMI), smoking status, hypertension (HTN), hyperlipidemia (HLD), diabetes mellitus (DM), cardiovascular disease (CVD), coronary artery disease (CAD), cardiac arrhythmias including conduction abnormalities, cerebrovascular accident (CVA), congestive heart failure (CHF), abdominal aortic aneurysm (AAA), pulmonary embolism (PE), deep vein thrombosis (DVT), and peripheral vascular disease (PVD). RA and OA groups were compared with the chi square test and the Mann-Whitney test.
Results: The RA and OA groups did not differ on the demographic characteristics of age or race. The presence of DM was similar in the two groups. The RA group had more women than the OA group (12.7% vs. 5.3%, p=0.026). The OA group had a higher mean BMI (33.1 vs 30.0, p<0.001) and higher prevalence of HLD (78.9% vs 64.6%, p=0.007) and HTN (79.3% vs. 66.7%, p=0.013). RA patients had a higher rate of smoking (70.0% vs 56.7%, p=0.017) and longer duration of smoking (34.3 years vs. 28.2 years, p=0.003). The RA group had a higher prevalence of CVD (58.7% vs. 42.7%, p= 0.006). Further data analysis among CVD showed there was no difference between the two groups for the prevalence of CAD, CHF, CVA, AAA, PVD or DVT/PE. RA patients had a higher prevalence of cardiac arrhythmias (31.3% vs. 12.0%, p<0.001). Among all types of cardiac arrhythmias, no significant difference was found between two groups for the prevalence of supraventricular tachycardia, ventricular arrhythmias, or conduction abnormalities. Patients with RA had a significantly higher prevalence of atrial fibrillation (15.3% vs. 6.0%, p = 0.015).
Conclusion: Cardiac arrhythmias occur more frequently in RA patients than in OA patients. Among all the arrhythmias, atrial fibrillation has a significantly higher prevalence in RA patients.
REFERENCES:

[1] Maradit-Kremers H, et al. Increased unrecognized coronary heart disease and sudden deaths in rheumatoid arthritis: A population-based cohort study. Arthritis Rheum. 2005; 52: 402-411
[2] Seferovic PM, et al. Cardiac arrhythmias and conduction disturbances in autoimmune rheumatic diseases. Rheumatology. 2006; 45: 39-42
[3] Avina-Zubiets JA, et al. Risk of incident cardiovascular events in patients with rheumatoid arthritis: A met-analysis of observational studies. Ann Rheum Dis 2012; 71: 1524-1529
[4] Lazzerini PE, Capechi L, et al. Systemic Inflammation and arrhythmic risk: Lessons from rheumatoid arthritis. European Heart Journal. 2017; 38: 1717-1727

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.243

POS0508

EVALUATION OF RESPONSE TO PNEUMOCOCCAL VACCINATION IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING UPADACITINIB: RESULTS FROM A PHASE 2 OPEN-LABEL EXTENSION STUDY

K. Winthrop[1], J. Ignacio Vargas[2], E. Drescher[3], C. Garcia Garcia[4], A. Friedman[5], J. Enejosa[5], N. Khan[5], Y. Li[5], J. Klaff[5], A. Kivitz[6]. [1]*Oregon Health & Science University, Infectious Disease, Portland, United States of America*; [2]*Quantum Research, Medicine, Puerto Varas, Chile*; [3]*Veszprém Csolnoky, Ferenc County Hospital, Veszprém, Hungary*; [4]*Hospital General de México,"Dr. Eduardo Liceaga", Mexico City, Mexico*; [5]*AbbVie Inc., Rheumatology, North Chicago, United States of America*; [6]*Altoona Center, Clinical Research, Duncansville, United States of America*

Background: Pneumococcal vaccination is recommended in patients with RA who are receiving conventional synthetic/biologic DMARDs.[1] Upadacitinib (UPA) is an oral Janus kinase (JAK) inhibitor engineered to have a greater selectivity for JAK1 versus JAK2, JAK3, and tyrosine kinase 2, and is approved for the treatment of RA.
Objectives: The aim of this analysis was to assess the impact of long-term treatment with UPA + background MTX on immunologic responses to Prevnar 13® (Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM_{197} Protein];

PCV13) in patients with RA enrolled in the ongoing Phase 2 open-label extension study BALANCE-EXTEND.

Methods: Patients from BALANCE-EXTEND receiving PCV13 vaccination were required to be on UPA 15 mg once daily (QD) or 30 mg QD and background MTX for ≥4 weeks prior to, and after, PCV13 vaccination; MTX was not interrupted prior to vaccination. Vaccination antibody titers were collected pre-vaccination (Week 0) and post-vaccination (Weeks 4 and 12). The primary variable was the proportion of patients with satisfactory humoral response to PCV13 (≥2-fold increase in antibody concentration from pre-vaccination [Week 0] in ≥6/12 pneumococcal antigens [1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F]) at 4 weeks post-vaccination.

Results: Of 111 patients (UPA 15 mg, n=87; UPA 30 mg, n=24), 86% were female, most (98%) were white, and mean (standard deviation) age was 58.4 (12.0) years. Prior to vaccination, patients had a median (range) duration of RA of 9.3 (3.4–35.0) years and had been receiving UPA for a median (range) of 3.9 (3.0–4.9) years. All but 3 patients were taking concomitant MTX, and 44.1% were taking a CS (median daily dose, 5.0 mg). All 111 patients received PCV13, none discontinued UPA during the first 4 weeks, and blood samples were available from 83/23 and 79/22 patients in the UPA 15/30 mg groups at Weeks 4 and 12, respectively. At 4 weeks, satisfactory humoral response to PCV13 occurred in 67.5% (95% confidence interval [CI]: 57.4–77.5) and 56.5% (95% CI: 36.3–76.8) of patients receiving UPA 15 and 30 mg, respectively. At 12 weeks, satisfactory humoral response to PCV13 occurred in 64.6% (95% CI: 54.0–75.1) and 54.5% (95% CI: 33.7–75.4) of patients receiving UPA 15 and 30 mg, respectively (Figure 1). There was no clear difference in response between patients receiving and not receiving concomitant CS. Within 30 days post-vaccination, 2 adverse events (AEs) were considered as possibly related to UPA (1 case of diverticulitis, UPA 15 mg; 1 case of anemia, UPA 30 mg) and no serious AEs were reported (Table 1). Two patients experienced pyrexia and 1 subject each experienced vaccination-site pain and headache within 1 day post-vaccination (all in UPA 15 mg group).

Table 1. Safety through 30 days post-PVC13 vaccination in UPA-treated patients

Event, n (%)	UPA 15 mg QD (n=87)	UPA 30 mg QD (n=24)
Any AE	15 (17.2)	3 (12.5)
Serious AE	0	0
AE leading to discontinuation of study drug	0	0
AE with reasonable possibility of being related to UPA[a]	1 (1.1)[b]	1 (4.2)[c]
Death	0	0

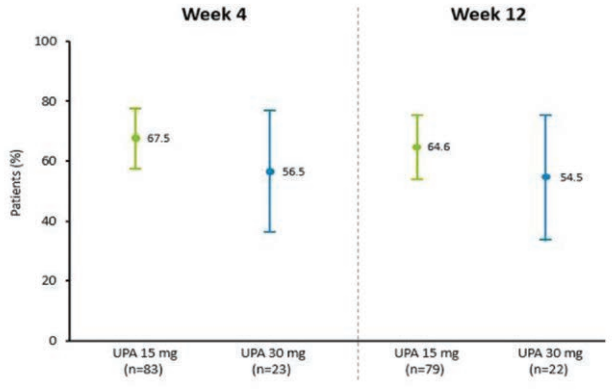
[a]As assessed by the investigator. [b]Diverticulitis. [c]Anemia. AE, adverse event; PVC13, Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM_{197} Protein]; QD, once daily; UPA, upadacitinib.

Conclusion: Satisfactory humoral response to PCV13 at 4 weeks occurred in ~two-thirds of patients with RA receiving long-term treatment with UPA 15 mg QD + background MTX. This is broadly consistent with pneumococcal vaccine humoral responses observed in patients with RA treated with other JAK inhibitors, biologics, or placebo.[2–4]

REFERENCES:

[1] Singh JA, et al. Arthritis Care Res 2016;68:1–25.
[2] Winthrop KL, et al. Arthritis Res Ther 2019;21:102.
[3] Bingham CO, et al. Ann Rheum Dis 2015;74:818–22.
[4] Winthrop KL, et al. Ann Rheum Dis 2016;75:687–95.

Figure 1. Proportion (%, 95% CI) of UPA-treated patients with satisfactory humoral response[a] to PVC13 at Weeks 4 and 12 (full analysis set)[b]



[a]Satisfactory humoral response was defined as ≥2-fold increase in antibody concentration from the vaccination baseline in ≥6 out of 12 pneumococcal antigens (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). [b]Number of patients based on availability of blood samples collected at Weeks 4 and 12.
CI, confidence interval; PVC13, Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM_{197} Protein]; UPA, upadacitinib.

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing assistance was provided by Frances Smith, PhD, of 2 the Nth, which was funded by AbbVie.

Disclosure of Interests: Kevin Winthrop Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead, Pfizer, Roche, and UCB., Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead, Pfizer, Roche, and UCB., Juan Ignacio Vargas Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead, Pfizer, Roche, and UCB, Edit Drescher: None declared, CONRADO GARCIA GARCIA: None declared, Alan Friedman Shareholder of: AbbVie, Employee of: AbbVie, Jeffrey Enejosa Shareholder of: AbbVie, Employee of: AbbVie, Nasser Khan Shareholder of: AbbVie, Employee of: AbbVie, Yihan Li Shareholder of: AbbVie, Employee of: AbbVie, Justin Klaff Shareholder of: AbbVie, Employee of: AbbVie, Alan Kivitz Shareholder of: Amgen, Novartis, Gilead, GlaxoSmithKline, Pfizer Inc., and Sanofi, Speakers bureau: AbbVie, Celgene, Eli Lilly, Flexion, Genzyme, Horizon, Merck, Novartis, UCB, Pfizer Inc., Regeneron, Sanofi, and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Genzyme, Gilead, Janssen, Pfizer Inc., Regeneron, Sanofi, SUN Pharma Advanced Research, and UCB

DOI: 10.1136/annrheumdis-2021-eular.559

POS0509 PREVALENCE OF RHEUMATOID CACHEXIA AND ITS ASSOCIATION WITH SERUM FETUIN-A LEVELS IN CAUCASIAN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Papichev[1], B. Zavodovsky[1], L. Seewordova[1], J. Polyakova[1], Y. Akhverdyan[1].
[1]*FSBI "Research Institute of Clinical and Experimental Rheumatology n.a. A.B. Zborovsky", Treatment and Prevention of Joint Disease Laboratory, Volgograd, Russian Federation*

Background: Rheumatoid cachexia is an under-recognized pathological condition, which is characterized by a loss of muscle strength and can be presented as a low fat-free mass and normal or high BMI in patients with rheumatoid arthritis determined by dual-energy X-ray absorptiometry (DEXA) [1]. Though fetuin-A is one of a major noncollagen proteins in bone tissue it is of interest to clarify its association with rheumatoid cachexia.

Objectives: To define the prevalence of rheumatoid cachexia in Caucasian patients with rheumatoid arthritis determined by DEXA method and to study the association of serum fetuin-A levels with body composition and rheumatoid cachexia in this group.

Methods: 110 Caucasian patients with rheumatoid arthritis undergone DEXA with «Total Body» program. All patients fulfilled the 2010 ACR/EULAR classification criteria for rheumatoid arthritis. The diagnosis of rheumatoid cachexia was based on Engvall I.L. criteria: fat-free mass index less than 10th percentile with fat mass index above 25th percentile [1]. We used values for these indexes from the study performed in 2008 by Coin A. et al. on Italian population due to a lack of standard values [2]. Fetuin-A in serum was determined by enzyme-linked immunosorbent assay. 72 patients have been taking glucocorticoids for more than 3 months in dose equivalent or higher than 5 mg of prednisolone daily. Statistical analysis was performed using a software package "Statistica 12.0". Parametric data is presented as M±St.dev, and nonparametric as Me [Q1-Q3].

Results: Rheumatoid cachexia was diagnosed in 25 patients (22,7%) with mean age of 52,2±8,14 years. The prevalence of cachexia was the same in groups of patients who took glucocorticoids (n=16, 22,2%) and who didn't (n=9, 23,7%; p = 0,465). Median cumulative dose of oral glucocorticoids in patients with rheumatoid cachexia was higher but fell just short of statistical significance (8,0 [2,9-13,5] g vs 5,4 [0,2-11,6] g; Z=-1,42; p = 0,156). Median serum fetuin-A levels were only slightly significantly lower in patients with rheumatoid cachexia (757,7 [700,5-932,0] μg/ml vs 769,3 [660,3-843,4] μg/ml; Z=-1,35; p=0,175). Positive statistically significant correlations were observed between serum fetuin-A levels and bone mass in right (r=0,222, p = 0,027) and left (r=0,263, p = 0,008) lower limbs, trunk (r=0,268, p = 0,007), gynoid region (r=0,293, p = 0,003), both lower limbs (r=0,246, p = 0,014) and whole-body (r=0,235, p = 0,019).

Conclusion: Rheumatoid cachexia was diagnosed in 22,7% of patients with rheumatoid arthritis. No association was observed between glucocorticoids intake and rheumatoid cachexia, despite the expected influence of them on muscle mass. We may suggest that occurrence and pathogenesis of this condition is complex and should be studied more precisely. It is well-known that patients with such condition have a higher risk for metabolic syndrome, arterial hypertension and mortality. We observed positive correlations between serum fetuin-A levels and bone mass in lower limbs, trunk, gynoid region and whole-body. Considering

that fetuin-A is also associated with bone mineral density [3], it may be regarded as a marker of bone remodeling.

REFERENCES:

[1] *Engvall I.L., Elkan A.C., Tengstrand B., Cederholm T., Brismar K., Hafstrom I.* Cachexia in rheumatoid arthritis is associated with inflammatory activity, physical disability, and low bioavailable insulin-like growth factor. Scand J Rheumatol. 2008; 37 (5): 321–328.

[2] *Coin A., Sergi G., Minicuci N., Giannini S., Barbiero E., Manzato E., Pedrazzoni M., Minisola S., Rossini M., Del Puente A., Zamboni M., Inelmen E.M., Enzi G.* Fat-free mass and fat mass reference values by dual-energy X-ray absorptiometry (DEXA) in a 20-80 year-old Italian population. Clinical Nutrition. 2008; 27 (1): 87-94.

[3] *Sari, A., & Uslu, T.* The relationship between fetuin-a and bone mineral density in postmenopausal osteoporosis. Turkish Journal of Rheumatology. 2013; 28 (3): 195-201.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.568

POS0510 EPIDEMIOLOGY OF COCAINE AND HALLUCINOGEN USE DISORDER HOSPITALIZATIONS IN RHEUMATIC DISEASES

J. Singh[1]. [1]*University of Alabama at Birmingham, Medicine, Birmingham, United States of America*

Background: Cocaine use disorder is a frequent cause of drug use disorders in the U.S. Although hallucinogen use disorder is less common, both are potentially preventable public health issues. To our knowledge, epidemiological studies estimating burden of cocaine or hallucinogen use disorders in common Musculoskeletal diseases (MSDs) are lacking.

Objectives: To assess national time-trends in cocaine use and hallucinogen use disorders in people with MSDs

Methods: This study used the U.S. National Inpatient Sample (NIS), a de-identified national all-payer inpatient health care database (https://www.hcup-us.ahrq.gov/nisoverview.jsp) from 1998-2014. The NIS is a 20% stratified sample of hospital discharges in the U.S. It is commonly used to derive national estimates of hospitalization and outcomes. Cocaine or hallucinogen use disorder hospitalization was defined in a validated approach as the presence of the following International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes: cocaine use disorder, 304.2x, or 305.6x; and hallucinogen use disorder, 304.5x or 305.3x; hospitalizations for drug use in remission, drug counseling, rehabilitation or detoxification were excluded, as in previous studies. MSDs were identified based on the respective ICD-9 codes, a validated approach (5-9), in non-primary position: Gout: 274.xx; rheumatoid arthritis (RA): 714.xx; Fibromyalgia: 729.1; osteoarthritis (OA): 715.xx; or low back pain (LBP): 724.

Results: In 1998-2000, the highest frequency of cocaine use hospitalizations was in people with LBP: LBP (n=5,914), followed by OA (n=4,931), gout (n=2,093), RA (n=2,026), and fibromyalgia (n=1,620). In 2013-2014, the order changed slightly with OA (n=22,185), followed by LBP (n=16,810), gout (n=10,570), RA (n=8,975), and fibromyalgia (n=5,680). Respective rates per 1 million U.S. NIS hospitalizations in 2013-2014 and the relative increase from 1998-2000 to 2013-2014 were: Gout, 10.2 (increase, 4.1-fold); OA, 21.4 (3.5-fold); fibromyalgia, 5.48 (2.5-fold); RA, 8.66 (3.4-fold); and LBP, 16.22 (1.8-fold; figure 1).

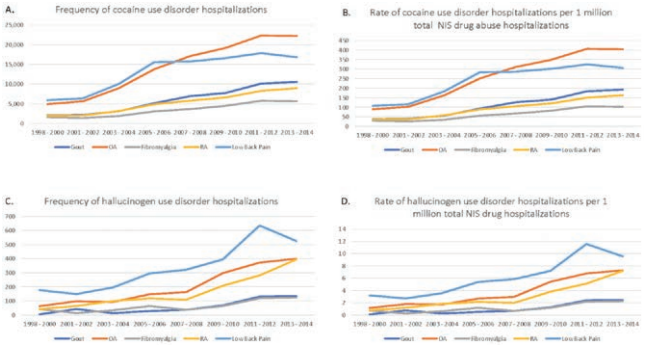


Figure 1. Time-trends in the rates of hospitalization with cocaine use and hallucinogen use disorder (A), non-home discharge (B), and in-hospital mortality (C) per 100,000 NIS hospitalization claims.The x-axis shows rate per 100,000 NIS hospitalization claims and the y-axis the study periods

In 1998-2000, hallucinogen use disorder hospitalizations were as follows: LBP (n=176), followed by OA (n=63), RA (n=42), fibromyalgia (n=41) and gout (n<10; cells with frequency of 10 of fewer are reported as <10 per NIS guidance). In 2013-2014, the frequency order was the similar, with the highest numbers for LBP (n=525) followed by OA (n=400), RA (n=395), gout (n=135) and fibromyalgia (n=125). Respective rates per 1 million US NIS hospitalizations in 2013-2014 and the relative increase from 1998-2000 to 2013-2014 were: Gout, 0.13 (increase, 25-fold); OA, 0.39 (5.5-fold); fibromyalgia, 0.12 (2-fold); RA, 0.38 (8.5-fold); and LBP, 0.51 (2-fold; figure 1).

Conclusion: This study confirmed an increasing rate of both, cocaine use and hallucinogen use disorder hospitalizations in people with 5 MSDs over a 17-year period from 1998-2014 in the U.S.

Acknowledgements: John D. Cleveland, MS of the University of Alabama at Birmingham for performing data analyses according to the protocol.

Disclosure of Interests: Jasvinder Singh Speakers bureau: JAS is on the speaker's bureau of Simply Speaking. JAS is a member of the executive of Outcomes Measures in Rheumatology (OMERACT), an organization that develops outcome measures in rheumatology and receives arms-length funding from 12 companies., Consultant of: consultant fees from Crealta/Horizon, Medisys, Fidia, UBM LLC, Trio Health, Medscape, WebMD, Two labs Inc., Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam associates, Focus forward, Navigant consulting, Spherix, MedIQ, Practice Point communications, the National Institutes of Health and the American College of Rheumatology.

DOI: 10.1136/annrheumdis-2021-eular.613

POS0511 USING HIP STRUCTURAL ANALYSIS MEASUREMENTS TO PREDICT FRACTURE IN RHEUMATOID ARTHRITIS

R. Ark[1,2], M. Bukhari[1,2]. [1]*Lancaster University, Lancaster Medical School, Bailrigg, United Kingdom*; [2]*University Hospitals of Morecambe Bay NHS Foundation Trust, Royal Lancaster Infirmary, Lancaster, United Kingdom*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease and increases the risk of developing osteoporosis. Incidence of fracture is higher in this group of patients compared to the general population and can lead to increased morbidity (1). Bone strength of the proximal femur is not only linked to bone mineral density; it also depends on the geometric properties of the bone mass (2). Hip structural analysis (HSA) is a technique used to assess hip bone structure that takes geometric measurements of the femur from dual-energy X-ray absorptiometry (DEXA) images (3).

Objectives: To determine whether HSA measurements help predict fracture in patients with RA.

Methods: Data were collected from June 2004 to August 2017 from RA patients who underwent a DEXA scan at a District General Hospital. This included hip axis length (HAL), cross-sectional area (CSA), cross-sectional moment of inertia (CSMI), distance from centre of femoral head to centre of femoral neck (D1) and to inter-trochanteric line (D2), mean femoral neck diameter (D3), shaft angle (A) neck/shaft angle (Θ) and proximal femur strength index (SI) and distance from centre of mass of femoral neck to superior neck margin (Y). Fracture was predicted by a series of binomial logistic regression models, adjusted for sex, age and bone mineral density (BMD). Odds ratios with 95% confidence intervals and area under the receiver operating characteristic curve (AUC) were calculated.

Results: 2077 patients with RA were identified, 1632 were female and the mean age was 66.7. HAL, D1, D2, D3, A, Θ and Y were not significant predictors of fracture in regression models; odds ratios are included in table 1. CSA, CSMI and SI predicted fracture risk. The AUC for CSA, CSMI and SI regression models were 0.632, 0.609 and 0.625 respectively.

Table 1. Odds ratios of fracture for different HSA parameters in RA patients

HSA Parameter	Odds Ratio (95% Confidence Interval)
HAL	1.01410 (0.99958 - 1.02883)
CSMI	0.99994 (0.99990 - 0.99998)
CSA	0.98523 (0.98065 - 0.98982)
D1	1.01683 (0.98925 - 1.04518)
D2	1.01286 (0.99886 - 1.02705)
D3	1.00664 (0.96958 - 1.04511)
Y	1.04580 (0.98633 - 1.10886)
A	1.00898 (0.98878 - 1.02959)
Θ	1.00276 (0.98672 - 1.01906)
SI	0.56769 (0.43400 - 0.74258)

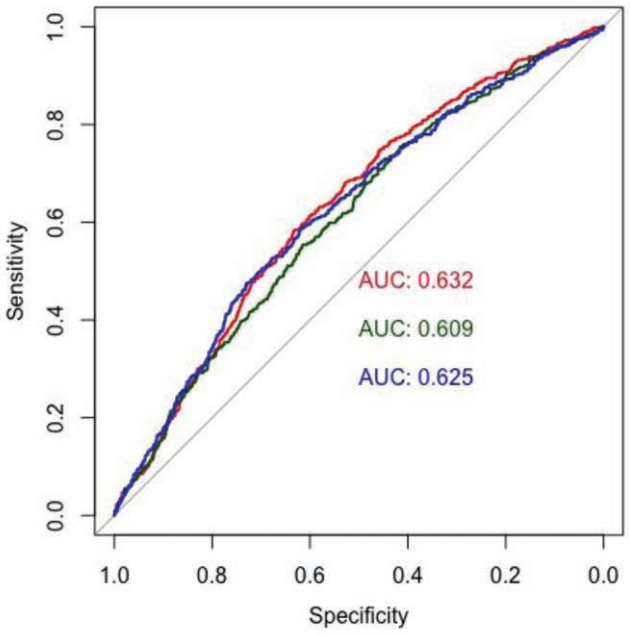


Figure 1. Receiver operating characteristic curves for CSA (red), CSMI (green) and SI (blue). AUC for CSA was 0.632, CSMI-0.609 and SI-0.625.

Conclusion: These data suggest that CSA, CSMI and SI help predict the fracture risk in patients with RA. HAL, D1, D2, D3, A, Θ and Y do not predict risk of fracture. The CSA regression model was the strongest predictor of fracture. HSA measurements can therefore help predict risk of fracture in conjunction with other factors. Limitations of the study are that it was retrospective and only studied patients who had a DEXA scan.

REFERENCES:

[1] Xue A, Wu S, Jiang L, Feng A, Guo H, Zhao P. Bone fracture risk in patients with rheumatoid arthritis: A meta-analysis. Medicine. 2017; 96 (36): e6983. Available from: doi: 10.1097/MD.0000000000006983.

[2] Faulkner KG, Wacker WK, Barden HS, Simonelli C, Burke PK, Ragi S, Del Rio L. Femur strength index predicts hip fracture independent of bone density and hip axis length. Osteoporos Int. 2006;17(4):593-9. doi: 10.1007/s00198-005-0019-4.

[3] Kaptoge S, Beck TJ, Reeve J, Stone KL, Hillier TA, Cauley JA, et al. Prediction of Incident Hip Fracture Risk by Femur Geometry Variables Measured by Hip Structural Analysis in the Study of Osteoporotic Fractures. Journal of Bone and Mineral Research. 2008; 23 (12): 1892-1904. Available from: doi: https://doi.org/10.1359/jbmr.080802.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.802

POS0512

DIFFERENCES IN TREATMENT SATISFACTION, PATIENT PREFERENCES, AND TREATMENT PATTERNS BETWEEN EUROPEAN, SOUTH AMERICAN, AND JAPANESE PATIENTS WITH SUBOPTIMALLY CONTROLLED RHEUMATOID ARTHRITIS: A SUBGROUP ANALYSIS OF THE SENSE STUDY

P. C. Taylor[1], P. Sidiropoulos[2], C. Ancuta[3], I. Lagunes-Galindo[4], M. Delavega[5], U. Kalyoncu[6], O. Nagy[4], A. Kawakami[7]. *[1]University of Oxford, Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; *[2]University of Crete, Faculty of Medicine, Heraklion, Greece*; *[3]"Grigore T. Popa" University of Medicine and Pharmacy, Department of Rheumatology, Iași, Romania*; *[4]AbbVie, Inc,., North Chicago, United States of America*; *[5]CEIM Investigaciones Medicas,., Buenos Aires, Argentina*; *[6]Hacettepe University, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; *[7]Nagasaki University Graduate School of Biomedical Sciences, Department of Immunology and Rheumatology, Nagasaki, Japan*

Background: Despite the availability of advanced therapies, many patients with rheumatoid arthritis (RA) do not achieve their treatment goals. Understanding geographic influence on patient perspectives and physicians' attitudes toward treatment adjustments may inform region-specific strategies to improve outcomes in RA.

Objectives: To explore differences in treatment satisfaction, patient preferences, and treatment strategies between patients from Europe (EU), South America (SA), and Japan (JP) with suboptimal control of RA.

Methods: This is a subgroup analysis of SENSE, a non-interventional cross-sectional study in adults with RA who had moderate/high disease activity as measured by Disease Activity Score in 28 joints with erythrocyte sedimentation rate (DAS28[ESR]) >3.2, despite disease-modifying antirheumatic drug (DMARD) treatment. Patient satisfaction and preferences, treatment adherence, patient-reported outcomes, and physicians' plans for DMARD switch were assessed as previously described.[1] Predictors of good treatment satisfaction and physician's decision not to switch DMARDs were identified using multiple logistic regression analyses.

Results: Of 1234, 272, and 118 patients enrolled from EU, SA, and JP, respectively, 13.9%, 15.4%, and 5.9% reported good treatment satisfaction. Irrespective of region, patients reported impaired quality of life and good treatment adherence, and around one-third of patients received targeted synthetic (ts) or biologic (b) DMARDs. Among patients treated with ts/bDMARDs, monotherapy was most common in SA (45.3%), followed by EU (26.3%) and JP (18.8%), consistent with a greater acceptance of combination therapy in JP. More than 80% of JP patients preferred oral treatments versus <60% of EU/SA patients. DMARD switches were planned in 51.8% (EU), 57.4% (SA), and 38.1% (JP) of patients, most commonly to a tumor necrosis factor inhibitor. Predictors for good treatment satisfaction included treatment with ts/bDMARDs and the presence of psychiatric disorders in EU and SA; however, current disease activity was not a common predictor (Table 1). Reluctance to switch treatments was predicted by lower disease activity assessed by DAS28(ESR) (all regions) and current treatment with ts/bDMARDs (EU/SA).

Table 1. Predictors for good treatment satisfaction and no treatment switch planned

OR (95% CI)	Europe (n=1234)	South America (n=272)	Japan (n=118)
Good treatment satisfaction (TSQM global treatment satisfaction ≥80)			
Current treatment with ts/bDMARDs	3.8 (2.7, 5.4)****	4.9 (2.2, 10.8)****	—
Psychiatric disorders	2.4 (1.3, 4.6)**	3.1 (1.2, 8.4)*	—
Number of comorbidities	—	—	2.3 (1.2, 4.3)*
Worst joint pain	—	1.3 (1.1, 1.5)**	
SF-36 MCS	1.0 (1.0, 1.1)****	—	1.3 (1.1, 1.5)**
SF-36 PCS	1.1 (1.0, 1.1)****	—	—
Work Productivity and Activity Impairment–Rheumatoid Arthritis: Total activity impairment	—	1.0 (1.0, 1.0)***	—
DAS28(ESR) >5.1	—	0.3 (0.1, 0.7)**	—
Female	—	—	0.1 (0.0, 0.9)*
No treatment switch planned			
Current treatment with ts/bDMARDs	3.9 (3.0, 5.2)****	2.4 (1.4, 4.2)**	—
Number of comorbidities	1.2 (1.1, 1.4)****	—	—
Age	—	—	1.0 (1.0, 1.1)*
TSQM effectiveness subscore	1.0 (1.0, 1.0)***	1.0 (1.0, 1.0)***	—
Number of concomitant medications	0.9 (0.8, 1.0)**	—	—
DAS28(ESR)	0.5 (0.5, 0.6)****	0.6 (0.5, 0.8)***	0.6 (0.4, 0.9)*

X^2 test: ****p<0.0001, ***p<0.001, **p<0.01, *p<0.05CI, confidence interval; OR, odds ratio; SF-36M/PCS, 36-Item Short-Form Survey mental/physical component summary; TSQM, Treatment Satisfaction Questionnaire for Medication

Conclusion: In patients with moderate to high RA disease activity, current disease control was a common determinant of treatment switches. Predictors for good treatment satisfaction revealed region-specific patient attitudes to treatment acceptance despite poor disease control.

REFERENCES:

[1] Taylor PC, et al. Ann Rheum Dis 2020;79:996–7

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of this abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Hilary Wong, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Disclosure of Interests: Peter C. Taylor Speakers bureau: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Eli Lilly, Fresenius, Galapagos, Gilead, GSK, Janssen, Nordic Pharma, Pfizer, Roche, Sanofi, and UCB., Consultant of: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Eli Lilly, Fresenius, Galapagos, Gilead, GSK, Janssen, Nordic Pharma, Pfizer, Roche, Sanofi, and UCB., Grant/research support from: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Eli Lilly, Fresenius, Galapagos, Gilead, GSK, Janssen, Nordic Pharma, Pfizer, Roche, Sanofi, and UCB., Prodromos Sidiropoulos Speakers bureau: AbbVie, Amgen, MSD, Novartis, Pfizer, Roche, and UCB., Consultant of: AbbVie, Amgen, MSD, Novartis, Pfizer, Roche, and UCB., Grant/research support from: AbbVie, Amgen, MSD,

Novartis, Pfizer, Roche, and UCB., CODRINA ANCUTA Speakers bureau: AbbVie, Eli Lilly, Ewopharma, MSD, Novartis, Pfizer, Roche, and UCB., Consultant of: AbbVie, Eli Lilly, Ewopharma, MSD, Novartis, Pfizer, Roche, and UCB., Ivan Lagunes-Galindo Employee of: AbbVie employee and may own stocks or options, Maria DeLaVega: None declared, Umut Kalyoncu Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB., Consultant of: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB., Orsolya Nagy Employee of: AbbVie employee and may own stocks or options, Atsushi Kawakami Speakers bureau: AbbVie, Actelion, Asahi Kasei, Astellas, Boehringer Ingelheim, Celltrion, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, GSK, Janssen, Kowa, MedPeer, Mitsubishi Tanabe, Novartis, ONO, Pfizer, Taisho, and Takeda, Grant/research support from: AbbVie, Actelion, Asahi Kasei, Astellas, AYUMI, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, Kyowa Hakko Kirin, MSD, Neopharma, Novartis, ONO, Sanofi, Taisho, Takeda Science Foundation, and Teijin.

DOI: 10.1136/annrheumdis-2021-eular.842

POS0513

ABATACEPT IN MONOTHERAPY VERSUS COMBINED IN INTERSTITIAL LUNG DISEASE OF RHEUMATOID ARTHRITIS. MULTICENTER STUDY OF 263 CAUCASIAN PATIENTS

C. Fernández-Díaz[1], B. Atienza-Mateo[1], S. Castañeda[2], R. Melero[3], F. Ortiz-Sanjuán[4], I. Casafont-Solé[5], J. Loricera[1], S. C. Rodriguez-García[6], I. Ferraz-Amaro[7], M. A. González-Gay[1], R. Blanco[1]on behalf of Spanish Collaborative Group of Interstitial Lung Disease Associated to Rheumatoid Arthritis Members of the Spanish Collaborative Group of Interstitial Lung Disease Associated to Rheumatoid Arthritis: Clara Aguilera-Cros (H.U. Virgen del Rocío, Sevilla), Ignacio Villa (H. Sierrallana, Torrelavega), Enrique Raya-Alvarez (H.U. San Cecilio, Granada), Clara Ojeda-García (H.U. Virgen Macarena, Sevilla), María G. Bonilla Hernán (H.U. La Paz, Madrid), Ana M. López-Robles (H.U. Vall d' Hebron, Barcelona), Luis Arboleya-Rodríguez (H.U. Central de Asturias, Asturias), Javier Narváez García (H.U. Bellvitge, Barcelona), Evelin C. Cervantes Pérez (H.U. de Santiago, Santiago de Compostela, A Coruña), OlgaMaiz-Alonso (H.U. Donostia, Gipuzkoa), María N. Alvarez-Rivas (H.U. Luca Augusti, Lugo), Iván Cabezas-Rodríguez (H.U. Río Hortega, Valladolid), Eva Salgado-Pérez (C.H.U. Ourense, Ourense), Cristina Hidalgo-Calleja (H.U. de Salamanca, Salamanca), Sabela Fernández-Aguado (H.U. Cabueñes, Asturias), Jesús C. Fernández-López (C.H.U. A Coruña), Alejandro Olivé, Samantha Rodríguez-Muguruza (H.U. GermansTrias i Pujol, Barcelona), Raquel Almodóvar-González (H.U. Fundación Alcorcón, Madrid), Carmen Carrasco-Cubero (C.H.U. Infanta Cristina, Badajoz), Antonio Juan-Mas (H. Son Llàtzer, Palma de Mallorca), Raúl Castellanos-Moreira (H.U. Clinic. Barcelona), Iñigo Hernández Rodríguez (C.H.U. de Vigo, Vigo), Neus Quillis-Marti (H. Vinalopo Elche), José A. Bernal-Vidal (H. Marina Baixa, Villajoyosa), Angel García-Aparicio (H. Virgen de la salud, Toledo), Sonia Castro-Oreiro (H.U. Joan XXIII, Tarragona), Julia Fernández-Melón (H. Son Espases, Palma de Mallorca), Paloma Vela Casasempere(H. U. Alicante, Alicante), María C. Fito, Carmen González-Montagut (C.U. Navarra, Navarra), Manuel Rodríguez-Gómez (C.H.U. Ourense, Ourense), Trinidad Pérez-Sandoval, Miriam Retuerto-Guerrero (H.U. León), Deseada Palma-Sánchez (H. Rafael Mendez, Lorca), José L. Andreu (H. U. Puerta del Hierro), Patricia Carreira-Delgado (H. 12 de Octubre, Madrid), Lorena Expósito-Pérez (H.U. de Canarias, Tenerife), Juan RD Jiménez- de Aberásturi, Ana Ruibal-Escribano (H.U. Txagorritxu, Araba), Ana Urruticoechea-Arana (H. Can Misses, Ibiza), Rosa Expósito-Molinero (H. Laredo, Laredo), Rubén López Sánchez (H. Negrín Las Palmas), Manuel J.Moreno-Ramos (H. Virgen de la Arrixaca, Murcia), Isabel Serrano-García (H. Puerta del Mar Cadiz), Blanca García-Magallón (H. San Jorge Huesca), José María Andreu Ubero (H. Virgen de las Nieves Granada), Natalia Mena-Vázquez (H.R.U Málaga), Iván Castellvi-Barranco (H.U. De la Santa Creu i Sant Pau, Barcelona), Carmen González-Montagut (H. U. Valladolid, Valladolid), Juan Blanco-Madrigal (H. Basurto, Bilbao), Pilar Morales-Garrido (H.U. San Cecilio, Granada), Cilia Peralta-Ginés (H. Lozano Blesa, Zaragoza), Mireia López-Corbeto (H.U. Vall d´Hebron, Barcelona), Sergio Ordóñez-Palau (H. Lleida, Lleida), Andrea García-Valle (H. U Palencia), Susana Romero-Yuste (H.U. Pontevedra, Pontevedra).. *[1]Marqués de Valdecilla University Hospital, Rheumatology, Santander, Spain*; *[2]Hospital de La Princesa, Rheumatology, Madrid, Spain*; *[3]Complejo Hospitalario Universitario de Vlgo, Rheumatology, Vigo, Spain*; *[4]Hospital La Fe, Rheumatology, Valencia, Spain*; *[5]Hospital Germans Trias i Pujol, Rheumatology, Badalona, Spain*; *[6]Hospital Clínic, Rheumatology, Barcelona, Spain*; *[7]Hospital Universitario de Canarias, Rheumatology, San Cristóbal de La Laguna, Spain*

Background: Interstitial lung disease (ILD) is a severe complication of RA. Abatacept (ABA) have demonstrated efficacy in RA-ILD [1,2], although combined treatment with MTX or others DMARDs remain controversial.

Objectives: To assess the efficacy and safety of ABA in monotherapy (ABA_{MONO}) versus combined-ABA, ABA plus MTX(ABA_{MTX}) or ABA plus other non-MTX DMARDs ($ABA_{NON-MTX}$), in RA-ILD.

Methods: Observational multicenter study of RA-ILD caucasian patients treated with ABA. We analyzed in three groups (ABA_{MONO}, ABA_{MTX}, $ABA_{NON-MTX}$) the following outcomes: **a)** Dyspnea, **b)** FVC and DLCO, **c)** HRCT, **d)** DAS28-ESR, **e)** corticosteroid-sparing effect. Differences between basal and final follow-up were evaluated. Multivariable linear regression was used between the three groups.

Results: We studied 263 RA-ILD patients (mean age 64.6±10 years) [ABA_{MONO} (n=111), ABA_{MTX} (n=46) and $ABA_{NON-MTX}$ (n=106)]. At baseline, ABA_{MONO} patients were older (67±10 years) and took higher prednisone dose (10 [IQR 5-15] mg/day). There was no statistically significant differences in sex, seropositivity, ILD patterns, FVC, DLCO or disease duration. In all groups, most patients experienced stabilization or improvement in FVC, DLCO, dyspnea, HRCT as well as improvement in DAS28-ESR. A statistically significant difference between basal and final follow-up was only found in corticosteroid-sparing effect in ABA_{MTX} or $ABA_{NON-MTX}$(Figure 1**).** However, in the multivariable analysis, there were no differences in any outcome between the three groups(Table 1).

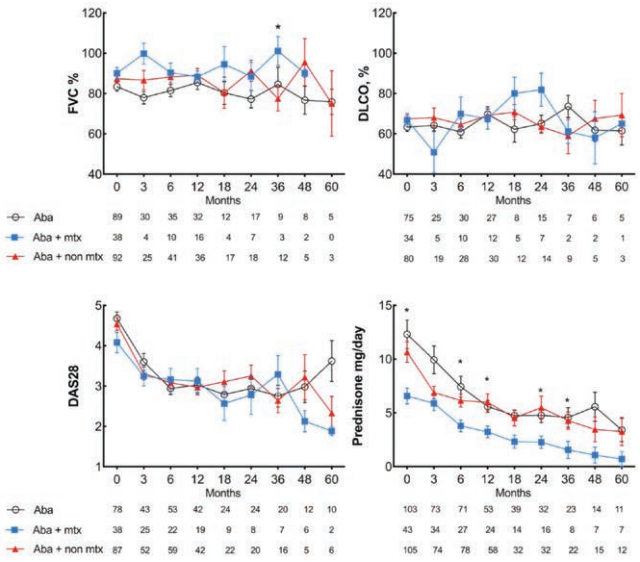


Figure 1.

Conclusion: In caucasian individuals with RA-ILD, ABA_{MONO} or ABA_{MTX} or $ABA_{NON-MTX}$ seems to be equally effective and safe. However, a corticosteroid-sparing effect is only observed in combined-ABA.

REFERENCES:

[1] Fernández-Díaz C, et al. Abatacept in patients with rheumatoid arthritis and interstitial lung disease: A national multicenter study of 63 patients. Semin Arthritis Rheum. 2018 Aug;48(1):22-27. doi: 10.1016/j.semarthrit.2017.12.012.

[2] Fernández-Díaz C, et al. Abatacept in interstitial lung disease associated with rheumatoid arthritis: national multicenter study of 263 patients. Rheumatology (Oxford). 2020 Dec 1;59(12):3906-3916. doi: 10.1093/rheumatology/keaa621.

Acknowledgements: Spanish Collaborative Group of Interstitial Lung Disease Associated to Rheumatoid Arthritis

Disclosure of Interests: Carlos Fernández-Díaz Speakers bureau: Roche, bristol myers squibb, Belén Atienza-Mateo: None declared, Santos Castañeda: None declared, Rafael Melero: None declared, Francisco Ortiz-Sanjuán: None declared, Ivette Casafont-Solé: None declared, J. Loricera: None declared, Sebastián C Rodriguez-García: None declared, Iván Ferraz-Amaro: None declared, Miguel A González-Gay: None declared, Ricardo Blanco Speakers bureau: bristol myers squibb

DOI: 10.1136/annrheumdis-2021-eular.892

Table 1. Effect in FVC, DLCO, dyspnea (mMRC) and HRCT pulmonary scan after abatacept.

	ABA_{MONO} N=111		ABA_{MTX} N=46		$ABA_{NON-MTX}$ N=106		ABA_{MTX} vs ABA_{MONO}			$ABA_{NON-MTX}$ vs ABA_{MONO}	
		p		p		p	p*	Unadjusted	Adjusted**	Unadjusted	Adjusted**
Follow-up, median [IQR] months	12 [6-36]		12 [6-36]		18[12-36]		0.40		0.67		0.17
Differences between basal and final follow-up											
FVC, %	-0.5 (-2.5, 1.5)	0.64	1.2(-0.6, 3.1)	0.17	-1.2 (-2.9, 0.5)	0.17	0.33	0.30	0.39	0.59	0.90
DLCO, %	1.8 (-0.7, 4.34)	0.16	0.5 (-3.8, 4.8)	0.82	-1.5 (-4.1, 1.1)	0.26	0.20	0.58	0.80	0.07	0.32
mMRC, n (%)											
Worsening	5 (5)		3 (8)		5 (5)		0.83		0.47		0.99
Stable or improving	93 (95)		36 (92)		87 (95)						
HRCT pulmonary scan, n (%)											
Worsening	13 (28)		2 (11)		15 (25)		0.24		0.10		0.78
Stable or improving	34 (72)		19 (89)		44 (75)						
DAS28-ESR	**-1.5 (-1.9, -1.0)**	**0.000**	**-1.2 (-1.8, -0.6)**	**0.000**	**-1.5 (-1.8, -1.2)**	**0.000**	0.74	0.58		0.92	
Prednisone, mg/day	-3.8 (-8.3, 0.8)	0.10	**-2.7 (-4.6, -0.8)**	**0.006**	**-4.8 (-6.3, -3.4)**	**0.000**	0.69	0.67		0.65	

Differences in DAS28-ESR, prednisone, FVC and DLCO are expressed as mean difference (95%CI) comparing final follow-up minus basal values.*Differences between the 3 groups.**Differences between ABA_{MTX} vs. ABA_{MONO}, and between $ABA_{NON-MTX}$ vs ABA_{MONO} are adjusted for age, disease duration until abatacept treatment, and DAS28 and prednisone dose at baseline.**Abbreviations (**DAS28-ESR: Disease activity score-erythrocyte sedimentation rate; DLCO: Carbon Monoxide Diffusing Capacity; HRCT: High resolution computed tomography; FVC: Forced vital capacity, mMRC: modified Medical Research Council scale

POS0514

IMPORTANCE OF BODY MASS MEASUREMENT AND THE GRIP STRENGTH TEST TO PREDICT FALLS IN PATIENTS WITH RHEUMATOID ARTHRITIS

M. Tada[1], Y. Yamada[2], K. Mandai[3], N. Hidaka[1]. [1]*Osaka City General Hospital, Orthopaedic Surgery, Osaka, Japan*; [2]*Osaka City University Medical School, Orthopaedic Surgery, Osaka, Japan*; [3]*Osaka Saiseikai Nakatsu Hospital, Orthopaedic Surgery, Osaka, Japan*

Background: We previously reported that the prevalence of sarcopenia was 28% in patients with rheumatoid arthritis (RA) in a cohort study [1]. RA patients have a high risk of falls and fractures [2]. However, the predictors of falls and fractures in RA patients are not known.

Objectives: Whether evaluation of muscle mass and function at baseline could predict falls and fractures during four-year follow-up was investigated.

Methods: The four-year follow-up data from a prospective, observational study (CHIKARA study: Correlation researcH of sarcopenIa, sKeletal muscle and disease Activity in Rheumatoid Arthritis) were used. Muscle mass was measured by a body impedance analyzer, and leg muscle mass was calculated. The leg muscle score (max: 100, min: 0) reflected the ratio of leg muscle mass to overall weight. Grip strength as an indicator of muscle function was evaluated using a digital, hand-held, isokinetic dynamometer. The correlations between muscle mass or function and falls or fractures were analyzed by survival rates and Cox hazard ratios. Leg muscle mass and grip strength were investigated by receiver operating characteristic (ROC) curve analysis for correlations with falls or fractures.

Results: A total of 100 RA patients (female: 78%, mean age: 66.1 years) were enrolled; 35 patients had falls, and 19 patients had fractures during the four-year follow-up. The leg muscle score, grip strength, age, and fractures at baseline were significantly correlated with falls. The cut-off values of the leg muscle score and grip strength were calculated to be 84.5 points (sensitivity: 0.79, specificity: 0.43) and 15.9 kg (sensitivity: 0.56, specificity: 0.70), respectively, by ROC curve analysis. The patients were divided into four groups by their leg muscle scores and grip strength; the numbers of falls and fractures are shown in Table 1 for each group. The fall-free survival rate was significantly lower in the group with low leg muscle score and low grip strength (35.3%) than in the other groups (P=0.002) (Figure 1). The hazard ratio for the both low group was significantly increased, 3.6-fold (95%CI: 1.1-11.5), compared to that in the both high group.

Table 1. Numbers of falls and fractures by category of leg muscle score and grip strength

	LG + GS+ (n=34)	LG - GS+ (n=12)	LG + GS- (n=37)	LG - GS- (n=17)	P value*
Falls, N	6	5	15	11	0.010
Fractures, N	3	4	6	6	0.072

LG+: leg muscle score >84.5 points, GS+: grip strength >15.9kg, LG-: leg muscle score ≤84.5 points, GS+: grip strength ≤15.9kg *: compared in four groups by Kruskal-Walls test.

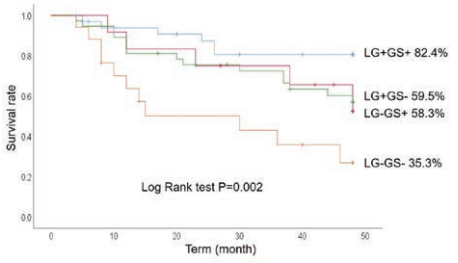


Figure 1. Fall-free survival rate in the four groups

Conclusion: RA patients with both low leg muscle score and low grip strength at baseline were at high risk for falls during the four-year follow-up period. Evaluation of muscle mass and function can predict falls in RA patients.

REFERENCES:

[1] Tada, M., Yamada, Y., Mandai, K. & Hidaka, N. Matrix metalloprotease 3 is associated with sarcopenia in rheumatoid arthritis - results from the CHIKARA study. *Int J Rheum Dis* **21**, 1962-1969, doi:10.1111/1756-185X.13335 (2018).

[2] van Staa, T. P., Geusens, P., Bijlsma, J. W., Leufkens, H. G. & Cooper, C. Clinical assessment of the long-term risk of fracture in patients with rheumatoid arthritis. *Arthritis Rheum* **54**, 3104-3112, doi:10.1002/art.22117 (2006).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.940

POS0515

FIBROMYALGIA IN MEXICAN PATIENTS WITH RHEUMATOID ARTHRITIS

L. D. Fajardo Hermosillo[1]. [1]*Instituto Mexicano del Seguro Social, Centro Médico Nacional de Occidente, Rheumatology, Guadalajara, Mexico*

Background: Rheumatoid Arthritis (RA) is a disabling chronic inflammatory disease that shows an unpredictable and severe clinical course [1]. Global assessment, functional status and disease activity of patients with RA can be influenced also by non-inflammatory factors as concomitant presence of fibromyalgia (FM) [1,2]. FM occur up to 20% in RA patients, who present chronic widespread pain, fatigue and cognitive symptoms that impacts achieving a complete disease remission, having more comorbidities, bearing a higher medical cost and finally exhibiting a worse quality of life [1,3,4]. Range of manifestations of FM varies according ethnical and cultural differences between patients [1]. Here is presented the impact of fibromyalgia in Mexican patients with RA.

Objectives: To determinate the frequency and factors associated to fibromyalgia in Mexican RA patients.

Methods: 624 patients with RA that fulfilled ACR/EULAR 2010 criteria (≥18 years) from a Mexican population recruited from 2012 to 2020 were examined. Patients with or without presence of FM diagnosed by ACR 2010/2011 criteria were included. Demographic factors, clinical features, disease activity measured using DAS28 (Disease Activity Score 28-joint counts), functional status evaluated by HAQ (Health Assessment Questionnaire), comorbidities and pharmacologic treatments were explored for RA patients with and without FM. Charlson's comorbidity index (CCI) was used to analyze comorbidities. Chi-square, Student´s-t, U Mann-Whitney tests were performed by univariate analysis and logistic regression was executed by multivariate analysis adjusted for age and gender. Statistical tests were conducted at 5% level of significance.

Results: Of 624 patients with RA 88.8% were women. The mean age [standard deviation (SD)] was 55.0 (12.3) years. The mean of time at onset of RA (SD) was 11.2 (9.1) years. A total of 311(49.8%) patients had FM; of them 91.6% were women and the mean age (SD) was 54.5 (12.2) years. In the univariate analysis RA patients with FM were more likely to be older and smokers, have seropositive RA, higher body mass index and longer time at onset of RA, show worse functional status by HAQ and more radiographic progression, present more extra-articular and Sicca manifestations, exhibit increased demand of hip and knee arthroplasty, also reveal a higher frequency of comorbidities including depression, osteoporosis and type 2 diabetes mellitus, besides to use a greater number of disease-modifying anti-rheumatic drugs (DMARDs), more biologic agents and higher doses of corticosteroids. Also, CCI was higher in RA patients with FM. Nevertheless, no differences were found for RA disease activity in both groups. In multivariate analysis, higher score of CCI (OR 1.21, 95% CI 1.01–1.44, p=0.037) remained significant in RA patients with FM.

Conclusion: This study suggests that RA patients from Mexico have high prevalence of the FM. Those with FM have a worse functional status, a higher frequency and score of comorbidities that impact in a reduction of their quality of life. On the other hand, no differences were found for RA disease activity in both groups. However, these observations must be confirmed in larger and prospective studies.

REFERENCES:

[1] Zhao SS et al. Best Pract Res Clin Rheumatol. 2019;33(3):101423;
[2] Duffield SJ et al. Rheumatology (Oxford). 2018;57(8):1453;
[3] Kim H et al. Arthritis Care Res (Hoboken) 2017;69(12):1871;
[4] Salaffi Fet al. Rheumatol Int. 2017;37(12):2035.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1013

POS0516 REDEFINING THE CLINICAL AND LABORATORY FEATURES OF RHEUMATIC PLEURAL EFFUSION: A 30-CASE SERIES

S. Minoda[1], R. Sada[2], S. Matsushita[2], Y. Nakayama[3], H. Akebo[2], Y. Tsugihashi[4], H. Ishimaru[2], K. Hatta[2]. *[1]Osaka University Graduate School of Medicine, Department of Respiratory Medicine and Clinical Immunology, Osaka, Japan*; *[2]Tenri Hospital, Department of General Internal Medicine, Nara, Japan*; *[3]Graduate School of Medicine, Kyoto University, Department of Rheumatology and Clinical Immunology, Kyoto, Japan*; *[4]Tenri Health Care University, Department of Health Care, Nara, Japan*

Background: Rheumatoid pleural effusion (RPE) is a common extra-articular complication in patients with rheumatoid arthritis (RA). Previous studies have shown that RPE usually occurs in middle-aged men with rheumatoid factor (RF)-positive RA. RPE usually has features of pleural fluid acidosis, high lactate dehydrogenase (LDH) levels, and very low glucose levels[(1)]. However, to the best of our knowledge, these findings were based on very few case series and reports, and most of these reports were published by the early 2000s[(1, 2)].

Objectives: To investigate the clinical and laboratory characteristics and typical clinical courses of patients with RPE in a single centre of Japan since the beginning of the 21st century.

Methods: Medical records of RPE patients were retrospectively reviewed between May 2006 and September 2020. RPE was identified by fulfilling these five conditions: (1) confirmation of the RA diagnosis; (2) having an exudative pleural effusion according to Light's criteria; (3) negative results of pleural fluid culture; (4) negative results of pleural fluid cytology; and (5) exclusion of a parapneumonic effusion or empyema defined as no antibiotic use or ineffectiveness of antibiotics during the clinical course. Patients were divided into two groups according to their age at diagnosis: <60 years (Group A) and ≥60 years (Group B).

Results: A total of 30 cases of RPE were included in the study. The median age was 71 years (interquartile range [IQR], 66–78 years). Of these patients, 16 (53%) were women. The median disease duration of RA was 98 months (IQR, 8–162 months). The two groups comprised six patients aged <60 years old and 24 patients ≥60 years. The median age was 54 years (IQR, 49–56 years) in Group A and 74 years (IQR, 69–78 years) in Group B. The median disease duration of RA was longer in Group B than that in Group A (132 *vs*. 3 months, p=0.008). Compared with Group A, Group B had fewer patients with fever (14% *vs*. 83%, p=0.003), and had lower serum C-reactive protein levels (3.3 *vs.* 11.1 mg/dL, p=0.03). Moreover, Group B was more likely to show mild inflammatory pleural fluids with higher pH (7.5 *vs.* 7.2, p=0.005) and lower LDH levels (155 *vs*. 1810 IU/L, p=0.046). Corticosteroids were started or increased in five (83%) and nine (38%) patients, and biologic disease-modifying anti-rheumatic drugs were started in one (17%) and two (8%) patients in groups A and B, respectively. One patient (16%) died within 5-years in Group A, and seven patients (29%) died in Group B.

Conclusion: In contrast to previous studies, RPE was seen in older patients as well as middle-aged adults, and the pleural fluid analysis in older patients with RPE showed milder inflammation than the middle-aged patients.

Table 1. Comparison of clinical and laboratory findings between Group A and Group B.

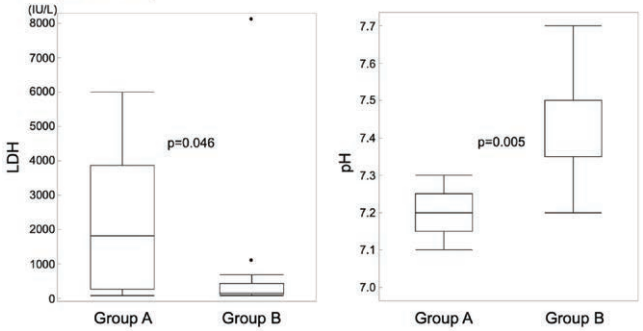
	Group A (n=6)	Group B (n=24)	P value
Age (years)	54 [49-56]	74 [69-78]	
Female	2 (n=6, 33.3)	14 (n=24, 58.3)	0.38
Disease duration of RA (months)	3 [1-9]	132 [44-199]	0.008
Fever ≥37.0℃	5 (n=6, 83.3)	3 (n=22, 13.6)	0.003
Serum			
CRP (mg/dL)	11.1 [5.6-1.4]	3.3 [0.9-10.5]	0.03
RF (IU/mL)	100 [19-816]	63 [23-193]	0.95
Anti-CCP ab positive	5 (n=6, 83.3)	12 (n=15, 80)	1.00
Pleural fluid analysis			
pH	7.2 [7.2-7.2]	7.5 [7.4-7.5]	0.005
LDH (IU/L)	1810 [594-2932]	155 [123-346]	0.046
Glu (mg/dL)	59 [10-123]	105 [91-122]	0.42
Tp (g/dL)	5.1 [4.9-5.6]	4.6 [3.6-5.2]	0.21
Number of cells (/μL)	5235 [3353-9300]	3300 [1490-5008]	0.27
Glu/serum Glu	0.41 [0.09-0.99]	1.05 [0.85-1.15]	0.71
Started or increased CS	5 (n=6, 83.3)	9 (n=24, 37.5)	0.18
Started bDMARDs	1 (n=6, 16.6)	2 (n=24, 8.3)	0.50
Died within 5 years	1 (n=6, 16.6)	7 (n=24, 29.1)	1.00

Data are median [interquartile range], or number (total number, percent).Abbreviations: RA, rheumatoid arthritis; CRP, C-reactive protein; RF, rheumatoid factor; Anti-CCP ab, anti-cyclic citrullinated peptide antibodies; LDH, lactate dehydrogenase; Glu, glucose; Tp, total protein; CS, corticosteroid; bDMARDs, biologic disease-modifying anti-rheumatic drugs

REFERENCES:

[1] Balbir-Gurman A, et al. Semin Arthritis Rheum. 2006 Jun; 35(6): 368-78.

Figure. Comparison of pleural fluid lactate dehydrogenase (LDH) and pH between Group A and Group B.



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1197

POS0517 A LONGITUDINAL STUDY OF SARCOPENIA, LOCOMOTIVE SYNDROME, AND FRAILTY IN PATIENTS WITH RHEUMATOID ARTHRITIS: FROM THE CHIKARA STUDY

K. Mandai[1], M. Tada[2], Y. Yamada[3], T. Koike[4,5], T. Okano[3], N. Hidaka[2], H. Nakamura[3]. *[1]Osaka Saiseikai Nakatsu Hospital, Department of Orthopedic Surgery, Osaka, Japan*; *[2]Osaka City General Hospital, Department of Orthopedic Surgery, Osaka, Japan*; *[3]Osaka City University Graduate School of Medicine, Department of Orthopedic Surgery, Osaka, Japan*; *[4]Osaka City University Graduate School of Medicine, Center for Senile Degenerative Disorders (CSDD), Osaka, Japan*; *[5]Search Institute for Bone and Arthritis Disease (SINBAD), Department of Orthopedic Surgery, Shirahama, Japan*

Background: Rheumatoid arthritis (RA) patients have a high frequency of sarcopenia, and they commonly have reduced physical function. We previously reported that the prevalence of sarcopenia was 28%, that of frailty was 18.9%, and that of pre-frailty was 38.9% in RA patients[1,2], and 13.2% of RA patients developed sarcopenia within a year [3].

Objectives: To investigate the risk factors for new onset of sarcopenia, locomotive syndrome, and frailty in patients with RA and the course of each disease.

Methods: Two-year follow-up data from the rural group of the prospective, observational CHIKARA study were used. Sarcopenia was diagnosed using the criteria of the Asian Working Group for Sarcopenia 2014, locomotive syndrome was diagnosed using locomotive 5, and frailty was diagnosed using the basic checklist. New onset of the disease over the 2-year follow-up period was studied, excluding cases that had the disease at baseline. Improvement was defined as cases with disease at baseline that no longer met the diagnostic criteria after 2 years. Differences in the characteristics of each disease were tested using the Chi-squared test and the paired *t*-test.

Results: The 81 patients with RA (82.7% female) had mean age 66.9±11.5 years, mean DAS28-ESR 2.9±1.2, methotrexate use in 81.5% (with a dose of 9.9±2.7 mg/week), and glucocorticoid (GC) use in 22.2% (with a dose of 3.1±1.7 mg/week). The baseline prevalence was 44.4% for sarcopenia, 35.8% for locomotive syndrome, and 25.9% for frailty, and the new onset rate was 4.4% for sarcopenia, 15.4% for locomotive syndrome, and 13.3% for frailty. Of the patients with each disease at baseline, 36.1% had sarcopenia, 20.7% had locomotive syndrome, and 33.3% had frailty, and of those with each disease at 2 years, 36.1% had sarcopenia, 20.7% had locomotive syndrome, and 33.3% had frailty. The new onset sarcopenia and locomotive syndrome groups had significantly higher rates of GC use (p=0.036, p=0.007, paired *t*-test) and significantly higher doses (p=0.01, p=0.001, paired *t*-test) than the groups without new onset sarcopenia and locomotive syndrome. High baseline disease activity was an independent predictor of new onset of locomotive syndrome on multivariate logistic regression analysis (OR=3.21, p=0.015).

Conclusion: The new onset rates at 2 years were 4.4% for sarcopenia, 15.4% for locomotive syndrome, and 13.3% for frailty. In the new onset sarcopenia and locomotive syndrome groups, both GC use and dosage were significantly higher.

REFERENCES:

[1] Tada M, et al. Matrix metalloprotease 3 is associated with sarcopenia in rheumatoid arthritis - results from the CHIKARA study. Int J Rheum Dis. 2018 Nov;21(11):1962-1969.
[2] Tada M, et al. Correlation between frailty and disease activity in patients with rheumatoid arthritis: Data from the CHIKARA study. Geriatr Gerontol Int. 2019 Dec;19(12):1220-1225.
[3] Yamada Y, et al. Glucocorticoid use is an independent risk factor for developing sarcopenia in patients with rheumatoid arthritis: from the CHIKARA study. Clin Rheumatol. 2020 Jun;39(6):1757-1764.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1245

POS0518

DIAGNOSTIC VALUE OF MUSCLE STRENGTH TESTS FOR THE DIAGNOSIS OF SARCOPENIA IN RHEUMATOID ARTHRITIS PATIENTS

O. Dobrovolskaya[1], A. Efremova[1], N. Toroptsova[1], O. Nikitinskaya[1], A. Feklistov[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Department of osteoporosis, Moscow, Russian Federation*

Background: Motor disorders in patients with rheumatoid arthritis (RA) may be associated with sarcopenia (SP). The frequency of secondary SP in RA patients reaches 17 - 37% [1, 2]. Currently, in patients with RA muscle strength is evaluated by methods proposed in geriatric practice [3].
Objectives: To determine the sensitivity, specificity, diagnostic accuracy, positive and negative predictive value of handgrip strength (HS) and chair stand test (5-times sit-to-stand, CST) for the diagnosis of sarcopenia (SP) in women with rheumatoid arthritis (RA).
Methods: 87 women (aged 40-75 years) with RA were enrolled in the study. We did not include patients with aseptic bone necrosis, femoral and knee endoprostheses and comorbidity that negatively affected on the bone tissue. All patients underwent handgrip strength by mechanical dynamometer and CST. Handgrip strength less than 16kg and CST more than 15 seconds were the criteria for probable SP. Assessment of muscle mass was carried out by dual-energy x-ray absorptiometry («Discovery A» Hologic, USA). Reduced muscle mass was determined as a decrease in appendicular muscle mass (AMM) < 15kg or appendicular mass index (AMI) < 5.5kg/m2. Confirmed SP was diagnosed when there was a combination of low muscle strength and reduced muscle mass. For both tests of muscle strength assessment, the sensitivity, specificity, diagnostic accuracy of the method, as well as their positive and negative predictor value for the diagnosis of SP were calculated.
Results: Low handgrip strength and 5-times CST more than 15 seconds were found in 63 (72%) and 54 (62%) women, respectively. Among them only 20 (23%) patients had low AMM or AMI, so in these women SP was confirmed. For the handgrip strength the sensitivity of the method was 95%, and the specificity - only 34%, the diagnostic accuracy was 48%. The positive prognostic value of this test was 30%, and the negative value - 96%. The sensitivity, specificity and diagnostic accuracy of the CST were significantly lower than the handgrip strength and amounted to 50%, 21% and 28%, respectively. The prognostic value of this test, both positive (16%) and negative (58%), was also significantly lower than the assessment of handgrip strength in RA patients.
We evaluated the diagnostic value of combination of two tests to identify individuals with probable SP: the sensitivity, specificity and diagnostic accuracy were 65%, 30% and 39%, respectively. Negative and positive predictive values were 71% and 24%, respectively, for combination of 2 tests, which was better than using only CST, but worse than using only hand dynamometry.
Conclusion: Muscle strength tests proposed by the European Working Group on Sarcopenia in Older People have a low specificity, diagnostic accuracy and positive predictive values for detecting SP in RA patients, which requires the development of other methods of the first step of diagnosis of SP in RA patients.
REFERENCES:

[1] Torii M, Hashimoto M, Hanai A, et al. Prevalence and factors associated with sarcopenia in patients with rheumatoid arthritis. Modern Rheumatology, 2018;29(4):589-595. doi:10.1080/14397595.2018.1510565
[2]Vlietstra L, Stebbings S, Meredith-Jones K et al. Sarcopenia in osteoarthritis and rheumatoid arthritis: The association with self-reported fatigue, physical function and obesity. PLoS ONE, 2019;14(6):e0217462. doi:10.1371/journal.pone.0217462
[3] Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16-31. doi:10.1093/ageing/afy169

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1322

POS0519

BONE MINERAL DENSITY, LEAN AND FAT MASS IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

N. Toroptsova[1], O. Dobrovolskaya[1], A. Feklistov[1], O. Nikitinskaya[1], A. Efremova[1], N. Demin[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Department of osteoporosis, Moscow, Russian Federation*

Background: The relationship between lean mass (LM), fat mass (FM) and bone mineral density (BMD) remains controversial. Some population studies have emphasized the positive association between them, while others have found an inverse relationship. RA patients are characterized by a decrease in muscle mass and an increase in fat mass. Such changes in body composition may be associated with low BMD.
Objectives: To study the relationship between BMD, LM and FM in postmenopausal women with RA.
Methods: 68 postmenopausal women with RA (median age 59 [54; 63] years) were included in the study. BMD and body composition were evaluated using two-energy X-ray absorptiometry. Correlation analysis between body composition parameters and BMD was performed with the Spearman method, correlation coefficients R for p<0.05 are presented.
Results: The average L1-L4 BMD was 0,92±0,16g/cm^2, total hip BMD - 0,84±0,15g/cm^2 and femoral neck - 0,73±0,13g/cm^2. 33 (48.5%) women had osteopenia, and 17 (25.0%) - osteoporosis (OP). Low appendicular LM was found in 5 (7.4%) and low appendicular muscle index (appendicular LM/height^2, AMI) – in 10 (14.7%) patients. Overfat was revealed in 47 (69.1%) women, but only 20 (29.4%) women had BMI corresponding to obesity. The positive correlations between BMD in L1-L4, total hip and femoral neck regions and body weight (R=0.46, R=0.56 and R=0.50, respectively), trunk fat (R=0.4, R=0.51 and R=0.37, respectively), total FM (R=0.27, R=0.43 and R=0.34, respectively), trunk LM (R=0.55, R=0.54 and R=0.51, respectively), total LM (R=0.51, R=0.50 and R=0.52, respectively), appendicular LM (R=0.31, R=0.29 and R=0.37, respectively) and AMI (R=0.26, R=0.33 and R=0.51, respectively) were found out. In the multivariate linear regression analysis total LM was associated with BMD of lumbar spine (β=0.638, p=0.001) and total hip (β=0.473, p=0.008), and AMI - with femoral neck BMD (β=0.360; p=0.014). We found that FM hadn't a significant effect on BMD in any region.
Conclusion: 73.5% of patients with RA had a reduced BMD, and 14.7% women – low AMI. LM was positively associated with BMDs in different regions of interest, but FM had no effect on BMD. Further researches are needed to identify associations between body composition, inflammatory activity and bone health in patients with RA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1331

POS0520

ASSOCIATIONS BETWEEN THE NEOVASCULARIZATION OF CAROTID ATHEROSCLEROTIC PLAQUES, LIPID PARAMETERS AND IMMUNOLOGICAL DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Gerasimova[1], T. Popkova[1], O. Pogorelova[2], O. Fomicheva[3], I. Kirillova[1], T. Balakhonova[2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases Laboratory, Moscow, Russian Federation*; [2]*National Medical Research Center of Cardiology, Department of functional diagnostics, Moscow, Russian Federation*; [3]*National Medical Research Center of Cardiology, 4 cardiology department, Moscow, Russian Federation*

Background: Development of carotid atherosclerotic plaques (CAP) in patients (pts) with rheumatoid arthritis (RA) is associated with accumulation of traditional risk factors and immunological disorders. CAP neovascularization is associated with its' inflammation and increasing vulnerability. Therefore, early detection of CAP neovascularization is important for prevention of potential cardiovascular complications, preferably using a non-invasive technique, such as contrast-enhanced ultrasound (CEUS) of the carotid arteries.
Objectives: to identify the relationship between the severity of CAP neovascularization, lipid parameters and RA-related parameters.
Methods: Evaluation of 23 RA pts, 8 males and 15 females, mean age 61 [58; 65] years, with a longstanding disease (7 [3;12] years), seropositivity for IgM rheumatoid factor (RF) (76%) and anti-cyclic citrullinated peptide (ACCP) (62%) and moderate clinical disease activity (DAS 28 3,9 [3,2;4,8]). Nineteen RA pts (83%) received Methotrexate, 35% - biological agents, 35% - low-dose glucocorticoids. All patients underwent bilateral CEUS of the carotid arteries using a PHILIPS IU22 ultrasound system with 3-9 MHz linear array transducer and i/v administration of SonoVue contrast agent. The severity of carotid intraplaque neovascularization (IPN) was visually assessed on a scale from 0 to 3 (Shah et al. 2007): 0 - no neovascularization, 1 (mild) - limited to moderate neovascularization, 2 (severe) - extensive appearance of neovascularization, 3 - in the presence of a pulsating vessel in the plaque image.
Results: Carotid IPN was found in all RA pts. Grade 1 of neovascularization was established in 39% pts (group I) and Grade 2 - in 61% pts (group II). Groups were comparable in terms of age, sex, body mass index, smoking, disease duration and activity RA (DAS 28 score). The degree of carotid IPN positively correlated with the LDL-C level (R = 0,46, p=0,04), and the TG level (R=0,56, p=0,01) and negatively correlated with the HDL-C level (R= -0,52, p=0,02) in all pts. The degree of neovascularization was also associated with RA duration (R=0,52, p<0,05) and ACCP-positivity (R=0,57, p=0,007). Aforementioned correlations were significant for both groups of RA pts. No association was found between the severity of IPN and the levels of RF, DAS28. Association between the degree of carotid stenosis and CRP concentrations (R=-0,73, p<0,05) was found in pts of group II.
Conclusion: CEUS of carotid arteries demonstrated the presence of a predominantly extensive carotid IPN in RA pts. Cases of more severe carotid IPN were associated with lipid parameters (positively with the LDL-C, TG levels and negatively with the HDL-C level), RA duration and ACCP-positivity. The relationship between the degree of carotid artery stenosis and CRP requires additional studies to determine the role of immunological disorders in the development of carotid intraplaque neovascularization in RA pts.
REFERENCES:

[1] Shah F., Balan P., Weinberg M., Reddy V., Neems R., Feinstein M., Dainauskas J., Meyer P., Goldin M., Feinstein S.B. Contrast-enhanced ultrasound imaging of atherosclerotic carotid plaque neovascularization: a new surrogate marker of atherosclerosis? Vasc Med. 2007;12(4):291-7. https://doi.org/10.1177/1358863x07083363

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1509

POS0521 FACTORS ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

N. Mena-Vázquez[1], F. G. Jiménez-Núñez[1], M. Rojas-Giménez[2], L. Cano Garcia[1], S. Manrique Arija[1], A. Fernandez-Nebro[1]. [1]*Instituto de Investigación Biomédica de Málaga (IBIMA). Hospital Regional Universitario de Málaga (HRUM), Reumatología, Málaga, Spain*; [2]*Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC). UGC de Reumatología, Hospital Universitario Reina Sofía de Córdoba., Reumatología, Córdoba, Spain*

Objectives: To describe the prevalence of subclinical atherosclerosis measured as carotid intima-media thickness (cIMT) in patients with rheumatoid arthritis (RA) and to analyze the associated factors.

Methods: We performed an observational study of 60 patients with RA and 60 sex and age-matched controls. Patients with dyslipidemia were excluded. The main variable was the cIMT measured by ultrasound. The maximum cIMT was measured and atheromatous plaque was defined as focal thickening of the arterial wall protruding toward the lumen and measuring >0.5 mm or more than 50% of the neighboring cIMT. The other variables included were clinical and laboratory values, lipid metabolism, the 28-joint Disease Activity Score (DAS28), International Physical Activity Questionnaire (METs) and Adherence to a Mediterranean diet (MEDAS). Descriptive, bivariate and two multivariate models were constructed to identify factors associated with pathologic cIMT in all subjects and other in RA patients.

Results: The baseline characteristics of both groups are shown in Table 1. The RA patients did not have differences in the mean (SD) of maximum cIMT in relation to the controls (0.77 [0.1] vs 0.75 [0.1]; p = 0.392), nor in the number of plaques (16 [26.7%] vs 10 [16.7]; p = 0.184). The factors associated with maximum cIMT in the total sample were male sex (ß= 0.182; p = 0.039), age (ß = 0.010; p <0.001), METs (ß= -2.19; p = 0.008), MEDAS (ß = -0.177; p = 0.038); While the factors associated with maximum cIMT in patients with RA were: male sex (ß = 0.155; p = 0.003), age (ß = 0.005; p = 0.007), MEDAS (ß = -0.022; p = 0.017), DAS28 (ß = 0.036; p = 0.003) and ACPA (ß = 0.082; p = 0.052).

Table 1. Baseline characteristics of 60 patients with RA and 60 controls.

Variable	Patients n=60	Controls n=60	p-value
Age in years, mean (SD)	54.0 (11.1)	54.2 (110.4)	0.943
Female sex; n (%)	53 (88.3)	51 (85.0)	0.591
Smoking			0.300
Never smoked, n (%)	27 (45.8)	30 (54.5)	
Exsmoker, n (%)	23 (39.0)	14 (25.5)	
Active smoker, n (%)	9 (15.3)	11 (20,0)	
BMI (kg/m^2), mean (SD)	28.0 (5.5)	27.3 (4.9)	0.540
MET-minute, median (IQR)	533.2 (605.1)	809 (716.9)	0.028
MEDAS, median (IQR)	9.4 (1.8)	9.1 (2.1)	0.349
Progression of RA, months, mean (SD)	119.7 (84.1-170.5)	-	-
Diagnostic delay, months, median (IQR)	5.7 (5.1-14.4)	-	-
Erosions, n (%)	25 (43.1)	-	-
RF >10, n (%)	45 (75.0)	0 (0.0)	<0,001
ACPA >20, n (%)	48 (80.0)	0 (0,0)	<0,001
High-sensitivity CRP (mg/dl), median (IQR)	8.1 (4.2)	2.0 (4.5)	0.009
ESR (mm/h), median (IQR)	21.1 (16.6)	13.9 (12.3)	0.008
DAS28 at protocol, mean (SD)	3.1 (2.2-4.2)	-	-
Synthetic DMARDs, n (%)	52 (88.1)	-	-
Methotrexate, n (%)	36 (61.0)	-	-
Leflunomide, n (%)	6 (10.2)	-	-
Sulfasalazine, n (%)	7 (11.9)	-	-
Hydroxychloroquine, n (%)	4 (6.8)		
Biologic DMARDs, n (%)	32 (54.2)	-	-
Anti TNF-α, n (%)	23 (39.0)	-	-
Jak inhibitor, n (%)	1 (1.7)	-	-
Anti-IL-6, n (%)	6 (10.2)	-	-
Abatacept, n (%)	1 (1.7)	-	-

Abbreviations: RA, rheumatoid arthritis; ACPA, anti-citrullinated peptide antibodies; RF, rheumatoid factor; SD, standard deviation; MEDAS: Mediterranean Diet Adherence Survey; DAS28, 28-joint Disease Activity Score; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; DMARD, disease-modifying antirheumatic drug; IL-6, interleukin 6; Anti TNF, anti–tumor necrosis factor.

Conclusion: In patients with well-controlled established RA, subclinical atherosclerosis is associated, in addition to sex, age, and mediterranean diet, with inflammatory activity and ACPA value.

Acknowledgements: Grant for Medical Researchers from "Fundación Española de Reumatología" 2019

Grant from "Fundación Española de Reumatología" 2018 for non-funded projects.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1561

POS0522 PREVALENCE OF BRONCHIECTASIS IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

L. Martin[1], L. Prisco[1], W. Huang[1], G. Mcdermott[1], N. Shadick[1], T. Doyle[2], J. Sparks[1]. [1]*Brigham and Women's Hospital, Rheumatology, Boston, United States of America*; [2]*Brigham and Women's Hospital, Pulmonology, Boston, United States of America*

Background: Bronchiectasis is a known extra-articular manifestation of rheumatoid arthritis (RA) and can lead to decreased quality of life as well as increased risk for infection and mortality. Understanding the burden of bronchiectasis in RA may lead to a better understanding of pathogenesis and improved management. We performed a systematic review and meta-analysis to determine the prevalence of bronchiectasis in RA.

Objectives: We investigated the prevalence of RA-related bronchiectasis (RA-BR) using a systematic review and meta-analysis.

Methods: We followed the PRISMA-P 2015 guideline for systematic reviews and registered this analysis (ID#199080) on PROSPERO. We queried PubMed and EMBASE databases using the search strategy "rheumatoid arthritis; AND; bronchiectasis" as of July 31, 2020. The inclusion and exclusion criteria were assessed for study eligibility by two independent abstractors. Exclusion criteria included: (1) non-primary literature (i.e., review articles, editorials); (2) case reports involving less than 5 patients; (3) published in a language other than English; (4) did not relate to both RA and bronchiectasis; and (5) studies not involving humans (e.g., mouse models). After the initial screen, we conducted a full text review to verify that inclusion criteria were met: (1) reported frequency of RA-BR and denominator of all RA patients in the study sample. Data including type of study design, method of RA-BR detection, and RA characteristics were extracted by two independent abstractors. We performed meta-analyses using random effects models to estimate prevalence of RA-BR among RA overall and restricted to retrospective or prospective studies.

Results: Out of a total of 208 studies, 37 studies were identified that reported frequency of RA-BR among RA. The included studies had heterogeneous methods to identify RA-BR that were based on either clinical or research chest computed tomography (CT) imaging and had varying methods to adjudicate images. Some studies focused on patients with respiratory symptoms or suspected RA-associated interstitial lung disease (RA-ILD). There were a total of 8,646 patients with RA, and 612 were identified as having RA-BR. The pooled overall prevalence of RA-BR in the random effects meta-analysis was 18.2% (95%CI 13.3-23.7%, Figure 1). Among prospective studies (n=24), the prevalence of RA-BR in the meta-analysis was 20.7% (95% CI 14.7-27.4%). Among retrospective studies (n=13) reporting RA-BR, the prevalence was 14.5% (95% CI 7.2-23.7%). Prevalence was lowest in retrospective studies where RA-BR was identified through clinical care (e.g., two large retrospective studies that investigated 4,000 and 1,129 RA patients reported RA-BR prevalence of 0.6% and 2.7%, respectively). The two largest prospective studies that incorporated a research protocol performing chest CT imaging on all enrolled patients investigated 150 and 332 patients with RA and reported a RA-BR prevalence of 8.0% and 9.6%, respectively. Smaller studies of both study design types generally reported higher prevalence of RA-BR.

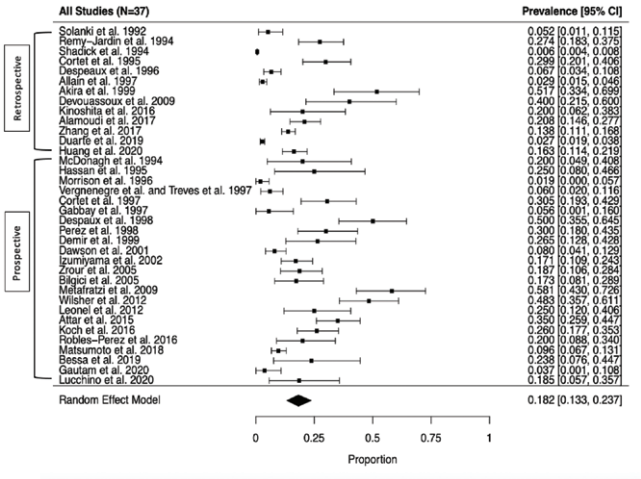


Figure 1. Pooled prevalence of RA-related bronchiectasis in RA among all studies identified (n=37).

Conclusion: The prevalence of RA-BR in this systematic review and meta-analysis was 18.2%, emphasizing that bronchiectasis is a common extra-articular feature of RA. However, some studies may have identified subclinical RA-BR through research imaging or RA-BR may have been secondary to RA-ILD. Future studies should standardize methods to identify RA-BR cases and investigate the natural history and clinical course given the relatively high prevalence that we report.

Disclosure of Interests: Lily Martin: None declared, Lauren Prisco: None declared, Weixing Huang: None declared, Gregory McDermott: None declared, Nancy Shadick Consultant of: Consultant < 5K Bristol-Myers Squibb, Grant/research support from: BMS Amgen Lilly, Mallinckrodt, and Sanofi, Tracy Doyle Consultant of: Boehringer Ingelheim (<5K), Grant/research support from: Bristol Myers Squibb and Genentech, Jeffrey Sparks Consultant of: Bristol-Myers Squibb, Gilead, Inova Diagnostics, Optum, and Pfizer, Grant/research support from: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.1650

POS0523 RISK OF CARDIOVASCULAR DISEASE IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS: A CURRENT RISK ASSESSMENT

R. Raadsen[1], R. Hansildaar[1], M. Heslinga[1,2], A. W. van Kuijk[1], M. Nurmohamed[1,2]. [1]*Amsterdam Rheumatology and Immunology Center, Location Reade, Rheumatology, Amsterdam, Netherlands*; [2]*Amsterdam Rheumatology and Immunology Center, Location VU University Medical Center, Rheumatology, Amsterdam, Netherlands*

Background: Patients with rheumatoid arthritis (RA) are known to have an increased risk of developing, mainly ischemic cardiovascular diseases (CVD). This is partly explained by a higher incidence of traditional CV risk factors as hypertension and/or hypercholesterolemia but also due to the systemic inflammation characteristic to RA. RA is considered an independent CV risk by National and International CVD risk management guidelines, and therefore CVD risk screening is recommended. However, the implementation of CV risk management is often poorly performed in daily clinical practice.

Objectives: The aim of the current study was to investigate the cardiovascular disease risk of newly diagnosed RA patients, and review if and to what extent implementation of CVD risk management had previously taken place.

Methods: Every newly diagnosed RA patient in a large Dutch outpatient rheumatology clinic had CV screening within their first year post-diagnosis during a regularly scheduled visit, where among others smoking habits, blood pressure and lipid profile were measured. A 10-year cardiovascular risk was calculated using a modified SCORE calculator from www.u-prevent.com, which predicts the risk of myocardial infarction, stroke, heart failure, peripheral arterial disease and CV death based on several CV risk factors. To account for RA as a risk factor, the calculator multiplies the risk by 1.5, in accordance with the Dutch CV risk management guideline. The calculated 10-year cardiovascular morbidity risk was categorized in low (<10%), intermediate (10-19%) and high (≥20%), and the 10-year mortality risk was also categorized in low (<1%), intermediate (1-4%) and high (≥5%).

Results: A total of 53 patients were included up to this point. Of these, the average age was 57 (±8.5), and 39 (74%) were women. Mean systolic blood pressure was 129 (±17.7) mmHg, with 38 (72%) patients having hypertension. Mean total cholesterol, LDL and HDL were respectively 5.5 (±1.0) mmol, 3.43 (±0.82) mmol and 1.78 (±0.54) mmol, with 30 patients having hypercholesterolemia. The average calculated 10-year morbidity risk of all patients was 13%, and the mortality risk was 3%. Distribution of the 10-year risk in low, intermediate and high is presented in figure 1. Only one patient reported having previous used medication for hypercholesterolemia, but not at the time of enrollment in this study.

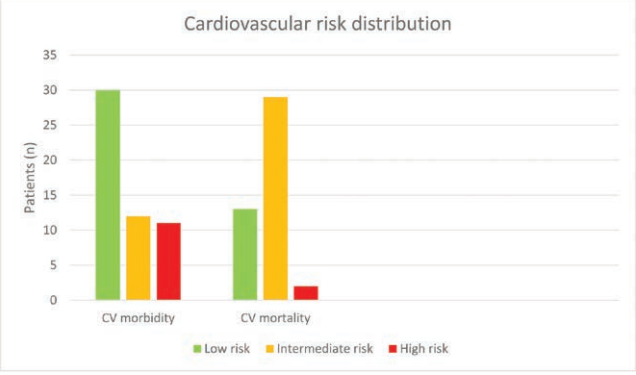


Figure 1. Distribution of 10-year cardiovascular risk in rheumatoid arthritis patients. CV = cardiovascular

Conclusion: 43% of newly diagnosed RA patients had an intermediate or high calculated 10-year CV morbidity risk, and 76% had an intermediate or high mortality risk. Patients with early RA still often have underdiagnosed and severely undertreated risk factors of CVD, such as hypertension and hypercholesterolemia. Early CV risk assessment and management in patients with RA is critical and needs to be implemented as standard care.

REFERENCES:

[1] Ortec. (2020, November 20). U-prevent. Retreived from U-prevent (u-prevent.nl)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1734

POS0524 CARDIOVASCULAR DISEASE RISK IN INFLAMMATORY ARTHRITIS PATIENTS STILL SUBSTANTIALLY ELEVATED IN 2020

R. Raadsen[1], F. Hooijberg[1], L. Boekel[1], E. Vogelzang[2], M. Leeuw[1], R. van Vollenhoven[3], W. Lems[1,4], G. J. Wolbink[1], A. W. van Kuijk[1], M. Nurmohamed[1,4]. [1]*Amsterdam Rheumatology and Immunology Center, location Reade, Rheumatology, Amsterdam, Netherlands*; [2]*Amsterdam University Medical Center, Vanderbilt University Medical Center, Medical Microbiology, Amsterdam, Netherlands*; [3]*Amsterdam Rheumatology and Immunology Center, Location Academic Medical Center, Rheumatology, Amsterdam, Netherlands*; [4]*Amsterdam Rheumatology and Immunology Center, Location VU University Medical Center, Rheumatology, Amsterdam, Netherlands*

Background: Patients with inflammatory rheumatic diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) are at a higher risk for developing cardiovascular diseases (CVD) than the general population. This increased risk is partly due to a higher incidence of traditional cardiovascular (CV) risk factors, such as hypertension and dyslipidemia, and partly due to the underlying systemic inflammation. During the past two decades, the burden of the systemic inflammation has been reduced by more efficacious anti-inflammatory treatment, which somewhat attenuated the increased CV risk of rheumatic patients. However, it remains important to monitor the effects of these new treatment strategies on the prevalence of CVD in patients with a rheumatic disease in systematically controlled cohorts.

Objectives: The aim of the current report was to evaluate whether the CV risk of patients with inflammatory rheumatic diseases still differs from the general population, despite advances In anti-rheumatic treatment strategies.

Methods: In March 2020, all adult patients with an inflammatory rheumatic disease from the Amsterdam Rheumatology and Immunology Center, location "Reade" were systematically asked to participate in a prospective cohort study. The primary aim of this study was to monitor the impact of the COVID-19 pandemic on patients with inflammatory rheumatic diseases compared to age and sex matched healthy controls. Between April 26, 2020 and May 27, 2020, participants completed the first online questionnaire of the study. Amongst others, information on demographic data, including CV comorbidities and risk factors, and medication use was collected. The baseline characteristics and prevalence of CVD were compared between RA, PsA or AS and healthy controls.

Results: In total, 1455 consecutive patients with an inflammatory rheumatic disease (979 RA patients, 261 PsA patients and 215 AS patients), and 414 healthy controls completed the first questionnaire, as shown in table 1. CV comorbidities were more frequently reported in RA, PsA and AS patients compared to healthy controls; 107 (11%), 28 (11%) and 22 (10%) compared to 30 (7%), respectively.

Table 1. Biological DMARD usage in RA, PsA and AS patients

Patient characteristics	All patients (n=1455)	RA (n=979)	PsA (N=261)	AS (n=215)	Controls (n=414)
Mean age - yr	55 ± 13	58 ± 12	55 ± 13	48 ± 13	53 ± 13
Female sex - no (%)	934 (64)	728 (74)	119 (46)	87 (41)	298 (72)
BMI (IQR)	25 (23-28)	25 (22-28)	26 (24-30)	25 (22-28)	24 (22-27)
Smoking - no (%)	178 (12)	126 (13)	17 (7)	35 (16)	34 (8)
Cardiovascular disease – no (%)	157 (11)	107 (11)	28 (11)	22 (10)	30 (7)
Rheumatic medication - no (%)					
csDMARDs	877 (60)	712 (73)	148 (57)	17 (8)	N.A.
Oral glucocorticoids	161 (11)	139 (14)	17 (7)	5 (2)	2 (0.4)
TNF inhibitor	563 (39)	336 (34)	121 (46)	106 (49)	N.A.
IL-6 inhibitor	19 (1)	19 (2)	0	0	N.A.
IL-17 inhibitor	17 (1)	2 (0.2)	7 (3)	8 (4)	N.A.

Table 1. Baseline characteristics. Values are displayed as mean ± standard deviation (SD), median with interquartile range (IQR) or frequencies with percentages (%). RA = rheumatoid arthritis, PsA = psoriatic arthritis, AS = ankylosing spondylitis, BMI = body mass index, TNF = anti-tumor necrosis factor, IL = interleukin.

Conclusion: We demonstrated that the prevalence of CVD is approximately 1.5 times higher in patients with rheumatic diseases compared to healthy controls (11% vs. 7%, respectively). This corresponds with previous research, although the reported prevalence of CVD in PsA and AS patients is even higher compared to prior studies. This suggests that the CVD risk of patients with rheumatic diseases is still elevated in 2020 compared to the general population, despite the improved management of rheumatic disease activity. Therefore, adequate and timely treatment of CV risk factors remains relevant, not only in patients with RA, but in patients other rheumatic diseases as well.

REFERENCES:

[1] Hooijberg F et al. (2020) Patients with rheumatic diseases adhere to COVID-19 isolation measures more strictly than the general population. *The Lancet rheumatology 2(10), 583-585.*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1739

POS0525 ARTHRITIC PAIN AS A SURROGATE MARKER FOR ASYMPTOMATIC CARDIOVASCULAR RISK FACTORS: OFFERING PRACTITIONERS A 'TEACHABLE MOMENT'

J. Sewell[1], S. M. Hussain[1], Y. Wang[1], A. Wluka[1], M. Carrrington[2], K. Samaras[3], F. Cicuttini[1]. *[1]Monash University, Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Melbourne, Australia*; *[2]Baker Heart and Diabetes Institute, Pre-Clinical Disease and Prevention, Melbourne, Australia*; *[3]University of New South Wales, St Vincent's Clinical School of Medicine, Sydney, Australia*

Background: Cardiovascular diseases (CVD) are the number one cause of death worldwide. CVDs are linked to well established risk factors: obesity, hypertension (HTN), dyslipidaemia (DL) and diabetes mellitus (DM)[1]. While targeting risk factors reduces the burden of CVD, this is often challenging because they are largely asymptomatic and patients are therefore unlikely to seek medical attention. Arthritis, in contrast, causes pain and functional impairment prompting presentation to a healthcare practitioner. Patients with arthritis of varying aetiologies (such as osteoarthritis[2], gout[3], rheumatoid arthritis[4]) have been shown to have an increased risk of CVD.

Objectives: To examine the relationship between arthritis and DM, HTN and DL in adults of all age groups. A secondary objective was to examine whether this relationship existed independent of obesity.

Methods: Data from the 2017-18 Australian Bureau of Statistics National Health Survey included 13,776 participants, categorised into young (18-39 years), middle aged (40-64 years) and older (≥65 years) adults. Blood pressure, height and weight were measured. BMI was calculated and participants classified as obese (≥30 kg/m^2) or non-obese. HTN was defined as > 140/90mmHg. Participants were asked if they had arthritis of any form, DL or DM diagnosed by a doctor. Logistic regression models estimated odds ratios with 95% CI for prevalence of arthritis associated with CVD risk factors.

Results: Arthritis was reported by 3.9% of young adults, 28.8% of middle-aged adults, and 54.5% ofolderadults. In all three age groups, arthritis was associated with significantly increased odds of obesity, HTN, DL and DM. For example, in middle-aged adults, having arthritis was associated with increased odds of obesity (1.75, 95% CI 1.54-2.01), HTN (1.78, 1.60-2.04), DL (2.14, 1.84-2.49) and DM (1.64, 1.33-2.03). These associations remained statistically significant after adjustment for obesity.

Conclusion: Compared to those without arthritis, adults with arthritis were at increased risk of obesity, HTN, DM and DL. The increased risk of HTN, DM and DL was independent of obesity and tended to be higher in younger adults. These data suggest that a patient's presentation with symptomatic arthritis of any aetiology and at any age, may be used opportunistically as a "teachable moment" for screening for asymptomatic CVD risk factors in higher-risk individuals. This provides practitioners an opportunity to manage both arthritis and CVD risk in parallel, rather than in silos.

REFERENCES:

[1] World Health Organisation. (2017). "Cardiovascular Diseases." from https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases(cvds).
[2] Wang, H., et al. (2016). "Osteoarthritis and the risk of cardiovascular disease: a meta-analysis of observational studies." Scientific reports **6**: 39672.
[3] Singh, J. (2015). "When gout goes to the heart: does gout equal a cardiovascular disease risk factor?" Annals of the Rheumatic Diseases **74**: 631-634.
[4] England, B. R., et al. (2018). "Increased cardiovascular risk in rheumatoid arthritis: mechanisms and implications." British Medical Journal **361**: k1036.

Table 1. Prevalence of CVD risk factors in adults with and without arthritis.

	Young 18-39 yo			Middle Aged 40-64 yo			Older ≥65 yo		
	No arthritis n = 3773	Arthritis n = 157	OR (95% CI) *adjusted for obesity	No arthritis n = 4055	Arthritis n = 1638	OR (95% CI) *adjusted for obesity	No arthritis n = 1891	Arthritis n = 2262	OR (95% CI) *adjusted for obesity
Obesity	473	32	2.07 (1.36-3.16)	868	527	1.75 (1.54-2.01)	326	610	1.89 (1.62-2.21)
HTN	131	14	2.72 (1.53-4.84) 2.35 (1.17-4.70)*	745	496	1.78 (1.60-2.04) 1.59 (1.37-1.84)	730	1091	1.48 (1.31-1.68) 1.35 (1.18-1.55)*
DM	19	4	5.7 (1.74-15.37) 4.87 (1.34-17.69))*	236	151	1.64 (1.33-2.03) 1.37 (1.08-1.73)*	256	399	1.37 (1.15-1.62) 1.15 (0.95-1.39)*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1763

POS0526 SEXUAL FUNCTION IN MALE AND FEMALE PATIENTS WITH RHEUMATOID ARTHRITIS: A POST-HOC ANALYSIS OF THE FINCH STUDIES

L. F. Perez-Garcia[1], M. Micu[2], L. Gheyle[3], Z. Yin[4], Y. Tan[5], K. Chen[6], P. Papazian[7,8], K. Van Beneden[9], R. Dolhain[1], R. Westhovens[10]. *[1]Erasmus University Medical Centre, Department of Rheumatology, Rotterdam, Netherlands*; *[2]Rehabilitation Clinical Hospital, Rheumatology Division, 2nd Rehabilitation Department, Cluj-Napoca, Romania*; *[3]Galapagos NV, Clinical Research, Mechelen, Belgium*; *[4]Gilead Sciences, Inc., Department of Clinical Data Science, Foster City, United States of America*; *[5]Gilead Sciences, Inc., Clinical Research (Inflammation Therapeutic Area), Foster City, United States of America*; *[6]Gilead Sciences, Inc., Department of Clinical Data Science, Foster City, United States of America*; *[7]Pitié-Salpêtrière Hospital, Infectious Diseases Department, Paris, France*; *[8]Galapagos France, Medical Affairs, Puteaux, France*; *[9]Galapagos NV, Medical Affairs, Mechelen, Belgium*; *[10]University Hospitals Leuven, Department of Development and Regeneration, Skeletal Biology and Engineering Research Centre, Division of Rheumatology, Leuven, Belgium*

Background: While sexual function is impaired in a high proportion of patients with rheumatoid arthritis (RA), it is often neglected in patient care.[1] FINCH 1 (NCT02889796), FINCH 2 (NCT02873936) and FINCH 3 (NCT02886728) were Phase 3 studies to assess the safety and efficacy of filgotinib (FIL) for moderate-to-severe RA; patient-reported sexual function was also evaluated.

Objectives: To analyse disease characteristics associated with sexual function and explore the effect of FIL and adalimumab (ADA) on sexual function in males and females in the FINCH studies.

Methods: Post-hoc analyses included data from patients who were randomised and received ≥1 dose of study drug in the FINCH studies. Male and female subgroup analyses were performed to describe the correlation between baseline disease characteristics and baseline visual analogue scale (VAS) sexual function score (using Pearson correlation coefficient) and to assess the treatment effect on the change from baseline in VAS sexual function (mm) up to Week 52 (FINCH 1 and 3) or Week 24 (FINCH 2). Patients indicated how RA affected their ability to have sex during the last week using an exploratory 0–100 VAS (0: no effect; 100: complete inhibition). Changes from baseline were analysed with a mixed-effects model for repeated measures. All P values are nominal for exploratory purposes.

Results: Baseline characteristics are shown in the Table 1. Univariate analyses revealed significant positive correlations (P<0.05) between disease duration and baseline VAS sexual function score in male and female subgroups in FINCH 1; no significant correlations were seen in male and female subgroups of FINCH 2 and 3. In all studies, significant correlations (P<0.05) were observed between baseline VAS sexual function score and baseline disease characteristics (swollen/tender joint count 28, Disease Activity Score-28, Health Assessment Questionnaire Disability Index, 36-Item Short Form Survey, patient global VAS, pain VAS or fatigue) in males or females. In all studies, analysis of least-squares mean changes from baseline in VAS sexual function revealed improvements in both males and females on FIL as early as Week 2, until Week 52 (Week 24 in FINCH 2). Figure 1 shows data for FINCH 1.

Conclusion: Sexual function should be considered as an important patient outcome in RA treatment. At baseline in the FINCH studies, disease activity

negatively impacted sexual function in both male and female patients. Active treatment with FIL or ADA resulted in early and sustained improvements from baseline in sexual function.

REFERENCES:

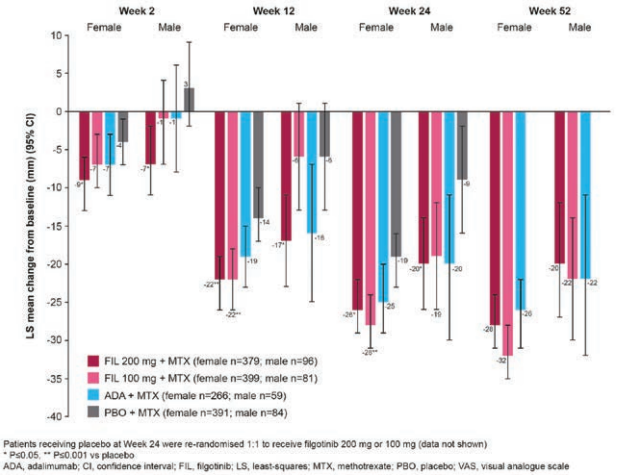
[1] Tristano AG. *World J Orthop* 2014;5:107–11

Table 1. Mean (standard deviation) baseline characteristics

	FINCH 1		FINCH 2		FINCH 3	
	Male n=258	Female n=990	Male n=79	Female n=270	Male n=233	Female n=691
Duration of RA, yr	**6.8 (7.38)**	**8.0 (7.63)**	11.3 (8.53)	12.7 (9.35)	2.1 (5.35)	2.2 (4.85)
SJC28	**11 (5.0)**	**11 (5.1)**	**13 (6.2)**	**12 (6.1)**	**11 (5.4)**	**11 (5.7)**
TJC28	**14 (6.5)**	**15 (6.4)**	**15 (7.5)**	**16 (7.0)**	**14 (6.6)**	**15 (6.7)**
HAQ-DI	**1.35 (0.614)**	**1.64 (0.601)**	**1.41 (0.689)**	**1.73 (0.634)**	**1.37 (0.651)**	**1.62 (0.617)**
DAS28 (CRP)	**5.6 (0.95)**	**5.8 (0.90)**	**5.8 (1.08)**	**5.9 (0.92)**	**5.7 (1.00)**	**5.7 (0.99)**
SF-36 PCS	**34.3 (7.72)**	**33.0 (7.34)**	**31.7 (8.48)**	**30.9 (7.75)**	**34.4 (7.72)**	**33.4 (7.47)**
SF-36 MCS	**45.9 (10.15)**	**43.6 (10.65)**	**43.7 (11.20)**	**44.5 (11.71)**	**46.2 (11.75)**	**43.0 (10.89)**
FACIT-fatigue	**30.0 (10.00)**	**26.8 (10.49)**	**26.3 (11.15)**	**24.0 (11.64)**	**30.7 (10.93)**	**26.6 (10.89)**
Patient global VAS (mm)	**64 (19.8)**	**67 (19.0)**	**66 (20.0)**	**70 (19.5)**	**65 (22.4)**	**66 (20.3)**
Pain VAS (mm)	**61 (20.6)**	**66 (19.5)**	**62 (22.3)**	**68 (20.6)**	**64 (22.3)**	**66 (20.9)**
VAS sexual function score	44 (30.2)	49 (32.3)	48 (34.6)	49 (36.8)	42 (34.4)	48 (35.1)

Variables in bold significantly correlated with VAS sexual function score (P<0.05)DAS28 (CRP), Disease Activity Score-28 using C-reactive protein; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; MCS, mental component summary; PCS, physical component summary; RA, rheumatoid arthritis; SF-36, 36-Item Short Form Survey; S/TJC28, swollen/tender joint count based on 28 joints; VAS, visual analogue scale

Figure. Change from baseline in VAS sexual function over time for female and male subgroups in FINCH 1



Patients receiving placebo at Week 24 were re-randomised 1:1 to receive filgotinib 200 mg or 100 mg (data not shown)
* P≤0.05, ** P≤0.001 vs placebo
ADA, adalimumab; CI, confidence interval; FIL, filgotinib; LS, least-squares; MTX, methotrexate; PBO, placebo; VAS, visual analogue scale

Acknowledgements: The FINCH studies were funded by Gilead Sciences, Inc (Foster City, CA, USA). Medical writing/editorial support was provided by Debbie Sherwood, BSc, CMPP (Aspire Scientific, Bollington, UK), funded by Galapagos NV (Mechelen, Belgium).

Disclosure of Interests: Luis Fernando Perez-Garcia Consultant of: Galapagos, Grant/research support from: CONACYT, ReumaNederland, and ZonMw, Mihaela Micu Speakers bureau: AbbVie, Angelini, Eli Lilly, Ewopharma, Novartis, UCB, Consultant of: Galapagos, Lien Gheyle Shareholder of: Galapagos, Employee of: Galapagos, Zhaoyu Yin Shareholder of: Gilead, Employee of: Gilead, YingMeei Tan Shareholder of: Gilead, Employee of: Gilead, Kun Chen Shareholder of: Gilead, Employee of: Gilead, Patrick Papazian Speakers bureau: Amgen, Gilead, Janssen, MSD, Consultant of: Gilead, Janssen, MSD, Employee of: Galapagos, part-time employee since Sept 2020, Katrien Van Beneden Shareholder of: Galapagos, Employee of: Galapagos, Radboud Dolhain Speakers bureau: AbbVie, Genzyme, Novartis, Roche, UCB, Consultant of: Galapagos, Grant/research support from: UCB, Rene Westhovens Speakers bureau: Celltrion, Galapagos/Gilead, Consultant of: Celltrion, Galapagos/Gilead

DOI: 10.1136/annrheumdis-2021-eular.1774

POS0527 ACUTE KIDNEY INJURY (AKI) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

A. Nakashima[1], K. Suzuki[1], H. Fujii[1], Y. Fujisawa[2], I. Mizushima[3], T. Zoshima[3], M. Kawano[3], H. Nomura[4]. *[1]Ishikawa Prefectural Central Hospital, Division of Nephrology and Rheumatology, Kanazawa, Japan; [2]Ishikawa-ken Saiseikai Kanazawa Hospital, Division of Internal Medicine and Rheumatology, Kanazawa, Japan; [3]Kanazawa University Hospital, Department of Rheumatology, Kanazawa, Japan; [4]Kanazawa University Hospital, Department of General Medicine, Kanazawa, Japan*

Background: Methotrexate has been an anchor drug for patients with rheumatoid arthritis (RA). However, it is strictly prohibited to prescribe MTX to patients with severely decreased renal function because it can induce a fatal adverse event such as pancytopenia in these patients. On the other hand, since the average age of RA patients is gradually increasing, and many of them already have mildly to moderately impaired renal function, their renal function can easily decrease to below the critical level of the estimated glomerular filtration rate. Therefore, new development of acute kidney injury (AKI) during MTX administration might induce a fatal adverse event, making the identification of patients susceptible to AKI very important.

Objectives: To clarify the frequency of AKI and the factors involved in it in RA patients.

Methods: Two hundred and fifty-two RA patients (211 females, 41 males, mean age 62.3 ± 12.5 years, disease duration 11.0 ± 9.5 years) diagnosed more than 3 years earlier and followed for more than 5 years, and also, others diagnosed ≥3 years earlier but followed for ≤5 years were enrolled. We measured BUN, Cr, RF and aCCP in patient serum, urinary proteins, urinary blood, and urinary casts and evaluated CDAI, SDAI, disease activity score (DAS) 28-CRP and DAS28-ESR. Steinbrocker functional classification and radiological grading were evaluated. History of diabetes mellitus, hypertension and hyperlipidemia was determined from the medical records. Medications for RA, including non-steroid anti-inflammatory drugs (NSAIDs), prednisolone, csDMARD (MTX, Tacrolimus, etc.), bDMARDs and tsDMARDs were evaluated. Estimated glomerular filtration rate (eGFR) was calculated by the new Japanese coefficient-modified Modification of Diet in Renal disease (MDRD) study equation. The criteria of AKI were that serum Cr increased by 0.3 mg /dl or increased by 1.5-fold between consecutive visits according to the KIDIGO criteria [1)] and the report of Leither et al[2)].

Results: Twenty (7.9%) patients developed AKI, 22 times. The causes of AKI were 10 infections, 6 dehydrations, 2 enteritis, 1 urticaria, 2 hypercalcemia due to VitD administration, and 1 ureteral stone. We divided our patients into group A (with AKI) and group B (without AKI). Group A was older (69.9±10.1 vs 61.7±12.6 years), had greater physician VAS (29.5±27.7 vs 15.7±18.3 mm), higher serum creatinine (0.79±0.19 vs 0.60±0.16 mg/dl), higher BUN (18.4±5.7 vs 15.1±4.4 mg/dl), lower eGFR(65.5±23.3 vs 86.4±22.4 ml/min), more frequent prednisolone administration (75.0% vs 41.9%), more frequent hyperlipidemia (50.0% vs 19.2%) and more frequent hypertension (60.0% vs 30.6%) than Group B by univariate analysis significantly (p<0.01). We then performed multifactorial analysis using logistic regression analysis. Greater physician VAS (OR 1.02, 1.00-1.04), lower eGFR (OR 1.04, 1.01-1.08) and prednisolone administration (OR 3.29, 1.02-10.63) were found as independent relevant factors for group A.

Conclusion: Our study indicated that AKI developed in RA patients and suggested that renal function decline and prednisolone administration may be implicated. RA patients with impaired renal function and prednisolone administration need to be treated with special attention to the onset of AKI.

REFERENCES:

[1] Kidney Disease: Improving Global Outcomes (KDIGO) Practice Guideline for Acute Kidney Injury. Kidney Int Suppl 2: 1-138, 2012

[2] Leither MD, Murphy DP, Bicknese L et al. The impact of outpatient acute kidney injury on mortality and chronic kidney disease: a retrospective cohort study. Nephrol Dial Transplant. 34:493-501, 2019

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1786

POS0528 SCORES OF CARDIOVASCULAR RISK CALCULATORS AS PREDICTORS OF EARLY ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Gerasimova[1], T. Popkova[1], D. Gerasimova[2], S. Glukhova[3], E. Nasonov[1,4], A. Lila[1,5]. [1]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases Laboratory, Moscow, Russian Federation*; [2]*Sechenov First Moscow State Medical University (Sechenov University), Department of Organization and Economics of Pharmacy, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Laboratories of Medical and Social Problems of Rheumatology, Moscow, Russian Federation*; [4]*Sechenov First Moscow State Medical University (Sechenov University), Department of Rheumatology, Moscow, Russian Federation*; [5]*Russian Medical Academy of Continuing Professional Education, Department of Rheumatology, Moscow, Russian Federation*

Background: Rheumatoid arthritis (RA) is a systemic inflammatory disease leading to significant increase in cardiovascular morbidity and mortality. Development of cardiovascular diseases (CVD) in RA patients is associated with the accumulation of traditional risk factors and immunological disorders. Carotid Artery Doppler Ultrasound (DUS) Exam is the gold standard to identify early atherosclerosis.
Objectives: To evaluate the cardiovascular risk and analyze its relationship with detection of early carotid artery atherosclerotic lesion in patients with rheumatoid arthritis (RA).
Methods: One hundred and nine RA patients (female/male 93/16), aged 45 to 60 without established CVD were included in the study. The median age was 52 [48; 54] years, duration of RA was 120 [36; 204] months, DAS28 was 4,7 [3,5; 5,6] points. 54% (n=59) of patients received methotrexate (median dose 20 [15;27]mg/week), 12% - leflunomide (20mg/day), 12% - sulfasalazine (2000mg/day), 40% - glucocorticoids (median dose 4 [2;8]mg/day), 44% - non-steroidal anti-inflammatory drugs. None of study participants had biologics or statins in their therapeutic regiments at the time of inclusion. CVD risk was calculated with mSCORE, RRS, ASSIGN, QRISK3, ERS-RA scales and results of Carotid Artery DUS imaging in all patients.
Results: Traditional risk factors were highly among RA patients without CVD, including: arterial hypertension - in 73%, dyslipidemia - 68%, overweight - 53%, family history of CVD - 43% and smoking - 39% patients. A combination of three traditional risk factors was found in 60% of patients with RA, and combination of two – in 25%. High risk was found in 5, 5, 14, 6, and 38% of patients according to mSCORE, RRS, ASSIGN, QRISK3, ERS-RA scales, respectively. Carotid atherosclerotic plaques were found in 30% of patients, more often in men (48%) than in women (28%, p=0,049), with similar prevalence regardless RA activity or stage od disease. Positive correlations of carotid intima-media thickness were established with scores of all CVD risk calculators: mSCORE (R = 0,50), RRS (R = 0,40), ASSIGN (R = 0,40), QRISK3 (R = 0,36), ERS-RA (R = 0,26), p <0,05 in all cases, as well as with age (R = 0,41; p = 0,04), the level of total cholesterol (R = 0,23; p = 0,01), systolic blood pressure (R = 0,66; p = 0,02), diastolic blood pressure (R = 0,33; P = 0,03), erythrocyte sedimentation rate (R = 0,26; p = 0,04), IL-6 levels (R = 0,65; p = 0,01). The sensitivity and specificity of the CVR algorithms in prognostication of atherosclerotic carotid artery lesions were 73 and 67% for mSCORE, 64 and 63% for RRS, 64 and 56% for ASSIGN, 73 and 49% for QRISK3, respectively, p<0.05 in all cases, 67 and 50% for ERS-RA, p=0,06.
Conclusion: RRS, mSCORE, ASSIGN, QRISK 3 calculators equally predicted the presence of carotid atherosclerotic plaques in RA patients. The optimal ratio of specificity and sensitivity is shown for the mSCORE scale. Stratification of CVR in RA patients should include assessment of the carotid intima-media thickness. mSCORE calculation and carotid intima-media thickness were the most informative methods identify CVR assessment in RA patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1787

POS0529 ANTI-TNF AND METHOTREXATE PROTECT AGAINST RHEUMATOID ARTHRITIS ATHEROSCLEROSIS

M. Rojas-Giménez[1], M. Á. Puche Larrubia[1], I. Gómez García[1], J. Calvo Gutierrez[1], M. C. Ábalos-Aguilera[2], A. Escudero Contreras[1]. [1]*Reina Sofia University Hospital, Cordoba, Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC), Córdoba University (UCO), Córdoba, Spain., Cordoba, Spain*; [2]*Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC), Córdoba, Spain, Cordoba, Spain*

Objectives: To analyze the effect of differents anti-rheumatic treatments on the carotid intima-medial thickness (cIMT) in patients with Rheumatoid Arthritis (RA).
Methods: Controlled cross-sectional observational study of a cohort of patients with RA. 146 patients with RA (ACR/EULAR2010).cIMT was measured by semi-automatic carotid ultrasound.Other variables: atheroma plaques, bilateral plaques, DAS28-VSG, lipid metabolism, apoB, apoA1, apoB/apoA1, uric acid, homocysteine. Biological or conventional synthetic disease-modifying antirheumatic drug therapy (bDMARDs/csDMARDs), glucocorticoids. Descriptive, bivariate, Spearman's test and multivariate model were constructed to identify factors associated with cIMT.
Results: The baseline characteristics are shown in Table 1.Significant positive correlation was found between cIMT and apoB (r=0.22; p=0.014), apoB/apoA1 (r=0.18; p=0.044), cholesterol(r=0.23; p=0.006),triglycerides(r=0,21, p=0.013),uric acid(r=0.26; p=0.009),age(r=0.65, p>0.001),RF(r=0.16, p=0.05) homocysteine (r=0.5, p<0.001), BMI (r=0.19, p=0.023),CRP(r=0.18, p=0.032) and negative correlation with anti-TNFα treatment time(r=-0.20, p=0.02).Patients receiving bDMARDs alone or combined with csDMARDs had less cIMT than those taking only csDMARDs[median (IQR): 0.54 (0.50-0.63), 0.57(0.53-0.65) and 0.65(0.53-0.75); p=0.046].The factors associated with cIMT were age(ß= 0.007, p<0.001),anti-tnf-α treatment ever(ß= -0.06, p=0.027) and methotrexate treatment ever(ß= -0.07, p=0,08).

Table 1. Baseline characteristics

Variables	RA n=146
Epidemiological characteristics and comorbidities	
Age (years), mean (SD)	55.9 (13.1)
Female sex; n (%)	112 (76.7)
Smoker, n (%)	30 (21.6)
Arterial hypertension, n (%)	45 (30.8)
Diabetes mellitus, n (%)	5 (3.4)
Previous Cardiovascular disease, n (%)	10 (14.6)
Hyperlipidemia, n (%)	46 (31.5)
BMI (kg/m^2), median (IQR)	26.8 (23.4-29.7)
Clinical-laboratory characteristics	
Disease duration, years, median (IQR)	6.77 (2.2-14.2)
Erosions, n (%)	53 (36.6)
RF positive, n (%)	119 (81.55)
ACPA positive, n (%)	123 (84.2)
CRP (mg/dl), median (IQR)	4.8 (1.6-11.5)
ESR (mm/h), median (IQR)	12 (6-24)
DAS28 at protocol, median (IQR)	2.8 (2.1-3.7)
HAQ, mean (SD)	0.78 (0.6)
ApoB (mg/dl), mean (SD)	86.8 (21.8)
ApoA1 (mg/dl), mean (SD)	149.8 (32.7)
Cholesterol (mg/dl), mean (SD)	198.7 (37.3)
cLDL (mg/dl), mean (SD)	119.3 (30.3)
cHDL (mg/dl), median (IQR)	56 (47-70)
Triglycerides (mg/dl), median (RIQ)	92 (73-121)
Homocisteyne (mg/dl), median (RIQ)	2.08 (1.7-2.8)
cIMT mean (mm), median (IQR)	0.6 (0.53-0.7)
Atherosclerotic plaques, n (%)	51 (34.9)
Bilateral plaques, n (%)	22 (15.1)
Anti-rheumatic treatment	
Synthetic DMARDs ever, n (%)	146 (100)
Methotrexate ever, n (%)	132 (90.4)
Time with methotrexate (years), median (IQR)	4.4 (1.04-9.5)
Leflunomide ever, n (%)	83 (56.8)
Sulfasalazine ever, n (%)	13 (8.9)
Hydroxychloroquine ever, n (%)	99 (67.8)
Biological DMARDs ever, n (%)	76 (52.05)
Anti TNFα ever, n (%)	47 (32.2)
Time with antiTNF-α (years), mean (SD)	1.18 (2.8)
Jak inhibitor ever, n (%)	10 (6.8)
Anti-IL-6 ever, n (%)	28 (19.2)
Rituximab ever, n (%)	15 (10.3)
Glucocorticoids at protocol, n (%)	82 (56.5)
Glucocorticoids dose at protocol (mg), median (IQR)	5 (0-5)

Abbreviations: RF: rheumatoid factor; ACPA: anti-citrullinated peptide antibodies, cIMT: carotid intima media thickness; ApoB: apolipoprotein B, ApoA1: apolipoprotein A1, LDL: low-density lipoprotein; HDL: high-density lipoprotein; DAS28: 28-joint Disease Activity Score; HAQ: Health Assessment Questionnaire; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; IL-6: interleukin 6; Anti TNF, anti–tumor necrosis factor

Conclusion: biological disease-modifying antirheumatic drug therapy, in particular Anti TNFα, could protect against the development of atherosclerosis in RA
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1796

POS0530 HOW DOES MULTIMORBIDITY IMPACT ON THE DIRECT AND INDIRECT COSTS IN PATIENTS WITH RHEUMATOID ARTHRITIS?

P. H. Hsieh[1,2], C. Geue[1], O. Wu[1], E. McIntosh[1]. [1]*Institute of Health and Wellbeing, University of Glasgow, Health Economics and Health Technology Assessment, Glasgow, United Kingdom*; [2]*Tri-Service General Hospital, National Defense Medical Centre, Clinical Pharmacy Department, Taipei, Taiwan, Republic of China*

Background: Comorbidities are prevalent in patients with rheumatoid arthritis (RA) and associated with worse outcomes as well as higher economic burden. Little is known about the impact of multimorbidity on the direct and indirect costs

of RA. Evidence of the incremental scale of these multimorbidity costs will usefully inform RA interventions and policies.

Objectives: The aim of this study was to describe how multimorbidity impacts on the cost-of-illness, including direct and indirect costs, in patients with RA.

Methods: The Scottish Early Rheumatoid Arthritis (SERA) is a registry of patients newly presenting with RA since 2011. It contains data on patient characteristics, clinical outcomes, health-related quality of life, and employment status data. These data were linked to routinely recorded hospital admissions and primary care prescribing data. Direct costs were estimated by applying relevant unit costs to healthcare resource use quantities. Indirect cost estimates were obtained from information on employment status and hospital admissions, valued by age and sex specific wages. Two-part models (probit followed by generalized linear model) were used to estimate direct and indirect costs, adjusting for age, gender, and functional disability. The Charlson Comorbidity Index (CCI) score was calculated using patient ICD-10 diagnoses from hospital records. The number of comorbidities was categorized into "RA alone", "single comorbidity" and "multimorbidity (>1 comorbidity)".

Results: Data were available for 1,150 patients, 65.7% were female and a mean age of 57.5±14 years. The majority of patients only had RA (54.1%), followed by a single comorbidity (23.4%) and multimorbidity (22.5%). Annual total costs were significantly higher for patients with multimorbidity (£6,669 95% CI £4,871-£8,466; OR 11.3 95% CI 8.14-15.87) and for patients with a single comorbidity (£2,075 95% CI £1,559-£2,591; OR 3.52 95% CI 2.61-4.79), when compared with RA alone (£590). The excess costs were mainly driven by direct costs (£6,281 versus £1,875 versus £556). Although the difference in indirect costs between patients with multimorbidity and a single comorbidity were not statistically significant (£1,218 versus £914, p=0.11), patients with multimorbidity were associated with significantly higher costs than those with RA only (£594, p<0.01).

Conclusion: The presence of comorbidity contributes significant excess to both direct and indirect costs among RA patients. In particular, patients with multimorbidity incurred substantially higher direct costs than those with a single comorbidity or RA only.

Acknowledgements: The study analysed the data from the Scottish Early Rheumatoid Arthritis (SERA) study with a linkage to routinely recorded health data from Information Service Division, National Service Scotland. We would like to thank all the patients, clinical and nursing colleagues who have contributed their time and support to the study, the SERA steering committee for the approval, and Allen Tervit from the Robertson Centre for Biostatistics, University of Glasgow for the timely technical supports.

Disclosure of Interests: Ping-Hsuan Hsieh: None declared, Claudia Geue: None declared, Olivia Wu Consultant of: OW has received consultancy fees from Bayer, Lupin and Takeda outside the submitted work., Emma McIntosh: None declared

DOI: 10.1136/annrheumdis-2021-eular.1817

POS0531 FACTORS ASSOCIATED WITH BASELINE HYPERTENSION IN EARLY RHEUMATOID ARTHRITIS: DATA FROM A REAL-WORLD LARGE INCIDENT COHORT

B. Hadwen[1], S. Stranges[1,2,3], N. Klar[1], K. Bindee[4], J. Pope[5], S. J. Bartlett[6,7], G. Boire[8], L. Bessette[9], C. Hitchon[10], G. Hazlewood[11], E. Keystone[4], O. Schieir[12], C. Thorne[13], D. Tin[13], M. F. Valois[6], V. Bykerk[14,15], L. Barra[1,3,5]on behalf of on behalf of CATCH Investigators. *[1]University of Western Ontario, Epidemiology and Biostatistics, London, Canada*; *[2]University of Western Ontario, Family Medicine, London, Canada*; *[3]Lawson Health Research Institute, London, Canada*; *[4]University of Toronto, Sinai Health System, Toronto, Canada*; *[5]University of Western Ontario, Department of Medicine, London, Canada*; *[6]McGill University, Department of Medicine, Montreal, Canada*; *[7]Johns Hopkins University, Department of Medicine, Baltimore, United States of America*; *[8]Université de Sherbrooke, Department of Medicine, Sherbrooke, Canada*; *[9]Université de Laval, Department of Medicine, Quebec City, Canada*; *[10]University of Manitoba, Department of Medicine, Winnipeg, Canada*; *[11]University of Calgary, Department of Medicine, Calgary, Canada*; *[12]University of Toronto, Dalla Lana School of Public Health, Toronto, Canada*; *[13]Southlake Regional Health Center, Division of Rheumatology, Newmarket, Canada*; *[14]Weill Cornell Medical College, Hospital for Special Surgery, New York City, United States of America*; *[15]University of Toronto, Department of Medicine, Toronto, Canada*

Background: It is not well understood why hypertension (HTN) is so common in rheumatoid arthritis (RA) patients. Reported prevalence of HTN in RA patients ranges from 4-73%.(1)

Objectives: This study explored the prevalence of HTN at time of RA diagnosis and which demographic, behavioural and clinical factors were associated with HTN.

Methods: Data from the Canadian Early Arthritis Cohort (CATCH), a prospective inception cohort of patients with RA <1 year duration, were used to analyze baseline demographic, behavioural and clinical characteristics associated with HTN, which was reported by physicians. Univariate logistic regression models were created to explore associations with baseline HTN. A multivariate logistic regression model was built based on goodness of fit indicated by likelihood ratio tests. Variables included in the model were age, sex, race, body mass index (BMI), education, smoking, alcohol servings, seropositivity, disease activity and comorbidities.

Results: In total, 2052 subjects were included with mean (±SD) age of 55 (±14) years and symptom duration 5.60(5.47, 5.73) months, 71% of subjects were female and 85% were Caucasian. HTN was reported in 26% of subjects at baseline. Hypertensive subjects were older and more likely to be male. Other factors significantly associated with HTN at baseline were lower education, ever smoking, high BMI, diabetes, hyperlipidemia, worse RA disease activity, longer duration of RA symptoms, being seropositive, as well as the use of NSAIDs and/or corticosteroids (Table 1). In multivariable analysis HTN was associated with older age, overweight and obese BMI, diabetes, and hyperlipidemia. Expression of anti-citrullinated protein antibodies was inversely associated with HTN (Table 1). Other RA disease factors and treatments were not significantly associated with HTN on multivariable analysis.

Table 1. Results of univariate and multivariate logistic regression analyses exploring the association between baseline characteristics and HTN in early RA.

		Univariate Logistic Regression	Multivariable Logistic Regression
	Variable	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**
Socio-Demographic	20-39 years old	0.15 (0.07, 0.26)	0.14(0.05, 0.34)
	40-59 years old	Reference	
	60-79 years old	2.81 (2.26, 3.50)	2.26(1.65, 3.11)
	80-99 years old	5.87 (3.36,10.25)	3.80(1.53, 9.41)
	Female	0.55 (0.45, 0.68)	1.10(0.78, 1.54)
Lifestyle/Behavioural	Normal weight (18.5- 24.9kg/m^2)	Reference	
	Overweight (25-29.9 kg/m^2)	2.33(1.74, 3.11)	1.63(1.10, 2.43)
	Obese (30+ kg/m^2)	3.19(2.38, 4.27)	2.84(1.91, 4.23
	Ever-smoking	1.41(1.15, 1.73)	1.02(0.75, 1.40)
	Post-secondary education	0.58(0.47, 0.71)	0.88(0.65, 1.20)
Clinical Characteristics	Symptom duration	0.99(0.99, 0.99)	1.00(1.00, 1.00)
	DAS-28	1.09(1.09, 1.17)	1.02(0.92, 1.13)
	ACPA+	0.68(0.56, 0.85)	0.64(0.44, 0.92)
	Corticosteroid use pre-baseline	1.37(1.04, 1.81)	Omitted
	NSAID use at baseline	0.68(0.55, 0.84)	Omitted
	Diabetes	5.62(4.09, 7.73)	3.20(1.99, 5.15)
	Hyperlipidemia	4.75(3.74, 6.03)	2.80(1.94, 4.02),
	CVD	15.59(3.35, 72.64)	Omitted

DAS-28; Disease activity score 28, ACPA; Anti-citrullinated protein antibody, CVD; Cardiovascular disease. Pre-baseline is 29 to 365 days before entering the cohort. Baseline is within 28 days before entering the cohort. Omitted variables either failed likelihood ratio test or were colinear. Additional variables tested but found insignificant: race, alcohol servings, depression, RF+, and use of DMARDs.

Conclusion: Approximately 1 in 4 diagnosed with RA had HTN reported by their rheumatologists, which is similar to that of the general population. This suggests that increased risk of HTN in RA patients may develop as RA disease or treatment time progresses. Factors that may be predictive of this excess risk will be explored in further analysis.

REFERENCES:

[1] Panoulas VF, Metsios GS, Pace AV, et al. Hypertension in rheumatoid arthritis. *Rheumatology (Oxford)* 2008;47:1286-98.

Acknowledgements: The CATCH study was designed and implemented by the investigators and financially supported through unrestricted research grants from: Amgen and Pfizer Canada - Founding sponsors since January 2007; AbbVie Corporation and Hoffmann-LaRoche since 2011; Medexus Inc. since 2013;, Merck Canada since 2017, Sandoz Canada, Biopharmaceuticals since 2019,Gilead Sciences Canada since 2020 and Fresenius Kabi Canada Ltd. since 2021. Previously funded by Janssen Biotech from 2011-2016, UCB Canada and Bristol-Myers Squibb Canada from 2011-2018, Sanofi Genzyme from 2016-2017, and Eli Lilly Canada from 2016-2020.

Disclosure of Interests: Brook Hadwen: None declared, Saverio Stranges: None declared, Neil Klar: None declared, Kuriya Bindee: None declared, Janet Pope Speakers bureau: UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, BMS, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead, Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB;, Grant/research support from: Abbvie, BMS, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Susan J. Bartlett Consultant of: Pfizer, UCB, Lilly, Novartis, Merck, Janssen, Abbvie, Gilles Boire Speakers bureau: Merck, BMS, Pfizer, Janssen, Grant/research support from: Amgen, Abbvie, BMS, Eli Lilly, Merck, Novartis, Pfizer, Sandoz, Louis Bessette Speakers bureau: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant of: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis., Grant/research

support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis., Carol Hitchon Grant/research support from: Pfizer and UCB Canada, Glen Hazlewood: None declared, Edward Keystone Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Consultant of:: AbbVie, Amgen, AstraZeneca Pharma, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Genentech Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis, Grant/research support from: AbbVie, Amgen, Gilead Sciences, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, PuraPharm, Sanofi, Orit Schieir: None declared, Carter Thorne Speakers bureau: Medexus/Medac, Consultant of: Abbvie, Centocor, Janssen, Lilly, Medexus/Medac, Pfizer, Grant/research support from: Amgen, Pfizer, Abbvie, Celgene, CaREBiodam, Novartis, Diane Tin: None declared, Marie-France Valois: None declared, Vivian Bykerk Consultant of: Amgen, BMS, Gilead, Sanofi-Genzyme/Regeneron, Scipher, Pfizer Pharmaceuticals, UCB, NIH, Lillian Barra: None declared
DOI: 10.1136/annrheumdis-2021-eular.1835

POS0532 AVERAGE PREDNISOLONE DOSE OF ONLY 1 MG PER DAY WAS RISK FACTOR FOR CLINICAL FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS - NINE-YEAR FINDINGS OF THE TOMORROW STUDY

H. Yoshimura[1], T. Koike[2,3], K. Mamoto[4], Y. Sugioka[2], T. Okano[4], M. Tada[5], K. Inui[6], H. Nakamura[4]. *[1]Izumi City General Hospital, Orthopaedic Surgery, Osaka, Japan*; *[2]Center for Senile Degenerative Disorders (CSDD), Osaka City University Medical School, Orthopaedic surgery, Osaka, Japan*; *[3]Search Institute for Bone and Arthritis Disease (SINBAD), Orthopaedic Surgery, Wakayama, Japan*; *[4]Osaka City University Medical School, Orthopaedic Surgery, Osaka, Japan*; *[5]Osaka City General Hospital, Orthopaedic Surgery, Osaka, Japan*; *[6]Osaka Saiseikai Nakatsu Hospital, Orthopaedic Surgery, Osaka, Japan*

Background: Previous cohort studies showed that the use of prednisolone (PSL) was a risk factor for clinical fractures in patients with rheumatoid arthritis (RA). However, there are few reports on relationship between PSL dose and clinical fractures.
Objectives: The present study aimed to determine the effect of PSL dose on the incidence of clinical fractures in the RA patients treated with PSL.
Methods: We evaluated anthropoetric parameters, bone mineral density (BMD), disease activity score 28-erythrocyte sedimentation rate (DAS28-ESR), RA medication (methotrexate (MTX) dose, use of biologic disease modified anti-rheumatic-drugs (bDMARDs), and PSL dose) and the incidence of clinical fractures during nine years in RA patients who participant the TOMORROW study (UMIN000003876), which is a 10-years prospective cohort study. Data on clinical fracture was self-reported on the questionnaires. In this analysis, the data of RA patients treated with PSL at least once during nine-year period were evaluated. We analyzed the average dose of PSL until the incidence of the clinical fractures. The risk factor for clinical fractures were analyzed by using Cox proportional hazard model with adjustment for age, sex, body mass index (BMI), and smoking history.
Results: We analyzed the data of 67 RA patients treated with PSL. Among them, median age was 61.8 year, 56 patients (83.6%) were female, 47 patients (70.1%) were never smoker and median disease duration was 12.1 year. The number of patients treated with PSL at baseline was 48 (69.1%). During 9 years, 23 clinical fractures were observed in 67 patients, and the incidence of clinical fracture was 0.046/person-year. In 19 patients, who were not treated with PSL at baseline but treated with PSL at least once during 9 years, 5 clinical fractures were observed. In 67 RA patients, Cox proportional hazard analysis revealed that baseline disease activities, BMD at thoracic vertebrae and medication were not significant risk factors for clinical fractures. However, average PSL dose of more than only 1 mg/day was a significant risk factor for the incidence of clinical fracture (hazard ratio (HR): 2.80; p=0.03) (Table 1).

Table 1. Adjusted hazard ratio for clinical fractures in patients with rheumatoid arthritis treated with PSL.

	* Adjusted Hazard ratio	95% Confidence interval	P value
CRP (mg/dL)	1.29	0.88-1.91	0.19
RF (IU/mL)	0.99	0.99-1.00	0.07
ACPA (U/mL)	0.99	0.98-1.00	0.18
DAS28-ESR	0.99	0.71-1.39	0.97
BMD at thoracic vertebrae (mg/cm^2)	0.02	0.00-1.00	0.05
bDMARDs use	0.55	0.23-1.32	0.18
Bisphosphonate use	2.33	0.95-5.71	0.07
average dose of MTX (mg/week)	1.02	0.92-1.12	0.74
average score of DAS28-ESR	1.15	0.76-1.75	0.52
average dose of PSL more than 1mg/day	2.8	1.09-7.24	0.03

*Hazard ratio was adjusted for age, sex, body mass index (BMI), and smoking history. RF, Rheumatoid factor; ACPA, Anti-cyclic citrullinated peptide antibody; DAS28-ESR, disease activity score 28-erythrocyte sedimentation rate; BMD, Bone mineral density; bDMARDs, biologic disease modified anti-rheumatic-drugs; MTX, methotrexate; PSL, prednisolone.

Conclusion: In RA patients treated with PSL, average PSL dose of only 1mg/day significantly increased the risk for the incidence of clinical fractures. Even for established RA patients, continuous use or initiation of low PSL dose was apparently significant risk factor for clinical fractures.
Disclosure of Interests: Hitoshi Yoshimura: None declared, Tatsuya Koike Grant/research support from: Takeda Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Chugai Pharmaceutical, Eisai, Abbott Japan, Teijin Pharma, Banyu Pharmaceutical and Ono Pharmaceutical, Kenji Mamoto: None declared, Yuko Sugioka: None declared, Tadashi Okano: None declared, Masahiro Tada: None declared, Kentaro Inui Grant/research support from: Janssen Pharmaceutical K.K. and Astellas Pharma Inc, Hiroaki Nakamura: None declared
DOI: 10.1136/annrheumdis-2021-eular.1868

POS0533 EFFECT OF CAROTID ULTRASOUND ON THE ACHIEVEMENT OF LDL-CHOLESTEROL TARGETS IN THE ROUTINE CLINICAL CARE OF PATIENTS WITH RHEUMATOID ARTHRITIS

I. Ferraz-Amaro[1], A. Corrales[2], N. Vegas-Revenga[2], B. Atienza-Mateo[2], V. Portilla[2], R. Blanco[2], J. Llorca[2], M. A. González-Gay[2]. *[1]Hospital Universitario de Canarias, Division of Rheumatology, Santa Cruz de Tenerife, Spain*; *[2]Hospital Universitario Marqués de Valdecilla, Division of Rheumatology, Santander, Spain*

Background: Cardiovascular disease (CVD) risk in patients with rheumatoid arthritis (RA) is substantially elevated compared to the general population. In RA, as in the general population, CVD control includes the detection and treatment of CV risk factors based, among others, on blood pressure, smoking, diabetes, and lipid profiles. Little is known about the real impact of the use of carotid ultrasound in the prevention of CVD in patients with RA.
Objectives: To determine whether the use of carotid ultrasound in the routine clinical care of patients with RA can improve the achievement of LDL-cholesterol targets over time.
Methods: We conducted a retrospective, real-world study of 327 RA patients in which a carotid ultrasound was performed as part of routine clinical care. Participants were followed from 2012 to 2018. LDL-c levels were measured before and after the carotid ultrasound intervention. The achievement of the LDL-c goals recommended by the international guidelines was compared before and after the carotid ultrasound. Predictive factors of achievement of LDL-cholesterol targets were studied.
Results: When considering the 2010 EULAR RA SCORE risk categories, serum LDL-c levels in the moderate CV risk category was significantly lower when follow-up finished (126 ± 33 to 109 ± 29 mg/dl, p=0.000) (Table 1). This was not the case for other CV risk categories. Similarly, LDL-c goal attainment in the moderate CV risk category was significant higher at the end of the study compared to baseline. Based on the 2016 European Society of Cardiology LDL-c targets, the achievement of a LDL-cholesterol inferior to 115 mg/dl for the moderate CV risk category significantly increased from 35 to 64% (p=0.000) after follow-up. However, significant changes were not observed in this regard for the low, high, and very-high CV risk categories.

Table 1. LDL cholesterol serum levels and LDL goals differences between baseline and final follow-up

			LDL, mg/dl			LDL (mg/dl) ESC 2016 goals			
	n	%	Baseline	Final follow-up		Goal	Baseline	Final follow-up	p
2010 EULAR RA SCORE									
Low	120	37	116 ± 37	119 ± 32	0.081	< 130	68%	66%	0.99
Moderate	195	60	126 ± 33	109 ± 29	**0.000**	< 115	35%	64%	**0.000**
High	7	2	121 ± 26	104 ± 22	0.14	< 100	14%	33%	0.99
Very High	5	0	131 ± 41	115 ± 46	0.080	< 70	0%	20%	0.99

ESC: European Society of Cardiology; EULAR: European League Against Rheumatism. SCORE: Systematic COronary Risk Evaluation; RA: Rheumatoid Arthritis; LDL: low-density lipoprotein. Significant 'p' value are depicted in bold.

When patients with RA, regardless the SCORE risk they had, were divided between those that attained LDL-cholesterol target or not, those that achieved their LDL goal, were more frequently female and had less diabetes mellitus. Moreover, the probability of achieving LDL-cholesterol goal was higher in those with an inferior total cholesterol, LDL-c and atherogenic index at baseline. Interestingly, no differences were observed in both populations regarding the baseline use of statins, aspirin or hypertension treatment at baseline. Concerning disease related data when study started, no differences about disease duration and activity or treatments were observed between dose that reached LDL-cholesterol goal and those that did not.
Those that achieved LDL-c objectives had a higher decrease in smoking quit and a superior control of hypertension. Besides, in those that attained objectives a

superior increase in statins prescription was observed (36% vs. 13%, p=0.000), as well in hypertension and aspirin treatment. However, no differences were noticed in the changes in disease-related data that occur during the time the study was carried out.

Conclusion: This real-world study demonstrates that incorporating carotid ultrasound into routine clinical practice in RA patients is effective in achieving LDL-cholesterol targets for the prevention of cardiovascular disease. This effect is not only mediated by the increase in the prescription of statins, but also by the better control of other cardiovascular risk factors that occurred after carotid ultrasound evaluation.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1883

POS0534 THE PREVALENCE OF HYPERTENSION AND ITS POTENTIAL ASSOCIATED FACTORS IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS

Y. W. Zou[1], C. Chen[2], J. Lin[1], J. D. Ma[2], Y. Y. Zou[1], L. Dai[1]. [1] *Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Department of Rheumatology, Guangzhou, China*; [2]*Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Department of Rheumatology, Guangzhou, China*

Background: Cardiovascular disease (CVD) is the leading cause of mortality in patients with rheumatoid arthritis (RA), and hypertension is a modifiable risk-factor for CVD. In addition, comorbidities may shorten the life span of RA patients, which appears to be the consequence of an increased prevalence of CVD. RA patients with comorbidities might not be given the equal treatment in daily practice compared with patients without comorbidities.

Objectives: To investigate the prevalence of hypertension and its associated factors in Chinese RA patients.

Methods: Consecutive patients with RA were recruited from August 2015 to September 2019 at Department of Rheumatology, Sun Yat-sen Memorial Hospital. Demographic and clinical characteristics were collected including indicators of disease activity, functional assessment and radiographic assessment and CV-related comorbidities.

Results: There were 674 RA patients recruited with 82.3% female and mean age 49.9±13.0 years. The prevalence rate of hypertension in RA patients was 32.9%, followed by dyslipidemia (9.9%), type 2 diabetes (8.8%), hyperuricemia (8.5%), fatty liver disease (8.0%), CVD (6.2%) and chronic kidney disease (3.3%). The prevalence of hypertension was 38.7% and 31.7% in male and female RA patients respectively (P = 0.144). Further age stratification showed no hypertension in RA patients at 16-19 years, 2.0% at 20-29 years and 8.1% at 30-39 years. The prevalence of hypertension greatly increased after 40 years old with 24.5%, 38.6%, 54.9%, and 63.6% in RA patients of 40-49, 50-59, 60-69, ≥ 70 years old respectively, and there was no significant difference between male and female RA patients of different age (Figure 1). Compared with those without hypertension, RA patients with hypertension had advanced age (57.3 ± 9.3 years vs. 46.3 ± 13.0 years), long-standing disease duration (median 60 months vs. 48 months), higher disease activity indicators [including PtGA (median 4 vs. 3), PrGA (median 3 vs. 3) and ESR (median 33 mm/h vs. 27 mm/h)], higher functional indicator [HAQ-DI (median 0.25 vs. 0.13)], worse joint destruction [JE subscore (median 10 vs. 6)] and higher proportions of comorbidities [including type 2 diabetes (14.9% vs. 5.8%), hyperuricemia (13.1% vs. 6.1%), chronic kidney disease (6.3% vs. 1.8%), dyslipidemia (15.8% vs. 7.1%), CVD (10.4% vs. 4.2%) and fatty liver disease (13.5% vs. 5.3%), all P < 0.005]. Multivariate logistic regression analysis showed that comorbidities including hyperuricemia (OR = 1.977, 95% CI: 1.002-3.900), dyslipidemia (OR = 1.903, 95% CI: 1.102-3.288) and fatty liver disease (OR = 2.335, 95% CI: 1.278-4.265) were associated factors of hypertension after adjustment for age and gender

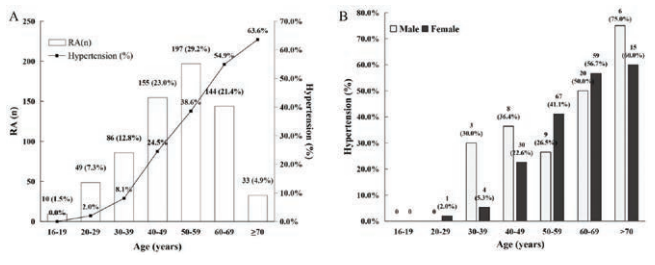


Figure 1. The prevalence of hypertension in different age and sex groups of RA patients.

Conclusion: Hypertension is the most common CV-related comorbidity in Chinese RA patients which is associated with hyperuricemia, dyslipidemia and fatty liver disease. Detection and management of hypertension and other CV-related comorbidities in RA patients should be emphasized.

Fund program:
National Natural Science Foundation of China (81801605, 81801606, 81971527); Guangdong Natural Science Foundation (2018A030313541, 2018A030313690, 2019A1515011928); Guangzhou Science and Technology Program (201904010088); Guangdong Basic and Applied Basic Research Foundation (2020A1515110061); Guangdong Medical Scientific Research Foundation (A2018062)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2078

POS0535 QUERY ALGORITHMS AND MACHINE LEARNING METHODS AS TOOLS TO IDENTIFY COMORBIDITIES IN LARGE-SCALE FREE-TEXT BASED FIELDS: A CASE-REPORT

D. Rohrich[1], T. Maarseveen[2], A. de Boer[1], C. van den Ende[1], A. den Broeder[1], C. Popa[1], R. Knevel[2]. [1]*Sint Maartenskliniek, Rheumatology, Ubbergen, Netherlands*; [2]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*

Background: Inflammatory rheumatic conditions (IRC) are associated with comorbidity, two most important being cardiovascular diseases (CVD) and infections [1, 2]. A crucial initial step when proceeding with studying CVD and infections in these patients is identification of events. The large scale EHR datasets enable studies to assess low incident and clinically important events, but requires both accurate as well as efficient data extraction. Studying Electronic Health Records (EHR) using query-based algorithms (QBA) and machine learning algorithms (MLA) offers a valuable tool to screen large-scale collections for rare events, thus replacing resource intensive manual chart review.

Objectives: To explore the (comparative) usefulness of QBA and MLA to identify CVD and infection events in EHR free-text data in patients with chronic IRC.

Methods: To independently develop and validate the algorithms we used two EHR databases, i.e. a training set with psoriatic arthritis patients (N=977, dataset A, Golden Standard) and a validation set of rheumatoid arthritis patients (N=1098, dataset B). Using both QBA and MLA, we aimed to identify (yes/no and timing) CVD and infections. We assessed the performances of the algorithms by calculating the specificity, sensitivity, positive predictive value (PPV) and the negative predictive value (NPV), respectively.

Results: In the final performance analysis on dataset B, both QBA and MLA showed a high performance in identifying CVD (sensitivity, specificity, PPV, NPV for QBA ((95% CI)= 0.69 (0.66-0.72), 0.99 (0.96-1.02), 0.84 (0.81-0.87), 0.98 (0.95-1.01)) and for MLA (sensitivity = 0.69 (0.66-0.72), 0.98 (0.95-1.01), 0.68 (0.65-0.71), 0.98 (0.95-1.01), respectively) Infections showed similar performance (QBA sensitivity, specificity, PPV, NPV is 0.64 (0.61-0.67), 0.96 (0.93-0.99), 0.66 (0.63-0.69), 0.96 (0.93-.0.99) and for MLA = 0.61 (0.58-0.64), 0.93 (0.90-0.96), 0.49 (0.46-0.52), 0.96 (0.93-0.99), respectively). For infections the specificity was slightly higher for QBA relative to MLA.

Conclusion: We found a consistent high performance of both the QBA and MLA algorithms for the identification of CVD and infections in our free text EHR of patients with chronic IRC (Table 1). The performance of QBA highly depends on the domain knowledge of the builders, which might allow it to outperform a Gold Standard. MLA is efficient as it does not require any domain knowledge, but its performance is restricted by the quality of the Gold Standard.

Table 1. Overlap and differences in event identification of the query based and machine learning based algorithms compared to the Gold Standard dataset B (chart review by specialized health care professional). The results of non-event and event identification by the algorithms is represented in numbers of events and percentages of the total non-event or event.

Dataset B Cardiovascular events				
	QBA -	**ML -**	**QBA +**	**ML +**
GS – (N=2123)	**2102 (99.0%)**	**2071 (97.6%)**	**21 (0.99 %)**	**52 (2.45%)**
GS + (N=159)	**49 (30.1%)**	**49 (30.1%)**	**110 (69.2%)**	**110 (69.2%)**
Total events GS =2282				
Dataset B Infection events				
	QBA -	**ML -**	**QBA +**	**ML +**
GS – (N= 2053)	**1979 (96.4%)**	**1910 (93.0%)**	**74 (3.6%)**	**143 (7.0%)**
GS + (N =228)	**83 (36.4%)**	**89 (39.0%)**	**145 (63.6%)**	**139 (61.0%)**
Total events GS = 2281				

(QBA = Query Based Algorithm, MLA = Machine Learning Algorithm, GS - = Non-event in Gold Standard dataset B, GS + = Event in Gold Standard dataset B)

REFERENCES:
[1] Kroot, E.J., et al., *Chronic comorbidity in patients with early rheumatoid arthritis: a descriptive study.* J Rheumatol, 2001. **28**(7): p. 1511-7.
[2] Castaneda, S., et al., *Additional proposals to reduce comorbidity in patients with chronic inflammatory rheumatic diseases: comment on 'Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative' by Baillet et al.* Ann Rheum Dis, 2016. **75**(8): p. e55.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2094

POS0536 FILGOTINIB DEMONSTRATES CLINICAL EFFICACY IN RHEUMATOID ARTHRITIS INDEPENDENT OF SMOKING STATUS: A POST-HOC SUBGROUP ANALYSIS OF THREE PHASE 3 CLINICAL TRIALS

P. Emery[1], B. Downie[2], J. Liu[2], R. Hawtin[2], J. R. Curtis[3], G. R. Burmester[4]. *[1]University of Leeds, School of Medicine, Leeds, United Kingdom*; *[2]Gilead Sciences, Inc., Foster City, United States of America*; *[3]University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, United States of America*; *[4]Charité – Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*

Background: Filgotinib (FIL), an oral janus kinase 1 (JAK1) inhibitor, has been evaluated in three phase 3 clinical studies (FINCH 1-3) in adults with moderately-to-severely active rheumatoid arthritis (RA). Patients with RA who currently smoke (a predisposing factor for RA) have been reported to be less likely to respond to anti-TNFα treatment and more likely to discontinue or switch treatment.[1,2,3] However, the impact of smoking on JAKi efficacy in RA patients is unknown.
Objectives: A post-hoc sub-group analysis of FINCH patient (pt) data was performed in order to identify associations with smoking status.
Methods: Data from 3452 RA pts participating in the FINCH3 (MTX-naïve; NCT02886728), FINCH1 (MTX-IR; NCT02889796), or FINCH2 (bDMARD-IR; NCT02873936) clinical trials were included for analysis of clinical response at weeks 12 and 24. Logistic regression models were fitted to assess the effects of smoking status on categorical clinical endpoints (ACR20/50/70, CDAI ≤ 10, DAS28(CRP) ≤3.2 or < 2.6). Adjustments were made for covariates selected based on previously published work[1] and listed in the Figure 1 caption. No adjustments of p-values were made for multiple testing.
Results: In the MTX-IR population (FINCH1), current (12% of enrolled patients) and former (13%) smokers treated with ADA+MTX had a lower week 12 ACR50 response rate compared to non-smokers (25% and 28% vs. 39%, nominal p = 0.095 and p=0.21, respectively). In contrast, the ACR 50 response at week 12 in FIL+MTX treated pts showed no association with smoking status. Former smokers had higher response rates than non-smokers in the MTX-IR (FINCH1) and MTX naïve (FINCH3) populations (Table 1). Direct comparison between non-smoking pts in the MTX-IR FIL200+MTX-arm and ADA+MTX-arm showed no significant difference in ACR50 response rate (46% vs. 39%, p=0.08). In contrast, former and current smokers showed significantly better week 12 ACR50 response rates under FIL200+MTX treatment compared to ADA+MTX patients (former smoker: 62% vs. 28%, p=0.0017, current smoker: 50% vs. 25%, p=0.016, Figure 1. Similar observations were made at both weeks 12 and 24 for other clinical endpoints, including ACR20/50/70, DAS28(CRP) < 2.6 or ≤3.2, and CDAI ≤ 10 response criteria.

Table 1. Difference in adjusted ACR50 response rate compared to non-smokers for FINCH1/2/3.

		PBO+MTX‡	FIL100+MTX	FIL200+MTX
FINCH1	Current	-1%	+2.4%	+3.3%
	Former	-6%	+12%	+16% (*)
FINCH2†	Current	0%	+13%	-9%
	Former	+9%	-7%	+4%
FINCH3	Current	0%	+1%	+4%
	Former	+4%	+20% (*)	+17% (*)

ACR50 response rate based on fully adjusted logistic regression model. †: FINCH2 patients received either MTX or csDMARD. ‡FINCH3 had active comparator arm of MTX together with PBO to maintain blind. *: p < 0.05, **: p < 0.01, ***: p < 0.001

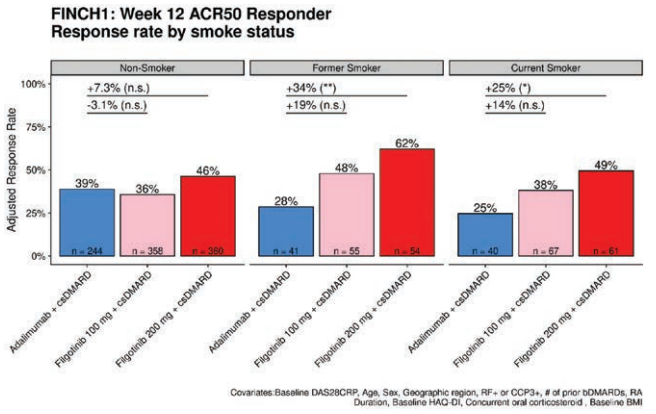


Figure 1. FINCH1 adjusted Week 12 ACR50 response rate stratified by smoking status. ACR50 response rate based on fully adjusted logistic regression model. *: p < 0.05; **: p < 0.01; ***: p < 0.001. Former and current smokers that received FIL200mg + MTX showed a higher response rate compared to similar ADA+MTX patients.

Conclusion: This exploratory analysis showed that current and former smokers with RA who received ADA+MTX trended toward a lower response rate compared to non-smokers. In contrast, FIL+MTX was found to be similarly efficacious independent of smoking status within both the MTX-IR and MTX-naïve RA populations. Current or former smokers were more likely to respond to FIL200mg + MTX compared to ADA+MTX across a range of endpoints. Given the small number of current and former smokers enrolled in these studies, further studies of the efficacy of JAK inhibitors and the mechanism of reduced response to anti-TNFs in patients with a history of smoking are warranted.
REFERENCES:
[1] Hyrich KL. Rheumatology 2006;45:1558–1565; 2. Canhao H. Rheumatology 2012;51:2020–2026; 3. McCulley CB. Clin Exp Rheumatol 2019;28(37):422–428
Disclosure of Interests: Paul Emery Consultant of: Pfizer, Abbvie, Amgen, MSD, Roche, Sanofi, BMS, Novartis, Lilly, Gilead, Samsung, Celltrion, Grant/research support from: Abbvie, BMS, Samsung, Bryan Downie Shareholder of: Gilead, Employee of: Gilead, Jinfeng Liu Shareholder of: Gilead, Roche, Employee of: Gilead, Rachael Hawtin Shareholder of: Gilead, Employee of: Gilead, Jeffrey R. Curtis Consultant of: Abbvie, Amgen, BMS, Corrona, Eli Lilly, Jannsen, Myriad, Pfizer, Regeneron, Roche, and UCB, Grant/research support from: Abbvie, Amgen, BMS, Corrona, Eli Lilly, Jannsen, Myriad, Pfizer, Regeneron, Roche, and UCB, Gerd Rüdiger Burmester Speakers bureau: Abbvie, Gilead, Lilly, Pfizer, Consultant of: Abbvie, Gilead, Lilly, Pfizer
DOI: 10.1136/annrheumdis-2021-eular.2128

POS0537 TRENDS AND PREDICTORS OF INPATIENT MORTALITY IN PATIENTS WITH CLOSTRIDIODES DIFFICILE INFECTION AMONG THOSE WITH AND WITHOUT RHEUMATOID ARTHRITIS: A NATIONWIDE ANALYSIS

M. Tahir[1,2], S. Alexander[3,4], R. Tariq[2], K. Wysham[5], J. Andrews[5], H. Aly[6], S. Khanna[7], N. Singh[5]. *[1]Rochester General Hospital, Internal Medicine, Rochester, United States of America*; *[2]1425 Portland Ave, Internal Medicine, Rochester, United States of America*; *[3]University of Connecticut, Internal Medicine, Storrs, United States of America*; *[4]263 Farmington Ave, Internal Medicine, Farmington, United States of America*; *[5]1959 NE Pacific St, Internal Medicine, Seattle, United States of America*; *[6]740 S Limestone, Internal Medicine, Lexington, United States of America*; *[7]200 1st St SW, Internal Medicine, Rochester, United States of America*

Background: People with rheumatoid arthritis (RA) have a higher risk of serious infections. The most common nosocomial infection in the United States (US) is *Clostridioides difficile* infection (CDI) and yet, little is known regarding the impact of comorbid RA on outcomes in persons hospitalized with CDI.
Objectives: To evaluate the trends over time and predictors of inpatient mortality in hospitalized patients with CDI comparing those with and without RA.
Methods: We used the National Inpatient Sample (NIS) database, the largest available all-payer database of inpatient hospitalizations in the US. Patients aged

≥18 years admitted with CDI from 2006-2018 were included. Patients with RA were identified using the International Classification of Diseases (ICD) 9 and 10 codes. Categorical variables between CDI patients with and without RA were compared using Chi-squared test. Temporal trends of hospitalization charges, length of stay (LOS) and inpatient mortality were assessed using the Cochrane Armitage test. Predictors of inpatient mortality were assessed using multivariable logistic regression adjusting for: age ≥65, sex, race, presence of RA, and Elixhauser comorbidity index.

Results: There were 4,396,945 hospitalizations with a discharge diagnosis of CDI in the study period, of which 111,336 (2.5%) had a coexisting diagnosis of RA. Over the study period, the proportion of CDI patients with a diagnosis of RA increased from 1.7% in 2006 to 3.3% in 2018 with a statistically significant trend of rise (p trend<0.001). There were significantly more females in the RA group (78.2%) than without RA (57.5%), p <0.001. RA group was significantly younger (68.0 vs 70.7, P<0.001). Races were similar between the groups.

The inflation-adjusted average charge for hospitalization for CDI without RA was significantly higher than for CDI with RA ($95,863 vs $73,025, p<0.001). There was an increasing trend in inflation-adjusted average charge for hospitalization for both CDI without RA ($76,966 in 2006 to $104,552 in 2018, p<0.001) and CDI with RA ($55,689 in 2006 to $77,295 in 2018, p<0.001). Patients with or without RA had the same median length of stay (LOS) of 7 days. But when trended over time, for patients without RA, the median LOS decreased from 8 days in 2006-08 to 6 days in 2016-18 whereas for patients with RA, the median LOS fluctuated between 6 and 7 days over the course of study period.

CDI patients without RA had a significantly higher mortality over the study period than those with RA (7.8% vs 6.1%, p<0.001). Among non-RA CDI patients, mortality decreased from 9.3% in 2006 to 6.3% in 2018 (p trend <0.001). Hospitalizations of people with CDI and comorbid RA showed an overall decreasing trend (p trend <0.001).

The multivariable analyses found age≥65 was associated with increased inpatient mortality (adjusted odds ratio [aOR], 1.77, 95% confidence interval [CI], 1.73-1.80), whereas a diagnosis of RA was associated with a decreased mortality (aOR 0.86, 95% CI, 0.81-0.91) (Table 1).

Table 1. Predictors of inpatient mortality

	aOR	95% C.I. for aOR		P-value
		Lower	Upper	
Age ≥ 65	1.765	1.730	1.801	<0.001
Hospitalization years				
-Years 2006-2011	Ref			
-Years 2011-2014	0.707	0.693	0.721	<0.001
-Years 2015-2018	0.582	0.569	0.594	<0.001
Elixhauser Comorbidity Index	1.056	1.055	1.056	<0.001
Rheumatoid Arthritis	0.859	0.810	0.911	<0.001
Female	0.870	0.855	0.885	<0.001
Race				
-White	Ref			
-African American	1.071	1.044	1.099	<0.001
-Hispanic	1.144	1.108	1.180	<0.001
-Asian/Pacific Islander	1.267	1.200	1.337	<0.001
-Native American	1.022	0.910	1.147	0.716
-Other races	1.263	1.201	1.329	<0.001

aOR = Adjusted Odds Ratio; C.I.= confidence interval

Conclusion: In this nationwide study, among hospitalized patients with CDI, those with comorbid RA had significantly decreased odds of inpatient mortality than those without RA. Further studies are needed to understand this association.

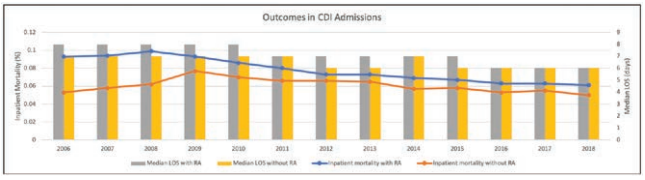


Figure 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2176

POS0538 RELATIONSHIP BETWEEN HINDFOOT DEFORMITIES AND ULTRASOUND TENOSYNOVITIS IN RHEUMATOID ARTHRITIS

K. Maatallah[1], H. Boussaa[1], H. Riahi[2], H. Ferjani[1], M. Habechi[1], W. Triki[1], D. Ben Nessib[1], M. Bouaziz[2], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab Institute of Orthopedics, Rheumatology, La Manouba, Tunisia*; [2]*Mohamed Kassab Institute of Orthopedics, Radiology, La Manouba, Tunisia*

Background: Rheumatoid arthritis (RA) is an inflammatory disease that frequently affects the joints and soft tissues of the feet. Tibialis posterior tenosynovitis has a reported prevalence between 13 and 64% in RA. The condition is associated with a progressive flat foot deformity and significant gait disability. However, few studies have investigated the relationship between foot deformities and the involvement of tendons. Recently, ultrasonography (US) has been reported as the gold standard for the investigation of tendons.

Objectives: This study aimed to assess the relationship between hindfoot deformities and US tenosynovitis in RA.

Methods: We conducted a cross-sectional study including patients with RA (ACR/EULAR 2010). Demographic data and disease parameters were collected. For each patient, a podoscope examination of both feet was performed by a rheumatologist. A radiologist experienced in musculoskeletal imaging performed a US examination using a Philips HD11 device with a high-frequency linear transducer. The assessed lesions were synovitis of the tibiotalar, talonavicular, and subtalar joints, and tenosynovitis of tibialis anterior (TA), extensor hallucis longus (EHL), extensor digitorum longus (EDL), tibialis posterior (TP), flexor digitorum longus (FDL), flexor hallucis longus (FHL), fibularis brevis (FB) and fibularis longus (FL) tendons. The presence or absence of synovitis and tenosynovitis was recorded, and the composite synovitis score (power doppler/grayscale ultrasound (PDUS)) was measured for each joint. The US score of each patient was defined by the sum of the composite scores of the joints studied (0-30). A p-value <0.05 was considered significant.

Results: Sixty-two feet were examined in 31 RA patients (25 women and six men) with a mean age of 54.8±10.8 years old [32-70]. The mean disease duration was 8.5±7.2 years [1-37]. Rheumatoid Factor (RF) and Anti-Citrullinated Peptides Antibodies (ACPA) were positive in respectively 61.3% and 83.8% of cases. The mean DAS28 ESR was 3.8±1.5 [0.6-7].

Podoscope examination revealed pes planus valgus (PPV) in 55.6% of cases and pes cavus varus (PCV) in 18.5% of cases. US showed tibiotalar synovitis in 59.3% of cases, talonavicular synovitis in 64.8% of cases, and subtalar synovitis in 46.3% of cases. In the anterior compartment, tenosynovitis of TA was noted in 5.6% of cases, of EHL in 1.9% of cases, and EDL in 9.3% of cases. In the medial compartment, tenosynovitis of TP was found in 22.2% of cases, of FDL in 5.6% of cases, and FHL in 0% of cases. In the lateral compartment, tenosynovitis of FB and FL was found in 25% and 11.1% of cases respectively.

An association between PPV and synovitis of the tibiotalar joint (p<0.001) and the subtalar joint (p=0.007) was found. An association was also noted with FL tenosynovitis (p=0.045) but not with the other assessed tendons.

No association was noted between PCV and synovitis or tenosynovitis of the assessed structures.

Conclusion: PPV was frequent among RA patients. This condition was associated with tibiotalar and subtalar synovitis and FL tenosynovitis. It is important to detect and correct foot deformities in order to ensure optimal control of the disease.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2223

POS0539 PAIN IS AN INDEPENDENT ASSOCIATED FACTOR ON FUNCTIONAL LIMITATION IN CHINESE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

Y. W. Zou[1], C. Chen[1], Q. Zhang[1], S. Y. Lian[1], K. M. Yang[1], Y. H. Xu[1], J. Lin[1], J. D. Ma[1], Y. Y. Zou[1], L. Dai[1]. [1]*Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Department of Rheumatology, Guangzhou, China*

Background: Rheumatoid arthritis (RA) is a leading cause of extremity disability in Chinese female population according to 2006 national survey. However, less epidemiological data about functional limitation in Chinese RA patients have been published.

Objectives: To investigate the prevalence, characteristics and associated factors of functional limitation in Chinese RA patients.

Methods: Consecutive patients with RA were recruited. The demographic and clinical data were collected including indicators of disease activity, functional assessment and radiographic assessment. According to Health Assessment

Questionnaire Disease Index (HAQ-DI), functional limitation was defined as: mild (0 < HAQ-DI ≤ 1), moderate (1 < HAQ-DI ≤ 2), and severe (2 < HAQ-DI ≤ 3).
Results: There were 643 RA patients recruited with 82.3% female and mean age 49.7 ± 12.9 years. The median (IQR) of total HAQ-DI was 0.25 (0.00-0.75) and there were 399 (62.1%) RA patients with functional limitation including 293 (45.6%), 73 (11.4%), 33 (5.1%) with mild, moderate, and severe functional limitation, respectively. The highest prevalence of functional limitation subdimension was "walking" (43.5%), followed by "grip" (36.1%), "reach" (35.5%), "common daily activities" (33.4%), "hygiene" (33.0%), "dressing and grooming" (29.7%), "arising" (29.1%), while the lowest was "eating" (18.4%). Further age stratification showed that the prevalence of functional limitation was increased with age ($P < 0.001$), but no difference between male and female RA patients (58.8% vs. 62.8%, $P = 0.426$). The prevalence of functional limitation of RA patients with disease duration < 1 years (early), 1-10 years (intermediate) and ≥ 10 years (long) were 70.2%, 55.9% and 74.5% respectively, showing a U-shaped curve (Figure 1A), which indicated that early RA also had high rate of functional limitation. Furthermore, early RA patients had the highest proportion of severe functional limitation (14.3% vs. 2.0% vs. 8.7%, Figure 1B), together with higher prevalence of functional limitation of all eight subdimension than those with intermediate disease duration ($P < 0.05$, Figure 1C). There were significant differences in Pain VAS, indicators of disease activity, functional and radiographic assessment among RA patients with different disease duration. Compared with those with intermediate disease duration, early RA patients had higher Pain VAS, higher disease activity indicator (including ESR, CRP, CDAI), higher HAQ-DI, but lower radiographic indicators (all $P < 0.05$). There was no significant difference in disease activity and functional indicators between early RA patients and those with long disease duration. Multivariate ordered logistic regression analysis showed that Pain VAS (*OR* = 2.116, 95% *CI*: 1.483-3.019), disease activity indicators [including CRP (*OR* = 1.047, 95% *CI*: 1.011-1.084) and CDAI (*OR* = 1.128, 95% *CI*: 1.054-1.208)] were associated factors of functional limitation in early RA patients.

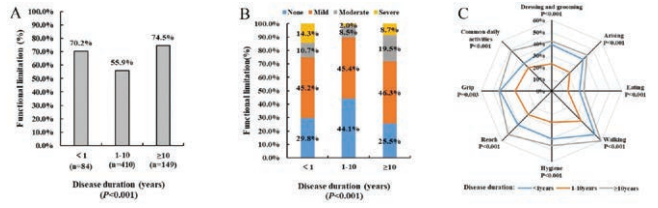


Figure 1. The prevalence of function limitation in RA patients. (A) The prevalence of functional limitation in different disease duration groups of RA patients. (B) The different degrees of functional limitation in different disease duration groups of RA patients. (C) The subdimension characteristics of functional limitation in different disease duration groups of RA patients.

Conclusion: Near two third early RA patients have functional limitation, in which both pain and active disease are independent associated factors. Management of pain and target treatment in early RA patients should be emphasized.
Fund program:
National Natural Science Foundation of China (81801605, 81801606, 81971527); Guangdong Natural Science Foundation (2018A030313541, 2018A030313690, 2019A1515011928); Guangzhou Science and Technology Program (201904010088); Guangdong Basic and Applied Basic Research Foundation (2020A1515110061); Guangdong Medical Scientific Research Foundation (A2018062)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2291

POS0540 SEXUAL DYSFUNCTION IN MALE PATIENTS WITH RHEUMATIC DISEASES

A. P. Stanciu[1], L. Groseanu[1,2], A. Balanescu[1,2], D. Predeteanu[1,2], D. Opris-Belinski[1,2], V. Bojinca[1,2], F. Berghea[1,2], C. L. Constantinescu[1,2], I. Saulescu[1,2], S. Daia-Iliescu[1,2], A. Borangiu[1,2], D. Mazilu[1,2], M. M. Negru[1,2], C. Cobilinschi[1,2], R. Ionescu[1,2]. [1]*Saint Mary Hospital, Rheumatology and Internal Medicine, București, Romania*; [2]*Carol Davila University of Medicine and Pharmacy, Rheumatology, București, Romania*

Background: Sexual health is an essential element of overall health and well-being. Rheumatic diseases may affect sexual functioning in many ways related to pain, fatigue, stiffness, functional impairment, depression, anxiety, negative body image, reduced libido, hormonal imbalance and drug treatment. However, these issues are rarely addressed in clinical practice.
Objectives: The aim of this study was to evaluate sexual function in a cohort of men with rheumatic disease compared to healthy controls.
Methods: This was an observational, single-center, cohort study conducted between august 2019 and march 2020 in the Rheumatology department of "Saint Mary" Clinical Hospital in Bucharest which included 120 men with ages between 18 and 60 years - 60 patients with rheumatic diseases and 60 healthy controls. The study tools were the Sexual Health Inventory for Men (SHIM) questionnaire and one questionnaire referring to personal data, history of the rheumatic disease, comorbidities, treatment and sexual impairment. Also, the disease activity was assessed using specific scores for each condition.
Results: In this cohort of 60 patients, the mean age was 45.26 (7.8) years and the diagnoses wereankylosing spondylitis (AS) - 37%,psoriatic arthritis (PsA) - 18%, rheumatoid arthritis (RA) - 17%, systemic sclerosis (SS) - 15% and gout - 13%. More than half of the patients (62%) had active disease based on specific scores (ASDAS for AS, DAS28-CRP for RA, EScSG disease activity indices for SS, DAPSA for PsA). Regarding sexual life, this study showed a significant decrease in sexual life quality after rheumatic disease diagnosis(before diagnosis: 71,67% - satisfying and 16,67% - not satisfyingversus after diagnosis: 21,67% - satisfying and 68,33% - not satisfying). Most patients (90%) reported impairment of their sexual life after diagnosis. In terms of sexual dysfunction (SD), a significantly higher proportion of patients (40%) mentioned reduced libido compared to the control group (18,33%) (p=0.043). Also, 21,66% of the patients reported erectile dysfunction (ED) in comparison with only 8,33% in the control group (p=0.009). Most patients with AS, RA, PsA and gout had mild ED while most patients with SS presented with mild to moderate ED. Also, the SHIM score mean value was significantly lower in the study group (17,65)compared to the control group (20,15) (p=0.009). The importance of SD in this cohort is emphasized by the fact that only one patient conceived after rheumatic disease diagnosis. Concerning treatment, more than half of the patients (55%) reported no effect of the therapy on their sexual life while 38.33% mentioned that medication improved their sexual life and very few (7%) reported a worsening.
Conclusion: This study revealed a higher prevalence of sexual dysfunction in male patients with rheumatic disease in comparison with healthy controls. Considering the importance of sexual and reproductive health, rheumatologists should approach this topic with their patients and offer them guidance.
REFERENCES:
[1] AG Tristano, *"The impact of rheumatic diseases on sexual function",* Rheumatol Int 2009 Jun;29(8):853-60
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2330

POS0541 LOW PREVALENCE OF SSA (anti-Ro) AND SSB (anti-La) AUTOANTIBODIES IN FEMALE RHEUMATOID ARTHRITIS PATIENTS WITH A WISH TO CONCEIVE

H. T. Smeele[1], L. F. Perez-Garcia[1], J. M. J. Cornette[2], M. W. Schreurs[3], R. Dolhain[1]. [1]*Erasmus MC, Rheumatology, Rotterdam, Netherlands*; [2]*Erasmus MC, Department of Gynaecology and Obstetrics, Rotterdam, Netherlands*; [3]*Erasmus MC, Department of Immunology, Rotterdam, Netherlands*

Background: The presence of SSA (anti-Ro) and SSB (anti-La) autoantibodies has important clinical implications for female patients with a wish to conceive. The association between maternal levels of these autoantibodies and complete congenital heart block and neonatal Lupus syndrome is well established. Currently guidelines advise to test for these antibodies in all Rheumatoid Arthritis (RA) patients with a wish to conceive (1).
Objectives: The objective was to determine the prevalence and titers of SSA and SSB autoantibodies in female patients with rheumatoid arthritis and a wish to conceive or who are pregnant.
Methods: Patients were derived from 2 large prospective cohorts on RA and pregnancy (PARA-cohort and PreCARA-cohort). The presence and titers of SSA and SSB were tested using Phadia, an automated system which uses fluorescence enzyme immunoassays (FEIA) (Thermo-Fisher Scientific).
Results: We included a total of 647 patients with RA and a wish to conceive, 417 (64.5%) conceived during the follow-up period. A detailed description of the study population, stratified for the presence of SSA and SSB antibodies autoantibodies is presented in table 1. A total of 25 out of 647 patients had detectable SSA or SSB antibodies: SSA n = 25 (SSA-52 n = 17, SSA-60 n = 19), SSB n = 7. This corresponds with a prevalence of 3.9% for SSA antibodies and 1.1% for SSB antibodies. 13 (52% of the SSA positive patients, 2.0% of the total population) patients had a titer of >240 units/ml of SSA antibodies, and 3 (42.9% of the SSB positive patients, 0.46% of the total

population) patients had a titers >340 units/ml of SSB antibodies. The percentage of patients positive for RF antibodies was higher in SSA and/or SSB positive patients (p = 0.01).

Table 1. Clinical and demographic features from 647 patients with rheumatoid arthritis and a wish to conceive.

Variable	SSA and SSB antibodies [-], n = 622	Positive SSA and/or SSB antibodies [+], n = 25	p-value
Age at inclusion in the cohort (y, SD)	32.3 (4.0)	32.3 (4.4)	0.98
Median disease duration at first visit, years (IQR)	5.2 (2.2 – 9.8)	4.9 (2.1 – 11.4)	0.77
ACPA positive, n (%)	408/614 (66.5)	16 (69.6)	0.75
Rheumatoid Factor positive, n (%)	426/617 (69.0)	23 (92.0)	0.01

Conclusion: Our study shows an overall low prevalence of SSA and SSB autoantibodies in female RA patients with a wish to conceive. Moreover, about half of the patients positive for SSA or SSB had, based on literature, moderate or low titers of these antibodies (2). Especially for RF negative patients, the current advise to test for SSA and SSB antibodies in all RA patients with a wish to conceive should be reconsidered.

REFERENCES:

[1] Sammaritano LR et al. 2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases. Arthritis Care Res (Hoboken). 2020 Apr; 72(4):461-488.

[2] Jaeggi E et al. The Importance of the Level of Maternal Anti-Ro/SSA Antibodies as a Prognostic Marker of the Development of Cardiac Neonatal Lupus Erythematosus: A Prospective Study of 186 Antibody-Exposed Fetuses and Infants. Journal of the American College of Cardiology. 2010 2010/06/15/; 55(24):2778-2784

Disclosure of Interests: Hieronymus TW Smeele: None declared, Luis Fernando Perez-Garcia Consultant of: Yes, Galapagos, J.M.J. Cornette: None declared, Marco WJ Schreurs: None declared, Radboud Dolhain Speakers bureau: Yes UCB, Roche, Abbvie, Genzyme, Novartis, Consultant of: Yes, Galapagos, Grant/research support from: Yes, UCB

DOI: 10.1136/annrheumdis-2021-eular.2435

POS0542

DISEASE ACTIVITY IN PREGNANT WOMEN WITH RHEUMATOID ARTHRITIS: IMPACT ON THE SOLUBLE FMS-LIKE TYROSINE KINASE-1 TO PLACENTAL GROWTH FACTOR RATIO

H. T. Smeele[1], R. I. Neuman[2,3], A. H. J. Danser[2], R. Dolhain[1], W. Visser[2,3].
[1]Erasmus MC, Rheumatology, Rotterdam, Netherlands; *[2]Erasmus MC, Department of Internal Medicine; Division of Pharmacology and Vascular Medicine, Rotterdam, Netherlands*; *[3]Erasmus MC, Department of Gynecology and Obstetrics, Rotterdam, Netherlands*

Background: An elevated sFlt-1 indicates soluble Fms-like tyrosine kinase-1 (sFlt-1)/ placental growth factor (PlGF) ratio has recently been validated as significant predictor of preeclampsia (PE)(1). However, raised sFlt-1 levels due to inflammation are observed in patients with rheumatoid arthritis (RA)(2). The use of the sFlt-1/PlGF ratio for the prediction of PE has not been evaluated in pregnant women with diseases that are characterized by high levels of inflammation, such as RA

Objectives: We investigated whether sFlt-1 and/or PlGF are altered in pregnant women with RA according to disease activity, and evaluated whether a sFlt-1/PlGF ratio of ≤38 could be used to predict the absence of PE in pregnant RA-patients.

Methods: This study was embedded in a nationwide, observational, prospective cohort study on pregnant women with RA (PARA-study). sFlt-1 and PlGF levels were measured, using automated analyzer (Cobas-6000, e-module; Roche-Diagnostics), in the third trimester of pregnancy.

Results: A total of 221 women, aged 21–42 years, were included. Values of sFlt-1, PlGF and sFlt-1/PlGF ratio were not significantly correlated with the DAS28-CRP (Figure 1). CRP correlated weakly with PlGF (r=-0.14, p=0.03), while no correlation was found with sFlt-1 or the sFlt-1/PlGF ratio.

Preeclampsia occurred in four out of 214 women with a ratio ≤38 (2%) in contrast to three out of seven women with a ratio >38 (43%), p<0.001 (Table 1). When stratified to a sFlt-1/PlGF ratio of ≤38 only 2% of women developed preeclampsia, compared to 43% of the women with a ratio >38. The observed sensitivity and specificity for a sFlt-1/PlGF ratio cut-off of ≤38 were 42.1% and 98.1%, respectively, with a negative predictive value (NPV) of 98%. All women that developed PE, developed PE >4 weeks after collecting of blood samples in the 3rd trimester, therefore the observed NPV could be even higher.

Table 1. Pregnancy Outcome according to sFlt-1/PlGF ratio with a cut-off value of 38.

Parameter	Ratio ≤38	Ratio >38	P-value
N	214	7	
GA at birth, weeks	39 (38 - 40)	37 (36 - 40)	0.05
<34	2 (1)	0(0)	1.00
34 - 37	18 (8)	2 (29)	0.12
Male, n (%)	113 (53)	5 (71)	0.45
Birth weight, grams	3420 (2998 - 3800)	2620 (2360 - 2850)	<0.01
Maternal Outcome			
Gestational Hypertension	15 (7)	2 (29)	0.09
Preeclampsia	4 (2)	3 (43)	<0.001
Time to delivery, days	66 (52 - 75)	52 (44 - 66)	0.08
Fetal Outcome			
Birth weight percentile <10	33 (15)	5 (71)	<0.01
Fetal/Neonatal Death	1 (1)	0 (0)	1.00

Data are reported as median (interquartile range) or number (percentage). sFlt-1 indicates soluble Fms-like tyrosine kinase-1; PlGF, placental growth factor; GA, gestational age. Time to delivery is defined as the amount of days between blood sampling and delivery.

Conclusion: Our study shows that in pregnant women with RA, the sFlt-1/PlGF ratio is not altered due to disease activity, and a cut-off of ≤38 of this ratio can be used to exclude preeclampsia.

REFERENCES:

[1] H. Zeisler et al. Predictive Value of the sFlt-1:PlGF Ratio in Women with Suspected Preeclampsia. N Engl J Med 2016; 374: 13-22. DOI 10.1056/NEJMoa1414838.

[2] S. Ballara et al. Paleolog. Raised serum vascular endothelial growth factor levels are associated with destructive change in inflammatory arthritis. *Arthritis Rheum* 2001; **44**: 2055-2064. DOI 10.1002/1529-0131(200109)44:9<2055::AID-ART355>3.0.CO;2-2.

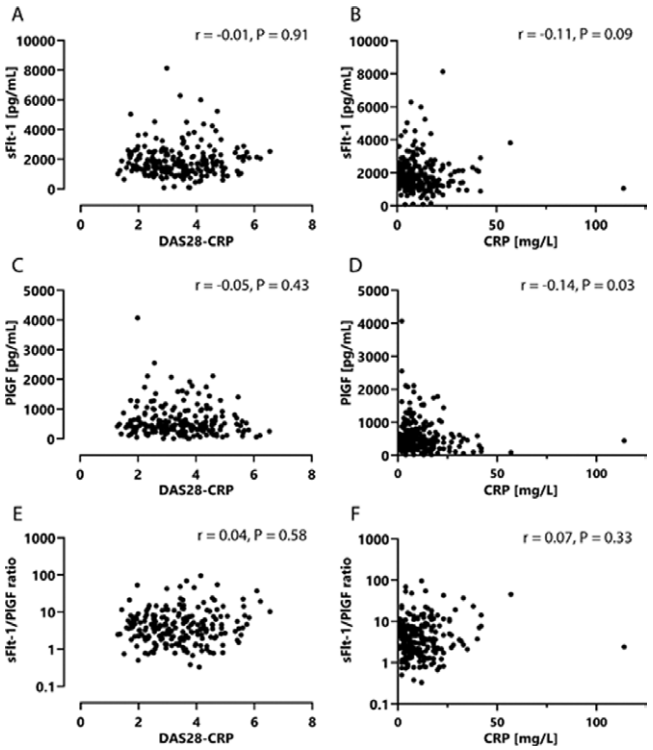


Figure 1. Correlations between sFlt-1, PlGF and sFlt-1/PlGF ratio with DAS28-CRP and CRP. Correlation coefficients for sFlt-1 (A-B), PlGF (C-D) and sFlt-1/PlGF ratio (E-F) with DAS28-CRP and CRP.

Acknowledgements: The kits for measurement of sFlt-1/PlGF ratio were a kind gift from Roche Diagnostics, Germany. We thank all participants of the PARA study. Additionally, we extend our gratitude to the laboratory workers, in particular Nadine Davelaar and Priyanka Bangoer, and research assistants for their contribution to the data collection. We thank ReumaNederland (LLP project number: LLP-26) for their financial support.

Disclosure of Interests: Hieronymus TW Smeele: None declared, R.I. Neuman: None declared, A.H.J. Danser: None declared, Radboud Dolhain Speakers bureau: Yes UCB, Roche, Abbvie, Genzyme, Novartis, Consultant of: Yes, Galapagos, Grant/research support from: Yes, UCB, W. Visser: None declared

DOI: 10.1136/annrheumdis-2021-eular.2438

POS0543

MORNING STIFFNESS IN CLINICALLY SUSPECT ARTHRALGIA IS EXPLAINED BY LOCAL SUBCLINICAL SYNOVITIS AND SYSTEMIC INFLAMMATION

D. Krijbolder[1], F. Wouters[1], E. van Mulligen[2], A. van der Helm - van Mil[1,2]. [1]*Leiden University Medical Centre, Department of Rheumatology, Leiden, Netherlands*; [2]*Erasmus Medical Center, Department of Rheumatology, Rotterdam, Netherlands*

Background: Morning stiffness (MS) is considered a cardinal symptom in the clinical appraisal of arthralgia patients, suggesting presence of subclinical inflammation, which could indicate an increased chance of progression to rheumatoid arthritis (RA). However, the pathophysiology behind MS in arthralgia patients that is clinically suspect for progressing to RA (clinically suspect arthralgia; CSA) has never been studied. In RA, it is presumed that both and local- and systemic inflammation underlie MS. We therefore hypothesize that, in patients with CSA, MS can also be explained by local- and systemic inflammation.
Objectives: To determine if MS can be explained by MRI-detected local inflammation (subclinical synovitis and tenosynovitis) and systemic inflammation (C-reactive protein(CRP)).
Methods: 514 CSA patients underwent a contrast-enhanced 1.5T MRI of metacarpophalangeal (MCP) 2-5, wrist and metatarsophalangeal (MTP) 1-5 joints, next to clinical assessment and laboratory investigations. MRIs were scored for synovitis and tenosynovitis in line with the RAMRIS-method. MS was dichotomized as present (duration ≥60 minutes) or absent (duration <60 minutes). Associations of MRI-detected synovitis, tenosynovitis and increased CRP with MS were tested with univariable and multivariable logistic regression. Since earlier research in arthritis patients showed that the effect of combined presence of MRI-detected synovitis and tenosynovitis was increased, compared to the effect of these features separately, interaction between MRI-detected synovitis and tenosynovitis, and between synovitis and increased CRP, was assessed.
Results: In the studied CSA-patients, mean age was 44 years (sd 13), 397 patients (77%) were female, median tender joint count (TJC-70) was 5 (interquartile range 2-10), and 67 (13%) patients were ACPA-positive. MS was present in 191 (37%) CSA-patients. Baseline characteristics among patients with and without MS were similar. MRI-detected synovitis was more often present in patients with MS compared to patients without MS (34% versus 19%), OR 2.12 (95% CI 1.41-3.19). Also, MRI-detected tenosynovitis was more frequently present in patients with MS (36% versus 24%), OR 1.74 (1.18-2.57). Likewise, increased CRP levels (≥5 mg/L) were more often found in patients with MS (31% versus 18%), OR 2.00 (1.32-3.04). In multivariable analyses, ORs were 1.90 (1.22-2.96) for MRI-detected synovitis and 1.82 (1.18-2.82) for increased CRP. With an OR of 1.20 (0.77-1.87) MRI-detected tenosynovitis was not significantly associated with MS in a multivariable analysis. Interaction between synovitis and tenosynovitis, and between synovitis and CRP was not significant (p-value of 0.13 and 0.15, respectively).
Conclusion: Presence of MRI-detected synovitis and increased CRP levels are associated with presence of MS in patients with CSA. This indicates that MS in CSA patients could indeed be induced by both local- and systemic inflammation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2474

POS0544

INFLUENCE OF EATING HABITS ON FRAILTY AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: KURAMA COHORT

M. Katsushima[1], H. Minamino[2], M. Torii[3], M. Hashimoto[4], W. Yamamoto[5], R. Watanabe[4], K. Murakami[1], K. Murata[4], M. Tanaka[4], H. Ito[4], A. Morinobu[1]. [1]*Kyoto University Graduate School of Medicine, Department of Rheumatology and Clinical Immunology, Kyoto, Japan*; [2]*Kyoto University Graduate School of Medicine, Department of Diabetes, Endocrinology and Nutrition, Kyoto, Japan*; [3]*Kyoto University Graduate School of Medicine, Department of Human Health Sciences, Kyoto, Japan*; [4]*Kyoto University Graduate School of Medicine, Department of Advanced Medicine for Rheumatic Diseases, Kyoto, Japan*; [5]*Kurashiki Sweet Hospital, Department of Health Information Management, Kurashiki, Japan*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder that contributes to accelerating frailty, a clinical state of increased vulnerability due to declined physiological function. Although accumulating evidence suggests the importance of nutritional therapy for frailty in the general population, there is little evidence on dietary recommendations for preventing frailty in patients with RA.
Objectives: The present study aimed to reveal clinical associations between frailty status, eating habits and RA disease activity.
Methods: We conducted a cross-sectional study of 306 female outpatients enrolled from the KURAMA (Kyoto University Rheumatoid Arthritis Management Alliance) cohort database. The participants were classified into three groups (robust, prefrail and frail) according to simplified frailty scale (SOF index), and dietary data were collected using a self-reported food frequency questionnaire as previously reported. We performed multivariate logistic analyses for the presence of frailty/prefrailty with or without eating habits.
Results: Frail group showed physical decline such as decreased skeletal muscle index, hand grip strength and walking speed, and DAS28-ESR in the frail group was significantly higher compared to that in the others. In multivariate logistic analysis, the presence of frailty/prefrailty was correlated with DAS28-ESR (OR 1.71, p=0.00004) and methotrexate use (OR 0.47, p=0.0097). Cochran-Armitage trend test also showed that the intake frequency of five ingredients (meat, fish, milk, fruits and vegetables) was inversely associated with the prevalence of frailty/prefrailty. In additional multivariate logistic analyses with dietary habits, habitual intake of fish (at least three times per week), rather than meat or other foods, was independently correlated with the presence of frailty/prefrailty (OR 0.33, p=0.00027).
Conclusion: Our results suggest that habitual intake of fish, rather than meat or other foods, may be beneficial in preventing frailty among RA patients.

REFERENCES:

[1] Ferrucci, L. & Fabbri, E. Inflammageing: chronic inflammation in ageing, cardiovascular disease, and frailty. *Nat Rev Cardiol* 15, 505-522, doi:10.1038/s41569-018-0064-2 (2018).
[2] Hernandez Morante, J. J., Gomez Martinez, C. & Morillas-Ruiz, J. M. Dietary factors associated with frailty in old adults: a review of nutritional interventions to prevent frailty development. *Nutrients* 11, doi:10.3390/nu11010102 (2019).

Table 1. Multivariate logistic analysis for RA patients with prefrailty or frailty

variables including eating habits	Fish + Meat		All	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
DAS28-ESR	**1.78 (1.34 - 2.37)**	**0.00003**	**1.73 (1.30 - 2.30)**	**0.00009**
MTX use	**0.43 (0.23 - 0.79)**	**0.0055**	**0.42 (0.23 - 0.78)**	**0.0050**
Age (1 year)	**1.02 (1.00 - 1.05)**	**0.037**	**1.03 (1.01 - 1.06)**	**0.0015**
PSL use	1.23 (0.69 - 2.21)	0.49	1.22 (0.67 - 2.20)	0.51
Duration of RA (1 year)	1.00 (0.98 - 1.02)	0.72	1.00 (0.98 - 1.02)	0.84
Body mass index	1.00 (0.93 - 1.07)	0.98	0.99 (0.92 - 1.07)	0.85
Biological agents use	1.02 (0.60 - 1.72)	0.94	1.04 (0.62 - 1.77)	0.87
Fish dish	**0.31 (0.17 - 0.55)**	**0.00004**	**0.33 (0.18 - 0.61)**	**0.00027**
Meat dish	0.86 (0.49 - 1.50)	0.60	0.89 (0.51 - 1.57)	0.69
Milk			0.71 (0.41 - 1.24)	0.23
Vegetable			0.95 (0.47 - 1.93)	0.89
Fruits			0.77 (0.41 - 1.42)	0.40

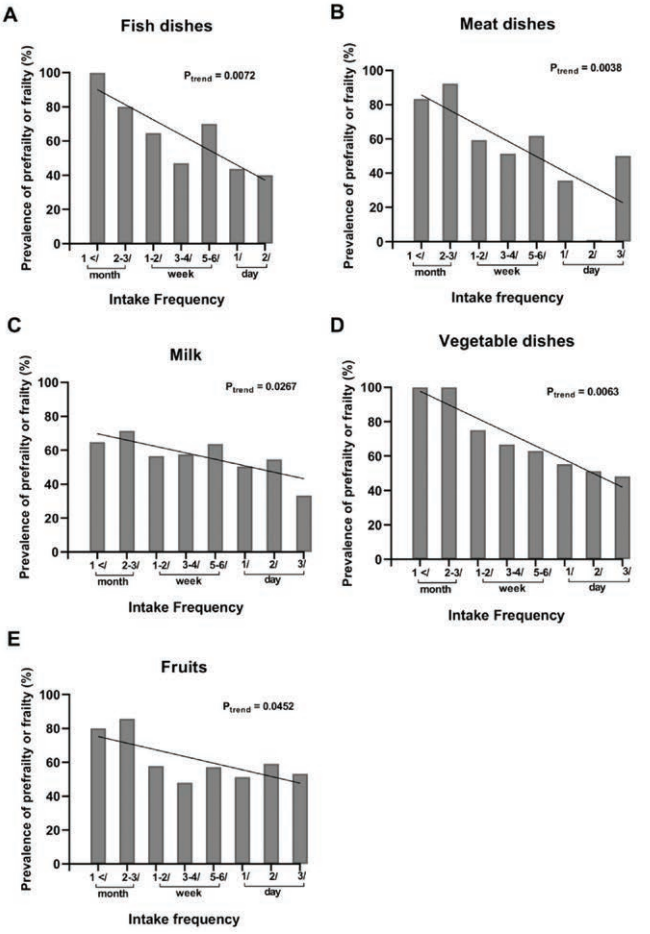


Figure 1. The prevalence of prefrailty or frailty for subjects by intake frequency

Acknowledgements: We thank S. Nakagawa and M. Iida for technical assistance.

Disclosure of Interests: Masao Katsushima: None declared, Hiroto Minamino: None declared, Mie Torii: None declared, Motomu Hashimoto Speakers bureau: M.H. receives grants and/or speaker fees from Bristol-Meyers, Eisai, Eli Lilly, and Tanabe Mitsubishi., Grant/research support from: M.H. belongs to the department financially supported by Nagahama City, Shiga, Japan, Toyooka City, Hyogo, Japan and five pharmaceutical companies (Tanabe-Mitsubishi, Chugai, UCB Japan, Ayumi and Asahi-Kasei).

KURAMA cohort study is supported by a grant from Daiichi Sankyo Co. Ltd., Wataru Yamamoto: None declared, Ryu Watanabe Grant/research support from: R.W. belongs to the department that is financially supported by Nagahama City, Shiga, Japan, Toyooka City, Hyogo, Japan and five pharmaceutical companies (Tanabe-Mitsubishi, Chugai, UCB Japan, Ayumi and Asahi-Kasei). KURAMA cohort study is supported by a grant from Daiichi Sankyo Co. Ltd., Kosaku Murakami: None declared, Koichi Murata Grant/research support from: K.M. belongs to the department that is financially supported by Nagahama City, Shiga, Japan, Toyooka City, Hyogo, Japan and five pharmaceutical companies (Tanabe-Mitsubishi, Chugai, UCB Japan, Ayumi and Asahi-Kasei).

KURAMA cohort study is supported by a grant from Daiichi Sankyo Co. Ltd., Masao Tanaka Grant/research support from: M.T. belongs to the department that is financially supported by Nagahama City, Shiga, Japan, Toyooka City, Hyogo, Japan and five pharmaceutical companies (Tanabe-Mitsubishi, Chugai, UCB Japan, Ayumi and Asahi-Kasei).

KURAMA cohort study is supported by a grant from Daiichi Sankyo Co. Ltd., Hiromu Ito Speakers bureau: H.I. receives a research grant and/or speaker fee from Bristol-Myers, Eisai, Mochida, Taisho, and Asahi-Kasei., Grant/research support from: H.I. belongs to the department that is financially supported by Nagahama City, Shiga, Japan, Toyooka City, Hyogo, Japan and five pharmaceutical companies (Tanabe-Mitsubishi, Chugai, UCB Japan, Ayumi and Asahi-Kasei). KURAMA cohort study is supported by a grant from Daiichi Sankyo Co. Ltd., Akio Morinobu Speakers bureau: A.M. has received speaking fees and/or research grants from Eli Lilly Japan K.K., Ono Pharmaceutical Co., Pfizer Inc., UCB Japan, AbbVie G.K., Asahi Kasei Pharma and Chugai Pharmaceutical Co. Ltd., Grant/research support from: A.M. has received speaking fees and/or research grants from Eli Lilly Japan K.K., Ono Pharmaceutical Co., Pfizer Inc., UCB Japan, AbbVie G.K., Asahi Kasei Pharma and Chugai Pharmaceutical Co. Ltd.

DOI: 10.1136/annrheumdis-2021-eular.2511

POS0545 DISCORDANCE BETWEEN PATIENT'S AND PHYSICIAN'S DISEASE ACTIVITY ASSESSMENT IN RHEUMATOID ARTHRITIS: WHICH DOMAINS CAN INFLUENCE THIS DISCREPANCY WHEN REMISSION IS ACHIEVED?

L. Moschetti[1,2], C. Bazzani[1], F. Villanova[2], R. Gorla[1], F. Franceschini[1,2]. [1]*ASST Spedali Civili, Rheumatology and Clinical Immunology Unit, Brescia, Italy*; [2]*University of Brescia, Clinical and Experimental Sciences, Brescia, Italy*

Background: In daily clinical practice, it is not rare to observe a relevant discordance between patient's global assessment (PGA) and physician's global assessment (PhGA), because of different illness perceptions.

Objectives: To evaluate the presence of PGA/PhGA discrepancy in patients with rheumatoid arthritis (RA) who achieved biological remission and to explore whether this discordance could be influenced by the presence of additional elements affecting patients' quality of life, such as comorbidities, sleep disturbances and psycho-emotional factors.

Methods: Our study included adult RA patients, followed in a single rheumatology centre, fulfilling three out of four Boolean remission criteria: tender joint count ≤1, swollen joint count ≤1 and C reactive protein ≤1 mg/dl[1]. Medical records including demographic data, clinical characteristics and outcomes measures were collected. To evaluate the impact of comorbidities we used the Rheumatic Disease Comorbidity Index (RDCI). Pain assessment, PGA and PhGA were rated on a visual analogue scale (0-100 mm) on the same day of the clinical evaluation. To analyse the discrepancy between PGA and PhGA, the [PGA-PhGA] variable was calculated, considering as discordant a difference ≥ 30 mm. All the subjects completed the following questionnaires: Health Assessment Questionnaire (HAQ), SF36 Health Survey, State-Trait Anxiety Inventory (STAI-Y1/Y2), Self-rating Depression Scale (SDS Zung) and Insomnia Severity Index (ISI). Statistical analysis was performed to compare concordant and discordant groups.

Results: The study included 90 patients (64 women, 26 men) with a median age of 60 [50-67] and a median RA duration of 10 [5-16] years; 80% of patients were RF and/or ACPA positive. According to DAS28 (median 1.7 [1.5-2.2]), 90% of patients achieved remission, 9% LDA and 1% MDA. Nevertheless, in 81% of cases PGA>PhGA and in 33% [PGA-PhGA] ≥30. The discordant group showed higher median disease activity scores (DAS28: 2.2 [1.9-2.4] vs 1.5 [1.4-1.9], *p<0,001*; SDAI: 6.7 [3.9-8.1] vs 2.0 [0.7-3.2], *p<0.001*). No differences were found in gender, age, comorbidities, RA duration, serology and treatment (cs-/b-DMARDs). Median prednisone dose was higher in the discordant group (0 [0-21] vs 0 [0-7.5] mg/week, *p:0,024*). Data about patient-reported outcomes and differences between two groups are reported in the table 1.

Conclusion: In our study we found discordance between the global disease assessment reported by patients, although considered in biological remission, and their physicians in 33% of the cases. As previously described[2], our data seems to confirm that potential causes for this discordance could be pain due to non-inflammatory processes, functional disability and compromised physical health. In the present study also psychological stress, particularly state anxiety, seems to negatively affect PGA/PhGA concordance. These results confirm the importance, in clinical practice, of exploring and managing inflammatory and non-inflammatory parameters separately, also in patients achieving biological remission.

REFERENCES:

[1] Svensson B et al. BMJ Open. 2013. [2] Craig ET et al. Arthritis Care Res. 2019.

Table 1. Data are expressed as median (1st-3rd quartile) and compared using Mann-Whitney test.

PATIENT-REPORTED OUTCOMEs	PATIENT NUMBER =90	CONCORDANT GROUP (PGA-PhGA) <30 =60 (67%)	DISCORDANT GROUP (PGA-PhGA) ≥30 =30 (33%)	*p <0,05*
PGA, [0-100]	20 (10-40)	10 (0-20)	50 (37-60)	-
PhGA, [0-100]	0 (0-10)	0 (0-10)	10 (0-10)	-
PGA-PhGA, [0-100]	10 (0-30)	10 (0-10)	40 (30-52)	-
VAS pain, [0-100]	20 (10-40)	10 (0-20)	50 (30-60)	***<0,001***
HAQ, [0-3]	0,13 (0-0,50)	0 (0-0,25)	0,31 (0,09-0,87)	***<0,001***
STAI Y1, [20-80]	36 (31-47)	35 (30-42)	40 (35-51)	***0,014***
STAI Y2, [20-80]	37 (33-45)	37 (33-45)	38 (33-47)	*ns*
SDS ZUNG, [25-100]	45 (40-51)	44 (39-49)	48 (40-53)	*ns*
ISI, [0-28]	2 (2-11)	5 (2-11)	8 (3-14)	*ns*
SF36 Physical, [0-100]	44 (36-52)	48 (40-54)	36 (28-46)	***<0,001***
SF36 Mental, [0-100]	50 (38-56)	51 (41-57)	47 (33-54)	*ns*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2555

POS0546 RENAL DYSFUNCTION AND METABOLIC CHANGES IN PATIENTS WITH RHEUMATOID ARTHRITIS ARE ASSOCIATED WITH ANGIOPOIETIN-LIKE PROTEIN TYPE 4

V. Aleksandrov[1,2], A. Aleksandrov[1,2]. [1]*Volgograd State Medical University, Department of Hospital Therapy, Volgograd, Russian Federation*; [2]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», Department of clinical and laboratory diagnostics, Volgograd, Russian Federation*

Background: Along with chronic inflammation, the development of renal damage in rheumatoid arthritis (RA) is promoted by the presence of metabolic syndrome (MS), which may be an independent risk factor for the progression of chronic kidney disease.

Objectives: To establish a correlation between serum angiopoietin-like protein type 4 (ANGPTL4) and the presence of renal dysfunction and metabolic disorders in RA patients.

Methods: We examined 158 patients with RA (91.8% - women and 8.2% - men) aged 21 to 80 years old with an average duration of the disease - 9 [4; 15] years. The majority of patients were seropositive for RF-IgM (57.6%) and for anti-citrullinated protein antibody (ACPA) (60.1%), with an advanced clinical stage (45.6%) and moderate activity (3.2 <DAS28 ≤ 5.1) of the pathological process (58.2%).

The laboratory examination included the determination of serum concentrations of angiopoietin-like protein type 3 (Human Angiopoietin-like Protein 3 ELISA, Bio Vendor, Czech Republic) and type 4 (RayBio Human ANGPTL4 ELISA Kit; RayBiotech, USA).

To assess renal function in RA patients, the estimated glomerular filtration rate (GFR) was used according to the 2009 CKD-EPI formula. On the basis of GFR measurements, the patients were divided into three groups: I - optimal renal function (> 90 ml / min); II - a slight decrease in renal function (89-60 ml / min); III - reduced renal function (<59 ml / min).

A combination of the increased blood pressure (≥140 / 90 mmHg), the increased triglyceride levels (≥1.7 mmol / L), and the impaired carbohydrate metabolism (increased fasting plasma glucose ≥6.1 mmol / L) with a background of central obesity (waist circumference> 94 cm in men and> 80 cm in women) served as the basis for inclusion into the group of RA patients with signs of MS.

Results: A multivariate analysis of variance was performed comparing ANGPTL indices depending on GFR in the groups of RA patients without signs of MS and

RA patients with MS. It was revealed that there are significant differences in the level of both ANGPTL3 (F = 8.86, p = 0.0034) and ANGPTL4 (F = 29.6, p <0.001) between RA patients with varying severity of metabolic disorders.
The study of the influence of several factors (MS and renal dysfunction) on the content of ANGPTL in RA patients showed that the presence of metabolic disorders had an insignificant effect on the parameters of ANGPTL3 in the groups of patients with optimal and slightly reduced GFR, acquiring significance only with a more intense decrease in GFR (<59 ml / min / 1.73 m2). These factors and their interactions explain the insignificant share of the variability in ANGPTL3 (R^2 = 0.11), which indicates a low quality of the model.
There was a more pronounced difference in the level of ANGPTL4 in the presence of metabolic disorders in the groups of RA patients with varying degrees of renal dysfunction. The factors under consideration and their interactions do not make this model significant (p = 0.1), although they can explain a significant proportion of the variability in ANGPTL4 (R^2 = 0.32).
We differentiated RA patients into patients with high or optimal GFR (≥89 ml / min) and patients with reduced GFR (<89 ml / min) when combining groups of RA patients with varying degrees of renal dysfunction (group II and group III). Multivariate analysis of variance using the new characteristics showed a significant increase in ANGPTL 4 in the blood serum of RA patients with reduced GFR (F = 18.5, p <0.001) and severe metabolic changes (F = 24.2, p <0.001).
Thus, the concentration of ANGPTL4 in RA patients is directly influenced by two factors (renal dysfunction and the presence of MS), which can describe the variability of this sign in more than 30% of cases. The squared multiple correlation coefficient (R^2) in this model is 0.33.
Conclusion: ANGPTL type 4 should be considered as a key factor linking the development of the renal dysfunction in RA patients and the metabolic changes caused by rheumatoid inflammation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2657

POS0547 METEOROLOGICAL VARIABLES HAVE DIFFERENT INFLUENCE ON CORE MEASURES OF DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

P. Mandl[1], P. Studenic[1], F. Alasti[1], R. Kaltenberger[2], A. Kerschbaumer[1], T. Krennert[3], J. S. Smolen[1], D. Aletaha[1]. [1]*Medical University of Vienna, Rheumatology, Vienna, Austria*; [2]*Central Institute for Meteorology and Geodynamics, Climate Research, Vienna, Austria*; [3]*Central Institute for Meteorology and Geodynamics, Weather Forecast, Vienna, Austria*

Background: The notion that weather conditions may influence the symptoms and course of rheumatic and musculoskeletal diseases goes back to ancient times. However, despite the seemingly obvious relationship, previous studies assessing how meteorological variables affect pain and disease activity have yielded contradictory results.
Objectives: To evaluate whether meteorological variables influence disease activity in patients with rheumatoid arthritis (RA).
Methods: We assessed correlations between clinical measures of disease activity (pain, patient global assessment [PGA], tender- and swollen 28 joint counts [TJC and SJC]) and individual meteorological variables: temperature (temp.), effective (eff.) temperature, saturation vapor pressure (SVP), absolute humidity (AH), relative humidity (RH), dew point, vapor pressure (VP) and precipitation. Assessments documented in the Care for Rheumatoid Arthritis database of our institution were matched with these meteorological variables on a daily basis for a period of 12 years between 2005 and 2017 and analyzed utilizing generalized estimating equations. Patients with <5 visits in the study period, those with <1 visit/quarter or with no pain (VAS=0) in ≥3 consecutive visits and those living outside of the catchment area were excluded. Patients were grouped into remission or low (≤11) vs. moderate or high (>11) disease activity based on the simplified disease activity index (SDAI).
Results: A total of 461 patients with an average disease duration at first visit of 5.7±7.4 years, average age of 55.3±14.5 years and a mean SDAI of 22.1±12.7 were analyzed. Among patients with moderate or high disease activity, higher temp./eff. temp. and SVP were associated with lower pain, TJC and SJC (Figure 1); on the contrary, higher RH was associated with higher pain and higher SJC. In those in remission or low disease activity, higher RH, AH, VP or dew point were associated with lower PGA. Higher precipitation was associated with lower SJC.

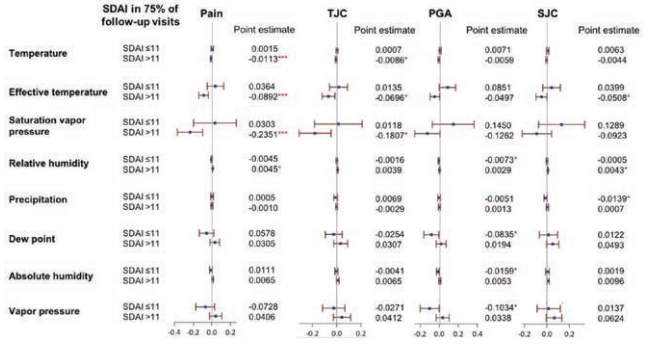


Figure 1. Association of meteorological parameters and clinical measures of disease activity. PGA: patient's global assessment, SDAI: simplified disease activity index, SJC: swollen joint count, TJC: tender joint count. * p≤ 0.05, ** p≤ 0.01, *** p≤ 0.001

Conclusion: In this large association study of meteorological parameters with RA, both temperature and humidity parameters were modestly inversely associated with pain, TJC and SJC.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2684

POS0548 OPTIMAL ASSESSMENT OF THE RHEUMATOID ARTHRITIS ANKLE AND HINDFOOT: A COMPARATIVE STUDY BETWEEN CLINICAL EXAMINATION AND ULTRASONOGRAPHY

K. Maatallah[1], H. Boussaa[1], H. Riahi[2], H. Ferjani[1], M. Habechi[1], W. Triki[1], D. Ben Nessib[1], M. Bouaziz[2], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab Institute of Orthopedics, Rheumatology, La Manouba, Tunisia*; [2]*Mohamed Kassab Institute of Orthopedics, Radiology, La Manouba, Tunisia*

Background: Foot disease is a common problem in rheumatoid arthritis (RA). Therapeutic decisions are often based on clinical examination (CE) alone, which can be adversely affected by factors such as deformity, obesity, and peripheral edema. Ultrasonography (US) has previously been shown to be more sensitive than CE for detecting synovitis and tenosynovitis in RA forefeet, but few data exist for the hindfoot and ankle.
Objectives: The aim of this study was to compare CE and US for the detection of hindfoot and ankle synovitis and tenosynovitis in patients with established RA.
Methods: We conducted a cross-sectional study including patients with RA (ACR/EULAR 2010). Demographic data and disease parameters were collected. CE was performed by a rheumatologist for the presence or absence of tenderness, swelling, and mobility restriction of both ankles. The following tendons were examined for tenosynovitis: tibialis anterior (TA) and posterior (TP), fibularis longus (FL), and brevis (FB) (assessed together). In a second time, US examination of the tibiotalar, talonavicular, and subtalar joints and the same tendons as CE was performed by a blinded radiologist experienced in musculoskeletal imaging using a Philips HD11 device with a high-frequency linear transducer. The presence or absence of synovitis and tenosynovitis was recorded, and the composite synovitis score (power doppler / grayscale ultrasound (PDUS)) was measured for each joint. The US score of each patient was defined by the sum of the composite scores of the joints studied (0-30). A p-value <0.05 was considered significant.
Results: Sixty-two feet were examined in 31 RA patients (25 women and six men) with a mean age of 54.8±10.8 years old [32-70]. The mean disease duration was 8.5±7.2 years [1-37]. Rheumatoid Factor (RF) and Anti-Citrullinated Peptides Antibodies (ACPA) were positive in 61.3% and 83.8% of cases. The mean DAS28 ESR was 3.8±1.5 [0.6-7].
Clinical examination of ankles revealed tenderness in 57.4% of cases, swelling in 38.8% of cases, and restriction in the range of motion in 11.1% of cases. TA tenosynovitis was noted in 14.8% of cases, TP tenosynovitis in 22.2% of cases, and FL and FB tenosynovitis in 31.5% of cases.
US showed tibiotalar synovitis in 59.3% of cases, talonavicular synovitis in 64.8% of cases, and subtalar synovitis in 46.3% of cases. TA tenosynovitis was noted in 5.6% of cases, TP tenosynovitis in 22.2% of cases, and FB and FL tenosynovitis in 25% and 11.1% of cases respectively.

An association was found between clinical tenderness and US synovitis of the tibiotalar joint (p=0.013) and the talonavicular joint (p=0.027). No association was noted between clinical swelling and US synovitis in these joints.
No association was noted between clinical and US tenosynovitis of TA (p=0.279), TP (p=0.436), FB (p=0.495) and FL (p=0.315).
Conclusion: Clinical examination of RA ankles may be challenging and needs to be coupled with US, which is more sensitive and accurate in the detection of synovitis and tenosynovitis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2720

POS0549 FUNCTIONAL IMPACT OF FOREFOOT INVOLVEMENT IN RHEUMATOID ARTHRITIS

K. Maatallah[1], H. Boussaa[1], H. Riahi[2], H. Ferjani[1], W. Triki[1], M. Habechi[1], D. Ben Nessib[1], M. Bouaziz[2], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab Institute of Orthopedics, Rheumatology, La Manouba,Tunisia*; [2]*Mohamed Kassab Institute of Orthopedics, Radiology, La Manouba,Tunisia*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that mainly affects small joints of the hands and feet. Foot deformities may affect the patient's gait, thus compromising their daily activities and autonomy.
Objectives: The aim of this study was to analyze its functional impact.
Methods: We conducted a cross-sectional study including patients diagnosed with RA according to the ACR/EULAR 2010 criteria. Demographic variables, Foot Function Index (FFI), and Health Assessment Questionnaire (HAQ) scores were analyzed. We collected data on the following clinical variables: The pain Visual Analog Scale (VAS), forefoot deformities, erythrocyte sedimentation rate (ESR), and Disease Activity Score 28 (DAS28). All patients had feet X-rays and the Larsen score was calculated. A blinded radiologist experienced in musculoskeletal imaging using a Philips HD11 device with a high-frequency linear transducer performed ultrasonography (US) of MTP joints. Synovitis was defined as an abnormal hypoechoic synovial tissue within the capsule that is not displaceable and poorly compressible and that may exhibit Doppler signals. The composite synovitis score (power doppler / grayscale ultrasound (PDUS)) was measured for each joint. The US score of each patient was defined by the sum of the composite scores of the joints studied (0-30). A p-value <0.05 was considered significant.
Results: We included 31 patients (25 men and six women) with a mean age of 54.8±10.8 years old [32-70]. The mean disease duration was 8.5±7.2 years [1-37]. The mean ESR and DAS28 ESR were 33±26 mm [5-102] and 3.8±1.5 [0.6-7], respectively. Twenty-nine percent of patients had a high disease activity.
Metatarsalgia was reported by 54.8% of patients with a mean VAS of 4.5±3.7 [0-9]. Forefoot deformities were noted in 42% of patients: round forefoot in 13% of cases, triangular forefoot in 29% of cases, hallux valgus in 29% of cases, Quintus varus in 29% of cases, and claw toes in 13% of cases. Corns and calluses were noted in 42% and 29% of cases respectively.
X-rays showed abnormalities in 75% of patients. The mean Larsen score was 9.8±6.2 [0-28].
US showed synovitis in 46.3% of MTP1, in 53.7% of MTP2, in 48.3% of MTP3, in 42.6% of MTP4, and in 37% of MTP5 joints. Doppler signal was detected in 5.6% of MTP1 and MTP2, and in 3.7% of MTP3, MTP4, and MTP5 joints. The mean US score was 5.3±4.3 [0-15].
The mean FFI was 66.5%. Mean rates of pain, difficulty, and disability were 89.5%, 40%, and 70% respectively. The mean HAQ score was 0.5±0.5 [0-2]. Severe disability was noted in 20% of patients.
A significant positive correlation was noted between FFI and, Larsen score (r=0.214, p=0.014) and US score (r=0.420, p=0.021). A significant positive correlation was also noted between HAQ score and, foot pain VAS (r=0.555, p=0.009).
Conclusion: Foot involvement is frequently seen in RA. This condition may affect patients' autonomy. Early diagnosis and appropriate treatment are necessary in order to preserve the quality of life.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2727

POS0550 EVALUATION OF THE INTIMA-MEDIA THICKNESS INDEX BY CAROTID DOPPLER IN PATIENTS WITH RHEUMATOID ARTHRITIS AT HOSPITAL DOCENTE PADRE BILLINI, DOMINICAN REPUBLIC

T. Polanco Mora[1], J. Santana Peralta[2], A. Cornelio[1], Y. Cruz[1], E. Rodriguez Bautista[1], T. Valdez[1], R. Muñoz[1], A. Feriz[1]. [1]*Hospital Docente Padre Billini, Reumatologia, Santo Domingo,*; [2]*Hospital Docente Padre Billini, Reumatologia, Santo domingo,*

Background: Rheumatoid arthritis (RA) is an autoimmune disease systemic, affects 0.5 - 1% of the world population, predominantly female. (1) Carotid Doppler is used to detect endothelial dysfunction by measuring intima-media thickening, flow velocities, subclinical atherosclerosis markers, and vascular tone.(2,3) Measurement of carotid intima-media thickness (cIMT) is useful in assessing cerebrovascular disease and cardiovascular risk in patients with rheumatoid arthritis (4) Intima-media thickness value> 0.9mm and presence of plaques Atheromatous cells in the carotid artery are predictive of increased cardiovascular risk and silent heart disease. (5,6)
Objectives: To evaluate the carotid intima-media thickness in patients with rheumatoid arthritis
Methods: A prospective, observational, cross-sectional study. Carotid Doppler was performed on outpatient patients with a diagnosis of rheumatoid arthritis from November 2019 to 2020 of the rheumatology service of the Hospital Docente Padre Billini and healthy controls. Inclusion criteria:> 18 years, diagnosis of RA according to ACR / EULAR 2010 classification criteria, carotid Doppler with measurement of the carotid intima-media thickness. Controls without disease, matched by sex and age. The data were analyzed with SPSS V23.
Results: Of 251 patients with a diagnosis of RA, 100 met criteria inclusion, 96.2% female, 100 healthy controls were included. Average evolution of the disease 7.5 years, 88%(88) Positive rheumatoid factor, 33% (33) Positive anti-CCP. 82% (82) concomitant scDMARD, 70% (70) bDMARD, 18% (18) ctDMARD. 53% (53) Dyslipidemia, 23% (23) obesity, 10% (10) hyperglycemia, 8% (8) smokers. DAS28 showed 57% (57) low activity, 20% (20) moderate activity, 15% (15) remission, 8% (8) high activity. Carotid Doppler in patients with RA showed 32% (32) atheromatous plaques, 18.75% (6) calcified plaques, 1.44% (1) stenosis bilateral carotid. C-reactive protein and erythrocyte sedimentation rate high 35% (35) / 58% (58) respectively. Carotid Doppler in healthy controls revealed 17% (17) atheromatous plaques, 47.05% (8) calcified plaques. 69% (69) of RA patients had increased cIMT, mean (SD) cIMT 3.82mm (1.11), controls 58% (58) increase in cIMT, Mean (SD) 3.12mm (0.93) (p = 0.0435).
Conclusion: Our study showed that 69% of patients with Arthritis Rheumatoid featured increased intima-media thickness associated with low DAS28, we recommend assessing cardiovascular risk using carotid Doppler in patients with low to moderate activity. It was observed that in patients with RA and healthy controls more than half present increased carotid intima-media thickness.
REFERENCES:
[1] JAMA. 2018;320(13):1360-1372.
[2] Villa-Forte, B.F. Mandell / Rev Esp Cardiol. 2011;64(9):809–817.
[3] Meune, C., Touzé, E., Trinquart, L., Allanore, Y. Trends in cardiovascular mortality in patients with rheumatoid arthritis over 50 years: A systematic review and meta-analysis of cohort studies. Rheumatology 2009; 48 (10): 1309-13.
[4] Choi, HK., Rho, Y-H., Zhu, Y., Cea-Soriano, L., Aviña-Zubieta, JA., Zhang, Y. The risk of pulmonary embolism and deep vein thrombosis in rheumatoid arthritis: A UK population-based outpatient cohort study. Ann Rheum Dis. 2013; 72 (7): 1182-7.
[5] Gkaliagkousi, E., Gavriilaki, E., Doumas, M., Petidis, K., Aslanidis, S., Stella, D. Cardiovascular risk in rheumatoid arthritis: Pathogenesis, diagnosis, and management. J Clin Rheumatol Pract Rep Rheum Musculoskelet Dis. 2012; 18 (8): 422-30.
[6] Corrales, A., González-Juanatey, C., Peiró, ME., Blanco, R., Llorca, J., González-Gay, MA. Carotid ultrasound is useful for the cardiovascular risk stratification of patients with rheumatoid arthritis: Results of a population-based study. Ann Rheum Dis. 2013.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2743

POS0551 MEDICAL COSTS FOR PATIENTS STARTING TREATMENT FOR RHEUMATOID ARTHRITIS WHO HAVE COMORBID DIABETES MELLITUS IN JAPAN

E. Tanaka[1], E. Inoue[1,2], R. Sakai[1], I. Katsuhiko[3], A. Shoji[3], M. Harigai[1]. [1]*Tokyo Women's Medical University School of Medicine, Department of Rheumatology, Tokyo, Japan*; [2]*Showa University, Showa University Research Administration Center (SURAC), Tokyo, Japan*; [3]*Medilead Inc., Tokyo, Japan*

Background: Rheumatoid arthritis (RA) patients can experience various comorbidities[1]. The incidence of diabetes mellitus (DM) is reported higher in patients with RA[2] and comorbid DM is likely to affect treatment outcomes[3] and then healthcare resource uses, however, no previous study has not focused on it.
Objectives: To evaluate medical costs and resource use in patients starting treatment for RA with and without DM using a large claims database in Japan.
Methods: We used a large Japanese administrative claims database constructed by the Japan Medical Data Center (JMDC)[4]. Patients with the International Classification of Diseases 10th revision (ICD-10) codes for RA who started medication with disease-modifying antirheumatic drugs (DMARDs) after 6 months without them in the period from 1/1/2012 to 12/31/2017 and who were observable for 12 months as a follow-up period were enrolled. These patients were categorized as DM or non-DM group with ICD-10 codes for DM plus use of antidiabetic drugs in 6 months before starting DMARDs (baseline period). To adjust baseline characteristics between the 2 groups, they were matched by sex, age, Charlson Comorbidity Index (CCI) except for DM, months from the first RA codes to starting DMARDs, and medications. The primary endpoint was mean medical cost per patient in the 12-month follow-up period. Costs in JPY were converted into EUR (1 EUR = 125 JPY in 2020). Costs for drugs, treatments, and materials and their subcategories were evaluated both with and without DM-specific costs. The secondary endpoints were the proportions of patients using the subcategories of each resource.
Results: Patients of 161 for the DM group and 2,974 for the non-DM group were eligible, and 109 patients were matched from each group. The medians of age and CCI were 59 years and 2.0 in both groups and no significant difference was observed in all baseline characteristics used for matching between the groups. Total mean costs were significantly higher in the DM group (DM, 5,331 EUR, non-DM 3,200 EUR; P< 0.05). After excluding DM-specific costs, drug costs were significantly higher in the DM group than in the non-DM group (DM 1,883 EUR, non-DM 896 EUR; P < 0.05), especially costs for biological DMARDs (DM 1,156 EUR, non-DM 292 EUR; P < 0.05), mainly because a higher proportion of patients used these drugs in the DM group (Table 1). Treatment costs (DM 2,380 EUR, non-DM 2,133 EUR) and material costs (DM 74 EUR, non-DM 149 EUR) were not different between the groups, but only costs for examinations were significantly higher in the DM group (DM 970 EUR, non-DM 779 EUR; P < 0.05).

Table 1. Number and proportion of patients who used drugs

Type of drug		Drug use, n (%)		
		DM (N = 109)	Non-DM (N = 109)	*P*-value
csDMARDs	Total	109 (100.0)	109 (100.0)	1.000
	Methotrexate	101 (92.7)	102 (93.6)	1.000
	Others	46 (42.2)	51 (46.8)	0.583
bDMARDs	Total	16 (14.7)	6 (5.5)	0.041
	TNFi	11 (10.1)	4 (3.7)	0.118
	IL6i	6 (5.5)	2 (1.8)	0.219
	T-cell	4 (3.7)	0 (0.0)	0.125
tsDMARDs		0 (0.0)	0 (0.0)	1.000
CSs		65 (59.6)	62 (56.9)	0.711
Analgesics	Total	103 (94.5)	96 (88.1)	0.167
	Acetaminophen	24 (22.0)	23 (21.1)	1.000
	Acetaminophen /Opioids	10 (9.2)	6 (5.5)	0.454
	NSAIDs	102 (93.6)	93 (85.3)	0.093
	Opioids	0 (0.0)	4 (3.7)	0.125
	Others	25 (22.9)	17 (15.6)	0.185

bDMARDs=biological disease-modifying antirheumatic drugs; CSs=corticosteroids; csDMARDs=conventional synthetic disease-modifying antirheumatic drugs; DM=diabetes mellitus; IL6i=interleukin-6 inhibitor; NSAID=non-steroidal anti-inflammatory drug; T-cell=selective T-cell co-stimulation modulator; TNFi=tumor necrosis factor α inhibitor; tsDMARDs=targeted synthetic disease-modifying antirheumatic drugs; P-values were calculated using McNemar test

Conclusion: Medical costs for RA were higher in the DM group than in the non-DM group because of more prevalent use of biological DMARDs in the DM group.
REFERENCES:
[1] Gabriel SE et al., *Arthritis Res Ther*. 2009;11(3):229.
[2] Giacomelli R et al., *Expert Rev Clin Immunol*. 2016;12(8):849-55.
[3] Crepaldi G et al., *PLoS One*. 2016;11(1):e0146991.
[4] JMDC claims database, Tokyo, Japan.
Disclosure of Interests: Eiichi Tanaka Speakers bureau: AbbVie GK, Asahi Kasei Pharma Corporation, Astellas Pharma Inc, Ayumi Pharmaceutical Corporation, Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., GlaxoSmithKline K.K., Kyowa Pharma Chemical Co., Ltd., Janssen Pharmaceutical K.K., Mochida Pharmaceutical Co., Ltd., Pfizer, Takeda Pharmaceutical Co., Ltd, and Teijin Pharma Ltd., Eisuke Inoue Speakers bureau: Pfizer Japan, Bristol-Myers Squibb K.K., Ryoko Sakai Speakers bureau: Bristol Myers Squibb Co., Ltd., Grant/research support from: Tokyo Women's Medical University (TWMU), particularly the Division of Multidisciplinary Management of Rheumatic Diseases, Department of Rheumatology, has received unrestricted research grants from Ayumi Pharmaceutical Co.; Chugai Pharmaceutical Co., Ltd.; Eisai Co., Ltd., Nippon Kayaku Co., Ltd.; Taisho Toyama Pharmaceutical Co., Ltd.; Takeda Pharmaceutical Co., Ltd.; Mitsubishi Tanabe Pharma Co.; and Teijin Pharma Ltd., with which TWMU paid the salaries of RS., Iwasaki Katsuhiko: None declared, Ayako Shoji: None declared, masayoshi harigai Speakers bureau: AbbVie GK, Ayumi Pharmaceutical Corporation, Bristol-Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., Pfizer Japan Inc., and Takeda Pharmaceutical Co., Ltd., Consultant of: AbbVie GK, Bristol-Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd., Eli Lilly Japan K.K., and Gilead Sciences Inc., Grant/research support from: AbbVie GK, and Asahi Kasei Corp., Astellas Pharma Inc., Ayumi Pharmaceutical Corporation, Bristol-Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd. Daiichi-Sankyo, Inc., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Corporation., Nippon Kayaku Co., Ltd., Taisho Pharmaceutical Co., Ltd., and Takeda Pharmaceutical Co., Ltd.
DOI: 10.1136/annrheumdis-2021-eular.2770

POS0552 DIASTOLIC DYSFUNCTION ASSOCIATED WITH INCREASED ACTIVITY IN RHEUMATOID ARTHRITIS

S. Lugo-Perez[1], D. Á. Galarza-Delgado[2], J. R. Azpiri-López[1], I. J. Colunga-Pedraza[2], N. Guajardo-Jauregui[2], A. B. Rodriguez-Romero[2], A. Cárdenas[2], H. Azpiri-Diaz[1], O. A. Cepeda-Ayala[1]. [1]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico*; [2]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*

Background: Cardiovascular disease (CVD) is the main cause of mortality in patients with rheumatoid arthritis (RA) reflected by a higher prevalence of cardiovascular risk factors (CVRFs), a chronic systemic inflammatory state and heart failure compared to the general population (1). Left ventricular diastolic dysfunction (LVDD) is attributable to structural abnormalities such as hypertrophy or interstitial fibrosis and impaired myocyte relaxation resulting from ischemia and is frequently asymptomatic (2). The presence of LVDD it could be considered as the first step to development of heart failure.
Objectives: The aim of the study is to identify the association of disease activity and the presence of LVDD in patients with RA.
Methods: A cross-sectional, observational, and comparative study of RA subjects that fulfilled ACR / EULAR 2010 classification criteria, aged 40-75 years. Subjects were evaluated by a transthoracic echocardiogram performed and reviewed by two certified echocardiographers. A total of fifty-one RA patients diagnosed with LVDD were included according to the 2016 American Society of Echocardiography (ASE). Distribution was evaluated with the Kolmogorov-Smirnov test. Descriptive analysis was done using measures of central tendency. Chi square, Student´s t test and Mann-Whitney U test were used for comparations between groups. A *p* value <0.05 was considered statistically significant.
Results: We found no statistical difference between groups regarding age, gender, comorbidities (type 2 diabetes mellitus, hypertension, dyslipidemia and, active smoking) and body mass index. Patients with LVDD demonstrated a higher disease activity evaluated by disease activity score using 28 joints-C reactive protein (DAS28-PCR) (4.88 vs 3.56, *p*= 0.004) (Table 1). It was observed that patients with LVDD have a higher prevalence of being in the high disease activity category (41.2% vs. 13.7%, *p*= 0.002) (Figure 1). When performing a binary logistic regression, it was found that a high disease activity was the only independent predictor for the presence of LVDD, with an OR 4.70, (95% CI 1.63-13.50, *p*= 0.004).

Table 1. Demographic and disease characteristics

	RA patients with LVDD (n=51)	RA patients without LVDD (n=51)	*p*
Women, n (%)	50 (98)	47 (92.2)	NS
Age, years ± SD	56.12 ± 8.76	53.91 ± 5.61	NS
HTN, n (%)	17 (33.3)	13 (25.5)	NS
T2DM, n (%)	6 (11.8)	10 (19.6)	NS
Dyslipidemia, n (%)	17 (33.3)	11 (21.6)	NS
Active smoking, n (%)	5 (9.8)	5 (9.8)	NS
BMI kg/m^2 ± SD	28.20 ± 4.89	29.40 ± 5.13	NS
Disease duration, years (p25-p75)	10.70 (5.16-17.87)	5.66 (2.67-15.64)	**0.033**
DAS28-CRP, median (p25-p75)	4.88 (3.53-5.45)	3.56 (3.00-4.69)	**0.004**

NS, no significative; HTN, hypertension; T2DM, type 2 diabetes mellitus; BMI, body mass index; DAS28, disease activity score using 28 joints; CPR, C reactive protein

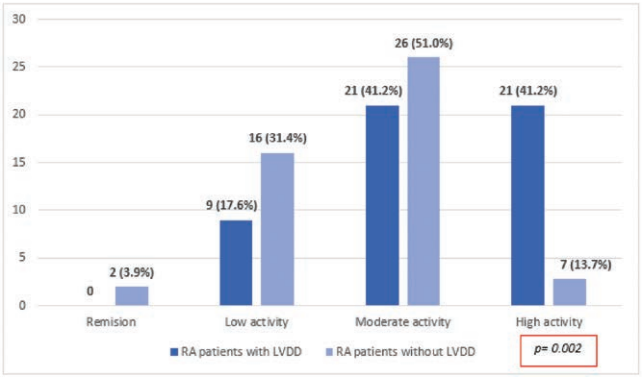
Conclusion: Patients with RA and LVDD have a higher disease activity, so emphasis should be placed on strict antirheumatic treatment and cardiovascular therapies to avoid the risk of developing CVD and the progression to heart failure. Logistic regression demonstrates that inadequate disease control is an independent factor from traditional CVRFs for the presence of LVDD.

REFERENCES:

[1] Dal Piaz EC, Cioffi G, Ognibeni F, et al. Incidence and predictors of new onset left ventricular diastolic dysfunction in asymptomatic patients with rheumatoid arthritis without overt cardiac disease. Monaldi Arch Chest Dis 2019;89(3) doi: 10.4081/monaldi.2019.1053

[2] Abdul Muizz AM, Mohd Shahrir MS, Sazliyana S, et al. A cross-sectional study of diastolic dysfunction in rheumatoid arthritis and its association with disease activity. Int J Rheum Dis 2011;14(1):18-30. doi: 10.1111/j.1756-185X.2010.01593.x

Figure 1. Classification of disease activity by DAS28-CRP



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2786

POS0553

IMPACT OF RHEUMATOID ARTHRITIS ON LEFT VENTRICULAR REMODELING

S. Lugo-Perez[1], J. R. Azpiri-López[1], I. J. Colunga-Pedraza[2], D. Á. Galarza-Delgado[2], A. B. Rodriguez-Romero[2], N. Guajardo-Jauregui[2], A. Cárdenas[2], H. Azpiri-Diaz[1], O. A. Cepeda-Ayala[1]. [1]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico*; [2]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*

Background: Patients with Rheumatoid Arthritis (RA) have a higher prevalence of cardiovascular diseases (1) and a strong association with abnormalities in the left ventricle (LV) geometry. Both concentric and eccentric remodeling have been determined as an independent factor for sudden cardiac arrest in the general population with normal or slightly decreased ventricular function (2) but there is still controversy about the factors involved and the pathophysiology in patients with RA.

Objectives: The aim of the study is to determine the characteristics of LV geometry and the impact of RA.

Methods: A cross-sectional, observational, and comparative study of fifty-two RA patients that fulfilled ACR / EULAR 2010 classification criteria, aged 40-75 years. Controls were included and matched by age, gender, and comorbidities. Subjects were evaluated using a transthoracic echocardiogram performed and reviewed by two certified echocardiographers. Ventricular geometry was evaluated with indexed left ventricular mass and relative wall thickness. Distribution was evaluated with the Kolmogorov-Smirnov test. Descriptive analysis was done using measures of central tendency. Chi square, Student's t test and Mann-Whitney U test were used for comparations between groups. A logistic binary regression was performed with the traditional cardiovascular risk factors (CVRFs), age and RA diagnosis. A p value <0.05 was considered statistically significant.

Results: No significant differences were found in the traditional CVRFs (type 2 diabetes mellitus, dyslipidemia, active smoking, and hypertension) (Table 1). Most of the subjects reported normal geometry in both groups (55.8% for RA group vs 64.0% for controls). A higher prevalence of eccentric hypertrophy was found in the RA group, 13 (25%) subjects versus 3 (6%) in the control group, p = 0.009. The binary regression showed that the diagnosis of RA was the only independent risk factor for the presence of eccentric hypertrophy, OR 7.22 95% CI (1.68-31.02, p = 0.008).

Table 1. Demographic characteristics and echocardiographic findings.

	RA (n=52)	Control (n=50)	*p*
Age, years ± DE	51.4 ±6.2	51.1 ± 5.5	NS
Women, n (%)	51 (98.1)	49 (98.0)	NS
Active smoking, n (%)	8 (15.4)	8 (16.0)	NS
Dyslipidemia, n (%)	11 (21.2)	13 (26.0)	NS
Type 2 Diabetes Mellitus, n (%)	5 (9.6)	5 (10.0)	NS
HTN, n (%)	8 (15.4)	10 (20.0)	NS
BMI kg/m^2, median (p25-p75)	27.8 (24.5-31.4)	28.3 (25.4-30.3)	NS
BSA, median (p25-p75)	1.7 (1.6-1.8)	1.8 (1.6-1.9)	**0.003**
Systolic blood pressure, mmHg (p25-p75)	119.5 (110.0-127.5)	120.0 (110.7-130.0)	NS
Echocardiography findings			
LVPWTd, median (p25-p75)	0.9 (0.8-1.0)	0.9 (0.8-1.0)	NS
LVIDd, median (p25-p75)	4.8 (4.3-5.2)	4.6 (4.5-4.9)	NS
LV mass, median (p25-p75)	131.2 (119.5-155.7)	131.2 (113.2-154.3)	NS
LV mass index, median (p25-p75)	78.6 (69.7-95.6)	76.0 (66.7-84.6)	NS
RWT, mean ± SD	0.4 ± 0.09	0.4 ± 0.07	NS

NS, no significant; BMI, body mass index; BSA, body surface area; LVPWTd, left ventricular posterior wall thickness at end-diastole; LVIDd, left ventricular internal dimension at end-diastole; RWT, relative wall thickness.

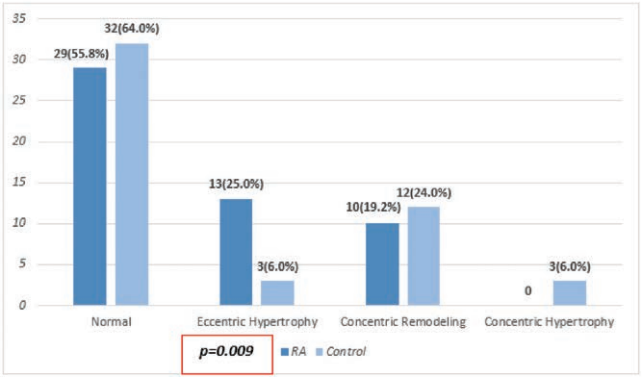
Conclusion: There is a higher prevalence of eccentric remodeling in patients with RA independently of traditional CVRF. The diagnosis of RA is an independent risk factor for the presence of eccentric hypertrophy that is associated with higher mortality. Treatment of cardiovascular comorbidities should be intensified in those patients with abnormalities in LV geometry in order to prevent cardiovascular diseases such as heart failure.

REFERENCES:

[1] You S, Cho CS, Lee I, et al. A systems approach to rheumatoid arthritis. PLoS One 2012;7(12):e51508. doi: 10.1371/journal.pone.0051508

[2] Pascale V, Finelli R, Giannotti R, et al. Cardiac eccentric remodeling in patients with rheumatoid arthritis. Sci Rep 2018;8(1):5867. doi: 10.1038/s41598-018-24323-0

Figure 1. Abnormalities in left ventricular geometry in patients with RA.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2790

POS0554

MEDICAL COST AND RESOURCE USE IN PATIENTS STARTING TREATMENT FOR RHEUMATOID ARTHRITIS TREATED WITH AND WITHOUT CORTICOSTEROIDS IN JAPAN

E. Tanaka[1], E. Inoue[1,2], R. Sakai[1], I. Katsuhiko[3], A. Shoji[3], M. Harigai[1]. [1]*Tokyo Women's Medical University School of Medicine, Department of Rheumatology, Tokyo, Japan*; [2]*Showa University, Showa University Research Administration Center (SURAC), Tokyo, Japan*; [3]*Medilead Inc., Tokyo, Japan*

Background: The 2019 update of the European League Against Rheumatism (EULAR) treatment recommendations strongly recommends co-administration of corticosteroids (CSs) with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) in patients with RA as bridging therapy to improve the success rate of the first-line treatment and to avoid disease flare-ups[1]; however, current treatment guidelines for RA in Japan do not clearly mention about their use. Poor disease management after the initial diagnosis can affect the overall use of health services and the economic burden on patients.

Objectives: To describe medical costs and resource use in patients with early RA treated with and without oral or injectable corticosteroids (CSs) as part of their initial treatment with disease-modifying antirheumatic drugs (DMARDs) in Japan.

Methods: We used a large Japanese administrative claims database constructed by the Japan Medical Data Center (JMDC)[2]. Patients with the International Classification of Diseases 10th revision (ICD-10) codes for RA were enrolled at the first DMARDs prescription after no DMARDs prescription period for 6-months (index date) in the period from 1/1/2012 to 12/31/2017. Patients who were observable for 12 months after the index date as a follow-up period were included. Patients treated with CSs within the follow-up period were compared with those without them (CS and non-CS group). The primary endpoint was mean medical cost per patient in the 12-month follow-up period. The secondary endpoints were costs for drugs, treatments, and materials and the proportions of patients using the subcategories of each resource. Drugs were divided into medications for RA or for comorbidities including adverse events (AEs). Costs in JPY were converted into EUR (1 EUR = 125 JPY in 2020).

Results: Eligible patients of 1,670 and 1,487 were identified as the CS and non-CS group (median age: 51 years and 50 years). Total mean costs were significantly higher in the CS group (CS, 4,448 EUR, non-CS 3,208 EUR; P< 0.05). Drug, treatment, and material costs were significantly higher in the CS group than in the non-CS group (drug for RA and AEs, CS 2,367 EUR, non-CS 1,581 EUR, P < 0.05; drug for RA only, CS 2,265 EUR, non-CS 1,516 EUR, P < 0.05; treatment, CS 1,987 EUR, non-CS 1,562 EUR, P < 0.05; material, CS 94 EUR, non-CS 65 EUR; P < 0.05). The resource use in almost all drug subcategories were higher in the CS group (Table 1), as well as in all treatment and material subcategories.

Table 1. Number and proportion of patients who used drugs

Type of drug		Drug use, n (%)		
		CS (N = 1,670)	Non-CS (N = 1,487)	*P*-value
csDMARDs	Total	1,635 (97.9)	1,447 (97.3)	0.328
	Methotrexate	1,481 (88.7)	1,315 (88.4)	0.870
	Others	790 (47.3)	551 (37.1)	< 0.001
bDMARDs	Total	342 (20.5)	181 (12.2)	< 0.001
	TNFi	252 (15.1)	129 (8.7)	< 0.001
	IL6i	93 (5.6)	40 (2.7)	< 0.001
	T-cell	40 (2.4)	17 (1.1)	0.012
Analgesics	Total	1,512 (90.5)	1,274 (85.7)	< 0.001
	Acetaminophen	379 (22.7)	273 (18.4)	0.003
	Acetaminophen / Opioids	84 (5.0)	37 (2.5)	< 0.001
	NSAIDs	1,459 (87.4)	1,214 (81.6)	< 0.001
	Opioids	16 (1.0)	10 (0.7)	0.491
	Others	198 (11.9)	101 (6.8)	< 0.001
Antibiotics	Total	1,086 (65.0)	873 (58.7)	< 0.001
	Antibacterial drugs	1,022 (61.2)	800 (53.8)	< 0.001
	Antifungal drugs	133 (8.0)	86 (5.8)	0.019
	Antiviral drugs	172 (10.3)	129 (8.7)	0.136
	Antiparasitic drugs	5 (0.3)	8 (0.5)	0.443
Anti-osteoporotic drugs		341 (20.4)	95 (6.4)	< 0.001

bDMARDs=biological disease-modifying antirheumatic drugs; CSs=corticosteroids; csDMARDs=conventional synthetic disease-modifying antirheumatic drugs; IL6i=interleukin-6 inhibitor; NSAID=non-steroidal anti-inflammatory drug; T-cell=selective T-cell co-stimulation modulator; TNFi=tumor necrosis factor α inhibitor; P-values were calculated using Chi-square test

Conclusion: Patients with early RA treated with CSs in the first year after starting DMARDs tended to use more resources and have higher medical costs than patients not treated with CSs.

REFERENCES:

[1] Smolen JS et al., *Ann Rheum Dis*. 2020;79(6):685-699.

[2] JMDC claims database, Tokyo, Japan.

Disclosure of Interests: Eiichi Tanaka Speakers bureau: AbbVie GK, Asahi Kasei Pharma Corporation, Astellas Pharma Inc, Ayumi Pharmaceutical Corporation, Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., GlaxoSmithKline K.K., Kyowa Pharma Chemical Co., Ltd., Janssen Pharmaceutical K.K., Mochida Pharmaceutical Co., Ltd., Pfizer, Takeda Pharmaceutical Co., Ltd, and Teijin Pharma Ltd., Eisuke Inoue Speakers bureau: Pfizer Japan, Bristol-Myers Squibb K.K., Ryoko Sakai Speakers bureau: Bristol Myers Squibb Co., Ltd., Grant/research support from: Tokyo Women's Medical University (TWMU), particularly the Division of Multidisciplinary Management of Rheumatic Diseases, Department of Rheumatology, has received unrestricted research grants from Ayumi Pharmaceutical Co.; Chugai Pharmaceutical Co., Ltd.; Eisai Co., Ltd., Nippon Kayaku Co., Ltd.; Taisho Toyama Pharmaceutical Co., Ltd.; Takeda Pharmaceutical Co., Ltd.; Mitsubishi Tanabe Pharma Co.; and Teijin Pharma Ltd., with which TWMU paid the salaries of RS., Iwasaki Katsuhiko: None declared, Ayako Shoji: None declared, masayoshi harigai Speakers bureau: AbbVie GK, Ayumi Pharmaceutical Corporation, Bristol-Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., Pfizer Japan Inc., and Takeda Pharmaceutical Co., Ltd., Consultant of: AbbVie GK, Bristol-Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd., Eli Lilly Japan K.K., and Gilead Sciences Inc., Grant/research support from: AbbVie GK, and Asahi Kasei Corp., Astellas Pharma Inc., Ayumi Pharmaceutical Corporation, Bristol-Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd. Daiichi-Sankyo, Inc., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Corporation., Nippon Kayaku Co., Ltd., Taisho Pharmaceutical Co., Ltd., and Takeda Pharmaceutical Co., Ltd.

DOI: 10.1136/annrheumdis-2021-eular.2805

POS0555 THE NATURAL COURSE OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE FOCUSING ON LUNG PHYSIOLOGY: A PROSPECTIVE OBSERVATIONAL COHORT STUDY (PART 1)

S. H. Chang[1], J. S. Lee[2], J. S. Lee[3], C. H. Park[4], M. U. Kim[5], Y. J. Ha[6], E. H. Kang[6], Y. A. Lee[7], Y. Park[8], J. Y. Choe[9], E. Y. Lee[10]on behalf of KOrean Rheumatoid Arthritis Interstitial Lung disease (KORAIL) cohort study group. *[1]Soonchunhyang University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Cheonan, Korea, Rep. of (South Korea)*; *[2]Clinical Research Center, Asan Institute for Life Sciences, Asan Medical Center, Department of Medical Stastics, Seoul, Korea, Rep. of (South Korea)*; *[3]GENOME INSIGHT Inc.,., Seoul, Korea, Rep. of (South Korea)*; *[4]Soonchunhyang University College of Medicine, Department of Radiology, Cheonan, Korea, Rep. of (South Korea)*; *[5]SMG-SNU Boramae Medical Center, Department of Radiology, Seoul, Korea, Rep. of (South Korea)*; *[6]Seoul National University Bundang Hospital, Division of Rheumatology, Department of Internal Medicine, Seongnam, Korea, Rep. of (South Korea)*; *[7]Kyung Hee University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; *[8]Yonsei University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; *[9]Catholic University of Daegu College of Medicine, Division of Rheumatology, Department of Internal Medicine, Daegu, Korea, Rep. of (South Korea)*; *[10]Seoul National University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*

Background: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). However, there are few prospective studies for the natural course of lung physiology in most patients with RA-ILD.

Objectives: To assess the natural course of lung physiology of RA-ILD and the relation between arthritis activity and pulmonary physiology in patients with RA-ILD.

Methods: The KOrean Rheumatoid Arthritis ILd (KORAIL) cohort is the prospective observational cohort and aims to investigate the natural course of RAILD. Based on either 1987 or 2020 ACR criteria, patients diagnosed with RA and ILD based on CT scan were recruited from six tertiary medical hospitals in Korea since January 2015. RA disease activity was assessed using swollen and tender joint count by treating physician, inflammatory markers including CRP and ESR, and patient's global assessment annually. Pulmonary function tests (PFT), including FVC, FEV1, DLCO, and chest CT scan, were conducted annually.

Results: We analyzed 163 patients at baseline (V1), 141 at 1-year (V2), 122 at 2-year (V3), and 88 at 3-year follow-up (V4). The mean (±SD) duration since RA diagnosis and since ILD diagnosis was 7.6±8.0 and 2.7±3.1 years, respectively. The female to male ratio was about 2:1, and 58.9% of patients (n=96) were 65 years old or older. Only two patients were negative for RF and anti-CCP; 98.7% of patients (n=161/163) were positive for RF (n=143, 87.7%) or anti-CCP antibody (n=154, 94.5%). At enrollment, one-hundred-nine patients (66.9%) had FVC ≥80 % of predicted. Twenty-five patients (15.3%) showed FEV1/FVC≥0.7, of which seventeen patients, only ten percent of a total cohort (10.4%), had FVC ≥80% of predicted, which corresponds to the obstructive pattern. Proportion of patients showed a ≥10-point decline from the enrollment in FVC of the predicted value were around 10% at every year (Table 1). The proportion of patients with a relative decline of ≥10% from the enrollment in FVC predicted was increased every year because of cumulation. The proportion of patients with a relative decline of ≥10% from the previous visit in FVC predicted was also around 10-15% every year. Proportions of patients with 55% or more DLco % pred. has been decreased annually; 78.5% (n=128/158) at V1, 72.9% (n=105/139) at V2, 68.7% (n=90/117) at V3, and 56.6% (n=56/85) at V4. Patients with a relative decline of ≥10% from the enrollment in DLco predicted was 38 (27.5 %) at V2 and 37 (31.9%) at V3. Patients with a relative decline of ≥10% from the previous visit in DLco predicted was 29 (25.2%) at V3. Of note, thirty patients (21.7%) showed a relative 10% or more increase from enrollment in DLco predicted at V2, and so did 30 patients (25.9%) at V3.

Table 1. The analysis of forced vital capacity (FVC) in KORIL cohort

	V1 (enrollment)	V2 (1-year)	V3 (2-year)	V4 (3-year)
FVC (mL), mean±SD	2549.5 ± 743.3	2479.5± 764.4	2435.8 ± 742.8	2405.7 ± 731.2
FVC % of predicted, mean±SD	84.70 ± 16.74	84.7±18.1	84.3 ± 17.6	83.1 ± 19.1
Rate of FVC decline, mL·year^{-1} (95% CI)	-	-14 (-49, 21)	-62 (-104, -21)	-
A 10-point decline from V1 in predicted FVC value, n (%)	-	10 (7.1)	16 (13.3)	8 (9.4)
Relative decline of 10% from V1 in predicted FVC value, n (%)	-	17 (12.1)	23 (18.9)	17 (19.3)
Relative decline of 10% from the previous visit in predicted FVC value, n (%)	-	17 (12.1)	17 (14.2)	13 (15.3)

Conclusion: Annually, about 10-15% of patients experience a relative ≥10% decline from the previous visit in FVC predicted value in RA-ILD.

Acknowledgements: This work was supported by the Korea Health Technology R&D Project through the Korea Health Industry Development Institute, funded by the Ministry of Health and Welfare, Republic of Korea (grant no.HI14C1277).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2810

POS0556 USEFULNESS OF FDG-PET/CT FOR PREDICTING SPONTANEOUS REGRESSION IN MTX ASSOCIATED LYMPHOPROLIFERATIVE DISORDER WITH RHEUMATOID ARTHRITIS

T. Kameda[1], S. Nakashima[1], H. Shimada[1], R. Wakiya[1], M. Mahmoud Fahmy Mansour[1], M. Kato[1], K. Sugihara[1], Y. Ushio[1], H. Dobashi[1]. [1]*Kagawa University, Department of Internal Medicine, Division of Haematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kita-gun, Japan*

Background: Recently, there are many reports from Japan about methotrexate associated lymphoproliferative disorder (MTX-LPD). We are investigating the predictive factor of spontaneous regression (SR) in MTX-LPD. On the other hand, FDG-PET/CT is used for diagnosis of LPD including malignant lymphoma. In addition, it was reported that imaging biomarkers such as metabolic tumor volume (MTV) and total lesion glycolysis (TLG) could predict the prognosis of malignant tumor (1, 2). However, there is no report that these imaging biomarkers could predict the SR of MTX-LPD.

Objectives: We investigate the usefulness of FDG-PET/CT for predictive factor of SR in MTX-LPD.

Methods: We enrolled 24 RA patients who diagnosed MTX-LPD and performed FDG-PET/CT from 2005 to 2019. We divided these cases into spontaneous regression cases (SR group; 15 cases) and cases that treated with chemotherapy after MTX discontinuation (CTx group; 9 cases), and compared the difference as follow subjects between two groups; clinical data including histopathological findings, SUVmax to evaluate malignant tumor activity by FDG-PET/CT, MTV and TLG which refer to metabolically active volume of the tumor segmented FDG-PET/CT. In addition, we analyzed cut off levels, sensitivity and specificity using statistical software JMP.

Results: Diffuse large B cell lymphoma (DLBCL) and Hodgkin lymphoma (HL) were 5 and 1 cases in SR group, and 1 and 5 cases in CTx group. In addition, MTV and TLG by FDG-PET/CT was significantly lower in SR group, although SUVmax is no difference between two groups (figure 1). Cut off levels of MTV and TLG were 103.12 ml (sensitivity; 88.9%, specificity; 86.7%) and 361.75 ml (sensitivity; 88.9%, specificity; 86.7%), respectively.

Conclusion: We suggested that MTV and TLG were useful for predict of SR in MTX-LPD.

REFERENCES:

[1] Chen HH, Chiu NT, Su WC. et al. Prognostic value of whole-body total lesion glycolysis at pretreatment FDG PET/CT in non-small cell lung cancer. Radiology. 2012 Aug;264(2):559-66.

[2] Chu KP, Murphy JD, La TH. et al. Prognostic value of metabolic tumor volume and velocity in predicting head-and-neck cancer outcomes. Int J Radiat Oncol Biol Phys. 2012 Aug 1;83(5):1521-7.

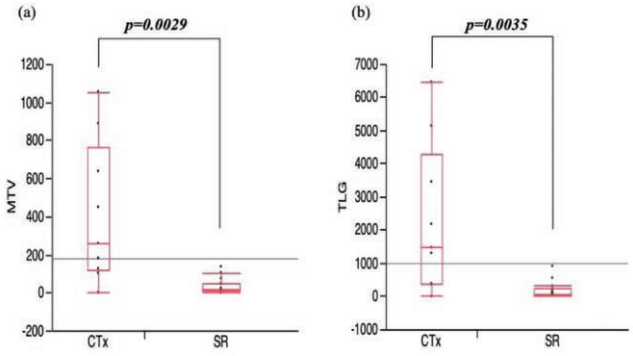


Figure 1. Comparison of the level of MTV(a) and TLG (b).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2812

POS0557 THE RELATION BETWEEN INVOLVEMENT OF INDIVIDUAL JOINTS OF THE UPPER EXTREMITY AND GRIP FORCE IN EARLY RHEUMATOID ARTHRITIS

M. Rydholm[1,2], A. Sharma[2], I. Wikström[1,2], L. T. H. Jacobsson[2,3], C. Turesson[1,2]. [1]*Skåne University Hospital, Department of Rheumatology, Malmö, Sweden*; [2]*Lund University, Rheumatology, Department of Clinical Sciences, Malmö, Malmö, Sweden*; [3]*Gothenburg University, Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, Gothenburg, Sweden*

Background: Rheumatoid arthritis (RA) has a major impact on hand function in many patients.

Objectives: The objective of this study was to investigate the relation between swelling and tenderness of individual joints in the upper extremities and grip force in patients with early RA.

Methods: An inception cohort of patients with early RA (symptom duration ≤12 months), recruited in 1995-2005, was investigated and followed in a structured program. All patients were examined by the same rheumatologist according to a structured protocol, and swelling and tenderness of individual joints was recorded. Grip force (Newton, N) was measured using the electronic instrument Grippit (AB Detektor, Gothenburg, Sweden). Average grip force values of each hand were evaluated and compared to the expected, based on age- and sex-specific reference values from the literature (1). Grip force was expressed as % of expected values. Linear regression analyses were used to assess the relation between upper extremity joint involvement in individual joints and grip force, using the presence/absence of synovitis/tenderness in each joint as covariates. For the multivariate analysis, covariates with $p<0.10$ in the univariate analyses were selected. In cases with major collinearity (Spearman's $r>0.3$), the covariate with the stronger association in the univariate analysis was included.

Results: A total of 215 patients with early RA (71 % women; mean age 60 years) were investigated. The median symptom duration at inclusion was 7 months; interquartile range 5-10. The median 28 joint counts for swollen joints was 7 (interquartile range, IQR 5-11) and for tender joints 4 (IQR 1-9). In univariate analyses, swelling of the wrist, each metacarpophalangeal (MCP) joint and proximal interphalangeal (PIP) joints III and V, as well as tenderness of the elbow, wrist and each MCP and PIP joint were associated with significantly reduced grip force in the right hand. In the left extremity, corresponding associations were observed for swelling of the wrist, each MCP joint and PIP joints I and V, and for tenderness of the wrist and each MCP and PIP joint. In multivariate analysis, wrist synovitis was associated with reduced grip force (β -11.0 and -14.3 % of expected, respectively). There were also independent significant associations for tenderness of MCP IV and the elbow with reduced grip force in the right hand, and for swelling of MCP I and MCP V with reduced grip force in the left hand (Table 1).

Table 1. Joint involvement associated with average grip force (% of expected value), multivariate linear regression

	Unstandardized β	95 % CI
Right hand		
Swollen Wrist	-11.0	-17.5 to -4.5
Tender MCP IV	-15.6	-25.2 to -6.0
Tender PIP V	-2.3	-12.0 to 7.3
Tender Elbow	-11.7	-22.1 to -1.3
Left hand		
Swollen Wrist	-14.3	-20.4 to -7.6
Swollen MCP I	-7.6	-14.6 to -0.6
Swollen MCP V	-11.7	-21.9 to -1.5
Swollen PIP I	-0.8	-9.2 to 7.5

MCP: Metacarpo phalangeal jointPIP: Proximal interphalangeal joint

Conclusion: Involvement of several different joints in the upper extremity contributes to impaired hand function. Clinical synovitis of the wrist was associated with reduced grip force in both hands. In the left hand, arthritis of the thumb had a major impact on grip force. In general, MCP involvement was found to be more important for the grip than PIP involvement.

REFERENCES:

[1] Nilsen T et al. Scand J Occup Ther 2012; 19: 288-96

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2837

POS0558 STATE OF ADIPOCYTOKINES IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH SUBCLINICAL ATHEROSCLEROSIS

I. Krivotulova[1], T. Chernysheva[1]. [1]*Orenburg State Medical University (OrSMU), Department of Internal Diseases, Orenburg, Russian Federation*

Background: The causes of accelerated atherosclerosis in rheumatoid arthritis (RA) are not completely understood [1]. Therefore, there is a need to identify new biomarkers of increased cardiovascular risk in RA.

Objectives: To establish the relationship of adipocytokines (adiponectin and leptin) with metabolic and inflammatory markers of subclinical atherosclerosis in RA patients.

Methods: The study included 88 women with RA according to the ACR (American College of Rheumatology)/EULAR (European League Against Rheumatism) criteria, 2010 [2] who visited the adaptation therapy clinic of Orenburg State Medical University. The mean±SD age was 46.43±8.5 years and the mean±SD disease duration was 8.21±5.56 years.

We evaluated the following laboratory parameters in all patients: erythrocyte sedimentation rate (ESR), total cholesterol, triglycerides (TAG), high-density lipoproteins (HDL), low-density lipoproteins (LDL) and C-reactive protein (CRP). Serum concentrations of adiponectin, leptin, rheumatoid factor (RF), tumor necrosis factor-α (TNF-α), and interleukin-17 (IL-17) were determined by enzyme-linked immunosorbent assay (ELISA).

We carried out ultrasound (US) duplex scanning of the carotid arteries by the device "Philips Epiq 7" with linear transducer with frequency of 4-18 MHz with the division into 2 groups of patients: group I consisted of 44 women with US signs of subclinical atherosclerosis, group II – 44 women without these signs. The control group included 30 women without inflammatory joint diseases and US signs of subclinical atherosclerosis and similar in gender, age and body mass index (BMI) to RA patients.

The program STATISTICA, 12.0 was used for statistical analysis.

Results: The serum adiponectin level was significantly higher in RA patients compared to the control group (p<0.0001): 40.88±13.60 ng/ml versus 22.75±11.27 ng/ml. The level of leptin in the blood serum of women with RA and healthy individuals was approximately the same and amounted to 18.07±14.02 ng/ml and 16.60±11.45 ng/ml respectively. When comparing the levels of adipocytokines in RA patients, the predominance of concentrations of both adipokines in patients with paraclinical atherosclerosis were noted. The adiponectin concentration was 46.08±14.44 ng/ml versus 35.70±10.51 ng/ml (p<0.001). The leptin level was 26.40±20.06 ng/ml versus 14.96±16.62 ng/ml (p<0.01).

Correlation analysis showed an negative relationship between adiponectin levels and metabolic markers of atherosclerosis: BMI (r=-0.52; p<0.05), neck circumference (NC) (r=-0.50; p<0.05), levels of LDL (r=-0.77; p<0.001) and TAG (r=-0.59; p<0.05) as well as proinflammatory cytokines: TNF-α (r=-0,48; p<0.05), IL-17 (r=-0.60; p<0.01) in patients of both groups. The increase in adiponectin concentration in group II patients was associated with the duration of administration of methotrexate (r=0.49; p<0.05) and glucocorticosteroids (r=0.71; p<0.001). Direct correlations were found between the level of leptin and BMI (r=0.48; p<0.05), NC (r=0.48; p<0.05), LDL (r=0.54; p<0.05) and TAG (r=0.45; p<0.05), CRP (r=0.49; p<0.05) and IL-17 (r= 0.52; p<0.05) in group I patients.

Conclusion: There is a significant increase in the production of adipocytokines in RA with subclinical atherosclerosis. Correlations of levels of adipokines with metabolic and inflammatory markers of atherosclerosis, on the one hand, indicate the influence of adipose tissue on systemic inflammation and, on the other hand, confirm the involvement of proinflammatory cytokines in the development of atherosclerotic vascular damage in patients with RA.

REFERENCES:

[1] Mahmoudi M, Aslani S, Fadaei R, Jamshidi AR. New insights to the mechanisms underlying atherosclerosis in rheumatoid arthritis. Int J Rheum Dis. 2017;20(3):287-297. doi: 10.1111/1756-185X.12999

[2] Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2010;69:1580—8. doi:10.1136/ard.2010.138461

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2853

POS0559 SPECKLE TRACKING BETTER DETECTS SUBCLINICAL MYOCARDIAL DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

I. Kirillova[1], T. Popkova[1], Y. Gorbunova[1], A. Volkov[1], E. Nasonov[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Systemic Rheumatic Diseases, Moscow, Russian Federation*

Background: The risk of developing cardiovascular complications and death in rheumatoid arthritis (RA) is 50% higher than in the total population. These clinical events depend from risk factors for cardiovascular diseases, chronic inflammation and inflammatory myocardial infiltration. A new method for detecting early myocardial dysfunction is echocardiography using speckle tracking echocardiography.

Objectives: to determine the frequency of myocardial dysfunction (lower global longitudinal epicardial strain of left ventrical (LV), diastolic dysfunction of left ventricle (LVDD)) using standard and novel echocardiographic methods in patients (pts) with RA prior to therapy with bDMARDs, examine its relationship with markers of inflammation.

Methods: a total of 28 pts with a valid diagnosis of RA (ACR/EULAR, 2010): 23 f (82%) /5 m (18%) were included, median (Me) age - 56 [interquartile range (IR) 34;65] years, Me RA duration-14,5 [IR 7;87] months; all pts with RA demonstrated a high disease activity (Me DAS28 6.06, [IR 5,4;6,6]), seropositive for IgM RF (88%) and/or ACCP (84%) without any experience of administration of bDMARDs. The control group consisted of 10 healthy subjects, which were matched by sex and age. All pts were assessed for traditional risk factors for cardiovascular disease (ESC guidelines, 2011), echocardiography, tissue Doppler imaging, and the speckle tracking assessment of left ventricle longitudinal strain. DD was allocated according to the ESC guidelines for the diagnosis and treatment of heart failure (2018). Arterial hypertension was detected in 5 pts with RA.

Results: In pts with RA LVDD was more often detected (8 (31%) vs 0%, p=0.05) than in controls. The values of E LV (0.77 [0.62;0.94] ms vs 1.25 [1.03;1.51] ms, p=0.0001) were lower than in control group. Speckle-tracking method detected lower global longitudinal epicardial strain (–16.5 [-18.9; -13.6]% vs –21.58 [-22.1;-20.4] %, p=0.0001). 17(61%) RA pts showed a decrease global longitudinal epicardial strain. There were no between-group differences in left ventricular ejection fraction, LV sizes, LV myocardial mass index in RA pts with controls. There were correlations between the global longitudinal epicardial strain and DAS28 (r=0,9, p<0,02), tender joint score (r=0,6, p<0,02), radiological stage (r=0,6, p<0,008); the presence of systemic manifestations (r=0,5, p<0,03).

Conclusion: In pts with RA frequently (61%) were detected lower global longitudinal epicardial strain, which are associated with a high activity of the inflammatory process. Speckle-tracking echocardiography is better at detecting early myocardial dysfunction than tissue Doppler.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2870

POS0560 CO-MORBIDITIES MAY NOT CHANGE TREATMENT CHARACTERISTICS OF THE RHEUMATOID ARTHRITIS PATIENTS

M. E. Tezcan[1], G. Geçmez[2], Ö. Volkan[1], N. Şen[1], S. Yilmaz-Oner[1]. [1]*Kartal Dr. Lütfi Kırdar Şehir Hastanesi, Rheumatology, İstanbul, Turkey*; [2]*Kartal Dr. Lütfi Kırdar Şehir Hastanesi, Internal Medicine, Istanbul, Turkey*

Background: Several co-morbidities may usually accompany rheumatoid arthritis (RA)(1). These can have direct or indirect implications for the severity of rheumatoid arthritis, the doctors' decision of disease-modifying treatment, and the functional disability of RA patients.

Objectives: It has been previously shown that various co-morbidities can have negative effects on the functional status, quality of life and life expectancy of RA patients individually (2). Here, we evaluated the effect of weight of all co-morbidities on treatment of RA patients and functional disability. Our hypothesis "The functional status of RA patients with moderate and severe co-morbidities is impaired compared to patients with mild co-morbidities, and the treatment characteristics of RA are different between these groups".

Methods: We included 246 RA patients who met the ACR / EULAR 2010 rheumatoid arthritis classification criteria. We divided the patients into two groups according to the Charlson comorbidity index (scores 0-2 mild,> 2 moderate and severe) (3). We compared the functional status of the two groups assessed by the health assessment questionnaire disability index (HAQ-DI). In addition, we compared disease-related characteristics between groups. We performed the Mann-Whitney U and chi-square tests where appropriate. Lastly, we also adjusted the age when comparing the continuous variables with ANCOVA.
Results: The patients with moderate and severe co-morbidities were older (p<0.001). All other demographic features were similar between the groups. Extra-articular involvement was more frequent in moderate and severe co-morbidity group (p=0.03). All other disease features and treatment modalities were similar between the groups. Additionally, after adjusting the age, none of the continuous features were different between the groups.

Table 1. Disease and demographic features and treatment characteristics of the patients.

	Mild co-morbidity group (n=180)	Moderate and severe co-morbidity group (n=66)	P	p** (age adjusted)
Age (year)	44.5±9.2	65.0±7.0	**P<0.001**	N/A
Gender (M/F)	34/146	16/50	0.5	
Smoking (%)	24 (13.3)	7 (10.6)	0.63	
Charlson co-morbidity index	1.38±0.48	3.3±0.6	**p<0.001**	**p<0.001**
Disease duration (month)	65.2±77.1	65.1±75.3	0.97	0.23
Swollen joint	0.3±1.5	0.2±0.6	0.92	0.86
Tender joint	0.6±1.6	0.3±1.0	0.38	0.50
ACPA positivity (%)	84 (46.6)	29 (43.9)	0.92	
RF positivity (%)	93 (51.6)	66 (58.3)	0.39	
DAS28-CRP	2.2±1.2	2.1±0.7	0.85	0.37
HAQ-DI	0.16±0.20	0.27±0.39	0.05	0.64
Extra-articular involvement (%)	3 (1.6)	5 (7.5)	**0.03**	
Joint deformity (%)	21 (11.6)	7 (10.6)	077	
Number of received DMARD	1.3±0.5	1.3±04	0.55	0.48
Steroid dosage (mg)	1.7±2.4	1.4±1.9	0.73	0.60
Ever receiving bDMARD (%)	21 (11.6)	3 (4.5)	0.09	

M: Male; F: Female; ACPA: Anti-Cyclic Citrullinated Peptide Antibody; RF: Rheumatoid factor; DAS-28: Disease activity score-28; HAQ-DI: Health assessment questionnaire disability index; DMARD: Disease modifying drugs; bDMARD: Biologic disease modifying drugs. **For continuous variables. Continuous variables shown as Mean ± SD. p<0.05 is significant

Conclusion: The only different disease feature was the increased frequency of extra-articular involvement in the more severe co-morbidity group. All other disease characteristics were similar. In addition, the severity of the co-morbidities may not change the doctors' decision to prescribe biological or synthetic DMARDs and steroid dosage.
REFERENCES:
[1] Dougados M, Soubrier M, Antunez A, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis 2014; 73:62-8.
[2]Luque Ramos A, Redeker I, Hoffmann F, et al. Comorbidities in Patients with Rheumatoid Arthritis and Their Association with Patient-reported Outcomes: Results of Claims Data Linked to Questionnaire Survey. J Rheumatol 2019; 46:564-571.
[3] D'Hoore W, Sicotte C, and Tilquin C. Risk adjustment in outcome assessment: the Charlson comorbidity index. Methods Inf Med 1993; 32:382-7.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2903

POS0561 OBESITY PHENOTYPES IN EARLY RHEUMATOID ARTHRITIS

Y. Gorbunova[1], T. Popkova[1], L. Kondrateva[1], M. Cherkasova[2], E. Nasonov[3], A. Lila[3]. *[1]VA Nasonova Research Institute of Rheumatology, Laboratory of Systemic Rheumatic Diseases, Moskva, Russian Federation*; *[2]VA Nasonova Research Institute of Rheumatology, Laboratory of Immunology, Moskva, Russian Federation*; *[3]VA Nasonova Research Institute of Rheumatology, Scientific Department, Moskva, Russian Federation*

Background: Patients with rheumatoid arthritis (RA) and obesity have a lower risk of early death than patients with normal weight due to the so-called "obesity paradox". Available publications discuss three phenotypes of obesity: classical obesity, metabolically healthy overweight/obesity, and latent obesity (normal weight associated with metabolic disorders, most importantly - with insulin resistance and adipocytokines imbalance).
Objectives: To clarify the prevalence of obesity phenotypes and to identify factors predisposing to «latent obesity» in early RA without diabetes mellitus or hyperglycemia.
Methods: The study included 35 pts (23 women, 12 men) with early RA (criteria ACR / EULAR, 2010), 56 [43,0; 60,0] years old, naïve to treatment with glucocorticoids and disease-modifying anti-rheumatics, without established diabetes mellitus. Pts were seropositive for IgM RF and anti-CCP, with highly active RA (DAS28 5,9 [5,2; 6,4]; SDAI 35,4 [27,0; 45,8], and CDAI 31,0 [26,0; 44,0]) scores, and median disease duration of 8.0 [6,0;15.0] months. Electrochemiluminescence assay Elecsys (Roche Diagnostics) was used to measure patients' insulin levels, and ELISA (DBS – Diagnostics Biochem Canada Inc.) - for evaluation of serum leptin concentrations. Insulin resistance (IR) was defined as Homeostasis Model Assessment of Insulin Resistance index (HOMA-IR) ≥2,77. Leptin levels were considered elevated at values ≥11,1 ng/ml for women, ≥5,6 ng/ml for men. The overweight/obesity status was determined by World Health Organization criteria in pts with body mass index (BMI) ≥25kg/m^2.
Results: Overweight/obesity were documented in 19 (54, 3%) pts with early RA, 4/19 (21%) had high leptin levels and IR, 11/19 (58%) had isolated hyperleptinemia. Normal BMI was found in 16 (45,7%) pts with early RA, 2/16 (12,5%) had elevated leptin levels and IR, and 6/16 (37,5%) – only hyperleptinemia. Four (21%) out of 19 overweight and 8 (50%) out of 16 pts with normal BMI did not show any metabolic disorders (p=0,02). Classical obesity was found in 15 (43%), and latent obesity – in 8 (23%) pts with early RA. Leptin levels correlated with waist circumference (r=0,58, *p*=0,02), BMI (r=0,71, *p*=0,0006), ESR (r=0,5, *p*=0,02) in the overweight/obese pts, and with waist circumference (r=0,59, *p*=0,03), IgM RF (r=0,58, *p*=0,03), triglyceride levels (r=0,77, *p*=0,003), and atherogenic index (r=0,62, *p*=0,03) in pts with normal weight.
Conclusion: The classical obesity phenotype associated with abdominal obesity and inflammation was the most common and prevailing over other phenotypes in early RA. Latent obesity was less common and was associated with an unfavorable lipid profile and accumulation of abdominal fat, therefore increasing the risk of cardiovascular diseases in RA. Metabolically healthy overweight/obesity in early RA was really a rare phenotype.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2961

POS0562 PULSE PRESSURE AS AN INDICATOR OF SUBCLINICAL ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS

S. Lugo-Perez[1], I. J. Colunga-Pedraza[2], J. R. Azpiri-López[1], D. Á. Galarza-Delgado[2], N. Guajardo-Jauregui[2], A. B. Rodriguez-Romero[2], A. Cárdenas[2], A. C. Garza Acosta[3]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico*; *[2]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*; *[3]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Radiology, Monterrey, Mexico*

Background: Pulse pressure (PP) is defined as the difference between systolic and diastolic blood pressure and represents arterial compliance and reflective properties of blood flow (1). It is well known that gender, age, and race / ethnicity are intrinsic factors of the patient that influence PP. Brachial PP has recently been associated with markers of subclinical cardiovascular disease after adjustment with traditional cardiovascular risk factors in the general population (2). However, this relationship has not been studied in patients with rheumatoid arthritis (RA) and its identification would allow earlier adjustments of cardiovascular therapies in this high-risk group.
Objectives: The aim of the study is to analyze the difference in PP between patients with RA and healthy controls. Additionally, to analyze the difference between patients with carotid plaque (CP) and without CP.
Methods: A cross-sectional, observational, and comparative study of ninety-two patients with RA aged 40-75 years and who fulfilled ACR/EULAR 2010 classification criteria. Also, we included ninety-two controls without RA, matched by gender, age and comorbidities. A carotid ultrasound was performed in patients with RA and it was divided into two subgroups, with the presence of CP and without CP. A blood pressure measurement was taken after 15 minutes of rest on the right arm of all patients. Distribution was evaluated with the Kolmogorov-Smirnov test. Descriptive analysis was done using measures of central tendency. Chi square, Student's t test and Mann-Whitney U test were used for comparations between groups. A *p* value <0.05 was considered statistically significant.
Results: We found no statistical difference between groups regarding age, gender and, comorbidities (type 2 diabetes mellitus, hypertension, dyslipidemia and, active smoking) (Table 1). There was a significant difference in PP between patients with RA and controls (50 mmHg vs 41 mmHg respectively, *p* = 0.032). Patients with RA had a significant difference in PP of patients with CP and without CP (50 mmHg vs 44 mmHg respectively, *p* = 0.008) (Figure 1). When performing a binary logistic regression, it was found that PP was the only independent factor for the presence of CP in patients with RA, OR 1.054 (95% CI 1.008-1.101, *p* = 0.020).
Conclusion: Patients with RA had a higher PP than controls. Binary logistic regression showed PP as the only independent factor for the presence of subclinical atherosclerosis in patients with RA. PP is a parameter that all rheumatologists should consider when evaluating cardiovascular risk in patients with RA.
REFERENCES:
[1] Winston GJ, Palmas W, Lima J, et al. Pulse pressure and subclinical cardiovascular disease in the multi-ethnic study of atherosclerosis. Am J Hypertens 2013;26(5):636-42. doi: 10.1093/ajh/hps092

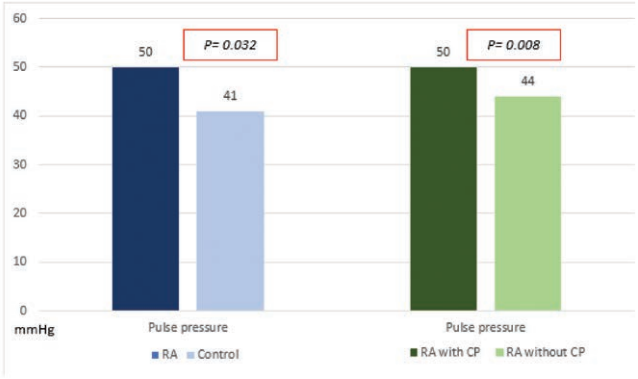
[2] Zureik M, Touboul PJ, Bonithon-Kopp C, et al. Cross-sectional and 4-year longitudinal associations between brachial pulse pressure and common carotid intima-media thickness in a general population. The EVA study. Stroke 1999;30(3):550-5. doi: 10.1161/01.str.30.3.550

Table 1. Demographic characteristics.

	RA (n=92)	Control (n=92)	p
Women, n (%)	85 (92.4)	85 (92.4)	NS
Age, years ± SD	58.0 (55.0-63.0)	56.5 (54.0-61.0)	NS
T2DM, n (%)	17 (18.5)	15 (16.3)	NS
Hypertension, n (%)	33 (35.9)	33 (35.9)	NS
Dyslipidemia, n (%)	30 (32.6)	29 (31.5)	NS
Obesity, n (%)	30 (32.6)	31 (33.7)	NS
Active smoking, n (%)	11 (12.0)	20 (21.7)	NS
	RA patients with CP (n=39)	**RA patients without CP (n=53)**	***p***
Women, n (%)	36 (92.3)	49 (92.5)	NS
Age, years ± SD	60.13 ± 5.98	58.08 ± 7.00	NS
T2DM, n (%)	9 (23.1)	8 (15.1)	NS
Hypertension, n (%)	16 (41.0)	17 (32.1)	NS
Dyslipidemia, n (%)	13 (33.3)	17 (32.1)	NS
Obesity, n (%)	15 (38.5)	15 (28.3)	NS
Active smoking, n (%)	6 (15.4)	5 (9.4)	NS
Disease duration, years (p25-p75)	8.44 (3.00-15.50)	12.86 (4.66-19.66)	NS

NS, no significant; T2DM, type 2 diabetes mellitus; CP, carotid plaque.

Figure 1. Comparison of pulse pressure between RA and controls and, RA with and without carotid plaque



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3005

POS0563 THE NATURAL COURSE OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE FOCUSING ON LUNG PHYSIOLOGY AND DISEASE ACTIVITY: A PROSPECTIVE COHORT STUDY (PART 2)

S. H. Chang[1], J. S. Lee[2], J. S. Lee[3], C. H. Park[4], M. U. Kim[5], Y. J. Ha[6], E. H. Kang[6], Y. A. Lee[7], Y. Park[8], J. Y. Choe[9], E. Y. Lee[10]on behalf of KOrean Rheumatoid Arthritis Interstitial Lung disease (KORAIL) cohort study group.
[1]Soonchunhyang University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Cheonan, Korea, Rep. of (South Korea); *[2]Clinical Research Center, Asan Institute for Life Sciences, Asan Medical Center, Department of Medical Stastics, Seoul, Korea, Rep. of (South Korea)*; *[3]GENOME INSIGHT Inc., -, Seoul, Korea, Rep. of (South Korea)*; *[4]Soonchunhyang University College of Medicine, Department of Radiology, Cheonan, Korea, Rep. of (South Korea)*; *[5]SMG-SNU Boramae Medical Center, Department of Radiology, Seoul, Korea, Rep. of (South Korea)*; *[6]Seoul National University Bundang Hospital, Division of Rheumatology, Department of Internal Medicine, Seongnam, Korea, Rep. of (South Korea)*; *[7]Kyung Hee University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; *[8]Yonsei University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; *[9]Catholic University of Daegu College of Medicine, Division of Rheumatology, Department of Internal Medicine, Daegu, Korea, Rep. of (South Korea)*; *[10]Seoul National University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*

Background: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). However, the effect of RA disease activity on the course of ILD is not yet known.
Objectives: To assess the natural course of lung physiology of RA-ILD and the relation between arthritis activity and pulmonary physiology in patients with RA-ILD.
Methods: The Korean Rheumatoid Arthritis ILd (KORAIL) cohort is the prospective observational cohort and aims to investigate the natural course of RAILD. Based on either 1987 or 2020 ACR criteria, patients diagnosed with RA and ILD based on CT scan were recruited from six tertiary medical hospitals in Korea since January 2015. RA disease activity was assessed using disease activity (DAS)28-ESR and CRP, annually. Pulmonary function tests (PFT), including FVC and DLCO were conducted annually. According to the transition of DAS28-ESR status, we classified patients into four groups: Group A. persistent remission or low disease activity, Group B. improvement, Group C. worsening, Group D. persistent moderate to high disease activity.
Results: We analyzed 143 patients who completed a 2-year follow-up (visit 2) or had died with available PFT results at least twice. Mean duration since RA diagnosis and since ILD diagnosis was 7.6±8.0 and 2.7±3.1 years, respectively. Twenty-four patients were Group A, 33 Group B, 10 Group C and 30 Group D. The mean of FVC (mL) and % of the predicted value in FVC was significantly lower in Group D than in other groups (Table 1). The annual rate of decline in FVC was -42 (95% CI -93~10) mL·year^{-1} in Group B while -113 (95% CI -206~-21) mL·year^{-1} in Group C (Figure 1A). The annual decline rate in Group C was further exaggerated in patients with ≥ 80% of FVC predicted (-141, 95% CI -251~-32 mL·year^{-1}). During two years of follow-up, patients ever experienced a relative decline of ≥10% from the enrollment in FVC predicted was 27.3%(n-9/33) in Group B whereas 30.0% (3/10) in Group C. The annual rate of decline in % of DLco predicted value was also the largest in Group C (-4.6 %·year^{-1}, 95%CI -8.5~-0.7), which further exaggerated in patients with ≥ 80% of FVC predicted (-4.9%·year^{-1}, 95 %CI -8.3~-1.5, Figure 1B). Of note, about half of patients with maintained not only low disease activity (Group A) but also moderate to severe disease activity (Group D) improved in DLco at least 10% or more from the enrollment of DLco predicted value (Group A: 54.2%, n=13/24, Group D: 46.7%, n=14/30).
Conclusion: RA disease activity is associated with the change of lung physiology in patients with RA-ILD; worsening disease activity associated with a further decrease of annual change in FVC and maintaining low disease activity associated with a further increase of annual change in % of DLco predicted value.

Table 1. The analysis of forced vital capacity (FVC) according to disease activity transition group.

	Group A	Group B	Group C	Group D
FVC (mL), mean±SD	2810.0±771.1	2528.8±735.3	2801.0±952.7	2048.3±575.7
FVC % of predicted, mean±SD	87.5±14.5	86.5±16.6	93.0±15.6	77.2±17.3
Rate of FVC decline, mL·year^{-1} (95% CI)	-52 (-112,7)	-42 (-93,10)	-113 (-206, -21)	1 (-52, 54)
A 10-point decline from V1 in predicted FVC value, n (%)	29 (20.3)	6 (25.0)	6 (18.2)	3 (30.0)
Relative decline of 10% from the enrollment in predicted FVC value, n (%)	35 (24.5)	5 (20.8)	9 (27.3)	3 (30.0)

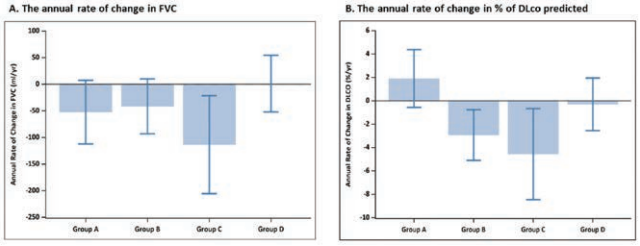


Figure 1. The annual change of pulmonary physiology according to disease activity transition group.

Acknowledgements: This work was supported by the Korea Health Technology R&D Project through the Korea Health Industry Development Institute, funded by the Ministry of Health and Welfare, Republic of Korea (grant no.HI14C1277).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3084

POS0564 THE EFFECT OF ARTHRITIS TREATMENT ON THE COURSE OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE FOCUSING ON BIOLOGIC DMARDS: FROM A PROSPECTIVE COHORT STUDY (PART 5)

S. H. Chang[1], J. S. Lee[2], J. S. Lee[3], C. H. Park[4], M. U. Kim[5], Y. J. Ha[6], E. H. Kang[6], Y. A. Lee[7], Y. Park[8], J. Y. Choe[9], E. Y. Lee[10]on behalf of KOrean Rheumatoid Arthritis Interstitial Lung disease (KORAIL) cohort study group.

[1]Soonchunhyang University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Cheonan, Korea, Rep. of (South Korea); [2]Clinical Research Center, Asan Institute for Life Sciences, Asan Medical Center, Department of Medical Stastics, Seoul, Korea, Rep. of (South Korea); [3]GENOME INSIGHT Inc., -, Seoul, Korea, Rep. of (South Korea); [4]Soonchunhyang University College of Medicine, Department of Radiology, Cheonan, Korea, Rep. of (South Korea); [5]SMG-SNU Boramae Medical Center, Department of Radiology, Seoul, Korea, Rep. of (South Korea); [6]Seoul National University Bundang Hospital, Division of Rheumatology, Department of Internal Medicine, Seongnam, Korea, Rep. of (South Korea); [7]Kyung Hee University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea); [8]Yonsei University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea); [9]Catholic University of Daegu College of Medicine, Division of Rheumatology, Department of Internal Medicine, Daegu, Korea, Rep. of (South Korea); [10]Seoul National University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)

Background: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). However, the effect of RA treatment on the course of ILD is not yet known.
Objectives: To assess the effect of RA treatment on the course of lung physiology of RA-focusing on biologic DMARDs treatment.
Methods: The Korean Rheumatoid Arthritis ILd (KORAIL) cohort is the prospective observational cohort and aims to investigate the natural course of RAILD. Based on either 1987 or 2020 ACR criteria, patients diagnosed with RA and ILD based on CT scan were recruited from six tertiary medical hospitals in Korea since January 2015. RA disease activity was assessed using disease activity (DAS)28-ESR and CRP, annually. Pulmonary function tests (PFT), including FVC and DLCO were conducted annually. In the current study, we analyzed patients who completed a 2-years follow-up or had died during those terms till October 2020. They classified patients into three groups: patients treated with abatacept ≥24 weeks ever (Group 1), those with other bDAMRDs ≥24 weeks ever (Group 2), and those without any bDMARDs or with bDMARDs <24 weeks (Group 3).
Results: Of a total of 125 patients who completed 2-year follow-up, 21 patients were classified as Group 1, 26 for Group 2, and 78 for Group 3. The mean age or the number of patients with ≥ 65-year-old was comparable between groups(Table 1). The mean duration since RA diagnosis was shorter in Group 3, but that since ILD diagnosis was comparable. DAS28-ESR score was comparable between Group 1 and 2 at enrollment, so was in 1-year-follow-up (p=0.75) and 2-year-follow-up (p=1.00). FVC and % of the predicted value in FVC, FEV1, and DLco were also comparable among the three groups at enrollment. The numbers of patients with ≥10-point decline in % of FVC predicted was 2 (10.0%) for Group 1, 1 (3.8%) for Group 2, 3 (3.9%) for Group3 during the first 1-year follow-up, and 3 (15.8%), 3 (11.5%), 10 (14.1%) during the last 1-year follow up. The percent of FVC predicted was 81.6 ± 17.5 %, 87.4 ± 17.9 %, 85.2 ± 17.7 % for Group 1,2 and 3, respectively, at 1-year-follow-up, and 79.5 ± 18.8 %, 89.0 ± 16.8 %, 83.5 ± 17.3 % at 2-year-follow-up. (Figure 1A). The percent of DLco predicted was 75.5 ± 23.4 %, 66.7 ± 18.1 %, 67.5 ± 16.7 % for Group 1,2 and 3, respectively, at 1-year-follow-up, and 74.0 ± 23.7 %, 69.1 ± 18.9 %, 67.0 ± 18.5 % at 1-year-follow-up (Figure 1B).
Conclusion: Treatment of bDMARDs did not exacerbate FVC than without bDMARDs treatment and mitigated the decline of DLCO compared to without bDMARDs treatment during 2-year-follow-up.

Table 1. Clinical characteristics at enrollment (V1)

	Total	Group 1.	Group 2.	Group 3.	P
N	125	21	26	78	
Age at enrollment	65.9±8.2	66.0±8.8	63.9±8.0	66.6±8.1	0.34
65, n (%)	72 (57.6)	13 (61.9)	11 (42.3)	48 (61.5)	0.21
Female, n (%)	89 (71.2)	16 (76.2)	17 (65.4)	56 (71.8)	0.71
RA duration, years	8.0±8.4	9.6±6.6	9.2±9.0	7.2±8.6	0.05
ILD duration, years	3.0±3.3	3.8±3.7	3.8±3.5	2.5±3.1	0.10
BMI, kg/m2	24.1±3.1	23.8±3.7	24.8±2.9	23.9±3.0	0.39
Ever-smoker	18	5	5	18	0.57
RF positive, n (%)	111 (88.8)	19 (90.5)	22 (84.6)	70 (89.7)	0.72
Anti-CCP positive, n (%)	119 (95.2)	20 (95.2)	25 (96.2)	74 (94.9)	1.00
Arthritis activity					
DAS28-ESR	4.0 ± 1.4	4.1 ± 1.1	4.3 ± 1.8	3.8 ± 1.4	0.60*
DAS28-CRP	3.1 ± 1.4	3.2 ± 1.2	3.4 ± 1.6	3.0 ± 1.4	0.76*
HAQ-DI	0.70 ± 0.76	0.64 ± 0.49	0.82 ± 0.82	0.67 ± 0.80	0.28*
Pulmonary function test					
FVC, ml	2522.5 ± 765.4	2406.2 ± 772.6	2617.3 ± 965.2	2522.2 ± 692.3	0.65
FVC, % of pred.	84.6 ± 16.9	80.9 ± 17.7	86.12 ± 17.82	85.08 ± 16.5	0.53
FEV1, % of pred.	92.4 ± 21.4	92.0 ± 24.8	90.6 ± 22.1	93.0 ± 20.4	0.88
DLco, % of pred.	71.5 ± 19.7	72.3 ± 26.7	69.1 ± 16.4	72.0 ± 18.7	0.80

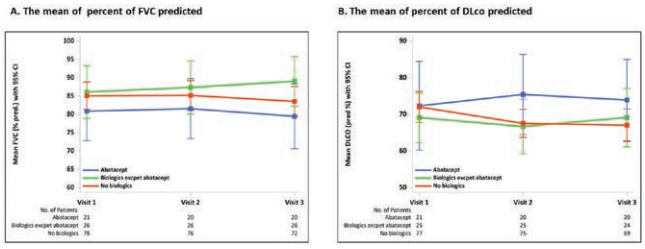


Figure 1.

Acknowledgements: This research was supported by Bristol Myers Squibb Inc.
Disclosure of Interests: Sung Hae Chang: None declared, Ji Sung Lee: None declared, Jeong Seok Lee: None declared, Chan Ho Park: None declared, Min Uk Kim: None declared, You-Jung Ha: None declared, Eun Ha Kang: None declared, Yeon Ah Lee: None declared, Yongbeom Park: None declared, Jung-Yoon Choe: None declared, Eun Young Lee Grant/research support from: Bristol Myers Squibb Inc.
DOI: 10.1136/annrheumdis-2021-eular.3094

POS0565

IS ACTIVE SYNOVITIS OF METACARPOPHALANGEAL JOINTS A NEUROPATHIC CONDITION IN RHEUMATOID ARTHRITIS PATIENTS? RESULTS FROM A ULTRASOUND STUDY AT LEVEL OF THE PALMAR DIGITAL NERVES

M. Di Carlo[1], J. Di Battista[1], R. Chiorrini[1], E. Cipolletta[1], G. Smerilli[1], A. Di Matteo[1], T. Okano[2], F. Salaffi[1], E. Filippucci[1]. [1]Università Politecnica delle Marche, Dipartimento di Scienze Cliniche e Molecolari - Rheumatology Clinic, Jesi, Italy; [2]Osaka City University Graduate School of Medicine, Department of Orthopedic Surgery, Osaka, Japan

Background: Rheumatoid arthritis (RA) is a chronic inflammatory arthritis that primarily affects the joints of hands, wrists, and feet. Anatomical damage (at bone, cartilage and tendon level) occurs as a consequence of a persistent synovial inflammation (1). In RA, periarticular soft tissues, including nerves, may also be involved. In particular, there is a high prevalence of neuropathic conditions such as carpal tunnel syndrome (CTS) in RA patients. In fact, the presence of inflammatory changes can frequently be documented by ultrasound (US) at the level of median nerve (2). Currently available very-high frequency US transducers allow high spatial resolution of small anatomical structures, including the palmar digital nerves.
Objectives: The objectives of this study were: to document the presence of dimensional alterations of the palmar digital nerves, particularly in terms of increased cross-sectional area (CSA), and to determine the variables associated with increased CSA, in RA patients.
Methods: From September 2020 to December 2020, adult RA patients from a tertiary outpatient clinic were consecutively included regardless of disease activity status. Patients underwent a clinical assessment to determine disease activity using the Clinical Disease Activity Index (CDAI), functional capacity using the QuickDASH, and the presence of neuropathic pain features using the PainDetect Questionnaire (PDQ). In the same visit, patients underwent a US examination of the 2nd to 5th metacarpophalangeal joints (MCPj) of the clinically more involved hand by an operator blinded to the clinical assessment. The presence/absence and US grading of synovitis was recorded for each joint. A third operator, blinded to the clinical and joint US assessment, measured the CSA of each pair of palmar digital nerves from 2nd to 5th finger scanned for assessment joint involvement. The CSA of the palmar digital nerves was measured at the MCPj. The US examinations were conducted with a MyLab Class C (Esaote, Genoa, Italy), with a 6-18 MHz probe for the articular examination, and with an 10-22 MHz probe for the examination of the palmar digital nerves. The serological status, respectively rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA), and the presence of radiographic erosive disease were also recorded for each patient. Statistical analysis was conducted by considering the sum of the CSA for each nerve pair of each finger. CSA was compared with respect to body mass index (BMI), disease duration, disease activity, US synovitis grading, functional capacity, neuropathic pain features, serological characteristics, and erosive status.
Results: Sixty-three patients with RA were included, 48 women, 15 men, with a mean age of 62.2 (11.8, standard deviation [SD]) years, a mean disease duration of 10.9 (8.2) years, for a total of 252 MCPj and 504 palmar digital nerves. The CSA of the palmar digital nerves taken individually was 2.3 (0.9) mm^2, ranging from 1 mm^2 to 8 mm^2, and 4.2 (1.5) mm^2 as a pair for finger. There was a statistically significant association with disease activity as assessed by the CDAI (p <0.001), and with the grading of US synovitis (p <0.001), while there were no significant associations with any of the other variables.

Conclusion: The presence of active RA, both in terms of clinical and ultrasonographic indices, correlates with an increased CSA of the palmar digital nerves. This alteration is probably due to inflammatory mechanisms of the perineural tissues at the level of the MCPj. Active synovitis during RA can somehow be framed as a condition capable of causing neuropathic damage to the palmar digital nerves.

REFERENCES:

[1] Filippucci E, Cipolletta E, Mashadi Mirza R, et al. Ultrasound imaging in rheumatoid arthritis. Radiol Med 2019;124(11):1087-1100.

[2] Smerilli G, Di Matteo A, Cipolletta E, et al. Ultrasound assessment of carpal tunnel in rheumatoid arthritis and idiopathic carpal tunnel syndrome. Clin Rheumatol 2020; doi: 10.1007/s10067-020-05293-z.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3116

POS0566 CATASTROPHIZING IN PATIENTS WITH RHEUMATOID ARTHRITIS

C. Traverson[1], B. Coste[1], E. Filhol[1,2], C. Daien[3,4], S. Laurent-Chabalier[5], S. Benamar[3], B. Combe[3,4], C. Lukas[2,3], J. Morel[3,4], C. Hua[1,2], C. Gaujoux-Viala[1,2]. *[1]Nîmes University Hospital, Rheumatology, Nîmes, France*; *[2]University of Montpellier, IDESP, UMR-INSERM, Montpellier, France*; *[3]CHU Lapeyronie, Rheumatology, Montpellier, France*; *[4]University of Montpellier, -, Montpellier, France*; *[5]Nîmes University Hospital, BESPIM, Nîmes, France*

Background: Catastrophizing is conceptualized as a negative cognitive–affective response to an anxiety-provoking stimulus, especially anticipated or actual pain. Catastrophizing can be assessed quickly using a validated questionnaire: the Pain Catastrophizing Scale (PCS)[1]. Catastrophizing plays a role in maintaining chronic pain and is associated with several pain-related outcomes in osteoarthritis and low back pain.

Objectives: To assess the prevalence of catastrophizing and associated factors in rheumatoid arthritis (RA).

Methods: We performed an observational, prospective, bi-centric study. All patients aged 18 or over with RA and fulfilling the ACR-EULAR 2010 criteria were consecutively included. Sociodemographic data, information on the disease and its treatments were collected as well as questionnaires for disease activity (DAS28), function (HAQ), quality of life (SF12, EQ5D), anxiety and depression (HADS, GAD7), fibromyalgia (FiRST), insomnia (ISI) and catastrophizing scores (PCS). Statistical analysis included the samples t-test, one-way variance analysis, the Spearman's correlation test, the Chi^2 test, Fisher's exact test, the Wilcoxon test, multivariate linear regression (considering catastrophizing as a continuous variable) and multivariate logistics regression (considering catastrophizing as a categorical variable: PCS ≥ 20 = high level catastrophizing).

Results: From September 2019 to March 2020, 201 patients with RA were included: 78.1% were women and the median age was 63.0 years. In all, 64.1% of patients were RF+, 65.7% ACPA+, and 46% had erosive disease. Median DAS28 CRP was 2.9 [2.1-4.0]. with 45% of patients in remission, 14.8% with low, 31.2% moderate and 9 % high activity. The majority of patients (92 %) had a disease lasting for more than 2 years.

The prevalence of a PCS score ≥20 was 48.0% [41.0;54.9]. The median PCS score was 18 [7-28]. In multivariate logistics regression, high-level catastrophizing was significantly associated with DAS28-CRP (OR= 1.61 [1.18-2.20]), HADS anxiety score (OR=1.25 [1.11-1.40]) and the HADS depression score (OR=1.19 [1.07-1.33]). In multivariate linear regression, catastrophizing was significantly associated with the HADS anxiety score (p< 0.0001), HADS depression score (p=0.0055), HAQ (p=0.0015) and the ISI insomnia score (p=0.005).

Conclusion: Almost half the patients with RA were high catastrophizers. Catastrophizing is linked to anxiety, depression, disease activity, function impairment and insomnia. It may be interesting to detect catastrophizing in order to improve the management of our patients.

REFERENCES:

[1] Sullivan MJL. et al. Psychological Assessment. 1995;7(4):524–32

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3144

POS0567 HEPCIDIN IS POTENTIAL BIOMARKER TO DISTINGUISH BETWEEN IRON DEFICIENCY ANEMIA AND ANEMIA OF INFLAMMATION IN RHEUMATOID ARTHRITIS

E. Galushko[1], A. Semashko[1], A. Gordeev[1], A. Lila[1]. *[1]V.A.Nasonova Research Institute of Rheumatology, Department of Early Arthritis, Moscow, Russian Federation*

Background: Anemia of inflammation (AI) and iron deficiency anemia (IDA) are the two most prevalent forms of anemia in patients with rheumatoid arthritis (RA). Diagnosis becomes challenging if AI is associated with true ID (AI/ID), as there is still a lack of a gold standard for differentiation between AI and AI/ID. However, as therapies to overcome anemia differ, proper diagnosis and understanding of underlying pathophysiological regulations are necessary.

Objectives: The aim of the study was to evaluate the clinical efficiency of hepcidin, a key regulator of iron metabolism, in the diagnosis of IDA, as well as the differential diagnosis of AI/ID and AI in patients with RA.

Methods: The study was undertaken 96 patients with RA, 67 of them were diagnosed anemia according to WHO criteria (104,3±21,4 g/l). Anemic patients and anemia-free patients with RA (n=29) were comparable (p>0.05) in age (44.4±14.8 and 49.8±9.3 years), disease duration (73.5±65.4 and 59.8±48.3 months) and DAS28 (6.3±1.6 and 5.9±1.9). All cases were subjected to following tests: complete blood count with peripheral smear, serum C-reactive protein, serum interleukin-6, iron studies, serum soluble transferrin receptor (sTfR), and serum hepcidin. Patients with RA and anemia were divided two groups: 25 patients with IDA and 42 - with AI. The AI cases were subdivided into pure AI and AI with coexistent ID (n=15).

Results: The mean serum hepcidin concentration was significantly increased in pure AI patients (123.85±25.8 ng/mL) as compared to those in IDA patients (63.9±22.8 ng/mL, P < 0.05) and anemia-free patients with RA (88.1±39.09 ng/mL). Also, compared to pure AI patients [normal sTfR levels (<3 μg/mL)], the serum hepcidin concentration was reduced significantly in AI patients with ID [high sTfR levels (≥3 μg/mL)] with a mean of 79.0±23.97 ng/mL.

Conclusion: Hepcidin measurement can provide a useful tool for differentiating AI from IDA and also help to identify an iron deficiency in AI patients. This might aid in the appropriate selection of therapy for these patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3303

POS0568 OBESITY RATES AND BMI ARE SIMILAR IN AGE AND SEX MATCHED RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND SPONDYLOARTHRITIS PATIENTS

G. K. Yardımcı[1], B. Farisoğulları[1], E. C. Bolek[1], E. Bilgin[1], E. Duran[1], G. Ayan[1], Z. Özsoy[1], G. Sandal Uzun[1], L. Kılıç[1], A. Akdoğan[1], O. Karadag[1], Ş. A. Bilgen[1], S. Kiraz[1], U. Kalyoncu[1], A. İ. Ertenli[1]. *[1]Faculty of Medicine; Hacettepe University, Rheumatology, Ankara, Turkey*

Background: Obesity has been suggested to be a chronic inflamatory condition and therefore, obesity may be considered as a risk factor for developing immune-mediated diseases, including inflammatory arthritis. In larger biologic registiries, obesity was found frequently in psoriatic arthritis than other inflammatory diseases such as rheumatoid arthritis and spondyloarthritis. [1-4]. However, obesity may be a reason of aging, moreover, there are strong sex differences between those diseases.

Objectives: The aim of this study was to evaluate the obesity rates in sex and aged matched patients with inflammatory arthritis before the initation of biological therapy.

Methods: HUR-BIO (Hacettepe University Biologic Registry) is a prospective, single center database of biological treatments since 2005 and to date 5635 patients have been recorded. Demographic, clinical and laboratory data before bDMARD of SpA, RA and PsA patients were noted. The patients were divided into two groups: non-obese patients (<30 kg/ m^2) and obese (≥30 kg/m^2) patients. When investigeting the changes in BMI by diagnosis, the effects of gender and age were adjusted using two-way ANOVA and ANCOVA tests. The selection was made for the gender and age indifferences of the relevant groups by using propensity score.

Results: 5059 patients' (1834 RA, 2741 SpA and 484 PsA) BMI data before the bDMARD treatments were avaliable and analysed. Baseline characteristics of RA, SpA and PsA patients were given in Table 1. 72.3% of the RA patients were seropositive. HLAB27 was positive in 64.7% and 22.9% of the SpA and PsA patients. Anti-TNF therapy was started as first bDMARD in 57.2% of the RA patients, others were started with non-Anti-TNF bDMARDs. In SpA (99.2%) and PsA (100%) patients anti-TNFs were the first biologics. Overall, the proportion of obese patients was significantly higher in RA and PsA than in SpA patients (Table 1) and age and sex affected BMI significantly (p<0.001) (Figure 1). After adjusting age and sex indifference between groups, the difference between the BMI of the patients disappeared (Table 1).

Table 1. Baseline characteristics and BMI of the patients

		RA	SpA	PsA	p
All bDMARD patients	**N**	1834	2741	484	
	Female, n (%)	1470 (80.2)	1257 (45.9)	334 (69.0)	0.000*
	Age, years*	52.9±13.4	43.1±11.4	47.4±12.2	0.000*
	Disease duration, years¥	11 (7-17)	8 (5-13)	7 (3-12)	0.000*
	Body mass index*	29.6 ± 6.5	27.7 ± 5.4	29.2 ± 5.8	0.000*
	Obesity, n (%)	811 (44.2)	815 (29.7)	199 (41.1)	0.000*
Age and sex matched group	**N**	481	483	484	
	Female, n (%)	315 (65.7)	324 (67.1)	334 (69.0)	0.545
	Age, years*	47 (36-59)	48 (39-57)	47 (38-56)	0.691
	Disease duration, years¥	10 (6-15)	5 (5-13)	7 (3-12)	0.000*
	Body mass index*	28.5 ± 6.1	28.5 ± 5.8	29.2 ± 5.8	0.150
	Obesity, n (%)	183 (38.0)	176 (36.4)	199 (41.1)	0.316

* Mean ±S.D ¥Median (IQR)

Conclusion: Although obesity was more frequently reported in RA and PsA patients, age and gender seemed to be the major factors in the occurrence of this difference rather than inflammatory arthritis subgroups. Therefore, when considering obesity as a factor in the registries, for instance biological registries, sex and age should be kept in mind.

REFERENCES:

[1] Højgaard, P., et al., The influence of obesity on response to tumour necrosis factor-α inhibitors in psoriatic arthritis: results from the DANBIO and ICEBIO registries. Rheumatology (Oxford), 2016. **55**(12): p. 2191-2199.
[2] Liu, Y., et al., Impact of Obesity on Remission and Disease Activity in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis. Arthritis Care Res (Hoboken), 2017. **69**(2): p. 157-165.
[3] Moroni, L., N. Farina, and L. Dagna, *Obesity and its role in the management of rheumatoid and psoriatic arthritis.* Clin Rheumatol, 2020. **39**(4): p. 1039-1047.
[4] Zurita Prada, P.A., et al., Influence of smoking and obesity on treatment response in patients with axial spondyloarthritis: a systematic literature review. Clin Rheumatol, 2020.

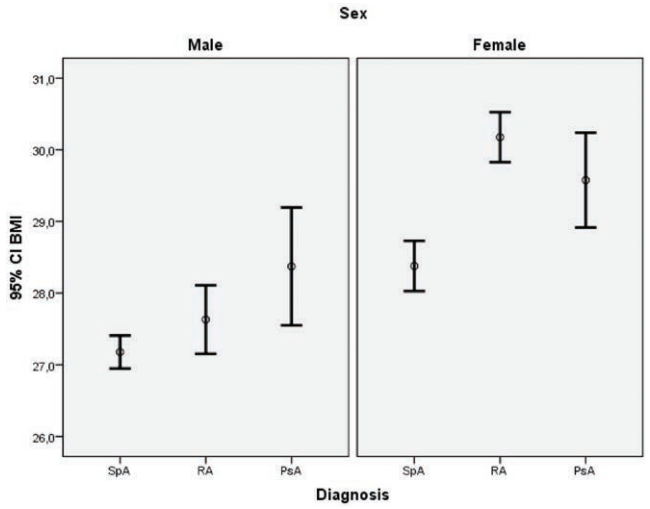


Figure 1. BMI regarding to sex and diseases subtypes

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3312

POS0569 LONG-TERM OUTCOMES OF CHILDREN BORN TO WOMEN WITH RHEUMATOID ARTHRITIS

N. Calin[1], A. T. Florescu[2], F. Bobirca[3], C. Tataru[4], I. Ancuta[1,2], M. Bojinca[1,2], C. Mihai[1,5], A. Balanescu[1,6], A. Musetescu[7], M. Micu[8], C. Ancuta[9], V. Stoica[1,2], L. Andreoli[10,11], B. Anca[1,2]. [1]*Carol Davila University of Medicine and Pharmacy, Rheumatology, Bucharest, Romania*; [2]*Cantacuzino Hospital, Internal Medicine and Rheumatology, Bucharest, Romania*; [3]*Carol Davila University of Medicine and Pharmacy, Surgery, Bucharest, Romania*; [4]*Emergency Hospital Saint Pantelimon, Rheumatology, Focsani, Romania*; [5]*Zurich University Hospital, Rheumatology, Zurich, Switzerland*; [6]*Sf Maria Clinical Hospital, Internal Medicine and Rheumatology, Bucharest, Romania*; [7]*University of Medicine and Pharmacy of Craiova, Rheumatology, Craiova, Romania*; [8]*Clinical Rehabilitation Hospital, Rehabilitation II, Cluj-Napoca, Romania*; [9]*Grigore T. Popa University of Medicine and Pharmacy, Clinical Hospital of Rehabilitation, Iasi, Romania*; [10]*University of Brescia, Clinical and Experimental Sciences, Brescia, Italy*; [11]*Spedali Civili Hospital, Rheumatology and Clinical Immunology, Brescia, Italy*

Background: Children born to women with rheumatoid arthritis (RA) have increased incidences of adverse neonatal outcomes and a potential excess risk of specific diseases during childhood and adolescence [1]. Further studies aimed at confirming long-term consequences in the offspring are needed.
Objectives: To evaluate whether maternal RA has an impact on the health and developmental outcomes of the offspring.
Methods: A retrospective descriptive study was conducted on data regarding 43 children born to mothers diagnosed with either RA or juvenile idiopathic arthritis (JIA) prior to conception. Participants were recruited from several Clinics of Rheumatology located across Romania. Data on neonatal outcomes, lactation, developmental milestones, childhood illnesses, and hospitalizations was collected using a patient-reported questionnaire completed by maternal participants in 2020.
Results: Favorable neonatal outcomes were found in 81% of the participants; however, children of mothers with RA had a higher occurrence of favorable outcomes than those with JIA (p = 0.009). Adverse neonatal outcomes reported include the following: small for gestational age (11.6%), intrauterine growth restriction (4.65%), and preterm births (2.75%). There were no incidences of congenital malformations. The mean birth weights of offspring born to mothers with RA are higher than those with JIA (p = 0.00829).
While the majority of the children were breastfed (88.4%), those who were not breastfed were hospitalized more often than those who were breastfed for any period of time (p = 0.03). Mothers who experienced a postpartum flare up within the first 4 months breastfed their children significantly less than those who did not have a flare up (14.62 versus 48 weeks, p = 0.00011).
The mean age of the children at inclusion was 7.6 ± 5.5 years.
Developmental milestones were considered to be within the expected average limits, except for an increased incidence of delayed speech (12%).
51.2% of the children were hospitalized at some point during their childhood, with viral enterocolitis, tonsilitis, bronchiolitis, and pneumonia being the most frequently encountered reasons for admission. Surprisingly, children with favorable neonatal outcomes were hospitalized more often than those with unfavorable outcomes (p = 0.0000436). Additionally, children born to mothers under the age of 35 were hospitalized more often than those over 35 (p = 0.02).
77.3% of offspring experienced recurrent ear/nose/throat (ENT) infections, 55.8% had allergies, and 39.5% were diagnosed with atopic dermatitis. Childhood allergies were strongly associated with an increased incidence of atopic dermatitis (p = 0.0000585), as was a concurrent maternal thrombophilia diagnosis (p = 0.03). Of the remaining childhood afflictions that were assessed asthma/chronic respiratory diseases (4.65%), juvenile idiopathic arthritis (2.33%), ulcerative colitis (2.33%), diabetes, anxiety/personality disorders, thyroid diseases, febrile seizures, and epilepsy did not yield statistically significant results.
Conclusion: Maternal RA was found to be associated with increased incidences of adverse neonatal outcomes, childhood hospitalizations, recurrent ENT infections, allergies, and atopic dermatitis. However, overall health outcomes of offspring did not show alarmingly significant excess morbidities.

REFERENCES:

[1] Rom AL, Wu CS, Olsen J, et al. Parental rheumatoid arthritis and long-term child morbidity: a nationwide cohort study. *Annals of the Rheumatic Diseases*. 2016;75(10):1831–1837. doi:10.1136/annrheumdis-2015-208072

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3322

POS0570 ASSOCIATION OF BODY FAT MASS AND ITS DISTRIBUTION WITH DISEASE ACTIVITY, PAIN AND DISABILITY IN RHEUMATOID ARTHRITIS

O. Lamkhanat[1], H. Azzouzi[1], I. Linda[1]. [1]*Mohammed VI University Hospital, Mohammed I University, Faculty of Medicine, Rheumatology, Oujda, Morocco*

Background: Rheumatoid arthritis (RA) and body composition are closely related. Recent studies have found a significant association between fat mass and disease activity and disability in RA [1].
Objectives: We aimed to study the association between body fat mass and its distribution with disease activity, disability, and pain in RA patients.
Methods: This is a cross-sectional study of patients with RA diagnosis according to ACR-EULAR 2010 classification recruited from first January 2021. Those with prior cancer, hyperparathyroidism, hyperthyroidism, diabetes, chronic kidney disease, and cirrhosis were excluded. Body fat mass (BFM) and its distribution (gynoid (GFM), android (AFM), visceral (VFM), limbs (LFM), trunk (TFM)) were measured with dual-energy X-ray absorptiometry (Hologic, Horizon QDR®). Clinical data and laboratory tests of the same day of the DXA scan were analyzed. The associations between BFM and its distribution with disease activity score (DAS28CRP), pain visual analogue scale (VAS), and disability measured by health assessment questionnaire (HAQ) were explored. Obesity was defined as a body mass index (BMI) ≥ of 25kg/m^2. Our statistical analysis was based on descriptive study, comparisons and linear regressions using SPSS 20.
Results: It is about 69 RA patients. Their mean age was 49.86 ± 14.33 years, mean DAS28CRP was 2.56 ± 1.27, and mean disease duration was 14.84 ± 10.99 years. Sixty-two (89.9%) were women. The mean BMI was 26.46 ± 5.26 kg/m^2, and 41 patients were obese (59.4%). Compared with non-obese patients, obese patients had a higher C-reactive protein (p = 0.03). DAS-28CRP was higher in obese patients (2.77 ± 1.41 vs 2.25 ± 0.97) but did not reach significance (p = 0.07). We did not find any difference between the two groups regarding pain and disability. In univariate regression analysis, the LFM was positively associated with disease activity (p = 0.001; β = 0.38), pain (p = 0.001; β = 0.38) and disability (p = 0.007; β = 0.32). Adjusted on BMI, LDL cholesterol, triglyceride, cumulative dose of corticosteroid, disease and corticosteroid duration, menopause duration, dose and duration of methotrexate, we found a significant association between LFM, disability (p = 0.02; β = 0.51), disease activity (p = 0.02; β = 0.54) and pain (p = 0.009; β = 0.57). However, we had no association between disease activity, pain, and disability with BFM and the other components.
Conclusion: Limbs fat mass was significantly associated with the activity, disability, and pain in RA patients.

REFERENCES:

[1] Kyeong Min Son, Seong Hun Kang, Young Il Seo, Hyun Ah Kim. Association of body composition with disease activity and disability in rheumatoid arthritis. Korean J Intern Med. 2021 Jan;36(1):214-222.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3337

POS0571 NON-OBESE RHEUMATOID ARTHRITIS PATIENTS WITH LOW LOW-DENSITY LIPOPROTEIN HAVE GREATER CORONARY ATHEROSCLEROSIS BURDEN, PLAQUE PROGRESSION AND CARDIOVASCULAR EVENT RISK

G. Karpouzas[1], S. Ormseth[1], E. Hernandez[1], M. Budoff[2]. [1]*The Lundquist Institute, Rheumatology, Torrance, United States of America*; [2]*The Lundquist Institute, Cardiology, Torrance, United States of America*

Background: Rheumatoid arthritis (RA) patients with low body weight incur higher mortality than obese patients. Paradoxically, RA patients in the lowest low-density lipoprotein group (LDL <70 mg/dl) may also experience higher cardiovascular disease (CVD) risk.

Objectives: We here explored whether abdominal obesity (waist-to-height ratio >0.58 in females and >0.63 in males) might moderate the effect of low LDL (<70mg/dl) on coronary atherosclerosis burden, progression and long-term CVD risk in RA.

Methods: One hundred fifty patients without symptoms or diagnosis of CVD underwent coronary computed tomography angiography. Plaque progression was evaluated 6.9±0.3 years later in 101 patients. Coronary artery calcium, number of segments with plaque (segment involvement score), and extensive (>4 segments with plaque) or obstructive disease (>50% stenosis) were assessed. CVD events were prospectively recorded, including cardiac death, myocardial infarction, unstable angina, revascularization, stroke, claudication, and heart failure hospitalization over 6.0±2.4 years of follow-up. Lipoprotein classes were directly measured. Oxidized LDL (oxLDL) was assessed with monoclonal antibody E06. Adjusted robust linear regression evaluated interactions between abdominal obesity and LDL groups on plaque outcomes. Per segment, adjusted robust logistic regression models explored obesity x LDL group interactions on new plaque formation and stenotic progression of prevalent plaques. Robust Cox regression models stratified by abdominal obesity evaluated the effect of LDL group (<70 vs. >70 mg/dl) on CVD events.

Results: Non-obese patients with low LDL had the highest plaque burden (Figure 1A, all p < 0.02). Obesity moderated the effect of LDL on likelihood of extensive/obstructive disease (*P* for interaction = 0.061); specifically, LDL<70 associated with an increased likelihood of extensive/obstructive plaque in non-obese (adjusted OR 4.75 [95% CI 1.18-19.07], *P* = 0.028) but not obese patients (adjusted OR 1.55 [95% CI 0.39-6.08], *P* = 0.532). No differences in disease activity or inflammatory markers were seen across groups. Compared to LDL>70 mg/dl, low LDL predicted an increased likelihood of high oxLDL (>median) in non-obese patients (adjusted OR 5.10 [95% CI 1.46-17.75], *P* = 0.011) but not obese patients (adjusted OR 0.50 [95% CI 0.11-2.21], *P* = 0.36, Figure 1B). Obesity further moderated the effect of LDL on likelihood of future development of plaque (*P* for interaction = 0.002) and increased stenotic severity of existing plaques (*P* for interaction = 0.040); in non-obese patients, low LDL associated with a greater likelihood of new plaque forming in segments without baseline plaque (adjusted OR 4.68 [95% CI 2.26-9.66]) and worsening stenotic severity in segments with prevalent plaque (OR 5.35 [95% CI 1.62-17.67]). This was not observed in obese patients (Figure 1C). Notably, in non-obese patients, low LDL associated with higher CVD event risk compared to those with LDL>70 mg/dl (HR 7.94 [95% CI 1.52-41.36], *P* = 0.015). This was not the case in obese patients (HR 0.32 [95% CI 0.04-2.40], *P* = 0.27, Figure 1D).

Conclusion: In non-obese RA patients, LDL<70 mg/dl may reflect higher LDL oxidation and was associated with higher baseline coronary atherosclerosis burden, new plaque formation, stenotic plaque progression and greater CVD risk than LDL>70 mg/dl.

Disclosure of Interests: George Karpouzas Speakers bureau: Sanofi/ Genzyme/ Regeneron, Consultant of: Sanofi/ Genzyme/ Regeneron, Grant/research support from: Pfizer, Sarah Ormseth: None declared, Elizabeth Hernandez: None declared, Matthew Budoff Consultant of: Pfizer

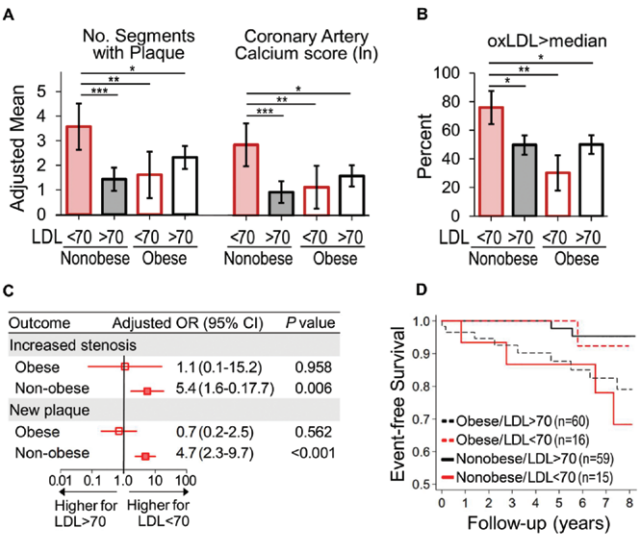


Figure 1 (A) Mean number of coronary segments plaque and log-transformed coronary artery calcium score across LDL/obesity groups, adjusted for age, gender, diabetes, and statin use. **(B)** Percent patients with elevated (>median) oxidized LDL (oxLDL) across LDL/obesity groups, adjusted for age, gender, hypertension, diabetes, and statin use. **(C)** Moderating effects of obesity on the association between low LDL and worsening stenosis of existing plaques and new plaque formation in coronary segments without baseline plaque, adjusted for age, time between scans, proximal segment location, time-averaged CRP, cumulative prednisone dose, and statin duration. New plaque formation model additionally adjusted for bDMARD duration. **(D)** The effect of low LDL on long-term cardiovascular risk stratified by obesity.
*p<0.050, **p<0.010, ***p<0.001.

DOI: 10.1136/annrheumdis-2021-eular.3419

POS0572 THE ASSOCIATED FACTORS OF ULTRASONOGRAPHIC TENOSYNOVITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REMISSION

R. Fakhfakh[1], N. El Amri[1], K. Baccouche[1], H. Zeglaoui[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*

Background: Tenosynovitis is a common manifestation of rheumatoid arthritis (RA), but, is difficult to assess appropriately by clinical examination. In clinical remission, musculoskeletal ultrasound (MSUS) showed a predictive value of tenosynovitis for flares and joint destruction in RA (1).

Objectives: To assess the prevalence, the characteristics, and the factors associated with tenosynovitis in ultrasound examination of patients with RA in clinical remission.

Methods: A Cross-sectional study including patients with RA in clinical remission (DAS28 ESR ≤ 2.6) for at least 6 months. MSUS of 20 tendons (in wrists, hands and ankles) was performed in mode B and power Doppler (PD). Tenosynovitis was defined and scored according to the Outcome Measures in Rheumatology Clinical Trials (OMERACT). A total score for the tenosynovitis in B-mode (TBI) and PD (TDI) was calculated by summing the grades for each patient. SDAI and CDAI were calculated. Functional disability was assessed by the Health Assessment Questionnaire (HAQ). For the radiographic evaluations, we used the Van der Heijde score.

Results: Thirty-seven patients were enrolled, the mean age was 54.2 years±12.7 years and the sex ratio was 0.37. The mean disease duration was 8.1 years±5.1. The mean remission duration was 36.5 months ± 32.7. The prevalence of tenosynovitis was 40.5% in B-mode and 13.5% for PD. The most affected tendons were: extensor carpi ulnaris (B-mode: 21.6%, PD: 8.1%), tibialis posterior (B-mode: 10%, PD: 2.7%), peroneal (B-mode: 8.1%, PD: 2.7%), flexor digitorum superficialis and profundus (B-mode: 5.4%, PD: 0%) and extensor digitorum (B-mode: 2.7%, PD: 2.7%). Tenosynovitis was most frequently grade1 in B-mode (32.4%) and grade 2 in PD (10.8%). Grade 3 was identified only in B-mode in the peroneal tendons. The mean of TBI was 7.1±5.3 and the mean of TDI was 2.2.±3.1. We found a significant association between remission duration and PD tenosynovitis (mean: 16.2 vs 39.7 months, p = 0.05). Tenosynovitis, in B-mode and PD, weren't associated with the swollen joints, the tender joints, the patient

global health assessment, the HAQ, erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor and anti-cyclic citrullinated peptide, DAS28, CDAI, SDAI, biologic treatment and radiographic structural damage. Multivariate logistic regression analysis didn't show any association.

Conclusion: Ultrasound tenosynovitis was commonly found in RA in remission and the extensor carpi ulnaris tendon was most involved. A shorter duration of remission was associated with PD tenosynovitis in univariate analysis. The MSUS assessment of tendons can be an additional feasible method to assess clinical remission.

REFERENCES:

[1] Janta I, Stanciu D, Hinojosa M, Nieto-González JC, Valor L, Bello N, et al. Structural damage in rheumatoid arthritis: comparison between tendon damage evaluated by ultrasound and radiographic damage. Rheumatology (Oxford). 2016;55(6):1042-6.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3511

POS0573 IMPACT OF JOINT DESTRUCTION IN THE HANDS, THE WRISTS AND THE ANKLES ON THE ULTRASOUND ASSESSMENT AND THE FUNCTIONAL OUTCOMES IN RHEUMATOID ARTHRITIS IN REMISSION

R. Fakhfakh[1], N. El Amri[1], K. Baccouche[1], H. Zeglaoui[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*

Background: Joint destruction is a strong predictive factor for residual synovitis among rheumatoid arthritis (RA) patients in clinical remission. Both of them were associated with functional impairment.

Objectives: To assess the ultrasound findings and functional outcomes of RA patients in remission according to the site of joint destruction.

Methods: A Cross-sectional study including RA patients in remission DAS28 ESR≤ 2.6 for at least 6 months. A B-mode and power doppler (PD) ultrasound of 42 joints was performed. Synovitis was defined and scored using the combined OMERACT-PDUS (gray scale and power doppler (PD)) scoring system graded from 0 to 3. The health assessment questionnaire (HAQ) and the radiological Sharp score of the wrists, hands and feet were calculated.

Results: Thirty-seven patients were included. The sex ratio was 0.37 and the mean age was 54.2 years ± 12.7. The mean disease duration was 8.1 years±5.1. The mean remission duration was 36.5 months ± 32.7. The mean DAS28vs was 2.1 ± 0.5. Rheumatoid factor and anti-citrullinated peptide antibodies were found in 62% and 75% of patients, respectively. The mean HAQ was 0.35 ± 0.38. Bone erosion was found in 81% of patients. In patients with hands and feet erosions (54%), synovitis was found in 90% of cases associated with PD in 70% of cases. The mean total score of synovitis was 7.8 ± 5.4. The mean HAQ was 0.37 ± 0.44. In patients with only erosions in the hands or wrists (18.9%), synovitis was found in 100% of cases associated with PD in 57% of cases. The mean total score of synovitis was 4.5±4.7. The mean HAQ was 0.48 ± 0.34. In patients with only feet erosions (8.1%), synovitis was found in 100% of cases associated with PD in 66.7% of cases. The mean total score of synovitis was 4.6±3.5. The mean HAQ was 0.31 ± 0.26. RA was not erosive in 18.9% of patients. In these patients, synovitis was found in 100% of cases associated with PD in 28.6% of cases. The mean total score of synovitis was 5.6±4.3. The mean HAQ was 0.21 ± 0.23. There is no significant difference between these groups(p>0.05).

Conclusion: In RA in remission, PD synovitis and functional incapacity were less frequent in the absence of erosion. PD synovitis was more frequently found in patients with erosions, especially, in the feet. The HAQ was higher in patients with hands erosions.

REFERENCES:

[1] Hamamoto Y, Ito H, Furu M, Hashimoto M, Fujii T, Ishikawa M, et al. Serological and Progression Differences of Joint Destruction in the Wrist and the Feet in Rheumatoid Arthritis - A Cross-Sectional Cohort Study. PLoS One. 2015;10(8):e0136611.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3601

POS0574 RELATIONSHIP BETWEEN INVOLVED JOINT FOR REGION AND MODIFIED HEALTH ASSESSMENT QUESTIONNAIRE SCORE IN JAPANESE PATIENT WITH RHEUMATOID ARTHRITIS

I. Yoshii[1]. [1]*Yoshii Hopital, Rheumatology and Musculoskeletal Medicine, Shimanto City, Japan*

Objectives: Rheumatoid arthritis (RA) is a chronic inflammatory disease that involves various joints in whole body. For evaluation of daily life activities (ADL), modified Health Assessment Questionnaire (mHAQ) is usually used. This index configures eight ADL functions these are separated by predominant extremities. This study aimed to evaluate how involved joint affect ADL predominantly in real world setting.

Methods: A total of 24,450 times of consultation with RA patient were visited in the institute. Here, patient with RA was interviewed every another visit, and involved joint in whole body, pain score with visual analog scale (PS-VAS), and mHAQ were recorded. Involved joints were divided by four regions in accordance with joint size and part; small joint in upper extremities (US), large joint in upper extremities (UL), small joint in lower extremities (LS), and large joint in lower extremities (LL). mHAQ was also separately evaluated in accordance with predominant regions; upper extremities predominant mHAQ (mHAQ_UE), and lower extremities predominant mHAQ (mHAQ_LE). Adding to these parameters, as an index for disease activity monitoring, components of the simplified disease activity index score (SDAI) was also recorded. Relationship between mHAQ for each predominant extremities, and these parameters and sex, age, disease duration of RA, anti-cyclic citrullinated polypeptide antibodies (ACPA), rheumatoid factor (RF), and Sharp/van der Heijde score (SHS), were statistically evaluated using linear regression analysis.

Results: mHAQ_UE significantly correlated with age, ACPA and RF titre, SHS, tenderness joint count (TJC), patient's global assessment (PGA), evaluator's global assessment (EGA), C-reactive protein (CRP), US, UL, LL, and PS-vas, whereas mHAQ-LE significantly correlated with all parameters that demonstrated significant correlation with mHAQ-UE and disease duration. mHAQ also correlated with all parameters those that demonstrated significant correlation with mHAQ-LE. Interestingly, all of mHAQ-UE, mHAQ-LE, and mHAQ did not correlated significantly with swollen joint count (SJC) and LS.

Conclusion: mHAQ is influenced by various factors, however, SJC and involvement of small joint in lower extremities did not affect mHAQ.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3644

POS0575 THE PATIENT GLOBAL ASSESSMENT (PGA) OF DISEASE ACTIVITY COLLECTS DIFFERENT INFORMATION IN EARLY COMPARED TO ESTABLISHED RHEUMATOID ARTHRITIS

L. De Stefano[1,2], S. Bugatti[1,2], B. D'Onofrio[1,2], E. Favalli[3], A. Manzo[1,2], R. Caporali[3,4], C. Montecucco[1,2]. [1]*Fondazione I.R.C.C.S. Policlinico San Matteo, Division of Rheumatology, Pavia, Italy*; [2]*The University of Pavia, Department of Internal Medicine and Therapeutics, Pavia, Italy*; [3]*ASST Pini-CTO - Presidio Gaetano Pini, Department of Rheumatology, Milano, Italy*; [4]*University of Milan, Department of Clinical Sciences & Community Health, Milano, Italy*

Background: The patient global assessment (PGA) is the most widely used patient-reported measure in rheumatoid arthritis (RA), being a component of disease activity scores and definitions of remission. Studies have however shown that, at least in established RA, PGA is mostly associated with pain, functional limitation, psychological distress and comorbidities, rather than with objective measures of inflammation. As such, the inclusion of PGA as a driver of intensification of immunosuppressive therapy is been questioned. Determinants of PGA may however differ in the earliest stages of RA, when pain processing mechanisms and damage accrual have not occurred yet. Whether the association of PGA with disease activity in RA changes over time is at present undetermined.

Objectives: To analyze the associations between PGA and disease activity measures in patients with RA across different phases of the disease.

Methods: 1.002 RA patients from two independent cohorts were included: 1) a prospective longitudinal cohort of early RA (<12 months of symptoms) (n=601) with an observation period of 24 months upon initiation of therapy with methotrexate; 2) a cross-sectional cohort of established RA (duration >5 years) (n=401) with inadequate response to methotrexate. Determinants of PGA were assessed by Pearson's correlation coefficients and multivariable linear regression.

Results: In early RA, median (IQR) symptom duration at inclusion was 15 (9-27) weeks, 71.5% of the patients were female, 49.3% were autoantibody-positive, and 30% had radiographic evidence of ≥1 erosion. The mean (SD) DAS28 was 4.94 (1.19), and the mean (SD) PGA 57.6 (26.6). The proportion of patients at least in low disease activity (DAS28 <3.2) after 6, 12 and 24 months of treatment was 49.9%, 57.4% and 67% respectively. The associations of PGA with pain and functional limitation were moderate to good (r >0.40) at all time points, and were independent of other co-variates (Table 1). Swollen joints (SJC28) were independently and directly associated with PGA at all time points until 12 months, whilst the association become indirect at 24 months (Table 1). In ACPA-positive patients, PGA at 6 and 12 months was weakly but still significantly associated with SJC28 even in low disease activity states (adj r 0.15 and 0.13, p<0.05). Patients with established RA had a mean [SD] DAS28 of 5.3 [1.2] and were ACPA-positive in 69.6% of the cases. Independent determinants of PGA were pain, HAQ and tender joints, whilst no associations with SJC28 and acute phase reactants were found neither in the overall cohort nor in ACPA-positive patients.

Conclusion: In established RA, PGA appears mostly related to factors outside the core domains of disease activity. In contrast, in the early phases of the disease, PGA may more strictly collect information on inflammatory-related symptoms. Better understanding of the relationship between patient reported outcomes and disease activity in the various phases of RA may thus be needed before introducing definitive changes in the current definitions of disease activity.

REFERENCES:
[1] Nikiphorou E et al. Arthritis Res Ther 2016;18:251
[2] Ferreira RJO et al. *Ann Rheum Dis* 2019;78:e109.

Table 1. Associations of PGA in early RA at different time points

	0 months		6 months		12 months		24 months	
	r (95% CI)	p	r (95% CI)	p	r (95% CI)	p	r (95% CI)	p
VAS pain	0.74 (0.70-0.77)	<0.001	0.83 (0.80-0.86)	<0.001	0.84 (0.80-0.86)	<0.001	0.83 (0.79-0.87)	<0.001
HAQ	0.47 (0.41-0.54)	<0.001	0.54 (0.46-0.62)	<0.001	0.57 (0.50-0.63)	<0.001	0.50 (0.41-0.59)	<0.001
SJC28	0.27 (0.19-0.35)	<0.001	0.27 (0.18-0.35)	<0.001	0.21 (0.12-0.30)	<0.001	0.23 (0.13-0.33)	<0.001
TJC28	0.34 (0.27-0.41)	<0.001	0.39 (0.31-0.47)	<0.001	0.39 (0.30-0.46)	<0.001	0.30 (0.20-0.40)	<0.001
CRP	0.08 (0.00-0.17)	0.05	0.09 (0.00-0.19)	0.07	0.19 (0.10-0.28)	<0.001	0.03 (0.09-0.14)	0.63
	β stand	p	β stand	p	β stand	p	β stand	p
VAS pain	0.66	<0.001	0.76	<0.001	0.74	<0.001	0.80	<0.001
HAQ	0.20	<0.001	0.18	0.01	0.20	0.03	0.22	0.003
SJC28	0.17	0.03	0.15	0.04	0.11	0.04	--	--
TJC28	--	--	--	--	--	--	--	--
CRP	--	--	--	--	--	--		

Acknowledgements: I have no acknowledgements to declare.
Disclosure of Interests: Ludovico De Stefano: None declared, Serena Bugatti Speakers bureau: BMS, Lilly, Sanofi, Pfizer, Galapagos, Bernardo D'Onofrio: None declared, Ennio Favalli Speakers bureau: AbbVie, MSD, Novartis, Pfizer, UCB Pharma, Antonio Manzo: None declared, Roberto Caporali Speakers bureau: AbbVie, BMS, Celgene, HSD, Lilly, Pfizer, Roche, UCB Pharma, Carlomaurizio Montecucco Speakers bureau: BMS, Lilly, Sanofi, Pfizer, Galapagos, Roche, Novartis
DOI: 10.1136/annrheumdis-2021-eular.3653

POS0576 EFFECTS OF ACUTE EXERCISE ON SERUM BDNF LEVEL IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Baglan Yentur[1], Z. Ercan[1], G. Deniz[2], A. Karatas[3], M. Gur[3], G. Alkan[4], S. S. Koca[3]. *[1]Firat University Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Elazig, Turkey*; *[2]Firat University School of Medicine, Department of Anatomy, Elazig, Turkey*; *[3]Firat University School of Medicine, Department of Rheumatology, Elazig, Turkey*; *[4]Firat University School of Medicine, Department of Physical Therapy and Rehabilitation, Elazig, Turkey*

Background: Brain derived neurotrophic factor (BDNF) is a neurotrofic factor that may show healing, survival-promoting and protective effects on neurons in central and peripheral nervous system. The effect of physical exercise on serum BDNF is unclear. Also, BDNF level was found significantly lower in rheumatoid Arthritis (RA) patients with depression.
Objectives: Aim of this study is to investigate the variation of BDNF levels following acute exercise and potential correlation between BDNF levels and depression.
Methods: This study included 44 RA patients and 44 age and sex matched healthy controls (HC). Aerobic exercise was performed to all participants for a single session. The intervention was performed on a treadmill and included 5 minutes of warm-up, 20 minutes of walking exercise reaching at 60- 80% of Maximal heart rate and 5 minutes of cool-down. Depression and anxiety levels were evaluated with Beck Depression Inventory (BDI) and Hospital Anxiety and Depression Scale (HADS). Blood samples from all subjects were taken and centrifuged before and immediately after the exercise intervention.
Results: Serum BDNF levels (both baseline and post-exercise) were similar in the RA and HC group (Table 1). Although after aerobic exercise serum BDNF levels were significantly decreased in both RA and HC groups (Wilcoxon Rank $P < 0.05$) ΔBDNF levels was significantly higher in the RA group than HC group. Serum BDNF level was increased in 30.2% of healthy subjects and 4.5% of RA patients ($P = 0.002$). On the other hand, BDI, HADS depression and HADS anxiety indices were correlated significantly with ΔBDNF levels in the RA group ($p<0.05$) but not in HC group.
Conclusion: A single bout of exercise may be effective on serum BDNF levels in patients with RA and healthy subjects. However, psychological comorbidities affect the amelioration of BDNF level, in RA. The long-term effect of alterations on BDF level is candidate to evaluate by prospective studies.

Table 1. Clinical and laboratory characteristics in the study groups

	RA (n=44)	HC (n=44)	P
Mean age, years	46.8±10.3	43.4±6.4	0.071*
Females, n (%)	32 (72.7)	31 (70.5)	0.813**
Active smokers, n (%)	12 (27.3)	10 (22.7)	0.622**
BMI, kg/m^2	26.8±4.6	25.6±2.4	0.127*
HADS Depression	10.2±3.9	2.2±2.1	<0.001*
HADS Anxiety	10.4±4.1	2.4±2.1	<0.001*
BDI	17.9±8.1	3.7±4.1	<0.001*
BDNF (baseline), pg/ml	798.9±381.1	688.7±469.9	0.069***
BDNF (post-exercise), pg/ml	469.5±193.5	509.9±380.4	0.593***
ΔBDNF, pg/ml	329.5±258.4	211.1±302.6	0.047***
BDNF increased, n (%)	2 (4.5)	13 (30.2)	0.002**

RA; rheumatoid arthritis, HC; healthy control, BMI; body mass index, HADS; Hospital Anxiety and Depression Scale, BDI; Beck Depression Inventory, BDNF; brain derived neurotrophic factor*Student's t test, **Chi square test and ***Mann Whitney U test

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3768

POS0577 EVALUATION OF COPING STRATEGIES IN RHEUMATOID ARTHRITIS PATIENTS

B. A. Hiba[1], S. Meriem[2], S. Miladi[2,2], F. Alia[2,2], S. Leila[2], O. Kmar[2], S. Kassab[2], S. Chikili[2], K. Ben Abdelghani[2], A. Laatar[2]. *[1]Mongi Slim University Hospital, Rheumatology, Tunis, Tunisia*; *[2]Mongi Slim University Hospital, Rheumatology, TUNIS, Tunisia*

Background: Studies have shown that the association of pain, stiffness, disability, and social restrictions in rheumatoid arthritis (RA) patients induce a significantly increased level of depressed mood and stress. The use of favorable coping strategies could lead to improve physical and psychological well-being.
Objectives: To evaluate coping strategies of RA patients and their associations with health-related quality of life (HRQoL) outcomes.
Methods: A cross-sectional sample of patients with established RA was evaluated using measures of coping: the Brief-COPE (scores presented for the two overarching coping styles: Approach coping including active coping, emotional support, use of informational support, positive reframing, planning and acceptance, and Avoidant coping including self-distraction, denial, substance use, behavioral disengagement, venting and self-blame), the HRQoL (Mental and Physical Components [MCS/PCS] of the Short Form 12), and the Rheumatoid Arthritis Impact of Disease score (RAID). Multiple linear regression analyses were performed to evaluate the associations between coping strategies and HRQoL outcomes.
Results: The study sample comprised 45 patients with a female predominance (91.9 %), and a mean age of 55.7± 9.9 years [38-77]. The median disease duration was 10 years [38-77]. The majority of patients (82.8 %) were positive for either rheumatoid factor or anti-CCP. Half of the patients were on biological disease-modifying antirheumatic drugs. Two active coping strategies were identified: Approach coping (E = 4.29) and Avoidant Coping (E=3.86), which explained 40% of the total variance. Mean RAID was 4.8± 1.6, while the mean PCS and MCS were 31.9 ± 9.4 and 39.7 ± 9.4, respectively. Approach coping and avoidant coping were associated with PCS (r= 0.4, p = 0.03), (r=0.3, p=0.008) respectively. However, no association was found between coping strategies and MCS or RAID (p>0.05). In the multivariate model, approach coping and avoidant coping were significant to explain lower disease-specific HRQoL (PCS) (Beta= 0.4, p= 0.008), (Beta=0.3, p=0.02) respectively.
Conclusion: Approach and avoidance are associated with lower disease-specific HRQoL (PCS) but not with lower disease-specific HRQoL (MCS). Doctors should not forget to help their patients developing adaptive coping strategies.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3781

POS0578 CORRELATION BETWEEN EXPRESSION LEVELS OF MIR-155 AND MIR-223 IN SYNOVIAL FLUID AND ULTRASOUND SCORES FOR ACTIVE SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS

R. Shumnalieva[1], D. Kachakova[2], R. Kaneva[2], Z. Kolarov[1], S. Monov[1]. *[1]Clinic of Rheumatology, Department of Rheumatology, Medical University-Sofia, Bulgaria, Sofia, Bulgaria*; *[2]Molecular Medicine Center, Department of Medical Chemistry and Biochemistry, Medical University-Sofia, Bulgaria, Sofia, Bulgaria*

Background: MicroRNAs (miRNAs) are a class of small, non-coding RNAs that negatively regulate gene expression at posttranscriptional level. In rheumatoid arthritis studies have shown that miRNA are differentially expressed systemically as well as locally in the inflamed joints [1,2]. The correlation between their systemic or local expression levels and scores for disease activity and progression in RA make them possible candidate for biomarkers in the clinical practice.
Objectives: To analyze the expression levels of miR-155 and miR-223 in synovial fluid (SF) from RA patients in regard to the ultrasound scores for disease activity.
Methods: A total number of 48 RA patients according to the 1987 ACR criteria were included in the study. Expression levels of miR-155 and miR-223 SF were determined by qPCR (SybrGreen technology) and compared to healthy controls (HCs). Relative changes of gene expression levels of the studied miRNAs were calculated by $2^{-\Delta\Delta Ct}$ method. Musculoskeletal ultrasound (MSUS) examination was performed by two

independent examiners on ESAOTE, MyLab60 using both grey scale and power Doppler technic. A semi-quantitative assessment of the peripheral joints was performed for detecting joint inflammation and determining the grade of synovial thickening and the degree of vascularization. Ultrasound features for active disease were correlated to the local expression of the studied miRNAs. SPSS was used for statistical analysis.

Results: RA SF showed overexpression of miR-155 (in 79.17%, $p=1.63x10^{-4}$) and of miR-223 (in 79.17%, $p=1.64x10^{-3}$) when compared to HCs and both miRNAs could be used to differentiate RA patients from HCs ($p=8.0x10^{-5}$ and $p=2.8x10^{-4}$, respectively). When we analyzed the correlation between the diagnosis, the expression of miRNAs and the changes on the musculoskeletal ultrasound examination we found a statistically significant correlation between the presence of synovitis and the degree of the power Doppler signal on MSUS and the local expression of miR-223 ($p=6.19 \times 10^{-4}$ and p=0.003, respectively). SF levels of miR-223 correlated also with the degree of synovial hypertrophy on MSUS (p=0.013). The results for miRNA-155 were not statistically significant.

Conclusion: The correlation between the local expression of miR-223 and the ultrasound features of active joint inflammation shows that this miRNA might be a better candidate for local disease biomarker than miR-155. Further analysis with larger sets is needed to confirm if altered local miRNA expression could be used in the clinical practice as biomarker for disease activity especially in cases with subclinical synovitis.

REFERENCES:

[1] Filková M, Aradi B, Šenolt L, et al. Association of circulating miR-223 and miR-16 with disease activity in patients with early rheumatoid arthritis. ARD, 2014; 73: 1898-1904.

[2]Kriegsmann, M., Randau, T.M., Gravius, S. et al. Expression of miR-146a, miR-155, and miR-223 in formalin-fixed paraffin-embedded synovial tissues of patients with rheumatoid arthritis and osteoarthritis. Virchows Arch, 2016; 469, 93–100.

Acknowledgements: The study was supported by Grant 14-D/2012 and Grant 60/2013 funded by Medical University-Sofia.

Disclosure of Interests: Russka Shumnalieva: None declared, Darina Kachakova: None declared, Radka Kaneva: None declared, Zlatimir Kolarov Speakers bureau: Amgen, Pfizer, Novartis, Abbvie, Roche, Astra-Zeneka, Simeon Monov Speakers bureau: Amgen, Pfizer, Novartis, Abbvie, Roche, Astra-Zeneka

DOI: 10.1136/annrheumdis-2021-eular.3828

POS0579 LOCAL ADAPTATION OF RECOMMENDATION-BASED MATERIALS FOR SHARED DECISION-MAKING AND MANAGEMENT OF COMORBIDITY IN RHEUMATOID ARTHRITIS

J. M. Alvaro-Gracia[1], C. Barbazan[2], J. F. Garcia Llorente[3], S. Muñoz-Fernández[4], A. Gomez-Centeno[5], A. Urruticoechea-Arana[6], M. A. Caracuel-Ruiz[7], E. Loza[8], J. Calvo[9]. *[1]University General Hospital Gregorio Marañón, Rheumatology, Madrid, Spain*; *[2]Complexo Hospitalario Universitario de Vigo, Rheumatology, `Vigo, Spain*; *[3]Hospital de Galdakao Usansolo, Rheumatology, Bilbao, Spain*; *[4]University Hospital 'Infanta Sofía', Rheumatology, Madrid, Spain*; *[5]University Hospital 'Parc Taulí', Rheumatology, Sabadell, Spain*; *[6]Hospital 'Can Misses', Rheumatology, Ibiza, Spain*; *[7]University Hospital 'Reina Sofía', Rheumatology, Cordoba, Spain*; *[8]Instituto de Salud Musculoesquelética, Rheumatology, Madrid, Spain*; *[9]University Hospital of Araba, Rheumatology, Vitoria-Gasteiz, Spain*

Background: Evolving the management of rheumatoid arthritis (eRA) is a European-wide educational initiative aiming to support improved patient care through practical and educational tools addressing specific unmet needs. The aims of the eRA program were: (1) To identify priority unmet needs with the greatest impact on disease outcomes; (2) To develop practical, educational and guidance tools in line with EULAR recommendations to address identified unmet needs; and (3) To improve RA management and patient care.

Objectives: To describe the process by which local adaptations were made of materials derived from evidence-based recommendations in a training programme in rheumatoid arthritis (RA).

Methods: A multidisciplinary Steering Committee (17 members, 12 countries) identified unmet needs within the management of RA and prioritised those with the greatest impact on patient outcomes. Practical educational tools addressing priority needs were then developed for dissemination and implementation by the rheumatology community across Europe, including shared decision making practises and a checklist for managing comorbidity in RA, among others. These materials were evaluated in detailed and discussed in small regional groups by practicing rheumatologists. Voting, open discussions and recommendations were extracted from the meetings.

Results: Thirty-five Spanish rheumatologists from diverse geographic regions discussed a comorbidity checklist and a shared decision making tool. The results of the local meetings were synthesised as (1) a judicious commitment to check agreed comorbidities, and (2) a list of barriers and facilitators for the implementation of shared decision making at the local settings. With regards to ways to implement the agreed list and periodicity, two issues standed-out: (1) patient education and (2) the need of easy access to information and the use of local organisational systems in place. With respect to shared decision-making, issues raised included messages for self-awareness, challenges, and practical facilitators.

Conclusion: Discussion, adaptation, and planning are needed before implementing any evidence-based recommendation and materials if we want to achieve a successful implementation. Further studies should demonstrate whether this initiative was successful in achieving the goals of improved patient care. Our experience could be used as a guidance or example for implementation elsewhere.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3922

POS0580 COMORBIDITY BURDEN IS HIGH IN RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS PATIENTS STARTING BIOLOGICS AND PREDICTS THE INCIDENCE OF SERIOUS ADVERSE EVENTS DURING THERAPY

I. Flouri[1], A. Repa[2], N. Avgustidis[2], N. Kougkas[2], A. Eskitzis[2], A. Molla Ismail Sali[2], S. Pitsigavdaki[2], K. Pateromichelaki[2], E. Kalogiannaki[2], M. Terizaki[2], G. Bertsias[2], P. Sidiropoulos[2]. *[1]University Hospital of Heraklion, Crete, Rheumatology Department, Heraklion, Crete, Greece*; *[2]University Hospital of Heraklion, Crete, Rheumatology Department, Heraklion, Crete, Greece*

Background: There is limited information on the burden of comorbidities in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA) in real-world clinical practice and its impact on the incidence of serious adverse events (SAE) during biologic disease-modifying anti-rheumatic drug (bDMARD) therapy.

Objectives: To evaluate the number of comorbidities in patients with RA and SpA initiating a bDMARD in everyday clinical practice and to explore its association with the occurrence of a SAE during therapy.

Methods: Prospective study of all patients who start any bDMARD treatment in a tertiary centre University Hospital. All comorbidities and SAEs (AEs necessitating hospitalization or resulting in significant incapacity/death) are registered by treating physicians. Comorbidities' number was evaluated using two different indices: total comorbidities count (CC) and Rheumatic Disease Comorbidity Index (RDCI). Statistical analysis was performed using multinomial logistic and Cox regression models.

Results: A total of 799 patients were analysed, of which 428 (54%) had ≥3 comorbidities (Table 1). Comorbidity burden was higher in RA, however in multivariable analyses, comorbidities were not significantly associated with diagnosis, but mainly with increasing patient age. Patients received 1701 bDMARD treatments. During a follow-up of 4019 patient-years, 198 patients (RA:134, SpA:64) had a total of 295 SAE (RA: 217, SpA:78). Each one additional comorbidity in CC index was resulting in 16% increased adjusted risk for the first SAE [HR (95%CI) = 1.16 (1.12-1.20), p<0.001], and each additional comorbidity of the RDCI index was resulting in 28% increased risk [HR (95%CI) = 1.28 (1.20-1.37), p<0.001]. Other baseline independent predictors of the first SAE were greater age [HR=1.04, p<0.001] and use of corticosteroids [HR=1.42, p=0.006].

Table 1. Biologic treatments and clinical characteristics at baseline

Patients, N	Total	RA	SpA	p
	799	501	298	
Females, N (%)	535 (67)	404 (81)	131 (44)	<0.001
Age, median (IQR) έτη	55 (45-65)	60 (51-68)	46 (36-54)	<0.001
Disease duration, median (IQR) έτη	6.0 (2.5-13)	5.4 (3-11)	7.4 (2.0-15)	<0.001
Comorbidities count, median (IQR)	3 (1-5)	3 (2-6)	2 (1-4)	<0.001
Patients with no comorbidities, N (%)	103 (13)	43 (9)	60 (20)	<0.001
Patients with 1 comorbidity, N (%)	134 (17)	77 (15)	57 (19)	0.172
Patients with 2 comorbidities, N (%)	134 (17)	76 (15)	58 (19,5)	0.118
Patients with ≥3 comorbidities, N (%)	428 (54)	305 (61)	123 (41)	<0.001
RDCI, median (IQR)	1 (0-2)	2 (0-3)	1 (0-2)	<0.001
Patients with RDCI = 0, N (%)	267 (33)	128 (25.5)	139 (47)	<0.001
Patients with RDCI = 1, N (%)	185 (23)	119 (24)	66 (22)	0.665
Patients with RDCI = 2, N (%)	163 (20)	113 (23)	50 (17)	0.057
Patients with RDCI ≥ 3, N (%)	184 (23)	141 (28)	43 (14)	<0.001
Total bDMARDs initiated by patients, N	**1701**	**1098**	**603**	
Co-administered methotrexate, N(%)	946 (56)	674 (61)	272 (45)	<0.001
Co-administered corticosteroids, N (%)	493 (29)	397 (36)	96 (16)	<0.001
DAS28, median (IQR) (in RA and perSpA)	5.8 (4.9-6.6)	5.8 (5.0-6.6)	5.4 (4.2-6.3)	<0.001
BASDAI, median (IQR) (in axSpA)	-	-	5.6 (4.5-7.0)	

Conclusion: Patients with RA and SpA initiating a bDMARD treatment in real-world clinical practice have a significant comorbidity burden which increases with age and is an independent predictor for an SAE during therapy.

Acknowledgements: This research is co-financed by Greece and the European Union (European Social Fund- ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning» in the context of the project "Reinforcement of Postdoctoral Researchers - 2nd Cycle" (MIS-5033021), implemented by the State Scholarships Foundation (IKY).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3956

POS0581

PERIODONTAL DISEASE IN RHEUMATOID ARTHRITIS: RESULTS FROM A COHORT AT TREATMENT WITH BIOLOGICAL, CLASSICAL AND TARGETED SYNTHETIC DMARDS

R. Dos-Santos[1], F. Otero[1], E. Perez-Pampín[1], A. Mera Varela[1]. [1]*Clinical University Hospital in Santiago de Compostela, Rheumatology Department, Universidad de Santiago de Compostela, Santiago de Compostela, Spain*

Background: Periodontal disease (PD) has been widely studied in the pathogenesis of rheumatoid arthritis (RA). As well, its relationship with severity and disease activity, has also been investigated with ambiguous results. It has been suggested that the improvement of oral health could enhance disease activity scores.[1] PD prevalence worldwide stands around 60% in older adults (>65 years) and its frequency increases with aging.[2]
Objectives: To asses oral health in RA patients and to identify predictors of PD in this population.
Methods: Patients diagnosed of RA at treatment with biological, classical or targeted synthetic disease modifying anti-rheumatic drugs (b/cs/tsDMARDs) in the aforementioned hospital during 2020 performed a dental review with a specialized periodontal odontologist. Oral health patterns were given for all patients, following criteria of American Academy of Periodontology, and reevaluation of disease activity was made 2 months later.
Clinical, demographic and treatment data were collected from participants.
Univariable logistic regression was performed to identify predictors of PD. Variables with p<0.20 were selected for multivariable analysis.
Stata 15.1 was used to perform statistical analysis.
Results: 81 patients were recruited. 82.72% were female. Mean age was 56.17 years (SD 14.15) and mean time since diagnosis was 15.58 years (SD 8.17). 25% were current or past smokers. 21 patients had comorbidities (arterial hypertension the most frequent). 66.67% were rheumatoid factor (RF) positive and 72.73% anti-citrullinated peptide autoantibody (ACPA) positive. Median erythrocyte sedimentation rate (ESR) was 12 mm (IQR 6;23) and mean C-reactive protein (CRP) was 0.48 mg/dl (SD 1.18). Mean disease activity score (DAS28-VSG) at the testing time was 2.62 (SD 1.21) and after 2 months was 2.39 (SD 0.97). 96.30% of patients were at treatment with csDMARDs, 64.20% with glucocorticoids, 96.30% with bDMARDs and 6 patients with tsDMARDs.
Univariable analysis identified higher age, at least one autoantibody positive and ESR/CRP as potential predictors of medium/severe PD (p<0.20). Multivariable testing including these variables pointed out higher age, lower ESR and at least one autoantibody positive (OR 1.09 [CI95% 1.04-1.14] p=0.001, OR 0.18 [CI95% 0.04-0.95] p=0.044 and OR 0.94 [CI95% 0.88-1.00] p=0.042, respectively) as predictors of medium or severe PD (≥3 mm interdental clinical attachment loss).
Univariable analysis identified higher age, the presence of any comorbidity and anti tumour-necrosis factor alpha treatment (anti-TNF) as potential predictors of severe PD (p<0.20). Multivariable testing including these variables pointed out higher age (OR 1.15 [CI95%1.02-1.30] p=0.026) as predictor of severe PD (≥5 mm interdental clinical attachment loss).
Conclusion: Periodontal disease is still an extended health problem among the entire population. Its prevalence in RA is increased, therefore higher age and RF or ACPA positive are risk factors for developing severe PD. This analysis might suggest that an aggressive management of PD could implement better responses in DAS28. Also anti-TNF treatment could delimit a "penumbra" group of patients at risk of developing severe PD, where intensive manage could modify the final outcome.
REFERENCES:
[1] C O Bingham, M Moni. Periodontal disease and rheumatoid arthritis: the evidence accumulates for complex pathobiologic interactions. Curr Opin Rheumatol. 2013;25(3):345-353.
[2] P Carvajal. Periodontal disease as a public health problem: the challenge for primary health care. Rev Clin Periodoncia inplantol. 2016;9(2):177-183.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3970

POS0582

RHEUMATOID ARTHRITIS AND ORAL MICROBIOME: PREDICTORS OF DISTURBANCES AND ITS IMPLICATIONS. RESULTS FROM A COHORT AT TREATMENT WITH cs/b/tsDMARD

R. Dos-Santos[1], F. Otero[1], E. Perez-Pampín[1], A. Mera Varela[1]. [1]*Clinical University Hospital in Santiago de Compostela, Rheumatology Department, Universidad de Santiago de Compostela, Santiago de Compostela, Spain*

Background: Oral microbiome (OM) seems to be significant in the pathogenesis of some immune-mediated diseases, such as rheumatoid arthritis (RA), psoriasis or inflammatory bowel disease.[1] Some microorganisms, as *Porphyromonas gingivalis* have been related with the production of autoantibodies. Also it has been suggested that composition of OM could change RA disease course, being more difficult-to-treat and having higher disease activity scores.[2]
Objectives: To identify which variables could predict the appearance of altered OM and its implications in clinical practice.
Methods: Patients were recruited if they were diagnosed of RA and were at active treatment (biological, classical or targeted synthetic disease modifying anti-rheumatic drugs [b/cs/tsDMARDs]). Patients performed a dental review with a specialized odontologist that made an OM test (semiquantitative PCR), and oral health standards were instructed (following criteria of American Academy of Periodontology). Recruitment was made during 2020 in the Clinical University Hospital in Santiago de Compostela, Spain. Disease activity reevaluation was made 2 months later.
Treatment, demographic and clinical data were collected from participants.
Univariable logistic and linear regression were performed to identify predictors of OM. Variables with p<0.20 were selected for multivariable analysis.
Stata 15.1 was used to perform statistical analysis.
Results: 47 patients were selected of whom 40 were female. Mean age was 55.43 years (SD 14.42). 30.77% were current or ex-smokers. Mean time since RA diagnosis was 14.89 years (SD 8.47). 63.83% were anti-citrullinated peptide autoantibody (ACPA) positive and 70.21% were rheumatoid factor (RF) positive, letting only 6 patients double negative. 46.81% had moderate/severe periodontal disease (PD). 32.61% of patients had any comorbidity. Mean DAS28 at the OM test was 2.67 (SD 1.28) and after 2 months 2.37 (SD 1.03). Mean C-reactive protein (CRP) was 0.64 mg/dl (SD 1.48) and median erythrocyte sedimentation rate (ESR) was 13 mm (IQR 7;27). All patients were under glucocorticoid treatment, 46 with bDMARD, 1 with tsDMARD and 46 with csDMARD. *Treponema denticola* was detected in 44.68% of patients, *P. gingivalis* in 29.79%, *Actinomyces* spp in 8.51%, *Tanerella forsythia* in 36.17% and *Prevotella intermedia* in 25.53%. Only 15 patients were full-negative for OM test.
Univariable analysis identified RF positive, double autoantibody positive (RF and ACPA) and moderate/severe PD as potential predictors of the presence of at least one oral microorganism (p<0.20). Multivariable testing pointed out moderate/severe PD as predictor of the presence of at least one oral microorganism (OR 22.91 [CI95% 2.38-220.4] p=0.007).
Univariable analysis identified higher age, presence of any comorbidity, RF positive, higher CRP, treatment with anti-tumour necrosis alpha (aTNF) and moderate/severe PD as potential predictors of the presence of multiple species in OM (p<0.20). Multivariable testing pointed out moderate/severe PD as predictor of the presence of multiple species in OM (ß 0.39 [95%CI 0.19-0.58] p=0.000).
Conclusion: Oral microbiome is closely related with periodontal disease, added to our results, a relationship between OM and disease activity has been exposed. In this analysis the role of OM and autoantibody profile is manifest, as being double positive or RF positive is associated with the presence of altered OM. Also patients with high acute-phase reactants, active disease and under aTNF treatment could delineate a specific RA population under risk of altered OM, where intensive strategies for changing oral microbiome could have any repercussion in the disease course.
REFERENCES:
[1] Chen, B., Zhao, Y., Li, S. *et al.* Variations in oral microbiome profiles in rheumatoid arthritis and osteoarthritis with potential biomarkers for arthritis screening. *Sci Rep* **8,** 17126 (2018).
[2] R Bodkhe, B Balakrishnan, V Taneja. The role of microbiome in rheumatoid arthritis treatment. Ther Adv Musculoskelet Dis. 2019;11:1759720.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3979

POS0583

ENGINEERED GLOVE TO EVALUATE THE SPEED OF THE HANDS' MOVEMENTS IN RHEUMATOID ARTHRITIS

M. Patanè[1], L. Carmisciano[2], E. Hysa[3], E. Gotelli[3], A. Signori[2], V. Smith[4], M. Cutolo[3]. [1]*Ospedale Alessandria, Internal Medicine, Alessandria, Italy*; [2]*University of Genoa, Department of Health Sciences, Genoa, Italy*; [3]*University of Genoa, Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, IRCCS "San Martino" Polyclinic Hospital, Genova, Italy*; [4]*Ghent University, Department of Internal Medicine; Department of Rheumatology; Unit for Molecular Immunology and Inflammation, Ghent University Hospital, Gent, Belgium*

Background: Rheumatoid arthritis (RA) is a long-term, progressive, and disabling autoimmune disease1. The disease activity can be quantified by the Disease Activity Score 28-joint count – C reactive protein (DAS28crp)2; the evaluation of disability function (DF) is actually mainly performed only by subjective Patient Reported Outcomes (PROs) like Health Assessment Questionnaire (HAQ)3; to investigate the functional aspects of RA hands it is usually used the grip strength (GS)4. However, in the scientific literature no tool, which objectively evaluates movement speed, has been reported. The Hand Test System (HTS, ETT) is an engineered glove (RAGLOVE), nowadays applied for neuroscience studies to evaluate hand motility5

Objectives: To objectively evaluate the RA hand's speed of the fine movements, through the HTS and to compared with a group of age and sex matched healthy controls. To verify the correspondence with the HAQ, DAS28, GS.
Methods: 55 consecutives RA patients (pts) (6 males, age 61 ± 16 years, mean duration of disease 12 ± 8 years), classified according to 2010 ACR/EULAR criteria6, and 50 matched healthy controls (HCs) were enrolled. After consent, all participants undergone HTS test that recognizes the touches between the finger tips during the opposition movements of the hands in standard sequences of movements, after dressed the glove. A multiple finger evaluation (MFE) and a single finger evaluation (SFE) were performed using a dedicated software that provided the physician the following quantitative parameters: Touch Duration (TD), Inter Tapping Interval (ITI) and Movement Rate (MR). Average time for hand 2 minutes. RA pts compiled the HAQ, performed the GS and a DAS28cpr was performed.
The student's t-test was used to compare the glove's parameters between the groups whereas the analysis of variance (ANOVA) was utilized to verify potential differences between the populations. In order to evaluate the single correlations, the r and p values of Pearson were employed.
Results: For MFE, glove parameters TD and ITI were significantly higher in RA pts than HCs, whereas; MR was significantly lower in RA pts compared to HCs (all p <0.001).
For SFE non-affected fingers (not swollen and not tender) of RA pts performed better than a clinically affected fingers, but in any case significantly worse than average HCs fingers (p < 0.001).
There is a statistically significant correlation between the GS and MR (r= 0.39 p=0.003) and TD (r=-0.33 p=0.015).
TD, ITI e MR of RA pts showed a significant correlation with the total score of the HAQ (r = 0.56, r = 0.39, r = -0.56, all p < 0.001;). DAS28, considered as a continuous variable, proved to be significantly correlated with the TD (r = 0.36, p = 0.009). When the RA patients were grouped according to the disease activity by DAS28cpr7, there was an increase of one third of the TD's logarithm for each increase in the activity class (linear regression with ordinal predictors, beta = 0.33; 95%CI 0.03, 0.63,p < 0.0297). Finally, even RA pts in remission showed a TD significantly higher compared with HCs (p= 0.034).
Conclusion: The RAGLOVE is shown as a new safe and fast tool to evaluate a new objective parameter in the hand's functionality: the speed of finger movements. In RA pts, an inversely proportional correlation emerges between the speed of movement and disease activity.
The significant correlation found with HAQ, highlights the loss of motility of the hands as one of the main determinant of disability. The RAGLOVE is now tested in RA patients undergoing treatment.
REFERENCES:
[1] Hakkinen et al Ann Rheum Dis. 2005;
[2] Van Der Heijde et al J of Rheum. 1993;
[3] Fries et al Arthritis Rheum. 1980;
[4] Mathiowetz et al J Hand Surg Am. 1984;
[5] Carmisciano et al Eur J Neurol. 2020;
[6] Aletaha et al. Ann Rheum Dis. 2010;
[7] Aletaha et al Arthritis Rheum 2005.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3991

POS0584 ULTRASONOGRAPHY OF THE MEDIAN NERVE IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDER SUSPICION OF CARPAL TUNNEL SYNDROME

S. Tsiami[1], E. Ntasiou[2], C. Krogias[2], R. Gold[2], J. Braun[1], M. Sarholz[3], X. Baraliakos[1]. [1]*Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*; [2]*Ruhr-University Bochum, St. Josef-Hospital, Bochum, Germany*; [3]*St. Marien-Hospital Vreden, Klinik fuer Rheumatologie, Vreden, Germany*

Background: Carpal tunnel syndrome (CTS) is the most common nerve compression syndrome and a common extra-articular manifestation of rheumatoid arthritis (RA). Different causes of CTS are known, among them inflammatory and non-inflammatory pathologies. Electroneurography (ENG) of the median nerve, the method of choice to diagnose CTS, measures impairment of nerve conduction velocity without explaining its underlying cause. However, because the electrical stimulation is often not well tolerated, ENG results may come out inconclusive. Using greyscale ultrasonography (GS-US) provides anatomic information including a structural representation of the carpal tunnel.
Objectives: To investigate the performance of nerve GS-US in the diagnosis of CTS in patients with RA.
Methods: Consecutive patients with active RA under suspicion of CTS presenting to a large rheumatologic center were included. Both hands were examined by an experienced neurologist including ENG and a GS-US (ML linear probe with 6-15 Hz) of the median nerve. An established grading system for ENG (1), and an established system for GS-US based on cut-offs for the nerve cross sectional area (CSA) [mild: 0,11-0,13cm^2, moderate: 0,14-0,15 cm^2, severe: > 0,15 cm^2 CTS (2)] were used. In addition, the Boston Carpal Tunnel Syndrome Questionnaire (BCTSQ) was used to assess CTS symptoms (3).
Results: Both hands of 58 patients with active RA (n=116) and clinical suspicion of CTS (in 38 cases bilaterally) were included. After clinical examination, CTS was suspicious in 96 hands (82.8%), and 59 of all hands had a final diagnosis of CTS (50.9%). Of the latter, 43 hands (72.9%) had a positive ENG and 16 (27.1%) a positive GS-US finding only, while 30 hands (50.8%) were positive in both examinations.

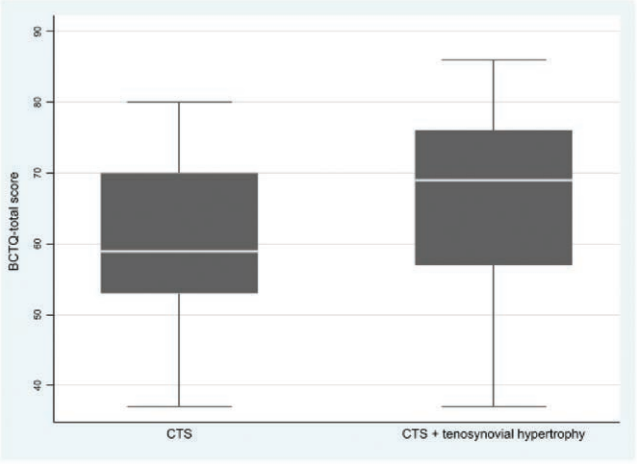


Figure 1. BCTSQ scores in patients with diagnosis of CTS and absence or presence of RA-related tenosynovial hypertrophy

There was a good correlation of the cross-sectional area (CSA) as well as the CSA-ratio to the ENG findings: the larger the CSA, the more severe was the CTS as assessed by ENG (Spearman's rho=0.554; p<0.001). The more severe the GS-US findings of CTS were, the more definite were the distal motor latency (Spearman's rho=0.554; p<0.001) and sensible nerve conduction velocity of the median nerve (Spearman's rho=-0.5411; p<0.001).
In the 46 hands positive in GS-US, tenosynovial hypertrophy of the flexor tendons was detected in 19 hands (41.3%), 7 of which (36.8%) also showed an additional cystic mass. In these 19 patients, clinical complains were more severely present than in patients with non-inflammatory CTS, as assessed by the BCTSQ with a total score of 68.8±13.4 vs. 59.3±13.7, respectively (p=0.007).
Conclusion: In patients with active RA and clinical complains of CTS, ultrasound examinations provide additional information about inflammation which is helpful for a diagnosis of CTS. Thus, ENG and nerve GS-US should be used complementary for a diagnostic workup of CTS in RA patients with a suspicion of CTS. Power-Doppler may further improve the diagnostic performance of GS-US.
REFERENCES:
[1] Padua L et al. Acta Neurol Scand 1997; 96:211–217
[2] El Miedany et al., Rheumatology (Oxford). 2004 Jul; 43(7):887-895
[3] Levine DW et al. J Bone Joint Surg Am 1993; 75: 1585-1592
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3994

POS0585 ORAL STATUS IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Ben Salem[1], M. Brahem[1], H. Hachfi[1], R. Sarraj[1], S. Abdellatif[1], R. Ben Tekaya[1], C. Baccouche[2], Y. Mohamed[1]. [1]*Tahar Sfar Hospital, Rheumatology, Mahdia, Tunisia*; [2]*Tahar Sfar Hospital, Dentistry, Mahdia, Tunisia*

Background: Rheumatoid arthritis (RA) is a systemic auto immune inflammatory disorder, which primarily affects the synovial joints, but it may have an impact on oral health.
Objectives: The present study aimed to describe oral manifestations in patients with Rheumatoid arthritis (RA).
Methods: A cross sectional study including RApatients, which consulted or were hospitalized in Rheumatology department in Taher Sfar Hospital of Mahdia Tunisia, during a period of 10 months. The diagnosis of RA was based on ACR/EULAR 2010 criteria. Oral and periodontal examination was practiced by a trained dentist in the same hospital. Oral hygiene, teeth status (missing teeth) and paradental parameters (bleeding index of Loe and Silness (IG), plaque indexed O'Leary (IP) were determined for each patient, to assess oral and periodontal diseases in RA.
Results: Our study included 51 patients with an average age of 51.11 years ±12.4 [21-74years].50patients (92.6%of cases) were women and 8patients (14.8%) were diabetic. Only one patient was a smoker. The mean duration of RA was 10.7 years 7.7± [10months-35years]. Rheumatoid factor (RF) was positive

in 25 Patients (46.3%of cases). Anti-citrullinated peptide antibody (ACPA) was positive in 32 patients (59.3 %).41patients (75.4%) had radiological impairments and 28(51.9%) had specific deformations of RA. The average disease activity score (DAS28-VS) and (DAS28-CRP) were respectively 4.1±1.5[1.4-7.3] 3.4±1.5 [1.24-6.71]. Oral examination revealed a poor oral hygiene in 36patients (69.2% of cases) and 4.7% of our patients (2 cases) were toothless. Xerostomia was observed in 32 patients (80%). Gingivitis was diagnosed in 26 Patients (52%): localized in 6 patients (26.1%) and generalized in 17 patients (73.9%). 21 patients had periodontitis (41.2%). Basing on bleeding index of Loe and Silness (IG),27 patients (55.1%) had degree 2 and9 patients (18.8 %) had degree 3. Supragingival plaque and subgingival plaque were detected respectively in 45 patients (90 %) and 47 patients (95.9 %). In our study, tooth loss was significantly correlated with increased age (p=0.001) and post-menopausal status (p=0.03). Xerostomia, gingivitis and periodontitis were associated with increased age. But no association was found between oral manifestations and DAS28 nor biological inflammatory parameters.

Conclusion: Rheumatoid arthritis is destructive and disabling rheumatism with a great risk to develop dental and periodontal diseases. So, it is important to systematically control oral hygiene of our patients to prevent complications.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4015

POS0586 RHEUMATOID ARTHRITIS IS AN INFLAMMATORY DISEASE WITH A HIGH CARDIOVASCULAR RISK

L. Nacef[1], H. Riahi[2], Y. Mabrouk[1], H. Ferjani[3], K. Maatallah[3], E. Labbene[4], D. Kaffel[1], M. Bouaziz[2], W. Hamdi[1]. [1]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Manouba, Tunisia*; [2]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Radiology, Tunis, Tunisia*; [3]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Tunis, Tunisia*; [4]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Radiology, Manouba, Tunisia*

Background: Hypertension, diabetes, and dyslipidemia are traditional risk factors of cardiac events. Carotid ultrasonography is an available way to detect subclinical atherosclerosis.

Objectives: This study aimed to compare the intima-media thickness in RA patients based on their personal cardiovascular (CV) history of hypertension (hypertension), diabetes, and dyslipidemia.

Methods: The present study is a prospective study conducted on Tunisian RA patients in the rheumatology department of Mohamed Kassab University Hospital (March and December 2020). The characteristics of the patients and those of the disease were collected.

The high-resolution B-mode carotid US measured the IMT, according to American Society of Echocardiography guidelines. The carotid bulb below its bifurcation and the internal and external carotid arteries were evaluated bilaterally with grayscale, spectral, and color Doppler ultrasonography using proprietary software for carotid artery measurements. IMT was measured using the two inner layers of the common carotid artery, and an increased IMT was defined as ≥0.9 mm. A Framingham score was calculated to predict the cardiovascular risk at 10-year.

Results: Forty-seven patients were collected, 78.7% of whom were women. The mean age was 52.5 ±11.06 [32-76]. The rheumatoid factor (RF) was positive in 57.8% of cases, and anti-citrullinated peptide antibodies (ACPA) were positive in 62.2% of cases. RA was erosive in 81.6% of cases. Hypertension (hypertension) was present in 14.9% of patients, diabetes in 12.8% of patients, and dyslipidemia in 12.8% of patients. Nine patients were active smokers. The mean IMT in the left common carotid (LCC) was 0.069 ±0.015, in the left internal carotid (LIC) was 0.069 ±0.015, in the left external carotid (LEC) was 0.060 ±0.023. The mean IMT was 0.068 ±0.01 in the right common carotid (RCC), 0.062 ±0.02 in the right internal carotid (RIC), and 0.060 ±0.016 in the right external carotid (REC). The IMT was significantly higher in the left common carotid (LCC) in patients with hypertension (p=0.025). There was no significant difference in the other ultrasound sites (LIC, LEC, RCC, RIC, and REC) according to the presence or absence of hypertension. The IMT was also significantly increased in patients with diabetes at LCC (p=0.017) and RIC (p=0.025). There was no significant difference in the IMT at different ultrasound sites between patients with and without dyslipidemia.

Conclusion: Hypertension was significantly associated with the increase in IMT at the LCC level in RA patients. Diabetes had an impact on IMT in LCC and RIC. However, dyslipidemia did not affect the IMT at the different ultrasound sites.

REFERENCES:

[1] S. Gunter and al. Arterial wave reflection and subclinical atherosclerosis in rheumatoid arthritis. Clinical and Experimental Rheumatology 2018; 36: Clinical *E.xperimental.*

[2] Aslan and al. Assessment of local carotid stiffness in seronegative and seropositive rheumatoid arthritis. SCANDINAVIAN CARDIOVASCULAR JOURNAL, 2017.

[3] Martin I. Wah-Suarez and al, Carotid ultrasound findings in rheumatoid arthritis and control subjects: A case-control study. Int J Rheum Dis. 2018;1–7.

[4] Gobbic C and al. Marcadores subclínicos de aterosclerosis y factores de riesgo cardiovascular en artritis temprana. Subclinical markers of atherosclerosis and cardiovascular risk factors in early arthritis marcadores subclínicos de aterosclerose e fatores de risco cardiovascular na artrite precoce.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4080

POS0587 EFFECT OF RHEUMATOID ARTHRITIS TREATMENTS ON THE INTIMA-MEDIA THICKNESS OF SUPRA-AORTIC TRUNKS AND ON CARDIOVASCULAR RISK

L. Nacef[1], H. Ferjani[2], K. Maatallah[1], Y. Mabrouk[2], H. Riahi[3], E. Labbene[4], D. Kaffel[2], W. Hamdi[1], M. Bouaziz[3]. [1]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Tunis, Tunisia*; [2]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Manouba, Tunisia*; [3]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Radiology, Tunis, Tunisia*; [4]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Radiology, Manouba, Tunisia*

Background: Patients with rheumatoid arthritis (RA) are exposed to a multifactorial cardiovascular risk: chronic inflammation, endogenous and exogenous factors, and treatment.

Objectives: The aim of this study was to investigate the impact of RA treatments on cardiovascular risk and the influence of supra aortic trunks.

Methods: This is a prospective study conducted on RA patients followed-up between March and December 2020 at the rheumatology department of the Mohamed Kassab Institute of Orthopedics and Traumatology. Socio-demographic data of patients and characteristics of the disease were collected. The disease activity was evaluated by the Disease Activity Score 28. Prescribed treatments were specified. Ultrasonography of the supra aortic trunks was performed by measuring, in centimeters, the Intima-media Thickness (IMT) at the level of the left (LCC) and right (RCC) common carotid arteries, the left (LIC) and right (RIC) internal carotid arteries and the left (LEC) and right (REC) internal carotid arteries.

Results: Of the 47 patients surveyed, 78.7% were female. The mean age was 52.5 ±11.06 [32-76]. The average RA progressed from 86.25 ±63 [5-288] and was erosive in 81.6% of cases. The rheumatoid factor (RF) was positive in 57.8% of patients, and citrullinated antipeptide antibodies (ACPA) were present in 62.2%. The treatments taken were: Methotrexate (MTX) (54.5%), Sulfasalazine (SLZ) (1.8%), Leflunomide (LFN) (3.6%), a combination of cs-DMARDs (5.5%), and biotherapy (10.9%). The prescribed biotherapies were: Etanercept (3.6%), Adalimumab (1.8%), Certolizumab (1.8%), Infliximab (3.6%). Corticosteroids (CT) were prescribed in 38.2% of patients, non-steroidal anti-inflammatory drugs (NSAIDs) (3.6%), and analgesics (41.8%).

CT had a protective effect on IMT in LIC (p=0.031) and RIC (p=0.016). MTX had a significant protective effect on IMT in RIC (p=0.002) and LEC (p=0.033).

SLZ was associated with an increase in IMT at the RIC level (p=0.05). There was no association between NSAID use and IMT. MTX and CT were significantly associated with a decrease in SCORE (p=0.02; p=0.05, respectively). There was a non-significant association between SLZ or LFN and decreased SCORE (p=0.140, p=0,970).

Conclusion: In our series, patients taking MTX and CT had a lower IMT than those not taking these drugs. SLZ was associated with an increase in IMT. NSAIDs did not affect IMT in our study.

REFERENCES:

[1] Pasquale Ambrosino and al, Subclinical atherosclerosis in patients with rheumatoid arthritis A meta-analysis of literature studies. Thrombosis and Haemostasis 113.5/2015

[2] Hyun-Je Kim and al, Effects of Methotrexate on Carotid Intima-media Thickness in Patients with Rheumatoid Arthritis. The Korean Academy of Medical Sciences 2015.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4120

POS0588 USUAL INTERSTITIAL PNEUMONIA DURING RHEUMATOID ARTHRITIS: PREVALENCE AND ASSOCIATED FACTORS

C. Daldoul[1], N. El Amri[1], A. Guiga[2], S. Laataoui[1], K. Baccouche[1], H. Zegaloui[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*; [2]*Farhat Hached Hospital, Internal Medicine, Sousse, Tunisia*

Background: Lung involvement is the second common extraarticular manifestation of rheumatoid arthritis (RA). Its prevalence varies widely according to the screening tool used and it could reach up to 80% of patients. This lung disease can affect all the lung compartments. However, interstitial lung disease during RA needs a particular attention due to the increased morbidity and usual interstitial pneumonia (UIP) pattern especially due to its higher rate of mortality.

Objectives: To determine the frequency and associated factors of UIP among RA patients
Methods: This was a retrospective study conducted at the Rheumatology department of Farhat Hached University Hospital from 2005 to 2020. We included all RA patients who had undergone high-resolution computed tomography (HRCT) scans of the lung. Demographic data, disease characteristics, pulmonary function tests (PFT) and drugs intake were collected at the time of the realization of the HRCT. UIP pattern and NON-UIP patterns were based on HRCT results. Khi-2 and T-student tests were used in the univariate analysis. Binary logistic regression was used in the multivariate analysis. Statistical significance level was set at 5%.
Results: Fifty-nine patients with RA patients having HRCT of the lung were identified among them 27.1% (16) were male. The mean age of the patients was 60.27± 11.3 years; the mean disease duration was 7.16 ± 2.9 years and current or previous smoking habits were recorded in 18.8% (11) of our population with a median. Secondary Sjogren's syndrome and cutaneous rheumatoid nodules were documented in 33.9% (20) and 10.17% (6) respectively. RA was erosive in 81.5% (48) of our population. The median tender joint count and the median swollen joint count were 10 and 4 respectively. The mean erythrocyte sedimentation rate (ESR) and the mean C-reactive protein (CRP) were 49±20.31 mm and 32±14.07 mg/dl respectively. The mean disease activity score (DAS 28 ESR) was 5.49±1.66. The median rheumatoid factor and Anti-CCP levels were 260UI/ml and 68 UI/ml respectively. Exertional dyspnea (stage 2 or higher) was present in 42.37% (25) and inspiratory crackles were found in 22.4% (13) of our patients. PFT revealed a restrictive ventilatory defect, an obstructive pattern and a mixed pattern were found in 20.3% (12), 13.6 (8) and 3.4% (2) respectively. The mean DLCO value was 70±24.6%. According to HRCT results, parenchymal involvement was found in 83.1% (49) of our patients and among them, we documented UIP pattern in 18 (36.73%), Non Specific Interstitial Pneumonia (NSIP) in 14.28% (7), unclassifiable fibrosis in 14.29 (7), organizing pneumonia in 2% (1) and isolated pulmonary nodules in 32.6% (16). Pleural effusion was found in 5.1% (3) and airways disease in 15.3% (9). Mediastinal lymphadenopathy was found in 15.25% (9). Abnormalities on HRCT lead to a change in treatment in 30.5% (18) of our patients. Compared to the group with a non-UIP pattern, male sex was significantly associated with UIP pattern on HRCT (47.4% vs. 17.5%, p=0.016). UIP pattern was significantly associated with smoking (37.5% vs. 9.4% p=0.022, Unadjusted OR=5.88, 95%IC=[1.217-27.634]), with cutaneous rheumatoid nodules (31.3% vs.3.4%, p=0.017, Unadjusted OR=12.72, 95IC=[1.331-121.658]) and with the presence of lymphadenopathy on HRCT (41.2% vs. 6.5%, p=0.004, Unadjusted OR=10.15, 95%IC=[1.803-57.140]). There was no significant difference between the two groups regarding age (p=0.454), disease duration (p=0.126), DAS28 (p=0.447), anti-CCP level (p=0.454). After multivariate analysis, male sex (Adjusted OR=11.58, 95%IC=[1.622-82.67] p=0.015), Presence of lymphadenopathy on HRCT (Adjusted OR=10.53, 95%IC=[1.146-96.87], p=0.037) and exertional dyspnea (Adjusted OR=6.43, 95%IC=[1.036-40.011], p=0.046) were independently associated with UIP pattern.
Conclusion: UIP was present in 36.73% and it was the most prevalent pattern of lung involvement in RA. It was associated with male sex, mediastinal lymphadenopathy and exertional dyspnea.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4178

POS0589 **PREVALENCE AND SEVERITY OF STRESS AT HOME AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: SINGLE CENTRE RESULTS FROM THE PRIME REGISTRY COHORT**

M. Haroon[1], F. Hashmi[1], S. Ullah[1], A. Ashraf[2], H. J. Shaheen[1], S. Asif[1], S. Batool[1]. [1]*Fatima Memorial Hospital & FMH College of Medicine and Dentistry, Department of Rheumatology, Lahore, Pakistan*; [2]*CMH Lahore Medical College & Institute of Dentistry, Medicine, Lahore, Pakistan*

Background: In chronic inflammatory diseases like rheumatoid arthritis (RA), psychological stress is widely recognised as an important risk factor to negatively affect the disease course. Stress activates the hypothalamic-pituitary adrenal axis and the autonomic nervous system, which associate with the release of neurotransmitters (i.e. norepinephrine), hormones (i.e. cortisol) and activation of immune cells. Perceived stress can potentially induce the disease exacerbation, but on the other hand, the disease itself might produce significant stress to patients thus the vicious circle is formed and maintained.
Objectives: We aimed to examine the prevalence of mental/emotional stress at home and its associations among patients with Rheumatoid arthritis. We addressed this question using real-world data from the PRIME registry.
Methods: This was a cross-sectional study conducted using data collected at the time of patient enrolment in the PRIME registry. The PRIME Registry is a large, independent, prospective, observational cohort initiated in October 2019 that comprises patients diagnosed with RA, SLE, PsA or AS by a rheumatologist, and is being actively followed up. IRB approval and informed consent was obtained. We assessed the data for RA patients. The clinical variables studied were gender, age, smoking habits, body mass index, education status, marital status, disease duration, comorbidities (using Charlson Comorbidity Index). Education status was stratified by whether participants completed secondary (high) school education. Evaluation of disease activity and severity was made as per internationally agreed definitions, such as: swollen joint counts, tender joint counts, deformed joint counts, and DAS-28. All participants were directly inquired at the interview during the time of patient enrolment about the presence or otherwise of mental/emotional stress at home, and to rate it from 1-3 (mild, moderate, severe). For better understanding and ease of statistical analysis, dichotomous variable was made with moderate-to-severe stress patients were categorised into one group and none-to-mild stress patients into second group.
Results: The data of consecutive 507 RA patients (mean age 42.3±12.6 years, 73.6% female, disease duration of 80±22 months) was reviewed. Forty-eight percent of patients accepted to have moderate-severe stress at home (moderate stress=29.9%, severe stress=18.3%). On univariate analysis, significant association of moderate-severe stress at home was noted with deformed joint counts (p=0.036), higher DAS-28 scores (p<0.001), and being married (p=0.001). Weak statistical association of age (p=0.11), disease duration (p=0.13), low education status (p=0.14), female gender (p=0.24) was noted. On multiple logistic regression analysis, a significant association of moderate-severe stress at home was observed with higher DAS-28 scores (OR 1.76, CI 1.29-2.41, p<0.001) and deformed joint counts (OR 1.15, CI 1.00-1.31, p=0.040). Following variables were included in multiple stepwise regression analysis: age, disease duration, low education status, married, Das-28 scores, and deformed joint counts. However, when gender was included in the regression analysis, a significant association of moderate-severe stress at home was observed with female gender (OR 3.99, CI 1.47-10.83, p=0.007), higher DAS-28 scores (OR 1.8, CI 1.31-2.51, p<0.001), with marginal association with deformed joint counts (OR 1.13, CI 0.99-1.30, p=0.061).
Conclusion: Stress at home is common among patients with RA, and nearly half of the cohort was noted to have moderate-severe level of stress at home. Ongoing stress at home has significant association with higher RA disease activity and deformities suggesting a bidirectional relationship. These findings demonstrate an important need for integration of rheumatologic, social workers and mental health services
Disclosure of Interests: Muhammad Haroon Speakers bureau: Roche, Novartis, Grant/research support from: Abbvie, Pfizer, Farzana Hashmi: None declared, Saadat Ullah: None declared, Arfa Ashraf: None declared, Hafiza Javeria Shaheen: None declared, Sadia Asif: None declared, Shabnam Batool: None declared
DOI: 10.1136/annrheumdis-2021-eular.4181

Rheumatoid arthritis - biological DMARDs

POS0590 **SAFETY AND EFFICACY OF BIOLOGICS IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS IN A REAL WORLD STUDY: USE OF INTRAVENOUS GOLIMUMAB AND INFLIXIMAB IN ADULTS WITH RHEUMATOID ARTHRITIS ≥65 YEARS OF AGE**

J. Schechtman[1], A. Broadwell[2], S. Kafka[3], S. Black[4], S. Xu[5], W. Langholff[5], S. Schwartzman[6]. [1]*Sun Valley Arthritis Center, Rheumatology, Peoria, United States of America*; [2]*Rheumatology and Osteoporosis Specialists, Rheumatology, Shreveport, United States of America*; [3]*Janssen Scientific Affairs, LLC, Immunology, Horsham, United States of America*; [4]*Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; [5]*Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; [6]*Weill Cornell Medical College, Rheumatology, New York, United States of America*

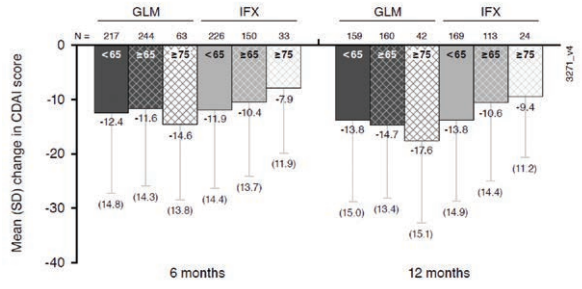
Background: AWARE is a real-world evidence-based (RWE) study evaluating the safety and efficacy of IV golimumab (GLM) and infliximab (IFX) in adults with RA.
Objectives: Evaluate safety and efficacy of IV GLM and IFX in elderly AWARE participants.
Methods: AWARE, a prospective non-interventional study (88 US sites), enrolled patients (pts) initiating either IV GLM or IFX. Pt management was at the discretion of treating rheumatologists. In a post hoc analysis, pts were grouped by age (<65/≥65/≥75 yrs). Adverse events (AEs) were collected through the Week (W) 52 database lock (DBL; completed W52 or discontinued study) and at the end-of-study DBL (W104). The primary endpoint was proportion of pts with ≥1 infusion reaction through W52. Change from baseline in Clinical Disease Activity Index (CDAI) scores at Months 6 and 12 were secondary endpoints evaluated in bionaïve pts, including those with IFX dose escalation.
Results: 1270 pts were enrolled (685 IV GLM; 585 IFX). 1047 (82%) pts were female; mean age was 60 yrs (57% <65 yrs, 43% ≥65 yrs, and 7% ≥75 yrs). Mean disease durations were 9 yrs (IV GLM) and 7 yrs (IFX). Comorbidities were generally similar between IV GLM and IFX groups but more common among pts ≥65

vs <65 yrs. Through W52, 66% of IV GLM pts and 62% of IFX pts discontinued the study. Discontinuation due to lack of efficacy was generally similar across age groups within treatment groups, although somewhat higher for IV GLM (29%) vs IFX (19%). For both treatments, AEs and discontinuations due to AE through W52 were more common in pts ≥65 vs <65 yrs (Table 1). Consistent with general trends observed in elderly individuals,[1] rates of serious AEs (SAEs) and serious infections increased with age for both IV GLM and IFX; however, increases were more notable in IFX- than IV GLM-treated pts ≥65 yrs. The incidence of serious infections was highest in pts ≥75 yrs for both treatments, although small sample size may limit data interpretation. No increase in opportunistic infections, including Varicella, was observed in pts ≥65 vs <65 yrs. Infusion reactions were more common in pts <65 yrs in both treatment groups, and more prevalent in IFX- than IV GLM-treated pts within each age group through W52. Generally similar safety results were seen between W52 and W104 for each treatment group (data not shown). Both IV GLM and IFX in bionaïve pts showed improvement in CDAI scores across age groups, which was maintained over time (Figure 1).

Table 1. % of pts with ≥1 AE through W52 DBL

	IV GLM			IFX		
	<65 yrs	≥65 yrs	≥75 yrs	<65 yrs	≥65 yrs	≥75 yrs
Patients, n	351	334	91	370	215	46
Discontinued due to AE	8.5%	12.6%	16.5%	15.1%	17.7%	21.7%
AE	52.4%	58.4%	57.1%	63.5%	66.5%	71.7%
Most common AEs (≥5% of pts in either treatment group)						
Nausea	3.7%	3.3%	3.3%	8.4%	6.0%	2.2%
Worsening of RA	5.4%	4.5%	3.3%	7.3%	7.0%	4.3%
Upper respiratory tract infection	5.7%	5.1%	4.4%	6.2%	5.6%	2.2%
Pruritis	1.4%	2.4%	3.3%	6.8%	2.8%	2.2%
Sinusitis	7.1%	3.3%	0%	3.8%	3.7%	2.2%
Urinary tract infection	4.8%	5.1%	5.5%	4.3%	5.1%	6.5%
SAE	7.7%	16.8%	20.9%	9.7%	18.6%	26.1%
Infection	30.5%	27.2%	27.5%	32.2%	28.8%	32.6%
Serious infection	3.7%	6.3%	7.7%	3.5%	7.9%	15.2%
Neoplasms benign, malignant and unspecified	0.6%	2.7%	1.1%	0.8%	2.3%	6.5%
Latent tuberculosis	0.3%	0%	0	0.3%	0%	0%
Opportunistic infection	1.4%	1.8%	4.4%	1.9%	1.4%	4.3%
Infusion reaction	5.1%	2.7%	1.1%	17.3%	8.8%	8.7%
Death	0.3%	2.4%	2.2%	0%	2.3%	6.5%

Figure. Mean (SD) change from baseline CDAI score at 6 months and 12 months (observed data) for bionaive population[a]



[a] Efficacy conducted for bionaive population including pts who had IFX dose escalation

Conclusion: Elderly RA pts receiving IV GLM or IFX in this RWE study demonstrated similar safety and efficacy as reported in Phase 3 trials.[2,3] The higher rates of AEs, discontinuations due to AE, and SAEs (mainly serious infections) observed in pts ≥65 yrs are in line with increased safety events seen in elderly vs younger individuals in the general population. Rates of AEs, SAEs, and infusion reactions were higher for IFX vs IV GLM. Infusion reactions were more common in pts <65 vs ≥65 yrs for both GLM and IFX, but more prevalent with IFX.

REFERENCES:

[1] Castle SC. Clin Infect Dis 2000;31:578–85.
[2] Lipsky PE, et al. N Engl J Med 2000;343:1594-602.
[3] Weinblatt ME, et al. Ann Rheum Dis 2013;72:381-9.

Disclosure of Interests: Joy Schechtman: None declared, Aaron Broadwell Speakers bureau: Amgen, AbbVie, Eli Lilly, Horizon, Janssen, Mallinckrodt, Novartis, Pfizer, Radius, Sanofi/Regeneron, and UCB, Consultant of: AbbVie, Amgen, Aurinia, Celegene, Eli Lilly, Janssen, Novartis, Pfizer, and Sandoz, Shelly Kafka Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Shawn Black Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Stephen Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Wayne Langholff Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Sergio Schwartzman Shareholder of: Amgen, Boston Scientific, Gilead, Medtronic, and Pfizer, Speakers bureau: AbbVie, Janssen, Eli Lily, Novartis, Pfizer, Regeneron, Sanofi, and UCB, Consultant of: AbbVie, Gilead, Eli Lilly, Janssen, Myriad, Novartis, Regeneron, Samsung, Sanofi, and UCB
DOI: 10.1136/annrheumdis-2021-eular.165

POS0591 SARILUMAB ATTENUATES DISEASE ACTIVITY IN SERONEGATIVE RA PATIENTS – PRELIMINARY DATA FROM A NON-INTERVENTIONAL STUDY IN REGULAR CARE IN GERMANY

H. Burkhardt[1], H. P. Tony[2], P. M. Aries[3], S. Zinke[4], K. Krueger[5], J. Ahlers[6], R. Hecker[6], I. Albrecht[7], S. Kalus[8], O. Bley[9], P. Sternad[10], A. D. Holst[11], N. T. Baerlecken[12], T. Klopsch[13], M. Welcker[10], E. Feist[14]. [1]*University Hospital Frankfurt, Division of Rheumatology, Frankfurt am Main, Germany*; [2]*University Hospital Würzburg, Rheumatology/Clinical Immunology, Department of Internal Medicine II, Würzburg, Germany*; [3]*Rheumatologie im Struenseehaus, Internal Medicine and Rheumatology, Hamburg, Germany*; [4]*Medical Practice Dr. Med. Zinke, Internal Medicine and Rheumatology, Berlin, Germany*; [5]*Praxiszentrum St. Bonifatius, Internal Medicine and Rheumatology, München, Germany*; [6]*Sanofi-Aventis Deutschland GmbH, Rheumatology, Berlin, Germany*; [7]*Sanofi-Aventis Deutschland GmbH, Future Indications, Berlin, Germany*; [8]*GKM Gesellschaft für Therapieforschung mbH, Biostatistics, München, Germany*; [9]*Sanofi-Aventis Deutschland GmbH, Clinical Study Unit, Berlin, Germany*; [10]*MVZ für Rheumatologie Dr. Martin Welcker, Internal Medicine and Rheumatology, Planegg, Germany*; [11]*Private Practice Dr. Med. Holst, Internal Medicine and Rheumatology, Ludwigslust, Germany*; [12]*Rheumatologie Köln - Dr. Niklas Baerlecken / Dr. Thomas Karger, Internal Medicine and Rheumatology, Cologne, Germany*; [13]*Private Practice Dr. Med. Klopsch, Internal Medicine and Rheumatology, Neubrandenburg, Germany*; [14]*HELIOS Clinic Vogelsang-Gommern, Department of Rheumatology and Immunology, Gommern, Germany*

Background: Although seronegative RA patients often present with substantial disease burden [1], patients are underrepresented in research cohorts or clinical trials. Consequently, less knowledge about this subgroup has been accumulated.
Objectives: To describe outcome of seronegative vs. seropositive RA patients treated with sarilumab in regular care in Germany.
Methods: The prospective, observational, 24-month single-arm PROSARA study (SARILL08661) is currently running in Germany at 96 sites, aiming to enroll up to 750 RA patients treated with sarilumab. RA patients are prospectively selected at physician's discretion according to label, and medical history is documented before treatment. This interim analysis included patients with data available up to 24 months. Here we focus on sustained treatment response after 6 and 12 months, respectively. Patients were stratified according to serostatus (RF- AND ACPA- as seronegative or RF+ AND/OR ACPA+ as seropositive). All analyses are descriptive only.
Results: To date 473 patients were included in the study, of which 22.2% (n=105) were seronegative and 59.0% (n=279) were seropositive (Table 1). For 89 patients (18.8%) serostatus was not specified.
The mean time since diagnosis of RA was shorter in seronegative than in seropositive patients (7.9±7.6 years vs. 11.5±9.9 years) (Table 1).
At baseline, CDAI score was 27.7±14.7 (n=104) and 23.0±12.9 (n=272) in seronegative and seropositive patients, respectively. After 12 months of sarilumab treatment, CDAI improved to 15.6±12.3 (n=38) and 9.1±8.7 (n=101) in seronegative and seropositive, respectively, for patients with post-baseline data available. At that time, remission/low disease activity according to CDAI was reached by 5.3% (n=2/38) / 39.5% (n=15/38) of seronegative patients, respectively and by 26.7% (n=27/101) / 68.3% (n=69/101) of seropositive patients, respectively (Fig. 1A, B).
Physical function, assessed by HAQ-DI, was slightly more impaired in seronegative patients (1.4±0.7) than in seropositive patients (1.2±0.7) at baseline. HAQ-DI improved over 12 months to 0.9±0.7 in seropositive patients (n=90) but showed no change in seronegative patients (1.4±0.7; n=37) (Fig. 1C).
Safety was consistent with the anticipated profile of IL-6-R-inhibition and no new safety signals occurred. Adverse events and serious adverse events were described in 61.7% and 12.8% of seronegative patients, respectively and in 55.2% and 13.7% of seropositive patients, respectively.

Table 1. Baseline data regarding patient characteristics, prior treatment and disease activity

		seronegative		seropositive	
	patients [n] (%)	105	(22.2)	279	(59.0)
patient characteristics	Sex female [n] (%)	81	(77.1)	207	(74.2)
	Age mean [years] (SD)	56.6	(12.5)	59.6	(10.9)
	BMI mean (SD) [kg/m^2]	29.2	(6.7)	28	(6.0)
	Smoking history current/ former [%]	22.1/11.5		25.5/20.4	
	Time since diagnosis of RA mean [years] (SD)	7.9	(7.6)	11.5	(9.9)
prior RA treatment	csDMARD [n] (%)	102	(97.1)	273	(97.8)
	bDMARD (TNFi) [n] (%)	54	(51.4)	167	(59.9)
	bDMARD (non-TNFi) [n] (%)	32	(30.5)	83	(29.7)
	tsDMARD (JAKi) [n] (%)	25	(23.8)	57	(20.4)
disease activity	CRP [mg/l] (SD)	12.9	(30.9)	14.2	(31.0)
	ESR [mm/h] (SD)	23.7	(20.5)	25.3	(22.4)
	SJC mean (SD)	5.3	(5.5)	4.6	(4.8)
	TJC mean (SD)	10.2	(8.2)	7.2	(6.6)
	HAQ-DI mean (SD)	1.4	(0.7)	1.2	(0.7)
	DAS28-ESR mean (SD)	5.0	(1.5)	4.6	(1.5)
	CDAI mean (SD)	27.7	(14.7)	23.0	(12.9)
	Fatigue [VAS] (SD)	64.0	(25.5)	51.1	(28.1)

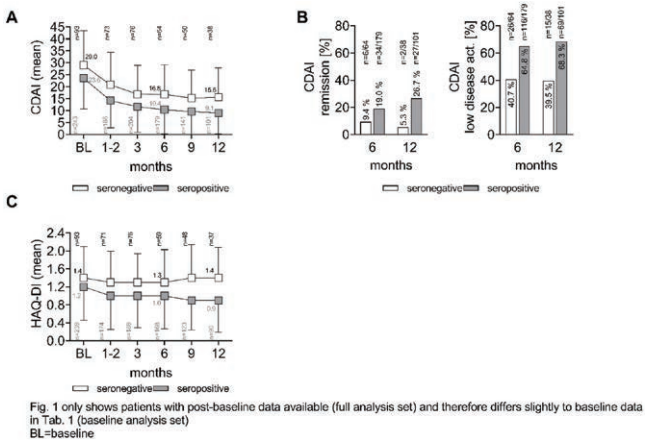


Fig. 1 only shows patients with post-baseline data available (full analysis set) and therefore differs slightly to baseline data in Tab. 1 (baseline analysis set)
BL=baseline

Figure 1. CDAI (A, B) and HAQ-DI (C) outcomes in seronegative and seropositive patients

Conclusion: Sarilumab treatment ameliorated CDAI in both seronegative (ΔCDAI -17.0±16.5) and seropositive (ΔCDAI -15.4±14.3) patients to the same extent over the course of 12 months, with a higher remission rate in seropositive patients. Functional capacity improved meaningfully in the seropositive cohort but had no significant impact in seronegative patients. The safety profile was consistent with data reported from controlled clinical trials.

REFERENCES:

[1] Choi S-T et al. (2018) PLoS ONE 13(4): e0195550.

Acknowledgements: We thank Cornelia Kühne (Haldensleben) for substantial contribution to patient recruitment in PROSARA.

Disclosure of Interests: Harald Burkhardt Speakers bureau: Sanofi, Pfizer, Roche, Abb- vie, Boehringer Ingelheim, UCB, Eli Lilly, Chugai, Bristol Myer Scribb, Janssen, and Novartis, Consultant of: Sanofi, Pfizer, Roche, Abbvie, Boehringer Ingelheim, UCB, Eli Lilly, Chugai, Bristol Myer Scripps, Janssen, and Novartis, Grant/research support from: Pfizer, Roche, Abbvie, Hans-Peter Tony Consultant of: AbbVie, Astra-Zeneca, BMS, Chugai, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, Peer-Malte Aries Speakers bureau: Abbvie, Biogen, Berlin Chemie, Celgene, GSK, Hexal, Mylan, Novartis, Pfizer, UCB, Consultant of: Abbvie, Celgene, Hexal, Janssen, Medac, Novartis, Pfizer, Sanofi, UCB, Silke Zinke: None declared, Klaus Krueger Speakers bureau: Sanofi, Jonas Ahlers Employee of: Sanofi, Rolf Hecker Employee of: Sanofi, Inka Albrecht Employee of: Sanofi, Stefanie Kalus Consultant of: Sanofi, Oliver Bley Employee of: Sanofi, Patrizia Sternad: None declared, Ann-Dörthe Holst: None declared, Niklas Thomas Baerlecken: None declared, Thilo Klopsch: None declared, Martin Welcker Speakers bureau: Abbvie, Aescu, Amgen, Biogen, Berlin Chemie, Celgene, GSK, Hexal, Mylan, Novartis, Pfizer, UCB, Consultant of: Abbvie, Actelion, Aescu, Amgen, Cel- gene, Hexal, Janssen, Medac, Novartis, Pfizer, Sanofi, UCB, Grant/research support from: Abbvie, Novartis, UCB, Hexal, BMS, Lilly, Roche, Celgene, Sanofi, Eugen Feist Speakers bureau: Novartis, Roche, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Sanofi, Consultant of: Novartis, Roche, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Sanofi

DOI: 10.1136/annrheumdis-2021-eular.232

POS0592

BIOSIMILAR INFLIXIMAB THERAPY IN RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS: A LONG-TERM FOLLOW-UP STUDY ON INFLIXIMAB-NAÏVE PATIENTS AND PATIENTS SWITCHED FROM THE ORIGINATOR TO THE BIOSIMILAR CT-P13

B. Fautrel[1], M. Assing[2], N. Mammar[2], H. Marotte[3]. [1]*Sorbonne University - Assistance Publique-Hopitaux de Paris, Pitié-Salpêtrière Hospital, Paris, France*; [2]*PFIZER, Inflammation & Immunology, Paris, France*; [3]*SAINBIOSE INSERM U1059 and Rheumatology department, University of Lyon and University Hospital of Saint-Etienne, Saint-Etienne, France*

Objectives: The ReFLECT study was carried out to investigate real life use of CT-P13, the first monoclonal antibody biosimilar to infliximab originator.

Methods: ReFLECT is a multicentre, prospective, observational study conducted in France to determine the characteristics of patients (pts) receiving CT-P13, its effectiveness and safety in a real-life setting. Eligible were both pts who had been switched from infliximab originator (IFX_S) and infliximab-naïve pts started on CT-P13 (IFX_N). Intermediate results in pts with rheumatic diseases using descriptive statistical analyses from inclusion to a 24-month-follow-up period are described here.

Results: Among the 1370 adult pts included between October 2016 and April 2019, data were analysed for 142 pts with rheumatoid arthritis (RA; 23.9% males; mean age: 61.5±10.9 years; 80 IFX_N/61 IFX_S), 411 with ankylosing spondylitis (AS; 58.9% males; 48.1±13.1 years; 228 IFX_N/179 IFX_S), and 96 with psoriatic arthritis (PsA; 41.7% males; 53.4±14.1 years; 55 IFX_N/40 IFX_S) after a median of between 8.7 and 12.9 years since diagnosis. At inclusion, 66.9%, 24.3% and 50% had one concomitant treatment, mainly methotrexate. At the time of the first administration of CT-P13, disease had been active in 94.2%, 76.6% and 83.3% of the IFX_N pts compared with 45.3%, 24.0% and 32.0% of the IFX_S pts. After 24 months of follow-up, both CRP levels and disease activity remained stable compared to baseline in the IFX_S pts: median $\Delta CRP/RA_S = 1$, $\Delta CRP/AS_S = 0$, $\Delta CRP/PsA_S = 0$ and median $\Delta DAS28/RA_S = 0$, $\Delta BASDAI/AS_S = 0$, $\Delta DAS28/PsA_S = 1$. As expected, improvement was observed in the IFX_N pts: median $\Delta CRP/RA_N = -2$, $\Delta CRP/AS_N = -2$, $\Delta CRP/PsA_N = 0$ and median $\Delta DAS28/RA_N = -1$, $\Delta BASDAI/AS_N = -2$, $\Delta DAS28/PsA_N = -1$. In naïve pts, CT-P13 brought both CRP and disease activity down to levels comparable to those seen in patients switched from the IFX originator: median [Q1;Q3] $CRP/RA_N = 5$ [2;9] *vs* $CRP/RA_S = 5$ [2;8]; $CRP/AS_N = 3$ [2;9] *vs* $CRP/AS_S = 3$ [2;5]; $CRP/PsA_N = 2$ [1;4] *vs* $CRP/PsA_S = 2$ [1;3] and median [Q1;Q3] $DAS28/RA_N = 3$ [3;4] *vs* $DAS28/RA_S = 2$ [2;3]; $BASDAI/AS_N = 3$ [1;4] *vs* $BASDAI/AS_S = 2$ [1;3]; $DAS28/PsA_N = 3$ [2;3] *vs* $DAS28/PsA_S = 3$ [2;3], (Figure 1). At 24 months, 62.7%, 74.9% and 75.0% remained on treatment with CT-P13 in RA, AS and PsA pts respectively. The reasons for treatment withdrawing and safety results are reported in Table 1.

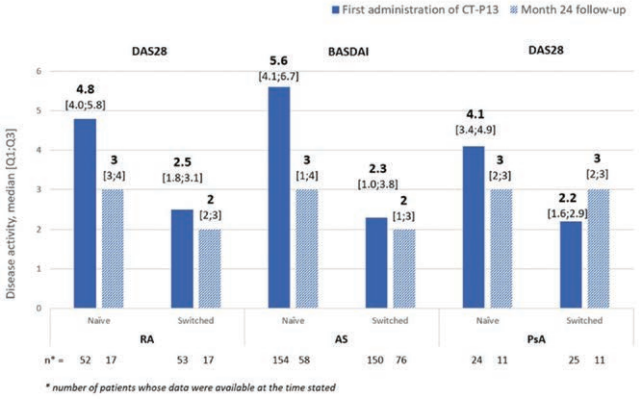


Figure 1. Disease activity at the time of first administration of CT-P13 and after 24 months

Table 1. Reasons for treatment withdrawing and safety results

Reasons for treatment withdrawing						
IFX pts, n (%)	**RA_N, 37**	**RAs, 15**	**AS_N, 64**	**ASs, 38**	**PsA_N, 11**	**PsAs, 12**
Missing	1	0	0	0	0	1
Remission	0	2 (13.3)	2 (3.1)	0	0	0
Therapeutic failure *	25 (69.4)	8 (53.3)	41 (64.1)	23 (60.5)	5 (45.5)	6 (54.5)
Intolerance	5 (13.9)	1 (6.7)	5 (7.8)	2 (5.3)	1 (9.1)	1 (9.1)
Other	6 (16.7)	4 (26.7)	16 (25.0)	13 (34.2)	5 (45.5)	4 (36.4)
Safety data, n (%)	**RA, 142**		**AS, 411**		**PsA, 96**	
Pts with ≥ 1 adverse event (AE)	67 (47.2)		222 (54.0)		48 (50.0)	
Pts with ≥ 1 AE related to CT-P13	33 (23.2)		84 (20.4)		19 (19.8)	
Pts with ≥ 1 serious AE	19 (13.4)		42 (10.2)		9 (9.4)	
Pts with ≥ 1 allergic infusion reaction †	4 (2.8)		11 (2.7)		1 (1.0)	
Pts with ≥ 1 infection ‡	10 (7.0)		18 (4.4)		3 (3.1)	

* Encompassing primary failure in IFX_N pts and loss of efficacy in IFX_N and IFX_S pts† Including acute and delayed hypersensitivity reactions‡ Including severe infections, tuberculosis, opportunistic infections, hepatitis

Conclusion: Year 2 follow-up data indicate that CT-P13 effectively induced improvement in disease activity in pts with RA, AS and PsA receiving infliximab for the first time and maintained stable disease activity in pts switched from

IFX originator to CT-P13. This real-life study did not highlight any new safety concerns.

Disclosure of Interests: Bruno Fautrel Speakers bureau: Lilly, SOBI, Roche-Chugaï, Consultant of: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Roche-Chugaï, Sanofi Aventis, SOBI and UCB, Grant/research support from: AbbVie, Lilly, MSD, Pfizer, Maryse Assing Employee of: Pfizer, Nadir Mammar Employee of: Pfizer, Hubert MAROTTE Speakers bureau: Sanofi-Aventis, Paid instructor for: Sanofi-Aventis, Consultant of: AbbVie, Biogen, Bristol Myers Squibb, Gilead, Lilly France, MSD, Medac, Nordic Pharma, Novartis, Pfizer, Sanofi-Aventis, UCB, Grant/research support from: Bristol Myers Squibb, Lilly France, MSD, Novartis, Nordic Pharma, Pfizer, Sanofi Aventis
DOI: 10.1136/annrheumdis-2021-eular.477

POS0593

THE REDUCTION OF RETINAL MICROVASCULAR ALTERATIONS AND THE DECREASE OF A POTENTIALLY RELATED T-CELL SUBSET IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS TREATED WITH ABATACEPT

S. Piantoni[1], F. Regola[1], S. Masneri[1], C. Nalli[1], C. Bazzani[1], C. Rossini[2], G. Chiarini[2], C. De Ciuceis[2], F. Franceschini[1], D. Rizzoni[2], P. Airò[1].
[1]Rheumatology and Clinical Immunology Unit, ASST Spedali Civili and University of Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy; *[2]Internal Medicine Unit, ASST Spedali Civili and University of Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy*

Background: T-cells play a pivotal role in the pathogenesis of rheumatoid arthritis (RA) and in its cardiovascular (CV) comorbidities, acting at microvascular level [1]. Since small artery remodeling is the earliest form of target organ damage in hypertension, the evaluation of microvascular alterations might provide clinically useful information. The evaluation of retinal arterioles is a non-invasive technique to identify a precocious microvascular damage, which is related to an increase of the wall-to-lumen ratio (WLR) [2]. CD3+CD31+CXCR4+ T-cells may be involved in damaged endothelium repair and are increased in patients with morphological microvascular alterations [3]. In addition to its effect on disease activity, abatacept (ABA), a co-stimulator blocker which is approved for the treatment of RA, may have specific CV protective action, modulating the numbers of certain subtypes of lymphocytes [4].

Objectives: To non-invasively investigate morphological characteristics of retinal arterioles and to evaluate CD3+CD31+CXCR4+T-cells in a cohort of RA patients treated with ABA.

Methods: Eleven RA patients [median (25th-75thpercentile) age=58 (50-65) years, baseline C-reactive protein (CRP)-DAS28=4.4 (3.8-4.6), body mass index (BMI)=23.4 (21.6-25.6) kg/m^2, rheumatoid factor (RF) positive:45%, anti-citrullinated peptide autoantibodies (ACPA) positive:73%] without known CV risk factors (arterial hypertension, diabetes, hypercholesterolemia, previous CV events, smoking) were evaluated by adaptive optics, a validated technique quantifying microvascular damage [5], before and every 6 months of therapy with ABA (T0, T6 and T12). Phenotypic analysis of peripheral blood T lymphocytes was made by flow-cytometry in 5 patients of the cohort at T0 and T6.

Results: A progressive significant reduction of the WLR of retinal arterioles was observed [T0=0.28 (0.25-0.30), T6=0.27 (0.24-0.31), T12=0.23 (0.23-0.26); p T0 vs T6=0.4; p T6 vs T12=0.01; p T0 vs T12=0.01] (Figure 1), without significant variations in the other parameters [internal diameter: T0=94.4 (84.1-104.0), T6=94.8 (84.6-107.7), T12=99.2 (89.1-109.1) µm; external diameter: T0=125.8 (111.1-131.0), T6=122.4 (109.1-134.5), T12=125.6 (113.9-134.4) µm; wall thickness: T0=13.2 (12.2-14.4), T6=13.4 (11.7-14.4), T12=12.5 (11.6-13.0) µm; wall cross-sectional area: T0=4581.0 (3788.7-5263.7), T6=4563.3 (3788.5-5295.2), T12=4099.7 (3899.0-5145.7) µm^2)]. In 5 patients evaluated also for T-cell immunophenotyping a negative correlation was observed between CD3+CD31+CXCR4+ T-cell number and the retinal wall thickness at baseline (R=0.871;p=0.05). After ABA therapy a trend for reduction of CD3+CD31+CXCR4+T-cells [19.0 (13.8-38.3) vs 12.4 (5.2-18.0) % of CD3+], was observed as well as of significant reduction of retinal wall cross-sectional area [5123.3 (4385.0-5470.3) vs 4852.3 (4118.3-5228.0) µm^2;p=0.04].

Conclusion: In a cohort of RA patients without known CV risk factors, a reduction in retinal microvascular alterations arterioles was demonstrated after treatment for 12 months with ABA. CD3+CD31+CXCR4+T-cell number was inversely related to the possible presence of subclinical CV involvement. These results may suggest the possibility of microvascular abnormalities regression induced by the immune system modulation.

REFERENCES:

[1] Dessein PH, J Rheumatol 2005.
[2] Rizzoni D, Am J Hypertens. 2018.
[3] Hur J, Circulation 2007.
[4] Kallikourdis M, Nat Commun 2017.
[5] De Ciuceis C, J Hypertens 2018.

Acknowledgements: Bristol-Myers-Squibb Italy provided an unrestricted research grant for the study conduct.

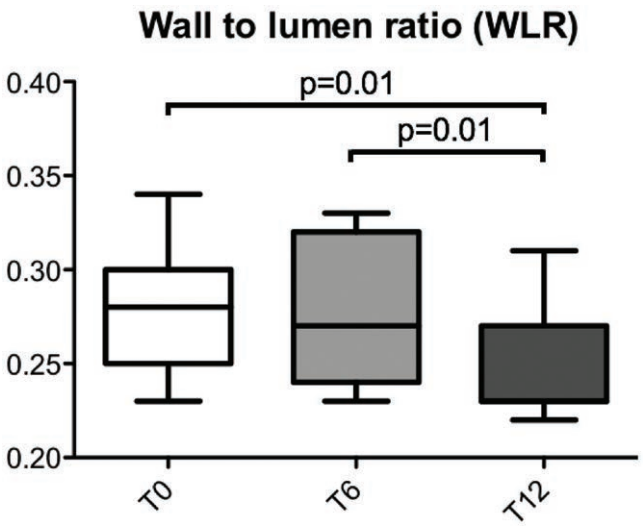


Figure 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.483

POS0594

MEANINGFUL IMPROVEMENT AND WORSENING IN PATIENTS WHO DO NOT ACHIEVE LDA AND SWITCH THERAPY TO A NEW BIOLOGIC OR TARGETED THERAPY: RESULTS FROM THE CORRONA REGISTRY

J. Curtis[1], S. Fiore[2], K. Ford[3], J. Janak[4], H. Chang[5], D. A. Pappas[4], T. Blachley[5], K. Emeanuru[6], V. Bykerk[7]. *[1]University of Alabama at Birmingham, Division of Clinical Immunology & Rheumatology, Birmingham, AL, United States of America*; *[2]Sanofi, Medical Affairs, Bridgewater, NJ, United States of America*; *[3]Sanofi, Medical Affairs, Cambridge, MA, United States of America*; *[4]Consortium of Rheumatology Researchers of North America (CORRONA), Clinical Epidemiology, Waltham, MA, United States of America*; *[5]Consortium of Rheumatology Researchers of North America (CORRONA), Bio-statistics, Waltham, MA, United States of America*; *[6]Consortium of Rheumatology Researchers of North America (CORRONA), Epidemiology, Waltham, MA, United States of America*; *[7]Inflammatory Arthritis Center, Hospital for Special Surgery, New York, NY, United States of America*

Background: Guidelines recommend adjusting therapy in patients with rheumatoid arthritis (RA) who fail to reach and sustain low disease activity (LDA) or remission (disease control). Many factors can affect the decision to change therapy, including the potential for improvement as well as the fear of potential worsening or loss of improvement already achieved. Although data exist on response to treatment in patients who switch therapy, data addressing the likelihood of worsening are limited.

Objectives: The aim of this analysis was to describe the demographic, clinical characteristics, and change in clinical outcomes in patients on biologic/targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs) who had some improvement in clinical disease activity index (CDAI) but did not achieve LDA after ~ 6-12 months of treatment and then switched to a different b/tsDMARD.

Methods: This study included adult inadequately responding RA patients from the CORRONA registry who: (1) started a biologic or Janus kinase inhibitor (JAKi) between January 2010 to November 2020 (V1), (2) had any CDAI improvement (i.e., decrease ≥1 unit) but were not in LDA or remission at a subsequent visit (baseline [BL]) occurring 3 to 15 months after V1; (3) had a third visit (follow-up [F/U]) 6 (±3) months after BL with a valid CDAI measure; (4) switched therapy at the BL or between BL and F/U, with the switch occurring at least 3 months prior to the F/U. CDAI >10 and ≤22 was defined as moderate disease activity (MDA) and CDAI >22 was defined as high disease activity (HDA). Two thresholds of change in CDAI (≥6 and ≥12 units) were used to define meaningful improvement and meaningful worsening after the switch. If there was no meaningful improvement or meaningful worsening, this was considered as no meaningful change (-5 to +5 for 6 units change and -11 to +11 for 12 units change). These thresholds for meaningful change were set for all switchers regardless of their pre-switch CDAI value. Descriptive statistics were generated for demographic and clinical characteristics for the switchers at BL, and the change of clinical outcomes was evaluated from BL to F/U.

Results: Of the 1,224 patients fulfilling the inclusion criteria, 93 (7.6%) switched therapy and 1,131 (92.4%) did not switch therampy after not achieving an adequate response on the initial b/tsDMARD. At BL, 42.5% and 70.0% of patients had no meaningful improvement to their prior therapy based on ≥6 and ≥12-unit change, respectively; mean (SD) age was 53.1 (14.0) years; duration of RA 10.7 (10.4) years; CDAI 22.2 (10.8); 81.7% were female; 64.5% had MDA, 35.5% had HDA; 21.5 % reported being disabled, 24.7% were current smokers, and 50% were obese. In terms of prior biologic use 57.0%, 22.6%, and 20.4% had been on 1, 2, and 3+, respectively. From BL to F/U, meaningful worsening occurred in 30.1% and 12.9% using a threshold of 6 and 12, respectively, with the remaining patients experiencing meaningful improvement or no meaningful change (Figure 1).

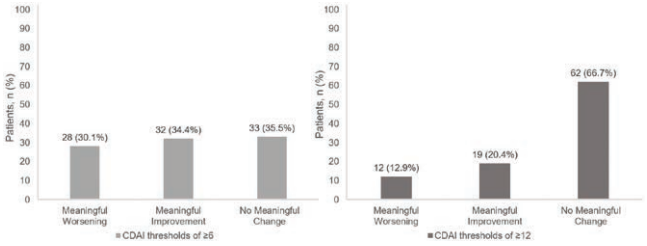


Figure 1. Meaningful Worsening, Meaningful Improvement, and No Meaningful Change Based on CDAI Change Thresholds of ≥6 and ≥12 From BL to F/U (N=93)

Conclusion: In our analysis, a large proportion of patients who initiated a biologic/JAKi and experienced some improvement but failed to attain LDA or remission, did not switch therapy within approximately a year. This analysis consisted of many patients who did not have a meaningful response to their prior biologic/JAKi, patients who had received multiple prior biologics, and a large portion of patients with poor prognostic factors. Despite this, the proportion of patients with meaningful worsening was low compared with most patients who had either meaningful improvement or no meaningful change. Additional research is warranted to understand the reasons for not switching and whether the likelihood of a meaningful change correlates with prior response, poor prognosis, or other factors.

Acknowledgements: Amy Praestgaard (Sanofi) contributed to the statistical analysis for this abstract. Medical writing support for this abstract was provided by Krishna Kammari (Sanofi).

Disclosure of Interests: Jeffrey Curtis Grant/research support from: and personal fees from AbbVie, Amgen, BMS, CORRONA, Eli Lily, Janssen, Myriad, Pfizer, Roche, Regeneron, Radius, UCB, outside the submitted work, Stefano Fiore Shareholder of: Sanofi, Employee of: Sanofi. In addition, he has a patent EP 19306553.9; USPTO #s 62/799,698; 62/851,474; 62/935,395 issued, Kerri Ford Shareholder of: Sanofi, Employee of: Sanofi, Judson Janak: None declared, Hong Chang: None declared, Dimitrios A Pappas Employee of: CORRONA LLC. He has previously acted as a consultant for Sanofi, Abbvie, Gtech Roche Hellas, and Novartis. He has an equity interest in CORRONA LLC. and is on the Board of directors of the CORRONA research foundation, Taylor Blachley: None declared, Kelechi Emeanuru: None declared, Vivian Bykerk Grant/research support from: reports grants from Amgen, BMS, UCB, and Novartis were given to institution, that grants from the NIH, PCORI, and CIHR were given to institutions which whom she is affiliated, and that she has received personal fees from Amgen, Gilead, BMS, Pfizer, Sanofi Aventis, Roche, UCB and Regeneron, outside the submitted work.

DOI: 10.1136/annrheumdis-2021-eular.544

POS0595

ABATACEPT IN USUAL AND IN NON-SPECIFIC INTERSTITIAL PNEUMONIA ASSOCIATED TO RHEUMATOID ARTHRITIS. NATIONAL MULTICENTER STUDY OF 190 PATIENTS

B. Atienza-Mateo[1], C. Fernández-Díaz[2], S. Castañeda[2], R. Melero[3], F. Ortiz Sanjuan[4], I. Casafont-Solé[5], S. C. Rodriguez-García[6], I. Ferraz-Amaro[7], M. A. González-Gay[1], R. Blanco[1]on behalf of Members of the Spanish Collaborative Group of Abatacept in Interstitial Lung Disease Associated with Rheumatoid Arthritis: Clara Aguilera-Cros (H.U. Virgen del Rocío, Sevilla), Ignacio Villa (H. Sierrallana, Torrelavega), Enrique Raya-Alvarez (H.U. San Cecilio, Granada), Clara Ojeda-García (H.U. Virgen Macarena, Sevilla), María G. Bonilla Hernán (H.U. La Paz, Madrid), Ana M. López-Robles (H.U. Vall d' Hebron, Barcelona), Luis Arboleya-Rodríguez (H.U. Central de Asturias, Asturias), Javier Narváez García (H.U. Bellvitge, Barcelona), Evelin C. Cervantes Pérez (H.U. de Santiago, Santiago de Compostela, A Coruña), OlgaMaiz-Alonso (H.U. Donostia, Gipuzkoa), María N. Alvarez-Rivas (H.U. Luca Augusti, Lugo), Iván Cabezas-Rodríguez (H.U. Río Hortega, Valladolid), Eva Salgado-Pérez (C.H.U. Ourense, Ourense), Cristina Hidalgo-Calleja (H.U. de Salamanca, Salamanca), Sabela Fernández-Aguado (H.U. Cabueñes, Asturias), Jesús C. Fernández-López (C.H.U. A Coruña), Alejandro Olivé, Samantha Rodríguez-Muguruza (H.U. GermansTrias i Pujol, Barcelona), Raquel Almodóvar-González (H.U. Fundación Alcorcón, Madrid), Carmen Carrasco-Cubero (C.H.U. Infanta Cristina, Badajoz), Antonio Juan-Mas (H. Son Llàtzer, Palma de Mallorca), Raúl Castellanos-Moreira (H.U. Clinic. Barcelona), Iñigo Hernández Rodríguez (C.H.U. de Vigo, Vigo), Neus Quillis-Marti (H. Vinalopo Elche), José A. Bernal-Vidal (H. Marina Baixa, Villajoyosa), Angel García-Aparicio (H. Virgen de la salud, Toledo), Sonia Castro-Oreiro (H.U. Joan XXIII, Tarragona), Julia Fernández-Melón (H. Son Espases, Palma de Mallorca), Paloma Vela Casasempere(H. U. Alicante, Alicante), María C. Fito, Carmen González-Montagut (C.U. Navarra, Navarra), Manuel Rodríguez-Gómez (C.H.U. Ourense, Ourense), Trinidad Pérez-Sandoval, Miriam Retuerto-Guerrero (H.U. León), Deseada Palma-Sánchez (H. Rafael Mendez, Lorca), José L. Andreu (H. U. Puerta del Hierro), Patricia Carreira-Delgado (H. 12 de Octubre, Madrid), Lorena Expósito-Pérez (H.U. de Canarias, Tenerife), Juan RD Jiménez- de Aberásturi, Ana Ruibal-Escribano (H.U. Txagorritxu, Araba), Ana Urruticoechea-Arana (H. Can Misses, Ibiza), Rosa Expósito-Molinero (H. Laredo, Laredo), Rubén López Sánchez (H. Negrín Las Palmas), Manuel J. Moreno-Ramos (H. Virgen de la Arrixaca, Murcia), Isabel Serrano-García (H. Puerta del Mar Cadiz), Blanca García-Magallón (H. San Jorge Huesca), José María Andreu Ubero (H. Virgen de las Nieves Granada), Natalia Mena-Vázquez (H.R.U Málaga), Iván Castellvi-Barranco (H.U. De la Santa Creu i Sant Pau, Barcelona), Carmen González-Montagut (H. U. Valladolid, Valladolid), Juan Blanco-Madrigal (H. Basurto, Bilbao), Pilar Morales-Garrido (H.U. San Cecilio, Granada), Cilia Peralta-Ginés (H. Lozano Blesa, Zaragoza), Mireia López-Corbeto (H.U. Vall d´Hebron, Barcelona), Sergio Ordóñez-Palau (H. Lleida, Lleida), Andrea García-Valle (H. U Palencia), Susana Romero-Yuste (H.U. Pontevedra, Pontevedra).. *[1]Hospital Universitario Marqués de Valdecilla, IDIVAL, Rheumatology, Santander, Spain*; *[2]Hospital Universitario La Princesa, Rheumatology, Madrid, Spain*; *[3]Complejo Hospitalario Universitario de Vigo, Rheumatology, Vigo, Spain*; *[4]Hospital Universitario La Fe, Rheumatology, Valencia, Spain*; *[5]Hospital Universitario Germans Trias i Pujol, Rheumatology, Barcelona, Spain*; *[6]Hospital Universitario Clinic, Rheumatology, Barcelona, Spain*; *[7]Hospital Universitario de Canarias, Rheumatology, Santa Cruz de Tenerife, Spain*

Background: Interstitial lung disease (ILD) is a severe complication of Rheumatoid Arthritis (RA). Usual interstitial pneumonia (UIP) is considered to be more frequent and severe in RA than non-specific interstitial pneumonia (NSIP). Abatacept (ABA) and Rituximab have demonstrated efficacy in RA-ILD **[1-3].**

Objectives: To compare the efficacy of ABA in RA-ILD patients according to radiological patterns of UIP or NSIP.

Methods: From an observational multicenter study of 263 RA-ILD patients treated with ABA, we selected those with UIP or NSIP **[2].** We analyzed in the 2 groups from baseline up to 24 months the following outcomes: **a)** Forced Vital Capacity (FVC), **b)** Carbon monoxide diffusing capacity (DLCO), **c)** Chest High Resolution Computed Tomography (HRCT), and **d)** dyspnea. Differences between final follow-up and basal visit were calculated as the average difference and 95% Confidence Interval (95% CI). Multivariable linear regression was used to assess the differences between the 2 groups.

Results: We studied 190 patients with UIP (n=106) and NSIP (n=84). Patients with UIP were older, had more positivity for rheumatoid factor and had received more sulfasalazine (Table 1). ILD duration up to ABA initiation was relatively short in both groups, with a median [IQR] of 16 [4-50] and 11 [2-36] months in UIP and NSIP patterns, respectively. Mean baseline values of FVC and DLCO were > 80% and > 60%, respectively, in the 2 groups, with a lower FVC in UIP (82% vs 89% in NSIP, p<0.05). The evolution of FVC and DLCO is shown in Figure 1. Both parameters remained stable during 24 months of ABA therapy. Available chest HRCT images improved/ stabilized in 73.1% and 72.9% of UIP and NSIP patterns, respectively. With multivariable linear regression analysis, no differences were found in the changes of FVC, DLCO, or HRCT images. Stabilization or improvement of dyspnea was found in 91% and 95% of UIP and NSIP patterns, respectively.

Conclusion: ABA seems to be equally effective in stabilizing of DLCO, FVC and HRCT in UIP and NSIP in RA-ILD. Our results suggest that an early administration of ABA in ILD, before significant structural lung damage development, may be preferable to prevent interstitial progression, regardless of the radiological pattern.

REFERENCES:

[1] Fernández-Díaz C, et al. *Semin Arthritis Rheum.* 2018 Aug;48(1):22-27. doi: 10.1016/j.semarthrit.2017.12.012

[2] Fernández-Díaz C, et al. *Rheumatology (Oxford).* 2020 Dec 1;59(12):3906-3916. doi: 10.1093/rheumatology/keaa621

[3] Atienza-Mateo B, et al. *J Clin Med.* 2020 Sep 23;9(10):3070. doi: 10.3390/jcm9103070

Table 1. Main general features at baseline.

	UIP (n=106)	NSIP (n=84)	p value
Age, years mean±SD	66±10	63±10	**0.049**
Women, n (%)	59 (56)	49 (58)	0.71
Smoker ever, n (%)	51 (48)	45 (54)	0.46
ILD duration up toABA, months, median [IQR]	16 [4-50]	11 [2-36]	0.57
RF	100 (94)	71 (85)	**0.041**
ACPA, n (%)	96 (91)	75 (89)	0.83
FVC (% of the predicted), mean±SD	82±21	89 ±19	**0.025**
DLCO (% of the predicted), mean±SD	63 ±19	65 ±16	0.46
ABA monotherapy, n (%)	45 (42)	41 (49)	0.38
ABA combined+ MTX // + other cDMARD, n (%)	15 (14) // 46 (43)	16 (19) // 27 (32)	0.17
Prednisone at baseline, mg/day, median [IQR]	7.5 [5-10]	10 [5-10]	0.20
Previous immunosuppressive therapy, n (%)			
MTX	81 (76)	68 (81)	0.45
Leflunomide	48 (45)	31 (37)	0.25
Sulfasalazine	16 (15)	5 (6)	**0.046**
Hydroxychloroquine	24 (23)	16 (19)	0.55
Anti-TNF drugs	37 (35)	30 (36)	0.80
Rituximab	19 (18)	15 (18)	0.99
Tocilizumab	12 (11)	12 (14)	0.54

ABA, abatacept; ACPA, anti-citrullinated protein antibodies; DMARD, disease-modifying antirheumatic drug, ILD, Interstitial lung disease; MTX, methotrexate; NSIP, non-specific interstitial pneumonia; RA, rheumatoid arthritis; TNF, tumor necrosis factor; UIP, usual interstitial pneumonia.

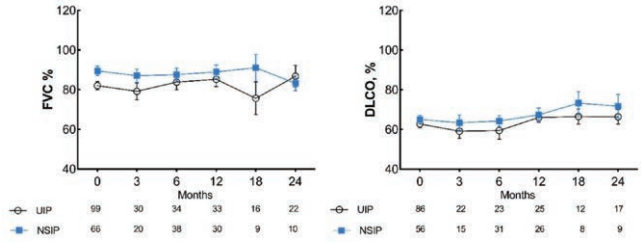


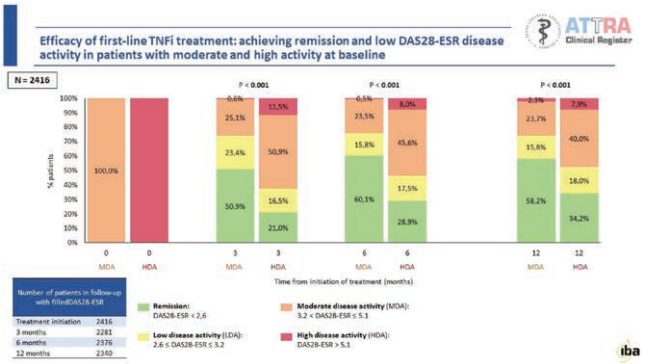
Figure 1. Evolution of pulmonary function tests in RA-ILD patients with UIP and NSIP patterns. FVC and DLCO are expressed as mean (95%CI) and compared between the 2 groups.

Acknowledgements: the Spanish Collaborative Group of Abatacept in Interstitial Lung Disease Associated with Rheumatoid Arthritis
Disclosure of Interests: Belén Atienza-Mateo: None declared, Carlos Fernández-Díaz Speakers bureau: Brystol Myers Squibb, Santos Castañeda: None declared, Rafael Melero: None declared, FRANCISCO ORTIZ SANJUAN: None declared, Ivette Casafont-Solé: None declared, Sebastián C Rodriguez-García: None declared, Iván Ferraz-Amaro: None declared, Miguel A González-Gay: None declared, Ricardo Blanco Speakers bureau: Brystol Myers Squibb
DOI: 10.1136/annrheumdis-2021-eular.711

POS0596 THE THERAPEUTIC TARGET IS REACHED MORE OFTEN IN RA PATIENTS STARTING TNF INHIBITORS WITH MODERATE ACTIVITY THAN WITH HIGH DISEASE ACTIVITY – AN ANALYSIS FROM THE ATTRA REGISTRY

K. Pavelka[1], L. Nekvindova[2], J. Zavada[1]. [1]*Institute of Rheumatology, Rheumatology, Praha 2, Czech Republic*; [2]*Institute of Biostatistics and Analyses LTD, Biotatistics, Brno, Czech Republic*

Background: Treat to target guidelines recommend achieving remission or low disease activity in rheumatoid arthritis (RA). In the Czech Republic, anti-TNF therapy has been reimbursed only for patients with highly active RA until 2019, when pts with LDA have been also included in the reimbursement policy.
Objectives: The aim of the study was to compare the results of treatment in patients with rheumatoid arthritis and moderate disease activity (MDA) or high disease activity (HDA) starting the therapy with the first anti-TNF drug in routine clinical practice.
Methods: This was a retrospective cohort study of patients treated with the first anti-TNF drug in the Czech Republic. Propensity score was used to match pts starting anti-TNF in MDA or HDA for other important predictive factors. The propensity score was obtained by logistic regression with 10 covariates (gender, age, disease duration, seropositivity, comedication with MTX, comedication with other csDMARDs, number of previosu csDMARDs, anti-TNF drug),.Within the paired groups, one-dimensional logistic models were then calculated to estimate the odds of remission / low activity after 6 and 12 months of treatment.
Results: A total of 2416 patients were analyzed in the study. 2231 patients had high activity (DAS 28> 5.1) and 185 patients had moderate activity (3.2 <DAS28 ≤ 5.1) at baseline. After 12 months, the low activity state (DAS28 < 3.2) was achieved by patients with MDA in 74.0% and patients with HDA in 52.2%, (p <0.001) (FIG 1). The differences btw groups were significant in all evaluated intervals of 0, 3, 6, 12 months. Furthermore, a comparison of patients with MDA and HAD by propensity score matching, who no longer differ in the baseline characteristics (except for disease activity and quality of life) was performed. Patients with MDA were 2.4x more likely to achieve remission or low activity according to DAS28-ESR after 6 months and 1.7x more likely to achieve remission or low activity after 12 months of treatment compared to patients with HDA at the beginning of treatment.



Conclusion: This analysis of the results of treatment with anti-TNF drugs in the ATTRA Registry has shown that starting anti-TNF therapy in patients with RA and MDA leads more often to the target of remission or low activity, than in pts with HDA.
Acknowledgement: Supported by the project of the Ministry of Health Care of the Czech Republic of the conceptual development of the research organization 00023728 Institute of Rheumatology
Disclosure of Interests: Karel Pavelka Speakers bureau: Abbvie, Pfizer, Elli-Lilly, BMS, UCB, Sanofi, Novartis, Gilead, Paid instructor for: Abbvie, Consultant of: Abbvie, Pfizer, Elli-Lilly, BMS, UCB, Sanofi, Novartis, Gilead, Lucie Nekvindova: None declared, Jakub Zavada Speakers bureau: Abbvie, Elli-Lilly, UCB, Sanofi, Consultant of: Abbvie, UCB, Sanofi, Gilead
DOI: 10.1136/annrheumdis-2021-eular.720

POS0597 EFFECTS OF RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS-RELATED INTERSTITIAL LUNG DISEASE: A SINGLE-CENTRE EXPERIENCE FROM TURKEY

D. Sahin Eroglu[1], A. Colaklar[2], S. Baysal[3], M. Torgutalp[1], A. Baygul[4], M. E. Yayla[1], T. M. Turgay[1], G. Kınıklı[1], A. Ates[1]. [1]*Ankara University Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; [2]*Ankara University Faculty of Medicine, Department of Radiology, Ankara, Turkey*; [3]*Ankara University Faculty of Medicine, Department of Internal Medicine, Ankara, Turkey*; [4]*Ankara University Faculty of Medicine, Department of Pulmonology, Ankara, Turkey*

Background: Rheumatoid arthritis-related interstitial lung disease (RA-ILD) is the most common type of lung involvement in rheumatoid arthritis (RA). The existence of RA-ILD is associated with worse survival. There is no mainstay treatment for RA-ILD. However, in recent studies, rituximab (RTX) seems to be effective in RA-ILD.
Objectives: To determine the effects of RTX in patients with RA-ILD from a single-centre.
Methods: In our biological treatment outpatient clinic, a retrospective study was conducted in patients with RA who were treated with RTX. Among them, patients with RA-ILD were analysed. For lung response to RTX, progression was defined as a decline of 10% ≥ in forced vital capacity (FVC) and/or a decline of 15% ≥ in diffusion capacity of carbon monoxide (DLCO). Computed tomography of the chest (chest-CT) were integrated to lung response so as to constitute missing data of pulmonary function tests (PFTs).
Results: A total of 165 patients who are followed-up in our biological treatment outpatient clinic have been using RTX for their RA diagnosis. Among 165 patients, 26 (15.8%) patients with RA-ILD were initiated RTX. Five patients were diagnosed with RA-ILD while using RTX (incidence rate 3%). Patients' characteristics were demonstrated in table 1. Of 26 patients, the most commonly used concomitant disease-modifying antirheumatic drugs was leflunomide (46.2%) followed by mycophenolate mofetil (11.5), methotrexate (11.5%) and azathioprine (3.8%). Twenty-four (92.3%) patients used steroids. For the evaluation of lung response, 20 patients who had follow-up PFTs and/or chest-CT were compared.

Median DLCO values for pre- and post RTX were 71.0% (60.0-77.0) and 63.0% (47.0-74.0), respectively (p= 0.061). Median pre and post-RTX FVC were 74.0% (61.0-99.0) and 84.0% (63.0-100.0), respectively (p= 0.28). After a median of 2.7 years, 11 (55.0%) patients had stable disease, 2 (10.0%) patients had regression of RA-ILD and 7 (35.0%) patients had progressive disease. Sex, age, seropositivity and radiographic patterns were not associated with progression. In total, 23 adverse events were detected in 11 (42.3%) patients. Five of them were serious infections requiring hospitalization, mostly pneumonia. Other adverse events were simple infections and surgeries such as arthroplasty. RTX was stopped in 4 (15.4%) patients due to infections secondary to hypogammaglobulinemia in 2, malignancy in 1 and allergic reaction in 1.

Conclusion: RTX seems to achieve stabilization/improvement of RA-ILD with fewer adverse events. However, given that RA-ILD develops post-RTX, it is not a panacea; therefore, we need more effective treatment modalities in the case of RA-ILD.

Table 1. Characteristics of 26 patients with RA-ILD treated with rituximab

Age at first RTX infusion, median (IQR), years	61.2 (57.1-65.1)
RA disease duration at first RTX, median (IQR), years	10.1 (4.3-29.7)
ILD disease duration at first RTX, median (IQR), years	1.9 (0.1-4.5)
Age at RA diagnosis, median (IQR), years	51.1 (40.0-60.6)
Age at ILD diagnosis, median (IQR), years	58.3 (53.9-63.3)
Male patient, n (%)	16 (61.5)
RF positivity, n (%)	25 (96.2)
ACPA positivity, n (%)	20 (90.9)
CRP levels,mg/L, mean (SD)	40.3 (58.9)
ESR levels, mean (SD)	37.7 (18.2)
Smoking status, n (%)	16 (64.0)
Prior TNF inhibitor treatment, n (%)	5 (19.2)
DAS28 at first RTX infusion, mean (SD)	5.3 (1.5)
Radiographic pattern, n (%)	
UIP	7 (26.9)
NSIP	8 (30.8)
OP	2 (7.7)
Indeterminate	8 (30.8)
Others	1 (3.8)
Follow-up duration, median (IQR), years	2.5 (1.2-3.7)

RA-ILD= Rheumatoid arthritis-related interstitial lung disease, RTX= rituximab, RA= rheumatoid arthritis, RF= rheumatoid factor, ACPA= anti-citrullinated protein antibody, TNF= tumor necrosis factor, CRP= C-reactive protein, ESR= erythrocyte sedimentation rate, UIP= usual interstitial pneumonia, NSIP= non-specific interstitial pneumonia, OP= organizing pneumonia

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.731

POS0598 COMPARISON OF INJECTION SITE REACTIONS AND INJECTION SITE ERYTHEMA BETWEEN YLB113 AND ETANERCEPT REFERENCE PRODUCT FROM PHASE 3 ACTIVE COMPARATOR STUDY (STUDY NO. YLB113-002)

D. Stefanidis[1], U. G[2], J. Sánchez-Bursón[3], C. Shah[4], D. Bakhle[4]. *[1]Viatris GmbH, Medical Affairs, Bad Homburg, Germany*; *[2]Viatris, Biostatistics, Bangalore, India*; *[3]Hospital Infanta Luisa, Rheumatology, Sevilla, Spain*; *[4]Lupin LTD, Clinical, Pune, India*

Background: YLB113 is an etanercept biosimilar approved in all indications of its etanercept Reference Product (RP). Therapeutic equivalence in terms of clinical efficacy, safety and immunogenicity was previously demonstrated in a pivotal multicenter, double-blind, randomized, parallel-group, active-control, comparative study (YLB113-002) in rheumatoid arthritis (RA) subjects.[1,2] Similar incidence of treatment emergent adverse events (TEAEs) was seen in both treatment arms except for injection site reactions (ISRs) and injection site erythema (ISE), both of which were less frequent in subjects treated with YLB113.

Objectives: This post-hoc analysis was performed to further evaluate the differences in the incidence of ISRs and ISE during the 24 week treatment when the subjects with RA were treated with 50 mg of YLB113 or RP given once a week as a SC injection along with methotrexate.

Methods: Safety analysis set (263 in YLB113 arm and 254 in RP arm) was considered for this analysis.

Local reactions at the site of injection were assessed at each of eight study visits. The number of subjects who experienced ISRs and ISE were statistically compared for YLB113 and RP. The risk difference and 95% confidence interval (CI) were computed between arms to understand the magnitude of difference in the incidence of events. The statistical significance of between group difference was tested using chi-square test.

Results: The result of this analysis showed a statistically significant difference in the incidences of ISRs and ISE between subjects who received YLB113 and RP. The risk difference between YLB113 and RP arms for ISR was -9.98% (95% CI, WALD -14.81%, -5.15%) and, for ISE it was -7.94% (95% CI, WALD -11.96%, - 3.92%; Table 1). This could be possibly explained by the absence of latex in the syringe needle cap of YLB113.[3]

Table 1. Differences in ISRs and ISEs between YLB113 and Reference Product (RP)

Event	YLB113 N=263	RP N=254	YLB113 vs RP	
	No of subjects with events [n(%)]	No of subjects with events [n(%)])	Risk Diff (95%CI, WALD)	P-value (Chi-Square)
Injection-site reactions	10 (3.8%)	35 (13.8%)	-9.98% (-14.81%, -5.15%)	<0.0001
Injection-site erythema	5 (1.9%)	25 (9.8%)	-7.94% (-11.96%, -3.92%)	0.0001

Conclusion: YLB113 has shown statistically significant lower incidences of ISRs (P-value <0.0001) and ISEs (P value 0.0001) compared to RP. This property may translate to a better acceptability by patients.

REFERENCES:

[1] EULAR Abstract AB0416 (2019). Ann Rheum Dis, volume 78, supplement 2, year 2019, page A1670.

[2] Yamanaka H, Kamatani N, Tanaka Y, et al. A Comparative Study to Assess the Efficacy, Safety, and Immunogenicity of YLB113 and the Etanercept Reference Product for the Treatment of Patients with Rheumatoid Arthritis. *Rheumatol Ther*. 2020;7(1):149-163.

[3] Viatris Etanercept Summary of Product Characteritics May 2020.

Disclosure of Interests: Dimitris Stefanidis Employee of: Viatris GmbH Sr. Director, Global Medical Affairs Lead, Immunology Biosimilars, Unmesh G Employee of: Viatris, Juan Sánchez-Bursón: None declared, Chirag Shah Shareholder of: As an employee, Shareholder of Lupin LTD, Employee of: Employee of Lupin LTD, Dhananjay Bakhle Shareholder of: As part of Employee Stock Options Plan from Lupin LTD, Employee of: Employee of Lupin LTD

DOI: 10.1136/annrheumdis-2021-eular.829

POS0599 DISEASE ACTIVITY IN PATIENTS WITH RA BY SEROSTATUS AND TREATMENT LINE, FOLLOWING TREATMENT WITH ABATACEPT: RESULTS FROM AN INTERNATIONAL OBSERVATIONAL STUDY

R. Alten[1], X. Mariette[2], R. M. Flipo[3], R. Caporali[4,5], M. H. Buch[6,7], Y. Patel[8], R. Sanmartí[9], S. Marsal[10], M. T. Nurmohamed[11], H. Griffiths[12], P. Peichl[13], B. Bannert[14], A. Forster[15], M. Chartier[16], Y. Elbez[17], C. Rauch[18], K. Lozenski[19], V. Khaychuk[20]. *[1]Schlosspark-Klinik University, Department of Internal Medicine, Rheumatology, Berlin, Germany*; *[2]Université Paris-Saclay, AP-HP, Hospital Bicêtre, Department of Rheumatology, Paris, France*; *[3]Centre Hospitalier Universitaire de France, Department of Rheumatology, Lille, France*; *[4]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy*; *[5]G. Pini Hospital, Clinical Rheumatology Unit, Milan, Italy*; *[6]University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[7]University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; *[8]Hull Royal Infirmary, Department of Rheumatology, Hull, United Kingdom*; *[9]Hospital Clínic de Barcelona, Rheumatology Department, Barcelona, Spain*; *[10]Hospital Universitari Vall d'Hebron, Rheumatology, Barcelona, Spain*; *[11]ARC Amsterdam University Hospitals – VU University Medical & Reade, Department of Rheumatology, Amsterdam, Netherlands*; *[12]University Hospital Geelong, Barwon Rheumatology Service, Geelong, Australia*; *[13]Evangelical Hospital, Department of Internal Medicine, Vienna, Austria*; *[14]Universitätsspital Basel, Rheumatologische Universitätsklinik, Basel, Switzerland*; *[15]Schulthess Klinik, Department of Rheumatology, Zürich, Switzerland*; *[16]Bristol Myers Squibb, Non-Registrational Data Generation, Rueil-Malmaison, France*; *[17]Deepscover, Biostatistics, Puteaux, France*; *[18]Bristol Myers Squibb, Medical Immunology & Fibrosis, Munich, Germany*; *[19]Bristol Myers Squibb, Immunology and Fibrosis, Princeton, United States of America*; *[20]Bristol Myers Squibb, US Medical Immunology and Fibrosis, Princeton, United States of America*

Background: RF and anti-citrullinated protein antibodies (ACPAs) are associated with a severe and aggressive disease course in patients with RA.[1] Abatacept is a selective co-stimulation modulator for the treatment of RA.[2] ASCORE (Abatacept SubCutaneOus in Routine Clinical PracticE; NCT02090556) was a 2-year, observational, prospective, multicentre study of SC abatacept for the treatment of RA in routine clinical practice.[3]

Objectives: To determine if serostatus and treatment line impacted disease activity in patients enrolled in the ASCORE study.

Methods: Eligible patients, aged ≥18 years, with active moderate-to-severe RA (ACR/EULAR 2010 criteria) who were IV abatacept-naive and initiated SC abatacept 125 mg once weekly, were enrolled into two cohorts: biologic (b) DMARD-naive patients and those with ≥1 prior bDMARD treatment failure. This *post hoc* analysis assessed the mean change in disease activity (CDAI, SDAI and DAS28 [ESR]) from baseline (BL) at 6, 12, 18 and 24 months in response to treatment with abatacept. Patients were stratified by BL serostatus (all patients, RF/ACPA double positive [+/+] RA; RF/ACPA single positive [+/–; RF+/ACPA– or RF–/ACPA+] RA and RF/ACPA double negative [–/–] RA) and by line of therapy (all patients, patients receiving abatacept as a first-line or ≥ second-line therapy and those receiving abatacept following 1 or ≥2 prior bDMARDs). Overall patient data, as well as data for patients who were +/– or those who had 1 or ≥2 previous bDMARDs, are not shown. Estimates of mean difference are from *t*-test.

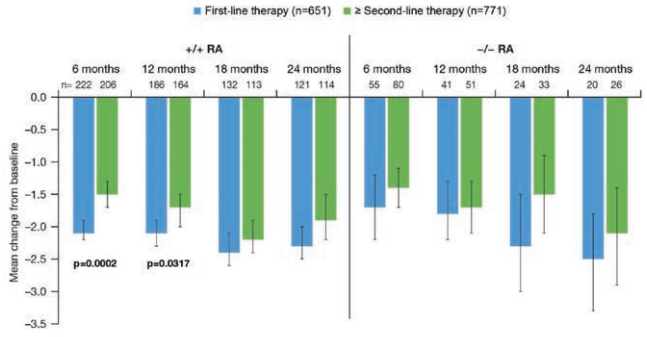
Results: Among 2892 eligible patients in ASCORE, 1748 patients with RF/ACPA status available at BL were included in this analysis (1079 +/+ RA, 326 +/– RA and 343 –/– RA). After 6 months, patients with +/+ RA on first-line abatacept therapy had better improvements in CDAI and SDAI scores from BL than patients on ≥ second-line abatacept therapy (mean difference [95% CI]: –3.4 [–5.6, –1.1]; p=0.0032 and –3.9 [–6.5, –1.3]; p=0.0035, respectively); better improvements in SDAI were also seen after 12 months (mean difference [95% CI]: –3.5 [–6.5, –0.5]; p=0.0207). Changes in CDAI and SDAI scores were comparable after 18 and 24 months. At 6 and 12 months, patients with +/+ RA on first-line therapy had better improvements from BL in DAS28 (ESR) than those on ≥ second-line therapy (mean differences [95% CI]: –0.5 [–0.8, –0.2]; p=0.0002 and –0.4 [–0.7, –0.0]; p=0.0317, respectively); changes were comparable at 18 and 24 months (Figure 1). For patients on ≥ second-line therapy, at 18 months those with +/+ RA had better improvements from BL in DAS28 (ESR) than those with –/– RA (mean difference [95% CI]: –0.7 [–1.2, –0.1]; p=0.0232). For patients not stratified by line of therapy, changes in DAS28 (ESR) were comparable between the +/+ and –/– RA subgroups over time, with the exception of 6 months where patients with –/– RA had better improvements from BL compared with patients with +/+ RA (mean difference [95% CI]: –0.3 [–0.6, –0.0]; p=0.0495).

Conclusion: In this real-world, *post hoc* analysis, patients with +/+ RA who received abatacept as a first-line therapy had greater early improvements in disease activity compared with patients who received abatacept as a ≥ second-line therapy. Improvements in disease activity at 24 months were comparable between patients who were +/+ and those who were –/–. Larger studies are needed to further corroborate these findings.

REFERENCES:

[1] Katchamart W, et al. *Rheumatol Int* 2015;35:1693–1699.
[2] Malmström V, et al. *Nat Rev Immunol* 2017;17:60–75.
[3] Alten R, et al. *Ann Rheum Dis* 2019;78(Suppl 2):A1639.

Figure 1. Mean change from BL in DAS28 (ESR) for patients with RA treated with abatacept



p values are for the mean difference between abatacept as a first-line and abatacept as a ≥ second-line therapy, determined by *t*-test.
+/+=RF/ACPA double positive; –/–=RF/ACPA double negative; ACPA=anti-citrullinated protein antibody.

Acknowledgements: Professional medical writing and editorial assistance was provided by Rachel Rankin, PhD, at Caudex and was funded by Bristol Myers Squibb. This study was funded by Bristol Myers Squibb.

Disclosure of Interests: Rieke Alten Speakers bureau: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Consultant of: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Grant/research support from: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Xavier Mariette Consultant of: Bristol Myers Squibb, Galapagos, Gilead, GlaxoSmithKline, Janssen, Pfizer, UCB, Rene-Marc Flipo Speakers bureau: AbbVie, Bristol Myers Squibb, Janssen, Lilly, Medac, Merck Sharp & Dohme, Novartis, Pfizer, Roche-Chugai, Grant/research support from: Amgen, Janssen, Novartis, Pfizer, Roberto Caporali Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Fresenius Kabi, Galapagos, Gilead, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Samsung Bioepis, Sanofi, UCB, Consultant of: Galapagos, Gilead, Janssen, Lilly, Merck Sharp & Dohme, Maya H Buch Speakers bureau: AbbVie, Consultant of: AbbVie, Eli Lilly, Gilead, Merck Serono, Pfizer, Roche, Sanofi, Grant/research support from: Gilead, Pfizer, Roche, UCB, Yusuf Patel: None declared, Raimón Sanmartí Speakers bureau: AbbVie, Bristol Myers Squibb, Gebro, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, Consultant of: AbbVie, Bristol Myers Squibb, Gebro, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, Grant/research support from: Bristol Myers Squibb, Merck Sharp & Dohme, Pfizer, Sara Marsal Speakers bureau: Bristol Myers Squibb, Celgene, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol Myers Squibb, Celgene, Galapagos, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, UCB, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Sanofi, UCB, M.T. Nurmohamed Speakers bureau: AbbVie, Bristol Myers Squibb, Eli Lilly, Roche, Sanofi, Consultant of: AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Mundipharma, Novartis, Pfizer, Roche, Sanofi, Hedley Griffiths Consultant of: AbbVie, Gilead, Janssen, Novartis, Peter Peichl: None declared, Bettina Bannert: None declared, Adrian Forster: None declared, Melanie Chartier Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Yedid Elbez Consultant of: Bristol Myers Squibb, Christiane Rauch Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Karissa Lozenski Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Vadim Khaychuk Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.928

POS0600 IMMUNOGENICITY OF RITUXIMAB BIOSIMILAR GP2013: A RARE EVENT, BUT NOT WITHOUT CONSEQUENCES ...

J. Avouac[1], R. Cougnaud Murail[1], C. Goulvestre[2], S. Dumas[3], A. Moltó[1], C. Miceli Richard[1], O. Conort[3], F. Batteux[2], Y. Allanore[1]. [1]*Cochin Hospital, Rheumatology Department, Paris, France*; [2]*Cochin Hospital, Immunology Department, Paris, France*; [3]*Cochin Hospital, Pharmacy Department, Paris, France*

Background: The bioequivalence between rituximab (RTX) originator and its biosimilar GP2013 has been demonstrated in rheumatoid arthritis (RA) (1). A recent randomized controlled trial suggested in a selected population a very low immunogenicity of GP2013 in RA (<1%) (2).

Objectives: To study in daily practice the risk of immunogenicity of patients treated with GP2013 for their chronic inflammatory rheumatic disorder.

Methods: Prospective routine care study carried out between September 2018 and August 2020 in the Rheumatology department of Cochin Hospital. We consecutively included patients treated with the biosimilar RTX GP2013, systematically used in the department since March 2018. Samples were taken before each infusion in order to detect anti-RTX antibodies (Ab) and RTX residual concentrations by ELISA (Lisa Tracker Duo Rituximab, LTR005, Theradiag).

Results: We included 159 consecutive patients treated with GP2013 (124 women, 78%) with a mean age of 59±13 years and a mean disease duration of 18±11 years. Among these 159 patients, 108 (68%) had RA and 51 had another disease (16 systemic sclerosis (SSc), 15 mixed connective tissue disease (MCTD), 5 systemic lupus (SLE), 5 inflammatory myopathies (MI), 5 undifferentiated polyarthritis, 2 juvenile idiopathic arthritis (JIA) and 3 primary Sjögren's syndromes). 137 patients (86%) were receiving associated disease-modifying therapy (DMARD), mainly methotrexate (111/137 patients, 81%). 120 patients (75%) were in maintenance therapy with originator RTX (cumulative dose of RTX: 3.5±6g) before the switch to GP2013 in March 2018. Originator RTX was not re-established during the entire treatment period. The other 39 patients (25%) treated with GP2013 were naïve of originator RTX.

The analysis of the first sample, performed before the second GP2013 infusion, identified 8 patients (5 RA, 1 SLE, 1 MCTD and 1 SSc) with positive anti-RTX antibodies (prevalence 5%), with rates varying between 6 and >100ng/mL and undetectable residual RTX concentrations. Among these 8 patients, 6 had previously received originator RTX and 2 were RTX-naïve patients. There was a trend for higher body mass index in patients with positive anti-RTX antibodies (28±7 vs. 25±6 kg/m^2, p=0.12), and no association was observed between anti-RTX immunization and age, disease duration, combination with conventional DMARD, mean interval between infusions or cumulative RTX dose.

Among the 8 immunized patients, two groups could be isolated: i) a group of 5 patients (3 RA, 1 SLE, 1 SSc) with low antibody levels (6-22 ng/mL) and no significant clinical consequences (absence of treatment discontinuation and loss of efficacy after 13±4 months of follow-up, only one minor allergic reaction) and ii) a group of 3 patients (2 RA, 1 MCTD) with a high antibody levels (≥100ng/mL) and meaningful clinical consequences: one severe allergic reaction during the second GP2013 infusion leading to treatment discontinuation, and a loss of efficacy with incomplete B depletion in 2 patients leading to RTX dose escalation from 500 mg to 1 g. Among the 151 patients not immunized at the time of the first sample, no severe allergic reaction and 6 minor allergic reactions were noted under GP2013.

Conclusion: The immunogenicity of patients treated with RTX is a rare event with possible clinical and biological consequences, especially in patients with high antibody levels.

REFERENCES:

[1] Smolen et al, Ann Rheum Dis 2017
[2] Tony et al, Arthritis Care Res 2019

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.954

POS0601 DIFFERENCES IN DRUG SURVIVAL BETWEEN ORIGINATOR AND BIOSIMILAR PRODUCTS AMONG FIRST USERS OF EACH MOLECULE

D. Di Giuseppe[1], H. Bower[1], B. Delcoigne[1], T. Frisell[1], K. Chatzidionysiou[1,2], U. Lindström[3], C. Sjowall[4], E. Lindqvist[5], J. Askling[1]on behalf of ARTIS. *[1]Karolinska Institute, Department of Medicine Solna, Stockholm, Sweden*; *[2]Nya Karolinska, Rheumatology Unit, Stockholm, Sweden*; *[3]Sahlgrenska Academy, University of Gothenburg, Rheumatology Unit, Karolinska University Hospital, Gothenburg, Sweden*; *[4]Linköping University, Division of Inflammation and Infection, Department of Biomedical and Clinical Sciences, Linköping, Sweden*; *[5]Lund University, Skåne University Hospital, Department of clinical sciences, Rheumatology, Lund, Sweden*

Background: Biosimilar products of biological disease-modifying antirheumatic drugs (bDMARDs) entered the Swedish market in 2015, with regulatory approvals based on head to head trials of limited duration. Longer-term comparative drug survival, in clinical practice, remains less well documented.

Objectives: To compare survival on drug between biosimilars and their originator products among first starters of etanercept, infliximab, adalimumab and rituximab.

Methods: Data from the Swedish Rheumatology Quality register (SRQ) was used to identify and follow patients who started a first ever treatment with etanercept since April 2015 (originator=ETA,biosimilar= SB4), infliximab since March 2014 (originator=IFX,biosimilar= CT-P13), adalimumab since January 2018 (originator=ADA biosimilars=SB5, ABP501), or rituximab since January 2018 (originator=RIT,biosimilar= GP2013), through December 31st, 2019, date of first discontinuation of the drug, or death. Discontinuation was defined as lack of effectiveness or adverse events, while other reasons for interruption of the drug (including non-medical switch) were considered censoring events. Descriptive characteristics were collected from the SRQ and tabulated. Hazard ratios (HR) of discontinuation were estimated using Cox regression, with each drug analyzed separately, adjusted for age,sex,indication,line of treatment,disease duration,year of treatment start,region and concomitant use of csDMARD.

Results: 9274 patients started etanercept(49% SB4), 3609 started infliximab(64% CT-P13), 3117 started adalimumab(27% SB5, 14% ABP 501), and 763 started rituximab(39% GP2013), Table 1. Patients starting CT-P13 and GP2013 were less likely to be biologics-naïve compared to those starting the originator product. Initiators of SB5,ABP501 and GP2013 were more likely,and those starting CT-P13 were less likely,to be on concomitant csDMARDs compared to those starting the originator products. Patients characteristics of ETA and SB4 were similar.

The introduction of a biosimilar was typically followed by a decrease in the uptake of the originator, but for ETA a change in pricing in 2018 later led to a reversal of this pattern (Figure 1).

For IFX,ADA,and RIT, survival on drug was similar for the originator and its biosimilar(s). For ETA,risk of discontinuation was somewhat lower for the biosimilar than for the originator(adjusted HR:0.87,95% confidence interval:0.79-0.95), Table 1.

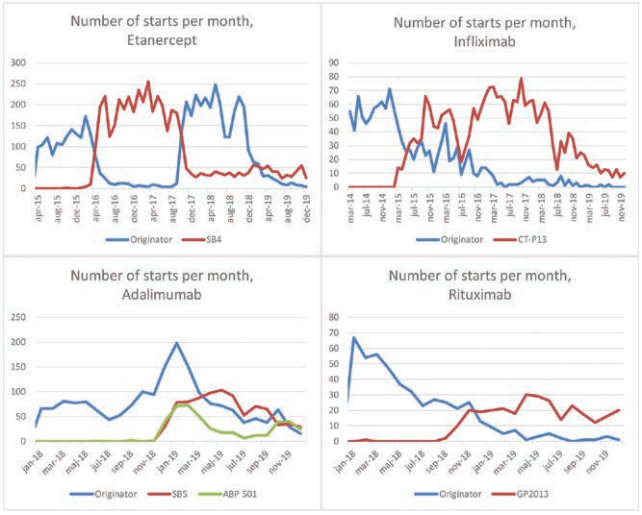


Figure 1. Number of starts of biosimilars compared to the originator during the follow-up time, by molecule

Conclusion: Despite their identical indications and therapeutic positioning, there are some differences in the baseline characteristics between patients who start ADA, IFX and RIT and their biosimilars. There are no differences in drug survival between originator and biosimilar with the possible exception of etanercept although the observed difference should be interpreted in light of possible unmeasured or residual channeling.

Disclosure of Interests: Daniela Di Giuseppe: None declared, Hannah Bower: None declared, Bénédicte Delcoigne: None declared, Thomas Frisell: None declared, Katerina Chatzidionysiou Consultant of: Eli Lilly, AbbVie and Pfizer, Ulf Lindström: None declared, Christopher Sjowall: None declared, Elisabet Lindqvist: None declared, Johan Askling Grant/research support from: Abbvie, AstraZeneca, BMS, Eli Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB,

DOI: 10.1136/annrheumdis-2021-eular.977

POS0602 ROLE OF INTRAARTICULAR BIOLOGICS AND METHOTREXATE IN THE MANAGEMENT OF ACTIVE INFLAMMATORY MONOARTHRITIS

F. Aslam[1], M. Meyer[1], M. Pham[2]. *[1]Mayo Clinic, Rheumatology, Scottsdale, United States of America*; *[2]Mayo Clinic, Medicine, Scottsdale, United States of America*

Background: Expansion of immunosuppressive medications has greatly improved disease activity control in rheumatoid arthritis (RA) patients. However, persistent symptomatic monoarthritis can be a problem in some patients who otherwise have satisfactory disease control. Intra-articular (IA) corticosteroid (CS) injections have remained a treatment cornerstone for these patients, but the need for other therapies is clear. Patients can fail such therapy, may develop adverse effects or have comorbidities that are exacerbated by IA CS. 50% of patients relapse after IA CS therapy. Several studies have looked at other agents such as methotrexate (MTX) or tumor necrosis factor inhibitors (TNF-i) as IA treatment options.

Objectives: To systematically review the evidence regarding utility of IA methotrexate and biologics in managing inflammatory monoarthritis in patients with RA.

Table 1. Hazard ratios of discontinuation and descriptive characteristics of biosimilar vs. originator among first starters of each molecule, until 31st December 2019.

	Etanercept		Infliximab		Adalimumab			Rituximab	
	Originator	SB4	Originator	CT-P13	Originator	SB5	ABP 501	Originator	GP2013
N	4721	4553	1308	2301	1834	852	431	465	298
Discontinuation	1289	1236	582	878	399	139	80	57	26
Adjusted hazard ratios*	**Ref**	0.87 (0.79-0.95)	**Ref**	1.14 (0.99-1.31)	Ref	1.02 (0.83-1.26)	1.16 (0.88-1.52)	Ref	1.12 (0.68-1.85)
Age, mean years (std)	51 (16)	51 (15)	49 (16)	49 (16)	48 (15)	52 (15)	51 (15)	59 (15)	60 (15)
Female, %	67%	65%	61%	64%	62%	64%	65%	75%	76%
RA, %	46%	48%	39%	35%	33%	42%	43%	61%	76%
Bionaïve, %	72%	72%	76%	69%	45%	52%	43%	53%	38%
Disease duration, mean years (std)	11 (12)	11 (11)	11 (11)	11 (11)	12 (13)	12 (11)	14 (15)	14 (19)	15 (11)
DAS28, mean	4.0 (1.3)	4.0 (1.4)	4.1 (1.4)	4.1 (1.4)	3.7 (1.4)	3.8 (1.3)	4.0 (1.3)	4.5 (1.4)	4.7 (1.4)
Concomitant csDMARDs, %	45%	47%	57%	48%	37%	49%	42%	36%	43%

Abbreviations: RA=rheumatoid arthritis. csDMARDs=conventional synthetic DMARD, std=standard deviation.

Methods: A systematic literature review, in accordance with PRISMA guidelines, was conducted looking at trials investigating the use of IA MTX and/or TNF-i, against IA CS, in managing inflammatory monoarthritis in patients with RA. A trained librarian conducted search of Ovid MEDLINE, Ovid EMBASE, Scopus, and Web of Science databases. Included studies were assessed for risk of bias as per the Cochrane tool.

Results: A total of 1013 citations were retrieved from the medical database searches. 12 studies were included in the final review. 6 studies investigated IA MTX while 5 studied IA etanercept. One study investigated different biologic agents: infliximab, etanercept, or adalimumab. Multitude of dosing regimens and administration protocols were used in various studies. 5 of the 6 MTX studies only included knees. IA MTX was compared against saline, CS and as combined MTX/CS vs CS alone. There was no evidence to support the use of IA MTX as a superior or equivalent agent to the comparator groups. Unlike MTX, etanercept was investigated in multiple joint types e.g. elbows, knees and wrists. IA etanercept was found to have utility as a successful IA alternative to CS. The only study investigating infliximab and adalimumab found them to be superior to IA CS across multiple joint types. All therapies were generally well tolerated. Etanercept studies had low risk of bias while the MTX studies mostly suffered from higher risk of bias.

Conclusion: Etanercept may be used as an IA agent in select patients with inflammatory arthritis when systemic treatment is not an option and IA corticosteroids cannot be used. Limited data also supports the utility of IA adalimumab and infliximab as better IA agents compared to CS. IA MTX, however, did not have such supporting data.

REFERENCES:

[1] Fisher BA, Keat A. (2006) Should we be using intraarticular tumor necrosis factor blockade in inflammatory monoarthritis? J Rheumatol. 33(10), 1934-5.
[2] Weitoft T, Uddenfeldt P. (2000) Importance of synovial fluid aspiration when injecting intra-articular corticosteroids. Ann Rheum Dis. 59(3), 233-5.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1016

POS0603 ANALYSIS OF FACTORS ASSOCIATED WITH THE EFFECTIVENESS OF ABATACEPT IN THE ORIGAMI STUDY

K. Misaki[1], E. Tanaka[2], E. Inoue[3], K. Tsuritani[4], S. Matsumoto[5], H. Yamanaka[2,6], M. Harigai[2]. *[1] Kita-Harima Medical Center, Rheumatology, Ono, Japan*; *[2]Tokyo Women's Medical University School of Medicine, Department of Rheumatology, Tokyo, Japan*; *[3] Showa University, Showa University Research Administration Center, Tokyo, Japan*; *[4]Bristol-Myers Squibb K.K., Immunology Medical, Tokyo, Japan*; *[5]Ono pharmaceutical Co, Ltd., Medical Affairs, Tokyo, Japan*; *[6] Sanno Medical Center, Rheumatology, Tokyo, Japan*

Background: The ORIGAMI study is a multicenter, observational study to evaluate the effectiveness, safety, and patient-reported outcomes of abatacept (ABA) in Japanese patients with csDMARD-resistant, Simplified Disease Activity Index (SDAI)-moderate, biologic-naïve rheumatoid arthritis (RA). ABA has shown better effectiveness/efficacy in RA patients with anti-cyclic citrullinated peptide antibody (ACPA) positive (1) and high ACPA titer (2) compared to ACPA negative and low ACPA titer, respectively. However, more accurate predictors of effectiveness in clinical practice are needed than ACPA status.

Objectives: This post-hoc analysis is aimed to determine the association between ACPA and ABA effectiveness (disease activity and physical function) or retention rate and to investigate other factors associated with the effectiveness of ABA in patients enrolled in the ORIGAMI study.

Methods: Of the 279 patients in the effectiveness analysis set of the ORIGAMI study, 270 patients with baseline ACPA measurement were analyzed. The patients were divided into the ACPA-positive group (ACPA +ve, ≥4.5 U/mL at baseline) and the ACPA-negative group (ACPA –ve, <4.5 U/mL). Patients' characteristics, changes in disease activity and physical function (Japanese Health Assessment Questionnaire; J-HAQ) through 52 weeks, and retention rates of ABA at week 52 were evaluated. Baseline characteristics and use of concomitant drugs were analyzed as independent variables by multiple regression analysis using a standard linear model adjusted by SDAI at week 0 to identify factors associated with SDAI change at week 52. In addition, the interaction effects among ACPA status, RF status, and the factor that was significantly associated with SDAI change in multiple regression analysis on changes in SDAI were explored.

Results: The numbers of ACPA +ve and –ve patients were 226 and 44, respectively. ACPA values (mean ± SD, U/mL) were 280.3 ± 376.8 and 0.9 ± 0.7, and rheumatoid factor (RF) values were 174.8 ± 302.6 and 20.9 ± 61.7 in the ACPA +ve and –ve groups, respectively. Mean (95% confidence interval) changes in SDAI at week 52 were −11.3 (−12.4 to −10.3) and −8.0 (−10.5 to −5.5), and those in J-HAQ were −0.27 (−0.34 to −0.20) and −0.16 (−0.34 to 0.01) in the ACPA +ve and –ve groups, respectively. In the Kaplan–Meier analysis, the retention rates of ABA at week 52 in the ACPA +ve and –ve groups were 72.1% and 58.7%, (discontinuation for any reason), and 91.6% and 75.7% (discontinuation because of lack of effectiveness), respectively. In a multiple regression analysis, the duration of disease (< 1 year) was associated with the change in SDAI at week 52. With respect to SDAI changes, the estimated difference of ACPA +ve and disease duration (< 1 year), ACPA +ve and disease duration (≥1 year), and ACPA –ve and disease duration (< 1 year), versus ACPA –ve and disease duration (≥ 1 year), were −4.26 (p = 0.022), −0.82 (p = 0.618), and −0.93 (p = 0.716), respectively (Fig. 1). The estimated difference of ACPA +ve and RF +ve, ACPA +ve and RF –ve, and ACPA –ve and RF +ve, versus ACPA –ve and RF –ve, were −2.48 (p = 0.060), −2.77 (p = 0.107), and −5.48 (p = 0.087), respectively.

Conclusion: A higher retention rate as well as better effectiveness of ABA on disease activity and physical function in ACPA +ve group versus ACPA –ve group were shown in the simple subgroup analysis. ABA effectiveness on the SDAI change was significantly better in patients with disease duration <1 year and ACPA +ve compared to those with ACPA –ve and disease duration ≥ 1 year.

REFERENCES:

[1] Harrold LR et al. J Rheumatol 2018;45(1):32–39.
[2] Sokolove J et al. Ann Rheum Dis 2016;75(4):709–714.

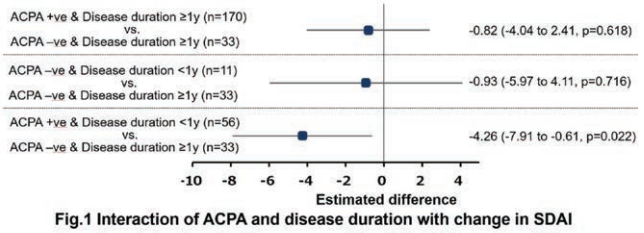


Fig.1 Interaction of ACPA and disease duration with change in SDAI

Interaction analysis adjusted for RF, age, sex, comorbidity, SDAI, J-HAQ, steroid use, MTX use and csDMARDs use (except for MTX) were performed.
ACPA, anti-cyclic citrullinated peptide antibody; SDAI, simplified disease activity index; RF, rheumatoid factor; J-HAQ, Japanese Health Assessment Questionnaire; MTX, methotrexate; csDMARDs, conventional synthetic disease modified anti-rheumatic-drugs.

Disclosure of Interests: Kenta Misaki Speakers bureau: Eisai Co., Ltd., AbbVie GK, Eli Lilly Japan K.K., Ono Pharmaceutical Co., Ltd., Grant/research support from: Ono Pharmaceutical Co., Ltd., Eiichi Tanaka Speakers bureau: AbbVie GK, Asahi Kasei Pharma Corporation, Astellas Pharma Inc, Ayumi Pharmaceutical Corporation, Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., GlaxoSmithKline K.K., Kyowa Pharma Chemical Co., Ltd., Janssen Pharmaceutical K.K., Mochida Pharmaceutical Co., Ltd., Pfizer, Takeda Pharmaceutical Co., Ltd, and Teijin Pharma Ltd., Eisuke Inoue Speakers bureau: Pfizer Japan, Bristol-Myers Squibb K.K., Katsuki Tsuritani Employee of: Bristol-Myers Squibb K.K., Shigeru Matsumoto Employee of: Ono Pharmaceutical Co., Ltd., Hisashi Yamanaka Consultant of: Bristol-Myers Squibb K.K., masayoshi harigai Speakers bureau: AbbVie GK, Ayumi Pharmaceutical Corporation, Bristol-Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., Pfizer Japan Inc., and Takeda Pharmaceutical Co., Ltd., Consultant of: AbbVie GK, Bristol-Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd., Eli Lilly Japan K.K., and Gilead Sciences Inc., Grant/research support from: AbbVie GK, and Asahi Kasei Corp., Astellas Pharma Inc., Ayumi Pharmaceutical Corporation, Bristol-Myers Squibb K.K., Chugai Pharmaceutical Co., Ltd. Daiichi-Sankyo, Inc., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Corporation., Nippon Kayaku Co., Ltd., Taisho Pharmaceutical Co., Ltd., and Takeda Pharmaceutical Co., Ltd.

DOI: 10.1136/annrheumdis-2021-eular.1028

POS0604

LONG TERM SAFETY AND TOLERABILITY WITH ETANERCEPT BIOSIMILAR (YLB113), RESULTS FROM A 2-YEAR OPEN LABEL EXTENSION STUDY (STUDY NO. YLB113-003)

Y. Hisashi[1], Y. Tanaka[2], T. Hibino[3], C. Shah[4], D. Bakhle[5], D. Stefanidis[6]. [1]*Sanno Medical Center, Rheumatology, Tokyo, Japan*; [2]*University of Occupational and Environmental Health, Japan, Professor, Fukuoka, Japan*; [3]*YL Biologics Ltd, Clinical, Tokyo, Japan*; [4]*Lupin LTD, Clinical Development, Pune, India*; [5]*Lupin LTD, Medical Research, Pune, India*; [6]*Viatris GmbH, Medical Affairs, Bad Homburg vor der Höhe, Germany*

Background: Eligible subjects with moderate-to-severely active rheumatoid arthritis (RA) who completed a phase 3 double-blind comparative efficacy and safety study (Study No. YLB113-002; Yamanaka et al, 2019) of 50 mg etanercept biosimilar (YLB113) or etanercept reference product (RP) by subcutaneous administration with concomitant MTX treatment for 52 weeks, were enrolled in this open label extension (OLE) study (Study No. YLB113-003) to assess the long-term safety and tolerability of YLB113 through to 3 years.

Objectives: This OLE study aimed to evaluate the long-term safety of YLB113 administration in subjects with RA who received RP or YLB113 in a phase 3 active comparator study. The main parameters assessed were safety and tolerability in terms of adverse events (AEs) and injection site reactions (ISRs), incidence of immunogenicity and efficacy as DAS28 improvement (disease activity score in 28 joints).

Methods: Subjects received 50 mg of YLB113 subcutaneously once every 1 to 2 weeks. Safety was assessed by AEs after study drug administration, ISRs, physical examination findings, and immunogenicity. Efficacy (DAS28 score) was assessed at the time of transition to the OLE study (Week 0), and at weeks 12, 24, 48, 72, 96 and at the end of the study.

Results: 201 (Full analysis set [FAS]) subjects received the study drug and 184 subjects completed the study (91.5% completion rate). The average drug exposure in 94 subjects who continued to receive YLB113 and completed the study (94.0% completion rate) and 90 subjects who switched from RP to YLB113 and completed the study (89.1% completion rate) was 103 weeks providing the long-term drug exposure data of YLB113.

The CTCAE Grade of TEAEs and ADRs observed were Grade 2 or less in severity (with no Grade ≥3). The overall incidence of ISRs was 10.0% (20/201 subjects) 77 events. All the ISRs reported were Grade 1 except for one Grade 2. An overview of the AEs experienced by the subjects is summarized in the Table 1.

Table 1. Overview of Adverse events in OLE study

FAS	n (%)	Number of events
Number of subjects	201	-
Treatment emergent adverse events (TEAEs)	188(93.5)	975
Adverse drug reactions (ADRs)	82(40.8)	221
Serious adverse events (SAEs)	21(10.4)	27
Serious adverse drug reactions (SADRs)	7(3.5)	7
AEs leading to premature study discontinuation	4(2.0)	6
ADRs leading to premature study discontinuation	3(1.5)	4
SAEs leading to premature study discontinuation	3(1.5)	4
SADRs leading to premature study discontinuation	2(1.0)	2

n - number of subjects with at least 1 AE in the category

The mean DAS28 (mean ± S.D.) of 2.22 ± 0.95 at the study transition was 2.10 ± 0.91 at Week 72 and 2.06 ± 0.89 at the end of the study. It was confirmed that DAS28 slightly decreased with time after the study transition and continued until the end of the study. The average DAS28 value remained low even with long-term administration of YLB113, suggesting that the effects of the study drug was sustained (Figure 1).

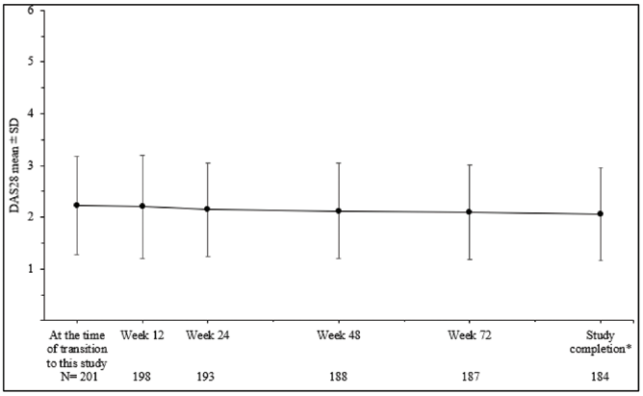


Figure 1. DAS28 over time with YLB113N: Number of subjects. * The administration period at the study completion differs for each subject, because the study transition time differs for each subject.

cts who tested positive for anti-drug antibodies (ADA) at least once in the OLE study were 1.0% (2/200 subjects). All ADA were transient and disappeared at study completion. Such transient ADA formation was reported in the phase 3 study as well. In the phase 3 study, ADA formation was more frequent in subjects who received RP at 24 weeks, but all subjects were negative in the OLE study after switching. Therefore, switching did not affect immunogenicity.

Conclusion: The safety, efficacy and immunogenicity profile of YLB113 was maintained over the long-term through to 3 years. Switching from RP to YLB113 did not impact safety or immunogenicity.

REFERENCES:

[1] Yamanaka H, Kamatani N, Tanaka Y, et al. A Comparative Study to Assess the Efficacy, Safety, and Immunogenicity of YLB113 and the Etanercept Reference Product for the Treatment of Patients with Rheumatoid Arthritis. Rheumatol Ther. 2020 Mar;7(1): 149-163.

Disclosure of Interests: Yamanaka Hisashi Speakers bureau: YL Biologics Ltd, Consultant of: YL Biologics Ltd, Yoshiya Tanaka Speakers bureau: Received speaking fees and/or honoraria from Daiichi-Sankyo, Eli Lilly, Novartis, YL Biologics, Bristol-Myers, Eisai, Chugai, Abbvie, Astellas, Pfizer, Sanofi, Asahi-kasei, GSK, Mitsubishi-Tanabe, Gilead, Janssen., Grant/research support from: Received research grants from Abbvie, Mitsubishi-Tanabe, Chugai, Asahi-Kasei, Eisai, Takeda, Daiichi-Sankyo., Toshihiko Hibino: None declared, Chirag Shah Shareholder of: Lupin LTD, Employee of: Lupin LTD, Dhananjay Bakhle Shareholder of: As part of Employee Stock Options Plan of Lupin LTD, Employee of: Lupin LTD, Dimitris Stefanidis Employee of: Sr. Director, Global Medical Affairs Lead, Immunology Biosimilars for Viatris GmbH

DOI: 10.1136/annrheumdis-2021-eular.1030

POS0606

DISEASE ACTIVITY AND PATIENTS-REPORTED OUTCOMES AFTER SWITCHING BETWEEN IL-6 RECEPTOR INHIBITORS AND JAK INHIBITORS: AN ANALYSIS FROM THE CORRONA REGISTRY

A. Dua[1], K. Ford[2], S. Fiore[3], D. A. Pappas[4], J. Janak[4], T. Blachley[5], C. Roberts-Toler[5], K. Emeanuru[6], J. Kremer[7,8], A. Kivitz[9]. [1]*Northwestern University Feinberg School of Medicine, Department of Medicine, Division of Rheumatology, Chicago, IL, United States of America*; [2]*Sanofi, Medical Affairs, Cambridge, MA, United States of America*; [3]*Sanofi, Medical Affairs, Bridgewater, NJ, United States of America*; [4]*Consortium of Rheumatology Researchers of North America (Corrona), Clinical Epidemiology, Waltham, MA, United States of America*; [5]*Consortium of Rheumatology Researchers of North America (Corrona), Biostatistics, Waltham, MA, United States of America*; [6]*Consortium of Rheumatology Researchers of North America (Corrona), Epidemiology, Waltham, MA, United States of America*; [7]*Albany Medical College, Department of Medicine, Center for Rheumatology, Albany, NY, United States of America*; [8]*Corrona LLC, Consortium of Rheumatology Researchers of North America (Corrona), Waltham, MA, United States of America*; [9]*Altoona Center for Clinical Research, Altoona Arthritis & Osteoporosis Center, Duncansville, PA, United States of America*

Background: Rheumatoid arthritis (RA) patients who fail therapy may be switched to any of the five classes of biological disease-modifying antirheumatic drugs (DMARDs) and targeted synthetic DMARDs, to meet treatment goals. Physicians may hesitate to switch between Janus Kinase inhibitors (JAKi) and interleukin-6 receptor inhibitors (IL-6Ri) since they both impact IL-6 signalling and due to limited data on switching between the two classes.

Objectives: This retrospective, observational study based on the real-world Corrona RA registry aimed to describe the response in RA patients switching between IL-6Ri and JAKi.

Methods: Adult RA patients who initiated either IL-6Ri or JAKi after November 2012 and had a six-month post-initiation follow-up visit were eligible. Patients in 'Cohort A' initiated an IL-6Ri following discontinuation of a JAKi and those in 'Cohort B' initiated a JAKi following discontinuation of an IL-6Ri. Disease activity measures and patient-reported outcomes (PROs) were evaluated at baseline and at six-month follow-up. Within each group, change from baseline was assessed for Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire (HAQ), pain, fatigue, tender joint count (TJC), swollen joint count (SJC), physician global assessment (MDGA), patient global assessment (PtGA) and morning stiffness duration. Proportion of patients achieving CDAI low disease activity (LDA), CDAI remission and minimal clinically important difference (MCID) for HAQ, pain, fatigue, MDGA, PtGA were assessed. Adjusted linear and logistic regression models were performed for between-group comparisons (Cohort A vs Cohort B) excluding initiators who switched therapy prior to six-month visit.

Results: Cohorts A and B included 122 and 144 initiators, respectively. Patients who switched to

IL-6Ri (vs JAKi) were younger (mean [SD] age, 56.2 [11.3] vs 58.9 [12.6] years), had higher baseline CDAI (23.2 [12.9] vs 20.2 [12.8]), had higher prior use of ≥2 csDMARDs (75% vs 65%), and were less likely to initiate therapy as monotherapy (44% vs 50%).

In Cohort A, significant changes from baseline were observed for all continuous outcomes except HAQ and fatigue. In Cohort B, a significant improvement was observed only for patient-reported pain (Table 1).

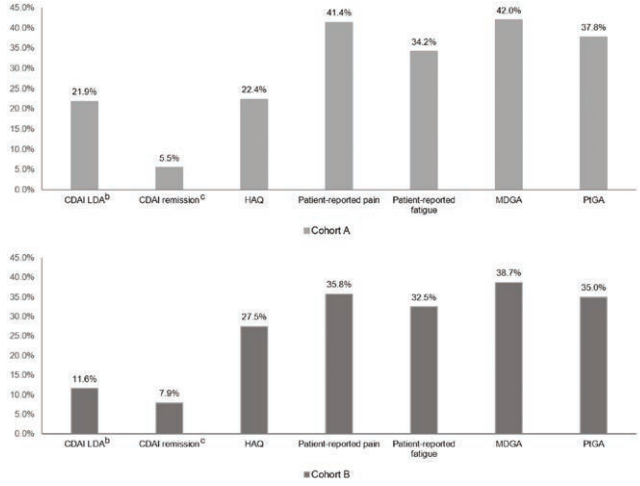
Table 1. Unadjusted Within-Group Change from Baseline to Six Months, Mean (95% CI), n

Outcomes	Cohort A, N = 122	Cohort B, N = 144
CDAI	-4.7 (-7.6, -1.9), 109	-2.4 (-5.2, 0.4), 116
HAQ	-0.0 (-0.1, 0.1), 105	-0.1 (-0.1, 0.0), 118
Patient-reported pain	-8.2 (-13.4, -3.0), 109	-5.9 (-11.5, -0.2), 120
Patient-reported fatigue	-4.4 (-9.0, 0.2), 109	-1.7 (-6.6, 3.3), 117
TJC	-1.6 (-3.0, -0.1), 112	-1.2 (-2.6, 0.3), 117
SJC	-1.5 (-2.5, -0.4), 112	-0.4 (-1.3, 0.6),117
MDGA	-10.9 (-15.6, -6.3), 112	-4.3 (-8.7, 0.2), 117
PtGA	-6.0 (-11.2, -0.8), 109	-4.8 (-10.5, 0.8), 120
Morning stiffness duration[a]	-1.3 (-2.2, -0.5), 109	-0.1 (-1.1, 0.8), 118

[a]Among those reporting morning stiffness at baseline.

In the adjusted between-group comparison (data not shown) of change from baseline, there were no significant differences in clinical outcomes between Cohorts A and B.

In both cohorts, patients achieved CDAI LDA, CDAI remission, and MCIDs across other PROs (Figure 1). In the adjusted between-group comparison (data not shown), the results were similar with the exception of achievement of CDAI LDA among patients with moderate to high disease activity at baseline.



[a]CDAI LDA: >2.8 to ≤10 units; CDAI remission: ≤2.8 units; MCID for PROs were assessed, MCID for HAQ: ≥0.3 units; MCID for VAS of pain, fatigue, MDGA, and PtGA: ≥10 units. [b]Among those in moderate or high disease activity at baseline. [c]Among those in low, moderate, or high disease activity at baseline.

Figure 1. Rates of CDAI LDA, CDAI Remission, and MCID for PROs[a] at Six Months

Conclusion: In general, in both cohorts a substantial proportion of patients achieved CDAI LDA and MCID across PROs. Despite some overlap of JAKi and IL-6Ri therapies' on the IL-6 pathway, there are some distinct mechanisms of action which may result in meaningful improvements for a subset of patients.

Acknowledgements: Amy Praestgaard (Sanofi) contributed to the interpretation of the statistical analysis for this abstract. Medical writing support for this abstract was provided by Nupur Chaubey (Sanofi).

Disclosure of Interests: Anisha Dua Speakers bureau: AbbVie, Consultant of: Consulting/advisory board for AbbVie, Novartis, and Chemocentryx, Employee of: Board member of Vasculitis foundation and Chicago Rheumatism Society, Kerri Ford Shareholder of: Sanofi, Employee of: Sanofi, Stefano Fiore Shareholder of: Sanofi, Employee of: Sanofi. In addition, Stefano Fiore has a patent EP 19306553.9; USPTO #s 62/799,698; 62/851,474; 62/935,395 issued, Dimitrios A Pappas Shareholder of: Corrona LLC, Consultant of: Sanofi, AbbVie, Gtech, Roche Hellas, and Novartis, Employee of: Corrona LLC. Board of directors, Corrona Research Foundation, Judson Janak: None declared, Taylor Blachley: None declared, Carla Roberts-Toler: None declared, Kelechi Emeanuru: None declared, Joel Kremer Consultant of: AbbVie, Lilly, Novartis, Pfizer, BMS, Genentech, Regeneron, Sanofi, and Corrona, Grant/research support from: AbbVie, Lilly, Novartis, and Pfizer, Alan Kivitz Shareholder of: Pfizer, Sanofi, GlaxoSmithKline, Gilead Sciences, Inc., and Novartis, Speakers bureau: Celgene, Merck, Lilly, Novartis, Pfizer, Sanofi, Flexion, and AbbVie, Consultant of: AbbVie, Boehringer Ingelheim, Flexion, Janssen, Pfizer, Sanofi, Regeneron, SUN Pharma Advanced Research, Gilead Sciences, Inc. In addition, Alan Kivitz reports other from Altoona Center for Clinical Research, PC, during the conduct of the study.

DOI: 10.1136/annrheumdis-2021-eular.1298

POS0607

PROMIS ASSESSMENT OF RESPONSE TO TREATMENT WITH GOLIMUMAB IV OR INFLIXIMAB IN RHEUMATOID ARTHRITIS PATIENTS: RESULTS FROM THE PHASE-4 AWARE STUDY

C. Bingham[1], S. Kafka[2], S. Black[3], S. Xu[4], W. Langholff[5], J. Curtis[6]. [1]*Johns Hopkins University, Division of Rheumatology, Baltimore, United States of America*; [2]*Janssen Scientific Affairs, Med Group Rheum, Horsham, United States of America*; [3]*Janssen R&D US, Immunology General, Horsham, United States of America*; [4]*Janssen Research & Development, Clinical Biostats, Spring House, United States of America*; [5]*Janssen Research & Development, Clinical Biostats, Horsham, United States of America*; [6]*University of Alabama at Birmingham, Dept of Medicine, Birmingham, United States of America*

Background: AWARE is a phase-4 observational study designed to provide real-world assessment of Golimumab (GLM) IV & infliximab (IFX) in patients (pts) with rheumatoid arthritis (RA).
Objectives: To assess patient-reported aspects of social, mental, & physical health through the 8th infusion (≈1 year of treatment) using Patient Reported Outcomes Measurement Information System (PROMIS), a validated, disease-agnostic set of health assessment instruments.
Methods: AWARE enrolled 1270 RA pts initiating treatment with GLM/IFX. The 52 week analysis set included pts with ≥1-year treatment or those discontinued and, while enrolled, completed PROMIS-29 or PROMIS short form (SF) questionnaires. PROMIS instruments were administered at baseline & prior to infusions 2, 5, & 8. The raw score was converted into a standardized T-score with a mean of 50 and SD of 10.
Results: At baseline, treatment groups were balanced on demographics & medical characteristics. Most pts were white (87.0% GLM, 86.2% IFX) & female (83.4% GLM, 82.4% IFX). Mean ages were 58.5 ±12.96 years for GLM & 59.6 ±13.24 years for IFX. Overall, 35.3% GLM & 42.9% IFX pts were bio-naïve. The proportion of GLM & IFX pts with prior exposure to 1 or 2 biologics was similar; however, 20.1% GLM pts vs 10.8% IFX pts had exposure to ≥3 biologics. Methotrexate use was similar between GLM (76.4%) & IFX pts (75.0%). Based on mean PROMIS T-scores at baseline (Table 1), Fatigue, Pain Interference, & Physical Function domains approached or exceeded 1 SD worse than those of general US population. Through the 8th infusion, GLM- & IFX-treated pts achieved meaningful improvement based on mean changes from baseline in most PROMIS-29 domains & respective SFs with no significant difference between GLM and IFX. The percentage of GLM or IFX pts with improvements of ≥3, ≥5, or ≥10 units change in T-scores increased from infusion 2 through infusion 8.
Conclusion: RA pts treated with GLM or IFX achieved comparable improvements across PROMIS-assessed social, mental, & physical health. PROMIS-29 was able to detect change to subsequent anti-tumor necrosis factor-α therapies.
Disclosure of Interests: Clifton Bingham Consultant of: AbbVie, BMS, Eli Lilly, Gilead, Janssen, Pfizer, Regeneron/Sanofi, Grant/research support from: Bristol-Myers Squibb, Shelly Kafka Employee of: Janssen Research & Development, LLC, Shawn Black Employee of: Janssen Research & Development, LLC, Stephen Xu Employee of: Janssen Research & Development, LLC, Wayne Langholff Employee of: Janssen Research & Development, LLC, Jeffrey Curtis Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, UCB
DOI: 10.1136/annrheumdis-2021-eular.1349

Table 1. Mean (SD) Change from Baseline PROMIS-29 Domain and Short Form T-Scores: 52 Week Analysis Set

	GLM	IFX	LSM difference (95% CI)*
Anxiety (4-item)	N=6	N=570	
Baseline	53.4 (10.13)	54.6 (10.53)	
Change from baseline at infusion 8	N=223 -2.6 (8.10)	N=286 -3.7 (7.86)	-0.29 (-1.54, 0.97)
Depression (4-item)	N=674	N=574	
Baseline	51.9 (9.83)	52.5 (10.21)	
Change from baseline at infusion 8	N=225 -2.1 (7.56)	N=287 -2.3 (7.89)	0.49 (-0.72, 1.70)
Fatigue (4-item)	N=671	N=574	
Baseline	58.4 (9.91)	59.4 (9.99)	
Change from baseline at infusion 8	N=225 -3.4 (8.72)	N=281 -3.1 (7.77)	0.69 (-0.64, 2.03)
Short form Fatigue 7a	N=681	N=576	
Baseline	59.1 (8.51)	59.7 (8.25)	
Change from baseline at infusion 8	N=228 -3.2 (7.40)	N=287 -2.4 (6.35)	1.01 (-0.11, 2.14)
Pain interference (4-item)	N=679	N=574	
Baseline	63.0 (7.56)	63.9 (7.80)	
Change from baseline at infusion 8	N=227 -4.2 (8.23)	N=284 -3.1 (7.77)	1.84 (0.55, 3.13)
Short form Pain interference 6b	N=680	N=576	
Baseline	61.9 (7.45)	62.8 (7.54)	
Change from baseline at infusion 8	N=228 -3.8 (7.88)	N=287 -3.2 (6.67)	1.31 (0.15, 2.48)
Physical function (4-item)	N=678	N=571	
Baseline	38.2 (6.79)	38.0 (6.90)	
Change from baseline at infusion 8	N=224 2.2 (5.64)	N=283 1.9 (5.85)	-0.76 (-1.73, 0.21)
Sleep disturbance (4-item)	N=671	N=569	
Baseline	54.6 (8.72)	N=55.5 (8.61)	
Change from baseline at infusion 8	N=221 -1.4 (7.45)	N=281 -1.7 (7.61)	0.23 (-0.96, 1.42)
Social participation (4-item)	N=673	N=574	
Baseline	43.7 (8.40)	42.9 (8.77)	
Change from baseline at infusion 8	N=225 3.2 (8.15)	N=283 3.4 (7.48)	-0.10 (-1.36, 1.16)

*Least squares mean (LSM) difference & confidence interval (CI) are based on analysis of covariance controlling for baseline PROMIS score using inverse probability of treatment weighted propensity score.

POS0608

SWITCHING OF TREATMENT FROM REFERENCE ETANERCEPT TO SANDOZ ETANERCEPT BIOSIMILAR IN PATIENTS WITH RHEUMATIC DISEASES: AN INTERIM ANALYSIS OF REAL-WORLD DATA FROM THE COMPACT STUDY

M. Schmalzing[1], A. Askari[2], T. Sheeran[3], D. Walsh[4], J. De Toro Santos[5], J. C. Vazquez Perez-Coleman[6], C. Both[7], F. Furlan[7], S. Hachaichi[7], H. Kellner[8]. [1]*University Hospital, Wuerzburg, Rheumatology/Clinical Immunology, Department of Internal Medicine II, Wuerzburg, Germany*; [2]*Robert Jones and Agnes Hunt Orthopedic Hospital NHS Foundation Trust, Department of Rheumatology, Oswestry, United Kingdom*; [3]*Cannock Chase Hospital, Department of Rheumatology, Cannock, United Kingdom*; [4]*University of Nottingham and Sherwood Forest Hospitals NHS Foundation Trust, Pain Centre Versus Arthritis, Nottingham, United Kingdom*; [5]*University Hospital Coruña, Servicio de Reumatología, A Coruña, Spain*; [6]*University Hospital Complex of Ferrol, Rheumatology Department, Ferrol, Spain*; [7]*Sandoz Hexal AG, Global Medical Affairs, Holzkirchen, Germany*; [8]*Hospital Neuwittelsbach, Center for Rheumatology and Gastroenterology, Munich, Germany*

Background: Sandoz etanercept (SDZ ETN) is a biosimilar of etanercept (ETN). COMPACT is an ongoing, non-interventional study, evaluating the effectiveness, safety, and quality of life with SDZ ETN treatment in patients (pts) with rheumatoid arthritis (RA), axial-spondyloarthritis (axSpA) or psoriatic arthritis (PsA) in real-world conditions.

Objectives: We have reported an interim analysis, with the effectiveness and safety data focusing on pts who were in clinical remission or low disease activity under treatment with reference ETN or biosimilar ETN other than SDZ ETN (initial ETN; iETN) and switched to SDZ ETN.

Methods: Pts aged ≥18 years for whom treatment with SDZ ETN were initiated are being enrolled. Pts were categorized under four treatment groups based on prior treatment status: Group A,
pts on clinical remission or low disease activity under treatment with iETN and switched to SDZ ETN; Group B, pts who received targeted therapies and switched to SDZ ETN; Group C, biologic naïve considered uncontrolled with conventional therapy; Group D, DMARD naïve with recent diagnosis of RA considered suitable for treatment initiation with a biologic and started on treatment with SDZ ETN. Effectiveness assessments included Disease Activity Score 28-joint count Erythrocyte Sedimentation Rate (DAS28-ESR) or Ankylosing Spondylitis Disease Activity Score (ASDAS) until Week 24 after enrollment (baseline; BL) in the study. Functional disability was measured by the Health Assessment Questionnaire Disability Index (HAQ-DI). The effectiveness and safety results are reported for the pts who switched from iETN (Group A).

Results: Of the 1437 pts recruited (analysis cut-off date: 16 Oct, 2020), 567 pts were switched from iETN, 163 were switched from other targeted therapies, 697 were biologic-naïve, and 10 were RA DMARD-naïve. Among pts who switched from iETN, 51.5% had RA, followed by axSpA (28.0%) and PsA (20.5%). Comorbidities were more frequent in pts with RA (70.2%) followed by PsA (58.6%) and axSpA (49.7%); musculoskeletal and connective tissue disorders were reported in 31.8% and 15.7% of pts with RA and axSpA, respectively. At BL, whilst receiving iETN, the mean (SD) DAS28-ESR scores were 2.5 (1.1) and 2.1 (1.1) in pts with RA and PsA, respectively (figure 1). The mean change from BL in DAS28-ESR score at Week 24 after switch to SDZ ETN was -0.1 (1.1) and 0 (1.0) in pts with RA and PsA, respectively. In pts with axSpA, the mean (SD) ASDAS score was 1.5 (0.7) at BL; mean change from BL in ASDAS score at Week 24 was 0.1 (0.5). At BL, the mean (SD) HAQ-DI scores were 0.8 (0.7), 0.5 (0.7) and 0.5 (0.6) in pts with RA, PsA and axSpA, respectively. Overall, the proportion of patients with at least one adverse event (AE) was 37.3%, 33.6% and 25.8% in pts with RA, PsA and axSpA, respectively. Serious AEs were reported in 6.5%, 1.7% and 3.1% of pts with RA, PsA, and axSpA, respectively. Injections site reactions were reported in 2.7%, 0.9% and 1.3% of pts with RA, PsA and axSpA, respectively.

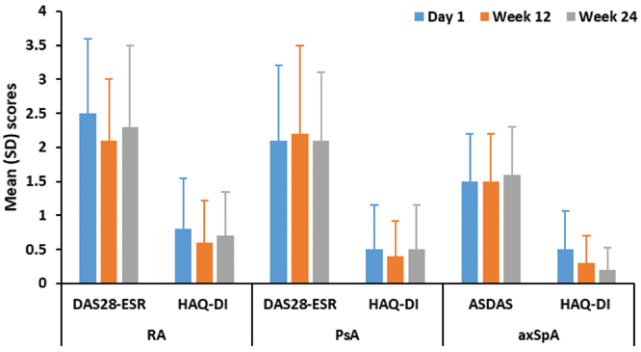


Figure 1. Disease activity in patients who switched from iETN to SDZ ETN

Conclusion: The interim analysis results shows that switch from iETN to SDZ ETN does not impact the effectiveness of ETN in pts with RA, axSpA or PsA, without any new safety signals.

Disclosure of Interests: Marc Schmalzing Speakers bureau: Novartis, AbbVie, Chugai/Roche, Janssen-Cilag, Lilly, Consultant of: AstraZeneca, Chugai/Roche, Hexal/Sandoz, Gilead, AbbVie, Janssen-Cilag, Boehringer/Ingelheim, Grant/research support from: Travel grants: Chugai/Roche, Boehringer/Ingelheim, Celgene, Medac, Ayman Askari: None declared, Tom Sheeran Speakers bureau: Pfizer, UCB, Roche, Consultant of: Novartis, Pfizer, Grant/research support from: Novartis, UCB, Roche, David Walsh: None declared, Javier de Toro Santos: None declared, JULIO CESAR VAZQUEZ PEREZ-COLEMAN Speakers bureau: Sandoz, Abbvie, Sanofi, Fresenius, Charlotte Both Employee of: Sandoz employee Global Medical Affairs, Fabricio Furlan Employee of: Sandoz employee Global Medical Affairs, Sohaib HACHAICHI Employee of: Sandoz employee Global Medical Affairs, Herbert Kellner: None declared

DOI: 10.1136/annrheumdis-2021-eular.1490

POS0609

A TOCILIZUMAB DOSING STRATEGY IN RHEUMATOID ARTHRITIS PATIENTS WITH STABLE DISEASE AIMING TO PREVENT OVERTREATMENT AND UNNECESSARY COSTS

K. van Soest[1], N. W. Boone[1], S. Ramiro[2,3], M. Starmans[2], N. C. Punt[4], R. B. M. Landewé[2,5]. [1]*Zuyderland MC, Clinical Pharmacy, Pharmacology and Toxicology, Heerlen, Netherlands*; [2]*Zuyderland MC, Rheumatology, Heerlen, Netherlands*; [3]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; [4]*Medimatics, PKPD/TDM, Maastricht, Netherlands*; [5]*Amsterdam UMC, locatie AMC, Rheumatology & Immunology, Amsterdam, Netherlands*

Background: Tocilizumab (TCZ) is a humanized interleukin 6 (IL-6) antibody that competitively inhibits IL-6 signalling by binding both membrane-bound and soluble IL-6 receptors. The EULAR recommends the use of TCZ, as a biological disease-modifying antirheumatic drug (DMARD), as second line therapy in rheumatoid arthritis (RA) when

conventional DMARDs have failed achieving treatment target. The labelled dosing regimen for TCZ in RA is 8mg/kg (maximum 800mg) every 4 weeks. A TCZ predose serum concentration (TCZpsc) >1mg/L normalizes C-reactive protein, while clinical trials found mean TCZpsc of 19.9 ±17.0 mg/L in patients receiving the standard regimen. On the basis of these data, it can be hypothesized that cost-effectiveness of therapy can be improved.

Objectives: In this study we evaluated TCZpsc in stable RA-patients to determine whether the TCZ 8mg/kg dose could be lowered while meeting the minimal required concentration for effective blockage of the IL-6 inflammatory cascade.

Methods: Adult RA patients with stable disease (i.e. at least 3 months without treatment change) treated with intravenous TCZ were investigated in a prospective cohort study. TCZpsc before two different TCZ infusions over time was assessed. A validated ELISA was used to measure TCZpscs, immunogenicity was measured by quantifying human antibodies using antigen-binding tests (radioimmunoassay).

A population pharmacokinetic (PK) model was constructed using maximum a posteriori Bayesian estimation applied on the available PK data in the literature combined with the collected data on dosing and predose concentrations in the study patients. Body surface area, creatinine clearance and gender were included as covariates in the model. A patient individual dose tapering strategy was predicted based on the derived model.

The target TCZpsc was set on 8-10mg/L taking the measurement error of 15%, the use of the entire content of the vials and intra-individual variation into consideration.

Results: A total of 44 patients were included [median (IQR) age: 63 (58-72), 75% female, mean (SD) DAS28-ESR: 1.5 (0.8)]. Half of the patients received TCZ in combination with a conventional DMARD, 32% used methotrexate (MTX). Patients received 7.7 ±0.8mg/kg (range 5.7-9.7) TCZ. Mean TCZpsc was 27.6 ±12.6mg/L. The intra-individual variance of TCZpsc was low; mean difference in individual TCZpscs was 0.56 (5.2)mg/L. Higher dosages (in mg/kg) were significantly associated with higher TCZpsc (regression coefficient 7.32 95%CI 2.73;11.9), suggesting overtreatment. No drug-neutralizing auto-antibodies were measured. Co-treatment with MTX did not influence the median TCZpsc (21.0mg/L versus 26.5mg/L without MTX, p=0.84).

According to the measured TCZpsc, TCZ dosage could be lowered in 36 patients (92%). In a 28-days regimen, target-TCZpsc would be reached with a 0.4-4.6mg/kg dose-reduction (Figure 1). Extending the interval between two administrations would lead to low TCZpsc (<1mg/L).

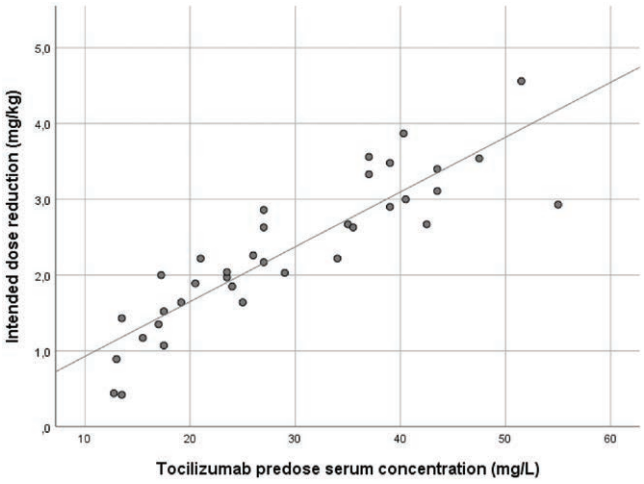


Figure 1. Intended dose reduction related to the measured tocilizumab predose serum concentration

Considering the aimed average dose-reduction of 2.1 mg/kg per administration, efficacy would be expected to maintain (TCZpsc >1 mg/L) while reducing yearly costs with ±€3.900,- per patient. On average patients were started on TCZ treatment 63 months (SD26) earlier. As maximum efficacy of TCZ treatment can be achieved after 3 months, TCZpsc-guided dose reduction 3 months after start could have resulted in a total drug cost reduction of ±€750.000,- in our study population (±€19.500,- per patient).

Conclusion: Measured TCZpsc under standard TCZ therapy was much higher than the minimal required concentration. These results suggest that the labelled TCZ dose leads to overtreatment and unnecessary costs in patients with stable RA. The TCZpsc seems supportive as an instrument for dose reduction strategies. Future prospective studies should assess its use in TCZ dose adjustment and confirm whether treatment efficacy is maintained.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1511

POS0610 EPIDEMIOLOGIC PROFILE AND CHANNELING TO TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT OVER THE LAST 5 YEARS: DATA FROM THE SPANISH REGISTER BIOBADASER 3.0

S. C. Rodriguez-García[1], C. Sánchez-Piedra[2], R. Castellanos-Moreira[3], D. Ruiz-Montesinos[4], M. Pombo[5], F. Sánchez-Alonso[2], J. J. Gómez-Reino[6]on behalf of the BIOBADASER Working group. [1]*Hospital de La Princesa, Rheumatology, Madrid, Spain*; [2]*Spanish Society of Rheumatology (SER), Research Unit, Madrid, Spain*; [3]*Hospital Clínic de Barcelona, Rheumatology, Barcelona, Spain*; [4]*Hospital Universitario Virgen Macarena, Rheumatology, Sevilla, Spain*; [5]*Hospital Clínico Universitario de Santiago, Rheumatology, Santiago de Compostela, Spain*; [6]*Fundación IDIS, Rheumatology, Madrid, Spain*

Background: Abatacept (ABA) is a selective T-cell co-stimulatory modulator. After its approval, changes in therapeutic recommendations, the arrival of new drugs (e.g., biosimilars or Janus kinase inhibitors) and growing focus on comprehensive patient care may have changed prescription patterns, channeling ABA use towards specific patient subtypes. To date, studies analyzing these aspects in clinical practice settings are scarce.
Objectives: We aimed to evaluate the epidemiological profile of ABA users and compare it to other DMARD groups included in the register.
Methods: We performed an observational study based on the nationwide Spanish register BIOBADASER, which includes patients with rheumatic diseases receiving biologic disease-modifying antirheumatic drugs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs) from 28 tertiary centers. For this analysis, all RA patients included from December 2015 to December 2020 were examined. Baseline features were analyzed descriptively grouping all b/tsDMARDs by mode of action. Clinical effectiveness was assessed through drug survival obtained by the Kaplan-Meier method. Patients were right-censored if data were not available if they were still on treatment at the time of data analysis. The safety profile was assessed by the adverse events (AE) and serious AE incidence rates (IR) expressed as events per 1000 patient-years.
Results: There were 628 ABA-treated patients, 471 (75%) using the subcutaneous presentation. Only 142 (23%) were on first-line while 381 (61%) were on third or later-line therapy. ABA users were older and more likely to present certain comorbidities compared to the other b/tsDMARD groups. The biggest relative differences were seen for interstitial lung disease (ILD), chronic obstructive pulmonary disease (COPD), diabetes and ischemic heart disease. (Table 1)

Table 1.

N	ABA	IL-6	CD20	JAKi	TNFi
	628	786	181	669	1787
Mean age, years (SD)	64.1 (12.0)	50.7 (12.7)	63.2 (12.3)	59.6 (12.3)	60.7 (13.1)
Female sex, n (%)	482 (77)	652 (83)	135 (75)	537 (80)	1418 (79)
Median disease duration	10.1	9.4	13.3	10.4	7.4
(p25-p75)	(5.1-16.5)	(4.6-15.9)	(8.3-20.6)	(5.0-17.2)	(3.2-13.7)
ACPA, n (%)	352 (72)	425 (71)	113 (79)	407 (70)	875 (70)
RF, n (%)	380 (77)	454 (75)	124 (86)	411 (70)	915 (72)
Current smokers, n (%)	98 (16)	137 (17)	338 (19)	90 (20)	259 (18)
ILD, n (%)	64 (13)	21 (3)	25 (2)	8 (2)	19 (2)
COPD, n (%)	38 (6)	23(3)	52 (3)	14 (3)	43 (3)
Chronic Kidney Disease, n (%)	18 (3)	13 (2)	19 (1)	13 (3)	18 (1)
Diabetes	73 (12)	66 (8)	13 (7)	46 (10)	100 (7)
Ischemic Heart Disease, n (%)	36 (6)	23 (3)	0	12 (3)	30 (2)
Hypertension, n (%)	197 (31)	198 (25)	416 (23)	131 (30)	338 (23)
Heart Failure, n (%)	19 (4)	12 (2)	10 (1)	6 (2)	5 (1)
Osteoporosis, n (%)	133 (21)	141 (18)	26 (14)	72 (16)	215 (15)

IL-6: Tocilizumab and Sarilumab; CD20: Rituximab and biosimilars; JAKi: Janus kinase inhibitors (Tofacitinib and Baricitinib); TNFi: TNF inhibitors and biosimilars; ACPA: anti-citrullinated peptide antibodies; RF: rheumatoid factor; ILD: interstitial lung disease; COPD: chronic obstructive pulmonary disease.

Overall, 63% of patients remained on ABA at 1 year, 48% at 2 and 31% at 5 years after drug initiation. The corresponding proportions were 79%, 65% and 52% for bionaïve and 59%, 43% and 30% for those in third or later-line therapy. From 394 total discontinuations, loss of efficacy in 225 (57%) and AE in 98 (25%) were the main reasons. This trend was consistent among all therapy lines.
The total IR of AE was 886.5 (837.3-938.5) and 156.4 (136.5-179.2) for SAE. Infections were the most frequent AE overall, IR 44.4 (34.4-57.3), and the highest IR was seen among bionaïve patients (69.6 (44.9-107.9)).
Conclusion: ABA-treated RA patients in Spain are older and have more comorbidities (vs other b/tsDMARDs), especially ILD, COPD, ischemic heart disease and diabetes and receive ABA as third or later-line therapy. Although these features are associated with worse response to treatment and a higher risk of infection, ABA presents a good drug survival and infectious AE are not the main cause of discontinuation.
Acknowledgements: On behalf of the BIOBADASER Working group

Disclosure of Interests: Sebastián C Rodriguez-García Speakers bureau: Sanofi, MSD, UCB-Pharma, Bristol-Myers-Squibb, Novartis, Janssen, Consultant of: Bristol-Myers-Squibb, Galápagos, Carlos Sánchez-Piedra: None declared, Raul Castellanos-Moreira Speakers bureau: Roche, Sanofi, MSD, UCB-Pharma, Bristol-Myers-Squibb, Novartis, Lilly, and Pfizer., Dolores Ruiz-Montesinos: None declared, Manuel Pombo: None declared, Fernando Sánchez-Alonso: None declared, Juan J. Gómez-Reino Consultant of: Pfizer, Grant/research support from: Abbvie, Lilly, MSD, Pfizer, Roche, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.1534

POS0611 THE EFFECT OF RITUXIMAB BIOSIMILAR THERAPY ON THE EXPRESSION OF INTERFERON-STIMULATED GENES ("INTERFERON SIGNATURE") IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Avdeeva[1], E. Tchetina[2], G. Markova[2], E. Nasonov[2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Early Arthritis Laboratory, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Early Arthritis Laboratory, Moscow, Russian Federation*

Background: Type I interferons (IFN-Is) are a group of molecules with pleiotropic effects on the immune system forming a crucial link between innate and adaptive immune responses. The type I interferon pathway has been implicated in the pathogenesis of a number of rheumatic diseases, including rheumatoid arthritis. IFN activity is usually quantified using expression of interferon-stimulated genes (ISGs) referred to as an IFN signature. Acellbia (BIOCAD) is the first Russian rituximab (RTX) biosimilar which was approved for medical use in rheumatoid arthritis (RA) patients in Russia and some CIS countries.
Objectives: To evaluate the changes in expression of ISGs in patients (pts) with RA during RTX biosimilar therapy
Methods: 20 RA pts (18 woman, Me;IQR age 61.5(54-66.5) years, disease duration 39.5(20-84) months, mean DAS 28 5.6(4.9-6.8)) received two intravenous RTX biosimilar infusions (600 mg №2) in combination with DMARDs and glucocorticoids. Laboratory biomarkers were assessed at baseline and 24 weeks after the first infusion of RTX. 5 genes (IFI44L, MX1, IFIT 1, RSAD2, EPSTI1) were selected for evaluation of the "interferon signature" (Type I IFN gene signature – IFNGS). IFI44L and IFIT1 expression was undetectable, therefore the remaining three genes (MSX1, EPSTI1, RSAD2) were included into further analysis. IFNGS was calculated as the average expression values of the three selected genes. The control group included 20 age and gender matching healthy donors.
Results: The baseline expression levels of MX1-11.48 (5.45-19.38), EPSTI1-12.83 (5.62-19.64), RSAD2-5.16 (2.73-10.4), and IFNGS-10.3 (5.18-17.12) in RA patients were significantly higher compared to healthy donors– 1,26 (0,73-1,6); 1,06 (0,81-1,48); 0,93 (0,72-1,19); 1,09 (0,92-1,42), (p<0.05, respectively). IFNGS was detected in 15 (75%) patients, and was not found in 5 (15%) patients. RTX induced reduction in disease activity, and the level of acute phase reactants (ESR, CRP) after 12 and 24 weeks of therapy, p<0.05 (fig.1). Increased RSAD 2 expression (p<0.05) and a trend to increasing IFNGS levels (p=0.06) were documented in the whole group, and also in patients with moderate treatment effects by week 24. Among patients with a good EULAR response to therapy, changes in expression were not significant (p> 0.05) (fig.1)

Parameters	Week	Patients with RA (n=20)	Moderate/no EULAR response by week 24 (n=15)	Good EULAR response by week 24 (n=5)
DAS 28	baseline	5.6 (4.9-6.8)	5.64 (4.68-6.99)	5.6 (5.2-6.57)
	week 12	4.28 (3.24-4.75)	4.4 (3.3-5.05)*	4.17 (2.6-4.4)*
	week 24	4.14 (3.11-4.66)	4.47 (3.8-4.8)*	2.5 (2.33-2.6)*
ESR, mm/h	baseline	45.0 (19.5-80.0)	50.0 (14.0-87.0)	40.0 (40.0-70.0)
	week 12	20.0 (16.0-38.0)*	22.0 (18.0-40.0)*	16.0 (12.0-18.0)*
	week 24	21.5 (12.0-31.0)*	28.0 (14.0-36.0)	12.0 (10.0-12.0)*
CRP mg/ml	baseline	12.3 (8.9-45.2)	14.4 (9.2-46.0)	10.2 (8.6-37.1)
	week 12	4.9 (2.2-11.3)*	5.7 (2.4-13.3)*	3.9 (1.6-5.1)*
	week 24	4.9 (2.3-21.9)*	10.4 (2.7-24.1)	2.6 (1.2-4.2)*
EPST1	baseline	12.83 (5.62-19.64)	13.1 (5.4-19.9)	12.6 (9.8-14.2)
	week 24	14.4 (3.38-43.9)	12.4 (2.9-49.5)	16.4 (10.3-19.9)
RSAD2	baseline	**5.16 (2.73-10.4)**	**5.12 (2.3-9.7)**	8.34 (3.7-18.2)
	week 24	**14.97 (5.04-42.1)***	**14.6 (1.3-43.9)***	15.4 (5.9-40.3)
MX1	baseline	11.48 (5.45-19.38)	10.6 (5.3-18.8)	13.5 (5.8-19.9)
	week 24	12.49 (3.4-69.1)	10.4 (3.2-80.4)	56.5 (9.7-57.7)
IFNGS	baseline	**10.3 (5.18-17.12)**	**11.7 (4.4-18.9)**	8.9 (8.3-15.3)
	week 24	**16.5 (5.05-55.8) p=0,06**	**14.8 (2.8-60.8), p=0,06**	27.4 (11.6-38.1)

*p<0.05 from baseline

Figure 1.

Conclusion: Expression of IFN-stimulated genes was increased in RA patients compared to healthy donors. Increased RSAD2 and IFNGS expression was documented in patients with moderate effect of RTX therapy, therefore, these findings have important clinical relevance as predictors of RA clinical course which necessitates personified approach to treatment.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1551

POS0612

EXPLORING EQUIVALENCE BETWEEN BIOSIMILAR SB4 AND REFERENCE ETANERCEPT BY ASSESSING EFFECTIVENESS IN RHEUMATOID ARTHRITIS PATIENTS TREATED IN ORDINARY CLINICAL PRACTICE

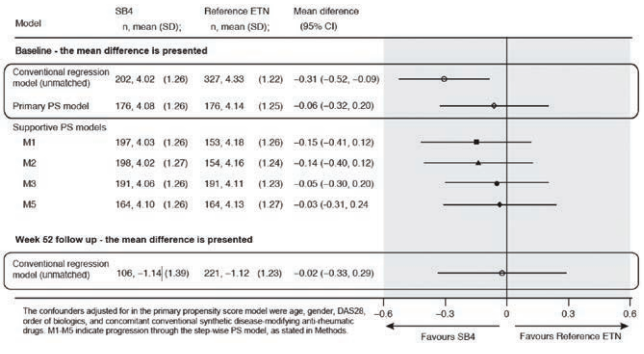
G. Haugeberg[1,2], G. Bakland[3], E. Rødevand[4], I. J. Widding Hansen[1], A. Diamantopoulos[5], A. H. Pripp[5]. *[1]Sørlandet Hospital, Division of Rheumatology, Department of Medicine, Kristiansand, Norway*; *[2]Norwegian University of Science and Technology, Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, NTNU, Trondheim, Norway*; *[3]University Hospital of Northern Norway, Department of Rheumatology, Tromsø, Norway*; *[4]St Olav's Hospital, Department of Rheumatology, Trondheim, Norway*; *[5]Martina Hansens Hospital, Oslo Centre of Biostatistics and Epidemiology, Oslo, Norway*

Background: Biosimilar drugs follow a tailored approval pathway that usually includes a Phase III comparative efficacy randomized controlled trial with a high internal but low external validity. Therefore, observational studies with high external validity are important to reassure patients and physicians that there are no clinically meaningful differences in effectiveness between a biosimilar and its reference drug. A EULAR Task Force systematic review and others have noted that recent comparative effectiveness studies often do not disclose applied analytical methods in sufficient detail, with many studies not adjusting for confounders nor accounting for attrition or missing data. [1,2]

Objectives: To apply the EULAR Points to Consider for Comparative Effectiveness Research (CER) in an analysis of reference etanercept (ETN) and SB4 biosimilar ETN in patients with rheumatoid arthritis (RA) treated in ordinary clinical practice in Norway.

Methods: ETN-naïve patients with RA starting ETN treatment between January 2010 and July 2018 at five centres in Norway were followed for at least 1 year; the 2 cohorts remained on either ETN or SB4 throughout. The primary outcome was DAS28 at Week 52. This CER has been designed to formally assess equivalence for DAS28, based on the accepted equivalence margin of 0.6.[3] Conventional regression and propensity score (PS) models have been applied for the primary outcome evaluation of DAS28 at Week 52. Based on clinical knowledge, the confounders adjusted for in the step-wise PS model were age, gender, DAS28, order of biologics, and concomitant conventional synthetic disease-modifying anti-rheumatic drugs. A standardized difference (d) of <0.1 indicates a good match.

Results: In the unmatched sample, there were 575 patients treated with reference ETN and 299 treated with SB4. Before PS matching, baseline mean (SD) DAS28 was different between the ETN and SB4 groups, 4.3 (1.2) vs 4.0 (1.3), (d) = 0.25. After PS matching, there were 176 RA patients in each group; baseline mean (SD) DAS28 was 4.1 (1.2) vs 4.1 (1.3), (d) = 0.05. At Week 52, the difference (mean [95% confidence interval (CI)]) between reference ETN and SB4 for primary outcome DAS28 at Week 52 was -0.02 (-0.33 to 0.29) in the unmatched analysis. Since the entire 95% CI is within the pre-defined equivalence margin of 0.6, equivalence at Week 52 has formally been shown. The analysis of the PS matched groups to Week 52 is ongoing and results will be presented in the poster.



Conclusion: Our results show the importance of adopting proper analytical techniques when comparing a biosimilar with its reference product. A conventional regression model may not fully account for differences in key clinical measures (in this instance, disease activity) between the two groups at baseline, and therefore the Week 52 results might be biased. The propensity score matched model ensures comparability of the groups at baseline and therefore the validity of the Week 52 results should be more robust.

REFERENCES:

[1] Cantini F and Benucci M. Mandatory, cost-driven switching from originator etanercept to its biosimilar SB4: possible fallout on non-medical switching. *Ann Rheum Dis* 2020; 79: e13.

[2] Lauper K KJ, De Wit M, Fautrel B, et al. A Systematic Review to Inform the EULRA Points to Consider When Analysing and Reporting Comparative Effectiveness Research With Observational Data in Rheumatology. *Annals of the Rheumatic Diseases* 2020; 79:

[3] Fransen J and van Riel PL. The Disease Activity Score and the EULAR response criteria. *Clin Exp Rheumatol* 2005; 23: S93-99.

Acknowledgements: The authors wish to acknowledge Janet Addison and Ulrich Freudensprung of Biogen for their intellectual contributions to this abstract and Bjørg Tilde Fevang for providing data from Haukeland University Hospital in Bergen. Editorial support for the preparation of this abstract was provided by Excel Scientific Solutions (Fairfield, CT, USA); funding was provided by Biogen International GmbH.

Disclosure of Interests: Glenn Haugeberg Grant/research support from: Biogen, Gunnstein Bakland: None declared, Erik Rødevand: None declared, Inger Johanne Widding Hansen: None declared, Andreas Diamantopoulos: None declared, Are Hugo Pripp: None declared

DOI: 10.1136/annrheumdis-2021-eular.1604

POS0613

TOCILIZUMAB DECREASES ANGIOGENESIS IN RHEUMATOID ARTHRITIS THROUGH ITS REGULATORY EFFECT ON EMMPRIN/CD147

D. Zisman[1,2], M. Safieh[1,3], E. Simanovich[3], J. Feld[1,2], A. Kinarty[3], L. Zisman[3], T. Gazitt[1], A. Haddad[1], M. Elias[1], I. Rosner[2,4], L. Kaly[4], M. Amit Rahat[2,3]. *[1]Carmel Medical Center, Rheumatology Unit, Haifa, Israel*; *[2]Technion-Israel Institute of Technology, Ruth and Bruce Rappaport Faculty of Medicine, Haifa, Israel*; *[3]Carmel Medical Center, Immunotherapy Laboratory, Haifa, Israel*; *[4]Bnei Zion Medical Center, Rheumatology Unit, Haifa, Israel*

Background: Angiogenesis is an important contributor to the development of Rheumatoid arthritis (RA). Tocilizumab (TCZ), an anti-IL-6 receptor antibody, is an immunosuppressant used in the treatment of RA patients, but its effects on angiogenesis and the molecular mechanisms regulating new blood vessel formation are not fully elucidated.

Objectives: To evaluate the concentrations of pro- and anti-angiogenic factors in serum samples of RA patients, before and after the initiation of TCZ treatment and to explore in an in vitro co-culture system the mechanisms of TCZ action.

Methods: We evaluated the concentrations of EMMPRIN, VEGF, MMP-9, IL-6, NGAL, endostatin and thrombospondin-1 (Tsp-1) using commercial ELISA kits from 40 RA patients, before and 4 months after the initiation of TCZ treatment. The levels of secreted EMMPRIN, VEGF MMP-9 and Tsp-1 were measured in an in vitro co-culture system of HT1080 fibroblasts and U937 monocytes with and without addition of anti-EMMPRIN blocking antibody. In the tube formation assay serum samples and supernatnats from the co-cultures were added to endothelial layer. Images were obtained after 6 hours of incubation and the number of closed lumens were counted in two separate fields. In the wound assay, supernatants from the co-cultures, with or without the addition of the anti-EMMPRIN antibody were added to the endothelial layer after scratching. The scratch site area was measured immediately and compared to the area after 24 hours of incubation to assess the distance of cell migration.

Results: Study population included 40 RA patients, 33 (82.5%) females, mean age of 57.5±11.1 years, disease duration of 7.7±5.6 years, and 53.9% positive for rheumatoid factor initiating treatment with TCZ. In this patient cohort, 25/40 (62.5%) patients were classified as "responders" according to EULAR criteria.

Following 4 mounts of treatment, statistically significant reductions in the levels of EMMPRIN/CD147 (p=0.035), without significant changes in serum levels of MMP-9, VEGF, MMP-3 and MMP-7 and of the anti-angiogenetic factors Tsp-1 and endostatin were found. A statistically significant decrease in the ratio between the pro-angiogenic factor EMMPRIN and the anti-angiogenic factor Tsp-1 that was calculated for each patient 4 months after initiating TCZ was found(p=0.031). The decrease in angiogenesis was manifested by the reduced number of closed lumen tube-like structures formed by EaHy926 endothelial cell line after incubation with serum samples 4 months after initiation of TCZ, relative to the number of closed lumens formed prior to TCZ initiation (p=0.007). The ratio between EMMPRIN and Tsp-1 was significantly reduced in the responding patients versus non-responders (p=0.033), while the levels of VEGF, MMP-9, Tsp-1, and EMMPRIN were unchanged.

In vitro, the accumulation of the pro-angiogenic factors EMMRPIN, VEGF and MMP-9 in the supernatants was increased in the co-culture, while the accumulation of the anti-angiogenic factor Tsp-1 was decreased. When EMMPRIN was neutralized with a blocking antibody, supernatants derived from these co-cultures exhibited reduced migration, proliferation, and tube-like structure formation in functional assays.

Conclusion: Our findings suggest an important role for EMMPRIN in mediating pro-angiogenic signals in RA patients, with EMMPRIN/Tsp-1 ratio serving as a marker of angiogenesis in RA. When administered to RA patients, TCZ in turn, exerts an anti-angiogenic effect through its regulation of EMMRPIN/CD147 levels.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1616

POS0614

PERFUSE: A FRENCH PROSPECTIVE/ RETROSPECTIVE NONINTERVENTIONAL COHORT STUDY OF INFLIXIMAB-NAÏVE AND TRANSITIONED PATIENTS RECEIVING INFLIXIMAB BIOSIMILAR SB2; 12-MONTH ANALYSIS

B. Fautrel[1], Y. Bouhnik[2], M. Dougados[3], U. Freudensprung[4], J. Addison[5]. *[1]Sorbonne University, Pitié-Salpêtrière Hospital, AP-HP, Paris, France*; *[2]Beaujon Hospital, Paris Diderot University, Department of Gastroenterology, AP-HP, Clichy, France*; *[3]CHU Paris Centre - Hôpital Cochin, Service de Rhumatologie B, Paris, France*; *[4]Biogen GmbH, Medical Data Science and Analytics, Biosimilars, Baar, Switzerland*; *[5]Biogen IDEC, Clinical Research, Biosimilars, Maidenhead, United Kingdom*

Background: SB2 is approved in the EU as an infliximab (IFX) biosimilar, having demonstrated bioequivalence and similar efficacy, safety and immunogenicity as the reference. PERFUSE is an ongoing non-interventional study of 1233 patients (496 with rheumatology diagnoses, 737 with gastroenterology diagnoses) receiving SB2 as routine therapy.

Objectives: The aim of the study is to provide data on long-term outcomes in patients initiating SB2 in the real-world setting.

Methods: Adult patients eligible for inclusion in the rheumatology study cohorts have a diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Axial Spondyloarthritis (axSpA) and had initiated SB2 in routine clinical practice after September 2017, either as their first IFX or transitioning from treatment with IFX reference or another IFX biosimilar. Outcome measures include SB2 dose, disease activity scores and persistence on SB2, over time and up to 24 months after initiation. This interim analysis is the first complete analysis of 12 month data on all rheumatology patients enrolled into the study at 9 specialist sites and followed up to the data extract date of 29th October 2020. The analysis provides an overview of baseline characteristics, disease scores, SB2 dose and persistence at 12 months post-initiation of SB2.

RESULTS:

Table 1. This 12-month interim analysis includes 496 patients (336 with axSpA, 98 with RA and 62 with PsA)

	axSpA cohort (N=336; IFX naïve 81, IFX-prior 255)		RA cohort (N=98; IFX naïve 22, IFX-prior 76)		PsA cohort (N=62; IFX naïve 14, IFX-prior 48)	
Baseline characteristics						
Age in years, mean (SD):						
IFX-naïve	43.1 (11.1)		53.1 (15.9)		48.5 (12.2)	
Transitioned from IFX	48.9 (12.4)		57.3 (13.1)		53.1 (13.0)	
Disease duration in years, mean (SD):						
IFX-naïve	7.2 (9.3)		11.3 (9.8)		4.2 (3.9)	
Transitioned from IFX	16.6 (11.6)		17.3 (8.8)		12.9 (11.3)	
Women, n (%):						
IFX-naïve	26 (32.1)		16 (72.7)		6 (42.9)	
Transitioned from IFX	79 (31.0)		60 (78.9)		15 (31.3)	
SB2 Dose: n, mean mg/kg (SD)						
IFX-naïve:						
Baseline	81	383.8 (85.5)	22	266.2 (145.9)	14	395.4 (108.9)
Month 12	47	436.8 (153.3)	13	285.5 (90.7)	6	508.0 (147.6)
Transitioned from IFX:						
Baseline	255	396.7 (109.6)	76	291.8 (103.4)	48	408.5 (91.3)
Month 12	195	392.1 (105.5)	60	287.8 (106.6)	41	421.4 (101.6)
Disease score, mean (SD)						
IFX-naïve:	**n**	**BASDAI**	**n**	**DAS28**	**n**	**DAS28**
Baseline	54	5.8 (2.1)	14	4.3 (1.6)	-*	-*
Month 12	30	3.5 (2.7)	9	3.2 (1.2)		
Transitioned from IFX:						
Baseline	206	3.0 (2.0)	62	2.6 (1.2)	20	2.2 (1.2)
Month 12	151	3.0 (2.1)	47	2.7 (1.2)	19	2.1 (0.9)
KM estimate of persistence on SB2 by Month 12; proportion, (95% CI)						
IFX-naïve	56.26 (44.43; 66.51)		59.09 (36.10; 76.21)		64.29 (34.33; 83.31)	
Transitioned from IFX	79.86 (74.37; 84.30)		80.26 (69.42; 87.60)		85.04 (71.11; 92.58)	

*Blank as disease score data for both baseline and Month 12 were provided by a single patient who was IFX-naïve and had PsA; IFX = infliximab; axSpA = Axial Spondyloarthritis; RA = Rheumatoid Arthritis; PsA = Psoriatic Arthritis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; DAS28 = Disease Activity Score 28; CI = confidence interval; SD = standard deviation; KM = Kaplan Meier.

Conclusion: This 12-month analysis indicates that patients with axSpA or RA can be successfully initiated on SB2 as the first infliximab therapy, and patients with axSpA, RA or PsA can be transitioned from originator or biosimilar IFX to SB2 without loss of disease control and with no dose penalty over 12 months post-transition. Over 56% of IFX- naïve patients and over 79% of patients transitioned from prior IFX remained on SB2 at 12 months post-initiation. With follow-up of patients ongoing to 24 months post-initiation of SB2, the study will continue to provide pertinent information about clinical outcomes of initiation on SB2 as first IFX or after transition from reference or IFX biosimilar to SB2.

Acknowledgements: Data management for the study was provided by Sanoïa E-health services, Digital CRO, Gémenos, France; funding was provided by Biogen International GmbH.

Disclosure of Interests: Bruno Fautrel Speakers bureau: AbbVie, Biogen, Boehringer-Ingelheim, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, SOBI, UCB., Consultant of: AbbVie, Biogen, Boehringer-Ingelheim, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, SOBI, UCB., Grant/research support from: AbbVie, MSD, Pfizer., Yoram Bouhnik Speakers bureau: AbbVie, Biogaran, Biogen, Boehringer Ingelheim, CTMA, Ferring, Gilead, Hospira, ICON, Inception IBD, Janssen, Lilly, Mayoly Spindler, Merck, Merck Sharp & Dohme, Norgine, Pfizer, Robarts Clinical Trials, Roche, Sanofi, Shire, Takeda, UCB, Vifor Pharma., Consultant of: AbbVie, Biogaran, Biogen, Boehringer Ingelheim, CTMA, Ferring, Gilead, Hospira, ICON, Inception IBD, Janssen, Lilly, Mayoly Spindler, Merck, Merck Sharp & Dohme, Norgine, Pfizer, Robarts Clinical Trials, Roche, Sanofi, Shire, Takeda, UCB, Vifor Pharma., Maxime Dougados Grant/research support from: Biogen, Ulrich Freudensprung Shareholder of: Biogen, Employee of: Biogen, Janet Addison Shareholder of: Biogen, Employee of: Biogen

DOI: 10.1136/annrheumdis-2021-eular.1642

POS0615

TOCILIZUMAB IS SAFE AND EFFECTIVE IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

C. Specker[1], M. Aringer[2], G. R. Burmester[3], M. Peters[4], M. W. Hofmann[5], H. Kellner[6], F. Moosig[7], H. P. Tony[8], G. Fliedner[9]. *[1]Clinic Essen-Mitte, Clinic of Rheumatology and Clinical Immunology, Essen, Germany*; *[2]Dresden University of Technology, University Medical Centre Carl Gustav Carus, Dresden, Germany*; *[3]Free University and Humboldt University Berlin, Department of Rheumatology and Clinical Immunology Charité - Universitätsmedizin Berlin, Berlin, Germany*; *[4]Roche Pharma AG, Grenzach-Wyhlen, Germany*; *[5]Chugai Pharma Germany GmbH, Rheumatology, Frankfurt am Main, Germany*; *[6]Rheumatology and Gastroenterology Specialty Practice, Rheumatology, Munich, Germany*; *[7]Rheumatology Centre Schleswig-Holstein Middle, Rheumatology, Neumünster, Germany*; *[8]Medical Clinic II, Department of Rheumatology and Clinical Immunology, University Clinic Würzburg, Würzburg, Germany*; *[9]Rheumatology Practice, Osnabrück, Germany*

Background: Average life spans of patients with rheumatoid arthritis (RA) are approaching those of the general population. This results in a large proportion of RA patients being elderly at some point and underlines effective RA treatments needed for this population. Pivotal clinical trials have demonstrated the efficacy of tocilizumab (TCZ) for the treatment of RA. However, real-world studies that explore the effectiveness of TCZ especially in the elderly are lacking. ICHIBAN was a large, observational study that followed patients with RA treated with TCZ under real-world conditions in Germany for up to 2 years.

Objectives: In this analysis of ICHIBAN, we examined the safety and effectiveness of long-term TCZ treatment according to patient baseline (BL) age (<50, 50–65, >65 years).

Methods: ICHIBAN (NCT01194401) was a prospective, non-interventional study that observed adult patients with active moderate to severe RA in German rheumatology clinics and practices. Patients were treated with TCZ according to the local label. The safety analyses set (SAF) included all patients who received at least one dose of TCZ. The effectiveness set (EFF) included all patients from the SAF who had no prior TCZ therapy. Patient-reported outcomes (PROs) were assessed using the visual analogue scale. Last observation carried forward was used to substitute for missing values.

Results: At baseline (BL), 3,164 patients were included in the SAF: 29.2% <50 years, 47.3% 50–65 years, and 23.5% >65 years old (1.2% ≥80 years). Patients >65 years old were not only the most likely to have comorbidities such as hypertension, anaemia, renal insufficiency, osteoporosis, diabetes, and coronary heart disease, but also had the highest BL disease activity according to Disease Activity Score-28 erythrocyte sedimentation rate (DAS28-ESR) and Clinical Disease Activity Index (CDAI) (Table 1).

Proportions of patients with adverse events (AEs) considered related to treatment were similar in patients <50 (22.3%), 50–65 (21.9%) and >65 years (22.2%). More patients >65 years (20.2%) and 50–65 years (14.4%) experienced serious AEs (SAEs) than patients <50 years (11.5%). Slightly more patients >65 years old experienced infectious SAEs (4.8%) than younger patients (<50 years, 3.2% and 50–65 years, 3.1%). Yet, similar proportions of patients across all age groups discontinued TCZ due to AE (7.0% <50 years; 9.6% 50–65 years; 7.8% >65 years).

2,902 patients were included in the EFF. Patients <50 years experienced DAS28-ESR remission at least once during the treatment period (65.4%) more often than patients aged 50–65 years (59.8%) or >65 years (59.5%). However, patients >65 years had numerically greater improvements in DAS28-ESR (Table 1). Patients <50 years had the best physical functioning at BL and the greatest reduction in

Health Assessment Questionnaire Disease Index (HAQ-DI) score (Figure 1A). All age groups had similar improvements in PROs such as fatigue, strength of pain, and sleep disturbances (Figure 1B).

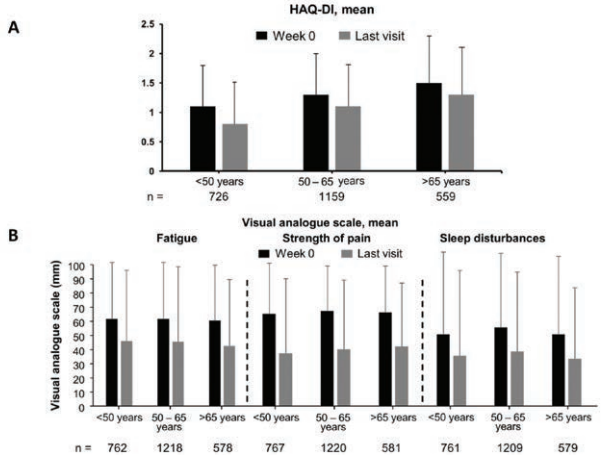
Table 1. Mean Disease Activity Score-28 erythrocyte sedimentation rate (DAS28-ESR) and Clinical Disease Activity Index (CDAI) over the course of ICHIBAN. BL, baseline; SD, standard deviation.

		<50 years	50–65 years	>65 years
DAS28-ESR, mean ± SD	n*	777	1237	617
	BL	4.9 ± 1.4	5.3 ± 1.3	5.4 ± 1.3
	Last visit	2.8 ± 1.7	3.1 ± 1.7	3.2 ± 1.7
	Change from BL	-2.0 ± 1.7	-2.2 ± 1.7	-2.2 ± 1.8
CDAI, mean ± SD	n*	768	1217	590
	BL	25.7 ± 12.8	28.4 ± 13.3	28.8 ± 12.8
	Last visit	13.3 ± 12.8	14.6 ± 13.2	14.5 ± 12.8
	Change from BL	-12.5 ± 13.6	-13.8 ± 14.0	-14.3 ± 13.8

*271 patients with missing data at BL**327 patients with missing data at BL

Conclusion: Although elderly patients experienced a higher rate of infections, the proportion of patients withdrawing due to AE was not higher than in the other age groups. Starting with higher baseline disease activity, patients >65 years had similar benefits to disease activity and PROs when compared with younger patients. Overall, these results indicate that long-term TCZ treatment of elderly patients is effective and has an acceptable safety profile.

Figure. Mean (SD) Health Assessment Questionnaire Disease Index (HAQ-DI) score and B) mean (SD) patient-reported outcomes over the course of ICHIBAN. SD, standard deviation.



Disclosure of Interests: Christof Specker Speakers bureau: AbbVie, Celgene, Chugai, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Chugai, Lilly, Novartis, Sobi, and UCB, Grant/research support from: Boehringer, Chugai, GSK, and Roche, Martin Aringer Speakers bureau: Roche and Chugai, Consultant of: Roche and Chugai, Grant/research support from: Roche, Gerd Rüdiger Burmester Consultant of: Lilly, Pfizer, Sanofi, and Roche, Grant/research support from: Roche, Marvin Peters Employee of: Roche Pharma AG, Michael W. Hofmann Employee of: Chugai Pharma Germany GmbH, Herbert Kellner Consultant of: Roche, Grant/research support from: Roche, Frank Moosig Grant/research support from: Roche, Hans-Peter Tony Speakers bureau: Roche, Abbvie, BMS, Chugai, Janssen, Novartis, Sanofi, and Lilly, Consultant of: Roche, Abbvie, BMS, Chugai, Janssen, Novartis, Sanofi, and Lilly, Grant/research support from: Roche, Gerhard Fliedner Grant/research support from: Roche, Chugai, Abbvie, and Lilly

DOI: 10.1136/annrheumdis-2021-eular.1711

POS0616

LONG-TERM EFFECTIVENESS AFTER MULTIPLE CYCLES WITH RITUXIMAB FOLLOWING AN ON-FLARE RETREATMENT STRATEGY IN PATIENTS WITH RHEUMATOID ARTHRITIS

D. Bertrand[1], N. Pype[1], T. Conings[1], D. De Cock[1], S. Pazmino[1], M. Doumen[1,2], J. Joly[2], B. Neerinckx[1,2], R. Westhovens[1,2], P. Verschueren[1,2]. [1]*KU Leuven, Skeletal Biology and Engineering Research Center, Leuven, Belgium*; [2]*UZ Leuven, Rheumatology, Leuven, Belgium*

Background: Rituximab is known as an efficacious drug for the treatment of Rheumatoid Arthritis (RA). The recommended administration schedule consist of 2 infusions of 1000 mg with a 2-week interval. In Belgium an on-flare retreatment strategy is followed, making evaluation of effectiveness over time challenging. Moreover the patient's view on this strategy is unclear.

Objectives: To explore long-term effectiveness and safety of rituximab in daily clinical practice in patients with RA.

Methods: Data of patients diagnosed with RA and treated with rituximab in a tertiary university hospital were retrospectively collected. For every cycle, clinical data were recorded at the time of the first and second infusion, the 16-week visit and the visit on which the treating rheumatologist decided to prescribe a new cycle. Data on demographics, previous RA treatment, disease activity, patient-reported outcomes, adverse events related to rituximab, dose and number of cycles were collected from 01/01/2006 until 01/12/2019 or until discontinuation of rituximab. The visit on which rituximab was prescribed for the first time was considered as the baseline visit. The data were analysed descriptively.

Results: Data of 66 patients with RA were collected. The median (IQR) age was 57.0 (47.0-65.0) years at baseline and 56% (37/66) were female. Most patients were seropositive (RF 91% and ACPA 92%), and had erosive (71%) or nodular disease (53%). The median (IQR) disease duration was 12.5 (4.0-18.3) years. In total, 94% of the patients had failed at least one other biological Disease-modifying Antirheumatic Drug (bDMARD) before starting rituximab. Overall, patients received a median (IQR) of 3 (2-7) cycles of rituximab. Seven of the 66 patients (11%) discontinued rituximab and changed to another bDMARD after a median (IQR) of 1 (1-6) cycles and 11% were treated with a lower dose than 2x1000mg. The median (IQR) interval between the first 2 cycles was 7.0 (6.0-10.0) months, after which this increased to up to one year (interval between cycle 2-3: 10.0 (7.0-13.0) months, cycle 3-4: 12.0 (7.3-15.5) months). The overall median (IQR) follow-up time was 45.5 (14.8-82.3) months. The efficacy of rituximab remained after repeated cycles: after every treatment with rituximab, a reduction in disease activity based on the disease activity score in 28 joints (DAS28) could be noticed (figure 1A). The evolution in patients' (PaGH) and physicians' global health (PhGH) assessment followed the same pattern as the DAS28-score (Figure 1B). High PaGH-scores could be noticed at every start of a new rituximab cycle. The proportion of patients with a PaGH-score above 20 ranged from 84% - 100%, 74% - 100% and 66% - 86% at the first infusion, second infusion and week 16 visits, respectively. Rituximab was considered to be well-tolerated. In total, 23 adverse events in 12 patients were recorded and none of them were serious.

Conclusion: Rituximab can be considered a highly efficacious drug for RA treatment in daily practice. There were no major side effects and there was an increasing treatment interval over time. However, a healthy survivor effect should be kept in mind when interpreting the results. It should be noted that with the on-flare retreatment strategy, every new rituximab cycle was preceded by a rise in PaGH-scores, which reflects a state of impaired wellbeing reported by patients. This should be further studied with qualitative methods and in a randomized trial setting comparing on-flare with fixed-interval retreatment to evaluate optimal effectiveness.

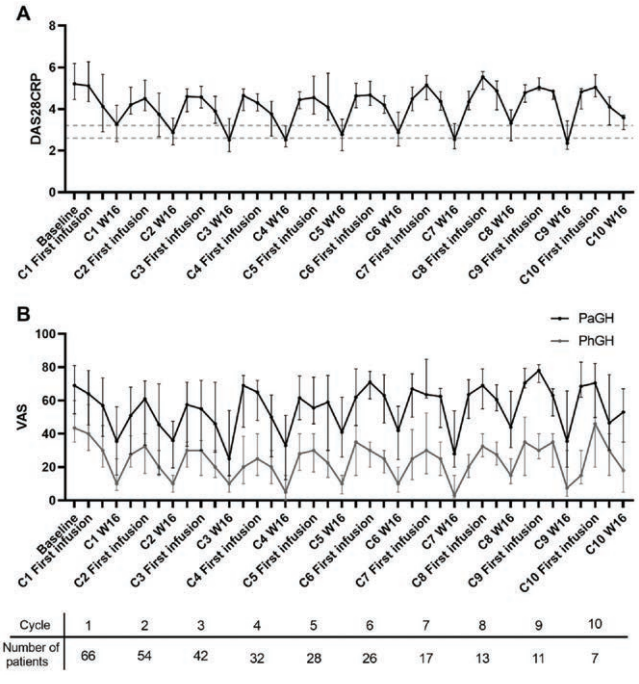


Figure 1. Evolution in median - interquartile range disease activity (DAS28CRP) (A) and patients' (PaGH) and physicians' global health (PhGH) (B) over the different rituximab cycles. The disease activity, PaGH and PhGH were measured at baseline, the time of the first and

second infusion, W16 and the visit on which a new rituximab cycle was prescribed. The dotted lines represent a DAS28CRP-score of 2.6 (remission cut-off) and 3.2 (low disease activity cut-off). C: cycle; W: week; VAS: visual analogue scale.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1783

POS0617 ANTI INFLIXIMAB ANTIBODIES DETECTED BY A DRUG TOLERANT ASSAY ARE FREQUENT BUT, IN MANY CASES, WITHOUT RELEVANT CLINICAL SIGNIFICANCE

A. Martínez-Feito[1,2], B. Hernández-Breijo[2], M. Novella-Navarro[2,3], V. Navarro-Compán[2,3], C. Diego[1], I. Monjo[2], L. Nuño[2], A. Villalva[3], D. Peiteado[3], D. Pascual-Salcedo[2], P. Nozal[1], A. Balsa[2,3], C. Plasencia[2,3]. [1]*La Paz University Hospital, Immunology, MADRID, Spain*; [2]*IdiPaz. La Paz University Hospital, Immuno-Rheumatology Research Group, MADRID, Spain*; [3]*La Paz University Hospital, Rheumatology, MADRID, Spain*

Background: Infliximab (Ifx) has proven effective in treating rheumatoid arthritis (RA) and spondyloarthropathies (SpA), although around 40% of cases fails, mainly due to immunogenicity. Formation of immunocomplexes between antibodies to Ifx (ATI) and Ifx can increase drug clearance, leading to treatment failure. Standard ELISA assays which are drug -sensitive are frequently used, being able to detect only free ATI. Interest in drug-tolerant assays to measure total ATI (free and complexed) is increasing.
Objectives: To compare the development of ATI using both drug-tolerant and drug-sensitive assays at early stages of Ifx therapy. To analyse the relationship of ATI detected by both assays with the drop-out of treatment.
Methods: This is a prospective observational study including 45 patients with RA and 61 with axial-SpA treated with standard doses of Ifx (3mg/kg and 5mg/kg, respectively) enrolled at Biological Therapy Unit of Hospital La Paz. Serum samples were obtained at 2, 6, 12 and 22 weeks (W) after Ifx initiation. The data about discontinuation for inefficacy was obtained from the database. ATI presence was evaluated by a drug-sensitive in-house two-site (bridging) ELISA (bELISA) and a drug-tolerant commercial ELISA assay (Immundiagnostik®,IDK). All comparisons were performed throughout non-parametrical test. In SpA group, due to the low number of ATI+ patients at W12 by bELISA the statistical analysis to compare both assays were not performed.
Results: ATI detection by both assays at early stages (≤22W) of treatment is shown in Table 1a. ATI were always detected earlier by IDK than bELISA and also in RA than in SpA patients probably reflecting the effect of lower Ifx doses. Three out of 106 (3%) vs 0 (0%) patients had ATI at W 2 and 62 (58%) vs 20 (18%) patients at W22, by IDK and bELISA, respectively.

Table 1.

	W2		W6		W12		W22	
	AR	SpA	AR	SpA	AR	SpA	AR	SpA
a) ATI+ patients (n, %) at early stages								
bELISA	0	0	3(7%)	0	10(22%)	1(2%)	13(29%)	7(12%)
IDK	1(2%)	2(3%)	7(16%)	2(3%)	16(36%)	16(26%)	28(62%)	34(56%)
b) Patients who discontinued (n, %) Ifx therapy considering ATI status at early stages								
bELISA+					9(90%)*	1(100%)*	12(92%)	4(57%)
bELISA-					23(66%)	22(37%)	20(63%)	19(35%)
IDK+					15(94%)*	7(44%)	24(86%)	13(38%)
IDK-					17(59%)	11(24%)	13(77%)	10(27%)

*p<0.05 comparing between ATI+ vs ATI- in each assay.

Once ATIs appeared, regardless both methods, they persisted throughout the follow-up, indicating that immunogenicity was not transient.
At W22, only 13/28 (46%) and 7/34 (21%) patients with ATI detected by IDK were also positive by bELISA in RA and SpA, respectively.
ATI levels by IDK were higher in ATI+ by bELISA than in ATI- patients at early stages: ATI levels by IDK at W12: 91[74-348] ng/ml ATI+ vs 21.7[15-59.5] ng/ml ATI- (p<0.01) and at W22: 132 [89-372] ng/ml ATI+ vs 23[13-66] ng/ml ATI- (p<0.001). However, only in 4% (2/45) patients with RA and in 13% (8/61) patients with SpA the detection by IDK was earlier than by bELISA at W12.
Free IFX in serum was not detected in bELISA ATI+ patients. In IDK ATI+ patients low circulating Ifx levels were present as compare to ATI- since W6 to the end of follow-up (p<0.01).
More ATI+ patients dropped out Ifx at W12 and W22 regardless de assay (Table 1.b), being statistically significant for both assays in patients with RA and only for bELISA in patients with SpA.
Conclusion: ATI measured by a drug-tolerant assay are always detected earlier than ATI detected by bELISA, indicating that immunogenicity, at least with Ifx, is usually an early event. High levels of ATI by IDK are associated with an earlier detection by bELISA in case of RA patients. ATI detected only by drug tolerant assays are associated with low levels of circulating Ifx but not with a complete drug neutralization and may do not have clinical relevance compared to ATI detected by bELISA. Many patients have low levels of ATI which can only be detected by drug tolerant assays after long-term of follow-up.
The reasons why ATI levels rise rapidly in some patients while in others remain low are currently unknown but may be relevant if the clinical effect of immunogenicity is to be minimized.
Acknowledgements: We are grateful to all the rheumatologists and nurses of the Daycare Department for Biologics and to the laboratory technicians of the Immunological Unit
Disclosure of Interests: ANA MARTÍNEZ-FEITO: None declared, Borja Hernández-Breijo: None declared, Marta Novella-Navarro: None declared, Victoria Navarro-Compán Grant/research support from: AbbVie, Janssen, Lilly, Novartis, Pfizer, and UCB, Cristina Diego: None declared, Irene Monjo: None declared, Laura Nuño: None declared, Alejandro Villalva: None declared, Diana Peiteado: None declared, DORA PASCUAL-SALCEDO: None declared, Pilar Nozal: None declared, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, Roche.Amgen, Sandoz, Lilly, UCB. Personal fees and non-financial support from BMS. Grants, personal fees and non- financial support from Nordic., Chamaida Plasencia Grant/research support from: AbbVie, Lilly, Novartis, Pfizer,Sanofi, Biogen and UCB.
DOI: 10.1136/annrheumdis-2021-eular.1791

POS0618 PERSISTENCE OF REMISSION AFTER TAPERING OF GOLIMUMAB IN INFLAMMATORY JOINT DISEASE (IJD)

A. Damiani[1], F. Bartoli[1], V. Gori[1], S. Bellando-Randone[1], G. Fiori[1], M. Matucci-Cerinic[1], S. Guiducci[1]. [1]*University of Florence, Rheumatology Unit, Firenze, Italy*

Background: In refractory IJD, remission may be obtained with antiTNFa drugs and other biological disease modifying anti-rheumatic drugs (bDMARDs). The last EULAR recommendations suggest tapering of bDMARD when remission persists[1]. However, best timing and modality of tapering are uncertain and specific knowledge on patients' characteristics associated to a better outcome is still lacking.
Objectives: To evaluate the persistency of remission after increasing the interval between injections of Golimumab in a group of patients affected by rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and juvenile idiopathic arthritis (JIA) and to identify any variables associated to disease flare after tapering.
Methods: Between 2011 and July 2020, 80 patients affected by RA, PsA, AS and JIA treated with Golimumab were enrolled. Their demographic and clinical data, including inflammation (ESR and cRP) and clinimetric indices (DAS28 or BASDAI), were collected at baseline and during the follow up visit (T1). In 22/80 patients that reached clinical remission at T1, the time between Golimumab injections has been prolonged (mean time between injection: 43.7 days); ESR and cRP, DAS28/BASDAI, and time since the start of the tapering (weeks) were evaluated in the next control visit (T2).
Results: 80 patients were enrolled (32 male, mean age 50.6 years +/- 13.91), 34 AS, 33 PsA, 9 RA and 4 JIA. At baseline they have an active disease with a DAS 28 of 4.74+/-0.85 and a BASDAI of 5.23+/- 1.31. At T1, 60/80 patients were in remission (75%), with a mean DAS 28 of 1.84+/- 0.6 and an average BASDAI of 1.32+/-0.6, and 22/60 patients started drug tapering. At T2, 20/22 patients (91%) were in remission, (DAS 28 1.9+/-0.49, BASDAI of 0.8+/- 0, 67). A significantly higher BASDAI was observed at T1, even though in the range of absence of disease activity (2.2, +/- 0.28 *vs* 0.58, +/- 0.47; p <0.001) in patients who, after extending the therapeutic interval (T1) were no longer in remission at T2. Patients with a flare of disease activity (2/22) were taken back to the 28 days window of Golimumab with a prompt recovery of disease remission. Out of the 38 patients maintained at the standard dose, 4 experienced a disease flare with necessity to switch or swope bDMARD, with a retention rate in this group of 90%. Difference of retention rate between patients on standard *vs* reduced dose was not statistically significative.
Conclusion: Tapering of Golimumab was successful in 91% of the cases without flare. Moreover, the prolongation of the increase of the treatment window provided the same result as that obtained in patients that continued in the standard time window. This evidence suggests that the extension of the gap between Golimumab administrations may be feasible and safely applied in practice.
REFERENCES:
[1] Smolen JS, Landewé RBM, Bijlsma JWJ, et al EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update Annals of the Rheumatic Diseases 2020;79:685-699.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1959

POS0619 MODELLING OF DISEASE ACTIVITY IN PATIENTS WITH INFLAMMATORY ARTHROPATHIES TREATED WITH ETANERCEPT ORIGINATOR OR BIOSIMILAR AS FIRST-LINE BIOLOGIC IN AN AUSTRALIAN REAL-WORLD DATASET

C. Deakin[1], G. Littlejohn[1,2], H. Griffiths[1,3], T. Smith[1], C. Osullivan[1], P. Bird[1,4]. *[1]OPAL Rheumatology, Ltd., Sydney, Australia*; *[2]Department of Medicine, Monash University, Clayton, Australia*; *[3]Barwon Rheumatology, Services, Geelong, Australia*; *[4]Department of Medicine, UNSW Sydney, Sydney, Australia*

Background: The availability of biosimilars as non-proprietary versions of established biologic disease-modifying anti-rheumatic drugs (bDMARDs) is enabling greater access for patients with rheumatic diseases to effective medications at a lower cost. Since April 2017 both the originator and a biosimilar for etanercept (trade names Enbrel and Brenzys, respectively) have been available for use in Australia.

Objectives:

[1] To model effectiveness of etanercept originator or biosimilar in reducing Disease Activity Score 28-joint count C reactive protein (DAS28CRP) in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis (AS) treated with either drug as first-line bDMARD

[2] To describe persistence on etanercept originator or biosimilar as first-line bDMARD in patients with RA, PsA or AS

Methods: Clinical data were obtained from the Optimising Patient outcomes in Australian rheumatoLogy (OPAL) dataset, derived from electronic medical records. Eligible patients with RA, PsA or AS who initiated etanercept originator (n=856) or biosimilar (n=477) as first-line bDMARD between 1 April 2017 and 31 December 2020 were identified. Propensity score matching was performed to select patients on originator (n=230) or biosimilar (n=136) with similar characteristics in terms of diagnosis, disease duration, joint count, age, sex and concomitant medications. Data on clinical outcomes were recorded at 3 months after baseline, and then at 6-monthly intervals. Outcomes data that were missing at a recorded visit were imputed.

Effectiveness of the originator, relative to the biosimilar, for reducing DAS28CRP over time was modelled in the matched population using linear mixed models with both random intercepts and slopes to allow for individual heterogeneity, and weighting of individuals by inverse probability of treatment weights to ensure comparability between treatment groups. Time was modelled as a combination of linear, quadratic and cubic continuous variables.

Persistence on the originator or biosimilar was analysed using survival analysis (log-rank test).

Results: Reduction in DAS28CRP was associated with both time and etanercept originator treatment (Table 1). The conditional R-squared for the model was 0.31. The average predicted DAS28CRP at baseline, 3 months, 6 months, 9 months and 12 months were 4.0 and 4.4, 3.1 and 3.4, 2.6 and 2.8, 2.3 and 2.6, and 2.2 and 2.4 for the originator and biosimilar, respectively, indicating a clinically meaningful effect of time for patients on either drug and an additional modest improvement for patients on the originator.

Median time to 50% of patients stopping treatment was 25.5 months for the originator and 24.1 months for the biosimilar (p=0.53). An adverse event was the reason for discontinuing treatment in 33 patients (14.5%) on the originator and 18 patients (12.9%) on the biosimilar.

Conclusion: Analysis using a large national real-world dataset showed treatment with either the etanercept originator or the biosimilar was associated with a reduction in DAS28CRP over time, with the originator being associated with a further modest reduction in DAS28CRP that was not clinically significant. Persistence on treatment was not different between the two drugs.

Table 1. Model summary for prediction of DAS28CRP using time and etanercept originator (relative to biosimilar)

Fixed Effect	Estimate	95% Confidence Interval	p-value
Time (linear)	0.90	0.89, 0.91	1.5e-63
Time (quadratic)	1.01	1.00, 1.01	1.3e-33
Time (cubic)	1.00	1.00, 1.00	7.1e-23
Originator	0.91	0.86, 0.96	0.0013

Acknowledgements: The authors acknowledge the members of OPAL Rheumatology Ltd and their patients for providing clinical data for this study, and Software4Specialists Pty Ltd for providing the Audit4 platform.

Supported in part by a research grant from Investigator-Initiated Studies Program of Merck & Co Inc, Kenilworth, NJ, USA. The opinions expressed in this paper are those of the authors and do not necessarily represent those of Merck & Co Inc, Kenilworth, NJ, USA.

Disclosure of Interests: Claire Deakin: None declared, Geoff Littlejohn Consultant of: Over the last 5 years Geoffrey Littlejohn has received educational grants and consulting fees from AbbVie, Bristol Myers Squibb, Eli Lilly, Gilead, Novartis, Pfizer, Janssen, Sandoz, Sanofi and Seqirus., Hedley Griffiths Consultant of: AbbVie, Gilead, Novartis and Lilly., Tegan Smith: None declared, Catherine OSullivan: None declared, Paul Bird Speakers bureau: Eli Lilly, abbvie, pfizer, BMS, UCB, Gilead, Novartis

DOI: 10.1136/annrheumdis-2021-eular.2265

POS0620 TREATMENT PATHWAYS OF RHEUMATOID ARTHRITIS PATIENTS LEADING TO BIOLOGIC THERAPY VISUALIZED IN A SANKEY DIAGRAM

T. Coppes[1], N. Jessurun[1], J. Jansen[1], K. Velthuis[1], P. ten Kloster[2,3], H. Vonkeman[3,4]. *[1]Netherlands Pharmacovigilance Centre Lareb, Monitoring, 's-Hertogenbosch, Netherlands*; *[2]Transparency in Healthcare B.V., Hengelo, Netherlands*; *[3]University of Twente, Psychology, Health & Technology, Enschede, Netherlands*; *[4]Medisch Spectrum Twente, Rheumatology and Clinical Immunology, Enschede, Netherlands*

Background: Treatment of rheumatoid arthritis (RA) has changed in the past 20 years due to the arrival of biologic disease-modifying antirheumatic drugs (bDMARDs) and the application of treat to target strategies. Many different combinations of conventional synthetic (cs)DMARDS and bDMARDS are being applied in daily practice. It is difficult to visualize and understand all the different treatment pathways that are sequentially being used over longer periods of time in a real-world setting. We therefore investigated whether a Sankey diagram is a suitable tool to study and visualize which treatment pathways exist and to what extent a RA treatment protocol is being followed.

Objectives: To illustrate the treatment pathways over longer periods of time in a cohort of early RA patients and to assess adherence to the treatment protocol using Sankey diagrams.

Methods: This single-centre retrospective, observational cohort study used data from the DREAM-RA registry. Patients were treated according to a treat to target strategy with a step-up DMARD treatment protocol when remission was not achieved, initial steps were starting with MTX 15 mg/wk, week 8 MTX 25 mg/wk, week 12 MTX+SSZ 2dd1000mg, week 20 MTX+SSZ 3dd1000mg, week 24 MTX+adalimumab 40mg/2wk, week 36 MTX+adalimumab 40mg/wk. Although the protocol met full consensus, adherence to the protocol in individual patients was at the discretion of the treating rheumatologist. In this study, patients were included if they received a continuous treatment with a conventional synthetic or biologic DMARD between 1 January 2002 and 30 April 2020. During treatment, corticosteroids per protocol were allowed but not considered as an individual treatment. Evaluated outcomes included: the consecutive treatments that patients followed including start- and stop-date of treatments, the proportion of patients that received bDMARDs, the number of switches until first bDMARD, and time to first bDMARD. Furthermore, the lower limit of adherence to the protocol was estimated by considering all patients (% of total) treated according to the protocol. This information was determined by verifying whether the patient was being treated according to the protocol after each switch.

Results: A total of 372 patients were included in this study (Table 1). The mean overall follow-up time of the cohort was 8.83 (± 3.59) years. The follow-up time for the first 4 treatments, depicted in the Sankey diagram was 6.28 (± 3.31) years. At least 45 (12%) patients started with a bDMARD before all previous protocol steps were followed. At the start of treatment, 81% of the patients were treated according to the protocol, this was reduced to 28% after one switch. The lower limit of adherence to the predefined protocol after 3 switches were roughly 5% of all patients.

Table 1. Patient characteristics of all included patients

	All patients (n=372)
Gender, female, n (%)	246 (66.1)
Age, year, mean ± SD	67.9 ± 13.61
Overall follow-up, years ± SD	8.83 ± 3.59
Follow-up first 4 treatments, years ± SD	6.28 ± 3.31
Baseline DAS-28 score, mean ± SD	3.60 ± 1.41
Rheumatoid factor positive, n (%)	336 (90.3)
Patients who eventually received a bDMARD, n (%)	108 (29.0)
Number of switches until first bDMARD, mean ± SD	2.7 ± 1.41
Time to first bDMARD, years ± SD	3.66 ± 3.00

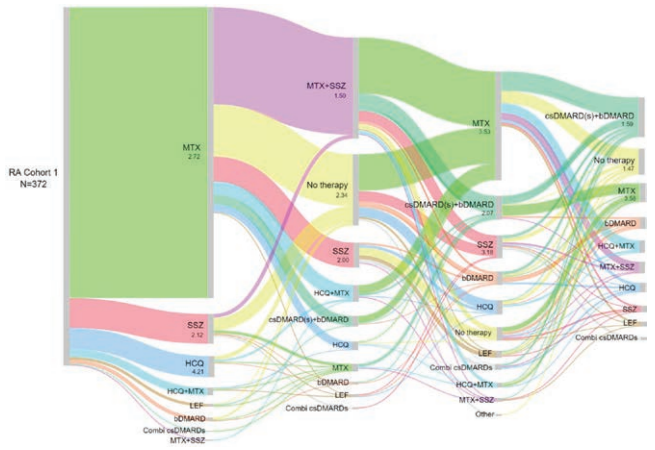


Figure 1. Sankey diagram of the treatment pathway of the first 3 switches of RA patients. The average duration of treatment of a flow is displayed in years if the flow included more than 20 patients. (MTX= methotrexate; SSZ= sulfasalazine; HCQ = hydroxychloroquine; LEF= leflunomide; bDMARD= monotherapy bDMARD; Combi csDMARDs= combination therapy of csDMARDS; csDMARD(s)+bDMARD= combination therapy of one or two csDMARD(s) + a bDMARD; No therapy= no treatment received >3 months; Other = medication that is not a (cs)(b)DMARD)

Conclusion: Sankey diagramming can be used to illustrate complex real-world treatment data of a treat to target cohort of RA patients. Treatment protocol adherence can be assessed with the help of a Sankey diagram. After 3 switches, the lower limit of adherence to the protocol was roughly 5%.

Disclosure of Interests: Tristan Coppes: None declared, Naomi Jessurun: None declared, Jurriaan Jansen: None declared, Kimberly Velthuis: None declared, Peter ten Klooster: None declared, Harald Vonkeman Consultant of: BMS, Celgene, Celltrion, Galapagos, Gilead, Janssen-Cilag, Lilly, Novartis, Pfizer, Sanofi-Genzyme, Grant/research support from: Abbvie
DOI: 10.1136/annrheumdis-2021-eular.2299

POS0621 DISEASE-SPECIFIC ADVERSE DRUG REACTION PROFILES OF ADALIMUMAB AND ETANERCEPT AS REPORTED BY IMMUNE-MEDIATED INFLAMMATORY DISEASE PATIENTS

L. Roest[1], L. Kosse[1], J. van Lint[1], J. Scholl[1], M. van Doorn[2], S. Tas[3], M. Nurmohamed[4], H. Vonkeman[5,6], R. Hebing[7], P. Spuls[8], F. Hoentjen[9], E. van Puijenbroek[10,11], B. van den Bemt[10,12], N. Jessurun[1]. *[1]Netherlands Pharmacovigilance Centre Lareb, Department of Monitoring,'s-Hertogenbosch, Netherlands*; *[2]Erasmus MC, Department of Dermatology, Rotterdam, Netherlands*; *[3]Amsterdam UMC, Location Academic Medical Center, University of Amsterdam, Amsterdam Infection & Immunity Institute and Amsterdam Rheumatology & Immunology Center (ARC), Department of Rheumatology & Clinical Immunology, Amsterdam, Netherlands*; *[4]Reade and Amsterdam Rheumatology & Immunology Center (ARC), Department of Rheumatology, Amsterdam, Netherlands*; *[5]Health & Technology, University of Twente, Department of Psychology, Enschede, Netherlands*; *[6]Medisch Spectrum Twente, Department of Rheumatology, Enschede, Netherlands*; *[7]Amsterdam Rheumatology and Immunology Center Location Reade, Department of Pharmacy, Amsterdam, Netherlands*; *[8]Amsterdam UMC, Amsterdam Public Health, Immunity and Infections, University of Amsterdam, Department of Dermatology, Amsterdam, Netherlands*; *[9]Radboud UMC, Department of Gastroenterology, Nijmegen, Netherlands*; *[10]Sint Maartenskliniek, Department of Pharmacy, Nijmegen, Netherlands*; *[11]Netherlands Pharmacovigilance Centre Lareb, Department of Signal Detection,'s-Hertogenbosch, Netherlands*; *[12]Radboud UMC, Department of Pharmacy, Radboud UMC, Netherlands*

Background: Information on adverse drug reactions (ADRs) is generally clustered for all indications of a drug in the patient information leaflet. However, previous research has shown that participants of the Dutch Biologic Monitor (DBM) that use a biologic for their immune-mediated inflammatory disease (IMID) prefer to receive ADR information tailored to their own biologic an IMID (1). Currently, it is unclear whether the ADR profile of a specific biologic may differ between patients with different IMIDs, which would be vital information for health care providers (HCPs) in their patient guidance.

Objectives: To determine whether the profiles of ADRs attributed to adalimumab (ADA) and etanercept (ETN) reported by patients in the DBM differ between IMIDs.

Methods: The DBM is a prospective cohort event monitoring system for patient-reported ADRs attributed to biologics (2). Study data was extracted from the DBM for the period Jan 2017 – Oct 2020. ADRs were coded according to their corresponding Preferred Term (PT) following MedDRA terminology. Unique PTs were selected per participant and grouped under System Organ Classes (SOCs) (Figure 1) for ADA and ETN. SOCs contributing for <1% to the total number of reported ADRs were grouped as 'other'. Participants with more than one of the included IMIDs, i.e. Psoriatic Arthritis (PsA), Inflammatory Bowel Disease (IBD, i.e. Crohn's disease and ulcerative colitis), rheumatoid arthritis (RA), and axial spondyloarthritis (axSpA) including Ankylosing Spondylitis (AS), were excluded. Differences in ADR profiles between IMIDs were tested using the Fisher-Freeman-Halton's Exact Test with Monte Carlo simulation. SOCs of interest were separately tested with the Fisher-Freeman-Halton's Exact Test (no simulation) and subsequently corrected for multiple comparisons using the Benjamini-Hochberg (BH) correction.

Results: A total of 572 ADR reports from 218 participants using ADA and 450 ADR reports from 185 participants using ETN were analyzed (Table 1).

Overall, a statistically significant difference in patient-reported ADR profile between the assessed indications was found for ADA (p=0.011), but not for ETN (p=0.057). The following separate tests for selected SOCs of interest showed a significant difference in the frequencies of 'respiratory, thoracic and mediastinal disorders' and 'musculoskeletal and connective tissue disorders' between the different IMIDs for ADA after BH correction, but none for ETN.

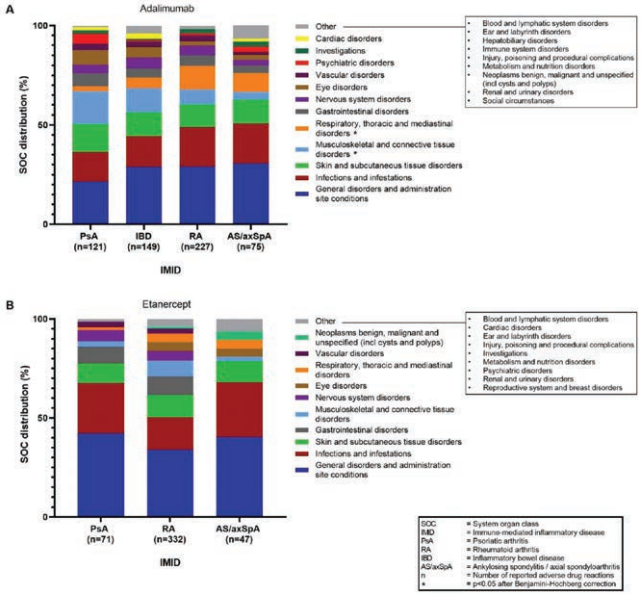


Figure 1. The disease-specific patient-reported ADR profile of ADA (A) and ETN (B) in IMID patients resulting from the Dutch Biologic Monitor

Table 1. Respondent characteristics.

Characteristics	ADA		ETN	
	n=218	%	*n*=185	%
Female gender, *n* (%)	140	64.2	129	69.7
Median age (IQR), years	56.0 (46.0-64.0)		58.0 (48.0-66.0)	
ADR reports	572	100.0	450	100.0
Indication for biologic therapy				
Rheumatoid arthritis	90	41.3	127	68.6
Psoriatic arthritis	46	21.1	35	18.9
Ankylosing spondylitis/axSpA	32	14.7	23	12.4
IBD[a]	50	22.9	0	0.0
Combination therapy[b]				
Methotrexate	63	30.3	70	40.2
Corticosteroids	25	12.0	21	12.1
Thiopurines	18	8.7	1	0.6
No combination therapy	87	41.8	59	33.9
Other	31	14.9	48	28.2

IQR: interquartile range; IBD: inflammatory bowel disease; axSpA: axial spondyloarthritis.[a]IBD includes Crohn's disease and ulcerative colitis.[b]The overall percentage exceeds 100% since patients can have a combination therapy consisting of one or more drugs.

Conclusion: Although only ADA shows a statistically significant difference in ADR profile between different IMIDs, more research with a larger sample size might show similar results for ETN. Furthermore, explanations for the differences found, such as disease-drug interactions, must be examined. This would help HCPs in providing disease-specific information and patient guidance.

REFERENCES:
[1] *Kosse LJ et al.; Expert Opin Drug Saf. 2020;19(8):1045-1054.*
[2] *Kosse LJ et al.; Rheumatol. 2020;59(6):1253-1261*
Disclosure of Interests: Lieke Roest: None declared, Leanne Kosse: None declared, Jette van Lint: None declared, Joep Scholl: None declared, Martijn van Doorn Grant/research support from: Leopharma, Novartis, Abbvie, BMS, Celgene, Lilly. Pfizer, Sanofi-Genzyme, Janssen Cilag, all outside the submitted work, Sander Tas Grant/research support from: AbbVie, Arthrogen, AstraZeneca, BMS, Celgene, Galapagos, GSK, MSD, Pfizer, Roche, Sanofi-Genzyme, all outside the submitted work, Michael Nurmohamed Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Roche, Sanofi, all outside the submitted work, Consultant of: AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, Sanofi, all outside the submitted work, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Mundipharma, Novartis, Pfizer, Roche, Sanofi, all outside the submitted work, Harald Vonkeman Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Celltrion, Galapagos, Gilead, GSK, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi-Genzyme, all outside the submitted work, Renske Hebing: None declared, Phyllis Spuls Grant/research support from: departmental independent research grant for TREAT NL registry from different companies for the TREAT NL registry, is involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of e.g. psoriasis and atopic dermatitis, for which financial compensation is paid to the department/hospital and, is Chief Investigator (CI) of the systemic and phototherapy atopic eczema registry (TREAT NL) for adults and children and one of the main investigators of the SECURE-AD registry, all outside the submitted work, Frank Hoentjen Speakers bureau: Abbvie, Janssen-Cilag, MSD, Takeda, Celltrion, Teva, Sandoz, Dr Falk, all outside the submitted work, Consultant of: Celgene, Janssen-Cilag, all outside the submitted work, Grant/research support from: Dr Falk, Janssen-Cilag, Abbvie, Takeda, all outside the submitted work, Eugène van Puijenbroek: None declared, Bart van den Bemt: None declared, Naomi Jessurun: None declared
DOI: 10.1136/annrheumdis-2021-eular.2300

POS0622 THE BLOOD T-CELL SUBSETS IN RHEUMATOID ARTHRITIS PATIENTS ON LONG-TERM IL-6 RECEPTOR BLOCKER THERAPY

E. Gerasimova[1], T. Popkova[1], A. Aleksankin[2], D. Tabakov[3]. *[1]V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases Laboratory, Moscow, Russian Federation*; *[2]Research Institute of Human Morphology, Reproductive Pathology Laboratory, Moscow, Russian Federation*; *[3]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*

Background: Pleiotropic effects of IL-6 receptor antagonist tocilizumab (TCZ) in rheumatoid arthritis (RA) involve circulating T-cells. Preliminary reports have suggested that TCZ therapy can modulate T cell function and humoral immune responses in RA [1,2]. According to other studies, TCZ had no influence on T-lymphocyte subdifferentiation [3].
Objectives: To assess the effect of 12 months (m) TCZ therapy on T-cell phenotype, and to analyze the association between T-cell subsets and RA activity.
Methods: 36 active RA pts (29F/7M); median age 55[46; 64] years; disease duration 120[72; 1928]m; DAS28 score 6,3[5,7;6,7]; RF+100%, ACCP+ 86% were treated with TCZ (8 mg/kg every 4 weeks) in an open-label study. Immunophenotyping was performed at baseline, 6m and 12m. T-cell subpopulations and key laboratory parameters (CRP, RF, ACCP, MCV, MMP-3) were assessed.
Results: At baseline, the absolute counts of T cell subpopulations in RA pts - (CD3+), Th (CD3+CD4+), Tc (CD3+CD8+), NK cells (CD3-CD56+) - were comparable with counts in healthy donors (table1). At baseline, the absolute NK cells (CD3-CD56+) count correlated with MCV (r=0,35, p<0,05) and with MMP-3 (r=0,57, p<0,05) in RA pts. After 6m of TCZ therapy, 34% of pts were classified as good responders, 66% - as moderate responders; after 12m of TCZ therapy 68% of pts - as good responders, 32% - as moderate responders, according to the response criteria of the EULAR. Tc (CD3+CD8+) absolute count reductions were documented after 6m of TCZ therapy, absolute of T cells (CD3+) count and Th (CD3+CD4+) count - after 12m of TCZ therapy (table1). A positive correlation between Tc (CD3+CD8+) absolute counts and RF (r=0,50, p<0,05) was found after 6m of TCZ therapy. A negative correlation of Δ CRP was established with Δ T cells (CD3+) (r=-0,45], Δ Th (CD3+CD4+) (r=-0.47), and Δ Tc (CD3+CD8+) (r=-0,59, p<0,05 in all cases) after 12m of TCZ. The median absolute counts of T cells (CD3+), Th (CD3+CD4+) was lower than on healthy donors after 12m of TCZ therapy. NK cells (CD3-CD56+) counts and Th/Tc index did not change after 12 m of TCZ therapy vs healthy donors and baseline values.
Conclusion: Immunophenotyping in pts with active RA showed no difference in the absolute counts of T-cell subpopulations (T cells (CD3+), Th (CD3+CD4+), Tc (CD3+CD8+), NK cells (CD3-CD56+)) compared to healthy donors. T cells (CD3+), Th (CD3+CD4+) and Tc (CD3+CD8+) T cell counts dropped after 6 or 12m of TCZ therapy. Significant correlation between the T-cell subpopulations counts and values of RA laboratory indicators (CRP, MCV, RF, MMP-3) suggest potential T-lymphocytes involvement in RA pathogenesis.
REFERENCES:
[1] Kasama T, Isozaki T, Takahashi R, Miwa Y.Clinical effects of tocilizumab on cytokines and immunological factors in patients with rheumatoid arthritis. Int Immunopharmacol. 2016 Jun;35:301-306. doi: 10.1016/j.intimp.2016.03.016.
[2] Schinnerling K, Aguillón JC, Catalán D, Soto L. The role of interleukin-6 signalling and its therapeutic blockage in skewing the T cell balance in rheumatoid arthritis. Clin Exp Immunol. 2017 Jul;189(1):12-20. doi: 10.1111/cei.12966.
[3] Schwaneck EC, Renner R, Junker L. et al. T cells, natural killer cells, and gammadeltaT cells in a large patient cohort with rheumatoid arthritis: influence of age and anti-rheumatic therapy. Scand J Rheumatol. 2020 Jan;49(1):8-12. doi: 10.1080/03009742.2019.1634755.

Table 1. Absolute counts of T-cell subpopulations at baseline, after 6 and 12 m of TCZ therapy

	Donors	Baseline	6m	12m
T cell (CD3+)	1,3 (1,2-1,8)^	1,2 (0,9; 1,7)*	1,1 (0,7; 1,4)	1,0 (0,7; 1,5)* ^
Th (CD3+CD4+)	0,9 (0,7-1,2) ^	0,8 (0,6; 1,0)*	0,7 (0,5; 1,0)	0,6 (0,4; 1,1) * ^
Tc (CD3+CD8+)	0,4 (0,3-0,5)	0,4 (0,2; 0,5)**	0,3 (0,2; 0,04)**	0,3 (0,3; 0,5)
Th/Tc	2,5 (1,9-3,1)	2,3 (1,4; 3,0)	2,3 (1,5; 3,6)	2,3 (1,4; 4,0)
NK (CD3-CD56+)	0,2 (0,2-0,5)	0,2 (0,1; 0,2)	0,2 (0,1; 0,3)	0,2 (0,1; 0,3)

Note: * - p<0,05 between pts at baseline and after 12 m of TCZ therapy; **- p= 0,02 between pts at baseline and after 6 m of TCZ therapy; ^ - p<0,05 between donors and pts after 12 m of TCZ therapy.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2310

POS0623 CYTOKINE PRODUCTION BY BLOOD LYMPHOCYTES DEFINES A PROFILE ASSOCIATED WITH NON-REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TNF INHIBITORS

B. Hernández-Breijo[1], E. Rodríguez-Martín[2], C. García-Hoz[2], V. Navarro-Compán[1,3], C. Sobrino[4], A. Martínez-Feito[1,5], I. Nieto-Gañán[2], J. Bachiller-Corral[4], P. Lapuente-Suanzes[2], G. Bonilla[3], C. Pijoán-Moratalla[4], M. Vázquez[4], A. Balsa[1,3], D. Pascual-Salcedo[1], L. M. Villar[2], C. Plasencia[1,3]. *[1]IdiPaz, La Paz University Hospital, Immuno-Rheumatology Research Group, Madrid, Spain*; *[2]Ramón y Cajal University Hospital and IRYCIS, Immunology, Madrid, Spain*; *[3]La Paz University Hospital, Rheumatology, Madrid, Spain*; *[4]Ramón y Cajal University Hospital and IRYCIS, Rheumatology, Madrid, Spain*; *[5]La Paz University Hospital, Immunology, Madrid, Spain*

Background: In clinical practice no more than 50% of the patients treated with TNF inhibitors (TNFi) achieve remission (REM). Previous investigations suggested that peripheral blood mononuclear cells (PBMC) may be markers associated with the TNFi treatment success[1].
Objectives: This study aims to analyse the intracellular cytokine production by PBMC and its association with REM achievement after 6 months (m) of TNFi treatment in patients with RA.
Methods: This was a prospective study including 62 patients with RA starting the 1st TNFi. PBMC were isolated from patients at baseline and after 6m of treatment with TNFi and cryopreserved until studied. In vitro stimulation and intracellular cytokine production by PBMC was performed as follow: in the presence of 2µg/mL brefeldin and 2µmol/L monensin monocytes were stimulated with 20ng/mL LPS during 4h whereas lymphocytes were stimulated with 50ng/mL phorbol 12-myristate 13-acetate and 750ng/mL ionomycin for 4h at 37ºC. To identify IL10-producing B cells, PBMC were pre-incubated with 3µg/mL of CpG oligonucleotide during 20h at 37°C prior to stimulation. Intracellular cytokine production (TNFα, IL6, GM-CSF, IL10) by the different cell subsets (monocytes, $CD4^+$ and $CD8^+$ T cells, naïve and memory B cells) was analysed by flow-cytometry. Clinical activity at baseline and after 6m was assessed by DAS28-ESR. REM was defined as DAS28≤2.6 at 6m. The association between cytokine production by each PBMC subset and REM was analysed through univariable and multivariable logistic regression models. Receiving operating curve (ROC) analysis was used to select the optimal ratio of cytokine production associated with REM status.
Results: After 6m of TNFi treatment, 30 (48%) patients achieved REM. No significant differences between REM and non-REM groups were observed for patients' characteristics at baseline except for DAS28, which was lower in the REM group (non-REM: 5.4±0.9; REM: 4.3±0.9; p<0.0001) (Table 1). Therefore, further analyses were adjusted by baseline DAS28. A lower ratio between calculated with the IL10 and TNFα production by B cells and by $CD4^+$ T cells (IL10 B/TNF CD4) at 6m was found for non-REM patients (non-REM: 0.31 vs REM: 0.54; p=0.007). Based on a ROC analysis, we found that a (IL10 B/TNF CD4)<0.54 at 6 m was

significantly associated with a higher probability of non-REM at 6 months (OR: 5.0; 95% CI: 1.1-21.7) (Figure 1).

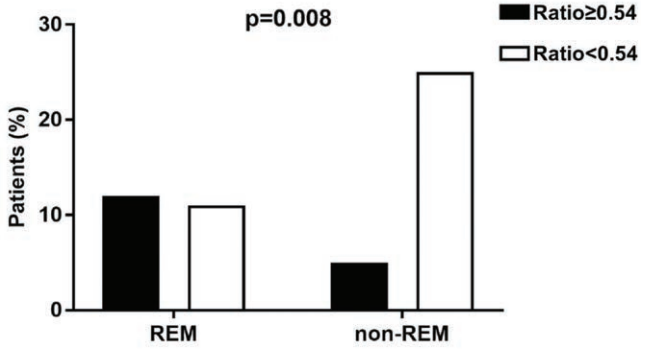
Table 1. The table shows mean±SD, median (IQR) or absolute number (percentage) for all patients included (n=62). RF, rheumatoid factor; ACPA, anti-citrullinated protein antibodies; DAS28, Disease Activity Score-28; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; MTX, methotrexate; OD, other conventional synthetic disease-modifying anti-rheumatic drugs than methotrexate. The differences between DAS28 groups were analysed considering p-value<0.05 as statistically significant result.

Baseline patients' characteristics	Total patients (n=62)	DAS28>2.6 (n=32; 52%)	DAS28≤2.6 (n=30; 48%)	p-value
Age (years)	53±12	53±13	52±10	0.8
Female	55 (89)	30 (94)	25 (83)	0.2
Disease duration (years)	8 (4-11)	8 (4-12)	7 (3-11)	0.7
RF positive	49 (79)	23 (72)	26 (87)	0.1
ACPA positive	54 (87)	26 (81)	28 (93)	0.2
Smoking habit (n=55)				0.2
Non-smokers	26 (47)	16 (55)	10 (38)	
Smoker	29 (53)	13 (45)	16 (51)	
Body mass index (kg/m^2)	25.9±5.6	25.8±5.7	26.0±5.6	0.9
DAS28	4.9±1.0	5.4±0.9	4.3±0.9	**<0.0001**
Concomitant csDMARDs	60 (97)	32 (100)	28 (93)	0.3
MTX [±OD]	46 (74)	26 (81)	20 (67)	0.3
Only OD	14 (23)	6 (19)	8 (26)	0.3
Prednisone	36 (58)	19 (59)	17 (57)	0.9

Conclusion: Our results show that the proinflammatory IL10 B/TNF CD4 ratio is associated with non-REM status. It could be useful to analyse the success of TNFi treatment in patients with RA.

REFERENCES:

[1] Rodríguez-Martín E, et al. Front Immunol. 2020; 11: 1913.



Acknowledgements: ISCIII (PI16/00474; PI16/01092)

Disclosure of Interests: Borja Hernández-Breijo: None declared, Eulalia Rodríguez-Martín: None declared, Carlota García-Hoz: None declared, Victoria Navarro-Compán Speakers bureau: Abbvie, Janssen, Lilly, MSD, Novartis, Pfizer and UCB, Grant/research support from: Abbvie, Janssen, Lilly, MSD, Novartis, Pfizer and UCB, Cristina Sobrino: None declared, ANA MARTÍNEZ-FEITO: None declared, Israel Nieto-Gañán: None declared, Javier Bachiller-Corral Speakers bureau: Abbvie, MSD, BMS and Roche, Grant/research support from: Pfizer, Paloma Lapuente-Suanzes: None declared, Gemma Bonilla: None declared, Cristina Pijoán-Moratalla: None declared, Mónica Vázquez: None declared, Alejandro Balsa Speakers bureau: Abbvie, BMS, Nordic, Novartis, Pfizer, Sandoz, Sanofi, Roche and UCB, DORA PASCUAL-SALCEDO: None declared, Luisa María Villar: None declared, Chamaida Plasencia Speakers bureau: AbbVie, Lilly, Novartis, Pfizer, Sanofi, Biogen and UCB

DOI: 10.1136/annrheumdis-2021-eular.2361

POS0624

EFFICACY AND SAFETY OF LEVILIMAB IN COMBINATION WITH METHOTREXATE IN SUBJECTS WITH ACTIVE RHEUMATOID ARTHRITIS: PHASE III, DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED TRIAL

V. Mazurov[1], M. Korolev[2], A. Kundzer[3], N. Soroka[4], A. Kastanayan[5], T. Povarova[6], T. Plaksina[7], O. Antipova[8], D. Kretchikova[9], S. Smakotina[10], O. Tciupa[11], T. Raskina[12], T. Kropotina[13], O. Nesmeyanova[14], T. Popova[15], E. Dokukina[16], A. Plotnikova[16], A. Lutskii[17], A. Zinkina-Orihan[17]. *[1]North-Western State Medical University n.a. I.I. Mechnikov, Department of Therapy and Rheumatology of Temporary Disability and Medical Care Quality Expertise Named After E. E. Eichwald, Saint-Petersburg, Russian Federation*; *[2]Federal Research Center Institute of Cytology and Genetics, Deputy Director for Clinical Issues, Novosibirsk, Russian Federation*; *[3]Academy for Postgraduate Education, Department of Cardiology and Rheumatology, Minsk, Belarus*; *[4]Belarus State Medical University, Department of Internal Diseases No.2, Minsk, Belarus*; *[5]Rostov State Medical University, Department of Internal Diseases No.2, Rostov-on-Don, Russian Federation*; *[6]Clinical Hospital Russian Railways-Medicine of the City of Saratov, Department of Cardiology, Saratov, Russian Federation*; *[7]N. A. Semashko Nizhny Novgorod Regional Clinical Hospital, Center of Rheumatology, Nizhniy Novgorod, Russian Federation*; *[8]Irkutsk City Clinical Hospital No. 1, Medical Rheumatological Center, Irkutsk, Russian Federation*; *[9]Departmental Hospital at Smolensk Station, JSC Russian Railways, Department of Rheumatology, Smolensk, Russian Federation*; *[10]Kemerovo Regional Clinical Hospital Named After S.V. Belyaev, Regional Rheumatological Center, Kemerovo, Russian Federation*; *[11]City Hospital No.4 of the City of Barnaul, Department of Rheumatology, Barnaul, Russian Federation*; *[12]Kemerovo State Medical University, Department of Internal Medicine Propaedeutics, Kemerovo, Russian Federation*; *[13]Regional Clinical Hospital, Deputy Chief Physician for Therapy, Omsk, Russian Federation*; *[14]Chelyabinsk Regional Clinical Hospital, Department of Rheumatology, Chelyabinsk, Russian Federation*; *[15]City Clinical Hospital No.40, Department of Rheumatology, Ekaterinburg, Russian Federation*; *[16]BIOCAD, Clinical Research, Saint-Petersburg, Russian Federation*; *[17]BIOCAD, Clinical Development, Saint-Petersburg, Russian Federation*

Background: Previously, the results of phase II AURORA clinical study of levilimab in subjects with active rheumatoid arthritis (RA) have been reported[1]. Here we report topline 24-weeks results of preliminary primary efficacy and safety analysis of phase 3 double-blind, placebo-controlled randomized clinical study (SOLAR).

Objectives: To confirm that levilimab in combination with methotrexate is superior to placebo in combination with methotrexate in achieving ACR20 at week 12 and low disease activity (LDA) at week 24 in subjects with methotrexate (MTX) resistant active RA.

Methods: The study is ongoing at 21 clinical sites in Russia and Belarus. All randomized subjects have completed 24 weeks of study between November 2019 and January 2021.

154 adults, aged ≥18 years with the diagnosis of RA (ACR 2010) for at least 24 weeks, and confirmed disease activity at screening despite treatment with MTX for the last 12 weeks (in a stable dose 15-25 mg/week, for at least 4 weeks) were randomly assigned (2:1) to receive either levilimab (162 mg, SC, QW) + MTX (n=102) or placebo + MTX (n=52). The randomization and treatment allocation were carried out by a central computer-based system. Subjects, caregivers, and those assessing the outcomes were blinded to group assignment.

The hypothesis of superiority of levilimab over placebo was tested for two co-primary efficacy outcomes: proportion of subjects who achieved ACR20 at week 12 and proportion of subjects who achieved LDA of RA (DAS28-CRP <3.2) at Week 24 of the study.

For ethical reasons, subjects who haven't achieved minimal clinical response at week 12 (≥20% reduction in the number of tender/swollen joints; 66/68) received rescue therapy at the discretion of the Investigator, and all subsequent efficacy assessments for those were considered missing.

For the primary efficacy analysis, subjects with missing data due to study discontinuation or rescue therapy prescription were considered non-responders (non-responder imputation, NRI). Otherwise, the analysis was performed on observed cases.

Safety was assessed through monitoring of adverse events (AEs).

Results: The primary analysis was based on 149 randomized subjects (n=99 and n = 50) for ACR20 and 154 randomized subjects (n= 102 and n = 52) for LDA. 70/99 (71%) of subjects who received levilimab and 20/50 (40%) who received placebo achieved ACR20 response at week 12. The difference in proportion was 30% with a lower bound of 97.5% CI 12.8%; p=0.0003 (Pearson's chi-squared test).

53/102 (52%) of subjects received levilimab and 3/52 (6%) received placebo achieved LDA at week 24. The difference in proportion was 46% with a lower bound of 97.5% CI 31.2 %; p<0.0001 (Pearson's chi-squared test).

The safety population included all subjects, who received investigational product (n=154).

The most common adverse events (reported in ≥5% of subjects) in levilimab and placebo arms, respectively were: blood cholesterol increase (19% vs. 10%), ALT increase (11% vs. 8%), lymphocyte count decrease (9% vs. 8%), blood bilirubin increase (11% vs. 0%), blood triglycerides increase (9% vs. 2%), AST increase (7% vs. 4%), IGRA with *M.tuberculosis* antigen positive (5% vs. 6%), ANC decrease (8% vs. 0%). No deaths were occurred.

Conclusion: The study confirmed superior efficacy of levilimab + MTX over placebo + MTX in subjects with MTX resistant active RA. No new safety signals were detected.

Trial registration: Clinicaltrials.gov identifier NCT04397562

REFERENCES:
[1] Mazurov V, Zotkin E, Ilivanova E, et al. FRI0114 EFFICACY OF LEVILIMAB, NOVEL MONOCLONAL ANTI-IL-6 RECEPTOR ANTIBODY, IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: 1-YEAR RESULTS OF PHASE 2 AURORA STUDY. Annals of the Rheumatic Diseases 2020;79:637-638.
Acknowledgements: We thank all contributors to the SOLAR clinical trial
Disclosure of Interests: V Mazurov: None declared, Maxim Korolev: None declared, Alena Kundzer: None declared, Nikolaj Soroka: None declared, Aleksander Kastanayan: None declared, Tatyana Povarova: None declared, Tatyana Plaksina: None declared, Olga Antipova: None declared, Diana Kretchikova: None declared, Svetlana Smakotina: None declared, Oksana Tciupa: None declared, Tatiana Raskina: None declared, Tatyana Kropotina: None declared, Olga Nesmeyanova: None declared, Tatiana Popova: None declared, Ekaterina Dokukina Employee of: JSC BIOCAD, Aleksandra Plotnikova Employee of: JSC BIOCAD, Anton Lutskii Employee of: JSC BIOCAD, Arina Zinkina-Orihan Employee of: JSC BIOCAD
DOI: 10.1136/annrheumdis-2021-eular.2443

POS0625 ASSOCIATIONS OF REMISSION AND PERSISTENCE OF BIOLOGICS AT 1 AND 12 YEARS

K. Murray[1], M. Turk[1], Y. Alammari[1], F. Young[1], P. Gallagher[1], T. P. Saber[1], U. Fearon[2], D. Veale[1]. [1]*Saint Vincent's University Hospital, Rheumatology, Dublin 4, Ireland*; [2]*Trinity College, Trinity Biomedical Sciences Institute, Dublin, Ireland*

Background: Biologic therapies have greatly improved outcomes in rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Yet, our ability to predict long-term remission and persistence or continuation of therapy remains limited.
Objectives: To compare RA and PsA outcomes at 1 and 12 years after commencing biologic DMARDs and to identify predictors of remission and persistence of therapy.
Methods: RA and PsA patients were prospectively recruited from a biologic clinic. Outcomes on commencing therapy, at 1 year and 12 years were reviewed. Demographics, medications, morning stiffness, patient global health score, tender and swollen joint counts, antibody status, CRP and HAQ were collected. Outcomes at 1 and 12 years are reported and predictors of EULAR-defined remission (DAS28-CRP <2.6) and biologic persistence are examined with univariate and multivariate analysis.
Results: A total of 403 patients (274 RA and 129 PsA) were analysed. PsA patients were more likely to be male, in full-time employment and have completed higher education. PsA had higher remission rates than RA at both 1 year (60.3% versus 34.5%, $p<0.001$) and 12 years (91.3% versus 60.6%, $p<0.001$). This difference persisted when patients were matched for baseline disease activity ($p<0.001$). Biologic continuation rates were high for RA and PsA at 1 year (49.6% versus 58.9%) and 12 years (38.2% versus 52.3%). In PsA, patients starting on etanercept had lower CRP at 12 years ($p=0.041$). Multivariate analysis showed 1-year continuation [OR 4.28 (1.28–14.38)] and 1-year low-disease activity [OR 3.90 (95% CI 1.05–14.53)] was predictive of a 12-year persistence. Persistence with initial biologic at 12 years [OR 4.98 (95% CI 1.83–13.56)] and male gender [OR 4.48 (95% CI 1.25–16.01)] predicted 12 year remission.
Conclusion: This is the first real world data to show better response to biologic therapy in PsA compared to RA at 12 years. Long-term persistence with initial biologic agent was high and predicted by biologic persistence and low-disease activity at 1 year. Interestingly, PsA patients had higher levels of employment, educational attainment, and long-term remission rates compared to RA patients.
Disclosure of Interests: Kieran Murray Grant/research support from: Bresnihan Molloy and Newman Fellowships, Matthew Turk: None declared, Yousef Alammari: None declared, Francis Young: None declared, Phil Gallagher: None declared, Tajvur Parveen Saber: None declared, Ursula Fearon: None declared, Douglas Veale: None declared
DOI: 10.1136/annrheumdis-2021-eular.2547

POS0626 MONEY MATTERS: ASSESSING THE VALUE OF THE ADALIMUMAB BIOSIMILAR SWITCH FOR RHEUMATOLOGY PATIENTS

S. Gohil[1]. [1]*University Hospitals of Coventry and Warwickshire NHS Trust, Pharmacy, Coventry, United Kingdom*

Background: The adalimumab biosimilar switch plan, actioned 2018-19 was one of the most complex of all biologic switches across several specialties. Non-medical switches are considered to ensure the best value medicines are prescribed for patients in line with NICE Technology Appraisals.
Objectives: This 2 year follow up review explores the value of the switch for Rheumatology (R) patients in comparison to two other major specialisms; Dermatology (R) and Gastroenterology (G).
Methods: 403 homecare (HC) patients had been identified as eligible for switch to a citrate containing biosimilar (R;189, G;176, D;38) between April-December 2019. 35 hospital FP10 patients receiving the citrate-free originator biologic were also identified for switch to the citrate containing biosimilar and prescription processing via HC (R; 24, G; 9, D;2). Biosimilar switch information was communicated via patient letters/clinic reviews. FP10 patients also received remote pharmacist telephone support, as part of a PDSA (Plan, Do, Study, Act) quality improvement pilot. Data in regard to switch refusal, treatment cessation, withheld treatment and patient satisfaction ratings for pharmacist phonecalls (1 = unsatisfactory, 5=very satisfied) was documented.
Results: 235/403 HC patients successfully switched (R;99, G;107, D;29). 64/403 HC patients switched back to the originator (R;47, G;12; D;5). Of the 64 switch back HC patients; 52% = reported lack of efficacy; 27% = injection site pain and 21% = various other factors such as blepharitis, insomnia and hair loss. 38/403 HC patients refused the switch and remained on the originator biologic (R;11, G;27, D;0). 31/403 HC patients switched to an alternative biologic (R;19, G;9, D;3). 32/403 HC patients stopped treatment (R;13, G;19, D;0). Treatment was withheld for 3/403 HC patients (R;0, G;2, D;1). 100% of FP10 patients switched to HC. 31/35 FP10 patients switched to the biosimilar (R; 22, G; 7, D; 2). 3/31 patients switched back to the originator due to lack of efficacy or side effects. 4 patients refused the switch to biosimilar (R;3, G;1, D;0). 89% of patients were very satisfied with the pharmacist telephone support.
Conclusion: In summary, 58% of all eligible HC patients switched in comparison to 89% of FP10 patients who received pharmacist telephone support; total cost saving following HC and FP10 switch = £270,000. Rheumatology demonstrated the least success in HC switching (52%) and the highest HC switch back figure (25%). Injection site pain and subjective lack of efficacy appear to be the main reasons for ongoing switch backs. The PDSA project demonstrates that a thorough pharmacist assessment of patient concerns in rationalising the use of a biologic agent versus biosimilar can be valuable for patients. Further cost effective adalimumab biosimilars have recently been launched. This seminal review emphasises the ongoing need for robust critical appraisals of biosimilars, with consideration for both clinical and cost effective parameters, before establishing their placement in treatment pathways.
Acknowledgements: Mark Easter, UHCW and Interim Integrated Care System Chief Pharmacist, Hardeep Bagga, Deputy Chief Pharmacist, UHCW Pharmacy Homecare Team and UHCW Specialist Rheumatology, Gastroenterology and Dermatology Clinical Teams.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2566

POS0627 SHORT-TERM EFFECT OF ANTI-IL-6 THERAPY ON ADIPONECTIN SERUM LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Remuzgo-Martínez[1], V. Pulito-Cueto[1], F. Genre[1], J. Calvo[2], E. Aurrecoechea[3], I. Llorente[4], A. Triguero-Martinez[4], R. Blanco[1], J. Llorca[5], M. E. Ruiz[6], N. Rivera[6], O. Gualillo[7], R. López-Mejías[1], S. Castañeda[4,8], M. A. González-Gay[1,9,10]. [1]*IDIVAL, Hospital Universitario Marqués de Valdecilla, Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, Santander, Spain*; [2]*Hospital Universitario Txagorritxu, University of Basque Country, Rheumatology Division, Araba, Spain*; [3]*Hospital Universitario Sierrallana, Rheumatology Division, Torrelavega, Cantabria, Spain*; [4]*Hospital Universitario de la Princesa, IIS-IP, Rheumatology Division, Madrid, Spain*; [5]*School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Epidemiology and Computational Biology Department, Santander, Spain*; [6]*Hospital Universitario Basurto, Rheumatology Division, Bilbao, Spain*; [7]*Santiago University Clinical Hospital, SERGAS (Servizo Galego de Saude) and IDIS (Instituto de Investigación Sanitaria de Santiago), NEIRID Lab (Neuroendocrine Interactions in Rheumatology and Inflammatory Diseases), Research Laboratory 9, Santiago de Compostela, Spain*; [8]*Universidad Autónoma de Madrid (UAM), Cátedra UAM-ROCHE, EPID Future, Department of Medicine, Madrid, Spain*; [9]*University of Cantabria, School of Medicine, Santander, Spain*; [10]*University of the Witwatersrand, Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, Johannesburg, South Africa*

Background: Adiponectin is an adipokine with anti-inflammatory, anti-atherosclerotic and cardioprotective effects that also contributes to the pathogenesis of metabolic syndrome (MetS) [1]. MetS is frequently observed in patients with rheumatoid arthritis (RA), increasing the risk of cardiovascular (CV) morbidity and mortality in these patients [1-3]. A recent study of our group disclosed a short-term effect of anti-IL-6 therapy on serum levels of leptin (another adipokine with pro-inflammatory functions, related with MetS and CV disease) in RA patients [4]. Accordingly, it is plausible to think that such treatment may also have an effect in adiponectin levels.
Objectives: To determine the short-term effect of the anti-IL-6 receptor tocilizumab (TCZ) administration on circulating adiponectin serum levels in patients with RA, as well as the potential association of adiponectin with demographic and clinical features of these patients.

Methods: 50 consecutive Spanish patients undergoing periodic treatment with TCZ who fulfilled the 2010 classification criteria for RA [5] were recruited. Adiponectin serum levels were assessed in samples obtained immediately prior to (pre-infusion) and 60 minutes after the end of a TCZ intravenous infusion (post-infusion) by a commercial Enzyme-Linked ImmunoSorbent Assay (ELISA) kit.
Results: Similar serum levels of adiponectin were found following the TCZ infusion (mean ± standard deviation: 23.01 ± 18.58 µg/mL *versus* 22.35 ± 17.84 µg/mL, pre- and post-infusion, respectively, p=0.69). Additionally, there was a negative correlation between adiponectin basal levels and body mass index (r=-0.45, p<0.01), insulin (r=-0.33, p=0.02), insulin/glucose index (r=-0.32, p=0.03) and C-peptide levels (r=-0.32, p=0.03) of RA patients, whereas a strong positive correlation was observed with HDL-cholesterol levels (r=0.51, p<0.01). Moreover, basal levels of adiponectin were significantly lower in obese patients when compared to those with normal weight (p=0.03).
Conclusion: Our study suggests that anti-IL-6 therapy has no short-term effect on adiponectin serum levels in patients with RA. Furthermore, our results support that low adiponectin levels are associated with MetS features and, therefore, with CV disease in RA.
REFERENCES:
[1] Biochem Pharmacol. 2019;165:196-206; [2] Clin Exp Rheumatol. 2008;26:596-603; [3] Mediators Inflamm. 2013;2013:710928; [4] Clin Exp Rheumatol 2020;38:1201-1205; [5] Arthritis Rheum. 2010;62:2569-2581.
Acknowledgements: Personal funds:
SR-M: RD16/0012/0009 (ISCIII-ERDF); VP-C: PREVAL 18/01 (IDIVAL); OG: GPC IN607B2019/10 (GAIN); RL-M: Miguel Servet type I programme CP16/00033 (ISCIII-ESF).
Disclosure of Interests: Sara Remuzgo-Martínez: None declared, Verónica Pulito-Cueto: None declared, Fernanda Genre: None declared, Jaime Calvo: None declared, Elena Aurrecoechea: None declared, Irene Llorente: None declared, Ana Triguero-Martinez: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD and Roche, Javier Llorca: None declared, M E Ruiz: None declared, Natalia Rivera: None declared, Oreste Gualillo: None declared, Raquel López-Mejías: None declared, Santos Castañeda: None declared, Miguel A González-Gay Speakers bureau: Pfizer, Abbvie, MSD, Grant/research support from: Pfizer, Abbvie, MSD.
DOI: 10.1136/annrheumdis-2021-eular.2739

POS0628 FAILURE TO SUSTAIN TREATMENT TARGET AFTER TAPERING TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: 4-YEAR LONGITUDINAL DATA FROM A NATIONWIDE COHORT

J. W. Park[1], M. J. Kim[2], H. A. Kim[3], J. Kim[4], E. B. Lee[1], K. Shin[2]. *[1]Seoul National University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; *[2]Seoul Metropolitan Government - Seoul Boramae Medical Center, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; *[3]Ajou University School of Medicine, Department of Rheumatology, Suwon, Korea, Rep. of (South Korea)*; *[4]Chungnam National University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Daejeon, Korea, Rep. of (South Korea)*

Background: Tapering biologic therapy after achieving clinical remission or low disease activity (LDA) has become a viable option in daily clinical practice of treating patients with rheumatoid arthritis (RA). There are yet few studies investigating its effectiveness and safety compared with those of standard biologic treatment, especially with non-tumor necrosis factor inhibitors.
Objectives: To investigate the effectiveness and safety of tapering tocilizumab (TCZ) in patients with RA who attained LDA after TCZ therapy.
Methods: Data were collected from a nationwide cohort of patients with RA receiving biologic therapy in South Korea (KOBIO-RA). This study included 350 patients who were treated with TCZ and achieved Clinical Disease Activity Index (CDAI)-LDA or remission (CDAI ≤ 10) after one year of treatment. We performed a longitudinal analysis utilizing clinical data measured in all 1-year intervals using generalized estimating equations (GEE). A total of 575 one-year intervals were divided into two groups according to the dose quotient (DQ, 0-100%) of TCZ within the interval (tapering group vs. standard treatment group). The main outcome of this study was loss of CDAI-LDA in the following 1-year interval.
Results: Tapering TCZ was conducted in 282 (49.0%) intervals with a mean (SD) DQ of 66.0 (15.5). Loss of CDAI-LDA occurred in 91 (15.1%) intervals. Multivariable GEE showed significantly increased loss of CDAI-LDA (adjusted OR (95% CI): 1.76 [1.01 to 3.07]) in the tapering group after adjusting for previous biologics use, route of TCZ administration, concomitant glucocorticoid use, and CDAI measured in the previous follow-up. In addition, the likelihood to achieve DAS28-deep remission (DAS28-ESR < 1.98) was also significantly lower in the tapering group (adjusted OR 0.68 [0.46 to 0.99]). In contrast, there was no significant difference in the proportion of fulfilling other remission criteria between the two groups (Table 1). Development any adverse drug event or event of special interest was comparable in both groups except for hypercholesterolemia, which was lower in the tapering group.

Table 1. The effect of tapering tocilizumab on achieving outcomes

	Loss of CDAI-LDA	DAS28-remission	DAS28-deep remission	CDAI-remission	SDAI-remission	ACR/EULAR remission
Unadjusted OR (95% CI) (vs. standard-dose group)	1.02 (0.67 to 1.55)	1.03 (0.71 to 1.49)	0.76 (0.54 to 1.06)	1.23 (0.75 to 2.00)	0.92 (0.59 to 1.44)	0.98 (0.65 to 1.48)
Adjusted OR (95% CI) (vs. standard-dose group)	**1.76 (1.01 to 3.07)**	0.87 (0.54 to 1.38)	**0.68 (0.46 to 0.99)**	0.94 (0.57 to 1.55)	0.87 (0.54 to 1.38)	0.76 (0.50 to 1.18)

CDAI, clinical disease activity index; CI, confidence interval; DAS, disease activity score; LDA, low disease activity; OR, odds ratio; SDAI, simplified disease activity index.

Conclusion: Tapering TCZ after achieving LDA in patients with RA increases the risk of losing the benefit of LDA without a significant merit in safety.
REFERENCES:
[1] Smolen JS et al. Maintenance, reduction or withdrawal of etanercept after treatment with etanercept and methotrexate in patients with moderate rheumatoid arthritis (PRESERVE): a randomised controlled trial. Lancet. 2013;381:918-29.
[2] Schett G et al. Tapering biologic and conventional DMARD therapy in rheumatoid arthritis: current evidence and future directions. Ann Rheum Dis. 2016;75:1428-37.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2818

POS0629 PREDICTORS OF CHANGE IN DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS AFTER START OF TREATMENT WITH ABATACEPT

J. Liukkonen[1], G. Cagnotto[1,2], J. Å. Nilsson[1,2], S. Saevarsdottir[3,4], C. Turesson[1,2]. *[1]Lund University, Rheumatology, Department of Clinical Sciences, Malmö, Malmö, Sweden*; *[2]Skåne University Hospital, Department of Rheumatology, Malmö, Sweden*; *[3]Karolinska Institutet, Division of Clinical Epidemiology, Department of Medicine, Stockholm, Sweden*; *[4]University of Iceland, Faculty of Medicine, School of Health Sciences, Reykjavik, Iceland*

Background: Abatacept is a biologic disease-modifying anti-rheumatic drug (bDMARD) used to treat rheumatoid arthritis (RA) since 2006, acting by inhibition of T-cell co-stimulation. There are limited data on factors predicting clinical outcomes in RA after start of treatment with abatacept.
Objectives: The primary aim was to identify predictors of change in disease activity in RA-patients after start of treatment with abatacept.
Methods: This cohort study was based on data from the Swedish Rheumatology Quality register (SRQ). All patients with RA who started treatment with abatacept between 2006 and 2017 were included. Clinical data from the SRQ included demographics, disease characteristics and antirheumatic treatment. Disease activity was measured according to DAS28-ESR (Disease Activity Score of 28 joints based on erythrocyte sedimentation rate) at inclusion and at follow-up visits at 6 and 12 months from start of treatment with abatacept. Baseline predictors of change in disease activity were investigated using linear regression models bivariately and adjusted for baseline values of DAS28. Covariates with a p-value of <0.1 were retained for the final multivariate model. In case of covariates with major collinearity, the one with the stronger association with change of DAS28 was selected.
Results: In a total of 2716 patients, 872 had data on change in DAS28 at 12 months. Among these, most patients were women (79.6%) and the mean age at start of abatacept was 58.4 years (SD 13.6). The majority of patients had established RA, with a mean disease duration of 13.5 years (SD 11.1). Most patients had severe, active disease, with substantial pain and disability, despite extensive treatment. The mean number of bDMARDs that a patient had been exposed to was 1.90 (SD 1.32). DAS28 decreased significantly over the first year (mean 1.22: 95 % CI 1.12, 1.32). The greatest decrease in DAS28 (mean 1.09) occurred during the first 6 months from start of abatacept. The multivariate regression model identified male sex and limited previous bDMARD exposure as independent predictors of change in DAS28 at 12 months from start of abatacept – adjusted for baseline DAS28, RA duration and current treatment with methotrexate or prednisolone (Table 1).
Conclusion: In this national register study, male sex and limited previous exposure to bDMARDs were independent predictors of reduction of disease activity one year after start of treatment with abatacept for RA, possibly reflecting a better prognosis overall in such patients.

Table 1. Baseline predictors of reduction of disease activity at 12 months from start of abatacept. Linear regression.

	Bivariate			Adjusted for baseline DAS28			Multivariate		
Variables	B	95% CI	*P-value*	B	95% CI	*P-value*	B	95% CI	*P-value*
Male sex	**0.39**	**[0.13, 0.64]**	**0.003**	**0.43**	**[0.20, 0.66]**	**<0.001**	**0.42**	**[0.19, 0.64]**	**<0.001**
Age (per SD)	0.10	[-0.004, 0.21]	0.058	0.044	[-0.051, 0.14]	0.37		N/A	
RA duration (per SD)	**-0.14**	**[-0.25, -0.037]**	**0.008**	**-0.11**	**[-0.21, -0.016]**	**0.022**	-0.030	[-0.13, 0.065]	0.54
HAQ (per SD)	**0.12**	**[0.007, 0.23]**	**0.037**	**-0.24**	**[-0.35, -0.13]**	**<0.001**		N/A	
VAS pain (per SD)	**0.26**	**[0.15, 0.37]**	**<0.001**	-0.058	[-0.17, 0.054]	0.31			
MTX[1]	0.20	[-0.013, 0.41]	0.066	0.17	[-0.018, 0.36]	0.076	0.11	[-0.076, 0.29]	0.25
Prednisolone[1]	-0.19	[-0.41, 0.017]	0.072	-0.17	[-0.36, 0.024]	0.087	-0.14	[-0.33, 0.043]	0.13
bDMARDs[2] (per SD)	**-0.30**	**[-0.40, -0.20]**	**<0.001**	**-0.32**	**[-0.41, -0.23]**	**<0.001**	**-0.31**	**[-0.40, -0.21]**	**<0.001**

B=beta coefficient; N/A=not applicable; SD=standard deviation; CI=confidence interval. Bold text indicates significant associations.DAS28, Disease activity Score of 28 joints; RA, rheumatoid arthritis; HAQ, Health Assessment Questionnaire; VAS, visual analogue scale; MTX, methotrexate; bDMARD, biologic disease-modifying antirheumatic drug.[1]Current treatment[2]Number of previous bDMARDs

Disclosure of Interests: Julia Liukkonen: None declared, Giovanni Cagnotto: None declared, Jan-Åke Nilsson: None declared, Saedis Saevarsdottir: None declared, Carl Turesson Speakers bureau: Abbvie, Bristol Myers-Squibb, Medac, Pfizer, Roche., Consultant of: Roche, Grant/research support from: This study was supported by an unrestricted grant from Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.2867

POS0630 COMPARISON OF THE EFFICACY AND SAFETY OF ORIGINAL AND BIOSIMILAR ADALIMUMAB MOLECULES IN CHILDHOOD RHEUMATIC DISEASES

K. Ulu[1], F. Demir[1], T. Coşkuner[1], Ş. Çağlayan[1], B. Sözeri[2]. *[1]Umraniye Training and Research Hospital, Pediatric Rheumatology, Istabul, Turkey*; *[2]Umraniye Training and Research Hospital, Pediatric Rheumatology, Istabul, Turkey*

Background: The TNF-α inhibitor adalimumab is a biological disease modifying anti-rheumatic drug (bDMARD) that has been used in different rheumatic diseases with a resistant course. ABP-501 is a biosimilar product (BP) of adalimumab, recently approved by the FDA and EMA. To our knowledge, there is no study assess the efficacy and safety of these two molecules on pediatric patients.

Objectives: We aimed to compare the efficacy and safety of the original and biosimilar adalimumab (ABP-501) molecules in childhood rheumatic diseases.

Methods: This non-interventional, retrospective, single-centre analysis carried out in Umraniye Training and Resrach Hospital, Pediatric Rheumatology Clinic, Istanbul, Turkey. The study group consisted of patients who were followed due to chronic rheumatic disease between January 1, 2016 and June 1, 2020, and received reference or biosimilar adalimumab therapy for at least three months. Demographic and clinical data of patients were collected at baseline, 3rd, 6th, and 12th months of treatment. Disease activity assessment was made with JADAS-27 in JIA patients, with SUN criteria in uveitis patients, and with Behçet's Disease Activity Index in BD patients. Efficacy and safety of treatments were compared between reference and biosimilar adalimumab groups.

Results: A total of 89 patients (65 with original and 24 with biosimilar molecule) treated with adalimumab, were included in the study. There were 45 female and 44 male in the study, and the median age at the initiation of the adalimumab was 166 months (min-max: 36-231). Of the 89 patients evaluated, the primary diagnoses of 62 were juvenile idiopathic arthritis, 13 were idiopathic uveitis, eight were Behçet's disease, three were Blau syndrome, two were chronic recurrent multifocal osteomyelitis and one was Vogt-Koyanagi-Harada syndrome. 63 of the patients were biologic-naïve, and 13 were switched from etanercept, 11 from infliximab, and two from other bDMARDs. The median exposure time of adalimumab was 16 months (min-max:3-70) in RP and 14.5 months (min-max: 3-23) in BP. All patients had active disease before treatment. In the group treated with RP, inactive disease was achieved in 60%, 76.6% and 87.2% of the patients at the 3rd, 6th and 12th months, respectively. Also, inactive disease was achieved in 62.5%, 78.2% and 78.2% of the patients at the 3rd, 6th and 12th months in the group treated with BP, respectively. There was no statistically significant difference in efficacy between the groups at the 3rd, 6th and 12th months (p=0.83, 0.07 and 0.32). Serious adverse events were seen in one patient in each groups (lymphoma in RP group, tuberculous meningitis in BP group). Non-serious adverse events were observed in eight patients (12.3%) in the RP group and in two patients (8.3%) in the BP group, without statistically significant difference between groups (p=0.86).

Conclusion: No significant difference was observed between the biosimilar adalimumab ABP-501 and RP adalimumab in terms of efficacy and safety.

REFERENCES:

[1] Renton, William D et al. *Pediatr Rheumatol Online J*. 2019;17(1):67.
[2] Lovell DJ, Ruperto N, Goodman S, et al. *N Engl J Med*. 2008;359(8):810-820.
[3] Kingsbury, Daniel J et al. Clin Rheumatol 2014;33(10):1433-41.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2979

POS0631 COMPARATIVE EFFICACY OF COMBINATION THERAPY WITH BIOLOGIC OR TARGET SYNTHETIC DRUGS FOR RHEUMATOID ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS

F. Cacciapaglia[1], V. Venerito[1], S. Stano[2], M. Fornaro[1], G. Lopalco[1], F. Iannone[1]. *[1]University and AOUC Policlinico of Bari, Department of Emergency and Organs Transplantation, Bari, Italy*; *[2]School of Medicine University of Bari, Department of Emergency and Organs Transplantation, Bari, Italy*

Background: Biologic agents and small molecules have shown long term benefit when added in patients with active RA non-responders to conventional DMARDs treatment (1). In head-to-head trials only adalimumab was compared to other drugs in combination with methotrexate, with some evidence of superiority but no data on multiple comparisons have been reported (2). The availability of biosimilar agents led in clinical practice to prefer mainly the cheaper one, so the choice of the most effective treatment remains a clinical unmet need (3).

Objectives: To assess the relative efficacy of different therapeutic strategies for achieving ACR50 response at 24 weeks of treatment in patients with active RA, based on direct and indirect evidence.

Methods: We performed systematic reviews of MEDLINE, EMBASE, and Cochrane Library databases, searching for all published phase 3 Randomised Controlled Trials (RCTs) comparing adalimumab originator to its biosimilars, abatacept, baricitinib, certolizumab pegol, tofacitinib or upadacitinib, combined to MTX, in patients with active RA inadequate responders to previous conventional DMARDs. American College of Rheumatology (ACR) 50% response at 24 weeks of treatment had to be evaluated both in adalimumab branch and in examined drug branch. Bayesian fixed-effect network meta-analysis was performed to combine the direct and indirect evidence using the WinBUGS 1.4 software (MRC Biostatistics Unit, Cambridge, UK).

Results: Eleven RCTs evaluating 6'004 patients were included in the analysis, namely originator (1) and biosimilars (2) adalimumab, abatacept (3), baricitinib (4), certolizumab pegol (5), tofacitinib (6) and upadacitinib (7). Convergence was reached at n.100'000 iterations. Upadacitinib seems to be more effective than both originator and biosimilar adalimumab in achieving ACR 50 (OR 1.65 95% CI 1.25-2.14 and OR 1.22 95%CI 1.10-2.18; see Figure 1). Similarly, tofacitinib was more effective of originator adalimumab (OR 1.25 95%CI 1.01-155). Upadacitinib was ranked first among treatments with a probability of being the agent more likely to induce ACR 50 response of 86.3%. In this regard tofacitinib had a probability of 4.8%, hence it was ranked second among treatments.

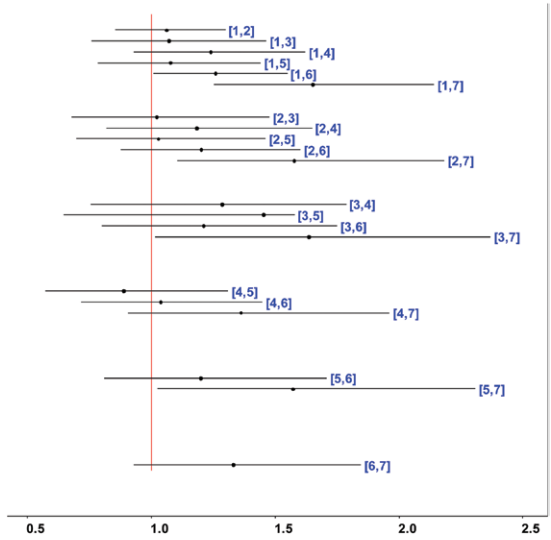


Figure 1. Caterpillar plot OR for ACR50 at 24 weeks (originator [1] and biosimilars [2] adalimumab; abatacept [3]; baricitinib [4]; certolizumab pegol [5]; tofacitinib [6]; upadacitinib [7]).

Conclusion: Although patients with active RA and inadequate response to MTX have different therapeutic combination of biologics or small molecules options, the best relative efficacy in terms of ACR50 response after 24 weeks of treatment is for upadacitinib 15 mg/day.

REFERENCES:

[1] Smolen JS, et al. Annals of the Rheumatic Diseases 2020;79:685-699.
[2] Combe B, Lukas C. Joint Bone Spine, 2020,105004.
[3] Caporali R, et al. Biomed Res Int. 2018 Sep 9;2018:3878953.

Disclosure of Interests: Fabio Cacciapaglia Speakers bureau: Roche, Pfizer, Eli Lilly, MSD, UCB, BMS, Abbvie, Vincenzo Venerito: None declared, Stefano Stano: None declared, Marco Fornaro: None declared, Giuseppe Lopalco Speakers bureau: Celgene, BMS, Abbvie, Novartis, Florenzo Iannone Speakers bureau: Roche, Pfizer, Eli Lilly, MSD, UCB, BMS, Abbvie, Novartis, Celgene

DOI: 10.1136/annrheumdis-2021-eular.3073

POS0632 THE LONGITUDINAL ASSOCIATIONS OF METHOTREXATE AND BIOLOGIC USE ON HOSPITAL ADMISSION FOR RHEUMATOID ARTHRITIS PATIENTS IN WESTERN AUSTRALIA POPULATION (1995- 2014)

K. Almutairi[1], J. Nossent[1], D. Preen[2], H. Keen[1], C. Inderjeeth[1]. [1]*The University of Western Australia, School of Medicine, Perth, Australia*; [2]*The University of Western Australia, School of Population and Global Health, Perth, Australia*

Background: Rheumatoid arthritis (RA) carries a substantial burden for patients and society in terms of morbidity, enduring disability, and costs [1]. The Australian Pharmaceutical Benefits Scheme (PBS) has subsidised biological disease-modifying anti-rheumatic drugs (B-DMARDs) since 2003 [2].

Objectives: We examined the impact of B-DMARDs availability on RA hospitalisation rate in the Western Australia (WA) population pre- and post- B-DMARDs introduction to the PBS (1995-2002 and 2003-2014).

Methods: Population PBS dispensing data for WA of DMARD were obtained and converted to defined daily doses (DDD)/1000 population/day using the WA population census. RA inpatient records were extracted from the WA Hospital Morbidity Data Collection using ICD-9 codes 714 and ICD-10 codes M05.00–M06.99). Principal component analysis (PCA) was applied to determine the relationship between DMARDs use and RA hospital admission rates.

Results: There was a total of 17,125 patients who had 50,353 admissions with a diagnostic code for RA during the study period. DMARD use for RA rose from 1.45 to 3.19 DDD/1000 population/day over 1995-2014 (Figure 1). In 1995-2002, the number of RA admissions fell from 7.9 to 2.6 per 1000 hospital separations, then dropped further from 2.9 to 1.9 per 1000 hospital separations in 2003-2014. Based on PCA analysis, conventional DMARDs (methotrexate) and B-DMARDs dispensing had an inverse association with hospital admissions for RA.

Conclusion: The increased availability of conventional and biological DMARDs for RA was associated with a significant decline in hospital admissions for RA patients in WA.

REFERENCES:

[1] Boonen A, Severens JL (2011) The burden of illness of rheumatoid arthritis. Clin Rheumatol 30:3-8.
[2] Medicare Australia (2020) Pharmaceutical Benefits Schedule statistics. http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp.

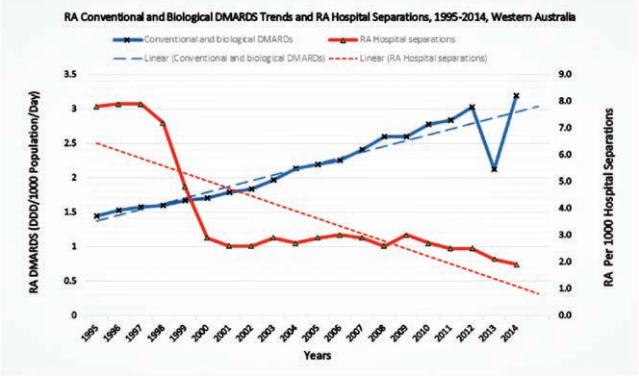


Figure 1. The hospital separations and total drugs use patterns of RA in 1995-2014 in Western Australia.

Acknowledgements: Supported by an Australian Government Research Training Program PhD Scholarship at the University of Western Australia.

Disclosure of Interests: Khalid Almutairi: None declared, Johannes Nossent Speakers bureau: Janssen, David Preen: None declared, Helen Keen Speakers bureau: Pfizer Australia, Abbvie Australia, Charles Inderjeeth Speakers bureau: bureau: Eli Lilly

DOI: 10.1136/annrheumdis-2021-eular.3230

POS0633 DURATION OF STARTING BDMARDS ARE ALMOST 3 TIMES LONGER IN RA PATIENTS THAN PSA PATIENTS: HUR-BIO REAL LIFE RESULTS

G. K. Yardımcı[1], B. Farisoğulları[1], E. C. Bolek[1], E. Bilgin[1], E. Duran[1], G. Ayan[1], Z. Özsoy[1], G. Sandal Uzun[1], L. Kılıç[1], A. Akdoğan[1], O. Karadag[1], Ş. A. Bilgen[1], S. Kiraz[1], A. İ. Ertenli[1], U. Kalyoncu[1]. [1]*Faculty of Medicine; Hacettepe University, Rheumatology, Ankara, Turkey*

Background: Before using biological DMARDs, EULAR suggests the use of synthetic DMARDs (especially methotrexate) for RA and PsA [1-2].

Objectives: It was aimed to evaluate the differences of disease duration and csDMARDs till first bDMARD in RA and PsA patients.

Methods: HUR-BIO (Hacettepe University Biologic Registry) is a prospective, single center database of biological treatments since 2005 and to date 2070 RA and 520 PsA patients have been recorded. Demographic, clinical and laboratory data before bDMARDs of the patients were noted. When investigating the differences between groups, the effects of gender, age and disease duration wereadjusted using two-way ANOVA and ANCOVA tests. The selection was made for the gender, age and for indifference of the relevant groups by using prospensity score matching.

Results: We incuded 481 RA, and 482 PsA age and gender matched patients in the study. Age, gender and disease duration information were given in the Table 1. 72.8% of the RA patients were RF or anti-CCP positive. Overall, 56.3, 100% of the RA, and PsA patients first biologic therapies were anti-TNFs, respectively. All RA patients started with csDMARDs before bDMARD treatments, whereas 450 of 482 (93.4%) PsA patients. Methotrexate was the anchor csDMARD for both diseases. RA patients more frequently used all csDMARDs included methotrexate, leflunomide, sulphasalazine hydroxychloroquine and corticosteroids as well. Median disease duration till bDMARD treatments in RA and PsA patients were 55 and 18.5 months respectively (p<0.001) (Table 1).

Table 1. Demographic characteristics and csDMARDs before first bDMARD

		RA (n=481)	PsA (n=482)	P value
Female, n (%)		319 (66.3)	332 (68.9)	0.218
Age, years (mean±SD)		48.2 ± 13.5	47.4 ± 12.2	0.332
Disease duration, years*		10 (6-16)	7 (3-12)	**0.000**
Symptom duration before diagnosis, years¥		0 (0-1)	1 (0-4)	**0.000***
The period of time between diagnosis and bDMARD initiation, months¥		55 (24-115)	18.5 (8-58)	**0.000***
The period of time between symptoms and bDMARD initiation, months¥		70 (35-151)	48 (20-124)	**0.000***
Methotrexate	**Ever n (%)**	400 (83.3)	373 (77.5)	**0.015**
	Just before bDMARD initiation n (%)	251 (52.2)	230 (47.7)	0.093
Hydroxychloroquine sulfate	**Ever n (%)**	292 (60.8)	170 (35.3)	**0.000***
	Just before bDMARD initiation n (%)	262 (54.5)	99 (20.5)	**0.000***
Leflunomide	**Ever n (%)**	237 (49.4)	129 (26.8)	**0.000***
	Just before bDMARD initiation n (%)	160 (33.3)	96 (19.9)	**0.000***
Sulphasalazine	**Ever n (%)**	353 (73.5)	265 (55.1)	**0.000***
	Just before bDMARD initiation n (%)	156 (32.4)	146 (30.3)	0.259*
Corticosteroids	**Ever n (%)**	419 (87.3)	281 (58.4)	**0.000***
	Just before bDMARD initiation n (%)	335 (69.6)	187 (38.8)	**0.000***

¥Median (IQR)

Conclusion: According to HUR-BIO real life data, for inflammatory arthritis patients who started bDMARDs, the periods of time between diagnosis and bDMARDs were more reasonable (18 months) in PsA patients than RA patient's periods which were approximately three times longer. RA patients were used much more and longer duration of csDMARDs. This explicit distinction may be explained by synthetic DMARDs on activity differences between the RA and PsA.

REFERENCES:

[1] Gossec, L., et al., EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis, 2020. 79(6): p. 700-712.
[2] Smolen, J.S., et al., EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Ann Rheum Dis, 2020. 79(6): p. 685-699.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3283

POS0634 DO BIOLOGICS IMPROVE FATIGUE IN PATIENTS WITH RHEUMATOID ARTHRITIS?

A. Fazaa[1], H. Boussaa[1], K. Ouenniche[1], S. Miladi[1], M. Sellami[1], L. Souabni[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim University Hospital, Rheumatology, Sidi Daoud, Tunisia*

Background: Fatigue is a significant issue in rheumatoid arthritis (RA) with no accepted evidence-based management guidelines. Several studies suggested that biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDs) have a direct role on fatigue in RA.
Objectives: This study aimed to compare fatigue between patients treated with bDMARDs and conventional synthetic Disease Modifying Anti-Rheumatic Drugs (cs DMARDs).
Methods: We conducted a longitudinal study including patients with RA (ACR/EULAR 2010). Patients with other acute or chronic diseases that may induce fatigue (such as cancer, infection or depression) were excluded. Demographic data and the following disease-related parameters were collected: pain Visual Analog Scale (VAS), Global Patient Assessment (GPA), tender joint count (TJC), swollen joint count (SJC), Erythrocyte Sedimentation Rate (ESR), C Protein Reactive (CRP), Disease Activity Score 28 (DAS28), Health Assessment Questionnaire (HAQ) and DMARDs used. Fatigue was assessed at baseline (T0), at 6 months (T6) and at 12months (T12) using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) which is a short 13-item questionnaire validated in RA. The score FACIT-F ranges between 0 and 52. Fatigue was considered mild if the FACIT-F score was ≥40, moderate if 20≤FACIT-F<40 and severe if 0≤FACIT-F<20. A p value inferior to 0.05 was considered significant.
Results: We included 100 RA patients (84 women and 16 men) with a mean age of 49.5±10 years old [18-65]. The mean disease duration was 87.3 months [1-360]. The mean pain VAS was 49 cm [0-100] and the mean GPA was 47.8 cm [0-100]. The mean TJC and SJC were 5.3 [0-36] and 1 [0-9] respectively. The mean levels of ESR and CRP were 38.1 mm [10-120] and 10.8 mg/l [2-61] respectively. The mean DAS28 ESR was 3.68 [1.90-8.33] and the mean HAQ score was 0.90 [0-2.75].
Eighty-three percent of patients used csDMARDs: Methotrexate (n=96), sulphasalazine (n=28), leflunomide (n=21), and hydroxychloroquine (n=12). bDMARDs were prescribed in 17% of patients: Rituximab (n=10), Infliximab (n=9), and Etanercept (n=5).
At baseline, the mean FACIT-F score was 27.1 [0-51]. Moderate fatigue was noted in 57% of cases and severe fatigue in 26% of cases. Patients on csDMARDs had a lower FACIT-F score when compared to patients on bDMARDs (26.89 versus 28.41), but the difference was not statistically significant (p=0.630).
The mean FACIT-F score was 27.41 in bDMARDs patients versus 29.80 in csDMARDs patients (p=0.497) at T6, and 32.35 versus 33.65 respectively at T12 (p=0.695).
The mean delta FACIT-F was 2.18 in bDMARDs patiens versus 2.73 in csDMARDs patients between T6 and T0 (p=0.815), and 3.94 versus 7.2 respectively between T12 and T0 (p=0.807).
When considering all patients, a significant positive correlation was noted between delta FACIT-F and delta DAS28 at T6 (r=0.418, p<0.001) and at T12 (r=0.338, p<0.001).
Conclusion: RA patients treated with bDMARDs didn't show significant improvement of fatigue in comparison with those treated with csDMARDs. Further studies are needed to determine if biologics improve fatigue, and whether the improvement results from a direct action on fatigue or indirectly through reduction in disease activity.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3351

POS0635 COMPARING THE ULTRASONOGRAPHIC EVALUATION IN PATIENTS WITH JAPANESE RHEUMATOID ARTHRITIS BETWEEN BARICITINIB AND TNF ANTAGONIST THERAPY

Y. Kanayama[1], A. Nagata[2], M. Shimotake[2], F. Miyachi[2], K. Fujita[2], M. Koyama[2], S. Uno[2]. [1]*Toyota Kosei Hospital, Orthopedic Surgery and Rheumatology, Toyota, Japan*; [2]*Toyota Kosei Hospital, Clinical Technology, Toyota, Japan*

Background: Baricitinib (BAR) and TNF antagonist are the important therapeutic agent for the treatment of rheumatoid arthritis.However there is still few studies of improvement of ultrasonographic findings in RA treated comparison with BAR and TNF.
Objectives: To evaluate the clinical efficacy of BAR and TNF therapy patients with rheumatoid arthritis (RA) using ultrasonography (US).
Methods: Participants comprised 16 and 45 Japanese RA patients who had recently received BAR and TNF. All patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria. Patients underwent clinical and laboratory assessments every 4 weeks from baseline to 24 weeks, and US assessments at baseline, 4, 12 and 24 weeks. Gray scale (GS) and power doppler (PD) signals were scored using a semi-quantitative scale from 0 to 3 at 26 (0-78) synovial sites (22 joints) in the following joints: bilateral first to fifth metacarpopharangeal (MCP) joints (dorsal recess); first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) (dorsal recess) joints; and the wrists (dorsal radial, median and ulnar). We evaluated the improvement of GS and PD score from baseline to week 24.
Results: In the patients receiving BAR (n=16) and TNF (n=45), the mean age was 55.9 vs 54.6 years old (p=0.682), disease duration was 10.2 vs 6.1 years (p=0.094), the rate of MTX use was 75% vs 89% (p=346), the mean MTX dose was 9.3 vs 10.2 mg/w (p=0.443), the rate of ACPA positive was 94% vs 82% (p=0.476), DAS28-ESR was 4.25 vs 4.61 (p=0.289), CDAI was 15.8 vs 18.5 (p=0.210), GS score was 21.6 vs 16.3 (p=0.436) and PD score was 15.0 vs 9.5 (p=0.260). The degree of improvement respective changes in GS and PD score after 4, 12 and 24 weeks were as follows: GS: -7.2 vs -3.7 (p=0.268) and PD: -7.6 vs -2.3 (p=0.158) after 4 weeks, GS: -10.9 vs -5.0 (p=0.161) and PD: -9.2 vs -3.8 (p=0.049) after 12 weeks, GS: -12.9 vs -6.1 (p=0.485) and PD: -11.3 vs -5.7 (p=0.062) after 24 weeks between BAR and TNF (Fig.1, 2). Next, The improvement rate of respective changes in GS and PD score after 4, 12 and 24 weeks were as follows: GS: -23.8% vs -11.6% (p=0.580) and PD: -30.3% vs -16.5% (p=0.343) after 4 weeks, GS: -39.6% vs -15.6% (p=0.129) and PD: -47.1% vs -30.8% (p=0.210) after 12 weeks, GS: -52.2% vs -22.2% (p=0.248) and PD: -77.1% vs -50.1% (p=0.048) after 24 weeks between BAR and TNF.
Conclusion: The present study provides evidence supporting both the BAR and TNF therapy showed improvement effect over time, but in a comparison between BAR and TNF, the PD score of BAR showed a siginificant improvement effect compared to TNF at 12 and 24 weeks. It was suggeted that BAR may improve inflammatory synovitis earlier compared to TNF.

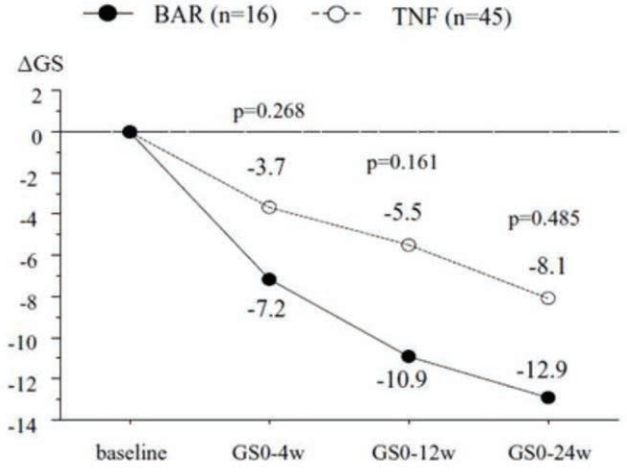


Figure 1 : The degree of improvement respective changesin GS score from baseline to Week 24 between BAR and TNF patients

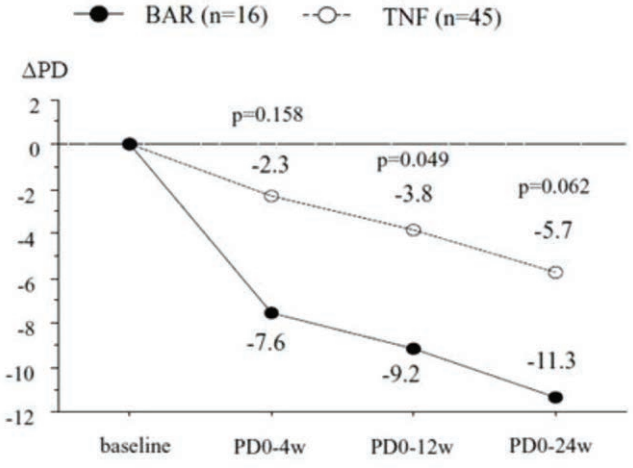


Figure 2 : The degree of improvement respective changesin PD score from baseline to Week 24 between BAR and TNF patients

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3483

POS0636

INFLUENCE OF DEMOGRAPHIC AND DISEASE RELATED FACTORS ON EFFICACY OF INFLIXIMAB OR GOLIMUMAB IN RHEUMATOID ARTHRITIS. A META-ANALYSIS ON RANDOMIZED PLACEBO-CONTROLLED TRIALS

M. A. Sparfel[1], S. Derolez[1], J. Law-Wan[1], N. Azzopardi[2], P. Goupille[1], D. Mulleman[1], T. Bejan-Angoulvant[3]. [1]*Université de Tours, EA 7501, Service de Rhumatologie CHRU de Tours, Tours, France*; [2]*Université de Tours, EA 7501, ERL CNRS 7001, Tours, France*; [3]*Université de Tours, EA 4245, Service de Pharmacologie Clinique, CHRU de Tours, Tours, France*

Background: TNF inhibitors have changed the course of rheumatoid arthritis (RA). Yet, detailed analysis on factors influencing clinical response to TNF inhibitors in RA is lacking.
Objectives: Herein we aimed at studying the impact of demographics and disease-related factors on therapeutic response to golimumab and infliximab in RA.
Methods: Randomized clinical trials (RCTs) that evaluated golimumab and infliximab versus placebo or conventional therapy were sought. We selected the following factors: age, sex, ethnicity, body mass index (BMI), smoking status, physical activity, disease duration, disease activity at baseline, presence of auto-antibodies. We studied the impact of these factors on clinical response using firstly aggregate data in a Mantel-Haenszel random effects model, and secondly individual data in a multivariate regression model.
Results: Individual data from 8 RCTs, 2 on infliximab (n=1477) and 6 on golimumab (total =3041) were obtained. In the aggregate model analysis, none of the selected factors had a significant impact on clinical response. In the multivariate analysis, male sex and physical activity were significantly associated with a lower DAS28-CRP after 6 months of treatment (regression coefficients -0.264 ($p<0.001$) and -0.193 ($p=0.004$) respectively), while a high initial DAS28-CRP was significantly associated with a higher DAS28-CRP (regression coefficient 0.579 ($p<0.001$)). The baseline disease activity was the only significant interaction factor with the effect of the treatment.
Conclusion: Male gender and practicing physical activity are associated with lower disease activity 6 months after golimumab or infliximab initiation. High baseline disease activity significantly influences negatively the effect of the treatment on disease activity score.
Acknowledgements: This study, carried out under YODA Project 2018-2931, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C. The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C.
Disclosure of Interests: Marc-Antoine SPARFEL: None declared, Sophie Derolez: None declared, Johan Law-Wan: None declared, Nicolas Azzopardi: None declared, Philippe Goupille Speakers bureau: Abbvie, Biogaran, BMS, Hospira, Janssen, MSD, Pfizer, Sanofi-Genzyme, UCB, Consultant of: Abbvie, Biogaran, BMS, Hospira, Janssen, MSD, Pfizer, Sanofi-Genzyme, UCB, Grant/research support from: Clinical trials sponsored by Abbvie, Roche, BMS, Boehringer, Lilly, Novartis, Pfizer, UCB, Janssen and MSD. Invitation to an international congresses by MSD, Roche, BMS and Abbvie, Denis Mulleman Speakers bureau: Pfizer and Novartis, Consultant of: Pfizer and Novartis, Grant/research support from: Invitation to an international congress by Janssen-Cilag, Theodora Bejan-Angoulvant: None declared
DOI: 10.1136/annrheumdis-2021-eular.3565

POS0637

INCIDENCE AND DETERMINANTS ASSOCIATED WITH RETRANSITIONING FROM BIOSIMILAR SB4 TO ORIGINATOR ETANERCEPT

R. Meijboom[1,2], H. Gardarsdottir[2,3,4], M. Becker[1,5], S. Ten Wolde[6], T. Egberts[2,3], T. Giezen[1,2,5]. [1]*Pharmacy Foundation of Haarlem Hospitals, Pharmacy Foundation of Haarlem Hospitals, Haarlem, Netherlands*; [2]*Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht, Netherlands*; [3]*University Medical Center Utrecht, Department of Clinical Pharmacy, Utrecht, Netherlands*; [4]*University of Iceland, Department of Pharmaceutical Sciences, Reykjavik, Iceland*; [5]*Spaarne Gasthuis, Department of Clinical Pharmacy, Haarlem and Hoofddorp, Netherlands*; [6]*Spaarne Gasthuis, Department of Rheumatology, Haarlem, Netherlands*

Background: The market entry of the etanercept biosimilar SB4 (BS-ETA) reduced prices; and, therefore, many patients in clinical practice are transitioned from originator etanercept (OR-ETA) to BS-ETA. However, previous studies demonstrated that 2.7-17.1% of patients who transitioned from OR-ETA to BS-SB4, retransitioned to OR-ETA (i.e. restarted originator), which might reduce the (financial) benefits of biosimilars. Insight in the incidence of retransitioning and characteristics of patients who are most likely to retransition, can provide lessons to clinicians for successful introduction of biosimilars.
Objectives: To assess the incidence of retransitioning from BS-ETA to OR-ETA in patients with a rheumatic disease (RD) and to identify determinants thereof.
Methods: All patients diagnosed with RD who transitioned in 2016 from OR-ETA to BS-ETA in a Dutch general teaching hospital (the Spaarne Gasthuis, Haarlem/Hoofddorp) were included in this cohort study. All patients were followed until retransitioning, switching to another biological, discontinuing of biological treatment death, loss to follow up or until censor date. The incidence of retransitioning and duration of BS-ETA use was assessed using the Kaplan-Meier method. Potential determinants for retransitioning, including age, gender, BS-SB4 dosing interval, use of other biologicals prior to OR-ETA, initiation or intensification of corticosteroids or immunomodulators, hospitalisations and the number of outpatient visits to the rheumatology department, were assessed in a nested case control study, using (multivariate) conditional logistic regression.
Results: In total, 342 patients (median age 57.8 years, 53.5% females, median follow-up 2.7 years) were included. 9.4% of patients had retransitioned to OR-ETA one year after transitioning. Additionally, one year after transitioning 69.7% of patients were still treated with BS-ETA, 3.8% switched to other treatment and 17.1% discontinued all biological treatment. At the end of follow-up (median 2,7 years), 46 patients (13.5%) retransitioned to OR-ETA; median time until retransitioning was 0.50 (IQR 0.98) years.
Univariate determinants for retransitioning included female gender (OR 2.37, 95% CI 1.18-7.74), initiating or intensifying corticosteroids or immunomodulators (OR 3.24, 95% CI 1.38-7.63) and number of visits to the rheumatology department (OR 2.32, 95% CI 1.70-3.17). Based on the multivariate analysis, only the number of visits to the rheumatology department was associated with retransitioning (OR 2.19 95% CI 1.60-3.00), as demonstrated in Table 1.
Conclusion: When introducing BS-SB4 in clinical care, clinicians should anticipate on about one in seven patients retransitioning to OR-ETA. These patients might be identified prior to retransitioning based on their contacts to the rheumatology department. Information specifically aiming for their concerns might prevent them from retransitioning. However, more qualitative studies are needed to explore patients' underlying reasons for retransitioning, in order to improve the introduction of biosimilars in clinical care.

Table 1. Determinants for retransitioning

	Cases n = 46	Controls n = 184	OR (univariate) 95% CI	OR (multivariate) 95% CI
Age, years (median, IQR)	59.0 (16.5)	56.5 (22.3)	1.01 (0.98–1.03)	-
Gender				
Male	15 (32.6%)	97 (52.7%)	Ref	Ref
Female	31 (67.4%)	87 (47.3%)	2.37 (1.18–7.74)	1.36 (0.60–3.07)
BS-SB4 dosing interval (index date)				
7 days	35 (76.1%)	129 (70.1%)	Ref	-
>7 days	11 (23.9%)	55 (29.9%)	0.72 (0.33–1.56)	
Previous use other biological				
No	43 (93.5%)	172 (93.5%)	Ref	-
Yes	3 (6.5%)	12 (6.5%)	1.00 (0.27–3.74)	
Initiation/ intensification corticosteroid/ immunomodulator				
No	35 (76.1%)	168 (91.3%)	Ref	Ref
Yes	11 (23.9%)	16 (8.7%)	3.24 (1.38–7.63)	2.31 (0.84–6.38)
Hospitalisation				
No	41 (89.1%)	166 (90.2%)	Ref	-
Yes	5 (10.9%)	18 (9.8%)	1.12 (0.40–3.18)	
No. visits rheumatology department				Ref
(median, IQR)	2 (2)	0 (1)	2.32(1.70–3.17)	2.19 (1.60–3.00)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3636

POS0638

DISEASE SEVERITY AND OUTCOMES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS WHO RECEIVE A NEWLY APPROVED BIOLOGIC: REAL-WORLD US EXPERIENCE WITH SARILUMAB FROM THE ACR RISE REGISTRY

S. Fiore[1], L. Chen[2], C. Clinton[2], H. Yun[2], A. Praestgaard[3], K. Ford[2], J. Curtis[2]. [1]*Sanofi, Sanofi, Bridgewater, United States of America*; [2]*University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, United States of America*; [3]*Sanofi, Sanofi, Cambridge, United States of America*

Background: Patients with rheumatoid arthritis (RA) who have received multiple biologics or targeted therapies over time tend to have more refractory and more severe disease, which may lead to worse clinical response to treatment.
Objectives: We used data from the ACR RISE registry to assess whether disease severity was greater in those who received sarilumab shortly after its FDA approval (May 2017) than in subsequent time periods and to evaluate the effectiveness of sarilumab in populations with various degrees of disease severity.
Methods: Patients with RA who initiated sarilumab treatment in the period 2017-2020 were identified in the ACR RISE registry and divided into Cohort 1 (2017, year of the FDA approval) and the calendar year-based Cohorts 2-4 (2018-2020). Patient demographics, RA-related features, and comorbidities were determined using data prior to sarilumab initiation. The cohorts were compared using chi-square test (categorical variables) and a nonparametric test (continuous variables). Sarilumab effectiveness was assessed using 3 cohorts assembled based on progressively restrictive criteria: Active Disease cohort (Clinical Disease Activity Index [CDAI] >10 or Routine Assessment of Patient Index Data 3 [RAPID3] >6, and C-reactive protein, if measured, ≥8 mg/L), TARGET Eligibility cohort (patients who satisfied enrolment criteria for TARGET,[1] a Phase 3 sarilumab trial in patients with RA and an inadequate response to TNF inhibitors), and TARGET Baseline cohort (patients from TARGET Eligibility cohort with characteristics weighted to match those from the TARGET trial baseline,[1] using the matching-adjusted indirect comparison method[2]). In all 3 effectiveness cohorts, mean changes in CDAI and RAPID3 at 6 and 12 months post-initiation of sarilumab were evaluated using a model adjusted for baseline score, age, sex, race, calendar year, and seropositivity.
Results: A total of 2949 patients, treated by 585 rheumatologists, initiated sarilumab treatment in the period 2017–2020. The 4 yearly cohorts were relatively similar in terms of patients' age, sex, race, and most clinical characteristics. However, patients receiving sarilumab shortly after FDA approval (Cohort 1) had more ambulatory visits, a greater number of previously used non-TNFi biologics (particularly tocilizumab), and a higher comorbidity burden, and were more likely to be current users of glucocorticoids or opioids than sarilumab initiators in the subsequent 3 years. In the 3 cohorts used to assess sarilumab effectiveness, the greatest improvement was observed in the TARGET Baseline cohort, which also had the greatest mean baseline CDAI score (43), compared with the other two (24 both).
Conclusion: In this real-world cohort, we observed modest evidence for channeling of patients with greater RA severity and greater prior exposure to non-TNFi biologics to sarilumab shortly after its FDA approval. This cohort effect did not diminish the effectiveness of sarilumab. All cohorts showed improvement, with the greatest clinical improvement observed in the cohort with the highest baseline CDAI score who most closely resembled those enrolled in a phase 3 trial of patients with an inadequate response to TNF inhibitors.
REFERENCES:
[1] Fleischmann R, et al. *Arthritis Rheumatol* 2017;69:277-290.
[2] Signorovitch JE et al. *Value Health* 2012;15:940-7.

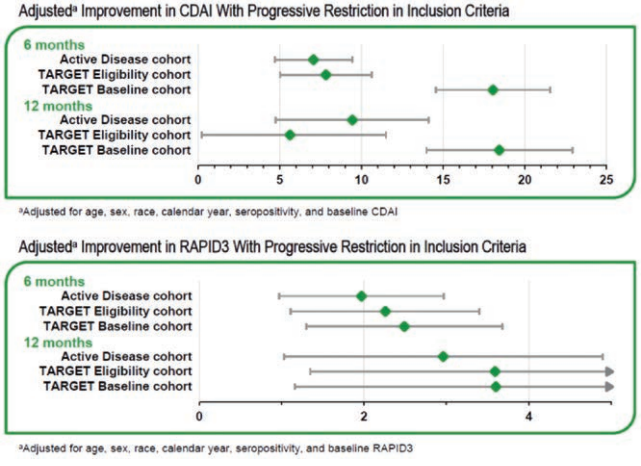


Figure 1. Adjusted improvements in CDAI and RAPID3

Acknowledgements: This study was sponsored by Sanofi. Medical writing support was provided by Vojislav Pejović, PhD (Eloquent Medical Affairs, division of Envision Pharma Group) and funded by Sanofi.
Disclosure of Interests: Stefano Fiore Employee of: Sanofi, Lang Chen: None declared, Cassie Clinton Consultant of: Information available in profile, Huifeng Yun Grant/research support from: Research support for Pfizer, Amy Praestgaard Employee of: Sanofi, Kerri Ford Employee of: Sanofi, Jeffrey Curtis Consultant of: Received consulting and research grants from AbbVie, Amgen, BMS, Lilly, Gilead, GSK, Janssen, Myriad, Pfizer, Roche, Samsung, Sandoz, Sanofi, UCB, Grant/research support from: Received consulting and research grants from AbbVie, Amgen, BMS, Lilly, Gilead, GSK, Janssen, Myriad, Pfizer, Roche, Samsung, Sandoz, Sanofi, UCB
DOI: 10.1136/annrheumdis-2021-eular.3655

POS0639 LONG-TERM EFFECTIVENESS OF THE RITUXIMAB HALF DOSE REGIMEN FOLLOWING A RESPONSE TO THE LICENSED DOSE IN RHEUMATOID ARTHRITIS

L. Garcia-Montoya[1,2], M. Y. Md Yusof[1,2], G. Eugénio[1,2], J. B. Candelier[1,2], S. Das[1,2], E. Vital[1,2], P. Emery[1,2]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*; [2]*Leeds Biomedical Research Centre, NIHR, Leeds, United Kingdom*

Background: Following initial treatment with rituximab (RTX) full dose (2x1000mg), B-cell numbers are often lower than baseline. The half dose regime (2x500mg) has been reported to be similarly effective [1]; however, there is limited long-term data on the effectiveness of switching to RTX half-dose from the real-world perspective.
Objectives: To compare the 3-year RTX regime retention between patients receiving retreatment with half-dose and full-dose of RTX, and assess factors associated with maintenance of 2x500mg, with a view to establish an optimal long-term retreatment strategy in RA.
Methods: An observational study was conducted on 755 consecutive RTX-treated RA patients in a single centre for over 20 years. Of these, 165/755 (22%) received at least one cycle of 2x500mg. Long-term effectiveness was assessed using RTX retention rate. Drug survival of patients treated with 2x500mg was compared with 200 RA patients receiving 2x1000mg throughout the study, matched to the number of cycle when the 2x500mg regime was initiated.
Results: Of the 165 patients who received 2x500mg, 81.8% were female; mean age was 63.4 (26-91) years; mean disease duration 15.5 (2-53) years; 57 (34.5%) were bDMARDs-naïve; 121 (74%) were on concomitant DMARDs and mean DAS-28 was 3.9 (SD 1.29) at the half dose initiation. At 3 years, the retention rate was 38% for patients recieving 2x500mg compared to 87% for those on 2x1000mg; HR for half dose discontinuation was 6.17 [95%CI (3.91-12.27); p<0.001] (Figure 1A).
The main reasons for 2x500mg discontinuation were poor EULAR response (30%); moderate EULAR response (30%); shorter duration of response compared to the full dose (22%); and incomplete B-cell depletion (17%). The majority of these patients (87.9%) were switched back to 2x1000mg, 5.1% received other bDMARDs and 7.1% did not receive further DMARDs.
In multivariable analysis, previous TNFi use was associated with 3-year maintenance of the 2x500mg dose [OR 2.63 (1.12-6.10); p=0.024]; while higher plasmablasts at 2x500mg initiation was associated with shorter maintenance of this regime [OR 0.78 (0.67-0.97); p=0.028].
There were no significant differences in 5-year RTX retention rates between patients receiving 2x500mg and switched back to 2x1000mg vs those receiving 2x1000mg throughout the study (Log-Rank=0.186) (Figure 1B).
Conclusion: The use of RTX half-dose regimen was associated with poor retention at 3 years. Nevertheless, where loss of effectiveness occurs post-2x500mg initiation, switching back to 2x1000mg appears to be a pragmatic option. Patients with previous TNFi exposure and lower plasmablasts may be most suited to be commenced on the 2x500mg dose for long-term disease control.
REFERENCES:
[1] Mariette X, et al. ARD 2014

Figure 1A

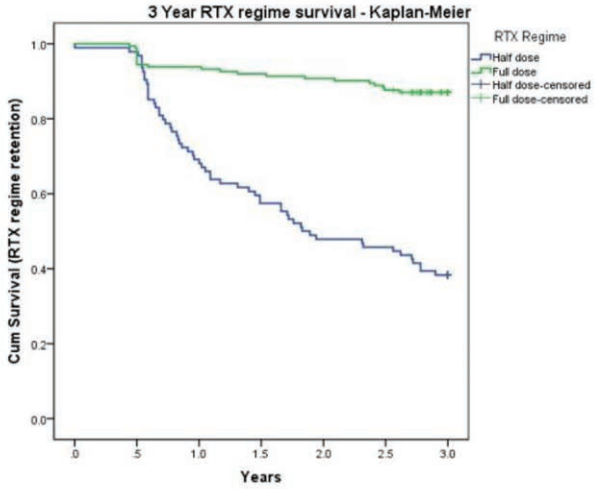
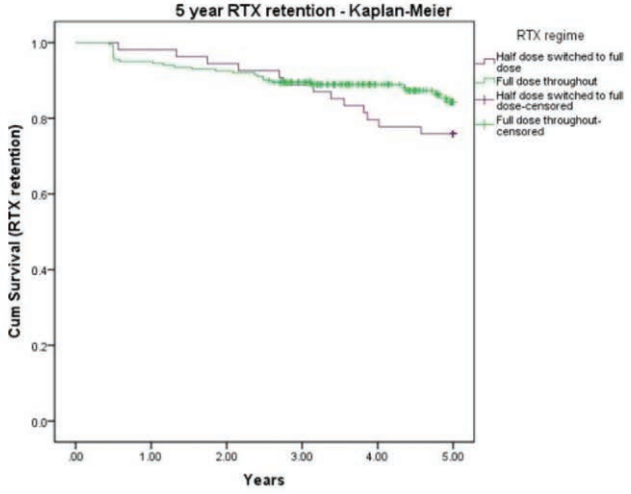


Figure 1B



Acknowledgements: Leeds Cares
Disclosure of Interests: Leticia Garcia-Montoya: None declared, Md Yuzaiful Md Yusof: None declared, Gisela Eugénio: None declared, Jean Baptiste Candelier: None declared, Sudipto Das Speakers bureau: Dr Das has received honoraria from Roche, Edward Vital Speakers bureau: Dr Vital has received honoraria from Roche, Consultant of: Dr Vital has received honoraria a from Roche, Grant/research support from: Dr Vital has received research grant support from Roche, Paul Emery Speakers bureau: Professor Emery has received honoraria from Roche, Consultant of: Professor Emery has received consultant fees from Roche, Grant/research support from: Professor Emery has received research grants paid to his employer from Roche.
DOI: 10.1136/annrheumdis-2021-eular.3691

POS0640

EFFECTIVENESS AND SAFETY OF ORIGINAL AND BIOSIMILAR ETANERCEPT IN BDMARD-NAÏVE PATIENTS IN A REAL-WORLD COHORT OF PORTUGAL

A. S. Pinto[1,2], M. Cunha[3], F. Oliveira Pinheiro[4], M. Bernardes[4], H. Assunção[5], J. Martinho[6], M. C. Tenazinha[6], A. M. Duarte Monteiro[6], S. Silva[7], F. R. Martins[8], L. Silva[9], M. Couto[10], M. Faria[11], F. Araújo[12], T. Fontes[13], D. Faria[2], J. Tavares-Costa[2]. [1]*Unidade Local de Saúde da Guarda, Rheumatology, Guarda, Portugal*; [2]*Unidade Local de Saúde do Alto Minho, Rheumatology, Ponte de Lima, Portugal*; [3]*Garcia de Orta Hospital, Rheumatology, Almada, Portugal*; [4]*Centro Hospitalar Universitário de São João, Rheumatology, Porto, Portugal*; [5]*Centro Hospitalar Universitário de Coimbra, Rheumatology, Coimbra, Portugal*; [6]*Centro Hospitalar Universitário Lisboa Norte, Rheumatology, Lisboa, Portugal*; [7]*Centro Hospitalar Baixo Vouga, Rheumatology, Aveiro, Portugal*; [8]*Centro Hospitalar Universitário do Algarve, Rheumatology, Faro, Portugal*; [9]*Centro Hospitalar Trás-Os-Montes e Alto Douro, Rheumatology, Vila Real, Portugal*; [10]*Centro Hospitalar Tondela-Viseu, Rheumatology, Viseu, Portugal*; [11]*Hospital Central do Funchal, Rheumatology, Funchal, Portugal*; [12]*Hospital de Sant'Ana, Rheumatology, Parede, Portugal*; [13]*Hospital do Divino Espírito Santo, Rheumatology, Ponta Delgada, Portugal*

Background: The patent expiration of the original etanercept in Europe has facilitated the development of biosimilar products. Non-significant differences in efficacy and safety were noted in clinical trials which are not expected to influence clinical performance. Nonetheless, daily practice data should be gathered to support the claim for biosimilarity.
Objectives: To compare the effectiveness and safety of original and biosimilar etanercept, in biological-Disease Modifying Antirheumatic Drug (bDMARD)-naïve patients.
Methods: A retrospective multicenter non-interventional study, using data collected prospectively from Reuma.pt (The Rheumatic Diseases Portuguese Register) was done, including patients with: age ≥ 18 years old; diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Spondyloarthritis (SpA) (axial or peripheral); active disease who initiated treatment with etanercept as first line of biological treatment after 2010. Kaplan-Meyer was used to calculate the persistence rate in treatment. Disease activity at baseline and follow-up data at 6, 12, 18 and 24 months of treatment was compared using the chi-square for categorical variables and t-student or Mann-Whitney tests for continuous variables. Reasons for discontinuing therapy were summarized using descriptive statistics. Statistical significance was assumed for 2-sided p-values >0.05.
Results: We included 1694 patients (413 on biosimilar and 1280 on original etanercept) 864 with RA, 335 with PsA and 494 with SpA. The population's baseline characteristics were not significantly different among both groups, except concomitant treatment in RA (higher use of conventional DMARDs in biosimilar group and higher use of NSAIDs in original group) and in SpA patients (higher use of corticosteroids in original group).
At baseline, a higher joint count was found in patients treated with original etanercept with a statistical difference for swollen (p=0.03) and tender (p=0.01) joints count (SJC and TJC, respectively) in RA and in TJC in SpA patients (p=0.02). In RA patients, CDAI and SDAI were higher in patients who started original (p=0.03; p=0.04, respectively). Pain measured by visual analogic scale was higher in SpA patients treated with biosimilar (p=0.03).
The 3-year PR was not significantly different between both treatment groups in RA, PsA and SpA (Figure1). In RA, PR in biosimilar was 72.6%, with a median time-on-drug (TOD) of 28.3 months; for original etanercept PR was 63.6%, with a median TOD of 27.4 months (p=0.566). In PsA patients, the PR for biosimilar was 70.6%, with a median TOD of 27.6 months, and in original drug 67.0%, with a median TOD of 28.1 months (p=0.743). In SpA patients, the PR were 78.4% for biosimilar (median TOD of 27.4 months) and 71.5% for original treatment (median TOD of 28.0 months (p=0.816)).

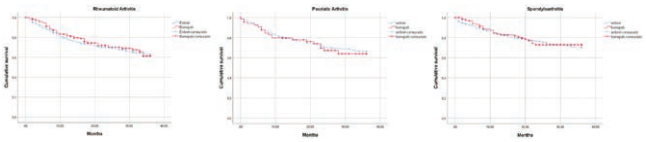


Figure 1. Drug survival in biosimilar and original etanercept in Rheumatoid Arthritis, Psoriatic Arthritis and Spondyloarthritis

In RA patients, we did not find differences between the two treatment groups for the proportion of patients in remission or low disease activity by CDAI ≤10, SDAI≤11 or DAS28 <3.2 at 6, 12, 18 and 24 months of treatment. For PsA, no differences were found in the same timelines for DAPSA≤14, DAS28<3.2, BASDAI<4, ASDAS<2.1 or PsARC response. Also, in SpA patients, no differences were found in BASDAI<4, BASFI<4, ASDAS<2.1, ASDAS response and BASDAI response in all the timelines with the exception of BASDAI response at 18 months, which was achieved in fewer patients in biosimilar therapy (p=0.02).
Overall, 535 (31.6%) patients stopped etanercept (428 patients on original and 107 patients on biosimilar). Discontinuations due to inefficacy were the most frequent, but there were no significant differences between both groups as for adverse events. Discontinuations due to "other reasons" were higher for the original group, both in RA (p=0.01) and in SpA (p=0.04).
Conclusion: Biosimilar and original used as first-line biological treatment showed similar effectiveness and safety in our long-term cohort of patients with RA, PsA, and SpA
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3706

POS0641

INCIDENCE OF GASTRO-INTESTINAL COMPLICATIONS IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING BIOLOGICAL DMARDS IN OBSERVATIONAL COHORT STUDIES: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

A. Charlotte[1], D. Jerome[2], C. Lukas[3], C. Rempenault[3], A. Constantin[4], J. Morel[3]. *[1]Lapeyronie Hospital, Montpellier, Rheumatology Department, Montpellier, France*; *[2]Purpan University Hospital and University Toulouse III – Paul Sabatier, Rheumatology Department, Montpellier, France*; *[3]Lapeyronie Hospital, Montpellier, Rheumatology Department, Montpellier, France*; *[4]Purpan University Hospital and University Toulouse III – Paul Sabatier, Rheumatology Department, Toulouse, France*

Background: Rheumatoid arthritis (RA) patients are at increased risk of gastro-intestinal (GI) perforations compared with non-RA patients, resulting in increased mortality. Clinical trials, post-marketing studies and registries have reported an increased risk of GI perforations in RA patients treated with tocilizumab.
Objectives: The aim of our study was to assess the incidence of GI complications among RA patients receiving bDMARDs in observational cohort studies
Methods: A systematic literature review was carried out through September 2020 on the Pubmed, Embase and international congress databases, selecting observational cohort studies assessing the incidence of GI complications, including perforations and diverticulitis, in RA patients receiving bDMARDS. Keywords were "gastrointestinal perforation", "gastrointestinal disease", "diverticulitis", "biological DMARDs" and "rheumatoid arthritis" with no publication date limit. Studies were selected independently by two readers. Data were extracted by one investigator and independently checked by another. A meta-analysis was performed with Review Manager Software, with random-effects models, whenever methodologically possible and relevant.
Results: The literature search revealed 232 articles and abstracts of potential interest, and further examination resulted in 7 studies fulfilling required criteria. Among bDMARDs, Tocilizumab was associated with an increased incidence of GI perforations, with an overall incidence of 2.40 per 1000 person-years (95% confidence interval [95% CI] 1.45-3.35). The overall incidences of GI perforations were 1.01 per 1000 PY [0.75-1.27] for TNF inhibitors, 1.07 per 1000 PY [0.53-1.62] for abatacept and 1.12 per 1000 PY [0.16-2.08] for rituximab (Figure 1). In RA patients treated with tocilizumab, most of the perforations were located in the lower GI tract, with an incidence of 2.24 per 1000 PY [1.24-3.52]. The incidences of upper GI perforations were similar across the different bDMARDs. The incidences of diverticulitis were 4.99 per 1000 PY [4.08-5.99] in RA patients receiving tocilizumab and 1.81 per 1000 PY [1.47-2.19] in those receiving TNF inhibitors.
Conclusion: In our meta-analysis, focused in RA patients receiving bDMARDs in observational cohort studies, tocilizumab was associated with an increased incidence of GI perforations, mainly located in the lower GI tract. An history of diverticulitis and long-term corticosteroid therapy were associated with an increased risk of GI perforations.

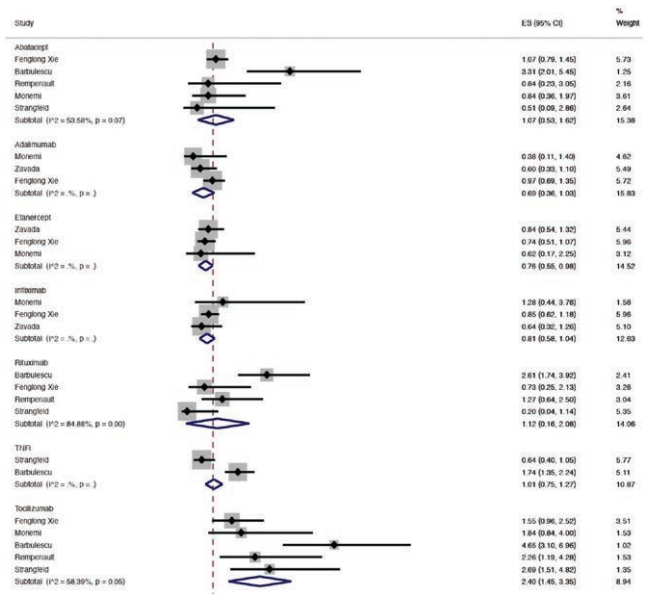


Figure 1. Meta-analysis of the incidences of gastro-intestinal perforations in RA patients receiving bDMARDs in observational cohort studies

Acknowledgements: We cannot express enough thanks to PhD Constantin and PhD Morel for their support and encouragement.
We would like to address a special word of thanks to PhD Lukas for his accuracy. Special Thanks to Claire Rempenault for her precious advices. You have been a role model for us.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3755

POS0642

THE IMPACT OF AGE ON DISCONTINUATION OF BIOLOGIC DMARDs IN PATIENTS WITH RHEUMATOID ARTHRITIS

V. Rivera Teran[1], S. Sicsik[1], D. Vega-Morales[2], F. Irazoque-Palazuelos[1], D. Miranda[2], J. C. Casasola[1], S. Carrilo[2], A. Peña[1], A. Castillo Ortiz[2], O. E. Muñoz-Monroy[1], S. Duran Barragan[2], A. Paz[1], E. Torres Valdéz[2], L. F. Valdés Corona[1], D. X. Xibille Friedmann[2], E. Zamora[1], A. Ramos[2], N. Santana[1], M. Vazquez[2], F. Guerrero[1], C. Zepeda[2], K. Alvarado[1], M. Rivera[2], D. Alpizar-Rodriguez[1]on behalf of Mexican Registry of Adverse Events involving Biological Therapies in Rheumatic Diseases (BIOBADAMEX). *[1]Colegio Mexicano de Reumatología, Unidad de Investigación, Mexico City, Mexico*; *[2]Colegio Mexicano de Reumatología, Unidad de Investigación, Ciudad de México, Mexico*

Background: Rheumatoid arthritis (RA) is the most common autoimmune disease. Older patients treated with biologic DMARDs (bDMARDs) are at a significantly greater risk of adverse effects (AEs) [1]. However, the rate of drug discontinuation because of adverse effects caused by bDMARDs has not differed in elderly compared to younger patients in different registries.
Objectives: Determine if drug discontinuation of bDMARDs differs by age in patients with rheumatoid arthritis in the Mexican Adverse Events Registry (BIOBADAMEX).
Methods: BIOBADAMEX is a Mexican ongoing cohort of patients using bDMARDs since 2016. In this analysis we included all patients with diagnosis of RA with at least two assessments. Survival on bDMARDs was estimated using Kaplan-Meier analysis. Predictors of discontinuation, including age older than median age in the sample were investigated by Cox regression analyses.
Results: Among 743 patients in the registry, 497 had RA diagnosis, from which, 214 had at least two assessments. At baseline, patients had a median (IQR) age of 53.4 (45-61) years old, median disease duration of 10.7 (6-17) months and median DAS28 of 4.7 (3-6). Conventional DMARDS were used by 185 (87%) patients and 94 (44%) patients used corticosteroids. Comorbidities were present in 194 (91%). The most common bDMARDs received at baseline were abatacept 59 (27%), tocilizumab 45(21%), adalimumab 31 (15%) and certolizumab 30 (14%). At the time of analysis, the median bDMARDs treatment duration was 21.0(13-34) months, 128 (59%) had discontinued treatment, 66 for inefficacy, 32 for adverse events and 30 for others. Fig 1 shows discontinuation rate curves in patients younger and older than median age. Cox proportional-hazards demonstrated no significant differences regarding age older than median age (HR 1.1, 95% CI 0.8-1.4, p=0.7), female sex (HR 1.2, 95% CI 0.7-1.9, p=0.44), use of corticosteroids (HR 1.2, 95% CI 0.9-1.6, p=0.20), comorbidities (HR 0.9, 95% 0.6-1.5, p=0.78), DAS28 (HR 0.9, 95% 0.9-1.1, p=0.93) or other factors.
Conclusion: This analysis did not show a role of age on discontinuation of bDMARDs in Mexican RA patients. Further longitudinal analyses will be performed including more patients to assess retention rate of bDMARDs and identify predictive variables of discontinuation in Mexican population.

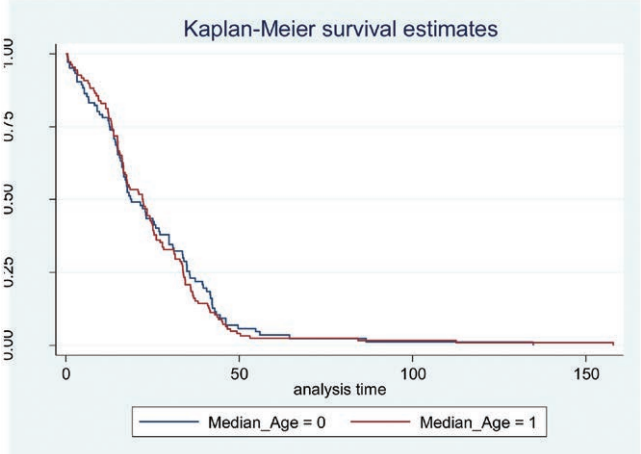


Figure 1. Discontinuation rate curves in patients younger and older than median age (< 53.4 and >=53.4 years old)

REFERENCES:
[1] Akter R, et al. Can Geriatr J. 2020 May 1;23(2):184-189.
[2] Ikari Y, et al. Medicine (Baltimore). 2020 Dec 24;99(52):e23861.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3759

POS0643 ARE BIOLOGIC AND TARGETED SYNTHETIC DMARDS SAFE TO USE IN PATIENTS WITH RENAL IMPAIRMENT?

F. Rees[1], M. Jasim[1]. [1]*Cannock Chase Hospital, Rheumatology, Cannock, United Kingdom*

Background: Chronic kidney disease (CKD) is defined as a permanent (minimum three month) reduction in glomerular filtration rate. [1] 10-30% of rheumatoid arthritis (RA) patients have CKD, compared to 5% of the general population.[1] There are several causes of CKD associated with RA including persistent inflammation, cardiovascular risk factors, frequent use of non-steroidal anti-inflammatory drugs and amyloidosis.[1] CKD in RA patients is associated with increased mortality.[2]
The use of biologic and targeted synthetic DMARDs for treating RA has increased significantly in recent years. Studies have shown these therapies might reduce the risk of developing CKD in RA. [3] However, conversely, biologics have been linked to the development of glomerulonephritis.[4]
Surprisingly few studies have explored the use of biologics in patients with pre-existing renal disease and whether they contribute to renal impairment themselves.
Objectives: Our objectives were to explore the renal safety profile of biologic and targeted synthetic DMARDs in a real-world cohort of RA patients with and without pre-existing CKD.
Methods: A retrospective observational study was completed using the Biologic Therapy Database at Cannock Chase Hospital. Inclusion criteria were a diagnosis of RA and current treatment with a biologic or targeted synthetic DMARD.
Demographic data, renal function at biologic initiation and any deterioration of renal function were among the recorded information for each patient. Patients with insufficient information available via electronic patient records were excluded.
Results: 998 RA patients on biologics were identified, of whom 213 were excluded. Of the 785 remaining patients, a 3:1 female to male ratio was noted with a mean age of 62. 40% of patients were on an anti-TNF, 22% rituximab, 15% abatacept, 15% JAK inhibitors and 9% anti-IL6 respectively. At biologic initiation 92% of the patients had a GFR of >60 ml/min per 1.73m^2, 4.8% had a GFR of 30-60 (CKD stage 3a-3b), <1% stage 4 CKD. No patients in the cohort had CKD stage 5 at biologic initiation.
Overall, 13 patients had significant pre-existing CKD (eGFR <45) of these, 6 were treated with abatacept. 7/13 patients had no co-morbid risk factors for CKD – of those remaining, 2 were hypertensive, 2 diabetic and 2 both. None of these 13 patients experienced a drop in renal function by more than 1 stage since initiation of current biologic.
Of those patients without prior CKD at the point of biologic initiation (GFR >45), only 15 patients (2%) developed new renal impairment whilst on biologic treatment. 10 patients' renal function dropped by one stage and five patients by two stages. Crucially, 12 of the 15 patients were aged ≥75yrs and 10 patients had at least one other associated risk factor (e.g. diabetes). Only one patient in the cohort developed renal impairment as a direct result of a biologic - minimal-change disease secondary to etanercept.
Conclusion: Our findings indicate that biologic treatments have a good renal safety profile – even with pre-existing CKD. RA patients most at risk of developing CKD whilst on biologics are likely to have other risk factors such as diabetes or hypertension. As previously stated, there is a very rare association of anti-TNF biologics causing glomerulonephritis.

REFERENCES:
[1] Couderc M, et al. Prevalence of Renal Impairment in Patients with Rheumatoid Arthritis: Results from a Cross-Sectional Multicenter Study. Arthritis Care Res. 2016 May 1;68(5):638–44.
[2] Chiu HY, et al. Increased risk of chronic kidney disease in rheumatoid arthritis associated with cardiovascular complications - A national population-based cohort study. PLoS One. 2015 Sep 25;10(9).
[3] Sumida K, et al. Treatment of rheumatoid arthritis with biologic agents lowers the risk of incident chronic kidney disease. Kidney Int. 2018 May 1;93(5):1207–16.
[4] Piga M, et al. Biologics-induced autoimmune renal disorders in chronic inflammatory rheumatic diseases: Systematic literature review and analysis of a monocentric cohort. Vol. 13, Autoimmunity Reviews. Elsevier; 2014. p. 873–9.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3817

POS0644 AIR POLLUTION IS A PREDICTOR OF POOR RESPONSE TO BIOLOGICAL THERAPIES IN CHRONIC INFLAMMATORY ARTHRITIDES

G. Adami[1], D. Gatti[1], A. Fassio[1], O. Viapiana[1], A. Giollo[1], E. Bertoldo[1], M. Rossini[1]. [1]*University of Verona, Rheumatology Unit, Verona, Italy*

Background: There is increasingly evidence that environmental air pollution is associated with both development of chronic inflammatory arthritides (CIA). The role of air pollutants on the treatment response of CIA (including psoriatic arthritis [PsA] and ankylosing spondylitis [AS]) is still unclear.
Objectives: The objective of the present study is to determine the association between the concentration of air pollutants and biological drug retention rates in CIA.
Methods: We retrieved longitudinal data of patients affected by CIA on biological therapies and of the daily concentration of air pollutants in the Verona area. We designed a case-crossover study to compare the exposure to pollutants in the 30-day and 60-day periods preceding a drug switch or swap due to disease progression referent to the 30-day and 60-day periods preceding a visit with stable treatment for at least 6 months.
Results: 1,286 patients with CIA (888 with RA, 260 with PsA and 138 with AS) with 5,454 follow-up visits were included in the study. 13,636 daily air pollution records were retrieved. We found an exposure-dependent relationship between exposure to air pollutants and CRP serum levels in CIA. At PM10 exposures of >50 µg/m3 and >40 µg/m3 we found a 150% and 65% higher risk of having CRP above 5 mg/L respectively (OR 2.564, 95% CI 2.114-3.110 and OR 1.659, 95% CI 1.440-1.910, respectively.). If the threshold was set at >30 µg/m3 of PM10 (below the European Union health protection limit) we still found a 38% higher risk of having altered CRP (OR 1.383, 95% CI 1.206-1.588). Among CIA patients, 280 patients (21.7%) had at least 2 follow-up visits with at least one drug switch or swap due to drug inefficacy and one visit with stable treatment for at least 6 months, serving as our sample for the case-crossover study. We found that air pollutants concentrations were higher before a switch or swap due to drug inefficacy (Figure 1A). Figure 1B shows the receiver operating characteristic (ROC) curve for the prediction of switch or swap due to drug inefficacy. Discriminatory capacity of disease activity alone was the highest (AUC 0.841) but when the prediction model included the concentrations of air pollutants in the 60 days before the visit the discriminatory capacity increased (AUC 0.879).
Conclusion: We found that environmental air pollution was a determinant of poor response to biological treatment in a cohort of patients with CIA followed over a 5-year period. Intervention aimed to decrease the fossil combustion emissions might have beneficial effects on biologics persistence rate of patients with CIA.

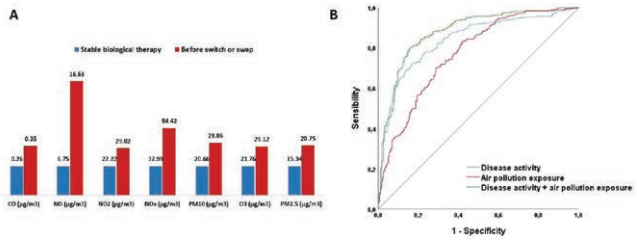


Figure 1. A) Mean concentrations of air pollutants in the 60-day period before switch or swap visit compared to the stable treatment visit. p <0.001 between all groups. B) Receiving operating characteristics (ROC) curves for the prediction of switch or swap due to drug inefficacy

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3863

POS0645 RITUXIMAB THERAPY IN THE INTERSTITIAL LUNG DISEASE OF RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

E. F. Vicente-Rabaneda[1], J. De la Macorra[1], J. P. Baldivieso[1], F. Gutiérrez-Rodríguez[1], A. García-Vadillo[1], R. Garcia de Vicuna[1], S. Castañeda[1]. [1]*Hospital Universitario de la Princesa, IIS-P, Rheumatology, Madrid, Spain*

Background: Interstitial lung disease (ILD) is a severe manifestation of rheumatoid arthritis (RA), linked to increased mortality. There is still no consensus on the best therapeutic strategy as there aren't yet randomized controlled trials.
Objectives: To analyze the available scientific evidence on the efficacy and safety of rituximab (RTX) treatment of interstitial lung disease (ILD) associated with rheumatoid arthritis (RA).
Methods: A systematic search was carried out in PubMed until April 2020 following the PRISMA recommendations. Studies were selected according to the

following inclusion criteria: (1) original research, including case series, case/control studies, cohort studies, and clinical trials; (2) population with RA and associated ILD, either monographically or together with other connective tissue diseases (CTD), provided that individualized data on patients with RA were provided; (3) patients treated with RTX; (4) objective and quantifiable results on the evolution of ILD after treatment with available data of FVC, DLCO and/or HRCT.

Results: Of the 64 papers identified, 9 articles were selected. The studies showed great heterogeneity in design, both in the sample selection criteria and in the objectives of the analysis. Most were observational, retrospective (n = 6) or prospective (n = 2) studies, with only one open prospective experimental study. Those focused on RA predominated, but 3 of them also included patients with other CTDs. The mean age of the patients in the different studies ranged between 52 and 70 years, predominantly women. 40-79% had a history of smoking and were mostly positive for rheumatoid factor (83-100%) and anti-CCP (82-100%). The most frequent radiological patterns were NSIP, UIP and undefined. The outcome measures were diverse: changes in respiratory function tests (LTF) and HRCT, incidence of pulmonary dysfunction, mortality rates, effect on glucocorticoid deprivation, delay in inclusion in the lung transplant list and/or serious adverse events. The initiation of RTX was motivated by pulmonary and/or joint pathology, in patients with failure to other synthetic or biological DMARDs. A total of 393 treatment cycles were collected in 114 patients, with a mean of 3.45 cycles per patient. The RTX regimen was 2 infusions of 1g 2 weeks apart in all patients, except for 1 who received the lymphoma-like regimen. With regard to the efficacy of the treatment with RTX, improvement and especially stabilization of HRCT and LFT predominated, with numerically greater improvement for DLCO than for FVC. There was also a favorable trend in the evolution of patients treated with RTX compared to controls, although it did not reach statistical significance, and a lower risk of deterioration of lung function in patients treated with RTX versus those who had received other DMARDs. The mortality rate found at 5 years was lower than that previously described for the disease and half for the patients treated with RTX compared to those treated with anti-TNF. The adverse events described in the studies did not show additional safety alerts to those already described for RTX.

Conclusion: RTX seems to be postulated as a promising therapy for patients with ILD associated with RA, showing a stabilizing effect on the lung function, with an acceptable safety profile. However, further research of higher methodological quality prospective studies is needed to confirm these favorable preliminary results.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4192

Rheumatoid arthritis - non biologic treatment and small molecules

POS0646 RAPID AND CONCURRENT IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES OF RHEUMATOID ARTHRITIS WITH BARICITINIB IN RA-BEAM

V. Strand[1], A. Sebba[2], B. Jia[3], J. Birt[3], A. Quebe[3], H. Zhang[4], P. C. Taylor[5]. [1]*Stanford University School of Medicine, Division of Immunology/Rheumatology, Palo Alto, United States of America*; [2]*University of South Florida, Department of Rheumatology, Tampa, United States of America*; [3]*Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, United States of America*; [4]*TechData Services, Statistics, King of Prussia, United States of America*; [5]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences and the Kennedy Institute of Rheumatology, Oxford, United Kingdom*

Background: The efficacy and safety of baricitinib (BARI), an oral selective Janus kinase (JAK)1/JAK2 inhibitor, were evaluated in the randomized, controlled trial, RA-BEAM (NCT01710358), in patients (pts) with active rheumatoid arthritis (RA) and inadequate responses (IR) to methotrexate (MTX).[1,2,3]

Objectives: To compare the time to onset and magnitude of improvement across different patient-reported outcomes (PROs) of BARI, adalimumab (ADA) and placebo (PBO) during the first 12 weeks of treatment in RA-BEAM.

Methods: 1,305 patients on stable background MTX were randomized 3:3:2 to PBO, BARI 4 mg, or ADA 40 mg. In this intent-to-treat analysis, least-squares mean changes and percentage changes from baseline were assessed up to Week 12 for pain (0-100 mm visual analog scale [VAS]), SF-36 physical component summary (PCS, 0-100), morning joint stiffness (MJS) severity (0-10), Health Assessment Questionnaire-Disability Index (HAQ-DI, 0-3), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F, 0-52), and Patient Global Assessment of disease activity (PtGA, 0-100 mm VAS) scores. PROs were compared between treatments with ANCOVA; the model included change from baseline as the response variable, baseline of interest, regional baseline, joint erosion status, and treatment as explanatory variables. Last-observation-carried-forward was applied to impute missing data. Speed of onset and magnitude of PRO improvement are presented in spydergrams.

Results: Statistically significant improvements (P<0.05) with BARI and ADA vs. PBO were reported as early as Week 1 for pain, MJS severity, HAQ-DI, and PtGA and at Week 4 for FACIT-F and SF-36 PCS scores. Statistically significantly larger improvements (P<0.05) with BARI vs. ADA were observed as early as Week 2 for pain, PtGA, Week 3 for MJS severity, and Week 4 for HAQ-DI and SF-36 PCS scores. These improvements were maintained to Week 12.

Conclusion: Among MTX-IR pts, BARI and ADA treatment resulted in improvements across all PROs by Week 4, and as early as Week 1, for all but FACIT-F and SF-36 PCS scores. Statistically significant larger improvements for BARI compared with ADA were reported for all PROs, except FACIT-F, by Week 12.

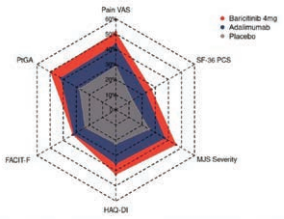
REFERENCES:

[1] Taylor et al. NEJM, 2017;376: 652-62
[2] Keystone et al. Ann Rheum Dis, 2017;76:1853-61
[3] Strand et al. Ann Rheum Dis, 2020; 79: 599-600

Table 1. Change from baseline in patient-reported outcomes at Weeks 4 and 12

	Week 4			Week 12		
LSM Change from Baseline	**PBO**	**ADA**	**BARI**	**PBO**	**ADA**	**BARI**
Pain VAS	-12.6	-22.3***	-27.1***††	-17.1	-26.4***	-31.5***††
SF-36 PCS	3.0	5.7***	6.9***††	4.2	7.2***	8.7***††
MJS severity	-0.9	-1.5***	-1.9***††	-1.4	-2.0***	-2.5***†††
HAQ-DI	-0.26	-0.47***	-0.54***†	-0.34	-0.56***	-0.66***††
FACIT-F	5.2	6.9**	7.8***	6.7	8.7***	9.1***
PtGA	-14.2	-23.7***	-26.8***†	-16.7	-26.6***	-31.2***††

*p≤0.05, **p≤0.01, ***p≤0.001 vs PBO; †p≤0.05, ††p≤0.01, †††p≤0.001 vs. ADA
ADA: adalimumab; BARI: baricitinib; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI: Health Assessment Questionnaire-Disability Index; MJS: morning joint stiffness; PBO: placebo; PCS: physical component scale; PtGA: Patient Global Assessment; VAS: visual analog scale



Pain VAS = Patient's Assessment of Pain Visual Analogue Scales; PCS = Physical Component Score; MJS = Morning Joint Stiffness; HAQ-DI = Health Assessment Questionnaire-Disability Index; FACIT-F = Functional Assessment of Chronic Illness Therapy-Fatigue; PtGA = Patient's Global Assessment of Disease Activity.

Figure 1. Percentage improvement from baseline to Week 12 in PROs of patients with RA in RA-BEAM

Acknowledgements: The authors would like to acknowledge Molly Tomlin, with Eli Lilly and Company, for medical writing and project management support

Disclosure of Interests: Vibeke Strand Consultant of: AbbVie, Amgen, Arena, AstraZeneca, Bayer Pharmaceuticals, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Eli Lilly and Company, Galapagos NV, Genentech, Gilead, GlaxoSmithKline, Ichnos, Inmedix, Janssen, Kiniksa, Merck, Myriad Genetics, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Scipher, Setpoint, Sun Pharma, and UCB Pharma, Anthony Sebba Speakers bureau: Eli Lilly and Company, Genentech, Sanofi, Regeneron, Consultant of: Amgen, Eli Lilly and Company, Genentech, Gilead Sciences, Novartis, Sanofi, Regeneron, Bochao Jia Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Julie Birt Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Amanda Quebe Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Hong Zhang Consultant of: Eli Lilly and Company, Peter C. Taylor Consultant of: AbbVie, Biogen, Galapagos, Gilead, GlaxoSmithKline, Janssen, Lilly, BMS, Pfizer, Roche, Celltrion, Sanofi, Nordic Pharma, Fresenius and UCB, Grant/research support from: Celgene, Galapagos, Janssen, Lilly

DOI: 10.1136/annrheumdis-2021-eular.65

POS0647 EFFICACY, SAFETY AND CHARACTERISTICS OF IGURATIMOD-BASED THERAPY IN THE TREATMENT OF UA, ERA AND RA PATIENTS FOR 24 WEEKS: A PROSPECTIVE COHORT STUDY

X. Liu[1], Z. Sun[1], W. Guo[1], F. Wang[1], L. Song[1], J. Li[1], Q. Liu[1], Q. Shu[1]. [1] *Qilu Hospital of Shandong University, Department of Rheumatology, Jinan, China*

Background: Experts emphasize early diagnosis and treatment in RA, but the widely used diagnostic criterias fail to meet the accurate judgment of early rheumatoid arthritis. In 2012, Professor Zhanguo Li took the lead in establishing ERA "Chinese standard", and its sensitivity and accuracy have been recognized by peers. However, the optimal first-line treatment of patients (pts) with undifferentiated arthritis (UA), early rheumatoid arthritis (ERA), and rheumatoid arthritis (RA) are yet to be established.

Objectives: To evaluate the efficacy and safety of Iguratimod-based (IGU-based) Strategy in the above three types of pts, and to explore the characteristics of the effects of IGU monotherapy and combined treatment.

Methods: This prospective cohort study (ClinicalTrials.gov Identifier NCT01548001) was conducted in China. In this phase 4 study pts with RA (ACR 1987 criteria[1]), ERA (not match ACR 1987 criteria[1] but match ACR/EULAR 2010 criteria[2] or 2014 ERA criteria[3]), UA (not match classification criteria for ERA and RA but imaging suggests synovitis) were recruited. We applied different treatments according to the patient's disease activity at baseline, including IGU monotherapy and combination therapies with methotrexate, hydroxychloroquine, and prednisone. Specifically, pts with LDA and fewer poor prognostic factors were entered the IGU monotherapy group (25 mg bid), and pts with high disease activity were assigned to combination groups. A Chi-square test was applied for comparison. The primary outcomes were the proportion of pts in remission (REM)or low disease activity (LDA) that is DAS28-ESR<2.6 or 3.2 at 24 weeks, as well as the proportion of pts, achieved ACR20, Boolean remission, and good or moderate EULAR response (G+M).

Results: A total of 313 pts (26 pts with UA, 59 pts with ERA, and 228 pts with RA) were included in this study. Of these, 227/313 (72.5%) pts completed the 24-week follow-up. The results showed that 115/227 (50.7%), 174/227 (76.7%), 77/227 (33.9%), 179/227 (78.9%) pts achieved DAS28-ESR defined REM and LDA, ACR20, Boolean remission, G+M response, respectively. All parameters continued to decrease in all pts after treatment (Fig 1).

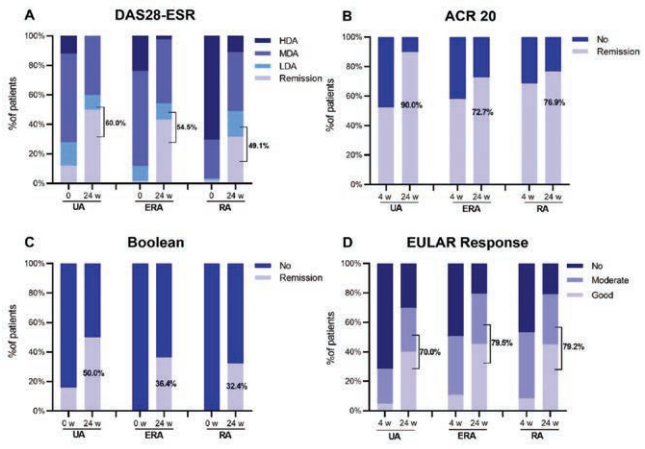
Compared with baseline, the three highest decline indexes of disease activity at week 24 were SW28, CDAI, and T28, with an average decline rate of 73.8%, 61.4%, 58.7%, respectively. Results were similar in three cohorts.

We performed a stratified analysis of which IGU treatment should be used in different cohorts. The study found that the proportion of pts with UA and ERA who used IGU monotherapy were significantly higher than those in the RA cohort. While the proportion of triple and quadruple combined use of IGU in RA pts was significantly higher than that of ERA and UA at baseline and whole-course (Fig 2).

A total of 81/313 (25.8%) pts in this study had adverse events (AE) with no serious adverse events. The main adverse events were infection(25/313, 7.99%), gastrointestinal disorders(13/313, 4.15%), liver dysfunction(12/313, 3.83%) which were lower than 259/2666 (9.71%) in the previous Japanese phase IV study[4].

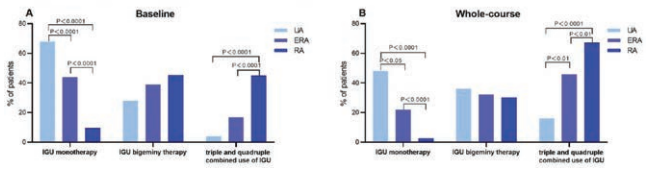
The most common reasons of lost follow-up were: 1) discontinued after remission 25/86 (29.1%); 2) lost 22/86 (25.6%); 3) drug ineffective 19/86 (22.1%).

Figure 1: Change of various disease activity assessment criteria of UA, ERA and RA



(A) DAS28-ESR disease activity of patients at baseline and week 24(Remission, DAS28-ESR≤2.6; Low disease activity (LDA), 2.6< DAS28-ESR ≤ 3.2; Moderate disease activity (MDA), 3.2< DAS28-ESR≤ 5.1; and High disease activity (HDA), DAS28-ESR> 5.1); (B) ACR20 response rate of all patients at week 4 and week 24; (C) Boolean remission rate of patients at baseline and week 24; (D) EULAR response rate of patients at week 4 and week 24.
DAS28=Disease Activity Score 28 joints; ESR=erythrocyte sedimentation rate; EULAR=European League Against Rheumatism; ACR=American College of Rheumatology;

Figure 2: Comparison of proportion of monotherapy and combined use of IGU in UA, ERA and RA



Conclusion: Both IGU-based monotherapy and combined therapies are tolerant and effective for treating UA, ERA, and RA, while the decline in joint symptoms was most significant. Overall, IGU combination treatments were most used in RA pts, while monotherapy was predominant in ERA and UA pts.

REFERENCES:

[1] Levin RW, et al. *Scand J Rheumatol* 1996, **25(5)**:277-281.
[2] Kay J, et al. *Rheumatology* 2012, **51(Suppl 6)**:vi5-9.
[3] Zhao J, et al. *Clin Exp Rheumatol* 2014, **32(5)**:667-673.
[4] Mimori T, et al. *Mod Rheumatol* 2019, **29(2)**:314-323.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.91

POS0648 SURVIVAL ANALYSIS OF TIME TO FIRST ADVERSE DRUG REACTION AND DRUG SURVIVAL IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH METHOTREXATE AND HYDROXYCHLOROQUINE MONOTHERAPIES OR COMBINATION THERAPY

K. Velthuis[1], M. Nguyen[1], J. Scholl[1], J. Jansen[1], J. Van Lint[1], P. Ten Klooster[2,3], H. Vonkeman[3,4], N. Jessurun[1]. [1]*Netherlands Pharmacovigilance Centre Lareb, Research Department, 's-Hertogenbosch, Netherlands*; [2]*Transparency in Healthcare B.V., Hengelo, Netherlands*; [3]*University of Twente, Department of Psychology, Health & Technology, Enschede, Netherlands*; [4]*Medisch Spectrum Twente, Department of Rheumatology and Clinical Immunology, Enschede, Netherlands*

Background: Methotrexate (MTX) and hydroxychloroquine (HCQ) are first line treatments of rheumatoid arthritis (RA). Adverse drug reactions (ADRs) during treatment with these drugs are common. Survival analysis on time to first ADR and on first time drug use duration have not yet been performed for these drugs in real-world settings.

Objectives: To compare proportions of patients with ADRs during first time use of either MTX monotherapy, HCQ monotherapy or MTX+HCQ combination therapy and to compare survival to first ADR and drug survival between these drugs.

Methods: Retrospective single centre cohort study including adult RA patients treated with either MTX monotherapy, HCQ monotherapy or MTX+HCQ combination therapy. First time users between 1 January 2003 and 30 April 2020 were followed until discontinuation of their first time drug use. The proportion of patients with ADRs was defined as the percentage of patients experiencing an ADR during their first time drug use. Survival to first ADR and drug survival of first time drug use were also assessed. MTX+HCQ use was considered combination therapy when the start dates of these drugs differed less than 14 days. For both monotherapies, end of first time drug use was defined as drug discontinuation for more than 90 days. For MTX+HCQ combination therapy, end of first time drug use was defined as discontinuation of either MTX, HCQ or both for more than 90 days. Differences in the proportion of patients experiencing an ADR during first time drug use of MTX, HCQ or a combination of both was statistically tested using Fisher's Exact Test. Survival to first ADR and drug survival were studied by Kaplan-Meier analysis and statistically tested by performing Log Rank tests.

Results: In total, 794 patients were included (MTX 363, HCQ 77, MTX+HCQ 354). For 156 patients (19.6%) at least one ADR was registered during first time drug use (MTX 59 [16.3%], HCQ 9 [11.7%], MTX+HCQ 88 [24.9%]). Proportions of ADRs differed significantly between MTX monotherapy and MTX+HCQ combination therapy (p=0.005) and between HCQ monotherapy and MTX+HCQ combination therapy (p=0.011). Survival to first ADR also differed significantly for both monotherapies compared to MTX+HCQ combination therapy (medians not reached, p<0.001 and p<0.008, respectively (figure 1A)). Drug survival differed significantly between MTX and HCQ monotherapy and between MTX monotherapy and MTX+HCQ combination therapy (median survival MTX 3.32 years (95% CI [2.81-3.83]; HCQ 1.39 years (95% CI [1.03-1.75]); MTX+HCQ 1.23 years (95% CI [1.11-1.34]), both p<0.001 (figure 1B)).

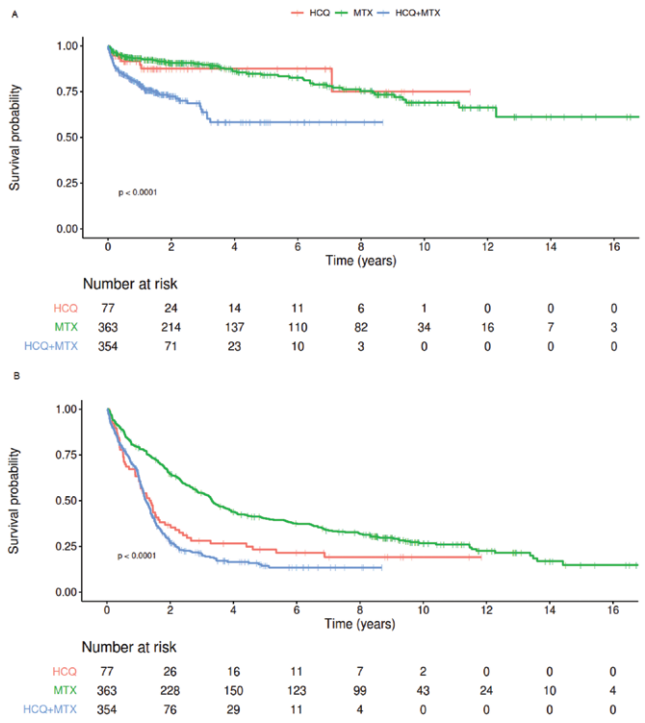


Figure 1. Kaplan-Meier curves of MTX and HCQ monotherapies and MTX+HCQ combination therapy, with (a) survival to first ADR and (b) drug survival.

Conclusion: Patients using MTX+HCQ combination therapy are more likely to experience an ADR during the first time drug use compared to MTX and HCQ monotherapies. MTX+HCQ combination therapy also leads to experiencing an ADR sooner compared to both monotherapies. Drug survival of patients treated with HCQ monotherapy as well as MTX+HCQ combination therapy is shorter compared to MTX monotherapy.

Disclosure of Interests: Kimberly Velthuis: None declared, My Nguyen: None declared, Joep Scholl: None declared, Jurriaan Jansen: None declared, Jette van Lint: None declared, Peter ten Klooster: None declared, Harald Vonkeman Consultant of: BMS, Celgene, Celltrion, Galapagos, Gilead, Janssen-Cilag, Lilly, Novartis, Pfizer, Sanofi-Genzyme, Grant/research support from: Abbvie, Naomi Jessurun: None declared

DOI: 10.1136/annrheumdis-2021-eular.181

POS0649 BARICITINIB PROVIDES GREATER IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES ACROSS ALL DISEASE ACTIVITY LEVELS COMPARED TO PLACEBO AND ADALIMUMAB IN RHEUMATOID ARTHRITIS

P. C. Taylor[1], R. Blanco[2], K. Ikeda[3], B. Jia[4], Y. F. Chen[4], C. Walls[4], E. Haladyj[4], B. Fautrel[5]. [1]*University of Oxford, Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; [2]*Hospital Universitario Marqués de Valdecilla, Department of Rheumatology, Santander, Spain*; [3]*Chiba University Hospital, Department of Allergy and Clinical Immunology, Chiba, Japan*; [4]*Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, United States of America*; [5]*Sorbonne University – Assistance Publique Hôpitaux de Paris, Pitie Salpetriere Hospital, Rheumatology Department, Paris, France*

Background: Baricitinib (BARI) is a JAK1/JAK2 inhibitor which provides improvements to clinical signs, symptoms, and patient-reported outcomes (PROs) in patients with rheumatoid arthritis [1, 2].

Objectives: The effect of BARI on the relationship between disease activity and pain has been explored previously [3]. The purpose of this post hoc analysis was to determine the association between additional PROs (physical function, fatigue, and duration of morning joint stiffness) and disease activity status after 12 weeks of treatment and to evaluate whether patients with an inadequate response to methotrexate treated with BARI 4 mg experienced greater PRO improvement than patients treated with either placebo (PBO) or adalimumab (ADA) across all levels of disease activity.

Methods: Data for these analyses were derived from the Phase 3 study RA-BEAM (N=1305; NCT01710358). Pain was evaluated using a 0-100 mm visual analog scale, physical function was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI), fatigue was measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale, and duration of morning joint stiffness (MJS, minutes) was reported by the patient. Disease activity was measured using the Clinical Disease Activity Index (CDAI) and categorized as remission (REM, ≤2.8), low disease activity (LDA, >2.8 to ≤10), moderate disease activity (MDA, >10 to ≤22), or high disease activity (HDA, >22). Linear regression was used to model the relationship between change in PROs at Week 12 (response) and CDAI values at Week 12 (primary explanatory variable) to evaluate the extent of improvement in PROs with BARI relative to PBO and ADA across a spectrum of disease activity levels. Last observation carried forward was used to impute missing values.

Results: At baseline, 91% of patients were classified as having HDA and 9% as having MDA by CDAI across all treatment groups. After 12 weeks of treatment, 2%, 7%, and 9% of patients achieved REM; 16%, 27%, and 33% of patients achieved LDA; and 33%, 40%, and 38% of patients achieved MDA with PBO, ADA, and BARI, respectively [3].

At Week 12, the estimated changes in measures of pain and physical function, as well as duration of MJS, for BARI 4 mg were greater than both PBO and ADA at all disease activity level threshold values of CDAI (Table 1). The estimated change in fatigue for BARI 4 mg was similar to that of ADA, and greater than PBO, at all disease activity level threshold values (Table 1).

Table 1. Estimate of PRO Improvement by Disease Activity Threshold Level (CDAI) at Week 12

PRO	CDAI=2.8			CDAI=10			CDAI=22		
	PBO	ADA	BARI 4 mg	PBO	ADA	BARI 4 mg	PBO	ADA	BARI 4 mg
Pain VAS[a] (mm)	-28.4	-37.9	-40.9	-24.5	-32.6	-36.1	-18.0	-23.7	-28.1
HAQ-DI[b]	-0.6	-0.7	-0.9	-0.5	-0.7	-0.7	-0.4	-0.5	-0.6
FACIT-F[c]	9.8	11.8	11.1	8.8	10.6	10.2	7.0	8.7	8.7
Duration of MJS (min)	-6.9	-37.8	-64.9	-6.3	-35.3	-55.7	-5.3	-31.3	-40.2

[a]Pain VAS scores range from 0 (no pain) to 100 (worst pain).
[b]HAQ-DI scores range from 0 (no disability) to 3 (completely disabled).
[c]FACIT-F scores range from 0 (worst fatigue) to 52 (no fatigue).
Abbreviations: ADA, adalimumab; BARI, baricitinib; CDAI, Clinical Disease Activity Index; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MJS, morning joint stiffness; PBO, placebo; PRO, patient-reported outcomes; VAS, visual analog scale.

Conclusion: Estimates of treatment differences suggest that patients treated with BARI 4 mg may experience greater improvements in pain, physical function, and MJS duration than patients treated with PBO or ADA regardless of their disease activity status reached after 12 weeks of treatment. Using this approach, improvements in fatigue with BARI 4 mg may be greater than with PBO and similar to ADA after 12 weeks.

REFERENCES:
[1] Taylor, P.C., et al., N Engl J Med, 2017. 376(7): p. 652-662.
[2] Keystone, E.C., et al., Ann Rheum Dis, 2017. 76(11): p. 1853-1861.
[3] Taylor, P., et al., Arthritis Rheumatol, 2019. 71(S10): p. 2455-2457.

Acknowledgements: The authors would like to acknowledge Catherine Lynch, with Eli Lilly and Company, for medical writing and project management support.

Disclosure of Interests: Peter C. Taylor Consultant of: AbbVie, Biogen, Galapagos, Gilead, GlaxoSmithKline, Janssen, Eli Lilly, BMS, Pfizer, Roche, Celltrion, Sanofi, Nordic Pharma, Fresenius and UCB, Grant/research support from: Celgene, Galapagos, Gilead, Eli Lilly, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, BMS, Janssen, Eli Lilly and MSD, Consultant of: Abbvie, Pfizer, Roche, BMS, Janssen, Eli Lilly and MSD, Grant/research support from: Abbvie, MSD, and Roche, Kei Ikeda Speakers bureau: Eli Lilly, Abbvie, Mitsubishi-Tanabe, Novartis, Paid instructor for: Abbvie, Grant/research support from: Mitsubishi-Tanabe, Bochao Jia Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Yun-Fei Chen Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Chad Walls Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Ewa Haladyj Employee of: Eli Lilly and Company, Bruno Fautrel Speakers bureau: Eli Lilly, Consultant of: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Janssen Pharmaceuticals, Eli Lilly and Company, Medac, MSD, NORDIC Pharma, Novartis, Pfizer Inc., Roche, Sanofi-Aventis, SOBI, UCB, Grant/research support from: AbbVie, Eli Lilly and Company, MSD, Pfizer Inc

DOI: 10.1136/annrheumdis-2021-eular.182

POS0650 PREDICTORS OF DURABLE CLINICAL RESPONSE TO TOFACITINIB 11 MG ONCE DAILY WITH OR WITHOUT METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: POST HOC ANALYSIS OF DATA FROM A PHASE 3B/4 METHOTREXATE WITHDRAWAL STUDY

K. Yamaoka[1], S. B. Cohen[2], N. Sugiyama[3], H. Shi[4], J. L. Rivas[5], A. Diehl[4], J. S. Smolen[6]. [1]*Kitasato University, Department of Rheumatology and Infectious Diseases, Sagamihara, Japan*; [2]*Metroplex Clinical Research Center, Dallas,*

TX, United States of America; [3]*Pfizer Japan Inc, Inflammation and Immunology, Tokyo, Japan*; [4]*Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America*; [5]*Pfizer SLU, Inflammation and Immunology, Madrid, Spain*; [6]*Medical University of Vienna, Department of Rheumatology, Vienna, Austria*

Background: ORAL Shift, a global Phase 3b/4 non-inferiority study, demonstrated sustained efficacy and safety of tofacitinib modified-release (MR) 11 mg once daily (QD) following methotrexate (MTX) withdrawal in patients with rheumatoid arthritis (RA) who achieved Clinical Disease Activity Index (CDAI) low disease activity (LDA) after treatment with tofacitinib + MTX.[1]

Objectives: To assess predictors of durable clinical response in patients receiving tofacitinib MR 11 mg QD in ORAL Shift.

Methods: ORAL Shift (NCT02831855) enrolled patients aged ≥18 years with moderate to severe RA and an inadequate response to MTX. Patients received open-label tofacitinib MR 11 mg QD + MTX for 24 weeks. Patients achieving LDA (CDAI score ≤10) at Week (W)24 entered the 24-week double-blind MTX withdrawal phase and were randomised 1:1 to receive tofacitinib MR 11 mg QD + placebo (tofacitinib monotherapy; ie blinded MTX withdrawal) or continue tofacitinib + MTX. In this post hoc analysis of randomised patients, we assessed predictors of durable response (maintenance of response from W24–48) per CDAI LDA and remission (CDAI score ≤2.8) criteria. All covariates were initially assessed for significance in a univariate logistic regression. Highly correlated covariates were reviewed to assess which would be removed prior to modelling in a multivariable logistic regression. Remaining significant (p≤0.10) covariates in the univariate regression were selected in the model using a stepwise selection process with p≤0.15 entry and p≤0.05 stay criteria. From the final model, estimated odds ratios (ORs) with 95% confidence intervals (CIs) are presented.

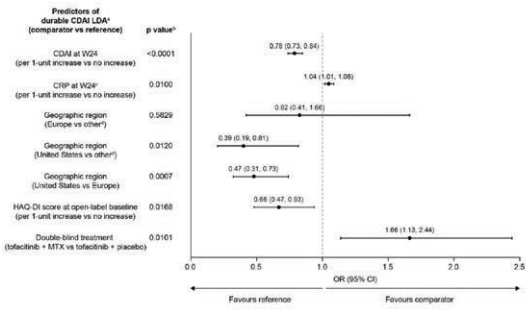
Results: In the double-blind phase of ORAL Shift, durable CDAI LDA and remission rates were: 66.2% and 14.7%, respectively, with tofacitinib + MTX (N=266); and 55.3% and 11.0%, respectively, with tofacitinib + placebo (N=264) (Table 1). In the multivariable analysis, five patient covariates significantly predicted durable CDAI LDA (Figure 1; discussed hereafter). Each unit increase in CDAI score at W24 reduced the likelihood of maintaining CDAI LDA by 22.0%. Each unit increase in C-reactive protein (CRP) at W24 increased the likelihood of maintaining CDAI LDA by 4.0%; this may have been due to imbalanced CRP levels at W24 (randomisation) between treatment groups (Figure 1, footnote c). The odds of durable CDAI LDA were 53.0% lower in the US vs Europe and 61.0% lower in the US vs 'other' regions. Each unit increase in baseline Health Assessment Questionnaire-Disability Index (HAQ-DI) score reduced the odds of durable CDAI LDA by 34.0%. Patients receiving tofacitinib + MTX had 66.0% greater odds of durable CDAI LDA vs patients receiving tofacitinib + placebo. CDAI at W24 was the only significant predictor of durable CDAI remission in the multivariable analysis: OR (95% CI) 0.32 (0.24, 0.43); p<0.0001. Each unit increase in CDAI score at W24 reduced the odds of durable CDAI remission by 68.0%.

Table 1. Durable CDAI LDA and remission[a] in patients receiving tofacitinib MR 11 mg QD with MTX or placebo in the double-blind phase of ORAL Shift

	Tofacitinib + MTX (N=266)	Tofacitinib + placebo (N=264)
Durable CDAI LDA, n (%)	176 (66.2)	146 (55.3)
Durable CDAI remission, n (%)	39 (14.7)	29 (11.0)

[a]Durable CDAI LDA or remission was defined as achievement of LDA (CDAI score ≤10) or remission (CDAI score ≤2.8), respectively, at W24–48
N, number of patients in each group; n, number of patients achieving outcome

Figure. Multivariable regression results for predictors of durable CDAI LDA[a] in patients receiving tofacitinib MR 11 mg QD with MTX or placebo in the double-blind phase of ORAL Shift



[a]Durable CDAI LDA was defined as achievement of LDA (CDAI score ≤10) at W24–48; [b]The Wald chi squared test p value for that comparison; [c]Mean CRP levels at W24 (randomisation) were 25.6% higher in the tofacitinib + MTX group (mean CRP=5.05 mg/L) vs tofacitinib + placebo group (mean CRP=4.02 mg/L). During the double-blind phase, CRP stabilised with tofacitinib + MTX but increased with tofacitinib + placebo. The CRP differences between treatment groups may have impacted the CDAI LDA durability outcome; [d]'Other' refers to Australia, Korea, Philippines, Mexico and South Africa

Conclusion: This post hoc analysis of data from ORAL Shift found that CDAI and CRP at W24, geographic region, baseline HAQ-DI and treatment could be predictors for durable CDAI LDA. As these findings were limited to patients who achieved CDAI LDA at W24 with tofacitinib MR 11 mg QD + MTX, additional data in the general patient population need to be investigated.

REFERENCES:

[1] Cohen et al. Lancet Rheumatol 2019; 1: E23-34.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Sarah Piggott, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: Kunihiro Yamaoka Speakers bureau: Actelion, Astellas, Chugai, Eisai, Eli Lilly, GlaxoSmithKline, Janssen, Mitsubishi Tanabe, Nippon Shinyaku, Pfizer Inc, Takeda, Consultant of: Actelion, Astellas, Chugai, Eisai, Eli Lilly, GlaxoSmithKline, Janssen, Mitsubishi Tanabe, Nippon Shinyaku, Pfizer Inc, Takeda, Stanley B. Cohen Consultant of: AbbVie, Eli Lilly, Genentech, Gilead Sciences, Pfizer Inc, Grant/research support from: AbbVie, Eli Lilly, Genentech, Gilead Sciences, Pfizer Inc, Naonobu Sugiyama Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Harry Shi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Jose Luis Rivas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Annette Diehl Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Josef S. Smolen Consultant of: AbbVie, AstraZeneca, Celgene, Celltrion, Chugai, Eli Lilly, Gilead Sciences, ILTOO, Janssen, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, Grant/research support from: AbbVie and AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.357

POS0651 CLINICAL AND FUNCTIONAL RESPONSE TO TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: PROBABILITY PLOT ANALYSIS OF RESULTS FROM A 48-WEEK PHASE 3B/4 METHOTREXATE WITHDRAWAL STUDY

S. B. Cohen[1], Y. H. Chen[2], N. Sugiyama[3], J. L. Rivas[4], A. Diehl[5], T. Lukic[6], J. Paulissen[6], H. Fan[5], T. Hirose[3], E. Keystone[7]. [1]*Metroplex Clinical Research Center, Dallas, TX, United States of America*; [2]*Taichung Veterans General Hospital, Division of Allergy, Immunology, and Rheumatology, Taichung, Taiwan, Republic of China*; [3]*Pfizer Japan Inc, Inflammation and Immunology, Tokyo, Japan*; [4]*Pfizer SLU, Inflammation and Immunology, Madrid, Spain*; [5]*Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America*; [6]*Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*; [7]*Mount Sinai Hospital, Toronto, ON, Canada*

Background: The Phase 3b/4 study ORAL Shift (NCT02831855) demonstrated sustained efficacy/safety of tofacitinib modified-release 11 mg QD following MTX withdrawal, that was non-inferior to continued tofacitinib + MTX use, in patients (pts) with moderate to severe RA who achieved LDA with tofacitinib + MTX at Week (W)24.[1]

Objectives: To assess differences and similarities in clinical/functional responses in pts receiving tofacitinib ± MTX in ORAL Shift.

Methods: In ORAL Shift, pts received open-label tofacitinib + MTX to W24; at W24, pts who achieved CDAI LDA were randomised to receive tofacitinib + MTX or tofacitinib + placebo (PBO) from W24–48. In this post hoc analysis, clinical efficacy endpoints were ACR-N (minimum % change from baseline [BL; Δ] at W48 achieved by each pt in 3 efficacy measures), ΔDAS28-4(ESR), and DAS28-4(ESR) remission/LDA (scores ≤3.2) and moderate/high disease activity (scores >3.2). Functional efficacy endpoints were ΔHAQ-DI and HAQ-DI clinically relevant functional progression (CRFP) status at W48, defined as failure to achieve improvement in HAQ-DI ≥ minimum clinically important difference (MCID; ≥0.22 decrease from BL in HAQ-DI). Thus, CRFP was defined as <0.22 decrease, no change or increase from BL in HAQ-DI at W48. All efficacy endpoints were summarised descriptively. Cumulative probability plots of ACR-N and ΔHAQ-DI were produced. Median of mean CRP values from BL–W24 and >W24–48 were assessed by response subgroups.

Results: 266 pts receiving tofacitinib + MTX and 264 pts receiving tofacitinib + PBO in W24–48 were included. At W48: mean ACR-N was numerically greater with tofacitinib + MTX vs tofacitinib + PBO (60.8 vs 53.1); mean decrease in HAQ-DI was generally similar between groups (-0.71 vs -0.67); mean decrease in DAS28-4(ESR) was numerically greater with tofacitinib + MTX vs tofacitinib + PBO (-2.95 vs -2.68). The differences/similarities between groups in ACR-N and ΔHAQ-DI were also seen in cumulative probability plots (Figure 1). CRFP rates were numerically lower with tofacitinib + MTX (18.7%) vs tofacitinib + PBO (23.5%), and in pts with remission/LDA (tofacitinib + MTX, 12.1%; tofacitinib + PBO, 16.8%) vs moderate/high disease activity (tofacitinib + MTX, 26.2%; tofacitinib + PBO, 30.8%). Median of mean CRP over time was generally numerically lower in pts with CRFP vs non-CRFP and DAS28-4(ESR)-defined remission/LDA vs moderate/high disease activity; and in those receiving tofacitinib + PBO vs tofacitinib + MTX, irrespective of CRFP or DAS28-4(ESR) disease status (Table 1).

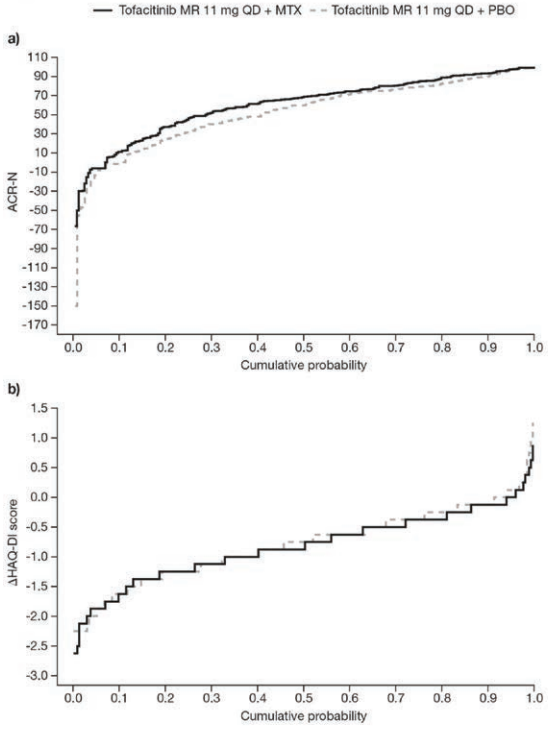
Table 1. Median of mean CRP[a] up to W48 by response subgroups

	Tofacitinib 11 mg QD + MTX		Tofacitinib 11 mg QD + PBO	
Mean CRP,[a] median (IQR) [n]	**>BL–W24**	**>W24–48**	**>BL–W24**	**>W24–48**
HAQ-DI CRFP	2.84 (1.15–7.30) [45]	2.30 (0.82–4.75) [46]	1.45 (0.77–4.42) [56]	2.28 (0.53–7.28) [56]
HAQ-DI non-CRFP	2.81 (1.09–6.19) [195]	2.91 (1.19–5.84) [195]	2.26 (0.98–4.63) [176]	2.47 (1.13–5.53) [178]
DAS28-4(ESR) remission/LDA	2.48 (1.05–4.95) [126]	2.46 (1.07–4.76) [127]	1.70 (0.89–4.14) [115]	1.95 (0.81–3.82) [117]
DAS28-4(ESR) moderate/ high disease activity	3.56 (1.17–7.13) [107]	3.58 (1.36–8.33) [107]	2.60 (0.87–5.16) [115]	2.68 (1.34–8.23) [115]

[a]Mean CRP was calculated as the average CRP value during each time period (>BL–W24 or >W24–48)

CRP, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; IQR, interquartile range; LDA, low disease activity; MTX, methotrexate; n, number of pts meeting assessment criteria; QD, once daily

Figure. Cumulative probability plot at W48 for a) ACR-N; b) ΔHAQ-DI score



Endpoints were assessed using the full analysis set (defined as all pts receiving ≥1 dose of study drug with ≥1 value post-baseline), with no imputation for missing values
ACR-N, American College of Rheumatology response, where N represents the minimum amount of improvement expressed by each pt in % ΔTJC28, % ΔSJC28, and the median of % Δ in PtGA, PGA, Pain, HAQ-DI and CRP; CRP, C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; MR, modified release; MTX, methotrexate; PGA, Physician Global Assessment; PtGA, Patient Global Assessment; QD, once daily; SJC28, swollen joint count in 28 joints; TJC28, tender joint count in 28 joints

Conclusion: Although clinical/functional responses were generally similar between treatment groups, numerical improvements were seen for some efficacy endpoints with tofacitinib + MTX vs tofacitinib + PBO. A numerically higher CRFP rate may be associated with higher DAS28-4(ESR) disease activity. CRP changes up to W48 may not trend with CRFP status.

REFERENCES:

[1] Cohen et al. Lancet Rheumatol 2019; 1: E23-34.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Anthony G McCluskey, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: Stanley B. Cohen Consultant of: AbbVie, Eli Lilly, Genentech, Gilead Sciences, Pfizer Inc, Grant/research support from: AbbVie, Eli Lilly, Genentech, Gilead Sciences, Pfizer Inc, Yi-Hsing Chen Grant/research support from: Bristol-Myers Squibb, GlaxoSmithKline, Pfizer Inc, Naonobu Sugiyama Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Jose Luis Rivas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Annette Diehl Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Tatjana Lukic Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Jerome Paulissen Consultant of: Pfizer Inc, Haiyun Fan Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Tomohiro Hirose Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Edward Keystone Speakers bureau: AbbVie, Amgen, F. Hoffman-La Roche, Janssen, Merck, Novartis, Pfizer Inc, Sanofi Genzyme, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celltrion, Eli Lilly, F. Hoffman-La Roche, Gilead Sciences, Janssen, Merck, Myriad Autoimmune, Pfizer Inc, Sandoz, Sanofi Genzyme, Samsung Bioepsis, Grant/research support from: Amgen, Merck, Pfizer Inc, PuraPharm

DOI: 10.1136/annrheumdis-2021-eular.358

POS0652

SEX DIFFERENCES IN THE EFFICACY AND SAFETY OF TOFACITINIB IN RHEUMATOID ARTHRITIS PATIENTS: A POST HOC ANALYSIS OF PHASE 3 AND LONG-TERM EXTENSION TRIALS

H. N. Jones[1], V. Strand[2], H. Schulze-Koops[3], E. Mysler[4], C. Kinch[5], D. C. Gruben[6], R. Germino[7], C. A. Connell[8], L. Eder[9]. *[1]University of Alberta, Division of Rheumatology, Edmonton, AB, Canada*; *[2]Stanford University, Division of Immunology/Rheumatology, Palo Alto, CA, United States of America*; *[3]University of Munich, Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, Munich, Germany*; *[4]Organización Médica de Investigación, Buenos Aires, Argentina*; *[5]Pfizer Canada ULC, Inflammation and Immunology, Kirkland, QC, Canada*; *[6]Pfizer Inc, Inflammation and Immunology, Groton, CT, United States of America*; *[7]Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*; *[8]Pfizer Inc, Clinical Development and Operations, Groton, CT, United States of America*; *[9]University of Toronto, Women's College Research Institute, Department of Medicine, Toronto, ON, Canada*

Background: Differences in efficacy outcomes favouring males vs females with rheumatoid arthritis (RA) have been reported with conventional synthetic (cs) disease-modifying antirheumatic drugs (DMARDs) and tumour necrosis factor inhibitors; results with Janus kinase inhibitors are less clear.

Objectives: To assess the impact of sex on efficacy, safety and persistence in tofacitinib RA clinical trials.

Methods: Efficacy and safety analyses included data pooled from Phase (P)3 randomised controlled trials (RCTs) of patients (pts) with RA and an inadequate response (IR) to methotrexate (NCT00847613; NCT00853385) or ≥1 DMARD (NCT00856544) who received tofacitinib 5 or 10 mg twice daily (BID), adalimumab (ADA) 40 mg Q2W or placebo (PBO), with background csDMARDs. Persistence analyses of pts receiving tofacitinib 5 or 10 mg BID ± csDMARDs used data pooled from two long-term extension trials (NCT00661661; NCT00413699). Efficacy outcomes to Month (M)12 included: ACR20/50/70 responses, changes from baseline (Δ; BL) in DAS28-4(ESR), CDAI, HAQ-DI and FACIT-F, and DAS28-4(ESR) remission (<2.6). Safety was evaluated to M24 for tofacitinib and ADA. Kaplan-Meier persistence analysis estimated time to discontinuation.

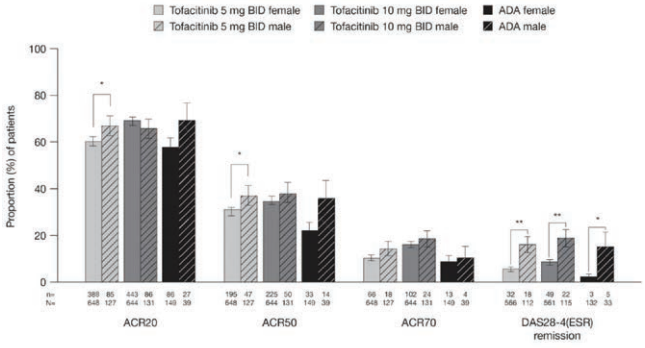
Results: 2265 pts were included from P3 RCTs. Demographics and BL characteristics were comparable across sexes and treatments. Tofacitinib or ADA vs PBO generally led to significantly higher ACR20/50/70 responses in both sexes through M6. To M12, ACR20/50/70 responses were broadly comparable across active treatments and between sexes, with significant differences favouring males at some time points, including M3 (Figure 1). Statistically significant differences favouring males vs females were observed in DAS28-4(ESR) remission rates at most time points, including M3 (Figure 1); a similar trend was observed for ΔDAS28-4(ESR). ΔCDAI, ΔHAQ-DI and ΔFACIT-F significantly favoured males vs females receiving tofacitinib 5 mg BID at most time points, while ΔHAQ-DI and ΔFACIT-F tended to favour females receiving tofacitinib 10 mg BID. Rates of adverse events (AEs), serious AEs (SAEs), severe AEs and discontinuations due to AEs were slightly higher in females vs males with tofacitinib 5 mg BID; this was generally reversed with tofacitinib 10 mg BID and ADA (Table 1). AEs of special interest (AESI) were comparable between sexes with tofacitinib and ADA, although low event numbers limit interpretation (Table 1). Time to all-cause discontinuation and discontinuation due to AEs/lack of efficacy with tofacitinib 5 mg BID was similar between sexes. Numerical differences favouring females vs males were observed for time to all-cause discontinuation and discontinuation due to AEs with tofacitinib 10 mg BID.

Table 1. Safety summary to M24 in pooled DMARD-IR P3 RCTs

	Tofacitinib 5 mg BID		Tofacitinib 10 mg BID		ADA	
Pts with events, n (%)	**Females (N=707)**	**Males (N=133)**	**Females (N=698)**	**Males (N=137)**	**Females (N=162)**	**Males (N=42)**
AEs	562 (79.5)	85 (63.9)	529 (75.8)	107 (78.1)	119 (73.5)	30 (71.4)
SAEs	107 (15.1)	17 (12.8)	71 (10.2)	24 (17.5)	13 (8.0)	6 (14.3)
Severe AEs	86 (12.2)	12 (9.0)	55 (7.9)	22 (16.1)	14 (8.6)	5 (11.9)
Discontinuations due to AEs	87 (12.3)	10 (7.5)	88 (12.6)	10 (7.3)	17 (10.5)	5 (11.9)
Death	6 (0.8)	4 (3.0)	0	3 (2.2)	1 (0.6)	2 (4.8)
AESI						
Serious infections	28 (4.0)	6 (4.5)	27 (3.9)	6 (4.4)	2 (1.2)	1 (2.4)
All HZ (non-serious/serious)	35 (5.0)	7 (5.3)	43 (6.2)	5 (3.6)	2 (1.2)	3 (7.1)
MACE	5 (0.7)	0	2 (0.3)	3 (2.2)	0	3 (7.1)
Malignancies (excl. NMSC)	7 (1.0)	1 (0.8)	9 (1.3)	1 (0.7)	0	1(2.4)
NMSC	2 (0.3)	5 (3.8)	4 (0.6)	2 (1.5)	1 (0.6)	1 (2.4)
Venous thromboembolism	3 (0.4)	0	3 (0.4)	1 (0.7)	0	0

HZ, herpes zoster; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer

Figure. Proportion of pts achieving ACR20/50/70 and DAS28-4(ESR) remission at M3, stratified by sex and treatment group (P3 RCTs)



*p<0.05, **p<0.001
Pts from ORAL Standard who were found to be non-compliant with study procedures were excluded; PBO data not presented
ACR20/50/70, American College of Rheumatology ≥20/50/70% response criteria; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; n, number of responders; N, number of patients assessed at each visit

Conclusion: Efficacy outcomes with tofacitinib and ADA were generally higher in males and comparable in females vs previously reported mixed population response rates for advanced therapies. Safety findings did not reveal a consistent pattern between sexes. Tofacitinib persistence was similar between sexes.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Christina Viegelmann, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: H Niall Jones Consultant of: Pfizer Inc, Vibeke Strand Consultant of: AbbVie, Amgen, Arena, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Corrona, Eli Lilly, Galapagos, Genentech/Roche, Gilead, GlaxoSmithKline, Ichnos, Inmedix, Janssen, Kiniksa, Merck, Myriad Genetics, Novartis, Pfizer Inc, Regeneron, Samsung, Sandoz, Sanofi, Scipher, SetPoint Medical, UCB, Hendrik Schulze-Koops Consultant of: AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead Sciences, Hexal Sandoz, Hospira, Janssen-Cilag, MSD, Novartis, Pfizer Inc, Roche, UCB, Grant/research support from: Novartis, Pfizer Inc, Eduardo Mysler Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer Inc, Roche, Sanofi, Grant/research support from: Eli Lilly, Pfizer Inc, Roche, Cassandra Kinch Shareholder of: Pfizer Canada ULC, Employee of: Pfizer Canada ULC, David C Gruben Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Rebecca Germino Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Carol A. Connell Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lihi Eder Speakers bureau: AbbVie, UCB, Consultant of: AbbVie, Celgene, Eli Lilly, Novartis, Pfizer Inc, UCB, Grant/research support from: AbbVie, Eli Lilly, Pfizer Inc, UCB

DOI: 10.1136/annrheumdis-2021-eular.359

POS0653

IMPACT OF UPADACITINIB OR ADALIMUMAB AS INITIAL THERAPY ON THE ACHIEVEMENT OF 48-WEEK TREATMENT GOALS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO METHOTREXATE: POST HOC ANALYSIS OF A PHASE 3 STUDY

E. Mysler[1], Y. Tanaka[2], A. Kavanaugh[3], D. Aletaha[4], P. C. Taylor[5], I. H. Song[6], T. Shaw[6], Y. Song[6], R. Demasi[6], M. Ali[6], R. Fleischmann[7]. [1]*Organización Medica de Investigación, Rheumatology, Buenos Aires, Argentina*; [2]*The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan*; [3]*Division of Rheumatology, Allergy, & Immunology, University of California San Diego Medical School, San Diego, United States of America*; [4]*Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Vienna, Austria*; [5]*Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom*; [6]*AbbVie Inc., Rheumatology, North Chicago, United States of America*; [7]*Department of Medicine, University of Texas Southwestern Medical Center, Metroplex Clinical Research Center, Dallas, United States of America*

Background: In the randomized, double-blinded, Phase 3 SELECT-COMPARE study, upadacitinib (UPA) + MTX demonstrated greater clinical and functional responses vs adalimumab (ADA) + MTX in patients (pts) with RA and inadequate response to MTX.[1,2] Pts with insufficient response to initial therapy were switched from UPA to ADA (and vice versa) according to treat-to-target (T2T) principles.

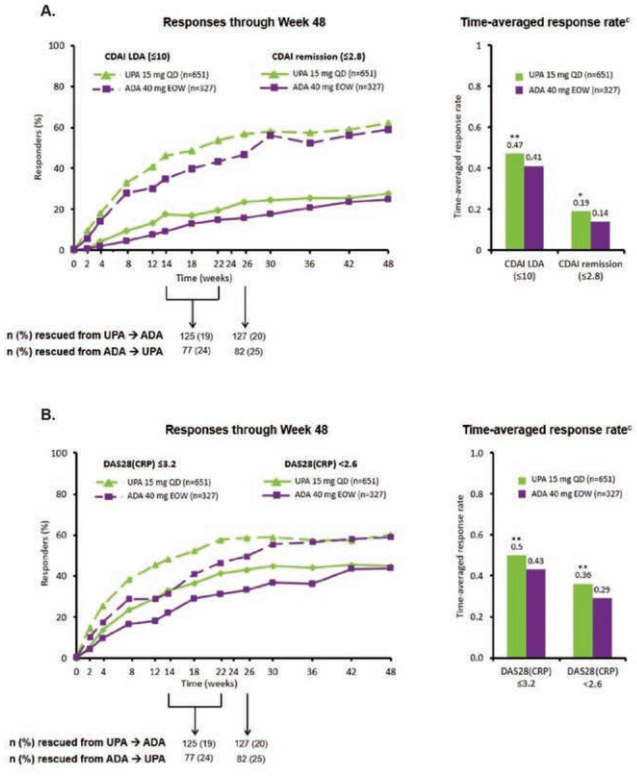
Objectives: We analyzed 1-year treatment outcomes in SELECT-COMPARE according to initial randomization group, regardless of whether pts subsequently switched therapy.

Methods: Pts initially randomized to UPA 15 mg once daily (QD) or ADA 40 mg every other week (EOW; both + MTX) for up to 48 weeks in SELECT-COMPARE were included in the analysis. As per the protocol-directed rescue strategy, pts experiencing <20% improvement in tender or swollen joint counts at Week 14, 18, or 22, or Clinical Disease Activity Index (CDAI) >10 at Week 26, were switched from UPA to ADA or ADA to UPA in a blinded fashion. Efficacy outcomes included CDAI remission (≤2.8) and low disease activity (LDA; ≤10), DAS of 28 joints using CRP (DAS28[CRP]) <2.6 and ≤3.2, and a composite of "deep response" (CDAI remission, HAQ-Disability Index <0.5, and pain score <20). Data are presented and attributed to initial randomized group (UPA or ADA) regardless of any subsequent switch in therapy. Time-averaged response rates were calculated as area under the curve of response rate standardized by 48 weeks. The proportions of pts who maintained Week 26 responses through 6 months of follow-up are also reported.

Results: This analysis included 651 pts initially randomized to UPA (of whom 245 switched to ADA) and 327 pts initially randomized to ADA (of whom 157 switched to UPA). Baseline characteristics including age, sex, and BMI were generally well balanced between randomized groups. At Week 48, similar proportions of pts initially randomized to UPA or ADA therapy achieved CDAI remission/LDA (27.6%/61.9% vs 24.8%/59.0%) and DAS28(CRP) <2.6/≤3.2 (45.0%/60.2% vs 43.7%/59.0%) (Figure 1). However, a small but significantly greater proportion of pts achieved a deep response with initial UPA vs initial ADA therapy (17.8% vs 12.8%; p<0.05). In addition, time-averaged response rates over 48 weeks were higher for initial UPA vs initial ADA therapy across efficacy outcomes. Similar trends were observed for other outcomes. Additionally, similar proportions of pts maintained Week 26 responses with initial UPA vs initial ADA therapy based on CDAI remission/LDA and DAS28(CRP) <2.6/≤3.2 during 6-month follow-up (Table 1).

Conclusion: Using a stringent T2T approach to RA management, rates of LDA or remission at 1 year were similar, regardless of whether pts were initially randomized to UPA or ADA. However, initial UPA therapy led to more frequent deep responses and higher time-averaged response rates vs initial ADA therapy.

Figure 1. Achievement of CDAI (A) and DAS28(CRP) (B) responses corresponding with time-averaged response rates over 48 weeks by initial therapy with UPA or ADA in SELECT-COMPARE



**p<0.01, *p<0.05 vs ADA.
[a]Non-responder imputation. [b]Blinded rescue from UPA to ADA or ADA to UPA was permitted at Weeks 14, 18, and 22 for <20% improvement in TJC/SJC and at Week 26 for CDAI <10. Data are presented and attributed to original randomized group (UPA or ADA) regardless of any subsequent switch in therapy. [c]Calculated as area under the curve of response rate standardized by length of study (48 weeks).
ADA, adalimumab; CDAI, Clinical Disease Activity Index; DAS28(CRP), DAS of 28 joints using CRP; EOW, every other week; QD, once daily; SJC, swollen joint count; TJC, tender joint count; UPA, upadacitinib.

REFERENCES:
[1] Fleischmann R, et al. Arthritis Rheumatol 2019;71:1788–800.
[2] Fleischmann R, et al. Ann Rheum Dis 2019;78:1454–62.

Table 1. Proportion of patients maintaining Week 26 CDAI and DAS28(CRP) responses during 6-month follow-up by initial therapy with UPA or ADA in SELECT-COMPARE[a-c]

	UPA 15 mg QD	ADA 40 mg EOW
CDAI LDA (≤10)	43.9	36.3
CDAI Remission (≤2.8)	35.0	22.7
DAS28(CRP) ≤3.2	39.1	35.3
DAS28(CRP) <2.6	30.5	30.1

[a]As observed.
[b]Blinded rescue from UPA to ADA or ADA to UPA was permitted at Week 14, 18, and 22 for patients with <20% improvement in TJC or SJC and at Week 26 for patients with a CDAI <10. Data are presented and attributed to original randomized group (UPA or ADA) regardless of any subsequent switch in therapy.
[c]Maintaining response defined as never losing response at any visit during ~6 months (22–26 weeks) follow up after first achieving response before or at Week 26.
ADA, adalimumab; CDAI, Clinical Disease Activity Index; DAS28(CRP), DAS of 28 joints using CRP; EOW, every other week; QD, once daily; SJC, swollen joint count; TJC, tender joint count; UPA, upadacitinib.

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing assistance was provided by Frances Smith, PhD, of 2 the Nth, which was funded by AbbVie.

Disclosure of Interests: Eduardo Mysler Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer, Roche, and Sandoz., Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer, Roche, and Sandoz., Yoshiya Tanaka Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Eli Lilly, Chugai, Daiichi-Sankyo, Eisai, Gilead, GlaxoSmithKline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer, Sanofi, and YL Biologics, Consultant of: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Eli Lilly, Chugai, Daiichi-Sankyo, Eisai, Gilead, GlaxoSmithKline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer, Sanofi, and YL Biologics, Grant/research support from: AbbVie, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Takeda, and UCB., Arthur Kavanaugh Consultant of: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Janssen, Pfizer, Roche, and UCB., Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Janssen, Pfizer, Roche, and UCB., Daniel Aletaha Consultant of: AbbVie, Amgen, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Roche, Sanofi, and UCB., Grant/research support from: AbbVie, Amgen, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Roche, Sanofi, and UCB., Peter C. Taylor Speakers bureau: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Celltrion, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Fresenius, Nordic Pharma, Pfizer, Roche, Sanofi, and UCB., Consultant of: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Celltrion, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Fresenius, Nordic Pharma, Pfizer, Roche, Sanofi, and UCB., Grant/research support from: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Celltrion, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Fresenius, Nordic Pharma, Pfizer, Roche, Sanofi, and UCB., In-Ho Song Shareholder of: AbbVie, Employee of: AbbVie, Tim Shaw Shareholder of: AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: AbbVie, Employee of: AbbVie, Ryan DeMasi Shareholder of: AbbVie, Employee of: AbbVie, Mira Ali Shareholder of: AbbVie, Employee of: AbbVie, Roy Fleischmann Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sanofi-Aventis, and UCB., Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sanofi-Aventis, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.474

POS0654

IMPACT OF CONCOMITANT GLUCOCORTICOIDS ON THE CLINICAL EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN AD HOC ANALYSIS OF DATA FROM THREE PHASE 3 STUDIES

B. Combe[1], F. Buttgereit[2], A. Ostor[3], R. Xavier[4], A. Saraux[5], C. Daridon[6], K. Famulla[7], Y. Song[8], I. Lagunes-Galindo[8], G. R. Burmester[2]. [1]*Department of Rheumatology, CHU Montpellier, Montpellier University, Montpelier, France*; [2]*Charité University Medicine, Rheumatology, Berlin, Germany*; [3]*Cabrini Hospital, Monash University & Emeritus Research Melbourne, Melbourne, Australia*; [4]*Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil*; [5]*Department of Rheumatology, UBO, CHU, INSERM 1227 (LBAI), Brest, France*; [6]*AbbVie France, Rheumatology, Rungis, France*; [7]*AbbVie Deutschland GmbH & Co. KG, Rheumatology, Wiesbaden, Germany*; [8]*AbbVie Inc., Rheumatology, North Chicago, United States of America*

Background: Glucocorticoid (GC) therapy has strong anti-inflammatory effects and helps slow radiographic progression in RA[1]; however, GCs can be associated with adverse events (AEs) such as infection, especially with long-term use and higher doses.

Objectives: To evaluate the impact of baseline GCs on the efficacy and safety of upadacitinib (UPA) with or without concomitant conventional synthetic DMARDs (csDMARDs).

Methods: In this ad hoc analysis of three Phase 3 studies, patients with inadequate response to MTX (MTX-IR) receiving UPA 15 mg once daily (QD) or placebo (PBO) + csDMARDs in SELECT-NEXT, and MTX-IR/MTX-naïve patients receiving UPA 15 mg QD monotherapy or MTX monotherapy in SELECT-MONOTHERAPY/SELECT-EARLY, respectively, were included. Efficacy outcomes, including measures of remission and low disease activity (LDA) determined by DAS in 28 joints using CRP (DAS28[CRP]; <2.6/≤3.2) and Clinical Disease Activity Index (CDAI; ≤2.8/≤10), were assessed and stratified by baseline GC use. Patients were permitted to receive oral GCs ≤10 mg/day (prednisone equivalent) at baseline with no adjustment permitted until Week 24/26/48. Safety was reported as number and proportion of patients with AEs. Data were analyzed descriptively with no statistical comparisons between groups or doses.

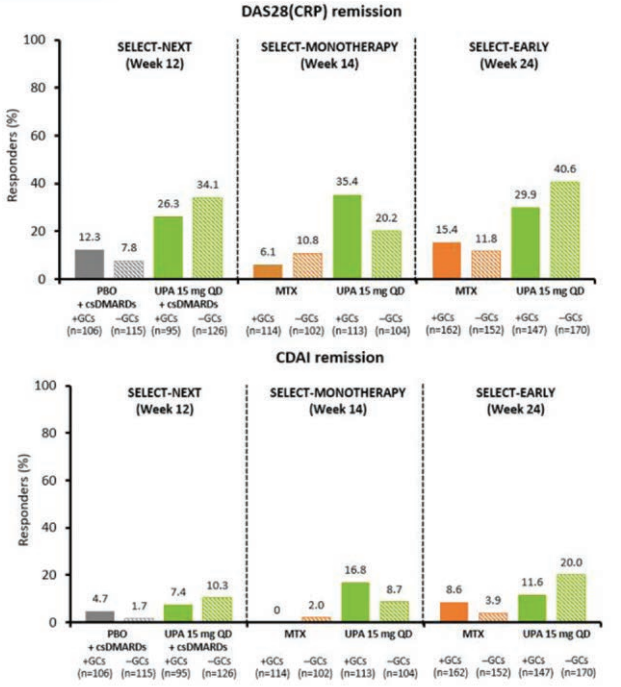
Results: Of 1,506 patients included in the analysis, 737 (48.9%) were receiving baseline GCs (mean dose 6.2 mg/day). Baseline characteristics were broadly similar across treatment groups; SELECT-EARLY, which enrolled MTX-naïve patients, generally had the shortest duration of RA and higher CRP levels. Across UPA treatment groups, concomitant GCs generally did not influence the proportions of patients achieving remission (Figure 1). In SELECT-NEXT, clinical responses with UPA 15 mg in combination with csDMARDs were similar irrespective of concomitant GC use (Figure 1). Within SELECT-MONOTHERAPY, responses in patients receiving UPA 15 mg without concomitant csDMARDs or GCs were higher than those in patients receiving MTX alone, but were numerically lower than in those receiving UPA 15 mg with GCs (Figure 1). However, this was not observed within SELECT-EARLY, where clinical responses in patients receiving UPA 15 mg monotherapy without GCs were higher than in those patients receiving UPA 15 mg with GCs for both DAS28(CRP) <2.6 (40.6% vs 29.9%, respectively) and CDAI ≤2.8 (20.0% vs 11.6%, respectively) (Figure 1). A similar trend was observed for LDA. Serious AEs, AEs leading to discontinuation, and AEs of special interest, including infections (such as herpes zoster), were broadly similar in the UPA groups irrespective of concomitant GC use (**table of safety data will be presented**).

Conclusion: UPA 15 mg in combination with csDMARDs or as monotherapy was effective in achieving remission and LDA, irrespective of concomitant GC use. Safety of UPA, including incidence of infection, appeared largely unaffected by concomitant GC use.

REFERENCES:

[1] Kirwan JR, et al. Cochrane Database Syst Rev 2007;1:CD006356.

Figure. Efficacy in patients receiving UPA or PBO with/without csDMARDs, and with/without GCs[a]



[a]Non-responder imputation.
CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic DMARD; DAS28(CRP), Disease Activity Score in 28 joints using CRP; GC, glucocorticoid; PBO, placebo; QD, once daily; UPA, upadacitinib.

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing assistance was provided by Frances Smith, PhD, of 2 the Nth, which was funded by AbbVie.

Disclosure of Interests: Bernard Combe Speakers bureau: AbbVie, Eli Lilly, Gilead, Janssen, Merck, Novartis, Pfizer, Roche-Chugai, Sanofi, and UCB Pharma, Consultant of: AbbVie, Eli Lilly, Gilead, Janssen, Merck, Novartis, Pfizer, Roche-Chugai, Sanofi, and UCB Pharma, Frank Buttgereit Speakers bureau: AbbVie, Eli Lilly, Pfizer, and Roche, Andrew Ostor Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Gilead, Janssen, Novartis, Paradigm, Pfizer, Roche, and UCB Pharma., Ricardo Xavier Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB Pharma, Consultant of: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB Pharma, Alain Saraux Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Eli Lilly, Nordic, Sanofi, and UCB Pharma, Consultant of: AbbVie, Bristol-Myers Squibb, Chugai, Eli Lilly, Nordic, Sanofi, and UCB Pharma, Capucine DARIDON Shareholder of: AbbVie, Employee of: AbbVie, Kirsten Famulla Shareholder of: AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: AbbVie, Employee of: AbbVie, Ivan Lagunes-Galindo Shareholder of: AbbVie, Employee of: AbbVie, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Eli Lilly, Gilead, Janssen, Merck, Pfizer, Roche, and UCB Pharma, Consultant of: AbbVie, Eli Lilly, Gilead, Janssen, Merck, Pfizer, Roche, and UCB Pharma

DOI: 10.1136/annrheumdis-2021-eular.480

POS0655 LONG-TERM SAFETY AND EFFICACY OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: 3-YEAR RESULTS FROM THE SELECT-EARLY STUDY

R. van Vollenhoven[1], T. Takeuchi[2], J. Aelion[3], N. Chávez[4], P. Mannucci Walter[5], A. Singhal[6], J. Swierkot[7], A. Friedman[8], N. Khan[8], Y. Li[8], X. Bu[8], J. Klaff[8], V. Strand[9]. [1]*Amsterdam UMC, Rheumatology, Amsterdam, Netherlands*; [2]*Keio University School of Medicine, Rheumatology, Tokyo, Japan*; [3]*Arthritis Clinic PLLC, Rheumatology, Jackson, United States of America*; [4]*Instituto Guatemalteco de Seguridad Social, Rheumatology, Ciudad de Guatemala, Guatemala*; [5]*Aprillus Asistencia e Investigación, Rheumatology, Buenos Aires, Argentina*; [6]*SouthWest Rheumatology Research, LLC, Rheumatology, Dallas, United States of America*; [7]*Wrocław Medical Hospital, Department and Clinic of Rheumatology and Internal Medicine, Wroclaw, Poland*; [8]*AbbVie Inc, Immunology, North Chicago, United States of America*; [9]*Stanford University, Division Immunology/Rheumatology, Palo Alto, United States of America*

Background: Upadacitinib (UPA), an oral Janus kinase inhibitor, demonstrated significant improvements in signs, symptoms, and structural inhibition as monotherapy (mono) vs methotrexate (MTX) in MTX-naïve patients (pts) with rheumatoid arthritis (RA) through 48 weeks (wks).[1]

Objectives: To report the efficacy and safety of UPA vs MTX mono up to 156 wks in pts with RA from the ongoing long-term extension (LTE) of the SELECT-EARLY trial.

Methods: During the 48-wk double-blind study period, pts were randomized to UPA 15 or 30 mg once daily (QD) or MTX (titrated to 20 mg/wk by Wk 8). At Wk 26, pts who did not achieve Clinical Disease Activity Index (CDAI) remission (≤2.8) and had <20% improvement from baseline in tender or swollen joint count received blinded rescue therapy (addition of MTX for UPA groups and UPA 15 or 30 mg for MTX group). In the LTE, pts received open-label treatment once the last pt reached Wk 48. Efficacy assessments up to Wk 156 were summarized by randomized group and included American College of Rheumatology (ACR) responses, remission and low disease activity (LDA) measures, and change in modified Total Sharp Score (mTSS; up to 96 wks). Treatment-emergent adverse events (AEs) per 100 pt-years (PY) for pts on continuous mono were summarized through 156 wks. Non-responder imputation was used for binary endpoints for missing data and when pts received rescue therapy or prematurely discontinued the study drug.

Results: Of 945 pts randomized and treated, 775 entered the LTE on study drug (including 57 rescued pts; MTX, 33; UPA 15 mg, 17; UPA 30 mg, 7). Overall, 161 (21%) pts discontinued during the LTE. At Wk 156, higher proportions of pts randomized to UPA achieved a 20/50/70% improvement in ACR response (ACR20/50/70), LDA, and remission vs MTX (Figure 1). Change from baseline in mTSS at Wk 96 favored UPA vs MTX (data not shown). Most AEs were numerically more frequent with UPA 30 mg. The overall rate of serious infection was numerically higher with UPA vs MTX (Table 1). Herpes zoster (HZ), neutropenia, non-melanoma skin cancer (NMSC), and creatine phosphokinase (CPK) elevation were more frequent with UPA vs MTX. Two active tuberculosis (TB) events were reported in each UPA arm; 3 adjudicated gastrointestinal (GI) perforation events were observed in the UPA 30 mg arm. Adjudicated major adverse cardiovascular events (MACEs) or venous thromboembolic events (VTEs) were comparable across treatment arms.

Conclusion: UPA monotherapy showed sustained clinically meaningful responses including remission vs MTX through Wk 156 but higher rates of several AEs, including HZ, neutropenia, and CPK elevations; no new safety risks were observed compared with previous results.[1,2]

REFERENCES:

[1] van Vollenhoven R, et al. Ann Rheum Dis 2019;78:376–7; 2. Cohen SB, et al. Ann Rheum Dis 2020;annrheumdis-2020-218510.

Table 1. Safety overview

E/100 PY (95% CI)	MTX mono (n=314; PY=601.9)	UPA 15 mg QD mono (n=317; PY=703.4)	UPA 30 mg QD mono (n=314; PY=687.6)
Any AE	240.2 (228.0, 252.9)	268.0 (256.0, 280.4)	292.5 (279.8, 305.5)
Any serious AE	10.8 (8.3, 13.8)	12.2 (9.8, 15.1)	16.3 (13.4, 19.6)
Any AE leading to discontinuation of study drug	6.5 (4.6, 8.9)	7.3 (5.4, 9.5)	7.7 (5.8, 10.1)
Any death[a]	0.7 (0.2, 1.7)	0.9 (0.3, 1.9)	1.0 (0.4, 2.1)
Serious infection	2.5 (1.4, 4.1)	3.3 (2.1, 4.9)	4.4 (2.9, 6.2)
Opportunistic infection excluding TB and HZ	0.2 (0.0, 0.9)	0.1 (0.0, 0.8)	0.3 (0.0, 1.1)
HZ	0.8 (0.3, 1.9)	4.5 (3.1, 6.4)	4.7 (3.2, 6.6)
Active TB	0	0.3 (0.0, 1.0)	0.3 (0.0, 1.1)
NMSC	0	0.4 (0.1, 1.2)	1.0 (0.4, 2.1)
Malignancy other than NMSC	1.0 (0.4, 2.2)	0.6 (0.2, 1.5)	1.2 (0.5, 2.3)
Hepatic disorder	14.1 (11.3, 17.5)	12.5 (10.0, 15.4)	15.0 (12.2, 18.2)
GI perforation[b]	0	0	0.4 (0.1, 1.3)
Neutropenia	2.2 (1.2, 3.7)	4.5 (3.1, 6.4)	5.7 (4.0, 7.8)
CPK elevation	1.8 (0.9, 3.3)	7.7 (5.8, 10.0)	15.4 (12.6, 18.6)
MACE[b]	0.3 (0.0, 1.2)	0.4 (0.1, 1.2)	0.6 (0.2, 1.5)
VTE[b]	0.3 (0.0, 1.2)	0.4 (0.1, 1.2)	0.6 (0.2, 1.5)

Data were censored at the time of MTX or UPA addition for rescued pts

[a]Includes treatment-emergent (≤30 days after the last dose of study drug) and non-treatment-emergent deaths. [b]Adjudicated

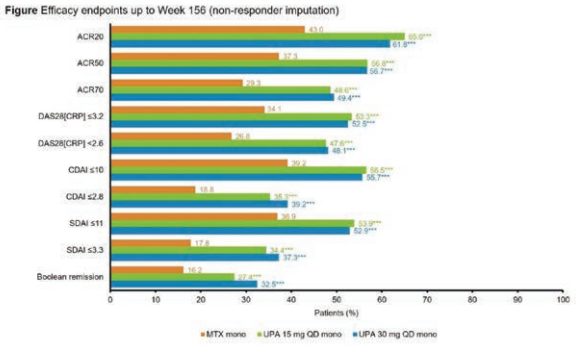


Figure Efficacy endpoints up to Week 156 (non-responder imputation)

***Nominal p<0.001 vs MTX mono
ACR20/50/70, 20/50/70% improvement in American College of Rheumatology response; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS28, Disease Activity Score in 28 joints; mono, monotherapy; QD, once daily; MTX, methotrexate; SDAI, Simple Disease Activity Index; UPA, upadacitinib

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Russell Craddock, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Disclosure of Interests: Ronald van Vollenhoven Speakers bureau: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Galapagos, Gilead, GSK, Janssen, Pfizer, Sanofi, Servier, UCB, and Viela Bio, Consultant of: AbbVie, AstraZeneca, Biogen, Biotest, Bristol-Myers Squibb, Galapagos, Gilead, GSK, Janssen, Pfizer, Sanofi, Servier, UCB, and Viela Bio, Grant/research support from: Bristol-Myers Squibb, GSK, Eli Lilly, Pfizer, Roche, and UCB, Tsutomu Takeuchi Speakers bureau: AbbVie, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Dainippon Sumitomo, Eisai, Gilead, Mitsubishi Tanabe, Novartis, Pfizer, and Sanofi, Consultant of: Astellas, Chugai, and Eli Lilly, Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi Sankyo, Eisai, Mitsubishi Tanabe, Nippon Kayaku, Shionogi, Takeda, and UCB, Jacob Aelion Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos/Gilead, Genentech, GSK, Horizon, Janssen, Mallinckrodt, Nektar, Nichi-Iko, Novartis, Pfizer, Regeneron, Roche, Sanofi, Selecta, and UCB, Nilmo Chávez Speakers bureau: AbbVie, Janssen, and Pfizer, Consultant of: AbbVie, Janssen, and Pfizer, Grant/research support from: AbbVie, Galapagos, Gilead, Pfizer, and Sanofi, Pablo Mannucci Walter Consultant of: AbbVie, Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Genentech/Roche, GSK, Janssen, and UCB, Atul Singhal Consultant of: AbbVie, Aclaris, Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Gilead, Idorsia, Novartis, Oscotec,

Pfizer, Regeneron, Roche/Genentech, Sanofi, Selecta, Takeda, UCB, and Viela Bio, Grant/research support from: AbbVie, Aclaris, Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Gilead, Idorsia, Novartis, Oscotec, Pfizer, Regeneron, Roche/Genentech, Sanofi, Selecta, Takeda, UCB, and Viela Bio, Jerzy Swierkot Speakers bureau: AbbVie, Accord, BMS, Janssen, MSD, Pfizer, Roche, Sandoz, and UCB, Consultant of: AbbVie, Accord, BMS, Janssen, MSD, Pfizer, Roche, Sandoz, and UCB, Grant/research support from: AbbVie, Accord, BMS, Janssen, MSD, Pfizer, Roche, Sandoz, and UCB, Alan Friedman Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Nasser Khan Shareholder of: May own stocks or options in AbbVie, Employee of: AbbVie, Yihan Li Shareholder of: May own stocks or options in AbbVie, Employee of: AbbVie, Xianwei Bu Shareholder of: May own stocks or options in AbbVie, Employee of: AbbVie, Justin Klaff Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Vibeke Strand Consultant of: AbbVie, Amgen, Arena, AstraZeneca, Bayer, Bristol-Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Genentech/Roche, Gilead, GSK, Ichnos, Inmedix, Janssen, Kiniksa, MSD, Myriad Genetics, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, Setpoint, and UCB

DOI: 10.1136/annrheumdis-2021-eular.530

POS0656 RELATIONSHIP BETWEEN CHANGES IN LIPID LEVELS AND IMPROVEMENT IN DISEASE ACTIVITY OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING UPADACITINIB TREATMENT: POOLED ANALYSIS OF DATA FROM TWO PHASE 3 STUDIES

C. Charles-Schoeman[1], J. T. Giles[2], N. Lane[3], E. Choy[4], H. Camp[5], Y. Song[5], S. Anyanwu[5], I. McInnes[6]. [1]*University of California, Rheumatology, Los Angeles, United States of America*; [2]*Columbia University, Rheumatology, New York, United States of America*; [3]*University of California, Davis, Sacramento, United States of America*; [4]*Cardiff University, School of Medicine, Cardiff, United Kingdom*; [5]*AbbVie Inc., Rheumatology, North Chicago, United States of America*; [6]*University of Glasgow, Rheumatology, Glasgow, United Kingdom*

Background: Upadacitinib (UPA) is an oral Janus kinase (JAK) inhibitor engineered to have greater selectivity for JAK1 vs JAK2, JAK3, and tyrosine kinase 2, and is approved for the treatment of RA. Across 2 double-blind, placebo (PBO)-controlled Phase 3 studies of UPA in patients with RA, after an initial increase through Week 8, lipid levels remained stable up to Week 24.[1,2] Previous studies of JAK or IL-6 receptor inhibitors have reported a negative correlation between changes in lipid levels and RA disease activity.[3,4]

Objectives: To determine the relationship between changes in lipid levels and disease activity outcomes in patients with RA treated with UPA.

Methods: Patients with RA and an inadequate response to conventional synthetic/biologic DMARDs (cs/bDMARD-IR) from SELECT-NEXT/SELECT-BEYOND, respectively, were randomized to receive UPA 15 mg once daily (QD), UPA 30 mg QD, or PBO for 12 weeks followed by an extension of up to 5 years; patients randomized to PBO switched to UPA 15 or 30 mg after 12 weeks. Spearman correlations of maximum changes from baseline (BL) through Week 12 in fasting-state lipid levels (low- and high-density lipoprotein cholesterol [LDL-C; HDL-C], and total cholesterol [TC]) with clinical disease activity outcomes measured by change from BL in Clinical Disease Activity Index (CDAI), DAS of 28 joints using CRP (DAS28[CRP]), tender/swollen joint count in 28 joints (TJC28/SJC28), and pain by visual analog scale (VAS) at Weeks 12 and 24, were determined. Spearman correlations of maximum changes from BL in lipid levels and CRP through Week 12 were also determined.

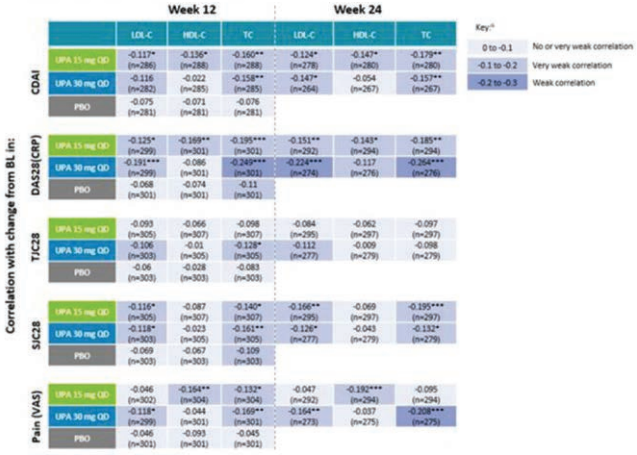
Results: Available fasting samples from 1,160 pooled patients (UPA 15 mg, n=386; UPA 30 mg, n=384; PBO, n=390) were included. Modest, but statistically significant, negative correlations were observed between maximum changes from BL in TC through Week 12 and change from BL in CDAI, DAS28(CRP), SJC28, and pain (VAS) at Week 12 with UPA 15 or 30 mg (Figure 1); similar trends were observed at Week 24. Significant correlations between changes in LDL-C and HDL-C and disease activity outcomes were also observed, but were not consistent across UPA doses and time points. No significant correlations were noted between changes in lipid levels and disease activity outcomes in the PBO group. Statistically significant weak negative relationships were observed between maximum changes from BL in lipid levels and CRP levels through Week 12 with UPA 15 mg (HDL-C and TC) or UPA 30 mg (LDL-C and TC) (Table 1).

Conclusion: In this large pooled data set of patients receiving UPA, increases in lipid levels showed modest, but statistically significant, correlations with improvement in clinical disease activity outcomes in patients with cs/bDMARD-IR RA. These results add to evidence suggesting a relationship between systemic inflammation and lipid metabolism in patients with RA, which is modifiable with effective interventions, and reinforce the importance of monitoring for hyperlipidemia in these patients.

REFERENCES:

[1] Burmester GR, et al. Lancet 2018;391:2503–12.
[2] Genovese MC, et al. Lancet 2018;391:2513–24.
[3] Kremer JM, et al. Arthritis Rheumatol 2017;69:943–52.
[4] Cacciapaglia F, et al. Mediators Inflamm 2018;2018:2453265.

Figure. Spearman correlations of maximum changes from BL in lipid levels through Week 12 with disease activity outcomes at Weeks 12 and 24



*p<0.05, **p<0.01, ***p<0.001.
BL, baseline; CDAI, Clinical Disease Activity Index; DAS28(CRP), DAS of 28 joints using CRP; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PBO, placebo; QD, once daily; SJC28, swollen joint count in 28 joints; TC, total cholesterol; TJC28, total joint count in 28 joints; UPA, upadacitinib; VAS, visual analog scale.

Table 1. Spearman correlation of maximum changes from BL in lipid levels through Week 12 with maximum change from BL in CRP through Week 12

	UPA 15 mg QD	UPA 30 mg QD	PBO
LDL-C	-0.099 (n=303)	-0.174** (n=302)	-0.053 (n=303)
HDL-C	-0.184** (n=305)	-0.087 (n=304)	-0.024 (n=303)
TC	-0.189*** (n=305)	-0.236*** (n=304)	-0.056 (n=303)

**p<0.01, ***p<0.001.
HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoproteincholesterol; PBO, placebo; QD, once daily; TC, total cholesterol; UPA, upadacitinib

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing assistance was provided by Frances Smith, PhD, of 2 the Nth, which was funded by AbbVie.

Disclosure of Interests: Christina Charles-Schoeman Consultant of: AbbVie, Gilead, Pfizer, and Regeneron-Sanofi., Grant/research support from: AbbVie, Bristol-Myers Squibb, and Pfizer, Jon T Giles Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, and Gilead, Grant/research support from: Pfizer, Nancy Lane Speakers bureau: Amgen and Mallinckrodt, Consultant of: Amgen, Mallinckrodt, Pfizer, and Roche, Ernest Choy Speakers bureau: AbbVie, Amgen, AstraZeneca, Bio-Cancer, Biogen, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai Pharma, Eli Lilly, Ferring Pharmaceuticals, GlaxoSmithKline, Hospira, Janssen, Merck Sharp & Dohme, Napp, Novimmune, Novartis, ObsEva, Pfizer, Regeneron, Roche, R-Pharm, Sanofi, SynAct Pharma, Synovate, Tonix, and UCB, Grant/research support from: AbbVie, Amgen, AstraZeneca, Bio-Cancer, Biogen, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai Pharma, Eli Lilly, Ferring Pharmaceuticals, GlaxoSmithKline, Hospira, Janssen, Merck Sharp & Dohme, Napp, Novimmune, Novartis, ObsEva, Pfizer, Regeneron, Roche, R-Pharm, Sanofi, SynAct Pharma, Synovate, Tonix, and UCB, Heidi Camp Shareholder of: AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: AbbVie, Employee of: AbbVie, Samuel Anyanwu Shareholder of: AbbVie, Employee of: AbbVie, Iain McInnes Consultant of: AbbVie, Celgene, Janssen, Novartis, and UCB, Grant/research support from: Celgene, Janssen, Novartis, Pfizer Inc., Roche, and UCB

DOI: 10.1136/annrheumdis-2021-eular.606

POS0657 GEOGRAPHIC VARIATION OF SAFETY IN THE FILGOTINIB RHEUMATOID ARTHRITIS PROGRAM

B. Combe[1], T. Matsubara[2], A. Pechonkina[3], Y. Tan[4], Z. Yin[5], J. Hong[5], R. Besuyen[6], A. Gomez-Centeno[7], M. H. Buch[8]. [1]*University of Montpellier, Department of Rheumatology, Montpellier, France*; [2]*Matsubara Mayflower Hospital, Department of Orthopaedic Surgery, Kato, Japan*; [3]*Gilead*

Sciences, Inc., Inflammation and Respiratory Therapeutic Area, Foster City, United States of America; [4]*Gilead Sciences, Inc., Inflammation Therapeutic Area, Foster City, United States of America*; [5]*Gilead Sciences, Inc., Biostatistics, Foster City, United States of America*; [6]*Galapagos BV, Clinical Development, Leiden, Netherlands*; [7]*Hospital Universitari Parc Taulí, Department of Rheumatology, Barcelona, Spain*; [8]*University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*

Background: The Janus kinase-1 preferential inhibitor filgotinib (FIL) improved signs and symptoms of rheumatoid arthritis (RA) in the FIL clinical program.[1–3]

Objectives: To assess FIL safety across regions.

Methods: This was an analysis of patients (pts) meeting 2010 ACR/EULAR RA criteria in pooled phase (P)2 DARWIN 1–2 (D1–2), P3 FINCH 1–3 (F1–3), and long-term extension studies (DARWIN 3, FINCH 4). Data were analyzed by region: North America, South and Central America, Western Europe, Eastern Europe, Asia, South East (SE) Asia, and Other. Week (W)12 placebo (PBO)-controlled analysis included data from pts receiving once-daily FIL 100 mg (FIL100), FIL 200 mg (FIL200), or PBO for ≤12W (D1–2, F1–2); long-term as-treated data included pts from all 7 studies receiving FIL100 or FIL200; data after rerandomization were included and contributed to treatment received. Data presented as exposure-adjusted incidence rates (EAIRs)/100 patient-years of exposure (PYE) of treatment-emergent (TE) adverse events (TEAEs).

Results: Table 1 shows EAIRs of TEAEs in PBO-controlled analysis. EAIRs/100 PYE of all TEAEs in Western Europe, Asia, and Other were higher than in remaining regions and for PBO vs FIL arms; EAIRs for FIL200/FIL100 in North America and SE Asia were higher vs PBO. EAIRs/100 PYE of TE serious AEs were higher in SE Asia for FIL100 and for FIL200/FIL100 in Other, with high PBO EAIRs in Western Europe. EAIRs/100 PYE of TEAEs leading to study discontinuation were higher in FIL arms vs PBO in Western Europe and Other (FIL200); in Asia and SE Asia, EAIRs were higher for PBO vs FIL200/FIL100.

Table 1. EAIR of TEAEs (placebo-controlled)

	North America N = 481	South and Central America N = 350	Western Europe N = 141	Eastern Europe N = 933	Asia N = 236	South East Asia N= 135	Other N = 70
TEAE							
FIL200[a]	216.9 (162.5, 289.5)	205.6 (155.1, 272.6)	285.0 (188.6, 430.8)	150.3 (119.3, 189.4)	248.9 (180.6, 343.1)	165.1 (104.0, 262.1)	298.4 (150.3, 592.5)
FIL100[b]	182.2 (136.8, 242.7)	159.2 (117.3, 216.1)	285.7 (183.7, 444.3)	146.4 (115.9, 185.0)	246.9 (180.3, 338.1)	153.7 (94.2, 251.0)	263.5 (113.9, 609.2)
PBO[c]	174.5 (130.3, 233.7)	162.1 (118.8, 221.2)	314.9 (200.7, 493.9)	148.4 (117.6, 187.4)	259.0 (188.0, 356.8)	81.6 (40.8, 163.3)	306.0 (142.8, 655.7)
TE serious AE							
FIL200[a]	14.3 (6.0, 34.4)	11.4 (3.7, 35.5)	8.3 (1.2, 59.0)	12.2 (5.2, 28.7)	5.5 (0.8, 38.9)	0.0 (0.0, ∞)	49.6 (10.2, 144.9)
FIL100[b]	10.6 (4.0, 28.3)	7.2 (1.8, 28.7)	19.9 (5.0, 79.7)	15.1 (6.8, 33.7)	16.2 (5.2, 50.2)	28.8 (9.3, 89.4)	20.5 (0.5, 114.0)
PBO[c]	16.1 (7.2, 35.9)	7.5 (1.9, 30.0)	29.6 (9.5, 91.7)	4.6 (1.3, 15.8)	11.4 (2.8, 45.5)	10.2 (1.4, 72.4)	0.0 (0.0, 69.2)
TEAE leading to discontinuation							
FIL200[a]	8.6 (2.8, 26.6)	3.8 (0.1, 21.2)	16.6 (4.2, 66.5)	12.9 (5.5, 30.5)	0.0 (0.0, 20.2)	9.2 (1.3, 65.1)	16.5 (0.4, 92.1)
FIL100[b]	10.6 (4.0, 28.3)	7.2 (0.9, 26.0)	19.9 (5.0, 79.7)	1.9 (0.2, 13.8)	5.4 (0.1, 30.1)	9.6 (1.4, 68.2)	0.0 (0.0, 75.5)
PBO[c]	5.4 (1.3, 21.5)	0.0 (0.0, 13.8)	9.9 (1.4, 70.0)	12.9 (5.4, 30.7)	17.1 (3.5, 49.9)	20.4 (5.1, 81.6)	0.0 (0.0, 69.2)

Data presented as EAIR (95% CI)/100 patient-years

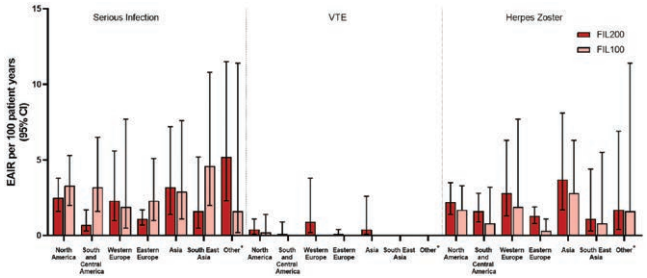
[a]N = 777, 179.8 PYE [b]N = 788, 181.6 PYE [c]N = 781, 178.4 PYE

A subject may contribute to more than one treatment group if they received more than one treatment of interest.

EAIR and corresponding 95% CI were estimated using Poisson regression model by treatment, including study and treatment with an offset of natural log of exposure time, except when 0 events occurred; Poisson model was not adjusted by study.

AE, adverse event; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; PBO, placebo; PYE, patient-years of exposure; TE, treatment-emergent

Figure shows serious infections (SI), venous thromboembolism (VTE) and herpes zoster (HZ) EAIRs.



EAIRs for SI were highest in Other for FIL200 and SE Asia for FIL100. While VTE EAIRs were low, pts in 5/7 regions had VTE. HZ EAIRs were highest in Asia.

Conclusion: Although EAIR of TEAEs varied between regions, no consistent trend was reflected in any particular region.

REFERENCES:

[1] Genovese et al. *JAMA*. 2019;322:315–25.
[2] Westhovens et al. *Ann Rheum Dis*. 2021; online first.
[3] Combe et al. *Ann Rheum Dis*. 2021; online first.

Disclosure of Interests: Bernard Combe Speakers bureau: BMS; Eli Lilly & Co.; Gilead Sciences, Inc.; MSD; Pfizer; Roche-Chugai; and UCB, Consultant of: AbbVie; Eli Lilly & Co.; Gilead Sciences, Inc.; Janssen; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Novartis, Pfizer, and Roche-Chugai, Tsukasa Matsubara Speakers bureau: Pfizer Japan, Nichi-Iko, Astellas, Meiji Seika, Bristol-Myers Squibb, AbbVie GK, Janssen, Chugai, Eisai, AYUMI, Alena Pechonkina Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., YingMeei Tan Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Zhaoyu Yin Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Jaehyung Hong Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Robin Besuyen Shareholder of: Galapagos, BV, Employee of: Galapagos, BV, Antonio Gomez-Centeno Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly & Co., Gebro, Janssen, Menarini, Merck Sharp & Dohme, Pfizer, Roche, Rubio, Sanofi, and UC, Consultant of: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Eli Lilly & Co., Gebro, Gilead Sciences, Inc., Hospira, Merck Sharp & Dohme, Pfizer, Roche, Rubio, Sandoz, Sanofi, Grant/research support from: Boehringer Ingelheim, Celltrion, Eli Lilly & Co., Galapagos NV, Gilead Sciences, Inc., Novartis, Pfizer, Roche, Sanofi, UCB, YL Biologics, Maya H Buch Speakers bureau: AbbVie; Eli Lilly and Company; Gilead Sciences, Inc.; Merck-Serono; Pfizer; Roche; Sandoz; Sanofi; and UCB, Consultant of: AbbVie; Eli Lilly and Company; Gilead Sciences, Inc.; Merck-Serono; Pfizer; Roche; Sandoz; Sanofi; and UCB, Grant/research support from: AbbVie; Eli Lilly and Company; Gilead Sciences, Inc.; Merck-Serono; Pfizer; Roche; Sandoz; Sanofi; and UCB

DOI: 10.1136/annrheumdis-2021-eular.643

POS0658 GEOGRAPHIC VARIATION OF EFFICACY IN THE FILGOTINIB RHEUMATOID ARTHRITIS PROGRAM

M. H. Buch[1], T. Matsubara[2], B. Combe[3], A. Pechonkina[4], Y. Tan[5], Z. Yin[6], J. Hong[6], R. Besuyen[7], A. Gomez-Centeno[8]. [1]*University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; [2]*Matsubara Mayflower Hospital, Department of Orthopaedic Surgery, Kato, Japan*; [3]*University of Montpellier, Department of Rheumatology, Montpellier, France*; [4]*Gilead Sciences, Inc., Inflammation and Respiratory Therapeutic Area, Foster City, United States of America*; [5]*Gilead Sciences, Inc., Inflammation Therapeutic Area, Foster City, United States of America*; [6]*Gilead Sciences, Inc., Biostatistics, Foster City, United States of America*; [7]*Galapagos BV, Clinical Development, Leiden, Netherlands*; [8]*Hospital Universitari Parc Taulí, Department of Rheumatology, Barcelona, Spain*

Background: The Janus kinase-1 preferential inhibitor filgotinib (FIL) improved signs and symptoms of rheumatoid arthritis (RA) across the FIL clinical program.[1–3]

Objectives: To assess FIL efficacy across geographic regions.

Methods: Pooled data from patients (pts) meeting 2010 ACR/EULAR RA criteria randomised to once-daily FIL 200 mg (FIL200), FIL100 mg (FIL100), or placebo (PBO) with background conventional synthetic disease-modifying antirheumatic drugs in DARWIN 1 (P2; up to week [W]12) and FINCH 1–2 (P3; up to W24) studies were evaluated. Data were analysed by region: North America, South and Central America, Western Europe, Eastern Europe, Asia, South East (SE) Asia, and Other. W12 American College of Rheumatology 20% improvement (ACR20) and W24 Disease Activity Score in 28 joints (C-reactive protein) (DAS28[CRP]) <2.6 and ≤3.2 response rates were analysed by a logistic regression model. Change from baseline (CFB) in Health Assessment Questionnaire-Disability

Index (HAQ-DI) at W12 was analysed by a mixed-effects model for repeated measures. Analyses were exploratory and not adjusted for multiplicity.

Results: Despite high PBO response rates in Eastern Europe and South and Central America, greater proportions of pts receiving FIL200 or FIL100 vs PBO achieved ACR20 at W12 (*P* <0.05) in all regions, except Other (with lowest sample size, n = 69), where both FIL doses were numerically greater than PBO (Table 1). At W12, least-squares mean CFB in HAQ-DI improved for pts receiving FIL200 or FIL100. vs PBO (*P* <0.05) in all regions, except SE Asia, where improvement was numeric (Table 1).

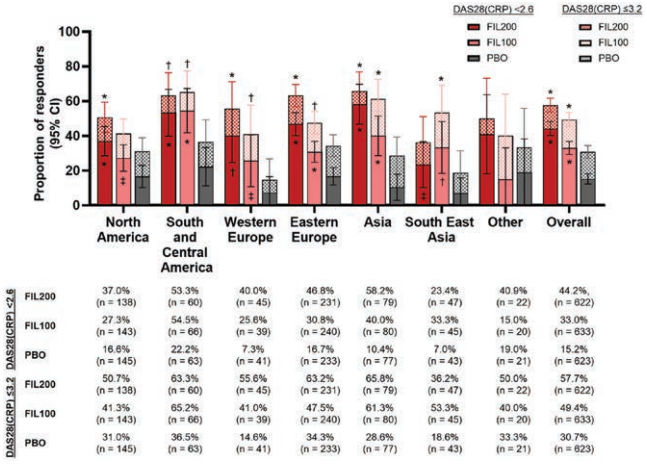
Table 1. Proportion of pts achieving ACR20 and LSM change from baseline HAQ-DI at week 1

	ACR20			HAQ-DI		
	FIL200	**FIL100**	**FIL200**	**FIL100**	**FIL200**	**FIL100**
North America	64.8*	58.3*	33.8	−0.63*	−0.58*	−0.34
n = 455	(56.7, 72.9)	(50.3, 66.4)	(26.0, 41.6)	(−0.70, −0.56)	(−0.65, −0.51)	(−0.41, −0.27)
South and Central America	77.2	77.3	57.4	−0.77*	−0.67*	−0.43
n = 283	(68.1, 86.3)†	(65.8, 86.2)†	(46.9, 68.0)	(−0.85, −0.68)	(−0.75, −0.59)	(−0.52, −0.35)
Western Europe	69.4*	68.3*	24.4	−0.69*	−0.61*	−0.28
n = 135	(55.5, 83.3)	(52.8, 83.8)	(10.8. 38.1)	(−0.80, −0.58)	(−0.73, −0.49)	(−0.40, −0.17)
Eastern Europe	77.1*	69.1*	54.6	−0.62*	−0.51*	−0.34
n = 822	(71.9, 82.3)	(63.5, 74.7)	(48.5, 60.7)	(−0.68, −0.56)	(−0.57, −0.45)	(−0.40, −0.28)
Asia	81.0*	60.0†	37.7	−0.83*	−0.61†	−0.42
n = 236	(71.7, 90.3)	(48.6, 71.4)	(26.2, 49.1)	(−0.92, −0.73)	(−0.70, −0.52)	(−0.52, −0.33)
South East Asia	70.2†	71.1†	39.5	−0.61	−0.57	−0.45
n = 135	(56.1, 84.4)	(56.8, 85.5)	(23.8, 55.3)	(−0.73, −0.49)	(−0.69, −0.45)	(−0.58, −0.33)
Other	60.0	52.4	39.1	−0.56‡	−0.60‡	−0.33
n = 69	(38.8, 81.2)	(28.6, 76.1)	(17.0, 61.2)	(−0.72, −41)	(−0.76, −0.43)	(−0.49, −0.17)
Overall	73.4*	66.4*	45.3	−0.71*	−0.61*	−0.40
N = 2135	(70.1, 76.8)	(62.9, 70.0)	(41.5, 49.0)	(−0.76, −0.66)	(−0.66, −0.56)	(−0.45, −0.35)

Includes only patients initially randomised to the treatment groups in each study for the comparison of interest. ACR20 presented as percentage (95% CI); 95% CI was based on normal approximation method with a continuity correction; P values calculated from the logistic regression.HAQ-DI presented as LSM (95% CI); LSM, 95% CI, and P value calculated from a mixed-effects model for repeated measures.*P <0.001, †P <0.01, ‡P <0.05; not adjusted for multiplicity.

ACR20, American College of Rheumatology 20% improvement; CI, confidence interval; FIL, filgotinib; HAQ-DI, Health Assessment Questionnaire-Disability Index; LSM, least square mean; PBO, placebo.

At W24, DAS28(CRP) <2.6 and ≤3.2 response rates were higher for both doses of FIL vs PBO (*P* <0.05) in all regions, with the exception of Other, where PBO was higher than FIL100 for DAS28(CRP) <2.6 (Figure 1).



Conclusion: In exploratory analyses, ACR20, DAS28(CRP) <2.6 and ≤3.2 response rates and HAQ-DI scores varied between regions; however, no stable trend was shown in any particular region. Small pt numbers in some subgroups may confound statistical analysis.

REFERENCES:

[1] Genovese et al. *JAMA*. 2019;322:315–25.
[2] Westhovens et al. *Ann Rheum Dis*. 2021; online first.
[3] Combe et al. *Ann Rheum Dis*. 2021; online first.

Disclosure of Interests: Maya H Buch Speakers bureau: AbbVie; Eli Lilly and Company; Gilead Sciences, Inc.; Merck-Serono; Pfizer; Roche; Sandoz; Sanofi; and UCB, Consultant of: AbbVie; Eli Lilly and Company; Gilead Sciences, Inc.; Merck-Serono; Pfizer; Roche; Sandoz; Sanofi; and UCB., Grant/research support from: AbbVie; Eli Lilly and Company; Gilead Sciences, Inc.; Merck-Serono; Pfizer; Roche; Sandoz; Sanofi; and UCB., Tsukasa Matsubara Speakers bureau: Pfizer Japan, Nichi-Iko, Astellas, Meiji Seika, Bristol-Myers Squibb, AbbVie GK, Janssen, Chugai, Eisai, AYUMI, Bernard Combe Speakers bureau: BMS; Eli Lilly & Co.; Gilead Sciences, Inc.; MSD; Pfizer; Roche-Chugai; and UCB, Consultant of: AbbVie; Eli Lilly & Co.; Gilead Sciences, Inc.; Janssen; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Novartis, Pfizer, and Roche-Chugai, Alena Pechonkina Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., YingMeei Tan Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Zhaoyu Yin Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Jaehyung Hong Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Robin Besuyen Shareholder of: Galapagos, BV, Employee of: Galapagos, BV, Antonio Gomez-Centeno Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly & Co., Gebro, Janssen, Menarini, Merck Sharp & Dohme, Pfizer, Roche, Rubio, Sanofi, and UCB, Consultant of: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Eli Lilly & Co., Gebro, Gilead Sciences, Inc., Hospira, Merck Sharp & Dohme, Pfizer, Roche, Rubio, Sandoz, Sanofi, Grant/research support from: Boehringer Ingelheim, Celltrion, Eli Lilly & Co., Galapagos NV, Gilead Sciences, Inc., Novartis, Pfizer, Roche, Sanofi, UCB, YL Biologics
DOI: 10.1136/annrheumdis-2021-eular.648

POS0659

REAL WORD EXPERIENCE WITH TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN INTERIM ANALYSIS FROM A FRENCH PROSPECTIVE OBSERVATIONAL STUDY DeFacTo

C. Gaujoux-Viala[1], A. Basch[2], S. Lassoued[3], F. Coury-Lucas[4], M. Kessouri[5], N. Mammar[5], T. Lequerre[6], C. Salliot[7]. *[1]University Hospital Carémeau, Rheumatology, NIMES, France*; *[2]Infirmerie Protestante de Lyon, Rheumatology, Caluire et Cuire, France*; *[3]Cahors Hospital Center, Rheumatology, Cahors, France*; *[4]Lyon Sud Hospital, Rheumatology, Pierre-Bénite, France*; *[5]Pfizer, Immunologie & Inflammation, Paris, France*; *[6]Rouen University Hospital & Inserm U905, Rheumatology, Rouen, France*; *[7]Orléans Régional Hospital Center, Rheumatology, Orléans, France*

Background: Tofacitinib is an oral JAK inhibitor indicated for moderate to severe active rheumatoid arthritis (RA).

Objectives: To present baseline patients characteristics and effectiveness data at 6 months of DeFacTo real life study ("I**De**ntification of **Fa**ctors predictive of **To**facitinib's survival").

Methods: DeFacTo is an observational, open-label, prospective, multi-center, national study designed to evaluate the predictive factors of tofacitinib's survival in patients with moderate-to-severe active rheumatoid arthritis according to the SmPC[1]. Here we present the 1st interim results involving a descriptive analysis of the 221 patients included between January 2019 and March 2020 (POP1). Effectiveness results at 6 months of 145 patients having ≥ 6 months follow-up (POP2) are also described.

Results: The baseline characteristics of the POP1 patients (n = 221) were: 78.3% women with a mean age (± SD) of 60.4 ± 11.1 years, disease duration of 12.0 ± 9.8 years, TJC: 7.3 ± 5.7 and SJC: 5.1 ± 4.7; 44.0% of patients had erosions, 79.5% were RF+ and 75.9% were ACPA+. The mean CRP was 15.3 ± 21.8 mg/l, the ESR at one hour was 28.7 ± 23.6 mm, DAS28-4 CRP was 4.6 ± 1.0, DAS28-4 ESR was 4.9 ± 1.1 and the FACIT-Fatigue score was 27.6 ± 11.3. A total of 97.3% of patients had been previously treated by ≥1 csDMARD (mean number 1.9 ± 1.0) and 66.1% by b/tsDMARDs (mean number 2.9 ± 2.5), tofacitinib was prescribed as monotherapy (without csDMARD) in 49.3% of patients. The characteristics of the POP2 patients were similar to those of POP1. At 6 months in POP2, 29 patients have discontinued their treatment with tofacitinib. The results showed a decrease from baseline in inflammatory markers (CRP from 14.2±17.1 to 4.7±4.2 mg/l), pain (Pain VAS from 58.3±23.4 to 27.6±22.1) and DAS28 activity scores with 23% of patients in DAS28-CRP remission and 36% of patients in DAS28-CRP LDA (figure 1). This interim analysis didn't identifyany new safety findings (Table 1).

Conclusion: *Preliminary results from this prospective observational study on the use of tofacitinib in patients suffering with RA in France indicate that its* effectiveness *and safety are similar to those found in the clinical studies*[1-3]. *In this study, tofacitinib was prescribed as monotherapy (without csDMARD) in more than 49% of cases.*

REFERENCES:

[1] *European Medicines Agency, Tofacitnibi SmPc (summary of product characteristics).*
[2] *Burmester G et al. Lancet. 2013; 381: 451-460.*

[3] *Fleischman R et al. Lancet 2017; 390: 457-6.*
[4] *Wollenhaupt et al. Arthritis Research & Therapy (2019) 21:89*

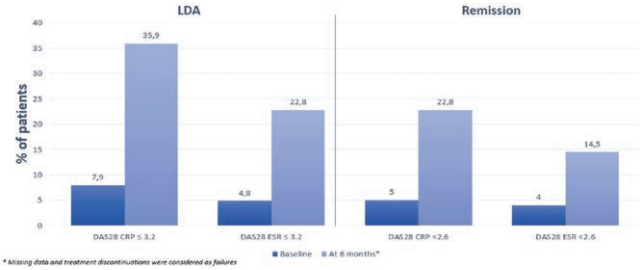


Figure 1. Patients with LDA or remission at baseline and 6 months

Table 1. ***Safety data***

Tolerability, n patients (%)	<65 years, n = 132	≥ 65 years, n = 86	Total n = 218
AE	*56 (42.4)*	*33 (38.4)*	*89 (40.8)*
Serious AE	*8 (6.1)*	*5 (5.8)*	*13 (6.0)*
Herpes Zoster	*4 (3.0)*	*2 (2.3)*	*6 (2.8)*
Infection	*27 (20.5)*	*15 (17.4)*	*42 (19.3)*
Severe infection	*2 (1.5)*	*2 (2.3)*	*4 (1.8)*

Acknowledgements: To all investigators involved in this study.
Disclosure of Interests: Cécile Gaujoux-Viala Speakers bureau: AbbVie; Amgen; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Consultant of: AbbVie; Amgen; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Andre BASCH Speakers bureau: Janssen, Novartis, Amgen, BMS, Abbvie, Lilly, Pfizer, MSD, UCB, Consultant of: Janssen, Novartis, Amgen, BMS, Abbvie, Lilly, Pfizer, MSD, UCB, Slim Lassoued: None declared, Fabienne COURY-LUCAS Consultant of: AbbVie, Bristol-Myers Squibb, Janssen, Lilly, MSD, Novartis and Pfizer, Grant/research support from: AbbVie, Biogen, Roche Chugai, Pfizer, and UCB, Meriem Kessouri Shareholder of: Pfizer, Employee of: Pfizer, Nadir Mammar Shareholder of: Pfizer, Employee of: Pfizer, Thierry Lequerre Consultant of: Abbvie, BMS, Boeringher, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Roche – Chugai, Sanofi, UCB, Carine Salliot Consultant of: Biogen, Lilly, Novartis, Roche Chugai, Pfizer
DOI: 10.1136/annrheumdis-2021-eular.870

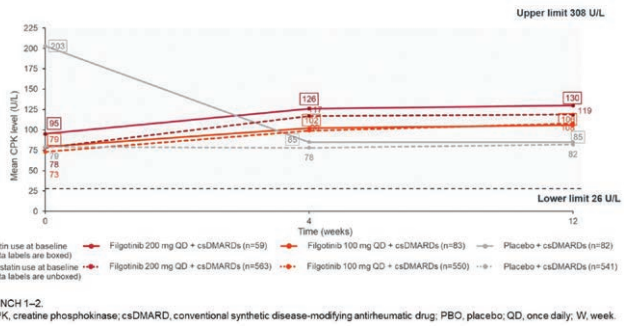
POS0660

CONCOMITANT USE OF STATINS IN FILGOTINIB-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS

P. C. Taylor[1], C. Charles-Schoeman[2], M. Alani[3,4], M. Trivedi[3], V. Castellano[5], I. Tiamiyu[3], D. Jiang[6], L. Ye[6], S. Strengholt[7], M. Nurmohamed[8], G. R. Burmester[9]. *[1]University of Oxford, Botnar Research Center, Oxford, United Kingdom*; *[2]UCLA Medical Center, Department of Medicine, Los Angeles, United States of America*; *[3]Gilead Sciences, Inc., Clinical Research, Foster City, United States of America*; *[4]University of Washington, Department of Rheumatology, Seattle, United States of America*; *[5]Gilead Sciences, Inc., Rheumatology Therapeutic Area, Foster City, United States of America*; *[6]Gilead Sciences, Inc., Biostatistics, Foster City, United States of America*; *[7]Galapagos BV, Department of Rheumatology, Leiden, Netherlands*; *[8]Amsterdam Rheumatology & Immunology Center, Department of Rheumatology, Amsterdam, Netherlands*; *[9]Charité - Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*

Background: The Janus kinase-1 preferential inhibitor filgotinib (FIL) improved rheumatoid arthritis (RA) signs and symptoms in phase (P)3 trials.[1–3] RA elevates cardiovascular disease risk; statins are used to reduce risk.
Objectives: To assess safety of statin and filgotinib coadministration across the clinical program.
Methods: Patients (pts) meeting 2010 ACR/EULAR RA criteria in P2 DARWIN 1–2 (D1–2; NCT01888874, NCT01894516), P3 FINCH 1–3 (F1–3; NCT02889796, NCT02873936, NCT02886728), and long-term extensions DARWIN 3 and FINCH 4 (D3, F4; NCT02065700, NCT03025308) receiving FIL 100 mg (FIL100) QD, FIL 200 mg QD (FIL200), adalimumab (ADA), methotrexate (MTX), or placebo (PBO) were included. Events related to statin use were analysed as exposed by treatment received. N and % were provided.
Week (W)12 PBO-controlled safety analysis included pts receiving FIL100, FIL200, or PBO for ≤12W (D1–2, F1–2); as-treated safety analysis included pts receiving long-term FIL100 QD (n=1647), FIL200 QD (n=2267), ADA (n=325), MTX (n=416), or PBO (n=781) (D1–3, F1–4); P3 as-randomised analysis included data up to W52 (F1–3) per assigned treatment.
Results: In each arm, similar proportions of pts took statins at baseline (9.4%–11.9%); initiation during study was low (1.2%–6.8%). Through W12 in PBO-controlled analysis, mean creatine phosphokinase (CPK; Figure 1), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels were similar regardless of statin use and remained within normal levels across all arms.

Figure: CPK levels through W12 in PBO-controlled analysis*



*FINCH 1–2.
CPK, creatine phosphokinase; csDMARD, conventional synthetic disease-modifying antirheumatic drug; PBO, placebo; QD, once daily; W, week.

Mean baseline ALT and AST levels were 20–23 and 20–22 U/L, respectively; at W12, ALT and AST ranged from 22–24 and 20–25 U/L, respectively. Graded CPK, ALT, and AST elevations are in Table 1.

Table 1. Graded laboratory abnormalities at week 12 by baseline statin use in PBO-controlled analysis

	Concomitant			None		
	FIL200 (n=68)	FIL100 (n=95)	PBO (n=93)	FIL200 (n=709)	FIL100 (n=693)	PBO (n=688)
CPK increased*	59	82	81	562	549	537
G1 (≤2.5×ULN)	10 (16.9)	13 (15.9)	6 (7.4)	71 (12.6)	47 (8.6)	18 (3.4)
G2 (>2.5 to 5×ULN)	3 (5.1)	0	0	6 (1.1)	2 (0.4)	3 (0.6)
G3 (>5 to 10×ULN)	0	0	0	1 (0.2)	0	3 (0.6)
G4 (>10×ULN)	0	0	0	1 (0.2)	2 (0.4)	0
AST increased**	68	94	92	708	692	684
G1 (≤3.0×ULN)	9 (13.2)	11 (11.7)	7 (7.6)	97 (13.7)	79 (11.4)	60 (8.8)
G2 (>3.0 to 5.0×ULN)	0	0	0	3 (0.4)	2 (0.3)	3 (0.4)
G3 (>5.0 to 20.0×ULN)	0	1 (1.1)	0	2 (0.3)	0	0
G4 (>20.0×ULN)	0	0	0	0	0	0
ALT increased**	68	94	92	708	692	684
G1 (≤3.0×ULN)	13 (19.1)	14 (14.9)	13 (14.1)	98 (13.8)	92 (13.3)	72 (10.5)
G2 (>3.0 to 5.0×ULN)	0	2 (2.1)	0	10 (1.4)	5 (0.7)	6 (0.9)
G3 (>5.0 to 20.0×ULN)	0	0	0	1 (0.1)	0	1 (0.1)
G4 (>20.0×ULN)	0	0	0	0	0	0

Data are n (%). Grading per Common Terminology Criteria for Adverse Events v4.03
*FINCH 1–2**DARWIN 1–2, FINCH 1–2ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; csDMARD, conventional synthetic disease-modifying antirheumatic drug; FIL200/100, filgotinib 200/100 mg + csDMARDs; Grade, G; PBO, placebo; ULN, upper limit of normal.

In the long-term as-treated analysis, 1 (0.5%)/6 (3.2%)/0/0/0 treatment-emergent adverse events (AE) of myalgia occurred in pts on statins at baseline receiving FIL200/FIL100/ADA/MTX/PBO and in 12 (0.6%)/8 (0.5%)/3 (1.0%)/2 (0.5%)/1 (0.1%) pts not on statins. Muscle spasms occurred in 2 (0.9%)/3 (1.6%)/1 (3.2%)/0/1 (1.1%) pts on statins at baseline receiving FIL200/FIL100/ADA/MTX/PBO and 21 (1.0%)/8 (0.5%)/0/3 (0.8%)/1 (0.1%) pts not on statins at baseline. One patient not on statins receiving FIL200 reported rhabdomyolysis. For all treatment arms in P3 as-randomised analysis, mean LDL and HDL increased similarly from baseline (108–110 and 56–59 mg/dL, respectively) to W52 (119–130 and 59–71 mg/dL, respectively).
Conclusion: No increases in statin-induced AEs such as muscle or liver toxicities occurred with statins and filgotinib coadministration; results are supported by a drug-drug interaction study.[4] Mean LDL and HDL increased at W52 in all treatment arms.
REFERENCES:
[1] Genovese et al. *JAMA.* 2019;322:315–25.
[2] Westhovens et al. *Ann Rheum Dis*. 2021; online first.
[3] Combe et al. *Ann Rheum Dis.* 2021; online first.
[4] Anderson et al. EULAR 2021 abstract.
Disclosure of Interests: Peter C. Taylor Consultant of: AbbVie, Biogen, Eli Lilly, Fresenius, Galapagos, Gilead, GlaxoSmithKline, Janssen, Nordic Pharma, Pfizer, Roche, BMS, Sanofi, Celltrion, and UCB, Grant/research support from: Celgene, Eli Lilly, Galapagos, and Gilead, Christina Charles-Schoeman

Consultant of: Gilead, Pfizer, and Regeneron-Sanofi, Grant/research support from: AbbVie, Bristol-Myers Squibb and Pfizer Inc, Muhsen Alani Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Mona Trivedi Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Vanessa Castellano Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Iyabode Tiamiyu Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Deyuan Jiang Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Lei Ye Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Sander Strengholt Shareholder of: Galapagos BV, Employee of: Galapagos BV, Michael Nurmohamed Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Roche, and Sanofi, Consultant of: AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, and Sanofi, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Mundipharma, Novartis, Pfizer, Roche, and Sanofi, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Eli Lilly, Pfizer, and Gilead Sciences, Inc., Consultant of: AbbVie, Eli Lilly, Pfizer, and Gilead Sciences, Inc.

DOI: 10.1136/annrheumdis-2021-eular.933

POS0661 RAPID RESPONSE TO BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO METHOTREXATE AND AT LEAST ONE BIOLOGIC DMARD: A CLINICAL AND POWER DOPPLER ULTRASOUND STUDY

C. Baldi[1], P. Falsetti[1], E. Conticini[1], S. G. Khayyat[1], M. Bardelli[1], S. Gentileschi[1], L. Cantarini[1], B. Frediani[1]. [1]*Rheumatology Unit, University of Siena, Siena, Italy*

Background: Baricitinib, an oral Janus kinase (JAK) 1-2 inhibitor, is currently used among biologic DMARDs (bDMARDs) after the failure of methotrexate (MTX) in rheumatoid arthritis (RA). Power Doppler ultrasound (PDUS) is a promising, non-invasive imaging method to assess synovitis in RA: results from numerous studies suggest that it provides additional information to clinical and conventional radiographic examinations.

Objectives: The main objective of our study was to evaluate short-term efficacy of Baricitinib in reducing synovitis, using the composite semi quantitative scale (0–3 grades) PDUS synovitis score, developed by the Outcome Measures in Rheumatology– European League Against Rheumatism (OMERACT–EULAR)-Ultrasound Task Force. Moreover both synovial hyperplasia and intrasynovial power Doppler (PD) signal were also scored as single components/parameters on 0-3 scales. Secondary objective was to assess the concordance between patient reported outcomes (PROs), markers of inflammation, physical examination and US.

Methods: We enrolled 30 patients fulfilling 2010 ACR and EULAR criteria for RA. All patients had failed at least one anti-TNF. Each patient was prescribed Baricitinib 4 mg/daily at T0, in addition to MTX and/or oral steroids at a dosage ≤ 7, 5 mg/day of Prednisone or equivalent, at T'. All patients were evaluated at baseline (T0) and then after one month (T1), 3 months (T2) and 6 months (T3) of treatment. Swollen and tender joints (out of 28)were evaluated and recorded, as well as patient (PGA) and physician global assessment (PhGA) and pain, expressed in a visual analog scale (VAS). Disease activity was evaluated at each visit using DAS28 (Disease activity score 28), CDAI (Clinical disease activity index)and SDAI(Simplified disease activity index), accompanied by a complete blood count, Erythrocyte sedimentation rate (ESR) and C- reactive protein (CRP) collection. Statistical analysis was performed using GraphPad version 9.0.0. PDUS examination, was carried out by two rheumatologists (PF and CB) blinded to clinical conditions of the patients, using an Esaote Mylab Twice (Genoa, Italy), equipped with a high-frequency (6-18 MHz) linear probe. With standardised Doppler parameters (pulse repetition frequency between 500-750 Hz; Doppler frequency between 7–11.1 MHz). PDUS was performed at each visit bilaterally for 22 joint sites [MCPs 1–5, proximal interphalangeal joints (PIPs) 1–5, wrist, elbow, glenohumeral, knee, tibiotalar, talonavicular and calcaneocuboidal and metatarsophalangeal joints (MTPs) 1–5] for a total of 44 joints for each patient.

Results: we observed a reduction of VAS pain (T0 vs, T6<0,0001) PDUS composite score (T0 vs. T6 p<0,0001), Power Doppler (T0 vs. T6 p<0,0001) synovial hyperplasia (T0 vs. T6 p=0,0002), CRP (T0 vs. T6 p<0,0001) and ESR (T0 vs. T6 p <0,0001) was observed in our patients. Accordingly, DAS-28, CDAI and SDAI displayed a significant reduction too (DAS-28: T0 vs. T6 p< 0, 0001; CDAI: T0 vs. T6 p< <0, 0001; SDAI: T0 vs. T6 p= 0, 0003).

Conclusion: We investigated the efficacy of Baricitinib in real life, evaluating both from a clinimetric and ultrasound point of view. Baricitinib, demonstrated a significant parallel and fast improvement in VAS, PDUS and CRP was found at follow up assessment as early as one month of therapy. In conclusion, these results demonstrated the short term efficacy of Baricitinib 4mg for up to 6 months and providing a prompt improvement of PROs within the first weeks of treatment.

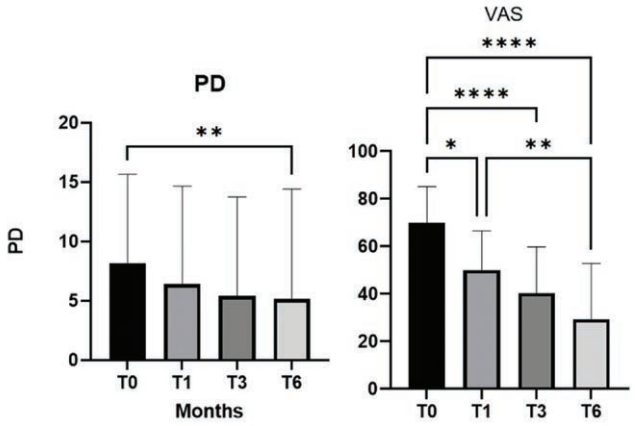


Figure 1. The difference between the means of PD and of the VAS pain over time (T0, T1, T3 and T6).Power Doppler (T0 vs. T6** p<0,0001), VAS: (T0 vs. T1 *p<0,0098;T0 vs. T3 **** p<0,0001; T0 vs. T6 ****p<0,0001)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1007

POS0662 PREDICTORS OF TOXICITY WITH HYDROXYCHLOROQUINE AND CHLOROQUINE USE: A SYSTEMATIC REVIEW

N. Citeroni[1], S. Rampes[1], P. Kotecha[1], J. Schoones[2], E. Nikiphorou[3,4], J. Galloway[3,4]. [1]*King's College London, GKT School of Medical Education, Faculty of Life Sciences & Medicine, London, United Kingdom*; [2]*Leiden University Medical Center, Walaeus Library, Leiden and the Hague, Netherlands*; [3]*King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; [4]*King's College Hospital, Rheumatology Department, London, United Kingdom*

Background: Hydroxychloroquine (HCQ) has attracted much attention especially during the COVID-19 pandemic. HCQ and closely related chloroquine (CQ) have known ocular and cardiac toxicity. However, although screening guidance now exists from the Royal College of Ophthalmologists for the former (RCOphth)[1], little is known regarding predictors of both forms of toxicity.

Objectives: To systematically explore the literature on predictors of toxicity limited to cardiac and ocular toxicity.

Methods: A detailed search of the following databases was conducted: PubMed, Medline, Embase, Web of Science, The Cochrane library, EMCare and Academic Search Premier. Studies addressing predictors of HCQ toxicity with relevant search terms used were included. Exclusion criteria were: non-English articles, pre-clinical and paediatric studies. Three authors (SR, NC, PK) independently screened titles and abstracts for inclusion, ensuring each article was screened twice. Disagreement over inclusion was adjudicated by senior reviewers (EN, JG). Data extraction (SR, NC, PK) focused on predictors of toxicity.

Results: The search strategy retrieved 3103 studies. 147 studies were included for data extraction, of which 92 were eventually excluded due to: not identifying predictors (n=17), reviews (n=19), not ocular or cardiovascular toxicity (n=18), case reports (n=3), paediatrics (n=1), screening articles that focused on detecting retinopathy (n=30), article unobtainable at time of abstract submission (n=4), leaving 55 studies for full review.

Studies addressing cardiac toxicity (n=16) included: cohort, retrospective observational, a comparative pharmacovigilance, systematic monitoring protocol and a randomised control trial (RCT). The majority of these involved high-dose (>5mg/kg/day) use for acute COVID-19 infection. The main significant predictors identified were: Hydroxychloroquine (HCQ) use in combination with azithromycin (6/7 studies), cumulative dose (2 studies), pre-existing cardiovascular morbidity (2/3 studies) and prolonged baseline QTc (2 studies). Individual associations were also identified in the following: longer treatment duration, daily dosage, increased age, male gender, severe COVID-19 infection, abnormal liver function tests (LFTs) and concurrent use of loop-diuretics.

Regarding predictors of ocular toxicity (n=39), only one study was a RCT. The remainder were observational studies: case-control, cohort, retrospective chart reviews and letters to the editor which included original patient data.

Several predictors of retinopathy and maculopathy were examined in two or more studies and included: duration of use (16/18 studies), daily dosage (7/13 studies), cumulative dose (11/14 studies), increased age (10/11 studies), body weight or BMI (3/5 studies), renal impairment (5 studies), HCQ blood levels (2 studies),

keratopathy (2 studies) and tamoxifen use (2 studies). Sex (2 studies) and history of cataract surgery (2 studies) were not found to be predictors of toxicity.
Only few studies performed regression analysis presenting odds and/or hazard ratios with confidence intervals.
Conclusion: The most recognised predictor of cardiac toxicity was co-administration with azithromycin. In ocular toxicity, commonly cited predictors included those already recognised by the RCOphth[1], as well as cumulative dose, increased age, weight considerations, HCQ blood levels and keratopathy. Further research is warranted on better characterising predictors of cardiac and ocular toxicity in patients on HCQ and CQ therapy.
REFERENCES:
[1] The Royal College of Ophthalmologists. Hydroxychloroquine and Chloroquine Retinopathy: Recommendations on Monitoring [Internet]. The Royal College of Ophthalmologists; 2020 [cited 2021 Jan 25].
Disclosure of Interests: Natasha Citeroni: None declared, Sanketh Rampes: None declared, Pinky Kotecha: None declared, Jan Schoones: None declared, Elena Nikiphorou: None declared, James Galloway Speakers bureau: JG has received honoraria / speaker fees from Abbvie, BMS, Celgene, Chugai, Gilead, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi, Sobi and UCB.
DOI: 10.1136/annrheumdis-2021-eular.1178

POS0663 SAFETY AND EFFICACY OF COMBINING METHOTREXATE AND LEFLUNOMIDE AMONG PATIENTS WITH INFLAMMATORY ARTHROPATHIES: FINDINGS FROM THE PRIME REGISTRY

M. Haroon[1], A. Ashraf[2], H. J. Shaheen[1], S. Asif[1], S. Batool[1], F. Hashmi[1], S. Ullah[1]. [1]*Fatima Memorial Hospital & FMH College of Medicine and Dentistry, Department of Rheumatology, Lahore, Pakistan*; [2]*CMH Lahore Medical College & Institute of Dentistry, Medicine, Lahore, Pakistan*

Background: Currently, conventional synthetic DMARDs (csDMARDs) are the most commonly prescribed drugs as first-line treatment for peripheral arthritis. In resource-constrained settings where biologic agents are not widely available, there are limited therapeutic options for patients with rheumatoid arthritis (RA) and seronegative inflammatory arthropathies refractory to other csDMARD therapies. Hence, in our practice, we are inclined to use combination of potent DMARDs after MTX failure, prior to considering biologic therapies. We believe that combination of DMARDs, especially combining MTX and Leflunomide (LEF) provides a potent and valuable low-cost treatment option. Efficacy of MTX and LEF is very well established, but there have been lot of concern as regards their combination use due to potential risk of hepatotoxicity.
Objectives: We aimed to review our inflammatory arthropathies cohort data especially examining the safety, efficacy and drug retention of the combination usage of MTX and Leflunomide. We addressed this question using real-world data from the PRIME registry.
Methods: This was a cross-sectional study conducted using data collected at the time of patient enrolment in the PRIME registry. The PRIME Registry is a large, independent, prospective, observational cohort initiated in October 2019 that comprises patients diagnosed with RA, SLE, PsA or AS by a rheumatologist, and is being actively followed up. IRB approval and informed consent was obtained. A number of clinical variables were recorded. Detailed history was gathered from every patient regarding their present and past medications usage. Questions were asked directly about the usage or otherwise of all available DMARDs and biologics. The duration of usage, any adverse events, or the reasons for discontinuation were recorded. Evaluation of disease activity and severity was made as per internationally agreed definitions.
Results: The data of 766 inflammatory arthritis patients (RA=663, PsA=103) was reviewed. Among them, 241 patients (RA=196, PsA=45) were using combination therapy of MTX and LEF (combo MTX+LEF) with mean age 42.3±6 years; 42% male]. These patients had failed MTX or LEF monotherapy. Among these 241 patients, 49 patients were also on concomitant hydroxychloroquine therapy. It was noted that median drug retention of combo MTX+LEF therapy has been 9.5 months (IQR 6-16). Regarding any adverse events of combo MTX+LEF therapy, hepatotoxicity (ALT ≤3 times the upper limit of normal) was noted among 15 (6.2%) patients, hepatotoxicity (ALT ≥3 times the upper limit of normal) was noted among 8 (3.3%) patients, and troublesome gastrointestinal upset (nausea, or vomiting, or diarrhoea) in 3 (1.2%). Overall, only 13 (5.4%) patients had to discontinue this combo MTX+LEF therapy due to adverse events. Disease activity among combo MTX+LEF users was as follows: 64% (n=29) of PsA patients had achieved MDA; 42% (n=83) of RA cohort were in DAS28 remission, 46% (n=91) of RA patients were having DAS low disease activity.
Conclusion: Combination of MTX and LEF was well tolerated and had good drug retention time, with 94.6% of patients having ongoing treatment to date. In low-income countries, where bDMARD availability is limited, financial arguments significantly influence decision making process, and our data provides initial evidence that MTX and LEF combination therapy could be an effective treatment option.
Disclosure of Interests: Muhammad Haroon Speakers bureau: Roche, Novartis, Grant/research support from: Abbvie, Pfizer, Arfa Ashraf: None declared, Hafiza Javeria Shaheen: None declared, Sadia Asif: None declared, Shabnam Batool: None declared, Farzana Hashmi: None declared, Saadat Ullah: None declared
DOI: 10.1136/annrheumdis-2021-eular.1272

POS0664 A MULTICENTER RANDOMIZED STUDY IN RHEUMATOID ARTHRITIS TO COMPARE IGURATIMOD, METHOTREXATE, OR COMBINATION: 52 WEEK EFFICACY AND SAFETY RESULTS OF THE SMILE TRIAL

F. Du[1], J. Xu[2], X. Li[3], Z. Li[4], X. Li[5], X. Zuo[6], L. Bi[7], D. Zhao[8], M. Zhang[9], H. Wu[10], D. He[11], Z. Wu[12], Z. Li[13], Y. Li[14], J. Xu[15], Y. Tao[16], J. Zhao[17], J. Chen[18], H. Zhang[19], J. Li[20], L. Jiang[21], Z. Xiao[22], Z. Chen[23], G. Yin[24], L. Gong[25], G. Wang[26], L. Dong[27], W. Xiao[28], C. Bao[1]. [1]*Renji Hospital of Shanghai Jiao Tong University School of Medicine, Department of Rheumatology, Shanghai, China*; [2]*The First Affiliated Hospital of Anhui Medical University, Department of Rheumatology and Immunology, Hefei, China*; [3]*The First Affiliated Hospital of USTC, Department of Rheumatology and Immunology, Hefei, China*; [4]*Peking University People's Hospital, Department of Rheumatology and Immunology, Beijing, China*; [5]*Qilu Hospital of Shandong University, Department of Rheumatology, Jinan, China*; [6]*Xiangya Hospital Central South University, Department of Rheumatology and Immunology, Changsha, China*; [7]*China-Japan Union Hospital of JiLin University, Department of Rheumatology and Immunology, Changchun, China*; [8]*Changhai Hospital of Shanghai, Department of Rheumatology and Immunology, Shanghai, China*; [9]*First Affiliated Hospital, Nanjing Medical University, Department of Rheumatology and Immunology, Nanjing, China*; [10]*The Second Affiliated Hospital Zhejiang University School of Medicine, Department of Rheumatology and Immunology, Hangzhou, China*; [11]*ShangHai GuangHua Hospital of Integrated Traditional Chinese and Western Medicine, Department of Rheumatology, Shanghai, China*; [12]*Xijing Hospital, Fourth Military Medical University, Department of Clinical Immunology, Xi'an, China*; [13]*First Affiliated Hospital, Bengbu Medical College, Department of Rheumatology and Immunology, Bengbu, China*; [14]*The Second Affiliated Hospital, Harbin Medical University, Department of Rheumatology and Immunology, Harbin, China*; [15]*First Affiliated Hospital of Kunming Medical University, Department of Rheumatology and Immunology, Kunming, China*; [16]*The Second Affiliated Hospital of Guangzhou Medical University, Department of Rheumatology and Immunology, Guangzhou, China*; [17]*Jining No.1 People's Hospital, Department of Rheumatology and Immunology, Jining, China*; [18]*The Second Xiangya Hospital of Central South University, Department of Rheumatology and Immunology, Changsha, China*; [19]*The Third Xiangya Hospital of Central South University, Department of Nephropathy and Rheumatology, Changsha, China*; [20]*Zhuzhou Central Hospital, Department of Rheumatology and Immunology, Zhuzhou, China*; [21]*Fudan University Zhongshan Hospital, Department of Rheumatology and Immunology, Shanghai, China*; [22]*The First Affiliated Hospital of Shantou University Medical College, Department of Rheumatology, Shantou, China*; [23]*The First Affiliated Hospital of Soochow University, Department of Rheumatology, Suzhou, China*; [24]*West China Hospital, Department of Rheumatology and Immunology, Chengdu, China*; [25]*Tianjin Medical University General Hospital, Department of Rheumatology and Immunology, Tianjin, China*; [26]*China-Japan Friendship Hospital, Department of Rheumatology and Immunology, Beijing, China*; [27]*Tongji Hospital Tongji Medical College of HUST, Department of Rheumatology and Immunology, Wuhan, China*; [28]*The First Hospital of China Medical University, Department of Rheumatology and Immunology, Shenyang, China*

Background: Iguratimod (IGU) has demonstrated efficacy and safety for active rheumatoid arthritis (RA) patients in double-blind clinical trials in China and Japan as a new disease-modifying anti-rheumatic drug (DMARD). There are no studies evaluating the radiographic progression of structural joint damage of IGU for the treatment of RA using the mTSS as the primary endpoint.
Objectives: Our study was to evaluate the efficacy and safety of IGU monotherapy and IGU combined methotrexate (MTX) compared with MTX monotherapy, including the inhibitory effects of joint destruction.
Methods: This randomized, double-blind, parallel-controlled, multicenter study in patients with active RA who have not previously used MTX and biological DMARDs (bDMARDs) (ClinicalTrials.gov Identifier NCT01548001) was carried out in China. Patients were randomized 1:1:1 to receive IGU 25 mg twice a day (bid), MTX 10mg once a week(qw) for the first 4 weeks and 15 mg once a week(qw) for week 5 to 52, or IGU combined MTX (IGU+MTX) for 52 weeks. The primary endpoints were to assess and compare American College of Rheumatology 20% (ACR20) response and the change of modified total Sharp scoring (mTSS) score over 52 weeks (Intention-to-treat, ITT analysis). The non-inferiority test was used to analyze the difference of ACR20 response at 52 weeks between the IGU monotherapy and the MTX monotherapy arms, and the non-inferiority

limit value was 10%. The difference test was used for the comparison between the IGU+MTX and MTX monotherapy arms. Two-way ANOVA was used to analyze the difference of the changes of mTSS score of each arm compared with baseline value (0 week).

Results: A total of 895 patients were randomized to IGU 25mg bid (n =297), MTX 10-15mg qw(n=293), and IGU+MTX (n=305). Baseline characteristics were comparable between the arms (Table 1).

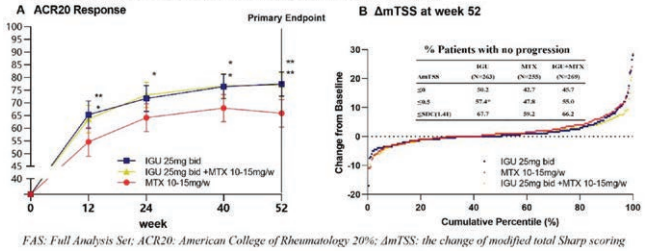
Table 1. Demographic and Other Baseline Characteristics (SAS)

	IGU	MTX	IGU+MTX
Number of Subjects	**297**	**293**	**305**
Age, mean (SD) years	46.87(10.67)	47.63(10.70)	48.37(10.69)
Female/male, %	77.44/22.56	79.18/20.82	78.03/21.97
Duration of RA, mean(SD) years	11.67±7.16	11.60±7.98	11.67±7.27
CRP, mean(SD) mg/L[2]	22.32±35.47	20.67±26.61	19.74±31.38
Tender joint count, mean (SD)	14.59±9.16	14.83±9.30	14.93±9.88
Swollen joint count, mean (SD)	9.81±6.63	9.73±7.20	9.51±6.22
DAS28-CRP, mean (SD)	5.084±0.994	5.102±0.979	5.103±0.956
HAQ score, mean (SD)	15.82±11.25	15.24±10.93	16.06±10.92

SAS: Safety Analysis Set; CRP: C-reactive protein;
DAS28: disease activity score; HAQ: Health Assessment Questionnaire

The study met its primary endpoints. More concretely, IGU monotherapy and IGU+MTX were found to be superior to MTX at week 52 with a higher ACR20 response of 77.44%(230/297, P=0.0019) and 77.05%(235/305, P=0.0028) versus 65.87%(193/293) (fig 1). As shown in fig 1
, the structural remission (ΔmTSS≤0.5) was statistically significant for IGU monotherapy (57.4%, P=0.0308) but not for IGU+MTX arm (55%) versus MTX monotherapy (47.8%).

Figure 1. ACR20 response and the percent of patients with no progression (FAS)



FAS: Full Analysis Set; ACR20: American College of Rheumatology 20%; ΔmTSS: the change of modified total Sharp scoring

Overall incidence of the adverse events (AEs) leading to study discontinuation were reported in 13.8% (41/297) in IGU monotherapy arm, 11.26% (33/293) in MTX monotherapy arm and 11.51% (35/305) patients in IGU+MTX arm. The incidence of adverse drug reactions (ADR) leading to study discontinuation were 11.45% (34/297), 8.53% (25/293) and 9.21% (28/305), respectively. There was no one death and no significant difference in all the safety indicators among the three arms.

Conclusion: Iguratimod alone or in combination with MTX demonstrated superior efficacy with acceptable safety compared to MTX for patients with active RA who have not previously used MTX bDMARDs.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1486

POS0665 TRAJECTORIES OF GLUCOCORTICOID-THERAPY IN EARLY RHEUMATOID ARTHRITIS: FIRST RESULTS OF A SCOPING SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL COHORT STUDIES

A. Palmowski[1], F. Buttgereit[1]. [1]*Charité – Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*

Background: Glucocorticoids (GCs) are regularly used as a bridging therapy in early rheumatoid arthritis (eRA). As long-term treatment, especially at higher dosages, may lead to undesirable adverse events, GCs should be tapered as rapidly as clinically feasible.

Objectives: To assess real-world trajectories of GC-therapy initiated in patients with eRA and in methotrexate-naïve RA patients.

Methods: We conducted a scoping search in MEDLINE (via PubMed) to find articles (years 2005 – 2020) reporting on eRA (or methotrexate-naïve RA) patients from observational cohorts who start or take GCs at baseline. Articles had to describe either dosages or proportions of patients who took GCs or were able to taper GCs at two (minimum) pre-specified time points. The articles were screened by one reviewer (AP). Random-effects meta-analyses pooled results per outcome and time point if ≥3 studies were available. *R* software with package *metafor* was used for statistical analyses. A research protocol was published with protocols.io (10.17504/protocols.io.bpyfmptn).

Results: Our highly specific search strategy yielded 165 results. Twelve articles on nine cohorts were finally included. Eight cohorts originated in Europe, one in Africa. At baseline, about half of the patients with eRA were prescribed GCs with a mean dosage of 8mg/d prednisone equivalent (fig 1
). Over time, both the proportion taking GCs and the mean dosage declined. There was substantial heterogeneity between studies.

Conclusion: Our results indicate that GCs remain regularly used drugs in eRA patients and in methotrexate-naïve patients with RA. While about 40% of patients still receive GCs after 24 months, mean dosages were tapered to "low" dosages (≤7.5mg/d prednisone equivalent)[1] in all cohorts that reported respective data. Heterogeneity might be caused by country-specific differences. Unfortunately, the validity of sensitivity analyses would be poor due to the paucity of published data regarding GC dosages and proportions of patients taking GCs in observational RA cohorts. Major limitations of this scoping review are the very specific (and consequently less sensitive) search strategy and that the screening was conducted by one reviewer only.

REFERENCES:

[1] Buttgereit F, Da Silva JAP, Boers M, et al. Standardised nomenclature for glucocorticoid dosages and glucocorticoid treatment regimens: current questions and tentative answers in rheumatology. *Ann Rheum Dis* 2002;61(8):718-22. doi: 10.1136/ard.61.8.718.

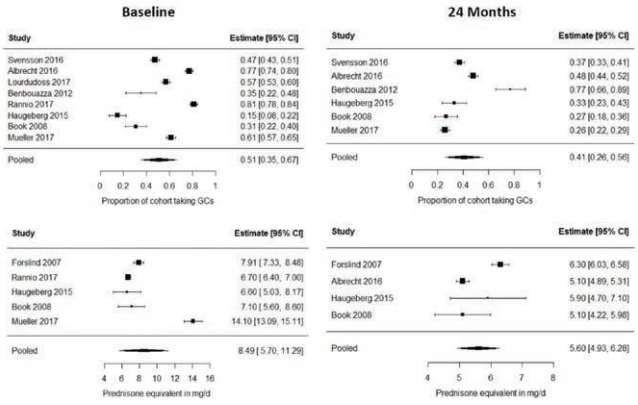


Figure 1. Meta-analyses of proportions taking glucocorticoids and mean dosages at baseline and 24 months. GCs: Glucocorticoids; CI: Confidence interval.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1526

POS0666 TREATMENT EFFECTIVENESS OF UPADACITINIB AT 3 MONTHS IN US PATIENTS WITH RHEUMATOID ARTHRITIS FROM THE UNITED RHEUMATOLOGY NORMALIZED INTEGRATED COMMUNITY EVIDENCE (NICE[TM]) REAL-WORLD DATA

A. Gibofsky[1], B. Dhillon[2], M. E. Pearson[3], N. Tundia[4], Y. Song[4], K. Dunlap[4], G. Wright[5]. [1]*Weill Cornell Medical College, Hospital for Special Surgery, New York, United States of America*; [2]*United Rheumatology, Rheumatology, Hauppauge, United States of America*; [3]*West Suburban Center for Arthritis, Rheumatology, Brookfield, United States of America*; [4]*AbbVie Inc, Immunology, North Chicago, United States of America*; [5]*Association of Women in Rheumatology, Rheumatology, New York, United States of America*

Background: Upadacitinib (UPA), an oral Janus kinase inhibitor (JAKi), has demonstrated efficacy in the phase 3 SELECT clinical program, conducted across a range of patients (pts) with rheumatoid arthritis (RA).[1–6] Real-world data for UPA, including in pts previously treated with a JAKi, have not yet been reported since global approvals beginning in 2019.

Objectives: To assess the characteristics of US-based pts receiving UPA and its effectiveness in clinical practice at 3 months.

Methods: This observational study included US-based pts from the United Rheumatology Normalized Integrated Community Evidence (UR-NICE) database who initiated UPA 15 mg once daily from FDA approval (August 2019) to July 31, 2020 and had ≥6-month pre-baseline data available. Effectiveness was assessed in pts with a reported Clinical Disease Activity Index (CDAI) score at 3 months after UPA initiation and included proportions of pts achieving CDAI remission (≤2.8), CDAI low disease activity (≤10), other disease activity measures, and pt-reported outcomes. A subgroup analysis assessed UPA effectiveness in pts with or without prior tofacitinib (TOFA) treatment.

Results: This analysis included 252 pts treated with UPA 15 mg, of whom 98 (38.9%) received UPA monotherapy and 154 (61.1%) received UPA combined with conventional synthetic (cs) disease-modifying antirheumatic drugs (DMARDs). 64.3% of pts were from the Southern region of the USA. 86.1%, 72.2%, and 47.6% of pts had been previously treated with csDMARDs, biologic DMARDs, and JAKis, respectively. Baseline characteristics were largely similar between UPA monotherapy and combination therapy groups and those with or without prior TOFA treatment (Table 1). Pts with prior TOFA treatment had a longer duration of RA since diagnosis and higher steroid use versus those without. UPA 15 mg improved disease activity scores (including CDAI) and pt-reported outcomes (including physical function and pain) after 3 months of treatment (Figure 1). Similar effectiveness was observed with UPA 15 mg in pts with or without prior TOFA treatment.

Conclusion: In the UR-NICE real-world database of US-based pts, improvements in clinical and pt-reported outcomes were observed at 3 months in UPA-treated pts with RA, including those with or without prior TOFA treatment, despite the treatment-refractory population included in this dataset.

REFERENCES:

[1] Burmester GR, et al. Lancet 2018;391:2503–12.
[2] Smolen JS, et al. Lancet 2019;393:2303–11.
[3] Fleischmann R, et al. Arthritis Rheumatol 2019;71:1788–800.
[4] Genovese MC, et al. Lancet 2018;391:2513–24.
[5] van Vollenhoven R, et al. Arthritis Rheumatol 2020;72:1607–20.
[6] Rubbert-Roth A, et al. N Engl J Med 2020;383:1511–21.

Table 1. Baseline characteristics

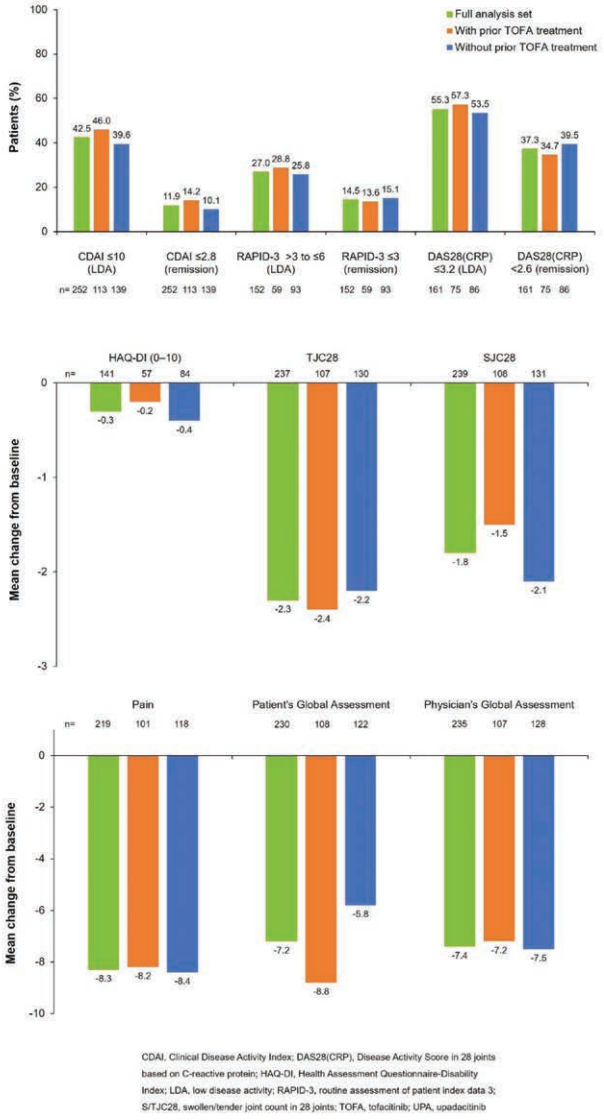
n (%), unless otherwise stated	Full analysis set (n=252)		Pts with prior TOFA treatment (n=113)		Pts without prior TOFA treatment (n=139)		
Mean (SD) exposure, days	219.7 (112.1)		215.7 (116.7)		222.9 (108.5)		
Female	199 (79.0)		85 (75.2)		114 (82.0)		
Age ≥65 years	75 (29.8)		34 (30.1)		41 (29.5)		
Oral steroid use	140 (55.6)		70 (61.9)		70 (50.4)		
Prior csDMARDs	217 (86.1)		102 (90.3)		115 (82.7)		
Prior TOFA	113 (44.8)		113 (100.0)		0		
Prior biologic DMARDs	182 (72.2)		86 (76.1)		96 (69.1)		
Tumor necrosis factor inhibitor	147 (58.3)		66 (58.4)		81 (58.3)		
Interleukin-6 receptor inhibitor	87 (34.5)		47 (41.6)		40 (28.8)		
	n	**Mean (SD)**	**n**	**Mean (SD)**	**n**	**Mean (SD)**	Duration of RA diagnosis, years
188	4.0 (3.0)	89	5.1 (2.9)	99	3.1 (2.8)	Methotrexate dose, mg/week	88
17.0 (5.1)	28	17.8 (5.0)	60	16.6 (5.2)	SJC28	239	4.8 (5.7)
108	4.5 (5.0)	131	5.0 (6.2)	TJC28	237	6.5 (6.7)	107
6.5 (6.8)	130	6.5 (6.6)	CDAI	225	20.4 (13.4)	105	20.2 (13.5)
120	20.6 (13.3)	Routine assessment of patient index data 3	165	4.2 (2.3)	72	4.2 (2.4)	93
4.3 (2.2)	Disease Activity Score in 28 joints based on C-reactive protein	167	3.9 (1.5)	83	3.9 (1.5)	84	3.9 (1.5)
Health Assessment Questionnaire-Disability Index (0–10)	170	2.5 (2.1)	74	2.4 (2.2)	96	2.5 (2.1)	Pain
229	56.5 (28.5)	104	56.9 (29.3)	125	56.1 (28.0)	SD, standard deviation; S/TJC, swollen/tender joint count	

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Hilary Wong, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Disclosure of Interests: Allan Gibofsky Shareholder of: AbbVie, Amgen, Johnson & Johnson, and Pfizer, Consultant of: AbbVie, Celgene, Eli Lilly, Flexion, Pfizer, Relburn Pharma, and Samumed. Paid consultant with investment analysts on behalf of the Gerson Lehrman Group, Bhavna Dhillon Shareholder of: May own stock or options in United Rheumatology, Employee of: United Rheumatology, Mark E. Pearson Shareholder of: May own AbbVie stock or options, Namita Tundia Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Kendall Dunlap Shareholder of: May own stocks or shares in AbbVie, Employee of: AbbVie, Grace Wright Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Exagen, Myriad Autoimmune, Novartis, Sanofi/Regeneron, UCB, and Vindico, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Exagen, Gilead, Janssen, Myriad Autoimmune, Novartis, Pfizer, Sanofi/Regeneron, and UCB, Employee of: President and Founder of the Association of Women in Rheumatology

DOI: 10.1136/annrheumdis-2021-eular.1565

Figure UPA 15 mg effectiveness at Month 3



POS0667 TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-WORLD SETTINGS: A NATIONAL MULTICENTER STUDY OF 167 PATIENTS FROM ARGENTINA

M. D. R. Maliandi[1], Y. S. Malvano[2], A. Cusa[3], M. J. Gamba[4], R. Gomez[4], J. Got[5], O. Gut[6], U. V. Paris[7], M. A. Spinetto[8], C. Mariach[8], A. I. Abalo[9], A. Estevez[9], J. L. Velazco Zamora[10], J. P. Vinicki[11]. [1]*Sanatorio Garay, Rheumatology, Santa Fe, Argentina*; [2]*Sanatorio Modelo Adrogué, Rheumatology, Burzaco, Argentina*;

[3]*MR Medicina Reumatológica, Rheumatology, GHP, Argentina*; [4]*Hospital Posadas, Rheumatology, El Palomar, Argentina*; [5]*Instituto Medico Humanitas, Rheumatology, Resistencia, Argentina*; [6]*Private Practice, Rheumatology, Ciudad Autonoma de Buenos Aires, Argentina*; [7]*Hospital Madariaga, Rheumatology, Posadas, Argentina*; [8]*Private Practice, Rheumatology, Buenos Aires, Argentina*; [9]*Hospital El Cruce - Nestor Kirchner, Rheumatology, Florencio Varela, Argentina*; [10]*Clinical Research Institute Quilmes, Rheumatology, Quilmes, Argentina*; [11]*Hospital De Quilmes, Rheumatology, Quilmes, Argentina*

Background: Tofacitinib (TOF), an oral JAK inhibitor, is approved for the treatment of rheumatoid arthritis (RA) either as monotherapy or in combination with background methotrexate (MTX). Despite the current evidence of efficacy from randomized controlled trials and open-label long-term extension studies, evidence of effectiveness and safety in real-world settings is limited, not only in Argentina but also in Latin America.

Objectives: To describe effectiveness, safety and persistence of TOF therapy in RA patients from public and private medical centers from Argentina. In addition, establish prognostic factors for clinical remission at 3 months and TOF monotherapy at 12 months.

Methods: A retrospective, observational and multicentre study was performed from an analysis of medical records of 10 medical centers. RA patients (ACR/EULAR, 2010) and age ≥ 18 years who had received or are under treatment with TOF until June 2020 were included. The data collection was done on a standard database that included baseline data and at 3, 6 and 12 months. Clinical remission was defined as DAS28-ESR < 2,6. Adverse events, treatment duration, TOF treatment persistence at last visit and discontinuation cause were assessed. Comparison to baseline values was performed using Wilcoxon sign for numerical variables and McNemar´s test for categorical variables. Treatment persistence was analyzed using Kaplan Meier´s technique. Multivariate analysis was performed using R software and its library packages (Lme4, Tidyverse and ggpubr). A p value < 0.05 was considered significant.

Results: A total of 167 patients were included (78.4% were female). At baseline, the median age was 53 years (IQR 43-63 years), median disease duration was 4 years (IQR 2-13 years). RF was positive in 85.6% of patients, ACPA in 80.8% and structural radiological damage was present in 71.8%. Previous use of MTX was 97%, leflunomide 74.8% and biologic therapy 42.5% (28.74% 1 biologic, 11.98% 2 biologics and 1.8% ≥ 3 biologics). TOF dose: 48% 11 mg/day and 52% 5 mg BID. A statistically significant difference was observed not only in disease activity (p<0.0001) but also in the requirement of MTX and PDN (p<0.0001) in the 12 months evaluated. Remission significantly increased from baseline to month 3 and to a much lesser extent to month 6 (p < 0.001). The mean duration of treatment with TOF was 20.10 ± 15.25 months. Treatment persistence was 93.84% at 3 months and 91.24% at 6 months. In those patient who achieved REM at month 3, a statistically significant differences in duration of RA (p 0.0002), structural radiological damage (p 0.011), basal disease activity (p 0.018) and prior treatment with biological therapy (p 0.017) was found when compared with patients who remained active. Furthermore, in univariate logistic regression analysis, 5 years or more of disease duration was associated with a 3 times higher risk of not achieving clinical remission at 3 months (odds ratio = 0.35, 95% CI = 0.15-0.83). In the multivariate logistic regression analysis, previous biological therapy was the only predictor associated with a decrease in the probability of clinical remission (p < 0.008). Adverse events were registered in 26 patients (herpes zoster, n = 9).

Conclusion: The effectiveness of TOF was observed not only in the clinical response achieved but also in the dose titration or withdrawal of MTX and PDN. The safety profile did not show any difference from long-term extension studies. At 12 months, 86.81% of the patients persisted with TOF therapy. We found prognostic factors associated with clinical remission at 3 months but those associated with monotherapy at 12 months could not be defined due to small number of patients analyzed that could have generated lack of statistical power, although more studies are required to confirm these assumptions.

Disclosure of Interests: Maria Del Rosario Maliandi: None declared, Yanina Silvia Malvano: None declared, Alejandra Cusa: None declared, María Julieta Gamba: None declared, Ramiro Gomez Speakers bureau: Abbvie, Novartis, Julio Got: None declared, Oscar Gut: None declared, Ursula Vanesa Paris: None declared, Maria Andrea Spinetto: None declared, Carolina Mariach: None declared, Alejandra Ines Abalo: None declared, Adrián Estevez Speakers bureau: Bristol-Meyer-Squibb, Jose Luis Velazco Zamora: None declared, Juan Pablo Vinicki: None declared

DOI: 10.1136/annrheumdis-2021-eular.1645

POS0668 REAL WORLD EFFECTIVENESS OF BARICITINIB IN THE SWISS RHEUMATOID ARTHRITIS REGISTER (SCQM-RA)

B. Gilbert[1], D. Courvoisier[1], D. Mongin[1], K. Lauper[1,2], C. Perrier[3], R. Muller[4], A. Finckh[1]. [1]*Geneva University Hospitals, Division of Rheumatology, Geneva, Switzerland*; [2]*University of Manchester, Centre for Musculoskeletal Research, Manchester, United Kingdom*; [3]*Eli Lilly SA (Suisse), Medical Department, Vernier, Switzerland*; [4]*Kantonsspital Aarau, Medical University Department, Aarau, Switzerland*

Background: When not responding to conventional synthetic DMARDs (csDMARDs), rheumatoid arthritis (RA) patients may receive biological DMARDs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs) including baricitinib (BARI). While BARI has demonstrated efficacy in randomized controlled trials, limited studies have established comparative effectiveness in real world settings, in particular when used in b/tsDMARD-naïve patients.

Objectives: To analyze the effectiveness of BARI versus alternative bDMARDs, as assessed by drug maintenance over time and by response rates at 12 months.

Methods: This is a nested study of RA patients, within the prospective Swiss Clinical Quality Management (SCQM) observational cohort.

All treatment courses (TC) with BARI or alternative bDMARDs initiated between 2017-09-01 and 2020-06-01, with at least one follow-up visit, were included. TC with BARI were compared to TC with alternative bDMARDs (non-BARI), including all b/tsDMARDs except rituximab. The non-BARI group was then subdivided into TNF inhibitors (TNFi) and other mode of action bDMARDs (OMA), excluding tsDMARDs. A secondary analysis focusing specifically on b/tsDMARD naïve patients was conducted.

Baseline characteristics were compared using ANOVA or $\chi 2$ tests. A Cox-model survival analysis assessed drug maintenance. 12-month response rates were estimated using an attrition-corrected, confounder-adjusted approach (1). CDAI score ≤10 defined low disease activity state (LDA), and CDAI score ≤2.8 defined remission.

Table 1. Baseline characteristics of studied population

Variable	Overall comparison: BARI vs non-BARI			Subgroup analysis 1: by bDMARD type (tsDMARD excluded)			Subgroup analysis 2: In b/tsDMARD-naïve patients			
	BARI (TC = 273; 273 patients)	Non-BARI (altogether) (TC = 945; 755 patients)	p values	TNFi (TC = 473; 408 patients)	OMA (TC = 318; 298 patients)	p values (vs BARI)	BARI (n = 46)	TNFi (n = 225)	OMA (n = 65)	p values
	Mean (SD) Otherwise: n %			Mean (SD) Otherwise: n %			Mean (SD) Otherwise: n %			
Concomitant csDMARD	41 %	46 %	0.17	54 %	41 %	**<0.01**	50 %	61 %	48 %	0.1
Line of Therapy	17 %	35 %	**<0.01**	48 %	20 %	**<0.01**	100 %	100 %	100 %	
-1st (= bio-naive)										
-2nd	20 %	23 %		23 %	23 %					
-3rd	19 %	16 %		11 %	24 %					
-4th or later	44 %	26 %		18 %	33 %					
Female	78%	74 %	<0.21	74 %	73 %	0.28	70 %	71 %	74 %	0.88
Age	59 (14)	56 (14)	**0.01**	52 (15)	58 (13)	**<0.01**	57 (15)	51 (14)	57 (16)	**<0.01**
Disease duration (years)	13 (10)	10 (9)	**<0.01**	8 (9)	11 (9)	**<0.01**	5.5 (6.45)	5 (7)	6.5 (9)	0.243
CDAI baseline	15 (9)	15 (10)	0.9	14 (9)	16 (11)	0.05	13 (7)	14 (9)	14 (10)	0.72
Previous tsDMARD (non-BARI)	33 %	8 %	**<0.01**	4 %	11 %	**<0.01**	0 %	0 %	0 %	
TC duration > 12-months	37 %	29 %	**0.01**	27 %	30 %	**0.02**	37 %	29 %	34 %	0.52

BARI = baricitinib, TNFi = TNF inhibitors, OMA = other mode of action, Non-BARI = TNFi + OMA + other tsDMARDs, SD = standard deviation.

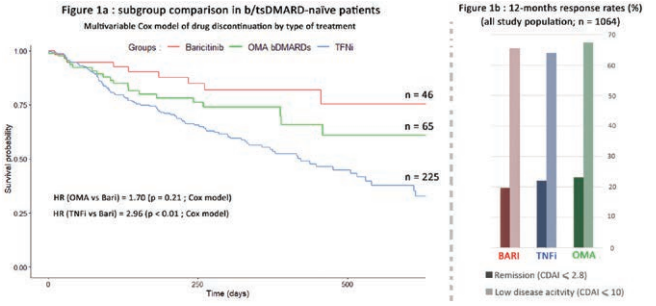
Results: Overall, 1218 eligible TC (from 1028 patients) were initiated during the study period (273 in BARI, 154 other tsDMARD, 473 in TNFi and 318 in OMA). Drug maintenance was significantly shorter for TNFi compared to BARI, even after adjustment for potential confounders (Hazard ratio (HR) for drug discontinuation 1.85 (95% CI [1,40 – 2,43]); p < 0.001). Drug maintenance was also numerically shorter for the OMA group compared to BARI, but the difference was not significant (HR 1.18 (95% CI [0.87 – 1.60]); p = 0.28). These differences were larger when analysing only bDMARD-naïve patients (Figure 1a).

All TC taken together, the rates of LDA and remission did not differ significantly between the 3 groups at 12 months. LDA ranged from 63% to 67% (BARI vs OMA p = 0.87; BARI vs TNFi p = 0.81) and remission from 19% to 23% (BARI vs OMA p = 0.30; BARI vs TNFi p = 0.77; Figure 1b).

Conclusion: BARI demonstrated a significantly higher overall drug maintenance than TNFi, and a similar drug maintenance to OMA, both in a bDMARD-naïve population and in the overall population. The adjusted 12-month response rates did not differ between BARI, TNFi and OMA groups. These results suggest that prescription of BARI after csDMARD has at least similar outcomes as alternative bDMARDs.

REFERENCES:

[1] Lauper, K., et al. Sat0588. Annals of the Rheumatic Diseases 78 (2019).



Disclosure of Interests: Benoit GILBERT: None declared, Delphine Courvoisier: None declared, Denis Mongin: None declared, Kim Lauper Consultant of: Gilead Galapagos, Grant/research support from: AbbVie, Clementine Perrier Shareholder of: Eli Lilly, Employee of: Eli Lilly, Rudiger Muller Consultant of: AbbVie, Novartis, Grant/research support from: GEBRO Pharma, Axel Finckh Speakers bureau: AbbVie, BMS, Pfizer, Eli-Lilly, Consultant of: AbbVie, BMS, Pfizer, Eli-Lilly, Grant/research support from: BMS, Pfizer, Eli-Lilly

DOI: 10.1136/annrheumdis-2021-eular.1781

POS0669

HYPOGLYCAEMIA FOLLOWING JAK INHIBITOR TREATMENT IN DIABETES MELLITUS PATIENTS WITH RHEUMATOID ARTHRITIS

J. van Lint[1], F. Van Hunsel[1], S. Tas[2], M. Nurmohamed[3], H. Vonkeman[4,5], R. Hebing[3], F. Hoentjen[6], M. van Doorn[7], B. van den Bemt[8,9], E. van Puijenbroek[1,10], N. Jessurun[1]. [1]*Netherlands Pharmacovigilance Centre Lareb, 's Hertogenbosch, Netherlands*; [2]*Amsterdam UMC, Rheumatology & Clinical Immunology, Amsterdam, Netherlands*; [3]*Amsterdam Rheumatology and Immunology Center, location Reade, Rheumatology, Amsterdam, Netherlands*; [4]*Medisch Spectrum Twente, Rheumatology, Enschede, Netherlands*; [5]*University of Twente, Psychology, Health & Technology, Enschede, Netherlands*; [6]*RadboudUMC, Gastroenterology, Nijmegen, Netherlands*; [7]*Erasmus MC, Dermatology, Rotterdam, Netherlands*; [8]*Sint Maartenskliniek, Pharmacy, Nijmegen, Netherlands*; [9]*RadboudUMC, Pharmacy, Nijmegen, Netherlands*; [10]*University of Groningen, Groningen Research Institute of Pharmacy, Pharmacotherapy, Epidemiology & Economics, Groningen, Netherlands*

Background: Janus kinase (JAK) inhibitors are effective small molecular drugs for rheumatoid arthritis (RA) and other immune mediated inflammatory diseases (IMIDs). JAK inhibitors exert their immunosuppressive effects by suppressing the action of JAK, an intracellular tyrosine. Although infections are the most reported side effects, potential glucose lowering effects in patients with diabetes mellitus (DM) have been described in literature and have also been reported as suspected adverse drug reactions (ADRs) to the National Pharmacovigilance Centre Lareb in the Netherlands (1).

Objectives: To assess and describe suspected adverse effects of JAK inhibitors on glucose levels in diabetic patients with rheumatic diseases and other IMIDs, as reported in daily practice.

Methods: We describe ADR reports of tofacitinib and baricitinib in the European pharmacovigilance Eudravigiliance (EV) database from initiation to 12 January 2021. All ADRs in EV are coded according to the Medical Dictionary for Regulatory Activities (MedDRA). We included all reports indicating hypoglycaemia in patients with reported DM type 1 and 2 or with antidiabetic drugs as concomitant medication. This could include oral antidiabetics as well as insulins.

Results: On 12 January 2021 the EV database included 32 ADR reports, concerning 32 diabetic patients, indicating hypoglycaemia associated with the use of JAK inhibitors (15 tofacitinib, 17 baricitinib), out of 32,484 ADR reports in total concerning tofacitinib or baricitinb (Table 1). Most patients (25 patients, 78%) used the JAK inhibitor for rheumatoid arthritis. The suspected ADR with MedDRA Preferred Term 'Hypoglycaemia' was reported for 16 patients and MedDRA Preferred Term 'Decreased blood glucose' was reported for 15 patients. In one case, increased insulin sensitivity was described as suspected ADR of baricitinib. In this case, the insulin dose had to be reduced to prevent hypoglycaemia. Of note, the insulin dose had to be increased after temporary discontinuation of baricitinib and was reduced again after baricitinib was restarted. Additionally, in six cases improvements of glycaemic control were described after discontinuation or dose reduction of the JAK inhibitor or antidiabetic drug. Improvements were also described after unknown action or unchanged treatment with JAK inhibitor in eight cases.

Conclusion: JAK inhibitors may induce hypoglycaemia by increasing insulin sensitivity, and consequently may reduce the need for antidiabetic medication (2-3). Healthcare professionals should be alert for these potential ADRs when starting a JAK inhibitor in patients with DM as comorbidity. More research is needed to support our findings and elucidate the underlying pharmacological mechanisms of this potentially beneficial effect of JAK inhibitors.

Table 1. Suspected adverse drug reaction reports indicating hypoglycaemia in diabetic patients using tofacitinib or baricitinib in the Eudravigilance database

	Tofacitinib N (%)	Baricitinib N (%)
No. of reports	15 (100)	17 (100)
Mean age years (range)	65 (56 - 78)	62.2 (48 - 78)
Female gender	13 (87)	13 (76)
Indication for JAK inhibitor		
Rheumatoid arthritis	11 (73)	14 (82)
Unknown	3 (20)	3 (18)
Arthritis	1 (7)	
Reported adverse drug reaction		
Hypoglycaemia	6 (40)	11 (65)[a]
Decreased blood glucose	9 (60)	6 (35)[a]
Time to onset after start JAK inhibitor[b]		
Within 1 month	6 (40)	3 (18)
2-6months	2 (13)	2 (12)
More than 6 months	1 (7)	
Improvement after action:		
Drug withdrawal	3 (20)[c]	1 (6)[d]
Dose adjustments		1 (6)[e]
Other	1 (7)[f]	

a.In one case of baricitinib hypoglycaemia as well as decreased blood glucose were reported as adverse drug reactions.
b.Time to onset was unknown in 6 reports of tofacitinib and 12 reports of baricitinib
c.Tofacitinib withdrawal: 1, sitagliptin withdrawal: 1, tofacitinib and insulin withdrawal: 1
d.Baricitinib withdrawal: 1
e.Baricitinib: after insulin dose adjustments: 1
f.After tofacitinib withdrawal and insulin dose adjustments

REFERENCES:

[1] Fujita Y, et al. Case Rep Rheumatol. 2019.
[2] Bako HY, et al. Life Sci. 2019.
[3] Chaimowitz NS, et al. N Engl J Med. 2020.

Disclosure of Interests: Jette van Lint: None declared, Florence van Hunsel: None declared, Sander Tas Consultant of: Gebro, GSK, AbbVie, Galvani, Arthrogen, Galapagos, Grant/research support from: Pfizer, GSK, Celgene, BMS, Sanofi, AstraZeneca, Michael Nurmohamed Speakers bureau: speaker's fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Roche, and Sanofi, Consultant of: consulting fees from AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, and Sanofi, Grant/research support from: research funding from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Mundipharma, Novartis, Pfizer, Roche, and Sanofi, Harald Vonkeman Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Celltrion, Galapagos, Gilead, GSK, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi-Genzyme, all outside the submitted work., Renske Hebing: None declared, Frank Hoentjen Speakers bureau: served on advisory boards or as speaker for Abbvie, Janssen-Cilag, MSD, Takeda, Celltrion, Teva, Sandoz and Dr Falk, Consultant of: Celgene, Janssen-Cilag, Grant/

research support from: Dr Falk, Janssen-Cilag, Abbvie, Takeda, Martijn van Doorn Grant/research support from: reports personal fees from Leopharma, grants and personal fees from Novartis, personal fees from Abbvie, personal fees from BMS, personal fees from Celgene, personal fees from Lilly, personal fees from MSD, personal fees from Pfizer, personal fees from Sanofi-Genzyme, personal fees from Janssen Cilag, outside the submitted work., Bart van den Bemt: None declared, Eugène van Puijenbroek: None declared, Naomi Jessurun: None declared
DOI: 10.1136/annrheumdis-2021-eular.1851

POS0670

ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3 (RAPID3) IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH LONG-TERM UPADACITINIB THERAPY

M. Bergman[1], M. H. Buch[2], Y. Tanaka[3], G. Citera[4], S. Bahlas[5], E. Wong[6], Y. Song[7], N. Tundia[7], J. Subotički[7], V. Strand[8]. *[1]Drexel University College of Medicine, Rheumatology, Philadelphia, Pennsylvania, United States of America*; *[2]School of Biological Sciences, University of Manchester and NIHR Manchester Biomedical Centre, Centre for Musculoskeletal Research, Manchester, United Kingdom*; *[3]University of Occupational and Environmental Health Japan, Rheumatology, Kitakyushu, Japan*; *[4]Instituto de Rehabilitación Psicofísica, Ciudad Autónoma de Buenos Aires, Rheumatology, Buenos Aires, Argentina*; *[5]King Abdulaziz University, Medicine, Jeddah, Saudi Arabia*; *[6]Queen Alexandra Hospital, Rheumatology, Portsmouth, United Kingdom*; *[7]AbbVie Inc., Immunology, North Chicago, Illinois, United States of America*; *[8]Stanford University, Division of Immunology/Rheumatology, Palo Alto, California, United States of America*

Background: Routine Assessment of Patient Index Data 3 (RAPID3) is a pooled index of 3 patient-reported measures: patient global assessment, pain, and physical function. RAPID3 was shown to correlate with other composite measures of disease activity[1] and is recommended by the American College of Rheumatology for use in clinical practice.[2]
Objectives: To evaluate the impact of upadacitinib (UPA) versus comparators on RAPID3 over 60 weeks, as well as the correlation of RAPID3 scores with other disease measures in the UPA phase 3 SELECT clinical program.
Methods: This post hoc analysis included placebo-controlled (SELECT-NEXT, -BEYOND, and
-COMPARE) and active comparator-controlled (SELECT-EARLY, -MONOTHERAPY, and
-COMPARE) trials. Patients received UPA as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs). Mean change from baseline in RAPID3 and the proportion of patients reporting RAPID3 remission (≤3), low (LDA, >3 to ≤6), moderate (MDA, >6 to ≤12), and high disease activity (HDA, >12) were assessed. Correlations between absolute scores for RAPID3 and Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), and 28-joint Disease Activity Score with C-reactive protein (DAS28[CRP]) were assessed using Spearman correlation coefficients. All data are as observed.
Results: A total of 661, 498, 648, 1629, and 945 patients were included from SELECT-NEXT,
-BEYOND, -MONOTHERAPY, -COMPARE, and -EARLY. At baseline, the majority of patients across all studies were in RAPID3 HDA (mean baseline RAPID3 [across all studies], 17.2–19.2) (Table 1 and Figure 1). Improvements from baseline in RAPID3 were observed with UPA 15 mg and 30 mg through Week 60, with numerically greater improvements observed with UPA compared with active comparators (Table 1). Across studies, mean improvements in RAPID3 exceeded the minimal clinically important difference (MCID) with UPA and adalimumab (ADA) treatment (MCID=3.8[3]). By Week 60, approximately one-half of UPA-treated patients were in RAPID3 remission or LDA, with only 10–25% remaining in HDA, except for the more refractory population in SELECT-BEYOND, in which ~38% of patients remained in HDA (Figure 1). RAPID3 scores moderately to strongly correlated with CDAI (ρ=0.69–0.83), SDAI (ρ=0.69–0.82), and DAS28(CRP) (ρ=0.58–0.77), across all studies, at Week 60 (all p<0.001).
Conclusion: UPA, as monotherapy or in combination with csDMARDs, was associated with improvements in patient-reported disease activity, pain, and physical function, as assessed by RAPID3 over 60 weeks in the phase 3 SELECT clinical program. RAPID3 continues to be an important tool in clinical practice to assess disease activity, as it was shown to correlate to other disease activity measures and allows for rapid scoring.

REFERENCES:

[1] Pincus T, et al. Arthritis Care Res (Hoboken) 2010;62:181–9.
[2] England BR, et al. Arthritis Care Res (Hoboken) 2019;71:1540–55.
[3] Ward MM, et al. J Rheumatol 2019;46:27–30.

Table 1. Change from BL in RAPID3 at Week 60 (as observed)

Phase 3 study	Group	n[a]	Mean (SD) BL score	Mean (SD) change from BL[b]
SELECT-EARLY[c]	MTX	236	18.5 (5.6)	–9.6 (7.5)
(MTX-naïve)	UPA 15 mg QD	269	18.9 (5.6)	–12.0 (7.6)
	UPA 30 mg QD	253	18.2 (5.6)	–13.4 (7.2)
SELECT-NEXT	UPA 15 mg QD	172	17.7 (5.1)	–11.1 (7.3)
(csDMARD-IR)	UPA 30 mg QD	172	17.6 (5.3)	–10.4 (6.8)
SELECT-MONOTHERAPY	UPA 15 mg QD	172	17.4 (5.8)	–9.6 (7.4)
(MTX-IR)	UPA 30 mg QD	180	17.2 (5.9)	–10.6 (7.2)
SELECT-COMPARE[c]	UPA 15 mg QD	552	18.5 (5.5)	–10.2 (7.1)
(MTX-IR)	ADA 40 mg EOW	264	18.7 (5.4)	–8.8 (6.7)
SELECT-BEYOND	UPA 15 mg QD	133	19.2 (5.1)	–8.6 (6.8)
(bDMARD-IR)	UPA 30 mg QD	118	18.5 (5.3)	–9.3 (7.3)

b, biologic; BL, baseline; EOW, every other week; IR, inadequate response; MTX, methotrexate; QD, once daily; SD, standard deviation
[a]Number of patients with RAPID3 values at both BL and Week 60. [b]Negative values indicate improvement from BL. [c]Observed data include patients rescued to UPA and/or ADA; treatment effect may include both the randomized and switch treatments in these patients

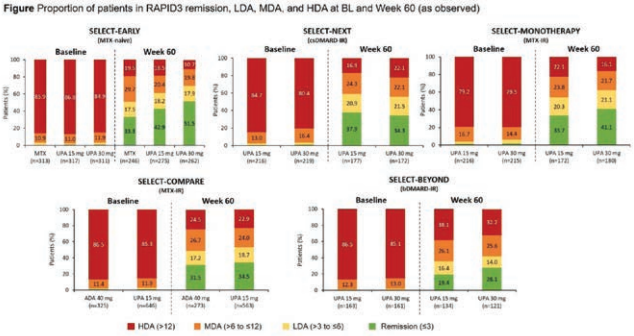


Figure Proportion of patients in RAPID3 remission, LDA, MDA, and HDA at BL and Week 60 (as observed)

ADA, adalimumab; bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD; DMARD, disease-modifying antirheumatic drug; HDA, high disease activity; IR, inadequate response; LDA, low disease activity; MDA, moderate disease activity; MTX, methotrexate; RAPID3, Routine Assessment of Patient Index Data 3; UPA, upadacitinib

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Grant Kirkpatrick, MSc, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.
Disclosure of Interests: Martin Bergman Shareholder of: Johnson & Johnson, Speakers bureau: AbbVie, Celgene, GSK, MSD, Novartis, Pfizer, and Sanofi/Regeneron, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Genentech/Roche, Gilead, Horizon, Janssen, MSD, Novartis, Pfizer, Sandoz, Sanofi/Regeneron, and Scipher, Maya H Buch Consultant of: AbbVie, Eli Lilly, Merck-Serono, Pfizer, Sandoz, and Sanofi, Grant/research support from: Pfizer, Roche, and UCB, Yoshiya Tanaka Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, GSK, Janssen, Mitsubishi Tanabe, Novartis, Pfizer, Sanofi, Takeda, UCB, and YL Biologics, Grant/research support from: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Mitsubishi Tanabe, MSD, Ono, Taisho Toyama, and Takeda, Gustavo Citera Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Genzyme, Pfizer, and Roche, Sami Bahlas: None declared, Ernest Wong Consultant of: AbbVie, Chugai, Eli Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Chugai, Novartis, and UCB, Yanna Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Namita Tundia Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Jessica Subotički Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Vibeke Strand Consultant of: AbbVie, Amgen, Arena, AstraZeneca, Bayer, Bristol-Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Gilead, Ichnos, Inmedix, Janssen, Kiniksa, MSD, Myriad Genetics, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Scipher, Setpoint, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.2090

POS0671

CLINICAL RESPONSES TO UPADACITINIB OR ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS BY TYPE OF PRIOR BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG: DATA FROM THE PHASE 3 SELECT-CHOICE STUDY

A. Rubbert-Roth[1], R. Xavier[2], B. Haraoui[3], H. S. B. Baraf[4,5], M. Rischmueller[6,7,8], N. Martin[9], Y. Song[9], J. Subotički[9], J. Cush[10].
[1]*Kantonsspital St Gallen, Division of Rheumatology, St Gallen, Switzerland*; [2]*Hospital de Clínicas de Porto Alegre, Division of Rheumatology, Porto Alegre, Brazil*; [3]*Institut de Rhumatologie de Montréal, Clinical Research Unit, Montreal, Quebec, Canada*; [4]*The Center for Rheumatology and Bone Research, Rheumatology, Wheaton, Maryland, United States of America*; [5]*The George Washington University, Rheumatology, Washington DC, United States of America*; [6]*The Queen Elizabeth Hospital, Rheumatology Department, Woodville South, Australia*; [7]*Basil Hetzel Institute, Rheumatology Research Group, Woodville South, Australia*; [8]*Adelaide Medical School, University of Adelaide, Rheumatology, Adelaide, Australia*; [9]*AbbVie Inc., Immunology, North Chicago, Illinois, United States of America*; [10]*The University of Texas Southwestern Medical School, Rheumatic Disease Division, Dallas, Texas, United States of America*

Background: In the phase 3 double-blind SELECT-CHOICE study of patients (pts) with prior inadequate response (IR) or intolerance to biologic disease-modifying antirheumatic drugs (bDMARDs), upadacitinib (UPA) showed superiority to abatacept (ABA) in change from baseline in 28-joint Disease Activity Score using C-reactive protein (DAS28[CRP]) and in the proportion of pts achieving DAS28(CRP) <2.6 at Week 12.

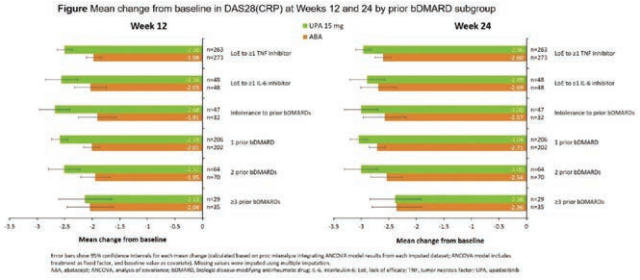
Objectives: To describe clinical responses in pts receiving UPA or ABA by number and mechanism of action of prior bDMARDs.

Methods: 612 pts were randomized to once-daily UPA 15 mg or monthly intravenous ABA (<60 kg, 500 mg; 60–100 kg, 750 mg; >100 kg, 1000 mg). All pts continued background therapy with stable conventional synthetic DMARDs. From Week 12, pts who did not achieve ≥20% improvement in both tender and swollen joint counts vs baseline at 2 consecutive visits had background medication(s) adjusted or added. In this post hoc analysis, pts were grouped by the number and/or type of bDMARD received prior to enrollment: 1) lack of efficacy (LoE) to ≥1 tumor necrosis factor (TNF) inhibitor; 2) LoE to ≥1 interleukin-6 (IL-6) inhibitor; 3) intolerance to prior bDMARDs; 4) number of prior bDMARDs (1, 2, or ≥3). Mean change from baseline in DAS28(CRP) and DAS28(CRP) <2.6 and other clinical endpoints were evaluated at Weeks 12/24.

Results: Most pts had LoE to ≥1 TNF inhibitor (536, 87.6%); 96 (15.7%) had LoE to an IL-6 inhibitor; 79 (12.9%) had intolerance to prior bDMARDs; 408 (66.7%), 134 (21.9%), and 64 (10.5%) had received 1, 2, or ≥3 prior bDMARDs, respectively. Mean change from baseline in DAS28(CRP) was generally greater with UPA vs ABA across the different pt subgroups at Weeks 12/24 (Figure 1). Across endpoints, regardless of prior bDMARD therapy (except in those who failed ≥3 prior bDMARDs), UPA and ABA demonstrated similar responses at Week 12 compared with those observed for the overall treatment groups, even with more stringent criteria such as ACR70 and Clinical Disease Activity Index (CDAI) ≤2.8 (Table 1. below) Responses at Week 24 followed a similar trend to those at Week 12 for DAS28(CRP) <2.6 and other endpoints (Table 1). The safety profile across subgroups was consistent with each respective treatment in the overall study population (data not shown).

Conclusion: Although sample sizes were small for some subgroups, treatment with UPA led to greater clinical responses vs ABA at Week 12, including in pts with LoE to TNF or IL-6 inhibitors, and those with IR or intolerance to 1, 2, or ≥3 prior bDMARDs.

Figure Mean change from baseline in DAS28(CRP) at Weeks 12 and 24 by prior bDMARD subgroup



Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Grant Kirkpatrick, MSc of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Disclosure of Interests: Andrea Rubbert-Roth Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Chugai, Eli Lilly, Gilead, Janssen, Novartis, Roche, and Sanofi, Ricardo Xavier Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Boulos Haraoui Consultant of: AbbVie, Amgen, Eli Lilly, Gilead, MSD, Pfizer, Sandoz, and UCB, Herbert S.B. Baraf Consultant of: Gilead, Janssen, and UCB, Grant/research support from: AbbVie, Eli Lilly, Genentech, Gilead, and Janssen, Maureen Rischmueller Consultant of: AbbVie, Bristol-Myers Squibb, CSL Behring, Eli Lilly, Gilead, Janssen, Pfizer, Sanofi, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi, and UCB, Naomi Martin Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Jessica Subotički Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, John Cush Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, and Novartis.

DOI: 10.1136/annrheumdis-2021-eular.2114

Table 1. Efficacy endpoints by prior bDMARD subgroup (Week 12 [top] and Week 24 [bottom])[a]

		ACR20	ACR50	ACR70	DAS28(CRP) ≤3.2	DAS28(CRP) <2.6	CDAI ≤10	CDAI ≤2.8	HAQ-DI MCID[b]
LoE to ≥1 TNF inhibitor	UPA 15 mg n=263	75.3	44.9	22.8	49.0	30.4	40.7	9.1	75.5
		77.9	59.7	38.8	61.2	46.8	58.6	22.8	74.3
	ABA	64.5	33.7	13.2	27.5	12.5	33.7	2.2	65.2
	n=273	72.9	48.4	24.9	46.5	29.7	49.8	12.5	66.3
LoE to ≥1 IL-6 inhibitor	UPA 15 mg n=48	70.8	37.5	20.8	45.8	25.0	41.7	6.3	78.3
		85.4	66.7	29.2	66.7	41.7	58.3	16.7	78.3
	ABA	77.1	41.7	22.9	25.0	14.6	27.1	2.1	75.0
	n=48	79.2	56.3	27.1	43.8	29.2	52.1	10.4	75.0
Intolerance to prior bDMARDs	UPA 15 mg	83.0	53.2	17.0	53.2	31.9	44.7	8.5	80.0
	n=47	76.6	57.4	27.7	57.4	29.8	44.7	14.9	73.3
	ABA	62.5	28.1	0.0	21.9	6.3	21.9	3.1	61.3
	n=32	71.9	50.0	31.3	56.3	31.3	56.3	9.4	67.7
1 prior	UPA 15 mg	77.2	51.9	21.8	52.4	32.5	41.7	9.2	79.6
	n=206	81.1	63.1	38.8	66.0	47.6	61.2	20.9	76.6
bDMARD									
	ABA	67.3	35.1	15.8	29.2	12.4	36.1	3.0	66.7
	n=202	77.7	53.5	33.7	51.5	35.6	55.9	16.3	71.7
2 prior	UPA 15 mg	78.1	34.4	23.4	51.6	26.6	45.3	4.7	73.8
	n=64	76.6	56.3	39.1	62.5	50.0	54.7	23.4	70.5
bDMARDs									
	ABA	64.3	28.6	4.3	27.1	11.4	28.6	1.4	55.7
	n=70	64.3	42.9	11.4	41.4	24.3	44.3	8.6	55.7
≥3 prior bDMARDs	UPA 15 mg n=29	55.2	24.1	17.2	27.6	20.7	27.6	10.3	58.6
		65.5	44.8	24.1	41.4	27.6	48.3	17.2	72.4
	ABA	65.7	40.0	20.0	28.6	20.0	37.1	2.9	77.1
	n=35	71.4	40.0	17.1	37.1	20.0	40.0	8.6	74.3

[a]Missing information was imputed using NRI. [b]HAQ-DI MCID=reduction from baseline of ≥0.22ACR20/50/70, 20/50/70% improvement in ACR criteria; HAQ-DI, Health Assessment Questionnaire-Disability Index

POS0672

FIRST-IN-HUMAN STUDY OF GS-5718, AN ORAL IRAK-4 INHIBITOR, IN HEALTHY SUBJECTS: PHARMACOKINETICS, SAFETY, TOLERABILITY, AND ASSESSMENT OF EFFECT OF FOOD AND ACID REDUCING AGENTS ON EXPOSURE

K. Anderson[1], C. H. Hsueh[1], O. Gurtovaya[1], A. Mathur[1], J. Taylor[1], A. Serone[1], A. A. Othman[1]. [1]*Gilead Sciences, Inc., Foster City, United States of America*

Background: GS-5718 is a potent and selective interleukin-1 receptor-associated kinase 4 (IRAK4) inhibitor in clinical development for treatment of inflammatory diseases.
Objectives: The aim of this first-in-human study was to evaluate the pharmacokinetics, safety, and tolerability of GS-5718; and the effect of food and acid-reducing agents (ARA) on GS-5718 pharmacokinetics in healthy subjects.
Methods: This was a blinded, randomized, placebo-controlled, single and multiple (once daily for 10 days) oral dose study. Healthy male and female subjects were enrolled in ascending dose cohorts and randomized to receive GS-5718 (15, 50 or 150 mg) or placebo. GS-5718 was administered fasted in the single ascending dose cohorts, and under fed conditions (standard meal) in the multiple dose cohorts. The effects of a high-fat meal and omeprazole (a representative ARA) on GS-5718 50 mg dose pharmacokinetics were also evaluated. Serial blood samples were collected and GS-5718 pharmacokinetic parameters were characterized. Safety was assessed by review of adverse events (AEs), clinical laboratory tests, and vital signs.
Results: A total of 74 subjects (n = 62 GS-5718; n = 12 placebo) enrolled and completed study drug treatments in this study. GS-5718 was generally well tolerated at all evaluated dose levels; AEs were mild in severity and no dose-limiting toxicities, serious AEs, nor clinically relevant electrocardiogram or vital sign abnormalities were observed in subjects administered GS-5718. GS-5718 exposure was approximately dose proportional across the evaluated multiple ascending dose range. GS-5718 showed low-to-moderate pharmacokinetic variability with median half-life of 25 to 33 hours and 1.6 to 2.4- fold accumulation at steady-state, which was achieved by Day 5-7 of dosing. Food had no clinically meaningful impact on GS-5718 exposure (AUC and C_{max}) at the 50 mg dose. Co-administration of omeprazole with GS-5718 reduced GS-5718 exposure (AUC and C_{max}) by 23% and 43%, respectively, at the 50 mg dose.
Conclusion: GS-5718, administered once daily, was well tolerated following single or multiple dosing up to 150 mg. The pharmacokinetic and safety profile of GS-5718 support the further development in inflammatory diseases with once-daily administrations.
Disclosure of Interests: Kacey Anderson Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Chia-Hsiang Hsueh Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Oksana Gurtovaya Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Anubhav Mathur Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, James Taylor Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Adrian Serone Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Ahmed A. Othman Shareholder of: Gilead Sciences, Employee of: Gilead Sciences
DOI: 10.1136/annrheumdis-2021-eular.2238

POS0673

TOLEROGENIC DENDRITIC CELLS IN RHEUMATOID ARTHRITIS PATIENTS: NEWS AND PROMISES

Y. Kurochkina[1], E. Chernykh[2], A. Sizikov[3]. [1]*Research Institute of Clinical and Experimental Lymphology - Branch of the Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences, Rheumatology, Novosibirsk, Russian Federation*; [2] *Federal State Budgetary Scientific Institution Research Institute of Fundamental and Clinical Immunology, Laboratory of Cells Immunotherapy, Novosibirsk, Russian Federation*; [3]*Federal State Budgetary Scientific Institution Research Institute of Fundamental and Clinical Immunology, Rheumatology, Novosibirsk, Russian Federation*

Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, the enhancing of tolerogenic properties of DCs seems to be a new important strategy in treatment of RA. Dexamethasone is widely used in clinical practice and can be used as a tolerogenic substance. Therefore, the properties of DCs generated in presence of dexamethasone are of great clinical interests.
Objectives: The aim of our study is to describe the properties of tolerogenic DCs, generated with dexamethasone in patients with RA and their influence on autologous T-cells.
Methods: Sixty five patients with RA with high and moderate activity of disease were recruited in this study. All patients follow ACR/EULAR criteria (2010). All studies were performed after receiving informed consent. All patients received conventional synthetic DMARDs. DCs were generated from blood monocytes culturing for 5 days with GM-CSF and IFN-α in the presence dexamethasone (dexDCS), applied on third day. LPS as maturation stimuli was added on fourth day. The expression of CD14, CD83, HLA-DR, TLR-2 on the surface of DCs was measured by flow cytometry. The functions of DCs were evaluated by measuring cytokine production and DCs allostimulatory activity in mixed lymphocyte culture. Mature DCs generated in absence of dexamethasone used as control.
Results: We revealed that dexDCs are characterized by enhanced expression of CD14+cells and decreased number of CD83+cells but percent of HLA-DR+cells were constant (about 85). DexDCs show high expression of TLR-2 is seen as tolerogenic molecule (75%vs51%, p=0.05 compared to control). DexDCs also have marked prominent increase of TNFα/IL-10 ratio in contrast to control (0.59 vs 1.8, p=0.03). DexDCs suppressed proliferation of allogenic T-cells (2005 vs 7980 cpm, p=0.0002). To assess the stability of the DC in the proinfflamatory micro-environment after assessing stimulatory activity dexDCs were then cultivated with LPS and allostimulatory activity were evaluated one more. The stimulation activity dexDCs after incubation with LPS were not increase (4692 vs 6053 cpm, p=0.7). Also earlier we showed possibility of dexDCs induse apoptosis of autologous T-cells, activation of CD4+IL10+Tr1 and possession of antigen-specific suppression.
Conclusion: The data obtained indicate that dexDCs from RA patients have the main tolerogenic features and stable in inflammatory environment that proves their potential in the treatment of rheumatoid arthritis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2261

POS0674

DIRECT COMPARISON OF EFFECTIVENESS AND SAFETY OF TOFACITINIB AND BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-WORLD SETTINGS

N. Iwamoto[1], T. Suzuki[2], A. Okada[3], K. Fujikawa[4], T. Aramaki[5], A. Mizokami[4], Y. Ueki[5], A. Kawakami[1]. [1]*Nagasaki University Graduate School of Biomedical Sciences, Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, Nagasaki, Japan*; [2]*Sasebo City General Hospital, Department of Internal Medicine, Sasebo, Japan*; [3]*Nagasaki Atomic Bomb Museum, Department of Rheumatology, Nagasaki, Japan*; [4]*Japan Community Healthcare Organization, Isahaya General Hospital, Department of Rheumatology, Isahaya, Japan*; [5]*Sasebo Chuo Hospital, Department of Rheumatology, Sasebo, Japan*

Background: Tofacitinib is a non-selective first-generation JAK inhibitor and baricitinib was approved for the treatment of Rheumatoid arthritis several years after approve of tofacitinib. Randomized controlled trials have shown good treatment response for RA in these two drugs. However, the evaluation of these two drugs in real-world setting have been rarely reported, moreover, until now, no published data of a direct comparison among JAK inhibitors in RA have been available.
Objectives: To compare the efficacy and safety of the JAK inhibitors tofacitinib and baricitinib in patients with rheumatoid arthritis (RA) by using propensity score matching in a real-world setting.
Methods: A total of 242 patients with RA who were treated with tofacitinib (n=161) or baricitinib (n=81) were enrolled. To avoid confounding, we performed propensity score matching based on multiple baseline characteristic variables, and then 80 baricitinib-treated patients and 57 tofacitinib-treated patients were extracted for the direct comparison. A mixed effect model with a repeated measures analysis of variance (ANOVA) was performed to ascertain whether there were significant differences in clinical efficacy between the two treatment groups during the treatment period.Finally, We evaluated the predictive factor of clinical responses by performing univariate and multivariable logistic regression analyses.
Results: The mean delta disease activity scores (DAS)28-ESR from baseline to 6 months were −1.60 (tofacitinib) and −1.46 (baricitinib). The remission rate defined by the DAS28-ESR at 24 weeks were 21.1% (tofacitinib) and 25.0% (baricitinib). There was no significant difference in the clinical response between the baricitinib-treated and tofacitinib-treated groups. Although there was no significant difference, the concomitant use of methotrexate (MTX) showed better clinical efficacy in the cases of baricitinib treatment as compared with in the case of tofacitinib treatment. In both groups, the most common AE was herpes zoster infection, and the AE rates were similar between the two groups. However, the predictive factors contributing to clinical response differed. The concomitant use of oral steroid was independently associated with the achievement of DAS-low disease activity in both groups, whereas in the baricitinib group, the number of biological and/or targeted synthetic DMARDs previously used and the DAS28-ESR at the time of initiation were associated with DAS-low disease activity.
Conclusion: This study indicate that tofacitinib and baricitinib had comparable efficacies and safety profiles in a real-world setting. However, the influence of clinical characteristics on the treatment response differed between these two drugs. Direct comparison between two JAK inhibitors provide useful information to optimal use of JAK inhibitors in real-world settings.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3469

POS0675 THE COMPARATIVE 3-YEAR RETENTION RATE OF TARGETED-SYNTHETIC AND BIOLOGIC DRUGS FOR RHEUMATOID ARTHRITIS: REAL-LIFE DATA FROM THE ITALIAN GISEA REGISTRY

E. G. Favalli[1], F. Iannone[2], E. Gremese[3], R. Gorla[4], R. Foti[5], F. Conti[6], M. Rossini[7], E. Fusaro[8], F. P. Cantatore[9], C. Montecucco[10], M. Sebastiani[11], A. Cauli[12], G. Ferraccioli[13], G. Lapadula[14], R. Caporali[1,15]on behalf of Gruppo Italiano di Studio sulla Early Arthritis, GISEA. [1]*ASST Gaetano Pini-CTO Institute, Division of Clinical Rheumatology, Milan, Italy*; [2]*University of Bari, Department of Medicine, Rheumatology Unit, Bari, Italy*; [3]*Fondazione Policlinico Universitario A.Gemelli-IRCCS, Università Cattolica del Sacro Cuore, Rheumatology Division, Rome, Italy*; [4]*Spedali Civili, UO Reumatologia e Immunologia Clinica, Brescia, Italy*; [5]*Policlinico Vittorio Emanuele, Department of Medicine, Rheumatology Unit, Catania, Italy*; [6]*Sapienza University of Rome, Dipartimento di Scienze Cliniche, Internistiche, Anestesiologiche e Cardiovascolari-Reumatologia, Rome, Italy*; [7]*University of Verona, Department of Medicine, Rheumatology Unit, Verona, Italy*; [8]*Città Della Salute E Della Scienza Hospital, Rheumatology Unit, Turin, Italy*; [9]*University of Foggia Medical School, Department of Medical and Surgical Sciences, Rheumatology Clinic, Foggia, Italy*; [10]*IRCCS Policlinico San Matteo Foundation, University of Pavia, Rheumatology Unit, Pavia, Italy*; [11]*University of Modena and Reggio Emilia, Rheumatology Unit, Modena, Italy*; [12]*Policlinico of the University of Cagliari, Department of Medical Sciences, Rheumatology Unit, Cagliari, Italy*; [13]*Gruppo Italiano di Studio sulla Early Arthritis, GISEA, Rome, Italy*; [14]*Gruppo Italiano di Studio sulla Early Arthritis, GISEA, Bari, Italy*; [15]*Università degli Studi di Milano, Department of Clinical Sciences & Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Milan, Italy*

Background: Long-term observational data on the real-life use of JAK inhibitors (JAKis) for rheumatoid arthritis (RA) and their comparison with biological drugs are still very limited. Large population-based registries have been increasingly used to investigate the performance of targeted drugs in a real-life setting.
Objectives: The aim of this study is to evaluate and compare the 3-year retention rate of JAKis, TNF inhibitors (TNFis) and biologic drugs with other mechanisms of action (OMAs) in the large cohort of RA patients included in the Italian national GISEA registry.
Methods: Data of all RA patients treated with targeted synthetic or biologic drugs were prospectively collected in the Italian multicentric GISEA registry. The analysis was limited to patients who started a first- or second-line targeted drug in the period after the first JAKi was marketed in Italy (1st December 2017). The 3-year retention rate was calculated by the Kaplan-Meier method and compared between different drug classes by a log-rank test. A descriptive analysis of reasons for discontinuation was performed.
Results: The study population included 1027 RA patients (79.8% females, mean age [±SD] 56.9 [±13.5] years, mean disease duration 9.8 [±9] years, mean baseline SDAI 17.5 [±11.9], ACPA positive 67.4%, RF positive 62.7%) who received JAKis (baricitinib or tofacitinib, n=297), TNFis (n=365), or OMAs (n=365) as first or second targeted drug. Main baseline characteristics of study population were overall well balanced between treatment groups. Retention rate was numerically but not statistically higher (p=0.18) in patients treated with JAKis compared with TNFis or OMAs (80.6, 78.9 and 76.4% at 1 year and 73, 56.8 and 63.8% at 3 years, respectively) (Figure 1). Drug survival was significantly higher in patients receiving concomitant methotrexate (MTX) compared with monotherapy only in TNFis (66.8 vs 47.1%, p=0.04) but not in JAKis (76.1 vs 70.1%, p=0.54) and OMAs (66.1 vs 61.9%, p=0.41) group. Therapy was discontinued in a total of 211 patients because of ineffectiveness (n=107), adverse events (n=88), or compliance/other reasons (n=16). The most frequent reason for treatment withdrawal was ineffectiveness in both JAKis (n=30 out of 56) and TNFis (n=45 out of 74) groups, whereas OMAs were discontinued more frequently because of adverse events (n=41 out of 81).

Conclusion: Our data confirmed in a real-life setting a favorable 3-year retention rate of all available targeted mechanisms of action for RA therapy. As expected, concomitant MTX significantly impacted persistence on therapy of TNFis only. Discontinuations of JAKis for adverse events were infrequent overall, confirming the safety profile observed in randomized clinical trials.

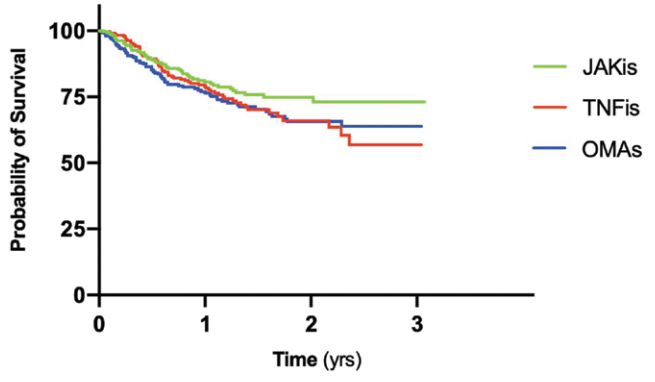


Figure 1. Three-year retention rate by treatment group

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3557

POS0676 SURVIVAL OF THE FIRST COURSE OF BIOLOGIC OR JAK INHIBITOR IN RHEUMATOID ARTHRITIS: ASSOCIATION WITH THE CHOICE OF AGENT AND CONCOMITANT CONVENTIONAL SYNTHETIC DMARDS

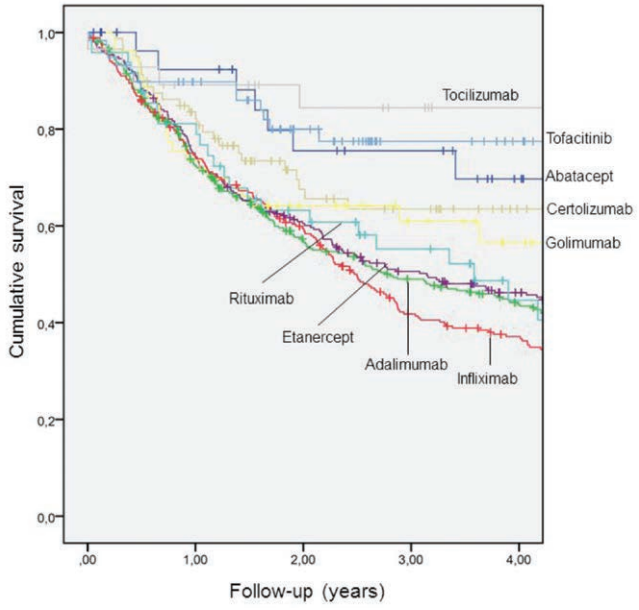
M. Bredemeier[1,2], A. Duarte[1], M. Pinheiro[1], B. Stadler[2], J. C. Macieira[1], R. Ranza[1], J. Miranda[1], V. Valim[2], G. Castro[1], M. Bertolo[2], M. D. F. Sauma[2], V. Fernandes[2], A. Medeiros[2], R. Botelho[2], C. Brenol[2], D. Negrão Gonçalo Dias[2], H. Carvalho[2], S. Studart[2], G. Da Rocha Castelar Pinheiro[2], L. Rocha[2], I. Pereira[2], M. Ohira Gazzeta[2], A. Maria Kakehasi[2], P. Louzada Jr[2], A. L. S. Hayata[2], F. Pina[2], C. Lupo[2], L. Balarini[2], I. Silveira[2], S. Kowalski[2], D. Titton[2], R. Chakr[2], A. Ranzolin[2], I. Laurindo[1], R. Xavier[1]on behalf of BiobadaBrazil. [1]*BiobadaBrasil, Brazilian Society of Rheumatology, SAO PAULO, Brazil*; [2]*BiobadaBrasil, Brazilian Society of Rheumatology, Sao Paulo, Brazil*

Background: After failure of conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) in the therapy of rheumatoid arthritis (RA), treatment may be escalated to biologic (bDMARDs) or JAK inhibitors (JAKi) (1). Analysis of drug survival can provide useful information on the effectiveness of these therapeutic schemes.
Objectives: to evaluate the association of the choice of therapeutic agent with the survival of treatment course in RA patients receiving their first bDMARD or JAKi.
Methods: BiobadaBrasil is a multicentric registry-based cohort study of Brazilian patients starting their first bDMARD/JAKi (2). This analysis includes RA patients recruited from Jan 2009 to Oct 2019, followed-up over the first course of treatment with a bDMARD/JAKi until censoring (latest date, Nov 19, 2019) or occurrence of the outcome of interest. A treatment course is defined as a period during which the medication scheme does not change, except for dose adjustments. The primary outcome was the interruption of treatment course for any reason (except for pregnancy or disease remission); interruption of treatment due to adverse events (AEs) or death and due to inefficacy served as secondary outcomes. Multivariate Cox proportional hazards models were used for analyses.
Results: In total, 1177 patients (3800 patient-years [PY]) were enrolled. The overall incidence of treatment interruption was 17.5/100 PY. Adalimumab was the most frequently prescribed agent, followed by infliximab (n= 267). The hazards ratios (HR) of the primary and secondary outcomes are presented in Table 1. Figure 1 compares the survival of treatment curves of different bDMARDs/JAKi.

Table 1. Hazard ratios (HR) of interruption of therapy course of each therapeutic agent (the reference category for bDMARDs/ JAKi is infliximab). Results are HR, 95% CIs, and P values*.

Agent (number of patients)	Interruption for any reason (665 events)	Interruption due to adverse events or death (196 events)	Interruption due to inefficacy (319 events)
Adalimumab (354)	0.83 (0.68 to 1.01), P= 0.062	0.68 (0.48 to 0.96), P=0.029	1.08 (0.80 to 1.44), P=0.621
Etanercept (257)	0.81 (0.66 to 1.01), P=0.063	0.56 (0.37 to 0.83), P=0.004	0.93 (0.68 to 1.29), P=0.674
Certolizumab (80)	0.74 (0.47 to 1.16), P=0.185	0.33 (0.13 to 0.86), P=0.024	1.32 (0.74 to 2.35), P=0.350
Golimumab (53)	0.86 (0.53 to 1.38), P=0.530	0.46 (0.18 to 1.19), P=0.111	1.07 (0.53 to 2.15), P=0.849
JAKi (tofacitinib) (59)	0.54 (0.30 to 0.99), P=0.047	0.19 (0.04 to 0.82), P=0.026	0.89 (0.41 to 1.96), P=0.779
Rituximab (48)	0.87 (0.55 to 1.37), P=0.540	0.48 (0.20 to 1.18), P=0.109	0.58 (0.26 to 1.34), P=0.205
Abatacept (30)	0.52 (0.25 to 1.07), P=0.077	0.46 (0.14 to 1.56), P=0.215	0.46 (0.14 to 1.52), P=0.203
Tocilizumab (29)	0.29 (0.14 to 0.63), P=0.002	0.40 (0.12 to 1.30), P=0.126	0.28 (0.09 to 0.90), P=0.033
Methotrexate (792)	0.95 (0.79 to 1.14), P=0.561	0.86 (0.62 to 1.19), P=0.362	0.98 (0.75 to 1.28), P=0.860
Leflunomide (497)	1.17 (0.99 to 1.39), P=0.061	1.44 (1.06 to 1.96), P=0.020	1.02 (0.80 to 1.30), P=0.856
Sulfasalazine (48)	1.18 (0.80 to 1.75), P=0.401	1.94 (1.07 to 3.54), P=0.030	0.85 (0.45 to 1.59), P=0.605
Antimalarials (230)	0.80 (0.65 to 0.98), P=0.027	0.67 (0.45 to 0.99), P=0.043	0.67 (0.50 to 0.92), P=0.011

* All tests adjusted for other variables presented in the table and for age, baseline DAS28, disease duration, gender, smoking, seropositivity (RF/anti-CCP), previous malignancy, diabetes, hypertension, hypercholesterolemia, renal failure, ischemic cardiomyopathy, COPD, heart failure, use of corticosteroids, starting year, hypercholesterolemia, osteoporosis, hepatitis B and C.



Conclusion: In our study, infliximab was related to an overall higher hazard of treatment course interruption than tolicizumab and tofacitinib, and higher hazard of interruption due to AEs than most other anti-TNF agents and tofacitinib. Maintaining antimalarials in patients receiving advanced therapies for RA may reduce interruption of treatment due to inefficacy and AEs.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3841

POS0677

THE ROLE OF MUSCULOSKELETAL ULTRASOUND IN PREDICTING THE RESPONSE TO JAK INHIBITORS: RESULTS FROM A LARGE MONOCENTRIC COHORT

C. Garufi[1], F. Ceccarelli[1], F. R. Spinelli[1], S. Mancuso[1], C. Pirone[1], F. Conti[1].
[1]*Sapienza University of Rome, Reumatologia, Dipartimento di Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Roma, Italy*

Background: In the management of chronic arthritis, such as Rheumatoid Arthritis (RA), Ultrasound (US) assessment can provide relevant information about the joint inflammatory status in the diagnostic phase and even more in the monitoring of disease activity and structural damage[1,2].
Objectives: In this longitudinal study, we aimed to assesse the role of US in predicting the efficacy of JAK-inhibitors (JAKi) in RA patients.
Methods: We enrolled RA patients starting baricitinib or tofacitinib. All patients were evaluated at baseline and after 4, 12, 24, 48 weeks. Disease activity was calculated by DAS28CRP. US examination in 22 joints (I–V MCPs and PIPs, wrists) aimed at evaluating inflammatory features (synovial effusion and hypertrophy, power Doppler-PD), through a semi-quantitative scale (0-3). The total US (0-198) and PD (0-66) scores were calculated. We scanned bilateral flexor (I–V fingers of hands) and extensor compartments (1-6) tendons: tenosynovitis was scored as absent/present (0/1), resulting in a total score (0-22).
Results: We studied 102 patients (M/F 15/87; median age 59.2 years, IQR 17.75; median disease duration 144 months, IQR 126), 61 treated with baricitinib and 41 with tofacitinib. At baseline, the median total US score was 18 (IQR 19) and the median PD score 2 (4). We observed a significant reduction in both total and PD US scores at all time-points (p<0.0001) (Figure 1). At baseline, 75.4% of patients showed tenosynovitis involving at least one tendon, with a median score of 2 (IQR 3.5) significantly decreasing after 24 weeks (p=0.02). Multivariate analysis, adjusted for baseline $DAS28_{CRP}$ and other concomitant treatments (including glucocorticoids and methotrexate treatment), confirmed the independent association between baseline US (PD and tenosynovitis) scores and the reduction of disease activity at follow-up evaluations.
Conclusion: The present study confirmed the early efficacy of JAKi in RA patients by using US evaluation. Furthermore, power doppler and tenosynovitis scores could play a predictive role in response to treatment.
REFERENCES:

[1] MUELLER RB, HASLER C, POPP F, et al. Effectiveness, Tolerability, and Safety of Tofacitinib in Rheumatoid Arthritis: A Retrospective Analysis of Real-World Data from the St. Gallen and Aarau Cohorts. J Clin Med. 2019;8(10):1548.
[2] COLEBATCH AN, EDWARDS CJ, ØSTERGAARD M, et al. EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. Ann Rheum Dis. 2013;72(6):804-14.

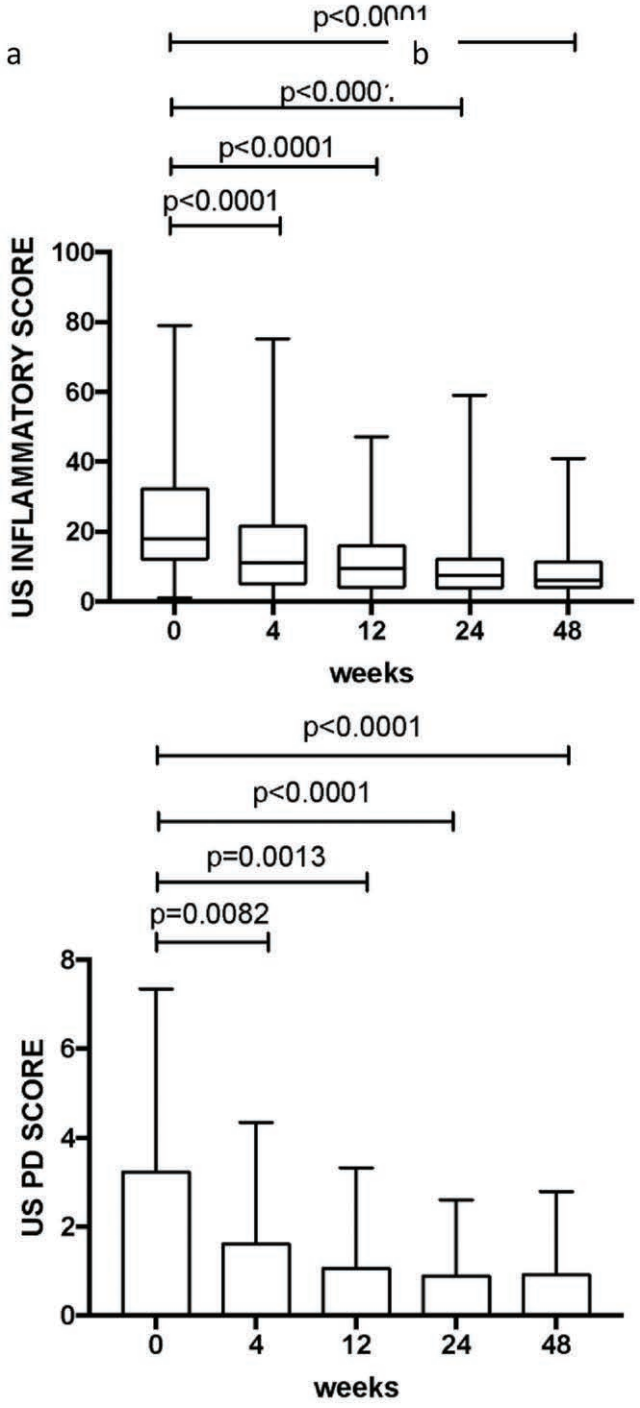


Figure 1. Ultrasound inflammatory score (a) and Ultrasound Power Doppler (PD) score (b) at baseline and follow-up.

WEEKS	0	4	12	24	48
US inflammatory score	18 (19)	11 (15.5)	9.5 (11.7)	7.5 (8)	6 (11)
US PD score	2 (4)	0 (2)	0 (1)	0 (1)	0 (0.7)

Disclosure of Interests: Cristina Garufi: None declared, Fulvia Ceccarelli: None declared, Francesca Romana Spinelli Speakers bureau: Abbvie, Eli Lilly, Consultant of: Gilead/Galapagos, Eli Lilly, Grant/research support from: Pfizer, Silvia Mancuso: None declared, Carmelo Pirone: None declared, Fabrizio Conti Speakers bureau: Abbvie, Eli Lilly, Sanofi, Pfizer, Consultant of: Gilead/Galapagos

DOI: 10.1136/annrheumdis-2021-eular.3850

POS0678

DOES SILDENAFIL IMPROVE ENDOTHELIAL DYSFUNCTION IN RHEUMATOID ARTHRITIS? – A PILOT CLINICAL TRIAL

K. Liang[1], D. Landsittel[2], Y. Li[2], L. Hope[3], L. Ruffalo[3], J. Peat-Fircak[3], J. Avolio[4], P. Biswas[3], E. Roth[3], M. Simon[5], L. Moreland[6]. [1]*University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, PA, United States of America*; [2]*University of Pittsburgh, Biomedical Informatics, Pittsburgh, United States of America*; [3]*University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America*; [4]*University of Pittsburgh, Clinical and Translational Science Institute, Pittsburgh, PA, United States of America*; [5]*University of California San Francisco, Cardiology, San Francisco, CA, United States of America*; [6]*University of Colorado, Rheumatology, Aurora, CO, United States of America*

Background: Rheumatoid arthritis (RA) is independently associated with an increased risk of cardiovascular disease (CVD). One of the early stages of atherosclerosis is endothelial dysfunction, which is increased in RA. Using drugs to target endothelial dysfunction is a promising novel strategy for CVD prevention in RA. Sildenafil has been shown to improve endothelial function in diabetics, who have similar increased CVD risk. Our hypothesis was that sildenafil use may be a novel primary CVD prevention strategy in RA.

Objectives: To determine if sildenafil use in RA patients improves endothelial dysfunction (as measured by brachial artery flow-mediated dilation [FMD] and peripheral arterial tone [PAT]), as well as serum inflammatory and atherosclerosis biomarkers.

Methods: This NIH-funded study was a phase II, randomized double-blind placebo-controlled crossover efficacy trial of 25 RA patients, with no known history of CVD, but at least one traditional CVD risk factor. Patients were randomized 1:1 to receive either sildenafil or placebo for 3 months, then after a 2-week washout, crossed over to each respective group for an additional 3 months. Vascular studies (FMD and PAT) and serum atherosclerosis biomarkers (e-Selectin, ICAM-1, VCAM-1) were performed at baseline, 3 months pre- and post-washout, and 6 months. Adverse events were collected. Given the cross-over design, analyses included a random effects model for within-subject comparisons of sildenafil versus placebo periods, adjusting for the baseline (FMD or EndoPAT) within that period and a term for treatment order. All tests were 2-sided with α=0.05.

Results: A total of 233 subjects were assessed for eligibility, with 25 subjects being randomized after written informed consent. A total of 13 subjects were randomized to placebo first, and 12 to sildenafil first. Baseline characteristics were similar between those randomized to Placebo vs. Sildenafil first. Mean age was 62.0+/-10.9 years; 84% were female; and 92% were white. A total of 6 adverse events experienced in 3 subjects occurred. The primary endpoint (increase in %FMD in Sildenafil period vs. Placebo period) was not significant (p=0.19). However, note the study was powered at 80% to detect an effect size of 0.37 for change in %FMD or biomarker with a sample size of 60, not 25. However, sildenafil use was associated with a significant increase (improvement) by 0.200 units of PAT ratio (p=0.003) compared with placebo, adjusted by treatment order and baseline PAT ratio (within the given treatment period). Exploratory linear mixed models comparing e-Selectin, ICAM-1, and VCAM-1 between Sildenafil vs. Placebo periods, adjusted for treatment order and the baseline biomarker level, did not show any significant differences except for ICAM-1 (55.3 units higher in Sildenafil vs. Placebo periods, p=0.011).

Conclusion: In this pilot trial of 25 RA subjects, sildenafil use was associated with a significant increase (improvement) in endothelial function as measured by PAT. However, there was no significant difference in FMD. The study is limited due to the small sample size, which was impacted by slow recruitment as well as the COVID-19 pandemic. Future larger studies are required to assess whether other PDE5 inhibitors may improve endothelial dysfunction in RA and other autoimmune disease patients at high risk of CVD.

REFERENCES:

[1] Maradit-Kremers H, Crowson CS, Nicola PJ, et al. Increased unrecognized coronary heart disease and sudden deaths in rheumatoid arthritis: a population-based cohort study. Arthritis Rheum 2005;52:402-11.

[2] Peters MJ, van Halm VP, Voskuyl AE, et al. Does rheumatoid arthritis equal diabetes mellitus as an independent risk factor for cardiovascular disease? A prospective study. Arthritis Rheum 2009;61:1571-9.

[3] Deyoung L, Chung E, Kovac JR, et al. Daily use of sildenafil improves endothelial function in men with type 2 diabetes. J Andrology 2012;33:176-80.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4069

POS0679

A NEW QUESTIONNAIRE AND SCORE (MISA) FOR ASSESSING METHOTREXATE INTOLERANCE IN RHEUMATOID ARTHRITIS

V. Dhir[1], D. V[1], S. Jain[1], V. Pai[2], A. Sharma[1], S. K. Sharma[1], G. Naidu[1], S. Jain[1]. [1]*Postgraduate Institute of Medical Education and Research, Rheumatology Division, Department of Internal Medicine, Chandigarh, India*; [2]*All India Institute of Medical Sciences, Rishikesh, Rheumatology, Medicine, Rishikesh, India*

Background: Methotrexate (MTX) intolerance refers to unpleasant symptoms that accompany use of MTX and may lead to its discontinuation. However, it lacks a validated score in RA patients; with the only option being to use the MISS score which was validated for use in children and not adults.

Objectives: To develop and validate a questionnaire and score (s) for measuring MTX intolerance and its severity in rheumatoid arthritis.

Methods: A 10-item questionnaire called 'Methotrexate Intolerance and Severity assessment in Adults' (MISA) was validated in 105 RA patients. A score was calculated by adding the scores of first 7 questions (0 to 3 based on severity on symptoms), to last 3 questions (0 or 1); it ranged from 0 to 24 (MISA score) and was assessed for correctly classifying MTX intolerance (compared to an interview) by ROC analysis. Its area-under-curve (AUC) was compared with 'Methotrexate Intolerance Severity Score' (MISS), developed for children. Subsequently, it was administered to 414 RA patients to assess the prevalence and associations of MTX intolerance. In addition, the MISA cross-products score, that was calculated by adding the cross-products (severity (1 to 3) x duration per week (0.5 to 7 days)) of symptoms, was compared to MISA and MISS for assessing severity of intolerance.

Results: In the initial phase, 105 RA patients on MTX≥6 months were included, a majority were female (87%), mean age was 51 (13.4) years and methotrexate dose was 18.8±6 mg/week. Thirty-five (33%) were found to be intolerant to MTX based on interview. MISA score had a good predictive ability (AUC of 0.904), to correctly classify MTX intolerance, and was better than MISS score (AUC of 0.823) (Figure 1A). The optimal cut-off for MISA was ≥1, with a sensitivity and specificity of 91.4% and 84.3%. Using the MISA score (≥1), 38.4% of 414 RA patients were found to have MTX intolerance: with nausea, lethargy and irritability being common symptoms. (Figure 1B, C) On multivariable analysis, age (OR 0.972) and BMI (OR 1.061) were significant predictors of MTX intolerance. (Table 1) On assessing for severity of intolerance, MISA cross product score performed the best, with an area-under-curve of 0.899 (95% CI 0.831-0.966), being higher than AUC for MISS and MISA score which were 0.847 (95% CI 0.768-0.927) and 0.837 (95% CI 0.754-0.920).

Conclusion: MISA is the first validated questionnaire for assessing methotrexate intolerance in rheumatoid arthritis, with the MISA score having a good accuracy (at cut-off ≥1), to detect MTX intolerance. Methotrexate intolerance was present in more than one-third of RA patients, with nausea, lethargy and irritability being most common.

Table 1. Baseline characteristics of 414 RA patients.

Variable	All (n=414)	Tolerant (n=255)	Intolerant (n=159)	p-value tol. vs ntol.	P-value multivariable model
Females, n (%)	370 (89)	231 (91)	139 (87)	0.31	
Age, yrs, mean (SD)	50 (12.5)	51.2 (12.6)	48.2 (12.2)	0.016*	0.008**
Duration of RA, yrs, mean (SD)	10.0 (7.0)	10.8 (7.4)	9.6 (6.3)	0.168	
BMI, Kg/m^2[a], mean (SD)	24.0 (4.9)	23.6 (4.9)	24.6 (4.7)	0.107	0.03*
RF positive[b], n (%)	300 (73)	191 (82)	109 (78)	0.29	
CDAI, mean (±SD)	14.0 (11.8)	14 (12.1)	14.1 (11.4)	0.69	
Dose of MTX, mg/wk, mean (SD)	18.6 (5.6)	18.6 (5.5)	18.7 (5.8)	0.83	
Injectable MTX, n (%)	47 (11)	25 (10)	22 (14)	0.21	
Use of FA, n (%)	395 (95)	241 (95)	154 (97)	0.27	
Use of other DMARD, n (%)	272 (66)	160 (62)	112 (70)	0.11	
HCQ n (%)	209 (51)	123 (48)	86 (54)	0.25	
Prednisolone n (%)	156 (38)	87 (34)	69 (43)	0.058	0.21
Using antiemetics, n (%)	12 (3)	1 (0.5)	11 (7)	<0.001	

[a] Available for 262 patients [b]Available for 372 patients

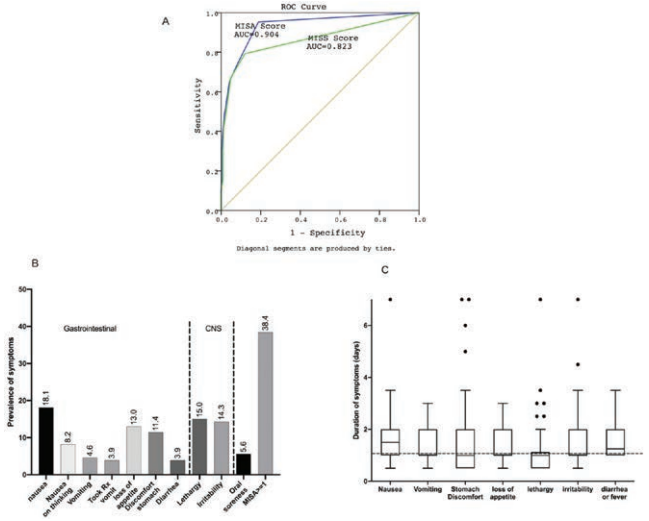


Figure 1. Figure showing the ROC curve for MISA and MISS questionnaires for MTX intolerance (A), Bar diagram showing the prevalence of various symptoms of intolerance in 414 RA patients (B), and Box-and-whiskers plot showing the duration of unpleasant symptoms (C).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4241

SLE, **Sjögren's and APS – treatment_**

POS0680 BELIMUMAB ADD-ON THERAPY MOBILISES MEMORY B CELLS INTO THE CIRCULATION OF PATIENTS WITH SLE

E. J. Arends[1], M. Zlei[2], C. M. Tipton[3], Z. Osmani[1], S. Kamerling[1], T. Rabelink[1], I. Sanz[3], J. J. M. Van Dongen[2], C. Van Kooten[1], Y. K. O. Teng[1]. *[1]Leiden University Medical Center (LUMC), Nephrology, Leiden, Netherlands*; *[2]Leiden University Medical Center (LUMC), Immunology, Leiden, Netherlands*; *[3]Emory University-School of Medicine, Division of Rheumatology, Department of Medicine, Atlanta, United States of America*

Background: Belimumab (BLM), a recombinant human monoclonal antibody directed against B-cell activating factor (BAFF), is the first approved biological agent for patients with active severe systemic lupus erythematosus (SLE) and lupus nephritis (LN). There is clinical evidence that combining BLM with B cell depleting therapy can ameliorate disease activity in severe, refractory SLE patients[1]. Although BLM is a B cell directed therapy and has been shown to significantly decrease total B cells, flow cytometry observations suggest a rapid increase of circulating memory B cells (MBC)[2].
Objectives: To investigate dynamics of B-cell subsets in SLE patients treated with or without BLM, with a focus on assessing MBC characteristics.
Methods: Extensive B cell subset phenotyping was performed by high-sensitivity (HS) flow cytometry (acquisition of 10^7 leukocytes; per EuroFlow protocols[3]) on samples from active LN or SLE patients with major organ involvement treated with standard of care (SOC) consisting of high dose steroids and mycophenolate mofetil combined with or without the addition of BLM. MBC gene expression profiles were characterized with single-cell RNA and V(D)J sequencing (ScRNA-SEQ).
Results: By employing HS flowcytometry, we established that the absolute increase in circulating MBC in SLE and LN patients was significant for patients who initiated BLM (Figure 1). The increase was observed in a broad range of MBC subsets (Unswitched, IgG1+, IgG2+, IgA1+, IgA2+) at 2 and 4 weeks following initiation of BLM treatment. This rise in MBC could hypothetically be attributed to either proliferation of blood MBC, BLM induced migration of tissue-resident MBCs or BLM related retention of tissue-destined MBC in the blood. ScRNA-SEQ analysis of cell cycle gene-expression was performed and established in both groups a non-proliferating phenotype [in approximately ~94%] of MBC post-treatment, including absence of MKI67 as active proliferation marker. Clonal diversity analysis comparing week 2 with baseline revealed an unexpected decrease of the largest MBC clones in BLM, whereas no change in clonality was observed with SOC alone. Together these data indicate that proliferation is unlikely to be responsible for the observed increase in MBC by BLM. Furthermore, a clear difference was found in gene-expression levels between both treatment groups:

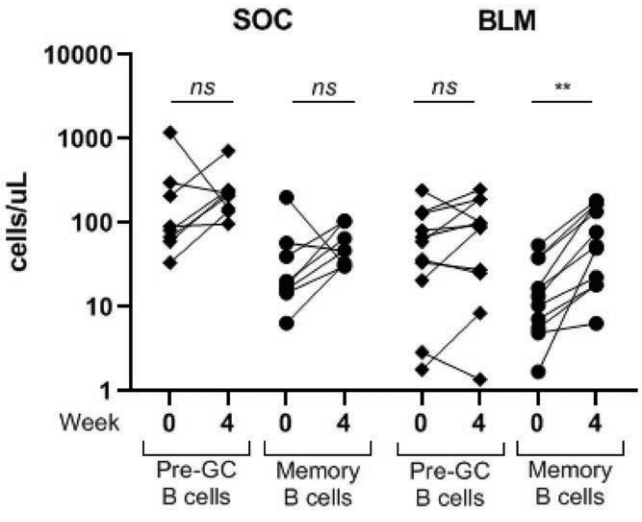


Figure 1. Change in pre-germinal center and memory B cell counts from baseline to week 4 of patients with SLE or LN treated with SOC (n=8) or SOC+BLM (n=11).

BLM was responsible for the upregulation of 72 vs 10 genes in SOC, likewise 162 vs 32 genes were downregulated. Most importantly, a significant downregulation of the migration genes SELL (CD62L), CCR7, ITGB1, RAC2 and ICAM2, were specifically seen in BLM treated patients. This may reflect disrupted lymphocyte trafficking, preventing MBCs from transmigrating from the blood into tissue owing to reduced migration molecules, or preventing MBCs from being retained at the tissue level owing to reduction in tissue adhesion proteins.
Conclusion: The addition of BLM to SOC significantly increases MBCs in patients with SLE independently of proliferation, accompanied by a strong modulation of gene expression, including reduced expression of migration markers pointing towards disrupted lymphocyte trafficking. These data may have important implications for improving treatment strategies in patients with LN or severe SLE, as a deeper depletion of autoreactive MBCs could be established by adding B-cell-depleting therapy after the initiation of BLM.

REFERENCES:

[1] Arends EJ et al. Long-term effects of combined B cell immunomodulation with rituximab and belimumab in severe, refractory systemic lupus erythematosus: 2-year results. Nephrol Dial Transplant. 2020 Jun 27 gfaa117.
[2] Stohl W et al. Belimumab reduces autoantibodies, normalizes low complement levels, and reduces select B cell populations in patients with SLE. Arthritis Rheum. 2012;64(7):2328-2337.
[3] Blanco et al, Age-associated distribution of B and plasma cell subsets in peripheral blood - J Allergy Clin Immunol 2018 141 2208-2219.

Disclosure of Interests: Eline J. Arends: None declared, Mihaela Zlei: None declared, Christopher M. Tipton: None declared, Zgjim Osmani: None declared, Sylvia Kamerling: None declared, Ton Rabelink: None declared, Ignacio Sanz: None declared, Jacques J.M. van Dongen Paid instructor for: BD Biosciences: Educational Services (fees for LUMC), Consultant of: BD Biosciences and Cytognos (fees for LUMC), Grant/research support from: GSK (flow cytometry studies for GSK BLISS-BELIEVE study NCT03312907), Cees van Kooten: None declared, Y.K. Onno Teng Consultant of: Aurinia provided financial compensation for consultancy, Grant/research support from: GSK provided belimumab for free for the Synbiose-2 clinical trial and provided an unrestricted grant to conduct the study.
DOI: 10.1136/annrheumdis-2021-eular.248

POS0681 VOCLOSPORIN FOR LUPUS NEPHRITIS: INTERIM ANALYSIS OF THE AURORA 2 EXTENSION STUDY

A. Saxena[1], P. Mina-Osorio[2], C. Mela[3], V. Berardi[2]. *[1]NYU Langone Health, Rheumatology, New York, United States of America*; *[2]Aurinia Pharmaceuticals, Inc., Medical Affairs, Victoria, Canada*; *[3]Aurinia Pharmaceuticals, Inc., Clinical Science, Victoria, Canada*

Background: Voclosporin, a novel calcineurin inhibitor (CNI), has been tested successfully in two pivotal trials in adult patients with lupus nephritis.
Previously reported results from the Phase 3 AURORA 1 study and the Phase 2 AURA-LV study showed that compared with mycophenolate mofetil (MMF) and low-dose steroids alone, the addition of voclosporin significantly increased the renal response rate and reduced proteinuria, as measured by urine protein creatinine ratio (UPCR), in patients with lupus nephritis (LN) at approximately one year of treatment (48 weeks in AURA-LV and 52 weeks in AURORA 1).
Objectives: Patients that completed one year of treatment in the AURORA 1 study were eligible to enroll into the two-year, blinded, controlled extension study, AURORA 2. Here we report the first interim analysis of the ongoing AURORA 2 study.
Methods: Patients completing AURORA 1 were eligible to continue the same randomized treatment of voclosporin (23.7 mg BID) or placebo, in combination with MMF (1 g BID) and low-dose oral steroids in the AURORA 2 extension. This interim analysis evaluated UPCR and estimated glomerular filtration rate (eGFR) in patients with up to two years of total treatment: one year from AURORA 1 and up to one year in AURORA 2.
Results: 116 patients in the voclosporin arm and 100 patients in the control arm enrolled in the extension study, of which 73 patients in the voclosporin arm and 51 patients in the control arm had received two years of treatment at the time of this interim analysis. Mean UPCR at pre-treatment (AURORA 1) baseline was 3.94 mg/mg in the voclosporin arm (n=116) and 3.87 mg/mg in the control arm (n=100). The LS mean change in UPCR from pre-treatment baseline to year two was -3.1 mg/mg for the voclosporin arm (n=73) and -2.1 mg/mg for control arm (n=51; Table 1). Mean eGFR at pre-treatment (AURORA 1) baseline was 79.6 mL/min for the voclosporin arm (n=116) and 78.9 mL/min for the control arm (n=100) and at year two, was 79.0 mL/min for the voclosporin arm (n=73) and 82.9 mL/min for the control arm (n=51). There was a small early decrease in mean eGFR in the first four weeks of treatment (in AURORA 1) after which eGFR remained stable throughout year one and year two. Additionally, there

were no unexpected new AEs observed in patients who continued with voclosporin treatment compared to control-treated patients for more than one year.

Table 1. UPCR

	Control (n=100)		Voclosporin (n=116)		Treatment Comparison of Voclosporin to Control	
	n	UPCR (mg/mg)	n	UPCR (mg/mg)	UPCR (mg/mg)	p-value
Pre-treatment baseline, mean	100	3.87	116	3.94	NC	NC
Change from pre-treatment baseline, LS mean						
Year 1	100	-2.4	116	-3.0	-0.6	0.0080
Year 2	51	-2.1	73	-3.1	-1.0	0.0004

LS, least squares; NC, not calculated; UPCR, urine protein creatinine ratio.Mixed effects model for repeated measures (MMRM) analysis of LS mean change from pre-treatment baseline for UPCR included terms for baseline covariate, treatment, visit and treatment by visit interaction. Integrated results include data from pre-treatment baseline of AURORA 1, the one-year treatment period in AURORA 1 and up to a one-year treatment period in AURORA 2.

Conclusion: Patients in the voclosporin treatment arm maintained meaningful reductions in proteinuria with no change in mean eGFR at two years of treatment. Additional AURORA 2 efficacy and safety data will be provided at the conclusion of the study.

Disclosure of Interests: Amit Saxena: None declared, Paola Mina-Osorio Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc., Christopher Mela Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc., Vanessa Berardi Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc.
DOI: 10.1136/annrheumdis-2021-eular.372

POS0682 RETROSPECTIVE ANALYSIS OF PREGNANCY OUTCOMES IN PATIENTS WITH OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (OAPS), NON-CRITERIA OAPS (NC-OAPS) AND ANTIPHOSPHOLIPID CARRIERS

M. E. D'amico[1], M. S. Ciliento[1], P. Melissa[1], M. Govoni[1]. [1]*Rheumatology Unit; Azienda Ospedaliera Universitaria Sant'Anna – Cona (Ferrara, Department of Medical Sciences - University of Ferrara, Ferrara, Italy*

Background: Antiphospholipid (aPL) antibodies are considered in obstetric morbidity even when Sydney criteria for OAPS are not met. Classification and treatment of NC-OAPS patients and aPL carriers during pregnancy are still debated.
Objectives: To increase knowledge, we evaluated and compared aPL serum profiles, exposure to antithrombotic therapies and pregnancy outcomes in OAPS, NC-OAPS and aPL carrier patients, accessing to our centre.
Methods: A retrospective observational study was conducted on pregnant outpatients from January 2003 to April 2020. According to Sydney revised classification criteria, we considered lupus anticoagulant (LA), IgM and IgG anti-cardiolipin antibodies (aCL), IgM and IgG antibeta2 glycoprotein I antibodies (aβ2-GPI), to stratify aPL risk profiles [Ref]. In each pregnancy, after case stratification into high (≥ 2 aPL or LA serum positivity) versus low (single aPL positivity) risk profile, we evaluated antithrombotic treatment strategy and subsequent pregnancy outcomes as live-births, spontaneous abortions (SA) or foetal losses.
Results: A total of 78 pregnancies were followed: 17 in OAPS, 9 in NC-OAPS and 52 in aPL carrier patients. Rheumatic diseases (RD) coexisted predominately in carriers (73.1%), mainly systemic lupus erythematosus (57.9%). As presented in Table 1, in OAPS and aPL plus RD carrier groups the association of acetyl-salicylic acid (ASA - mean dose 100 mg q.d.) and low-molecular weight heparin (LMWH - mean dose 4000 UI q.d.) showed a better rate of positive outcomes (97.8% of pregnancies) in high aPL risk profile, compared to monotherapy, especially with LA or triple aPL positivity. Conversely, negative outcomes occurred mostly with triple aPL positivity in the first group and double aPL in the second, despite therapy approaches. No significant data were obtained in NC-OAPS group, due to its paucity, though adverse outcomes were observed with monotherapy both in high and low risk profiles. Except aPL carriers with RD, in all other low risk subgroups, a prevalence of negative outcomes occurred using ASA alone, without statistical significance (OR 0; p= 0.45). Similarly, considering the whole population, the use of a mono or a combination therapy in high risk subgroups had not a significant correlation with pregnancy outcomes (OR 1.79; 95%CI 0.31-10.15; p= 0.50).
Conclusion: In our study, negative pregnancy outcomes were sporadic, occurring mostly with ≥ 2 aPL positivity. Combination treatment showed better results overall in high aPL risk profile patients, both in OAPS and NC-OAPS or aPL carriers. Though no significant correlation between outcomes and treatments were found, we hinted how aPL-based risk stratification may be useful in adopting personalised therapies to prevent obstetric failures.

REFERENCE:

[1] Miyakis S, et al (2006) International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome. J Thromb Haemost 4:295–306.

Table 1. Population groups, aPL risk profiles, antithrombotic therapies and pregnancy outcomes.

Population group	aPL risk profile	Type/n° of aPL	Therapy (n° of pregnancies)	Pregnancy outcomes
OAPS	**High**	LA	ASA (1)	1 live-birth
			ASA + LMWH (1)	1 live-birth
		2 aPL	ASA + LMWH (3)	3 live-births
		3 aPL	ASA + LMWH (9)	7 live-births
				2 foetal losses
	Low	1 aPL	ASA (2)	1 live-birth
				1 foetal loss
			ASA + LMWH (1)	
				1 live-birth
NC-OAPS	**High**	LA	-	-
		2 aPL	ASA (1)	1 live-birth
			LMWH (1)	*1 SA*
		3 aPL	-	-
	Low	1 aPL	ASA (6)	5 live-births
				1 SA
			ASA + LMWH (1)	
				1 live-birth
aPL carriers without RD	**High**	LA	ASA (1)	1 live-birth
			LMWH (1)	1 live-birth
		2 aPL	ASA (1)	1 live-birth
			LMWH (2)	2 live-births
		3 aPL	ASA (1)	1 live-birth
			ASA + LMWH (3)	3 live-births
	Low	1 aPL	ASA (5)	4 live-births
				1 foetal loss
aPL carriers with RD	**High**	LA	ASA (4)	3 live-birth
				1 foetal loss
			ASA + LMWH (7)	
				6 live-births
				1 SA
		2 aPL	ASA (6)	6 live-births
			ASA + LMWH (4)	2 live-births
				1 SA
				1 foetal loss
		3 aPL	LMWH (2)	2 live-births
			ASA + LMWH (5)	5 live-births
	Low	1 aPL	ASA (8)	8 live-births
			ASA + LMWH (3)	3 live-births

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.394

POS0683 NOVEL STRINGENT OUTCOME MEASURES APPLIED TO THE PHASE 2 AND 3 ANIFROLUMAB TRIALS

D. Isenberg[1,2], I. N. Bruce[3], R. Furie[4], E. F. Morand[5], Y. Tanaka[6], S. Manzi[7], K. Kalunian[8], K. Psachoulia[9], E. Maho[10], R. Tummala[9]. [1]*University College London, Centre for Rheumatology and Bloomsbury Rheumatology Unit, London, United Kingdom*; [2]*University College Hospital, Department of Rheumatology, London, United Kingdom*; [3]*The University of Manchester and NIHR Manchester Biomedical Research Centre, Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Division of Musculoskeletal and Dermatological Sciences, Manchester, United Kingdom*; [4]*Zucker School of Medicine at Hofstra/Northwell, Division*

of Rheumatology, Great Neck, United States of America; [5]*Monash University, Centre for Inflammatory Disease Monash Health, Melbourne, Australia*; [6]*University of Occupational and Environmental Health, Japan, First Department of Internal Medicine, Kitakyushu, Japan*; [7]*Lupus Center of Excellence, Autoimmunity Institute, Allegheny Health Network, Rheumatology, Pittsburgh, United States of America*; [8]*University of California, San Diego, Division of Rheumatology, Allergy and Immunology, La Jolla, United States of America*; [9]*AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, United States of America*; [10]*AstraZeneca, BioPharmaceuticals R&D, Cambridge, United Kingdom*

Background: Patients with systemic lupus erythematosus (SLE) who received anifrolumab, a type I interferon receptor antibody, had greater BILAG–based Composite Lupus Assessment (BICLA) response rates vs placebo at Week (W)52 in the phase 2 MUSE[1] and the phase 3 TULIP-1[2] and TULIP-2[3] trials. Patients receiving anifrolumab also had fewer flares, and more patients were able to taper glucocorticoids (GC) vs placebo.[1–3]

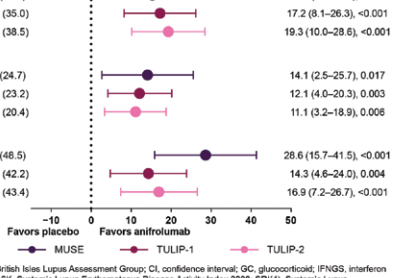
Objectives: To evaluate anifrolumab treatment response vs placebo in patients with SLE from MUSE, TULIP-1, and TULIP-2 using more stringent BICLA definitions, as well as a novel endpoint that requires dual BICLA and SLE Responder Index (SRI[4]) responses.

Methods: MUSE (NCT01438489), TULIP-1 (NCT02446912), and TULIP-2 (NCT02446899) were randomized, placebo-controlled, 52-week trials of intravenous anifrolumab (every 4 weeks for 48 weeks) in patients with moderate to severe SLE despite standard therapy.[1–3] Sustained GC taper was defined as taper to ≤7.5 mg/day in patients receiving GC ≥10 mg/day at baseline, or to less than or equal to baseline dose in patients receiving GC <10 mg/day at baseline, achieved by W40 and sustained through W52. Response rates were compared between anifrolumab 300 mg vs placebo groups for patients who **1)** attained a W52 BICLA response with sustained GC taper; **2)** attained a W52 BICLA response and no flares after W12 (flare defined as ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B scores vs the prior visit); **3)** attained a W52 BICLA response with sustained GC taper and no flares after W12; **4)** attained an enhanced BICLA (eBICLA) response at W52 that required complete resolution of all baseline BILAG-2004 activity (all baseline A/B scores to D; no worsening of C or D scores); and **5**) met both BICLA and SRI(4) response criteria.

Results: Evaluated patients received anifrolumab 300 mg (MUSE, n=99; TULIP-1 and TULIP-2, n=180) or placebo (MUSE, n=102; TULIP-1, n=184; TULIP-2, n=182). Response rate differences favoring anifrolumab 300 mg over placebo were observed for all 5 endpoints across MUSE, TULIP-1, and TULIP-2 (Figure 1). A greater proportion of patients had BICLA responses at W52 with sustained GC taper with anifrolumab vs placebo. More patients had BICLA responses at W52 with no flares after W12 with anifrolumab vs placebo. More patients had BICLA responses at W52 with both sustained GC taper and no flares after W12 with anifrolumab vs placebo (treatment difference, 15.3%–19.3%; nominal $P \leq 0.006$). More patients attained eBICLA responses (requiring complete resolution of baseline disease activity) at W52 with anifrolumab vs placebo (treatment difference, 11.1%–14.1%; nominal $P \leq 0.017$). In addition, more patients were dual BICLA and SRI(4) responders at W52 with anifrolumab vs placebo (treatment difference, 14.3%–28.6%; nominal $P \leq 0.004$).

Figure. Stringent BICLA response definitions and dual BICLA and SRI(4) response at Week 52 in patients with SLE

W52 endpoint, Trial	Placebo, n/N (%)	Anifrolumab 300 mg, n/N (%)	Treatment difference (95% CI)	Treatment difference (95% CI), nominal *P*
BICLA response				
MUSE	26/101 (25.7)	53/99 (53.5)		28.0 (15.1–41.0), <0.001
TULIP-1	54/184 (29.6)	83/180 (46.1)		16.4 (6.7–26.2), 0.001
TULIP-2	57/182 (31.5)	86/180 (47.8)		16.3 (6.3–26.3), 0.001
BICLA response + sustained GC taper				
MUSE	9/102 (8.5)	22/99 (24.0)		15.5 (4.3–26.6), 0.006
TULIP-1	48/184 (26.1)	77/180 (42.9)		16.8 (7.1–26.4), <0.001
TULIP-2	49/182 (27.0)	77/180 (43.0)		16.0 (6.3–25.8), 0.001
BICLA response + no flares after W12				
MUSE	21/102 (20.0)	45/99 (45.9)		25.9 (13.0–38.7), <0.001
TULIP-1	39/184 (21.4)	70/180 (38.8)		17.3 (8.0–26.7), <0.001
TULIP-2	43/182 (23.8)	75/180 (41.8)		18.0 (8.4–27.6), <0.001
BICLA response + no flares after W12 + sustained GC taper				
MUSE	8/102 (7.6)	21/99 (22.9)		15.3 (4.4–26.2), 0.006
TULIP-1	33/184 (17.9)	63/180 (35.0)		17.2 (8.1–26.3), <0.001
TULIP-2	35/182 (19.2)	69/180 (38.5)		19.3 (10.0–28.6), <0.001
Enhanced BICLA response (complete resolution)				
MUSE	11/102 (10.7)	24/99 (24.7)		14.1 (2.5–25.7), 0.017
TULIP-1	20/184 (11.1)	42/180 (23.2)		12.1 (4.0–20.3), 0.003
TULIP-2	17/182 (9.4)	37/180 (20.4)		11.1 (3.2–18.9), 0.006
BICLA response + SRI(4) response				
MUSE	21/102 (19.9)	48/99 (48.5)		28.6 (15.7–41.5), <0.001
TULIP-1	51/184 (27.9)	76/180 (42.2)		14.3 (4.6–24.0), 0.004
TULIP-2	48/182 (26.4)	78/180 (43.4)		16.9 (7.2–26.7), <0.001



BICLA, BILAG–based Composite Lupus Assessment; BILAG, British Isles Lupus Assessment Group; CI, confidence interval; GC, glucocorticoid; IFNGS, interferon gene signature; PGA, Physician's Global Assessment; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SRI(4), Systemic Lupus Erythematosus Responder Index of 4; W, Week.

Rates, differences, 95% CIs, and nominal *P* values were calculated using a stratified Cochran–Mantel–Haenszel approach (stratification factors SLEDAI-2K score at screening, Day 1 GC dose, and IFNGS test status at screening). Response for all endpoints required no trial treatment discontinuation and no use of protocol-restricted medications.

BICLA response, vs baseline: improvement in all BILAG-2004 organ domains (A and B scores to B/C/D and C/D, respectively), no BILAG-2004 domain worsening; no SLEDAI-2K worsening; no PGA worsening (≥0.3 points).

SRI(4) response, vs baseline: reduction ≥4 points in SLEDAI-2K; no new BILAG-2004 organ involvement (≥1 A or ≥2 B items); no PGA worsening (≥0.3 points).

Conclusion: In phase 2 and 3 trials in patients with SLE, anifrolumab treatment was consistently associated with improved disease control vs placebo using stringent endpoint definitions, including BICLA response with sustained GC taper and no flares, an enhanced BICLA response requiring complete resolution of baseline disease activity, and dual BICLA and SRI(4) responses.

REFERENCES:

[1] Furie R, et al. *Arthritis Rheumatol*. 2017;69:376–86.

[2] Furie RA, et al. *Lancet Rheumatol*. 2019;1:e208–19.

[3] Morand EF, et al. *N Engl J Med.* 2020;382:211–21.

Acknowledgements: Writing assistance by Rosie Butler, PhD, of JK Associates Inc., part of Fishawack Health. This study was sponsored by AstraZeneca.

Disclosure of Interests: David Isenberg Consultant of: AstraZeneca, Celgene, Merck Serono, UCB, and Servier, Ian N. Bruce Speakers bureau: AstraZeneca, GSK, and UCB, Consultant of: Eli Lilly, GSK, ILTOO, Merck Serono, and UCB, Grant/research support from: Genzyme/Sanofi, GSK, Roche, and UCB, Richard Furie Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Eric F. Morand Speakers bureau: AstraZeneca, Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Yoshiya Tanaka Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, GSK, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer, Sanofi, and YL Biologics, Grant/research support from: AbbVie, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Takeda, and UCB, Susan Manzi Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Kenneth Kalunian Consultant of: AstraZeneca, Konstantina Psachoulia Employee of: AstraZeneca, Emmanuelle Maho Employee of: AstraZeneca, Raj Tummala Employee of: AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.702

POS0684 RELATIONSHIP OF ANIFROLUMAB PK WITH EFFICACY AND SAFETY IN PATIENTS WITH SLE

Y. L. Chia[1], J. Zhang[2], R. Tummala[3], T. Rouse[4], R. Furie[5], E. F. Morand[6]. [1]*AstraZeneca, BioPharmaceuticals R&D, South San Francisco, United States of America*; [2]*Fate Therapeutics Inc, Department of Data Science, San Diego, United States of America*; [3]*AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, United States of America*; [4]*AstraZeneca, BioPharmaceuticals R&D, Gothenburg, Sweden*; [5]*Zucker School of Medicine at Hofstra/Northwell, Division of Rheumatology, Great Neck, United States of America*; [6]*Monash University, Centre for Inflammatory Disease Monash Health, Melbourne, Australia*

Background: In patients with systemic lupus erythematosus (SLE), the type I interferon (IFN) receptor inhibitor anifrolumab was well tolerated and was associated with greater percentages of patients with BILAG–based Composite Lupus Assessment (BICLA) responses vs placebo in 2 phase 3 trials: TULIP-1[1] (secondary endpoint) and TULIP-2[2] (primary endpoint).

Objectives: To characterize the relationship of anifrolumab pharmacokinetics (PK) with BICLA response and safety using pooled data from the TULIP trials.

Methods: This analysis included patients with moderate to severe SLE despite standard therapy who had ≥1 dose of investigational product and ≥1 quantifiable PK observation in the randomized, placebo-controlled, 52-week TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) trials of intravenous anifrolumab (every 4 weeks).[1,2] The distributions of average anifrolumab serum concentrations (C_{ave}) during treatment were similar between TULIP-1 and TULIP-2, allowing for data pooling for all analyses. For the exposure–BICLA analysis, the proportions of patients with BICLA responses at Week (W)52 (and corresponding 95% confidence intervals [CIs]) in each quartile/tertile of C_{ave} were compared for anifrolumab 300 mg and placebo groups in all patients, patients who completed treatment, and IFN gene signature (IFNGS) test–high patients who completed treatment, using average marginal effect logistic regression (stratified by SLE Disease Activity Index 2000 total score at screening, IFNGS status at screening, and Day 1 glucocorticoid dosage [mg/day]). The relationships between exposure and key safety events were similarly assessed. Analyses presented focus on the anifrolumab 300 mg dose.

Results: Of the patients in TULIP-1/TULIP-2 who received anifrolumab 300 mg (n=356) or placebo (n=366), 574 completed treatment, of whom 470 were IFNGS test–high at screening. In the exposure–BICLA response analyses, differences favoring anifrolumab 300 mg vs placebo were observed across C_{ave} subgroups among all patients, patients who completed treatment, and IFNGS test–high patients who completed treatment (Table 1). Among IFNGS test–high patients who completed treatment, logistic regression identified C_{ave} as a significant covariate for BICLA response. There was no evidence that the incidence of non-opportunistic serious infections, or increased incidence of herpes zoster (HZ) or infusion-related reactions associated with anifrolumab, were exposure-driven (Figure 1); the incidence of malignancy was low in the anifrolumab 300 mg and placebo groups (<1%), with no evidence that malignancy was exposure-driven through W52.

Conclusion: Consistent benefit in favor of anifrolumab 300 mg vs placebo was observed in W52 BICLA responses across C_{ave} subgroups. C_{ave} was a significant covariate of efficacy in IFNGS test–high patients who completed treatment. There was no evidence of exposure-driven HZ, non-opportunistic serious infections, infusion-related reactions, or malignancy during the TULIP trials.

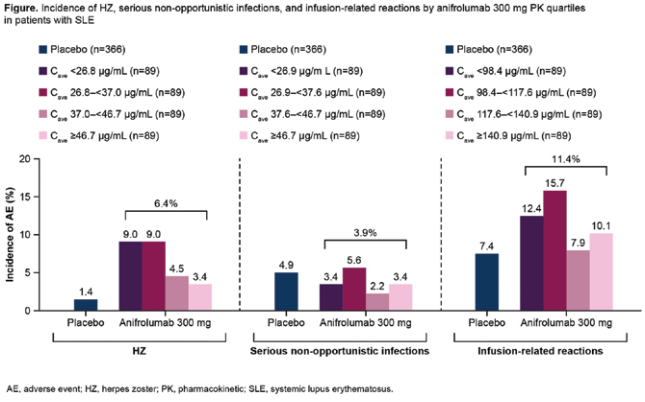
REFERENCES:

[1] Furie R. *Lancet Rheumatol.* 2019;1:e208–19.
[2] Morand E. *N Engl J Med.* 2020;382:211–21.

Table 1. Exposure–BICLA Analysis for Pooled TULIP Data

BICLA response, W52	PK subgroup[a]	Anifrolumab 300 mg, n/N[b] (%)	Anifrolumab vs placebo difference, % [95% CI]
All patients (n=722)	Q1	40/100 (40)	9.6 [–1.0, 20.3]
	Q2	44/98 (44)	13.4 [2.6, 24.2]
	Q3	43/81 (53)	22.5 [10.7, 34.3]
	Q4	44/77 (58)	27.4 [15.4, 39.4]
	Placebo	112/366 (31)	–
Patients completing treatment (n=574)	Q1	40/75 (54)	12.7 [0.1, 25.2]
	Q2	44/74 (57)	15.5 [2.7, 28.3]
	Q3	43/74 (58)	17.2 [4.7, 29.8]
	Q4	44/75 (60)	18.7 [6.2, 31.2]
	Placebo	112/276 (41)	–
IFNGS test–high patients completing treatment (n=470)	T1	44/81 (54)	15.4 [3, 27.8]
	T2	46/81 (54)	15.4 [2.8, 27.9]
	T3	52/81 (66)	26.7 [14.7, 38.7]
	Placebo	88/227 (39)	–

BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment;CI, confidence interval; IFNGS, interferon gene signature; PK, pharmacokinetic; Q, quartile; T, tertile.[a]PK was stratified by quartiles/tertiles based on sample size.[b]n, number of BICLA responders; N, number of patients in the subgroup.



AE, adverse event; HZ, herpes zoster; PK, pharmacokinetic; SLE, systemic lupus erythematosus.

Acknowledgements: Writing assistance by Alexus Rivas, PharmD, and Rosie Butler, PhD, of JK Associates Inc., part of Fishawack Health.
This study was sponsored by AstraZeneca.

Disclosure of Interests: Yen Lin Chia Employee of: AstraZeneca, Jianchun Zhang Employee of: Fate Therapeutics, AstraZeneca (former), Raj Tummala Employee of: AstraZeneca, Tomas Rouse Employee of: AstraZeneca, Richard Furie Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Eric F. Morand Speakers bureau: AstraZeneca, Consultant of: AstraZeneca, Grant/research support from: AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.803

POS0685 MYCOPHENOLATE MOFETIL IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: FIVE-YEARS DRUG SURVIVAL IN RENAL AND NON-RENAL INVOLVEMENT

G. Olivieri[1], F. Ceccarelli[1], F. Natalucci[1], F. R. Spinelli[1], C. Alessandri[1], F. Conti[1]. *[1]Lupus Clinic, Sapienza Università di Roma, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Roma, Italy*

Background: The updated EULAR recommendations for the management of systemic lupus erythematosus (SLE) underline the use of Mycophenolate Mofetil (MMF) in the treatment of different disease related manifestations (1). Several randomized controlled trials have demonstrated the efficacy of MMF in lupus nephritis (LN) patients but only case series and open-labelled trials have analyzed the use of this drug in other than LN features. Moreover, no data are available about the MMF retention rate in a real-life setting.

Objectives: The present study aims at evaluating the 5-years drug retention rate (DRR) of MMF in a large monocentric SLE cohort. Secondly, we investigated the influence of MMF in disease activity changes and chronic damage progression.
Methods: We performed a longitudinal study including all the SLE patients (ACR 1997 criteria) starting MMF treatment in our Lupus Clinic. Data about indications, mean dosage, duration of treatment and reasons for drug withdrawal were registered. The DRR was estimated using the Kaplan–Meier method. Disease activity and chronic damage were assessed by SLE Disease Activity Index 2000 (SLEDAI-2K) and SLICC Damage Index (SDI), respectively.
Results: The present analysis included 162 SLE patients (M/F 22/140, median age at the disease diagnosis 25.5 years, IQR 13). At the beginning of MMF treatment, we registered a median age of 34 months (IQR 21) and a median disease duration of 72 months (IQR 123). The most frequent indications for prescribing MMF were LN (101 patients, 62.3%) and musculoskeletal manifestations (39, 24.1%), followed by neuropsychiatric involvement (10, 6.2%), and others disease related manifestations (12, 7.4%; in particular skin involvement, hematological features, myositis, vasculitis). MMF was administered at a mean daily dosage of 2.1±0.6 grams; no differences in dosage were found between the different indications (p=ns).
At the longitudinal analysis, we registered a median treatment duration of 30 months (IQR 55). Figure 1 reported data about DRR: in particular, at 60 months follow-up we observed a DRR of 61.1% for LN patients, which was similar to that registered for patients without renal involvement (NLN) (60.5%; p=ns). Interestingly, the DRR at 60 months was higher in the subgroup of patients treated for joint involvement (75.4%), even without reaching a statistically significant difference. During the observation period, 92 patients (59.2%) discontinued MMF (median treatment duration at discontinuation 25 months, IQR 35). Interestingly, the main cause of withdrawal was the achievement of persistent remission, observed in 20 patients (21.7%), followed by loss of efficacy (19 patients, 20.5%), drug intolerance and pregnancy planning (17 patients for both reasons, 18,4%). Furthermore, our analysis confirmed MMF efficacy, as demonstrated by the significant reduction in SLEDAI-2k values after 4, 12 and 24 months of treatment (p< 0.0001 for all the time-points in comparison with baseline). In addition, MMF resulted able to control chronic damage progression, as demonstrated by the lack of significant increase in SDI values (baseline: 0.6, IQR 1; last observation: 0.93, IQR 1; p=ns).
Conclusion: The evaluation of a large SLE cohort demonstrated a good retention rate for MMF. In particular, our results demonstrated that MMF is also a safe and effective drug for SLE manifestation other than LN, in particular for joint involvement. Moreover, it is able to control disease activity and to prevent the progression of chronic damage.

REFERENCES:

[1] Fanouriakis A et al. Ann Rheum Dis. 2019 Jun;78(6):736-745.

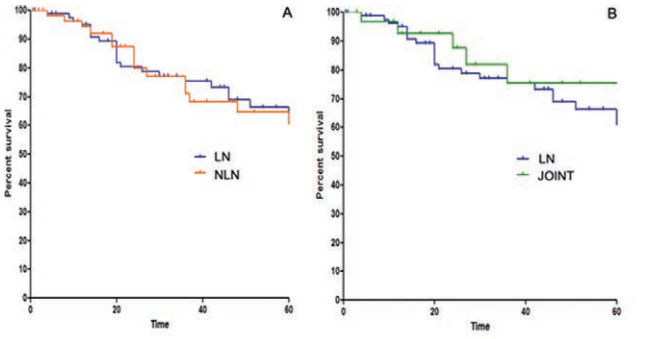


Figure 1. Kaplan–Meier survival curve of MMF treatment. The time of MMF treatment is expressed as months. DRR of MMF therapy at 60 months was similar in LN patients and NLN patients (Figure 1A). Interestingly, the DRR was higher in in the subgroup of patients with joint involvement (75.4%), even without reaching a significant difference (Figure 1B).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.925

POS0686 BARICITINIB DECREASES ANTI-DSDNA AND IGG ANTIBODIES IN ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS FROM A PHASE 2 DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL

T. Dörner[1], R. Van Vollenhoven[2], A. Doria[3], B. Jia[4], D. Fantini[4], J. Ross Terres[4], M. Silk[4], S. De Bono[4], P. Fischer[4], D. J. Wallace[5]. *[1]Charite Universitätsmedizin Berlin and Deutsches Rheumaforschungszentrum (DRFZ), Division of Rheumatology, Berlin, Germany*; *[2]University Medical Center, Department of Rheumatology, Amsterdam, Netherlands*; *[3]University of Padova, Department of Medicine, Padova, Italy*; *[4]Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, United States of America*; *[5]Cedars-Sinai Medical Center/ University California at Los Angeles, Division of Rheumatology, Los Angeles, United States of America*

Background: Baricitinib (BARI), an oral, selective Janus kinase (JAK)1 and JAK2 inhibitor, improved disease severity in adults with systemic lupus erythematosus (SLE) receiving standard background therapy in a phase 2 trial[1]. There were no meaningful reductions in least squares mean change from baseline (BL) in levels of serologic biomarkers for SLE with BARI treatment, including anti-double-stranded deoxyribonucleic acid (anti-dsDNA) antibodies and complement component (C)3 and C4[1].

Objectives: Evaluate the median change from BL in serologic biomarkers in subgroups and the overall population of BARI-treated SLE patients, in addition to the Systemic Lupus Erythematosus Responder Index-4 (SRI-4) response by normalization of anti-dsDNA.

Methods: Data were assessed from the phase 2 trial JAHH (NCT02708095). The median change from BL in anti-dsDNA, IgG, C3, and C4 was evaluated over time among the following populations at BL: anti-dsDNA positive (≥30 IU/mL), low C3 (<90 mg/dL), low C4 (<10 mg/dL), and all patients for IgG. Statistical tests were conducted for BARI 2-mg and 4-mg compared with placebo (PBO). Among patients who were anti-dsDNA positive at BL, SRI-4 responder rate was compared for those who stayed positive or achieved normal levels by Week (Wk) 24.

Results: Among patients who were anti-dsDNA positive at BL, significant decreases of anti-dsDNA antibodies were observed for BARI 2-mg and 4-mg compared to PBO beginning at Wks 2 and 4, respectively, and continuing through Wk 24 (Figure 1 and Table 1). Moreover, reductions of IgG levels were found for BARI-treated patients including significant decreases for BARI 4-mg compared to PBO at Wks 12 and 24 (Table 1). Among patients who had low levels of C3 and C4 at BL, no significant differences in median change from BL were observed over time with BARI compared to PBO. For patients who were anti-dsDNA positive at BL, no relationship in SRI-4 responder rate was observed for those who stayed positive or achieved normal levels by Wk 24, possibly due to the limited sample size.

Conclusion: BARI treatment resulted in a rapid and sustained significant decrease in anti-dsDNA antibodies compared to PBO among anti-dsDNA positive SLE patients at BL, as well as a significant decrease in IgG levels in the 4-mg group at Wks 12 and 24. These data suggest that BARI may have an effect on B cell activity in SLE.

REFERENCES:

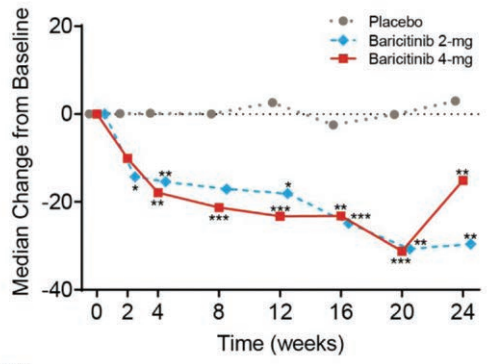
[1] Wallace D et al. Lancet. 2018;392:222-231.

Table 1.

	PBO			BARI 2-mg			BARI 4-mg		
Week	4	12	24	4	12	24	4	12	24
Anti-dsDNA (IU/mL)[a]	0.2 (-17.2, 17.3)	2.6 (-14.8, 18.4)	3.0 (-14.9, 28.3)	-15.4** (-31.4, 1.9)	-18.1* (-42.0, 4.1)	-29.6** (-55.1, 10.3)	-17.9** (-42.7, 1.8)	-23.3*** (-50.9, -5.9)	-15.1** (-71.9, -4.6)
IgG (g/L)[b]	-0.31 (-1.1, 0.4)	0.09 (-1.1, 0.7)	-0.04 (-0.9, 0.9)	-0.60 (-1.3, 0.6)	-0.30 (-1.3, 0.4)	-0.51 (-1.7, 0.6)	-0.56 (-1.2, 0.2)	-0.65** (-1.3, 0.2)	-0.60** (-1.7, 0.2)

Data are median change from baseline (25th, 75th percentiles). [a]Data were assessed for patients that were anti-dsDNA positive (≥30 IU/mL) at baseline (PBO N=51, BARI 2-mg N=56, BARI 4-mg N=53). [b]Data were assessed for all patients (PBO N=105, BARI 2-mg N=105, BARI 4-mg N=104). *p≤0.05, **p≤0.01, ***p≤0.001 for BARI vs. PBO.

Figure. Median change from baseline in anti-dsDNA (IU/mL)[a]



Number of patients								
Placebo	51	50	49	47	47	43	40	40
Baricitinib 2-mg	56	55	53	51	48	46	42	43
Baricitinib 4-mg	53	53	52	48	46	45	43	40

[a]Data were assessed for patients that were anti-dsDNA positive (≥30 IU/mL) at baseline. dsDNA=double-stranded deoxyribonucleic acid.
*p≤0.05, **p≤0.01, ***p≤0.001 for baricitinib compared with placebo

Acknowledgements: The authors would like to acknowledge Nicole L. Byers, of Eli Lilly and Company, for medical writing and process support.

Disclosure of Interests: Thomas Dörner Speakers bureau: Eli Lilly and Company, Roche, and Samsung, Consultant of: AbbVie, Celgene, Eli Lilly and Company, Janssen, Novartis, Roche, Samsung, and UCB, Grant/research support from: Janssen, Novartis, Roche, Sanofi, and UCB, Ronald van Vollenhoven Consultant of: Abbvie, Biotest, BMS, Celgene, Crescendo, Eli Lilly and Company, GSK, Janssen, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, Grant/research support from: Abbvie, Amgen, BMS, GSK, Pfizer, Roche, and UCB, Andrea Doria Speakers bureau: GSK, Janssen, Pfizer, and Roche, Consultant of: Celgene, Eli Lilly and Company, and GSK, Bochao Jia Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Damiano Fantini Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jorge Ross Terres Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Maria Silk Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Stephanie de Bono Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Peter Fischer Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Daniel J. Wallace Consultant of: Amgen, Aurunia, Eli Lilly and Company, EMD Merck Serono, GSK, and Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1015

POS0687

A RANDOMISED DOSE RANGING, PLACEBO-CONTROLLED, PHASE II STUDY ASSESSING THE EFFICACY AND SAFETY OF BI 655064, AN ANTAGONISTIC ANTI-CD40 ANTIBODY, IN PATIENTS WITH LUPUS NEPHRITIS

D. Jayne[1], J. Steffgen[2], J. Romero-Diaz[3], H. Amano[4], K. Noppakun[5], H. M. Gomez[6], R. Recto[7], V. Belsack[8], N. Fagan[9], S. Padula[10], I. Revollo[11], J. Wu[12], S. Visvanathan[13], R. Furie[14]. [1]*University of Cambridge, Department of Medicine, Cambridge, United Kingdom*; [2]*Boehringer Ingelheim International GmbH, TA Inflammation Medicine, Biberach, Germany*; [3]*Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubiran", Immunology and Rheumatology, Mexico City, Mexico*; [4]*Juntendo University Hospital, Department of Medicine, Japan, Japan*; [5]*Chiang Mai University, Thailand, Department of Internal Medicine, Chiang Mai, Thailand*; [6]*Angeles University Foundation Medical Center, Rheumatology, Angeles City, Philippines*; [7]*Mary Mediatrix Medical Center, Internal Medicine, Lipa City, Philippines*; [8]*SCS Boehringer Ingelheim, Clinical Operations, Brussels, Belgium*; [9]*Boehringer Ingelheim Pharmaceuticals Inc., Biostatistics & Data Science, Ridgefield, United States of America*; [10]*Boehringer Ingelheim International GmbH, Ingelheim, TA Inflammation Medicine, Ingelheim, Germany*; [11]*Boehringer Ingelheim International GmbH, Pharmacovigilance Corporate, Ingelheim, Germany*; [12]*Boehringer Ingelheim Pharmaceuticals Inc., Translational Medicine and Clinical Pharmacology, Ridgefield, United States of America*; [13]*Boehringer Ingelheim Pharmaceuticals Inc., Translational Medicine and Clinical Pharmacology, Ridgefield, United States of America*; [14]*Northwell Health and Zucker School of Medicine at Hofstra/Northwell, Department of Rheumatology, Great Neck, United States of America*

Background: In patients with SLE, activation of the CD40–CD40L pathway results in stimulation and proliferation of B cells and other inflammatory cell types. The subsequent generation of autoantibodies and their deposition in the kidney, as well as activation of myeloid and resident kidney cells, result in local inflammation and eventually, kidney injury. Thus, CD40 is an appealing therapeutic target in lupus nephritis (LN). BI 655064 is a humanised anti-CD40 monoclonal antibody that blocks the CD40 pathway in a nanomolar range and downregulates activated B cells.

Objectives: To assess the efficacy and safety over 52 weeks of three doses of subcutaneous BI 655064 compared with placebo, as add-on to mycophenolate and steroids, in patients with active proliferative LN (ClinicalTrials.gov number: NCT02770170).

Methods: Overall, 121 patients with LN were randomised, double blind, in a 2:1:1:2 ratio to placebo or BI 655064 120 mg, 180 mg or 240 mg, and received a weekly loading dose for the first 3 weeks, followed by dosing every 2 weeks for the 120 and 180 mg doses, and weekly (120 mg) for the 240 mg group. Key inclusion criteria included an active ISN/RPS class III or IV (±V) renal biopsy within 3 months prior to screening and a screening protein/creatinine ratio of ≥1 mg/mg. Randomisation was stratified based on race (Asian vs non-Asian) and screening protein/creatine (UP/UC) ratio (<3 vs ≥3). The primary efficacy endpoint was complete renal response (CRR), defined as 24 h proteinuria <0.5 g/day and stable eGFR at Week 52.

Results: The placebo response in this trial was higher than expected (48.3%; Table 1); none of the

BI 655064 doses increased rates of CRR at Week 52 compared with placebo. However, CRR at Week 52 based on creatinine-adjusted proteinuria, assessed using spot urine, showed a better response in the 180 mg group (50%) vs placebo (42.5%), and the 180 mg dose showed a greater change from baseline over

time vs placebo from Week 4. Time to CRR was shorter in the 180 mg group (17.3 weeks) vs placebo (20.4 weeks). The 180 mg group also showed improvement vs placebo in total SLEDAI (SELENA) and its subscores.

The unexpected high placebo response prompted a post hoc analysis evaluating confirmed CRR (cCRR), whereby confirmation of the endpoint was required at both Weeks 46 (penultimate visit on treatment) and 52. A 15.2% higher cCRR in the 180 mg group (44.3%) vs placebo (29.1%) was observed (p=0.26).

While based on a small sample size, there were more reports of infection-related severe and serious adverse events and neutropenia in the 240 mg group compared with placebo. Of note, in those who experienced neutropenia, a clinical impact (e.g. increase in infections) was not established. Aside from these observations, safety data were comparable across treatment groups.

Larger decreases from baseline were observed in the percentage of CD27–IgD–CD95+, CD27–IgD+CD95+, CD27+IgD+CD95+ and CD27+IgD–CD95+ B-cell subsets in the 180 and 240 mg groups compared with placebo.

Treatment-emergent anti-drug antibodies (ADAs) were detected in five patients treated with BI 655054, all at low titre, and in one who received placebo; ADAs had no impact on pharmacokinetics or safety.

Conclusion: The trial did not meet its primary CRR endpoint. However, when confirmation of CRR was required at both Weeks 46 and 52, the resultant decrease in the placebo response generated an effect size of 15.2% and 9.1% in favour of 180 mg and 240 mg BI 655064, respectively.

Table 1. Efficacy endpoints at Week 52

	Placebo (n=40)	BI 655064		
		120 mg (n=21)	180 mg (n=20)	240 mg (n=40)
Observed CRR, n	20	8	9	18
Adjusted* CRR, %	48.3	38.3	45	44.6
Observed cCRR, n	13	5	9	16
Adjusted* cCRR, %	29.1	22.5	44.3	38.2
Mean change from baseline in SLEDAI				
Total score	–6.5	–6.1	–9.7	–8.2
Non-renal score	–1.4	–3.0	–2.8	–3.1
Renal score	–5.1	–3.7	–6.8	–5.0
Clinical score	–5.7	–3.9	–7.9	–6.5

CRR based on 24 h proteinuria; cCRR based on UP/UC (spot urine) at Weeks 46 and 52. *Logistic regression model including treatment and the covariates race and proteinuria at screening.

Disclosure of Interests: David Jayne Consultant of: DRJ has received consulting fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline Research & Development Ltd, Novartis, and Roche, Juergen Steffgen Employee of: JS is employed by Boehringer Ingelheim., Juanita Romero-Diaz Consultant of: JRD has received research consulting fees from Boehringer Ingelheim, Hirofumi Amano Grant/research support from: HA has received research grants from Boehringer Ingelheim, Kajohnsak Noppakun Consultant of: KN has received honoraria from Boehringer Ingelheim, Novartis, Roche, Jansen, AstraZeneca, Otsuka Pharmaceuticals, Astellas Pharma, Abbott, Sanofi and Novo Nordisk, Grant/research support from: KN has received research grants from Boehringer Ingelheim, GlaxoSmithKline Research & Development Ltd, Visterra Inc., Kalbe Genexine Biologics, Aurinia Pharmaceuticals Inc., and Omeros Corporation., Harold Michael Gomez Speakers bureau: HMG has received speaker's fees for Pfizer, MSD, Unilab, Astellas Pharma, AstraZeneca, GlaxoSmithKline Research & Development Ltd, and Aurinia Pharmaceuticals Inc., Rhona Recto: None declared, Valérie Belsack Employee of: Boehringer Ingelheim, Nora Fagan Employee of: Boehringer Ingelheim, Steven Padula Employee of: Boehringer Ingelheim, Ivette Revollo Employee of: Boehringer Ingelheim, Jing Wu Employee of: Boehringer Ingelheim, Sudha Visvanathan Employee of: Boehringer Ingelheim, Richard Furie Consultant of: RF has received research consulting fees, Grant/research support from: RF has received clinical trial support

DOI: 10.1136/annrheumdis-2021-eular.1401

POS0688 CHARACTERIZATION OF PK/PD OF ANIFROLUMAB IN PATIENTS WITH MODERATE TO SEVERE SLE

Y. L. Chia[1], R. Tummala[2], T. Mai[3], T. Rouse[4], W. White[2], E. F. Morand[5], R. Furie[6]. *[1]AstraZeneca, BioPharmaceuticals R&D, South San Francisco, United States of America*; *[2]AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, United States of America*; *[3]Genentech, Clinical Pharmacology and Modeling & Simulation, South San Francisco, United States of America*; *[4]AstraZeneca, BioPharmaceuticals R&D, Gothenburg, Sweden*; *[5]Monash University, Centre for Inflammatory Disease Monash Health, Melbourne, Australia*; *[6]Zucker School of Medicine at Hofstra/Northwell, Division of Rheumatology, Great Neck, United States of America*

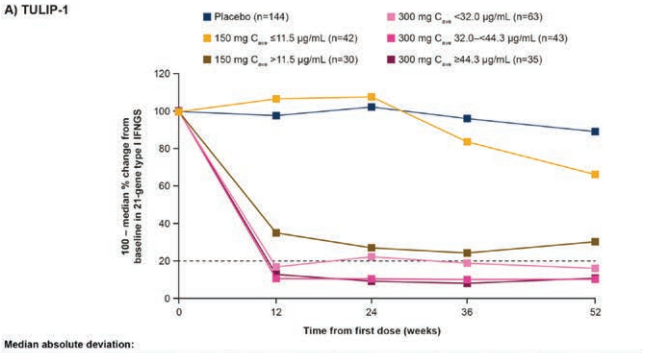
Background: In the TULIP-1 and TULIP-2 trials, anifrolumab, a type I interferon (IFN) receptor antibody, at a dosage of 300 mg once every 4 weeks (Q4W), demonstrated consistent median pharmacokinetic (PK) concentrations[1] and sustained neutralization of the pharmacodynamic (PD) 21-gene type I IFN gene signature (IFNGS)[2–4] in patients with moderate to severe systemic lupus erythematosus (SLE) despite standard therapy.

Objectives: To characterize the PK/PD relationship of anifrolumab and to confirm anifrolumab 300 mg provides adequate PD neutralization in IFNGS test–high patients.

Methods: This study included IFNGS test–high patients from the phase 3 randomized, placebo-controlled, 52-week TULIP-1[2] (NCT02446912) and TULIP-2[3] (NCT02446899) trials of intravenous anifrolumab 150 mg or 300 mg Q4W plus standard therapy. IFNGS test status (high or low) at screening was classified with an analytically validated 4-gene qPCR based test on whole blood.[2] PD neutralization was measured with 21-gene type I IFNGS and expressed as a percentage change from baseline.[3] For the graphic PK/PD analysis, patients with ≥1 quantifiable serum PK sample and ≥1 PD measurement before discontinuation were categorized depending on C_{ave} (individual predicted average anifrolumab concentration over treatment duration) median and tertiles (T) for anifrolumab 150 mg and 300 mg, respectively. Median PD IFNGS neutralization and medium absolute deviations were compared across C_{ave} subgroups. PK/PD modeling was assessed in patients with ≥1 quantifiable serum PK sample and a baseline and ≥1 postbaseline PD measurement before discontinuation, using a nonlinear mixed-effects model (NONMEM; version 7.3; ICON) to estimate parameters and characterize the PK/PD data. The PD/efficacy analysis included patients with ≥1 postbaseline PD measurement before discontinuation. BILAG-based Combined Lupus Assessment (BICLA) response rates at Week (W)52 were compared across median PD neutralization quartiles (Q) for pooled anifrolumab 300 mg and 150 mg groups.

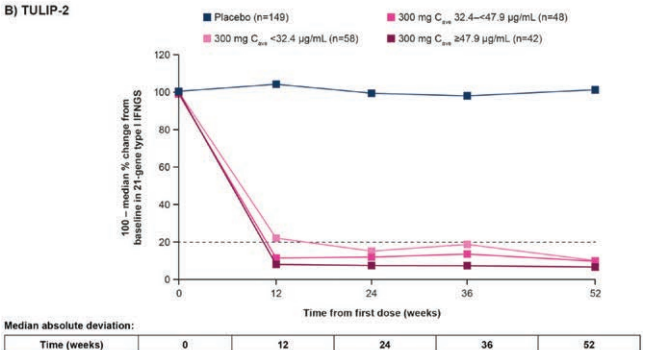
Results: The PK/PD graphic analysis included 654 IFNGS test–high patients (placebo [n=293]; anifrolumab 150 mg [n=72] or 300 mg [n=289]). C_{ave} was generally higher with anifrolumab 300 mg (μg/mL, TULIP-1: T1 <32, T2 32–<44.3, T3 ≥44.3; TULIP-2: T1 <32.4, T2 32.4–<47.9, T3 ≥47.9) than with anifrolumab 150 mg (median 11.5 μg/mL); overlap between anifrolumab 300 mg and 150 mg C_{ave} subgroups was small owing to nonlinearity. Anifrolumab 300 mg elicited rapid

Figure. Observed PD neutralization of the 21-gene type I IFNGS according to C_{ave} subgroup over the 52-week treatment duration in A) TULIP-1 and B) TULIP-2



Median absolute deviation:

Time (weeks)		0	12	24	36	52
Placebo		0	29.5	33.3	32.7	29.0
150 mg	C_{ave} ≤11.5	0	26.6	36.6	41.6	28.5
	C_{ave} >11.5	0	26.5	20.7	18.3	19.0
300 mg	C_{ave} <32.0	0	8.9	15.9	12.4	11.2
	C_{ave} 32.0–<44.3	0	4.7	4.9	5.1	5.9
	C_{ave} ≥44.3	0	6.8	5.0	4.1	8.0



Median absolute deviation:

Time (weeks)		0	12	24	36	52
Placebo		0	38.7	34.4	27.4	34.3
300 mg	C_{ave} <32.4	0	16.6	10.1	11.8	4.0
	C_{ave} 32.4–<47.9	0	7.3	7.8	10.6	4.5
	C_{ave} ≥47.9	0	3.6	3.2	4.1	2.8

C_{ave}, average anifrolumab concentration over the treatment period; IFNGS, interferon gene signature; PD, pharmacodynamic; PK, pharmacokinetic. Figure includes patients with ≥1 quantifiable serum PK observation and ≥1 PD measurement prior to discontinuation; PD collected after discontinuations were not included.

(by W4[4]) and sustained median PD neutralization >80%, vs a lower and delayed PD neutralization (median >50% at W52) with anifrolumab 150 mg, and minimal PD neutralization with placebo. The median PD neutralization increased with higher C_{ave} subgroups, plateauing at ~90% at W12–W52. All anifrolumab 300 mg C_{ave} tertiles had a median PD neutralization ~80%; however, the variability was greater in the lowest C_{ave} tertiles vs higher C_{ave} tertiles across trials (Figure 1). The PK/PD modeling, which included 646 IFNGS test–high patients (placebo [n=289], anifrolumab 150 mg [n=70] or 300 mg [n=287]), gave an IC_{80} estimate of 3.88 µg/mL. The median W24 (study midpoint) C_{trough} was higher with anifrolumab 300 mg vs 150 mg (15.6 vs 0.2 µg/mL); thus, the W24 C_{trough} exceeded the IC_{80} in a higher proportion of patients treated with anifrolumab 300 mg vs 150 mg (~83% vs ~27%). The PD/efficacy analysis included 341 patients who received anifrolumab. Higher median percentage PD neutralization quartiles (Q1 <51.7%, Q2 51.7%–85.3%, Q3 85.3%–92.6%, Q4 >92.6%) were associated with higher W52 BICLA response rates (Q1 37.6%, Q2 49.4%, Q3 51.8%, Q4 58.1%).

Conclusion: In TULIP-1 and TULIP-2, anifrolumab 300 mg yielded higher anifrolumab C_{ave} vs 150 mg. High C_{ave} was associated with rapid (W4[4]–W12), substantial, and sustained PD neutralization of the 21-gene IFNGS in IFNGS test–high patients, which in turn was associated with higher efficacy.

REFERENCES:

[1] Kuruvilla D. Poster 360, AAPS 2020.
[2] Furie RA. *Lancet Rheumatol.* 2019;1:e208–19.
[3] Morand EF. *N Engl J Med.* 2020;382:211–21.
[4] Furie R. *Arthritis Rheumatol.* 2017;69:379–86.

Acknowledgements: Writing assistance by Matilda Shackley, MPhil, of JK Associates Inc., part of Fishawack Health. This study was sponsored by AstraZeneca.

Disclosure of Interests: Yen Lin Chia Employee of: AstraZeneca, Raj Tummala Employee of: AstraZeneca, Tu Mai Employee of: Genentech, Tomas Rouse Employee of: AstraZeneca, Wendy White Employee of: AstraZeneca, Eric F. Morand Speakers bureau: AstraZeneca, Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Richard Furie Consultant of: AstraZeneca, Grant/research support from: AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.1464

POS0689

A 6-MONTH OPEN-LABEL EXTENSION STUDY OF THE SAFETY AND EFFICACY OF INTRAVENOUS BELIMUMAB IN PATIENTS WITH LUPUS NEPHRITIS

R. Furie[1], B. H. Rovin[2], F. Houssiau[3], G. Contreras[4], P. Curtis[5], A. Madan[6], A. Jones-Leone[7], M. Okily[8], D. Roth[9]. [1]*Northwell Health, Division of Rheumatology, Great Neck, NY, United States of America*; [2]*The Ohio State University, Division of Nephrology, Columbus, OH, United States of America*; [3]*Cliniques Universitaires Saint-Luc, Pôle de Pathologies, Brussels, Belgium*; [4]*University of Miami Miller School of Medicine, Division of Nephrology, Division of Hypertension, Department of Medicine, Miami, FL, United States of America*; [5]*GlaxoSmithKline, Department of Quantitative Sciences, Brentford, United Kingdom*; [6]*GlaxoSmithKline, Clinical Sciences, Collegeville, PA, United States of America*; [7]*GlaxoSmithKline, Medical Affairs, Collegeville, PA, United States of America*; [8]*GlaxoSmithKline, R&D ImmunoInflammation, Collegeville, PA, United States of America*; [9]*GlaxoSmithKline, Research and Development, Collegeville, PA, United States of America*

Background: BLISS-LN (GSK Study BEL114054; NCT01639339), the largest lupus nephritis (LN) study to date, showed that intravenous (IV) belimumab (BEL) + standard therapy (ST) improved outcomes compared with ST alone in patients (pts) with active LN.[1]

Objectives: To assess additional safety and efficacy data of BEL + ST in pts with LN in a 6-month open-label (OL) phase beyond 2 years of double-blind (DB) treatment in BLISS-LN.

Methods: In this OL phase, eligible completers of the DB phase received monthly BEL 10 mg/kg IV + ST for 6 months. Endpoints: safety; Primary Efficacy Renal Response (PERR; uPCR ≤0.7; eGFR no worse than 20% below OL baseline eGFR or ≥60 ml/min/1.73 m^2; no prohibited medications) and Complete Renal Response (CRR; uPCR <0.5; eGFR no worse than 10% below OL baseline eGFR or ≥90 ml/min/1.73 m^2; no prohibited medications) at OL Week 28; proportion of pts with SLEDAI score <4; corticosteroid use; biomarkers. Analyses were based on observed data and summarised relative to the OL baseline (last value measured prior to the first dose of OL treatment).

Results: We enrolled 257 pts (57.4% of pts in BEL114054) and treated 255 pts. All treated pts were included in the safety population (123 pts switched from placebo [PBO] to BEL; 132 pts remained on BEL). Efficacy was assessed in the safety population, excluding 1 pt due to non-compliance (mITT population; PBO to BEL: 122 pts; BEL to BEL: 132 pts). 96.5% of pts completed the OL phase; 3.5% withdrew, mainly due to adverse events (AE; 2.0%).

Overall, 168/255 (65.9%) pts had ≥1 AE (76/123 [61.8%] PBO to BEL pts; 92/132 [69.7%] BEL to BEL pts); 15/255 (5.9%) pts had ≥1 serious AE (5/123 [4.1%] PBO to BEL pts; 10/132 [7.6%] BEL to BEL pts); 1 (0.8%) pt died in the PBO to BEL group.

Proportions of PERR and CRR responders increased from OL baseline to OL Week 28 (Table 1. below)

Proportions of pts who attained SLEDAI scores <4 increased from OL baseline to OL Week 28 in the BEL to BEL group and decreased in the PBO to BEL group.

Among pts receiving average daily prednisone-equivalent doses of ≤5 mg or ≤7.5 mg dose was maintained from OL baseline to OL Week 28 (Table 1. below)

In pts with autoantibodies at OL baseline, anti-dsDNA and anti-C1q levels decreased from OL baseline to OL Week 28 in both groups. Among pts with low C3/C4 levels at OL baseline, C3/C4 levels increased from OL baseline to OL Week 28 in both groups (Table 1. below)

Conclusion: In this OL phase of BLISS-LN, proportions of PERR and CRR responders increased in both the BEL-naïve and BEL-experienced groups; and no new safety signals were observed. Improvements in biomarker levels were observed, especially in pts who switched from PBO to BEL.

Table 1. Responses at OL baseline and OL Week 28 (mITT population, N=254)

	OL baseline*		OL Week 28	
	PBO to BEL (n=122)	**BEL to BEL (n=132)**	**PBO to BEL (n=122)**	**BEL to BEL (n=132)**
n	122	132	118	122
PERR, n (%)	73 (59.8)†	93 (70.5)†	79 (66.9)	91 (74.6)
CRR, n (%)	44 (36.1)†	63 (47.7)†	57 (48.3)	76 (62.3)
SLEDAI score <4				
n	122	132	120	122
Responders, n (%)	44 (36.1)†	64 (48.5)†	40 (33.3)	64 (52.5)
Prednisone-equivalent dose				
n	122	132	121	128
≤5 mg, n (%)	59 (48.4)	78 (59.1)	60 (49.6)	75 (58.6)
≤7.5 mg, n (%)	62 (50.8)	85 (64.4)	66 (54.5)	83 (64.8)
Anti-dsDNA (IU/ml)‡				
n	85	64	81	61
Median (IQR) levels	107.0 (49.0, 212.0)	65.5 (42.5, 126.5)	-	-
Median (IQR) % change from baseline	-	-	-30.2 (-46.3, -6.8)	-10.7 (-27.2, 9.1)
Anti-C1q (U/ml)§				
n	64	60	58	54
Median (IQR) levels	71.7 (36.6, 167.5)	47.1 (33.0, 75.7)	-	-
Median (IQR) % change from baseline	-	-	-23.0 (-41.5, 0.5)	-16.5 (-33.0, 6.1)
C3 (mg/dl)‖				
n	45	37	44	35
Median (IQR) levels	78.0 (72.0, 83.0)	80.0 (71.0, 84.0)	-	-
Median (IQR) % change from baseline	-	-	6.2 (-4.2, 14.6)	4.7 (-4.8, 16.9)
C4 (mg/dl)‖				
n	18	12	18	11
Median (IQR) levels	7.5 (6.0, 8.0)	7.0 (7.0, 8.5)	-	-
Median (IQR) % change from baseline	-	-	23.6 (11.1, 37.5)	11.1 (0.0, 57.1)

*DB Week 104 visit and the OL baseline visit were the same visit; †*Post hoc* analyses; ‡Among anti-dsDNA positive pts at OL baseline (≥30 IU/ml); §Among anti-C1q positive pts at OL baseline (≥22.2 U/ml); ‖Among pts with low C3 (<90 mg/dl)/C4 (<10 mg/dl) levels at OL baseline.

Funding: GSK.

REFERENCES:

[1] Furie R, et al. *N Engl J Med.* 2020;383(12):1117-28.

Acknowledgements: Medical writing assistance was provided by Olga Conn, PhD, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.

Disclosure of Interests: Richard Furie Consultant of: GSK, Grant/research support from: GSK, Brad H Rovin Consultant of: GSK, Frederic Houssiau Consultant of: GSK, Grant/research support from: UCB, Gabriel Contreras Consultant of: Genentech, Merck, Grant/research support from: Genentech, Merck, Paula Curtis Shareholder of: GSK, Employee of: GSK, Anuradha Madan Shareholder of: GSK, Employee of: GSK, Angela Jones-Leone Shareholder of: GSK, Employee of: GSK, Mohamed Okily Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK

DOI: 10.1136/annrheumdis-2021-eular.1583

POS0690 RANDOMIZED, CONTROLLED, PHASE 2 TRIAL OF TYPE 1 IFN INHIBITOR ANIFROLUMAB IN PATIENTS WITH ACTIVE PROLIFERATIVE LUPUS NEPHRITIS

D. Jayne[1], B. H. Rovin[2], E. Mysler[3], R. Furie[4], F. Houssiau[5], T. Trasieva[6], J. Knagenhjelm[6], E. Schwetje[7], Y. L. Chia[8], R. Tummala[7], C. Lindholm[6]. [1]*University of Cambridge, Department of Medicine, Cambridge, United Kingdom*; [2]*Ohio State University, Department of Internal Medicine–Nephrology, Columbus, United States of America*; [3]*Organización Médica de Investigación, Uruguay, Rheumatology, Buenos Aires, Argentina*; [4]*Zucker School of Medicine at Hofstra/Northwell, Division of Rheumatology, Great Neck, United States of America*; [5]*Cliniques Universitaires Saint-Luc and Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Service de Rhumatologie, Brussels, Belgium*; [6]*AstraZeneca, BioPharmaceuticals R&D, Gothenburg, Sweden*; [7]*AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, United States of America*; [8]*AstraZeneca, BioPharmaceuticals R&D, South San Francisco, United States of America*

Background: Anifrolumab, a type I interferon receptor antibody, has shown efficacy in patients with systemic lupus erythematosus (SLE),[1,2] >30% of whom develop lupus nephritis (LN).

Objectives: To evaluate the efficacy and safety of anifrolumab vs placebo alongside standard therapy in patients with active proliferative LN.

Methods: TULIP-LN (NCT02547922) was a phase 2 double-blind trial in adult patients with active, biopsy-proven LN and 24-hour (h) urine protein–creatinine ratio (UPCR) >1 mg/mg. Patients were randomized (1:1:1) to anifrolumab basic regimen (BR, 300 mg, based on SLE dosing[1,2]), anifrolumab intensified regimen (IR, 900 mg for 3 doses, 300 mg thereafter), or placebo, intravenously every 4 weeks alongside standard therapy of oral glucocorticoids (GCs; mandatory taper ≤10 mg/day by Week [W]12, ≤7.5 mg/day by W24) and mycophenolate mofetil (target 2 g/day by W8). The primary endpoint was the relative difference in change from baseline to W52 in 24-h UPCR, measured with a geometric mean ratio (GMR) of the change in the combined anifrolumab vs placebo groups (GMR <1 favors anifrolumab). The key secondary endpoint was complete renal response (CRR) at W52 (24-h UPCR ≤0.7 mg/mg, estimated glomerular filtration rate ≥60 mL/min/1.73 m^2 or no decrease ≥20%, no treatment discontinuation, and no restricted medication use). Sustained GC taper (≤7.5 mg/day, W24–52) was an exploratory endpoint. $CRR_{0.5}$ (CRR with UPCR ≤0.5 mg/mg) and time to $CRR_{0.5}$ sustained to W52 were analyzed post hoc. Responder rates were calculated with a stratified Cochran–Mantel–Haenszel approach.

Results: Patients received anifrolumab BR (n=45) or IR (n=51) or placebo (n=49); demographics and baseline disease characteristics were generally balanced between groups. No difference in change from baseline to W52 in 24-h UPCR was observed for combined anifrolumab vs placebo groups (Table 1). Anifrolumab clearance was higher in patients with LN vs SLE; proteinuria in LN elicited suboptimal anifrolumab serum concentrations (early trough from BR 50%–60% lower than in SLE trials[1,2]), so anifrolumab IR results are presented. CRR rate at W52 was numerically higher with the IR vs placebo (45.5% vs 31.1%) (Table 1). Time to sustained $CRR_{0.5}$ (Figure 1), rate of $CRR_{0.5}$ at W52, and rate of sustained GC taper to ≤7.5 mg/day (Table 1) were improved with the IR vs placebo. Most adverse events were nonserious, mild, or moderate and did not lead to discontinuation; rates were similar in the combined anifrolumab vs placebo groups (89.8% vs 93.8%). In the combined anifrolumab vs placebo groups, there was a higher incidence of herpes zoster (HZ, 16.7% vs 8.2%); most HZ cases were of mild to moderate intensity, cutaneous, and resolved with treatment.

Conclusion: Although the primary endpoint was not met, the anifrolumab IR was associated with numeric improvements across clinical endpoints vs placebo; thus, intensified dosing may be required to reach clinical efficacy in LN vs SLE without active renal disease. Anifrolumab had a similar safety profile in patients with LN and SLE; despite higher frequency of HZ vs placebo, anifrolumab was well tolerated.

REFERENCES:

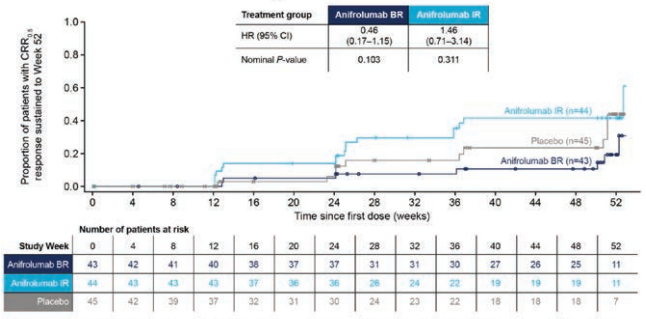
[1] Morand EF. *N Engl J Med*. 2020;382:211–21.
[2] Furie RA. *Lancet Rheumatol.* 2019;1:e208–19.

Table 1. Summary of Clinical Efficacy Endpoints

Endpoint		Anifrolumab			Placebo
		Combined	Basic	Intensified	
24-hour urine protein–creatinine ratio improvement W52	N	91	41	50	41
	GMR vs placebo	1.031	1.104	0.963	–
	95% CI	0.621, 1.713	0.612, 1.992	0.548, 1.693	
CRR rate W52	n/N (%)	27/87 (31.0)	7/43 (16.3)	20/44 (45.5)	14/45 (31.1)
	Δ	−0.08	−14.83	14.34	–
	95% CI	−16.92, 16.76	−32.89, 3.22	−5.77, 34.46	
$CRR_{0.5}$ rate W52	n/N (%)	25/87 (28.7)	7/43 (16.3)	18/44 (40.9)	12/45 (26.7)
	Δ	2.07	−10.39	14.24	–
	95% CI	−14.25, 18.39	−28.07, 7.29	−5.42, 33.90	
Glucocorticoid ≤7.5 mg/day W24–52	n/N (%)	31/67 (46.3)	11/31 (35.5)	20/36 (55.6)	11/33 (33.3)
	Δ	12.94	2.15	22.22	–
	95% CI	−7.26, 33.13	−21.40, 25.70	−0.79, 45.23	

Δ Percentage difference vs placebo.CI, confidence interval; CRR, complete renal response; GMR, geometric mean ratio; n, number of responders; N, number analyzed; W, Week.

Figure. Kaplan–Meier plot of time to first $CRR_{0.5}$ (24-hour UPCR ≤0.5 mg/mg criteria) sustained to Week 52



BR, basic regimen; CI, confidence interval; CRR, complete renal response; HR, hazard ratio; IR, intensified regimen; UPCR, urine protein–creatinine ratio. $CRR_{0.5}$ includes 24-hour UPCR ≤0.5 mg/mg cutoff. Time to sustained $CRR_{0.5}$ is defined as the visit of first $CRR_{0.5}$ response that is sustained up to and including Week 52. HRs, 95% CIs, and *P*-values were calculated with a Cox regression model.

Acknowledgements: Writing assistance by Matilda Shackley, MPhil, of JK Associates, Inc, a member of Fishawack Health. This study was sponsored by AstraZeneca.

Disclosure of Interests: David Jayne Grant/research support from: AstraZeneca, Aurinia, Boehringer-Ingelheim, GSK, Roche/Genentech and Sanofi-Genzyme, Brad H Rovin Consultant of: AstraZeneca, Eduardo Mysler Grant/research support from: AstraZeneca, GSK, Eli Lilly, Sandoz, Roche, AbbVie, Pfizer, Janssen, Gemma, and Amgen, Richard Furie Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Frederic Houssiau Consultant of: GSK, Teodora Trasieva Employee of: AstraZeneca, Jacob Knagenhjelm Employee of: AstraZeneca, Erik Schwetje Employee of: AstraZeneca, Yen Lin Chia Employee of: AstraZeneca, Raj Tummala Employee of: AstraZeneca, Catharina Lindholm Employee of: AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.1605

POS0691 EFFECTS OF ANIFROLUMAB ON RENAL DISEASE IN PATIENTS WITH SLE

E. F. Morand[1], R. Furie[2], Y. Tanaka[3], T. Takeuchi[4], G. Abreu[5], R. Tummala[6], C. Lindholm[5]. [1]*Monash University, Centre for Inflammatory Disease Monash Health, Melbourne, Australia*; [2]*Zucker School of Medicine at Hofstra/Northwell, Division of Rheumatology, Great Neck, United States of America*; [3]*University of Occupational and Environmental Health, Japan, First Department of Internal Medicine, Kitakyushu, Japan*; [4]*Keio University School of Medicine, Department of Internal Medicine, Tokyo, Japan*; [5]*AstraZeneca, BioPharmaceuticals R&D, Gothenburg, Sweden*; [6]*AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, United States of America*

Background: The type I interferon (IFN) receptor antibody anifrolumab has shown efficacy in patients with systemic lupus erythematosus (SLE) in the phase 3 TULIP-1 and TULIP-2 trials.[1,2] Type I IFN dysregulation is associated with lupus nephritis (LN) pathogenesis.[3]
Objectives: Pooled TULIP data were analyzed post hoc to assess baseline characteristics of patients with and without renal involvement and to evaluate the effects of anifrolumab on renal disease.
Methods: TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) were randomized, placebo-controlled, 52-week trials of intravenous anifrolumab every 4 weeks in patients with moderate to severe SLE despite standard therapy, which excluded patients with severe active LN.[1,2] Renal involvement at baseline was defined as any of the following: BILAG-2004 renal score A–C; SLEDAI-2K renal score >0; urine protein–creatinine ratio (UPCR) >0.5 mg/mg. Baseline characteristics were evaluated in patients with and without renal involvement, and the following endpoints were compared for the anifrolumab 300 mg and placebo groups: cumulative UPCR (area under the curve, AUC) through Week (W)52; percentage of patients with UPCR >0.5 mg/mg at baseline who improved to UPCR ≤0.5 mg/mg at W52; percentage of patients with renal flares (new BILAG-2004 A/B renal score vs prior visit); cumulative glucocorticoid (GC) use (AUC) through W52; and percentage changes in complement C3/C4 from baseline to W52.
Results: Of the 726 patients in TULIP-1/-2 (anifrolumab, n=360; placebo, n=366), 99 had renal involvement at baseline (anifrolumab, n=45; placebo, n=54), 57 of whom had UPCR >0.5 mg/mg (anifrolumab, n=24; placebo, n=33). Patients with renal involvement vs without renal involvement had a lower mean age (37.8 vs 42.4 years) and were more likely to be male (14.1% vs 6.1%), Asian (16.2% vs 9.6%), IFN gene signature test–high (89.9% vs 81.5%), and anti-dsDNA positive (69.7% vs 40.4%); have a SLEDAI-2K score ≥10 (91.9% vs 68.4%); and be receiving GC ≥10 mg/day (67.7% vs 49.1%) or mycophenolate (26.3% vs 11.5%) at baseline. Among patients with baseline renal involvement, anifrolumab treatment was associated with a numerically greater improvement vs placebo in cumulative UPCR (AUC) through W52 (LS mean difference [SE]: –54.1 [54.26]) (Table 1). Numerically more patients improved from UPCR >0.5 mg/mg at baseline to ≤0.5 mg/mg at W52 with anifrolumab vs placebo (difference [SE], 4.9% [13.3]). Among all TULIP patients, fewer had ≥1 BILAG-2004 renal flare with anifrolumab vs placebo (5.0% vs 7.4%).[4] Among patients with renal involvement, cumulative GC use (AUC) through W52 was lower with anifrolumab vs placebo (LS mean difference [SE]: –210.3 mg [332.6]) and there were numerically greater improvements in C3 and C4 from baseline to W52 (Table 1).
Conclusion: TULIP data suggest renal benefit with anifrolumab in patients with SLE with mild/stable renal disease, supporting further investigation into anifrolumab's efficacy in patients with active LN.
REFERENCES:
[1] Furie R. *Lancet Rheumatol*. 2019;1:e208–19.
[2] Morand E. *N Engl J Med.* 2020;382:211–21.
[3] Feng X. *Arthritis Rheum*. 2006;54:2951–62.
[4] Furie R [abstract]. *Arthritis Rheumatol*. 2020;72(supp 10).

Table 1. Renal Endpoints in TULIP-1 and TULIP-2

Endpoint (baseline to Week 52)	Placebo	Anifrolumab 300 mg
UPCR AUC[a]		
n	54	45
LS mean (SE)	271.8 (54.8)	217.7 (60.0)
LS mean difference (SE), 95% CI	–54.1 (54.3), –161.9, 53.6	
Improvement from >0.5 to ≤0.5 mg/mg UPCR[b]		
n	33	24
Patients with improvement (%)	36.3	41.2
Difference, % (SE), 95% CI	4.9 (13.3), –21.1, 30.9	
Glucocorticoid AUC[a]		
n	54	45
LS mean (SE)	3524.5 (339.0)	3314.2 (365.2)
LS mean difference (SE), 95% CI	–210.3 (332.6), –870.7, 450.1	
Change in C3/C4 (%)[c]		
C3		
N	31	21
Mean (SE)	20.3 (6.2)	26.6 (5.0)
C4		
N	19	14
Mean (SE)	29.1 (12.0)	38.7 (13.8)

AUC, area under the curve; CI, confidence interval; LS, least squares; UPCR, urine protein–creatinine ratio; SE, standard error.n, number satisfying baseline inclusion criteria for subgroup.[a]Patients with baseline renal involvement; analysis of covariance.[b]Stratified Cochran–Mantel–Haenszel.[c]Patients with renal involvement and abnormal C3/C4 at baseline.

Acknowledgements: Writing assistance by Rosie Butler, PhD, of JK Associates Inc. part of Fishawack Health. This study was sponsored by AstraZeneca.
Disclosure of Interests: Eric F. Morand Speakers bureau: AstraZeneca, Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Richard Furie Consultant of: AstraZeneca, Grant/research support from: AstraZeneca, Yoshiya Tanaka Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, GSK, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer, Sanofi, and YL Biologics, Grant/research support from: AbbVie, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Takeda, and UCB, Tsutomu Takeuchi Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co,. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Astellas Pharma Inc, Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co., Ltd., Novartis Pharma K.K., Consultant of: AstraZeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Abbvie GK, Nipponkayaku Co.Ltd, Janssen Pharmaceutical K.K., Astellas Pharma Inc,. Taiho Pharmaceutical Co., Ltd., Chugai Pharmaceutical Co, Ltd., Grant/research support from: Astellas Pharma Inc, Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Takeda Pharmaceutical Co., Ltd., AbbVie GK, Asahikasei Pharma Corp., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Eisai Co., Ltd., AYUMI Pharmaceutical Corporation, Nipponkayaku Co.Ltd., Novartis Pharma K.K., Gabriel Abreu Employee of: AstraZeneca, Raj Tummala Employee of: AstraZeneca, Catharina Lindholm Employee of: AstraZeneca
DOI: 10.1136/annrheumdis-2021-eular.1618

POS0692

IANALUMAB (VAY736) SAFETY AND EFFICACY IN PATIENTS WITH SJOGREN'S SYNDROME: 52 WEEK RESULTS FROM A RANDOMISED, PLACEBO-CONTROLLED, PHASE 2B DOSE-RANGING TRIAL

T. Dörner[1], S. J. Bowman[2,3,4], R. Fox[5], X. Mariette[6], A. Papas[7], T. Grader-Beck[8], B. A. Fisher[2,3,4], F. Barcelos[9], S. De Vita[10], H. Schulze-Koops[11], R. J. Moots[12,13], G. Junge[14], J. Woznicki[15], M. Sopala[14], W. L. Luo[15], W. Hueber[14].
[1]Charite Universitätsmedizin, Department Medicine/Rheumatology and Clinical Immunology, Berlin, Germany; [2]University Hospitals Birmingham NHS Foundation Trust, Department of Rheumatology, Birmingham, United Kingdom; [3]University of Birmingham, Rheumatology, Birmingham, United Kingdom; [4]NIHR Birmingham Biomedical Research Centre, Rheumatology, Birmingham, United Kingdom; [5]Scripps Memorial Hospital and Research Institute, Rheumatology, California, United States of America; [6]Université Paris- Saclay, Rheumatology, Paris, France; [7]Tufts School of Dental Medicine, Division of Oral Medicine, Massachusetts, United States of America; [8]Johns Hopkins School of Medicine, Division of Rheumatology, Baltimore, United States of America; [9]Instituto Português de Reumatologia, Rheumatology, Lisbon, Portugal; [10]DAME, University Hospital of Udine, Division of Rheumatology, Udine, Italy; [11]Ludwig-Maximilians-University of Munich, Division of Rheumatology and Clinical Immunology, Munich, Germany; [12]Aintree University Hospital, Academic Rheumatology Department, Liverpool, United Kingdom; [13]Edge Hill University, Faculty of Health, Social Care and Medicine, Ormskirk, United Kingdom; [14]Novartis Pharma AG, Immunology, Hepatology and Dermatology, Basel, Switzerland; [15]Novartis Pharmaceuticals Corporation, Immunology, Hepatology and Dermatology, East Hanover, United States of America

Background: Sjogren's syndrome (SS) is an autoimmune disease affecting excretory glands and characterised by B-cell hyperactivity. Ianalumab (VAY736) is a human monoclonal antibody to B-cell activating factor receptor, engineered for direct ADCC-mediated B-cell depletion. A Phase 2b study evaluated the dose-response of VAY736 vs placebo (PBO) in EULAR SS Disease Activity Index (ESSDAI) change from baseline (CHB) and other secondary endpoints.
Objectives: Primary results at Week (Wk) 24 were reported previously[1]. Here we report 52 Wk safety and efficacy from extended blinded treatment period 2 (TP2).
Methods: 190 patients (pts) were randomised equally to receive s.c. doses of VAY736 (5, 50, 300 mg) or PBO every 4 Wks (q4w). Eligible pts fulfilled American European Consensus Group (AECG) criteria, were anti-Ro/SSA+, had ESSDAI ≥6 and EULAR SS Patient Reported Index (ESSPRI) ≥5. At Wk 24, after completion of the first blinded TP (TP1), PBO-treated pts were switched to VAY736 150 mg, and pts on 300 mg were re-randomised to continue 300 mg or PBO for 28 Wks in TP2. Pts were followed post-treatment for ≥20 Wks. Safety was assessed for all periods. Due to lack of PBO-control in TP2, descriptive efficacy analysis was performed for ESSDAI, ESSPRI, Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F), Physician's (PhGA) and Patient's Global Assessments (PaGA), SF-36, and SS symptom diary (SSSD).
Results: Overall, there was no dose dependency of treatment emergent adverse events (TEAEs) except for injection site reactions, which were mostly mild to moderate in severity. Lymphopenia and neutropenia were mostly grade (G)1 and G2, no G4. Most common TEAEs were infections and infestations in exposure-adjusted analysis of incidence rates. Nasopharyngitis and upper

respiratory tract infections were the most common TEAEs, with no dose response (Table 1). Tracheobronchitis and pneumonia, were mild to moderate severity, not associated with absolute neutrophil count G3, and none led to treatment withdrawal.

At Wk 52, efficacy was sustained for pts who continued 300 mg in TP2 (ESSDAI, ESSPRI, PaGA, PhGA CHB: –9.06, –1.91, –22.03, –35.80, respectively). Efficacy was partially lost for pts switched to PBO at Wk 24 (Figure 1). Improvement was noted for PBO pts switched to 150 mg. Stimulated whole salivary flow at Wk 24 was improved for 300 mg (PBO-adjusted CHB 0.20 ml/min; P=0·037); last measurement at Wk 48 was 0.45 and 0.22 ml/min CHB in pts who continued 300 mg or PBO in TP2, respectively.

Conclusion: Ianalumab 300 mg was well tolerated up to 52 Wks. Exploratory efficacy showed that continuous dosing of 300 mg s.c. q4w provided sustained clinical benefit. PaGA was the outcome that showed the most prominent change following switch to PBO or VAY736.

REFERENCES:

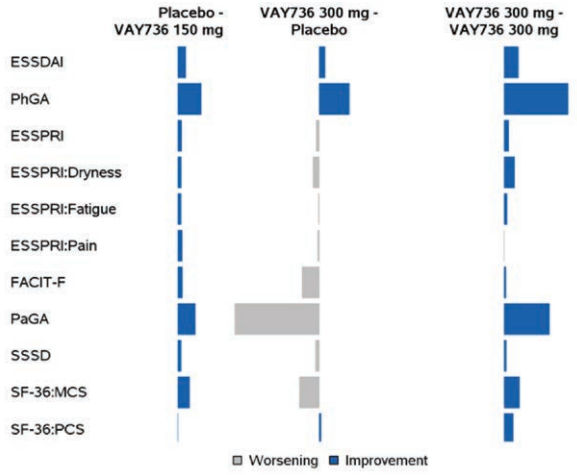
[1] Dörner T, et al. [OP0302]. *Ann Rheum Dis*. 2020; 79 (suppl 1).

Table 1. Key Safety Data (All Study Periods up to Week 52)*

n (%)	5 mg	50 mg	150 mg	Any 300 mg (N=47)
[EAIR][1]	24 Wks	24 Wks	28 Wks	
	(N=47)	(N=47)	(N=47)	
Any AE	**43 (91.5) [517.5]**	**43 (91.5) [423.3]**	**44 (93.6) [621.0]**	**45 (95.7) [544.6]**
Any SAE	**3 (6.4) [5.9]**	**5 (10.6) [10.7]**	**8 (17.0) [19.9]**	**8 (17.0) [13.6]**
Infections and infestations (SOC)[2]	**33 (70.2) [154.1]**	**31 (66.0) [119.2]**	**34 (72.3) [162.0]**	**38 (80.9) [127.7]**
Nasopharyngitis[3]	7 [15.5]	4 [8.5]	9 [22.1]	9 [16.5]
Upper respiratory tract infections[3]	6 [12.8]	8 [17.8]	5 [11.6]	8 [13.6]
Bronchitis[3]	3 [6.2]	3 [6.2]	4 [9.5]	4 [6.6]
Tracheobronchitis[3]	1 [2.0]	0 [0.0]	0 [0.0]	3 [5.0]
Pneumonia[3]	1 [2.0]	0 [0.0]	1 [2.2]	2 [3.3]
Blood & Lymphatic Disorders (SOC)[2]	**8 (17.0) [18.0]**	**9 (19.1) [20.8]**	**6 (12.8) [14.3]**	**9 (19.1) [16.8]**
Lymphopenia[3]	4 [8.4]	4 [8.6]	3 [6.8]	2 [3.3]
Neutropenia[3]	5 [10.7]	1 [2.1]	2 [4.5]	4 [6.9]
Injection site reaction[3]	**4 (8.5)**	**9 (19.1)**	**17 (36.2)**	**27 (57.4)**

*Includes all safety data from TP1, TP2 and post-treatment follow-up; cut-off 06-Feb-2020[1]EAIR, incidence rate per 100 subject years. For patient with an event, exposure time is censored at time of first event;[2]Number of pts with at least one AE in SOC;[3]PT, preferred term;SOC, system organ class

Figure: Summary of Efficacy data at Week 52 (Treatment Period from Wk 24 to Wk 52)



ESSDAI, EULAR Sjögren's Syndrome Disease Activity index; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; EULAR, European League Against Rheumatism; FACIT-F, Functional Assessment of Chronic Illness Therapy Fatigue; MCS, mental component summary; PaGA, patient global assessment; PCS, physical component summary; PhGA, physician global assessment; SF, short form; SSSD, Sjögren's syndrome symptom diary

Disclosure of Interests: Thomas Dörner Consultant of: Novartis, GSK, Sanofi, Janssen, Eli Lilly, Grant/research support from: Deutsche Forschungsgemeinschaft, Simon J. Bowman Consultant of: Astrazeneca, Biogen, BMS, Celgene, Medimmune, MTPharma, Novartis, Ono, UCB, xtlbio, Robert Fox Consultant of: Novartis, Pfizer and Lilly, Xavier Mariette Consultant of: BMS, Galapagos, Gilead, Medimmune, GSK, Grant/research support from: Servier, Athena Papas Consultant of: Novartis, Grant/research support from: Novartis, Thomas Grader-Beck Consultant of: Novartis, Lilly, Grant/research support from: Abbvie, Celgene, Ben A Fisher Consultant of: Novartis, Roche, BMS and Servier, Filipe Barcelos Consultant of: Pfizer and Lilly, Salvatore De Vita Consultant of: Roche, Human Genome Science, Glaxo Smith Kline and Novartis, Hendrik Schulze-Koops Consultant of: Novartis, Robert J Moots Consultant of: Amgen, Chugai, Gilead, Lilly, Novartis, Pfizer, Roche, Grant/research support from: Amgen, Chugai, Gilead, Lilly, Novartis, Pfizer, Roche, Guido Junge Shareholder of: Novartis, Employee of: Novartis, Janice Woznicki Shareholder of: Novartis, Employee of: Novartis, Monika Sopala Shareholder of: Novartis, Employee of: Novartis, Wen-Lin Luo Shareholder of: Novartis, Employee of: Novartis, Wolfgang Hueber Shareholder of: Novartis, Employee of: Novartis

DOI: 10.1136/annrheumdis-2021-eular.1700

POS0693

EFFICACY AND SAFETY OF BELIMUMAB IN PATIENTS WITH LUPUS NEPHRITIS IN REAL-LIFE SETTING: RESULTS FROM A LARGE, NATIONWIDE, MULTICENTRIC, PROSPECTIVE COHORT

F. Saccon[1], M. Gatto[2], M. Zen[2], M. Fredi[3], F. Regola[3], F. Franceschini[3], A. Tincani[3], G. Emmi[4], F. Ceccarelli[5], F. Conti[5], A. Bortoluzzi[6], M. Govoni[6], M. Mosca[7], C. Tani[7], M. Gerosa[8], T. Ubiali[8], E. Bozzolo[9], G. A. Ramirez[9], L. Moroni[9], A. Gabrielli[10], P. Cardinaletti[10], E. Gremese[11], G. Tanti[12], S. De Vita[13], G. De Marchi[13], S. Fasano[14], F. Ciccia[14], G. Pazzola[15], C. Salvarani[15], G. Orsolini[16], M. Rossini[16], P. Faggioli[17], A. Laria[18], S. Scarpato[19], A. De Paulis[20], E. Brunetta[21], E. Bartoloni Bocci[22], R. Gerli[22], F. Benvenuti[1], L. Iaccarino[2], A. Doria[2]on behalf of BeRLiSS Study Group. *[1]University of Padua, Division of Rheumatology, Department of Medicine DIMED, Padua, Italy*; *[1]University of Padua, Division of Rheumatology, Department of Medicine DIMED, Padua, Italy*; *[3]ASST Spedali Civili di Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy*; *[4]University of Firenze, Department of Experimental and Clinical Medicine, Firenze, Italy*; *[5]Sapienza University of Roma, Dipartimento Universitario di Scienze Cliniche, Internistiche, Anestesiologiche e Cardiovascolari (SCIAC), Rome, Italy*; *[6]University of Ferrara, Rheumatology Unit, Ferrara, Italy*; *[7]University of Pisa, Rheumatology, Pisa, Italy*; *[8]Milan ASST Gaetano Pini, Department of Clinical Sciences and Community Health, Milan, Italy*; *[9]Milan San Raffele, Medicina Generale e delle Cure Avanzate, Milan, Italy*; *[10]Università Politecnica delle Marche, Dipartimento di Scienze Cliniche e Molecolari, Ancona, Italy*; *[11]Rome Fondazione Policlinico Universitario A. Gemelli-IRCCS, Division of Rheumatology, Rome, Italy*; *[12]Università Cattolica del Sacro Cuore Sede di Roma, Division of Rheumatology, Rome, Italy*; *[13]University of Udine, Rheumatology Unit, Udine, Italy*; *[14]Università degli Studi della Campania Luigi Vanvitelli, Deparment of Precision Medicine, Naples, Italy*; *[15]Reggio Emilia, Division of Rheumatology, Reggio Emilia, Italy*; *[16]University of di Verona, Unit of Rheumatology, Verona, Italy*; *[17]ASST OVEST Milanese presidio di Legnano, Rheumatology Unit, Legnano, Italy*; *[18]ASST OVEST Milanese presidio di Magenta, Division of Rheumatology, Magenta, Italy*; *[19]Salerno Ospedale M. Scarlato, Rheumatology, Salerno, Italy*; *[20]University of Napoli Federico II, Dipartimento di Scienze Mediche Traslazionali e Centro di Ricerca Immunologia Base e Clinica (CISI), Naples, Italy*; *[21]Istituto Clinico Humanitas, Rheumatology, Milan, Italy*; *[22]University of Perugia, Department of Medicine, Perugia, Italy*

Background: LN is still a severe manifestation of Systemic lupus erythematosus (SLE) and multitarget therapy is needed to control the disease especially in refractory cases.

Objectives: To evaluate renal response in SLE patients with glomerulonephritis (GN) treated with Belimumab in real-life setting.

Methods: Patients with proteinuria >0.5 g/24 h and/or active sediment at baseline enrolled in a multicentre Italian cohort of SLE patients (BeRLiSS study), treated with monthly iv Belimumab 10 mg/kg plus standard of care were considered in this study. *Complete renal response (CRR)* was defined as proteinuria <0.5 g/24 h, estimated glomerular filtration rate (eGFR)≥90ml/min/1.73m^2 and no rescue therapy. *Primary efficacy renal response (PERR)* was defined as proteinuria ≤0.7 g/24 h, eGFR ≥60ml/min/1.73m^2 and no rescue therapy. Prevalence and predictive factors of CRR and PERR at 12 and 24 months after Belimumab initiation were analyzed by multivariate logistic regression analysis.

Results: A total of 91 patients were considered in this study, 79 female, mean age 40.51±9.03 years, mean disease duration 12.18±8.15 years, median follow-up time after Belimumab initiation 22 months. Twenty patients had baseline proteinuria ≥0.5 <1 g/day, 17 ≥1 <2 g/day, 13 ≥2 g/day. Belimumab was started at GN onset in 20 (22%) patients and at the time of a renal flare in all other cases. Seventy-five patients underwent a renal biopsy: 1 class I, 4 class II, 14

class III, 47 class IV and 9 class V. Baseline serum creatinine was 82.44±29.26 umol/L; 15 patients showed eGFR<60ml/min/1.73m^2 at baseline. Immunosuppressants were taken by 70 (76.9%) patients: 47 micofenolate, 15 azathioprine and 5 ciclosporine. Sixty patients (65.9%) were on antimalarials. During follow-up 34 (37.4%) patients achieved CRR. Among them 5 (14.7%) patients relapsed and 29 (85.3%) patients maintained remission. Mean time to achieved CRR was 9.71±5.91 months.

High levels of baseline proteinuria were a negative independent predictor of CRR and PERR at 6 months (OR 0.044 CI95% 0.006-0.320 *p=0.002* and OR 0.232 CI95% 0.091-0.596 *p=0.002)* and 12 months (OR 0.029 CI95% 0.002-0.556 *p=0.019* and OR 0.056 CI95% 0.009-0.327 *p=0.001)*. High levels of baseline creatinine were a negative independent predictor of renal response. Renal response at 6 months was a strong predictive factor of renal response at 12 and 24 months.

Conclusion: Belimumab is an effective add-on therapy in the treatment of GN in real-life practice setting.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1757

POS0694 REAL-WORLD ECONOMIC IMPLICATIONS OF ACHIEVING LOW DISEASE ACTIVITY IN LUPUS NEPHRITIS

M. Dall'era[1], T. Hermes[2], M. Eaddy[3], A. Ogbonnaya[3], E. Farrelly[3], P. Mina-Osorio[4]. *[1]UCSF, Rheumatology, San Francisco, United States of America*; *[2]Aurinia Pharmaceuticals Inc., Commercial, Rockville, United States of America*; *[3]Xcenda, Health Economics, Carrollton, United States of America*; *[4]Aurinia Pharmaceuticals Inc., Medical Affairs, Victoria, Canada*

Background: Lupus nephritis (LN) is a common and severe manifestation of systemic lupus erythematosus (SLE) affecting 50% of SLE patients and leading to end-stage kidney disease (ESKD) in up to 30% of patients with LN.[1] Previous studies have reported higher healthcare costs in patients with SLE that develop LN compared to patients without LN.[2-5] These studies captured overall treatment costs associated with LN, regardless of disease activity or severity, and were conducted in small patient populations.

Objectives: The aim of this study was to assess the real-world economic implications of achieving low disease activity compared to active disease or ESKD in a large LN population.

Methods: This study was a retrospective observational analysis of patients with LN within Optum's health plan identified with ICD9 or ICD10 codes to have LN between January 1, 2015, and December 31, 2019. Patients were ≥18 years of age and had ≥2 months of follow-up data available. Patients were followed until death, loss to follow-up, or December 31, 2019. Low disease activity was defined by evidence of glucocorticoid doses ≤5 mg/day, evidence of mycophenolate mofetil (MMF) doses ≤2 g/day, and no use of cyclophosphamide for ≥6 consecutive months. Follow-up time that could not be defined as low disease activity was defined as active disease periods, except for periods with evidence of ESKD. Healthcare payer costs for medical and pharmacy services were compared between periods of low disease activity, active disease, and ESKD. A univariate generalized estimating equation model accounting for interdependence was used to compare differences in costs between periods of active and low disease activity.

Results: A total of 21,251 patients with LN met study criteria with a mean follow-up time of 31.0 months. The mean age was 60.3 years; 86.9% of patients were female and 35.2% of patients were non-White race. Low disease activity was evident in 51.3% of patients with a mean duration of 27.5 months. Mean monthly medical costs were $2,523 during periods of low disease activity and $4,777 during periods of active disease. After factoring in pharmacy costs, mean monthly total costs were $3,584 during periods of low activity and $6,612 during periods of active disease (P<0.001). The mean monthly costs of ESRD were $18,084 for medical and $3,760 for pharmacy.

Conclusion: Achieving low disease activity in patients with LN is associated with reduced economic burden to healthcare payers, with monthly medical costs averaging $2,254 less and total monthly costs averaging $3,028 less than costs during periods of active disease.

REFERENCES:

[1] Parikh SV et al. Update on Lupus Nephritis: Core Curriculum 2020. *Am J Kidney Dis*. 2020;76(2):265-281.

[2] Bartels-Peculis L et al. Treatment patterns and health care costs of lupus nephritis in a United States payer population. *Open Access Rheumatol*. 2020;12:117-124.

[3] Furst DE et al. Medical costs and healthcare resource use in patients with lupus nephritis and neuropsychiatric lupus in an insured population. *J Med Econ*. 2013;16(4):500-509.

[4] Li T et al. Long-term medical costs and resource utilization in systemic lupus erythematosus and lupus nephritis: a five-year analysis of a large Medicaid population. *Arthritis Rheum*. 2009;61(6):755-763.

[5] Pelletier EM et al. Economic outcomes in patients diagnosed with systemic lupus erythematosus with versus without nephritis: results from an analysis of data from a US claims database. *Clin Ther*. 2009;31(11): 2653-2664.

Disclosure of Interests: Maria Dall'Era Speakers bureau: Consulting agreement with Aurinia for Advisory Boards and educational lectures, Tim Hermes Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc., Michael Eaddy Consultant of: Aurinia Pharmaceuticals Inc., Augustina Ogbonnaya Consultant of: Aurinia Pharmaceuticals Inc., Eileen Farrelly Consultant of: Aurinia Pharmaceuticals Inc., Paola Mina-Osorio Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc.

DOI: 10.1136/annrheumdis-2021-eular.1928

POS0695 KZR-616, A SELECTIVE IMMUNOPROTEASOME INHIBITOR FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE COMPLETED DOSE ESCALATION PHASE 1B PORTION OF THE MISSION STUDY

R. Furie[1], S. Parikh[2], J. Wang[3], D. Bomba[4], R. Leff[5], C. Kirk[6], N. Henig[7]. *[1]Northwell Health, Chief, Division of Rheumatology, Great Neck, United States of America*; *[2]Ohio State University Wexner Medical Center, Division of Nephrology, Columbus, United States of America*; *[3]Kezar Life Sciences, Drug Metabolism, South San Francisco, United States of America*; *[4]Kezar Life Sciences, Clinical Operations, South San Francisco, United States of America*; *[5]Kezar Life Sciences, Clinical Science, South San Francisco, United States of America*; *[6]Kezar Life Sciences, Chief Science Officer, South San Francisco, United States of America*; *[7]Kezar Life Sciences, Chief Medical Officer, South San Francisco, United States of America*

Background: KZR-616 is a first-in-class selective inhibitor of the immunoproteasome, which is active in >15 autoimmune disease models, including murine models of systemic lupus erythematosus (SLE)/lupus nephritis (LN).[1,2,3] Selective inhibition of the immunoproteasome modulates both innate and adaptive immune effector cells, resulting in reduced inflammatory T helper cell subsets (Th1 and Th17), increased regulatory T cells, and decreased plasma cells and autoantibodies. KZR-616 was well tolerated in two healthy volunteer studies of 100 subjects receiving up to 75 mg subcutaneously (SC). Target levels of immunoproteasome inhibition were observed at doses ≥30 mg.[3,4] KZR-616 is currently in Phase 2 studies for several autoimmune indications, including the ongoing Phase 2 portion of the MISSION Study (KZR-616-002; NCT0339013) in patients with LN.

Objectives: Results of the completed MISSION Phase 1b dose escalation portion of the study are reported.

Methods: In the open-label, multicenter, dose escalation Phase 1b portion, SLE patients (per SLICC Classification Criteria) with SLEDAI ≥4 despite stable background immunosuppressant, anti-malarial, and/or corticosteroid therapy were administered weekly KZR-616 subcutaneously at doses of 45 mg (cohort 1), 60 mg (cohort 2), 60 mg following step-up doses of 30 mg and 45 mg (cohort 2a), 60 mg following a step-up dose of 30 mg (cohorts 2b, 2c) or 75 mg following a step-up dose of 30 mg (cohort 3) for 13 weeks with follow-up through Week 25 (W25); a lyophilized formulation was used for cohorts 2b, 2c and 3. The disease activity measures assessed were: SLEDAI-2K, Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), 28 tender and swollen joint counts, Physician and Patient Global Assessments, and Patient Assessment of Pain. Safety and tolerability were assessed in the safety population (patients receiving at least one dose of KZR-616).

Results: The Phase 1b portion of MISSION enrolled 47 SLE patients, including 2 patients with active proliferative LN. The most common treatment-emergent adverse events (TEAE) were injection site reactions, which were mostly mild. Infections occurred at a low rate, and there were no reports of peripheral neuropathy, prolonged hematologic AEs, or clinically significant laboratory abnormalities. No discontinuations were observed in cohorts 2b and 2c; no serious AEs were reported in cohort 3 and TEAEs were consistent with those reported in earlier cohorts. Mean values of all measures of disease activity improved in evaluable patients who completed the 13-week treatment period, and improvements were generally maintained at W25. All patients with

elevated anti-double-stranded DNA antibody (anti-dsDNA) levels at baseline (n=7) had a reduction in levels with 3 of 7 experiencing a >50% reduction in their levels. Two of two patients with active proliferative LN had a >50% reduction in UPCR and experienced reductions in SLEDAI-2K scores as well as anti-dsDNA levels. Exposure to KZR-616, similar to that reported in healthy volunteers, was dose-proportional across doses, and no accumulation was observed.

Conclusion: KZR-616 SC, once weekly for 13 weeks up to 75 mg, appears to be safe and well-tolerated in patients with active SLE on stable background therapy in the MISSION Phase 1b. At doses ≥45mg, efficacy was noted, including improvements in proteinuria in two of two patients with LN and serologic improvement in all 7 patients with quantifiable levels of anti-dsDNA antibodies at baseline. KZR-616 60 mg SC weekly for 24 weeks is currently being evaluated in the MISSION Phase 2 in patients with LN. Based on the results of MISSION, inhibition of the immunoproteasome with KZR-616 represents a novel strategy to treat autoimmune diseases.

REFERENCES:

[1] Basler M et al. Clin Exp Rheumatol 2015 (suppl 92);S74.

[2] Muchamuel T et al. Ann Rheumatol Dis 2018;77(suppl 2);685.

[3] Muchamuel T et al. ASN 2020 Virtual Conference.

[4] Snyder B et al. ACR/ARP 2019 Annual Meeting.

[5] Fan RA et al. ACR/ARP 2019 Annual Meeting.

Acknowledgements: Kezar Life Sciences acknowledges the support of site investigators and patient participants in the MISSION study

Disclosure of Interests: Richard Furie Consultant of: Genentech;Kezar Life Sciences, Grant/research support from: Kezar Life Sciences, SV Parikh Consultant of: Aurinia Pharmaceuticals, BMS, GlaxoSmithKline, and Kezar Life Sciences, Grant/research support from: Aurinia Pharmaceuticals;EMD-Serono, Jinhai Wang Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences, Darrin Bomba Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences, Richard Leff Employee of: Kezar Life Sciences [part-time], Christopher Kirk Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences -- full-time employee, Noreen Henig Shareholder of: Kezar Life Sciences, Employee of: Kezar Life Sciences

DOI: 10.1136/annrheumdis-2021-eular.2158

POS0696 SAFETY AND EFFICACY OF BELIMUMAB IN OLDER ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF AN INTEGRATED ANALYSIS

D. D'cruz[1], G. Eriksson[2], Y. Green[3], A. Hammer[4], B. Ji[5], P. Meizlik[6], D. Roth[7]. *[1]Guy's Hospital, Louise Coote Lupus Unit, London, United Kingdom*; *[2]GlaxoSmithKline, Global Clinical Delivery, Collegeville, PA, United States of America*; *[3]GlaxoSmithKline, Clinical Development, Brentford, Middlesex, United Kingdom*; *[4]GlaxoSmithKline, Biostatistics, Collegeville, PA, United States of America*; *[5]GlaxoSmithKline, Research and Development, Brentford, Middlesex, United Kingdom*; *[6]GlaxoSmithKline, Global Safety, Collegeville, PA, United States of America*; *[7]GlaxoSmithKline, Research and Development, Collegeville, PA, United States of America*

Background: Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease characterised by persistent B-cell activation. Belimumab (BEL), a monoclonal antibody that inhibits B-lymphocyte stimulator, is approved in patients aged ≥5 years with active autoantibody-positive SLE; however, safety and efficacy data of BEL in older adults are limited.

Objectives: Assess the safety and efficacy of BEL in older adults with SLE.

Methods: A meta-analysis (GSK study 116559) was performed on the subpopulation of patients aged ≥65 years and compared with the overall population pooled from six controlled, repeat-dose (CRD) BEL trials in adults with SLE (GSK studies: 110752, 110751, LBSL02 [safety only], 112341, 113750, and 115471). Additional safety data were obtained from GSK study 115467.

In each trial, patients were randomised to BEL or placebo (PBO) and received ≥1 treatment dose (GSK studies 110752 and 110751: intravenous [IV] BEL 1 or 10 mg/kg; LBSL02: IV BEL 1, 4, or 10 mg/kg; GSK study 112341: subcutaneous BEL 200 mg; GSK studies 113750, 115471, and 115467: IV BEL 10 mg/kg) plus standard therapy. Safety assessments included: incidence of serious adverse events (SAE), mortality and adverse events of special interest (AESI). The primary efficacy analysis for the CRD trials was the SLE Responder Index 4 (SRI4) response rate.

Results: Older adults (CRD studies: N=63; study 115467: N=156) had lower disease activity and more organ damage compared with the overall populations, and a greater proportion were of white race compared with the overall population in the CRD studies. There were no clinically relevant differences in the incidence of SAE or death between older adults and the overall populations (Table 1). Rates of AESI (post-infusion/injection systemic reactions [PISR], serious infections of special interest, malignancies, psychiatric events) were generally similar or lower in older adults compared with the overall populations with no imbalances between BEL and PBO in older adults (Table 1). No malignancies were reported in older adults. The SRI4 response rate in older adults favoured BEL vs PBO (OR [95% CI], 1.49 [0.49, 4.58]), consistent with the overall populations of the individual CRD studies (110752 and 110751 pooled [10 mg/kg IV]: 1.68 [1.32, 2.15]; 112341: 1.68 [1.25, 2.25]; 113750: 1.99 [1.40, 2.82]; 115471: 1.42 [0.94, 2.15]).

Conclusion: In patients with SLE, the safety and efficacy of BEL in older adults were generally consistent with the overall population and suggest a favourable benefit–risk profile. Due to the small number of older adults analysed, these data should be interpreted with caution.

Funding: GSK

Table 1. SAE, deaths, and AESI

N (%)*	Study 115467				CRD studies†			
	Older adults (N=156)		Overall (N=4003)		Older adults (N=63)		Overall (N=4170)	
	PBO N=82	BEL N=74	PBO N=2001	BEL N=2002	PBO N=27	BEL N=36	PBO N=1355	BEL N=2815
SAE	9 (11.0)	6 (8.1)	222 (11.1)	220 (11.0)	5 (18.5)	10 (27.8)	230 (17.0)	421 (15.0)
Death‡	1 (1.2)	1 (1.4)	11 (0.5)	12 (0.6)	0	0	6 (0.4)	16 (0.6)
AESI								
PISR§,‖,¶	-	-	-	-	0	2 (5.6)	110 (8.1)	286 (10.2)
Serious PISR	0	0	2 (<0.1)	8 (0.4)	0	0	2 (0.1)	13 (0.5)
Infections of SI (opportunistic, herpes zoster, tuberculosis, sepsis)§	0	2 (2.7)	50 (2.5)	36 (1.8)	1 (3.7)	0	97 (7.2)	173 (6.1)
Serious infections of SI	0	2 (2.7)	17 (0.8)	17 (0.8)	0	0	17 (1.3)	40 (1.4)
Malignancies ex. non-melanoma skin cancer§	0	0	5 (0.2)	5 (0.2)	0	0	2 (0.1)	8 (0.3)
Depression (inc. mood disorders / anxiety)/ suicide/self-injury§,¶,**	-‖	-	-	-	3 (11.1)	3 (8.3)	92 (6.8)	210 (7.5)
Serious depression/ suicide/self-injury	0	1 (1.4)	6 (0.3)	18 (0.9)	1 (3.7)	0	5 (0.4)	9 (0.3)

*Patients counted once/category; †Pooled data from all studies except 115467; ‡Study 115467: fatal SAEs that started during on-treatment period; death may have occurred after period end. CRD studies: all deaths during double-blind period; §Per custom MedDRA query; ‖Occurring on/within 3 days of infusion/injection; ¶Study 115467: only serious PISR and serious depression/suicide/self-injury events collected; **Per standard MedDRA query.MedDRA, Medical Dictionary for Regulatory Activities; SI, special interest

Acknowledgements: Medical writing assistance was provided by Helen Taylor, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.

Disclosure of Interests: David d'cruz Speakers bureau: GSK, Consultant of: GSK, Eli Lilly, Gina Eriksson Shareholder of: GSK, Employee of: GSK, Yulia Green Shareholder of: GSK, Employee of: GSK, Anne Hammer Shareholder of: GSK, Employee of: GSK, Beulah Ji Shareholder of: GSK, Employee of: GSK, Paige Meizlik Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK

DOI: 10.1136/annrheumdis-2021-eular.2217

POS0697 SAFETY OF BELIMUMAB IN ADULT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A LARGE INTEGRATED SAFETY ANALYSIS OF CONTROLLED CLINICAL TRIAL DATA

D. J. Wallace[1], T. Atsumi[2], M. Daniels[3], A. Hammer[4], P. Meizlik[5], H. Quasny[6], A. Schwarting[7], F. Zhang[8], D. Roth[9]. *[1]Cedars-Sinai, Division of Rheumatology, Los Angeles, CA, United States of America*; *[2]Hokkaido University Hospital, Department of Rheumatology, Sapporo, Japan*; *[3]GlaxoSmithKline, Clinical Science Lupus, Collegeville, PA, United States of America*; *[4]GlaxoSmithKline, Biostatistics, Collegeville, PA, United States of America*; *[5]GlaxoSmithKline,*

Global Safety, Collegeville, PA, United States of America; [6]*GlaxoSmithKline, Global Medical Affairs, Chapel Hill, NC, United States of America*; [7]*University Medical Center, Division of Rheumatology and Clinical Immunology, Mainz, Germany*; [8]*Peking Union Medical College Hospital, Internal Medicine Department, Beijing, China*; [9]*GlaxoSmithKline, Research and Development, Collegeville, PA, United States of America*

Background: Belimumab (BEL), a monoclonal antibody that antagonizes B-lymphocyte stimulator, was first approved in 2011 for active, autoantibody-positive systemic lupus erythematosus (SLE). BEL has been studied for over 10 years; and while safety data from individual trials have been informative, a large integrated safety analysis has not yet been conducted.

Objectives: Perform pooled analyses to evaluate the safety of BEL in adult patients with SLE.

Methods: Aggregate analyses were performed using safety data for patients ≥18 years of age pooled from six randomised, placebo (PBO)-controlled BEL clinical trials (GSK studies: LBSL02, 110752, 110751, 112341, 113750, and 115471). Patients from GSK studies LBSL02, 110752, and 110751 received intravenous (IV) BEL 1, 4 (LBSL02 only), or 10 mg/kg, or PBO on Days 1, 14, 28, and every 28 days thereafter. Patients from GSK studies 113750 and 115471 received IV BEL 10 mg/kg or PBO on Days 1, 14, 28, and every 28 days thereafter. Patients from GSK study 112341 received subcutaneous (SC) BEL 200 mg, or PBO weekly. Safety analyses included the incidence of adverse events (AEs), serious AEs (SAEs), severe AEs, AEs of special interest (AESI), and mortality of BEL (all doses and formulations combined) vs PBO at Week 52.

Results: The pooled analysis included 4170 patients. Overall, 81.0% (n=2280/2815) of patients receiving BEL and 76.6% (n=1038/1355) of patients receiving PBO completed their respectively enrolled study; the most common reason for withdrawal was occurrence of an AE in both groups. The majority of patients were female (BEL: 94.5%; PBO: 93.6%), the mean age in both groups was 38 years, and baseline characteristics (race, SLE duration, disease activity, SLE damage, complement levels, anti-dsDNA binding, SLE medication usage) were similar between treatments.

The incidence of patients experiencing ≥1 AE, ≥1 SAE, and mortality was similar across treatments (Table 1); the most commonly reported SAEs in both groups were infections and infestations (BEL: 5.4% [n=151/2815]; PBO: 5.9% [n=80/1355]). The mean duration of treatment exposure was similar between groups (BEL: 334.1 days; PBO: 325.3 days).

A greater proportion of patients experienced AESI with BEL vs PBO for post-infusion/injection systemic reactions (from IV or SC administration) and depression/suicide/self-injury (Table 1). The proportion of patients experiencing an AESI of infections and malignancies was similar between groups.

Conclusion: Consistent with individual studies, BEL demonstrated a similar safety profile to PBO in this large integrated safety analysis of six trials. These results support a positive benefit–risk profile of BEL in the treatment of adult SLE.

Funding: GSK

Table 1. Pooled AE data

N (%)	PBO (IV + SC) N=1355	BEL (IV + SC) N=2815
AE	1184 (87.4)	2440 (86.7)
SAE	230 (17.0)	421 (15.0)
Severe AE (severe or life threatening)	209 (15.4)	377 (13.4)
AE resulting in study drug discontinuation	109 (8.0)	184 (6.5)
Death	6 (0.4)	16 (0.6)
AESI		
Post-infusion/injection systemic reactions*	110 (8.1)	286 (10.2)
Serious	2 (0.1)	13 (0.5)
All infections of special interest (OIs, HZ, TB, sepsis)	97 (7.2)	173 (6.1)
Serious	17 (1.3)	40 (1.4)
All OIs	92 (6.8)	157 (5.6)
Active TB	5 (0.4)	4 (0.1)
All HZ	59 (4.4)	106 (3.8)
All sepsis	10 (0.7)	20 (0.7)
Malignancies excluding NMSC	2 (0.1)	8 (0.3)
Including NMSC	3 (0.2)	12 (0.4)
Depression (inc. mood disorders and anxiety)/suicide/self-injury	92 (6.8)	210 (7.5)
Serious	5 (0.4)	9 (0.3)

*Occurring on or within 3 days of infusion/injection date.HZ, herpes zoster; NMSC, non-melanoma skin cancer; OIs, opportunistic infections; TB, tuberculosis

Acknowledgements: Medical writing assistance was provided by Helen Taylor, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.

Disclosure of Interests: Daniel J. Wallace Speakers bureau: GSK, Consultant of: GSK, Tatsuya Atsumi Speakers bureau: GSK, Consultant of: GSK, Grant/research support from: GSK, Mark Daniels Shareholder of: GSK, Employee of: GSK, Anne Hammer Shareholder of: GSK, Employee of: GSK, Paige Meizlik Shareholder of: GSK, Employee of: GSK, Holly Quasny Shareholder of: GSK, Employee of: GSK, Andreas Schwarting Speakers bureau: Novartis, Roche, GSK, Pfizer, Amgen, Consultant of: GSK, Grant/research support from: AbbVie, Pfizer, Novartis, GSK, Actelion, Fengchun Zhang: None declared, David Roth Shareholder of: GSK, Employee of: GSK

DOI: 10.1136/annrheumdis-2021-eular.2373

POS0698

BIIB059 DEMONSTRATED A CONSISTENT THERAPEUTIC EFFECT ON SRI-4 RESPONSE ACROSS SUBGROUPS OF PARTICIPANTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN THE LILAC PHASE 2 STUDY

R. Van Vollenhoven[1], R. Furie[2], K. Kalunian[3], S. Navarra[4], J. Romero-Diaz[5], V. Werth[6,7], X. Huang[8], H. Carroll[9], C. Musselli[10], C. Barbey[11], N. Franchimont[10]. [1]*Amsterdam University Medical Centers, Department of Rheumatology and Clinical Immunology, Amsterdam, Netherlands*; [2]*Northwell Health, Division of Rheumatology, Great Neck, United States of America*; [3]*University of California San Diego, Division of Rheumatology, Allergy and Immunology, La Jolla, United States of America*; [4]*University of Santo Tomas, Rheumatology, Manila, Philippines*; [5]*Salvador Zubirán National Institute of Health Sciences and Nutrition, Department of Immunology and Rheumatology, Ciudad de México, Mexico*; [6]*University of Pennsylvania, Dermatology, Philadelphia, United States of America*; [7]*Corporal Michael J. Crescenz VA Medical Center, Department of Dermatology, Philadelphia, United States of America*; [8]*Biogen, Biostatistics, Cambridge, United States of America*; [9]*Biogen, Medical Evaluation/Global Safety, Cambridge, United States of America*; [10]*Biogen, Clinical Development, Cambridge, United States of America*; [11]*Biogen, Clinical Development, Baar, Switzerland*

Background: Type I interferons and other inflammatory mediators derived from plasmacytoid dendritic cells (pDCs) are implicated in systemic lupus erythematous (SLE) pathology. BIIB059 is a humanized monoclonal antibody that targets blood dendritic cell antigen 2 (BDCA2), a pDC-specific receptor. The binding of BIIB059 to BDCA2 leads to rapid internalization of BDCA2 from the surface of pDCs and subsequent inhibition of interferon, cytokine, and chemokine production. In Part A of the 2-part, phase 2 LILAC study (NCT02847598), BIIB059 significantly reduced SLE activity, as evidenced by reduced total active joint count (primary endpoint) and higher SLE Responder Index (SRI-4)[1] response (a secondary endpoint) versus placebo.[2]

Objectives: To evaluate SRI-4 response for BIIB059 versus placebo at Week 24 in SLE participant subgroups.

Methods: Enrollment in LILAC Part A was open to adults fulfilling ≥ 4 of 11 revised 1997 ACR criteria for classification of SLE, with ≥ 4 tender and ≥ 4 swollen joints, active skin disease, and positive lupus antibodies. Participants were randomized to receive either BIIB059 450 mg or placebo subcutaneously every 4 weeks for 20 weeks (with an additional dose at Week 2). SRI-4 response at Week 24 was analyzed in subgroups, though analyses were limited by small sample sizes and were not powered for statistical testing.

Results: In LILAC Part A, 64 and 56 participants were dosed with BIIB059 450 mg and placebo, respectively. At week 24, SRI-4 response rate was observed in favor of BIIB059 regardless of the baseline disease activity, such as SLEDAI-2K <10 versus ≥10, presence of BILAG-2004 grade A or B arthritis, oral corticosteroid usage, positivity for anti-ds DNA autoantibody and/or complement status, with point estimates for least-squares mean differences as well as corresponding 95% CIs consistently favoring BIIB059 (Figure 1). The incidence of adverse events in the overall study population was similar between the placebo and BIIB059 groups.[2]

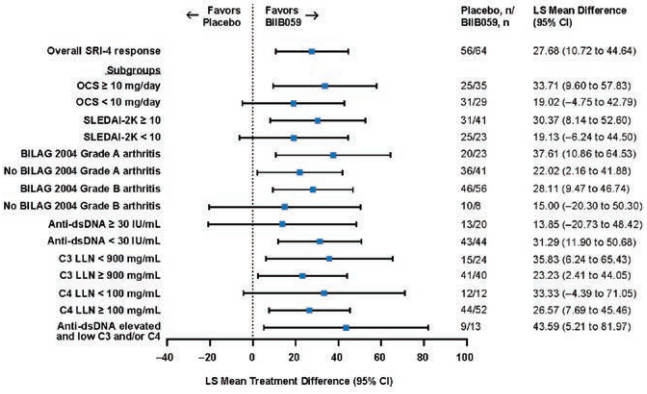
Conclusion: BIIB059 treatment was associated with greater SRI-4 response rate, consistent among different subgroups of baseline disease activity as measured by SLEDAI-2K and BILAG-2004, glucocorticoid dosage, and serology. These findings provide additional evidence of the potential benefit of BIIB059 for the treatment of patients with active SLE.

REFERENCES:

[1] Furie RA, et al. *Arthritis Rheum.* 2009;61(9):1143-1151. 2. Furie RA, et al. *Arthritis Rheumatol.* 2020;72(suppl 10). Abstract 0935.

Acknowledgements: This study was sponsored by Biogen (Cambridge, MA, USA). Writing and editorial support was provided by Excel Scientific Solutions (Fairfield, CT, USA); funding was provided by Biogen.

Figure. Subgroup Analysis of SRI-4 Response Between BIIB059 and Placebo at Week 24



BILAG 2004 = British Isles Lupus Assessment Group 2004; dsDNA = double-stranded DNA; LLN = lower limit of normal; LS = least-squares; OCS = oral corticosteroid; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SLE = systemic lupus erythematosus; SRI-4 = SLE Responder Index

SRI-4 was defined as a reduction from baseline of ≥ 4 points in SLEDAI-2K, no new BILAG-2004 Grade A domain score or no more than 1 new BILAG-2004 Grade B domain score, no worsening from baseline in Physician's Global Assessment (< 10%), and no violations of protocol-specified medication rules. Participants who were considered as treatment failures or discontinued treatment were considered as nonresponders at visits after treatment failure or discontinuation. Participants who completed treatment but had a missing score at a primary timepoint were classified as nonresponders for that timepoint. Results are based on a generalized linear regression model adjusted for treatment using an identity link function (linear probability model) for the LS mean differences. Only BIIB059 450 mg and placebo are included in the statistical modeling.

Disclosure of Interests: Ronald van Vollenhoven Consultant of: AbbVie, AstraZeneca, Biotest, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Lilly, Medac, Merck, Novartis, Pfizer, Roche, UCB, Grant/research support from: AbbVie, Arthrogen, Bristol Myers Squibb, GlaxoSmithKline, Lilly, Pfizer, UCB, Richard Furie Consultant of: Biogen, Grant/research support from: Biogen, Kenneth Kalunian Consultant of: AbbVie, Amgen, AstraZeneca, Biogen, Bristol Myers Squibb, Eli Lilly, Equillium, Genentech, Gilead, ILTOO, Janssen, Nektar, Roche, Viela, Grant/research support from: Lupus Research Alliance, Pfizer, Sanford Consortium, Sandra Navarra Speakers bureau: Astellas, Johnson & Johnson, Novartis, Pfizer, Consultant of: Biogen, Grant/research support from: Biogen, Juanita Romero-Diaz Consultant of: Biogen, Boehringer Ingelheim, Victoria Werth Consultant of: AbbVie, Amgen, AstraZeneca, Biogen, Bristol Myers Squibb, Eli Lilly, EMD Serono, Gilead, GlaxoSmithKline, Janssen, Kyowa Kirin, Resolve, Viela, Grant/research support from: Biogen, Celgene, Gilead, Janssen, Viela, XIAOBI HUANG Shareholder of: Biogen, Employee of: Biogen, HUA CARROLL Shareholder of: Biogen, Employee of: Biogen, Cristina Musselli Shareholder of: Biogen, Employee of: Biogen, Catherine Barbey Shareholder of: Biogen, Employee of: Biogen, NATHALIE FRANCHIMONT Shareholder of: Biogen, OMass Therapeutics, Employee of: Biogen
DOI: 10.1136/annrheumdis-2021-eular.2570

POS0699

GREATER REDUCTION IN CLASI-A SCORES ACHIEVED WITH BIIB059 VERSUS PLACEBO INDEPENDENTLY OF DISEASE SEVERITY AT BASELINE

V. Werth[1,2], R. Furie[3], K. Kalunian[4], R. Van Vollenhoven[5], S. Navarra[6], F. Nyberg[7], J. Romero-Diaz[8], M. Tee[9], X. Huang[10], H. Carroll[11], C. Barbey[12], C. Musselli[13], N. Franchimont[13]. [1]*University of Pennsylvania, Dermatology, Philadelphia, United States of America*; [2]*Corporal Michael J. Crescenz VA Medical Center, Department of Dermatology, Philadelphia, United States of America*; [3]*Northwell Health, Division of Rheumatology, Great Neck, United States of America*; [4]*University of California San Diego", Division of Rheumatology, Allergy and Immunology, La Jolla, United States of America*; [5]*Amsterdam University Medical Centers, Department of Rheumatology and Clinical Immunology, Amsterdam, Netherlands*; [6]*University of Santo Tomas, Rheumatology, Manila, Philippines*; [7]*Karolinska University Hospital, Department of Medicine, Stockholm, Sweden*; [8]*Salvador Zubirán National Institute of Health Sciences and Nutrition, Department of Immunology and Rheumatology, Mexico City, Mexico*; [9]*Medical Center Manila, College of Medicine, Manila, Philippines*; [10]*Biogen, Biostatistics, Cambridge, United States of America*; [11]*Biogen, Medical Evaluation/Global Safety, Cambridge, United States of America*; [12]*Biogen, Clinical Development, Baar, Switzerland*; [13]*Biogen, Clinical Development, Cambridge, United States of America*

Background: Patients with cutaneous lupus erythematosus (CLE) experience symptoms including photosensitivity, rash, pain, and skin damage that can impact their quality of life. No targeted therapies are approved for CLE. BIIB059 is a humanized monoclonal antibody that targets blood dendritic cell antigen-2 (BDCA2), expressed exclusively on the surface of plasmacytoid dendritic cells (pDCs). The binding of BIIB059 to BDCA2 leads to rapid internalization of BDCA2 from the cell surface of pDCs, thereby inhibiting the production of pDC-derived type I interferons, cytokines, and chemokines, which are involved in CLE pathology. In Part B of the 2-part, phase 2 LILAC study (NCT02847598), the primary endpoint was met: BIIB059 significantly reduced CLE activity, as evidenced by a statistically significant dose response and statistically significant differences in least-squares mean percent changes in Cutaneous Lupus Erythematosus Disease Area and Severity Index – Activity (CLASI-A) score[1] versus placebo.[2]

Objectives: To determine the proportion of patients with CLE who presented at baseline with moderate or severe disease (CLASI-A ≥ 10) or with the higher category of mild disease (CLASI-A < 10 [i.e., 8 or 9]) and experienced a shift in CLASI-A score to a mild skin disease category or clear/almost clear skin status.

Methods: Adults with histologically confirmed CLE with or without systemic manifestations were enrolled if they had CLASI-A ≥ 8 at baseline, despite prior use of or intolerance to topical corticosteroids (CS) and/or antimalarials, in addition to ≥ 1 lesion diagnostic of subacute CLE (CLASI-A erythema score ≥ 2) and/or chronic CLE (CLASI-A erythema score ≥ 2 and CLASI-Damage scarring score ≥1). Concomitant CLE/SLE therapy was allowed if doses were initiated ≥ 12 weeks and kept stable ≥ 4 weeks before randomization and throughout the treatment period. Systemic corticosteroid doses could not exceed 15 mg/day of prednisone (or equivalent). BIIB059 (50, 150, 450 mg) or placebo was subcutaneously administered once every 4 weeks for 12 weeks, with an additional dose at Week 2. An ad hoc analysis was conducted to determine the proportion of participants (CLASI-A ≥ 10 or < 10 at baseline) with a shift in CLASI-A score to ≤ 1, ≤ 3, ≤ 6, and ≤ 8 at Week 16.

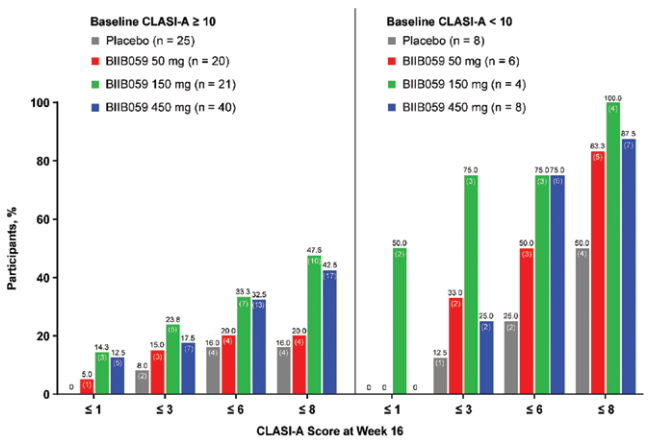
Results: In this ad hoc analysis from LILAC Part B, 106 (80.3%) and 26 (19.7%) of participants had a baseline CLASI-A score ≥ 10 and < 10, respectively. Compared with placebo, higher proportions of participants treated with BIIB059 achieved a shift in CLASI-A score from either ≥ 10 or < 10 at baseline to ≤ 1, ≤ 3, ≤ 6, and ≤ 8 at Week 16 (Figure 1). Treatment with BIIB059 resulted in higher proportions of participants achieving reduced scores, indicating shifts to more mild disease activity, compared with placebo. A score ≤ 1 (clear or almost clear skin) at Week 16 was achieved by 0.0% (0/25), 5.0% (1/20), 14.3% (3/21), and 12.5% (5/40) of participants with baseline CLASI-A ≥ 10 who were treated with placebo and BIIB059 50, 150, and 450 mg, respectively. Two of 26 participants with baseline CLASI-A < 10 achieved a score ≤ 1 (both received BIIB059 150 mg).

Conclusion: A greater proportion of participants achieved milder skin disease or clear/almost clear skin status in the BIIB059 groups as compared with the placebo group. This effect was observed in participants with moderate or severe disease as well as in those in the higher range of the mild category of disease severity at baseline, indicating the ability of BIIB059 to improve skin lesions in patients with a broad range of cutaneous disease activity.

REFERENCES:

[1] Albrecht J, et al. *J Invest Dermatol*. 2005;125(5):889-894.
[2] Werth V, et al. *Arthritis Rheumatol*. 2020;72(suppl 10). Abstract 0986.

Figure. Percentage of Participants With Baseline CLASI-A ≥ 10 and < 10 Achieving a Decrease to CLASI-A Score Thresholds ≤ 1, ≤ 3, ≤ 6, and ≤ 8 at Week 16



CLASI-A = Cutaneous Lupus Erythematosus Disease Area and Severity Index – Activity

The denominator is the number of participants who had a CLASI-A score ≥ 10 or < 10 at baseline and a nonmissing CLASI-A score at Week 16. Participants who were treatment failures or who discontinued treatment were considered nonresponders at visits after the treatment failure or discontinuation. Participants who completed treatment but had a missing score at the primary timepoint were classified as nonresponders for that timepoint.

Acknowledgements: This study was sponsored by Biogen (Cambridge, MA, USA). Writing and editorial support was from Excel Scientific Solutions (Fairfield, CT, USA); funding was provided by Biogen.

Disclosure of Interests: Victoria Werth Consultant of: AbbVie, Amgen, AstraZeneca, Biogen, Bristol Myers Squibb, Eli Lilly, EMD Serono, Gilead, GlaxoSmithKline, Janssen, Kyowa Kirin, Resolve, Viela, Grant/research support from: Biogen, Celgene, Gilead, Janssen, Viela, Richard Furie Consultant of: AstraZeneca, Biogen, Grant/research support from: AstraZeneca, Biogen, Kenneth Kalunian Consultant of: AbbVie, Amgen, AstraZeneca, Biogen, Bristol Myers Squibb, Eli Lilly, Equillium, Genentech, Gilead, ILTOO, Janssen, Nektar, Roche, Viela, Grant/research support from: Lupus Research Alliance, Pfizer, Sanford Consortium, Ronald van Vollenhoven Consultant of: AbbVie, AstraZeneca, Biotest, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Lilly, Medac, Merck, Novartis, Pfizer, Roche, UCB, Grant/research support from: AbbVie, Arthrogen, Bristol-Myers Squibb, GlaxoSmithKline, Lilly, Pfizer, UCB, Sandra Navarra Speakers bureau: Astellas, Johnson & Johnson, Novartis, Pfizer, Consultant of: Biogen, Filippa Nyberg Consultant of: Biogen, Juanita Romero-Diaz Consultant of: Biogen, Boehringer Ingelheim, Michael Tee Speakers bureau: Pfizer, Novartis, Johnson & Johnson, Celltrion, Consultant of: Neovacs, Grant/research support from: Celltrion, Johnson & Johnson, Pfizer, XIAOBI HUANG Shareholder of: Biogen, Employee of: Biogen, HUA CARROLL Shareholder of: Biogen, Employee of: Biogen, Catherine Barbey Shareholder of: Biogen, Employee of: Biogen, Cristina Musselli Shareholder of: Biogen, Employee of: Biogen, NATHALIE FRANCHIMONT Shareholder of: Biogen, OMass Therapeutics, Employee of: Biogen

DOI: 10.1136/annrheumdis-2021-eular.2716

POS0700

TREATMENT OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH PRIMARY SJOGREN SYNDROME: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

T. Y. Lan[1], H. T. Huang[2], J. H. Kao[1], C. F. Cheng3, C. H. Lu3, C. Y. Shen3, K. J. Li3, S. C. Hsieh[1]. [1]*National Taiwan University Hospital, Department of Internal Medicine, Rheumatology Division, Taipei, Taiwan, Republic of China*; [2]*National Taiwan University Hospital, Department of Oncology, Taipei, Taiwan, Republic of China*; [1]*National Taiwan University Hospital, Department of Internal Medicine, Rheumatology Division, Taipei, Taiwan, Republic of China*

Background: Interstitial lung disease (ILD) is one of the main contributor to morbidity and mortality in patients with primary Sjogren syndrome (pSS), and whether immunosuppressive treatments are effective for pSS-ILD is uncertain. Cyclophosphamide (CYC) and rituximab (RTX) are effective in stabilizing pulmonary function in patients with ILD caused by systemic sclerosis, inflammatory myositis, and rheumatoid arthritis[1,2]. Reports regarding the treatment response for cyclophosphamide or rituximab in pSS-ILD patients are lacking.

Objectives: To investigate whether add-on CYC or RTX in addition to steroid and oral DMARDs leads to greater improvement in pulmonary function test than conventional treatment in patients with pSS-ILD with impaired baseline pulmonary function.

Methods: pSS-ILD patients with ILD confirmed by a chest computed tomography were screened. Those with imparied baseline pulmonary function test (FVC<80% and DLCO<80%) and available results of pulmonary function tests at 6th-18th month post-treatment were retrospectively enrolled. The patients were clustered into two groups: steroid and oral DMARDs alone (steroid/oDMARD group), and add-on CyC and/or RTX (Add-on CyC/RTX group).

Results: This study enrolled 22 patients. The median age of these patients was 65. Among them, 68% were female and 18% were smokers. The median baseline FVC was 63.5% and the median DLCO was 54.4%. The predominant CT pattern was NSIP (54%), followed by UIP (22%), LIP (13.6%) and OP (9%) (table 1).

Five patients received steroid and oral DMARDs alone (hydroxychloroquine +/- azathioprine), while 17 patients received add-on CYC and/or RTX (8 patients received CYC, 3 received RTX, and 6 received CYC and RTX). There was no significant difference in baseline characteristic between these two groups (table 1).

With a median follow-up period of 9.8 months (interquartile range 7.6 - 13.4 months) after treatment, the FVC improved significantly from 61.3% to 65.5% (p=0.013) in CYC/RTX group, while the FVC improvement was not significant in steroid/oDMARD group (figure 1A). In CYC/RTX group, patients with non-UIP pattern (NSIP, LIP and OP) on chest CT had significant FVC improvement (p=0.021), contrasting to the patients with UIP pattern on chest CT (figure 1B).

Conclusion: In pSS patients with ILD and impairment of pulmonary function at baseline (FVC<80%, DLCO<80%), FVC improved significantly in patients received add-on cyclophosphamide and/or rituximab therapy.

REFERENCES:

[1] Wells AU, Denton CP. Interstitial lung disease in connective tissue disease--mechanisms and management. Nat Rev Rheumatol. 2014 Dec;10(12):728-39.

[2] Gao Y, Moua T. Treatment of the Connective Tissue Disease-Related Interstitial Lung Diseases: A Narrative Review. Mayo Clin Proc. 2020 Mar;95(3):554-573.

Table 1. Baseline characteristics of patients with Sjögren's syndrome and interstitial lung disease

	Total (n = 22)	Steroid/oDMARDs (n = 5)	Add-on CYC/RTX (n = 17)	Comparison between two groups (p-value)
Age, year, median (IQR)	65.1 (61.7 - 69.1)	64 (64.6 - 67.4)	65.6 (61.6 - 69.2)	0.88
Female sex, n (%)	15 (68%)	4 (80%)	12 (70%)	1.00
Smoking, n (%)	4 (22%)	0 (0%)	4 (21%)	0.54
Baseline FVC, % of predicted value, median (IQR)	63.6% (53.8 - 68.2)	63.9% (63.7 - 67.5)	61.3% (50.2 - 68.2)	0.43
Baseline DLCO, % of predicted value, median (IQR)	54.4% (39.4 - 66.4)	69.1% (57.8 - 75.5)	52.1% (38.5 - 58.1)	0.12
CT pattern, n (%)				
	NSIP - 12 (54%)	NSIP 1 (20%)	NSIP - 11 (65%)	-
	UIP - 5 (22%)	UIP 1 (20%)	UIP - 4 (24%)	
	LIP - 3 (13.6%)	LIP 2 (40%)	LIP -1 (6%)	
	OP - 2 (9%)	OP 1 (20%)	OP -1 (6)	
UIP pattern, n (%)	5 (22%)	1 (20%)	4 (24%)	1.00

CYC, cyclophosphamide; oDMARDs, oral DMARDs; RTX, rituximab

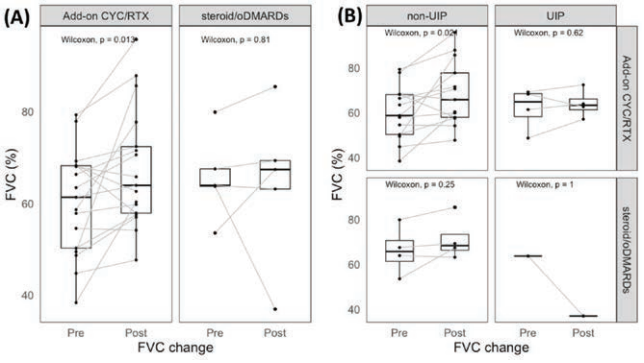


Figure 1. FVC change before and after the immunosuppressive treatment

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2758

POS0701 ANIFROLUMAB, AN ANTI-INTERFERON-A RECEPTOR MONOCLONAL ANTIBODY IN SYSTEMIC LUPUS ERYTHEMATOSUS- A META ANALYSIS

A. Abdul Razzack[1], S. Abdul Razzack[1], P. Shenasan[2], N. Shenasan[2], S. Mishra[2], R. Zarrar[2], J. Pablo Sosa[2], M. Mercedes Ferreira Caceres[2], R. Garimella[1], K. Andrews[3], S. Mukhtar[2], A. Agolli[2], O. Agolli[2], S. Hassan[4], D. M. Rocha Castellanos[5], S. Pothuru[6], K. Theja Reddy[7]. [1]*Dr. N.T.R University of Health Sciences, Department of Medicine, Vijaywada, India*; [2]*Larkin Community Hospital, Department of Clinical and Translational Research, South Miami, United States of America*; [3]*Prince Mohammad Bin Fahad University, Department of Mathematics and Natural Sciences, Al Khobar, Saudi Arabia*; [4]*University of Louisville, Department of Medicine, Louisville, United States of America*; [5]*Tecnológico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Departamento de Cirugía, Nuevo León, Mexico*; [6]*Ascension Via Christi Hospital, Department of Medicine, Manhattan, United States of America*; [7]*UHS Southern California Medical Education Consortium, Department of Medicine, California, United States of America*

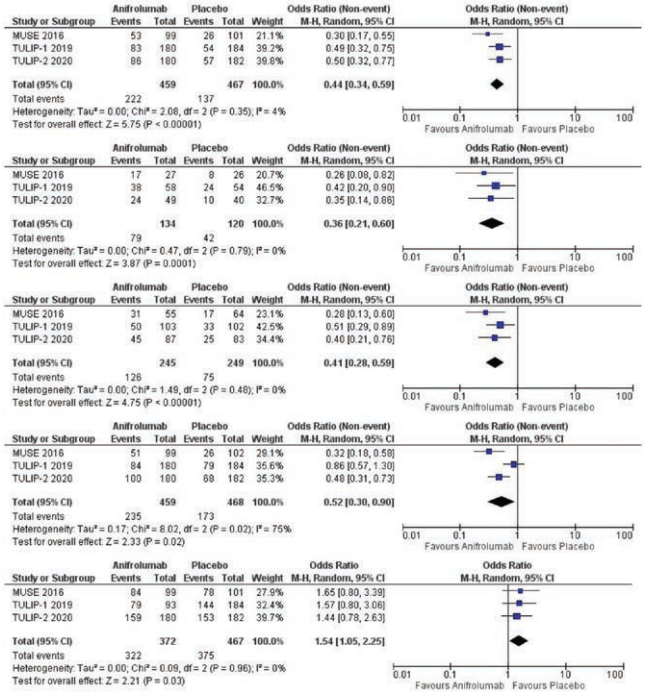
Background: Type I interferons such as Anifrolumab have been implicated in Systemic lupus erythematosus (SLE) pathogenesis on the basis of increased interferon-stimulated gene expression and genetic susceptibility. Little is known regarding its efficacy and safety profile.

Objectives: To assess the efficacy and safety of Anifrolumab in patients with SLE.

Methods: Electronic databases (PubMed, Embase, Scopus, Cochrane) were searched from inception until December 15th, 2020. Unadjusted odds ratios (OR) were calculated from dichotomous data using Mantel Haenszel (M-H) random-effects with statistical significance to be considered if the confidence interval excludes 1 and p<0.05. The primary outcome of interest was British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA). Secondary outcomes included the proportion of patients who achieved an SLE responder index of 4 (SRI-4) reduction of 50% or more in the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), reductions in the glucocorticoid dose and adverse effects.

Results: A total of three studies[1,2,3] with 839 participants (Anifrolumab=372, Placebo=467) were included in our analysis. Follow-up duration was at week 52. A statistically significant different was observed in the Anifrolumab arm in terms of BICLA response (OR 0.44 95%CI 0.34-0.59;p<0.00001, I^2=4), ≥50% reduction in CLASI activity score (OR 0.36 95%CI 0.21-0.60;p=0.0001, I^2=0), glucocorticoid reduction (OR 0.41 95%CI 0.28-0.59;p<0.00001; I^2=0) and SRI-4 response (OR 0.52 95% CI 0.30-0.90; p=0.02, I^2=75). However, Adverse events were less likely in the placebo arm as compared to Anifrolumab (OR 1.54 95%CI 1.05-2.25; p=0.03; I^2=0).

Conclusion: Anifrolumab was found to be more effective than placebo for the management of SLE, but may also cause more severe adverse effects.



REFERENCES:

[1] Morand EF, Furie R, Tanaka Y, Bruce IN, Askanase AD, Richez C, Bae SC, Brohawn PZ, Pineda L, Berglind A, Tummala R; TULIP-2 Trial Investigators. Trial of Anifrolumab in Active Systemic Lupus Erythematosus. N Engl J Med. 2020 Jan 16;382(3):211-221. doi: 10.1056/NEJMoa1912196. Epub 2019 Dec 18. PMID: 31851795.

[2] Furie R, Khamashta M, Merrill JT, Werth VP, Kalunian K, Brohawn P, Illei GG, Drappa J, Wang L, Yoo S; CD1013 Study Investigators. Anifrolumab, an Anti-Interferon-α Receptor Monoclonal Antibody, in Moderate-to-Severe Systemic Lupus Erythematosus. Arthritis Rheumatol. 2017 Feb;69(2):376-386. doi: 10.1002/art.39962. PMID: 28130918; PMCID: PMC5299497.

[3] Furie RA, Morand EF, Bruce IN, et al. Type I interferon inhibitor anifrolumab in active systemic lupus erythematosus (TULIP-1): a randomised, controlled, phase 3 trial. Lancet Rheumatol 2019; 1(4):e208-e219.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2782

POS0702 PREGNANCY IN SLE PATIENTS TREATED WITH BELIMUMAB: EXPERIENCE FROM 3 ITALIAN CENTERS

F. Crisafulli[1], M. C. Gerardi[1], L. Moschetti[1], M. Fredi[1], C. Nalli[1], M. L. Urban[2], G. Emmi[2], F. Saccon[3], M. Zen[3], L. Iaccarino[3], A. Doria[3], F. Franceschini[1], L. Andreoli[1], A. Tincani[1]. [1]*ASST Spedali Civili and University of Brescia, Rheumatology and Clinical Immunology Unit, Brescia, Italy*; [2]*University of Florence, Department of Experimental and Clinical Medicine, Firenze, Italy*; [3]*University of Padova, Unit of Rheumatology, Padova, Italy*

Background: Belimumab (BEL) is a monoclonal antibody approved for SLE treatment but few data are available about its use before or during pregnancy.

Objectives: Our study aims to describe pregnancies in SLE patients who have discontinued BEL before conception, at positive pregnancy test or during pregnancy.

Methods: Data from prospectively-followed pregnancies (2014-2020) in SLE patients treated with BEL in 3 Italian centers where retrospectively collected, focusing on maternal disease activity, obstetric and neonatal outcome. Continuous data are expressed as median [min-max].

Results: Thirteen SLE pregnancies were analyzed (median age at conception 32 [24-41] years; 77% spontaneous, 69% primigravidae). All patients had positive ANA and anti-dsDNA antibodies; 4 had anti-Ro antibodies (31%); 4 had anti-phospholipid antibodies (aPL; 1 single, 2 double and 1 triple positivity). Seven patients (54%) had a history of lupus nephritis (LN); 2 patients (15%) had a concomitant diagnosis of antiphospholipid syndrome (1 thrombotic-APS and 1 thrombotic+obstetric-APS).

Ten (77%) pregnancies were planned and the use of BEL with regard to pregnancy was agreed with the patient during preconception counseling. At preconception visit, 8 patients were in remission while 5 had active disease (median SLEDAI 3 [0-8]).

BEL (11 intravenous, 2 subcutaneous) was stopped in 2 cases before conception, in 7 at positive pregnancy test and in 4 during pregnancy (2 at 11th week, 1 at 22nd, 1 at 24th); median duration of treatment at discontinuation was 29 [4-68] months. Other treatments during pregnancy were: oral prednisone in 12 cases (92%); intravenous methylprednisolone in 1 (8%); hydroxychloroquine in 10 (77%); chloroquine in 1 (8%); azathioprine in 5 (39%); calcineurin inhibitors in 5 (39%); low-dose acetylsalicylic acid in 10 (77%); low molecular weight heparin in 9 (69%).

Three flares occurred during the 3rd trimester in patients who stopped BEL at positive pregnancy test.

Live-births occurred in 92% of the pregnancies. A patient with thrombotic+obstetric-APS and LN, underwent assisted reproductive technology (embryo donation) and developed eclampsia (25thweek), an urgent cesarean section was performed and the newborn died after 3 days. One pre-eclampsia occurred in a patient with history of LN, double aPL positivity and active disease. One miscarriage at 11th week occurred; no early miscarriages (<10th week) were recorded. Pregnancy complications and outcomes are reported in Table 1.

No malformations were recorded. Two newborns were transferred to the Intensive Care Unit (1 for milk protein intolerance and 1 for desaturation).

Table 1. Pregnancy complications and outcomes according to the timing of discontinuation of BEL.

	BEL STOPPED PRECONCEPTIONALLY (2)	BEL STOPPED AT POS PREGNANCY TEST (7)	BEL STOPPED DURING PREGNANCY (4)
Pre-eclampsia	0/2	0/7	1/4 (25%)
Eclampsia	0/2	0/7	1/4* (25%)
Gestational Diabetes	0/2	1/7 (14%)	0/4
IUGR	0/2	1/7 (14%)	1/4* (25%)
pPROM/PROM	0/2	0/7	1/4 (25%)
Live birth	***1/2 (50%)***	***7/7 (100%)***	***4/4 (100%)***
Severe pre-term birth (≤ 34thweek)	0/2	0/7	1/4* (25%)
Late pre-term birth (35th- 37thweek)	0/2	3/7 (43%)	0/4
Small for Gestational age neonate	0/2	4/7 (54%)	1/4 (25%)
Late miscarriage (>10thweek)	***1/2 (50%)***	0/7	0/4
Perinatal death	0/2	0/7	***1/4* (25%)***

IUGR: IntraUterine Growth Restriction; PROM: Premature Rupture of Membrane; pPROM: pretermPROM;*in the same patient (history of thrombotic and obstetric-APS and lupus nephritis) who underwent Assisted Reproductive Technologies (embryo donation).

Eight newborns received vaccinations according to national schedule (missing data for 3). Five newborns were breastfed, 1 received formula milk and 5 mixed-feeding. BEL was resumed in 7/13 patients after pregnancy (in 4 cases for flare), after a median period of 5 [4-22] months.

Conclusion: While more data are needed, this small series suggests that BEL might be a therapeutic option for SLE patients during pregnancy planning, similarly to other biological drugs used in chronic forms of arthritis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2862

POS0703 CARDIAC ADVERSE EFFECTS OF LONG-TERM USE OF HYDROXYCHLOROQUINE IN SYSTEMIC LUPUS ERYTHEMATOSUS. SINGLE UNIVERSITY CENTER STUDY OF 109 PATIENTS

A. Herrero-Morant[1], A. Margarida-de Castro[1], R. Pérez-Barquín[1], J. Zubiaur-Zamacola[1], M. Á. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology and Cardiology, Santander, Spain*

Background: Hydroxychloroquine (HCQ) is a widely used drug especially in connective tissue disorders such as Systemic Lupus Erythematosus (SLE). Cardiac adverse effects of long-term use of HCQ remains controversial.

Objectives: To assess cardiac adverse effects of long-term use of HCQ in SLE.

Methods: Observational single center study of 109 patients with SLE treated with HCQ for more than 3 months. The main outcomes were cardiac structural and conduction disorders in a 12-lead electrocardiogram and/or echocardiogram at baseline and during HCQ treatment.

Results: We studied 109 patients (95 women/14 men; mean age 66.9±14.7 years). Main cardiovascular history was hypertension (n=61, 56.0%), diabetes mellitus (n=16, 14.7%) and renal impairment (n=11, 10.1%). HCQ was used for 11.7±8.9 years. Initial median SLE Disease Activity Index 2000 (SLEDAI-2K) was 7 [3.75-11]. At baseline, 27 (24.8%) patients had conduction disorders and 15 (13.7%) had structural abnormalities: Most prevalent cardiac alterations were Left Anterior Fascicular Block (LAFB) (n=9, 8.3%), left ventricular hypertrophy (n=9, 8.3%) and right bundle branch block (n=8, 7.3%). After 11.7±8.9 years of follow-up (mean HCQ cumulative dose: 1042.2±267.5 g; median SLEDAI-2K 1 [0-4]), there was a significant increase in conductions disorders (n=41, 37.6%, p=0.011) and in LAFB (n=16, 14.7%, p=0.021). There was no statistically significant increase in structural abnormalities (n=21, 19.7%, p=0.629).

Table 1. Main cardiac abnormalities at baseline and after follow-up.

	Baseline	After follow-up	*p*
Conduction disorders, n (%)	27 (24.8)	41 (37.6)	0.011
Left anterior fascicular block	9 (8.3)	16 (14.7)	0.021
Right bundle branch block	7 (6.4)	8 (7.3)	1.0
Atrioventricular block	4 (3.6)	11 (10.1)	0.092
Incomplete right bundle branch block	4 (3.6)	5 (4.6)	1.0
Short PR interval	2 (1.8)	4 (3.7)	0.5
Prolonged QT corrected interval	2 (1.8)	4 (3.7)	0.625
Left bundle branch block	1 (0.9)	5 (4.6)	0.125
Atrial Fibrillation	1 (0.9)	5 (4.6)	0.219
Structural abnormalities, n (%)	15 (13.7)	21 (19.7)	0.629
Ventricular hypertrophy	9 (8.3)	9 (8.3)	1.0
Atrial enlargement	6 (5.5)	13 (11.9)	0.096

Main cardiac abnormalities at baseline and after 11.7±8.9 years of follow-up are summarized in Table 1. Time of occurrence of cardiac adverse effect in relation to HCQ cumulative dose is shown in Figure 1.

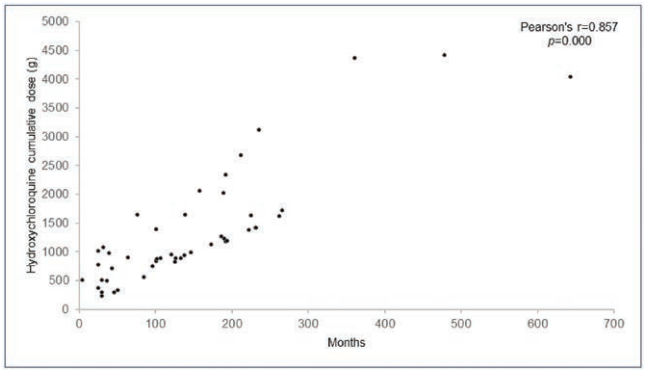


Figure 1. Time of occurrence of cardiac adverse effect in relation to hydroxychloroquine cumulative dose.

Conclusion: Conduction disorders were more prevalent than structural abnormalities. Patients with SLE treated with HCQ had a significant increase in LAFB. Use of electrocardiogram and/or echocardiogram may be helpful in monitoring cardiac adverse effects.

Disclosure of Interests: Alba Herrero-Morant: None declared, Adrián Margarida-de Castro: None declared, Raquel Pérez-Barquín: None declared, Jon Zubiaur-Zamacola: None declared, Miguel Á. González-Gay Speakers bureau: AbbVie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Grant/research support from: AbbVie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, Sanofi, Lilly and MSD, Grant/research support from: AbbVie, MSD, and Roche

DOI: 10.1136/annrheumdis-2021-eular.3471

POS0704 LONG-TERM CLINICAL OUTCOMES OF PATIENTS WITH LUPUS NEPHRITIS TREATED WITH AN INTENSIFIED B-CELL DEPLETION PROTOCOL: A PROSPECTIVE STUDY

D. Roccatello[1], S. Sciascia[1], C. Naretto[1], M. Alpa[1], R. Fenoglio[1], M. Ferro[1], G. Quattrocchio[1], E. Rubini[1], E. Rahbari[1], D. Rossi[1]. [1]*University of Torino, Department of Clinical and Biological Sciences, Turin, Italy*

Background: B cells play a key role In the pathogenesis of Lupus Nephritis (LN).

Objectives: we aim to investigate the safety and efficacy of an intensified B-cell depletion induction therapy (IBCDT)without immunosuppressive maintenance regimen compared to standard of care in biopsy-proven LN.

Methods: Thirty patients were administered an IBCDT (4 weekly Rituximab 375mg/m2 and 2more doses after 1&2 months;2 infusions of 10 mg/kg cyclophosphamide (CYC),3 methylprednisolone pulses), followed by oral prednisone (tapered to 5 mg/day by the 3rd month). No immunosuppressive maintenance therapy was given. Thirty patients matched for LN class and age were selected as controls: 20 received 3 methylprednisolone pulses days followed by oral prednisone and mycophenolate mofetil (MMF) 2-3 g/day, while 10 were given the Euro Lupus CYC.

Results: At 12 months, complete renal remission was observed in 93% of patients on IBCDT, in 62.7% on MMF, and in 75% on CYC (p=0,03); the dose of oral prednisone was lower in the IBCDT group (mean±SD 2.9±5.0mg/dl) than MMF (10.5±8.0 mg/day,p<0.01) or CYC group (7.5±9.0mg/day,p<0.01). Mean follow-up after treatment was 44.5 months (IQR 36–120months), 48.6 months (IQR36–120months), and 45.3 (IQR36–120months) for IBCDT, MMF and CYC, respectively. At their last follow-up visit, we observed no significant differences in proteinuria and serum creatinine, nor in the frequency of new flares among the three groups.

Conclusion: In biopsy proven LN, the IBCDT without further immunosuppressive maintenance therapy was shown to be as effective as conventional regimen of MMF or CYC followed by a 3-year maintenance MMF regimen. Moreover, the use of IBCDT was associated with a marked reduction of glucocorticoid cumulative dose.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3803

SLE, Sjögren's and APS - clinical aspects (other than treatment)

POS0705 BILAG-2004 INDEX ACTIVE DISEASE PREDICTS DEVELOPMENT OF DAMAGE

C. S. Yee[1], V. Farewell[2], M. Akil[3], P. Lanyon[4], C. J. Edwards[5], D. Isenberg[6], A. Rahman[6], L. S. Teh[7], S. Tosounidou[8], R. Stevens[1], A. Prabu[9], B. Griffiths[10], N. Mchugh[11], I. N. Bruce[12], Y. Ahmad[13], M. Khamashta[14], C. Gordon[9]on behalf of British Isles Lupus Assessment Group (BILAG). [1]*Doncaster & Bassetlaw Teaching Hospitals NHS Foundation Trust, Department of Rheumatology, Doncaster, United Kingdom*; [2]*University of Cambridge, MRC Biostatistics Unit, Cambridge, United Kingdom*; [3]*Sheffield Teaching Hospitals NHS Foundation Trust, Department of Rheumatology, Sheffield, United Kingdom*; [4]*Nottingham University Hospitals NHS Trust, Department of Rheumatology, Nottingham, United Kingdom*; [5]*University Hospital Southampton NHS Foundation Trust, Department of Rheumatology, Southampton, United Kingdom*; [6]*University College London, Centre for Rheumatology Research, London, United Kingdom*; [7]*Royal Blackburn Hospital, Department of Rheumatology, Blackburn, United Kingdom*; [8]*Sandwell and West Birmingham Hospitals NHS Trust, Department of Rheumatology, Birmingham, United Kingdom*; [9]*University of Birmingham, Rheumatology Research Group, Birmingham, United Kingdom*; [10]*Newcastle upon Tyne Hospitals NHS Foundation Trust, Department of Rheumatology, Newcastle, United Kingdom*; [11]*Royal National Hospital for Rheumatic Diseases NHS Trust, Department of Rheumatology, Bath, United Kingdom*; [12]*The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [13]*Betsi Cadwaldr University Health Board, Department of Rheumatology, Wales, United Kingdom*; [14]*Guy's and St Thomas' NHS Foundation Trust, Department of Rheumatology, London, United Kingdom*

Background: BILAG-2004 Index (BILAG-2004) has undergone construct and criterion validity and is used to assess disease activity in SLE. However, its predictive validity has yet to be established.

Objectives: This study was to determine if disease activity according to BILAG-2004 was predictive of development of damage in an inception cohort.

Methods: This was a prospective multi-centre longitudinal study in the UK of an inception cohort of SLE patients (recruited within 12 months of achieving 1997 ACR revised criteria for SLE). Data were collected on disease activity (BILAG-2004 and BILAG2004-Pregnancy Index during pregnancy), SLICC/ACR DI (SDI), cumulative drug exposure and death at every visit. Information on cardiovascular risk factors (hypertension, diabetes mellitus, hypercholesterolaemia and smoking status) and antiphospholipid syndrome status were also collected. This study ran from 1st January 2005 to 31st December 2017. Longitudinal analysis using Poisson regression with random effects model was used to determine predictors of development of new damage. Death was not included in the analysis due to small numbers.

Results: 273 patients were recruited (91.2% female, 59.3% Caucasian, 17.2% African/Caribbean, 17.2% South Asian) with mean age at recruitment of 38.5 years (SD 14.8). 97.8% had no damage at recruitment (2.2% had SDI score of 1). Median follow-up was 73.4 months (range: 1.8, 153.8) with total follow-up of 1767 patient-years. Prevalence of risk factors during follow-up were: hypertension 23.1%, hypercholesterolaemia 35.5%, diabetes mellitus 5.5%, smoker or ex-smoker 44% and antiphospholipid syndrome 7%. There were 13 deaths and 114 new damage items occurred during follow-up.

There were 6674 assessments with disease activity score: 293 assessments with Grade A activity in 95 patients (92.4% had only 1 system with grade A, range: 1 - 4) and 1704 assessments with Grade A or B activity in 239 patients (78.7% had only 1 system with Grade A or B, range: 1 - 5).

Univariate analysis showed that gender, cardiovascular risk factors, antiphospholipid syndrome and most drug exposure (except hydroxychloroquine, glucocorticoids, mycophenolate and cyclophosphamide) were not associated with new damage (they were not included in the multivariate analysis).

Table 1 summarises multivariate analysis. Similar results were obtained when the disease activity variable was changed to Number of Systems with Grade A per assessment (RR 2.04 with 95% CI: 1.05, 3.94). Analysis using BILAG-2004 systems tally showed that persistent minimal disease was protective of development of damage (RR 0.74 with 95% CI: 0.57, 0.95). Cumulative drug exposure since recruitment for mycophenolate was protective against new damage (RR 0.99 with 95% CI 0.99, 0.99) but not cumulative drug exposure since last visit.

Variable	Risk Ratio (95% CI) for New Damage
Ethnicity	
Afro-Caribbean	1.21 (0.68, 2.17)
South Asian	1.81 (0.97, 3.36)
Others	2.37 (0.68, 8.20)
Age at diagnosis	**1.06 (1.04, 1.08)**
Prior SDI score	0.69 (0.44, 1.08)
Constitutional A or B	unreliable estimate due to low numbers
Mucocutaneous A or B	**1.80 (1.04, 3.14)**
Neuropsychiatric A or B	**4.68 (1.68, 13.05)**
Musculoskeletal A or B	0.76 (0.33, 1.73)
Cardiorespiratory A or B	0.35 (0.05, 2.59)
GIT A or B	unreliable estimate due to low numbers
Ophthalmic A or B	unreliable estimate due to low numbers
Renal A or B	2.08 (0.99, 4.40)
Haematological A or B	**4.37 (1.15, 16.65)**
Hydroxychloroquine since last visit (per g)	**0.99 (0.98, 0.99)**
Prednisolone since last visit (per 100mg)	**1.01 (1.00, 1.02)**
Cyclophosphamide since last visit (per g)	1.42 (0.94, 2.14)

Conclusion: Active disease (Grade A or B) according to BILAG-2004 index is predictive of development of new damage in SLE patients.

REFERENCES:

[1] Yee C. S., et al. The BILAG-2004 systems tally – a novel way of representing the BILAG-2004 index scores longitudinally. Rheumatology (Oxford) 2012; 51[11]: 2099-2105.

Acknowledgements: Versus Arthritis and Vifor Pharma

Disclosure of Interests: Chee-Seng Yee Consultant of: Bristol Myers Squibb, ImmuPharma, Grant/research support from: Vifor Pharma, Vernon Farewell: None declared, Mohammed Akil: None declared, Peter Lanyon: None declared, Christopher John Edwards Consultant of: Glaxo Smith Kline, Roche, Grant/research support from: Glaxo Smith Kline, Roche, David Isenberg: None declared, Anisur Rahman: None declared, Lee-Suan Teh: None declared, Sofia Tosounidou: None declared, Robert Stevens: None declared, Ahtiveer Prabu: None declared, Bridget Griffiths: None declared, Neil McHugh: None declared, Ian N. Bruce: None declared, Yasmeen Ahmad: None declared, Munther Khamashta: None declared, Caroline Gordon Speakers bureau: UCB, Consultant of: Center for Disease Control, Astra-Zeneca, MGP, Sanofi and UCB

DOI: 10.1136/annrheumdis-2021-eular.9

POS0706 PERFORMANCES OF DIFFERENT CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN A SINGLE CENTER COHORT FROM TURKEY

E. S. Torun[1], E. Bektaş[2], F. Kemik[2], M. Bektaş[1], C. Cetin[1], Y. Yalçınkaya[1], B. Artim-Esen[1], A. Gül[1], M. Inanc[1]. [1]*Istanbul University Istanbul Medical Faculty, Departmemt of Rheumatology, Istanbul, Turkey*; [2]*Istanbul University Istanbul Faculty of Medicine, Department of Internal Medicine, Istanbul, Turkey*

Background: Recently developed EULAR/ACR classification criteria for systemic lupus erythematosus (SLE) have important differences compared to the 2012 Systemic Lupus International Collaborating Clinics (SLICC) SLE classification criteria and the revised 1997 American College of Rheumatology (ACR) criteria: The obligatory entry criterion of antinuclear antibody (ANA) positivity is introduced and a "weighted" approach is used[1]. Sensitivity and specificity of these three criteria have been debated and may vary in different populations and clinical settings.

Objectives: We aim to compare the performances of three criteria sets/rules in a large cohort of patients and relevant diseased controls from a reference center with dedicated clinics for SLE and other autoimmune/inflammatory connective tissue diseases from Turkey.

Methods: We reviewed the medical records of SLE patients and diseased controls for clinical and laboratory features relevant to all sets of criteria. Criteria sets/rules were analysed based on sensitivity, positive predictive value, specificity and negative predictive value, using clinical diagnosis with at least 6 months of follow-up as the gold standard. A subgroup analysis was performed in ANA positive patients for both SLE patients and diseased controls. SLE patients that did not fulfil 2012 SLICC criteria and 2019 EULAR/ACR criteria and diseased controls that fulfilled these criteria were evaluated.

Results: A total of 392 SLE patients and 294 non-SLE diseased controls (48 undifferentiated connective tissue disease, 51 Sjögren's syndrome, 43 idiopathic inflammatory myopathy, 50 systemic sclerosis, 52 primary antiphospholipid syndrome, 15 rheumatoid arthritis, 15 psoriatic arthritis and 20 ANCA associated

vasculitis) were included into the study. Hundred and fourteen patients (16.6%) were ANA negative.
Sensitivity was more than 90% for 2012 SLICC criteria and 2019 EULAR/ACR criteria and positive predictive value was more than 90% for all three criteria (Table 1). Specificity was the highest for 1997 ACR criteria. Negative predictive value was 76.9% for ACR criteria, 88.4% for SLICC criteria and 91.7% for EULAR/ACR criteria.
In only ANA positive patients, sensitivity was 79.6% for 1997 ACR criteria, 92.2% for 2012 SLICC criteria and 96.1% for 2019 EULAR/ACR criteria. Specificity was 92.6% for ACR criteria, 87.8% for SLICC criteria 85.2% for EULAR/ACR criteria.
Eleven clinically diagnosed SLE patients had insufficient number of items for both 2012 SLICC and 2019 EULAR/ACR criteria. Both criteria were fulfilled by 16 diseased controls: 9 with Sjögren's syndrome, 5 with antiphospholipid syndrome, one with dermatomyositis and one with systemic sclerosis.

Table 1. Sensitivity, positive predictive value, specificity and negative predictive value of 1997 ACR, 2012 SLICC and 2019 EULAR/ACR classification criteria

	SLE (+)	SLE (-)	Sensitivity (%)	Positive Predictive Value (%)	Specificity (%)	Negative Predictive Value (%)
1997 ACR	(+) **308**	15	78.6	95.4	94.9	76.9
	(-) 84	**279**				
2012 SLICC	(+) **357**	26	91.1	93.2	91.2	88.4
	(-) 35	**268**				
2019 EULAR/ ACR	(+) **368**	28	93.8	92.9	90.5	91.7
	(-) 24	**266**				

Conclusion: In this cohort, although all three criteria have sufficient specificity, sensitivity and negative predictive value of 1997 ACR criteria are the lowest. Overall, 2019 EULAR/ACR and 2012 SLICC criteria have a comparable performance, but if only ANA positive cases and controls are analysed, the specificity of both criteria decrease to less than 90%. Some SLE patients with a clinical diagnosis lacked sufficient number of criteria. Mostly, patients with Sjögren's syndrome or antiphospholipid syndrome are prone to misclassification by both recent criteria.

REFERENCES:

[1] Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Ann Rheum Dis* 2019;78:1151-1159.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.366

POS0707 SALIVARY GLAND ULTRASONOGRAPHY AND THE CLINICAL FEATURES USING ESSDAI IN PATIENTS OF EARLY-ONSET VERSUS LATE-ONSET WITH PRIMARY SJÖGREN'S SYNDROME

N. Hashimoto[1], S. Uchiyama[2], T. Nakazawa[3], T. Iwasaki[4], T. Hashimoto[1]. *[1]Hashimoto Rheumatology Clinic, Rheumatology, Osaka, Japan*; *[2]Kansai Medical University,Temmabashi General Clinic, Osaka, Japan*; *[3]Osaka Saiseikai Nakatsu Hospital, Department of Rheumatology, Osaka, Japan*; *[4]Keiseikai Medical Corporation, Department of Internal Medicine, Higashiosaka, Japan*

Background: Primary Sjögren's syndrome (pSS) is a chronic inflammatory autoimmune disease characterized by lymphocyte infiltration in salivary and lacrimal glands. pSS affects primarily middle-aged and elderly patients, although younger age groups may also be involved. However, differences of etiology and pathogenesis between early-onset pSS (EOpSS) and late-onset pSS (LOpSS) are unknown. Recently, standardized outcome tools for measuring disease-specific activity and patients' reported symptoms have been formulated by the European League Against Rheumatism (EULAR) SS study group: the EULAR SS Disease Activity Index (ESSDAI) for systemic features of pSS [1]. Also, as the new imaging techniques, salivary gland ultrasonography (SGUS) proved valuable for assessing salivary gland involvement in SS and seemed to exhibit good diagnostic properties. In addition, previous studies have demonstrated usefulness of SGUS for the prognostic stratification of patients with pSS [2], [3], [4].
Objectives: The aim of this study was to examine the differences of etiology and pathogenesis between EOpSS and LOpSS using ESSDAI and SGUS.
Methods: Fifty-six pSS patients who fulfilled the American College of Rheumatology (ACR) / European League Against Rheumatism (EULAR) classification criteria for SS were studied. Based on the disease onset age, all pSS patients were divided into two groups as those with the onset age of 40 years old or younger (EOpSS: n=26) and those with the onset age of older than 65 years old (LOpSS: n=30). The clinical findings were evaluated ESSDAI and OMERACT SGUS score at the first visit to our hospital. The ESSDAI (0–123) proposes the evaluation of 12 domains or organ systems (constitutional, lymphadenopathy, glandular, articular, cutaneous, pulmonary, renal, peripheral nervous system, central nervous system, muscular, hematological and biology). All patients were examined SGUS by a single investigator who was blinded to device (TUS-A300; Canon Medical Systems, Tokyo, Japan) with a linear transducer (7.5-10MHz). The OMERACT SGUS score was used for graded changes in the parenchymal homogeneity of salivary glands: grade 0, normal-appearing salivary gland parenchyma; grade 1, minimal change: mild inhomogeneity without hypo/anechoic areas; grade 2, moderate change: moderate inhomogeneity with focal hypo/anechoic areas; grade 3, severe change: diffuse inhomogeneity with hypo/anechoic areas occupying the entire gland surface [5].
Results: The proportions of positive sera of RF, anti-SS-A and anti-SS-B antibodies were not different in the two groups, but the disease activities were higher in the EOpSS than in the LOpSS patients by measuring ESSDAI (7.30 vs 4.23, p=0.008), especially in constitutional domain (1.50 vs 0.60, p=0.03), articular domain (1.54 vs 0.40, p=0.0002) and biological domain (1.35 vs 0.90, p=0.04). No difference in salivary secretion was found between two groups (EOpSS: 8.02 vs LOpSS: 6.31 mL/10min.), but the OMERACT SGUS score was higher in LOpSS than in EOpSS patients (2.00 vs 2.70, p=0.0002).
Conclusion: Although serological findings were not different, EOpSS patients had higher disease activity but less severe salivary gland degeneration than that in LOpSS patients, suggesting the pathogenesis of these two groups was different.

REFERENCES:

[1] Seror R, et al. Ann Rheum Dis. 2010 Jun;69(6):1103-9.
[2] Arthritis Care Res (Hoboken). 2014 Jul;66(7):1102-7.
[3] Hammenfors DS, et al. Clin Exp Rheumatol. 2015 Jan-Feb;33(1):56-62.
[4] Milic V, et al. PLoS One. 2019 Dec 31;14(12): e0226498.
[5] Jousse-Joulin S, et al. Ann Rheum Dis. 2019 Jul;78(7):967-973.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.419

POS0708 PSYCHIATRIC DISORDERS IN PATIENTS WITH DIFFERENT PHENOTYPES OF NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (NPSLE)

R. Monahan[1], A. Blonk[2], H. Middelkoop[3], M. Kloppenburg[1,4], T. Huizinga[1], N. Van der Wee[2], G. M. Steup-Beekman[1]. *[1]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; *[2]Leiden University Medical Center, Department of Psychiatry, Leiden, Netherlands*; *[3]Leiden University Medical Center, Department of Neurology, Leiden, Netherlands*; *[4]Leiden University Medical Center, Department of Clinical Epidemiology, Leiden, Netherlands*

Background: Patients with systemic lupus erythematosus (SLE) may present with psychiatric disorders. These are important to recognize, as they influence quality of life and treatment outcomes and strategies.
Objectives: We aimed to study the frequency of psychiatric morbidity as classified by the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) in patients with SLE and neuropsychiatric symptoms of different origins.
Methods: In the neuropsychiatric SLE (NPSLE) clinic of the Leiden University Medical Center, patients undergo a standardized multidisciplinary assessment by a neurologist, neuropsychologist, vascular internal medicine, rheumatologist, physician assistant and psychiatrist. After two weeks, a multidisciplinary consensus meeting takes place, in which the symptoms are attributed to SLE requiring treatment (major NPSLE) or to minor involvement of SLE or other causes (minor/non-NPSLE). Consecutive patients visiting the NPSLE clinic between 2007-2019 were included. Data of psychiatric evaluation and current medication use were extracted from medical records. The presence of cognitive dysfunction was established during formal neuropsychological assessment.
Results: 371 consecutive SLE patients were included, of which 110 patients had major NPSLE (30%). Mean age was 44 ± 14 years and 87% was female.
The most frequently diagnosed psychiatric disorders in the total group were cognitive dysfunction (42%) and depression (23%), as shown in Table 1. Furthermore, anxiety was present in 5% and psychotic disorders in 4% of patients. In patients with minor/non-NPSLE, especially depression (26% vs 15%) and anxiety (6% vs 2%) were more common than in major NPSLE. Cognitive dysfunction (54% vs 36%) and psychotic disorders (6% vs 4%) were more common in patients with major NPSLE than minor/non-NPSLE.
Psychiatric medication was used in 33% of patients, of which antidepressants and benzodiazepines the most frequently (both: 18% in both subgroups). Antipsychotics were more often used in patients with NPSLE (10% vs 7%) and benzodiazepines more often in minor/non-NPSLE (20% vs 14%).
In addition, 17 patients (5%) had a history of suicide attempt, which was more common in patients with minor/non-NPSLE than major NPSLE (6% vs 2%).
Conclusion: Psychiatric morbidity, especially cognitive dysfunction and depression, are common in patients with lupus and differ between underlying cause of the neuropsychiatric symptoms (minor/non-NPSLE vs major NPSLE).

Table 1. Presence of psychiatric diagnoses in patients with SLE and neuropsychiatric symptoms

	All patients (n = 371)	Minor/ non-NPSLE (n = 261)	Major NPSLE (n = 110)
DSM V diagnosis, n (%)			
Neurodevelopmental disorder	5 (1)	2 (1)	3 (2)
Schizophrenia Spectrum and Other Psychotic Disorders	16 (4)	10 (4)	6 (6)
Bipolar and related disorders	7 (2)	5 (2)	2 (2)
Depressive disorders	84 (23)	68 (26)	16 (15)
Anxiety disorders	17 (5)	15 (6)	2 (2)
Obsessive-Compulsive and Related Disorders	1 (0)	1 (0)	0 (0)
Trauma- and Stressor-Related Disorders	16 (4)	12 (5)	4 (3)
Dissociative Disorders	2 (1)	2 (1)	0 (0)
Somatic Symptom and Related Disorders	1 (0)	1 (0)	0 (0)
Feeding and Eating Disorders	0 (0)	1 (0)	0 (0)
Elimination Disorders	0 (0)	0 (0)	0 (0)
Sleep-wake disorders	2 (1)	2 (1)	0 (0)
Sexual dysfunctions	0 (0)	0 (0)	0 (0)
Gender dysphoria	0 (0)	0 (0)	0 (0)
Disruptive, Impulse-Control, and Conduct Disorder	0 (0)	0 (0)	0 (0)
Substance-related and addictive disorders	9 (2)	8 (3)	1 (1)
Cognitive dysfunction	154 (42)	95 (36)	59 (54)
Personality disorders	10 (3)	9 (3)	1 (1)
Paraphilic disorders	0 (0)	0 (0)	0 (0)
Other mental disorders	12 (3)	7 (3)	5 (5)
Medication-Induced Movement Disorders and Other Adverse Effects of Medication	0 (0)	0 (0)	0 (0)
Unknown	3 (1)	3 (1)	0 (0)

NPSLE = neuropsychiatric systemic lupus erythematosus.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.423

POS0709 LUPUS FOG IS NOT DISSOCIATIVE FOG

R. Monahan[1], A. Blonk[2], H. Middelkoop[3], M. Kloppenburg[1,4], T. Huizinga[1], N. Van der Wee[2], G. M. Steup-Beekman[1]. [1]*Leiden University Medical Center (LUMC), Department of Rheumatology, Leiden, Netherlands*; [2]*Leiden University Medical Center, Department of Psychiatry, Leiden, Netherlands*; [3]*Leiden University Medical Center, Department of Neurology, Leiden, Netherlands*; [4]*Leiden University Medical Center, Department of Clinical Epidemiology, Leiden, Netherlands*

Background: The presence of a 'fog' is frequently reported by patients with systemic lupus erythematosus (SLE). However, little is known about this lupus fog: it is thought to be a result of cognitive dysfunction, but fogs can also be the result of dissociation. The Dissociative Experience Scale-II (DES) is a standardized tool to study dissociation. In the general adult population, scores range from 4.4-14.[1-3]
Objectives: We aimed to study the prevalence of dissociative symptoms including dissociative fog in patients with SLE and neuropsychiatric symptoms.
Methods: Patients visiting the tertiary referral center for neuropsychiatric systemic lupus erythematosus (NPSLE) of the LUMC between 2007-2019 were included. All patients underwent a standardized multidisciplinary assessment. Patients were classified as NPSLE if neuropsychiatric symptoms were attributed to SLE and immunosuppressive or anticoagulant therapy was initiated, otherwise patients were classified as minor/non-NPSLE. Dissociation was studied using the DES. The DES separates different types of dissociative symptoms: amnesia, absorption/imagination and derealization/depersonalization. It also contains one question regarding evaluating the presence of a dissociative fog: *"Some people sometimes feel as if they are looking at the world through a fog, so that people and objects appear far away or unclear".* All statements (n = 28) regarding dissociative symptoms are rated from 'none of the time' to 'all of the time' (0-100%); scores >25 are considered abnormal. A multiple regression analysis (MRA) were performed to compare dissociation in patients with and without NPSLE. DES results are presented as median (range) and MRA as odds ratio (OR) and 95% confidence interval (CI).
Results: DES questionnaires were available for 337 patients, of which 97 had the diagnosis NPSLE (29%). Mean age in patients with NPSLE was 41 ± 13 years and 84% was female. In minor/non-NPSLE, median age was 44 ± 14 years and 87% was female.
Median dissociation was 7 (0-75) and did not differ between patients with minor/non-NPSLE and NPSLE (OR: 1.0 (95% CI: -0.9; 1.1)). The most common type of dissociation was absorption/imagination (median: 12, range 0-75) and depersonalization/derealization was infrequent (median: 1, range 0-84). 43 patients (13%) had an abnormal score (>25) on the dissociative fog question.
Conclusion: Dissociative symptoms are within normal range in patients with SLE and neuropsychiatric symptoms, regardless of underlying etiology. Dissociative fog seems uncommon and therefore lupus fog is most likely not the result of dissociation.

REFERENCES:
[1] Bernstein EM and Putnam FW. Development, reliability, and validity of a dissociation scale. J Nerv Ment Dis 1986; 174: 727-735. 1986/12/01. DOI: 10.1097/00005053-198612000-00004.
[2] Maaranen P, Tanskanen A, Honkalampi K, et al. Factors associated with pathological dissociation in the general population. Aust N Z J Psychiatry 2005; 39: 387-394. 2005/04/30. DOI: 10.1080/j.1440-1614.2005.01586.x.
[3] van IJzendoorn MH and Schuengel C. The measurement of dissociation in normal and clinical populations: Meta-analytic validation of the Dissociative Experiences Scale (DES). Clinical Psychology Review 1996; 16: 365-382. DOI: 10.1016/0272-7358(96)00006-2.

Table 1. Presence of dissociation in patients with SLE and neuropsychiatric symptoms

	Total cohort (n = 337)	Minor/non-NPSLE (n = 240)	NPSLE (n = 97)
DES (median, range)			
Total questionnaire	7 (0 - 75)	8 (0 - 66)	6 (0 – 75)
Amnesia	5 (0 - 76)	5 (0 - 68)	4 (0 - 76)
Absorption/imagination	12 (0 – 75)	13 (0 – 75)	10 (0 – 73)
Depersonalization/derealization	1 (0 – 84)	1 (0 – 73)	1 (0 – 84)
Dissociative fog*	0 (0-100)	0 (0-100)	0 (0-100)

DES = Dissociative Experience Scale *NPSLE* = neuropsychiatric systemic lupus erythematosus.*Dissociative fog is question 28 of the DES-II

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.424

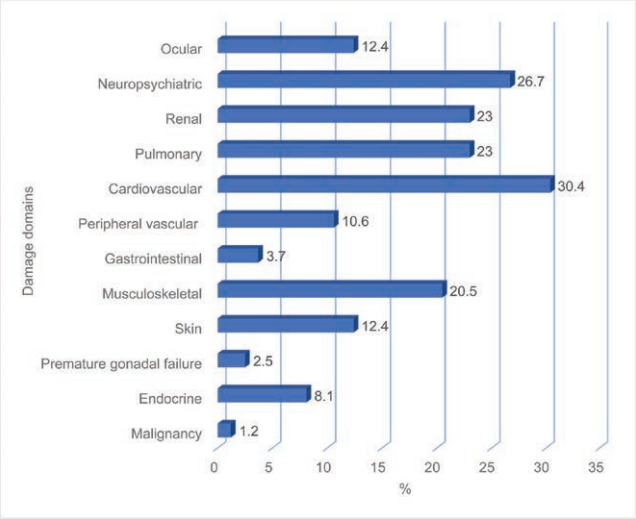
POS0710 ANALYSIS OF 5-YEAR HOSPITALIZATION DATA OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DAMAGE IS A RISK FACTOR FOR FREQUENT AND LONGER STAYS

C. Cetin[1], M. G. Can[2], S. Oztaskin[2], Y. Yalçınkaya[1], A. Gül[1], M. Inanc[1], B. Artim-Esen[1]. [1]*Istanbul Faculty of Medicine, Rheumatology, İstanbul, Turkey*; [2]*Istanbul Faculty of Medicine, Internal Medicine, İstanbul, Turkey*

Background: The rates of hospitalization in patients with SLE is around 10% per year.[1]
Objectives: In this study, we aimed to examine the hospitalization data of patients with SLE in the last 5 years at our center and determine the factors that affect hospitalization.
Methods: Hospitalization data of patients with SLE (2012 SLICC classification) admitted to our rheumatology ward between January 2015 and 2020 were analyzed. Cumulative clinical and laboratory findings were retrieved from the existing SLE database and revised. SLICC SLE damage index (SDI), and the disease activity at admission were determined (SLEDAI-2K).
Results: Eighty-six % (n=138) of 161 hospitalized patients were female. The mean age of the patients was 38 ± 13 years whilst mean duration of disease was 97.3 ±96.9 months. Thirty-eight% of the patients were hospitalized more than once and the mean number of hospitalizations was 1.8±1.5 The mean hospitalization duration covering all stays for each patient was 25±27 days. Active disease followed by infection and damage-related complications ranked the first three among all causes of hospitalization.
Compared to patients hospitalized for active disease or other reasons, patients hospitalized for infection had a significantly higher number of readmissions (**p<0.05)** and their total duration of hospitalization was longer **(p<0.01**). Duration of disease was significantly shorter in patients hospitalized for active disease compared to patients hospitalized for infection and damage related causes (p<0.05).
The frequency of patients with damage and the mean SDI score was significantly lower in the group with active disease (68% and 1.9 ± 2) compared to patients hospitalized for infection (90% and 2.7±1.6) and other causes (96% and 3±1.7) (p<0.05 for both). Distribution of damage according to organ/systems is presented in Graph 1. Highest frequency of damage was detected in the cardiovascular (30%), followed by neuropsychiatric (26.7%), renal (23%), pulmonary (23%) and musculoskeletal (20.5%) domains. A positive correlation was found between the mean SDI score and duration of hospitalization (r=0.551, **p<0.001**) as well as the number of hospitalizations (r=0.393, **p<0.001**). Regarding disease activity at the time of admission, the mean score of patients hospitalized for active disease was 11.0 ± 6.1 whilst was 3.2 ± 2.8 in patients hospitalized for infection and 2.9 ± 3.3 in patients hospitalized for other reasons (**p<0.001**). Renal active disease was the most common (44%), followed by hematological (34.8%), articular (21.7%) and mucocutaneous (21%) activity. Ten% of the patients all of whom had damage were admitted to intensive care unit (ICU). **Total hospitalization duration** (p=0.012), **mean SDI** (p=0.008), **antiphospholipid syndrome** (p=0.033), **lupus anticoagulant** (p=0.010), **thrombocytopenia** (p=0.015),

serositis (p=0.034), **pulmonary hypertension** (p=0.021), history of **alveolar haemorrhage** (p<0.001) and **cardiac valve involvement** (p=0.002) were associated with ICU hospitalization.

Conclusion: Disease activity, infections and damage are the leading causes of hospitalization in patients with SLE. Damage increases the frequency of hospitalizations, prolongs the duration of stay, and increases the need for follow-up in the ICU. Tight control of disease activity with rational use of immunosuppressive treatment is important to reduce damage and hospitalizations.



Graphic 1. Distribution of damage according to organs/systems in hospitalized patients

REFERENCES:

[1] Gu K, Gladman DD, Su J, Urowitz MB. Hospitalizations in patients with systemic lupus erythematosus in an academic health science center. The Journal of rheumatology 2017;44:1173-8.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.529

POS0711 SUICIDAL BEHAVIOUR IN SLE PATIENTS: A SYSTEMATIC LITERATURE REVIEW

A. Kyriakou[1], A. Chatzittofis[1], K. Parperis[1,2]. [1]*University of Cyprus, Medical School, Nicosia, Cyprus*; [2]*The University of Arizona College of Medicine - Phoenix, Rheumatology, Phoenix, United States of America*

Background: Previous studies have demonstrated that SLE patients have a higher risk of suicidal behaviour, including suicidal ideation, attempt and complete suicide (1,2). Data describing the SLE patients' clinical characteristics and risk factors of suicidal behaviour are lacking.

Objectives: To determine the magnitude of suicidal behaviour among SLE patients and to examine predictors associated with suicidal behaviour.

Methods: According to the PRISMA guidelines, we conducted a systematic literature review of the online databases, PubMed/Medline, EMBASE, and Web of Science, from inception to December 2020 (Figure 1). Full-text original articles that examined the relationship between SLE patients with suicidal behaviour were eligible for our review. Two reviewers independently review articles to assess eligibility using the Newcastle-Ottawa Scale and the Joanna Briggs Institute tools. Systematic reviews, metanalysis, narrative review, case reports, case series, including less than 10 patients and conference abstracts, were excluded.

Results: Of the 64 articles identified, 22 were relevant to the study question; cross-sectional (n=8) and prospective cohorts (n=6) were the most frequently retrieved studies. Among the 27106 SLE patients with SLE, 802 had suicidal behaviour (2.9%), and of those, 87.9% were female. Suicide attempt occurred in 573/802 (71.4%) and complete suicide in 18/802 (2,3%). Major depressive disorder (MDD) was the most frequently reported coexisting psychiatric condition associated with suicidal behavior, followed by psychosis and social phobia. Several clinical manifestations were linked to suicidal behaviour, particularly neuropsychiatric lupus, mucocutaneous, renal involvement and serositis. Further, high scores in disease activity and damage indices were associated with suicidal behaviour.

Conclusion: Suicidal behavior in SLE patients was associated with MDD, NPSLE, active disease and damage. Awareness of these findings can guide clinicians to recognize suicide behavior promptly and prevent suicide attempts.

REFERENCES:

[1] Hajduk A, Nowicka-Sauer K, Smoleńska Ż, Czuszyńska Z, Zdrojewski Z. Prevalence and correlates of suicidal thoughts in patients with neuropsychiatric lupus. Lupus. 2016 Feb;25(2):185-92. doi: 10.1177/0961203315603136.

[2] Buji RI, Abdul Murad NA, Chan LF, Maniam T, Mohd Shahrir MS, Rozita M, Shamsul AS, Mohamad Hussain R, Abdullah N, Jamal R, Nik Jaafar NR. Suicidal ideation in systemic lupus erythematosus: NR2A gene polymorphism, clinical and psychosocial factors. Lupus. 2018 Apr;27(5):744-752. doi: 10.1177/0961203317742711.

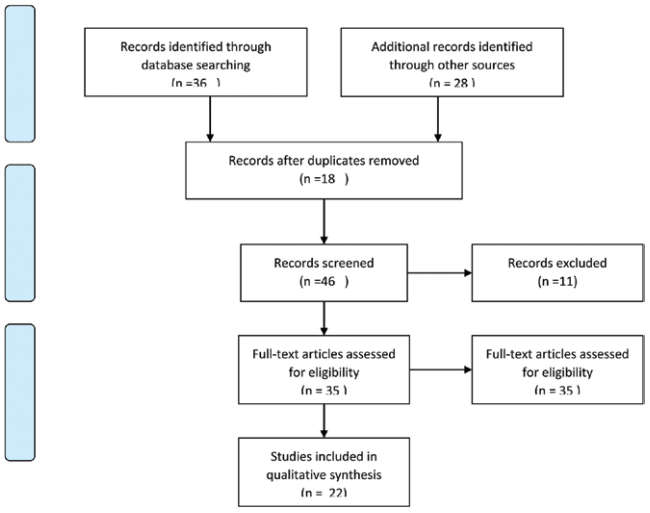


Figure 1. A PRISMA chart describing the inclusion/exclusion process

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.741

POS0712 "EXTRA"- CRITERIA ANTIPHOSPHOLIPID ANTIBODIES IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS (PRELIMINARY DATA)

F. Cheldieva[1,2], T. Reshetnyak[1,2], M. Cherkasova[1], N. Seredavkina[1], A. Lila[1,2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Vascular Rheumatology, Moscow, Russian Federation*; [2]*Russian Medical Academy of Continuing Professional Education, Ministry of Health of Russia, Department of Rheumatology, Moscow, Russian Federation*

Background: The study of antiphospholipid antibodies (aPL), not included in the Sydney diagnostic criteria, in antiphospholipid syndrome (APS) and systemic lupus erythematosus (SLE) is poorly understood.

Objectives: To determine the frequency of detection of IgA-aCL and IgA-aβ2GP1 and IgG antibodies to β2GP1 domain 1 (IgG-aβ2GP1-D1) in patients with APS with and without SLE.

Methods: ELISA and chemiluminescence assays (CMA) were used to test 63 sera of patients: 22 (35%) with primary APS (pAPS) and 41 (65%) patients with APS and with SLE (secondary APS (sAPS)), with mean age 38,0 [33,0 – 43,0] years and disease duration 4,0 [0,1 – 9,9]. Both methods were used to test of IgG/IgM-aCL and IgG/IgM-aβ2GP1. CMA was used for research IgG/IgM/IgA-aCL, IgG/IgM/IgA-aβ2GPI and IgG-aβ2GP1-D1. Of them 49 (78%) (18 – with pAPS; 31 – with sAPS) displayed major thrombotic events and 18 of 22 pregnant women had pregnancy morbidity in past history. Lupus anticoagulant (LA) positivity was in 9 out of 12 patients who had it determined. LA was not investigated due to anticoagulant therapy in the remaining 52 patients.

Results: IgG/IgM-aCL and IgG/IgM-aß2GP1 were recorded in 44/18 and 50/17 patients by ELISA and in 55/19 and 59/16 by CMA, respectively.

IgA-aCL positivity was found in 35 (56%) of 63 patients. Thirty IgA-positive patients were positive for IgG-aCL by ELISA: 22 – IgG-aCL – highly positive, 6 – medium positive and 2 – low positive patients. IgM-aCL by ELISA was detected in 13 (37%) of 35 IgA-aCL positive patients: 11 – highly positive, 1 – medium positive and 1 – low positive. IgA-aCL was combined with IgG-aCL in 34 patients and with IgM-aCL in 16 patients in the CMA. IgG-aß2GP1 in ELISA was detected in 32 patients with IgA-aCL (24 –highly positive, 5 – medium positive and 3 – low

positive) and in 34 – in CMA. IgM-aß2GP1 was combined with IgA-aß2GP1 with the same frequency in both methods (in 13 patients).
IgA-aß2GP1 was detected in 30 (48%) of 63 patients. They were combined with both IgG-aCL and IgG-aß2GP1 in all cases in both methods. IgM-aCL and IgM-aß2GP1 were detected in 14 and 11 of 30 patients with IgA-aß2GP1, respectively. The combination of IgA-aß2GP1 with IgG-aCL by ELISA was in 27 (in most cases highly positive – 20) and with IgM-aCL – in 10 (highly positive - 8). IgG-aß2GP1 was detected in 28 patients with IgA-aß2GP1 (high positive – 21) and in 11 patients with IgM-aß2GP1 (high positive –7).
IgG-aß2GP1-D1 was revealed in 48 (76%) patients. It was combined with IgG-aCL – in 38, with IgM-aCL – in 15 patients by the ELISA. The combination of IgG-aß2GP1-D1 by CMA was as follows: with IgG-aCL – in 46, with IgM-aCL – in 17, and with IgA-aCL – in 33 patients. In most cases, IgG-aß2gp1-D1 was combined with highly positive aCL levels. IgG-aß2GP1-D1 positivity was associated with IgG-aß2GP1 positivity in 42 – by ELISA and 47 – by CMA, IgM-aβ2GP1 – in 13 and 14 patients by ELISA and CMA, respectively, and IgA-aß2GP1 – in 29. Isolated IgG-aß2GP1-D1 positivity was not observed.
Conclusion: The frequency of IgA-aCL detection was 56% (35 patients out of 63), IgA-aβ2GP1 – 48% (30 patients out of 63), IgG-aβ2GP1-D1 – 76% (48 patients out of 63). There was not isolated positivity of this "extra" criterial antibodies. The presence of IgA-aCL, IgA-aβ2GP1, IgG-aβ2GP1-D1 was associated with highly positivity of IgG/IgM-aCL and IgG/IgM- aβ2GP1.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.818

POS0713 PREDICTORS OF HOSPITALIZATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A 10-YEAR COHORT STUDY OF 398 PATIENTS FROM A TERTIARY CENTRE

H. Assunção[1], M. Rodrigues[2], A. R. Prata3, J. A. P. Da Silva[1,4], L. Inês[1,5].
[1]Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal; *[2]Hospital Distrital de Leiria, Rheumatology, Leiria, Portugal*; *[1]Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal*; *[4]University of Coimbra, Coimbra Institute for Clinical and Biomedical Research (iCBR), Faculty of Medicine, Coimbra, Portugal*; *[5]University of Beira Interior, School of Health Sciences, Covilhã, Portugal*

Background: Patients with systemic lupus erythematosus (SLE) often require hospitalization. The cause of admission may vary, but active disease and infection are consistently reported as the main reasons for hospitalization and are associated with worse survival and damage accrual. Recent improvements in the standard of care, including minimization of glucocorticoid dose and more effective and safe immunosuppressive regimens, may have changed the incidence and risk factors for hospitalization due to these causes. Hence, it is useful to identify predictors of hospitalization to further reduce the risk of admission for disease activity and severe infection in patients with SLE.
Objectives: To identify predictors of hospitalization in patients with SLE, according to the underlying cause.
Methods: Patients with SLE fulfilling classification criteria (ACR'97 and/or SLICC), regularly followed at an academic lupus clinic from January 2009 to December 2020 and with at least two outpatient visits were included in this cohort study. Time to first hospitalization up to 120 months was identified separately for the following admission causes: (a) any cause; (b) active SLE; (c) infection. Predictors of hospitalization were sought through survival analysis, with distinct models for each of the major admission causes. Univariate analysis was performed using Kaplan-Meier curves and Log-Rank tests. Tested variables assessed at baseline included: gender; age at SLE onset; age; disease duration; SLE Disease Activity Index (SLEDAI-2K) score; ongoing antimalarial use; ongoing immunosuppressants; ongoing prednisolone daily dose; lupus nephritis up to baseline; SLICC Damage Index (SDI) score. Variables with p<0.1 were further tested in multivariate Cox regression models. Hazard ratios (HR) were determined with 95% confidence intervals (95%CI).
Results: We included 398 patients (female: 86.2%, mean age: 41.2±15.1 years, mean disease duration: 10.1±9.2 years; previous lupus nephritis: 28.9%; mean SLEDAI-2K score: 3.4±2.7; ongoing antimalarials: 78.9%; ongoing immunosuppressant: 29.9%; ongoing prednisolone >7.5 mg/day: 17.1%; SDI score ≥1: 28.4%). During the follow-up period, 50.5%, 23.6% and 17.3% were hospitalized at least once for any cause, active SLE or infection, respectively.
In the multivariate model, significant baseline predictors for hospitalization due to active disease were (table 1): SLEDAI-2K score >5; disease duration ≤2 years; ongoing immunosuppressants; SDI score ≥1. Baseline independent predictors of hospitalization for infection included (table 1): male gender; SDI score ≥1; ongoing antimalarials were protective.

Table 1. Predictors of hospitalization in multivariate Cox regression according to the admission cause

Predictors	Hospitalization for active SLE	Hospitalization for infection
SLEDAI-2K score >5	2.43 (1.53-3.88)	n.s.
SLE duration ≤2 years	1.70 (1.04-2.77)	n.s.
Ongoing immunosuppressant	1.91 (1.24-2.95)	n.s.
SDI score ≥1	1.82 (1.16-2.86)	2.14 (1.33-3.45)
Male gender	n.s.	2.19 (1.23-3.89)
No antimalarial treatment	n.s.	2.20 (1.34-3.60)

Risk for each predictor reported as Hazard Ratio (95% Confidence Interval); n.s.: non-significant

Conclusion: Tight control of disease activity, prevention of damage accrual, and treatment with antimalarials may contribute to minimize the risk of hospitalization for these two major causes of admission in patients with SLE.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.832

POS0714 WHITE MATTER HYPERINTENSITIES LEAD TO REDUCED PSYCHOMOTOR SPEED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND NEUROPSYCHIATRIC SYMPTOMS

R. Monahan[1], F. Inglese[2], H. Middelkoop[3], M. Van Buchem[2], T. Huizinga[1], M. Kloppenburg[1,4], I. Ronen[2], G. M. Steup-Beekman[1], J. De Bresser[2]. *[1]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; *[2]Leiden University Medical Center, Department of Radiology, Leiden, Netherlands*; *[3]Leiden University Medical Center, Department of Neurology, Leiden, Netherlands*; *[4]Leiden University Medical Center, Department of Clinical Epidemiology, Leiden, Netherlands*

Background: Cognitive impairment is common in patients with systemic lupus erythematosus (SLE) and neuropsychiatric (NP) symptoms, but the exact underlying structural brain correlates are unknown.
Objectives: We aimed to compare cognitive function between groups of patients with different phenotypes of (NP)SLE and assessed the association between brain volumes, white matter hyperintensity (WMH) volume and cognitive function.
Methods: Patients who visited the NPSLE clinic of the Leiden University Medical Center between 2007-2015 were included in this study (n=151; 42 ± 13 years, 91% female). In a multidisciplinary consensus meeting, phenotypes were established and neuropsychiatric symptoms were attributed to SLE (NPSLE, inflammatory (n=24) or ischemic (n=12)) or to minor involvement of SLE or other causes (minor/non-NPSLE (n=115)). All patients underwent standardized cognitive assessment of the four cognitive domains: global cognitive functioning (GCF), learning and memory (LM), executive functioning and complex attention (EFCA) and psychomotor speed (PS)). Cognitive dysfunction was defined as a T-score <40, with age, sex, gender and education matched individuals of the Dutch population as reference. In addition, automated volume measurements on brain MRI (white matter, grey matter, white matter hyperintensities (WMH) and total brain volume (TBV)) were performed. Patients with brain infarcts >1.5 cm were excluded. Cognitive function (Z-score) was compared between different NPSLE phenotypes using multiple regression analyses corrected for age, sex and education. Associations between brain volumes, WMH and cognitive function were assessed per phenotype using multiple regression analyses corrected for age, sex and intracranial volume.
Results: Global cognitive functioning was impaired in 5%, learning & memory in 46%, and executive functioning & complex attention in 39% and psychomotor speed in 46% of all patients. Patients with inflammatory NPSLE showed the most cognitive impairment and reduced cognitive function compared to ischemic NPSLE (all domains) and minor/non-NPSLE (EFCA) (p <0.05).
Lower total brain volume and grey matter volume were associated with lower cognitive functioning in all domains (β: 0.00/0.01 (0.00; 0.01)) and lower white matter volume associated with lower LM, EFCA and PS (β: 0.00/0.01 (0.00; 0.01)) in all patients. Higher WMH volume associated with lower psychomotor speed (β: -0.14 (-0.32; -0.02)), especially in patients with inflammatory NPSLE (β: -0.36 (-0.60; -0.12).
Conclusion: Reduced brain volume leads to reduced cognitive function in multiple cognitive domains in all patients with SLE and neuropsychiatric symptoms. Increased WMH volume leads to reduced psychomotor speed, especially in patients with inflammatory NPSLE.

Table 1. Prevalence of cognitive impairment in patients with minor/non-NPSLE, inflammatory NPSLE and ischemic NPSLE

	Global cognitive functioning	Learning & memory	Executive functioning & complex attention	Psychomotor speed
All patients	8 (5)	70 (46)	57 (39)	69 (46)
(n = 151) Inflammatory NPSLE	3 (13)	14 (58)	12 (50)	12 (50)
(n = 24) Ischemic NPSLE	0 (0)	6 (50)	2 (17)	2 (17)
(n = 12) Minor/non-NPSLE	5 (4)	50 (44)	43 (38)	55 (49)
(n = 115)				

NPSLE = neuropsychiatric systemic lupus erythematosus.Data represent n (%) of patients with cognitive impairment in the mentioned cognitive domain. Cognitive impairment was defined as cognitive function at least 1SD lower than the mean of an age, sex and education matched general Dutch population. The percentages were calculated from total number of patients with available scores: Global functioning: 23/24 inflammatory NPSLE and 113/115 minor/non-NPSLE; psychomotor speed 113/115 minor/non-NPSLE, executive function & complex attention: also 113/115. All tests were available for ischemic NPSLE.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.881

POS0715 QUANTIFYING THE PSYCHOSOCIAL IMPACT OF UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE (UCTD)

C. Siegel[1,2], E. Sevim[3,4], B. Stamm[5], J. Vega[5], J. Kleinman[6], J. Barnhill[7], M. Lockshin[2,5], L. Sammaritano[2,5], M. Barbhaiya[2,5]. *[1]Hospital for Special Surgery, Rheumatology, New York, United States of America*; *[2]Weill Cornell Medicine, Internal Medicine, New York, United States of America*; *[3]Montefiore Medical Center, Internal Medicine, Bronx, United States of America*; *[4]Albert Einstein College of Medicine, Internal Medicine, Bronx, United States of America*; *[5]Hospital for Special Surgery, Barbara Volcker Center for Women and Rheumatic Diseases, New York, United States of America*; *[6]Hospital for Special Surgery, Department of Social Work Programs, Division of Rheumatology, New York, United States of America*; *[7]Weill Cornell Medicine, Psychiatry, New York, United States of America*

Background: Only half of patients diagnosed with SLE fulfill classification criteria; the rest have "SLE-like" illnesses such as UCTD. SLE patients are known to experience impaired health-related quality of life (HRQoL) and significant anxiety, depression, and fatigue,[1] yet the psychosocial aspects of UCTD are less established. In a qualitative study, we found that most UCTD patients had engaged in psychotherapy and felt additional support was needed.[2]
Objectives: Using multiple validated instruments, this study aims to quantify the psychosocial impact of UCTD.
Methods: The Hospital for Special Surgery UCTD and Overlap Registry includes UCTD patients aged ≥ 18 years with ANA ≥ 1:80 and ≥ 1 sign or symptom of rheumatic disease who do not fulfill classification criteria for a defined CTD. We administered the 36-Item Short Form Health Survey (SF-36), General Anxiety Disorder-7 (GAD-7), Beck Depression Inventory (BDI), and Fatigue Severity Scale (FSS) to all patients to assess HRQoL, anxiety, depression, and fatigue. Instruments were scored based on established algorithms and results were summarized using predefined scales and severity thresholds.
Results: The composite questionnaire was administered to 85 UCTD patients and completed by 75 (97.3% female, 60% white, mean age ± SD 48.8 ± 13.6 years). The SF-36 Physical Component Summary mean score was 37.8 and Mental Component Summary mean score was 41.1. Across the 8 SF-36 subscales, mean scores were lowest for role limitations due to physical health (39.3) and vitality (39.7) and highest for physical functioning (67.2), role limitations due to emotional health (67.1), and mental health (67.1). Approximately half of UCTD patients reported anxiety (GAD-7 ≥ 6); 20% had moderate/severe anxiety (GAD-7 ≥ 10). The prevalence of depression (BDI ≥ 14) was 26.7%; 13.3% had moderate/severe depression (BDI ≥ 20). Fatigue (FSS ≥ 3) was reported by 82.8% of patients (median FSS score of 4.7) [Table 1].

Table 1. Psychosocial Survey Scores of Patients with Undifferentiated Connective Tissue Disease (n=75)

36-Item Short Form Health Survey (SF-36)	Physical Component Summary	38.2 (11.2)
	◦Physical functioning	67.2 (26.3)
	◦Role-Physical	39.3 (46.3)
*Range 1-100 – Mean (SD)**	◦Bodily Pain	49.5 (22.1)
	oGeneral Health	42.9 (21.5)
	Mental Component Summary	41.3 (10.7)
	◦Vitality	39.7 (21.7)
	◦Social Functioning	59.3 (25.9)
	◦Role-Emotional	67.1 (41.9)
	oMental Health	67.1 (18.3)
Generalized Anxiety Disorder-7 (GAD-7)	None [0-5]	38 (50.7)
	Mild [6-10]	22 (29.3)
	Moderate [11-15]	14 (18.7)
*Range 0-21 – N (%)***	Severe [16-21]	1 (1.3)
Beck Depression Inventory (BDI)	Minimal [0-13]	55 (73.3)
	Mild [14-19]	10 (13.3)
*Range 0-63 – N (%)***	Moderate [20-28]	7 (9.3)
	Severe [29-63]	3 (4.0)
Fatigue Severity Scale (FSS) *Range 1-7 – Median (IQR)***		4.7 (1.5)

*Higher number indicates better health state. **Higher number indicates greater severity.

Conclusion: UCTD patients have significantly impaired HRQoL and a high prevalence of anxiety, depression, and fatigue, suggesting substantial psychosocial impact of UCTD comparable to that reported in SLE.[3,4] Impaired HRQoL in UCTD is driven to similar degrees by aspects of physical and mental health. In future studies, we will compare age- and sex- matched UCTD to SLE patients and longitudinally evaluate psychosocial metrics alongside clinical trajectories.
REFERENCES:
[1] Dietz B, Katz P, Dall'Era M, et al. Major depression and adverse patient-reported outcomes in systemic lupus erythematosus: Results from a prospective longitudinal cohort. *Arthritis Care Res*. 2021;73(1):48-54.
[2] Siegel CH, Kleinman J, Barbhaiya M, et al. The psychosocial impact of undifferentiated connective tissue disease on patient health and well-being: A qualitative study. *J Clin Rheumatol*. In press.
[3] Gu M, Cheng Q, Wang X, et al. The impact of SLE on health-related quality of life assessed with SF-36: A systemic review and meta-analysis. *Lupus*. 2019;28(3):371-382.
[4] Zhang L, Fu T, Yin R, Zhang Q, Shen B. Prevalence of depression and anxiety in systemic lupus erythematosus: A systematic review and meta-analysis. *BMC Psychiatry*. 2017;17(1).
Acknowledgements: This project was supported by the Barbara Volcker Center for Women and Rheumatic Diseases and the Robin J. Sillau Memorial Research Fund for Connective Tissue Disease. Dr. Barbhaiya is supported by the Rheumatology Research Foundation Investigator Award.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.929

POS0716 FACTORS ASSOCIATED WITH FERTILITY OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW

S. Giambalvo[1], C. Garaffoni[1], E. Silvagni[1], F. Furini[2], M. Govoni[1], A. Bortoluzzi[1]. *[1]Unit of Rheumatology, Azienda Ospedaliera-Universitaria Sant'Anna, Department of Medical Sciences, University of Ferrara, Ferrara, Italy*; *[2]Unit of Rheumatology, Ospedale Maggiore, Bologna, Italy*

Background: Fertility is thought to be not reduced in women affected by systemic lupus erythematosus (SLE), however disease-related factors, psychosocial effects of chronic disease as well as medication exposure might impair gonadal function.
Objectives: The aim of this systematic review was to explore clinical, hormonal, serological, instrumental and management factors associated with fertility outcomes in women of childbearing age with SLE.
Methods: This systematic review was conducted following the Preferred Reporting Items for systematic reviews and Meta-analysis (PRISMA) statement. All articles available in English, published from 1972 to 15th August 2020 in Pubmed, EMBASE, Scopus and Cochrane Library. Study selection and data collection were performed by two independent reviewers. All data were extracted using a standardized template. Risk of bias of the included studies was assessed by using the NIH risk-of-bias tool [1].

Results: Of 788 abstracts, we included in the review 45 studies of which 1 systematic literature reviews, 16 cross-sectional studies, 15 cohort studies, 12 observational studies and 1 case-series study, with a total of 4656 patients. The mean age was 33.5 ± 5.4 years, while the mean disease duration was 97.4 ± 65.2 months. Figure 1 illustrates the quality of the included studies. Definitions of fertility/premature ovarian failure (POF) adopted in the studies varied in terms of the number of months of amenorrhea considered. Most studies did not use a hormonally based definition of fertility. Clinical factors associated with the development of POF were older age at the time initiation of therapy and older age at the onset of SLE disease. Cyclophosphamide exposure (CYC) and its cumulative dose influenced gonadal function in SLE women, leading to amenorrhoea and ovarian failure, as reported in 19 studies. Mycophenolate, azathioprine, calcineurin inhibitors and steroids seem to be associated with a lower risk of ovarian failure compared to CYC. 3 studies demonstrated that POF was more frequent in patients treated with CYC not receiving gonadotropin-releasing hormone analogues (GnRH) in comparison to those co-treated with GnRH. 11 studies evaluated the impact of damage and disease activity on ovarian reserve in patients with SLE with conflicting evidence. Finally, 18 studies investigated exposure to hormonal and serological factors able to influence fertility outcomes; among others nor Anti-Müllerian Hormone, neither anti-corpus luteum antibodies were associated with POF.

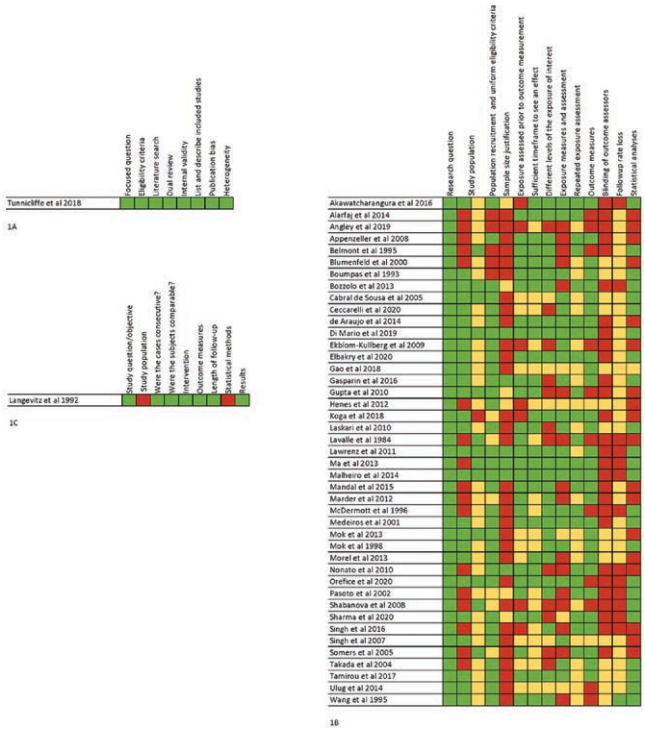
Conclusion: The role of disease activity on fertility in SLE patients is contradictory. Regarding management factors associated with fertility in SLE women of childbearing age, the strongest evidence is about the treatment with CYC and its cumulative dose. Hormonal and serological factors did not impact on fertility outcome but might be used as a surrogate of fertility, especially after treatment with disease-specific drugs.

REFERENCES:

[1] Study Quality Assessment Tools NIH. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools.

[2] Andreoli L. et al. EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome. Ann Rheum Dis. 2017; 76: 476–485.

Figure 1 - Risk of bias graph: review authors' judgements about each risk of bias using NIH risk-of-bias tool. 1A: systematic literature review/meta-analysis; 1B: observational studies; 1C: case series; green box = "yes/low risk of bias"; yellow box = "not applicable/not reported"; red box = "no/potential risk of bias"



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.937

POS0717 AUTOIMMUNE LIVER DISEASE IN ANTICENTROMERE ANTIBODY POSITIVE PRIMARY SJOGREN'S SYNDROME

B. Chalcev[1], A. Torgashina[1], E. Sokol[1], J. Khvan[1], V. Vasiliev[2], S. Palshina[3]. *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Intensive Care of Rheumatic Diseases, Moscow, Russian Federation*; *[2]MEDSI, Department of Rheumatic Diseases, Moscow, Russian Federation*; *[3]Clinic of Heart and Joint Diseases, Department of Rheumatic Diseases, Moscow, Russian Federation*

Background: studies have shown that anticentromere antibody (ACA) positivity in primary Sjogren's syndrome (pSS) is associated with autoimmune liver diseases, most often primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) [1, 2, 3], but detailed characteristics of the frequency and severity of liver disease in these patients is not presented in the literature.

Objectives: to identify the frequency, structure and characterize the course of autoimmune liver diseases in pSS+ACA.

Methods: we observe 82 patients with pSS+ACA. The diagnosis of pSS was established on the basis of Russian 2001 criteria, SSc was excluded based on the ACR/EULAR 2013 criteria [4]. 18 of 82 patients (22%) had a persistent increase in alkaline phosphatase, 11 of them were positive for antimitochondrial antibodies (AMA) and, according to the recommendations of the American Association for the Study of Liver Diseases [5], they were diagnosed with PBC. 7 of 18 patients were AMA-negative, 2 of them had a liver biopsy and the diagnosis of AMA-negative PBC was confirmed, 4 patients who did not have a liver biopsy and 1 patient with hepatitis B were excluded from the study. Also, in 6 of 64 patients without signs of liver damage, an increase in AMA was detected, in 1 of them a liver biopsy was performed and the diagnosis of PBC was confirmed. Thus, the group of patients with pSS+ACA and autoimmune liver diseases included 19 patients: 12 patients with AMA-positive PBC, 2 patients with AMA-negative PBC, and 5 patients with asymptomatic AMA positivity.

Results: The median follow-up for 19 patients with pSS+ACA and autoimmune liver diseases was 4 years. AMA were detected in 89.5% of patients, an increase in IgM - in 42.1%, an increase in ALT / AST - 63.2%, a decrease in albumin, prothrombin index and cytopenia - 15.8% (were associated with the development of liver cirrhosis). In most cases, the clinical course of liver disease was characterized by an asymptomatic, slowly progressing course, with no signs of progression during observation. Cirrhosis and portal hypertension were detected in 15.8% of patients, hepatic encephalopathy - in 10.5%. Liver biopsy was performed in 9 patients, PBC was diagnosed in all cases (overlap syndrome with AIH was established in 3 cases). Assessment of PBC histological stages showed signs of stage 1 in 5 patients, stage 2 in 1 patient, stage 3 in 3 patients. Observation of 5 patients with stage 1 PBC and 5 AMA-positive patients without signs of liver damage (median follow-up was 2 years), showed the absence of clinical, laboratory and instrumental progression of liver disease, which is why we believe that these patients have epithelitis of the biliary ducts as manifestation of glandular lesions in pSS, but not PBC.

Conclusion: autoimmune liver diseases in pSS+ACA are detected in 23.2% of patients, most of whom develop PBC and epitheliitis of the biliary ducts with the same frequency, less often overlap syndrome of PBC and AIH, and characterized by a mild, slowly progressing course and rarely lead to liver cirrhosis.

REFERENCES:

[1] Masako Kita et al. Abnormal Liver Function in Patients with Sjogren's Syndrome. Acta Med. Nagasaki 41: 31-37.

[2] Baldini, Chiara et al. "Overlap of ACA-positive systemic sclerosis and Sjögren's syndrome: a distinct clinical entity with mild organ involvement but at high risk of lymphoma." *Clinical and experimental rheumatology* vol. 31,2 (2013): 272-80.

[3] Bournia, Vasiliki-Kalliopi K et al. "Anticentromere antibody positive Sjögren's Syndrome: a retrospective descriptive analysis." *Arthritis research & therapy* vol. 12,2 (2010): R47. doi:10.1186/ar2958.

[4] van den Hoogen, Frank et al. "2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism collaborative initiative." *Arthritis and rheumatism* vol. 65,11 (2013): 2737-47. doi:10.1002/art.38098.

[5] Lindor, Keith D et al. "Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases." *Hepatology (Baltimore, Md.)* vol. 69,1 (2019): 394-419. doi:10.1002/hep.30145.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.949

POS0718 CLINICAL CHARACTERISTICS ASSOCIATED WITH GLANDULAR INVOLVEMENT EVALUATED BY SALIVARY GLAND ULTRASONOGRAPHY IN SJÖGREN'S SYNDROME

T. Shimizu[1], H. Nakamura[1], Y. Takagi[2], S. Y. Nishihata[1], R. Sumiyoshi[1], T. Igawa[1], T. Koga[1], S. Y. Kawashiri[1], N. Iwamoto[1], K. Ichinose[1], M. Tamai[1], T. Origuchi[1], A. Kawakami[1]. *[1]Nagasaki University Graduate School of Biomedical Sciences, Department of Immunology and Rheumatology, Nagasaki, Japan*; *[2]Nagasaki University Graduate School of Biomedical Sciences, Department of Radiology and Cancer Biology, Nagasaki, Japan*

Background: Sjögren's syndrome (SS) is a systemic autoimmune disease characterized by periductal lymphocytic infiltration of the salivary and lacrimal glands, which results in reduced secretory functions and oral and ocular dryness (1). In addition, patients often have extraglandular manifestations, such as interstitial pneumonia and interstitial nephritis, and the appearance of autoantibodies such as anti-Ro/SS-A and La/SS-B antibodies. Salivary gland ultrasonography (SGUS) is typically used to evaluate the findings of salivary glands; thus, we can evaluate the severity of salivary gland disorders due to SS using SGUS in real time (2).
Objectives: To identify clinical indices, including disease activity, associated with glandular involvement evaluated using SGUS in patients with SS.
Methods: We enrolled patients with SS (n=115) and non-SS sicca subjects (n=90) who visited Nagasaki University Hospital between 1995 and 2019. The patients' SS classifications were based on the 2002 American–European Consensus Group (AECG) SS classification criteria (3). The non-SS sicca subjects exhibited sicca symptoms but did not fulfill the AECG SS classification criteria. SGUS and clinical indices such as age, sex, the focus score (FS), sicca symptoms, the Saxon test results, Schirmer's test results, anti-SS-A/Ro antibody positivity, anti-SS-B/La antibody positivity, anti-centromere antibody (ACA) positivity, serum immunoglobulin G levels, and the clinical European League Against Rheumatism SS disease activity index were examined. The ultrasonography (US) score was calculated based on SGUS imaging (hypoechoic area, hyperechoic band, and irregular border) (4).
Results: The US score was significantly higher in patients with SS than that in non-SS sicca subjects. In addition, we found significant correlations between the US score and FS in patients with SS. Multivariate analysis revealed the FS, Saxon test positivity, and ACA positivity as the variables independently associated with the US score in patients with SS. These results were the same in the primary SS patient group (n=96). Patients with ACA positivity had significantly higher US scores compared to those in patients with ACA negativity, whereas the FS was not significantly high. In addition, patients with ACA positivity had significantly greater positivity of hyperechoic bands than that in patients with ACA negativity.
Conclusion: This study indicated that ACA positivity, which is not reflected in sialadenitis of SS, is associated with the US score in patients with SS. These results suggest that US findings of patients with ACA positivity might show specific changes in salivary glands, such as fibrosis, and not only sialadenitis (5).
REFERENCES:
[1] Ramos-Casals M, Tzioufas AG, Font J. Primary Sjogren's syndrome: new clinical and therapeutic concepts. Ann Rheum Dis. 2005;64(3):347-54.
[2] van Ginkel MS, Glaudemans A, van der Vegt B, Mossel E, Kroese FGM, Bootsma H, et al. Imaging in Primary Sjogren's Syndrome. J Clin Med. 2020;9(8).
[3] Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, et al. Classification criteria for Sjogren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis. 2002;61(6):554-8.
[4] Takagi Y, Nakamura H, Sumi M, Shimizu T, Hirai Y, Horai Y, et al. Combined classification system based on ACR/EULAR and ultrasonographic scores for improving the diagnosis of Sjogren's syndrome. PLoS One. 2018;13(4):e0195113.
[5] Nakamura H, Kawakami A, Hayashi T, Iwamoto N, Okada A, Tamai M, et al. Anti-centromere antibody-seropositive Sjögren's syndrome differs from conventional subgroup in clinical and pathological study. BMC Musculoskelet Disord. 2010;11:140.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1110

POS0719 ADVERSE OUTCOMES AND REHOSPITALIZATION AFTER DELIVERY AMONG WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS OR RHEUMATOID ARTHRITIS AND THEIR INFANTS

J. Sabo[1], N. Singh[1], D. A. Crane[2], D. R. Doody[3], M. A. Schiff[4,5,6], B. A. Mueller[3,6]. *[1]University of Washington, Division of Rheumatology, Seattle, United States of America*; *[2]University of Washington, Department of Rehabilitation Medicine, Seattle, United States of America*; *[3]Fred Hutchinson Cancer Research Center, Public Health Sciences Division, Seattle, United States of America*; *[4]University of Washington, Department of Obstetrics and Gynecology, Seattle, United States of America*; *[5]University of New Mexico, Albuquerque, Division of Epidemiology, Biostatistics & Preventive Medicine, Albuquerque, United States of America*; *[6]University of Washington School of Public Health, Department of Epidemiology, Seattle, United States of America*

Background: Women with rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) have greater risk of adverse obstetric and birth outcomes than women without these conditions. Infant outcomes are less well-studied. It is unknown whether re-hospitalization after delivery occurs more often for affected mothers and their infants.
Objectives: We compared obstetric outcomes among women with and without RA or SLE, and birth outcomes among their infants. Maternal and infant rehospitalizations <2 years of delivery were also compared.
Methods: This population-based cohort study used linked birth-hospital discharge data from Washington State for 1987-2014. International Classification of Disease 9th revision (ICD9) codes identified all women with RA (ICD9 714.X, 725.X) and SLE (ICD9 710, 710.0, 710.1) in the hospital discharge record at delivery, and a 10:1 comparison group of women without these codes. Analyses were restricted to singleton live births (1,223 RA; 1,354 SLE). Poisson regression with robust standard errors estimated relative risks (RR) and 95% confidence intervals (CI) for selected outcomes, accounting for delivery year, maternal age, and parity.
Results: Many adverse outcomes were more common among RA and SLE cases than among comparison women. Preeclampsia occurred more often during pregnancies of women with RA (RR 1.42, 95% CI 1.17-1.71) or SLE (RR 2.33, 95% CI 2.01-2.70), as did preterm rupture of membranes (PROM, RR 2.85, 95% CI 2.20-3.72 for RA; RR 3.28, 95% CI 2.54-4.23 for SLE). Cesarean deliveries were more common among nulliparous women in both groups (RR 1.32, 95% CI 1.18-1.48 for both conditions). Infants of women with RA or SLE were more likely to weigh <2500 g (RR 2.08, 95% CI 1.72-2.52 for RA; RR 4.88, 95% CI 4.27-5.58 for SLE), be small for gestational age (RR 1.25, 95% CI 1.07-2.50; RR 2.30; 2.04-2.59, respectively), delivered at <32 weeks gestation (RR 1.83, 95% CI 1.13-2.97; RR 5.13, 95% CI 3.75-7.01, respectively), and require neonatal intensive care unit admission (NICU, RR 1.89, 95% CI 1.56-2.30; RR 2.71, 95% CI 2.25-3.28, respectively). Infants of women with SLE were more likely to have a malformation (RR 1.46, 95% CI 1.21-1.75) or die within 2 years (RR 2.11, 95% CI 1.21-3.67). Rehospitalization levels among both women with RA (RR 2.22; 1.62-3.04) and SLE (RR 2.78, 95% CI 2.15-3.59) were greatest <6 months of delivery and declined over time. Infants of women with SLE had increased rehospitalization <6 months (RR 1.64, 95% CI 1.36-1.98).
Conclusion: Consistent with prior literature, we found women with RA or SLE experienced many adverse outcomes. In our data, these included preeclampsia, PROM, and cesarean deliveries, with increased risks more notable among women with SLE. Infants of women with either condition were more likely to weigh <2500g, be <32 weeks gestation, small for gestational age, and require NICU admission than infants of comparison women. Only infants of women with SLE had increased malformations. Maternal rehospitalization after delivery was more common in both groups; most marked at <6 months. Infant rehospitalizations were increased in both cohorts to a lesser extent. Close follow-up during this time period is crucial to minimize adverse outcomes.
Disclosure of Interests: Julianna Sabo: None declared, Namrata Singh: None declared, Deborah A. Crane: None declared, David R. Doody: None declared, Melissa A. Schiff: None declared, Beth A. Mueller Shareholder of: Household owns shares in AstraZeneca
DOI: 10.1136/annrheumdis-2021-eular.1127

POS0720 MORTALITY PATTERNS AND THEIR PROGNOSTIC VALUE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN CUBA

H. Hernández-Negrín[1], Y. Roque-Dapresa[2]. *[1]Universidad de Ciencias Médicas de Villa Clara, Internal Medicine, Santa Clara, Cuba*; *[2]Hospital Universitario Arnaldo Milián, Internal Medicine, Santa Clara, Cuba*

Background: There is an increase over time in studies adopting cluster analysis (CA) to identify causes, patterns and severity in rheumatic diseases.[1] However, CA has not been used to identify patterns of causes-of-death in patients with systemic lupus erythematosus (SLE).
Objectives: 1) to identify homogeneous groups of patients according to their causes-of-death, 2) to identify homogeneous groups of cause-of-death combinations and 3) to determine the potential prognostic value of the identified patterns.
Methods: This is a population-based study using the mortality register of Villa Clara (province of Cuba) between 1990 and 2019. Based on International Classification of Disease (ICD), Nine and Tenth Revision (ICD-9, code 710.0 and ICD-10, code M32), there were identified the SLE-related deaths (any mention on the death certificate) and their associated causes-of-death. Two hierarchical CA with Ward's method was carried out, based on the associated causes-of-death: one to conglomerate patients and another one to conglomerate variables. To identify differences in socio-demographic characteristics and causes-of-death between each cluster, Chi-square test, Fisher's exact test and Kruskal-Wallis test were used as appropriate. Multivariate Poisson regression model corrected for over-dispersion was used to determine the prognostic value of the clusters. Years of potentially life lost (YPLL) was defined as a dependent variable. To calculate

YPLL, each decedent's age at death was subtracted from a predetermined age of 75 years.

Results: A total of 141 patients were analyzed, which were grouped into three clusters. The socio-demographic features and causes-of-death that characterized each cluster are summarized in Table 1. Figure 1 shows the cause-of-death patterns identified by clustering the variables. After adjusting for sex, skin color, and the presence of pregnancy in the last year, cluster 1 was significantly associated with the number of YPLL in the multivariate analysis (adjusted rate ratios= 1.32; 95% confidence interval= 1.03 to 1.70; p= 0.028).

Table 1. Socio-demographic characteristics and top ten causes-of-death according to clusters.

Variable	Cluster 1	Cluster 2	Cluster 3	*P* value
	n=40	n=71	n=30	
Age at death median (IR)	36(28.5 to 50.2)	46(30.0 to 56.0)	49(39.0 to 63.2)	0.022
Sex n(%)				
Male	4(28.6)	8(57.1)	2(14.3)	0.873
Female	36(28.3)	63(49.6)	28(22.0)	
Skin color n(%)				
White	18(21.4)	45(53.6)	21(25.0)	0.070
Non White	22(38.6)	26(45.6)	9(15.8)	
Associated causes-of-death n(%)				
Acute respiratory failure	2(11.8)	6(35.3)	9(52.9)	0.006
Chronic kidney disease	31(96.9)	0(0)	1(3.1)	0.000
Essential hypertension	2(22.2)	6(66.7)	1(11.1)	0.734
Heart failure	3(25.0)	9(75.0)	0(0)	0.093
Lupus nephritis	39(95.1)	2(4.9)	0(0)	0.000
Multiple organ failure	2(18.2)	5(45.5)	4(36.4)	0.496
Pericarditis	4(40.0)	5(50.0)	1(10.0)	0.569
Pneumonia	5(14.7)	6(17.6)	23(67.6)	0.000
Pulmonary embolism	4(20.0)	15(75.0)	1(5.0)	0.043
Septicemia	4(22.2)	0(0)	14(77.8)	0.000

YPLL: Years of potentially life lost. IR: interquartile rank.

Conclusion: Three clusters of patients were identified, the one with higher prevalence of causes-of-death expressing renal damage presented higher mortality burden. The patterns of causes-of-death were mainly shaped by renal, cardiovascular and infectious causes. Better understanding of the association among causes of death, improves our comprehension of SLE and facilitate its clinical management.

REFERENCES:

[1] Han L, Benseler SM, Tyrrell PN. Cluster and Multiple Correspondence Analyses in Rheumatology. Rheum Dis Clin N Am. 2018; 44:349-60. https://doi.org/10.1016/j.rdc.2018.01.013

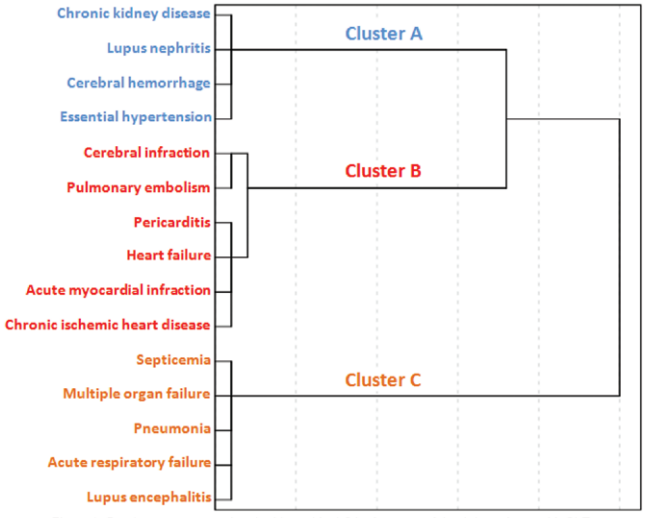


Figure 1: Dendogram representing the hierarchical CA of causes of death in patients with SLE.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1149

POS0721

ARE ANTIMALARIALS SAFE FOR THE HEART OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS? ANALYSIS OF FACTORS ASSOCIATED WITH THE DEVELOPMENT OF HEART FAILURE IN PATIENTS IN THE SPANISH SOCIETY OF RHEUMATOLOGY LUPUS REGISTRY (RELESSER)

I. Rúa-Figueroa[1], D. Rua-Figueroa[2], A. M. Anzola Alfaro[3], N. Pérez-Veiga[4], M. Galindo-Izquierdo[5], J. Calvo-Alén[6], A. Fernandez-Nebro[7], R. Menor-Almagro[8], C. Sanguesa[9], E. Tomero Muriel[10], N. Del-Val[11], E. Uriarte Isacelaya[12], R. Blanco[13], A. Boteanu[14], J. Narváez[15], J. L. Andréu Sánchez[16], T. Cobo-Ibáñez[17], C. A. Montilla-Morales[18], M. Freire González[19], C. Bohórquez[20], F. J. Toyos Sáenz de Miera[21], E. Salas[22], J. A. Bernal[23], E. Salgado Perez[24], L. Expósito[25], A. J. Mas[26], J. A. Hernandez Beriain[27], M. Velloso Feijoo[28], N. Lozano Rivas[29], G. Bonilla[30], V. Quevedo Vila[31], M. Moreno[32], I. Jiménez-Moleón[33], O. Ibarguengoitia[34], A. Pecondon[35], E. Aurrecoechea[36], E. Valls-Pascual[37], C. Mouriño[38], T. R. Vazquez Rodriguez[39], J. M. Pego-Reigosa[38]on behalf of RELESSER and EAS-SER.

[1]Hospital de Gran Canaria Doctor Negrin, Rheumatology, Las Palmas GC, Spain; [2]Hospital de Gran Canaria Doctor Negrin, Cardiology, Las Palmas GC, Spain; [3]Hospital Gregorio Marañón, Rheumatology, Madrid, Spain; [4]natalia.perez.veiga@gmail.com, Statistics, Las Palmas GC, Spain; [5]Hospital Doce de Octubre, Rheumatology, Madrid, Spain; [6]Hospital de Araba, Rheumatology, Vitoria, Spain; [7]Hospital Carlos Haya, Rheumatology, Malaga, Spain; [8]Hospital Jerez de la Frontera, Rheumatology, Jerez de la Frontera, Spain; [9]Hospital Germán Trias i Pujol, Rheumatology, Barcelona, Spain; [10]Hospital de la Princesa, Rheumatology, Madrid, Spain; [11]Hospital de Navarra, Rheumatology, Navarra, Spain; [12]Hospital Universitario Donostia, Rheumatology, San Sebastian, Spain; [13]Hospital Marqués de Valdecilla, Rheumatology, Santander, Spain; [14]Hospital Ramón y Cajal, Rheumatology, Madrid, Spain; [15]Hospital de Belvitge, Rheumatology, Barcelona, Spain; [16]Hospital Puerta de Hierro-Majadahonda, Rheumatology, Madrid, Spain; [17]Hospital Infanta Sofia, Rheumatology, Madrid, Spain; [18]Hospital de Salamanca, Rheumatology, Salamanca, Spain; [19]Complejo Hospitalario Universitario de A Coruña (CHUAC), Rheumatology, A Coruña, Spain; [20]Hospital Príncipe de Asturias, Rheumatology, Alcalá de Henares, Spain; [21]Hospital Virgen Macarena, Rheumatology, Sevilla, Spain; [22]Hospital Marina Baixa, Rheumatology, Villajoyosa, Spain; [23]Hospital de Alicante, Rheumatology, Alicante, Spain; [24]Complejo Hospitalario De Orense, Rheumatology, Orense, Spain; [25]Hospital Universitario de Canarias, Rheumatology, Tenerife, Spain; [26]Hospital Universitari Son Llàtzer, Rheumatology, Palma de Mallorca, Spain; [27]Hospital Insular de Gran Canaria, Rheumatology, Las Palmas GC, Spain; [28]Hospital de Valme, Rheumatology, Sevilla, Spain; [29]Hospital Virgen de la Arrixaca, Rheumatology, Murcia, Spain; [30]Hospital La Paz, Rheumatology, Madrid, Spain; [31]Hospital de Monforte, Rheumatology, Lugo, Spain; [32]Consorci Corporació Sanitària Parc Taulí, Rheumatology, Barcelona, Spain; [33]Hospital Clínico San Cecilio, Rheumatology, Granada, Spain; [34]Hospital de Basurto, Rheumatology, Bilbao, Spain; [35]Hospital Miguel Servet, Rheumatology, Zaragoza, Spain; [36]Hospital de Sierrallana, Rheumatology, Torrelavega, Spain; [37]Hospital Universitario Dr. Peset, Rheumatology, Valencia, Spain; [38]Galicia Sur Health Research Institute, Rheumatology, Vigo, Spain; [39]Hospital Lucus Augusti, Rheumatology, Lugo, Spain

Background: Factors associated with the development of chronic heart failure (CHF) in systemic lupus erythematosus (SLE) have received little attention. On the other hand, recent data from the use of hydroxychloroquine in the treatment of SARS-CoV-2 infection during the COVID19 pandemic have cast some doubts on its cardiological safety.

Objectives: To identify factors associated to CHF in SLE.

Methods: Retrospective cross-sectional study, including all patients with SLE (≥4 ACR-1997 criteria) recruited in RELESSER registry. The objectives and methodology of the registry have been described previously (1). CHF was defined according to the Charlson index item. Patients with CHF before diagnosis of SLE were excluded. Cumulative damage was measured with the SLICC/ACR index, excluding cardiovascular (CV) items (mSDI). Multivariate analysis exploring factors associated with CHF was carried out.

Results: 117 patients (3% of the entire cohort) with SLE and CHF and 3,506 controls with SLE without CHF were included. 90% were women. Disease duration: mean (SD), 120.2 (87.7) months. CHF appeared after a median (P25-P75) of 9.40 (4.2-18.3) years from SLE diagnosis. Patients with CHF were older (59.8 ± 18.2 vs. 46.2 ± 4.3). In the bivariate analysis, the

association of CHF with greater severity [Katz severity index: median (IQR): 4 (3-5) vs. 2 (1-3)], damage [mSDI: 3 (2-4) vs 0 (0-1)], comorbidity [modified Charlson- excluding CV items: 4 (3-6) vs 1(1-3)] and both CV (37.5% vs 6.7%) and overall mortality (43.2% vs 4.7%) (p<0.0001 for all comparisons). Also, CHF patients were more refractory to SLE treatments (33.3% vs 24%, p=0.0377) and were more frequently hospitalised due SLE [median 3 (1-5) vs 1(0-2), p<0.0001]. The results of the multivariable model are depicted in table 1.

Table 1. Congestive heart failure associated factors (multivariable analysis)

	Odds Ratio	95% CI	P-value
Sex (female)	0.46	0.25 - 0.88	0.0147
Ischaemic cardiopathy	7.96	4.01 - 15.48	<0.0001
Cardiac arrhythmia	7.38	4.00 - 13.42	<0.0001
Pulmonary hypertension	3.71	1.84 - 7.25	0.0002
Cardiac valvulopathy	6.33	3.41 - 11.62	<0.0001
Hospitalization (due to SLE)	3.74	1.81 - 8.65	0.0008
Calcium or vitamin D	5.29	2.07 - 16.86	0.0015
Antimalarials	0.28	0.17 - 0.45	<0.0001
mSDI *	1.29	1.16 - 1.44	<0.0001

*mSDI = modified SLICC/ACR damage index (without cardiovascular items)

Conclusion: - CHF is a rather late complication of SLE.
- Patients with SLE and CHF have more severe SLE, with greater refractoriness to SLE treatments and higher overall mortality.
- Treatment with antimalarials, as routinely used in SLE patients, is not only safe to heart, but even appears to have a cardioprotective effect.

REFERENCES:

[1] Rúa-Figueroa I, López-Longo FJ, Calvo-Alén J, et al. National registry of patients with systemic lupus erythematosus of the Spanish Society of Rheumatology: objectives and methodology. Reumatol Clin. 2014;10(1): 17-24.

Acknowledgements: Research Unit of Spanish Society of Rheumatology

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1208

POS0722 HISTOPATHOLOGICAL ANALYSIS OF LUPUS NEPHRITIS INCORPORATING BANFF CRITERIA EMPHASIZES THE IMPORTANCE OF TUBULOINTERSTITIAL CHANGES FOR CREATININE AND PROTEINURIA AT 12 MONTHS AFTER RENAL BIOPSY

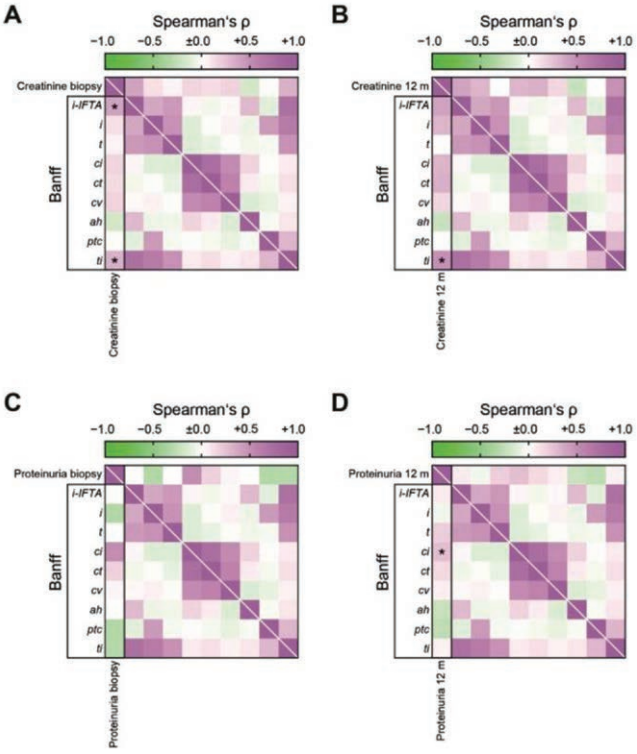
M. Plüß[1], S. Hakroush[2], N. Niebusch[1], B. Tampe[1], P. Korsten[1].
[1]Universitätsmedizin Göttingen, Department of Nephrology and Rheumatology, Göttingen, Germany; *[2]Universitätsmedizin Göttingen, Institute of Pathology, Göttingen, Germany*

Background: Lupus nephritis (LN) occurs in about 30-60% of patients with systemic lupus erythematosus (SLE). LN is associated with increased mortality. Currently, the diagnosis relies on histopathologic characteristics according to the ISN/RPS classification (1). This classification relies heavily on glomerular changes and may not accurately reflect all changes occurring in LN. For the description of transplanted kidney, the BANFF classification has been established which, in addition to glomerular changes, also incorporates tubular pathologies (2).

Objectives: With the present study, we aim to describe histopathologic changes according to the BANFF classification in a single-center cohort of LN patients.

Methods: We retrospectively recorded epidemiological, clinical and laboratory data of 58 patients with LN over a ten-year period. Histopathologic diagnoses according to ISN/RPS classification or the former WHO classification were also documented. We then re-analyzed representative kidney samples according to the BANFF classification and performed Spearman rank correlation for BANFF findings and creatinine at biopsy and 12 months as well as proteinuria at biopsy and at 12 months.

Results: We analyzed 58 patients with LN. 9 were male, 49 were female. Median age was 38 (15-78) years. According to ISN/RPS, 3 had class I LN, 6 had class II, 14 had class III, 16 had class IV, 6 had class V, and 0 had class VI. Median eGFR at biopsy was 60 ml/min/1.73m2 (13-137). According to the BANFF classification, tubulointerstitial inflammation (ti) was associated with creatinine at 12 months. Proteinuria at 12 months was associated with interstitial fibrosis (ci) (Figure 1).



Conclusion: In LN, the current ISN/RPS classification puts emphasis on glomerular changes. Nevertheless, for the long-term outcome, tubulointerstitial changes (tubulointerstitial inflammation and interstitial fibrosis) may at least be as important as glomerular changes. These findings have to be corroborated in larger cohorts with prespecified renal endpoints.

REFERENCES:

[1] Weening et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. JASN 2004.
[2] Jeong HY. Diagnosis of renal transplant rejection: Banff classification and beyond. Kidney Res Clin Pract 2020.

Disclosure of Interests: Marlene Plüß: None declared, Samy Hakroush: None declared, Noah Niebusch: None declared, Björn Tampe: None declared, PETER KORSTEN Speakers bureau: Abbvie, Pfizer, Chugai, Sanofi, Boehringer-Ingelheim, GSK, Novartis, Consultant of: Abbvie, Pfizer, Chugai, Sanofi, Boehringer-Ingelheim, GSK, Novartis, Lilly, Gilead, Grant/research support from: GSK

DOI: 10.1136/annrheumdis-2021-eular.1213

POS0723 HERPES ZOSTER IN A MULTI-ETHNIC SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COHORT: CLINICAL FEATURES AND RISK FACTORS

S. S. Shaharir[1], S. Rajalingham[1], R. Mohd[2], N. Kori[3], A. Jamil[4]. *[1]Universiti Kebangsaan Malaysia Medical Centre, Rheumatology Unit, Department of Internal Medicine, Kuala Lumpur, Malaysia*; *[2]Universiti Kebangsaan Malaysia Medical Centre, Nephrology Unit, Department of Internal Medicine, Kuala Lumpur, Malaysia*; *[3]Universiti Kebangsaan Malaysia Medical Centre, Infectious Disease Unit, Department of Internal Medicine, KL, Malaysia*; *[4]Universiti Kebangsaan Malaysia Medical Centre, Dermatology Unit, Department of Internal Medicine, Kuala Lumpur, Malaysia*

Background: Systemic Lupus Erythematosus (SLE) patients are at risk of Herpes Zoster (HZ) infection due to the underlying immunosuppressed state. The reported incidence of HZ in SLE is 6 to 10-times higher than the general population.

Objectives: To determine the clinical characteristics of SLE patients who develop Herpes Zoster (HZ) infection and their associated risk factors.

Methods: Medical records review was performed on consecutive SLE patients in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) from 2018 until 2019. Previous history of HZ and their demographic characteristics, clinical and medications used at the time of infection were recorded. Univariate and multivariate analyses were performed to compare the clinical and treatment characteristics

between SLE patients with history of HZ and patients who had never had experienced HZ.

Results: A total of 229 patients with predominantly Malay patients (n=123, 53.7%), followed by Chinese (n=90, 39.3%) and others (n=16, 7.0%) were included. A total of 37 patients had history of HZ (16.2%). Their mean age during HZ episode was 34.4 ± 13.8 years and their SLE disease duration was 68.7 ±57.1 months. More than half of them (n=21, 56.8%) developed HZ when the SLE disease was active with the mean dose of prednisolone at the time of infection was 20.7 ± 9.2 mg daily. A total of 21 HZ patients (56.8%) had ever received cyclophosphamide with the median interval of the last infusion was 6 (0.2-84) months. Almost half of the HZ patients (n=18, 48.6%) developed the infection while on cyclosporine A. Meanwhile, 4 (10.8%) were on azathioprine and mycophenolate mofetil respectively. Chinese patients tend to have HZ as compared to other ethnics (27% vs 41.7%), p=0.07. HZ occurred in a higher proportion among male patients (29%) as compared to female patients (14.1%), p=0.05. The use of azathioprine (10.8% vs 55.2%, p<0.01) and mycophenolate mofetil (10.8% vs 31.8%, p=0.009) were less associated with HZ. On the other hand, the use of cyclosporine A (48.6% vs 32.3%, p=0.05) and prednisolone ≥ 60mg daily (44.4% vs 28%, p=0.04) were associated with HZ. Higher HZ patients had hematological manifestation (81.1% vs 62.5%, p=0.04) and positive lupus anticoagulant (LA), 32.4% vs 14.6%, p=0.02. A forward logistic regression which included all factors with p<0.1 in the univariate analyses revealed that the use of prednisolone ≥ 60mg daily and hematological manifestation were the independent predictors of HZ with OR= 2.28 (95% C.I = 1.01-5.17), p=0.049 and OR= 2.78 (95% C.I = 1.09-7.04), p=0.03 respectively. The use of azathioprine was associated with a lower risk of HZ with OR 0.08 (95% C. I= 0.03-0.25), p=<0.01.

Conclusion: Our study demonstrated the possible influence of male gender, Chinese ethnicity and disease characteristics such as hematological manifestation and lupus anticoagulant positivity with the occurrence of HZ. In addition, the use high dose oral prednisolone ≥ 60mg daily was the independent predictor of HZ while on the other hand, the use of azathioprine was associated with a lower risk of developing HZ as compared to other immunosuppressive agents. Further larger studies are needed to confirm these associations.

REFERENCES:

[1] Chen D, Li H, Xie J, Zhan Z, Liang L, Yang X. Herpes zoster in patients with systemic lupus erythematosus: Clinical features, complications and risk factors. Exp Ther Med. 2017;14(6):6222-6228.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1216

POS0724 GENDER DIFFERENCES IN THROMBOTIC PRIMARY ANTIPHOSPHOLIPID SYNDROME IN A LARGE COHORT OF PATIENTS FROM FOUR EUROPEAN CENTERS

L. Moschetti[1], L. Dal Pozzolo[1], V. Le Guern[2], N. Morel[2], C. M. Yelnik[3], M. Lambert[3], E. Hachulla[3], Y. Benhamou[4], F. Franceschini[1], L. Andreoli[1], N. Costedoat-Chalumeau[2], A. Tincani[1]. *[1]ASST Spedali Civili - University of Brescia, Rheumatology and Clinical Immunology Unit - Clincal and Experimental Sciences, Brescia, Italy*; *[2]2AP-HA Cochin Hospital - Université Descartes-Sorbonne Paris Cité, Internal Medicine Departement, Centre de Référence Maladies auto-immunes et systémiques rares d'ile de France, Paris, France*; *[3]Univ Lille, INSERM, CHU Lille, Service de médecine interne et d'immulogie clinique, Centre de Réference des Maladies auto-immunes systèmiques rares du nord-ouest de France (CeRAINO), U1167 - RID AGE, Lille, France*; *[4]CHU Charles Nicolle - Normandie University, UNIROUEN, Départemend de Médecine Interne - INSERM U1096 EnVI, Rouen, France*

Background: Autoimmune diseases occur more frequently in females and their course and severity can be affected by gender. Antiphospholipid syndrome (APS) is a systemic autoimmune disorder in which antiphospholipid antibodies (aPL) exert a pathogenic role resulting in vascular thrombosis and/or pregnancy morbidities. Data about gender differences in thrombotic APS (t-APS) are still scarce[1,2].

Objectives: To evaluate the differences in frequency, disease expression and severity between females and males affected by primary t-APS.

Methods: Retrospective study enrolling subjects with a formal diagnosis of primary APS (Miyakis 2006) with vascular thrombosis at onset. Women who presented with obstetric events as first aPL-related manifestation were excluded. All the patients were followed from 1967 to 2019 in four European centers: three French centers and one Italian center.

Results: The study included 433 patients (68% females, 32% males). Median age at t-APS onset [31 (24-46) vs 41 (29-53) years, *p<0.001*] and at diagnosis [34 (27-50) vs 46 (34-57) years, *p<0.001*] was significantly lower in females.

The most common presenting manifestations were venous thrombosis (60%) followed by arterial events (37%) and catastrophic APS (3%). Venous events were more frequent in women as compared to men (64% vs 51% *p:0.012* OR:1.7 [1.1-2.5]). Sites of venous thrombosis included: limbs (35%), pulmonary (17%), cerebral (3%), portal and inferior cava (2%) and retinal (1%) veins, without gender differences. The arterial events were more frequent among men (43% vs 34% *p:0.053*). Strokes (27%) and myocardial infarctions (4%) were the most frequent manifestations, followed by thrombosis of limbs (2%), retina (2%) and abdominal organs (1%). Noteworthy, only men presented with visceral ischemia. During the follow-up, new thrombosis occurred in 41% of patients (179/433). 33% out of them had at least two episodes and these occurred especially among males (22% vs 10% *p:0.001* OR:2.5 [1.3-4.8]). New events were mostly of the same type, but ⅓ of patients presented a switch from venous to arterial side and viceversa, with no gender differences.

Complete aPL profile was available in 357 subjects: 33% had single aPL positivity, 24% double positivity and 43% triple positivity, with no differences between women and men. About 80% of the patients had a concomitant risk factor (RF) for thrombosis. Established cardiovascular RFs were more represented among men as shown in table 1. In women, estrogenic exposure was the main RFs, present in almost 40% of them.

Table 1.

	MALES n= 137	FEMALES n= 296	*P* OR [IC 95%]
Traditional cardiovascular RFs, n (%)			
Smoke	66 (48)	81 (27)	*<0.001* 2.5 [1.6-3.8]
Arterial hypertension	59 (43)	75 (25)	*<0.001* 2.2 [1.5-3.4]
Dyslipidemia	52 (38)	72 (24)	*0.004* 1.9 [1.2-2.9]
Diabetes	16 (12)	15 (5)	*0.014* 2.5 [1.8-5.1]
Obesity	13 (10)	38 (13)	*ns*
Other thrombophilic factors, n (%)			
Estrogenic stimuli*	0	116 (39)	-
Trauma / surgery / immobilization	21 (15)	32 (11)	*ns*
Congenital thrombophilia	9/94 (10)	33/204 (16)	*ns*

Data were compared using contingency tables, *p value* was calculated with Chi-Squared or Fisher exact test. *= hormonal therapy, pregnancy, post-partum

Conclusion: This gender-oriented analysis of patients with primary t-APS showed that women had the first vascular event at a younger age and mostly on the venous side, while men presented mainly with arterial events, later in life and suffered from more recurrent events. No differences were observed in the distribution of the aPL profile. The different frequency of arterial and venous events in the two groups could be attributed mainly to the presence of additional RFs rather than to biological gender-specific issues. However, it should be underlined that some RFs, such as the use of estrogens or classic cardiovascular RFs, are exclusive or more represented in one gender rather than the other, making it difficult to assess the link of causality between gender and manifestations of t-APS.

REFERENCES:

[1] JF de Carvalho. Rheumatol Int. 2011.
[2] LJ Jara. Lupus. 2005.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1228

POS0725 CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS OF PATIENTS WITH JUVENILE-, ADULT- AND LATE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

O. Iaremenko[1], D. Koliadenko[1], I. Matiyashchuk[2]. *[1]Bogomolets National Medical University, Department of Internal Medicine #3, Kyiv, Ukraine*; *[2]Medical Center "Consilium Medical", Rheumatology Department, Kyiv, Ukraine*

Background: Systemic lupus erythematosus (SLE) predominantly develops in women of child-bearing age. However, nearly 20% of cases present during childhood, generally after puberty (juvenile-onset SLE, JSLE). On the other hand, 10-20% of patients develop SLE after the age of 45-50 years (late-onset SLE, LSLE) [1]. It is known that age at disease onset can influence the clinical presentation and course of SLE, but the findings are not always consistent across the studies [2].

Objectives: The aim of this study was to evaluate the spectrum of clinical manifestations and autoantibody profile in patients with SLE in the central region of Ukraine regarding age at onset.

Methods: The study included 258 SLE patients before starting an adequate therapy, comprising 225 females (87.2%) and 33 males (12.8%). The median age at SLE onset was 28 (20-39) years. The patients were classified into 3 groups: I – age at SLE onset ≤18 years (JSLE; n=52; 20.2%), II – SLE onset at age 19-44 years (adult-onset SLE, ASLE; n=161; 62.4%), III – age at disease onset ≥45 years (LSLE; n=45; 17.4%). The clinical and demographic data, SLE Disease Activity Index (SLEDAI), erythrocyte sedimentation rate (ESR), C-reactive protein

(CRP) and autoantibody profile were analyzed. Quantitative and categorical data were compared using Kruskal-Wallis test and chi-square test, respectively.
Results: There was a difference in prevalence of malar rash between the groups (p=0.022): it was more common in JSLE (40.4%) and ASLE (34.4%) than in LSLE patients (15.6%; p=0.04 and 0.05, respectively). Similar distribution was found for renal involvement: JSLE and ASLE patients presented higher rates of nephritis (55.8% and 49.4%, respectively) than LSLE patients (23.8%; p=0.012 and 0.014, respectively). But the groups did not differ significantly with regard to nephrotic syndrome (p=0.224). ASLE was associated with more frequent alopecia (38.8%) comparing with JSLE (19.2%; p=0.04). Moreover, ASLE patients also had the highest frequency of lymphadenopathy (56.3%) whereas in LSLE it was observed only in 25.0% of patients (p=0.001). Serositis was more common in LSLE (54.5%) and ASLE (43.8%) than in JSLE (23.1%; p=0.011 and 0.034, respectively). Although secondary Sjögren's syndrome was more frequently observed in ASLE (7.6%) and LSLE (7.3%) than in JSLE (0.0%), the difference did not achieve statistical significance (p=0.157). Also, no differences were observed in the occurence of arthritis, pulmonary and neurological manifestations, constitutional symptoms, SLEDAI score among the groups. Median CRP level in LSLE was significantly higher (14.0 (1.1-46.4) mg/L) than in JSLE (0.7 (0.0-12.0) mg/L) (p<0.05). But all groups did not differ significantly with regard to ESR levels. When differences in antinuclear antibodies were analyzed, we disclosed that the frequency of anti-dsDNA positive results was significantly higher in JSLE (68.6%) and ASLE (70.1%) patients when compared with that found in LSLE patients (31.3%) (p=0.016 and 0.001, respectively). There were no significant differences between groups with regard to positivity for other antibodies (anti-Sm, -Ro, -La, -RNP, antiphospholipid antibodies).
Conclusion: JSLE and ASLE patients are more likely to have malar rash, nephritis and anti-dsDNA positivity. Alopecia and lymphadenopathy are most frequent in ASLE patients. JSLE are far less likely to have serositis than any other group. Patients with LSLE demonstrate comparatively low frequency of major organ involvement, but they have higher levels of CRP.
REFERENCES:
[1] Ambrose N., et al. Differences in disease phenotype and severity in SLE across age groups. Lupus. 2016;25(14):1542-1550.
[2] Livingston B., et al. Differences in autoantibody profiles and disease activity and damage scores between childhood- and adult-onset systemic lupus erythematosus: a meta-analysis. Seminars in Arthritis and Rheumatism. 2012;42(3):271-280.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1237

POS0726 POST-TRAUMATIC STRESS DISORDER AND QUALITY OF LIFE IN SYSTEMIC LUPUS ERYTHEMATOSUS. A CROSS SECTIONAL WEB SURVEY-BASED STUDY

L. Moroni[1,2], M. Mazzetti[3], G. A. Ramirez[1,2], S. Zuffada[3], N. Farina[1,2], E. Bozzolo[1], V. Di Mattei[2,3], L. Dagna[1,2]. *[1]San Raffaele Hospital, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milano, Italy*; *[2]Vita-Salute San Raffaele University, Milano, Italy*; *[3]San Raffaele Hospital, Clinical and Health Psychology Unit, Milano, Italy*

Background: Exposure to severe or chronic life stressors may alter immune function and high levels of subsequent distress have been implicated in autoimmune disease pathogenesis. Post-traumatic stress disorder (PTSD) is a debilitating psychiatric condition affecting 1-12% of the general population[1], occurring in response to traumatic events. Growing evidence supports an association between trauma exposure and PTSD with systemic lupus erythematosus (SLE) onset[2].
Objectives: To cross-sectionally assess PTSD prevalence in a cohort of patients with SLE and to examine its correlation with quality of life.
Methods: A 189-item anonymous questionnaire including demographics, disease features, the 9-domain Trauma and Loss Spectrum – Self Report (TALS-SR) and the 8-domain Lupus Quality of Life (Lupus QoL) was administered via web to a cohort of patients with SLE. Patients were classified as PTSD cases based on TALS-SR items corresponding to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for PTSD.
Results: Ninety-nine (95% female and 5% male) patients with a median follow-up of 16.5 years completed the questionnaire. Self-reported fatigue prevalence was 75%. Fifteen patients (15%) reportedly were on psychological and/or psychiatric support. Thirty-one patients (31%) met the DSM-5 criteria for PTSD. The average LupusQoL interdomain score was 80/100. PTSD cases reported significantly lower scores compared to non-cases in three LupusQoL domains: planning (83 vs. 100, p=0.035), body image (85 vs. 95, p=0.031), and fatigue (67 vs. 92, p=0.001). An inverse correlation between TALS-SR scores and Lupus QoL subscales was found (Table1). In particular, the degree of stress secondary to losses or upsetting events was strongly correlated to fatigue intensity (rho= -0.458, p<0.001).
Conclusion: PTSD prevalence might be higher in SLE than in the general population and have a detrimental influence on quality of life. Fatigue perception might be more significantly affected by PTSD. Intervention studies are needed to assess the therapeutical effects of psychological support in patients with SLE.
REFERENCES:
[1] Shalev A et al. *Post-Traumatic Stress Disorder.* New England Journal of Medicine, June 2017.
[2] Roberts AL et al. *Association of Trauma and Posttraumatic Stress Disorder With Incident Systemic Lupus Erythematosus in a Longitudinal Cohort of Women.* Arthritis & Rheumatology, November 2017.

Table 1. Spearman rho coefficients outlining correlation across Lupus QoL and TALS-SR domains. The highest negative correlation has been found between fatigue and reaction to traumatic events. Significant correlations boxes are coloured in yellow (weak, rho 0.20-0.39) and red (moderate, rho 0.40-0.59). * p<0.05, ** p<0.01.

		LupusQoL Domains								
		Physical health	Pain	Planning	Intimate relationships	Burden to others	Emotional health	Body image	Fatigue	Lupus QoL Total Score
TALS-SR Domains	Loss events	-.217	-.217	-.096	-.031	.047	-.022	.076	-.009	-.061
	Grief reactions	-.145	-.104	-.041	-.018	-.124	-.172	-.192	-.149	-.107
	Potentially traumatic events	.039	-.082	-.169	-.167	-.207	-.185	-.046	-.229	-.096
	Reaction to losses or upsetting events	-.221	-.256*	-.289*	-.218	-.290*	-.369**	-.371**	-.458**	-.341**
	Re-experiencing	-.139	-.215	-.245*	-.228	-.320**	-.275*	-.287*	-.342**	-.274*
	Avoidance and numbing	-.176	-.246*	-.279*	-.257*	-.337**	-.405**	-.413**	-.406**	-.338**
	Maladaptive coping	-.190	-.238	-.294*	-.282*	-.324**	-.340**	-.358**	-.405**	-.327**
	Arousal	-.134	-.177	-.263*	-.320**	-.283*	-.279*	-.321**	-.397**	-.282*
	Personal characteristics / risk factors	-.044	-.115	-.266*	-.189	-.409**	-.231	-.197	-.253*	-.199

Disclosure of Interests: Luca Moroni: None declared, Martina Mazzetti: None declared, Giuseppe Alvise Ramirez: None declared, Simone Zuffada: None declared, Nicola Farina: None declared, Enrica Bozzolo: None declared, Valentina Di Mattei: None declared, Lorenzo Dagna Consultant of: Abbvie, Amgen, Biogen, BristolMyers Squibb, Celltrion, Galapagos, GlaxoSmithKline, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI, Grant/research support from: The Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR) received unrestricted research/educational grants from Abbvie, Bristol-Myers Squibb, Celgene, GlaxoSmithKline,Janssen, Merk Sharp & Dohme, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi Genzyme, and SOBI
DOI: 10.1136/annrheumdis-2021-eular.1238

POS0727 INSULIN RESISTANCE AND LEPTIN LEVELS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITHOUT DIABETES MELLITUS OR FASTING HYPERGLYCEMIA

L. Kondrateva[1], T. Panafidina[1], T. Popkova[2], M. Cherkasova[3], A. Lila[4], E. Nasonov[4]. *[1]V.A. Nasonova Research Institute of Rheumatology, Department of Systemic Rheumatic Diseases, Moscow, Russian Federation*; *[1]V.A. Nasonova Research Institute of Rheumatology, Department of Systemic Rheumatic Diseases, Moscow, Russian Federation*; *[3]V.A. Nasonova Research Institute of Rheumatology, Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*; *[4]V.A. Nasonova Research Institute of Rheumatology, Scientific Department, Moscow, Russian Federation*

Background: Insulin resistance (IR) is considered as initial stage of diseases continuum from development of prediabetes to eventual progression to type 2 diabetes mellitus (T2DM). Individuals with prediabetes have also elevated leptin levels, so this adipocytokine along with IR can be considered as predictive laboratory markers of higher risk of T2DM. It is not yet clear whether presence of individual or multiple SLE-related and/or known traditional risk factors of T2DM (such as unhealthy diet, physical inactivity, family history of diabetes, or being overweight) can precipitate the development of IR.
Objectives: To analyze the relationship between IR and increasing leptin levels rates. To identify the presence and evaluate the potential role of traditional and disease-related risk factors for IR in SLE patients without T2DM or hyperglycemia.

Methods: A total of 49 SLE pts (46 women, 3 men, 40 [33;48] years old) without established DM and with normal fasting glucose levels (<6,1 mmol/l) were enrolled in the study. Median disease duration was 3,0[0,7;8,0] years, SLEDAI-2K was 5[2;8]. SLE pts were treated with glucocorticoids (GC) (84%), hydroxychloroquine (78%), immunosuppressive drugs (20%) and biological agents (10%). Insulin levels were measured using electrochemiluminescence assay Elecsys (Roche Diagnostics), serum leptin concentrations were estimated using ELISA (DBS-Diagnostics Biochem Canada Inc.). IR was defined as Homeostasis Model Assessment of Insulin Resistance index (HOMA-IR) ≥2,77. Leptin levels were considered elevated at values ≥11,1 ng/ml for women, ≥5.6 ng/ml for men. Eight traditional T2DM risk factors from the FINDRISK (Finnish Type 2 Diabetes Risk Assessment Form) questionnaire (older age, being overweight, abdominal obesity, family history of diabetes, sedentary lifestyle, lack of regular dietary fiber intake, taking antihypertensive medications as a surrogate marker of high blood pressure, documented episodes of hyperglycemia) were evaluated. This study used 5 risk categories for developing T2DM proposed by FINDRISK questionnaire: low, slightly elevated, moderate, high or very high.

Results: Median HOMA-IR levels were 1,7 [1,2;2,5]. HOMA-IR correlated with leptin levels (r=0,7, p<0,001), body mass index (BMI) (r=0,6, p<0,001), waist circumference (WC) (r=0,5, p<0,001), T2DM risk categories by FINDRISK (r=0,3, p=0,03), SLEDAI-2K (r= -0,4, p<0,01), and duration of GCs therapy (r=0,3, p=0,03). Current GC use had no influence on HOMA-IR in SLE. IR was detected in 10 (20%) SLE pts. The traditional T2DM risk factors profiles were similar in pts with (Group 1) or without IR (Group 2) except for higher anthropometric parameters in group 1 (for BMI 27,2[24,8;32,2]kg/m^2 vs 23,7[20,6;26,7]kg/m^2, p<0,01; for WC: 93[86;102]cm vs 83[76;93]cm, p=0,02). Leptin levels were also higher in SLE pts with IR compared to pts without IR (74,2[30,4;112,7]ng/ml vs 25,0[6,7;42,4]ng/ml, p<0,01). Increased leptin levels were found in 35 (71%) pts, more often in pts with IR (100 vs 64%, p=0,04).

Conclusion: IR was found in 20% of SLE pts without T2DM having normal serum fasting glucose concentration. Emergence of IR was commonly preceded by increased leptin levels. IR values were closely associated with accumulation of adipose tissue facilitated by long-term GCs use and disease activity decrease. Contribution of other traditional risk factors of T2DM seemed insignificant.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1307

POS0728 QRISK3 RELATION TO CAROTID PLAQUE IS HIGHER THAN THAT OF SCORE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

J. C. Quevedo-Abeledo[1], C. Palazuelos[2], J. Llorca[2], L. Cáceres Martín[1], I. Ferraz-Amaro[3], M. A. González-Gay[4]. [1]*Hospital Universitario de Gran Canaria Dr Negrín, Rheumatology, Las Palmas de GC, Spain*; [2]*University of Cantabria, CIBER Epidemiología y Salud Pública (CIBERESP), Santander, Spain*; [3]*Hospital Univeritario de Canarias, Rheumatology, La Laguna, Spain*; [4]*Hospital Universitario Marqués de Valdecilla, University of Cantabria, Rheumatology, Santander, Spain*

Background: Systemic lupus erythematosus (SLE) has been described as an independent risk factor for the development of cardiovascular (CV) disease. Recently, QRESEARCH risk estimator version 3 (QRISK3) calculator has been released for the assessment of CV risk in general population. QRISK3 now includes the presence of SLE as one of its variables for the calculation of CV risk.

Objectives: We aim to compare, in patients with SLE, the predictive capacity between QRISK3 and Systematic COronary Risk Evaluation (SCORE) for the presence of carotid subclinical atherosclerosis.

Methods: 296 patients with SLE were recruited. The presence of carotid plaque and carotid intima media thickness (cIMT) were assessed through ultrasound. QRISK3 and SCORE were calculated. The relation of QRISK3 and SCORE between themselves and to the presence of carotid subclinical atherosclerosis (both carotid plaque and cIMT) was studied.

Results: Most of the patients were female (95%) and average age was 51 ± 12 years. Traditional cardiovascular risk factors were prevalent, as shown in table 1. Most SLE patients were in the no activity (41%) or mild activity (29%) categories as shown by the SLEDAI scores. SLICC and Katz indexes were, respectively, 1 (IQR 0-2) and 2 (IQR 1-4). Seventy-one percent of the patients had a SLICC/ACR DI score equal to or higher than 1, and 39% had a Katz index equal to or higher than 3. Almost half of the patients (47%) were taking prednisone (the median dose of those 139 patients on prednisone was 5 [IQR 2.5-5] mg/day at the time of the study). DMARDs use was reported in 77% of the patients and 69% were taking hydroxychloroquine at the time the study was performed. SCORE and QRISK3 did not correlate between them in patients with SLE. In this sense, QRISK3, both calculated including the SLE item (Rho Spearman r=-0.008, p=0.90) or not (Rho Spearman r=-0.009, p=0.96), did not correlate with SCORE. This lack of correlation was also found when the corresponding categorizations of both scores were used. For example, patients with a QRISK> = 10 did not show a higher SCORE when compared to patients with a QRISK3 <10 (1.26 vs. 1.30, p=0.90). Similarly, QRISK3 was not different between the low, moderate, high and very-high SCORE CV risk categories.

Relation of QRISK3 and SCORE to cIMT and to the presence of carotid plaque is shown in Figure 1. QRISK3 was statistically significantly correlated with cIMT (Rho Spearman r=-0.420, p=0.000). However, this relation was not found between SCORE and cIMT (Rho Spearman r=-0.005, p=0.93). Moreover, QRISK3 showed a statistically significant discrimination for the presence of carotid plaque (AUC 0.765 (95%CI 0.711-0.820). This relation was found to be significant both when QRISK3 was calculated with the SLE variable item or not. However, in patients with SLE, SCORE did not show a significant discrimination for the presence of carotid plaque (0.561 (95%CI 0.494-0.629). Additionally, a statistical significant difference was observed between the AUC of QRISK3 and SCORE (p=0.000).

Table 1. Characteristics of SLE patients

	SLE patients (n=296)
Age, years	51 ± 12
Female, n (%)	280 (95)
Body mass index, kg/m2	27 ± 6
Systolic blood pressure, mmHg	127 ± 19
Cardiovascular co-morbidity	
Smoking, n (%)	74 (25)
Diabetes, n (%)	14 (5)
Hypertension, n (%)	119 (40)
Dyslipidemia, n (%)	115 (39)
Analytical and lipid profile	
CRP, mg/dl	1.9 (0.9-4.9)
Cholesterol, mg/dl	198 ± 38
LDL cholesterol, mg/dl	110 ± 29
SLE related data	
Disease duration, years	17 (10-25)
SLICC	1 (0-2)
SLEDAI	2 (0-4)
Current prednisone, n (%)	139 (47)
Hydroxychloroquine, n (%)	205 (69)
Subclinical atherosclerosis	
Carotid IMT, microns	630 ± 122
Carotid plaques, n (%)	108 (36)

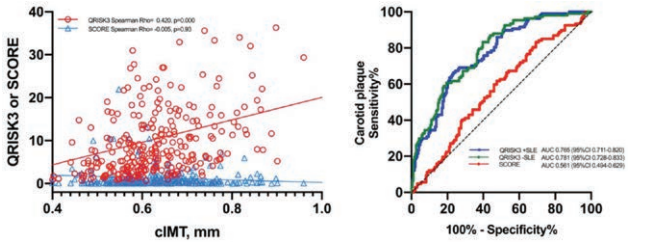


Figure 1. Relation of QRISK3 and SCORE to cIMT and carotid plaque.

Conclusion: QRISK3 discrimination for carotid plaque is higher than that of the SCORE. QRISK3, and not SCORE, should be use for the calculation of CV risk in patients with SLE.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1376

POS0729 INFLUENCE OF VARIOUS FACTORS ON THE IMMUNOGENICITY OF 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

G. Tarasova[1], B. Belov[1], M. Cherkasova[2], E. Aseeva[3], T. Reshetnyak[4], N. Kosheleva[4], T. Popkova[5]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Drug Therapy, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Intensive Therapy Laboratory, Moscow, Russian Federation*; [4]*V.A. Nasonova Research Institute of Rheumatology, Vascular Rheumatology Laboratory, Moscow, Russian Federation*; [5]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases Laboratory, Moscow, Russian Federation*

Background: Immunosuppressive therapy increases the risk of pneumococcal infection in patients with systemic lupus erythematosus (SLE). The therapy, as well as some features of the course of the disease, can lead to a decrease in the immunogenicity of the pneumococcal vaccine in these patients.
Objectives: The aim of the study was to identify "risk factors" that negatively affect the immunogenicity of the 23-valent polysaccharide pneumococcal vaccine (PPV-23) in patients with SLE.
Methods: The study included 60 patients aged 19 - 68 years with a reliable diagnosis of SLE, disease duration from 9 months. up to 42 years old. Nine patients had high disease activity, 12 had medium, 33 had low, and 6 had remission. Therapy: 58 patients received glucocorticoids (GC) 5-40 mg / day, 46-hydroxychloroquine, 33- cytostatics (CS), 23- biologics: 12-rituximab (RTM), 10-belimumab (BLM), 1- RTM and BLM. 1 dose (0.5 ml) of PPV-23 was administered subcutaneously. During the year, standard clinical and laboratory studies were carried out, the level of antibodies to polysaccharides of the S. pneumoniae cell wall in the blood serum was determined.
Results: After 1-2 months. after vaccination, 78.7% of patients showed a more than twofold increase in protective antibodies, a year later - in 56.7% of patients ("responders"). The severity of the vac-cine response did not depend on age: in the subgroup of patients under 50 years of age (n = 46), the proportion of "responders" remained 52.2%, and in patients over 50 years of age (n = 14) -50%. With different duration of the disease, the vaccine response did not differ significantly: with a disease period of up to 5 years, the vaccine response was observed in 47.6%, from 5 to 10 years - in 66.7%, over 10 years - in 55.6% of patients. Patients in remission had the lowest vaccine response (33.3%), while with high SLE activity, 100% response to the vaccine was recorded (p = 0.02), which is probably due to the fact that remission requires long-term and active immunosuppressive therapy, and patients with high activity such therapy has just been initiated or is to be. With an average and low degree of activity, the number of "respondents" was the same (50% and 51.5%, respectively). In patients receiving biologics therapy, a full-fledged vaccine response was observed less frequently than in patients without biologics (39% and 68%, respectively, p = 0.03), while no differences were found against the background of RTM and BLM therapy (41.6% and 40% of "respondents", respectively). The effect of the duration of biologics therapy on the severity of the vaccine response was analyzed.
There was a tendency for the predominance of "responders" in the group with a duration of therapy before vaccination up to 1 year, as well as in the group of initiation of biologics after vaccination, however, the differences were not statistically significant.
Conclusion: RTM and BLM have a negative effect on the immunogenicity of the PPV-23 vaccine. However, if the timing of administration is observed (initiation of biologics therapy after vaccination or vaccination against the background of biologics therapy lasting less than a year), the number of "responders" increases. Further recruitment of patients is needed to clarify and confirm the results obtained.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1445

POS0730 DECREASED RISK OF OSTEONECROSIS OVER TIME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS USING JAPANESE HEALTH INSURANCE DATABASE

R. Sakai[1], E. Tanaka[1], M. Yamagishi[1], M. Majima[1], M. Harigai[1]. [1]*Tokyo Women's Medical University School of Medicine, Department of Rheumatology, Tokyo, Japan*

Background: In patients with systemic lupus erythematosus (SLE), prevalence of osteonecrosis (ON) was 20–40% [1], and 4–10 times higher risk of ON than the general population was observed [2,3]. Because ON can influence patients' physical activity and quality of life, it is essential for rheumatologists to manage ON appropriately. Recently, medications such as mycophenolate mofetil (MMF) and hydroxychloroquine (HCQ) were approved for SLE in Japan. Considering the changes in treatments for SLE over time, it is clinically important to investigate the risk and risk factors of ON in patients with the disease. However, to date, only evidence is found in the literature.
Objectives: To estimate incidence rate (IR) and identify risk factors of ON in patients with SLE using a Japanese health insurance database.
Methods: This retrospective longitudinal population-based study was conducted using claims data provided by Medical Data Vision Co., Ltd (Tokyo, Japan). We defined individuals as SLE cases if they met all of the following: 1) having at least one ICD10 code (M321 or M329); 2) having at least one prescription of oral corticosteroids (CS), methylprednisolone (mPSL) pulse therapy, immunosuppressive drugs (IS) (azathioprine, mizoribine, tacrolimus, MMF, cyclophosphamide, methotrexate), biologics (belimumab, rituximab) or HCQ between January 2010 and January 2017; 3) being 16 years old or over. The start of observation was defined by the first month in which cases met all of the above criteria. Patients were followed until the earliest of date of first ON, date of loss of follow-up, or the end of follow-up (December 2017). ON was defined when patients had at least one ICD code (M87.0, M87.1, M87.2, M87.3, M87.8, M87.9, M90.5) during the observation period. Patients were excluded if they had a previous diagnosis of ON during the first 3 months of the observation period. We defined baseline characteristics using the data in the month of starting observation, and calculated incidence rate (IR) in each year, adjusted relative risk (RR [95% CI]) of ON using a Poisson regression model, and adjusted odds ratio (OR [95% CI]) of risk factors of ON after adjusting for age and sex at baseline, and medications and comorbidities during the observation period using a logistic regression model.
Results: In this study, 16,386 cases were included. The median age was 55 years and 81.3% were female. Median observation period was 33 months, and total observation period was 47,138 patient-years (PY). IR/1,000 PY of ON in each year from 2010 to 2017 was 13.2, 10.6, 11.0, 13.3, 13.1, 9.8, 8.5, and 7.3, respectively. Adjusted RR in each year from 2011 to 2017 compared to 2010 was 0.5 [0.2–1.4], 0.3 [0.1–0.9], 0.6 [0.3–1.4], 0.7 [0.3–1.6], 0.4 [0.2–0.8], 0.4 [0.2–0.8], and 0.3 [0.1–0.7], respectively. Adjusted OR was 1.22 [1.10–1.34] for younger age by decade, 1.41 [1.11–1.79] for male, 2.69 [1.52–4.76] for use of oral CS (> 0 and < 5 mg/day of prednisolone [PSL] equivalent dose versus no use), 2.21 [1.26–3.86] for oral CS (≥ 5 and < 10mg/day versus no use), and 1.25 [1.02–1.54] for dyslipidemia.
Conclusion: Significant decrease in IR of ON after 2015 was observed in Japanese patients with SLE for the first time. Younger age, use of CS, and dyslipidemia were identified as significant risk factors of ON.
REFERENCES:
[1] Rheumatology 2018;57(5):844-9.
[2] BMJ Open. 2017;7(7):e016788.
[3] Eur J Intern Med. 2016;35:e23-e4.
Disclosure of Interests: Ryoko Sakai Speakers bureau: RS received fees from Bristol Myers Squibb Co., Ltd., Grant/research support from: Tokyo Women's Medical University (TWMU), particularly the Division of Multidisciplinary Management of Rheumatic Diseases, Department of Rheumatology, has received unrestricted research grants from Ayumi Pharmaceutical Co.; Chugai Pharmaceutical Co., Ltd.; Eisai Co., Ltd., Nippon Kayaku Co., Ltd.; Taisho Toyama Pharmaceutical Co., Ltd.; Takeda Pharmaceutical Co., Ltd.; Mitsubishi Tanabe Pharma Co.; and Teijin Pharma Ltd., with which TWMU paid the salaries of RS., Eiichi Tanaka Speakers bureau: ET has received lecture fees from Abbvie, Asahi Kasei pharma co., Astellas Pharmaceutical, Ayumi Pharmaceutical, Chugai Pharmaceutical, Eisai Pharmaceutical, Eli Lilly Japan K.K., GlaxoSmithKline K.K., Kyowa Pharma Chemical CO.,LTD., Janssen Pharmaceutical K.K., Mochida Pharmaceutical CO.,LTD., Pfizer, Takeda Pharmaceutical, and Teijin Pharma Ltd., Consultant of: ET has received lecture fees from Abbvie, Asahi Kasei pharma co., Astellas Pharmaceutical, Ayumi Pharmaceutical, Chugai Pharmaceutical, Eisai Pharmaceutical, Eli Lilly Japan K.K., GlaxoSmithKline K.K., Kyowa Pharma Chemical CO.,LTD., Janssen Pharmaceutical K.K., Mochida Pharmaceutical CO.,LTD., Pfizer, Takeda Pharmaceutical, and Teijin Pharma Ltd., Miku Yamagishi: None declared, masako majima: None declared, masayoshi harigai Speakers bureau: MH has received speaker's fee from AbbVie Japan GK, Ayumi Pharmaceutical Co., Boehringer Ingelheim Japan, Inc., Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Ltd., Eisai Co.,Ltd., Eli Lilly Japan K.K., GlaxoSmithKline K.K., Kissei Pharmaceutical Co., Ltd., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd., Consultant of: MH is a consultant for AbbVie, Boehringer-ingelheim, Bristol Myers Squibb Co., Kissei Pharmaceutical Co., Ltd. and Teijin Pharma., Grant/research support from: MH has received research grants from AbbVie Japan GK, Asahi Kasei Corp., Astellas Pharma Inc., Ayumi Pharmaceutical Co., Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Daiichi-Sankyo, Inc., Eisai Co., Ltd., Kissei Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Nippon Kayaku Co., Ltd., Sekisui Medical, Shionogi & Co., Ltd., Taisho Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd.
DOI: 10.1136/annrheumdis-2021-eular.1484

POS0731

CLINICAL ASSOCIATIONS OF COGNITIVE DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

S. Raghunath[1,2], V. Golder[1,2], R. Kandane-Rathnayake[1], E. F. Morand[1,2], Y. Glikmann-Johnston[3], J. C. Stout[3], A. Hoi[1,2]. [1]*Monash University, Centre for Inflammatory Diseases, Melbourne, Australia*; [2]*Monash Health, Rheumatology Department, Melbourne, Australia*; [3]*Monash University, Turner Institute for Brain and Mental Health, School of Psychological Sciences, Melbourne, Australia*

Background: Cognitive symptoms are commonly reported by SLE patients, but the prevalence and clinical associations of cognitive dysfunction (CD) is poorly understood.

Objectives: To examine the relationship between SLE disease parameters and CD.

Methods: Patients with SLE were consecutively recruited from 2018-2020. Cognitive assessment was performed using the one-hour conventional neuropsychiatric test battery recommended by the American College of Rheumatology for SLE[1]. Three binary definitions of CD and seven cognitive test z-scores were included in analysis. Clinical parameters included disease activity (SLEDAI-2K) and damage (SDI). Multivariate regression analysis was performed to determine associations with cognitive endpoints using variables with p <0.1 on univariate testing; likelihood ratio tests were used to select for inclusion from collinear pairs. A subgroup univariate analysis was performed to look for associations with interferon gene signature (IGS) and metabolic indices.

Results: 91 SLE patients and 48 age, sex, and premorbid IQ matched controls were recruited. The median (range) age was 45 (21-64) and median disease duration 13 years (0.2-39). 60% were Caucasian and the rest predominantly Asian, and all had good English proficiency. Prevalence of CD varied based on definition used; 18% had ≥2 cognitive domains ≥2 SD below the healthy control mean, whereas 48% were considered impaired if this threshold was reduced to ≥1.5 SD below. Age and premorbid IQ were significantly associated with multiple cognitive endpoints, and SDI was associated with four endpoints including the most severe definition of CD. Increased parity and past strokes correlated with poorer cognition in two endpoints. In contrast, clinical variables such as SLEDAI, antiphospholipid antibodies and past seizures only correlated with one endpoint each. There were no associations with other antibodies or any medications including glucocorticoids. Subgroup analysis showed univariate associations of CD with increased waist circumference, hypertriglyceridemia and low IGS.

Conclusion: Clinical associations of CD in SLE vary according to the cognitive domain or impairment definition used. SDI was the disease-related factor most consistently associated with CD, while IGS was negatively and metabolic features positively associated with CD. Studies of CD in SLE should use standardised methods to determine CD.

REFERENCES:

[1] Liang et al. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum. 1999;42(4).

Acknowledgements: We would like to acknowledge the patients who contribute to the Australian Lupus Registry and Biobank (ALRB) and participated in this study. The ALRB has received sponsorship from AstraZeneca, UCB and Arthritis Victoria.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1487

POS0732

IDENTIFICATION OF AUTOPHAGY-RELATED PHENOTYPES IN PRIMARY SJOGREN'S SYNDROME

R. Zhao[1,2,3], S. X. Zhang[1,2,3], J. Qiao[1,2,3], S. Song[1,2,3], Y. Zhang[1,2,3], M. J. Chang[1,2,3], Q. Wang[4,5], G. Y. Liu[1], P. F. He[5], X. Li[1,2,3]. [1]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [2]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [3]*Ministry of Education, Key laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [4]*Shanxi Medical University, Department of Basic Medical College, Taiyuan, China*; [5]*Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Primary Sjogren's syndrome (pSS) is a chronic systemic autoimmune disease characterized by disorders of effector T cell subpopulations such as Th1, Th2, Th17, regulatory T cells, and follicular helper T cells [1 2]. Autophagy is an evolutionarily conserved self-digestion process that plays an important role in T cell-mediated immune response[3]. The relationship between autophagy and T cell subsets was unclear in pSS up till now.

Objectives: To landscape the autophagy-related multiple gene expression signature in pSS classification and discover the influence of autophagy in T cell subsets.

Methods: Gene expression profiles of pSS samples (GSE66795, GSE51092, GSE154926) were acquired from GEO database. A set of significant G-ATGs were intersected from the global gene of patients and 232 autophagy genes (ATGs) which were obtained from the Human Autophagy Database (HADb, http://www.autophagy.lu/). In training dataset (GSE66795, including 155 patients and 29 healthy controls), non-negative matrix factorization was used to divided patients by G-ATGs expression microarray data. An autophagy score model divided patients into the high-autophagy score and low groups by ssGSEA scores of gene according to normalized G-ATGs training data. Further, new classifications were validated by both peripheral blood samples (GSE51092, 90 patients) and salivary gland tissue (GSE154926, 43 participants).

Results: Two distinct subtypes were identified and validated by 206 selected significant G-ATGs in training datasets (figure 1A,B) and validation datasets according to the autophagy score (figure 1D,E,F) Combined with clinical information of salivary gland dataset, it was found that most patients with early pSS were grouped in the high autophagy, while advanced patients were grouped in the low (figure 1G). Patients in high-autophagy group had higher levels of Treg cells and Th2 cells but lower concentrations of Th17 and Th1 in peripheral blood (figure 1C, P <0.05). Similar results were also observed in salivary gland tissue (figure 1H, P <0.05).

Conclusion: Patients with different autophagy status differs from each other. Autophagy is closely corelated with lymphocyte subpopulations in patients with pSS. This work may help inform therapeutic decision-making for the treatment of pSS.

Table 1. Multivariate Analysis of Clinical Predictors of Cognitive Dysfunction in SLE

	Cognitive Dysfunction Definitions[1]			Individual Cognitive Domains (Tests)						
	2 domains -1.5 SD	1 domain -2 SD	2 domains -2 SD	Visual Memory (ROCF recall)	Verbal Memory (CVLT 1-5)	Verbal Fluency (COWAT FAS)	Working Memory (LNS score)	Processing Speed (Coding score)	Complex attention (TMT B time)	Psychomotor Speed (Finger tap)
	Odds ratio (logistic regression)			Coefficient (linear regression)						
Age	**1.06***	**1.06***		**-0.03***				**-0.014***		**-0.03****
Premorbid IQ	**0.89****	**0.86****	**0.85***	**0.056****	**0.044****	**0.072****	**0.028****	**0.026***	**0.05****	0.017
SLEDAI	0.86	0.89								
Time-adjusted mean SLEDAI					**0.14****					-0.012
PGA									**0.79****	0.44
SDI			**1.91***	**-0.25****				**-0.15****	**-0.22****	
Past stroke or TIA	7.94	**13.19***					**-0.97****			
Past seizures					**-0.65***					-0.24
Methotrexate								-0.23		
Anti Ro			0.22							
Anti-cardiolipin								**0.38***		
Any APLS abs			**0.037****							
Parity			**2.21****		-0.05		-0.051		**-0.22****	
Substance use			2.58					**-0.49***		**-0.62***

[1]Impairment defined by number of cognitive domains either 1.5 or 2 SD below healthy control group mean*p value <0.05 **p value <0.005Abbreviations: SLEDAI - SLE Disease Activity Index, PGA - Physician global assessment, SDI - SLE International Collaborating Clinics Damage Index, TIA - Transient Ischaemic Attack, abs - Antibodies, APLS - Antiphospholipid Syndrome, ROCF - Rey-Ostrrieth Complex Figure Test, CVLT - California Verbal Learning Test, COWAT - Controlled Oral Word Association Test, LNS and Coding - Letter Number Sequencing & Coding subsets of Wechsler Adult Intelligence Scale IV, TMT - Trail Making Test

REFERENCES:

[1] Colafrancesco S, Vomero M, Iannizzotto V, et al. Autophagy occurs in lymphocytes infiltrating Sjögren's syndrome minor salivary glands and correlates with histological severity of salivary gland lesions. Arthritis research & therapy 2020;22(1):238. doi: 10.1186/s13075-020-02317-6 [published Online First: 2020/10/15].

[2] Alessandri C, Ciccia F, Priori R, et al. CD4 T lymphocyte autophagy is upregulated in the salivary glands of primary Sjögren's syndrome patients and correlates with focus score and disease activity. Arthritis research & therapy 2017;19(1):178. doi: 10.1186/s13075-017-1385-y [published Online First: 2017/07/27].

[3] Wei J, Long L, Yang K, et al. Autophagy enforces functional integrity of regulatory T cells by coupling environmental cues and metabolic homeostasis. Nature immunology 2016;17(3):277-85. doi: 10.1038/ni.3365 [published Online First: 2016/01/26].

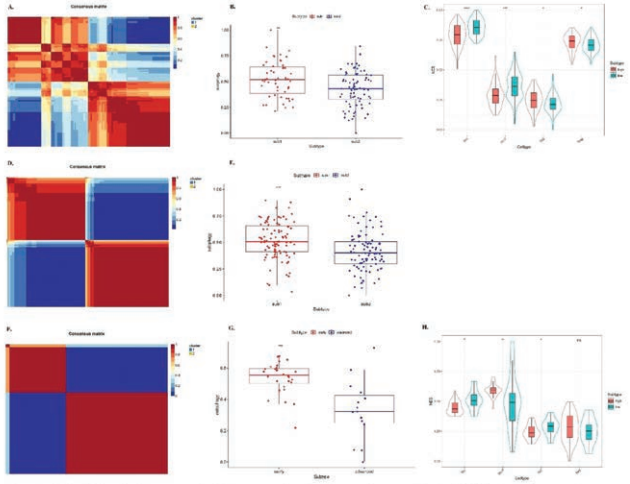


Figure 1: **(A)** Identification of training dataset using NMF consensus clustering in the autophagy set. **(B)** Boxplot visualizing the autophagy score between two subtypes. **(C)** ssGSEA was used to estimate the proportion of 4 immune cell types in 155 pSS patients. Th1; Th2; Th17; Treg cells remained statistically significant. **(D)** identification subclasses using NMF consensus clustering in the autophagy set in GSE5 1092. **(E)** Boxplot visualizing the autophagy score between two subtypes remained statistically significant. **(F)** NMF clustering using 206 ferroptosis-related genes. Salivary gland tissues from pSS patients were divided into cluster 1 and cluster 2. **(G)** The early group showed a higher autophagy score than the advanced group. **(H)** ssGSEA was used to estimate the proportion of 4 immune cell types in 43 pSS patients. Th1; Th2; Th17 cells remained statistically significant. ***P< 0.001; **P< 0.01, *P< 0.05, ns P>0.05

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1769

POS0733 REAL-LIFE PHYSICAL ACTIVITY IN SLE PATIENTS: ASSOCIATIONS WITH FATIGUE AND QUALITY OF SLEEP

H. Wohland[1], N. Leuchten[1], M. Aringer[1]. [1]*University Medical Center and Faculty of Medicine TU Dresden, Department of Medicine III, Division of Rheumatology, Dresden, Germany*

Background: Fatigue is among the top complaints of patients with systemic lupus erythematosus (SLE), but only in part associated with SLE disease activity. Physical activity can help to reduce fatigue and should therefore be recommended to SLE patients. Vice versa, fatigue may arguably lead to reduced physical activity.

Objectives: To investigate the extent of physical activity and the perception of fatigue and sleep quality in patients with SLE.

Methods: Starting in February 2019, SLE patients were invited to participate in a cross-sectional survey study of fatigue and physical exercise during their routine outpatient clinic visits. Participants filled out a ten-page paper questionnaire focused on physical activity. To evaluate fatigue, we primarily used a 10 cm visual analogue scale (0-100 mm, with 100 meaning most fatigued), but also the FACIT fatigue score (range 0-52). Sleep quality was estimated using grades from 1 (excellent) to 6 (extremely poor).

Results: 93 SLE patients took part in the study. All patients fulfilled the European League Against Rheumatism/ American College of Rheumatology (EULAR/ ACR) 2019 classification criteria for SLE. 91% of the patients were female. Their mean (SD) age was 45.5 (14.3) years and their mean disease duration 12.1 (9.4) years. The mean BMI was 25.2 (5.6). Of all patients, 7.5% had a diagnosis of (secondary) fibromyalgia. The mean fatigue VAS was 32 (27) mm and the mean FACIT fatigue score 35.7 (10.3). As expected, fatigue by VAS and FACIT was correlated (Spearman r=-0.61, p<0.0001). The mean SLEDAI was 1 (1) with a range of 0 to 6. Median glucocorticoid doses were 2 mg prednisolone equivalent, with a range from 0 to 10 mg.

Out of 66 patients in payed jobs, 64 (97%) reported details on their working space. One person (2%) worked in a predominanty standing position, 37 (58%) worked in essentially sedentary jobs and 26 (40%) were in positions where they were mildly physically active in part. The mean fatigue VAS was 31 (24) mm for patients with partly active jobs and 27 (30) mm for those in sedentary jobs. Sleep was graded 2.9 (0.9) by those with active and 3.1 (1.3) by those with sedentary jobs.

Half of the patients (51%) reported more than one physical recreational activity. 44 (47%) were walking and for five persons (5%) this was the only form of activity. Cycling was reported by 19 patients (20%), 18 of whom also practiced other activities. For transport, 52 (56%) in part chose active modes, such as walking and cycling. Patients who reported any of the above activities showed a mean fatigue VAS of 28 (25) mm, compared to 36 (28) mm in the patient group without a reported activity. Sleep quality was very similar: 3.1 (1.2) and 3.2 (1.1) for more active and more passive patients, respectively.

65 (70%) patients regularly practiced sports. Of these, 39 (60%) practiced one kind of sport, 15 (23%) two, 7 (11%) three, and 2 (3%) each four and five kinds of sports. Fatigue VAS of patients practicing sports was 27 (25) mm versus 43 (28) in those who did not (p=0.0075). Sleep quality was 2.9 (1.1) in the sports cohort and 3.5 (1.1) in the no-sports cohort (p=0.0244).

Conclusion: A majority of SLE patients in remission or low to moderate disease activity regularly practiced sports, and those doing so reported lesser fatigue and better sleep quality. The absolute values on the fatigue VAS were in a moderate range that made fatigue as the main cause of not performing sports rather unlikely for most patients.

Disclosure of Interests: Helena Wohland: None declared, Nicolai Leuchten Speakers bureau: AbbVie, Janssen, Novartis, Roche, UCB, Consultant of: AbbVie, Janssen, Novartis, Roche, Martin Aringer Speakers bureau: AbbVie, Astra Zeneca, BMS, Boehringer Ingelheim, Chugai, Gilead, GSK, HEXAL, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Astra Zeneca, BMS, Boehringer Ingelheim, GSK, Lilly, MSD, Roche, Sanofi, UCB

DOI: 10.1136/annrheumdis-2021-eular.1775

POS0734 EXTRAPOLATION OF LONG-TERM OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS: REPLICATING A HOPKINS LUPUS COHORT ANALYSIS WITH THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS (SLICC) INCEPTION COHORT

A. E. Clarke[1], Y. St-Pierre[2], V. Paly[3], I. N. Bruce[4], C. Malmberg[5], A. Briggs[6], Y. Zhang[7], J. Choi[7], A. Brennan[8]on behalf of Systemic Lupus International Collaborating Clinics. [1]*University of Calgary, Division of Rheumatology, Calgary, Canada*; [2]*McGill University Health Centre, Research Institute, Montreal, Canada*; [3]*ICON plc, Global Health Economics and Outcomes Research (GHEOR), New York, United States of America*; [4]*University of Manchester, The Kellgren Centre for Rheumatology, Manchester, United Kingdom*; [5]*ICON plc, Global Health Economics and Outcomes Research (GHEOR), Stockholm, Sweden*; [6]*London School of Hygiene & Tropical Medicine, Department of Health Services Research and Policy, London, United Kingdom*; [7]*Bristol Myers Squibb, Worldwide HEOR, Lawrenceville, United States of America*; [8]*University of Sheffield, Health Economics and Decision Science, School of Health and Related Research, Sheffield, United Kingdom*

Background: A disease model of systemic lupus erythematosus (SLE) that predicts short-term outcomes (disease activity and prednisone use) and links them to long-term outcomes (accrual of organ damage and mortality) was previously developed in a single center SLE cohort (Johns Hopkins [JH]) to support health economic analyses (Watson 2015), which has not been comprehensively replicated in other cohorts or contexts.

Objectives: As part of an effort to develop and refine this existing disease model, the aim of this study was to replicate the previously estimated network of risk equations for short- and long-term outcomes in the SLICC Inception Cohort, an international cohort of patients (33 centers,11 countries).

Methods: The SLICC Inception Cohort enrolled patients fulfilling ACR Classification Criteria for SLE within 15 months of diagnosis from 1999-2011 with annual follow-up through April 2020. The network of risk equations included two linear random effects models to predict (1) change in annual average Systemic Lupus Disease Activity Index (SLEDAI) score based on patient characteristics and the presence of renal, hematological, and immunological involvement in the prior year and (2) average annual prednisone dose based on SLEDAI score in the same year. These equations were then linked to parametric survival models that predicted time to the occurrence of organ damage (system-specific based on the ACR/SLICC Damage Index) and mortality. We compared model performance between the SLICC Cohort and the original analysis from the JH Cohort.

Results: In comparison to the JH cohort (N=1354), the SLICC cohort (N=1697) had a smaller fraction of patients of African descent (39% vs 17%) and shorter

disease duration at entry (4.8 vs 0.5 years). In the first equation predicting change in annual SLEDAI score, predictors were generally aligned with the same direction and significance, with the exception of renal involvement in the prior period, which had a positive association with change in SLEDAI in the SLICC cohort but was negatively associated in the JH cohort (Table 1). The second equation predicting prednisone dose was also consistent with the original analysis showing a significant positive association between higher disease activity and prednisone use. In all of the parametric survival analyses (individual organ damage and mortality models), coefficients were generally in the same direction and magnitude, though some were no longer significant in the SLICC cohort.

Conclusion: The relationships identified in the original analysis were broadly replicated in the SLICC Inception Cohort. Observed differences may reflect differences in the patient populations, structure of the two cohorts (prevalent vs inception), and frequency of visits (quarterly visits in the JH cohort vs annual visits with the SLICC cohort may more closely capture a decrease in SLEDAI associated with treatment specifically related to renal involvement). Additional analyses relaxing the requirement to completely align with the original structure are underway to further assess the predictive accuracy of these models.

REFERENCES:

[1] Watson P, et al. *Rheumatology* (Oxford). 2015;54(4):623-32.

Table 1.

	JH Cohort (N=1354)		SLICC Cohort (N=1697)	
Female, %	92.9		88.8	
African descent, %	38.8		16.7	
Disease duration at entry, mean (SD), years	4.8 (6.3)		0.5 (0.3)	
SLEDAI at first visit, mean (SD)	3.7 (4.1)		5.4 (5.4)	
Change in average annual SLEDAI	**Coefficient**		**Coefficient**	
Constant	1.491	*	5.762	*
Annual average SLEDAI in prior period	–0.460	*	–0.755	*
Male gender	–0.080		–0.207	
Log transformation of age	–0.241	*	–1.134	*
Renal involvement in prior period	–0.301	*	0.627	*
African descent	0.383	*	0.126	
Increased DNA binding in prior period	0.276	*	0.939	*
Low complement in prior period	0.484	*	0.775	*
Hematological involvement in prior period	0.104		–0.025	
Anemia in prior period	0.152	**	0.144	
Associated annual average prednisone dose (mg/day)				
Constant	3.475	*	2.738	*
SLEDAI in same period	0.777	*	0.648	*

*p<0.001; **p<0.05

Acknowledgements: We acknowledge the support on this abstract of the following investigators of the Systemic Lupus International Collaborating Clinics:
John Hanly - john.hanly@nshealth.ca
Caroline Gordon - p.c.gordon@bham.ac.uk
Sang-Cheol Bae - scbae@hanyang.ac.kr
Juanita Romero-Diaz - juanita.romerodiaz@gmail.com
Jorge Sanchez-Guerrero - jorge.sanchez-guerrero@uhn.ca
Sasha Bernatsky - sasha.bernatsky@mcgill.ca
Ann Clarke - aeclarke@ucalgary.ca
Daniel Wallace - dwallace@ucla.edu/danielwallac@gmail.com
David Isenberg - d.isenberg@ucl.ac.uk
Anisur Rahman - anisur.rahman@ucl.ac.uk
Joan Merril - JTMmail@aol.com
Paul Fortin - paul.fortin@crchudequebec.ulaval.ca
Dafna Gladman - dafna.gladman@utoronto.ca
Murray Urowitz - m.urowitz@utoronto.ca
Ian Bruce - ian.bruce@manchester.ac.uk
Michelle Petri - mpetri@jhmi.edu
Ellen Ginzler - ellen.ginzler@downstate.edu
MA Dooley - Mary_Dooley@med.unc.edu
Rosalind Ramsey-Godman - rgramsey@northwestern.edu
Susan Manzi - susan.manzi@ahn.org; Susanmanzi@gmail.com
Andreas Jonsen - andreas.jonsen@med.lu.se
Graciela Alarcon - galarcon@uab.edu
Ronald van Vollenhoven - r.vanvollenhoven@amsterdamumc.nl
Cynthia Aranow - CAranow@Northwell.edu
Meggan Mackay – mmackay@northwell.edu
Guillermo Ruiz-Irastorza - r.irastorza@outlook.es
Sam Lim - sslim@emory.edu
Murat Inanc - drinanc@istanbul.edu.tr; minanc2008@gmail.com
Kenneth Kalunian - kkalunian@ucsd.edu
Soren Jacobsen - sj@dadlnet.dk
Christine Peschken - christine.peschken@umanitoba.ca
Diane Kamen - kamend@musc.edu
Anca Askanase - ada20@columbia.edu

Disclosure of Interests: Ann E Clarke Consultant of: BMS, AstraZeneca, GSK, and Exagen Diagnostics., Yvan St-Pierre: None declared, Victoria Paly: None declared, Ian N. Bruce Speakers bureau: GSK, UCB, Consultant of: BMS, Eli Lilly, GSK, Astra Zeneca, Merck Serono; UCB, ILTOO, Aurinia, Grant/research support from: Genzyme/Sanofi, GSK, Roche, UCB, Chiara Malmberg: None declared, Andrew Briggs Speakers bureau: Alexion, AstraZeneca, Bayer, BMS, Daiichi Sankyo, Eisai, Gilead, GSK, Kite, Merck, Novartis, Rhythm, Roche, Sanofi, Takeda, Consultant of: Alexion, AstraZeneca, Bayer, BMS, Daiichi Sankyo, Eisai, Gilead, GSK, Kite, Merck, Novartis, Rhythm, Roche, Sanofi, Takeda, Yuanhui Zhang Shareholder of: Bristol Myers Squibb., Employee of: Bristol Myers Squibb., Jiyoon Choi Shareholder of: JNJ., Employee of: BMS, Alan Brennan Consultant of: Alan Brennan is a paid consultant on advisory boards regarding cost-effectiveness modelling., Grant/research support from: Alan Brennan received research grants.

DOI: 10.1136/annrheumdis-2021-eular.1790

POS0735 ULTRASOUND-GUIDED CORE NEEDLE BIOPSY FOR SALIVARY GLAND ENLARGEMENT IN SJÖGREN'S SYNDROME: PROCEDURE SAFETY AND PATIENT TOLERANCE

A. Zabotti[1], I. Giovannini[1], S. Z. Callegher[1], V. Manfrè[1], M. Lorenzon[2], E. Pegolo[3], C. A. Scott[3], A. Tel[4], M. Robiony[4], C. Zuiani[2], S. De Vita[1].
[1]Rheumatology Clinic, Department of Medicine, University of Udine, c/o Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy; *[2]Institute of Radiology, Dipartimento di Diagnostica per Immagini, Udine, Italy*; *[3]Institute of Anatomic Pathology, Department of Medical and Biological Sciences, Udine, Italy*; *[4]Maxillofacial Surgery, Department of Specialistic Surgery, Udine, Italy*

Background: Persistent enlargement of major salivary glands (SGs) is one of the main risk factors for B-cell lymphoma in primary Sjögren's syndrome (pSS). The Ultrasound-guided Core Needle Biopsy (US-guided CNB) could be a novel technique for the management of SGs enlargement in pSS (1).

Objectives: To evaluate the procedure safety and the patient tolerance of US-guided CNB in pSS patients with major SGs enlargement.

Methods: Consecutive patients, with either definite or clinically suspected pSS, and with clinical indication for SGs biopsy due to persistent glandular enlargement were screened for US-guided CNB from September 2019 to December 2020. All patients were evaluated clinically between 1 and 2 weeks and 12 weeks following US-guided CNB. All patients were asked to complete a questionnaire to report post-procedural complications (Figure 1, *English version*) and intra- and post-procedural pain Visual Analogue Scale (VAS). The complications were classified as transient (<12 weeks) or persistent (≥12 weeks).

Results: US-guided CNB was performed in 21 glands (12 parotid and 9 submandibular glands) in 20 pSS patients. 16/20 (80%) patients fulfilled the ACR-EULAR classification criteria for pSS (2). The mean age at the time of biopsy was 62.1 (±11.7) years. US-guided CNB was well tolerated, no long-term complications were reported in the follow-up period (mean 9.5 ±5.7 months). Only transient complications were noticed in 11 patients (55%). In particular, two cases of local swelling at the biopsy site lasting no more than 6 days, one case of local bleeding and subsequently hematoma of the submandibular area, one case of transient facial paresis (lasting less than one hour), seven cases of post-procedural mild local pain, that resolved within 10 days without the need of analgesics (Table 1). The procedure was well tolerated, with a very low reported intra-operative pain (mean VAS 1.74 ±2.49) and a mean post-operative pain VAS of 1.39 (±2.33). The biopsy sampling was diagnostic in 19/20 patients (95%).

Conclusion: US-guided CNB represents a novel approach for the management of pSS patients with SGs enlargement. This procedure shows a remarkable patient safety and tolerance, allowing an adequate glandular sampling and definite diagnosis in almost all the studied patients.

REFERENCES:

[1] Zabotti A, Zandonella Callegher S, Lorenzon M, Pegolo E, Scott CA, Tel A, et al. Ultrasound-guided core needle biopsy compared with open biopsy: a new diagnostic approach to salivary gland enlargement in Sjögren's syndrome? Rheumatology (Oxford) 2020.

[2] Shiboski CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM, Rasmussen A, Scofield H, Vitali C, Bowman SJ, Mariette X; International Sjögren's Syndrome Criteria Working Group. 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts. Arthritis Rheumatol. 2017 Jan;69(1):35-45. doi: 10.1002/art.39859. Epub 2016 Oct 26. PMID: 27785888; PMCID: PMC5650478.

Table 1. Description of complications

Complications of US-guided CNB	
Patients presenting complications, *n*/*N* (%)	11/20 (55%)
Description of **transient** complications	
Swelling at biopsy site, *n*	2
Bleeding, *n*	1
Hematoma, *n*	1
Local Pain, *n*	7
Local infection, *n*	0
Sialocele or fistula, *n*	0
Anaesthesia/paraesthesia, *n*	0
Transient facial palsy (< 1 hour), *n*	1
No **persistent** complications reported	

All the above specified complications were transient (< 12 weeks). No persistent complications were reported in the follow up.

POST-BIOPSY COMPLICATIONS QUESTIONNAIRE

1. Did you have any swelling at biopsy site?	YES	NO
If yes, how long?	.....	
Physician control	YES	NO
2. Did you have any hematoma at biopsy site?	YES	NO
If yes, how long?	.....	
Physician control	YES	NO
3. Did you have any bleeding at biopsy site?	YES	NO
If yes, how long?	.....	
Physician control	YES	NO
4. Did you have pain at biopsy site?	YES	NO
If yes, choose a number from 0 to 10 to describe pain intensity	.....	
If yes, how long?	.....	
5. Did you have any local infection?	YES	NO
Physician control	YES	NO
6. Did you have any anesthesia / paresthesia in the biopsy area?	YES	NO
If yes, how long?	.....	
Physician control	YES	NO
7. Did you have any sialocele or fistula in the biopsy area?	YES	NO
Physician control	YES	NO

Figure 1. Post-biopsy complication Questionnaire

Disclosure of Interests: Alen Zabotti Speakers bureau: UCB, Novartis, Janssen, Paid instructor for: Amgen, Consultant of: Janssen, Ivan Giovannini: None declared, Sara Zandonella Callegher: None declared, Valeria Manfrè: None declared, Michele Lorenzon Consultant of: not relevant for this study, Enrico Pegolo: None declared, Cathryn Ann Scott: None declared, Alessandro Tel: None declared, Massimo Robiony Consultant of: not relevant for this study, Grant/research support from: not relevant for this study, Chiara Zuiani Consultant of: not relevant for this study, Grant/research support from: not relevant for this study, Salvatore De Vita Consultant of: GSK, Roche, Grant/research support from: not relevant for this study

DOI: 10.1136/annrheumdis-2021-eular.1804

POS0736 IDENTIFICATION OF MOLECULAR PHENOTYPES AND IMMUNE CELL INFILTRATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS ACCORDING TO LONGITUDINAL GENE EXPRESSION

S. Song[1,2,3], S. X. Zhang[1,2,3], J. Qiao[1,2,3], R. Zhao[1,2,3], J. Shi[1,2,3], Y. Hu[1,2,3], J. Chen[1], G. Y. Liu[1], P. F. He[4], X. Li[1,2,3]. [1]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [2]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [3]*Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [4]*Shanxi Medical University, Institute of Medical Data Sciences, Taiyuan, China*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with highly heterogeneous clinical presentation characterized by disease unpredictable flares and multi-systemic involvement[1 2]. This clinical heterogeneity calls for design a molecular stratification to improve clinical trial design and formulate personalization treatment therapies.

Objectives: This research was conducted to develop a reliable method to stratify SLE patients combined gene expression information and disease status.

Methods: The mRNA expression profile of GSE138458 (contained 307 patients and 23 controls) and GSE49454 (contained 111 patients and 16 controls) were downloaded from the publicly GEO databases. After background adjustment, batch correction, and other pre-procession, obtaining a big gene matrix to identify the differentially expressed genes (DEGs) in SLE compared with healthy controls, which were screened by P value < 0.01. SLE subtypes were identified by non-negative matrix factorization (NMF) based on DEGs. Acquired signature genes in different SLE subtypes were conducted to process pathway enrichment analysis in Metascape. SLEDAI score and immune cell infiltration was also performed between subtypes by software package R (version 4.0.3).

Results: Total 1202 DEGs were imputed to NMF unsupervised machine learning method. Patients with SLE were stratified into two subsets based on 184 signature genes derived from obtained DEGs(Fig.1A, 1B). GO and KEGG enrichment analysis showed that signature genes were mainly involved in negative regulation of innate immune response, toll-like receptor signaling pathway, regulation of immune effector process and so on(Fig.1C). Patients in Sub1 group had severe disease activity measures compared with those in Sub2(Fig.1D). SLEDAI scores from GSE49454 dataset were also higher in Sub1 compare with Sub2(-Fig.1E). Further, immune cell infiltration results revealed an insufficient of regulatory T cell, CD8 T cells and naive CD4 T cells in Sub1 and neutrophils cells in Sub2(P<0.05)(Fig.1F).

Conclusion: Our findings indicate that patients with SLE could be stratified into 2 subtypes which had different lymphocyte status and closely related to disease activity. This phenotyping may help us understand the etiology of the disease, inform patient in the design of clinical trials and guide treatment decision.

REFERENCES:

[1] Dorner T, Furie R. Novel paradigms in systemic lupus erythematosus. Lancet 2019;393(10188):2344-58. doi: 10.1016/S0140-6736(19)30546-X [published Online First: 2019/06/11].

[2] Fanouriakis A, Tziolos N, Bertsias G, et al. Update on the diagnosis and management of systemic lupus erythematosus. Annals of the rheumatic diseases 2021;80(1):14-25. doi: 10.1136/annrheumdis-2020-218272 [published Online First: 2020/10/15].

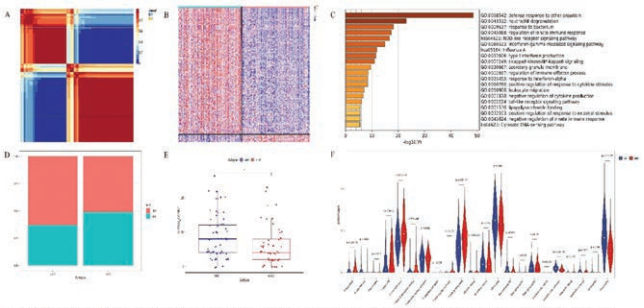


Fig.1 (A) NMF consensus clustering of 418 SLE patients based on 1202 differentially expressed genes. Columns and rows represent patients and signature genes, respectively. (B) Heatmap of two clusters defined by signature genes. Colors indicates relative gene expression value, with red for high expression and blue for low expression. (C) GO and KEGG pathway enrichment analysis of signature genes indicate possible differential pathways. (D) Disease activity distribution in the two subtypes. (E) Boxplot show the difference of SLEDAI scores among two subgroups in GSE49454. (F) Violin plot show the fraction of 22 immune cells subpopulations in two subtypes based on CIBERSORT algorithm.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1812

POS0737 LOW PRECONCEPTIONAL COMPLEMENT LEVEL IS RELATED WITH ADVERSE OBSTETRIC OUTCOME IN A MULTICENTRIC COHORT OF PREGNANCY IN PATIENTS WITH APS AND APL POSITIVITY

D. Lini[1], C. Nalli[1], L. Andreoli[1], F. Crisafulli[1], M. Fredi[1], M. G. Lazzaroni[1], V. Bitsadze[2], A. Calligaro[3], V. Canti[4], R. Caporali[5], F. Carubbi[6], C. Chighizola[7], P. Conigliaro[8], F. Conti[9], C. De Carolis[10], T. Del Ross[11], M. Favaro[11], M. Gerosa[12], A. Iuliano[13], J. Khizroeva[2], A. Makatsariya[2], P. L. Meroni[12], M. Mosca[14], P. Melissa[15], R. Perricone[8], P. Rovere-Querini[16], G. D. Sebastiani[13], C. Tani[12], M. Tonello[11], S. Truglia[9], D. Zucchi[12], F. Franceschini[1], A. Tincani[1]. [1]*University and ASST Spedali Civili of Brescia, Rheumatology Unit, Brescia, Italy*; [2]*I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University), Department of Obstetrics and Gynecology, Moscow, Russian Federation*; [3]*University Hospital of Padua, Padua, Rheumatology Unit, Department of Medicine, Padua, Italy*;

[4]RCCS San Raffaele Hospital, Immunology, Rheumatology, Allergology and Rare Disease - Laboratory of Autoimmunity and Vascular Inflammation, Milan, Italy; [5]ASST Gaetano Pini-Cto Institute, Division of Clinical Rheumatology - Department of Clinical Sciences and Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Milan, Italy; [6]School of Medicine, University of L'aquila, Department of Biotechnological and Applied Clinical Science, Rheumatology Unit, L'aquila, Italy; [7]Istituto Auxologico Italiano, University of Milan, Department of Clinical Sciences and Community Health -; Experimental Laboratory of Immunorheumatological Researches, Milan, Italy; [8]University of Rome Tor Vergata, Rheumatology, Allergology and Clinical Immunology, Department of "Medicina Dei Sistemi", Rome, Italy; [9]Sapienza University of Rome, Reumatologia, Dipartimento di Scienze Cliniche, Internistiche, Anestesiologiche E Cardiovascolari, Rome, Italy; [10]Polymedical Center for Prevention of Recurrent Spontaneous Abortion, Polymedical Center for Prevention of Recurrent Spontaneous Abortion, Rome, Italy; [11]University Hospital of Padua, Rheumatology Unit, Department of Medicine, Padua, Italy; [12]Ospedale Gaetano Pini, University of Milan, Division of Rheumatology, Department of Clinical Sciences and Community Health, Milan, Italy; [13]Azienda Ospedaliera San Camillo-Forlanini, Rheumatology Unit, Roma, Italy; [14]University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy; [15]University Of Ferrara, Division of Rheumatology, Department of Clinical Sciences, Ferrara, Italy; [16]IRCCS San Raffaele Hospital - San Raffaele University, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy

Background: The role of complement in the antiphospholipid (aPL) related pathology has been widely studied in animal models. Antiphospholipid antibodies can induce fetal loss in experimental animals but mice deficient in specific complement components (C4, C3, C5) appear somehow protected. In addition, in pregnant mice injected with aPL, antibody deposition has been found at decidual level causing focal necrosis, apoptosis and neutrophil infiltrates and supporting aPL pathogenetic potential. On the other hand, human studies did find hypocomplementemia associated to pregnancy complications in patients with obstetric antiphospholipid syndrome (APS). These results, however, are not unanimously confirmed and, in addition, some studies only show increased levels of complement activation products (i.e. Bb) and not decreased levels of C3 and/or C4. A recently study focusing on complement level in early pregnancy and before pregnancy showed a significant correlation with pregnancy complications and loss in a large cohort of primary APS.

Objectives: To investigate if the simple detection of low C3 and/or C4 could be considered a risk factor for adverse pregnancy outcome in APS and aPL carriers pregnancies.

Methods: We performed a multicentric study including patients from 10 Italian and 1 Russian Centers. Data on pregnancies in women with primary APS (n=434) and asymptomatic carriers with persistently positive aPL but not fulfilling clinical criteria for APS (n=218) were retrospectively collected. Serum C3 and C4 levels were evaluated by nephelometry; hypocomplementemia was defined by local laboratory reference values. Statistical analysis was performed using GraphPad.

Results: Preconceptional complement levels and gestational outcome were available for 107 (25%) pregnancies in APS out of 434 and for 196 (90%) pregnancies in aPL carriers women out of 218. In pregnancies with low preconceptional C3 and/or C4, a significantly higher prevalence of pregnancy losses was observed (p=0.019). A subgroup analysis focusing on triple aPL positive patients was also performed. Preconceptional low C3 and/or C4 levels were found to be associated with an increased rate of pregnancy loss (p = 0.027) in this subgroup also. Otherwise, adverse pregnancy outcomes in single or double aPL positive women were not related to preconception complement levels (p = 0.44) (Table 1). Of note, all the pregnancy losses in the triple positive group occurred in patients treated with low dose aspirin and low molecular weight heparin from the time of positive pregnancy test.

Conclusion: Our findings confirm that decreased complement levels before pregnancy are associated with increased risk of adverse outcome. This has been seen only in in women with triple aPL positivity, indeed single or double positivity does not show this trend. Complement levels are cheap and easy to be measured therefore they could represent a useful aid to identify patients at increased risk of pregnancy loss. test positivity.

REFERENCES:

[1] De Carolis S, et al. Complementemia and obstetric outcome in pregnancy with antiphospholipid syndrome. Lupus (2012) 21:776–8.

[2] Kim MY, et al. Complement activation predicts adverse pregnancy outcome in patients with systemic lupus erythematosus and/or antiphospholipid antibodies. Ann Rheum Dis (2018) 77:549–55.

[3] Fredi M, et al. Risk Factors for Adverse Maternal and Fetal Outcomes in Women With Confirmed aPL Positivity: Results From a Multicenter Study of 283 Pregnancies. Front Immunol. 2018 May 7;9:864.

Table 1.

	Triple aPL positivity			Single or double aPL positivity		
Gestational outcome	**Low C3/C4 (n=49)**	**Normal C3/C4 (n=17)**	**p**	**Low C3/C4 (n=57)**	**Normal C3/C4 (n=165)**	**p**
Term live birth (>37w)	15 (31%)	6 (35%)	ns	34 (60%)	110 (67%)	ns
Preterm live birth (≤37w)	22 (45%)	11 (65%)	ns	15 (26%)	38 (23%)	ns
Pregnancy losses (abortion and miscarriages)	12 (24%)	0 (0%)	0.027	8 (14%)	17 (10%)	ns

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1824

POS0738

BLUNTED CEREBRAL OXYGENATION DURING EXERCISE IN NON-NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

N. Koletsos[1], K. Dipla[2], A. Triantafyllou[1], A. Lazaridis[1], N. Papadopoulos[3], A. Zafeiridis[2], S. Aslanidis[4], S. Douma[1], E. Gkaliagkousi[1]. [1]Papageorgiou General Hospital, Aristotle University of Thessaloniki, ESH Hypertension Excellence Center, 3rd Department of Internal Medicine, Thessaloniki, Greece; [2]Aristotle University of Thessaloniki, Exercise Physiology & Biochemistry Laboratory, Department of Sport Sciences, Serres, Greece; [3]Papageorgiou General Hospital, Rheumatology Department, Thessaloniki, Greece; [4]Hippokration General Hospital, Rheumatology Department-2nd Propedeutic Department of Internal Medicine, Thessaloniki, Greece

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease affecting multiple organs, including the central nervous system. Subclinical brain lesions have been reported in SLE patients, even without overt neuropsychiatric manifestations (non-NPSLE). Studies using PET/MRI, examining structural or functional brain abnormalities in SLE, have been previously performed, either at rest or during a mental task (1–3). Exercise can be used to identify early alterations in brain oxygenation that might not detectable during resting conditions (4).

Objectives: Our study aimed to examine possible differences in cerebral oxygenation during a handgrip exercise test between SLE patients without neuropsychiatric manifestations and age-matched controls.

Methods: Fifty-two participants (26 non-NPSLE and 26 controls), following evaluation of handgrip strength, underwent a protocol involving a seated rest (baseline), a 3-min handgrip exercise (at 30% of maximal strength), and a 3-min recovery. Continuous-near-infrared-spectroscopy (NIRS) was used to monitor changes in cerebral-oxygenated hemoglobin (O2Hb), de-oxygenated (HHb) and total-hemoglobin (tHb). Beat-by-beat blood pressure (Finapres) was continuously monitored.

Results: There were no differences between the two groups in age, body mass index, blood pressure, and smoking status. Median SLE duration was 7.5 (3.0 – 16.0) years. During exercise, cerebral -O2Hb increased in both groups; however, non-NPSLE exhibited a significantly lower increase in O2Hb vs. controls (average response:1.20±0.89 vs. 2.33±1.61μM, respectively, p<0.005) and lower tHb responses (p<0.05), with no differences in HHb.

Conclusion: Our data show, for the first time, that SLE patients even without overt neuropsychiatric manifestations exhibit a blunted increase in cerebral-O2Hb during a submaximal exercise stimulus compared to age-matched controls. Examining brain oxygenation during a simple exercise task may assist in identifying patients with early alterations in cerebral function.

REFERENCES:

[1] Mak A, Ren T, Fu EH yun, Cheak AA cia, Ho RCM. A Prospective Functional MRI Study for Executive Function in Patients with Systemic Lupus Erythematosus Without Neuropsychiatric Symptoms. Semin Arthritis Rheum. 2012;41(6):849–58.

[2] Kozora E, Brown MS, Filley CM, Zhang L, Miller DE, West SG, et al. Memory impairment associated with neurometabolic abnormalities of the hippocampus in patients with non-neuropsychiatric systemic lupus erythematosus. Lupus. 2011;20(6):598–606.

[3] Mackay M, Vo A, Tang CC, Small M, Anderson EW, Ploran EJ, et al. Metabolic and microstructural alterations in the SLE brain correlate with cognitive impairment. JCI Insight. 2019;4(1).

[4] Triantafyllou GA, Dipla K, Triantafyllou A, Gkaliagkousi E, Douma S. Measurement and Changes in Cerebral Oxygenation and Blood Flow at Rest and During Exercise in Normotensive and Hypertensive Individuals. Vol. 22, Current Hypertension Reports. Springer; 2020.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1867

POS0739

DEVELOPMENT OF A CONCEPTUAL MODEL TO UNDERSTAND DISEASE BURDEN IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND LONG-TERM ORGAN DAMAGE

L. Broderick[1], W. H. Chen[2], R. Levy[3], A. Foster[1], C. Umanzor[1], D. Chauhan[4].
[1]QualityMetric, Johnston, RI, United States of America; *[2]GlaxoSmithKline, Value Evidence and Outcomes, Collegeville, PA, United States of America*; *[3]GlaxoSmithKline, Global Medical Affairs, Collegeville, PA, United States of America*; *[4]GlaxoSmithKline, Value Evidence and Outcomes, Brentford, Middlesex, United Kingdom*

Background: Systemic lupus erythematosus (SLE) is a chronic, multisystem, autoimmune disease resulting in increased morbidity and mortality and reduced health-related quality of life (HRQoL). Patients with SLE are at risk of developing irreversible long-term organ damage (LTOD) caused by both disease activity and cumulative medication toxicities. Data regarding the overall disease burden and impact of LTOD in patients with SLE are limited.
Objectives: The primary objective of this qualitative study was to develop a conceptual model to describe the burden experienced by patients with SLE and LTOD.
Methods: This study (GSK Study 209754) was conducted in three phases. First, a targeted literature review was performed to aid the development of an initial draft conceptual model. Key opinion leaders (KOLs) with experience in SLE and LTOD were then interviewed to assess the clarity, language, comprehensibility, and potential use of the conceptual model, and to help shape the patient interview materials. Finally, one-on-one interviews were performed with patients with SLE and LTOD in any of the 12 organ areas (defined by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index [SDI]), to gather patient perspectives on the common symptoms, functional impacts, treatment experiences, and HRQoL factors associated with LTOD. Data from the interviews were coded and analysed using NVivo software to identify patterns in responses concerning the key concepts of the overall patient burden of LTOD, and used to identify concepts to include in the model.
Results: The literature review produced the preliminary conceptual model of LTOD. Results of the KOL interviews (n=5 clinicians and n=1 patient advocate) indicated that the preliminary conceptual model broadly captured the patient experience of LTOD. KOLs emphasised the difference between SLE activity (flares) and LTOD; the conceptual model was subsequently updated in accordance with these recommendations. Interviews conducted with patients with confirmed single (n=9) and multiple LTOD (n=31) indicated that the burden of LTOD associated with SLE was more severe, debilitating, and life threatening than that caused by SLE flares. Almost all patients (39/40) reported aspects of their lives that were more severely affected since their LTOD diagnosis. All 40 patients reported LTOD-related physical impacts, which often affected patients' ability to perform everyday tasks. The most frequent physical impacts reported were a loss of vitality (39/40), long-term complications (e.g. unstable blood pressure, extreme pain, poor mobility, inflammation, dialysis, infection; 36/40), and severe fatigue (29/40). Cognitive impairments that became more pronounced after their LTOD diagnosis were reported by 27/40 of patients. Typically characterised as "brain fog," these impairments were described as slower cognitive processing, forgetfulness, confusion, and aphasia. Economic impacts associated with LTOD included patients' inability to work (31/40), costs of care (33/40), and non-medical-related costs (17/30). Psychosocial impacts reported by patients with LTOD affected their emotional state (39/40), ability to socialise (40/40) and relationships (30/40). Additionally, 30/40 patients reported symptoms as more severe since their LTOD diagnosis, including pain (14/40), fatigue (9/40), and oedema (8/40). Patients' treatment goals were largely aligned with their experienced impacts of LTOD, including managing the disease and symptoms (25/40), limiting further organ damage (15/40), and improving HRQoL (11/40).
Conclusion: The findings from this research clearly indicate that the patient burden of LTOD far surpasses that of SLE without LTOD. These data were incorporated and refined into a conceptual model that fully represents the patient experience of LTOD. The model will help researchers, clinicians, and patients to better understand the impact of SLE-related LTOD progression.
Funding: GSK
Acknowledgements: Medical writing assistance was provided by Casmira Brazaitis, PhD, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.
Disclosure of Interests: Lynne Broderick Consultant of: GSK, Wen-Hung Chen Shareholder of: GSK, Employee of: GSK, Roger Levy Shareholder of: GSK, Employee of: GSK, April Foster Consultant of: GSK, Cindy Umanzor Consultant of: GSK, Deven Chauhan Shareholder of: GSK, Employee of: GSK
DOI: 10.1136/annrheumdis-2021-eular.1907

POS0740

EPIDEMIOLOGY AND CLINICAL FEATURES OF OCULAR SARCOIDOSIS. STUDY OF 65 PATIENTS OF A SERIES OF 384 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL

C. Álvarez-Reguera[1], J. J. Gaitán-Valdizán[2], R. Fernández-Ramón[2], R. Demetrio-Pablo[2], J. L. Martín-Varillas[3], L. Sanchez-Bilbao[1], D. Martínez-López[1], I. González-Mazón[1], M. Á. González-Gay[1], R. Blanco[1].
[1]Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain; *[2]Hospital Universitario Marqués de Valdecilla, Ophthalmology, Santander, Spain*; *[3]Hospital de Sierrallana, Rheumatology, Santander, Spain*

Background: Ocular involvement in sarcoidosis can be present in up to 80% of patients. If not treated, it can lead to significant visually complications **(1-5).**
Objectives: Our aim was to assess the main **a)** epidemiology and **b)** clinical features of ocular sarcoidosis in a wide and unselected series from a single university hospital.
Methods: Study of a large cohort (n=384) of all consecutive patients diagnosed with sarcoidosis from January 1, 1999 to December 31, 2019. Finally, 344 patients were included according to the ATS/ERS/WASOG criteria *(Eur Respir J. 1999;14:735-7).*
Results: 65 (33 men/32 women) of 344 (18.9%) patients had ocular involvement. Mean age at diagnosis was 45.6±15.9 years. The most frequent extraocular clinical clusters were respiratory (80%), osteoarticular (30.8%) and cutaneous (29.2%) (figure 1). Ocular manifestations and complications are shown in table 1. Uveitis (83.1%), orbital lesions (7.7%) and retinal vasculitis (6.2%) were the most common ocular lesions. Median Best Corrected Visual Acuity (BCVA) at diagnosis and after one year of follow-up was 0.6 [0.3-0.8] and 0.9 [0.30-1], respectively. Retinal vasculitis was associated to the worst BCVA outcome, and panuveitis to more frequent and severe complications.
Conclusion: Ocular manifestations, especially uveitis, are frequent in sarcoidosis. A more aggressive and early treatment may be indicated in panuveitis and retinal vasculitis.
REFERENCES:
[1] Riancho-Zarrabeitia L, et al. Semin Arthritis Rheum 2015;45:361-8.
[2] Riancho-Zarrabeitia L et al. Clin Exp Rheumatol 2014; 32:275-84.
[3] Vegas-Revenga N, et al. Am J Ophthalmol 2019; 200:85-94.
[4] Calvo-Río V, et al. Clin Exp Rheumatol 2014; 32 (4 Suppl 84): S54-7. Epub 2014 Jul 8.
[5] Cordero-Coma et al. Mediators Inflamm. 2014; 2014:717598.

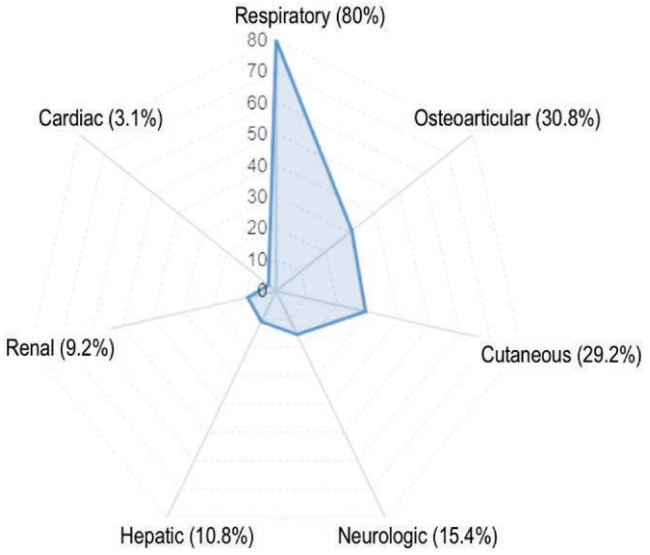


Figure 1. Clinical clusters of associations in ocular sarcoidosis.

Table 1. Ocular manifestations and associated complications after 1 year of follow-up of 65 patients with ocular sarcoidosis.

Type of ocular affectation	N (%)	Median BCVA at onset [IQR]	Median BCVA after 1 year of follow-up [IQR]	Cataract N (%)	OP N (%)	OHT N (%)	CME N (%)	ERM N (%)
Uveitis, pattern	54 (83.1)	0.6 [0.3-0.8]	0.9 [0.6-1]	18 (27.7)	11 (16.9)	7 (10.8)	7 (10.8)	8 (12.3)
Anterior	31 (47.7)	0.7 [0.3-0.8]	0.8 [0.5-1]	13 (41.9)	2 (6.5)	2 (6.5)	2 (6.5)	2 (6.5)
Panuveitis	16 (24.6)	0.4 [0.2-0.7]	0.9 [0.5-1]	5 (31.3)	7 (43.8)	4 (25)	5 (31.3)	5 (31.3)
Posterior	5 (5.2)	0.5 [0.1-0.9]	0.9 [0.9-1]	0	2 (40)	1 (20)	0	0
Intermediate	2 (3.1)	0.5	0.7	0	0	0	0	1
Orbitary lesions	5 (7.7)	0.5 [0.1-0.6]	1 [0.1-1]	1 (20)	0	1 (20)	0	0
Retinal vasculitis	4 (6.2)	0.6 [0.5-0.8]	1 [0.6-1]	0	0	0	0	1 (25)
Dry eye	4 (6.2)	1	0.9	0	0	0	0	0
Scleritis	1	0.6	1.0	0	0	0	0	0

Abbreviations: BCVA: Best corrected visual acuity; CME: Cystoid macular edema ERM: Epiretinal membrane; OP: Optic Papillitis; OHT: Ocular hypertension.

Disclosure of Interests: Carmen Álvarez-Reguera: None declared, Jorge Javier Gaitán-Valdizán: None declared, Raúl Fernández-Ramón: None declared, Rosalía Demetrio-Pablo: None declared, José Luis Martín-Varillas: None declared, Lara Sanchez-Bilbao: None declared, David Martínez-López: None declared, Iñigo González-Mazón: None declared, Miguel Á. González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi and MSD., Grant/research support from: Abbvie, MSD, Janssen and Roche., Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myer, Janssen, Lilly and MSD., Grant/research support from: Abbvie, MSD and Roche.

DOI: 10.1136/annrheumdis-2021-eular.1930

POS0741 HISTOPATHOLOGIC PATTERNS OF LUPUS NEPHRITIS PREDICT THE RISKS OF MORTALITY-A SINGLE-CENTER RETROSPECTIVE STUDY

Y. W. Liao[1], W. T. Hung[1], Y. M. Chen[1], C. W. Hsieh[1], T. Y. Hsieh[1], Y. H. Chen[1], W. N. Huang[1]. [1]*Taichung Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Taichung, Taiwan, Republic of China*

Background: Lupus nephritis is a significant complication of systemic lupus erythematosus and is associated with increased risks of end-stage kidney disease and mortality.

Objectives: The retrospective observational study aims to investigate which component of the National Institutes of Health activity and chronic indices of lupus nephritis can predict mortality.

Methods: We identified 528 SLE patients with biopsy-proven lupus nephritis between 2006 and 2019. Two patients with class VI lupus nephritis were excluded, and a total of 526 patients were analyzed. Serum creatinine, urine protein-to-creatinine ratio (UPCR), and serologic markers for SLE disease activity were measured at the time of the renal biopsy. The histopathologic findings of renal biopsies were classified by utilizing the International Society of Nephrology/ Renal Pathology Society (ISN/RPS) classification.

Results: Among 526 patients enrolled, 64 expired, and 44 were female (68.8%, p=0.004). Class IV (± V) comprised the most (n= 39, 60.9%), followed by class V (n= 18, 29.7%). Lower eGFR was observed in the death group, compared with the survival group (median: 24.7 vs. 80.5, p<0.001). There were no significant differences in UPCR and serologic markers for SLE (dsDNA, C3, and C4). Total scores of chronicity index and the scores for each index were higher in the death group. Interestingly, although total scores of activity index in death and survival groups did not differ significantly, the scores for cellular crescents tended to be higher in the death group (1.38 ±1.77 vs. 0.72 ±1.24, p=0.002)

In the univariable analysis, age, male sex, eGFR, activity index scores, cellular crescents, chronicity index scores, and all CI components (global obsolete glomeruli, tubular atrophy, interstitial fibrosis, fibrous crescents) and tubulointerstitial nephritis were significantly associated with an increased risk of death. When patient characteristics and NIH activity/ chronicity indices were jointly examined in a multivariable analysis, fibrous crescents were significantly associated with increased risk of death in females (HR 5.23 [95% CI: 1.51, 18.09]) (Table 1). In males, the risks of death increased with cellular crescents (HR 1.73 [95% CI: 1.10, 2.73]) but decreased with global obsolete glomeruli (HR 0.12 [95% CI: 0.02, 0.91]).

Conclusion: In this single-center observational study, fibrous crescents in females and cellular crescents in males were significantly associated with increased risks of mortality.

REFERENCES:

[1] Doria A, Iaccarino L, Ghirardello A, et al. Long-term prognosis and causes of death in systemic lupus erythematosus. Am J Med 2006; 119: 700–706.

[2] Faurschou M, Starklint H, Halberg P, Jacobsen S. Prognostic factors in lupus nephritis: diagnostic and therapeutic delay increases the risk of terminal renal failure. J Rheumatol. 2006;33(8):1563-1569.

[3] Chen YM, Hung WT, Liao YW, et al. Combination immunosuppressant therapy and lupus nephritis outcome: a hospital-based study. Lupus. 2019;28(5):658-666.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2006

POS0742 SCREENING AND BIOINFORMATICS ANALYSIS OF HUB GENES AND PATHWAYS FOR PRIMARY SJÖGREN'S SYNDROME BASED ON GEO DATABASE

T. Kong[1], S. X. Zhang[2,3,4], S. Song[2,3,4], X. Sun[1], C. Zheng[1], S. Feng[5], L. Cheng[1], G. Shi[6], X. Li[2,3,4], P. F. He[7], Q. Yu[1,7]. [1]*Shanxi Medical University, School of Management, Taiyuan, China*; [2]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [3]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [4]*Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [5]*Shanxi Medical University, School of Humanities and Social Sciences, Taiyuan, China*; [6]*Shanxi Medical University, Basic Medical College, Taiyuan, China*; [7]*Shanxi Medical University, Institute of Medical Data Sciences, Taiyuan, China*

Background: Primary Sjögren's syndrome (pSS) is an autoimmune disease that featured as lymphoplasmacytic infiltration of the exocrine glands leading to sicca symptoms[1]. However, its underlying molecular mechanisms remain elusive.

Objectives: This study aims to identify differentially expressed genes (DEGs) and pathways associated with the progression of pSS using bioinformatics analysis and explore its pathogenesis.

Methods: The pSS-associated gene chip data set GSE66795 was obtained from the Gene Expression Omnibus (GEO) database, which included 131 cases of fully-phenotyped pSS patients' whole blood samples and 29 cases of control samples. DEGs were screened Using R software. Online tool Metascape[2] was used to make Gene Ontology (GO) and KEGG pathway enrichment. The PPI network was performed using String database. Hub genes were identified by Cytoscape.

Results: A total of 108 DEGs were captured, including 101 up-regulated genes and 7 down-regulated genes. GO enrichment showed that these DEGs were primarily enriched in defense response to virus, response to interferon-gamma, regulation of innate immune response, response to interferon-beta, double-stranded RNA binding, response to interferon-alpha. KEGG pathway enrichment analysis showed these DEGs were principally enriched in Influenza A, RIG-I-like receptor signaling pathway, necroptosis, Staphylococcus aureus infection. Finally, 9 hub genes (STAT1, IRF7, OAS2, GBP1, OAS1, IFIT3, IFIH1, OAS3, DDX60) had highest degree value.

Conclusion: The findings identified molecular mechanisms and the key hub genes that may involve in the occurrence and development of pSS.

REFERENCES:

[1] Francois H, Mariette X. Renal involvement in primary Sjogren syndrome. *Nat Rev Nephrol* 2016;12(2):82-93. doi: 10.1038/nrneph.2015.174 [published Online First: 2015/11/17].

[2] Zhou Y, Zhou B, Pache L, et al. Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. *Nat Commun* 2019;10(1):1523. doi: 10.1038/s41467-019-09234-6 [published Online First: 2019/04/05].

Table 1. Logistic regression of predictors for mortality in patients with lupus nephritis

	Univariable			Multivariable (Female)			Multivariable (Male)		
	HR	95% CI	*p* value	HR	95% CI	*p* value	HR	95% CI	*p* value
Age	1.03	(1.01-1.05)	0.002	1.02	(0.98-1.07)	0.267	1.01	(0.95-1.08)	0.670
Male sex	2.10	(1.23-3.55)	0.006						
UPCR	1.02	(0.95-1.09)	0.616						
eGFR	0.97	(0.96-0.99)	<0.001	0.99	(0.96-1.00)	0.183	0.98	(0.96-1.00)	0.086
Activity Index	1.06	(1.01-1.11)	0.027						
Cellular crescents	1.29	(1.12-1.50)	<0.001	1.03	(0.63-1.67)	0.917	1.73	(1.10-2.73)	0.017
Chronicity Index	1.16	(1.07-1.26)	<0.001						
global obsolete glomeruli	1.37	(1.08-1.76)	0.011	1.24	(0.55-2.77)	0.606	0.12	(0.02-0.91)	0.040
Tubular atrophy	1.65	(1.28-2.13)	<0.001	0.41	(0.06-2.82)	0.362	4.77	(0.30-75.32)	0.267
Interstitial fibrosis	1.71	(1.32-2.23)	<0.001	3.70	(0.52-26.24)	0.191	1.37	(0.07-27.40)	0.837
Fibrous crescents	2.38	(1.40-4.03)	0.001	5.23	(1.51-18.09)	0.009	0.00	(0-extremely large)	0.989
Tubulointerstitial nephritis	1.70	(1.03-2.80)	0.037						

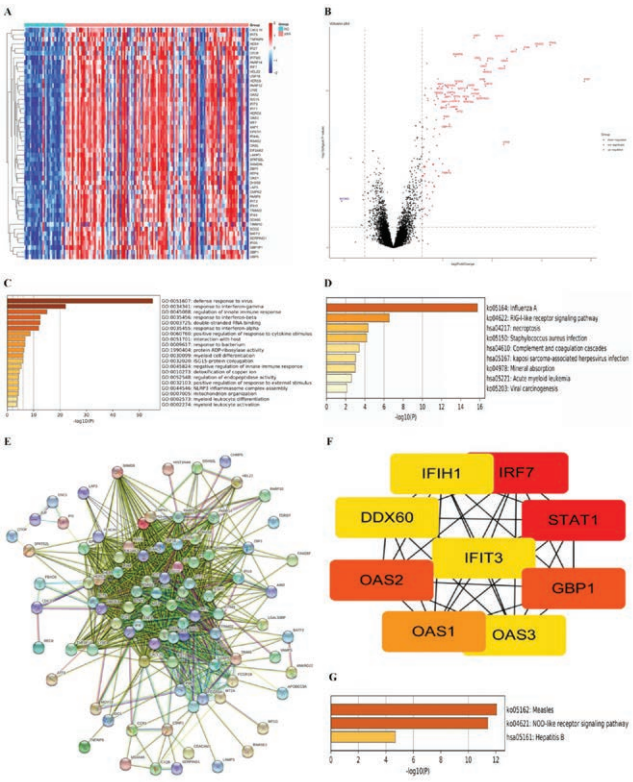


Figure 1: (A)Heat map of the top 50 up-regulated differentially expressed genes: Each small square represents a gene; the color indicates the expression level of the gene. Each column indicates the expression level of the genes in a sample; each row indicates the expression level of a gene in different samples; the right side is the gene name. **(B)Volcano map of gene expression:** The horizontal axis is log2 FC, the vertical axis is log10 adj.P.Val. Each dot represents a gene, blue indicates low expression genes, red indicates high. **(C,D)Visualization GO enrichment analysis and KEGG pathway enrichment analysis. (E,F,G)PPI network and hub gene identification:** Top 9 hub genes in the PPI network were screened by Cytoscape plugin cytoHubba based on their degree value from red (high degree value) to yellow (low degree value).

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2021

POS0743 GENE EXPRESSION MICROARRAY IN LUPUS NEPHRITIS BY BIOINFORMATIC ANALYSIS

C. Wang[1,2,3], S. X. Zhang[1,2,3], S. Song[1,2,3], J. Qiao[1,2,3], R. Zhao[1,2,3], M. J. Chang[1,2,3], Y. Zhang[1,2,3], G. Y. Liu[1], P. F. He[4], X. Li[1,2,3]. [1]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [2]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [3]*Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [4]*Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Nephritis is one of the predominant causes of morbidity and mortality in patients with lupus[1,2].The lack of understanding regarding the molecular mechanisms of lupus nephritis(LN) hinders the development of specific targeted therapy for this progressive disease[3].
Objectives: In this study, we use bioinformatics method to analyze the genes involved in regulating the potential pathogenesis of LN.
Methods: The expression profile of LN(GSE104948 and GSE32591) was obtained from the GEO database.GSE104948 was a memory chip, which included 32 LN glomerular biopsy tissues and 3 glomerular tissues from living donors.GSE32591 dataset included 32 LN glomerular biopsy tissues and 15 glomerular tissues from living donors. The Oligo package was used to process the data to obtain the expression matrix files of all the related genes.P<0.05 and |log2(FC)|>2 were setted as cut-off criteria for the DEGs.Ggplot2, heatmap packages were used to DEGs visualization. Metascape online tool was used to annotating DEGs for Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis performed.We used STRING online database to construct protein-protein interaction (PPI) network. Hub genes were identified by Cytoscape.
Results: In differential expression analysis,357 DEGs were identified,including 248 up-regulated genes and 109 down-regulated genes (Figure 1A,B). GO enrichment showed that these DEGs were primarily enriched in biological pathways, cell localization and molecular function and revealed that LN-related genes mainly involved in immune response.KEGG pathway annotation enrichment analysis revealed these DEGs were closely associated with Staphylococcus aureus infection,Complement and coagulation cascades (Figure 1D). Fourteen hub genes(IFT3,IRF7,OAS3,GBP2,RSAD2,MX1,IFIT2,IFI6,MX2,ISF15,IFIT1,QAS2,OASL,OAS1) were identified from PPI network (Figure 1C,E).
Conclusion: Illuminating the molecular mechanisms of LN was help for deep understanding of LN.
REFERENCES:

[1] Song J, Zhao L, Li Y. Comprehensive bioinformatics analysis of mRNA expression profiles and identification of a miRNA-mRNA network associated with lupus nephritis. Lupus 2020;29(8):854-61. doi: 10.1177/0961203320925155 [published Online First: 2020/05/22].
[2] Yao F, Sun L, Fang W, et al. HsamiR3715p inhibits human mesangial cell proliferation and promotes apoptosis in lupus nephritis by directly targeting hypoxiainducible factor 1alpha. Mol Med Rep 2016;14(6):5693-98. doi: 10.3892/mmr.2016.5939 [published Online First: 2016/11/24].
[3] Dall'Era M. Treatment of lupus nephritis: current paradigms and emerging strategies. Curr Opin Rheumatol 2017;29(3):241-47. doi: 10.1097/BOR.0000000000000381 [published Online First: 2017/02/17].

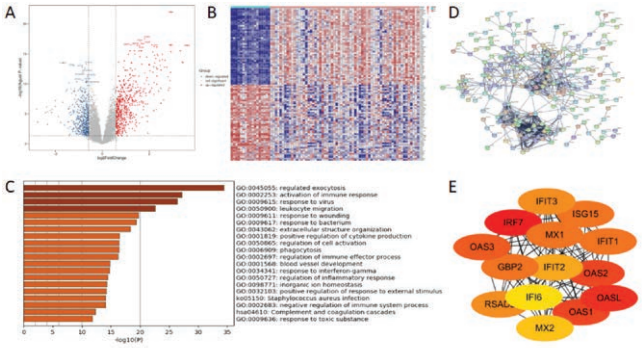


Figure1:**(A)**Volcano plots of DEGs between LN and healthy controls.Each dot represents a gene, where red represent up-regulated, blue represent down-regulated genes, and black represent genes with no significant difference.**(B)**Heatmap of the top 50 up-regulated and 50 down-regulated DEGs.Red represent up-regulated, blue represent down-regulated genes. Each row represents the expression level of a gene in a sample, sample grouping information is on the right. Each column represents the expression level of a gene in different samples.**(C)**Heatmap of enriched terms across input gene lists,colored by p-values.**(D,E)**PPI network and hub gene identification.Top 14 hub genes in the PPI network were screened by Cytoscape plugin cytoHubba based on their degree value from red (high degree value) to yellow (low degree value).

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2062

POS0744 A NEGATIVE INTERFERON BIOMARKER CD169 / SIGLEC-1 RULES OUT SYSTEMIC LUPUS ERYTHEMATOSUS

L. Zorn-Pauly[1], A. S. L. Von Stuckrad[2], J. Klotsche[3], T. Rose[1], T. Kallinich[2], F. Hiepe[1], P. Enghard[4], L. Ostendorf[4], T. Dörner[1], C. Meisel[5], U. Schneider[1], N. Unterwalder[5], G. R. Burmester[1], T. Alexander[1], R. Biesen[1]. [1]*Charité - Universitätsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany*; [2]*Charité - Universitätsmedizin Berlin, Pediatric Pneumology and Immunology, Berlin, Germany*; [3]*German Rheumatism Research Centre, Epidemiologic Unit, Berlin, Germany*; [4]*Charité – Universitätsmedizin Berlin, Nephrology and Intensive Care Medicine, Berlin, Germany*; [5]*Institute for Medical Immunology, Labor Berlin – Charité Vivantes, Immunology, Berlin, Germany*

Background: While there have been advances in the therapy of systemic lupus erythematosus (SLE) in recent years, there have been no major new findings in SLE biomarkers [1, 2]. Type I interferon (IFN) plays a pivotal role in the pathogenesis of SLE [3]. In 2008, we first described CD169 / SIGLEC-1 (sialic acid-binding immunoglobulin-like lectin-1), an interferon-induced adhesion molecule on monocytes in SLE patients [4]. For over five years SIGLEC-1 has been routinely assessed in our clinic.
Objectives: To evaluate and compare the diagnostic utility of the type I IFN induced SIGLEC-1 with established biomarkers in the initial diagnosis of the disease.
Methods: We analyzed retrospectively 232 patients who were on suspicion of SLE at Charité University Hospital Berlin between October 2015 and September 2020. Patients underwent full clinical characterization, and biomarkers were

determined in the routine laboratory. Based on the final diagnosis, we divided patients into two groups: A) initial diagnosis of SLE and B) Non-SLE mimicking condition.

Results: In 76 patients (32.3 %) SLE was confirmed by fulfilling the EULAR / ACR 2019 classification criteria [5]. SIGLEC-1 was dramatically increased in patients with an initial diagnosis of SLE compared to patients without SLE ($p<0.0001$). For a threshold of 2500 molecule per monocyte, a sensitivity of 98.7 %, a specificity of 82.1 %, a negative predictive value (NPV) of 99.2 %, and a positive predictive value (PPV) of 72.8 % were calculated for SIGLEC-1. Adjusted to the prevalence of SLE in Germany (36.7 per 100,000 inhabitants [6]) NPV and PPV turned out to > 99.9 % and 0.2 %. We further aimed to compare not only the performance of the tests at a given cutoff but also across all possible measured values. Therefore, we conducted ROC curves analyses (see figure 1). The area under the curve (AUC) of SIGLEC-1 test was significantly higher than that of ANA test (AUC=0.88, p=0.031), C3 (AUC = 0.83, p=0.001), C4 (AUC=0.83, p=0.002), but not than that of the Anti-dsDNA ELISA (AUC=0.90, p=0.163).

Conclusion: Our study shows that IFN activity is a hallmark at the onset of the disease and that the interferon biomarker SIGLEC-1 is valuable to rule out SLE in suspected cases.

REFERENCES:

[1] Ostendorf L, Burns M, Durek P, Heinz GA, Heinrich F, Garantziotis P, Enghard P, Richter U, Biesen R, Schneider U *et al*: **Targeting CD38 with Daratumumab in Refractory Systemic Lupus Erythematosus**. *N Engl J Med* 2020, **383**(12):1149-1155.

[2] Furie R, Rovin BH, Houssiau F, Malvar A, Teng YKO, Contreras G, Amoura Z, Yu X, Mok CC, Santiago MB *et al*: **Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis**. *N Engl J Med* 2020, **383**(12):1117-1128.

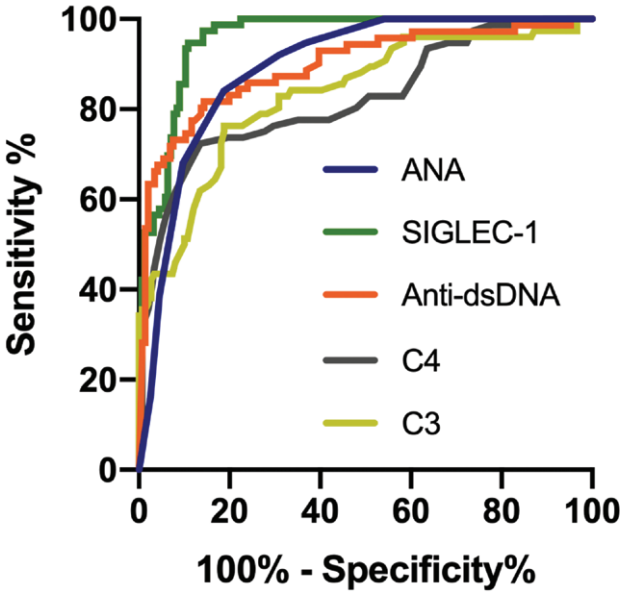
[3] Ronnblom L, Leonard D: **Interferon pathway in SLE: one key to unlocking the mystery of the disease**. *Lupus Sci Med* 2019, **6**(1):e000270.

[4] Biesen R, Demir C, Barkhudarova F, Grun JR, Steinbrich-Zollner M, Backhaus M, Haupl T, Rudwaleit M, Riemekasten G, Radbruch A *et al*: **Sialic acid-binding Ig-like lectin 1 expression in inflammatory and resident monocytes is a potential biomarker for monitoring disease activity and success of therapy in systemic lupus erythematosus**. *Arthritis Rheum* 2008, **58**(4):1136-1145.

[5] Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, Smolen JS, Wofsy D, Boumpas DT, Kamen DL *et al*: **2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus**. *Annals of the Rheumatic Diseases* 2019, **78**(9):1151-1159.

[6] Brinks R, Fischer-Betz R, Sander O, Richter JG, Chehab G, Schneider M: **Age-specific prevalence of diagnosed systemic lupus erythematosus in Germany 2002 and projection to 2030**. *Lupus* 2014, **23**(13):1407-1411.

Figure 1: Comparing ROC Curves



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2096

POS0745

RISK FACTORS FOR HOSPITALIZATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A LATIN COHORT

I. E. Garcia Cañas[1], E. Cuevas Orta[1], D. A. Herrera Van Oostdam[1], C. Abud-Mendoza[1]. [1]*Hospital Central Dr. Ignacio Morones Prieto, Rheumatology, San Luis Potosí, Mexico*

Background: Systemic lupus erythematosus (SLE) is the prototype of autoimmune diseases and is characterized by multisystemic affection. Hospitalization is a frequent eventuality in the course of the disease with a rate of 0.50 admissions/person-year estimated; infections and disease activity explain the highest percentage of admissions, risk factors depend on the population studied, among which are cardiopulmonary disease, elevated creatinine, thrombocytopenia, high disease activity and use of immunosuppression, however, the risk factors in the Mexican population are unknown.

Objectives: To identify risk factors for hospitalization in patients with generalized lupus erythematosus, and as a secondary result, identify the main causes of hospitalization in our population.

Methods: Observational, analytical, case-control and ambilective study of patients with a diagnosis of SLE at the Hospital Central Dr. Ignacio Morones Prieto in San Luis Potosí, Mexico, evaluated from January 2019 to October 2020; for each hospitalized patient with SLE, a non-hospitalized patient with SLE evaluated in the Rheumatology outpatient clinic was taken as a control, to establish a 1: 1 relationship. Continuous variables were expressed as mean or median; and standard deviation or interquartile ranges (IQR) according to the distribution. The categorical variables were expressed in proportion. The comparison of continuous variables was carried out with the unpaired Student's t test or Mann Whitney's U according to their distribution, while the categorical variables were compared with Fisher's exact test or X^2 and logistic regression analysis was performed.

Results: A total of 202 patients were collected, 179 were women (88.6%); of all patients, 89 (45.1%) were hospitalized, who were younger at diagnosis and time of evolution of the disease and greater SLEDAI and accumulated damage than non-hospitalized patients. The main causes of hospitalization were disease activity in 60.7% of cases, with kidney disease being the most important, followed by infectious in 22.5% and pharmacological toxicity in 5.6%. In the multivariate analysis, the risk factors associated with hospitalization identified were creatinine (p 0.018), CRP (p 0.046), neutrophils (p 0.013), constitutional condition (p 0.044), hematological (p 0.003) and renal (p. p 0.004), see Table 1. Factors associated with mortality were creatinine (p 0.022), INR (0.019), days of ICU stay (p 0.020) and the use of vasopressors (p 0.003). The use of antimalarials was a protective factor for hospitalization with p 0.0003. Survival analysis was performed where it was observed that patients with infection acquired in the hospital had a lower probability of survival with p 0.012.

Conclusion: In our center, disease activity continues to be the most frequent cause of hospitalization and elevated creatinine is a risk factor for hospitalization and mortality in patients with SLE. In-hospital infections were a factor of poor survival.

REFERENCES:

[1] Lee J, Park D, Kang J, Choi S, Yim Y, Kim J, et al. The rate of and risk factors for frequent hospitalization in systemic lupus erythematosus: results from the Korean lupus network registry. Lupus 2016. DOI: 10.1177/0961203316640916.

[2] Li D, Madhoun H, Jarjour W. Determining risk factors that increase hospitalizations in patients with systemic lupus erythematosus. Lupus 2018. DOI. 10.1177/0961203318770534.

Table 1. Multivariate analysis of factors associated with hospitalization in patients with SLE

	OR	CI 95%	p
Age of diagnosis	1.04	0.993 - 1.11	0.097
Previos prednisone dose	1.17	1.030 – 1.41	0.069
Use of antimalarials	0.04	0.006 - 0.21	**0.003**
Hemoglobin	0.78	0.57 – 1.01	0.074
Neutrophils	1.58	1.13 – 2.39	**0.013**
Creatinine	2.96	1.40 – 8.86	**0.018**
CRP	1.16	0.99 – 1.36	**0.046**
Constitutional condition	9.19	1.24 – 105.22	**0.044**
Hematological condition	34.5	3.82 – 517.49	**0.003**
Renal condition	16.05	2.66 – 133.42	**0.004**
Cardiopulmonary condition	19.79	0.84 – 843.46	0.081

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2178

POS0746

THE ARTHRITIS COMPONENT OF THE SLEDAI SHOULD ONLY BE SCORED IF THERE IS JOINT SWELLING

K. Mahmoud[1,2], A. Zayat[3], M. Y. MD Yusof[1,2], K. Dutton[1,2], L. S. Teh[4], C. S. Yee[5], D. D'cruz[6], N. Ng[6], D. Isenberg[7], C. Ciurtin[8], P. G. Conaghan[1,2], P. Emery[1,2], C. J. Edwards[9], E. Hensor[1,2], E. Vital[1,2]. *[1]NIHR Leeds Biomedical Research Centre, Rheumatology, Leeds, United Kingdom*; *[2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, Rheumatology, Leeds, United Kingdom*; *[3]Bradford Teaching Hospitals NHS Foundation Trust, Rheumatology, Bradford, United Kingdom*; *[4]Royal Blackburn Hospital, Rheumatology, Blackburn, United Kingdom*; *[5]Doncaster & Bassetlaw Hospitals NHS Trust, Rheumatology, Doncaster, United Kingdom*; *[6]Guy's and St Thomas' Hospital, Rheumatology, London, United Kingdom*; *[7]University College Hospital, Rheumatology, London, United Kingdom*; *[8]Centre for Adolescent Rheumatology, Rheumatology, London, United Kingdom*; *[9]University Hospital Southampton NHS Foundation Trust, Rheumatology, Southampton, United Kingdom*

Background: SLE disease activity tools do not optimally define disease activity and response. The SLEDAI arthritis item is common, and sufficient to define SRI response. Lupus patients with arthralgia often have no swelling. Glossary definitions of arthritis in different versions of the SLEDAI have included: swelling, swelling between visits, effusion, tenderness, warmth and erythema. MSK ultrasound in SLE can identify synovitis without swelling, ultrasound synovitis is associated with worse symptoms and serology, predicts response to therapy, and is more responsive to therapy than clinical variables.

Objectives: To validate different glossary definitions for SLEDAI arthritis using musculoskeletal ultrasound.

Methods: We analysed baseline data from a multicentre longitudinal study. Physicians scored SLEDAI-2K in 133 patients with joint pain that was considered inflammatory, but not necessarily swelling. Stable immunosuppressants and prednisolone <=5mg were permitted. If the arthritis criterion was scored, we asked physicians to report which glossary features drove their decision. Musculoskeletal ultrasound of hands and wrists was performed on the same day, blinded to clinical findings. We defined abnormal grey-scale in joints as 1 joint with GS>=2, and in tendons as >=1 tendon with GS >=1, and abnormal power Doppler as >=1 joint or tendon with PD >=1.

Results: 78/133 patients had arthritis scored on SLEDAI-2K. In 21/78, swelling was not a reason for that decision. These 21 patients had either tenderness (16/21), swelling reported between visits (4/21) or both of these (1/21). No patient was scored for warmth, erythema or effusion alone. Comparison of SLEDAI definitions and ultrasound is shown in Table 1. Of 57 patients with SLEDAI arthritis scored due to swelling, 90% had an abnormal ultrasound. The positive predictive value was 89% (95% CI 79 – 94). Of 21 patients with SLEDAI arthritis scored without swelling, 48% had an abnormal ultrasound. The positive predictive value was 48% (95% CI 31 – 67). There was no substantive difference in clinical and serological variables comparing patients with SLEDAI arthritis without swelling and patients without SLEDAI arthritis. In contrast, patients with SLEDAI arthritis with swelling had worse ESR (p=0.0003), Physician MSK disease activity VAS (p<0.001) and patient EMS VAS (p=0.0019) and IgG (p=0.0625) compared to the other two groups.

Conclusion: Although ultrasound proven synovitis in the absence of swelling is not uncommon, it is not reliably identified using other signs or symptoms. The arthritis item of the SLEDAI was likely to be associated with ultrasound synovitis if scored because of swelling, but not if scored because of tenderness or swelling between visits. Our results support raising the threshold criteria for arthritis so that it should only be scored when there is joint swelling. Previous clinical trial datasets could be re-analysed excluding SLEDAI arthritis scores not confirmed by a swollen joint count greater than one.

Disclosure of Interests: Khaled Mahmoud: None declared, Ahmed Zayat: None declared, Md Yuzaiful Md Yusof: None declared, Katherine Dutton: None declared, Lee-Suan Teh: None declared, Chee-Seng Yee: None declared, David d'cruz: None declared, Nora Ng: None declared, David Isenberg: None declared, Coziana Ciurtin: None declared, Philip G Conaghan: None declared, Paul Emery: None declared, Christopher John Edwards Shareholder of: Research grant support from; Abbvie, Biogen, Pfizer, Consultant of: Personal fee from; Abbvie, BMS, Biogen, Celgene, Celltrion, Fresenius, Gilead, GSK, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Grant/research support from: Research grant support from; Abbvie, Biogen, Pfizer, Elizabeth Hensor: None declared, Edward Vital Speakers bureau: AstraZeneca, Genentech, Aurinia, Lilly, Modus, Consultant of: AstraZeneca, Genentech, Aurinia, Lilly, Modus, Grant/research support from: Sandoz, AstraZeneca,

DOI: 10.1136/annrheumdis-2021-eular.2199

POS0747

MAPPING THE NATIONWIDE CLINICAL PROFILE AND PATTERNS OF CARE OF SLE IN BRAZIL – FINDINGS FROM THE MACUNAÍMA STUDY

M. Abreu[1,2], O. Monticielo[3], V. Fernandes[4], A. Cristovão Maiorano[2], F. Dos Santos Beserra[2], F. Lamarao[5], N. David[5], B. De Veras[5], B. Bica[1], D. Sávio Nunes de Lima[6], M. Maria Das Chagas Medeiros[7]. *[1]Universidade Federal do Rio de Janeiro, Faculdade de Medicina, Rio de Janeiro, Brazil*; *[2]Universidade Federal do Rio de Janeiro, Laboratório para Pesquisa em Desfechos Centrados no Paciente, Rio de Janeiro, Brazil*; *[3]Universidade Federal do Rio Grande do Sul, Serviço de Reumatologia do Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil*; *[4]Universidade de Cuiabá, Department of Medicine, Cuiabá, Brazil*; *[5]GlaxoSmithKline, Medical Department, Rio de Janeiro, Brazil*; *[6]Universidade Federal do Amazonas, Serviço de Reumatologia do Hospital Universitário Getúlio Vargas, Manaus, Brazil*; *[7]Universidade Federal do Ceará, Faculdade de Medicina, Fortaleza, Brazil*

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with wide clinical variability. Brazil has vast regional diversity, both from an ethnic and socio-cultural point of view.

Objectives: To map the clinical profile of SLE in Brazil and explore how this distribution is associated with regional disparities.

Methods: This cross-sectional study (GSK Study 207353) evaluated 300 Brazilian patients ≥18 years old with SLE (American College of Rheumatology [ACR] criteria, 1997) who had been under SLE care for ≥1 year. Five SLE reference teaching facilities were selected, one in each of the following Brazilian regions: North (NO), Northeast (NE), Midwest (CO), Southeast (SE), and South (SU). Each region included 60 patients. Clinical and demographic characteristics, and patterns of care were measured through questionnaires completed by physicians or nurses. The SLE Disease Activity Index (SLEDAI) score described disease activity and the Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI) described damage accrual. To assess the potential association between regional disparities and clinical outcomes, a hospitalisation profile was described. A bootstrapping approach of logistic regression was used to explore potential factors associated with hospitalisation.

Results: Overall, 92.3% of patients were female, with a mean (standard deviation; SD) age of 41.8 (12.7) years and a mean (SD) disease duration of 11.8 (7.9) years. Overall, 161 (53.7%) patients were of Latino origin; in the NO this proportion was 88%. White patients predominated in the SU (58.3%); and black patients in the SE (31.7%). The mean (SD) number of years of schooling was 11.3 (4.6), and was highest in the NO (14.2 [3.6]) and lowest in the SU (9.0 [4.0]; p<0.001). With regard to the distribution of the SLE clinical profile according to ACR criteria, arthritis was found in 221 patients and predominated in all regions (mean 73.7%), with a lower prevalence in the CO (40%; p<0.001; Figure 1A). The mean (SD) SLEDAI score was 4.33 (5.39) at the time of interview. The main contributing factors to disease activity, according to SLEDAI, were complement consumption (18%), arthritis (15.3%), and alopecia (15%). The SDI scale was scored for cataracts (15%), proteinuria (8.7%), and thrombosis (7.3%). Among the associated comorbidities, hypertension was predominant in the NO (35%; p=0.001). Smoking predominated in the SU (23%; p<0.001); obesity (27%; p=0.059) and dyslipidemia (35%; p=0.023), in the SE. Regarding patterns of care (Figure 1B), antimalarials were most frequently prescribed in the SE (88.3%) and the SU (91.7%). Corticosteroids prevailed in the NO (96.7%). The mean (SD) time between home and care facility was 4.5 (12.6) hours. Patients in the NO reported the longest transport time to reach the care facility (11.5 [25.4] hours; p<0.001). The hospitalisation rate during the study period was 21.3% across all regions, with no statistical difference between centres (p=0.651). Reasons for

SLEDAI-2K at baseline	Ultrasound Abnormalities at Baseline					Test statistics for any ultrasound abnormality			
	GS joints	PD joints	GS tendons	PD tendons	Any abnormality	Sensitivity	Specificity	PPV	NPV
	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
All patients (n=133)	77/133 (58)	33/133 (25)	36/133 (27)	27/106 (20)	83/133 (62)	-	-	-	-
MSK SLEDAI = No (n=55)	20/55 (36)	2/55 (4)	9/55 (16)	3/55 (6)	22/55 (40)	-	-	-	-
MSK SLEDAI = Yes (n=78)	57/78 (73)	31/78 (40)	27/78 (35)	24/78 (31)	61/78 (78)	73 (62, 82)[b]	66 (51, 78)[b]	78 (70, 84)[b]	60 (49, 69)[b]
-Due to swelling (n=57)	48/57 (84)	28/57 (49)	21/57 (37)	19/57 (33)	51/57 (90)	61 (50, 71)[c]	88 (75, 95)[c]	89 (79, 94)[c]	57 (50, 64)[c]
-Without swelling (n=21)[a]	9/21 (43)	3/21 (14)	6/21 (29)	5/21 (24)	10/21 (48)	31 (16, 50)[d]	75 (60, 87)[d]	48 (31, 67)[d]	60 (45, 68)[d]

hospitalisation included disease activity (36 [12%]), infection (19 [6.3%]), surgery (10 [3.3%]), and management of clinical morbidities (6 [2.0%]). Hospitalisation was associated with ethnicity (p<0.016), occupational status (p<0.001), age (p=0.02), and the use of hydroxychloroquine (HCQ) or chloroquine (CQ; p<0.001).

Conclusion: This nationwide study highlights ethnic, social, and patterns-of-care disparities among Brazilian patients with SLE. The modelling shows evidence that such disparities contribute to the divergent clinical spectrum observed in Brazil.

Funding: GSK

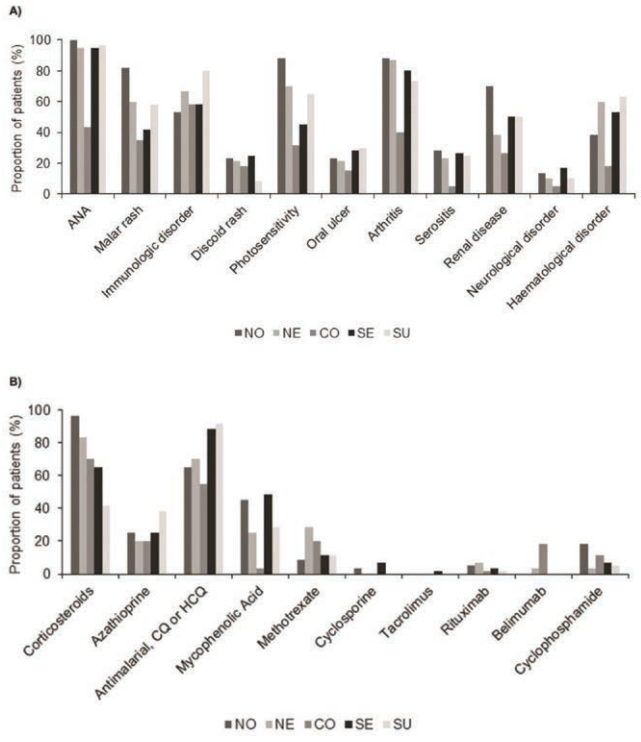


Figure 1. Distribution of the A) Brazilian SLE clinical profile according to the ACR Classification Criteria and B) Brazilian prescriptive profile for SLE treatment according to the use of immunosuppressive drugs, biological agents, and corticosteroids during the study (12 months)

ANA, antinuclear antibody

Acknowledgements: Medical writing assistance was provided by Helen Taylor, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.

Disclosure of Interests: Mirhelen Abreu Grant/research support from: GSK, Amgen, Biogen, Libbs, Odirlei Monticielo Speakers bureau: GSK, AbbVie, UCB, Roche, Novartis, Consultant of: GSK, AbbVie, Janssen, Vander Fernandes Speakers bureau: Janssen, Novartis, Roche, AbbVie, Pfizer, Grant/research support from: Novartis, GSK, Pfizer, Alexandre Cristovão Maiorano: None declared, Fernando dos Santos Beserra: None declared, Flavia Lamarao Employee of: GSK, Nathalie David Shareholder of: GSK, Employee of: GSK, Bruna de Veras Employee of: GSK, Blanca Bica: None declared, Domingos Sávio Nunes de Lima Grant/research support from: GSK, Marta Maria das Chagas Medeiros: None declared

DOI: 10.1136/annrheumdis-2021-eular.2421

POS0748 EASY-BILAG: A NEW TOOL FOR FASTER AND MORE ACCURATE RECORDING OF BILAG-2004 DISEASE ACTIVITY IN SLE

L. M. Carter[1], C. Gordon[2], C. S. Yee[3], I. N. Bruce[4], D. Isenberg[5], S. Skeoch[6], E. Vital[1]. *[1]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[2]University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom*; *[3]Department of Rheumatology, Doncaster and Bassetlaw NHS Foundation Trust, Doncaster, United Kingdom*; *[4]University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; *[5]University College London, Centre for Rheumatology, London, United Kingdom*; *[6]Department of Rheumatology, Royal National Hospital For Rheumatic Diseases, Bath, United Kingdom*

Background: BILAG-2004 index is an important disease activity instrument for SLE which is widely used in clinical trials and in treatment commissioning. It is more comprehensive and responsive than SLEDAI. However, BILAG-2004 may be difficult or time-consuming to complete during routine clinic visits. To derive the eventual scores from A (highly active) to E (no current or prior disease involvement) for each of the 9 organ domains, the current BILAG-2004 relies on a separate index form, glossary and scoring algorithm.

Objectives: The Easy-BILAG project aimed to develop and validate a simplified tool for scoring the original BILAG-2004 index more rapidly and accurately in routine clinical care.

Methods: Data from the UK BILAG-Biologics Registry (BILAG-BR) were used to measure the frequency with which the 97 BILAG-2004 clinical items occurred in a population with active SLE. These data and a series of prototypes were used to draft a new tool for simplified scoring of the BILAG-2004 index - the "Easy-BILAG". After preliminary testing, a validation study was conducted to test accuracy, speed and usability of Easy-BILAG compared to the standard BILAG-2004 template. Rheumatologists and specialty trainees from centres around the UK were invited to score BILAG-2004 disease activity in a timed workbook of 10 exemplar case vignettes, using either Easy-BILAG or standard BILAG-2004 reference documents. The case vignettes tested clinicians in scoring both frequent and uncommon SLE manifestations as well as longitudinal scoring of items in flare and remission. All workbooks contained an overview and detailed instructions on BILAG-2004.

Results: Among 2395 submissions to BILAG-BR the 6 most frequently scored clinical items were each present in more than 20% of records; arthralgia (72%), mild skin eruption (47%), moderate arthritis (38%), mild mucosal ulceration (34%), mild alopecia (34%), pleurisy / pericarditis (22%). Twenty-five items were active in less than 1% of assessments. Easy-BILAG was therefore designed to enhance the visibility of the most frequently scored items and capture all clinical items scoring >5% in a rapid single-page assessment. All remaining, less common items, are scored, only when necessary, on a second page. Easy-BILAG incorporates an abridged glossary definition immediately adjacent to clinical each item. A new colour-blindness compatible, colour-coding system directs clinicians instantly to the overall A-E score for each domain.

In the validation exercise, clinicians were asked to identify active disease and assign BILAG-2004 scores, from A-E, for all 9 organ domains in a workbook of 10 case vignettes. Twenty clinicians, with a range of prior experience, have so far participated. Among clinicians working with the standard BILAG-2004 reference documents (n = 11), scoring 10 case vignettes took 90 +/- 9 minutes (mean +/- SEM) to complete. Clinicians using Easy-BILAG (n = 9) completed the exercise significantly faster at 66 +/- 8 minutes (p = 0.05). Crucially, Easy-BILAG yielded significantly higher percentage accuracy (mean +/- SEM) at 95.3 +/- 0.8 % across all domains, as compared with 81.8 +/- 6.2 % achieved by clinicians using standard BILAG-2004 documentation (p = 0.05). The difference was most apparent when specifically comparing accuracy across domains where the case exercises registered active disease. Here, Easy-BILAG showed no decline in accuracy at 94.9 +/- 1.0 % compared 75.7 +/- 5.3% achieved with standard BILAG-2004 documents (p = 0.005). In a usability survey, all (9/9) clinicians testing the Easy-BILAG template rated it as intuitive and simple to navigate.

Conclusion: Easy-BILAG facilitates more rapid and accurate scoring of BILAG-2004 and provides a format which is amenable to use in routine clinical practice. Following completion of validation, it will be made widely available to clinicians.

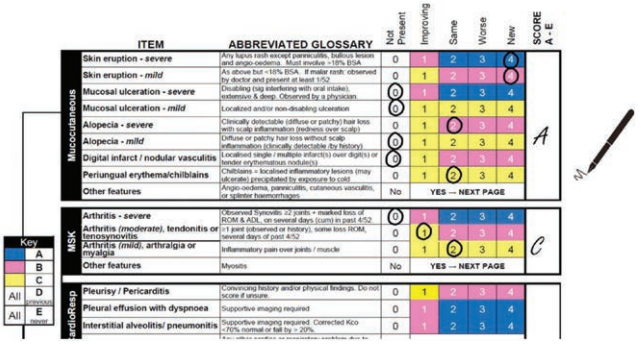


Figure 1. Illustration of the Easy-BILAG template shows format, colour scheme and method of scoring highest prevalence items mucocutaneous and musculoskeletal domain.

Disclosure of Interests: Lucy Marie Carter: None declared, Caroline Gordon: None declared, Chee-Seng Yee: None declared, Ian N. Bruce Speakers bureau: GlaxoSmithKline, UCB Pharma, Consultant of: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, MedImmune, Merck Serono, Grant/

research support from: Genzyme Sanofi, GlaxoSmithKline, David Isenberg: None declared, Sarah Skeoch: None declared, Edward Vital Consultant of: Roche, GSK and AstraZeneca, Grant/research support from: GSK and AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.2496

POS0749 ASSOCIATION BETWEEN IMMUNE-SEROLOGICAL PROFILE AND PULMONARY MANIFESTATIONS IN COLOMBIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (LES)

S. Herrera[1], J. C. Diaz-Coronado[1,2], S. Monsalve[2], S. Guerra-Zarama[2], M. F. Saavedra Chacón[2], J. Barbosa[2], J. D. Serna Giraldo[2], J. D. Lopez[2], J. M. Gutiérrez[2], T. Vega[2], D. Orozco[2], D. Ocampo[2], N. Zuluaga[2], D. Hernandez-Parra[1], D. Rojas-Gualdrón[3], R. Pineda.Tamayo[1]. *[1]Artmedica, Clinical Information Group, Medellín, Colombia*; *[2]CES University, Department of Internal Medicine, Medellín, Colombia*; *[3]CES University, Facultad de Medicina, Medellín, Colombia*

Background: Pulmonary involvement is common in Systemic Lupus Erythematosus (SLE) patients with varying degrees of parenchymal, vascular, and pleural compromise. In GLADEL, pulmonary involvement was reported in 28.4% of the cohort, but its occurrence ranges between 30-90% due to diversity in populations and the methods used to define it.

Objectives: To describe the immune-serological profile of a Colombian cohort of SLE patients and to establish its association with pulmonary manifestations.

Methods: Retrospective analysis of observational data from the follow-up of a cohort of adult patients with SLE. We included 559 patients that fulfilled the SLICC 2012 classification criteria with at least 6 months of disease history and being treated in a rheumatology specialized medical center between 2015 and 2018. The immuno-serological profile was characterized, and pulmonary involvement was monitored for 1 year. Diagnosis of pulmonary involvement was performed with the rheumatologist report in the clinical chart. Prevalence of pulmonary manifestations and immune-serological profile was determined, and logistic regression was performed afterward adjusted by age, sex, and level of education to establish the association between pulmonary manifestations and a positive auto-antibodies profile.

Results: The median age of the cohort was 45 years, 96.5% were female. Pulmonary involvement was documented in 113 patients (20.5%) at the beginning of the study. Their frequency was: pleuritis (14.3%), lupus pneumonitis (3.6%), pulmonary hypertension (3.2%), interstitial lung disease (ILD) (2.3%), pulmonary embolism (2.3%), lung fibrosis (2.14%), alveolar hemorrhage (1.4%), shrinking lung (0.2%). At 1 year of follow up. there were no statistically significant differences in the frequency of pulmonary manifestations. As for the immune-serological profile, there were positive ANA in 92%, anti-dsDNA in 53.1%, anti-B2GP IgM 15.2%, anti- B2GP IgG in 17.2%, and ENA in 97.2%; as for the ENA 41.7% had positive anti-RNP, 40.2% anti-Ro, 36.4% anti-SM and 16.5% anti-La. Low complement levels was characterized as follows: C3 53.1% and C4 29.2%. In the logistic regression adjusted by age, sex and level of education, there was an association between anti-SM and pulmonary manifestations with an adjusted OR of 1.85; 95% CI 1.13-3.01.

Conclusion: An association between anti-SM positivity and pleuro-pulmonary manifestations was found. In other cohorts with a greater size, anti-La and anti-RNP have been associated with pulmonary involvement (OR 2.51; 95% CI 1.39-4.57 and OR 1.32; 95% CI 1-1.75 respectively). Anti-RNP positivity has been associated in particular with ILD, pulmonary hypertension and shrinking lung. Although these manifestations prevalence was similar in our cohort, an association with this antibody was not found (OR 1.01, 95% CI: 0.2-4.9). This could be explained by the smaller sample size. As for anti-La positivity, its prevalence in our cohort was less than what was found in the GLADEL cohort (16.5% vs 24.3% respectively). It is possible that this could explain the poor association between anti-La positivity with the presence of pulmonary manifestations in our study compared with those of the GLADEL cohort. There are data that indicates that anti-SM and anti-RNP simultaneous positivity is related mainly to pleuritis OR 1.98 (95% CI: 1.31-3); and this kind of involvement was found to be more frequent in our study. Our results suggest an association between positive anti-SM and pulmonary manifestations in Colombian patients with SLE, pleuritis in particular.

REFERENCES:

[1] Haye Salinas MJ, Caeiro F, Saurit V et al. Pleuropulmonary involvement in patients with systemic lupus erythematosus from a Latin American inception cohort (GLADEL). Lupus. 2017;26(13):1368–77.

[2] Emad Y, Gheita T, Darweesh H, Klooster P, et al. Antibodies to extractable nuclear antigens (ENAS) in systemic lupus erythematosus patients: Correlations with clinical manifestations and disease activity. Reumatismo. 2018;70(2):85–91.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2577

POS0750 THE CHARACTERISTICS OF SYSTEMIC LUPUS ERYTHEMATOSUS WHO HAVE CONSTITUTIONAL SYMPTOMS AND LYMPHADENOPATHY

Y. Erez[1], S. Gulle[1], A. Karakas[1], R. Bekis[2], A. Balcı[3], M. Birlik[1], G. Can[1], F. Onen[1], İ. Sari[1]. *[1]Dokuz Eylul University School of Medicine, Division of Rheumatology, İzmïr,Turkey*; *[2]Dokuz Eylul University School of Medicine, Division of Nuclear Medicine, İzmïr,Turkey*; *[3]Dokuz Eylul University School of Medicine, Division of Radiology, İzmïr,Turkey*

Background: Systemic lupus erythematosus (SLE) is the prototype of systemic autoimmune diseases. It may affect any organ system and may present with a variety of clinical symptoms. Lymphadenopathy (LAP) is a nonspecific finding of SLE and often associated to the active disease state. LAP associated SLE pose a significant diagnostic challenge especially in the presence of constitutional symptoms.

Objectives: In this retrospective cohort study, we evaluated the clinical and imaging characteristics of SLE patients who presented with LAP and constitutional symptoms.

Methods: SLE Patients with lymphadenopathy who had constitutional symptoms were reviewed retrospectively. The characteristics of the patients such as age, sex, disease duration, clinical features, and laboratory tests including autoantibodies against ANA, dsDNA and ENA were recorded. Imaging findings such as positron emission tomography–computed tomography (PET/CT), thoracal or abdominal CT or diagnostic lymph node biopsy were identified.

Results: There were 28 patients in this study. The mean age at the time of LAP was 38.9±15.2 years, 22 (78.6%) were female. All patients were fulfilling SLICC 2012 classification criteria for SLE. LAP was the presenting feature of SLE in 15 (53.6%) patients. The most common clinical features associated with LAP were arthritis (42.8%), fever (35.7%), acute lupus rash (32.1%) and serositis (28.5%). There were 11 (39.2%) who had significant proteinuria and 4 (14.3%) had class III or IV renal histology. Anti-phospholipid antibodies were present in nearly one-third of the patients and 12 of them had venous or arterial thrombosis or pregnancy co-morbidity. Cervical LAP was present in 57.1%, axillary LAP in 82.1% and inguinal in 36%. On CT, the prevalence of thoracal and abdominal LAP and hepatomegaly and splenomegaly were 61.5%, 37,5%, 40% and 16% respectively. The pericardial and pleural effusion and intra-abdominal free fluid were 19.2%, 30.8% and 10.2% respectively. There were 19 (67.8%) patients who underwent PET/CT imaging and all were reported as reactive LAP. In terms of SUV max 7 (36.8%) of them had a threshold ≥2.5. 17 (60.7%) patients required lymph node biopsy; 2 did not include lymphoid tissue, 4 (30.7%) with atypical lymphoid hyperplasia suggestive of viral infection and remaining were reactive lymphoid hyperplasia. Autoantibody testing showed that anti-dsDNA was positive in 66.7% and the most common anti-ENAs were anti-nucleosome (35.7%) and anti-Sm-RNP (35.7%) followed by anti-SSA (25%), anti-ribosomal P (17.9%) and anti-histone (14%). The clinical and laboratory features of the clinical and laboratory features of the group is summarized in Table 1.

Table 1. Data at the time of LAP

Age, years	38.9±15.2
Disease duration, months	3 (2- 300)
SLE-DAI, median (min-max)	9 (2-30)
Sex, female n(%)	22 (78.6)
Clinical features	**n (%)**
Acute cutaneous	9 (32.1)
Arthritis	12 (42.8)
Fever	10 (35.7)
Other constitutional symptoms	18 (64.2)
Serositis	8 (28.5)
Renal involvement	11 (39.2)
Neurologic involvement	1 (3.6)
Leucopenia	7 (25.0)
Trombositopenia	5 (17.8)
Hemolitic anemia	7 (25.0)
ANA (+)>1/320	28 (100)
Anti-dsDNA (+)	18 (66.7)
Anti-Sm(+)	5 (17.9)
Anti-phospholipid antibody (+)	9 (32.1)
Low complement	16 (88.5)

Conclusion: We showed that SLE patients who had constitutional findings and LAP could be the presenting feature and may confer a significant diagnostic challenge in which the patients might require invasive procedures and advanced imaging modalities. PET/CT revealed reactive changes in lymph nodes in all patients but lymph node biopsy revealed atypical changes in some patients suggestive of viral infections. On the other hand, LAP patients with constitutional symptoms represents a severe phonotype of the SLE as there were significant renal and thrombotic disease.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2588

POS0751 COMORBIDITY AND LONG-TERM OUTCOME IN PATIENTS WITH CONGENITAL HEART BLOCK: PRELIMINARY DATA OF THE ITALIAN REGISTRY ON THE IMMUNE-MEDIATED CONGENITAL HEART BLOCK

M. Fredi[1], G. Rizzo[2], L. Andreoli[1], B. Bacco[3], T. Bertero[3], A. Bortoluzzi[4], F. Ceccarelli[5], R. Cimaz[6], P. Conigliaro[7], F. Corradi[3], S. De Vita[8], E. DI Poi[8], E. Elefante[9], G. Emmi[10], M. Gerosa[11], M. Govoni[4], A. Hoxha[12], A. Lojacono[13], E. Marrani[14], L. Marozio[15], A. Mathieu[16], M. Mosca[9], P. Melissa[4], C. Picchi[17], M. Piga[16], R. Priori[5], V. Ramoni[18], A. Ruffatti[19], G. Simonini[14], C. Tani[9], M. Tonello[19], L. Trespidi[20], M. L. Urban[10], M. Vezzoli[21], S. Zatti[22], S. Calza[21], A. Brucato[23], F. Franceschini[1], A. Tincani[1]. [1]*UO Reumatologia e Immunologia Clinica, Dipartimento Scienze Cliniche e Sperimentali, ASST Spedali Civili e Università degli Studi di Brescia, Brescia, Italy*; [2]*University of Brescia, Brescia, Italy*; [3]*S.S.d.D.U. Immunologia, Allergologia, A.O. Ordine Maurziano di Torino, Torino, Italy*; [4]*UO e Sezione di Reumatologia, Dipartimento di Scienze Mediche, Universita' degli Studi di Ferrara, Ferrara, Italy*; [5]*UO Complessa, Reumatologia, Policlinico Umberto I- University La Sapienza, Roma, Italy*; [6]*Department of Clinical Sciences and Community Health, University of Milan, Milano, Italy*; [7]*Rheumatology, Allergology and Clinical Immunology, Department of Systems Medicine, University of Rome Tor Vergata, Roma, Italy*; [8]*Clinica di Reumatologia, Azienda Sanitaria Universitaria Integrata di Udine, Udine, Italy*; [9]*UO Reumatologia, Dipartimento di Medicina Clinica e Sperimentale, Universita' di Pisa, Pisa, Italy*; [10]*Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy*; [11]*Istituto Ortopedico Gaetano Pini, University of Milan, Milan, Italy*; [12]*Internal Medicine Unit, Department of Medicine, San Bortolo Hospital, Vicenza, Italy*; [13]*Ostetricia e Ginecologia, Ospedale di Desenzano, ASST Garda, Desenzano del Garda, Italy*; [14]*Servizio di Reumatologia Pediatrica, Azienda Ospedaliero-Universitaria "Anna Meyer", Firenze, Italy*; [15]*Ginecologia e Ostetricia 1, Dipartimento di Scienze Chirurgiche, Università di Torino, Turin, Italy*; [16]*Cattedra e Struttura Complessa di Reumatologia, Universita' degli Studi e AOU di Cagliari, Cagliari, Italy*; [17]*Medicina Interna, ASST Fatebenefratelli, Milano, Italy*; [18]*Rheumatology, IRCCS Policlinico San Matteo Foundation, University of Pavia, Pavia, Italy*; [19]*Unità di Reumatologia, Dipartimento di Medicina, Università di Padova, Padova, Italy*; [20]*Dipartimento per la Salute della Donna, Bambino e Neonato, Fondazione Ospedale Maggiore, Milan, Italy*; [21]*Unit of Biostatistics, Biomathematics, and Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy*; [22]*Department of Obstetrics and Gynecology, ASST Spedali Civili and University, Brescia, Italy*; [23]*Dipartimento di Scienze Biomediche e Cliniche "Sacco", Università degli Studi di Milano, Milan, Italy*

Background: Congenital heart block (CHB) is due to placental transfer of maternal anti-Ro/SSA autoantibodies to the fetus. The prevalence of CHB has been estimated as 1-2% in anti-Ro/SSA women while the recurrence rate is 16-19% (1). This condition is associated with a high rate of fetal/neonatal mortality and most of the cases requires pacemaker (PM) pacing. Given the rarity of CHB, limited data are available regarding the long-term follow-up of the offspring other than the cardiovascular complications.

Objectives: The results of the Italian Registry of the autoimmune congenital heart block were recently described (2). A peculiarity of this cohort was that most of the mothers had an established diagnosis of systemic autoimmune disease at CHB detection, in contrast with other registries where CHB was mostly incidentally detected in healthy women. Here we report an update, with the preliminary data regarding the long-term outcome of patients with CHB, their unaffected siblings and health controls born from mothers positive for Ro/SSA.

Methods: Data regarding demography, treatment, maternal, neonatal outcome, and follow-up were collected through an online electronic datasheet. A dedicated questionnaire was created with the aim to investigate general health, cardiovascular follow-up, and frequency of autoimmune diseases.

Results: One-hundred and five cases of CHB in 99 patients were included from 1969 to December 2020. CHB was mostly detected in utero (97 cases, 92.3%) with 8 neonatal cases. Third degree CHB occurred in 71 cases (67.6%). Child mortality was observed in 29 (27.6%) cases: 20 in utero, 7 during neonatal period and 2 during childhood. Overall, a PM was implanted in 54 out of the 85 live births (63.5%). Then, our cohort was divided into 2 subgroups: pregnancy that occurred before (N=61) and after 2010 (N=44) with the aim to evaluate possible differences among the subgroups. Whereas mortality, PM, CHB degree were similar, CHB more frequently occurred in the last 10 years among Ro/SSA asymptomatic carriers than in the group of pregnancies before 2010 (53.6% vs 32.8%, p=0.038). Questionnaires from 14 surviving CHB cases, 8 unaffected siblings 12 controls born from mothers Ro/SSA positive were collected. Among CHB cases, 6 were males and 8 females, median age 12 years (range 6-28). All presented a third degree CHB, 10 required a neonatal PM pacing and one had an implantable ECG recorder. PM was substituted at least once in 9 patients, the oldest patient had to change it four times. No dilated cardiomyopathy occurred and most of the patients maintain an annual follow-up. Two cases of autoimmune diseases were registered among CHB cases, one idiopathic juvenile arthritis and one Cogan's vasculitis, both born from mothers with Sjogren Syndrome. Four cases of neurodevelopmental disorders occurred: three cases of learning disabilities (one in each group) and one case of speech disorder in the sibling group. In addition, a CHB case presented a stress disorder linked to frequent hospitalizations.

Conclusion: This registry is an ongoing project aiming at collecting all Italian CHB. Moreover, here we reported the preliminary data concerning the evaluation of long-term follow-up of CHB patients. Our data, even if need to be confirmed in larger cohort, seems reassuring: no differences were reported comparing CHB patients with unaffected siblings or controls.

REFERENCES:

[1] Brito-Zéron et al. Nat Rev Rheumatol 2015;11:301-312.
[2] Fredi M et al. Front Cardiovasc Med. 2019 Feb 28;6:11.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2697

POS0752 INTERSTITIAL LUNG INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS: RELEVANT CLINICAL CHARACTERISTICS. OUR EXPERIENCE IN A THIRD LEVEL HOSPITAL

I. González Fernández[1], C. Moriano[1], E. Diez Álvarez[1], X. E. Larco Rojas[1], A. López Robles[1], M. E. Vallejo Pascual[2], M. T. Perez Sandoval[1]. [1]*Complejo Asistencial Universitario de León, Reumatología, León, Spain*; [2]*Universidad de León, Facultad de CC. EE y Empresariales, León, Spain*

Background: Lung involvement[1] in Systemic Lupus Erythematosus (SLE) is heterogeneous, with the pleura being more frequently affected. Associated diffuse interstitial lung disease (ILD) is rare (3-13%) with difficult diagnosis and therapeutic management.

Objectives: Assess the main clinical-epidemiological characteristics of patients diagnosed with SLE with ILD in a third level hospital and analyze the possible relationship between them.

Methods: Descriptive observational study of patients diagnosed with SLE (SLICC criteria) with ILD in our hospital between 1973 and 2020. The following clinical-epidemiological characteristics were evaluated such as sex, mean age at diagnosis, presence of cardiovascular risk factors (CVRF), smoking, baseline cardiac and respiratory comorbidities, laboratory markers (autoimmunity, CRP and vitamin D), baseline SLEDAI, manifestations of SLE, interstitial pattern on HRCT, correlation with conventional radiology (Rx), respiratory function tests, clinical and physical examination at diagnosis.

Results: 455 patients diagnosed with SLE were included, of whom 20 had ILD (4.4%). 65% were women with a mean age at diagnosis of 63 ± 16.23 years. 30% presented ILD as the first clinical data for the diagnosis of SLE. 30% had jobs with exposure to chemicals. 25% were ex-smokers and 10% were active smokers. 10% had associated CVRF, highlighting HT (35%). 30% had valve disease on echocardiography such as mitral regurgitation (30%) and tricuspid regurgitation (20%). Only 10% had associated bronchopathy. 35% and 25% associated, respectively, pleural serositis and secondary Sjogren's syndrome. Arthritis and skin involvement were documented in 60% for both clinical domains. 40% had SLEDAI> 6.

At the diagnosis of ILD, 90% had symptoms such as dyspnea (75%) and cough (60%). 80% had crackles on examination. 85% had alterations in the X-ray and 100% in the CT scan with the NINE patterns as the main one (65%) with progression at 2 years despite treatment in 25%. Spirometry differentiated an obstructive pattern (25%), restrictive (20%) and normal (55%) with a tendency to stability at one year (40%) with the prescribed treatment. 90% had a decrease in diffusion, the majority being mild (67%). Analytically, 67% had elevated levels of CRP and hypovitaminosis D; 40% elevated DNA titers, 50% hypocomplementemia and 60% ENAS positive, highlighting Ro (45%); La (15%) and RNP (15%). Leukopenia and thrombopenia (30% and 10% respectively) were also observed.

In our study, we did not find any statistical significance between the variables analyzed, due to the small sample size.

Conclusion: 1)ILD is an infrequent manifestation in SLE, it usually associates respiratory symptoms and pulmonary functional repercussions with the diagnosis. The most characteristic radiological pattern is the NINE.

2)In our study, ILD was more frequently associated with women and joint or skin symptoms, as well as with data on immunological activity, without statistical significance.

REFERENCES:

[1] Aguilera-Pickens G, Abud-Mendoza C. Pulmonary Manifestations in Systemic Lupus Erythematosus: Pleural Involvement, Acute Pneumonitis, Chronic Interstitial Lung Disease and Diffuse Alveolar Hemorrhage. Clinical rheumatology. Vol.14 Issue. 5. Pages 294-300 (September-October 2018).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2726

POS0753 SUBSPECIALTY LUPUS CLINIC CARE IS ASSOCIATED WITH HIGHER QUALITY FOR PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

S. Sreedharan[1,2], A. Hoi[1,2], N. Li[2], G. Littlejohn[2], R. Buchanan[3], M. Nikpour[4], E. F. Morand[1,2], V. Golder[1,2]. [1]*Monash Health, Department of Rheumatology, Melbourne, Australia*; [2]*Monash University, School of Clinical Sciences, Melbourne, Australia*; [3]*Austin Hospital, Department of Rheumatology, Heidelberg, Australia*; [4]*St. Vincent's Hospital Melbourne, Department of Rheumatology, Fitzroy, Australia*

Background: Healthcare quality for systemic lupus erythematosus (SLE) is a modifiable target for improving patient outcomes. Disease-specific subspecialty clinics offer experienced healthcare professionals, collaborative multidisciplinary teams and streamlined care processes. A single centre study in the USA has suggested superior performance of the subspecialty lupus clinic in the provision of quality care (1), but this has not been examined outside the USA where access to care may be influential.

Objectives: To assess the quality of SLE care provided in a subspecialty lupus clinic compared with hospital general rheumatology and private rheumatology clinics in a non-US, universal healthcare setting.

Methods: Lupus patients (n = 258) were recruited in 2016 from various clinic settings in Australia, including a subspecialty lupus clinic (n = 147), two hospital general rheumatology clinics (n = 56) and two private clinics (n = 55). Quality of care was assessed using 31 validated SLE quality indicators (QI) encompassing diagnostic work-up, disease and comorbidities assessment, drug monitoring, preventative care and reproductive health (2,3). Data were collected from medical records and patient questionnaires. Overall and individual QI performance was calculated and compared between the three clinic settings, and multivariable regression was performed to adjust for sociodemographic, disease and healthcare factors.

Results: Median [IQR] overall performance on eligible QIs was higher in the lupus clinic (66.7% [16.9]) than the hospital general rheumatology (52.7% [10.6]) and private rheumatology (50.00% [18.0]) clinics ($p < 0.01$), and remained significant with multivariable adjustment. This trend was still observed when the overall performance was reassessed to include patient self-report (73.1% [14.8] vs 68.1% [11.5] vs 63.2% [13.4], $p < 0.01$). This difference may be due to consistent formal assessments of disease activity (100% vs 0% vs 0%, $p < 0.01$) and disease damage (95.9% vs 0% vs 0%, $p < 0.01$) at the lupus clinic. Performance was high across all clinic settings for diagnostic work-up, comorbidity assessment, drug monitoring, prednisolone taper, osteoporosis management, lupus nephritis and pregnancy quality indicators. However, the lupus clinic significantly outperformed the other clinic settings on eligible quality indicators for new medication counselling, pre-immunosuppression hepatitis and tuberculosis screening, drug toxicity assessment, sun avoidance education, vaccinations, cardiovascular risk factor assessment and contraception counselling.

Conclusion: SLE patients managed in a subspecialty lupus clinic received higher overall quality of care when compared to hospital general rheumatology and private rheumatology clinics. Regular assessment of QI performance can improve quality of care for patients in all clinic settings.

REFERENCES:

[1] Arora, S et al. Does Systemic Lupus Erythematosus Care Provided in a Lupus Clinic Result in Higher Quality of Care Than That Provided in a General Rheumatology Clinic? Arthritis Care Res. 2018;70(12):1771-1777.

[2] Mosca, M et al. Development of quality indicators to evaluate the monitoring of SLE patients in routine clinical practice. Autoimmune Rev. 2011;10(7):383-8.

[3] Yazdany, J et al. A quality indicator set for systemic lupus erythematosus. Arthritis Rheum. 2009;61(3):370-7.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2760

POS0754 DEVELOPMENT OF A RISK PREDICTION MODEL FOR VENOUS THROMBOEMBOLISM IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: THE SLE-VTE SCORE

H. You[1,2], M. Li[1], J. L. Zhao[1], L. Wu[3], X. Duan[4], H. Luo[5], C. Zhao[6], F. Zhan[7], Z. Wu[8], H. Li[9], M. Yang[10], J. Xu[11], W. Wei[12], Y. Wang[13], J. Shi[14], J. Qu[1], Q. Wang[1], X. Leng[1], X. Tian[1], Y. Zhao[1], X. Zeng[1]. [1]*Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Sciences, Department of Rheumatology, Beijing, China*; [2]*The First Affiliated Hospital of Nanjing Medical University, Department of Rheumatology, Nanjing, China*; [3]*People Hospital of Xinjiang Uygur Autonomous Region, Department of Rheumatology, Urumchi, China*; [4]*The Second Affiliated Hospital of Nanchang University, Department of Rheumatology, Nanchang, China*; [5]*Xiangya Hospital, Central South University, Department of Rheumatology, Changsha, China*; [6]*The First Affiliated Hospital of Guangxi Medical University, Department of Rheumatology, Nanning, China*; [7]*Hainan General Hospital, Department of Rheumatology, Haikou, China*; [8]*Xijing Hospital Affiliated to the Fourth Military Medical University, Department of Rheumatology, Xi'an, China*; [9]*Affiliated Hospital of Inner Mongolia Medical College, Department of Rheumatology, Hohhot, China*; [10]*Nanfang Hospital, Southern Medical University, Department of Rheumatology, Guangzhou, China*; [11]*First Affiliated Hospital of Kunming Medical University, Department of Rheumatology, Kunming, China*; [12]*Tianjin Medical University General Hospital, Department of Rheumatology, Tianjin, China*; [13]*Institute of Basic Medical Sciences, China Academy of Medical Sciences & Peking Union Medical College, Department of Epidemiology and Bio-Statistics, Beijing, China*; [14]*Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Sciences, Department of Respiratory and Critical Care Medicine, Beijing, China*

Background: Patients with systemic lupus erythematosus (SLE) have a substantially increased risk of venous thromboembolism (VTE). An individual VTE risk assessment is important to ensure that all patients are assessed and given adequate thromboprophylaxis.

Objectives: We conducted this study to develop a risk score for VTE in patients with SLE.

Methods: Patients with SLE who participated in the Chinese SLE Treatment and Research group were enrolled in this study. Patient baseline information and clinical laboratory indicators were obtained, and VTE events were recorded every 3-6 months during follow-up visits. The risk prediction model was created and internally validated using the bootstrap methods, and a scoring system was established (Figure 1).

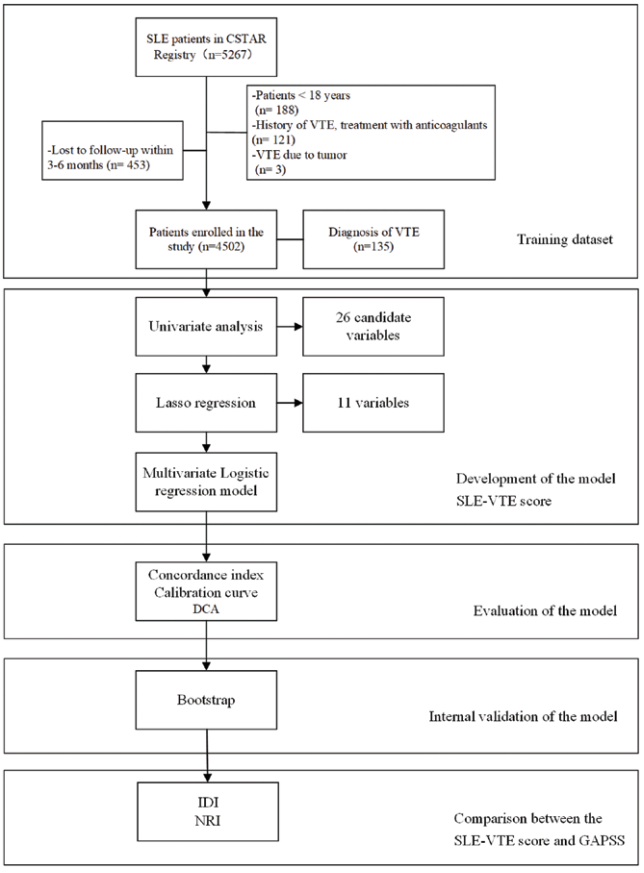


Figure 1. Flow chart of study design.

Results: Out of 4,502 patients included in this study, 135 had a VTE event. After univariate analysis and Lasso regression, the following 11 variables were identified and included in the risk prediction model: male sex, age, BMI ≥25 kg/m2, hyperlipidemia, hypoalbuminemia, hsCRP>3 mg/L, renal involvement, nervous system involvement, anti-β2-glycoprotein I antibody positivity, lupus anticoagulant positivity, and no use of hydroxychloroquine. The AUC for the SLE-VTE score (Table 1) was 0.947 (95% CI, 0.9249-0.9694). The SLE-VTE score's sensitivity and specificity with the optimal cutoff value of 13 were 0.919 and 0.881, respectively. The SLE-VTE score was superior to the GAPSS system in predicting the risk of VTE in patients with SLE (AUC= 0.947 vs. 0.680, P< 0.001; integrated discrimination improvement (IDI)= 0.6652, P< 0.001; net reclassification improvement (NRI)= 0.6652, P< 0.001).

Table 1. Final multivariable analysis for venous thromboembolism risk in patients with SLE

	β coefficients	Odds ratio* (95% CI)	P-value	Points in scoring system
Male	0.621	1.86 (0.953-3.503)	0.061	2
Age at study entry(≥50)	0.837	2.308 (1.339-3.915)	**0.002**	3
BMI02(kg/m^2	0.792	2.209 (1.333-3.627)	**0.002**	3
Hyperlipemia	0.838	2.313 (1.246-4.166)	**0.006**	3
Hypoalbuminemia	2.163	8.697 (5.185-14.794)	**< 0.001**	7
hsCRP>3 mg/L	1.452	4.272 (2.618-6.968)	**< 0.001**	5
Anti β2GPI	1.013	2.754 (1.543-4.853)	**0.001**	3
LA	1.559	4.752 (2.799-8.072)	**< 0.001**	5
Nervous system	2.382	10.832 (6.163-18.998)	**< 0.001**	8
Lupus nephritis	0.835	2.305 (1.414-3.756)	**0.001**	3
No use of hydroxychloroquine	1.771	5.876 (3.722-9.401)	**< 0.001**	6

BMI: body mass index; hsCRP: Hypersensitive c-reactive protein; ACL: anticardiolipin, antiβ2GPI: anti-β2-glycoprotein I, LA: lupus anticoagulantm;Values in bold are statistically significant at p <0.05.

Conclusion: Various factors are related to the occurrence of VTE in patients with SLE. The proposed SLE-VTE risk score can accurately predict the risk of VTE and help identify SLE patients with a high risk of VTE who may benefit from thromboprophylaxis.

REFERENCES:

[1] Ramirez GA, Efthymiou M, Isenberg DA, Cohen H. Under crossfire: thromboembolic risk in systemic lupus erythematosus. Rheumatology. 2018;58:940-952.
[2] Chung WS, Lin CL, Chang SN, Lu CC, Kao CH. Systemic lupus erythematosus increases the risks of deep vein thrombosis and pulmonary embolism: a nationwide cohort study. J Thromb Haemost. 2014;12:452-458.
[3] Liew NC, Alemany GV, Angchaisuksiri P, et al. Asian venous thromboembolism guidelines: updated recommendations for the prevention of venous thromboembolism. Int Angiol. 2017;36:1.
[4] Savino S, Giovanni S, Veronica M, Dario R, Khamashta MA, Laura BM. GAPSS: the Global Anti-Phospholipid Syndrome Score. Rheumatology. 2013:8.
[5] Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41:543-603.
[6] Moghadamyeghaneh Z, Hanna MH, Carmichael JC, Nguyen NT, Stamos MJ. A Nationwide Analysis of Postoperative Deep Vein Thrombosis and Pulmonary Embolism in Colon and Rectal Surgery. J Gastrointest Surg. 2014;18:2169-2177.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2769

POS0755 PREVALENCE AND RELEVANCE OF ANTIBODIES AGAINST CITRULLINATED ALPHA ENOLASE (ANTI-CEP1) IN CONNECTIVE TISSUE DISEASES

A. Alunno[1], O. Bistoni[1], F. Carubbi[2], M. Antonucci[1], S. Calvacchi[1], E. Bartoloni Bocci[1], M. Zen[3], A. Ghirardello[3], R. Depascale[3], A. Doria[3], R. Gerli[1]. *[1]Rheumatology Unit, University of Perugia, Department of Medicine, Perugia, Italy; [2]Internal Medicine and Nephrology Unit, University of L'Aquila, Department of Life, Health and Environmental Sciences, L'Aquila, Italy; [3]Division of Rheumatology, University of Padua, Department of Medicine DIMED, Padua, Italy*

Background: Anti-citrullinated alpha enolase antibodies have been investigated in rheumatoid arthritis and associated with bone erosion and interstitial lung disease but little is known about their prevalence and role in connective tissue diseases (CTDs).

Objectives: The aim of this study was to investigate the prevalence and relevance of anti-CEP1 antibodies in CTDs.

Methods: Serum samples from five independent patient cohorts were assessed: 1) established (est) primary Sjogren's syndrome (pSS) N=78, 2) est-systemic lupus erythematosus (SLE) N=52, 3) est-systemic sclerosis (SSc) N=71, 4) pSS at disease onset N=30, 5) SLE at disease onset N=46 (cohorts 4 and 5 had at least 3 years of follow-up). Samples from ninety sex and age matched healthy donors (HD) and 200 patients with est-RA (disease controls) were also tested. Anti-CEP1 IgG antibodies were measured with a commercially available ELISA kit (Euroimmun, Luebeck, Germany).

Results: Anti-CEP1 titer was significantly higher in est-pSS, est-SLE and est-SSc compared to HD, significantly lower in est-pSS and est-SSc compared to est-RA and comparable in est-SLE versus est-RA. We divided patients in every CTD group based on whether their anti-CEP1 titer was below or above the 25th, 50th and 75th percentile. In est-SLE anti-CEP1 values over the 25th percentile were associated with articular involvement (odds ratio, OR (95% confidence interval, CI)=11.5; 1.9-70.6, p=0.008). In est-pSS, no relationship between anti-CEP1>25th percentile and articular involvement was found but rather an association with rheumatoid factor positivity (OR (95% CI)=4.8, 1.6-14.1, p=0.004) and salivary gland swelling (OR (95% CI)=6.2, 1.3-29.1, p=0.021). In est-SSc no difference could be detected across the 3 groups. Anti-CEP-1 titers in pSS and SLE at onset did not differ from each other, were comparable also to those of HD and significantly lower than those of est-pSS, est-SLE and est-RA patients (all p<0.0001).). Of interest, we could retrieve a serum sample collected at the time of diagnosis for 5 patients from the cohort of established pSS and we observed that anti-CEP1 titers were significantly lower at pSS onset than during follow up (at least 12 months after the diagnosis, p=0.0024). No difference was observed in the clinical presentation at disease onset according to different anti-CEP1 titer and they did not predict the development of new clinical manifestations during follow-up.

Conclusion: Anti-CEP-1 antibodies can be detected in CTDs at different title during the disease course and may increase overtime, at least in pSS. Although anti-CEP1 antibodies are associated with specific clinical manifestation in est-CTDs, such as articular involvement in est-SLE, they seem to lack a predictive value for future manifestations when measured at disease onset.

REFERENCES:

[1] Alunno A, Bistoni O, Pratesi F et al Rheumatology (Oxford) 2018.
[2] Manca ML, Alunno A, D'Amato C et al. Joint Bone Spine 2018.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2825

POS0756 HOW HAS OUR MANAGEMENT OF SLE CHANGED OVER THE LAST THREE DECADES? REAL LIFE DATA FROM A MONOCENTRIC COHORT

V. Signorini[1], C. Tani[2], E. Elefante[2], D. Zucchi[2], C. Stagnaro[2], F. Ferro[2], L. Carli[2], M. Mosca[2]. *[1]University of Pisa, Rheumatology Unit, Pisa, Italy; [2]University of Pisa, Rheumatology Unit, Pisa, Italy*

Background: Over the last decades new therapies have been approved and new treatment strategies have been proposed in the treatment of SLE. In particular, recently, EULAR recommendations[1] and the Treat to Target[2] approach established a new paradigm for the treatment of SLE based on the early introduction of immunosuppressive treatment and glucocorticoids (GC) minimization.

Objectives: to evaluate changes in therapeutic approach and outcomes over the last three decades in a monocentric cohort of SLE patients.
Methods: This is a retrospective analysis of prospectively collected data from a monocentric cohort of patients with SLE with disease diagnosis between 1990 and 2020. Based on the year of diagnosis, patients were divided in three groups, each of them corresponding to a decade: group 1: decade 1990-1999; group 2: decade 2000-2009; group 3: decade 2010-2020. For each patient, epidemiological and demographic characteristics, cumulative organ involvement and serology, previous and ongoing therapies, comorbidities were collected and compared among the 3 groups. Organ damage was evaluated by the SLICC-DI (SDI)[3] at 1 and 5 years from diagnosis, as comorbidities we considered hypertension, diabetes, osteoporosis and cardiovascular (CV) events occurred during the follow-up.
Results: A total of 262 SLE patients were enrolled in the study (97% Caucasian, 90.5% females): 69 patients in group 1, 100 in group 2 and 93 in group 3. Demographic and clinical characteristics of whole cohort and of the three groups are summarized in table 1. Differences in therapies during the first year from diagnosis among the groups are summarized in table 1. In group 3 the use of Micophenolate Mofetil was significantly more common with respect to the group 1 (25% *vs* 1.4%, p= 0.001) and similar to group 2 (25% vs 25.5%, p=ns); on the contrary, in group 3, Azathioprine (AZA) and Cyclosporine (Cya) were less used (13.2% *vs* 27.5%, p=0.003 and 3.3% vs 14.3%, p= 0.019 respectively). As Cyclophosphamide (CYC) is concerned, it was used with the same frequency in the three decades, but in group 1, the total dose of CYC was significantly higher than second and third group (4.8 g *vs* 2.3 and 0.9, p=0.02 and p=0.001 respectively). In group 2 and 3, during the first year of disease, biological drugs (Rituximab or Belimumab) have been used more frequently (2% and 2.2% *vs* 0%, p=0.04). Any differences have not been showed for GC among the groups. However, in group 3 a significantly higher proportion of patients stopped GC therapy within 5 years from diagnosis (34.5% *vs* 8.8% and 12.5%, p=0.001) and in the same group the duration of GC therapy was significantly shorter with respect to previous two decades (3.1 years *vs* 16.8 and 10.5 respectively, p=0.001). As regard damage accrual, at 1 and 5 years from diagnosis, no significant differences among groups were observed; however, hypertension resulted significantly less common in group 3 (10% vs 26% and 37.3%, p=0.001), even adjusting for age (OR=0.2); less CV events were recorded in group 3, but significance is lost adjusting for age.

Table 1.

	Whole cohort	Group 1	Group 2	Group 3	p
Patients (n)	262	69	100	93	
Caucasian (%)	97%	99%	98%	94.6%.	n.s.
Females (%)	90.5%	94.2%	95%	92.5%	n.s.
Median age at	29	27	28.5	34	**0.001**
diagnosis IQR)	(20-36)	(20-32)	(20-36)	(23-44)	
Cumulative organ involvement					
Renal	48.1%	52.2%	57%	35.5%	**0.007**
Articular	74.4%	75.3%	66%	82.8%	n.s.
Serositic	19.5%	20.3%	22%	16.1%	n.s.
Neuropsychiatric	8%	11.6%	6%	7.5%	n.s.
Cutaneous	63%	70%	60%	61.3%	n.s.
Hematological	58.4%	51.5%	61%	61.3%	n.s.
Therapies 1st year					
AZA	17.2%	8.7%	27.5%	13.2%	**0.003**
MMF	18.7%	1.4%	25.5%	25.3%	**0.001**
CYC	22.5%	21.7%	27%	17%	n.s.
Cya	9.9%	13%	14.3%	3.3	**0.019**
Biologicals	1.5%	0%	2%	2.2%	n.s

Conclusion: These data show that new therapies and new treatment strategies have actually been implemented in clinical practice over the past 30 years; further studies with a longer follow-up are necessary to appreciate the impact of these advancement on clinical outcomes.
REFERENCES:
[1] Bertsias G, et al. *Ann Rheum Dis* 2008.
[2] van Vollenhoven RF, et al.*Ann Rheum Dis* 2014.
[3] Gladman DD, et al. *J Rheumatol* 2000.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2842

POS0757

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) DIAGNOSED DURING HOSPITALIZATION: CLINICAL PHENOTYPE AND PERFORMANCE OF THE SLE RISK PROBABILITY INDEX (SLERPI)

N. Kapsala[1], D. Nikolopoulos[1], S. Flouda[1], K. Chavatza[1], A. Pieta[1], A. Grivas[1], A. Ntourou[1], K. Togia[1], P. Rapsomaniki[1], T. Gerogianni[1], D. Tseronis[1], M. Aggelakos[1], T. Karageorgas[1], P. Katsimpri[1], G. Bertsias[2], A. Fanouriakis[1,3], D. Boumpas[1]. *[1]"Attikon" University Hospital of Athens, Rheumatology and Clinical Immunology, Medical School, National and Kapodistrian University of Athens, Athens, Greece*; *[2]University of Crete, Rheumatology, Clinical Immunology and Allergy, Heraklion, Greece*; *[3]"Asklepieion" General Hospital, Department of Rheumatology, Voula, Athens, Greece*

Background: Systemic Lupus Erythematosus (SLE) can first present with severe or critical disease leading to hospitalization. Prompt recognition of the disease in hospitalized patients may lead to early institution of treatment and improve outcomes. We have recently developed a clinician-friendly algorithm for SLE diagnosis based on classical clinical and serological SLE features [SLE Risk Probability Index (SLERPI)][1].
Objectives: To determine the clinical phenotype of SLE patients first diagnosed during hospitalization, the interval between hospitalization and SLE diagnosis and the potential impact of SLERPI on early diagnosis.
Methods: Mixed prospective (from June 2020 to January 2021) and retrospective study of SLE patients from "Attikon" cohort (n=820)[2]. Clinical phenotype was divided into 10 core domains (neuropsychiatric, thrombosis, nephritis, serosal, haematologic, pulmonary, cardiovascular, gastrointestinal, skin-joints, other). Chart review and patient interview was performed to assess the lag time between 1) the onset of symptoms and 2) the hospitalization and the final diagnosis. Demographic and clinical characteristics, SLERPI and SLICC damage index were recorded for each patient at the time of diagnosis. SLE diagnosis was based on at least one of the three existing classification criteria.
Results: Out of 820 SLE patients, 202 (24.6%) diagnosed during hospitalization were included. Among them, 185 patients (91.5%) were hospitalized because of a lupus related feature, while in the remaining 17 SLE patients, hospitalization was due to non-lupus related manifestations. The most common lupus-related clinical phenotype leading to hospital admission was neuropsychiatric lupus (n=51, 25.2%) with cerebrovascular events constituting the dominant clinical syndrome (n=8/51). Thrombotic events (n=32, 15.8%), mainly pulmonary embolism (n=20/32), cytopenias (n=32, 15.8%), lupus nephritis (n=30, 14.8%), skin-joint disease (n=26, 12.8%) and serositis (n=24, 11.8%) were also common as dominant manifestations. Pulmonary disease (n=16, 7.9%), heart disease (n= 4, 1.9%) and gastrointestinal disease (n=2, 0.9%) were less common. On admission, 11.3% of patients (n=23) had symptoms from at least 2 clinical domains as defined. Most patients (93.5%) had multisystem disease while only 6.5% had organ-dominant disease. Early diagnosis (within 3 months from hospitalization) was established in 86.6% while 27 patients had their SLE diagnosis more than 3 months from hospitalization. The mean lag time between the hospitalization and the diagnosis was approximately 14 months (SD 19.9). Overall, the mean interval between the onset of symptoms and the diagnosis was 48.2 months (SD 73.2). Importantly, a SLERPI >7 (suggesting probable SLE) at hospitalization was present in 92.5% of SLE patients with delayed diagnosis.
Conclusion: One out of four SLE patients first present with moderate to severe disease necessitating hospitalization, while in approximately 15% of such patients, diagnosis is initially missed. Application of the SLERPI may facilitate early SLE diagnosis.
REFERENCES:
[1] Adamichou C et al. Ann Rheum Dis. 2021; DOI: 10.1136/annrheumdis-2020-219069.
[2] D Nikolopoulos et al. Lupus 2020; doi: 10.1177/0961203320908932.
Acknowledgements: This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 742390)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2905

POS0758

DOES EXPERIENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS INFLUENCE THE PHYSICIAN GLOBAL ASSESSMENT SCORING? A CROSS-SECTIONAL STUDY ON TWO EUROPEAN COHORTS

E. Chessa[1], M. Piga[1], F. Sagez[2], R. Felten[2], A. Floris[1], A. Cauli[1], L. Arnaud[2]. *[1]Rheumatology Unit, AOU and University of Cagliari, Department of Medical Sciences and Public Health, Cagliari, Italy*; *[2]Hôpitaux Universitaires de Strasbourg, Université de Strasbourg, Service de Rhumatologie, Centre National de Référence des Maladies Systemiques et Autoimmunes Rares Est Sud-Ouest (RESO), Strasbourg, France*

Background: The Physician Global Assessment (PGA) is an outcome instrument based on physician judgement of disease activity in patients with Systemic Lupus Erythematosus (SLE). Due to the subjectivity of the score and lack of standardization, the PGA could represent a source of heterogeneity, because the same manifestations could be rated differently by physicians with different backgrounds (1).

Objectives: The purpose of this study was to evaluate the inter-rater reliability of PGA between a rheumatology trainee and rheumatologists expert in SLE from 2 european countries.

Methods: SLE patients classified according to SLICC 2012 criteria were enrolled between May 2019 and December 2019 during a SLEuro traineeship program. Demographic, clinical (SLEDAI-2k, PGA), serological and ongoing medication data were collected. PGA was evaluated before (pre-lab) and after (post-lab) knowledge of laboratory exams, using a Visual Analogue Scale (VAS) ranging from 0 to 3, anchored at point 1 (mild), 2 (moderate) and 3 (severe activity). A trainee in Rheumatology (EC) and three rheumatologists experts in SLE (LA, MP, FS) independently scored the PGA for each patient.

The trainee preliminarily received a standardization training with her tutor (MP), consisting of a shared discussion about 10 consecutive SLE outpatients to increase reliability in PGA scoring.

Inter-rater reliability was analysed using the intraclass correlation coefficient (ICC) with a two-way single-rating model (2,1); 95% confidence interval (CI) was calculated.

Results: Fifty-seven patients (86% female) affected from SLE (29 belonging to a French cohort and 28 to an Italian cohort) with a mean (SD) age 43.2 (15.9) years and a median [IQR] disease duration 6.4 [2.0-15.4] years were enrolled. Clinical features are presented in table 1. Pre-lab PGA scores were obtained from all patients and ranged from 0 to 2.3; post-lab PGA scores were obtained from 51 patients and ranged from 0 to 2.9. Inter-rater reliability of the PGA among the trainee was good to excellent for each lupus expert comparison: a) pre-lab PGA ICC 0.94, 95% CI 0.87-0.97; post-lab PGA ICC 0.94, 95% CI 0.87-0.97 (MP); b) pre-lab PGA ICC 0.84, 95% CI 0.63-0.93; post-lab PGA ICC 0.96 CI 0.88-0.99 (LA); c) pre-lab PGA ICC 0.91, 95% CI 0.65-0.98; post-lab PGA ICC 0.91, 95% CI 0.65-0.98 (FS).

Conclusion: After an adequate standardization, PGA scoring reaches good to excellent reliability between trainee and experts.

REFERENCES:

[1] Chessa E, Piga M, Floris A, Devilliers H, Cauli A, Arnaud L. Use of Physician Global Assessment in systemic lupus erythematosus: a systematic review of its psychometric properties. Rheumatology (Oxford). 2020 Dec 1;59(12):3622-3632.

Clinical Data	
Caucasian	44 (77.2%)
anti-dsDNA titre (median,IQR)	14 (0-75)
Hypocomplementemia (n,%)	30 (54%)
SLEDAI≥6 (n,%)	18 (31.6%)
SLEDAI (median,IQR)	4 (2-6)
Flares (n,%)	18 (31.6%)
Ongoing prednisone treatment (n,%)	41 (71.9%)
Prednisone dose mg (mean±sd)	5 (0 - 8.9)
Hydroxychloroquine (n,%)	44 (77.2%)
Immunosuppressant (n,%)	35 (61.4%)

Acknowledgements: Elisabetta Chessa gratefully acknowledges the SLEuro European Lupus Society for its financial support in her traineeship in Strasbourg.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2945

POS0759

THE JOURNEY OF PATIENTS FROM FIRST SYMPTOMS TO DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): AN OBSERVATIONAL STUDY

N. Kapsala[1], S. Flouda[1], D. Nikolopoulos[1], K. Chavatza[1], A. Pieta[1], A. Grivas[1], A. Ntourou[1], K. Togia[1], P. Rapsomaniki[1], T. Gerogianni[1], D. Tseronis[1], M. Aggelakos[1], T. Karageorgas[1], P. Katsimpri[1], G. Bertsias[2], A. Fanouriakis[1,3], D. Boumpas[1]. *[1]"Attikon" University Hospital of Athens, Rheumatology and Clinical Immunology, Medical School, National and Kapodistrian University of Athens, Athens, Greece*; *[2]University of Crete, Rheumatology, Clinical Immunology and Allergy, Heraklion, Greece*; *[3] "Asklepieion" General Hospital, Department of Rheumatology, Voula, Athens, Greece*

Background: The lack of pathognomonic features poses a considerable challenge in SLE diagnosis. The time from symptom onset to diagnosis has been reported to range from two to six years[1].

Objectives: To document the initial symptoms of the disease and the time lapse until its diagnosis.

Methods: We examined 438 patients from the "Attikon" SLE cohort[2]. For diagnosis, we used the classification criteria (ACR, SLICC, EULAR-ACR) or in few cases clinical diagnosis (n=32, 7.3%). Data were collected using patient interviews, in-person clinical visits and medical charts review. Initial symptoms were recorded and determined chronologically using prespecified forms with a list of typical manifestations (skin, joints, renal, nervous system, pleuropulmonary, cardiovascular, anti-phospholipid syndrome) as well as characteristic disease features (Raynaud's phenomenon, fatigue, fever, sicca symptoms). Questions also included the time between symptom onset and initial physician visit, the time from first medical consultation until first rheumatologist assessment, the time from rheumatologist assessment to SLE definite diagnosis, the number of physicians seen before SLE diagnosis, the specialty of first physician and of diagnosing physician. Information on demographic and clinical characteristics, disease activity and disease damage, was collected both at enrolment and at last follow-up visit.

Results: 88.5% of patients were females, mean (±SD) age at diagnosis was 41.9 years ± 15.4 and disease duration was 6.7 ± 7 years. Most common systems involved were joints (94.5%), skin (73.7%), blood (39.2%) and renal (17.5%). At diagnosis, 9.8% of patients were ANA negative. The most common initial symptoms at disease onset were arthritis/arthralgia (74.4%), followed by fatigue (53.1%) and photosensitive rash (50.9%) (Table 1). Among non-criteria features, Raynaud's phenomenon was reported by 146 patients (33.3%) prior the diagnosis. The median interval between symptoms onset and the SLE diagnosis was 16 months (IQR 5-60). SLE was diagnosed earlier in ANA-positive than -negative patients [median time 14 months (IQR 5-60) vs 36 months (IQR 10.5-84); P=0.1, t-test]. Approximately half of the patients (52.5%) were diagnosed after 12 months from disease onset with only 15.9% diagnosed within 3 months of symptoms presentation. The median lag time between onset of symptoms and the first medical consultation was 2 months (IQR 1-12). Internists were the most common first consultants (27.8%) followed by orthopedists (15.9%), dermatologists (13.6%) and rheumatologists (13.4%). The median interval between the first medical assessment and first rheumatologist evaluation was 3 months (IQR 0-11.5) while the median time from rheumatologist assessment to definite diagnosis was 0 months (IQR 0-4). SLE patients consulted an average of 3 different physicians before the definite diagnosis, which in 95.8% was established by rheumatologists.

Conclusion: Approximately 50% of patients were diagnosed with SLE after 12 months from symptom onset with a mean time from symptoms to definite diagnosis almost 4 years. Increasing awareness of internists to SLE and avoidance of strict adherence to ANA as a requirement for diagnosis may improve early diagnosis.

Table 1. Initial symptoms prior to diagnosis

Symptoms	*N=438 (%)*	*Duration* (mean months ±SD)*
Arthralgias	326 (74.4)	37.5 ±69.4
Photosensitive rash	223 (50.9)	30.6 ±70.2
Malar rash	168 (38.3)	22.6 ±62
Alopecia	167 (38.1)	19.6 ±54.6
Ulcers	106 (24.2)	16.8 ±54.4
Fever	103 (23.5)	9.3 ±43.8
Raynaud's phenomenon	146 (33.3)	22.3 ±68.5
Fatigue	233 (53.1)	19.7 ±45.7

*Mean time from symptom onset to established diagnosis

REFERENCES:
[1] Nightingale AL, Davidson JE, Molta CT et al. Lupus Science & Medicine 2017; doi:10.1136/lupus-2016-000172.
[2] D Nikolopoulos et al. Lupus 2020; doi: 10.1177/0961203320908932.

Acknowledgements: This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 742390)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2975

POS0760

MONITORING C3 AND C4 VARIATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PREGNANCIES IS USEFUL TO RECOGNIZE COMPLICATIONS. DATA FROM 2 ITALIAN CENTERS

F. Crisafulli[1], R. Reggia[2], M. Filippini[1], M. Fredi[1], M. C. Gerardi[1], R. Gorla[1], M. G. Lazzaroni[1], D. Lini[1], C. Nalli[1], M. Taglietti[1], A. Lojacono[3], S. Zatti[3], C. Zanardini[3], C. Tani[4], D. Zucchi[4], M. Mosca[4], F. Franceschini[1], L. Andreoli[1], A. Tincani[1]. *[1]ASST Spedali Civili and University of Brescia, Rheumatology and Clinical Immunology Unit, Brescia, Italy*; *[2]Casa di Cura San Camillo, Internal Medicine, Cremona, Italy*; *[3]ASST Spedali Civili and University of Brescia, Obstetrics and Gynecology Unit, Brescia, Italy*; *[4]University of Pisa, Rheumatology Unit, Pisa, Italy*

Background: In SLE pregnancies adverse pregnancy outcomes (APO) are more frequent than in general obstetric population (GOP). In clinical practice, low C3 and C4 levels are associated with active disease and, during pregnancy, complement activation products are shown to be associated with APO.
Objectives: To analyse complement variations during SLE pregnancies, focusing on disease flares and APO.
Methods: Data on SLE pregnancies prospectively-followed by multidisciplinary team in 2 Italian Centers from 1987 to 2018 were retrospectively analysed. C3 and C4 normal levels were calculated in general obstetric population (GOP) as previously described[1], and related to maternal and fetal outcome. Non categorical variables were compared using Mann-Whitney test or Wilcoxon test when appropriate.
Results: Two hundred forty-six pregnancies in 172 SLE patients were analysed (mean age at conception 31.3 ±4.9 years; mean disease duration 8.3 ±7.1). Anti-Ro antibodies were positive in 64 patients (37%) and anti-phospholipid antibodies (aPL) were positive in 84 (48%), with single positivity in 54%, double in 24% and triple in 21%; 9 patients (5%) had also a diagnosis of obstetric-antiphospholipid syndrome (APS) and 8 (4%) had thrombotic-APS. Seventy-one patients (41%) had history of Lupus Nephritis.
Thirty-five flares were recorded in 30 pregnancies (12%). APO occurred in 47 pregnancies (19%) and were: 27 fetal loss (20 early miscarriage <10th week and 7 intrauterine fetal death), 11 severe preterm birth (<34th week) and 15 hypertensive disorder (11 pre-eclampsia and 5 pre-eclampsia+HELLP syndrome).

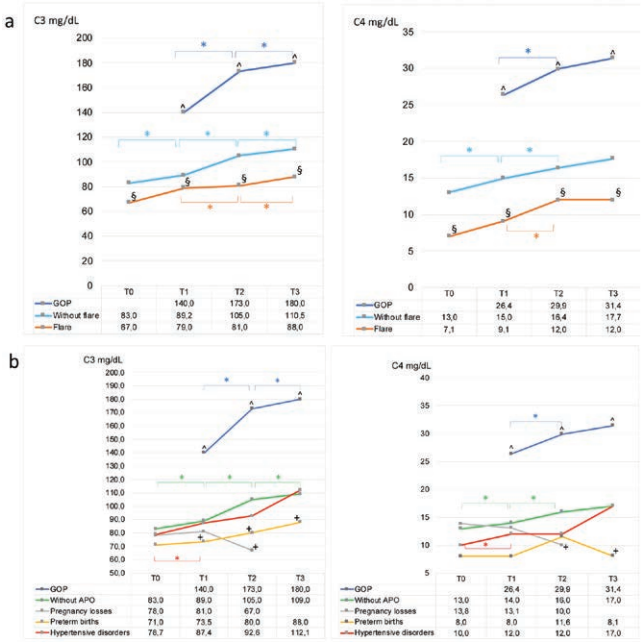


Figure 1. Variations of C3 and C4 median levels (mg/dL) throughout pregnancy in GOP[1] and in SLE pregnancies without and with flare (a) and without and with APO (b).

In GOP, C3 progressively increased throughout pregnancy and C4 increase from the 1st trimester to the 2nd trimester, as well as in SLE pregnancies without flares and without APO, from preconception (Fig 1). In the other SLE groups, C3 and C4 showed a different trend: in pregnancies with flares, they did not increase from preconception to the 1st trimester; in fetal losses and severe pre-term births, they remained stable throughout pregnancy; in hypertensive disorders they increased only between preconception and the 1st trimester.
C3 and C4 levels were higher in GOP than in all SLE pregnancies groups (including those without flares and without APO) in each trimester. SLE pregnancies without flares showed higher C3 and C4 levels than pregnancies with flares, at preconception and in each trimester. SLE pregnancies without APO had higher C3 and C4 levels than pregnancies with fetal death at 2nd trimester, higher C3 levels than severe pre-term births in each trimester and higher C4 at 3rd trimester (Fig.1).
At preconception, pregnancies with flares showed a higher frequency of low C3 and of low C4 than in pregnancies without flares (76% vs 42%, p=0.01; 76% vs 26%, p<0.001, respectively). Using the normality range previously calculated in GOP, SLE pregnancies with flares had higher frequency of low C4 in every trimester as compared with pregnancies without flares (1st: 82% vs 48%, p=0.003; 2nd: 82% vs 64%, p=0.01; 3rd: 64% vs 30%, p=0.002). At multivariate analysis, low C4 at preconception was associated with flare (OR [95% CI]: 10.34 [2.52-42.39]; p=0.001).
** p <0.05*
^as compared with SLE groups: p<0.05; § as compared with SLE pregnancies without flare: p<0.05; + as compared with SLE pregnancies without APO: p<0.05
Conclusion: In SLE pregnancies, monitoring of C3 and C4 is important: its failure to increase can be useful to recognize potential risk situations which deserve particular monitoring.

REFERENCES:
[1] Reggia R. et al. Rheumatology 2012;51:2186-2190.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3056

POS0761

INVESTIGATION ON THE EFFECT AND MECHANISM OF ABNORMALLY ACTIVATED CD8+ T CELLS FROM BONE MARROW ON HEMATOPOIETIC STEM CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

T. Fu[1], Y. Yang[1], X. Gu[2], C. Dong[2], R. Zhao[1], J. Ji[2], Z. Xue[1], X. Zhang[3], Z. Gu[2]. [1]*Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China*; [2]*Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*; [3]*Institute Pasteur of Shanghai Chinese Academy of Sciences, Key Laboratory of Molecular Virology & Immunology, Shanghai, China*

Background: SLE is an autoimmune disease characterized by the abnormal function of lymphocytes. The impairment of hematopoietic function of bone marrow participates in its pathogenesis, in which T cells play an important role. However, study on bone marrow T cells in SLE patients is very limited.
Objectives: This study aims to characterize the phenotype and molecular characteristics of abnormally activated CD8+T cells in bone marrow of SLE patients and explore the mechanism of hematopoietic stem cells (HSCs) reduction caused by the abnormally activated CD8+T cells in bone marrow of patients with SLE.
Methods: A total of 8 SLE patients and 5 age- and sex-matched controls were recruited in our study. Among them, 3 SLE patients and 4 donors were collected bone marrow and peripheral blood samples for Single-cell RNA sequencing (scRNA-seq) and functional studies. BM and peripheral T cell subsets were measured by flow cytometry. Plasma cytokines and secreted immunoglobulins were detected by Luminex. Disease activity of SLE patients was measured using the SLE Disease Activity Index (SLEDAI). All analyses were performed using R language and Flowjo 9.
Results: In the present study, SLE patients had increased CD8+T%αβT cells and decreased CD4+T%αβT cells in bone marrow of SLE, compared to healthy controls. A large number of CD38+HLADR+CD8+T cells existed in the bone marrow and peripheral blood of SLE patients. Those patients also showed reduced number of HSCs, and with a downward trend of the numbers of peripheral red blood cells, white blood cells, neutrophils, hemoglobin, and platelets. By scRNA-seq, the CD38+HLADR+CD8+T cells contained high levels of GZMK, GZMA, PRF1, IFNG, and TNF in the bone marrow of SLE patients. the CD38+HLADR+CD8+T cells exhibited significant relationship with HSCs, white blood cells, neutrophils, and platelets.
Conclusion: These findings demonstrated that the abnormally activated CD8+T cells in bone marrow can reduce the number of HSCs by the expression of killer molecules, which contributes to the impairment of hematopoietic function and the development of SLE. This project focuses on the specific bone marrow T cell subset in SLE. The completement of this project provides information for exploring the mechanism of hematopoiesis involvement.

REFERENCES:

[1] Anderson E, Shah B, Davidson A, Furie R. Lessons learned from bone marrow failure in systemic lupus erythematosus: Case reports and review of the literature. Semin Arthritis Rheum. 2018;48(1):90-104.
[2] Sun LY, Zhou KX, Feng XB, Zhang HY, Ding XQ, Jin O, Lu LW, Lau CS, Hou YY, Fan LM. Abnormal surface markers expression on bone marrow CD34+cells and correlation with disease activity in patients with systemic lupus erythematosus. Clin Rheumatol. 2007;26(12):2073-2079.

Acknowledgements: We want to thank Lu Meng, Teng Li, Wei Zhou, and Jiaxin Guo for their assistance with this study.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3060

POS0762

CAN THE SLE-DAS SUBSTITUTE BILAG TO MEASURE LUPUS DISEASE ACTIVITY IN CLINICAL TRIALS? POST-HOC ANALYSIS OF THE BLISS-76 TRIAL

D. Jesus[1,2], A. Matos[3,4], C. Henriques[3,5], A. Doria[6], L. Inês[2,7]. [1]*Centro Hospitalar de Leiria, Rheumatology Department, Leiria, Portugal*; [2]*University of Beira Interior, Faculty of Health Sciences, Covilhã, Portugal*; [3]*Institute of Viseu, Technology and Management, Viseu, Portugal*; [4]*Research Centre in Digital Services, CISeD, Viseu, Portugal*; [5]*University of Coimbra, Centre for Mathematics, Coimbra, Portugal*; [6]*University of Padova, Division of Rheumatology, Padova, Italy*; [7]*Centro Hospitalar e Universitário de Coimbra, CHUC Lupus Clinic, Rheumatology Department, Coimbra, Portugal*

Background: The primary endpoint for randomized clinical trials (RCT) in Systemic lupus erythematosus (SLE) is usually defined as proportion of responders in a composite index. The most widely used are British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA) and Systemic Lupus Responder Index (SRI). Both comprise BILAG along with SLE Disease Activity Index (SLEDAI). BICLA and SRI are complex and time-consuming to assess.
The SLE Disease Activity Score (SLE-DAS) is an easy to apply, validated, continuous disease activity measure, highly correlated with SLEDAI, with higher accuracy and sensitivity-to-change as compared to SLEDAI[1].
We hypothesize that SLE-DAS can also identify the SLE disease activity information from BILAG, thus dispensing the use of composite indexes for RCT.
Objectives: To compare the ability of the SLE-DAS and the Safety of Estrogen in Lupus National Assessment (SELENA)-SLEDAI to discriminate between BILAG classification of mild *vs.* moderate *vs.* severe disease activity.
Methods: Post-hoc analysis of all intention-to-treat patients in the BLISS-76 (NCT00410384) RCT at the baseline study visit. SELENA-SLEDAI and BILAG were assessed at time of the study visits and SLE-DAS was retrospectively scored from the study database. Patients' disease activity was classified as: (i) mild (no BILAG B or A scores in any organ domain); (ii) moderate (1 BILAG B, no A scores); (iii) severe (≥2 BILAG B and/or ≥1 BILAG A). Ability of the SLE-DAS and SELENA-SLEDAI to differentiate between: (i) mild *vs.* moderate/severe disease activity; (ii) mild/moderate *vs.* severe disease activity (according to BILAG), were evaluated using receiver operating characteristic (ROC) analysis. The area under the ROC curves (AUCs) with 95% confidence intervals (95%CI) as a measure of discriminatory ability of the SLE-DAS and SELENA-SLEDAI were compared using Delong's test for two correlated curves. Because AUC measurements might have restricted accuracy for imbalanced datasets, precision-recall (PR) curves and area under PR curves (AUC-PR) were also performed. Statistical significance was set at 0.05.
Results: We included 819 patients, classified by BILAG as presenting mild (7.7%), moderate (28.8%) or severe (63.5%) disease activity. To differentiate mild *vs.* moderate/severe disease activity, the discriminatory ability of SLE-DAS was outstanding (AUC 0.948; 95%CI 0.923-0.973), while that of SELENA-SLEDAI was acceptable (AUC 0.729; 95%CI 0.657-0.801) (p<0.005) (figure 1A). To differentiate mild/moderate *vs.* severe disease activity, the discriminatory ability of SLE-DAS was excellent (AUC 0.873; 95%CI 9.846-0.899), while that of SELENA-SLEDAI was acceptable (AUC 0.707; 95%CI 0.670-0.744) (p<0.005) (figure 1B). The AUC-PR confirmed the higher performance of SLE-DAS over SELENA-SLEDAI to differentiate mild *vs.* moderate/severe disease activity (0.995 *vs.* 0.965, respectively) (figure 1C) and mild/moderate *vs.* severe disease activity (0.902 *vs.* 0.794, respectively) (figure 1D).

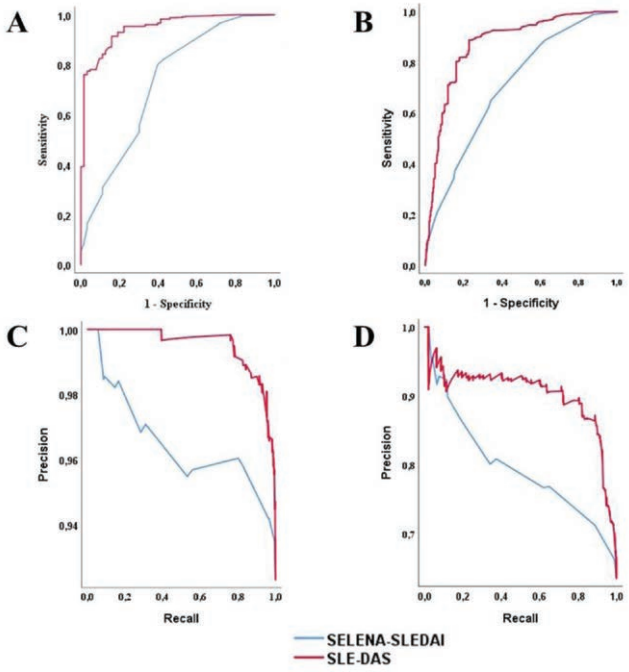


Figure 1. Receiver operating characteristics (ROC) curves comparing the ability of the SLE-DAS and SELENA-SLEDAI to differentiate (A) mild *vs.* moderate/severe disease activity and (B) mild/moderate *vs.* severe disease activity, as assessed by BILAG; and Precision-recall (PR) curves comparing the performance of the SLE-DAS and SELENA-SLEDAI to differentiate (C) mild *vs.* moderate/severe disease activity and (D) mild/moderate *vs.* severe disease activity.

Conclusion: The SLE-DAS presents excellent performance in assessing SLE disease activity categorized by BILAG scores, which is not the case for SELENA-SLEDAI. Further studies will aim to better define ability of SLE-DAS to substitute composite responder indices.

REFERENCES:

[1] Jesus D, *et al.* Derivation and validation of the SLE Disease Activity Score (SLE-DAS): a new SLE continuous measure with high sensitivity for changes in disease activity. *Ann Rheum Dis* 2019;78:365-71.

Acknowledgements: The authors would like to thank GlaxoSmithKline (Uxbridge, UK) for granting access to the data from the BLISS-76 trial through the Clinical Study Data Request consortium.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3162

POS0763 PERFORMANCE OF THE NEW ACR/EULAR 2019 CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN A COHORT OF ARGENTINIAN PATIENTS

J. M. Dapeña[1], E. R. Serrano[1], J. M. Bande[1], M. A. Medina[1], D. S. Klajn[1], J. A. Caracciolo[1], C. Castro[2], J. Morbiducci[2], A. L. Mercé[2], R. Tralice[1,2], G. V. Espasa[3], S. Yessika Jackeline[3], M. L. Leguizamón[3], M. A. Pera[3], V. I. Bellomio[3], M. S. Yacuzzi[4], M. Machado Escobar[4], M. Cosentino[5], L. Garcia[5], M. García[5], C. Aeschlimann[6], G. Gomez[7], N. Perez[7], S. Papasidero[1]. *[1]Hospital General de Agudos Dr. Enrique Tornú, Servicio de Reumatología, Buenos Aires, Argentina*; *[2]Hospital General de Agudos Bernardino Rivadavia, Servicio de Reumatología, Buenos Aires, Argentina*; *[3]Hospital Ángel C. Padilla Juan Bautista Alberdi, Servicio de Reumatología, San Miguel de Tucumán, Argentina*; *[4]Hospital Eva Perón de Tucumán, Servicio de Reumatología, Banda del Río Salí, Argentina*; *[5]H.I.G.A. San Martín de La Plata, Servicio de Reumatología, La Plata, Argentina*; *[6]Hospital Provincial de Rosario, Servicio de Reumatología, BZL, Argentina*; *[7]Instituto de Investigaciones Médicas Alfredo Lanari, Servicio de Reumatología, Buenos Aires, Argentina*

Background: In 2019 ACR and EULAR published in joint collaboration the new classification criteria for Systemic Lupus Erythematosus (SLE). Compared to the previous ones, these criteria have shown higher sensitivity and specificity in multiple cohorts. To our knowledge, its performance has not been evaluated in a cohort of patients with rheumatological diseases living in Argentina.
Objectives: The aim of this study was to evaluate the sensitivity and specificity of the ACR/ EULAR 2019 criteria in a cohort of patients with connective tissue diseases residing in Argentina. Secondary objectives were to determine the Likelihood Ratio (LR) of these criteria and the correlation of their global score with activity and damage indexes of the disease.
Methods: Multicentre, retrospective and analytical study. Patients ≥ 18 years old with diagnosis of SLE (ACR 1997/SLICC 2012) without other associated collagen diseases (case group), and patients with other non-SLE connective tissue diseases (control group) were included. Those with active infectious disease, oncohematological disease, drug-induced lupus and overlap syndrome were excluded. Sociodemographic data, characteristics of the disease and treatment were recorded. In addition, activity and damage indexes were recorded in the group with SLE.
Three SLE experts, blinded to the diagnosis determined, for every individual if the patient had SLE or another rheumatological disease. An interrater agreement of 100% (including the 3 evaluators) was considered "defined SLE" and used as gold standard. In all cases, ACR 1997/SLICC 2012/ACR / EULAR 2019 criteria were applied and compared with the gold standard. Statistical analysis: Descriptive statistics was estimated. Sensitivity, specificity, positive and negative LR of the criteria were determined. The association between the final score of the ACR-EULAR 2019 criteria and the disease activity and damage indexes were estimated with Spearman correlation test. STATA 15.0 was used for data analysis.
Results: A total of 365 patients from 7 centres in Argentina were included. A One hundred and eighty-three belonged to the SLE group: 92.3% women, mean age 39 years (SD 13.3), median disease duration 92 months (IQR 37-150). The most frequent manifestations of the disease were mucocutaneous (94%), musculoskeletal (82.5%) and haematological (69%). All patients presented ANA +, 88% hypocomplementemia, 69.4% Anti-DNA and 19.5% antiphospholipid antibodies. Median SLEDAI and SLICC were 2 (IQR 0-6) and 0 (IQR 0-1), respectively.
In the control group, 182 patients were recruited: 84% women, mean age 53.6 years (SD 14.2) and median disease duration 82.5 months (IQR 38-151). The most frequent diseases were Rheumatoid Arthritis (46.1%), Scleroderma (18.1%) and Sjögren's Syndrome (16.5%) and most common manifestations were musculoskeletal (81.9%), immunological (73.6%) and constitutional (25.3%). A total of 62.6% of patients presented ANA+, 8.6% hypocomplementemia, and 1.3% Antiphospholipid antibodies.
Ninety-one percent of patients in the case group were classified as defined SLE and 3.8% in the control group.
The ACR / EULAR 2019 Criteria showed a 99.4% sensitivity and an 89.1% specificity, with a LR+ of 9.1 and a LR- of 0.007. The sensitivity and specificity of SLICC 2012 criteria were 98.3% and 88%, respectively with a LR+ of 8.2 and a LR- of 0.02; and the ACR 1997 criteria showed a 93.96% sensitivity and 90.1% specificity, with LR + of 8.21 and LR - of 0.07.
The correlations between the ACR/EULAR 2019 Criteria global score, and activity and damage indexes were 0.19 and -0.006, respectively.
Conclusion: The new ACR / EULAR 2019 criteria have shown high sensitivity, a specificity comparable to its predecessors, and a higher ability to distinguish SLE from other diseases and to exclude it in non-SLE patients. No correlation was observed between the criteria scores and activity and damage indexes.

REFERENCES:
[1] Aringer M, Costenbader K, Daikh D, et al 2019 EULAR/ACR classification criteria for SLE. Ann Rheum 2019; 78: 1151-1159.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3172

POS0764 EULAR RECOMMENDATION-BASED QUALITY INDICATORS (QIS) FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): ELABORATION, FINAL SET, PERFORMANCE AND INITIAL VALIDATION

K. Chavatza[1], M. Kostopoulou[2], D. Nikolopoulos[1], O. Gioti[3], K. Togia[1], S. Flouda[1], N. Kapsala[1], M. Kosmetatou[1], G. S. Moysidou[1], A. Grivas[1], A. Pieta[1], A. Ntourou[1], P. Rapsomaniki[1], T. Gerogianni[1], D. Tseronis[1], M. Aggelakos[1], T. Karageorgas[1], P. Katsimpri[1], L. Andreoli[4,5], M. Aringer[6], J. N. Boletis[7], A. Doria[8], F. Houssiau[9], D. Jayne[10], M. Mosca[11], E. Svenungsson[12], A. Tincani[13], G. Bertsias[14], A. Fanouriakis[1,3], D. Boumpas[1,15]. *[1]"Attikon" University Hospital of Athens, Rheumatology and Clinical Immunology, Medical School, National and Kapodistrian University of Athens, Athens, Greece*; *[2]"G. Gennimatas" General Hospital, Department of Nephrology, Athens, Greece*; *[3]"Asklepieion" General Hospital, Voula, Department of Rheumatology, Athens, Greece*; *[4]University of Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy*; *[5]Spedali Civili, Unit of Rheumatology and Clinical Immunology, Brescia, Italy*; *[6]University Medical Center & Faculty of Medicine Carl Gustav Carus, Technical University of Dresden, Division of Rheumatology, Department of Medicine III, Dresden, Germany*; *[7]"Laikon" Hospital, National and Kapodistrian University of Athens, Medical School, Nephrology Department and Renal Transplantation Unit, Athens, Greece*; *[8]University of Padova, Rheumatology Unit, Department of Medicine, Padova, Italy*; *[9]Université catholique de Louvain, Cliniques Universitaires Saint-Luc, Brussels, Belgium*; *[10]Addenbrooke's Hospital, Department of Medicine, Cambridge, United Kingdom*; *[11]University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy*; *[12]Karolinska Institutet and Karolinska University Hospital, Department of Medicine, Rheumatology Unit, Stockholm, Sweden*; *[13]University of Brescia, Rheumatology and Clinical Immunology, Brescia, Italy*; *[14]University Hospital of Heraklion, Rheumatology, Clinical Immunology and Allergy, Heraklion, Greece*; *[15]Biomedical Research Foundation of the Academy of Athens, Laboratory of Autoimmunity and Inflammation, Athens, Greece*

Background: Targets of therapy and quality of care are receiving increased attention in systemic lupus erythematosus (SLE).
Objectives: To develop Quality Indicators (QIs) for the care of SLE patients based on the EULAR recommendations, and assess their performance.
Methods: Using the published EULAR recommendations for SLE, we developed 44 candidate QIs. These were independently rated for validity and feasibility by 12 experts, analysed by a modified RAND/UCLA model and further scrutinized based on the scorings and expert opinion. (Fig.1) Adherence to the final set of QIs was tested in a cohort of 220 SLE patients combined with an assessment on its impact on disease outcomes such as flares, hospitalizations and organ damage.
Results: The panel rated 18 QIs as valid and feasible. These involve diagnosis; disease and damage assessment; monitoring for lupus nephritis and drug toxicity; therapy and targets of therapy; fertility and pregnancy; and adjunct therapy (preventive measures for osteoporosis, vaccination, cardiovascular disease). On average, SLE patients received 54% (95%CI 52–56%) of the indicated care with adherence ranging from 41% for QIs related to monitoring to 88% for treatment-related QIs. Regarding targets of therapy, sustained remission or low disease activity were achieved in 27%, while 94% of patients received low-dose glucocorticoids, and 92% the recommended hydroxychloroquine dose. Dependent upon individual QI tested, adherence for lupus nephritis-related QIs was 88% for receiving appropriate adjunct therapy (ACE inhibitors) to 100% for being treated with the indicated immunosuppressive treatment. In contrast, adherence to QIs related to preventive measures and other adjunct therapies was moderate to low. Notably, patients who were eligible for cardiovascular risk modification, vaccination, and osteoporosis management received lower quality of care (40.5%, 47.7% and 45.5% respectively) while 91.4% had sunscreen protection. In reference to laboratory work-up and monitoring, complete laboratory work-up at diagnosis was performed in 48%, while disease activity and damage, were fully assessed only in 14.1% (in three consecutive visits) and 28.6% (annually) respectively, Similarly, reproductive health and pregnancy counselling adherence rates were modest estimated at 50% and 62% respectively. Higher adherence to the indicated care during follow-up (monitoring QIs) was associated with reduced risk for adverse outcomes during the last year of observation (OR 0.97, 95%CI 0.96-0.99). Patients who achieved sustained remission or LLDAS, exhibited fewer flares (OR=0.15, p-value<0.001) and damage accrual (OR=0.35, p-value<0.001). Of interest, patients who received low-dose of GCs or were appropriately vaccinated, had a lower risk of experiencing a flare (OR=0.23 and 0.46 respectively).

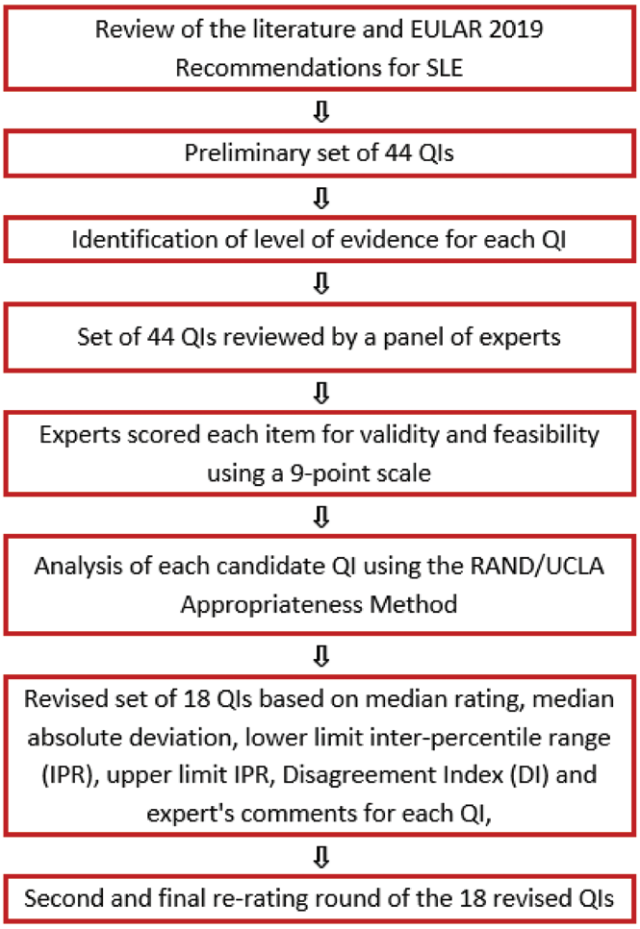
Conclusion: A set of 18 QIs based on the EULAR recommendations for SLE was developed to be used towards improving care in SLE. Initial real-life data suggest variable degree of adherence with higher adherence resulting in reduced adverse outcomes.

REFERENCES:

[1] Fanouriakis, et al., 2019 Update of the EULAR recommendations for the management of systemic lupus erythematosus. In *Annals of the Rheumatic Diseases* (Vol. 78, Issue 6, pp. 736–745). BMJ Publishing Group. https://doi.org/10.1136/annrheumdis-2019-215089.

[2] Nikolopoulos, D., et al., Evolving phenotype of systemic lupus erythematosus in Caucasians: low incidence of lupus nephritis, high burden of neuropsychiatric disease and increased rates of late-onset lupus in the 'Attikon' cohort. *Lupus*, *29*(5), 514–522. https://doi.org/10.1177/0961203320908932.

Figure 1.



Acknowledgements: This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 742390)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3181

POS0765 LABORATORY RATIOS: A SUBROGATE BIOMARKER FOR DETECTION OF INFECTION IN SLE PATIENTS

Y. Santamaria-Alza[1], J. Sanchez-Bautista[2], T. Urrego Callejas[1], J. Moreno[2], F. Jaimes[2], J. Rodello[3], D. Fernández[4], L. A. González[1], G. Vásquez[1].

[1]Universidad de Antioquia, Rheumatology, Medellín, Colombia; *[2]Universidad de Antioquia, Internal Medicine, Medellín, Colombia*; *[3]Universidad de Antioquia, Nephrology, Medellín, Colombia*; *[4]Polytechnic University of Catalonia-BarcelonaTech, Statistics and Operations Research, Medellín, Colombia*

Background: The most common complication in patients with SLE is infection, and its clinical presentation is often indistinguishable from SLE flares. Therefore, laboratory ratios have been evaluated to differentiate between those events. Among them, ESR/CRP[1], neutrophil/lymphocyte (NLR)[2], and platelet/lymphocyte (PLR)[3] ratios have been previously assessed with acceptable performance; however, there is no validation of those ratios in our SLE population.

Objectives: To examine the predictive capacity of infection of the lymphocyte/C4 (LC4R), lymphocyte/C3 (LC3R), and ferritin/ESR (FER) ratios in SLE patients, and to evaluate the performance of ESR/CRP, NLR, AND PLR ratios in our SLE population.

Methods: We conducted a cross-sectional study of SLE patients admitted to the emergency service at Hospital San Vicente Fundación (HSVF). The HSVF ethics committee approved the execution of the project.

Patients were categorized into four groups according to the main cause of hospitalization: (1) infection, (2) flare, (3) infection and flare and, (4) neither infection nor flare. We calculated the median values of the ratios and their respective interquartile ranges for each group. Then, we compared those summary measures using the Kruskal-Wallis test. Subsequently, we assessed the predictive capacity of infection of each ratio using ROC curve. Finally, we carried out a logistic regression model.

Results: A total of 246 patients were included, among them 90.7% were women. The median age was 28 years (IQR: 20-35 years). Regarding the outcomes, 37.0% of the patients had flares, 30.9% had neither infection nor flare, 16.7% had an infection and, 15.5% had simultaneously infection and flare. When compared the four groups, statistical significance ($p<0.05$) was observed. Area under the ROC curve (AUC) for infection prediction was as follows: 0.752 (sensitivity 60.5%, specificity 80.5%) for LC4R, 0.740 (sensitivity 73.2%, specificity 68.3%) for FER, 0.731 (sensitivity 77.6%, specificity 80.5%) for LC3R.

In the logistic regression modeling, we observed that an increase in the risk of infection was associated with an LC4R below 66.7 (OR: 6.3, CI: 2.7 – 14.3, $p<0.0001$), a FER greater than 13.6 (OR: 5.9, CI: 2.8 – 12.1, $p<0.0001$) and an LC3R below 11.2 (OR: 4.9, CI: 2.4 – 9.8, $p<0.0001$).

The ESR/CRP and PLR performed poorly with an AUC of 0.580 and 0.655, respectively. In contrast, the NLR showed better performance (AUC of 0.709, with a sensitivity of 80.2% and specificity of 55.7%).

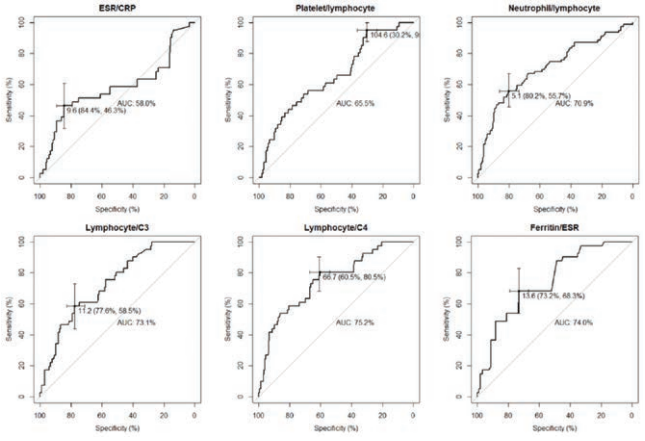


Figure 1. ROC curves of the evaluated ratios

Conclusion: These laboratory ratios could be easy to assay and inexpensive biomarkers to differentiate between infection and activity in SLE patients. The LC4R, FER, and LC3R have a significant diagnostic performance for detecting infection among SLE patients. Of the ratios previously evaluated, ESR/CRP, LPR, NLR, only the latest has an adequate performance in our population.

REFERENCES:

[1] Littlejohn E, Marder W, Lewis E, et al. The ratio of erythrocyte sedimentation rate to C-reactive protein is useful in distinguishing infection from flare in systemic lupus erythematosus patients presenting with fever. *Lupus*. 2018;27(7):1123-1129.

[2] Broca-Garcia BE, Saavedra MA, Martínez-Bencomo MA, et al. Utility of neutrophil-to-lymphocyte ratio plus C-reactive protein for infection in systemic lupus erythematosus. *Lupus*. 2019;28(2):217-222.

[3] Soliman WM, Sherif NM, Ghanima IM, EL-Badawy MA. Neutrophil to lymphocyte and platelet to lymphocyte ratios in systemic lupus erythematosus: Relation with disease activity and lupus nephritis. *Reumatol Clin*. 2020;16(4):255-261s.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3184

POS0766 CLUSTER ANALYSIS AND COMPARISON OF CUMULATIVE DAMAGE BY DIAPS IN A SINGLE CENTER COHORT OF APS PATIENTS

O. Uludag[1], E. Gurel[1], C. Cetin[1], E. Cene[2], Y. Yalçınkaya[1], A. Gül[1], M. Inanc[1], B. Artim-Esen[1]. *[1]Istanbul Faculty of Medicine, Division of Rheumatology, Department of Internal Medicine, İstanbul, Turkey*; *[2]Faculty of Arts and Science, Yıldız Technical University, Department of Statistics, Istanbul, Turkey*

Background: Antiphospholipid syndrome (APS) is a chronic autoimmune disease with significant morbidity and mortality. The recently developed damage index for APS (DIAPS) considers thrombotic APS specific damage.
Objectives: Herein we aimed to identify disease clusters based on clinical characteristics and compare DIAPS between these clusters in a single center cohort of patients with APS ± systemic lupus erythematosus (SLE).
Methods: This retrospective study included 237 consecutive patients with APS [114 primary APS (PAPS) and 123 SLE+APS]. Data regarding demographics, clinical and laboratory characteristics and cardiovascular risk factors were retrieved from the existing database and revised. Two-step cluster analysis was performed. Cumulative damage was calculated for all patients by applying DIAPS as described previously.
Results: 237 patients were classified into 4 subgroups by cluster analysis. Cluster 1 (*n*=74) consisted of older patients with arterial-predominant VT, livedo reticularis and increased cardiovascular risk, cluster 2 (*n*=70) of SLE+APS patients with thrombocytopenia and heart valve disease, cluster 3 (*n*=59) of patients with venous-predominant VT, less extra-criteria manifestations and cluster 4 (*n*=34) of patients with only PM with a lower frequency of extra-criteria features and cardiovascular risk (table 1).

Table 1. Demographic, clinical and laboratory characteristics of clusters

	All (*n*=237)	Cluster 1 (*n*=74)	Cluster 2 (*n*=70)	Cluster 3 (*n*=59)	Cluster 4 (*n*=34)	*P*
Age (years), median (range)	43 (20-81)	51 (20-81)	40 (27-72)	42 (24-69)	40.5 (26-65)	<0.001
Duration of disease (years), median (range)	9.5 (1-37.7)	13.1 (1-37.7)	10.4 (1-28.7)	8.5 (1-32.8)	7 (1-22.4)	0.028
Female, *n* (%)	198 (83.5)	56 (75.7)	61 (87.1)	47 (79.7)	34 (100)	<0.05
SLE, *n* (%)	123 (51.9)	31 (41.9)	46 (65.7)	32 (54.2)	14 (41.2)	<0.05
Vascular thrombosis, *n* (%)	191 (80.6)	73 (98.6)	59 (84.3)	59 (100)	0 (0)	<0.001
Arterial thrombosis, *n* (%)	109 (46)	50 (67.6)	31 (44.3)	28 (47.5)	0 (0)	<0.001
Venous thrombosis, *n* (%)	112 (47.3)	36 (48.6)	37 (52.9)	39 (66.1)	0 (0)	<0.001
Pregnancy morbidity, *n* (%)	117 (49.4)	22 (29.7)	46 (65.7)	15 (25.4)	34 (100)	<0.001
Livedo reticularis, *n* (%)	38 (16)	21 (28.4)	10 (14.3)	5 (8.5)	2 (5.9)	<0.01
Thrombocytopenia, *n* (%)	81 (34.2)	4 (5.4)	65 (92.9)	4 (6.8)	8 (23.5)	<0.001
Heart valve disease, *n* (%)	92 (38.8)	32 (43.2)	46 (65.7)	8 (13.6)	6 (17.6)	<0.001
Arterial hypertension, *n* (%)	101 (42.6)	49 (66.2)	34 (48.6)	18 (30.5)	0 (0)	<0.001
Hyperlipidemia, *n* (%)	103 (43.5)	69 (93.2)	26 (37.1)	0 (0)	8 (23.5)	<0.001
Smoking, *n* (%)	58 (24.5)	31 (41.9)	7 (10)	17 (28.8)	3 (8.8)	<0.001
Lupus anticoagulant, *n* (%)	156 (65.8)	53 (71.6)	48 (68.6)	35 (59.3)	20 (58.8)	0.36
Anticardiolipin IgG/IgM, *n* (%)	155 (65.4)	46 (62.2)	46 (65.7)	38 (64.4)	25 (73.5)	0.71
Anti-β2-glycoprotein I IgG/IgM, *n* (%)	93 (39.2)	25 (33.8)	33 (47.1)	26 (44.1)	9 (26.5)	0.13
Triple aPL positivity, *n* (%)	45 (19)	12 (16.2)	16 (22.9)	13 (22)	4 (11.8)	0.46

Cluster 2 had the highest cumulative damage (mean DIAPS 2.48 ± 1.67) followed by cluster 1 (2.24 ± 1.44), cluster 3 (1.69 ± 1.27) and cluster 4 (0.32 ± 0.68). Comparison of DIAPS (total and major domains) between the clusters is shown in figure 1.
Patients with SLE+APS had a higher mean DIAPS compared to those with PAPS (2.10 ± 1.61 vs 1.69 ± 1.47, *P*=0.046). Cardiovascular domain was the most frequently affected DIAPS domain in both groups. Proteinuria and avascular necrosis were significantly more frequent in SLE+APS (9.8% vs 2.2%, *P*=0.02 and 5.7% vs 0%, *P*=0.009, respectively). DIAPS was positively correlated with disease duration (r=0.192, *P*=0.003).
Conclusion: Elder APS patients with arterial thrombosis and increased cardiovascular risk and SLE+APS patients with extra-criteria manifestations had higher cumulative DIAPS. Longer disease duration, higher frequency of major organ involvement and higher immunosuppressive usage may have contributed to this difference. Therefore, control of cardiovascular risk factors, prevention and effective treatment of SLE flares may help to reduce damage in these subgroups.

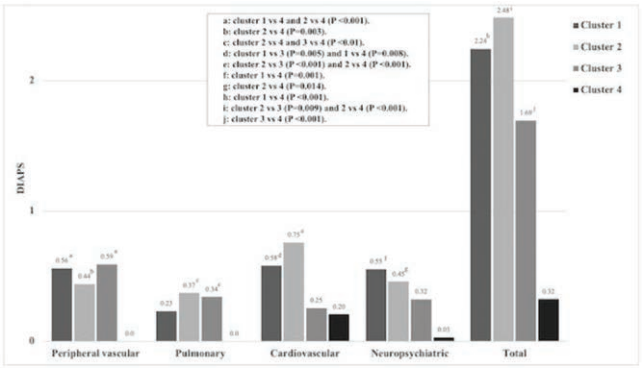


Figure 1. Comparison of mean DIAPS (total and major domains) between the clusters

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3260

POS0767

CLINICAL MANIFESTATIONS, TREATMENT, AND OUTCOMES OF "NON-CRITERIA" ANTIPHOSPHOLIPID SYNDROME IN COMPARISON WITH DEFINITE ANTIPHOSPHOLIPID SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

G. Pires Da Rosa[1,2], E. Ferreira[2,3], B. Sousa-Pinto[4,5], I. Rodriguez-Pubto[6], P. Bettencourt[2,7], R. Cervera[1], G. Espinosa[1]. [1]*Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS), University of Barcelona, Department of Autoimmune Diseases, Barcelona, Catalonia, Spain*; [2]*University of Porto, Faculty of Medicine, Porto, Portugal*; [3]*Centro Hospitalar Universitário de São João, Department of Internal Medicine, Porto, Portugal*; [4]*CINTESIS – Center for Health Technology and Services Research, Porto, Portugal*; [5]*Faculty of Medicine, University of Porto, MEDCIDS – Department of Community Medicine, Information and Health Decision Sciences, Porto, Portugal*; [6]*Hospital Universitari Mútua de Terrassa, Autoimmune Diseases Unit, Terrassa, Catalonia, Spain*; [7]*Hospital CUF, Department of Internal Medicine, Porto, Portugal*

Background: Patients with laboratorial or clinical manifestations suggestive of antiphospholipid syndrome (APS) but not fulfilling the classification criteria [1] constitute a challenge in clinical practice.
Objectives: To establish a comparison between patients with "non-criteria" versus those with definite APS on the frequency of clinical manifestations, prescribed therapies and reported outcomes.
Methods: A systematic review of observational studies comparing "non-criteria" with definite APS patients was performed searching 4 electronic databases. Data was extracted on clinical manifestations, therapies and outcomes. Studies were analyzed globally and, where possible, grouped under four potential "non-criteria" APS subsets. Random-effects meta-analyses were performed.
Results: Fourteen studies were included, assessing a total of 3,238 participants (Table 1). In the meta-analysis, no difference was detected in the frequency of arterial events or thrombosis recurrence between "non-criteria" and definite APS. However, a lower frequency of venous events was observed in "non-criteria" patients (risk ratio [RR]=0.9; 95%CI 0.7-1.0; p-value=0.047, I^2=0%; Q Cochran p-value=0.226). Regarding obstetric morbidity, no difference was observed in most outcomes, but previous history of intrauterine growth restriction was less frequent (RR=0.7; 95%CI=0.6-0.9; p-value=0.003, I^2=0%; Q Cochran p-value=0.228) and the risk of prematurity in followed pregnancies lower in "non-criteria" patients. There was no significant difference in treatment frequency between groups, except for less use of hydroxychloroquine in "non-criteria" APS (RR=0.7; 95%CI=0.5-0.9; p-value=0.007, I^2=46.5%; Q Cochran p-value=0.642). There was no significant difference in the risk of fetal loss between groups either with or without treatment (Figure 1). It should be noted that significant heterogeneity was observed in some outcomes across the studied categories. Most studies focused on "seronegative" and "incomplete laboratory" APS.

Table 1. Description of studies included in the systematic review.

	Number of Patients	
Author, year (reference)	**Definite APS**	**NC-APS (global)**
Mekinian, 2012 [2]	25	53
Rodriguez-Garcia, 2012 [3]	87	67
Conti, 2014 [4]	25	24
Ofer-Shiber, 2015 [5]	126	117
Mekinian, 2016 [6]	83	96
Omar, 2018 [7]	30	30
Signorelli, 2017 [8]	77	13
Fredi, 2018 [9]	85	81
Litvinova, 2018 [10]	41	17
Alijotas-Reig, 2019 [11]	1000	640
Ferreira, 2020 [12]	15	21
Liu, 2020 [13]	192	90
Li, 2020 [14]	34	94
Lo, 2020 [15]	12	24

Abbreviations – APS: Antiphospholipid Syndrome; NC-APS: Non-criteria antiphospholipid syndrome.

Conclusion: This review suggests an absence of marked differences in most of the evaluated variables regarding clinical manifestations, treatment and outcomes between "non-criteria" and definite APS. These results should be interpreted with caution in light of the low-quality evidence available and heterogeneity observed in some outcomes.
REFERENCES:
[1] S Miyakis et al., J Thromb Haemost **4** (2), 295 (2006).

[2] A Mekinian et al., Journal of Reproductive Immunology **94** (2), 222 (2012).
[3] JL Rodriguez-Garcia et al., Ann Rheum Dis **71** (2), 242 (2012).
[4] F Conti et al., J Immunol Res **2014**, 389601 (2014).
[5] S Ofer-Shiber and Y Molad, Blood Coagul Fibrinolysis **26** (3), 261 (2015).
[6] A Mekinian et al., Semin Arthritis Rheum **46** (2), 232 (2016).
[7] G Omar et al., Egyptian Rheumatologist **40** (2), 111 (2018).
[8] F Signorelli et al., Annals of the Rheumatic Diseases **76**, 887 (2017).
[9] M Fredi et al., Front Immunol **9**, 864 (2018).
[10] E Litvinova et al., Front Immunol **9**, 2971 (2018).
[11] J Alijotas-Reig et al., Rheumatology (Oxford) (2019).
[12] TG Ferreira et al., Clin Rheumatol **39** (4), 1167 (2020).
[13] T Liu et al., Arthritis Res Ther **22** (1), 33 (2020).
[14] X Li et al., Clinical Rheumatology (2020).
[15] HW Lo et al., Eur J Obstet Gynecol Reprod Biol **244**, 205 (2020).

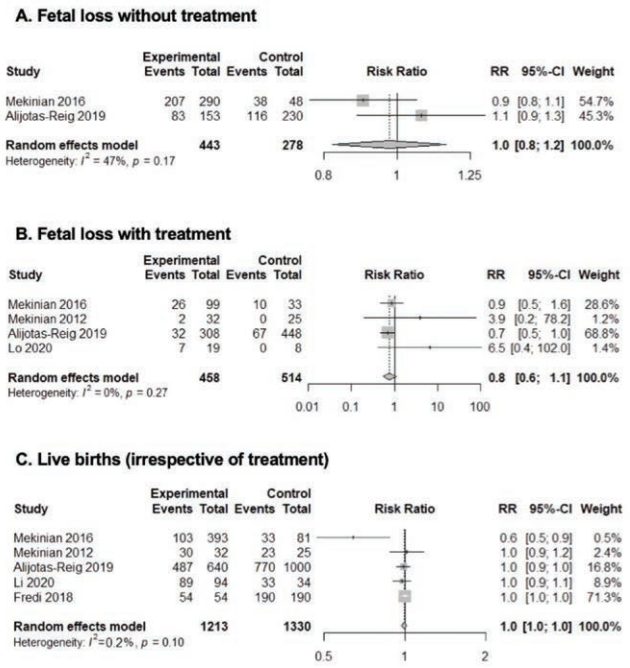


Figure 1. Forest plot of studies included in the meta-analysis regarding pregnancy and treatment outcomes.

Acknowledgements: The authors wish to thank Helena Donato, from the Documentation Unit, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, for her assistance performing the search for the systematic review.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3353

POS0768 THE IMPACT OF ANTI-RO ANTIBODIES IN PREGNANT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SJÖGREN'S SYNDROME

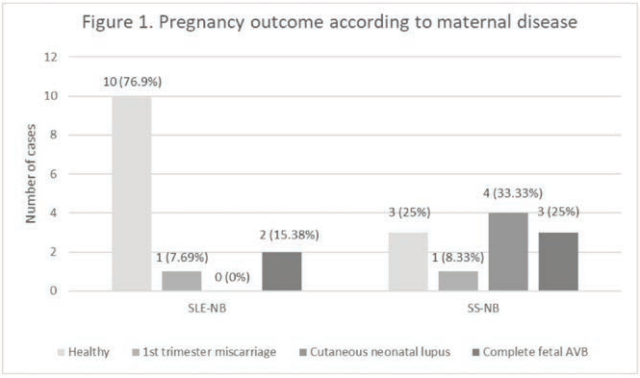
D. A. Vaida-Voevod[1,2], L. E. Mera[3], S. C. Vesa[4], M. M. Tamas[1,2], I. Felea[2], L. Muntean[1,2], I. Filipescu[1,2], C. Pamfil[1], L. Damian[2], S. P. Simon[1,2], S. Rednic[1,2]. *[1]Iuliu Hatieganu University of Medicine and Pharmacy, Rheumatology, Cluj-Napoca, Romania*; *[2]Emergency Clinical County Hospital, Rheumatology, Cluj-Napoca, Romania*; *[3]University Hospital C.F.R, ENT, Cluj-Napoca, Romania*; *[4]Iuliu Hatieganu University of Medicine and Pharmacy, Pharmacology, Toxicology and Clinical Pharmacology, Cluj-Napoca, Romania*

Background: The presence of anti-Ro antibodies in female patients diagnosed with systemic lupus erythematosus (SLE) and primary Sjögren syndrome (SS) in their fertile years raises concern among the medical team due to the risk of neonatal lupus in their newborns (NB).(1)
Objectives: The aim of this study was to determine whether there are differences between the outcome of anti-Ro positive pregnancies in SLE and SS.
Methods: This is a retrospective observational study carried out in a Rheumatology tertiary center. We included anti-Ro positive female SLE and SS patients, who were diagnosed before or during pregnancy and followed in our clinic between 2003-2020. The diagnosis of SLE or SS was established according to the 2012 SLICC criteria and the 2016 EULAR/ACR criteria, respectively. Clinical, immunological and pregnancy parameters were recorded before (where available), during and after pregnancy, as well as maternal risk factors (smoking, BMI, disease and medication history). Statistical analysis for continuous variables were performed with T-student test and categorical variables with Person Chi-square test, using IBM SPSS Statistics version 20.
Results: Eleven out of 65 anti-Ro positive SLE patients and 10 out of 153 anti Ro-positive SS patients met the inclusion criteria and had 13 and 12 pregnancies, respectively. The mean age at diagnosis was 24,75 ± 5,19 years for SLE and 31,92 ± 4,05 years for SS, and the mean pregnancy age was 28,33 ± 4,05 years for SLE and 33,17 ± 3,63 years for SS. Nine (81,81%) SLE patients were diagnosed before pregnancy, while 6 (60%) of the SS patience were diagnosed during pregnancy. Two (18,18%) SLE and 1 (10%) SS were smokers, median BMI was 21 for both SLE and SS (1 SS patient was obese), 2 (18,18%) had a history of lupus nephritis, 6 (54.54%) LES patients had secondary antiphospholipid syndrome, out of which 1 had a previous miscarriage. In the SS group there were 3 previous miscarriages, one patient had a history of parotid lymphoma. The majority of both SLE and SS patients had moderate anti-Ro antibody titers (<200 U/ml) before as well as during pregnancy: 6 (46.5%) and 8 (61.53%) in SLE, 5 (41.6%) and 7 (58.3%) in SS. More preterm NB and stillbirths were encountered in SLE mothers, possibly due to the association of secondary antiphospholipid syndrome, both groups encountered 1 pregnancy loss, and cesarean delivery outweighed vaginal ones in both SLE and SS patients. (Table 1)

Table 1. Gestational age and delivery type according to maternal disease

		SLE number (%)	SS number (%)
Gestational age			
	Full-term pregnancy	4 (30.76%)	10 (83.33%)
	Late preterm births	4 (30.76%)	1 (8.33%)
	Very preterm births	2 (15.38%)	0
	Stillbirth	2 (15.38%)	0
	Pregnancy loss	1 (7.69%)	1 (8.33%)
Delivery type			
	Vaginal	3 (25%)	4 (36.36%)
	Cesarean	9 (75%)	7 (63.63%)

Distribution of pregnancy outcome is exhibited in figure 1. There were 4 (33.33%) NB with cutaneous neonatal lupus all from SS mothers, 3 of whom used HCQ before and/or during pregnancy; and there were 5 NB with complete fetal atrioventricular block (AVB), 3 (25%) from SS mothers and 2 (15.38%) from SLE mothers. A history of HCQ usage was recorded in 3 out of these 5 mothers, and all 5 NB with complete fetal AVB were treated with dexamethasone, without success. Two NB died (both from SLE mothers) and 3 NB (all from SS mothers) needed pacemaker implantation. From the latter, 1 developed pacemaker cardiomyopathy and 1 developed sepsis.



Conclusion: Neonatal lupus seems to be more prevalent in anti-Ro positive SS patients than SLE patients, even though no difference was seen in anti-Ro titer between the two diseases. Fetal cardiac arrhythmia may lead to SS diagnosis. Dexamethasone did not improve the outcome of the fetal AVB.
REFERENCES:
[1] Mollerach FB, Scolnik M, Catoggio LJ, Rosa J, Soriano ER. Causes of fetal third-degree atrioventricular block and use of hydroxychloroquine in pregnant women with Ro/La antibodies. Clin Rheumatol. 2019 Aug;38(8):2211-2217.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3378

POS0769 VALIDATION OF THE SIMPLE INDEX FOR DISEASE ACTIVITY OF SYSTEMIC LUPUS ERYTHEMATOSUS IN CHINESE PATIENTS

C. C. Mok[1], L. Y. Ho[1], K. L. Chan[1], J. Meenakshi[2]. *[1]Tuen Mun Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[2]Rush University, Medicine, New York, United States of America*

Objectives: To validate the SIMPLE index for systemic lupus erythematosus (SLE) disease activity assessment in Chinese patients.
Methods: Adult patients (age ≥18 years) who fulfilled the 2013 SLICC criteria for SLE and were followed in the Rheumatology clinics of Tuen Mun Hospital, Hong Kong were recruited in a cross-sectional study. Participants were invited to complete the SIMPLE questionnaire before seeing doctors on the same day. The two laboratory results were supplemented by research nurses. Physicians, who were blinded to the SIMPLE results, were asked to complete disease activity assessment by the SELENA-SLEDAI and physicians' global assessment (PGA) after consultation. Correlation was made between the SIMPLE score and the SLEDAI/PGA scores by Spearman's rank correlation test. Receiver operating characteristic (ROC) analysis was performed to find the best cut-off SIMPLE score that predicted a clinical SLEDAI score of 1-6 (mild SLE activity) and ≥7 (moderate/severe activity).
Results: 364 SLE patients were studied (94% women; age 45.4±13.4 years; disease duration 13.2±8.0 years). The proportion of patients having a history of neuropsychiatric and renal disease that required immunosuppressive therapies was 9.3% and 56%, respectively. At the time of questionnaire completion, 69 (19%) patients had SLEDAI ≥6 and 192 (53%) had SLEDAI 1-5. The mean SLEDAI was 3.04±2.85 and PGA score was 0.62±0.55. A total of 161 (44%) had SDI score ≥1. The mean SIMPLE index was 26.0±12.9. SIMPLE index correlated significantly with SLEDAI (ρ=0.76; p<0.001) and PGA score (ρ=0.48; p<0.001). ROC analysis showed that a SIMPLE index of >27 points best predicted a clinical SLEDAI score of 1-6 (area under the curve [AUC] 0.78[0.73-0.84]; sensitivity 0.75; specificity 0.71), and >36.8 points best predicted a clinical SLEDAI score of ≥7 (AUC 0.87[0.69-1.00]; sensitivity 0.88, specificity 0.85).
Conclusion: SIMPLE shows a good correlation with SELENA-SLEDAI and PGA. It is a simple tool that enables patients to self-report disease activity and communicate with the health care team more efficiently.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3386

POS0770 DIFFERENTIAL CLINICAL PRESENTATION BETWEEN SLE RUPHUS PATIENTS AND SLE NON-RHUPUS PATIENTS: A CASE-CONTROL STUDY

J. Sanchez-Bautista[1], Y. Santamaria-Alza[2], C. Quintero[2], M. Muñoz[2], A. Ramírez[1], C. Muñoz[2,3], A. L. Vanegas-García[2,3], G. Vásquez[2], L. A. González[2]. [1]*Universidad de Antioquia, Internal Medicine, Medellín, Colombia*; [2]*Universidad de Antioquia, Rheumatology, Medellín, Colombia*; [3]*Hospital San Vicente Fundación, Rheumatology, Medellín, Colombia*

Background: Rhupus is a term that describe the coexistence of systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Rhupus patients have symmetrical, erosive arthritis, characteristic SLE manifestations and an array of autoantibodies including rheumatoid factor (RF), anti-cyclic citrullinated peptides (anti-CCP), anti-dsDNA, and anti-Sm.[1] Joint involvement is common in SLE patients (90%), but only 1% to 9,7% have rhupus.[2] Due to its low prevalence, there is still a lack of evidence on its presentation and differences with other SLE patients without rhupus.
Objectives: To examine the rhupus prevalence and to compare the clinical and serological characteristics between rhupus, and non-rhupus SLE patients (SLE with arthritis (SLEa), and SLE without arthritis (SLEwa)).
Methods: We performed a case-control study. Rhupus patients (cases) were matched 1:1 with non-rhupus SLE patients (controls). Descriptive statistics were calculated and rhupus, SLEa, and SLEwa were compared.
Results: A total of 72 patients were included, 24 patients in each group; most were female (87.5%). The median age at rhupus onset was 36.5 years (IQR 30-42.5). RA preceded rhupus in half of the patients, 29% were initially diagnosed as SLE, and 21% were initially diagnosed as rhupus. The median duration of RA was 66 months (IQR 30-144).
In the descriptive analysis of rhupus patients, the most affected joints were the proximal interphalangeal and metacarpophalangeal joints (87.5%), followed by the wrists (79.1%). Regarding immunological findings, RF and anti-CCP were positive in 87.5% and 50% of the patients, respectively. As to radiographic findings, the median number of erosions in the hands and wrists was 2 (IQR 0-5) and the median number of joints with narrowed joint space was 7 (IQR: 1.5 - 13.5). In terms of treatment, 95.8% received corticosteroids (median 10 mg/day), 91.6% antimalarials, 79.1% methotrexate, 41.6% leflunomide, and 25.0% rituximab.
Patients with rhupus were older and had less renal and hematological involvement than patients with SLEa and SLEwa. SLEa patients had higher seropositivity for anti-RNP and anti-Sm, higher neurological involvement, and higher SLEDAI-2K scores than rhupus patients. Comparisons of other clinical and serological variables between SLE rhupus and non-ruphus patients are shown in table 1 and figure 1.

Table 1. Clinical and serological manifestations in rhupus, articular SLE, and non-articular SLE

Variables	RHUPUS M (IQR)	SLE with arthritis M (IQR)	SLE without arthritis M (IQR)	P value RHUPUS vs. SLE with arthritis	p value RHUPUS vs. SLE without arthritis
Age (years) M (IQR)	40 (31.5 – 49)	29 (21.5 – 45)	33 (19.5 – 37.5)	0.043	0.013
CPR M (IQR)	2.3 (1– 8.5)	1.6 (0.3– 3.6)	0.9 (0.2– 2.5)	0.337	0.032
Positive anti-RNP N (%)	7 (29.1%)	14 (58.3%)	7 (29.1%)	0.042	1.000
Positive anti-Sm N (%)	5 (20.8%)	15 (62.5%)	6 (25%)	0.003	0.500
SLEDAI – 2K score M (IQR)	4.5 (1 – 7)	9 (2 – 18)	7 (3.5 – 15)	0.045	0.082

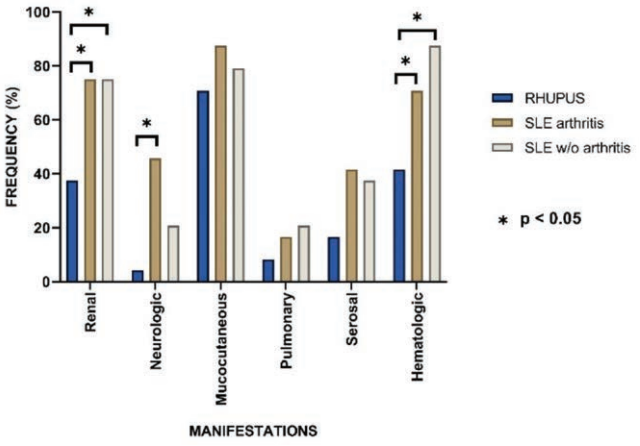


Figure 1. Differences in the frequencies of organic alterations. w/o: without.

Conclusion: Patients with rhupus were older and had lower SLEDAI-2K scores compared with those non-rhupus. Furthermore, renal, neurological, and hematological manifestations were more common in non-rhupus patients than in rhupus patients.
REFERENCES:
[1] Antonini L, et al. Rhupus: a systematic literature review. Autoimmun Rev. 2020;19(9):102612.
[2] Tani C, et al. Rhupus syndrome: Assessment of its prevalence and its clinical and instrumental characteristics in a prospective cohort of 103 SLE patients. Autoimmun Rev. 2013; 12:537–41.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3393

POS0771 VALIDATION OF THE 2019 EUROPEAN LEAGUE AGAINST RHEUMATISM/AMERICAN COLLEGE OF RHEUMATOLOGY (EULAR/ACR) CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN HONG KONG CHINESE

C. C. Mok[1], Y. K. Chung[2], C. Lee[2], L. Y. Ho[1], C. H. To[2]. [1]*Tuen Mun Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; [2]*Pok Oi Hospital, Medicine, Hong Kong, Hong Kong (SAR)*

Objectives: To validate the 2019 EULAR/ACR classification criteria for SLE in Hong Kong Chinese patients and compare its performance with the 2012 Systemic Lupus International Collaborating Clinics (SLICC) and 1997 American college of rheumatology (ACR) criteria.
Methods: We retrospectively reviewed the medical records of consecutive patients who attended the Rheumatology clinics in Tuen Mun and Pok Oi hospitals between May and September 2019. Patients with anti-nuclear antibody (ANA) ≥1:80 were included and patients with ANA <1:80 or no ANA results were excluded. Patients were evaluated and cross-checked for the fulfilment of the 1997 ACR, 2012 SLICC and 2019 EULAR/ACR criteria by two investigators (YKC,CL). Medical records were then reviewed by an expert panel consisting of 3 senior rheumatologists, who were blinded for the results of the criteria evaluation, for a diagnosis of SLE based on the clinical judgement and therapeutic decisions. Teleconferences were arranged by the panel to discuss the discrepancies of the final diagnosis and agreement was made by voting. The three SLE criteria

were evaluated against the clinical diagnosis of SLE as judged by the expert panel on the sensitivity and specificity, which was calculated by 2x2 contingency tables ("condition positive" = clinical diagnosis of SLE; "test positive" = criteria positive for SLE) with standard formulas (sensitivity = true positive/[true positive + false negative]; specificity = true negative / [true negative + false positive]). Receiver operating characteristic (ROC) curve was used to study the optimal cut-off points from the EULAR/ACR criteria for the highest summation of specificity and sensitivity.

Results: 3967 patients were screened; 1542 patients who were positive for ANA (≥1:80) were included (88.3% women). The mean age of these patients at first rheumatology clinic attendance was 45.6±15.0 years and the duration of follow-up was 7.5±7.0 years. A total of 567 patients were judged to have SLE by the expert panel (discrepancy of clinical diagnosis in 135 patients resolved with voting). The sensitivity and specificity of the three SLE classification criteria in our patients are listed in Table 1. ROC analysis showed that the best cut-off for a clinical diagnosis of SLE using the EULAR/ACR criteria was 10 points (area under the curve [AUC] 0.977; sensitivity 89.2% and specificity 89.6%). Similar figures were obtained for subgroups of patients stratified by gender and different age ranges.

Conclusion: In our cohort of Hong Kong Chinese patients, the 2019 EULAR/ACR criteria is more sensitive but less specific when compared with 1997 ACR criteria for classifying SLE. On the other hand, the EULAR/ACR criteria is less sensitive but more specific than the 2012 SLICC criteria. The specificity of the EULAR/ACR criteria for SLE is higher in male than female patients. In our patients older than 50 years, the EULAR/ACR criteria is less sensitive but more specific for a classification of SLE. Overall, the performance of the EULAR/ACR criteria for a diagnosis of SLE in our study is similar to that reported in recent Asian studies although the sensitivity is lower, which may be related to the inclusion of ANA+ patients only.

REFERENCES:

Classification criteria	Sensitivity	Specificity
1997 ACR	85.9%	94.4%
2012 SLICC	97.5%	86.4%
2019 EULAR/ACR with 10 points as cut-off	89.2%	89.6%
2019 EULAR/ACR with 9 points as cut-off	93.6%	68.7%
2019 EULAR/ACR with 11 points as cut-off	86.9%	92.4%
2019 EULAR/ACR with 10 points as cut-off (men)	88.9%	94.5%
2019 EULAR/ACR with 10 points as cut-off (women)	89.2%	88.8%
2019 EULAR/ACR with 10 points as cut-off (age >50 years)	78.7%	94.1%
2019 EULAR/ACR with 10 points as cut-off (age ≤50 years)	91.7%	84.1%

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3394

POS0772 PREVALENCE AND RISK FACTORS FOR HERPES ZOSTER REACTIVATION IN 1542 PATIENTS WITH RHEUMATIC DISEASES

C. C. Mok[1], L. Y. Ho[1], S. M. Tse[1], K. L. Chan[1], C. H. To[2]. *[1]Tuen Mun Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[2]Pok Oi Hospital, Medicine, Hong Kong, Hong Kong (SAR)*

Objectives: To study the prevalence and risk factors of herpes zoster (HZ) infection in patients with rheumatic diseases.

Methods: Medical records of patients with rheumatic diseases who attended our out-patient rheumatology clinics between 2019 March and 2019 August were retrospectively reviewed. Patients who were using biological or targeted DMARDs were excluded. Episodes of HZ infection since disease diagnosis were identified and the prevalence over time was calculated. Laboratory parameters (total white cell count, neutrophil-to-lymphocyte ratio, serum albumin, globulin & creatinine), history of diabetes mellitus and the highest doses of immunosuppressive medications within 6 months of the first episode of HZ infection were compared with those within 6 months of last follow-up in patients who did not have HZ infection. Cox regression analysis was performed to identify factors associated with the first HZ infection in all patients.

Results: 1542 patients were studied (88% women, age 46.4±15.0 years). The underlying diseases were systemic lupus erythematosus (SLE) (38%), rheumatoid arthritis (26%) and other rheumatic diseases (36%). After a total follow-up of 11,515 patient-years since diagnosis (7.5±7.0 years), 122 (7.9%) patients developed 146 episodes of HZ infection, giving an overall prevalence of 1.27/100-patient years. The prevalence rates of HZ in SLE, RA and non-SLE/RA patients were 1.70, 0.64 and 0.76 per 100 patient-years, respectively. Patients who experienced HZ reactivation were younger (41.6±14.7 vs 46.8±15.0 years; p<0.001), more likely to have SLE (74% vs 35%; p<0.001) and diabetes mellitus (17% vs 7.3%; p=0.01), and had a significantly lower albumin (38.6±5.6 vs 41.3±3.5; p<0.001) and higher neutrophil-to-lymphocyte ratio (4.9±6.2 vs 2.8±2.6; p<0.001). More patients with HZ reactivation were treated with prednisolone (54% vs 22%; p<0.001), azathioprine (20% vs 8%; p<0.001), mycophenolate mofetil [MMF] (21% vs 12%; p=0.006), cyclophosphamide [CYC] (4.9% vs 0.1%; p<0.001) and hydroxychloroquine (48% vs 34%; p=0.002) in the preceding 6 months compared with those who did not have HZ infection. Among those using immunosuppressive drugs, the doses of MMF (1.42±0.64 vs 1.02±0.31g; p=0.005) and prednisolone (15.6±15.9 vs 5.5±4.5mg; p<0.001) were significantly higher in those with HZ infection. The cumulative risk of having HZ reactivation in SLE patients at 24 and 48 months since diagnosis was 5.9% and 8.6%, respectively, which was significantly higher than that in non-SLE patients (1.9% and 2.5%, respectively; p<0.001 by log rank test). Cox regression analysis revealed that having a diagnosis of SLE (HR 1.97 [1.17-3.31]), albumin level (HR 0.93 [0.90-0.97] per g/L; p=0.001), serum creatinine (HR 0.995 [0.990-1.00] per umol/L), higher neutrophil/lymphocyte ratio (HR 1.08 [1.05-1.11]) and the use of CYC (HR 6.69 [2.56-17.5]) and prednisolone (HR 1.61 [1.02-2.45]) in the preceding 6 months were independently associated with the development of HZ infection.

Conclusion: Reactivation of HZ is fairly common in patients with rheumatic diseases. Underlying SLE, prednisolone/cyclophosphamide therapy and the neutrophil/lymphocyte ratio, but not age, sex or other laboratory parameters, are the major risk factors for HZ reactivation.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3398

POS0773 CLINICAL PRESENTATION AND OUTCOMES OF THE ANTIPHOSPHOLIPID SYNDROME (APS) IN SOUTHERN CHINESE PATIENTS: THE HONG KONG APS REGISTRY

C. C. Mok[1], C. Lee[2], M. C. Leung[3], Y. K. Tang[4], C. Ho[5], S. Woo[6], M. L. Lee[7], M. C. Wan[6], M. Y. Lee[8]on behalf of Hong Kong APS registry working group. *[1]Tuen Mun Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[2]Pok Oi Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[3]United Christian Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[4]Kwong Wah Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[5]Queen Mary Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[6]Rutonjee Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[7]Yan Chai Hospital, Medicine, Hong Kong, Hong Kong (SAR)*; *[8]Tai Po Hospital, Medicine, Hong Kong, Hong Kong (SAR)*

Objectives: To report the clinical presentation and outcomes of the APS in Hong Kong Chinese patients.

Methods: The HKAPS registry was established in early 2020 by the Hong Kong Society of Rheumatology to study the outcomes of Chinese patients with APS treated in public hospitals in Hong Kong. Patients aged ≥18 years were identified by the Hospital Authority Clinical Data retrieval system using the ICD-10 diagnostic code of APS. The medical history and APS diagnosis was verified by sub-investigators in different hospitals using the 2006 modified consensus criteria for the APS. Eligible patients were classified into definite APS or probable APS, which was further categorized into primary (without underlying rheumatic diseases) and secondary types. The presentation, treatment and outcomes of these patients were summarized.

Results: 232 APS patients (76.3% women) were identified. All were ethnic Chinese. A total of 160 patients fulfilled the 2006 criteria for APS (definite APS) while 72 patients had probable APS (anti-phospholipid [aPL] antibodies positive once or with non-criteria manifestations). In those with definite APS, the mean age at diagnosis was 44.9±15.8 years and the female to male ratio was 3.1:1. APS was primary in 82 patients while 78 patients had concomitant rheumatic diseases (SLE in 95% of patients). 130(81%) patients had thromboembolic manifestations, 20(13%) had obstetric morbidities and 10(6%) had both. In patients with secondary APS, 23% thrombotic or obstetric manifestations occurred before diagnosis of the rheumatic diseases (ie. evolved from primary APS). Lupus anticoagulant was present in 81(51%) patients, moderate/high titers of anti-cardiolipin were present in 90(56%) patients and anti-$\beta_2$glycoprotein-1 was present in 6(4%) patients. Sixteen (10%) patients were double positive while 1 patient was triple positive for these aPL antibodies. Among the thromboembolic manifestations, arterial thrombosis (n=84) (ischemic stroke 77%, myocardial infarction 4.8%, peripheral vascular disease with limb/digital gangrene 2.4%, retinal artery 2.4%, splenic artery 1.2%, bowel infarct 1.2%) was more common than venous thrombosis (n=73) (calf vein thrombosis ± pulmonary embolism 86%, cerebral veins 2.7%, inferior vena cava/iliac veins 6.8%, retinal vein 2.7%, splenic vein 1.4%). The following treatment regimens were used in our APS patients: warfarin (71%), aspirin plus subcutaneous heparin (4%), aspirin + warfarin (3.1%), aspirin alone (17%) and the direct oral anticoagulant (DOAC) (5%). Bleeding complications developed in 35(22%) patients. Over a mean follow-up of 9.9±7.0years, recurrence of thromboembolic or obstetric manifestations recurred in 39(24%) and 6(4%) patients, respectively. A total of 29(18%) patients succumbed (median time to death: 6.4 years) and the causes of death were: pneumonia (24%), septicemia (17%), intracranial hemorrhage (14%), myocardial infarction (10%), ischemic stroke (3%), bowel infarct (3%), pulmonary hypertension (6.9%) and sudden death with unknown causes (14%).

Conclusion: APS in southern Chinese is relatively uncommon and most cases were associated with SLE. In contrast with the Caucasians, venous thrombosis related to APS is less frequent than arterial thrombosis in Chinese patients. With long-term anticoagulation treatment, the outcome is satisfactory with relatively low rates of recurrence and mortality. Expansion of the sample size to study factors associated with recurrence and mortality by involving more hospitals is in progress.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3403

POS0774 INFLUENZA INFECTION AS A TRIGGER FOR SYSTEMIC LUPUS ERYTHEMATOSUS FLARES RESULTING IN HOSPITALIZATION

Y. B. Joo[1], Y. J. Park[2]. [1]*Hanyang University Guri Hospital, Rheumatology, Guri, Korea, Rep. of (South Korea)*; [2]*St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Rheumatology, Seoul, Korea, Rep. of (South Korea)*

Background: Infections have been associated with a higher risk of systemic lupus erythematosus (SLE) flares, but the impact of influenza infection on SLE flares has not been evaluated.
Objectives: We evaluated the association between influenza infection and SLE flares resulting in hospitalization.
Methods: SLE flares resulting in hospitalization and influenza cases were ascertained from the Korean national healthcare insurance database (2014-2018). We used a self-controlled case series design. We defined the risk interval as the first 7 days after the influenza index date and the control interval was defined as all other times during the observation period of each year. We estimated the incidence rates of SLE flares resulting in hospitalization during the risk interval and control interval and compared them using a Poisson regression model.
Results: We identified 1,624 influenza infections among the 1,455 patients with SLE. Among those, there were 98 flares in 79 patients with SLE. The incidence ratio (IR) for flares during the risk interval as compared with the control interval was 25.75 (95% confidence interval 17.63 – 37.59). This significantly increased the IRs for flares during the risk interval in both women (IR 27.65) and men (IR 15.30), all age groups (IR 17.00 – 37.84), with and without immunosuppressive agent (IR 24.29 and 28.45, respectively), and with and without prior respiratory diseases (IR 21.86 and 26.82, respectively).
Conclusion: We found significant association between influenza infection and SLE flares resulting in hospitalization. Influenza infection has to be considered as a risk factor for flares in all SLE patients regardless of age, sex, medications, and comorbidities.
REFERENCES:

[1] Kwong, J. C. et al. Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection. N Engl J Med 2018:378;345-353.

Table 1. Incidence ratios for SLE flares resulting in hospitalization after influenza infection

Risk interval	Incidence ratio	95% CI
During risk interval for 7 days / control interval	25.75	17.63 – 37.59
Days 1-3 / control interval	21.81	14.71 – 32.35
Days 4-7 / control interval	7.56	3.69 – 15.47

SLE, systemic lupus erythematosus; CI, confidence interval

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3409

POS0775 APLS-ASSOCIATED RETINAL VASCULOPATHY AS A PRESENTATION OF THROMBOTIC MICROANGIOPATHY

W. Qi[1], Z. Xie[1], J. L. Zhao[1], X. Tian[1], M. Li[1], X. Zeng[1]. [1]*Peking Union Medical College Hospital, Department of Rheumatology, Beijing, China*

Background: Persistent antiphospholipid antibodies (aPL) positivity was a recognized risk factor for thrombotic events, obstetric morbidity and a variety of manifestations beyond thrombosis. The presence of some non-criteria manifestations including thrombocytopenia, hemolytic anemia, and APS nephropathy should prompt consideration for thrombotic microangiopathy (TMA).[1] Patients with APS can also present with a variety of ocular and neuro-ophthalmic manifestations, such as retinal artery/vein occlusion, retinal arteritis, optic neuritis and ischemic optic neuropathy, with underlying mechanisms remained elusive. Retinal vasculopathy including retinal artery occlusion (RAO) or retinal vein occlusion (RVO) was recently found occurred more frequently in APS patients with thrombocytopenia[2], suggested other possible mechanisms besides thromboembolism.
Objectives: To explore risk factors and possible mechanisms of retinal vasculopathy among APS patients.
Methods: In this single-center case-control study among APS patients, we evaluated patients who fulfilled 2006 Sapporo APS Classification Criteria[3] with or without retinal vasculopathy during 2018-2020 at Peking Union Medical College Hospital. Demographic data, aPL-related manifestations, cardiovascular risk factors and antibodies profile were compared and a logistical regression model was built. Hierarchical cluster analysis with the Euclidean distance and the Ward method was applied to identify clusters of variables.
Results: A total of 310 APS patients (67.4% female, mean age 38.1 years) were included, of whom 18 patients were diagnosed with retinal vasculopathy (9 with RVO and 9 with RAO). No significant differences was found among most demographic characteristics, clinical manifestations, or antibody profile. However, APS-related heart valve disease (OR 13.66, 95% confidence interval [CI] 4.55-40.98), APS nephropathy (OR 12.77, 95% CI 4.04-40.35), thrombocytopenia (OR 2.63, 95% CI 1.01-6.89) and high serum IgM (OR 3.67, 95% CI 1.30-10.40) were predictive of retinal vasculopathy (Figure 1 A). APS-related heart valve disease and nephropathy were also found statistical significant in multivariate logistical regression (Figure 1 B). They and other non-criteria manfestations were aggregated with retinal vasculopathy from cluster analysis of variables (Figure 1 C).
Conclusion: Patients with APS-related heart valve disease and nephropathy suffered a higher risk of retinal vasculopathy including RAO and RVO. The underlying mechanisms of aPLs-associated retinal vasculopathy may involve TMA, leading to a poor prognosis and therapeutic changes.
REFERENCES:

[1] Kotzen ES, Roy S, Jain K. Antiphospholipid Syndrome Nephropathy and Other Thrombotic Microangiopathies Among Patients With Systemic Lupus Erythematosus. Adv Chronic Kidney Dis. 2019 Sep;26(5):376-386.
[2] Ermakova NA, Alekberova ZS, Reshetniak TM, Kalashnikova LA, Kosheleva NM. [Retinal vascular lesions in systemic lupus erythematosus and secondary antiphospholipid syndrome]. Vestn Oftalmol. 2005 Sep-Oct;121(5):31-6.
[3] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost. 2006 Feb;4(2):295-306.

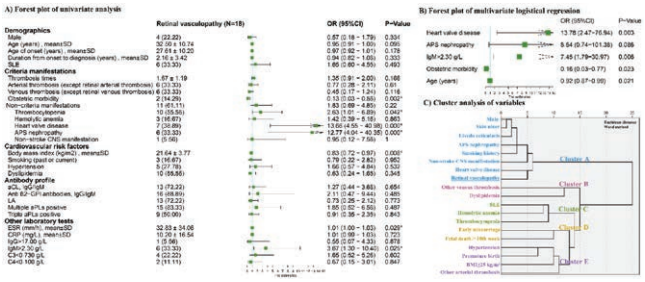


Figure 1. A) Forest plot of univariate analysis; B) Forest plot of multivariate logistic regression; C) Cluster analysis of variables.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3441

POS0776 CORRELATION OF PERIPHERAL CD4+GRANZB+CTLS WITH DISEASE SEVERITY IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

Q. Wang[1], L. Gu[2], M. Zhang[1]. [1]*The First Affiliated Hospital of Nanjing Medical University, Department of Rheumatology, Nanjing, China*; [2]*The First Affiliated Hospital of Nanjing Medical University, Department of Rheumatology, Nanjing, China*

Background: Sjögren's syndrome (SS) is a chronic autoimmune disorder. The major histopathologic lesion of it is a focal lymphocytic infiltrate around ductal and acinar epithelial cells, which include a majority of CD4+T. Several studies have shown that the epithelial cells in SS present diverse phenomena, such as MHC class II overexpression. CD4+T cells with cytotoxic activity (CD4 CTL) have been detected in various immune responses. They are characterized by their ability to secrete perforin and granzyme B to kill the target cells in an MHC class II-restricted fashion.
Objectives: So this study was to investigate the correlation of peripheral CD4+GranzB+CTLs with disease severity and organ involvement in patients with primary Sjögren's syndrome.
Methods: We recruited 116 pSS patients and 46 healthy controls using flow cytometry to examine proportion of CD4+GranzB+CTLs in their peripheral blood, and immunofluorescence to test the expression of CD4+GranzB+CTLs in labial gland. The correlations of CD4+GranzB+CTLs and the relevant clinical data were analyzed.

Results: We analyzed the percentage of CD4+GranzB+cytotoxic T cells in peripheral blood mononuclear cells (PBMCs) by flow cytometry. Frequency of peripheral CD4+GranzB+CTLs were measured in 116 patients with pSS and 46 healthy controls matched for age and sex. The percentage of CD4+GranzB+CTLs were significantly up-regulated in pSS patients than healthy controls (7.1%±4.9% vs 3.1%±1.9%, p <0.0001) and positive correlation with ESSDAI in pSS patients(r = 0.6332, p<0.001). The percentage of CD4+GranzB+CTLs were markedly higher in pSS patients with extraglandular manifestations. Moreover, CD4+GranzB+CTLs were observed in the lymphocytic foci and periductal areas of the LSGs and were elevated with increased foci index (FI). After excluding the other risk factors associated with pSS, CD4+GranzB+CTLs were still related to ESSDIA and extraglandular manifestations independently(p<0.05). ROC curve analysis indicated that the area under the curve (AUC) of CD4+GranzB+CTLs was 0.796 to predict the activity of pSS, and 0.851 to presume extraglandular manifestations. The best diagnostic cut-off point was 4.865 for pSS patients.
Conclusion: In this study, We provide new evidence indicating involvement of CD4+GranzB+CTLs over activation in the disease pathophysiology of pSS, which may serve as a new biomarker to evaluate the activity and severity of pSS.
REFERENCES:
[1] Takeuchi A, Saito T. Front Immunol. (2017) 23:194.
[2] Brown DM, et al. Front Immunol. (2016) 9:93.
[3] Polihronis M, et al. Clin Exp Immunol. (1998) 114:485-90.
[4] Xanthou G, et al. Clin Exp Immunol. (1999) 118:154-63.
[5] Maehara T, et al. Ann Rheum Dis. (2017) 76:377-385.
[6] Goules AV, et al. Clin Immunol. (2017) 182:30-40.
[7] Hashimoto K, et al. Proc Natl Acad Sci U S A. (2019) 116:24242-24251.
[8] Croia C, et al. Arthritis Rheumatol. (2014) 66:2545-57.
[9] Schmidt D,et al. J Clin Invest. (1996) 97:2027–37.
[10] Pandya JM, et al. Arthritis Rheum. (2010) 62:3457–66.
[11] Moosig F, et al. Clin Exp Immunol. (1998) 114:113–8.
[12] Peeters LM, et al. Front Immunol. (2017) 20:1160.

Table 1. Multivariate analysis of CD4+GranzB+CTLs influenced by pSS-related factors

	regression coefficient	standard error	t-statistics	*p* value	95%CI
CD8+GranzB+CTLs(%)	0.144	0.033	4.334	6.9E-5	0.077, 0.211
ESSDAI	0.256	0.122	2.095	0.041	0.011, 0.502
extraglandular manifestations	2.612	1.268	2.059	0.045	0.065, 5.158

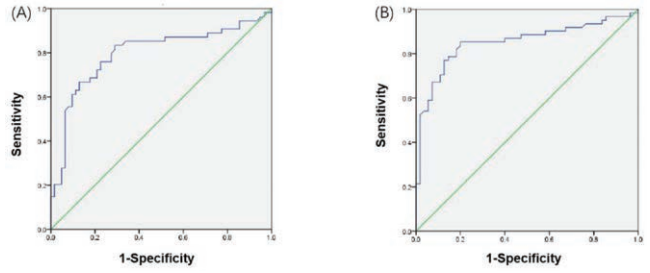


Figure 1. Receiver operating characteristic (ROC) curve of the frequency of CD4+GranzB+CTLs to predict ESSDAI and extraglandular manifestations response

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3450

POS0777

ANTIPHOSPHOLIPID RELATED LARGE VESSEL LESIONS: NOT ONLY THROMBOSIS

H. Jiang[1], W. Qi[1], J. Zhao[1], Y. Zhao[1]. [1]*Peking Union Medical College Hospital, Department of Rheumatology, National Clinical Research Center for Dermatologic and Immunologic Diseases, Beijing, China*

Background: Antiphospholipid syndrome (APS) is demonstrated as recurrent venous/arterial thromboses or obstetric morbidities with persistent antiphospholipid antibodies(aPLs). Recently, several cases reported that non-thrombotic lesions of large vessels may exist in APS, while less report described the characteristics of these patients.
Objectives: The study investigated patients with chronic large vessel lesions (stenosis or occlusion) (LVL) in APS, to detect the features of non-thrombotic arterial vasculopathy in APS (VAPS) by comparing with thrombotic APS (TAPS).
Methods: This is a single-center study involved the APS database from Peking Union Medical College Hospital (PUMCH) from 2013 to 2020. The study analyzed demography and laboratory index of 18 patients with LVL by comparing with 216 patients with thrombotic APS. Patients with LVL presented no specific vasculitis or in situ thrombosis at the lesion.
Results: Radiographic analysis in patients with LVL showed widespread thickening/enhancement of vessel wall or multiple segments stenoses, without intraluminal thrombus or atherosclerosis. In comparing with 216 patients with TAPS, the 18 patients with LVL complicated no other autoimmune diseases, had more cardiovascular risks (72.22% vs. 30.09%, $P < 0.01$), lower inflammatory index such as erythrocyte sedimentation rate (ESR) (6 vs. 11, p<0.05), increased cerebrovascular symptoms which maybe related to cerebral/carotid vessel occlusions (55.56%vs. 25.93%, p=0.01). Population characteristics, complications and antibody profiles in VAPS are similar to TAPS.
Conclusion: Large vessel lesions in APS could present non-thrombotic and non-inflammatory manifestations which is different from TAPS.

Table 1. Demographic characteristics

	TAPS(n=216)	VAPS(n=18)	P-value
Age (years), Mean±SD	39.36±13.69	40.06±13.86	.290
Male, n (%)	88(40.74)	9(50.00)	.300
SLE, n (%)	53(24.54)	0	***.008***
Other autoimmune diseases, n (%)	4(1.85)	0	.724
B.M.I. (kg/m2), Mean±SD	24.10±4.12	23.93±3.31	.469
Cardiovascular risk factors, n (%)	65(30.09)	13(72.22)	***.001***
Non-criteria manifestations, n (%)	109(50.46)	7(38.89)	.243
Triple positive antibodies, n (%)	124(57.4)	13(72.22)	.165
Double positive antibodies, n (%)	46(21.30)	4(22.22)	.563
Single positive antibody, n (%)	45(20.83)	1(5.56)	.096
Arterial thrombosis, n(%)	100(46.30)	16(88.89)	***.000***
Stroke	56(25.93)	10(55.56)	***.010***
Venous thrombosis, n(%)	152(70.37)	8(44.44)	***.025***
ESR (mm/h), Median (Quartile)	11(5.00,29.00)	6(2.75,14.00)	***.035***
CRP (mg/L), Median (Quartile)	1.52(0.59,4.44)	1.28(0.26,1.91)	.054
Hcy(umol/L), Median (Quartile)	13.45(11.1,17.1)	13.55(10.9,16.38)	.406

* **SLE**: systemic lupus erythematosus; **B.M.I**: Body Mass Index; **Cardiovascular risks positive**: patients with at least one positive of smoke, coronary heart disease, hypertension, diabetes, obesity or hyperlipidemia; **Non-criteria manifestations**: at least one positive of thrombocytopenia, hemolytic anemia, vulve vegetation, nephropathy, livedo reticularis, skin ulcer or non-stroke central nervous system manifestations; **ESR**: erythrocyte sedimentation rate; **CRP**: C-reactive protein; **Hcy**: homocysteine.

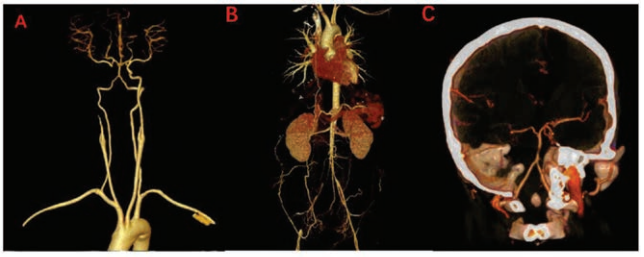


Figure: APS related Large Vessel Lesions in CT angiography and 3D Reconstruction
A. Severe stenosis of right internal carotid artery (RICA). B. Severe occlusion of right iliac artery.
C. Occlusion of right middle cerebral artery.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3459

POS0778

ULTRA HIGH-RESOLUTION ULTRASOUND (UHFUS) OF LABIAL GLANDS IS A STRONG PREDICTOR OF SALIVARY GLAND HISTOPATHOLOGY IN SJÖGREN'S SYNDROME (PSS)

G. Fulvio[1], F. Ferro[1], R. Izzetti[2], S. Fonzetti[1], G. La Rocca[1], G. Governato[1], G. Aringhieri[3], D. Caramella[3], M. Mosca[1], V. Donati[4], C. Baldini[1]. [1]*University of Pisa, Rheumatology Unit, Clinical and Experimental Medicine, Pisa, Italy*; [2]*University of Pisa, Unit of Dentistry and Oral Surgery, Surgical, Medical and Molecular Pathology and Critical Care Medicine, Pisa, Italy*; [3]*University of Pisa, Diagnostic and Interventional Radiology, Translational Research and of New Technologies in Medicine and Surgery, Pisa, Italy*; [4]*Unit of Pathological Anatomy 2, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy*

Background: Last-generation ultra high-resolution ultrasound (UHFUS) transducers, producing frequencies up to 70 MHz and achieving tissue resolution up to 30 µm, are opening up new possibilities for the study of labial salivary glands (LSG) in patients clinically suspected with primary Sjögren's syndrome (pSS).
Objectives: To explore the value of LSG-UHFUS as a predictor of the intensity of the histological inflammation in LSG biopsy in an inception cohort of patients with sicca symptoms derived from daily clinical practice.

Methods: Consecutive patients undergoing a LSG for clinically suspected pSS were included in this study from January 2018 to October 2020. UHFUS of LSG was performed by using VEVO MD, equipped with a 70 MHz probe, scanning first the central compartment of the inferior lip, and then both peripheral compartments. Parenchymal homogeneity was graded on a scale of 0 (normal) to 3 (evident). UHFUS imaging was used to locate the LSG for the US-guided biopsy. For each of the LSG specimens the area of the glandular tissue, the presence and number of foci and the focus score (FS) were assessed. Immunostaining for CD21 was performed to evaluate the presence of follicular dendritic cells (FDC) in foci.

Results: We included a total of 171 patients with suspected pSS: out of them, 83 (48.5%) received a diagnosis of pSS (ACR 2016 criteria) and 88 (51.5 %) were diagnosed as no-SS sicca controls. Out of the 171 LSG biopsies, 73/171 (42.7%) were characterized by a nonspecific chronic sialadenitis (NSCS) whereas a focal lymphocytic sialadenitis (FLS) was described in the remaining 98/171 (57.3%). UHFUS-LSG scores were differently distributed in pSS patients with respect to no-SS sicca controls: a score 0 was detected in 16/88 no-SS sicca controls and in none of the 83 pSS patients, whereas a score 3 was detected in 12/83 pSS and in none of no-SS sicca controls. (p<0.001). The higher was the UHFUS grading, the higher was the number of foci (from a mean (S.D) = 0.38 (0.72) in UHFUS-score 0 to 4.58 (3.11) in UHFUS-score 3, p<0.001) and the focus score (from 0.17 (0.32) in UHFUS-score 0 to 1.88 (0.90) in UHFUS-score 3, p<0.001) of the samples. Overall, out of the 16 no-SS controls with LSG-UHFUS score 0, only 4/16 showed histological features of focal lymphocytic infiltrate; however, the mean FS of those 4/16 samples was 0.17 (0.32). In fact, considering a FS≥1, negative UHFUS-LSG was highly predictive of a negative histology (100 %). By contrast, out of the 12 pSS patients with the highest score at LSG-UHFUS (score 3), 10/12 presented FDC networks in their biopsies, with a positive predictive value of 83% of the severity of the infiltrate.

Conclusion: UHFUS of LSG appeared feasible and sensitive in pSS; due to its striking negative predictive value this novel tool can help to identify negative patients on subsequent lip biopsy, thus avoiding invasive procedures in selected cases. Besides its diagnostic role, considering the association with the presence of FDC networks, UHFUS-LGS may also have a role in patients prognostic stratification.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3484

POS0779 MYOCARDIAL INFARCTIONS, SUBTYPES, LOCATIONS AND CORONARY ATHEROSCLEROSIS IN SLE - A COMPARATIVE STUDY WITH MATCHED CONTROLS

I. Samuelsson[1], I. Parodis[1,2], I. Gunnarsson[1,2], A. Zickert[1,2], C. Hofman-Bang[3,4], H. Wallén[3,4], E. Svenungsson[1,2]. *[1]Karolinska Institutet, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden*; *[2]Karolinska University Hospital, Unit of Rheumatology, Stockholm, Sweden*; *[3]Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, Stockholm, Sweden*; *[4]Danderyd Hospital, Unit of Cardiology, Stockholm, Sweden*

Background: Myocardial infarction (MI) is estimated to be 2- to 3-fold elevated in systemic lupus erythematosus (SLE) as compared to gender- and age-matched controls (1-2). Even though some risk factors have been purposed, mechanisms of increased MI incidence remains to be determined.

Objectives: To explore underlying mechanisms, we compared MI characteristics and risk factors between SLE patients with MI (MI-SLE), MI patients without SLE (MI-nonSLE) and SLE patients without MI (nonMI-SLE).

Methods: We performed retrospective medical file review including angiography and echocardiography reports in 34 MI-SLE patients, 34 MI-nonSLE patients and 34 nonMI-SLE patients – all individually matched for gender and age in a ratio of 1:1:1.

Results: Median age was 61 years and 88% were females. MI-SLE patients had more coronary arteries involved (table 1; p=0.038), and ≥50% coronary atherosclerosis/occlusion at MI was numerically more common compared to MI-nonSLE controls (88% versus 66%; p=0.065). The left anterior descending artery was most frequently involved in both MI groups (73% versus 59%; p=0.11). Decreased (<50%) left ventricular ejection fraction occurred with similar frequency (45% versus 36%; p=0.79) in MI-SLE patients compared to MI-non-SLE patients. Cardiovascular disease (CVD) (44%, 5.9%, 12%; p<0.001) and coronary artery disease excluding MI (CAD, 32%, 2.9%, 0%; p<0.001) preceded MI/inclusion more commonly in MI-SLE than in MI-nonSLE and nonMI-SLE patients, respectively. MI-SLE patients differed from nonMI-SLE patients through lower plasma albumin levels (35 (29-37) versus 40 (37-42) g/L; p=0.002) and longer disease duration (22 (14-32) versus 14 (6.3-24) years; p=0.038).

Conclusion: We demonstrate that non-procedural MIs in SLE are in 88% of cases associated with significant coronary atherosclerosis. Increased prevalence of CAD prior MI and higher number of coronary arteries involved at MI, suggest accelerated coronary atherosclerosis in SLE patients. This calls for attentive surveillance of CVD and early atheroprotective treatment in this patients group.

REFERENCES:

[1] Hak AE et al. Systemic lupus erythematosus and the risk of cardiovascular disease: Results from the nurses' health study. Arthritis and rheumatism 2009;61:1396-402.

[2] Fischer LM et. Effect of rheumatoid arthritis or systemic lupus erythematosus on the risk of first-time acute myocardial infarction. The American journal of cardiology 2004;93:198-200.

Table 1. MI characteristics

	MI-SLE	N_{total}	MI-nonSLE	N_{total}	P-value
ECG findings	23 (72%)	32	21 (66%)	32	1.0
NSTEMI					
STEMI	9 (28%)	32	11 (34%)	32	
Presence of atherosclerosis					
0-VD	3 (12%)	26	10 (35%)	29	0.065
MI-CAD (≥1-VD)	23 (88%)	26	19 (66%)	29	
Number of involved arteries					
0-VD	3 (12%)	26	10 (35%)	29	0.038
1-VD	13 (50%)	26	9 (31%)	29	
≥2-VD	10 (39%)	26	10 (35%)	29	
Involvement of specific arteries	3 (12%)	26	0 (0%)	29	0.50
LMCA					
LAD	19 (73%)	26	17 (59%)	29	0.11
RCA	7 (27%)	26	9 (31%)	29	0.75
Cx	6 (23%)	26	6 (21%)	29	1.0
Left ventricular ejection fraction					
<50%	13 (45%)	29	12 (36%)	33	0.79
≥50%	16 (55%)	29	21 (64%)	33	

0-VD = 0-Vessel disease. 1-VD = 1-Vessel disease. 2-VD = 2-Vessel disease. Cx = Circumflex artery. LAD = Left anterior descending artery. LMCA = Left main coronary artery. MI-CAD = MI with coronary artery disease. NSTEMI = Non-ST-elevation MI. RCA = Right coronary artery. STEMI = ST-elevation MI.

Disclosure of Interests: Isak Samuelsson: None declared, Ioannis Parodis Grant/research support from: The author declare that he has no conflict of interest related to this work, Iva Gunnarsson Grant/research support from: The author declare that she has no conflict of interest related to this work, Agneta Zickert: None declared, Claes Hofman-Bang: None declared, Håkan Wallén Grant/research support from: The author declare that he has no conflict of interest related to this work, Elisabet Svenungsson Grant/research support from: The author declare that she has no conflict of interest related to this work

DOI: 10.1136/annrheumdis-2021-eular.3547

POS0780 SKIN LESIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

A. Shumilova[1], F. Cheldieva[2,3], T. Reshetnyak[2,3], A. Lila[3,4]. *[1]V.A. Nasonova Research Institute of Rheumatology, 4th Department of Rheumatology, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Vascular Rheumatology Department, Moscow, Russian Federation*; *[3]Russian Medical Academy of Continuing Professional Education, Department of Rheumatology, Moscow, Russian Federation*; *[4]V.A. Nasonova Research Institute of Rheumatology, Head of the Institute, Moscow, Russian Federation*

Background: In more than 40% of cases, systemic lupus erythematosus (SLE) is associated with the presence of highly positive antiphospholipid antibodies, with 50-70% of patients developing antiphospholipid syndrome (APS) over the next 10 years of the disease. Both diseases have similar and different clinical manifestations of skin lesions. The variety of skin lesions in SLE and APS requires a differential diagnosis and can make it difficult to diagnose a systemic autoimmune disease in a timely manner.

Objectives: To study the frequency of skin manifestations in SLE and APS, depending on the positivity of aPL.

Methods: The study included 116 patients with SLE (104 women and 12 men), mean age 37.9±12.9, disease duration 8.5 [1.15-13.0]; 40 patients with APS (33 women and 7 men), mean age 36.2±9.39. All patients were evaluated for skin lesions, and patients with APS were determined by IgG/IgM-aCL and IgG/IgM-aß2HP1 by enzyme immunoassay (ELISA), 19 of them were determined by IgA-aCL, IgA-aß2HP1 and IgG-aß2HP1-D1 chemiluminescence analysis (CMA).

Results: Acute skin lesions in past history were noted in 58 (50%) patients, chronic lesions -I n 21 (18.1%) patients; photosensivity and alopecia were indicated in 46 (39.6%) patients, mucosal lesions were noted in 36 (31%) of 116 patients, which corresponds to the literature data on the frequency of skin lesions and its appendages in SLE. At the time of inclusion in the study, skin lesions were detected in 20 patients. Score according to the CLASI index in patients with skin lesions: activity index=1.55 [0-22]; damage index=1.81 [0-36].

Skin lesions are the second most common signs of SLE onset (debut in 26 (22.4%) patients), second only to arthritis (38 (32.5%) patients), while the

detection of immunological disorders (highly positive ab to dsDNA) was observed in 7 patients (6%) with reliable APS and probable SLE, who may not have had time to develop a clinic for reliable SLE.
Livedo, as one of the most frequent skin manifestations of APS, was detected in 60 patients and was significantly associated with IgM-aCL and IgM-aß2HP1 positivity (p<0.0001). Significantly, positivity for IgG-aCL, IgG-aß2HP1 and IgG-aß2HP1-D1 (p=0.0001) and IgA-aCL (p=0.008) was associated with the development of comminuted hemorrhages, which occurred in 7 patients with APS and was associated with positivity of IgG-aCL, IgG-aß2HP1, IgG-aß2HP1-D1 (p=0.0001) and IgA-aCL (p=0.008).
The development of ulcerative-necrotic vasculitis with deep skin necrosis was observed in 3 patients, 2 of them were highly positive for IgG-aCL, IgG-aß2HP1, IgG-aß2HP1-D1. Melanoma was detected in the past history in 2 patients with highly positive for IgG-aCL, which is not a manifestation of the underlying disease, but confirms an increased risk of malignancy with aPL-positivity.
Conclusion: More than half of the patients had acute skin lesions, and about a quarter of the cases had skin lesions at the onset of the disease. The presence of comminuted hemorrhages was associated with positivity of IgG-aCL, IgG-aß2HP1, IgG-aß2HP1-D1) and IgA-aCL. Assessment of skin activity and damage (in particular, according to the CLASI index) is necessary for a comprehensive analysis of the dynamics of the disease and the response to therapy. The detection of aPL is necessary not only for the purpose of predicting thrombotic catastrophes, but also for the development of skin manifestations of APS.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3548

POS0781 PERFORMANCE OF MAJOR SALIVARY GLAND ULTRASOUND FOR THE DIAGNOSIS OF SJÖGREN'S SYNDROME IN CLINICAL PRACTICE

M. C. Tenazinha[1,2], V. C. Romão[1,2,3], J. Polido-Pereira[1,2,4], N. Khmelinskii[1,2], R. Barros[1], F. M. Diamantino Saraiva[1,2], J. E. Fonseca[1,2,3,4]. *[1]Hospital de Santa Maria, Rheumatology and Metabolic Bone Diseases, Lisboa, Portugal*; *[2]Instituto de Medicina Molecular (IMM), João Eurico Fonseca Lab, Lisboa, Portugal*; *[3]Faculty of Medicine, University of Lisbon, Clinical Semiotics Institute, Lisboa, Portugal*; *[4]Faculty of Medicine, University of Lisbon, Rheumatology, Lisboa, Portugal*

Background: There is no specific test to diagnose Sjögren's Syndrome (SS) although available classification criteria intended for research purposes help guide the diagnosis. Major salivary gland ultrasound (MSGUS) may contribute to SS diagnosis.
Objectives: To study the performance of MSGUS for the clinical diagnosis of SS and its relationship with other relevant markers of disease.
Methods: We included patients with a clinical suspicion of SS that underwent MSGUS evaluation at our Department. Parotid and submandibular glands were classified bedside on a 0-4 scale, based on tissue inhomogeneity. The score of the highest graded gland was considered and a score ≥2 was defined as a positive MSGUS. Minor salivary gland biopsy (mSGB) was considered positive if a focus score ≥1 was reported. We compared MSGUS findings across diagnoses and against mSGB result and anti-SSA status. Categorical variables were compared using the chi-square test. Continuous variables were compared using Student's t-test, Mann-Whitney U test, or ANOVA. P-value was considered significant at <0.05.
Results: A total of 219 patients were included (Table 1). MSGUS was positive in a higher proportion of patients with primary and secondary SS, in comparison to non-Sjögren's sicca syndrome (nSSS) and undifferentiated connective tissue disease (UCTD; p<0.001). Mean MSGUS score was higher in SS patients in comparison to nSSS and UCTD (p<0.001). A positive MSGUS was associated with anti-SSA positivity (61.4% vs 38.6% in anti-SSA negative patients; p<0,001). Patients positive for anti-SSA had a higher mean MSGUS score (2.12 ± 1.03) in comparison with anti-SSA negative patients (1.31 ± 0.97, p<0.001). While MSGUS and mSGB were not significantly associated (p=0.237), the mean MSGUS score was higher in patients with a positive mSGB (1.95 ± 1.17) in comparison with those with a negative mSGB (1.61 ± 0.99; p=0.027).

Table 1. General sample characteristics

	Overall (n=219)	pSS (n=131)	sSS (n=17)	nSSS (n=62)	UCTD (n=9)	p-value
Age, years (mean ± sd)	60 ± 14	58 ± 17	56 ± 19	60 ± 13	48 ± 16	0.07
Female, n (%)	210 (95.9)	127 (97.0)	15 (88.2)	59 (95.2)	9 (100)	<0.001
Anti-SSA positive, n (%)	105 (47.9)	91 (69.5)	10 (5.8)	3 (4.8)	1 (11.1)	<0.001
Positive mSGB, n (%)	85 (46.4)	69 (63.3)	7 (46.7)	8 (15.7)	1 (12.5)	<0.001
MSGUS score, mean ± sd	1.70 ± 1.09	1.98 ± 1.09	1.76 ± 1.11	1.13 ± 1.09	1.44 ± 1.12	<0.001
Grade 0, n (%)	35 (16.0)	17 (13.0)	3 (17.7)	15 (24.2)	0 (0.0)	<0.001
Grade 1, n (%)	62 (28.3)	25 (19.1)	4 (23.5)	27 (43.6)	6 (66.7)	
Grade 2, n (%)	62 (28.3)	39 (29.8)	4 (23.5)	17 (27.5)	2 (22.2)	
Grade 3, n (%)	54 (24.7)	44 (33.6)	6 (35.3)	3 (4.9)	1 (11.1)	
Grade 4, n (%)	6 (2.7)	6 (4.6)	0 (0.0)	0 (0.0)	0 (0.0)	
MSGUS score ≥ 2, n (%)	122 (55.7)	89 (67.9)	10 (58.8)	20 (32.3)	3 (33.3)	<0.001

Conclusion: MSGUS is a valuable resource in the investigation of SS. It is associated with clinical diagnosis, anti-SSA and MSGB findings. Together with these other complementary exams, it can be used to assist in the diagnosis of patients presenting with sicca features suggestive of SS.
REFERENCES:
[1] Jousse-Joulin S, Milic V, Jonsson MV, Plagou A, Theander E, Luciano N, et al. Is salivary gland ultrasonography a useful tool in Sjögren's syndrome? A systematic review. Rheumatology (Oxford). 2016 May;55(5):789–800.
[2] Zhou M, Song S, Wu S, Duan T, Chen L, Ye J, et al. Diagnostic accuracy of salivary gland ultrasonography with different scoring systems in Sjögren's syndrome: a systematic review and meta-analysis. Sci Rep. 2018 Dec;8(1):17128.
[3] Cornec D, Jousse-Joulin S, Pers J-O, Marhadour T, Cochener B, Boisramé-Gastrin S, et al. Contribution of salivary gland ultrasonography to the diagnosis of Sjögren's syndrome: toward new diagnostic criteria? Arthritis Rheum. 2013 Jan;65(1):216–25.
Disclosure of Interests: Maria Catarina Tenazinha: None declared, Vasco C Romão: None declared, Joaquim Polido-Pereira: None declared, Nikita Khmelinskii Speakers bureau: GSK, Rita Barros: None declared, FERNANDO MANUEL DIAMANTINO SARAIVA: None declared, Joao Eurico Fonseca: None declared
DOI: 10.1136/annrheumdis-2021-eular.3597

POS0782 FOLLICULAR DENDRITIC CELL NETWORKS IN MINOR SALIVARY GLAND BIOPSIES: A MARKER OF DISEASE ACTIVITY AT BASELINE AND DURING THE FOLLOW-UP IN SJÖGREN'S SYNDROME

C. Baldini[1], F. Ferro[1], G. Fulvio[1], G. La Rocca[1], S. Fonzetti[1], G. Governato[1], M. De Francesco[1], M. Mosca[1], R. Izzetti[2], V. Donati[3]. *[1]University of Pisa, Rheumatology Unit, Clinical and Experimental Medicine, Pisa, Italy*; *[2]University of Pisa, Unit of Dentistry and Oral surgery, Surgical, Medical and Molecular Pathology and Critical Care Medicine, Pisa, Italy*; *[3]Unit of Pathological Anatomy 2, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy*

Background: Minor salivary gland biopsy (MSGB) has been increasingly recognized as an important tool for the stratification of patients with primary Sjögren's syndrome (pSS). Recently, the presence of follicular dendritic cell (FDC) networks in the inflammatory infiltrate has been associated with more severe biological and serological abnormalities compared with less organized infiltrates.
Objectives: To investigate the associations between the presence and number of FDC networks in foci and pSS glandular and extra-glandular disease activity at baseline and during the follow-up.
Methods: Consecutive MSGBs performed in daily practice for clinically suspected pSS from January 2017 to October 2020 were reviewed. Patients' demographic, clinical, biological and serological data were obtained from medical records. The ESSDAI was used to measure disease activity at baseline and at the end of the follow-up in pSS patients. For histopathology, 3 µm sections were cut from each formalin-fixed paraffin-embedded block of MSGBs and stained with haematoxylin and eosin (H&E). Immunohistochemical stainings were performed on additional 3 µm sections in order to detect T lymphocytes (CD3), B lymphocytes (CD20) and follicular dendritic cells (CD21). Glandular tissue areas, number of foci, focus score (FS) and the presence and number of FDC networks were assessed.
Results: We reviewed 330 consecutive MSGBs from patients with suspected pSS: out of them 146/330 (44%) were classified as nonspecific chronic sialadenitis (NSCS) whereas 184/330 (56%) as focal lymphocytic sialadenitis (FLS). According to the ACR/EULAR criteria the diagnosis of pSS was confirmed in 130 patients (117 F:13 M, age 56±13 yrs). The mean (S.D) surface area of the MSGBs was 7.8 (3.9) mm^2. The number of foci in the FLS samples ranged from 1 to 12 (mean (S.D)=3.1 (2.6)), whereas the FS ranged from 0.3 to 9.0 (mean (S.D) = 1.4 (1.2)).The presence of FDC networks was documented in 106/330 (32%) of the samples; in 54/106 (51%) of these MSGBs the number of FDC networks ranged from 2 to 8 (mean (S.D)=3.1 (1.4)). The number of FDC networks significantly correlated with the number of foci (r=0.721**) and FS (r=0.707**). Patients with FDC networks in the inflammatory infiltrate presented more serological abnormalities (i.e anti-Ro/SSA, anti-LA/SSB, Rheumatoid factor) and elevated IgG levels (p<0.001). In pSS patients, the number of FDC networks slightly correlated also with C4 levels (r=-0.216*), peripheral lymphocyte count (r=-0.274**) and with glandular (r=0.213*), and biological (r=0.230**) domains of the ESSDAI at baseline. After a mean (S.D) follow-up of 21(13) months, the number of FDC networks still correlated with the final total ESSDAI (r=0.312**).
Conclusion: The presence and number of FDC networks in foci represent a useful histopathological parameter able to reflect disease activity at baseline and during the follow-up, thus allowing more personalized interventions.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3620

POS0783

LUPUS NEPHRITIS: HISTOLOGICAL FEATURES AND LONG TERM OUTCOMES IN A LARGE SINGLE-CENTRE COHORT

A. I. Celia[1], F. R. Spinelli[1], C. Garufi[1], S. Truglia[1], V. A. Pacucci[1], F. Ceccarelli[1], C. Pirone[1], F. Natalucci[1], M. Speziali[1], C. Alessandri[1], F. Conti[1]. [1]*Department of Clinical Internal, Anaesthesiological and Cardiovascular Sciences, Sapienza University, Rome, Italy*

Background: In Systemic Lupus Erythematosus (SLE) patients the incidence of lupus nephritis (LN) is about 40% [(1)]. The rate of progression to end stage renal disease (ESRD) is 4.3-10.1% [(2)] and renal involvement is a strong predictor of morbidity and mortality.
Objectives: To describe clinical, histological features and renal outcomes of LN patients included in our single-center registry reporting data from more than 30 years. Moreover, we examined the correlation between clinical features at LN diagnosis and therapeutic lines used during the course of a 24 years follow-up.
Methods: A total of 71 patients were diagnosed with LN from 1989 to 2020. Demographic features and laboratory abnormalities (serum creatinine, 24 hours urine protein, urinary sediment, ds-DNA) at the time of LN diagnosis and at last available follow-up, were evaluated. We also examined renal biopsy performed and the histological classes (proliferative vs non-proliferative). We considered the increase number of therapeutic lines adopted as a negative prognostic factor in response to therapy.
Mean (SD) or median (IQR) were used according the variable distribution. T-test and Chi square and Mann-Whitney were used and p-value <0.05 were considered significant.
Results: Among 71 patients with LN, 63 (88.7%) were females and 8 (11.3%) males, with a F/M ratio of 6. Median SLE duration was 180 (162) months. The median age at the onset of nephritis was 28 (19.5) years and occurred in median after 12 (60) months from SLE diagnosis.
Sixty patients underwent a biopsy: the histology showed class III or IV proliferative glomerulonephritis in 49 patients (81.6%) and a non-proliferative class in 11 (18.3%) (p< 0.0001). Median serum creatinine value, 24 hours urine protein, urinary sediment, anti-ds-DNA at LN onset are reported in Table 1. Induction therapy was performed with cyclofosfamide in 14.5% of cases, mycophenolate in 21.1%, rituximab in 1.3%, cyclosporine A in 1.9% and azathioprine in 4.6%. The lines of therapies adopted during the follow-up ranged between a minimum of 0 and a maximum of 6 lines with a median value of 1.
Overall, the median follow-up was 180 (111) months and 30 (21.3%) patients had at least 120 months of follow-up. Median serum creatinine value, 24 hours urine protein, urinary sediment and eGFR last available follow-up are reported in Table 1. Three patients underwent dialysis and 3 kidney transplantation.
Eight patients underwent a re-biopsy: 7 (87.5%) had a proliferative class and 1 (12.5%) had a membranous class (p=0.01). Median serum creatinine value, 24 hours urine protein, urinary sediment at re-biopsy are reported in Table 1. In re-bioptized subgroup patients, induction therapies were cyclofosfamide in 50% of cases, mycophenolate in 12.5%, cyclosporine A in 25% and azathioprine in 12.5%. There were not statistically significant differences among the age on LN onset, the time from renal onset to the onset of the disease and the number of therapeutic lines adopted (Figure 1).
Conclusion: Among patients with LN the proliferative classes are the most common. At the 15-year follow-up 2,1% had renal transplantation and 2,1% dyalisis. We did not detect any association between age at diagnosis, time from renal impairment and the number of therapeutic lines.
REFERENCES:
[1] Fanouriakis A et al. Update EULAR/ERA–EDTA recommendations for the management of lupus nephritis. Ann Rheum Dis 2019.
[2] Hanly JG et al. The frequency and outcome of lupus nephritis: results from an international inception cohort study. Rheumatology 2016.

Table 1. Laboratory features in SLE patients at LN onset, at last available follow-up and in re-bioptized patients.

	LN onset (n 71)	AFTER 10 years long FOLLOW-UP (n 30)	P value	Re-bioptized patients (n 8)
Serum creatinine (mg/dl)	0.81 (+/- 0.4)	0.87 (+/- 0.60)	0,07	1.05 (0.45)
24 hours urine protein (mg/24h)	3000 (+/- 3707)	330 (+/- 793)	<0,00001	5068 (2392)
Active urinary sediment	64 patients (45,44%)	2 patients (6.66%)	<0,00001	8 patients (100%)
Anti-ds-DNA + eGFR <50ml/h	30 patients	12 patients (3.6%)		

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3710

POS0784

AUDIOLOGIC EVALUATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AND IMPACT OF HYDROXYCHLOROQUINE THERAPY

S. Tharwat[1], W. Elshawaf[2], M. K. Nassar[3]. [1]*Mansoura University, Internal Medicine, Rheumatology & Immunology, Mansoura, Egypt*; [2]*Mansoura University, Audiology Unit, ORL Department, Mansoura, Egypt*; [3]*Mansoura University, Mansoura University Nephrology and Dialysis Unit, Internal Medicine Department, Mansoura, Egypt*

Background: Hydroxychloroquine (HCQ) is a commonly used agent in the treatment of rheumatic diseases including systemic lupus erythematosus (SLE). **[1]**
Objectives: The aim of this study was to evaluate the hearing function in SLE patients and assess the impact of chronic HCQ.
Methods: This study was carried out on 60 individuals (48 SLE and 12 healthy controls). The SLE patients were divided into HCQ group (n=36) and non-HCQ group (n=12) according to the chronic administration of HCQ. All participants were assessed by full audiological history and extended high frequency audiometry at frequencies 9, 10, 11, 2, 12.5, 14, 16,18 and 20 KHz.
Results: When comparing the study SLE patients with healthy controls,there was a statistically significant difference regarding patient reported otological manifestations such as tinnitus (p=.021), vertigo (p=.002) and hearing impairment (p=.042) while there was no significant difference regarding deafness or ear buzzing in one or both ears. HCQ group showed more hearing impairment at frequency 9000 and 20000 Hz than non-HCQ group (p=.004, <.001 respectively).
Conclusion: Otological symptoms and sensorineural hearing loss are prevalent among SLE patients. Chronic administration of HCQ may have an ototoxic effect.
REFERENCES:
[1] Fiehn, C., et al. "Safety management in treatment with antimalarials in rheumatology. Interdisciplinary recommendations on the basis of a systematic literature review." *Zeitschrift für Rheumatologie* (2020): 1-9.

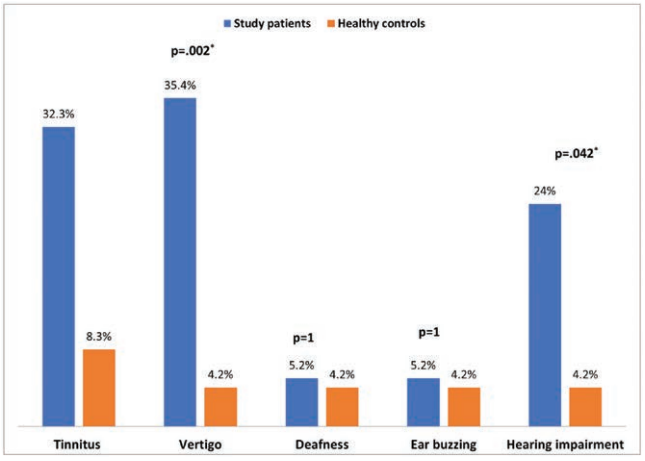


Figure 1. Otological manifestations in the study SLE patients (n=48) and the healthy controls (n=12)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3742

POS0785

CHANGING EXPRESSION PROFILES OF LONG NONCODING RNAS, MIRNAS, MRNAS AND CIRCULAR RNAS IN LABIAL SALIVARY GLANDS OF PRIMARY SJÖGREN'S SYNDROME (PSS)

G. Feng[1], L. Huang[2], J. Ji[3], C. Dong[3], Y. Xia[3], C. Cheng[4], Z. Gu[3]. [1]*Affiliated Hospital of Nantong University, Department of Stomatology, Nantong, China*; [2]*Affiliated Hospital of Nantong University, Department of Critical Care Medicine, Nantong, China*; [3]*Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*; [4]*Nantong University, Jiangsu Province Key Laboratory for Inflammation and Molecular Drug Target, Nantong, China*

Background: Primary Sjögren's syndrome (pSS) is a relatively common autoimmune disease characterized by oral and ocular dryness. An increasing number of studies have revealed that long non-coding RNA (lncRNA), miRNA, mRNA and circular RNA (circRNA) contributes to the pathogenesis of autoimmune diseases.
Objectives: To explore lncRNA, miRNA, mRNA and circRNA expression profiles in labial salivary glands (LSGs) in pSS patients and their biological functions in the regulation of pSS.
Methods: The expression of 75,550 lncRNAs, 2,318 miRNA, 20,292 mRNAs and 6,877 circRNAs were determined in the LSG of six pSS patients and six healthy controls using microarray experiments. Validation was performed in pSS patients and controls using real-time PCR. LncRNA-mRNA co-expression and gene-pathway networks were constructed using bioinformatics software.
Results: A total of 599 lncRNAs (upregulated: 279, downregulated: 320), 78 miRNAs (upregulated: 26, downregulated: 52), 615 mRNAs (upregulated: 590, downregulated: 25) and 160 mRNAs (upregulated: 110, downregulated: 50) were differentially expressed in the LSGs of pSS patients. Five of these lncRNAs were validated using real-time PCR. lncRNA HCP5, lncRNA SNHG5, lncRNA IFI44L, lncRNA CMPK2 were significantly upregulated and lncRNA TTYH1 were downregulated in pSS. GO

and KEGG biological pathway analysis were performed to predict the functions of differentially expressed lncRNAs and co-expressed potential targeting genes. Subsequently, a ceRNA (lncRNA-miRNA-mRNA) network including 2320 ceRNA pairs was constructed based on predicted miRNAs shared by lncRNAs and mRNAs.
Conclusion: The expression profile provided a systematic perspective on the potential functions of lncRNAs miRNAs, mRNAs and circRNAs in the pathogenesis of pSS. Therefore, this study will aid in the development of new diagnostic biomarkers and drug therapies.
REFERENCES:
[1] Le Dantec C, Varin MM, Brooks WH, Pers JO, Youinou P, Renaudineau Y. Epigenetics and Sjogren's syndrome.Curr Pharm Biotechnol. 2012 Aug;13(10):2046-53.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3784

POS0786 UNMET TREATMENT NEEDS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A CROSS-SECTIONAL ASSESSMENT OF DISEASE ACTIVITY IN SLE PATIENTS DURING THEIR LAST VISIT

O. Gioti[1], K. Chavatza[2], G. Belevonis[1], S. Koutsoviti[1], C. Katsimpari[1], I. Sofianos[1], A. Tatsi[1], P. Tzanis[1], A. Lazarini[1], K. Klavdianou[1], I. Giannakopoulou[1], E. Kalavri[1], E. Theotikos[1], A. Elezoglou[1], D. Boumpas[2], A. Fanouriakis[1,2]. [1]*"Asklepieio" General Hospital, Department of Rheumatology, Athens, Greece*; [2]*"Attikon" University Hospital, Rheumatology and Clinical Immunology Unit, Athens, Greece*

Background: The current goal of treatment in SLE is remission or low disease activity (LDA) and prevention of flares, achieved with the lowest possible dose of glucocorticoids. Nevertheless, in current clinical practice a significant number of patients still has active disease.[1,2]
Objectives: To assess the current disease activity state of SLE patients during their most recent visit in two centers (Department of Rheumatology in "Asklepieio" Hospital and Rheumatology Unit in "Attikon" Hospital, both in Athens, Greece).
Methods: Cross-sectional study of patients with a diagnosis of SLE for at least one year. Patients were divided into four groups: 1) *Remission off-therapy*: SLE Disease Activity Index (SLEDAI)=0 without prednisone or immunosuppressive drugs (IS), 2) *Remission on-therapy:* SLEDAI=0, prednisone dose ≤5mg/day and/or IS (conventional and biologic, maintenance phase), 3) *LDA*: SLEDAI ≤4, prednisone dose ≤7.5mg/day and/or IS (maintenance phase), 4) *Active disease*: SLEDAI >4 and/or prednisone dose >7.5mg/day and/or IS (induction phase).[2] Hydroxychloroquine was allowed in all groups.
Results: 205 patients were included [95.1% female, mean (SD) age 48.4 (14.9) years and median disease duration (IQR) 6.2 (12.6) years]. A history of lupus nephritis and neuropsychiatric SLE was present in 16.6% and 17.1% of our patients, respectively, and 39% of patients had SLICC/ACR damage index (SDI) > 0. At last visit, remission off-therapy and remission on-therapy was present in 8.3% (n=17) and 15.1% (n=31) of our patients, respectively. Seventy-five patients (36.6%) had LDA, whereas 82 patients (40%) had active disease. More than 85% (86.3%) of patients were in treatment with hydroxychloroquine and 64.4% were receiving immunosuppressive drugs. Regarding glucocorticoids, 50.2% (n=103) were treated with prednisone dose ≤7.5mg/day and over 40% (42.4%, n=87) did not receive prednisone at all. A SLEDAI score 0 and 1-4 was achieved in 24.4% and 42.9% of patients, respectively, but only 3.9% had a SLEDAI > 8, indicative of high disease activity.
Conclusion: Although the majority of our patients were treated with hydroxychloroquine and glucocorticoids in acceptable levels of daily dose, four out of ten patients in our practice have active disease during their last visit. Achieving treatment goals in SLE patients remains a challenge for future novel therapies.
REFERENCES:
[1] Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. *Ann Rheum Dis* 2019; 78: 736–745.
[2] Ugarte-Gil MF, Wojdyla D, Pons-Estel GJ, et al. Remission and Low Disease Activity Status (LDAS) protect lupus patients from damage occurrence: data from a multiethnic, multinational Latin American Lupus Cohort (GLADEL). *Ann Rheum Dis* 2017; 76: 2071–2074.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3832

POS0787 BERBERINE MODULATE LUPUS SYNDROME VIA THE REGULATION OF GUT MICROBIOTA IN MRL/LPR MICE

Y. Bao[1], J. Ji[1], Z. Xue[2], Z. Gu[1]. [1]*Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*; [2]*Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China*

Background: Intestinal flora disorder and immune abnormalities have been reported in systemic lupus erythematosus (SLE) patients[1,2]. Berberine (BBR) showed significant effects in regulating the intestinal flora, repairing gut barriers and regulating immune cells[3,4]. While few reports mentioned the abnormal gut microbiota and metabolites in Chinese SLE patients.
Objectives: Our investigation tried to illustrate the relationship between gut microbiota, intestinal metabolites and disease activity in Chinese SLE patients. And the effect of BBR to intestinal dysbacteriosis, multiple organ damages and over-activated immune system in MRL/Lpr mice.
Methods: 16S high-throughput (16S rRNA) sequence, qRT-PCR and gas chromatography technology were used to determine the gut microbiota and metabolites in 104 SLE patients from Affiliated Hospital of Nantong University, China. BBR was orally treated to the MRL/Lpr mice in low, medium and high doses. After 6 weeks treatment, mice were sacrificed. Serum, faeces and organs were collected for further studies.
Results: Chinese SLE patients showed higher abundance of *Bacteroidetes* and lower abundance of *Firmcutes*. The results of qRT-PCR showed high *Firmcutes*/*Bacteroidetes* (F/B) ratio of SLE patients. The F/B ratio was negative correlated with SLE disease activity index (SLEDA) score. Almost all the tested short-chain fatty acids (SCFAs) found statistically significant results in SLE and LN (lupus nephritis) patients, especially the propanoic acid and butyric. BBR altered the relative abundance of *Bacteroides* and *Verrucomicrobia* and the butyric acid content in colon of MRL/Lpr mice. The increase of tight junction protein also indicated the gut barrier was repaired by BBR. Treg and Tfr cells in spleen and mesenteric lymph node (MLN) were increased. These results revealed a positive therapeutic effect of berberine on SLE from gut microbiota to immune status.
Conclusion: Our study highlights current status of intestinal dysbacteriosis in Chinese patients with SLE and differences in intestinal metabolites among patients with different disease states. The regulation of intestinal flora and the repairment of gut barrier by intestinal metabolites in BBR treated mice seemed to be the factor that directed the immune responses and disease outcomes. The ultimate goal of our study was to determine the beneficial effects of regulating the gut microbiota on the treatment of SLE. The application of berberine is a relatively safe and convenient way. In the coming investigations, we plan to focus on the study of berberine and its metabolites on intestinal function and systemic immunity.
REFERENCES:
[1] Guo, M. *et al.* Alteration in gut microbiota is associated with dysregulation of cytokines and glucocorticoid therapy in systemic lupus erythematosus. *Gut microbes* **11**, 1758-1773, doi:10.1080/19490976.2020.1768644 (2020).
[2] Mu, Q. *et al.* Control of lupus nephritis by changes of gut microbiota. *Microbiome* **5**, 73, doi:10.1186/s40168-017-0300-8 (2017).
[3] Habtemariam, S. Berberine pharmacology and the gut microbiota: A hidden therapeutic link. *Pharmacological research* **155**, 104722, doi:10.1016/j.phrs.2020.104722 (2020).
[4] Cui, H. *et al.* Berberine Regulates Treg/Th17 Balance to Treat Ulcerative Colitis Through Modulating the Gut Microbiota in the Colon. *Frontiers in pharmacology* **9**, 571, doi:10.3389/fphar.2018.00571 (2018).

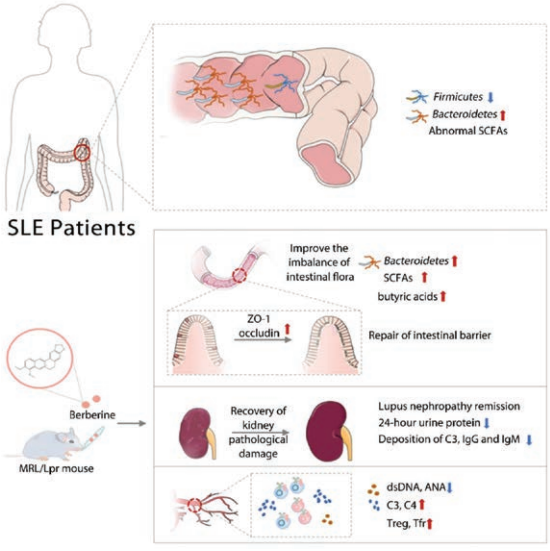


Figure 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3838

POS0788 CIRCULATING EXOSOMES PROMOTE LUPUS NEPHRITIS IN MRL-LPR MICE

X. Sha[1], X. Ge[1], Y. Jin[1], T. Chen[1], X. Ni[1], W. Zheng[2], J. Ji[1], Z. Gu[1]. [1]*Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*; [2]*Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China*

Background: Systemic Lupus Erythematosus (SLE) is a prototypic autoimmune disease that characterized by the loss of self-tolerance and the production of autoantibodies (autoAbs) [1, 2]. Lupus nephritis (LN), the severe organ-threatening manifestations of SLE, could cause massive damage to patients[3, 4]. Currently, some exosomal microRNAs (miRNAs) are considered as potential biomarkers in SLE. However, the role of exosomal miRNAs in Lupus Nephritis (LN) remains unclear.
Objectives: The purpose of this study was to investigate molecular mechanism of plasma exosomal miRNAs in the development of Lupus Nephritis.
Methods: Circulating exosomes were isolated from plasma of patients with LN, SLE without LN (NLN). Plasma exosomes were authenticated by Western Blot, Nanosight Tracking Analysis (NTA) and transmission electron microscopy (TEM). Fluorescence microscopy of co-cultured plasma exosomes and podocytes demonstrated that exosomes were uptaken into podocytes. Moreover, cell apoptosis and the inflammation factors was assessed using Western Blot. We analyzed the expression profiles of miRNAs in LN and NLN exosomes and the expression profiles of mRNAs of podocytes stimulated with LN and NLN exosomes with the help of next generation sequencing (NGS).
Results: We demonstrate that exosomes derived from LN plasma could be taken by neighboring podocytes and promote the apoptosis of podocytes and the expression of inflammation factors. In addition, the sequencing found that miRNAs were differentially expressed in LN and NLN exosomes and mRNAs were differentially expressed in podocytes stimulated with LN and NLN exosomes.
Conclusion: LN plasma exosomes have a potency to stimulate the apoptosis of podocytes and the expression of inflammation factors. Moreover, differentially expressed miRNAs in exosomes play a potential role in the development of LN.
REFERENCES:
[1] T. Colasanti, A. Maselli, F. Conti, M. Sanchez, C. Alessandri, C. Barbati, D. Vacirca, A. Tinari, F. Chiarotti, A. Giovannetti, F. Franconi, G. Valesini, W. Malorni, M. Pierdominici, E. Ortona, Autoantibodies to estrogen receptor α interfere with T lymphocyte homeostasis and are associated with disease activity in systemic lupus erythematosus, Arthritis and rheumatism, 64 (2012) 778-787.
[2]H.A. Al-Shobaili, A.A. Al Robaee, A.A. Alzolibani, Z. Rasheed, Antibodies against 4-hydroxy-2-nonenal modified epitopes recognized chromatin and its oxidized forms: role of chromatin, oxidized forms of chromatin and 4-hydroxy-2-nonenal modified epitopes in the etiopathogenesis of SLE, Disease markers, 33 (2012) 19-34.
[3]A. Kaul, C. Gordon, M.K. Crow, Z. Touma, M.B. Urowitz, R. van Vollenhoven, G. Ruiz-Irastorza, G. Hughes, Systemic lupus erythematosus, Nat Rev Dis Primers, 2 (2016) 16039.
[4]M.G. Tektonidou, A. Dasgupta, M.M. Ward, Risk of End-Stage Renal Disease in Patients With Lupus Nephritis, 1971-2015: A Systematic Review and Bayesian Meta-Analysis, Arthritis & rheumatology (Hoboken, N.J.), 68 (2016) 1432-1441.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3904

POS0789

APPLICATION OF THE NEW ACR/EULAR 2019 CLASSIFICATION CRITERIA OF SYSTEMIC LUPUS ERYTHEMATOSUS TO A INCEPTION, MONOCENTRIC COHORT OF UNDIFFERENTIATED CONNECTIVE TISSUE DISEASES POPULATION AT ONSET OF THE DISEASE

E. Elefante[1,2], A. Parma[1], V. Nannipieri[1], V. Signorini[3], C. Stagnaro[3], D. Zucchi[3], L. Carli[3], F. Ferro[3], C. Tani[3], M. Mosca[3]. *[1]University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy*; *[2] University of Siena, Department of Medical Biotechnology, Siena, Italy*; *[1]University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy*

Background: undifferentiated connective tissue diseases (UCTDs) are a group of systemic autoimmune diseases that share clinical and serological manifestations with definite connective tissue diseases (CTDs), but do not satisfy existing classification criteria[1]. Within this group, it is possible to identify very heterogeneous conditions: transitory and self-limiting forms, stable conditions over time and forms that will evolve towards definite CTDs, in particular Systemic Lupus Erythematosus (SLE). The availability of new classification criteria for CTDs could be useful in identifying major CTDs from their onset and help in the differentiation from stable UCTDs, which will maintain their undifferentiated profile over time.
Objectives: the aim of this study was to apply the new ACR/EULAR 2019 classification criteria of SLE[2] to patients included, at the onset of UCTD, to evaluate how many patients could be re-classified as SLE.
Methods: this is a retrospective observational study that enrolls patients who received the diagnosis of UCTD at the Rheumatology Unit of Pisa, according to the classification criteria proposed by Mosca et al[1], and were then regularly followed in the same clinic (inception cohort). For each patient, demographics, comorbidities, treatment, clinical and serological data were collected, at baseline and during follow-up. The new ACR/EULAR 2019 classification criteria of SLE were applied to the inception cohort at the onset of the disease. The characteristics of patients re-classified as SLE according to the new classification criteria and those of patients who "remained" classified as UCTD were compared.
Results: we enrolled 202 patients with a diagnosis of UCTD, mainly female (F:M 193:9) and of Caucasian ethnicity (97.5%), mean age at the diagnosis 38,5 ± 13,2 years and a median follow-up of 5 years (IQR 2-10).
During the follow-up, 10 patients (4.9%) in our cohort developed clinical and serological characteristics that led to a diagnosis of a definite CTD, in particular: 7 SLE, 2 Mixed Connective Tissue Disease (MCTD) and 1 Sjogren's syndrome.
Applying the ACR/EULAR 2019 classification criteria of SLE to patients enrolled at the onset of the disease, 38/202 (18.8%) would have been classified as SLE (with a median score of 12 (IQR 11-15)) on the basis of the presenting clinical and serological manifestations. Interestingly, 6/7 patients who received a diagnosis of SLE during the follow-up were among these 38 patients.
Among the items of the new classification criteria of SLE, the most frequently satisfied by patients "re-classified" were arthritis (63.2%), hematological (44.7%) and skin (23.7%) manifestations; as for the "immunological" items, hypocomplementemia (71%), SLE-specific (52.6%) and antiphospholipid (35.1%) autoantibodies.
Comparing the subgroup of patients "re-classified" as SLE with that of patients who "remained" UCTD, we found that the first group presented more frequently hematological manifestations, hypocomplementemia and anti-dsDNA, anti-Sm, anti-RNP, anti-beta2GPI positivity at the onset of the disease ($p<0.01$). Moreover, during the follow-up, the subgroup of patients "re-classified" as SLE developed more frequently malar ($p<0.05$) and discoid rash and arthritis ($p<0.01$) compared to patients who "remained" UCTD.
Conclusion: The development of increasingly sensible and specific classification criteria for definite CTDs may guide in the identification of stable UCTDs since their early stages and consequently in better definition of these conditions that can be considered as a distinct clinical entity.
The early identification of stable UCTD is of great importance not only for clinical management (follow-up schedules as well as therapeutic protocols) but also for scientific implications.
REFERENCES:
[1] Mosca M. et al., Clin Exp Rheumatol. Sep-Oct 1999;17(5):615-20; 2. Fanouriakis A. et al., Ann Rheum Dis. 2020 Jun;79(6):713-723.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3909

POS0790

RELATIONSHIPS BETWEEN SALIVA IMMUNOGLOBULINS FREE LIGHT CHAINS CONCENTRATION AND CLINICAL, IMMUNOLOGICAL, HISTOLOGICAL PARAMETERS IN PATIENT WITH PRIMARY SJOGREN'S SYNDROME

E. Kuvardin[1], I. Kholopova[2], E. Belyakova[3], I. Grigor'eva[1], I. Bekhtereva[3], A. Maslyanskiy[1], Y. Krivolapov[3], S. Lapin[2]. *[1]Almazov National Medical Research Centre, Rheumatology Department, Saint - Petersburg, Russian Federation*; *[2]Pavlov First Saint - Petersburg State Medical University, Center for Molecular Medicine, Laboratory of Autoimmune Diagnostics, Saint - Petersburg, Russian Federation*; *[3]North-Western State Medical University named after I.I. Mechnikov, Pathological Department of Clinical Molecular Morphology, Clinic named after E.E. Eichwald, Saint - Petersburg, Russian Federation*

Background: Patients with primary Sjogren's syndrome (pSS) exhibit biological signs of B cell activation such as serum polyclonal hypergammaglobulinaemia, increased levels of free light chains (FLC) and positivity for autoantibodies. B-cells may comprise up to 50% cells of lymphocytic infiltrates in salivary glands of patents with the disease. For that reasons measuring saliva B-cells products might have diagnostic value in pSS.
Objectives: To evaluate relationships between saliva free light chains concentration and clinical, immunological, histological parameters in patient with pSS.
Methods: Saliva and blood FLC concentrations were measured in patient with pSS (n = 24) and healthy volunteers (n = 11). Patients fulfilled the ACR/EULAR 2016 criteria of pSS. Saliva collected during assessment unstimulated salivary flow was used for analysis. Quantitative assessment of $CD3^+$, $CD4^+$, $CD8^+$, $CD20^+$, $CD21^+$, $CD68^+$, $CD138^+$ cells was performed in minor salivary glands of 9 patient by immunohistochemistry. Cells quantity was calculated in 4 mm^2 (area of section).
Results: FLC concentration in saliva of pSS patients was higher than in healthy volunteers ($p<0,01$). Medians of saliva κ - and λ – free light chains concentrations in patients and healthy persons were 1,08 mg/L [25-;75- percentiles 0,58;1,91], 1,038 mg/L [0,55;2,03] and 0,36 mg/L [0,32; 0,54], 0,35 mg/L [0,21; 0,52] respectively. Median of saliva κ: λ chains ratio in pSS patient was 0,94 [0,6;1,5]. The ratio didn't differ from healthy persons ($p=0,24$). Saliva κ – and λ – free light chain concentrations in patient with pSS correlated with patients age ($r_s = 0,51$, $p=0,033$ and $r_s=0,43$, $p= 0,011$, respectively) and unstimulated salivary flow ($r_s = -0,48$, $p=0,02$ and $r_s=-0,49$, $p= 0,017$, respectively). Concentration of κ – free light chain correlated with number of $CD138^+$-cells ($r_s = 0,733$, $p=0,025$). Interesting that saliva λ – free light chain concentration didn't correlate with quantity of plasmatic cells.
Conclusion: Measuring saliva FLC concentration might be offered as diagnostic marker of pSS. Concentration κ – free light chain can directly mirror the glands quantity of plasmatic cells.
REFERENCES:
[1] Nocturne, Gaëtane; Mariette, Xavier (2018): B cells in the pathogenesis of primary Sjögren syndrome. In Nature reviews. Rheumatology 14 (3), pp. 133–145. DOI: 10.1038/nrrheum.2018.1.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3926

POS0791

DOSE-DEPENDENT RELATIONSHIP BETWEEN HISTORY OF DENTAL CARIES AND INCREASED RISK OF NEWLY-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: A NATIONWIDE POPULATION-BASED COHORT STUDY

K. S. K. Ma[1]. [1]*National Taiwan University, Taipei, Taiwan, ROC, Department of Life Science, Taipei, Taiwan, Republic of China*

Background: The relationship between oral bacterial invasion caused by periodontal pathogens and risk of systemic lupus erythematosus (SLE) has been identified. However, there is a lack of knowledge on the relationship between carious lesions and risk of SLE, as well as longitudinal studies on the effect of restorative materials on SLE.
Objectives: This study investigated whether patients with history of dental caries are associated with an increased risk of newly-onset systemic lupus erythematosus (SLE).
Methods: A total of 541,461 carious patients and 258,918 controls without carious teeth were enrolled between 1997 and 2013 from the National Health Insurance Research Database. Subgroup analyses were conducted based on restorative materials included amalgam, resins or both. Cumulative incidences and hazard ratios (HRs) of developing SLE were derived after adjusting for age, gender, comorbidities and co-medications in a multivariable model.
Results: The risk of SLE was significantly higher in carious patients (HR = 1.984, 95% = 1.652-2.382) compared to controls. Dose-dependent relationship between caries and risk of SLE was identified. The risks of SLE were higher among those who had over 11 dental visits (HR = 2.525, 95% C.I = 1.859-3.429), followed by those with 3-10 dental visits (HR = 1.863, 95% C.I= 1.356-2.543), then those with 1-2 visits, and were higher among those who had over 5 carious teeth extractions (HR = 1.877, 95% C.I= 1.186-2.970), followed by those with 1-4 carious teeth extractions (HR = 1.363, 95% CI = 1.167-1.593), then those without extraction. The risk of SLE among different restorative materials, including amalgam or resins, for caries management, were not significantly different.
Conclusion: Patients with caries were associated with higher SLE risks. The relationship between caries and risk of SLE was dose-dependent, regardless of used restorative materials.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3945

POS0792

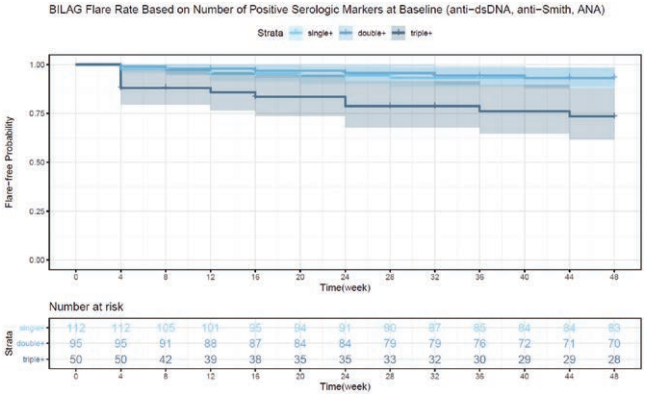
BASELINE FACTORS ASSOCIATED WITH LUPUS FLARES: A POST-HOC ANALYSIS OF PATIENTS WITH MODERATE TO SEVERE ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS ENROLLED IN A 48 WEEK PHASE II RANDOMIZED CLINICAL TRIAL

L. Lindsay[1], H. A. Mao[2], J. E. Cheng[2], C. Y. Chuo[3], N. Jones[4], M. D. Cascino[4], K. Tuckwell[4]. [1]*Genentech, Inc., Personalized Healthcare Data Science, South San Francisco, United States of America*; [2]*Hoffmann-La Roche Limited, Product Development Biometrics, Mississauga, Canada*; [3]*Genentech, Inc., Personalized Healthcare Analytics, South San Francisco, United States of America*; [4]*Genentech, Inc., Product Development Clinical Science, South San Francisco, United States of America*

Background: Systemic lupus erythematosus (SLE) is a chronic disease characterized by periodic flares associated with poor outcomes and subsequent organ damage (1-2). Flare prevention is important for optimal patient management and development of effective therapies.
Objectives: To identify patient-level factors associated with flares among patients with moderate/severe SLE.
Methods: We conducted a post-hoc analysis of 260 patients with active, autoantibody+ SLE enrolled in a phase II randomized clinical trial (Fenebrutinib) (3). The relationship between baseline demographic (age, gender, ethnicity, BMI), region (US/EU, outside US/EU), disease severity (PGA, SLEDAI-2K, BILAG domain involvement), disease duration, serologic markers (C3, C4, ANA, anti-dsDNA Ab, anti-Smith Ab), treatment arm, standard of care (SOC) and flares (BILAG and SFI) over 48 wks was assessed by survival analysis and multiple Cox Proportional Hazard models. We examined concordance between BILAG and SFI flares using Cohen's Kappa Index.
Results: The overall rate of flare was low (n=37 SFI flare, n=25 BILAG flare). Median time to first flare was 8 wks for SFI flares compared to 12 wks for BILAG flares. There was no difference in flare rate by treatment arm. Cumulative flare hazard increased over time. Concordance between SFI and BILAG flares was 0.14. Multivariable analyses identified a higher flare rate for both SFI and BILAG-defined flares in patients with severe disease at baseline (PGA >1.7, SLEDAI-2K ≥10) and <7 y disease duration.
Flares were more common in patients ANA, anti-dsDNA and anti-Smith+ at baseline compared to patients with <3 + markers (p<.001). Furthermore, anti-dsDNA (p = .03) and/or anti-Smith (p = .001) positivity at baseline were better indicators of higher flare rate compared to ANA (p = 0.5). Low baseline complement level (C3 and C4) was associated with a higher flare rate (p = .03 and p = .03 respectively).
Patients from non-US/EU regions had a higher flare rate compared to patients from the US/EU, despite receiving more frequent SOC therapy and higher baseline corticosteroid doses (≥10 mg/d). Overall, flare-free probability was comparable at 48 wks regardless of baseline corticosteroid dose but patients receiving <10 mg/d had a median time to flare of 4 vs 24 wks for those receiving ≥10 mg/d (p = .004).
Conclusion: In this study, flares were more common among patients with more severe disease, shorter disease duration, multiple serologic markers, were from outside the US/EU, and received lower steroid doses at baseline.
REFERENCES:
[1] Fernandez D and Kirou KA. Curr Rheumatol Rep 2016 18:14.
[2] Stoll T, et al. Rheum (Oxford) 2004 43(8):1039–44.
[3] Isenberg D, et al. Arth Rheum 2019 71 suppl 10.

Baseline Factors (%)	No Flare n=206	Flare		
		BILAG n=25	SFI n=37	BILAG and SFI n=8
Age (mean (SD))	41.8 (12)	35.2 (9)	40.4 (10)	34.9 (8)
Female	199 (97)	24 (96)	35 (95)	7 (88)
PGA (mean (SD))	1.7 (0.5)	1.7 (0.4)	1.9 (0.5)	1.7 (0.6)
BILAG A/B any domain	197 (96)	23 (92)	35 (95)	7 (88)
SLEDAI 2K >=10	87 (42)	18 (72)	17 (46)	4 (50)
Disease duration (y) (mean (SD))	9.4 (7)	5.3 (4)	6.6 (6)	2.9 (3)
ANA +	203 (99)	24 (96)	35 (95)	8 (100)
anti-dsDNA +	102 (50)	18 (72)	21 (57)	5 (63)
anti-Smith +	45 (22)	13 (52)	12 (32)	4 (50)
Low C3	57 (28)	12 (48)	13 (35)	3 (38)
Low C4	26 (13)	7 (28)	4 (11)	1 (13)
Non US/EU	157 (76)	21 (84)	32 (87)	8 (100)
Corticosteroid ≥10 mg/d	130 (63) 80 (39)	14 (56) 9 (36)	21 (57) 14 (38)	5 (63) 4 (50)
Immunosuppressant	74 (36)	12 (48)	15 (41)	3 (38)
Antimalarial	135 (66)	14 (56)	21 (57)	5 (63)

Notes: included patients 18-75 y; 1+ serologic marker of SLE; SLEDAI-2K >=8, PGA>=1; 1+ oral SOC treatment
SFI = SELENA- SLEDAI Flare Index



Disclosure of Interests: Lisa Lindsay Shareholder of: Employee of Genentech, Inc., Employee of: Employee of Genentech, Inc., Huiyan (Ashley) Mao Shareholder of: Employee of Hoffmann-La Roche Limited, Employee of: Employee of Hoffmann-La Roche Limited, Ji (Emmy) Cheng Shareholder of: Employee of Hoffmann-La Roche Limited, Employee of: Employee of Hoffmann-La Roche Limited, Ching-Yi Chuo Shareholder of: Employee of Genentech, Inc., Employee of: Employee of Genentech, Inc., Nicholas Jones Shareholder of: Employee of Genentech, Inc., Employee of: Employee of Genentech, Inc., Matthew D. Cascino Shareholder of: Employee of Genentech, Inc., Employee of: Employee of Genentech, Inc., Katie Tuckwell Shareholder of: Employee of Genentech, Inc., Employee of: Employee of Genentech, Inc.
DOI: 10.1136/annrheumdis-2021-eular.4042

POS0793

PREDICTORS OF END STAGE RENAL DISEASE IN THE RENAL BIOPSY PROVEN LUPUS NEPHRITIS

E. Duran[1], T. Yıldırım[2], U. Kalyoncu[1], A. Taghiyeva[3], E. Arzu Sağlam[4], M. Üner[4], E. Bilgin[1], J. Jabrayilov[2], E. C. Bolek[1], C. Önal[2], B. Farisoğulları[1], N. S. Koç[2], G. K. Yardımcı[1], S. Girgin[2], G. Ayan[1], Z. Özsoy[1], G. Sandal Uzun[1], L. Kılıç[1], Ş. R. Yılmaz[2], A. Akdoğan[1], Ş. A. Bilgen[1], O. Karadag[1], S. Kiraz[1], B. Altun[2],

A. İ. Ertenli[1], M. Arıcı[2], Y. Erdem[2]. *[1]Hacettepe University School of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; *[2]Hacettepe University School of Medicine, Department of Internal Medicine, Division of Nephrology, Ankara, Turkey*; *[3]Hacettepe University School of Medicine, Department of Internal Medicine, Ankara, Turkey*; *[4]Hacettepe University School of Medicine, Department of Department of Pathology, Ankara, Turkey*

Background: Although focusing on the proliferative form of lupus nephritis (LN), recent reports also highlight the importance of recognizing and treating non-proliferative forms of LN.

Objectives: In this study, we aimed to compare the clinical features and outcomes between proliferative and non-proliferative LN and to investigate the predictor factors of end stage renal disease (ESRD).

Methods: This retrospective study included 139 SLE patients who had at least one kidney biopsy between 2001 and 2020. 116 patients were diagnosed as LN. Biopsy findings had been classified according to the International Society of Nephrology and the Renal Pathology Society (ISN/RPS) classification. Demographics, disease involvements, laboratory values, treatment regimens, and outcomes in LN course were compared according to the proliferative and non-proliferative LN. Complete renal response within first 24 months was defined as ACR response criteria. Factors predicting the ESRD were analysed by the logistic regression analysis.

Results: A total of 116 lupus nephritis patients were categorised class 3 (n=17, 14.7%) or 4 (n=77, 66.4%) as proliferative LN and class 2 (n=9, 7.8%) or 5 (n=13, 11.2%) as non-proliferative LN. Of these patients, 80.2% was female. Mean age at the SLE diagnosis and SLE manifestations were similar for both group. ANA (+) ≥ 1:320, ds-DNA level, APS antibodies, anti-Sm (+) were similar for proliferative and non-proliferative LN, but ds DNA positivity and low level of C3 and C4 were more frequent in proliferative LN. LN duration was similar. Median renal SLEDAI scores were higher in proliferative LN group. Induction treatment regimens included pulse steroid 72.3%, CyC 51.8%, MMF 24.6%, Rtx 6.1%, CsA 4.4%, and plasma exchange 12.9%. ESRD, renal transplantation and exitus were major complications of LN. Predictors of ESRD were duration of lupus nephritis (OR 1.32 [1.09-1.61]; 95% CI), decrease in GFR at the biopsy time (OR 0.97 [0.95-0.99]; 95% CI), and being in complete renal response within 24 months (OR 21.07 [2.28-194.36]; 95% CI).

Conclusion: Unfortunately, LN patients still have worse outcomes, such as high ESRD rate, regarding to current effective immunosuppressive treatment regimens. Although patients' number were not enough for conclusion, interestingly, worse outcomes were not related with proliferative or non-proliferative LN. Complete remission within 24 months was most relevant good prognostic factor, and clinicians should be kept in mind to these windows of opportunity period.

Table 1. Demographic, clinical characteristics, and outcomes of the patients with lupus nephritis

Variables*	All patients (n=116)	Class 3 or 4 LN (n=94)	Class 2 or 5 LN (n=22)	p
Age at the SLE diagnosis, years	22.5±13.1	23±13.3	20.3±14	0.32
Sex, female	93 (80.2)	74 (78.7)	19 (86.4)	0.42
SLE disease duration	8 (8.7)	8 (9.7)	8.3 (7.5)	0.66
Lupus nephritis at diagnosis time	67 (58.8)	54 (58.7)	13 (59.1)	0.97
Manifestation of SLE				
-Musculoscletal	75 (66.4)	63 (68.5)	12 (57.1)	0.32
-Mucocutaneous	60 (52.6)	50 (54.3)	10 (45.5)	0.45
-Hematologic	47 (40.9)	38 (40.4)	9 (42.9)	0.83
-Serosal	26 (23.2)	21 (23.1)	5 (23.8)	0.94
-Neurological	6 (5.3)	5 (5.4)	1 (4.8)	0.91
Laboratory values for kidney biopsy				
-Creatinine level (mg/dL)	0.7 (0.5)	0.8 (0.5)	0.6 (0.2)	**0.01**
-GFR (ml/min)	110 (67)	92 (55)	145 (59)	**0.03**
-≥ 60 ml/min	79 (79.8)	63 (77.8)	16 (88.9)	
-30-59 ml/min	8 (8.1)	7 (8.6)	1 (5.6)	0.55
-< 30 ml/min	12 (12.1)	11 (13.6)	1 (5.6)	
-24-hour urine protein				
≥ 1 gr/day	72 (71.3)	62 (76.5)	10 (52.6)	**0.04**
≥ 3 gr/day	36 (35.6)	32 (39)	4 (21.1)	0.14
-Active urinary sediment	91 (83.5)	78 (89.7)	13 (59.1)	**0.001**
Renal SLEDAI at the biopsy	12 (8)	12 (8)	8 (8)	**0.001**
Lupus nephritis duration (years)	5.5 (8)	5.1 (8.3)	6.4 (4.8)	0.73
Complete renal response within 24 months	69 (71.1)	55 (72.4)	14 (66.7)	0.61
End-stage renal disease	13 (11.2)	11 (11.7)	2 (9.1)	0.72
Renal transplantation	5 (4.3)	4 (4.3)	1 (4.5)	0.95
Exitus	8 (7)	7 (7.5)	1 (4.5)	0.62

** n (%), if otherwise specified. Med (IQR) for numerical data excluding age; mean ± SD for age.*

GFR: Glomerular filtration rate, LN: Lupus nephritis, SLEDAI: Systemic lupus erythematosus disease activity index

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4054

POS0794 INCIDENCE AND PHENOTYPE OF ANTIPHOSPHOLIPID SYNDROME (APS) AFTER PREECLAMPSIA

S. Amylidi-Mohr[1], M. Karakitsiou[1], R. Braun[1], F. Förger[2], E. Rexhaj[3], L. Raio[1]. *[1]Inselspital, Obstetrics, Bern, Switzerland*; *[2]Inselspital, Rheumatology, Bern, Switzerland*; *[3]Inselspital, Cardiology, Bern, Switzerland*

Background: Obstetric Antiphospholipid syndrom (oAPS) is induced by antiphospholipid antibodies (aPL) and associated with specific pregnancy complications. oAPS requires the combination of at least one obstetrical and one laboratory criteria (in 2 or more occasions at least 12 weeks apart). Multiple aPL positivity, lupus anticoagulant (LA) or persistently high aPL titers is defined as high risk aPL profile. *"Non-criteria" oAPS* are cases not fulfilling the clinical criteria.

Objectives: To investigate the incidence of aPL after preeclampsia and the association of phenotypes of oAPS and pregnancy outcome.

Methods: The present retrospective cohort analysis included women followed up after preeclampsia. Anti-PL (LA, aCL, anti-β2GBI of IgG and IgM isotype) are assessed 8 to 12 weeks after PE and if positive, again at least 12 weeks apart. According to the ISSHP PE is classified as severe if the blood pressure exceeds 160/110mmHg, or is associated with HELLP syndrome, or eclampsia. FGR is defined as estimated fetal weight <5th, and birth weight <10th percentile, and/or pathologic fetal Doppler.

Results: Complete clinical and laboratory data were available for 99 women over a period of 6 years. 38.4% delivered <34+0 weeks. PE was severe in 63.6% of cases, and the incidence of FGR was 58.9%. HELLP syndrome was diagnosed in 34.3% and in 4 cases it was isolated. The prevalence of aPL was 35 (35.4%) at first evaluation, and 23 (23.2%) were still positive 12 weeks apart. 14/99 (14.1%) cases fulfilled the definition of classical oAPS, and 9/99 (9.1%) delivered >34 weeks ("non-criteria oAPS"). Of interest, the incidende og high risk aPL profiles was similar in both groups (64.3% vs. 77.8%; p=NS). The incidence of HELLP syndrome was higher in the presence of APS (APS: 9/23 [39.1%] vs. 21/76 [27.6%]; p=NS). 3 out of 4 cases with isolated HELLP syndrome were associated with high risk aPL profiles. Overall, aCL IgG was the dominant aPL. 32/35 (91.4%) and 22/23 (95.7%) had positive aCL at first and second investigation, respectively (p=NS). An aCL IgG titer >32.8CU at first assessment yield a LR of 10 for persistent aCL with a sensitivity and specificity of 91.3% and 90.9%, respectively.

Conclusion: Classical and "non-criteria" obstetrical APS show a similar aPL pattern and distribution of aPL phenotypes regardless of gestational age at delivery. aCL IgG is the dominant aPL antibody and is highly predictive for aPL persistence at follow up. HELLP syndrome may be an additional feature of oAPS, in particular the isolated form. However, more studies are necessary to explore this possible association.

REFERENCES:

[1] Tektonidou MG et al, EULAR recommendations for the management of antiphospholipid syndrome in adults Ann Rheum Dis. 2019 Oct;78(10):1296-1304. doi: 10.1136/annrheumdis-2019-215213. Epub 2019 May 15.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4074

POS0795 ULTRASOUND-GUIDED CORE NEEDLE BIOPSY: AN EFFECTIVE AND SAFE TOOL TO DIAGNOSE SJÖGREN`S SYNDROME AND LYMPHOMA OF THE MAJOR SALIVARY GLANDS

U. Borner[1], L. Nisa Hernandez[1], A. C. Sarbu[2], L. Christ[2], Y. Banz[3], B. Maurer[2], M. D. Caversaccio[1], F. Kollert[2]. *[1]Inselspital, University Hospital Bern, University of Bern, Otorhinolaryngology, Head and Neck Surgery, Bern, Switzerland*; *[2]Inselspital, University Hospital Bern, University of Bern, Rheumatology & Immunology, Bern, Switzerland*; *[3]Pathology, University of Bern, Bern, Switzerland*

Background: Histopathology is a cornerstone of diagnostics in Sjögren`s syndrome (SjS). The current widely accepted standard, minor salivary gland (lip) biopsy, is a surgical procedure with several disadvantages including permanent sensory loss of the lips as a well-known complication (reviewed in 1). Moreover, lymphoma of salivary glands cannot be excluded. Ultrasound-guided core needle biopsy (CNB) is an excellent diagnostic tool with good safety (2) and encouraging results as compared to open biopsy (3).

Objectives: To retrospectively analyze safety and diagnostic outcome of ultrasound-guided CNB in patients with known or suspected SjS.

Methods: A retrospective analysis of a case series of four patients with known or suspected SjS. All patients were treated at the outpatient clinic of the Department of Rheumatology & Immunology, and the Department of Otorhinolaryngology. All patients underwent ultrasound-guided CNB: We clean and disinfect the ultrasound transducer and the skin of the patient before and after the procedure. We use a sterile probe cover and gloves. Only sterile ultrasound gel or ultrasound compatible disinfectant should be used. Core-needle biopsy was

performed using a 20 g needle (Bard). A Logiq S8 GE ultrasound device with a 6-15 MHz matrix linear transducer was used. We performed a local anesthesia at the entry point and a 2mm skin incision. The sampling length was set on 20mm. The CNB was performed at the most suspicious focal sonographic lesion. 2-3 needle passes were carried out through the same skin access.

Results: Representative histopathological samples were obtained from all patients. In patient 1 (62y) with known SjS and parotid swelling, mucosa-associated lymphoid tissue (MALT) lymphoma was diagnosed (previous lip biopsy with no proof of malignancy). Also in patient 2 (35y) with known SjS and a 20-years history of parotid swelling, MALT lymphoma was diagnosed. In this patient a lip biopsy was performed in the previous year supporting the diagnosis of SjS, but without proof of malignancy. In patient 3 (64y) with SSc, anti-Ro/SSA positivity and dry eyes and mouth, the biopsy established the diagnosis of SjS. In patient 4 (59y) with SSc, negative anti-Ro/SSA antibodies and dry eyes/mouths, SjS could be excluded. In the corresponding ultrasound, all patients showed hypoechogenic lesions and inhomogeneous parenchyma of major salivary glands reflecting OMERACT grade II-III SjS ultrasound score (4). No safety signals were observed. Patients with prior lip biopsies perceived ultrasound-guided CNB as preferable.

Conclusion: This pilot study suggests that ultrasound-guided CNB in SjS is a safe procedure with an excellent diagnostic yield allowing the diagnosis of lymphoma of the salivary glands, which is superior to lip biopsy. Given these encouraging results, we will now increase patient numbers for further validation.

REFERENCES:

[1] Pijpe, J., et al., *Parotid gland biopsy compared with labial biopsy in the diagnosis of patients with primary Sjogren's syndrome.* Rheumatology (Oxford), 2007. **46**(2): p. 335-41.

[2] Kim, H.J. et al., *Ultrasound-guided core needle biopsy in salivary glands: A meta-analysis.* Laryngoscope, 2018. **128**(1): p. 118-125.

[3] Zabotti, A. et al., *Ultrasound-guided core needle biopsy compared with open biopsy: a new diagnostic approach to salivary gland enlargement in Sjögren's syndrome? Rheumatology (Oxford). 2020. **17**:keaa441. Epub ahead of print.*

[4] Jousse-Joulin, S., et al., *Video clip assessment of a salivary gland ultrasound scoring system in Sjogren's syndrome using consensual definitions: an OMERACT ultrasound working group reliability exercise.* Ann Rheum Dis, 2019. **78**(7): p. 967-973.

Disclosure of Interests: Urs Borner: None declared, Lluis Nisa Hernandez: None declared, Adela-Cristina Sarbu: None declared, Lisa Christ Shareholder of: Roche, Grant/research support from: Gilead, Roche, Pfizer, Yara Banz: None declared, Britta Maurer Speakers bureau: Boehringer-Ingelheim, Grant/research support from: Abbvie, Protagen, Novartis Biomedical Research and congress support from Pfizer, Roche, Actelion, mepha, and MSD. BM has a patent for mir-29 for the treatment of systemic sclerosis issued (US8247389, EP233143)., Marco D. Caversaccio Grant/research support from: Medel, Cochlear, Oticon, Storz, Florian Kollert Shareholder of: Roche, Consultant of: Actelion, BMS, Boehringer-Ingelheim, Pfizer, Grant/research support from: Gilead, Pfizer, Employee of: In the past at Novartis, currently at Roche

DOI: 10.1136/annrheumdis-2021-eular.4077

Vasculitis – large vessel vasculitis

POS0796 SURVIVAL OF GIANT CELL ARTERITIS PATIENTS IN SLOVENIA

A. Hočevar[1,2], A. Viršček[3], R. Jese[1], M. Tomsic[1,2], Z. Rotar[1,2]. [1]*University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia*; [2]*Medical Faculty, University of Ljubljana, Internal Medicine, Ljubljana, Slovenia*; [3]*Statistical Office of the Republic of Slovenia, Ljubljana, Slovenia*

Background: Recent meta-analysis reported no difference in the long-term mortality of GCA patients at a population level, but an increased mortality in hospital-based cohorts[1].

Objectives: The aim of our study was to evaluate for the first time the survival of GCA patients in Slovenia.

Methods: We included patients with clinical diagnosis of GCA supported by histology or imaging diagnosed between September 2011 and December 2019 and prospectively followed at our secondary/tertiary rheumatology center. To evaluate mortality the censor date of 24. June 2020 was used. Kaplan–Meier analysis was used to analyze mortality. Standardized mortality ratio (SMR) was calculated using data of age matched Slovenian population as the reference.

Results: Between September 2011 and December 2019 we identified 309 new GCA patients (203 (65.7%) females, median (IQR) age 74.9 (67.7–80.1.7), range 53.7 to 97.5 years). Patients were followed (until death or censor date) of a median (IQR) 33.3 (17.5-60.8) months. Until the censor date 51 (16.5%) GCA patients died (24 females, 27 males). We found no significant sex related differences in the net survival estimates during the first five years of follow up (p=0.68).

Figure 1 shows the survival curve of GCA patients and general population as a comparator according to Kaplan–Meier analysis. In the first year following GCA diagnosis the mortality rate was 1.9 times higher compared to general Slovenian population (95% CI 1.19 - 2.88, p=0.03). For patients who survived the first year after diagnosis the mortality was comparable to the general population (Table 1).

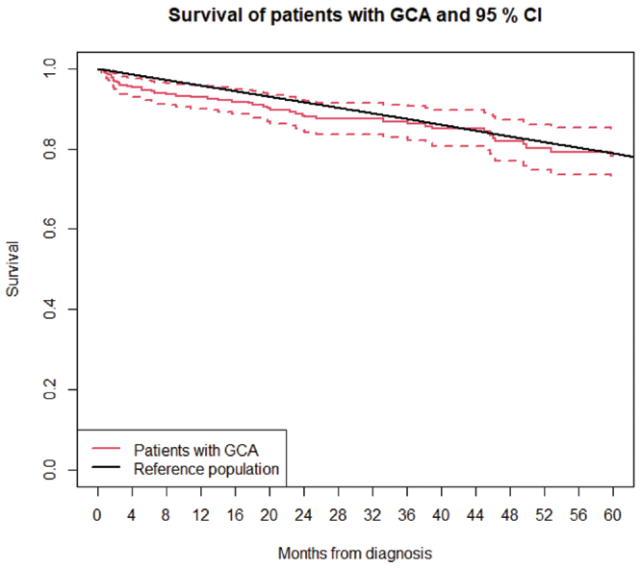


Figure 1. Survival curve according to Kaplan–Meier analysis in GCA

Table 1. Standardized mortality ratios of patients who survived the first year after diagnosing GCA (ie. were followed at least one year) compared to the general population

Years of FU	Observed deaths	Expected deaths	SMR (95%CI)	P-value
2	11	9.7	1.14 (0.57-2.03)	0.753
3	14	16.5	0.85 (0.46-1.43)	0.626
4	21	21.6	0.97 (0.60-1.49)	0.987
5	25	25.0	1.00 (0.65-1.48)	0.921
6	26	27.6	0.94 (0.61-1.38)	0.831

Legend: FU follow up; SMR Standardized mortality ratios; CI confidence interval

Conclusion: GCA patients had an increased risk of death in the first year from the GCA diagnosis.

REFERENCES:

[1] Hill CL, et al. *Semin Arthritis Rheum*. 2017;46(4):513-9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.321

POS0797 LARGE VESSEL-GCA: A DIAGNOSTIC CHALLENGE

F. Regola[1], F. Franceschini[1], G. Bosio[2], P. Toniati[1]. [1]*ASST Spedali Civili and University of Brescia, Rheumatology and Clinical Immunology Unit, Brescia, Italy*; [2]*ASST Spedali Civili, Nuclear Medicine Unit, Brescia, Italy*

Background: GCA is the most frequent systemic vasculitis in patients older than 50 years involving medium-sized and large arteries. Inflammation of the extracranial branches of the carotid artery gives rise to the classic symptoms of GCA. However, in almost two-thirds of patients GCA involves also the aorta and its major branches (1,2). Large vessel involvement leads to a different atypical clinical picture which can be challenging to diagnose (3,4). More information on clinical presentation and vessel involvement in large-vessel GCA are needed to better diagnose it.

Objectives: To analyze clinical presentation of large-vessel GCA compared to classical cranial disease.

Methods: 100 consecutive patients with a clinical diagnosis of GCA were enrolled in this retrospective study. All patients were older than 50 years of age, met the ACR criteria for GCA or had a positive biopsy of the temporal artery or evidence of large vessel vasculitis at FDG-PET/CT scan.

Results: Based on vascular involvement, patients were classified into three group: 61 patients with only cranial arteritis (C-GCA), 16 patients with only extracranial large vessel vasculitis (LV-GCA) and 23 patients with both cranial and large vessel involvement (LV-C-GCA).

Compared to C-GCA, patients with large vessel involvement (LV-GCA and LV-C-GCA) were younger and more frequently women, and the difference was further significant for patients with isolated LV-GCA. Patients with isolated LV-GCA had also the longer duration of symptoms at GCA diagnosis [LV-GCA 20(16-82) *vs* LV-C-GCA 12(4-16) *vs* C-GCA 4(3-12) weeks; p<0.001]. Systemic symptoms, as fever and fatigue, were associated with large vessel involvement, both in LV-GCA and LV-C-GCA groups. Polymyalgia rheumatica was equally reported in all three cohorts of patients and no significant differences were found in inflammatory markers levels according to vessel involvement.

In patients with large vessels involvement (LV-GCA and LV-C-GCA) thoracic aorta, subclavian arteries and abdominal aorta were the most frequently involved arteries.

Conclusion: GCA is not a single entity but includes several patterns of disease. Female gender, younger age and systemic symptoms are associated with large vessel involvement, regardless the presence or absence of cranial symptoms. The different clinical manifestations of large vessel GCA lead to a longer time to diagnosis if compared to C-GCA. For these reasons, in patients with the aforementioned characteristics, a large vessel involvement should be considered in order to reduce the time to diagnosis.

REFERENCES:

[1] De Boysson H, et al. Clin Exp Rheumatol 2019.
[2] Prieto-González S, et al. Ann Rheum Dis 2012.
[3] Brack A, et al. Arthritis Rheum 1999.
[4] Muratore F, et al. Rheumatol 2015.

	GCA (n: 100)	C-GCA (n: 61)	LV-C-GCA (n: 23)	LV-GCA (n: 16)	p
Age: median (IQR)	76 (67-79)	75 (71-80)	74 (69-77)	63 (59-72)	0.001
Female/ Male	68 (68%) / 32 (32%)	38 (62%) / 23 (38%)	17 (74%) / 6 (26%)	13 (81%) / 3 (19%)	0.276
Time between symptom onset and diagnosis (weeks)	8 (4-20)	4 (3-12)	12 (4-16)	20 (16-82)	<0.001
Cranial symptoms (overall)	84 (84%)	61 (100%)	23 (100%)	0 (0%)	<0.001
New temporal headache	77 (77%)	58 (95%)	19 (83%)	0 (0%)	<0.001
Visual symptoms	39 (39%)	34 (56%)	5 (22%)	0 (0%)	<0.001
Jaw or tongue claudication	35 (35%)	27 (44%)	8 (35%)	0 (0%)	0.004
Fever	48 (48%)	23 (38%)	14 (61%)	11 (69%)	0.032
Fatigue	75 (75%)	40 (66%)	21 (91%)	14 (88%)	0.023
Weight loss	52 (52%)	28 (46%)	13 (57%)	11 (69%)	0.235
Polymyalgia rheumatica	43 (43%)	27 (44%)	13 (57%)	3 (19%)	0.061
Arm or leg claudication	5 (5%)	0 (0%)	4 (17%)	1 (6%)	0.005
CRP (C-reactive protein)	83 (45-127)	77 (39-115)	89 (50-134)	95 (20-124)	0.461
ESR (erythrocyte sedimentation rate)	72 (47-96)	70 (46-88)	75 (28-105)	66 (44-91)	0.711
Cranial arteries	84 (84%)	61 (100%)	23 (100%)	0 (0%)	<0.001
Carotid arteries	19 (19%)	0 (0%)	12 (52%)	7 (44%)	<0.001
Subclavian and upper limb arteries	21 (21%)	0 (0%)	10 (43%)	11 (69%)	<0.001
Thoracic aorta	29 (29%)	0 (0%)	15 (65%)	14 (88%)	<0.001
Abdominal aorta	21 (21%)	0 (0%)	10 (43%)	11 (69%)	<0.001
Iliac and inferior limb arteries	10 (10%)	0 (0%)	6 (26%)	4 (25%)	<0.001

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.510

POS0798 GIANT CELL ARTERITIS TREATMENT PATTERNS AND RATES OF SERIOUS INFECTIONS

S. Tedeschi[1], Y. Jin[2], S. Vine[2], H. Lee[2], A. Pethoe-Schramm[3], V. Yau[4], S. Kim[1,2]. *[1]Brigham and Women's Hospital, Rheumatology, Inflammation and Immunity, Boston, United States of America*; *[2]Brigham and Women's Hospital, Pharmacoepidemiology and Pharmacoeconomics, Boston, United States of America*; *[3]F. Hoffmann-La Roche Ltd., Global Medical Affairs - Immunology, Basel, Switzerland*; *[4]Genentech, Personalized Healthcare Data Science, South San Francisco, United States of America*

Background: Giant cell arteritis (GCA) afflicts older adults, who may have age- and comorbidity-related risks for infection, and is treated with glucocorticoids and other immunosuppressants that might increase the risk of serious infections.

Objectives: To examine GCA treatment patterns and rates of serious infections in two real-world cohorts in the U.S.

Methods: Using claims data from two U.S. health insurance databases, Medicare (public, 2007-2017) and MarketScan (commercial, 2015-2019), we selected a cohort of patients with GCA based on a validated claims-based algorithm requiring ≥2 diagnosis codes for GCA plus dispensing of high-dose oral glucocorticoid (PPV 84.8%) [1]. The Medicare cohort included Medicare enrollees aged ≥65 years with GCA who were treated at a large Massachusetts-based healthcare system; the MarketScan cohort included a nationwide sample of GCA patients aged ≥50 years. GCA index date was the date of 1st glucocorticoid prescription. We assessed baseline comorbidities in the year prior to index date. Immunosuppressants and prophylactic antibiotics dispensed within 30 days of index date were recorded. Influenza vaccine administration in the year after index date was identified. We calculated the incidence rate of serious infections, defined as infections requiring hospitalization, after index date through end of cohort follow-up (12/31/17 in Medicare; 12/31/2019 in MarketScan), disenrollment, or death.

Results: The Medicare cohort included 734 patients, 28% male, mean age 77.1 (SD 7.4); the MarketScan cohort included 1022 patients, 30% male, mean age 68.4 (SD 10.9). The most common comorbidity was hypertension (80% Medicare; 72% MarketScan) followed by hyperlipidemia, cancer, coronary artery disease, and diabetes (Table 1). High-dose prednisone was the most common initial treatment; a small percentage received tocilizumab within 30 days of index date. Prophylaxis against pneumocystis pneumonia was similar in Medicare (13%) and MarketScan cohorts (10%). Influenza vaccination was more common in the Medicare (56%) than MarketScan (22%) cohort in the year after GCA index date. During the mean follow-up time of 2.6 (SD 2.5) years in Medicare and 1.5 (SD 0.9) years in MarketScan, 27.9% of the Medicare and 7.2% of MarketScan patients developed serious infections: incidence rate per 100 person-years = 10.7 (95% CI 9.3, 12.2) in Medicare and 6.3 (95% CI 5.0, 7.9) in MarketScan.

Conclusion: In these 2 real-world GCA cohorts in the US, over 25% of Medicare and 7% of MarketScan patients developed serious infection during follow-up. The incidence rate of serious infection was similar to ANCA-associated vasculitis [2]. Use of prophylactic antibiotics and influenza vaccination was suboptimal among GCA patients.

REFERENCES:

[1] Lee H, et al. ACR Open Rheum 2020 (in press).
[2] Rathmann J, et al. Rheumatology 2020; doi: 10.1093/rheumatology/keaa699.

Table 1. Comorbidities, medication use, and infection rates in GCA cohorts

	Medicare cohort (n=734)	MarketScan cohort (n=1022)
Baseline comorbidities		
Hypertension	80%	72%
Hyperlipidemia	71%	61%
Cancer	38%	24%
Coronary artery disease	34%	25%
Diabetes	34%	31%
No. rheumatology visits, mean (SD)	1.4 (2.2)	0.8 (1.7)
Medications within 30 days of index date		
Prednisone maximum dose ≥60mg daily	87%	91%
Tocilizumab IV or SC	<2%	5%
Methotrexate	3%	4%
Bactrim, atovaquone, or dapsone	13%	10%
Vaccines in the year after index date		
Influenza vaccine	56%	22%
Serious infection incidence rate (95% CI) per 100 person-years	10.7 (9.3, 12.2)	6.3 (5.0, 7.9)

Disclosure of Interests: Sara Tedeschi: None declared, Yinzhu Jin: None declared, Seanna Vine: None declared, Hemin Lee: None declared, Attila Pethoe-Schramm Employee of: F. Hoffmann-La Roche, Vincent Yau Employee of: F. Hoffmann-La Roche/Genentech, Seoyoung Kim Grant/research support from: Roche, Pfizer, AbbVie and Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.561

POS0799 THE EFFICACY AND SAFETY OF TOCILIZUMAB IN PATIENTS WITH GIANT CELL ARTERITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Koster[1], K. J. Warrington[1], J. Han[2], S. Mohan[3]. *[1]Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; *[2]Genentech, Inc., Biometrics, South San Francisco, United States of America*; *[3]Genentech, Inc., Immunology, South San Francisco, United States of America*

Background: Tocilizumab (TCZ) has been proven to be safe and effective for the treatment of giant cell arteritis (GCA) in 2 randomized controlled trials; however, data from additional types of studies provide valuable information related to the treatment of GCA with TCZ.

Objectives: To review and analyze efficacy and safety data for TCZ in GCA based on peer-reviewed publications to date.

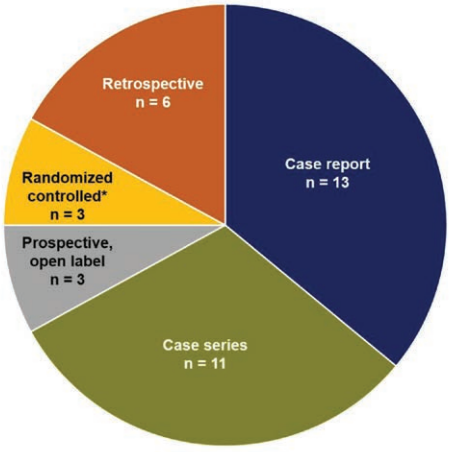
Methods: A systematic literature review was conducted according to the PRISMA guidelines. Publications were retrieved from the MEDLINE, Embase, Cochrane, Scopus and Web of Science databases. Publications of clinical trials and retrospective or prospective observational studies (April 11, 2005-October 8, 2019) including patients with GCA (classified based on ACR criteria and/or positive biopsy vs imaging) treated with TCZ and reporting a measure of efficacy were eligible for inclusion. Extracted data included year of publication, year(s) when the study was conducted, number of patients with GCA, method of GCA diagnosis, age and sex, TCZ treatment details (dose, route of administration, frequency, duration), clinical outcome (remission, relapse), serious adverse events

(SAEs) following treatment with TCZ, corticosteroid dose before and following TCZ initiation and imaging data following TCZ treatment. Results are presented for the studies (unweighted) and as the weighted population mean. Unweighted mean proportions were calculated as the average of the proportions reported from each study; unweighted means were calculated by computing the mean of individual reported study means. The weighted population proportion was estimated by calculating the total number of patients achieving an outcome and dividing by the total number of patients in all of the studies. The weighted population mean was equivalent to the sum of the individual patient's outcome values divided by the total number of patients in all of the studies.

Results: The search retrieved 664 references; 55 full-text articles were reviewed for eligibility, and 36 studies were included in the meta-analysis (Figure 1); the once-weekly and every-2-weeks subcutaneous (SC) TCZ arms of the GiACTA trial were counted as separate studies. A total of 519 patients were included. The median (IQR) duration of treatment with intravenous and SC TCZ was 26.0 (20.0-37.3) and 52.0 (26.0-52.0) weeks, respectively, across all studies in the unweighted analysis and 25.8 (20.8-41.9) and 38.9 (32.4-45.5) weeks in the weighted analysis. The mean (SE) proportion of patients achieving investigator-defined remission at the end of the study was 86.3% (4.3%) and 79.3% (6.0%) in the unweighted and weighted analyses, respectively (Table 1). The mean (SE) proportion of patients who relapsed while receiving TCZ was 2.6% (1.3%) and 12.0% (4.5%) in the unweighted and weighted analyses, respectively. The median prednisone dose at the end of the study was < 5 mg/day, and the mean proportion of patients with SAEs after TCZ initiation was ≈ 14.0%.

Conclusion: A high proportion of patients with GCA treated with TCZ were in investigator-defined remission at the end of the study across all studies analyzed. These meta-analysis findings add to the evidence of the efficacy and safety of TCZ in GCA.

Figure 1. Study Types Included in Meta-Analysis



*The subcutaneous TCZ once-weekly and every-2-weeks treatment arms of the GiACTA trial were counted as separate studies.

Table 1. Summary of Remission, Relapse and Adverse Events

Mean (SE) [95% CI]	Across GCA Studies; Unweighted (n = 36 studies)	Weighted Population Mean (n = 519 patients)
Percentage of patients in investigator-defined remission at the end of the study	n=35	n=411
	86.3 (4.3) [77.6 to 94.9]	79.3 (6.0) [67.2 to 91.4]
Percentage of patients who relapsed while receiving TCZ	n=31	n=39
	2.6 (1.3) [–0.18 to 5.3]	12.0 (4.5) [2.8 to 21.2]
Percentage of patients who relapsed after TCZ discontinuation	n=20	n=41
	26.4 (7.8) [10.1 to 42.7]	14.8 (5.8) [2.7 to 26.9]
Percentage of patients receiving no steroids at the end of follow-up	n=31	n=170
	41.8 (6.8) [27.8 to 55.8]	49.4 (8.1) [32.8 to 66.0]
Percentage of patients with SAEs after TCZ initiation	n=35	n=72
	14.0 (4.1) [5.5 to 22.4]	14.3 (1.3) [11.7 to 17.0]

Acknowledgements: This study was sponsored by Genentech, Inc. Support for third-party writing assistance, furnished by Health Interactions, Inc., was provided by Genentech, Inc.

Disclosure of Interests: Matthew Koster: None declared, Kenneth J Warrington Grant/research support from: Lilly and Kiniksa.(clinical trial support), Jian Han Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Shalini Mohan Shareholder of: Genentech, Inc., Employee of: Genentech, Inc.

DOI: 10.1136/annrheumdis-2021-eular.600

POS0800 VISUAL ISCHEMIA DURING RELAPSE AND FOLLOW-UP OF GIANT CELL ARTERITIS: A SYSTEMATIC REVIEW

K. Bugdayli[1], P. Ungprasert[2], K. J. Warrington[3], M. Koster[3]. [1]*Case Western Reserve University School of Medicine, Internal Medicine, Cleveland, United States of America*; [2]*Cleveland Clinic Main Campus, Rheumatology, Cleveland, United States of America*; [3]*Mayo Clinic College of Medicine and Science, Rheumatology, Rochester, United States of America*

Background: Visual ischemia (VI) is one of the most feared complications in giant cell arteritis (GCA). While the frequencies of VI development at or near diagnosis are better studied, limited information is available regarding the frequency of VI during relapse.

Objectives: The purpose of this study was to characterize the frequency of visual ischemia (VI) as a manifestation of relapse or during follow-up in patients with GCA through performance of a systematic literature review.

Methods: Potentially eligible studies were identified from Medline and EMBASE databases from inception to November 31, 2019 using a search strategy that comprised of terms for "giant cell arteritis," "temporal arteritis," or "Horton's disease," with "relapse," "recurrence," "flare," "outcome," "follow-up," or "prognosis." VI was defined as transient or permanent, full or partial, monocular or binocular visual field loss. VI occurring within 4 wks of GCA diagnosis was considered due to active disease and not included as a relapse event. Inclusion criteria used: (1) original research reported in English, (2) GCA definition provided, (3) VI outcome described as one of the following: (a) relapse rate/frequency denoting the presence or absence of VI, or (b) absolute number of VI events (> 4 weeks after GCA diagnosis) even if total cohort relapse rate/frequency was not provided. In order to reduce bias from under-reporting of negative results, studies that reported relapse rates/frequencies with accompanying relapse characteristics but did not provide initial detail regarding the presence/absence of VI were also identified. In such circumstances, the primary authors were directly contacted for patient-level data regarding VI and these studies were included in the final analysis if such data were available and provided.

Results: A total of 913 unique articles were identified and underwent screening. Among these, 148 articles underwent independent full-text review by two physicians (K.B. and M.J.K). 33 articles met full inclusion criteria and an additional 21 articles included data on relapse but did not report VI patient data in the publication. Responses were received from authors of 11 of these 21 studies allowing for inclusion. 44 studies accounting for 3,649 patients with GCA were identified. Average percentage of baseline VI was 19% (range 0-66%). The average length of follow-up was 3.4 years (range 0.4 to 8.7). VI developing > 4 weeks after GCA diagnosis was recorded in a total of 53 patients (1.5%).

Study-defined relapses were reported in 36 studies. A total of 1,215 patients with at least one or more relapses were recorded among 2,592 patients under observation (47%). Among these 36 studies, VI occurred in 37 patients (3.0%) with at least one study defined relapse event.

Comparing trial design, retrospective studies (n=25) reported 27 of 2,718 (1%) patients developed VI during follow-up whereas 19 of 541 (3.5%) patients in randomized controlled trials (n=8) developed VI during the trial or post-trial follow-up.

Conclusion: This report outlines the first systematic review evaluating VI as a manifestation of relapse and during follow-up in GCA. Overall, VI > 4 weeks after GCA diagnosis is uncommon (1.5%) but is noted in up to 3% of patients with at least one relapse event. Frequencies of reported VI were 3.5 times higher in randomized controlled trials compared to retrospective studies.

Disclosure of Interests: Kubra Bugdayli: None declared, Patompong Ungprasert: None declared, Kenneth J Warrington Grant/research support from: Financial support for research from Kiniksa, Eli Lilly, Matthew Koster: None declared

DOI: 10.1136/annrheumdis-2021-eular.697

POS0801 VASCULITIS IN PATIENTS WITH SARCOIDOSIS: A SINGLE-INSTITUTION CASE SERIES OF 17 PATIENTS

A. Kimbrough[1], K. J. Warrington[2], H. Langenfeld[3], C. S. Crowson[2,3], E. Carmona[4], A. Virata[5], M. Koster[2]. [1]*Mayo Clinic College of Medicine and Science, Internal Medicine, Rochester, United States of America*; [2]*Mayo Clinic College of Medicine and Science, Rheumatology, Rochester, United States of America*; [3]*Mayo Clinic School of Health Sciences, Bioinformatics and Statistics, Rochester, United States of America*; [4]*Mayo Clinic College of Medicine and Science, Pulmonology and Critical Care Medicine, Rochester, United States of America*; [5]*Mayo Clinic College of Medicine and Science, Pathology, Rochester, United States of America*

Background: Vasculitis in patients with sarcoidosis is rare and can affect blood vessels of any size. Limited information describing this association is available.
Objectives: To describe a large, single-institution case-series of patients with sarcoidosis and vasculitis.
Methods: A single-institution retrospective study was performed reviewing all patients with a diagnosis code for sarcoidosis and vasculitis between January 1, 1998 and December 31, 2019. Medical records were individually reviewed, and data regarding diagnosis, treatment, and outcomes were abstracted. Sarcoidosis was diagnosed based on histologic, radiographic, and clinical data with exclusion of alternative diagnoses. Diagnosis for small vessel vasculitis (SVV) required biopsy confirmation. Patients with large or medium-vessel vasculitis (L/MVV) required biopsy and/or arterial imaging. Comparison between patients presenting with L/MVV versus patients with only SVV was performed.
Results: Seventeen patients were identified during the study period. Nine patients (56% female) had L/MVV and 8 (50% female) had SVV. Sarcoidosis preceded the diagnosis of vasculitis in 4 (44%) patients in the L/MVV group compared to 3 (38%) patients in the SVV group. Mean±SD age at sarcoidosis diagnosis was 53.2±17.8 and 51.9±11.4 years and mean±SD age at vasculitis diagnosis was 57.4±19.6 and 59.0±13.4 years in L/MVV and SVV groups, respectively. Number of organ systems involved by sarcoidosis was similar [median (IQR) 3 (1,4) L/MVV vs. 2.5 (1.75, 3.25) SVV]. Sarcoid organ involvement and vasculitis vessel distributions are noted in Table 1. Mean length of follow-up was 11.5±12.8 years in L/MVV and 13.1±14.3 years in SVV. All patients were treated with glucocorticoids for vasculitis. More patients with L/MVV were treated with at least one DMARD/biologic (8/9, 89%) compared to SVV (3/8, 38%, p=0.05). Complete response to therapy for vasculitis was observed in 8/9 L/MVV and 7/8 in SVV. Four patients in SVV group were able to stop all immunosuppression but only one patient with L/MVV was off all therapy at last follow-up.

Case	Sex	Age Sarcoid / Vasculitis Dx, yr	WASOG Organ Involvement*	Vessel size	Arterial involvement on imaging†¥ or biopsy**
1	M	44/44	B-J, ET-LN, Sk	LVV, MVV	AA (e), Ant Tib (s), Ax (s), Br (o), V (s), Ca (s), CF (b), I (b), Innom (b), Mes (b, o, s), Per (b), Pop (a), Re (b), SF (b), Sub (o, pa, wt), TA (a)
2	F	66/68	BM, ET-LN, Li, Lu, NS, S	LVV	TA (hm)
3	F	55/55	Lu, Sp	MVV	IMA (a, s, o, wt), Sp (a)
4	M	81/80	Lu	LVV	AA (hm), Car (hm), Innom (hm), Sub (hm), TA (hm)
5	F	72/72	Eye, NS, Lu	LVV, MVV	ACA (b), ICA (b, en, s), MCA (b), SMA (wt)
6	M	43/45	Lu	LVV, MVV	Br (o, s), Ce (s), SMA (s), Sp (s), TA (wt)
7	F	53/54	B-J, Eye, Lu, Sk	MVV	Skin – medium vessel**
8	M	24/20	Eye, Li, Lu, Sp	MVV	Hep (a), Sp (a)
9	F	40/79	Lu	LVV	Temporal artery**
10	M	55/57	Li, Lu, NS	SVV	Sural nerve**
11	F	53/50	ET-LN, Lu, Sk	SVV	Skin**
12	M	60/62	Lu	SVV	Skin**
13	F	67/82	ET-LN, Lu	SVV	Skin**
14	F	52/56	Eye, Lu, NS, Sk	SVV	Skin**
15	M	39/37	Eye, Lu, NS, Sk	SVV	Skin**
16	F	57/56	Lu, Sk	SVV	Skin**
17	M	32/71	Lu	SVV	Skin**

*WASOG Organ Involvement: B-J, bone-joint; BM, bone marrow; ET-LN, extra-thoracic lymph node; Li, liver; Lu, lung; NS, nervous system; Sk, skin; Sp, spleen
† a, aneurysm; b, beaded irregularities; e, ectasia; en, enhancement; hm, hypermetabolism (on positive emission tomography); o, occlusion; pa, pseudoaneurysm; s, stenosis; wt, wall thickening
¥ AA, abdominal aorta; ACA, anterior cerebral artery; Ant Tib, anterior tibial; Ax, axial; Br, brachial; Ca, carotid; Ce, celiac; CF, common femoral; Hep, hepatic; I, iliac; ICA, internal carotid artery; IMA, inferior mesenteric artery; Innom, innominate; MCA, middle cerebral artery; Mes, mesenteric branch; PCA, posterior cerebral artery; Per, peroneal; Pop, popliteal; Re, renal; SF, superficial femoral; Sp, splenic; Sub, subclavian; TA, thoracic aorta; V, vertebral

Conclusion: Vasculitis in patients with sarcoidosis is uncommon. Variability exists in the vessels involved and the treatments utilized. Overall this series observed favorable outcomes with a high percentage achieving complete response, regardless of vessel size affected.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1146

POS0802

18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY AS A PREDICTOR OF ANGIOGRAPHIC PROGRESSION OF DISEASE IN LARGE-VESSEL VASCULITIS

K. A. Quinn[1], M. Ahlman[2], H. Alessi[1], A. Malayeri[2], J. Marko[2], E. Novakovich[1], P. Grayson[1]. [1]*National Institutes of Health, NIAMS, Bethesda, United States of America*; [2]*National Institutes of Health, Clinical Center, Radiology and Imaging Sciences, Bethesda, United States of America*

Background: Giant cell arteritis (GCA) and Takayasu's arteritis (TAK) are the two main forms of large-vessel vasculitis (LVV). Although angiography is essential to detect vascular disease in patients with LVV, there is limited prospective data characterizing change in arterial lesions over time, and factors that predict angiographic change remain unknown.
Objectives: The objectives of this study were to: 1) describe longitudinal change in angiographic studies in patients with GCA and TAK and 2) determine whether FDG-PET activity predicts angiographic progression of disease.
Methods: Patients with GCA or TAK were recruited into a prospective, observational cohort. All patients underwent baseline magnetic resonance (MR) or computed tomography (CT) angiography and a follow-up study (same modality) ≥6 months after baseline per a standardized imaging protocol. For patients who had multiple angiograms, the baseline and most recent images were compared. Arterial lesions, defined as stenosis, occlusion, or aneurysm, were evaluated by visual inspection in 4 segments of the aorta and 13 branch arteries by a single reader blinded to clinical status. On follow up angiography, the development of new lesions in these same territories was recorded, and existing lesions were characterized as improved, worsened, or unchanged by visual inspection, with confirmation by an independent reader.
All patients underwent FDG-PET on the same date as angiography. Qualitative assessment of FDG uptake was performed in each corresponding arterial territory evaluated by angiography. Active vasculitis was defined as greater FDG uptake in the arterial wall compared to the liver by visual inspection.
Results: At the baseline visit, there were 248 arterial lesions (21%) out of 1162 arterial territories evaluated from 70 patients with LVV (TAK=38; GCA=32). Baseline characteristics were as follows: Age [TAK=29.5 years (18.4-39.5), GCA=69.6 years (60.7-75.5)], Female gender [TAK=30 patients (79%), GCA=23 patients (72%)], Disease duration [TAK=2.2 years (0.6-5.5), GCA=0.7 years (0.1-2.6)], Active clinical disease [TAK=17 patients (45%), GCA=20 patients (63%)].
Over 1.6 years (1.0-2.7) of median follow-up, no angiographic change was observed in 1,132 (97%) arterial territories. New lesions developed in 8 arterial territories, exclusively in 5 patients with TAK. Arterial lesions improved in 16 territories (GCA = 7, TAK = 9) and worsened in 6 territories (GCA = 1, TAK = 5). Patients with angiographic improvement were initially imaged earlier in the disease course compared to patients with new/worsening lesions (median 1.1 vs 16.4 months, p=0.09). Patients with angiographic improvement had significantly lower acute phase reactants at follow-up compared to patients with new/worsening arterial lesions [median ESR 3.0 (2.0-15.0) vs. 27.0 (7.3-39) mm/h, p<0.01; median CRP 0.7 (0.3-1.4) vs. 6.1 (3.1-19.6) mg/L, p<0.01]. Seventy-nine percent of patients with new/worsening arterial lesions had received increased treatment over the follow-up interval compared to 100% patients with improved arterial lesions, p=0.09. FDG-PET activity was evaluated in 1091/1162 (94%) of corresponding arterial territories. PET activity in an arterial territory at baseline was significantly associated with change in that arterial territory (either new/worsening or improvement) on follow-up angiography (p<0.01) (FIGURE 1). PET activity had a sensitivity of 80% and specificity of 74% for predicting change in arterial lesions. Most arterial territories without PET activity at baseline remained unchanged over time by angiography, yielding a negative predictive value of 99%. (FIGURE 1).
Conclusion: Development of new arterial lesions is infrequent in LVV. Change in arterial lesions is dynamic, and improvement can occur. FDG-PET activity predicts change in angiographic lesions, and lack of PET activity is strongly associated with stable angiographic disease. These data may inform guideline recommendations for imaging monitoring in LVV.

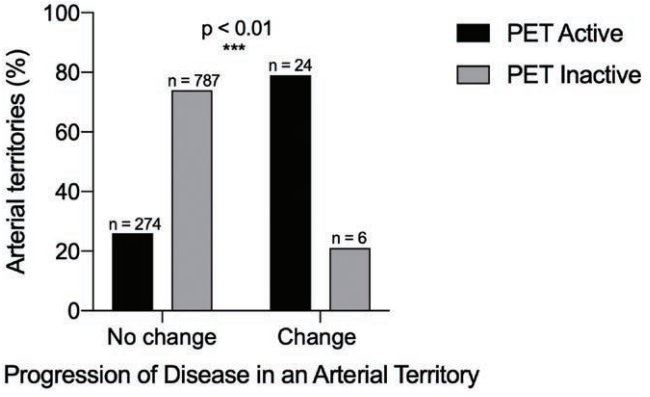


Figure 1.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1278

POS0803 TRENDS IN THE INCIDENCE OF GIANT CELL ARTERITIS ACROSS SEVEN DECADES AND CHANGES IN DIAGNOSTIC MODALITIES: A POPULATION-BASED STUDY

T. Garvey[1], C. S. Crowson[1], M. Koster[1], K. J. Warrington[1]. [1]*Mayo Clinic, Rheumatology, Rochester, United States of America*

Background: Diagnostic methods for giant cell arteritis (GCA) have evolved over recent decades, and large vessel imaging plays an increasing role in disease detection.
Objectives: This study aims to estimate the incidence of GCA over the past 10 years in a population and compare it to preceding incidence estimates. It also explores trends in the diagnostic modalities used to identify GCA.
Methods: A pre-existing population-based cohort of patients diagnosed with GCA between 1950 and 2009 was extended with incident cases from 2010 to 2019. The diagnosis of GCA was confirmed by review of medical records of patients with ICD9/10 codes for GCA between 1/1/2010 and 12/31/2019. Incident cases that met either one of the following sets of inclusion criteria were added to the cohort: one, American College of Rheumatology 1990 GCA classification criteria; or two, patients aged ≥50 years with elevation of erythrocyte sedimentation rate or C-reactive protein and radiographic evidence of large vessel vasculitis attributed to GCA. Incident cases were classified into one of three groups: group 1, temporal artery biopsy (TAB) positive; group 2, TAB negative or not done with positive large-vessel imaging; or group 3, clinical diagnosis of GCA.
Results: The study cohort included 305 patients diagnosed with GCA from 1950 until 2019. Fifty-five incident cases were diagnosed between 2010 and 2019; 37 females (67%) and 18 males (33%). The age and sex adjusted incidence rates (95% CI) per 100,000 between 2010 and 2019 for females, males, and the total population were 13.0 (8.8, 17.3), 8.6 (4.6, 12.7), and 10.8 (8.0, 13.7), respectively. The corresponding incidence rates from 2000-2009 were 28.0 (21.0, 35.1), 10.2 (5.0, 15.5), and 20.5 (15.9, 25.1), respectively. This represents a significant decline in the incidence rates in females (p<0.001) and the total group (p<0.001) between the 2000-2009 and 2010-2019 cohorts but no change in males (p=0.64). Of the 55 patients diagnosed between 2010 and 2019, there were 37 (67%) in group 1, 10 (18%) in group 2, and 8 (15%) in group 3. In contrast, of the 250 patients diagnosed between 1950 and 2009 there were 209 (84%) in group 1, 4 (2%) in group 2, and 37 (15%) in group 3. There was a significant difference between the 1950-2009 and 2010-2019 cohorts in the composition of these groups (p<0.001).
Conclusion: In this population-based cohort of patients with GCA diagnosed over a 70-year period, the incidence of GCA has declined in recent years. The total decline is driven by a decline in females but not in males. The reasons for this are unclear but should be followed over time and investigated in other population-based cohorts. There has also been a shift in the diagnostic modalities for GCA. In recent years, there are fewer TAB positive patients, and more patients diagnosed with large vessel imaging. This is the first population-based incidence cohort demonstrating a trend towards increased use of large vessel imaging for the diagnosis of GCA.

REFERENCES:

[1] Chandran AK, et al. Incidence of Giant Cell Arteritis in Olmsted County, Minnesota, over a 60-year period 1950-2009. Scand J Rheumatol. 2015;44(3):215-218.
[2] Gonzalez-Gay MA, et al. Giant cell arteritis: is the clinical spectrum of the disease changing? BMC Geriatr. 2019; Jul 29;19(1):200.
[3] Rubenstein E, et al. Sensitivity of temporal artery biopsy in the diagnosis of giant cell arteritis: a systemic literature review and meta-analysis. Rheumatology (Oxford). 2020 May 1:59(5):1011-1020.

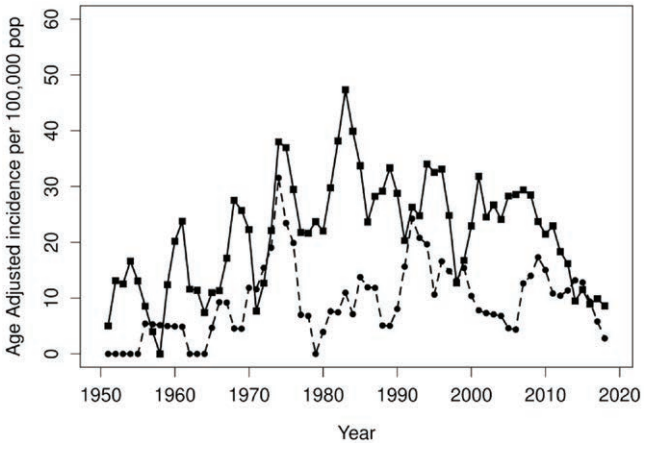


Figure 1. Trends in the incidence of GCA in Olmsted County by sex (1950-2019).

Acknowledgements: This study was made possible using the resources of the Rochester Epidemiology Project, which is supported by the National Institute on Aging of the National Institutes of Health (NIH) under Award Number R01 AG034676, and CTSA Grant Number UL1 TR000135 from the National Center for Advancing Translational Sciences (NCATS), a component of the NIH. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.
Disclosure of Interests: Thomas Garvey: None declared, Cynthia S. Crowson: None declared, Matthew Koster: None declared, Kenneth J Warrington Grant/research support from: Clinical research support from Eli Lilly and Kiniksa
DOI: 10.1136/annrheumdis-2021-eular.1415

POS0804 OUTCOMES OF SURGICALLY RESECTED THORACIC AORTITIS: RESULTS FROM A PROSPECTIVE MULTI-CENTRE REGISTRY

H. Caterson[1], A. Li[2], L. March[3], P. Bannon[4], J. Kench[5], T. Davidson[6], H. C. Soh[7], A. Sammel[8]. [1]*Royal Prince Alfred Hospital, Rheumatology, Camperdown, Australia*; [2]*The University of Sydney, Charles Perkins Centre and Boden Institute, Camperdown, Australia*; [3]*Royal North Shore Hospital, Rheumatology, St Leonards, Australia*; [4]*Royal Prince Alfred Hospital, Cardiothoracic Surgery, Camperdown, Australia*; [5]*Royal Prince Alfred Hospital, Anatomical Pathology, Camperdown, Australia*; [6]*Prince of Wales Hospital, Anatomical Pathology, Randwick, Australia*; [7]*Royal North Shore Hospital, Anatomical Pathology, St Leonards, Australia*; [8]*Prince of Wales Hospital, Rheumatology, Randwick, Australia*

Background: Inflammatory thoracic aortitis is a cause of aneurysm and is often diagnosed incidentally following aortic replacement surgery. It may be due to systemic diseases such as giant cell arteritis (GCA) and Takayasu arteritis (TAK) or a topographically isolated variant termed clinically isolated aortitis (CIA). While CIA is identified in 2-12% of thoracic aortic surgical pathology,[1] its short-term post-operative outcome is unknown.
Objectives: This study was undertaken to examine the short-term post-operative mortality and morbidity of patients with surgically resected thoracic aortitis compared to those with non-inflammatory thoracic aortic aneurysms and assess if outcomes varied based on post-operative corticosteroid therapy.
Methods: The study was based at three tertiary referral hospitals in Sydney, Australia, for the years 2004-2018. Prospectively collected data was accessed from a national surgical registry for all patients who underwent thoracic aortic aneurysm replacement. Aortitis patients were identified from histopathology records.
Inpatient medical records were reviewed to categorise aortitis cases as CIA, GCA, TAK or other aortitis and to audit the use of corticosteroids. Outcomes were compared between aortitis cases and the non-inflammatory cohort using logistic regressions, controlling for age, sex, year of procedure, and hospital.
Results: 41 aortitis cases were identified from the cohort of 1119 surgical patients (3.7%). 27 (66%) met criteria for CIA, 11 (27%) for GCA, 2 (5%) for TAK, and 1 (2%) for Other. 8 (20%) received corticosteroid therapy for aortitis.
Compared with non-inflammatory patients, the aortitis cohort was predominantly female (54% vs 28%, p < 0.01), older (mean 70 vs 62 years, p < 0.01), and had higher rates of hypertension (83% vs 67%, p = 0.03) and pre-operative immunosuppression (10% vs 1%, p < 0.01).
There was no difference (p > 0.05) between the aortitis and the non-aortitis groups for 30-day mortality (7% vs 7%), composite significant morbidity (15% vs 22%), composite infection (10% vs 6%), return to theatre for bleeding (7% vs 13%), stroke (5% vs 5%) or readmission (12% vs 10%). Similar results were also seen for CIA and the aortitis subgroup who did not receive corticoid steroid therapy when compared to the non-aortitis group (table 1).

Table 1. 30-day mortality and morbidity

	Non-aortitis		All aortitis		Aortitis, not treated for aortitis		CIA	
	n=1078		n=41		n=33		n=27	
	%	n	%	n	%	n	%	n
Mortality	7	70	7	3	6	2	4	1
Stroke	5	57	5	2	6	2	4	1
Return to theatre bleed	13	137	7	3	6	2	4	1
Composite morbidity	22	241	15	6	15	5	11	3
Composite infection	6	69	10	4	9	3	11	3
Readmission	10	108	12	5	12	4	11	3

Note: Differences in outcomes between the aortitis groups and the no aortitis group were modelled using logistic regression, controlling for age, sex, year of procedure, and hospital. There were no statistically significant differences in outcomes (p > 0.05).
CIA; clinically isolated aortitis. Composite morbidity; an outcome comprised of return to theatre for bleeding, stroke, new renal failure, acute myocardial infarction or aortic dissection. Composite infection; an outcome comprised of 30-day pneumonia, septicaemia, deep sternal wound infection or deep thoracotomy infection.

Conclusion: The finding of thoracic aortitis following aortic replacement surgery does not affect short-term post-operative mortality or morbidity. Corticosteroid therapy in the immediate post-operative period did not impact upon short-term outcomes.

REFERENCES:

[1] Quimson L, Mayer A, Capponi S, *et al*. Comparison of aortitis versus non-inflammatory aortic aneurysms among patients who undergo open aortic aneurysm repair. *Arthritis Rheum* 2020;72:1154-59.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1531

POS0805 TREATMENT OF GIANT CELL ARTERITIS WITH TOCILIZUMAB: A RETROSPECTIVE COHORT STUDY OF 119 PATIENTS

J. Rakholiya[1], M. Koster[1], H. Langenfeld[2], C. S. Crowson[1,2], A. Abril[3], P. Bansal[4], L. Mertz[5], A. Rodriguez-Pla[5], R. Sehgal[4], B. Wang[3], K. J. Warrington[1]. *[1]Mayo Clinic, Rheumatology, Rochester, United States of America*; *[2]Mayo Clinic School of Health Sciences, Biomedical Statistics and Informatics, Rochester, United States of America*; *[3]Mayo Clinic, Rheumatology, Jacksonville, United States of America*; *[4]Mayo Clinic Health System, Rheumatology, Eau Claire, United States of America*; *[5]Mayo Clinic, Rheumatology, Scottsdale, United States of America*

Background: Giant cell arteritis (GCA) is an inflammatory condition of medium- and large-sized arteries. Prospective clinical trials have demonstrated the efficacy of tocilizumab (TCZ) for treatment of patients with GCA (1). However, there is a limited data on the use of TCZ in routine clinical practice.

Objectives: To evaluate the efficacy and safety of TCZ in a retrospective cohort study of patients with GCA treated with TCZ.

Methods: Patients with GCA treated with TCZ at 4 clinical centers of a single tertiary care institution (2000-2020) were identified. The diagnosis of GCA was confirmed by at least one of the following modalities: 1. Arterial biopsy 2. Large vessel imaging 3. Clinical diagnosis of GCA meeting ACR classification criteria and established by a rheumatologist. Patient demographics, clinical presentation, laboratory studies, treatment course and adverse events were abstracted from the medical record; only patients with at least 6 months of follow-up after TCZ initiation were included. Kaplan-Meier methods were used to estimate time to TCZ discontinuation and time to first relapse after TCZ discontinuation. Poisson regression models were used to compare relapse rates before and after TCZ initiation.

Results: The study cohort included 119 patients [61% female; mean (SD) age at GCA diagnosis 70.3 (8.2) years]. The majority of patients (89%) had a biopsy-proven and/or imaging-based diagnosis of GCA, while 13 (11%) had a clinical diagnosis of GCA. In addition to glucocorticoids, 40 (34%) patients received other immunosuppressive agents prior to TCZ. The method of initial TCZ administration was subcutaneous (162mg/ml) weekly in 48 (41%), subcutaneous every other week in 20 (17%), monthly 4mg/kg infusions in 34 (29%), monthly 8mg/kg infusions in 14 (12%) and non-standard dosing in 3 remaining patients. The median (IQR) duration from GCA diagnosis to TCZ initiation was 4.8 (1.2-22.0) months and the median (IQR) duration of TCZ treatment was 18 (11-28) months. The mean (SD) dose of prednisone at TCZ initiation was 31 (19) mg/day and was reduced to a mean (SD) dose of 3.9 (6.7) mg/day at TCZ discontinuation/last follow-up visit. The relapse rate per year decreased 43% from 0.77 to 0.44 after the initiation of TCZ (RR=0.57; 95% CI: 0.44-0.75; p<0.001). The mean (SD) ESR and CRP decreased from 22 (20) mm/hour to 6 (9.2) mm/hour and from 19.1 (25) mg/L to 5.4 (16.6) mg/L, respectively from TCZ initiation to TCZ discontinuation/last follow-up visit. At 2 years of follow-up, 67% of patients had discontinued glucocorticoids. At last follow up, 46 patients had discontinued TCZ, only 14 of which were due to adverse events. The median time to TCZ discontinuation was 2.9 years. Only 17% (95%CI: 10-24%) had discontinued by 1 year after TCZ initiation and 38% (95% CI: 26-47%) had discontinued by 2 years. The most common adverse events were infections and cytopenias. While on TCZ, 1 patient developed new onset vision loss related to GCA and 1 patient, without history of diverticulitis, had bowel perforation. Among those discontinuing TCZ, 61% had relapsed at least once by 1 year after TCZ discontinuation.

Conclusion: In this large single institution cohort of patients with GCA, TCZ use resulted in a significantly reduced relapse rate and reduction in glucocorticoid dosage. Overall, patients tolerated long-term use with only 12% discontinuing due to adverse events. However, over half of patients stopping TCZ had a subsequent flare; highlighting ongoing use may be required beyond two years in several patients with GCA to maintain remission.

REFERENCES:

[1] Stone JH, et al. Trial of Tocilizumab in Giant-Cell Arteritis. N Engl J Med. 2017 Jul 27;377(4):317-328. doi: 10.1056/NEJMoa1613849. PMID: 28745999.

[2] Calderón-Goercke M, et al. Tocilizumab in giant cell arteritis. Observational, open-label multicenter study of 134 patients in clinical practice. Semin Arthritis Rheum. 2019 Aug;49(1):126-135. doi: 10.1016/j.semarthrit.2019.01.003. Epub 2019 Jan 5. PMID: 30655091.

Disclosure of Interests: Jigisha Rakholiya: None declared, Matthew Koster: None declared, Hannah Langenfeld: None declared, Cynthia S. Crowson: None declared, Andy Abril: None declared, Pankaj Bansal: None declared, Lester Mertz: None declared, Alicia Rodriguez-Pla: None declared, Rahul Sehgal: None declared, Benjamin Wang: None declared, Kenneth J Warrington Grant/research support from: Research support: Kiniksa, Eli Lilly

DOI: 10.1136/annrheumdis-2021-eular.1674

POS0806 FINDINGS CONSISTENT WITH SUBCLINICAL VASCULITIS IN PATIENTS WITH NEW ONSET POLYMYALGIA: A SYSTEMATIC LITERATURE REVIEW AND A META-ANALYSIS OF COHORT DATA

D. S. Gozzoli[1], A. Hemmig[2], L. Hemkens[3,4,5], L. Werlen[3], H. Ewald[6], C. Berger[7], D. Kyburz[2,8], S. Imfeld[9], M. Aschwanden[9], M. Stegert[2], D. Camellino[10], M. A. Cimmino[11], C. Campochiaro[12], A. Tomelleri[12], L. Henckaerts[13], D. Blockmans[13], P. Moya[14], H. Corominas[15], R. Buchanan[16,17], C. Owen[16,17], Y. Van Sleen[18], E. Brouwer[18], H. Ymashita[19], T. Daikeler[2]. *[1]University Hospital of Basel, Department of Internal Medicine, Basel, Switzerland*; *[2]University Hospital of Basel, Department of Rheumatology, Basel, Switzerland*; *[3]University Hospital of Basel, Department of Clinical Research, Basel, Switzerland*; *[4]Stanford University, Meta-Research Innovation Center at Stanford (METRICS), Palo Alto, CA 94305, United States of America*; *[5]Berlin Institute of Health, Meta-Research Innovation Center Berlin (METRIC-B), Berlin, Germany*; *[6]University of Basel, Medical Library, Basel, Switzerland*; *[7]University Hospital of Basel, Departments of Biomedicine and Internal Medicine, Translational Immunology and Medical Outpatient Clinic, Basel, Switzerland*; *[8]University of Basel, Department of Biomedicine, Basel, Switzerland*; *[9]University Hospital of Basel, Department of Angiology, Basel, Switzerland*; *[10]"La Colletta" Hospital, Division of Rheumatology, Arenzano, Italy*; *[11]University of Genoa, Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, Genoa, Italy*; *[12]San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), Milan, Italy*; *[13]KU Leuven, University Hospitals Leuven, Department of General Internal Medicine, Department of Microbiology, Immunology and Transplantation, Leuven, Belgium*; *[14]Hospital de la Santa Creu i Sant Pau, Rheumatology Unit, Department of Internal Medicine, Barcelona, Spain*; *[15]Hospital Universitari de la Sant creu i Sant Pau, Servei de Reumatologia, Barcelona, Spain*; *[16]Austin Health, Department of Rheumatology, Heidelberg, Victoria, Australia*; *[17]University of Melbourne, Department of Medicine, Parkville, Victoria, Australia*; *[18]University of Groningen, University Medical Center Groningen, Groningen, Netherlands*; *[19]National Center for Global Health and Medicine, Division of Rheumatic Diseases, Tokyo, Japan*

Background: GCA is characterized by cranial symptoms but imaging techniques show that patients with non-specific symptoms such as systemic inflammation or PMR may have undiagnosed large vessel (LV) GCA[1]. Although silent GCA in patients with clinically isolated PMR may have consequences for patients' outcome, little is known about its prevalence and characteristics of affected patients.

Objectives: To review data on the prevalence of silent GCA in newly diagnosed PMR patients without cranial GCA symptoms and to analyze which characteristics are associated with vascular involvement among PMR patients.

Methods: We systematically screened PubMed, Embase and Web of Science databases and included studies screening for GCA in steroid naïve PMR patients without cranial symptoms consistent with GCA. Authors of the publications that used PET for vasculitis screening were invited to share their individual patient data (IPD) for a meta-analysis. We sought to define patient characteristics that were associated with vasculitis using univariable mixed effects logistic regression models with vascular involvement as the outcome, missing values were imputed using multilevel joint modeling multiple imputation. To fit a multivariable model with the candidate predictors we excluded variables that were hypothesized to have less medical relevance for the outcome and highly correlated inflammation markers (ESR, Lc).

Results: Out of the 3047 studies screened independently by 2 authors (DG and TD), 13 fulfilled the inclusion criteria. These studies (published 1963-2019) reported on 543 PMR patients examined by temporal artery biopsy (n=175), ultrasound (n=110), PET or PET-CT (n=258). 115 PMR patients were diagnosed with GCA (21.2%), with prevalence ranging from 0-92%.

We collected IPD for 243 patients from 4 cohorts using PET and 3 using PET/CT for GCA diagnosis. The overall median age of patients was 72.3 years (IQR 66.4-78.0) and vasculitis was found in 65 patients (26.7%) (table 1).

Table 1.

	Overall	PMR	PMR+GCA
n (%)	243	178 (73.3)	65 (26.7)
Female sex (%)	146 (60.1)	98 (55.1)	48 (73.8)
Shoulder girdle pain (%)	236 (97.1)	174 (97.8)	62 (95.4)
Pelvic girdle pain (%)	174 (71.6)	127 (71.3)	47 (72.3)
Inflammatory back pain (%)			
No	107 (44.0)	83 (46.6)	24 (36.9)
Yes	106 (43.6)	70 (39.3)	36 (55.4)
Lower limb pain (%)			
No	87 (35.8)	61 (34.3)	26 (40.0)
Yes	81 (33.3)	68 (38.2)	13 (20.0)
Weight loss (%)	112 (46.1)	78 (43.8)	34 (52.3)
CRP (mg/l) (median [IQR])	46.0 [19.0, 77.7]	44.0 [16.9, 74.2]	52.0 [27.9, 85.0]
ESR (mm/h) (mean (SD))	65.2 (30.3)	62.7 (30.2)	72.3 (29.7)
Hemoglobin (g/dl) (mean (SD))	12.1 (1.5)	12.2 (1.5)	11.7 (1.6)
Thrombocytes (1e+09/ml) (mean (SD))	341.9 (106.3)	323.9 (103.2)	375.8 (104.6)

In the univariable analyses the following factors were most strongly associated with vasculitic PET findings: female sex (OR 2.31, CI 1.17-4.58), inflammatory back pain (OR 2.73, CI 1.32-5.64), temperature >37° (OR 1.83, CI 0.90-3.7), weight loss (OR 1.83, CI 0.96-3.51), thrombocytosis (i.e., patients with a thrombocyte count 1 SD above mean have an OR of 1.51, CI 1.05-2.18), anemia (i.e., 1 g/dl decrease in Hb below mean corresponds to an OR of 1.25, CI 1.00-1.56). Patients with lower limb pain were less likely to have vasculitis (OR 0.43, CI 0.19–0.95). The estimated ORs were very similar in the multivariable model although the 95%CIs became wider.

Conclusion: Although the prevalence across published studies showed substantial variation, 6 out of 13 studies reported a prevalence of silent GCA in 18-40% of all PMR patients. The exploratory analysis of the collected IPD identified female sex, inflammatory back pain, fever, weight loss, absence of lower leg pain, thrombocytosis and anemia as factors associated with LV-GCA. These findings should be validated in future prospective cohort studies. The presence or absence of these factors may further aid in diagnosing LV-GCA in PMR patients.

REFERENCES:

[1] Buttgereit F, Dejaco C, Matteson EL, Dasgupta B. Polymyalgia Rheumatica and Giant Cell Arteritis: A Systematic Review. JAMA. 2016 Jun 14;315(22):2442–58.

Acknowledgements: The study is funded by the "Schweizerische Stiftung für die Erforschung der Muskelkrankheiten (SSEM)".

Disclosure of Interests: Daniele Silvio Gozzoli: None declared, Andrea Hemmig: None declared, Lars Hemkens: None declared, Laura Werlen: None declared, Hannah Ewald: None declared, Christoph Berger: None declared, Diego Kyburz Grant/research support from: DK reports personal fees from Abbvie, Gilead, Lilly, Novartis and Pfizer, outside of the submitted work, Stephan Imfeld: None declared, Markus Aschwanden: None declared, Mihaela Stegert: None declared, Dario Camellino: None declared, Marco Amedeo Cimmino: None declared, Corrado Campochiaro Grant/research support from: personal fees from Roche, Alessandro Tomelleri: None declared, Liesbet Henckaerts: None declared, Daniel Blockmans Speakers bureau: Paid speaker for Roche, Consultant of: Paid consultant for Roche, Patricia Moya: None declared, Hector Corominas: None declared, Russell Buchanan: None declared, Claire Owen Speakers bureau: CO has received speaking honoraria from Roche, Janssen, Novartis and Pfizer, and meeting sponsorship from Roche, UCB and Janssen, Yannick van Sleen: None declared, Elisabeth Brouwer Speakers bureau: E. Brouwer as an employee of the UMCG received speaker fees and consulting fees from Roche in 2017, 2018 which were paid to the UMCG, Consultant of: E. Brouwer as an employee of the UMCG received speaker fees and consulting fees from Roche in 2017, 2018 which were paid to the UMCG, Hiroyuki Ymashita: None declared, Thomas Daikeler: None declared

DOI: 10.1136/annrheumdis-2021-eular.1803

POS0807 RETINAL VESSEL CALIBERS AS A NON-INVASIVE BIOMARKER OF INFLAMMATORY BURDEN IN PRIMARY SYSTEMIC VASCULITIS

O. Argyropoulou[1], E. Aissopou[1], A. Argyris[1], A. Goules[1], C. Mavragani[2], N. Tentolouris[3], P. Sfikakis[3], P. Vlachoyiannopoulos[1], A. Tzioufas[1], A. Protogerou[1]. [1]*School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece*; [2]*School of Medicine, National and Kapodistrian University of Athens, Physiology, Athens, Greece*; [3]*Medical School, National and Kapodistrian University of Athens, Athens, First Department of Propaedeutic Internal Medicine, Athens, Greece*

Background: Primary Systemic Vasculitides (PSV) constitute a heterogeneous group of rare and potentially life-threatening autoimmune diseases, characterized by a varying degree of inflammatory response, leading to local or generalized vascular disease. Vessel involvement accounts for the micro- and macrovascular complications of the disease, along with the classic risk factors including, among others age and chronic use of steroids (1). Early identification of high-risk patients for cardiovascular disease (CVD) development and the contribution of inflammation towards this adverse outcome are still unmet needs. Alterations of retinal microcirculation have been independently associated with increased CVD risk in the general population (2). The potential changes of retinal vasculature and their association with disease activity and the magnitude of inflammation have not been studied in PSV so far.

Objectives: To explore the effect of disease activity and inflammation on retinal microcirculation in PSV, classified according to vessel size as large, medium or small vessel vasculitides (LVV, MVV or SVV respectively), and polymyalgia rheumatica (PMR) without vasculitis.

Methods: Fifty-nine patients, 43 with active disease [30 active vasculitis (12 LVV, 4 MVV, 14 SVV) and 13 PMR] and 16 with chronic inactive disease (13 vasculitis, 3 PMR) were studied. All patients were matched at 1:1 ratio with 59 controls, without underlying autoimmune/autoinflammatory disorder, neoplasia or infection, according to age, gender, CVD history, BMI, smoking, arterial hypertension, dyslipidemia, diabetes mellitus and treatment related to comorbidities. A total of 32 rheumatoid arthritis (RA) patients with mild to moderate inflammatory component as defined by standard of care acute phase reactants (ESR and CRP) and 16 chronic RA patients with normal ESR and CRP levels, matched 1:1 according to all the above parameters with 32 active and 16 inactive vasculitis/PMR patients respectively, served as disease controls. Digital retinal images were obtained and retinal vessel calibers were measured with a validated software to determine central retinal arteriolar and venular equivalents ratio (CRAE and CRVE respectively). For 16 patients with active vasculitis/PMR, retinal examination was performed in two time points (baseline and ≤ 6 months later).

Results: In the overall population, patients with active Vasculitis/PMR had increased CRVE (213.8±21.7 vs 201.3±17.1, p<0.001) and CRAE (180.0±19.2 vs 164.1±17.5 p<0.001) compared to healthy controls. Separating patients according to disease type, we found that in LVV, MVV and PMR, CRAE (p≤0.05) and CRVE (p<0.05) were increased compared to control group, while in SVV only CRAE was increased (p<0.001). Interestingly, chronic patients with disease in remission displayed higher CRAE compared to matched controls (179.8±17.2 vs 169.1±11.1, p=0.006). After immunosuppressive treatment for ≤ 6 months CRVE and to a lesser extent CRAE were reduced (p=0.048 and 0.149 respectively) with a stronger statistical significance found in the Vasculitis group (p=0.026 and 0.069 respectively). Pearson's linear correlation coefficient in active disease state (at baseline examination) revealed positive bivariate correlation only between CRVE with ESR and CRP. Patients with Vasculitis/PMR had also increased CRAE when compared to RA patients in both active and inactive disease status (182.8±19.4 vs 170.1±18.4, p<0.001 and 179.8±17.2 vs 166.3±17.9, p=0.005 respectively).

Conclusion: Systemic inflammation alters retinal microcirculation in both a reversible (venules) and irreversible (arterioles) way, independently of PSV form. Thus, common disease specific pathogenetic mechanisms related to inflammation may be implicated in vascular remodeling. Sequential follow-up of PSV patients will address whether retinal vessel calibers may serve as a biomarker of disease activity and CVD development.

REFERENCES:

[1] Argyropoulou OD et al. Curr Opin Rheumatol 2017.
[2] Shaohua G et al. Current Atherosclerosis reports 2020.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1950

POS0808 CHARACTERISTICS OF GIANT CELL ARTERITIS FLARES AFTER SUCCESSFUL TREATMENT WITH TOCILIZUMAB: RESULTS FROM THE LONG-TERM EXTENSION OF A RANDOMIZED CONTROLLED PHASE 3 TRIAL

S. Unizony[1], S. Mohan[2], J. Han[2], J. H. Stone[1]. [1]*Harvard Medical School, Massachusetts General Hospital Rheumatology Unit, Boston, United States of America*; [2]*Genentech, US Medical Affairs, South San Francisco, United States of America*

Background: GiACTA investigated tocilizumab (TCZ) for the treatment of giant cell arteritis (GCA).

Objectives: To investigate disease flare characteristics after successful treatment with TCZ in GiACTA.

Methods: We report a post hoc analysis from part 2 of GiACTA. Part 1 was a 52-week, double-blind, randomized controlled period and part 2 was a 2-year open-label follow-up. In part 1, patients received TCZ 162 mg subcutaneously every week or every other week with a 26-week prednisone taper or placebo plus a 26- or 52-week prednisone taper. Patients who were in remission at week 52 were to enter part 2 on no TCZ treatment. Part 2 treatment was at the investigator's discretion. We report characteristics of first disease flare in patients assigned to TCZ in part 1 who were in sustained remission at week 52 and experienced flare in part 2. Flare was defined as reappearance of cranial symptoms (headaches, jaw claudication, visual manifestations, scalp tenderness) or polymyalgia rheumatica (PMR) symptoms or elevation of erythrocyte sedimentation rate (ESR) ≥30 mm/h attributable to GCA that required treatment.

Results: Of 149 patients assigned to TCZ in part 1, 81 (54%) were in sustained remission on entering part 2. Of these 81 patients, 37 (46%) experienced at least one flare in part 2, including 17 with new-onset GCA and 20 with relapsing GCA at baseline. Median time to flare was 26.6 weeks. In patients with new-onset GCA, flares included cranial (53%) more often than PMR symptoms (18%). Cranial and PMR symptoms were balanced (both 60%) at the time of flare in patients with relapsing GCA. Visual manifestations occurred in two patients (5%) (Table 1). ESR and CRP were elevated in 65% and 36% of patients, respectively, at the time of flare. Three (8%) flares occurred with elevated ESR without clinical symptoms.

Table 1. Clinical manifestations during flare in part 2

	Part 1 Treatment[a]		
	TCZ QW+Pred	TCZ Q2W+Pred	All TCZ
New-onset disease			
Patients, n	28	14	42
Patients with ≥1 flare, n (%)[b]	9 (32.1)	8 (57.1)	17 (40.5)
Patients with ESR ≥30 mm/h during flare, n (%)[b]	6 (66.7)	6 (75.0)	12 (70.6)
Patients with CRP ≥10 mg/L during flare, n (%)[b]	4 (44.4)	2 (25.0)	6 (35.3)
Patients with GCA signs or symptoms during flare, n (%)[c]	7 (77.8)	7 (87.5)	14 (82.4)
PMR symptoms	1 (11.1)	2 (25.0)	3 (17.6)
Cranial symptoms[d]	4 (44.4)	5 (62.5)	9 (52.9)
Amaurosis fugax	0	0	0
Blurred vision	1 (11.1)	0	1 (5.9)
Diplopia	0	0	0
Blindness	0	0	0
Ischemic optic neuropathy	0	0	0
Fever	1 (11.1)	0	1 (5.9)
Other[e]	3 (33.3)	2 (25.0)	5 (29.4)
Relapsing disease			
Patients, n	28	11	39
Patients with ≥1 flare, n (%)[b]	14 (50.0)	6 (54.5)	20 (51.3)
Patients with ESR ≥30 mm/h during flare, n (%)[b]	8 (57.1)	4 (66.7)	12 (60.0)
Patients with CRP ≥10 mg/L during flare, n (%)[b]	5 (35.7)	3 (50.0)	8 (40.0)
Patients with GCA signs or symptoms during flare, n (%)[c]	14 (100)	6 (100)	20 (100)
PMR symptoms	8 (57.1)	4 (66.7)	12 (60.0)
Cranial symptoms[d]	8 (57.1)	4 (66.7)	12 (60.0)
Amaurosis fugax	1 (7.1)	0	1 (5.0)
Blurred vision	0	0	0
Diplopia	0	0	0
Blindness	0	0	0
Ischemic optic neuropathy	1 (7.1)	0	1 (5.0)
Fever	0	0	0
Other[e]	6 (4.3)	1 (16.7)	7 (35.0)

[a]Patients from part 1 TCZ+Pred groups who were in sustained remission at week 52 entered part 2 on no treatment.
[b]Percentage based on N in disease-onset group.
[c]Percentage based on number of flare patients in disease-onset group. Individual signs or symptoms are shown as number of patients with each symptom; patients could have ≥1 sign or symptom at the time of flare.
[d]New-onset localized headache, scalp tenderness, temporal artery tenderness or decreased pulsation, ischemia-related vision loss, or jaw pain claudication.
[e]Includes fatigue, malaise, subjective weakness, and night sweats.

Conclusion: Overall, 46% of GCA patients successfully treated with TCZ for 1 year experienced disease flare within the next 2 years. Flares in patients with new-onset disease occurred more often with cranial than PMR symptoms. Visual manifestations were rare, and no blindness occurred. ESR and CRP were normal in a sizable percentage of patients experiencing flare.

Disclosure of Interests: Sebastian Unizony Consultant of: Sanofi and Kiniksa Pharmaceuticals, Grant/research support from: Genentech, Inc., Shalini Mohan Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Jian Han Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., John H. Stone Consultant of: Roche/Genentech and Sanofi
DOI: 10.1136/annrheumdis-2021-eular.2602

POS0809 A BIOMARKER PROFILE AIDING AN EARLY DIAGNOSIS OF GIANT CELL ARTERITIS

Y. Van Sleen[1], P. Therkildsen[2], A. Boots[1], B. Dalsgaard Nielsen[2], K. Van der Geest[1], P. Heeringa[3], M. G. Huitema[1], M. D. Posthumus[4], M. Sandovici[1], E. Toonen[5], J. Zijlstra[1], E. M. Hauge[2], E. Brouwer[1]. *[1]University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*; *[2]Aarhus University Hospital, Rheumatology, Aarhus N, Denmark*; *[3]University Medical Center Groningen, Pathology and Clinical Immunology, Groningen, Netherlands*; *[4]Martini Ziekenhuis Groningen, Rheumatology, Groningen, Netherlands*; *[5]Hycult Biotech, R&D Department, Uden, Netherlands*

Background: Diagnosing patients with giant cell arteritis (GCA) remains difficult. Due to its non-specific symptoms, it is challenging to identify GCA in patients presenting with polymyalgia rheumatica (PMR), which is a more common disease (1). In addition, commonly used acute-phase markers fail to discriminate between GCA patients and (infectious) mimicry patients.
Objectives: To investigate a selection of biomarkers for their utility in the accurate diagnosis of GCA in two cohorts.
Methods: Treatment-naïve GCA patients participated in the Aarhus GCA/PMR cohort (N=52) and the Groningen GPS cohort (N=48). Symptoms and biomarker levels were compared to patients presenting phenotypically as isolated PMR, disease controls and healthy controls (HCs). Diagnosis or exclusion of diagnosis of GCA was based on clinical assessment and in the majority of cases aided by imaging. Serum/plasma levels of 12 biomarkers were measured by ELISA or Luminex.
Results: In both the Aarhus and the GPS cohort, we found that weight loss, elevated erythrocyte sedimentation rate (ESR) and higher angiopoietin-2/-1 ratios but lower matrix metalloproteinase (MMP)-3 levels identify concomitant GCA in PMR patients (Figure 1). In addition, we confirmed (1) that elevated platelet counts are characteristic of GCA but not of GCA look-alikes, and that low MMP-3 and proteinase 3 (PR3) levels may help to discriminate GCA from other diseases (Figure 1). Multiple biomarkers of inflammation were found elevated in patient and disease control groups when compared to HCs.
Conclusion: This study, performed in two independent cohorts, consistently shows the potential of angiopoietin-2/-1 ratios and MMP-3 levels to identify GCA in patients presenting with PMR. These biomarkers may be used to select which PMR patients require further diagnostic workup. Platelet counts may be used to discriminate GCA from GCA look-alike patients.

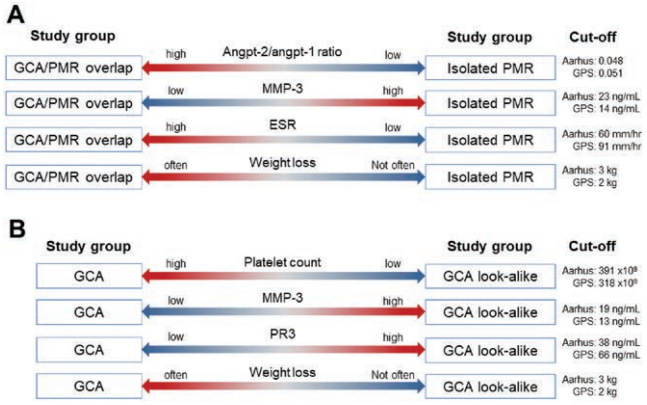


Figure 1. Summary of the most important and consistent findings in both cohorts. A shows the four factors that perform best in discriminating GCA/PMR patients overlap from isolated PMR patients in both cohorts. B shows the four factors that perform best in discriminate GCA patients from GCA look-alike patients in both cohorts. Cut-off values for the biomarkers are calculated by the Youden index.

REFERENCES:

[1] van der Geest, KSM, Sandovici M, Brouwer E, Mackie SL. Diagnostic accuracy of symptoms, physical signs, and laboratory tests for giant cell arteritis: A systematic review and meta-analysis. JAMA internal medicine. 2020.

Disclosure of Interests: Yannick van Sleen: None declared, Philip Therkildsen: None declared, Annemieke Boots: None declared, Berit Dalsgaard NIelsen: None declared, Kornelis van der Geest: None declared, Peter Heeringa: None declared, Minke G. Huitema: None declared, M.D. Posthumus: None declared, Maria Sandovici: None declared, Erik Toonen Employee of: Is an employee of Hycult Biotech, Jannik Zijlstra: None declared, Ellen-Margrethe Hauge: None declared, Elisabeth Brouwer: None declared
DOI: 10.1136/annrheumdis-2021-eular.2636

POS0810 PULMONARY FINDINGS ON HIGH-RESOLUTION COMPUTED TOMOGRAPHY IN TAKAYASU ARTERITIS

X. Kong[1], J. Zhang[2], J. Lin[3], P. LV[3], H. Chen[1], Z. Ji[1], X. Dai[1], X. Jin[4], L. Ma[1], L. Jiang[1]. *[1]Zhongshan Hospital Fudan University, Department of Rheumatology, Shanghai, China*; *[2]Zhongshan Hospital Fudan University, Department of Pulmonary Medicine, Shanghai, China*; *[3]Zhongshan Hospital Fudan University, Department of Radiology, Shanghai, China*; *[4]Zhongshan Hospital Fudan University, Department of Clinical Epidemiology Center, Shanghai, China*

Background: Takayasu arteritis (TA) is a chronic granulomatous large-vessel vasculitis most commonly seen in women under 50 years of age[1]. The pulmonary arteries are less often involved, with the frequency of involvement varying widely between countries (from 4% to >50%) [2–5]. Respiratory symptoms or signs and pulmonary imaging findings in TA have not been fully investigated [6–7].
Objectives: This study aimed to describe pulmonary high-resolution computed tomography (HRCT) findings in TA and to determine possible causes.
Methods: A total of 243 TA patients were enrolled from a prospective cohort after excluding 260 patients with other pulmonary disorders or incomplete data. Clinical data including symptoms, lab results, imaging information were collected. Pulmonary HRCT were interpreted by two radiologist who were blinded to patients' clinical information. Abnormal pulmonary features were recorded as nodules, stripe opacity (linear opacity), patchy opacity, ground-glass opacity, pleural thickening, pleural effusion, pulmonary infarction, mosaic attenuation, pulmonary bronchiectasis, pulmonary oedema. After evaluation, patients were divided into two groups: those with normal lung HRCT and those with abnormal lung HRCT. Clinical characteristics were compared between groups and binary logistic regression analysis was applied to identify potential risk factors for the lung lesions. Follow-up HRCT (obtained in 64 patients) was analysed to study changes in pulmonary lesions after at least 6 months' treatment.
Results: Of the 243 patients, 107 (44.0%) had normal lung HRCT while 136 (56.0%) had abnormal lung HRCT, including stripe opacity (60.3%), nodules (44.9%), patchy opacity (25.0%), pleural thickening (15.4%), pleural effusion (10.3%), ground-glass opacity (8.1%), pulmonary infarction (6.6%), mosaic attenuation (4.4%), bronchiectasis (3.7%), and pulmonary oedema (2.2%). Patients with abnormal HRCT were significantly more likely to have type II arterial involvement (25% vs. 12.2%, P = 0.04), pulmonary arterial involvement (PAI; 21.3% vs. 5.6%, P < 0.001), pulmonary hypertension (20.6% vs. 8.4%, P = 0.01), and abnormal heart function (27.9% vs. 7.6%, P < 0.001). Logistic regression analysis demonstrated that PAI (OR = 3.0, 95% CI= 1.1-8.4, P=0.03), worsened heart function (OR = 2.7, 95% CI = 1.1-6.6, P=0.03), and age (OR = 1.1, 95% CI = 1.0-1.1, P<0.01) were associated with presence of pulmonary lesions. Pulmonary infarction, pleural effusion, and patchy opacities improved partially after treatment.
Conclusion: Pulmonary lesions are not rare in patients with TA. Age, PAI, and worsened heart function are potential risk factors for presence of pulmonary lesions in TA.
REFERENCES:
[1] Jennette JC, Falk RJ, Bacon PA, et al. 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013;65:1-11.
[2] Kong X, Ma L, Wu L, et al. Evaluation of clinical measurements and development of new diagnostic criteria for Takayasu arteritis in a Chinese population. Clin Exp Rheumatol. 2015; 33(2 Suppl 89): S-48-55.
[3] Nooshin D, Neda P, Shahdokht S, Ali J. Ten-year Investigation of Clinical, Laboratory and Radiologic Manifestations and Complications in Patients with Takayasu's Arteritis in Three University Hospitals. Malays J Med Sci. 2013; 20(3):44-50.
[4] Bicakcigil M, Aksu K, Kamali S, et al. Takayasu's arteritis in Turkey – clinical and angiographic features of 248 patients. Clin Exp Rheumatol. 2009; 27(1 Suppl 52):S59-64.
[5] Kechaou M, Frigui M, Ben Hmida M, Bahloul Z. Takayasu arteritis in Southern Tunisia a study of 29 patients. Presse Med. 2009; 38(10):1410-4.
[6] Dou JB, Gong JN, Ma ZH, Kuang TG, Yang YH. The analysis of the clinical records diagnosed as Takayasu's arteritis with pulmonary vascular involvement. Zhonghua Jie He Hu Xi Za Zhi. 2016; 39(8):603-7.
[7] Nd Perera G, C Jayasinghe A, D Dias L, Kulatunga A. Bronchiectasis and hoarseness of voice in takayasu arteritis: a rare presentation. BMC Res Notes. 2012; 5:447.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2789

POS0811 EULAR RECOMMENDATIONS ON GIANT CELL ARTERITIS IN REAL LIFE

F. Regola[1], F. Franceschini[1], G. Bosio[2], P. Toniati[1]. [1]*ASST Spedali Civili and University of Brescia, Rheumatology and Clinical Immunology Unit, Brescia, Italy*; [2]*ASST Spedali Civili of Brescia, Nuclear Medicine Unit, Bresica, Italy*

Background: GCA is the most frequent systemic vasculitis in patients older than 50 years involving medium-sized and large arteries. On July 2019 EULAR published its updated recommendations for the management of large vessel vasculitis, including GCA.
Objectives: To analyze how the application of the updated EULAR recommendations changed clinical practice in GCA patients in our Hospital.
Methods: All patients with a new diagnosis of GCA between January 1st, 2018 and December 31st, 2020 were enrolled in this study. Two cohorts were analyzed: patients who received GCA diagnosis in the eighteen months before EULAR recommendations publication (between January 1st, 2018 and June 30th, 2019: cohort A) and patients who received GCA diagnosis in the following eighteen months (between July 1st, 2019 and December 31st, 2020: cohort B). Data are expressed as median (IQR).
Results: 70 patients were enrolled in the study (F: 47, M: 23, age: 76 (69-79) years): 39 patients in cohort A, 31 in cohort B. Table 1 summarize main clinical features and treatment of patients. Sixteen patients of cohort A (41%) and eleven patients of cohort B (35%) presented large vessel involvement demonstrated by FDG-PET/CT. Thirty-one patients in cohort A (79%) and twenty-seven in cohort B (87%) presented cranial symptoms and were studied with temporal arteries ultrasound (US) and/or biopsy (TAB). More specifically, in cohort A US was performed in 42% of patients with cranial symptoms and TAB in 58% of them. After EULAR recommendations publication (cohort B) the percentage of patients with cranial symptoms who performed US increased to 56% and the percentage of TAB decreased to 52%.
After EULAR recommendations publication, time between symptoms onset and first rheumatologic evaluation was reduced by 30% (from 61 (23-131) to 43 (22-92) days).
No difference in treatment regiments were found between groups, whether in glucocorticoid initial dose or DMARDs adjunctive therapy.
Conclusion: After EULAR recommendations publication, two major improvement were achieved in our cohort. EULAR suggests GCA patients should be urgently referred to a specialist team. Consistently with this recommendation, time between symptoms onset and first rheumatologic evaluation was markedly reduced. Moreover, EULAR suggests always confirming GCA diagnosis by imaging or TAB, with US as first choice. In line with these recommendations, in our cohort US became more and more frequently performed and progressively preferred over TAB. On the other hand, no differences in treatment regiments were found over time, with EULAR recommendations satisfied both before and after their publication.
REFERENCES:
[1] Hellmich B, et al. Ann Rheum Dis 2019.

	ALL GCA (n: 70)	Before EULAR recommendations (n: 39)	After EULAR recommendations (n: 31)
Time between symptoms onset and first rheumatologic evaluation (days)	53 (22-110)	61 (23-131)	43 (22-92)
Temporal artery US	28/58 (48%)	13/31 (42%)	15/27 (56%)
Temporal artery biopsy	32/58 (55%)	18/31 (58%)	14/27 (52%)
Large vessel involvement (FDG-PET/CT)	27 (39%)	16 (41%)	11 (35%)
Glucocorticoid initial dose (mg/die prednisone equivalent)	50 (47-50)	50 (50-50)	50 (38-50)
DMARDs	43 (61%)	24 (61%)	19 (61%)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2971

POS0812 SUBCLAVIAN ARTERIES INVOLVEMENT IN PATIENTS WITH GIANT CELL ARTERITIS: DO WE NEED A MODIFIED HALO SCORE?

J. Molina Collada[1], J. Martínez-Barrio[1], B. Serrano-Benavente[1], I. Castrejon[1], J. C. Nieto González[1], L. R. Caballero Motta[1], L. Trives Folguera[1], J. M. Alvaro-Gracia[1]. [1]*Hospital General Universitario Gregorio Marañón, Rheumatology, Madrid, Spain*

Background: EULAR recommendations propose temporal and axillary arteries ultrasound (US) as first-line investigation when predominantly cranial giant cell arteritis (GCA) is suspected. Recently, two novel US scoring systems, the halo count and the Southend Halo Score, have been developed to quantify the extent of inflammation by US in GCA.
Objectives: To assess whether adding the subclavian arteries examination into the ultrasound (US) Southend Halo Score, as proposed in the modified Halo Score, improves the diagnostic accuracy of GCA and its relationship with systemic inflammation.
Methods: Retrospective observational study of patients referred to a GCA fast track pathway (FTP) over a 1-year period. Patients underwent US exam of temporal and large vessel (LV) (carotid, subclavian and axillary) arteries. The extent of inflammation was measured by the halo count, the Southend Halo Score and the modified Halo Score (Image 1). The gold standard for GCA diagnosis was clinical confirmation after 6 months follow-up.
Results: 64 patients were evaluated in the FTP, 17(26.5%) had GCA. Subclavian arteries involvement was present only in patients with GCA (29.4% versus 0%,p<0.001) (Table 1). Overall, the three scores showed excellent diagnostic accuracy for GCA (ROC AUC 0.906, 0.930 and 0.928, respectively) and moderate correlations with acute phase reactants (0.35-0.51, p<0.01). However, in the subgroup of patients presenting LV involvement, moderate correlations were

found between the modified Halo Score and ESR (rho 0.712, p<0.05), haemoglobin (rho 0.703, p<0.05) and platelets (rho 0.734, p<0.05), but not with the other two US scores.

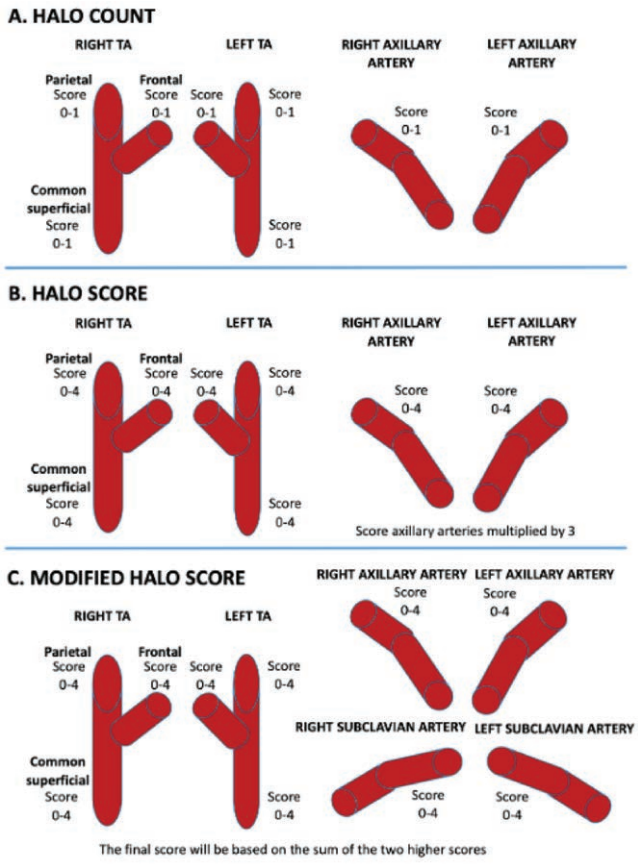


Figure 1. Proposed scores to quantify the extent of vascular inflammation by ultrasound in giant cell arteritis. A. Halo count, B. Halo Score, C: Modified Halo Score

Table 1. Clinical, laboratory and ultrasound findings of patients included in the fast track pathway with or without GCA clinical confirmation.

	Total n=64	Patients with GCA n=17	Patients without GCA n=47	p
Age, median (IQR)	78 (69.3-83)	78 (72.5-83)	78 (66-83)	0.5
Female, n (%)	42 (65.6%)	10 (58.8%)	32 (68.1%)	0.491
Temporal artery biopsy positive n=13, no. of patients	5 (38.5%)	5 (50%)	0 (0%)	0.231
^{18}F-FDG-PET/CT positive n=14, no. of patients	7 (50%)	5 (62.5%)	2 (33.3%)	0.592
Fulfilling 1990 GCA criteria, no. of patients	16 (25%)	8 (47.1%)	8 (17%)	0.022
PMR diagnosis before US examination, no. of patients	21 (32.8%)	4 (23,5%)	17 (36,2%)	0.386
Headache, no. of patients	31 (48.4%)	12 (70.6%)	19 (40.4%)	0.033
Jaw claudication, no. of patients	12 (18.8%)	9 (52.9%)	3 (6.4%)	<0.001
Ocular ischaemia, no. of patients	4 (6.3%)	2 (11.8%)	2 (4.3%)	0.285
Abnormal TA clinical examination, no. of patients	5 (7.8%)	3 (17.6%)	2 (4.3%)	0.112
CRP (mg/dL), median (IQR)	1.7(0-6.5)	7 (2.1-14)	1.1 (0-5.1)	0.001
ESR (mm/h), mean (SD)	52.8 (34.6)	68.3 (33.3)	46.8 (33.3)	0.044
Haemoglobin (g/dL), mean (SD)	12.5 (1.7)	11.8 (1.6)	12.7 (1.7)	0.059
Platelets 10^9/L, mean (SD)	276.1 (105.8)	323.4 (116.3)	258.7 (97.3)	0.52
Positive US findings, no. of patients	17 (26.6%)	15 (88.2%)	2 (4.3%)	<0.001
Temporal artery positive US findings, no. of patients	13 (20.3%)	12 (70.6%)	1 (2.1%)	<0.001
Axillary positive US findings, no. of patients	9 (14.1%)	8 (47.1%)	1 (2.1%)	<0.001
Subclavian positive US findings, no. of patients	5 (7.8%)	5 (29.4%)	0 (0%)	<0.001
Temporal artery + axillary or subclavian positive US findings, no. of patients	5 (7.9%)	5 (29.4%)	0 (0%)	0.003
Halo Count, median (IQR)	0 (0-0.75)	2 (1-4.5)	0 (0-0)	<0.001
Halo Score, median (IQR)	0 (0-4.5)	18 (7-22.5))	0 (0-0)	<0.001
Modified Halo Score, median (IQR)	0 (0-2.75)	8 (3-13.5)	0 (0-0)	<0.001

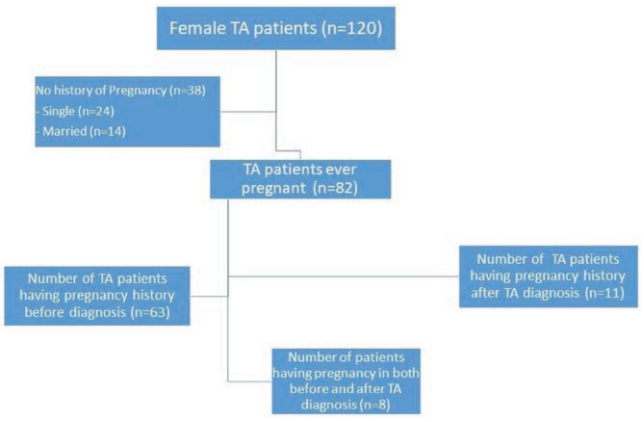
Conclusion: The inclusion of subclavian arteries examination in the modified Halo Score does not improve the diagnostic accuracy of GCA. Nevertheless, it correlates better with markers of systemic inflammation in LV-GCA

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3129

POS0813 FERTILITY AND PREGNANCY OUTCOMES IN TAKAYASU'S ARTERITIS

A. Taghiyeva[1], L. Kılıç[2], M. Cagan[3], E. C. Bolek[2], G. K. Yardımcı[2], O. Karadag[2], O. Ozyuncu[3], Ş. A. Bilgen[2]. [1]*Hacettepe University Faculty of Medicine, İnternal Medicine, Ankara, Turkey*; [2]*Hacettepe University Faculty of Medicine, Department of Internal Diseases Rheumatology, Ankara, Turkey*; [3]*Hacettepe University Faculty of Medicine, Department of Obstetrics and Gynecology, Ankara, Turkey*

Background: Takayasu's arteritis (TA) is commonly seen in women of childbearing ages; therefore, reproductive health of TA patients is an important issue.
Objectives: We aimed to evaluate the fertility and pregnancy (PG) outcomes of TA patients before and after diagnosis.
Methods: In the prospective database of the Hacettepe University Vasculitis Research Centre (HUVAC), 202 TA patients (female =184) meeting the 1990 ACR criteria were registered by the end of February 2020. 120 patients who could be reached out gynaecological records and marriage status, were included in the study. We identified 233 PG in 82 of included these 120 TA patients (Figure 1). Demographic and clinical features, comorbidities, distribution of vascular involvement, obstetrical histories and outcomes were retrospectively evaluated. Patients were classified according to a novel proposed disease clusters (C1: Abdominal Predominant, C2: Aortic Arch Predominant, C3: Focal Disease) using the defined decision tree.
Results: 12 of 96 (12.5%) married TA patients had infertility being defined as not being able to get pregnant after one year (or longer) of unprotected sex. 20 (16.7%) women had menopause before the age of 45, being defined as early menopause (EM). Compared to normal population, infertility (12.5% vs. 8.1%) and EM ratios (16.7% vs. 7.6%) seem to be increased in TA patients. (1, 2)
200 PG had occurred before TA diagnosis (bTA) in 71 women, and 33 PG were observed after TA diagnosis (aTA) diagnosis in 19 women (two patients diagnosed during PG). According to novel disease subsets, aTA patients classified into C1 (n=3; 15.7%), C2 (n=9; 47.3%) and C3 (n=6; 31.5%). One patient could not be classified.
GHT was seen in 4 (12.1%) patients being the most frequent maternal complication in aTA group. Most common fetal complications were prematurity, IUGR and LBW in both groups (Table 1). Even fetal complications were more frequent in aTA group, it was not statistically significant [11 (33.3%) vs. 43 (21.5%), p=0.18 respectively]. However, maternal complications were significantly more common in aTA group [22 (11.0%) vs. 8 (24.2%), p=0.048]. There was no difference for the obstetrical outcomes in terms of novel TA classification.



Conclusion: This study showed increased infertility and EM ratios in TA patients. PG of aTA had more complications in terms of maternal complications. Fetal complications were more frequent in PG of aTA but not statistically significant. Larger cohort data is required.

REFERENCES:
[1] doi:10.1017/s0021932017000244.
[2] doi:10.1016/j.maturitas.2019.03.008.

	Pregnancies		p
	Before TA (n=200)	After TA (n=33)	
Number of Patients	71	19	*NP*
Age at TA diagnosis, years mean (SD)	38.2 (13.1)	24.0 (6.6)	
Age at first pregnancy	21.7 (5.0)	27.6 (5.0)	
Comorbidities/CV Risk factors n(%)	**n (%)**		**p**
- Smoking	22 (31)	3 (15.8)	>0.05
- Dyslipidemia	14 (19.7)	1 (5.3)	
- Hypertension	29 (40.8)	9 (47.4)	
- Diabetes mellitus	8 (11.3)	0 (0)	
Maternal Complications	**n (%)**		
Numbers of pregnancies with any maternal complications	22 (11.0)	8 (24.2)	0.048
- Gestational hypertension	6 (3.0)	4 (12,1)	*NP*
- PROM	6 (3.0)	1 (3.0)	
- GDM	0 (0)	0 (0)	
- Bleeding (Antepartum/ postpatum)	6 (3.0)	2 (6.1)	
- Preeclampsia	0 (0.0)	0 (0.0)	
- İnfection	5 (2.5)	1 (3.0)	
- Placenta previa	0 (0)	1 (3.0)	
Fetal Complications	**n (%)**		**p**
Numbers of pregnancies with any fetal complications	43 (21.5)	11 (33.3)	0.180
- LBW	16 (8.0)	6 (18.2)	*NP*
- IUGR	20 (1.0)	5 (15.2)	
- Preterm birth	13 (6.5)	7 (21.2)	
- CNS complications	2 (1.0)	1 (3.0)	
- Cardiovascular complications	3 (1.5)	0 (0)	
- RDS_BPD	4 (2.0)	0 (0)	
- NICU admission	12 (6.0)	1 (3.0)	
- Other	5 (2.5)	0 (0)	
- Neonatal death	5 (2.5)	0 (0)	
- Retinopathy of prematurity	1 (0.5)	0 (0)	
- Stillbirth	7 (3.5)	0 (0)	
Delivery	**n (%)**		**P**
Vaginal delivery	128 (64)	6 (18.2)	<0.001
Cesarean	24 (12)	13 (39.4)	<0.001
Spontaneous abortus	21 (10.5)	7 (21.2)	0.088
Termination of pregnancy	18 (9.0)	7 (21.2)	0.061

Abbreviations: BPD: Bronchopulmonary dysplasia, **CNS:** Central nervous system, **GDM:** Gestational diabetes mellitus, **IUGR:** Intrauterin growth restriction, **LBW:** Low birth weight, **NICU:** Neonatal Intensive Care Unit, **NP:** Not performed **PROM:** Premature rupture of membranes, **RDS:** Respiratory distress syndrome

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3231

POS0814

DRUG RETENTION RATE, REASONS FOR DISCONTINUATION AND OUTCOME OF INFLIXIMAB USE IN BEHÇET SYNDROME

S. N. Esatoglu[1,2], B. Tukek[3], S. S. Taflan[3], Y. Ozyazgan[4], D. Ucar[4], V. Hamuryudan[1,2], Y. Ozguler[1,2], E. Seyahi[1,2], M. Melikoglu[1,2], U. Uygunoglu[5], A. Siva[5], Z. Kutlubay[6], I. Fresko[1,2], S. Yurdakul[1], H. Yazici[1,2], G. Hatemi[1,2].
[1]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey; *[2]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Behcet Disease Center, Istanbul, Turkey*; *[3]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Istanbul, Turkey*; *[4]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Ophthalmology, Istanbul, Turkey*; *[5]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Neurology, Istanbul, Turkey*; *[6]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Dermatology, Istanbul, Turkey*

Background: Infliximab (IFX) plays a key role in the management of severe and refractory manifestations of Behçet syndrome (BS). However we had previously shown that its sustained use may be limited due to adverse events and lack of patient compliance (1).
Objectives: To assess the retention rate of IFX, adverse events, causes of discontinuation and outcome after cessation of IFX in a larger group of BS patients who were followed in a tertiary center.
Methods: The charts of BS patients who were prescribed IFX between 2004 and 2020 were reviewed to determine demographic features, reasons for IFX use, previous and concomitant drugs, IFX duration, reasons for cessation of IFX and time to flare following cessation of IFX. Follow-up was censored on March 2020.
Results: A total of 252 patients (195 men, mean age 40±10 years) received IFX for uveitis (n=122), vascular involvement (n=82), parenchymal neurologic involvement (n=32), gastrointestinal involvement (n=11), arthritis (n=10), mucocutaneous involvement (n=4), and secondary amyloidosis (n=1). Ten patients had more than 1 involvement requiring IFX.
During a median follow-up of 52 (IQR: 30-88) months, 122 (48%) patients were still receiving IFX for a median period of 33 (IQR: 15-56) months while 130 (52%) patients had discontinued IFX after a median follow-up of 17 (IQR: 7-31) months. Reasons for discontinuation were remission in 25 (19%) patients, adverse events in 39 (30%), lack of efficacy in 23 (18%) (4 primary and 19 secondary), lack of patient compliance in 36 (28%), pregnancy in 4, and preparation for surgery in 3 patients.
Adverse events (n=39) that required the cessation of IFX were infusion reaction (n=17), infection (n=7), hepatotoxicity (n=4), malignancy (n=4), palmoplantar psoriasis (n=3), lichen planus (n=1), drug induced lupus (n=1), splenic infarction (n=1), and a decrease in left ventricular ejection fraction (n=1).
Among the 25 patients who discontinued IFX due to remission, 5 (20%) had a relapse after 4, 21, 26, 29, 38 and 46 months. The remaining patients did not experience a relapse during a median follow-up of 35 (IQR: 24-68) months.

Reasons for infliximab treatment	No of patients	No (%) of patients who were still receiving infliximab	Number (%) of patients who discontinued infliximab	Reasons for discontinuation	Duration of infliximab use (median (IQR) months)
Eye involvement	122	59 (48)	63 (52)	Remission (n=17) Inefficacy (n=10) Lack of patient compliance (n=19) Adverse event (n=12) Others (n)=5)	28 (12.5-52)
Vascular involvement	82	40 (49)	42 (51)	Remission (n=10) Inefficacy (n=7) Lack of patient compliance (n=12) Adverse event (n=12) Others (n=4)	18.5 (9-33.5)
Parenchymal neurologic involvement	32	21 (66)	11 (34)	Adverse event (n=8) Inefficacy (n=2) Lack of patient compliance (n=1)	25 (14.5-50)
Gastrointestinal involvement	11	4 (36)	7 (64)	Remission (n=1) Inefficacy (n=1) Adverse event (n=2) Lack of patient compliance (n=4)	7 (2-17)
Joint involvement	10	2 (20)	8 (80)	Inefficacy (n=1) Adverse event (n=5) Lack of patient compliance (n=2)	20 (4-35)
Mucocutaneous involvement	4	3	1	Inefficacy (n=1)	6, 10, 12, 104 months
AA amyloidosis	1	0	1	Inefficacy (n=1)	6 years

At the end of the follow-up, 2 patients had died due to lung adenocarcinoma during IFX treatment and 3 patients had died 1 year, 3 and 8 years after IFX discontinuation. The causes of death were with right heart failure due to pulmonary hypertension in 1, and severe nervous system involvement in 2 of the patients.

Conclusion: Despite its successful use for the management of potentially organ and life-threatening manifestations in more than half of our patients with BS, long term maintenance was not possible in 42%, mainly due to adverse events, lack of patient compliance and inefficacy.

REFERENCE:

[1] Esatoglu SN, Tukek B, Taflan SS, et al. SAT0258 Drug Retention Rate and Prognosis After Discontinuation of Infliximab in Patients with Behçet Syndrome. Annals of the Rheumatic Diseases 2020;79: 1071-1072.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3262

POS0815 CLINICAL CHARACTERISTICS, IMAGING PHENOTYPE, AND LONG-TERM OUTCOMES OF TAKAYASU ARTERITIS PATIENTS WITH HYPERTENSION

Y. Sun[1], L. Ma[1], H. Chen[1,2], C. Rongyi[2], L. Jiang[2]. [1]*Zhonngshan Hospital, Fudan University, Rheumatology, Shanghai, China*; [2]*Zhonngshan Hospital, Fudan University, Rheumatology, Shanghai, China*

Background: Hypertension occurred in 30-80% of TAK patients around the world. The occurrence of hypertension might severely worsen TAK prognosis. Nevertheless, data describing the specific imaging features in hypertensive TAK patients and the associations between hypertensive severity, blood pressure control status and long-term outcome were still lacking.

Objectives: To investigate the characteristics and associations of hypertensive characteristics with adverse events-free survival in Takayasu arteritis (TAK) patients with hypertension.

Methods: This research was based on a prospectively on-going observational cohort-East China Takayasu Arteritis (ECTA) cohort. In all, 618 TAK patients, who registered in the ECTA cohort up to December 2019, were enrolled. The main outcome was the adverse-events-free survival among hypertensive TAK patients during the follow-up ended on August 2020.

Results: Totally, 204 (33.0%) patients suffered from hypertension, with 48 (23.5%), 62 (30.4%), and 94 (46.1%) mild, moderate, and severe hypertension, respectively. Cluster analysis indicated three imaging phenotypes for hypertensive TAK patients: Cluster 1: involvement of the abdominal aorta and/or renal artery (n=56, 27.5%); Cluster 2: involvement of the ascending aorta, thoracic aorta, and the aortic arch and its branches (n=38, 18.6%); Cluster 3: combined involvement of Cluster 1 and Cluster 2 (n=111, 54.4%). By the end of the follow-up, the blood pressure control rate was 50.8%, while the adverse-events-free survival was 67.9% in the entire hypertensive population. Multivariate Cox regression analysis indicated that well-controlled blood pressure (HR=2.13, 95%CI 1.32–3.78, p=0.047), co-existence of severe aortic valve regurgitation (HR=0.87, 95%CI 0.64–0.95, p=0.043), Cluster 1 (HR=0.69, 95%CI 0.48–0.92, p=0.017) and Cluster 3 (HR=0.72, 95%CI 0.43–0.94, p=0.048) imaging phenotype was associated with the adverse-events-free survival.

Conclusion: Patients with controlled hypertension showed better adverse-events-free survival, while those with the Cluster 1 imaging phenotype were more likely to suffer from worse adverse-events-free survival. Hypertension occurred in 30-80% of TAK patients around the world. The occurrence of hypertension might severely worsen TAK prognosis.

REFERENCES:

[1] Johnston SL, Lock RJ, Gompels MM. Takayasu arteritis: a review. *J Clin Pathol* 2002; 55:481–6.

[2] Watanabe Y, Miyata T, Tanemoto K. Current clinical features of new patients with Takayasu arteritis observed from a cross-country research in Japan: age and sex specificity. *Circulation* 2015; 132:1701–9.

[3] Yilmaz N, Can M, Oner FA, et al. Impaired quality of life, disability and mental health in Takayasu's arteritis. *Rheumatol.* (Oxford) 2013; 52:1898–904.

[4] Laurent A, Julien H, Nicolas L, et al. Takayasu arteritis in France: a single-center retrospective study of 82 cases comparing white, North African, and black patients. *Medicine* 2010; 89:1–17.

[5] Mwipatayi BP, Jeffery PC, Beningfield SJ, et al. Takayasu arteritis: clinical features and management: report of 272 cases. *ANZ J Surg* 2005; 75:110–7.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3494

POS0816 PROGNOSTIC FACTORS FOR AGGRAVATED VASCULAR DAMAGE IN TAKAYASU ARTERITIS

R. Chen[1,1], L. Ma[1], Y. Liu[1], L. Ma[1], L. Jiang[1]. [1]*Zhongshan Hospital Fudan University, Rheumatology, Shanghai, China*

Background: Takayasu arteritis is a rare disease characterized by inflammation in the aorta and its branches. Some patients were discovered to suffer the aggravated vascular damage (AVD), monitored by imaging techniques, even with the effective anti-inflammation treatment. But the general characteristics and the related prognostic factors of AVD in TA were unclear yet.

Objectives: We aimed to describe the characteristics of the AVD and identify its prognostic factors in TA.

Methods: From the living East China Takayasu arteritis cohort, patients who underwent at least two magnetic resonance angiography (MRA) examinations at Zhongshan Hospital from April 2009 to April 2019 were enrolled as the derivation cohort to explore the prognostic factors of AVD in MRA. An independent group of patients from May 2019 to July 2020 comprising the validation cohort were used to validate the nomogram formed by these prognostic factors.

Results: Among 235 enrolled patients, 69 patients (29.3%) suffered AVD with the median follow-up of 14 months. The limb arteries were the most vulnerable and the aggravated vascular stenosis were the most commonly seen in AVD. Patients with AVD were younger, had higher complement 4 levels at baseline, and lower disease remission rate at 6 months. Multivariate cox regression analysis revealed that younger age (HR: 0.25-0.42, 95%CI: 0.09-0.91), higher CRP levels (HR = 2.57, 95%CI: 1.51–4.36) at baseline, and lower remission rate at 6 months (HR = 0.36, 95%CI: 0.21–0.64) were significant predictors. In the validation cohort of 65 patients, 19 cases had AVD. The predictive nomogram based on these factors achieved C-indices of 0.745 and 0.641 in the derivation and validation cohort respectively.

Conclusion: Totally, 29.3% of patients suffered AVD, among which the aggravated vascular stenosis and limb arteries involvement were most commonly seen. Younger age, higher CRP at baseline, and lower disease remission rate at 6 months were prognostic factors for AVD.

REFERENCES:

[1] M. Bredemeier, C.M. Rocha, M.V. Barbosa, E.H. Pitrez. One-year clinical and radiological evolution of a patient with refractory Takayasu's arteritis under treatment with tocilizumab. Clin Exp Rheumatol 2012; 30 (Suppl. 70): S98-S100.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3720

POS0817 A NOVEL MODEL TO ASSESS DISEASE ACTIVITY IN TAKAYASU ARTERITIS BASED ON 18F-FDG-PET/CT: A CHINESE COHORT STUDY

L. Ma[1], B. Wu[2], X. Jin[3], Y. Sun[1], X. Kong[1], Z. Ji[1], R. Chen[1], X. Cui[1], H. Shi[2], L. Jiang[1]. [1]*Zhongshan Hospital, Fudan University, Department of Rheumatology, Shanghai, China*; [2]*Zhongshan Hospital, Fudan University, Department of Nuclear Medicine, Shanghai, China*; [3]*Zhongshan Hospital, Fudan University, Department of Medical Statistics, Shanghai, China*

Background: Takayasu arteritis (TA) is a condition characterized by major large-vessel vasculitis (LVV), and is most commonly found in young women (age <40 years) of East Asia countries. 18F-FDG-PET/CT has been widely used in the diagnosis and follow-up of cancers to gather functional information based on metabolic activity. In the present study, we evaluated the value of different parameters in 18F-FDG-PET/CT for assessing active TA disease, and we establish a simple, quantifiable, and effective disease activity evaluation model based on 18F-FDG-PET/CT. A comparison in the ability to identify active disease was performed between the established Kerr score and the new 18F-FDG-PET/CT was also performed.

Objectives: To investigate the utility of 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG-PET/CT) in assessing disease activity in TA.

Methods: Ninety-one patients with TA, were recruited from a Chinese cohort from October 2017 to January 2019. Clinical data, acute-phase reactants (APRs), and 18F-FDG-PET/CT findings were simultaneously recorded. The Physician Global Assessment was used as the gold standard to assess TA disease activity. The value of using 18F-FDG-PET/CT to identify active disease

was evaluated, using erythrocyte sedimentation rate (ESR) as a reference. Disease activity assessment models were constructed and concordance index (C-index), net reclassification index (NRI), and integrated discrimination index (IDI) were evaluated to compare the benefits of the new modes with ESR and Kerr score.

Results: In total, 64 (70.3%) cases showed active disease. Higher levels of ESR and CRP, and lower interleukin (IL)-2R levels, were observed in active cases. 18F-FDG-PET/CT parameters, including SUVmean, SUVratio1, SUVratio2, sum of SUVmean, and sum of SUVmax, were significantly higher in active disease groups. The C index threshold of ESR to indicate active disease was 0.78 (95% CI: 0.69-0.88). The new activity assessment model combining ESR, sum of SUVmean, and IL-2R showed significant improvement in C index over the ESR method (0.96 vs. 0.78, P < 0.01; NRI 1.63, P < 0.01; and IDI 0.48, P < 0.01). The new model also demonstrated modest superiority to Kerr score assessment (0.96 vs. 0.87, P = 0.03; NRI 1.19, P < 0.01; and IDI 0.33 P < 0.01).

Conclusion: A novel 18F-FDG-PET/CT-based method that involves combining the sum of SUVmean with ESR score and IL-2R levels demonstrated superiority in identifying active TA compared to conventional methods.

REFERENCES:

[1] Kerr GS, Hallahan CW, Giordano J, Leavitt RY, Fauci AS, Rottem M, et al. Takayasu arteritis. Ann Intern Med 1994;120:919-29.
[2] Hoffman GS, Ahmed AE. Surrogate markers of disease activity in patients with Takayasu arteritis. A preliminary report from The International Network for the Study of the Systemic Vasculitides (INSSYS). Int J Cardiol 1998;66 Suppl 1:S191-4; discussion S195.
[3] Misra R, Danda D, Rajappa SM, Ghosh A, Gupta R, Mahendranath KM, et al. Development and initial validation of the Indian Takayasu Clinical Activity Score (ITAS2010). Rheumatology (Oxford) 2013;52:1795-801.
[4] Bardi M, Diamantopoulos AP. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice summary. Radiol Med 2019;124:965-972.
[5] Spick C, Herrmann K, Czernin J. 18F-FDG PET/CT and PET/MRI Perform Equally Well in Cancer: Evidence from Studies on More Than 2,300 Patients. J Nucl Med 2016;57:420-30.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3739

POS0818 TREATMENT OF POLYMYALGIA RHEUMATICA WITH TOCILIZUMAB: RESULTS OF AN OBSERVATIONAL RETROSPECTIVE MULTICENTER STUDY

M. Assaraf[1], B. Chevet[2], P. Philippe[1], J. Avouac[3], M. Delacour[4], E. Houvenagel[5], T. Pascart[5], J. Henry[6], C. Roux[7], D. Wendling[8], J. Paccou[1], B. Cortet[1], V. Devauchelle-Pensec[2], R. M. Flipo[1]. *[1]Lille University Hospital, Rheumatology, Lille, France*; *[2]Brest University Hospital, Rheumatology, Brest, France*; *[3]Cochin University Hospital, Rheumatology, Paris, France*; *[4]Arras Hospital Medical Center, Rheumatology, Arras, France*; *[5]Saint Philibert University Hospital, Rheumatology, Lomme, France*; *[6]Kremlin Bicêtre Univeristy Hospital, Rheumatology, Paris, France*; *[7]Nice University Hospital, Rheumatology, Nice, France*; *[8]Besançon University Hospital, Rheumatology, Besançon, France*

Background: In 2017, TOCILIZUMAB (TCZ) obtained marketing authorization for treatment of giant cell arteritis (GCA); however, this doesn't extend to polymyalgia rheumatica (PMR) therapy. Based on efficacy data for TCZ in GCA, TCZ is sometimes used as a glucocorticoid (GC) sparing agent when PMR is GC dependent or when a rapid steroid withdraw is needed. Currently, there are no available recommendations on the use of this therapeutic class in for this particular indication.

Objectives: Here, we present the results of an observational French multicentric study of patients with PMR treated with TCZ.

Methods: Thirteen medical centers were included in this study. The data was collected retrospectively between 2015 and 2020. The minimum duration of treatment was 3 months. Patients were included when receiving TCZ for isolated PMR or associated with a non-active GCA (asymptomatic, no vascular fixation on PET scanner).

Results: Overall, 34 patients were included (24 women; mean age 70.1 years (+/-10.3)). At TCZ introduction, patients had been treated with GC for a mean duration of 27,9 months (+/-25.9) and the mean GC dose was 16,8mg/d (+/-10). Fifteen patients (44%) had one or more complications from GC therapy. Another immunosuppressant was added before TCZ treatment for 25 (74%); mostly METHOTREXATE (24/25).

TCZ was initiated intravenously at 8mg/kg every 4 weeks for 27 patients (79%) and subcutaneously at 162mg/week for 7 patients (21%).

The reasons for TCZ introduction included GC dependence (n=30, 88%), and necessity of quick GC sparing (n=4 patients,12%).

Of all patients, 76% (26 patients) had stopped GC treatment definitively, with a mean time of 9,4 (0-32) months.

The mean TCZ treatment period was 19,2 months (3-66). Fifteen patients (44%) permanently stopped TCZ at the end of the observation period (8 prolonged remissions;1 myocardial infarction; 1 cutaneous lymphoma; 1 primary failure, 3 lost to follow up).

Eighteen patients (60%) benefited from an attempted tapering of TCZ (infusion spacing or dose reduction), 6 attempts (1/3) led to a relapse. 1/2 patients had side effects mostly benign (cytopenia n=6, infections n=5).

Conclusion: This is the largest cohort presenting results of the use of TCZ in PMR. Despite the small number of participants, our study suggests TCZ is effective as a GC sparing agent in PMR. As there are no official recommendations of use, indications for TCZ use within this population are no defined. Randomized Controlled Trial would be beneficial to validate these first results.

REFERENCES:

[1] Toussirot, « Biothérapies, pseudo- polyarthrite rhizomélique et artérite à cellules géantes État des lieux en 2018 ».
[2] Devauchelle-Pensec et al., « Efficacy of First-Line Tocilizumab Therapy in Early Polymyalgia Rheumatica ».
[3] Genovese et al., « Longterm Safety and Efficacy of Tocilizumab in Patients with Rheumatoid Arthritis ».
[4] Stone et al., « Trial of Tocilizumab in Giant-Cell Arteritis ».

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3885

POS0819 EMERGENCE OF DE NOVO MANIFESTATIONS DURING INFLIXIMAB TREATMENT IN BEHÇET SYNDROME

B. Tukek[1], S. N. Esatoglu[2,3], G. Hatemi[2,3], E. B. Caliskan[1], Y. Ozyazgan[4], D. Ucar[4], Y. Ozguler[2,3], E. Seyahi[2,3], M. Melikoglu[2,3], U. Uygunoglu[5], A. Siva[5], Z. Kutlubay[6], I. Fresko[2,3], S. Yurdakul[2,3], H. Yazici[2,3], V. Hamuryudan[2,3]. *[1]Istanbul University - Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Istanbul,Turkey*; *[2]Istanbul University - Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul,Turkey*; *[3]Istanbul University - Cerrahpasa, Cerrahpasa Medical Faculty, Behcet Disease Center, Istanbul,Turkey*; *[4]Istanbul University - Cerrahpasa, Cerrahpasa Medical Faculty, Department of Ophthalmology, Istanbul,Turkey*; *[5]Istanbul University - Cerrahpasa, Cerrahpasa Medical Faculty, Department of Neurology, Istanbul,Turkey*; *[6]Istanbul University - Cerrahpasa, Cerrahpasa Medical Faculty, Department of Dermatology, Istanbul,Turkey*

Background: Infliximab (IFX) is increasingly used in the management of severe, relapsing or refractory manifestations of Behçet Syndrome (BS). Emergence of de novo manifestations have been reported during IFX treatment, despite efficacy for the initial manifestation that required IFX use[1].

Objectives: We aimed to survey a sizeable cohort of BS patients treated with IFX for the development of de novo manifestations during treatment.

Methods: A chart review was conducted to identify all BS patients who were given IFX in our Behçet Disease Research Center between 2004 and 2020. Demographic data, indications for IFX initiation, concomitant drugs, prior treatments, and outcomes were recorded. De novo manifestations were defined as new BS manifestations that had not occurred before IFX treatment.

Results: A total of 252 patients used IFX with the main indications being uveitis in 122, vascular involvement in 82, parenchymal central nervous system involvement in 32, gastrointestinal involvement in 11, arthritis in 10, mucocutaneous involvement in 4, and secondary amyloidosis in 1. Of these patients, 17 (6%) had developed a total of 21 de-novo manifestations during a mean follow-up of 38.4 ± 92 (SD) months (Table 1). Vascular involvement was the main indication for IFX in the majority (n=12; 71%) of these 17 patients followed by eye involvement (n=3; 18%), central nervous system involvement (n=1), and joint involvement (n=1). Concomitant medications were prednisolone in 14 patients, azathioprine in 6 patients, mycophenolate mofetil, cyclosporine-A and methotrexate in 1 patient each. Thirteen patients (76%) were in remission for the main indication when de-novo manifestations emerged. In 10 patients IFX treatment was intensified either by increasing the dose to

10 mg/kg (2 patients) or by shortening the infusion intervals to 4 weeks (2 patients) along with the addition of corticosteroids or immunosuppressives. In the remaining 7 patients IFX was switched to another agent (cyclophosphamide in 5, adalimumab in 1 and anakinra in 1). At the time of this survey 8/17 patients were still on IFX for a mean follow-up of 32.5 ± 24.6 (SD) months, with concomitant low dose prednisolone in 5, azathioprine in 3 and mycophenolate mofetil in 3. In addition to the 7 patients who discontinued IFX at the time of de-novo manifestations, 2 more patients had discontinued IFX due to allergic reactions.

Conclusion: De novo manifestations developed during IFX treatment in 6% of BS patients, despite efficacy for the initial manifestation. Appearance of de novo manifestations mostly in patients with vascular involvement is noteworthy. Intensification of IFX treatment was efficacious in managing de novo manifestations in more than half of these patients.

REFERENCES:

[1] Hamuryudan V et al. Semin Arthritis Rheum. 2015;45(3):369-73.

Table 1. Distribution of de novo manifestations that have emerged in 17 patients

De-novo manifestations	21
Pulmonary artery aneurysm	1
Pulmonary artery thrombosis	2
Coronary artery involvement	3
Superficial thrombophlebitis	5
Arthritis	5
Erythema nodosum	3
Gastrointestinal involvement	1
Central nervous system involvement	1

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3887

POS0820 INFLIXIMAB FOR VASCULAR INVOLVEMENT IN BEHÇET SYNDROME

G. Hatemi[1,2], B. Tukek[3], S. N. Esatoglu[1,2], Y. Ozguler[1,2], M. Melikoglu[1,2], E. B. Caliskan[3], S. Ugurlu[1,2], I. Fresko[1,2], S. Yurdakul[1,2], H. Yazici[1,2], V. Hamuryudan[1,2]. *[1]Istanbul University - Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*; *[2]Istanbul University - Cerrahpasa, Cerrahpasa Medical Faculty, Behcet Disease Center, Istanbul, Turkey*; *[3]Istanbul University - Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Istanbul, Turkey*

Background: Vascular involvement is an important cause of morbidity and mortality in patients with Behçet syndrome (BS). TNF inhibitors have been reported to be effective for almost all serious manifestations of BS but data on vascular involvement is still limited.

Objectives: To survey the efficacy and safety of infliximab (IFX) in BS patients with vascular involvement followed in a dedicated tertiary center.

Methods: We reviewed the charts of all BS patients who used IFX and identified those who used this drug for vascular involvement. A standard form was used for extracting data on demographic and clinical features, type of vascular involvement, concomitant immunosuppressives, duration of IFX use, relapses, adverse events and outcome.

Results: 83 patients (67 men, 16 women, mean age 39.5 ± 8.4 SD years) had used IFX for vascular involvement. The number of patients with each type of vascular involvement as the main indication for IFX, and previous treatment modalities right before IFX are presented in the Table 1. 33 patients had more than 1 type of vascular lesion. Additional organ manifestations were eye involvement in 32, central nervous system involvement in 4 and gastrointestinal involvement in 3 patients. All but one patient used IFX at a dose of 5 mg/kg every 6-8 weeks. All patients used concomitant prednisolone and 51 received pulse methylprednisolone during induction. Other concomitant medications were azathioprine in 21 and mycophenolate mofetil in 4 patients. Outcome of IFX treatment at the end of a mean follow-up of 25.9 months (range 1-103) is tabulated according to arterial and venous involvement (Table 1). Overall, 57/83 (68%) patients obtained remission with no further relapses and IFX could be stopped in 12 (14%) of them. IFX was discontinued due to adverse events in 15 patients. These were allergic reactions in 8, tuberculosis, disseminated zona, lung adenocarcinoma, fibromyxoid sarcoma, heart failure, systemic lupus erythematosus, and palmoplantar pustulosis in 1 patient each. Three patients had died. Causes of death were lung adenocarcinoma in one patient and pulmonary hypertension related right heart failure due to pulmonary artery thrombosis in 2 patients.

Conclusion: Infliximab seems to be beneficial in Behçet syndrome patients with vascular involvement, even in those who are refractory to immunosuppressives and corticosteroids. No further relapses occurred in 68% of the patients, and adverse events leading to discontinuation were observed in 18%.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3971

Table 1.

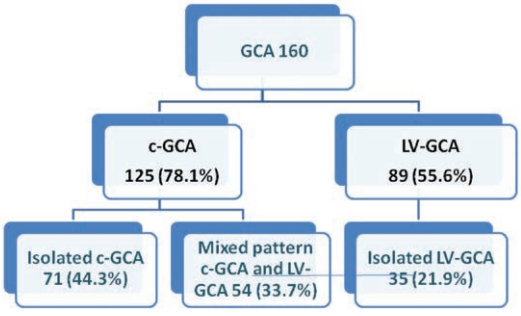
	Arterial Involvement (n=36)	Venous Involvement (n=47)
Main reason for infliximab use	Pulmonary artery aneurysm and/or thrombosis, n=29 Peripheral artery aneurysm, n=4 Aortic aneurysm, n=3	Vena cava superior and/or inferior thrombosis, n=5 Lower extremity DVT, n=24 Budd-Chiari syndrome, n=4 Intracardiac thrombosis, n=2 Dural sinus thrombosis, n=7 Leg ulcer, n=5
		Previous treatment
First line infliximab	4	13
Corticosteroids	34	38
Cyclophosphamide (CYC)	25 (15/25 refractory to CYC; 10/25 for maintenance after CYC)	11 (8/11 refractory to CYC; 3/11 for maintenance after CYC)
Interferon-alpha	-	13
Azathioprine	21	17
Mycophenolate Mofetil	1	2
Cyclosporine A	-	2
None due to non-compliance	2	1
Outcome		
Remission, still on infliximab	16	23
Discontinued due to remission	4	8
Discontinued due to adverse events	5	9
Discontinued due to relapse	5	3
Discontinued due to non-compliance	5	3
Died	2 (1 had previously discontinued due to relapse)	1

POS0821

THE DIFFERENT SUBTYPES OF GIANT CELL ARTERITIS BY ULTRASOUND: RESULTS FROM A FAST-TRACK CLINIC

I. Monjo[1], E. Fernández-Fernández[1], J. Ortega[2], E. De Miguel[1]. [1]*La Paz University Hospital, Rheumatology, Madrid, Spain*; [2]*Universidad Autónoma de Madrid, School of Medicine, Madrid, Spain*

Background: Giant cell arteritis (GCA) is a vasculitis that affects the medium and large vessels (LV). Although cranial artery involvement is better known, awareness of the importance of LV involvement is increasing. Imaging techniques currently constitute the basis for the diagnosis of LV-GCA and have improved its diagnosis and prevalence. In recent years, differences in clinical patterns and different inflammatory and etiopathogenic mechanisms of the disease have been suggested. Therefore, improving sensitivity to diagnosis is essential to improve the knowledge and care of our population.
Objectives: The aim of this study was to know the prevalence of the different ultrasound patterns of GCA in our area.
Methods: Retrospective records of available data were collected from all patients referred to our ACG fast track clinic in the past three years. The clinical and laboratory characteristics were evaluated at the time of referral. All patients underwent an ultrasound scan of cranial vessels (superficial temporal arteries (TA) and their frontal and parietal branches) and large vessels (axillary, subclavian and carotid arteries). The doctor confirmed the GCA diagnosis after at least six months of follow-up. The OMERACT definitions of halo sign with a hypoechoic wall thickness ≥ 0.34 mm were used for TA pathology for the ultrasound diagnosis of GCA and for axillary, subclavian and carotid arteries and homogeneous hypoechoic thicknesses ≥ 1 mm of the arterial wall were applied. Atherosclerosis lesions were evaluated to detect this disease as a possible false positive halo sign. An Esaote Mylab Twice with a 13 MHz probe in BT and 22 MHz for cranial vessels in 2017-2019 and an Esaote Mylab X8plus with a 15 MHz probe for BT and a 24 MHz probe for cranial arteries in 2019-2020 were used by two rheumatologist with long experience in ACG ultrasound.
Results: A total of 261 patients (180 women / 81 men) with suspected GCA were evaluated in our fast track clinic. The mean age (± SD) was 76 ± 9.2 years and CRP at diagnosis was 75.7 ± 68.6 mg/L. The time elapsed since the first symptoms was less than 6, 6-12, 12-24 or >24 weeks in 37.5%, 19.9%, 12.3% and 15.7% respectively. Of the 261 cases explored, 160 had GCA, of which 102 were women and 58 men, and had a mean age of 77.21 ± 7.9 years. The ultrasound patterns of GCA were: 71 patients had exclusive involvement of the TA (cranial-GCA), 54 had a mixed pattern with involvement of both TA and LV (mixed-CGA), and 35 had isolated involvement of the LV (LV-GCA). That is, 125 patients had cranial involvement with or without LV involvement and 89 had LV-GCA associated or not with cranial involvement (Figure 1).



GCA= Giant Cell Arteritis; c-GCA= Cranial Giant Celll Arteritis; LV-GCA= Large Vessell Giant Cell Arteritis

Figure 1. Ultrasound patters of GCA

Conclusion: Ultrasound is a useful tool for the screening of GCA and its different subtypes of vascular involvement. The isolated cranial subtype or associated with LV-GCA is the most common (78% of cases), but LV-GCA is also very common (55.6% of cases of GCA) and 21.9% presents as an isolated LV-GCA standard. The LV arteries should be included in the ultrasound examination for suspected GCA.
Disclosure of Interests: Irene Monjo Speakers bureau: Roche, Novartis, UCB, Gedeon Richter, Consultant of: Roche, Elisa Fernández-Fernández: None declared, Javier Ortega: None declared, Eugenio de Miguel Speakers bureau: AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi, Paid instructor for: Janssen, Novartis, Roche, Consultant of: AbbVie, Novartis, Pfizer, Galapagos, Grant/research support from: Abbvie, Novartis, Pfizer
DOI: 10.1136/annrheumdis-2021-eular.4154

Vasculitis – small vessel vasculitis

POS0822

NEW FACES OF POLYARTERITIS NODOSA: 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY FINDINGS IN A SERIES OF 10 PATIENTS

C. Rousselin[1], T. Machet[1], G. Collet[2], T. Quéméneur[1], R. Ben Ticha[2], M. Verstraete[2], N. Le Gouellec[1], F. Demailly[2], A. Fagart[2]. [1]*Hôpital de Valenciennes, Internal Medicine and Nephrology, Valenciennes, France*; [2]*Hôpital de Valenciennes, Nuclear Medicine, Valenciennes, France*

Background: ^{18}F-fluorodeoxyglucose positron emission tomography with computed tomography (FDG-PET/CT) is widely used in patients with large-vessel vasculitis (1). The benefits of FDG-PET/CT in polyarteritis nodosa (PAN) has only been assessed in a few case reports (2-3).
Objectives: Our aim was to describe FDG-PET/CT findings in 10 patients with newly diagnosed PAN.
Methods: This was a retrospective study of patients with PAN who underwent FDG-PET/CT at the time of diagnosis, between 2017 and 2020. The FDG-PET/CT data were analysed retrospectively and compared with clinical, biological, histological and conventional imaging data.
Results: Ten patients were included: 9 men and 1 woman, median age of 67 (43–78) years. PAN was diagnosed according to ACR criteria (6) in 9 patients, and histologically in the remaining patient. The clinical manifestations were: systemic (n=10), muscular (n=6), joint (n=3), skin (n=3), peripheral nervous system (n=3), and gastrointestinal (n=2). All patients had high C-reactive protein levels (median, 223 mg/L). One patient had incomplete FDG-PET exploration. Three patients had begun corticosteroid therapy before their FDG-PET/CT scan. The main FDG-PET/CT abnormality was increased tracer uptake in the muscles, particularly in the connective tissue (perimysium, epimysium) (n=7), in linear (n=5) or focal (n=2) patterns. Increased FDG uptake in large-diameter vessels was observed in 4 patients, in the humeral (n=4), femoral (n=1) and the common interosseous (n=1) arteries. Nine patients had bone-marrow FDG uptake, six had splenic FDG uptake. Three patients had synovitis. Three had lymph-node uptake. One patient had subcutaneous FDG uptake, with a "leopard skin" appearance.
Conclusion: FDG-PET/CT seems to be a useful non-invasive imaging technique for diagnosing PAN, particularly in patients with non-specific systemic features. Tracer uptake in muscular connective tissue seems to be a recurrent sign in patients with PAN.
REFERENCES:
[1] Prieto-González S, Depetris M, García-Martínez A, Espígol-Frigolé G, Tavera-Bahillo I, Corbera-Bellata M et al. Positron emission tomography assessment of large vessel inflammation in patients with newly diagnosed, biopsy-proven giant cell arteritis: a prospective, case-control study. Ann Rheum Dis. 2014;73(7):1388-92.
[2] Mino N, Yamashita H, Takahashi Y, Kaneko H. Polyarteritis Nodosa With Reversible FDG Accumulation in Vessels and Kidneys. Clin Nucl Med. 2019;44(11):889-891.
[3] Schollhammer R, Schwartz P, Jullie ML, Pham-Ledard A, Mercie P, Fernandez P et al. 18F-FDG PET/CT Imaging of Popliteal Vasculitis Associated With Polyarteritis Nodosa. Clin Nucl Med. 2017;42(8):e385-e387.
[4] Lightfoot RW Jr, Michel BA, Bloch DA, Hunder GG, Zvaifler NJ, McShane DJ et al. The American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa. Arthritis Rheum. 1990;33(8):1088-93.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.120

POS0823

ARTHRITIS IN ADULT IGA VASCULITIS

A. Hočevar[1,2], V. Jurčić[3], M. Tomsic[1,2], Z. Rotar[1,2]. [1]*University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia*; [2]*Medical Faculty, University of Ljubljana, Internal Medicine, Ljubljana, Slovenia*; [3]*Medical Faculty, University of Ljubljana, Institute of Pathology, Ljubljana, Slovenia*

Background: Arthritis is one of the main clinical features of IgA vasculitis (IgAV). Joint involvement represents the second most common manifestation in childhood IgAV with the predilection for the knees and ankles.
Objectives: We aimed to describe the characteristics of arthritis in adult IgAV cohort.
Methods: We analysed medical records of histologically proven adult IgAV cases, diagnosed between January 2010 and December 2020 at our secondary/

tertiary rheumatology centre. The frequency, temporal occurrence and the localization of arthritis was recorded. In addition, we searched for potential differences in other IgAV features between patients with and without arthritis.

Results: During the 132-month observation period we identified 328 new IgAV cases (59.5% males, median (IQR) age 64.3 (45.1; 76.1) years). Forty-eight (14.6%) patients developed arthritis. Arthritis was the first IgAV manifestation in 16 (4.9%) patients. Arthritis was mono-, oligo- and poly- articular (involving up to 15 joints) in 13 (4.0%), 25 (7.6%) and 10 (3.0%) patients, respectively. Arthritis was most common in wrists and ankles (each in 18 (37.5%) patients); metacarpophalangeal joints and knees (each in 11 (22.9%)); proximal interphalangeal joints (9 (18.8%)); elbows (8 (16.7%)) and metatarsophalangeal joints (4 (8.3%)). Clinical differences between IgAV patients with and without arthritis are presented in table 1. Patients with arthritis were significantly younger, more commonly developed gastrointestinal tract involvement compared to those without arthritis. Arthritis remitted in all with immunomodulatory treatment (given predominantly for necrotic skin purpura or visceral involvement). Follow up (FU) data accessible for 42/48 (87.5%) patients with arthritis showed that IgAV relapsed in 10 (23.8%) patients during a median (IQR) 24.5 (12.9; 40.7) month FU. Relapses were limited to skin and/or kidneys, there were no relapses of arthritis.

Table 1. Clinical characteristics of IgA vasculitis patients with and without arthritis

Clinical characteristics	Arthritis IgAV (48)	Non-arthritis IgAV (280)	P value
Male gender (%)	56.3	60.0	0.636
Age (years)*	49.9 (36.1-66.9)	65.4 (48.4;77.5)	<0.001
Ever smoker (%)	50.0	43.6	0.435
Prior infection (%)	43.8	30.4	0.094
Generalized purpura	50.0	50.0	1.0
Skin necroses (%)	35.4	49.6	0.085
GI involvement (%)	47.9	25.0	0.002
Renal involvement (%)	47.9	46.8	1.0
Elevated serum IgA (%)	33.3 (11/33)	52.0 (115/221)	0.061

Legend: * median and IQR; GI gastrointestinal;

Conclusion: Arthritis in adult IgAV was frequently oligoarticular, involved large and small joints of both upper and lower extremities, and was not prone to chronic course and recurrence. In addition, we found an association between arthritis and gastrointestinal tract involvement.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.324

POS0824 THE LONG-TERM CLINICAL COURSE OF MUSCULAR VASCULITIS DEPENDING ON THE ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY STATUS: A RETROSPECTIVE OBSERVATIONAL STUDY

T. Yoshida[1], K. Nishimura[1], D. Waki[1], K. Mizukawa[1], N. Tanaka[1], H. Murabe[1], T. Yokota[1]. [1]*Kurashiki Central Hospital, Department of Endocrinology and Rheumatology, Kurashiki, Okayama, Japan*

Background: Skeletal muscle is known as one of the organ involvements of primary systemic vasculitis.[1,2] Muscle inflammation is detected by magnetic resonance imaging, and necrotizing vasculitis is proved by muscle biopsy.[3] As with systemic vasculitis or single organ vasculitis, glucocorticoid (GC) and immunosuppressants are used in its treatment.[4] There are not many reports about muscular vasculitis, and its long-term clinical course after initial treatment, including the rates of relapse and mortality, remains unclear.

Objectives: To identify the predictors of relapse and mortality in patients with muscular vasculitis, especially focusing on the status of anti-neutrophil cytoplasmic antibody (ANCA).

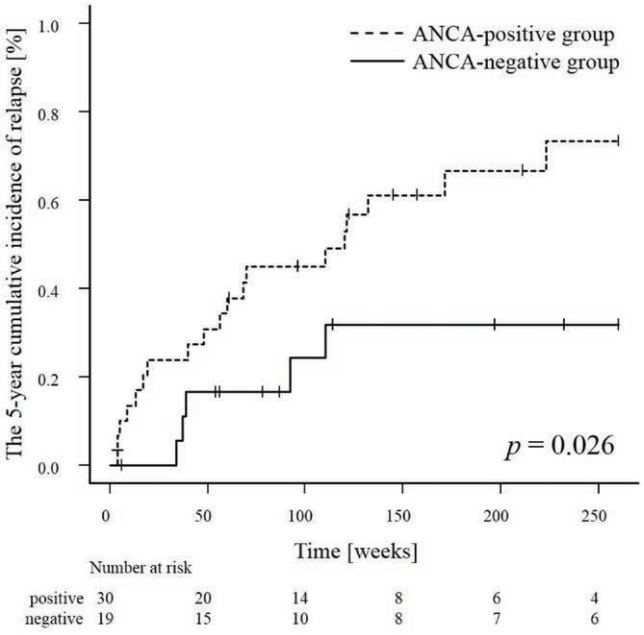
Methods: We retrospectively reviewed patients diagnosed with necrotizing vasculitis with muscle involvements in our hospital between 2004 and 2020. In all cases, muscular vasculitis was identified by muscle biopsy or magnetic resonance imaging. To focus on the clinical features of muscular vasculitis, we excluded patients with such severe organ involvements as cardiovascular, abdominal, cerebral, severe renal, and severe pulmonary involvements. We compared the 5-year cumulative incidence of relapse, the overall survival rate, and the dose of GC over 5 years between the ANCA-positive and ANCA-negative groups. A relapse was defined as any new or worsened state of disease activity requiring an escalation of GC dose. Gray's method was used for assessing the cumulative incidence of relapse. The log-rank test was used for assessing overall survival. The Mann-Whitney U test was used for assessing the dose of GC. The possible factors for relapse in 5 years in a univariate analysis were selected for a multivariate analysis using the Cox proportional hazards model.

Results: Forty-nine patients were enrolled. The median age of onset was 77 (69-82) years and 71.4% were women. There were 30 ANCA-positive patients (90.0% with anti-myeloperoxidase) and 19 ANCA-negative patients. The median age and the number of patients with renal involvements were higher in the ANCA-positive group than in the ANCA-negative group (73.0 ± 9.29 years vs. 79.5 ± 20.28 years, p=0.0062 and 7/30 [23.3%] vs. 0/19 [0.0%], p=0.034, respectively). The Birmingham Vasculitis Activity Score (ver. 3), the induction dose of GC, and the rate of immunosuppressants use were not significantly different between the two groups. During the observational period, 24 patients relapsed. The 5-year cumulative incidence of relapse was significantly higher in the ANCA-positive group than in the ANCA-negative group (p=0.026) (Figure 1). The Cox proportional hazards model revealed that the presence of ANCA was an independent risk factor for relapse (hazard ratio: 3.15; 95% confidence interval 1.06–9.38; p=0.040). During the observational period, 9 patients died (3 died from cancer, 1 from interstitial pneumonia, 1 from cerebral hemorrhage, 1 from infection, and 3 from unknown reasons). The ANCA-positive group exhibited a higher mortality rate than the ANCA-negative group without a statistical significance (p=0.12). The 5-year cumulative dose of GC was larger in the ANCA-positive group than in the ANCA-negative group without a statistical significance (14786 [11246–19138] mg vs. 10088 [7129–12634] mg, p=0.12).

Conclusion: In muscular vasculitis, the presence of ANCA is an independent risk factor for long-term relapse. Stratified treatment depending on the ANCA status may reduce the relapse rate and the occurrence of side effects of GC in patients with muscular vasculitis.

REFERENCES:

[1] Kitching AR et al. Nat Rev Dis Primers 2020; 6(1): 71.
[2] Hernández-Rodríguez J et al. J Autoimmun 2014; 48-49: 84-9.
[3] Ushiyama S et al. Rheumatol Int 2020; 40(10): 1667-74.
[4] Ganeshanandan LR et al. Semin Arthritis Rheum 2020; 50(3): 503-8.



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.815

POS0825 DEVELOPMENT OF A NEW AND SIMPLIFIED FORMULA TO PREDICT MORTALITY IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS ADMITTED TO THE INTENSIVE CARE UNIT

P. Korsten[1], F. Kück[2], K. Tejiozem Donfack[1], R. Vasko[1], A. Lena[2], B. Tampe[1]. [1]*Universitätsmedizin Göttingen, Department of Nephrology and Rheumatology, GÖTTINGEN, Germany*; [2]*Universitätsmedizin Göttingen, Department of Medical Statistics, Göttingen, Germany*

Background: ANCA-associated vasculitis (AAV) can present with a wide range of symptoms, including acute kidney injury (AKI) requiring renal replacement therapy or diffuse alveolar hemorrhage (1). These two manifestations often require admission to an intensive care unit (ICU) and are associated with increased mortality. To predict ICU mortality, the Simplified Acute Physiology Score version 2 (SAPS2) is often used but has not been formally tested in AAV patients (2). In addition, it is cumbersome to assess.

Objectives: To develop a novel, simplified formula to predict ICU mortality in an AAV ICU population from an academic tertiary care center.

Methods: We retrospectively recorded clinical and laboratory parameters in patients admitted to our ICU from 2000-2018. We performed risk factor analysis using univariate and multivariate logistic regression. In the multivariate case we applied the least absolute shrinkage and selection operator (lasso) method for variable selection. We considered average marginal effects and partial dependence plots in order to describe the influence of various independent variables on the probability of death more specifically. We evaluated our new score by comparing the corresponding area under the curve (AUC) to the AUC corresponding to the established SAPS2 score.
Results: We analyzed 58 patients with AAV (39 granulomatosis with polyangiitis, 19 with microscopic polyangiitis) with a mean age of 74±14 (GPA) and 73±12 (MPA). 19/39 (48.7%) of GPA and 9/19 (47.4%) were female. Reasons for admission included disease manifestations or infectious complications from treatment (e. g. pneumonia, urinary tract infection). In total, 13/58 (22.4%) patients died throughout the study (10 GPA, 3 MPA patients). Using a cut-off threshold of 40 for SAPS2, sensitivity and specificity for mortality were 0.92 and 0.60, respectively. Confidence interval for the AUC was [0.68,0.95]. In the fitted multivariate logistic regression model, lasso was applied for variable selection. The identified variables included: disease duration, pH, procalcitonin, hemoglobin, leukocytes on admission, coronary heart disease, and pneumonia on admission. The estimated mortality is given by the formula $f(\beta 0 + \beta 1\chi 1 + \ldots + \beta 7\chi 7)$, where $f(u)=1/(1+\exp(-u))$. Table 1 shows the estimated mortality for various values of the new score.

Table 1. Example scores predicting mortality using the novel formula.

Score	Predicted mortality
-2.2	0.1
-1.1	0.25
0	0.5
1.1	0.75
2.2	0.9

Testing if the AUC corresponding to the new model is significantly larger than the one corresponding to the SAPS2 score as independent variable resulted in p-value of 0.037. To identify possible overfitting, a 5-fold cross validation was performed. This resulted in a CI for the AUC of [0.64,0.96], suggesting that the new score allows for simpler prediction of mortality.
Conclusion: We developed a novel formula corresponding to a score which is able to simpler predict mortality in patients with AAV admitted to the ICU. We will test our formula in the available ICU database MIMIC III, which comprises a large dataset of ICU patients.
REFERENCES:
[1] Kitching AR, Anders H-J, Basu N, Brouwer E, Gordon J, Jayne DR, et al. ANCA-associated vasculitis. Nature Reviews Disease Primers. 2020 Aug 27;6(1):1–27.
[2] Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA. 1993 Dec 22;270(24):2957–63.
Disclosure of Interests: PETER KORSTEN Speakers bureau: Chugai, Boehringer-Ingelheim, Sanofi Aventis, Abbvie, GSK, Novartis, Consultant of: Lilly, Gilead, Abbvie, Boehringer-Ingelheim, GSK, Novartis, Grant/research support from: GSK, Fabian Kück: None declared, Karaine Tejiozem Donfack: None declared, Radovan Vasko: None declared, Andreas Lena: None declared, Björn Tampe: None declared
DOI: 10.1136/annrheumdis-2021-eular.1209

POS0826 SKIN LIMITED IGA VASCULITIS IN ADULTS

A. Hočevar[1,2], J. Ostrovrsnik[1], K. Perdan-Pirkmajer[1], M. Tomsic[1,2], Z. Rotar[1,2]. [1]*University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia*; [2]*Medical Faculty, University of Ljubljana, Internal Medicine, Ljubljana, Slovenia*

Background: IgA vasculitis (IgAV) could be limited to skin or evolve into a systemic disease, affecting characteristically joints, gastrointestinal tract and/or kidneys.
Objectives: We aimed to look for differences between adult IgAV patients with disease limited to skin compared to systemic IgAV.
Methods: Medical records of histologically proven adult IgAV cases, diagnosed between January 2010 and December 2020 at our secondary/tertiary rheumatology centre were analyzed.
Results: During the 132-month observation period we identified 328 new IgAV cases (59.5% males, median (IQR) age 64.3 (45.1; 76.1) years). Ninety-four (40.2%) patients had skin limited disease, and the rest systemic IgAV.

Clinical differences between skin limited and systemic adult IgAV are presented in table 1. Adults with IgAV limited to skin were significantly older, had less commonly skin lesions above the waistline and a lower level of C reactive protein compared to patients with a systemic disease. There were no differences in the frequency of skin necroses between the compared IgAV subgroups. The frequency of potential vasculitis triggers (prior infections, new medications, malignancy) was similar between the compared subgroups.

Table 1. Clinical characteristics of IgA vasculitis patients with skin limited and systemic disease

Clinical characteristics	Skin limited IgAV (94)	Systemic IgAV (234)	P value
Male gender (%)	54.3	61.5	0.263
Age (years)*	68.0 (55.0-80.5)	61.5 (41.7-75.8)	0.007
Current smoker (%)	13.8	21.8	0.123
Antecedent infection (%)	28.7	33.8	0.434
New medication	23.4	23.5	1.0
History of cancer	12.8	10.7	0.569
Symptom duration (days)*	7 (5-21)	8 (5-14)	0.756
Purpura above waistline	36.2	55.6	0.002
Skin necroses (%)	52.1	45.7	0.329
ESR /mm/h) *	32 (18-52)	34 (17-53)	0.873
CRP (g/l) *	13.5 (1-32)	30 (11-68)	<0.001
Elevated serum IgA (%)	50.6	49.1	0.892

Legend: * median and IQR;

Follow up data were available for 250 (76.2%) patients. During the follow up of median (IQR) 12.5 (6.8 – 22.4) months 35 patients relapsed (13/70 (18.6%) with skin limited IgAV and 22/180 (12.2%) with systemic IgAV, p= 0.224).
Conclusion: Skin limited IgAV was associated with older age and less extensive skin puprura in adults. However, relapses of purpura were as common as in systemic IgAV.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1383

POS0827 HEPATOTROPIC VIRUSES WITH HIGHER RHEUMATOID FACTOR, BUT NOT RHEUMATIC DISEASES LINK TO PREVALENT CRYOGLOBULINEMIA. CORRELATION OF CLINICAL AND SEROLOGICAL MARKERS WITH ETIOLOGICAL CAUSES

S. Jeria Navarro[1], T. Franco[2], L. Alserawan[2], D. Lobo Prat[1], A. García-Guillén[1], L. Sainz Comas[1], H. Park[1], A. M. Millán Arciniegas[1], P. Moya[1], B. Magallares[1], C. Díaz-Torné[1], E. Moga[2], C. Juarez[2], H. Corominas[1]. [1]*Hospital Universitari de la Santa Creu i Sant Pau & Dos de Maig, Rheumatology Unit, Barcelona, Spain*; [2]*Hospital Universitari de la Santa Creu i Sant Pau, Immunology Unit, Barcelona, Spain*

Background: Cryoglobulinemia (CG) is a rare phenomenon, which is defined as the persistent presence in serum of abnormal immunoglobulins (Igs) that precipitate in vitro at less than 37ºC and dissolve when the temperature rises again. Is related to hematological disorders, infections and autoimmunes diseases.
Objectives: To describe the differential clinical features, serological and demographics in a cohort of patients diagnosed with CG.
Methods: We describe a retrospective cohort of 252 cryoglobulin (Cg) positive samples, obtained from a database from the immunology laboratory of a tertiary hospital (November 2018-November 2019). We obtained 182 patients with CG, classified according to their etiology into 4 groups: 1)Rheumatic diseases (RD) that includes rheumatoid arthritis, Systemic lupus erythematosus, Sjögren´s syndrome and Systemic scleroderma, 2)Hepatotropic viruses (HV) with patients diagnosed with Hepatitis C virus, B virus and both, 3)Hematological diseases (HD) and 4)Essential cryoglobulinemia (CGE). Demographic variables, clinical and serological data were collected. A comparative analysis was performed with the Mann-Whitney U test and the multivariate Kruskal-Wallis test, nonparametric variables were compared using a Wilcoxon test. Ten patients, with more than one disease from 4 groups, were excluded from the study.
Results: Out of 182 reviewed patients, 172 were included in the study. Mean age at diagnosis was 59.7(±14.0). Demographic, clinical and laboratory characteristics are described in table 1. Mixed CG was the predominant subtype, in 116 (67.4%) patients. The most prevalent CG-associated diseases were HV infection with 91(53%) patients. CGE mostly presented with cutaneous manifestations (p=0.0001), particularly purpura. In RD group the presence of Raynaud and non-erosive arthritis (p=0.0001) was relevant. Laboratory findings showed that CG titration varies according to the etiology, being HD the one with the highest values with 292.2 (±546.2). There is significant difference in

terms of the average of rheumatoid factor (RF) being higher in the group by CGE. On other hand, the group HV presented more consumption of complement, and showed the lowest average p=0.0001, without more severe clinical manifestations.

Table 1.

	RD (n=47)	HV (n=91)	HD (n=17)	CGE (n=17)	
Gender,n(%) F	42 (89.4)	57 (62.6)	7 (41.2)	11 (64.7)	
Age at dg, years, (± SD)	60.6 (±14)	59.6 (±13.1)	61.1(±16.6)	56.3(±20.8)	p=0.8
CLINICAL CHARACTERISTICS					
Skin n (%)	18 (38.3)	10 (11.0)	2 (11.8)	9 (52.9)	p<0.001
Raynaud n (%)	14 (29.8)		1 (5.9)	3 (17.6)	p<0.001
Purpura n (%)	6 (12.8)	9 (9.9)	2 (11.8)	6 (35.3)	p=0.04
Acrocyanosis n (%)	6 (12.8)			1 (5.9)	p=0.0033
Ulcers n (%)	3 (6.4)	2 (2.2)	-	2 (11.8)	p=0.19
Peripheric Neuro n (%)	10 (21.3)	9 (9.9)	1 (5.9)	4 (23.5)	p=0.13
N-E arthritis n (%)	22 (46.8)	8 (8.8)	1 (5.9)	4 (23.5)	p<0.001
GMN n (%)	5 (10.6)	3 (3.3)	1 (5.9)	3 (17.6)	p=0.11
LABORATORY					
Cg (mg/dL) x̄ (± SD)	26.7 (±63.2)	65.8 (±256.5)	292.4 (±546.2)	47.59 (±79.1)	p<0.001
Isotype IgG, n (%)	G+M 26 (55.3)	G+M 72 (79.1)	M 8 (47.1)	G+M 12 (70.6)	
β2M (≥1.8 mg/L), n (%)	7/40 (17.5%)	1/5 (20.0%)	3/12 (25.0%)	-	p= 0.44
RCP (mg/L) p 50	10.3 (±26.2)	3.9 (±3.0)	13.4 (±18.3)	8.5 (±12.0)	p= 0.47
ESR (mm/h) p50	40.0 (±28.5)	20.3 (±20.2)	35.4 (±35.1)	24.5 (±25.0)	p= 0.0003
RF + (>20UI/mL), n (%)	19/46 (41.3)	44/86 (51.2)	5/11 (45.5)	7/17 (41.2)	p= 0.09
p50	90.6 (±175.9)	161.0 (±219.5)	94.8 (±135.6)	284.5 (±619.3)	p<0.001
C3 (<85mg/dL), n %)	20 (42.6)	47 (51.6)	3 (17.6)	3 (17.6)	p= 0.13
x̄ (± SD)	90.1 (±28.6)	68.5 (±10.8)	99.1 (±29.0)	114.8 (±12.7)	p<0.001
C4 (<12mg/dL), n (%)	17 (36.2)	36 (39.6)	-	3 (17.6)	p= 0.02
x̄ (± SD)	15.6 (±9.0)	7.6 (±3.5)	20.4 (±7.4)	21.1 (±9.5)	p<0.001

Conclusion: In our cohort, not all patients with CG presented clinical manifestations being those associated with CGE and RD those with the highest skin and joint expression. The most prevalent association of CG continues to be the HV and we confirmed the characteristic decrease in C3 and C4 complement levels, together with the positivity for RF.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1758

POS0828

CONSISTENT EFFICACY WITH APREMILAST IN MEN AND WOMEN TO TREAT ORAL ULCERS ASSOCIATED WITH BEHÇET'S SYNDROME: PHASE 3 RELIEF STUDY RESULTS

G. Hatemi[1], A. Mahr[2], M. Takeno[3], D. Kim[4], M. Melikoglu[1], S. Cheng[5], S. Richter[5], S. Jardon[5], M. Paris[5], M. Chen[5], Y. Yazici[6]. [1]*Istanbul University-Cerrahpaşa, Cerrahpaşa Medical School and Behçet's Disease Research Center, Division of Rheumatology, Department of Internal Medicine, Istanbul, Turkey*; [2]*Cantonal Hospital St. Gallen, Department of Rheumatology, St. Gallen, Switzerland*; [3]*Nippon Medical School, Rheumatology, Kawasaki, Japan*; [4]*Yonsei University College of Medicine and Severance Hospital, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; [5]*Amgen Inc., Global Medical Affairs, Thousand Oaks, United States of America*; [6]*New York University School of Medicine, Department of Medicine, New York, United States of America*

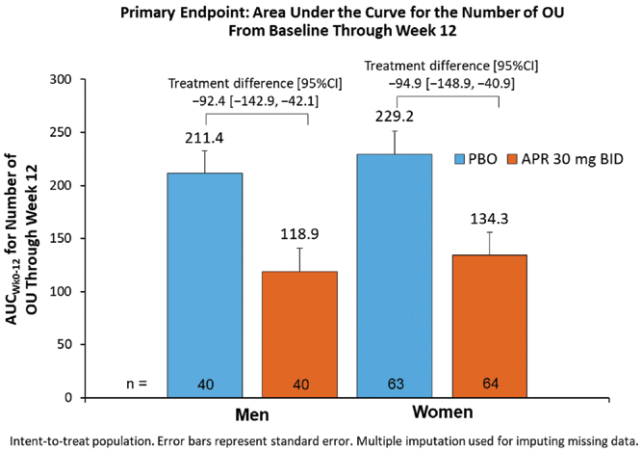
Background: Painful, recurring oral ulcers (OU) associated with Behçet's syndrome negatively affect quality of life (QoL). Differences across sexes were reported in the frequency of disease manifestations, disease course, and response to colchicine. The phase 3, randomized, double-blind, placebo (PBO)-controlled RELIEF study showed overall efficacy of apremilast (APR) for OU associated with Behçet's syndrome, including improvements in OU pain, disease activity, and QoL.

Objectives: To evaluate the consistency of efficacy with APR in men and women with Behçet's syndrome.

Methods: Adults with active Behçet's syndrome and ≥3 OU at randomization or ≥2 OU at screening and randomization, without active major organ involvement, were randomized to APR 30 mg BID or PBO during the 12-wk PBO-controlled phase. Randomization was stratified by sex. The primary endpoint was area under the curve for the number of OU through Wk 12 (AUC_{Wk0-12}) to assess continued efficacy over the time period in a symptom that waxed and waned. Key secondary endpoints included OU pain, complete response (OU-free), maintenance of complete response, and QoL at Wk 12. Disease activity was also assessed using Behçet's Syndrome Activity Score (BSAS) and Behçet's Disease Current Activity Index Form (BDCAF). QoL was assessed using Behçet's Disease QoL (BDQoL). Prespecified subgroup analyses in men and women were performed to assess treatment effect in primary and secondary endpoints.

Results: Eighty men and 127 women were randomized and received ≥1 dose of study medication. Mean age was 38.7 yrs (men) and 40.8 yrs (women). Mean (SD) OU count at baseline was 3.4 (1.4) (PBO) and 3.7 (1.5) (APR) for men and 4.3 (3.2) (PBO) and 4.5 (4.5) (APR) for women. Greater improvements in favor of APR vs PBO were observed in AUC_{Wk0-12} in men and women (Figure 1). Consistency in efficacy with APR was observed between men and women, with greater reduction in pain and achievement of OU complete response (OU-free) and maintenance of response at Wk 12 vs PBO (Table 1). In men and women, consistent treatment effects in favor of APR vs PBO were observed for disease activity and QoL measures, although moderate treatment differences were observed in BDCAI (men/women) and BDQoL (men) (Table 1).

Conclusion: Consistent treatment effects in favor of APR vs PBO in clinically relevant outcomes, including OU number and pain, OU complete response, and disease activity measures, were observed in men and women with OU associated with Behçet's syndrome.



Intent-to-treat population. Error bars represent standard error. Multiple imputation used for imputing missing data.

Key Secondary Efficacy Outcomes at Wk 12

	Men			Women		
	PBO (n = 40)	APR (n = 40)	Tx Difference [95% CI]	PBO (n = 63)	APR (n = 64)	Tx Difference [95% CI]
OU CR, n/N (%)	8/40 (20.0)	21/40 (52.5)	32.6 [12.8, 52.4]	15/63 (23.8)	34/64 (53.1)	29.3 [13.2, 45.4]
OU CR 6+6*, n/N (%)	1/40 (2.5)	10/40 (25.0)	22.8 [8.8, 36.8]	4/63 (6.3)	21/64 (32.8)	26.5 [13.6, 39.3]
Pain (VAS)†	-12.0 (4.8)	-37.6 (4.9)	-25.6 [-37.2, -14.1]	-17.4 (4.4)	-41.5 (4.3)	-24.1 [-34.9, -13.3]
BSAS†	-1.3 (2.4)	-14.4 (2.4)	-13.1 [-18.8, -7.3]	-7.7 (2.4)	-19.7 (2.4)	-12.0 [-18.0, -6.0]
BDCAF†						
BDCAI	-0.1 (0.3)	-0.5 (0.3)	-0.4 [-1.1, 0.4]	-0.7 (0.3)	-1.3 (0.3)	-0.6 [-1.2, 0.0]
Patient's Perception of Disease Activity	-0.2 (0.3)	-1.4 (0.3)	-1.2 [-1.9, -0.5]	-1.0 (0.2)	-1.8 (0.2)	-0.9 [-1.4, -0.3]
Clinician's Overall Perception of Disease Activity	-0.2 (0.3)	-1.5 (0.3)	-1.3 [-1.9, -0.7]	-1.0 (0.2)	-1.7 (0.2)	-0.7 [-1.3, -0.2]
BDQoL†	-0.7 (1.0)	-2.2 (1.0)	-1.5 [-3.8, 0.8]	-0.3 (0.9)	-4.4 (0.9)	-4.1 [-6.3, -2.0]

LOCF analyses. *Proportion of patients achieving an OU CR by Wk 6, and remaining OU-free for ≥6 additional wks during the 12-wk PBO-controlled treatment phase. †LS mean (SE) change from baseline. BSAS = Behçet's Syndrome Activity Scores; BDCAF = Behçet's Disease Activity Form; CR = complete response; n = number of patients randomized to treatment; Tx = treatment.

Acknowledgements: This study was funded by Celgene. Additional analyses were funded by Amgen Inc. Writing support was funded by Amgen Inc. and provided by Kristin Carlin, RPh, MBA, of Peloton Advantage, LLC, an OPEN Health company.

Disclosure of Interests: Gulen Hatemi Speakers bureau: AbbVie, Novartis, and UCB, Grant/research support from: Celgene, Alfred Mahr Speakers bureau: Chugai and Roche, Consultant of: Celgene and Chugai, Mitsuhiro Takeno Speakers bureau: AbbVie, Esai, and Mitsubishi-Tanabe, Consultant of: Celgene, Grant/research support from: Novartis, Doyoung Kim: None declared, Melike Melikoglu: None declared, Sue Cheng Employee of: Amgen Inc., Sven Richter Employee of: Amgen Inc., Shauna Jardon Employee of: Amgen Inc., Maria Paris Employee of: Amgen Inc., Mindy Chen Employee of: Amgen Inc., Yusuf Yazici Consultant of: Bristol-Myers Squibb, Celgene, Genentech, and Sanofi
DOI: 10.1136/annrheumdis-2021-eular.1926

POS0829 SPECIFICITY OF PANCA AUTOANTIBODIES IN AUTOIMMUNE DISEASES

O. Argyropoulou[1], A. Tsirogianni[2], C. Sfontouris[3], G. Boutzios[1], P. Vlachoyiannopoulos[1], A. Tzioufas[1], E. Kapsogeorgou[1]. [1]*School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece*; [2]*Evangelismos General Hospital, Immunology and Histocompatibility, Athens, Greece*; [3]*Evangelismos General Hospital, Rheumatology, Athens, Greece*

Background: The clinical significance of pANCA by indirect immunofluorescence is well-established. However, their clinical utility is sometimes hindered by the fact that pANCA are also detected in various autoimmune diseases. Myeloperoxidase (MPO) is considered as the major autoantigen recognized by pANCA in ANCA-associated vasculitides (AAV) and predominantly in microscopic polyangiitis (MPA). However, information regarding the targets of pANCA in other autoimmune diseases is still elusive.
Objectives: To investigate the specific autoantigens recognized by pANCA in autoimmune diseases.
Methods: Sera from all patients that were found positive for pANCA in the diagnostic laboratories of the Department of Pathophysiology, School of Medicine, National and Kapodistrian University of Athens and the Department of Immunology and Histocompatibility, Evangelismos General Hospital, Athens, Greece during the last two years were studied. The pANCA+ sera were evaluated for reactivity with the major antigens that are recognized by pANCA [MPO, lactoferrin, neutrophil elastase, cathepsin G and bactericidal/permeability increasing protein (BPI)] by a commercially available multiplex ELISA (ANCA profile ELISA, Euroimmun, Lubeck, Germany).
Results: A total of 82 patients were included in the study. All patients had positive pANCA by indirect immunofluorescence with a title ranging from 1/160 to 1/640. According to respective classification criteria, 21 patients had systemic vasculitides (15 MPA, 1 granulomatosis with polyangiitis; GPA, 1 Behcet's disease; BD, 1 aortitis, 2 Henoch-Schonlein purpura; HSP and 1 cryoglobulinemic vasculitis; CV), 29 had systemic lupus erythematosus (SLE), 6 antiphospholipid syndrome (APS), 8 Sjögren's syndrome (SS), 2 rheumatoid arthritis (RA), 1 systemic scleroderma (SScl), 14 Hashimoto thyroiditis and 1 sarcoidosis. The specificities of pANCA in each entity are shown in the following table.

Autoimmune Diseases		Antigens recognized by pANCA+ sera				
		MPO	**Elastase**	**Cathepsin G**	**BPI**	**Lactoferrin**
Vasculitides	MPA	66.7 (10/15)	0 (0/15)	0 (0/15)	0 (0/15)	0 (0/15)
	GPA	100 (1/1)	0 (0/1)	0 (0/1)	0 (0/1)	0 (0/1)
	BD	100 (1/1)	0 (0/1)	0 (0/1)	0 (0/1)	0 (0/1)
	Aortitis	0 (0/1)	0 (0/1)	0 (0/1)	0 (0/1)	0 (0/1)
	HSP	0 (0/2)	0 (0/2)	0 (0/2)	0 (0/2)	0 (0/2)
	CV	0 (0/1)	0 (0/1)	0 (0/1)	0(0/1)	100 (1/1)
SLE		6.9 (2/29)	0 (0/29)	0 (0/29)	0 (0/29)	6.9 (2/29)
APS		16.6 (1/6)	16.6 (1/6)	0 (0/6)	0 (0/6)	0 (0/6)
SS		0 (0/8)	12.5 (1/8)	0 (0/8)	12.5 (1/8)	0 (0/8)
RA		50 (1/2)	0 (0/2)	0 (0/2)	0 (0/2)	0 (0/2)
SScl		100 (1/1)	0 (0/1)	0 (0/1)	0 (0/1)	0 (0/1)
Hashimoto		0 (0/14)	0 (0/14)	0 (0/14)	0 (0/14)	0 (0/14)
Sarcoidosis		0 (0/1)	0 (0/1)	0 (0/1)	0 (0/1)	0 (0/1)

Conclusion: pANCA positive staining in AAVs is highly restricted to MPO specificity. On the contrary, pANCA staining pattern in other autoimmune diseases, involves unknown autoantigens that are under investigation in our laboratory.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1949

POS0830 FACTORS INFLUENCING PATIENT-REPORTED OUTCOMES IN ANCA-ASSOCIATED VASCULITIS

S. Monti[1,2], P. Delvino[1,2], C. Klersy[3], G. Coppa[4], A. Milanesi[1], C. Montecucco[1]. [1]*Pavia, Rheumatology, IRCCS Policlinico S. Matteo Fondazione, Pavia, Italy*; [2]*Pavia, PhD in Experimental Medicine, University of Pavia, Pavia, Italy*; [3]*Pavia, Biometry and Clinical Epidemiology, IRCCS Policlinico S. Matteo Fondazione, Pavia, Italy*; [4]*Pavia, University of Pavia, School of Medicine and Surgery, Pavia, Italy*

Background: Patient-reported outcomes (PROs) are currently poorly integrated in the clinical evaluation of disease activity in patients with ANCA-associated vasculitis (AAV).
Objectives: To assess the distribution of the Patient Global Assessment (PtGA) in patients with AAV in stable remission, and to identify correlates of PtGA; to assess the discordance between PtGA score and PhGA.
Methods: Patients with a diagnosis of AAV [eosinophilic granulomatosis with polyangiitis, granulomatosis with polyangiitis, microscopic polyangiitis] in stable, complete remission (defined by a BVAS=0) and with a Physician Global Assessment (PhGA)=0 were included. A questionnaire including several aspects of disease captured by PROs was collected. PtGA on a 0-100 mm visual analogue scale (VAS) was assessed, with higher scores representing higher/worse levels of disease activity. Similarly, VAS for pain, chronic damage according to the patient's opinion, general health (GH), fatigue, and sleep quality were collected. The worst symptom in the patient's opinion affecting the overall assessment of disease activity was recorded. The Cragg Hurdle model was used to assess the predictors of PtGA.
Results: 65 patients were included, female 57%, mean age 61±12 years. Mean disease duration at enrollment was 8±6 years. Mean vasculitis damage index (VDI) was 4.4 ±2.3, with 45% of patients having a VDI ≥ 5. Despite having been classified as being in remission, PtGA was elevated in 37% of patients. We explored several correlates of PtGA. Higher degree of damage accrual (VDI) did not influence the patient's evaluation of current disease activity. Similarly, we did not identify a correlation between older age, educational level, number of organ-systems involved, number of comorbidities, the number of previous major or minor relapses, higher disease duration, nor the type of AAV diagnosis (figure 1, panel A). Only sex significantly correlated with PtGA scores: 19 (51%) of female patients reported an elevated PtGA compared to only 5 (18%) of male (p=0.009). PtGA resulted to be significantly correlated with other (mostly modifiable) PROs including VAS pain, perception of the level of chronic damage accrual, GH, and fatigue (figure 1, panel B). The agreement between patients' and physicians' assessments of disease activity was 63%. Patients reported pain, followed by chronic respiratory symptoms to be the worst-experienced ongoing manifestations affecting their evaluation of disease activity.
Conclusion: A significant proportion of patients with AAV considered to be in remission by the physician still declares to have persistent aspects of uncontrolled disease. PtGA is significantly influenced by persistent pain and fatigue, which warrant better assessment in the future.

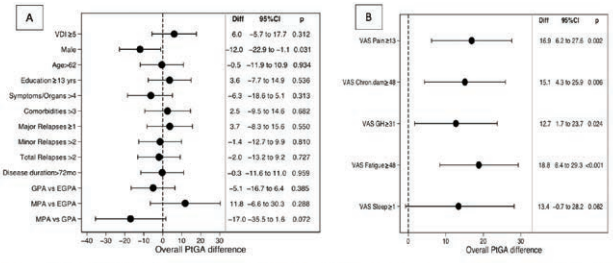


Figure 1. Forrest plots of correlates of the Patient Global Assessment (PtGA): patient- and disease-related items (Panel A); influence of other patient-reported outcomes (Panel B). Cut-off values were identified based on the median value of the population.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2367

POS0831

EARLY INFECTIOUS RISK IN PATIENTS WITH NEWLY-DIAGNOSED ANTI-NEUTROPHILCYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS ACCORDING TO THE REMISSION-INDUCTIONTHERAPY: A FRENCH MONOCENTRIC RETROSPECTIVE STUDY INCLUDING 145 PATIENTS

M. Gérard[1], H. De Boysson[1], R. Morello[1], N. M. Silva[1], A. C. Leroux[2], A. Dumont[1], G. Maigné[1], J. Boutemy[1], K. Khoy[1], D. Mariotte[1], T. Lobbedez[1], A. Aouba[1], S. Deshayes[1]. [1]*Centre Hospitalier et Universitaire de Caen, Calvados, Caen, France*; [2]*Centre Hospitalier et Universitaire de Caen, Manche, Saint-Lô, France*

Background: Few comparative data exist on early infections secondary to remission-induction therapy (RIT) with rituximab versus cyclophosphamide in newly-diagnosed ANCA-associated vasculitis (AAV) patients.
Objectives: We compared and analyzed the rate and predictors of severe infections in such patients within the first six months following RIT.

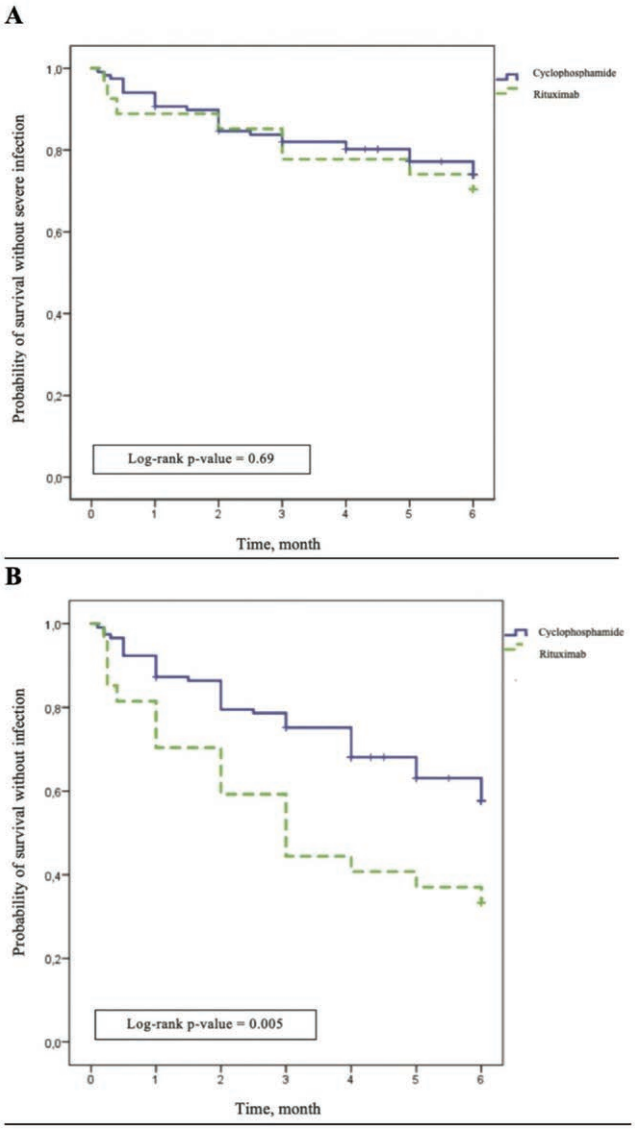


Figure 1. Comparison of the 6-month survival without severe infection (A) or without infection of any severity (B) in patients with newly-diagnosed ANCA-associated vasculitis treated by rituximab or cyclophosphamide

Methods: We included, from the databases of Caen University Hospital, all consecutive adults newly-diagnosed with granulomatosis with polyangiitis or microscopic polyangiitis between January 2006 and December 2019. We compared the survival without severe infections (WSI) and the survival without infection of any severity (WIOAS) within 6 months from the RIT, and used a multivariate cox analysis to identify predictors of infection.
Results: We included 145 patients, 27 in rituximab group and 118 in cyclophosphamide group. Patients in the rituximab group more frequently had pneumococcal vaccination ($p<0.01$) and creatinine level <150 µmol/L, while other characteristics, including Birmingham Vasculitis Activity Score, were comparable between both groups.
Overall, 37 severe infections and 65 infections of any severity were recorded. The survival WSI was similar in both groups ($p=0.69$), but survival WIOAS was lower in rituximab group ($p=0.005$).
In multivariate analysis, risk factors at diagnosis for severe infections were chronic urinary tract disease, dialysis and absence of prophylaxis with trimethoprim-sulfamethoxazole ($p<0.01$ each).
Conclusion: The survival WIS within the 6 months following RIT was similar in patients with newly-diagnosed AAV treated by rituximab or cyclophosphamide, but survival WIOAS appeared to be lower within the 6 months following rituximab despite a better pneumococcal vaccination coverage.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3098

Scleroderma, myositis and related syndromes

POS0832

A NOVEL GREY SCALE AND POWER DOPPLER ULTRASONOGRAPHIC SCORE FOR IDIOPATHIC INFLAMMATORY MYOPATHIES: SIENA MYOSITIS ULTRASOUND GRADING SCALE

E. Conticini[1], P. Falsetti[1], S. G. Al Khayyat[1], C. Baldi[1], F. Bellisai[1], M. Bardelli[1], L. Cantarini[1], B. Frediani[1]. [1]*University of Siena, Rheumatology Unit, Siena, Italy*

Background: No clear-cut guidelines exist about the use of diagnostic procedures for idiopathic inflammatory myopathies (IIM) and only scanty and conflicting data report the use of ultrasound (US).
Objectives: We aimed to assess if grey-scale (GS) and Power Doppler (PD) US, graded with a 0-3-points-scale, may be a reliable tool in a cohort of patients affected by IIM.
Methods: We prospectively collected, since July to October 2020, all patients referred to Vasculitis and Myositis clinic, Rheumatology Unit, University of Siena, for suspected IIM, as well as patients with a previous, definite diagnosis of IIM and evaluated during follow-up or referred from other centers for a second opinion. All patients underwent US examination of both thighs in axial and longitudinal scans. Edema and atrophy, both assessed in GS, and PD, were graded with a 0-3-points-scale. Spearman test was used to identify the correlations between US and clinical and serological variables.
Results: A total of 18 patients was included. Four of them were evaluated twice, at baseline and within 3 months of therapy. Muscle edema was found to be directly correlated with physician global assessment (PhGA), serum myoglobin and PD and negatively with disease duration. PD score was positively correlated to PhGA and negatively to disease duration. Muscle atrophy directly correlated with Myositis Damage Index and patients' age. The single-thigh sub-analysis evidenced a direct correlation between PD score and Manual Muscle Test.
Conclusion: In our cohort, we found that edema and PD are strictly related to early, active myositis, suggesting that an inflamed muscle should appear swollen, thickened and with Doppler signal. Conversely, muscle atrophy reflects the age of the patient and the overall severity of the disease. Such findings shed a new, promising, light in the role of US in diagnosis and monitoring of IIMs.

Table 1. Siena Myositis Ultrasound Grading Scale (SMUGS).

	Grey-scale edema	Grey-scale atrophy	Power Doppler
0	Normal muscle echotexture with hyperechoic septa and hypoechoic muscle fibers, conserved thickness.	Normal muscle echotexture, with hyperechoic septa and hypoechoic muscle fibers, conserved thickness.	No PD signal.
1	Focal hypoechoic areas, where septa are less evident. Conserved thickness.	Focal heterogeneously hyperechoic areas, where septa are thicker and more evident, and muscle fibers are thinner. Conserved muscle thickness.	One or two PD signals in at least one muscle (PD vascular spots, small vessels of homogenous diameters, vessel diameters approximately not superior to fibrous intramuscular septa)
2	Diffuse and heterogeneous hypo echogenicity (rectus femoris as hypoechoic or more than vastus intermedius), septa diffusely less evident. Conserved thickness.	Diffuse and heterogeneously hyperechoic muscle, with thicker septa and thinner muscle fibers. Conserved muscle thickness.	More than 2 PD signals for each muscle (as vascular spots, small vessels of homogenous diameters, vessel diameters approximately not superior to fibrous intramuscular septa).
3	Diffuse and heterogeneous hypo echogenicity (rectus femoris as hypoechoic or more than vastus intermedius), septa diffusely less evident. Increased thickness (rectus femoris became thicker than vastus intermedius).	Diffuse and heterogeneously hyperechoic muscle, with thicker septa and thinner muscle fibers. Reduced muscle thickness.	More than 2 PD signals for each muscle with larger diameter of the vessel (at least superior to fibrous intramuscular septa), or vessels with different diameters or branched vessels.

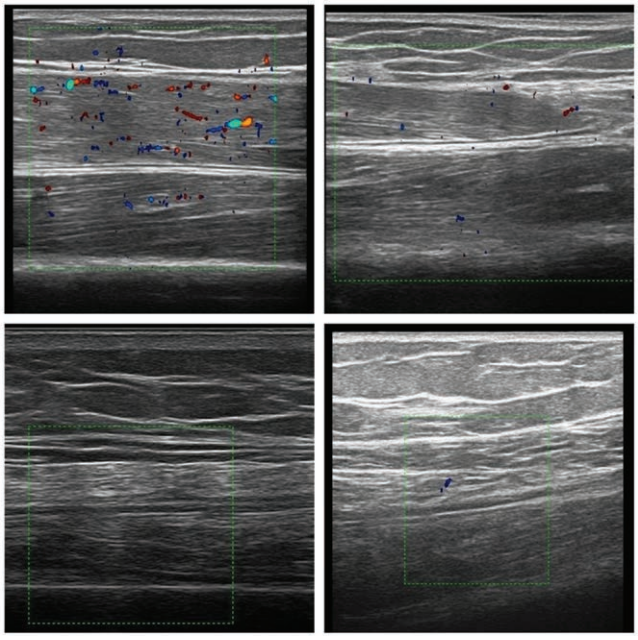


Figure 1. Different PD findings (clockwise) in longitudinal anterior scans of the thigh: PD 3 in a patient with a recent diagnosis of anti-Mi2 DM; PD 2 in the same patient after one month of treatment with steroids and Methotrexate; PD 1 in a patient affected by anti-SAE DM, with a suspected disease flare; PD 0 in a patient affected by an advanced polymyositis diagnosed in 2000, currently not in treatment.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.197

POS0833 A RETROSPECTIVE COHORT STUDY IN CHINESE PATIENTS WITH ADULT POLYMYOSITIS AND DERMATOMYOSITIS: RISK OF COMORBIDITIES AND SUBCLASSIFICATION USING MACHINE LEARNING

J. Zhu[1], L. Wu[2], Y. Zhou[3], R. Wang[1], S. Chen[1], S. Yu[4], S. Zheng[1], F. Xiao[1], J. Li[1]. [1]*Nanfang Hospital, Southern Medical University, Department of Rheumatic & TCM Medical Center, Guangzhou, China*; [2]*School of Traditional Chinese Medicine, Southern Medical University, Department of Internal Medicine of Traditional Chinese Medicine, Guangzhou, China*; [3]*Guangdong Women and Children Hospital, Department of Obstetrics, Guangzhou, China*; [4]*Nanfang Hospital, Southern Medical University, Department of Rheumatology, Guangzhou, China*

Background: Idiopathic inflammatory myopathy (IIM), also known as myositis, refers to a group of heterogeneous disorders including polymyositis (PM), dermatomyositis (DM), inclusion body myositis and immune-mediated necrotising myopathy. Phenotype, pathogenesis, and prognosis vary due to multi-organ involvement and comorbidities. With the clinical application of MSAs, a new classification system for myositis was explored to reduce confusion between subgroups. But it is far from showing the full picture of myositis due to high heterogeneity. Therefore, it is necessary to systematically evaluate the relevant risk factors of myositis for ILD, other rheumatic diseases, and malignancy for better clinical vigilance. And further exploring the subclassification of myositis is critical.
Objectives: To identify the risk factors in Chinese patients with adult polymyositis and dermatomyositis for their comorbidities and explore a subclassification system.
Methods: Clinical records of 397 patients with idiopathic inflammatory myopathies were retrospectively reviewed. Logistic regression was used to identify potential risk factors for interstitial lung disease (ILD), other rheumatic diseases, and malignancy after bivariate analysis. Hierarchical clustering and decisional tree were utilized to identify subgroups and explore a subclassification system.
Results: A total of 119 polymyositis and 191 dermatomyositis patients were included. Anti-PM/Scl, anti-Ro52, anti-aminoacyl-tRNA synthetase and anti-MDA5 (adjusted odds ratios (AOR)=4.779, 1.917, 5.092 and 7.714 respectively) antibodies were risks (p<0.05), whereas overlapping malignancy was protective (AOR=0.107; p=0.002) for ILD across polymyositis, dermatomyositis and the total group. In subgroup models, Raynaud's phenomenon, arthralgia and semi-quantitative anti-nuclear antibody (AOR=51.233, 4.261, 3.047 respectively) were risks for other overlapping rheumatic diseases (p<0.05). For overlapping malignancy, male and anti-TIF1γ antibodies (AOR=2.533, 16.949) were risks (p<0.05), whereas disease duration and combination of ILD (AOR=0.954, 0.106) were protective in the total group (p<0.05); while anti-NXP2 antibodies were identified as risk factors (AOR=73.152; p=0.038) in polymyositis. Hierarchical clustering suggested a subclassification with 6 subgroups: malignancy overlapping dermatomyositis, classical dermatomyositis, polymyositis with severe muscle involvement, dermatomyositis with ILD, polymyositis with ILD, and overlapping of myositis with other rheumatic diseases according to the characteristics of grouped patients. Accuracy of the classification and regression trees model was 0.768 (95% CI 0.711 to 0.819) on training set and 0.633 (95%CI 0.499 to 0.754) on test set.
Conclusion: Accompanying ILD, other rheumatic diseases and malignancy are strongly associated with clinical manifestation and myositis-specific or myositis-associated autoantibodies among Chinese polymyositis and dermatomyositis patients. The subclassification system proposed a more precise phenotype defining toward stratified treatments.
Acknowledgements: The study was supported by the Natural Science Foundation of China [No. 81803932] and the Natural Science Foundation of Guangdong Province [No. 2018030310025 and 2017A030313868]. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.590

POS0834 LONG-TERM OUTCOME OF SSC ASSOCIATED ILD: IMPROVED SURVIVAL IN PPI TREATED PATIENTS

M. Kreuter[1], F. Bonella[2], K. Kathrin[3], J. Henes[4], E. Siegert[5], G. Riemekasten[6], N. Blank[7], C. Pfeiffer[8], U. Müller-Ladner[9], A. Kreuter[10], P. Korsten[11], A. Juche[12], M. Schmalzing[13], M. Worm[14], I. Jandova[15], L. Susok[16], T. Schmeiser[17], C. Guenther[18], G. Keyszer[19], J. Ehrchen[20], A. Ramming[21], I. Kötter[22], H. M. Lorenz[2], P. Moinzadeh[23], N. Hunzelmann[23]. [1]*Center for Interstitial and Rare Lung Diseases, Thoraxclinic, Heidelberg, Germany*; [2]*Ruhrlandklinik University Hospital Essen, Center for Interstitial Lung Disease, Essen, Germany*; [3]*Faculty of Medicine University of Cologne, Institute of Medical Statistics and Computational Biology, Cologne, Germany*; [4]*University Hospital Tuebingen, Rheumatology, Tübingen, Germany*; [5]*Charite Universitätsmedizin Berlin, Rheumatology, Berlin, Germany*; [6]*University Medical Center UKSH Luebeck, Rheumatology, Lübeck, Germany*; [7]*University Hospital Heidelberg, Rheumatology, Heidelberg, Germany*; [8]*University Medical Center Ulm, Dermatology, Ulm, Germany*; [9]*Kerckhoff Clinic Bad Nauheim, Rheumatology, Bad Nauheim, Germany*; [10]*HELIOS St. Elisabeth Clinic Oberhausen, Dermatology, Oberhausen, Germany*; [11]*University Medical Center, Department of Nephrology and Rheumatology, Göttingen, Germany*; [12]*Immanuel Hospital Berlin-Buch, Rheumatology,*

Berlin, Germany; [13]*University Hospital Wurzburg, Rheumatology, Würzburg, Germany*; [14]*Charite Universitätsmedizin Berlin, Dermatology, Berlin, Germany*; [15]*University Hospital Freiburg, Rheumatology, Freiburg, Germany*; [16]*St. Josef Hospital Bochum, Dermatology, Bochum, Germany*; [17]*Hospital St. Josef Wuppertal, Rheumatology, Wuppertal, Germany*; [18]*University Hospital Carl Gustav Carus Dresden, Dermatology, Dresden, Germany*; [19]*University Hospital Halle, Rheumatology, Halle, Germany*; [20]*University Hospital Muenster, Dermatology, Münster, Germany*; [21]*University Hospital Erlangen, Rheumatology, Erlangen, Germany*; [22]*Klinikum Bad Bramstedt, Rheumatology, Bad Bramstedt, Germany*; [23]*University Hospital Cologne, Dermatology, Cologne, Germany*

Background: Gastroesophageal reflux disease (GERD) occurs frequently in patients with systemic sclerosis (SSc) and SSc-associated interstitial lung disease (SSc-ILD). PPI use has to been shown to improve survival in patients with idiopathic pulmonary fibrosis, whereas to date there are no data on the use of PPI in SSc-ILD.

Objectives: This study was aimed to assess whether use of PPI is associated with progression of SSc-ILD and survival.

Methods: We retrospectively analysed 1931 patients with SSc and SSc-ILD from the German Network for Systemic Sclerosis (DNSS) database (2003 onwards). Kaplan–Meier analysis compared overall survival (OS) and progression-free survival (PFS) in patients with vs. without GERD (SSc and SSc-ILD), and PPI vs. no PPI use (SSc-ILD only). Progression was defined as a decrease in either % predicted forced vital capacity ≥10% or single-breath diffusing capacity for carbon monoxide ≥15%, or death.

Results: GERD was not associated with decreased OS or PFS in patients with either SSc or SSc-ILD. In patients with SSc-ILD, PPI use was associated with improved OS vs. no PPI use after 1 year (98.4% [95% confidence interval: 97.6–99.3]; n=760 vs. 90.8% [87.9–93.8]; n=290) and after 5 years (91.4% [89.2–93.8]; n=357 vs. 70.9% [65.2–77.1]; n=106; p<0.0001). PPI use was also associated with improved PFS vs. no PPI use after 1 year (95.9% [94.6–97.3]; n=745 vs. 86.4% [82.9–90.1]; n=278) and after 5 years (66.8% [63.0–70.8]; n=286 vs. 45.9% [39.6–53.2]; n=69; p<0.0001).

Conclusion: GERD had no effect on survival in SSc or SSc-ILD. PPIs improved survival in patients with SSc-ILD; however, controlled, prospective trials are needed to confirm this finding.

Disclosure of Interests: Michael Kreuter Speakers bureau: Boehringer, Consultant of: Boehringer, Grant/research support from: Boehringer, Francesco Bonella Speakers bureau: Boehringer, Roche, GSK, Consultant of: Boehringer, Roche, GSK, Grant/research support from: Boehringer, Kuhr Kathrin: None declared, Jörg Henes Speakers bureau: Abbvie, Boehringer, Chugai, Roche, Janssen, Novartis, SOBI, Pfizer and UCB, Consultant of: Boehringer, Celgene, Chugai, Roche, Janssen, Novartis, SOBI, Grant/research support from: Chugai, Roche, Janssen, Novartis, SOBI, Pfizer, Elise Siegert: None declared, Gabriela Riemekasten Speakers bureau: Novartis, Janssen, Roche, GSK, Boehringer, Consultant of: Janssen, Actelion, Boehringer, Norbert Blank Consultant of: Sobi, Novartis, Roche, UCB, MSD, Pfizer, Actelion, Abbvie, Boehringer, Grant/research support from: Novartis, Sobi, Christiane Pfeiffer: None declared, Ulf Müller-Ladner: None declared, Alexander Kreuter Speakers bureau: MSD, Boehringer, InfectoPharm, Paid instructor for: MSD, PETER KORSTEN Consultant of: Glaxo, Abbvie, Pfizer, BMS, Chugai, Sanofi, Lilly, Boehringer, Novartis, Grant/research support from: Glaxo, Aaron Juche: None declared, Marc Schmalzing Speakers bureau: Chugai Roche, Boehringer, Celgene, Medac, UCB, Paid instructor for: Novartis, Abbvie, Astra Zeneca, Chugai Roche, Janssen, Consultant of: Chugai Roche, Hexal Sandoz, Gilead, Abbvie, Janssen, Boehringer, Margitta Worm Speakers bureau: Boehringer, Ilona Jandova Speakers bureau: Boehringer, Novartis, Abbvie, Laura Susok Speakers bureau: MSD, Novartis, BMS, Sunpharma, Consultant of: MSD, Tim Schmeiser Consultant of: Abbvie, Boehringer, Novartis, UCB, Claudia Guenther Paid instructor for: Advisory Board Boehringer January 2020, Employee of: Novartis 2002-2005, Gernot Keyszer Consultant of: Boehringer, Jan Ehrchen Speakers bureau: Boehringer, Janssen, Chugai, Sobi, Employee of: Pfizer, Actelion (now Janssen), Andreas Ramming Speakers bureau: Boehringer, Gilead, Janssen, Pfizer, Roche, Consultant of: Boehringer, Pfizer, Grant/research support from: Novartis, Pfizer, Ina Kötter Speakers bureau: several companies, Consultant of: several companies, Grant/research support from: several companies, Hanns-Martin Lorenz Speakers bureau: Abbvie, Astra Zeneca, Actelion, Alexion Amgen, Bayer Vital, Baxter, Biogen, Boehringer, BMS, Celgene, Fresenius, Genzyme, GSK, Gilead, Hexal, Janssen, Lilly, Medac, MSD, Mundipharm, Mylan, Novartis, Octapharm, Pfizer, Roche Chugai, Sandoz, Sanofi, Shire SOBI, Thermo Fischer, UCB, Grant/research support from: basic research studies: Pfizer, Novartis, Abbvie, Gilead, Lilly, MSD, Roche Chugai, Pia Moinzadeh Speakers bureau: Boehringer, Actelion, Grant/research support from: Actelion, Nicolas Hunzelmann Speakers bureau: Boehringer Janssen, Roche, Sanofi, Consultant of: Boehringer

DOI: 10.1136/annrheumdis-2021-eular.878

POS0835 DECLINE IN FORCED VITAL CAPACITY (FVC) IN SUBJECTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) IN THE SENSCIS TRIAL VERSUS HYPOTHETICAL REFERENCE SUBJECTS WITHOUT LUNG DISEASE

T. Maher[1,2,3], A. Bourdin[4,5], E. Volkmann[6], S. Vettori[7], J. H. W. Distler[8], M. Alves[9], C. Stock[10], O. Distler[11]on behalf of the SENSCIS investigators..
[1]*Imperial College London, National Heart and Lung Institute, London, United Kingdom*; [2]*Royal Brompton Hospital, National Institute for Health Research Clinical Research Facility, London, United Kingdom*; [3]*University of Southern California, Keck School of Medicine, Los Angeles, United States of America*; [4]*University of Montpellier, PhyMedExp, Montpellier, France*; [5]*University of Montpellier, CHU Montpellier, Department of Respiratory Diseases, Montpellier, France*; [6]*University of California, David Geffen School of Medicine, Department of Medicine, Division of Rheumatology, Los Angeles, United States of America*; [7]*Ospedale Monaldi, UOC di Fisiopatologia e Riabilitazione Respiratoria, Napoli, Italy*; [8]*Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Universitätsklinikum Erlangen, Department of Internal Medicine 3-Rheumatology and Immunology, Erlangen, Germany*; [9]*Boehringer Ingelheim International GmbH, TA Inflammation Med, Ingelheim, Germany*; [10]*Boehringer Ingelheim Pharma GmbH & Co. KG, Biostatistics + Data Sciences, Ingelheim am Rhein, Germany*; [11]*University Hospital Zurich, University of Zurich, Department of Rheumatology, Zurich, Switzerland*

Background: In the randomized SENSCIS trial in subjects with SSc-ILD, nintedanib reduced the rate of decline in FVC over 52 weeks (mL/year) by 44% compared to placebo. Healthy individuals have varied FVC depending on age, sex, ethnicity and height; expected values can be determined using internationally recognised reference equations.

Objectives: To provide further context to the FVC declines observed in the SENSCIS trial, we compared the decline in FVC observed in subjects with SSc-ILD in the SENSCIS trial with the decline in FVC that would be expected in hypothetical subjects without ILD matched for age, sex, ethnicity and height.

Methods: The SENSCIS trial enrolled subjects with SSc-ILD aged ≥18 years with first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD ≥10% on HRCT, FVC ≥40% predicted and DLco 30–89% predicted. Baseline FVC (mL) and changes in FVC (mL) at week 52 were assessed in the nintedanib and placebo groups, with missing values at week 52 imputed using predictions from the primary analysis model (random slope and intercept model). Changes in FVC in the SENSCIS trial were compared to values in hypothetical healthy reference subjects matched to the SENSCIS subjects for age, sex, ethnicity and height. FVC values in these healthy reference subjects were derived from the equations published by the European Respiratory Society Global Lung Function Initiative in 2012, which were derived from data from over 70,000 subjects.[1]

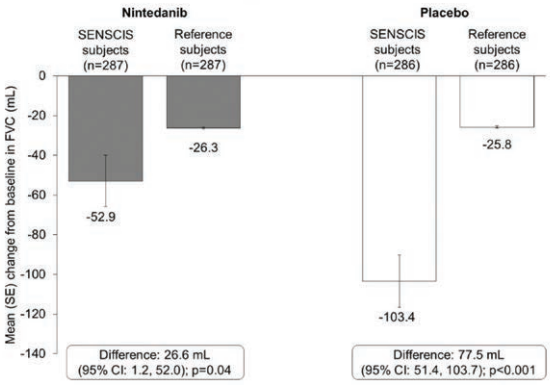
Results: In the nintedanib and placebo groups of the SENSCIS trial, respectively, mean (SD) time since onset of first non-Raynaud symptom was 3.5 (1.6) and 3.5 (1.8) years. In the nintedanib group, mean (SD) FVC at baseline was 2460 (737) mL, compared with 3403 (787) mL in the healthy reference subjects. In the placebo group, mean (SD) FVC at baseline was 2544 (817) mL compared with 3516 (887) mL in the healthy reference subjects. The difference in the change from baseline in FVC at week 52 between the nintedanib-treated subjects in the SENSCIS trial (n=287) and the healthy reference subjects was 26.6 mL ([95% CI: 1.2, 52.0]; p=0.04). The difference in the change from baseline in FVC at week 52 between the placebo-treated subjects in the SENSCIS trial (n=286) and the reference subjects was 77.5 mL ([95% CI: 51.4, 103.7]; p<0.001) (Figure 1).

Conclusion: Subjects with SSc-ILD who participated in the SENSCIS trial had marked lung function impairment at baseline compared with healthy matched reference subjects, despite a mean duration of SSc of 3.5 years. Over 52 weeks, the decline in FVC in subjects with SSc-ILD who received placebo was 4-fold greater than in healthy reference subjects. Subjects with SSc-ILD who were treated with nintedanib had a decline in FVC that was only slightly greater than the decline observed in the matched healthy subjects. These data support the clinical relevance of the reduction in the rate of FVC decline provided by nintedanib in patients with SSc-ILD.

REFERENCES:

[1] Quanjer et al. Eur Respir J 2012;40:1324–43.

Figure. Absolute change from baseline in FVC (mL) at week 52 in subjects in the SENSCIS trial versus hypothetical reference subjects without ILD matched for age, sex, ethnicity and height.



Acknowledgements: The SENSCIS trial was funded by Boehringer Ingelheim. Medical writing support was provided by FleishmanHillard Fishburn, London, UK. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE).

Disclosure of Interests: Toby Maher Speakers bureau: Boehringer Ingelheim and Roche/Genentech, Consultant of: Acelleron Pharma, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline and Roche/Genentech, Arnaud Bourdin Speakers bureau: Actelion/Janssen (personal fees and other), AstraZeneca (personal fees and other), Boeringher Ingelheim (personal fees and other), Chiesi (personal fees and other), GlaxoSmithKline (personal fees and other), Novartis (personal fees and other), Pulsar Therapeutics (other), Roche (personal fees and other), Sanofi Regeneron (personal fees and other), Teva (other) and United Therapeutics (other), Consultant of: Actelion/Janssen (personal fees and other), AstraZeneca (personal fees and other), Boeringher Ingelheim (personal fees and other), Chiesi (personal fees and other), GlaxoSmithKline (personal fees and other), Novartis (personal fees and other), Pulsar Therapeutics (other), Roche (personal fees and other), Sanofi Regeneron (personal fees and other), Teva (other) and United Therapeutics (other), Grant/research support from: Actelion/Janssen (grants and other), AstraZeneca (grants and other), Boeringher Ingelheim (grants and other), Chiesi (other), GlaxoSmithKline (grants and other), Novartis (other), Pulsar Therapeutics (other), Roche (other), Sanofi Regeneron (other), Teva (other) and United Therapeutics (other), Elizabeth Volkmann Consultant of: Boehringer Ingelheim, Grant/research support from: Corbus and Forbius, Serena Vettori Paid instructor for: Boehringer Ingelheim, Consultant of: Boehringer Ingelheim, Jörg H.W. Distler Speakers bureau: Actelion, Active Biotech, AnaMar, Arxx Therapeutics, Bayer, Boehringer Ingelheim, Celgene, Galapagos NV, GlaxoSmithKline, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, Consultant of: AnaMar, Arxx Therapeutics, Bayer, Boehringer Ingelheim, Galapagos NV, Inventiva, JB Therapeutics and UCB, Grant/research support from: Active Biotech, AnaMar, Array BioPharma, Arxx Therapeutics, aTyr, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Galapagos NV, GlaxoSmithKline, Inventiva, Novartis, Sanofi-Aventis, Redx and UCB, Margarida Alves Employee of: Currently an employee of Boehringer Ingelheim, Christian Stock Employee of: Currently an employee of Boehringer Ingelheim, Oliver Distler Consultant of: AbbVie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Bayer, Blade Therapeutics, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos NV, GlaxoSmithKline, Glenmark Pharmaceuticals, Horizon (Curzion) Pharmaceuticals, Inventiva, IQVIA, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Merck Sharp & Dohme, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Target Bioscience, Topadur Pharma and UCB, Grant/research support from: Kymera Therapeutics and Mitsubishi Tanabe Pharma

DOI: 10.1136/annrheumdis-2021-eular.897

POS0836 CONDUCTION AND RHYTHM DISORDERS AMONG PATIENTS WITH SYSTEMIC SCLEROSIS: A US POPULATION BASED STUDY

Y. Radwan[1,2], R. Kurmann[3], E. El-Am[3], A. Sandhu[2], C. S. Crowson[2,4], E. Matteson[2], T. G. Osborn[2], K. J. Warrington[2], R. Mankad[3], A. Makol[2]. *[1]Michigan State University, Department of Internal Medicine, Lansing, United States of America*; *[2]Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; *[3]Mayo Clinic, Department of Cardiovascular Disease, Rochester, United States of America*; *[4]Mayo Clinic, Department of Health Sciences Research, Rochester, United States of America*

Background: Systemic sclerosis (SSc) can impact multiple areas of the heart through fibrotic and vascular processes; leading to variable cardiac involvement including electrocardiogram (ECG) abnormalities. Conduction and rhythm disorders are associated with worse prognosis in patients with SSc. (1, 2)

Objectives: To study the incidence, risk factors and outcomes of conduction and rhythm disorders in a US population-based cohort of patients with SSc and non-SSc comparators from the same geographic area.

Methods: A previously identified incident cohort of SSc patients (1980-2016) in a well-defined geographic area was compared to a randomly selected 2:1 cohort of age- and sex-matched non-SSc subjects from the same population base. Demographics, disease characteristics, cardiovascular risk factors and laboratory tests were abstracted by manual record review. ECGs and Holter ECGs were reviewed to determine the occurrence of any conduction or rhythm abnormalities. The need for cardiac interventions was also abstracted.

Results: 78 incident SSc cases and 156 non-SSc comparators were identified [age 56 years± 15.7, 91% female]. Prevalence of any conduction disorders before SSc diagnosis compared to non-SSc comparators was 15% vs. 7% (p=0.06), and any rhythm disorder was 18% vs. 13% (p=0.33). During a median follow up of 10.5 years in patients with SSc and 13.0 years in non-SSc comparators, conduction disorders developed in 25 SSc patients with a cumulative incidence (ci) of 20.5% (95% CI: 12.4-34.1%) compared to 28 non-SSc patients with ci of 10.4% (95% CI: 6.2-17.4%) (HR: 2.57; 95% CI: 1.48-4.45), while rhythm disorders developed in 27 SSc patients with ci of 27.3% (95% CI: 17.9-41.6%) vs 43 non-SSc patients with ci of 18.0% (95% CI: 12.3-26.4%) (HR: 1.62; 95% CI: 1.00-2.64). (Figure 1).

Conduction disorders in patients with SSc during follow up included: 1st-degree atrioventricular block (AVB) (n=12), 2nd-degree AVB (n=1), 3rd-degree AVB (n=1), right bundle branch block (n=10), left bundle branch block (n=4), bifascicular block (n=6), and prolonged-QT (n=13). Rhythm disorders included: atrial fibrillation (n=10), atrial flutter (n=4), supraventricular tachycardia (n=4), ventricular tachycardia (n=1), and premature ventricular contractions (n=16).

Pulmonary hypertension (PHT) was the only significant risk factor identified for development of both conduction and rhythm disorders (HR=8.38, 95% CI: 1.32-53.40 and HR=8.07, 95% CI: 1.60-40.74, respectively). Current smoking significantly increased the risk for development of rhythm disorders (HR=2.91, 95% CI: 1.19-7.12). Conduction and rhythm disorders were associated with increased mortality among patients with SSc (HR=7.60, 95% CI: 3.49-16.55 and HR=4.87, 95% CI: 2.28-10.42, respectively, after adjusting for age, sex and calendar year of diagnosis).

Conclusion: Patients with SSc have a significantly higher prevalence of conduction disorders at disease onset than non-SSc comparators. During the course of their disease, their risk of developing conduction disorders is 2.6-fold, and risk of rhythm disorders is 1.6-fold increased, compared to non-SSc subjects.

PHT was significantly associated with increased risk of developing conduction and rhythm disorders among patients with SSc, a finding that should warrant increased vigilance and screening for ECG abnormalities in this population.

REFERENCES:

[1] Tyndall A.J. et al. Ann Rheum Dis, 2010. 69(10): p. 1809-15.
[2] Desai C.S. et al. Curr Opin Rheumatol, 2011. 23(6): p. 545-54.

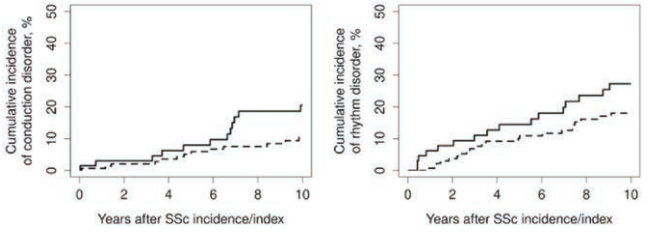


Figure 1. Cumulative incidence of any conduction or any rhythm disorder in SSc (solid line) vs non-SSc comparators (dashed line).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.911

POS0837 THE USE OF CANNABIDIOL IN THE TREATMENT OF PAIN RELATED TO SCLERODERMA DIGITAL ULCERS

D. Giuggioli[1], M. De Pinto[1], L. Parenti[1], L. Magnani[2], P. Castrignanò[1], C. Salvarani[1,2], A. Spinella[1]. *[1]University of Modena and Reggio Emilia, Scleroderma Unit, Rheumatology Unit, Modena, Italy*; *[2]AUSL-IRCCS of Reggio Emilia, Italy, Rheumatolgy, Reggio Emilia, Italy*

Background: Systemic Sclerosis-SSc is an autoimmune disease, characterized by fibrosis due to immune-mediated microangiopathy. Digital ulcers-DUs represent frequent complications, they are recurrent, painful and often resistant to traditional treatments. Standard therapy, in particular oral opioids, is often

inadequate or limited by side effect. Cannabidiol-CBD, is the major non-psychotropic component of the Cannabis sativa, recent studies on its effectiveness as an anxiolytic, anti-inflammatory, and antipsychotic drug showed promising results, in the setting of chronic pain too.

Objectives: We evaluated the efficacy of CBD drop in pain management in a cohort of SSc patients using standard rating scale VAS, PSQI and HAQ. We further assessed the safety profile and the potential use as opioid-sparing.

Methods: From January to November 2019 we consecutively enrolled 31 SSc patients (F/M 26/5, mean age 53.0±14.6SD-years) referred to our Scleroderma Unit. All patients satisfied the EULAR/ACR SSc classification criteria. All cases were complicated by painful DUs resistant to analgesics and pain was classified as severe, according to WHO guidelines. CBD drops consist of cannabis sativa seed in olive oil, 10% CBD, laboratory tested to confirm a tetrahydrocannabinol-THC level<0.3%. The CBD oil was administrated sublingually twice-a-day. All patients started with CBD 3 drops twice-a-day, and progressively increased to the maximum dosage of 6 drops twice-a-day (from 27.6 g to 55.2 g dose/day). All patients continued local/systemic treatments for SSc: 24/31 subjects performed calcium-channel blockers, 31/31 prostanoids infusion, 24/31 anti-endothelin drugs. All subjects were provided with a daily diary to record self-evaluation of pain using VAS, PSQI, hours of sleep per night, use of other analgesics, eventual side effects. HAQ-DI was also administrated. These indicators were assessed baseline and during follow-up. Safety of CBD was evaluated by patient's records of side effects. All data were analyzed by paired t-test. This investigation was a monocentric, prospective study. Ethical approval was obtained from the Competent Ethics Committee (protocol n. 282/15) and all participants gave written consent.

Results: CBD was administered for a mean period of 5.9±3.2SD-months. After the first month, VAS decreased from 94.80±8.72SD to 54.70±9.40SD ($p<0.0001$), PSQI decreased from 9.27±2.9SD to 4.47±1.06SD ($p<0.001$), total hours of sleep increased from 2.56±1.28 SD to 5.67±0.85SD ($p< 0.0001$). The additional analgesic therapy was necessary in 22/31 patients: 6/22 only paracetamol, 12/22 paracetamol+oxycodone reducing the dosage of oxycodone at the minimum, 2/22 oxycodone 20 mg twice-a-day, 2/22 need fentanyl transdermal patch. After 3 months, VAS further reduced to 40.90±12.90, PSQI decreased to 3.1±1.4SD, the mean total hours of sleep per night was 6.10±0.79SD and the HAQ-DI decreased from 2.19±0.67SD (baseline) to 0.79±0.46SD at the last patients' evaluation. At the end of the observation, 18/31 patients (58%) showed DUs healing. We also interestingly reported improvement of dysphagia and appetite in 70%, and an improvement in constipation related to opiods in 48%. No patients experienced severe side effects in particular no psychoactive aspects. Mild side effects, namely dry mouth was referred by 9/31 (29%), mild abdominal pain and changes in appetite by 10/31 (32%). No interaction with other drugs was observed.

Conclusion: Our study suggests that oral CBD is effective and safe in maintaining analgesia in SSc patients with DUs. Furthermore, CBD could be helpful in opioids tapering and to treat dysphagia, even if these observations need focused investigations. In conclusion, CBD might be a useful tool to manage chronic pain in SSc-DUs. These data provide a compelling rationale for further research to clarify the therapeutic potential of CBD in SSc.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.918

POS0838 EPIDEMIOLOGY AND TRENDS IN SURVIVAL OF SYSTEMIC SCLEROSIS IN OLMSTED COUNTY: A POPULATION-BASED STUDY (1980-2018)

C. Coffey[1], Y. Radwan[2], A. Sandhu[3], C. S. Crowson[1,4], P. Bauer[5], E. Matteson[1,4], A. Makol[1]. [1]*Mayo Clinic, Division of Rheumatology, Rochester, MN, United States of America*; [2]*Michigan State University, Internal Medicine, Lansing, MI, United States of America*; [3]*Kettering Health, Internal Medicine, Kettering, OH, United States of America*; [4]*Mayo Clinic, Health Sciences Research, Rochester, MN, United States of America*; [5]*Mayo Clinic, Division of Pulmonary and Critical Care, Rochester, MN, United States of America*

Background: Systemic sclerosis (SSc) is a complex immune-mediated disease with heterogeneous manifestations, which is characterized by vasculopathy and fibrosis of the skin and visceral organs. Mortality associated with SSc exceeds that of other rheumatic diseases, though population-based studies assessing recent trends in survival are lacking.

Objectives: We aimed to determine the incidence and prevalence of physician-diagnosed SSc in a population-based cohort over a 39-year time period, and assess for trends in survival over time.

Methods: Medical records of patients with a diagnosis or suspicion of SSc in a geographically well-defined area from Jan 1, 1980 to Dec 31, 2018 were reviewed to identify incident cases of SSc. Cases were defined by physician diagnosis of SSc, and fulfillment of the 2013 ACR/EULAR classification criteria was ascertained. Prevalent cases of SSc on Jan 1, 2015 were also identified. Incidence and prevalence rates were age- and sex-adjusted to the 2010 U.S. white population. Survival rates were compared with expected rates in the general population.

Results: 85 incident cases of SSc (91% female, mean age 55.4 ± 16 y) and 49 prevalent cases on Jan 1, 2015 were identified. Patients had a mean 11.7 (SD 9.4) years of follow-up available. The overall age and sex adjusted annual incidence for 1980-2018 was 2.5 (95% CI: 2.0-3.1) per 100,000 population, with no change in incidence over time (p=0.32). The age-adjusted incidence was 4.4 (95% CI: 3.4-5.4) for females, and 0.56 (95% CI: 0.16-0.96) for males per 100,000 population. The age- and sex-adjusted prevalence on Jan 1, 2015 was 43.6 (95% CI: 31.3-55.8) per 100,000 population.

77 (91%) patients fulfilled the 2013 classification criteria; 38 (45%) fulfilled 1980 criteria. 70 (82%) had limited cutaneous involvement, 12 (14%) had diffuse cutaneous involvement, and 3 (4%) had sine scleroderma. At SSc diagnosis, 80 (94%) patients had Raynaud's, 43 (51%) had sclerodactyly, 39 (46%) had telangiectasias, 14/48 (29%) had abnormal nailfold capillaries, 16/35 (46%) had digital ulcers or fingertip scarring, 8 (9%) had interstitial lung disease (ILD), and 7 (8%) had pulmonary arterial hypertension (PAH). 77/82 patients (91%) had a positive antinuclear antibody. 44 (52%) had a known SSc-related autoantibody: 32 (73%) with anti-centromere, 9 (20%) with anti-Scl-70, and 4 (9%) with anti-RNA-polymerase III.

Survival was 77% (95% CI: 69-87) at 5 years, 66% (95% CI: 56-78) at 10 years, and 42% (95% CI: 30-57) at 20 years, with no evidence of improved survival over time (p=0.46). Age (Hazard ratio [HR]: 1.49 per 10 year increase; 95% CI 1.19-1.88), smoking at time of diagnosis (HR: 2.37; 95% CI: 1.05-5.34), digital ischemia (HR: 2.54; 95% CI: 1.33-4.87), ILD (HR: 4.00; 95% CI: 2.11-7.59), and PAH (HR: 4.30; 95% CI: 2.24-8.25) had significant associations with mortality. Survival of patients with SSc was poorer than the general population (standardized mortality ratio: 2.48; 95% CI: 1.76-3.39).

Conclusion: The average incidence of SSc in this population-based cohort spanning 39 years was 2.5 per 100,000 population, with no change in incidence over time. Age, smoking, digital ischemia, ILD and PAH were risk factors for poorer survival. Overall survival for patients with SSc is worse than that of the general population and shows no improvement over time, suggesting continued need for improved diagnostic and treatment measures.

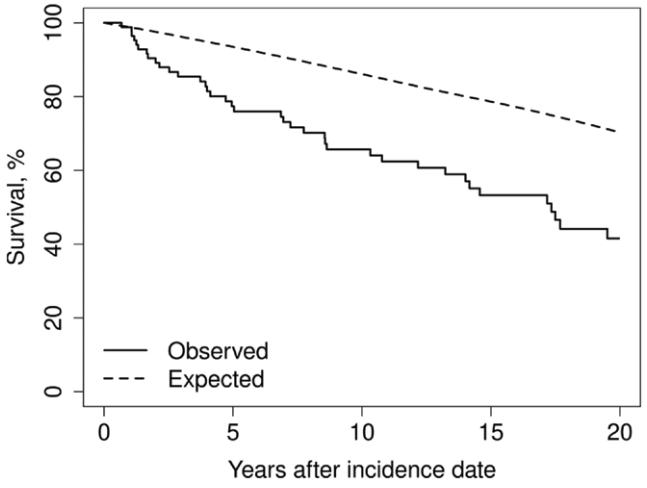


Figure 1. Survival of 85 Olmsted County residents with SSc compared with expected survival rates from Minnesota lifetables (observed: solid line, expected: dashed line).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.919

POS0839 BODY COMPOSITION AND FREQUENCY OF SARCOPENIA IN PATIENTS WITH SYSTEMIC SCLEROSIS

A. Efremova[1], O. Nikitinskaya[1], N. Toroptsova[1], O. Dobrovolskaya[1], N. Demin[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Department of Osteoporosis, Moscow, Russian Federation*

Background: Sarcopenia can be age associated (primary form) or secondary to chronic disorders, including rheumatic inflammatory disorders. Systemic sclerosis (SSc) is a chronic autoimmune rheumatic disease characterized by widespread vasculopathy, progressive fibrosis of the skin and other internal organs, such as lung, kidneys, gastrointestinal tract, cardiovascular system. Different from the other chronic rheumatic inflammatory disorders, sarcopenia has not been well evaluated in SSc patients.

Objectives: To assess the body composition (BC) and to identify the frequency of sarcopenia (SP) in SSc patients.
Methods: A total of 44 women who met the ACR/EULAR 2013 classification criteria were included. Mean age was 53,2 + 8,8 years. The median disease duration was 7,0 [4,0;12,0] years. 26 (59,1%) patients had limited and 18 (40,9%) - diffuse cutaneous subtype. Body composition was measured using Dual-energy X-ray absorptiometry (DXA) of whole body. The appendicular lean mass index (ALMI) was calculated as the ratio of appendicular lean mass (ALM) to height (kg/m2). Handgrip measurement and chair stand test were performed. Physical function was measured with the Short Physical Performance Battery (SPPB). SP was diagnosed in agreement with the 2019 revised consensus on definition and diagnosis of SP of the European Working Group on Sarcopenia in Older People 2 (EWGSOP2): handgrip <16kg, chair stand test > 15 seconds for 5 rises, ALM <15 kg or ALMI <5.5 kg/m2. Severe SP was detected if the patient additionally had gait speed ≤0.8 m/s or SPPB ≤ 8-point score. Overfat was defined as body fat percentage >35%.
Results: The median bone mineral content was 2.0 [1.8; 2.2] kg, total lean mass - 39,5 [35,7; 45,5] kg, ALM - 16,3 [14,5;19,4] kg, ALMI – 6,5 [5,7; 7,2] kg/m2, trunk fat mass – 13,5 [9,1; 16,7] kg and total fat mass - 26,6 [20,1; 34,5] kg. Body fat percentage was 38,8% [34,2; 42,7].
9 (20,5%) women had low ALM and low ALMI, 6 (13,6%) – only low ALM. Healthy BC was found in 5 (11,3%), low ALM or low ALMI – in 7 (15,9%), overfat – in 24 (54,5%), low ALM + overfat – in 8 (18,2%) patients. We found no differences in BC between SSc patients with limited and diffuse cutaneous subtype.
Low muscle strength (SP probable) was found in 21 (47,7%) women, meanwhile confirmed SP (low muscle strength and muscle mass) was diagnosed in 10 (22,7%) patients, among them 5 (11,4%) persons had severe SP. No significant difference in SP frequency among patients with limited and diffuse cutaneous SSc 4 (15,4%) and 6 (33,3%), respectively, (p=0,27). Osteoporosis was found in 6 (60%) patients with SP without differences in SSc subtypes.
Conclusion: Healthy BC was found only in 11,3% cases, while overfat - in 72,7% and low ALM – in 34,1% SSc patients. SP was detected in 22.7% of women, among them in half of cases - severe SP, without any differences between the limited and diffuse subtypes of the disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.970

POS0840 RISK OF MALNUTRITION IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD): FURTHER ANALYSES OF THE SENSCIS TRIAL

E. Volkmann[1], Z. Mcmahan[2], S. Johnson[3], V. Smith[4], S. Jouneau[5], C. Miede[6], M. Alves[7], A. Herrick[8]on behalf of the SENSCIS trial investigators.. *[1]University of California, David Geffen School of Medicine, Department of Medicine, Division of Rheumatology, Los Angeles, United States of America*; *[2]Johns Hopkins University School of Medicine, Division of Rheumatology, Baltimore, United States of America*; *[3]Toronto Western and Mount Sinai Hospitals, University of Toronto, Toronto Scleroderma Program, Department of Medicine, Toronto, Canada*; *[4]Ghent University Hospital, Department of Rheumatology and Internal Medicine, Ghent, Belgium*; *[5]Competences Centre for Rare Pulmonary Diseases, University of Rennes, CHU Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail) - UMR_S 1085, Department of Respiratory Medicine, F-35000 Rennes, France*; *[6]mainanalytics GmbH, Statistics, Sulzbach (Taunus), Germany*; *[7]Boehringer Ingelheim International GmbH, TA Inflammation Med, Ingelheim am Rhein, Germany*; *[8]The University of Manchester, Salford Royal NHS Foundation Trust, Centre for Musculoskeletal Research, Manchester, United Kingdom*

Background: Gastrointestinal (GI) involvement is common in patients with SSc and may lead to weight loss and malnutrition. In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks, with mainly GI adverse events. The Malnutrition Universal Screening Tool (MUST) was developed to identify adults who are at risk of malnutrition and has been used in studies of patients with SSc.
Objectives: To evaluate nutritional status over 52 weeks in the SENSCIS trial based on a modified MUST score.
Methods: The SENSCIS trial enrolled patients with SSc-ILD with first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD ≥10% on HRCT and FVC ≥40% predicted. Patients who had taken a stable dose of mycophenolate for ≥6 months were eligible to participate. Patients were randomised to receive nintedanib 150 mg bid or placebo. Dose reductions to 100 mg bid and treatment interruptions were allowed to manage adverse events and specific recommendations were provided for the management of diarrhoea. We calculated a modified MUST score at baseline and weeks 12, 24, 36 and 52 based on (A) BMI, (B) weight loss (week 12 vs baseline; week 24 vs week 12; week 36 vs week 24; week 52 vs week 36), and (C) a surrogate for acute disease effect (if the patient had any serious adverse event that led to hospitalisation between weight assessments and received ≥1 medication from the WHO classification code for "solutions for parenteral nutrition" for ≥5 days). MUST score at baseline was based solely on BMI. With scores ranging from 0 to 6, the risk of malnutrition is defined as low (score = 0), medium (score = 1) or high (score ≥2).
Results: Among 576 patients who received nintedanib (n=288) or placebo (n=288), mean (SD) age at baseline was 54.0 (12.2) years, weight was 69.7 (15.9) kg and BMI was 25.9 (5.0) kg/m^2; median time since onset of first non-Raynaud symptom was 3.4 years; and 75.2% of patients were female. In the nintedanib and placebo groups, respectively, MUST scores suggested that 74.0% and 78.1% of patients were at low risk of malnutrition at baseline and remained at low risk at their last measurement (Table 1). At weeks 12 and 52, respectively, mean (SD) MUST scores were 0.3 (0.6) and 0.4 (0.7) in the nintedanib group and 0.2 (0.5) and 0.2 (0.6) in the placebo group. At weeks 12, 24, 36 and 52, respectively, the proportions of patients at low risk of malnutrition were 81.8%, 80.9%, 72.9% and 76.5% in the nintedanib group and 86.6%, 86.4%, 88.3% and 80.8% in the placebo group; the proportions at medium risk were 12.1%, 13.1%, 18.0% and 13.5% in the nintedanib group and 8.5%, 8.6%, 5.8% and 13.1% in the placebo group; and the proportions of patients at high risk were 6.1%, 5.6%, 8.3% and 9.6% in the nintedanib group and 4.9%, 4.3%, 4.7% and 5.4% in the placebo group.

Table 1. Risk of malnutrition at baseline and at last assessment over 52 weeks in the SENSCIS trial.

Last assessment of risk	Nintedanib (n=288)				Placebo (n=288)			
	Baseline risk				Baseline risk			
	Low	Medium	High	Total	Low	Medium	High	Total
Low	213 (74.0)	1 (0.3)	0	214 (74.3)	225 (78.1)	7 (2.4)	0	232 (80.6)
Medium	31 (10.8)	8 (2.8)	0	39 (13.5)	20 (6.9)	14 (4.9)	4 (1.4)	38 (13.2)
High	13 (4.5)	8 (2.8)	7 (2.4)	28 (9.7)	3 (1.0)	2 (0.7)	10 (3.5)	15 (5.2)
Missing	7 (2.4)	0	0	7 (2.4)	3 (1.0)	0	0	3 (1.0)
Total	264 (91.7)	17 (5.9)	7 (2.4)	288 (100)	251 (87.2)	23 (8.0)	14 (4.9)	288 (100)

MUST score ranges from 0 to 6. Score of 0 = low risk: score of 1 = medium risk; score of ≥2 = high risk. Baseline MUST score was based solely on BMI.

Conclusion: In the SENSCIS trial, scores based on a modified MUST indicated that most patients treated with nintedanib were at low risk of malnutrition at baseline and remained at low risk over 52 weeks. The proportions of patients at high risk of malnutrition were low but were numerically greater in patients who received nintedanib than placebo. Management of disease manifestations and gastrointestinal adverse events that may be associated with weight loss is important to reduce the risk of malnutrition in patients with SSc-ILD treated with nintedanib.
Acknowledgements: The SENSCIS trial was funded by Boehringer Ingelheim. Medical writing support was provided by FleishmanHillard Fishburn, London, UK. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE).
Disclosure of Interests: Elizabeth Volkmann Consultant of: Boehringer Ingelheim, Grant/research support from: Corbus and Forbius, Zsuzsanna McMahan: None declared, Sindhu Johnson Consultant of: Boehringer Ingelheim, CSL Behring and Ikaria, Grant/research support from: Bayer, Boehringer Ingelheim, Corbus, GlaxoSmithKline, Merck and Roche, Vanessa Smith Speakers bureau: Boehringer Ingelheim and Janssen, Consultant of: Boehringer Ingelheim, Grant/research support from: Belgian Fund for Scientific Research in Rheumatic diseases (FWRO), Boehringer Ingelheim, Research Foundation - Flanders (FWO) and Janssen, Stéphane Jouneau Speakers bureau: Actelion, AIRB, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Chiesi, Genzyme, GlaxoSmithKline, LVL Mediphar, Mundipharma, Novartis, Pfizer, Roche and Sanofi, Consultant of: AIRB, Boehringer Ingelheim, Novartis and Roche, Grant/research support from: AIRB, Boehringer Ingelheim, LVL Mediphar, Novartis and Roche, Corinna Miede Employee of: Currently an employee of mainanalytics GmbH, contracted by Boehringer Ingelheim, Margarida Alves Employee of: Currently an employee of Boehringer Ingelheim, Ariane Herrick Speakers bureau: Janssen, Consultant of: Boehringer Ingelheim, Camurus, CSL Behring and Gesynta Pharma, Grant/research support from: Actelion and Gesynta Pharma
DOI: 10.1136/annrheumdis-2021-eular.1083

POS0841 RISK FACTORS OF LOW BONE MINERAL DENSITY IN WOMEN WITH SYSTEMIC SCLEROSIS

A. Efremova[1], N. Toroptsova[2], N. Demin[2], O. Dobrovolskaya[2], O. Nikitinskaya[2]. *[1]V.A. Nasonova Research Institute of Rheumatology, Department of Osteoporosis, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Department of Osteoporosis, Moscow, Russian Federation*

Background: Chronic inflammatory rheumatic diseases are risk factors of bone loss and fractures. Systemic sclerosis (SSc) has been recognized to be another potential inflammatory joint disease that may affect bone tissue.
Objectives: to evaluate bone mineral density (BMD) and risk factors of low BMD in women with SSc.
Methods: 173 women, among them 110 postmenopausal (median age 60[55,63] years) and 63 premenopausal (median age 35[31,44] years). BMD was measured at lumbar spine (LS), femoral neck (FN) and total hip (TH) by dual energy X-ray absorptiometry (DXA, Hologic 4500A). Low BMD was diagnosed if the T-score was < -1.0 standard deviation (SD) in postmenopausal women and if the Z-score was < -2.0 SD in premenopausal women. The relationship between BMD and SSc patients' characteristics was evaluated using univariate linear regression analysis.
Results: Low BMD was found in 66% patients: 79% - in postmenopausal and 18% - in premenopausal women. Among postmenopausal persons osteoporosis was discovered in 47% and osteopenia – in 32% cases. In postmenopausal woman BMD of LS, FN and TH were associated with body mass index (BMI) (β=0.27, p=0.010; β=0.47, p<0,001 and β=0.45, p<0,001, respectively), duration of glucocorticoids (GCs) using (β=-0.31, p=0.008; β=-0.34, p=0.003 and β=-0.27, p=0.022, respectively); BMD of FN and TH with C-reactive protein (β= -0.32, p=0.016 and β= -0.29, p=0.029, respectively) and LS BMD with current and cumulative GCs dose (β= -0.24, p=0.039 and β= -0.29, p=0.014, respectively). In premenopausal women BMD of LS, FN and TH were associated with BMI (β=0.51, p<0,001; β=0.45, p=0.003 and β=0.47, p=0.002, respectively), duration of GCs using (β= -0.45, p=0.004; β= -0.47, p=0.003 and β= -0.48, p=0.002, respectively) and GCs cumulative dose (β= -0.48, p=0.002; β= -0.51, p=0.001 and β= -0.46, p=0.004, respectively); BMD of FN and TH with 25(OH)D level (β=0.52, p=0.008 and β=0.54, p=0.005, respectively), and LS BMD with SSc duration (β= -0.44, p=0.004).
Conclusion: Low BMD was diagnosed in 66% of women with SSc. Low BMI, GCs cumulative dose and duration of GCs using were independent risk factors for low BMD in both premenopausal and postmenopausal persons. Additional factors as SSc duration and low vitamin D level were found out for premenopausal and current GCs dose and C-reactive protein level for postmenopausal women.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1339

POS0842 LUNG ULTRASOUND TO ASSESS THE SEVERITY OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS

C. Bruni[1], L. Mattolini[1], L. Tofani[1], L. Gargani[2], N. Landini[3,4], G. Lepri[1], M. Orlandi[1], S. Guiducci[1], S. Bellando Randone[1], M. Matucci-Cerinic[1].
[1]Careggi University Hospital, Experimental and Clinical Medicine, Division of Rheumatology, Firenze, Italy; *[2]National Research Council (CNR) PISA, Institute of Clinical Physiology, Pisa, Italy*; *[3]Cà Foncello General Hospital, Radiology, Treviso, Italy*; *[4]University of Florence, Experimental and Clinical Biomedical Sciences, Division of Radiology, Firenze, Italy*

Background: Interstitial lung disease (ILD) is one of the most common complications and one of the main causes of morbidity and mortality in Systemic Sclerosis (SSc). High-resolution computed tomography (HRCT) is the gold standard for the diagnosis of ILD and it allows its quantification. Among semi-quantitative methods, Goh et al proposed a semi-quantitative scoring system to visually quantify ILD extent, with categorical cut-off of 20% to distinguish limited and extensive parenchymal involvement with prognostic implications. More recently, the use of radiomics has allowed the objective quantification of ILD through the use of dedicated software, which calculate different parameters of lung density. Given the exposure to ionizing radiation that the procedure entails, other methods of ILD evaluation are being studied, among which lung ultrasound (LUS) identifies the B-lines as a main feature of ILD. So far, different evidences have proposed the use of LUS for the screening of ILD, even in the early phases of the disease and in subclinical lung involvement.
Objectives: the aim of this study is to test the role of LUS in quantifying the severity of SSc-ILD, evaluated with both semi-quantitative visual radiological and quantitative radiomic scores.
Methods: Adult SSc patients classified according to the ACR/EULAR 2013 criteria patients were assessed with pulmonary function test (PFTs), lung ultrasound and HRCT over 60 days. CT images were analysed qualitatively (by presence/absence of ILD), semi-quantitatively (categorical Goh score <20% vs> 20% of extent and the continuous extent Goh score made from 5 levels' assessment– 0 to 100%) and quantitatively [with the densitometric radiomic data obtained through the Horos software - Mean lung attenuation (MLA), Standard Deviation (SD), Kurtosis, Skewness and Lung volume (LV)]. LUS was used to quantify the B-lines detected in each patient by scanning a total of 13 intercostal spaces, on both anterior and posterior chest wall.
Results: Among 59 SSc patients (81% women, mean age 48±14 years, 45% anti-Scl70 positive), 23 (39%) presented ILD on HRCT, of which 14 limited and 9 extensive. The mean visual semi-quantitative score was 6%, ranging from 0 to 66%. Our data showed a significantly different number of B-Lines in ILD vs non-ILD patients (median 38 vs 9, p <.005), a result which was further confirmed among non-ILD vs ILD> 20% (median 47 vs 9, p=.001) and ILD <20% (median 36 vs 9, p=.001) patients. Conversely, the number of B-lines was not statistically different between patients with ILD <20% and >20% (median 47 vs 36, p=.78). We observed a significant negative correlation between the number of B-lines and FVC (r=-.472, p<.05) TLC (r=-.436, p=.003), DLco (r=-.515, p<.001), DLCO/VA (r=.-306, p=.03). Finally, the number of B-lines showed a statistically significant correlation with the Goh score on 5 levels (r=.437, p=.001), MLA (r=.571, p<.001), kurtosis (r=-.285, p=.028), skewness (r=-.370, p = .004) and LV (r=-.277, p=.033). All data were confirmed analysing anterior and posterior B-Lines separately.
Conclusion: Our study confirms that LUS represents a useful tool for the identification of SSc-ILD. In addition, we showed that LUS may be useful also for the quantification of the severity of SSc-ILD, by correlating with PFT parameters, radiomics parameters and visual radiological evaluation. Together with the PFTs, LUS could be used to increase the accuracy of the screening and, potentially, of the follow-up of SSc-ILD patients.
Disclosure of Interests: Cosimo Bruni: None declared, Lavinia Mattolini: None declared, Lorenzo Tofani: None declared, Luna Gargani Consultant of: GE Healthcare, Philips Healthcare and Caption Health, Nicholas Landini: None declared, Gemma Lepri: None declared, Martina Orlandi: None declared, Serena Guiducci: None declared, Silvia Bellando Randone: None declared, Marco Matucci-Cerinic: None declared
DOI: 10.1136/annrheumdis-2021-eular.1350

POS0843 A NEW RISK MODEL IS ABLE TO IDENTIFY SYSTEMIC SCLEROSIS PATIENTS WITH A LOW RISK OF DISEASE PROGRESSION

N. Van Leeuwen[1], M. Maurits[1], S. Liem[1], J. Ciaffi[1], N. Ajmone-Marsan[2], M. Ninaber[3], C. Allaart[1], H. Gillet-van Dongen[4], R. Goekoop[5], T. Huizinga[1], R. Knevel[1], J. De Vries-Bouwstra[1]. *[1]Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; *[2]Leiden University Medical Center, Cardiology, Leiden, Netherlands*; *[3]Leiden University Medical Center, Pulmonology, Leiden, Netherlands*; *[4]Haaglanden Medisch Centrum, Rheumatology, Den Haag, Netherlands*; *[5]HagaZiekenhuis, Rheumatology, Den Haag, Netherlands*

Background: Disease course in Systemic Sclerosis (SSc) ranges from mild, to severe with progressive organ involvement within months. Guidelines for follow-up are mainly based on expert consensus, and advocate annual assessment. So far, no data driven guidelines exist that describe tailormade systematic assessments for individual patients in line with individual disease course.
Objectives: To develop a prediction model to guide annual assessment of SSc patients tailored in accordance to disease activity.
Methods: A machine learning approach was used to develop a model that can identify patients without disease progression. SSc patients included in the prospective Leiden SSc cohort and fulfilling the ACR/EULAR 2013 criteria were included. The primary endpoint in the prediction model was disease progression which was defined as progression in ≥1 organ system, and/or start of immunosuppression or death between the two most recent visits. Using elastic-net-regularization, and including 90 independent clinical variables (100% complete), we trained the model on 75% and validated it on 25% of the patients in order to perform internal validation of the final model. We optimized the model on negative predictive value (NPV) to minimize the likelihood of missing progression. By expert assessment of the test characteristics, including swarm plots of the probability scores, cut-offs were identified for low, intermediate and high risk for disease progression.
Results: Of the 492 SSc patients (range of follow-up: 2-10yrs), disease progression during follow-up was observed in 52% (median time 4.9yrs), including myocardial progression in 29%, lung progression in 23%, skin progression in 16%,

Baseline characteristics	Total n=492	Non-Progressors N=235	Progressors N=257
Demographics			
Female, n (%)	389 (79)	193 (82)	196 (76)
Age, mean (SD)	55 (14)	55 (15)	55 (13)
Disease duration nonRP, median (IQR)	3.2 (0.9-10.3)	3.5 (0.8-10.5)	3.6 (1.1-9.3)
Organ involvement			
DcSSc, n (%)	118 (24)	**34 (15)**	**84 (33)**
DLCO% of pred, mean (SD)	66 (18)	69 (18)	64 (17)
FVC% of pred, mean (SD)	98 (23)	96 (24)	97 (21)
ILD on HRCT, n (%)	183 (37)	**66 (28)**	**117 (46)**
PAH, n (%)	26 (5)	10 (4)	16 (6)
GAVE, n (%)	9 (2)	4 (2)	5 (2)
Cardiac involvement, n (%)	28 (6)	14 (6)	14 (5)
Myositis, n (%)	8 (2)	6 (3)	2 (1)
Renal crisis, n (%)	14 (3)	6 (3)	8 (3)
Autoantibodies			
Anti-centromere, n (%)	194 (39)	**118 (50)**	**76 (30)**
Anti-topoisomerase, n (%)	116 (24)	**42 (18)**	**74 (29)**

RP=raynaud phenomenon, dcSSc= diffuse cutaneous systemic sclerosis, mRSS=modified rodnan skin score, DU=digital ulcera, DLCO= single-breath diffusing capacity for carbon monoxide, FVC= forced vital capacity, ILD=interstitial lung disease, HRCT= high resolution computed tomography, PAH= pulmonary arterial hypertension, GAVE= gastric antral vascular extasia.

and death in 12%. Performance of the model in the test set showed an AUC-ROC of 0.66. Probability score cutoffs were defined: low risk for disease progression (<0.197, NPV:1.0; 29% of patients), intermediate risk (0.197-0.223, NPV:0.82; 27%) and high risk (>0.223, NPV:0.78; 44%). The predictive variables included in the model were: previous use of cyclophosphamide or corticosteroids, start with immunosuppressive drugs, previous gastrointestinal progression, previous cardiovascular event, pulmonary arterial hypertension, modified Rodnan Skin Score, creatinine kinase, and diffusing capacity for carbon monoxide.
Conclusion: Our machine-learning-assisted model for disease progression enabled us to classify 29% of SSc patients as 'low risk'. In this group annual assessment programs could be less extensive than indicated by international guidelines.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1418

POS0844 EFFECTS OF SERIAL LOCALLY APPLIED WATER-FILTERED INFRARED A RADIATION IN PATIENTS WITH SYSTEMIC SCLEROSIS WITH SEVERE RAYNAUD'S SYNDROME RECEIVING PROSTAGLANDINE TREATMENT – A RANDOMIZED CONTROLLED TRIAL

P. Klemm[1], J. Bär[1], I. Aykara[1], K. Frommer[1], E. Neumann[1], U. Müller-Ladner[1], U. Lange[1]. [1]*Justus Liebig University Giessen, Campus Kerckhoff, Rheumatology, Clinical Immunology, Osteology and Physical Medicine, Bad Nauheim, Germany*

Background: More than 95% of patients with systemic sclerosis (SSc) suffer from Raynaud's syndrome (RS) leading to digital ulcerations (DU). In severe RS, intravenous application of prostaglandins is required. Moreover, these patients profit from an additional non-pharmacological treatment using hyperthermia to increase vasodilatation and perfusion, and to reduce pain.
Serial locally applied water-filtered infrared A radiation (sl-wIRAR) is a hyperthermia treatment modality using infrared heat radiation in the range of 780-1400nm with high tissue penetration and low thermal load on the skin surface [1]. wIRAR has both, temperature-dependent and non-dependent effects, which do not inherit thermal energy transfer and/or relevant temperature changes [1]. It is therefore not only used in acute and chronic wound healing as it promotes perfusion, alleviates pain and has anti-infectious effects [2], but is also used in oncology [3] and rheumatology [4].
Objectives: We conducted a randomized controlled trial with a follow-up visit after 2 weeks to evaluate the value of a high-frequent hyperthermia treatment using sl-wIRAR in comparison to a low-frequent hyperthermia treatment (our standard) in SSc patients with severe RS receiving Iloprost treatment.
Methods: Eligible patients had SSc according to the 2013 ACR/EULAR classification criteria, were 18 to 80 years old and had RS requiring treatment with Iloprost in an in-patient setting. Key exclusion criteria were contraindications to any hyperthermia treatment such as infection or heat insensitivity. The trial was conducted at Campus Kerckhoff of Justus-Liebig University Giessen. Eligible patients were equally randomized to the intervention group (IG) receiving additional sl-wIRAR treatment (2 treatments for 30 min per day for 8 days) plus the standard of care (Iloprost treatment over 8 days plus daily carbon dioxide hand baths of 20 min) and the control group (CG) receiving only the standard of care. Primary outcome was the between-group difference in pain measured on a numeric rating scale (NRS) after intervention. Key secondary outcomes included a change in RS frequency, RS duration, and a change in Interleukin (IL) -6 and VEGF levels.
Results: From 01.03.2020 to 31.12.2020 49 SSc patients met the inclusion criteria. 42 patients were enrolled (IG: 21, CG: 21). 38 patients (IG:19, CG: 19) completed the full trial period and were analyzed. There was no statistically significant between-group difference in pain levels (NRS) (p=0.284, Z -1.082 (Mann-Whitney U Test)) and thus the primary outcome was not met. Therefore, all p values for secondary outcomes are nominal. Intensity (Visual analogue scale 0-100mm) and duration (min) of RS were reduced in the IG (mean ± standard error) -14.579 ± 7.214 mm (p=0.058) and -2.917 ± 1.510 min (p=0.08), respectively. Intra- and inter-group comparison of IL-6 and VEGF levels showed no relevant change.
Conclusion: The additive and frequent use of sl-wIRAR in the treatment of SSc patients with RS requiring Iloprost treatment does not improve outcomes regarding pain levels, RS intensity or frequency nor IL-6 and VEGF levels when compared to Iloprost treatment and low-frequent hyperthermia application.
REFERENCES:
[1] Hoffmann G. Clinical applications of water-filtered infrared-A (wIRA) – a review. Phys Med Rehab Kuror. 2017;27(05):265–274.
[2] Hoffmann G, Harte M, Mercer JB. Heat for wounds – water-fil- tered infrared-a (wIRA) for wound healing – a review. GMS Ger Med Sci. 2016;14:Doc08.
[3] Notter M, Thomsen AR, Nitsche M, et al. Combined wIRA-hyperthermia and hypofractionated re-irradiation in the treatment of locally recurrent breast cancer: evaluation of therapeutic outcome based on a novel size classification. Cancers (Basel). 2020;12(3): 606.
[4] Klemm P, Eichelmann M, Aykara I et al. Serial locally applied water-filtered infrared a radiation in axial spondyloarthritis – a randomized controlled trial, International Journal of Hyperthermia, 37:1, 965-970.
Acknowledgements: We acknowledge the help of Carina Schreiyäck.
This study was in part supported by the Dr. med. h.c. Erwin Braun Foundation, Basel, a charitable, nonprofit Swiss scientific foundation approved by the Swiss Federal Administration. The foundation supports clinical investigation of waterfiltered infrared-A. The foundation was not involved in any content- or decision-related aspect of the study.
This study was prospectively registered at www.drks.de (German Registry of Clinical Studies): DRKS00021098
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1735

POS0845 SCLERODERMIC HAND SENSOR: SMART TECHNOLOGY APPLIED TO RHEUMATOLOGY

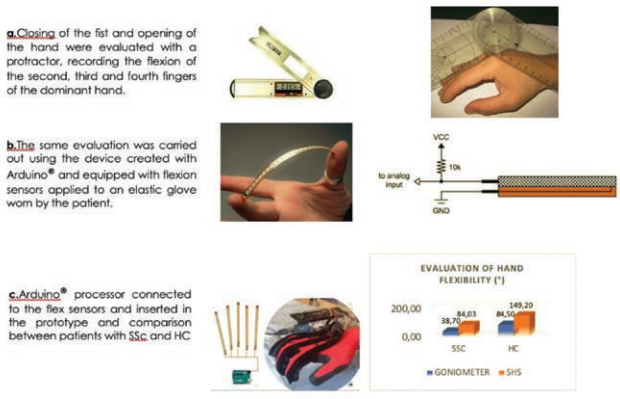
S. Parisi[1], M. C. Ditto[1], C. L. Peroni[1], A. Laganà[1], E. Fusaro[1]. [1]*AOU Città della Salute e della Scienza di Torino, Rheumatology Unit, Turin, Italy*

Background: Systemic Sclerosis (SSc) is an autoimmune rheumatic disease characterized by excessive production and accumulation of collagen in the skin and internal organs and by injuries to small arteries.
Impairment of the musculoskeletal system is one of the main causes of disability in SSc, indeed, about 90% of these patients have a loss of hand function. To date, the degree of skin involvement is evaluated through a semi-quantitative method called Rodnan Skin Score (RSS) or Modified-RSS (MRSS). However, MRSS is a method that has limitations related to the operator and his experience and does not provide information on joint mobility.
Arduino® is an open source integrated online platform based on easy to use hardware and software. It is a system for creating interactive projects by inserting a special configuration code, using the Arduino® development environment. Through this platform it is possible to create electronic devices with specific purposes to lead the possibility of integrating different kits (eg types of sensors) in relation to the object of study.
Objectives: We have therefore created an electronic instrument (Sclerodermic Hand Sensor - SHS) independent operator and easily reproducible in order to measure the degree of mobility (flexion) of the hand in patients with SSc (Fig.1). The aim was to evaluate whether the SHS was able to highlight significant differences between patients with SSc and healthy patients.
Methods: We recruited 20 female patients with SSc according to ACR criteria with a mean age of 50.8 ± 15.5 years and 20 healthy (HC) patients with a mean age of 44.3 ± 10.8 years (Tab.1), in order to test the effectiveness and sensitivity of the SHS tool.
Results: The results showed a significant difference between the two groups of patients (SSc vs HC) independent of the measurement method used as expected (Goniometer SSc / HC: Δ45.80 ° p: 0.003 SHS SSc / HC: Δ65.17 ° p: 0.002, Fig.1c), however the device created with Arduino® proved to be more sensitive than the goniometric measurement in detecting the degree of joint flexion (p: 0.002). The flexion sensor, indeed, unlike the goniometer, evaluates the simultaneous articular excursion of the entire finger (MCF, IFP and IFD) and not just one segment (Fig.1).
Conclusion: This technology application, thanks to the creation of dedicated electronic devices, allows the physicians to be supported in clinical practice with independent operating tools.

Table 1. SSc Patients Characteristics

Chararcteristics	SSc
Patients (n°, subset D=Diffuse; L=Limited)	20 (9D/11L)
Age, mean ± SD years	50.8 ± 15.5
Duration of Raynaud's Phenomenon (mean ± SD years)	12.8 ± 4.4
Duration of SSc (mead ± SD years)	8.4 ± 3.6
MRSS (mean ± SD years)	15.9 ± 5.3

Fig.1. Comparison between the use of the goniometer and SHS in SSc patients



The tool we propose could be a valid support in accurately assessing the joint and indirectly skin involvement of sclerodactyly in this type of patient, especially in the context of a clinical trial to evaluate the efficacy of a treatment.
Further studies are needed to compare with other methods to assess hand disability in SSc such as the use of HAMIS (Hand Mobility in Scleroderma) test.

REFERENCES:

[1] Sandqvist G et al. J Rheumatol. 2016 Jul;43(7):1356-62.
[2] https://www.arduino.cc.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1826

POS0846 SEXUAL FUNCTION IS IMPAIRED IN WOMEN WITH SYSTEMIC SCLEROSIS COMPARED TO HEALTHY CONTROLS

B. Heřmánková[1,2], M. Špiritović[1,2], S. Oreska[2,3], H. Štorkánová[2,3], H. Smucrova[2], K. Pavelka[2,3], J. Vencovský[2,3], L. Šenolt[2,3], R. Bečvář[2,3], M. Tomčík[2,3].
[1]Faculty of Physical Education and Sport, Charles University, Department of Physiotherapy, Prague, Czech Republic; *[2]Institute of Rheumatology, Department of Rheumatology, Prague, Czech Republic*; *[3]First Faculty of Medicine, Charles University, Department of Rheumatology, Prague, Czech Republic*

Background: Systemic sclerosis (SSc) is a multisystem, connective tissue disorder characterized by fibrosis of the skin and internal organ involvement, which can influence all aspects of life, including sexual life.
Objectives: This study aimed to compare sexual function in patients with SSc to age-/sex-matched healthy controls (HC) and determine the potential impact of clinical features on sexual function.
Methods: In total, 90 women with SSc (mean age: 49.1, disease duration: 6.1 years, lcSSc/dcSSc: 62/28, mRSS: 9.3, ESSG activity index: 2.1), who fulfilled the ACR/EULAR 2013 criteria, and 90 healthy controls (mean age: 49.1) without rheumatic diseases filled in 12 well-established and validated questionnaires assessing sexual function (FSFI, BISF-W, SFQ-28, SQoL-F), pelvic floor function (PISQ-12, PFIQ-7), fatigue (FIS, Fatigue Impact Scale), physical activity (HAP, Human Activity Profile), disability (HAQ, Health Assessment Questionnaire), depression (BDI-II, Beck's Depression Inventory-II) and quality of life (SF-36, Medical outcomes study Short Form 36 – PCS, Physical Component Summary; MCS, Mental Component Summary). A routine laboratory testing was performed. Data are presented as median (IQR).
Results: Patients with SSc reported significantly greater prevalence and severity of sexual dysfunction (FSFI, BISF-W, SFQ28 – in all subscales as well as total scores), worse sexual quality of life (SQoL-F) and pelvic floor dysfunction (PISQ-12, PFIQ-7) compared to HC (table 1). The prevalence of sexual dysfunction in patients with SSc according to the FSFI cut-off score was 77%. Worse scores in SSc patients were associated with longer disease duration [BISF-W-total (r=-0.243,p=0.026), FSFI-lubrication (r=-0.229,p=0.035)], higher disease activity [ESSG activity index: BISF-W-total (r=-0.291,p=0.010), FSFI-arousal (r=-0.299,p=0.007)], increased inflammation [CRP: BISF-W-receptivity/initiation (r=-0.301,p=0.007)], more pronounced fatigue [FIS-total: BISF-W-total (r=-0.412,p<0.0001)], more severe depression [BDI-II: FSFI-total (r=-0.506,p<0.0001), SQoL-F (r=-0.369, p<0.0001)], worse functional disability [HAQ: FSFI-total (r=-0.394,p<0.0001)], reduced physical activity [HAP: FSFI-total (r=0.535,p<0.0001)], and decreased overall quality of life [SF-36 PCS: FSFI-total (r=0.428,p<0.0001), SF-36 MCS: SQoL-F (r=0.472, p<0.0001)].

Table 1. Sexual function and pelvic floor function in women with SSc and healthy controls

Questionnaire: score range (meaning)	SSc (n=90)	HC (n=90)	p-value
FSFI: Female sexual function index: 2 (worst) - 36 (best)	19.4 (3.9-26.8)	30.1 (23.1-32.9)	**p<0.0001**
BISF-W: Brief Index of Sexual Function for Women: -16 (worst) - 75 (best)	14.3 (2.1-35.1)	38.2 (19.3-46.2)	**p<0.0001**
SQoL-F: Sexual Quality of Life Questionnaire-Female: 0 (worst) - 100 (best)	61.1 (34.4-81.1)	91.1 (70.0-96.7)	**p<0.0001**
PISQ-12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0 (best) - 48 (worst)	13.0 (9.0-17.0)	7.0 (5.0-12.0)	**p<0.0001**
PFIQ-7: Pelvic Floor Distress Inventory Questionnaire: 0 (best) - 300 (worst)	9.5 (0.0-48.8)	0.0 (0.0-8.3)	**p<0.0001**
SFQ-28: Sexual Functioning Questionnaire-28 desire: 5 (worst) - 31 (best)	17.0 (12.0-20.0)	21.0 (17.0-23.0)	**p<0.0001**
SFQ-28 arousal sensation: 4 (worst) - 20 (best)	10.0 (8.0-13.0)	12.0 (9.0-15.0)	**p=0.0031**
SFQ-28 arousal lubrication: 2 (worst) - 10 (best)	5.0 (4.0-7.0)	8.0 (5.2-9.0)	**p<0.0001**
SFQ-28 arousal cognitive: 2 (worst) - 10 (best)	5.0 (4.0-6.0)	7.0 (5.0-8.0)	**p<0.0001**
SFQ-28 orgasm: 1 (worst) - 15 (best)	10.0 (6.5-12.0)	12.0 (10.0-13.0)	**p<0.0001**
SFQ-28 pain: 2 (worst) - 15 (best)	12.0 (9.5-15.0)	15.0 (13.0-15.0)	**p<0.0001**
SFQ-28 enjoyment: 6 (worst) - 30 (best)	19.0 (12.5-24.0)	24.0 (20.0-25.8)	**p<0.0001**
SFQ-28 partner: 2 (worst) - 10 (best)	9.0 (8.0-10.0)	10. (9.0-10.0)	**p=0.0182**

Conclusion: Women with SSc reported significantly impaired sexual function and pelvic floor function compared to age-/sex-matched healthy controls. Worse scores in SSc were associated with disease-related features.

Acknowledgements: Supported by MHCR 023728, GA UK 1578119, and SVV 260373.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1829

POS0847 IDENTIFICATION OF MOLECULAR PHENOTYPES IN SYSTEMIC SCLEROSIS BY INTEGRATIVE SYSTEMS ANALYSIS

M. J. Chang[1,2,3], S. X. Zhang[1,2,3], Q. Wang[4,5], J. Qiao[1,2,3], R. Zhao[1,2,3], S. Song[1,2,3], Y. Zhang[1,2,3], Q. Yu[6], P. F. He[5], X. Li[1,2,3]. *[1]The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; *[2]Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; *[3]Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; *[4]Shanxi Medical University, Basic Medical College, Taiyuan, China*; *[5]Shanxi Medical University, Medical Data Sciences, Taiyuan, China*; *[6]Shanxi Medical University, Medical Data Sciences/School of Management, Taiyuan, China*

Background: Systemic sclerosis (scleroderma, SSc) is a systemic autoimmune disease characterized by inflammation, fibrosis and vasculopathy and associated with high mortality and high morbidity[1]. Stratification based on whole-genome gene expression data could provide a new basis for clinical diagnosis from a micro perspective[2].
Objectives: The objective of this study is to stratify patients with SSc, combine with clinical skin scores and clinical features, and provide a preliminary assessment and novel insights for assessing disease severity, and treatment design.
Methods: The original data mRNA expression profiles of GSE95065 (including 18 SSc patients and 4 healthy controls) and GSE130955 (including 58 SSc patients and 33 healthy controls) were downloaded from the public Gene Expression Omnibus (GEO) database. After batch correction, background adjustment, and other pre-processing, a large gene matrix was obtained to identify the differently expressed genes (DEGs) of SSc compared with healthy controls. Then the gene expression matrix decomposition was used to identify SSc subtypes by NMF algorithm. The cluster-based signature genes were applied to pathway enrichment analysis by Metascape[3]. Immune infiltrating cells and clinical skin scores were evaluated in all SSc subtypes.
Results: Total 325 DEGs were imputed to NMF unsupervised machine learning algorithm. Patients were divided into 2 subtypes (Figure 1A), one of which (sub1) was mostly enriched in the defense response to bacterium and cellular response to lipopolysaccharide pathway and another subtype (sub2) was enriched in the PPAR signaling and alcohol metabolic process pathway (Figure 1B-C). According to immune infiltration, sub1 had higher level of immune cells such as B cells, CD4+T cells, DC cells, Th2 cells and Tregs compared with sub2 ($P < 0.01$). Sub2 had more skin-related cells, including Epithelial cells, Fibroblasts and Sebocytes ($P < 0.05$). Interestingly, combined with clinical information, sub1 showed a severe clinical skin score over those of Sub2 patients ($P < 0.05$)(Figure 1D-E).
Conclusion: Our findings indicated that SSc patients could be stratified into 2 subtypes which had different molecular profiles of disease progression and

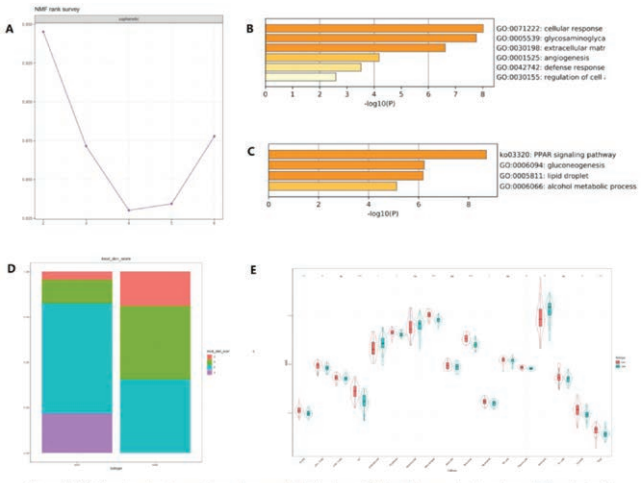


Figure 1 NMF clustering function enrichment, immune cells infiltration and clinical skin scores in SSc patients. **(A)**The relationship between cophenetic with respect to number of clusters. **(B-C)** Genetic functional enrichment for sub1 and sub2. **(D)** The box plot shows the difference in the clinical skin scores between the two subtypes. **(E)**Violin plot visualizing the differently infiltrated immune cells and skin cells (red represents sub1 and blue represents sub2) (ns, no significant;P> 0.05; *P< 0.05; **p< 0.01; **P< 0.001.)

clinical disease activities. This result could serve as a template for future studies to design stratified approaches for SSc patients.

REFERENCES:

[1] Xu X, Ramanujam M, Visvanathan S, et al. Transcriptional insights into pathogenesis of cutaneous systemic sclerosis using pathway driven meta-analysis assisted by machine learning methods. *PLoS One* 2020;15(11):e0242863. doi: 10.1371/journal.pone.0242863 [published Online First: 2020/12/01].

[2] Xu C, Meng LB, Duan YC, et al. Screening and identification of biomarkers for systemic sclerosis via microarray technology. *Int J Mol Med* 2019;44(5):1753-70. doi: 10.3892/ijmm.2019.4332 [published Online First: 2019/09/24].

[3] Zhou Y, Zhou B, Pache L, et al. Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. *Nat Commun* 2019;10(1):1523. doi: 10.1038/s41467-019-09234-6 [published Online First: 2019/04/05].

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1846

POS0848 IDENTIFICATION OF POTENTIAL CRUCIAL GENES AND KEY PATHWAYS IN PULMONARY ARTERIAL HYPERTENSION WITH SYSTEMIC SCLEROSIS BY BIOINFORMATIC ANALYSIS

S. Feng[1], S. X. Zhang[2,3,4], R. Zhao[2,3,4], C. Zheng[5], L. Cheng[5], T. Kong[5], X. Sun[5], Q. Wang[6], X. Li[2,3,4], Q. Yu[5,7], P. F. He[7]. *[1]Shanxi Medical University, School of Humanities and Social Sciences, Taiyuan, China*; *[2]The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; *[3]Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; *[4]Ministry of Education, Key laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; *[5]Shanxi Medical University, School of Management, Taiyuan, China*; *[6]Shanxi Medical University, Basic Medical College, Taiyuan, China*; *[7]Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Pulmonary arterial hypertension with systemic sclerosis (SSc-PAH) is the main cause of death in patients with SSc. Early diagnosis and timely treatment are very important to reduce the mortality of patients with SSc-PAH[1]. At present, there are not many sensitive markers for the diagnosis of SSc-PAH. Therefore, it is necessary to mine more sensitive markers as more accurate and practical predictors, which is of great significance for the diagnosis and treatment of SSc-PAH.

Objectives: To discover the differentially expressed genes (DEGs) and activated signaling pathways in SSc-PAH.

Methods: Fifty-five samples (27 SSc-PAH v.s 28 normal controls) in GSE33463 chip data obtained from Gene Expression Omnibus (GEO) were included in this study. DEGs in SSc-PAH patients were screened by R, key pathways and hub genes were discoved by Metascape[2], STRING[3] and Cytoscape.

Results: Total 431 genes with large differences were identified, including 238 up-regulated genes and 193 down-regulated genes, after standardizing the data ($|logFC| > 1$; $P < 0.05$). GO analysis showed that the upregulated genes were mainly involved in defense response to virus, hemoglobin complex, platelet alpha granule membrane and cytokine binding. The downregulated genes were mainly characterized by positive regulation of cell death, regulation of MAPK cascade, regulation of DNA-binding transcription factor activity and transcription factor AP-1 complex. Several significant enriched pathways obtained in the KEGG pathway analysis were Influenza A, Hepatitis C, IL-17 signaling pathway, MAPK signaling pathway, Toll-like receptor signaling pathway. Finally, after the selected differential genes were introduced into STRING online software, the data information of protein interaction network was derived, and 12 core genes in the network were identified, they were CXCL8, PPBP, LPAR1, FPR2, GNG11, CXCL10, LPAR5, JUN, C3AR1, CCR2, CCR3, IRF2.

Conclusion: The genes and signal pathways related to SSc-PAH discovered by bioinformatics methods could not only provided new molecular markers for its diagnosis and treatment, but also provided new ideas for its related biological research.

REFERENCES:

[1] Zheng JN, Li Y, Yan YM, et al. Identification and Validation of Key Genes Associated With Systemic Sclerosis-Related Pulmonary Hypertension. *Front Genet* 2020;11:816. doi: 10.3389/fgene.2020.00816 [published Online First: 2020/08/15].

[2] Zhou Y, Zhou B, Pache L, et al. Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. *Nat Commun* 2019;10(1):1523. doi: 10.1038/s41467-019-09234-6 [published Online First: 2019/04/05].

[3] Szklarczyk D, Gable AL, Lyon D, et al. STRING v11: protein-protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. *Nucleic Acids Res* 2019;47(D1):D607-D13. doi: 10.1093/nar/gky1131 [published Online First: 2018/11/27].

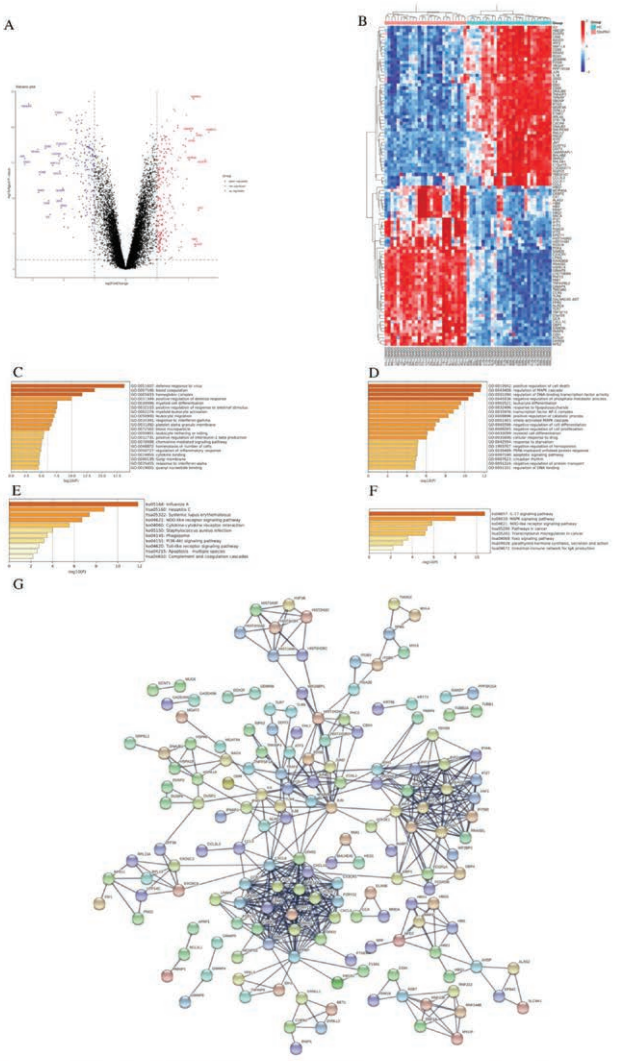


Figure 1: **(A) Volcano map of gene expression:** The horizontal axis is log2 FC, the vertical axis is log10 adj.P.Val . Each dot represents a gene, blue indicates low expression genes, red indicates high. **(B)Heat map of the top 100 up-regulated differentially expressed genes:** Each small square represents a gene; the color indicates the expression level of the gene. Each column indicates the expression level of the genes in a sample; each row indicates the expression level of a gene in different samples; the right side is the gene name. **(C,D,E and F) Visualization GO enrichment analysis and KEGG pathway enrichment analysis. (G) Protein-protein interactions network.**

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1947

POS0849 SEXUAL FUNCTION IS IMPAIRED IN WOMEN WITH IDIOPATHIC INFLAMMATORY MYOPATHIES COMPARED TO HEALTHY CONTROLS

B. Heřmánková[1,2], M. Špiritović[1,2], S. Oreska[2,3], H. Štorkánová[2,3], H. Smucrova[2], M. Komarc[4], M. Klein[2,3], K. Pavelka[2,3], L. Šenolt[2,3], H. Mann[2,3], J. Vencovský[2,3], M. Tomčík[2,3]. *[1]Faculty of Physical Education and Sport, Charles University, Department of Physiotherapy, Prague, Czech Republic*;

[2]*Institute of Rheumatology, Department of Rheumatology, Prague, Czech Republic*; [3]*First Faculty of Medicine, Charles University, Department of Rheumatology, Prague, Czech Republic*; [4]*Faculty of Physical Education and Sport, Charles University, Department of Methodology, Prague, Czech Republic*

Background: Idiopathic inflammatory myopathies (IIM) are rare diseases characterized by chronic muscle inflammation and multiple organ involvement. These serious clinical manifestations can be associated with significant impairment of quality of life, including sexual life.

Objectives: This study aimed to compare sexual function in patients with IIM to age-/sex-matched healthy controls (HC) and determine the potential impact of clinical features on sexual function.

Methods: In total, 62 women with IIM [mean age: 53.1, disease duration: 5.2 years, dermatomyositis (DM, 29)/ polymyositis (PM, 27)/ necrotizing myopathy (IMNM, 5)/ inclusion body myositis (IBM, 1)], who fulfilled the Bohan/ Peter 1975 criteria for DM/PM, or ENMC criteria for IMNM or IBM, and 62 healthy controls (HC) (mean age: 53.1) without rheumatic diseases filled in 11 well-established and validated questionnaires assessing sexual function (FSFI, SFQ28, BISF-W, SQoL-F), pelvic floor function (PFIQ-7, PISQ-12), fatigue (FIS, Fatigue Impact Scale), physical activity (HAP, Human Activity Profile), disability (HAQ, Health Assessment Questionnaire), depression (BDI-II, Beck's Depression Inventory-II), and quality of life (SF-36, Medical outcomes study Short Form 36 – PCS, Physical Component Summary; MCS, Mental Component Summary). A routine laboratory testing was performed. Data are presented as median (IQR).

Results: Patients with IIM reported significantly greater prevalence and severity of sexual dysfunction (FSFI, BISF-W, SFQ28, SQoL-F) and pelvic floor dysfunction (PISQ-12, PFIQ-7) compared to HC (Table 1). The prevalence of sexual dysfunction in patients with IIM according to the FSFI cut-off score was 59%. Worse scores in IIM patients were associated with greater muscle weakness of m. gluteus maximus [MMT: FSFI (r=0.289, p=0.035), PFIQ-7 (r=-0.407, p=0.003)], m. gluteus medius [MMT: PFIQ-7 (r=-0.381, p=0.005)], more pronounced fatigue [FIF: SQoL-F (r=-0.412, p=0.003)], severer depression [BDI-II: SQoL-F (r=-0.459, p=0.0007)], worse functional disability [HAQ: FSFI (r=-0.436, p=0.005)], reduced physical activity [HAP: FSFI (r=0.403, p=0.001), SQoL-F (r=0.368, p=0.007)], and decreased quality of life [SF-36 PCS: FSFI-total (r=0.381,p=0.002), SF-36 MCS: SQoL-F (r=0.407, p=0.002)]. We did not observe any associations with disease duration, the current prednisone dose, or serum levels of muscle enzymes.

Conclusion: Women with IIM reported significantly impaired sexual function and pelvic floor function compared to age-/sex-matched healthy controls. Worse scores in IIM were associated with disease-related features.

Table 1. Sexual function and pelvic floor function in women with IIM and healthy controls

Questionnaire: score range (meaning)	IIM (n=62)	HC (n=62)	p-value
FSFI: Female Sexual Function Index: 2 (worst) - 36 (best)	18.2 (3.2-28.5)	28.4 (14.4-32.1)	**p=0.006**
BISF-W: Brief Index of Sexual Function for Women: -16 (worst) - 75 (best)	18.6 (2.7-32.3)	34.0 (8.0-44.7)	**p=0.004**
SQoL-F: Sexual Quality of Life Questionnaire – Female: 0 (worst) - 100 (best)	60.0 (41.4-83.6)	86.7 (70.8-95.6)	**p<0.0001**
PISQ–12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0 (best) - 48 (worst)	14.5 (9.0-18.0)	8.0 (5.0-12.0)	**p<0.0001**
PFIQ7: Pelvic Floor Impact Questionnaire – short form 7: 0 (best) - 300 (worst)	4.8 (0.0-23.8)	0.0 (0.0-4.8)	**p=0.052**
SFQ-28: Sexual Functioning Questionnaire-28 desire: 5 (worst) - 31 (best)	18.0 (13.3-20.0)	19.0 (17.0-22.0)	**p=0.042**
SFQ-28 arousal sensation: 4 (worst) - 20 (best)	9.5 (7.0-11.0)	12.0 (9.0-14.3)	p=0.082
SFQ-28 arousal lubrication: 2 (worst) - 10 (best)	6.0 (4.0-8.0)	7.0 (5.0-9.0)	p=0.112
SFQ-28 arousal cognitive: 2 (worst) - 10 (best)	6.0 (4.3-7.0)	6.0 (5.0-7.3)	p=0.235
SFQ-28 orgasm: 1 (worst) - 15 (best)	11.0 (8.0-13.0)	12.0 (9.8-13.0)	p=0.279
SFQ-28 pain: 2 (worst) - 15 (best)	12.0 (10.0-15.0)	15.0 (13.0-15.0)	**p=0.004**
SFQ-28 enjoyment: 6 (worst) - 30 (best)	19.0 (14.3-24.3)	23.0 (19.0-25.0)	**p=0.027**
SFQ-28 partner: 2 (worst) - 10 (best)	9.0 (8.0-10.0)	10.0 (9.0-10.0)	**p=0.012**

Acknowledgements: Supported by MHCR 023728, GA UK 1578119, and SVV 260373

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1955

POS0850 NAILFOLD CAPILLARY DILATIONS IN RAYNAUD'S PHENOMENON: QUANTIFYING A PREDICTIVE THRESHOLD FOR THE 'SCLERODERMA PATTERN'

G. Pacini[1], M. Pendolino[1], C. Pizzorni[1], E. Gotelli[1], A. Sulli[1], L. Carmisciano[2], S. Paolino[1], V. Smith[3,4], M. Cutolo[1]. [1]*IRCCS Polyclinic San Martino, University of Genova, Laboratory of Experimental Rheumatology and Academic Division of Rheumatology, Postgraduate School of Rheumatology, Department of Internal Medicine and Specialties, Genova, Italy*; [2]*University of Genova, Biostatistics Unit, Department of Health Sciences, Genova, Italy*; [3]*Ghent University Hospital, Department of Internal Medicine, Department of Rheumatology, Gent, Belgium*; [4]*VIB-UGent Center for Inflammation Research, Unit for Molecular Immunology and Inflammation, Gent, Belgium*

Background: Non-specific abnormalities could be detected by nailfold videocapillaroscopy (NVC) in subject with primary Raynaud's Phenomenon (RP) several years before the clinical onset of connective tissue diseases (CTD)s [1]. Previous findings from our group proved that ≤30 µm capillary dilations in RP patients have a negative predictive value for developing the 'scleroderma pattern' during follow-up [2].

Objectives: To investigate the role of NVC >30 µm capillary dilations as positive predictive factors of the 'scleroderma pattern' in RP patients later developing systemic sclerosis (SSc)-related RP.

Methods: A 10-year retrospective NVC-based investigation evaluated the dataset of sequential NVCs of 18 RP patients later developing SSc (cases) and 19 sex- and age-matched RP patients later developing other CTDs (controls). Both cases and controls had ≥1 NVC performed before the 'scleroderma pattern'/CTD diagnosis (basal NVC) showing >30 µm dilated capillaries. Each NVC was qualitatively and semi-quantitatively assessed, recording number of total capillaries, number and average/site-specific diameters (arterial, apical, venous) of >30 µm dilated capillaries [3]. Statistical analysis was performed to stratify the risk of developing the 'scleroderma pattern'.

Results: Significant differences of capillary diameters were observed between cases and controls both at basal NVC and during follow-up (p<0.001). The proportion of >30 µm dilated capillaries in basal NVC was the strongest predictor of 'scleroderma pattern' in a median 3-year time, with a 27% cut-off (PPV 0.79, 95%CI 0.54,0.94; p<0.001). Additional "Higher risk" NVC hallmarks for 'scleroderma pattern' development were apical diameter >40 µm (p<0.001), venous diameter >25 µm (p<0.05) and average diameter ≥35 µm (p<0.005). Conversely, CTDs patients showed a stable NVC 'non-scleroderma pattern' over a median 10-year time.

Conclusion: This is the first study to show that NVC-detected homogeneous and progressive capillary loop dilations in RP patients significantly contribute to predict the 'scleroderma pattern' evolution within a median 3-year time, possibly providing a "very early" window of opportunity in SSc pre-clinical stages.

REFERENCES:

[1] Cutolo M et al. Expert Rev Clin Immunol. 2019;15(7):753–64. [2] Trombetta AC et al. J Rheumatol 2016;43:599–606. [3] Smith et al. Autoimmun Rev 2020; 19(3):102458.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2014

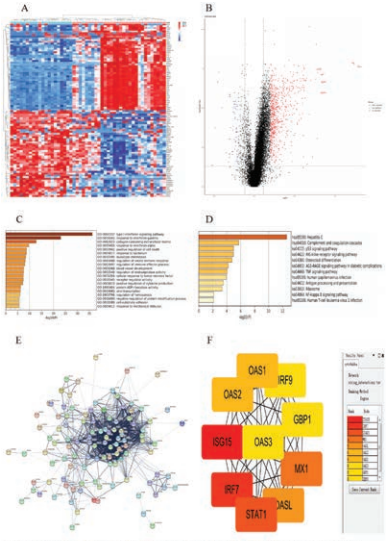
POS0851 IDENTIFICATION OF HUB GENES AND PATHWAYS IN DERMATOMYOSITIS BY BIOINFORMATICS ANALYSIS

C. Zheng[1], S. X. Zhang[2,3,4], R. Zhao[2,3,4], L. Cheng[1], T. Kong[1], X. Sun[1], S. Feng[5], Q. Wang[6], X. Li[2,3,4], Q. Yu[7], P. F. He[8]. *[1]Shanxi Medical University, School of Management, Taiyuan, China*; *[2]The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; *[3]Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; *[4]Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; *[5]Shanxi Medical University, School of Humanities and Social Sciences, Taiyuan, China*; *[6]Shanxi Medical University, Basic Medical College, Taiyuan, China*; *[7]Shanxi Medical University, Medical Data Sciences/School of Management, Taiyuan, China*; *[8]Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Dermatomyositis (DM) is a chronic systemic autoimmune disease characterized by inflammatory infiltrates in the skin and muscle[1]. The genes and pathways in the inflamed myopathies in patients with DM are poorly understood[2].
Objectives: To identify the key genes and pathways associated with DM and further discover its pathogenesis.
Methods: Muscle tissue gene expression profile (GSE143323) were acquired from the GEO database, which included 39 DM samples and 20 normal samples. The differentially expressed genes (DEGs) in DM muscle tissue were screened by adopting the R software. Gene ontology (GO) and Kyoto Encyclopedia of Genome (KEGG) pathway enrichment analysis was performed by Metascape online analysis tool. A protein-protein interaction (PPI) network was then constructed by STRING software using the genes in significantly different pathways. Network of DEGs was analyzed by Cytoscape software. And degree of nodes was used to screen key genes.
Results: Totally, 126 DEGs were obtained, which contained 122 up-regulated and 4 down-regulated. GO analysis revealed that most of the DEGs were significantly enriched in type I interferon signaling pathway, response to interferon-gamma, collagen-containing extracellular matrix, response to interferon-alpha and bacterium, positive regulation of cell death, leukocyte chemotaxis. KEGG pathway analysis showed that upregulated DEGs enhanced pathways associated with the hepatitis C, complement and coagulation cascades, p53 signaling pathway, RIG-I-like receptor signaling, Osteoclast differentiation, and AGE-RAGE signaling pathway. Ten hub genes were identified in DM, they were ISG15, IRF7, STAT1, MX1, OASL, OAS2, OAS1, OAS3, GBP1, and IRF9 according to the Cytoscape software and cytoHubba plugin.
Conclusion: The findings from this bioinformatics network analysis study identified the key hub genes that might provide new molecular markers for its diagnosis and treatment.

REFERENCES:

[1] Olazagasti JM, Niewold TB, Reed AM. Immunological biomarkers in dermatomyositis. *Curr Rheumatol Rep* 2015;17(11):68. doi: 10.1007/s11926-015-0543-y [published Online First: 2015/09/26].
[2] Chen LY, Cui ZL, Hua FC, et al. Bioinformatics analysis of gene expression profiles of dermatomyositis. *Mol Med Rep* 2016;14(4):3785-90. doi: 10.3892/mmr.2016.5703 [published Online First: 2016/09/08].
[3] Zhou Y, Zhou B, Pache L, et al. Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. *Nat Commun* 2019;10(1):1523. doi: 10.1038/s41467-019-09234-6 [published Online First: 2019/04/05].



(**A**)In the volcano, each dot represents a gene, blue indicates low expression genes, red indicates high expression genes, and black indicates no markedly expressed genes. (**B**)In the heat map, each square represents a gene, and the color indicates that the higher the expression level of the gene, the darker the color (red up, blue down).(**C**)The results of GO analysis show that the functions of differently expressed genes are mainly concentrated in the above 20 aspects. (**D**)The results of KEGG show that the functions of differently expressed genes are mainly concentrated in 12 aspects.(**E,F**)Among the 126 DEGs, the 10 up-regulated genes with the largest differences are ISG15, IRF7, STAT1, MX1, OASL, OAS2, OAS1, OAS3, GBP1, IRF9.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2026

POS0852 HIGH DOSE INTRAVENOUS PULSE METHOTREXATE IN REFRACTORY EOSINOPHILIC FASCIITIS: WHAT ARE THE ADVERSE EVENTS?

G. Geurts[1], J. Mertens[2], N. Van Herwaarden[1], E. De Jong[3], R. M. Thurlings[1]. *[1]Radboudumc, Rheumatology, Nijmegen, Netherlands*; *[2]Jeroen Bosch Ziekenhuis, Internal Medicine, Nijmegen, Netherlands*; *[3]Radboudumc, Dermatology, Nijmegen, Netherlands*

Background: Eosinophilic Fasciitis (EF) is a disease of unknown origin initially characterized by limb or trunk edema, and collagenous thickening of the subcutaneous fascia in later stages. Eosinophilia in peripheral blood is commonly observed. Being a rare disease, evidence regarding treatment is mainly based on case series and anecdotal evidence. The mainstay systemic treatment is prednisone, and Methotrexate (MTX) up to doses of 25 mg/week is the leading prednisone-sparing agent. Mycophenolate can be considered in refractory cases. As an alternative we explored the use of intravenous (i.v.) pulse MTX. We already showed this to be a potentially effective and safe treatment option in a prospective single-arm study[1], but more data on adverse events (AEs) are needed.
Objectives: To present an overview of AEs of high dose i.v. pulse MTX in refractory EF.
Methods: Adult patients with EF based on clinical appearance combined with histology and/or MRI, who were unresponsive to prednisone combined with low-dose MTX or presenting with severe disease, were selected for this retrospective cohort study. Patients received 6-9 monthly infusions of 4 mg/kg MTX followed by oral folinic acid rescue therapy, which is comparable to treatment schedules for trophoblast disease. An additional number of six pulses could be administered in case of a partial effect or flare. Safety data were monitored during each visit and classified according to the Common Terminology Criteria for Adverse Events (CTCAE) from the National Institute of Health (2009).
Results: Twenty-seven patients (26 with EF, one with deep linear morphea) were included in this study (five males), with a mean age of 59 (sd 11.5) years, based on clinical presentation and histology and/or MRI. Previous treatment data were available for 22 patients of which 21 received oral prednisone (20-60 mg) whether or not combined with low dose MTX and/or UVA1 therapy. All patients reported ≥ 1 AEs at some stage, exactly 100 in total. '*Gastro-intestinal disorders*' (n=36) and '*General disorders and administration site conditions*' (n=15) were most common; especially nausea (n=6) and fatigue (n=11). One patient was hospitalized for blood transfusion. In four cases, treatment was discontinued due to AEs (acute kidney injury (AKI), depression, nausea/vomiting, and leukopenia resp.). Each reported AE appeared reversible. The patient with AKI had an MTX level in the toxic range; methotrexate-induced crystal nephropathy seemed the most likely explanation, probably due to a combination of high body weight (and thus high absolute dosage of MTX) and the concomitant use of omeprazole. Oral folinic acid rescue therapy was prolonged, together with 500 cc i.v. fluid, after which kidney function normalized.

Organ system	AE	Frequency
Gastro-intestinal disorders	Nausea, oral mucositis, diarrhea, vomiting, abdominal pain, anorexia	36
General disorders, administration site conditions	Malaise, fatigue	15
Respiratory, thoracic, mediastinal disorders	Cough and dyspnea	10
Skin and subcutaneous tissue disorders	Skin hyperpigmentation, hair loss, alopecia, other	9
Nervous system	Headache, nerve abducens disorder	7
Infections and infestinations	Skin, urinary tract, upper respiratory tract, other	6
Blood, lymphatic system disorders	Anemia, leukopenia, pancytopenia	4
Psychiatric conditions	Depression	3
Renal, urinary disorders	Acute Kidney Injury	1
Other systems		9
		100

Conclusion: AEs were common among patients receiving high dose i.v. pulse MTX, especially nausea and fatigue, but were generally mild and reversible in all cases. This is in line with studies performed with patients with trophoblast disease. One episode of reversible AKI occurred that seemed to be related to high body weight and the use of concomitant medication. The safety profile of i.v. pulse MTX thus seems auspicious, but the case of AKI illustrates that further data on safety is needed.

REFERENCES:
[1] *Mertens JS et al. High-dose intravenous pulse methotrexate in patients with eosinophilic fasciitis. JAMA Dermatol 2016; 1(152):1262-5.*
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2029

POS0853 DECREASE IN ANTI-TOPOISOMERASE-1 ANTIBODY TITER IN PATIENTS WITH SYSTEMIC SCLEROSIS DURING LONG-TERM RITUXIMAB THERAPY

L. Garzanova[1], L. P. Ananyeva[1], O. Koneva[1], O. Desinova[1], O. Ovsyannikova[1], M. Starovoytova[1], R. Shayakhmetova[1], S. Glukhova[2], M. Cherkasova[3]. *[1]VA Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, MOSCOW, Russian Federation*; *[2]VA Nasonova Research Institute of Rheumatology, Educational and Methodical Department, Moscow, Russian Federation*; *[3]VA Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology, Moscow, Russian Federation*

Background: Rituximab (RTX) is a new option in the treatment of systemic sclerosis (SSc) [1]. There is not enough data on changes in the level of autoantibodies and their clinical significance during RTM therapy. There are only a few reports on the higher efficiency of RTX in patients (pts) with SSc positive for anti-topoisomerase-1 antibodies (a-Topo-1), therefore the study of this issue might be interested.
Objectives: To compare clinical parameters and B-lymphocytes (B-lymph) level in SSc pts depending on the presence or absence of a-Topo-1 during RTX therapy with prospective long-term follow-up.
Methods: This study included 88 pts with SSc. The mean follow-up period was 26,3±10,7 months. The mean age was 47years (17-71), female-73 pts (83%), the diffuse cutaneous subset of the disease had 50 pts (57%). Symptoms of the interstitial lung disease (ILD) were observed in 70 pts (80%). The mean disease duration was 5,9±4,8 years. The cumulative mean dose of RTX was 2,9±1,1 grams. All patients received prednisone at a dose of 11,7±4,4 mg, immunosuppressants received 42% of them. There were 63 pts positive for a-Topo-1 and 25 pts - negative. The pts of the compared groups did not differ in the main demographic and clinical parameters, excepting lung involvement. In a-Topo-1 positive group 55 (87%) pts had ILD and only 15 (60%) – in a-Topo-1-negative group (p=0,02). The results at baseline and at the end of the follow up are presented in the form of mean values and changes in parameters (delta).
Results: Considering the entire cohort, an improvement of almost all outcome parameters was found. When a-Topo-1 positive and a-Topo-1-negative pts were analyzed separately, we observed a significantly higher decrease in the activity score, depletion of B-lymph, an increase in forced vital capacity (FVC) and diffusion capacity for carbon monoxide (DLCO) in a-Topo-1 positive group of pts (table 1).

Table 1. Changes of the main outcome parameters depending on the presence of a-Topo-1 on RTX therapy.

Parameters	a-Topo-1 positive pts	a-Topo-1 negative pts	P
Delta Activity score (EScSG-AI)	1,79	0,9	0,001
Delta Rodnan skin score (mRSS)	4,9	5,2	NS
Delta B-lymphocytes (absolute count)	0,212	0,193	0,001
Delta FVC*, %	8,64	6,46	0,001
Delta DLCO**, %	2,86	0,032	0,001

*FVC - forced vital capacity % predicted, **DLCO - diffusion capacity for carbon monoxide % predicted

The a-Topo-1 level decreased from 174,2±50,1 to 148,1±66,1 units/ml (p=0,0009). In this group, a-Topo-1 became negative in 5 pts (7,9%). The disappearance of a-Topo-1 positivity was accompanied by a more pronounced decrease in mRSS (delta mRSS=7,4) and a higher depletion of B-lymph. There was a higher cumulative dose of RTX (4±1,4grams) in this 5 pts compared with the pts who sustained a-Topo-1 positivity. There was a moderate negative statistically significant correlation between the a-Topo-1 and the total dose of RTX (r=-0,298, p=0,017). A moderate negative statistically significant correlation was found between the a-Topo-1 and FVC (r=-0,322, p=0,009).
Conclusion: In our study, the a-Topo-1 level significantly decreased during RTX therapy in Russian pts. The decrease in a-Topo-1 titers correlated with the total dose of RTX and was accompanied by a decrease in mRSS, disease activity index and an increase in FVC and DLCO. A higher efficacy of RTX in the a-Topo-1 positive group with prevalence of ILD was revealed, therefore a-Topo-1 positivity could be considered as a predictor of a better response to RTX therapy.
REFERENCES:
[1] Jordan S, et al. Effects and safety of rituximab in systemic sclerosis: an analysis from the European Scleroderma Trial and Research (EUSTAR) group. Ann Rheum Dis.2015;74:1188–94.Doi:10.1136/annrheumdis-2013-204522.
[2] Ebata S, Yoshizaki A, et.al. Rituximab therapy is more effective than cyclophosphamide therapy for Japanese patients with anti-topoisomerase I-positive systemic sclerosis-associated interstitial lung disease. J Dermatol.2019. Nov;46(11):1006-1013.doi:10.1111/1346-8138.15079.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2038

POS0854 SEX DIFFERENCES IN SYSTEMIC SCLEROSIS PATIENTS IN A SINGLE CENTER IN EASTERN EUROPE

A. Petre[1], L. Groseanu[1,2], A. Balanescu[1,2], V. Bojinca[1,2], D. Opris-Belinski[1,2], F. Berghea[1,1], I. Saulescu[1,2], D. Mazilu[1,2], S. Daia[1,1], A. Borangiu[1,2], C. L. Constantinescu[1,2], M. Abobului[1,2], M. M. Negru[1,2], C. Cobilinschi[1,2], D. Predeteanu[1], R. Ionescu[1,2]. *[1]Sf Maria Clinical Hospital, Bucharest, Romania, Department of Internal Medicine and Rheumatology, Bucharest, Romania*; *[2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, Department of Internal Medicine and Rheumatology, Bucharest, Romania*

Background: The low overall prevalence of systemic sclerosis (SSc) and the low proportion of male patients have resulted in a scarcity of studies assessing sex differences in SSc patients, and contradictory results have often been observed.
Objectives: The aim of the study was to assess differences in disease manifestations in a cohort of SSc patients according to gender.
Methods: We performed a retrospective observational study using data extract from the EULAR scleroderma trials and research (EUSTAR) cohort 096.We looked at sex influence on disease characteristics at baseline and then focused on patients with at least 2 years of follow-up to estimate the effects of sex on disease progression and survival.
Results: 173 patients with SSc were available for the baseline analyses. Males were older (52,96 vs 45,88, p=0.009), were more likely to smoke (73% vs 7%, p<0,001), had more frequent diffuse skin involvement (73,1% vs 56,5%,p<0.01), higher modified Rodnan skin score (34,61% vs 17%, p=0.01) and activity score(84,62% vs 46,26%,p<0.001) and were more often associed with positive acute phase reactants (65,38% vs 38,77%, p=0.01). Severe interstitial lung disease was more common in males (59,09% vs 27,53%, p=0.003), also the presence of tendon friction rubs was more frequent in this sex group (23,07% vs 8,84%, p=0.032).
In the longitudinal analysis after a mean follow-up of 3,5(±0,65) years, male sex was associated with a higher risk of scleroderma renal crisis (OR:9.45 (1.49 to 59.69); p=0.004), digital contractures (OR:8,2 (3,1 to 21,9); p<0,001), arrhythmias (OR:3,37 (1.36 to 8,34); p=0.006), pulmonary fibrosis (OR: 3.56, (1.51 to 8.41); p=0.003), pulmonary hypertension (OR: 3.01 (1.19 to 7,59); p=0.016), severe vascular involvement (OR:2,86, (1,22 to 6,73); p=0.013) and low ventricular ejection fraction (OR: 2,84, (1.2 to 6,73); p=0.014). Males had significantly reduced survival time after diagnosis (p=0,004). The most frequent causes of death were scleroderma renal crisis in males and pulmonary hypertension in females.
Conclusion: Although more common in women, SSc appears as strikingly more severe in men. Our results demonstrate a higher risk of severe organ involvement and poor prognosis in men. These results raise the point of including sex in the management and the decision-making process.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2110

POS0855 PATIENT PREFERENCES, TRADE-OFFS AND ACCEPTABLE RISKS IN THE TREATMENT OF SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: A STEP TOWARDS SHARED DECISION-MAKING

C. Bruni[1], S. Heidenreich[2], A. Duenas[2], A. M. Hoffmann-Vold[3], A. Gabrielli[4], Y. Allanore[5], E. Chatelus[6], J. H. W. Distler[7], E. Hachulla[8], V. Hsu[9], N. Hunzelmann[10], D. Khanna[11], M. E. Truchetet[12], U. Walker[13], M. Alves[14], N. Schoof[15], L. A. Saketkoo[16], O. Distler[17]. *[1]University of Florence, Department of Experimental and Clinical Medicine, Division of Rheumatology, Florence, Italy*; *[2]Evidera, Patient-Centered Research, London, United Kingdom*; *[3]Oslo University Hospital, Department of Rheumatology, Oslo, Norway*; *[4]Università Politecnica delle Marche, Department of Clinical and Molecular Sciences, Ancona, Italy*; *[5]Cochin Hospital, Paris Descartes University, Department of Rheumatology A, Paris, France*; *[6]University Hospital of Strasbourg, Hôpital de Hautepierre, Department of Rheumatology, Strasbourg, France*; *[7]University of Erlangen-Nuremberg, Department of Internal Medicine 3, Erlangen, Germany*; *[8]Claude Huriez Hospital, Lille University School of Medicine, Department of Internal Medicine and Clinical Immunology, Lille, France*; *[9]Rutgers–Robert Wood Johnson Medical School, Department of Medicine, Division of Rheumatology, New Jersey, United States of America*; *[10]University of Cologne,*

Department of Dermatology, Cologne, Germany; *[11]University of Michigan, Scleroderma Program, Ann Arbor, United States of America*; *[12]Department of Rheumatology, CHU Bordeaux, Bordeaux, France*; *[13] University Hospital Basel, Department of Rheumatology, Basel, Switzerland*; *[14]Boehringer Ingelheim International GmbH, Inflammation Medicine, Ingelheim am Rhein, Germany*; *[15]Boehringer Ingelheim International GmbH, Inflammation Medicine, Ingelheim am Rhein, Germany*; *[16] Tulane University Schools of Medicine, Department of Medicine, New Orleans, United States of America*; *[17]University Hospital, Department of Rheumatology, Zurich, Switzerland*

Background: Current treatments for systemic sclerosis-associated interstitial lung disease (SSc-ILD) are characterised by different attributes such as mode of administration, adverse events (AE) and efficacy. Physicians and patients often have different perspectives on treatments, thus shared decision-making between patients and physicians is essential. An understanding of patients' decision processes when weighing treatment attributes and the trade-offs they are willing to make is important for shared decision-making.
Objectives: The study aimed to 1) identify relevant treatment attributes, 2) elicit patient preferences for these attributes and 3) quantify preference as relative attribute importance (RAI; a higher RAI indicates that more of the variability in patients' responses may be explained by changes in the attribute); and maximum acceptable risk (MAR) of diarrhoea, nausea and/or vomiting (MAR is a trade-off measure that evaluates attributes in risk-equivalences as a unit of measurement).
Methods: A discrete choice experiment (DCE) was created, based on a literature review, a patient advisory board, qualitative patient interviews, and a workshop involving SSc-ILD expert physicians. Seven SSc-ILD treatment attributes were identified: 1) mode of administration; 2) shortness of breath; 3) skin tightness; 4) cough; 5) tiredness; 6) risk of gastrointestinal tract (GIT) AEs; and 7) risk of serious and non-serious infections. The levels of AE risk were informed by frequencies observed in clinical trials and patient input during the interviews. The DCE was integrated into an online survey, which asked patients to make repeated choices between two alternatives described by varying levels of included attributes. Patients with SSc-ILD were recruited by physician referral from Switzerland, Norway, France, Germany and the USA. DCE data were analysed using a logit model, and RAI and MAR measures were calculated.
Results: A total of 231 patients with physician-confirmed SSc-ILD (mean age 52.6±13.2 years; 54% diagnosed for >5 years) completed the survey. Patients with SSc-ILD mostly preferred twice-daily oral treatments ($p<0.001$) and infusion every 6–12 months ($p<0.001$) over monthly infusions. Patients' choices were mostly affected by the risk of GIT AEs (RAI=25%; 95% CI 22–28%) and risk of infections (RAI=20%; 95% CI 16–24%). Improvements in shortness of breath and type and severity of cough were jointly more important than improvement in skin tightness ($p<0.001$).
Patients accepted an additional 21% risk (95% CI 13–29%) of GIT AEs if they could reduce the frequency of infusions from monthly to 6–12 monthly, or accepted an extra 15% (95% CI 7–23%) increase in risk if changing to an oral treatment twice daily. Among symptoms, an additional 28% (95% CI 20–36%) risk of GIT AEs was considered acceptable if the severity of patients' persistent cough was reduced to a level that was easier to tolerate, even if it remained persistent. Similarly, a 37% (95% CI 28–46%) increase in the risk of GIT AEs was acceptable if it resulted in breathlessness during routine activities rather than breathlessness at rest. Finally, patients were willing to accept an additional 36% risk (95% CI 27–45%) of GIT AEs if it reduced their risk of non-serious infections from 30% to 15% and of serious infections from 10% to 5%.
Conclusion: This is the first study to quantitatively elicit patients' preferences for attributes of SSc-ILD treatments. Preferences were driven by safety, efficacy and technical considerations. Patients showed willingness to make trade-offs, providing a firm basis for shared decision-making in routine clinical practice.
Disclosure of Interests: Cosimo Bruni Speakers bureau: Actelion, Consultant of: Eli Lilly, Grant/research support from: Gruppo Italiano Lotta alla Scleroderma (GILS), Fondazione Italiana per la Ricerca sull'Artrite (FIRA), New Horizon Fellowship, European Scleroderma Trial and Research (EUSTAR), Foundation for Research in Rheumatology (FOREUM)., Sebastian Heidenreich Consultant of: Sebastian Heidenreich, PhD is employed by Evidera Inc, a business unit of PPD. Evidera is a CRO that offers paid research services to pharmaceutical companies., Ashley Duenas Consultant of: Yes. I am an employee of Evidera which received funding from Boehringer Ingelheim for work related to this study., Anna-Maria Hoffmann-Vold Speakers bureau: Boehringer Ingelheim, Actelion, Roche, Merck Sharp & Dohme, Lilly, Consultant of: Actelion, Boehringer Ingelheim, Roche, Bayer, Merck Sharp & Dohme, ARXX, Lilly and Medscape, Grant/research support from: Boehringer Ingelheim, Armando Gabrielli Grant/research support from: Pfizer Bhering, Yannick Allanore Consultant of: Honorarium received from Boehringer, Medsenic,
Sanofi, Menarini, Grant/research support from: Grants received from Alpine, Ose Immunogenetics, Emmanuel Chatelus: None declared, Jörg H.W. Distler Shareholder of: JHWD is stock owner of 4D Science, Consultant of: JHWD has consultancy relationships with Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, Grant/research support from: JHWD has received research funding from Anamar, Active Biotech, Array Biopharma, ARXX, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB, Eric Hachulla: None declared, Vivian Hsu Speakers bureau: I am a speaker for Boehringer Ingelheim Pharmaceuticals, Consultant of: with Boehringer Ingelheim Pharmaceuticals, Grant/research support from: Principal Investigator for several clinical trials, currently with Genentech, Corbus Pharmaceutical, and EICOS, Nicolas Hunzelmann Speakers bureau: Boehringer, Roche, Sanofi, Dinesh Khanna Shareholder of: Eicos Sciences, Inc (less than 5%), Consultant of: Paid Consultant for: Acceleron, Actelion, Abbvie, Amgen, Bayer, Boehringer Ingelheim, CSL Behring, Corbus, Gilead, Galapagos, Genentech/Roche, GSK, Horizon, Merck, Mitsubishi Tanabe Pharma, Sanofi-Aventis, and United Therapeutics, Grant/research support from: Research Grant support from: Immune Tolerance Network, Bayer, BMS, Horizon, Pfizer, Employee of: Leadership/Equity position – Chief Medical Officer, CiviBioPharma/Eicos Sciences, Inc – recieves a stipend for role as Chief Medical Officer, which would technically qualify as emplyoment., Marie-Elise Truchetet Speakers bureau: Abbvie, Lilly, Sobi, Boehringer, Paid instructor for: Lilly, Consultant of: UCB, Sobi, Abbvie, Grant/research support from: UCB, Gilead, Ulrich Walker Shareholder of: Bayer, NASDAQ, MSCI-World ETF's, Speakers bureau: All companies producing pharmaceuticals used in AIDS, Paid instructor for: Roche, Abbvie, Novartis, Consultant of: All companies producing pharmaceuticals used in AIDS, Grant/research support from: Gilead, Abbvie, (in the last two years). Other companies in previous years., Margarida Alves Employee of: Boehringer Ingelheim, Nils Schoof Employee of: Employee of Boehringer Ingelheim International GmbH, Lesley Ann Saketkoo Speakers bureau: Boehringer Ingelheim, Actelion, Janssen, Mallinckrodt, United Therapeutics, Consultant of: Actelion, Boehringer Ingelheim, Bayer, Bristol Meyer Squibb, Corbus, EICOS, Janssen, Horizon, United Therapeutics, Inc, Grant/research support from: Mallinckrodt, United Therapeutics, Oliver Distler Speakers bureau: Boehringer Ingelheim, Medscape, IQone, Roche, Consultant of: OD has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years):
Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Grant/research support from: Kymera Therapeutics, Mitsubishi Tanabe
DOI: 10.1136/annrheumdis-2021-eular.2112

POS0856 CLINICAL UTILITY OF BREATH-HOLDING TEST FOR MEASURING CARDIOPULMONARY FUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS

J. Yeo[1], M. H. Kim[2], J. W. Park[2], J. K. Park[2,3], E. B. Lee[2,3,4]. *[1]Seoul National University Hospital, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; *[2]Seoul National University Hospital, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; *[3]Seoul National University College of Medicine, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; *[4]Seoul National University, Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul, Korea, Rep. of (South Korea)*

Background: Interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH) are major causes of death in systemic sclerosis (SSc). Six-minute-walk test (6MWT) is a standard outcome measure for exercise capacity in cardiopulmonary diseases. However, the results of 6MWT may not reflect real cardiopulmonary function of SSc patients in whom musculoskeletal system is frequently inflicted.
Objectives: This study aimed to evaluate the clinical utility of breath-holding test (BHT) in evaluating cardiopulmonary function in SSc patients, as compared with 6MWT.
Methods: Seventy-two patients with SSc were prospectively enrolled and underwent BHT and 6MWT with measurement of Borg score and Scleroderma Health Assessment Questionnaire (SHAQ). Data on diffusing capacity for carbon monoxide (DLCO, %), forced vital capacity (FVC, % and liters), and ejection fraction and pulmonary arterial systolic pressure (PASP) measured by transthoracic echocardiography (TTE), were also collected. For BHT, participants were required to make a maximum expiration followed by a maximum inspiration and to hold the breath as long as possible at maximum inspiratory level. This procedure was repeated three times, with 5-minute intervals. 6MWT was performed according to the American Thoracic Society guidelines. Pearson's correlation test was applied to demonstrate the relationship between BHT results and each clinical parameter.

Results: Among 72 (66 female) patients, mean (SD) age was 57.1 (11.1) years, modified Rodnan skin score 10.6 (10.5), SHAQ 0.64 (0.61) and 6MWT distance 473.5 (95.5) m. Mean BHT time was 35.05 (14.90) sec at the first time, 38.92 (16.14) sec at the second time, and 41.11 (17.71) sec at the third time. The BHT time showed a statistically significant negative correlation with Borg scale (pre-test, r = -0.336, p = 0.002; post-test, r = -0.252, p = 0.034; Figure 1 and Table 1), while 6MWT showed a negative correlation with only post-test Borg scale (pre-test, r = -0.113 p = 0.343; post-test, r = -0.351 p = 0.002; Table 1). The BHT time was positively correlated with DLCO (%, r = 0.409, p < 0.001) and FVC (liters, r = 0.402, p < 0.001) (Table 1). We also found a statistically significant correlation between BHT time and SHAQ score (r = -0.451, p < 0.001; Table 1). However, EF and PASP by TTE showed no significant relationship with BHT time (EF, r = -0.108, p = 0.374; PASP, r = -0.246, p = 0.054; Table 1).

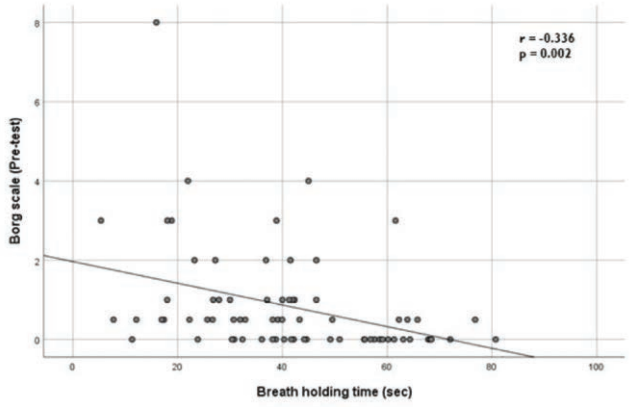


Figure 1. Association of Borg dyspnea scale with breath-holding time.

Table 1. Pearson's correlation coefficients (r) for the relation between BHT and clinical parameters in comparison to 6MWT.

	Pre-test Borg scale	Post-test Borg scale	DLCO (%)	FVC (L)	FVC (%)	FVC /DLCO	EF (%)	PSAP (mm Hg)	SHAQ (score)
BHT (sec)	-0.366**	-0.252*	0.409***	0.402**	0.191	-0.244***	-0.108	-0.246	-0.451***
6MWT (m)	-0.113	-0.351**	0.297*	0.321**	0.063	-0.250*	0.137	-0.354**	-0.531***

BHT, breath-holding test; 6MWT, 6-minute-walk test; DLCO, diffusing capacity for carbon monoxide; FVC, forced vital capacity; EF, ejection fraction estimated by transthoracic echocardiography; SHAQ, Scleroderma Health Assessment Questionnaire.
* p < 0.05, ** p < 0.01, *** p < 0.001

Conclusion: The BHT is a simple, safe, and less time-consuming test, reflective of pulmonary parameters and SHAQ, as compared with 6MWT. Our results suggest that the BHT might be a useful surrogate marker of cardiopulmonary capacity in SSc patients.

REFERENCES:

[1] Villalba WO, Sampaio-Barros PD, Pereira MC, Cerqueira EM, Leme CA, Jr., Marques-Neto JF, et al. Six-minute walk test for the evaluation of pulmonary disease severity in scleroderma patients. Chest. 2007;131(1):217-22.
[2] Garin MC, Highland KB, Silver RM, Strange C. Limitations to the 6-minute walk test in interstitial lung disease and pulmonary hypertension in scleroderma. J Rheumatol. 2009;36(2):330-6.
[3] Barnai M, Laki I, Gyurkovits K, Angyan L, Horvath G. Relationship between breath-hold time and physical performance in patients with cystic fibrosis. Eur J Appl Physiol. 2005;95(2-3):172-8.

Acknowledgements: This study would not have been possible without help from research assistant, Sung-Soon Cho.

Disclosure of Interests: Jina Yeo: None declared, Mi Hyeon Kim: None declared, Jun Won Park: None declared, Jin Kyun Park: None declared, Eun Bong Lee Consultant of: Pfizer, Grant/research support from: GC Pharma and Handok Inc.

DOI: 10.1136/annrheumdis-2021-eular.2273

POS0857 IMMUNOSUPPRESSANTS (CYCLOPHOSPHAMIDE AND MYCOPHENOLATE MOFETIL) VERSUS RITUXIMAB A SINGLE-AGENT THERAPY IN SCLERODERMA-RELATED INTERSTITIAL LUNG DISEASE: REAL CLINICAL PRACTICE

O. Koneva[1], L. P. Ananyeva[1], L. Garzanova[1], O. Desinova[1], O. Ovsyannikova[1], M. Starovoytova[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*

Background: Although interstitial lung disease (ILD) occurs in the majority of patients with systemic sclerosis (SSc), treatment options for this manifestation is empirical and at present consists of Cyclophosphamide (CyP) or Mycophenolate Mofetil (MMF). However, the immunosuppressants (IS) use leads to rather limited improvement of ILD and is associated with many adverse reactions. The search for novel, more efficacious agents has been continued, such as attracting much attention RTM. However, the limited number of RTM-treated patients, considerably different dose regimens, cumulative doses, and observation periods does not allow univocal conclusions on RTM efficacy or definitive recommendations on RTM use in the patients with SSc.

Objectives: To compare the impact of IS and RTM a single-agent therapy on SSc clinical manifestation and activity, and the safety of these agents in the open-label prospective non-randomized study.

Methods: 116 patients with the confirmed SSc diagnosis and ILD evidence based on MSCT findings were enrolled into the study. All patients received low and moderate-dose glucocorticoids regimens. Group A(n=35) received RTM as a single therapy agent for 13.3±2.3 months at total dose 1.35±0,5g (the patient's average age was 45.0±15 years, with female proportion 80%; SSc duration 6.3±2.3 years; diffused/localized forms 1.3/1). Group B (n=36) received parenteral CyP for 12±6 months at total dose 10.6±5 g (the average age 47±12 years, females 92%, SSc duration 5.0±4.8 years, diffused/localized forms 1.6/1). Group C (n=45) received MMF for 12±6 months at a dose of 2 grams per day (the average age 49±13 years, females 91%, SSc duration 7.1±5 years, diffused/localized forms 1/1.3). The time courses of FVC, modified skin count (mRss, points), activity index (EScSG, points) were assessed into the study.

Results: In Groups A, B and C the therapy was associated with significant decrease in mRss (p=0.02, 0.008, 0.007, respectively) and EScSG (p=0.00017, 0.000165, 0.01, respectively).

Evaluation of FVC time course revealed significant FVC increase only in Groups A (p= 0.002) and B (p=0.034), with median increment about 5%.

In Groups A and B 10% FVC increase was found in the third of the patients thus exceeding respective parameter twice in Group C (p=0.15 and 0.008, respectively). The patient percentage with FVC decrease by ≥10% did not differ significantly between groups.

The therapy was better tolerated in RTM-treated group: during RTM therapy adverse reactions emerged in lower proportion of the patients (4/11%) compared with CyP (19/53%, p=0.0000) and MMF-treated group (12/27%, p=0,5).

Parameters	Group A	Group B	Group C
Activity Index 1 *M ± SD*	2.8±1.4*	3.2±1.9*	1.9±1.5*
Activity Index 2 *M ± SD*	1.4±1.2*	1.4±1.2*	1.2±0.9*
Skin count 1 *M ± SD*	11.5±9.5 *	11.2±7.9 *	7.5±6.9 *
Skin count 2 *M ± SD*	8.2±6.2 *	7.9±6.8 *	4.8±3.9 *
FVC 1 *M ± SD*	78.7±20.0 *	80.5±20.1*	90.3±20.8
FVC 2 *M ± SD*	84.2±20.0*	85.8±20.4*	92.2±21.0
Δ FVC %	5.3 [0.8; 11.1]	5.7 [0; 11.2]	1.9 [-3.5; 6.0]
FVC increment by ≥10%, n/%	9/26	14/31	6/13.3
FVC decrement by ≥10% n/%	2/5.7	2/4.4	4/8.9

Notes: *in Parameters column 1 = before treatment, 2 = after treatment; M ± SD = mean value and standard deviation; * = significant difference between the vales measured before and after the treatment*

Conclusion: All agents effectively alleviated skin induration and EScSG, but only RTM and CyP significantly improved FVC. The RTM single therapy was better tolerated compared to IS. The study findings substantiate potential use an RTM single therapy both as a first-line agent for ILD treatment in the patients with a progressive course of ILD damage SSc, and in the event of CyP inefficacy of poor tolerability. The MMF use is more preferable in patients with less pronounced ILD.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2288

POS0858 POTENTIAL EFFICACY PREDICTORS OF ANTI-B-CELL THERAPY IN THE PATIENTS WITH SYSTEMIC SCLEROSIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE

O. Koneva[1], L. P. Ananyeva[1], L. Garzanova[1], O. Desinova[1], O. Ovsyannikova[1], M. Starovoytova[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*

Background: Rituximab (RTM) is considered as a promising therapeutic agent for treatment of With Interstitial Lung Disease (ILD) in the patients with systemic sclerosis (SSc). However, the limited number of RTM-treated patients, considerably

varying dose regimens, cumulative doses and observation periods, lack of data on potential predictors of RTM therapy response do not allow univocal conclusions on RTM efficacy or definitive recommendations on RTM use in the patients with SSc.
Objectives: The study of potential efficacy predictors of anti-B-cell therapy in the patients with SSc associated with ILD.
Methods: 90 patients with SSc-ILD verified by multispiral computed tomography were enrolled to the study and received RTM therapy for 12-42 months at cumulative dose 2.9±1.1 grams (disease duration 5.9±4.8 years, diffused/limited SSc 1.3/1, average age 47 ± 13.6 years, females 83%). All patients received low or moderate dose glucocorticoids. 45 patients received RTM in addition to immunosuppressive therapy (cyclophosphamide and mycophenolate mofetil) because of inadequate efficacy of immunosuppressants. After evaluation of FVC trends in the patients receiving RTM the overall study population was divided into two patient groups for the analysis: group A (n=35) comprised the patients with ≥10% FVC increase (disease duration 6.1±5.8 years, diffused/limited SSc 1,3/1, average age 50±12 years, females 86%, cumulative RTM dose 3.2±1.24 grams), and group B (n=11) comprised the patients with ≥5% FVC decrease (disease duration 5.2±4, diffused/limited SSc 0.8/1, average age 43±16, females 72%, cumulative RTM dose 2.5±0.99 grams). Subsequently correlation analysis was made to clarify the association between delta FVC and a number of clinical (age, gender, duration and form of SSc, modified skin count, presence of gastroesophageal reflux, mPAP, SSc activity (EScSG, points), cumulative RTM dose, immunosuppressive therapy) and laboratory parameters (ESR, ANA-HEP-2, a-Scl-70, CRP, B cell count).
Results: In the overall patient population RTM therapy was associated with significant FVC increase from 77.0±19.9 % to 84.7±20.9% (p=0.000000), with median FVC increment 6.6% [0;14.1].
In group A FVC increased from 75.3±19.9 to 94.3±20.4) (p=0.000000), with median FVC increment 16.3 [12.6; 24.7].
In group B FVC decreased from 82.5 ±23.2 to 72,3±19.4 (p=0,000176), with median FVC decrement 10.4% [-13.4; -6].
Correlation analysis in groups A and B showed significant association of between delta FVC and the patient age (R=0.36), cumulative RTM dose (R=0.34) and EScSG during the last examination (1.2±.,0 and 3.1±1.4 in groups A and B, respectively; R=-0.42).
No significant correlation between delta FVC and any other tested parameters was found.
Conclusion: Therefore, older patients who received the cumulative rituximab dose more than 3 grams with suppressed SSc activity achieved greater FVC increase at the background of therapy. These data allow to consider the above parameters as potential predictors of response to anti-B-cell therapy in the patients with SSc-ILD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2313

POS0859 DEEP PHENOTYPING OF DERMATOMYOSITIS BASED ON LIPID FERROPTOSIS-RELATED GENES BY MACHINE LEARNING

J. Q. Zhang[1,2,3], S. X. Zhang[1,2,3], R. Zhao[1,2,3], J. Qiao[1,2,3], M. T. Qiu[1,2,3], S. Song[1,2,3], M. J. Chang[1,2,3], Y. Zhang[1,2,3], G. Y. Liu[1], P. F. He[4], X. Li[1,2,3]. [1]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [2]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [3]*Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [4]*Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Dermatomyositis (DM) is an idiopathic inflammatory myopathy with heterogeneous clinical manifestation that raise challenges regarding diagnosis and therapy[1]. Ferroptosis is a newly discovered form of regulated cell death that is the nexus between metabolism, redox biology, and rheumatic immune diseases[2]. However, how ferroptosis maintains the balance of lymphocyte T cells and affect disease activity in DM is unclear.
Objectives: To investigate an ferroptosis-related multiple gene expression signature for classification by assessing the global gene expression profile, and calculate the lymphocyte T cells status in the different subsets.
Methods: Gene expression profiles of skeletal muscle from DM samples were acquired from GEO database. GSE143323 (30 patients and 20 HCs) was selected as the training set. The GSE3307 contained 21 DM patients and was selected as the validation set. The 60 ferroptosis genes were obtained from previous literature[3]. The intersection of the global gene and ferroptosis genes was considered the set of significant G-Ferroptosis genes for further analysis. The "NMF" (R-package) was applied as an unsupervised clustering method for sample classification by using G-Ferroptosis genes expression microarray data from the training datasets. An ferroptosis score model was constructed. The performance of the ferroptosis genes-based risk score model constructed by the DM training set was validated in the batch-1 and batch-2 DM sets. Normalized ferroptosis genes training data was used to compare the ssGSEA scores of gene sets between the high risk and low risk group. The statistical software package R (version 4.0.3) was used for all analyses. *P* value < 0.05 were considered statistically significant.
Results: We selected 54 significant G-Ferroptosis genes for further analysis in training set. There were 2 distinct subtypes (high-ferroptosis-score groups and low-ferroptosis-score groups) identified in G-Ferroptosis genes cohort which were also identified in validation datasets (Fig.1A, C, D). Metallothionein 1G (MT1G) was a characteristic gene of low-ferroptosis-score group. The characteristic genes of high-ferroptosis-score group were acyl-CoA synthetase family member 2(ACSF2) and aconitase 1(ACO1) (Fig.1B). Patients in high-ferroptosis-score group had a lower level of Tregs compared with that of low-ferroptosis-score patients in both training and validation set (*P* <0.05, Fig.1E).
Conclusion: The biological process of ferroptosis is associated with the lever of Tregs, suggesting the process of ferroptosis may be involved in the disease progression of DM. Identificating ferroptosis-related features for DM might provide a new idea for clinical treatment.
REFERENCES:
[1] DeWane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogenesis. Journal of the American Academy of Dermatology 2020;82(2):267-81. doi: 10.1016/j.jaad.2019.06.1309 [published Online First: 2019/07/08].
[2] Liang C, Zhang X, Yang M, et al. Recent Progress in Ferroptosis Inducers for Cancer Therapy. Advanced materials (Deerfield Beach, Fla) 2019;31(51):e1904197. doi: 10.1002/adma.201904197 [published Online First: 2019/10/09].
[3] Liang JY, Wang DS, Lin HC, et al. A Novel Ferroptosis-related Gene Signature for Overall Survival Prediction in Patients with Hepatocellular Carcinoma. International journal of biological sciences 2020;16(13):2430-41. doi: 10.7150/ijbs.45050 [published Online First: 2020/08/08].

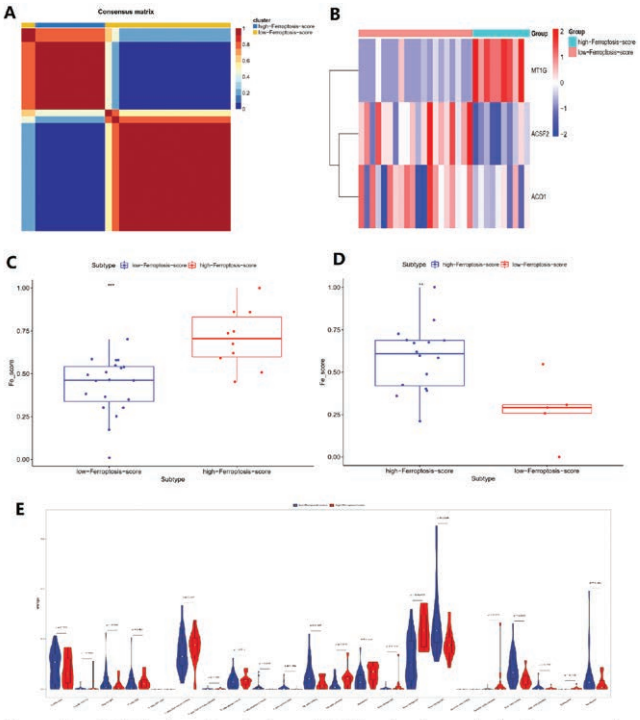


Figure : (**A** and **B**) Molecular typing of patients with DM based on ferroptosis-related gene expression profiles consensus clustering of GEO samples by NMF. Comparison of ferroptosis score levels between the two subgroups of the training set(**C**) and the validation set(**D**). (**E**) Comparison of the ssGSEA scores between different score groups. The scores of 22 immune cells are displayed in boxplots. ^{ns}P> 0.05; *P< 0.05; **P< 0.01; ***P< 0.001.

Acknowledgements: This project was supported by National Science Foundation of China (82001740).Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2323

POS0860 EFFICACY AND SAFETY OF TWO COURSES OF RITUXIMAB BIOSIMILAR ACELLBIA IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS: A PROSPECTIVE OBSERVATIONAL STUDY

L. P. Ananyeva[1], L. Garzanova[1], O. Desinova[1], M. Starovoytova[1], O. Koneva[1], O. Ovsyannikova[1], R. Shayakhmetova[1]. [1]*VA Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*

Background: Interstitial lung disease associated with systemic sclerosis (ILD-SSc) is a frequent manifestation of the disease, impairing the quality of life and the prognosis of the disease. The efficacy of rituximab (RTX) in patients (pts) with ILD-SSC have been shown [1]. The "biosimilar" versions of RTX might reduce the cost of therapy and increase pts accessibility to this treatment option. The RTX biosimilar Acellbia (ACB), "BIOCAD", has received approval in Russian Federation in 2014 for all indications held by reference RTX.
Objectives: to investigate the efficacy and safety of ACB in naive to biological therapy pts with ILD-SSc during at least 12 month of follow-up.
Methods: Twenty pts were included in prospective observational study. The pts were aged 49,7 (s.d.14) years, 14 (70%) were females, mean disease duration was 3,5±2,7years, with diffuse subset in 11 (55%), 13 (65%) were anti-topoisomerase positive, all pts has NSIP-pattern by HRCT. All pts were naive to ACB, received glucocorticoids in low doses, 10 (50%) pts were previously treated with immunosuppressants and 4(20%) of them continued to take mycophenolate mofetil as a concomitant therapy. Pts received two courses of ABC with the same scheme: 1 g repeated 1 week apart (4 g ACB in total). An assessment of basic measurements was obtained at baseline (Point 0), before the second course (after 7,2±1,7 mo, Point 1) and at the end of follow-up (13,4±1,6 mo, Point 2). The results are presented in the form of mean values and standard deviations.
Results: We observed a gradual improvement in the main parameters from Point 0 to Point 2 (table). Importantly, that at Point 1 there were no differences in most parameters, except for Rodnan skin score (mRSS) and the absolute number of B-lymphocytes (B-lymph), but at Point 2 there were significant differences between most basic outcome measures.

Table 1. Follow-up data of ACB treatment in ILD-SSC pts

Parameters	Point 0 (n=20)	Point 1 (n=20)	Point 2 (n=18)#	P 1-2	P 1-3
mRSS	12,75±11,1	8,25±7,72	6,16±5,65	0,002	0,002
FVC*, % pred	89,1±18,2	92,31±19,21	98,26±16,13	NS	0,0002
DLCO, % pred**	56,67±15,7	58,11±17,71	61,86±17,16	NS	0,019
SHAQ	1,13±0,628	0,98±0,678	0,61±0,495	NS	0,00001
IgG, g/l	12,61±2,348	11,5±1,61	10,19±2,18	NS	0,002
a-Topo-1, unit/ml	109,68±86,92	96,46±81,72	72,46±69,46	NS	0,004
B-lymph, absolute count	0,329±0,34	0,0016±0,003	0,00189±0,003	0,0004	0,001
Glucocorticoids, mg/day	11,0±2,7	10,75±2,0	9,4±2,3	NS	0,03

**FVC - forced vital capacity % predicted, **DLCO - diffusion capacity for carbon monoxide % predicted.# Of the 20 patients who received the second course, 2 (10%) dropped out the follow-up due to pregnancy (1) and lung cancer (1).*

The frequency and spectrum of adverse events (AE) corresponds to the known in the treatment of RTX, most AEs were classified as mild ones.There were 11 (55%) of AE in 9 (45 %) pts. Infections were observed in 7 (35%) pts: 4 cases of acute respiratory tract infections, 2 cases of positivity in interferon-gamma release assayand one case each of otitis, cystitis, cholecystitis (9 AE in total). One pts developed low limb vein thrombosis and one - lung cancer. There were no infusion-related reactions.
Conclusion: The data from this prospective pilot study showed the effectiveness of the ACB in ILD-SSc. The clinical effect of ACB arises gradually and the baseline outcome measures reliably improve by the end of the first year. Our study have demonstrated a well-tolerated safety profile. We believe that ACB can be prescribed at SSc-ILD as a first-line drug and/or in the form of monotherapy.
REFERENCES:
[1] Erre G.L., et.al. Efficacy, Safety, and Tolerability of Treatments for Systemic Sclerosis-Related Interstitial Lung Disease: A Systematic Review and Network Meta-Analysis. J.Clin.Med.2020,9,2560;doi:10.3390/jcm90825-60.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2338

POS0861 EFFECTIVENESS AND SAFETY OF TOCILIZUMAB IN PATIENTS WITH SYSTEMIC SCLEROSIS: A PROPENSITY SCORE CONTROL MATCHED OBSERVATIONAL STUDY OF THE EUSTAR COHORT

S. Kuster[1], S. Jordan[1], M. D. Elhai2, U. Held[3], K. Steigmiller[3], C. Bruni[4], F. Iannone[5], S. Vettori[6], E. Siegert[7], S. Rednic[8], V. Codullo[9], P. Airò[10], Y. Braun-Moscovici[11], N. Hunzelmann[12], M. J. Salvador[13], V. Riccieri[14], A. M. Gheorghiu[15], J. J. Alegre Sancho[16], K. Romanowska-Prochnicka[17], I. Castellvi[18], I. Koetter[19], M. E. Truchetet[20], F. J. López-Longo[21], P. Novikov[22], A. Giollo[23], Y. Shirai[24], L. Belloli[25], E. Zanatta[26], E. Hachulla[27], V. Smith[28], C. Denton[29], R. Ionescu[30], T. Schmeiser[31], J. H. W. Distler[32], A. Gabrielli[33], A. M. Hoffmann-Vold[34], M. Kuwana[24], Y. Allanore[35], O. Distler[2]on behalf of EUSTAR. *[1]University of Zurich, University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland*; *[1]University of Zurich, University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland*; *[3]University of Zurich, Department of Biostatistics at Epidemiology, Biostatistics and Prevention Institute, Zurich, Switzerland*; *[4]University of Florence, Division of Rheumatology, Department of Experimental and Clinical Medicine, Florence, Italy*; *[5]GISEA, University Hospital of Bari, Bari, Italy*; *[6]University of Campania 'Luigi Vanvitelli', Department of Precision Medicine, Naples, Italy*; *[7]Charité-Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; *[8]University of Medicine & Pharmacy "Iuliu Hatieganu" Cluj, Clinica Reumatologie, Cluj Napoca, Romania*; *[9]University and IRCCS Policlinico S. Matteo Foundation, Division of Rheumatology, Pavia, Italy*; *[10]University of Brecsia, ASST Spedali Civili of Brescia, Rheumatology and Clinical Immunology, Brescia, Italy*; *[11]Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion, B. Shine Rheumatology Unit, Hailfa, Israel*; *[12]Universtätsklinikum Köln, Universitätshautklinik Köln, Köln, Germany*; *[13]University of Coimbra, University Hospitals, Department of Rheumatology, Coimbra, Portugal*; *[14]Sapienza University, Department of Internal Medicine and Medical Specialties, Rome, Italy*; *[15]Ion Cantacuzino Clinical Hospital, Department of Internal Medicine and Rheumatology Clinic, Bucharest, Romania*; *[16]University of Valencia, University Hospital Dr. Peset, Department of Rheumatology, Valencia, Spain*; *[17]Institute of Rheumatology, Department of Connective Tissue Disease, Warsaw, Switzerland*; *[18]Hospital Universitari de La Santa Creu I Sant Pau, Department of Rheumatology, Barcelona, Spain*; *[19]Asklepios Clinic Altona, Medical Department 4, Rheumatology, Immunology, Nephrology, Hamburg, Germany*; *[20]National Reference Center for Systemic Autoimmune Rare Diseases, Hopital Pellegrin, Department of Rheumatology, Bordeaux, France*; *[21]Hospital General Universitario Gregorio Marañón, Department of Rheumatology, Madrid, Spain*; *[22]Sechenov First Moscow State Medical University, Clinic of Nephrology, Internal and Occupational Diseases, Moscow, Russian Federation*; *[23]University of Verona, Rheumatology Section, Department of Medicine, Verona, Switzerland*; *[24]Nippon Medical School Hospital, Allergy and Rheumatology, Tokyo, Japan*; *[25]Niguarda Ca' Granda Hospital, Rheumatology Unit, Milano, Italy*; *[26]University of Padova, Rheumatology Unit, Department of Clinical and Experimental Medicine, Padova, Italy*; *[27]Referral Centre for Rare Systemic Auto-immune Diseases for North and North-West of France, University of Lille, Department of Internal Medicine, Claude Huriez Hospital, Lille, France*; *[28]University of Ghent, Department of Rheumatology, Ghent, Belgium*; *[29]Royal Free and University College London Medical School, Royal Free Campus, Centre for Rheumatology, London, United Kingdom*; *[30]University of Medicine and Pharmacy, Department of Rheumatology - St. Maria Hospital, Carol Davila, Bucharest, Romania*; *[31]Krankenhaus St. Josef, Innere Medizin und Rheumatologie, Wuppertal-Elberfeld, Germany*; *[32]Universitätsklinikum Erlangen, Department of Internal Medicine 3, Erlangen, Germany*; *[33]Istituto di Clinica Medica Generale, Università Politecnica delle Marche Polo Didattico, Ematologia ed Immunologia Clinica, Ancona, Italy*; *[34]Rikshospitalet University Hospital, Department of Rheumatology, Oslo, Norway*; *[35]Cochin Hospital, APHP, Paris Descartes University, Rheumatology A Department, Paris, France*

Background: Tocilizumab (TCZ) showed trends for improving skin fibrosis and prevented progression of lung fibrosis in patients with systemic sclerosis (SSc) in placebo-controlled randomised clinical trials (RCTs). However, safety and effectiveness of TCZ beyond these selected and enriched clinical trial populations in SSc is still unknown.
Objectives: To assess safety and effectiveness of TCZ treatment compared to standard of care in SSc patients from the large, multicentre, observational, real-life EUSTAR network/database using propensity score matching.
Methods: SSc patients from the EUSTAR network/database, who fulfilled the ACR/EULAR 2013 classification criteria, with a baseline and a follow-up visit at 12±3 months, receiving TCZ or standard of care (controls), were selected. The following variables were used for the propensity score matching (1:1): age at diagnosis, gender, disease subtype, baseline modified Rodnan skin score (mRSS), forced vital capacity (FVC), and diffusing capacity for carbon monoxide (DLCO), co-therapy with immunosuppressives, disease duration, and year of treatment. Primary endpoints were mRSS and FVC at 12±3 months follow-up compared between the groups, using paired t-tests. Secondary endpoints were the percentage of progressive/regressive patients for skin and lung at 12±3 months follow-up according to standard definitions (1,2). Sensitivity analyses assessed pre-processing decisions (selection of most recent vs. random observation for control patients with multiple suitable time intervals), as well as the matching method (optimal vs. exact matching). Missing values were addressed with 100-fold multiple imputation using chained equations. Safety data were analysed in all patients. The study including the statistical analysis plan was pre-registered at www.drks.de (DRKS-ID: DRKS00015537).
Results: We identified 93 SSc patients treated with TCZ and 2370 SSc patients with standard of care who fulfilled the inclusion criteria. Forty nine (57.7%) of the TCZ treated patients were diffuse, eight patients were not classified, disease duration was (mean±SD) 6.35±5.40 years, their baseline mRSS was 15.05±10.85, and 76 (81.7%) received immunosuppressive therapy in addition to TCZ.Through multiple imputation and propensity score matching, 100 imputed

sets of 93 pairs of TCZ/controls were generated. Comparison between groups showed consistent effects of TCZ across all pre-defined primary and secondary endpoints: mRSS was lower in the TCZ group (mean difference (95% confidence interval (CI)) -1.8 (-4.79 to 1.19), p=0.24, Figure 1A). Similarly, FVC % predicted was higher in the TCZ group mean difference (2.25, 95% CI -4.57 to 9.06), p=0.51, Figure 1B). Considering secondary endpoints, the percentage of skin progressors as well as lung progressors at follow up was lower in the TCZ group (odds ratio OR 0.67 (95% CI 0.07 to 6.41), p=0.74 and OR 0.53 (95% CI 0.16 to 1.7); p=0.2, respectively. Consistently, the percentage of regressors for skin (OR 1.6 (95% CI 0.56 to 4.54), p=0.38) and for lung (OR 1.74 (95% CI 0.66 to 4.58), p=0.26) was higher in TCZ. These results were robust regarding the sensitivity analyses. Safety analysis confirmed previously reported adverse event profiles.

Conclusion: In this large, observational, controlled, real-life EUSTAR study, effectiveness of TCZ did not reach statistical significance compared to standard of care treatment but showed consistent positive effects of TCZ on skin and lung fibrosis across all pre-defined primary and secondary endpoints confirming data from recent RCTs.

REFERENCES:

[1] Prediction of improvement in skin fibrosis in diffuse cutaneous systemic sclerosis: a EUSTAR analysis. Ann Rheum Dis 2016:1743-8.

[2] Progressive interstitial lung disease in patients with systemic sclerosis-associated interstitial lung disease in the EUSTAR database. Ann Rheum Dis 2021:219-227.

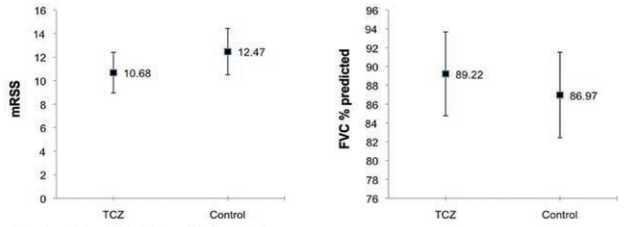


Figure 1. mRSS and FVC at follow up (12±3months)

A) **Mean mRSS (95% CI) TCZ 10.68 (8.96 to 12.4) vs control 12.5 (10.5 to 14.5), between group mean difference -1.8 (-4.79 to 1.19), p=0.24**

B) **Mean FVC% predicted (95% CI) TCZ 89.22 (84.77 to 93.67) vs control 86.97 (82.43 to 91.52), between group difference 2.25 (-4.57 to 9.06), p=0.51**

Disclosure of Interests: Simon Kuster: None declared, Suzana Jordan: None declared, Muriel Daniele Elhai: None declared, Ulrike Held: None declared, Klaus Steigmiller: None declared, Cosimo Bruni: None declared, Florenzo Iannone: None declared, Serena Vettori: None declared, Elise Siegert: None declared, Simona Rednic: None declared, Veronica Codullo: None declared, Paolo Airò Consultant of: Dr. Airo' reports personal fees (consultancies) from Bristol Myers Squibb, Bohringer Ingelheim, non-financial support from CSL Behring, SOBI, Janssen, Roche, Sanofi, Pfizer, Yolanda Braun-Moscovici: None declared, Nicolas Hunzelmann: None declared, Maria Joao Salvador: None declared, Valeria Riccieri: None declared, Ana Maria Gheorghiu: None declared, Juan Jose Alegre Sancho: None declared, Katarzyna Romanowska-Prochnicka: None declared, Ivan Castellví: None declared, Ina Koetter: None declared, Marie-Elise Truchetet Consultant of: Marie-Elise Truchetet has had consultancy relationships and/or has received research funding from Boehringer Ingelheim, Genentech/Roche, and Sanofi in the area of potential treatments of scleroderma and its complications., Grant/research support from: Marie-Elise Truchetet has had consultancy relationships and/or has received research funding from Boehringer Ingelheim, Genentech/Roche, and Sanofi in the area of potential treatments of scleroderma and its complications., Francisco J López-Longo: None declared, Pavel Novikov: None declared, Alessandro Giollo: None declared, Yuichiro Shirai: None declared, Laura Belloli: None declared, Elisabetta Zanatta: None declared, Eric Hachulla: None declared, Vanessa Smith: None declared, Christopher Denton: None declared, Ruxandra Ionescu: None declared, Tim Schmeiser: None declared, Jörg H.W. Distler: None declared, Armando Gabrielli: None declared, Anna-Maria Hoffmann-Vold Consultant of: AMHV has received research funding and/or consulting fees and/or other remuneration from Actelion, Boehringer Ingelheim, Roche, Bayer, Merck Sharp & Dohme, ARXX, Lilly and Medscape, Grant/research support from: AMHV has received research funding and/or consulting fees and/or other remuneration from Actelion, Boehringer Ingelheim, Roche, Bayer, Merck Sharp & Dohme, ARXX, Lilly and Medscape. Masataka Kuwana: None declared, Yannick Allanore: None declared, Oliver Distler Speakers bureau: Oliver Distler has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Consultant of: Oliver Distler has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Grant/research support from: The study was partially supported by a grant from Roche. Roche was not involved in analysis or interpretation of the results.

DOI: 10.1136/annrheumdis-2021-eular.2392

POS0862 NAILFOLD CAPILLAROSCOPY IN UNDIFFERENTIATED AND MIXED CONNECTIVE TISSUE DISEASES

C. Pizzorni[1], G. Ferrari[1], C. Schenone[1], E. Gotelli[1], S. Paolino[1], A. Sulli[1], G. Pacini[1], E. Alessandri[1], V. Smith[2], M. Cutolo[1]. *[1]Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic, Genoa, Italy*; *[2]Department of Rheumatology – Department of Internal Medicine – Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent University Hospital, Ghent, Belgium*

Background: Microvascular damage is a frequent feature in connective tissue diseases (CTDs) and can be easily detected trough nailfold videocapillaroscopy (NVC) (1,2). Mixed and Undifferentiated connective tissue diseases (MCTD and UCTD) do not show a specific and unique NVC pattern (3). However, a variety of microvascular abnormalities can occur in these two CTDs, both non-specific or specific for the scleroderma like-pattern (3-5).

Objectives: To retrospectively assess and compare nailfold microangiopathy observed by NVC in MCTD and stable UCTD versus primary Raynaud's phenomenon (PRP) (6). In addition, the aim was to correlate NVC findings with serum levels of autoantibodies (Abs) against extractable nuclear antigen (ENA) detected in UCTD.

Methods: Files of fourty-six MCTD patients (Kasukawa's criteria) (mean age 42.8±16 SD years), fourty-seven UCTD patients (mean age 47.7±16.1 SD years), fifty-one PRP (mean age 45.9±17.3 SD years) were retrospectively evaluated in the study. Among UCTD and MCTD patients 95% of both showed Raynaud's phenomenon. Main NVC parameters (i.e. dilated capillaries, giant capillaries, microhemorrhages, abnormal shapes and number of capillaries) and related semiquantitative scale (score 0–3 for every parameter), were analyzed and compared between the two distinct CTD groups and PRP. Furthermore, ENA Abs (in particular, Ro/SSA, La/SSB, Scl70 and Jo1) were evaluated. The CTD patients were receiving different immunosuppressive treatments. Statistical analysis was performed by non-parametric tests.

Results: Among UCTD group, 36% of patients showed a normal NVC pattern, 53% had non-specific NVC abnormalities and 11% had a scleroderma like-pattern. The latter was significantly more frequent in MCTD than in UCTD ($p<0.001$), in fact 22 out of 46 (48%) MCTD patients presented a scleroderma-like pattern. On the other hand, normal pattern or non-specific NVC abnormalities were respectively found in 9% and 43% MCTD patients. Therefore, CTD patients showing giant capillaries, abnormal shapes (i.e. angiogenesis) and lower capillary density were significantly more affected by MCTD than UCTD ($p<0.001$). Finally, the absolute number of capillaries was found significantly lower in MCTD versus UCTD patients (mean 7±1.7 SD vs mean 9.2±1 SD, respectively, $p<0.001$). Not any statistical correlation was observed between NVC parameters and specific Abs ENA in UCTD. PRP showed a normal NVC pattern in 2% and non-specific capillary abnormalities in 98%, (including dilated capillaries and microhemorrhages).

Conclusion: NVC features in UCTD patients seem very close to the pattern observed in PRP (mostly non-specific capillary abnormalities), conversely in MCTD the scleroderma-like pattern was found significantly prevalent together with a significant capillary number reduction. The transition from the scleroderma-like to the scleroderma pattern (mean systemic sclerosis) is matter of actual investigation.

REFERENCES:

[1] Cutolo M. et al. Best Pract Res Clin Rheumatol 2008; 22:1093-108.

[2] Sulli A, Ann Rheum Dis. 2008;67:885-7.

[3] Smith V. et al. Autoimmunity Reviews 2020; 19:102458.

[4] De Holanda Mafaldo DA, et al. Lupus. 2007; 16:254–8.

[5] Smith V, et al. Ann Rheum Dis 2010; 69: 1092-96.

[6] Antunes M, et al. RMD Open. 2019, 26;4.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2562

POS0863

DIFFERENTIATING THE DOMINANCE OF PULMONARY VASCULAR DISEASE OR INTERSTITIAL LUNG DISEASE ON HEMODYNAMIC ABNORMALITIES IN SYSTEMIC SCLEROSIS AND CLARIFYING EACH CHARACTERISTIC BY USING QUANTITATIVE EVALUATION OF CHEST CT

K. Ninagawa[1], M. Kato[1], M. Kono[1], Y. Fujieda[1], K. Oku[1], T. Atsumi[1]. [1]*Hokkaido University, Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Sapporo, Japan*

Background: Group 1 and 3 pulmonary hypertension (PH) develop through different pathological mechanisms but have similar hemodynamic abnormalities. Systemic sclerosis (SSc) is associated with both pulmonary vascular disease (PVD) and interstitial lung disease (ILD), making it challenging to differentiate group 1 and 3 PH in those patients. A previous study using quantitative evaluation of chest computed tomography (CT) demonstrated that normal lung volume was inversely correlated with mean pulmonary arterial pressure (mPAP) in patients with group 3 PH (1).
Objectives: In this study, we aimed to assess the dominance of PVD or ILD in SSc patients by quantitative evaluation of chest CT and to evaluate each characteristic.
Methods: A total of 76 SSc patients who underwent right heart catheterization (RHC) were included. Chest CT was evaluated by using a software (Synapse Vincent Ver.3.0, Fujifilm) which quantified normal and total area of the lung. Then, we calculated abnormal area by drawing normal area from total area in the lung (%). Pulmonary function test (PFT) and serum biomarkers, such as KL-6 and LDH, were also evaluated. The dominance of PVD or ILD was defined as divergent or parallel change between the first and last assessments, respectively, in mPAP and abnormal area in the lung calculated using the software. Increase or decrease by over 10% in the last assessment compared to the first assessment was considered as a significant change in mPAP or abnormal area in the lung. P values were calculated by Mann-Whitney U test, and correlation coefficients were calculated by direct regression variance.
Results: The median [range] values of mPAP and abnormal area in the lung at baseline were 23 [9-65] mmHg and 30.2 [0-100] %, respectively. Of 37 SSc and PH patients, 18 were defined as having PVD dominance while 19 as ILD dominance. Abnormal area in the lung at baseline was greater in patients with ILD dominance compared to those with PVD dominance (39.1 [16.3-98.3] v.s. 14.0 [0-99] %, p=0.002), whereas mPAP was higher in patients with PVD dominance than those with ILD dominance (42.5 [23.0-65.0] v.s. 26.0 [16.0-42.0] mmHg, p=0.002). PFT parameters including forced vital capacity were not different between the two groups. The ratio of mPAP/KL-6 showed a great difference between the two groups with its significant elevation in patients with PVD dominance (p=0.007).
Conclusion: Quantitative evaluation of chest CT showed great efficiency in differentiating the dominance of PVD or ILD in patients with SSc and PH. In addition, the ratio of mPAP/KL-6 may easily be used as a parameter for dominance evaluation.
REFERENCES:

[1] Iwasawa T, Kato S, Ogura T, Kusakawa Y, Iso S, Baba T, et al. Low-normal lung volume correlates with pulmonary hypertension in fibrotic idiopathic interstitial pneumonia: computer-aided 3D quantitative analysis of chest CT. AJR Am J Roentgenol. 2014;203(2):W166-73.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2569

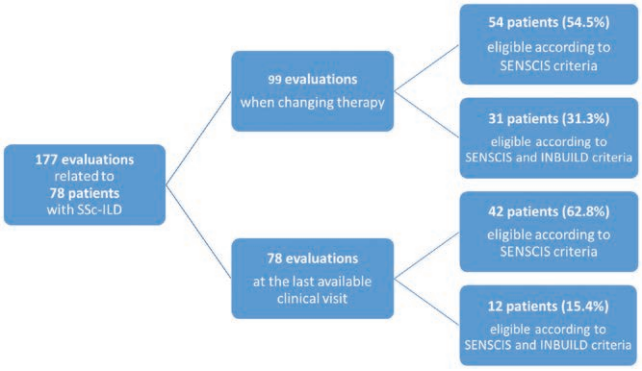
POS0864

ELIGIBILITY FOR ANTI-FIBROTIC TREATMENT WITH NINTEDANIB OF PATIENTS WITH SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE

E. De Lorenzis[1], G. Natalello[1], L. Verardi[1], L. Gigante[1], M. A. D'agostino[1], S. L. Bosello[1]. [1]*Fondazione Policlinico Universitario A. Gemelli IRCCS - Catholic University of the Sacred Heart, Rheumatology Unit, Rome, Italy*

Background: Pulmonary involvement is the main determinant of disease-related mortality in systemic sclerosis (SSc). The SENSCIS and INBUILD trials have documented the efficacy of the antifibrotic drug Nintedanib (NTN) in the treatment of SSc-related interstitial lung disease (SSc-ILD) and progressive forms of ILD other than Idiopathic Pulmonary Fibrosis[1,2]. The criteria for the use of this drug in patients with SSc-ILD in clinical practice are currently being defined.
Objectives: To evaluate the proportion of patients eligible for NTN treatment based on the enrollment criteria fof the SENSCIS and INBUILD studies in a real-life cohort of SSc-ILD patients.
Methods: We considered consecutive patients with ILD extension on CT ≥10% and disease duration ≤7 years with at least one visit in the period between September 2016 and December 2019. Data of the clinical visits were retrospectively evaluated. For each patient, we examined the visits during which a well-tolerated immunosuppressive therapy was modified because of progression of SSc-ILD and the most recent follow-up visit. Eligibility of patients for NTN was defined according to the inclusion criteria of the SENSCIS and INBUILD trials. Patients with more than 2 acral ulcers at the time of evaluation, history of digital amputation, pulmonary hypertension (functional class III-IV) and increased hemorrhagic or thrombotic risk were judged not eligible to NTN in trials.
Results: A total of 177 visits regarding 78 patients were examined (females 80.8%, diffuse skin disease 51.3%, anti-Scl70 antibodies positivity 55.7%, age 54.8±16.0 years, disease duration 4.0±2.4 years). Considering the visits in which indication for a therapeutic change was given, 54 patients (54.5%) were eligible for NTN according to SENSCIS criteria and of these 31 (31.3%) also according to INBUILD criteria (Figure 1). In this group, 25 patients were treated with mycophenolate mofetil, 11 with azathioprine, 10 with cyclophosphamide, 7 with methotrexate and 8 with rituximab (2 in combination). At the latest available evaluation, 42 patients (62.8%) were eligible for NTN according to SENSCIS criteria and of these 12 (15.4%) also according to INBUILD criteria (Figure 1). In this group, 30 patients were in mycophenolate mofetil (6 in combination with biologic treatment), 5 in azathioprine, 1 in cyclophosphamide, 1 in methotrexate, 6 in rituximab, 2 in tocilizumab and 1 in pirfenidone. Overall, the factors limiting NTN start according to the trial enrollment criteria would have been: uncompromised (19.2%) or too low (6.4%) DLco values, too low FVC (3.4%), severe acral disease with ulcers (16.9%), severe pulmonary arterial hypertension (6.2%), increased thrombotic or haemorrhagic risk (6.2%). In the scenario of eligibility, skin progression was detectable in 43.4% of all visits.
Conclusion: Treatment that can modify the progression of SSc-ILD are currently limited. Based on our retrospective analysis, the use of NTN in accordance with current clinical evidence could be considered in a significant percentage of patients with SSc-ILD.
REFERENCES:

[1] Flaherty KR, et al. Nintedanib in Progressive Fibrosing Interstitial Lung Diseases. N Engl J Med. 2019.
[2] Distler O, et al. Nintedanib for Systemic Sclerosis-Associated Interstitial Lung Disease. N Engl J Med. 2019.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2711

POS0865

REDUCED BONE MINERAL DENSITY IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: A CASE CONTROL STUDY

Y. K. Tang[1], V. Lao[1], H. T. Pang[1], T. L. V. Wong[1], T. H. Luk[1], H. So[2]. [1]*Kwong Wah Hospital, Medicine and Geriatrics, Hong Kong, Hong Kong (SAR)*; [2]*The Chinese University of Hong Kong, Department of Medicine and Therapeutics, Hong Kong, Hong Kong (SAR)*

Background: Idiopathic Inflammatory Myopathies (IIMs) patients are at risk of bone mineral density (BMD) loss due to systemic inflammation, use of glucocorticoids (GCs) and disability. Cross sectional study showed 70% of IIMs patients had reduced BMD but whether they were at excessive risk compared to controls were unknown.
Objectives: To compare the prevalence of reduced BMD between IIMs patients, non-rheumatological controls, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients and to determine the clinical determinants of BMD in IIMs patients.
Methods: This was a single centre retrospective case control study. BMD at lumbar spine L1-L4 and neck of femur (NOF) were assessed by dual-energy X-ray absorptiometry (DXA) scans. The prevalence of reduced BMD and osteoporosis in Chinese IIMs patients and age-and-sex-matched non-rheumatological controls were compared. The BMD of female IIMs were then compared to age matched female RA and SLE patients in the secondary analysis. Binary logistic regression was used for adjustment of confounders. The demographics and

clinical variables independently associated with BMD were determined by linear regression.

Results: A total of 230 patients were recruited including 65 IIMs, 65 non-rheumatological controls, 50 RA and 50 SLE patients. The mean age was 58.6±10.96 years and 76.9% were female. There was no significant difference on demographics between the two groups. Almost all IIMs patients (98%) and 52% of controls had exposed to GCs (p<0.001). Significantly more IIMs patients had used immunosuppressants (92.3% vs 38.5%, p<0.001) and biologics (13.8% vs 1.5%, p=0.01). The prevalence of reduced BMD and osteoporosis were significantly higher in IIMs patients than non-rheumatological control (Reduced BMD: 73.8% vs 43.1%, p=0.043; Osteoporosis: 29.2% vs 13.8%, p=0.033) (Table 1). The mean lumbar spine and hip BMD were 0.886±0.181 g/cm^2 and 0.651±0.144 g/cm^2 in IIMs patients, which were significantly lower than that of the control group (0.960±0.143g/cm^2, p=0.011 and 0.751±0.127g/cm^2, p<0.001) (Figure 1). Multivariate analysis confirmed IIMs were associated with increased risk of reduced BMD (Odds ratio:2.118, p=0.048, 95% CI 1.005-4.461). The prevalence of reduced BMD and osteoporosis were not significantly different between IIMs, RA and SLE patients but the mean hip BMD was the lowest in the IIM group (0.641±0.152g/cm^2 vs 0.663±0.102g/cm^2 in the RA group vs 0.708±0.132 g/cm^2 in the SLE group, p=0.035). Lower BMI (p=0.035) and more advanced age (p<0.001) were associated with lower BMD in the IIM patients.

Conclusion: Reduced BMD was more prevalent in IIM patients than non-rheumatological controls. Lower BMI and more advanced age were associated with lower BMD. Vigilant monitoring of BMD and use of antiresorptive treatment should be considered in IIM patients.

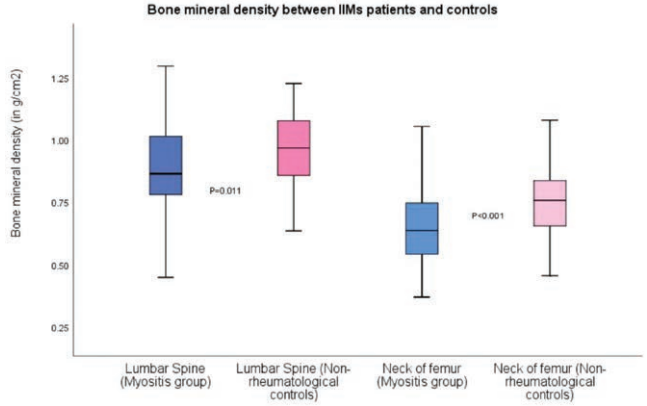
REFERENCES:

[1] Briot K, Geusens P, Em Bultink I et al. Inflammatory diseases and bone fragility. Osteoporos Int. 2017;28:3301-14.

[2] So H, Yip ML, Wong AKM. Prevalence and associated factors of reduced bone mineral density in patients with idiopathic inflammatory myopathies. Int J Rheum Dis. 2016;19:521-8.

Table 1. Prevalence of reduced BMD in IIM patients and non-rheumatologcial controls

	Myositis (n=65)	Non-rheumatological controls (n=65)	Significance
Osteopenia at LS	25 (38.5%)	20 (30.8%)	0.357
Osteoporosis at LS	13 (20%)	6 (9.2%)	0.082
Osteopenia at NOF	29(44.6%)	26 (40%)	0.542
Osteoporosis at NOF	12(18.5%)	6 (9.2%)	0.119
Osteopenia overall	29(44.6%)	28 (43.1%)	0.860
Osteoporosis overall	19(29.2%)	9(13.8%%)	0.033
Reduced BMD overall	48 (73.8%)	37 (56.9%)	0.043
Occurrence of fragility fracture	None=52 Vertebral =5 Femoral=1Femoral=1 Wrist=4 Other sites=3	None=54 Vertebral=4 Femoral=0 Wrist=3 Other sites=3	0.651



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2824

POS0866 TWO-DIMENSIONAL HRCT-BASED RADIOMIC FEATURES IN SSC-ILD DISTINGUISH DRUG RESPONDERS FROM NON-RESPONDERS

C. Meier[1], M. Maciukiewicz[1], M. Brunner[1], J. Schniering[1], H. Gabrys[2], A. Kühnis[2], O. Distler[1], T. Frauenfelder[3], S. Tanadini-Lang[2], B. Maurer[1].

[1]University of Zurich, University Hospital Zurich, Department of Rheumatology, Center of Experimental Rheumatology, Zurich, Switzerland; *[2]University of Zurich, University Hospital Zurich, Department of Radiation Oncology, Zurich, Switzerland*; *[3]University of Zurich, University Hospital Zurich, Institute for Diagnostic and Interventional Radiology, Zurich, Switzerland*

Background: Management of patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) is complicated by high inter-patient variability. To date, no validated predictors of treatment response are available for routine use. High resolution computed tomography (HRCT)-based radiomics, i.e. the high-dimensional, quantitative analysis of imaging metadata, have previously been shown to be successful in discriminating (SSc-)ILD phenotypes in preclinical and clinical studies[1]. Since HRCT is an integral part of the routine work-up in SSc, HRCT-based radiomic features may hold potential as non-invasive biomarkers.

Objectives: To predict treatment response using two-dimensional (2D) HRCT-based radiomics in SSc-ILD patients from a prospectively followed cohort.

Methods: Inclusion criteria were diagnosis of SSc-ILD in HRCT, availability of a suitable chest HRCT scan within 12 months prior to initiation of a new treatment, and availability of clinical baseline and follow-up information. Treatment response was defined as the absence of all of the following over a follow-up period of 12-24 months: relative decrease in forced vital capacity (FVC) ≥5%, increase of ILD in HRCT as assessed by a radiologist, change in treatment regimen due to insufficient response, ILD-related death or lung transplantation. Of each pre-treatment HRCT, 6 slices (15±5 mm apart, starting from the basal lung margin) were manually segmented and 1513 2D radiomic features were extracted using the in-house software Z-Rad (Python 2.7). Features were Z-score transformed and pre-filtered for inter- and intra-reader robustness (intraclass correlation coefficient >0.85) and inter-feature correlation (Spearman's rho <0.9). A categorical linear regression model was created using 3-fold cross-validated elastic nets for feature selection. Features were then summarized and divided by their number. For generation of a score cut-off, Youden's score was used. For two-group analyses of continuous variables, Wilcoxon's test was performed, whereas categorical data was assessed using Fisher's exact test.

Results: A total of 64 pre-treatment HRCTs from 54 patients were analyzed. In 9 patients, >1 asynchronous treatments were assessed, while 45 patients had only 1 eligible treatment approach. The response rate within the assessed follow-up period was 45.3% (n=29). For score generation, 13 radiomic features were selected and an optimal cut-off value of -0.1589 was determined. Univariate linear regression showed significant association between our categorical radiomics-based score and treatment response (p=0.007, area under the curve = 0.65 (0.51-0.79), sensitivity=0.90, specificity=0.43), whereby a high score was predictive for treatment response.

No differences between patients with high (n=46) or low (n=18) scores were detected for baseline age (mean±SD=55.5±12.0 and 55.5±13.6 years, p=0.84), duration of SSc (mean±SD=6.2±8.4 and 4.7±4.4 years, p=0.79), time since ILD diagnosis (2.7±2.9 and 2.4±3.1 years, p=0.59), FVC (77.6±20.6 and 80.1±17.9, p=0.41) or DLco (54.4±21.0 and 57.6±18.9, p=0.40). Distribution of anti-Scl-70 positivity (45.7% vs. 55.6%, p=0.58) and diffuse cutaneous disease (47.7% vs. 61.1%, p=0.41) was not significantly different between patients with high and low scores, respectively, although a trend towards higher percentages in the high score group was observed.

Conclusion: Our results indicate that, following validation in external cohorts, radiomics may be a promising tool for future pre-treatment patient stratification. Moreover, our radiomics-based score seems not to be associated with commonly studied clinical predictors such as anti-Scl-70 positivity or lung function, underlining a possible additive value to 'traditional' clinical parameters.

REFERENCES:

[1] Schniering, J., *et al.* Resolving phenotypic and prognostic differences in interstitial lung disease related to systemic sclerosis by computed tomography-based radiomics. *medRxiv* [Preprint] doi:10.1101/2020.06.09.20124800 (2020).

Disclosure of Interests: Chantal Meier: None declared, Malgorzata Maciukiewicz: None declared, Matthias Brunner: None declared, Janine Schniering: None declared, Hubert Gabrys: None declared, Anja Kühnis: None declared, Oliver Distler Speakers bureau: Speaker fee on Scleroderma and related complications: Bayer, Boehringer Ingelheim, Medscape, Novartis, Roche. Speaker fee on rheumatology topic other than Scleroderma: MSD, iQone, Novartis, Pfizer, Roche, Consultant of: Consultancy fee for Scleroderma and its complications: Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Bayer, Baecon Discovery, Boehringer, CSL Behring, ChemomAb, Corbus Pharmaceuticals, Horizon Pharmaceuticals, Galapagos NV, GSK, Glenmark Pharmaceuticals, Inventiva, Italfarmaco, iQvia, Kymera, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Roche, Roivant Sciences, Sanofi, UCB. Consultancy fee for rheumatology topic other than Scleroderma: Abbvie, Amgen, Lilly, Pfizer, Grant/research support from: Research Grants to investigate the pathophysiology and potential treatment

of Scleroderma and its complications: Kymera Therapeutics, Mitsubishi Tanabe, Thomas Frauenfelder: None declared, Stephanie Tanadini-Lang: None declared, Britta Maurer Speakers bureau: Speaker fees from Boehringer-Ingelheim, Grant/research support from: Grant/research support from AbbVie, Protagen, Novartis Biomedical Research, congress support from Pfizer, Roche, Actelion, mepha, and MSD

DOI: 10.1136/annrheumdis-2021-eular.2884

POS0867

ALTERATION OF DUODENAL HISTOLOGY IN SYSTEMIC SCLEROSIS PATIENTS AFTER FECAL MICROBIOTA TRANSPLANTATION

H. Didriksen[1], N. Strahm[2], Ø. Molberg[1], H. Fretheim[1], T. Garen[1], Ø. Midtvedt[1], O. Distler[2], G. Kania[2], A. M. Hoffmann-Vold[1]. [1]*Oslo universitetssykehus Rikshospitalet, Rheumatology, Oslo, Norway*; [2]*University Hospital of Zürich, Rheumatology, Zürich, Switzerland*

Background: Systemic sclerosis (SSc) is a complex autoimmune, multi-organ disease with gastro-intestinal tract (GIT) involvement significantly contributing to comorbidity. While understanding of mechanisms behind SSc-related GIT disease is incomplete, recent work shows that altered gut microbiota (dysbiosis) is present in many patients and associates with specific GIT symptoms. Intending to improve dysbiosis, we set up the controlled ReSScue pilot trial, where fecal microbiota transplantation (FMT) was conducted by duodenal infusions of Anaerobic Cultivated Human Intestinal Microbiome (ACHIM) or placebo. The results indicated that FMT by ACHIM induced short-term improvement on patient reported GIT symptoms, as evaluated by the validated UCLA GIT score (1). Duodenal biopsies were taken before and after FMT to assess potential effects of ACHIM on small intestinal mucosa.

Objectives: Assessment of duodenal histology and GIT symptoms before and after FMT by ACHIM compared to placebo.

Methods: In this explorative study, we assessed duodenal biopsies collected prior to first FMT (week 0), prior to second FMT (week 2) and at study end (week 16) from ReSScue trial patients who either received ACHIM (n=5) or placebo (n=4). To examine potential effects of FMT on the duodenal mucosa, we performed immunohistochemistry (IHC) staining on paraffin-embedded tissue samples using the following markers: Sirius red (SIR) for collagen fibers and monoclonal antibodies against gp38 (podoplanin, as marker for lymphatic vessels and fibroblasts), CD38 (as preliminary marker for adaptive immune cells) and CD64 (as preliminary marker for innate immune cells). We determined staining per area in the individual tissue slides for each marker using ImageJ Fiji. The mean total UCLA GIT score for the patients were calculated at week 0, 2 and 16, as well as the mean staining per area of the duodenum biopsies at week 0, 2 and 6 for all the markers. Finally, correlations between mean staining per area and mean total UCLA GIT score were assessed for ACHIM and placebo patient groups by Pearson correlation (r).

Results: All nine patients included in the pilot trial were female and had limited cutaneous SSc. Groups receiving ACHIM and placebo had comparable disease duration (1). We found that relative change in staining per area for SIR from week 0 to week 2 differed between the ACHIM group and the placebo group (Figure 1A, left panel). Similar changes were observed for anti-gp38, anti-CD38 and anti-CD64 (left panel in Figures 1B-D). Strong correlations were found between mean total UCLA GIT score and the mean staining per area of the markers SIR (r=0.98), anti-gp38 (r=0.94), anti-CD34 (r=0.85) and CD64 (r=0.93) in the ACHIM group (Figure 1, A-D). In the placebo group, there was no correlation between the UCLA GIT score and anti-gp38 (r=0.22) and anti-CD64 (r=0.21), however, a strong correlation were observed to SIR (r=0.86) and anti-CD38 (r=0.92) staining (Figure 1A-D, right panel).

Conclusion: This explorative data set indicates different effects of FMT by ACHIM and placebo on the duodenal mucosa of SSc patients with GIT affection. Interestingly, we observed correlations between mucosal markers and improved patient reported GIT symptoms in the ACHIM group.

REFERENCES:

[1] Fretheim H, Chung BK, Didriksen H, Bækkevold ES, Midtvedt Ø, Brunborg C, et al. Fecal microbiota transplantation in systemic sclerosis: A double-blind, placebo-controlled randomized pilot trial. PLoS One. 2020;15(5):e0232739.

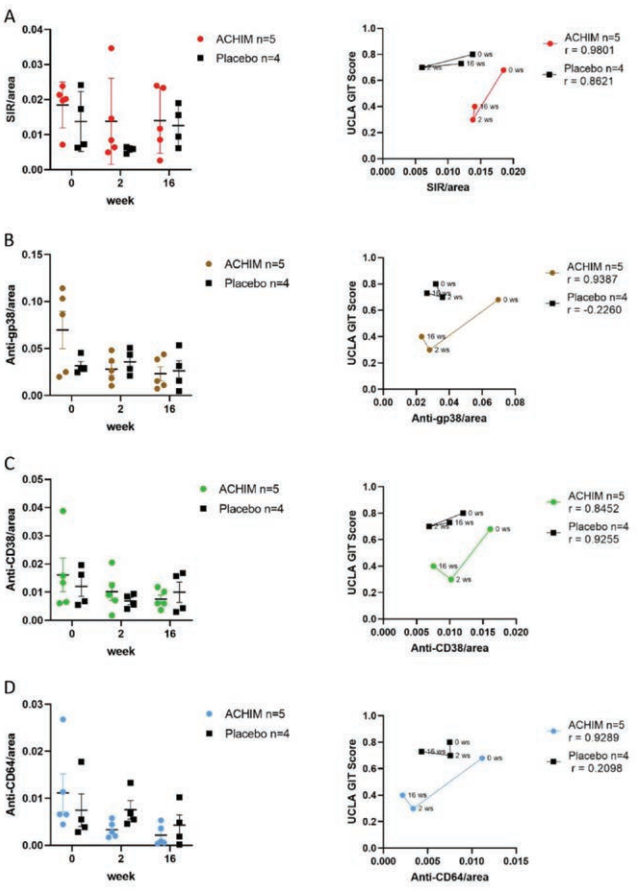


Figure 1. Relative staining per area in ACHIM and placebo group (left panel) and correlation between total UCLA GIT score and staining ratios at time point 0, 2 and 16 weeks in patients receiving ACHIM and placebo (right panel).

Acknowledgements: We will like to thank Maria Comazzi for all the work she have done with the IHC stainings

Disclosure of Interests: Henriette Didriksen Speakers bureau: Travel bursary - GSK

Travel bursary and speaker - Actelion, Noemi Strahm: None declared, Øyvind Molberg: None declared, Håvard Fretheim Speakers bureau: Received travel bursaries from Actelion, and remuneration from Bayer., Torhild Garen: None declared, Øyvind Midtvedt: None declared, Oliver Distler Speakers bureau: Actelion, Kymera Therapeutics, Mitsubishi Tanabe Pharma, Abbvie, Acceleron, Alexion, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Corbus Pharmaceuticals, Drug Development International Ltd, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Kymera Therapeutics, Lilly, Novartis, Pfizer, Topadur and UCB, Grant/research support from: Boehringer Ingelheim, Beyer, Gabriela Kania: None declared, Anna-Maria Hoffmann-Vold Speakers bureau: Actelion, Roche, Bayer, Merck Sharp & Dohme, Lilly, ARXX and Medscape, Grant/research support from: Boehringer Ingelheim

DOI: 10.1136/annrheumdis-2021-eular.2936

POS0868

THE FORMULA TO PREDICT TACROLIMUS CONCENTRATION ACCORDING TO GENOTYPING OF CYP3A5 IS USEFUL FOR EFFECTIVE TREATMENT IN INTERSTITIAL LUNG DISEASE WITH DERMATOMYOSITIS

M. Katayama[1], S. Horibata[2,3], S. Takahashi[1,3], M. Takahashi[3], T. Saito[3], N. Amano[1], K. Yoshida[1], S. Hatachi[1], K. Yorifuji[2,3], S. Kumagai[1,3]. [1]*Shinko Hospital, Center for Rheumatic Disease, Kobe, Japan*; [2]*Shinko Hospital, Department of Pharmacy, Kobe, Japan*; [3]*Shinko Institute for Medical Research, Kobe, Japan*

Background: Tacrolimus (TAC), an immunosuppressant, can be used in second-line maintenance therapy for interstitial lung disease (ILD) in patients with dermatomyositis (DM) [1]. Although some studies reported the clinical efficacy of initial high-trough levels of TAC in combination with GC and IVCY in induction therapy for severe DM-ILD [2], there have been no useful clinical tools for deciding suitable initial dose of TAC. Genotype of polymorphisms in cytochrome P450 (CYP) 3A5 enzyme was reported to play an important role in pharmacokinetics of TAC [3], and we made a formula for deciding initial dose of TAC according to CYP3A5 genotypes in our previous study.
Objectives: In our previous study (retrospective study), we set the target trough according to the severity for nine DM-ILD patients, six of whom were CYP3A5 *3/*3 and investigated the dose of TAC that could attain the trough using their CYP3A5 genootyping. Using these results, we developed a formula for deciding initial daily dose of TAC (target trough*weight / [(151.1, if CYP3A5 *3/*3) or (86.5, if CYP3A5 *1 allele)]). In this study, we prospectively examined the usefulness and accuracy of this formula.
Methods: We introduced TAC for new six DM-ILD patients who visited our hospital between November 2019 and May 2020 (prospective study). The starting dose of TAC was decided by using the formula. We assessed the association between predicted and observed trough concentration of TAC at first measurement date (from day 2 to day4), using linear regression analysis. We also assessed the days for attaining the target trough concentration between the patients using the formula (prospective group) and six patients with CYP3A5 *3/*3 (retrospective group).
Results: CYP3A5 genotype of all six DM-ILD patients were *3/*3 and underwent the TAC treatment by using the formula. The predicted and observed trough concentration of first measurement date were significantly correlated in the patients (r 2= 0.897, p=0.0041) (Fig.1). Compared with our retrospective study, target trough was more quickly attained in patients of the prospective study (Fig.2).
Conclusion: The formula which we made for attainment target trough concentration based on CYP3A5 genotype was useful for deciding the starting dose of TAC. We also showed that we could attain the target trough concentration at early stage of initial treatment by using the formula.
REFERENCES:
[1] Oddis CV and Aggarwal R. Nat Rev Rheumatol 2018;14(5):279-89.
[2] Suzuka T et al. Int J Rheum dis 2019;22: 303-13.
[3] Y. Muraki et al. Exp Ther Med 2018;15:532-38.

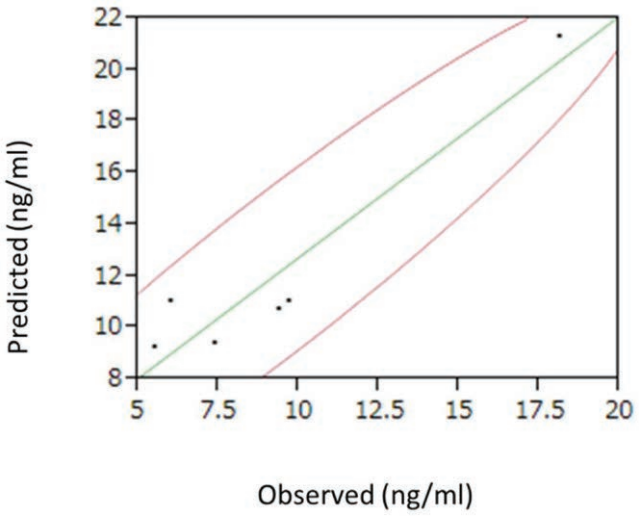


Figure 1. Correlation of predicted and observed tacrolimus trough concentration at first measurement in the prospective study

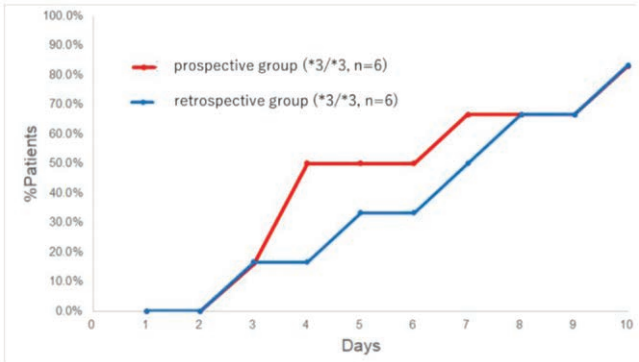


Figure 2. Days to attain the target trough concentration of tacrolimus in the prospective group and the retrospective group

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3018

POS0869 PREDICTIVE VALUE OF ANTI-INTERFERON-INDUCIBLE PROTEIN 16 ANTIBODIES FOR DIGITAL ULCERS OF SYSTEMIC SCLEROSIS

C. Chen[1], S. Yang[1], Z. Jiang[1], W. Wan[1], H. Zou[1], M. Liang[1]. [1]*Huashan Hospital Affiliated to Fudan University, Department of Rheumatology, Shanghai, China*

Background: Interferon-inducible protein 16 (IFI-16) is constitutively expressed in vascular endothelial cells and can inhibit the proliferation of human endothelial cells and the formation of capillary-like structures *in vitro*. Anti-IFI-16 antibodies were reported in 21%-29% of patients with systemic sclerosis (SSc) and were associated with digital vascular events in a few retrospective studies.
Objectives: To evaluate the presence and the clinical implication of anti-IFI-16 antibodies in Chinese SSc cohort, focusing on the associations with vasculopathy indexes, and to investigate the predictive value of anti-IFI-16 antibodies for the development of digital ulcers (DUs) in SSc prospectively.
Methods: Patients with SSc presenting to our center between July 2018 and September 2018 were prospectively enrolled. Serum from 42 SSc patients and 42 age- and sex-matched healthy controls were analyzed for anti-IFI-16 antibodies by enzyme-linked immunosorbent assay (ELISA), and was considered positive if the optical density (OD) value was above the mean OD of controls plus two standard deviations. Tissue immunofluorescence was used to evaluate the expression of IFI16 in skin biopsy samples obtained from SSc patients and normal controls. At baseline, nailfold video-capillaroscopy was performed to assess nailfold capillary density of SSc patients. Power Doppler ultrasound was used to grade finger pulp blood flow (0-no observed flow; 1-decreased flow; 2-normal flow), and to measure ulnar and radial artery blood flow and resistive index (RI). All patients were followed up for 6 months to see whether they experienced new onset or recurrent DUs. The association of anti-IFI-16 antibodies with DUs was analyzed using logistic regression.
Results: Of the 42 SSc patients, 8 (19.0%) were positive for anti-IFI-16 antibodies. Immunofluorescence of skin biopsy samples from SSc patients exhibited enhanced staining of IFI-16 in the dermis, and colocalization with endothelial marker CD31. SSc patients who were positive for anti-IFI-16 antibodies showed higher ulnar artery RI at baseline (0.95±0.09 vs. 0.86±0.09, p=0.015), while no significant differences were found for other vascular parameters, nor for clinical or demographic profiles. Within 6-month follow-up, 14 (33.3%) patients experienced new-onset or recurrent DUs. Univariate logistic regression revealed the presence of DUs at enrollment (p=0.009), anti-IFI-16 antibody (p=0.012), finger pulp blood flow (p=0.027), and ulnar artery RI (p=0.008) could be the predictors for the development of DUs. Multivariate analysis further identified DUs at enrollment (odds ratio [OR]: 10.85; 95% confidence interval [CI]: 1.61-73.18; p=0.014) and anti-IFI-16 antibody (OR: 15.00; 95% CI: 1.13-199.18; p=0.040) as independent risk factors. Among patients without DUs at enrollment, new-onset ulcers occurred in 80% (4/5) and 4.5% (1/22) of those with and without anti-IFI-16 antibody, respectively (p=0.001).
Conclusion: Anti-IFI-16 antibody is associated with vasculopathy in SSc and could be used as a novel biomarker for indicating the development of DUs.
REFERENCES:
[1] McMahan ZH, Shah AA, Vaidya D, et al. Anti-interferon-inducible protein 16 antibodies associate with digital gangrene in patients with Scleroderma. Arthritis Rheumatol. 2016; 68(5): 1262-71.
[2] McMahan ZH, Cottrell TR, Wigley FM, et al. Autoantigens targeted in scleroderma patients with vascular disease are enriched in endothelial lineage cells. Arthritis Rheumatol. 2016; 68(10): 2540–49.

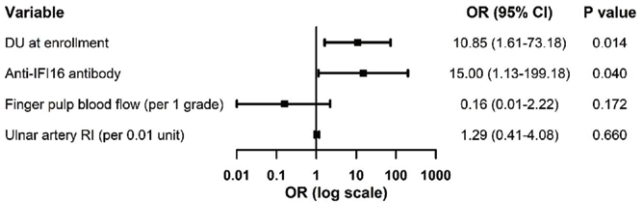


Figure 1. Multivariate logistic analysis for new or recurrent digital ulcers.
Acknowledgements: The authors would like to thank Doctor Yi Cheng for performing Power Doppler ultrasound assessment.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3058

POS0870 CLINICAL CHARACTERIZATION OF PORTUGUESE PATIENTS WITH ANTISYNTHETASE SYNDROME

P. Martins[1,2], E. Dourado[1,2], A. T. Melo[1,2], B. Samões[3], M. Sousa[4], R. Freitas[5], M. H. Fernandes Lourenco[6], B. M. Fernandes[7], E. Costa[8], H. Parente[9], F. R. Martins[10], J. E. Fonseca[1,2], V. C. Romão[1,2], N. Khmelinskii[1,2],

R. Campanilho-Marques[1,2], I. Cordeiro[1,2]. *[1]Hospital de Santa Maria, Centro Hospitalar Universitário de Lisboa Norte, Centro Académico de Medicina de Lisboa, Lisbon, Portugal, Serviço de Reumatologia e Doenças Ósseas Metabólicas, Lisbon, Portugal*; *[2]Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Lisboa, Portugal, Lisbon, Portugal, Unidade de Investigação em Reumatologia, Lisbon, Portugal*; *[3]Centro Hospitalar Vila Nova de Gaia/Espinho, Serviço de Reumatologia, Vila Nova de Gaia, Portugal*; *[4]Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, Serviço de Reumatologia, Coimbra, Portugal*; *[5]Hospital Garcia de Orta, Almada, Portugal, Serviço de Reumatologia, Almada, Portugal*; *[6]Centro Hospitalar Lisboa Ocidental, Hospital Egas Moniz, Lisboa, Portugal, Serviço de Reumatologia, Lisbon, Portugal*; *[7]Centro Hospitalar e Universitário São João, Porto, Portugal, Serviço de Reumatologia, Porto, Portugal*; *[8]Serviço de Reumatologia, Hospital de Braga, Braga, Portugal*; *[9]Serviço de Reumatologia, Unidade Local de Saúde Do Alto Minho, Ponte de Lima, Portugal, Ponte de Lima, Portugal*; *[10]Centro Hospitalar Universitário do Algarve, Faro, Portugal, Serviço de Reumatologia, Faro, Portugal*

Background: Antisynthetase syndrome (ASyS) may have different clinical phenotypes and outcomes associated with different anti-aminoacyl RNA-synthetase (anti-ARS) antibodies. Its wide clinical spectrum can include inflammatory myopathy, interstitial lung disease (ILD), arthritis, fever, mechanic's hands, and Raynaud phenomenon (RP).
Objectives: To describe a nationwide, multicentre cohort of Portuguese patients with ASyS.
Methods: Retrospective analysis of patients with ASyS from nine Portuguese Rheumatology centers. Data on patients' signs and symptoms, laboratory results, pulmonary radiological findings (computed tomography) and treatment (immunomodulators) were collected.
Results: Among the 70 patients included, 42 patients (60%) were anti-Jo1–positive, 11 (15.7%) were anti-PL12–positive, 10 (14.3%) were anti-PL7–positive, 4 (5.7%) were anti-EJ–positive and 2 (2.9%) were anti-OJ positive. In one patient it was not possible to identify the type of antibody. Antibody overlap was found in 15 patients (21.4%), who were positive for anti-Ro52 antibodies. The general clinical characteristics are shown in Table 1. The diagnostic delay was greater in patients positive for anti-OJ, followed by anti-Jo-1 and anti-PL12. The follow-up was shorter for anti-PL7 and anti-OJ-positive patients. Anti-PL7-positive patients had lower rates of arthritis when compared to anti-Jo1 ($p< 0.01$). When compared with anti-Jo-1 ARS, myositis was less common in anti-PL12 ($p < 0.01$). ILD prevalence was similar in the different ARS subgroups. Glucocorticoids (GCs) were the most frequently used class of drugs. A more conservative treatment plan (e.g. GCs plus methotrexate or azathioprine) was the treatment of choice in ASyS with myositis and/or arthritis involvement. Rituximab or mycophenolate mofetil were preferred when lung involvement occurred. Only two deaths were reported, being one associated with lung neoplasia.
Conclusion: This is the first study investigating the clinical phenotypes of Portuguese patients with ASyS. These results are generally concordant with data retrieved from international cohorts.

REFERENCES:

[1] Mahler M, Miller FW, Fritzler MJ. Idiopathic inflammatory myopathies and the anti-synthetase syndrome: a comprehensive review. Autoimmun Rev 2014;13:367–71.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3068

POS0871

CHARACTERISTICS OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS DURING LONG TERM FOLLOW-UP, SINGLE CENTER EXPERIENCE

S. Keret[1], Y. Braun-Moscovici[2], M. Yigla[3], V. Shataylo[4], L. Guralnik[5], A. Balbir-Gurman[2]. *[1]Rambam Health Care Campus, Internal Medicine C, Haifa, Israel*; *[2]Rambam Health Care Campus, Rheumatology Institute, Rappaport Faculty of Medicine, Technion, Haifa, Israel*; *[3]Rambam Health Care Campus, Pulmonary Institute, Haifa, Israel*; *[4]Rambam Health Care Campus, Rheumatology Institute, Haifa, Israel*; *[5]Rambam Health Care Campus, Imaging Department, Rappaport Faculty of Medicine, Technion, Haifa, Israel*

Background: ILD is one the leading causes of morbidity and mortality in patients with SSc. Diagnosis of SScILD is based on signs of fibrosis on chest x-rays or HRCT. Particular measurement of lung volumes by FVC and in gas exchange by DLCO supports the diagnosis. Associations between clinically significant SSc ILD and male gender, age, DcSSc, topoisomerase antibodies, low FVC at baseline, widespread lung involvement on baseline HRCT, and higher decline rate of FVC and DLCO during followup were reported. A standardized approach to assessing and treating SSc and SScILD in particular have been proposed. Main treatment regimens include cyclophosphamide and mycophenolate mofetil; recently antifibrotic drug nintedanib showed significant efficacy in hindering FVC decline rate in patients with SSc ILD. The data on survival changes in SSc generally and SScILD are conflicting.
Objectives: To analyze demographic and clinical features and mortality of patients with SSc ILD.
Methods: A retrospective study on Rambam Health Care Campus prospective cohort of SSc patients fulfilled ACR and EULAR Classification Criteria 2013 for the period between January 2000 and September 2020 was performed. Patients were recruited at one of their early visits to the clinic. The majority of recruited patients were included into EUSTAR prospective cohort 042, since 2004 the Rheumatology Institute at Rambam is affiliated to EUSTAR registry project. Data on patients not registered in EUSTAR database but treated at our institution was extracted via hospital electronic records. Patients with lung involvement underwent baseline and annual HRCT and pumonary function tests in addition to clinical assessment during their visit to combined rheumatology-pulmonology clinic. We registered age, gender, ethnicity, date of SSc diagnosis and ILD diagnosis, disease duration, SSc subset, pulmonary, cardiac, renal, and muscle involvement, treatment used, autoantibodies, FVC, DLCO, HRCT and pulmonary artery pressure. Statistical analysis included t-test, Pearson's Chi-squared test, Fisher's test, and Cox Regression analysis with p value less than 0.05 as significant.
Results: Among 446 SSc patients (female 82.3%, mean age 46.5 and disease duration 11.6 years, DcSSc 39.2%; 27.4% dead during follow-up) 141 patients had ILD. Comparison between patient with ILD and witout ILD showed significant differences in term of nationality (Arabs 34% vs 18.7%), SSc related death 78.3% vs 50.7%), DcSSc (68.8% vs 25.6%), topoisomerase antibodies

Table 1. Patient characteristics according to the anti-ARS. ILD - interstitial lung disease; IQR- interquartile range; NSIP - Non-specific interstitial pneumonia; UIP - Usual interstitial pneumonia; yrs - years

Variables	Overall, n=70	Jo-1, n=42 (60%)	PL-12, n=11 (15.7%)	PL-7, n=10 (14.3%)	EJ, n=4 (5.7%)	OJ, n=2 (2.9%)
Mean age at onset, yrs	52 ± 15	46.6 ± 14.4	55.2 ± 14.7	56.5±12.5	56.3±11.2	73.5±2.1
Female, n (%)	49 (70)	29 (69)	9 (81.8)	7 (70)	2 (50)	2 (100)
Median age in years at disease onset (IQR)	52 (15-75)	48 (15-70)	59 (20-70)	62 (39-73)	60 (40-65)	73.5 (72-75)
Median follow-up time in yrs (IQR)	3 (0-32)	5 (0-32)	3 (0-13)	1 (1-4)	4 (2-21)	1 (0-2)
Median diagnostic delay in yrs (IQR)	6 (1-33)	7 (1-33)	7 (2-19)	4 (1-23)	1.5 (1-2)	12.5 (2-21)
Myositis, n (%) and Comparison Anti-Jo.1 ARS vs PL-12 and PL-7	36 (51.4)	25 (59.5)	3 (27.3)	4 (40)	3 (75)	0
			***p < 0.01**	p=0.7	-	-
ILD, n (%) and Comparison Anti-Jo.1 ARS vs PL-12 and PL-7	53 (75.7)	33 (78.6)	8 (72.7)	6 (60) p=0.56	4 (100)	1 (50)
			p = 0.98		-	-
ILD pattern - NSIP, n (%)	30 (56.6)	18 (54.5)	6 (75)	3 (50)	1 (25)	0
ILD pattern - UIP, n (%)	6 (11.3)	3 (9.1)	1 (12.5)	1 (16.7)	1 (25)	0
ILD pattern - other specific pattern, n (%)	6 (11.3)	4 (12.1)	0	2 (33.3)	1 (25)	0
ILD pattern - non-specific pattern, n (%)	11 (15.7)	8 (24.2)	1 (12.5)	0	1 (25)	1 (100)
Mechanic's hands (%), n (%)	23 (32.9)	14 (33.3)	3 (27.3)	2 (20)	0	1 (50)
General impairment, n (%)	18 (25.7)	11 (26.2)	3 (27.3)	2 (20)	2 (50)	0
Fever, n (%)	7 (10)	4 (9.5)	2 (20.2)	0	1 (25)	0
Raynaud phenomenon, n (%)	22 (31.4)	11 (26.2)	7 (63.6)	0	2 (50)	0
Arthritis, n (%) and Comparison Anti-Jo.1 ARS vs PL-12 and PL-7	43 (61.4)	29 (69)	5 (45.4)	2 (20)	2 (50)-	1 (50)-
			p=0.07	***p < 0.01**		
Malignancy, n (%)	4 (5.7)	3 (7.1)	1 (9.1)	0	0	0
Deaths, n (%)	2 (2.9)	2 (2.4)	0	0	0	1 (50)

(61.7% vs 24.9%), myopathy (21.3% vs 10.2%) and pulmonary hypertension (34.8% vs 22.3%). Significantly more SSc ILD patients were treated with cyclophosphamide, mycophenolate mofetil and azathioprine. Survival Kaplan-Meier curve patiets demonstrate reduced survival in patients with ILD ($p<0.01$). Five years survival rates between years 2000 and 2015 have not changed significant. Mortality risk assessed with Cox regression analysis in the whole group was significantly higher in males, Arabs, DcSSc, elder age, heart and muscle involvement, and treatment with CYC. In the ILD group, the mortality was significantly higher in Arabs (3.3 times), elder age (8.9 times), presence of PAH (3.1 times) and treatment with CYC (2.8 times) compared to patients without ILD.

Conclusion: In our SSc cohort, ILD affected about third of patients and had major impact on patients' outcome. Male gender, Arab nationality, elder age, DcSSc, topoisomerase antibodies, heart and muscle involvement were significantly associated with worst prognosis. Despite active approach to assessing and treatment, survival rates of patients with SSc and SSc-ILD have not improved in last decades. Enrichment of the cohort with severe patients to a tertiary center due to reference bias and low efficacy of existed immunomodulatory drugs in SSc and in SSc related ILD particularly, could explain our results.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3105

POS0872 CLINICAL FEATURES AND OUTCOME OF 1054 PATIENTS WITH SYSTEMIC SCLEROSIS: AN ANALYSIS OF THE PORTUGUESE REUMA.PT REGISTRY FOR SCLERODERMA (REUMA.PT/SSC)

R. Freitas[1], P. Martins[2], E. Dourado[2], M. J. Salvador[3,4], T. Santiago[3,4], I. Cordeiro[2], B. M. Fernandes[5], F. Guimarães[6], S. Garcia[5], B. Samões[7], N. Gonçalves[8], M. H. Fernandes Lourenco[8], A. S. Pinto[9], M. Rocha[10], M. Couto[11], E. Costa[12], F. Araújo[13], C. Resende[2], F. Godinho[1], A. Cordeiro[1], M. J. Santos[1,14]. *[1]Hospital Garcia de Orta, Rheumatology Department, Almada, Portugal*; *[2]Centro Hospitalar Lisboa Norte, Rheumatology Department, Lisboa, Portugal*; *[3]Centro Hospitalar e Universitário de Coimbra, Rheumatology Department, Coimbra, Portugal*; *[4]University of Coimbra, Rheumatology Department, Coimbra, Portugal*; *[5]São João Universitary Hospital Center, Rheumatology Department, Porto, Portugal*; *[6]Centro Hospitalar do Alto Minho, Rheumatology Department, Ponte de Lima, Portugal*; *[7]Centro Hospitalar Vila Nova de Gaia, Rheumatology Department, Vila Nova de Gaia, Portugal*; *[8]Centro Hospitalar Lisboa Ocidental, Rheumatology Department, Lisboa, Portugal*; *[9]Unidade de Saúde Local da Guarda, Rheumatology Department, Guarda, Portugal*; *[10]Centro Hospitalar Universitário do Algarve, Rheumatology Department, Faro, Portugal*; *[11]Centro Hospitalar Tondela - Viseu, Rheumatology Department, Viseu, Portugal*; *[12]Hospital de Braga, Rheumatology Department, Braga, Portugal*; *[13]Hospital de Sant'Ana, Rheumatology Department, Parede, Portugal*; *[14]Lisbon University, Medical School, Lisboa, Portugal*

Background: Systemic sclerosis (SSc) may present distinctive manifestations and survival in different ethnic and geographic groups.

Objectives: To describe the clinical features, treatments, and survival of adult SSc patients registered in Reuma.pt/SSc.

Methods: Demographic features, SSc subsets, fulfilment of classification criteria, clinical and immunologic characteristics, comorbidities, medication and deaths were reviewed. Survival was calculated for patients included in the registry within the first 2 years of diagnosis.

Results: In total, 1054 patients were included, 87.5% female, mean age at diagnosis 52.7 ± 14.8 years. The most common subset was limited cutaneous (lc)SSc (56.3%), followed by diffuse cutaneous (dc)SSc (17.5%), preclinical SSc (13%), overlap syndrome (9.8%) and SSc sine scleroderma (3.3%). Raynaud's phenomenon (93.4%) and skin thickening (76.9%) were the most observed manifestations. Gastrointestinal (62.8% *vs* 47.8%), pulmonary (59.5% *vs* 23%) and cardiac (12.8% *vs* 6.9%) involvement were significantly more prevalent in dcSSc compared to lcSSc (Table 1). 52.5% of patients were ACA positive and 21% anti-topoisomerase positive, with significant differences between lcSSc and dcSSc. One third of patients was treated with immunomodulators, 53.6% with vasodilators, 23% received glucocorticoids and 2.3% biologics.

During the median follow-up 12.4 years, 83 deaths (7.9%) were verified. The overall 1, 2 and 5 years survival was 98.0%, 96.8% and 92.6% respectively, without significant differences between lcSSc and dcSSc (Figure 1).

Conclusion: Reuma.pt/SSc register is useful in routine patient monitoring and contributes to improve knowledge about this rare and complex disease. Clinical features of Portuguese SSc patients are similar to what has been described in other populations although the overall 5-year survival in recently diagnosed patients appears to be higher than previously reported.

Table 1. Cumulative clinical and immunologic characteristics of Portuguese SSc patients

Clinical and immunologic features	Total N=1054	Limited cutaneous SSc N= 576 (56.3%)	Diffuse cutaneous SSc N=180 (17.5%)	*P value*
Skin involvement – N(%) N=987	688 (90.6)	525 (90.7)	180 (100)	<0.01
Skin thickening * – N (%) N= 962	680 (76.9)	512 (88.9)	180 (100)	<0.01
Digital ulcers – N (%) N=970	325(33.5)	186 (34.7)	4 (51.5)	<0.01
Raynaud's Phenomenon – N (%) N=1010	943 (93.4)	539 (95.7)	157 (92.4)	0.06
Musculoskeletal involvement – N(%) N=972	346 (45.6)	247 (42.7)	99 (55)	<0.01
Cardiac involvement –N(%) – N=924	71 (7.7)	36 (6.9)	19 (12.8)	0.02
Renal involvement –N(%) – N= 917	17 (1.9)	8!1.5)	6 (4.1)	0.07
Gastrointestinal involvement - N(%) N=933	508 (48.2)	277 (47.8)	113 (62.8)	<0.01
Pulmonary involvement – N(%) N=915	261 (28.5)	119 (23)	88 (59.5)	<0.01
PAH – N(%) N= 871	14 (1.6)	10 (2)	1 (0.7)	0.23
Interstitial lung disease – N(%) N=765	218 (28.5)	100 (22.7)	75 (57.7)	<0.01
Antinuclear antibodies - N(%) N=1040	934 (89.8)	522 (90.2)	154 (88.5)	0.57
Anti-centromere – N(%) N= 1027	540 (52.6)	383 (67.1)	16 (9.5)	<0.01
Anti-Scl70 – N(%) N=1020	214 (21)	12 (3.3)	104 (60.1)	<0.01
Anti-RNA polymerase III – N(%) N=710	25 (3.5)	12 (3.3)	7 (5.6)	0.38
Comorbidities				
Hypertension – N(%) N=431	117 (27.1)	76 (29.7)	67 (20.7)	0.1
Hyperlipidemia – N(%) N=431	71 (13.4)	72 (12.2)	24 (15.9)	0.08
Neoplasia – N(%) N=1054	29 (2.8)	12 (2.1)	7 (3.9)	0.14

PDE-5 (phosdiasterase-5); PPIs (proton pump inhibitors); PAH-Pulmonary arterial hypertension confirmed by right heart catheterization. Immunomodulators includes Metothrexate, Leflunomide, Hydroxycloroquine; Azathioprine, Mycophenolate Mofetil and Cyclophosphamide; * Does not include sclerodactyly.

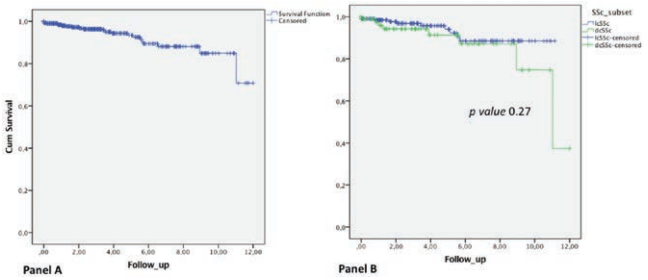


Figure 1. Panel A - Survival in years from diagnosis of patients with SSc included in Reuma.pt in the first 2 years of disease (N=472). Panel B - survival according to SSc subset (lcSSc and dcSSC).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3159

POS0873 IMPROVEMENT IN MODIFIED RODNAN SKIN SCORE (MRSS) IN SYSTEMIC SCLEROSIS PATIENTS TREATED WITH RITUXIMAB: A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE SCIENTIFIC LITERATURE

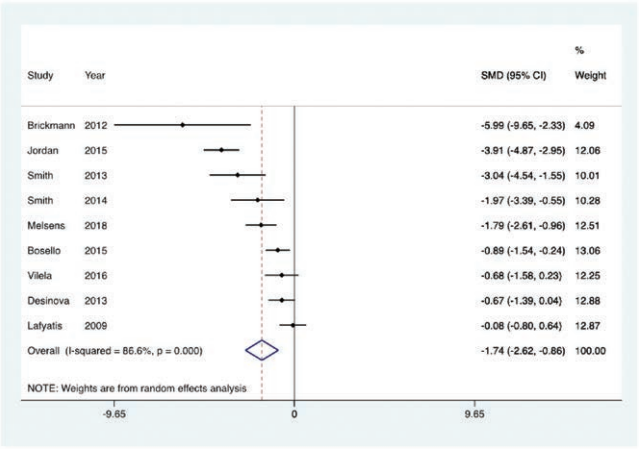
J. L. Puga Guzmán[1], D. Fernández Fernández[2,3], R. Dos-Santos[2,3], I. González Fernández[2,3], E. Perez-Pampín[3,4], A. Souto Vilas[3,4], A. Mera Varela[3,4]. *[1]Facultade de Medicina e Odontoloxía - USC, Medicine, Santiago de Compostela, Spain*; *[2]Hospital Clínico Universitario de Santiago, Rheumatology, Santiago de Compostela, Spain*; *[3]University of Santiago de Compostela, Medicine, Santiago de Compostela, Spain*; *[2]Hospital Clínico Universitario de Santiago, Rheumatology, Santiago de Compostela, Spain*

Background: Systemic sclerosis (SSc) is a chronic autoimmune disease of the connective tissue characterized by vascular disease and fibrosis in different organs and systems such as lung and skin (1). Recently, several case reports and small series of patients reported on the efficacy of rituximab in SSc, showing a possible improvement in skin and lung affectations (2). However, registered clinical trials are lacking to determine factors associated with response, maintenance regimen, and long-term efficacy of rituximab in SSc.

Objectives: To analyze the efficacy of Rituximab in the treatment of skin fibrosis using the changes of the modified Rodnan Skin Score (mRSS) of patients diagnosed with systemic sclerosis from the data published in Registered Clinical Trials (RCTs) in the scientific literature.

Methods: We perform a systematic review and a meta-analysis using the main electronic databases to locate all the articles available so far: Medline, Embase, Cochrane Library and Web of science and ACR and EULAR abstracts congress were extracted to assess efficacy outcomes. That efficacy was measured based on the variation of mRSS at 12, 24 and 48 weeks for patients treated with Rituximab versus patients treated with another drug or placebo.

Results: 3 RCTs contained data regarding mRSS at week 12 of treatment with Rituximab. The estimated SMD was -1.071 (95% CI -1.608, -0.535 [p <0.001]) with a non-significant P value in the Egger Test (P = 0.703) and non-significant heterogeneity through I2 (I2 = 0.00%).
9 studies contained data regarding mRSS at week 24 of treatment with Rituximab. The estimated SMD was -1.743 (CI95% -2.622, -0.864 [p <0.001], *see image below*) with a non-significant P value in the Egger Test (P = 0.072) and significant heterogeneity through I2 (I2 = 86.6%). Meta-regression analysis could not be performed to assess such heterogeneity, due to the lack of comparable data.



8 RCTs contained data regarding mRSS at week 48 of Rituximab treatment. The estimated SMD was -1.327 (CI95% -2.018, -0.636 [p <0.001]) with a significant P value in the Egger Test (P = 0.018), estimating that there may be publication bias in the studies analyzed and significant heterogeneity by I2 (I2 = 85.2%). Meta-regression analysis could not be performed to assess such heterogeneity, due to the lack of comparable data.
Conclusion: Our meta-analysis shows that Rituximab treatment in patients affected with systemic sclerosis shows efficacy in the treatment of cutaneous fibrosis measured by the mRSS, turning this molecule into a potential drug to add to the therapeutic armamentarium of systemic sclerosis. However, more studies are necessary to try to elucidate whether this change is powerful enough to become the new gold standard for the treatment of systemic sclerosis skin involvement.
REFERENCES:
[1] Stern EP, Denton CP. The pathogenesis of systemic sclerosis. Rheum Dis Clin North Am 2015;41:367–82. https://doi.org/10.1016/j.rdc.2015.04.002.
[2] Thiebaut M, Launay D, Rivière S, et al. Efficacy and safety of rituximab in systemic sclerosis: French retrospective study and literature review. Autoimmun Rev. 2018;17(6):582-587. https://doi:10.1016/j.autrev.2017.12.010.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3161

POS0874 CLOT LYSIS TIME PREDICTS RECURRENT DIGITAL ULCERS IN SYSTEMIC SCLEROSIS AFTER ONE YEAR OF FOLLOW-UP: A NESTED CASE-CONTROL STUDY

J. Colic[1], A. Antovic[2], I. Pruner[3], J. Vojinovic[4], N. Damjanov[5], M. Sefik Bukilica[5,6]. [1]*Institute of Rheumatology, Department of Rheumatology IVb Unit, Belgrade, Serbia*; [2]*Karolinska Institutet,Karolinska University Hospital Solna, Department of Medicine, Rheumatology Unit, Stockholm, Sweden*; [3]*Karolinska Institute, Department of Molecular Medicine and Surgery, Stockholm, Sweden*; [4]*Medical Faculty, University of Nis, Department of Pediatrics, Nis, Serbia*; [5]*School of Medicine, University of Belgrade, Internal Medicine, Belgrade, Serbia*; [6]*Institute of Rheumatology, Department of Rheumatology Unit, Belgrade, Serbia*

Background: Digital ulcers (DU) are a common visible manifestation of vasculopathy in systemic sclerosis (SSc), which could be recurrent and associated with disability and mortality (1). Although vasculopathy is connected with impaired coagulation/fibrinolysis system and aberrant expression of adhesion molecules, there are few data about their role in developing recurrent DU.
Objectives: To evaluate the possible role of Fibrin generation/Fibrinolysis parameters and adhesion molecules in the prediction of new ischaemic DU oncet during a 1-year follow-up and their impact on the time to new DU onset (TD).
Methods: From 58 consecutive patients with SSc who fulfilled the 2013 ACR/EULAR SSc criteria and have never been treated with endothelin receptor antagonist, phosphodiesterase 5 inhibitors or prostanoids, a total of 38 patients with ever had DU, either active at inclusion or in past, were enrolled in a prospective cohort study. Each patient was given a "DU diary". Demografic, clinical and serologycal data were recorded. The serum concentration of ICAM1 and E selectin were measured by ELISA. Haemostatic potential parameters: overall haemostasis (OHP), overall coagulation (OCP) and overall fibrinolysis (OFP) potential were assessed. Maximum absorbance (Cmax), reflects the fibrin clot density and clot lysis time (Lys50t0, time from initiation of clot formation to the time at which a 50% fall in absorbance from Cmax in the lysis assay), reflects fibrinolytic susceptibility, were calculated (2). Fibrin structure was visualised using scanning electron microscopy (SEM).
Results: Over the follow-up period,18 patients (45.5%) developed new DU with the average TD of 7.4±2.9 months. There was no differance in ASA and CCB treatment among two groups (p>0.05). The OFP value was significantly decreased (p<0.01), Lys50t0 prolonged (p<0.05), while OHP was increased (p<0.05) in patients experienced new DU. Lys50t0 showed good validity in identifying patients with new DU oncet (AUC 0.683 95% CI 0.5 - 0.9). By multivariate analysis including clinical data in model the Lys50t0 (HR 1.2, 95% CI 1.1-1.3, p=0.018) and active DU at enrollment (HR 9.6, 95% CI 1.4-66.8, p=0.022) were identified as independent risk factors for the occurrence of new DU. TD was inversly correlated with ICAM1(p<0.001), E selectin (p<0.05), Cmax (p <0.05) and Lys50t0 (p<0.001). Model explaining 81.6% of the TD variability included Lys50t0 (β=- 0.55,p=0.003), E selectin (β=- 0.44,p=0.014) and fibrinogen (β=- 0.49,p=0.017). SEM revealed denser fibrin clots with thinner fibres in group experienced new DU compared to clots formed in plasma of patient without DU.
Conclusion: Our results provide evidence that impaired fibrinolysis has critical role in the progression of microvascular disease, identifing clot lysis time as a strong predictor in the oncet of new digital ulcers in Systemic sclerosis. The higher level of E selectin and the longer lysis time are, the shorter is time until the onset of new digital ulcer. These results could be used in selection of patients at high risk of developing recurrent digital ulcer and therefore allow earlier therapeutic intervention.
REFERENCES:
[1] Allanore Y, Distler O, Matucci-Cerinic M, Denton CP. Review: Defining a Unified Vascular Phenotype in Systemic Sclerosis. Arthritis Rheumatol. 2018 Feb;70(2):162-170
[2] Carter AM, et al. Heritability of clot formation, morphology, and lysis: the EuroCLOT study. Arterioscler Thromb Vasc Biol. 2007 Dec;27(12):2783-9.

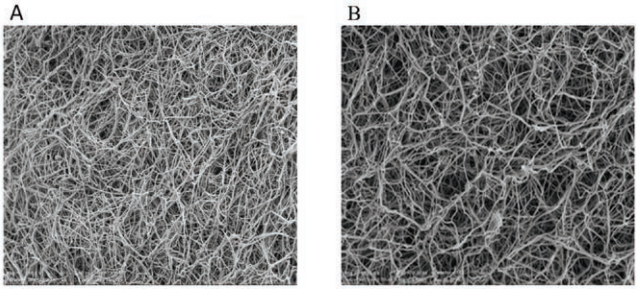


Figure 1. SEM images of fibrin network in 1 representative sample from a SSc patient with (A) and 1from patient without (B) new DU oncet
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3163

POS0875 MYOSITIS-SPECIFIC ANTIBODIES IN A RETROSPECTIVE SINGLE-CENTER OBSERVATIONAL STUDY

J. Álvarez Troncoso[1], S. Carrasco Molina[1], J. Valdivieso[2], P. Nozal[2], Á. Robles Marhuenda[1], E. Martínez Robles[1], C. Soto Abánades[1], J. J. Rios[1], A. Noblejas Mozo[1], F. Arnalich Fernández[1]. [1]*Hospital Universitario La Paz, Internal Medicine, Madrid, Spain*; [2]*Hospital Universitario La Paz, Clinical Immunology, Madrid, Spain*

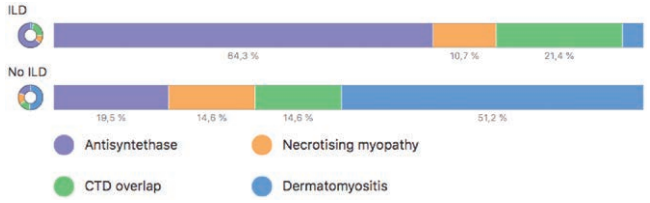
Background: Myositis-specific antibodies (MSA) are highly specific and useful to classify patients as having syndromes with distinct clinical features and prognosis. MSA are almost always mutually exclusive and quite specific, adding value as a useful biomarker for diagnosis. Although individual autoantibodies aren't sensitive enough to detect the full spectrum of idiopathic inflammatory myopathies (IIM), the sensitivity of a myositis panel is increasing as more autoantibodies are discovered, and as better assays become available.
Objectives: We aimed to analyze the usefulness of a myositis-specific immunoblot for the diagnosis of IIM in a hospital cohort from January 2019 to December 2020. We also seek to correlate immunological findings with the risk of associated interstitial lung disease (ILD), cancer, or death.

Methods: Retrospective single-center observational study conducted in a Spanish tertiary hospital. In patients with high clinical suspicion of IIM, a myositis immunoblot was performed including Jo1, PL-7, PL-12, EJ, SRP, Mi2, Ku, MDA-5, TIF1-γ, HMGCR, PM-Scl and Ro52 antibodies. The demographic characteristics, the risk of ILD, cancer and death were analyzed.

Results: In a cohort of 313 patients with high suspicion of IIM, 87 patients (27.8%) presented a positive MSA (MSA+ve). The mean age at diagnosis was 56.7±16.9 years, with no significant differences between MSA+ve and MSA-ve (p=0.597). Most of the patients were women with significant differences between both groups (80.5% MSA+ve vs 68.1% MSA-ve, p=0.030).

IIM were classified as antisynthetase syndrome (ARS) (38%), dermatomyositis (DM) (31%), overlap myopathy (OM) (16.9%) and necrotizing myopathy (NM) (14.1%) according to the manifestations and MSA found (Jo1, PL-12, PL-7, EJ in ARS; Mi-2, MDA-5 and TIF1-γ in DM; Ku and PM-Scl in OM; HMGCR and SRP in NM). The most frequent MSA were anti-Jo1 (16.9%), TIF1-γ (15.5%), Ku (12.7%), Mi-2 (9.9%), PL-7 (9.9%), HMCGR (8.5%), PL-12 (7%), MDA-5 (5.6%), SRP (5.6%) and EJ (4.2%). The presence of Ro52 associated with other MSA was found in 20 patients (22.9%).

ILD was the most frequent manifestation (45.2% of the MSA+ve). Non-specific interstitial pneumonia (NSIP) was the most frequent ILD (39.5%), followed by usual interstitial pneumonia (34.2%). The main risk factors associated with IIM-ILD were some subtypes of the MSAs (p<0.001), the association of Ro52 (p<0.001), and older age (p=0.027). Among the IIM, ARS and OM (p<0.001) were more frequently associated with IIM-ILD. The MSAs most associated with IIM-ILD were Jo1, PL-7, PM-Scl, Ku and SRP (p<0.001).



Cancer was found in 9.6% of MSA+ve patients. The most frequent tumors were gynecological (37.5%), followed by gastrointestinal (25%) and breast cancer (12.5%). Factors associated with cancer were age (p=0.010), TIF1-γ (p<0.001), SRP (p=0.004), PL-12 (p=0.013), PL-7 (p=0.047) and HMGCR (p=0.027).

The mortality of these patients was 3.5%. There were no differences regarding MSA+ve/-ve (p = 0.911). However, MDA-5 (p=0.033) and older age (p=0.001) were associated with higher mortality. There were no significant differences between the IIM classifications, the associated SAD, the presence of cancer or ILD. However, longer follow-up periods and future studies are necessary to confirm these results.

Conclusion: The use of a myositis blot allowed classifying, stratifying the risk of ILD, the risk of cancer and the risk of mortality in IIM. IIM-ILD was the most frequent complication, usually manifested as NSIP. The associated risk factors were ARS, OM, some MSAs, Ro52+ and older age. Cancer was a serious and frequent manifestation in these patients, especially in patients with TIF1-γ and other MSAs, so it is essential to know the risk factors and perform an early screening, especially in older patients.

A better knowledge of the serological profiles of IIM will provide more individualized approaches and better risk stratification, helping in the management and treatment of these patients.

REFERENCES:

[1] Satoh et al. Clin Rev Allergy Immunol. 2017 Feb;52(1):1-19.
[2] Betteridge et al. J Intern Med. 2016 Jul;280(1):8-23.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3234

POS0876 SARCOPENIA IN MYOSITIS PATIENTS: A MARKER OF MUSCLE DAMAGE ASSOCIATED WITH HANDICAP

M. Giannini[1], A. L. Charles[2], M. Pizzimenti[3], L. Debrut[3], D. A. Levy[1], R. M. Javier[4], B. Geny[3], A. Meyer[1]. *[1]University of Strasbourg, Service de Physiologie et d'explorations fonctionnelles, Nouvel Hopital Civil, Centre de Référence des Maladies Autoimmunes Rares, Fédération de Médecine Translationnelle, UR3072, Strasbourg, Strasbourg, France*; *[2]University of Strasbourg, Fédération de Médecine translationnelle, UR3072, Strasbourg, Strasbourg, France*; *[3]University of Strasbourg, Service de Physiologie et d'explorations fonctionnelles, Nouvel Hopital Civil, Fédération de Médecine Translationnelle, UR3072, Strasbourg, Strasbourg, France*; *[4]Centre Hospitalier Universitaire, Strasbourg, Department of Rheumatology, Strasbourg, France*

Background: Myositis are systemic autoimmune rare diseases characterized by muscle inflammation and weakness. Even though the signs of active disease have been resolved, myositis patients frequently present residual muscle weakness, decreased physical performance and sustained disability. This condition has been coined on the term "damage" (as opposed to "activity").

Sarcopenia is a frequent, progressive and generalized skeletal muscle disorder characterized by low muscle strength and mass leading to handicap, decreased quality of life and increased mortality.[1]

Prevalence and significance of sarcopenia in myositis patients has never been reported.

Objectives: To study sarcopenia in myositis patients with low or no disease activity.

Methods: Adult myositis patients (2017 ACR/EULAR criteria), with disease duration greater than 12 months, creatine kinase serum level (CK) less than 500 U/l, stable medication for 6 months were enrolled. Patients with inclusion body myositis were excluded. Total (LM) and appendicular (ALM) muscle mass were measured using dual-energy X-ray absorptiometry (DXA, Hologic) and muscle grip strength was measured using Jamar dynamometer. Sarcopenia was defined according to the EWGSOP2 consensus.[1]

Results: 29 patients (20 female, 68.9%), with a median age of 61 years (50.5-71) were enrolled. They suffered from dermatomyositis (DM, n=4), immune-mediated necrotizing myopathy (IMNM), n=8), anti-synthetase syndrome (ASS, n=9), scleromyositis (SM, n=8) since 4.7 years (2.8-8.3). At the evaluation, muscle strength assessed with MMT-8 was 139/150 (136-147), MMT-12 was 210/220 (204-216) and CK were 131.5 U/l (105.5-202). Four patients (13.8%) were sarcopenic. Sarcopenic patients were older (73.4 years (66.2-80.5) vs 58.7 years (44.2-79.6), p=0.03), with a longer disease duration (7.3 years (5.3-11.8) vs 4.3 (2.7-8.3), p = 0.1), longer time with increased CK (449 days (169.8-954) vs 255.5 (124-872.8)), higher maximum CK values (6000 U/l (2205-7000) vs 1636 (900-4457)). They suffered from IMNM (2/4, 50%); DM (n=1) and SM (n=1), had more frequently disease-related cardiac involvement (50% vs 4%, p=0.04), and tended to a longer steroid therapy duration (2.4 years (0.8-5) vs 1.8 (1.3-3.9), p=0.9) and a higher number of immunomodulatory drugs (2.5 (2-5.3) vs 2 (2-3), p=0.3).

At the evaluation, sarcopenic patients were globally weaker as highlighted by lower MMT-12 (201 (196.8-206.8) vs 213 (207-217.5), p=0.02). Head flexo-extensors and proximal upper muscles were especially weaker (respectively, p=0.04 and p=0.03). Muscle performance was also lower in sarcopenic patients as assessed by distance covered at 6-minute walk test (6mWT, p=0.003) and number of squats in 30 seconds (p=0.005). Time to drink a glass of water was significantly longer in sarcopenics (p=0.04) even if any patient referred dysphagia. Health assessment questionnaire score was greater (1.4 (0.8-2) vs 0.6 (0.2-1), p=0.04) indicating higher handicap. LM positively correlated with MMT-8 (ρ=0.5, p=0.01) and MMT-12 (ρ=0.5, p=0.004), with number of squats in 30 seconds (ρ=0.7, p=0.0003) and 6mWT distance covered/lower limit (ρ= 0.5, p=0.01). Moreover, LM negatively correlated with time to drink a glass of water (ρ=-0.6, p=0.002).

Conclusion: Muscle mass measured by DXA is a relevant parameter for muscle damage and disability in myositis patients. Sarcopenic myositis patients represent a subgroup with important muscle damage and handicap.

REFERENCES:

[1] Cruz-Jentoft AJ et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 1 Jan 2019;48(1):16-31.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3248

POS0877 THE EFFECT OF PLATELET INHIBITORS ON DIGITAL ULCERS IN SYSTEMIC SCLEROSIS - A DERIVATION AND VALIDATION EUSTAR STUDY

A. Garaiman[1], K. Steigmiller[2], C. Gebhard[3], C. Mihai[1], R. Dobrota[1], M. Matucci-Cerinic[4], J. Henes[5], J. De Vries-Bouwstra[6], V. Smith[7], A. Doria[8], Y. Allanore[9], L. Dagna[10], B. Anic[11], C. Montecucco[12], O. Kowal-Bielecka[13], M. Martin[14], Y. Tanaka[15], A. M. Hoffmann-Vold[16], U. Held[2], O. Distler[1], M. O. Becker[1]. *[1]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zürich, Switzerland*; *[2]Department of Biostatistics, at Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland*; *[3]Department of Nuclear Medicine, University Hospital Zurich, University of Zurich, Zürich, Switzerland*; *[4]Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Scleroderma Unit, AOUC, Florence, Italy*; *[5]Centre for Interdisciplinary Clinical Immunology, Rheumatology and Autoinflammatory Diseases and Department of Internal Medicine II (Hematology, Oncology, Immunology and Rheumatology), University Hospital Tuebingen, Tuebingen, Germany*; *[6]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands*; *[7]Department of Internal Medicine, Ghent University, Belgium; Department of Rheumatology, Ghent University Hospital, Belgium; Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent, Belgium*; *[8]Rheumatology Unit, Department of Medicine, University of Padova, Padova, Italy*; *[9]Department of Rheumatology A, Descartes University, APHP, Cochin Hospital, Paris, France*; *[10]Unit of Immunology, Rheumatology,*

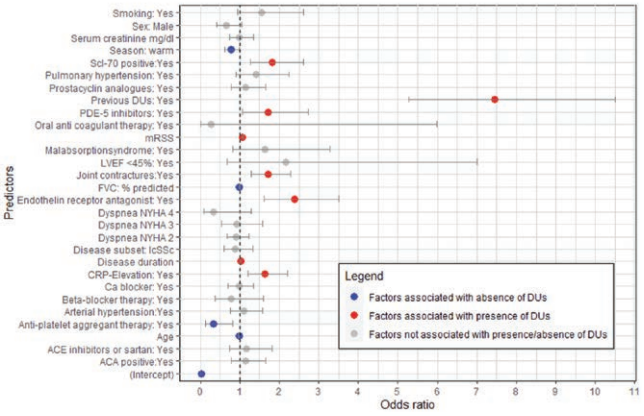
Allergy and Rare Diseases (UnIRAR), IRCCS San Raffaele Scientific Institute, Milan, Italy; Vita-Salute San Raffaele University, Milan, Italy; [11]*Division of Clinical Immunology and Rheumatology, Department of Internal Medicine, University Hospital Centre Zagreb and University of Zagreb, School of Medicine, Zagreb, Croatia*; [12]*Department of Rheumatology, Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy*; [13]*Department of Rheumatology and Internal Medicine, Medical University of Bialystok, Bialystok, Italy*; [14]*Department of Internal Medicine, Poitiers University Hospital, Poitiers, France*; [15]*The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health Japan, Kitakyushu, Japan*; [16]*Department of Rheumatology, Oslo University Hospital, Oslo, Norway*

Background: Digital ulcers (DUs) affect half of the patients with systemic sclerosis (SSc) and can be complicated by gangrene and amputation. The direct involvement of platelets in the development of DUs has been suggested by *in vitro* studies, which encouraged physicians to consider platelet inhibitors as a therapeutic option in the management of DUs. However, until now, there is no clinical study to assess the efficacy of platelet inhibitors for DUs in SSc patients.
Objectives: To demonstrate a possible relationship between treatment with platelet inhibitors and the occurrence of DUs at the next follow-up visit in patients with SSc.
Methods: This study used prospectively collected data from the European Scleroderma Trials and Research group (EUSTAR) registry. Patients fulfilling the 2013 ACR/EULAR SSc classification criteria with complete longitudinal data on the presence of DUs and platelet inhibitors were included in the analysis. Multiple imputation using a random forest algorithm was implemented to handle missing values.
The dataset was split into a derivation and validation cohort. To investigate the response for the binary dependent variable of DUs, a generalized linear mixed model (GLMM) was developed in the derivation cohort and validated using ROC analysis and Brier scores to address discrimination and calibration, respectively.
Results: Of 3,463 patients (2,961 in the derivation cohort, 722 in the validation cohort), 453 had current DUs at the baseline and 245 were exposed to platelet inhibitors (table 1). Our GLMM revealed that the exposure to platelet inhibitors is associated with a reduced risk of DUs at the next follow up visit (OR = 0.33, 95% CI = [0.13 to 0.82]). Further factors associated with absence or presence of DUs at the next follow-up visit are shown in figure 1. This confirmed the previously identified risk factors for the presence of DUs, supporting the overall robustness and the validity of our model.
The performance was evaluated by ROC curve analysis and showed an AUC = 97.97% (95% CI = [96.93% to 97.67%]) for the derivation cohort and AUC = 77.3% (95% CI = [74.01% to 81.39%]) for the validation cohort, respectively, showing an acceptable discrimination. The Brier score was 0.05 in the derivation cohort and 0.07 in the validation cohort, suggesting a good calibration of the model.
Conclusion: Our model, with acceptable discrimination and good calibration, suggests a positive treatment effect of platelet inhibitors on DUs in clinical practice.

Table 1. Baseline characteristics of patients before imputation

Characteristics	Overall	Derivation set	Validation set
n	3,463	2,691	772
Age (median [IQR])	56.00 [47.00, 66.00]	56.00 [47.00, 65.00]	57.00 [48.00, 67.00]
Disease duration (median [IQR])	9.00 [4.00, 16.00]	9.00 [4.00, 16.00]	8.00 [4.00, 15.00]
Disease subset = Limited cutaneous SSc (%)	1562 (65.2)	1164 (64.6)	398 (66.9)
DUs (%): Current	453 (13.1)	378 (14.0)	75 (9.7)
DUs (%): Never	1783 (51.5)	1326 (49.3)	457 (59.2)
DUs (%): Previously	1227 (35.4)	987 (36.7)	240 (31.1)
mRSS (median [IQR])	5.00 [2.00, 11.00]	6.00 [2.00, 12.00]	4.00 [1.00, 11.00]
Joint Contractures = Yes (%)	881 (26.8)	770 (29.4)	111 (16.5)
LVEF (median [IQR])	62.00 [60.00, 65.00]	60.00 [60.00, 65.00]	65.00 [60.00, 67.00]
Dyspnea NYHA III and IV (%)	300 (9.5)	214 (8.6)	86 (12.7)
Pulmonary hypertension = Yes (%)	244 (10.7)	200 (11.3)	44 (8.4)
Lung fibrosis on HRCT = Yes (%)	685 (46.6)	600 (47.7)	85 (39.7)
FVC % predicted (median [IQR])	97.00 [82.00, 111.00]	95.00 [81.00, 110.00]	101.00 [85.00, 115.00]
Serum creatinine mg/dl (median [IQR])	0.70 [0.60, 0.90]	0.70 [0.60, 0.90]	0.70 [0.70, 0.90]
Anti-Scl-70 positive = Yes (%)	1147 (33.1)	958 (35.6)	189 (24.5)
CRP elevation = Yes (%)	639 (21.1)	490 (20.8)	149 (22.1)
Platelet inhibitors therapy = Yes (%)	245 (7.1)	206 (7.7)	39 (5.1)
Oral anti-coagulants therapy = Yes (%)	53 (1.5)	50 (1.9)	3 (0.4)

Figure 1: The coefficient plot of the GLMM:



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3272

POS0878 ULTRASOUND ASSESSMENT OF DERMAL THICKNESS AND SKIN STIFFNESS IN UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE AT RISK FOR SYSTEMIC SCLEROSIS

T. Santiago[1,2], M. Luis[1], J. Lima[2], C. Gaspar[2], M. J. Salvador[1,2], J. A. P. Da Silva[1,2]. [1]*Centro Hospitalar e Universitário de Coimbra, Rheumatology Department, Coimbra, Portugal*; [2]*Faculty of Medicine, University of Coimbra, Institute for Clinical and Biomedical Research (iCBR), Coimbra, Portugal*

Background: High-frequency ultrasound (HFUS) and shear-wave elastography (SWE) allow an objective assessment of skin involvement in systemic sclerosis (SSc) patients.[1] Till now it has been applied to patients with established diagnosis.[2,3] However, there is no data concerning its application in Undifferentiated Connective Tissue Disease at risk for SSc (UCTD-risk-SSc), i.e., patients with Raynaud's phenomenon and either SSc marker autoantibodies or typical capillaroscopic findings or both, not satisfying classification criteria for SSc.[4]
Objectives: To compare ultrasound-dermal thickness (DT) and skin stiffness, using high-frequency ultrasound and shear-wave elastography, in UCTD-risk-SSc and healthy controls.
Methods: Forty UCTD-risk-SSc patients and 40 age- and gender-matched healthy controls were included. Ultrasound-DT was measured using an 18MHz probe, and skin stiffness (i.e. shear-wave velocity values, SWV) using the VTIQ software with a 9MHz probe, at the 17 Rodnan skin sites. The mRSS score was, by definition, zero in all sites, both in cases and controls. Continuous data were expressed as the mean (SD), and Mann-Whitney U test was performed to compare differences between the groups, as variables were not normally distributed. Associations between variables were analysed using the Spearman's correlation.
Results: SWV values were significantly higher in patients with UCTD-risk-SSc compared with controls at the right and left hands, and in the right and left fingers (table 1). Higher values of ultrasound dermal-thickness were found in the fingers and hands bilaterally, although differences were only significantly at the hands, compared with healthy controls (table 1). There were no significant differences in the other Rodnan skin sites. There was no significant correlation between ultrasound-dermal thickness and stiffness at the same skin site.
Conclusion: This study provides the first evidence suggesting that ultrasound-DT and stiffness can discriminate patients with UCTD-risk-SSc from healthy controls. Prospective studies including a larger number of patients with different subsets of UCTD-risk-SSc are needed to investigate diagnostic and prognostic value of the ultrasound parameters in this group.

REFERENCES:

[1] Santiago T, et al. Arthritis Care Res (Hoboken). 2019;71:563-574.
[2] Hesselstrand R, et al. Rheumatology (Oxford). 2008;47:84-7.
[3] Flower V et al. jrheum.200234.
[4] Valentini, G., et al. Arthritis Care Res, 66: 1520-1527.

Table 1. Clinical and ultrasound parameters in UCTD-risk-SSc and healthy control groups.

	UCTD-risk-SSc (n=40)	Healthy controls (n=40)	p value
Age, mean (SD)	51.4 (14.9)	49.8 (13.9)	Ns
Female, n (%)	36 (90.0)	36 (90.0)	
Raynaud phenomenon, %	100.0%	-	
ANAs	100.0	-	
Anti-centromere, %	60.0		
Anti-Scl70+, %	11.5		
Scleroderma/non-scleroderma pattern in capillaroscopy, %	5.0/95.0	-	-
Ultrasound parameters			
Dermal thickness (mm)			
Dorsal hand right	0.77 (0.32)	0.62 (0.12)	0.02
Dorsal hand left	0.79 (0.39)	0.62 (9.13)	0.02
Proximal phalanx right	0.64 (0.14)	0.61 (0.11)	Ns
Proximal phalanx left	0.66 (0.16)	0.60 (0.09)	Ns
SWV values (m/s)			
Dorsal hand right	1.94 (0.40)	1.61 (0.24)	0.0001
Dorsal hand left	1.82 (0.36)	1.65 (0.25)	0.025
Proximal phalanx right	2.09 (0.60)	1.68 (0.24)	0.001
Proximal phalanx left	2.13 (0.82)	1.66 (0.27)	0.004

Legend: ANA: Antinuclear antibodies; Ns: Non-significant; UCTD: Undifferentiated Connective Tissue Disease; SD: Standard Deviation

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3384

POS0879 CLINICAL FEATURES, PROGNOSTIC FACTORS, AND OUTCOME OF ANTI-MDA5 POSITIVE DERMATOMYOSITIS WITH RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE: A MULTICENTER STUDY OF 238 PATIENTS

L. Xu[1], L. Wang[1], C. LV[1], W. Tan[1]on behalf of Myositis Study Group Jiangsu cohort. [1]*The First Affiliated Hospital of Nanjing Medical University, Department of Rheumatology, Nanjing, China*

Background: Anti-melanoma differentiation-associated gene 5 positive dermatomyositis (anti-MDA5$^+$ DM) is typically amyopathic and associated with a life-threatening, therapy-resistant, rapidly progressive interstitial lung disease (RP-ILD).
Objectives: The present study aims to characterize the prognostic factors and long-term outcome of MDA5$^+$ DM -associated RP-ILD.
Methods: A multicenter retrospective study was performed across ten tertiary hospitals in China between January 1, 2018 to December 31, 2019.
Results: A total of 238 patients (170 women) with MDA5$^+$ DM enrolled into this retrospective clinical study. The mean age was 53.0 ± 12.2 years. The median follow-up duration was 6.3 ± 12.2 months. Of those 238 anti-MDA5+ patients, ILD is commonly observed in 213 patients, and RP-ILD occurred in 35.29% (84/213) of these patients (RP-ILD defined as progressive dyspnea occurs within 1 month after the onset of respiratory symptoms, and chest radiography or pulmonary function test show progressive interstitial abnormalities). The mortality rate of RP-ILD patients within the 6 months was 58.3% (49/84) in our cohort. Death peaked the first three months after diagnosis, occupying 84.8% (39/46) of died RP-ILD patients. Cox univariate proportional hazard analysis showed that age, gender, disease duration, abnormal laboratory features (LDH, CK, ESR and CRP), anti-Ro52 autoantibody and anti-MDA5 grade were related to the risk of occurrence of RP-ILD in patients with MDA5$^+$ DM. The Cox proportional hazards model identified the disease duration [odds ratio (OR) 0.81 (95% CI 0.68, 0.96), P=0.016] as a protective factor, and anti-Ro52 autoantibody [OR 5.82 (95% CI 1.72, 19.73), P=0.005] as independent risk factors for the occurrence of RP-ILD in MDA5$^+$ DM patients. The 6-month all-cause mortality rate of RP-ILD patients was 58.3% (49/84).
Conclusion: Combined with anti-Ro52 in Myositis-specific antibodies was associated with the occurrence and long-term mortality in MDA5$^+$ DM -associated RP-ILD patients. The results suggest poor overall survival among patients with MDA5$^+$ DM -associated RP-ILD. Survival during the first 6 months is crucial for long-term survival. Early recognition and prompt treatment of this high-risk group of MDA5$^+$ DM -associated RP-ILD patients are therefore important.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3401

POS0880 TWO-MINUTE WALK TEST AS A SIMPLE AND OBJECTIVE OUTCOME MEASURE IN IDIOPATHIC INFLAMMATORY MYOSITIS

S. K. Dunga[1], C. Kavadichanda[2], V. Negi[2]. [1]*Jawaharlal Institute of Postgraduate Medical Education and Research, Department of Clinical Immunology, Puducherry, India*; [2]*Jawaharlal Institute of Postgraduate Medical Education and Research, Department of Clinical Immunology, Puducherry, India*

Background: Manual muscle testing (MMT) and Functional index 2(FI-2) are the usual methods in assessing disease activity in IIM[1]. Limitations of MMT8 include low sensitivity to change, floor/ceiling effect, and under-representation of certain important muscle groups[1] while FI-2 takes a longer time to administer. Several Timed function tests (TFTs) like the 2-minute walk test (2MWT) or 30s raise from a chair test and 30s 1kg arm rise test may be better alternatives and less time taking[2]. Data looking at the performance of these tests are limited to small controlled studies.
Objectives: To assess the performance of timed function tests against MMT8 and FI-2 in assessing muscle strength and endurance at baseline, 3 and 6 months of therapy.
Methods: An observational cohort study, included 41 patients with polymyositis and dermato-myositis attending OPD and IPD service of tertiary centre. MMT8, FI-2 and Timed function tests were done at baseline, at 3 months and at 6 months. (Figure 1)

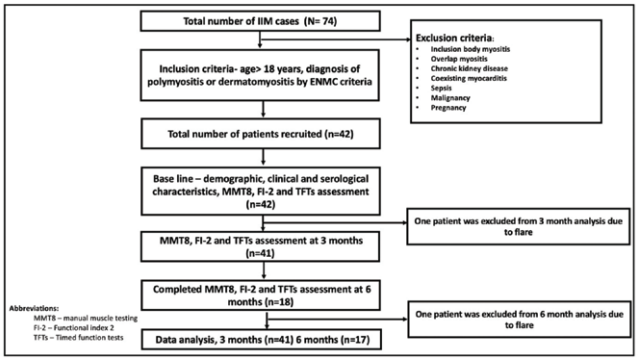


Figure 1. Consort diagram showing the workflow in study population

Results: Forty one patients included in the study had completed three month follow-up assessment, while 17 patients achieved a six-month evaluation. Out of 41 patients, 11 (27%) were polymyositis, and 30 (73%) were dermatomyositis. The mean MMT8 of the total study population at baseline was 57±15, at three months (n=41) was 66 ±10 and at six months (n=17) was 71 ± 10, while in active subgroup was 50 ± 18, 64 ± 9 (n=41), 67 ± 9.6 (n=17)at baseline, three months and six months respectively. The change in TFTs showed a moderate to strong correlation with the change in Fi-2 among the study population at three months and six months (Table 2). Among the TFTs 2MWT showed moderate correlation with both MMT8 and FI-2 in active disease.

Table 1. Spearman Rho Correlation between change in timed function tests with change in MMT8, change in FI-2 at 3 months and 6 months

		At 3 months (n=41)		At 6 months (n=17)	
		Active disease (n=18)	Inactive disease (n=23)	Active disease (n=7)	Inactive disease (n=10)
Correlation of Δ MMT8 with	**Δ30s rise form chair**	0.143	0.346	0.200	0.347
	Δ30s1kg arm lift	0.018	0.284	0.362	0.168
	Δ2MWD	**0.755***	0.313	**0.482***	0.334
Correlation of ΔFI-2 with	**Δ30s rise form chair**	**0.784***	**0.495***	**0.486***	**0.424***
	Δ30s1kg arm lift	**0.671***	0.107	**0.704***	0.301
	Δ2MWD	**0.834***	**0.623***	**0.808***	**0.506***

***p<0.05**

Conclusion: Using timed function tests can be an excellent alternative to FI-2 in assessing muscle endurance. 2-minute walk distance is a better alternative to conventional muscle testing as it measures both power and endurance, and this can overcome the ceiling effect of MMT-8.

REFERENCES:

[1] Rider LG, Aggarwal R, Machado PM, Hogrel J-Y, Reed AM, Christopher-Stine L, et al. Update on outcome assessment in myositis. Nat. Rev. Rheumatol. 2018;14:303–18.
[2] Agarwal S, Kiely PD. Two simple, reliable and valid tests of proximal muscle function, and their application to the management of idiopathic inflammatory myositis. Rheumatology. 2006 Jul 1;45(7):874-9.

Acknowledgements: I would like to acknowledge my patients, my teachers, colleagues, and paraclinical staff of the department of Clinical Immunology JIPMER
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3461

POS0881

DETECTION OF THE GENE EXPRESSIONS IN PERIPHERAL BLOOD INVOLVED IN THE PROGRESSION OF PULMONARY VESSEL DISEASE AT THE SUBCLINICAL STAGE OF PULMONARY HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS

Y. Koyama[1], Y. Sato[2], T. Shoji[2], S. Fuke[3], T. Umayahara[4], M. Sakamoto[1]. [1]*Japanese Red Cross Okayama Hospital, Rheumatology, Center for Autoimmune Diseases, Okayama, Japan*; [2]*DNA Chip Research Inc., N/A, Tokyo, Japan*; [3]*Japanese Red Cross Okayama Hospital, Cardiology, Okayama, Japan*; [4]*Japanese Red Cross Okayama Hospital, Dermatology, Okayama, Japan*

Background: Pulmonary hypertension (PH) is prominent as a vascular involvement of systemic sclerosis (SSc), which remains a leading cause of death in spite of current best treatments. Recently, hemodynamic definition of PH was updated from mPAP≥25mmHg to mPAP>20mmHg and PVR≥3WU. Although new definition may improve the prognosis of PH associated with SSc by giving a chance to start management early, it may be insufficient as more than 2/3 of the pulmonary circulation is already impaired by the time of meeting the definition. Therefore, the ideal therapeutic intervention should be started at the subclinical stage of PH in SSc patients, but little is known about underlying pathological mechanisms at the stage. In this study, we investigate progression to exercise-induced PH (exPH)[1)], which is considered subclinical PH, in the prospective registry of high-risk population for developing PH associated with SSc.

Objectives: To detect the gene expressions in peripheral blood involved in the progression of pulmonary vessel disease (PVD) at the subclinical stage of PH associated with SSc.

Methods: Total of 180 patients who had not met PH criteria with Raynaud phenomenon, skin sclerosis or SSc-related autoantibody was registered. To detect the early PVD, exercise Doppler echocardiography (exDE) was carried out every 6 or 12 months for up to 6 years. The definition of exPH was maximum sPAP>40mmHg or increase in sPAP>20mmHg estimated by exDE during exercise. For gene expression analysis, total RNAs from whole peripheral blood cells were extracted by PAXgene system, and then multiplex sequencing was done. To identify candidate genes involved in the progression to exPH, random forest machine learning method was employed. Volcano plots, a scatter plots to visualize fold-changes and p-values of differentially expressed genes (DEGs) between exPH and others (exN), were also used for seeking the important genes for disease progression.

Results: At the time of registration, 34.4% of patients met exPH criteria, and 15.6% of patients developed exPH during follow-up period (35.0±18.1 months). Expression of TNF gene was selected as the most useful genes to predict progression to exPH by random forest, and the accuracy of the model was about 87%. Volcano plots indicated that expressions of TMEM176A and TMEM176B were prominent (fold-change >2.4 and -log10 p-value >3.5) in exPH patients. The accuracy was improved to 90% if the expression of TNF and TMEMA/B were used for the prediction of progression to exPH. We found that statistically significant increase in the expression of TNF was eliminated at the time of fulfilling the exPH criteria, while increase in expressions of TMEM A/B were still kept.

Conclusion: It was reported that TNFα drives pulmonary arterial hypertension by suppressing the BMP type-II receptor and altering NOTCH signalling[2)]. Our findings suggest that TNFα plays important role only in the period of pre-exPH. On the other hand, increase in expressions of TMEM A/B were observed through the period of pre-exPH to post-exPH. It suggests that there are multiple phases before developing PH associated with SSc. It is very important to understand the phases for the precise treatment to arrest the progression of PVD.

REFERENCES:

[1] R. Naeije et al., Am J resp and critical care med 187, 576-583 (2013). 2) LA. Hurst et al., Nat Commun. 13;8:14079 (2017).

Disclosure of Interests: Yoshinobu Koyama Speakers bureau: Asahikasei, Ayumi, BMS, Mitsubishi Tanabe, Shin-nihon, Paid instructor for: Asahikasei, Asteras, BMS, Grant/research support from: Eli-Lilly, Yoshiharu Sato: None declared, Tatsuma Shoji: None declared, Soichiro Fuke: None declared, Takatsune Umayahara: None declared, Moe Sakamoto: None declared

DOI: 10.1136/annrheumdis-2021-eular.3609

POS0882

AMINAPHTONE LONG-TERM TREATMENT IN SYSTEMIC SCLEROSIS

A. Sulli[1], E. Gotelli[1], A. Cere[1], E. Hysa[1], G. Pacini[1], C. Pizzorni[1], S. Paolino[1], M. Cutolo[1]. [1]*Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic Hospital, Genova, Italy*

Background: Aminaphtone has been used since many years to treat microvascular disorders. Aminaphtone seems to improve clinical symptoms of Raynaud's phenomenon (RP), either primary or secondary to systemic sclerosis (SSc) by increasing peripheral blood perfusion as assessed by Laser speckle contrast analysis (1).

Objectives: To evaluate long-term survival and tolerability of Aminaphtone in SSc patients with secondary RP.

Methods: Eighty SSc patients (mean age 64±12 years; mean disease duration 9±8 years) treated with Aminaphtone due to active RP were enrolled (ACR/EULAR 2013 criteria). Patients were taking also various concomitant treatments, including aspirin, cyclic intravenous iloprost, immunomodulators, endothelin receptor antagonists. SSc patients performed periodic clinical and laboratory assessments on average every four months per our clinical practice. Duration of Aminaphtone administration, side effects, and self-assessment of Raynaud Condition Score (RCS) with a scale from 0 (absence of pain) to 10 (maximal pain) were retrospectively assessed.

Results: The observation period was between twelve and seventy months (mean 36±19 months). Aminaphtone was administered at 75 mg twice daily, as standard initial posology per our clinical practice. During the follow-up, five patients (6.2%) referred headache as side effect: three of them had to reduce Aminaphtone posology to 75 mg per day, while maintaining clinical benefits; two patients had to stop the treatment. No other side effects related to the drug appeared during the treatment period, and repeated blood tests did not reveal any significant alteration ascribable to Aminaphtone. After 3 months of treatment sixty-six patients (83%) referred a subjective improvement of RP (RCS 3.6±0.8, vs baseline RCS 7.4±0.8, p=0.032), whereas fourteen patients (17%) were clinically unsatisfied (RCS 6.1±0.4, p=0.12). In this last group of patients, Aminaphtone posology was increased to 75 mg three times a day with a satisfactory amelioration in further nine patients (94% of total) (RCS 4.0±0.6, p=0.04), while five patients (6.2%) definitively discontinued therapy for subjective ineffectiveness within six months. Patients referred a sustained improvement of RCS along the observational period (36±19 months) (last RCS 3.6±0.7 vs baseline, p=0.031).

Conclusion: During an average observation period of three years, Aminaphtone showed a good tolerability profile along with sustained efficacy in 94% of patients with SSc-related RP, without disabling side effects. The absence of a placebo-control group, the retrospective design limit the results, and a randomized controlled trial for Aminaphtone use in the management of SSc-related RP is needed.

REFERENCES:

[1] Ruaro B et al. 2019. *Front Pharmacol* 10:293.

Disclosure of Interests: Alberto Sulli: None declared, Emanuele Gotelli: None declared, ANDREA CERE: None declared, Elvis Hysa: None declared, Greta Pacini: None declared, Carmen Pizzorni: None declared, Sabrina Paolino: None declared, Maurizio Cutolo Grant/research support from: Laboratori Baldacci s.p.a.

DOI: 10.1136/annrheumdis-2021-eular.3614

POS0883

DETECTION OF AUTOANTIBODIES AGAINST MUSCLE-SPECIFIC FOUR-AND-A-HALF-LIM DOMAIN 1 (FHL1) IN INFLAMMATORY MYOPATHIES: RESULTS FROM A SINGLE-CENTER COHORT

A. S. Galindo-Feria[1,2], B. Horuluoglu[1,2], J. Day[3], C. Cerqueira[1,2], S. Proudman[3], I. E. Lundberg[1,2], V. Limaye[3]. [1]*Karolinska Institutet, Solna, Karolinska University Hospital, Division of Rheumatology, Department of Medicine, Stockholm, Sweden*; [2]*Karolinska Institutet and Karolinska University Hospital Solna, Center for Molecular Medicine, Stockholm, Sweden*; [3] *Royal Adelaide Hospital, University of Adelaide, Rheumatology Unit and Discipline of Medicine, Adelaide, Australia*

Background: Autoantibodies targeting a muscle-specific autoantigen, four-and-a-half-LIM-domain 1 (FHL1), have been previously identified in patients with idiopathic inflammatory myopathies (IIM) (1).

Objectives: The aim of this project was to determine the prevalence and associations of anti-FHL antibody in South Australian patients with histologically-confirmed IIM and in an autoimmune disease control (systemic sclerosis (SSc)).

Methods: Sera from patients with IIM (n=267) from the South Australian Myositis Database (SAMD), and SSc (n=174) from the Australian Scleroderma Cohort Study (ASCS) followed at the Royal Adelaide Hospital, and healthy controls (HC, n=100) were analyzed for anti-FHL1 autoantibodies by Enzyme-Linked ImmunoSorbent Assay (ELISA). Clinical, serological and histological details were retrieved from the SAMD and the ASCS.

Results: Autoantibodies to FHL1 were more frequent in patients with IIM (55/267, 20.5%) compared with SSc (18/174, 10%) ($p<0.001$) and HC (4/100, 4%) ($p<0.001$). Muscular vessel inflammation and atrophy were seen more frequently in IIM anti-FHL1$^+$ patients compared with anti-FHL1$^-$ ($p<0.01$ and $p<0.05$). Dysphagia, marked muscle atrophy, and high CK levels were frequent in anti-FHL1$^+$ patients with inclusion body myositis (IBM) and immune-mediated necrotizing myopathy (IMNM). In 35/54 anti-FHL1$^+$ patients, there were no other myositis-specific autoantibodies present. Anti-FHL1 autoantibodies in patients with SSc were associated with gastric antral vascular ectasia.

Conclusion: Anti-FHL1 autoantibodies were detected in 20.5% of IIM patients. In IBM and IMNM, the presence of anti-FHL1-autoantibodies was associated with a severe myopathy as suggested by presence of dysphagia and muscle atrophy.

REFERENCES:

[1] Albrecht I, Wick C, Hallgren A, Tjarnlund A, Nagaraju K, Andrade F, et al. Development of autoantibodies against muscle-specific FHL1 in severe inflammatory myopathies. J Clin Invest. 2015;125(12):4612-24.

Disclosure of Interests: Angeles Shunashy Galindo-Feria: None declared, Begum Horuluoglu: None declared, Jessica Day: None declared, Catia Cerqueira: None declared, Susanna Proudman: None declared, Ingrid E. Lundberg Consultant of: Consulting fees from Corbus Pharmaceuticals, Inc, Grant/research support from: Research grants from Bristol Myers Squibb and Astra Zeneca, Vidya Limaye Consultant of: Scientific adviser for Actelion and Boehringer-Ingelheim, Grant/research support from: PI for clinical trials for Bayer, Boehringer-Ingelheim, Corbus, and CSL

DOI: 10.1136/annrheumdis-2021-eular.3640

POS0884 THE ENHANCED LIVER FIBROSIS (ELF) SCORE AS A BIOMARKER OF SKIN FIBROSIS IN SYSTEMIC SCLEROSIS

C. Chen[1], S. Yang[1], Z. Jiang[1], W. Wan[1], H. Zou[1], M. Liang[1]. [1]*Huashan Hospital Affiliated to Fudan University, Department of Rheumatology, Shanghai, China*

Background: Serum fibrotic markers for systemic sclerosis (SSc) remain limited. The Enhanced Liver Fibrosis (ELF) score, originally derived and validated in patients with chronic liver disease, is an algorithm combining 3 serum markers, known as procollagen type III amino terminal propeptide (PIIINP), tissue inhibitor of metalloproteinases 1 (TIMP-1), and hyaluronic acid (HA). The combined score was proved to be superior to the single components in reflecting the severity of liver fibrosis. However, the performance of ELF score and its components has not been fully validated in SSc.

Objectives: To investigate PIIINP, TIMP-1, HA, and the combined algorithm ELF score as fibrotic markers for SSc skin involvement.

Methods: Eighty SSc patients (44 dcSSc and 36 lcSSc), fulfilling the 2013 ACR/EULAR criteria with the absence of chronic liver diseases, were enrolled. Eighty age- and sex- matched healthy controls were also included. Serum PIIINP and HA levels were quantified by chemiluminescence immunoassay. Serum TIMP-1 levels were determined by enzyme-linked immunosorbent assay. The ELF score was calculated using the formula *ELF score= 2.494+0.846*ln(HA) + 0.735*ln(PIIINP) + 0.391*ln(TIMP-1)*. Results were correlated with clinical profiles including modified Rodnan skin score (mRSS) and interstitial lung disease (ILD).

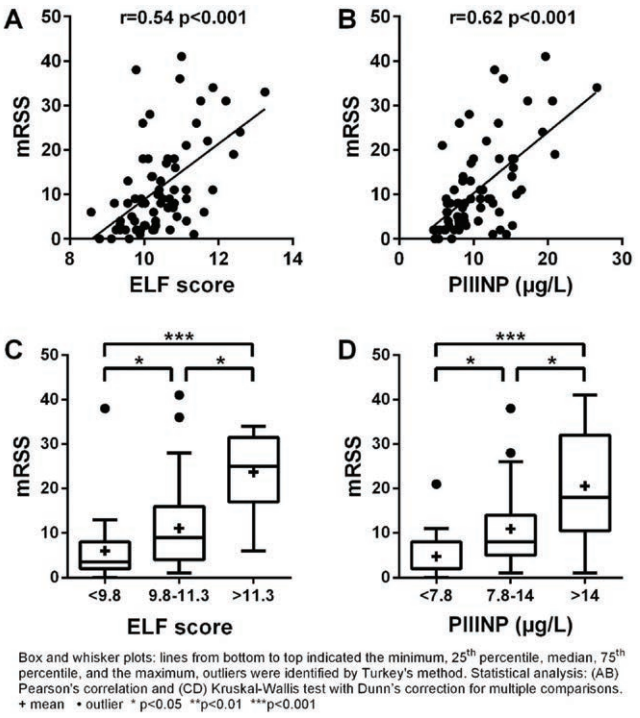
Results: Compared with healthy controls, patients with SSc showed significantly elevated serum PIIINP (11.2±4.8 vs. 5.73±1.4μg/L, p<0.001), TIMP-I (123.7±78.6 vs. 67.8±26.5 ng/ml, p<0.001), and ELF score (10.5±0.9 vs. 9.7±0.4, P<0.001). Even higher levels of PIIINP, TIMP-1, and ELF score were observed in dcSSc patients, compared with lcSSc patients (p<0.001, p=0.024, p=0.003, respectively). No significant difference was found in the levels of serum HA between patients and controls. Strong correlations were observed between mRSS and ELF score (r=0.54, p<0.001), and between mRSS and PIIINP(r=0.62, p<0.001), whereas only weak correlations could be observed between mRSS and TIMP-1 (r=0.28, p=0.02), and between mRSS and HA (r=0.26, p=0.03). When stratified by ELF score, using cutoffs proposed for liver fibrosis and cirrhosis, SSc patients with ELF<9.8 showed the lowest mRSS on average, while patients with ELF>11.3 showed the highest (p<0.001). When stratified by serum PIIINP levels, using the 25th and 75th percentiles, SSc patients with serum PIIINP levels<7.8μg/L showed the lowest mRSS on average, while patients with PIIINP>14.0μg/L showed the highest (p<0.001). Neither the ELF score nor its components showed significant difference between patients with and without ILD.

Conclusion: The ELF score could be used for reflecting the severity of overall skin involvement in SSc, and serum PIIINP also increased in parallel with the increase of mRSS. Longitudinal prospective studies exploring ELF score or serum PIIINP as fibrotic markers and outcome measures of SSc are warranted.

REFERENCES:

[1] Lichtinghagen R, Pietsch D, Bantel H, et al. The Enhanced Liver Fibrosis (ELF) score: Normal values, influence factors and proposed cut-off values. Journal of Hepatology. 2013; 59: 236-42.

[2] Abignano G, Blagojevic J, Bissell LA, et al. European multicentre study validates enhanced liver fibrosis test as biomarker of fibrosis in systemic sclerosis. Rheumatology. 2019; 58: 254-59.



Box and whisker plots: lines from bottom to top indicated the minimum, 25th percentile, median, 75th percentile, and the maximum, outliers were identified by Turkey's method. Statistical analysis: (AB) Pearson's correlation and (CD) Kruskal-Wallis test with Dunn's correction for multiple comparisons. + mean • outlier * p<0.05 **p<0.01 ***p<0.001

Figure 1. Correlations of mRSS with ELF score (A) and serum PIIINP (B) and distribution of mRSS among different ELF (C) and PIIINP (D) ranges.

Acknowledgements: The authors have no acknowledgements to declare.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3648

POS0885 HIGH INCIDENCE AND MORTALITY OF PNEUMOCYSTIS JIROVECI INFECTION IN ANTI-MDA5-ANTIBODY POSITIVE DERMATOMYOSITIS: EXPERIENCE FROM A SINGLE CENTER

Q. Yan[1], S. Chen[1], L. Huang[1], Q. Fu[1], Y. Ye[1]. [1]*Renji Hospital, Shanghai Jiaotong University, School of Medicine, Department of Rheumatology, Shanghai, China*

Background: Idiopathic inflammatory myopathies (IIM) was associated with a significantly higher risk of opportunistic infections that including Pneumocystis jiroveci pneumonia(PJP) which is potentially fatal opportunistic infection. However, no prior studies have evaluated the PJP infection in subtypes of IIM.

Objectives: To investigate the incidence rate and mortality rate of PJP infection in subgroups of IIM patients according to myopathy specific antibodies.

Methods: In the first part, we reviewed 463 consecutive patients with IIM retrospectively to analyze incidence of PJP infection. In the next part, we enrolled 30 consecutive PJP infection patients with any rheumatic disease was to identify the mortality rate and risk factors. Kaplan-Meier curve with log rank test was used to access differences in survival. Univariate and multivariate analyses were performed to identify prognostic factors using Cox regression.

Results: We found that 12(7.5%) PJP cases occurred in 160 anti-MDA5-ab-positive DM patients, while only two (0.7%) PJP cases were found in 303 anti-MDA5-ab-negtive DM/PM patients($P < 0.05$). PJP infection typically happened in the first two months of the treatment for anti-MDA5-ab-positive DM patients who have a significant decrease in the CD4+ T cell counts and Lymphocyte counts ($P < 0.05$). Only two (16.7%) anti-MDA5-ab-positive DM patients recover from PJP, with lethally higher mortality than those PJP infection with other rheumatic diseases (83.3% vs. 38.9%, $P < 0.05$). We found no association between the time to anti-PJP treatment and treatment outcomes in anti-MDA5-ab-positive DM; yet we confirmed in PJP infection with other rheumatic diseases that anti-PJP treatment within 6 days crucially increased the survival ($P < 0.05$).

Conclusion: PJP infection has alarming high incidence and mortality in anti-MDA5-ab-positive DM patients. Unlike PJP infection with other rheumatic diseases, timely treatment for PJP doesn't improve the prognosis of this particular subtype. Therefore, the necessity of further study of PJP prophylaxis treatment in anti-MDA5-ab-positive DM patients is verified.

REFERENCES:
[1] Hsu CY, et al. Comparing the burdens of opportunistic infections among patients with systemic rheumatic diseases: a nationally representative cohort study. ARTHRITIS RES THER 2019, 21(1):211.
Acknowledgements: The authors thank Dr. An Sun,
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3693

POS0886 COULD BE INTERSTITIAL MYOCARDITIS A FEATURE OF THE ANTISYNTHETASE SYNDROME?

A. Gil-Vila[1], G. Burcet[2], A. Anton-Vicente[1], D. Gonzalez-Sans[1], A. Nuñez-Conde[1], E. Trallero-Araguás[3], J. L. Reyes-Juárez[2], C. P. Simeón-Aznar[1], A. Selva-O'callaghan[1]. [1]*Vall d'Hebron University Hospital, Internal Medicine, Barcelona, Spain*; [2]*Vall d'Hebron University Hospital, Cardiovascular Imaging, Radiology, Barcelona, Spain*; [3]*Vall d'Hebron University Hospital, Rheumatology, Barcelona, Spain*

Background: Antisynthetase syndrome (ASS) is characterized by inflammatory myopathy, interstitial lung disease, arthritis, mechanical hands and Raynaud phenomenon, among other features. Recent studies have shown that idiopathic inflammatory myopathies (IIM) may develop cardiac involvement, either ischemic (coronary artery disease) or inflammatory (myocarditis). We wonder if characteristic lung interstitial involvement (interstitial lung disease) that appears in patients with the ASS may also affect the myocardial interstitial tissue. New magnetic resonance mapping techniques could detect subclinical myocardial involvement, mainly as edema (increase extracellular volume in interstitium and extracellular matrix), even in the absence of visible late Gadolinium enhancement (LGE).
Objectives: Our aim was to describe the presence of interstitial myocarditis in a group of patients with ASS.
Methods: Cross-sectional, observational study performed in a tertiary care center. We included 13 patients diagnosed with ASS (7 male, 53%, mean (SD) age at diagnosis 56,8 years (±11,8)). The patients were consecutively selected from our outpatient myositis clinic. Myositis specific and associated antibodies were performed by means of line immunoblot (EUROIMMUN©). Cardiac magnetic resonance (CMR) was performed on all patients. The study protocol includes functional cine magnetic resonance and standard late gadolinium enhancement (LGE), as well as novel parametric T1 and T2 mapping sequences (modified look locker inversion recovery sequences - MOLLI) with extracellular volume (ECV) calculation 20 minutes after the injection of a gadolinium-based contrast material.
Results: CMR could not be performed in one patient due to anxiety. All patients studied (12) had a normal biventricular function, without alteration of segmental contraction. A third (4 out of 12, 33%) of the studied patients showed elevated T2 myocardial values without focal LGE, half of them (2/4) with an elevated ECV, consistent with myocardial edema. Two patients with normal T2 values showed unspecific LGE focal patterns, one in the right ventricle union points and another with mild interventricular septum enhancement (Figure 1). None of the patients studied refer any cardiac symptomatology. All the four patients with T2 mapping alterations (100%) had interstitial lung involvement, but only 4 out of 8 (50%) of the rest ASS patients without T2 mapping positivity. The autoimmune profile was as follows: 10 anti-Jo1/Ro52, 1 anti-EJ/Ro52, 2 anti-PL12.

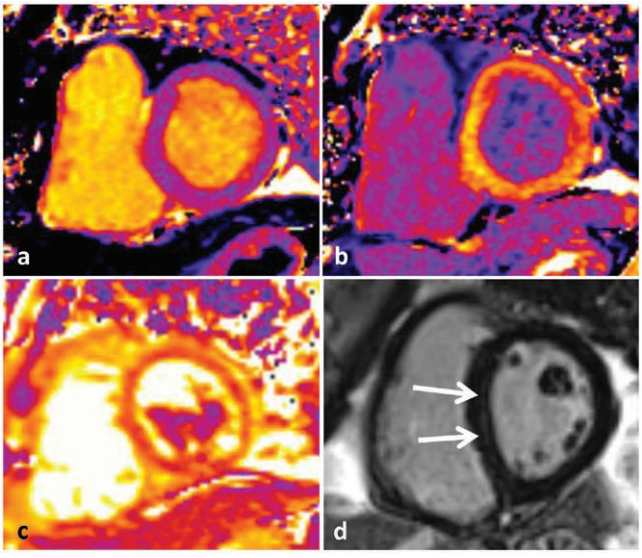


Figure 1. Cardiac magnetic resonance images from ASS patients.

Conclusion: Myocarditis, although subclinical, appears to be a feature in ASS patients. T1 and T2 mapping sequences might be valuable to detect and monitor subclinical cardiac involvement in these patients. The possibility that the same etiopathogenic mechanism may be involved in the interstitial tissue in lung and myocardium is raised. More studies must be done in order to assert the prevalence of myocarditis in ASS.
REFERENCES:
[1] Dieval C et al. Myocarditis in Patients With Antisynthetase Syndrome: Prevalence, Presentation, and Outcomes. Medicine (Baltimore). 2015 Jul;94(26):e798.
[2] Myhr KA, Pecini R. Management of Myocarditis in Myositis: Diagnosis and Treatment. Curr Rheumatol Rep. 2020 Jul 22; 22:49.
[3] Sharma K, Orbai AM, Desai D, Cingolani OH, Halushka MK, Christopher-Stine L, Mammen AL, Wu KC, Zakaria S. Brief report: antisynthetase syndrome-associated myocarditis. J Card Fail. 2014 Dec;20(12): 939-45.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3696

POS0887 TRANSCRANIAL ELECTRICAL STIMULATION IS SAFE AND EFFICIENT IN PATIENTS WITH SYSTEMIC AUTOIMMUNE MYOPATHIES

L. F. Adsuara de Sousa[1], R. G. Misse[1], L. De Macedo Dos Santos[2], A. Fontes Baptista[3], C. Tanaka[2], J. M. D'andréa Greve[4], S. Katsuyuki Shinjo[1]. [1]*Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Division of Rheumatology, Sao Paulo, Brazil*; [2]*Speech Therapy and Occupational Therapy, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Department of Physical Therapy, Sao Paulo, Brazil*; [3]*Universidade Federal do ABC, Center for Mathematics, Computing and Cognition, Santo Andre, Brazil*; [4]*Institute of Orthopedics and Traumatology, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Laboratory of Movement Studies, Sao Paulo, Brazil*

Background: There is currently few information regarding rehabilitation in patients with systemic autoimmune myopathies (SAMs). Transcranial direct current stimulation (tDCS) has shown promising results for the motor performance of healthy individuals as for patients with, e.g., post-stroke hemiparetic limbs.
Objectives: The present study was aimed to assessing the safety and efficiency of tDCS in patients with SAMs.
Methods: This study is a prospective, randomized, sham controlled, double blind, and clinical trial with ethical approval. Eighteen adult patients with dermatomyositis, polymyositis, antisynthetase syndrome or immune-mediated necrotizing myopathies in remission or with minimal disease activity were enrolled from 2018 to 2019. Patients were allocated randomly in two groups to receive sham or active tDCS with 2mA amplitude submitted for 20 minutes for three consecutive days. The 5x7cm sponge-electrodes were positioned with the anode over the left (C1) or right (C2) - contralateral to the dominant limb, whereas the cathode over the FP2 or FP3, respectively (10-10 EEG electrodes placement). The groups were evaluated in four moments: pre-stimulation, and 30 minutes, 3 weeks and 8 weeks post-tDCS. They were evaluated in the different moments with International Myositis Assessment and Clinical Studies Group set scores, Short-Form health survey (SF-36), state-trait anxiety inventory (STAI), Beck depression inventory (BDI), timed up-and-go test (TUG), time-stands test (TST), isokinetic extension and flexion testing of bilateral knee and elbow. A specific security questionnaire for tDCS was used after the active or sham stimulation in all patients.
Results: The demographic data, kind of myositis, disease duration, and disease status (all with low disease activity) were comparable between both active and sham tDCS groups. After interventions, there was improvement of values of patient's VAS (P=0.042) and serum levels of creatine phosphokinase (P=0.005), independent of the group. Moreover, in active tDCS group, the physical aspects of SF-36 in week 8 (P<0.001), mean and better TST at each evaluation (P<0.001), absolute peak tork (P<0.001) and peak tork adjusted for body weight values (P<0.001) of stimulated inferior limb extension also improved. No differences were observed in the STAI, BDI, or TUG in both groups. The patients' adherence to the protocol was 100% and no adverse event was reported, including disease relapsing.
Conclusion: This unprecedented study evidences the safety of tDCS, besides the potential efficiency in improving rehabilitation of tDCS in SAMs. More studies with a large samples and period of tDCS sessions are necessaries to corroborate with the present study.
REFERENCES:
[1] Lundberg IE, et al. 2017 European league against rheumatism/ American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. Arthritis Rheum. 2017;69:2271-82.

[2] Tanaka S, et al. Single session of transcranial direct current stimulation transiently increases knee extensor force in patients with hemiparetic stroke. Neurorehabil Neural Repair. 2011;25:565-9.
Acknowledgements: This work was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) 303.379/2018-9, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) 2019/11776-6, Faculdade de Medicina da USP/SP to SKS.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3723

POS0888 EPIDEMIOLOGICAL AND CLINICAL DIFFERENCES BETWEEN ANTI-MDA5 PHENOTYPES: DATA FROM A LARGE COHORT (MEDRA5) STUDY

E. Trallero-Araguás[1], F. Romero[2], I. Castellví[3], V. Ortiz-Santamaria[4], S. Castañeda[5], O. Sanchez Pernaute[2], X. Solanich[6], R. Coto-Hernández[7], R. Garcia de Vicuna[5], Á. Robles Marhuenda[8], I. Rodriguez-Pubto[9], M. E. Ruiz-Lucea[10], L. Sáez-Comet[11], A. Selva-O'callaghan[12]on behalf of MEDRA5 (Spanish anti-MDA5 syndrome Register) group (listed contributors at the end of the abstract). *[1]Hospital Vall d'Hebron, Rheumatology, Barcelona, Spain*; *[2]Hospital Universitario Fundación Jiménez Díaz, Rheumatology, Madrid, Spain*; *[3]Hospital Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*; *[4]Hospital General de Granollers, Rheumatology, Granollers, Spain*; *[5]Hospital La Princesa, Rheumatology, Madrid, Spain*; *[6]Hospital de Bellvitge, Internal Medicine, Hospitalet de Llobregat, Spain*; *[7]Hospital Universitario Central de Asturias, Internal Medicine, Oviedo, Spain*; *[8]Hospital Universitario La Paz, Internal Medicine, Madrid, Spain*; *[9]Hospital Universitario Mutua de Terrassa, Internal Medicine,Terrassa, Spain*; *[10]Hospital Universitario Basurto, Rheumatology, Bilbao, Spain*; *[11]Hospital Miguel Servet, Internal Medicine, Zaragoza, Spain*; *[12]Hospital Vall d'Hebron, Internal Medicine, Barcelona, Spain*

Background: Idiopathic inflammatory myopathies are a heterogenous group of systemic autoimmune diseases. Several phenotypes have been linked to specific autoantibodies. Clinically amyopathic dermatomyositis with rapidly progressive interstitial lung disease, the most severe form of ILD, is associated with the anti-MDA5 antibodies. However not all the patients with dermatomyositis and anti-MDA5 positive antibodies develop this severe condition.
Objectives: We aim to define different phenotypes from a large cohort of patients diagnosed with dermatomyositis who were positive to anti-MDA5 antibodies.
Methods: We retrospective analyzed the clinical and immunological data of 90 anti-MDA5 patients [50 female, 55.6%, mean (SD) age at diagnosis 47 (15.4) yrs.] with dermatomyositis recruited from a multicenter register in Spain (MEDRA5) including 30 hospitals. All the patients fulfill de International Myositis Classification Criteria (EULAR/ACR) for dermatomyositis (score >90%). Anti-MDA5 were detected by means of commercial immunoblot (EUROIMMUN©). The chi-square test was used to assess the relationships between qualitative variables. The Kruskal-Wallis test was used to compared medians between groups.
Results: Sixty-six patients (73.3%) were diagnosed with clinically amyopathic dermatomyositis. Three different phenotypes linked with the anti-MDA5 antibody were identified. Group 1: patients with rapidly-ILD phenotype (28 patients, 31.1%), group 2: antisynthetase-like phenotype (23 patients, 25.5%), and group 3: non-ILD phenotype (39 patients, 43.3%). Clinical and immunological comparison between the groups disclosed that age at disease onset was higher (median, IQR) in patients from group 1 [53 (43-60)] vs. group 2 [46 (40-56)] or group 3 [42(41-51)] (p=0.01); disease onset was more frequent in spring in patients from group 1 (46.5%) than in the rest of the groups (21.7% and 28.9%) (p<0.01). Cancer was detected in 7 patients, only associated with myositis in 3 cases (3 years interval between cancer and dermatomyositis) without significant differences between phenotypes. Vasculitis (one case ANCA positive) was detected in 9 cases (6 limited to skin, 1 renal and 1 intestinal), 6 of them in the group 3 (statistical significance, in comparison with group 1 and 2, p<0.01). Mortality rate was higher in group 1 (51.9%, 16 out of 17 due to refractory respiratory failure) vs group 2 (12.5%) or 3 (0%) (p<0.001). Anti Ro52 positivity was more frequent in group 1 (65.4%) vs. group 2 (25%) or 3 (35.5%) (p<0.017), although it did not reach statistical significance in terms of mortality (p=0.173) or patients admitted in the intensive care unit (p=0.173). Mechanic hands were more frequent in group 2 (40.6%) than in groups 1 (25%) and 3 (34.4%) (p=0.05). Fever was significantly most frequent in group 1(52.6%) than in group 2 (21.1%) and 3 (26.3%) (p=0.001). Other clinical or immunological features such as arthritis, myositis, or the number of characteristic skin lesions among others were not more frequent in one group or another.
Conclusion: Three different phenotypes of patients positive to anti-MDA5 were identified. The presence or not of ILD, or the different type (rapidly progressive or not) of ILD were the main feature that allow to differentiate these phenotypes, which are relevant in clinical practice.

REFERENCES:
[1] Allenbach Y, Uzunhan Y, Toquet S, et al; French Myositis Network. Different phenotypes in dermatomyositis associated with anti-MDA5 antibody: Study of 121 cases. Neurology. 2020;95: e70-e78.
Acknowledgements: List of contributors of MEDRA5 group: Aguilar-García J (Internal Medicine, Hospital Costa del Sol, Marbella), Carrión-Barberá I (Rheumatology, Hospital del Mar, Barcelona), Cobo-Ibañez T (Rheumatology, Hospital Infanta Sofía, San Sebastián de los Reyes), de Escalante-Yangüela B (Internal Medicine, Hospital Clínico Lozano Blesa, Zaragoza), Fonseca-Aizpuru EM (Internal Medicine, Hospital de Cabueñes, Gijón), González-Cubillo L (Intensive Medicine, Hospital Universitario de Cruces, Barakaldo), González-Gay MA (Rheumatology, Hospital Marqués de Valdecilla, Santander), Prieto-González S (Internal Medicine, Hospital Clinic, Barcelona), Ruiz-Román A (Rheumatology, Hospital Universitario Virgen del Rocío, Sevilla), Calero-Paniagua I (Internal Medicine, Hospital Virgen de la Luz, Cuenca), Callejas-Rubio JL (Internal Medicine, Hospital Clínico San Cecilio, Granada), Gil-Vila A (Internal Medicine, Hospital Vall d'Hebron, Barcelona), de Miguel-Campo B (Internal Medicine, Hospital Doce de Octubre, Madrid), García-Sevilla R (Pneumology, Hospital General Universitario de Alicante, Alicante), Iriarte-Fuster A (Internal Medicine, Hospital de Bellvitge, Hospitalet de Llobregat), Jovani-Casano V (Rheumatology, Hospital General Universitario de Alicante, Alicante), Lozano-Rivas N (Rheumatology, Hospital Virgen de la Arritxaca, Murcia), Martín-Gascón M (Internal Medicine, Hospital Morales Meseguer, Murcia), Martinez-González O (Rheumatology, Hospital Universitario de Salamanca, Salamanca), Monteagudo-Jiménez M (Internal Medicine, Hospital Parc Taulí, Sabadell), Mora-Ortega GM (Pneumology, Hospital Universitario Infanta Sofía, San Sebastián de los Reyes), Moral-Moral Pedro (Internal Medicine, Hospital Universitari i Politecnic La Fe, Valencia), Pérez-De Pedro I (Interna Medicine, Hospital Regional Universitario de Málaga, Málaga), Picazo-Talavera MR (Rheumatology, Hospital del Sureste, Madrid), Rubio-Rivas M (Internal Medicine, Hospital de Bellvitge, Hospitalet de Llobregat)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3837

POS0889 CO PRESCRIPTION OF ANTI-ACID THERAPY REDUCES THE BIO AVAILABILITY OF MYCOPHENOLATE MOFETIL IN SYSTEMIC SCLEROSIS PATIENTS

G. Alex[1], S. K C[2], D. Reachel Varghese[1], S. Babu A S[2], R. Reji[2], P. Shenoy[2]. *[1]Center for Arthritis and Rheumatism Excellence (CARE), Rheumatology, Kochi, India*; *[2]Center for Arthritis and Rheumatism Excellence (CARE), Rheumatology, Kochi, India*

Background: Mycophenolate mofetil (MMF) is an effective treatment option for systemic sclerosis (SSC). However, many patients require co administration of proton pump inhibitors (PPI) or H2 receptor blockers (HRB) because of significant gastrointestinal manifestations in SSC. Co-treatment with PPI or HRB have shown to be associated with reduced drug exposure in post-transplant patients.[1, 2] There is scarcity of data among patients with SSC. We evaluated the drug concentration of MMF over 12 hours of exposure and assessed the impact of ranitidine and PPI in twenty patients with SSC.
Objectives: To assess the effect of esomeprazole or ranitidine on the bioavailability of MMF in SSC patients who are on a stable dose of MMF.
Methods: Twenty SSC patients, who were on a stable dose of MMF (1.5-3 g) for the past 3 months were selected for the study after obtaining informed written consent. All patients were given either MMF (without PPI or HRB), MMF + esomeprazole, MMF + ranitidine for one month each. At the end of each month, EDTA plasma samples were collected at various time points including 0, 1/2, 1, 1½, 2, 2½, 3, 4, 5, 6, 8 and 12 hours following drug administration to determine the 12-hour area under curve (AUC) of mycophenolic acid (MPA) levels. Estimation of MPA levels was carried out using reverse phase high performance liquid chromatography (HPLC). Total gastrointestinal score was calculated at the end of each month using UCLA Scleroderma Clinical Trial Consortium GIT 2.0 scoring. To compare the mean AUC, linear mixed effect model was fit by considering treatment as the fixed effect and subject as the random effect. MMF was set as the reference treatment for the other three treatments and these were analysed together using Linear mixed effect model.
Results: All patients were females with mean age of 45 years. Addition of either ranitidine or esomeprazole significantly reduced the mean AUC and C max of the MMF over 12-hour time period. On the other hand, PPI or HRB helped in reduction of the total GI score at the end of 1 month. Details of pharmacokinetics are depicted in the table 1.

Table 1. Pharmacokinetics and GI score with MMF in combination with PPI / HRB

	MMF	MMF+ R	MMF + E	p
AUC	67.97 (62.73, 73.20)	53.04 (44.80, 61.27)	45.69 (41.10, 50.28)	<0.001*
mean (95% CI) **T- MAX**	42.00 (33.60, 50.40)	46.50 (32.48, 60.52)	79.50 (58.99, 100.01)	<0.001*
mean (95% CI) **C-MAX**	29.61(26.74, 32.48)	15.14 (11.32, 18.97)	12.62 (10.58, 14.66)	<0.001*
mean (95% CI) **Mean GI score**	0.28 (0.15,0.40)	0.19 (0.09, 0.30)	0.14 (0.06,0.23)	0.009
mean (95% CI)				

AUC, area under curve Mycophenolic acid; C-MAX, maximum concentration of MPA in 12 hours following MMF; CI confidence interval;Mean GI score, UCLA Scleroderma Clinical Trial Consortium GIT 2.0 scoring; MMF, mycophenolate mofetil; MMF+E, mycophenolate mofetil + esomeprazole; MMF+R, mycophenolate mofetil+ ranitidine;*p value < 0.05 considered as significant

Conclusion: As co administration of PPI or HRB can significantly reduce the bio-availability of MMF in patients with systemic sclerosis. To avoid therapeutic failure of MMF drug level monitoring is essential when these agents re prescribed with MMF.

REFERENCES:

[1] Schaier M, Scholl C, Scharpf D, Hug F, Bönisch-Schmidt S, Dikow R, et al. Proton pump inhibitors interfere with the immunosuppressive potency of mycophenolate mofetil. Rheumatology (Oxford, England). 2010;49:2061–7.

[2] Rissling O, Glander P, Hambach P, Mai M, Brakemeier S, Klonower D, et al. No relevant pharmacokinetic interaction between pantoprazole and mycophenolate in renal transplant patients: a randomized crossover study. British Journal of Clinical Pharmacology. 2015;80:1086–96.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3898

POS0890 MACROVASCULAR DYSFUNCTION AND ITS CLINICAL IMPLICATION IN SYSTEMIC SCLEROSIS

D. Bairwa[1], C. Kavadichanda[1], V. Negi[1]. [1]*Jawaharlal Institute of Postgraduate Medical Education and Research, Clinical Immunology, Puducherry, India*

Background: Even though microvascular dysfunction has been implicated in pathogenesis of scleroderma (SSc), there is minimal evidence to suggest presence of macrovascular dysfunction. The clinical implication of macrovascular dysfunction in SSc is unknown. Moreover, data on the correlation between dysfunction in small and large blood vessel is inconclusive. [1-2]

Objectives: To study the correlation between macrovascular dysfunction as assessed by percent change in flow mediated vasodilation (FMD) of brachial artery and microvascular dysfunction as assessed by nail fold capillaroscopy (NFC) findings in SSc. To assess the clinical impact of macrovascular dysfunction.

Methods: This cross-sectional comparative study enrolled patients with SSc and age and gender matched healthy controls. FMD change was calculated using standard USG probe of 5 to 6 MHz in right brachial diameter from the average of 3 consecutive end diastolic frames. NFC was performed using portable nail fold capillary microscope at 800X magnification. Clinical features of SSc were compared between SSc patients with and without macrovascular dysfunction.

Results: This study enrolled 59 SSc patients including 29 (49.2%) diffuse, 20 (20.4%) limited, 08 (10.2%) sine SSc and 2 patients (3.4%) with myositis overlap. SSc patients had significantly (p-<0.0001) lower % FMD change compared to healthy controls. NFC showed significantly higher architecture distortion (p-<0.0001), loss of capillaries (p-<0.0001) and abnormal capillaries (p-<0.0001). There was no correlation between FMD change and capillary density (p-0.381), avascular area (p-0.266) and abnormal capillaries (p-0.899). None of the clinical features like pulmonary hypertension, digital ulcer burden, acro-osteolysis and auto amputation were different between SSc with and without macrovascular dysfunction.

Conclusion: Macrovascular dysfunction in SSc is substantial and it seems to be independent of the microvascular dysfunction. The clinical implications of macrovascular dysfunction are yet to be identified.

REFERENCES:

[1] Schioppo T, Orenti A, Boracchi P, De Lucia O, Murgo A, Ingegnoli F. Evidence of macro- and micro-angiopathy in scleroderma: An integrated approach combining 22-MHz power Doppler ultrasonography and video-capillaroscopy. Microvasc Res. 2019 Mar;122:125–30.

[2] Rollando D, Bezante GP, Sulli A, Balbi M, Panico N, Pizzorni C, et al. Brachial Artery Endothelial-dependent Flow-mediated Dilation Identifies Early-stage Endothelial Dysfunction in Systemic Sclerosis and Correlates with Nailfold Microvascular Impairment. J Rheumatol. 2010 Jun 1;37(6):1168–73.

Table 1. Comparison of various parameters between the SSc patients with healthy controls.

Parameter	Frequency (percentage)/median (interquartile range)	
	SSc patients (n=59)	Healthy controls (n=64)
Demographic details		
Age in years	38 (27-46)	36.5 (28.25-42)
Gender		
Male	03 (5.1%)	03 (4.7%)
Female	56 (95.1%)	61 (95.3%)
FMD findings		
FMD % change*	4.54 (3.13-8.82)	10.30 (8.33-13.16)
NFC findings		
Number of capillaries*	51 (38-63)	121 (113-128)
Average capillary density*	3.19 (2.38-3.94)	7.56 (7.06-8)
Disorganized architecture (%)*	37.5 (12.5-37.5)	0
U shape (%)*	50 (36.59-68.09)	85.51 (82.97 – 88.53)
Abnormal (%)*	36.11 (14.03-55.26)	0
Enlarged (%)*	10.63 (2.94-23.68)	0
Giant (%)*	21.05 (0-45.45)	0
Microhemorrhages (%)*	6.25 (0-12.5)	0
Neoangiogenesis (%)*	3.85 (0-20)	0
Avascular area (%)*	50 (31.25- 75)	0

*parameters with statistically significant (p value< 0.0001) difference among two groups. SSc; Systemic Sclerosis, FMD; flow mediated vasodilatation, NFC; nail fold capillaroscopy

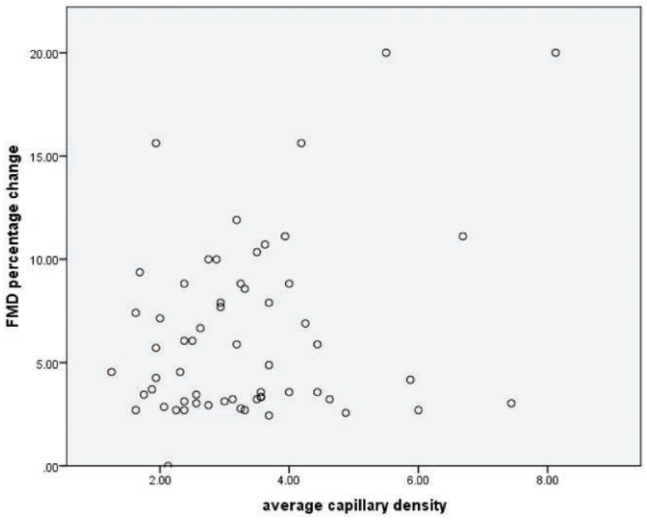


Figure 1. Scatter plot showing correlation between FMD percentage change and average capillary density. (r= 0.116) (P-value - 0.381)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3916

POS0891 IMPROVED SURVIVAL IN SYSTEMIC SCLEROSIS PATIENTS DURING LAST DECADE: CURRENT FINDINGS AND COMPARISON WITH DIFFERENT PREVIOUS ITALIAN COHORTS

F. Cacciapaglia[1], E. De Lorenzis[2], M. G. Lazzaroni[3], A. Corrado[4], M. Fornaro[1], G. Natalello[2], F. Montini[1], A. Altomare[4], L. Urso[1], F. P. Cantatore[4], S. L. Bosello[2], P. Airò[3], F. Iannone[1]. [1]*Rheumatology Unit - University and AOUC Policlinico of Bari, Department of Emergency and Organ Transplantations, Bari, Italy*; [2]*Division of Rheumatology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Roma, Italy*; [3]*Rheumatology and Clinical Immunology Unit, ASST Spedali Civili, Brescia, Italy*; [4]*Rheumatology Clinic, Department of Medical and Surgical Sciences - University of Foggia, Foggia, Italy*

Background: Systemic Sclerosis (SSc) is a chronic rheumatic disease characterized by an autoimmune disorder with vasculopathy that leads to an excess in collagen and other extracellular matrix proteins deposition. This process results in progressive fibrotic and vascular damage of skin and visceral organs.

According to observational studies conducted in last decades, mean survival of SSc patients had improved with significant changes in causes of death.
Objectives: To assess the 10-years survival in a large Italian multicentre cohort of SSc patients in the last decade compared to previous periods published since the 1980s, and to identify features that can justify any change.
Methods: We retrospectively analysed all medical records of our longitudinal SSc cohorts, fulfilling 1980 ARA and/or 2013 EULAR/ACR Classification Criteria, with a median (IQR) follow-up of 91.5 (51-120) months from 4 Scleroderma Units since January 2009. All clinical, laboratory and instrumental findings have been recorded and analysed. Survival rate was calculated with Kaplan-Meier curves and log-rank tests, and Cox proportional hazards models were used to identify any predictor. Then, observed SSc survival was compared to those previously published and to that expected in the general population, calculated using official data published on the website United Nation World Population Prospects (www.macrotrends.net/countries/ITA/italy/death-rate).
Results: Of 912 SSc patients (91.6% female; mean (SD) age at first non-Raynaud symptom (RS) 51 (15.4) years; median (IQR) disease duration from non-RS 24 (0-84.7) months) diffuse cutaneous involvement was defined in 182 (20%) patients. Anti-centromere and anti-topoisomerase-I were detected in 390 (42.8%) and 302 (33.1%) patients, respectively, while 220 (24.1%) presented antibodies for other extractible nuclear antigens. Prevalent non-Raynaud manifestations were interstitial lung disease detected in 459 (50.3%), digital ulcers in 395 (43.3%) and oesophagopathy in 371 (40.7%) patients, respectively, while other gastrointestinal manifestations were reported in 234 (25.7%) patients. Chronic renal failure was observed in 61 (6.7%) patients and pulmonary arterial hypertension (PAH) was confirmed at right heart catheterization in 38 (4.2%) patients. Three hundred twenty-two (35.3%) patients received immunosuppressant, 215 (23.5%) assumed an endothelin receptor antagonist and/or a 5-phosphodiesterase inhibitor, and 72 (7.9%) were treated with a biologic agent. The global 10-years survival was 89.4%; female gender (HR 0.33, CI95% 0.17-0.67), diffuse cutaneous involvement (HR 2.14, CI95% 1.17-3.91), presence of pulmonary hypertension (HR 2.61, CI95%1.31-5.16) and older age at non-RS (HR 1.1, CI95% 1.06-1.12) affected survival. Furthermore, as compared to previous Italian studies, our cohort showed a significant improvement in rate (see Figure 1).
Conclusion: Survival in SSc patients has improved in last 5 decades but still reduced compared to that expected in general population above all 5 years after diagnosis. Early diagnosis, with reduced renal involvement, along with better screening and innovative therapeutic strategies may explain these achievements.

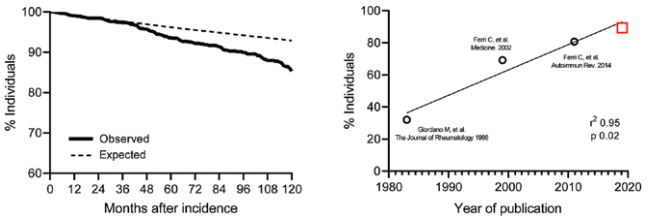


Figure 1. Ten-years survival in SSc patients since 2009 (left); comparison of survival across different Italian SSc cohorts (box: current analysis) (right).

REFERENCES:
[1] Giordano M, et al. The Journal of Rheumatology. 1986; 13:911-916.
[2] Ferri C, et al. Medicine. 2002; 81:139-53.
[3] Vettori S, et al. Reumatismo. 2010; 62(3):202-209.
[4] Ferri C, et al. Autoimmun Rev. 2014; 13(10):1026-34.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3943

POS0892 QUANTITATIVE CT INDEXES: PROMISING TOOLS FOR OBJECTIVE ASSESSMENT OF PULMONARY FIBROSIS IN SYSTEMIC SCLEROSIS

D. Temiz Karadağ[1,2], O. Cakir[3], S. Şan[1], A. Yazici[1], A. Cefle[1]. [1]*Kocaeli University Faculty of Medicine, Department of Rheumatology, Kocaeli, Turkey*; [2]*Canakkale Mehmet Akif Ersoy State Hospital, Department of Rheumatology, Canakkale, Turkey*; [3]*Kocaeli University Faculty of Medicine, Department of Radiology, Kocaeli, Turkey*

Background: Pulmonary fibrosis (PF) occurs in the majority of patients with SSc and is a leading cause of SSc-related death. SSc related PF has heterogeneous disease progression: many patients will have a chronic, indolent course while others may develop the progressive, life-threatening disease.
Objectives: The objective of this study is to investigate the discrimination performance of quantitative CT indexes in identifying the parenchymal differences between the SSc and the control groups. We also aimed to demonstrate the correlation among quantitative indexes (QI), spirometric pulmonary function tests, and visual CT scores in patients with PF.
Methods: A total of 135 SSc patients (female 87.4%; age, 50±13 years), 41 of whom had pulmonary fibrosis (PF), and 38 healthy subjects (female 89.5%; age, 52±6 years) were enrolled. All participants underwent volume thin-section CT in the supine position at full inspiration and spirometry. Quantitative indexes (QIs) were obtained using dedicated software for the segmentation of the lung (Vital Images Vitrea Workstation; Version 7.12.3.133). QIs included total lung volume (TLV), low attenuation (LA) volume (-1020 HU<pixel<-920 Hounsfield units [HU]), medium attenuation (MA) volume (-920 HU<pixel<-920 HU), and high attenuation (HA) volume (-720<pixel<0 HU). The global extent of pulmonary parenchymal abnormality was measured semiquantitatively by visual scoring (VS) and functional lung volume was derived. The functional lung volume, total MA volume, and ratio of total MA to total lung volume were assumed as the indexes of normal lung parenchyma.
Results: MA volumes, HA volumes, total lung volumes and the ratio of MA volume to total lung volume differed significantly between the patients with PF, patients without PF, and the control group. In the PF group, FVC showed significant correlation with functional lung volume (r=0.45, p=0.014) and total MA volume (r=0.48, p=0.009); DLCO showed significant correlation with VS of normal lung parenchyma (r=0.65, p<0.001), functional lung volume (r=0.53, p=0.006), total MA volume (r=0.54, p=0.005) and ratio of total MA to total lung volume (r=0.42, p=0.031). The functioning lung volume obtained by VS and total MA volume showed excellent correlation (r=0.78, p<0.001).
Conclusion: Quantitative indexes measured by soft-ware differentiated the patients with PF from the patients without PF and healthy subjects. The indexes used to evaluate the normal lung parenchyma showed a good correlation with pulmonary function test results. Quantitative indexes can be used as an objective complementary tool for the evaluation of the lung areas unaffected by PF.

Table 1. Quantitative Indexes of CT in the Control, SSc without PF and SSc with PF Groups

	Control	SSc without PF	SSc with PF	*p*
Right lung LA volume (ml)	372±375	420±446	254±308	0.102
Right lung MA volume (ml)	1230±408	1377±441	987±451	<0.001
Right lung HA volume (ml)	531±152	494±177	625±215	0.004
Left lung LA volume (ml)	342±370	367±383	221±271	0.089
Left lung MA volume (ml)	1014±383	1170±433	805±402	<0.001
Left lung HA volume (ml)	563±176	516±251	620±289	0.037
Total lung LA volume (ml)	712±736	827±959	517±653	0.119
Total lung MA volume (ml)	2212±863	2548±862	1756±850	<0.001
Total lung HA volume (ml)	1072±343	1009±406	1290±522	0.005
Total lung volume (ml)	3996±1237	4385±1256	3563±1236	0.002
Mean lung density (HU)	-799±61.4	-798±63	-730±75	<0.001
Total MA volume/Total lung volume	0.55±0.12	0.59±0.13	0.49±0.15	0.002

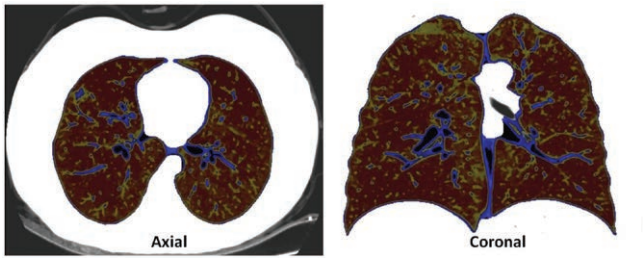


Figure 1. Segmentation of lung parenchyma

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3992

POS0893 NON-INVASIVE CUTANEOUS ASSESSMENT OF SYSTEMIC SCLEROSIS- THE NEW OUTLOOKS

P. S. Wong[1], D. Kurzeja[1], B. Ahmed Abdi[1], R. Stratton[1]. [1]*Royal Free Hospital and University College Medical School, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom*

Background: Systemic sclerosis (SSc) is a rare connective tissue disease with abnormalities in vasculopathy, immune dysregulation and fibrosis resulting in skin and internal organ damages. Severity of skin involvement is known to correlate with organ-related mortality in particular pulmonary involvement. Variables skin assessment tools are available, modified Rodnan Skin Score (mRSS) is currently best validated and used widely. The immediate action of finding an ideal,

clinically convenient objective methods is crucial to better clinicians' care for SSc patents.

Objectives: Explore the potential of commercially available handheld, non-invasive devices for SSc skin analysis.

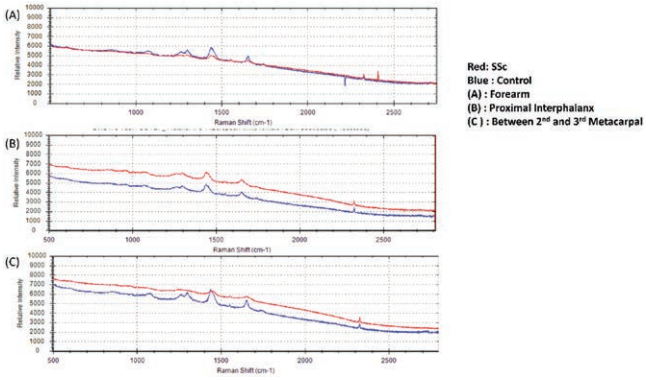
Methods: 1.Measure skin surface Adenosine Triphosphate (ATP) level with handheld ATP bioluminator (SystemSURE Plus, Hygiena) over the forearm of SSc(n= 51) and controls (n=50) 60seconds after sterilization to eliminate extrinsic factors. The bioluminometer expresses ATP test results in Relative Light Units (RLU) that is directly proportional to the amount of ATP on the test sample (Unit conversion: 1RLU = 1fM).

2.In-vivo Raman Spectra measurement of SSc skin comparing with matched healthy controls on proximal phalangeal, area between 2nd and 3rd metacarpal and forearm. Our measurments include laser power of 250mw, excitation length of 785nm and spectral range from 500 to 2800cm^{-1}.

Measurements were analysed with patients' phenotypes and clinical characteristics.

Results: Flow cytometry showed increase expression of P2X7 (purinergic) receptor and CD206 in M2-Macrophage in SSc compare to controls [(724.4 vs 472.9, 776.1 vs 632.2)]. CD206 expression positively correlated with P2X7 levels (p<0.001, r2=0.76) and mRSS (p<0.05, r2=0.26). In real life scenario, measurement of purinergic metabolites is laboratorial tedious. ATP bioluminator measurement reviewed significant higher skin surface ATP in SSc than controls (188fM ± 53 [95% CI = 84, 300] vs 44fM ± 6 [95% CI = 33, 56], p< 0.003). And the intensity is negatively correlate with duration of disease in SSc (r = - 0.25, p = 0.096).

We obtain Raman spectra in SSc patient and control. Our study both groups have similar Raman curve when Raman Spectrometry were performed on skin surfaces. However, the relative intensity of each peaks of the curve were overtly flatter in SSc. This finding were similar for both Limited and Diffuse SSc in gross review of the graph representative. In addition to that, our analysis reviewed a peak at Raman shift of 2410 cm^{-1} that is characteristically present in forearm of a SSc but not in controls (Figure 1). Its significant yet to be determined.



Conclusion: Both ATP bioluminator and Raman Spectrometry is widely available commercially which are widely used in industrial, agriculture and cosmetology and dermatology in particular for Raman Spectrometry. It is commonly for assessing physically property of skin, determine drug administration and diagnosis of variable skin condition in particular cancer diagnosis. The advantages of these tools in SSc skin analysis include:

1.Non-invasive nature of skin analysis (compares to skin biopsy),
2.Portable devices easily mobilized in clinic setting,
3.Advanced technology allows molecular analysis of skin hence able to objectively classify grades of skin inflammation and determine drug efficacy
4.Possible better accuracy compares to other methods (eg. Ultrasound) which are operators dependent,
5.Widely available Raman signal database of different types of chemical compounds and expertise made the collection and analysis of date convenient

Our study has provide preliminary outlook and idea of utilizing commercially available devices on skin analysis in SSc. Further study in larger cohort are to be considered.

REFERENCES:

[1] Burnstock G, Knight GE, Greig AV. Purinergic signaling in healthy and diseased skin. The Journal of investigative dermatology. 2012;132(3 Pt 1):526-46.

[2] Franzen L, Windbergs M. Applications of Raman spectroscopy in skin research. Advanced Drug Delivery Reviews.Volume 89.2015. Pages 91-104.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4044

POS0894 ANTI-IL-6 THERAPY EFFECT FOR REFRACTORY JOINT AND SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS: A REAL-WORLD, SINGLE CENTER EXPERIENCE

S. Panopoulos[1], M. Tektonidou[1], V. K. Bournia[1], A. Arida[1], P. Sfikakis[1]. [1]*National and Kapodistrian University of Athens, First Propedeutic and Internal Medicine, Joint Rheumatology Program, Medical School, Athens, Greece*

Background: Emerging evidence during the last two decades supports a pivotal role of Interleukin 6 (IL-6) in the pathogenesis of Systemic Sclerosis (SSc). Standard immunosuppressive agents are often inadequate to control disease activity in SSc patients and treatment failure of multiple regimens is frequent in real-world practice.

Objectives: To examine the efficacy and safety of interleukin-6 receptor inhibition by tocilizumab in selected real-world patients with SSc.

Methods: Twenty-one patients (20 women, 16 diffuse SSc, mean age: 52±10 years, mean disease duration: 6.4±3.7 years, all with negative rheumatoid factor and anti-cyclic citrullinated antibodies, none with overlap syndrome with RA) with active joint and skin involvement refractory to corticosteroids (n=21), methotrexate (n=17), cyclophosphamide (n=10), mycophenolate (n=7), rituximab (n=1), leflunomide (n=2), hydroxychloroquine (n=2), and hematopoietic stem cell transplantation (n=2) who received weekly tocilizumab (162 mg subcutaneously) in an academic center, were monitored prospectively. Changes in Eustar modified activity index (MAI), modified Rodnan skin score (mRSS), disease activity score (DAS)28, lung function tests (LFTs) and patient reported outcomes (PROs) were analyzed at one year of treatment and at the end of follow-up.

Results: One patient discontinued tocilizumab after 3 months due to inefficacy. During the first year of treatment, 12 patients achieved low disease activity (mean MAI change -2.9±1.8, p<0.001) and significant clinical improvement was evident in 12 patients regarding skin involvement (mean mRSS change: -6.9±5.9, p<0.001) and in 16 patients regarding polyarthritis (mean DAS28 change: -1.9±0.8, p<0.001); Accordingly, improvements were recorded for all PROs (all p<0.001) (Table 1). Lung function tests' stabilization was also observed in 16/20 patients. During the second year, 3 patients discontinued tocilizumab (cytomegalovirus infection in 1, inefficacy in 2) and one died. Beneficial effects were sustained in all 16 patients at follow-up end (mean duration of Tocilizumab treatment 2.2 ± 1.1 years), apart from LFTs deterioration in 3. Except for recurrent digital ulcer infection in 3 patients, tocilizumab was well-tolerated.

Conclusion: Tocilizumab was effective in refractory joint and skin involvement irrespective of SSc disease duration or subtype. Long-term retention rates and disease stabilization for most real-world patients suggest that tocilizumab might be a valuable choice for difficult-to-treat SSc.

Table 1. Clinical and laboratory parameters and measures (mean ± SD) at baseline and after one year of treatment with tocilizumab in 20 patients with Systemic Sclerosis

	Baseline	1st year	change	p
Modified activity index	4.9 ± 1.6	2.0± 1.2	-2.9 ± 1.8	**<0.001**
mRSS	21.5 ± 9.5	14.6 ± 6.6	-6.9 ± 5.9	**<0.001**
DAS28	5.3 ± 0.7	3.4 ± 0.6	-1.9 ± 0.8	**<0.001**
FVC (% of predicted)	82 ± 19.5	79 ± 19.1	-2.9 ± 12	0.389
DLCO (% of predicted)	60.4 ± 16.3	61.1 ± 18.4	0.7 ± 12.3	0.844
ESR (mm/1st hr)	35.6 ± 17.2	12.9 ± 11.8	-22.8 ± 19.1	**0.001**
CRP (mg/l)	13.2 ± 12.5	1.2 ± 2.1	-12 ± 13.1	**0.006**
SHAQ	1.6 ± 0.8	1.0 ± 0.7	-0.6 ± 0.5	**<0.001**
VAS patient global score	37.8 ± 16.8	60.5 ± 15.4	22.7 ± 20.3	**<0.001**
VAS physician global score	33.4 ± 13.2	63.2 ± 13.9	29.8 ± 15.6	**<0.001**

mRSS: modified Rodnan skin score; DAS28: disease activity score 28; FVC: forced vital capacity; DLCO: diffusing lung capacity for carbon monoxide; ESR: erythrocyte sedimentation rate; CRP: c-reactive protein; SHAQ: scleroderma health assessment questionnaire; VAS: visual analogue scale

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4131

Spondyloarthritis – treatment

POS0895 EFFECT OF TOFACITINIB ON PATIENT-REPORTED OUTCOMES IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM A PHASE 3 TRIAL

V. Navarro-Compán[1], J. C. C. Wei[2], F. Van den Bosch[3], M. Magrey[4], L. Wang[5], D. Fleishaker[5], J. C. Cappelleri[5], C. Wang[5], J. Wu[5], O. Dina[6], L. Fallon[7], V. Strand[8]. *[1]University Hospital La Paz, Rheumatology Department, Madrid, Spain*; *[2]Chung Shan Medical University Hospital, Department of Internal Medicine, Taichung, Taiwan, Republic of China*; *[3]Ghent University Hospital, Department of Rheumatology, Ghent, Belgium*; *[4]Case Western Reserve University, Division of Rheumatology, Cleveland, OH, United States of America*; *[5]Pfizer Inc, Inflammation and Immunology, Groton, CT, United States of America*; *[6]Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*; *[7]Pfizer Inc, Inflammation and Immunology, Kirkland, QC, Canada*; *[8]Stanford University, Division of Immunology/Rheumatology, Palo Alto, CA, United States of America*

Background: Ankylosing spondylitis (AS) can significantly impact quality of life. Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of adult patients (pts) with AS. The safety/efficacy (including pt-reported outcomes [PROs]) of tofacitinib in pts with AS was assessed in a Phase 3 trial (NCT03502616).[1]

Objectives: To evaluate the effect of tofacitinib on pt-reported pain, fatigue, overall health and work productivity in pts with active AS enrolled in the Phase 3 trial.

Methods: Pts with an inadequate clinical response or intolerance to ≥2 oral NSAIDs were randomised in a double-blind fashion to tofacitinib 5 mg twice daily (BID) or placebo (PBO) for 16 weeks. At Week (W)16, all pts received open-label tofacitinib 5 mg BID up to W48. Least squares (LS) mean changes from baseline (Δ) up to W48 are reported for the following outcomes: pt assessment of nocturnal spinal pain, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Short Form-36 Health Survey version 2 (SF-36v2; W16 and W48 only), and Work Productivity and Activity Impairment Questionnaire (WPAI; W16 and W48 only).

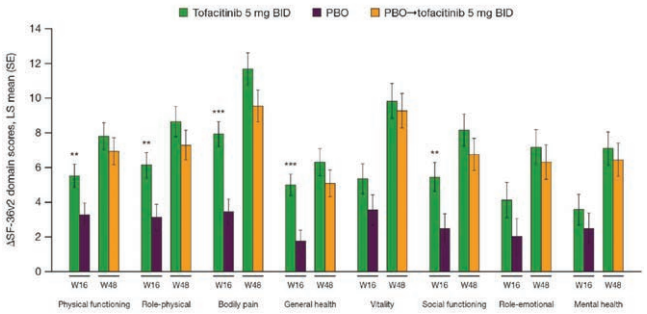
Results: At W16, there were greater improvements from baseline in pain (total back pain [previously published[1]] and nocturnal spinal pain) and fatigue (FACIT-F total score; experience and impact domain scores) with tofacitinib vs PBO ($p \leq 0.05$; Table 1); improvements were observed as early as W2. Also, improvements in SF-36v2 physical component summary (PCS) (Table 1), and physical functioning, role-physical, bodily pain, general health and social functioning domains (Figure 1) were greater with tofacitinib vs PBO at W16 ($p \leq 0.05$). Similarly, improvements in WPAI scores at W16 were greater with tofacitinib vs PBO ($p \leq 0.05$), except for % work time missed (Table 1). Improvements with tofacitinib continued up to W48 (Table 1/Figure 1). Generally, pts receiving PBO who advanced to tofacitinib at W16 reported similar improvements after switching to tofacitinib (Table 1/Figure 1).

Table 1. PROs at baseline and Δ at W16 and W48

	Baseline, mean (SD) [N1]		Δ, W16, LS mean (SE)			Δ, W48, LS mean (SE)	
	Tofacitinib 5 mg BID (N=133)	PBO (N=136)	Tofacitinib 5 mg BID	PBO	p value	Tofacitinib 5 mg BID	PBO→ tofacitinib 5 mg BID
Nocturnal spinal pain[a]	6.8 (1.9)	6.8 (1.9)	-2.67 (0.20)	-0.84 (0.20)	<0.0001	-3.52 (0.23)	-3.01 (0.23)
FACIT-F total score[a,b]	27.2 (10.7)	27.4 (9.3)	6.54 (0.80)	3.12 (0.79)	0.0008	9.54 (0.90)	7.35 (0.89)
FACIT-F experience domain[a]	8.9 (4.3)	8.7 (4.0)	2.85 (0.36)	1.29 (0.36)	0.0007	4.22 (0.40)	3.40 (0.40)
FACIT-F impact domain[a]	18.3 (6.9)	18.8 (5.9)	3.68 (0.49)	1.81 (0.49)	0.0028	5.32 (0.54)	3.95 (0.54)
SF-36v2 PCS[b,c]	33.5 (7.3)	33.1 (7.0) [135]	6.69 (0.59)	3.14 (0.59)	<0.0001	8.81 (0.720)	7.39 (0.71)
SF-36v2 MCS[c]	39.4 (11.1)	39.8 (12.7) [135]	3.45 (0.91)	2.13 (0.92)	0.2529	7.07 (0.93)	6.35 (0.92)
WPAI[c]							
% activity impairment	56.5 (23.4)	56.0 (21.4)	-19.03 (1.97)	-5.63 (1.97)	<0.0001	-27.37 (2.34)	-19.77 (2.31)
% work time missed	9.9 (22.4) [81]	11.5 (24.6) [88]	-3.65 (2.66)	0.88 (2.62)	0.1784	-8.10 (2.14)	-5.79 (2.05)
% impairment while working	48.4 (26.3) [79]	49.6 (22.2) [85]	-19.83 (2.27)	-6.94 (2.30)	<0.0001	-25.35 (2.77)	-23.00 (2.66)
% overall work impairment	50.8 (27.4) [79]	53.5 (23.1) [85]	-21.49 (2.51)	-7.64 (2.56)	<0.0001	-27.63 (3.01)	-23.22 (2.90)

[a]MMRM [b]Global type I error-controlled endpoint [c]Analysis of covariance model for W16 and MMRM for W48MCS, mental component summary; MMRM, Mixed Model for Repeated Measures; N, number of pts in full analysis set; N1, number of pts included in the analysis (if different from N); SD, standard deviation; SE, standard error

Figure. LS mean ΔSF-36v2 domain scores (norm-based) at W16 and W48



**p<0.01, ***p<0.001 for tofacitinib 5 mg BID vs PBO (analysis of covariance model)

Conclusion: In pts with active AS, improvements in spinal pain, fatigue, overall health and work productivity were greater with tofacitinib vs PBO at W16; improvements continued up to W48. These PRO findings support the primary efficacy results of this Phase 3 trial,[1] and add to the overall understanding of the benefit/risk profile of tofacitinib in patients with AS.

REFERENCES:

[1] Deodhar et al. Arthritis Rheumatol 2020; 72 (S10): Abs L11.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Emma Mitchell, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer Inc, UCB, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer Inc, UCB, Grant/research support from: AbbVie, Novartis, James Cheng-Chung Wei Speakers bureau: Eli Lilly, Janssen, Novartis, Pfizer Inc, Consultant of: Eli Lilly, Novartis, Pfizer Inc, Grant/research support from: AbbVie, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, UCB, Filip van den Bosch Shareholder of: AbbVie, Celgene, Eli Lilly, Galapagos, Gilead, Merck, Novartis, Pfizer Inc, UCB, Marina Magrey: None declared, Lisy Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Dona Fleishaker Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Joseph C Cappelleri Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Cunshan Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Joseph Wu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Oluwaseyi Dina Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lara Fallon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Vibeke Strand Consultant of: AbbVie, Amgen, Arena, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Corrona, Eli Lilly, Galapagos, Genentech/Roche, Gilead, GSK, Ichnos, Inmedix, Janssen, Kiniksa, Merck, Myriad Genetics, Novartis, Pfizer Inc, Regeneron, Samsung, Sandoz, Sanofi, Scipher, SetPoint Medical, UCB

DOI: 10.1136/annrheumdis-2021-eular.106

POS0896 PREDICTORS OF RESPONSE IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS RECEIVING CERTOLIZUMAB PEGOL IN THE C-AXSPAND STUDY

W. P. Maksymowych[1], T. Kumke[2], S. Auteri[3], B. Hoepken[2], L. Bauer[2], M. Rudwaleit[4,5]. *[1]University of Alberta, Department of Medicine, Division of Rheumatology, Edmonton, Canada*; *[2]UCB Pharma, N/A, Monheim am Rhein, Germany*; *[3]UCB Pharma, N/A, Brussels, Belgium*; *[4]Klinikum Bielefeld, Clinic for Internal Medicine and Rheumatology, Bielefeld, Germany*; *[5]Charité – Universitätsmedizin Berlin, Department of Gastroenterology, Infectiology and Rheumatology, Berlin, Germany*

Background: Identification of predictive clinical factors of long-term treatment response in non-radiographic axial spondyloarthritis (nr-axSpA) may contribute to improved management of patients with this chronic disease. Certolizumab pegol (CZP) is currently the only FDA-approved tumour necrosis factor inhibitor (TNFi) for treatment of nr-axSpA.[1]

Objectives: To identify whether any demographic or baseline characteristics of nr-axSpA patients from the C-axSpAnd study[2] are predictive of achieving a clinical response after 1 year of CZP treatment.

Methods: C-axSpAnd (NCT02552212) was a phase 3, interventional multicentre study including a 52-week double-blind, placebo-controlled period. Full

study design is reported elsewhere.[2] Multivariate stepwise logistic regression analysis was used to identify predictors of response for the primary efficacy variable (Ankylosing Spondylitis Disease Activity Score – major improvement [ASDAS-MI] at Week 52) and the main secondary efficacy variable (Assessment of SpondyloArthritis international Society 40% [ASAS40] at Week 52) in patients randomised to CZP 200 mg every 2 weeks (Q2W). Predictive factors used in the model included demographic and baseline characteristics, and clinical outcomes at Week 12. A p value ≤0.05 was required for forward selection into the model and p=0.1 for backward elimination from the model. Non-responder imputation was used to account for missing data or values collected after switching to open-label treatment. A sensitivity analysis was conducted to account for patients who had changes in their non-biologic background medication during the 52-week placebo-controlled period.

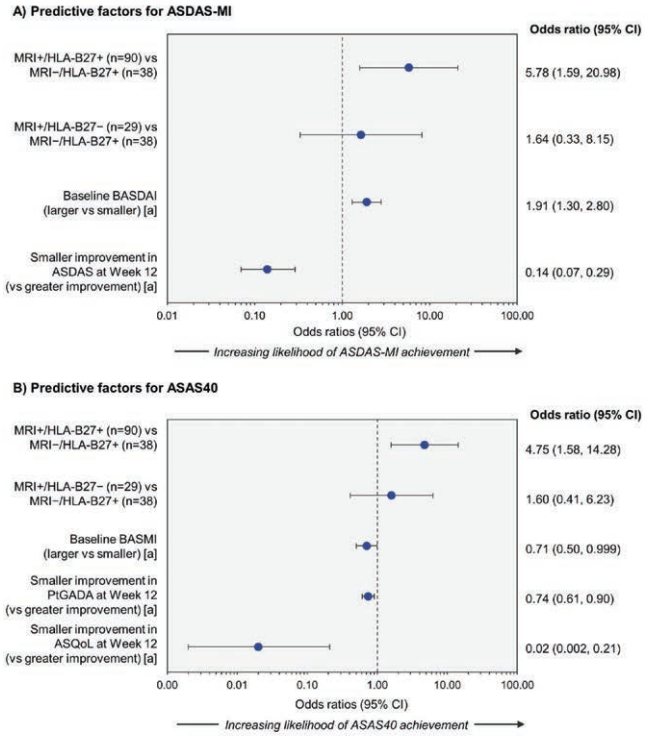
Results: A total of 159/317 patients were randomised to CZP 200 mg Q2W and 158/317 to placebo. Predictive factors identified for Week 52 ASDAS-MI in the CZP-treated patients included being positive for both presence of sacroiliitis on MRI (MRI+) and human leukocyte antigen (HLA)-B27 (HLA-B27+), having a higher Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at baseline, and having a larger Week 12 improvement in ASDAS (Figure 1A). For ASAS40 response, MRI+/HLA-B27+ was also identified as a predictor of Week 52 response, along with a lower baseline Bath AS Metrology Index (BASMI) and larger Week 12 improvements in Patient Global Assessment of Disease Activity (PtGADA) and AS Quality of Life (ASQoL; Figure 1B). Sensitivity analysis identified the same predictors for ASDAS-MI and ASAS40, with the exception of change from baseline in PtGADA as a predictor of ASAS40. Sensitivity analysis also identified achievement of Week 12 ASAS40 as a predictor of Week 52 ASAS40. In placebo-treated patients, no meaningful predictors of response at Week 52 were identified.

Conclusion: Presence of sacroiliitis on MRI and HLA-B27 positivity were identified as consistent predictors of Week 52 response (ASDAS-MI and ASAS40) in nr-axSpA patients treated with CZP. To our knowledge, this is the first report from an interventional 52-week placebo-controlled study in nr-axSpA to identify objective clinical features, particularly the presence of sacroiliac joint inflammation, as being predictive of response.

REFERENCES:

[1] Ashrafi M. Curr Opin Rheumatol 2020;32:321–9.
[2] Deodhar A. Arthritis Rheumatol 2019;71:1101–11.

Figure. Predictive factors of Week 52 response in CZP-treated patients



[a] Included in the predictive model as continuous variables; for these factors, an odds ratio >1 indicates a higher probability of larger values being predictive of a response. For Week 12 change from baseline measures, a lower (negative) value is indicative of improvement, while larger (positive) values indicate worsening. ASAS40: Assessment of SpondyloArthritis international Society 40%; ASDAS-MI: Ankylosing Spondylitis Disease Activity Score – major improvement; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CI: confidence interval; HLA: human leukocyte antigen; MRI+/−: presence/absence of sacroiliitis on magnetic resonance imaging; PtGADA: Patient Global Assessment of Disease Activity; vs: versus.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical.

Disclosure of Interests: Walter P Maksymowych Speakers bureau: AbbVie, Janssen, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, BMS, Boehringer, Eli Lilly, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Novartis, Pfizer, Thomas Kumke Shareholder of: UCB Pharma, Employee of: UCB Pharma, Simone Auteri Shareholder of: UCB Pharma, Employee of: UCB Pharma, Bengt Hoepken Shareholder of: UCB Pharma, Employee of: UCB Pharma, Lars Bauer Shareholder of: UCB Pharma, Employee of: UCB Pharma, Martin Rudwaleit Speakers bureau: AbbVie, Eli Lilly, Novartis, UCB Pharma, Consultant of: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, UCB Pharma

DOI: 10.1136/annrheumdis-2021-eular.108

POS0897 REDUCTION OF ANTERIOR UVEITIS FLARES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS DURING CERTOLIZUMAB PEGOL TREAT MENT: 96-WEEK RESULTS FROM THE C-VIEW STUDY

I. Van der Horst-Bruinsma[1], R. Van Bentum[1], F. Verbraak[2], T. Rath[3], B. Hoepken[4], O. Irvin-Sellers[5], T. Kumke[4], L. Bauer[4], M. Rudwaleit[6,7].
[1]Amsterdam University Medical Centre, Location VUmc, Department of Rheumatology, Amsterdam, Netherlands; *[2]Academic Medical Centre, University of Amsterdam, Department of Ophthalmology, Amsterdam, Netherlands*; *[3]St Franziskus-Hospital, Department of Ophthalmology, Münster, Germany*; *[4]UCB Pharma, N/A, Monheim am Rhein, Germany*; *[5]UCB Pharma, N/A, Slough, United Kingdom*; *[6]Klinikum Bielefeld, Clinic for Internal Medicine and Rheumatology, Bielefeld, Germany*; *[7]Charité – Universitätsmedizin Berlin, Department of Gastroenterology, Infectiology and Rheumatology, Berlin, Germany*

Background: Acute anterior uveitis (AAU) is the most common extra-articular manifestation in axial spondyloarthritis (axSpA), affecting up to 40% of patients and causing significant burden.[1] Previous studies have shown that tumour necrosis factor inhibitors (TNFi) can reduce the incidence of AAU flares in patients with radiographic axSpA (ankylosing spondylitis),[2-4] but few have focused on patients across the full axSpA spectrum.[1]

Objectives: To report 2-year outcomes from the phase 4, open-label C-VIEW study (NCT03020992), which investigated the impact of certolizumab pegol (CZP) treatment on AAU in patients with active axSpA and a recent history of AAU.

Methods: C-VIEW prospectively investigated patients with active axSpA who were HLA-B27 positive and had recurrent AAU, with a history of ≥1 AAU flare in the year prior to baseline (additional study criteria and study design are described elsewhere[5]). The primary efficacy variable was the incidence of AAU flares during 96 weeks of CZP treatment versus the 2-year pre-baseline period. AAU incidence was evaluated using Poisson regression adjusted for duration of time in each period, with period (pre- and post-baseline) and axSpA disease duration as covariates. Secondary efficacy variables were Assessment of SpondyloArthritis international Society 20%/40% (ASAS20/40) response rates, as well as mean Ankylosing Spondylitis Disease Activity Score (ASDAS) and mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) to Week 96.

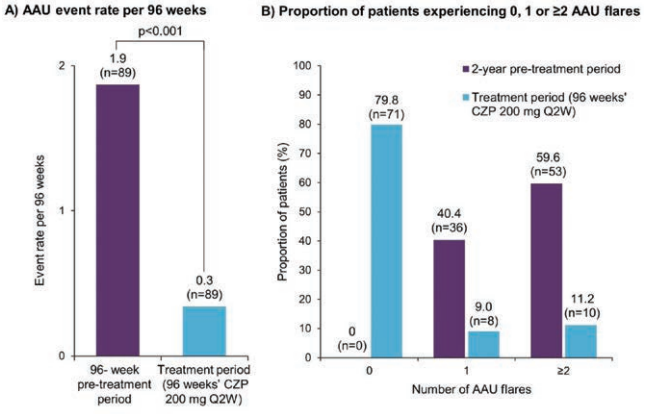
Results: Of 115 enrolled patients, 89 initiated CZP treatment; 83 completed Week 96. The primary analysis revealed an 82% reduction in the incidence of AAU flares during CZP treatment compared with pre-baseline (Figure 1A; rate ratio [95% CI]: 0.18 [0.12, 0.28], p<0.001). The percentage of patients experiencing ≥1 and ≥2 AAU flares reduced from 100% and 59.6% pre-baseline to 20.2% and 11.2% during treatment (Figure 1B). There were also improvements in axSpA disease activity (Table 1): by Week 96, 75.6% and 58.5% of patients had achieved ASAS20 and ASAS40 responses, respectively. ASDAS and BASDAI also improved substantially over the 96-week treatment period. No new safety signal was identified, compared to previous reports.[5]

Conclusion: These data support the use of CZP for the treatment of patients with axSpA and a history of recurrent AAU. During 96 weeks' CZP treatment, there was a significant reduction of 82% in the AAU flare rate compared to pre-baseline. There were also substantial improvements in patients' axSpA disease activity.

REFERENCES:

[1] Martin TM. Curr Opin Rheumatol 2002;14:337–41.
[2] van der Heijde D. Rheumatology (Oxford) 2017;56:1498–509.
[3] van Bentum RE. J Rheumatol 2019;46:153–9.
[4] van Denderen JC. J Rheumatol 2014;41:1843–8.
[5] van der Horst-Bruinsma I. RMD Open 2020;6:e001161.

Figure. Summary of AAU flares (observed data)



Treatment period: after start of study medication until Week 96 or discontinuation visit. Pre-treatment period: 24 months prior to treatment start. Flares on the same eye are combined and counted as one flare if the time interval between two subsequent flares is <3 months (90 days). Patients received CZP 400 mg at Weeks 0/2/4, then 200 mg Q2W through 96 weeks. a) Poisson regression analysis, with period (pre-/post-baseline) and axSpA disease duration as covariates and adjusting for the length of time in the pre- and post-baseline periods. AAU: acute anterior uveitis; CZP: certolizumab pegol; Q2W: every 2 weeks.

Table 1. Changes in axSpA disease activity to Week 96

Disease activity measure	Week 0 (n=89)	Week 48 (n=86)	Week 96 (n=82)
ASAS responder rates, n (%)			
ASAS20	N/A	65 (75.6)	62 (75.6)
ASAS40	N/A	46 (53.5)	48 (58.5)
ASDAS, mean (SD)	3.5 (1.0)	2.0 (0.9)	1.9 (1.0)
BASDAI, mean (SD)	6.5 (1.5)	3.3 (2.1)	3.0 (2.1)

Observed data are shown. Patients received CZP 400 mg at Weeks 0/2/4, then 200 mg Q2W through 96 weeks. ASAS20/40: Assessment of SpondyloArthritis international Society 20%/40%; ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CZP: certolizumab pegol; Q2W: every 2 weeks; SD: standard deviation.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical.

Disclosure of Interests: Irene van der Horst-Bruinsma Speakers bureau: AbbVie, BMS, MSD, Pfizer, UCB Pharma, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, UCB Pharma, Grant/research support from: AbbVie, MSD, Pfizer, Rianne van Bentum: None declared, Frank Verbraak Speakers bureau: Bayer, IDxDR, Novartis, UMC, Consultant of: Bayer, Novartis, Grant/research support from: Bayer, Thomas Rath Speakers bureau: AbbVie, BMS, Chugai, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma, Consultant of: AbbVie, BMS, Chugai, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma, Bengt Hoepken Shareholder of: UBC Pharma, Employee of: UCB Pharma, Oscar Irvin-Sellers Shareholder of: UCB Pharma, Employee of: UCB Pharma, Thomas Kumke Shareholder of: UCB Pharma, Employee of: UCB Pharma, Lars Bauer Shareholder of: UCB Pharma, Employee of: UCB Pharma, Martin Rudwaleit Speakers bureau: AbbVie, Eli Lilly, Novartis, UCB Pharma, Consultant of: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, UCB Pharma

DOI: 10.1136/annrheumdis-2021-eular.115

POS0899

HOW DOES GENDER AFFECT SECUKINUMAB TREATMENT OUTCOMES AND RETENTION RATES IN PATIENTS WITH ANKYLOSING SPONDYLITIS? - REAL WORLD DATA FROM THE GERMAN AQUILA STUDY

U. Kiltz[1], J. Brandt-Juergens[2], P. Kästner[3], E. Riechers[4], D. Peterlik[5], H. P. Tony[6]. *[1]Rheumazentrum Ruhrgebiet / Ruhr-Universität Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*; *[2]Rheumatologische Schwerpunktpraxis, Rheumatologische Schwerpunktpraxis, Berlin, Germany*; *[3]Ambulantes Rheumazentrum, Ambulantes Rheumazentrum, Erfurt, Germany*; *[4]Medizinische Hochschule Hannover, Klinik für Immunologie und Rheumatologie, Hannover, Germany*; *[5]Novartis Pharma GmbH, Immunology, Hepatology & Dermatology, Nuremberg, Germany*; *[6]Medizinische Klinik II, Universitätsklinik, Rheumatology/ Immunology, Würzburg, Germany*

Background: Current studies suggest that the phenotype of spondyloarthritis differs between genders and that this may influence the subsequent diagnostic approach and therapeutic decisions[1]. The German non-interventional study AQUILA provides real-world data on the influence of gender on therapeutic effectiveness and retention rate under treatment with secukinumab, a fully human monoclonal antibody that selectively inhibits interleukin-17A.

Objectives: The aim of this interim analysis is to describe selected baseline (BL) demographics, to evaluate secukinumab treatment outcomes on disease activity, global functioning and health and retention rate depending on the gender of AS patients.

Methods: AQUILA is an ongoing, multi-center, non-interventional study including more than 3000 patients with active AS or psoriatic arthritis. Patients were observed from BL up to week (w) 52 according to clinical routine. Real-world data was assessed prospectively and analyzed as observed. Validated questionnaires were used to collect data on disease activity (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI), global functioning and health (Assessment of SpondyloArthritis-Health Index, ASAS-HI) and severity of depressive mood (Beck´s Depression Inventory version II, BDI-II). Patient reported outcomes were reported using patient´s global assessment (PGA). In addition, retention rates (time from study inclusion until premature secukinumab treatment discontinuation) were assessed through Kaplan-Meier plots. This interim analysis focuses on the subgroups of male and female AS patients.

Results: At BL, 683 AS patients were included: 59.7% (n=408) male and 40.3% (n=275) female. Demographic data (Table 1) of male and female AS patients differed numerically in the following parameters: proportion of obese patients, smokers, pretreatment with disease-modifying antirheumatic drugs (csDMARDs), and biologicals/biosimilars (b-bsDMARDs).

Mean BASDAI and PGA were comparable between male and female AS patients over time (♂: 5.2 at BL to 3.8 at w52, ♀: 5.3 at BL to 4.1 at w52 and ♂: 5.9 at BL to 4.1 at w52, ♀: 5.6 at BL to 4.3 at w52, respectively). Mean ASAS-HI over time was higher in women; nevertheless, improvements in global functioning were comparable for both genders from BL to week 52 (Fig. 1A). Severity of depressive mood was numerically lower in male patients; nevertheless, BDI-II reductions were comparable across the genders (♂: 11.2 at BL to 10.0 at w52, ♀: 13.1 at BL to 11.0 at w52). Secukinumab treatment retention rate for men was (not significantly) higher than for women (Fig. 1B).

Conclusion: In a real-world setting, secukinumab improved disease activity, global functioning and severity of depressive mood in AS patients in both men and women. Women showed overall higher disease burden. Altogether, real-world data of this interim analysis are in line with those of Phase 3 studies and show that secukinumab is an effective treatment up to 52 weeks with high treatment retention rates, irrespective of gender.

REFERENCES:

[1] Landi, M., *et al. Medicine (Baltimore)* **95**, e5652 (2016).

Table 1. Overview of baseline characteristics in AS patients depending on gender

Demographics*	Male (N=408)	Female (N=275)
Age, years	45.6 (12.1)	47.8 (12.2)
BMI, kg/m^2	27.4 (4.5)	27.6 (5.7)
BMI >25 to ≤30 kg/m^2, n (%)	178 (45.1)	88 (32.4)
BMI >30 kg/m^2, n (%)	94 (23.8)	83 (30.5)
Smoker, n (%)	150 (36.8)	67 (24.4)
BASDAI	5.2 (1.9)	5.3 (1.9)
PGA	5.8 (4.9)	5.6 (5.6)
ASAS-HI	7.4 (3.5)	8.2 (3.5)
BDI-II	11.2 (10.2)	13.1 (13.0)
Medication prior to secukinumab initiation, n (%):		
NSAID	330 (80.9)	222 (80.7)
csDMARD	145 (35.5)	137 (49.8)
b-bsDMARD	249 (61.0)	190 (69.1)

*variables given as mean (SD)

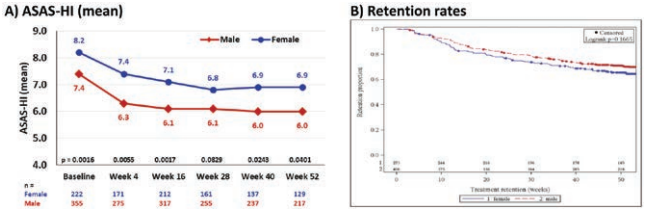


Figure 1. Global functioning and secukinumab treatment retention in AS patients stratified by genderNote: P-values are of exploratory nature

Disclosure of Interests: Uta Kiltz Consultant of: AbbVie, Biocad, Chugai, Eli Lilly, Gruenenthal, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Grant/research support from: AbbVie, Biogen, Novartis, Pfizer, Jan Brandt-Juergens Consultant of: Abbvie, Affibody, BMS, Gilead, Janssen, Lilly, Medac, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, Peter Kästner Consultant of: Chugai, Novartis, Elke Riechers Consultant of: AbbVie, Chugai, Novartis, UCB, Grant/research support from: AbbVie, Chugai, Lilly, Janssen, Novartis, Pfizer, Roche, UCB, Daniel Peterlik

Employee of: Novartis Pharma GmbH, Hans-Peter Tony Consultant of: AbbVie, Astra-Zeneca, BMS, Chugai, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi
DOI: 10.1136/annrheumdis-2021-eular.141

POS0900

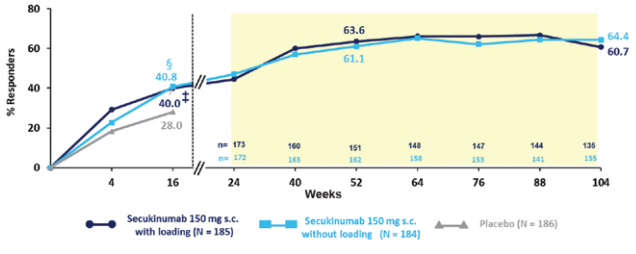
SECUKINUMAB 150 MG PROVIDES SUSTAINED IMPROVEMENT IN SIGNS AND SYMPTOMS OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 2-YEAR RESULTS FROM THE PREVENT STUDY

D. Poddubnyy[1], A. Deodhar[2], X. Baraliakos[3], R. Blanco[4], E. Dokoupilova[5], S. Hall[6], A. Kivitz[7], M. G. H. Van de Sande[8], A. Stefanska[9], P. Pertel[10], H. Richards[10], J. Braun[11]. *[1]Charité - Universitätsmedizin Berlin, German Rheumatism Research Centre, Berlin, Germany*; *[2]Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America*; *[3]Rheumazentrum Ruhrgebiet, Rheumatology Division, Herne, Germany*; *[4]Hospital University Marqués de Valdecilla, IDIVAL, Division of Rheumatology, Santander, Spain*; *[5]Medical Plus, s.r.o., Uherske Hradiste, Masaryk University, Department of Pharmaceutical Technology, Faculty of Pharmacy, Brno, Czech Republic*; *[6]Monash University, Department of Medicine, Melbourne, Australia*; *[7]Altoona Center for Clinical Research, Clinical Research Division, Pennsylvania, United States of America*; *[8]Amsterdam UMC, University of Amsterdam, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands*; *[9]Novartis Ireland Limited, Immunology, Hepatology and Dermatology, Dublin, Ireland*; *[10]Novartis Pharma AG, Immunology, Hepatology and Dermatology, Basel, Switzerland*; *[11]Rheumazentrum Ruhrgebiet, Herne, and Ruhr-University Bochum, Department of Rheumatology, Bochum, Germany*

Background: Axial spondyloarthritis (axSpA) is an inflammatory disease characterised by chronic back pain, and it comprises radiographic axSpA and non-radiographic axSpA (nr-axSpA).[1] Secukinumab (SEC) 150 mg, with (LD) or without loading (NL), dose significantly improved the signs and symptoms of patients with nr-axSpA in the PREVENT (NCT02696031) study through Week 52.[2]
Objectives: To report the long-term clinical efficacy and safety of secukinumab from the PREVENT study through 2 years.
Methods: A detailed study design, key primary and secondary endpoints have been reported previously.[2] In total, 555 patients fulfilling ASAS criteria for axSpA plus abnormal C-reactive protein (CRP) and/or MRI, without evidence of radiographic changes in sacroiliac (SI) joints according to modified New York Criteria for AS were randomised (1:1:1) to receive SEC 150 mg with LD, NL, or placebo (PBO) at baseline. LD patients received SEC 150 mg at Weeks 1, 2, 3, and 4, and then every 4 weeks (q4wk) starting at Week 4. NL patients received SEC 150 mg at baseline and PBO at weeks 1, 2, and 3, and then 150 mg q4wk. 90% patients were anti-tumour necrosis factor (anti-TNF) naïve, 57% had elevated CRP and 73% had evidence of SI joint inflammation on MRI. All images were assessed centrally before inclusion. All patients continued to receive open-label SEC 150 mg treatment after Week 52. Efficacy assessments through Week 104 included ASAS40 in anti-TNF-naïve patients, ASAS40, BASDAI change from baseline, BASDAI50, ASAS partial remission, and ASDAS-CRP inactive disease in the overall population. The safety analyses included all patients who received ≥1 dose of study treatment for the entire treatment period up to Week 104. Data are presented as observed.
Results: Overall, 438 patients completed 104 weeks of study: 78.9% (146/185; LD), 77.7% (143/184; NL) and 80.1% (149/186; PBO). Efficacy results at Week 52 were sustained through Week 104 and are reported in the Table 1. The safety profile was consistent with the previous reports with no deaths reported during the entire treatment period up to Week 104.[2]
Conclusion: Secukinumab 150 mg demonstrated sustained improvement in the signs and symptoms of patients with nr-axSpA through 2 years. Secukinumab was well tolerated with no new or unexpected safety signals.

REFERENCES:

[1] Strand V, et al. *J Clin Rheumatol*. 2017; 23(7):383–91.
[2] Deodhar A, et al. *Arthritis Rheumatol*. 2020. Online ahead of print.



§p<0.01 and ‡p<0.05 vs placebo (unadjusted p-values at Week 16). **Data presented as non-responder imputation till week 16 and as observed from Week 24 to Week 104. At Week 52 all patients remaining on blinded treatment switched to open-label secukinumab.**
ASAS, Assessment of SpondyloArthritis International Society; N, total number of patients randomised; n, number of evaluable patients including those who switched to open label secukinumab or standard of care after Week 20. After Week 52, only patients who continued to receive open-label secukinumab are presented; s.c., subcutaneous

Figure 1. ASAS40 response was maintained through Week 104 in the overall population

Table 1. Summary of clinical efficacy (Observed data)

Endpoints	Week	SEC 150 mg LD (N=185)	SEC 150 mg NL (N=184)	PBO-SEC 150 mg (N=186)
*ASAS40 in anti-TNF-naïve patients, n/M (%)	52[a]	90/137 (65.7)	95/145 (65.5)	85/151 (56.3)
	104	78/123 (63.4)	83/123 (67.5)	83/134 (61.9)
BASDAI change from baseline, mean±SD	52[a]	–3.7±2.8	–3.7±2.6	–3.3±2.4
	104	–4.1±2.6	–3.9±2.6	–3.7±2.5
BASDAI50, n/M (%)	52[a]	90/153 (58.8)	92/163 (56.4)	90/161 (55.9)
	104	88/137 (64.2)	84/136 (61.8)	87/142 (61.3)
ASAS partial remission, n/M (%)	52[a]	46/152 (30.3)	56/163 (34.4)	46/161 (28.6)
	104	51/137 (37.2)	50/135 (37.0)	50/142 (35.2)
ASDAS CRP inactive disease, n/M (%)	52[a]	49/152 (32.2)	58/163 (35.6)	48/160 (30.0)
	104	50/132 (37.9)	53/133 (39.8)	53/142 (37.3)

*For anti-TNF-naïve patients, N=164, LD; 166, NL; 171, PBO-SEC.[a] total number of evaluable patients including open-label SEC and standard of care (SOC; 2 patients in LD, 1 patient in NL continued on SOC). After Week 52, only patients who continued to receive open-label SEC are presented.ASAS, Assessment of SpondyloArthritis International Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; M, number of patients with evaluation; N, total randomised patients; n, number of patients who are responders; SD, standard deviation

Disclosure of Interests: Denis Poddubnyy Speakers bureau: AbbVie, BMS, Eli Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: AbbVie, Biocad, BMS, Eli Lilly, Gilead, MSD, Novartis, Pfizer, Samsung Bioepis, UCB, Grant/research support from: AbbVie, MSD, Novartis, Pfizer, Atul Deodhar Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, GSK, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, and UCB, Xenofon Baraliakos Speakers bureau: AbbVie, BMS, Celgene, Chugai, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, BMS, Celgene, Chugai, Galapagos, Gilead, MSD, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie and Novartis, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, UCB pharma and MSD and Eli Lilly, Consultant of: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, UCB pharma and MSD, Grant/research support from: AbbVie, MSD, and Roche, Eva Dokoupilova Grant/research support from: AbbVie, Affibody AB, Eli Lilly, Galapagos, Gilead, GSK, Hexal AG, MSD, Novartis, Pfizer, R-Pharm, Sanofi-Aventis, and UCB, Stephen Hall Speakers bureau: Novartis, Merck, Janssen, Pfizer, Eli Lilly, and UCB, Consultant of: Novartis, Merck, Janssen, Pfizer, Eli Lilly, and UCB, Grant/research support from: AbbVie, UCB, Janssen, and Merck, Alan Kivitz Shareholder of: Pfizer, Sanofi, Novartis, Amgen, GlaxoSmithKline, Gilead Sciences, Inc., Speakers bureau: Celgene, GlaxoSmithKline, Eli Lilly, Merck, Novartis, Pfizer, Sanofi, Genzyme, Flexion, AbbVie, UCB, Consultant of: AbbVie, Boehringer Ingelheim, Flexion, Janssen, Pfizer, Sanofi, Regeneron, SUN Pharma Advanced Research, Gilead Sciences, Inc., Marleen G.H. van de Sande Speakers bureau: Novartis, MSD, Consultant of: Abbvie, Novartis, Eli Lily, Grant/research support from: Novartis, Eli Lilly, Janssen, UCB, Anna Stefanska Shareholder of: Novartis, Employee of: Novartis, Patricia Pertel Shareholder of: Novartis, Employee of: Novartis, Hanno Richards Shareholder of: Novartis, Employee of: Novartis, Juergen Braun Speakers bureau: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB pharma, Eli Lilly, Consultant of: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, Eli Lilly, Grant/research support from: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, Eli Lilly
DOI: 10.1136/annrheumdis-2021-eular.143

POS0901

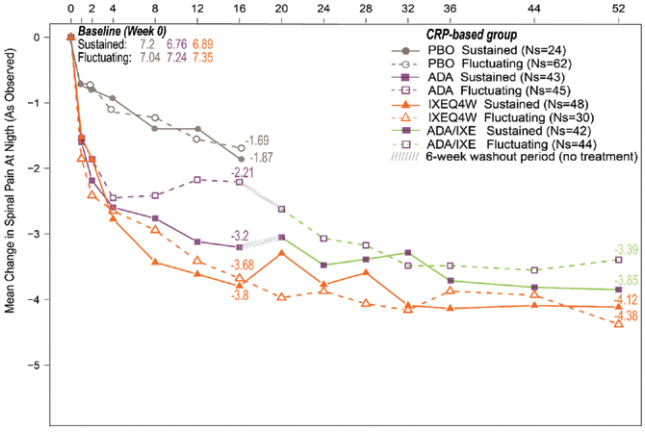
IXEKIZUMAB SHOWS A DISTINCT PATTERN OF PAIN IMPROVEMENT BEYOND INFLAMMATION IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

K. De Vlam[1], G. Gallo[2], P. J. Mease[3], P. Rahman[4], V. Krishnan[2], D. Sandoval[2], C. Y. Lin[2], R. Bolce[2], P. G. Conaghan[5]. *[1]University Hospital Leuven, Rheumatology, Leuven, Belgium*; *[2]Eli Lilly and Company, Lilly Corporate Centre, Indianapolis, United States of America*; *[3]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology, Seattle, United States of America*; *[4]Memorial University of Newfoundland, Medicine, St. John's, Canada*; *[5]University of Leeds, School of Medicine, Leeds, United Kingdom*

Background: The efficacy of ixekizumab (IXE) in biologic-naïve patients with radiographic axial spondyloarthritis (r-axSpA) has been previously presented using traditional axSpA outcome measures, such as BASDAI and ASAS.

Objectives: In patients with active r-axSpA, to assess the analgesic efficacy of IXE as it relates to patient-reported and objective measures of inflammation.
Methods: The Phase III COAST-V (NCT02696785) multi-center, randomized, double-blind, placebo (PBO)-controlled and active reference arm with adalimumab (ADA) trial investigated the efficacy of IXE in 341 patients (pts) with active r-axSpA for 52 weeks (W). Pts were initially randomized to IXEQ4W, IXEQ2W, PBO, and ADAQ2W. At W16, pts assigned to PBO and ADA were re-randomized to IXEQ2W or Q4W. Changes in spinal pain at night (SP-N) and spinal pain were measured at each study visit and analysed while controlling for CRP levels or mean of BASDAI questions 5 & 6 (Q5: Duration and Q6: Intensity of morning stiffness). Observed data analyses are presented for each group stratified by treatment arm and compared to PBO. In the initial analysis, pts were categorized into 2 sub-groups defined as "Sustained" and "Fluctuating" depending on: CRP <5 mg/L W4-16 vs. CRP ≥5 mg/L at any point beyond W4 between weeks 4-16 respectively. In a second analysis, pts were categorized based on BASDAI Q5/6 improvement: "Sustained" if ≥2-pt improvement W12-16 vs. "Fluctuating" if <2-pt improvement at any point beyond W12 between W12-16.
Results: Between W0 and W16, pts treated (tx) with IXEQ4W experienced greater reduction in SP-N than pts tx with ADA, in both CRP sustained and fluctuating groups (Fig 1a). Pts in the IXEQ4W and ADA arms showed different trajectories of pain improvement in the CRP fluctuating groups. For the pts with a fluctuating CRP ≥5 mg/L, pts in IXEQ4W arm demonstrated a greater reduction in SP-N compared to pts in PBO arm ($p < .001$) at W16, whereas pts in ADA arm did not experience a reduction in SP-N compared to PBO ($p = .416$). For the pts with a sustained CRP <5mg/L, IXEQ4W and ADA treatments both significantly demonstrated reduction in SP-N compared to PBO at W16 (IXEQ4W: $p = .002$; ADA: $p = .02$), with IXEQ4W treatment showing a greater level of reduction (Fig 1a). The pts randomized to ADA and re-randomized to IXEQ2W or Q4W (ADA/IXE) experienced further improvement in SP-N. This effect was sustained over the 52-wk period (Fig 1b). The same pattern of improvement in SP-N was observed when controlling for the BASDAI Q5/6; the SP-N improvement was greater in pts with a sustained BASDAI Q5/6 compared to pts with a fluctuating BASDAI Q5/6, regardless of treatment (Table 1). In the fluctuating BASDAI Q5/6, for pts in ADA/IXE arm, further reduction of both spinal pain and SP-N were observed (Table 1).

Figure 1: Change in Spinal Pain at Night (SP-N) over 52 weeks by CRP, in active treatment arms, showing IXE and ADA re-randomized to IXE (Q2W and Q4W combined: ADA/IXE)



Conclusion: IXE reduced SP-N and spinal pain irrespective of CRP or morning stiffness. Additionally, pts treated with ADA re-randomized to IXE experienced a further reduction in SP-N and spinal pain. Collectively, these results support the additive benefits of IXE in reducing pain above measurable effects on inflammation.

Acknowledgements: The authors would like to thank Eglantine Julle-Daniere for writing and editorial contributions
Disclosure of Interests: Kurt de Vlam Speakers bureau: Eli Lilly, Novartis, Pfizer, Paid instructor for: Celgene, Amgen, Consultant of: Elil Lillyn Novartis, UCB, Galapagos, Sandoz, Pfizer, Grant/research support from: Celgene, Gaia Gallo Shareholder of: Eli Lilly, Employee of: Eli Lilly, Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sun, UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, Sun, UCB, Proton Rahman Speakers bureau: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, UCB, Grant/research support from: Janssen, Novartis, Venkatesh Krishnan Shareholder of: Eli Lilly, Employee of: Eli Lilly, David Sandoval Shareholder of: Eli Lilly, Employee of: Eli Lilly, Chen-Yen Lin Shareholder of: Eli Lilly, Employee of: Eli Lilly, Rebecca Bolce Shareholder of: Eli Lilly, Employee of: Eli Lilly, Philip G Conaghan Consultant of: personal fees from: AbbVie, AstraZeneca, BMS, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, Gilead, Novartis, Pfizer
DOI: 10.1136/annrheumdis-2021-eular.211

POS0902 EFFICACY AND SAFETY OF INTRAVENOUS GOLIMUMAB IN ANKYLOSING SPONDYLITIS PATIENTS WITH EARLY VS LATE DISEASE THROUGH WEEK 52 OF GO-ALIVE STUDY

A. Deodhar[1], S. Kafka[2], E. C. Hsia[3,4], K. H. Lo[5], L. Kim[5], S. Xu[5], J. D. Reveille[6].
[1]*Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America*; [2]*Janssen Scientific Affairs, LLC, Immunology, Horsham, United States of America*; [3]*Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; [4]*University of Pennsylvania, Rheumatology, Philadelphia, United States of America*; [5]*Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; [6]*University of Texas McGovern Medical School, Rheumatology And Clinical Immunogenetics, Houston, United States of America*

Background: The GO-ALIVE study assessed efficacy and safety of intravenous golimumab (IV GLM) in patients (pts) with ankylosing spondylitis (AS).[1,2]
Objectives: In this post hoc analysis, we assessed IV GLM efficacy and safety in AS pts with early disease (ED) vs late disease (LD) based on pt-reported duration of inflammatory back pain (IBP).
Methods: In this Phase 3, double-blind, placebo (PBO)-controlled trial, pts with active AS were randomized (1:1) to receive IV GLM 2 mg/kg at Week (W) 0, W4, then Q8W or PBO at W0, W4, and W12 with crossover to IV GLM at W16, W20, then Q8W through 52. The primary endpoint was achievement of SpondyloArthritis International Society 20% improvement response (ASAS 20) at W16. In this post hoc analysis, 208 pts were grouped into quartiles based on self-reported duration of IBP symptoms. Efficacy and safety in 60 pts with ED (1st quartile) were compared with 52 pts with LD (4th quartile).
Results: For the overall study population, mean duration of IBP symptoms was 10.9 yr and mean time since diagnosis was 5.5 yr. For ED pts, the mean duration of IBP symptoms ranged from 2.3 yr (IV GLM) to 2.6 yr (PBO), and for LD pts ranged from 23.5 yr (IV GLM) to 24.4 yr (PBO). At W16, ASAS 20 was achieved by 72% IV GLM vs 32% PBO pts with ED and by 67% IV GLM vs 21% PBO pts with LD. Pts with ED had numerically better response than those with LD in Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), and across more stringent endpoints, including ASAS 40, Bath Ankylosing Spondylitis Disease Activity Index 50% improvement

Table 1. Change in Pain Outcome at baseline, week 16 and week 52 by Inflammation Status as assessed by BASDAI or CRP levels for patients receiving placebo (PBO), adalimumab (ADA), and ixekizumab every 4 weeks (IXE Q4W)

		Change from baseline								
		PBO			ADA			IXEQ4W		
		baseline	Week 16 (as observed)	Week 52 PBO/IXE (as observed)	baseline	Week 16 (as observed)	Week 52 ADA/IXE (as observed)	baseline	Week 16 (as observed)	Week 52 (as observed)
Spinal pain	BASDAI Q5/6 sustained	7.54	-3.33	-4.65	7.21	-4.07	-4.5	7.4	-4.52	-4.94
	BASDAI Q5/6 fluctuating	7.37	-1.32	-2.82	6.76	-1.2	-2.24	6.97	-1.3	-2.52
	CRP sustained	7	-1.53	-1.93	6.83	-2.9	-3.6	7.23	-3.57	-4.21
	CRP fluctuating	7.51	-1.96	-3.63	7.28	-2	-2.89	7.24	-2.91	-3.93
Spinal pain at night	BASDAI Q5/6 sustained	7.12	-3.21	-4.61	7.26	-4.63	-4.92	7.12	-4.73	-4.91
	BASDAI Q5/6 fluctuating	7.05	-1.15	-2.88	6.6	-1.2	-2.49	7.03	-2.17	-2.92
	CRP sustained	7.2	-1.87	-2.27	6.76	-3.2	-3.85	6.89	-3.8	-4.12
	CRP fluctuating	7.04	-1.69	-3.6	7.24	-2.21	-3.39	7.35	-3.68	-4.38

(BASDAI 50), and Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease and major improvement (Table 1). Response rates at W16 among IV GLM-treated pts were generally consistent through 1 year in both ED and LD subgroups; also in ED and LD subgroups, pts crossing over to IV GLM at W16 demonstrated response at W52 consistent with pts who started IV GLM at W0. At W16, improvements in enthesitis score were similar for pts with ED (mean change -2.9 for IV GLM vs 0.1 for PBO) and LD (mean change -2.5 for IV GLM vs 0.6 for PBO); improvements were maintained at W52 for ED and LD pts. Treatment-emergent adverse events and serious adverse events through 1 year were 46% and 3% for pts with ED compared with 61% and 2% for pts with LD, respectively.

Conclusion: While IV GLM provided clinically meaningful improvements in signs and symptoms of AS in pts regardless of disease duration, response generally appeared numerically better in pts with ED than in pts with LD. This supports the principle of prompt diagnosis and early treatment.

REFERENCES:

[1] Deodhar A, et al. *J Rheumatol*. 2018;45:341-348.
[2] Reveille J, et al. *J Rheumatol*. 2019;46:1277-1283.

Table 1. Efficacy Outcomes

	ED				LD			
	Week 16		Week 52		Week 16		Week 52	
	PBO (n=25)	IV GLM (n=35)	PBO→IV GLM (n=25)	IV GLM (n=35)	PBO (n=28)	IV GLM (n=24)	PBO→IV GLM (n=28)	IV GLM (n=24)
ASAS 20	32%	71%	68%	71%	21%	67%	68%	63%
ASAS 40	12%	46%	56%	60%	4%	42%	57%	42%
BASDAI 50	12%	40%	64%	60%	7%	33%	57%	42%
ASDAS inactive disease (score <1.3)	4%	17%	44%	37%	0%	8%	14%	4%
ASDAS major improvement (decrease ≥2.0)	n=24 4%	57%	n=24 54%	51%	0%	n=23 48%	46%	n=23 30%
ASDAS clinically important improvement (decrease ≥1.1)	n=24 29%	77%	n=24 75%	77%	18%	n=23 91%	61%	n=23 65%
Mean change from baseline (SD) in BASFI	n=23 -0.4 (2.0)	-2.3 (2.1)	n=23 -2.7 (2.7)	-2.8 (2.6)	n=27 -0.3 (1.8)	n=24 -2.2 (1.7)	n=27 -2.4 (2.2)	n=23 -2.3 (1.7)
Mean change from baseline (SD) in BASMI	n=23 -0.3 (0.7)	-0.4 (0.7)	n=23 -0.6 (0.7)	-0.3 (0.5)	n=27 0.01 (0.5)	n=21 -0.3 (0.6)	n=27 -0.4 (0.7)	n=20 -0.3 (0.7)
Mean change from baseline (SD) in enthesitis score	n=23 0.1 (3.6)	-2.9 (2.9)	n=23 -2.0 (4.4)	-3.2 (2.5)	n=27 -0.6 (3.4)	n=21 -2.5 (3.0)	n=27 -2.5 (3.1)	n=20 -3.5 (5.9)

SD=standard deviation

Disclosure of Interests: Atul Deodhar Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer, and UCB, Shelly Kafka Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Kim Hung Lo Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Lilianne Kim Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Stephen Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, John D Reveille Consultant of: Eli Lilly and UCB, Grant/research support from: Eli Lilly and Janssen

DOI: 10.1136/annrheumdis-2021-eular.220

POS0903

CLINICAL AND RADIOLOGICAL MANIFESTATIONS OF COXITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS (AS) TREATED WITH TNF-ALPHA INHIBITOR GOLIMUMAB: RESULTS OF A 24-MONTHS OBSERVATION (GO-COX STUDY)

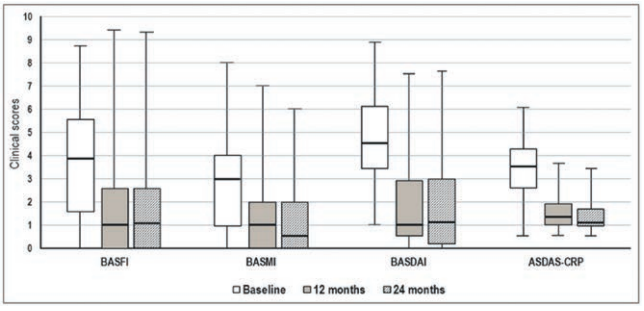
S. Erdes[1], E. Agafonova[1], D. Rumiantceva[1], S. Davidian[2], E. Zemerova[3], A. Kulikov[4], O. Markova[5], E. Lukyanova[6], V. Achikyan[6]. [1]*Federal Rheumatology Research Institute n.a. V.A.Nasonova, Laboratory of Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*; [2]*National Medical and Surgical Center named after N.I. Pirogov, Rheumatology, Moscow, Russian Federation*; [3]*Khanty-Mansiysk Autonomous Region - Yugra Regional Clinical Hospital, Rheumatology, Khanty-Mansiysk, Russian Federation*; [4]*Rostov-on-Don Regional Clinical Hospital #2, Rheumatology, Rostov-on-Don, Russian Federation*; [5]*Yakutsk Clinic Lotos, Rheumatology, Yakutsk, Russian Federation*; [6]*MSD Pharmaceuticals LLC, Medical Affairs, Moscow, Russian Federation*

Background: Coxitis (hip joint inflammation) in AS is associated with worse BASFI scores due to hip joint involvement and more severe axial disease [1]. Radiological index of BASRI-hip, US and MRI findings may be used for evaluation of hip joint impairment [2, 3, 4]. Number of studies on coxitis in AS patients treated with biologics was limited at time of this study initiation.

Objectives: To evaluate clinical changes measured by BASFI, BASMI, BASDAI, ASDAS-CRP and radiological changes in AS patients with coxitis (BASRI-hip, hip MRI [STIR- and T1-weighted sequences], hip US) after 12 and 24 months of treatment with TNF alpha inhibitor golimumab from baseline.

Methods: A non-interventional prospective cohort study. Bio-naïve patients with AS and coxitis were treated with golimumab according to daily clinical practice in 5 clinics across Russia and followed up for 24 months. 39 patients participated. This analysis includes data from 30 patients who completed the follow up. The whole cohort's data to be presented after consolidation of safety data. MRI and US data were collected for 12 months in up to 28 of 30 patients. The primary endpoint was mean change of BASFI which was expected to be -2.5 (± 2.12) from baseline at week 52 weeks (12 months) of therapy [5]. The power of the study was 90% with minimum sample size of 18 patients. Student's paired t-criteria, Wilcoxon signed rank test were used to compare quantitave and Chi-square test for qualitative variables.

Results: Majority of participants (66,7%; 20 out of 30) were male, with mean (SD) age of 33.2 (9.4) years, mean (SD) duration of AS was 36.2 (42.1) months, mean (SD) duration of coxitis was 36.9 (44.1) months. Baseline mean (SD) scores were: BASFI 3.9 (2.5), BASMI 3.1 (2.5), BASDAI 4.9 (2.0), ASDAS-CRP 3.5 (1.2). Changes of mean clinical scores from baseline after 12 and 24 months of treatment with golimumab were: ΔBASFI= -2.2 (p=0.0001), -2.1 (p=0.0000); ΔBASMI= -1.5 (p=0.0000), -1,8 (p=0.0000); ΔBASDAI= -3.0 (p=0.0000), -3.1 (p=0.0000); ΔASDAS-CRP= -2.0 (p=0.0000), -2.1 (p=0.0000), correspondingly (n=30). The clinical results (medians, interquartile ranges, min and max) are presented below.



Baseline mean (SD)/median BASRI-hip was 1.1 (0.8)/1.0 on the right and on the left. Changes of mean/median BASRI-hip score at 12 and 24 months compared to baseline were: 0.3/0.0 (n=25; p=0.2344) and 0.3/0.0 (n=25; p=0.1368) on the right; 0.4/0.0 (n=25; p=0.0352) and 0.4/1.0 (n=25; p=0.0735) on the left. Rates of patients with MRI and US findings are presented below.

Hip	MRI, paired analysis	Patients (%), n=27		Patients (%), n=23	
		Baseline	At 6 months	Baseline	At 12 months
Right	No findings	33.3	48.1	39.1	56.5
	Subchondral bone marrow edema (SBME)	37.0	11.1	34.8	8.7
	Joint effusion	74.1	25.9*	73.9	17.4*
	Enthesitis	33.3	11.1	34.8	21.7
	Fatty degeneration	37.0	55.6	34.8	52.2
Left	No findings	29.6	51.9	30.4	52.2
	SBME	18.5	3.7	8.7	4.3
	Joint effusion	63.0	22.2*	60.9	21.7
	Enthesitis	22.2	18.5	17.4	21.7
	Fatty degeneration	33.3	55.6	30.4	52.2
Hip	US, paired analysis	Patients (%), n=28		Patients (%), n=27	
		Baseline	At 6 months	Baseline	At 12 months
Right	No findings	14.3	50.0*	18.5	51.9*
	Joint effusion	46.4	25.0	51.9	11.1*
	Enthesitis	25.0	14.3	18.5	14.8
Left	No findings	14.3	50.0*	18.5	55.6*
	Joint effusion	42.9	28.6	48.1	25.9
	Enthesitis	17.9	17.9	11.1	18.5

*$p<0.05$

Conclusion: Therapy with TNF alpha inhibitor golimumab for 24 months in AS patients with coxitis was accompanied with statistically significant improvement of clinical scores with primary endpoint achieved (mean BASFI change -2.5 at 12 months), improvement of MRI and US findings without obvious structural progression measured with BASRI-hip score compared to baseline.

REFERENCES:

[1] Cruyssen B.V. et al. Rheumatology 2010; 49: 73-81.
[2] Boonen A. et al. J Rheumatol 2009; 36; 1249-1255.
[3] Cruyssen B.V. et al. Curr Opin Rheumatol 2013, 25: 448-454.
[4] Zhen-Guo H. et al. European Journal of Radiology 82 (2013) 1487-1493.
[5] Konsta et al. Clin Rheumatol (2013) 32:1229-1232.Braun J. et al. Ann Rheum Dis 2012; 71: 661–667.

Disclosure of Interests: Shandor Erdes Speakers bureau: Paid as a speaker during educational activities supported by pharmaceutical companies (MSD, Pfizer, AbbVie, BIOCAD), Ekaterina Agafonova Speakers bureau: Paid as a speaker during educational activities supported by pharmaceutical companies (MSD)., Daria Rumiantceva Speakers bureau: Paid as a speaker during educational activities supported by pharmaceutical companies (Novartis), Satenik Davidian: None declared, Elena Zemerova Speakers bureau: Paid as a speaker during educational activities supported by pharmaceutical companies (MSD, Pfizer), Aleksey Kulikov Speakers bureau: Paid as a speaker during educational activities supported by pharmaceutical companies (MSD, AbbVie, UCB, BIOCAD, Novartis, Sanofi), Olga Markova Speakers bureau: Paid as a speaker during educational activities supported by pharmaceutical companies (MSD, Novartis, Medac, GSK), Ekaterina Lukyanova Employee of: MSD Pharmaceutical LLC (Russia), Director of Medical Affairs., Vladimir Achikyan Employee of: MSD Pharmaceutical LLC (Russia), Therapeutic Area Lead
DOI: 10.1136/annrheumdis-2021-eular.299

POS0904 FACTORS ASSOCIATED WITH SWITCHING FROM ONE ANTI-TNF AGENT TO ANOTHER ANTI-TNF, OR IL17 AGENT IN PATIENT WITH ANKYLOSING SPONDYLITIS

M. Hwang[1], M. Weisman[2], L. S. Gensler[3], A. Tahanan[4], M. Ishimori[2], T. Hunter[5], R. Bolce[5], J. Lisse[5], M. Rahbar6, M. Shan[5], J. D. Reveille[7]. *[1]McGovern Medical School at UTHealth, Rheumatology, Houston, United States of America*; *[2]Cedars-Sinai Medical Records Office, Rheumatology, Los Angeles, United States of America*; *[3]University of California San Francisco Parnassus Campus, Rheumatology, San Francisco, United States of America*; *[4]University Of Texas Professional Building, Medicine, Houston, United States of America*; *[5]Eli Lilly, Medical Affairs, Indianapolis, United States of America*; *[4]University Of Texas Professional Building, Medicine, Houston, United States of America*; *[7]University of Texas McGovern Medical School, Rheumatology, Houston, United States of America*

Background: A recent study examining Commercial Claims Insurance database found that many patients with ankylosing spondylitis (AS) do not remain on their initial TNF inhibitor two years after initiation, particularly women and those taking opioids.

Objectives: To examine factors associated with switching from one TNF inhibitor (i)agent to either another TNFi, IL-17i or JAKi over time (at <2years and >2 years) in a longitudinal cohort of AS patients.

Methods: Patients enrolled in the Prospective Study of Outcomes in AS (PSOAS), an observational longitudinal study of predictors of AS severity operative since 2002-2020 including over 1250 patients meeting modified New York criteria. Data collected included age, gender, ethnicity, HLA-B27 status, disease activity (BASDAI or ASDAS), erythocyte sedimentation rate (ESR), C-reactive protein (CRP), disease severity,(functional (BASFI) or radiographic (mSASSS)), comorbidities, smoking, exercise, disease duration, depression (either by self report or by the Center for Epidemiologic Studies Depression Scale (CES-D) and other medication usage (NSAIDs, including the NSAID index, nonbiologic DMARDs, opioids, anti-depressants, anxiolytics and hypnotics). Logistic regression models were built to identify clinical and sociodemographic characterstics associated with medication switching to another TNFi, IL-17i, or other biologic therapy (another TNFi, Il-17i, or JAKi) within 2 years and after 2 years of initiation).

Results: Of those patients in PSOAS who had at least two years of follow-up, 496 were prescribed anti-TNF, 34 anti-IL-17 and 3 anti-JAK agents. According to the multinomial logistic regression analysis, patients who switched from their original TNFito another TNFi, IL-17i or JAKi within two years after initiating their original TNFi were more likely to be older, have higher baseline subjective disease activity (BASDAI), less radiographic severity by MSASSS, exercise > 120 minutes/week and less likely to be currently smoking. Patients who switched after two years were less likely be depressed, had shorter disease duration, had greater subjective disease activity, were more likely to be exercising > 120 minutes/week, and had more comorbidities.

Conclusion: Different factors were encountered in AS patients who switched from their initial TNFi to another TNFi, IL-17i or JAKi within 2 years versus after 2 years of treatment.

Table 1. Factors Associated With Switching From One TNFi To A Second TNFi or IL-17i or JAKi Before or After Two Years Based On Multinomial Logistic Regression Model (N=496 Patients)

Variable	Switched within 2 years vs. not switched	p-value*	Switched after 2 years vs. not switched	p-value*
Gender (Male vs. Female)	0.99 (0.637, 1.549)	0.98	0.95 (0.528, 1.719)	0.87
HLA-B27_(+ vs. -)	0.99 (0.639, 1.523)	0.95	0.66 (0.365, 1.192)	0.17
Depression (CESD≥ 16 or self-report)(Yes vs. No)	0.99 (0.676, 1.445)	0.95	0.35 (0.182, 0.672)	0.002
Disease duration at baseline (≥20 vs. <20 years)	0.72 (0.485, 1.062)	0.10	0.27 (0.146, 0.491)	<0.001
Age at baseline (≥40 vs. <40) (years)	2.00 (1.291, 3.101)	0.002	1.23 (0.693, 2.193)	0.48
CRP (≥0.8 vs. <0.8)	1.94 (1.230, 3.056)	0.004	0.90 (0.454, 1.789)	0.77
BASFI (≥40 vs. <40)	1.34 0.852, 2.118)	0.20	0.87 (0.450, 1.688)	0.68
BASDAI (≥4 vs. <4)	1.73 (1.064, 2.797)	0.03	2.31 (1.202, 4.427)	0.01
NSAID index (≥50 vs. <50)	1.32 (0.822, 2.128)	0.25	0.83 (0.437, 1.586)	0.58
NSAIDs used (Yes vs. No)	0.84 (0.534, 1.309)	0.43	0.85 (0.479, 1.510)	0.58
Exercise (≥120 vs. <120) (minutes/week)	1.95 (1.396, 2.731)	<0.001	1.66 (1.057, 2.613)	0.03
ASDAS (≥3 vs. <3)	0.78 (0.454, 1.356)	0.39	1.07 (0.478, 2.399)	0.87
Number of comorbidities (≥2 vs. <2)	1.40 (0.997, 1.951)	0.05	1.63 (1.029, 2.575)	0.04
mSASSS (≥4, vs. <4)	0.63 (0.421, 0.957)	0.03	0.81 (0.474, 1.392)	0.03
Current smoker (Yes vs No)	0.69 (0.385, 1.225)	<0.001	0.79 (0.297, 2.076)	0.20

*p-values calculated based on multinomial logistic regression model when switching is defined as being prescribed a second TNFi or taking IL-17i or JAKi before or after 2 years from first TNFi initiation

Disclosure of Interests: Mark Hwang Consultant of: UCB, Novartis, Michael Weisman Consultant of: Novartis, GSK, UCB, Lilly, Lianne S. Gensler Consultant of: AbbVie, GlaxoSmithKline, Eli Lilly, Novartis, Pfizer, UCB Pharma, Amirali Tahanan: None declared, Mariko Ishimori: None declared, Theresa Hunter Employee of: Eli Lilly, Rebecca Bolce Employee of: Eli Lilly, Jeffrey Lisse Employee of: Eli Lilly, Mohammad Rahbar: None declared, Minyang Shan Employee of: Eli Lilly, John D Reveille Consultant of: UCB, Grant/research support from: Eli Lilly
DOI: 10.1136/annrheumdis-2021-eular.515

POS0905 ACHIEVEMENT OF PARTIAL REMISSION AND INACTIVE DISEASE IN UPADACITINIB-TREATED PATIENTS WITH ANKYLOSING SPONDYLITIS

A. Deodhar[1], A. Ostor[2], A. Maniccia[3], F. Ganz[4], T. Gao[3], A. Chu[3], D. Poddubnyy[5]. *[1]Oregon Health & Science University, Rheumatology, Portland, United States of America*; *[2]Cabrini Hospital, Monash University & Emeritus Research, Melbourne, Australia*; *[3]AbbVie Inc., Rheumatology, North Chicago, United States of America*; *[4]AbbVie, Rheumatology, Baar, Switzerland*; *[5]Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité-Universitätsmedizin, and Epidemiology Unit, German Rheumatism Research Centre, Berlin, Germany*

Background: Assessment of SpondyloArthritis international Society (ASAS) response criteria and AS Disease Activity Score (ASDAS) are both commonly used, rigorous composite indices consisting of components with relevance to patients. Clinically meaningful thresholds for these measures have been defined to reflect partial remission (PR), inactive disease (ID), and low disease activity (LDA).

Objectives: To study the association of ASAS PR and ordinal ASDAS disease categories (including ASDAS ID, which is the most stringent category of this composite score) in upadacitinib (UPA)-treated patients with AS.

Methods: In the SELECT-AXIS 1 (NCT03178487) study, biologic DMARD naïve-patients (pts; ≥18 y) with active AS and intolerance/contraindication or inadequate response to ≥2 NSAIDs were randomized 1:1 to UPA 15 mg once daily (QD) or placebo (PBO).[1] At wk 14, pts entered an open-label extension (OLE) of UPA 15 mg QD; pts randomized to PBO were switched to UPA. This post hoc analysis assessed the responsiveness of individual ASAS and ASDAS core components among pts who achieved ASAS PR. The association of ASAS PR with achievement of ASDAS ID (ASDAS <1.3), ASDAS LDA (ASDAS <2.1 but ≥1.3) or ASDAS high disease activity (HDA)/very HDA (VHDA) (ASDAS ≥2.1 for HDA/VHDA) was also assessed by measures including Youden index, distance to perfect point, and sensitivity/specificity

equality. These evaluations were performed in pts randomized to UPA from baseline (BL; continuous UPA, assessed at wk 14) and those who were randomized to PBO and switched to UPA upon entry in the OLE (PBO to UPA; re-baselined at wk 14 and assessed at wk 32, representing 18 wks of UPA exposure).

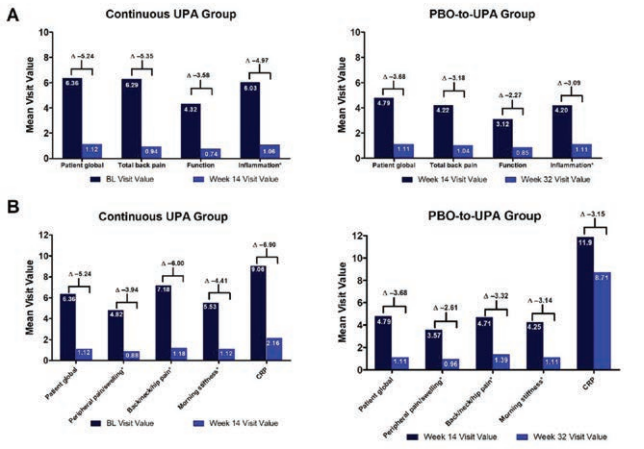
Results: At wk 14, for the continuous UPA group, 16 pts (19%) achieved ASAS PR. At wk 32, following 18 wks of UPA exposure for the PBO-to-UPA group, 28 pts (33%) achieved ASAS PR. Among both groups (continuous UPA and PBO-to-UPA), improvements were seen across all core components (Figure 1). Of the 44 total pts who achieved ASAS PR, 91% achieved either ASDAS ID or LDA. The majority of patients who achieved ASAS PR achieved ASDAS ID in the continuous UPA and PBO-to-UPA groups: 11/16 (69%) and 16/28 (57%), respectively. For the continuous UPA group, the remaining 5 pts who achieved ASAS PR also achieved ASDAS LDA (Table 1). ASAS PR was associated with ASDAS categories in the following manner: the highest rate of ASAS PR was achieved for ASDAS ID followed by ASDAS LDA followed by ASDAS HDA/VHDA. The cutoff of 1.3 (the upper threshold for ASDAS ID) was a better discrimination threshold for ASAS PR than the cutoff of 2.1 (the upper threshold for ASDAS LDA).

Conclusion: Nineteen percent of pts receiving UPA from BL achieved ASAS PR after 14 wks of treatment, with similar results seen in pts who were originally randomized to PBO and switched to UPA at wk 14. A consistent improvement was seen across all core components of ASAS among those who achieved ASAS PR with UPA treatment. The achievement of ASAS PR was most closely associated with the achievement of ASDAS ID, providing further clarity on the reduction of disease activity in AS pts treated with UPA.

REFERENCES:

[1] van der Heijde, et al. *Lancet*. 2019;394(10214):2108-2117.

Figure. Core ASAS (A) and ASDAS (B) Components Among Patients Who Achieved ASAS PR



*Inflammation based on mean of BASDAI question 5 and 6; peripheral pain/swelling based on BASDAI question 3; Back/neck/hip pain based on BASDAI question 2; duration of morning stiffness based on BASDAI question 6.
ASAS, Assessment of SpondyloArthritis international Society response criteria; ASDAS, AS Disease Activity Score; PBO, placebo; PR, partial remission; UPA, upadacitinib.

Table 1. Association Between ASAS PR and ASDAS Clinical Thresholds (ID/LDA/HDA or VHDA)

	ASDAS ID (<1.3)	ASDAS LDA (1.3 to <2.1)	ASDAS HDA or VHDA (≥2.1)
Continuous UPA Group	n=15	n=31	n=39
ASAS PR Responders (n=16)	11	5	0
ASAS PR Non-responders (n=69)	4	26	39
PBO to UPA Group	n=25	n=35	n=25
ASAS PR Responders (n=28)	16	8	4
ASAS PR Non-responders (n=57)	9	27	21

P<0.001 for association of ASAS PR with the ordered ASDAS categories of ID-LDA-HDA, for both Continuous UPA Group and PBO to UPA Group. *P*-value calculated from Cochran-Armitage trend test for association of ordinal categories.ASAS, Assessment of SpondyloArthritis international Society response criteria; ASDAS, AS Disease Activity Score; HDA, high disease activity; ID, inactive disease; LDA, low disease activity; PBO, placebo; PR, partial remission; UPA, upadacitinib; VHDA, very high disease activity.

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing support was provided by J Urbanik of AbbVie and M Hovenden and J Matsuura of Complete Publication Solutions, LLC (funded by AbbVie).

Disclosure of Interests: Atul Deodhar Speakers bureau: Novartis and Pfizer, Consultant of: Novartis, Pfizer, AbbVie, Eli Lilly, UCB Pharma, GlaxoSmithKline, Galapagos, Janssen, Boehringer Ingelheim and Celgene, Amgen., Grant/research support from: AbbVie, Eli Lilly, UCB Pharma, GlaxoSmithKline, Andrew Ostor Consultant of: AbbVie, BMS, Roche, Janssen, Lilly, Novartis, Pfizer, UCB, Gilead, and Paradigm, anna maniccia Shareholder of: AbbVie, Employee of: AbbVie, Fabiana Ganz Shareholder of: AbbVie, Employee of: AbbVie, Tianming Gao Shareholder of: AbbVie, Employee of: AbbVie, Alvina Chu Shareholder of: AbbVie, Employee of: AbbVie, Denis Poddubnyy Speakers bureau: AbbVie, BMS, Lilly, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Biocad, Gilead, GSK, Lilly, MSD, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Lilly, MSD, Novartis, and Pfizer

DOI: 10.1136/annrheumdis-2021-eular.566

POS0906

PREVALENCE OF SLEEP DISTURBANCE IN PATIENTS WITH ANKYLOSING SPONDYLITIS WITHIN THE AUSTRALIAN CLINICAL SETTING (ASLEEP STUDY): A REAL-WORLD OBSERVATIONAL STUDY USING THE OPAL DATASET

K. Tymms[1,2], B. Butcher[3,4], T. Sletten[5], T. Smith[2], C. Osullivan[2], G. Littlejohn[2,6], R. Sadler[7], R. Tronnberg[7], H. Griffiths[2,8]. [1]*Canberra Rheumatology, Rheumatology, Canberra, Australia*; [2]*OPAL Rheumatology, Ltd., Sydney, Australia*; [3]*WriteSource Medical, Pty Ltd, Lane Cove, Australia*; [4]*UNSW Sydney, Sydney, Australia*; [5]*Turner Institute for Brain and Mental Health, Monash University, Clayton, Australia*; [6]*Dept of Medicine, Monash University, Clayton, Australia*; [7]*Novartis Australia, Rheumatology, Macquarie Park, Australia*; [8]*Barwon Rheumatology Services, Rheumatology, Geelong, Australia*

Background: Sleep disorders are more prevalent in patients with ankylosing spondylitis (AS) compared to the general population. Sleep disturbance in AS, in addition to pain and fatigue, can lead to impaired physical function and reduced quality of life.

Objectives: The primary objective was to determine the prevalence of sleep disturbance in patients with AS in a real-world Australian cohort using the Insomnia Severity Index (ISI) and Multivariate Apnoea Prediction Index (MAPI). ISI score of ≥ 15 is considered clinical insomnia. MAPI values below 0.05 are suggestive of clinical apnoea.

Methods: Routinely collected, de-identified clinical data were sourced from the OPAL dataset. Patients aged between 18 and 95 years with a diagnosis of AS and who had completed at least one ISI or MAPI questionnaire between Jan-2019 and Sept-2020 were included. ISI and MAPI questionnaires were emailed to patients using OPAL's electronic patient reported outcome (ePRO) delivery method or completed in the clinic using a smart device and returned to the patient's file using a QR code. Disease activity was assessed using BASDAI collected at the same time as the sleep questionnaires. Age, sex and duration of symptoms were used to propensity match patients in the Il-17ai and TNFi group in a 1:2 ratio.

Results: 495 of the 5,323 patients identified with AS completed a questionnaire and were included in the analysis (n=395 TNFi, n=48 Il-17ai (secukinumab), n=52 other therapies). 142 were included in the propensity score matched population (n = 94 TNFi, and n = 48 Il-17ai). In the overall population the mean (SD) age was 48.3 (13.6), 55.4% were males, the mean (SD) BMI was 30.1 (19.6) at the index date and 4.8% reported depression. 51.7% had an optimal disease control (BASDAI <4). The mean (SD) ISI score was 8.6 (6.2). 48.1% reported no clinical significant insomnia, 32.7% reported subthreshold insomnia, 16% reported clinical insomnia (moderate severity) and 3.2% reported clinical insomnia (severe). The mean (SD) MAPI score was 0.4 (0.3). 292 patients (59.0%) had low risk of clinical apnoea, 134 patients (27.1%) had high risk of clinical apnoea and 69 patients 13.9% had not completed the MAPI questionnaire. In the propensity scored matched population, the TNFi and Il-17ai groups had mean (SD) ISI scores of 9.1 (6.6) and 8.9 (5.9) at index, respectively (p = 0.83) and mean (SD) MAPI scores of 0.3 (0.2) and 0.4 (0.3) at index, respectively (p=0.046), however a higher percentage of overweight and obese patients were identified in the Il-17ai treatment group. Ordered logistic regression analysis of the relationship between demographics and ISI in the matched population found that patients with BASDAI ≥4 were seven times more likely to experience greater sleep disturbance (OR 7.29, 95%CI 2.37 to 22.46, p=0.001) than those with BASDAI <4.

Conclusion: In this real-world AS cohort, poor disease control was associated with sleep disturbance, despite bDMARD therapy. Little difference was observed between TNFi and Il-17ai treatment. Screening for sleep disturbance and fatigue in routine clinical care may provide a more holistic view of the burden of this disease.

Table 1. Patient characteristics and outcome scores in the propensity score matched population at index.

	TNFi (n=94)	Il-17ai (n=48)	p value
BMI category Underweight	2 (2%)	1 (2%)	0.094
Normal weight	33 (35%)	8 (17%)	
Overweight	24 (26%)	16 (33%)	
Obese	27 (29%)	21 (44%)	
Missing	8 (9%)	2 (4%)	
Duration of treatment (months), mean (SD)	61.0 (156.7)	23.7 (20.1)	0.18
BASDAI <4	43 (46%)	23 (48%)	0.89
BASDAI > 4	16 (17%)	8 (17%)	
Missing	35 (37%)	17 (35%)	
ISI score, mean (SD)	9.1 (6.6)	8.9 (5.9)	0.83
ISI category (n (%)			0.83
No clinically significant insomnia	44 (57%)	24 (50%)	
Subthreshold insomnia	30 (32%)	15 (31%)	
Clinical insomnia (moderate)	15 (16%)	8 (17%)	
Clinical insomnia (severe)	5 (5%)	1 (2%)	
MAPI score, mean (SD)	0.3 (0.2)	0.4 (0.3)	0.046
MAPI, high apnoea risk Yes	17 (18%)	16 (33%)	0.051
No	62 (66%)	26 (54%)	
Missing	15 (16%)	6 (12%)	

Acknowledgements: The authors acknowledge the members of OPAL Rheumatology Ltd and their patients for providing clinical data for this study, and Software4Specialists Pty Ltd for providing the Audit4 platform. We acknowledge WriteSource Medical Pty Ltd for providing statistical services. Funding for this study was provided by Novartis.

Disclosure of Interests: Kathleen Tymms: None declared, Belinda Butcher: None declared, Tracey Sletten: None declared, Tegan Smith: None declared, Catherine OSullivan: None declared, Geoff Littlejohn Consultant of: AbbVie, Bristol Myers Squibb, Eli Lilly, Gilead, Novartis, Pfizer, Janssen, Sandoz, Sanofi and Seqirus., Ricky Sadler Employee of: Current employee of Novartis, Rebecca Tronnberg Employee of: Current employee of Novartis, Hedley Griffiths Consultant of: AbbVie, Gilead, Novartis and Lilly.

DOI: 10.1136/annrheumdis-2021-eular.578

POS0907 EFFECT OF UPADACITINIB ON REDUCING PAIN IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS AND INADEQUATE RESPONSE TO NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

A. Deodhar[1], X. Baraliakos[2], I. Mcinnes[3], K. De Vlam[4], L. Bessette[5], A. Maniccia[6], R. Lippe[7], C. Saffore[6], T. Gao[6], I. H. Song[6], A. Ostor[8]. [1]*Oregon Health & Science University, Rheumatology, Portland, United States of America*; [2]*Ruhr-University Bochum, Rheumatology, Bochum, Germany*; [3]*University of Glasgow, Rheumatology, Glasgow, United Kingdom*; [4]*University Hospitals Leuven, Rheumatology, Leuven, Belgium*; [5]*Laval University, Rheumatology, Québec City, Canada*; [6]*AbbVie Inc., Rheumatology, North Chicago, United States of America*; [7]*AbbVie Deutschland GmbH & Co. KG, Rheumatology, Wiesbaden, Germany*; [8]*Cabrini Hospital, Monash University & Emeritus Research, Melbourne, Australia*

Background: Pain is a debilitating symptom of ankylosing spondylitis (AS) and negatively impacts patient (pt) lives. Upadacitinib (UPA), a Janus kinase (JAK) inhibitor engineered for increased selectivity for JAK1 over JAK2, JAK3, and tyrosine kinase 2, [1] showed significant efficacy vs placebo (PBO) in the randomized phase 2/3 SELECT-AXIS 1 study in active AS.[2]

Objectives: To evaluate the efficacy of UPA on multiple pain assessments through 64 weeks (wks).

Methods: SELECT-AXIS 1 (NCT03178487) enrolled adults with active AS, who had an inadequate response, intolerance or contraindications to ≥2 NSAIDs, were biologic DMARD naive and met the modified New-York Criteria. Pts were randomized 1:1 to UPA 15 mg once daily (QD, n=93) or PBO (n=94) for 14 wks (Period 1), followed by open-label UPA 15 mg QD during 90-wk extension (Period 2); reported here are data through wk 64. Pain endpoints included the proportion of pts achieving ≥30%/≥50%/≥70% reduction in Pt's Global Assessment (PGA) of pain on a 0–10 numeric rating scale (NRS), minimal clinically important difference (MCID, defined as ≥1 point reduction or ≥15% reduction from baseline [BL]) in PGA of pain, and much better improvement (MBI, defined as ≥2 point reduction and ≥33% reduction from BL) in PGA of pain. In addition, mean change from baseline in PGA of pain, BASDAI questions 2 (neck/back/hip pain) and 3 (peripheral pain/swelling), and pt's assessment of back pain and nocturnal back pain NRS scores (NRS 0–10) were assessed. Non-responder imputation (binary endpoints) and mixed-effects model for repeated measurements (continuous endpoints) were used for missing data/dropouts in Period 1; as-observed analysis was used for Period 2.

Results: A significantly higher proportion of pts receiving UPA vs PBO achieved reductions in all PGA of pain assessments as early as wk 2 that was sustained at all time points in Period 1; the only exception was ≥70% reduction in PGA of pain that was significant at wk 4 and sustained thereafter (Figure 1). For ≥30%/≥50%/≥70% reduction and MBI, the response rate increased over time with UPA; the difference for UPA vs PBO also continued to increase over time for ≥50% and ≥70% reduction endpoints. For MCID, an increase from BL to wk 2 was observed and plateaued thereafter. The mean change from BL in PGA of pain, BASDAI Q2, back pain, and nocturnal back pain NRS scores were significantly greater for UPA vs PBO at all time points in Period 1; BASDAI Q3 was significant at wk 8 and 14 (Figure 1). The effect of UPA on pain reduction was sustained through wk 64. PBO pts who switched to open-label UPA at wk 14 generally reached the same level of pain reduction as those initially randomized to UPA (Figure 1).

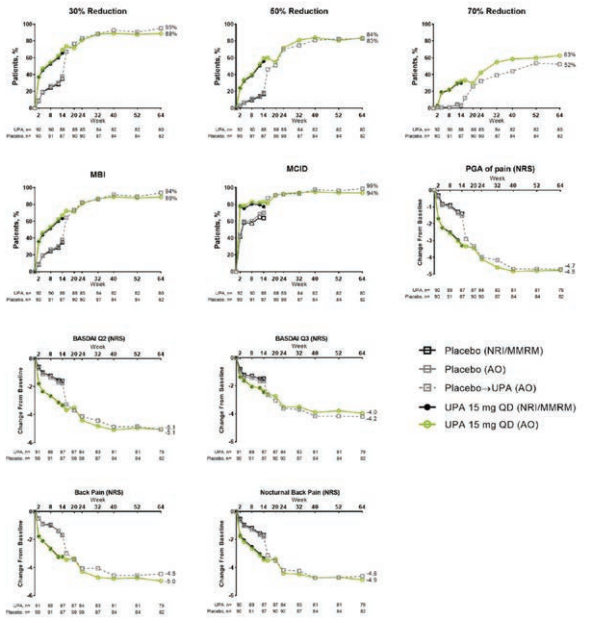
Conclusion: In pts with active AS and an inadequate response/contraindication to NSAIDs, a greater proportion of patients treated with UPA achieved rapid, significant, and clinically meaningful reductions in pain vs PBO through 14 wks across multiple pain assessments. The reductions in pain were sustained over time, and pts who switched from PBO to UPA reached the same level of improvement as the continuous UPA group.

REFERENCES:

[1] Parmentier JM, et al. *BMC Rheumatology*. 2018;2(23).

[2] van der Heijde D, et al. *Lancet*. 2019;394(10214):2108-2117.

Figure. Proportion of Patients Achieving Pain Endpoints (≥30%/50%/70% Reduction from Baseline and MBI or MCID in PGA of Pain) and Mean Change from Baseline in PGA of Pain, BASDAI Q2 and Q3, Back Pain, and Nocturnal Back Pain



AO, as observed; MBI, much better improvement; MCID, minimal clinically important difference; MMRM, mixed-effects model for repeated measurements; NRI, non-responder imputation; NRS, numeric rating scale; PGA, patient's global assessment; UPA, upadacitinib.
Dashed line: all patients randomized to placebo received open-label UPA starting from week 14.
UPA vs PBO comparison was calculated using Cochran-Mantel-Haenszel test adjusting for stratification factor of high-sensitivity CRP level; nominal *P* values:
***P<0.001, †P<0.05.
Patient's Global Assesment of Pain based on: "How much pain have you had because of your condition during the last week?"
BASDAI Q2 based on a question: "How would you describe the overall level of AS neck, back or hip pain you have had?"
BASDAI Q3 based on a question: "How would you describe the overall level of pain/swelling in joints other than neck, back or hips you have had?"
Patient's assessment of back pain based on question: "What is the amount of back pain that you experienced at any time during the last week?
Patient's assessment of nocturnal back pain based on a question:"What is amount of back pain at night that you experienced during the last week?"

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing support was provided by M Hovenden and J Matsuura of ICON plc and was funded by AbbVie.

Disclosure of Interests: Atul Deodhar Speakers bureau: Novartis, Pfizer, AbbVie, Eli Lilly, UCB Pharma, GlaxoSmithKline, Consultant of: Novartis, Pfizer, AbbVie, Eli Lilly, UCB Pharma, GlaxoSmithKline, Grant/research support from: Novartis, Pfizer, AbbVie, Eli Lilly, UCB Pharma, GlaxoSmithKline, Xenofon Baraliakos Consultant of: Novartis, Pfizer AbbVie, Eli Lilly, UCB Pharma, Galapagos Janssen, Celgene and Amgen, Grant/research support from: Novartis, Pfizer AbbVie, Eli Lilly, UCB Pharma, Galapagos Janssen, Celgene and Amgen, Iain McInnes Consultant of: AbbVie, AstraZeneca, Boehringer Ingelheim, Bristol

Myers, Celgene, Janssen, Leo, Lilly, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, AstraZeneca, Boehringer Ingelheim, Bristol Myers, Celgene, Janssen, Leo, Lilly, Novartis, Pfizer, and UCB, Kurt de Vlam Speakers bureau: Celgene Eli Lilly, Galapagos, Novartis, and UCB, Consultant of: Celgene, Eli Lilly, Galapagos, Novartis, and UCB, Grant/research support from: Celgene and Galapagos, Louis Bessette Speakers bureau: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, and Sanofi, Consultant of: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, Gilead, Grant/research support from: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, and Gilead, anna maniccia Shareholder of: AbbVie, Employee of: AbbVie, Ralph Lippe Shareholder of: AbbVie, Employee of: AbbVie, Christopher Saffore Shareholder of: AbbVie, Employee of: AbbVie, Tianming Gao Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie, Employee of: AbbVie, Andrew Ostor Consultant of: AbbVie, BMS, Roche, Janssen, Lilly, Novartis, Pfizer, UCB, Gilead, and Paradigm

DOI: 10.1136/annrheumdis-2021-eular.604

POS0908

EFFICACY OF IXEKIZUMAB THROUGH 52 WEEKS FOR IMPROVING PERIPHERAL JOINT INVOLVEMENT AMONG PATIENTS WITH RADIOGRAPHIC-AXIAL SPONDYLOARTHRITIS

M. Magrey[1], K. De Vlam[2], A. Kronbergs[3], R. Bolce[3], D. Sandoval[3], X. Li[3], S. Liu Leage[3], D. Poddubnyy[4]. [1]*The MetroHealth System and School of Medicine, Case Western Reserve University, Division of Rheumatology, Cleveland, United States of America*; [2]*Univeristy Hospitals Leuven, Rheumatology Department, Leuven, Belgium*; [3]*Eli Lilly and Company, Lilly Corporate Center, Indianapolis, United States of America*; [4]*Universitätsmedizin Berlin, Division of Rheumatology, Berlin, Germany*

Background: Radiographic-axial spondyloarthritis (r-axSpA) is a progressive chronic inflammatory disease primarily affecting the spine and sacroiliac joints. However, about 30-40% of patients (pts) with axSpA can have peripheral joint involvement, including joint tenderness and swelling, which can contribute significantly to burden of disease. Ixekizumab (IXE), a monoclonal antibody that neutralizes the pro-inflammatory cytokine interleukin-17A, has demonstrated a high level of efficacy in the treatment of r-axSpA.

Objectives: The aim of this study is to evaluate the efficacy of IXE through 52 weeks (wks) in improving peripheral joint pain and swelling for pts with r-axSpA.

Methods: Data was derived from two phase III randomised, double-blind, placebo (PBO)-controlled trials: one in pts with r-axSpA, who were biological disease-modifying anti-rheumatic drug (bDMARD)-naïve (COAST-V: NCT02696785), and the other in pts who were tumor necrosis factor inhibitor-experienced (COAST-W: NCT02696798). All pts had a confirmed diagnosis of r-axSpA and had to meet ASAS (Assessment of SpondyloArthritis international Society) criteria. IXE (80 mg) or PBO were administered subcutaneously every 2 (Q2W) or 4 (Q4W) wks during a 52-wk treatment period, after receiving a starting dose of 80 mg or 160 mg at wk 0. COAST-V/W pts originally randomised to PBO were re-randomised 1:1 to IXE Q4W or Q2W at wk 16. We present a post-hoc analysis of data from an integrated dataset from COAST-V and W (COAST-V/W); with intent to treat (ITT) pts categorized by baseline (BL) peripheral joint status. The presence of peripheral joint involvement was defined using a 46-joint tender joint count (TJC) >0 or 44-joint swollen joint count (SJC) >0. Treatment response through wk 52 was evaluated based on % improvement (20%, 50% or 70%) and resolution of tender or swollen joints of pts with BL TJC>0 or SJC>0, respectively. Missing data were imputed by non-responder imputation (NRI). Treatment comparison vs PBO at wk 16 was performed using Cochran-Mantel-Haenszel test.

Results: This analysis includes 359 pts (63.4% of ITT) with baseline TJC>0 and 203 pts (35.9% ITT) with baseline SJC>0. The mean (SD) baseline TJC and SJC were 7.7 (8.3) and 4.3 (4.5), respectively. Mean BL TJC and SJC values by treatment group are presented in Table 1. A significant improvement of SJC by 20% and 50% was seen in pts treated with IXE Q4W compared to PBO at wk 16. Pts treated with IXE resulted in a numerically higher improvement in TJC and SJC symptoms up to wk 16 compared to PBO, and efficacy was sustained up to wk 52 (Table 1). A higher proportion of IXE-treated pts achieved high-hurdle efficacy endpoints (50% and 70% improvements) in comparison to PBO at wk 16 (Table 1). Over this time period, IXE treatment led to a high proportion of pts experiencing complete resolution of TJC or SJC vs PBO at wk 16, which was sustained up to wk 52 (Fig 1).

Conclusion: In this post hoc analysis, pts with r-axSpA treated with IXE showed substantial improvement in peripheral joint pain and swelling.

Table 1. Improvement of Tender or Swollen Joint Counts for pts with radiographic-axSpA with TJC>0 or SJC>0 at baseline (COAST-V/W)[a] - NRI Results

% Improvement		Radiographic-AxSpA				
Wk		16			52[b]	
		PBO	IXE Q4W	IXE Q2W	IXE Q4W	IXE Q2W
N (TJC>0)		116	129	114	129	114
BL TJC mean (SD)		7.4 (8.8)	8.4 (8.4)	7.3 (7.5)		
%TJC improvement	20%	66.4	75.2	71.1	68.2	72.8
	50%	52.6	61.2	64.9*	65.1	67.5
	70%	37.9	47.3	50	55.8	54.4
N (SJC>0)		67	72	64	72	64
BL SJC mean (SD)		3.8 (4.6)	5.2 (5.2)	3.8 (3.3)		
%SJC improvement	20%	64.2	83.3*	76.6	77.8	78.1
	50%	56.7	77.8†	70.3	75	76.6
	70%	46.3	62.5	60.9	69.4	71.9

Abbreviations: COAST-V/W= integrated COAST-V and COAST-W; PBO = placebo; IXE= ixekizumab; Q4W = 80 mg IXE every 4 wks; Q2W = 80 mg IXE every 2 wks[a]Improvement in the number of tender or swollen joints were summarized on ITT patients who had tender (TJC>0) or swollen (SJC>0) joints at baseline, respectively[b]COAST-V/W PBO data are not available at wk 52 as pts originally randomised to PBO were re-randomised 1:1 to IXE Q4W or IXE Q2W at wk 16p-value vs. PBO at wk 16: *P<0.05, †P<0.01, ‡P<0.001

Figure 1. Complete Resolution of Tender or Swollen Joint Counts for pts with radiographic-axSpA with TJC>0 or SJC>0 at baseline (COAST-V/W) [a] - NRI Results

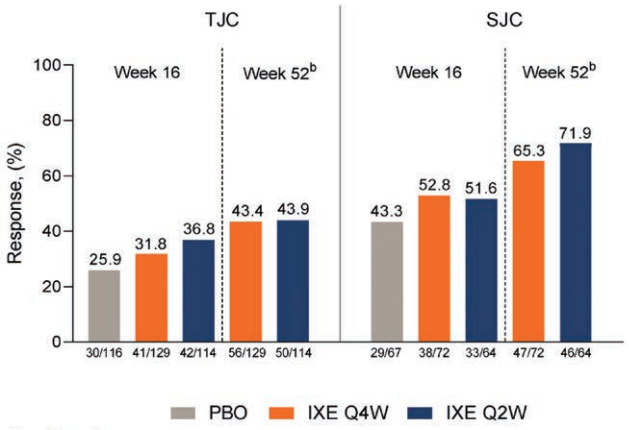


Figure Legend
Abbreviations: COAST-V/W= integrated COAST-V and COAST-W; PBO = placebo; IXE= ixekizumab; Q4W = 80 mg IXE every 4 wks; Q2W = 80 mg IXE every 2 wks
[a]Complete Resolution in the number of tender or swollen joints were summarized on ITT patients who had tender (TJC>0) or swollen (SJC>0) joints at baseline, respectively
[b]COAST-V/W PBO data are not available at wk 52 as patients originally randomised to PBO were re-randomised 1:1 to IXE Q4W or IXE Q2W at wk 16
p-value vs. PBO at wk 16: *P<0.05, †P<0.01, ‡P<0.001

Acknowledgements: Writing support was provided by Sinéad O' Loughlin, an employee of Eli Lilly and Company

Disclosure of Interests: Marina Magrey Consultant of: Novartis, UCB, Pfizer, Eli Lilly, Abbvie, Janssen, Kurt de Vlam Speakers bureau: UCB, Novartis, Pfizer, Eli Lilly, Amgen, Celgene, Paid instructor for: UCB, Amgen, Celgene, Consultant of: UCB, Novartis, Pfizer, Eli Lilly, Amgen, Celgene, Grant/research support from: Pfizer, Amgen, Celgene, Andris Kronbergs Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Rebecca Bolce Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Xiaoqi Li Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Soyi Liu Leage Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Denis Poddubnyy Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb,

Biocad, Gilead, GlaxoSmithKline, Eli Lilly, MSD, Novartis, Pfizer, Samsung Bioepis, and UCB, Grant/research support from: AbbVie, Eli Lilly, MSD, Novartis, and Pfizer

DOI: 10.1136/annrheumdis-2021-eular.761

POS0909 IXEKIZUMAB IMPROVES SIGNS, SYMPTOMS AND QUALITY OF LIFE OF ANKYLOSING SPONDYLITIS IN PATIENTS IRRESPECTIVE OF HLA-B27 STATUS: POOLED RESULTS FROM THE COAST-V AND COAST-W TRIALS

J. D. Reveille[1], P. Rahman[2], D. Sandoval[3], T. Muram[4], R. Bolce[4], S. Y. Park[4], M. Rudwaleit[5]. *[1]University of Texas Houston, Department of Internal Medicine, Houston, United States of America*; *[2]Memorial University of Newfoundland, Clinical Research, St. John's, Canada*; *[3]Eli Lilly and Company, Immunology, Indianapolis, United States of America*; *[4]Eli Lilly and Company Corporate Center, Immunology, Indianapolis, United States of America*; *[5]Charité - Campus Benjamin Franklin (Berlin), Rheumatology, Berlin, Germany*

Background: Human leukocyte antigen-B27 (HLA-B27) is found in most patients (pts) with ankylosing spondylitis (AS). Although a subset of pts with AS are HLA-B27 negative (NEG), ensuring treatment efficacy in this subpopulation is important.

Objectives: This analysis evaluated the efficacy of ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A, in AS pts who are either HLA-B27 positive (POS) or NEG.

Methods: COAST-V (NCT02696785) and COAST-W (NCT02696798) were 2 phase 3, multicenter, randomized, double-blind, PBO-controlled trials investigating the efficacy of 80-mg IXE administered every 4 weeks (Q4W) and every 2 weeks (Q2W) in pts naïve to biological disease-modifying anti-rheumatic drugs (bDMARDs; COAST-V) and in those who were inadequate responders or intolerant to 1 or 2 tumor necrosis factor inhibitors (TNFi; COAST-W). Only data from pts randomized at baseline to PBO, IXE Q4W or Q2W in both trials who met per protocol eligibility criteria were integrated and stratified based on HLA-B27 status (POS, NEG) for an *ad hoc* subgroup analysis. Efficacy was assessed using the Assessment of Spondyloarthritis International Society 40 (ASAS40), Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) and Short Form 36 Physical Component Scores (SF-36 PCS). Missing data were imputed by non-responder imputation (NRI) for binary measure and by modified baseline observation carried forward (mBOCF). Data from PBO was reported up to Week 16 and for pooled IXE Q4W and Q2W up to Week 52.

Results: This analysis includes pts with AS who are HLA-B27 POS (N=453; PBO=155, IXE=298) or NEG (N=62, PBO=21, IXE=41). Overall, more pts were male (82.6%, POS; 77.4%, NEG), and for IXE treated pts, the duration of disease since r-axSpA diagnosis was 10.3 (SD=9.1) and 6.9 (SD=5.6) years, among POS and NEG pts respectively (Table 1). Among IXE treated patients, the mean age of HLA-B27 NEG pts was approximately 7-8 years older than HLA-B27 POS pts. At Week 16, 39.6% (n=118/298) of HLA-B27 POS and 29.3% (n=12/41) of HLA-B27 NEG pts achieved ASAS40, and 34.6% (n=103) of HLA-B27 POS and 17.1% (n=7) of HLA-B27 NEG pts achieved BASDAI50; improvements were seen as early as Week 1 and sustained or improved up to Week 52. The mean baseline SF-36 PCS was 33.2 (SD=7.63) for HLA-B27 POS and 31.4 (SD=7.67) for HLA-B27 NEG pts. At Week 16, the mean change from baseline in SF-36 PCS was 7.3 (SD 7.6) for HLA-B27 POS and 3.7 (SD=6.83) for HLA-B27 NEG pts. Improvements were sustained to Week 52 (Figure 1).

Conclusion: IXE improves signs, symptoms, patient-reported outcomes and health-related quality of life in HLA-B27 POS and NEG pts with AS, however the HLA-B27 POS pts have a faster and more robust response than HLA-B27 NEG pts.

Table 1. Baseline Characteristics by HLA-B27 Positive and Negative Status

	Positive HLA-B27		Negative HLA-B27	
	PBO (N=155)	IXE (N=298)	PBO (N=21)	IXE (N=41)
Male, n (%)	133 (85.8)	241 (80.9)	18 (85.7)	30 (73.2)
Age of r-axSpA onset (yr), mean (SD)	25.2 (9.28)	26.3 (8.38)	35.4 (8.43)‡	34.6 (10.32)‡
Duration of symptoms since r-axSpA onset (yr)	18.7 (11.82)	17.1 (10.38)	16.0 (9.69)	15.9 (12.40)
C-Reactive protein (mg/L), mean (SD)	16.7 (22.43)	16.9 (25.50)	18.1 (21.69)	13.7 (14.38)
ASDAS score, mean (SD)	4.0 (0.78)	4.0 (0.83)	4.3 (0.76)	4.1 (0.73)
BASDAI score, mean (SD)	7.1 (1.25)	7.2 (1.37)	7.6 (1.31)*	7.4 (1.41)
SF-36 PCS, mean (SD)	33.7 (7.50)	33.2 (7.63)	34.1 (8.28)	31.4 (7.67)

Abbreviations: ASDAS, Assessment of Spondyloarthritis International Society 40; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HLA-B27, Human leukocyte antigen-B27; IXE, pooled ixekizumab every 2 weeks and every 4 weeks; N, total number of patients in group; n, number of patients in category/subgroup; PBO, placebo; r-axSpA, axial spondyloarthritis; SD, standard deviation; SF-36 PCS, Short Form 36 Physical Component Scores; yr, years.*p-value*: vs. HLA-B27 positive: *≤0.05, ‡ <0.0001

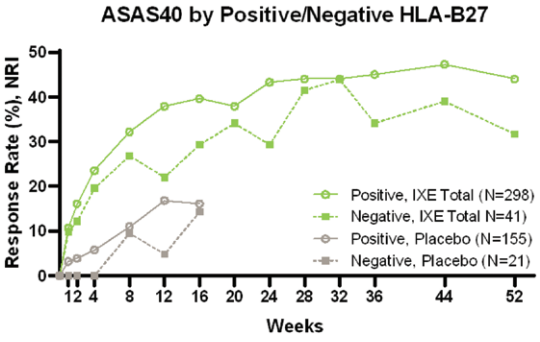


Figure 1. Proportion of patients achieving ASAS40by HLA-B27 Positive and Negative Status in patients randomized to placebo up to Week 16 and ixekizumab up to Week 52

Abbreviations: ASAS40, Assessment of Spondyloarthritis International Society 40; HLA-B27, Human leukocyte antigen-B27; IXE, pooled ixekizumab every 2 weeks and every 4 weeks; NRI, nonresponder imputation

Figure 1. Comparisons done using t-test and chi-square test for continuous and categorical variables.

Disclosure of Interests: John D Reveille Consultant of: UCB (Union Chimique Belge), Eli Lilly, Novartis, and Pfizer, Grant/research support from: Janssen 2018; Eli Lilly 2020, Proton Rahman Speakers bureau: Abbott, AbbVie, Amgen, Bristol-Meyers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and Pfizer, Consultant of: Abbot, AbbVie, Amgen, Bristol-Meyers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and Pfizer, Grant/research support from: Janssen and Novartis, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Talia Muram Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Rebecca Bolce Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, So Young Park Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Martin Rudwaleit Speakers bureau: AbbVie, Bristol-Meyers Squibb, Chugai, Janssen, Eli Lilly, MSD (Merck Sharp and Dohme), Novartis, Pfizer, UCD (Union Chimique Belge), Consultant of: AbbVie, Janssen, Eli Lilly, Novartis, Pfizer, UCB (Union Chimique Belge)

DOI: 10.1136/annrheumdis-2021-eular.801

POS0910 EVALUATION OF THE NONSTEROIDAL ANTI-INFLAMMATORY DRUG-SPARING EFFECT OF SECUKINUMAB IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS OF THE MULTICENTER, RANDOMISED, DOUBLE-BLIND, PHASE IV ASTRUM-TRIAL

U. Kiltz[1,2], X. Baraliakos[1,2], J. Brandt-Juergens[3], U. Wagner[4], S. Lieb[5], C. Sieder[5], C. Mann[5], J. Braun[1,2]on behalf of The study was sponsored by Novartis Pharma GmbH, Germany.. *[1]Rheumazentrum Ruhrgebiet, Claudiusstraße, Herne, Germany*; *[2]Ruhr-Universität Bochum, Universitätsstraße, Bochum, Germany*; *[3]Rheumatologische Schwerpunktpraxis, Seelbergstraße, Berlin, Germany*; *[4]Universitätsklinikum Leipzig AöR, Medizinische Klinik und Poliklinik 3 für Endokrinologie,*

Nephrologie, Rheumatologie, Sektion Rheumatologie, Leipzig, Germany; [5]*Novartis Pharma GmbH, Immunology, Hepatology and Dermatology, Nürnberg, Germany*

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to treat inflammatory back pain in patients (pts) with ankylosing spondylitis (AS). However, an increased risk of side effects associated with NSAIDs and their dosage has been reported[1]. Therefore, lower doses and a dose reduction is desirable.

Objectives: To evaluate the short-term NSAID sparing effect of secukinumab (SEC) in AS pts with NSAID intake.

Methods: In a prospective controlled trial, 211 adult pts with active AS (BASDAI ≥4) and an inadequate response (IR) to at least 2 NSAIDs at the highest recommended/tolerated dose and pts with an IR, or those who were naïve/intolerant to a maximum of 2 tumour necrosis factor inhibitors (TNFi) were enrolled. NSAID intake was evaluated using the ASAS-NSAID score. To be eligible, pts had to take at least 50% of the highest recommended/tolerated NSAID dose regularly. Pts were randomised (1:1:1) to receive SEC 150 mg s.c. from Week (Wk) 0 (group [gp] 1), Wk 4 (gp 2) and Wk 16 (gp 3). All groups received SEC 150 mg from Wk 16. NSAID tapering was allowed in all groups from Wk 4 onwards. The primary endpoint (PE) was an ASAS20 response of pooled gp 1 and gp 2 *vs.* gp 3 at Wk 12.

Results: There were 71 pts in gp 1, 70 in gp 2 and 70 in gp 3. Baseline (BL) characteristics were comparable across groups; mean age (SD) was 45.2 (12.3) years (yrs), time since diagnosis was 7.4 (9.8) yrs, 57.8% male, 79.0% HLA-B27 positive, 48.6% pts had an elevated CRP 40.8% were current/ever smoker and 72.0% were TNFi-naïve. The ASAS-NSAID (SD) scores at BL were: gp 1 *vs.* gp 2 *vs.* gp 3: 82.9 (37.7) *vs.* 79.9 (45.3) *vs.*82.3 (39.1). BASDAI and ASDAS-CRP scores were similar between groups: 6.0 (1.4) *vs.* 6.2 (1.5) *vs.* 6.2 (1.3), and 3.4 (0.7) *vs.* 3.3 (0.8) *vs.* 3.4 (0.7), respectively. The ASAS20 response at Wk 12 of pooled gp 1 and 2 *vs.* gp 3 was 51.1% *vs.* 44.3% but PE was not met (p=0.35). A higher proportion of pts in gp 1 and 2 achieved ASAS40 and BASDAI50 and other secondary outcomes at Wk 16 (Table 1). More pts in gp 1 and 2 reduced their NSAID intake from BL through Wk 16 *vs.* gp 3 (Table 1 **and** Figure 1).

Table 1. Effect of SEC 150 mg s.c. in AS pts (Intention-to-Treat population) at Wk 16

(%), unless otherwise specified	Group 1 (N=71) (SEC 150 mg from BL until Wk 20)	Group 2 (N=70) (PBO from BL until Wk 4; SEC 150 mg from Wk 4)	Group 3 (N=70) (PBO from BL until Wk 16; SEC 150 mg from Wk 16)
ASAS20*	56.3	50.0	41.4
ASAS40*	43.7§	32.9	21.4
ASAS5/6*	39.4‡	32.9	21.4
ASAS-PR*	8.5	20.0‡	5.7
ASAS20			
TNF-IR^*	60.0†‡	26.3	45.0
TNF-naïve^^*	54.9	58.8‡	40.0
ASAS40			
TNF-IR^*	45.0	15.8	25.0
TNF-naïve^^*	43.1‡	39.2‡	20.0
ASDAS-CRP change (mean±SD)**	-1.2±0.9§	-1.0±0.9‡	-0.7±0.8
BASDAI change (mean±SD)***	-2.3±1.9‡	-2.0±2.0	-1.7±2.0
BASDAI50+	32.4	28.6	22.9
ASAS-NSAID score change (mean±SD)++	-51.5±46.2‡	-42.5±68.6	-33.7±38.8
ASAS-NSAID score			
decrease ≥50%*	64.8‡	58.6	42.9
<10*	52.1§	45.7‡	28.6
=0*	32.4‡	38.6§	17.1

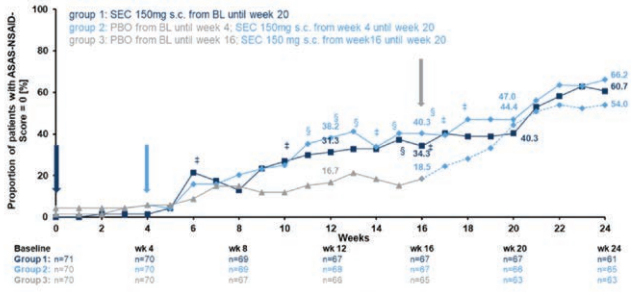
AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis International Society; ASDAS, AS Disease Activity score; BASDAI, Bath AS Disease Activity Index; BL, baseline; CRP, C-reactive protein; IR, inadequate responder; NSAID, nonsteroidal anti-inflammatory drug; N, total number of subjects in each treatment gp; PBO, placebo; PR, partial remission; pts, patients; SEC, secukinumab; TNFi, tumour necrosis factor inhibitor; Wk, week.†p<0.001; §p<0.01 and ‡p<0.05 *vs.* gp 3; ‡‡p<0.05 *vs.* gp 2*p-values are from a logistic regression model with treatment, TNFi status (IR / naïve) and CRP status (>/ ≤ central lab ULN) as factors.*p-values are from MMRM with treatment, TNFi status (IR / naïve), CRP status (>/ ≤ central lab ULN) and visit as factors, BL value as continuous covariate.**Missing values were imputed as non-response.Observed data (pts) for gp 1, 2, 3, respectively:**67, 66, 62***67, 66, 63++67, 67, 65^20, 19, 20^^51, 51, 50

Conclusion: In this population of pts with AS, SEC provided clinical improvements in conventional clinical outcomes and a short-term NSAID sparing effect.

REFERENCES:

[1] Burmester G, et al. Ann Rheum Dis 2011;70:818-822.

Figure: Proportion of patients reaching ASAS-NSAID score=0 through Week 24



ASAS, Assessment of SpondyloArthritis international Society; NSAID, non-steroidal-anti-inflammatory drug; N, total number of pts in each treatment group; n, number of observed pts; PBO, placebo; pts, patients; SEC, secukinumab; s.c., subcutaneous; Wk, week;
Data presented descriptively as observed through Wk 24;
As PE failed, statistical analysis is exploratory; p-values are from a logistic regression model with treatment, TNF inhibitor status (inadequate responder / naïve) and CRP status (> central lab ULN / ≤ lab ULN) as factors †p<0.001; §p<0.01 and ‡p<0.05 vs group 3; Arrows indicate first application of SEC in group 1, group 2 and group 3.

Disclosure of Interests: Uta Kiltz Speakers bureau: AbbVie, Biocad, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Consultant of: AbbVie, Biocad, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: Abbvie, Amgen, Biogen, Fresenius, GSK, Novartis and Pfizer, Xenofon Baraliakos Consultant of: AbbVie, Biocad, Chugai, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: AbbVie, Biocad, Chugai, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Jan Brandt-Juergens Speakers bureau: Abbvie, Pfizer, Roche, Sanofi-Aventis, Novartis, Lilly, MSD, UCB, BMS, Janssen, Medac, Consultant of: Abbvie, Pfizer, Roche, Sanofi-Aventis, Novartis, Lilly, MSD, UCB, BMS, Janssen, Medac, Ulf Wagner Speakers bureau: Pfizer, Novartis and Roche, Consultant of: Pfizer, Novartis and Roche, Grant/research support from: Roche, Novartis, BMS, Pfizer, Sebastian Lieb Employee of: Novartis, Christian Sieder Employee of: Novartis, Christian Mann Employee of: Novartis, Juergen Braun Speakers bureau: Abbvie, Amgen, Celltrion, Chugai, Medac, MSD, Novartis, Pfizer, Roche, and UCB, Consultant of: Abbvie, Amgen, Celltrion, Chugai, Medac, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Abbvie, Amgen, Celltrion, Chugai, Medac, MSD, Novartis, Pfizer, Roche, and UCB

DOI: 10.1136/annrheumdis-2021-eular.1033

POS0911

SIMILAR CLINICAL RESPONSES ACHIEVED WITH LOWER VERSUS STANDARD DOSES OF INFLIXIMAB BIOSIMILAR CT-P13 IN PATIENTS WITH ANKYLOSING SPONDYLITIS: REAL-WORLD RESULTS FROM THE RAAS STUDY

S. S. Lee[1], T. H. Kim[2], W. Park[3], Y. W. Song[4], C. H. Suh[5], S. Kim[6], D. Yoo[2]. *[1]Chonnam National University Medical School & Hospital, Department of Rheumatology, Gwangju, Korea, Rep. of (South Korea)*; *[2]Hanyang University Hospital for Rheumatic Diseases, Department of Rheumatology, Seoul, Korea, Rep. of (South Korea)*; *[3]Inha University, School of Medicine, Incheon, Korea, Rep. of (South Korea)*; *[4]Seoul National University College of Medicine, Seoul National University Hospital, Department of Internal Medicine, Division of Rheumatology, Seoul, Korea, Rep. of (South Korea)*; *[5]Ajou University School of Medicine, Department of Rheumatology, Suwon, Korea, Rep. of (South Korea)*; *[6]Celltrion Healthcare Co., Ltd., Medical Affairs Department, Incheon, Korea, Rep. of (South Korea)*

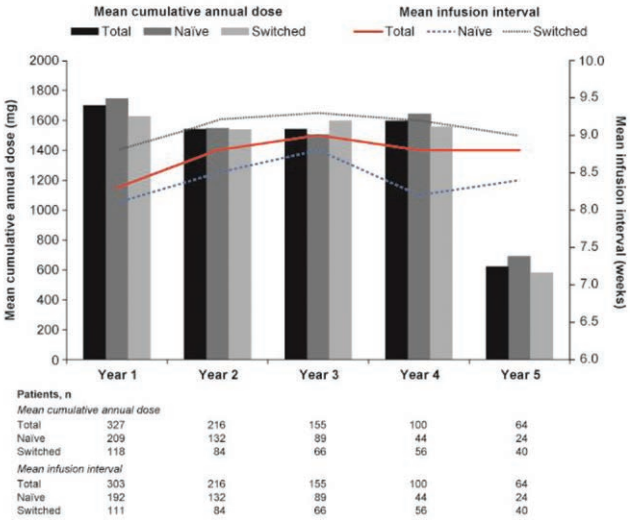
Background: CT-P13, an infliximab biosimilar, is effective for treating ankylosing spondylitis (AS) at a dose of 5 mg/kg infused once every 6–8 weeks. Evidence suggests that patients with AS may benefit from a lower dose, and individualised dose/interval adjustments should be based on treatment response.
Objectives: To analyse real-world treatment patterns (doses and infusion intervals) and outcomes for CT-P13-treated patients with AS over 5 years.
Methods: The RAAS study collected medical record data for adults with AS treated with CT-P13 at five referral hospitals in the Republic of Korea (2012–2017). Patients were infliximab naïve at CT-P13 initiation ('naïve') or had switched to CT-P13 from reference infliximab ('switched'). Patients were analysed by baseline dose (BD) (<4 mg/kg; ≥4–<5 mg/kg; ≥5 mg/kg), defined as the third (naïve) or first (switched) infusion dose. Baseline infusion intervals were the average of the three infusion intervals after BD. Over time, patients with both constant dose and infusion interval were compared with those with changes in dose and/or infusion interval. Data were analysed by Kruskal–Wallis test, chi-squared test and one-way analysis of variance, and drug survival by log-rank test.
Results: Overall, 337 patients (219 naïve; 118 switched) were identified. Of those with BD data, 71, 117 and 82 patients had BDs of <4 mg/kg, ≥4–<5 mg/kg and ≥5 mg/kg, respectively. Most patients were male (74.8%). Patients with higher BDs tended to have higher Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores; switched patients had lower scores than naïve patients. Of 186 evaluable patients (118 naïve; 68 switched), 85 (46 naïve; 39 switched) did not have dose and/or interval changes ('combined constant' group). More naïve (n=72; 61.0%) versus switched (n=29; 42.6%) patients had dose and/or interval changes ('combined changed' group). Considering dose and interval separately, 18/235 evaluable patients (152 naïve; 83 switched) had dose changes (12 increased; 6 decreased) and 110/224 evaluable patients (140 naïve; 84 switched) had interval changes (79 increased; 31 decreased). Cumulative annual doses were similar between naïve and switched patients; switched patients had longer infusion intervals than naïve patients (Figure 1). There were no significant differences in drug survival between BD groups overall or for naïve and switched patients. BASDAI scores over time showed that disease activity was well controlled (Table 1). Patients in the combined changed versus combined constant group had greater improvements in BASDAI score.

Table 1. BASDAI scores

Group		Statistic	W0	W54	W102	W156	W210
Combined constant	Total (N=85)	n	72	73	57	42	31
		Mean	5.50	2.50	2.35	2.42	2.36
		(SD)	(3.12)	(1.71)	(1.66)	(1.66)	(1.68)
		Median	6.32	2.60	2.40	2.55	2.60
	Naïve (n=46)	n	39	39	26	18	12
		Mean	7.86	2.49	2.41	2.34	1.94
		(SD)	(1.45)	(1.82)	(1.75)	(1.70)	(1.58)
		Median	7.80	2.20	1.75	1.90	1.44
	Switched (n=39)	n	33	34	31	24	19
		Mean	2.71	2.50	2.31	2.48	2.63
		(SD)	(2.07)	(1.60)	(1.60)	(1.67)	(1.73)
		Median	2.58	2.75	2.50	2.80	2.70
Combined changed	Total (N=101)	n	87	85	76	53	35
		Mean	5.68	1.81	1.58	1.49	1.40
		(SD)	(2.89)	(1.45)	(1.27)	(1.34)	(1.24)
		Median	6.70	1.32	1.19	1.20	1.00
	Naïve (n=72)	n	63	60	54	34	18
		Mean	7.18	2.01	1.65	1.54	1.52
		(SD)	(1.37)	(1.44)	(1.22)	(1.26)	(0.97)
		Median	7.30	1.83	1.35	1.31	1.35
	Switched (n=29)	n	24	25	22	19	17
		Mean	1.74	1.33	1.42	1.39 (1.50)	1.28
		(SD)	(1.94)	(1.36)	(1.41)		(1.50)
		Median	0.92	0.80	0.85	0.70	0.58

SD, standard deviation; W, Week

Figure. Mean cumulative annual dose and mean infusion interval by treatment group



Conclusion: These real-world data demonstrate that adjusting dose and infusion interval can improve clinical outcomes for CT-P13-treated patients with AS. Drug survival and BASDAI results show that patients with lower baseline BASDAI receiving low CT-P13 doses can achieve the same outcomes as those dosed with ≥5 mg/kg. Findings support the lack of impact of switching from reference infliximab to CT-P13 on efficacy, underlining conclusions previously drawn for efficacy and safety.[1]

REFERENCES:

[1] Kim T-H, et al. *Clin Drug Investig* 2020;40:541–53.

Acknowledgements: Funding: This study was supported by Celltrion Healthcare Co., Ltd. (Incheon, Republic of Korea). Medical writing support was provided by Beatrice Tyrrell, DPhil (Aspire Scientific, Bollington, UK), and funded by Celltrion Healthcare Co., Ltd. (Incheon, Republic of Korea).

Disclosure of Interests: Shin-Seok Lee: None declared, Tae-Hwan Kim: None declared, Won Park Consultant of: Celltrion, Inc., Yeong Wook Song: None declared, Chang-Hee Suh Speakers bureau: AbbVie Inc., Astellas Pharma Inc., Samsung Bioepis Co., Ltd, Consultant of: Celltrion Healthcare Co., Ltd., Eli Lilly and Company, GlaxoSmithKline plc, Janssen Pharmaceuticals, Yungjin Pharmaceutical, Co., Ltd, SooKyoung Kim Shareholder of: Celltrion Healthcare Co., Ltd., Employee of: Celltrion Healthcare Co., Ltd., DaeHyun Yoo Speakers bureau: Celltrion, Consultant of: Celltrion, Grant/research support from: Celltrion

DOI: 10.1136/annrheumdis-2021-eular.1055

POS0912

LONG-TERM TREATMENT WITH IXEKIZUMAB IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: TWO-YEAR RESULTS FROM COAST-Y

J. Braun[1,2], U. Kiltz[1,2], A. Deodhar[3], T. Tomita[4], M. Dougados[5], R. Bolce[6], D. Sandoval[6], D. Adams[6], C. Y. Lin[6], J. A. Walsh[7]. *[1]Rheumazentrum Ruhrgebiet, Rheumatology, Herne, Germany*; *[2]Ruhr-Universität Bochum, Rheumatology, Herne, Germany*; *[3]Oregon Health & Science University, Rheumatology, Portland, United States of America*; *[4]Osaka University Graduate School of Medicine, Rheumatology, Osaka, Japan*; *[5]Hôpital Cochin, Rheumatology, Paris, France*; *[6]Eli Lilly and Company, Biomedicines, Indianapolis, United States of America*; *[7]University of Utah, Rheumatology, Salt Lake City, United States of America*

Background: The efficacy and safety of the interleukin-17 inhibitor ixekizumab (IXE) for the treatment of radiographic (r-) and non-radiographic (nr-) axial spondyloarthritis (axSpA) has been shown for up to 52 weeks.[1-2]
Objectives: To study the efficacy and safety of ixekizumab in the treatment of patients with r- and nr-axSpA for up to 116 weeks.
Methods: COAST-Y (NCT03129100) is the 2-year extension of the COAST-V, -W, and -X trials. Patients continued with the dose received at the end of the originating trial at Week 52, either with 80 mg IXE every 4 weeks (Q4W) or every 2 weeks (Q2W). Patients who had been assigned to adalimumab or placebo were re-randomized to IXE Q4W or Q2W at Week 16 in COAST-V and -W. Patients who had received placebo for 52 weeks in COAST-X were switched to IXE Q4W in COAST-Y. Patients who switched from placebo or adalimumab treatment to IXE (COAST-V, -W, or -X) or from IXE Q4W to open-label IXE Q2W (COAST-X) during the originating studies were analyzed separately from patients continuously treated with IXE. Standardized efficacy measures were used (Table 1). Missing data were handled by non-responder imputation for categorical data

and modified baseline observation carried forward for continuous data. Safety data were analyzed for all patients who received ≥1 dose of IXE.

Table 1. Demographic and efficacy results for patients continuously treated with IXE for 116 weeks

	IXE Q4W N=157		IXE Q2W N=195	
Demographics				
Age	**42.7 (13.0)**		**41.8 (11.2)**	
Male (n, [%])	**124 (79.0)**		**132 (67.7)**	
Baseline ASDAS	**3.92 (0.80)**		**3.95 (0.76)**	
Baseline BASDAI	**7.07 (1.26)**		**7.18 (1.35)**	
Baseline BASFI	**6.57 (1.76)**		**6.74 (1.86)**	
Baseline BASMI	**4.08 (1.46)**		**3.97 (1.52)**	
Baseline SF-36 PCS	**33.90 (7.27)**		**33.26 (6.88)**	
Outcome measure				
Response (n, [%])	**Week 52**	**Week 116**	**Week 52**	**Week 116**
ASDAS <2.1	**75 (47.8)**	**69 (43.9)**	**88 (45.1)**	**96 (49.2)**
ASAS partial remission	**34 (21.7)**	**31 (19.7)**	**35 (17.9)**	**39 (20.0)**
ASAS40	**82 (52.2)**	**89 (56.7)**	**99 (50.8)**	**108 (55.4)**
BASDAI50	**78 (49.7)**	**75 (47.8)**	**83 (42.6)**	**99 (50.8)**
Change from baseline				
ASDAS	**-1.64 (1.05)**	**-1.60 (1.15)**	**-1.63 (1.03)**	**-1.78 (1.04)**
BASFI	**-2.88 (2.31)**	**-2.76 (2.39)**	**-2.83 (2.38)**	**-3.15 (2.34)**
BASMI	**-0.57 (0.95)**	**-0.57 (0.93)**	**-0.53 (0.92)**	**-0.60 (1.00)**
SF-36 PCS	**9.03 (8.62)**	**8.43 (8.70)**	**8.87 (7.57)**	**9.86 (8.45)**

Data are mean (SD) unless otherwise noted. Non-responder imputation was used for categorical variables, and modified baseline observation carried forward for continuous variables.

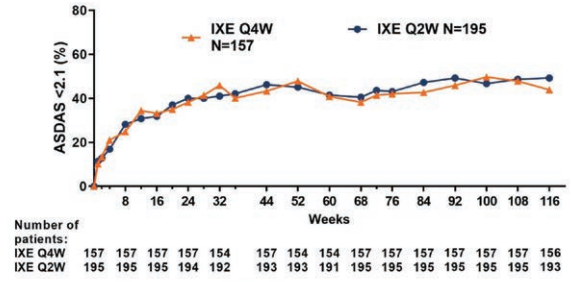
Results: Of the 773 patients enrolled in COAST-Y, 86.0% completed Week 116 of treatment (52 weeks of one of the originating trials and 64 weeks of COAST-Y). Among the patients continuously treated with IXE for 116 weeks (IXE Q4W: N=157; IXE Q2W: N=195), 46.9% achieved low disease activity (ASDAS <2.1), and 19.9% achieved ASAS partial remission at 116 weeks (Table 1; Figure 1). In comparison to baseline, 56.0% achieved ASAS40 (Table 1). The mean change from baseline at Week 116 was –1.70 for ASDAS, –2.98 for BASFI, and 9.22 for SF-36 Physical Component Summary (Table 1). Similar observed responses were achieved between the patients continuously treated with IXE and patients initially treated with placebo or adalimumab. For the 932 patients in the safety population, no new safety signals were identified.

Conclusion: Ixekizumab treatment led to consistent and sustained long-term improvements in disease activity and quality of life in patients with r- and nr-axSpA, with no new safety signals after up to 2 years of treatment.

REFERENCES:

[1] Dougados, et al. Ann Rheum Dis 2020;79:176-185.
[2] Deodhar, et al. Lancet 2020; 395:53-64.

Figure: ASDAS <2.1 responses for patients continuously treated with IXE for 116 weeks



Non-responder imputation was used for ASDAS <2.1.

Abbreviations (Table and Figure): ASAS40=achieving 40% improvement in Assessment of SpondyloArthritis International Society (ASAS) criteria, ASDAS=Ankylosing Spondylitis Disease Activity Score; BASDAI50=achieving 50% improvement in Bath Ankylosing Spondylitis Disease Activity Index; BASFI=Bath Ankylosing Spondylitis Functional Index; BASMI=Bath Ankylosing Spondylitis Metrology Index; IXE=ixekizumab; Q2W=every 2 weeks; Q4W=every 4 weeks; SF-36 PCS=36-item Short-Form Health Survey Physical Component Summary.

Disclosure of Interests: Juergen Braun Speakers bureau: Abbvie, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Eli Lilly and Company, Medac, MSD, Mundipharma, Novartis, Pfizer, Roche, Sanofi-Aventis, and UCB, Consultant of: Abbvie, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Eli Lilly and Company, Medac, MSD, Mundipharma, Novartis, Pfizer, Roche, Sanofi-Aventis, and UCB, Grant/research support from: Abbvie, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Eli Lilly and Company, Medac, MSD, Mundipharma, Novartis, Pfizer, Roche, Sanofi-Aventis, and UCB, Uta Kiltz Speakers bureau: AbbVie, Hexal, MSD, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Biocad, Eli Lilly and Company, Grünenthal, Hexal, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Biogen, Hexal, Novartis, and Pfizer, Atul Deodhar Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Giliad, GlaxoSmith & Kline, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Boehringer Ingelheim, Eli Lilly and Company, GlaxoSmith & Kline, Novartis, Pfizer, and UCB, Tetsuya Tomita Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Eisai, Eli Lilly and Company, Janssen, Mitsubishi Tanabe, Novartis, Takeda, Pfizer, Consultant of: AbbVie, Astellas, Bristol-Myers Squibb, Eisai, Eli Lilly and Company, Janssen, Mitsubishi Tanabe, Novartis, Takeda, Pfizer, Maxime Dougados Consultant of: AbbVie, BMS, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, BMS, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, and UCB, Rebecca Bolce Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Adams Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Chen-Yen Lin Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jessica A. Walsh Consultant of: AbbVie, Amgen, Eli Lilly and Company, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Merck, and Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1124

POS0913 UVEAL CATARACT IN PATIENTS WITH SPONDYLOARTHRITIS AND OTHER IMMUNO-INFLAMMATORY DISEASES AND ITS SURGICAL TREATMENT

S. Avetisov[1,2], I. Razumova[3], K. Avetisov[4], A. Godzenko[5]. [1]*Federal State Budgetary Scientific Institution Research Institute of Eye Diseases, Chief Scientific Adviser, Moscow, Russian Federation*; [2]*I.M. Sechenov First Moscow State Medical University (Sechenov University), Department of Eye Diseases, Moscow, Russian Federation*; [3]*Federal State Budgetary Scientific Institution Research Institute of Eye Diseases, Retinal and Optic Nerve Pathologies, Moscow, Russian Federation*; [4]*Federal State Budgetary Scientific Institution Research Institute of Eye Diseases, Department of Modern Methods of Treatment, Moscow, Russian Federation*; [5]*Federal State Budgetary Educational Institution of Additional Professional EducationRussian Medical Academy of Continuous Professional Education, Rheumatology, Moscow, Russian Federation*

Background: Uveitis is a common extra-skeletal manifestation of various systemic diseases, in particular, spondyloarthritis (SpA). Uveal cataract is the frequent complication of endogenous uveitis. Surgical treatment of uveal cataracts is associated with certain problems, the main being a potential risk of recurrence of uveitis, especially in the case of intraocular lens (IOL) implantation.

Objectives: To analyse the results of surgery of complicated uveal cataract in patients with SpA and other rheumatic disorders.

Methods: 30 pts (34 eyes) with uveal cataract as a result of systemic immuno-inflammatory diseases were assessed in the "Research Institute of Eye Diseases" in the period from 2006 to 2018. The postoperative follow-up period ranged from 2 to 12 years. 20 pts had different variants of SpA (Group 1):7 (7 eyes) - ankylosing spondylitis, 1 (1 eye) –reactive arthritis, 1 (1 eye) - psoriatic arthritis, 4 (6 eyes) – juvenile spondyloarthritis, 8 (8 eyes) non-radiological SpA. 10 patients (11 eyes) had other systemic diseases (Group 2): 1 (1 eye) Behcet's disease, 1 (1 eye) - multiple sclerosis, 3 (3 eyes) - Fuchs heterochromic cyclitis, 2 (2 eyes) -cutaneous psoriasis, and 3 (4 eyes) -uveitis of unknown etiology. 4 pts (6 eyes) with juvenile arthritis and pronounced corneal ribbon degeneration were underwent standard intracapsular cryoextraction of the cataract, followed by optical correction of aphakia using spectacle lenses. In other cases, ultrasound phacoemulsification with IOL implantation was used as a surgical aid. All patients had a period of uveitis remission before opreation for at least 2 months.Anti-inflammatory therapy using local glucocorticoid and local and systemic nonsteroidal antiinflammatory drugs was prescribed 2 weeks before and within a month after the operation. Intra and postoperative complications, fluctuations in intraocular pressure (IOP), improvement of visual acuity, and the frequency of uveitis flares after surgery were assessed as the main criteria for analyzing the results of surgery.

Results: A statistically significant decrease in the number of uveitis exacerbations was observed in all pts: in group 1 - from 2,5 ± 0,65 to 1, 2 ± 0,65 per year (p<0.0001), in group 2 - from 2,55 ± 0,21 to 0,89 ± 0,21 per year (p<0.0001), while there were no statistically significant differences between the groups (p=0.31). Statistically significant increase in maximum visual acuity was observed in all groups: in group 1 - from 0,2± 0,38 to 0,58 ± 0,74, p<0.0001, in group 2 – from 0,24 ± 0,05 to 0,69 ± 0,07, p<0.0001. No complications were observed during operations. The phenomena of bullous keratopathy after intracapsular extraction were noted in 2 pts with juvenile arthritis and ribbon-like corneal degeneration. No progression of corneal changes was observed. Opacity in the central zone of the posterior capsule in the period from 2 to 24 months after surgery occurred in 7 cases. In all cases, laser dissection of the posterior lens capsule was performed. Transient increase in IOP in the early postoperative period, normalized by local hypotensive therapy, occurred in 8 cases in groups I. In the long- term follow-up period (2-24 months), persistent IOP decompensation occurred in 6

cases in groups 1 and in 3 cases in groups 2, which required various types of anti-glaucoma operations. Cystic macular edema developed in one case 5 months after surgery as a result of uveitis exacerbation and was stopped by corticosteroid therapy.

Conclusion: Surgery of uveal cataracts in pts with SpA and other immuno-inflammatory diseases providing adequate pre- and postoperative anti-inflammatory therapy improves visual acuity and reduces the frequency of uveitis relapses. Monitoring of IOP is necessary in the postoperative period.

REFERENCES:

[1] Mora P., Gonzales S., Ghirardini S. et al. Perioperative prophylaxis to prevent recurrence following cataract surgery in uveitis patients a two-centre, prospective, randomized trial. Acta Ophthalmol. Scandinavica Fondation. 2016 Sept.; 94(6): e 390-394. http//doi. 10.1111/aos.12955. Epub 2016 Feb 5.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1193

POS0914 IS THERE AN ASSOCIATION BETWEEN AUTOANTIBODIES INDUCTION AND LOSS OF THERAPEUTIC EFFICACY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS TREATED WITH ANTI-TNF-α AGENTS?

A. Martins[1], D. Santos Oliveira[1,2], F. R. Martins[3], M. Rato[1], F. Oliveira Pinheiro[1], D. Fonseca[4], B. M. Fernandes[1], S. Garcia[1], S. Pimenta[1,5], M. Bernardes[1,5], L. Costa[1]. *[1]Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*; *[2]Faculdade de Medicina da Universidade do Porto - FMUP, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; *[3]University Hospital Center of Algarve, Rheumatology, Faro, Portugal*; *[4]Centro Hospitalar Vila Nova de Gaia / Espinho - Unit 1, Rheumatology, Vila Nova de Gaia, Portugal*; *[5]Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal*

Background: Induction of autoantibodies is frequently observed in patients treated with a TNF-α blocker. According to other authors, the incidence of induction of antinuclear antibodies (ANA) and anti-double stranded DNA antibodies (anti-dsDNA) varies between 23-57% and 9-33%, respectively. However, it is unknown whether the induction of these autoantibodies affects the pharmacokinetics and bioavailability of biotherapy and, consequently, reduces the efficacy and safety of the drug.

Objectives: To analyze if there is an association between autoantibodies induction and therapeutic efficacy in a monocentric cohort of patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) treated with anti-TNF-α agents.

Methods: The authors performed a retrospective analysis of patients with axSpA and PsA treated in our University Hospital with a TNF-α blocker as first biologic agent, and analysed the autoantibodies induction rate after 12 (T12) and 24 (T24) months of therapy. Then, they investigated the influence of autoantibodies in therapeutic efficacy at T12 and T24. Clinical evaluation, laboratory findings including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) and disease activity and functional scores (Bath Ankylosing Spondylitis Disease Activity Index – BASDAI, AS Disease Activity Score with CPR - ASDAS-CRP, Bath AS Functional Index - BASFI) were collected from reuma.pt and medical records. For PsA patients, Disease Activity Score-28-CRP (DAS28-CRP), Simple Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI) and Health Assessment Questionnaire (HAQ) scores were also collected. Patients with positive ANA (titer > 1/100) prior to anti-TNF-α therapy were excluded. Continuous variables were analyzed using a t-test and categorical variables using a Chi-square test. P-value <0.05 was considered statistically significant.

Results: In the axSpA group, 235 patients were included, 44.5% were females, mean age at diagnosis of 42.3 ± 12.4 years and median disease duration of 11.5 (IQR 6.0-21.0) years. Positive ANA were observed in 16.9% at T12 and 26.3% at T24 and positive anti-dsDNA in 3.4% at T12 and 3.8% at T24, with similar conversion rates between different anti-TNF drugs and no significant gender difference. A significant difference in ASDAS-CPR was found in axSpA patients with and without ANA at T12 (p=0.047). ASDAS-CPR was 1.16 times higher in patients with ANA comparing to patients without them. However, no difference was found in the others disease activity and functional scores at T12. Furthermore, no significant difference, including ASDAS-CPR, was found at T24. Also, there was no significant difference found when comparing patients with and without anti-dsDNA.

In the PsA group, 94 patients were included, 46.8% were females, mean age at diagnosis of 46.7 ± 11.7 years and median disease duration of 11.5 (IQR 6.5-16.5) years. Positive ANA were found in 14.9% at T12 and 21.3% at T24 and positive anti-dsDNA in 2.1% at T12 and 3.2% at T24. When comparing the groups with and without ANA and with and without anti-dsDNA at T12 and T24, no significant difference in disease activity and functional scores was found.

Conclusion: This study revealed high rates of serology conversion, similar to the rates described before. The authors found that ASDAS-CPR was higher in axSpA patients with ANA after 12 months of therapy. However, this difference was no longer evident after 24 months. No other significant difference was found between patients with and without ANA or with and without anti-dsDNA. The authors consider that the induction of autoantibodies may interfere with the response to anti-TNF-α therapy in a short and initial period of time. Long-term follow-up data are lacking to say whether that influence will disappear consistently over the long run, as they observed after 12 months of therapy. However, they can state that, *a priori*, seroconversion should not lead to treatment suspension because of concerns about loss of efficacy.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1287

POS0915 SUSTAINABILITY OF IXEKIZUMAB RESPONSE AT THE INDIVIDUAL PATIENT LEVEL OVER TIME IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

S. Ramiro[1], R. Bolce[2], D. Sandoval[2], A. Kronbergs[2], S. Y. Park[2], B. Wu[3], J. A. Walsh[4]. *[1]Leiden University Medical Center (LUMC), Department of Rheumatology, Leiden, Netherlands*; *[2]Eli Lilly and Company, Lilly Corporate Center, Indianapolis, United States of America*; *[3]IQVIA RDS Canada ULC, QC, Canada, Kirkland, Canada*; *[4]University of Utah, Division of Rheumatology and the Department of Dermatology, Salt Lake City, United States of America*

Background: Ixekizumab (IXE) has demonstrated efficacy in treating the signs and symptoms of radiographic axial spondyloarthritis (r-axSpA) in patients (pts) up to week (Wk) 52 [1]. Pts may experience fluctuations in the improvements of their symptoms, which may impact their overall quality of life [2]. Providing data at the pt level is important to support consistency and sustainability of efficacy.

Objectives: To analyse IXE response for sustainability at the individual pt level, between Wks 16 and 52.

Methods: COAST-V (NCT02696785) and COAST-W (NCT02696798) were two phase 3, multicentre, randomised, double-blind, placebo-controlled studies (adalimumab was the active control in COAST-V). Pts with active r-axSpA who were either biologic disease modifying anti-rheumatic drug (bDMARD) naïve (COAST-V) or, inadequate responders or intolerant to up to 2 TNF inhibitors (COAST-W) received IXE every 4 weeks (Q4W) or every 2 weeks (Q2W). Only IXE Q4W pts were included in the present analysis (approved dosage for the indication). Separate analyses were conducted on pts who achieved either endpoint; ASAS40 or ASDAS<2.1. The proportion (%) of pts who achieved either ASAS40 or ASDAS<2.1, at Wk 16 and at each visit out to Wk 52 (total of 8 visits) was assessed. Missing data were imputed as non-response. Heatmaps were used to depict the data analysed at the individual patient level across all visits.

Results: In COAST-V, 81 pts enrolled in the trial were initially randomised to IXE Q4W. Of those, 48% (N=39) of pts achieved ASAS40 at Wk 16 (Figure 1), of which 59% (N=23) maintained ASAS40 at every visit afterwards. In total, 85% (N=33) of the ASAS40 achievers at Wk 16 maintained ASAS40 with some (26% (N=10)) fluctuations, between ASAS40 and ASAS20. In COAST-W, 114 pts enrolled in the trial were initially randomised to IXE Q4W. Of those, 25.4% (N=29) pts achieved ASAS40 at Wk 16, of which, 69% (N=20) maintained ASAS40 at every visit afterwards. In total, 83% (N=24), of the ASAS40 achievers at Wk 16 maintained ASAS40 with some (14% (N=4)) fluctuations, between ASAS40 and ASAS20.

Of the 81 pts initially randomised to IXE Q4W in COAST-V, 35 pts achieved low disease activity (ASDAS<2.1, LDA) at Wk 16. Of those, 54% (N=19) of pts maintained LDA at every visit afterwards. In total, 91% (N=32) of the ASDAS-LDA

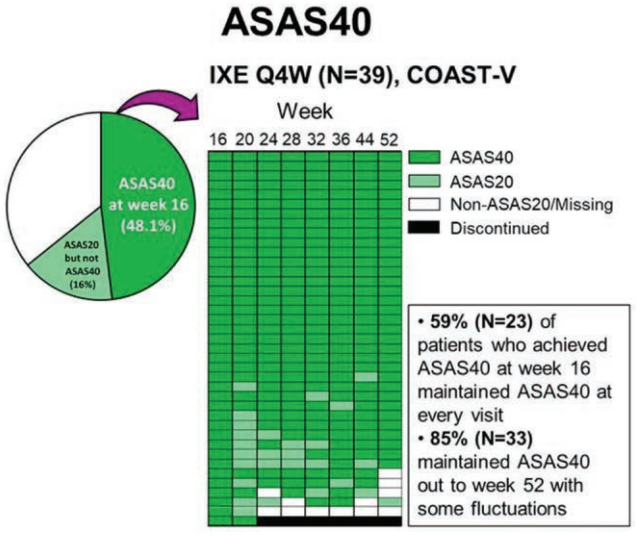


Figure 1. Heatmap diagram depicting the sustained effect of IXE over time at the pt level in pts with r-axSpA from COAST-V. Each row corresponds to an individual ASAS40 responder at Wk 16.

achievers at Wk 16 maintained LDA with some (37% (N=13)) fluctuations, between LDA and high disease activity (ASDAS 2.1-3.5, HDA). Of the 114 pts initially randomised to IXE Q4W in COAST-W, 20 pts achieved LDA at Wk 16. Of those, 50% (N=10) of pts maintained LDA at every visit afterwards. In total, 95% (N=19) of the ASDAS-LDA achievers at Wk 16 maintained LDA with some (45% (N=9)) fluctuations between LDA and HDA.

Conclusion: This analysis demonstrates that pts with r-axSpA and treated with IXE Q4W who achieve ASAS40 or ASDAS-LDA at Wk 16 show a sustainable response, at the individual patient level, with similar levels of efficacy over time and at each visit out to week 52.

REFERENCES:

[1] Dougados et al., Ann Rheum Dis. 2020; 79(2):176-185.
[2] Essers et al., Rheumatology. 2016;55(11):2014-22.

Acknowledgements: Edel Hughes, an employee of Eli Lilly and Company, provided editorial and writing support.

Disclosure of Interests: Sofia Ramiro Speakers bureau: AbbVie, Eli Lilly, MSD, Novartis, UCB, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Sanofi, UCB, Grant/research support from: MSD, Rebecca Bolce Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Andris Kronbergs Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, So Young Park Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, Beilei Wu: None declared, Jessica A. Walsh Consultant of: AbbVie, Amgen, Janssen, Lilly, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Merck, Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1340

POS0916 SAFETY OF BIOLOGIC TREATMENTS IN SOLID ORGAN TRANSPLANT RECIPIENTS: A SYSTEMATIC REVIEW

M. Frederic[1], W. V. Delphine[2], C. Prati[1], D. Wendling[1], F. Verhoeven[1]. [1]*CHRU Besancon, Rheumatology, Besancon, France*; [2]*CHRU Besancon, Hepatology, Besancon, France*

Background: The management of a broad spectrum of autoimmune/inflammatory diseases has been transformed with the development of biological treatments. However, little is known about their use in solid organ transplant recipients, a group of patients with high risk of serious infections and malignancies.

Objectives: To evaluate complications occurring with biologic treatments in solid-organ transplant recipients.

Methods: A systematic review of the literature was performed on the PubMed including Medline, Embase and Cochrane databases, up to 01/10/2020, to identify published case reports/series regarding the use of biologic treatments in solid organ transplant recipients in the context of chronic inflammatory diseases. Collected data were patient's characteristics (age, sex, reason for transplantation, antirejection regimen, type of biological treatment used, autoimmune/inflammatory disease treated, time between transplantation and biotherapy initiation, treatment duration) and their reported complications (deaths, infections, malignancies, graft dysfunction).

Results: 55 papers were included, representing 177 patients (131 liver, 42 kidney, 3 heart, and 1 liver-kidney transplant recipients). Inflammatory bowel diseases represented largely the most common indication of biologic treatment initiation (80.2%), followed by rheumatic diseases (7.3%), hereditary periodic fever syndromes (6.2%) and psoriasis (5.1%). Anti-TNFα were mainly used (81.4%) before anti- $\alpha4\beta7$ integrin Vedolizumab (23.7%) and anti-IL1R Anakinra (7.3%). 25/177 patients had several lines of different treatments. Median treatment duration was 13.5 months. Infections occurred in 48 patients (27.1%) through 76 recorded flares (mostly bacterial 68.4% and viral 19.7%). No therapeutic or epidemiological factor was associated with the occurrence of an infection. 16 patients (9.0%) developed malignancies, especially colorectal (4 cases, 2.3%) and skin cancers (4 cases, 2.3%) or Post-transplantation lymphoproliferative disorders (3 cases, 1.7%). Acute graft rejections occurred in 5 patients (2.8%), mostly in kidney transplants (4/5). Among a total of 177 patients, 6 deaths were identified (3.4%).

Conclusion: This review gathers, to our knowledge, the largest number of published case series/reports about the use of biological treatments in solid organ transplant recipients, providing data about their safety. Caution must be taken about eventual publication bias and the necessity of further head-to-head analysis comparing complications occurring in solid organ transplant recipients cohorts with and without biologic treatments.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1372

POS0917 EFFECTIVENESS AND SAFETY OF COMBINED BIOLOGICAL THERAPY IN PATIENTS WITH REFRACTORY SPONDYLOARTHRITIS

C. Valero[1], J. P. Baldivieso[1], I. Llorente[1], E. Tomero Muriel[1], I. González-Álvaro[1], S. Castañeda[1], R. Garcia de Vicuna[1]. [1]*Hospital La Princesa, Rheumatology, Madrid, Spain*

Background: Biological therapy in combination is discouraged in the guidelines for the treatment of immune-mediated inflammatory diseases, attending to safety reasons. However, combined biological therapy could be a valid alternative in patients with highly refractory spondyloarthritis (SpA) as has been previously demonstrated in some reluctant inflammatory bowel disease patients. Published experiences in the literature are very scarce and the follow-up is limited.

Objectives: The aim of this study is to determine the effectiveness and safety of the association of biological drugs in patients with SpA and describe the clinical profile of these patients.

Methods: This is a retrospective, cross-sectional and descriptive study. We included patients with SpA who had received simultaneously at least two biological drugs with different therapeutic targets. We reviewed the database of our hospital that included all patients diagnosed with SpA meeting the ASAS criteria for axial SpA under active biological treatment.

Demographics, clinical and laboratory data, previous treatments, disease activity index (ASDAS CRP) and adverse events were collected. Remission and low activity criteria were considered according to cut-off descriptions in ASDAS CRP, <1.3 and 2.1, respectively.

Results: We identified six patients with SpA receiving combined biological therapy (Table 1). All patients showed high disease activity at the start of combination treatment and most of them presented several disease domains involvement. The average of previous biologics drugs was 5.33 ± 1.75. Four patients received an anti-TNF in combination with an anti-IL17 agent and one patient with concomitant Crohn disease was prescribed an anti-TNF combined with an anti-IL23 agent. The sixth patient, with SpA and concomitant systemic lupus erythematosus, received rituximab with an anti-IL17 (Table 1). The median treatment duration of the combined biological therapy was 12.5 months (IQR 4-43.5; range: 4-117). All patients achieved low disease activity or clinical remission at some point during follow-up, allowing for initial de-escalation of initial dose in some patients. Only one patient experienced a transient relapse (unic uveitis episode). No relevant adverse effects have been found clearly attributable to combination therapy. A 60-year-old patient with multiple comorbidities has stopped treatment due to aggravation of a previous liver cirrhosis.

Conclusion: Combined biological therapy could be an effective therapeutic alternative to patients with multidomain and refractory SpA. In our series, we provide acceptable safety data for follow-up periods that it are longer than the majority of reported cases to date.

Table 1. Main characteristics of patients with SpA and treatment schedules.

Characteristics	Patients (N= 6)		
Male, n	3		
Age at diagnosis (years) mean (IQR)	25 (8-52)		
Ethnicity, n	5 Caucasian; 1 Hispanic		
Smoker, n	1		
Diagnosis	3 Juvenile SpA-ERA, 2 PsA, 1 SpA + SLE		
Duration of disease (years) mean (IQR)	20.5 (5.25-33.5)		
Domains involved, n	6		
Axial	6		
Peripheral	6		
Enthesis	5		
Extra-articular	2 psoriasis (1 with aortic insufficiency), 2 uveitis, 1 Crohn disease		
HLA-B27 +, n	4		
Previous biological or targeted therapy, n			
Anti-TNF	6 (5 etanercept, 5 adalimumab, 4 infliximab, 4 golimumab, 3 certolizumab)		
Anti-IL17	6 (5 secukinumab, 1 ixekizumab)		
Jakinibs	1 (1 tofacitinib)		
Other	3 (1 anakinra, 1 tocilizumab, 1 apremilast)		
Combined biological Therapy	Treatment 1 + Treatment 2	Time of follow-up (months)	Actual state
	1.GOL 100 mg/4w + SEC 150 mg/1w	117	Remission
	2.ETN 50 mg/1w + SEC 150 mg/2w	9	*Low activity
	3.ETN 50 mg/1w + SEC 150 mg/4w;	16	Remission
	4.GOL 100 mg/4w + SEC 150 mg/2w	4	Low activity
	5.GOL 100 mg/3w + RIS 250 mg/12w	4	Low activity
	6.RTX 2g infusion + SEC 150 mg/4w	19	Remission

At treatment interruption*Abbreviations:* ERA: enthesitis-related arthritis; ETN: etanercept; GOL: golimumab; IQR: interquartile range; PsA: psoriatic arthritis; RIS: risankizumab; RTX: rituximab SEC: secukinumab; SLE: systemic lupus erythematosus; SpA: spondyloarthritis; w: week.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1473

POS0918

EVALUATION OF SPINAL RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS RECEIVING IXEKIZUMAB THERAPY OVER 2 YEARS

D. Van der Heijde[1], M. Østergaard[2], J. D. Reveille[3], X. Baraliakos[4,5], A. Kronbergs[6], D. Sandoval[6], X. Li[6], H. Carlier[6], D. Adams[6], W. P. Maksymowych[7]. *[1]Leiden University Medical Centre, Department of Rheumatology, Leiden, Netherlands*; *[2]University of Copenhagen, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Denmark*; *[3]University of Texas-McGovern Medical School, Division of Rheumatology and Clinical Immunogenetics, Houston, United States of America*; *[4]Ruhr-University Bochum, Bochum, Germany*; *[5]Rheumazentrum Ruhrgebiet, Herne, Germany*; *[6]Eli Lilly and Company, Indianapolis, United States of America*; *[7]University of Alberta, Department of Medicine, Edmonton, Canada*

Background: It is important to understand the potential effect long-term therapy with biologics can have on structural changes in the spine among patients with active radiographic axial spondyloarthritis (r-axSpA, ankylosing spondylitis).
Objectives: We examined radiographic progression in the spine among patients with active r-axSpA treated with ixekizumab, an IL-17A antagonist, for 2 years, and potential predictors of spinal radiographic progression.
Methods: Patients with active r-axSpA, biologic-naive (COAST-V, NCT02696785) or with prior experience with a maximum of 2 TNF inhibitors (COAST-W, NCT02696798), received 80 mg ixekizumab every 2 or 4 weeks for 2 years (108 weeks, of which 56 weeks were the COAST-Y extension study, NCT03129100). Mean change from baseline of modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) (average score from 2 selected readers, blinded for time order) for patients treated with ixekizumab for 2 years with data at both baseline and year 2 is presented (N=230; 54% of total randomized patients). Non-progression is presented for all patients and subgroups based on TNFi-experience. Predictors were identified in multivariate logistic regression models with stepwise selection criteria of p-value <0.1. All data are observed.
Results: At baseline, patients (N=230) were predominately male (82%) with an average age of 43 years, mean symptom duration of 16 years, 52% were TNFi-experienced, mean (SD) ASDAS score was 4.0 (0.7), most were HLA-B27 positive (87%) and 40% had syndesmophytes (identified by both selected readers at the same location). Baseline mSASSS (SD) was 11.0 (16.3) and change from baseline at year 2 of treatment was 0.3 (1.8) (Table 1). The proportion of non-progressors (mSASSS change from baseline <2) over 2 years was 89.6% (total IXE [all patients]), 90.9% (biologic-naive) and 88.3% (TNFi-experienced), and, if defined as mSASSS change from baseline ≤0, 75.7% (total IXE [all patients]), 78.2% (biologic-naive) and 73.3% (TNFi-experienced) (Table 1). Predictors of structural progression at year 2 (mSASSS change >0) were age, baseline syndesmophytes, HLA-B27 status and gender (Table 1). Week 52 inflammation in MRI SPARCC spine was also identified as a predictor for structural progression at year 2 in a separate model for patients from COAST-V where MRI measures were available at baseline and Week 52 (N=109).
Conclusion: The majority of patients treated with ixekizumab for 2 years did not show radiographic progression, and the overall mean progression was low. Similar levels of non-progression were observed in biologic-naive patients and patients previously exposed to TNFis. Predictors were generally consistent with previous studies.

Table 1. Spinal radiographic changes for patients with active r-axSpA treated with ixekizumab for 2 years

Change in mSASSS at year 2	All patients[a] N=230	Biologic-naive N=110	TNFi-experienced N=120
Baseline mSASSS, mean (SD)	11.0 (16.3)	10.1 (15.5)	11.7 (17.0)
Change at year 2, mean (SD)	0.3 (1.8)	0.3 (2.0)	0.4 (1.6)
Change in total mSASSS <2, n (%)	206 (89.6)	100 (90.9)	106 (88.3)
Change in total mSASSS ≤0, n (%)	174 (75.7)	86 (78.2)	88 (73.3)
Multivariable logistic regression model			
Prediction for change in total mSASSS >0, OR (95% CI), p-value			
All patients[a,b]		**N=228**	
Age (≥40 years vs. <40 years)		2.97 (1.41, 6.28)	p=0.004[c]
Baseline syndesmophytes[b] (yes vs. no)		2.31 (1.18, 4.54)	p=0.015[c]
Baseline HLA-B27 (positive vs. negative)		3.78 (1.04, 13.75)	p=0.044[c]
Gender (male vs. female)		3.16 (1.01, 9.86)	p=0.047[c]
Baseline ASDAS state (>3.5 vs. [2.1, 3.5])		2.26 (0.96, 5.34)	p=0.063

[a]Combined ixekizumab group of Q2W and Q4W patients with baseline and year-2 mSASSS data[b]Identified by both selected readers at the same location (2 patients were not evaluable by both readers)[c]p<0.05Abbreviations: ASDAS=Assessment of Disease Activity, CI=confidence interval, IXE=ixekizumab, mSASSS=modified Stoke Ankylosing Spondylitis Spinal Score, OR=odds ratio, Q2W=every 2 weeks, Q4W=every 4 weeks, SD=standard deviation, TNFi=tumor necrosis factor inhibitor

Disclosure of Interests: Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma, Employee of: Director of Imaging Rheumatology bv., Mikkel Østergaard Consultant of: AbbVie, BMS, Boehringer-Ingelheim, Eli Lilly and Company, Janssen, Merck, Pfizer, Roche, UCB, Celgene, Sanofi, Regeneron, Novartis, Grant/research support from: AbbVie, BMS, Merck, UCB, Celgene, Novartis, John D Reveille Paid instructor for: UCB, Eli Lilly and Company, Consultant of: UCB, Eli Lilly and Company, Pfizer, Novartis, Grant/research support from: Janssen, Eli Lilly and Company, Xenofon Baraliakos Speakers bureau: Abbvie, BMS, Lilly, Janssen, Novartis, MSD, Pfizer, Galapagos, Gilead, UCB, Paid instructor for: Abbvie, BMS, Lilly, Janssen, Novartis, MSD, Pfizer, Galapagos, Gilead, UCB, Consultant of: Abbvie, BMS, Lilly, Janssen, Novartis, MSD, Pfizer, Galapagos, Gilead, UCB, Andris Kronbergs Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Xiaoqi Li Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Hilde Carlier Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Adams Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Walter P Maksymowych Speakers bureau: Abbvie, Janssen, Novartis, Pfizer, UCB, Consultant of: Abbvie, Boehringer, BMS, Eli Lilly and Company, Novartis, Pfizer, UCB, Grant/research support from: Abbvie, Novartis, Pfizer
DOI: 10.1136/annrheumdis-2021-eular.1620

POS0919

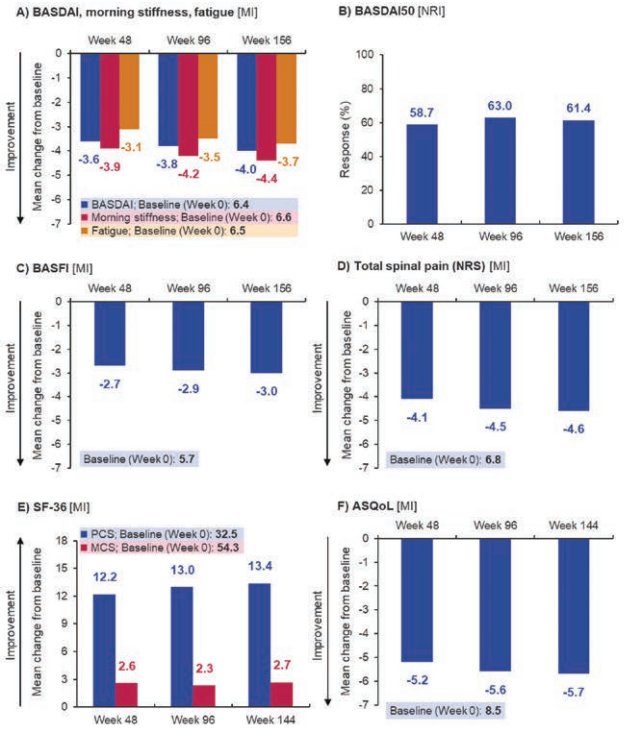
BIMEKIZUMAB SHOWS SUSTAINED LONG-TERM IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES AND QUALITY OF LIFE IN ANKYLOSING SPONDYLITIS: 3-YEAR RESULTS FROM A PHASE 2B STUDY

X. Baraliakos[1], M. Dougados[2], K. Gaffney[3], R. Sengupta[4], M. Magrey[5], N. De Peyrecave[6], M. Oortgiesen[7], T. Vaux[8], C. Fleurinck[6], A. Deodhar[9]. *[1]Ruhr-University Bochum, Rheumazentrum Ruhrgebiet Herne, Herne, Germany*; *[2]Hôpital Cochin, Department of Rheumatology, Paris, France*; *[3]Norfolk and Norwich University Hospital NHS Trust, Rheumatology Department, Norwich, United Kingdom*; *[4]The Royal National Hospital for Rheumatic Diseases, Department of Rheumatology, Bath, United Kingdom*; *[5]Case Western Reserve University, MetroHealth Medical Center, Cleveland, United States of America*; *[6]UCB Pharma, N/A, Brussels, Belgium*; *[7]UCB Pharma, N/A, Raleigh, United States of America*; *[8]UCB Pharma, N/A, Slough, United Kingdom*; *[9]Oregon Health & Science University, Division of Arthritis & Rheumatic Diseases, Portland, United States of America*

Background: Bimekizumab (BKZ), a monoclonal antibody that selectively inhibits interleukin (IL)-17A and IL-17F, has demonstrated clinical efficacy and safety in patients with ankylosing spondylitis (AS) treated over a period up to 96 weeks.[1,2]
Objectives: To report 3-year interim patient-reported outcomes (PROs) in patients with active AS treated with BKZ in a phase 2b dose-ranging study (BE AGILE; NCT02963506) and its open-label extension (OLE; NCT03355573).
Methods: BE AGILE study design has been described previously.[1] Patients treated with BKZ 160 mg or 320 mg every 4 weeks (Q4W) at Week 48 in BE AGILE were eligible for OLE entry. All OLE patients received BKZ 160 mg Q4W. Outcome measures are reported for the OLE full analysis set (patients who entered the OLE and had ≥1 dose of BKZ and ≥1 valid efficacy variable measurement in the OLE), and include: BASDAI, BASDAI50 responder rate, BASFI, fatigue (BASDAI Q1), morning stiffness (mean of BASDAI Q5+6), total spinal pain (numeric rating scale [NRS]), SF-36 PCS and MCS, and ASQoL. Missing data were imputed using multiple imputation (MI; based on the missing at random assumption) for continuous variables and non-responder imputation (NRI) for dichotomous variables.
Results: 262/303 (86%) patients randomised at BE AGILE study baseline (BL) completed Week 48 on BKZ 160 mg or 320 mg, of whom 255/262 (97%) entered the OLE (full analysis set: 254). From baseline to Week 48 in BE AGILE, BKZ-treated patients showed clinically relevant improvements in disease activity (BASDAI, BASDAI50), physical function (BASFI), fatigue, morning stiffness, spinal pain, and quality of life (SF-36 PCS and MCS, ASQoL) (Figure 1). Group-level improvements in all reported continuous efficacy measures exceeded published minimally important difference (MID), minimum clinically important improvement (MCII), and/or minimum clinically important difference (MCID) thresholds (Figure 1).[3,4] Efficacy in all reported outcome measures was maintained or continued to improve from Week 48 to Week 144 or 156 (Figure 1).
Conclusion: BKZ treatment was associated with sustained and consistent efficacy in patients with active AS over 3 years, including patient-reported disease activity, physical function, fatigue, morning stiffness, spinal pain, and quality of life.

REFERENCES:
[1] van der Heijde D. Ann Rheum Dis 2020;79:595–604.
[2] Baraliakos X. Arthritis Rheumatol 2020;72 (suppl 10).
[3] Ogdie A. Arthritis Care Res 2020;72 (S10):47–71.
[4] Maruish ME. User's manual for the SF-36v2 Health Survey (3rd ed). 2011; Lincoln, RI: QualityMetric Incorporated.

Figure. Patient-reported outcomes over 3 years of BKZ treatment



Full analysis set (N=254). Weeks 0 and 48 refer to the BE AGILE and OLE baseline, respectively. All patients received BKZ 160 mg during the OLE after completing BKZ 160 mg or 320 mg in BE AGILE. SF-36 PCS, MCS and ASQoL were recorded to Week 144. Arrows indicate improvement: positive change from baseline represents improvement in SF-36 PCS and MCS; negative change from baseline represents improvement for all other outcomes. MID/MCII/MCID thresholds: BASDAI total score MCII = 0.7; fatigue (BASDAI Q1) MCID = 1.1; morning stiffness (mean of BASDAI Q5+6) MCID = 1.7; BASFI MCII = 0.4; total spinal pain MCID = 1.6; SF-36 PCS score MID = 2; ASQoL total score MCID = -2.[3,4] SF-36 MID values are appropriate for groups with baseline mean T-scores of 30–40; for higher T-score ranges, MID values tend to be higher.[4] MID are not applied for improvement for baseline mean SF-36 T-scores >47, which are considered at least as good as the standard US population, hence no improvement is expected.[4] Since mean SF-36 MCS at baseline was 54.3, the MID was not applied here. ASQoL: Ankylosing Spondylitis Quality of Life questionnaire; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASDAI50: BASDAI 50% improvement from baseline; BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; MCII: minimum clinically important improvement; MCID: minimum clinically important difference; MI: multiple imputation; MID: minimally important difference; NRI: non-responder imputation; NRS: numeric rating scale; OLE: open-label extension; SF-36 MCS: 36-Item Short-Form Survey Mental Component Summary; SF-36 PCS: 36-Item Short-Form Survey Physical Component Summary.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical.
Disclosure of Interests: Xenofon Baraliakos Speakers bureau: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma, Paid instructor for: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer, UCB Pharma, Maxime Dougados Consultant of: AbbVie, Eli Lilly, Novartis, Pfizer and UCB Pharma, Grant/research support from: AbbVie, Eli Lilly, Novartis, Pfizer and UCB Pharma, Karl Gaffney Speakers bureau: AbbVie, Eli Lilly, Novartis, UCB Pharma, Consultant of: AbbVie, Eli Lilly, Novartis, UCB Pharma, Grant/research support from: AbbVie, Gilead, Eli Lilly, Novartis, UCB Pharma, Raj Sengupta Speakers bureau: AbbVie, Biogen, Celgene, MSD, Novartis, UCB Pharma, Consultant of: AbbVie, Biogen, Celgene, Eli Lilly, MSD, Novartis, UCB Pharma, Grant/research support from: AbbVie, Celgene, UCB Pharma, Marina Magrey Consultant of: AbbVie, Eli Lilly, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, UCB Pharma, Natasha de Peyrecave Employee of: UCB Pharma, Marga Oortgiesen Employee of: UCB Pharma, Thomas Vaux Employee of: UCB Pharma, Carmen Fleurinck Employee of: UCB Pharma, Valerie Ciaravino Employee of: UCB Pharma, Atul Deodhar Speakers bureau: Janssen, Novartis, Pfizer, Consultant of: AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Gilead, GSK, Janssen, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB Pharma
DOI: 10.1136/annrheumdis-2021-eular.1840

POS0920 TARGETED SERUM PROTEOMIC ANALYSIS FOLLOWING UPADACITINIB TREATMENT IN ANKYLOSING SPONDYLITIS SHOWS ROBUST SUPPRESSION OF INNATE AND ADAPTIVE IMMUNE PATHWAYS WITH TISSUE REPAIR MODULATION

T. Sornasse[1], I. H. Song[2], T. Radstake[2], D. Mcgonagle[3]. [1]*AbbVie Inc., Immunology Clinical Development, Redwood City, United States of America*; [2]*AbbVie Inc., Immunology Clinical Development, North Chicago, United States of America*; [3]*University of Leeds, School of Medicine, Leeds, United Kingdom*

Background: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients with active ankylosing spondylitis (AS) with an inadequate response (IR) to nonsteroidal anti-inflammatory drugs (NSAID) therapy in the SELECT-AXIS 1[1] trial.
Objectives: To identify pathways modulated by UPA in AS patients with emphasis on those associated with response to treatment.
Methods: A subgroup of patients from the SELECT-AXIS 1 study, with available baseline and at least one follow up plasma sample during the placebo-controlled period, were selected for analysis (PBO, n= 65; UPA 15 mg QD, n=63). The levels of 92 inflammation related protein biomarkers (BioMs) were analyzed using the Olink® platform; change from baseline were expressed as Log_2 Fold Change; a repeated measure mixed linear model identified BioMs differentially modulated by UPA. Relationship between change in BioMs and change in clinical disease activity measures were derived using Pearson's correlation (ASDAS-CRP, BASDAI, and CRP) and Spearman's correlation (MRI Spine SPARCC). Pathway analysis was performed with Ingenuity® Pathway Analysis (Qiagen Inc.).
Results: Treatment with UPA 15 mg QD reduced the levels of BioMs associated with IFN, IL6, T Cells, M1 or "inflammatory" Macrophages, and Dendritic Cells (DC); and increased those of BioMs associated with tissue repair and hematopoiesis. The type of pathways, inferred *in silico* based on BM data, suggests that UPA exerts broad inhibitory activity directly on multiple JAK1-dependent (IFNα/β, IFNγ, IL6, IL2, IL5, IL7, and OSM) and indirectly on JAK1-independent upstream pathways (IL1, IL23, IL17, IL18, and TNFα), resulting in the inhibition of key functional pathways such as leukocyte activation and mobility, inflammatory response, and damage to connective tissue. Improvement in ASDAS-CRP, BASDAI, and MRI spine SPARCC correlated with increase in BioMs associated with tissue repair (FGF5, DNER [Delta/Notch Like EGF Repeat Containing]) and hematopoiesis (FLT3LG,and SCF/KITLG), while improvement in ASDAS-CRP and CRP correlated with decrease in CCL23, CSF1, IL-6, and MMP1; and reduction in only CRP correlated with decrease in IFN- and of TNFα-related BioMs (**Data tables will be presented**).
Conclusion: Treatment of NSAID-IR AS patients with UPA 15 mg QD resulted in the coordinated decrease in multiple BioMs associated with the innate and adaptive immune responses, and in the increase in BioMs generally associated with tissue repair and hematopoiesis. In silico pathway prediction indicates that treatment with UPA directly inhibits JAK1-dependent and indirectly JAK1-independent pathways, resulting in the down modulation of functional pathways related to inflammation and tissue damage which are known to be dysregulated in AS[2]. Based on this observation and on the correlation of change in BioMs with change in clinical measures, we hypothesize that both increase in BioMs associated with tissue repair and hematopoiesis, and decrease in BioMs associated with inflammation may contribute to the clinical activity of UPA in AS patients.
REFERENCES:
[1] van der Heijde, D. et al. **Lancet** 394, 2108-2117 (2019).
[2] Stoll, M.L. **Clin Exp Rheumatol** 29, 322-330 (2011).
Acknowledgements: AbbVie, Inc was the study sponsor, contributed to the study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of the final version
Disclosure of Interests: Thierry Sornasse Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie, Employee of: AbbVie, Timothy Radstake Shareholder of: AbbVie, Employee of: AbbVie, Dennis McGonagle Speakers bureau: AbbVie, Grant/research support from: AbbVie
DOI: 10.1136/annrheumdis-2021-eular.1894

POS0921 EFFICACY AND SAFETY OF ACEMETACIN IN THE TREATMENT OF 1215 ACTIVE ANKYLOSING SPONDYLITIS PATIENTS: DATA FROM A PROSPECTIVE COHORT MANAGED BY SMARTPHONE SPONDYLOARTHRITIS MANAGEMENT SYSTEM

J. Zhang[1], L. Hu[1], X. Ji[1], Y. Wang[1], F. Huang[1]. [1]*Chinese PLA General Hospital, Rheumatology, Beijing, China*

Background: Biological DMARDs have widely used in the treatment of AS in last two decades, but NSAIDs still serves as a cornerstone in the treatment.

Given the wide use of Acemetacin in AS and relative lack of clinical evidence on the selection of NSAIDs in the treatment of AS, the investigation on acemetacin treating AS is of great significance.

Objectives: Our study aims to investigate efficacy and safety of acemetacin in the treatment of AS.

Methods: Data on efficacy and safety is available in 1215 patients from the Chinese Ankylosing Spondylitis Imaging Cohort (CASPIC), which is collected through the Smart-phone SpondyloArthritis Management System (SpAMS)[1]. Patients' self-assessments are completed online at baseline and every subsequent clinic visit. Physician-reported assessments, laboratory tests, and treatments were recorded by rheumatologists at every clinic visit.

Results: 1215 patients with AS were registered, of whom 992 were treated with acemetacin and 123 were treated with other NSAIDs. The results showed that total back pain and BASFI were significantly improved after three-month treatment of acemetacin, while comparing to other NSAIDs (P=0.027 and 0.015, respectively). After six-month treatment, patients taking acemetacin showed greater improvement in PGA (P=0.013), total back pain (P=0.049), night back pain (P=0.047), BASFI (P=0.042), ASDAS (P=0.007) and CRP (P=0.032) compared to those taking other NSAIDs. During the follow-up periods, no serious adverse events were reported. Mild abnormal liver function occurred in nine patients (9/992) treated with acemetacin and in six patients treated with other NSAIDs (6/123). See Table 1 for details.

Conclusion: Acemetacin showed better efficacy and acceptable safety profile in the treatment of active ankylosing spondylitis comparing with other NSAIDs.

REFERENCES:

[1] Ji, X., et al., Improvement of Disease Management and Cost Effectiveness in Chinese Patients with Ankylosing Spondylitis Using a Smart-Phone Management System: A Prospective Cohort Study. BioMed research international, 2019. 2019: p. 2171475.

Table 1. The comparation of two groups at 0, 3 and 6 months after treatment

	Baseline		3 months		6 months	
	95%CI	P	95%CI	P	95%CI	P
PGA	-0.13(-0.49, 0.24)	0.494	-0.28(-0.74, 0.18)	0.235	-0.59(-1.06, -1.13)	0.013*
Total back pain	-0.03(-0.37, 0.32)	0.889	-0.50(-0.94, -0.06)	0.027*	-0.44(-0.88, -0.002)	0.049*
Night back pain	0.01(-0.36, 0.38)	0.956	-0.30(-0.75, 0.16)	0.203	-0.46(-0.91, -0.006)	0.047*
BASFI	-0.30(-0.59, 0.004)	0.053	-0.55(-0.99, -0.11)	0.015*	-0.34(-0.67, -0.01)	0.042*
ASDAS	-0.10(-0.29, 0.08)	0.287	-0.15(-0.46, 0.16)	0.342	-0.41(-0.70, -0.11)	0.007*
CRP	-4.39(-8.87, 0.10)	0.055	0.91(-10.39, 12.21)	0.874	-7.86(-15.03, -0.68)	0.032*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1958

POS0922 NON-STEROIDAL ANTI-INFLAMMATORY DRUG USE IS ASSOCIATED WITH DISEASE ACTIVITY AND REDUCED SIGNIFICANTLY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH TUMOR NECROSIS FACTOR INHIBITORS; DATA FROM A REAL LIFE EXPERIENCE

E. Durak Ediboglu[1], D. Solmaz[1], G. Kabadayi[1], E. Otman Akat[1], H. Cinakli[1], G. Alp[1], E. Erpek[1], S. Gucenmez[1], M. Ozmen[1], S. Akar[1]. *[1]Izmir Katip Çelebi University, Rheumatology, Izmir, Turkey*

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) is the first line treatment option in axial spondyloarthritis (axSpA) patients suffering from pain and stiffness. However there is only limited data regarding the concomitant use of NSAIDs during tumour necrosis factor inhibitor (TNFi) treatment.

Objectives: To evaluate longitudinal concomitant NSAIDs use with the TNFi treatment and the determinant of the ASAS-NSAID index in patients with axSpA.

Methods: In total 429 axSpA patients (253 [59%] male; 272 [63%] with AS and 157 [37%] with non-radiographic (nr)-axSpA) who have followed up one year were included in this observational study. The data regarding disease activity and serum CRP levels were collected on 12, 24 and 52nd week. At each visit NSAID usage, type, dosage and frequency were recorded in order to calculate ASAS-NSAID index. The longitudinal relationship between NSAID-index and other factors tested by using generalized estimating equations (GEE) which is a technique for longitudinal data analysis allowing the use of all available data even deviated from normality.

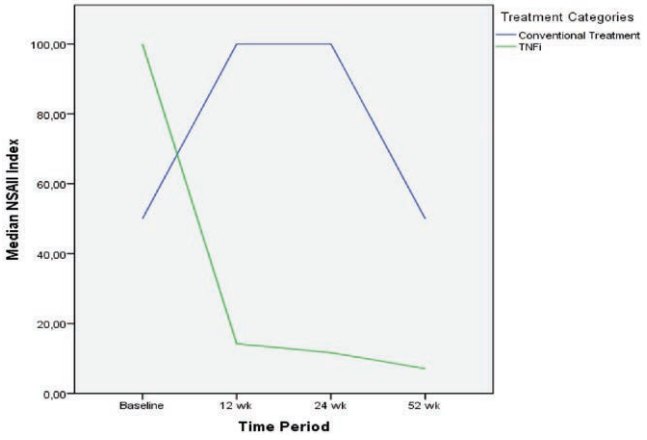
Results: At baseline 127/138 (92%) patients starting TNFi and 239/291 (82%) conventionally treated patients were using NSAID. Both the rate (p=0.007) and the median (IQR) ASAS-NSAID index were higher in biologic treatment group (100 [50] vs 70.8 [89.4]; p<0.001). During follow-up ASAS-NSAID index was decreased significantly in patients treated with TNFi (median 100 to 8.0;p<0.001), however ASAS-NSAID index was not changed in conventionally treated patients (p=0.154) (Figure 1). In univariate longitudinal analysis revealed that ASAS-NSAID index was significantly associated with BASDAI, ASDAS, BASFI scores and patient global assessment of disease activity, serum levels of CRP and education. We established two multivariable models (Table 1) to assess the associated factors/covariates with ASAS-NSAID index over time (one with ASDAS and the other BASDAI+CRP as disease activity index) and showed that BASDAI and patient global assessment of disease activity were independent determinants of NSAID dosage in biologic treated patients. However, in multivariate analysis there was no significant predictor for NSAID index in conventional treatment group.

Conclusion: Our results showed that NSAID prescription was significantly higher in axSpA patients who have TNFi indication. NSAID use was decreased significantly over time with TNFi and still independently determined by disease activity. However, it is stable in conventionally treated axSpA patients.

Table 1. The factors associated with ASAS-NSAII index in biologic treated patients

	Model 1			Model 2		
	B	95%CI	p	B	95% CI	p
BASFI	-0.55	-4.384; 4.275	*0.980*	0.943	-3.795; 5.682	*0.696*
BASMI	0.951	-1.511; 3.413	*0.449*	-0.098	-2.430; 2.234	*0.934*
PGA	0.535	0.210; 0.860	***0.001***	0.759	0.432; 1.086	***0.000***
CRP	-0.068	-0.220; 0.084	*0.380*			
BASDAI	5.718	2.487; 8.949	***0.001***			
ASDAS-CRP				1.771	-6.571; 10.113	*0.677*

PGA:Patient global assessment



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1961

POS0923 INFLUENCE OF BASELINE DEMOGRAPHICS ON IMPROVEMENTS IN DISEASE ACTIVITY MEASURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS RECEIVING UPADACITINIB: A POST HOC SUBGROUP ANALYSIS OF SELECT-AXIS 1

F. Van den Bosch[1], D. Poddubnyy[2,3], J. Stigler[4], A. Ostor[5], S. D'angelo[6], V. Navarro-Compán[7], I. H. Song[4], T. Gao[4], F. Ganz[8], L. S. Gensler[9]. *[1]Ghent University Hospital, Department of Rheumatology, Ghent, Belgium*; *[2]Infectious Diseases and Rheumatology, Campus Benjamin Franklin, Charité – Universitätsmedizin Berlin, Department of Gastroenterology, Berlin, Germany*; *[3]German Rheumatism Research Centre, Epidemiology Unit, Berlin, Germany*; *[4]AbbVie Inc., Immunology, North Chicago, Illinois, United States of America*; *[5]Cabrini Medical Center, Department of Rheumatology, Melbourne, Victoria, Australia*; *[6]"San Carlo" Hospital of Potenza and "Madonna delle Grazie" Hospital of Matera, Rheumatology Institute of Lucania (IReL) – Rheumatology Department of Lucania, Potenza, Italy*; *[7]University Hospital La Paz, IdiPaz, Department of Rheumatology, Madrid, Spain*; *[8]AbbVie AG, Immunology, Baar, Switzerland*; *[9]University of California, San Francisco, Rheumatology, San Francisco, California, United States of America*

Background: Upadacitinib (UPA), an oral Janus kinase inhibitor, has demonstrated efficacy and safety through 14 weeks in the SELECT-AXIS 1 study in biologic disease-modifying antirheumatic drug-naïve patients with active ankylosing spondylitis (AS).[1]

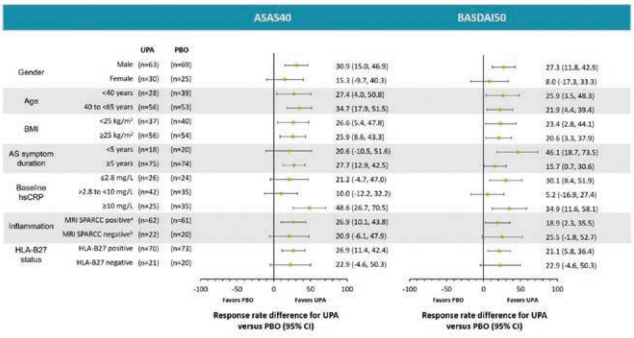
Objectives: To evaluate the efficacy of UPA 15 mg once daily (QD) in selected subgroups of patients with AS based on different baseline characteristics.
Methods: In SELECT-AXIS 1, patients were randomized to 14 weeks of blinded treatment with UPA 15 mg QD or placebo (PBO). This post hoc analysis evaluated the proportions of patients achieving ≥40% improvement in Assessment of SpondyloArthritis International Society criteria (ASAS40), ≥50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI50), and change from baseline in Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS[CRP]) at Week 14 across subgroups based on the following baseline patient characteristics: gender, age, body mass index, AS symptom duration, C-reactive protein (CRP) levels, Spondyloarthritis Research Consortium of Canada Magnetic Resonance Imaging index, and human leukocyte antigen B27 status. For missing data, non-responder imputation analysis was used for ASAS40 and BASDAI50, and mixed model repeated measures analysis was used for ASDAS(CRP).
Results: Baseline disease characteristics were balanced between the treatment groups at randomization, as previously reported.[1] ASAS40 and BASDAI50 response rates at Week 14 were numerically higher with UPA 15 mg versus PBO across the demographic and disease characteristic subgroups evaluated (Figure 1), including some subgroups with small sample sizes, such as patients with disease duration <5 years and female patients. Improvements from baseline in ASDAS(CRP) were also consistently greater with UPA 15 mg versus PBO across the subgroups evaluated (Table 1).
Conclusion: Within subgroups evaluated, most patients with active AS receiving UPA 15 mg demonstrated greater improvements versus PBO in disease activity measures assessed by ASAS40, BASDAI50, and change from baseline in ASDAS(CRP). There was some evidence that gender, AS symptom duration, and baseline CRP levels seemed to influence outcomes, though results should be interpreted with caution due to small sample sizes for some subgroups.
REFERENCES:
[1] van der Heijde D, et al. Lancet 2019;394:2108–17.

Table 1. PBO-corrected mean change from baseline (95% CI) in ASDAS(CRP) at Week 14 in patients receiving UPA 15 mg by baseline subgroups (MMRM)

Subgroup		n		ASDAS(CRP)
		UPA 15 mg	PBO	PBO-corrected mean change from baseline (95% CI)
Gender	Male	58	62	–1.11 (–1.37, –0.84)
	Female	26	22	–0.44 (–0.92, 0.03)
Age	<40 years	24	36	–1.00 (–1.42, –0.58)
	40–<65 years	51	46	–0.88 (–1.17, –0.59)
Body mass index	<25 kg/m^2	32	37	–0.92 (–1.30, –0.55)
	≥25 kg/m^2	52	47	–0.89 (–1.20, –0.59)
AS symptom duration	<5 years	16	17	–0.90 (–1.46, –0.34)
	≥5 years	68	67	–0.92 (–1.18, –0.66)
Baseline hsCRP	≤2.8 mg/L	23	19	–0.59 (–1.02, –0.15)
	>2.8–<10 mg/L	39	34	–0.59 (–0.95, –0.23)
	≥10 mg/L	22	31	–1.64 (–2.01, –1.27)
Inflammation based on SPARCC MRI scores	Positive[a]	56	57	–0.98 (–1.27, –0.69)
	Negative[b]	21	16	–0.60 (–1.08, –0.12)
HLA-B27 status	Positive	62	66	–0.97 (–1.24, –0.71)
	Negative	20	17	–0.73 (–1.28, –0.17)

[a]Spine SPARCC score ≥2 or sacroiliac joint SPARCC score ≥2. [b]Spine SPARCC score <2 and sacroiliac joint SPARCC score <2ASDAS(CRP), Ankylosing Spondylitis Disease Activity Score with C-reactive protein; CI, confidence interval; HLA-B27, human leukocyte antigen B27; hsCRP, high-sensitivity C-reactive protein; MMRM, mixed model repeated measures; MRI, magnetic resonance imaging; PBO, placebo; SPARCC, Spondyloarthritis Research Consortium of Canada; UPA, upadacitinib

Figure Response rate difference for UPA versus PBO (95% CI) for ASAS40 and BASDAI50 responses at Week 14 in patients receiving UPA 15 mg by baseline subgroups (non-responder imputation)



[a]Spine SPARCC score ≥2 or sacroiliac joint SPARCC score ≥2. [b]Spine SPARCC score <2 and sacroiliac joint SPARCC score <2
AS, ankylosing spondylitis; ASAS40, ≥40% improvement in Assessment of SpondyloArthritis International Society criteria; BASDAI50, ≥50% improvement in Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; CI, confidence interval; HLA-B27, human leukocyte antigen B27; hsCRP, high-sensitivity C-reactive protein; MRI, magnetic resonance imaging; PBO, placebo; SPARCC, Spondyloarthritis Research Consortium of Canada; UPA, upadacitinib

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Laura Chalmers, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.
Disclosure of Interests: Filip van den Bosch Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Janssen, and UCB, Denis Poddubnyy Speakers bureau: AbbVie, Celgene, Eli Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Celgene, Eli Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Jayne Stigler Employee of: AbbVie employee and may own stock or options, Andrew Ostor Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Salvatore D'Angelo Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Victoria Navarro-Compán Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, In-Ho Song Employee of: AbbVie employee and may own stock or options, Tianming Gao Employee of: AbbVie employee and may own stock or options, Fabiana Ganz Employee of: AbbVie employee and may own stock or options, Lianne S. Gensler Consultant of: AbbVie, Eli Lilly, Gilead, GSK, Novartis, Pfizer, and UCB, Grant/research support from: Pfizer and UCB
DOI: 10.1136/annrheumdis-2021-eular.1975

POS0924

PREDICTORS OF 1-YEAR TREATMENT RESPONSE AMONG UPADACITINIB-TREATED PATIENTS WITH ANKYLOSING SPONDYLITIS: A POST HOC ANALYSIS OF SELECT-AXIS 1

M. Magrey[1], S. Ramiro[2,3], M. Pinheiro[4], T. Gao[5], F. Ganz[6], I. H. Song[5], A. Biljan[5], N. Haroon[7,8,9], M. Rudwaleit[10]. *[1]MetroHealth System and School of Medicine, Case Western Reserve University, Division of Rheumatology, Cleveland, Ohio, United States of America*; *[2]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; *[3]Zuyderland Medical Center, Department of Rheumatology, Heerlen, Netherlands*; *[4]Universidade Federal de São Paulo, Rheumatology, São Paulo, Brazil*; *[5]AbbVie Inc., Immunology, North Chicago, United States of America*; *[6]AbbVie AG, Immunology, Baar, Switzerland*; *[7]University of Toronto, Rheumatology, Ontario, Canada*; *[8]University Health Network, Rheumatology, Toronto, Canada*; *[9]Krembil Research Institute, Rheumatology, Toronto, Canada*; *[10]Klinikum Bielefeld Rosenhöhe, Internal Medicine and Rheumatology, Bielefeld, Germany*

Background: Upadacitinib (UPA) is an oral Janus kinase inhibitor that has demonstrated efficacy and safety among patients with ankylosing spondylitis (AS) in the phase 2/3 SELECT-AXIS 1 study.[1] If identified, early predictors of treatment response may inform treat-to-target strategies and optimize patient outcomes in AS.

Objectives: To determine whether baseline (BL) characteristics or early responses predict clinical response at 1 year in UPA-treated patients with AS.
Methods: In the double-blind, randomized, placebo (PBO)-controlled SELECT-AXIS 1 study, patients received UPA 15 mg once daily or PBO until Week 14.[1] At Week 14, PBO-treated patients switched to UPA 15 mg; patients originally randomized to UPA continued UPA therapy. Data from patients in the PBO and UPA arms were combined based on overall exposure to UPA; in the switch arm, exposure was defined as current visit minus 14 weeks (time of switch). The following outcomes were assessed at 1 year: Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS[CRP]) inactive disease (ID; <1.3) and low disease activity (LDA; <2.1), Assessment of SpondyloArthritis International Society (ASAS) partial remission (PR), and ≥40% improvement in ASAS criteria (ASAS40) response. The ability of BL characteristics, efficacy at Week 12, and back pain at Week 12 to predict 1-year outcomes was assessed using a univariable logistic regression model generating odds ratios (ORs; 95% confidence intervals). LASSO regression was used to select the best-fitted multivariable model at Week 12 for each outcome measure.
Results: Among 187 patients who received or switched to UPA 15 mg, 70 (37.4%), 134 (71.7%), 73 (39.0%), and 131 (70.1%) achieved ASDAS(CRP) ID, ASDAS(CRP) LDA, ASAS PR, and ASAS40, respectively, following 1 year of UPA treatment. No meaningful predictors of 1-year efficacy outcomes were identified based on BL demographics (including disease duration, gender, and human leukocyte antigen B27 status) or BL disease characteristics (including ASDAS, Bath Ankylosing Spondylitis Disease Activity Index, and CRP levels). In univariable analyses, Week 12 responses based on several disease activity measures and patient-reported outcomes (PROs), including reductions (much better improvement [MBI], ≥30/≥50/≥70% reduction, or improvement) in back pain score, along with lower scores for back pain at Week 12, were associated with the achievement of ASDAS(CRP) ID, ASDAS(CRP) LDA, ASAS PR, and ASAS40 at 1 year (Figure 1). In a multivariable analysis, improvement from BL to Week 12 in back pain score consistently predicted several efficacy outcomes at 1 year.
Conclusion: In upadacitinib-treated patients with AS, improvement in PROs and reduction in back pain score at 12 weeks predicted clinical outcomes at 1 year.
REFERENCES:
[1] van der Heijde D, et al. Lancet 2019;394:2108–17.

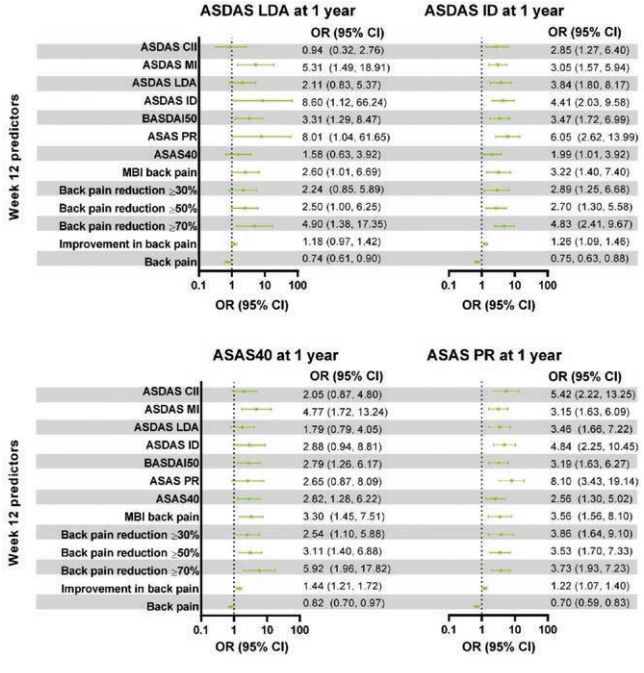


Figure 1. Association between Week 12 response or back pain at Week 12 and achievement of efficacy outcomes at 1 year (univariable analysis)

All ASDAS scores are calculated using C-reactive protein
ASDAS CII: change from BL ≥1.1; ASDAS MI: change from BL ≥2.0; MBI back pain: ≥2-point reduction in absolute score and ≥33% reduction from BL on a 0–10 NRS
ASAS, Assessment of SpondyloArthritis International Society; ASAS40, ≥40% improvement in ASAS criteria; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI50, ≥50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index; BL, baseline; CI, confidence interval; CII, clinically important improvement; ID, inactive disease; LDA, low disease activity; MBI, much better improvement; MI, major improvement; NRS, numeric rating scale; OR, odds ratio; PR, partial remission
Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Laura Chalmers, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.
Disclosure of Interests: Marina Magrey Consultant of: Consultant for Janssen and Novartis; member of advisory boards for Eli Lilly, Janssen, Novartis, and UCB, Grant/research support from: AbbVie, Sofia Ramiro Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Sanofi, and UCB, Grant/research support from: MSD, Marcelo Pinheiro Consultant of: AbbVie, Eli Lilly, Janssen, and Novartis, Tianming Gao Employee of: AbbVie employee and may own stock or options, Fabiana Ganz Employee of: AbbVie employee and may own stock or options, In-Ho Song Employee of: AbbVie employee and may own stock or options, Ana Biljan Employee of: AbbVie employee and may own stock or options, Nigil Haroon Consultant of: AbbVie, Amgen, Eli Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Martin Rudwaleit Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, and UCB
DOI: 10.1136/annrheumdis-2021-eular.1986

POS0925 EFFICACY OF SECUKINUMAB IN TNFI-NAÏVE PATIENTS ACROSS THE AXIAL SPONDYLOARTHRITIS SPECTRUM OVER 52 WEEKS: A POST HOC ANALYSIS OF THE MEASURE AND PREVENT CLINICAL TRIALS

M. Magrey[1], J. A. Walsh[2], F. Huang[3], H. Kameda[4], J. Wang[5], C. Herrem[6], P. Pertel[7], H. Marzo-Ortega[8]. *[1]Case Western Reserve University School of Medicine, Division of Rheumatology, Ohio, United States of America*; *[2]Salt Lake City Veteran Affairs Medical Center; University of Utah Medical Center, Salt Lake City, Division of Rheumatology, Utah, United States of America*; *[3]Chinese PLA General Hospital, Beijing, Department of Rheumatology and Immunology, Beijing, China*; *[4]Toho University (Ohashi Medical Center), Department of Internal Medicine, Division of Rheumatology, Tokyo, Japan*; *[5]Novartis Pharmaceuticals Corporation, Immunology, Hepatology and Dermatology, East Hanover, United States of America*; *[6]Novartis Pharma AG, Rheumatology, Basel, Switzerland*; *[7]Novartis Pharma AG, Immunology, Hepatology and Dermatology, Basel, Switzerland*; *[8]NIHR Leeds Biomedical Research Centre, Leeds Training Hospitals NHS Trust and LIRMM, University of Leeds, NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom*

Background: Secukinumab (SEC) has demonstrated significant efficacy in patients (pts) with ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA).[1-5] However, evidence regarding the efficacy of SEC across the axSpA disease spectrum is limited.
Objectives: To assess the efficacy of SEC on key efficacy endpoints in pts with axSpA (nr-axSpA and AS) over 52 weeks from 6 pooled phase 3 clinical trials.
Methods: This post hoc analysis included pooled data from tumour necrosis factor inhibitors (TNFi)-naïve pts in the MEASURE 1-5 (AS) and PREVENT (nr-axSpA) phase 3 trials. Assessments included proportion of patients achieving ASAS40, ASAS 5/6, ASAS partial remission (ASAS-PR), ASDAS-CRP major improvement, ASDAS-CRP inactive disease (ASDAS-CRP ID), BASDAI50 and mean change from baseline in nocturnal back pain and morning stiffness with any SEC 150 mg or SEC 300 mg or placebo (PBO) at Week 16, and sustainability was measured in pts treated with SEC at Week 52. Data are reported as non-responder imputation.
Results: A total of 1558 TNFi-naïve pts (SEC 150 mg, N=932; SEC 300 mg, N=57 and PBO, N=569) with a mean age of 39.3 ± 11.58 years were included in the study. At Week 16, significantly higher improvements in pts treated with SEC versus PBO were observed in all efficacy endpoints (Table 1) with improvements sustained up to Week 52.
Conclusion: SEC 300 mg and 150 mg provided significant and sustained improvement in the signs and symptoms of TNFi-naïve pts with axSpA regardless of radiographic status.
REFERENCES:
[1] Baeten D, et al. *N Engl J Med* 2015;373:2534–48.
[2] Pavelka K, et al. *Arthritis Res Ther* 2017;19:285.
[3] Kivitz AJ, et al. *Rheumatol Ther* 2018;5:447–62.
[4] Feng H, et al. *Chin Med J* 2020;133:2521–31.
[5] Deodhar A, et al. *Arthritis Rheumatol* 2021;73:110–20.

Table 1. Efficacy endpoints at Week 16 and Week 52 in TNFi-naïve patients with axSpA

Endpoints	Week	Any secukinumab 150 mg (N = 932)	Secukinumab 300 mg (N = 57)	Placebo (N = 569)
ASAS40, n (%)	16	399 (42.8)†	25 (43.9)†	134 (23.6)
	52	508 (54.5)	33 (57.9)	-
ASAS 5/6, n (%)	16	414 (44.4)†	24 (42.1)†	125 (22.0)
	52	508 (54.5)	33 (57.9)	-
ASAS partial remission, n (%)	16	166 (17.8)†	12 (21.1)†	35 (6.2)
	52	240 (25.8)	13 (22.8)	-
ASDAS-CRP major improvement, n (%)	16	266 (28.5)†	16 (28.1)†	43 (7.6)
	52	336 (36.1)	20 (35.1)	-
ASDAS-CRP ID, n (%)	16	171 (18.3)†	11 (19.3)†	31 (5.4)
	52	247 (26.5)	13 (22.8)	-
BASDAI50, n (%)	16	356 (38.2)†	22 (38.6)§	110 (19.3)
	52	459 (49.2)	27 (47.4)	-
Nocturnal back pain, mean change from baseline ± SE	16	−31.82 ± 0.87	−37.99 ± 3.56†	−18.12 ±1.13
	52*	−41.31 ± 27.58	−46.56 ± 24.30	-
Overall level of morning stiffness, mean change from baseline ± SE	16	−3.23 ± 0.09†	−3.62 ± 0.35†	−1.95 ± 0.11†
	52*	−4.24 ± 2.75	−4.71 ± 2.74	-

Data presented as NRI.†P <0.001; §P<0.01 vs placebo; *mean change ± SD.ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C-reactive protein; ID, inactive disease; NRI, non-responder imputation; SD, standard deviation; SE, standard error; TNFi, tumour necrosis factor inhibitor.

Disclosure of Interests: Marina Magrey Consultant of: Novartis, Pfizer, Abbvie, UCB, Eli Lilly, Grant/research support from: Clinical trials with Abbvie and UCB, Jessica A. Walsh Consultant of: AbbVie, Novartis, Eli Lilly and Company, UCB, Grant/research support from: AbbVie, Pfizer, Janssen, feng huang: None declared, Hideto Kameda Speakers bureau: AbbVie, Asahi-Kasei, Astellas, Bristol-Myers Squibb, Chugai, Eisai, Eli Lilly, Gilead Sciences, Janssen, Kyowa Kirin, Mitsubishi-Tanabe, Novartis, Pfizer and UCB., Consultant of: AbbVie, Asahi-Kasei, Astellas, Bristol-Myers Squibb, Chugai, Eisai, Eli Lilly, Gilead Sciences, Janssen, Kyowa Kirin, Mitsubishi-Tanabe, Novartis, Pfizer and UCB., Grant/research support from: AbbVie, Asahi-Kasei, Astellas, Behringer, Chugai, Eisai, Mitsubishi-Tanabe, Novartis, Jianyuan Wang Employee of: Novartis, Christopher Herrem Employee of: Novartis, Patricia Pertel Employee of: Novartis, Helena Marzo-Ortega Speakers bureau: AbbVie, Celgene, Janssen, Eli Lilly and Company, Novartis, Pfizer, Takeda, and UCB., Consultant of: AbbVie, Celgene, Janssen, Eli Lilly and Company, Novartis, Pfizer, Takeda, and UCB., Grant/research support from: Janssen, Novartis
DOI: 10.1136/annrheumdis-2021-eular.2005

POS0926

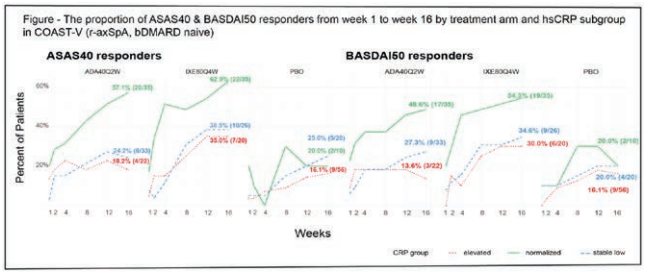
NORMALIZATION OF HIGH SENSITIVITY CRP VERSUS CLINICAL RESPONSE TO IXEKIZUMAB AT WEEK 16 IN PATIENTS WITH RADIOGRAPHIC & NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE COAST STUDIES

H. Marzo-Ortega[1], X. Juanola[2], T. Okano[3], Y. Schymura[4], A. Bradley[5], J. Gerwien[5], B. Monsberger[6], S. Liu Leage[5], D. Aletaha[7], M. Østergaard[8].
[1]Leeds Teaching Hospitals NHS Trust & LIRMM, University of Leeds, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom; *[2]University Hospital Bellvitge, Rheumatology Service, Barcelona, Spain*; *[3]Osaka City University, Graduate School of Medicine, Osaka, Japan*; *[4]Eli Lilly and Company, Statistics, Indianapolis, United States of America*; *[5]Eli Lilly and Company, Medical Rheumatology, Indianapolis, United States of America*; *[6]Eli Lilly and Company, Dermatology, Indianapolis, United States of America*; *[7]Medical University of Vienna, Division of Rheumatology, Wien, Austria*; *[8]University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark*

Background: C-reactive protein (CRP), an objective marker of inflammation, can be used to monitor treatment response to biologics in patients with axial spondyloarthritis (axSpA) in addition to evaluating signs & symptoms. CRP is not elevated in all patients with active axSpA questioning its validity as a universal biomarker of response. Ixekizumab (IXE) demonstrated efficacy in axSpA treatment irrespective of baseline (BL) CRP levels. However, response to IXE categorized on CRP change from BL is unknown.
Objectives: To evaluate response to IXE treatment from BL through week (wk) 16 in patients with axSpA categorized according to change in high sensitivity (hs) CRP.
Methods: COAST-V (NCT 02696785),-W (NCT02696798), & -X (NCT02757352), were phase 3, multicentre, randomized, controlled trials, investigating the efficacy of IXE 80 mg every 4 & 2 wks in patients with: r-axSpA naïve to biologic disease-modifying antirheumatic drugs (bDMARDs; COAST-V); or who were inadequate responders/intolerant to tumour necrosis factor inhibitors (TNFi; COAST-W); or who fulfilled Assessment of SpondyloArthritis International Society (ASAS) criteria for non-radiographic (nr)axSpA (COAST-X).
This post hoc analysis focuses on approved dosing regimens. Depending on BL and wk 16 hsCRP values, patients were categorised as stable low (hsCRP ≤5 mg/L at BL & ≤5 mg/L at wk 16), normalized (hsCRP >5 mg/L at BL & ≤5 mg/L at wk 16) or elevated (hsCRP >5 mg/L at wk 16, irrespective of BL hsCRP). An absolute cutoff of 5 mg/L was used as the stratification factor in all COAST studies. Data were analyzed by treatment arm. Each trial was analyzed separately.
For hsCRP subgroups, patient demographics & other characteristics at BL, as well as trajectory over time for the endpoints ASAS40 & Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 are described. Non-responder imputation was used for missing values.
Results: In all studies at BL, disease activity & MRI SPARCC score were higher in normalized & elevated subgroups compared to the stable low subgroup - **a**.
In COAST-V, ASAS40 & BASDAI50 response was observed in IXE-treated patients regardless of hsCRP change status by wk 16 vs placebo. The highest ASAS40 & BASDAI50 response rate was reported in patients with normalized hsCRP - **b**. Similar findings were observed in COAST-W & -X.

Table 1. ***Baseline Patient demographics & other characteristics - ITT population, per CRP subgroup***

	COAST-V (r-axSpA, bDMARD naive)			COAST-W (r-axSpA, inadequate responders /intolerant to TNFi)			COAST-X (non-radiographic axSpA, bDMARD naïve)		
	Stable low (n=79)	Normalized (n=80)	Elevated (n=98)	Stable low (n=58)	Normalized (n=34)	Elevated (n=126)	Stable low (n=78)	Normalized (n=40)	Elevated (n=81)
Parameter									
Age (years)	43.7 (12.1)	38.9 (10.9)	42.7 (12.0)	50.4 (13.3)	46.1 (13.8)	45.7 (12.5)	44.0 (12.8)	37.2 (14.6)	38.7 (12.8)
Male gender, n (%)	63 (79.7)	71.0 (88.8)	78 (79.6)	39.0 (67.2)	30 (88.2)	109 (86.5)	35 (44.9)	23 (57.5)	34 (42)
Duration of symptoms since axSpA onset (years)	17.5 (11.2)	14.4 (9.3)	16.1 (9.9)	21.7 (12.9)	16.8 (11.6)	18.9 (10.9)	12.1 (9.9)	10.3 (9.7)	9.5 (9.0)
HLA-B27 positive, n (%)	69 (87.3)	75.0 (93.8)	89 (90.8)	31.0 (91.2)	101 (80.2)	101 (80.2)	48 (61.5)	31 (77.5)	67 (82.7)
BASDAI Total Score	6.5 (1.4)	6.7 (1.5)	7.0 (1.1)	7.4 (1.5)	7.3 (1.3)	7.4 (1.3)	6.9 (1.5)	7.1 (1.6)	7.2 (1.5)
ASDAS Total Score	3.1 (0.5)	3.9 (0.6)	4.2 (0.7)	3.5 (0.6)	4.3 (0.6)	4.4 (0.8)	3.2 (0.6)	4.2 (0.8)	4.2 (0.9)
Spinal Pain due to AS	7.0 (1.5)	7.0 (1.5)	7.5 (1.3)	7.8 (1.5)	7.7 (1.5)	7.9 (1.4)	7.2 (1.7)	7.5 (1.7)	7.5 (1.6)
Patients with peripheral articular manifestations (>=1 TJC or >=1 SJC)	47 (59.5)	40 (50)	62 (63.3)	43 (74.1)	24 (70.6)	86 (68.3)	56 (71.8)	33 (82.5)	66 (81.5)
	MRI Spine SPARCC Score						MRI SIJ SPARCC Score		
MRI SPARCC Score	6.7 (11.2)	21.8 (27.3)	20.7 (25.7)	1.2 (2.3)	7.0 (7.6)	10.4 (17.0)	5.2 (6.6)	6.1 (8.2)	6.2 (10.5)



Conclusion: IXE reduced clinical disease activity in patients with axSpA irrespective of hsCRP change from BL to wk 16. Improvement in hsCRP level was associated with overall response rates.
Acknowledgements: The authors would like to acknowledge Philana Fernandes, an employee of Eli Lilly and Company, for her for writing and editorial support.
Disclosure of Interests: Helena Marzo-Ortega Consultant of: Celgene, Janssen, Eli Lilly, Novartis, Pfizer, UCB, Grant/research support from: Janssen, Novartis, Xavier Juanola: None declared, Tadashi Okano Speakers bureau: Asahi Kasei, Astellas, Abbvie, Ayumi, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Janssen, Mitsubishi Tanabe,

Novartis, Ono, Pfizer, Sanofi and Takeda, Grant/research support from: Asahi Kasei, Abbvie, Chugai, Eisai, Yves Schymura Employee of: Eli Lilly, Andrew Bradley Shareholder of: Eli Lilly, Employee of: Eli Lilly, Jens Gerwien Shareholder of: Eli Lilly, Employee of: Eli Lilly, Brigitte Monsberger Shareholder of: Eli Lilly, Employee of: Eli Lilly, Soyi Liu Leage Employee of: Eli Lilly, Daniel Aletaha Speakers bureau: Abbvie, Amgen, Celgene, Lilly, Medac, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi/Genzyme, Grant/research support from: Abbvie, Lilly, Novartis, Roche, Mikkel Østergaard Speakers bureau: Abbvie, Celgene, Eli-Lilly, Janssen, Novartis, Pfizer, Roche, Sanofi and UCB, Consultant of: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: Abbvie, BMS, Merck, Celgene, Novartis

DOI: 10.1136/annrheumdis-2021-eular.2079

POS0927

EFFECTIVENESS AND SAFETY OF SECUKINUMAB IN NAÏVE OR TNF-INHIBITORS FAILURE AXIAL SPONDYLOARTHRITIS PATIENTS IN REAL LIFE: A 24-MONTHS PROSPECTIVE MULTICENTRIC STUDY

M. Lorenzin[1], A. Ortolan[1], M. S. Chimenti[2], A. Marchesoni[3], E. Lubrano[4], L. Santo[5], A. Semeraro[6], C. Salvarani[7,8], N. Girolimetto[8], E. Praino[9], G. L. Fonti[2], R. Foti[10], A. Carletto[11], A. Doria[12], R. Ramonda[12]On behalf of Italian Society of Rheumatology (SIR) "Spondyloartritis and Psoriatic Arthritis Study Group—A. Spadaro". *[1]University of Padova, Rheumatology Unit, Department of Medicine DIMED, Padova, Italy*; *[2]University of Rome "Tor Vergata", Rheumatology, Allergology and Clinical Immunology Department of "Medicina dei Sistemi", Roma, Italy*; *[3] ASST Gaetano Pini-CTO, Milan, Department of Rheumatology, Milano, Italy*; *[4]University of Molise, Campobasso, Academic Rheumatology Unit, Dipartimento di Medicina e Scienze per la Salute "Vincenzo Tiberio", Campobasso, Italy*; *[5] ASL BT Andria – DSS4 Barletta, Italy, Barletta-Andria-Trani, Rheumatology Unit, Barletta-Andria-Trani, Italy*; *[6]Martina Franca-ASL Taranto, Rheumatology Unit, Taranto, Italy*; *[7]University of Modena and Reggio Emilia, Rheumatology Unit, Reggio Emilia, Italy*; *[8]Azienda USL-IRCCS, Istituto di Ricovero e Cura a Carattere Scientifico, Rheumatology Unit, Department of Internal Medicine, Reggio Emilia, Italy*; *[9]ASL BT Andria – DSS4 Barletta, Italy, Barletta-Andria-Trani, Rheumatology Unit, Barletta-Andria-Trani, Italy*; *[10]A.O.U. Policlinico S. Marco, Catania, Italy, Rheumatology Unit, Catania, Italy*; *[11]AOUI University of Verona, Rheumatology Unit, Department of Medicine, Verona, Italy*; *[1]University of Padova, Rheumatology Unit, Department of Medicine DIMED, Padova, Italy*

Background: Axial Spondyloarthritis (axSpA) can be distinguished in radiographic axSpA (r-axSpA) and non-radiographic (nr-axSpA). Secukinumab (SEC) is a novel treatment for axSpA, but data from real-life are still missing.
Objectives: 1)to evaluate the effectiveness and safety of a wide cohort of axSpA patients on SEC followed in 8 Italian Rheumatologic centers for 24-months;2) to compare the features and disease-activity indices of SEC-treated axSpA patients subdivided in naïve biological drugs (**group A**) and in TNF-inhibitors failure patients (**group B**).
Methods: Consecutive patients with active axSpA (diagnosis according Assessment of SpondyloArthritis International Society ASAS criteria), who started SEC treatment, were evaluated prospectively.Data on disease characteristics, previous/ongoing treatments and imaging were collected. Disease-activity/functional/clinical scores and biochemical values were recorded at baseline (T0), at 6 (T6), 12 (T12), and 24 (T24) months. Effectiveness was evaluated over-time with descriptive statistics. Anova (Kruskal Wallis) and generalized linear models were used to compare variables over-time. Infections,adverse events were collected.
Results: One-hundred-seven patients [49.53% men; median age 49years; median treatment duration 18.5years] were enrolled;53(49.53%) had HLA-B27, 47.66% were r-axSpA and 52.34% nr-axSpA. Signs of sacroiliitis were present on MRI in 97 (90.65%) and X-rays in 51 (47.66%). SEC was prescribed as first line biologic treatment in 32 (29.9%) patients and as second or more line biological treatment in 75 (70.1%) patients (Figure 1). In all population significant decrease was achieved in:Visual Analogue Scale of pain and general-health; Leeds Enthesitis Index;Health Assessment Questionnaire modified for spondyloarthritis (HAQ-s);Bath Ankylosing Spondylitis Functional Index (BASFI);C-reactive protein. Bath Ankylosing Spondylitis Metrology Index and Erythrocyte-sedimentation-rate not significantly decreased. Effectiveness was associated to an improvement in Ankylosing Spondylitis disease activity score (ASDAS) [T0=3.4 (2.9-3.9) vs T24=1.9 (1.2-2.7);p=0.02] and in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [T0=6.6 (5.0-7.8) vs T24=3.2 (2.0-5.0);p=0.03].At T0 **group B** had a longer disease duration (p=0.04),a greater prevalence of peripheral arthritis (p=0.02),enthesitis (p=0.04) and psoriasis (p=0.05) and was mostly male (p=0.05),while no significant difference was observed for functional and disease-activity indices and signs of sacroiliitis on MRI/X-rays. At T24 **group A** showed better physical functioning and lower disease activity compared to **group B** [HAQs A vs. B=0.1(0.0-0.5) vs 0.3(0.1-0.8); BASFI A vs B=1.6(0.8-4.8) vs 4.0(2.5-4.6); BASDAI A vs B=2.2(1.0-3.8) vs 3.9(2.7-5.0);ASDAS A vs B=1.3(1.0-2.2) vs 2.1(1.6-2.9)].After T24 of treatment 70.2% of **Group A** and 68.4% of **Group B** had a low disease activity,accordingly to ASDAS<2.1. Twenty-three patients (21.5%) stopped the treatment during the follow-up mainly because of primary (7) or secondary loss of efficacy (9).Only 7 patients suspended SEC because of adverse events.A low number of episodes of mild infections (19) occurred;SEC was instead permanently discontinued in 4 cases for:oral refractory mucositis (2);recurrent aphthosis (1);recurrent broncopneumoniae (1).The retention rate at t24 was good in the whole population (73%).Survival curves for **Group A** and **B** were similar (log-rank test=0.81;p=0.69).
Conclusion: In a real-life clinical setting,SEC was safe and effective in axSpA, as shown by a significant decrease of BASDAI and ASDAS over a 24-months follow-up.

Baseline characteristics of 107 axSpA patients treated with secukinumab in the period January 2017- December 2020.

axSpA Features	Total patients	GROUP A vs.	GROUP B	p
Male sex (N,%)	53 (49.53%)	23 (71.88%)	30 (40%)	0.05
Age (years), median (IQR)	49 (40.5-58)	44 (35.75-58)	52 (42-58.5)	0.04
Age of diagnosis (years), median (IQR)	43 (32.5-51)	39.5 (30.5-50)	43 (33.5-53)	ns
Age of disease onset (years), median (IQR)	39 (29.5-49)	36.5 (22.75-46)	40 (30.5-49)	ns
Disease duration (years), median (IQR)	9 (4-13.5)	7 (2-14.25)	10 (6-13)	0.04
axSpA (n,%)	107	32 (29.91%)	75 (70.09%)	NA
r-axSpA	51 (47.66%)	15 (46.88%)	36 (48%)	ns
nr-axSpA	56 (52.34%)	17 (53.13%)	39 (52%)	ns
HLA-B27 positive, N (%)	53 (49.53%)	16 (50%)	37 (49.33%)	ns
SIJ-MRI positive, N (%)	97 (90.65%)	28 (87.5%)	69 (92%)	ns
SIJ-X-rays positive, N (%)	51 (47.66%)	15 (46.9%)	36 (48%)	ns
Peripheral arthritis, N (%)	62 (57.94%)	15 (46.9%)	47 (62.67%)	0.02
Enthesitis, N (%)	66 (61.68%)	17 (53.13%)	49 (65.33%)	0.04
Dactylitis, N (%)	14 (13.08%)	5 (15.63%)	9 (12%)	ns
Psoriasis, N (%)	50 (46.73%)	13 (40.63%)	37 (49.33%)	0.05
Onicopathy, N (%)	22 (20.56%)	6 (18.75%)	16 (21.33%)	ns
IBD, N (%)	4 (3.74%)	2 (6.25%)	2 (2.67%)	ns
Uveitis, N (%)	5 (4.67%)	0 (0%)	5 (6.67%)	ns
Familiarity with psoriasis or SpA	36 (33.64%)	12 (37.5%)	24 (32%)	ns
Smoking, N (%)	26 (24.30%)	8 (25%)	18 (24%)	ns
Weight (kg), median (IQR)	70 (60.5-82)	70.50 (64.5-82.25)	70 (60-81.5)	ns
Height (cm), median (IQR)	169 (161-177)	174 (165-178)	168 (160-175.5)	ns
BMI, median (IQR)	24.69 (21.95-28.05)	23.97 (22.65-26.20)	24.9 (21.79-28.24)	ns
BASMI [0-10], median (IQR)	3 (1-6)	2 (0-4)	4 (1-7)	0.03
LEI [0-6], median (IQR)	1 (0-2)	0 (0-1.5)	1 (0-2)	ns
ESR [0-25](mm/h), median (IQR)	16 (9-28)	13.5 (5-27.25)	18.5 (10-28)	ns
CRP [0-6](mg/L), median (IQR)	5 (2.9-11)	3.45 (2.4-15.3)	5 (2.9-11)	0.04
VAS-pain [0-10], median (IQR)	7 (6-8)	6.65 (6-7.45)	7 (6-8)	ns
VAS-gh [0-10], median (IQR)	5.6 (4-7)	5.0 (4.25-7.0)	6 (4-7.1)	ns
HAQ-S [0-8], median (IQR)	1 (0.5-1.5)	0.75 (0.2-1.0)	1 (0.75-1.50)	0.05
BASFI [0-10], median (IQR)	6 (4.95-7.03)	5.5 (3.63-7.05)	6 (5.1-7.0)	ns
BASDAI [0-10], median (IQR)	6.6 (5-7.8)	6 (3.7-6.95)	7 (5.25-8.2)	ns
ASDAS [0-6], median (IQR)	3.35 (2.85-3.86)	3.33 (2.67-3.68)	3.35 (2.90-3.86)	ns
Mean treatment duration (months), median (IQR)	18.5 (12-32.5)	18.10 (12-30)	18.93 (12-32.5)	ns
Dosage 300 mg/injection (N,%)	33 (30.84%)	6 (18.75%)	27 (36%)	0.04
Dosage 150 mg/injection (N,%)	74 (69.16%)	26 (81.25%)	48 (64%)	0.04
1st line (N,%)	32 (29.91%)	32 (100%)	0 (0%)	NA
Failure biological drugs (N,%)	75 (70.10%)	0 (0%)	75(100%)	NA
2nd line (N,%)	33 (30.84%)	0 (0%)	33 (44%)	NA
3rd line (N,%)	23 (21.50%)	0 (0%)	23 (30.67%)	NA
4th line (N,%)	13 (12.15%)	0 (0%)	13 (17.33%)	NA
>5th line (N,%)	6 (5.61%)	0 (0%)	6 (8%)	NA
Concomitant NSAIDs, N (%)	68 (63.55%)	21 (65.63%)	47 (62.67%)	ns
Concomitant glucocorticosteroid, N (%)	22 (20.56%)	6 (18.75%)	16 (21.33%)	ns
Concomitant csDMARDs, N (%)	23 (21.50%)	6 (18.75%)	17 (22.67%)	ns

Legend: Data are expressed as median (interquartile range=IQR) unless otherwise specified; range of possible values are indicated in square brackets. p§ Anova (Kruskal Wallis) a t0: p<0.05. GROUP A= naive to anti-TNFalpha inhibitors; GROUP B= TNFalpha failure inhibitors; SpA, Spondyloarthritis; axSpA, axial Spondyloarthritis; r-axSpA, radiographic axial spondyloarthritis; nr-axSpA, non-radigraphic axial spondyloarthritis; IBD, inflammatory bowel disease; HLA-B27, Human leukocyte antigen (HLA) B27; SIJ, Sacroiliac Joints; MRI, Magnetic Resonance Imaging; X-rays; Conventional Radiography; Kg, kilogram; cm,centimeter; BMI, body mass index;BASMI, Bath Ankylosing Spondylitis Metrology Index; LEI, Leeds Enthesitis Index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; VAS, Visual Analogue Scale; gh, Global Health, BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASDAS, Ankylosing Spondylitis disease activity score; HAQ-S, Health Assessment Questionnaire modified for spondyloarthritis; NSAIDS, non -steroidal inflammatory drugs; csDMARDs, conventional synthetic diseasemodifying antirheumatic drugs. ns=not statistical significant. NA= not applicable

Disclosure of Interests: Mariagrazia Lorenzin: None declared, Augusta Ortolan: None declared, Maria Sole Chimenti: None declared, Antonio Marchesoni Grant/research support from: AM has received honoraria and speaker fees from Abbvie, Pfizer, MSD, UCB, Novartis, Janssen, Eli-Lilly., Ennio Lubrano: None declared, Leonardo Santo Speakers bureau: Speaker from Jansen, Novartis, Pfizer, UCB, MSD, Sanofi, Angelo Semeraro: None declared, Carlo Salvarani: None declared, Nicolò Girolimetto: None declared, Emanuela Praino: None declared, Giulia Lavinia Fonti: None declared, Rosario Foti: None declared, Antonio Carletto: None declared, Andrea Doria Grant/research support from: ADhas received honoraria and speaker fees from Novartis, Abbvie, Pfizer, MSD, Janssen., Roberta Ramonda Grant/research support from: RR has received honoraria and speaker fees from Novartis, Abbvie, Pfizer, MSD, Janssen.
DOI: 10.1136/annrheumdis-2021-eular.2121

POS0928

NETAKIMAB EFFICACY IN ANTI-TNF-NAIVE AND ANTI-TNF-EXPERIENCED PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS OF SUBANALYSIS OF PHASE 3 ASTERA TRIAL

S. Erdes[1], V. Mazurov[2], T. Dubinina[3], I. Gaydukova[2,4], A. Kundzer[5], N. Soroka[6], A. Eremeeva[7]. *[1]Nasonova Research Institute of Rheumatology, Laboratory of Spondyloarthritides, Moscow, Russian Federation*; *[2]Mechnikov North-Western State Medical University, Department of Therapy and Rheumatology*

of Temporary Disability and Medical Care Quality Expertise, St-Petersburg, Russian Federation; [3]*Nasonova Research Institute of Rheumatology, Laboratory of Medical and Social Problems of Rheumatology, Moscow, Russian Federation*; [4]*Clinical Rheumatology Hospital No 25, Consultative Outpatient Department, St-Petersburg, Russian Federation*; [5]*Belarusian Medical Academy of Postgraduate Education, Department of Cardiology and Rheumatology, Minsk, Belarus*; [6]*Belarusian State Medical University, Department of Internal Diseases №2, Minsk, Belarus*; [7]*JSC BIOCAD, Clinical Development Department, St-Petersburg, Russian Federation*

Background: According to previous studies, the effectiveness of interleukin-17 (IL-17) inhibitors was higher in anti-TNF-naïve patients with ankylosing spondylitis (AS) [1,2]. Netakimab (NTK) is a humanized anti-IL-17A antibody approved for the treatment of AS, psoriatic arthritis, moderate-to-severe plaque psoriasis in Russia and Belarus.
Objectives: To compare the efficacy of NTK in anti-TNF-naïve patients with anti-TNF-experienced patients with active AS at week 16 of therapy.
Methods: ASTERA (NCT03447704) is an ongoing phase 3 placebo (PBO)-controlled clinical study, aimed at evaluating NTK efficacy in AS [3]. 228 adult patients with active AS (BASDAI ≥ 4) were randomly assigned (1:1) to receive 120 mg NTK or PBO subcutaneously at week 0,1,2 and then q2w. This analysis includes 112 patients in NTK group. Efficacy endpoints included ASAS20/40, ASAS5/6 and ASAS partial remission (PR) at week 16 of therapy.
Results: 28 (25.0%) of 112 patients in NTK group had previous inadequate response/intolerance to anti-TNF (anti-TNF-IR): 24 (21.4%) – one anti-TNF, and 4 (3.6%) – two anti-TNF. 84 (75.0%) patients were TNF-naive. Achievement of ASAS criteria response at week 16 was similar in both groups (Table 1).

Table 1. Efficacy of NTK at week 16

Parameter	TNF-naïve (n = 84)	anti-TNF-IR (n = 28)	p-value*
ASAS20, n (%)	52 (61.9%)	17 (60.7%)	0.91
ASAS40, n (%)	35 (41.7%)	11 (39.3%)	0.82
ASAS5/6, n (%)	39 (46.4%)	11 (39.3%)	0.51
ASAS(PR), n (%)	15 (17.9%)	4 (14.3%)	0.78

*- Fisher's exact test

Conclusion: NTK 120 mg provided sustained improvements in signs and symptoms of AS in anti-TNF-naive and anti-TNF-IR patients at 16 weeks of therapy.
REFERENCES:
[1] Blair HA, Dhillon S. Secukinumab: A Review in Ankylosing Spondylitis. Drugs. 2016;76(10):1023-30.
[2]Dougados M, et al. Efficacy and safety of ixekizumab through 52 weeks in two phase 3, randomised, controlled clinical trials in patients with active radiographic axial spondyloarthritis (COAST-V and COAST-W). Ann Rheum Dis. 2020;79(2):176-185.
[3] Mazurov VI, et al. Efficacy and safety of Netakimab, anti-IL-17A monoclonal antibody, in patients with ankylosing spondylitis. Results of phase III international, multicenter, randomized double-blind clinical trial BCD-085-5/ASTERA. Nauchno-Practicheskaya Revmatologia=Rheumatology Science and Practice. 2020;58 (4):376–386 (In Russ).
Acknowledgements: This study was sponsored by JSC BIOCAD.
Disclosure of Interests: Shandor Erdes: None declared, V Mazurov: None declared, Tatiana Dubinina: None declared, Inna Gaydukova Speakers bureau: Abbvie, Biocad, Eli Lilly, MSD, Novartis, Pfizer, Sandoz, Alena Kundzer: None declared, Nikolaj Soroka: None declared, Anna Eremeeva Employee of: Biocad
DOI: 10.1136/annrheumdis-2021-eular.2209

POS0929

FACTORS ASSOCIATED WITH THE DEVELOPMENT OF ANTI-DRUG ANTIBODIES TO TUMOUR NECROSIS FACTOR INHIBITORS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS; A TWO YEAR FOLLOW-UP STUDY

E. Durak Ediboglu[1], D. Solmaz[1], G. Kabadayi[1], M. Ozmen[1], M. Çınar[2], G. Sargin[3], O. Karadag[4], G. Kınıklı[5], Ö. Gerçik[6], U. Kalyoncu[4], S. Yilmaz[2], A. Cefle[7], G. Hatemi[8], T. Senturk[3], G. Keser[9], B. Kıcasık[10], F. Yargucu[9], L. Kozaci[11], S. Akar[1].
[1]*Izmir Katip Çelebi University, Rheumatology, Izmir, Turkey*; [2]*University of Health Sciences, Gulhane Faculty of Medicine, Rheumatology, Ankara, Turkey*; [3]*Adnan Menderes University, Rheumatology, Aydın, Turkey*; [4]*Hacettepe University, Rheumatology, Ankara, Turkey*; [5]*Ankara University, Rheumatology, Ankara, Turkey*; [6]*Tepecik Education and Research Hospital, Rheumatology, Izmir, Turkey*; [7]*Kocaeli University, Rheumatology, Kocaeli, Turkey*; [8]*Istanbul University, Cerrahpasa School of Medicine, Rheumatology, Istanbul, Turkey*; [9]*Ege University, Rheumatology, Izmir, Turkey*; [10]*Medical Park Hospital, Rheumatology, Gaziantep, Turkey*; [11]*Yıldırım Beyazit University, Biochemistry, Ankara, Turkey*

Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease affecting sacroiliac joints and spine as well as peripheral joints and entheses. Tumour necrosis factor inhibitors (TNFi) are widely used in patients with persistently high disease activity despite non-steroidal anti-inflammatory drugs. Some patients fail to respond or loose responsiveness during therapy with TNFi. The development of anti-drug antibodies (ADA) might play a role in non-response or some adverse events. However it has never been evaluated for 2-years period.
Objectives: Therefore, the aim of the present study was to evaluate the development of ADA against TNFi longitudinally during 2-years period in axSpA patients and factors associated with it.
Methods: In total 180 axSpA patients according to ASAS classification criteria with a new TNFi prescription in the last two weeks period were included in this observational study. Clinical data and serum samples were collected at baseline and at every 12 weeks. Serum drug levels and ADAs were measured on 12, 24, 52 and 104 weeks of treatment by ELISA in one center to avoid inter-assay variability. The development of ADA over time was investigated by using generalized estimating equations (GEE) which is a technique for longitudinal data analysis allowing the use of all available data even deviated from normality.
Results: 180 biologic naive axSpA patients (116 male, median [IQR] 44,5 [14,5] years) who started anti-TNF agents (infliximab [20%], adalimumab [27,2%], etanercept [32,2%] and golimumab [20,6%]) were included in the analysis. In comparison to baseline values BASDAI, ASDAS-CRP and CRP values were significantly decreased in third months of follow-up (Figure 1). In total 172 patients had at 12 weeks, 154 at 24, 121 at 52, and 73 at 104 week serum samples available for ADA determination. In longitudinal analysis; baseline age and TNFi type, as well as longitudinal BASDAI, ASDAS, serum CRP levels and the development of adverse events and discontinuation of the drug were found to be associated with the development of ADA. In order to determine independent association/s with the development of ADA two longitudinal multivariable models were run; (a) with ASDAS as an activity measure, (b) with BASDAI and CRP levels and produced that all the variables were independently associated with longitudinally development of anti-drug antibodies (Table 1). Antibodies to adalimumab were related with lower serum drug levels.
Conclusion: The results of the present study with up to 2 years of follow-up, revealed that the development of ADA against TNFi therapy is associated with high disease activity, the development of adverse events and treatment discontinuation in patients with axSpA. And etanercept might be negatively associated with the development of ADA.

Table 1. Factors associated with the development of anti-drug antibodies

	Model 1			*Model 2*		
	B	95% CI	*P*	B	95% CI	*P*
Age years	-0.061	-0.109;-0.012	***0.015***	-0.058	-0.107;-0.010	***0.018***
TNFi Treatment						
ETN	-1.981	-4.369; -0.134	*0.104*	-2.475	-4.791; -0.076	***0.036***
ADA	1.438	-0.002; 0.407	*0.073*	1.275	-0.119; -0.160	*0.064*
INF	1.550	3.010; 3.102	*0.050*	1.255	2.666; 2.629	*0.073*
GOL	0[a]			0[a]		
Presence of advers event, no	-0.824	-1.451; -.0198	***0.010***	-0.835	-1.461; -0.208	***0.009***
TNF treatment discontinuation	1.289	0.043;2.534	***0.043***	1.248	-0.075; 2.571	*0.065*
BASDAI	0.035	0.015; 0.055	***0.001***			
CRP	0.020	-0.035; 0.005	***0.008***			
ASDAS-CRP				0.852	0.466; 1.238	***0.000***

0[a]:set to zero because this parameter is redundant.

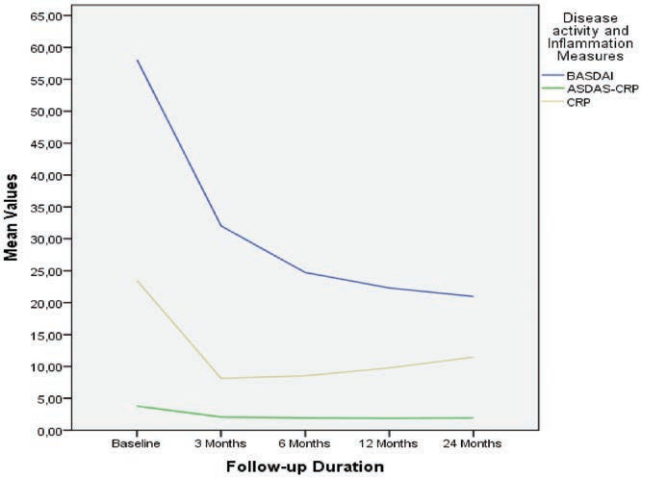


Figure 1. Mean change in disease activity and CRP levels during follow-up duration. (P values for 3rd months BASDAI<0.0001, CRP<0.001, ASDAS-CRP<0.001 respevtively)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2215

POS0930 SECUKINUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS AND AXIAL MANIFESTATIONS: PREDICTORS OF RESPONSE FROM THE DOUBLE-BLIND, RANDOMISED, PHASE 3B MAXIMISE TRIAL

X. Baraliakos[1], E. Pournara[2], L. Gossec[3], H. Marzo-Ortega[4], P. J. Mease[5], R. White[6], E. O'brien[6], B. Schulz[2], L. C. Coates[7]. [1]*Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*; [2]*Novartis Pharma AG., Immunology, Hepatology and Dermatology, Basel, Switzerland*; [3]*Sorbonne Universite, Hopital Pitie-Salpetriere, Paris, France*; [4]*University of Leeds, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*; [5]*Providence St Joseph Health and University of Washington, Swedish Medical Centre, Seattle, United States of America*; [6]*Novartis Ireland Limited, NBS CONEXTS, Dublin, Ireland*; [7]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*

Background: Psoriatic arthritis (PsA) is a heterogeneous disease with variability of response to different therapeutic modalities.[1] Identifying potential demographic and disease characteristics as predictors of treatment response may define personalised treatment optimisation strategies.[2–3]

Objectives: This post-hoc exploratory analysis of the MAXIMISE trial[4] investigated the differential treatment effect of demographics and baseline characteristics as predictive factors in biologic naïve patients with active PsA and symptoms of active spinal disease.

Methods: The full analysis set (FAS) comprised of all patients from the randomised set assigned to study treatment, fulfilling the predefined clinical criteria for active axial disease and for whom Assessment of SpondyloArthritis International Society (ASAS) 20 data were available at Week 12. The research hypothesis was that the odds ratio associated with the effect of treatment on ASAS20 responder status at Week 12 would be different depending on 12 pre-specified predictor variables. A logistic regression model was initially fitted to the FAS that included 12 pre-specified covariates. A second logistic regression model was then fitted to the FAS that allowed for all 12 pre-specified variables to interact with treatment.[5] The log-likelihood of the two fitted models were compared using a likelihood ratio test at a pre-specified significance level of 20% (i.e. *P*-value ≤0.20) to test whether any of the predefined variables interacted with treatment. If the above test was statistically significant at the 20% level of statistical significance the variables of the second model were formally examined to determine whether the overall effect of treatment is not applicable. Three forest plots were produced, one for each treatment group. Hypothesis tests were employed to determine the strength of evidence for each individual variable.

Results: The likelihood ratio test provided evidence against the assumption that the overall effect of treatment is applicable to all patients (*P*-value = 0.08). Notably, the odds of being an ASAS20 responder if nail dystrophy is present at baseline were 3 times greater in the secukinumab 150mg group and 5 times greater in the 300mg group compared with placebo (interaction *P*-value = 0.029). Although males fare worse than females in the placebo group, in the secukinumab 150mg and 300mg treatment groups the odds of being a responder were similar to females (interaction *P*-value = 0.039). Current smokers were less likely to be ASAS20 responders compared to never smokers regardless of treatment group (interaction *P*-value = 0.589) (Figure 1). Age, CRP level, Berlin MRI spine/SIJ score, time since first axial signs, number of swollen joints, new bone formation and BMI did not show a differential treatment effect on ASAS20 responses.

Conclusion: Of the 12 baseline variables of a unique population of 473 PsA patients with active axial disease diagnosed by clinical criteria, our analyses showed evidence of a differential treatment effect most notably for nail dystrophy suggesting that the presence of nail dystrophy may predict a better response to secukinumab in PsA patients with axial manifestations.

REFERENCES:

[1] Coates LC, Helliwell PS. *Clin Med (Lond).* 2017;17(1):65–70.
[2] Watson DS, et al. *BMJ*. 2019;364:l886.
[3] Hügle M, et al. *Rheumatol Adv Pract.* 2020;4(1):rkaa005.
[4] Baraliakos X, et al. *Ann Rheum Dis.* Published Online First: 17 Dec 2020. doi:10.1136/annrheumdis-2020-218808.
[5] Peto R, et al. *Br J Cancer.* 1977;35(1):1–39.

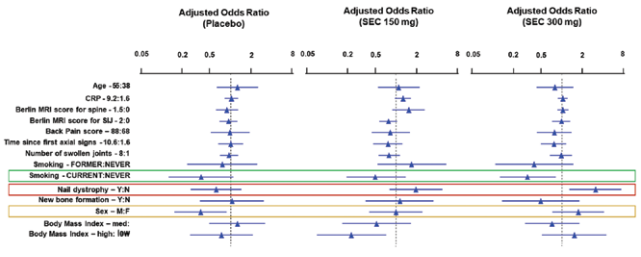


Figure 1. Forest plots of the adjusted odds ratio by treatment using interaction modelDisclosure of Interests:

Xenofon Baraliakos Speakers bureau: AbbVie, BMS, Celgene, Chugai, MSD, Novartis, Pfizer, and UCB., Consultant of: AbbVie, BMS, Celgene, Chugai, Galapagos, Gilead, MSD, Novartis, Pfizer, and UCB., Grant/research support from: AbbVie, and Novartis., Effie Pournara Shareholder of: Novartis, Employee of: Novartis, Laure Gossec Consultant of: AbbVie, Amgen, BMS, Biogen, Celgene, Gilead, Janssen, Lilly, Novartis, Pfizer, Samsung Bioepis, Sanofi-Aventis, and UCB., Grant/research support from: Amgen, Lilly, Janssen, Pfizer, Sandoz, Sanofi, and Galapagos., Helena Marzo-Ortega Consultant of: Janssen, Novartis, AbbVie, Celgene, Lilly, Pfizer, Takeda and UCB., Grant/research support from: Janssen, Novartis, AbbVie, Celgene, Lilly, Pfizer, Takeda and UCB., Philip J Mease Speakers bureau: AbbVie, Amgen, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer and UCB., Consultant of: AbbVie, Amgen, BMS, Boehringer Ingelheim, Galapagos, Celgene, Genentech, Gilead, Janssen, Lilly, Novartis, Pfizer, SUN Pharma, and UCB., Grant/research support from: AbbVie, Amgen, BMS, Celgene, Galapagos, Genentech, Gilead, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB., Roisin White Shareholder of: Novartis, Employee of: Novartis, Eamonn O'Brien Shareholder of: Novartis, Employee of: Novartis, Barbara Schulz Employee of: Novartis, Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Gilead, Eli Lilly, Janssen, Medac, Novartis, Pfizer, and UCB., Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB., Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Pfizer, and Novartis.

DOI: 10.1136/annrheumdis-2021-eular.2456

POS0931 RETENTION RATE AND TREATMENT RESPONSE OF BIOLOGICAL AGENTS IN ADVANCED SPINAL ANKYLOSIS AND BAMBOO SPINE: THE REAL LIFE DATA FROM THE HUR-BIO REGISTRY

B. Farisoğulları[1], G. K. Yardımcı[1], E. C. Bolek[1], E. Bilgin[1], E. Duran[1], G. Ayan[1], Z. Özsoy[1], G. Sandal Uzun[1], L. Kılıç[1], A. Akdoğan[1], Ş. A. Bilgen[1], O. Karadag[1], S. Kiraz[1], A. İ. Ertenli[1], U. Kalyoncu[1]. [1]*Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*

Background: Axial spondyloarthritis (axSpA) may lead to linear radiographic progression and progress to advanced spinal disease and finally to the bamboo spine (1).

Objectives: To assess the demographic, clinical, disease activity and retention rates of patients using biological disease-modifying antirheumatic drugs (bDMARD) with advanced spinal disease and bamboo spine in the Hacettepe University Rheumatology Biologic Registry (HUR-BIO) cohort.

Methods: In the HUR-BIO spondyloarthritis (SpA) registry were available 2952 patients. Of these, 774 patients with lumbar and cervical radiographs were included in the study. Advanced spinal ankyloses (99 patients) was defined as the presence of at least two intervertebral adjacent bridges at the lumbar and/or cervical spine level without bamboo spine. Bamboo spine (78 patients) was defined with a complete fusion of all lumbar and cervical spines. In addition, patients who diagnosed with axSpA for at least 10 years but no develop syndesmophytes on lumbar and cervical spine (92 patients) were used as a control group.

Results: Both the bamboo spine and advanced spinal disease had higher age, higher BMI, more smoking (ever) and hip involvement compared to the without syndesmophytes group. Acute phase reactants, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing spondylitis disease activity Score-CRP (ASDAS-CRP) parameters were similar at the beginning of bDMARD in all groups. BASFI was higher in the bamboo spine group than in the without syndesmophytes group at last visit (Table 1). There were no differences between all groups in terms of the retention rate of the first bDMARD (Log rank p=0.86) (Figure 1).

Conclusion: Data on the use of bDMARDs in SpA patients with bamboo spine are limited. This study showed that bDMARDs are an effective treatment option in SpA patients with bamboo spine with high disease activity. Similar drug retention rates were found compared to SpA patients with no syndesmophytes. Although the disease activity decreased similar rates in the groups, functional limitation continued in approximately half of the patients in bamboo spine patients.

REFERENCES:

[1] Braun J et al. Staging of patients with ankylosing spondylitis: a preliminary proposal. Annals of the rheumatic diseases, 2002, 61.suppl 3: iii19-iii23.

Table 1. Demographic, clinical characteristics and response to treatment in SpA groups.

	Without syndesmophytes n= 92		Advanced spinal disease n= 99		Bamboo spine n= 78		p	
Age, years˚	42.2 ± 8.8		51.3 ± 10.2		55.5 ± 9.3		**< 0.001***	
Age at disease onset, years˜	25.01 (11)		36.6 (20)		33.3 (18)		**< 0.001***	
Male, n (%)	55 (59.8)		78 (78.8)		66 (84.6)		**< 0.001***	
Disease duration, years˜	13.8 (5)		12.3 (15)		17.6 (13)		**< 0.001***	
Delay in diagnosis, months˜	12.02 (43)		36.01 (89)		36.01 (100)		**0.013***	
HLA-B27 positivity/total, n (%)	21/42 (50)		31/45 (69)		16/28 (57)		0.19	
BMI˜	26.3 (8)		29.7 (7)		29.4 (7)		**< 0.001***	
Smoking (ever), n (%)	56 (61)		78 (79)		58 (74)		**0.019***	
Hip involvement, positivity/total (%)	11/84 (13.1)		34/86 (39.5)		37/75 (49.3)		**< 0.001***	
	Onset	**Last**	**Onset**	**Last**	**Onset**	**Last**	**p (onset)**	**p (last)**
ESR, mm/h˜	21.5 (34)	12.5 (18)	25.5 (29)	14.5 (17)	23 (31)	14 (14)	0.6	0.59
CRP, mg/dL˜	1.5 (4)	0.4 (0.6)	1.7 (2)	0.65 (1)	1.8 (3)	0.64 (0.8)	0.4	**0.001***
ASDAS-CRP˜	3.6 (0.8)	1.9 (1)	3.4 (0.9)	2 (1.2)	3.4 (0.8)	1.9 (1.4)	0.4	0.23
BASDAI score˜	5.7 (2.6)	2.4 (4.5)	5.6 (3.3)	2.8 (3.1)	5.6 (3.2)	2.4 (3.3)	1	0.31
BASFI score˜	5.4 (4)	2 (4)	4.5 (4)	3 (4)	6.5 (3)	3.9 (4.5)	0.1	**0.002***
BASFI score > 4, n (%)	29 (59)	23 (25)	29 (56)	32 (32)	27 (75)	36 (46)	0.1	**0.014***
ASAS PR, n (%)		26 (28)		15 (15)		17 (22)		0.09

*p <0.05, ˚mean ± SD, ˜median (IQR)SD: Standard deviation; IQR: Inter-quartile rangeBASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BMI: Body mass index; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; ASAS PR: Assessment in SpondyloArthritis International Society partial remission; ASDAS: Ankylosing spondylitis disease activity score

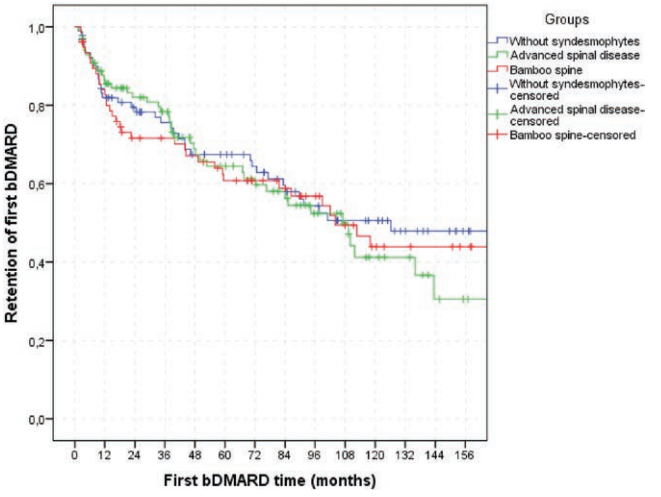


Figure 1. Retention rate of the first bDMARD

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2468

POS0932

REGULATION OF INTESTINAL FLORA RESTORES IMMUNE BALANCE IN PATIENTS WITH UNDIFFERENTIATED SPONDYLOARTHRITIS

T. Cheng[1,2,3], J. Guo[2], S. X. Zhang[1,2,3], Y. Zhang[1,2,3], Y. Li[1,2,3], X. Liu[1,2,3], X. F. Yin[1,2,3], X. Li[1,2,3]. [1]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [2]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [3]*Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*

Background: Undifferentiated spondyloarthritis (USpA) is the most common subtype of the spondyloarthritides with a prevalence between 0.7% and 2.0%[1]. Inflammatory back pain, peripheral arthritis and less frequently enthesitis are the main clinical features of USpA[2]. Resently the role of dysregulated microbiome along with migration of T lymphocytes and other cells from gut to the joint ("gut-joint" axis) has been recognized[3 4]. However, the detailed lymphocyte statuses of USpA patients and the effect of regulating the intestinal flora on the lymphocyte subsets is unclear.

Objectives: To investigate the status of lymphocyte subsets in peripheral blood (PB) of USpA patients and the variation after regulation of intestinal flora.

Methods: A total of 39 newly diagnosed patients with USpA who fulfilled the European Spondyloarthropathy Study Group (ESSG) classification criteria and 60 age- and sex- matched healthy controls (HC) were enrolled in this study. All patients were given intestinal flora regulation therapy for six months, including clostridium butyricum capsule or bacillus coagulans tablet. The peripheral lymphocyte subsets of these participants were assessed by flow cytometry. Methane hydrogen breath test as well as cytokines were measured in all patients before and after treatment. Mann-Whitney U test was applied for the lymphocyte status between USpA patients and HC and Wilcoxon test for the comparison before and after treatment. The results of methane hydrogen breath were counted by the Chi-Square test. All *P*-values reported herein are two-tailed and *P*-value<0.05 was taken as statistically significant.

Results: Compared with HC, patients with USpA had a lower numbers of T cells (*P*=0.001), NK cells (*P*=0.026), CD8+T cells (*P*=0.046) and Treg cells (*P*<0.05) but higher ratios of Th17/Tregs (*P*=0.001), indicating a disturbance of immune microenvironment (Figure 1). After given therapy, T cells (*P*=0.003), B cells (*P*=0.018), NK cells (*P*=0.003), $CD8^+$T cells (*P*=0.001) and Treg cells (*P*=0.009) were distinctly increased while the ratio of Th17/Treg decreased (*P*=0.046), suggesting a rebalance of immune systems (Figure 2a-c). Moreover, there were increase in the level of IL-6 (*P*<0.001), IL-17 (*P*=0.029) and TNF-α (*P*=0.003) as well as decrease in IL-10 (*P*=0.045) and IFN-γ (*P*=0.001) (Figure 2d). Further, the positive rate of intestinal bacterial overgrowth decreased significantly after regulation (*P*=0.029) (Figure 2e).

Conclusion: Imbalance of immune environment is closely related to the incidence of undifferentiated spondyloarthrosis. The regulation of intestinal flora restores the balance and improve the growth of bacteria in the small intestine simultaneously. Therefore it is essential to focus on the alteration of intestinal flora to prevent the outbreak of inflammation and disease progression.

REFERENCES:

[1] Cruzat V, Cuchacovich R, Espinoza LR. Undifferentiated spondyloarthritis: recent clinical and therapeutic advances. Curr Rheumatol Rep 2010;12(5):311-7. doi: 10.1007/s11926-010-0115-0 [published Online First: 2010/07/16].

[2] Deodhar A, Miossec P, Baraliakos X. Is undifferentiated spondyloarthritis a discrete entity? A debate. Autoimmun Rev 2018;17(1):29-32. doi: 10.1016/j.autrev.2017.11.006 [published Online First: 2017/11/08].

[3] Sheth T, Pitchumoni CS, Das KM. Management of Musculoskeletal Manifestations in Inflammatory Bowel Disease. Gastroenterol Res Pract 2015;2015:387891. doi: 10.1155/2015/387891 [published Online First: 2015/07/15].

[4] Fragoulis GE, Liava C, Daoussis D, et al. Inflammatory bowel diseases and spondyloarthropathies: From pathogenesis to treatment. World J Gastroenterol 2019;25(18):2162-76. doi: 10.3748/wjg.v25.i18.2162 [published Online First: 2019/05/31].

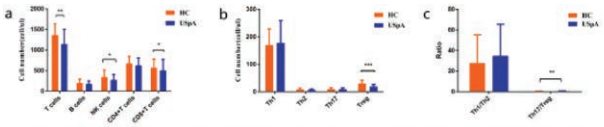


Figure1 **(a-c)** Comparison of lymphocyte subsets in peripheral blood between healthy controls and untreated USpA patients.

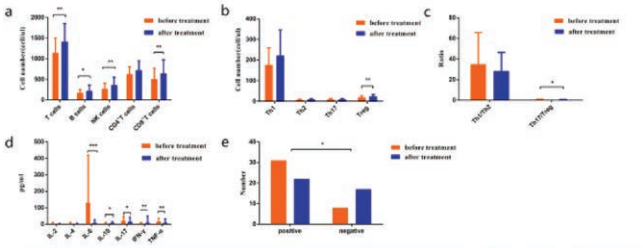


Figure2 **(a-c)** Variation of peripheral lymphocyte subsets cytokines after regulation of intestinal flora. **(d)** Variation of after regulation of intestinal flora. **(e)** Change of positive rate of methane hydrogen breath test after treatment. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3004

POS0933 TREATMENT ACCESS AND ADHERENCE DURING SOCIAL PREVENTIVE AND MANDATORY ISOLATION IN ARGENTINIAN PATIENTS WITH SPONDYLARTHRITIS

C. Airoldi[1], V. Martire[2], M. S. Gálvez Elkin[3], P. Girard Bosch[2], V. Duarte[4], S. Scarafia[5], F. Sommerfleck[6], M. Machado Escobar[7], N. Callahuara[8], J. Alcivar Navarrete[9], M. A. Medina[9], E. Buschiazzo[10], M. Cosatti[11], R. Garcia Salinas[12], E. Saturansky[6], V. Cosentino[13], D. Vila[14], M. J. Gamba[15], E. Kerzberg[13], G. P. Pendon[16], D. Zelaya[13], R. Águila Maldonado[17], L. Abbas[18], R. Nieto[1], S. Nasi[19], R. Luis[13], M. L. Acosta Felquer[20], M. Benegas[6]on behalf of Grupo de estudio de la Sociedad Argentina de Reumatología de Espondiloartritis axial yArtritis reactiva (GESAR EspAax-ARe). *[1]Hospital Provincial, Rheumatology, Rosario, Argentina*; *[2]Instituto Médico Platense, Rheumatology, La Plata, Argentina*; *[3]Instituto Cardiológico Santiago del Estero, Rheumatology, Santiago del Estero, Argentina*; *[4]Monte Grande Clinic, Rheumatology, Buenos Aires, Argentina*; *[5]Hospital Municipal San Cayetano, Rheumatology, Buenos Aires, Argentina*; *[6]Hospital Mendez, Rheumatology, Buenos Aires, Argentina*; *[7]Hospital Eva Perón, Rheumatology, Tucumán, Argentina*; *[8]Hospital Rivadavia, Rheumatology, Buenos Aires, Argentina*; *[9]Hospital Tornú, Rheumatology, Buenos Aires, Argentina*; *[10]Hospital Sr. Del Milagro, Rheumatology, Salta, Argentina*; *[11]CEMIC, Rheumatology, Buenos Aires, Argentina*; *[12]Hospital Italiano de La Plata, Rheumatology, La Plata, Argentina*; *[13]Hospital Ramos Mejía, Rheumatology, Buenos Aires, Argentina*; *[14]Centro Médico Ginecológico, Rheumatology, Buenos Aires, Argentina*; *[15]Hospital Posadas, Rheumatology, Buenos Aires, Argentina*; *[16]Hospital Ricardo Gutierrez, Rheumatology, La Plata, Argentina*; *[17]Hospital San Martin, Rheumatology, La Plata, Argentina*; *[18]PSORIAHUE, Rheumatology, Buenos Aires, Argentina*; *[19]Hospital El Carmen, Rheumatology, Mendoza, Argentina*; *[20]Hospital Italiano de Buenos Aires, Rheumatology, Buenos Aires, Argentina*

Background: Access to high-cost treatments is especially limited in low-resource countries. This issue is becoming stronger today given the health and economic crisis caused by the SARS-CoV2 pandemic. There are no reports in our country on limitations to access and adherence to treatment in patients with Spondyloarthritis (SpA) during social preventive and mandatory isolation.
Objectives: Evaluate access and adherence to treatment in patients with Spondyloarthritis during social preventive and mandatory isolation.
Methods: Patients with axial spondyloarthritis (axSpA) radiological (r-axSpA), non-radiological (nr-axSpA) and peripheral spondyloarthritis (pSpA), according to ASAS criteria and psoriatic arthritis (PsA) according to CASPAR criteria, were included. Sociodemographic data, comorbidities, disease activity and treatments were collected at baseline. Data on treatment discontinuation, medical attention for suspected COVID-19 disease, RT-qPCR for SARS-CoV-2 detection and outcome of COVID-19 disease were collected from April to September 2020. Numerical variables were summarized as means and standard deviations (SD) or as medians and interquartiles 25-75 (IQ 25-75).
Results: 320 patients were included, 55% were male, with a mean age of 50 years (SD 13), 21.6% had diagnosis of r-axSpA, 6.9% nr-axSpA, 6.9% pSpA, and 64.7% PsA. Disease duration was 11 (IQ 5-16) years and activity parameters were as follow: BASDAI 3.65 (SD 3), BASFI 3 (1.5-9), PASI 0.3 (0-7), BSA 0.2 (0-6). 14 (4.4%) patients with COVID-19 disease were reported, 10 were confirmed by positive RT-qPCR and 4 by symptoms and history of close contact with SARS patients. 4 (28.6%) received anti TNF (3 adalimumab, 1 certolizumab), 4 (28.6%) anti IL17 (3 secukinumab and 1 ixekizumab), 8 (57%) methotrexate (MTX) and 2 (14%) leflunomide (LF). Among the 320 patients included, 59 (18.4%) discontinued at least one treatment during follow-up. The discontinued medications were: adalimumab (16), MTX (15), secukinumab (9), etanercept (6), certolizumab(4), ustekinumab (3), NSAIDs (2), apremilast (1), golimumab (1), ixekuzumab (1), LF (1), MTX plus LF (1). The main reason for treatment discontinuation was drug shortage: 36 (62%), followed by patient's decision: 12 (21%) and medical indication: 11 (17%). Of the 36 patients who discontinued due to shortage, 11 received adalimumab, 8 secukinumab, 5 MTX, 3 etanercept, 3 certolizumab, 3 ustekinumab, 2 NSAIDs and 1 golimumab.
Conclusion: In our Argentinian cohort of patients with SpA, drug shortage was the main reason for treatment discontinuation. The SARS-CoV2 pandemic exposed limitations to access to treatment for patients with SpA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3147

POS0934 BIOLOGICAL THERAPY IN UVEITIS ASOCIATED TO AXIAL SPONDYLOARTHRITIS. SINGLE CENTER UNIVERSITY STUDY

A. Herrero-Morant[1], I. González-Mazón[1], V. Calvo-Río[1], J. Rueda-Gotor[1], M. Á. González-Gay[1], R. Blanco[1]. *[1]Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*

Background: Uveitis is the most frequent extraarticular manifestation of axial Spondyloarthritis (axSpA). Effects of Biological Therapy (BT) on uveitis associated to axSpA are contradictory (1-3).
Objectives: To assess in uveitis associated to axSpA a) frequency and features of uveitis, and b) efficacy and relation of BT in a single-center university study.
Methods: Observational study from a cohort of 301 consecutive unselected patients with axSpA classified according to the Assessment of SpondyloArthritis International Society criteria. Episodes of uveitis were analyzed before and after BT initiation. Likewise, uveitis incidence rate *(episodes/100 patients/year)* at baseline and after first BT was calculated.
Results: Uveitis was observed in 44 (25 men/19 women) out of 301 (14.6%) patients. Mean age was 45.6 ± 10.3 years. Demographic and clinical features in patients who developed uveitis and those that did not are summarized in Table 1. After 18.6 ± 10.4 years of follow-up, 44 (14.6%) patients suffered from at least one episode of uveitis. Uveitis was anterior and acute in all cases and unilateral in 37 (84.1%) patients. Mean anterior chamber cells was 1.7 ± 1.2 cells.
Per episode of uveitis, 20 patients received BT with: secukinumab (SECU) (n=7, 35%), adalimumab (n=6, 30%), golimumab (n=3, 15%), infliximab (n=2, 10%), certolizumab (n=1, 5%), and etarnecept (ETN) (n=1, 5%). Before the initiation of BT, patients treated with SECU developed 29.7 *episodes/100 patients/year* while those treated with monoclonal anti-TNFα 16.3 *episodes/100 patients/year* and patients with ETN 5.8 *episodes/100 patients/year*. After 5.9 ± 3.7 years of follow-up, patients treated with SECU developed 16.1 *episodes/100 patients/year* while those treated with monoclonal anti-TNFα 7.6 *episodes/100 patients/year* and patients with ETN 0 *episodes/100 patients/year* (Figure 1). No serious adverse effects were observed.
Conclusion: Uveitis was observed in 14.6% of axSpA. Most of them were HLA-B27 positive. Acute, anterior and unilateral was the most frequent pattern of uveitis in axSpA. There was a similar decrease in incidence rate between patients treated with SECU and those treated with monoclonal anti-TNFα.
REFERENCES:
[1] Deodhar AA, et al. ACR Open Rheumatol. 2020; 2:294-299.
[2] Roche D, et al [abstract]. Arthritis Rheumatol 2019; 71 (suppl 10).
[3] Lindström U, et al Annals of the Rheumatic Diseases 2020;79:9-10.

Table 1. Main general features and differences between patients with and without uveitis.

	Overall	Uveitis	Non uveitis	*p*
	n= 301	n= 44	n= 257	
Age, years (mean±SD)	44.9 ± 11.8	45.6 ± 10.3	44.8 ± 12.1	0.47
Gender, n (m/w) (%)	179/122 (59.5/40.5)	25/19 (56.8/43.2)	154/103 (59.9/40.1)	0.71
HLAB27 positive,n (%)	190 (63.1)	37 (84.1)	153 (60.0)	**0.00**
Follow-up of axSpA, year (mean±SD)	13.5 ± 11.2	18.6 ± 10.5	12.6 ± 11.1	0.33
Family history, n (%)	84 (27.9)	15 (34.1)	69 (27.2)	0.35
r-axSpA, n (%)	217 (72.1)	36 (81.8)	181 (70.4)	0.12
nr-axSpA, n (%)	84 (27.9)	8 (18.2)	76 (29.6)	0.12
Enthesitis, n (%)	108 (35.9)	14 (31.8)	94 (36.6)	0.54
Peripheral arthritis, n (%)	96 (31.9)	12 (27.3)	84 (32.7)	0.47
Psoriasis, n (%)	35 (11.6)	6 (13.6)	29 (11.3)	0.65
Inflammatory bowel disease, n (%)	22 (7.3)	2 (4.5)	20 (7.8)	0.45
Hip involvement, n (%)	20 (6.6)	3 (6.8)	17 (6.6)	0.96
Dactylitis, n (%)	17 (5.7)	3 (6.8)	14 (5.4)	0.72
Cardiovascular event, n (%)	7 (2.3)	1 (2.3)	6 (2.3)	0.98

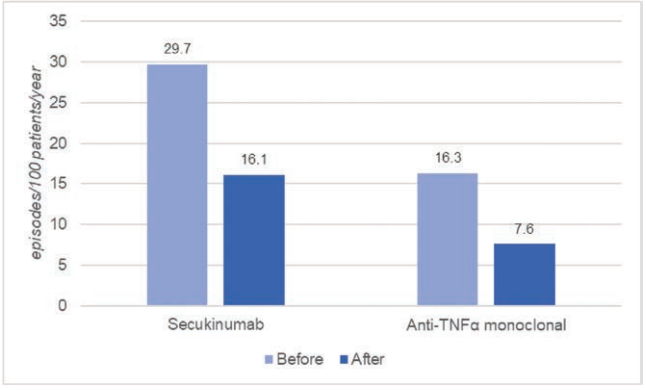


Figure 1. Uveitis incidence rate before and after biological therapy.

Disclosure of Interests: Alba Herrero-Morant: None declared, Iñigo González-Mazón: None declared, Vanesa Calvo-Río Speakers bureau: Abbott, Lilly, Celgene, Grünenthal, UCB Pharma, Grant/research support from: MSD and Roche, Javier Rueda-Gotor: None declared, Miguel Á. González-Gay Speakers bureau: AbbVie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Grant/research support from: AbbVie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, Sanofi, Lilly and MSD, Grant/research support from: AbbVie, MSD and Roche

DOI: 10.1136/annrheumdis-2021-eular.3229

POS0935 DO PERIPHERAL AND EXTRA MUSCULOSKELETAL MANIFESTATIONS HAVE AN IMPACT ON BIOLOGIC DMARD PRESCRIBING PATTERNS IN AXIAL SPONDYLOARTHRITIS: THE RESULTS OF TREASURE EXPERIENCE

E. Durak Ediboglu[1], D. Solmaz[1], O. Karadag[2], Y. Pehlivan[3], M. Çınar[4], A. İ. Ertenli[2], B. N. Coşkun[3], D. Ersözlü[5], O. Küçükşahin[6], A. Ateş[7], S. Kiraz[2], B. Yağız[3], E. Tekgoz[4], H. Emmungil[8], E. Gönüllü[9], G. Kabadayi[1], T. Kaşifoğlu[10], R. Mercan[11], G. Kimyon[12], S. Colak[4], C. Bes[13], N. S. Yasar Bilge[10], V. Yazısız[14], S. S. Koca[15], P. Atagündüz[16], N. A. Kanıtez[17], U. Kalyoncu[2], S. Akar[1]. *[1]Izmir Katip Çelebi University, Rheumatology, Izmir, Turkey*; *[2]Hacettepe University, Rheumatology, Ankara, Turkey*; *[3]Uludag University, Rheumatology, Bursa, Turkey*; *[4]University of Health Sciences, Gulhane Faculty of Medicine, Rheumatology, Ankara, Turkey*; *[5]University of Health Sciences, Adana Education and Research Hospital, Rheumatology, Adana, Turkey*; *[6]Yıldırım Beyazıt University, Rheumatology, Ankara, Turkey*; *[7]Ankara University, Rheumatology, Ankara, Turkey*; *[8]Trakya University, Rheumatology, Edirne, Turkey*; *[9]Sakarya University, Rheumatology, Sakarya, Turkey*; *[10]Osmangazi University, Rheumatology, Eskişehir, Turkey*; *[11]Namık Kemal University, Rheumatology, Tekirdağ, Turkey*; *[12]Mustafa Kemal University, Rheumatology, Hatay, Turkey*; *[13]Sadi Konuk Education and Research Hospital, Rheumatology, Istanbul, Turkey*; *[14]Akdeniz University, Rheumatology, Antalya, Turkey*; *[15]Fırat University, Rheumatology, Elazıg, Turkey*; *[16]Marmara University, Rheumatology, Istanbul, Turkey*; *[17]Koc University, Rheumatology, Istanbul, Turkey*

Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease mainly affecting sacroiliac joints and spine. Peripheral arthritis, dactylitis and enthesitis may also occur. Extra musculoskeletal manifestations (EMMs; uveitis [AAU], inflammatory bowel disease [IBD] and psoriasis [Pso] are among the most common ones) are important features and might have an impact on the disease burden in patients with axSpA. The presence of EMM, in particular IBD and AAU could influence the choice of TNFi however little is known regarding the role of peripheral manifestations together with the EMM on the prescribing patterns in axSpA patients.

Objectives: To examine the frequency of peripheral and EMMs in a real-world axSpA cohort and their effect on the choice of first advanced treatment.

Methods: In total 1687 axSpA patients (58% male and the mean age (±SD) was 38.5 ± 10.9) who initiated his/her first biologic were included in the present analysis. The data for the current study was obtained from the TReasure web-based registry; in which RA and SpA patients treated with bDMARDs from different regions of Turkey. Baseline demographic, disease related characteristics, peripheral and EMMs were extracted. Characteristics of patients with and without peripheral/extra-musculoskelatal involvement were compared as well as factors/covariates associated with the choice of first TNFi and secukinumab was analysed.

Results: Enthesis (28.2%) was found the most common peripheral manifestations and peripheral arthritis (26.4%) and hip arthritis (24.4%) followed it. Symptom duration to the first advanced treatment initiation was significantly shorter in axSpA patients with peripheral arthritis, enthesitis, dactylitis and psoriasis and longer in hip arthritis and AAU. HLA-B27 positivity was significantly lower in patients with arthritis, psoriasis and IBD and higher with hip arthritis and AAU. In multivariate analysis the presence of IBD is significantly associated with the preference of monoclonal TNFi (mab) over etanercept (ETA) (OR 5,770; 95%CI 1.788-18.616). However ETA was preferred in patients with hip arthritis (p=0.003), longer symptom duration (p=0.049), and using sulfasalazine (p=0.043). In comparison with mabs, secukinumab (SEC) prescription was found to be significantly associated with higher age (p=0.001), sulfasalazin (p=0.001) and methotrexate usage (p=0.053) among axSpA patients need their first advanced treatment.

Conclusion: The results of the current study confirm the pathophsyologic associations of peripheral involvement and EMM in axSpA patients. Apart from hip arthritis the presence of IBD has an impact on the prescription of advanced treatment in real-life.

Table 1. Clinical characteristics of patients in cohort

	All patients (n=1678)	Peripheral arthritis (n=445)	Dactilitis (n=81)	Enthesis (n=476)	Uveitis (n=193)	Psoriazis (n=152)	IBD (n=78)	Hip involvemet (n=412)
Age, mean±SD	38,5± 10,9	38,3± 11,6	37,4± 11,1	37,9± 10,7	41,3± 11,4	39,9± 11,3	41,6± 12,2	39,2± 11,2
Male sex, n (%)	974 (57,7)	184 (41,3)	34 (42)	238 (50)	96 (49,7)	54 (35,5)	43 (55,1)	272 (66)
Symptom duration, mean month±SD	108,5± 98,9	96,9± 92,9	79,1± 76,5	100,4± 92,7	144,7± 110,2	87,7± 94	94,5± 98	133,3± 108,2
HLA B27 positivity, n (%)	621 (53,7)	142 (46,3)	27 (51,9)	174 (49,4)	104 (77)	34 (36,2)	16 (27,1)	186 (59,8)
Concomitant cDMARD usage (yes), n (%)	420 (24,9)	170 (38,2)	39 (48,1)	133 (27,9)	53 (27,5)	58 (38,2)	24 (30,8)	99 (24)
BASDAİ, mean±SD	5,1±2,5	5,1±3	5,3±3,1	5,3±2,9	4,7±2,5	5,6±2,4	4,8±2,3	5,3±2,1
ASDAS-CRP, mean±SD	3,1±1,5	2,6±1,9	2,5±1,8	2,8±1,7	2,9±1,7	3,4±1,3	3,1±1,5	3,7±1,4

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3236

POS0936 TREATMENT OF ANKYLOSING SPONDYLITIS WITH TUMOR NECROSIS FACTOR-ALPHA INHIBITORS LOWERS THE RISK OF RENAL FUNCTION DECLINE

S. J. Lee[1], J. S. Lee[1], U. C. Cha[1], E. J. Nam[1]. *[1]School of Medicine, Kyungpook National University, Korea, Internal Medicine, Daegu, Korea, Rep. of (South Korea)*

Background: Ankylosing spondylitis (AS) is associated with reduced renal function, possibly due to chronic inflammation or the use of nephrotoxic drugs. However, the long term effect of tumor necrosis factor (TNF) inhibitors on renal function in patients with AS has not been well established.

Objectives: We therefore investigated the association of TNF inhibitors treatment and change in estimated glomerular filtration rate (GFR) using the Korean College of Rheumatology Biologics (KOBIO) registry (ClinicalTrials.gov, NCT01965132), a prospective nationwide biologics registry.

Methods: We enrolled 1846 patients with AS in KOBIO registry and as disease controls, 471 patients with AS who did not take biologics in Kyungpook National University Hospital. The estimated glomerular filter rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) equation was evaluated in both groups. Renal insufficiency was defined as eGFR <60 mL/min/1.73 m2. Changes and differences of eGFR in each group were assessed at every follow-up year using paired t-test. Risk factors for renal function decline were identified using multivariable analysis.

Results: The changes of eGFR values in patients treated with TNF inhibitors were not significantly decreased during 5 years follow up period. However, those in patients not treated with TNF inhibitors were significantly decreased. Moreover, among patients with renal insufficiency, use of TNF inhibitors did not affect further renal function deterioration during follow up period. Using multivariable logistic regression models, patients treated (versus not treated) with TNF inhibitors had a lower risk of renal function decline after 5 years follow up period (p<0.045).

Conclusion: The use of TNF inhibitors was independently associated with lower risk of renal function decline and TNF inhibitors may be a safe treatment option in AS patients with renal insufficiency.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3605

POS0937 TREATMENT SURVIVAL ON BIOLOGICS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS – DATA FROM MOSCOW UNIFIED ARTHRITIS REGISTRY (MUAR)

K. Lytkina[1], E. Koltsova[2], E. Rozochkina[3], E. Shmidt[4], G. Lukina[3,5], A. Zagrebneva[6,7], E. Zhilyaev[8,9]. *[1]City Clinical Hospital#4, Rheumatology Department, Moscow, Russian Federation*; *[2]Rheumatology Research Institute of the Organization of Health and Healthcare Management, The Organizational-Methodical Division, Moscow, Russian Federation*; *[3]A.S.Loginov Moscow Clinical Scientific Center, Rheumatology Department, Moscow, Russian Federation*; *[4]department City Clinical Hospital 1 named after N.I. Pirogov, Rheumatology Department, Moscow, Russian Federation*; *[5]V.A. Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*; *[6]City Clinical Hospital 52, Rheumatology, Moscow, Russian*

Federation; [7]*RSMU named after N.I.Pirogov, Department of General Medicine, Moscow, Russian Federation*; [8]*Russian Medical Academy of Continuing Professional Education, Rheumatology, Moscow, Russian Federation*; [9]*CJSC «European Medical Center», Rheumatology, Moscow, Russian Federation*

Background: The number of new biologics in treatment of axial spondyloarthritis (axSpA) is rapidly increasing. It is important to assess timely their place in the treatment of axSpA, especially with regard to retention on therapy.
Objectives: To compare retention on therapy with different biologics in patients with axSpA.
Methods: We retrospectively analyzed the data of axSpA patients receiving biologics from the MUAR register. Predictors of retention on therapy were selected by forward stepwise variable selection within Cox regression proportional hazard model. These predictors were considered as confounders when comparing the risks of biologics withdrawal.
Results: 990 treatment episodes in 640 patients with axSpA were analyzed (non-radiographic axSpA – 4.1%, ankylosing spondylitis - 95.9%). The duration of episodes was 824±920 days. Men were 66,6%, mean age 46,4±11,4.The patients were treated with Adalimumab (ADA) (n= 252 treatment episodes), Golimumab (GOL) (n=82), Infliximab (INF) (n=167), Netakimab (NET) (n=9), Secukinumab (SEC) (n=75), Certolizumab pegol (CER) (n=66), Etanercept (ETA) (n=339).
The following predictors of withdrawal risk were identified –
1.The total duration of the disease
2.The duration of the disease before the onset of biologic treatment
3.Gender
4.Family history of non-inflammatory spondylopathy (degenerative spinal disease)
5.The line of biologic treatment
6.The level of education
The severity of radiographic sacroiliitis and HLA B-27 positivity were not associated with the risk of discontinuation of biologics.
The identified predictors were further considered as confounders. Adjusted for confounders, ETA had the lowest treatment withdrawal risk (Figure 1). ADA, GOL, INF, SEC, CER had significantly higher risk of withdrawal compared with ETA (Table 1).
Conclusion: Our analysis detected predictors associated with risk of biologics withdrawal in axSpA patients in real clinical practice. There are significant differences between biologics regarding retention on treatment.

Table 1. Hazard ratio for treatment withdrawal

Drug	Hazard ratio (Exp B)	p
ADA	1.52*	0.004
GOL	2.95*	0.000
INF	2.574*	0.000
NET	3.680*	0.073
SEC	2.133*	0.005
CER	2.922*	0.000

*- withdrawal risk relative to ETA

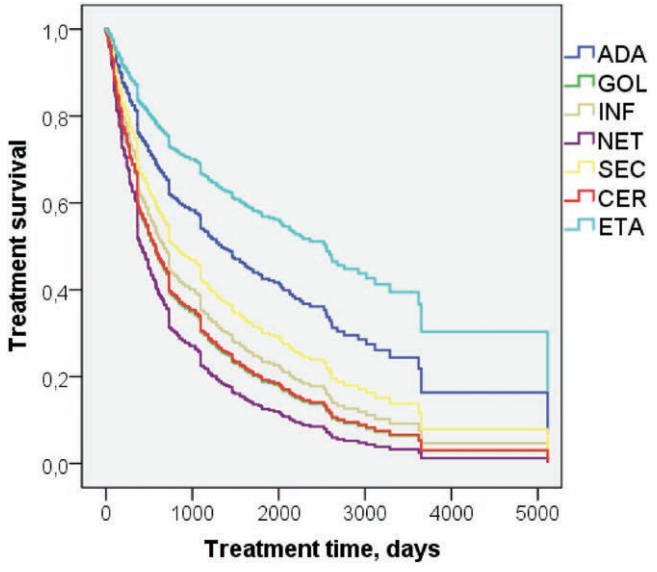


Figure 1. Picture 1. Treatment withdrawal risk

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3642

POS0938 A NEW APPROACH FOR ULTRASOUND GUIDED SACROILIAC JOINT INJECTIONS IN SPONDYLOARTHRITIS

P. Todorov[1], A. Batalov[1]. [1]*Medical University of Plovdiv, Rheumatology and Internal Diseases Propaedeutics, Plovdiv, Bulgaria*

Background: Sacroiliac joints (SIJ) inflammation and pain is particularly common in patients with Spondyloarthritis (SpA). SIJs injections represent a valuable therapeutic option in this condition. Traditionally this procedure (irrespective of the guidance method) aims at the lower (synovial) part of the joint. However, there is growing body of evidence that enthesitis rather than synovitis is the cardinal pathological lesion in SpA. Thus, an approach targeting the more superior (ligamentous) part of the joint, with the numerous entheses of the intraspinous sacroiliac ligaments placed there, could be more beneficial in SpA patients with active sacroiliitis. The Posterior sacroiliac ligament (PSIL) is the most superficial of the SIJ ligaments, covering the other dorsally. Thus, using PSIL as a landmark and placing the needle tip beneath it, the injected solution will inevitably spread in the ligamentous portion of the joint.
Objectives: To assess the feasibility and efficacy of a new technical approach of ultrasound (US) guided SIJ injections in SpA targeting the ligamentous part of the joint.
Methods: The feasibility and efficacy of our approach was tested on 22 consecutive SpA patients, after an inform consent, with pain in the SIJ that did not respond to NSAIDS and who were otherwise on a stable medical treatment. A solution consisting of 7 mg Betamethasone (1ml) and 1% Lidocaine (1.5 ml) was administered to all injected SIJs. The efficacy of the procedure was assessed by patients reported outcome measures: mean reported pain level (on VAS), level of disability due to the back pain (Roland Morris Disability Questionnaire – RMDQ) and quality of the night sleep (Jenkins Sleep Evaluation Questionnaire – JSEQ). They were filled by the patients at baseline and two months after the intervention. Methodology of the procedure: All injections were done with patients in a prone position using an Esaote My Lab 7 machine and a linear transducer (3-12 MHz). After visualization of the SIJ cleft, the probe was slide caudally to the level of the second sacral foramen. Then the probe was rotated to a slightly oblique position with its lateral part higher and the medial part lower. In this way the probe became parallel to the PSIL, and latter is visualized sufficiently well in its long axis. Then, in this position, a 22G, 9 mm spinal needle (Spinocan) was inserted at the medial side of the probe following an in-plane free-hand technique and advanced in cranio-lateral direction. When the needle tip was seen to penetrate the PSIL, and thus enter the SIJ ligamentous part, 0.2 ml of the solution was injected to confirm that it spreads beneath the PSIL, rather than above or in this ligament. After that, a Color Doppler (CD) box was activated and placed over the SIJ to monitor the spread of the injected solution and ensure that it keeps bellow the PSIL. The whole solution was injected under this direct US and CD visualization and the needle tip was repositioned again beneath the PSIL if needed during the procedure.
Feasibility of this injection approach was assessed on the basis of the encountered difficulties in adequate visualization of the PSIL and the injected solution flow beneath it from the start until the end of the intervention.
Results: The results of the procedure, assessed in two months showed that the mean pain score decreased by 68% (VAS from7.22±1.23 to 2.28±2.37), the disability score - by 46% (RMDQ from 11.86±5.12 to 6.42±6.39), and the sleep quality improved by 41% (JSEQ from 9.86±4.76 to 5.84±3.43). The procedure was found completely feasible by the performing operator and the visualization of the landmark (PSIL) was adequate in all patients and throughout the whole procedure. The CD allowed to confirm reliably that the solution is injected under the PSIL at any time point.
Conclusion: The SIJ injections performed by our approach and targeting the ligamentous part of the joint, proved to be completely feasible and furthermore – efficient, in alleviating the symptoms of active sacroiliitis in SpA patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3820

POS0939 WHEN DO THE ACTIVE SACROILIITIS MRI FINDINGS LOSS IN ANKYLOSING SPONDYLITIS? A RETROSPECTIVE, CROSS-SECTIONAL, OBSERVATIONAL STUDY

A. C. Genç[1], F. Turkoglu Genc[2], Z. Öztürk[3], D. Karatas[3], S. M. Turk[3], E. Gönüllü[3]. [1]*Geyve Government Hospital, Internal Medicine, Sakarya, Turkey*; [2]*Sakarya University, Internal Medicine, Sakarya, Turkey*; [3]*Sakarya Unıversıty, Rheumatology, Sakarya, Turkey*

Background: Ankylosing Spondylitis (AS) is an inflammatory rheumatic disease that affects the spine and sacroiliac joints (SIJ). Non-steroidal anti-inflammatory drugs (NSAIDs), modifying antirheumatic drugs (DMARDs), and recently anti-TNF blockers, which are more costly than NSAIDs but used in resistant cases, are generally used in its treatment (1).
Objectives: While SIJ-MRI is one of the imaging methods in the diagnosis of the disease, it is not yet used in its follow-up (2). We wanted to define when the activated SIJ-MRI findings, which showed early sacroiliitis, regressed according to the treatment option.
Methods: Among the 8100 SIJ-MRIs taken in our hospital in the last 5 years, those that were reported normally were excluded from the study. Among the remaining 1150 patients with active or chronic SIJ findings, a total of 87 patients who were diagnosed with AS and had active SIJ findings in the first imaging and had a second SIJ-MRI examination for any reason were included in our retrospective, cross-sectional and observational study. According to the treatment option, how long the active SIJ-MRI findings disappeared was calculated in months using the Kaplan-Meier method.
Results: Of the 87 patients examined in the study, 41 were women and 46 were men. The average age is 32.7. Active SIJ-MRI findings disappeared in a mean of 30.6 months for 11 of 24 patients who did not use any medication, in a mean of 33.9 months for 6 of 16 patients using NSAIDs, in a mean of 40.7 months for 14 of 34 patients using sulfasalazine, in a mean of 28.2 months for 3 of 6 patients using adalimumab, in a mean of 24.4 months for 3 of 5 patients using methotrexate, 11.9 month for 2 of 1 patient using certolizumab. There was no statistically significant difference between the groups.
Conclusion: The signs of active sacroiliitis disappeared in less time in patients who did not receive any treatment than those using NSAIDs and sulfasalazine. Patients using anti-TNF blockers had earlier results than those using no medication. The reason for this may be the progressive course of patients who are switched to the next level of treatment and their late response to treatment, as well as the mechanism of the disease (2-3). This situation brings to the agenda the tendency of physicians to over-treat the disease. More randomized controlled studies are needed regarding new treatment options.
REFERENCES:

[1] Braun J. 'Axial spondyloarthritis including ankylosing spondylitis' Rheumatology (Oxford). 2018 1;57(suppl_6):vi1-vi3.
[2] Braun J, Baraliakos X, Golder W, Brandt J, Rudwaleit M, Listing J, Bollow M, Sieper J, van der Heijde D. Magnetic resonance imaging examinations of the spine in patients with ankylosing spondylitis, before and after successful therapy with infliximab. Arthritis & Rheumatism Vol. 48, No. 4, April 2003, pp 1126–1136.
[3] Jee WH, McCauley TR, Lee SH, Kima SH, Ima SA, Had KY. Sacroiliitis in patients with ankylosing spondylitis: association of MR findings with disease activity. Magnetic resonance imaging 2004:22;245–250.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4031

POS0940 THE IMPACT OF TUMOUR NECROSIS FACTOR-ALPHA INHIBITOR TREATMENT ON WNT SIGNALING INHIBITORS, NOGGIN AND CYTOKINE LEVELS IN AXIAL SPONDYLOARTHRITIS

N. Atas[1], B. Çakır[2], F. Bakır[3], M. Uçar[4], H. Satış[1], G. T. Güz[5], H. Babaoglu[1], R. Bilici Salman[1], A. Avanoglu Guler[1], H. Karadeniz[1], S. Haznedaroglu[1], B. Goker[1], M. A. Ozturk[1], A. Tufan[1]. [1]*Gazi University, Division of Rheumatology, Department of Internal Medicine, Ankara, Turkey*; [2]*Alab Laboratory, Department of Clinical Biochemistry, Ankara, Turkey*; [3]*Lokman Hekim University, Department of Clinical Biochemistry, Ankara, Turkey*; [4]*Gazi University, Department of Radiology, Ankara, Turkey*; [5]*Gazi University, Department of Internal Medicine, Ankara, Turkey*

Background: Axial spondyloarthritis (axSpA) is a common chronic inflammatory disease of the axial skeleton. Some cytokines have important roles in initiation and progression of disease and are elevated in active disease. Additionally, Wnt signaling pathway inhibitors and noggin also appear to be involved in pathogenesis of ankylosing spondylitis. Anti-tumor necrosis factor-alpha (TNF) agents have dramatically improved the clinical outcome of axSpa; however, acceptable clinical improvement is not achieved in all patients and capacity of anti-TNF to slow or prevent structural damage still remains controversial.
Objectives: To evaluate the effect of anti-TNF on inflammatory and noninflammatory milieu in patients with axSpA.
Methods: In this prospective study we included 30 biologic treatment naive adult patients with axSpA and 30 healthy controls. All patients with high disease activity were treated with anti-TNF therapy for 6 months. Laboratory and clinical evaluation of all patients were performed at baseline and after 6 months of anti-TNF treatment. Following cytokines and wnt/BMP antagonists were measured; TNF-Alpha, COX-2, IL-6, IL-17, IL-22, IL-23, IL-33, dickkopf-1, sclerostin, noggin.
Results: The mean age of patients with axSpA and healthy controls were 38.1±13.3 and 37.7±7.7 years, respectively (p>0.005). At baseline, the median (IQR) TNF-alpha was higher in axSpA patients when compared to healthy controls, 34.4 pg/ml (31.4-37.03) vs 18.1 pg/ml (12.1-28.4), (p<0.001), while the median (IQR) dickkopf-1 and sclerostin were lower in axSpA patients, 446.7 pg/ml (356.9-529.3) vs 1088.7 pg/ml (951.7-1244.4), (p<0.001) and 312.4 pg/ml (140.8-412.7) vs 412.3 pg/ml (295.4-512.8), (p<0.001), respectively. IL-17, IL-22, IL-33, dickkopf-1 and sclerostin increased with anti-TNF treatment (table 1).
Conclusion: Elevation of some cytokines which are important in pathogenesis of axSpA and nonincrease in noggin with anti-TNF drugs may affect effectiveness of anti-TNF treatment.

Table 1. Changes of cytokines, dickkopf-1, sclerostin and noggin with anti-TNF treatment.

	Pre-Anti-TNF	Post-Anti-TNF	P value
IL-6	45(39.1-68.8)	47.6(27.3-61.1)	0.750
IL-17	93.3 (85.1-104.8)	102.1(86.6-114.6)	**0.026**
IL-22	159,2 (151,9-178.4)	183.5(156.3-304.6)	**0.033**
IL-23	36.5 (26.1-52.9)	41.3(28.4-55.5)	0.658
IL-33	127.8 (106.6-186.1)	147.06(128.5-213.4)	**0.016**
COX2	0.176 (0-0.374)	0.202(0.051-1.151)	0.469
TNFalpha	34.4(31.4-37.03)	30.7(12.8-35.6)	**0.004**
Dickkopf-1	446.7(356.9-529.3)	881.3(663.1-972.2)	**<0.001**
Sclerostin	312.4 (140.8-412.7)	405.1(276.3-452.5)	**0.018**
Noggin	48.3(17.04-153.9)	31.2(11.3-103.7)	0.264

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4130

POS0941 IN SPONDYLOARTHRITIS PATIENTS THE PRESENCE OF COMORBIDITIES IS AN INDEPENDENT PREDICTOR OF INSUFFICIENT RESPONSE TO THERAPY WITH BIOLOGIC AGENTS AND TREATMENT DISCONTINUATION

I. Flouri[1], N. Kougkas[1], N. Avgustidis[1], A. Repa[1], A. Eskitzis[1], A. Molla Ismail Sali[1], S. Pitsigavdaki[1], K. Pateromichelaki[1], E. Kalogiannaki[1], G. Bertsias[1], P. Sidiropoulos[1]. [1]*University Hospital of Heraklion, Crete, Rheumatology Department, Heraklion, Crete, Greece*

Background: Long-term observational studies of patients under biologic disease-modifying anti-rheumatic drug (bDMARD) therapies in routine clinical practice can provide us with important data regarding patients with comorbidities, who are usually excluded from randomized controlled studies.
Objectives: To study the impact of comorbidities in the outcome (response and persistence to therapy) of patients with spondyloarthritis (SpA) receiving bDMARDs in real-world clinical practice.
Methods: Prospective study of all patients who start a bDMARD in a tertiary centre University Hospital after their consent. All patient comorbidities [among a list of approximately 100 pre-specified major comorbidities] are registered by treating physicians at baseline and during follow-up.
Comorbidities were studied as total Comorbidities Count (CC) and rheumatic disease comorbidity index (RDCI). Statistical analyses were performed using logistic and Cox regression models, adjusting for the potential confounding of age, sex, disease duration, diagnosis (axial vs. peripheral SpA), number of previous conventional synthetic and biologic DMARDs, year of therapy start, and co-administered methotrexate and corticosteroids (yes/no). Analyses of response to therapy also included baseline BASDAI or ASDAS indices as confounding variables.
Results: A total of 603 biologic treatments (1st: 298, 2nd: 157, ≥3rd: 148) were analyzed. Half (51%) of the patients were female, 413 patients had axial SpA (AxSpA) and 190 peripheral SpA (perSpA). At baseline, median (IQR) age: 48 (38-57) years, disease duration: 11 (4-19) years, CC: 2 (1-4) and RDCI: 1 (0-2). Both comorbidity indices were significantly higher in perSpA compared to AxSpA (p<0.001).
At 6 months of therapy, 31% of patients with AxSpA achieved BASDAI50 and 39% had ASDAS-ESR < 2.1. Higher CC was an independent predictor of insufficient response according to BASDAI50 [OR (95%) = 0.70 (0.52-0.94), p=0.019] and higher RDCI was predicting failure to achieve ASDAS-ESR < 2.1 [OR (95%) = 0.59 (0.37-0.94), p=0.027]. Other independent predictors of non-response were age, longer disease duration and (for ASDAS-ESR<2.1) higher baseline disease activity.
During 1405 patient-years of follow-up, 349 (58%) treatments were discontinued. The adjusted hazard ratio for bDMARD discontinuation within the first 2 years of treatment due to insufficient response was doubled in patients with CC ≥2 versus those with CC ≤1 [HR = 2.27 (1.14-4.53), p=0.020] or with RDCI ≥1 (vs. RDCI =

0) [HR = 2.23 (1.22-4.07), p=0.009]. Comorbidities' indices were not significant predictors of treatment discontinuations due to adverse events.
Conclusion: The presence of comorbidities in patients with SpA is an independent predictor for insufficient 6-month response to bDMARDs and resultant treatment discontinuation due to failure.
Acknowledgements: This research is co-financed by Greece and the European Union (European Social Fund- ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning» in the context of the project "Reinforcement of Postdoctoral Researchers - 2nd Cycle" (MIS-5033021), implemented by the State Scholarships Foundation (IKY).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4222

Spondyloarthritis - clinical aspects (other than treatment)

POS0942 **THE NEGATIVE IMPACT OF UNDIAGNOSED DEPRESSION IN AXIAL SPONDYLOARTHROPARTHY: RESULTS OF A SCREENING STUDY**

S. Maguire[1,2], F. B. O'shea[1,2]. [1]*St James' Hospital, Rheumatology, Dublin, Ireland*; [2]*Trinity College Dublin, Medicine, Dublin, Ireland*

Background: Previous research in axial spondyloarthropathy(axSpA) has shown this population to have a high prevalence of depression. This co-morbidity has been previously shown to impact disease activity in patients with rheumatic disease.
Objectives: The purpose of this study was to screen for early signs of depression using two validated tools, the Patient Health Questionaire-9 (PHQ-9) and the Hospital Anxiety and Depression Scale for depression (HADs-D) in patients with known axSpA.
Methods: AxSpA patients attending the Rheumatology department in St James' Hospital between February and October 2020 were invited to take a self-administered survey which included the PHQ-9 and the HADs-D. Scores from the HADs-D yielded a numerical result which was then categorised as normal, borderline or abnormal. PHQ-9 numerical results were categorised as normal, mild, moderate, moderate/severe or severe. Patients with a known diagnosis of depression were excluded. In addition to baseline demographics, patient reported outcomes from the clinic visit were also recorded.
Data analysis was performed using IBM SPSS version 26. Continuous variables were recorded as means, categorical variables as frequencies with percentages. A one-way analysis of variance analysis (ANOVA) was used to determine significance of variation in outcomes between patient outcomes as determined by the HADs-D and PHQ-9. A p-value of <0.05 was deemed significant. Consent was obtained prior to participation. Approval was received from the St James'/Tallaght Hospital Joint Ethics Committee.
Results: In total 71 axSpA patients took part in the survey. The population was 70.4%(50) males and 29.5%(21) female, with an average age 47.9 years and mean disease duration 19.7 years (mean outcomes: BASDAI 4.08, BASFI 3.62, BASMI 3.54, ASQoL 6.79). Overall, 7 (9.9%) participants recorded abnormal HADs-D scores, while 17 (23.9%) recorded moderate to severe PHQ-9 scores indicative of underlying depression. AxSpA females had higher mean HADs-D scores (7.5 vs 4.8, p=0.01) than males, with abnormal scores in 19%(4) of females and 6% (3) of males. No significant differences were found in PHQ-9 scores between genders.
Analysis revealed significantly worse BASDAI (6.27 vs 3.42, p<0.01) and AQoL scores (12.57 vs 5.26, p<0.01) in axSpA patients with abnormal compared to normal HADs-D scores. No significant differences were noted in BASFI, BASMI or baseline demographics. A similar pattern was noted on analysis of PHQ-9 scores, with significantly worse BASDAI (7.9 vs 2.55, p<0.01), BASFI (8.05 vs 2.33, p<0.01) and ASQoL (19.5 vs 2.62, p<0.01) noted in those scoring as severe compared to normal. No significant differences were detected in BASMI scores or baseline demographics.
Conclusion: A high percentage of axSpA patients recorded high HADs-D and PHQ-9 scores concerning for undiagnosed depression. These patients were noted to have significantly worse disease activity and quality of life as compared to patients with normal scores. Clinicians treating axSpA should consider screening for depression in this population.
Disclosure of Interests: Sinead Maguire Speakers bureau: Speaker fee from Jassen, Grant/research support from: Recipient of the Gilead Inflammation Fellowship Grant, Finbar Barry O'Shea: None declared
DOI: 10.1136/annrheumdis-2021-eular.145

POS0943 **GEOGRAPHIC VARIATION OF ANKYLOSING SPONDYLITIS (AS) DIAGNOSIS AND TREATMENT IN THE UNITED STATES: A REAL-WORLD EVIDENCE STUDY**

A. Deodhar[1], D. Kruzikas[2], L. Zhou[2], A. Biljan[2], C. Saffore[2]. [1]*Oregon Health & Science University, Portland, United States of America*; [2]*AbbVie Inc., North Chicago, United States of America*

Background: AS is a chronic inflammatory immune-mediated disease primarily affecting the sacroiliac joints and spine, with a prevalence of 0.2%–0.5% in the United States.[1] Because radiographic features of the disease can take years to develop, diagnosis may be delayed by up to 10 years[2], which can negatively affect patients' function, ability to work, and overall quality of life.
Objectives: To describe geographic variations in AS diagnostic prevalence and treatment in the United States.
Methods: This study utilized the IBM® MarketScan® Administrative Claims Database from 2014–2019. Patients (pts) ≥18 years of age with AS, continuous medical and pharmacy enrollment during the calendar year, and complete geographic information during the study period were included. Pts were identified by having ≥1 claim with ICD-9-CM or ICD-10-CM codes for AS (720.0 or M45.x, respectively). Two AS diagnosis definitions were used; Definition 1 (D1): Pts with ≥1 claim for an AS diagnosis in the year by any provider and Definition 2 (D2): Pts with ≥2 claims for an AS diagnosis within 18 months by rheumatologists. Annual AS diagnostic prevalence rates were calculated for both groups; treatment was evaluated among pts with D2. Diagnosis and treatment rates were assessed from 2014–2019 at the national and state levels and reported for states where >20 pts received an AS diagnosis (D1 or D2) or respective treatment (D2). The effect of age, sex, race (surrogate for HLA-B27), and rheumatologist per capita on geographic variation was assessed.
Results: The number of pts included per year ranged between 10,811–13,077 (D1) and 3,775–4,901 (D2). AS diagnostic prevalence increased over time for both groups, with the annual prevalence rate per 10,000 persons for D2 pts increasing from 2.5 in 2014 to 3.5 in 2019 (Table 1). The AS diagnostic prevalence by D2 in 2019 was highest for Idaho (13) and Colorado (6), and lowest for Michigan (2). The state variations in prevalence did not appear to be explained by age, sex, racial distribution, or rheumatologists per capita. The percentage of D2 pts receiving advanced therapies (all FDA-approved indicated biologic disease-modifying antirheumatic drugs [bDMARDs] for AS) were >70% and increased each year, whereas the use of conventional synthetic DMARDs (csDMARDs) decreased (Figure 1. next page). While opioid use decreased, 37% of D2 pts were prescribed such treatment in 2019. Percentage of D2 pts receiving advanced therapy in 2019 was highest (91) in Minnesota and South Carolina and lowest in Idaho (69) and Indiana (70). In 2019, the percentage of D2 pts using csDMARDs in 2019 was highest in Oklahoma (33) and lowest (16) in North Carolina and New York, while for opioids it was highest in Idaho (69) and lowest in Wisconsin (28).
Conclusion: The prevalence of AS is increasing each year nationally, with significant variability observed across states that is not explained by differences in age, sex, race, or rheumatologists per capita. Among pts with confirmed AS diagnosis (D2), national rates of csDMARDs and opioids are decreasing although opioid use is still high, and high treatment rates exist for advanced therapies. Rates of all treatments also vary substantially across states. Observed variations may indicate the opportunity for further education that can be targeted based on regional need to improve diagnosis and treatment.
REFERENCES:
[1] Reveille JD. *Am J Med Sci*. 2011. 2. Deodhar A, et al. *Arthritis Rheumatol*. 2016.

Table 1. AS diagnostic prevalence by calendar year, 2014–2019

		Patients with ≥1 AS diagnosis (D1)		Patients with ≥2 AS diagnoses by rheumatologists (D2)	
Year	Number of annual enrollees	Number of patients with AS	Prevalence rate/10,000	Number of patients with AS	Prevalence rate/10,000
2014	19,470,780	13,077	6.7	4,901	2.5
2015	15,159,118	11,863	7.8	4,278	2.8
2016	14,836,594	12,801	8.6	4,473	3.0
2017	12,618,301	10,811	8.6	3,775	3.0
2018	13,460,224	12,259	9.1	4,302	3.2
2019	12,105,049	11,646	9.6	4,294	3.5

Acknowledgements: Medical writing services provided by Alan Saltzman of Fishawack Facilitate Ltd, part of Fishawack Health, and funded by AbbVie.
The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract. No honoraria or payments were made for authorship.
Disclosure of Interests: Atul Deodhar Speakers bureau: Novartis, Pfizer, Consultant of: Novartis, Pfizer, AbbVie, Eli Lilly, UCB Pharma, GlaxoSmith-Kline, Galapagos, Janssen, Boehringer Ingelheim, Celgene, Amgen, Grant/ research support from: Novartis, Pfizer, AbbVie, Eli Lilly, UCB Pharma, GlaxoSmithKline, Denise Kruzikas Shareholder of: AbbVie, Employee of: AbbVie, Lili Zhou Employee of: AbbVie, Ana Biljan Shareholder of: AbbVie, Employee of: AbbVie, Christopher Saffore Shareholder of: AbbVie, Employee of: AbbVie

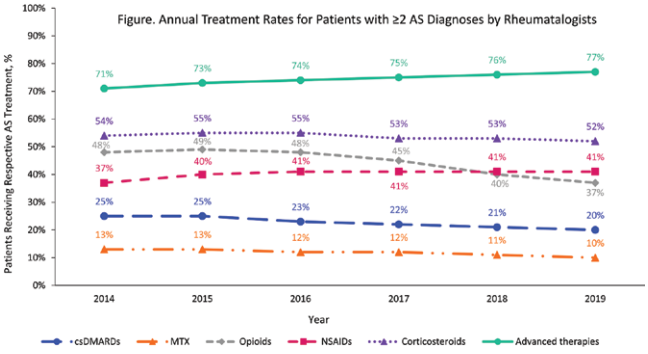


Figure 1.

DOI: 10.1136/annrheumdis-2021-eular.202

POS0944 AGE AT ONSET IN AXIAL SPONDYLOARTHRITIS AROUND THE WORLD: DATA FROM THE INTERNATIONAL ASAS-PERSPA STUDY

A. Boel[1], C. López-Medina[2], D. Van der Heijde[1], F. A. Van Gaalen[1]. [1]*Leiden University Medical Centre, Rheumatology, Leiden, Netherlands*; [2]*Cochin Hospital, Assistance Publique Hôpitaux de Paris, Rheumatology, Paris, France*

Background: Axial spondyloarthritis (axSpA) typically begins in young adulthood and age at onset is therefore very useful in identifying chronic back patients at an increased risk of axSpA. Age at onset below the age of 45 has been incorporated into the 2009 ASAS classification criteria for axSpA as a mandatory feature. However, inclusion of age at onset before the age of 45 was based on a small number of Western European studies and it is therefore unknown if this age at onset applies to patients in other parts of the world.
Objectives: The aim of this study was to assess age at onset of axSpA as well as its relationship with HLA-B27 throughout the world, using data from the Assessment in SpondyloArthritis international Society (ASAS) peripheral involvement in Spondyloarthritis (ASAS-perSpA) study.
Methods: Analyses were restricted to patients with an axSpA diagnosis who had information available on age at onset of axial complaints. Cumulative probability plots were used to graphically display the cumulative distribution of age at onset of axial symptoms. Linear regression models were built to assess the effect of HLA-B27 status on age at onset of axial symptoms. As axSpA is a multifactorial, multigenetic disease, geographical region was investigated as an effect modifier.
Results: The majority (92%) of patients with axSpA had an age at onset of axial symptoms below 45 years, with only small variation across the various geographical regions (table 1). Cumulative distribution plots showed age at onset of axial symptoms was consistently lower in HLA-B27 positive patients (in blue) than in HLA-B27 negative patients (in red) across all geographical regions (Figure 1 below). Linear regression models showed a significant effect of HLA-B27 status on the age at onset of axial symptoms in the total study population (p<0.001), and Latin American (p<0.001), European & North American (p<0.001), Asian (p=0.006) and Middle Eastern & North African (p=0.005) populations. There was no effect modification of geographical region (p=0.50) on the association between HLA-B27 status and age at onset of axial symptoms.

Conclusion: Irrespective of geographical region, the majority of axSpA patients had an age at onset of axial disease before the age of 45. In all populations, HLA-B27 was associated with earlier disease onset. These results provide crucial data for diagnosis, classification, and policies aimed at improving recognition of axSpA.

Table 1. Percentage of axSpA patients with an age at onset of axial symptoms <40, <45 and <50 years stratified by geographical region and HLA-B27 status.

	HLA-B27 positive				HLA-B27 negative			
	N	Age at onset <40	Age at onset <45	Age at onset <50	*N*	Age at onset <40	Age at onset <45	Age at onset <50
Asia	*469*	91%	94%	97%	*56*	79%	88%	95%
Europe & North America	*678*	88%	94%	98%	*184*	74%	85%	93%
Latin America	*157*	81%	94%	96%	*38*	45%	76%	84%
Middle East & North Africa	*320*	88%	94%	98%	*161*	84%	88%	94%
Total	*1624*	88%	94%	97%	*439*	76%	86%	93%

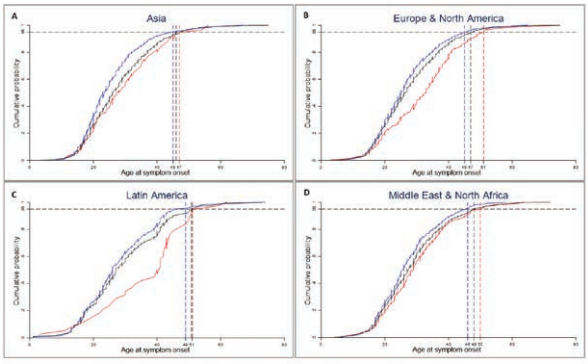


Figure Cumulative distribution of the age at onset of axial symptoms for Asia (A), Europe & North America (B), Latin America (C), and Middle East & North Africa (D). The black lines represent all patients in a given continent, the blue lines represent HLA-B27 positive patients, and the red lines represent the HLA-B27 negative patients. The horizontal black dashed line represents the 95% point, and the black, blue and red vertical lines represent the age at which 95% of patients developed axial complaints in the total population, HLA-B27 positive and HLA-B27 negative patients respectively.

Figure 1.

Acknowledgements: We would like to thank all ASAS-perSpA investigators and members of the scientific committee
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.218

POS0945 NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN THE AFRO-CARIBBEAN POPULATION, CLINICAL ASPECTS AND PARTICULARITIES

F. Louis-Sidney[1], D. Morillon[2], M. Blettery[1], L. Brunier[1], P. Numeric[3], M. De Bandt[2]. [1]*Hopital La Maynard Martinique, Rheumatology, Fort-de-France, Martinique*; [2]*Hopital La Maynard Martinique, Radiology, Fort-de-France, Martinique*; [3]*Hopital La Maynard Martinique, Rheumatology, Fort-de-France, Martinique*

Background: Spondyloarthritis is a polymorphic disease and the absence of diagnostic marker has led to propose diagnostic criteria for recognition. All the criteria, established in Caucasian populations, place at the center of the approach sacroiliac imaging and genetic terrain (HLA B27). For this reason, these criteria are not appropriate in populations lacking HLA B27. SPA is known to be rare in African populations and this rarity correlates with that of HLA B27.Prevalence of B27 in French West Indies is 2% (identical to the African populations).
Objectives: We report clinical manifestations of SpA seen at the Fort de France University Hospital, with an emphasis on the so-called "non-radiographic SpA" (NRSPA).
Methods: Adult patients with spondyloarthritis seen over a period of three consecutive months, were invited to participate in a survey and filled-in a self-administered questionnaire. The consulting rheumatologist specified the rheumatologic and extra-articular involvement, BASDAI score, HLAB27 data, markers of inflammation and imaging.

Results: There were 93 patients, 47 with radiographic sacroilitis (RSPA) and 46 patients without but all - these 46 - had magnetic sacroilitis. This population is Afro-Caribbean for 98%. Mean age at onset of clinical signs is 38.5 ± 15.0 years and median age is 37.0 (13-77). An evocative family history is noted in 37%. All these 93 patients suffer from rachialgia.

But the axial complaint is often secondary to the peripheral involvement. 3 patients have a mechanical spinal complaint. All the others have intermittent inflammatory complaint evolving by flares affecting all the spinal stages. 15/93 patients have isolated axial complain without peripheral disease. Enthesopathies are seen in 70%.

Peripheral inflammatory joint complain is observed in 78 patients (84%), it is a bilateral and symmetrical chronic polyarticular pattern affecting (70/78) the small joints of the hands, forefeet and wrists. Ankle bi-arthritis is almost systematic and is observed in 71/78 patients; 8 patients with RSPA had no polyarthritis but oligo (6) or monoarthritis (2). Peripheral inflammatory joint is more frequent in NRSPA than in RSPA (98% vs 70%). Ultrasound individualises grade II synovitis (78/78), rarely with a Doppler effect (5/78). On average, more painful and swollen joints are observed in NRSPA than in RSPA. Extra articular and immunological aspects and activity scores are in table 1.

Good sensitivity of peripheral arthritis to NSAIDs and MTX is noted in 94 and 91%.

Conclusion: NRSpA are not uncommon in the Afro-Caribbean population, but are distinct from Caucasian SpA by several points: female predominance, rarity of B27 and syndesmophytes, frequency of polyalgic pattern, frequency of peripheral arthritis, rarity of extra-articular manifestations, more frequent but less marked inflammation, good response of arthritis to NSAIDs and MTX. Appropriate classification criteria for Afro-descendant populations is an urgent unmet need.

REFERENCES:

[1] (López-Medina C, et al. RMD Open 2019;5:e001108).

Table 1. Extra articular manifestations, activity scores and immunological aspects of the patients.

Item	Results (%) NRSPA n=46	Results (%) RSPA n=47
Dactylitis	11 (23 %)	13 (27 %)
Uvéïtis	5 (11 %) (p 0.02)	15 (32%)
Psoriasis	1 (2 %)	1 (2 %)
IBD	4 (9 %) (p 0.02)	10 (21 %)
Balanitis	0	0
Non gonococcal urethritis	0	0
Non gonococcal cervicitis	0	0
High CRP (at least 2 measure)	21 (45%) (p 0.03)	30 (63%)
Mean CRP mg/l	6 ± 4	17 ± 7
BASDAI	4.1 ± 0.2	4 ± 0.2
EVA pain	4.5 ± 0.4	4,5 ± 0.2
HAQ	0.6 ± 0.3	0,5 ± 0.2
EVA Global	4.9 ± 0.8	4,8 + 0.8
EVA Spine	5 ± 0.5	4,1 + 0.9
FIRST score >5	5 /46 patients (10.9%)	6 / 47 patients (12.5%)
HLA B27 presence	4/46 (8.7%) (p 0.01)	14/47 (29.8%)
Sexe	male 10 (21.3%) (p 0.001)	male 19 (51.3%)
ACPA	0	0
Latex Waaler-Rose	1 (low titer, > 65 years)	1 (low titer, > 65 years)
ANA	2 (low titer, < 1/320°)	3 (low titer, < 1/320°)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.260

POS0946 DISTRIBUTION OF COMORBIDITIES IN SPONDYLOARTHRITIS WITH REGARD TO THE PHENOTYPE AND THE PRESENCE OF PSORIASIS: DATA FROM THE ASAS-COMOSPA STUDY

M. Á. Puche Larrubia[1], M. L. Ladehesa Pineda[1], F. U. Pilar[2], A. Moltó[3], C. López-Medina[1,3], E. Collantes-Estevez[1]. [1]*Reina Sofía University Hospital, Rheumatology, Córdoba, Spain*; [2]*University of Cordoba, Rheumatology, Córdoba, Spain*; [3]*Cochin Hospital, Rheumatology, Paris, France*

Background: Comorbidities have been reported to be more prevalent in patients with Spondyloarthritis (SpA) compared to the general population. Previous studies have suggested that patients with peripheral phenotypes exhibit a higher prevalence of traditional cardiovascular risk (CV) factors compared to those with a predominantly axial phenotype. However, the role of psoriasis in such differences has not been deeply studied.

Objectives: To compare the prevalence of comorbidities (CV, malignancies and osteoporosis (vertebral or peripheral fracture, or low bone mineral density)) between patients with axial and peripheral phenotypes and to evaluate the role of psoriasis in such comorbidities in the whole spectrum of SpA (including psoriatic arthritis).

Methods: Patients from the cross-sectional ASAS-COMOSPA study were classified as having either axial (presence of sacroiliitis on x-ray or MRI) or peripheral phenotype (absence of sacroiliitis AND presence of arthritis, enthesitis or dactylitis). Patients with each phenotype were divided into two groups depending on the presence or history of psoriasis. Pair-wise comparisons among the four groups (axial and peripheral with psoriasis/without psoriasis phenotypes) were conducted through univariate logistic regressions and generalized linear mixed models using disease duration and country as fixed and random effects, respectively. Multivariate analysis using were used to evaluate whether psoriasis and the phenotype are independently associated with each comorbidity.

Results: A total of 3291 patients were included in this analysis (mean age 43.6 years, 65% males). The peripheral phenotype with psoriasis showed the highest prevalence of hypertension (44.9%), dyslipidaemia (34%) and diabetes (8.8%), while axial phenotype without psoriasis exhibited the lowest prevalence of dyslipidaemia (14.2%), diabetes (4.1%) and stroke (0.9%) (Table 1). Among patients with psoriasis, the axial phenotype showed a significantly [OR, 95%CI] lower prevalence of hypertension [OR 0.5, 0.4-0.8] and lower Framingham score [OR 0.97, 0.95-0.99] compared to peripheral patients even after adjusting for disease duration and country. Among patients with axial phenotype, patients with psoriasis showed higher prevalence of hypertension [OR 1.8, 1.4-2.2], dyslipidaemia [OR 2.0, 1.7-2.5], diabetes [OR 2.1, 1.4-3.0] and Framingham score [OR 1.0, 1.0-1.1] than non-psoriatic patients. Multivariate analysis confirmed that hypertension, dyslipidaemia and the Framingham score are independently associated with both the psoriasis and the peripheral phenotype.

Prostatic cancer and colon cancer were independently associated with the presence of psoriasis but not with the phenotype. No differences were found across groups concerning osteoporosis.

Conclusion: Both a peripheral phenotype and the presence of psoriasis were independently associated with an increased CV risk. Psoriasis seems to be associated with a higher prevalence of some malignant diseases, while osteoporosis do not seem to be associated with either phenotype or the presence of cutaneous involvement.

Table 1. Description of comorbidities across the four groups.

	Psoriatic axial N = 460 n (%)	Non-psoriatic axial N = 2541 n (%)	Psoriatic peripheral N = 147 n (%)	Non-psoriatic peripheral N = 136 n (%)	p-value*
BMI, mean (SD)	27.4 (5.5)	25.5 (5.5)	27.3 (5.7)	26.6 (5.3)	**<0.001**
Hypertension	135 (29.5)	487 (19.2)	66 (44.9)	25 (18.4)	**<0.001**
Dyslipidemia	113 (24.8)	359 (14.2)	50 (34)	23 (17)	**<0.001**
Diabetes	37 (8.1)	104 (4.1)	13 (8.8)	7 (5.2)	**<0.001**
Ischemic heart disease	16 (3.5)	51 (2)	5 (3.4)	2 (1.5)	0.162
Stroke	11 (2.4)	22 (0.9)	3 (2)	2 (1.5)	**0.028**
Framingham score, mean (SD)	9.6 (8.7)	6.6 (7.5)	11.8 (8.8)	5.8 (6)	**<0.001**
Prostatic cancer	5 (1.8)	5 (0.3)	0 (0)	0 (0)	**0.006**
Breast cancer	(1.7)	3 (0.4)	1 (1.4)	0 (0)	0.181
Colon cancer	4 (0.9)	4 (0.2)	1 (0.7)	1 (0.7)	**0.046**
Basal cell carcinoma	6 (1.3)	9 (0.4)	1 (0.7)	4 (3)	**<0.001**
Lymphoma	0 (0)	4 (0.2)	3 (2)	0 (0)	**<0.001**

*ANOVA or chi-square for continuous and qualitative variables, respectively.

Acknowledgements: This study was conducted under the umbrella of the International Society for Spondyloarthritis Assessment (ASAS).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.306

POS0947 PSORIATIC ARTHRITIS WITH HYPERURICEMIA: MORE PERIPHERAL, DESTRUCTIVE AND CHALLENGING TO TREAT

L. Widawski[1], T. Fabacher[2], J. E. Gottenberg[3], L. Spielmann[1], P. M. Duret[1], J. Sibilia[3], L. Messer[1], R. Felten[3]. [1]*Hôpitaux Civils de Colmar, Rheumatology, Colmar, France*; [2]*Nouvel Hôpital Civil - Hôpitaux Universitaires de Strasbourg, Epidemiology and Public Health, Strasbourg,*

France; [3]*Hôpital de Hautepierre - Hôpitaux Universitaires de Strasbourg, Rheumatology, Strasbourg, France*

Background: Gout and psoriatic arthritis (PsA) can co-exist in the same patient. These 2 diseases seem strongly linked, but the pathophysiological mechanisms of this link have not yet been defined. Hyperuricemia could be an important determinant of PsA[1].
Objectives: To study the impact of hyperuricemia on clinical presentation, severity and associated comorbidities of PsA.
Methods: We conducted a retrospective bicenter case–control study in Strasbourg and Colmar, France. Patients with PsA (according to "L40.5 arthropathic psoriasis" ICD-10 coding) and at least one available serum urate level measurement, were included from 2009 to 2019. Demographic, comorbidities, clinical and radiographic data were collected. Hyperuricemia was defined as serum urate level ≥ 360 µmol/L. We defined "good responders to ongoing PsA treatment" as patients with no outbreak of PsA, biological inflammatory syndrome and therapeutic modification at the last follow-up. Patients with "destructive" disease had one or more erosion(s) seen on standard X-ray, ultrasonography, MRI or TDM.
Results: We included 242 patients. 73 (30.2%) had hyperuricemia and 15 (6.2%) met criteria for gout. On univariate analysis, as compared with normo-uricemic patients, hyperuricemic patients were more often male (72.6% vs. 39.1%, p = $1.6x10^{-06}$), had higher BMI (30.9 vs. 28.7 kg/m^2, p = 0.015) and had more comorbidities (Charlson Comorbidity Index: 2.6 vs. 1.8, p = 0.005). In hyperuricemic versus normo-uricemic patients, PsA started at an older age (47.5 vs 43 years, p = 0.016); PsA was more polyarticular (56.2% vs 41.9%, p = 0.049) than axial (9.6% vs 22.8%, p = 0.019) and more destructive (52.8% vs. 37.4%, p = 0.032). Median uricemia was higher in patients with destructive than non-destructive PsA (321 vs 288.8 µmol/l, p = 0.0038), and hyperuricemia was more frequent with than without joint destruction (37.6% vs 25.8%, p = 0.047). The multivariate analysis confirmed hyperuricemia associated with peripheral joint involvement (OR 2.98, p = 0.025) and less good response to PsA treatment (OR 0.35, p = 0.024).

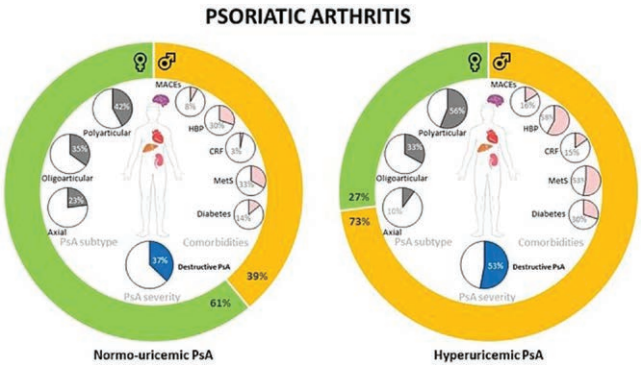


Figure 1. Description of normo- and hyperuricemic psoriatic arthritis

CRF: moderate to severe chronic renal failure. MACEs: major adverse cardiovascular events. HBP: high blood pressure. MetS: metabolic syndrome. PsA: psoriatic arthritis
Conclusion: Patients with hyperuricemic PsA have less good response to PsA treatment than those with normo-uricemia and more peripheral and destructive joint damage. Recognition of PsA in which hyperuricemia would play an aggravating role could modify the management. This would justify a diagnostic reassessment in case of doubt, the possible introduction of hypouricemic treatment and the careful use of NSAIDs in the context of multiple morbidities.
REFERENCES:
[1] Felten R, Duret P-M, Gottenberg J-E, Spielmann L, Messer L. At the crossroads of gout and psoriatic arthritis: « psout ». Clin Rheumatol. Febr 2020.
Acknowledgements: We thank all participating patients. We also thank the medical secretaries for their help with the ICD-10 extraction, and Dr Thomas Lavaux for helping with serum urate tests at Strasbourg University Hospital.
Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.308

POS0948

HYPERKYPHOSIS IN AXIAL SPONDYLOARTHRITIS: FACTORS THAT PRODUCE ITS APPEARANCE AND EFFECT ON MOBILITY AND FUNCTION

J. L. Garrido-Castro[1], M. L. Ladehesa Pineda[2], C. López-Medina[2], C. Garrido-González[3], F. U. Pilar[3], C. Gonzalez-Navas[1], E. Collantes Estevez[2]On behalf of CASTRO. [1]*Instituto Maimónides de Investigación Biomédica de Córdoba, Motion Analysis Lab, Córdoba, Spain*; [2]*Hospital Universitario Reina Sofia, Rheumatology, Córdoba, Spain*; [3]*Facultad de Medicina y Enfermería, Departamento Medicina, Córdoba, Spain*

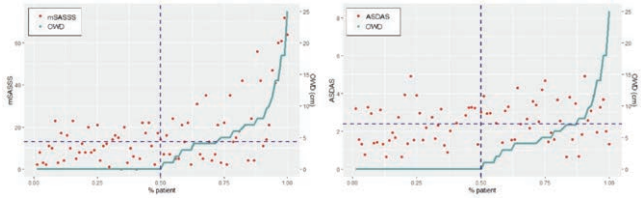
Background: Hyperkyphosis (HK) is a characteristic sign in patients with a large level of axial spondyloarthritis (axSpA) involvement. Kyphosis is defined as a sagittal deviation in the spinal alignment. Kyphosis can be graded in severity by the Cobb angle. The occiput-wall distance (OWD) is a surrogate measure of kyphosis. When this distance is greater than 0 cm, it is because the patient has an advanced affectation level that produces a reduction of physical function and other comorbidities. It is important that HK does not appear in the patient.
Objectives: To analyze contributors and effects of HK in patients with axSpA.
Methods: Nonparametric preprocessing for parametric causal inference was used for selection of two matched groups, formed by 42 axSpA patients each one, from the CASTRO cohort with similar covariate distributions (age and sex). Outcomes analyzed, besides OWD, included activity (BASDAI, ASDAS), physical function (BASFI) and mobility (BASMI). An inertial sensor-based system (ViMove) was used to analyze cervical and lumbar mobility and to calculate the UCOASMI index[1]. Structural damage was assesed according the mSASSS and its components (cervical and lumbar).
Results: Mean (sd) values of the different variables for each group are shown in table 1. Significant differences according to an independent t-test (p), variation coefficient (V.C.), effect size (E.S.) and correlation with OWD (Pearson r), are also included in this table.

	OWD=0 (n=42)	OWD>0 (n=42)	P	V.C.	E.S.	r
Age (y)	47.6 (8.9)	48.7 (8.7)	N.S.	2%	0.13	0.2
Sex (female %)	12%	14%	N.S.	-	-	-
B27 (positive %)	87%	86%	N.S.	-	-	-
Disease duration (y)	19.7 (11.4)	24.9 (13.4)	*	26%	0.42	0.30**
Diagnostic delay (y)	6.4 (9.6)	6.6 (8.4)	N.S.	2%	0.01	-0.09
BMI (kg/m^2)	25.8 (3.1)	29.5 (4.6)	***	14%	0.94¥	0.39***
ASDAS	2.2 (1.0)	2.7 (1.0)	*	21%	0.43	0.08
BASDAI	3.6 (2.4)	4.1 (2.5)	N.S.	6%	0.17	-0.02
mSASSS	10.6 (6.9)	22.6 (19.2)	***	113%	0.92¥	0.75***
Cervical mSASSS	5.4 (4.4)	11.2 (11.2)	**	106%	0.74	0.69***
Lumbar mSASSS	5.1 (3.6)	11.3 (10.0)	***	121%	0.91¥	0.67***
BASFI	2.6 (2.51)	4.6 (2.8)	***	74%	0.74	0.26*
BASMI	2.4 (1.1)	4.2 (1.5)	***	77%	1.40	0.77***
UCOASMI	3.7 (1.0)	5.6 (1.4)	***	51%	1.53	0.77***
Cervical flexion (º)	101 (20)	74 (29)	***	-26%	-1.07	-0.71***
Cervical rotation(º)	133 (20)	103 (37)	***	-23%	-1.04	-0.68***
Cervical lat. flex.(º)	67 (21)	44 (24)	***	-33%	-0.96¥	-0.64***

Sign.: *p<0.05, **p<0.01, *** p<0.001. ¥: Large effect size (ES>0.8)

There were not significant differences in age, sex as expected. HK group patients started earlier (5.2 years). The percentage of HLAB27+ is similar, so this antigen has not a relationship with HK. BMI is greater in HK group (14%); this can be a factor for HK appearance or a consequence of HK (less physical activity). Activity (according ASDAS) was slightly higher in HK. There were very significant differences in structural damage, and HK appears to be equally affected by damage at cervical and lumbar regions. BASFI also shown a significant reduction in HK. There was great reduction of mobility according to mobility indexes and cervical range of movement (23%-33%). In a multivariate regression analysis using all variables of the table and OWD as dependent variable, only mSASSS and BMI were included in the final model (adj. r^2= 0.61). In a ROC analysis, mSASSS shown to and acceptable variable to distinguish between groups (AUC=0.70, cutoff=13). ASDAS

obtained lower results (AUC=0.60, cutoff=2.38). Figure 1 shows cumulative probability plots of mSASSS and ASDAS versus OWD, showing cutoff values determined by ROC analysis.



Conclusion: Structural damage, in cervical and lumbar spine, are the main contributor to HK appearance in axSpA patients. Inflammation it is not so determinant and acts only in the short term. HK produces a significant reduction of cervical mobility and physical function. New treatments that decrease radiographical progression, and overweight reduction are the most important factor to avoid HK.

REFERENCES:

[1] Measuring Spinal Mobility Using an Inertial Measurement Unit System: A Validation Study in Axial Spondyloarthritis. Diagnostics 2020, 10(6), 426.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.346

POS0949 HIGH PREVALENCE OF ABDOMINAL OBESITY IN FEMALES WITH AXIAL SPONDYLOARTHROPATHY

S. Maguire[1,2], P. Gallagher[3], F. Wilson[4], F. B. O'shea[1,2]. [1]*St James' Hospital, Rheumatology, Dublin, Ireland*; [2]*Trinity College Dublin, School of Medicine, Dublin, Ireland*; [3]*St Vincent's Hospital, Rheumatology, Dublin, Ireland*; [4]*Trinity College Dublin, Discipline of Physiotherapy, Dublin, Ireland*

Background: Worldwide prevalence of obesity has been steadily increasing, despite significant public health campaigns to raise health awareness. In axial spondyloarthropathy (axSpA) obesity has been shown to be associated with higher levels of disease activity and decreased response to treatment. The waist to hip ratio (WtHpR) is a tool to screen for abdominal obesity. Abdominal deposition of adipose tissue is associated with increased risk of cardiovascular disease, type II diabetes and premature death. Abdominal obesity is more commonly found in males, while females are more prone to gluteal-femoral fat deposition. The Ankylosing Spondylitis Registry of Ireland (ASRI) is a source of epidemiological data of axSpA patients in Ireland.

Objectives: To capture the prevalence of abdominal obesity in a large cohort of axSpA patients and assess for variation in prevalence between sexes.

Methods: Participants were analysed on the basis of sex and presence of obesity by BMI and WtHpR. Obesity was defined by body mass index (BMI) with a result of >30 categorised as obese as per CDC definitions. Abdominal obesity was assessed by WtHpR and defined as per WHO guidelines. Categorical variables were recorded as frequencies, with a chi^2 test for independence used to test for statistical significance. Numerical variables were recorded as means within each group and an independent t-test or Mann Whitney U test was used to test for statistical significance between groups. A p-value of <0.05 was deemed significant. IBM SPSS version 26 was used for statistical analysis of the patient population captured within the ASRI.

Results: At the time of analysis, physical measurements were available on 692 patients in the ASRI made up of 96.2% (666) Caucasians with 22.3% (154) females and 77.7% (538) males. The average age was 45.9 years with a mean disease duration of 18.8 years (mean scores: BASDAI 4.09, BASFI 3.71, BASMI 3.99, HAQ 0.54, ASQoL 6.72). 80.9% (560) of patients had radiographic sacroiliitis while 49.1% (340) had sacroiliitis on MRI.

Overall 29.5% (215) patients were obese based on BMI results, while 37.5% (274) were centrally obese as per the WtHpR. Analysis on the basis of sex revealed no significant variation in mean BMI (28.1 vs 27.7, p=0.45) or prevalence of obesity as assessed by BMI (29.9% vs 28.6%, p=0.49) between males and females(table 1). As expected analysis of WtHpR revealed higher mean ratios in males compared to females (0.96 vs 0.89, p<0.01), however there was a significantly higher prevalence of abdominal obesity in females (29.9% vs 68.2%, p<0.01).

Conclusion: There is a high prevalence of abdominal obesity as assessed by WtHpR in axSpA, this is especially high in females with axSpA. Use of WtHpR should be considered when screening for obesity in this population.

Disclosure of Interests: Sinead Maguire Grant/research support from: Recipient of the Gilead Inflammation fellowship grant, Phil Gallagher: None declared, Fiona Wilson: None declared, Finbar Barry O'Shea: None declared

Table 1. Assessment of Obesity by Sex

	Males	Females	p value
n	77.7% (538)	22.3% (154)	
Weight (kg)	84.98	72.76	*<0.01*
BMI	28.08	27.69	*0.45*
Underweight	0.9% (5)	0.06% (1)	*0.49*
Normal Weight	29.2% (157)	36.4% (56)	
Overweight	39.2% (211)	34.4% (53)	
Obese	29.9% (161)	28.6% (44)	
Waist Circumference (cm)	97.43	90.03	*<0.01*
Hip Circumference (cm)	102.11	101.27	*0.56*
Waist to Hip Ratio	0.956	0.8901	*<0.01*
Normal Weight	23.8% (128)	17.5% (27)	*<0.01*
Overweight	46.3% (249)	14.3% (22)	
Obese	29.9% (161)	68.2% (105)	

DOI: 10.1136/annrheumdis-2021-eular.350

POS0950 ARE THERE GENDER DIFFERENCES IN AXIAL SPONDYLOARTHRITIS: DATA FROM A PORTUGUESE SPONDYLOARTHRITIS COHORT

A. R. Cunha[1], R. Aguiar[1], M. J. Santos[2], V. Afreixo[3], A. Barcelos[1,4,5]. [1]*Centro Hospitalar do Baixo Vouga, Rheumatology, Aveiro, Portugal*; [2]*Hospital Garcia de Orta, Rheumatology, Almada, Portugal*; [3]*University of Aveiro, Department of Mathematics and CIDMA - Center for Research & Development in Mathematics and Applications, Aveiro, Portugal*; [4] *University NOVA, Lisbon, NOVA National School of Public Health, Public Health Research Centre, Lisbon, Portugal*; [5] *University NOVA, Lisbon, Comprehensive Health Research Center (CHRC), Lisbon, Portugal*

Background: Historically, axial spondyloarthritis (particularly ankylosing spondylitis) was considered a men's disease and has been under-recognized in women.

Emerging evidence reveals gender differences in patophysiology, disease presentation and therapeutic efficacy.

Objectives: To determine if there are differences between genders in a Portuguese cohort of patients with axSpA as regards clinical manifestations, disease activity, functional capacity, patient related outcomes and radiographic findings.

Methods: Patients with ≥18 years fulfilling the *ASAS- Assessment of Spondyloarthritis International Society classification criteria* for axSpA and registered in the electronic national database- *Reuma.pt* were included in a multicentric cross-sectional study. Sociodemographic data, clinical features and radiographic findings were collected from the first record in Reuma.pt. These variables were compared between genders using Mann-Whitney test and Chi-Square test. Variables with a significant association with group variable (gender) were considered in the multiple variable analysis to adjust the gender effect on the outcome variables.

Results: A total of 1995 patients were included, 1114 (55.9%) men and 881 (44.1%) women. Men had a lower median age at onset of disease (25.1 vs 28.4, p=0.000) and median age at diagnosis (26.9 vs 30.4, p=0.000) and were more frequently smokers (32.1% vs 15.7%, p=0.000). Comparing to women, men had worse BASMI scores (4.0 vs 3.4, p=0.000), higher levels of CPR (10.5 vs 6.9, p=0.000) and were more often HLA-B27 positive (67.8% vs 54%, p=0.000). In univariable analysis, sacroiliitis on radiograph or/and MRI (95.5% vs 91.7%, p=0.04) was more common in men, however that wasn't confirmed in multivariable analysis.

In contrast, women more frequently had more inflammatory bowel disease (8.8% vs 4.9%, p=0,004), higher levels of ESR (25.0 vs 21.0, p=0.003) and worse PROs- BASDAI (5.7 vs 4.5, p=0.000), PGA (60.0 vs 55.0, p=0.000) and fatigue (6.2 vs 5.4, p=0,000).

Conclusion: Physicians must be aware of differences between genders in axial spondyloarthritis because this can result in less underdiagnosis and misdiagnosis, allow optimization of treatment strategies, and decrease overall disease burden in women with axSpA patients.

REFERENCES:

[1] Rusman T, van Vollenhoven RF, van der Horst-Bruinsma IE. Gender Differences in Axial Spondyloarthritis: Women Are Not So Lucky. Curr Rheumatol Rep. 2018;20(6):35.

[2] Tournadre A, Pereira B, Lhoste A, Dubost JJ, Ristori JM, Claudepierre P, et al. Differences between women and men with recent-onset axial spondyloarthritis: results from a prospective multicenter French cohort. Arthritis Care Res (Hoboken). 2013;65(9):1482-9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.497

	BASDAI		BASMI		PGA		Fatigue		Sacroiliitis on radiograph or/and MRI	
	β	p	β	p	β	p	β	p	OR	p
Male gender	-0.963881	**1.25×10^{-8}**	0.647295	**0.000856**	-5.76893	**0.00568**	-1.319037	**1.09×10^{-10}**	1.8793034	0.074607
Age at diagnosis	-0.003272	0.62910	0.025231	**0.001720**	-0.05975	0.47469	0.006319	0.4384	0.9995867	0.977807
HLA-B27	-0.503885	**0.00182**	-0.247478	0.164533	-7.96053	**6.89×10^{-5}**	-0.359688	0.0640	0.8436131	0.627840
CRP	0.004264	0.16449	0.004137	0.213673	0.02060	0.58906	-0.002740	0.4566	1.0014834	0.837317
Smoker	0.062283	0.73877	0.865084	**0.000104**	4.09464	0.08010	0.252386	0.2612	1.4020156	0.424626
Ex-smoker	0.171008	0.41963	0.627238	**0.009923**	3.94157	0.13256	0.304220	0.2324	2.4690088	0.150762
IBD	-0.699610	**0.01762**	-0.334230	0.288871	-1.95205	0.59487	-0.804620	**0.0242**	0.9475121	0.932460
ESR	0.024332	**1.22×10^{-14}**	0.011760	**0.000525**	0.31131	**1.08×10^{-15}**	0.024713	**5.52×10^{-11}**	1.0060363	0.400118

Table 1: Multiple variable analysis to adjust the gender effect on the outcome variables.

OR: Odds ratio; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrological Index; **PGA: Patient Global Assessment; HLA-B27:** Human Leukocyte Antigen-B27; **CPR: C-reactive protein; ESR: erythrocyte sedimentation rate; IBD: inflammatory bowel disease; MRI: magnetic resonance imaging**

POS0951

ASSOCIATION BETWEEN INDIVIDUAL AND COUNTRY-LEVEL SOCIOECONOMIC FACTORS AND HEALTH OUTCOMES IN AXIAL AND PERIPHERAL SPONDYLOARTHRITIS: ANALYSIS OF THE ASAS PERSPA STUDY

D. Capelusnik[1], S. S. Zhao[2], A. Boonen[3,4], N. Ziade[5,6], C. López-Medina[7,8], M. Dougados[7], E. Nikiphorou[9,10], S. Ramiro[11,12]. *[1]Instituto de Rehabilitación Psicofísica, Rheumatology, CABA, Argentina*; *[2]University of Liverpool, Musculoskeletal Biology, Institute of Life Course and Medical Sciences, Liverpool, United Kingdom*; *[3]Maastricht University Medical Center, Rheumatology, Maastricht, Netherlands*; *[4]Maastricht University, Care and Public Health Research Institute (CAPHRI), Maastricht, Netherlands*; *[5]Saint Joseph University, Rheumatology, Beirut, Lebanon*; *[6]Hotel-Dieu De France, Rheumatology, Beirut, Lebanon*; *[7]Cochin Hospital, Rheumatology, Paris, France*; *[8]Reina Sofia Hospital, Rheumatology, Córdoba, Spain*; *[9]King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; *[10]King's College Hospital, Rheumatology, London, United Kingdom*; *[11]Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; *[12]Zuyderland Medical Center, Rheumatology, Heerlen, Netherlands*

Background: Health outcomes in spondyloarthritis (SpA) are largely determined by socioeconomic (SE) factors, leading to the great inequity observed between countries across the world. However, the impact of these SE factors on health outcomes across the different SpA phenotypes (axSpA, pSpA and PsA), is less well known.

Objectives: To investigate (1) the association between individual and country-level SE factors and health outcomes in different SpA phenotypes, and (2) to explore whether any effect of these SE factors is mediated by the use of b/tsDMARD therapy.

Methods: Patients with axSpA, pSpA or PsA from the multinational cohort ASAS-perSpA were included in the analysis. The effect of individual (age, gender, education and marital status) and country-level SE factors (Gross Domestic Product [GDP], Healthcare Expenditure [HCE], Human Development Index [HDI], Gini Index) over health outcomes (ASDAS≥2.1, continuous ASDAS, BASFI, fatigue and ASAS-HI) were assessed in multivariable mixed-effects logistic and linear regression models (as appropriate), adjusting for confounders. Interactions between each individual and country-level SE factors and disease phenotype and between both levels of SE factors, were tested. Finally, a mediation analysis was conducted to explore whether the impact of country-level SE factors on ASDAS is mediated through b/tsDMARD uptake.

Results: A total of 4185 patients from 23 countries were included: 61% males, mean age 45 (SD 14), 65% axSpA, 10% pSpA and 25% PsA. Female gender, lower educational level and marital status (single vs married) were associated with higher ASDAS, without significant differences across disease phenotype. Living in lower-(vs higher) GDP countries was also associated with higher ASDAS (β=0.39 [95%CI 0.16; 0.63], with similar results for other economic indicators (Figure 1). 7% of the association between GDP and ASDAS was mediated by b/tsDMARD uptake. The above-mentioned individual and country-level SE factors remained significant to discriminate active disease (ASDAS≥2.1), with greater impact of gender (OR=1.32 [1.13; 1.54]), educational level (primary vs university OR=1.76 [1.40;2.20]) and lower GDP (OR= 1.74 [1.22;2.46]). Higher BASFI was also associated with gender (female vs male: β=0.12 [0.01; 0.24]), lower education (primary vs university: β=0.29 [0.11; 0.46], and marital status (single vs married: β=0.23 [0.09; 0.38]), without effect of country-level SE factors, and no differences across SpA phenotype. Gender and lower educational level were similarly associated with worse ASAS-HI scores (female vs male β=0.88 [0.68;1.09], and primary vs university β=0.61 [0.31;0.91]), while more fatigue was only associated with female gender and, in an opposite direction, with higher country-level SE factors (Figure 1). No interactions were found between individual and country-level SE factors for any of the outcomes.

Conclusion: Individual (female gender and lower education) and country-level SE factors are independently associated with higher disease activity in SpA. Uptake of b/tsDMARD had a small mediating effect on the association between GDP and ASDAS. Lower education and female gender are also associated with worse outcomes of functional disability, global functioning and fatigue. Country-level SE factors are not associated with functional disability or global functioning; in contrast, there is a paradoxical effect with fatigue: living in a country with a higher SE status is independently associated with higher levels of fatigue. Management of disease outcome in SpA requires also awareness of the role of individual and country level SE-factors.

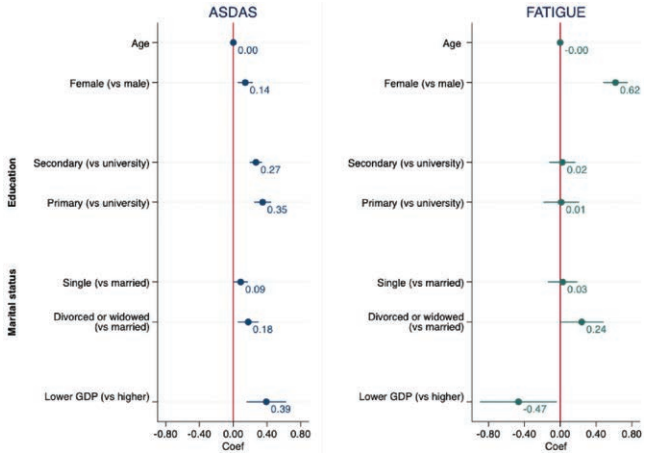


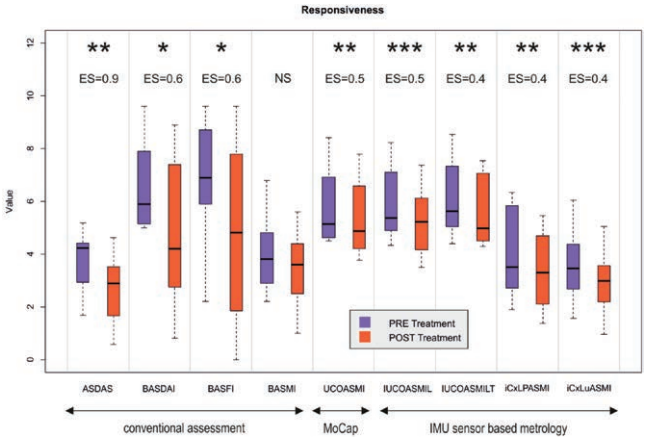
Figure 1. Effect of individual and country-level socioeconomic factors on ASDAS and fatigue, derived from multivariable mixed-effects models adjusted by clinical confounders.

Disclosure of Interests: Dafne Capelusnik Speakers bureau: BMS, Grant/research support from: Pfizer, Sizheng Steven Zhao: None declared, Annelies Boonen: None declared, Nelly Ziade Speakers bureau: Roche, Abbvie, Eli Lilly, Pfizer, Janssen, Novartis, Pierre Fabre, Apotex, Pharmaline, Paid instructor for: Abbvie, Eli Lilly, Sanofi-Aventis, Pfizer, Janssen, Consultant of: Roche, Abbvie, Eli Lilly, Pfizer, Janssen, Novartis, Gilead, NewBridge, Grant/research support from: Abbvie, NewBridge, Algorithm/Celgene, Clementina López-Medina: None declared, Maxime Dougados: None declared, Elena Nikiphorou Speakers bureau: Pfizer, Lilly, AbbVie, Sofia Ramiro Speakers bureau: Lilly, MSD, Novartis, UCB, Consultant of: AbbVie, Lilly, MSD, Novartis, UCB, Sanofi, Grant/research support from: MSD
DOI: 10.1136/annrheumdis-2021-eular.504

POS0952 RESPONSIVENESS OF SPINAL MOBILITY MEASUREMENTS IN AXIAL SPONDYLOARTHRITIS USING CONVENTIONAL AND ADVANCED METROLOGY: A PILOT STUDY

J. L. Garrido-Castro[1], I. C. Aranda-Valera[2], P. Gardiner[3], P. Machado[4], J. Condell[5], C. Gonzalez-Navas[1], E. Collantes Estevez[2]On behalf of the iMaxSpA study group.. *[1]Maimónides Biomedical Research Institute of Córdoba, Motion Analysis Lab, Córdoba, Spain*; *[2]Hospital Universitario Reina Sofia, Rheumatology, Córdoba, Spain*; *[3]Western Health and Social Care Trust, Rheumatology, Londonderry, United Kingdom*; *[4]University College London, Rheumatology, London, United Kingdom*; *[5]Ulster University, School of Computing, Eng & Intel. Sys, Londonderry, United Kingdom*

Background: Spinal mobility is an important outcome in axial spondyloarthritis (axSpA). Standardized metrology tests have been defined and validated. Nevertheless, conventional metrology measures lack responsiveness, particularly in the context of assessing short term response to treatments. Advanced metrology devices have also been used in axSpA, namely optical motion capture systems (MoCap) and Inertial Measurement Systems (IMU). These systems have better psychometric properties in terms of accuracy and reliability for analysing spinal mobility.
Objectives: To compare the responsiveness of spinal mobility using conventional and advanced metrology.
Methods: Spinal mobility was measured using an IMU based system (ViMove©) with sensors located at: occiput and T3 for cervical mobility, L1 and sacrum for lumbar mobility, and T3 and sacrum for thoracic+lumbar mobility. A MoCap system (UCOTrack©) using 13 markers was also used to record the movements in 3 planes (flexion+extension, rotation, and lateral flexion). The UCOASMI [1] index was calculated using measures obtained by MoCap and by the IMU system. Other metrology indexes based on IMU measures developed by the authors [2} were also calculated. Patients were assessed before (PRE) and 3 months after (POST) TNF blocker treatment. The Wilcoxon signed-rank test was used to test differences between pairs of pre- and post-treatment. Cohen's d was use for calculating the effect size of improvement.
Results: 12 axSpA patients were recruited from the CASTRO cohort (42% female, age 46±11 years, disease duration 16±13 years). Results PRE and POST are shown in Table 1: means (sd), statistical significance, and effect size. Disease activity and functional indexes were lower in POST and these differences were significant, especially in ASDAS. Conventional metrology lacked responsiveness, except for cervical rotation. MoCap showed moderate responsiveness in cervical rotation, in thoracolumbar mobility and with regards to the UCOASMI. Using IMU measures, responsiveness was good in terms of cervical flexion and rotation. For Lumbar (L_) and Lumbar Thoracic (LT_), lateral flexion shown significant improvement and lumbar rotation shown the best responsiveness.



	PRE	POST	Sign	ES		PRE	POST	Sign	ES
Activity					*IMU*				
BASDAI	6.5 (1.6)	4.9 (2.7)	*	0.64	C_FLEX	77 (22)	83 (19)	*	-0.25
BASFI	6.5 (2.3)	4.8 (3.2)	*	0.58	C_ROT	78 (25)	84 (22)	*	-0.22
ASDAS	3.6 (1.0)	2.5 (1.2)	**	0.87	C_FL	54 (19)	54 (17)	NS	
Metrology					L_FLEX	46 (16)	44 (19)	NS	
LatFlex	9.3 (4.1)	10.6 (3.3)	NS		L_ROT	21 (9)	27 (9)	***	-0.66
TWD	13.2 (4.2)	12.8 (3.6)	*	0.06	L_FL	32 (1)	38 (10)	*	-0.52
Schober	4.7 (1.5)	4.9 (1.5)	NS		LT_FLEX	62 (28)	63 (24)	NS	
IMD	89 (15)	90 (15)	NS		LT_ROT	63 (19)	70 (19)	NS	
CervRot	104 (28)	118 (24)	**	-0.51	LT_FL	52 (15)	60 (15)	**	-0.51
BASMI	3.8 (1.3)	3.4 (1.2)	NS		Trk_FLEX	109 (28)	112 (24)	NS	
MoCap					Trk_ROT	98 (31)	116 (21)	**	-0.59
C_FLEX	81 (22)	87 (20)	*	-0.28	Trk_FL	39 (9)	46 (10)	**	-0.7
C_ROT	101 (28)	112 (25)	***	-0.38	TTrk_FLEX	119 (36)	128 (30)	NS	
C_FL	58 (20)	58 (18)	NS		TTrk_ROT	137 (34)	161 (35)	**	-0.67
L_FLEX	107 (24)	114 (21)	***	-0.26	TTrk_FL	59 (15)	69 (16)	**	-0.6
L_ROT	67 (21)	73 (20)	NS		iUCOASMIL	5.7 (1.5)	5.0 (1.4)	***	0.48
L_FL	57 (18)	65 (20)	**	-0.41	iUCOASMILT	6.0 (1.5)	5.4 (1.3)	**	0.39
UCOASMI	6.1 (1.6)	5.3 (1.6)	**	0.50	iCxLPASMI	3.9 (1.8)	3.2 (1.5)	**	0.40
					iCxLuASMI	3.2 (1.4)	2.7 (1.3)	***	0.40

NS, not significant; *, p<0.05; **, p<0.01

Conclusion: Conventional metrology lacks short-term responsiveness. Advanced metrology using MoCap and IMU showed, in this pilot study, better responsiveness compared to conventional measures. Furthermore, IMU provide a feasibility similar to conventional metrology, and could be easily implemented in the context of clinical trials and observational studies.

REFERENCES:

[1] Validation of a new objective index to measure spinal mobility: the University of Cordoba Ankylosing Spondylitis Metrology Index (UCOASMI). Rheumatol Int. 2014 Mar;34(3):401-6.
[2] Validity and Reliability of a Sensor-Based Electronic Spinal Mobility Index for Axial Spondyloarthritis. Rheumatology (Oxford). 2020 Apr 28;keaa122.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.562

POS0953 PERIPHERAL ARTHRITIS AND HIGHER DISEASE ACTIVITY LEAD TO MORE FUNCTIONAL IMPAIRMENT IN AXIAL SPONDYLOARTHRITIS: LONGITUDINAL ANALYSIS FROM ESPAXIA

D. Capelusnik[1], S. Ramiro[2,3], E. E. Schneeberger[1], G. Citera[1]. *[1]Instituto de Rehabilitación Psicofísica, Rheumatology, CABA, Argentina*; *[2]Leiden University Medical Centre, Rheumatology, Leiden, Netherlands*; *[3]Zuyderland Medical Centre, Rheumatology, Heerlen, Netherlands*

Background: Preserving functional ability is among the main goals when treating patients with axSpA. Higher disease activity, reduced axial mobility, and increase spinal radiographic damage, and smoking status have shown to be longitudinally associated with functional worsening. The presence of peripheral arthritis has also been associated with worse functional ability during follow-up, though not in a true longitudinal analysis.
Objectives: To investigate whether peripheral arthritis together with disease activity independently contribute to functional impairment over time in patients with axSpA and to evaluate if there are contextual factors modifying this relationship.
Methods: Patients with axSpA from the ESPAXIA cohort were followed-up annually over 7 years. Physical function was assessed by the self-reported questionnaire BASFI, disease activity by ASDAS and peripheral arthritis was also recorded. The association between BASFI (outcome), peripheral arthritis and ASDAS (main variables of interest) over time was tested in generalized estimating equations (GEE) models. Models were autoregressive, i.e. adjusted for BASFI 1 year earlier, to allow for a truly longitudinal interpretation. Interactions between each of ASDAS and peripheral arthritis with contextual factors were tested.
Results: 185 patients were included (77 % male, mean age 42 (SD 13), mean disease duration 9.4 (SD 9.6) years. Mean baseline ASDAS was 2.3 (1.4), mean BASFI

3.9 (2.7) and 17% presented peripheral arthritis during the first visit. After a mean of 3.7 (2.4) years of follow-up, ASDAS and peripheral arthritis independently contributed to explaining BASFI changes over time. Contextual factors did not modify either of the relationships. A true longitudinal relation was proved with the autoregressive GEE model, showing that, adjusted for age, gender, spinal mobility and use of NSAIDs, an increase of one ASDAS unit led to a BASFI 0.48 units higher (ß 0.48 [95% CI 0.39-0.57]), and the presence of peripheral arthritis, to a BASFI 0.44 units higher (ß 0.44 [0.08-0.8]) (Table 1). A gradient was found for ASDAS disease activity states: ASDAS low disease activity (vs ASDAS inactive disease) with an increase in BASFI of 0.67 (0.35-0.98) units compared to ASDAS very high disease activity (vs ASDAS inactive disease) with a BASFI increase of 2.30 (1.90-2.72) units. (Figure 1) No interaction was found between peripheral arthritis and disease activity on BASFI, and similarly, no interactions were found between either ASDAS or peripheral arthritis with age, gender, educational level, smoking status, job type or comorbidities on BASFI.

Table 1. Factors longitudinally associated with BASFI

Assessment	Model with ASDAS continuous ß (95% CI) n=179	Model with ASDAS categorical ß (95% CI) n=179
Previous BASFI (0-10)	0.47 (0.41 to 0.52) †	0.44 (0.39 to 0.50)†
Age (years)	0.007 (-0.005 to 0.02)	0.008 (-0.004 to 0.02)
Male gender (vs female gender)	-0.42 (-0.79 to -0.06) †	-0.38 (-0.74 to -0.02)†
Peripheral arthritis	0.44 (0.08 to 0.80) †	0.38 (0.03 to 0.74) †
ASDAS-CRP	0.48 (0.39 to 0.57) †	-
ASDAS-CRP categorical		
Moderate vs inactive disease	-	0.67 (0.35 to 0.98) †
High vs inactive disease	-	1.70 (1.37 to 2.02) †
Very high vs inactive disease	-	2.30 (1.90 to 2.72) †
BASMI (0-10)	0.32 (0.24 to 0.41) †	0.32 (0.23 to 0.40) †
NSAIDs (%)	0.38 (0.09 to 0.66) †	0.37 (0.09 to 0.64) †

† Significant at p<0.05.

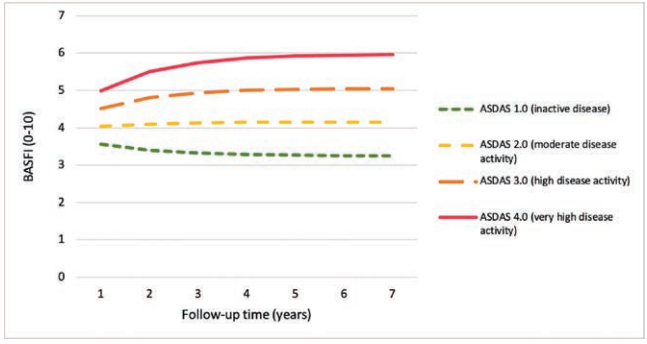


Figure 1. Longitudinal relationship between ASDAS and BASFI

Conclusion: Peripheral arthritis and higher disease activity independently lead to more functional impairment in axSpA. Contextual factors do not modify these relationships.
Disclosure of Interests: Dafne Capelusnik Speakers bureau: BMS, Grant/research support from: Pfizer, Sofia Ramiro Speakers bureau: Lilly, MSD, Novartis, UCB, Consultant of: AbbVie, Lilly, MSD, Novartis, UCB, Sanofi, Grant/research support from: MSD, Emilce Edith Schneeberger Speakers bureau: Abbvie, BMS, Janssen, Eli Lilly, Boehringer Ingelheim, Pfizer, Grant/research support from: Pfizer, Gustavo Citera Speakers bureau: Abbvie, BMS, Janssen, Pfizer, Grant/research support from: Pfizer, BMS, Janssen
DOI: 10.1136/annrheumdis-2021-eular.743

POS0954

QUALITY OF LIFE IN CHRONIC BACK PAIN PATIENTS, A 2-YEAR COMPARISON BETWEEN PATIENTS WITH AND WITHOUT A DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS: DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY COHORT

A. Boel[1], M. Van Lunteren[1], K. M. Fagerli[2], S. Exarchou[3], R. Ramonda[4], M. Van de Sande[5], D. Van der Heijde[1], F. A. Van Gaalen[1]. [1]*Leiden University Medical Centre, Rheumatology, Leiden, Netherlands*; [2]*Diakonhjemmet Hospital, Rheumatology, Oslo, Norway*; [3]*Lund University, Clinical Sciences, Section of Rheumatology, Malmö, Sweden*; [4]*University of Padova, Medicine, Rheumatology Unit, Padova, Italy*; [5]*Amsterdam University Medical Center, Rheumatology and Clinical Immunology, Amsterdam, Netherlands*

Objectives: To study quality of life (QoL) in patients with a diagnosis of axial spondyloarthritis (axSpA) and how this relates to the QoL of patients without axSpA, after two-years of protocolised follow-up.
Methods: QoL was assessed using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). Age, sex and country weighted scale scores were calculated for each of the 8 subscales. Numeric scales ranged from 0 (worst health) to 100 (best health), after recoding and recalibration. The physical (PCS) and mental component summary (MCS) scores were calculated from the adjusted scores; and transformed to enable comparison to the general population mean of 50.
Additionally, the proportion of patients with an improvement or worsening of the PCS and MCS above the minimal clinically important difference (MCID) were assessed. We applied the commonly used MCID in clinical trials with bDMARDs in axSpA of 3 points for the PCS and MCS.
In this study we included patients from the SPACE cohort (patients aged >16 years with chronic back pain suspected of axSpA) with a diagnosis axSpA or no axSpA all with a level of confidence ≥7 (on a 0-10 scale) after locally read imaging. The PCS and MCS had to be available at baseline and 2-year follow-up too.
Linear regression models were used to test the difference between patients with and without axSpA at two-year follow-up for PCS and MCS scores. Baseline PCS and MCS scores and NSAID-use over time were tested as confounders.
Results: Patients with a diagnosis of axSpA were more frequently male (57% vs 27%) and HLA-B27 positive (75% vs 31%) and had more SpA features at baseline [mean (SD) 5(2) vs 3(1)] compared to the patients without axSpA. Age, symptom duration and NSAID-use were similar between groups.
In both groups the PCS significantly improved over two years. The PCS was significantly better in the group with an axSpA diagnosis compared to the no axSpA group at two-year follow-up, after correction for baseline PCS scores and NSAID-use over time (table 1). Despite the improvements over time, PCS scores were still well below the general population mean of 50 in both groups at two-year follow-up. MCS scores were not significantly different between groups at follow-up, and they were close to the general population mean.
In linear regression models with baseline values and NSAID-use over time as covariates, axSpA was an independent predictor of better PCS scores.

Table 1. PCS and MCS scores at baseline and 2-year follow-up for the group with an axSpA diagnosis and those without axSpA (no axSpA)

	Diagnosis axSpA (N=186) Baseline	2 years	no axSpA (N=74) Baseline	2 years	p-values between groups at 2yrs
SF-36 PCS, mean (SD) %	28.0 (14.8)	40.5 (12.3)†	26.4 (13.6)	34.7 (15.6)†	p<0.001*
Improvement >MCID, n(%)		143 (78)		49 (66)	
Worsening >MCID, n(%)		22 (12)		12 (16)	
SF-36 MCS, mean (SD) %	47.3 (13.7)	47.9 (11.8)	46.5 (11.2)	48.9 (10.6)	p=0.364
Improvement >MCID, n(%)		76 (42)		35 (47)	
Worsening >MCID, n(%)		69 (38)		26 (35)	

*Significant difference between groups at two years; after correction for baseline PCS scores and NSAID use over time†Significant improvement within group over timeaxSpA, axial Spondyloarthritis; MCID, Minimal Clinically Important Difference; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, Medical Outcomes Study 36-Item Short-Form Health SurveyPCS scores of the majority of patients in both groups improved more than the MCID over two-years of protocolised follow-up. The proportions of patients who improved or worsened more than the MCID in MCS scores were similar.

Conclusion: After two years of protocolised follow-up physical functioning was better in patients with an axSpA diagnosis compared to patients without axSpA, but remained significantly compromised in both groups in comparison to the general population.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.769

POS0955 EXTRACELLULAR MATRIX PROTEIN TURNOVER MARKERS ARE ASSOCIATED WITH AXSPA – A COMPARISON WITH CONTROL SUBJECTS WITH OR WITHOUT PELVIC, BUTTOCK OR BACK PAIN

H. Port[1,2], S. Holm Nielsen[1,3], J. Blair[1], S. F. Madsen[1], A. C. Bay-Jensen[1], M. Karsdal[1], S. Seven[4,5], I. J. Sørensen[4,5], L. Morsel-Carlsen[6], M. Østergaard[4,5], S. Juhl Pedersen[4]. [1]*Nordic Bioscience A/S, Immunoscience, Herlev, Copenhagen, Denmark*; [2]*Panum - University of Copenhagen, School of Health and Medical Sciences, København, Denmark*; [3]*Technical University of Denmark, Biomedicine and Biotechnology, Kgs. Lyngby, Denmark*; [4]*Rigshospitalet, Center for Arthritis Research, Glostrup, Denmark*; [5]*University of Copenhagen, Clinical Medicine, København, Denmark*; [6]*Frederiksberg Hospital, Radiology, Frederiksberg, Denmark*

Background: Axial spondyloarthritis (axSpA) is a common chronic inflammatory disease, associated with extracellular matrix (ECM) remodeling of the cartilage, bone and connective tissues. The primary symptom of axSpA is back pain, caused by inflammation. However, there is a medical need to truly identify patients with axSpA from other subjects with buttock or low back pain attributable to other reasons. Tissue-derived extracellular (ECM) markers quantified in serum may serve to differentiate axSpA patients from other diagnostic entities.

Objectives: To investigate circulating ECM turnover markers as potential biomarkers to differentiate patients with axSpA from a control group of subjects with buttock or pelvic pain attributed to other reasons, including postpartum women and healthy subjects.

Methods: Biomarkers of ECM degradation/chronic inflammation (C1M, C3M, C4M, C6M, CRPM, C10C and COL10NC) and ECM formation (PRO-C3 and PRO-C6) were measured in 204 participants from the MASH study [1] (Table 1). Biomarker levels were compared among patients with axSpA and control group, and two new variables (Type 3 and Type 6) were included, corresponding to the index of formation/degradation of type III and type VI collagen respectively. The biomarker data was log10 transformed for normalization when necessary and linear regression models with pairwise comparisons were performed. Clinical scores and the SPARCC MRI scores for sacroiliac joint (SIJ) inflammation were correlated with the biomarkers data (data not shown).

Table 1. Comparison of blood-tested biomarkers levels in MASH study. Data was adjusted for confounders age, gender, and body mass index (BMI).

Biomarkers (Mean (SD))	Patients with axSpA (n = 41)	Control groups (n=163)	p
C1M	84.3 (85.8)	36.2 (22.1)	<0.0001
C3M	15.6 (4.0)	13.9 (3.0)	0.011
C4M	34.9 (10.2)	27.9 (7.7)	<0.0001
C6M	20.5 (5.8)	17.4 (4.2)	<0.0001
CRPM	11.9 (2.9)	11.0 (5.9)	0.027
C10C	2567 (462)	2568 (560)	0.31
COL10NC	9.15 (5.81)	9.43 (8.27)	0.43
PRO_C3	10.2 (2.5)	11.3 (3.0)	0.0052
PRO_C6	6.94 (2.45)	6.86 (2.53)	0.93
Type 3 (PRO-C3/C3M)	0.70 (0.28)	0.86 (0.31)	0.0004
Type 6 (PRO-C6/C6M)	0.36 (0.16)	0.41 (0.14)	0.0024

Results: We found that patients with axSpA had significantly increased MMP-mediated degradation of type I (C1M), type III (C3M), type IV (C4M) and type VI (C6M) collagens (p<0.0001, p=0.01,p<0.001,p<0.001, respectively), and CRP-metabolite (CRPM, p=0.027), and significantly decreased formation of type III collagen (p= 0.052) compared with control groups when adjusting for age, gender and body mass index (BMI). Significantly decreased rates of Type 3 and Type 6 variables were also observed in patients with axSpA (p=0.004, p=0.002, respectively). We further adjusted the analyses by the SPARCC SIJ inflammation scores since differences in these were found among the two groups [1], and similar differences in biomarker levels were found, indicating that the relationship between the level of biomarkers and the SPARCC SIJ inflammation scores was independent between the two groups.

Conclusion: Biomarkers of type I, III, IV and V collagen and a CRP-metabolite showed an altered turnover in patients with axSpA compared with the control group including subjects with or without buttock or pelvic pain attributable to other reasons. Such biomarkers may be used in combination with MRI or independently to separate patients with axSpA from other back pain conditions.

REFERENCES:

[1] Seven, S., Østergaard, M., Morsel-Carlsen, L., Sørensen, I. J., Bonde, B., Thamsborg, G., ... & Pedersen, S. J. (2019). Magnetic Resonance Imaging of Lesions in the Sacroiliac Joints for Differentiation of Patients With Axial Spondyloarthritis From Control Subjects With or Without Pelvic or Buttock Pain: A Prospective, Cross-Sectional Study of 204 Participants. Arthritis & Rheumatology, 71(12), 2034-2046.

Acknowledgements: The study was supported by Innovation Fund Denmark, Rigshospitalet and the Danish Rheumatism Association (grant no. R102-A2132-B98, R159-A5061 and R150-A4467-B98).

Disclosure of Interests: Helena Port Employee of: Industrial PhD student at Nordic Bioscience and University of Copenhagen, Signe Holm Nielsen Employee of: Full time employee at Nordic Bioscience, Joseph Blair Employee of: Full time employee at Nordic Bioscience, Sofie Falkenløve Madsen Employee of: Full time employee at Nordic Bioscience A/S, Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Full time employee at Nordic Bioscience A/S, Morten Karsdal Shareholder of: Nordic Bioscience A/S, Employee of: Full time employee at Nordic Bioscience A/S, Sengül Seven: None declared, Inge Juul Sørensen: None declared, Lone Morsel-Carlsen: None declared, Mikkel Østergaard: None declared, Susanne Juhl Pedersen: None declared

DOI: 10.1136/annrheumdis-2021-eular.786

POS0956 MEDITERRANEAN DIET IN AXIAL SPONDYLOARTHRITIS: A NUTRITIONAL INTERVENTION STUDY

F. Ometto[1], D. M. Farber[1], M. Lorenzin[1], A. Ortolan[1], G. Dellamaria[2], M. Felicetti[1], M. Favero[1], R. Valentini[2], A. Doria[1], R. Ramonda[1]. [1]*University of Padova, Rheumatology Unit, Department of Medicine, DIMED, Padova, Italy*; [2]*University of Padova, Dietetics and Clinical Nutrition Unit, Department of Medicine DIMED, Padova, Italy*

Background: Mediterranean diet (MD) proved to be beneficial on disease activity in patients affected by rheumatoid arthritis. A few data are available in other rheumatic conditions.

Objectives: A prospective monocentric study was conducted to evaluate the effect of a nutritional intervention based on the MD and to investigate the impact of such modification on disease activity of axial spondyloarthritis (ax-SpA).

Methods: Patients affected by ax-SpA randomized to a nutritional intervention arm (N) or a control arm (C) and were assessed at baseline (T0) and at month 6 (T6). Patients in N underwent a nutritional evaluation and received suggestions for dietary modification at T0, and then every 2 months. Adherence to the MD was evaluated with the PREDIMED questionnaire (range 0-10) [1]. A multivariable regression analysis was conducted to identify independent predictors of PREDIMED and of ASDAS-CRP improvement at T6.

Results: Eligible patients (161) were randomized to either N (81) or C (80); 47 in N and 63 in C completed the study. No relevant change of anthropometric or laboratory measures was observed at T6 in either group. A ≥20%PREDIMED improvement was more frequent in N (22/47, 46.8%) compared to C (13/63, 20.6%) (p<0.01). Also, a ≥20%ASDAS-CRP improvement was more frequent in N (8/47, 57.1%) compared to C (39/63, 40.6%) (p=0.020); and especially in those who achieved a ≥20%PREDIMED improvement (12/35, 34.3%) vs those who did not (2/73, 2.7%) (p<0.01). The nutritional intervention, a higher age, and a lower BMI increased the odds of achieving a ≥20%PREDIMED improvement; the ≥20%PREDIMED improvement was associated higher odds of achieving a ≥20%ASDAS-CRP improvement; psoriasis was negatively associated to the ASDAS-CRP improvement (Figure 1).

Conclusion: A nutritional intervention is effective in improving adherence to the MD in ax-SpA. A higher adherence to the MD may have a beneficial impact on activity of ax-SpA. Patients with psoriasis may have a limited benefit from the dietary improvement.

REFERENCES:

[1] Martínez-González, M.A. et al. A 14-item mediterranean diet assessment tool and obesity indexes among high-risk subjects: The PREDIMED trial.*PLoS One* **2012**,*7*.

Table 1. Characteristics of the patients.

	All patients	Nutrition	Controls	All patients	Nutrition	Controls
		Baseline			Month 6	
Females, n, (%)	40 (36.4)	18 (38.3)	22 (34.9)			
Age, years, mean±SD	51.7±1.3	53.0±1.3	49.6±1.3			
HLA-B27 positivity, n (%)	58 (52.7)	22 (46.8)	37 (57.1)			
Psoriasis, n (%)	58 (50.7)	26 (55.3)	32 (50.8)			
Disease duration (years), mean±SD	15.3±9.7	15.7±10	15±9.5			
Duration of b/tsD-MARD treatment overall, years, mean±SD	5±4.1	5.8±4.5	4.5±3.8			
NSAID, n (%)	76 (69.1)	30 (63.8)	46 (73)			
csDMARD, n (%)	14 (12.7)	5 (10.6)	9 (14.3)			
BMI, Kg/meters^2, mean±SD	26.5±5.4	26.5±4.3	26.6±6.1	26.4±5.3	26.3±4	26.6±6.1
ASDAS-CRP, mean±SD	2.1±1	2.1±0.9	2.1±1	2±1.1	1.8±0.9	2.1±1.2
BASDAI, mean±SD	37.6±23	37.4±23.2	37.7±22.9	39.3±24.1	37.3±23.6	41.2±24.6
BASFI, mean±SD	20.5±21.4	21.6±19.2	19.7±23	19.8±19.6	19.1±18.8	20.5±20.4
BASMI, mean±SD	1.6±2	1.9±2.2	1.4±1.7	1.8±2.1	1.9±2.4	1.7±1.9
Tender joint count, mean±SD	1.1±2.3	0.8±2.1	1.4±2.5	0.9±2	0.8±2	0.9±1.9
Swollen joint count, mean±SD	0.3±1.3	0.4±2	0.1±0.5	0.2±1.3	0.3±1.8	0.2±0.8
Leeds Enthesitis Index, mean±SD	0.2±0.8	0.3±1	0.2±0.6	1.1±2	1.3±2.2	1±1.8
CRP, mg/L, mean ±SD	3.4±6.2	3.2±3.9	3.7±7.4	3.5±5.6	2.6±3.1	4.1±6.9
LDL-c, mg/dl, mean ±SD	130.8±36.5	132.3±35	129.7±38.4	130.6±34.7	125.7±34.8	134.4±34.5
PREDIMED score, mean ±SD	6.7±1.8	7±2.1	6.6±1.6	7.6±2.1	8.6±1.9	6.8±2

b/tsDMARD biological/targeted synthetic DMARDs; csDMARD conventional DMARDs. PREDIMED questionnaire to assess adherence to the Mediterranean diet.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.812

POS0957 THE PREVALENCE AND FACTORS RELATED TO SLEEP APNOEA IN ANKYLOSING SPONDYLITIS

H. Forsblad-D'elia[1], A. Wiginder[2], C. Sahlin-Ingridsson[2], M. Geijer[3], K. Franklin[2], A. Blomberg[2]. [1]*Institute of Medicine, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; [2]*Umeå University, Department of Public Health and Clinical Medicine, Umeå, Sweden*; [3]*Institute of Clinical Sciences, Department of Radiology, Gothenburg, Sweden*

Background: An increased prevalence of obstructive sleep apnoea (OSA) has been suggested in ankylosing spondylitis (AS), but few controlled studies have been performed.
Objectives: We thus aimed to study the prevalence of OSA in patients with AS compared to controls and to study if disease-related and non-disease-related factors were determinants of OSA in AS patients.
Methods: One hundred and fifty-five patients with AS were included in the Backbone study that investigates severity and comorbidities in AS. Controls were recruited from the Swedish CardioPulmonary bioImage Study (SCAPIS). Participants were asked to be examined with a home sleep-monitoring device during one night's sleep to evaluate the presence of OSA. For each AS patient, 45-70 years, four controls were matched for sex, age, weight and height. OSA was defined as an apnoea-hypopnea-index ≥5 events/hour.
Results: In total, 63/155(40.6%) patients with AS were examined with a home sleep-monitoring device out of which 46 patients were 45-70 years and therefore matched (mean age 57.2±7.5years, 30(65.2%) men) with 179 controls (mean age 57.2±4.5years, 123(68.7%) men). Twenty-two out of 46(47.8%) patients with AS vs. 91/179(50.8%) controls had OSA, p=0.72. No differences measurements evaluating OSA were noted in AS vs. controls. In logistic regression analysis, based on all 63 examined AS-patients, several AS-related variables were associated with OSA but after adjusting for age and sex, only higher age and BMI, remained to be significant determinants of OSA, Table 1.

Table 1. Univariable and age- and sex-adjusted logistic regression analyses with obstructive sleep apnoea as dependent variable in 63 patients with ankylosing spondylitis.

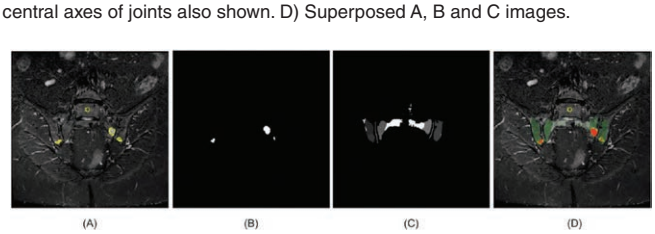
Variables	Univariable logistic regression analyses, Odds Ratio (95%CI)	P	Age- and sex-adjusted logistic regression analyses, Odds Ratio (95%CI)	P
Sex, male	1.9(0.6-5.5)	0.25	1.5(0.4-4.8)	0.53
Age	1.1(1.0-1.2)	**0.002**	1.1(1.0-1.2)	**0.002**
BMI	1.4(1.1-1.7)	**0.001**	1.6(1.2- 2.2)	**0.001**
Duration of symptoms	1.1(1.0-1.1)	**0.028**	1.0(0.9-1.1)	0.79
BASMI	1.9(1.3-2.9)	**0.002**	1.5(0.9 -2.5)	0.87
BASFI	1.4(1.0-2.0)	**0.038**	1.3(0.9-2.0)	0.88
≥1 Syndesmophyte	3.9(1.3-12.2)	**0.017**	3.0(0.8-11.3)	0.10
mSASSS	1.0(1.0-1.1)	**0.047**	1.0(0.98-1.05)	0.25
Metabolic syndrome	4.3(1.5-12.9)	**0.008**	1.4(0.3-6.6)	0.69
Epworth Sleep Scale	1.2(1.0-1-3)	**0.023**	1.2(1.0-1.4)	0.29

Conclusion: In this case-control study, patients with AS did not have a higher prevalence of OSA compared to controls. AS patients with OSA had higher BMI and were older compared to patients without OSA.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.823

POS0958 RESPONSIVENESS OF CONVENTIONAL, SEMI-AUTOMATIC AND FULL-AUTOMATIC METHODS TO QUANTIFY MARROW BONE EDEMA LESIONS IN MRI OF AXIAL SPONDYLOARTHRITIS PATIENTS: A PILOT STUDY

C. Garrido-González[1], M. L. Ladehesa Pineda[2], J. L. Garrido-Castro[3], Z. Tabor[4], I. Kucybała[5], W. Wojciechowski[5], P. Zarco-Montejo[6], R. Almodovar[6], E. Collantes Estevez[2]on behalf of CASTRO. [1]*Universidad de Córdoba, Facultad de Medicina, Enfermería y Fisioterapia, Córdoba, Spain*; [2]*Hospital Universitario Reina Sofía, Rheumatology, Córdoba, Spain*; [3]*Maimónides Biomedical Research Institute of Córdoba, Rheumatology, Córdoba, Spain*; [4]*AGH University of Science and Technology, Department of Biocybernetics and Biomedical Engineering, Krakow, Poland*; [5]*Jagiellonian University Medical College, Department of Radiology, Krakow, Poland*; [6]*Fundación Hospital Alcorcón, Rheumatology, Madrid, Spain*

Background: The presence or absence of marrow bone edema (MBE) in the sacroiliac joints (SIJ) is very important in the diagnosis of axial Spondyloarthritis (axSpA). The quantification of this lesion and its extension may be important to analyze responsiveness of the treatment. Several scoring systems have been proposed for MRI images of SIJ, some of them being observer dependent (Berlin, SPARCC). Others, works in a semi-automatically way, such as the s-SCAISS[1], which makes it possible to quantify the size of the lesion, based on the indication of the expert. Recently, methods like the KITs4R[2], based on a deep patch-based classification network. allow a fully automated detection and quantification of the MBE lesions.
Objectives: To analyze responsiveness of several scores (observer independent, semiautomatic and full automatic) for quantify MBE in SIJ of axSpA patients.
Methods: Two rheumatologists independently quantified SIJ images from axSpA patients by visual inspection methods (Berlin and SPARCC indexes) and a semiautomatic system (s-SCAISS) on a single semi-coronal MRI slide (STIR). Full semi-coronal MRI images (15 to 18 slices) were used for an automatic detection algorithm (KITs4R), where total MBE was calculated as sum of areas of MBE in each slice. Patients were assessed before TNF-α therapy (PRE) and 3 months later (POST). Spearman correlations was used to analyze relationship between variables, Wilcoxon signed-rank test for significant differences and Cohen's d for calculating the effect size of improvement. Figure 1 shows processing of the MRI images: A) Area of MBE selected by the SCAISS, when the rheumatologist "click" on each MBE; B) Lesions detected automatically by KITs4R; C) Automated deep segmentation of bones and subchondral regions (with split into quadrants with central axes of joints also shown. D) Superposed A, B and C images.



Results: 12 axSpA patients were recruited from the CASTRO cohort (42% female, age 46±11 years, disease duration 16±13 years, BMI 28±5). Results PRE and POST are shown in Table 1: mean values (sd), statistical significance (NS, not significant; *, p<0.05; **, p<0.01), and effect size. Activity indexes and CRP were lower. ASDAS and CRP shown significant differences and a large effect size. All MRI scores showed good responsiveness (ES medium-large, p<0.01), specially KITs4R. Agreement between all MRI scores were high (r>0.8;p<0.01). Between semiautomatic and automatic methods, this agreement was also excellent (r=0.92;p<0.001). Correlation in improvements (reductions in scores) were also significant between all MRI scores (r>0.7;p<0.05).

	PRE	POST	Sign	ES
BASDAI	6.12 (2.45)	4.96 (2.74)	N.S.	0.44-Small
ASDAS	3.61 (1.04)	2.58 (1.25)	*	0.89-Large
CRP	11.26 (8.93)	4.81 (4.08)	**	0.84-Large
BERLIN	2.58 (1.98)	1.17 (1.85)	**	0.74-Medium
SPARCC	3.92 (3.42)	1.58 (2.43)	**	0.69-Medium
SCAISS	295 (332)	95 (163)	**	0.68-Medium
KITs4R	1671 (1596)	258 (421)	**	1.04-Large

NS, not significant; *, p<0.05; **, p<0.01

Conclusion: All MRI scores have good level of agreement between them and good responsiveness. Berlin and SPARCC are observer dependent, and do not quantify the extension of the MBE area. s-SCAIS helps to this quantification. KITs4R is not observer dependent but clinimetric validation, analizing agreement level with human expert, is necessary. New advanced tools are improving quantitative and objective measurement of BME which is important to analyze responsiveness.

REFERENCES:

[1] Development and validation of SCAISS, a tool for semi-automated quantification of sacroilitis by magnetic resonance in spondyloarthritis. Rheumatol Int. 2018 Oct;38(10):1919-1926.
[2] The semi-automated algorithm for the detection of bone marrow oedema lesions in patients with axial spondyloarthritis. Rheumatol Int. 2020 Apr;40(4):625-633.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.864

POS0959 DIAGNOSTIC DELAY IN AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE NATIONAL EARLY INFLAMMATORY ARTHRITIS AUDIT

M. Russell[1], F. Coath[2], M. Yates[1], K. Bechman[1], S. Norton[1], J. Galloway[1], J. Ledingham[3], R. Sengupta[4], K. Gaffney[2]. *[1]King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; *[2]Norfolk and Norwich University Hospital, Rheumatology Department, Norwich, United Kingdom*; *[3]Portsmouth Hospitals University NHS Trust, Rheumatology Department, Portsmouth, United Kingdom*; *[4]Royal National Hospital for Rheumatic Diseases, Department of Rheumatology, Bath, United Kingdom*

Background: Diagnostic delay is a significant problem in axial spondyloarthritis (axSpA), and there is a growing body of evidence showing that delayed axSpA diagnosis is associated with worse clinical, humanistic and economic outcomes.[1] International guidelines have been published to inform referral pathways and improve standards of care for patients with axSpA.[2,3]

Objectives: To describe the sociodemographic and clinical characteristics of newly-referred patients with axSpA in England and Wales in the National Early Inflammatory Arthritis Audit (NEIAA), with rheumatoid arthritis (RA) and mechanical back pain (MBP) as comparators.

Methods: The NEIAA captures data on all new patients over the age of 16 referred with suspected inflammatory arthritis to rheumatology departments in England and Wales.[4] We describe baseline sociodemographic and clinical characteristics of axSpA patients (n=784) recruited to the NEIAA between May 2018 and March 2020, compared with RA (n=9,270) and MBP (n=370) during the same period.

Results: Symptom duration prior to initial rheumatology assessment was significantly longer in axSpA than RA patients (p<0.001), and non-significantly longer in axSpA than MBP patients (p=0.062): 79.7% of axSpA patients had symptom durations of >6 months, compared to 33.7% of RA patients and 76.0% of MBP patients; 32.6% of axSpA patients had symptom durations of >5 years, compared to 3.5% of RA patients and 24.6% of MBP patients (Figure 1A). Following referral, median time to initial rheumatology assessment was longer for axSpA than RA patients (36 vs. 24 days; p<0.001), and similar to MBP patients (39 days; p=0.30). The proportion of axSpA patients assessed within 3 weeks of referral increased from 26.7% in May 2018 to 34.7% in March 2020; compared to an increase from 38.2% to 54.5% for RA patients (Figure 1B). A large majority of axSpA referrals originated from primary care (72.4%) or musculoskeletal triage services (14.1%), with relatively few referrals from gastroenterology (1.9%), ophthalmology (1.4%) or dermatology (0.4%).

Of the subset of patients with peripheral arthritis requiring EIA pathway follow-up, fewer axSpA than RA patients had disease education provided (77.5% vs. 97.8%; p<0.001), and RA patients reported a better understanding of their condition (p<0.001). HAQ-DI scores were lower at baseline in axSpA EIA patients than RA EIA patients (0.8 vs 1.1, respectively; p=0.004), whereas baseline Musculoskeletal Health Questionnaire (MSK-HQ) scores were similar (25 vs. 24, respectively; p=0.49). The burden of disease was substantial across the 14 domains comprising MSK-HQ in both axSpA and RA (Figure 1C).

Conclusion: We have shown that diagnostic delay remains a major challenge in axSpA, despite improved disease understanding and updated referral guidelines. Patient education is an unmet need in axSpA, highlighting the need for specialist clinics. MSK-HQ scores demonstrated that the functional impact of axSpA is no less than for RA, whereas HAQ-DI may underrepresent disability in axSpA.

REFERENCES:

[1] Yi E, Ahuja A, Rajput T, George AT, Park Y. Clinical, economic, and humanistic burden associated with delayed diagnosis of axial spondyloarthritis: a systematic review. Rheumatol Ther. 2020;7:65-87.
[2] NICE. Spondyloarthritis in over 16s: diagnosis and management. 2017.
[3] van der Heijde D, Ramiro S, Landewe R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017;76(6):978-91.
[4] British Society for Rheumatology. National Early Inflammatory Arthritis Audit (NEIAA) Second Annual Report. 2021.

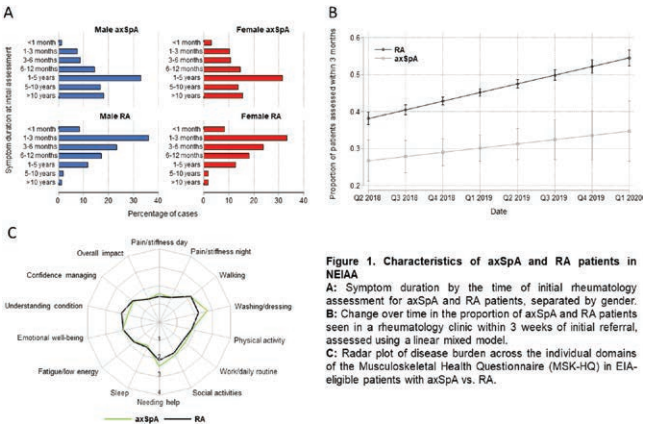


Figure 1. Characteristics of axSpA and RA patients in NEIAA
A: Symptom duration by the time of initial rheumatology assessment for axSpA and RA patients, separated by gender.
B: Change over time in the proportion of axSpA and RA patients seen in a rheumatology clinic within 3 weeks of initial referral, assessed using a linear mixed model.
C: Radar plot of disease burden across the individual domains of the Musculoskeletal Health Questionnaire (MSK-HQ) in EIA-eligible patients with axSpA vs. RA.

Acknowledgements: The National Early Inflammatory Arthritis Audit is commissioned by the Healthcare Quality Improvement Partnership, funded by NHS England and Improvement, and the Welsh Government, and carried out by the British Society for Rheumatology, King's College London and Net Solving.

Disclosure of Interests: Mark Russell Grant/research support from: UCB, Pfizer, Fiona Coath: None declared, Mark Yates Grant/research support from: UCB, Abbvie, Katie Bechman: None declared, Sam Norton: None declared, James Galloway Grant/research support from: Abbvie, Celgene, Chugai, Gilead, Janssen, Lilly, Pfizer, Roche, UCB, Jo Ledingham: None declared, Raj Sengupta Grant/research support from: AbbVie, Biogen, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Karl Gaffney Grant/research support from: AbbVie, Biogen, Cellgene, Celltrion, Janssen, Lilly, Novartis, Pfizer, Roche, UCB.

DOI: 10.1136/annrheumdis-2021-eular.894

POS0960 PRESENCE AND ASSOCIATED FACTORS OF FATIGUE IN PATIENTS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

M. Garrido-Cumbrera[1], V. Navarro-Compán[2], L. Christen[3], C. Bundy[4], R. Mahapatra[5], S. Makri[6], C. J. Delgado-Domínguez[1], J. Correa-Fernández[1], S. Sanz-Gómez[1], D. Poddubnyy[7]on behalf of IMAS working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; *[2]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*; *[3]Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; *[4]Cardiff University, School of Healthcare Sciences, Cardiff, United Kingdom*; *[5]Axial Spondyloarthritis International Federation (ASIF), Patient Advocacy, London, United Kingdom*; *[6]Cyprus League Against Rheumatism (CYPLAR), Patient Advocacy, Nicosia, Cyprus*; *[7]Charité - Universitätsmedizin Berlin, Rheumatology Department, Berlin, Germany*

Background: Fatigue/tiredness is an essential aspect of disease for patients with axial spondyloarthritis (axSpA). However, little is known about its prevalence and associated factors.

Objectives: The aim is to assess the prevalence of fatigue and associated factors in a large sample of patients with axSpA patients from 13 European countries.
Methods: Data from 2,846 unselected patients of the European Map of Axial Spondyloarthritis (EMAS) through an online survey (2017-2018) across 13 European countries were analyzed.
The presence of fatigue/tiredness was evaluated using the Visual Analogue Scale from the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI): "How would you describe the overall level of fatigue/tiredness you have experienced? (0-10)". Risk of poor mental health was assessed using the 12-Item General Health Questionnaire (GHQ-12; 0-12).
Possible associated factors included: Socio-demographic and disease characteristics, disease activity and function and mental health disorders.
The Mann-Whitney test was used to compare the means of variables of two categories vs. the numerical variables, the χ^2 test was used to compare the distribution between the categorical variables. Binary logistic regression and multiple linear regression were used to identify possible predictors.
Results: A total of 2,846 axSpA patients participated in the EMAS survey: mean age was 43.9 years, 61.3% female, 48.1% had a university degree, 67.9% were married and 71.3% were HLA-B27 positive. Fatigue/tiredness was associated with younger age (6.4±2.3 vs 5.5±2.4), being female (6.6±2.2 vs 5.7±2.4), lower educational level (6.9±2.4 vs 6.0±2.0) and separated or divorced persons (6.8±2.2 vs 6.2±2.3; all p<0.001). Those reporting work impact (6.8±2.1 vs 5.8±2.4), physically inactive (6.9±2.2 vs 6.1±2.3) or those with sleep disorders (7.0±2.0 vs 5.8±2.4), anxiety (7.0 ± 2.0 vs 5.9±2.4) or depression (7.2±1.9 vs 5.9±2.4; all p<0.001) also presented greater fatigue, as did those with higher morning stiffness (r=0.499) and functional limitation (r=0.257), and poorer mental health GHQ-12 (r=0.419). Finally, the variables independently associated with fatigue were female gender (B=0.427), being physical inactive (B=-0.395) and those with greater morning stiffness severity (B=0.349; see Table 1). In addition, those on temporary and permanent sick leave, along with the unemployed, presented greater fatigue (7.1, 6.8 and 7.1 respectively).

Table 1. Linear regression analysis to predict presence of fatigue/tiredness (N = 2052)

	Simple			Multivariate		
	B	95% CI	p-value	B	95% CI	p-value
Age	-0.018	-0.025, -0.011	**<0.001***	-0.015	-0.022, -0.008	**<0.001**
Gender (female)	0.838	0.659, 1.017	**<0.001***	0.427	0.264, 0.590	**<0.001**
Marital status (married)	0.190	0.042, 0.339	**0.012***	0.162	0.021, 0.302	**0.024***
Educational level (university)	-0.274	-0.402, -0.146	**<0.001***	-0.128	-0.245, -0.012	**0.031***
BMI (Overweight/Obesity)	0.151	-0.026, 0.328	0.094	NA	NA	NA
Morning stiffness severity (0-10) *	0.473	0.442, 0.505	**<0.001***	0.349	0.314, 0.385	**<0.001***
Functional limitation (0-54)	0.038	0.032, 0.044	**<0.001***	0.014	0.008, 0.019	**<0.001***
Reported Work impact (yes)	0.936	0.753, 1.119	**<0.001***	0.228	0.068, 0.389	**0.005***
Physical activity (yes)	-0.726	-0.968, -0.485	**<0.001***	-0.395	-0.611, -0.178	**<0.001***
Sleep disorder (yes)	1.191	1.013, 1.368	**<0.001***	0.276	0.095, 0.458	**0.003***
Anxiety (yes)	1.139	0.950, 1.327	**<0.001***	0.002	-0.215, 0.220	0.982
Depression (yes)	1.274	1.079, 1.469	**<0.001***	0.223	0.001, 0.446	**0.049***
GHQ-12 (0-12) **	0.234	0.215, 0.254	**<0.001**	0.110	0.088, 0.132	**<0.001***

*As measured by the respective item of the BASDAI scale**12-item General Health Questionnaire. A value of 3 or above indicates a risk of poor mental health

Conclusion: Fatigue/tiredness was highly prevalent among axSpA European patients with female gender, engage in physical activity and those with greater morning stiffness severity most strongly associated, and the unemployed presenting greatest fatigue.
Acknowledgements: This study was supported by Novartis Pharma AG. The authors would like to thank all patients who participated in the study.
Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Laura Christen Employee of: Novartis Pharma AG, Christine Bundy Speakers bureau: Abbvie, Celgene, Janssen, Lilly, Novartis, and Pfizer., Raj Mahapatra: None declared, Souzi Makri: None declared, Carlos Jesús Delgado-Domínguez: None declared, José Correa-Fernández: None declared, Sergio Sanz-Gómez: None declared, Denis Poddubnyy Speakers bureau: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB., Grant/research support from: Abbvie, MSD, Novartis, and Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.968

POS0961

PREVALENCE AND ASSOCIATED FACTORS OF SLEEP DISORDERS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

M. Garrido-Cumbrera[1], V. Navarro-Compán[2], L. Christen[3], C. Bundy[4], R. Mahapatra[5], S. Makri[6], C. J. Delgado-Domínguez[1], J. Correa-Fernández[1], D. Poddubnyy[7] on behalf of IMAS working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; *[2]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*; *[3]Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; *[4]Cardiff University, School of Healthcare Sciences, Cardiff, United Kingdom*; *[5]Axial Spondyloarthritis International Federation (ASIF), Patient Advocacy, London, United Kingdom*; *[6]Cyprus League Against Rheumatism (CYPLAR), Patient Advocacy, Nicosia, Cyprus*; *[7]Charité - Universitätsmedizin Berlin, Rheumatology Department, Berlin, Germany*

Background: Sleep is an essential health aspect that is often impacted in patients with axial spondyloarthritis (axSpA).
Objectives: This analysis aims to assess the prevalence and associated factors of sleep disorders in a large sample of European axSpA patients.
Methods: Data were analyzed from 2,846 unselected patients with self-reported clinician-given diagnosis of axSpA of the European Map of Axial Spondyloarthritis (EMAS) through an online survey (2017-2018) across 13 European countries. Socio-demographic data; BASDAI [0-10] scores; engagement in physical activity; axSpA influence on work choice (assessed with yes/no question "Was your current or past work choice in any way determined by axSpA?"); risk of psychological distress (12-item General Health Questionnaire [GHQ-12; 0-12]); functional limitation [0-54] and self-reported anxiety and depression were evaluated. Presence of sleep disorders was assessed by the question: "Please indicate whether you have been diagnosed with any of the following: sleep disorders". A Mann-Whitney test was used to compare the means of numerical variables between dichotomous variables, the Chi-Square test was used to compare the distribution between the categorical variables. Simple and multivariable logistic regression models were used to identify associations between sleep disorders and disease characteristics, mental health and work-related variables.
Results: Age of respondents was 43.9 years; 61.3% were female; 48.1% had a university degree; 67.9% were married and 71.3% were HLA-B27 positive. The prevalence of sleep disorders was 39.0%. In the bivariate analysis, presence of sleep disorders was associated with female gender (68.3% vs. 31.7%; p<0.001); overweight/obese (56.5% vs. 49.8%; p<0.001); increased BASDAI scores (6.1±1.8 vs. 5.0±2.1; p<0.001); fatigue (7.0±2.0 vs. 5.8±2.4; p<0.001); morning stiffness (5.8±2.4 vs. 4.8±2.4; p<0.001), work impact (56.5% vs. 38.2%; p< 0.001); anxiety (56.8% vs. 12.5%; p<0.001); depression (51.8% vs. 10.1%; p<0.001) and higher GHQ-12 scores (6.4±4.0 vs. 3.9±3.9; p<0.001). However, factors that remained independently associated with sleep disorders in the multivariable analysis were anxiety (OR=3.8 p<0.001) and depression (OR=3.1 p<0.001) and female gender (OR=1.4; p=0.002) [Table 1].

Table 1. Regression analysis to predict presence of sleep disorders (N=2191)

	Simple logistic regression			Multivariable logistic regression		
	OR	95% CI	p-value	OR	95% CI	p-value
Gender (female)	1.59	1.36-1.87	**<0.001**	1.40	1.13-1.73	**0.002**
Marital status (married)	1.13	0.99-1.28	0.074	NA	NA	NA
Overweight/Obesity	1.31	1.12-1.53	**0.001**	1.39	1.14-1.71	**0.001**
BASDAI (0-10)	1.33	1.27-1.39	**<0.001**	1.07	0.95-1.21	0.246
Fatigue/Tiredness (0-10)*	1.28	1.23-1.33	**<0.001**	1.04	0.97-1.12	0.271
Morning Stiffness intensity (0-10)*	1.19	1.15-1.23	**<0.001**	1.05	0.98-1.13	0.188
Reported Work impact (yes)	2.10	1.78-2.48	**<0.001**	1.29	1.05-1.58	**0.015**
Anxiety (yes)	9.18	7.58-11.11	**<0.001**	3.84	2.99-4.94	**<0.001**
Depression (yes)	9.53	7.78-11.66	**<0.001**	3.09	2.37-4.02	**<0.001**
GHQ-12 (0-12)**	1.16	1.14-1.19	**<0.001**	1.03	1.00-1.06	**0.029**

*As measured by the respective item of the BASDAI scale.**12-item General Health Questionnaire. A value of 3 or above indicates a risk of poor mental health.

Conclusion: Sleep disorders were highly prevalent among axSpA European patients and strongly associated with female gender and reporting worse mental health, and spinal stiffness. Patients on permanent and temporary sick leave were more likely to report sleep disorders. The strong association between sleep disorders with both anxiety and depression should encourage rheumatologists to screen their patients with sleep disturbance in case they require additional specialist support.
Acknowledgements: This study was supported by Novartis Pharma AG. The authors would like to thank all patients who participated in the study.
Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB., Laura Christen Employee of: Novartis Pharma AG, Christine Bundy Speakers bureau: Abbvie, Celgene, Janssen, Lilly, Novartis, and Pfizer, Raj Mahapatra: None declared, Souzi Makri: None declared, Carlos Jesús Delgado-Domínguez: None declared, José Correa-Fernández: None declared, Denis Poddubnyy Speakers bureau: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Abbvie, MSD, Novartis, and Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.981

POS0962

PATIENT-REPORTED IMPACT OF AXIAL SPONDYLOARTHRITIS ON WORKING LIFE. RESULTS FROM THE SPANISH ATLAS

M. Garrido-Cumbrera[1], E. Collantes-Estévez[2], V. Navarro-Compán[3], P. Zarco Montejo[4], C. Sastré[5], S. Sanz-Gómez[1], J. Correa-Fernández[1], J. Gratacos-Masmitja[6]on behalf of Atlas working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; *[2]Reina Sofia University Hospital, Rheumatology Department, Cordova, Spain*; *[3]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*; *[4]Hospital Universitario Fundación Alcorcón, Rheumatology Department, Madrid, Spain*; *[5]Novartis Farmacéutica Spain, Immunology, Hepatology and Dermatology, Barcelona, Spain*; *[6]Hospital Universitaria Parc Taulí, Rheumatology Department, Sabadell, Spain*

Background: Axial spondyloarthritis (axSpA) impacts negatively on multiple dimensions of patient's life, including their working life.
Objectives: The present study aims to evaluate burden of disease ox axSpA patients by working status, work-related issues and their associations and determinants in a Spanish sample.
Methods: The Atlas 2017 is an extensive cross-sectional patient survey conducted in Spain (2016), validated by a multidisciplinary group of experts on spondyloarthritis. Participants were recruited through an on-line panel and patient organizations. Participants were classified as active (employed, unemployed between 15-64 years) and inactive (retirees, on sick leave, students and homemakers). Those employed were asked to report work-related issues (WRIs) due to axSpA (sick-leave, difficulty fulfilling work hours, missing work for doctors' appointments, reducing working hours or taking days off) in the past 12 months. Diagnostic delay, disease activity (BASDAI), spinal stiffness (3-12), functional limitation (0-54) and psychological distress (General Health Questionnaire, GHQ-12 [0-12]) were compared between employed patients with or without WRIs using a Mann-Whitney and Kruskal-Wallis test.
Results: Data from 680 patients were collected: mean age was 47±11 years, 52.5% were female and 36.9% were university educated. Mean disease duration and diagnostic delay were 20.9±12.2 and 8.5±7.7 years, respectively, and mean BASDAI was 5.5±2.2. A total of 63.6% (n=415) were considered active population, of which 49.8% (n=325) were employed. Of those employed, 54.3% reported a WRI, specifically 37.1% took sick leave, 44.1% had difficulties in fulfilling the working hours, 42.9% missed work due to doctor's appointments 37.1% took sick leave, 18.2% reported that their professional life had suffered, 12.3% asked for some days off, 12.3% changed shift sometimes and 7.6% had to give up their previous job. Among all patients, 95.5% faced (or believed they would) difficulties finding a job due to axSpA. Experiencing WRIs due to axSpA was significantly associated in the univariable analysis with higher disease activity, self-reported spinal stiffness, longer diagnostic delay, higher functional limitation and higher level of psychological distress (p<0.001). However, the highest levels of disease burden were reported by unemployed participants (see Table 1).

Table 1. Differences between employees with/without work-related issues and between employed/unemployed participants in relation to sociodemographic and patient-reported outcomes

Reference group	Employed		Active Population	
Subgroup	Any WRI	With no WRIs	Employed	Unemployed
N size	n: 170	n: 143	n: 325	n: 90
Sociodemographic characteristics				
Age (years)	41.9 ± 7.9	44.2 ± 9.4	42.9 ± 8.6*	42.0 ± 9.1*
Gender (Male)	79 (46.5)	75 (52.4)	159 (48.9)	36 (40.0)
Education level (University)	80 (47.1)*	68 (47.6)*	153 (47.1)	21 (23.3)
Marital status (Married)	110 (64.7)	109 (76.2)	231 (71.1)	54 (60.0)
Patient-reported outcomes				
BASDAI (0-10)	5.7 ± 1.8**	4.5 ± 1.9**	5.2 ± 1.9**	6.3 ±1.9**
Spinal Stiffness (3-12)	6.7 ± 2.7**	6.1 ± 2.4**	6.5 ± 2.6**	7.8 ± 2.3**
Functional Limitation (0-54)	43.9 ± 8.8**	36.9 ± 10.3**	40.6 ± 10.1**	45.0 ± 8.4**
GHQ-12 (0-12)	6.6 ± 4.2**	3.0 ± 3.5**	4.9 ± 4.3**	7.6 ± 4.2**
Anxiety	35 (20.6)*	16 (11.2)*	52 (16.0)*	25 (27.8)*
Depression	29 (17.1)*	4 (2.8)*	33 (10.2)**	21 (23.3)**

*Note: WRI: Work-related issue** p-value <0.001; * p-value <0.05*

Conclusion: Results reveal a relevant impact of axSpA in patient working life. Approximately two out of three patients employed experienced WRIs due to axSpA, being associated to worse disease outcomes and poorer psychological health. However, those who were unemployed faced a harsher situation reporting even poorer disease-related and psychological health outcomes. As psychological health appears impaired severely in axSpA patients regardless of their employment status it should be key for a holistic approach to patient care.
Acknowledgements: This study was supported by Novartis Spain. The authors would like to thanks all patients who participated in the Atlas study.

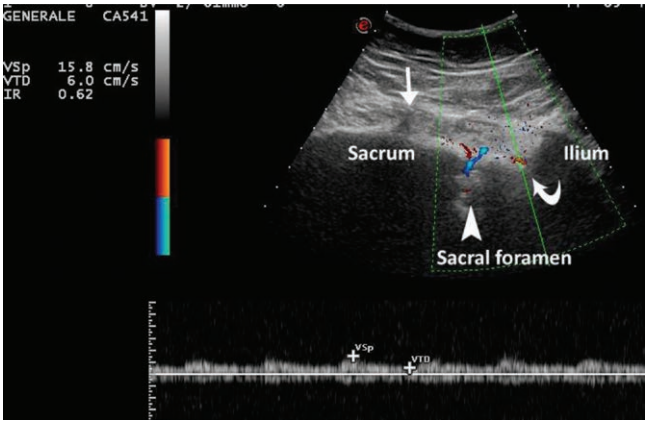
Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Eduardo Collantes-Estévez Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB., Pedro Zarco Montejo: None declared, Carlos Sastré Employee of: Novartis Farmacéutica Spain, Sergio Sanz-Gómez: None declared, José Correa-Fernández: None declared, Jordi Gratacos-Masmitja Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.985

POS0963

POWER AND SPECTRAL DOPPLER ULTRASOUND AS A SCREENING TOOL IN THE DIAGNOSTIC COURSE OF SUSPECTED AXIAL SPONDYLOARTHRITIS: PRELIMINARY DATA FROM A LARGE MONOCENTRIC COHORT

P. Falsetti[1], E. Conticini[1], C. Baldi[1], M. Bardelli[1], R. D'alessandro[1], S. G. Al Khayyat[1], M. A. Mazzei[2], L. Cantarini[1], B. Frediani[1]. *[1]University of Siena, Rheumatology Unit, Siena, Italy*; *[2]University of Siena, Diagnostic Imaging Unit, Siena, Italy*

Background: Sacroiliac joints (SIJs) involvement is a characteristic feature of Spondylarthritis (SpA). Magnetic resonance imaging (MRI) has been included in the new Assessment of SpA International Society (ASAS) criteria for the classification of non-radiographic axial SpA. Power Doppler ultrasound (PDUS) and spectral Doppler US have been used in few works, also from our group, to evaluate the inflammatory activity of the SIJs, in comparison with MRI, with different results.
Objectives: We aimed to evaluate the value of PDUS with spectral wave analysis (SWA) in the assessment of suspected active sacroiliitis (SI). PDUS of SIJs was used as a screening tool alongside the routine PDUS assessment of peripheral joints.
Methods: 143 patients (114 females and 29 males, mean age 46,2 years, mean BMI 25.9) with new onset of inflammatory back pain (IBP), were included. Peripheral symptoms were allowed. Every patient underwent a PDUS examination of SIJs as previously reported. The sonographer was blinded to the clinical data. An Esaote Twice US machine, with convex 1-8 MHz and linear 6-18 MHz probes, was used, with standardized parameters. PD signals detected in the SIJs, were scored with a 3-points scale: 0= absence of signals, 1= isolate vessels, 2= more than one vessel. The signals were also classified as intra-articular (vascularity from deep joint and inter-osseous ligament) or peri-articular (vascularity along posterior sacroiliac ligament). SWA was applied to the same vessels calculating the Resistive Index (RI) (Figure 1). A PDUS diagnosis of active SI was made with a grade 1 of vascularity and RI<0,60, or grade 2 of vascularity and RI<0,70. PDUS multi-site examination of peripheral joints and entheses was also performed; entheseal involvement was scored with Belgrade Ultrasound Enthesitis Score (BUSES) and as global enthesitic charge (GEC). Every patient underwent MRI of SIJs within 2 weeks, and before to start pharmacologic treatment. The non-parametric Spearman rank test and univariate linear regression analysis was applied using InStat GraphPad statistical package.
Results: A time of 5-8 minutes was sufficient to set and to complete PDUS/SWA examination on both SJJs. All patients considered this examination quick, not painful and substantially comfortable. PD signals were detected in 124 patients (mean RI 0,56). Bone marrow edema (BME) lesions (active SI on MRI) were detected in 94 patients. A final diagnosis of SpA was made in 103 patients (81 females, 22 males). Among SpA patients 24 had psoriasis, 3 inflammatory bowel disease, 3 uveitis, 5 were B27+, and they had mean BUSES of 4,1 and GEC of 1,2. The mean SIJs PDUS score was 1,3 in SpA and 0,52 in not-SpA patients. The mean SIJs RI was 0,53 in SpA and 0,68 in not-SpA patients. A significant correlation was demonstrated between MRI and PDUS diagnosis of SI (r=0,6486, p<0,0001), between MRI diagnosis and PD grading (r=0,4937, p<0,0001). The split analysis of peculiar parameters of imaging between the two methods also showed significant correlation: periarticular vascularity showed correlation with post-contrast MRI evidence of posterior capsulitis and enthesitis (p=0,001), as SIJs BME correlated with intra-articular PD signals (p<0,001). RI from SWA analysis was inversely correlated with MRI diagnosis of active SI (p<0.0001). SIJs PD demonstrated a significant correlation with SIJs pain (p<0,001), but not with inflammatory reactants, GEC, peripheral synovitis, and a weak correlation with BUSES (p=0,038).
Conclusion: SIJs PDUS/SWA may be an optional method for preliminary screening of active SI, as a feasible, cheap and an accurate diagnostic tool, compared with MRI as a gold standard for nr-Axial SpA. PD US in SI. Right SI joint with a PD signal within inter-osseous ligament (curved arrow), where spectral PD analysis shows a RI of 0,62. Normal vessels (with high RI, unshowed) can be observed into the first sacral foramen (arrowhead). The first sacral apophysis (arrow) protrudes from the sacrum profile.



Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.998

POS0964

CHARACTERISTICS AND BURDEN OF DISEASE IN PATIENTS WITH RADIOGRAPHIC VERSUS NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN THE ANKYLOSING SPONDYLITIS REGISTRY OF IRELAND COHORT

S. Quinn[1], S. Maguire[2], F. B. O'shea[2], L. O'neill[1], E. Molloy[1], U. Fearon[3], P. Gallagher[1], D. Veale[1]. *[1]St. Vincent's University Hospital, Rheumatology, Dublin, Ireland*; *[2]St James's Hospital, Rheumatology, Dublin, Ireland*; *[3]Trinity Biomedical Sciences Institute, Molecular Rheumatology, Dublin, Ireland*

Background: Axial spondyloarthritis (axSpA) is an umbrella term for types of inflammatory arthritis that primarily affect the spine and the sacroiliac joints. It is comprised of patients with both radiographic (r-axSpA) and non-radiographic features (nr-axSpA). R-axSpA was historically known as Ankylosing Spondylitis. Previous studies have shown the burden of disease to be largely similar in patients with radiographic versus non-radiographic axial spondyloarthritis in cohorts both in the US and Europe [1]. The Ankylosing Spondylitis Registry of Ireland (ASRI) was formed with the objective to measure the burden of axial spondyloarthritis in the population and identify early predictors of a poor outcome. All patients in the registry are 18 years or older and meet Assessment of Spondyloarthritis International Society (ASAS) criteria for a diagnosis of SpA.
Objectives: To compare the characteristics and burden of disease in patients with radiographic versus non-radiographic axial spondyloarthritis in the ASRI cohort.
Methods: Patients with radiographic axial spondyloarthritis (r-axSpA) were defined as those with x-ray evidence of sacroiliitis. Patients with non-radiographic axial spondyloarthritis (nr-axSpA) were defined as having MRI evidence of sacroiliitis but no x-ray evidence of sacroiliitis. A standardised clinical assessment was performed on each patient and structured interviews provided patient-reported data. For each patient the following scores were captured: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), Health Assessment Questionnaire (HAQ) assesses the self-reported functional status for performing activities of daily living, and the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire. Categorical variables were summarized as percentages with frequency counts, and continuous variables with a mean and standard deviation. Statistical comparisons between subgroups were evaluated using 2 sample t-tests for continuous variables and chi-square tests for categorical variables.
Results: 764 patients were available for analysis. Analysis of radiographic status showed 88.1% (n=673) of patients with r-axSpA and 11.9% (n=91) with nr-axSpA. Patients with nr-axSpA were younger (41.3 vs. 46.6 years, p<0.01), had shorter disease duration (14.8 vs. 20.2 years, p<0.01), lower proportion of males (66.6% vs. 78.4%, p=0.02) with lower rates of HLA-B27 positivity (73.6% vs. 90.5%, p<0.01). The nr-axSpA group had lower BASDAI (3.37 vs. 4.05, p=0.01), BASFI (2.46 vs. 3.88, p<0.01), BASMI (2.33 vs. 4.34, p<0.01), ASQoL (5.2 vs. 6.67, p=0.02), and HAQ scores (0.38 vs. 0.57, p<0.01). There were no significant differences in the prevalence of extra-articular manifestations.
Conclusion: This study provides evidence that the burden of disease is less in patients with non-radiographic axial spondyloarthritis than radiographic axial spondyloarthritis, as demonstrated by better BASDAI, BASFI, BASMI, HAQ and ASQoL scores.

REFERENCES:

[1] López-Medina C, et al. Characteristics and burden of disease in patients with radiographic and non-radiographic axial Spondyloarthritis: a comparison by systematic literature review and meta-analysis. RMD Open, 2019. 5(2) p1108.

Table 1.

	r-axSpA	nr-axSpA	*p value*
n	673	91	
Age (years)	46.6 (+/-12.4)	41.3 (+/-12.4)	<0.01
Disease duration (years)	20.2 (+/-12.4)	14.8 (+/-11.7)	<0.01
Delay to diagnosis (years)	8.41 (+/-8.6)	6.34 (+/-7.2)	0.03
Males	78.8% (528)	65.9% (60)	0.02
Females	21.5% (145)	34.1% (31)	0.02
HLA-B27+	90.50% (440 of 486 available results)	73.60% (53 of 72 available results)	<0.01
BASDAI	4.05 (+/-2.39)	3.37 (+/-2.31)	0.01
BASFI	3.88 (+/-3.00)	2.46 (+/-2.39)	<0.01
BASMI	4.34 (+/-2.08)	2.33 (+/-1.42)	<0.01
ASQoL	6.67 (+/-5.55)	5.2 (+/-5.53)	0.02
HAQ	0.57 (+/-0.54)	0.38 (+/-0.44)	<0.01
Psoriasis	17.8% (120)	15.4% (14)	0.31
IBD	11% (74)	8.8% (8)	0.58
Uveitis	33.9% (228)	34.1% (31)	0.54

Disclosure of Interests: Sean Quinn: None declared, Sinead Maguire: None declared, Finbar Barry O'Shea: None declared, Lorraine O'Neill: None declared, Eamonn Molloy: None declared, Ursula Fearon Speakers bureau: Abbvie, Grant/research support from: Janssen, Abbvie, Pfizer, UCB, Phil Gallagher: None declared, Douglas Veale Speakers bureau: AbbVie, BMS, Celgene, Pfizer, MSD, Roche, Consultant of: AbbVie, Actelion, BMS, Novartis, Pfizer, MSD, Roche, Regeneron/Sanofi, Grant/research support from: AbbVie, Pfizer, MSD, Novartis, Roche, Janssen.
DOI: 10.1136/annrheumdis-2021-eular.1056

POS0965

ARE SMOKING AND ALCOHOL ASSOCIATED WITH PERIPHERAL MUSCULOSKELETAL INVOLVEMENT IN PATIENTS WITH SPONDYLOARTHRITIS? RESULTS FROM THE ASAS-PERSPA STUDY

M. L. Ladehesa Pineda[1], R. Ortega Castro[1], M. Á. Puche Larrubia[1], M. Dougados[2], E. Collantes Estevez[1], C. López-Medina[1,2]. *[1]Córdoba, Rheumatology Department, Reina Sofia University Hospital, IMIBIC, University of Córdoba, Córdoba, Spain, Córdoba, Spain*; *[2]Paris, Rheumatology Department, Cochin Hospital, Paris, France, Paris, France*

Background: The harmful effect of smoking on axial spondyloarthritis (axSpA) in relation to radiographic progression is well known, but there are controversies around the role of cigarettes in other manifestations of SpA, such as peripheral involvement. Besides, it has been observed an inverse association between alcohol consumption and disease activity and functional impairment[1], although it is still unclear its association with peripheral manifestations of SpA.
Objectives: To evaluate the association between smoking/alcohol intake and the prevalence of peripheral articular manifestations (arthritis, enthesitis or dactylitis).
To assess the association between smoking/alcohol intake and the location of such manifestations.
Methods: Patients from the cross-sectional ASAS-PerSpA study with available data for both the smoking status and alcohol intake were included. Mixed logistic regressions using the peripheral manifestation (or location) as dependent variable, the smoking status or alcohol intake as fixed effect and the country as random effect were used. The interaction between smoking and alcohol was tested.
Results: A total of 4451 patients with either axSpA, peripheral SpA or Psoriatic Arthritis were included. 59.5% had smoked at any moment and 42.7% had been alcohol drinkers. Patients who had ever suffered arthritis showed lower frequency of smoking habit (OR 0.72, 95%CI 0.63-0.82) and lower alcohol intake (OR 0.82, 95%CI 0.71-0.94) (Table 1). Among patients with arthritis, smoking was associated with predominantly upper limbs vs. lower limbs involvement (OR 0.78, 95%CI 0.65-0.94), while alcohol was associated with predominant mono/oligoarticular vs. polyarticular involvement (OR 1.13, 95%CI 0.94-1.36).
Patients who had ever suffered enthesitis also showed lower frequency of smoking habit and alcohol intake (OR 0.75, 95%CI 0.63-0.89 and OR 0.69, 95%CI 0.57-0.83, respectively). No association was found with regard to the prevalence of dactylitis.
At the moment of the study visit, 20.4% patients were current smokers and 32.2% consumed alcohol. Current alcohol intake was associated with lower prevalence of current arthritis (26.9% vs. 33.6% (OR 0.76, 95%CI 0.64-0.91) and current enthesitis (21.1% vs. 34.6% (OR 0.78, 95%CI 0.62-0.96), while current smoking did not show significant differences.
No interaction was found in the association between alcohol and tobacco with regard to the prevalence of peripheral symptoms in the past. However, when assessing current arthritis, current smoking and no drinking was associated with arthritis in the lower limbs.
Conclusion: These results suggest that, taking into account the country, smoking and alcohol are associated with lower prevalence of peripheral manifestations (arthritis

and enthesitis), with no interaction effect between both habits. Smoking seems to be associated with predominantly upper limbs arthritis while alcohol intake seems to be associated with a predominantly oligo/mono articular involvement. Future studies are required including the influence of psoriasis and psoriatic arthritis in the relationship between alcohol and smoking and its association with peripheral manifestations.

REFERENCES:

[1] Zhao S, Thong D, Duffield SJ, et al. Alcohol and disease activity in axial spondyloarthritis: a cross-sectional study. Rheumatol Int 2018. 38(3):375-381.

Table 1. Association between peripheral musculoskeletal manifestations and smoking and alcohol.

	Peripheral joint disease with objective signs in the past			Peripheral enthesitis with objective signs in the past			Dactylitis in the past		
	Yes 2292	No 2169	OR (95%CI)*	Yes 765	No 3696	OR (95%CI)*	Yes 685	No 3776	OR (95%CI)*
Smoker ever	887 (38.7%)	1013 (46.7%)	**OR 0.72 (0.63-0.82)**	312 (40.8%)	1588 (43.0%)	**OR 0.75 (0.63-0.89)**	277 (40.4%)	1623 (43.0%)	OR 0.89 (0.75-1.06)
Alcohol ever	929 (40.4%)	882 (40.7%)	**OR 0.82 (0.71-0.94)**	276 (36.1%)	1535 (41.5%)	**OR 0.69 (0.57-0.83)**	299 (43.6%)	1512 (40.0%)	OR 1.01 (0.84–1.22)

*Mixed logistic regression using the country as a random effect.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1064

POS0966

IDENTIFICATION OF PATIENTS AFFECTED WITH ANKYLOSING SPONDYLITIS AND INFLAMMATORY BOWEL DISEASE OVERLAP USING COLLAGEN BIOMARKERS

S. Holm Nielsen[1], A. Stahly[2], E. H. Regner[2], A. C. Bay-Jensen[3], M. Karsdal[4], K. A. Kuhn[2]. [1]*Nordic Bioscience & Technical University of Denmark, ImmunoScience, Herlev, Denmark*; [2]*University of Colorado Anschutz Medical Center, Department of Medicine, Division of Rheumatology, Aurora, United States of America*; [3]*Nordic Bioscience, ImmunoScience, Herlev, Denmark*; [4]*Nordic Bioscience, RnD, Herlev, Denmark*

Background: Chronic inflammatory arthritis is a hallmark of Ankylosing Spondylitis (AS), where co-existence of inflammatory bowel disease, such as Crohn's Disease (CD) is prominent. The clinical overlap of AS and CD has raised the hypothesis that these conditions may have similar pathophysiological mechanisms. Both indications are characterized by an altered extracellular matrix turnover, where particularly collagens are remodeled.

Objectives: We investigated the association between biomarkers of collagen degradation in healthy controls and patients with AS, CD and AS/CD overlap, with the aim to investigate the biomarkers' ability to identify patients with AS/CD overlap.

Methods: Patients with AS fulfilling ASAS criteria (n=13), biopsy-proven CD (n=14), subjects with AS and CD overlap (n=10) and healthy controls (n=11) undergoing standard of care colonoscopies were included in the study. The collagen degradation biomarkers measuring type III, IV, VI and X collagen (C3M, C4M, C6M and C10C, respectively) were measured in EDTA plasma samples from all subject groups. Biomarkers were measured by competitive ELISAs. Statistical analysis was performed using an ANCOVA adjusted for age, an AUROC analysis and spearman correlations.

Results: The collagen biomarker C4M was significantly higher in patients with AS/CD overlap compared to AS, CD and HCs (all p<0.0001, Figure 1A). The blood levels of C4M in AS patients were significantly lower than HC (p=0.0003), while CD also showed a lower level compared to HC though not significant (p=0.0798). No difference was found between AS and CD alone. In an AUROC analysis, C4M showed a complete separation between the patients with AS/CD overlap compared to HC, AS and CD with an AUC=1.00; p=0.0001. No differences were found between the patient groups for C3M, C6M and C10C (Figure 1, B-D). 91.3 % of patients with AS, 92.8% of patients with CD and 60 % of patients with AS and IBD overlap were actively treated with TNF-α inhibitors, which may explain the suppression of the collagen degradation biomarker levels in AS, CD and AS/IBD overlap compared to healthy controls[1,2]. No correlations were found between the collagen biomarkers and CRP, BASDAI, SCCAI or HBI scores.

Conclusion: Degradation of type IV collagen quantified by C4M showed a complete separation of patients with AS/IBD overlap, compared to AS, CD and HC patients, which indicates an excessive collagen degradation and epithelial turnover. This biomarker could potentially be used to identify patients affected by both manifestations, and guide treatment decisions.

REFERENCES:

[1] van Haaften WT, Mortensen JH, Dige AK, Grønbæk H, Hvas CL, Bay-Jensen AC, et al. Serological Biomarkers of Tissue Turnover Identify Responders to Anti-TNF Therapy in Crohn's Disease: A Pilot Study. Clin Transl Gastroenterol. 2020;11:e00217.

[2] Siebuhr AS, Bay-Jensen AC, Karsdal MA, Lories RJ, de Vlam K. CRP and a biomarker of type I collagen degradation, C1M, can differentiate anti-inflammatory treatment response in ankylosing spondylitis. Biomark Med. 2016;10:197–208.

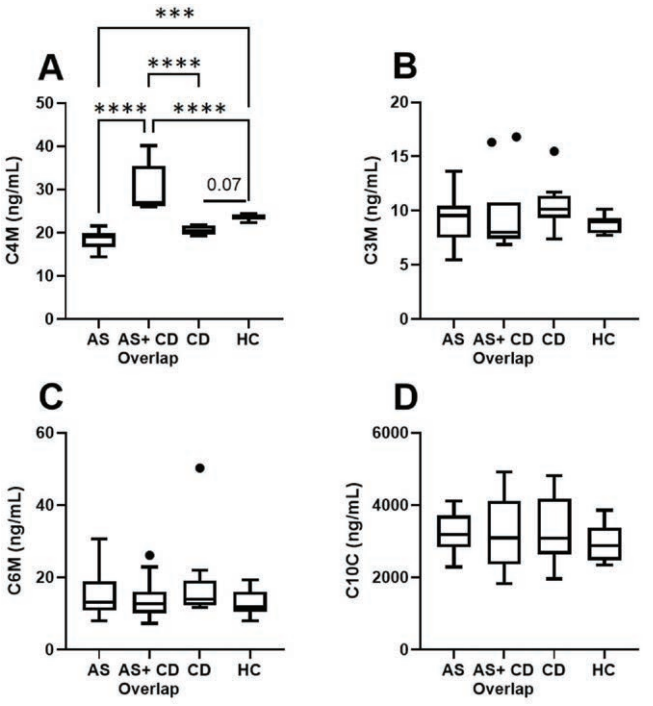


Figure 1. Levels of C4M (A), C3M (B), C6M (C) and C10C (D) in EDTA plasma from patients diagnosed with AS (n=13), CD (n=14), AS and CD overlap (n=10) and HC (n=11). Graphs are presented as Tukey box plots. Statistical significance: ****p<0.0001.

Disclosure of Interests: Signe Holm Nielsen Employee of: Full time PostDoc at Nordic Bioscience and Technical University of Denmark, Andrew Stahly: None declared, Emilie H. Regner: None declared, Anne-Christine Bay-Jensen Shareholder of: Stocks at Nordic Bioscience, Employee of: Full-time employee at Nordic Bioscience, Morten Karsdal Shareholder of: Stocks at Nordic Bioscience, Employee of: Full-time employee at Nordic Bioscience, Kristine A. Kuhn: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1206

POS0967

DESCRIPTION OF SACROILIAC CT FINDINGS IN PATIENTS WITH ANKYLOSING SPONDYLITIS AGED OVER 50 YEARS: PRELIMINARY RESULTS OF THE CASIAGE STUDY

O. Fakih[1], M. Chouk[1], C. Prati[1,2], D. Wendling[1,3], F. Verhoeven[1,2]. [1]*Centre hospitalier régional universitaire de Besançon, Rhumatologie, Besançon, France*; [2]*UFR Santé, Université de Franche-Comté, EA 4267 'PEPITE', Besançon, France*; [3]*UFR Santé, Université de Franche-Comté, EA 4266 'EPILAB', Besançon, France*

Background: Diagnosis of axial spondyloarthritis (SpA) is nowadays commonly made with the help of pelvic radiography or MRI. However, there is an important inter-observer variability for radiographs, and MRI is subject to possible false positives, and is not the best modality for studying structural lesions. Conversely, pelvic CT has an excellent specificity and appears to be more effective than radiography for the diagnosis of SpA [1]. However, CT findings in patients over 50 years of age have not been studied.

Objectives: To describe sacroiliac (SI) joint CT characteristics in patients with ankylosing spondylitis (AS), aged 50 years or older.

Methods: An observational, cross sectional study was performed using medical records from Besançon University Hospital's rheumatology department, which were screened to identify patients with AS. A search was then carried out for patients over 50 years old in the hospital's imaging archiving system to identify those who had benefited from a CT which included the SI joints in their entirety. Non-inclusion criteria were the existence of pelvic bone lesions and a history of pelvic radiotherapy. For each patient, CT was interpreted using a score previously used by Diekhoff et al. [2], dividing each SI joint into 12 regions, for each of which joint space narrowing (JSN), erosions, and sclerosis are assessed. For this study, we also observed the existence of

intra-articular gas and diffuse idiopathic skeletal hyperostosis (DISH) lesions for each region. Quantitative variables are expressed as mean ± standard deviation, qualitative variables as numbers and percentages. Wilcoxon rank-sum test was used to determine factors associated with a higher CT score.

Results: A total of 66 patients were included. Mean (SD) age was 65.10 ± 10.59 with a mean (SD) duration of disease of 22.87 ± 14.95 years. 60.29% were male, and 87.04 % were HLA-B27 positive. 40.30% had a bamboo spine. CT findings are described in Table 1. The vast majority of patients have a positive JSN score but significant erosions are found in only a minority of cases. This is partly explained by the fact that 55.9% of the patients had at least one complete bilateral ankylosis (and therefore no erosions) on one of the three slices studied. Bilateral anklylosis was associated with a longer duration of disease (p<0.001) and presence of bamboo spine (p<0.001). Also noteworthy is the low proportion of DISH compared to the general population in this age group, which is 15-25%. Factors associated with a higher total CT score were male sex (p=0.017), longer duration of disease (p<0.001), tobacco use (p=0.033), presence of bamboo spine (p=0.004), absence of DISH (p=0.045) and absence of intra-articular gas (p<0.001). The distribution of lesions appeared to be homogenous over all 24 regions studied (Figure 1).

Conclusion: CT findings in AS patients over 50 years of age are mostly represented by changes in joint space, with bilateral ankylosis present in half of the patients. AS appears to be a protective factor for DISH.

REFERENCES:

[1] Devauchelle-Pensec V, D'Agostino MA, Marion J, *et al.* Computed tomography scanning facilitates the diagnosis of sacroiliitis in patients with suspected spondylarthritis: Results of a prospective multicenter French cohort study. *Arthritis Rheum* 2012;**64**:1412–9. doi:10.1002/art.33466

[2] Diekhoff T, Hermann K-GA, Greese J, *et al.* Comparison of MRI with radiography for detecting structural lesions of the sacroiliac joint using CT as standard of reference: results from the SIMACT study. *Ann Rheum Dis* 2017;**76**:1502–8. doi:10.1136/annrheumdis-2016-210640

Table 1. Sacro-iliac CT findings using a score modified from Diekhoff et al.

Mean total score (range 0-108)	70.36±38.90
Presence of joint space narrowing	58 (85.29 %)
Presence of erosion	20 (29.41 %)
Presence of sclerosis	15 (22.06 %)
Presence of Intra-articular gas	22 (32.35 %)
Presence of DISH	3 (4.41 %)

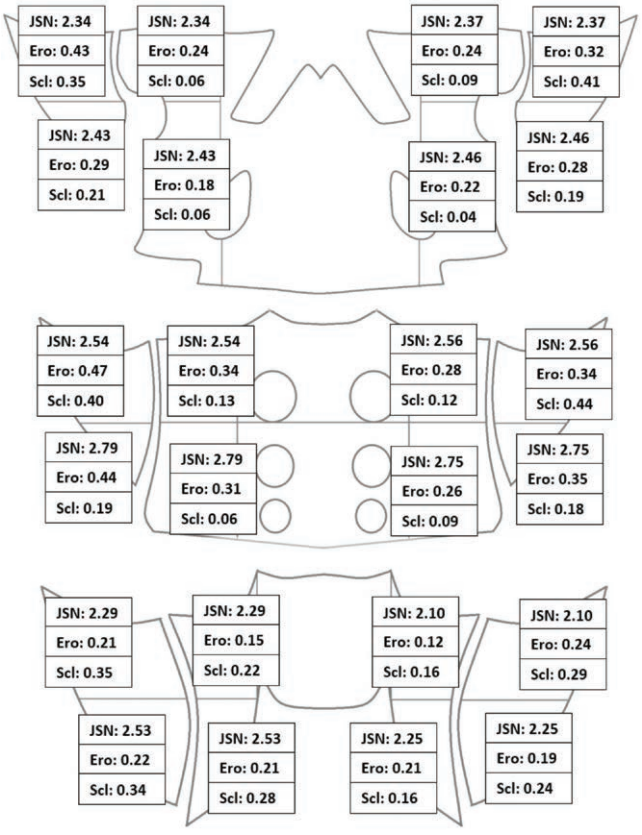


Figure 1. Mean scores per region in the anterior, central and posterior SI slices (JSN: joint space narrowing (0-4), Ero: erosions (0-3), Scl: sclerosis (0-2)).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1211

POS0968

ARE THERE CLUES FOR THE SCREENING OF SPONDYLOARTHRITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES?

B. Farisoğulları[1], O. Keskin[2], B. Usta[3], G. K. Yardımcı[1], E. Parlak[2], T. Kav[2], O. Karadag[1], U. Kalyoncu[1]. [1]*Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; [2]*Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Gastroenterology, Ankara, Turkey*; [3]*Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Ankara, Turkey*

Background: SpA is the most frequent extra-intestinal manifestation in patients with IBD (1). Questioning IBD patients in terms of SpA and referring patients to the rheumatology clinic is important for early diagnosis and treatment management.

Objectives: We aimed to diagnose SpA early by using the DETAIL questionnaire to IBD patients and to compare it with the study validated for each question (2).

Methods: In the Hacettepe University Gastroenterology Clinic, patients with IBD were questioned for musculoskeletal symptoms between March 2019 and September 2020. For this purpose, a validated DETAIL questionnaire consisting of 6 questions was asked. Patients with at least 1 positive out of 6 questions were consulted in the rheumatology clinic, and patients were evaluated for SpA by physical examination, laboratory, and imaging. For each question in the detection of arthritis in inflammatory bowel diseases (DETAIL) questionnaire, sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio (LR) were calculated.

Results: 217 IBD patients were included in the study. Twenty patients with previously known rheumatologic diseases were excluded from the study. 49 (24%) of the remaining 197 patients had a positive answer to at least one question in the DETAIL query. 39 (20%) of these patients were evaluated in the rheumatology clinic, and 16 (8.1%) of them were diagnosed with SpA (spondylitis: 9, peripheral arthritis: 7) (Figure 1). In the DETAIL questionnaire, two patients answered 5/6 yes, five patients answered 4/6 yes, eleven patients answered 3/6 yes, ten patients answered 2/6 yes, and eleven patients answered 1/6 yes. In the six items of DETAIL, the best performances in discriminating patients affected by SpA were found in the second and fourth questions (LR + 2.9 and 1.57, respectively) (Table 1).

Conclusion: 41% of IBD patients who answered yes to at least one question in the DETAIL questionnaire were diagnosed with SpA. Especially those with sausage fingers or low back pain for at least 3 months seem more likely probability to be diagnosed with SpA. Unlike the validated study, the probability of having diagnosis of SpA was not observed in questions five and six, which questioning the inflammatory back pain parameters. The DETAIL questionnaire may be used as a useful screening tool for the detection of SpA.

REFERENCES:

[1] Fragoulis GE et al. Inflammatory bowel diseases and spondyloarthropathies: From pathogenesis to treatment. World J Gastroenterol. 2019;25(18):2162-76.

[2] Benfaremo D et al. Multicenter validation of the DETAIL questionnaire for the screening of spondyloarthritis in patients with inflammatory bowel diseases. The Journal of Rheumatology, 2020.

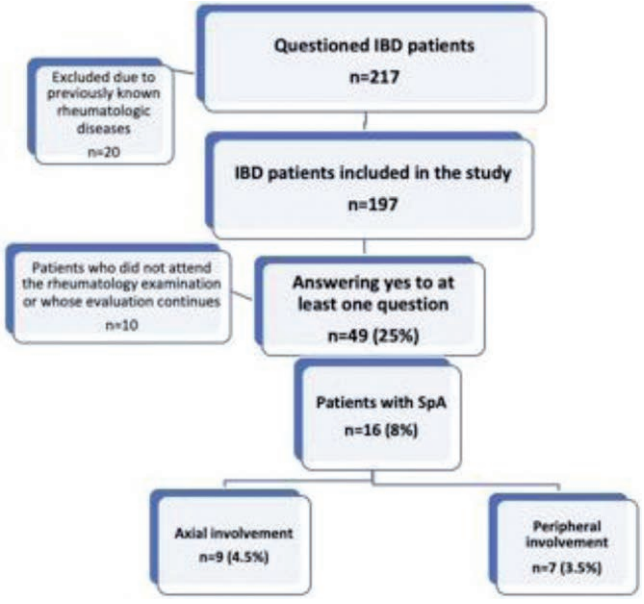


Figure 1. Flow chart of IBD patients in the study

Table 1. Sensitivity, specificity, positive and negative predictive values, likelihood ratios of the DETAIL questionnaire both in our study and in the other study

DETAIL questionnaire

Questions	Sensitivity (%)		Specificity (%)		Positive predictive value (%)		Negative predictive value (%)		Positive likelihood ratio		Negative likelihood ratio	
	Current study	Other study	Current study	Other study	Current study	Other study	Current study	Other study	Current study	Other study	Current study	Other study
1. Have you ever had a finger or a toe and/or another joint swollen and painful for no apparent reason?	68.8	69.6	34.8	67.7	42.3	41	61.5	87.3	1.05	2.16	0.9	0.45
2. Occasionally, has an entire finger or toe becomes swollen, making it look like a 'sausage'?	12.5	27.4	95.7	89.2	66.7	45.1	61.1	79.2	2.9	2.55	0.91	0.81
3. Have you had pain in your heels?	43.6	45.1	56.5	86.3	41.2	51.6	59.1	82.9	1.01	3.3	0.99	0.64
4. Have you ever had back pain lasting at least 3 months that was not injury related?	75	77.4	52.2	73.4	52.2	48.4	75	90.9	1.57	2.9	0.48	0.31
5. Do you have low back pain in the morning and/or after resting that improves with exercise?	43.6	82.3	56.5	67.7	41.2	45.1	59.1	92.2	1.01	2.5	0.99	0.26
6. Do you wake up at night because of low back pain?	18.8	54.9	78.3	85.4	37.5	54.9	58.1	85.4	0.87	3.7	1.04	0.53

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1231

POS0969

UNVEILING AXIAL INVOLVEMENT IN PSORIATIC ARTHRITIS: AN ANCILLARY ANALYSIS OF THE ASAS-PERSPA STUDY

D. Benavent[1], C. Plasencia[1], D. Poddubnyy[2], M. Kishimoto[3], F. Proft[2], H. Sawada[4], C. López-Medina[5,6], M. Dougados[5,7], V. Navarro-Compán[1].
[1]Hospital Universitario la Paz-IdiPaz, Rheumatology Service, Madrid, Spain; *[2]Charité Universitätsmedizin Berlin, Department of Gastroenterology, Infectiology and Rheumatology, Berlin, Germany*; *[3]Kyorin University School of Medicine, Department of Nephrology and Rheumatology, Tokyo, Japan*; *[4]Juntendo University School of Medicine, Department of Internal Medicine and Rheumatology, Tokyo, Japan*; *[5]Hôpital Cochin. Assistance Publique- Hôpitaux de Paris, Rheumatology Department, Paris, France*; *[6]Reina Sofia University Hospital, IMIBIC, University of Córdoba, Rheumatology Department, Córdoba, Spain*; *[7]INSERM U1153, Clinical Epidemiology and Biostatistics, Paris, France*

Background: Heterogeneity in psoriatic arthritis (PsA) is a current matter of discussion, especially concerning axial involvement.
Objectives: To determine the profile of axial PsA (axPsA) in a worldwide setting. Secondly, to identify predictive factors associated with the development of axial involvement in patients with PsA.
Methods: Data from 3684 patients with axial spondyloarthritis (axSpA) or PsA from the ASAS-PerSpA study were analysed. The ASAS-PerSpA is an observational, cross-sectional study that recruited consecutive patients with SpA from 68 centers worldwide. For this analysis, 367 PsA patients ever presenting axial involvement according to their rheumatologist were defined as axPsA and compared with 2651 axSpA patients, using logistic regression to later identify predictive factors for rheumatologist diagnosis of axPsA. In addition, the axPsA patients were also compared with 666 PsA patients without axial involvement (pPsA) and the characteristics associated with axial manifestations were determined by logistic regression analysis.
Results: Among all patients, 2651 were identified as axSpA and 1033 patients as PsA. Among those with axial involvement, 2651 were identified as axSpA (100% of axSpA) and 367 as axPsA (35.5 % of PsA). In comparison with axSpA, axPsA patients were less frequently males, older, less frequently HLA-B27 positive and had a higher body mass index (Table 1). Additionally, while patients with axPsA had more peripheral manifestations and psoriasis, concomitant IBD and uveitis were higher in axSpA. In the multivariable analysis, older age at diagnosis (OR= 1.04), peripheral arthritis (OR= 7.32) and dactylitis (OR= 2.82) were significantly associated with a diagnosis of axPsA. However, uveitis (OR= 0.22), IBD (OR= 0.12) or HLA*B27 carriership (OR= 0.26) were inversely associated with axPsA diagnosis as compared to axSpA. Furthermore, axial involvement in patients with PsA was significantly associated with male gender (OR= 1.68), elevated CRP (OR= 2.87), and the absence of psoriasis (OR= 0.33).
Conclusion: In this worldwide setting, axPsA was defined by rheumatologists as a unique phenotype, with disease features lying between axSpA and pure pPsA. Male gender, elevated CRP and the absence of psoriasis were associated with axial involvement in patients with PsA.

Table 1. Demographic and disease characteristics of patients with axial involvement included in the ASAS PerSpA study. Results shown as absolute numbers (percentages) or as the mean ± standard deviation

	axSpA n= 2651	axPsA n= 367	p-value
Sex (male)	1816 (68.5)	196 (53.4)	<0.001
Age at study visit	42.1(13.0)	50.0 (12.7)	<0.001
Body Mass Index	25.9 (5.1)	27.4 (5.7)	<0.001
Family history of SpA	944 (35.6)	135 (36.8)	0.684
Past history or current symptoms of back pain	2625 (99.0)	358 (97.5)	0.04
Inflammatory back pain (ASAS definition), n/N(%)	2500/2632 (94.9)	317/362 (87.6)	<0.001
Sacroiliitis on imaging, n/N (%) by:			
xRay mNY criteria	1997/2586 (77.2)	185/298 (62.1)	<0.001
MRI-SIJ, ASAS definition	1449/1757 (82.4)	141/225 (62.6)	<0.001
mNY criteria or ASAS definition	2446/2634 (92.9)	243/339 (71.7)	<0.001
HLA B27 positive	1674 /2126 (78.7)	54/182 (29.6)	<0.001
Elevated CRP (>5 mg/dL)	1863/2569 (72.5)	274/356 (76.9)	0.2
Classification criteria			
ASAS criteria	2339 (88.2)	185 (50.4)	<0.001
CASPAR criteria	123 (4.6)	274 (74.4)	<0.001
Peripheral Arthritis	946 (35.7)	318 (86.6)	<0.001
Enthesitis	1086 (41.0)	198 (54.0)	<0.001
Dactylitis	155 (5.8)	125 (34.1)	<0.001
Psoriasis	185 (7.0)	324 (88.3)	<0.001
IBD	129 (4.9)	3 (0.8)	<0.001
Uveitis	576(21.7)	13 (3.5)	<0.001
csDMARD (ever)	1359 (51.3)	339 (92.4)	<0.001
bDMARD (ever)	1585 (59.8)	263 (71.7)	<0.001
Specific drug for axial involvement			
NSAIDs	2465 (98.6)	317 (96.1)	0.002
csDMARD	828 (33.1)	187 (56.7)	<0.001
bDMARD	1288 (51.5)	180 (54.4)	0.32

axSpA: axial spondyloarthritis; axPsA: axial psoriatic arthritis; IBD: Inflammatory Bowel Disease; CRP: C-Reactive Protein; mNY: modified New York; csDMARDs: conventional synthetic DMARDs; bDMARDs: biological DMARDs; NSAID: Non-steroidal anti-inflammatory drugs

Disclosure of Interests: Diego Benavent: None declared, Chamaida Plasencia: None declared, Denis Poddubnyy: None declared, Mitsumasa Kishimoto Consultant of: AbbVie, Amgen-Astellas BioPharma, Asahi-Kasei Pharma, Astellas, Ayumi Pharma, BMS, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Kyowa Kirin, Novartis, Ono Pharma, Pfizer, Tanabe-Mitsubishi, Teijin Pharma, and UCB Pharma., Fabian Proft Grant/research support from: AbbVie, AMGEN, BMS, Celgene, MSD, Novartis, Pfizer, Roche, UCB, Haruki Sawada: None

declared, Clementina López-Medina: None declared, Maxime Dougados: None declared, Victoria Navarro-Compán: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1410

POS0970 ASSESSMENT OF THE ASSOCIATION BETWEEN ESTIMATED CARDIOVASCULAR RISK AND MASEI INDEX IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

I. C. Aranda-Valera[1,2,3], I. Gómez García[1,2,3], M. L. Ladehesa Pineda[1,2,3], M. C. Ábalos-Aguilera[1,2,3], C. López-Medina[1,2,3], E. Collantes Estevez[1,2,3]. [1]*Reina Sofía Hospital, Rheumatology Service, Córdoba, Spain*; [2]*IMIBIC, Rheumatology Service, Córdoba, Spain*; [3]*University of Córdoba, Rheumatology Service, Córdoba, Spain*

Background: It has been shown that the cardiovascular risk (CV) in spondyloarthritis (SpA) patients is higher than that of the general population. Furthermore, an association has recently been described between structural damage at the axial level and an increase in estimated CV risk [1].
Objectives: To evaluate the association between the estimated cardiovascular risk (CV) and the presence of subclinical atherosclerosis with the MASEI index (Madrid Sonographic Enthesis Index) in patients with axial spondyloarthritis (Ax-SpA) as an expression of peripheral enthesitis.
Methods: Cross-sectional study performed in 103 patients with ax-SpA from the Córdoba AxSpA Task force, Registry and Outcomes (CASTRO), in which patients undergoing treatment with biological therapy and with a previous history of CV event were excluded. Clinical data, disease activity data and factors related to CV risk were collected, as well as the presence of persistently elevated CRP levels in the five years prior to the study visit. The SCORE index was calculated, as well as the thickness of the carotid intima media (CIMT) and the MASEI index, both measured by ultrasound. The association between MASEI-SCORE and MASEI-atheroma plaques was evaluated using generalized linear models (GLM), adjusted for time of evolution of the disease, disease activity and smoking.
Results: Of the patients included, 35 were men (34.0%), with a mean age of 45.2 (±12.1) years and time of evolution of the disease of 18.5 (±13.0) years. The mean MASEI score was 13.6 (±9.1), and the mean SCORE score was 8.1 (±8.9). The GLM regressions showed that the MASEI was independently associated with the SCORE (coefficient β 0.22; 95% CI 0.02-0.43) adjusted for the duration of the disease, smoking, and the presence of persistent CRP (Table 1A). The MASEI index was also significantly associated with the CIMT, although these differences disappeared when the model was adjusted for other factors (Table 1B).

Table 1. A. Association between MASEI and SCORE adjusting for disease duration, smoking status and CRP.

	Crude model		Adjusted for disease duration		Adjusted for disease duration and smoking		Adjusted for disease duration, smoking and CRP	
	β *coefficient (95%CI)*	**p-value**	β *coefficient (95%CI)*	**p-value**	β *coefficient (95%CI)*	**p-value**	β *coefficient (95%CI)*	**p-value**
MASEI	0.37 (0.20-0.55)	<0.001	0.25 (0.08-0.42)	0.006	0.25 (0.09-0.42)	0.004	0.22 (0.02-0.43)	0.039

Conclusion: In patients with ax-SpA, peripheral enthetic damage measured by the MASEI index is associated with an increase in estimated CV risk independently of the time of evolution, smoking and levels of CRP.
REFERENCES:
[1] Ladehesa-Pineda ML, Arias-de la Rosa I, López-Medina C, et al. Assesment of the relationship between estimated cardiovascular risk and structural damage in patients with axial spondyloarthritis. Ther Adv Musculoskelet Dis 2020;12:1-15

Table 1. B. Association between MASEI and intima media thickness (IMT) adjusting for disease duration, smoking status and CRP.

	Crude model		Adjusted for disease duration		Adjusted for disease duration and smoking		Adjusted for disease duration, smoking and CRP	
	β *coefficient (95%CI)*	**p-value**	β *coefficient (95%CI)*	**p-value**	β *coefficient (95%CI)*	**p-value**	β *coefficient (95%CI)*	**p-value**
MASEI	*0.01 (0.00-0.01)*	0.041	*0.003 (-0.01-0.004)*	0.178	*0.002 (-0.001-0.004)*	0.149	*0.002 (-0.001-0.005)*	0.226

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1525

POS0971 HOW DO CLINICAL AND SOCIOECONOMIC FACTORS IMPACT ON WORK DISABILITY IN EARLY AXIAL SPONDYLOARTHRITIS? FIVE-YEAR DATA FROM THE DESIR COHORT

E. Nikiphorou[1,2], A. Boonen[3,4], B. Fautrel[5], P. Richette[6], R. B. M. Landewé[7,8], D. Van der Heijde[9], S. Ramiro[7,9]. [1]*King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; [2]*King's College Hospital NHS Trust, Rheumatology, London, United Kingdom*; [3]*Maastricht University Medical Center and Care and Public Health Research Institute (CAPHRI), Rheumatology, Maastricht, Netherlands*; [4]*Academic Hospital Maastricht, Internal Medicine, Division of Rheumatology, Maastricht, Netherlands*; [5]*Sorbonne University – Assistance Publique Hopitaux de Paris, Pitie Salpetriere Hospital, Pierre Louis Institute for Epidemiology and Public Health, INSERM UMRS 1136, PEPITES Teams, Rheumatology, Paris, France*; [6]*Université de Paris, Hopital Lariboisière, Rheumatology, Paris, France*; [7]*Zuyderland MC, Rheumatology, Heerlen, Netherlands*; [8]*Amsterdam University Medical Center, Rheumatology, Amsterdam, Netherlands*; [9]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*

Background: There remains substantial unmet need to study work disability (WD) in early axSpA. Previous studies suggest that treatment interventions alone do not improve work outcomes and that socioeconomic (SE) as well as clinical factors may play an important role.
Objectives: To investigate the occurrence of WD and the impact of clinical and SE factors on WD in early axial spondyloarthritis (axSpA).
Methods: Patients with a clinical diagnosis of axSpA from the DESIR cohort up to 5 years of follow-up (6-month visits in the first 2 years, followed by annual visits) were studied. Time to WD and potential baseline and time-varying predictors were explored, with a focus on SE variables: age, gender, smoking status since last visit, ethnicity (Caucasian vs other), job type based on 'collar' (blue vs white), educational status (low vs high -university), marital status (married vs not) and parental status (number of children); and clinical factors: disease activity (ASDAS/BASDAI), function (BASFI), mobility (BASMI), at each time point. The incidence of WD was calculated as the number of WD events over the total number of person-days under observation. Univariable analyses, followed by collinearity and interaction tests, guided subsequent multivariable Cox survival analyses.
Results: A total of 704 axSpA patients with work-related data, mean (SD) age 33.8 (8.6), were studied. The estimated incidence of WD amongst those at risk and across the five years of DESIR, was 0.05 (95% CI 0.03, 0.06) per 1000 days (total person-days of observation of 999,999). Mean (SD) time to WD was 976 days (SD 476), (min 163, max 2021 days). In people who developed WD, 25% did so at 595 days; 50% and 75% at 1050 and 1433 days, respectively. Significant differences in age, level of education, marital and parental status as well as disease activity, function and mobility, all at baseline, were seen between those developing WD vs those who never did. In multivariable models (Table 1), older age, higher ASDAS and BASFI all strongly predicted more WD (p<0.005). In separate models adjusted for age, gender and education, BASFI and BASMI both predicted WD. SE factors, including education attained, were not associated with a risk for WD. There were no relevant interactions between clinical variables and SE factors.

Table 1. Univariable and multivariable model analyses with WD as outcome.

Type of analysis	**Univariable**	**Multivariable model Focus on ASDAS**	**Multivariable model Focus on BASFI/ BASMI**
	HR (95% CI)	**HR (95% CI) (N=653)**	**HR (95% CI) (N=639)**
Explanatory variables			
Age	1.07 (1.04, 1.11)	1.06 (1.02, 1.10)	1.03 (0.99, 1.08)
Male gender	0.68 (0.37, 1.23)	1.10 (0.58, 2.08)	1.00 (0.50, 2.02)
High education	0.25 (0.14, 0.48)	0.57 (0.29, 1.11)	0.42 (0.19, 0.90)
Parental status	1.36 (1.09, 1.70)	NS	NS
ASDAS (CRP)	2.40 (1.77, 3.26)	1.79 (1.27, 2.54)	Not tested
BASFI, 0-10	1.54 (1.36, 1.75)	1.42 (1.22, 1.65)	1.53 (1.29, 1.81)
BASMI, 0-10	2.13 (1.65, 2.75)	NS	1.49 (1.10, 2.00)
Symptom duration	0.79 (0.56, 1.12)	NS	NS
HLA B27 positive	0.64 (0.36, 1.13)	NS	NS
Hip involvement (baseline) vs not	1.98 (1.02, 3.82)	NS	NS
Comorbidity count	2.33 (1.68, 3.21)	NS	NS
NSAID use last 6m (vs no use)	1.01 (1.00, 1.02)	NS	NS
Oral Corticosteroid use (vs no)	2.72 (1.27, 5.83)	NS	NS
csDMARD use last 6m (vs no)	2.20 (0.90, 5.41)	NS	NS
TNFi use	2.15 (1.19, 3.87)	NS	NS

NS=Not significant

Conclusion: In this early axSpA cohort, WD was an infrequent event. Nevertheless, clinical factors are amongst the strongest predictors of WD, over SE factors,

with worse disease activity, function and mobility all independently implicated with more WD in early axSpA. Disease severity remains a strong predictor of adverse work outcome, despite substantial advances in therapeutic strategies in axSpA.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1596

POS0972 CLUSTER ANALYSIS OF ANKYLOSING SPONDYLITIS PATIENTS REVEALS DIFFERENTIAL DRUG SURVIVAL OF ANTI-TNF AGENTS ACCORDING TO DISTINCT CLINICAL PHENOTYPE

S. Lee[1], S. Y. Kang[1], Y. H. Eun[1], H. Kim[1], H. S. Cha[1], E. M. Koh[1], J. Lee[1].
[1]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medicine, Seoul, Korea, Republic of (South Korea)*

Background: Previous studies using cluster analysis technique in ankylosing spondylitis (AS) patients have consistently identified distinct groups of patients in terms of their clinical characteristics: those with pure axial symptoms and those with a high frequency of peripheral manifestations [1,2]. Due to the cross-sectional nature of these studies, however, prognostic information such as drug survival of anti-TNF agents in these group were not provided.
Objectives: Using the data retrieved from Korean College of Rheumatology Biologics (KOBIO) registry, which includes longitudinal data of AS patients using anti-TNF agents, this study aims to perform cluster analysis to differentiate AS patients in terms of clinical phenotypes and to examine the differential drug survival of anti-TNF agents in these groups.
Methods: Clinical characteristics and demographic data of AS patients in KOBIO registry were analyzed using hierarchical clustering analysis. After clustering, drug survivals of anti-TNF agents were compared between these groups.
Results: 1,046 patients were included in the study with no missing data. The hierarchical cluster analysis classified patients in two groups; one with predominant isolated axial manifestations (axial group, n=823) and the other with more frequent extra-axial symptoms (extra-axial group, n=223). Almost all extra-axial symptoms (peripheral arthritis, enthesitis, uveitis, dactylitis, and psoriasis) were more frequently observed in extra-axial group than axial group. In addition, patients with shorter disease duration, late disease onset, and high disease activity were classified in extra-axial group (Table 1). Interestingly, the extra-axial group had lower drug survival probability than the axial group (p=0.008, Figure 1).
Conclusion: Cluster analysis of AS patients using anti-TNF agents classified two distinct groups of patients in terms of their clinical phenotypes and revealed that the patients with prominent extra-axial manifestations had lower drug survival with anti-TNF agents.

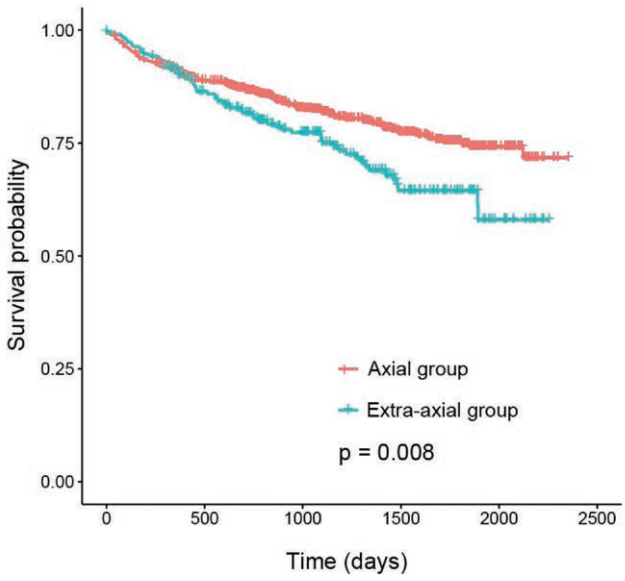
REFERENCES:

[1] Costantino F, et al. Two Phenotypes Are Identified by Cluster Analysis in Early Inflammatory Back Pain Suggestive of Spondyloarthritis: Results From the DESIR Cohort. Arthritis Rheumatol. 2016 Jul;68(7):1660-8.
[2] Porcher R, et al. Two major spondylarthropathy phenotypes are distinguished by pattern analysis in multiplex families. Arthritis Rheum. 2005 Apr 15;53(2):263-71.

Table 1. Clinical characteristics of divided groups

Group	1 (axial group)	2 (extra-axial group)	p
Number of patients	823	223	
Age at start of TNFi (yr)	38.21 (12.78)	38.58 (14.17)	0.713
Disease duration (yr)	3.95 (5.26)	2.29 (4.32)	<0.001
Age at diagnosis	34.27 (13.05)	36.29 (14.11)	0.044
Sex (male) (%)	645 (78.4)	152 (68.2)	0.002
HLA-B27 positivity (%)	736 (89.4)	197 (88.3)	0.732
Inflammatory back pain (%)	699 (84.9)	191 (85.7)	0.872
Peripheral arthritis (%)	201 (24.4)	191 (85.7)	<0.001
Enthesitis (%)	65 (7.9)	154 (69.1)	<0.001
Uveitis (%)	163 (19.8)	59 (26.5)	0.039
Dactylitis (%)	12 (1.5)	13 (5.8)	<0.001
Psoriasis (%)	15 (1.8)	12 (5.4)	0.006
Good response to NSAIDs (%)	205 (24.9)	155 (69.5)	<0.001
Family history (%)	88 (10.7)	27 (12.1)	0.632
Smoking (%)	408 (49.6)	102 (45.7)	0.347
CRP (mg/dl)	2.10 (2.74)	2.89 (3.57)	<0.001
ESR (mm/hr)	35.52 (28.73)	46.33 (32.94)	<0.001
BASDAI	5.93 (1.92)	6.41 (1.80)	0.001
BASF	3.42 (2.56)	3.64 (2.58)	0.255
Drug change after one year (%)	160 (19.4)	61 (27.4)	0.013

Figure 1. Kaplan-Meier survival analysis of TNFi use in two groups.



Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1772

POS0973 CONTEXTUAL FACTORS SHOULD COMPLETE THE ASSESSMENT OF FUNCTIONING IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS (AXSPA)

U. Kiltz[1], E. Ahomaa[2], B. Buehring[1], X. Baraliakos[1], D. Kiefer[1], J. D. Leicht[1], J. Braun[1]. [1]*Rheumazentrum Ruhrgebiet at Ruhr-University Bochum, Rheumatology, Herne, Germany*; [2]*St. Franziskus-Hospital, Department of Orthopedic Surgery, Cologne, Germany*

Background: Functioning of patients (pts.) with axial spondyloarthritis (axSpA) is influenced by a variety of factors. In contrast to clinical factors, the influence of contextual factors on functioning has not been well studied. According to the According to the International Classification of Functioning, Disability and Health (ICF), functioning is a complex interaction between health status and contextual factors such as social support, relationships and attitudes.
Objectives: The aim of this study is to understand limitations in participation and to investigate barriers and facilitators of contextual factors in pts. with axSpA.
Methods: Consecutive axSpA pts. underwent a standardized assessment with collection of patient and disease characteristics, patient-reported outcomes (ASDAS, BASFI, BASMI, PHQ-9, ICF Measure of Participation and ACTivities questionnaire (IMPACT-S (0-100%)), ASAS Health Index (ASAS HI and environment factor item set (EFIS) (1). The EFIS contains 9 dichotomous questions addressing ICF categories of products and technologies (e1), support and relationship (e3), attitudes (e4) and health services (e5). Validated cut-offs of ASAS HI were used to categorize global functioning.
Results: A total of 200 axSpA pts. were included: 69% males, 44.3±12.5 years, symptom duration 17.9±12.6 years, ASDAS 2.5±1.1, BASFI 4.0±2.7, BASMI 3.5±1.8, ASAS HI 7.0±4.1. Pts. reported limitations in the IMPACT-S activity and participation domain (82.3% (15.2) and 83.5% (16.8), respectively. The majority of pts. reported as barrier that treatment of axSpA requires time (e4, 58.5%). A minority of pts. but quite a few reported as barrier the need for support by family members (e3, 43.5%), the need to modify home and work environment (e1, 39.5%) and that they cannot rely on family members for help (e3, 22%). Some pts. (< 20%) reported that they have problems to be understood by health care professionals when experiencing a flare (e5, 18.5%), that pts. at home are not adequately taken care of (e4, 18.5%), disliking friends' behavior toward them (e4, 13.5%), and that friends are too demanding (e4, 13%). The majority of pts. (e4, 75.9%) identified attitudes of friends as the only and major facilitator. All pts. reporting at least one barrier had significantly worse global functioning (ASAS HI, IMPACT-S), and depression (PHQ-9) compared to patients who reported no barriers in the respective ICF categories (p< 0.01). Similarly, pts. with poor functioning are more likely to report barriers in contextual factors compared to pts. with good functioning (Table 1). Pts. having to ask for more support from their families expressed the feeling that they cannot rely on that.

Conclusion: Barriers more than facilitators of contextual factors are present in pts. with axSpA. This study shows that barriers in contextual factors are more common in pts. with impairments in self-reported and performed functioning as in those without impairments. This underlines the importance of contextual factors in the management of axSpA pts.

REFERENCES:

[1] Kiltz et al. Ann Rheum Dis 2013;72(s3):572

Table 1. Presence of contextual factors, stratified for global functioning categories

ICF category	EFIS Item	Global Functioning (ASAS HI 0-17)		
		Good ≤ 5 (n= 69)	Moderate <5 to <12 (n= 106	Poor ≥ 12 (n= 25)
e3	EFIS 1: As a result of my rheumatic disease, the children take more responsibility for household tasks.	11 (15.9)	55 (51.9)	21 (84)
e3	EFIS 2: I don't like the way my friends acts around me.	0 (0)	15 (14,2)	12 (48,0)
e3	EFIS 3: I can't count on my relatives to help me with my problems	11 (15,9)	24 (22,6)	9 (36)
e1	EFIS 4: I modify my home and work environments.	16 (23,2)	47 (44,3)	9 (36)
e5	EFIS 5: I have difficulties getting worsening of my disease acknowledged by a health care professional	3 (4,3)	21 (19,8)	16 (64)
e5	EFIS 6: Treatment of my rheumatic disease is taking up time	22 (31,9)	73 (68,9)	22 (88)
e4,	EFIS 7: My friends expect too much of	1 (1,4)	18 (17,0)	7 (28)
e4	EFIS 8: No one pays much attention to me at home	10 (14,5)	20 (18,9)	7 (28)
e4	EFIS 9: My friends understand me	56 (17,4)	83 (78,3)	12 (48)

values given as number (%)

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1776

POS0974

IMPROVEMENT IN THE DIAGNOSTIC DELAY OF AXIAL SPONDYLOARTHRITIS, RESULTS FROM REAL WORLD DATA

J. Feld[1,2], O. Elkayam[3,4], A. Druyan[4,5], T. Reitblat[6], A. Balbir-Gurman[2,7], A. Hadad[1], T. Gazitt[1], M. Elias[1], V. Furer[3], T. Mashiach[7], D. Zisman[1,2]. *[1]Carmel Medical Center, Rheumatology, Haifa, Israel*; *[2]Technion - Israel Institute of Technology, Medicine, Haifa, Israel*; *[3]ביבא לת בוליכיא מילוח תיב, Rheumatology, Tel Aviv-Yafo, Israel*; *[4]רלקאס ש"ע ביבא לת תטיסרבינוא האופרל הטלוקפה, Rheumatology, ופי ביבא לת, Israel*; *[5]Sheba Medical Center, Rheumatology, Ramat Gan, Israel*; *[6]Barzilai Medical Center, Rheumatology, Ashkelon, Israel*; *[7]Rambam Health Care Campus, Rheumatology, Haifa, Israel*

Background: Diagnostic delay is a major challenge in axial spondyloarthritis (axSpA) with an extended interval of 8-10 years in Europe and 14 years in the United States between symptom onset and disease diagnosis (1, 2).

Objectives: To assess the delay in the diagnosis of axSpA over time in a real world axSpA cohort diagnosed in the last 3 decades and to evaluate factors associated with this delay.

Methods: A cohort of axSpA patients was recruited from a national multicenter registry of inflammatory arthritis. This cohorts' demographic, clinical and diagnostic variables were studied. The diagnostic delay was defined as the time interval between the year of first symptom and year of diagnosis. The mean and median diagnostic delay were calculated. A survival analysis was performed evaluating the association between the demographic, clinical and diagnostic variables on the diagnostic delay.

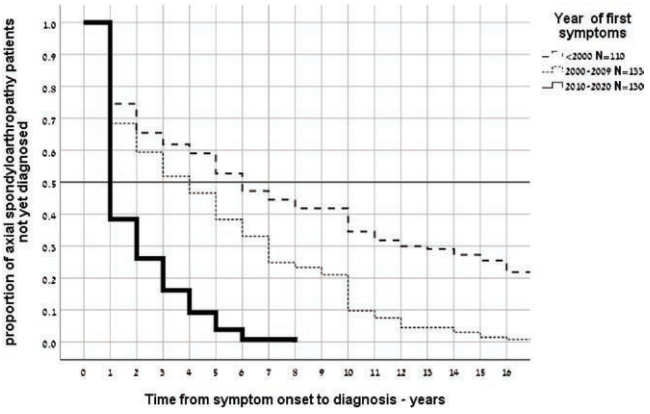
Results: Of the 373 axSpA patients in the registry, 198 (47%) are men. Ankylosing spondylitis fulfilling New York criteria was diagnosed in 73% of the patients. HLA-B*27 positivity was found in 64% of patients. The majority of the patients (63%) reported symptom onset between the age of 21-45, 21% before the age of 21 and 16% after the age of 45. Nine percent were diagnosed before the age of 21, 28% between 21-30, 23% between 31-40, 21% between 41-50 and 18% after the age of 50. One hundred and ten patients were diagnosed before 2000, 133 between 2001-2009 and 130 between 2010-2020. The mean and median delay in diagnosis was 9.1, 6 (±8.4) years when diagnosed before 2000, 5, 4 (±4.1) years when diagnosed 2001-2009, and 2, 1 (±1.5) years when diagnosed 2010-2020, respectively (graph 1). The only variable which was found to be associated with a shorter delay was the interval between symptom onset and first rheumatology consult: HR of 5.86 (4.3-8, p<0.001) if the rheumatology visit was within the first year of symptoms, HR 3.5 (2.4-5, p<0.001) if assessed 2-3 years after symptom onset. Additionally, age <21 at symptom onset was associated with a shorter delay (p=0.005). Sex, type of axSpA (radiographic vs. non radiographic axSpA), level of education, and HLA-B*27 positivity were not associated with a delay in diagnosis.

Conclusion: Delay in axSpA diagnosis has significantly improved in this real-world cohort during the last decade. The most significant factor associated with a faster diagnosis was the time of the first rheumatology consult relative to symptom onset. Increasing the awareness of disease manifestations and early referral to a rheumatology service can improve the diagnosis delay of axSpA.

REFERENCES:

[1] Sorensen J, Hetland ML, all departments of rheumatology in D. Diagnostic delay in patients with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis: results from the Danish nationwide DANBIO registry. Ann Rheum Dis. 2015;74(3):e12.

[2] Deodhar A, Mittal M, Reilly P, Bao Y, Manthena S, Anderson J, et al. Ankylosing spondylitis diagnosis in US patients with back pain: identifying providers involved and factors associated with rheumatology referral delay. Clin Rheumatol. 2016;35(7):1769-76.



Graph 1. The improvement in the delay in diagnosis of axial spondyloarthropathy over the last 3 decades

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1802

POS0975

CLINICAL CHARACTERISTICS OF NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN ASIAN COUNTRIES COMPARED TO OTHER REGIONS: RESULTS OF THE INTERNATIONAL CROSS-SECTIONAL ASAS-COMOSPA STUDY

K. Ono[1], M. Kishimoto[1], S. Fukui[2], S. Kawaai[2], G. A. Deshpande[3], K. Yoshida[4], N. Ichikawa[5], Y. Kaneko[6], T. Kawasaki[7], K. Matsui[8], M. Morita[9], K. Tada[10], N. Takizawa[11], N. Tamura[10], A. Taniguchi[5], Y. Taniguchi[12], S. Tsuji[13], S. Kobayashi[14], M. Okada[2], C. López-Medina[15], A. Moltó[15], D. Van der Heijde[16], M. Dougados[15], Y. Komagata[1], T. Tomita[17], S. Kaname[1]. *[1]Kyorin University School of Medicine, Department of Nephrology and Rheumatology, Tokyo, Japan*; *[2]St. Luke's International Hospital, St Luke`s International University, Immuno-Rheumatology Center, Tokyo, Japan*; *[3]Juntendo University School of Medicine, Department of General Internal Medicine, Tokyo, Japan*; *[4]Brigham and Women's Hospital and Harvard Medical School, Division of Rheumatology, Inflammation, and Immunity, Department of Medicine, Boston, Massachusetts, United States of America*; *[5]Tokyo Women's Medical University, Institute of Rheumatology, Tokyo, Japan*; *[6]Keio University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan*; *[7]Shiga University of Medical Science, Department of Orthopedic Surgery, Shiga, Japan*; *[8]Teine Keijinkai Hospital, Department of Rheumatology, Hokkaido, Japan*; *[9]Fujita Health University, Department of Orthopaedic Surgery, Aichi, Japan*; *[10]Juntendo University School of Medicine, Department of Internal Medicine and Rheumatology, Tokyo, Japan*; *[11]Chubu Rosai Hospital, Department of Rheumatology, Aichi, Japan*; *[12]Kochi Medical School, Department of Endocrinology, Metabolism and Nephrology, Kochi, Japan*; *[13]National Hospital Organization Osaka Minami Medical Center, Department of Orthopedics and Rheumatology, Osaka, Japan*; *[14]Juntendo University Koshigaya Hospital, Department of Internal Medicine, Saitama, Japan*; *[15] University of Paris, Cochin Hospital, Department of Rheumatology, Paris, France*; *[16]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; *[17]Osaka University Graduate School of Medicine, Department of Orthopaedic Biomaterial Science, Osaka, Japan*

Background: Clinical characteristics of nonradiographic axial spondyloarthritis (nr-ax-SpA) are highly variable across patients, and may potentially vary across patient populations, particularly due to differing distributions of human leukocyte antigens (HLA) and other genetic factors. The majority of nr-ax-SpA studies have been conducted in Europe, the United States, and small studies are reported from Asia [1].
Objectives: To delineate clinical characteristics of patients with nr-ax-SpA in Asian countries in comparison to other areas of the world.
Methods: Utilizing the ASAS-COMOSPA data, an international cross-sectional observational study of SpA patients, we analyzed information on demographics, disease characteristics, comorbidities, and risk factors. Patients were classified by region: Asia (China, Japan, Singapore, South Korea, and Taiwan), and non-Asian countries (Europe, Americas, and Africa); patient characteristics, including diagnosis and treatment, were compared.
Results: Among 3984 SpA patients included in the study, 1094 were from centers in Asian countries, and 2890 from other regions. 112/780 (14.4%) of axial SpA patients in Asian countries were nr-ax-SpA, substantially less than in other countries (486/1997, 24.3%). Nr-ax-SpA patients in Asian countries compared to nr-ax-SpA in other countries were more likely male (75.9 vs 47.1%), have onset (22.8 vs 27.8 years) and diagnosis (27.2 vs 34.5 years) at younger age, and experience less diagnostic delay (1.88 vs 2.92 years) (Table 1). Nr-ax-SpA patients in Asian countries have higher prevalence of positive HLA-B27 (90.6% vs 61.9%) and fewer peripheral signs such as arthritis, enthesitis, or dactylitis (53.6% vs 66.3%) but have similar rate of extra-articular manifestations (psoriasis, IBD, or uveitis) and co-morbidities. Disease activity, functional impairment, and inflammation on MRI were less in nr-ax-SpA patients in Asian countries. NSAIDs response was higher and use of methotrexate and b-DMARDs were lower among nr-ax-SpA in Asian countries.
Conclusion: Among axial SpA patients, substantially lower frequency of nr-ax-SpA was observed in Asian countries compared to other regions of the world. Nr-ax-SpA patients in Asian countries were predominantly male, and had younger disease onset with higher HLA-B27 positivity rate and less peripheral signs, and better response to NSAIDs. These results offer an opportunity to improve both early diagnosis and treatment of nr-ax-SpA patients in Asian countries.

Table 1. Characteristics of nonradiographic axial SpA in Asia versus non-Asian regions

Variables	Asia	non-Asian regions	p value
N	112	486	
Age at disease diagnosis, yrs	27.2 [21.1, 39.6]	34.5 [27.7, 41.7]	<0.001
Diagnostic delay, yrs	1.88 [0.27, 5.56]	2.92 [0.59, 9.58]	0.011
Male (%)	85 (75.9)	229 (47.1)	<0.001
Sacroiliitis on MRI among tested (%)	49 (67.1)	341 (82.2)	0.005
HLA B27 positivity among measured (%)	96 (90.6)	273 (61.9)	<0.001
Inflammatory Back Pain (%)	107 (95.5)	478 (98.4)	0.076
Arthritis, enthesitis, or dactylitis (%)	60 (53.6)	322 (66.3)	0.016
Psoriasis (%)	12 (10.7)	82 (16.9)	0.142
Uveitis (%)	20 (17.9)	81 (16.7)	0.870
Inflammatory bowel disease (%)	5 (4.5)	27 (5.6)	0.817
Elevated CRP (%)	37 (33.0)	213 (43.8)	0.048
Physician global assessment (0-10)	2.0 [1.0, 5.0]	2.0 [1.0, 4.0]	0.741
Patient global assessment (0-10)	3.0 [1.0, 6.0]	4.0 [2.0, 6.0]	0.012
ASDAS-CRP	1.40 [0.95, 2.08]	1.97 [1.21, 2.78]	<0.001
BASFI	0.8 [0.05, 2.65]	2.9 [0.8, 5.6]	<0.001
Good response to NSAIDs (%)	80 (71.4)	272 (56.0)	0.004
Methotrexate use (%)	18 (16.1)	134 (27.6)	0.016
Biological DMARDs use (%)	27 (24.1)	191 (39.3)	0.004

REFERENCES:

[1] López-Medina C, Ramiro S, van der Heijde D, et al. Characteristics and burden of disease in patients with radiographic and non-radiographic axial Spondyloarthritis: a comparison by systematic literature review and meta-analysis. RMD Open. 2019 Nov 21;5(2): e001108.

Acknowledgements: This study was conducted under the umbrella of the International Society for Spondyloarthritis Assessment (ASAS) and COMOSPA study was supported by unrestricted grants from Pfizer, AbbVie and UCB.

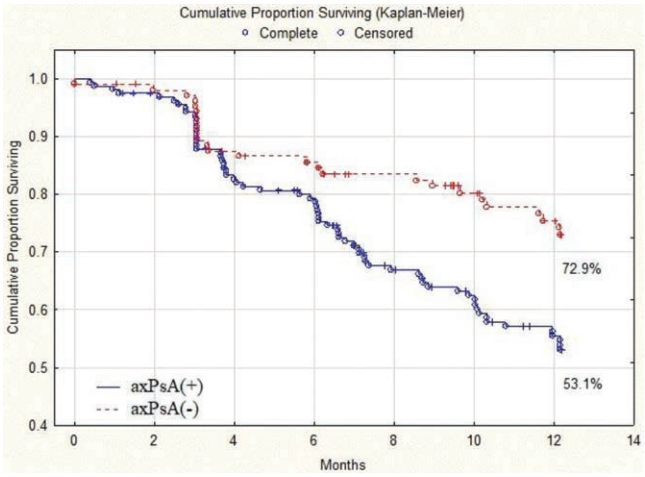
Disclosure of Interests: Keisuke Ono: None declared, Mitsumasa Kishimoto Speakers bureau: AbbVie, Amgen-Astellas BioPharma, Asahi-Kasei Pharma, Astellas, Ayumi Pharma, BMS, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Kyowa Kirin, Novartis, Ono Pharma, Pfizer, Tanabe-Mitsubishi, Teijin Pharma, and UCB Pharma, Consultant of: AbbVie, Amgen-Astellas BioPharma, Asahi-Kasei Pharma, Astellas, Ayumi Pharma, BMS, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Kyowa Kirin, Novartis, Ono Pharma, Pfizer, Tanabe-Mitsubishi, Teijin Pharma, and UCB Pharma, Sho Fukui: None declared, Satoshi Kawaai: None declared, Gautam A. Deshpande: None declared, Kazuki Yoshida Consultant of: OM1, Inc., Grant/research support from: Corrona, LLC, Naomi Ichikawa: None declared, Yuko Kaneko Speakers bureau: AbbVie, Astellas, Ayumi, Bristol-Myers Squibb, Chugai, Eisai, Eli Lilly, Hisamitsu, Jansen, Kissei, Pfizer, Sanofi, Takeda, Tanabe-Mitsubishi, and UCB, Taku Kawasaki: None declared, Kazuo Matsui: None declared, Mitsuhiro Morita: None declared, Kurisu Tada: None declared, Naoho Takizawa: None declared, Naoto Tamura: None declared, Atsuo Taniguchi: None declared, Yoshinori Taniguchi: None declared, Shigeyoshi Tsuji: None declared, Shigeto Kobayashi: None declared, Masato Okada: None declared, Clementina López-Medina: None declared, Anna Moltó Consultant of: AbbVie, Pfizer, MSD, Novartis, Gilead, Lilly and UCB, Grant/research support from: AbbVie, Pfizer, MSD, Novartis, Gilead, Lilly and UCB, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma, Employee of: Imaging Rheumatology bv. (Director), Maxime Dougados: None declared, Yoshinori Komagata: None declared, Tetsuya Tomita: None declared, Shinya Kaname: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1942

POS0976 ANALYSIS OF BIOLOGIC THERAPY RETENTION RATE IN PSORIATIC ARTHRITIS PATIENTS WITH AND WITHOUTV AXIAL INVOLVEMENT. DATA FROM CLINICAL PRACTICE

E. Gubar[1], Y. Korsakova[1], E. Loginova[1], S. Glukhova[2], T. Korotaeva[1], E. Nasonov[1,3], N. Kuznetsova[4], I. Umnova[5], V. Sorotskaya[6], I. Patrikeeva[7]. *[1]V.A. Nasonova Research Institute of Rheumatology, Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Medical and Social Problems in Rheumatology, Moscow, Russian Federation*; *[3]I.M. Sechenov First Moscow State Medical University, Rheumatology, Moscow, Russian Federation*; *[4]Municipal Autonomous Institution "City Clinical Hospital No. 40", Rheumatology, Yekaterinburg, Russian Federation*; *[5]Omsk region "Regional clinical hospital", Rheumatology, Omsk, Russian Federation*; *[6]Medical Institute of the Tula State University, Rheumatology, Tula, Russian Federation*; *[7]Tyumen Regional Clinical Hospitai №1, Rheumatology, Tyumen, Russian Federation*

Background: Limited data are available on retention rates of biologic therapy in psoriatic arthritis (PsA) patients (pts) with axial involvement. It has been shown that in the subset of pts with prevalent axial involvement (AS versus PsA and AxSpA versus PsA) a longer duration of anti-TNF-α-therapy was observed as compared to peripheral arthritis [1].
Objectives: To compare retention rates of biologic therapy in PsA pts with and without axial involvement in routine clinical practice.
Methods: 731 pts with PsA according to CASPAR criteria were included in the study. Data were collected from 43 rheumatology clinics over various regions of the Russian Federation. Among the pts, 243 (33.0%) (M/F 132/111) were given biologic therapy. Pts' age 45.9±12.8 years (yrs), disease duration 8.6±6.5 yrs. Pts underwent standard clinical examination of PsA activity and were split into two groups (gr.), with and without axial PsA (axPsA): axPsA(+) and axPsA(-). Pts in the axPsA(+) gr. had inflammatory back pain by ASAS criteria and/or radiographic sacroiliitis (SI) (unilateral grade≥3 or bilateral grade≥2) and/or active MRI SI and/or typical of axPsA changes of the cervical and/or lumbar spine (marginal/paramarginal syndesmophytes, ankylosis of the facet joints). Pts in the axPsA(-) gr. had only peripheral arthritis. The axPsA(+) gr. included 143 (58.8%) pts, the axPsA(-) gr. 100 (41.2%) pts. 163 (67.1%) pts were treated with TNF inhibitors (TNF-i), 80 (32.9%) pts with interleukin inhibitors (IL-i): 55 pts with Ustekinumab, 25 pts with Secukinumab. During the TNF-i treatment courses Infliximab was given to 34 pts, Adalimumab to 53 pts, Etanercept to 36 pts, Golimumab to 27 pts and Certolizumab Pegol to 8 pts. The observation period lasted 12 months. Treatment retention rates were analyzed using Kaplan-Meier curves and the log-rank test.
Results: Analysis of the treatment retention rates revealed statistically significant differences between the axPsA(+) and the axPsA(-) grs. After 12 months of observation, 72.9% of pts in the axPsA(-) gr. continued receiving biologic therapy, while in the axPsA(+) gr. only 53.1% of pts (p=0.0027) received it. The same kind of differences in anti-TNF therapy were found between the axPsA(-) gr. and the axPsA(+) gr.: 82.2% and 62.3% pts respectively (p=0.011) continued receiving TNF-i after 12 months. However no statistically significant differences were found between the two grs. in the treatment retention rates of IL-i therapy: after 12 months of observation 55.5% of axPsA(-) pts and 37% of axPsA(+) pts (p=0.086) continued receiving IL-i.
Conclusion: In routine clinical practice, retention rates of biologic therapy were found to be worse in PsA pts with axial involvement. In clinical practice, TNF-i are prescribed twice as often than IL-i. However, considering the need of personalized therapy, in case of axPsA the use of IL-i is preferable because their treatment retention rates don't depend on axial involvement.
REFERENCES:

[1] M. Fabbroni et al. Mediators of Inflammation, 2014.



Retention rates of biologic therapy. Differences between axPsA(+) and axPsA(-) pts are statistically significant (p=0.00265, log rank test).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2007

POS0977 CARDIOVASCULAR AND DISEASE RELATED FEATURES IN AXIAL SPONDYLITIS WITH AND WITHOUT CONCOMITANT PSORIASIS. A MULTICENTER STUDY WITH 882 PATIENTS

I. González-Mazón[1], J. Rueda-Gotor[1], I. Ferraz-Amaro[2], L. Sanchez-Bilbao[1], F. Genre[3], V. Calvo-Río[1], S. Remuzgo-Martínez[3], V. Pulito-Cueto[3], A. Corrales[1], L. Lera-Gómez[3], V. Portilla[1], V. Hernández-Hernández[2], J. C. Quevedo-Abeledo[4], C. Rodríguez-Lozano[4], C. López-Medina[5], M. L. Ladehesa Pineda[5], S. Castañeda[6], E. F. Vicente-Rabaneda[6], C. Fernández-Carballido[7], M. P. Martínez-Vidal[7], D. Castro-Corredor[8], J. Anino-Fernández[8], D. Peiteado[9], C. Plasencia[9], M. L. García Vivar[10], E. Galindez[10], E. Montes Pérez[11], C. Fernández-Díaz[1], R. Blanco[1], M. A. González-Gay[1,3]. *[1]Universitary Hospital Marques de Valdecilla, Rheumatology, Santander, Spain*; *[2]Hospital Universitario de Canarias, Rheumatology, Tenerife, Spain*; *[3]IDIVAL, Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Santander, Spain*; *[4]Hospital Universitario de Gran Canaria Dr. Negrín, Rheumatology, Las Palmas, Spain*; *[5]Reina Sofia Hospital, Rheumatology, Cordoba, Spain*; *[6]Hospital de La Princesa, Rheumatology, Madrid, Spain*; *[7]Hospital Universitario San Juan de Alicante, Rheumatology, Alicante, Spain*; *[8]Hospital General Universitario de Ciudad Real, Rheumatology, Ciudad Real, Spain*; *[9]Hospital Universitario La Paz-IdiPaz, Rheumatology, Madrid, Spain*; *[10]Hospital Universitario Basurto, Rheumatology, BIlbao, Spain*; *[11]Diagnóstico Médico Cantabria, DMC, Santander, Spain*

Background: Patients with axial spondyloarthritis (axSpA) may present with concomitant psoriasis (Ps) in approximately 10% of cases. As with axSpA, Ps is also associated with an accelerated atherosclerosis process[1]. However, it is unknown whether the presence of Ps confers an increased cardiovascular (CV) risk in patients with axSpA.

Objectives: To compare factors related to the disease, CV risk factors, atherosclerotic burden, and CV events in patients with axSpA with and without Ps.

Methods: Cross-sectional analysis of the AtheSpAin cohort, a Spanish multicenter cohort designed for the study of atherosclerosis in axSpA. We compared axSpA patients with and without concomitant psoriasis, focusing mainly on CV risk characteristics. Background information on CV risk factors, CV events, and disease-related factors was reviewed, and data on maximum body index, blood pressure, lipid profile, and disease status at the time of the study were also obtained. Carotid ultrasound (US) was performed in all patients at the time of the study, including measurement of carotid intima-media wall thickness (cIMT) and plaque detection according to the Mannhein consensus criteria.

Results: A set of 882 axSpA patients were included. 786 (89.1%) of them had no concomitant Ps, which was present in 96 (10.9%) patients. Although the mean age was similar, male sex was more prevalent in axSpA patients with Ps (79.1% Vs 66.5%, p=0.01) (Table 1).

Furthermore, it was found that axSpA with Ps had a more frequent history of synovitis (50% vs 33%, p = 0.001), dactylitis (13% vs 6%, p = 0.011) and concomitant inflammatory bowel disease (13% vs 6%, p = 0.01). AxSpA patients with Ps had a non-significant trend towards a higher prevalence of asymmetric sacroiliitis (23 vs 16%, p = 0.064) and had a lower frequency of positive HLA-B27 status (56% vs 72%, p = 0.003). Regarding the management of the disease, prednisone (23% vs 12%, p = 0.02), methotrexate (30% vs 15%, p = 0.000) and anti-TNFα therapy (50% vs 34%, p = 0.002) were more commonly used in the group with Ps.

Regarding CV risk characteristics, no differences were observed either in the prevalence of traditional CV risk factors (Table 1), nor in the total serum level, HDL and LDL, blood pressure and body mass index at that time of the study. However, axSpA patients with Ps showed a higher prevalence of CV events (9% vs 4%, p = 0.05), including ischemic heart disease (6% vs 3%, p = 0.042) and ischemic stroke (4% vs 1%, p = 0.016) (Table 1). The subclinical atherogenic burden was also more severe in the group with Ps, with a higher prevalence of carotid plaques (39% vs 31%, p = 0.098), and higher values of cIMT (0.664 ± 0.170 mm vs 0.642 ± 0.142 mm, p = 0.16), although the differences did not reach statistical significance.

Table 1. Main sociodemographic and cardiovascular differences among axSpA patients with and without psoriasis.

	axSpA without psoriasis (n=786)	axSpA with psoriasis (n=96)	p
Men/Women, n	523/268	76/20	**0.010**
Mean age (years) ±SD at the time of study	49 ± 13	49 ± 13	0.81
AS/nr-AxSpa	625/166	77/19	0.79
History of CV risk factors			
Current smokers	267 (34)	30 (31)	0.60
Obesitty	174 (22)	26 (27)	0.29
Dyslipidemia	262 (33)	35 (36)	0.48
Hypertension	211 (27)	28 (29)	0.57
Diabetes Mellitus	56 (7)	8 (8)	0.65
Chronic Kidney Disease	19 (2)	3 (3)	0.72
History of cardiovascular events, n (%)	33 (4)	9 (9)	**0.023**
Ischemic heart disease	20 (3)	6 (6)	**0.042**
Congestive heart failure	2 (0)	1 (1)	0.29
Ischemic stroke	6 (1)	4 (4)	**0.016**
Peripheral artery disease	6 (1)	0 (0)	0.99
CV data at the time of study			
Carotid plaques	244 (31)	38 (39)	0.098
IMT mm	0.642 ± 0.142	0.664 ± 0.170	0.16
IMT >= 900 mm	40 (5)	6 (6)	0.66

Abbreviations: AS = ankylosing spondylitis. AxSpA= axial spondylitis. CV = cardiovascular. IMT = intima-media wall thickness. Nr-axSpA = no-radiographic axial spondylitis.

Conclusion: The presence of Ps may confer additional CV risk to axSpA patients and is associated with particular disease related factors.

REFERENCES:

[1] Fang N, Jiang M, Fan Y. Association Between Psoriasis and Subclinical Atherosclerosis: A Meta-Analysis. *Medicine (Baltimore)*. 2016;95(20):e3576.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2025

POS0978 DISEASE CONTROL IN PSORIATIC ARTHRITIS PATIENTS WITH OR WITHOUT AXIAL MANIFESTATIONS IN REAL CLINICAL PRACTICE IN SPAIN: RESULTS FROM THE MIDAS STUDY

E. De Miguel[1], J. Gratacos-Masmitja[2], A. P. Cacheda[3], J. M. Rodríguez-Heredia[4], A. Gallego[5], E. Beltrán[6], B. Font Ramos[7], C. Sastré[7], C. Sanabra[7]on behalf of MIDAS group. *[1]Hospital Universitario La Paz, Rheumatology Service, Madrid, Spain*; *[2]Hospital Universitario Parc Taulí, Rheumatology Service, Sabadell, Spain*; *[3]Hospital Universitario Son Llatzer, Rheumatology Service, Palma, Spain*; *[4]Hospital Universitario Getafe, RheumatologySservice, Madrid, Spain*; *[5]Complejo Hospitalario Universitario Badajoz, Rheumatology Service, Badajoz, Spain*; *[6]Hospital del Mar, Rheumatology Service, Barcelona, Spain*; *[7]Novartis Farmacéutica, Rheumatology, Barcelona, Spain*

Background: MIDAS study assessed the disease activity in psoriatic arthritis (PsA) patients treated in clinical practice in Spain.

Objectives: This sub-analysis compared disease activity between PsA patients with or without axial manifestations.

Methods: MIDAS is an observational, non-interventional, cross-sectional, multicenter study conducted in Spain. Patients included were ≥18 years old with ≥6 months since diagnosis, were classified by CASPAR criteria and had initiated treatment ≥3 months. Disease activity was measured by Disease Activity in Psoriatic Arthritis (DAPSA) and Minimal Disease Activity (MDA). Axial involvement was defined according to the presence of inflammatory back pain assessed by rheumatologist.

Results: 312 evaluable PsA patients were included in this analysis, 12.2% of which presented with axial involvement. PsA patients with axial manifestations reported longer time from onset of symptoms to diagnosis and disease duration, higher presence of concomitant diseases, HLA-B*27+ status, C-reactive protein

(CRP) levels, perception of uncontrolled disease and presence of swollen and tender joints compared to patients without axial involvement. A higher proportion of PsA patients with axial manifestations were treated with a biologic compared with those without axial involvement 68.4% vs 57.3% (Table 1). Patients with axial involvement showed a higher impairment of their quality of life compared to those without axial manifestations by a worse higher mean (SD) Psoriatic Arthritis Impact of Disease 12-item questionnaire (PSAID12) score (5.0 [2.4] vs 2.7 [2.2], respectively). In terms of disease control more patients with axial manifestations presented with moderate to high disease activity (DAPSA>14: 65.7% vs 36.8%, respectively) and did not meet the MDA criteria for remission (89.5% vs 42.7%, respectively) (Figure 1).

Conclusion: PsA patients with axial manifestations presented with a higher burden of disease and showed a worse disease control compared to those without axial involvement.

Table 1. Baseline demographic and clinical characteristics

	With axial manifestations (n=38)	Without axial manifestations (n=274)	PsA (n=312)
Age (years), mean (SD)	53.1 (10.4)	54.1 (12.4)	54.0 (12.2)
Sex (male), n (%)	17 (44.7%)	153 (55.8%)	170 (54.5%)
Time since diagnosis (years), mean (SD)	13.6 (10.1)	10.1 (8.8)	10.5 (9.0)
Time from onset of symptoms to diagnosis (years), mean (SD)	4.3 (6.1)	2.8 (4.8)	3.0 (5.0)
Presence of concomitant diseases, mean (SD)	26 (68.4%)	166 (60.6%)	192 (61.5%)
Anemia, n (%)	3 (7.9%)	7 (2.6%)	7 (2.2%)
Anxiety, n (%)	6 (15.8%)	9 (3.3%)	1 (0.3%)
Asthma, n (%)	2 (5.3%)	7 (2.6%)	1 (0.3%)
Depression, n (%)	6 (15.8%)	1 (0.4%)	1 (0.3%)
Dyslipidemia, n (%)	3 (7.9%)	8 (2.9%)	9 (2.9%)
Hypertension, n (%)	3 (7.9%)	7 (2.6%)	9 (2.9%)
Others (excluding skin psoriasis, uveitis, or IBD), n (%)	3 (7.9%)	17 (6.2%)	19 (6.1%)
Presence of HLA-B*27+, n (%)	6 (15.8%)	28 (10.2%)	34 (10.9%)
CRP levels (mg/l), mean (SD)	7.3 (11.3)	4.6 (6.5)	4.9 (7.3)
Patient perceived disease control (PASS), n (%)	30 (78.9%)	228 (83.5%)	258 (83.0%)
Presence of swollen (SJC≥1), n (%)	22 (57.9%)	117 (42.7%)	139 (44.6%)
Presence of tender joints (TJC≥1), n (%)	14 (36.8%)	74 (27.0%)	88 (28.2%)
Patients treated with biological	26 (68.4%)	157 (57.3%)	183 (58.7%)

COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; HLA-B*27, human leukocyte antigen B27; IBD, inflammatory bowel disease; PASS, patient acceptable symptom state; PsA, psoriatic arthritis; SD, standard deviation; SJC, swollen joint counts; TJC, tender joint counts.

Figure 1. Disease status according to clinical phenotype of PSA **A)** Disease activity according to DAPSA **B)** Disease activity according to MDADAPSA, Disease Activity in Psoriatic Arthritis; MDA, Minimal Disease Activity; PsA, psoriatic arthritis.

Acknowledgements: We thank to MIDAS group investigators and patients included in the study.

Disclosure of Interests: Eugenio de Miguel Speakers bureau: AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi., Paid instructor for: Janssen, Novartis, Roche, Consultant of: AbbVie, Novartis, Pfizer, Galapagos, Grant/research support from: Abbvie, Novartis, Pfizer, Jordi Gratacos-Masmitja Speakers bureau: During the course of the year I have received funding in relation to courses and / or conferences, and / or have participated as a speaker or in advisory boards from: MSD, Pfizer, AbbVie, Janssen Cilag, Novartis, Lilly and Amgen., Consultant of: During the course of the year I have received funding in relation to courses and / or conferences, and / or have participated as a speaker or in advisory boards from: MSD, Pfizer, AbbVie, Janssen Cilag, Novartis, Lilly and Amgen., Grant/research support from: During the course of the year I have received a private grand from Pfizer.
I have not received any private influence in the elaboration of the contents of this talk., Ana Paula Cacheda: None declared, José M. Rodríguez-Heredia Speakers bureau: Amgen, Novartis, Sanofi, Consultant of: Amgen, Biogen, Fresenius, MSD, Janssen, Roche, Novartis, Pfizer, Sanofi, Adela Gallego Speakers bureau: During the course of the year I have received funding in relation to courses and / or conferences, and / or have participated as a speaker or in advisory boards from: MSD, Pfizer, AbbVie, Janssen, Novartis, Lilly, Amgen and Sanofi.
I have not received any private influence in the elaboration of the contents of this talk., Grant/research support from: During the course of the year I have received funding in relation to courses and / or conferences, and / or have participated as a speaker or in advisory boards from: MSD, Pfizer, AbbVie, Janssen, Novartis, Lilly, Amgen and Sanofi.
I have not received any private influence in the elaboration of the contents of this talk., Emma Beltrán Speakers bureau: Abbvie, Bristol, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Consultant of: Abbvie, Bristol, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Beatriz Font Ramos Employee of: Novartis employee, Carlos Sastré Employee of: Novartis employee, Cristina Sanabra Employee of: Novartis employee.
DOI: 10.1136/annrheumdis-2021-eular.2041

POS0979

ASSOCIATION BETWEEN HIGHER INTAKE OF CARBOHYDRATES AND FREE SUGAR WITH HIGHER DISEASE ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

V. Rios Rodriguez[1], M. D'urso[1], C. Höppner[1], F. Proft[1], M. Protopopov[1], J. Rademacher[1], B. Muche[1], S. Lüders[1], H. Haibel[1], M. Verba[1], J. Sieper[1], D. Poddubnyy[1,2]. [1]*Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Gastroenterology, Infectiology and Rheumatology, Berlin, Germany*; [2]*Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), ein Institut der Leibniz-Gemeinschaft, Epidemiology, Berlin, Germany*

Background: Diet has been previously described as an impact factor on the course of rheumatic diseases, such as rheumatoid arthritis and systemic lupus erythematosus (SLE). It has been previously reported that dietary sugar intake may contribute to subclinical inflammation and disease activity in SLE. However, there is very little investigation on the possible association between nutritional parameters and their influence on spondyloarthritis (SpA).

Objectives: To investigate the possible impact of nutritional parameters on the disease activity in patients with SpA.

Methods: Patients with radiographic axial SpA and starting a biological therapy were recruited between 2015 and 2019 in an extension of the prospective German Spondyloarthritis Inception Cohort (GESPIC). Dietary habits were collected at baseline using the country-specific validated food frequency questionnaire (FFQ) developed for the use in the German Health examination Survey for Adults 2008-2011. The FFQ includes questions about the frequency and amount of 53 food items, consumed during the past 4 weeks, and enabled to compute individual mean consumptions of foods in grams per day. Total energy intake (in Kcal per day) and nutritional parameters: carbohydrates, free sugars, total fats, saturated fats, mono and poly-unsaturated fats, proteins and dietary fiber, were calculated for each patient using a nutrition organization software and the database of Federal Food Code (Bundeslebensmittelschlüssel), version 3.02. Disease activity measures (BASDAI, CRP and ASDAS), as well as height, weight and body mass index (BMI) were assessed at baseline before starting the biological treatment.

Results: A total of 104 patients from 129 patients with axial SpA enrolled in the cohort were included in this nutritional analysis. The mean age (mean±SD) was 37.0±11.0 years old with symptoms duration of 11.3±9.9 years, 68.3% were males, and 86.5% were HLA-B27 positive. Patients presented BMI of 25.1±4.3 kg/m^2, BASDAI 5.6±1.4, CRP 14.0±18.2 mg/l, and ASDAS 3.5±1.0.

In the univariable and multivariable regression analysis, a higher energy intake and carbohydrates were associated with higher disease activity, measured by ASDAS, BASDAI and CRP. This association was attributable to the full intake of carbohydrates and specifically to the total of free sugars (monosaccharides

and disaccharides) and the decrease of dietary fiber as shown in the multivariable analyses (Figure 1). This effect was independent of age, sex, smoker status and BMI.

Conclusion: A higher intake of carbohydrates and a higher consumption of free sugars are associated with higher disease activity in patients with AS.

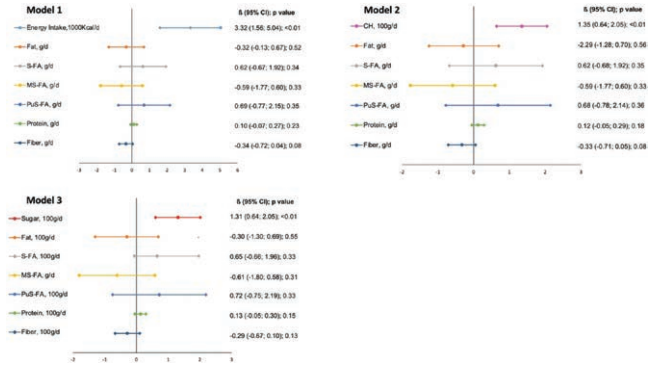


Figure 1. Multivariable linear regression analysis of the association between CRP and nutritional parameters in patients with radiographic axial SpA (n=104), adjusted for age, sex, body mass index and smoker status. Model 1 included variable of total energy intake, model 2 included variable of total intake of carbohydrates (CH) and model 3 included variable of free-sugar (monosaccharides and disaccharides).

B, linear regression coefficient; CH, carbohydrates; CI, confidence interval; MS-FA, monosaturated fatty acids; PuS-FA, polyunsaturated fatty acids, S-FA, saturated fatty acids.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2052

POS0980

ANALYSIS OF PRIMARY CARE CONSULTATION PATTERNS TO AID DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS – AN EXPLORATORY CASE SERIES

M. Al-Attar[1], W. J. Gregory[1,2], J. Mcbeth[3,4], W. Dixon[1,3,4]. [1]*Rheumatology Department, Salford Royal NHS Foundation Trust, Salford, United Kingdom*; [2]*Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, Manchester, United Kingdom*; [3]*Centre for Epidemiology Versus Arthritis, University of Manchester, Manchester, United Kingdom*; [4]*NIHR Manchester Musculoskeletal Biomedical Research Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, United Kingdom*

Background: Patients with Axial Spondyloarthritis (AxSpA) often suffer a significant delay to diagnosis. This is associated with poorer outcomes in quality of life, functional capabilities and work productivity [1]. These patients are frequent consulters to primary care in the years preceding rheumatology referral [2]. We hypothesise that analysis of primary care consultation patterns may identify as-yet undiagnosed disease, and suggest that implementing an automated diagnostic algorithm may support early action in primary care.

Objectives: To undertake a preliminary exploration of primary care consultation patterns in patients with a delayed diagnosis of AxSpA and identify themes for further research.

Methods: The study was run in Salford, UK, where unique linkage exists across electronic health records (EHR) from primary and secondary care. A dataset of patients with AxSpA was obtained from 2018-2020 hospital physiotherapy clinic records. Ten patients with a time to diagnosis ≥ 5 years were randomly selected for this exploratory analysis. Diagnostic delay was calculated based on rheumatology clinic letter documentation. Age, sex, and HLA-B27 status were recorded. All "Problem" codes from the primary care EHR up to the point of diagnosis were manually reviewed.

Results: Age at diagnosis was 32-49 years with seven males and three females. Seven were HLA-B27 positive. The average delay to diagnosis was 15.8 years (range 5-30).

On average, patients had 15 primary care consultations (range 5-24) between first coded AxSpA-related symptom and rheumatology referral. Around half of these codes were potentially AxSpA-related (for example, see Figure 1).

Six patients had a coded history of back pain. Two patients presented with other axial symptoms, including: rib pain, MSK chest pain and sciatica.

Five patients presented with peripheral joint symptoms, including: ankle pain, shoulder pain, knee problem, pain in arm, medial epicondylitis elbow, hip pain and groin pain. Of these, four had multiple presentations and three had a previous visit with axial pain.

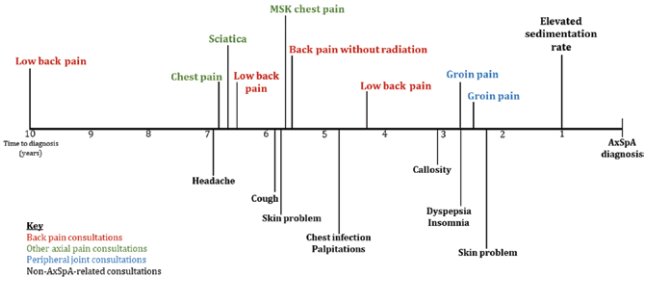
Two patients had uveitis preceding axial symptoms. One patient had peripheral joint symptoms (hip pain) preceding uveitis.

Inconsistent codes were used for the same problem presenting at different times in nine cases, including: back pain, backache, low back pain, lower back pain.

Other relevant codes were used in seven cases, including: stiffness, arthritis, saw physiotherapist and referred to pain clinic.

Figure 1 illustrates the consultation pattern for a male patient who first presented to primary care with back pain at the age of 35. Despite a relatively typical presentation, his diagnosis was made incidentally 10 years later after an ESR was checked for unrelated reasons. He was significantly disabled in function at the point of being referred to rheumatology.

Figure 1: Example of a patient's primary care consultation pattern



Conclusion: Our preliminary analysis suggests that patients with a delayed diagnosis of AxSpA have repeated primary care visits with potentially recognisable symptoms of their disease. These findings support the feasibility of future automated detection, with areas of focus including recognition of non-back pain axial symptoms, extra-articular manifestations, and peripheral joint symptoms.

Whilst half of presentations were not directly AxSpA-related, modern machine learning techniques have the ability to explore whether the pattern or frequency of these consultations are relevant to identifying undiagnosed disease. Such methods can also highlight patterns obscured by extensive data sets and inconsistent coding, with opportunity for implementation back into primary care.

REFERENCES:

[1] Redeker I et al. Determinants of diagnostic delay in axial spondyloarthritis: an analysis based on linked claims and patient-reported survey data. Rheumatology (Oxford) 2019;58:1634–8.

[2] Yi E et al. Clinical, Economic, and Humanistic Burden Associated With Delayed Diagnosis of Axial Spondyloarthritis: A Systematic Review. Rheumatol Ther. 2020;7(1):65–87

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2124

POS0981

COMPUTED TOMOGRAPHY-BASED ASSESSMENT OF RADIOGRAPHIC PROGRESSION IN SPINE AND SACROILIAC JOINTS AFTER PREGNANCY IN WOMEN WITH ANKYLOSING SPONDYLITIS

K. A. Lee[1], S. Y. Lee[2], H. S. Kim[1], H. R. Kim[3], S. H. Lee[2]. *[1]Soonchunhyaung University Seoul Hospital, Internal Medicine, Seoul, Korea, Republic of (South Korea)*; *[2]Kyung Hee University Hospital at Gangdong, Internal Medicine, Seoul, Korea, Republic of (South Korea)*; *[3]Konkuk University Medical Center, Internal Medicine, Seoul, Korea, Republic of (South Korea)*

Background: Mechanical stress are one of the pathogenesis of ankylosing spondlitis (AS). During pregnancy, the mechanical overload on the spine and pelvis increases due to gravid uterus. Recently, computed tomography syndesmophyte score (CTSS) has been developed to analysis of the spinal damage in patients with AS. Indeed, CT has higher sensitivity and reliability compared to conventional radiography in the detection of sacroiliitis.
Objectives: We aimed to investigate whether pregnancy and delivery affect radiographic progression of spine and SIJ in women with AS based on CT evaluation.
Methods: This retrospective study included women aged 19-49 years with AS who performed at least twice CT scans of whole-spine or sacroilliac joints (SIJ) at intervals of 2 to 4 years. To compare the radiographic progression after delivery, we classified into 2 groups: delivery group or controls. Delivery group was restricted to subjects who had the first CT scans ~2 years before delivery and the second CT scans ~2 years after delivery. CTSS (0-522) and SIJ scores (0-40) were used to evaluate the spinal syndesmophyte and erosion, joint space narrowing, and sclerosis of SIJ.
Results: A total of 21 women in delivery group and 38 women in controls were included. The median (Q1-Q3) CTSS at baseline in delivery group and controls were 19 (16-23) and 20 (13.25-27.75), and median progression was 1 (0-3) and 0 (0-1) during the median 2.9 year follow-up. The median (Q1-Q3) SIJ scores at baseline in delivery group and controls were 13 (8-22) and 11 (6-22), and median progression was 1.5 (0-3) and 1 (0-2). The CTSS and SIJ scores significantly increased in both groups, but no difference in absolute score changes per time point between was observed. The changes in SIJ scores was comparable according to the delivery methods.
Conclusion: This study suggests that pregnancy and delivery had no effect on radiographic progression of spine and SIJ in female with AS.
REFERENCES:

[1] de Bruin F, de Koning A, van den Berg R, Baraliakos X, Braun J, Ramiro S. Development of the CT Syndesmophyte Score (CTSS) in patients with ankylosing spondylitis: data from the SIAS cohort. 2018;77(3):371-7.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2251

POS0982

DIAGNOSTIC VALUE OF SPECT/CT IN AXIAL SPONDYLOARTHRITIS AND OTHER LOW BACK PAIN

J. S. Kim[1], K. Hyun-Sook[1], L. Kyung-Ann[1]. *[1]Soonchunhyang University Seoul Hospital, Soonchunhyang University College of Medicine, Internal Medicine, Seoul, Korea, Republic of (South Korea)*

Background: Spondyloarthropathies (SpA) including ankylosing spondylitis are characterized by inflammatory arthritis involving the spine and peripheral joints. Bone SPECT/CT is in the spotlight as it can reflect the current level of inflammation.
Objectives: We aimed to investigate the diagnostic performance of bone SPECT/CT for axial SpA (axSpA) at the level of sacroiliac joints.
Methods: Patients with low back pain who had undergone SPECT/CT of the SI joints were selected for inclusion in this study through a retrospective review of medical records from August 2016 and July 2018. We used semi-quantitative scoring methods for SPECT/CT. For visual scoring, a score of 0 was assigned when tracer uptake in the sacroiliac joint was less than that in the sacrum; a score of 1, when equal to that in the sacrum; and a score of 2, when greater than that in the sacrum. A score of 2 was considered positive for the diagnosis of sacroiliitis on SPECT/CT (Figure 1). The diagnosis of axSpA was retained when patients fulfilled the Assessment of SpA International Society criteria.
Results: A total of 164 patients were enrolled (34 patients with axSpA). The remaining 130 patients had non-axSpA rheumatic inflammatory disease (n=24), vertebral disk herniation (n=13), avascular necrosis (n=11), and others such as bursitis, and fracture (n=85). The mean age of aSpA (37.8±15.6 years) was lower than controls (49.8±16.4 years) (p<0.001), and axSpA (64.5 %) had more male than others (42.1 %) (p=0.024). The sensitivity, specificity, positive and negative predictive values of bone SPECT/CT for axSpA were 83.9%, 63.2%, 34.7%, and 94.4%, respectively. The bone SPECT/CT maximal score and BASDAI score has positive correlation (r=0.481, p=0.007). The bone SPECT/CT compared with MRI is marginal correlation (k=0.369, p<0.001).
Conclusion: In patients with low back pain, the bone SPECT/CT has a high negative predictive value that can exclude AS. In addition, when contraindication in MRI the bone SPECT/CT can be an alternative test.
REFERENCES:

[1] Rahul V. Parghane, Baljinder Singh, Aman Sharma, Harmandeep Singh, Paramjeet Singh, and Anish Bhattacharya. Role of 99mTc-Methylene Diphosphonate SPECT/CT in the Detection of Sacroiliitis in Patients with Spondyloarthropathy: Comparison with Clinical Markers and MRI. *J Nucl Med Technol 2017; 45:280–28*
[2] Anuj Jain, Suruchi Jain, w A n i l A g a r w a l, Sanjay Gambhir, Chetna Shamshery, and Amita Agarwal(2015). Evaluation of Efficacy of Bone Scan With SPECT/CT in the Management of Low Back Pain. A Study Supported by Differential Diagnostic Local Anesthetic Blocks. *Clin J Pain 2015;31:1054–1059*
[3] Yong-il Kim, Minseok Suh, Yu Kyeong Kim, Ho-Young Lee and Kichul Shin. The usefulness of bone SPECT/CT imaging with volume of interest analysis in early axial spondyloarthritis. *BMC Musculoskeletal Disorders (2015) 16:9*
[4] Jennifer Saunders, Mel Cusi, and Hans Van der Wall. What's Old Is New Again: The Sacroiliac Joint as a Cause of Lateralizing Low Back Pain. *Tomography (2018) VOLUME 4 NUMBER 2*
[5] Satoshi Kato, Satoru Demura, Hidenori Matsubara, Anri Inak2, Kazuya Shinmura, Noriaki Yokogawa, Hideki Murakam1, Seigo Kinuya and Hiroyuki Tsuchiya. Utility of bone SPECT/CT to identify the primary cause of pain in elderly patients with degenerative lumbar spine disease. *Journal of Orthopaedic Surgery and Research (2019) 14:185*
[6] Romain De Laroche, Erwan Simon, Nicolas Suignard, Thomas Williams, Marc-Pierre Henry, Philippe Robin, Ronan Abgral, David Bourhis Pierre-Yves Salaun, Frédéric Dubrana, Solène Querellou. Clinical interest of quantitative bone SPECT-CT in the preoperative assessment of knee osteoarthritis. *De Laroche et al. Medicine (2018) 97:35*
[7] Inki Lee, Hendra Budiawan, Jee Youn Moon, Gi Jeong Cheon, Yong Chul Kim, Jin Chul Paeng, Keon Wook Kang, June-Key Chung, and Dong Soo Lee. The Value of SPECT/CT in Localizing Pain Site and Prediction of Treatment Response in Patients with Chronic Low Back Pain. *J Korean Med Sci 2014; 29: 1711-1716*

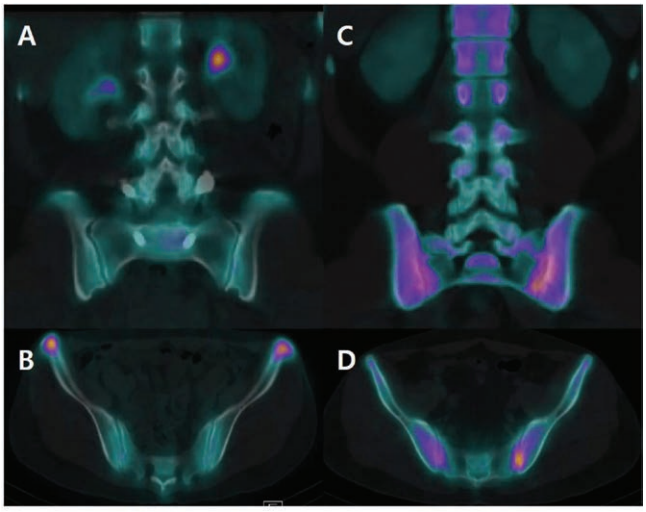


Figure 1. There is two bone SPECT/CT imaging. (A,B) 44 years old female diagnosed with ankylosing spondylitis (AS) and her Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score is 2.2. For visual scoring is 1 because sacroiliac joint was equal to sacrum. (C,D) 26 years old male, he diagnosed AS and BASDAI score is 4. sacroiliac joint uptake is greater than the sacrum, so semi-quantitative scoring is 2.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2296

POS0983

WORK PARTICIPATION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN GERMANY: RESULTS FROM A MULTICENTER, OBSERVATIONAL SURVEY (ATTENTUS-AXSPA)

U. Kiltz[1], K. Hoeper[2], L. Hammel[3], S. Lieb[4], A. Haehle[4], D. Meyer-Olson[5]on behalf of The study was sponsored by Novartis Pharma GmbH, Germany.. *[1]Rheumazentrum Ruhrgebiet; Ruhr Universität, Department of Rheumatology, Herne, Bochum, Germany*; *[2]Regionales Kooperatives Rheumazentrum Niedersachsen e. V.; Medizinische Hochschule Hannover, Klinik für Rheumatologie und Immunologie, Department of Rheumatology, Hannover, Germany*; *[3]Deutsche Vereinigung Morbus Bechterew e.V., Patient representative, Schweinfurt, Germany*; *[4]Novartis Pharma GmbH, Immunology, Hepatology and Dermatology, Nürnberg, Germany*; *[5]Medizinische Hochschule Hannover, Klinik für Rheumatologie und Immunologie; m&i Fachklinik Bad*

Pyrmont/MVZ Weserbergland, Rheumatology and Immunology, Hannover; Bad Pyrmont, Germany

Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory condition often associated with impaired working participation[1] not only translating to devastating outcomes for patients (pts) but also increased economic and social burden due to a significant amount of indirect costs. Data on the different work participation domains in axSpA pts with access to biologic therapies are limited.
Objectives: To characterise the different domains of work participation [presenteeism, absenteeism, sick leave, unemployment, disability pensions] in axSpA pts and their associations with demographic and clinical confounders.
Methods: Pts with confirmed clinical diagnosis of axSpA were enrolled in a multicenter, observational ATTENTUS survey conducted across Germany (Nov-2019 to Jul-2020). To ensure high data quality, inclusion criteria was verified by external monitoring, followed by evaluation of the domains of impaired work participation, including absenteeism and presenteeism (WPAI). Demographics, clinical parameters and patient related outcomes (PROs) were collected via tablet. This analysis included working age (18–65 years) pts; and excluded students and retired pts. Pts without absenteeism (value=0) and presenteeism ≤20% were defined as no impairment at work.
Results: A total of 787 axSpA pts were enrolled in the survey. Seven students, 68 retired pts and 17 pts not fulfilling the inclusion criteria were excluded from this analysis, leaving 695 pts with complete data sets. Baseline data are outlined in Table 1. 50 pts received disability pensions, 29 pts received unemployment benefits, 590 (84.9%) pts reported paid work [part-time: n=132 (22.4%); full-time: n=458 (65.9%)], with 242 (41.0%) pts having no impairments at work. 379 (64.2%) employed pts took sick leave within the previous 12 months (mo) (<3 mo: n=351; 3–6 mo: n=17; >6 mo: n=11). Absenteeism and presenteeism occurred in 140 (23.7%) and 496 (84.1%) pts, respectively. Pts without impairments were mostly of young age, male sex, well-educated, with low disease activity, less fatigue and shorter duration of morning stiffness, and preserved global and physical functioning. No apparent differences between pts with and without impairment of work participation were observed in terms of biologic treatment, disease duration and BMI.

Table 1. Descriptive characteristics of the study population

Mean (SD), unless specified	Impaired WP (n=453)	Full WP (n=242)	p-value	Total (n=695)
Age (yrs)	46.7 (11.1)	42.8 (10.1)	**<0.001**	45.3 (10.9)
BMI	28.5 (14.0)	27.0 (6.8)	0.146	28.0 (12.0)
Male, n(%)	246 (54)	177 (73)	**<0.001**	423 (61)
Disease duration (yrs)	12.7 (11.3)	12.4 (10.2)	0.813	12.6 (11.0)
University-Education, n(%)	104 (23.0)	82 (33.9)	**0.001**	186 (26.8)
In a committed relation, n(%)	310 (68.4)	159 (65.7)	0.464	469 (6.6)
ASAS-HI	8.0 (3.3)	3.7 (3.0)	**<0.001**	6.5 (3.8)
BASDAI	4.8 (1.9)	2.1 (1.6)	**<0.001**	3.9 (2.2)
BASDAI > 4, n(%)	286 (63.1)	28 (11.6)	**<0.001**	314 (45.2)
Fatigue [BASDAI #1]	5.8 (2.1)	2.8 (2.1)	**<0.001**	4.7 (2.5)
Duration morning stiffness [BASDAI #6]	3.5 (2.4)	1.6 (1.8)	**<0.001**	2.8 (2.4)
BASFI	4.2 (2.3)	1.5 (1.5)	**<0.001**	3.3 (2.4)
Biologic treatment, n(%)	230 (50.8)	134 (55.4)	0.390	364 (52.4)
Full time employment, n(%)	256 (56.5)	202 (83.5)	**<0.001**	458 (65.9)
Absenteeism	17.9 (32.1)	0	-	10.6 (26.2)
Presenteeism	48.6 (21.00)	9.6 (8.3)	-	32.6 (25.6)

ASAS-HI, Assessment of SpondyloArthritis International Society-Health Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BMI, basal metabolic index; n, number of pts; SD, standard deviation; WP, work productivity; years, yrs

Conclusion: There was a substantial impact on work participation for axSpA pts, despite numerous available therapeutic options. Pts with impaired work participation compared to pts with no impairment, reported increased fatigue, longer duration of morning stiffness, decreased functional capacity, female sex and a lower level of education.

REFERENCES:

[1] Ramoda R et al. *Arthritis Res Ther*. 2016;78

Disclosure of Interests: Uta Kiltz Speakers bureau: AbbVie, Biocad, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Consultant of: AbbVie, Biocad, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: Abbvie, Amgen, Biogen, Fresenius, GSK, Novartis and Pfizer, Kirsten Hoeper Speakers bureau: Abbvie, Chugai, Gilead, Lilly, Novartis, Sandoz Hexal and Sanofi. Consultant of: Abbvie, Chugai, Gilead, Lilly, Novartis, Sandoz Hexal and Sanofi. Ludwig Hammel: None declared, Sebastian Lieb Employee of: Employee of Novartis, Andreas Haehle Employee of: Employee of Novartis, Dirk Meyer-Olson Speakers bureau: Abbvie, Amgen, Berlin Chemie, Bristol Myers Squibb, Cellgene, Chugai, Fresenius Kabi, GSK, Jansen Cilag, Lilly, Medac, Merck Sharp & Dome, Mylan, Novartis, Pfizer, Sandoz Hexal, Sanofi and UCB, Consultant of: Abbvie, Amgen, Berlin Chemie, Bristol Myers Squibb, Cellgene, Chugai, Fresenius Kabi, GSK, Jansen Cilag, Lilly, Medac, Merck Sharp & Dome, Mylan, Novartis, Pfizer, Sandoz Hexal, Sanofi and UCB.
DOI: 10.1136/annrheumdis-2021-eular.2369

POS0984

PREVALENCE OF AXIAL SPONDYLOARTHRITIS AMONG YOUNG PEOPLE CONSULTING BECAUSE OF CHRONIC LOW BACK PAIN IN A UNIVERSITY HOSPITAL IN ARGENTINA

M. A. Tobar Jaramillo[1], N. Marin Zucaro[1], J. Rosa[1], J. Marin[1], M. L. Acosta Felquer[1], L. Ferreyra[1], J. F. Jaramillo Gallego[1], J. Marcos[2], V. Duarte[2], E. Soriano[1]. [1]*Hospital Italiano De Buenos Aires, Buenos Aires, Buenos Aires, Argentina*; [2]*Novartis, Buenos Aires, Buenos Aires, Argentina*

Background: Axial spondyloarthritis (SpA) is an umbrella term encompassing a number of inflammatory conditions involving the axial skeleton. A substantial delay between disease onset, diagnosis and treatment often occurs, related in part to under-recognition of SpA symptoms. Although several studies have investigated since the publication of the ASAS classification criteria in 2009, the prevalence and incidence of axial SpA in the general population and in patients with SpA-related conditions, the actual prevalence of SpA in many countries (including Argentina) is unknown.
Objectives: To estimate the prevalence of axial SpA and the amount of undiagnosed axial SpA in people under 45 years of age that contacted the health care system for chronic low back pain.
Methods: The setting was a university hospital-based health management organization with a population distribution similary to that of Buenos Aires. All electronic medical records of patients < 45 years of age at the time of onset of symptoms (as per the ASAS 2009 criteria) and chronic low back pain for 3 or more months) seen at the university hospital-based health management organization between 2009 and 2019, were reviewed. If the patient fulfilled the ASAS criteria, was classified as having axial SpA [ankylosing spondylitis (AS) or non-radiographic axial SpA (nr-axSpA)]. Among this group, if the diagnosis was already established in the medical records by the treating physicians, these patients were also classified as diagnosed with axial SpA; if not, they were classified as undiagnosed with axial SpA. We are reporting the results of descriptive analysis.
Results: A total of 796 patients were included (Table 1), 426 were women (53.52%, 95% CI 50.1-57) with a median age of 34 years (IQR 29-40) at initiation of low back pain with a median follow up of 77.7 months (IQR 35.7-136.4). The prevalence of axial SpA among patients with chronic low back pain was 5.78% (n= 46, 95% CI 4.2-7.4). 22 patients had AS (2.76%, 95% CI 1.6-3.9) with a median lag time between the onset of low back pain and diagnosis of 58.7 months (IQR 33.5 - 92). All AS cases were already diagnosed. 24 patients had nr-axSpA (3.02%, 95% CI 1.8 - 4.2). Of those, 14 were diagnosed by treating physicians with a lag time median of 23.2 months (IQR 13.1 - 36.5) between the onset of low back pain and diagnosis. Ten patients fulfilled the ASAS criteria (41.7%, CI 95% 22 - 61.4) but were not diagnosed by the treating physicians (22%, 95% CI 9.82-33.66) among the patients with axial SpA.

Table 1. Demographic, clinical features and therapeutic characteristics of patients with chroniclow back pain stratified by diagnosis

	Axial spondyloarthritis N=46	Ankylosing spondylitis N=22	Diagnosed nr-axSpA N=14	Undiagnosed nr-axSpA N=10	Other diagnosis N=749
Female, n (%, CI)	18 (39.13%, 25.04-53.23)	4 (18.18%, 2.06-34.29)	10 (71.42%,47.76-95.09)	4 (40%, 9.63-70.36)	407 (54.34,50.77-579)
Age at chronic LBP initiation, years, median (IQR)	36 (29.25-40)	32 (32-40)	38 (22-36.75)	39 (35.25-41.5)	34 (29-40)
Follow up, median months (IQR)	88 (33.43-148.66)	33.67 (23.38-90.34)	16.73 (7.64-24.02)	64.77 (11.21-164.7)	77.69 (35.83-135.32)
Inflammatory chronic LBP by any criteria n (%)	44 (95.7)	21 (95.5)	13 (92.8)	10 (100)	56 (7.5, 5.6-9.4)
Seen by a Rheumatologist, n (%)	42 (91.3)	22 (100)	14 (100)	6 (60)	36 (5.1)
Lag time between first LBP to SpA diagnosis, months, median (IQR)	34.6 (22.6-63.2)	58.7 (33.5 – 92)	23.1 (13.1-36.5)	-	-
bDMARDs treatment n, (%, CI)	15 (33; 19.5–48)	10(45; 24.4–67.8)	5(36; 13–64.9)	-	-
Lag time between NSAIDs failure and first bDMARDs, months, median (IQR)	2.66 (2.05-4.63)	2.76 (2.07-11.3).	2.66 (2.04-3.25)	-	-

CI: 95% confidential interval, IQR: interquartile range, bDMARDs: biologic disease modifying anti-rheumaticdrugs, **LBP:** low back pain

Conclusion: In our cohort, 5.78% of the patients < 45 years with chronic low back pain had axial SpA (AS: 2.76%; and nr-axSpA: 3.02%). Approximately, one in every five patients had undiagnosed axial SpA. *Original manuscript made in collaboration with Novartis Argentina S.A*

Disclosure of Interests: Mayra Alejandra Tobar Jaramillo: None declared, Nicolas Marin Zucaro: None declared, Javier Rosa: None declared, Josefina Marin: None declared, Maria Laura Acosta Felquer: None declared, LEANDRO FERREYRA: None declared, JOHN FREDY JARAMILLO GALLEGO: None declared, Josefina Marcos Employee of: Novartis, Vanesa Duarte Employee of: Novartis, Enrique Soriano Speakers bureau: AbbVie, Amber, Bristol-Myers Squibb, Eli Lilly, Novartis, Pfizer Inc, Roche, Consultant of: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer Inc, Sandoz, Grant/ research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer Inc, Sandoz.

DOI: 10.1136/annrheumdis-2021-eular.2391

POS0985 DISEASE CONTROL PERCEPTION BY PHYSICIANS AND PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS IN REAL CLINICAL PRACTICE IN SPAIN: MIDAS STUDY RESULTS

J. L. Pablos[1], X. Juanola[2], C. Barbazán[3], M. L. García Vivar[4], A. C. Valenciano[5], C. Rodriguez-Lozano[6], M. Estadella[7], A. Venegas[8], C. Sanabra[8], C. Sastré[8]on behalf of MIDAS group. [1]*Instituto de Investigación Hospital 12 de Octubre,Rrheumatology Service, Madrid, Spain*; [2]*Hospital Universitari Bellvitge, IDIBELL, Rheumatology Service, L'Hospitalet de Llobregat, Barcelona, Spain*; [3]*Complexo Hospitalario Universitario de Vigo,Rrheumatology Service, Vigo, Spain*; [4]*Hospital Universitario Basurto, Rheumatology Service, Bilbao, Spain*; [5]*Hospital Universitario Severo Ochoa, Rheumatology Service, Leganés, Madrid, Spain*; [6]*Hospital Universitario de Gran Canaria Doctor Negrín, Rheumatology Service, Las Palmas de Gran Canaria, Spain*; [7]*Syneos Health, Rheumatology, Barcelona, Spain*; [8]*Novartis Farmacéutica, Rheumatology, Barcelona, Spain*

Background: There are few published data regarding physician' and patient' perception of the disease control for ankylosing spondylitis (AS) and psoriatic arthritis (PsA).

Objectives: To evaluate the relationship between physician' and patient' disease control perception compared to clinical outcomes for controlled disease (BASDAI<4 in AS or DAPSA≤14 in PsA).

Methods: MIDAS is an observational, non-interventional, cross-sectional, multicenter study. Patients ≥18 years with ≥6 months AS or PsA diagnosis according to ASAS and modified New York criteria or CASPAR criteria, respectively, undergoing treatment ≥3 months before inclusion. The endpoint of this analysis was the relationship between disease control perception by physicians and patients and disease control (BASDAI<4 in AS or DAPSA≤14 in PsA).

Results: 313 AS patients included: 75.7% male, 78.5% HLA-B*27+, a mean (SD) age of 50.4 (12.0) years, a mean (SD) disease duration of 15.5 (11.6) years and a mean (SD) CRP of 5.1 (8.2) mg/l. 313 PsA patients included: 54.3% male, 17.95% HLA-B*27+, a mean (SD) age of 54.1 (12.2) years, a mean (SD) disease duration of 10.5 (9.0) years and a mean (SD) CRP of 4.91 (7.3) mg/l. AS group: in 95.5% of AS patients with BASDAI<4, physician's perception matched the clinical evaluation, while only 42.3% of the patients with BASDAI≥4 matched physician's perception. Positive Predictive Value (PPV) was 75.1%, Negative Predictive Value (NPV) was 83.9% and precision was 76.7%. Patients perceived their own disease as controlled in 95.0% of cases with BASDAI scores <4 and as not controlled in 29.7% of cases with BASDAI score ≥4. PPV was 71.1%, NPV was 76.7% and precision was 71.9%. The same trend was observed when assessing disease control through ASDAS-CRP index. PsA group: in 96.2% of patients with DAPSA≤14, physician's perception matched the clinical evaluation, while only 47.6% of patients with DAPSA>14 matched the physician's perception. PPV was 73.1%, NPV was 89.6% and precision was 76.4%. Patients perceived their own disease as controlled in 93.5% of the cases with DAPSA scores ≤14 and as not controlled in 32.3% of the cases with DAPSA>14. PPV was 66.8%, NPV was 77.4% and precision was 68.4%. The same trend was observed when assessing disease control through the MDA criteria (Table 1).

Table 1. Physician's and patient's perception of the disease control related to disease control variables in AS and PsA

			Controlled disease by physician's perception?			Controlled disease by patient's perception?	
		Valid N	Yes N (%)	No N (%)	Valid N	Yes N (%)	No N (%)
AS							
Disease control (BASDAI)	Controlled (BASDAI<4)	202 (100%)	**193 (95.5%)**	9 (4.5%)	202 (100%)	**192 (95.0%)**	10 (5.0%)
	Not controlled (BASDAI≥4)	111 (100%)	64 (57.7%)	**47 (42.3%)**	111 (100%)	78 (70.3%)	**33 (29.7%)**
Disease activity (ASDAS-CRP)	Inactive (ASDAS-CRP<1.3)	92 (100%)	**90 (97.8%)**	2 (2.2%)	92 (100%)	**91 (98.9%)**	1 (1.1%)
	Active (ASDAS-CRP≥1.3)	221 (100%)	167 (75.6%)	**54 (24.4%)**	221 (100%)	179 (81.0%)	**42 (19.0%)**
PsA							
Disease control (DAPSA)	Controlled (DAPSA≤14)	186 (100%)	**179 (96.2%)**	7 (3.8%)	185 (100%)	**173 (93.5%)**	12 (6.5%)
	Not controlled (DAPSA>14)	126 (100%)	66 (52.4%)	**60 (47.6%)**	127 (100%)	86 (67.7%)	**41 (32.3%)**
Active disease (MDA)	Inactive (MDA criteria ≥5)	161 (100%)	**154 (95.7%)**	7 (4.3%)	160 (100%)	**152 (95.0%)**	8 (5.0%)
	Active (MDA criteria<5)	151 (100%)	91 (60.3%)	**60 (39.7%)**	152 (100%)	107 (70.4%)	**45 (29.6%)**

AS, ankylosing spondylitis; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; DAPSA, Disease Activity in Psoriatic Arthritis; MDA, Minimal Disease Activity; PsA, psoriatic arthritis.

Conclusion: A higher agreement between physician's and patient' perception with the current clinical evaluation was observed when patients were controlled. MiDAS study showed that in real clinical practice in Spain, physicians perceived more disease control than the patients

Acknowledgements: We thank to MIDAS group investigators and patients included in the study.

Disclosure of Interests: José Luis Pablos Speakers bureau: Janssen, Pfizer, Lilly, Novartis, Roche, Celgene, Bristol, Abbvie, Sanofi, Consultant of: Janssen, Pfizer, Lilly, Novartis, Roche, Celgene, Bristol, Abbvie, Sanofi, Gilead, Galápagos, Xavier Juanola Speakers bureau: Novartis, Abbvie, Pfizer, Lilly, Consultant of: Novartis, Lilly, Abbvie, Ceferino Barbazán Speakers bureau: Sanofi, Pfizer, Novartis, Amgen, Abbvie, Roche, Galápagos, Lilly, BMS, Biogen, UCB, Consultant of: Sanofi, Pfizer, Novartis, Amgen, Abbvie, Roche, Galápagos, Lilly, BMS, Biogen, UCB, María L. García Vivar Speakers bureau: Lilly, Novartis, Pfizer, Amgen, Bristol, Abbvie, Sanofi, Janssen and UCB, Consultant of: Lilly, Novartis, Pfizer, Amgen, Bristol, Abbvie, Sanofi, Janssen and UCB, Ana Cruz Valenciano Speakers bureau: Novartis, Consultant of: Novartis, Carlos Rodriguez-Lozano: None declared, Maria Estadella Employee of: I'm employed at Syneos Health providing services for Novartis., Ana Venegas Employee of: employee at Novartis, Cristina Sanabra Employee of: Novartis employee, Carlos Sastré Employee of: Novartis employee.

DOI: 10.1136/annrheumdis-2021-eular.2397

POS0986 GENDER DIFFERENCES IN DISEASE CONTROL AND HEALTH STATUS IN PATIENTS WITH ANKYLOSING SPONDYLITIS IN CLINICAL PRACTICE IN SPAIN: RESULTS OF THE MIDAS STUDY

C. Fernández-Carballido[1], J. Gratacos-Masmitja[2], E. De Miguel[3], P. S. Del Río Martínez[4], O. Martínez González[5], A. Fernandez-Nebro[6], P. Vela-Casasempere[7], C. Sanabra[8], C. Sastré[8]on behalf of MIDAS group. [1]*Hospital Universitario San Juan de Alicante, Rheumatology Service, Alicante, Spain*; [2]*Hospital Universitario Parc Taulí, Rheumatology Service, Sabadell, Spain*; [3]*Hospital Universitario La Paz, Rheumatology Service, Madrid, Spain*; [4]*Hospital Clínico Universitario Lozano Blesa, Rheumatology Service, Zaragoza, Spain*; [5]*Hospital Universitario de Salamanca, Rheumatology Service, Salamanca, Spain*; [6]*Hospital Regional Universitario de Málaga, Rheumatology Service, Málaga, Spain*; [7]*Hospital General Universitario Alicante, Rheumatology Service, Alicante, Spain*; [8]*Novartis Farmacéutica, Rheumatology, Barcelona, Spain*

Background: Data on disease activity status and health status (HS) in clinical practice in Spain for patients with ankylosing spondylitis (AS) are scarce. The MIDAS study assessed the disease activity and the relationship with the reported HS in patients with AS treated in clinical practice in Spain.

Objectives: This is a sub-analysis to evaluate the differences in disease activity and HS by gender of the patients with AS included in the MIDAS study.
Methods: MIDAS is an observational, non-interventional, cross-sectional, multicenter study. Patients included were ≥18 years old with ≥6 months since diagnosis, were classified by ASAS and modified New York criteria; undergoing treatment ≥3 months. The primary variable was the disease control assessed by the percentage of patients in remission and low disease activity (measured by BASDAI and ASDAS-CRP)[1-2].
Results: We analyzed 313 AS patients; 237 (75.7%) were male and 76 (24.3%) female (Table 1). Disease control: According to BASDAI <4 (total 64.5% (mean (SD) 3.1 (2.2)); 69.2% (2.9 (2.1)) of the males vs 50.0% (3.8 (2.4)) of the females had a BASDAI <4 (Figure 1A). According to ASDAS-CRP, 57,5% of the AS patients showed low disease activity (ASDAS-ID + ASDAS-LDA), with a mean (SD) ASDAS-CRP of 1.9 (1.1); 138 (58.2%) males and 42 (55.3%) females showed low disease activity (Figure 1B). HS impact was low, with a mean (SD) ASAS-HI of 5.8 (4.4) for AS patients, that was 5.5 (4.4) for males and 6.8 (4.2) for females.

Table 1. Baseline demographic and clinical characteristics of the AS patients analysed.

	Total (n=313)	Male (n=237)	Female (n=76)
Age (years), mean (SD)	50.4 (12.0)	50.1 (12.2)	51.2 (11.5)
Years since diagnosis, mean (SD)	15.5 (11.6)	16.8 (12.2)	11.4 (8.5)
Years since the symptoms' onset to the study visit, mean (SD)	20.5 (12.7)	22.2 (13.0)	15.2 (9.9)
Years since the symptoms' onset to diagnosis, mean (SD)	5.0 (7.2)	5.4 (7.7)	3.9 (5.6)
BMI (kg/m^2), mean (SD)	27.0 (4.9)	27.5 (4.6)	25.5 (5.6)
Obesity (BMI>30), n (%)	67 (23.0%)	53 (23.7%)	14 (20.9%)
Smoking habit			
Current smoker, n (%)	75 (24.0%)	61 (25.7%)	14 (18.4%)
Ex-smoker (>6 months), n (%)	81 (25.9%)	68 (28.7%)	13 (17.1%)
Non-smoker, n (%)	137 (43.8%)	96 (40.5%)	41 (53.9%)
Family history of AS, n (%)	66 (21.1%)	48 (20.3%)	18 (23.7%)
Presence of HLA-B27, n (%)	245 (78.5%)	187 (79.2%)	58 (76.3%)
Patients previously treated with bDMARD	99 (31.6%)	77 (32.5%)	22 (28.9%)
Active disease, n (%)*			
BASDAI ≥4	111 (35.5%)	73 (30.8%)	38 (50.0%)
ASDAS-CRP ≥2.1	133 (42.4%)	99 (41.8%)	34 (44.7%)
CRP levels (mg/l), mean (SD)	5.1 (8.2)	5.7 (9.0)	3.3 (4.3)
PASS, n (%)	270 (86.3%)	208 (87.8%)	62 (81.6%)
ASAS-HI, mean (SD)	5.8 (4.4)	5.5 (4.4)	6.8 (4.2)

*Refers to the percentage of patients with active disease according to BASDAI≥4 and ASDAS-CRP ≥2.1.AS, ankylosing spondylitis; ASAS-HI, Assessment of Spondyloarthritis International Society - Health index; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD: biologic disease modifying anti-rheumatic drug; BMI, body mass index; CRP, C-reactive protein; HLA-B27, human leukocyte antigen B27; PASS, patient acceptable symptom state; SD, standard deviation.

Conclusion: Our analysis showed a higher proportion of females with active disease when using the BASDAI definition. However, when using the ASDAS-CRP definition, these differences by gender seem to be less pronounced. Also, the impact of disease activity on the HS seems to be higher in females than males. As far as we know, this is the first Spanish study to evaluate gender in this patient population.
REFERENCES:
[1] Smolen JS et al. Ann Rheum Dis 2018;77:3-17
[2] Gratacós J et al. Reumatol Clin 2018;14:320-33

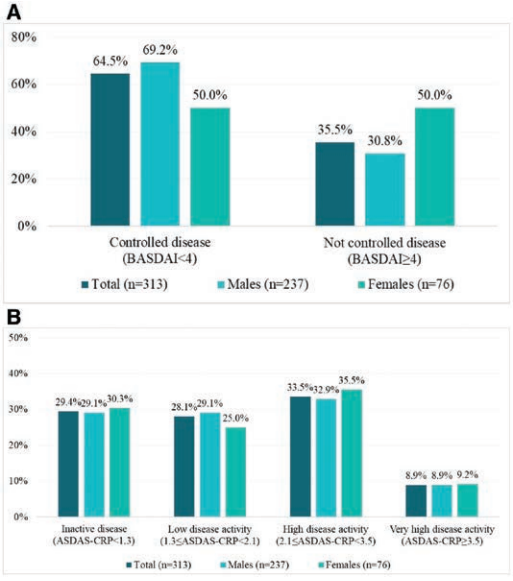


Figure 1. Disease status by sex **A)**Disease control according to BASDAI **B)**Disease status according to ASDAS-CRP

ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score- C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index.
Acknowledgements: We thank to MIDAS group investigators and patients included in the study.
Disclosure of Interests: Cristina Fernández-Carballido Speakers bureau: I have received lectures fees from Abbvie, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB., Consultant of: I have worked as a paid consultant for Abbvie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB., Jordi Gratacos-Masmitja Speakers bureau: MSD, Pfizer, AbbVie, Janssen Cilag, Novartis, Lilly and Amgen., Consultant of: MSD, Pfizer, AbbVie, Janssen Cilag, Novartis, Lilly and Amgen., Grant/research support from: During the course of the year I have received a private grand from Pfizer.
I have not received any private influence in the elaboration of the contents of this talk., Eugenio de Miguel Speakers bureau: AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi., Paid instructor for: Janssen, Novartis, Roche, Consultant of: AbbVie, Novartis, Pfizer, Galapagos, Grant/research support from: Abbvie, Novartis, Pfizer, Pilar Susana Del Río Martínez Speakers bureau: Novartis, Pfizer, Janssen, Sanofi., Paid instructor for: Lilly, Consultant of: Lilly, Sanofi Aventis, Olga Martínez González Speakers bureau: Novartis, Antonio Fernandez-Nebro Speakers bureau: MSD, Pfizer, AbbVie, Janssen Cilag, Novartis, Celgene, GSK, and Lilly, Consultant of: MSD, Pfizer, AbbVie, Janssen Cilag, Novartis, Celgene, GSK, and Lilly, Paloma Vela-Casasempere Speakers bureau: Astra-Zeneca, AbbVie, Boehringer, GSK, Novartis, UCB, Fresenius-Kabi, Sobi and Lilly, Consultant of: Astra-Zeneca, AbbVie, Boehringer, GSK, Novartis, UCB, Fresenius-Kabi, Sobi and Lilly, Grant/research support from: My unit has received also research support from Roche, MSD, Novartis, Lilly, BMS, and Fresenius-Kabi., Cristina Sanabra Employee of: Novartis employee, Carlos Sastré Employee of: Novartis employee.
DOI: 10.1136/annrheumdis-2021-eular.2420

POS0987 INFLAMMATION OF THE HIP JOINTS IN EARLY AXIAL SPONDYLOATRITIS: DATA ANALYSIS OF VISUALIZATION METHODS

E. Agafonova[1], T. Dubinina[1], A. Demina[1], D. Rumiantceva[1], S. Erdes[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*

Background: According to epidemiological studies in Russia, the inflammation of the hip joints occurs in half of patients with ankylosing spondylitis (AS). There have been practically no studies devoted to the investigations of coxitis in patients with early axial spondyloarthritis (axSpA). It is still unknown what factors cause the development of coxitis in axSpA; there is no generally accepted algorithm for diagnosing this condition, especially at an early stage. Previous studies have shown that coxitis in patients with AS develops on average 5–10 years after the onset of the disease, some patients already have irreversible changes in the hip joint at the time of diagnosis, and some do not develop coxitis never.
Objectives: To compare the clinical manifestations of coxitis with the results of magnetic resonance imaging (MRI), ultrasound (US), and radiography of the hip.
Methods: We examined 175 patients (mean age 28.0 ± 5.92 years) with axSpA (ASAS, 2009), with a duration of inflammatory back pain of no more than 5 years, from the CoRSaR cohort. The median duration of the disease was 21 [3–60] months. BASDAI - 4.0 ± 2.0, BASFI - 2.0 [0.4; 3.5]. Among the included patients, 69 (39.4%) had nr-axSpA, and 106 - AS; 87% were HLA-B27 positive. All patients underwent US examination of the hip joint. When synovitis was detected, the patients underwent MRI examination of the hip joint. The increase in the cervical-capsular distance (CCD) more than 7 mm was considered as an ultrasonic coxitis. The median CCD was 7.5 [7.0; 8.2] mm. For coxitis in MRI, osteitis of the head of the hip or acetabulum and synovitis were taken. Radiographic severity of coxitis was determined by BASRI hip.
Results: According to the US data, synovitis of the hip joint was detected in 54 from 175 (30.9%) patients. Pain in the hip joint had 33 (61%) patients. There was no correlation between the intensity of pain and CCD. CCD significantly correlated with laboratory indicators of disease activity, such as ESR (r = 0.34; p <0.05) and CRP (r = 0.3; p <0.05). Only 7 (13.0%) patients had BASRI hip stages II or III and the rest had normal hip joints. 39 (72%) had MRI manifestations of coxitis: 36 (66%) patients had synovitis, 1 (2%) had bone marrow edema, and 2 (4%) had a combination of synovitis with osteitis. Patients with and without radiographic coxitis did not differ in terms of disease activity and functional indices.
Conclusion: In early axSPA:
- 30.9% of patients have hip synovitis, and among them, MRI signs of coxitis have 72%, and X-ray coxitis - 13%;
- ultrasound synovitis is only confirmed by MRI in 70% of cases;
- it seems that the radiological progression of coxitis does not depend on the activity of the disease.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2432

POS0988 FACTORS ASSOCIATED WITH PAIN INTENSITY IN AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

M. Garrido-Cumbrera[1], V. Navarro-Compán[2], C. Bundy[3], L. Christen[4], R. Mahapatra[5], S. Makri[6], C. J. Delgado-Domínguez[1], J. Correa-Fernández[1], P. Plazuelo-Ramos[7], D. Poddubnyy[8]on behalf of IMAS working group.
[1]*Universidad de Sevilla, Health & Territory Research (HTR), Sevilla, Spain*; [2]*Hospital Universitario La Paz, IdiPaz, Madrid, Spain*; [3]*Cardiff University, School of Healthcare Sciences, Cardiff, United Kingdom*; [4]*Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; [5]*Axial Spondyloarthritis International Federation (ASIF), Patient Advocacy, London, United Kingdom*; [6]*Cyprus League Against Rheumatism (CYPLAR), Patient Advocacy, Nicosia, Cyprus*; [7]*Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; [8]*Charité - Universitätsmedizin Berlin, Rheumatology Department, Berlin, Germany*

Background: Pain is a hallmark of axial spondyloarthritis (axSpA) and can significantly deteriorate patients' health status.
Objectives: This analysis aims to investigate factors associated with pain intensity in a large sample of European axSpA patients.
Methods: 2,846 unselected patients participated in EMAS, a cross-sectional study (2017-2018) across 13 European countries. Data from 2,636 participants who reported pain were analysed. Pain was measured by the mean of two BASDAI questions (range 0 "no pain" to 10 "most severe pain"): "How would you describe the overall level of AS neck, back or hip pain you have had?" and "How would you describe the overall level of pain/swelling in joints other than neck, back, hips you have had?". Linear regression analysis was applied to identify associations between pain intensity and sociodemographic factors, patient-reported outcomes [BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), mental health using the 12-item General Health Questionnaire GHQ-12 (0-12)], work life, physical activity and comorbidities, for which 850 patients were included.
Results: The mean age of the sample was 44 years, 61.4% were female, 49.4% had a university degree and 67.7% were married. The average reported pain intensity was 5.3 (±2.2); 76.2% reported pain intensity ≥4, with the greatest intensity reported by women (5.5 vs 4.9, p<0.001), those not university educated (5.6 vs 5.0, p<0.001), separated or divorced compared to singles (5.8 vs 5.2, p=0.004), and not physically active (5.7 vs 5.2, p<0.001). In addition, employed patients who experienced work-related issues reported greater pain (5.2 vs 3.9) as did those who experienced/ believed they would face difficulties finding work due to axSpA (5.9 vs 4.3), and those whose employment choice was determined by axSpA (5.7 vs 4.9; all p<0.001). Moreover, associations with anxiety (5.9 vs 5.0), depression (6.1 vs 5.0) and sleep disorders (5.9 vs 4.9; all p<0.001) were also found. The multiple linear regression model showed that those with higher pain intensity reported at least one work-related issue (B=0.65), difficulties finding work due to axSpA (B=0.48), not having attended university (B=0.38), greater spinal stiffness (B= 0.29), being female (B=0.26) and poorer mental health (GHQ-12) (B=0.10) (Table 1).

Table 1. Regression analysis of the variables associated with pain intensity (0-10 NRS), n=850

	Univariable		Multivariable	
	B	95% CI	B	95% CI
Gender. Female[1]	0.604	**0.432, 0.775**	0.260	**0.003, 0.517**
Educational level. No University[2]	0.671	**0.504, 0.838**	0.376	**0.118,0.634**
Marital Status. Divorced/Separated[3]	0.495	**0.209, 0.780**	-0.044	-0.468, 0.380
Body Mass Index. Obese[4]	0.362	-0.097, 0.821	NA	NA
GHQ-12 (0-12)	0.182	**0.163, 0.201**	0.100	**0.064, 0.137**
Functional Limitation (0-54)	0.036	**0.030, 0.041**	0.009	-0.001, 0.018
Spinal Stiffness (3-12)	0.357	**0.326, 0.388**	0.288	**0.234, 0.342**
Diagnostic Delay, years	0.020	**0.010, 0.030**	-0.015	-0.032, 0.002
Work-Related Issues. Yes	1.338	**1.095, 1.582**	0.654	**0.338, 0.970**
Difficulty finding job due to axSpA. Yes	1.568	**1.362, 1.774**	0.476	**0.176, 0.776**
Work choice determinate by axSpA. Yes	0.808	**0.633, 0.983**	0.199	-0.069, 0.467
Physical activity. No	0.494	**0.263, 0.725**	-0.128	-0.497, 0.242
Anxiety diagnosis. Yes	0.935	**0.753, 1.117**	-0.047	-0.416, 0.321
Depression diagnosis. Yes	1.107	**0.919, 1.295**	0.115	-0.270, 0.500
Sleep disorder diagnosis. Yes	1.042	**0.871, 1.213**	-0.091	-0.392, 0.211

[1]Female vs Male; [2]No university studies (no schooling, primary and high school) vs University studies; [3]Divorced/separated vs single, married and widow; [4]Obese vs not obese (underweight, normal and overweight).

Conclusion: Pain was most strongly associated with working life impairment, as well as with spinal stiffness. Pain was also associated with suffering from depression, anxiety and sleep disorders. Understanding how pain affects individuals and shared-decision making between rheumatologists and patients are essential for long-term disease management and preserving quality of life of axSpA patients.
Acknowledgements: This study was supported by Novartis Pharma AG. The authors would like to thank all patients who participated in the EMAS study.
Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Christine Bundy Consultant of: Abbvie, Celgene, Janssen, Lilly, Novartis, and Pfizer, Laura Christen Employee of: Novartis Pharma AG, Raj Mahapatra: None declared, Souzi Makri: None declared, Carlos Jesús Delgado-Domínguez: None declared, José Correa-Fernández: None declared, Pedro Plazuelo-Ramos: None declared, Denis Poddubnyy Consultant of: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Abbvie, MSD, Novartis, and Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.2439

POS0989 FACTORS ASSOCIATED WITH INABILITY TO WORK AND DISABILITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

M. Garrido-Cumbrera[1], C. Bundy[2], V. Navarro-Compán[3], L. Christen[4], R. Mahapatra[5], S. Makri[6], C. J. Delgado-Domínguez[1], D. Gálvez-Ruiz[1], P. Plazuelo-Ramos[7], D. Poddubnyy[8]on behalf of IMAS working group.
[1]*Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; [2]*Cardiff University, School of Healthcare Sciences, Cardiff, United Kingdom*; [3]*Hospital Universitario La Paz, IdiPaz, Madrid, Spain*; [4]*Novartis Pharma AG, Patient Engagement, Basel, Spain*; [5]*Axial Spondyloarthritis International Federation (ASIF), Patient Advocacy, London, United Kingdom*; [6]*Cyprus League Against Rheumatism (CYPLAR), Patient Advocacy, Nicosia, Cyprus*; [7]*Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; [8]*Charité - Universitätsmedizin Berlin, Rheumatology Department, Berlin, Germany*

Background: Axial spondyloarthritis (axSpA) is associated with a high burden of disease, which may lead to inability to work and disability.
Objectives: This analysis aims to identify factors associated with inability to work and disability among European axSpA patients.
Methods: Data from 2,846 unselected patients participating in EMAS, a cross-sectional study (2017-2018) across 13 European countries were analysed. The sample was divided into those on permanent sick leave or with a recognised disability (Group 1) and those with neither permanent sick leave nor a recognized disability (Group 2). Mann-Whitney and Pearson's χ^2 tests were used to analyse possible differences between groups regarding sociodemographic characteristics, patient-reported outcomes [BASDAI (0-10), GHQ-12 (0-12), functional limitation (0-54) and spinal stiffness (3-12)], lifestyle habits, working life, and comorbidities). Univariable and multivariable binary logistic regression were used to analyse variables possibly explaining being on permanent sick leave and disability, for which 1,657 patients were included.
Results: Mean age was 43.9 years, 61.3% were female, 48.1% had a university degree, and 67.9% were married. Patients in Group 1 (34.4%; n=978) were more likely to be women (54.3%), married (71.1%), with higher disease activity (BASDAI 5.9 vs. 5.3), functional limitation (25.1 vs. 18.0), spinal stiffness (8.6 vs. 7.3; all p<0.001), and longer diagnostic delay (8.1 vs 7.1 years; p = 0.01) than those in Group 2 (65.6%; n=1,868). In addition, 88.0% of Group 1 (n=728) had difficulties in finding a job due to axSpA throughout life; and more than 30.0% reported a diagnosis of anxiety, depression, or sleep disorders. Moreover, being in Group 1 was associated with higher functional limitation in all daily activities. In the multivariable binary logistic regression, the qualitative variables associated with permanent sick leave or disability were: difficulties finding work (OR= 2.52), belonging to a patient organisation (OR= 1.54) and work choice determined by axSpA (OR= 1.38). The quantitative variables associated with permanent sick leave or disability were: higher spinal stiffness (OR= 1.09), older age (OR= 1.03), longer disease duration (OR= 1.03), shorter diagnostic delay (OR= 0.98), and higher functional limitation (OR= 1.01) (Table 1).

Table 1. Regression analysis for variables explaining being on permanent sick leave or disability (n=1,657)

	Univariable logistic analysis		Multivariable logistic analysis	
Qualitative variables	**OR**	**95% CI[3]**	**OR**	**95% CI[3]**
Gender[1]	1.57	**1.34, 1.83**	1.24	0.97, 1.57
Educational level[2]	1.71	**1.46, 2.00**	1.08	0.86, 1.35
Member of a patient organisation. Yes	1.96	**1.67, 2.29**	1.54	**1.23, 1.94**
Smoking. Yes	1.28	**1.08, 1.51**	1.22	0.96, 1.55
Difficulty finding job due to axSpA. Yes	3.71	**2.89, 4.77**	2.52	**1.83, 3.47**
Work choice determined by axSpA. Yes	1.69	**1.43, 1.99**	1.38	**1.09, 1.75**
Anxiety diagnosis. Yes	1.27	**1.07, 1.51**	0.98	0.72, 1.34
Depression diagnosis. Yes	1.58	**1.33, 1.89**	1.25	0.92, 1.69
Sleep disorder diagnosis. Yes	1.33	**1.13, 1.56**	0.95	0.73, 1.23
Quantitative variables	**OR**	**95% CI[3]**	**OR**	**95% CI[3]**
Age. Years	1.04	**1.03, 1.04**	1.03	**1.01, 1.04**
BASDAI (0-10)	1.18	**1.13, 1.24**	1.06	0.98, 1.13
Functional limitation (0-54)	1.03	**1.02, 1.03**	1.01	**1.00, 1.02**
Spinal stiffness (3-12)	1.25	**1.20, 1.29**	1.09	**1.03, 1.15**
Diagnostic delay	1.01	**1.01, 1.02**	0.98	**0.96, 0.99**
Disease duration	1.04	**1.03, 1.05**	1.03	**1.01, 1.04**

[1]Male vs Female; [2]No university studies vs university studies. [3]95% CI for test H_0: OR=1

Conclusion: One third of patients reported being on permanent sick leave or having a recognised disability. They were more likely to have higher spinal stiffness scores, were older in age, experiencing difficulty finding a job, and belonged to a patient organisation. Increased efforts in relation to early access to effective treatments and the creation of flexible working environments are essential for axSpA patients to continue working and remain active, which benefits their quality of life.

Acknowledgements: This study was supported by Novartis Pharma AG.The authors would like to thank all patients who participated in this study.

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Christine Bundy Consultant of: Abbvie, Celgene, Janssen, Lilly, Novartis, and Pfizer, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Laura Christen Employee of: Novartis Pharma AG, Raj Mahapatra: None declared, Souzi Makri: None declared, Carlos Jesús Delgado-Domínguez: None declared, David Gálvez-Ruiz: None declared, Pedro Plazuelo-Ramos: None declared, Denis Poddubnyy Consultant of: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Abbvie, MSD, Novartis, and Pfizer.

DOI: 10.1136/annrheumdis-2021-eular.2450

POS0990

FACTORS ASSOCIATED WITH ENGAGING IN PHYSICAL ACTIVITY IN AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

M. Garrido-Cumbrera[1], D. Poddubnyy[2], C. Bundy[3], L. Christen[4], R. Mahapatra[5], S. Makri[6], C. J. Delgado-Domínguez[1], D. Gálvez-Ruiz[1], P. Plazuelo-Ramos[7], V. Navarro-Compán[8]on behalf of IMAS working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; *[2]Charité - Universitätsmedizin Berlin, Rheumatology Department, Berlin, Germany*; *[3]Cardiff University, School of Healthcare Sciences, Cardiff, United Kingdom*; *[4]Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; *[5]Axial Spondyloarthritis International Federation (ASIF), Patient Advocacy, London, United Kingdom*; *[6]Cyprus League Against Rheumatism (CYPLAR), Patient Advocacy, Nicosia, Cyprus*; *[7]Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; *[8]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*

Background: Physical activity is an essential component in axial spondyloarthritis (axSpA) care, improving physical and mental well-being.

Objectives: This analysis aims to identify factors associated with engaging in physical activity among axSpA patients.

Methods: Data from 2,424 unselected patients participating in EMAS (N=2,846), a cross-sectional study (2017-2018) across 13 European countries, were analysed. Engaging in physical activity was assessed by the following item: "Do you do any physical or sporting activity?" for which participants could report at least 1 physical activity or that they did not do any physical activity. BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and mental health using General Health Questionnaire GHQ-12 (0-12) were assessed. Mann-Whitney and Pearson's χ^2 tests were used to analyse relationships between engaging in physical activity and sociodemographic factors, patient-reported outcomes, employment, lifestyle and comorbidities. Univariable and multivariable binary logistic regression were used to analyse variables possibly explaining engagement in physical activity.

Results: Mean age was 43.9±12.3 years, 61.3% were female, 48.1% had a university degree and 67.9% were married. 81.8% (n= 2,329) engaged in at least one kind of physical activity. Those physically active were typically male (85.3% vs 79.7% female, p<0.001), university educated (86.0% vs 78.0%, p<0.001), married (83.1% vs 79.2% unmarried, p=0.046), and members of a patient organisation (86.4% vs 78.9% non-member, p<0.001). 25.1% of obese patients (n=533) did not engage in physical exercise (v. 16.6% not obese, p<0.001). Those not engaging in physical activity reported greater disease activity (6.0 vs 5.4 BASDAI, p<0.001), functional limitation (21.6 vs 20.2, p=0.010), spinal stiffness (8.3 vs 7.6, p<0.001), and poorer mental health (5.9 vs 4.8 GHQ-12, p<0.001). Furthermore, 83.9% of those employed (n=1,457) were physically active, versus 73.7% unemployed (n=205; p<0.001). In the multivariable binary logistic regression, the qualitative variables associated with engaging in physical activity were belonging to a patient organisation (OR= 1.91), not being obese (OR= 1.58), being university educated (OR= 1.54), and being male (OR= 1.39). The quantitative variables associated with engaging in physical activity were lower spinal stiffness (OR=0.90), better mental health (OR=0.96), and one-year age increase (OR=1.02). (Table 1).

Table 1. Regression analysis for variables explaining engagement in physical activity (n=2,424)

	Univariable logistic analysis		Multivariable logistic analysis	
Qualitative variables	**OR**	**95% CI[7]**	**OR**	**95% CI[7]**
Gender. Male[1]	1.48	**1.21, 1.81**	1.39	**1.06, 1.82**
Educational level. University[2]	1.73	**1.42, 2.11**	1.54	**1.18, 2.00**
Marital Status. Married[3]	1.73	**1.06, 1.58**	1.18	0.91, 1.54
Patient organization. Member[4]	1.71)	**1.39, 2.10**	1.91	**1.43, 2.55**
Body Mass Index. Not Obese[5]	1.69	**1.35, 2.12**	1.58	**1.17, 2.13**
Employment status. Employed[6]	1.28	**1.06, 1.56**	1.00	0.76, 1.32
Quantitative variables	**OR**	**95% CI[7]**	**OR**	**95% CI[7]**
Age	1.01	**1.00, 1.02**	1.02	**1.01, 1.03**
BASDAI (0-10)	0.86	**0.82, 0.91**	0.96	0.89, 1.04
GHQ-12 (0-12)	0.94	**0.92, 0.96**	0.96	**0.93, 0.99**
Functional Limitation (0-54)	0.99	0.99, 1.00	1.00	0.99, 1.01
Spinal Stiffness (3-12)	0.90	**0.86, 0.94**	0.90	**0.84, 0.95**
Proportion of life with axSpA (0-1)	2.83	**1.50, 5.35**	2.00	0.91, 4.39

[1]Male vs Female; [2]University vs no university; [3]Married vs unmarried; [4]Member vs not; [5]Not obese (underweight, normal and overweight) vs obese; [6]Employed vs not (unemployed, sick leave, retirement, housework and student).[7]95% CI for test H_0: OR=1

Conclusion: These results show that increasing age, being male, university educated, member of a patient organisation, not obese, having lower spinal stiffness, and better mental health increase the probability of engaging in physical activity. Physical activity is an important part of axSpA care and patient organizations play a critical role in enhancing access to and participation in physical activity.

Acknowledgements: This study was supported by Novartis Pharma AG. The authors would like to thank all patients who participated in the study.

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Denis Poddubnyy Consultant of: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB., Grant/research support from: Abbvie, MSD, Novartis, and Pfizer, Christine Bundy Consultant of: Abbvie, Celgene, Janssen, Lilly, Novartis, and Pfizer, Laura Christen Employee of: Novartis Pharma AG, Raj Mahapatra: None declared, Souzi Makri: None declared, Carlos Jesús Delgado-Domínguez: None declared, David Gálvez-Ruiz: None declared, Pedro Plazuelo-Ramos: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2469

POS0991

THE IMPACT OF AXIAL SPONDYLOARTHRITIS ON PATIENTS' SEXUAL LIFE: RESULTS FROM THE SPANISH ATLAS

M. Garrido-Cumbrera[1], J. Gratacos-Masmitja[2], E. Collantes-Estevez[3], P. Zarco-Montejo[4], C. Sastré[5], S. Sanz-Gómez[1], P. Plazuelo-Ramos[6], V. Navarro-Compán[7]on behalf of Atlas working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; *[2]Hospital Universitaria Parc Taulí, Rheumatology Department, Barcelona, Spain*; *[3]Reina Sofía University Hospital, Rheumatology Department, Cordova, Spain*; *[4]Hospital Universitario Fundación Alcorcón, Rheumatology Department, Madrid, Spain*; *[5]Novartis Farmacéutica Spain, Immunology, Hepatology and Dermatology, Barcelona, Spain*; *[6]Spanish Federation of Spondyloarthritis Associations (CEADE), Patient Advocacy, Madrid, Spain*; *[7]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*

Background: Axial Spondyloarthritis (axSpA) can impact patients' sexual life.

Objectives: The aim is to assess the prevalence of functional limitation in sexual activity in axSpA patients in Spain and its associated factors.

Methods: Data from an online survey of 680 unselected axSpA patients pertaining to the Atlas of Axial Spondyloarthritis in Spain were collected. Functional limitation in intimate relations was assessed through a 3-point Likert scale (low, medium, and high) and the sample was divided into 1) low-medium and 2) high. Mann-Whitney and χ^2 tests were used to analyse relations between sociodemographic, employment, lifestyle, patient-reported outcomes, and comorbidities with respect to functional limitation in intimate relations. Univariate and multivariate binary logistic regression was used to analyse its associated factors.

Results: 605 axSpA patients were included: the mean age was 45.5 years, 51.4% were female, 38.3% had a university degree, and 70.7% were married. A total of 57.7%, 28.9%, and 13.4% participants presented high, medium, and low limitation in intimate relations, respectively. Patient with high functional limitation in intimate relations were younger (44.6 vs 46.7, p=0.032), female (67.2% vs 47.6% of male, p<0.001), did not belong to a patient organisation (62.7% vs 51.5% of members, p=0.006), were on sick leave (73.3% vs 51.9% of employed, p<0.001) and smoked more (67.3% vs 52.6%, p<0.001). The high limitation group presented higher disease activity (6.3 vs 4.9), functional limitation (48.2 vs 34.4) and spinal stiffness (7.9 vs 6.9, all p<0.001), worse mental health (7.0 vs 4.1, p<0.001), longer diagnostic delay (9.2 vs 7.6, p=0.019), and more comorbidities such as anxiety (73.3% vs 53.2%), depression (80.0% vs 53.3%) and sleep disorders (70.9% vs 53.9%, all p<0.001). In addition, 80.3% of patients with decreased frequency of intimate relations presented high functional limitation in intimate relations (vs 10.0% with more frequency) and 81.4% had experienced a worsening relationship with their spouse (vs 55.6% with better relation, all p<0.001). In the multivariate binary logistic regression, the qualitative factors associated with high functional limitation in intimate relations were a reduction in the frequency of intimate relations (OR= 18.66) and smoking (OR= 2.89), while the quantitative factor associated with high functional limitation in the intimate relation was higher overall functional limitation (B= 0.292; Table 1).

Table 1. Logistic regression to analyse factor associated with high functional limitation in intimate relation (N= 302)

	Univariate logistic analysis		Multivariate logistic analysis	
	OR	**p-value[1]**	**OR**	**p-value[1]**
Qualitative factors				
Gender. Female	2.254	**<0.001**	1.311	0.569
Patient Organization. Member	0.632	**0.006**	0.515	0.171
Employment. Sick leave	2.354	**<0.001**	1.060	0.910
Smoking. Yes	1.852	**0.001**	2.885	**0.020**
Anxiety diagnosis. Yes	2.420	**<0.001**	0.569	0.306
Depression diagnosis. Yes	3.509	**<0.001**	1.665	0.408
Sleep disorder diagnosis. Yes	2.081	**0.001**	0.625	0.381
Frequency of intimate relation. Less than before vs same or more than before	12.605	**<0.001**	18.655	**<0.001**
Relation with spouse. Worse than before	5.480	**<0.001**	1.256	0.636
Quantitative factors	**B**	**p-value[2]**	**B**	**p-value[2]**
Age	-0.018	**0.021**	0.010	0.718
BASDAI (0-10)	0.398	**<0.001**	-0.155	0.284
GHQ-12 (0-12)	0.154	**<0.001**	0.003	0.952
Functional Limitation (0-54)	0.237	**<0.001**	0.292	**<0.001**
Spinal Stiffness (3-12)	0.131	**<0.001**	-0.116	0.226
Diagnostic Delay	0.030	**0.013**	0.020	0.474

[1]p-value for test H_0: OR = 1 [2]p-value for test H_0: B = 0

Conclusion: More than half of patients with axSpA in Spain presented high functional limitation in intimate relations, who more likely presented decreased frequency of relations. This may indicate that avoidance of sexual encounters is a common coping mechanism for the functional limitation accompanying this disease. Healthcare providers can play a key role in the sexual health of axSpA patients by improving patient-physician communication and raising awareness about the benefits of counselling on a healthy sexual life.

Acknowledgements: This study was supported by Novartis Spain. The authors would like to thank all patients who participated in this study.

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Jordi Gratacos-Masmitja Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Eduardo Collantes-Estevez Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Pedro Zarco-Montejo: None declared, Carlos Sastré Employee of: Novartis Farmacéutica Spain, Sergio Sanz-Gómez: None declared, Pedro Plazuelo-Ramos: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2491

POS0992

PREVALENCE AND ASSOCIATED FACTORS OF SLEEP DISORDERS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE SPANISH ATLAS

M. Garrido-Cumbrera[1], V. Navarro-Compán[2], E. Collantes-Estevez[3], P. Zarco-Montejo[4], S. Sanz-Gómez[1], C. Sastré[5], P. Plazuelo-Ramos[6], J. Gratacos-Masmitja[7]on behalf of Atlas working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; *[2]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*; *[3]Reina Sofia University Hospital, Rheumatology Department, Cordova, Spain*; *[4]Hospital Universitario Fundación Alcorcón, Rheumatology Department, Madrid, Spain*; *[5]Novartis Farmacéutica Spain, Immunology, Hepatology and Dermatology, Barcelona, Spain*; *[6]Spanish Federation of Spondyloarthritis Associations (CEADE), Patient Advocacy, Madrid, Spain*; *[7]Hospital Universitaria Parc Taulí, Rheumatology Department, Barcelona, Spain*

Background: Sleep is an essential aspect of health that is commonly disrupted in patients with axial spondyloarthritis (axSpA).

Objectives: This analysis aims to assess the prevalence and associated factors of sleep disorders in a large sample of axSpA patients.

Methods: In 2016, a sample of 680 unselected patients with axSpA participated in the Atlas of Axial Spondyloarthritis in Spain through an online survey. The sample was divided into: 1) Patients with sleep disorders and 2) Patients without sleep disorders. Disease activity through BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54) and, mental health through a 12-item General Health Questionnaire GHQ-12 (0-12) were assessed. The Mann-Whitney and Pearson's chi-square tests were used to analyse possible relationships between independent sociodemographic characteristics, employment, lifestyle, patient-reported outcomes and comorbidity variables with sleep disorders. Univariate and multivariate binary logistic regression was used to determine the possible association of the independent variables on sleep disorders.

Results: Mean age was 45.7 years, 52.5% female, 36.9% had a university degree, and 71.5% were married. The prevalence of sleep disorders was 19.7%. Those who reported sleep disorders presented higher disease activity (6.3 vs 5.4, p<0.001), worse mental health (7.7 vs 5.0, p<0.001), greater functional limitation (45.7 vs 41.4, p<0.001), greater spinal stiffness (8.0 vs 7.3, p=0.008), and longer diagnostic delay (10.5 vs 7.9, p=0.021). 29.9% of the patients on sick leave had sleep disorders, compared to only 15.4% of employees (p=0.013). In addition, 23.0% of those who were physically active had sleep disorders compared to only 7.1% of those not physically active (p<0.001). Sleep disorders were more prevalent in patients with other comorbidities such as anxiety (60.0% vs 9.7%, w/o anxiety, p<0.001) and depression (66.0% vs 11.7% w/o depression, p<0.001). In the multivariate binary logistic regression, depression (OR= 3.89), anxiety (OR= 3.84), and a longer diagnostic delay (B=0.034) remained significantly associated with sleep disorders. Excluding mental comorbidity parameters from the model, physical activity (OR= 3.52) and disease activity (B= 0.175) remained significantly associated with sleep disorders (Table 1).

Table 1. Logistic regression to analyses factor associated with sleep disorders (N= 366)

	Univariate logistic analysis		Multivariate logistic analysis		Multivariate logistic analysis*	
	OR	**p-value[1]**	**OR**	**p-value[1]**	**OR**	**p-value[1]**
Qualitative factors						
Employment. Sick leave	1.937	**0.003**	1.554	0.180	1.540	0.131
Physical activity. Yes	3.914	**<0.001**	2.410	0.196	3.516	**0.048**
Anxiety diagnosis	13.925	**<0.001**	3.840	**<0.001**	--	--
Depression diagnosis	14.616	**<0.001**	3.886	**<0.001**	--	--
Quantitative factors	**B**	**p-value[2]**	**B**	**p-value[2]**	**B**	**p-value[2]**
BASDAI (0-10)	0.238	**<0.001**	0.036	0.673	0.175	**0.015**
GHQ-12	0.141	**<0.001**	0.045	0.204	--	--
Functional Limitation (0-54)	0.049	**<0.001**	-0.011	0.560	0.022	0.166
Spinal Stiffness (3-12)	0.104	**0.008**	0.016	0.775	0.020	0.683
Diagnostic Delay	0.041	**0.001**	0.034	**0.044**	0.025	0.083

*Excluding mental health factors. [1]p-value for test H_0: OR = 1 [2]p-value for test H_0: B = 0

Conclusion: One of five patients with axSpA reported sleep disorders. The presence of mental comorbidities such as anxiety and depression increases the likelihood of sleep disorders. Moreover, physical activity and disease activity also seem to increase the probability on sleep disorders. Referral to mental health specialists together with optimal healthcare management should be key for the reduction of sleep disorders in axSpA.

Acknowledgements: This study was supported by Novartis Spain. The authors would like to thank all patients who participated in this study.

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Eduardo Collantes-Estevez Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Pedro Zarco-Montejo: None declared, Sergio Sanz-Gómez: None declared, Carlos

Sastré Employee of: Novartis Farmacéutica Spain, Pedro Plazuelo-Ramos: None declared, Jordi Gratacos-Masmitja Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.2537

POS0993 THE IMPORTANCE OF PHYSICAL ACTIVITY IN RELATION TO BEING OVERWEIGHT/OBESE WITH AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE SPANISH ATLAS

M. Garrido-Cumbrera[1], E. Collantes-Estevez[2], V. Navarro-Compán[3], P. Zarco-Montejo[4], J. Correa-Fernández[1], C. Sastré[5], P. Plazuelo-Ramos[6], J. Gratacos-Masmitja[7]on behalf of Atlas working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; *[2]Reina Sofia University Hospital, Rheumatology Department, Cordova, Spain*; *[3]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*; *[4]Hospital Universitario Fundación Alcorcón, Rheumatology Department, Madrid, Spain*; *[5]Novartis Farmacéutica Spain, Immunology, Hepatology and Dermatology, Barcelona, Spain*; *[6]Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; *[7]Hospital Universitaria Parc Taulí, Rheumatology Department, Barcelona, Spain*

Background: Evidence on the negative effects of being overweight/obese on the health outcomes of patients with axial spondyloarthritis (axSpA) is increasing.
Objectives: This study aimed to identify associations between Body Mass Index (BMI) categories and disease activity, functioning, quality of life, and mental health in a large sample of axSpA patients.
Methods: In 2016, a sample of 680 unselected patients with axSpA participated in the Atlas of Axial Spondyloarthritis in Spain through an online survey. The sample was divided in two groups: 1) Patients with a BMI of 18.5 to <25 Kg/m2 (normal weight), and 2) Patients with a BMI of ≥ 25 Kg/m2 (overweight/obesity), excluding the underweight category (BMI <18.5 Kg/m2). The Mann-Whitney and Pearson's chi-square tests were used to analyse possible relationships between independent sociodemographic characteristics, employment, lifestyle, patient-reported outcomes, and comorbidity variables with those who are overweight/obese. Univariate and multivariate binary logistic regression was used to determine the association of the possible factors with those who are overweight/obese.
Results: Of the 663 patients analysed, the mean age was 45.9 years, 51.4% were female, 37.0% had a university degree, and 72.5% were married. The prevalence of overweight/obese patients was 53.4% compared to 46.6% who were of a normal weight. The patients with the highest prevalence of being overweight/obese were older (49.3 vs 42.0, p<0.001), with no university education (59.8% vs 42.4% of university, p<0.001), often widowers (75.0% vs 30.8% of single people, p<0.001), and reported membership of patient organisations (61.7% vs 46.6%, p<0.001). With respect to patients of normal weight, those who were overweight/obese presented greater spinal stiffness (8.2 vs 6.6, p<0.001) and a longer diagnostic delay (9.2 vs 7.8, p=0.005). In addition, patients who were overweight/obese were more likely physically inactive (63.7% vs 36.3%, p=0.007). In the multivariable binary logistic regression analysis, the qualitative factors associated with the presence of being overweight/obese were physical inactivity (OR= 2.40) and males (OR= 1.81), while the quantitative factor most associated with the presence of being overweight/obese were greater spinal stiffness (B= 0.121) and older in age (B= 0.052) (Table 1).

Table 1. Logistic regression to analyses factor associated with being overweight/obese (N= 469)

	Univariate logistic analysis		Multivariate logistic analysis	
	OR	**p-value[1]**	**OR**	**p-value[1]**
Qualitative factors				
Gender. Male	2.376	**<0.001**	1.811	**0.005**
Educational level. No university	2.018	**<0.001**	1.188	0.422
Marital Status. Widowed	2.647	0.235	NA	NA
Member of PAGs. Yes	1.851	**<0.001**	1.095	0.680
Employment. Retired / early retirement	4.414	**<0.001**	1.732	0.195
Physical activity. No	1.703	**0.007**	2.400	**0.038**
Quantitative factors	B	**p-value[2]**	B	**p-value[2]**
Age	0.070	**<0.001**	0.052	**<0.001**
Spinal Stiffness (3-12)	0.220	**<0.001**	0.121	**0.004**
Diagnostic Delay	0.024	**0.035**	0.008	0.568

[1]p-value for test H_0: OR = 1 [2]p-value for test H_0: B = 0.

Conclusion: Being overweight/obese is a common comorbidity among patients with axSpA. The lack of physical activity, male gender, higher spinal stiffness, and older age increase the probability of prevalence of being overweight/obese. Physicians should encourage physical activity in patients with axSpA, especially among men and older people to prevent the factors of being overweight/obese.
Acknowledgements: This study was supported by Novartis Spain. The authors would like to thank all patients who participated in the study.

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Eduardo Collantes-Estevez Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Pedro Zarco-Montejo: None declared, José Correa-Fernández: None declared, Carlos Sastré Employee of: Novartis Farmacéutica Spain, Pedro Plazuelo-Ramos: None declared, Jordi Gratacos-Masmitja Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.2545

POS0994 NON-RHEUMATOLOGISTS FIND IT DIFFICULT TO IDENTIFY AXIAL SPONDYLOARTHRITIS IN WOMEN AND YOUNG PEOPLE. RESULTS FROM THE SPANISH ATLAS

M. Garrido-Cumbrera[1], V. Navarro-Compán[2], J. Gratacos-Masmitja[3], P. Zarco-Montejo[4], J. Correa-Fernández[1], C. Sastré[5], P. Plazuelo-Ramos[6], E. Collantes-Estevez[7]on behalf of Atlas working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; *[2]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*; *[3]Hospital Universitaria Parc Taulí, Rheumatology Department, Barcelona, Spain*; *[4]Hospital Universitario Fundación Alcorcón, Rheumatology Department, Madrid, Spain*; *[5]Novartis Farmacéutica Spain, Immunology, Hepatology and Dermatology, Barcelona, Spain*; *[6]Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; *[7]Reina Sofia University Hospital, Rheumatology Department, Cordova, Spain*

Background: Delayed diagnosis in axial spondyloarthritis (axSpA) in Spain seems to be influenced by the patient diagnostic pathway. In particular, not all patients are diagnosed by rheumatologists, the profession better suited to make an axSpA diagnosis.
Objectives: The aim of this study is to evaluate the differences between patients diagnosed by a rheumatologist and those diagnosed by other healthcare professionals (HCPs).
Methods: In 2016, a sample of 680 unselected patients with axSpA participated in the Atlas of Axial Spondyloarthritis in Spain, an online survey. The sample was divided into: 1) Patients diagnosed by rheumatologists and 2) Non-Rheumatologist diagnosis including general practitioner, orthopaedic specialist, and physiotherapist. The Mann-Whitney and Pearson's chi-square tests were used to assess possible differences between both groups in sociodemographic characteristics, employment, lifestyle, patient-reported outcomes, and comorbidities. Univariate and multivariate binary logistic regression was used to analyse the possible factors associated with diagnosis by a non-Rheumatologist.
Results: A total of 522 axSpA patients participated in this study: the mean age was 45.3 years, 51.0% were female, 38.5% had a university degree, and 71.6% and were married. Prior to diagnosis, axSpA patients visited different HCPs such as a General Practitioner (GP) (88.5%), orthopaedic specialists (71.6%), rheumatologists (71.0%), and physiotherapists (46.9%). The greatest number of visits (mean, median) were made to physiotherapists (3.4, 3), followed by orthopaedic specialists (3.0, 2), rheumatologists (2.0, 1) and GPs (2.6, 2). The majority (81.4%) of patients were diagnosed by a rheumatologist, while 18.6% received their diagnosis from a non-rheumatologist (10.9% orthopaedic specialist, 7.3% general practitioner, and 0.4% physiotherapist). With respect to other specialists such as the GP, orthopaedic specialist or physiotherapist, patients diagnosed by the rheumatologist were younger (44.3 vs 49.5, p<0.001), more frequently female (54.8% vs 45.2% of male, p<0.001), with worse mental health (5.9 vs 4.8, p=0.039), who visited more professionals before being diagnosed (3.0 vs 2.5, p=0.001), were more frequently smokers (40.2% vs 26.0%, p=0.010) and used more biologicals (45.9% vs 33.0%, p=0.021). In the multivariate binary logistic regression, the qualitative factors associated with diagnosis by non-rheumatologists are males (OR= 1.80), and the quantitative factors associated with the diagnosis by non-rheumatologists are older age (B=0.027; Table 1).

Table 1. Logistic regression to analyses factor associated with non-rheumatologist diagnosis (N= 440)

	Univariate logistic analysis*		Multivariate logistic analysis*	
	OR	**p-value[2]**	**OR**	**p-value[2]**
Qualitative factors				
Gender. Female[1]	2.354	**<0.001**	1.797	**0.030**
Smoking. Yes	0.523	**0.010**	0.611	0.095
Used of Biologics. Yes	0.581	**0.022**	0.640	0.086
Quantitative factors	**B**	**p-value[3]**	**B**	**p-value[3]**
Age, in years	0.044	**<0.001**	0.027	**0.028**
GHQ-12 (0-12)	-0.059	**0.038**	-0.011	0.721
Number of HCPs seen before diagnosis	-0.294	**0.001**	-0.153	0.151

*Reference category of the dependent variable: Non-Rheumatologist; [1]Female vs male; [2]p-value for test H_0: OR = 1 [3]p-value for test H_0: B = 0

Conclusion: One out of five patients with axSpA in Spain were not diagnosed by rheumatologists. Patients diagnosed by non-rheumatologists were more likely male and older, suggesting that the suspicion of axSpA in females and younger patients is low among these healthcare professionals. Beside the rheumatologist, it is essential to educate other HCPs on axSpA diagnostic criteria in order to facilitate correct referrals to rheumatologists and shorten the time to diagnosis and effective treatment.

Acknowledgements: This study was supported by Novartis Spain. The authors would like to thank all patients who participated in the study

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Jordi Gratacos-Masmitja Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Pedro Zarco-Montejo: None declared, José Correa-Fernández: None declared, Carlos Sastré Employee of: Novartis Farmacéutica Spain, Pedro Plazuelo-Ramos: None declared, Eduardo Collantes-Estevez Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2551

POS0995 EFFECT OF SEX IN CO-EXISTENT FIBROMYALGIA AND ENTHESITIS IN SPONDYLOARTHRITIS: ANCILLARY ANALYSIS OF THE ASAS-PERSPA STUDY

G. Fitzgerald[1], S. Maguire[2,3], F. B. O'shea[2,3], C. López-Medina[4], M. Dougados[4], N. Haroon[5,6]. [1]*Galway University Hospital, Rheumatology, Galway, Ireland*; [2]*Trinity College Dublin, Medicine, Dublin, Ireland*; [3]*St. James's Hospital, Rheumatology, Dublin, Ireland*; [4]*Cochin Hospital, Rheumatology, Paris, France*; [5]*University Health Network, Rheumatology, Toronto, Canada*; [6]*Toronto Western Hospital, Rheumatology, Toronto, Canada*

Background: Enthesitis is a common feature of axial spondyloarthropathy (axSpA) and psoriatic arthritis (PsA). Up to 25% of individuals with axSpA and PsA have a co-existing diagnosis of fibromyalgia syndrome (FMS). The anatomic overlap between tender points in FMS and sites of entheses is a challenge when differentiating between active SpA and FMS. Literature investigating the co-existence of enthesitis and FMS in individuals with SpA is sparse, in particular the effect of sex. The ASAS Peripheral involvement in Spondyloarthritis (PerSpA) study aims to characterize peripheral musculoskeletal in individuals with SpA across the world.

Objectives: (1)To characterise the co-existence of enthesitis and FMS in individuals with SpA.

(2)To explore the effect of sex on the presence of FMS and enthesitis.

Methods: All individuals from the cross-sectional multinational ASAS-PerSpA study with a diagnosis of axSpA, peripheral SpA (pSpA) or PsA according to their rheumatologist were included. The Fibromyalgia Rapid Screening Tool (FiRST) was used to make the diagnosis of FMS. The baseline descriptive and clinical differences between sexes were performed using T-tests and crosstabs. Sex-stratified comparisons within the following categories were conducted using chi-square analysis and ANOVA as appropriate: (1) enthesitis & fibromyalgia; (2) enthesitis only; (3) fibromyalgia only; (4) neither.

Results: Baseline characteristics of the 4465 included patients are outlined in Table 1, stratified by sex. Enthesitis occurred in 44% (n=1984) of the population and was more common in females than males (48% vs 42%, p<0.01). The majority affected had intermittent episodes of enthesitis (55%, n=1088), with the Achilles tendon and plantar fascia the two most common sites in both sexes. Enthesitis was more often confirmed on imaging in females than males (44% v 35%, p<0.01). The most common treatment for enthesitis was non-steroidal anti-inflammatories (97%, n=1318), with no difference when stratified by sex. FMS occurred in 19% (n=775) of patients and was more common in females than males (28% vs 13%, p<0.01).

Table 1. Participant characteristics, stratified by sex. Values are mean (SD), median (25th, 75th) or n (%). P-values are independent T-tests or Mann-Whitney as appropriate.

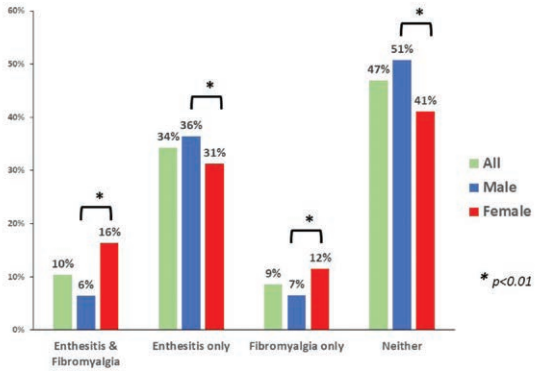
Variable	Total	Male	Female	P value
N	4465	2724	1741	
Age, years	45 (14)	43 (14)	46 (13)	<0.01
Disease duration, years	11 (6, 20)	12 (6, 21)	11 (5, 19)	0.01
Delay to diagnosis, years	3 (1, 9)	3 (1, 9)	3 (1, 10)	0.11
HLA-B27 positive	2066 (66)	1457 (73)	609 (54)	<0.01
Radiographic sacroiliitis	2517 (61)	1788 (70)	729 (46)	<0.01
Sacroiliitis on MRI	1817 (65)	1128 (68)	689 (60)	<0.01
axSpA ASAS criteria	2910 (65)	1953 (72)	957 (55)	<0.01
pSpA ASAS criteria	555 (12)	250 (9)	305 (18)	<0.01
CASPAR criteria	1043 (23)	508 (19)	535 (31)	<0.01
BMI, kg/m^2	26 (23, 29)	26 (23, 29)	26 (23, 30)	0.24
Axial involvement	3428 (76.8)	2243 (82.3)	1185 (68.1)	<0.01
Peripheral involvement	2541 (56.9)	1404 (51.5)	1137 (65.3)	<0.01
Enthesitis	1984 (44.4)	1149 (42.2)	835 (48.0)	<0.01
Uveitis	738 (17)	482 (18)	256 (15)	0.01
Psoriasis	1212 (27)	615 (23)	597 (34)	<0.01
Inflammatory bowel disease	275 (6)	150 (6)	125 (7)	0.02

Enthesitis and FMS occurred together in 10% of the cohort, was more common in women than men (see Figure 1) and was associated with a significantly (p<0.01) longer delay to diagnosis of 1.8 years and a higher BMI of 2.1 kg/m^2 than people with enthesitis only. Objective confirmation of enthesitis was similar in those with and without FMS (38% vs 38%, p=0.92).

The presence of FMS added to the burden of disease in those with enthesitis as assessed by BASDAI (6.4 vs 3.6, p<0.01) and ASDAS-CRP (3.5 vs 2.5, p<0.01), with no difference between sexes (p>0.05).

Conclusion: In this large cross-sectional multinational analysis, FMS affected 19% of individuals with SpA. The co-existence of enthesitis and FMS occurred in 16% of females compared to 6% of males. The presence of FMS increased the burden of disease in those with enthesitis, as assessed by BASDAI and ASDAS-CRP, with no difference between men and women.

Figure 1: Prevalence of co-existent enthesitis & FMS in individuals with SpA, stratified by sex. P<0.01 denotes significant difference between sex.



Disclosure of Interests: Gillian Fitzgerald: None declared, Sinead Maguire Grant/research support from: Recipient of Gilead Inflammation Fellowship, Finbar Barry O'Shea: None declared, Clementina López-Medina: None declared, Maxime Dougados: None declared, Nigil Haroon Speakers bureau: Received honorarium from AbbVie, Eli Lilly, Jannsen, Novartis, UCB, Consultant of: AbbVie, Eli Lilly, Jannsen, Novartis, UCB, Grant/research support from: AbbVie, Eli Lilly, Jannsen, Novartis, UCB.

DOI: 10.1136/annrheumdis-2021-eular.2556

POS0996 SIX-YEAR RESULTS FROM THE ESPERANZA COHORT: EVALUATION OF CLINICAL FEATURES, DISEASE ACTIVITY MEASURES AND TREATMENT ASPECTS IN AXIAL AND PERIPHERAL EARLY SPONDYLOARTHRITIS

C. Tornero[1], V. Navarro-Compán[1], B. Joven-Ibáñez[2], R. Almodovar[3], X. Juanola-Roura[4], C. Fernández-Carballido[5], J. C. Quevedo-Abeledo[6], J. Rosas[7], A. Hernández[8], C. A. Montilla-Morales[9], J. R. Maneiro[10], A. Juan-Mas[11], J. A. Pinto Tasende[12], M. Moreno[13], J. Sanz[14], T. Ruiz Jimeno[15], M. Moreno[16], M. L. Ladehesa Pineda[17], E. De Miguel[18]on behalf of Esperanza study group. [1]*Hospital Universitario La Paz., Department of Rheumatology., Madrid, Spain*; [2]*Hospital Universitario 12 de Octubre, Department of Rheumatology, Madrid, Spain*; [3]*Hospital Universitario Fundación Alcorcón, Department of Rheumatology, Madrid, Spain*; [4]*Hospital Universitari de Bellvitge, Department of Rheumatology, Barcelona, Spain*; [5]*Hospital General Universitario de Elda, Department of Rheumatology, Alicante, Spain*; [6]*Hospital Universitario de Gran Canaria Doctor Negrín, Department of Rheumatology, Las Palmas de Gran Canaria, Spain*; [7]*Hospital Marina Baixa, Department of Rheumatology, Alicante, Spain*; [8]*Hospital Virgen de la Salud, Department of Rheumatology, Toledo, Spain*; [9]*Hospital Universitario de Salamanca, Department of Rheumatology, Salamanca, Spain*; [10]*Complejo Hospitalario Universitario de Santiago de Compostela, Department of Rheumatology, Santiago de Compostela, Spain*; [11]*Hospital Universitario Son Llàtzer, Department of Rheumatology, Palma de Mallorca, Spain*; [12]*Complejo Hospitalario Universitario de A Coruña, Department of Rheumatology, La Coruña, Spain*; [13]*Hospital Parc Tauli, Department of Rheumatoloy, Barcelona, Spain*; [14]*Hospital Universitario Puerta de Hierro, Department of Rheumatology, Madrid, Spain*; [15]*Hospital de Sierrallana, Rheumatology, Torrelavega, Spain*; [16]*Hospital Clínico Universitario Virgen de la Arrixaca, Department of Rheumatology, Murcia, Spain*; [17]*Hospital Universitario Reina Sofía, Department of Rheumatology, Córdoba, Spain*; [18]*Hospital Universitario La Paz, Department of Rheumatology, Madrid, Spain*

Background: Esperanza was a multicenter national health program developed to facilitate an early diagnosis of patients with Spondyloarthritis (SpA) in Spain.

Objectives: To compare the clinical evolution of patients with axial SpA (axSpA) and peripheral SpA (pSpA) included in this program.
Methods: Patients from the Esperanza cohort fulfilling ASAS criteria for axSpA or pSpA and completed the 6-year follow-up were included. Patients were classified according to the predominant symptom. In case of having axSpA and pSpA, they were classified as axSpA. Clinical features, disease activity and treatment aspects at baseline and 6-year visit were evaluated.
Results: From 775 patients recruited at baseline, 6-year follow-up data from 178 (83.5%) fulfilling ASAS criteria at the final visit were available: 133 (74.7%) for axSpA and 45 for pSpA (25.3%). 118 (66.3%) were males (50.6% with axSpA and 62.2%, pSpA, p=0.4). Patients with axSpA had more frequently positive HLA-B27 (90.5%) vs. (9.5%), p<0.001. Follow-up clinical features are shown in Table 1. At the final visit, both axSpA and pSpA presented an improvement in clinical symptoms, disease activity (CRP, BASDAI, ASDAS and VAS-pt) and quality of life (ASQoL). A worsening of mobility (BASMI) was observed in both groups. The prevalence of uveitis, psoriasis and inflammatory bowel disease (IBD) at baseline was 10.7%, 18% and 5.6%, respectively. At the 6-year visit, the cumulative prevalence (CP) was 14% for uveitis (16.5% in axSpA and 6.7% in pSpA), 22.5% for psoriasis (12.8% in axSpA and 51.1% in pSpA) and 7.9% for IBD (5.3% in axSpA and 15.6% in pSpA). Most of the patients were prescribed NSAIDS at baseline and more patients maintained this treatment at the 6-year visit in axSpA compared with pSpA (96.9% vs 87.5%, p=0.02). At the final visit, a higher percentage with pSpA received csDMARDs in comparison with axSpA (81% vs. 35.7%, p<0.001). Sixty (44.4%) patients received biologic therapy at the final visit and no differences were observed in their prescription: 43% in axSpA and 48.6% in pSpA(p=0.6).
Conclusion: The early diagnosis of recent-onset SpA achieves a significant improvement in clinical features, disease activity and quality of life in patients with axSpA and pSpA after 6 years of follow-up. Although previous publications revealed a low radiographic progression in this cohort[1], the worsening of BASMI must aware clinicians of possible evolutive structural damage.
REFERENCE:
[1] Fernández-Carballido et al. RMD Open. 2020 Sep;6(2):e001345

able 1. Follow-up clinical features at baseline and 6-year visit in patients with axSpA and pSpA.

	Baseline visit			Six-year visit				
	1 AxSpA n=133	2 pSpA n=45	P value 1-2	3 AxSpA n=133	4 pSpA n=45	P value 3-4	P value 1-3	P value 2-4
Age (years), mean ± SD	33.2 ± 7.5	35.3 ± 7	0.09	39.6 ± 9.6	40.9 ± 6.9	0.107	<0.001	<0.001
Back pain, n (%)	125 (94%)	21 (46.7%)	<0.001	40 (30%)	6 (13.3%)	0.083	<0.001	0.002
Arthritis, n (%)	32 (24.1%)	40 (89%)	<0.001	8 (6%)	10 (22.2%)	0.006	<0.001	0.061
Enthesitis, n (%)	46 (34.6%)	23 (51.1%)	0.11	10 (7.5%)	1 (2.2%)	0.39	<0.001	<0.001
Dactylitis, n (%)	13 (9.8%)	15 (33.3%)	0.01	1 (0.8%)	2 (4.4%)	0.24	<0.001	<0.001
CP uveitis, n (%)	17 (12.8%)	2 (4.4%)	0.28	22(16.5%)	3 (6.7%)	0.5	<0.001	<0.001
CP Psoriasis, n (%)	11 (8.3%)	21 (46.7%)	<0.001	17(12.8%)	23(51.1%)	0.02	<0.001	<0.001
CP IBD, n (%)	4 (3%)	6 (13,3%)	0,029	7 (5.3%)	7 (15.6%)	0,69	<0.001	<0.001
SJC (0-68), mean ± SD	0.2 ± 0.9	2.1 ± 2.8	<0,001	0.2 ± 1.1	0.5 ± 1.1	0.11	0.62	<0.001
CRP (mg/L), mean ± SD	8.3 ± 11.6	8.9 ± 12.7	0.77	3.6 ± 4.9	5.1 ± 7.7	0.26	<0.001	0.045
BASDAI (0-10), mean ± SD	4 ± 2.2	4.2 ±2.4	0.59	2.4 ± 2.1	2.3 ± 2.1	0.67	<0.001	0.001
BASFI (0-10), mean ± SD	2.4 ± 2.2	2.4 ± 2.4	0.94	2.1 ± 2.2	1.6 ± 1.9	0.2	0.17	0.289
BASDAS, mean ± SD	2.3 ± 1.1	2.5 ± 1.3	0.264	1.6 ± 1.4	1.6 ± 0.9	0.690	<0.001	0.001
BASMI, mean ± SD	1.4 ± 1.3	1.2 ± 0.9	0.43	1.9 ± 1	1.6 ± 0.7	0.19	<0.001	0.002
VAS (0-10) physician,mean ± SD	3.1 ± 2.4	2.9 ± 2.4	0.61	1.8 ± 1.8	1.8 ± 1.6	0.92	<0.001	0.04
VAS (0-10) patient, mean ± SD	4.1 ± 2.7	4.8 ± 3	0.23	2.8 ± 2.3	2.4 ± 2.2	0.32	<0.001	0.03
ASQoL, mean ± SD	5.9 ± 4.7	6.4 ± 5.6	0.6	2.9 ± 3.8	3.9 ± 4.9	0.38	<0.001	0.008

Data are expressed as mean ± standard deviation (SD) for cuantitative variables and number (percentage) for cualitative variables. Abbreviations: AxSpA, axial spondyloarthritis. PspA, peripheral spondyloarthritis. SD, (standard deviation). Impr, improvement. CP, cumulative prevalence. IBD: Inflammatory Bowel Disease. CRP: C-Reactive Protein. SJC: Swollen Joint Count. VAS: Visual Analogic Scale. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index. BASFI: Bath Ankylosing Spondylitis Functional Index. ASQoL: Ankylosing Spondylitis quality of life. BASDAS: BASDAI-based ASDAS, similar to the ASDAS-CRP but uses only the BASDAI and CRP.

Acknowledgements: The Spanish Foundation of Rheumatology received funding from Pfizer (formerly Wyeth) to develop the Esperanza Program. Later, the Program has been supported by restricted grants from the Instituto de Salud Carlos III and Fondos FEDER (FIS PI13/02034 and PI17/01840) and AbbVie.
Disclosure of Interests: Carolina Tornero: None declared, Victoria Navarro-Compán: None declared, Beatriz Joven-Ibáñez: None declared, RAQUEL ALMODOVAR: None declared, Xavier Juanola-Roura: None declared, Cristina Fernández-Carballido: None declared, Juan Carlos Quevedo-Abeledo: None declared, Jose Rosas: None declared, Azucena Hernández: None declared, Carlos A. Montilla-Morales: None declared, Jose Ramón Maneiro: None declared, A. Juan-Mas: None declared, Jose Antonio Pinto Tasende: None declared, Mireia Moreno: None declared, Jesus Sanz: None declared, Teresa Ruiz Jimeno: None declared, Manuel Moreno: None declared, María Lourdes Ladehesa Pineda: None declared, Eugenio de Miguel Speakers bureau: AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi., Paid instructor for: Janssen, Novartis, Roche, Consultant of: AbbVie, Novartis, Pfizer, Galapagos, Grant/research support from: Abbvie, Novartis, Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.2725

POS0997 PERFORMANCE OF ASDAS VERSUS BASDAI DURING PREGNANCY

P. Fischer[1], A. Zbinden[1], F. Foerger[1]. [1]*University Hospital and University of Bern, Rheumatology and Immunology, Bern, Switzerland*

Background: Disease activity in patients with axial spondyloarthritis (axSpA) can be measured by BASDAI and ASDAS. Both instruments were validated in non-pregnant patients with cutoff values for active diseases. In pregnant women with axSpA, however, BASDAI and ASDAS scores might be biased by signs and symptoms of pregnancy itself.
Objectives: To compare the performance of ASDAS and BASDAI during pregnancy
Methods: Patients with axSpA were prospectively followed before pregnancy, at each trimester and 6 to 12 weeks postpartum. Disease activity was assessed by BASDAI, ASDAS, patient global assessment (PGA) and physician global assessment (PhGA). We analysed the disease course throughout pregnancy and postpartum, the correlation between BASDAI and ASDAS and the agreement in the classification of active disease. We applied receiver operating curves (ROC) to evaluate the cut-off points in pregnant patients.
Results: The study involved 40 women with axSpA. Disease activity scores were higher during pregnancy (median ASDAS score: 2.5, median BASDAI score 3.1) than during a non-pregnant state (median ASDAS score 2.3, median BASDAI score 2.1). Median BASDAI scores were highest at the first trimester, median ASDAS scores were highest at the second trimester. ASDAS strongly correlated with BASDAI, both in the pregnant and in the non-pregnant state (r=0.796, r=0.727). However, there was a discordance when analysing the proportion of patients with high disease activity using the common cut-off values (ASDAS >2.1, BASDAS >4). More patients had high disease activity when measured by ASDAS (1st trimester (T): 63%, 2nd T: 76%, 3rd T: 61%) compared to those measured by BASDAI (1st T 43%, 2nd T: 39%, 3rd T: 34%). The κ coefficient showed only fair agreement (κ=0.39). ROC analysis among pregnant patients showed that the cut-off point estimation for high disease activity using ASDAS >2.75 corresponded to a BASDAI >4. The ASDAS >2.75 cut-off for high disease activity had a good agreement with BASDAI >4 (κ=0.657). When ASDAS >2.75 was applied in pregnant women with axSpA, about 40% experienced high disease activity.
Conclusion: During pregnancy, the majority of women with axSpA experience ongoing disease activity. However, the cut-off values defining low and high disease activity might differ between pregnant and non-pregnant individuals since BASDAI and ASDAS are biased by pregnancy related symptoms like fatigue and mechanical back pain.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2859

POS0998 SPONDYLOARTHRITIS AND SLEEP DISORDERS

S. Lahrichi[1], K. Nassar[1], S. Janani[1]. [1]*University Hospital of IBN ROCHD, Rheumatology, Casablanca, Morocco*

Background: Spondyloarthropathies (SpA) are a group of chronic and progressive diseases, characterized in particular by a progressive stiffening of the spine, spreading to neighboring joints or to certain tissues, which could lead in the long term to progressive stiffening and functional impairment. This conditioncancauseinsomnia problems and impaired sleep quality.
Objectives: To assess the impact of SpA on the quality of sleep.
Methods: This is a retrospective study over a period of 4 years from January 2015 to December 2019, including all the medical records of patients with SpA followed in the Department of Rheumatology of the University Hospital of Ibn Rochd, Casablanca. We evaluated for each patient two validated scores: the Epworth somnolence scale rated from 0 to 24, and the Pittsburgh sleep score rated from 0 to 21 with 7 components. Patients with a psychiatric history or who were followed up for neurological pathologies were excluded.
Results: 178 patients were included. 60.67% were men with an average age of 36.32 years (14-68 years). 45.01% had axial SpA, 29.77% had psoriatic arthritis, and 25.22% were followed for SpA associated with inflammatory bowel disease. 45% had associated comorbidities: there were 18 diabetics and 34 hypertensive, 16.58% were smokers. Clinically, 85.42% presented a back pain initially on examination, 55% presented a polyarthralgia, and 39.88% an oligoarthritis. 63% had radiological sacroiliitis, and 35.14% had bilateral coxitis. 13.48% had a positive HLA B27 and 58.89% had a

positive inflammatory assessment with very high activity indices,with a mean of 4.6. 64.66% of the patients received NSAIDs,of which 11% responded well. 57% were treated with csDMARDs, and 17.86% were treated with biologics. At the time of our study, the mean visual analog scale was 5.84 ± 1.7 out of 10 (2-9). The mean Epworth score was 8.38 ± 5.2 (0-21). 56.1% of patients had no sleep debt, 33.3% had a sleep deficit, and only 10.6% had signs of drowsiness. For the overall Pittsburgh score, the mean was 7.02 ± 3.6 (1-18). The mean of "subjective quality of sleep" was 1.12, "sleep latency" was 1.22, "duration of sleep" was 1.06, "usual sleep efficiency" was 0.74, "Sleep disturbance" of 1.28, "use of a sleep medication" of 0.54, and the average of the component concerning "poor shape during the day" was 1.03 out of 3. The LEQUESNE index went from an average of 6 to 8, which corresponds to an average handicap (P = 0.2) over a period of 3 years. 68% of the patients had an alteration in the quality of sleep, starting on average three years after the onset of symptoms. 11% reported having experiencedanxiety and depressive symptoms, and reported having used antidepressants or anxiolytics in the past 5 years.

Conclusion: Our study showed the negative impact of SpA on the duration and overall quality of sleep. The degree of pain as well as functional impairment can cause and worsen sleep disturbances in SpA. We have shown that the Pittsburg score increases significantly with the increase of pain.The Lequesne score and that the Epworth score increase with disease activity[1].

REFERENCES:

[1] StolwijkC,vanTubergenA,Castillo-OrtizJD,BoonenA.Prevalenceofextra-articularmanifestationsinpatientswithankylosingspondylitis:asystematicreviewandmeta-analysis.AnnRheumDis2015;74:65—73.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2909

POS0999 HIGH CORRELATIONS BETWEEN QUESTION 1 & 2 OF THE BASFI: AN OPPORTUNITY TO STREAMLINE THE BASFI

M. Maclean[1], S. Maguire[1], F. B. O'shea[1]. [1]*St. James' Hospital, Rheumatology, Dublin, Ireland*

Background: The Bath Ankylosing Spondylitis Functional Index (BASFI) is a useful tool to quantitatively characterise functional ability in a patient with axial spondyloarthropathy (axSpA). Whether first presentation, decompensated, or routine follow-up, BASFI can help establish a more accurate understanding of disease progression, or response. As with any questionnaire, relevance and absence of redundancy is required. This analysis questions the redundancy of the first two questions of the BASFI:

1) How difficult is it to put socks on your feet?
2) How difficult is it to pick a pen up off the floor?

Objectives: To compare variation in reporting of questions one and two of the BASFI, to establish redundancy or exclusivity of these questions.

Methods: IBM SPSS version 26 was used for data analysis. Data from axSpA patients who attended the Rheumatology department during the study period were included in the analysis where BASFI scores were available. Both variables (pen scores and sock scores) were assessed with a Shapiro-Wilk's test for normal distribution. The variables were also assessed for the presence of a monotonic relationship by visual inspection of a scatterplot of the variables. Once a monotonic relationship was established a Spearman's rank order correlation between the sock score and pen scores for each participant was analysed.

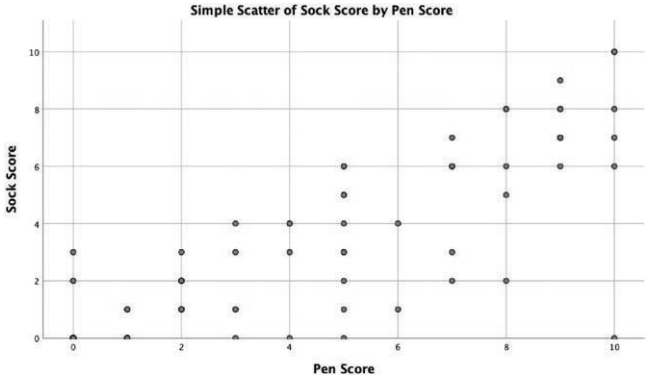
Results: In total data from 82 axSpA patients were included in this analysis. Population was made up of 28% (23) females, 72% (59) males with mean BASDAI score 4.33 and mean BASFI score 3.88(Table 1). Both variables were not normally distributed as assessed by Shapiro-Wilk's test ($p < 0.05$) necessitating a Spearman's rank-order correlation for analysis. Preliminary analysis variables demonstrated the relationship between the variables to be monotonic as determined by visual inspection of the scatterplot (graph 1) with no outliers detected. There was a statistically significant, strong positive correlation between sock scores and pen scores in this axSpA population, $r_{partial}(80) = 0.809$ significant at the $p < 0.01$ level.

Table 1. Descriptive output of data

	% (n)
n	82
Females	28% (23)
Males	72% (59)
Age	45.03
BASDAI	4.33
BASFI	3.88
Pen score	3.93
Sock score	2.88
Sock score greater	7.3% (6)
Pen score greater	50% (41)
Same scores	42.7% (35)

Conclusion: There is a strong positive correlation between sock (question 1) and pen scores (question 2) as captured by the BASFI. It appears that both questions are capturing a similar functional limitation in patients with axSpA. In order to minimise redundancy and improve the relevance of the BASFI our results support the removal of one of these questions to simplify the BASFI. From a practical perspective, putting on socks (question 1) would be a more commonly encountered daily activity than picking up a
pen from the floor(question 2). As such, we would suggest removal of question 2 from the BASFI.

Table 1 & Figure 1



Graph 1. Spread of Data points demonstrating a monotonic relationship with no outliers

Disclosure of Interests: Michael MacLean: None declared, Sinead Maguire Grant/research support from: Recipient of the Gilead Inflammation Fellowship, Finbar Barry O'Shea: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2913

POS1000 COMORBIDITIES ASSOCIATED TO SPONDYLOARTHRITIS

S. Bouden[1], L. Kharrat[1], A. Ben Tekaya[1], O. Saidane[1], R. Tekaya[1], I. Mahmoud[1], L. Abdelmoula[1]. [1]*Hospital Charles Nicolle, Rheumatology, Tunis, Tunisia*

Background: In contrast to other chronic rheumatic diseases such as rheumatoid arthritis, comorbidities associated to spondyloarthritis (SpA) and their impact on disease outcomes are less well studied.

Objectives: The aim of our study was to investigate the prevalence of comorbidities among SpA patients and to determine factors influencing their appearance.

Methods: We conducted a retrospective study including patients meeting the Assessment of SpondyloArthritis International Society (ASAS) criteria between 2000 and 2020.

The following comorbidities were collected: cardiovascular pathologies and their risk factors (smoking, arterial hypertension, diabetes, dyslipidemia and obesity), neoplasms, osteoporosis, depression, infections, gastrointestinal and pulmonary disorders.

Results: We included 138 patients. Sixty-eight per cent of them were males. The mean age was 45.73 ± 12.66 years. The mean age at the disease onset was 28.89 ± 12.54 years. The mean CRP was 33.38 ± 39.65 mg/dL. The mean BASDAI and ASDAS-CRP were 4.21 ±2.23 and 3.06 ± 1.26, respectively. The mean BASFI was 4.77 ± 2.58.

Sixty patients had at least one comorbidity (43.5%): 53 patients had one comorbidity (38.4%), 21 accumulated two types of comorbidities (15.2%) and 7 patients accumulated three types or more (5%).

Osteoporosis was the most frequent comorbidity, it was present in 23.1% of the cases (n=32), followed by tuberculosis 8.7% (n=12), stomach ulcers 5.1% (n=7), pulmonary superinfection 2.9% (n=4), neoplasia 2.2% (n=3) and then depression 1.4% (n=2).

Cardiovascular risk factors were noted in 44 patients (31.9%): hypertension (15.9%), diabetes (12.3%), dyslipidemia (9.4%) and obesity (8.7%).

Thirty-seven per cent of our patients were smokers.

SpA patients with comorbidities were significantly older than those without (50.2±11.07 *versus* 42.3±12.8 years, p<0.0001).

The presence of comorbidities was significantly associated to a higher disease activity evaluated by BASDAI (p=0.005) and ASDAS-CRP (p=0.002). Furthermore, BASFI was significantly higher among patients with comorbidities (5.47±2.38 *versus* 4.31±2.62, p=0.028).

However, no association was found between presence of comorbidities and smocking or CRP.

Conclusion: Our results show that more than 40% of our SpA patients presented with at least one comorbidity. Remarkably, the presence of comorbidities

was associated with high disease activity, suggesting that that inflammation might promotes comorbidities. For optimal management of SpA, a systemic screening for comorbidities is essential.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2929

POS1001 CLINICAL AND SURROGATE CARDIOVASCULAR RISK ASSESSMENT AND ITS RELATIONSHIP WITH PSORIATIC ARTHRITIS PATHOGENESIS

N. Barbarroja Puerto[1], I. Arias de la Rosa[1], C. Román-Rodriguez[2], I. Gómez García[2], C. Perez-Sanchez[2], C. López-Medina[2], M. L. Ladehesa Pineda[2], D. Ruiz[2], A. M. Patiño-Trives[2], M. Luque-Tévar[2], C. Lopez-Pedrera[2], A. Escudero Contreras[2], E. Collantes Estevez[2], M. D. López Montilla[2]. *[1]Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/Reina Sofia Hospital/ University of Cordoba, Medicine Department, Cordoba, Spain*; *[2]Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/Reina Sofia Hospital/University of Cordoba, Rheumatology Department, Cordoba, Spain*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease associated with an increased prevalence of cardiovascular (CV) events. Traditional CV risk factors do not account for the increased CV disease mortality in PsA. Inflammation seems to have a key role in the development of this comorbidity, however the specific molecular mechanisms involved are not defined yet.

Objectives: To evaluate clinical CV risk factors and surrogate markers and their relationship with inflammation, disease activity and metabolic comorbidities in PsA patients

Methods: This is a cross-sectional study including 100 PsA patients without CV disease recruited in the routine clinical practice at the Rheumatology Department, Reina Sofia Hospital of Cordoba and 100 age-matched healthy donors (HDs). Different parameters related to the cardiometabolic risk were analyzed. Clinical and analytical parameters were collected: lipid profile (cholesterol, HDL, LDL, TG, ApoA and ApoB), glucose and insulin, body surface area (BSA) affected by psoriasis, number of tender and swollen joints, DAPSA, VAS, CRP and ESR. To measure the persistence of inflammation, CRP levels were recorded retrospectively once, twice, or three times during the 5 years prior to study and at the moment of the study. Increased levels of CRP in at least 50% of the determinations was considered as persistent inflammation. Plasma and peripheral blood mononuclear cells (PBMCs) were isolated from peripheral blood of patients and HDs. A panel of 92 proteins involved in CV disease and an adipocytokine profile was measured in plasma and PBMCs. In addition, activation of 18 intracellular pathways involved in cell activation was also measured in PBMCs. *In vitro* experiments in adipocytes treated with serum from PsA patients were also carried out.

Results: Traditional CV risk factors including atherogenic risk, insulin resistance (IR), metabolic syndrome, smoking, obesity, arterial hypertension, apolipoprotein B/A risk, type 2 diabetes mellitus and the levels of SCORE were significantly increased in PsA patients. The presence of IR was associated with disease activity markers (DAPSA, ESR and CRP). In fact, the HOMA-IR index was related to the CRP persistence. PsA patients with obesity had significantly increased the number of tender and swollen joints, the levels of DAPSA and CRP. Twenty-eight proteins involved in CV disease and six adipocytokines were significantly elevated in the plasma of PsA patients. Several of these cardiovascular molecules were associated with higher levels of DAPSA (CTSD, GAL3, CD163, FABP4, IL6 and IL1RT2), acute phase reactants (GAL3, TNFα, Adiponectin, TNFR1 and IL6), affected body surface area (IL2RA, GAL3, CCL15, TRAP, CSTB, CD163, OPG and CNTN1) and onychopaty (TRAP, VWF, MCP-1, GAL3, LTBR, TFPI, CHI3L1, CTSZ and JAM-A). In addition, the mRNA expression of most of those 28 CV molecules were significantly increased in PBMCs from PsA patients. At intracellular level, the activation of 11 kinases (ERK1/2, AKT, S6 Ribosomal, mTOR, HSP27, Bad, p70 S6 kinase, PRAS40, p53 and caspase-3) involved in insulin signaling, inflammation, cell survival and apoptosis were altered in PBMCs. Finally, serum from PsA patients was able to modify the expression of these molecules in adipocytes.

Conclusion: 1) Disease activity and inflammatory burden are closely associated with the presence of metabolic alterations, specifically obesity and IR in patients with PsA. 2) The development of IR is extremely related to the persistence of CRP levels in the previous 5 years. 3) Inflammation is closely associated to the adipose tissue dysfunction in PsA and 4) FABP4, CD163 and GAL3 are surrogate CV markers commonly associated with clinical features of PsA, suggesting the role of these molecules linking CVD and PsA pathogenesis.

Funded by ISCIII (PI17/01316 and RIER RD16/0012/0015) co-funded with FEDER.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2990

POS1002 BASELINE CALPROTECTIN AND VISFATIN LEVELS PREDICT RADIOGRAPHIC SPINAL PROGRESSION AFTER 2 YEARS IN ANKYLOSING SPONDYLITIS PATIENTS ON TNF INHIBITOR THERAPY

J. Rademacher[1,2], M. Siderius[3], L. Gellert[1], F. Wink[4], M. Verba[1], F. Maas[3], L. M. Tietz[1], D. Poddubnyy[1,5], A. Spoorenberg[3], S. Arends[3]. *[1]Charité - Universitätsmedizin Berlin, Department of Gastroenterology, Infectiology and Rheumatology, Berlin, Germany*; *[2]Berlin Institute of Health, BIH, Berlin, Germany*; *[3]University Medical Center Groningen, Department of Rheumatology and Clinical Immunology, Groningen, Netherlands*; *[4]Medical Center Leeuwarden, Department of Rheumatology, Leeuwarden, Netherlands*; *[5]Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), ein Institut der Leibniz-Gemeinschaft, Epidemiology, Berlin, Germany*

Background: Radiographic spinal progression determinates functional status and mobility in ankylosing spondylitis (AS)[1].

Objectives: To analyse whether biomarker of inflammation, bone turnover and adipokines at baseline or their change after 3 months or 2 years can predict spinal radiographic progression after 2 years in AS patients treated with TNF-α inhibitors (TNFi).

Methods: Consecutive AS patients from the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort[2] starting TNFi between 2004 and 2012 were included. The following serum biomarkers were measured at baseline, 3 months and 2 years of follow-up with ELISA:

- Markers of inflammation: calprotectin, matrix metalloproteinase-3 (MMP-3), vascular endothelial growth factor (VEGF)
- Markers of bone turnover: bone-specific alkaline phosphatase (BALP), serum C-terminal telopeptide (sCTX), osteocalcin (OC), osteoprotegerin (OPG), procollagen typ I and II N-terminal propeptide (PINP; PIINP), sclerostin.
- Adipokines: high molecular weight (HMW) adiponectin, leptin, visfatin

Two independent readers assessed spinal radiographs at baseline and 2 years of follow-up according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Radiographic spinal progression was defined as mSASSS change ≥2 units or the formation of ≥1 new syndesmophyte over 2 years. Logistic regression was performed to examine the association between biomarker values at baseline, their change after 3 months and 2 years and radiographic spinal progression. Multivariable models for each biomarker were adjusted for mSASSS or syndesmophytes at baseline, elevated CRP (≥5mg/l), smoking status, male gender, symptom duration, BMI, and baseline biomarker level (the latter only in models with biomarker change).

Results: Of the 137 included AS patients, 72% were male, 79% HLAB27+; mean age at baseline was 42 years (SD 10.8), ASDAScrp 3.8 (0.8) and mSASSS 10.6 (16.1). After 2 years of follow-up, 33% showed mSASSS change ≥2 units and 24% had developed ≥1 new syndesmophyte. Serum levels of biomarkers of inflammation and bone formation showed significant changes under TNFi therapy, whereas adipokine levels were not altered from baseline (Figure 1).

Univariable logistic regression revealed a significant association of baseline visfatin (odds ratio OR [95% confidence interval] 1.106 [1.007-1.215]) and sclerostin serum levels (OR 1.006 [1.001-1.011]) with mSASSS progression after 2 years. Baseline sclerostin levels were also associated with syndesmophyte progression (OR 1.007 [1.001-1.013]). In multivariable logistic analysis, only baseline visfatin level remained significantly associated (OR 1.465 [1.137-1.889]) with mSASSS progression. Furthermore, baseline calprotectin showed a positive association with both, mSASSS (OR 1.195 [1.055-1.355]) and syndesmophyte progression (OR 1.107 [1.001-1.225]) when adjusting for known risk factors for radiographic progression.

Univariable logistic regression showed that change of sclerostin after 3 months was associated with syndesmophytes progression (OR 1.007 [1.000-1.015), change of PINP level after 2 years was associated with mSASSS progression (OR 1.027 [1.003-1.052]) and change of visfatin after 2 years was associated with both measures of radiographic progression – mSASSS (OR 1.108 [1.004-1.224]) and syndesmophyte formation (OR 1.115; [1.002-1.24]). However, those associations were lost in multivariable analysis.

Conclusion: Independent of known risk factors, baseline calprotectin and visfatin levels were associated with radiographic spinal progression after 2 years of TNFi. Although biomarkers of inflammation and bone formation showed significant changes under TNFi therapy, these changes were not significantly related to radiographic spinal progression in our cohort of AS patients.

REFERENCES:

[1] Poddubnyy et al 2018

[2] Maas et al 2019

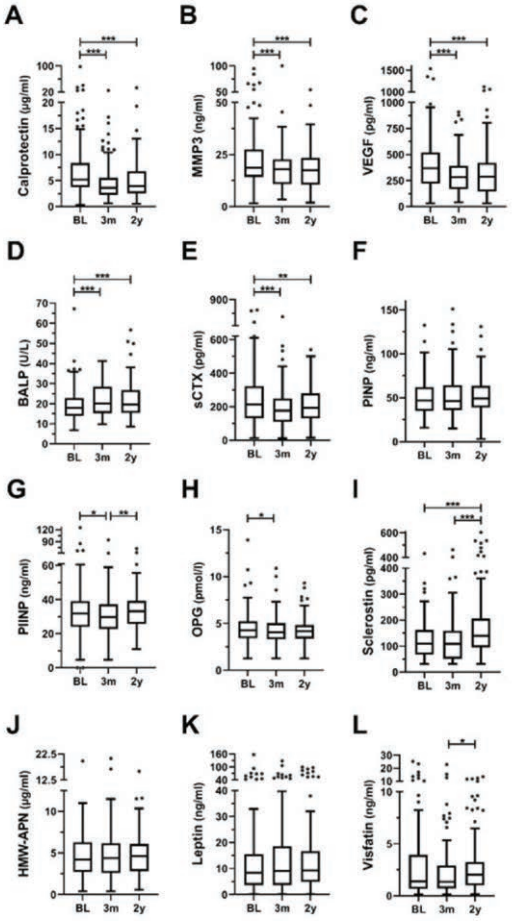


Figure. Levels of markers of inflammation (A-C), bone turnover markers (D-I) and adipokines (J-L) under treatment with TNF inhibitors: serum levels at baseline (BL; before start of TNFi), after 3 months (3m) and 2 years (2y) of treatment. Wilcoxon Signed Rank Test: * p value <0.05; ** p value <0.01; *** p value <0.001

Acknowledgements: Dr. Judith Rademacher is participant in the BIH-Charité Clinician Scientist Program funded by the Charité –Universitätsmedizin Berlin and the Berlin Institute of Health.

Disclosure of Interests: Judith Rademacher: None declared, Mark Siderius: None declared, Laura Gellert: None declared, Freke Wink Consultant of: AbbVie, Maryna Verba: None declared, Fiona Maas: None declared, Lorraine M Tietz: None declared, Denis Poddubnyy: None declared, Anneke Spoorenberg Consultant of: Abbvie, Pfizer, MSD, UCB, Lilly and Novartis, Grant/research support from: Abbvie, Pfizer, UCB, Novartis, Suzanne Arends Grant/research support from: Pfizer.

DOI: 10.1136/annrheumdis-2021-eular.3059

POS1003 CATASTROPHIZING IN PATIENTS WITH SPONDYLOARTHRITIS

B. Coste[1], C. Traverson[1], E. Filhol[1,2], C. Lukas[2,3], S. Laurent-Chabalier[4], J. Morel[3,5], B. Combe[3,5], C. Daien[3,5], C. Hua[1,2], C. Gaujoux-Viala[1,2]. *[1]Nîmes University Hospital, Rheumatology, Nîmes, France*; *[2]University of Montpellier, IDESP, UMR-INSERM, Montpellier, France*; *[3]CHU Lapeyronie, Rheumatology, Montpellier, France*; *[4]Nîmes University Hospital, BESPIM, Nîmes, France*; *[5]University of Montpellier, -, Montpellier, France*

Background: Catastrophizing is a negative cognitivo-affective response to an anxiety-provoking stimulus, especially anticipated or actual pain. It can be assessed quickly using a validated questionnaire: the Pain Catastrophizing Scale (PCS)[1]. Catastrophizing plays a role in maintaining chronic pain and is associated with several pain-related outcomes in osteoarthritis and low back pain. There is a lack of knowledge about catastrophizing in axial spondyloarthritis (AS) with only one study[2] so far.

Objectives: To assess the prevalence of catastrophizing and associated factors in spondyloarthritis.

Methods: We performed an observational, prospective, bi-centric study. All patients aged 18 or over with AS fulfilling the 2009 Assessment in Spondyloarthritis International Society (ASAS) criteria were consecutively included. Sociodemographic data, information on the disease and its treatments were collected as well as questionnaires regarding disease activity (BASDAI), function (HAQ, BASFI), quality of life (SF12, EQ5D), anxiety and depression (HADS, GAD7), fibromyalgia (FiRST), insomnia (ISI) and catastrophizing scores (PCS). Statistical analysis included a samples t-test, one-way variance analysis, Spearman's correlation coefficient, the Chi^2 test, Fisher's exact test, the Wilcoxon test, multivariate linear regression (considering catastrophizing as a continuous variable) and multivariate logistics regression (considering catastrophizing as a categorical variable: PCS ≥ 20 = high level catastrophizing).

Results: From September 2019 to March 2020, 168 AS patients were included: 48.5% were women, the median age was 48.5 years and 100 patients (60.2%) were professionally active. Almost all patients (95.8%) had a disease lasting for more than 2 years; 110 (72%) were HLA-B27+; 84 (50%) had MRI sacroiliitis and 62 (37.6%) radiographic sacroiliitis. In all, 166 (98.8%) had axial involvement, 99 (58.9%) had peripheral involvement and 44 (26.2%) had enthesitic involvement. The median BASDAI score was 6.30 [Q1-Q3 4.65-6.30].

The prevalence of a PCS score ≥20 was 45.5% [38.0;53.0]. The median PCS score was 18 [7-27]. In multivariate logistics regression, high-level catastrophizing was significantly associated with the HADS anxiety score (OR=1.54 [1.22-2.0]), HADS depression score (OR=1.25 [1.10-1.43]) and disease activity (BASDAI OR=1.14 [1.01-1.26]). In multivariate linear regression, catastrophizing was also significantly associated with anxiety (p<0.0001), depression (p<0.0001) and disease activity (p=0.0008).

Conclusion: Almost half the patients with AS were high catastrophizers. Catastrophizing is linked to anxiety, depression, and disease activity. It may be interesting to detect catastrophizing in order to improve the management of our patients.

REFERENCES:

[1] Sullivan MJL. et al. Psychological Assessment. 1995;7(4):524–32
[2] Penhoat M. et al. Joint Bone Spine. 2014;81(3):235–9

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3171

POS1004 BOTH SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS HAVE STRONG FAMILY HISTORIES

G. K. Yardımcı[1], B. Farisoğulları[1], E. C. Bolek[1], E. Bilgin[1], E. Duran[1], G. Ayan[1], Z. Özsoy[1], G. Sandal Uzun[1], L. Kılıç[1], A. Akdoğan[1], O. Karadag[1], Ş. A. Bilgen[1], A. İ. Ertenli[1], U. Kalyoncu[1], S. Kiraz[1]. *[1]Faculty of Medicine; Hacettepe University, Rheumatology, Ankara, Turkey*

Background: Family history is one of the hallmarks of spondyloarthritis (SpA) and psoriatic arthritis (PsA) [1, 2]. Some patients have a strong family history that more than 2 relatives have spondyloarthritis related diseases. The effects of strong family history on SpA features were not known very well.

Objectives: The aim of this study is to evaluate the effects of family history in SpA and PsA patients.

Methods: HUR-BIO (Hacettepe University Biologic Registry) is a prospective, single center database of biological treatments since 2005, and to date 3071 SpA and 526 PsA patients have been recorded. Demographic, clinical characteristics, disease activity parameters, a detailed family history of SpA and SpA features (presence of SpA including PsA, psoriasis, inflammatory bowel disease and uveitis) and laboratory data before anti-TNF treatments of the patients were noted.

Results: 2807 SpA (53.6% male) and 506 PsA (31.4% male) patients' family history were available and analysed. A positive family history was noted in 27.6% of the SpA and 31.0% of the PsA patients (ns). 7.4% of the SpA patients and 8.9% of the PsA patients had family history in more than one relative (Table 1). In SpA patients with a family history, uveitis was more frequent than patients without (14.4% vs 10.6%, p=0.006). Except for a higher male predominance and uveitis (53% vs 32% p=0.006 and 9% vs 2% p=0.003 respectively) in patients with ≥2 relatives with SpA features, there were no differences in PsA patients regarding family history. The presence of family history and HLA-B27 (63.7% vs 37.6%, p<0.001) positivity were associated in SpA patients but not in PsA patients (31.2% vs 20.0, p=0.13).

Conclusion: Family history was present in about one third of the patients of PsA and SpA. It is not uncommon for two or more family members to have a SpA feature. Presence of family history may be associated with some clinical conditions, such as uveitis.

REFERENCES:

[1]Solmaz, D., et al., Impact of Having Family History of Psoriasis or Psoriatic Arthritis on Psoriatic Disease. Arthritis Care Res (Hoboken), 2020. **72**(1): p. 63-68.
[2] Zurita Prada, P.A., et al., Influence of smoking and obesity on treatment response in patients with axial spondyloarthritis: a systematic literature review. Clin Rheumatol, 2020.

Table 1. Family history in PsA and SpA patients

	PsA (n=506)	SpA (n=2807)
≥ 1 family history, n (%)	157 (31.0)	774 (27.6)
≥1 first-degree relative, n (%)	114 (22.5)	489 (17.4)
≥2 first-degree relatives, n (%)	21 (4.2)	77 (2.7)
≥2 relatives (both first- and second-degree), n (%)	45 (8.9)	208 (7.4)
Family history		
➢**Psoriasis, n (%)**	120 (23.7)	155 (5.5)
➢**Psoriatic arthritis, n (%)**	14 (2.8)	9 (0.3)
➢**Spondyloarthritis, n (%)**	38 (7.5)	643 (22.9)
➢**Inflammatory bowel disease, n (%)**	1 (0.2)	10 (0.4)
➢**Uveitis, n (%)**	0	2 (0.1)

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3330

POS1005 ASSESSMENT OF DAREA AND MODIFIED DAREA IN AN ARGENTINIAN-GUATEMALAN REACTIVE ARTHRITIS COHORT

M. Benegas[1], C. Orozco[2], P. Giorgis[2], E. E. Schneeberger[2], J. M. Bande[3], M. A. Medina[4], I. Iraheta[5], C. Airoldi[6], P. Girard Bosch[7], S. Scarafia[8], E. Velozo[9], O. Rillo[10], M. Guinsburg[11], M. P. Cowan[12], M. Piovesan[12], V. Martire[7], L. Casalla[12], V. Cosentino[13], P. Gonzalez[14], C. Peon[14], R. Gomez[14], A. Benitez[14], M. J. Gamba[14]. [1]*Sanatorio Méndez, Reumatologia, CABA, Argentina*; [2]*Instituto de Rehabilitación psicofísica, Reumatologia, caba, Argentina*; [3]*Hospital tornú, Reumatologia, CAB, Argentina*; [4]*Hospital tornú, Reumatologia, CABA, Argentina*; [5]*Asociación Guatemalteca antienfermedades reumáticas, Reumatologia, Guatemala, Guatemala*; [6]*Hospital Provincial de Rosario, Reumatologia, Rosario, Argentina*; [7]*Instituto médico platense, Reumatologia, La plata, Argentina*; [8]*Hospital Municipal de San Fernando, Reumatologia, Buenos Aires, Argentina*; [9]*Sanatorio y Universidad Adventista del Plata, Reumatologia, Entre Rios, Argentina*; [10]*Hospital Pirovano, Reumatologia, CABA, Argentina*; [11]*Hospital Glassman, Reumatologia, Bahia Blanca, Argentina*; [12]*Consultorio privado, Reumatologia, CABA, Argentina*; [13]*Hospital Ramos Mejía, Reumatologia, CABA, Argentina*; [14]*Hospital Alejandro Posadas, Reumatologia, Buenos Aires, Argentina*

Background: Reactive Arthritis (ReA) is an inflammatory joint disease and, as in rheumatoid or psoriatic arthritis, composite indices are the most useful tools to measure disease activity. The Disease Activity Index for Reactive Arthritis (DAREA) is the only developed index for ReA, which requires a 66/68 joint count and CRP for its assessment, the latter being difficult to acquire in our setting. Therefore, we developed a simplified index, the modified DAREA (DAREAm), with a lower joint count and ESR for its evaluation.
Objectives: 1) To evaluate the DAREA and the DAREAm in a cohort of patients with diagnosis of ReA and post-infectious arthritis 2) To assess the correlation of the DAREA and DAREAm with several clinical variables, functional capacity and quality of life in a cohort of patients with ReA.
Methods: Patients with diagnosis of ReA (Calin'79) and post-infectious arthritis were included. Demographic data were collected, patient´s pain and global assessment were evaluated through a visual analog scale (VAS) and a 3-point scale (no pain = 0, mild = 1, moderate = 2, severe = 3), physician´s global assessment, morning stiffness (MS) and VAS fatigue. Functional capacity was assessed by HAQ and quality of life according to EuroQol-5 dimensions (EQ-5D), and the activity indices DAS28, DAREA and DAREAm were calculated. Statistical analysis: a descriptive analysis of the variables and correlation between numerical variables with Spearman rank correlation were performed.
Results: 57 patients were included, 53 with diagnosis of ReA, the majority post urogenital (63%) and gastrointestinal (17%), and 4 with diagnosis of post-infectious arthritis. Fifty six percent were male, mean age: 40 years old (SD ± 14) and median ReA duration: 15 months (IQR 2-45). The number of painful and swollen joints in a 66/68 joint count showed a median of 2 (IQR 0-3) and 1 (IQR 1-2) respectively. Median VAS pain 43 (IQR 15-70), patient´s disease activity 40 (IQR 20-60) and physician´s 40 (IQR 20-60), MS 10 (IQR 0-50) and fatigue 30 (IQR 0-80). Median DAS28 3.6 (IQR 2.3-4.3), DAREA 7.4 (IQR 2.5-10.6), DAREAm 8.6 (IQR 4.6-12.7), HAQ 0.625 (IQR 0.125-1). The dimensions with the greatest compromise in the EQ-5D were pain/discomfort (63%) and anxiety/depression (51%), and the median VAS EQ-5D was 60 (IQR 32-80). DAREA correlated with DAREAm (rs= 0.89; p <0.001), DAS28 (rs= 0.84; p <0.001), medical VAS (rs= 0.60; p <0.001), MS (rs= 0, 50; p <0.001), HAQ (rs= 0.53; p <0.001), VAS fatigue (rs= 0.57; p <0.001) and mobility subscales of the EQ5D (rs= 0.56; p <0.001), pain/discomfort (rs= 0.49; p <0.001) and anxiety/depression (rs= 0.61; p <0.001). The DAREAm correlated with DAS28 (rs= 0.93; p <0.001), physician VAS (rs= 0.58; p <0.001), fatigue VAS (rs= 0.53; p <0.001), HAQ (rs= 0 .51; p <0.001) and the EQ5D subscales: mobility (rs= 0.64; p <0.001), pain/discomfort (rs= 0.56; p <0.001) and anxiety/depression (rs= 0.66; p <0.001)
Conclusion: This is the first study that assess activity indices in a cohort of patients with ReA. The DAREAm demonstrated a very good correlation with both DAREA and DAS28. We encourage the use of this simplified index in daily practice to evaluate patients with ReA.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3374

POS1006 ABERRANT TH17 CELLS EXPANSION AND RISK FACTORS IN ANKYLOSING SPONDYLITIS PATIENTS COMPLICATED WITH CARDIOVASCULAR EVENTS

T. Ding[1], B. C. LI[2], R. Su[2], X. F. LI[2], C. Wang[2]. [1]*The Second Hospital of Shanxi Medical University, Rheumatology, Taiyuan, China*; [2]*Rheumatology, The Second Hospital of Shanxi Medical university, Taiyuan, China, Rheumatology, Taiyuan, China*

Background: The incidence of Ankylosing Spondylitis (AS) complicated with cardiovascular diseases (CVD) has increased in recent years [1]. However, identification of risk factors indicating the development of CAD in AS patients is lacking. Th17 cells are increasingly recognized to be important in atherogenesis [2]. However, the role of these cells in the pathogenesis of ankylosing spondylitis patients complicated with cardiovascular events remains elusive.
Objectives: This study aimed to assess the level of circulating Th17 cells as well as other lymphocyte subsets such as Treg, Th, Ts, and NK cells in AS combined with CVD, and further to evaluate whether elevations in special PBMC subpopulations in AS patients indicate an increased risk of CVD.
Methods: Samples were assessed from 141 AS patients hospitalized at the Second Hospital of Shanxi Medical University (60 AS patients combined with CVD and 81 AS patients without CVD) and 100 healthy controls. The absolute numbers of lymphocytes and CD4+ T cells in peripheral blood were determined using Flow Cytometer. The association between PBMC subpopulations and CVD development in AS patients were analyzed using multivariable logistic regression.
Results: 1. Compared with AS group, AS with CVD group exhibited significant increases in the number of Th17 cells (P=0.001) and Treg cells (P=0.046). The ratio of Th17/Treg was also increased (P=0.085).
2. Analogous increases in the absolute number (P<0.001) and frequency (P<0.001) of Th1 cells, as well as the ratio of Th1/Th2 (P<0.001) and Th1/Treg (P=0.004) were also present in AS with CVD patients, compared to those without CVD.
3. Compared to HCs, 141 AS patients showed significantly decreased Treg cells (P<0.012) and increased Th17/Treg (P=0.001).
4. Logistic regression showed age (odds ratio: 1.09; 95% CI: 1.035-1.137), hypertension (odds ratio: 3.31; 95% CI: 1.152-9.528), diabetes (odds ratio: 8.03; 95% CI: 1.251-51.503), and elevated level of Th1 number (odds ratio: 1.01; 95% CI: 1.003-1.016) and DD (D-dimer) (odds ratio: 1.00; 95% CI: 1.000-1.002) were significantly correlated with the onset of CVD in AS patients.
5. Smoke, increased Th17 level, and use of NSAIDS were also positively correlated with the onset of CVD although the P-values did not reach significant.
Conclusion: Our data indicates aberrant expansion of Th17 cells in AS with CVD patients. Moreover, age, hypertension, diabetes, and increased level of Th1 in PBMC and DD are single independent risk factors for the presence of CVD in AS. The mechanisms of atherogenesis in AS may associate with the elevations in Th1 and Th17 cells. Imbalance of Th1/Th2 and Th17/Treg may be shared etiologic pathways of AS and CVD, providing attractive targets for the prevention and therapy of CVD development in AS patients.
REFERENCES:
[1]Kim JH, Choi IA. Cardiovascular morbidity and mortality in patients with spondyloarthritis: A meta-analysis. Int J Rheum Dis (2020). doi: 10.1111/1756-185x.13970.
[2] Saigusa R, Winkels H, Ley K. T cell subsets and functions in atherosclerosis. Nat Rev Cardiol. 2020 Jul;17(7):387-401. doi: 10.1038/s41569-020-0352-5.

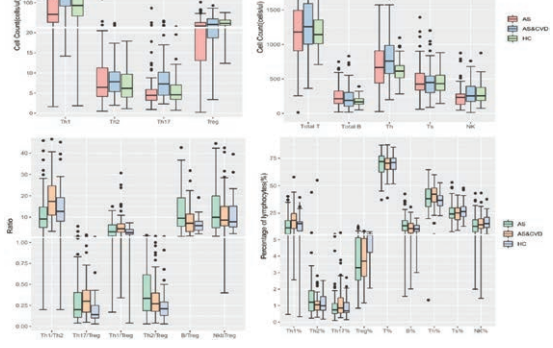


Figure 1. Compared with AS group, AS with CVD group exhibited significant increases in the number of Th17 cells (P=0.001) and Treg cells (P=0.046). The ratio of Th17/Treg was also increased (P=0.085). The absolute number (P<0.001) and frequency (P<0.001) of Th1 cells, as well as the ratio of Th1/Th2 (P<0.001) and Th1/Treg (P=0.004) were also present in AS with CVD patients.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3442

POS1007 OPTIMIZING A REFERRAL STRATEGY FOR PATIENTS WITH A HIGH PROBABILITY OF AXIAL SPONDYLOARTHRITIS: THE ROLE OF AGE AND SYMPTOM DURATION

F. Proft[1], L. Spiller[1], B. Muche[1], M. Protopopov[1], J. Rademacher[1], V. Rios Rodriguez[1], M. Torgutalp[1], D. Poddubnyy[1], I. Redeker[2]. [1]*Charité - Universitätsmedizin Berlin, Division of Gastroenterology, Infectious Diseases and Rheumatology; Department of Rheumatology, Berlin, Germany*; [2]*German Rheumatism Research Centre; Deutsches Rheuma-Forschungszentrum Berlin (DRFZ);, Programmbereich Epidemiologie, Beerlin, Germany*

Background: One of the most important prerequisites for a timely diagnosis of axial spondyloarthritis (axSpA) is the early referral of a patient with back pain to a rheumatologist. In the past years a number of referral strategies has been proposed,

most of them in line with the ASAS referral recommendations [1] and with a similar performance – about 30-40% of the referred patients can be diagnosed with axSpA after examination by a rheumatologist. In addition to physician-based strategies, an online self-referral (OSR) strategy has been recently proposed and evaluated about 20% of the patients being diagnosed with axSpA after rheumatologic evaluation [2].
Objectives: The objective of the current analysis was to investigate the role of age and symptom duration for the optimization of a physician-based and an OSR strategy for axSpA.
Methods: In the OptiRef study, patients with chronic back pain and suspicion of axSpA either referred by primary care physicians /orthopedists using the Berlin referral tool (=physician based) or based on a referral recommendation of an OSR were evaluated by rheumatologists in a specialized center [2]. All patients underwent a structured examination including imaging that resulted into the final diagnosis of axSpA or no axSpA. The relationship between age, symptom duration and the likelihood of axSpA diagnosis was evaluated in this analysis.
Results: A total of 360 patients (180 presented via the OSR and 180 referred by the physician based referral strategy) were included in this analysis. Patient's characteristics are shown in Table 1. A total of 71 patients (39.4%) in the physician-based group and 35 patients (19.4%) in the OSR group were finally diagnosed with axSpA. The heatmaps depicting the relationship between the proportions of patients diagnosed with axSpA and age plus symptom duration (Figure 1) showed a clear decline of the axSpA probability with increasing age. In the physician-referred group, however, axSpA was diagnosed even in patients who were above 50 years at the time-point of the examination, while there were only few patients with axSpA in the self-referred group aged 40-49 years, and none in the age group ≥50 years. Interestingly, there was no clear relationship between symptom duration and probability of the diagnosis: axSpA was diagnosed in a substantial proportion of patients even with a long history of back pain (>12 years) in both subgroups.
Conclusion: The probability of axSpA is high in patients suffering from back pain and aged <40 years with a substantial decline thereafter. Therefore, a referral strategy based on self-evaluation of symptoms should be more focused on a younger patient population, while physician-based strategies do not require such a restriction.
REFERENCES:
[1] Poddubnyy D, et al. Ann Rheum Dis 2015 Aug; 74(8):1483-1487.
[2] Proft F, et al. Semin Arthritis Rheum. 2020; 50(5):1015-1021.

Table 1. Patient characteristics

	Total N=360	Berlin tool N=180	Self-referral N=180	p-value
Diagnosis of axial SpA, n (%)	106 (29.4%)	71 (39.4%)	35 (19.4%)	<0.0001
Age, years, mean (SD)	36.9 (10.4)	37.2 (11.5)	36.6 (9.2)	>0.99
Male sex, n (%)	177 (49.2%)	100 (55.6%)	77 (42.8%)	0.02
Back pain duration, years, mean (SD)	7.9 (7.6)	6.5 (6.9)	9.2 (8.1)	<0.0001
HLA-B27 positive, n (%)	141 (40.9%)	104 (59.8%)	37 (21.6%)	<0.0001
CRP elevation, n (%)	52 (14.8%)	34 (19.4%)	18 (10.2%)	0.02
Inflammatory back pain, n (%)	204 (56.7%)	103 (57.2%)	101 (56.1%)	0.92

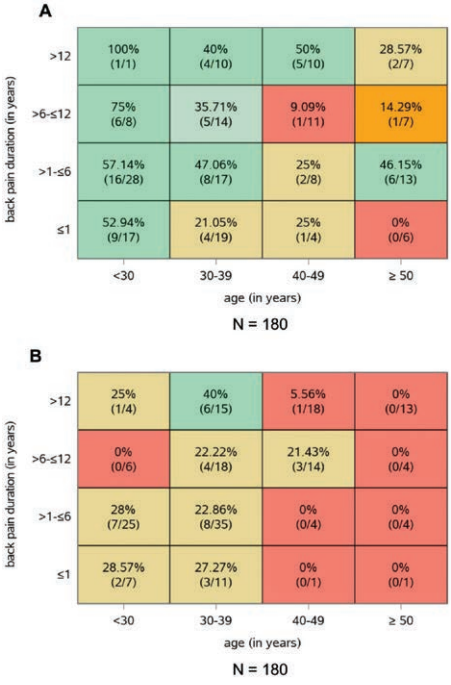


Figure 1. Heatmaps depicting the proportions of patients diagnosed with axSpA in relation to age and symptom duration in the physician-based (A) and OSR (B) groups.

Acknowledgements: We would like to thank all orthopaedists and primary care physicians who referred their patients. Further, we thank Dr. Anne-Katrin Weber and Dr. Susanne Lüders for the data collection support, Annegret Langdon for the data management support and Torsten Karge for set-up and support of the online screening tool.
Funding statement
The OptiRef study was supported by an unrestricted research grant from Novartis.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3567

POS1008 THE ROLE OF SERUM CALPROTECTIN IN THE DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

P. Kulakova[1], G. Lukina[1], E. Alexandrova[2], A. Novikov[2], A. Klimets[3], N. Savenkova[3], A. Kovshik[3], E. Volnukhin[3]. *[1]The Loginov Moscow Clinical Scientific Center of Moscow Healthcare Department" (The Loginov MCSC MHD), Rheumatology, Moscow, Russian Federation*; *[2]The Loginov Moscow Clinical Scientific Center of Moscow Healthcare Department" (The Loginov MCSC MHD), Immunology, Moscow, Russian Federation*; *[1]The Loginov Moscow Clinical Scientific Center of Moscow Healthcare Department" (The Loginov MCSC MHD), Rheumatology, Moscow, Russian Federation*

Background: Ankylosing spondylitis (AS) and inflammatory bowel diseases (IBD) have many common features. Approximately one in two patients with axial spondyloarthritis have subclinical (histologically confirmed) inflammation of the intestine, and 5-10% of subclinical inflammation turns into Crohn's disease (CD) or Ulcerative colitis (UC) [1]. Colonoscopy is usually used to diagnose IBD, but this procedure is invasive. Laboratory biomarkers, as fecal calprotectin (FC) and serum calprotectin (SC) can used to diagnosis of IBD. But there is no consensus regarding SC clinical utility. SC is exposed to proteolytic enzymes, but its level also increases with inflammation in the intestine and is associated with a higher disease activity [2]. SC levels positively correlate with CRP, ESR, disease activity in AS, but not as obvious as with FC [3,4].
Objectives: The aim of this study was to evaluate the possibility of using SC in the diagnosis of IBD in patients with AS.
Methods: In the analysis were included 50 patients with AS, fulfilling the modified New York criteria, among them man -36 (72%), woman -14 (28%), mean age of patients was 42.5 ±9.9, mean disease duration – 13.4±8.7 years. All patients were examined with ESR, CRP, FC (range: 100-1800 µg /g), esophagogastroduodenoscopy, colonoscopy and quantitative analysis of the SC level using ELISA (BUHLMANN MRP8/14 ELISA, range: 0.4-3.9 µg /ml).
Results: All patients had a high disease activity, mean BASDAI was 5.3 ± 1.8, mean ASDAS CRP 3.7 ± 1.01, mean ASDAS ESR 3.6 ± 1.01. 80 % patients had high FC level (more than 100 µg / g), while only 18% patients had an increase of SC level. IBD were diagnosed in 11 cases: 6 patients (12 %) with CD and 5 patients (10 %) - UC, in the remaining cases (78%) was no intestinal pathology. Only 2 patients with IBD had a high SC level. SC level was more correlated with ESR (r=0.5) and CRP (r=0.5) (p <0.05) levels, than with FC level (r=0.4) (p <0.05).
Conclusion: The results showed that there is currently insufficient data to assess the possibility of using SC in the diagnosis of IBD in patients with AS. There is a significant association between the SC, CRP and ESR, but not fecal calprotectin. Potentially SC may be more representative of systemic inflammation than an intestinal inflammation.
REFERENCES:
[1] Klingberg, E., Strid, H., Stahl, A.et al. A longitudinal study of fecal calprotectin and the development of inflammatory bowel disease in ankylosing spondylitis. A longitudinal study of fecal calprotectin and the development of inflammatory bowel disease in ankylosing spondylitis. Arthritis Res Ther 2017. 19(1):21
[2] Kalla R, Kennedy NA, Ventham NT, Boyapati RK, Adams AT, Nimmo ER, Visconti MR, Drummond H, Ho GT, Pattenden RJ, Wilson DC, Satsangi J. Serum Calprotectin: A Novel Diagnostic and Prognostic Marker in Inflammatory Bowel Diseases. Am J Gastroenterol. 2016 Dec;111(12):1796-1805
[3] Hu H, Du F, Zhang S, Zhang W. Serum calprotectin correlates with risk and disease severity of ankylosing spondylitis and its change during first month might predict favorable response to treatment. Mod Rheumatol. 2019 Sep;29(5):836-842.
[4] Azramezani Kopi T, Shahrokh S, Mirzaei S, Asadzadeh Aghdaei H, Amini Kadijani A. The role of serum calprotectin as a novel biomarker in inflammatory bowel diseases: a review study. Gastroenterol Hepatol Bed Bench. 2019;12(3):183-189.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3584

POS1009

ASYMPTOMATIC ENTHESITIS AND DOMINANT SIDE RELATED PATTERNS IN SPONDYLOARTHRITIS – THE ROLE OF ULTRASONOGRAPHY IN EVERYDAY PRACTICE

R. Decianu[1], V. Bojinca[2,3], L. Groseanu[2,3], S. Daia-Iliescu[2,3], A. Borangiu[2,3], C. L. Constantinescu[2,3], C. Cobilinschi[2,3], M. Duna[2], I. R. Gheorghe[4], D. Mazilu[2,3], M. M. Negru[2,3], D. Opris-Belinski[2,3], I. Saulescu[2,3], O. Vutcanu[5], A. Balanescu[2,3], M. Bojinca[3,5], R. Ionescu[2,3]. *[1]National Institute of Rehabilitation, Physical Medicine and Balneoclimatology, III, Bucharest, Romania*; *[2]"Sfanta Maria" Clinical Hospital, Internal Medicine and Rheumatology, Bucharest, Romania*; *[3]"Carol Davila" University of Medicine and Pharmacy, Rheumatology, Bucharest, Romania*; *[4]"Carol Davila" University of Medicine and Pharmacy, Marketing and Medical Technology, Bucharest, Romania*; *[5]"Dr. I. Cantacuzino" Clinical Hospital, Internal Medicine and Rheumatology, Bucharest, Romania*

Background: The spondyloarthritis (SpA) family includes a heterogeneous spectre of inflammatory diseases with several common features, such as the axial and peripheral joint involvement, but also trigger factors, as for instance, mechanical stress, infectious diseases or gut dysbiosis.[1,2]
Entheseal inflammation is the common background in the pathogenesis of SpA, leading to osteitis, periostitis and osteoproliferation. Despite being a central feature in SpA, enthesitis remains underdiagnosed in everyday practice.[3,4]
Objectives: The primary objective is to assess the frequency of ultrasound versus clinically detected enthesitis in a sample of Romanian patients with highly active SpA. A secondary objective is to determine the existence of an enthesitis pattern according to the dominant side in this sample of patients.
Methods: Out of 140 SpA patients, 106 were diagnosed with axial/peripheral SpA and 34 with psoriatic arthritis (PsA), and were clinically (medical history, clinical examination) evaluated, scanned using MSUS during the same visit, then asked which was their dominant side, in order to avoid any biases. The evaluation targeted 16 entheseal sites (Achilles tendon, plantar fascia, quadriceps tendon, proximal and distal patellar tendon, triceps tendon, extensor and flexor tendons of the hand, all evaluated on both sides), reaching a total of 2240 entheses. The medical history form included questions related to present or past spontaneous pain in any of the 16 evaluated sites as well as the clinical examination that evaluated the entheseal pain upon pressure (digital pressure on the enthesis overlying skin).
The MSUS evaluations were conducted using Esaote My Lab machines with 6-12/8-18 MHz linear probes. The same clinician/ultrasonographer performed all evaluations, in order to avoid interobserver variability.
Results: In the studied sample of patients, 68.6% were men, had a mean age of 43,46 (+/- 11,77), 51.4% were diagnosed with peripheral SpA, with a mean disease duration of 61,60 (+/- 71,03) months, and entheseal abnormalities were found in up to 62.7% of the asymptomatic entheses, lacking both spontaneous and elicited pressure pain.
The best performance of clinical and ultrasound examination was observed in the evaluation of the flexor tendons of the hand, with strong agreement between the two methods (kappa = 0,718, p = 0.001). Conversely, the lowest performance of clinical and ultrasound examination was noticed in Achilles (kappa = 0,292, p = 0.001) and distal patellar tendons (kappa = 0,202, p = 0.001), with low agreement indices. Both GS and PD abnormalities were more frequently detected on the right side, in a sample of 98.57% right handed patients. The differences were higher regarding the insertions of the triceps tendon (2.2%) and the plantar fascia (2.1%), in favour of the dominant side.
Conclusion: Entheseal reported pain (spontaneous and elicited by pressure) correlates poorly with MSUS detected enthesitis. This study highlights the high rates of imaging detected, but clinically overlooked entheseal abnormalities in SpA patients. Enthesitis was more frequently detected on the dominant side, emphasizing the role of mechanical stress in the pathogenesis of this feature. This outcome also requires the selection of the most reliable entheseal sites for SpA, being a future direction of research for this ongoing study.

REFERENCES:

[1] Barnett R, Ingram T, Sengupta R. Axial spondyloarthritis 10 years on: still looking for the lost tribe. *Rheumatology (Oxford)*. 2020; 59(4): iv25-iv37
[2]Kehl AS, Corr M, Weisman MH, et al. Enthesitis - New Insights Into Pathogenesis, Diagnostic Modalities, and Treatment. *Arthritis Rheumatol*. 2016; 68(2): 312–322
[3]Ruta S, Gutierrez M, Pena C, et al. Prevalence of subclinical enthesopathy in patients with spondyloarthropathy: an ultrasound study. *J Clin Rheumatol*. 2011; 17: 18–22
[4] Yi E, Ahuja A, Rajput T, et al. Clinical, economic, and humanistic burden associated with delayed diagnosis of axial spondyloarthritis: a systematic review. *Rheumatol Ther*. 2020; 7: 65–87

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3612

POS1010

PREDICTING CARDIOVASCULAR EVENTS IN PATIENTS WITH SPONDYLOARTHRITIS: 3 RISK ALGORITHMS

A. S. Pinto[1,2], F. Cunha Santos[1], S. P. Dinis[1], F. Guimarães[2], D. Esperança Almeida[3], H. Parente[2], S. Azevedo[2], C. Vaz[1,4], D. Faria[2], J. F. Ferreira[1,4]. *[1]Unidade Local de Saúde da Guarda, Rheumatology, Guarda, Portugal*; *[2]Unidade Local de Saúde do Alto Minho, Rheumatology, Ponte de Lima, Portugal*; *[3]Hospital de Braga, Rheumatology, Braga, Portugal*; *[4]Universidade da Beira Interior, Faculdade de Ciências da Saúde, Covilhã, Portugal*

Background: In the most recent European League Against Rheumatism (EULAR) cardiovascular risk reduction recommendations[1], the use of the SCORE algorithm has been advocated as a useful tool to identify an increased 10-year cardiovascular risk of first fatal atherosclerotic event. Even though validated inflammatory disease-specific CV risk score algorithms are still lacking, the EULAR task force advocated the use of a 1.5 multiplication factor for RA, but not clear for other inflammatory diseases.
Objectives: To assess the accuracy of several CV risk algorithms to predict an event and determine its sensibility and specificity.
Methods: A retrospective analysis of Spondyloarthritis (SpA) patients, registered in REUMA.PT, followed in two Portuguese centres was done. We calculated risk prediction algorithms such as Framingham, the American College of Cardiology/American Heart Association (ACC/AHA) risk score and the Systematic Coronary Risk Evaluation (SCORE) for low-risk countries. The adaptation of risk algorithms was done, accordingly to EULAR recommendations. Primary outcome was the first CV event. Discriminatory ability for CV risk prediction was evaluated by the area under the ROC curves. Sensibility and specificity were calculated for low-to-intermediate and intermediate-to-high risk cut-offs. Cut-off values of high risk were defined in 5% for SCORE, 20% for Framingham and ACC/AHA.
Results: 362 patients with SpA were included, 53.9% male (195), with a mean age of 51.1 ± 12.7 years. 67.8% of the patients were HLA B27 positive. Overall, the mean BMI was 26.3± 4.4 Kg/m^2 and 24.0% of the patients (87) were smokers in their lifetime. The mean of systolic blood pressure was 130± 16.4 mmHg, diastolic blood pressure of 73.5 ± 10.4 mmHg, total cholesterol of 190.1± 37.2 mg/dL and high-density lipoprotein cholesterol of 53.0 ± 14.8 mg/dL. Anti-hypertensive medication was reported in 24.3% of the patients, cholesterol medication in 19.3% and antidiabetic medications in 6.1%. Twenty-five patients (6.9%) presented a cardiovascular event. Patients with a cardiovascular event were older, with higher BMI, prescribed with medication for CV comorbidities and higher diastolic and systolic blood pressure (p<0.05).
Patients were under biologic therapy in 30.9% (112), 16.9% (61) with methotrexate; 16.3% (59) with sulfasalazine and 2.8% (10) with leflunomide; 68.5% (248) prescribed with NSAID and 10.8% (39) with corticosteroids. Area under the ROC in original and adapted scores were equal: 0.709 (95% CI 0.598 to 0.819) for SCORE, 0.805 (95% CI 0.737 to 0.872) for Framingham and 0.776 (95% CI 0.695 to 0.857) for ACC/AHA (Figure 1).

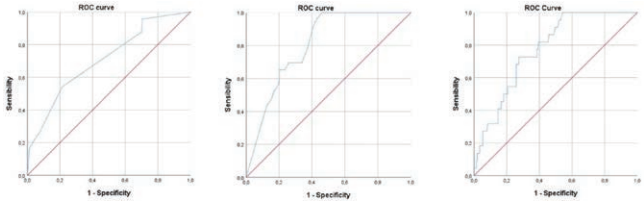


Figure 1. ROC curves for SCORE, Framingham and ACC/AHA

SCORE>1% showed the best sensitivity (96%) but lower specificity. Framingham>20% presented the best specificity (80%) with lower sensitivity (61%). In all cases, specificity raises with higher cut-off with corresponding reduction in sensibility. (Table 1)

Table 1. Sensibility, specificity, positive predictive value (PPV) and negative predictive value (NPV) of CV risk algorithms

	Sensibility (%)	Specificity (%)	PPV (%)	NPV (%)
SCORE > 1%	96	29	12	99
SCORE > 5%	54	78	20	94
Framingham >10%	78	63	15	97
Framingham >20%	61	80	21	96
ACC/AHA >5%	82	55	16	97
ACC/AHA >20%	32	86	20	92

Conclusion: A good discrimination between patients with or without CV events has been demonstrated by area under the ROC curve. The adaptation of CV risk algorithms according EULAR recommendations did not provide an improvement in discriminative ability. Overall, the algorithms studied presented a low sensibility or specificity. Better algorithms are needed to correctly assess cardiovascular risk for SpA patients and they should take into consideration the risk associated with the disease.

REFERENCES:

[1] Agca R, Heslinga SC, Rollefstad S, *et al.* EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. *Annals of the Rheumatic Diseases* 2017;76:17-28.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3622

POS1011 PREDICTORS OF ENDOTHELIAL DYSFUNCTION IN ANKYLOSING SPONDYLITIS

A. Syngle[1], N. Garg[2], I. Verma[3], P. Krishan[4]. [1]*Healing Touch City Clinic, Chandigarh, & 2. Fortis Multi-specialty Hospital, 1. Cardio Rheuma Division; Internal Medicine and Rheumatology, Chandigarh, India*; [2]*Chitkara University, Chitkara College of Pharmacy, Department of Pharmacy Practice, Patiala, India*; [3]*MM College of Pharmacy, Maharishi Markandeshwar, Department of Pharmacy Practice, Mullana, Ambala, India*; [4]*Punjabi University, Department of Pharmaceutical Sciences and Drug Research, Patiala, India*

Background: Cardiovascular (CV) disease is the leading cause of death in Ankylosing Spondylitis (AS). Chronic systemic inflammation driven endothelial dysfunction leading to accelerated atherosclerosis results in premature mortality. Endothelial dysfunction is potentially treatable hence a therapeutic target. Predictive biomarkers for endothelial dysfunction would allow tailoring therapy to the individual.
Objectives: To assess the endothelial dysfunction in AS in context of markers of inflammation and oxidative stress in AS patients.
Methods: Sub group–analysis of our previous studies of AS[1-3] was carried out and 80 AS patients were compared with 40 healthy controls matched for age and sex that were also part of these studies.[2,3] Such analysis had so far not been performed in this cohort. Patients with traditional CV risk factors had been excluded in these studies. Flow-mediated dilatation (FMD), as a measure of endothelial function, was assessed by AngioDefender (Everist Health, Ann Arbor, MI). Inflammatory measures included: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS) in AS. We also assayed markers of inflammation, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), proinflammatory cytokines (interleukin [IL]-1, IL-6, and tumor necrosis factor [TNF]-α), and endothelial dysfunction, including lipids and nitrite and marker of oxidative stress, TBARS.
Results: FMD was significantly lower in AS patients compared with controls [(5.80±0.35% vs. 9.09±0.35%, p≤0.05) reduced by approximately 36%] whereas serum nitrite, TBARS, total cholesterol and LDL levels were significantly higher in AS compared with controls (p≤0.05). Compared with controls, AS patients had significantly high BASDAI, ASDAS and increased concentrations of ESR, CRP, TNF-α, and IL-6. In AS, FMD inversely correlated with ASDAS, CRP (Figure 1A), TNF-α (Figure 1B), nitrite (Figure 1C) and TBARS (Figure 1) and positively correlated with HDL (p≤0.05).
Conclusion: In AS, FMD was impaired, indicating endothelial dysfunction. ASDAS, CRP, TNF-α, nitrite, and TBARS were independent predictors of FMD in AS. AS-related inflammatory mechanisms (TNF-α, IL-6) and markers of vascular function and oxidative stress (CRP, nitrite and TBARS) may all be involved in the development of cardiovascular disease in AS and these predictors could serve as a novel therapeutic targets for preventing CV risk in AS.

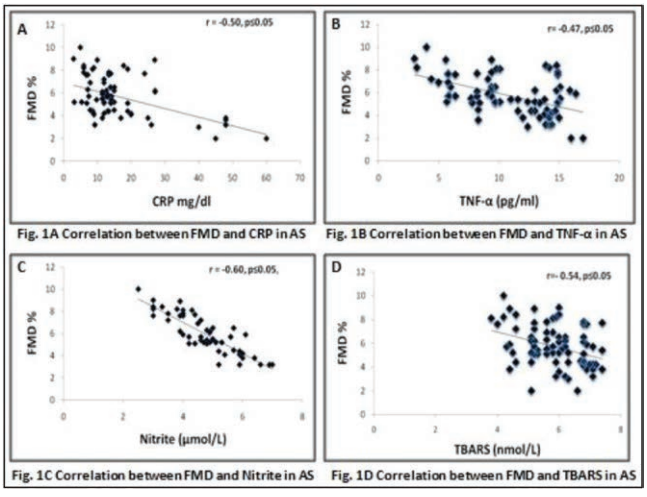


Fig. 1A Correlation between FMD and CRP in AS
Fig. 1B Correlation between FMD and TNF-α in AS
Fig. 1C Correlation between FMD and Nitrite in AS
Fig. 1D Correlation between FMD and TBARS in AS

Figure 1. Correlation of FMD with CRP, TNF-α, Nitrite and TBARS

REFERENCES:

[1] Garg N, Krishan P, Syngle A. Rosuvastatin improves endothelial dysfunction in ankylosing spondylitis. *Clin Rheumatol.* 2015;34:1065-1071.
[2] Verma I, Syngle A, Krishan P, Garg N. Endothelial Progenitor Cells as a Marker of Endothelial Dysfunction and Atherosclerosis in Ankylosing Spondylitis. *International Journal of Angiology.* 2017;26:36–42.
[3] Verma I, Krishan P, Syngle A. Predictors of Atherosclerosis in Ankylosing Spondylitis. *Rheumatol Ther.* 2015;2(2): 173–182.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3635

POS1012 HOW IMPORTANT WOULD BE THE IMPACT OF SPONDYLOARTHRITIS ON MILITARY POPULATION'S WORKING LIFE?

T. Mehmli[1], R. Dhahri[1], M. Slouma[1], E. Hannech[1], B. Louzir[2], L. Metoui[1], I. Gharsallah[1]. [1]*Military Hospital of Tunis, Rheumatology department, Tunis, Tunisia*; [2]*Military Hospital of Tunis, Internal medecine department, Tunis, Tunisia*

Background: Spondyloarthritis is a group of chronic inflammatory diseases involving axial and peripheral joints. It mainly affects young patients typically of working age. Therefore, its impact on work outcomes may be considerable particularly in military patients.
Objectives: The aim of this study was to evaluate the impact of spondyloarthritis on work ability and productivity in military patients, and to assess relationship between work productivity loss and disease activity.
Methods: Thirty Three patients diagnosed with spondyloarthritis in the militay hospital of Tunis were included in the study. Age, gender and C-reactive protein were recorded. Data related to duration of the disease, Ankylosing Spondylitis Disease Activity Score (ASDAS) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) were also recorded. Employed patients completed Work Productivity and Activity Impairment (WPAI) questionnaire witch assesses four subscales: presenteism, absenteism, overall work impairemend and daily activity impairement in the 7 past days.
Results: Among the thirty three patients, 63 % were men and 37% were women. The average age was 43,7 ± 13,5. The average duration of disease was 8,5 ± 7,75 years. Mean C-Reactive protein was 27,5 ± 39,3. Mean ASDAS and BASDAI were 3,12 ± 1,39 and 4,26 ± 1,78 respectively. 22 patients (66%) had an active disease and 11 (33%)were in remission. 48,4% of patients were using NSAIDs, 48,4% were under DMARDs and 42% were under biologics (12 patients using TNF-alpha blockers and 2 patients were given IL-17 inhibitors). Among this patients, 27 were employed. Three patients (11%) had a total work disability and were retired from work and two have been outplaced.
Employed patients worked an average of 35,6 ± 10,3 hours per week and missed an average of 3,48 ± 6,49 hours per week. The mean rates of absenteeism, presenteeism and work productivity loss were 8,8 ± 16,9 %, 48,4 ± 19,9 % and 48,6 ± 19,7 %.
There was a statistically significant correlation between BASDAI and work missed hours (p<0,05, r=0,48), absenteeism (p<0,05, r=0,48), presenteeism (p<0,01, r=0,669), work impairement (p<0,01, r=0,669), activity impairement (p<0,05, r=0,475) and work productivity loss (p<0,05, r=0,475), as well as between ASDAS CRP and presenteeism (p<0,05, r= 0,593), work impairement (p<0,05, r=0,593), activity impairement(p<0,05, r=0,460) and work productivity loss (p<0,05, r=0,460). No relation was found between WPAI indexes and C-reactive protein.
Conclusion: This study demonstrates that spondyloarthritis has a major impact on military patients' work productivity with a significant correlation between WAPI indexes and disease activity scores (ASDAS CRP and BASDAI). No relation was found with C-reactive protein.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3740

POS1013 LET'S TAKE A LOOK AT THE SYMPHYSIS PUBIC AREA IN SPONDYLARTHRITIS

H. Hajji[1], H. Ferjani[1], K. Maatallah[1], S. Miri[1], C. Ines[1], M. Yasmine[1], D. Kaffel[1], W. Hamdi[1]. [1]*Kassab Institute, Tunis; Rheumatology, Tunis, Tunisia*

Background: Symphysis pubic (SP) is the frequent site of enthesitis in spondylarthritis (SpA). Radiological changes in SP appear later in the course of the disease. Underdiagnosed, its prevalence varies from 4% to 47% (1), depending on imaging modalities.
Objectives: This study aimed to evaluate the prevalence of SP involvement in patients with spondyloarthritis (SpA). We also focused on the relation between radiographical changes and clinical findings.
Methods: It was a cross-sectional study, including patients with SpA according to the Assessment of SpondyloArthritis International Society (ASAS) criteria. We collected the following data: age, gender, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), and Bath Ankylosing Spondylitis Functional Index (BASFI).
Pelvic radiographs were examined by 2 experimented rheumatologists. Grading symphysial involvement was made as follow: scores ranged from 0-4 per reading: grade 0 = normal; grade 1 = subtle irregularity and/or subchondral sclerosis, grade 2 = clear erosions, 3 = marked sclerosis, grade 4 = ankylosis.
We divided our patients into two groups: G0 patients without SP changes and G1 patients with SP changes.
Results: One hundred and thirty-one patients were included, 84 were male, and 48 were female. The sex ratio M/F was 1.72. The mean age was 41.32±12.42

years. The mean disease duration was 12.65 ± 9.49 years. The clinical presentation of SpA was peripheral in 61 cases and axial in 118 cases. The mean disease scores activity was: BASDAI: 3.94±2.046 and ASDASCRP: 2.75±1.05. The mean BASFI was 4.17±2.7

SP changes were observed in 31 patients: score 1 (n=14), score 2 (n=8), score 3 (n=8) and score 4 (n=4). Sex ratios M/F were 2.1 and 1.65 in G1 and G0, respectively (p=0.23). No statistically significant differences were reported between the two groups G0 and G1: mean age (40.48 vs. 43.45, p=0.324), mean disease duration (11.19 vs. 14.45, p=0.218), mean BASDAI (3.8 versus 3.9, p=0.850), mean ASDAS-ESR (3.09 vs. 2.55, p=0.113) and mean BASFI (3.76 versus 4.96, p=0.06) respectively. In G1, nine patients had hip involvement (p=0.203). Enthesitis was more common in patients with SP changes (p=0.02).

Conclusion: In our study, the presence of enthesitis was associated with SP changes. Surprisingly, age and disease duration did not influence SP changes (1).

REFERENCES:

[1] Kang Y, Ahn JM, Lee E, Lee JW, Kang HS. Active inflammatory changes around the pubic symphysis in patients with axial spondyloarthritis: Magnetic resonance imaging characteristics and association with clinical factors. Eur J Radiol. mars 2020;124:108802.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4013

POS1014 CENTRAL SENSITIZATION HAS MAJOR IMPACT ON QUALITY OF LIFE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

S. Kieskamp[1], D. Paap[1], M. Carbo[1], F. Wink[2], R. Bos[2], H. Bootsma[1], S. Arends[1], A. Spoorenberg[1]on behalf of Groningen Leeuwarden Axial Spondyloarthritis (GLAS). [1]*University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*; [2]*Medical Center Leeuwarden, Rheumatology, Leeuwarden, Netherlands*

Background: Maintaining optimal health-related quality of life (QoL) is the ultimate goal of treatment in axial spondyloarthritis (axSpA). Chronic pain has a large potential impact on QoL. Central sensitization (CS) may explain part of the chronic pain in axSpA. However, the role of central sensitization (CS) herein has only been studied to a limited degree and current axSpA guidelines pay little attention to identification and treatment of CS.

Objectives: To explore the relationship between CS and QoL in axSpA.

Methods: Consecutive outpatients with axSpA from the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort were included. CS was assessed with the Central Sensitization Inventory (CSI; 0-100), QoL with the AS Quality of Life questionnaire (ASQoL; 0-18) and disease activity with the AS Disease Activity Score ($ASDAS_{CRP}$). A high probability of CS was defined as CSI score ≥40 and active disease as $ASDAS_{CRP}$ score ≥2.1. Patient characteristics and clinical assessments were compared between groups with CSI score <40 and ≥40.(1) Multivariable regression analysis was conducted to investigate the relationship between CSI and ASQoL scores, correcting for potential confounders.

Results: Of the 178 axSpA patients with available CSI score, 149 completed the ASQoL. Mean age of the 178 included patients was 47.4 ± 14.1 years, 78 (44%) were female, mean symptom duration was 21.4 ± 13.6 years and 88 (52%) were using bDMARDS. Mean CSI score was 38.0 ± 14.1, mean ASQoL 6.0 ± 5.3 and mean $ASDAS_{CRP}$ 2.1 ± 1.0. CSI score ≥40 was significantly associated with higher mean ASQoL (9.7 vs. 3.3), higher mean $ASDAS_{CRP}$ (2.6 vs. 1.7), female gender (60% vs. 29%) and more often entheseal involvement (61% vs. 26%) (Table 1).

Table 1. Selection of patient characteristics, disease activity and clinical outcome variables for patients with axSpA, divided in subgroups for CSI score with a cutoff point of 40.

Characteristics	All patients n = 178	CSI<40 n = 98 (55%)	CSI≥40 n = 80 (45%)
Age (years)	47.4 ± 14.1	48.7 ± 15.0	45.8 ± 12.7
Female	78 (44)	27 (29)	44 (60)*
Symptom duration (years)	21.4 ± 13.6	21.5 ± 13.5	21.2 ± 13.8
HLA-B27+	133 (79)	70 (79)	54 (79)
Smoker	45 (27)	28 (32)	15 (23)
BMI (kg/m^2)	26.7 ± 5.0	26.2 ± 4.4	27.5 ± 5.8
Completed higher education[1]	81 (71)	48 (70)	34 (76)
Biological use	88 (52)	49 (52)	39 (51)
RDCI (0-9)	0.0 (0.0 – 1.0)	0.0 (0.0 – 1.0)	0.0 (0.0 – 1.8)
Peripheral arthritis[2]	10 (6)	5 (6)	5 (8)
Entheseal involvement[3]	64 (40)	23 (26)	38 (61)*
$ASDAS_{CRP}$	2.1 ± 1.0	1.7 ± 0.9	2.6 ± 1.0*
CRP (mg/ml)	2.9 (1.1 – 6.8)	2.6 (1.1-6.0)	3.6 (1.4 – 7.0)
ASQoL (0-18)	6.0 ± 5.3	3.3 ± 3.6	9.7 ± 4.9*
CSI (0-100)	38.0 ± 14.1	28.0 (23 – 34)	50.0 (43.0 –56.0)[N/A]

Values are n (%), mean ± SD or median (IQR).1International Standard Classification of Education (ISCED) level >4; 2Swollen Joint Count >0; 3Maastricht Ankylosing Spondylitis Enthesitis Score >0. *p<0.001. ASDASCRP: Ankylosing Spondylitis Disease Activity Score; ASQoL: Ankylosing Spondylitis Quality of Life questionnaire; CRP: C-reactive protein; CSI: Central Sensitization Inventory; RDCI: Rheumatic Disease Comorbidity Index.

Patients with low $ASDAS_{CRP}$ (<2.1) and also low CSI score (<40) showed good QoL (median ASQoL 1.1). Patients with low $ASDAS_{CRP}$ combined with high CSI score (≥40) and patients with high $ASDAS_{CRP}$ (≥2.1) combined with low CSI score reported worse QoL (median ASQoL 5.6 and 4.1, respectively). Patients with high $ASDAS_{CRP}$ and also high CSI score reported the worst QoL (median ASQoL 12.0). (Figure 1).

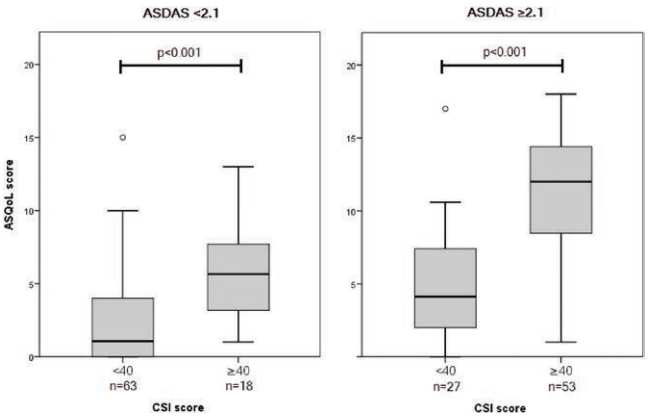


Figure 1. ASQoL score in patients with axSpA with CSI score ≥40 and <40, divided for $ASDAS_{CRP}$ (cutoff 2.1)

Additionally, in univariable analysis, the CSI score explained a large proportion of the variation of the ASQoL (R^2=0.46). This association remained significant after correction for $ASDAS_{CRP}$, gender, symptom duration, entheseal involvement, smoking status, BMI category, educational level and comorbidities in multivariable analysis (CSI p<0.001).

Conclusion: In daily clinical practice, CS seems strongly related to patient-reported QoL in patients with long-term axSpA.

REFERENCES:

[1] Neblett R et al. J Pain. 2013;14:438–45.

Acknowledgements: The authors would like to thank all patients who participated in the GLAS cohort. Furthermore, the authors wish to acknowledge Mrs. B. Burmania, Mrs. B. Hollander, Mrs. S. Katerbarg, Mrs. S. Lange, Mrs. E. Markenstein, Mrs. R. Rumph and Mrs. M. de Vries-Veldman for their contribution to clinical data collection.

Disclosure of Interests: Stan Kieskamp: None declared, Davy Paap: None declared, Marlies Carbo: None declared, Freke Wink Consultant of: Abbvie, Reinhard Bos: None declared, Hendrika Bootsma Grant/research support from: Roche, Suzanne Arends Grant/research support from: Pfizer, Anneke Spoorenberg Consultant of: Abbvie, Pfizer, MSD, UCB, Lilly, Novartis, Grant/research support from: Abbvie, Pfizer, UCB, Novartis.

DOI: 10.1136/annrheumdis-2021-eular.4035

POS1015 ANTI-TNF DRUGS AND CARDIOVASCULAR EVENTS IN PATIENTS WITH SPONDYLOARTHRITIS

C. W. S. Chan[1], P. H. LI[1], C. S. Lau[1], H. Y. Chung[1]. [1]*The University of Hong Kong, Queen Mary Hospital, Hong Kong, Division of Rheumatology and Clinical Immunology, Department of Medicine, Hong Kong, Hong Kong (SAR)*

Background: Cardiovascular (CVS) diseases are the leading cause of death worldwide and patients with rheumatic diseases have an increased CVS risk including stroke and myocardial infarction (MI) (1-3). CVS risk factors and CVS events are common in SpA (4). Delineating the CVS risk and the association with medications in patients with SpA would be useful.

Objectives: The objective of this study was to delineate the CVS risk and the association with medications in patients with SpA.

Methods: Patients with SpA and patients with non-specific back pain (NSBP) were identified in rheumatology and orthopedics clinics respectively. Clinical information and CVS events were retrieved. Incidence rates were calculated. Association analysis was performed to determine the CVS risk of SpA and other modifiable risk factors.

Results: A total of 5046 patients (SpA 2616 and NSBP 2430) were included from eight centers. Over 56 484 person-years of follow-up, 160 strokes, 84 MI and 262 major adverse cardiovascular events (MACE) were identified. Hypercholesterolemia was more prevalent in SpA (SpA 34.2%, NSBP 28.7%, P<0.01). Crude incidence rates of stroke and MI were higher in SpA patients. SpA was associated with a higher risk of MACE (HR 1.66, 95%CI 1.22-2.27, P<0.01) and cerebrovascular events (HR 1.42, 95%CI 1.01-2.00, p=0.04). The use of anti-tumor necrosis factor (TNF) drugs was associated with a reduced risk of MACE (HR 0.37, 95%CI 0.17-0.80, P=0.01) and cerebrovascular events (HR 0.21, 95%CI 0.06-0.78, P=0.02).

Conclusion: SpA is an independent CVS risk factor. Anti-TNF drugs were associated with a reduced CVS risk in these patients.

REFERENCES:

[1] Crowson CS, Liao KP, Davis JM, 3rd, Solomon DH, Matteson EL, Knutson KL, et al. Rheumatoid arthritis and cardiovascular disease. Am Heart J. 2013;166(4):622-8 e1.
[2] Verhoeven F, Prati C, Demougeot C, Wendling D. Cardiovascular risk in psoriatic arthritis, a narrative review. Joint Bone Spine. 2020;87(5):413-8.
[3] Liew JW, Ramiro S, Gensler LS. Cardiovascular morbidity and mortality in ankylosing spondylitis and psoriatic arthritis. Best Pract Res Clin Rheumatol. 2018;32(3):369-89.
[4] Molto A, Etcheto A, van der Heijde D, Landewe R, van den Bosch F, Bautista Molano W, et al. Prevalence of comorbidities and evaluation of their screening in spondyloarthritis: results of the international cross-sectional ASAS-COMOSPA study. Ann Rheum Dis. 2016;75(6):1016-23.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4133

POS1016 ANKYLOSING SPONDYLITIS IN WEST AFRICAN PATIENTS: A SERIES OF 37 CASES REPORTED IN TOGO

P. Houzou[1], V. E. S. Koffi-Tessio[2], S. Oniankitan[3], K. Kakpovi[1], E. Fianyo[2], K. Tagbor[2], O. Oniankitan[2], M. Mijiyaw[2]. *[1]University of Kara, Rheumatology, Kara,Togo*; *[2]University of Lomé, Rheumatology, Lomé,Togo*; *[3]University of Lomé, Rheumatology, Kara,Togo*

Background: Spondyloarthritis (SpA) is generally uncommon in sub-Saharan Africa, in part because of the rarity of HLA-B27 in this region.

Objectives: The aim of our study was to determine the epidemiological, semiological, paraclinical and therapeutic aspects of ankylosing spondylitis in rheumatology in Togo.

Methods: This was a retrospective multicenter descriptive study on the files of patients suffering from ankylosing spondylitis seen in an outpatient setting or hospitalized in one of the four Rheumatology departments of Togo in the period from January 1, 2000 to December 31, 2019. The diagnosis was essentially radio-clinical based on the modified New York criteria.

Results: In 20 years, and out of a population of 35,304 rheumatic patients, we have collected 37 cases of ankylosing spondylitis, meaning a hospital frequency of 0.10% and an annual frequency of 1.85 cases. There was clearly a male predominance with an M / F ratio of 4.28. The onset of the disease was on average of 29.62 ± 10.27 years and the diagnosis delay on average of 9.45 ± 9.20 years. The clinic was dominated by spinal pain in the form of chronic inflammatory cervical-dorsal-lumbar pain (41.2%) or lumbar pain (29.4%). Common joint injuries were those of the knees (57.69%), ankles (26.9%) and shoulders (23.1%). The most frequent extra-articular manifestations were ocular with conjunctivitis (62.5%) and uveitis (37.5%). Due to the delayed diagnosis, significant spinal deformities including hypercyphosis, straightness and ankylosis were found; the radiography of the spine objectified syndesmophytes (50.0%) with ankyloses and the bamboo column (23.5%) and that of the pelvis objectified sacroiliitis at stage 3 (54.6%) and at stage 4 (27.3%). The HLA B27 antigen was positive in 10.8% of cases. NSAIDs and sulfasalazine were the most commonly used drugs in management, respectively in 94.3% of symptomatic treatment and 92.6% of background therapy.

Conclusion: Ankylosing spondylitis is relatively rare in Togo, affecting more men and young adults. There are no clinical or paraclinical particularity. The delay in diagnosis reflects the importance of the radiological signs. Treatment is mainly done by NSAIDs and DMRADs in particular sulfasalazine, due to their accessibility.

REFERENCES:

[1] Dean LE, Jones GT, MacDonald AG, Downham C, Sturrock RD, Macfarlane GJ. Global Prevalence of Ankylosing Spondylitis. Rheumatology (Oxford). 2014;53:650-7.
[2] Zabsonre TWJ, Sawadogo SA, Kabore F, Ilboudo A, Sougue C, Zongo E, et al. Ankylosing Spondylitis in Sub-Saharan Africa: A Series of 48 Cases Reported in Burkina Faso (West Africa). Open J Rheumatol Autoimmune Dis. 2018;8:87-92.
[3] Mijiyawa M. Ankylosing Spondylitis in Togolese Patients. Med Trop. 1993;53:185-9.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4199

POS1017 CARDIOVASCULAR RISK IN DIFFERENT CLINICAL VARIANTS OF SPONDYLOARTHRITIS

A. Dadalova[1], E. Vasilenko[1], R. Samigullina[1], V. Mazurov[1]. *[1]North-Western State Medical University named after I.I. Mechnikov, Department of Therapy, Rheumatology, Examination of Temporary Disability and Quality of Medical Care named after E.E.Eichwald, St. Petersburg, Russian Federation*

Background: Numerous studies have shown that the life expectancy of patients with spondyloarthritis (SPA) is, on average, 5-7 years less compared to the population, and the overall mortality rate is 1.6-1.9 times higher than the population, while mortality from cardiovascular disease increases by 20-40%.

Objectives: of the current study were to assess the cardiovascular risk in pts with with ankylosing spondylitis, psoriatic arthritis and psoriatic spondyloarthritis and to compare different cardiovascular risk scales in these pts.

Methods: The study included 54 patients with SpA aged 45 to 65 years. The patients were divided into 3 groups: patients with ankylosing spondylitis (AS) who meet the modified New York criteria for AS (1984) (n = 14), patients with psoriatic arthritis (PsA) who meet the CASPAR criteria (Classification criteria of Psoriatic Arthritis, 2006) (n = 18) and patients with psoriatic spondyloarthritis (PsSpA) meeting the modified New York criteria for AS and CASPAR criteria for PsA (n = 22).

The average age in the AS group was 55.5 ± 6.43 years, in the PsA group - 57.4 ± 5.76 years, in the PsSpA group - 55.0 ± 6.45 years. Men made up 64.3% in the AC group, 50% in the PsA group, and 49% in the PsSpA group.

Three indices of cardiovascular risk evaluation (Systematic COronary Risk Evaluation (SCORE) with increasing coefficient 1.5 for inflammatory diseases, Reynolds Risk Score (RRS), and the third modification of QRESEARCH Cardiovascular Risk Algorithm (QRISK3) were calculated.

After the numerical assessment of the indicators, each patient was graded in the degree of CVR with the allocation of low, medium, high and very high degree. To stratify the degrees, an estimate of the total risk on the SCORE scale was used: with a value of less than 1%, the risk was considered low, from> 1% to 5% - medium or moderately increased, from> 5% to 10% - high, and> 10% - very high.

Results: The values of the indices were in the AS group SCORE – 3,05±2,41%, RRS – 5,05±2,67%, QRISK3 – 6,68±3,11%, in pts with PsA SCORE - 4,11±2,22%, RRS - 5.72 ± 2.46%, QRISK3 - 7.25 ± 2.51% and in pts with PsSpA SCORE - 4.78 ± 2.65%, RRS - 6.35 ± 2.34 %, QRISK3 - 8.02 ± 3.25%.

Table 1. The number of pts corresponding to different degrees of risk depending on the used CVD risk assessment scale, n = 54

Degrees of risk	SCORE	RRS	QRISK3
Low	9	2	0
Medium	32	26	16
High	12	23	28
Very high	1	3	10

When assessing CVR using various risk assessment scales (RRS, QRISK3, SCORE), the highest values were obtained in the PsSpA group.

When comparing the results obtained, it was found that the majority of the surveyed belonging to a low degree of CVR according to SCORE (9 people), when evaluated using other scales, fell into the group of medium or high risk. The assessment of the risks of 10-year significant cardiovascular events in patients with SPA using the SCORE index does not coincide with the QRISK3 index data in 70.4% of cases, with the RRS data - in 42.6% of cases, and the SCORE index shows lower values of the expected risk. The highest values were obtained when assessing CVR using the scale QRISK3.

Conclusion: The highest CVR values were obtained in the PsSpA group using various risk assessment scales (RRS, QRISK3, SCORE). There was a discrepancy in the severity of CVR calculated using different rating scales in SpA patients. The largest values were obtained when using the scale QRISK3, and the smallest when calculating the CVR using the scale SCORE.

REFERENCES:

[1] Horreau C, Pouplard C, Brenaut E, Barnetche T, Misery L, Cribier B, et al. Cardiovascular morbidity and mortality in psoriasis and psoriatic arthritis: a systematic literature review. J Eur Acad Dermatol Venereol 2013;27 Suppl 3:12–29.
[2] Bengtsson K, Forsblad-d'Elia H, Lie E, et al. Are ankylosing spondylitis, psoriatic arthritis and undifferentiated spondyloarthritis associated with an increased risk of cardiovascular events? A prospective nationwide population-based cohort study. Arthritis Res Ther. 2017 May 18;19(1):102. doi: 10.1186/s13075-017-1315-z

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4209

POS1018 IMPORTANCE OF LATERAL SPINE VIEW IN DXA BONE DENSITOMETRY IN PATIENTS WITH SPONDYLOARTHRITIS

S. Miri[1], H. Ferjani[1], K. Maatallah[1], A. Kasraoui[1], D. Kaffel[1], W. Hamdi[1]. *[1]Mohamed Kassab Institute of Orthopedics, Rhumatology, Manouba,Tunisia*

Background: Osteoporosis is an increasingly important health problem among patients with spondyloarthritis (SPA). The Measure of Bone Mineral Density BMD is routinely carried out in an anteroposterior (AP) view of the spine. However, the syndesmophytes, ligaments calcifications, and the posterior part of vertebrae affect AP scanning. A lateral spine view is a more sensitive tool in assessing bone loss in trabecular bone.
Objectives: We aimed to evaluate the association between lateral lumbar DXA and syndesmophyte grading in patients with SPA.
Methods: We conducted a retrospective study including 75 patients with SPA. Bone density of the hip and lumbar spine was measured with a GE Lunar Prodigy Advance Bone Densitometer equipment. All patients had lumbar lateral, AP, and proximal femur DXA scans. The T-score, which measures the difference between a patient's BMD and young-normal subjects, was computed and age-matched.
Results: The mean age of the patients was 36±11 years. Male predominance was noted with a sex ratio of 4.76. The mean BMI was 25±5 kg/m2. Eight percent were obese. Fifty-two percent had Vitamin D deficiency.
Forty-eight percent of the patients had axial SPA, while 52% had axial and peripheral symptoms.
The mean age of onset was 27±7 years. Fifty-two percent of the patients had high inflammatory biomarkers. The BASDAI, ASDAS-VS, and ASDAS-CRP mean levels were respectively: 3.5±2.4, 3.1±0.9, and 3±0.8. The mean BASRI and mass were respectively 8+4.8 and 16.4+19.4. Analyses of T-score values obtained over the femoral neck revealed osteoporosis in 18.7% of the cases and osteopenia in 32% of the cases. On the other hand, analyses of AP, spine views revealed osteoporosis in 25.3% and osteopenia in 45.3% of patients (p=0.028, r=0.254). We detected the highest percentage of osteoporosis in lateral lumbar view and T-scores matched more closely with femoral neck values; osteoporosis in 29.3%, and osteopenia in 22.7% of the patients (p<10-3, r=0.562). BMD measured in AP, and lateral views were in good agreement (p<10-3, p=0.592). Age was inversely but not significantly associated with BMD in lateral (p=0.442, r=-0.09), AP (p=0.319, r=-0.117) and femoral neck projections (p=0.179, r=-0.157). Femoral neck BMD was associated with the activity of SPA (ASDAS vs (p=0.027, r= -0.295), and the mobility limitation BASMI (p=0.032, r= -0.247). Coxitis, BASRI, or mSASS were independent of BMD.
Conclusion: We conclude that spine lateral view in DXA accurately measures BMD exceeding the AP spine views and femoral neck values. Therefore, structural changes do not affect this measurement
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4294

POS1019

INCONSISTENCY OF THE DEGREE OF CARDIOVASCULAR RISK WHEN ASSESSED USING DIFFERENT INDICES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

E. Vasilenko[1], A. Dadalova[1], R. Samigullina[1], V. Mazurov[1]. *[1]North-Western State Medical University named after I. I. Mechnikov, St. Petersburg, Russia, Department of Therapy, Rheumatology, Examination of Temporary Disability and Quality of Medical Care named after E.E. Eichwald, St. Petersburg, Russian Federation*

Background: Evaluation of indicators of cardiovascular risk is one of the main tasks facing a rheumatologist in the tactics of choosing a therapy for patients (pts) with axial spondyloarthritis (axSpA). It is known that pts suffering from axSpA are characterized by a significant increase in cardiovascular risk (CVR). However, there are still no recommendations regulating risk assessment scales in pts with axSpA.
Objectives: were to assess the CVR in pts with axSpA and to compare different cardiovascular risk scales in these pts.
Methods: The study included 55 pts at the age of 45-65 years with diagnosis of axSpA fulfilling ASAS criteria (2009) from St. Petersburg' axSpA register. Three indices of cardiovascular risk evaluation (Systematic COronary Risk Evaluation (SCORE) with increasing coefficient 1.5 for inflammatory diseases, Reynolds Risk Score (RRS), and the third modification of QRESEARCH Cardiovascular Risk Algorithm (QRISK3) were calculated. Risk gradation: low risk (<1%), medium (1.0-4.9%), high (5.0-9.9%), very high (> 10%).
Results: Mean age of the pts was 45.8±10.3 years; males - 37 (67.3%) pts, HLA-B27 positive – 34 (61.8%); mean disease duration 12.5±8.7 years. Mean value of SCORE was 2.83±1.89%, of RRS – 5.04±3.98%, of QRISK3 – 7.91±4.91%.
The gradation of the degree of risk depending on the applied assessment index is presented in Table 1.

Index	Results		
Risk degree	SCORE	RRS	QRISK3
Low	21 (38,2%)	8 (14,5%)	0 (0,0%)
Medium	26 (47,3%)	23 (41,8%)	17 (30,9%)
High	8 (14,5%)	17 (30,9%)	22 (40,0%)
Very high	0 (0,0%)	7 (12,7%)	16 (29,1%)

Particular attention is drawn to the 100% discrepancy of low risk values when comparing SCORE and QRISK3. A similar trend persisted when comparing medium, high and very high risk. Thus, the assessment of the risks of 10-year significant cardiovascular events in pts with axSpA using the SCORE index does not coincide with the QRISK3 index data in 87.27% of cases, and with the RRS data - in 58.18% of cases. In 84.3% of cases, the mismatch between the SCORE and RRS indexes was due to the presence of an increased CRP level.
Conclusion: When assessing cardiovascular risk in pts with axial spondyloarthritis, a discrepancy was found between the degrees of risk when assessed using different scales. SCORE scores were significantly different from Reynolds' and QRISK3 scores. These features can be interrelated with a small number of factors assessed when calculating the SCORE, even though there is a correction factor for rheumatic diseases. For pts with axial spondyloarthritis, it is necessary to use additional indicators that influence cardiovascular risk, such as CRP.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4311

Psoriatic arthritis – treatment

POS1020

EFFICACY OF TOFACITINIB ON DACTYLITIS IN INDIVIDUAL DIGITS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

A. M. Orbai[1], P. J. Mease[2,3], P. Helliwell[4], O. Fitzgerald[5], M. Bdewi[6], D. Fleishaker[7], R. Mundayat[8], P. Young[9]. *[1]Johns Hopkins University School of Medicine, Division of Rheumatology, Baltimore, MD, United States of America*; *[2]Swedish Medical Center/Providence St Joseph Health, Rheumatology Clinical Research Division, Seattle, WA, United States of America*; *[3]University of Washington School of Medicine, Rheumatology Clinical Research Division, Seattle, WA, United States of America*; *[4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*; *[5]Conway Institute for Biomolecular Research, University College Dublin, Dublin, Ireland*; *[6]College of Medicine, King Saud University Medical City, King Saud University, Division of Rheumatology, Riyadh, Saudi Arabia*; *[7]Pfizer Inc, Inflammation and Immunology, Groton, CT, United States of America*; *[8]Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*; *[9]Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America*

Background: Dactylitis, a hallmark of psoriatic arthritis (PsA), is a uniformly diffuse and sometimes painful swelling of the fingers and/or toes.[1] Up to 50% of patients (pts) with PsA may experience dactylitis;[1,2] as such, dactylitis is an accepted domain of PsA that should be considered in treatment decisions.[3] In PsA, dactylitis typically involves feet more than hands; dactylitic joints more frequently have erosive damage, compared with non-dactylitic joints.[2] There remains a need for effective therapies to treat dactylitis in pts with PsA. Improvements in dactylitis have been associated with tofacitinib, an oral Janus kinase inhibitor for the treatment of PsA.[4,5]
Objectives: To assess the effect of tofacitinib on dactylitis by location (hands/feet) and individual digit involvement in pts with PsA.
Methods: These post hoc analyses used data pooled from two Phase 3 studies (12-month OPAL Broaden [NCT01877668];[5] 6-month OPAL Beyond [NCT01882439][4]) in pts with active PsA treated with tofacitinib 5 mg twice daily (BID; approved dose; to Month [M] 6), tofacitinib 10 mg BID (to M6) or placebo (PBO; to M3); pts were treated continuously with a single conventional synthetic disease-modifying antirheumatic drug. Pts were categorised by the presence of dactylitis at baseline (BL) in the hands and/or feet. Endpoints included change from BL in Dactylitis Severity Score (DSS),[6] the number of dactylitic digits and the proportion of pts with dactylitis in individual digits at M1, M3 and M6. Descriptive statistics were generated by visit and treatment arm.
Results: Data were pooled from 373 pts with DSS >0 at BL. BL characteristics, including gender, age, race, body mass index, PsA duration, BL DSS and dactylitic digits count were similar across dactylitis groups and treatment groups, except for pts with dactylitis in both the hands and feet, who had higher DSS compared to those with dactylitis in the hands or feet only, likely due to having more dactylitic digits (data not shown). Regardless of location, pts treated with tofacitinib had cumulative improvements from BL to M6 in DSS (Figure 1a) and in the number of dactylitic digits (Figure 1b); improvements in DSS were greater at M1 and M3, compared with PBO. Pts treated with tofacitinib 10 mg BID typically had numerically greater improvements in DSS, compared with pts treated with tofacitinib 5 mg BID (Figure 1a). Most pts treated with tofacitinib experienced improvement of dactylitis across all fingers and toes (Figure 1c–f); mean dactylitis presence was ≤15% at M6 in pts treated with tofacitinib for all digits. Generally, at M1 and M3, fewer pts treated with tofacitinib had dactylitis in any digit, compared with PBO (Figure 1c–f).
Conclusion: Among pts with pre-existing dactylitis, treatment with tofacitinib resulted in improvements in dactylitis in hands, feet, or both, and in all digits as early as M1, and up to M6.

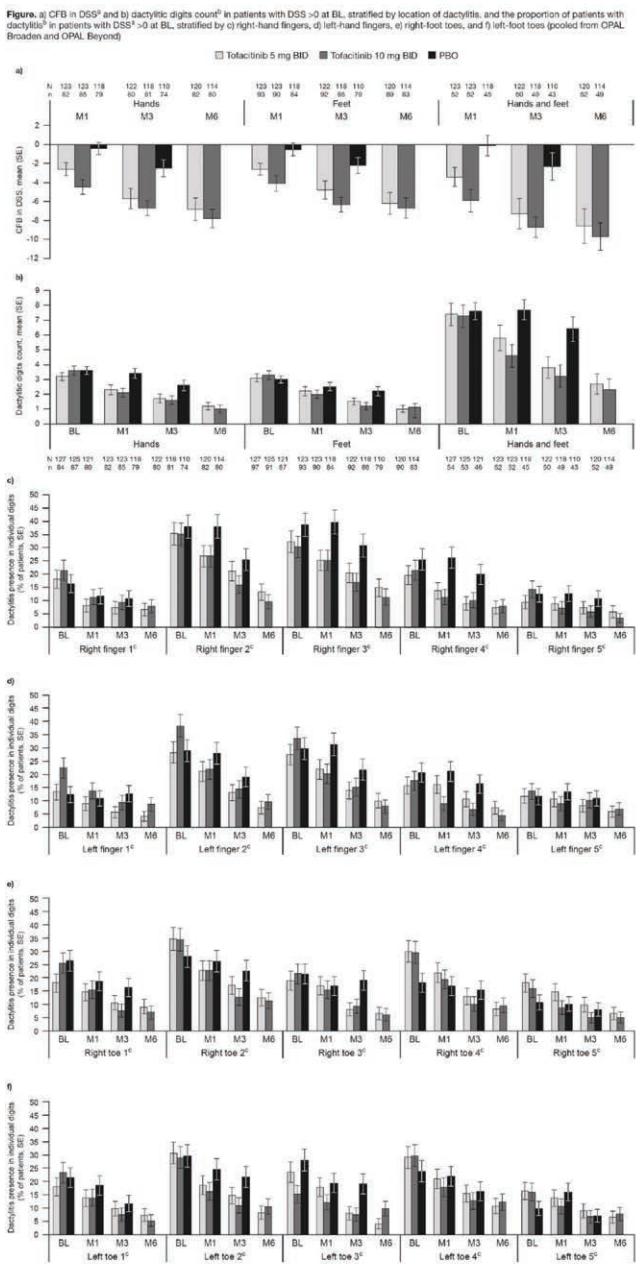


Figure. a) CFB in DSS[a] and b) dactylitic digits count[b] in patients with DSS >0 at BL, stratified by location of dactylitis, and the proportion of patients with dactylitis[b] in patients with DSS[a] >0 at BL, stratified by c) right-hand fingers, d) left-hand fingers, e) right-foot toes, and f) left-foot toes (pooled from OPAL Broaden and OPAL Beyond)

[a]A blinded assessor squeezed each digit of the hands and feet with moderate pressure, and assigned a score for each digit on a scale of 0–3, where 0 = no tenderness, 1 = tender, 2 = tender and winces, and 3 = tender and withdraws. DSS is calculated as the sum of those scores, ranging from 0–60, with a score of 60 being the highest dactylitis severity.[6] [b]Dactylitis was defined as swelling of an entire digit. [c]N ranged from 121–127 at BL, 118–123 at M1, 110–122 at M3 and 113–120 at M6 for all digits. CFB, change from baseline; N, total number of patients with DSS >0 at BL; n, total number of patients with dactylitis in that particular location; SE, standard error

REFERENCES:

[1] Kaeley et al. Semin Arthritis Rheum 2018; 48: 263-273.
[2] Brockbank et al. Ann Rheum Dis 2005; 64: 188-190.
[3] Coates et al. Arthritis Rheumatol 2016; 68: 1060-1071.
[4] Gladman et al. N Engl J Med 2017; 377: 1525-1536.
[5] Mease et al. N Engl J Med 2017; 377: 1537-1550.
[6] Helliwell et al. J Rheumatol 2005; 32: 1745-1750.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Eric Comeau, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: Ana-Maria Orbai Consultant of: Eli Lilly, Novartis, Pfizer Inc, Grant/research support from: AbbVie, Eli Lilly, Horizon, Janssen, Novartis, Philip J Mease Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Genentech, Janssen, Novartis, Pfizer Inc, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer Inc, Sun, UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer Inc, Sun, UCB, Philip Helliwell Paid instructor for: Janssen, Novartis, Pfizer Inc, Consultant of: Eli Lilly, Oliver FitzGerald Speakers bureau: AbbVie, Janssen, Pfizer Inc, Consultant of: Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Pfizer Inc, Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Novartis and Pfizer Inc, Mohammed Bdewi Speakers bureau: AbbVie, Pfizer Inc, Dona Fleishaker Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Rajiv Mundayat Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Pamela Young Shareholder of: Pfizer Inc, Employee of: Pfizer Inc.

DOI: 10.1136/annrheumdis-2021-eular.73

POS1021

THE PSABIO STUDY IN ITALY: A REAL-WORLD COMPARISON OF THE PERSISTENCE, EFFECTIVENESS AND SAFETY OF USTEKINUMAB AND TUMOUR NECROSIS FACTOR INHIBITORS IN PATIENTS WITH PSORIATIC ARTHRITIS

E. Gremese[1], F. Ciccia[2], C. Selmi[3], G. Cuomo[4], R. Foti[5], M. Matucci Cerinic[6], F. Conti[7], E. Fusaro[8], G. Guggino[9], F. Iannone[10], A. Delle Sedie[11], R. Perricone[12], L. Idolazzi[13], P. Moscato[14], E. Theander[15], W. Noel[16], P. Bergmans[17], S. Marelli[18], L. Gossec[19,20], J. S. Smolen[21]. *[1]Catholic University of the Sacred Heart, Fondazione Policlinico A Gemelli-IRCCS, Rome, Italy*; *[2]University of Campania 'L Vanvitelli', Rheumatology Unit, Naples, Italy*; *[3]Humanitas Clinical and Research Center IRCCS and Humanitas University, Rheumatology and Clinical Immunology Unit, Milan, Italy*; *[4]University of Campania 'L Vanvitelli', Department of Precision Medicine, Naples, Italy*; *[5]Presidio Ospedaliero San Marco – AOU Policlinico Vittorio Emanuele, Rheumatology Unit, Catania, Italy*; *[6]University of Florence, Department of Experimental and Clinical Medicine, Florence, Italy*; *[7]Sapienza University of Rome, Department of Internal Medicine, Anesthesiology and Cardiovascular Sciences, Rheumatology Unit, Rome, Italy*; *[8]City of Health and Science University Hospital of Turin, Department of Rheumatology, Turin, Italy*; *[9]University of Palermo, Biomedical Department of Internal and Specialized Medicine, Rheumatology Section, Palermo, Italy*; *[10]University of Bari 'Aldo Moro', Rheumatology Unit, Bari, Italy*; *[11]University of Pisa, Rheumatology Unit, Pisa, Italy*; *[12]University of Rome 'Tor Vergata' and Policlinico 'Tor Vergata', Rheumatology, Allergology and Clinical Immunology, Department of Internal Medicine, Rome, Italy*; *[13]University of Verona, Rheumatology Unit, Department of Medicine, Verona, Italy*; *[14]AOU San Giovanni di Dio e Ruggi D'Aragona, Rheumatology Unit, Department of Medicine, Salerno, Italy*; *[15]Janssen-Cilag AB, Medical Affairs, Solna, Sweden*; *[16]Janssen Pharmaceutica NV, Medical Affairs, Beerse, Belgium*; *[17]Janssen-Cilag BV, Biostatistics, Breda, Netherlands*; *[18]Janssen-Cilag SpA, Medical Affairs, Milan, Italy*; *[19] Sorbonne University, INSERM, Pierre Louis Institute of Epidemiology and Public Health, Paris, France*; *[20]Pitié-Salpêtrière Hospital, AP-HP, Department of Rheumatology, Paris, France*; *[21]Medical University of Vienna, Division of Rheumatology, Department of Medicine III, Vienna, Austria*

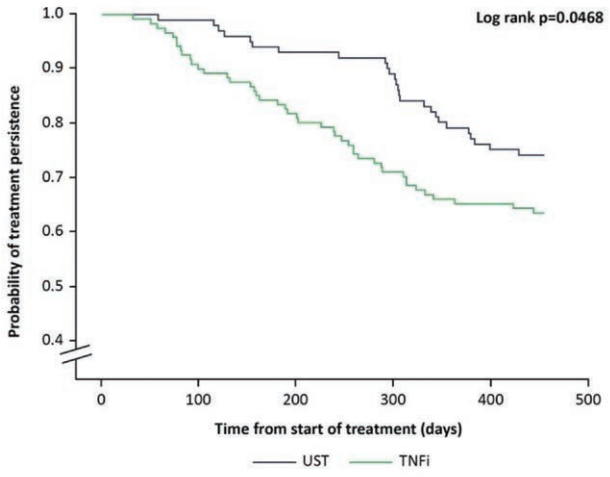
Background: There are still unmet needs in the treatment of psoriatic arthritis (PsA), including in terms of treatment persistence, which is a function of effectiveness, safety and patient satisfaction. Ustekinumab (UST) was the first new biologic drug to be developed for the treatment of PsA after tumour necrosis factor inhibitors (TNFi).

Objectives: To compare treatment persistence, effectiveness and safety of UST and TNFi in Italian patients within the PsABio cohort.

Methods: PsABio (NCT02627768) is an observational study of 1st/2nd/3rd-line UST or TNFi treatment in PsA in 8 European countries. The current analysis set includes 222 eligible patients treated in 15 Italian centres, followed to Month 12 (±3 months). Treatment persistence/risk of stopping was analysed using Kaplan–Meier (KM) and Cox regression analysis. Proportions of patients reaching minimal disease activity (MDA)/very low disease activity (VLDA) and clinical Disease Activity Index for PsA (cDAPSA) low disease activity (LDA)/remission were analysed using logistic regression, including propensity score (PS) adjustment for imbalanced baseline covariates, and non-response imputation of effectiveness endpoints if treatment was stopped/switched before 1 year. Last observation carried forward data are reported.

Results: Of patients starting UST and TNFi, 75/101 (74.3%) and 77/121 (63.6%), respectively, persisted with treatment at 1 year. The observed mean persistence was 410 days for UST and 363 days for TNFi. KM curves and PS-adjusted hazard ratios confirmed significantly higher persistence (hazard ratio [95% confidence interval (CI)]) for UST versus TNFi overall (0.46 [0.26; 0.82]; Figure 1). Persistence was also higher for UST than TNFi in patients receiving monotherapy without methotrexate (0.31 [0.15; 0.63]), in females (0.41 [0.20; 0.83]), and in patients with body mass index (BMI) <25 kg/m^2 (0.34 [0.14; 0.87]) or >30 kg/m^2 (0.19 [0.06; 0.54]). There was no significant difference in persistence between treatments in patients with BMI 25–30 kg/m^2. While patients receiving 1st- and 3rd-line UST or TNFi showed similar risk of discontinuation (0.60 [0.27; 1.29] and 0.36 [0.10; 1.25], respectively), patients receiving 2nd-line UST showed better persistence than those receiving 2nd-line TNFi (0.33 [0.13; 0.87]). Other factors added to the PS-adjusted Cox model did not show significant effects. In patients with available follow-up data, the mean (standard deviation) baseline cDAPSA

Kaplan–Meier estimates of treatment persistence for ustekinumab and TNFi in the overall PsABio Italian cohort



TNFi, tumour necrosis factor inhibitor

was 26.3 (15.4) for UST and 23.5 (12.3) for TNFi; at 1-year follow-up, 43.5% of UST- and 43.6% of TNFi-treated patients reached cDAPSA LDA/remission. MDA was reached in 24.2% of UST- and 28.0% of TNFi-treated patients, and VLDA in 12.5% of UST- and 10.2% of TNFi-treated patients. After PS adjustment (stoppers/switchers as non-responders), odds ratios (95% CI) at 1 year did not differ significantly between UST and TNFi groups for reaching cDAPSA LDA/remission (1.08 [0.54; 2.15]), MDA (0.96 [0.45; 2.05]) or VLDA (0.98 [0.35; 2.76]). In total, 23 (20.4%) patients reported ≥1 treatment emergent adverse event with UST and 30 (22.2%) with TNFi; 6 (5.3%) and 10 (7.4%) patients, respectively, discontinued treatment because of an adverse event.

Conclusion: In the Italian PsABio cohort, UST had better overall persistence compared with TNFi, as well as in specific subgroups: females, patients on monotherapy without methotrexate, with BMI <25 or >30 kg/m^2, and patients receiving UST as 2nd-line treatment. At 1 year, both treatments showed similar effectiveness, as measured by cDAPSA responses and MDA/VLDA achievement.

Acknowledgements: This study was funded by Janssen. Contributing author: Prof. Piercarlo Sarzi-Puttini, ASST Fatebenefratelli-Sacco, University of Milan, Italy

Disclosure of Interests: Elisa Gremese: None declared, Francesco Ciccia Speakers bureau: AbbVie, Abiogen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Roche, Consultant of: Celgene, Janssen, Lilly, Novartis, Pfizer, Roche, Grant/research support from: Celgene, Janssen, Novartis, Pfizer, Roche, Carlo Selmi Speakers bureau: AbbVie, Alfa-Wassermann, Amgen, Biogen, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme, Consultant of: AbbVie, Alfa-Wassermann, Amgen, Biogen, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Sanofi-Genzyme, Grant/research support from: AbbVie, Amgen, Janssen, Pfizer, Giovanna CUOMO: None declared, Rosario Foti Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Lilly, MSD, Janssen, Roche, Sanofi, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Lilly, MSD, Janssen, Roche, Sanofi, Marco Matucci Cerinic Speakers bureau: Actelion, Biogen, Janssen, Lilly, Consultant of: Chemomab, Grant/research support from: MSD, Fabrizio Conti Consultant of: AbbVie, Bristol-Myers Squibb, Galapagos, Lilly, Pfizer, Enrico Fusaro Speakers bureau: AbbVie, Amgen, Lilly, Grant/research support from: AbbVie, Pfizer, Giuliana Guggino Speakers bureau: AbbVie, Celgene, Novartis, Pfizer, Sandoz, Grant/research support from: Celgene, Pfizer, Florenzo Iannone Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Lilly, MSD, Novartis, Pfizer, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Lilly, MSD, Novartis, Pfizer, Sanofi, UCB, Andrea Delle Sedie: None declared, Roberto Perricone: None declared, Luca Idolazzi Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Sandoz, Paolo Moscato: None declared, Elke Theander Employee of: Janssen, Wim Noel Employee of: Janssen, Paul Bergmans Shareholder of: Johnson & Johnson, Employee of: Janssen, Silvia Marelli Employee of: Janssen, Laure Gossec Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Biogen, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Samsung Bioepis, Sanofi-Aventis, UCB, Grant/research support from: Amgen, Galapagos, Janssen, Lilly, Pfizer, Sandoz, Sanofi, Josef S. Smolen Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO, Janssen, Lilly, MSD, Novartis- Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Grant/research support from: AbbVie, AstraZeneca, Lilly, Novartis, Roche.

DOI: 10.1136/annrheumdis-2021-eular.81

POS1022

BIMEKIZUMAB SAFETY AND EFFICACY IN PATIENTS WITH PSORIATIC ARTHRITIS: 3-YEAR RESULTS FROM A PHASE 2B OPEN-LABEL EXTENSION STUDY

L. C. Coates[1], R. B. Warren[2], C. T. Ritchlin[3], L. Gossec[4], J. F. Merola[5], D. Assudani[6], J. Coarse[7], J. Eells[6], B. Ink[6], I. Mcinnes[8]. [1]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Diseases, Oxford, United Kingdom*; [2]*The University of Manchester, Dermatology Centre, Manchester NIHR Biomedical Research Centre, Manchester, United Kingdom*; [3]*University of Rochester, Medical Center, Rochester, United States of America*; [4]*Sorbonne Université and Pitié-Salpêtrière Hospital, Department of Rheumatology, Paris, France*; [5]*Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America*; [6]*UCB Pharma, N/A, Slough, United Kingdom*; [7]*UCB Pharma, N/A, Raleigh, United States of America*; [8]*University of Glasgow, School of Medicine, Glasgow, United Kingdom*

Background: Bimekizumab (BKZ), a monoclonal antibody inhibitor of interleukin (IL)-17A and IL-17F, demonstrated clinical improvements in joint and skin outcomes up to 108 weeks (wks) in patients (pts) with active psoriatic arthritis (PsA).[1,2]

Objectives: To report up to 3-year safety and efficacy of BKZ in pts with active PsA from a 48-week phase 2b dose-ranging study (BE ACTIVE; NCT02969525) and its open-label extension (OLE; NCT03347110).

Methods: BE ACTIVE and OLE study design has been described previously.[1] All OLE pts received BKZ 160 mg Q4W, irrespective of prior dosing regimen. Treatment-emergent adverse events (TEAEs) are reported for the safety set (SS; pts who received ≥1 dose BKZ in the dose-ranging study). Data are presented from dose-ranging study baseline (BL) to Wk 152. Efficacy outcomes are reported for the full analysis set (FAS): ACR50, minimal or very low disease activity (MDA/VLDA), Psoriasis Area and Severity Index (PASI) 90/100, body surface area affected by psoriasis (BSA) 0% and dactylitis/enthesitis resolution.

Results: Over 152 wks, the exposure-adjusted incidence rate (EAIR) per 100 patient-years (PY) was 126.4 for all TEAEs, 4.1 for serious TEAEs, 0.7 for serious infections and 4.6 for *Candida* infections (Table 1). One event was adjudicated by an independent committee as inflammatory bowel disease (microscopic colitis). All *Candida* infections were localised, mild/moderate, and resolved with appropriate anti-fungal therapy. Overall, the proportions of patients with ACR50 response were sustained through Wk 152 (52.9%, non-responder imputation [NRI]; Figure 1). Response rates were also sustained through Wk 152 for MDA (51.5%), VLDA (30.1%), PASI90 (64.2%), PASI100 (57.7%) and resolution of dactylitis (71.2%) and enthesitis (62.6%) (NRI; Table 1).

Table 1. Safety and efficacy outcomes up to 3 years

Safety (SS) n (%) [EAIR/100 PY]	BKZ 160 mg [a] (n=126)		BKZ 320 mg [b] (n=78)		Total (N=206)	
Any TEAE	114 (90.5) [136.1]		70 (89.7) [113.3]		184 (89.3) [126.4]	
Serious TEAEs	17 (13.5) [5.2]		5 (6.4) [2.3]		22 (10.7) [4.1]	
Key TEAEs of special monitoring						
Serious infections	3 (2.4) [0.9]		1 (1.3) [0.5]		4 (1.9) [0.7]	
Candida infections	15 (11.9) [4.7]		9 (11.5) [4.4]		24 (11.7) [4.6]	
Inflammatory bowel disease [c]	1 (0.8) [0.3]		0		1 (0.5) [0.2]	
Malignancies [d]	1 (0.8) [0.3]		0		1 (0.5) [0.2]	
Injection site reactions	0		3 (3.8) [1.4]		3 (1.5) [0.5]	
Suicidal ideation	1 (0.8) [0.3]		0		1 (0.5) [0.2]	
Liver function analyses	13 (10.3) [4.1]		11 (14.1) [5.3]		24 (11.7) [4.6]	
Study discontinuation due to TEAEs	12 (9.5) [3.5]		4 (5.1) [1.8]		16 (7.8) [2.8]	
Efficacy (FAS)	BKZ 160 mg [a]		BKZ 320 mg [b]		Total (N=206)	
n (%)	(n=124)		(n=82)			
	OC	NRI, %	OC	NRI, %	OC	NRI, %
MDA, Wk 152	64/95 (67.4)	51.6	42/62 (67.7)	51.2	106/157 (67.5)	51.5
VLDA, Wk 152	41/95 (43.2)	33.1	21/62 (33.9)	25.6	62/157 (39.5)	30.1
PASI90 [e] Wk 152	51/61 (83.6)	64.6	37/46 (80.4)	63.8	88/107 (82.2)	64.2
PASI100 [e] Wk 152	47/61 (77.0)	59.5	32/46 (69.6)	55.2	79/107 (73.8)	57.7
BSA 0% [e] Wk 48	48/72 (66.7)	60.8	38/55 (69.1)	65.5	86/127 (67.7)	62.8
Wk 152	46/61 (75.4)	58.2	31/45 (68.9)	53.4	77/106 (72.6)	56.2
Dactylitis [f]/Enthesitis [g] resolution, Wk 48	–	70.6/56.9	–	84.0/57.1	–	76.3/57.0
Wk 152	–	67.6/63.1	–	76.0/61.9	–	71.2/62.6

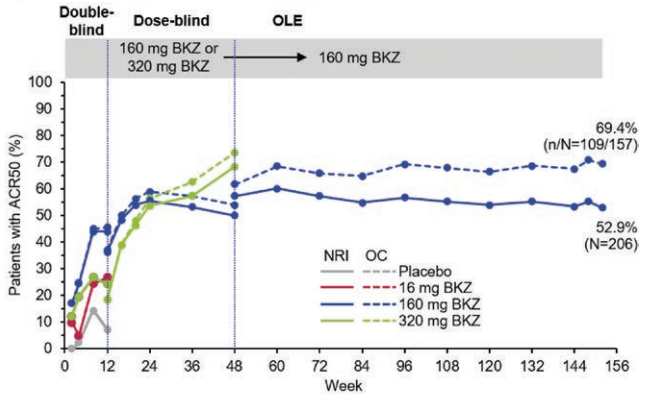
No anaphylactic reactions or major adverse cardiac events were reported. [a] Includes pts within the indicated analysis set originally assigned to all arms who were subsequently re-randomized to 160 mg, or [b] 320 mg, after double-blind period; [c] Microscopic colitis; [d] Malignant melanoma in situ; [e] Pts with BL BSA ≥3%, NRI: n=79, 58, 137 respectively; [f] Pts with BL LDI >0, NRI: n=34, 25, 59 respectively; [g] Pts with BL MASES >0, NRI: n=65, 42, 107 respectively. LDI: Leeds Dactylitis Index; MASES: Maastricht AS Enthesitis Score; OC: observed case.

Conclusion: The safety profile of BKZ in pts with PsA reflects previous observations[1,2] for up to 3 years. High threshold disease control was achieved by >50% of BKZ-treated pts up to 3 years, reflected in long-term improvements in joint and skin outcomes.

REFERENCES:

[1] Ritchlin CT. Lancet 2020;395:427–40;
[2] McInnes I. Ann Rheum Dis 2020;79:1153–4.

Figure. ACR50 responders up to 3 years



NRI and OC data shown for all timepoints from BL to Wk 152; pts randomised to placebo and 16 mg shown through double-blind period; pts re-randomised at start of dose-blind period to either 160 mg or 320 mg BKZ; 190/206 (92.2%) patients randomised at BE ACTIVE study baseline completed Week 48. At Week 48, 181/206 (FAS; 87.9%) patients entered the OLE; 157 patients had an efficacy assessment at Week 152; all OLE pts received 160 mg BKZ regardless of prior dosing regimen.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical.

Disclosure of Interests: Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Gilead, GSK, Janssen, Lilly, Medac, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celgene, Domain, Gilead, Janssen, Lilly, Grant/research support from: AbbVie, Amgen, Celgene, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB Pharma, Richard B. Warren Consultant of: AbbVie, Almirall, Amgen, Arena, Avillion, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, UCB Pharma, Grant/research support from: AbbVie, Almirall, Amgen, Janssen, LEO Pharma, Novartis, UCB Pharma, Christopher T. Ritchlin Consultant of: Amgen, AbbVie, Lilly, Pfizer, Novartis, Gilead, Janssen, UCB Pharma, Grant/research support from: AbbVie, Amgen, UCB Pharma, Laure Gossec Speakers bureau: AbbVie, Amgen, Biogen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Samsung, Sanofi, UCB Pharma, Consultant of: AbbVie, Amgen, Biogen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Samsung, Sanofi, UCB Pharma, Grant/research support from: Eli Lilly, Pfizer, Sandoz, Joseph F. Merola Consultant of: AbbVie, Amgen, Bayer, Biogen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Sanofi-Regeneron, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Amgen, Bayer, Biogen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Sanofi-Regeneron, Pfizer, UCB Pharma, Principal investigator for Dermavant, LEO Pharma, UCB Pharma, Deepak Assudani Employee of: UCB Pharma, Jason Coarse Employee of: UCB Pharma, Jason Eells Shareholder of: UCB Pharma, Employee of: UCB Pharma, Barbara Ink Shareholder of: GSK, UCB Pharma, Employee of: UCB Pharma, Iain McInnes Consultant of: AbbVie, BMS, Boehringer Ingelheim, Celgene, Lilly, Janssen, Novartis, UCB Pharma, Grant/research support from: BMS, Boehringer Ingelheim, Celgene, Janssen, UCB Pharma.

DOI: 10.1136/annrheumdis-2021-eular.124

POS1023 HOW DOES GENDER AFFECT SECUKINUMAB TREATMENT OUTCOMES AND RETENTION RATES IN PATIENTS WITH PSORIATIC ARTHRITIS? – REAL WORLD DATA FROM THE GERMAN AQUILA STUDY

U. Kiltz[1], J. Brandt-Juergens[2], P. Kästner[3], E. Riechers[4], D. Peterlik[5], H. P. Tony[6]. *[1]Rheumazentrum Ruhrgebiet/Ruhr-Universität Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*; *[2]Rheumatologische Schwerpunktpraxis, Rheumatologische Schwerpunktpraxis, Berlin, Germany*; *[3]Ambulantes Rheumazentrum, Ambulantes Rheumazentrum, Erfurt, Germany*; *[4]Medizinische Hochschule Hannover, Klinik für Immunologie und Rheumatologie, Hannover, Germany*; *[5]Novartis Pharma GmbH, Immunology, Hepatology & Dermatology, Nürnberg, Germany*; *[6]Medizinische Klinik II, Universitätsklinik, Rheumatology/Immunology, Würzburg, Germany*

Background: Gender disparities in PsA can affect natural course of disease, clinical presentation and response to medication[1]. The German non-interventional study AQUILA provides real-world data on the influence of gender of patients with psoriatic arthritis (PsA) on therapeutic effectiveness and retention rate under treatment with secukinumab, a fully human monoclonal antibody that selectively inhibits interleukin-17A.

Objectives: The aim of this interim analysis is to describe selected baseline (BL) demographics, to evaluate secukinumab treatment outcomes on disease activity, depressive mood and retention rate depending on the gender of PsA patients.

Methods: AQUILA is an ongoing, multi-center study including more than 3000 patients with active PsA or ankylosing spondylitis. Patients were observed from BL up to week (w) 52. Real-world data was assessed prospectively and analyzed as observed. Data was collected on impact of disease (Psoriatic Arthritis Impact of Disease - 12 items, PsAID-12 score), skin disease activity (Psoriasis Area and Severity Index, PASI), joint counts and severity of depressive mood (Beck´s Depression Inventory version II, BDI-II), in addition to patient´s global assessment (PGA). Moreover, retention rates (time from study inclusion until premature secukinumab treatment discontinuation) were assessed through Kaplan-Meier plots. This interim analysis focuses on the subgroups of male and female PsA patients.

Results: At BL, 1278 PsA patients were included: 41.5% (n=531) male and 58.5% (n=747) female. Demographic data (Table 1) of male and female PsA patients differed most obviously regarding proportion of overweight patients, smokers, pretreatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and biologicals/biosimilars (b-bsDMARDs).

Mean PsAID-12 values over time were higher in women; nevertheless, PsAID-12 improved comparably for both genders from BL to week 52 (♂: 4.8 at BL to 2.9 at w52, ♀: 5.3 at BL to 3.5 at w52, Figure 1A). This was similar to the course of improvements for mean PGA across genders (♂: 4.9 at BL to 3.0 at w52, ♀: 5.6 at BL to 3.5 at w52). In terms of PASI scores, both BL mean values and improvements over time were similar across genders (♂: 6.8 at BL to 1.9 at w52, ♀: 7.0 at BL to 1.0 at w52). Mean joint counts (tender/swollen) also improved similarly (♂: 6.8/3.7 at BL to 3.1/0.9 at w52, ♀: 7.3/3.7 at BL to 2.8/0.9 at w52). Over time, male patients showed overall reduced BDI-II values; nevertheless, BDI-II reductions were comparable across the genders (♂: 10.2 at BL to 8.1 at w52, ♀: 13.0 at BL to 10.6 at w52). Secukinumab treatment retention rate for men was (not significantly) higher than for women (Figure 1B).

Conclusion: In a real-world setting, secukinumab improved disease activity and depressive mood of PsA patients in both men and women. Women showed overall higher burden of disease. Altogether, this interim analysis shows that secukinumab is an effective treatment up to 52 weeks with high treatment retention rates in real-world setting, irrespective of gender.

REFERENCES:

[1] Eder, L., Chandran, V. & Gladman, D.D. *Int J Clin Rheumtol* **7**, 641-649 (2012).

Table 1. Overview of baseline characteristics in PsA patients depending on gender

Demographics*	Male (N=531)	Female (N=747)
Age, years	51.9 (11.6)	53.1 (11.2)
BMI, kg/m^2	29.1 (4.9)	29.0 (6.4)
BMI >25 to ≤30 kg/m^2, n (%)	219 (42.8)	211 (29.5)
BMI >30 kg/m^2, n (%)	188 (36.7)	285 (39.8)
Smoker, n (%)	103 (19.4)	196 (26.2)
PsAID-12	4.8 (2.2)	5.3 (2.2)
PGA	4.9 (2.6)	5.6 (2.4)
PASI	6.8 (9.8)	7.0 (11.1)
Tender joint counts	6.8 (7.9)	7.3 (7.4)
Swollen joint counts	3.7 (5.3)	3.7 (5.0)
BDI-II	10.2 (8.8)	13.0 (9.4)
Medication prior to secukinumab initiation, n (%):		
NSAID	290 (54.6)	467 (62.5)
csDMARD	460 (86.6)	678 (90.8)
b-bsDMARD	299 (56.3)	477 (63.9)

*variables given as mean (SD)

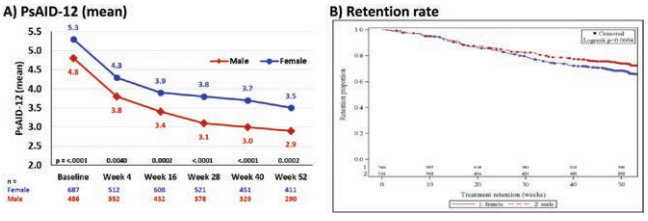


Figure 1. Impact of disease and treatment retention in PsA patients stratified by gender A) PsAID-12 (mean) B) Retention rate

Note: P-values are of exploratory nature

Disclosure of Interests: Uta Kiltz Consultant of: AbbVie, Biocad, Chugai, Eli Lilly, Gruenenthal, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Grant/research support from: AbbVie, Biogen, Novartis, Pfizer, Jan Brandt-Juergens Consultant of: Abbvie, Affibody, BMS, Gilead, Janssen, Lilly, Medac, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, Peter Kästner Consultant of: Chugai, Novartis, Elke Riechers Consultant of: AbbVie, Chugai, Novartis, UCB, Grant/research support from: AbbVie, Chugai, Lilly, Janssen, Novartis, Pfizer, Roche, UCB, Daniel Peterlik Employee of: Novartis Pharma GmbH, Hans-Peter Tony Consultant of: AbbVie, Astra-Zeneca, BMS, Chugai, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi.
DOI: 10.1136/annrheumdis-2021-eular.142

POS1024

GUSELKUMAB PROVIDES SUSTAINED DOMAIN-SPECIFIC AND COMPREHENSIVE EFFICACY AS ASSESSED USING COMPOSITE ENDPOINTS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

L. C. Coates[1], C. T. Ritchlin[2], L. Gossec[3], P. Helliwell[4], P. Rahman[5], E. C. Hsia[6,7], A. Kollmeier[8], X. L. Xu[8], C. Karyekar[9], M. Shawi[9], W. Noel[10], Y. Jiang[11], S. Sheng[11], Y. Wang[11], P. J. Mease[12]. *[1]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; *[2]University of Rochester Medical Center, Department of Medicine, Allergy/Immunology and Rheumatology, Rochester, United States of America*; *[3]Sorbonne Université, Rheumatology, Paris, France*; *[4]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[5]Memorial University of Newfoundland, Craig L Dobbin Genetics Research Centre, St. John's, Canada*; *[6]Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; *[7]University Pennsylvania Medical Center, Rheumatology, Philadelphia, United States of America*; *[8]Janssen Research & Development, LLC, Immunology, La Jolla, United States of America*; *[9]Janssen Global Services, LLC, Immunology, Horsham, United States of America*; *[10]Janssen Scientific Affairs, LLC, Immunology, Brussels, Belgium*; *[11]Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; *[12]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America*

Background: Guselkumab (GUS) is a human monoclonal antibody specific to the p19-subunit of interleukin-23. GUS significantly improved signs and symptoms of PsA through Week24 (Wk24), and improvements were maintained through Wk52 in the Phase 3 DISCOVER-1[1] and DISCOVER-2[2] studies.
Objectives: Assess GUS efficacy through Wk52 in both studies utilizing composite indices.
Methods: Adult patients (pts) enrolled had active PsA despite standard therapies. Pts in DISCOVER-1 had ≥3 swollen and ≥3 tender joints and C-reactive protein (CRP) ≥0.3 mg/dL; in DISCOVER-2, pts had ≥5 swollen and ≥5 tender joints and CRP ≥0.6 mg/dL. 31% of DISCOVER-1 pts received 1-2 prior tumor necrosis factor inhibitors; DISCOVER-2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Wk0, Wk4, then every 8 weeks (Q8W); or placebo (PBO); PBO pts crossed over to GUS 100 mg Q4W at Wk24. Composite endpoints pooled across the two studies were: Disease Activity Index for Psoriatic Arthritis (DAPSA), Psoriatic Arthritis Disease Activity Score (PASDAS), Minimal Disease Activity (MDA), and Very Low Disease Activity (VLDA). GUS vs PBO comparisons through Wk24 employed a Cochran-Mantel-Haenszel test with baseline stratification factors or Fisher's exact test; no treatment group comparisons were performed beyond Wk24. P-values were not adjusted for multiplicity. From Wk24 -Wk52, pts with missing data were considered nonresponders (>90% of pts completed study treatment through Wk52).
Results: In randomized and treated pts from DISCOVER-1 (N=381) and DISCOVER-2 (N=739), pooled baseline characteristics were generally well-balanced across treatment groups and reflected active disease. Differences in response rates between GUS Q4W or Q8W and PBO were seen as early as Wk8 and increased over time through Wk24. In pts continuing GUS Q4W or Q8W, respectively, post-Wk24 response rates associated with these composite indices continued to increase through Wk52, at which time they were 54.2% and 52.5% for DAPSA LDA, 45.3% and 41.9% for PASDAS LDA, 35.9% and 30.7% for MDA, 18.2% and 17.6% for DAPSA remission, and 13.1% and 14.4% for VLDA, with no discernable difference between the GUS Q4W and Q8W dosing regimens (Table 1 and Figure 1). After PBO pts crossed over to GUS Q4W at Wk24, response rates increased through Wk52.
Conclusion: GUS 100 mg Q4W and Q8W provided robust and sustained benefits to pts with active PsA across multiple domains, indicating that GUS may provide an alternative treatment option for the diverse manifestations of PsA.

REFERENCES:

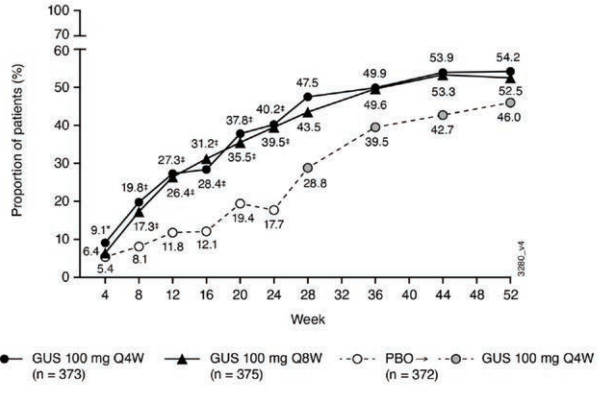
[1] Ritchlin CR et al. RMD Open 2021; 1–11. doi: rmdopen-2020-001457
[2] McInnes IB, et al. Arthritis Rheumatol 2020 Oct 11. doi: 10.1002/art.41553.

Table 1. Pooled response rates for DISCOVER-1 and DISCOVER-2 randomized and treated patients.

	DISCOVER-1&2		
	GUS Q4W	GUS Q8W	PBO --> GUS Q4W[1]
Randomized and treated patients, n	373	375	372
PASDAS[2] LDA			
Wk 24	27.9%**	30.1%**	8.9%
Wk 52	45.3%	41.9%	36.8%
MDA[3]			
Wk 24	22.8%**	24.3%**	7.8%
Wk 52	35.9%	30.7%	28.2%
DAPSA[4] Remission			
Wk 24	10.2%**	8.3%**	2.2%
Wk 52	18.2%	17.6%	11.0%
VLDA[3]			
Wk 24	6.4%**	4.3%*	1.3%
Wk 52	13.1%	14.4%	8.3%

Data reported as proportions of patients, %. Unadjusted p values at Wk24 vs PBO: *p<0.05; **p<0.001.
[1] Pts randomized to PBO crossed over to GUS Q4W at Wk24.
[2] PASDAS is derived from Pt global assessment of arthritis and psoriasis (0-100), Physician global assessment (0-100), swollen joint count (0-66), tender joint count (0-68), CRP (mg/L), Leeds enthesitis index score, tender dactylitis count, and the 36-item Short-Form Health Survey Physical Component Summary score. PASDAS LDA ≤3.2.
[3] MDA is 5/7 criteria met; VLDA is 7/7 criteria met: tender joint count ≤1, swollen joint count ≤1, Psoriasis Activity and Severity Index ≤1, Pt assessment of pain ≤15 (0-100), Pt global assessment of disease activity ≤20 (0-100), Health Assessment Questionnaire-Disability Index score ≤0.5, Tender entheseal points ≤1.
[4] DAPSA Remission: score ≤4 (definition in Figure 1 legend).

Figure. Proportions of Pooled DISCOVER-1 and DISCOVER-2 Patients Achieving DAPSA LDA[a] Through Week 52.



Missing data imputed as nonresponse.
*, +, ‡ p < 0.05, 0.01, 0.001, respectively, vs placebo. Unadjusted (nominal) p values are not controlled for multiplicity and are descriptive/supportive only; no statistical significance should be implied.
a The DAPSA score is derived from tender joint count (0–68), swollen joint count (0–66), CRP (mg/dL), patient assessment of pain (0–10 cm VAS), and patient global assessment of disease activity (arthritis, 0–10 cm VAS). DAPSA LDA: ≤14. DAPSA Remission: ≤4.

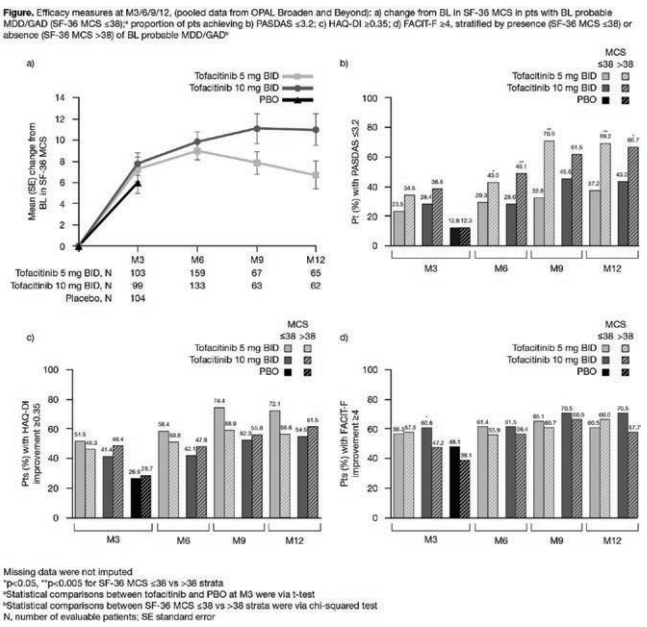
Disclosure of Interests: Laura C Coates Consultant of: AbbVie, Amgen, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Domain, Eli Lilly, Gilead, Janssen, Medac, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Novartis, Pfizer, Christopher T. Ritchlin Consultant of: Amgen, AbbVie, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, and UCB, Laure Gossec Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Biogen, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Samsung Bioepis, Sanofi-Aventis, and UCB., Grant/research support from: Amgen, Eli Lilly, Galapagos, Janssen, Pfizer, Sandoz, and Sanofi, Philip Helliwell Consultant of: Galapagos, Janssen, and Novartis, Grant/research support from: AbbVie, Janssen, Pfizer, Proton Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis,

Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Chetan Karyekar Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Wim Noel Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Yusang Jiang Employee of: Cytel, Inc. providing statistical support (funded by Janssen), Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Yanli Wang Employee of: IQVIA providing statistical support (funded by Janssen), Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.167

POS1025 TOFACITINIB TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS AND PROBABLE DEPRESSION AND/OR ANXIETY: A POST HOC ANALYSIS OF TWO PHASE 3 CLINICAL TRIALS

L. Gossec[1], G. Citera[2], A. Sellas-Fernández[3], D. C. Gruben[4], M. Valderrama[5], S. Gómez[5]. [1]*Sorbonne Université/Hôpital Pitié-Salpêtrière, Paris, France*; [2]*Instituto de Rehabilitación Psicofísica, Section of Rheumatology, Buenos Aires, Argentina*; [3]*University Hospital Vall d'Hebron, Secció de Reumatologia, Barcelona, Spain*; [4]*Pfizer Inc, Inflammation and Immunology, Groton, CT, United States of America*; [5]*Pfizer Inc, Inflammation and Immunology, Madrid, Spain*

Background: Depression and anxiety are highly prevalent in patients (pts) with psoriatic arthritis (PsA),[1] with inflammation a key pathogenic feature of depression in these pts.[2] Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. It acts by modulating immune and inflammatory responses. The link between major depressive disorder/generalised anxiety disorder (MDD/GAD), inflammation and tofacitinib effectiveness has not been fully explored.
Objectives: Analyse the prevalence of probable MDD/GAD in pts with PsA initiating tofacitinib treatment and the impact of baseline (BL) probable MDD/GAD status on tofacitinib efficacy in these pts.
Methods: This was a post hoc analysis of data from pts who received tofacitinib 5 or 10 mg twice daily (BID), or placebo (PBO), pooled from two Phase 3 trials (12-month OPAL Broaden [NCT01877668];[3] 6-month OPAL Beyond [NCT01882439][4]). Pts with BL probable MDD and/or GAD were identified by a Short Form-36 Health Survey (SF-36) Mental Component Summary score (MCS) ≤38. Pt demographics/BL characteristics and outcomes were stratified by the presence (SF-36 MCS ≤38) or absence (SF-36 MCS >38) of BL probable MDD/GAD. At Months (M)3/6/9/12, changes from BL in SF-36 MCS were evaluated, and efficacy assessed by the proportions of pts who achieved: Psoriatic Arthritis Disease Activity Score (PASDAS) ≤3.2, Health Assessment Questionnaire-Disability Index (HAQ-DI) improvement ≥0.35 and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) improvement ≥4. BL global pain was measured via visual analogue scale.
Results: Of the 706 pts included in this analysis, BL probable MDD/GAD was identified in 46.2%, 44.9% and 46.2% of pts in the tofacitinib 5 mg BID (108/234), tofacitinib 10 mg BID (106/236) and PBO (109/236) groups, respectively. BL disease activity was similar across the three treatment groups, independent of probable MDD/GAD status (mean PASDAS: 6.1–6.4 in pts with vs 5.8–6.1 in pts without probable MDD/GAD). In the tofacitinib 5 mg BID group, mean BL scores for HAQ-DI (1.4 vs 1.0), FACIT-F total score (20.5 vs 32.4) and global pain (61.3 vs 51.5) indicated worse disability, fatigue and pain, respectively, for pts with vs without BL probable MDD/GAD. Similar findings were seen in the tofacitinib 10 mg BID and PBO groups. At M3, improvements from BL in SF-36 MCS in pts with probable MDD/GAD were numerically, but not significantly, greater with tofacitinib 5 and 10 mg BID vs PBO, and these changes were largely sustained to M12 (Figure 1a). At M3, numerically greater proportions of pts achieved improvements in PASDAS, HAQ-DI and FACIT-F with tofacitinib 5 or 10 mg BID vs PBO, regardless of BL probable MDD/GAD status (Figure 1b–d). Through M3–12, the proportions of pts who achieved PASDAS ≤3.2 with tofacitinib 5 or 10 mg BID were generally significantly greater in pts without vs with probable MDD/GAD (Figure 1b). At all timepoints, rates of improvement in HAQ-DI with tofacitinib 5 mg BID were numerically greater in pts with vs without probable MDD/GAD, whereas the opposite was true for tofacitinib 10 mg BID (Figure 1c). FACIT-F improvement rates with tofacitinib 10 mg BID were consistently numerically greater in pts with vs without probable MDD/GAD, while findings were mixed for tofacitinib 5 mg BID (Figure 1d).



Missing data were not imputed
*p<0.05, **p<0.005 for SF-36 MCS ≤38 vs >38 strata
[a]Statistical comparisons between tofacitinib and PBO at M3 were via t-test
[b]Statistical comparisons between SF-36 MCS ≤38 vs >38 strata were via chi-squared test
N, number of evaluable patients; SE standard error

Conclusion: Around 46% of pts with PsA treated with tofacitinib had BL probable MDD/GAD (SF-36 MCS ≤38). Pts with BL probable MDD/GAD treated with tofacitinib had sustained changes in SF-36 MCS. Rates of clinical improvement with tofacitinib were generally greater in pts without vs with probable MDD/GAD, whereas findings for disability and fatigue improvements varied between tofacitinib doses. Further research is required to evaluate the relationship between PsA and depression, to improve treatment targets and the quality of life of pts with PsA.

REFERENCES:

[1] Zhao et al. Clin Rheumatol 2020; 39: 217-225.
[2] Mathew & Chandran. Rheumatol Ther 2020; 7: 287-300.
[3] Mease et al. N Engl J Med 2017; 377: 1537-1550.
[4] Gladman et al. N Engl J Med 2017; 377: 1525-1536.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Emma Deeks, CMC Connect, and funded by Pfizer Inc.
Disclosure of Interests: Laure Gossec Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer Inc, Roche, UCB, Gustavo Citera Consultant of: AbbVie, Amgen, Eli Lilly, Gema, Genzyme, Novartis, Pfizer Inc, Sanofi Genzyme, Grant/research support from: AbbVie, Amgen, Eli Lilly, Gema, Genzyme, Novartis, Pfizer Inc, Sanofi Genzyme, Agustí Sellas-Fernández: None declared, David C Gruben Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Monica Valderrama Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Susana Gómez Shareholder of: Pfizer Inc, Employee of: Pfizer Inc.
DOI: 10.1136/annrheumdis-2021-eular.176

POS1026 GUSELKUMAB PROVIDES SUSTAINED IMPROVEMENTS IN WORK PRODUCTIVITY AND NON-WORK ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS THROUGH 1 YEAR OF A PHASE 3 TRIAL

J. Curtis[1], I. Mcinnes[2], S. Peterson[3], P. Agarwal[4], F. Yang[3], A. Kollmeier[5], E. C. Hsia[6,7], C. Han[6], W. Tillett[8], P. J. Mease[9], P. Rahman[10]. [1]*University of Alabama at Birmingham, Department of Medicine, Immunology and Rheumatology, Birmingham, United States of America*; [2]*University of Glasgow, Institute of Infection, Immunity & Inflammation, Glasgow, United States of America*; [3]*Janssen Global Services, LLC, Immunology, Horsham, United States of America*; [4]*Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; [5]*Janssen Research & Development, LLC, Immunology, San Diego, United States of America*; [6]*Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; [7]*University of Pennsylvania Medical Center, Rheumatology, Philadelphia, United States of America*; [8]*Royal National Hospital for Rheumatic Diseases, Department of Pharmacy & Pharmacology Centre for Therapeutic Innovation, Bath, United Kingdom*; [9]*Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Rheumatology Research, Seattle, United States of America*; [10]*Memorial University of Newfoundland, Craig L Dobbin Genetics Research Centre, St. John's, Canada*

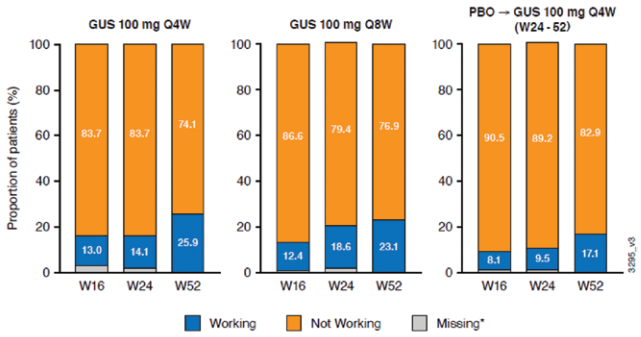
Background: DISCOVER-2 was a Phase 3 trial of the first-in-class anti-IL-23-specific mAb guselkumab (GUS) in patients (pts) with psoriatic arthritis (PsA). PsA impacts patients' productivity at work and in daily activity.1
Objectives: To evaluate the effect of GUS on work productivity and daily activity in DISCOVER-2 through 1 year using the Work Productivity and Activity Impairment Questionnaire: PsA (WPAI- PsA).
Methods: Bio-naïve adults with active PsA despite nonbiologic DMARDs &/or NSAIDs received subcutaneous GUS 100 mg every 4 weeks (Q4W); GUS 100 mg W0, W4, then Q8W; or placebo (PBO). At W24, PBO pts crossed over to GUS 100 mg Q4W. WPAI-PsA assesses PsA-related work time missed (absenteeism), impairment while working (presenteeism), impaired overall work productivity (absenteeism + presenteeism), and daily activity during the previous week. A shift analysis evaluated proportions of pts employed vs unemployed (regardless of desire to work) over time. Among pts working at baseline, least-squares (LS) mean changes from baseline in WPAI-PsA domains were determined using a mixed-effects model for repeated measures analysis, whereby mean changes in WPAI-PsA domains were calculated for each multiple imputation (MI) dataset using an analysis of covariance (ANCOVA); the reported LSmean is the average of all MI datasets. Also, among pts employed at baseline, indirect savings from improved overall work productivity were estimated using 2020 EU mean yearly wage estimate (all occupations).2
Results: In pts working at baseline, significant improvement in work productivity and non-work activity vs PBO was observed at W24. Productivity gains seen with GUS at W24 continued to improve through 1 year (Table 1). Shift analysis showed relatively stable employment in pts employed at baseline (62% of shift analysis cohort) through 1 year of GUS (>91% continued to work when assessed at W16, W24, and W52 [data not shown]). For those unemployed at baseline (38% of cohort), the proportion of pts working increased by ~10% following 1 year of GUS (Figure 1). Potential yearly indirect savings from improved overall work productivity were: *€7409* GUS Q4W and *€7039* GUS Q8W vs *€4075* PBO at W24 and were *€8520* GUS Q4W, *€9632* GUS Q8W, and *€6668* PBO→GUS Q4W at W52.
Conclusion: Improvement in work productivity and non-work activity was greater with GUS vs PBO among pts with active PsA through W52. Improvements demonstrated may result in reduction in PsA costs associated with work productivity.
REFERENCES:
[1] Tillett W et al. Rheumatol (Oxford). 2012;51:275–83.
[2] OECD (2020). Average wages (indicator). https://data.oecd.org/earnwage/average-wages.htm

Table 1. Model-based estimates of LSmean change[a] (95% CI) from baseline in WPAI-PsA domains among pts working at baseline and with an observed change through W24 (N=474) and W52 (N=475)

Change from baseline	GUS 100mg Q4W		GUS 100mg Q8W		PBO (W0-24)	PBO → GUS 100 mg Q4W (W24-52)
Visit	**W24**	**W52**	**W24**	**W52**	**W24**	**W52**
Absenteeism, N	145	145	147	147	162	163
LSmean	-3.4 (-6.5,-0.3)	-4.1 (-6.8,-1.5)	-3.0 (-6.0,0.1)	-4.0 (-6.6,-1.3)	-3.0 (-6.0, 0.04)	-3.0 (-5.5,-0.4)
Diff vs. PBO	-0.4 (-4.6,3.8)		-0.01 (-4.2, 4.2)			
Presenteeism, N	145	145	147	147	162	163
LSmean	-20.1 (-23.7,-16.6)	-22.4 (-26.3,-18.6)	-19.6 (-23.2,-16.1)	-25.7 (-29.5,-21.8)	-10.5 (-13.9,-7.0)	-18.5 (-22.2,-14.7)
Diff vs PBO	-9.7* (-14.4,-5.0)		-9.2* (-13.9,-4.5)			
Work productivity, N	145	145	147	147	162	163
LSmean	-20.1 (-24.1,-16.1)	-22.6 (-26.8,-18.3)	-19.2 (-23.1,-15.2)	-25.9 (-30.0,-21.7)	-10.6 (-14.4,-6.8)	-17.6 (-21.7,-13.6)
Diff vs PBO	-9.5* (-14.8,-4.2)		-8.6* (-13.9,-3.3)			
Non-work Activity, N	242	242	246	246	245	245
LSmean	-20.5 (-23.3,-17.7)	-25.7 (-28.6,-22.7)	-21.2 (-23.9,-18.4)	-25.4 (-28.4,-22.5)	-9.9 (-12.6,-7.1)	-22.3 (-25.3,-19.4)
Diff vs PBO	-10.6* (-14.4,-6.8)		-11.3* (-15.1,-7.5)			

CI=Confidence interval
a. LSmean for each MI dataset is calculated based on an ANCOVA model for the change from baseline at W24/W52. The combined LSmean, which is the average of the LSmean, taken over all the MI datasets, is presented.
*p<0.05

Figure. Shift Analysis of Working Status: Not Employed at Baseline



GUS 100 mg Q4W (N = 92), GUS 100 mg Q8W (N = 97), PBO → GUS 100 mg Q4W (W24-52) (N = 74)
* GUS 100 mg Q4W: W16, 3.3%; W24, 2.2%. GUS 100 mg Q8W: W16, 1.0%; W24, 2.1%. PBO → GUS 100 mg Q4W (W24-52): W16, 1.4%; W24, 1.4%.

Disclosure of Interests: Jeffrey Curtis Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, and UCB, Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Steve Peterson Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Prasheen Agarwal Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Feifei Yang Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Chenglong Han Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer Inc, and UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer Inc, and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, and UCB, Philip J Mease Speakers bureau: Boehringer Ingelheim and GlaxoSmithKline, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB, Proton Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis.
DOI: 10.1136/annrheumdis-2021-eular.244

POS1027

EFFICACY AND SAFETY OF GUSELKUMAB, A MONOCLONAL ANTIBODY SPECIFIC TO THE P19-SUBUNIT OF INTERLEUKIN-23, THROUGH 2 YEARS: RESULTS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY CONDUCTED IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

I. Mcinnes[1], P. Rahman[2], A. B. Gottlieb[3], E. C. Hsia[4,5], A. Kollmeier[4], X. L. Xu[4], S. Sheng[6], Y. Jiang[6], M. Shawi[7], S. D. Chakravarty[8,9], D. Van der Heijde[10], P. J. Mease[11]. [1]*University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; [2]*Memorial University of Newfoundland, Craig L Dobbin Genetics Research Centre, St. John's, Canada*; [3]*Icahn School of Medicine Mt. Sinai, Dermatology, New York, United States of America*; [4]*Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; [5]*University of Pennsylvania Medical Center, Rheumatology, Philadelphia, United States of America*; [6]*Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; [7]*Janssen Scientific Affairs, LLC, Immunology, Horsham, United States of America*; [8]*Janssen Scientific Affairs, LLC, Immunology, Horsham, United States of America*; [9]*Drexel University College of Medicine, Rheumatology, Philadelphia, United States of America*; [10]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [11]*Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America*

Background: Guselkumab (GUS), a selective IL-23 inhibitor dosed every 4 or 8 weeks (Q4W or Q8W), demonstrated efficacy for joint and skin symptoms, inhibition of structural damage progression (Q4W), and safety vs. placebo (PBO) through Week 24 (W24) of the Ph3, double-blind, PBO-controlled trial in biologic-naïve pts with PsA (DISCOVER-2).[1] Favorable benefit-risk was also seen through 1 year.[2]
Objectives: To assess GUS efficacy and safety through 2 years.

Methods: Biologic-naïve adults with active PsA (≥5 swollen joint count [SJC] + ≥5 tender joint count [TJC]; CRP ≥0.6 mg/dL) were randomized (1:1:1) to GUS 100 mg Q4W; GUS 100 mg at W0, W4, Q8W; or PBO with crossover to GUS 100 mg Q4W (PBO→Q4W) at W24. Clinical efficacy (ACR/PASI/IGA/HAQ-DI) was assessed in the modified intention to treat (mITT) population through W100 with missing data imputation (nonresponse for categorical endpoints; no change/multiple imputation for continuous endpoints). Observed PsA-modified van der Heijde Sharp (vdH-S) scores derived from blinded radiographic images collected at W0, W24, W52, W100 (or at discontinuation [d/c]) and adverse events (AEs) through W112 were collected.

Results: 712/739 (96%) randomized pts continued study agent at W24; 687/739 (93%) continued at W52; 652/739 (88%) completed W100. ACR20 response rates in the mITT population continued to increase after W24, and at W100 were 76% for Q4W and 74% for Q8W (Figure 1). Similar response patterns were seen for ACR50/70, HAQ-DI and PASI90/100 (Table 1), and IGA0/1 and PASI75 response rates were consistent through W100 in pts randomized to Q4W and Q8W; W100 data for PBO→Q4W pts were consistent with pts treated with Q4W and Q8W (Table 1). GUS improvements in SF-36 PCS/MCS at W52 also persisted through W100 (data not shown). Low rates of radiographic progression (as measured by PsA-modified vdH-S scores) were observed during W52-100 for Q4W (n=227; 0.75) and Q8W (n=232; 0.46). In the PBO→Q4W group (n=228), radiographic progression was 1.12 during W0-24 (while on PBO), 0.51 during W24-100 (while on Q4W), and 0.13 during W52-100. Through W112, the incidences of AEs, serious AEs (SAEs), AEs leading to d/c, infections, serious infections, and injection site reactions were generally consistent with the PBO-controlled period and through 1 year. Of the pts in the Q4W (n=245), Q8W (n=248), and PBO→Q4W (n=238) groups, 9%, 9% and 7% had ≥1 SAE; 2%, 3% and 3% had ≥1 serious infection; 2 Q8W pts (fungal esophagitis, disseminated herpes zoster) and 1 PBO→Q4W pt (listeria meningitis) had opportunistic infections; 1 PBO→Q4W pt died (road traffic accident); 1 PBO-randomized pt had IBD; no pt had anaphylactic or serum sickness reaction, or active TB.

Conclusion: In biologic-naïve PsA pts, GUS improvements in joint and skin symptoms, physical function, and low rates of radiographic progression persisted through 2 years. GUS safety in PsA through 2 years was comparable with safety at 6 months and 1 year, similar between Q4W and Q8W, and consistent with GUS safety in psoriasis.

REFERENCES:

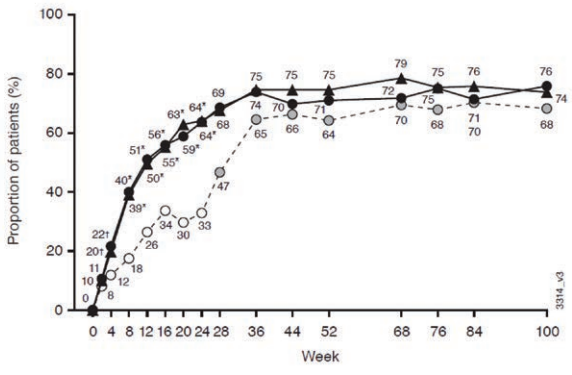
[1] Mease PJ. *Lancet*. 2020 Apr 4;395(10230):1126-1136. [2] McInnes IB. *Arthritis Rheumatol*. 2020 Oct 11. doi: 10.1002/art.41553.

Table 1. Efficacy Through W100 (NRI)

Data are %	GUS Q4W			GUS Q8W			PBO→GUS Q4W		
	W24	W52	W100	W24	W52	W100	W24	W52	W100
Analysis set, n		245			248			246	
ACR 50	**33**	**46**	**56**	**32**	**48**	**55**	**14**	**41**	**48**
ACR 70	**13**	**26**	**35**	**19**	**28**	**36**	**4**	**18**	**30**
BL HAQ-DI ≥0.35, n		228			228			236	
Improvement ≥0.35[a]	**56**	**59**	**63**	**50**	**58**	**64**	**31**	**48**	**56**
BL ≥3% BSA psoriasis + IGA ≥2, n		184			176			183	
IGA0/1	**69**	**63**	**62**	**71**	**58**	**55**	**19**	**63**	**67**
PASI75	**78**	**87**	**83**	**79**	**86**	**82**	**23**	**83**	**80**
PASI90	**61**	**77**	**74**	**69**	**74**	**70**	**10**	**72**	**77**
PASI100	**45**	**58**	**59**	**45**	**53**	**53**	**3**	**52**	**61**

BL, Baseline; BSA, Body surface area; HAQ-DI, Health assessment questionnaire disability index; IGA, Investigator global assessment; NRI, nonresponder imputation; PASI, Psoriasis area and severity index. [a]≥0.35 improvement among pts with HAQ-DI ≥0.35 at BL.

Figure. ACR 20 Response Through W100 (NRI)
(Note: Patients randomized to PBO crossed over to GUS 100 mg Q4W at W24)



Disclosure of Interests: Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Proton Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis, Alice B Gottlieb Consultant of: Avotres Therapeutics, Beiersdorf, Boehringer Ingelheim, Bristol-Myers Squibb Co, Incyte, Janssen, LEO Pharma, Eli Lilly, Novartis, Sun Pharmaceutical Industries Inc, UCB, and Xbiotech, Grant/research support from: Boehringer Ingelheim, Incyte, Janssen, Novartis, Sun Pharmaceuticals Industries Inc, UCB, and Xbiotech, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Yusang Jiang Employee of: Cytel, Inc. providing statistical support (funded by Janssen), May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Soumya D Chakravarty Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, LLC, Désirée van der Heijde Paid instructor for: Director of Imaging and Rheumatology BV, Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, and UCB, Philip J Mease Speakers bureau: Boehringer Ingelheim and GlaxoSmithKline, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.409

POS1028 PATIENT CHARACTERISTICS & CLINICAL FEATURES ASSOCIATE WITH HEALTH-RELATED QUALITY OF LIFE IN BIO-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS THROUGH WEEK 24 OF THE DISCOVER-2 STUDY

J. Curtis[1], I. Mcinnes[2], D. D. Gladman[3], F. Yang[4], S. Peterson[4], P. Agarwal[5], A. Kollmeier[6], E. C. Hsia[6,7], C. Han[6], M. Shawi[4], W. Tillett[8], P. J. Mease[9], P. Rahman[10]. *[1]University of Alabama at Birmingham, Department of Medicine, Immunology and Rheumatology, Birmingham, United States of America*; *[2]University of Glasgow, Institute of Infection, Immunity and Inflammation, Rheumatology, United Kingdom*; *[3]Centre for Prognosis in the Rheumatic Diseases, Toronto Western Hospital, Professor of Medicine, Toronto, Canada*; *[4]Janssen Global Services, LLC, Immunology, Horsham, United States of America*; *[5]Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; *[6]Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; *[7]University of Pennsylvania Medical Center, Rheumatology, Philadelphia, United States of America*; *[8]Royal National Hospital for Rheumatic Diseases, Department of Pharmacy & Pharmacology Centre for Therapeutic Innovation, Bath, United Kingdom*; *[9]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America*; *[10]Memorial University of Newfoundland, Craig L Dobbin Genetics Research Centre, St. John's, Canada*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by peripheral arthritis, axial inflammation, dactylitis, enthesitis, & skin/nail psoriasis. Patients (pts) with PsA often experience reduced health-related quality of life (HRQoL) due to these features.

Objectives: Using EuroQoL-5 dimension-5 level (EQ-5D-5L) questionnaire index & visual analog scale (EQ-VAS) scores, we assessed HRQoL in pts with PsA & its association with pt characteristics & clinical features of PsA, including fatigue.

Methods: The Phase 3 DISCOVER-2 trial evaluated guselkumab (GUS), a human monoclonal antibody targeting the IL-23p19-subunit, in bio-naïve adults with active PsA (swollen joint count [SJC] ≥5, tender joint count [TJC] ≥5, C-reactive protein [CRP] ≥0.6 mg/dL) despite standard therapies.[1] Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Week 0 (W0), W4, then Q8W; or placebo (PBO). EQ-5D-5L index assesses mobility, self-care, usual activities, pain/discomfort, & anxiety/depression. EQ-VAS assesses pt health state. Spearman correlation testing was used to evaluate relationships between baseline (BL) pt characteristics & PsA clinical features & BL EQ-5D-5L index & EQ-VAS scores (Figure 1). Employing absolute observed scores at both W0 & W24, univariate linear regression was used to assess the association between EQ-5D-5L index & EQ-VAS scores & pt characteristics/PsA clinical features. Variables with $p<0.20$ in the univariate analysis were included in a multivariate analysis employing mixed-effect model for repeated measures (MMRM), controlling for all other variables; resulting p values <0.05 were considered statistically significant. Least-squares (LS) mean changes in EQ-5D-5L index & EQ-VAS were assessed at W24 using MMRM.

Results: Among 738 pts, BL EQ-5D-5L index & EQ-VAS scores were moderately to strongly correlated (ie, ≥0.4) with BL pt-reported pain (0-10 VAS), physical function (Health Assessment Questionnaire-Disability Index [HAQ-DI]),

fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F] scale), & 36-item Short Form Health Survey (SF-36) physical & mental component summary (PCS & MCS) scores & weakly correlated with other variables (Figure 1). Based on univariate analyses (p<0.20) & evaluation of collinearity between variables, attributes at W0 & W24 included in the multivariate models were age, sex, CRP, FACIT-F, pain, psoriasis area & severity index (PASI) score, TJC, SJC, enthesitis, & dactylitis. In the final model, CRP, FACIT-F, pain, PASI score, & the presence of dactylitis were significantly associated with EQ-5D-5L index & EQ-VAS scores. A higher TJC was significantly associated with a worse EQ-5D-5L index score. A higher SJC was significantly associated with a worse EQ-VAS score (Table 1). For reference, in the GUS Q4W (N=244), GUS Q8W (N=246), & PBO (N=244) groups, the LS mean changes from baseline at W24 were 0.12, 0.12, & 0.05, respectively, for EQ-5D-5L index & 18.1, 18.4, & 6.8, respectively, for EQ-VAS.

Conclusion: Joint & skin symptoms, dactylitis, fatigue, pain, & elevated levels of CRP were significantly associated with reduced HRQoL (measured by EQ-5D-5L index & EQ-VAS) in bio-naïve pts with active PsA. Treatment of multiple PsA domains may help optimize HRQoL. Improvement across clinical domains[1] & in HRQoL has been observed in GUS-treated pts with PsA.

REFERENCES:

[1] Mease P, et al. Lancet 2020;395:1126-36.

Figure. Spearman correlations between BL pt characteristics/clinical features & BL EQ-5D-5L index & EQ-VAS scores at W0

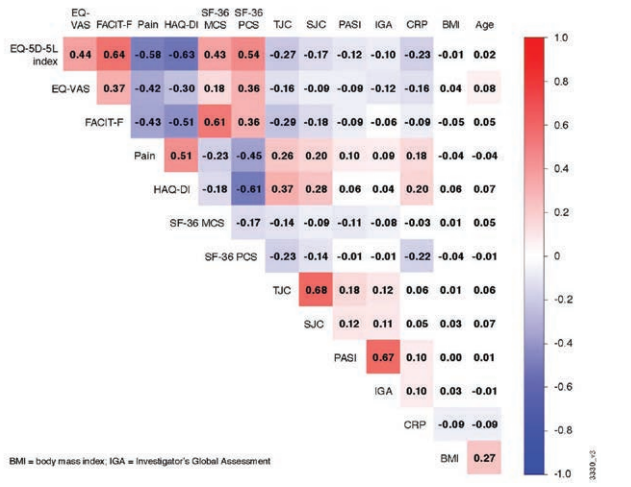


Table 1. Multivariate analysis of pt characteristics/clinical features & EQ-5D-5L index & EQ-VAS scores at W0 & W24

Parameter	EQ-5D-5L Index		EQ-VAS	
	Estimate	p value	Estimate	p value
Age (y)	-0.0001	0.69	0.06	0.12
Female	-0.003	0.53	1.11	0.20
CRP (mg/dL)	-0.005	**<0.001**	-0.51	**0.007**
FACIT-F (0-52)	0.007	**<0.001**	0.57	**<0.001**
Pain (0-10)	-0.02	**<0.001**	-3.47	**<0.001**
PASI (0-72)	-0.001	**0.03**	-0.17	**<0.001**
SJC (0-66)	-0.001	0.21	-0.17	**0.02**
TJC (0-68)	-0.001	**0.04**	-0.04	0.41
Dactylitis (Y/N)	0.01	**0.02**	1.74	0.49
Enthesitis (Y/N)	-0.004	0.33	-0.98	0.22

Disclosure of Interests: Jeffrey Curtis Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Eli Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Eli Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, Iain McInnes Consultant of: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, and UCB, Dafna D Gladman Consultant of: Abbvie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer and UCB, Grant/research support from: Abbvie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer and UCB, Feifei Yang Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Steve Peterson Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Prasheen Agarwal Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Chenglong Han Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, MSD, Pfizer, and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB, Proton Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis.

DOI: 10.1136/annrheumdis-2021-eular.432

POS1029 GUSELKUMAB-TREATED PATIENTS WITH PSORIATIC ARTHRITIS ACHIEVED CLINICALLY MEANINGFUL IMPROVEMENTS IN GENERAL HEALTH OUTCOMES MEASURED WITH PROMIS-29 THROUGH 52 WEEKS: RESULTS FROM THE PHASE 3 DISCOVER-1 TRIAL

A. M. Orbai[1], L. C. Coates[2], A. Deodhar[3], P. Helliwell[4], C. T. Ritchlin[5], A. Kollmeier[6], E. C. Hsia[6,7], X. L. Xu[6], S. Sheng[8], Y. Jiang[8], Y. Liu[6], C. Han[6]. *[1]Johns Hopkins University School of Medicine, Psoriatic Arthritis Program, Baltimore, United States of America*; *[2]Oxford University, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; *[3]Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America*; *[4]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[5]University of Rochester Medical Center, Department of Medicine, Allergy/Immunology and Rheumatology, Rochester, United States of America*; *[6]Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; *[7]University of Pennsylvania School of Medicine, Rheumatology, Philadelphia, United States of America*; *[8]Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*

Background: In the DISCOVER-1 study, the interleukin-23 p19 subunit inhibitor guselkumab (GUS) demonstrated robust efficacy across joint and skin clinical manifestations of psoriatic arthritis (PsA).[1] Patients (pts) with PsA also experience a broad range of symptoms that negatively impact health-related quality of life (eg, pain, fatigue, anxiety, depression, sleep disturbance, poor physical function).[2]

Objectives: Assess the treatment effect of GUS on general health outcomes in pts with PsA in the DISCOVER-1 trial through Week (W) 52 using the Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) instrument.

Methods: Pts with active PsA (≥3 swollen + ≥3 tender joints; C-reactive protein ≥0.3 mg/dL) and inadequate response to standard conventional therapies were randomized 1:1:1 to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or placebo (PBO). PBO pts switched to GUS 100 mg Q4W at W24. PROMIS-29 contains 4 items for each of 7 domains (anxiety, depression, fatigue, pain interference, physical function, sleep disturbance, social participation) and 1 pain intensity item; 28 items are scored on a 5-point Likert-type scale, and pain intensity is rated from 0-10. The raw score of each domain is converted to a standardized T-score, with norms based on a general population mean score=50 and a standard deviation (SD)=10. Higher scores in anxiety, depression, fatigue, pain interference, and sleep disturbance indicate more severe symptoms; higher physical function and social participation scores indicate better health outcomes. Changes ≥5 points (1/2 SD of T-score) are considered clinically meaningful. Analyses were performed using both observed (mean scores/changes, effect sizes) and imputed (clinically meaningful response, whereby change from baseline was set to 0 at W24/52 for pts who had missing data or at W24 for pts who met treatment failure criteria prior to W24).

Results: At baseline, mean PROMIS-29 T-scores for physical function, social participation, sleep disturbance, pain, and fatigue were worse in the 381 PsA pts enrolled in DISCOVER-1 than in the general US population. Across all 7 domains, observed mean PROMIS-29 T-scores showed improvements in GUS-treated pts from baseline to W24 and W52 (Figure 1). Observed mean changes from baseline to W24 and W52, with calculated effect size, are shown (Table 1). In all pts, including those with imputed data, significantly higher percentages of pts in both GUS treatment groups vs PBO had ≥5-point improvements in fatigue, pain interference, physical function, sleep disturbance, social participation, and pain intensity domains at W24 (all nominal p<0.05). Mean improvements in PROMIS-29 domains were maintained through W52.

Conclusion: In pts with active PsA, PROMIS-29 results indicate that GUS treatment was associated with clinically meaningful reductions in fatigue and pain and improvement in physical function and social participation, which were maintained through 1 year.

REFERENCES:

[1] Deodhar A et al. Lancet. 2020;395:1115-25.
[2] Orbai A et al. Ann Rheum Dis. 2017;76:673-80.

Figure. Mean PROMIS-29 T-scores at Baseline, W24, and W52 (Observed Data)*

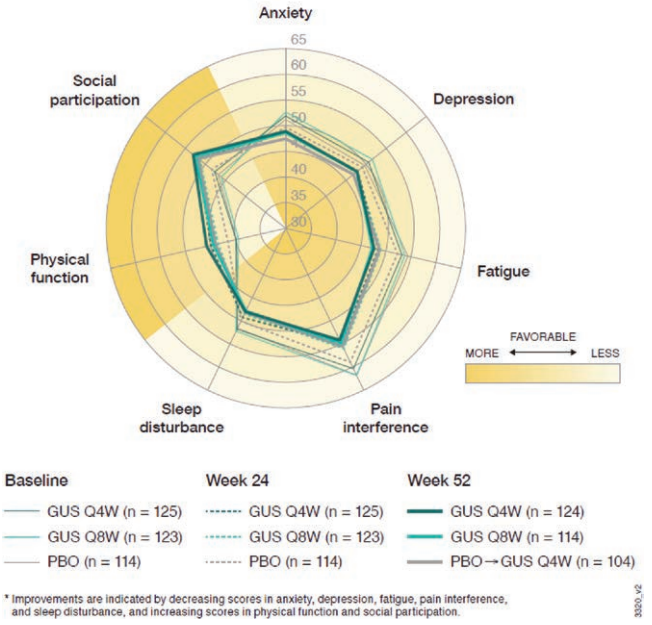


Table 1. Mean Change and Effect Size of Change From Baseline in PROMIS-29 Domain Scores at W24 and W52 (Observed)

	Mean Change From Baseline [Effect Size]					
	GUS Q4W		GUS Q8W		PBO W0-24	GUS Q4W W24-52
	W24	W52	W24	W52	W24	W52
Anxiety	−3.1 [−0.3]	−3.1 [−0.3]	−3.7 [−0.4]	−4.3 [−0.5]	−1.5 [−0.2]	−3.6 [−0.4]
Depression	−2.7 [−0.3]	−3.0 [−0.4]	−4.0 [−0.4]	−4.0 [−0.4]	−0.6 [−0.1]	−2.5 [−0.3]
Fatigue	−4.8 [−0.5]	−5.6 [−0.6]	−4.8 [−0.5]	−6.8 [−0.7]	−2.1 [−0.2]	−5.7 [−0.6]
Pain interference	−5.4 [−0.8]	−6.2 [−1.0]	−5.8 [−1.0]	−7.0 [−1.1]	−2.8 [−0.4]	−6.3 [−1.0]
Physical function	5.0 [0.8]	5.9 [0.9]	4.1 [0.6]	5.0 [0.7]	1.7 [0.2]	4.2 [0.6]
Sleep disturbance	−2.5 [−0.4]	−3.9 [−0.6]	−3.8 [−0.6]	−4.4 [−0.6]	−1.5 [−0.2]	−3.3 [−0.5]
Social participation	4.2 [0.5]	5.3 [0.7]	5.3 [0.6]	6.6 [0.8]	1.7 [0.2]	4.9 [0.6]
Pain intensity*	−2.3 [−1.2]	−2.8 [−1.5]	−2.1 [−1.1]	−2.7 [−1.4]	−0.7 [−0.4]	−2.5 [−1.3]

*Raw score; all other domains reported as T-score.

Disclosure of Interests: Ana-Maria Orbai Consultant of: Eli Lilly, Janssen, Novartis, Pfizer, UCB, Grant/research support from: Abbvie, Eli Lilly and Company, Celgene, Novartis, Janssen, Horizon, Laura C Coates Consultant of: AbbVie, Amgen, Biogen, Bristol Myers Squibb, Boehringer Ingelehim, Celgene, Domain, Eli Lilly, Gilead, Janssen, Medac, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Novartis, Pfizer, Atul Deodhar Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, GSK, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, and UCB, Philip Helliwell Consultant of: Galapagos, Janssen, and Novartis, Grant/research support from: Abbvie, Janssen, and Pfizer, Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Amgen, UCB Pharma, Alexa Kollmeier Shareholder of: Johnson & Johnson, of which Janssen Research & Development, LLC is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, of which Janssen Research & Development, LLC is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, of which Janssen Research & Development is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC, Shihong Sheng Shareholder of: Johnson & Johnson, of which Janssen Research & Development, LLC is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC, Yusang Jiang Employee of: Cytel, Inc., providing statistical support (funded by Janssen), Yan Liu Shareholder of: Johnson & Johnson, of which Janssen Research & Development, LLC is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC, Chenglong Han Shareholder of: Johnson & Johnson, of which Janssen Research & Development, LLC is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC.
DOI: 10.1136/annrheumdis-2021-eular.471

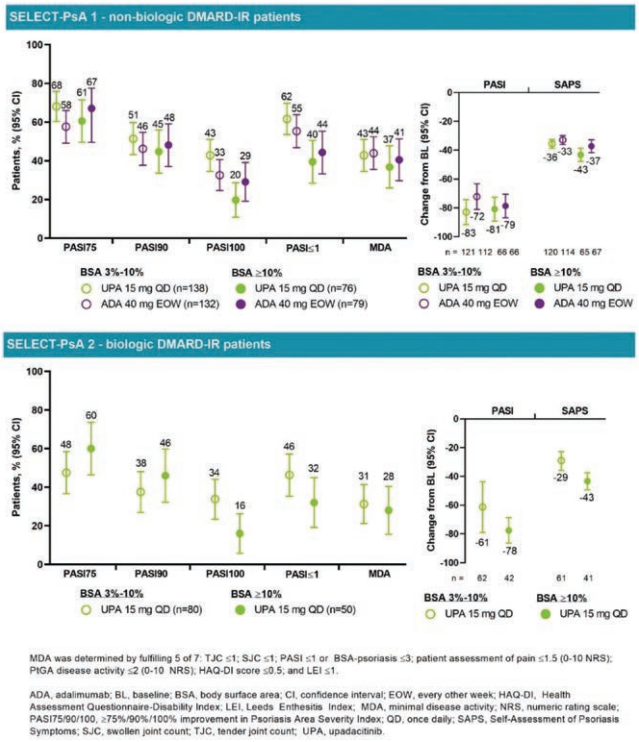
POS1030

EFFICACY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS STRATIFIED BY BASELINE SKIN SEVERITY: A SUBGROUP ANALYSIS OF TWO PHASE III TRIALS

J. F. Merola[1,2], P. Richette[3], E. Lubrano[4], E. Drescher[5], L. Soto[6], C. Lovan[7], K. Kato[7], R. Lippe[8], M. Lane[7], M. Kishimoto[9]. [1]*Brigham and Women's Hospital, Division of Rheumatology, Immunology and Allergy, Boston, United States of America*; [2]*Harvard Medical School, Division of Rheumatology, Boston, United States of America*; [3]*Hopital Lariboisiere Centre Viggo Petersen and Inserm UMR1132 Bioscar, Universite Paris Diderot UFR de Medecine, Service de Rhumatologie, Paris, France*; [4]*University of Molise, Department of Medicine and Health Sciences Vincenzo Tiberio, Campobasso, Italy*; [5]*Veszprém Csolnoky Ferenc County Hospital, Veszprém, Hungary*; [6]*Universidad de Chile, Facultad de Medicina, Santiago, Chile*; [7]*AbbVie, Immunology, North Chicago, United States of America*; [8]*AbbVie Deutschland GmbH & Co. KG, Immunology, Wiesbaden, Germany*; [9]*Kyorin University School of Medicine, Department of Nephrology and Rheumatology, Tokyo, Japan*

Background: In the SELECT-PsA 1 and 2 clinical trials, upadacitinib (UPA) demonstrated efficacy and safety in patients (pts) with active psoriatic arthritis (PsA).[1,2] PsA is associated with varying degrees of psoriatic symptoms; however, the impact of skin severity on treatment outcomes is not well understood.
Objectives: This post-hoc analysis assessed the effects of baseline skin severity on UPA efficacy.
Methods: SELECT-PsA 1 and SELECT-PsA 2 enrolled pts with PsA and prior inadequate response (IR) or intolerance to ≥1 non-biologic disease-modifying antirheumatic drug (DMARD)[1] or ≥1 biologic DMARD[2], respectively. In both trials, pts received once daily UPA 15 mg or UPA 30 mg or placebo (switched at Wk 24 to either UPA 15 mg or 30 mg); SELECT-PsA 1 also included the active comparator adalimumab (ADA). Only continuous UPA 15 mg and ADA are presented here. In this analysis, pts were divided into subgroups based on the extent of psoriasis at baseline (body surface area [BSA] of ≥3%-<10% or BSA ≥10%); efficacy endpoints were analyzed at Wk 56. Results for binary endpoints are based on non-responder imputation; continuous endpoints are based on mixed model repeated measures analysis with as-observed data.
Results: In the UPA 15 mg and ADA groups, respectively, 32% (138/429) and 31% (132/429) of pts had a BSA ≥3-<10% at baseline in SELECT-PsA 1; 18% (76/429) in each treatment group had a BSA ≥10%. In SELECT-PsA 2, 38% (80/211) had a BSA ≥3-<10% and 24% (50/211) had a BSA ≥10% at baseline in the UPA 15 mg group. Across pt populations (non-biologic DMARD-IR and biologic DMARD-IR), generally consistent results were observed between patients in both skin severity subgroups (Figure 1). In non-biologic DMARD-IR pts, a numerically greater proportion of UPA 15 mg pts with lower skin involvement compared with higher skin involvement achieved PASI100 and PASI≤1, two more stringent

Figure. Efficacy Outcomes at Week 56 Stratified by the Severity of Skin Involvement at Baseline



MDA was determined by fulfilling 5 of 7: TJC ≤1; SJC ≤1; PASI ≤1 or BSA-psoriasis ≤3; patient assessment of pain ≤1.5 (0-10 NRS); PtGA disease activity ≤2 (0-10 NRS); HAQ-DI score ≤0.5; and LEI ≤1.

ADA, adalimumab; BL, baseline; BSA, body surface area; CI, confidence interval; EOW, every other week; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; NRS, numeric rating scale; PASI75/90/100, ≥75%/90%/100% improvement in Psoriasis Area Severity Index; QD, once daily; SAPS, Self-Assessment of Psoriasis Symptoms; SJC, swollen joint count; TJC, tender joint count; UPA, upadacitinib.

Table 1. Additional Efficacy Outcomes at Week 56 Stratified by Severity of Skin Involvement at Baseline

	SELECT-PsA 1	
n/N (%) [95% CI]	**UPA 15 mg**	**ADA**
sIGA 0/1 w/at least 2 point improvement from BL[a]		
≥3%-<10%	71/128 (55.5) [46.9, 64.1]	53/124 (42.7) [34.0, 51.4]
≥10%	29/76 (38.2) [27.2, 49.1]	33/77 (42.9) [31.8, 53.9]
MDA + skin[b]		
≥3%-<10%	58/138 (42.0) [33.8, 50.3]	56/132 (42.4) [34.0, 50.9]
≥10%	19/76 (25.0) [15.3, 34.7]	28/79 (35.4) [24.9, 46.0]
SELECT-PsA 2		
n/N (%) [95% CI]	**UPA 15 mg**	
sIGA 0/1 w/at least 2 point improvement from BL[a]		
≥3%-<10%	24/71 (33.8) [22.8, 44.8]	
≥10%	18/50 (36.0) [22.7, 49.3]	
MDA + skin[b]		
≥3%-<10%	22/80 (27.5) [17.7, 37.3]	
≥10%	9/50 (18.0) [7.4, 28.6]	

[a] defined as achieving an sIGA score of 0 or 1 and at least a 2 point improvement from BL, evaluated in pts with BL sIGA ≥2.

[b] defined as achieving 5 of the 7 criteria, with PASI ≤1 or BSA-psoriasis ≤3 as a required component.

ADA, adalimumab; BL, baseline; CI, confidence interval; MDA, minimal disease activity; sIGA, Static Investigator Global Assessment of psoriasis; UPA, upadacitinib

skin endpoints. The achievement of MDA was generally consistent across skin severity subgroups; when pts were required to achieve the skin component of MDA, results were numerically better in the ≥3-<10% skin severity group (Table 1). In non-biologic DMARD-IR pts, results were similar between UPA 15 mg and ADA.

Conclusion: UPA is a viable treatment option for pts with active PsA regardless of the extent of psoriasis at baseline. Although these results are of interest and hypothesis-generating, they should be interpreted with caution due to low sample size.

REFERENCES:

[1] McInnes IB et al. *Ann Rheum Dis*, 2020; 79:12

[2] Mease PJ et al. *Ann Rheum Dis*, 2020;doi:10.1136/annrheumdis-2020-218870

Acknowledgements: AbbVie and the authors thank the patients, study sites, and investigators who participated in this clinical trial. AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. No honoraria or payments were made for authorship. Medical writing support was provided by Ramona Vladea, PhD and Jamie Urbanik, PharmD both of AbbVie Inc.

Disclosure of Interests: Joseph F. Merola Consultant of: Merck, Bristol-Myers Squibb, AbbVie, Dermavant, Eli Lilly, Novartis, Janssen, UCB, Celgene, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Sorono, Avotres and Leo Pharma, Pascal Richette Consultant of: AbbVie, Biogen, Janssen, BMS, Roche, Pfizer, Amgen, Sanofi-Aventis, UCB, Lilly, Novartis, and Celgene, Ennio Lubrano Speakers bureau: AbbVie, Celgene, Janssen, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Celgene, Janssen, MSD, Novartis, and Pfizer, Grant/research support from: AbbVie, Celgene, Janssen, MSD, Novartis, and Pfizer, Edit Drescher: None declared, Lilian Soto: None declared, Charles Lovan Shareholder of: AbbVie, Employee of: AbbVie, Koji Kato Shareholder of: AbbVie, Employee of: AbbVie, Ralph Lippe Shareholder of: AbbVie, Employee of: AbbVie, Michael Lane Shareholder of: AbbVie, Employee of: AbbVie, Mitsumasa Kishimoto Consultant of: AbbVie, Amgen-Astellas BioPharma, Asahi-Kasei Pharma, Astellas, Ayumi Pharma, BMS, Celgene, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Kyowa Kirin, Novartis, Ono Pharma, Pfizer, Tanabe-Mitsubishi, Teijin Pharma, and UCB Pharma.

DOI: 10.1136/annrheumdis-2021-eular.536

POS1031

LOW INCIDENCE OF GASTROINTESTINAL-RELATED AND OVERALL SERIOUS ADVERSE EVENTS AMONG GUSELKUMAB-TREATED PATIENTS: POOLED ANALYSES OF VOYAGE 1 & 2 AND DISCOVER 1 & 2 THROUGH 1-YEAR

P. J. Mease[1], P. Foley[2], K. Reich[3], J. Bagel[4], M. Lebwohl[5], Y. W. Yang[6], M. Shawi[6], M. Miller[7], A. Kollmeier[8], E. C. Hsia[7,9], X. L. Xu[7], M. Izutsu[7], P. Ramachandran[7], S. Sheng[10], Y. You[10], P. Helliwell[11], W. H. Boehncke[12]. *[1]Swedish Medical Center/Providence St. Joseph Health, University of Washington, Rheumatology Research, Seattle, United States of America*; *[2]The University of Melbourne, St. Vincent's Hospital Melbourne and Probity Medical Research, Skin Health Institute, Department of Medicine, Carlton, Australia*; *[3] University Medical Center Hamburg-Eppendorf, Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, Hamburg, Germany*; *[4]Psoriasis Treatment Center of Central New Jersey, Department of Dermatology, East Windsor, United States of America*; *[5]Icahn School of Medicine at Mount Sinai, Department of Dermatology, New York, United States of America*; *[6]Janssen Global Services, LLC, Immunology, Horsham, United States of America*; *[7]Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; *[8]Janssen Research & Development, LLC, Immunology, San Diego, United States of America*; *[9]University of Pennsylvania Health System, Rheumatology, Philadelphia, United States of America*; *[10]Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; *[11]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[12]Geneva University Hospitals, Department of Dermatology, Geneva, Switzerland*

Background: Guselkumab (GUS), a human monoclonal antibody that specifically binds to the p19-subunit of interleukin (IL)-23, demonstrated efficacy in the Phase 3 VOYAGE 1&2 trials of patients (pts) with moderate to severe plaque psoriasis (PsO)[1,2] and in the DISCOVER 1&2 trials of pts with active psoriatic arthritis (PsA).[3,4] IL-17 inhibitors used to treat PsO and PsA have been associated with exacerbation or new onset of inflammatory bowel disease (IBD) (e.g., Crohn's disease or ulcerative colitis).[5]

Objectives: Evaluate the incidence of gastrointestinal (GI)-related and overall serious adverse events (SAEs) from pooled safety data through 1-year of GUS 100 mg treatment from the VOYAGE 1&2 and DISCOVER 1&2 trials.

Methods: Using pooled safety data from the VOYAGE 1&2 PsO trials and DISCOVER 1&2 PsA trials, SAEs related to GI disorders were identified using the Medical Dictionary for Regulatory Activities (MedDRA) system-organ class "GI disorders". Pts with a previous history of IBD were not excluded in these trials; medical history of IBD was collected at baseline in DISCOVER 1&2. Rates of overall SAEs and GI-related SAEs were calculated as the number of SAEs per 100 pt-years (PY) of follow-up (95% confidence intervals). Data are presented for the placebo (PBO)-controlled period (Weeks 0-16 for VOYAGE 1&2; Weeks 0-24 for DISCOVER 1&2) and through 1-year (defined as through Week 48 for VOYAGE 1&2; through Week 60 for DISCOVER 1, and through Week 52 for DISCOVER 2). Events of uveitis and opportunistic infections were also analyzed.

Results: Through the PBO-controlled period, the overall rates of GI-related SAEs per 100 PY for pooled VOYAGE 1&2 were: PBO 0.78 (0.02, 4.34), GUS q8w 0; and for pooled DISCOVER 1&2: PBO 0.58 (0.01, 3.23), GUS q8w 0.58 (0.01, 3.21), GUS q4w 0. The GI-related SAEs included: gastrointestinal hemorrhage (PBO; n=1) for pooled VOYAGE 1&2; and inflammatory bowel disease (PBO; n=1) and mechanical ileus (GUS q8w; n=1) for pooled DISCOVER 1&2. Through 1-year, the overall rates of GI-related SAEs for pooled VOYAGE 1&2 were: Combined GUS group (GUS q8w and PBO→GUS groups) 0.51 (0.17, 1.20); and for pooled DISCOVER 1&2: GUS q8w 0.52 (0.06, 1.88), GUS q4w 0, Combined GUS group (GUS q8w, GUS q4w, and PBO→GUS groups) 0.21 (0.02, 0.74). The GI-related SAEs in the Combined GUS group for pooled VOYAGE 1&2 included: gastritis, hemorrhoids, inguinal hernia, pancreatitis, and umbilical hernia (0.10/100PY [0.00, 0.57]; n=1 for each); and in the Combined GUS group for pooled DISCOVER 1&2: mechanical ileus and pancreatitis chronic (0.10/100PY [0.00, 0.57]; n=1 for each). Overall, no cases of exacerbation or new onset of IBD were reported in GUS-treated pts, including 2 pts with a prior history of IBD in DISCOVER 1&2 (total PY of follow-up for the Combined GUS groups in VOYAGE and DISCOVER were 974 and 973, respectively). Through the PBO-controlled period, rates of overall SAEs for GUS-treated pts were comparable to PBO-pts and SAE rates remained low through 1-year of follow-up in the VOYAGE 1&2 and DISCOVER 1&2 trials. There were no reported cases of uveitis, opportunistic infections, or tuberculosis in GUS-treated pts through 1-year.

Conclusion: Through 1-year of follow-up with GUS treatment in pooled VOYAGE 1&2 and DISCOVER 1&2, GI-related SAE rates were low. There were no reported cases of uveitis, opportunistic infections, or new onset/exacerbation of IBD in GUS-treated pts. No new safety concerns were identified through 1-year.

REFERENCES:

[1] Blauvelt A., et al. *J Am Acad Dermatol*. 2017;76:405-17.

[2] Reich K., et al. *J Am Acad Dermatol.* 2017;76:418-31.

[3] Deodhar A., et al. *Lancet*. 2020;395:1115-25.

[4] Mease P.J., et al. *Lancet*. 2020; 395:1126-36.

[5] Hohenberger M., et al. *J Dermatolog Treat*. 2018;29:13-8.

Disclosure of Interests: Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB, Peter Foley Speakers bureau: AbbVie, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Valeant, Galderma, GSK, Leo Pharma, and Roche, Consultant of: Janssen, Lilly, Novartis, Pfizer, Galderma, AbbVie, Amgen, AstraZeneca, Arcutis, Aslan, Boehringer Ingelheim, Celgene, Hexima, Merck, Sun Pharma, UCB Pharma, Valeant, BMS, Celtaxsys, CSL, Cutanea, Dermira, Genentech, GSK, Leo Pharma, Regeneron Pharmaceuticals Inc, Reistone, Roche, and Sanofi, Grant/research support from: AbbVie, Amgen, Celgene, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Sanofi, and Sun Pharma; travel grants from AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, Galderma, Leo Pharma, Roche, Sun Pharma, and Sanofi
, Kristian Reich Consultant of: AbbVie, Amgen, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB Pharma, Grant/research support from: AbbVie, Amgen, and UCB Pharma, Jerry Bagel Speakers bureau: AbbVie, Celgene Corporation, Eli Lilly, Janssen Biotech, and Novartis, Consultant of: AbbVie, Amgen, Celgene Corporation, Eli Lilly and Company, Janssen Biotech, Leo Pharma, Novartis, Sun Pharmaceutical

Industries Ltd, and Valeant Pharmaceuticals, Grant/research support from: AbbVie, Amgen, Arcutis Biotherapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Celgene Corporation, Corrona, LLC, Dermavant Sciences, LTD, Dermira/UCB, Eli Lilly and Company, Glenmark Pharmaceuticals Ltd, Janssen Biotech, Kadmon Corporation, Leo Pharma, Lycera Corp, Menlo Therapeutics, Novartis, Pfizer, Regeneron Pharmaceuticals, Sun Pharma, Taro Pharmaceutical Industries Ltd, and Valeant Pharmaceuticals, Mark Lebwohl Consultant of: Aditum Bio, Allergan, Almirall, Arcutis, Inc., Avotres Therapeutics, BirchBioMed Inc., BMD skincare, Boehringer-Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Evelo, Evommune, Facilitate International Dermatologic Education, Foundation for Research and Education in Dermatology, Inozyme Pharma, Kyowa Kirin, LEO Pharma, Meiji Seika Pharma, Menlo, Mitsubishi, Neuroderm, Pfizer, Promius/Dr. Reddy's Laboratories, Serono, Theravance, and Verrica, Grant/research support from: Abbvie, Amgen, Arcutis, Boehringer Ingelheim, Dermavant, Eli Lilly, Evommune, Incyte, Janssen, Leo Pharmaceutucals, Ortho Dermatologics, Pfizer, and UCB, Ya-Wen Yang Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Megan Miller Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Miwa Izutsu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Paraneedharan Ramachandran Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Yin You Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Philip Helliwell Consultant of: Galapagos, Janssen, Novartis, Grant/research support from: Abbvie, Janssen, Pfizer, Wolf-Henning Boehncke Speakers bureau: AbbVie, Almirall, Celgene, Janssen, Leo, Lilly, Novartis, and UCB Pharma, Consultant of: AbbVie, Almirall, Celgene, Janssen, Leo, Lilly, Novartis, and UCB Pharma, Grant/research support from: Pfizer

DOI: 10.1136/annrheumdis-2021-eular.558

POS1032

EFFICACY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS STRATIFIED BY NUMBER OF PRIOR BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

P. J. Mease[1], A. Lertratanakul[2], B. Strober[3], S. Tsuji[4], P. Richette[5], C. Lovan[2], D. Feng[2], J. Anderson[2], F. Van den Bosch[6]. [1]*Department of Rheumatology, Swedish Medical Center and University of Washington, Seattle, United States of America*; [2]*AbbVie Inc., Rheumatology, North Chicago, United States of America*; [3]*Yale University School of Medicine, New Haven and Central Connecticut Dermatology, Cromwell, United States of America*; [4]*Department of Orthopaedics/Rheumatology, National Hospital Organization, Osaka Minami Medical Center, Osaka, Japan*; [5]*Department of Rheumatology, Lariboisière Hospital, Paris, France*; [6]*Department of Internal Medicine, Ghent University Hospital, Ghent, Belgium*

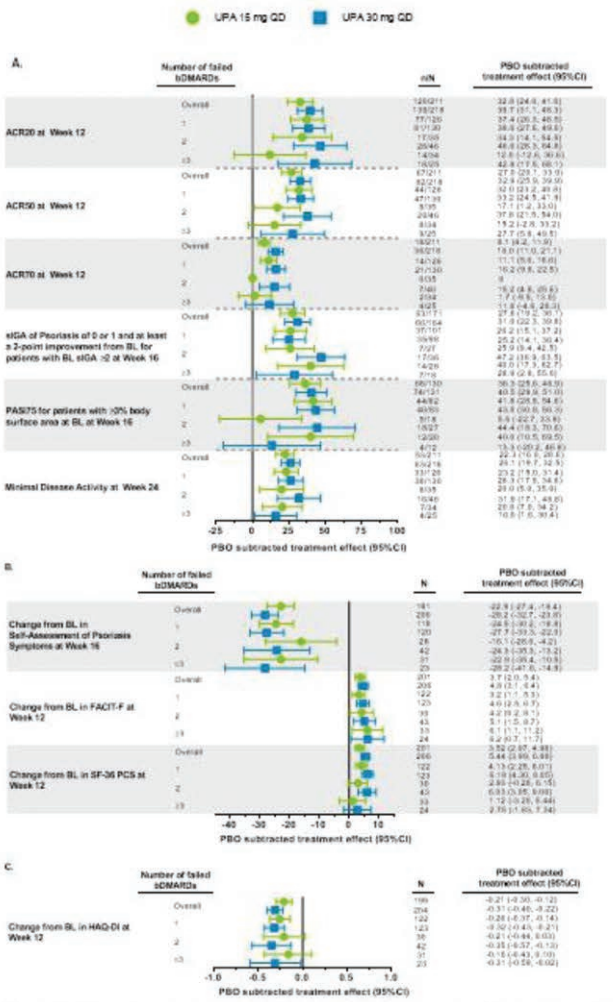
Background: Upadacitinib (UPA) has shown efficacy and safety in patients (pts) with active PsA in the Phase 3 SELECT-PsA 1 and SELECT-PsA 2 clinical trials.[1,2] Historically efficacy has been lower with second- and third-line therapy compared with first-line anti-TNF therapy in PsA;[3,4] however, clinical trial data that describe efficacy in pts who have had an inadequate response (IR) to multiple biologic DMARDs (bDMARDs) are limited.

Objectives: This analysis assessed the effects of prior bDMARD failure on UPA efficacy in the SELECT-PsA 2 trial.

Methods: The SELECT-PsA 2 study enrolled pts with prior IR or intolerance to ≥1 bDMARD (N=642). Pts were randomized to placebo (PBO), UPA 15 mg once daily (QD, UPA15), or UPA 30 mg QD (UPA30). Stable background treatment of ≤2 non-bDMARDs was permitted; background therapy was not required. Only the pts who had IR to ≥1 bDMARD were included in this analysis; pts were subgrouped based on the number of bDMARDs failed prior to enrollment (1, 2, or ≥3). This analysis includes assessment of proportion of pts achieving ACR20/50/70, and change in HAQ-DI, FACIT-Fatigue, and SF-36 Physical Component Summary at Wk 12; static Investigator Global Assessment of Psoriasis of 0 or 1 and at least a 2-point improvement from baseline, PASI75, and change in Self-Assessment of Psoriasis Symptoms at Wk 16; and proportion of pts achieving minimal disease activity (MDA) at Wk 24. Non-responder imputation was used for binary endpoints. Mixed-effects model for repeated measures was used for continuous endpoints. Point estimates and 95% confidence intervals (CIs) of the PBO subtracted treatment effect were calculated.

Results: 641 pts were randomized and received study drug; 92% were bDMARD-IR: 391 (61%) of pts failed 1 bDMARD, 116 (18%) failed 2 bDMARDs, and 83 (13%) failed ≥3 bDMARDs. In the overall study population, UPA15 and UPA30 demonstrated superiority vs placebo for all endpoints evaluated. In this post hoc analysis, the PBO subtracted treatment effect demonstrates generally consistent efficacy as compared to the overall study population for UPA15 and UPA30 across efficacy endpoints in the subgroups of pts with IR to 1, 2, or ≥3 prior bDMARDs (Figure 1). Due to limited sample sizes for pts with IR to >1 bDMARD and the pt subsets analyzed for psoriasis-related endpoints, results should be interpreted with caution.

Figure. Efficacy Outcomes by Prior bDMARD Exposure: Placebo Subtracted Treatment Effect



ACR20/50/70, American College of Rheumatology 20%/50%/70% improvement criteria; BL, baseline; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire - Disability Index; MDA, minimal disease activity; PASI, Psoriasis Area Severity Index; PBO, placebo; QD, once daily; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary Score; sIGA, Static Investigator Global Assessment of Psoriasis.

Conclusion: Upadacitinib demonstrated consistent efficacy in treating clinical manifestations of PsA including musculoskeletal symptoms, psoriasis, physical function, fatigue, and quality of life in pts with IR to 1 or multiple prior bDMARDs. In addition, comprehensive disease control as measured by MDA, was generally consistently achieved with upadacitinib regardless of number of prior bDMARDs tried.

REFERENCES:

[1] McInnes IB, et al. Ann Rheum Dis, 2020; 79:12.
[2] Genovese MC, et al. Ann Rheum Dis, 2020; 79:139.
[3] Costa L, et al. Drugs R D. 2017;17:509-522.
[4] Reddy SM, et al. 2016;35:2955-2966.

Acknowledgements: AbbVie and the authors thank the patients, study sites, and investigators who participated in this clinical trial. AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. No honoraria or payments were made for authorship. Medical writing support was provided by Ramona Vladea, PhD of AbbVie Inc.

Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Genentech, Gilead, GlaxosmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB., Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Genentech, Gilead, GlaxosmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB., Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Genentech, Gilead, GlaxosmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB., Apinya Lertratanakul Shareholder of: AbbVie, Employee of: AbbVie, Bruce Strober Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Ortho Dermatologics, Consultant of: AbbVie, Almirall,

Amgen, Arcutis, Arena, Aristea, Boehringer Ingelheim, Bristol-Myers-Squibb, Cara, Celgene, Dermavant, Dermira, Janssen, Leo, Eli Lilly, Meiji Seika Pharma, Novartis, Pfizer, GlaxoSmithKline, UCB Pharma, Sun Pharma, Ortho Dermatologics, Regeneron, Sanofi-Genzyme, Shigeyoshi Tsuji Speakers bureau: AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, Consultant of: AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, Pascal Richette Speakers bureau: AbbVie, Biogen, Janssen, BMS, Roche, Pfizer, Amgen, Sanofi-Aventis, UCB, Lilly, Novartis, and Celgene, Consultant of: AbbVie, Biogen, Janssen, BMS, Roche, Pfizer, Amgen, Sanofi-Aventis, UCB, Lilly, Novartis, and Celgene, Charles Lovan Shareholder of: AbbVie, Employee of: AbbVie, Dai Feng Shareholder of: AbbVie, Employee of: AbbVie, Jaclyn Anderson Shareholder of: AbbVie, Employee of: AbbVie, Filip van den Bosch Speakers bureau: AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, Consultant of: AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB.

DOI: 10.1136/annrheumdis-2021-eular.564

POS1033 SAFETY OF IXEKIZUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS: AN INTEGRATED ANALYSIS OF 4 CLINICAL TRIALS

C. Sesin[1], G. Gallo[2], A. Gellett[2], A. Kronbergs[2], A. T. Sprabery[2], W. Xu[2], H. Patel[2], A. Deodhar[3], B. Combe[4], G. R. Burmester[5]. *[1]Mount Sinai Medical Center, Miami Beach, United States of America*; *[2]Eli Lilly and Company, Indianapolis, United States of America*; *[3]Oregon Health & Science University, Portland, United States of America*; *[4]Montpellier University, CHU Montpellier, Montpellier, France*; *[5]Universitatsklinikum Charite, Berlin, Germany*

Background: Patients with psoriatic arthritis (PsA) require long-term treatment, which may lead to adverse events (AEs). Ixekizumab, an interleukin-17A antagonist, is approved for the treatment of adults with active PsA.

Objectives: We report a summary of safety outcomes for patients enrolled in 4 PsA studies with up to 3 years of exposure to ixekizumab.

Methods: This integrated safety analysis included all patients with PsA who received at least 1 dose of ixekizumab (80 mg every 2 or 4 weeks) in 4 clinical trials (NCT01695239, NCT02349295, NCT02584855, NCT03151551). Safety outcomes included treatment-emergent adverse events (TEAEs), serious AEs (SAEs), discontinuations due to AEs, deaths, and AEs of special interest.

Results: A total of 1401 patients were included in this safety analysis (51.5% female; mean age 49 years), with 2247.6 patient-years of exposure (Table 1). In all, 1131 patients (80.7%) reported ≥1 TEAE (exposure-adjusted incidence rate per 100 patient-years [IR] 50.3, 95% CI 47.5–53.3), mostly mild (32.9%) or moderate (39.7%) in severity. The most common TEAEs were nasopharyngitis (n=202, IR 9.0), upper respiratory infections (n=186, IR 8.3), and injection site reaction (n=156, IR 6.9). SAEs were reported by 134 patients (IR 6.0, 95% CI 5.0–7.1). 115 (8.2%) patients discontinued due to AEs (IR 5.1, 95% CI 4.3–6.1). Six deaths were reported (IR 0.3, 95% CI 0.1–0.6). Allergic reactions/hypersensitivity were reported in 102 patients (IR 4.5, 95% CI 3.7–5.5). Three cases were adjudicated as de novo inflammatory bowel disease (IR 0.13, 95% CI 0.04–0.41); 1 was ulcerative colitis (IR 0.04, 95% CI 0.01–0.32), 2 were Crohn's disease (IR 0.09, 95% CI 0.02–0.36). Major adverse cardiac events occurred in 12 patients (IR 0.5) and malignancies in 15 (IR 0.7), 9 of which were non-melanoma skin cancer. Opportunistic infections occurred in 40 (2.9%) patients (IR 1.8, 95% CI 1.3–2.4). Candidiasis occurred in 24 patients (oral: IR 0.7, 95% CI 0.4–1.2; oral fungal infection: IR 0.3, 95% CI 0.1–0.6; esophageal infection: IR 0.1, 95% CI 0.0–0.4). No active or reactive cases of tuberculosis were reported. Other opportunistic infections included hepatitis B (IR 0.0, 95% CI 0.0–0.3), herpes simplex (IR 1.8, 95% CI 1.3–2.5), and herpes zoster (IR 0.7, 95% CI 0.4–1.2).

Conclusion: The safety profile of ixekizumab across 4 clinical trials and up to 3 years of continuous treatment in patients with active PsA was consistent with the known safety profile reported in previous studies for psoriasis and PsA. No new safety events were found in this analysis.

Disclosure of Interests: Carlos Sesin Speakers bureau: Amgen, AbbVie, Sanofi, Radius, Pfizer, Eli Lilly and Company, Novartis, Gaia Gallo Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Amanda Gellett Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Andris Kronbergs Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Aubrey Trevelin Sprabery Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Wen Xu Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Himanshu Patel Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Atul Deodhar Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Galapagos, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Eli Lilly and Company, Glaxo Smith & Kline, Novartis, Pfizer, UCB, Bernard Combe Speakers bureau: AbbVie, BMS, Gilead-Galapagos, Eli Lilly and Company, MSD, Pfizer, Roche Chugai, Consultant of: AbbVie, Bayer, Gilead-Galapagos, Janssen, Eli Lilly and Company, Novartis, Roche Chugai, Grant/research support from: AbbVie, Eli Lilly and Company, Pfizer, Roche Chugai, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Janssen, Novartis, Eli Lilly and Company, MSD, Pfizer, Consultant of: AbbVie, Janssen, Novartis, Eli Lilly and Company, MSD, Pfizer.

DOI: 10.1136/annrheumdis-2021-eular.567

	Pooled Ixekizumab (N=1401; Total Patient-Years=2247.6)				
	n (IR) 95% CI	Year 0–1 (n=1401) n (IR) 95% CI	Year 1–2 (n=946) n (IR) 95% CI	Year 2–3 (n=510) n (IR) 95% CI	Year ≥3 (n=89) n (IR) 95% CI
Total Patient-Years	2247.7	1207.3	689.8	347.7	2.9
Patients with ≥1 TEAE	1131 (50.3)	1050 (87.0)	496 (71.9)	234 (67.3)	6 (206.2)
	47.5–53.3	81.9–92.4	65.9–78.5	59.2–76.5	92.6–458.9
SAEs	134 (6.0)	72 (6.0)	53 (7.7)	19 (5.5)	1 (34.4)
	5.0–7.1	4.7–7.5	5.9–10.1	3.5–8.6	4.8–243.9
Discontinuations due to AEs	115 (5.1)	61 (5.1)	37 (5.4)	17 (4.9)	0 (0)
	4.3–6.1	3.9–6.5	3.9–7.4	3.0–7.9	0.0–274.7
Hepatic reactions	112 (5.0)	80 (6.6)	32 (4.6)	14 (4.0)	0 (0)
	4.1–6.0	5.3–8.3	3.3–6.6	2.4–6.8	0.0–274.7
Allergic reaction/hypersensitivity	102 (4.5)	83 (6.9)	23 (3.3)	5 (1.4)	0 (0)
	3.7–5.5	5.5–8.5	2.2–5.0	0.6–3.5	0.0–274.7
Serious infection	28 (1.2)	18 (1.5)	9 (1.3)	3 (0.9)	0 (0)
	0.9–1.8	0.9–2.4	0.7–2.5	0.3–2.7	0.0–274.7
Malignancies	15 (0.7)	4 (0.3)	8 (1.2)	4 (1.2)	0 (0)
	0.4–1.1	0.1–0.9	0.6–2.3	0.4–3.1	0.0–274.7
Major adverse cardiac events	12 (0.5)	3 (0.2)	8 (1.2)	1 (0.3)	0 (0)
	0.3–0.9	0.1–0.8	0.6–2.3	0.0–2.0	0.0–274.7
Inflammatory bowel disease	3 (0.1)	3 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)
	0.0–0.4	0.1–0.8	0.0–1.0	0.0–2.3	0.0–274.7
Ulcerative colitis	1 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	**0 (0.0)**
	0.0–0.3	0.0–0.6	0.0–1.0	0.0–2.3	0.0–274.7
Crohn's disease	2 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	**0 (0.0)**
	0.0–0.4	0.0–0.7	0.0–1.2	0.0–2.3	0.0–274.7

AE, adverse event; CI, confidence interval; IR, exposure-adjusted incidence rate per 100 patient-years; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

POS1034 RESPONSE TO SEQUENTIAL LINES OF BIOLOGICAL THERAPY IN PSORIATIC ARTHRITIS: A SINGLE CENTRE COHORT STUDY

A. Abdalla[1], A. Rambojun[2], L. C. Coates[3], E. Korendowych[1], N. Mchugh[2], W. Tillett[1,2]. *[1]Royal National Hospital for Rheumatic Diseases, Rheumatology Department, Bath, United Kingdom*; *[2]University of Bath, Department of Pharmacy and Pharmacology, Bath, United Kingdom*; *[3]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*

Background: Biologic interventions using highly specific immuno-modulatory biologic disease-modifying anti-rheumatic drugs (bDMARDs) represent a rapidly developing therapeutic approach to the treatment of Psoriatic Arthritis (PsA). However, despite high rates of response, adverse events, primary and secondary inefficacy are common, and multiple sequential lines of bDMARDs are often required. Data on drug persistence, as a surrogate for response, from national registries indicates switching has become accepted routine practice. One third of patients will fail or discontinue their first biologic with a significant proportion switching on to a 3rd biologic or higher.[1-4] Due to a lack of evidence on the response to sequential therapies, individual patients may not have further lines routinely funded after three bDMARDs in the UK. While limiting lines of therapy remains a UK concern, many countries with rationed healthcare systems follow the UK model of drug usage.

Objectives: To describe the response to sequential lines of bDMARD therapy prescribed in routine care in a UK single centre cohort.

Methods: A retrospective sample of patients with PsA who fulfilled CASPAR criteria and had received at least one bDMARD were taken from the Bath longitudinal cohort for inclusion in the study. Clinical and laboratory variables that constitute physician and patient-reported outcome measures were collected at baseline and after a median (range) follow-up of 3 months (2-5) into their respective therapy line in accordance with the National Institute for Health and Care Excellence (NICE) rules. The mean change with a 95% confidence interval (CI) was used to report the difference between the baseline and follow-up measures. All patients provided consent to use their data collected during routine care, and ethical approval by the local committee was granted.

Results: The patients mean age was 57.7 (SD 12.2) with a median (range) disease duration of 14.4 years (9.7 – 23.2). Data was available for 194 patients commencing 1st line bDMARD, 106 (2nd line), 93 (3rd line), 33 (4th line), 12 (5th line), and 9 (6th line and higher) from a total of 759 patients in the cohort. Mean tender and swollen joint count at baseline 1st bDMARD was 7 (SD 4.7) and 22 (SD 14.0), pain visual analogue scale 50 (SD 27.6) and PASI 1.3 (SD 2.2). Reasons for changing biological therapies include lack or loss of efficacy, intolerance, side effects, and comorbidities. Mean levels of joint disease at drug initiation did not diminish with subsequent lines of therapy. Clinical and patient

reported outcomes by line of therapy are reported in Figure 1. Clinical responses were greatest to first line bDMARD, however clinically relevant DAPSA improvements were seen up to 5th line. Absolute levels of psoriasis in the cohort were low, however improvement in PASI was achieved across all lines of therapy. Patient and Physician Global Assessments (1-5 on Likert scale) and the Pain Visual analogue score (VAS on 1-10 Likert scale) showed a similar trend with greatest improvement to first line treatment across all lines of therapy.

Conclusion: In this study we report the clinical response to sequential lines of bDMARD therapy for active PsA in routine clinical practice. Clinical response was greatest to the first line bDMARD but overall improvement in DAPSA, PASI or pain response did not appear to diminish up to 5th line. Further study in larger cohorts is required to confirm this finding and build on our understanding of clinical response to sequential lines of bDMARD therapy.

REFERENCES:

[1] Hyrish et al 2006 *Rheum* 45, 1558-65
[2] Kawabe A. 2020 *Arth Res Ther* 22, 136
[3] Park DJ. 2017 *Clin Rheum* 36, 1013-22
[4] Karlsson. 2007 JA *Rheum* 47,507-13

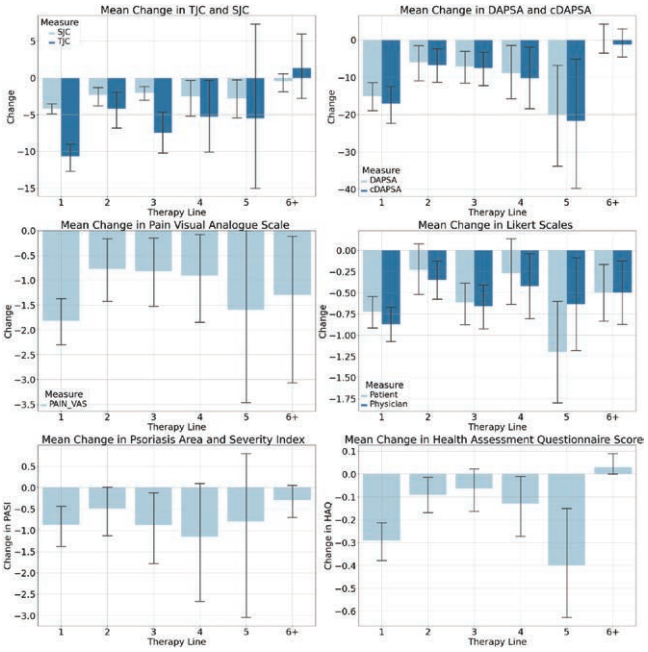


Figure 1. Clinical and patient reported outcomes by line of therapy

Disclosure of Interests: Abuelmagd Abdalla: None declared, Adwaye Rambojun: None declared, Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Gilead, Eli Lilly, Janssen, Medac, Novartis, Pfizer, and UCB., Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Pfizer, and Novartis, Eleanor Korendowych Consultant of: Abbvie, Celgene, Janssen, Lilly and Novartis., Neil McHugh: None declared, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer Inc., and UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer Inc., and UCB., Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc., and UCB.
DOI: 10.1136/annrheumdis-2021-eular.659

POS1035 UPADACITINIB AS MONOTHERAPY AND IN COMBINATION WITH NON-BIOLOGIC DMARDs FOR THE TREATMENT OF PSORIATIC ARTHRITIS: SUBGROUP ANALYSIS FROM TWO PHASE 3 TRIALS

P. Nash[1], P. Richette[2], L. Gossec[3], A. Marchesoni[4], C. T. Ritchlin[5], K. Kato[6], E. Mcdearmon-Blondell[6], E. Lesser[6], R. Mccaskill[6], D. Feng[6], J. Anderson[6], E. Ruderman[7]. [1]*School of Medicine, Griffith University, Brisbane, Australia*; [2]*Service de Rhumatologie, Hopital Lariboisiere Centre Viggo Petersen and Inserm UMR1132 Bioscar, Universite Paris Diderot UFR de Medecine, Paris, France*; [3]*Sorbonne Universite, Pitie Salpetriere Hospital, Paris, France*; [4]*ASST Gaetano, Pini-CTO, Milan, Italy*; [5]*Allergy, Immunology and Rheumatology Division, Center for Musculoskeletal Medicine, University of Rochester Medical Center, Rochester, United States of America*; [6]*AbbVie Inc., Rheumatology, North Chicago, United States of America*; [7]*Northwestern University, Feinberg School of Medicine, Chicago, United States of America*

Background: Approximately 40% of PsA patients (pts) on advanced therapy are on monotherapy.[1,2] Upadacitinib (UPA) showed efficacy and safety in pts with active PsA in the Phase 3 SELECT-PsA 1 and SELECT-PsA 2 clinical trials.[3,4]
Objectives: Assess efficacy and safety in subgroups of pts treated with UPA as monotherapy or in combination with non-biologic disease-modifying antirheumatic drugs (non-bDMARDs).
Methods: The SELECT-PsA program enrolled pts with prior inadequate response (IR) or intolerance to ≥1 non-bDMARD (N=1705) and prior IR or intolerance to ≥1 bDMARD (N=642). Data from both trials was integrated for pts receiving placebo (PBO), UPA 15 mg once daily (QD) and UPA 30 mg QD. Stable background treatment of ≤2 non-bDMARDs was permitted, but not required. Analysis includes UPA monotherapy vs combination therapy for endpoints: ACR20/50/70 responses and change from baseline in pain and HAQ-DI (Wk 12); Static Investigator Global Assessment of Psoriasis of 0 or 1 and at least a 2-point improvement from baseline and PASI75/90/100 responses (Wk 16); proportion of pts achieving resolution of enthesitis, dactylitis, and minimal disease activity (Wk 24). Binary outcomes, using the Cochran-Mantel-Haenszel-method and continuous outcomes, using mixed-effects model, were analyzed for repeated measures in the subgroups of UPA monotherapy and combination therapy. Point estimates and 95% confidence intervals (CIs) of PBO subtracted treatment effect were calculated. Treatment-emergent adverse events (TEAEs) were analyzed.
Results: Of 1916 pts, 574 (30%) received monotherapy and 1342 (70%) received combination therapy; 84% in combination therapy group received MTX +/- another non-bDMARD. Both UPA monotherapy and combination therapy led to improvements in efficacy vs PBO and across endpoints, for each dose, generally consistent point estimates of PBO subtracted treatment effect and associated overlapping CIs were observed (Figure 1). Generally, frequency of AEs and serious AEs, were comparable with UPA administered as monotherapy and combination therapy (Table 1). Frequency of AEs of serious infections and hepatic disorder were lower with monotherapy while frequency of AEs leading to discontinuation of study drug were lower with combination therapy. Most hepatic disorders were transient transaminase elevations.
Conclusion: In the SELECT PsA trials, efficacy and safety of UPA was generally consistent when administered as monotherapy or when given in combination with non-bDMARDs. Results from this analysis support the use of UPA with or without concomitant non-bDMARDs.

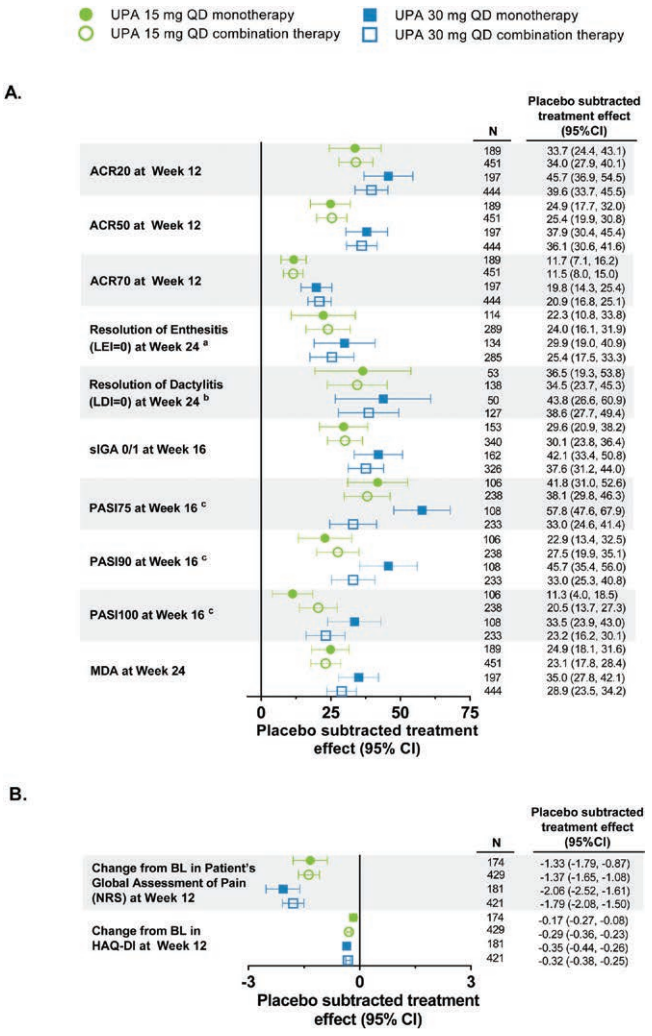
REFERENCES:

[1] Ianculescu I and Weisman MH, Clin Exp Rheumatol 2015; 33:S94–S97.
[2] Mease PJ, et al. RMD Open 2015; 1:e0000181.
[3] McInnes IB, et al. Ann Rheum Dis, 2020; 79:12.
[4] Genovese MC, et al. Ann Rheum Dis, 2020; 79:139.

Acknowledgements: AbbVie and the authors thank the patients, study sites, and investigators who participated in this clinical trial. AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. No honoraria or payments were made for authorship. Medical writing support was provided by Ramona Vladea of AbbVie Inc.
Disclosure of Interests: Peter Nash Speakers bureau: AbbVie, BMS, Roche, Pfizer, Janssen, Amgen, Sanofi-Aventis, UCB, Eli Lilly, Novartis, and Celgene, Consultant of: AbbVie, BMS, Roche, Pfizer, Janssen, Amgen, Sanofi-Aventis, UCB, Eli Lilly, Novartis, and Celgene, Grant/research support from: AbbVie, BMS, Roche, Pfizer, Janssen, Amgen, Sanofi-Aventis, UCB, Eli Lilly, Novartis, and Celgene, Pascal Richette Speakers bureau: AbbVie, Biogen, Janssen, BMS, Roche, Pfizer, Amgen, Sanofi-Aventis, UCB, Lilly, Novartis, and Celgene, Consultant of: AbbVie, Biogen, Janssen, BMS, Roche, Pfizer, Amgen, Sanofi-Aventis, UCB, Lilly, Novartis, and Celgene, Laure Gossec Speakers bureau: Abbvie, Amgen, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, Janssen, Sandoz, Sanofi-Aventis, UCB, Consultant of: Abbvie, Amgen, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, Janssen, Sandoz, Sanofi-Aventis, UCB, Grant/research support from: Abbvie, Amgen, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, Janssen, Sandoz, Sanofi-Aventis, UCB, Antonio Marchesoni Speakers bureau: AbbVie, BMS, Celgene, Eli-Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, BMS, Celgene, Eli-Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Janssen, Novartis, UCB, Grant/research support from: UCB, Koji Kato Shareholder of: AbbVie, Employee of: AbbVie, Erin McDearmon-Blondell Shareholder of: AbbVie, Employee of: AbbVie, Elizabeth Lesser Shareholder of: AbbVie, Employee of: AbbVie, Reva McCaskill Shareholder of: AbbVie, Employee of: AbbVie, Dai Feng Shareholder of: AbbVie, Employee of: AbbVie, Jaclyn Anderson Shareholder of: AbbVie, Employee of: AbbVie, Eric Ruderman Consultant of: AbbVie, Amgen, Gilead, Janssen, Lilly, Novartis, and Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.662

POS1036 COLLAGEN TURNOVER MARKERS ARE ASSOCIATED WITH ACTIVE PSORIATIC ARTHRITIS AND DECREASE WITH GUSELKUMAB TREATMENT IN A PHASE-3 CLINICAL TRIAL

G. Schett[1], M. J. Loza[2], A. Palanichamy[2], O. Fitzgerald[3], C. T. Ritchlin[4], F. Baribaud[2], K. Sweet[2]. [1]*Friedrich Alexander University Erlangen-Nuremberg and*



Universitätsklinikum Erlangen, Internal Medicine, Erlangen, Germany; [2]*Janssen Research & Development, LLC, Spring House, PA, United States of America*; [3]*University College Dublin, School of Medicine, Dublin 4, Ireland*; [4]*University of Rochester, Department of Medicine, Rochester, NY, United States of America*

Background: Guselkumab (GUS), an interleukin-23p19-subunit monoclonal antibody, demonstrated efficacy compared to placebo (PBO) in reducing skin and musculoskeletal signs and symptoms in patients with active psoriatic arthritis (PsA) in two phase-3 studies, DISCOVER-1 & -2, and in retarding structural damage in DISCOVER-2.[1,2]

Objectives: To evaluate tissue-derived extracellular matrix (ECM) products[3,4] in serum of PsA patients in the DISCOVER-2 study and their relationship with radiographic damage, clinical response, and impact of treatment.

Methods: In DISCOVER-2, patients were treated with GUS 100 mg at Week (w) 0, 4, then every 8w (q8w); GUS 100 mg every 4w (q4w); or matching PBO. At w24, PBO patients were crossed over to GUS q4w. A total of 11 serum biomarkers of ECM collagen formation (PRO-C1, PRO-C2, PRO-C3, PRO-C4, and PRO-C6) and degradation (C1M, C2M, C3M, C4M, C6M, and COL10) were measured (by Nordic Bioscience) in a subset of 260 patients from the DISCOVER-2 program at Weeks 0, 4, 24, & 52 and in 76 healthy controls matched for age, sex, and ethnicity. PsA patients were selected randomly, though enriching for subjects with greatest radiographic changes, at Weeks 24 and 52. Significance defined by $p<0.05$ and |fold difference| ≥1.25.

Results: At baseline, collagen degradation markers C1M, C3M, C4M, C6M and collagen formation markers PRO-C3 and PRO-C6 were significantly higher in the serum of PsA patients compared to matched healthy controls. Baseline C3M, C4M, and C6M were positively correlated to baseline skin and joint disease; baseline C1M, C3M, C4M, C6M, and PRO-C1 were positively correlated to baseline radiographic damage (data not shown). Levels of C1M (a maker indicating breakdown of collagen type I, the major collagen subtype in the bone) were significantly decreased after 24w treatment with GUS (Figure 1), reaching significant differences from placebo with the GUS 100 mg q4w group. For the PBO patients who crossed over to GUS at w24, there was also a reduction in this marker observed at w52 (Figure 1). In patients treated with GUS or PBO, there were no significant differences in baseline expression levels of the analytes in responders (patients achieving ACR20 at w24) compared with non-responders. However, ACR20 responders in the combined GUS group had a significantly greater reduction in C1M levels compared to non-responders (p=0.0065) at w24.

Conclusion: This work provides evidence that collagen biomarkers in serum are dysregulated in patients with PsA compared to healthy controls, and that GUS impacts levels of these proteins. Importantly, C1M serves as a biomarker that tracks with joint response. We observed a greater reduction in C1M in ACR responders compared to non-responders, providing insight into how GUS may be working to protect from degradation of bone in PsA.

REFERENCES:

[1] Deodhar A et al. *Lancet* 2020;395:1115-1125
[2] Mease PJ et al. *Lancet* 2020;395:1126-1136
[3] Gudmann NS et al. *Clin Exp Rheumatol* 2017;35:653-659
[4] Sardar S et al. *Annals of the Rheum Dis* 2019;78(Suppl 2): https://ard.bmj.com/content/78/Suppl_2/867.1

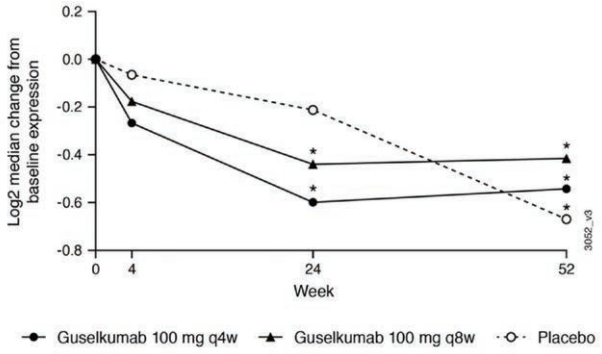


Figure. Collagen degradation marker C1M decreases with guselkumab treatment.
* Significant change from baseline defined by p < 0.05 and |fold difference| ≥1.25

Disclosure of Interests: Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Roche, UCB, Consultant of: AbbVie, BMS, Celgene,

Table 1. Safety Summary Through Week 24 by Monotherapy and Combination Therapy

Event, n (%)	Monotherapy			Combination		
	PBO (N=188)	UPA 15mg QD (N=189)	UPA 30mg QD (N=197)	PBO (N=447)	UPA 15mg QD (N=451)	UPA 30mg QD (N=444)
Any AE	127 (67.6)	124 (65.6)	145 (73.6)	264 (59.1)	298 (66.1)	331 (74.5)
Serious AE	8 (4.3)	9 (4.8)	9 (4.6)	9 (2.0)	17 (3.8)	35 (7.9)
AE leading to D/C of study drug	13 (6.9)	14 (7.4)	14 (7.1)	11 (2.5)	14 (3.1)	27 (6.1)
Deaths	1 (0.5)	0	0	1 (0.2)	0	0
Infection	65 (34.6)	67 (35.4)	88 (44.7)	148 (33.1)	173 (38.4)	203 (45.7)
Serious infection	2 (1.1)	1 (0.5)	2 (1.0)	3 (0.7)	5 (1.1)	15 (3.4)
Opportunistic infection excl. tuberculosis and herpes zoster	0	0	2 (1.0)	0	1 (0.2)	2 (0.5)
Herpes zoster	2 (1.1)	2 (1.1)	6 (3.0)	3 (0.7)	5 (1.1)	7 (1.6)
Active tuberculosis	0	0	0	0	0	0
Malignancy other than NMSC	0	3 (1.6)	1 (0.5)	0	0	2 (0.5)
NMSC	0	0	0	1 (0.2)	1 (0.2)	3 (0.7)
MACE (adjudicated)	0	0	0	1 (0.2)	1 (0.2)	0
VTE (adjudicated)	1 (0.5)	0	0	0	1 (0.2)	1 (0.2)
Hepatic disorder	5 (2.7)	8 (4.2)	14 (7.1)	14 (3.1)	35 (7.8)	56 (12.6)

AE, adverse event; CPK, creatine phosphokinase; D/C, discontinuation; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PBO, placebo; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolic events.

Janssen, Lilly, Novartis, Roche, UCB, Matthew J Loza Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Arumugam Palanichamy Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Oliver FitzGerald Speakers bureau: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Consultant of: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Christopher T. Ritchlin Speakers bureau: AbbVie, Amgen, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, Frederic Baribaud Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Kristen Sweet Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC.

DOI: 10.1136/annrheumdis-2021-eular.779

POS1037 CORRELATION BETWEEN SKIN INVOLVEMENT, JOINT INVOLVEMENT AND ENTHESITIS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: POST-HOC ANALYSIS OF EQUATOR/EQUATOR2

P. J. Mease[1,2], L. C. Coates[3], F. Van den Bosch[4], D. D. Gladman[5], L. Gheyle[6], M. Trivedi[7], M. Alani[7,8], E. Vetters[9], F. O. Le Brun[10], R. Besuyen[11], P. Helliwell[12]. *[1]Swedish Medical Center, Rheumatology Clinical Research Division, Seattle, United States of America*; *[2]University of Washington, School of Medicine, Seattle, United States of America*; *[3]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; *[4]Ghent University, VIB Center for Inflammation Research, Ghent, Belgium*; *[5]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Canada*; *[6]Galapagos NV, Clinical Research, Mechelen, Belgium*; *[7]Gilead Sciences, Inc., Clinical Research, Foster City, United States of America*; *[8]University of Washington, Rheumatology Department, Seattle, United States of America*; *[9]Galapagos NV, Biometrics, Mechelen, Belgium*; *[10]Galapagos GmbH, Biometrics, Basel, Switzerland*; *[11]Galapagos BV, Clinical Research, Leiden, Netherlands*; *[12]University of Leeds, School of Medicine, Leeds, United Kingdom*

Background: Psoriatic arthritis (PsA) is a heterogeneous, inflammatory disease involving multiple clinical domains including arthritis/synovitis, enthesitis, dactylitis, spondylitis and psoriasis. Effects on each domain should be assessed to determine the overall quality of treatment. Filgotinib (FIL) is a novel preferential Janus kinase 1 inhibitor that is in development for inflammatory conditions including PsA. EQUATOR (NCT03101670) was a 16-week, Phase 2, double-blind, randomised, placebo (PBO)-controlled trial of FIL for patients with active PsA.[1] EQUATOR2 (NCT03320876) is an open-label extension (OLE) of the study.

Objectives: This post-hoc analysis of EQUATOR and EQUATOR2 assessed the patient-level correlation between changes over time in the three PsA clinical disease domains of skin, joint and enthesitis in patients treated with FIL.

Methods: In EQUATOR, patients with active moderate-to-severe PsA (≥5 swollen joints and ≥5 tender joints, fulfilling Classification for PsA criteria) were randomised 1:1 to receive oral FIL 200 mg or PBO once daily (QD) for 16 weeks. At Week 16, patients could continue into the 304-week OLE, with all patients receiving FIL 200 mg QD regardless of previous treatment in EQUATOR. This post-hoc analysis was limited to patients with skin involvement (≥3% body surface area), joint involvement and enthesitis at baseline, with changes from baseline in the three domains assessed using the Psoriasis Area and Severity Index (PASI), swollen/tender joint count (S/TJC), and the Leeds Enthesitis Index (LEI) and Spondyloarthritis Research Consortium of Canada (SPARCC) index, respectively. Analyses that used LEI as the enthesitis index to assess change from baseline included patients with LEI score ≥1 at baseline; those using SPARCC included patients with SPARCC score ≥1 at baseline.

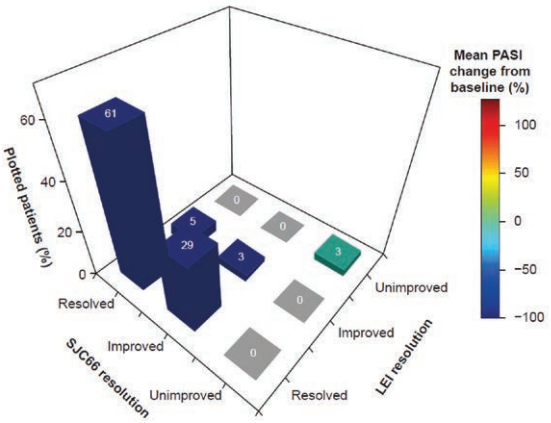
Results: The EQUATOR study enrolled 131 patients and 122 patients continued into the EQUATOR2 OLE. Of the 131 patients enrolled in EQUATOR, 49 and 56 patients had PsA involving all three domains at core study baseline when enthesitis was assessed using LEI and SPARCC index, respectively. Pooled data for all patients receiving FIL during the OLE indicate that improvements from baseline in the clinical domains continued with long-term treatment, with 22/42 (52%) and 23/38 (61%) patients having both SJC66 and LEI resolution at Weeks 52 and 100, respectively. For the 22 patients with both SJC and LEI resolution at Week 52, the mean percent change from baseline for PASI was –64%; for the 23 patients with both SJC and LEI resolution at Week 100, the mean percent change from baseline for PASI was –60%. The Figure 1 shows correlation between SJC, LEI and PASI at Week 100. A relationship between the three clinical domains was observed at the individual level; within a single patient, an improvement in one domain was generally followed by improvements in the other two domains. With regard to the sequence in which changes were observed, joints improved first, followed by improvements in the skin and enthesitis. There were no notable differences between changes in LEI and SPARCC enthesitis index in terms of their correlation with improvements in joint and skin involvement. Similarly, there were no notable differences in correlation between the three domains when joints were assessed using TJC rather than SJC.

Conclusion: Patients with improvements in skin, joints or enthesitis following treatment with FIL generally also had improvements in the other clinical domains of PsA. The joints were found to be the first of the three domains to improve.

REFERENCES:

[1] Mease P et al. *Lancet* 2018;392:2367–77

Figure: Correlation between SJC, LEI and PASI at Week 100 of the OLE



Plot shows observed cases. Number of plotted patients: 38 out of 49 patients with involvement in all three clinical domains at baseline.
Resolved: −100% percent change from baseline; Improved: −100% < percent change from baseline < 0%;
Unimproved: 0% ≤ percent change from baseline.
Patients were on placebo or filgotinib (200 mg) during the core study (initial 16 weeks).
LEI, Leeds Enthesitis Index; OLE, open-label extension; PASI, Psoriasis Area and Severity Index; SJC(66), (66-)swollen joint count.

Acknowledgements: EQUATOR and EQUATOR2 were sponsored by Galapagos NV (Mechelen, Belgium) and co-funded by Galapagos NV and Gilead Sciences, Inc (Foster City, CA, USA). Medical writing/editorial support was provided by Debbie Sherwood, BSc, CMPP (Aspire Scientific, Bollington, UK), funded by Galapagos NV.

Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead Sciences, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead Sciences, Janssen, Novartis, Pfizer, SUN and UCB, Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Gilead, Janssen, Medac, Novartis, Pfizer and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Novartis, and Pfizer, Filip van den Bosch Consultant of: AbbVie, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Merck and UCB, Dafna D Gladman Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB, Lien Gheyle Shareholder of: Galapagos, Employee of: Galapagos, Mona Trivedi Shareholder of: Gilead Sciences, Amgen, Employee of: Gilead Sciences, Muhsen Alani Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Eline Vetters Employee of: Galapagos, Franck Olivier Le Brun Shareholder of: Galapagos, Employee of: Galapagos, Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, Philip Helliwell Speakers bureau: Janssen and Novartis, Paid instructor for: Pfizer, Consultant of: Eli Lilly.

DOI: 10.1136/annrheumdis-2021-eular.883

POS1038 THE EFFECT OF FILGOTINIB ON ENTHESITIS: 100-WEEK DATA FROM AN OPEN-LABEL EXTENSION STUDY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

P. Helliwell[1], L. C. Coates[2], F. Van den Bosch[3], D. D. Gladman[4], L. Gheyle[5], M. Trivedi[6], M. Alani[6,7], F. O. Le Brun[8], R. Besuyen[9], P. J. Mease[10,11]. *[1]University of Leeds, School of Medicine, Leeds, United Kingdom*; *[2]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; *[3]Ghent University, VIB Center for Inflammation Research, Ghent, Belgium*; *[4]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Canada*; *[5]Galapagos NV, Clinical Research, Mechelen, Belgium*; *[6]Gilead Sciences, Inc., Clinical Research, Foster City, United States of America*; *[7]University of Washington, Rheumatology Department, Seattle, United States of America*; *[8]Galapagos GmbH, Biometrics, Basel, Switzerland*; *[9]Galapagos BV, Clinical Research, Leiden, Netherlands*; *[10]Swedish Medical Center, Rheumatology Clinical Research Division, Seattle, United States of America*; *[11]University of Washington, School of Medicine, Seattle, United States of America*

Background: Filgotinib (FIL), a novel preferential Janus kinase 1 inhibitor, was assessed in patients with active psoriatic arthritis (PsA) in the 16-week, Phase 2, EQUATOR trial (NCT03101670).[1] EQUATOR2 (NCT03320876) is the open-label extension (OLE). As previously reported, an interim analysis of the OLE showed that the majority of patients had clinical resolution of enthesitis by Week 52.[2]

Objectives: This post-hoc analysis evaluated the effect of FIL on clinical enthesitis after 100 weeks of treatment in the OLE, as assessed using the Leeds Enthesitis Index (LEI) and Spondyloarthritis Research Consortium of Canada (SPARCC) index, and evaluated the discriminatory capacity of the two indices. In addition, we assessed which of the sites included in LEI and SPARCC were most frequently involved and whether treatment effect was consistent across sites.
Methods: In EQUATOR, patients with active moderate-to-severe PsA (≥5 swollen joints and ≥5 tender joints, fulfilling Classification for PsA criteria) were randomised 1:1 to receive oral FIL 200 mg or placebo (PBO) once daily (QD) for 16 weeks. At Week 16, all patients could continue into the OLE, receiving FIL 200 mg QD for up to an additional 304 weeks. We compared changes from core baseline in LEI and SPARCC measures, the effect on enthesitis at sites included in LEI and SPARCC assessments and the discriminatory capacity of both enthesitis indices.
Results: Of 131 patients randomised to EQUATOR, 122 entered the OLE. There was strong agreement between LEI and SPARCC at baseline. While most patients had enthesitis at baseline according to either index (76/131 [58.0%] by LEI; 85/131 [64.9%] by SPARCC), a minority had enthesitis at a large number of sites (6.9% with 5–6 LEI sites; 12.2% with ≥9 SPARCC sites). The sites most frequently involved at baseline were the lateral epicondyle humerus and Achilles tendon, sites common to both LEI and SPARCC. There was greater variability in the change from baseline to Week 16 in SPARCC compared with LEI (Table 1). LEI showed a greater discriminatory capacity than SPARCC when change from baseline was compared for FIL vs PBO at Week 16, as shown by higher absolute standardised mean difference: –0.70 (LEI) and –0.30 (SPARCC) (observed cases; Table 1). Subgroup analyses indicated that the treatment effect of FIL vs PBO at Week 16 for all sites was consistent with the overall treatment effect seen for LEI or SPARCC, and indicative of an improvement with FIL vs PBO for nearly all sites. The proportion of patients with enthesitis decreased from baseline up to OLE Week 100 (Figure 1). There were no major differences in long-term effect on enthesitis between sites.
Conclusion: FIL improved enthesitis consistently across sites compared with PBO. Rapid improvement in enthesitis was seen up to Week 16 of the core study and improvements continued up to Week 52, after which responses were generally stable up to Week 100. LEI assesses fewer locations than SPARCC, but reassuringly captured the sites most commonly affected by enthesitis; LEI also had greater discriminatory capacity.

TABLE: Mean change from baseline in enthesitis assessed by LEI and SPARCC

Index	Imputation	Filgotinib		Placebo		Pooled SD	Mean difference	Standardised mean difference	Guyatt effect size
		n	Mean (SD) change from baseline at Week 16	n	Mean (SD) change from baseline at Week 16				
SPARCC	OC	34	−2.9 (3.43)	47	−1.9 (3.24)	3.32	−1.0	−0.30	−0.90
SPARCC	LOCF	37	−2.8 (3.29)	47*	−1.9 (3.24)	3.26	−0.9	−0.28	−0.86
LEI	OC	30	−1.7 (1.49)	43	−0.7 (1.37)	1.42	−1.0	−0.70	−1.24
LEI	LOCF	33	−1.8 (1.49)	43	−0.7 (1.37)	1.42	−1.1	−0.77	−1.31

Includes patients with enthesitis at core study baseline

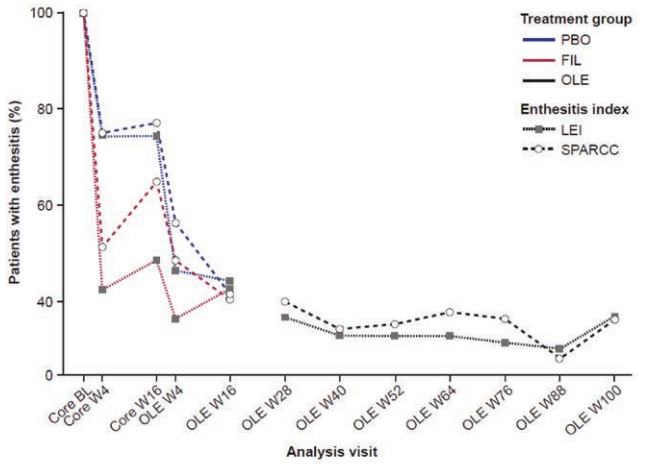
*One patient with SPARCC enthesitis at baseline had no post-baseline value

LEI, Leeds Enthesitis Index; LOCF, last observation carried forward; OC, observed case; SD, standard deviation; SPARCC, Spondyloarthritis Research Consortium of Canada

REFERENCES:

[1] Mease P, et al. *Lancet* 2018;392:2367–77
[2] Mease P, et al. *Arthritis Rheumatol* 2020;72(suppl 10): abstract 0910

Figure: Proportion of patients with enthesitis over time



Includes patients with enthesitis at baseline. Non-responder imputation.
From core Week 16 to OLE Week 16, patients are presented according to original treatment, but all received filgotinib during this time and for the remainder of the OLE.
BL, baseline; FIL, filgotinib; LEI, Leeds Enthesitis Index; OLE, open-label extension; PBO, placebo; SPARCC, Spondyloarthritis Research Consortium of Canada; W, Week.

Figure 1.

Acknowledgements: EQUATOR and EQUATOR2 were sponsored by Galapagos NV (Mechelen, Belgium) and co-funded by Galapagos NV and Gilead Sciences, Inc (Foster City, CA, USA). Eline Vetters, Leen Gilles, Benjamin Pett and his team, all employees of Galapagos, provided assistance with statistical analyses. Medical writing/editorial support was provided by Debbie Sherwood, BSc, CMPP (Aspire Scientific, Bollington, UK), and funded by Galapagos NV.

Disclosure of Interests: Philip Helliwell Speakers bureau: Janssen, Novartis, Paid instructor for: Pfizer, Consultant of: Eli Lilly, Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Gilead, Janssen, Medac, Novartis, Pfizer and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Novartis, and Pfizer, Filip van den Bosch Consultant of: AbbVie, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Merck and UCB, Dafna D Gladman Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB, Lien Gheyle Shareholder of: Galapagos, Employee of: Galapagos, Mona Trivedi Shareholder of: Gilead Sciences, Amgen, Employee of: Gilead Sciences, Muhsen Alani Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Franck Olivier Le Brun Shareholder of: Galapagos, Employee of: Galapagos, Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead Sciences, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead Sciences, Janssen, Novartis, Pfizer, SUN and UCB.
DOI: 10.1136/annrheumdis-2021-eular.884

POS1039 PSORIATIC ARTHRITIS AND PHYSICAL ACTIVITY, A SYSTEMATIC REVIEW

J. Kessler[1], M. Chouk[2], T. Ruban[1], C. Prati[1], D. Wendling[1], F. Verhoeven[1].
[1]Besançon University Hospital, Rheumatology, Besançon, France; *[2]Besançon University Hospital, Rheumatology, Besançon, France*

Background: The beneficial effects of physical activity (PA) have been demonstrated in rheumatoid arthritis and ankylosing spondylitis on disease and co-morbidities while they are not clearly established in psoriatic arthritis.
Objectives: Thus, the aim of this study was, on the basis of a systematic review of the literature, (i) to assess the level of physical activity in these patients and (ii) to determine the effects of physical activity on joint and extra articular symptoms and on well-being.
Methods: The research strategy was performed on Pubmed, Cochrane,and PEDro databases using the following keywords: “psoriatic arthritis AND physical activity” without restriction. Articles published in English before October 2019 were identified and selected according to the PRISMA methodology by two independent investigators. In case of disagreement, a third investigator was interviewed. To be included in the qualitative synthesis, the studies had to meet the PICOS criteria.
Results: Among the 259 studies identified, 13 were finally included. 241 were excluded because they did not address the topic or were not in English and 5 were duplicated. Two epidemiological studies revealed that 17 and 68 % of patients comply with WHO recommendations for the general population in terms of physical activity. The main explanations expressed by patients are; a lack of promotion of physical activity by the rheumatologist and the fear of pain during the movement also called “kinesiophobia”. Among the three prospective randomized clinical trials, one of them showed a significant 20% reduction in the BASDAI (Bath Ankylosing Spondylitis Disease) and a 25% reduction in pain. Fatigue was significantly reduced by 15% following a physical activity protocol on a cyclergometer for 11 weeks. Muscle strength and maximum VO2 were significantly improved after participation in the physical activity protocol in two of the clinical trials. Four retrospective studies evaluated the effect of physical activity on the risk of enthesitis or dactylitis. None were associated with an increased risk of enthesitis. However, physical activity was found to be a risk factor for structural remodelling of the Achilles tendon. And, avoiding physical activity seems to be a protective factor against the risk of enthesitis. On the other hand, the three clinical trials did not mention any increase in the disease’s activity score. Finally, the effects of four rehabilitation programs have been evaluated in psoriatic arthritis and other inflammatory rheumatism. The beneficial effects were modest and concerned the reduction of pain for all the programs and of fatigue for two of the programs.
Conclusion: The studies showed a beneficial effect of physical activity on disease activity, on well-being and on comorbidities. The data on the risk of enthesitis are reassuring. Further investigations are necessary to confirm these results and to precise the modalities of exercise.

Table 1. PICOS criteria according to PRISMA methodology.

Participants	Adults > 18 years old, Psoriatic Arthritis defined to CASPAR classification criteria (2006) or Moll Wright criteria (1973)
Intervention	Any type of physical activity regardless of intensity and duration
Comparison	Control group (not mandatory)
Outcomes	Level of physical activity Disease activity score Comorbidities
Study design	No restriction

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.926

POS1040

IMPLEMENTATION OF THE OMERACT PSAMRIS IN A PHASE IIB, RANDOMISED PLACEBO-CONTROLLED STUDY OF ABATACEPT IN PSORIATIC ARTHRITIS

M. Østergaard[1,2], P. Bird[3], C. Pachai[4], S. Du[4], C. Wu[5], J. Landis[5], T. Fuerst[6], H. A. Ahmad[7], S. Connolly[8], P. G. Conaghan[9]. *[1]Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen Center for Arthritis Research, Glostrup, Denmark*; *[2]University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark*; *[3]University of New South Wales (NSW), Division of Medicine, Sydney, Australia*; *[4]Bristol Myers Squibb, Translational Medicine, Princeton, United States of America*; *[5]Bristol Myers Squibb, Translational Bioinformatics, Princeton, United States of America*; *[6]BioClinica, Inc., Medical and Scientific Affairs, Newark, United States of America*; *[7]Bristol Myers Squibb, Medical Affairs, Immunology & Fibrosis, Princeton, United States of America*; *[8]Bristol Myers Squibb, Global Drug Development, Princeton, United States of America*; *[9]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*

Background: The semi-quantitative Outcome Measures in Rheumatology (OMERACT) Psoriatic Arthritis Magnetic Resonance Imaging Score (PsAMRIS) was developed for the evaluation of inflammatory and destructive changes in PsA,[1] but has limited trial usage.

Objectives: To retrospectively utilise the PsAMRIS in a multi-dose, randomised Phase IIb study of abatacept in patients with PsA who have inadequate response to DMARDs (NCT00534313).[2]

Methods: Patients were randomised to abatacept (3, 10 or 30/10mg/kg [the 30-mg/kg group switched to 10mg/kg after the first two doses]) or placebo and treated for 169 days, after which all patients received abatacept 10mg/kg through to Day 365. MRI scans of one hand or foot from 123 patients with PsA collected at baseline and on Days 85, 169 and 365 were centrally evaluated by two readers blinded to chronological order and treatment arm. Synovitis, bone oedema, tenosynovitis, periarticular inflammation, bone erosion, bone proliferation and joint space narrowing were assessed as per OMERACT PsAMRIS; a novel total inflammation score was calculated from the sum of synovitis, bone oedema, tenosynovitis and periarticular inflammation. Variables were analysed using all cases (hand or foot) and by hand and foot cases separately.

Results: At Day 169, the abatacept 30/10mg/kg or 10mg/kg group showed the most decrease (improvement) in each inflammatory assessment (Figure 1). The Day 169 change from baseline severity in synovitis and tenosynovitis in the abatacept 30/10mg/kg and 10mg/kg groups, respectively, were significantly reduced (improved) compared with placebo (estimated differences of –0.966 [p=0.039] and –1.652 [p=0.014], respectively) (Table 1). Patients originally randomised to placebo and then switched to abatacept 10mg/kg at Day 169 showed significant improvements in synovitis, tenosynovitis and total inflammation from Day 169 to Day 365 (Table 1, Figure 1). The structural outcomes joint space narrowing and bone erosion remained stable within each treatment group, showing little change from baseline to Days 85, 169 and 365. After separating hand and foot analyses (72 hand and 51 foot cases), only hand tenosynovitis in the 10-mg/kg group and foot synovitis in the 3-mg/kg group were significantly reduced (improved) at Day 169 compared with placebo (differences of –2.331 [p=0.017] and –1.689 [p=0.010], respectively). In general, more comparisons in the hand analysis were statistically significant versus in the foot analysis.

Conclusion: This analysis confirmed the efficacy of abatacept 10 and 30/10mg/kg when assessed with the OMERACT PsAMRIS. The inflammatory pathologies, synovitis and tenosynovitis, appeared to be the most responsive MRI outcomes. Analysing hand and foot cases together yielded results consistent with the primary clinical efficacy endpoint (ACR20 response rate), as the abatacept 10- and 30/10-mg/kg groups showed significant differences versus placebo at Day 169;[2] reduced sample size in separate hand and foot assessments may have prevented finding significant results corresponding to the combined analysis. These results also demonstrate the responsiveness of the PsAMRIS in PsA randomised clinical trials.

REFERENCES:

[1] Glinatsi D, et al. *J Rheumatol* 2015;42:2473–2479.
[2] Mease P, et al. *Arthritis Rheum* 2011;63:939–948.

Table 1. MRI variables showing significant treatment effects[a]

Between groups at Day 169

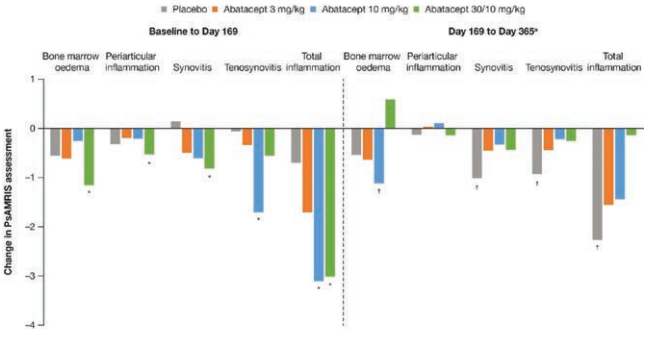
MRI score	Comparator	Comparator	Difference	SE	p value
Synovitis	Placebo	Abatacept 30/10 mg/kg	–0.966	0.461	0.039
Tenosynovitis	Placebo	Abatacept 10 mg/kg	–1.652	0.662	0.014

Placebo group before/after switch[b]

MRI score	Treatment, Day 169	Treatment, Day 365	Difference	SE	p value
Synovitis	Placebo	Abatacept 10 mg/kg	–1.018	0.458	0.029
Tenosynovitis	Placebo	Abatacept 10 mg/kg	–0.940	0.390	0.018
Total inflammation	Placebo	Abatacept 10 mg/kg	–2.275	1.067	0.036

[a]Based on change from baseline at the stated time points (unadjusted p values).
[b]Patients were switched to abatacept 10 mg/kg after Day 169.

Figure 1. Change in PsAMRIS assessments of inflammation



*All patients switched to abatacept 10 mg/kg after Day 169.
†Significant change from baseline based on least squares mean and 95% CI.
‡Significant difference in change from baseline from Day 169 to Day 365, based on unadjusted p value <0.05.
PsAMRIS=Psoriatic Arthritis Magnetic Resonance Imaging Score.

Acknowledgements: Professional medical writing and editorial assistance was provided by Rob Coover, MPH, at Caudex and was funded by Bristol Myers Squibb.
Disclosure of Interests: Mikkel Østergaard Speakers bureau: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, UCB, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Merck, Novartis, Paul Bird Speakers bureau: AbbVie, Bristol Myers Squibb, Eli Lilly, Novartis, Pfizer, UCB, Grant/research support from: Gilead, Chahin Pachai Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Shuyan Du Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Chun Wu Employee of: Bristol Myers Squibb, Jessica Landis Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Thomas Fuerst Employee of: Bioclinica, Inc., a contract research service providing radiology central reading services to pharmaceutical, biotech and medical device companies, Harris A Ahmad Employee of: Bristol Myers Squibb, Sean Connolly Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Philip G Conaghan Speakers bureau: AbbVie, Novartis, Consultant of: AstraZeneca, Bristol Myers Squibb, Eli Lilly, EMD Serono, Flexion Therapeutics, Galapagos, Gilead, Novartis, Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.972

POS1041

PREVALENCE, INCIDENCE AND ANTIRHEUMATIC DRUG USE IN PSORIATIC ARTHRITIS (PsA) IN NORWAY

A. Kerola[1,2], J. Sexton[1], S. Rollefstad[1], G. Wibetoe[1], C. S. Crowson[3], E. Haavardsholm[1], T. K. Kvien[1], A. G. Semb[1]. [1]*Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway*; [2]*Päijät-Häme Joint Authority for Health and Wellbeing, Rheumatology, Lahti, Finland*; [3]*Mayo Clinic, Department of Quantitative Health Sciences, Rochester, Minnesota, United States of America*

Background: Incidence estimates of PsA in Norway have varied from 6.9/100,000 person-years (pyrs) in Northern Norway to 41.3/100,000 pyrs in Central Norway, and point prevalence estimates have ranged from 1.3 to 6.9 per 1,000 adult inhabitants[1,2], while nationwide epidemiologic data on PsA in Norway have been lacking.
Objectives: To estimate prevalence, incidence and use of disease-modifying antirheumatic drugs (DMARDs) among PsA patients in Norway.
Methods: The Norwegian Cardio-Rheuma register includes pseudonymized data from the total Norwegian population ≥18 years of age during 2008-2017, identified from the National Population register. Demographic and socioeconomic data were retrieved from Statistics Norway. Data on public or private somatic specialized care episodes were collected from the Norwegian Patient register (NPR) [ICD-10 codes for diagnoses and medical procedure codes for biologic DMARD infusions]. Information on dispensed DMARD prescriptions was captured from the Norwegian Prescription Database. Based on NPR data, PsA cases were defined as persons fulfilling three criteria: 1) 1st episode with ICD-10 code M07.0-M07.3 or L40.5 as main or contributory diagnosis (index date), 2) 2nd episode with code M07.0-M07.3 or L40.5 within 2-year period following index date, 3) an episode in internal medicine or rheumatology clinic with recorded M07.0-M07.3 or L40.5 within 2 years from index date. Years 2008-2010 served as a look-back period to identify prevalent PsA cases. To estimate pyrs at risk, we calculated number of individuals aged ≥ 18 years living in Norway on the 1st of January of each year 2011-2015 multiplied by one year (prevalent PsA cases excluded). Age- and sex-standardized incidence rates were calculated with 5-year age groups using the Norwegian adult population on January 1st 2015 as the standard.
Results: During the look-back period 2008-2010, 7,697 cases fulfilled the PsA definition. In total, 6,183 incident PsA cases were identified during 2011-2015 (incidence 32/100,000 pyrs, 28 among men and 35 among women). Based on a sensitivity analysis comprising 5,065 PsA cases with no dispensed DMARD prescriptions ≥12 months before index date, incidence was slightly lower (26/100,000 pyrs). Patient characteristics and DMARD use are shown in Table 1. The incidence was highest among those aged 50-59 years in both sexes (Figure 1). PsA incidence was lower among those with higher education level (crude/age- and sex-standardized incidence per 100,000 pyrs for those below upper secondary education 34/38, upper secondary or post-secondary non-tertiary education 36/36, higher education 26/25). Point prevalence of PsA was 3.3/1,000 adult inhabitants on January 1st 2016.

Table 1. Characteristics and treatment penetration of incident PsA patients 2011-2015

	All		Excluding cases with DMARDs >1 yr prior to index date	
N	6183		5065	
Women, n (%)	3442 (55.7)		2783 (54.9)	
Age at index date, median (IQR)	50.5 (40.7 - 59.8)		49.9 (40.2 - 59.3)	
Use of DMARDs after index date, n (%)	**12 months**	**24 months**	**12 months**	**24 months**
Any conventional DMARD	3706 (59.9)	4048 (65.4)	2894 (57.1)	3184 (62.9)
Methotrexate	3313 (53.6)	3650 (59.0)	2638 (52.1)	2933 (57.9)
Sulfasalazine	440 (7.1)	586 (9.5)	330 (6.5)	457 (9.0)
Any biologic DMARD	842 (13.6)	1197 (19.4)	485 (9.6)	771 (15.2)
TNF-inhibitors	810 (13.1)	1154 (18.7)	477 (9.4)	758 (15.0)
Oral glucocorticoids	1773 (28.7)	2240 (36.2)	1449 (28.6)	1807 (35.7)
Any DMARD or glucocorticoids	4365 (70.6)	4742 (76.7)	3384 (66.8)	3725 (73.5)

Conclusion: Our estimate of PsA incidence and prevalence are in the mid-range compared to studies from smaller regions in Norway. Methotrexate was initiated for more than half of PsA cases within one year from index date, whereas 19% had used biologic DMARDs within two years.

REFERENCES:

[1] Hoff M, Gulati A, Romundstad P et al. Prevalence and incidence rates of psoriatic arthritis in central Norway: data from the Nord-Trondelag health study. Ann Rheum Dis 2015;74:60-64.
[2] Nossent J & Gran J. Epidemiological and clinical characteristics of psoriatic arthritis in northern Norway. Scand J Rheumatol 2009; 8:251-5.

Acknowledgements: This work has been supported by a research grant from FOREUM Foundation for Research in Rheumatology.

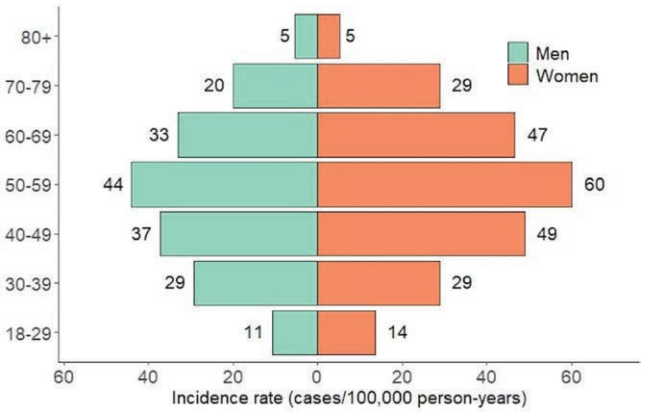


Figure 1.

Disclosure of Interests: Anne Kerola Speakers bureau: Boehringer-Ingelheim, Consultant of: Pfizer, Gilead and Boehringer-Ingelheim, Joseph Sexton: None declared, Silvia Rollefstad: None declared, Grunde Wibetoe: None declared, Cynthia S. Crowson: None declared, Espen Haavardsholm: None declared, Tore K. Kvien Speakers bureau: Amgen, Celltrion, Egis, Evapharma, Ewopharma, Hikma, Oktal, Sandoz, Sanofi, Consultant of: AbbVie, Amgen, Biogen, Celltrion, Eli Lilly, Gilead, Mylan, Novartis, Pfizer, Sandoz, Sanofi, Grant/research support from: research funding to Diakonhjemmet Hospital from AbbVie, Amgen, BMS, MSD, Pfizer and UCB, Anne Grete Semb Speakers bureau: AbbVie, Bayer, Lilly, Novartis, Sanofi, Consultant of: Sanofi, Grant/research support from: Collaborative research support from Lilly, outside the submitted work.
DOI: 10.1136/annrheumdis-2021-eular.980

POS1042

EFFICACY AND SAFETY OF DEUCRAVACITINIB, AN ORAL, SELECTIVE TYROSINE KINASE 2 (TYK2) INHIBITOR, COMPARED WITH PLACEBO AND APREMILAST IN MODERATE TO SEVERE PLAQUE PSORIASIS: RESULTS FROM THE PHASE 3 POETYK PSO-1 STUDY

A. Armstrong[1], M. Gooderham[2], R. B. Warren[3], K. Papp[4], B. Strober[5,6], D. Thaçi[7], E. Colston[8], J. Throup[9], S. Kundu[10], S. Banerjee[11], A. Blauvelt[12]. [1]*Keck School of Medicine, University of Southern California, Los Angeles, United States of America*; [2]*SKiN Center for Dermatology, Queen's University and Probity Medical Research, Peterborough, Canada*; [3]*Dermatology Center, Salford Royal NHS Foundation Trust Hospital, Manchester NIHR Biomedical Research Center, University of Manchester, Manchester, United Kingdom*; [4]*Clinical Research and Probity Medical Research, K. Papp Clinical Research, Waterloo, Canada*; [5]*Yale University, Dermatology, New Haven, United States of America*; [6]*Central Connecticut Dermatology Research, Co-founder, Cromwell, United States of America*; [7]*University of Lübeck, Comprehensive Centre for Inflammation Medicine, Lübeck, Germany*; [8]*Bristol Myers Squibb, Dermatology, Princeton, United States of America*; [9]*Bristol Myers Squibb, Immunoscience R&D, Princeton, United States of America*; [10]*Bristol Myers Squibb, Global Biometrics Sciences, Princeton, United States of America*; [11]*Bristol Myers Squibb, Rheumatology and Dermatology, Princeton, United States of America*; [12]*Oregon Medical Research Center, Dermatology, Portland, United States of America*

Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates interleukin (IL)-23, IL-12, and interferon (IFN)α/β signaling. Deucravacitinib is a novel, oral, selective inhibitor of TYK2 acting via binding to the TYK2 regulatory domain.[1] Phase 2 results showed deucravacitinib was efficacious and well tolerated versus placebo in patients with moderate to severe plaque psoriasis or active psoriatic arthritis.[2,3] No herpes zoster infections, opportunistic infections, thromboembolic events, or hematologic or lipid abnormalities characteristic of Janus kinase (JAK) 1–3 inhibitors were reported in the Phase 2 trials.[2,3]
Objectives: To compare the efficacy and safety of deucravacitinib versus placebo and apremilast in plaque psoriasis.
Methods: This Phase 3, double-blinded, 52-week study (NCT03624127) randomized patients with moderate to severe plaque psoriasis (BSA ≥10%, PASI ≥12, sPGA ≥3) to deucravacitinib 6 mg once daily, placebo, or apremilast 30 mg twice daily (2:1:1). Patients receiving placebo were switched to deucravacitinib at Week 16; apremilast-treated patients not achieving PASI 50 at Week 24 were switched to deucravacitinib. Coprimary endpoints were PASI 75 and sPGA 0/1 response versus placebo at Week 16. Key secondary endpoints included superiority versus apremilast, assessed via multiple measures.
Results: 666 patients were randomized. Demographic and baseline disease characteristics were balanced across groups; mean age was 46.1 years, mean

disease duration was 17.3 years, 18.2% of patients had psoriatic arthritis at baseline, and 38.9% had previously used biologic therapy. Mean BSA involvement at baseline was 26.3%, mean PASI was 21.4, and the percentage with severe sPGA (score=4) at baseline was 21.2%. Significantly greater proportions of patients in the deucravacitinib versus placebo and apremilast arms achieved PASI 75 (58.7% vs 12.7% vs 35.1%, respectively; *P*<0.0001) and sPGA 0/1 (53.6% vs 7.2% vs 32.1%, respectively; *P*<0.0001) response at Week 16 (Figure 1). Deucravacitinib was also superior to apremilast at Week 24, with 69.0% versus 38.1% of patients achieving PASI 75 and 58.4% versus 31.0% achieving sPGA 0/1 (*P*<0.0001 for both). In addition, DLQI 0/1 responses at Week 16 were significantly higher with deucravacitinib versus placebo and apremilast, demonstrating improved quality of life (40.7% vs 10.6% vs 28.6%, respectively; Figure 1). During the 16-week, placebo-controlled period, the most common AEs (≥5% in any arm) were nasopharyngitis, upper respiratory tract infection, headache, diarrhea, and nausea (Table 1). Frequencies of SAEs and treatment discontinuations due to AEs were low (Table 1).

Table 1. Summary of adverse events (AEs) through Week 16

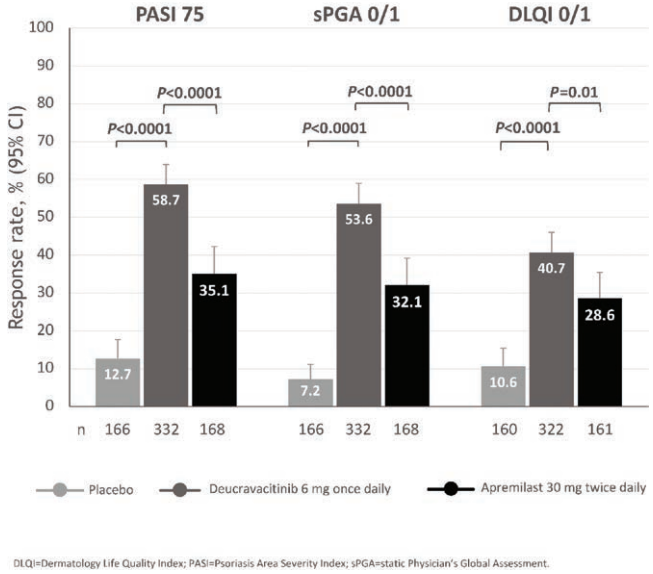
Patients, n (%)	Deucravacitinib n=332	Placebo n=165	Apremilast n=168
Any AEs	176 (53.0)	70 (42.4)	93 (55.4)
Severe AEs	5 (1.5)	7 (4.2)	5 (3.0)
Serious AEs	7 (2.1)	9 (5.5)	4 (2.4)
AEs leading to treatment discontinuation	6 (1.8)	7 (4.2)	10 (6.0)
Most common AEs (≥5% in any arm)			
Nasopharyngitis	21 (6.3)	7 (4.2)	14 (8.3)
Upper respiratory tract infection	21 (6.3)	6 (3.6)	3 (1.8)
Headache	16 (4.8)	5 (3.0)	17 (10.1)
Diarrhea	13 (3.9)	6 (3.6)	17 (10.1)
Nausea	7 (2.1)	4 (2.4)	19 (11.3)

Conclusion: Deucravacitinib demonstrated superiority versus placebo and apremilast across multiple efficacy endpoints in patients with moderate to severe plaque psoriasis, and was generally well tolerated. Overall, the efficacy and safety profile of deucravacitinib was consistent with that observed in the Phase 2 plaque psoriasis and psoriatic arthritis trials.[2,3]

REFERENCES:

[1] Burke JR et al. *Sci Transl Med.* 2019;11:1-16.
[2] Papp K et al. *N Engl J Med.* 2018;379:1313-21.
[3] Mease PJ et al. Presented at: Annual Scientific Meeting of the American College of Rheumatology; November 5-9, 2020; Virtual meeting.

Figure. Efficacy responses at Week 16



DLQI=Dermatology Life Quality Index; PASI=Psoriasis Area Severity Index; sPGA=static Physician's Global Assessment.

Acknowledgements: This study was sponsored by Bristol Myers Squibb. Professional medical writing assistance was provided by Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

Disclosure of Interests: April Armstrong Consultant of: Grants and personal fees from AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, Novartis; Personal fees from Boehringer Ingelheim/Parexel, Celgene, Dermavant, Genentech, GlaxoSmithKline, Menlo Therapeutics, Merck, Modernizing Medicine, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Science 37, Sun Pharma, Valeant, Grant/research support from: Grants: Dermira, Kyowa Hakko Kirin, and UCB, outside the submitted work; Grants and personal fees from AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, Novartis, Melinda Gooderham Shareholder of: Speakers bureau, consultant, investigator/advisor: AbbVie, Akros, Amgen, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Janssen, Kyowa Hakko Kirin, Leo Pharma, Merck, MedImmune, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Takeda, UCB, Valeant, Richard B. Warren Consultant of: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, Leo Pharma, Eli Lilly, Novartis, Pfizer, Sanofi, Xenoport, UCB, Grant/research support from: AbbVie, Almirall, Amgen, Celgene, Janssen, Eli Lilly, Leo Pharma, Novartis, Pfizer, UCB, Kim Papp Speakers bureau: AbbVie, Amgen, Astellas, Celgene, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Leo Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Valeant, Consultant of: Scientific officer/steering committee/advisory board: AbbVie, Akros, Amgen, Anacor, Astellas, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Merck Sharp & Dohme, Merck Serono, Novartis, Pfizer, Regeneron, Sanofi-Aventis/Genzyme, Valeant, Grant/research support from: AbbVie, Akros, Allergan, Amgen, Anacor, Arcutis, AstraZeneca, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Leo Pharma, MedImmune, Meiji Seika Pharma, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant;
Consultant: AbbVie, Akros, Amgen, Arcutis, Astellas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, CanFite, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Forward Pharma, Galderma, Genentech, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, Merck Sharp & Dohme, Merck Serono, Mitsubishi Pharma, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant; Honoraria: AbbVie, Akros, Amgen, Baxter, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Forward Pharma, Galderma, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Merck Sharp & Dohme, Merck Serono, Novartis, Pfizer, Takeda, UCB, Valeant, Bruce Strober Speakers bureau: AbbVie, Janssen, Eli Lilly, Ortho Dermatologics, Consultant of: Honoraria or consultation fees: AbbVie, Almirall, Amgen, Arena, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly, GSK, Janssen, Kyowa Hakko Kirin, Leo Pharma, Medac, Meiji Seika Pharma, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi-Genzyme, Sun Pharma, UCB; Scientific Director (consulting fee): Corrona Psoriasis Registry; Investigator: AbbVie, Corrona Psoriasis Registry, Dermavant, Dermira., Diamant Thaçi Paid instructor for: Lectures: AbbVie, Almirall, Amgen, DS-Pharma, Janssen, Leo Pharma, MSD, Novartis, Pfizer, Roche-Posay, Sandoz-Hexal, Sanofi, Target-Solution, UCB; Scientific advisory board: AbbVie, Amgen, Celgene, DS Pharma, Eli Lilly, Galapagos, Janssen-Cilag, Leo Pharma, Morphosis, MSD Novartis, Pfizer, Sandoz, Sanofi, UCB., Consultant of: Consultant: AbbVie, Almirall, Celgene, Dignity, Galapagos, Leo Pharma, Maruho, Mitsubishi, Novartis, Pfizer, Xenoport, Grant/research support from: Research support/principal investigator (clinical trials): AbbVie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Celgene, Chugai, Dermira, DS-Pharma, Eli Lilly, Galderma, GSK, Janssen-Cilag, Leo, MSD, Novartis, Pfizer, Regeneron, Roche, Sandoz-Hexal, Sanofi, UCB, Elizabeth Colston Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, John Throup Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Sudeep Kundu Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Subhashis Banerjee Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Andrew Blauvelt Consultant of: Scientific adviser and/or clinical study investigator for AbbVie, Aligos, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Evommune, Forte, Galderma, Incyte, Janssen, Leo Pharma, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, UCB Pharma.

DOI: 10.1136/annrheumdis-2021-eular.1002

POS1043

NETAKIMAB REDUCES PSORIATIC ARTHRITIS ACTIVITY IN PATIENTS WITH OR WITHOUT AXIAL DISEASE: SUBANALYSIS OF THE PATERA STUDY

T. Korotaeva[1], I. Gaydukova[2], V. Mazurov[2], A. Samtsov[3], V. Khayrutdinov[3], A. Bakulev[4], A. Kundzer[5], N. Soroka[6], A. Eremeeva[7]. *[1]Nasonova Research Institute of Rheumatology, Laboratory of Spondyloarthritides and Psoriatic Arthritis, Moscow, Russian Federation*; *[2]Mechnikov North-Western State Medical University, Department of Therapy and Rheumatology of Temporary Disability and Medical Care Quality Expertise, St-Petersburg, Russian Federation*; *[3]Kirov Military Medical Academy, Department of Skin and Veneral Diseases, St-Petersburg, Russian Federation*; *[4]Razumovsky Saratov State Medical University, Department of Dermatovenereology and Cosmetology, Saratov, Russian Federation*; *[5]Belarusian Medical Academy of Postgraduate Education, Department of Cardiology and Rheumatology, Minsk, Belarus*; *[6]Belarusian State Medical University, Department of Internal Diseases*

№2, Minsk, Belarus; [7]*JSC BIOCAD, Clinical Development Department, St-Petersburg, Russian Federation*

Background: PATERA is an ongoing phase 3 international double-blind, placebo-controlled clinical study of netakimab (NTK) in psoriatic arthritis (PsA) (NCT03598751). Netakimab (NTK) is an anti-interleukin-17A monoclonal antibody approved for psoriasis, ankylosing spondylitis, PsA in Russia and Belarus.
Objectives: A subanalysis was performed to define the impact of NTK on PsA activity depending on the presence of axial disease: a subset of patients with inflammatory back pain (IBP) according to self-reported ASAS IBP criteria, 2009 (IBP(+) was compared to those without IBP (IBP(-)).
Methods: 194 eligible adult patients with PsA fulfilling the CASPAR criteria, with inadequate response to csDMARD or one TNFi, were randomly assigned to receive NTK 120mg or placebo at weeks 0,1,2,4,6,8,10,14,18,22. Patients with missing values for categorical variables were considered as non-responders in the analysis. For quantitative variables, missing values were replaced using the multiple imputation method.
Results: 97 PsA patients (N=54 IBP(+), N=43 IBP(-)) received NTK. Both subpopulations were comparable in gender, age and PsA activity at baseline. The treatment led to a pronounced decline in PsA activity in both subpopulations, significant differences between arms were observed only in DAPSA remission and very low disease activity (VLDA) at week 24 (Figure 1A). Changes from baseline in DAS28-CRP were consistent between IBP(+) and IBP(-) patients with a rapid decline during the first month with further improvement up to week 24 (Figure 1B). A similar trend was observed PsA-specific composite responder index (PSARC) (data not shown). A comparable percentage of IBP(+) and IBP(-) patients achieved PSARC at each timepoint of evaluation with 87% and 86% of responders respectively at week 24.
Conclusion: NTK significantly improved PsA activity regardless of the presence of IBP.

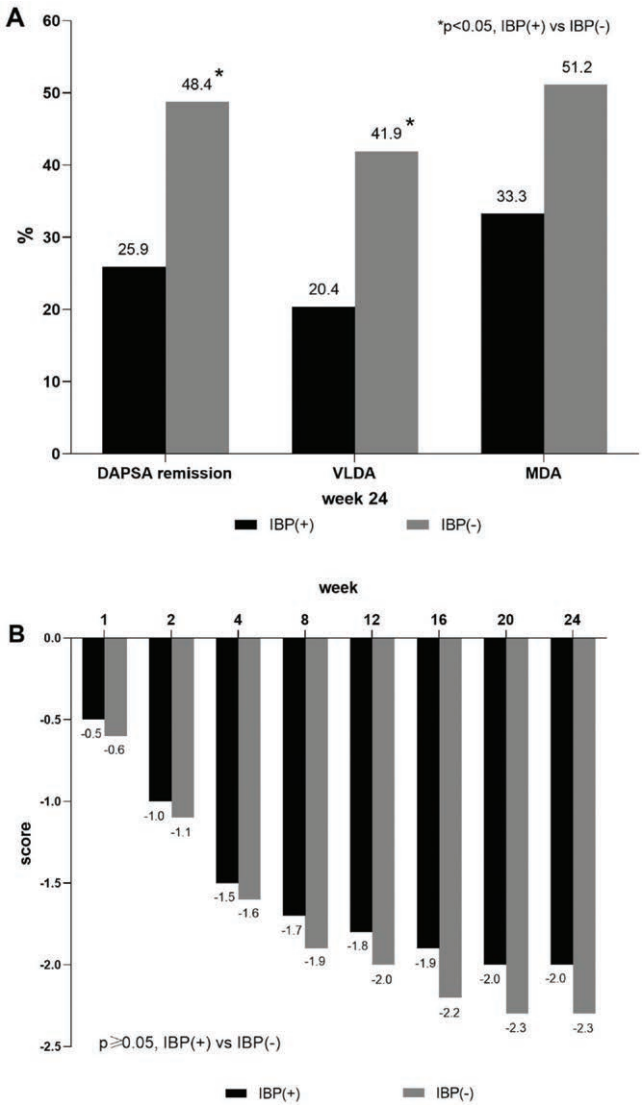


Figure 1. PsA activity after 24-week treatment with NTK. (A) Percentage of patients with DAPSA remission (0-4), very low disease activity (VLDA), minimal disease activity (MDA) at week 24; (B) change from baseline in DAS28-CRP

Acknowledgements: This study was sponsored by JSC BIOCAD.
Disclosure of Interests: Tatiana Korotaeva Speakers bureau: Abbvie, Biocad, Eli Lilly, Johnson & Johnson, Janssen, Novartis, Pfizer, UCB, Inna Gaydukova Speakers bureau: Abbvie, Biocad, Eli Lilly, MSD, Novartis, Pfizer, Sandoz, V Mazurov: None declared, Aleksey Samtsov: None declared, Vladislav Khayrutdinov: None declared, Andrey Bakulev: None declared, Alena Kundzer: None declared, Nikolaj Soroka: None declared, Anna Eremeeva Employee of: Biocad.
DOI: 10.1136/annrheumdis-2021-eular.1555

POS1044

EFFECT OF SECUKINUMAB VERSUS ADALIMUMAB ON ACR CORE COMPONENTS AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM THE EXCEED STUDY

P. Goupille[1], F. Behrens[2], L. C. Coates[3], J. Gratacos-Masmitja[4], P. J. Mease[5], D. D. Gladman[6], P. Nash[7], A. Kavanaugh[8], R. Martin[9], W. Bao[9], C. Gaillez[10], I. Mcinnes[11]. [1]*University of Tours, Department of Rheumatology and INSERM-CIC1415, Tours, France*; [2]*Goethe University, Rheumatology University Hospital and Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Branch for Translational Medicine and Pharmacology TMP and Fraunhofer Cluster of Excellence for Immune-Mediated Diseases CIMD, Frankfurt, Germany*; [3]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; [4]*University Hospital Parc Taulí, Sabadell, Universitat Autònoma de Barcelona, Rheumatology Department, Barcelona, Spain*; [5]*Swedish Medical Centre/Providence St. Joseph Health and University of Washington, Rheumatology Research Division, Seattle, United States of America*; [6]*Toronto Western Hospital, University of Toronto, Schroeder Arthritis Institute, Ontario, Canada*; [7]*Griffith University, Department of Medicine, Brisbane, Australia*; [8]*University of California San Diego, School of Medicine, Rheumatology, Allergy, Immunology Division, La Jolla, United States of America*; [9]*Novartis Pharmaceuticals Corporation, Immunology, Hepatology and Dermatology, East Hanover, United States of America*; [10]*Novartis Pharma AG, Immunology, Hepatology and Dermatology, Basel, Switzerland*; [11]*University of Glasgow, Institute of Infection, Immunity and Inflammation, College of Medical, Veterinary and Life Sciences, Glasgow, United Kingdom*

Background: EXCEED (NCT02745080) was the first fully blinded head-to-head trial to evaluate the efficacy and safety of secukinumab (SEC) versus (vs) adalimumab (ADA) monotherapy in patients with active psoriatic arthritis (PsA) with a primary endpoint of American College of Rheumatology (ACR) 20 at Week 52. Although SEC narrowly missed statistical significance for superiority vs ADA, numerically higher response for other musculoskeletal endpoints and composite indices were observed with SEC.[1]
Objectives: To explore the effect of SEC and ADA on ACR core components, function and Health-related Quality of Life (HRQoL) outcomes.
Methods: Patients were randomised 1:1 to receive SEC 300 mg (N=426) subcutaneous (s.c.) at baseline, Week 1-4, followed by every 4 weeks until Week 48 or ADA 40 mg (N=427) s.c. at baseline followed by same dosing every 2 weeks until Week 50. The primary, key secondary and some exploratory endpoints at Week 52 were previously reported.[1] A supportive analysis for ACR50 response using logistic regression model and trimmed means model for Health Assessment Questionnaire-Disability Index (HAQ-DI) with gender and smoking status as factors was performed to adjust for imbalances in baseline characteristics. An exploratory analysis of ACR core components with SEC vs ADA at Week 52 was conducted using a mixed-effects repeated measures model that included tender and swollen joint counts, patient and physician global assessment, PsA pain (VAS) and erythrocyte sedimentation rate. HRQoL variables were also exploratory and assessed based on Short Form Health Survey Physical/Mental Component Summary (SF-36 PCS/MCS) scores and Dermatology Life Quality Index (DLQI).
Results: The demographic and baseline disease characteristics were comparable across treatment groups, except for an imbalance in sex (females: 51.2% vs 46.4%) and smoking status (yes: 21.8% vs 17.8%) in SEC and ADA group, respectively. At Week 52, ACR50 responses were 49.0% and 44.8% (P=0.0929) and HAQ-DI mean change from baseline were −0.69 and −0.58 (P=0.0314) in SEC and ADA treatment groups, respectively after adjusting for gender and smoking status. No major difference across ACR core components was observed in both treatment groups at Week 52 (Table 1). At Week 52, SEC presented similar improvement in SF-36 PCS/MCS score and numerically higher improvement in DLQI compared to ADA (Figure 1).
Conclusion: Secukinumab provided similar improvements in ACR core components and SF-36 based quality of life at Week 52 with adalimumab. Greater improvement in HAQ-DI response and DLQI was demonstrated with secukinumab compared to adalimumab.

REFERENCES:
[1] McInnes IB, et al. *Lancet*. 2020; 395:1496–505.

Table 1. ACR Core Components at Week 52

Variables	Secukinumab 300 mg (N=426)		Adalimumab 40 mg (N=427)		*P*-value
	BL, mean ± SE	LSM change from BL ± SE	BL, mean ± SE	LSM change from BL ± SE	
Tender joint score (based on 78 joints)	19.4 ± 13.86	–14.27 ± 0.44	20.6 ± 14.81	–13.90 ± 0.45	0.5549
Swollen joint score (based on 76 joints)	9.7 ± 7.30	–8.41 ± 0.19	10.2 ± 7.86	–8.06 ± 0.20	0.1962
Patients global assessment	64.0 ± 19.67	–33.81 ± 1.14	61.9 ± 20.75	–31.61 ± 1.19	0.1825
Physicians global assessment	60.0 ± 17.12	–46.24 ± 0.80	61.4 ± 15.92	–43.63 ± 0.84	0.0243
Psoriatic arthritis pain (VAS)	58.6 ± 23.49	–30.21 ± 1.18	57.9 ± 22.42	–29.44 ± 1.23	0.6500
Erythrocyte sedimentation rate (mm/h)	23.8 ± 18.93	–9.63 ± 0.62	23.9 ± 17.99	–9.28 ± 0.64	0.7029

LS mean and nominal *P*-values are from a mixed-effects repeated measures model with treatment group, analysis visit as factors, weight and BL score as covariates, and by treatment and BL score as interaction terms, unstructured covariance structure. ACR, American College of Rheumatology; BL, baseline; LSM, least squares mean; N, total number of randomised patients; SE, standard error; VAS, visual analogue scale

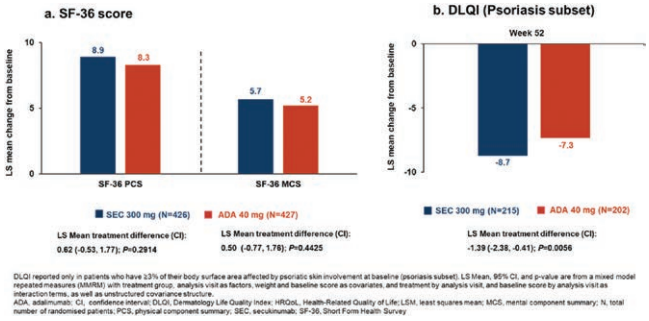


Figure 1. HRQoL Analysis at Week 52

Disclosure of Interests: Philippe Goupille Speakers bureau: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Eli Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Consultant of: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Eli Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Grant/research support from: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Eli Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Frank Behrens Paid instructor for: Eli Lilly, Consultant of: Pfizer, AbbVie, Sanofi, Eli Lilly, Novartis, Genzyme, Boehringer Ingelheim, Janssen, MSD, Celgene, Roche and Chugai, Grant/research support from: Pfizer, Janssen, Chugai, Celgene and Roche, Laura C Coates Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Biogen, BMS, Celgene, Domain, Eli Lilly, Gilead, GSK, Janssen, Medac, Novartis, Pfizer, Serac and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB, Jordi Gratacos-Masmitja Speakers bureau: AbbVie, Amgen, BMS, Celgene, Janssen, Eli Lilly, Novartis and Pfizer, Consultant of: AbbVie, Amgen, BMS, Celgene, Janssen, Eli Lilly, Novartis and Pfizer, Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Eli Lilly, Novartis and Pfizer, Philip J Mease Speakers bureau: AbbVie, Amgen, Genentech, Janssen, Eli Lilly, Merck, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Boehringer Ingelheim, Galapagos, Celgene, Genentech, Gilead, Janssen, Eli Lilly, Novartis, Pfizer, SUN Pharma, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Genentech, Gilead, Janssen, Eli Lilly, Merck, Novartis, Pfizer, SUN Pharma, and UCB, Dafna D Gladman Consultant of: Amgen, AbbVie, BMS, Celgene, Eli Lilly, Gilead, Galapagos, Janssen, Novartis, Pfizer and UCB, Grant/research support from: Amgen, AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB, Peter Nash Speakers bureau: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, Celgene, UCB, Eli Lilly, MSD, Sanofi, Gilead, Consultant of: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, Celgene, UCB, Eli Lilly, MSD, Sanofi, Gilead, Grant/research support from: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, Celgene, UCB, Eli Lilly, MSD, Sanofi, Gilead, Arthur Kavanaugh Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, and UCB, Ruvie Martin Shareholder of: Novartis, Employee of: Novartis, Weibin Bao Shareholder of: Novartis, Employee of: Novartis, Corine Gaillez Shareholder of: Novartis and BMS, Employee of: Novartis, Iain McInnes Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.1562

POS1045

IXEKIZUMAB EFFICACY ON SPINAL PAIN, DISEASE ACTIVITY AND QUALITY OF LIFE IN PATIENTS WITH PSORIATIC ARTHRITIS PRESENTING WITH SYMPTOMS SUGGESTIVE OF AXIAL INVOLVEMENT

A. Deodhar[1], D. D. Gladman[2], R. Bolce[3], D. Sandoval[3], S. Y. Park[3], S. Liu Leage[3], P. Nash[4], D. Poddubnyy[5]. *[1]Oregon Health and Science University, School of Medicine, Oregon, United States of America*; *[2]University of Toronto, Krembil Research Unit, Toronto, Canada*; *[3]Eli Lilly and Company, Lilly Corporate Center, Indianapolis, United States of America*; *[4]Griffith University, School of Medicine, Brisbane, Australia*; *[5]Charité University Hospital, Department of Gastroenterology, Infectiology and Rheumatology, Berlin, Germany*

Background: Many patients with psoriatic arthritis (PsA) experience back pain and stiffness, which may suggest axial involvement [1]. The prevalence of axial involvement in PsA varies between 25-70% [2]. Ixekizumab (IXE), a monoclonal antibody with high affinity for IL17-A, has been studied in Phase 3 trials in patients with PsA (SPIRIT-P1 [Biologic-naïve; NCT01695239] and SPIRIT-P2 [Inadequate response or intolerant to 1 or 2 TNF inhibitors (TNFi); NCT02349295]) [3] [4].
Objectives: To determine the efficacy of IXE up to 52 weeks (Wks) in reducing axial symptoms in patients with active PsA presenting with symptoms suggestive of axial involvement.
Methods: This post-hoc analysis included data from two subpopulations of patients with PsA (pooled SPIRIT-P1 and -P2). Symptoms suggestive of axial involvement were defined as Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Q2 (back pain) ≥4, and an average of Q5 + Q6 (intensity and duration of morning stiffness in the spine) ≥4 at baseline. Patients included in the sensitivity analysis subgroup 1 were, in addition to the above-mentioned overall analysis criteria, <45 years of age, while patients included in sensitivity analysis subgroup 2 were aged <45 but also had elevated C-reactive protein (CRP) (> 5 mg/l) at baseline. Efficacy of IXE was analysed using BASDAI questions, total BASDAI, mBASDAI (without Q3), and Ankylosing Spondylitis Disease Activity Score (ASDAS) change from baseline, as well as BASDAI50 response and Short-Form-36 physical component summary (SF-36 PCS) improvement, at Wks 16, 24 and 52. Treatment comparison was done using logistic regression for BASDAI50, and analysis of covariance (ANCOVA) model for other endpoints. Missing data for binary and continuous endpoints were imputed by non-responder imputation and modified baseline observation carried forward (mBOCF), respectively.
Results: A total of 313 patients (placebo (PBO), N=151; IXE Q4W, N=162) met the overall analysis inclusion criteria. Baseline values for BASDAI and ASDAS related endpoints were balanced across treatment arms (Table 1). Improvement in axial symptoms were significantly greater in patients treated with IXE compared to PBO at Wks 16 and 24 (Figure 1. next page) Improvement in quality of life (QoL) measures (SF-36 PCS) were also significantly greater in patients treated with IXE compared to PBO at Wks 16 and 24 (Table 1). Similar results were observed for patients < 45 years, and in patients < 45 years with CRP > 5 mg/l at baseline (sensitivity analysis, data not shown).
Conclusion: IXE is effective in reducing axial symptoms and improving QoL in patients with active PsA presenting with symptoms suggestive of axial involvement.

Table 1. Baseline values and change from baseline (mBOCF) in the overall analysis population at Wks 16, 24 and 52 for BASDAI and ASDAS related endpoints in patients with PsA and axial pain. Data presented as mean (SD) unless otherwise specified. ‡p<0.001 vs PBO.

	PBO (N=151)		IXE Q4W (N=162)		
Baseline values	**Wk 0**		**Wk 0**		
BASDAI	6.7 (1.4)		6.6 (1.3)		
Q2	7.0 (1.7)		6.7 (1.7)		
Q5	7.3 (1.5)		7.3 (1.5)		
Q6	5.8 (2.7)		5.5 (2.7)		
mBASDAI	6.7 (1.4)		6.6 (1.3)		
ASDAS	3.7 (0.8)		3.6 (0.9)		
SF-36 PCS	29.9 (7.4)		30.0 (8.4)		
Outcome measures	**Wk 16**	**Wk 24**	**Wk 16**	**Wk 24**	**Wk 52**
ASDAS	-0.4 (0.8)	-0.4 (0.8)	-1.2 (1.2)‡	-1.3 (1.2)‡	-1.4 (1.2)
BASDAI50, n (%)	16 (11)	12 (8)	51 (32)‡	61 (38)‡	64 (40)
mBASDAI	-1.0 (1.7)	-1.0 (1.7)	-2.1 (2.1)‡	-2.4 (2.3)‡	-2.7 (2.1)
SF-36 PCS	1.9 (7.3)	2.0 (6.9)	5.8 (8.8)‡	6.8 (9.9)‡	8.8 (9.5)

REFERENCES:
[1] Yap KS. Ann Rheum Dis. 2018;77(11)
[2] Feld J. Nat Rev Rheumatol. 2018;14
[3] Orbai A. Clin Exp Rheumatol. 2020[online]
[4] Genovese MC. Rheumatol. 2018;57(11)

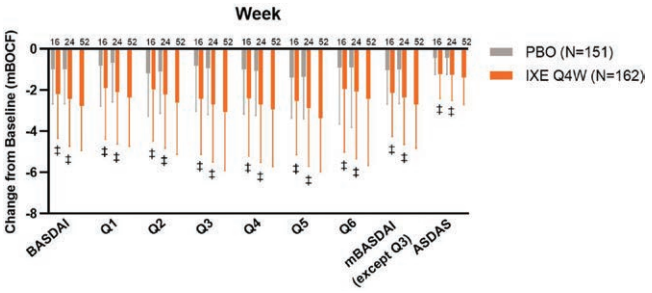


Figure 1. Change from baseline (mBOCF) in BASDAI and ASDAS related endpoints in patients with PsA and axial pain in the overall analysis population. Data presented as mean (SD). ‡p<0.001 vs PBO.

Acknowledgements: Edel Hughes, an employee of Eli Lilly and Company, provided editorial and writing support.
Disclosure of Interests: Atul Deodhar Speakers bureau: Janssen, Novartis, Pfizer, Paid instructor for: Boeheringer Ingelheim, Pfizer, Consultant of: AbbVie, Amgen, Boeheringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Glaxo Smith Kline, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Eli Lilly, Glaxo Smith Kline, Novartis, Pfizer, UCB, Dafna D Gladman Consultant of: Abbvie, Amgen, BMS, Galapagos, Gilead, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Grant/research support from: Abbvie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Rebecca Bolce Shareholder of: Employee and shareholder of Eli Lilly and Company, Employee of: Employee and shareholder of Eli Lilly and Company, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Currently employed by Eli Lilly and Company, So Young Park Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, Soyi Liu Leage Shareholder of: Owns Lilly shares (company producing drug/devices for use in rheumatology), Employee of: Employee of Eli Lilly and Company, Peter Nash Speakers bureau: Honoraria for lectures on behalf Abbvie, BMS, Celgene, Roche, Sanofi, Lilly, Novartis, Janssen, Pfizer, Boehringer, Samsung, Consultant of: Advice on behalf Abbvie, BMS, Celgene, Roche, Sanofi, Lilly, Novartis, Janssen, Pfizer, Boehringer, Samsung, Grant/research support from: Research funding for clinical trials on behalf Abbvie, BMS, Celgene, Roche, Sanofi, Lilly, Novartis, Janssen, Pfizer, Boehringer, Samsung, Denis Poddubnyy Speakers bureau: AbbVie, Bristol-Myers Squibb, Lilly, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Biocad, Gilead, GlaxoSmithKline, Eli Lilly, MSD, Novartis, Pfizer, Samsung Bioepis, and UCB, Grant/research support from: AbbVie, Eli Lilly, MSD, Novartis, and Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.1570

POS1046

IMPROVEMENTS IN PATIENT-REPORTED IMPACT OF PSORIATIC ARTHRITIS WITH IL-12/23 (USTEKINUMAB) OR TUMOUR NECROSIS FACTOR INHIBITORS: 1-YEAR DATA FROM THE LARGE, REAL-WORLD PsABIO STUDY

L. Gossec[1,2], S. Siebert[3], P. Bergmans[4], K. De Vlam[5], E. Gremese[6], B. Joven-Ibáñez[7], T. Korotaeva[8], W. Noel[9], M. Nurmohamed[10], P. Sfikakis[11], E. Theander[12], J. S. Smolen[13]. [1]*Sorbonne University, INSERM, Pierre Louis Institute of Epidemiology and Public Health, Paris, France*; [2]*Pitié-Salpêtrière Hospital, AP-HP, Department of Rheumatology, Paris, France*; [3]*University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; [4]*Janssen-Cilag BV, Biostatistics, Breda, Netherlands*; [5]*University Hospitals Leuven, Division of Rheumatology, Leuven, Belgium*; [6]*Catholic University of the Sacred Heart, Fondazione Policlinico A Gemelli-IRCCS, Rome, Italy*; [7]*University Hospital 12 de Octubre, Department of Rheumatology, Madrid, Spain*; [8]*VA Nasonova Research Institute of Rheumatology, Department of Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*; [9]*Janssen Pharmaceutica NV, Medical Affairs, Beerse, Belgium*; [10]*Reade and VU University Medical Center, Department of Rheumatology, Amsterdam, Netherlands*; [11]*National and Kapodistrian University of Athens Medical School, First Department of Propaedeutic and Internal Medicine, Athens, Greece*; [12]*Janssen-Cilag AB, Medical Affairs, Solna, Sweden*; [13]*Medical University of Vienna, Division of Rheumatology, Department of Medicine III, Vienna, Austria*

Background: Psoriatic arthritis (PsA) negatively impacts patients' (pts) quality of life (QoL), with a high burden of pain, fatigue and psychological distress. The 12-item Psoriatic Arthritis Impact of Disease questionnaire (PsAID-12) is a validated measure of pt-reported disease impact.
Objectives: To analyse PsAID-12 score changes in the overall population and specific subgroups of interest, and assess correlation of these changes using Health Assessment Questionnaire Disability Index (HAQ-DI).
Methods: PsABio (NCT02627768) is a multinational, prospective, observational study in pts with PsA receiving ustekinumab (UST) or a tumour necrosis factor inhibitor (TNFi) as a 1st/2nd/3rd-line biologic. Descriptive statistics, including 95% CI, are presented at baseline (BL) and 1 year. Linear regression, including propensity score (PS) adjustment for BL covariates, was used to compare change in PsAID-12 total from BL to 1 year between treatments. The relationship between changes in PsAID-12 and HAQ-DI was investigated using Spearman's correlation.
Results: Data were available for 438 UST and 455 TNFi pts. From BL to 1 year, significant improvements were seen in total PsAID-12 scores and in all domains with both treatments (Figure 1). PS-adjusted treatment comparison showed no difference in total PsAID-12 improvement (regression coefficient [95% CI]: 0.14 [-0.22; 0.51], p=0.4433), or in any domain, except skin problems, which improved significantly more with UST than TNFi (-0.55 [-1.04, -0.06], p=0.0277). Improvements in PsAID-12 and HAQ-DI showed strong positive correlation with both treatments (UST: r=0.63, p<0.0001; TNFi: r=0.70, p<0.0001). Effectiveness was demonstrated with UST and TNFi in subgroups of interest, including biologic treatment line, sex and psoriasis extent (Table 1. next page).
Conclusion: Treatment with IL-12/23 (UST) or TNF inhibitors significantly improved pt-reported disease impact at 1 year. PS-adjusted PsAID-12 improvements did not differ significantly between treatments, except skin problems (better with UST). Improvements in disease impact and physical functioning (HAQ-DI) were strongly correlated, emphasising the effect of these biologics on QoL in PsA pts.

Mean PsAID-12 overall and domain scores at baseline and 1 year with UST and TNFi

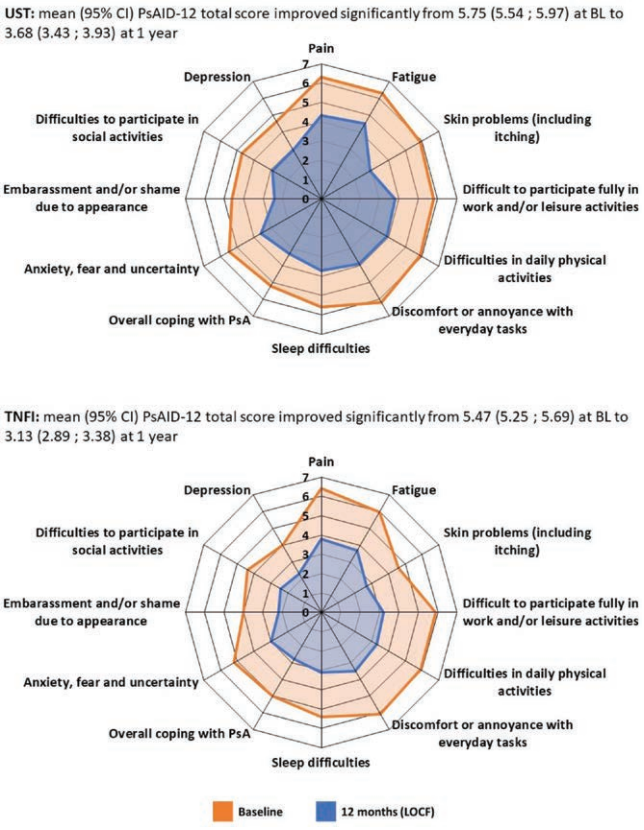


Figure 1.

Table 1. PsAID-12 scores by BL characteristic subgroup

Mean (95% CI)	UST		TNFi	
	BL	Unadjusted change from BL at 1 year (LOCF)	BL	Unadjusted change from BL at 1 year (LOCF)
Biologic line				
1st	5.51	-2.14	5.44	-2.41
	(5.19; 5.82)	(-2.49; -1.79)	(5.15; 5.72)	(-2.72; -2.09)
2nd	6.05	-2.14	5.57	-2.37
	(5.69; 6.41)	(-2.55; -1.72)	(5.19; 5.95)	(-2.79; -1.94)
3rd	5.84	-1.81	5.34	-1.89
	(5.33; 6.35)	(-2.45; -1.17)	(4.52; 6.15)	(-2.62; -1.16)
Sex*				
Male	5.27	-2.35	4.89	-2.49
	(4.95; 5.59)	(-2.70; -1.99)	(4.56; 5.23)	(-2.83; -2.15)
Female	6.14	-1.86	5.95	-2.20
	(5.86; 6.43)	(-2.20; -1.52)	(5.67; 6.23)	(-2.53; -1.87)
Enthesitis				
Yes	5.95	-2.19	5.89	-2.65
	(5.66; 6.24)	(-2.51; -1.86)	(5.61; 6.17)	(-2.98; -2.31)
No	5.51	-1.98	4.99	-2.02
	(5.19; 5.83)	(-2.36; -1.59)	(4.65; 5.32)	(-2.35; -1.68)
Psoriasis BSA, %				
<3	5.66	-1.60	4.97	-1.89
	(5.32; 6.00)	(-2.03; -1.18)	(4.63; 5.31)	(-2.25; -1.52)
3–10	5.44	-2.16	5.78	-2.99
	(5.05; 5.83)	(-2.59; -1.74)	(5.43; 6.14)	(-3.38; -2.59)
>10	6.15	-2.93	6.13	-2.86
	(5.70; 6.60)	(-3.43; -2.43)	(5.55; 6.71)	(-3.49; -2.23)
Joint involvement†				
Mono/ oligoarticular	5.07	-1.96	4.82	-2.18
	(4.56; 5.58)	(-2.47; -1.45)	(4.38; 5.25)	(-2.66; -1.70)
Polyarticular	5.98	-2.21	5.78	-2.47
	(5.75; 6.22)	(-2.51; -1.92)	(5.52; 6.04)	(-2.75; -2.18)
FiRST score*				
<5	5.15	-2.18	5.10	-2.44
	(4.87; 5.44)	(-2.50; -1.87)	(4.83; 5.36)	(-2.71; -2.16)
≥5	6.72	-1.95	6.49	-2.09
	(6.43; 7.00)	(-2.38; -1.53)	(6.15; 6.83)	(-2.57; -1.61)

*At BL, female pts and pts with FiRST score ≥5 (chronic widespread pain) were significantly more impacted than male pts and pts with FiRST score <5, and remained significantly more impacted at 1 year. †Polyarticular pts were significantly more impacted at BL, but not 1 year.BSA, body surface area; CI, confidence interval; FiRST, Fibromyalgia Rapid Screening Tool; LOCF, last observation carried forward

Acknowledgements: This study was funded by Janssen.

Disclosure of Interests: Laure Gossec Consultant of: AbbVie, Amgen, Bioepis, Biogen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Samsung, Sanofi-Aventis, UCB, Grant/research support from: Amgen, Galapagos, Janssen, Lilly, Pfizer, Sandoz, Sanofi, Stefan Siebert Speakers bureau: AbbVie, Amgen (previously Celgene), Biogen, Janssen, Novartis, UCB, Consultant of: AbbVie, Janssen, UCB, Grant/research support from: Amgen (previously Celgene), Boehringer Ingelheim, Bristol-Myers Squibb, GSK, Janssen, Novartis, Pfizer, UCB, Paul Bergmans Shareholder of: Johnson & Johnson, Employee of: Janssen, Kurt de Vlam Speakers bureau: AbbVie, Amgen, Eli Lilly, Novartis, UCB, Paid instructor for: Amgen, Galapagos, UCB, Consultant of: Eli Lilly, Galapagos, Johnson & Johnson, Novartis, UCB, Grant/research support from: Celgene, Elisa Gremese: None declared, Beatriz Joven-Ibáñez Speakers bureau: AbbVie, Celgene, Janssen, MSD, Novartis, Pfizer, Tatiana Korotaeva Speakers bureau: AbbVie, Amgen, Biocad, Lilly, Janssen, MSD, Novartis, Novartis-Pfizer, Sandoz, UCB, Consultant of: AbbVie, Amgen, Biocad, Lilly, Janssen, MSD, Novartis, Novartis-Sandoz, Pfizer, UCB, Grant/research support from: Pfizer, Wim Noel Employee of: Janssen, Michael Nurmohamed Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi, UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi, UCB, Petros Sfikakis Consultant of: AbbVie, Actelion, Boehringer Ingelheim, Enorasis, Farmaserv-Lilly, Genesis, Gilead, Pfizer, MSD, Novartis, UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Faran, Janssen, Pfizer, Roche, Elke Theander Employee of: Janssen, Josef S. Smolen Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO, Janssen, Lilly, MSD, Novartis- Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Grant/research support from: AbbVie, AstraZeneca, Lilly, Novartis, Roche.

DOI: 10.1136/annrheumdis-2021-eular.1607

POS1047

IMPACT OF UPADACITINIB ON REDUCING PAIN IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM TWO PHASE 3 TRIALS IN PATIENTS WITH INADEQUATE RESPONSE TO NON-BIOLOGIC OR BIOLOGIC DMARDs

I. Mcinnes[1], W. Tillett[2], P. J. Mease[3], K. De Vlam[4], L. Bessette[5], R. Lippe[6], A. Maniccia[7], P. Zueger[7], D. Feng[7], K. Kato[7], A. Ostor[8]. [1]*University of Glasgow, Rheumatology, Glasgow, United Kingdom*; [2]*Royal National Hospital, Rheumatic Diseases, Bath, United Kingdom*; [3]*Swedish Medical Center, Providence St Joseph Health and University of Washington, Seattle, United States of America*; [4]*University Hospitals Leuven, Rheumatology, Leuven, Belgium*; [5]*Laval University, Rheumatology, Québec City, Canada*; [6]*AbbVie Deutschland, GmbH & Co. KG, Wiesbaden, Germany*; [7]*AbbVie Inc., Rheumatology, North Chicago, United States of America*; [8]*Cabrini Hospital, Monash University & Emeritus Research, Melbourne, Australia*

Background: Pain is a dominant symptom of psoriatic arthritis (PsA), and pain reduction is a priority for patients (pts) that is often assessed in clinical trials. Upadacitinib (UPA), a Janus kinase (JAK) inhibitor engineered for increased selectivity for JAK1 over JAK2, JAK3, and tyrosine kinase2, has demonstrated safety and efficacy in pts with active PsA in the SELECT-PsA 1 and 2 studies.[1,2]

Objectives: The objective of this analysis was to compare the efficacy of UPA vs placebo (PBO) and adalimumab (ADA) on pain using different assessments through 24 weeks (wks).

Methods: The SELECT-PsA program enrolled adult pts with active PsA with prior inadequate response (IR) or intolerance to ≥1 non-biologic DMARD (SELECT-PsA 1; NCT03104400) or prior IR or intolerance to ≥1 biologic DMARD (SELECT-PsA 2; NCT03104374). Concomitant background therapy with ≤2 non-biologic DMARDs was allowed but not required. Pts were randomized to UPA 15 mg or UPA 30 mg once daily (QD) or PBO (both studies), or ADA 40 mg every other week (EOW; SELECT-PsA 1 only). Pain was assessed as proportion of pts achieving ≥30%, ≥50%, or ≥70% reduction from baseline (BL) in Pt's global assessment (PGA) of pain numeric rating scale (NRS) score (0–10), proportion of pts achieving minimal clinically important difference (MCID) in pain (defined as ≥1 point reduction or 15% reduction from BL on a 0–10 NRS)[3,4] and change from baseline in pain NRS (0–10) at all time points. In addition, change from BL in BASDAI questions 2 (spinal pain) and 3 (joint pain/swelling) and *36*-Item Short Form Survey (SF-36) questions 7 (bodily pain) and 8 (pain interference) at weeks 12 and 24 were assessed. Non-responder imputation was used for binary endpoints and mixed-effects model for repeated measurements for continuous endpoints. The statistical significance defined as $P<0.05$ was exploratory in nature.

Results: In both studies, a significantly higher proportion of pts receiving UPA 15 mg QD and UPA 30 mg QD vs PBO achieved improvements in most pain endpoints as early as wk 2, and improvements were generally either sustained or increased through wk 24 (nominal $P<0.05$). A significant improvement with UPA vs PBO was also observed for change from BL in PGA of pain NRS scores over time, as well as in BASDAI spinal pain and joint pain/swelling and SF-36 bodily pain and pain interference at weeks 12 and 24. In SELECT-PsA 1 significantly higher proportions of pts receiving UPA 30 mg QD vs ADA 40 mg EOW achieved improvements in most pain assessments as early as wk 2 which were sustained through wk 24; improvements in several assessments were also significantly greater with UPA 15 mg QD vs ADA 40 mg EOW at wk 24 (nominal P <0.05; **Data will be presented**).

Conclusion: In pts with active PsA who had inadequate response to non-biologic or biologic DMARDs, a greater proportion of pts treated with UPA vs PBO achieved rapid, significant, and clinically meaningful reductions in pain across multiple pain assessments. The reductions in pain were sustained over 24 wks.

REFERENCES:

[1] McInnes I. et al. *Ann Rheum Dis*. 2020;79(Suppl 1):12-13.
[2] Genovese M.C. et al. *Ann Rheum Dis.* 2020;79(Suppl 1):139.
[3] Dworkin, R.H. et al. *J Pain.* 2008;9(2):105-121.
[4] Salaffi F. et al. *Eur J Pain*. 2004;8:283–291.

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing support was provided by M Hovenden and J Matsuura of ICON plc (North Wales, PA) and was funded by AbbVie.

Disclosure of Interests: Iain McInnes Consultant of: AbbVie, AstraZeneca, Boehringer Ingelheim, Bristol Myers, Celgene, Janssen, Leo, Lilly, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, AstraZeneca, Boehringer Ingelheim, Bristol Myers, Celgene, Janssen, Leo, Lilly, Novartis, Pfizer, and UCB, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, and UCB, Philip J Mease Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Leo, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Leo, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Leo, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Kurt de Vlam Speakers bureau: Celgene Eli Lilly, Galapagos, Novartis, and UCB, Consultant of: Celgene, Eli Lilly, Galapagos, Novartis, and UCB, Grant/research support from: Celgene and Galapagos, Louis Bessette Speakers bureau: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, and Sanofi, Consultant of: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, Gilead, Grant/research support from: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, and Gilead, Ralph Lippe Shareholder of: AbbVie, Employee of: AbbVie, anna maniccia Shareholder of: AbbVie, Employee of: AbbVie, Patrick Zueger Shareholder of: AbbVie, Employee of: AbbVie, Dai Feng Shareholder of: AbbVie, Employee of: AbbVie, Koji Kato Shareholder of: AbbVie, Employee of: AbbVie, Andrew Ostor Consultant of: AbbVie, BMS, Roche, Janssen, Lilly, Novartis, Pfizer, UCB, Gilead, and Paradigm.
DOI: 10.1136/annrheumdis-2021-eular.1633

POS1048

IN PHASE-3 TRIALS DISCOVER 1 & 2, GUSELKUMAB REDUCED FATIGUE OVER 52 WEEKS IN PATIENTS WITH PSORIATIC ARTHRITIS AND DEMONSTRATED INDEPENDENT TREATMENT EFFECTS ON FATIGUE AFTER ADJUSTMENT FOR CLINICAL RESPONSE (ACR20)

P. Rahman[1], P. Helliwell[2], A. Deodhar[3], A. Kollmeier[4], E. C. Hsia[4,5], B. Zhou[6], X. Lin[7], C. Han[8], P. J. Mease[9]. *[1]Memorial University of Newfoundland, Disicpline of Medicine, Faculty of Medicine, St. Johns, Canada*; *[2]University of Leeds, Clinical Rheumatology, Leeds, United Kingdom*; *[3]Oregon Health & Science University, Division of Arthritis & Rheumatic Diseases, Oregon, United States of America*; *[4]Janssen Research & Development, LJ IMMUNOLOGY, Spring House, United States of America*; *[5]University of Pennsylvania School of Medicine, Division of Rheumatology, Philadelphia, United States of America*; *[6]Janssen Research & Development, CLINICAL BIOSTATS PA, Spring House, United States of America*; *[7]Janssen Research & Development, SMM-PA, Spring House, United States of America*; *[8]Janssen Research & Development, STRATEGIC MKT ACCESS, Spring House, United States of America*; *[9]Swedish Medical Center/Providence St Joseph Health and University of Washington School of Medicine, Department of Internal Medicine, Seatle, United States of America*

Background: DISCOVER 1 & 2 are phase-3 trials of guselkumab (GUS, an IL-23 inhibitor) in patients with psoriatic arthritis (PsA). In both trials, treatment with GUS led to significantly more improvement than placebo (PBO) in the primary endpoint (American College of Rheumatology 20% improvement criteria [ACR20]) and in other measures of arthritis and psoriasis at week (w) 24,[1,2] and these improvements were maintained through 1 year of active treatment.[3,4]
Objectives: To evaluate the effect of GUS on fatigue in DISCOVER 1 & 2 using the patient reported outcome (PRO) FACIT-Fatigue, which has demonstrated content validity and strong psychometric properties in clinical trials.[5]
Methods: DISCOVER 1 & 2 enrolled patients with active PsA, despite non-biologic DMARDS or NSAIDS, who were biologic naïve except ~30% of patients in DISCOVER 1 who had received 1-2 TNFi. Patients were randomized (1:1:1) in a blinded fashion to subcutaneous GUS 100 mg at w0, w4, then every (q) 8w; GUS 100 mg q4w; or matching PBO. At w24, PBO patients were switched to GUS q4w. Concomitant treatment with select non-biologic DMARDS, oral corticosteroids, and NSAIDs was allowed. The FACIT-Fatigue is a 13-item PRO assessing fatigue and its impact on daily activities and function over the past 7 days, total score ranging from 0 to 52, higher score denoting less fatigue. A change of ≥4 points is considered clinically meaningful.[5] The change from baseline in FACIT-Fatigue presented below is based on observed data. Mediation analysis[6] was applied to the treatment effect of GUS on FACIT-Fatigue to estimate the natural direct and indirect effects, after adjusting for ACR20 response (Table 1).
Results: At baseline in DISCOVER 1 & 2, the mean FACIT-fatigue scores (SD) were 30.4 (10.4) and 29.7 (9.7), respectively, indicating that patients with PsA experienced fatigue worse than the general population. At w24 in the DISCOVER trials, treatment with GUS led to significant improvements in FACIT-Fatigue scores compared with PBO, as early as w16 in DISCOVER 1 and w8 in DISCOVER 2. Improvements in fatigue were similar between GUS q4w and q8w doses, and the improvements at w24 were maintained through w52 (Figure 1). After a switch to GUS q4w at w24, PBO patients achieved FACIT-Fatigue scores that were comparable to those of GUS patients (Figure 1). 54%-63% of GUS patients compared with 35%-46% of PBO patients achieved clinically meaningful improvement (≥4 points) in FACIT-Fatigue at w24 (P≤0.003). At w52, 61%-70% of both GUS and PBO to GUS groups reached this improvement. As evaluated by mediation analysis at w24, GUS had independent positive treatment effects on fatigue (12%-36% in the q8w GUS dosing group and 69%-70% in the q4w GUS group) after adjustment for ACR20 response (Table 1).
Conclusion: In 2 phase-3 trials, GUS treatment improved fatigue when compared to PBO during PBO-controlled periods and maintained improvements through 1 year of active treatment. Substantial proportions of those effects were independent of the effects on ACR20, especially for the q4W dosing group.

REFERENCES:

[1] Deodhar et al. *Lancet* 2020;395:1115
[2] Mease et al. *Lancet* 2020;395:1126
[3] Ritchlin et al. *EULAR20*. SAT0397
[4] McInnes et al. *EULAR20*. SAT0402
[5] Cella et al. *J Patient-Reported Outcomes* 2019;3:30
[6] Valeri et al. *Psychologic Meth* 2013;18:137

Table 1. Mediation Analysis: Guselkumab Has Direct Effects and Indirect Effects (Mediated through ACR20) on Fatigue in PsA

	Effect	GUS 100 mg q8w vs. PBO (95% CI)	GUS 100 mg q4w vs. PBO (95% CI)
DISCOVER-1	Total Effect	3.1 (1.0, 5.2)	3.8 (1.9, 5.4)
		(p<0.02)	(p<0.02)
	% Direct Effect	11.7%	68.5%
	% Indirect effect mediated by ACR20	88.3%	31.5%
DISCOVER-2	Total Effect	4.0 (2.4, 5.5)	3.6 (2.1, 5.0)
		(p<0.02)	(p<0.02)
	% Direct Effect	36.3%	69.7%
	% Indirect effect mediated by ACR20	63.7%	30.3%

ACR, American College of Rheumatology; CI, confidence interval; GUS, guselkumab; PBO, placebo; PsA, psoriatic arthritis; q4W, every 4 weeks; q8W, every 8 weeks

Disclosure of Interests: Proton Rahman Speakers bureau: Received speakers fees from Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, Pfizer, Grant/research support from: Received grant/research support from Janssen and Novartis, consultation fees from Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, and Pfizer, Philip Helliwell Consultant of: Consultation fees paid to charity (AbbVie, Amgen, Pfizer, UCB) or himself (Celgene, Galapagos), Grant/research support from: Received grants/research support paid to charity (AbbVie, Janssen, Novartis), Atul Deodhar Speakers bureau: Received speakers fees from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant of: Received consultation fees from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Grant/research support from: Received grant/research support from AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB, Alexa Kollmeier Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Bei Zhou Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Xiwu Lin Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Chenglong Han Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Philip J Mease Speakers bureau: Received speakers fees from Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, Consultant of: Received consultation fees from Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB, Grant/research support from: Received grant/research support from Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB.
DOI: 10.1136/annrheumdis-2021-eular.1686

POS1049

EFFECT OF FILGOTINIB ON PASDAS: DRIVERS OF LOW AND VERY LOW ACTIVITY UP TO WEEK 100

L. C. Coates[1], P. J. Mease[2,3], P. Helliwell[4], F. Van den Bosch[5], M. Trivedi[6], M. Alani[6,7], F. O. Le Brun[8], R. Besuyen[9], L. Gheyle[10], E. Gvozdenovic[11], D. D. Gladman[12]. *[1]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*;

[2]Swedish Medical Center, Rheumatology Clinical Research Division, Seattle, United States of America; [3]University of Washington, School of Medicine, Seattle, United States of America; [4]University of Leeds, School of Medicine, Leeds, United Kingdom; [5]Ghent University, VIB Center for Inflammation Research, Ghent, Belgium; [6]Gilead Sciences, Inc., Clinical Research, Foster City, United States of America; [7]University of Washington, Rheumatology Department, Seattle, United States of America; [8]Galapagos GmbH, Biometrics, Basel, Switzerland; [9]Galapagos BV, Clinical Research, Leiden, Netherlands; [10]Galapagos NV, Clinical Research, Mechelen, Belgium; [11]Galapagos NV, Biometrics, Mechelen, Belgium; [12]Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Canada

Background: EQUATOR (NCT03101670) was a Phase 2, double-blind, randomised placebo (PBO)- controlled trial of the preferential Janus kinase 1 inhibitor filgotinib (FIL) for the treatment of psoriatic arthritis (PsA); EQUATOR2 (NCT03320876) is the open-label extension (OLE).

Objectives: This post-hoc analysis assessed the effect of FIL on individual Psoriatic Arthritis Disease Activity Score (PASDAS) components; and the association between PASDAS disease activity (DA) levels and DA levels achieved for each PASDAS component and patient-reported outcomes (PROs) up to OLE Week (Wk) 100.

Methods: In EQUATOR, patients with active moderate-to-severe PsA were randomised 1:1 to oral FIL 200 mg or PBO once daily (QD) for 16 wks.[1] At Wk 16, patients could continue into the 304-wk OLE, in which all patients received FIL 200 mg QD. The proportions of patients with PASDAS of very low DA (VLDA; ≤1.9), LDA (>1.9–<3.2), moderate DA (MoDA; ≥3.2–<5.4), and high DA (HDA; ≥5.4) at core Wk 16 and OLE Wk 52 and 100 were assessed. The proportion with improved PASDAS status vs baseline (BL) at OLE Wk 52 and 100 was calculated. Percent change from BL in PASDAS components and PROs were assessed at core Wk 16 and OLE Wk 52 and 100 by PASDAS status (VLDA, LDA, other). Multivariate logistic regression analyses performed cross-sectionally identified PASDAS components and PROs associated with not achieving VLDA or LDA at core Wk 16 and OLE Wk 52 and 100; all analyses were observed cases.

Results: At OLE Wk 52, LDA and VLDA were achieved by 27.5% and 16.8% of randomised patients, respectively (44.3% combined). At OLE Wk 100, LDA and VLDA were achieved by 26.0% and 17.6% of patients (43.6% combined; Figure 1). Of patients with HDA at BL, 69% improved to MoDA/LDA/VLDA, <4% remained in HDA and 27% did not reach Wk 100; of those in MoDA at BL, 63% improved to VLDA/LDA, 11% remained stable, <4% worsened and 22% did not reach Wk 100. Patient Global Assessment of Disease Activity (PtGDA), Short Form-36 physical component scale (SF-36 PCS), Functional Assessment of Chronic Illness Therapy, and Health Assessment Questionnaire Disability Index were found to be important components/PRO measures in achieving VLDA vs LDA (Table 1). Logistic regression indicated that factors associated with not achieving LDA at Wk 52 were PtGDA (odds ratio [OR]: 1.20, 95% confidence interval [CI]: 1.07–1.35), physician GDA (PhGDA; OR: 1.58, 95% CI: 1.18–2.12), and SF-36 PCS (OR: 0.79, 95% CI: 0.67–0.95); PtGDA was associated with not achieving VLDA (OR: 1.30, 95% CI: 1.15–1.47).

Conclusion: The proportion of patients achieving PASDAS VLDA or LDA increased over time and remained stable between OLE Wk 52 and 100. Important factors in determining whether VLDA/LDA was met were PtGDA, PhGDA, and SF-36 PCS, although the low patient numbers is a limitation.

REFERENCES:

[1] Mease P, et al. *Lancet*. 2018;392:2367–77

Figure. Proportion of patients with VLDA, LDA, MoDA, and HDA at baseline, Core Week 16, OLE Week 52, and OLE Week 100

Proportions are based on the all randomised population
*Patients are presented according to original treatment in the core study. During the OLE all patients received filgotinib
†Missing includes patients who did not reach the timepoint or had a missing assessment
HDA, high disease activity; LDA, low disease activity; MoDA, moderate disease activity; OLE, open-label extension; VLDA, very low disease activity

Table 1. Mean % change from baseline in PASDAS components and PROs (observed cases)

	Core Wk 16 (FIL + PBO groups combined) n=122			OLE Wk 52 n=110			OLE Wk 100 n=97		
	VLDA n=8 (7%)	LDA n=22 (18%)	Others n=92 (75%)	VLDA n=22 (20%)	LDA n=36 (33%)	Others n=52 (47%)	VLDA n=23 (24%)	LDA n=34 (35%)	Others n=40 (41%)
PhGDA	–93	–75	–44	–94	–82	–56	–96	–84	–54
PtGDA	**–87**	**–69**	–13	**–86**	**–58**	–24	**–90**	**–57**	–13
Tender joint count 68	–94	–80	–42	–99	–84	–64	–98	–87	–61
Swollen joint count 66	–99	–80	–64	–99	–96	–78	–99	–94	–80
LEI	–100	–86	–32	–96	–100	–78	–100	–99	–78
Dactylitis	–100	–100	–73	–100	–100	–97	–100	–100	–98
C-reactive protein	–66	–22	17	138*	–32	–25	–12	–13	24
SF-36 PCS	**53**	**26**	11	**33**	**23**	9	**47**	**23**	16
FACIT	**119**	**50**	32	**97**	**51**	34	**99**	**46**	36
HAQ-DI	**–84**	**–68**	–18	**–85**	**–51**	–18	**–88**	**–45**	–19
PASI	–84	–66	–29	–54	–59	–56	–49	–76	–42

Components or PRO measures in bold are those for which numerical differences between VLDA and LDA are greatest across timepoints*Due to outlier (3784)FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; LEI, Leeds Enthesitis Index; PASI, Psoriasis Area Severity Index; PhGDA, Physician Global Assessment of Disease Activity; PtGDA, Patient Global Assessment of Disease Activity; SF-36 PCS, Short Form-36 physical component summary; (V)LDA, (very) low disease activity

Acknowledgements: EQUATOR and EQUATOR2 were sponsored by Galapagos NV Mechelen, Belgium) and co-funded by Galapagos NV and Gilead Sciences, Inc (Foster City, CA, USA). Benjamin Pett and his team, employees of Galapagos, provided assistance with statistical analyses. Medical writing/editorial support was provided by Debbie Sherwood, BSc, CMPP (Aspire Scientific, Bollington, UK), and was funded by Galapagos NV.

Disclosure of Interests: Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Gilead, Janssen, Medac, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Novartis, and Pfizer, Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead Sciences, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead Sciences, Janssen, Novartis, Pfizer, SUN, and UCB, Philip Helliwell Paid instructor for: Janssen, Novartis, and Pfizer, Consultant of: Eli Lilly, Filip van den Bosch Consultant of: AbbVie, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Merck, and UCB, Mona Trivedi Shareholder of: Gilead Sciences, Amgen, Employee of: Gilead Sciences, Muhsen Alani Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Franck Olivier Le Brun Shareholder of: Galapagos, Employee of: Galapagos, Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, Lien Gheyle Shareholder of: Galapagos, Employee of: Galapagos, Emilia Gvozdenovic Employee of: Galapagos, Dafna D Gladman Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB., Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.1721

POS1050

SECUKINUMAB LEADS TO IMPROVEMENT ACROSS PSORIATIC ARTHRITIS MANIFESTATIONS OVER 2 YEARS REGARDLESS OF PREVIOUS EXPOSURE TO A TNF INHIBITOR: A POST HOC ANALYSIS OF FUTURE 5

A. M. Orbai[1], M. E. Husni[2], D. D. Gladman[3,4,5], B. Parikh[6], X. Meng[7], C. Gaillez[8], P. J. Mease[9,10]. [1]Johns Hopkins University School of Medicine, Division of Rheumatology, Baltimore, United States of America; [2]Cleveland Clinic, Rheumatologic and Immunologic Disease, Cleveland, United States of America; [3]Krembil Research Institute, Division of Rheumatology, Toronto, Canada; [4]Toronto Western Hospital, Division of Rheumatology, Toronto, Canada; [5]University of Toronto, Division of Rheumatology, Toronto, Canada; [6]Novartis Pharmaceuticals Corporation, Rheumatology, East Hanover, United States of America; [7]Novartis Pharmaceuticals Corporation, Biostatistics, East Hanover, United States of America; [8]Novartis Pharma AG, Rheumatology, Basel, Switzerland; [9]Swedish Medical Center/Providence St. Joseph Health, Rheumatology, Seattle, United States of America; [10]University of Washington, Rheumatology, Seattle, United States of America

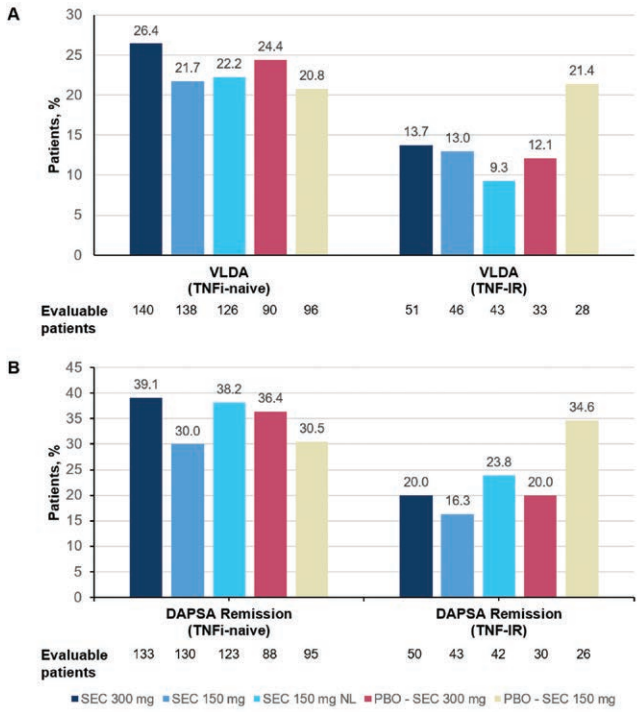
Table 1. Achievement of Key Outcomes Across PsA Manifestations at Week 104 Among TNF-IR and TNFi-Naive Patients Treated With SEC

	SEC 300 mg		SEC 150 mg[a]		SEC 150 mg No Load[b]		PBO–SEC 300 mg		PBO–SEC 150 mg[c]	
Outcomes, n/M (%)	**TNFi-naive n=154**	**TNF-IR n=68**	**TNFi-naive n=153**	**TNF-IR n=67**	**TNFi-naive n=157**	**TNF-IR n=65**	**TNFi-naive n=109**	**TNF-IR n=44**	**TNFi-naive n=114**	**TNF-IR n=39**
TJC/SJC resolution	51/140 (36.4)	19/51 (37.3)	46/136 (33.8)	11/46 (23.9)	53/125 (42.4)	14/43 (32.6)	40/90 (44.4)	11/31 (35.5)	32/96 (33.3)	10/28 (35.7)
Resolution of dactylitis	42/48 (87.5)	11/16 (68.8)	37/43 (86.0)	16/19 (84.2)	56/62 (90.3)	11/13 (84.6)	35/41 (85.4)	5/7 (71.4)	30/33 (90.9)	10/12 (83.3)
Resolution of enthesitis	70/88 (79.5)	22/30 (73.3)	70/85 (82.4)	24/32 (75.0)	50/69 (72.5)	16/26 (61.5)	37/50 (74.0)	12/17 (70.6)	39/56 (69.6)	14/20 (70.0)
mNAPSI75	61/73 (83.6)	15/26 (57.7)	66/76 (86.8)	16/23 (69.6)	61/80 (76.3)	13/18 (72.2)	42/51 (82.4)	13/17 (76.5)	34/64 (53.1)	7/14 (50.0)
PASI100	34/68 (50.0)	14/29 (48.3)	41/85 (48.2)	5/19 (26.3)	33/73 (45.2)	4/18 (22.2)	23/45 (51.1)	9/18 (50.0)	19/46 (41.3)	6/13 (46.2)

IR, inadequate responder; M, number of evaluable patients; mNAPSI, modified Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; PBO, placebo; SEC, secukinumab; TJC/SJC resolution, 0 tender/swollen joints; TNFi, tumor necrosis factor inhibitor.a Includes 53 TNFi-naive and 23 TNF-IR patients with dose escalation.b Includes 58 TNFi-naive and 19 TNF-IR patients with dose escalation.c Includes 40 TNFi-naive and 12 TNF-IR patients with dose escalation.

Background: The goal of treating psoriatic arthritis (PsA) is to achieve very low disease activity or remission across disease manifestations. In the phase 3 FUTURE 5 study (NCT02404350), patients receiving secukinumab (SEC) demonstrated sustained clinical improvements across PsA manifestations through Week 104.[1] However, the effect of previous tumor necrosis factor inhibitor (TNFi) exposure on achievement of remission across PsA manifestations was not explored.
Objectives: To report exploratory efficacy analyses of SEC at Week 104 on stringent endpoints across PsA manifestations in patients who were TNFi naive or inadequate responders (TNF-IR).
Methods: Patient data from FUTURE 5 were stratified by previous TNFi exposure and analyzed by treatment arm. At Week 104, patients received SEC 300 or 150 mg with subcutaneous loading dose (LD), SEC 150 mg without LD, or had received placebo up to Week 16 and were switched to SEC 300 or 150 mg between Weeks 16 or 24 based on tender and swollen joint count response. Patients with suboptimal clinical response to SEC 150 mg could escalate to SEC 300 mg after Week 52 per investigator judgment.[2] Exploratory efficacy analyses at Week 104 included resolution of TJC/SJC (0 tender/swollen joints), resolution of enthesitis and dactylitis, 75% improvement in the modified Nail Psoriasis Severity index (mNAPSI75), 100% improvement in the Psoriasis Area and Severity Index (PASI100), very low disease activity (VLDA), and Disease Activity in Psoriatic Arthritis (DAPSA) remission. Descriptive statistics are provided for each endpoint using an observed-case approach.

Figure. Proportion of Patients Achieving **(A)** VLDA and **(B)** DAPSA Remission at Week 104



DAPSA, Disease Activity in Psoriatic Arthritis; IR, inadequate responders; NL, no subcutaneous loading dose; PBO, placebo; SEC, secukinumab; VLDA, very low disease activity based on body surface area.

Results: Regardless of previous TNFi exposure, SEC-treated patients achieved several stringent endpoints across PsA domains, including TJC/SJC resolution, resolution of dactylitis/enthesitis, mNAPSI75, and PASI100 at Week 104 (Table 1). TNFi-naive patients generally experienced greater improvements than TNF-IR patients (Table 1 above). Similar trends were observed for achievement of VLDA and DAPSA remission at Week 104 (Figure 1).
Conclusion: SEC treatment resulted in sustained achievement of stringent endpoints across key PsA manifestations through Week 104 in both TNFi-naive and TNF-IR patients, with generally greater clinical responses among TNFi-naive patients.

REFERENCES:

[1] Mease P, et al. *Ann Rheum Dis*. 2018;77:890-897.
[2] Mease P, et al. *Arthritis Rheumatol*. 2019;71:(suppl 10) [abstract 1554].

Acknowledgements: This study was funded by Novartis Pharma AG. The authors thank Prasanthi Mandalay, PhD, of ArticulateScience LLC, for providing medical writing support/editorial support, which was funded by Novartis Pharmaceuticals Corporation, East Hanover, NJ, in accordance with Good Publication Practice (GPP3) guidelines (http://www.ismpp.org/gpp3).

Disclosure of Interests: Ana-Maria Orbai Consultant of: Janssen, Eli Lilly, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Celgene, Horizon, Janssen, Eli Lilly, and Novartis, M Elaine Husni Consultant of: AbbVie, Amgen, Gilead, Janssen, Eli Lilly, Novartis, Pfizer, Regeneron, and UCB, Grant/research support from: Pfizer, Dafna D Gladman Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Galapagos, Gilead, Janssen, Eli Lilly, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Novartis, Pfizer, and UCB, Bhumik Parikh Employee of: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, Xiangyi Meng Employee of: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, Corine Gaillez Employee of: Novartis Pharma AG, Basel, Switzerland, Philip J Mease Speakers bureau: AbbVie, Amgen, Janssen, Eli Lilly, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Galapagos, Gilead, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Pfizer, Sun Pharma, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Gilead, Janssen, Eli Lilly, Novartis, Pfizer, Sun Pharma, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.1862

POS1051

SECUKINUMAB IMPROVES PHYSICAL FUNCTION AND INHIBITS STRUCTURAL DAMAGE IN PsA PATIENTS WITH SUSTAINED REMISSION OR LOW DISEASE ACTIVITY: RESULTS FROM A PHASE 3 STUDY

L. C. Coates[1], P. J. Mease[2], D. D. Gladman[3], S. Navarra[4], W. Bao[5], C. Gaillez[6].
[1]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; [2]*Swedish Medical Center/Providence St. Joseph Health and University of Washington, Department of Rheumatology, Seattle, Washington, United States of America*; [3]*Toronto Western Hospital, University of Toronto, Schroeder Arthritis Institute, Ontario, Canada*; [4]*University of Santo Tomas Hospital, Section of Rheumatology, Manila, Philippines*; [5]*Novartis Pharmaceuticals Corporation, Immunology, Hepatology and Dermatology, East Hannover, New Jersey, United States of America*; [6]*Novartis Pharma AG, Immunology, Hepatology and Dermatology, Basel, Switzerland*

Background: Disease Activity Index for Psoriatic Arthritis (DAPSA) or the minimal disease activity (MDA) are considered for defining remission (REM) or low disease activity (LDA) in secukinumab (SEC) treated patients (pts) with PsA (Psoriatic Arthritis).[1] Currently, limited SEC data are available on pts with PsA achieving sustained REM in clinical trials or real-world evidence, using these stringent criteria.
Objectives: To report an exploratory analysis on achievement of sustained REM/LDA in pts with PsA treated with SEC and impact on structural outcomes, physical function and health-related quality of life (HRQoL) in the FUTURE 5 study (NCT02404350).

Methods: FUTURE 5 is a randomised, double-blind, placebo-controlled 2-year phase 3 trial in pts with active PsA.[2] Pts randomised to SEC 150 mg could be escalated to 300 mg from Week (Wk) 52 to 104, based on investigators' judgement. The pts were categorised as either not achieving REM/LDA, achieving it once only or sustained REM/LDA, which was defined as pts who achieved REM/LDA between Wks 24-52 and maintained the same response at least 2 of the next 6 visits (visit every 8 Wks). Of pts who did not achieve REM/LDA, achieved REM/LDA (VLDA, DAPSA REM, MDA, DAPSA LDA+REM) between Wk 24 and 52, the relationship between absence of REM/LDA, REM/LDA, sustained REM/LDA, proportion of pts with non-radiographic progression (assessed using the van der Heijde [mTSS]), physical function (health assessment questionnaire disability index [HAQ-DI]), and short form-36 physical component score [SF-36 PCS])[3] were assessed.

Results: In total, 996 pts were randomised to one of 4 treatment groups: SEC 300 mg loading dose (LD; N=222), SEC 150 mg LD (N=220), SEC 150 mg no loading dose (NL; N=222), and placebo (N=332). The baseline clinical characteristics were comparable across treatment groups. Majority of pts could achieve either sustained MDA/sustained DAPSA LDA+REM (Figure 1). Pts achieving REM/LDA, whether at one visit or consistently, showed improved physical function and SF36-PCS at Wk 104.[3]A high proportion of pts did not show radiographic progression at Wk 104 irrespective of achievement of REM/LDA category (Table 1**).**

Conclusion: The majority of patients treated with secukinumab were able to achieve sustained LDA. Sustained LDA/REM was associated with improved HRQoL, physical function and inhibition of structural damage progression.

REFERENCES:

[1] Coates LC, et al. *J Rheumatol.* 2018;46(1):38–42.
[2] Van der Heijde D, et al. *Rheumatology*. 2020;59(6):1325–1334.
[3] Coates L, et al. [0353]. *Arthritis Rheumatol*. 2020;72 (suppl 10).

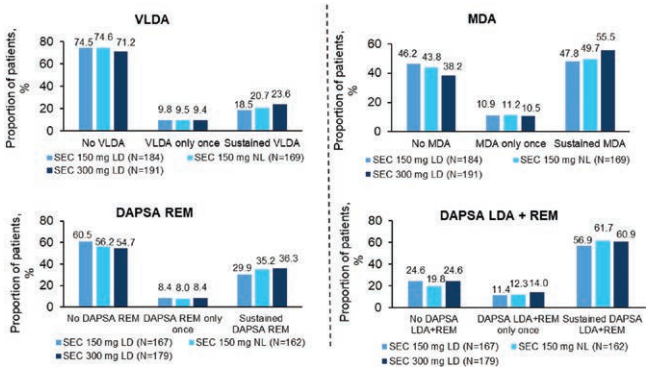


Figure 1. Proportion of patients achieving VLDA/MDA/DAPSA REM/DAPSA REM+LDASustained REM/LDA was defined if the same response was achieved at least 2 out of the next 6 visits (every 8 weeks), respectively. DAPSA, Disease activity in Psoriatic Arthritis; LD, loading dose; LDA, Low Disease Activity; MDA, Minimal Disease Activity; N, number of randomised patients assessed at both Week 24 and 104; NL, without loading dose; REM, remission; SEC, secukinumab; VLDA, Very Low Disease Activity

Table 1. Percentage of vdH-mTSS no progression at Week 104 (change from baseline ≤0.5) by REM/LDA and sustained REM/LDA status

REM and LDA composite indices, n (%)	Treatment group	No REM/LDA	REM/LDA only once	Sustained REM/LDA
MDA	SEC 150 mg LD	64 (75.3)	16 (80.0)	76 (86.4)
	SEC 150 mg NL	56 (75.7)	15 (78.9)	69 (82.1)
	SEC 300 mg LD	58 (79.5)	19 (95.0)	100 (94.3)
VLDA	SEC 150 mg LD	108 (78.8)	15 (83.3)	30 (88.2)
	SEC 150 mg NL	95 (75.4)	13 (81.3)	32 (91.4)
	SEC 300 mg LD	115 (84.6)	17 (94.4)	45 (100.0)
DAPSA REM	SEC 150 mg LD	77 (76.2)	11 (78.6)	46 (92.0)
	SEC 150 mg NL	65 (71.4)	10 (76.9)	50 (87.7)
	SEC 300 mg LD	82 (83.7)	14 (93.3)	63 (96.9)
DAPSA LDA + REM	SEC 150 mg LD	29 (70.7)	16 (84.2)	80 (84.2)
	SEC 150 mg NL	23 (71.9)	15 (75.0)	79 (79.0)
	SEC 300 mg LD	39 (88.6)	21 (84.0)	97 (89.0)

Sustained REM/LDA was defined if the same response was achieved at least twice out of the next 6 visits (every 8 weeks), respectively. n, number of evaluable patients; vdH-mTSS, van der Heijde- modified total Sharp score

Disclosure of Interests: Laura C Coates Consultant of: Abbvie, Amgen, Biogen, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer and UCB, Grant/research support from: Abbvie, Celgene, Lilly, Novartis and Pfizer, Philip J Mease Speakers bureau: AbbVie, Amgen, Janssen, Lilly, Novartis, Pfizer and UCB, Consultant of: AbbVie, Amgen, BMS, Boehringer Ingelheim, Galapagos, Celgene, Genentech, Gilead, Janssen, Lilly, Novartis, Pfizer, SUN Pharma, and UCB, Grant/research support from: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, SUN, and UCB, Dafna D Gladman Consultant of: Abbvie, Amgen, BMS, Celgene, Eli Lilly, Gilead, Galapagos, Janssen, Novartis, Pfizer and UCB, Grant/research support from: Abbvie, Amgen, BMS, Celgene, Eli Lilly, Gilead, Galapagos, Janssen, Novartis, Pfizer and UCB, Sandra Navarra Speakers bureau: Pfizer, Novartis, Astra-Zeneca, Janssen, Lilly, and Astellas, Consultant of: Pfizer, Novartis, Astra-Zeneca, Janssen, Lilly, and Astellas, Weibin Bao Shareholder of: Novartis, Employee of: Novartis, Corine Gaillez Shareholder of: Novartis and BMS, Employee of: Novartis.
DOI: 10.1136/annrheumdis-2021-eular.1971

POS1052

PSORIATIC ARTHRITIS AND OBESITY IMPACT DRUG PERSISTENCE IN USTEKINUMAB-TREATED PATIENTS WITH PSORIASIS IN THE BRITISH ASSOCIATION OF DERMATOLOGISTS BIOLOGIC AND IMMUNOMODULATORS REGISTER (BADBIR): A 10-YEAR FOLLOW-UP STUDY

A. Ogdie[1], W. Tillett[2], A. Passey[3], P. Gorecki[4]. [1]*University of Pennsylvania, Perelman School of Medicine, Philadelphia, United States of America*; [2]*Royal National Hospital for Rheumatic Diseases, Rheumatology, Bath, United Kingdom*; [3]*Janssen Real World Evidence, HEMAR EMEA, High Wycombe, United Kingdom*; [4]*Janssen, Medical Affairs, High Wycombe, United Kingdom*

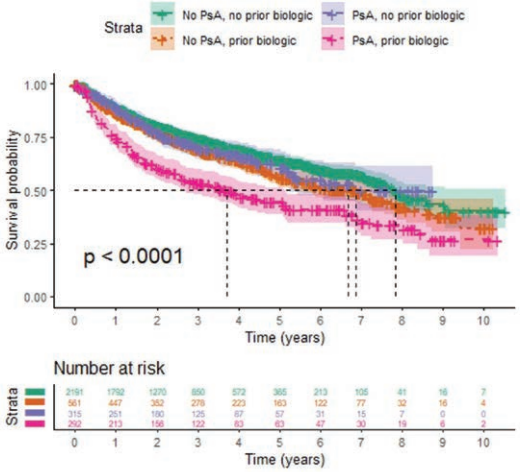
Background: Up to 80% of patients with psoriatic arthritis (PsA) have comorbid psoriasis (PsO).[1] However, data on the impact of comorbid PsA on treatment persistence in PsO patients are limited with mixed findings.[2–4] Other factors have been implicated in predicting response to treatment, including obesity, which is associated with PsA and has demonstrated a varying effect on biologic persistence.[2,3,5,6]

Objectives: The primary objective of this study was to evaluate whether comorbid PsA and obesity impact ustekinumab (UST) persistence in PsO patients using the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR). Additionally, the effect of line of therapy was investigated.

Methods: This retrospective observational study used data from PsO patients receiving UST in the BADBIR (first enrolled 07/2009; 10/2020 data cut-off). Time to discontinuation (TTD) was defined as time from treatment start date until treatment stop date, censoring for loss to follow-up where patients are lost to follow-up or active in the registry without a recorded treatment stop date. Kaplan–Meier survival analysis was used to estimate probability of discontinuation over time and median TTD. Patients were stratified by PsA diagnosis (recorded as a comorbidity at enrolment) and prior biologic experience (history of treatment with ≥1 other biologic). The log-rank test was used to compare persistence among groups. Hazard ratios (HRs), confidence intervals (CI) and p-values for effect of obesity, PsA status and prior biologic exposure on TTD were generated using Cox proportional hazards regression.

Results: Univariate analysis found that median TTD was shorter for patients with comorbid PsO and PsA (5.04 years; n=585) vs. patients with PsO alone (7.19 years; n=2698; p<0.0001). Biologic-experienced patients with comorbid PsO and PsA (n=292) had a significantly higher likelihood of discontinuation than any other group, with a median TTD of 3.84 years (p<0.0001; Figure 1). In

Fig. 1: Drug survival in patients with PsO treated with UST, stratified by presence of comorbid PsA and prior biologic experience.



p-value for drug survival probability across all groups. PsA, psoriatic arthritis; PsO, psoriasis; UST, ustekinumab.

multivariable models, biologic-experienced patients were more likely to discontinue treatment (HR 1.21 [95% CI 1.04–1.43]; p=0.017) vs. biologic-naïve patients, while PsA had no significant effect on TTD alone vs. no PsA (HR 1.12 [95% CI 0.9–1.4]; p=0.31). However, comorbid PsA increased the likelihood of treatment discontinuation for biologic-experienced patients (HR 1.45 [95% CI 1.06–1.97]; p=0.018). Obesity was a further predictor of discontinuation (HR 1.15 [95% CI 1.02–1.31]; p=0.027) and this was independent of comorbid PsA and prior biologic exposure (Table 1).

Conclusion: Comorbid PsA was associated with reduced time-to-discontinuation of UST in biologic-experienced patients, but not biologic-naïve patients. Obesity also impacted TTD but independently of PsA status.

REFERENCES:

[1] Coates and Helliwell. *Clin Med* 2017;17:65–70
[2] Menter et al. *J Eur Acad Dermatol Venereol* 2016;30:1148–58
[3] Mourad et al. *Br J Dermatol* 2019;181:450–8
[4] Yiu et al. *Br J Dermatol* 2020;183:294–302
[5] Mease et al. *RMD Open* 2015;1:e000181
[6] Costa et al. *Clin Rheumatol* 2019;38:2355–62

Table 1. Multivariate analysis of UST discontinuation in PsO patients (N=3,174).

Covariate	Status (n)	HR	95% CI	p-value
Comorbid PsA	No PsA	ref	-	-
	(n=2609)			
	PsA	1.12	0.90–1.40	0.31
	(n=565)			
Biologic experience	No prior biologic (n=2371)	ref	-	-
	Prior biologic (n=803)	1.21	1.04–1.43	0.017
PsA*prior biologic experience	No PsA, prior biologic	ref	-	-
	(n=539)			
	PsA, prior biologic	1.45	1.06–1.97	0.018
	(n=264)			
Obesity (BMI, kg/m^2)	<30	ref	-	-
	(n=1554)			
	≥30	1.15	1.02–1.31	0.027
	(n=1620)			

BMI, body mass index; CI, confidence interval; HR, hazard ratio; PsA, psoriatic arthritis; PsO, psoriasis; ref, reference; UST, ustekinumab.

Disclosure of Interests: Alexis Ogdie Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Janssen, Eli Lilly, Novartis and Pfizer, Grant/research support from: Pfizer to Penn, Novartis to Penn, Amgen to Forward/NDB, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB, Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, MSD, Pfizer and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen and UCB, Alun Passey Employee of: Janssen-Cilag Ltd, Patricia Gorecki Employee of: Janssen-Cilag Ltd.

DOI: 10.1136/annrheumdis-2021-eular.1997

POS1053 COMPARISON OF BASELINE CHARACTERISTICS BETWEEN PATIENTS CONTINUING OR DISCONTINUING APREMILAST AT TWELVE MONTHS IN THE REWARD STUDY (THE NETHERLANDS)

R. Bos[1], T. Jansen[2], S. De Jong[3], A. Castiglia[4], M. Vis[5]. [1]*Medisch Centrum Leeuwarden, Rheumatology, Leeuwarden, Netherlands*; [2]*Viecurie MC, Rheumatology, Venlo, Netherlands*; [3]*Amgen BV, Medical Affairs, Breda, Netherlands*; [4]*Amgen Europe GmbH, Medical, Rotkreuzt, Switzerland*; [5]*Erasmus MC, Rheumatology, Rotterdam, Netherlands*

Background: Previous analysis of the REWARD study reported that patients with limited joint involvement have a considerable burden of disease[1]. Recent data suggest that patients with moderately active psoriatic arthritis (PsA) and a limited joint involvement have a high likelihood of achieving treatment goals when treated with apremilast[2]. According to EULAR recommendations a PDE4 inhibitor may be considered in patients with mild disease and an inadequate response to at least one csDMARD, in whom neither a bDMARD nor a JAK inhibitor is appropriate and the value of apremilast may be found in treating patients with relatively mild disease (oligoarticular)[3].

Objectives: The objective of this prospective, multicentre, non-interventional study is to describe patient reported outcomes, effectiveness and real-life use of apremilast in patients with PsA. Patients will be followed up for a maximum of 12 months. This interim analysis compared the baseline characteristics and experience on apremilast for two subgroups of patients, those remaining on apremilast versus the ones that discontinued.

Methods: In this interim analysis we included patients with data available at cut-off date of 03 November 2020. Patient enrollment and follow up of current subjects is ongoing. Descriptive statistics (n's and percents for categorical data, means for continuous data) were used to summarize the baseline data by subgroup. Kaplan Meier plots are presented to show patients' experience on apremilast by subgroup.

Results: 85 patients were included in the analysis. 30 patients have completed the study, 39 patients have discontinued and 16 are ongoing. At baseline 22 (26%) patients were biologic experienced and 62 (74%) were biologic naïve. Both groups had a comparable disease activity measured with clinical disease activity in psoriatic arthritis (cDAPSA) scores. Biologic experienced patients had a longer disease duration compared to biologic naïve patients (mean 9.7 vs 6.2 years). Inefficacy of previous medication was the main reason for starting apremilast in both subgroups. Overall, 86% (n=69) of patients were still receiving apremilast at month 3, 60% (n=46) at month 6, and 41% (n=26) at month 12 (Figure 1). Drug survival (length of time until discontinuation of apremilast) for biologic naïve patients was 93% at month 3, 73% at month 6 and 58% at month 12. Drug survival of biologic experienced patients was 67%, 20%, and 0% at months 3, 6, and 12, respectively. At baseline mean values of body mass index (BMI), swollen joint count (SJC), tender joint count (TJC), psoriatic arthritis impact of disease (PsAID) were comparable between both groups (Table 1). Reasons for discontinuation were mainly lack of efficacy (49%) and adverse events (44%). In this analysis the nature and frequency of adverse events is in line with the known profile of apremilast.

Conclusion: In this interim analysis, patients who were biologic naïve had a better probability to remain on treatment than those who were biologic experienced. Baseline characteristics were similar between the two groups, apart from disease duration that was longer in the biologic experienced group. Best drug survival is achieved when apremilast is prescribed earlier in the PsA treatment course, before biologics and after csDMARDs, as per apremilast EU label.

REFERENCES:

[1] Jansen TL, et al. Ann Rheum Dis. 2019;78:913 [abstract FRI0442]
[2] Mease PJ, et al. Arthritis Care Res 2020 72 6 814–821
[3] Gossec L, et al. Ann Rheum Dis 2020;79:700–712

Disclosure of Interests: Reinhard Bos Consultant of: AbbVie BV, Genzyme Europe, Janssen-Cilag, Novartis, Pfizer, Grant/research support from: Galapagos, Tim Jansen Consultant of: AbbVie, Celgene Corporation – consultant, Speakers bureau: Grunenthal, Sobi – speakers bureau, Grant/research support from: ReumaNederland, Olatec, Grunenthal – grant/research support, Sylvia de Jong Shareholder of: Employee of Amgen Inc, Employee of: Employee of Amgen Inc, Antonio Castiglia Shareholder of: Employee of Amgen Inc, Employee of: Employee of Amgen Inc, Marijn Vis Consultant of: AbbVie, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, AbbVie, Celgene Corporation, Eli Lilly, Novartis, Pfizer.

DOI: 10.1136/annrheumdis-2021-eular.2081

POS1054 UPADACITINIB PHARMACOKINETICS AND EXPOSURE-RESPONSE RELATIONSHIPS FOR EFFICACY AND SAFETY IN PSORIATIC ARTHRITIS – ANALYSES OF THE PHASE 3 SELECT-PsA STUDIES

E. Muensterman[1], B. Engelhardt[1], S. Gopalakrishnan[2], J. Anderson[3], M. E. Mohamed[1]. [1]*AbbVie, Clinical Pharmacology and Pharmacometrics, North Chicago, United States of America*; [2]*Merck KGaA, Translational Medicine, Darmstadt, Germany*; [3]*AbbVie, Clinical Development, North Chicago, United States of America*

Background: Upadacitinib (UPA) is an oral, reversible, JAK inhibitor approved for the treatment of rheumatoid arthritis (RA). The efficacy and safety profile of UPA in psoriatic arthritis (PsA) has been established in the SELECT-PsA program which includes two global Phase 3 studies.

Objectives: These analyses characterize UPA pharmacokinetics and exposure-response relationships for efficacy and safety endpoints using data from the SELECT-PsA studies.

Methods: The SELECT-PsA program enrolled patients with prior inadequate response (IR) or intolerance to ≥1 non-bDMARD1 (N=1705) and prior IR or intolerance to ≥1 bDMARD2 (N=642). Data from both trials was integrated for patients receiving placebo (PBO), UPA 15mg once daily (QD) and UPA 30mg QD; adalimumab data was excluded from this analysis. UPA pharmacokinetics were characterized in PsA patients using Bayesian population pharmacokinetics analyses and utilizing prior information from analyses in healthy subjects and RA patients. Exposure-response analyses were conducted using logistic regression to characterize the relationships between upadacitinib average plasma concentration during a dosing interval (Cavg) and the percentage of patients achieving

ACR20/50/70 at Weeks 12 and 24, static Investigator Global Assessment of psoriasis (sIGA) of 0 or 1 (clear or almost clear) and at least a 2-point improvement from baseline, and PASI75 at Weeks 16 and 24 or experiencing selected clinically relevant safety events through week 24.

Results: Analyses were conducted using data from 1694 subjects (for pharmacokinetics) and 1916 subjects (for exposure-response analyses). UPA model-estimated plasma exposures in subjects with PsA who received 15mg and 30mg QD doses were comparable to previously estimated exposures in subjects with RA. Body weight and methotrexate use had no clinically relevant effects on UPA exposures. There was a statistically significant relationship between UPA Cavg and the percentage of subjects who achieved Week 12 ACR50/70, Week 16 sIGA 0/1, and Week 24 sIGA 0/1 (Figure 1). No statistically significant exposure-response relationship was observed for Week 12 ACR20, Week 16 PASI75, or Week 24 ACR20/50/70 or PASI75, indicating that the 15mg QD exposures are approximately at the plateau of response for these endpoints. No statistically significant relationships were observed between upadacitinib Cavg and the percentage of subjects experiencing pneumonia, herpes zoster, hemoglobin < 8 g/dL, Grade ≥3 lymphopenia, Grade ≥3 neutropenia. There was a shallow but statistically significant exposure-response relationships with the occurrence of serious infections and decrease in hemoglobin from baseline (>2 g/dL and >2 g/dL in combination with hemoglobin < lower limit for normal).

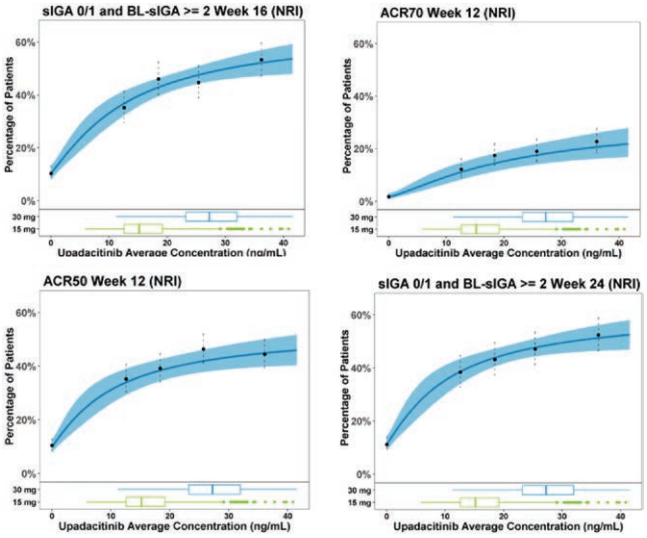


Figure 1. Observed and Model Predicted Efficacy Responses at Week 12 (for ACR50/70) or at Weeks 16 and Week 24 (for sIGA 0/1) Versus Upadacitinib Plasma Exposures

Conclusion: Exposure-response analyses demonstrated that plasma exposures associated with UPA 15 mg QD achieves robust efficacy in subjects with PsA with limited effects on the evaluated safety endpoints. UPA plasma exposures associated with UPA 15 and 30mg QD are predicted to provide similar ACR responses by week 24 while a small additional efficacy benefit with UPA 30mg is predicted for the achievement sIGA 0/1.

REFERENCES:

[1] van Vollenhoven R, et al. Monotherapy with Upadacitinib in MTX-naïve Patients with Rheumatoid Arthritis: Results at 48 Weeks from the SELECT-EARLY Study. 2019 EULAR; THU0197

[2] Fleischmann R, et al. Safety and Effectiveness of Upadacitinib or Adalimumab in Patients with Rheumatoid Arthritis: Results at 48 weeks from the SELECT-COMPARE Study. 2019 EULAR; FRI0147

Disclosure of Interests: Elena Muensterman Shareholder of: AbbVie, Employee of: AbbVie, Benjamin Engelhardt Shareholder of: AbbVie, Employee of: AbbVie, Sathej Gopalakrishnan Shareholder of: AbbVie, Employee of: AbbVie, Jaclyn Anderson Shareholder of: AbbVie, Employee of: AbbVie, Mohamed-Eslam Mohamed Shareholder of: AbbVie, Employee of: AbbVie.

DOI: 10.1136/annrheumdis-2021-eular.2182

POS1055 HIGH SATISFACTION WITH USTEKINUMAB TREATMENT IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS – FINAL RESULTS OF THE NON-INTERVENTIONAL STUDY SUSTAIN DEMONSTRATE EARLY AND LONG-TERM TREATMENT RESPONSE AND HIGH TOLERABILITY

J. Wendler[1], E. Movshovich[2], N. Damann[2], F. Hamann[3], P. Wagener[4], F. Behrens[5]. *[1]Rheumatologische Schwerpunktpraxis, Erlangen, Erlangen, Germany*; *[2]Janssen-Cilag, Neuss, Neuss, Germany*; *[3]Gemeinschaftspraxis für internistische Rheumatologie, Leipzig, Leipzig, Germany*; *[4]Fachpraxis für Rheumatologie und Osteologie, Bruchhausen-Vilsen, Bruchhausen-Vilsen, Germany*; *[5]Goethe-Universität, Rheumatologie and Fraunhofer Institut IME -TMP, Frankfurt, Germany*

Background: From February 2015 to April 2020, patients with active psoriatic arthritis under treatment with ustekinumab in routine clinical care in Germany were included into the prospective, multi-center non-interventional study SUSTAIN.

Objectives: Here, we present final data from SUSTAIN including final week 160 on long term efficacy and safety of ustekinumab treatment, quality of life and further patient reported outcomes.

Methods: In SUSTAIN, 337 patients were treated with ustekinumab according to routine clinical care at 75 centers for 160 weeks with documentation intervals at week 0 and 4 and then every 12 weeks. The collected data included demographics, number of swollen and tender joints, tender entheses, amount of skin symptoms (BSA and PASI), patient reported outcome concerning disease activity and pain, Health Assessment Questionnaire (HAQ), quality of life (SF-12), sleep quality (VAS), satisfaction with therapy of patient and physician, safety (adverse events [AE]/serious adverse events [SAE]), pharmacoeconomic aspects, number of patients with „Minimal Disease Activity“ (MDA) and number of patients with MDA at week 28 und 52. For this analysis, final data of all 337 patients of all documented visits were analyzed.

Results: The visit at week 4 was documented for 31 patients, at week 28 for 282, at week 52 for 216, and at week 160 for 129 of the 337 patients. At baseline, the patients had a mean age of 53.6 years (22-85) and 192 (57%) were female. The patients' mean BMI was 29.6 kg/m^2 (18.6-52). 54.3 % of the patients had at least one TNF inhibitor as prior medication. 54.1 % of the patients used MTX as concomitant medication. At time of inclusion, 73.3% of the patients showed arthritis at small and 52.2% at large joints. 16.9% showed spinal involvement and 13.1% enthesitis. In the course of the treatment, the number of tender joints improved from a mean of 10.0 (CI 95% 8.6/11.3) at baseline to 4.1 (3.2/4.9) at week 28, 3.6 (2.7/4.6) at week 52 and 1.0 (0.6/1.4) at week 160. Number of swollen joints improved from 4.1 (3.4/4.9) at baseline to 1.8 (1.2/2.3) at week 28, to 1.3 (0.8/1.8) at week 52 and to 0.4 (0.2/0.6) at week 160. BSA declined from a mean of 15.6% (rage from 0 to 80.0%) at baseline to 5.2% (0 to 60%) at week 28, to 3.0% (0 to 45.0%) at week 52 and to 1.7 (0 to 35%) at week 160. PASI declined from a mean of 7.3 (range from 0 to 43.0) at baseline to 1.7 (0 to 24.8) at week 28, to 1.3 (o to 28.5) at week 52 and to 0.5 (0 to 3.2) at week 160. Efficacy of the therapy with ustekinumab was assessed as “very good” or “good” by 85.3% of the treating physicians at week 52 and by 94.1% at week 160. The patients assessed the efficacy as “very good” or “good” by 82.8% at week 52 and by 89.8% at week 160. At the end of the study, 96 SAEs have been documented, of which only 16 were related to ustekinumab. All in all, safety of therapy with ustekinumab was assessed as “very good” or “good” by 99% of the treating physicians after 52 weeks and by 99.2 % after 160 weeks. The patients assessed the safety as “very good” or “good” by 97.5% at week 52 and by 100% at week 160.

Conclusion: The non-interventional study SUSTAIN showed relevant disease improvements and good safety with an outstanding high therapy satisfaction in patients with active psoriatic arthritis treated with ustekinumab. Treatment effect was observed as early as after 4 weeks. The treatment effects and satisfaction sustained up end of documentation at week 160 in daily practice life.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2495

POS1056 COMPARATIVE EFFICACY OF TNF INHIBITORS VERSUS OTHER CYTOKINE INHIBITOR BDMARDS ON PSORIATIC ARTHRITIS IMPACT OF DISEASE (PSAID) SCORE AND DOMAINS

A. Rauf[1], C. Hughes[1], D. Hill[1], P. Kiely[1,2]. *[1]Rheumatology, Rheumatology, London, United Kingdom*; *[2]St George's, University of London, Institute of Medical and Biomedical Education, London, United Kingdom*

Background: Psoriatic arthritis (PsA) has many consequences, reflecting musculoskeletal and skin inflammation, with the potential to adversely affect overall quality of life. Patient reported outcome measures (PROM) assess a holistic range of aspects of quality of life, including physical and mental components, and provide broad detailed information of the impact of disease. Biologic DMARDs (bDMARDs) targeting TNF have been used to treat PsA for over 10 years whereas inhibitors of IL-17, IL-12/23 and Janus kinases (JAK) have only been available more recently. They all target differing cytokines, including JAK inhibitors which inhibit IL-12 and IL-23 signaling but not TNF signaling. Their relative impact on PROMs is unknown.

Objectives: To assess, in routine care, the relative impact in PsA of TNF inhibitors (TNFi) versus non-TNFi bDMARDs, targeting IL-17, IL-12/23 and JAK, on PROMs.

Methods: We performed a cross section analysis of PsA patients with established disease treated with bDMARDs and JAKi, under routine care at St George's University Hospital, London, UK. Patients completed the 12-item psoriatic arthritis impact of disease (PsAID) tool. The total PsAID score was calculated using the on-line EULAR toolkit (see reference). The PsAID total and individual domain scores were compared between TNFi and non-TNFi groups using the

Mann Whitney U test. A total PsAID score below 4 out of 10 is considered a 'patient-acceptable state'.

Results: A total 95 patients (female n= 53, 56%) completed the PSAID; TNFi n=72 (female 50%, adalimumab n=41, Etanercept n= 24, Golimumab n=4, Infliximab n =2, Certolizumab n=1) and non-TNFi n= 23 (female 74%, Secukinumab n=9, Ixekizumab n=1, Ustekinumab n=9, Tofacitinib n=4). The mean age was 53.6 (TNFi 53.5, non-TNFi 53.7) years, and duration of time on bDMARD treatment was TNFi 49.5 (range 1- 141) months, non-TNFi 25.3 (range 4 -59) months. The total and individual domain PsAID scores are shown in the Table 1. A 'patient acceptable state' total score <4 was recorded in TNFi 36/72 (50%) and non-TNFi 11/23 (48%). There was no significant difference between TNFi and non-TNFi groups in the mean total PsAID score, or proportion achieving a patient acceptable state. Patients on TNFi had lower (better outcome) mean scores for all 12 domains except skin, and the differences, versus non-TNFi treated patients, were significant for pain, functional capacity, discomfort and depression.

PSAID domain	TNFi	Non-TNFi	P value
Total score	3.31	4.64	N.S.
Pain	3.67	5.43	0.02
Fatigue	4.04	5.65	N.S.
Skin problems	3.11	2.78	N.S.
Work/leisure activities	3.56	4.78	N.S.
Functional capacity	3.29	5.04	0.02
Discomfort	3.88	5.65	0.02
Sleep disturbance	3.42	4.78	N.S.
Coping	3.01	4.09	N.S.
Anxiety, fear, uncertainty	2.64	4.17	N.S.
Embarrassment/shame	2.28	3.39	N.S.
Social participation	2.6	3.48	N.S.
Depression	2.11	3.91	0.03

Conclusion: In PsA, TNFi appear to have a greater impact over non-TNFi bDMARDs on some aspects of quality of life, including pain and functional capacity. TNFi and non-TNFi were no different with respect to patients' perspective on skin disease, embarrassment or shame, despite less good cutaneous responses in clinical trials from TNFi agents. Overall, the PsAID tool reveals an unmet burden on quality of life in PsA patients treated with all classes of bDMARDs and JAKi, as 50% fail to achieve a 'patient acceptable state'. This should prompt scrutiny of the high scoring domains and utilization of additional treatment modalities to achieve better holistic outcomes for PsA patients in routine care.

REFERENCES:

[1] PsAID tool: http://pitie-salpetriere.aphp.fr/psaid/raid_psaid_quest_home.php

Disclosure of Interests: Atif Rauf: None declared, Catherine Hughes: None declared, Diane Hill: None declared, Patrick Kiely Speakers bureau: Abbvie.

DOI: 10.1136/annrheumdis-2021-eular.2887

POS1057 DISCONNECT BETWEEN TREATMENT SWITCHES AND DISEASE ACTIVITY STATE IN EARLY PSORIATIC ARTHRITIS

J. Luime[1], M. Kok[2], I. Tchetverikov[3], M. Vis[1], C. Collaboration of Rheumatologists[4]on behalf of DEPAR studygroup. *[1]ErasmusMC, Rheumatology, Rotterdam, Netherlands*; *[2]Maasstad hospital, Rheumatology, Rotterdam, Netherlands*; *[3]Albert Schweitzer Hospital, Rheumatology, Dordrecht, Netherlands*; *[4]Cicero, Rheumatology, Rotterdam, Netherlands*

Background: Receiving adequate treatment early in the disease course is one of the most important prognostic factors to achieve optimal disease outcome in most rheumatological conditions. Treat-to-target strategies and early step-up of treatment are important ingredients to accomplish this. While for Rheumatoid Arthritis this is common practice on accepted targets, for Psoriatic Arthritis (PsA) this is less outspoken practice. In PsA multiple domains must be taken into account and also there is a less established practice to use PsA specific targets, such as MDA, although this is associated with a better quality of life.[1,2] Whether this affects optimal disease outcome is not well described

Objectives: To describe treatment strategies in newly diagnosed PsA with at least one synovitis and, treatment switches over time in those that not achieved MDA.

Methods: For this study we used data from the DEPAR study between August 2013 and February 2019. The DEPAR study is a cohort that includes newly diagnosed PsA patients and follows them for up to 6 years. Patients are classified at baseline according to their prominent features: mono-, oligo-, polyarthritis, enthesitis, dactylitis or axial phenotype. For this study we used the data from the first 2 years for the patients with an articular phenotype. Methotrexate (MTX) and MTX plus another s-DMARD or GCs were addressed separately as they form the cornerstone of treatment in PsA. Next treatment was grouped in the usual drug classes: sDMARD (conventional), bDMARD and Glucocorticoids (GCs). Descriptive statistics were applied in STATA16 and Tableau 2020.3

Results: Out of 620 patients, 478 patients had at least one swollen joint at baseline and were included in this analysis. 349 (73%) had data at 1 year and 267 (56%) at 2 years. Average age was 50.3 years(sd 14.1), and 50% was female. Half of the patients had oligo-arthritis, 30% poly-arthritis and 20% mono-arthritis. At baseline, clinical characteristics were 3.8 swollen joints (sd 4.9), 5.5 tender joints (sd 6.2), 3.1 PASI points (sd 3.7, skin), 0.8 entheseal points (LEI; sd 1.2) and 0.1 dacylitis count (basic count of digits; sd 0.6). Treatment was initiated with Monotherapy MTX in 51% of the patients, while 25% did not start any DMARD, 10% started a combination of s-DMARDs, 9% a single s-DMARD, 3% a b-DMARD and 2% GCs. This differed for the different phenotypes as shown in Table 1.

Minimal Disease Activity (MDA) was achieved by 32% after 3 months increasing to 58% at 24 months. Treatment switches in the non-MDA mono-, oligo- and polyarthritis groups are shown in Figure 1. In the patients not in MDA treatment was not switch in: 70% of patients with mono-arthritis, 50-66% with oligo-arthritis and 50% poly-arthritis. Similar observations were found when using the DAS28(<=3.2) or DAPSA(<14), both including only articular disease activity (data not shown).

Conclusion: Achieving MDA is associated with a better quality of life, though it is not yet common practice to make treatment adjustments based on MDA. Of the newly diagnosed PsA patients not in MDA, more than half of the clinical evaluations did not result in a switch of medication.

REFERENCES:

[1] Wervers, K, et al ART 2019

[2] Coates, L, et al. Lancet 2015

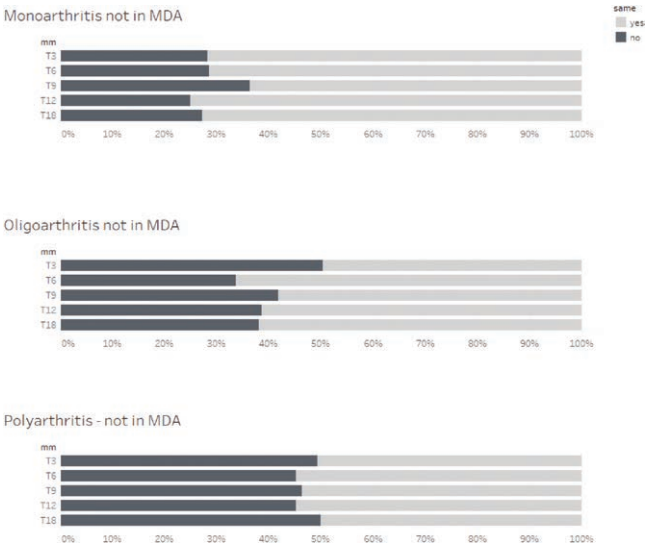


Figure 1. *Medication change in patients not in MDA at each timepoint (dark bars = change and light bars = no change)*

table 1 baseline medication

diagnosis	MTX mono	none	combi s-dmard	s-DMARDs	b-DMARDs	MTX+ GCs	GCs
monoarthritis	28%	58%	5%	6%	1%		2%
oligoarthritis	54%	20%	10%	10%	3%		2%
polyarthritis	62%	10%	13%	9%	4%	1%	1%
Grand Total	51%	25%	10%	9%	3%	0%	2%

Disclosure of Interests: Jolanda Luime: None declared, Marc Kok Grant/research support from: Pfizer, Novartis, BMS, Abbvie, Ilja Tchetverikov: None declared, Marijn Vis Grant/research support from: Novartis, CICERO collaboration of rheumatologists: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3748

POS1058 SUBCLINICAL DACTYLITIS: COMPARATIVE STUDY OF THERAPEUTIC RESPONSE WITH TNF INHIBITORS, SECUKINUMAB AND USTEKINUMAB

C. Guillén-Astete[1], Á. Andreu-Suárez[1], V. García García[1]. *[1]Hospital Ramón y Cajal, Rheumatology, Madrid, Spain*

Background: Non tender dactylitis has been recently associated with synovitis, tenosynovitis and enthesitis without fat tissue hyperemia. Dactylitis is a remarkable hallmark of spondyloarthritis and particularly in psoriatic arthritis. Also, dactylitis has been recognized as one of the most difficult musculoskeletal feature of the disease to treat. It has been of interest to compare the effectiveness of available therapies in cases of clinical dactylitis, however, the efficacy on subclinical dactylitis has not studied yet.

Objectives: To determine the effectiveness of three different biological therapy approaches in subclinical (non-tender) dactylitis in patients diagnosed by psoriatic arthritis in terms of changes detected by ultrasound scan.

Methods: A retrospective ultrasound record-based study was conducted to compare the findings of ultrasonographic studies performed before and 6 months after the start of one of the following biologic therapies in patients diagnosed by psoriatic arthritis: TNF-inhibitors, secukinumab and ustekinumab. We included patients with a complete before-after ultrasound scan of the hands from three different rheumatology clinics. To be considered as a subclinical dactylitis two conditions were had to be achieved: non tender finger and absence of fat tissue hyperemia.
Results: Patients included: 22 on TNF-inhibitors (28 subclinical dactylitis), 14 on secukinumab (17 subclinical dactylitis) and 13 on ustekinumab (16 subclinical dactylitis). Median of line of treatment of each biologic therapy: 1, 3 and 3, respectively. In the TNF-inhibtors group, 14/28 achieved synovitis resolution, 12/26 achieved tenosynovitis resolution and 2/28 achieved enthesitis resolution. In the secukinumab group, 11/17 achieved synovitis resolution, 11/17 achieved tenosynovitis resolution and 13/17 achieved enthesitis resolution. In the ustekinumab group, 10/16 achieved synovitis resolution, 10/15 achieved tenosynovitis resolution and 13/16 achieved enthesitis resolution. Complete dactylitis resolution was achieved in 12/28, 11/17 and 10/16 patients, respectively. Differences on independent success ratio of secukinumab and ustekinumab were not statistically significative, however both groups had higher rates of independent success compared to TNF-inhibitors group (P<0.05, both cases). The line of treatment did not affect the resolution rate of non-TNF-inhibitors group.
Conclusion: This is –as far as our knowledge know- the first study comparing the effect of different therapies on subclinical dactylitis. Besides the inherit limitations of a retrospective study, it seems to point that both secukinumab and ustekinumab are better therapeutic options than TNF-inhibitors. Of course, prospective further studies are needed.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4203

Psoriatic arthritis - clinical aspects (other than treatment)

POS1059 ULTRASOUND SYNOVITIS, UNLIKE ENTHESITIS OR CLINICAL JOINT ASSESSMENT, IS ASSOCIATED WITH JOINT DAMAGE PROGRESSION IN PATIENTS WITH PSORIATIC ARTHRITIS

Y. Yamada[1], K. Inui[2], T. Okano[1], K. Mandai[2], K. Mamoto[1], T. Koike[1], C. Tateishi[3], D. Tsuruta[3], H. Nakamura[1]. [1]*Osaka City University Graduate School of Medicine, Department of Orthopedic Surgery, Osaka city, Japan*; [2] *Saiseikai Nakatsu Hospital, Department of Orthopedic Surgery, Osaka city, Japan*; [3]*Osaka City University Graduate School of Medicine, Department of Dermatology, Osaka city, Japan*

Background: We previously reported that ultrasound assessment of enthesitis (US enthesitis) is not consistent with tenderness of the enthesis (clinical enthesitis) in patients with psoriatic arthritis (PsA). Although US enthesitis reflects inflammatory condition and clinical enthesitis is associated with disease activity and physical function, each of them was not associated with joint destruction by cross-sectional analysis1. It is reported that the utility of US for predicting joint destruction remains unclear among patients with PsA2.
Objectives: This study is aimed to longitudinally investigate the relationships between enthesitis or synovitis and joint damage progression in patients with PsA.
Methods: Forty-seven patients with PsA (average age of 56.5 years) underwent US and clinical examination of wrist and finger joints and 14 entheses (the bilateral humeral medial epicondyles and insertions of the triceps, distal quadriceps, proximal/distal patella, Achilles tendons, and plantar fascia). Tender or swollen joint count (TJC/SJC), Gray Scale (GS) and Power Doppler (PD) score of the joints, and US/clinical enthesitis counts were calculated. The relationships between the yearly progression in modified total sharp score (ΔmTSS) at two-time points (baseline and average follow-up of 20.4 months) and US or clinical findings were investigated.
Results: ΔmTSS was significantly correlated with age (r=0.44, p=0.01), joint GS score (r=0.44, p=0.01), and joint PD score (r=0.38, p=0.03). TJC, SJC, inflammatory marker, and disease activity showed no associations with ΔmTSS. US/clinical enthesitis counts also showed no associations with ΔmTSS (Table 1). The joint PD score, adjusted by age, was significant factor for ΔmTSS by multiple regression analysis (b=0.50, p<0.001).
Conclusion: The joint PD score or US synovitis, unlike clinical joint assessment, was significant predictive factor for joint damage progression. It is important to assess joints by US as well as clinical examination.
References: 1) Yutaro Yamada et al. Ultrasound assessment, unlike clinical assessment, reflects enthesitis in patients with psoriatic arthritis. Clin Exp Rheumatol. 2020 Apr 17. Online ahead of print.
2) van der Heijde et al. Assessing structural damage progression in psoriatic arthritis and its role as an outcome in research. Arthritis Res Ther. 2020, 22(1): 18.

Table 1. Univariate analysis of predictive factors for joint damage progression in PsA patients.

	mTSS at baseline		ΔmTSS	
	R value	p value	R value	p value
age	0.55	<0.001	0.44	0.01
PASE	0.04	0.81	0.12	0.52
PASI	-0.25	0.15	-0.01	0.96
DAS28CRP	-0.05	0.75	0.07	0.71
DAPSA	-0.01	0.94	-0.01	0.97
HAQ	0.17	0.27	-0.07	0.73
CRP	-0.13	0.38	0.23	0.20
MMP-3	0.04	0.80	0.29	0.12
biologics use	0.19	0.19	-0.11	0.54
Clinical enthesitis counts	-0.01	0.97	-0.19	0.30
TJC	-0.05	0.76	-0.10	0.58
SJC	0.21	0.18	0.13	0.48
US enthesitis counts	0.12	0.44	-0.13	0.48
joint GS score	0.08	0.60	0.44	0.01
joint PD score	0.08	0.60	0.38	0.03

PsA: psoriatic arthritis, mTSS: modified Total Sharp Score, PASE: Psoriatic Arthritis Screening and Evaluation, PASI: Psoriasis Area Severity Index, DAPSA: Disease Activity in Psoriatic Arthritis, DAS: Disease Activity Score, CRP: C-reactive protein, HAQ: Health Assessment Questionnaire, MMP-3: matrix metalloproteinase 3, TJC: tender joint counts, SJC: swollen joint counts, GS: Gray Scale, PD: Power Doppler

Disclosure of Interests: Yutaro Yamada: None declared, Kentaro Inui Speakers bureau: Abbvie, Eisai, Eli Lilly, Grant/research support from: Abbvie, Eisai, Chigai, Eli Lilly, Daiichi Sankyo, Mitusbishi Tanabe, Pfizer, UCB, Tadashi Okano Speakers bureau: Abbvie, Koji Mandai: None declared, Kenji Mamoto: None declared, Tatsuya Koike Grant/research support from: Abbvie, Chugai, Chiharu Tateishi: None declared, Daisuke Tsuruta Speakers bureau: Abbvie, Astellas, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Sanofi, Grant/research support from: Abbvie, Eli Lilly, Bristol-Myers Squibb, UCB, Hiroaki Nakamura Grant/research support from: Astellas, Asahi Kasei
DOI: 10.1136/annrheumdis-2021-eular.281

POS1060 A PROSPECTIVE, LONGITUDINAL STUDY TO EVALUATE REAL-WORLD PATIENT EXPERIENCES AND TREATMENT SATISFACTION WITH SECUKINUMAB FOR PSORIATIC ARTHRITIS

M. E. Husni[1], M. Bozyczko[2], D. Wolin[3], C. Sweeney[3], E. Davenport[3], S. Hass[4], E. Yi[4], P. Hur[4], L. Grinnell-Merrick[5]. [1]*Cleveland Clinic, Rheumatology, Cleveland, United States of America*; [2]*National Psoriasis Foundation, Patient Advocate, Portland, United States of America*; [3]*RTI Health Solutions, Surveys and Observational Studies, Research Triangle Park, United States of America*; [4]*Novartis Pharmaceuticals Corporation, Health Economics and Outcomes Research, East Hanover, United States of America*; [5]*University of Rochester, Rheumatology, Rochester, United States of America*

Background: Psoriatic arthritis (PsA) is an inflammatory disease that impairs quality of life. Despite therapeutic advances, up to a third of patients do not respond or are unable to sustain a treatment response. Thus, data on patient treatment experience in PsA is critical.
Objectives: To assess real-world experiences of patients with PsA treated with secukinumab.
Methods: This is an ongoing 12-month, prospective, longitudinal, web-based survey study of patients with PsA initiating secukinumab. Patient demographics and medical history are collected at baseline using a rheumatologist case report form. Patient experience data are collected at baseline, 3, 6, 9, and 12 months by patient surveys. The primary endpoint is change in the Psoriatic Arthritis Impact of Disease 12-item questionnaire (PsAID12) from baseline to 3 months. In addition, this study will explore other changes at 3 months, including PsA symptoms, treatment satisfaction with secukinumab, and other patient-reported outcome measures. Baseline and available month 3 data from patients enrolled to date were analyzed descriptively.
Results: Baseline demographic and medical history data were available for 72 patients; 32 (44.4%) were male, 59 (81.9%) were White, and 15 (20.8%) reported modifying their diet because of PsA. The mean (SD) time since symptom onset (n = 29) and since PsA diagnosis (n = 53) was 56.3 (45.6) and 34.4 (44.7) months, respectively. More than half of the patients who started treatment with secukinumab were biologic experienced (38/62; 61.3%). Primary and secondary loss of effectiveness were the main reasons for previous biologic discontinuation (Table 1). At 3 months (n = 49), the mean (SD) PsAID12 change from baseline was –1.8 (1.8) points. Additionally, 24.5% of patients reported their PsA symptoms to be "much better," 40.8% reported "moderately better," and 32.7% "a little better" compared with baseline; none reported "no change" or worsened symptoms. On a scale of 1-10, patients rated their overall satisfaction with secukinumab treatment at month 3 with a mean (SD) score of 6.8 (2.1). Patients were also highly

satisfied with their symptom improvement, speed to symptom improvement, and the mode and frequency of secukinumab administration (Table 1).

Table 1. Summary of Prior PsA Treatment and Treatment Satisfaction with Secukinumab at Month 3

Physician-reported treatment characteristics	Baseline measure (N = 62)
Most recent PsA biologic prior to secukinumab, n (%)	n = 31
Adalimumab	12 (38.7)
Certolizumab pegol	8 (25.8)
Etanercept	6 (19.4)
Infliximab, including -dyyb	3 (9.7)
Golimumab	1 (3.2)
Unknown/not sure	1 (3.2)
Primary reasons for discontinuing previous PsA biologic treatment, n (%)[a]	n = 30
Primary and secondary loss of effectiveness	25 (83.3)
Disease progression	6 (20.0)
Worsening of or new comorbidities	1 (3.3)
How the medication was taken	2 (6.7)
Adverse effects/intolerance	4 (13.3)
Other[b]	1 (3.3)
Patient-reported treatment satisfaction with secukinumab, mean (SD)[c]	**Month 3 (N = 49)**
Symptom improvement	6.7 (2.3)
Speed of symptom improvement	6.9 (2.0)
Dose frequency	7.4 (1.9)[c]
Method of administration	7.2 (1.5)
Ease of use	8.2 (1.5)
Side effects, if any	7.9 (1.9)
Patient support services by manufacturer	8.3 (1.7)

PsA, psoriatic arthritis.[a] Rheumatologists may list > 1 reason. Data tabulated based on the number of case report forms received from rheumatologists at analysis cutoff (n = 30).[b] Other reasons included availability of new treatment, patient request, or family history of disease.[c] n = 48.

Conclusion: Most patients were biologic experienced and reported primary or secondary loss of effectiveness as the main reason for discontinuation of their previous biologic. Patients reported overall symptom improvement and satisfaction with secukinumab treatment at 3 months after initiation.

Disclosure of Interests: M Elaine Husni Consultant of: AbbVie, Amgen, Janssen, Novartis, Eli Lilly, UCB, and Regeneron, Michael Bozyczko Employee of: National Psoriasis Foundation, Daniel Wolin Employee of: RTI Health Solutions, Carolyn Sweeney Employee of: RTI Health Solutions, Eric Davenport Employee of: RTI Health Solutions, Steven Hass Employee of: Novartis, Esther Yi Employee of: Novartis, Peter Hur Employee of: Novartis, Linda Grinnell-Merrick Consultant of: AbbVie, Amgen (previously Celgene), Novartis, Pfizer, and Regeneron.

DOI: 10.1136/annrheumdis-2021-eular.436

POS1061

THE ITALIAN PROSPECTIVE SIRENA STUDY: FOCUS ON EARLY PSORIATIC ARTHRITIS COHORT AND GENDER DIFFERENCES

A. Zabotti[1], M. M. Luchetti[2], C. Selmi[3], R. Ramonda[4], R. D. Grembiale[5], L. Dagna[6], S. D'angelo[7], G. Cafaro[8], S. De Vita[1], M. Felicetti[4], S. Marelli[9], D. Frigerio[9], E. Favalli[10]on behalf of SIRENA Study Group. *[1]University of Udine, Academic Hospital S. Maria della Misericordia, Rheumatology Clinic, Department of Medical Area, Udine, Italy*; *[2]Università Politecnica delle Marche, Clinica Medica, Dipartimento Scienze Cliniche e Molecolari, Ancona, Italy*; *[3]Humanitas Research Hospital and Humanitas University, Rheumatology and Clinical Immunology, Milan, Italy*; *[4]University of Padova, Rheumatology Unit, Department of Medicine-DIMED, Padova, Italy*; *[5]Università "Magna Graecia", Rheumatology Research Unit, Dipartimento di Scienze della Salute, Catanzaro, Italy*; *[6]IRCCS San Raffaele Scientific Institute and Vita-Salute San Raffaele University, Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), Milan, Italy*; *[7]San Carlo Hospital, Rheumatology Institute of Lucania (IReL) and Rheumatology Department of Lucania, Potenza, Italy*; *[8]Università di Perugia, Reumatologia, Dipartimento di Medicina, Perugia, Italy*; *[9]Janssen-Cilag, Medical Affairs Department, Immunology, Cologno Monzese (MI), Italy*; *[10]ASST Centro Specialistico Ortopedico Traumatologico Gaetano Pini – CTO, S.C. Reumatologia, Milan, Italy*

Background: Limited data on early Psoriatic Arthritis (PsA) are available[1,2].

Objectives: To describe baseline data of PsA patients naive to any DMARDs.

Methods: SIRENA study is an Italian, prospective Registry of Spondyloarthritis patients diagnosed according to ASAS criteria and naïve to any DMARDs. Data on demographic and clinical characteristics of PsA cohort were collected and analysed, also by gender.

Results: 203/350 (58%) subjects included in SIRENA Registry had PsA (mean age 51.9 years) and in 190/203 (94%) CASPAR classification criteria were fulfilled. In 70% of patients the diagnosis was performed within 24 months from symptom onset. At baseline, 194/203 (95.6%) had mainly peripheral manifestations, 74.4% of patients had skin psoriasis, 40% nail psoriasis, 39.3% clinical enthesitis and 25.9% dactylitis. Mean SJC66 and TJC68 were, respectively, 3 and 7.2; mean PhGA was 46.3; 14.7% of patients were in MDA.

The higher tender joint count in women (mean TJC68 9.3 in women *vs* 5.3 in men) resulted in a higher disease activity according to DAPSA (high disease activity: 11.5% women *vs* 4.1% men), a higher joint VAS score (mean score 47.1 women *vs* 39.8 men) and a lower prevalence of MDA (8.3% women *vs* 20% men). We observed a higher prevalence of moderate or severe psoriasis in men (BSA≥3%: 37% men *vs* 27.8% women) while all PROs collected (PtGA, pain VAS score, sleep VAS score, BASFI, BASDAI, HAQ-DI, WPAI) were worse in women. The most common comorbidities were cardiometabolic (35.5%), endocrine (9.4%), and gastrointestinal disorders (7.4%). Cardiometabolic disorders were more frequently reported by men, endocrine and gastrointestinal disorders by women; depression exclusively by women.

Conclusion: This analysis provides real-life data in a cohort of early PsA subjects. Relevant gender differences were observed, with women showing a higher disease activity and more joint pain and men having more severe psoriasis. Women also perceived a worse disease burden.

REFERENCES:

[1] Theander E, et al. Ann Rheum Dis 2014; 73:407–413.

[2] Nas K, et al. Mod Rheumatol 2017; 27(2):345-349.

Disclosure of Interests: Alen Zabotti: None declared, Michele Maria Luchetti Speakers bureau: Honorary fees for conferences and workshops by Janssen, Abbvie, Novartis, Lilly, Celgene, Pfizer, Carlo Selmi Speakers bureau: Honoraria and/or speaker bureau from AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer, Sanofi-Regeneron, Grant/research support from: Research support from Amgen, Janssen, Novartis, Pfizer, Roberta Ramonda Speakers bureau: Honoraria and speaker fees from Novartis, Abbvie, Pfizer, MSD, Janssen, Rosa Daniela Grembiale:

Table 1. Baseline data

	PsA		
	All patients (n=203)	**Women (n=98)**	**Men (n=105)**
Age (years), mean (SD)	51.9 (13.1)	51.1 (13.2)	52.7 (13.0)
Men, n (%)	105 (51.7)	0 (0)	105 (100)
BMI (kg/m^2), mean (SD)	25.9 (4.4)	25.4 (4.9)	26.4 (3.9)
BMI categories^, n (%)			
Obese	40 (21.2)	20 (22.2)	20 (20.2)
Overweight	44 (23.3)	15 (16.7)	29 (29.3)
Under/normal weight	105 (55.6)	55 (61.1)	50 (50.5)
Comorbidities > 5%*, n (%)			
Cardiometabolic	72 (35.5)	28 (28.6)	44 (41.9)
Endocrine disease	19 (9.4)	15 (15.3)	4 (3.8)
Gastrointestinal	15 (7.4)	10 (10.2)	5 (4.8)
Depression/Anxiety	8 (3.9)	8 (8.2)	0 (0)
Hepatic diseases	7 (3.5)	1 (1.0)	6 (5.7)
Clinical assessment			
CRP (mg/dl), median (min-max)	0.40 (0 – 7.12)	0.31 (0 - 5.40)	0.49 (0 - 7.12)
SJC66, mean (SD)	3.0 (4.0)	3.2 (4.0)	2.7 (4.0)
TJC68, mean (SD)	7.2 (8.8)	9.3 (10.3)	5.3 (6.6)
Dactylitis, n/tot assessed (%)	35/135 (25.9)	12/63 (19.1)	23/72 (31.9)
Enthesitis, n/tot assessed (%)	66/168 (39.3)	39/80 (48.8)	27/88 (30.7)
Psoriasis skin, n (%)	151 (74.4)	68 (69.4)	83 (79.1)
Psoriasis nails, n/tot assessed (%)	62/155 (40.0)	29/75 (38.7)	33/80 (41.3)
Fibromyalgia, n (%)	6 (3.0)	5 (5.2)	1 (1.0)
VAS, mean (SD) [range: 0-100]			
PhGA score	46.3 (25.8)	51.2 (25.4)	41.7 (25.4)
Joint score	43.3 (26.8)	47.1 (25.2)	39.8 (27.8)
Skin score	20.3 (24.0)	17.8 (23.1)	22.6 (24.8)
DAPSA, mean (SD)	22.3 (14.1)	26.8 (15.4)	18.7 (11.9)
DAPSA categories^, n (%)			
High disease activity	13 (7.4)	9 (11.5)	4 (4.1)
Moderate disease activity	83 (47.2)	43 (55.1)	40 (40.8)
Low disease activity	71 (40.3)	24 (30.8)	47 (48.0)
Remission	9 (5.1)	2 (2.6)	7 (7.1)
MDA°, n (%)	23 (14.7)	6 (8.3)	17 (20.0)
BSA categories, n (%)			
3-10% (moderate psoriasis)	35 (24.6)	13 (21.2)	22 (27.1)
>10% (severe psoriasis)	12 (8.5)	4 (6.6)	8 (9.9)

* A patient could report one or more comorbidities. ^The sum does not add up to the total because of some missing values. ° According to Coates et al. (Ann Rheum Dis. 2010;69: 48).

None declared, Lorenzo Dagna Consultant of: Consultation honoraria from Abbvie, Amgen, Biogen, Celltrion, GlaxoSmithKline, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI, Salvatore D'Angelo Speakers bureau: Consulting fees and/or speakers bureau from AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, Giacomo Cafaro: None declared, Salvatore De Vita: None declared, Mara Felicetti: None declared, Silvia Marelli Employee of: Janssen-Cilag SpA, Daniela Frigerio Employee of: Janssen-Cilag SpA, Ennio Favalli Speakers bureau: Consulting fees and/or speaking engagements from AbbVie, Bristol-Myers Squibb, Lilly, Merck Sharp & Dohme, Pfizer, Galapagos, Sanofi-Genzyme, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.607

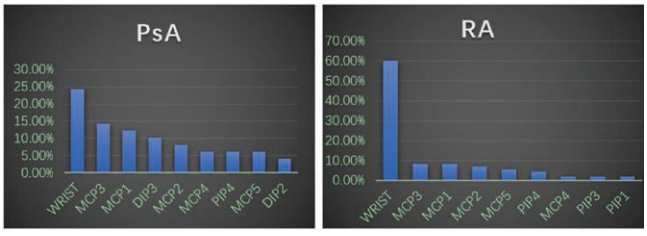
POS1062 ULTRASOUND ASSESSMENT OF SUB-CLINICAL HAND JOINT SYNOVITIS: A COMPARATIVE STUDY BETWEEN PSORIATIC AND RHEUMATOID ARTHRITIS

F. Liu[1], Y. Xin[2], D. LI[2], W. LI[2], J. Zhu[1]. [1]*Peking University People' s Hospital, Department of Ultrasound, Beijing, China*; [1]*Peking University People' s Hospital, Department of Ultrasound, Beijing, China*

Background: Ultrasound (US) detected subclinical synovitis can be present in early psoriatic arthritis (PsA) and rheumatoid arthritis (RA), and also in patients fulfilling clinical remission criteria[1-2]. Numerous evidences support that the persistence of subclinical synovitis detected by US is associated with a high risk of disease progression [2-3].
Objectives: To evaluate sub-clinical synovitis of PsA and RA at the level of small joints of the hand and wrist by B-mode and Power Doppler US.
Methods: 21 patients of early PsA and 25 patients of early RA (no clinical evidence of hand joint involvement, PsA disease duration <2 years, and RA disease duration <1 year) were recruited. DAS28 and DAPSA score used for assessment of articular disease activity for RA and PsA, respectively. US [grey scale (GS) and power Doppler (PD)] was performed to assess synovitis of bilateral wrists, metacarpophalangeal joints, proximal and distal interphalangeal joints, altogether 30 joints. A GS score ≥2 and/or a PD score ≥1 were used to identify US detected synovitis.
Results: A total of 25 patients were included in the RA group, including 5 males and 20 females. A total of 21 patients were included in the PsA group, including 7 males and 14 females. There were no significant differences in gender composition, age, and duration of disease between the two groups (*P*>0.05) (Table 1). 14 (66.67%) PsA patients and 12 (48%) RA patients had sub-clinical hand joint synovitis. Among 630 hand joints scanned in PsA group, 49 (7.78%) joints showed evidence of sub-clinical synovitis. Wrist joint was most commonly involved (24.49%), followed by MCP3 (14.29%), MCP1 (12.24%) and DIP3 (10.20%). Among 750 hand joints scanned in RA group, 110 (14.67%) joints showed evidence of sub-clinical synovitis. Wrist joint was most commonly involved (60.00%), followed by MCP3 (8.24%), MCP1 (8.24%) and MCP2 (7.06%). No correlation noted between numbers of joints with subclinical synovitis with DAPSA and DAS28 score. There was no correlation between number of joints with sub-clinical synovitis and disease activity indices.
Conclusion: Almost two-thirds patients with PsA and half patients with RA had US evidence of sub-clinical synovitis in wrist and hand joints, most commonly in wrist. There are some similarities in the joint involvement of sub-clinical synovitis between RA and PsA, physicians should take this into account in clinical work.

Table 1. Demographic characteristics of RA and PsA patients

	RA (n=25)	PsA (n=21)	*P*
Female, n(%)	20 (80.00%)	14 (66.67%)	0.305
Age, years, mean±SD	56.32±12.18	54.31±15.82	0.637
Disease duration, years, mean±SD	1.06±0.59	0.90±0.58	0.363



REFERENCES:
[1] Freeston JE, Coates LC, Nam JL, Moverley AR, Hensor EM, Wakefield RJ, et al. Is there subclinical synovitis in early psoriatic arthritis? A clinical comparison with gray-scale and power Doppler ultrasound. Arthritis care & research 2014, 66:432-439.
[2] Kawashiri SY, Suzuki T, Nakashima Y, Horai Y, Okada A, Iwamoto N, et al. Ultrasonographic examination of rheumatoid arthritis patients who are free of physical synovitis: Power doppler subclinical synovitis is associated with bone erosion. Rheumatology (Oxford), 2014, 53:562-569.
[3] Vreju FA, Filippucci E, Gutierrez M, Di Geso L, Ciapetti A, Ciurea ME, et al. Subclinical ultrasound synovitis in a particular joint is associated with ultrasound evidence of bone erosions in that same joint in rheumatoid patients in clinical remission. Clinical and experimental rheumatology, 2016, 34:673-678.
Acknowledgements: This work was supported by National Natural Science Foundation of China (No. 82071930 and 81571684).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.838

POS1063 RHEUMATOLOGIST AND PATIENT PERSPECTIVES ON IMPLEMENTING CARDIOVASCULAR RISK PREVENTION IN THE MANAGEMENT OF PSORIASIS: A QUALITATIVE STUDY

A. Ogdie[1], A. Gustafson[2], A. Lieberman[2], J. Mason[3], A. Armstrong[4], N. Mehta[5], R. Beidas[2], J. Gelfand[3]. [1]*University of Pennsylvania, Medicine/Rheumatology, Philadelphia, United States of America*; [2]*University of Pennsylvania, Implementation Science, Philadelphia, United States of America*; [3]*University of Pennsylvania, Dermatology, Philadelphia, United States of America*; [4]*University of Southern California, Dermatology, Los Angeles, United States of America*; [5]*National Institutes for Health, NHLBI, Rockville, United States of America*

Background: Psoriatic arthritis (PsA) is an immune-mediated musculoskeletal disease associated with excess risk for cardiovascular disease (CVD). New US-based guidelines recognize psoriasis as a CVD risk enhancer; however, patients with PsA often do not have CVD risk factors identified nor managed.
Objectives: This study examines strategies to improve CVD prevention care from the perspective of rheumatologists and patients with PsA.
Methods: Semi-structured qualitative interviews were conducted using an interview guide based on the Consolidated Framework for Implementation Research to examine the perspectives of rheumatologists (N = 8) and patients with psoriatic arthritis managed by rheumatologists (N = 8) on barriers/facilitators to CVD prevention. Interviews were transcribed and coded using an integrated approach designed to enhance reliability and validity facilitated by NVivo software.
Results: Most rheumatologists confirmed that they were not regularly engaging in CVD prevention care with psoriatic arthritis patients. Providers reported sometimes counseling and screening for CVD risk, but they were not regularly prescribing statins and not as willing to do so. Reasons included a lack of familiarity or comfort with guidelines, concern about working outside of their scope of practice, confusing boundaries between other clinicians, and time constraints. Most patients confirmed that it was uncommon for their rheumatologists to engage them in CVD prevention care but expressed desire for their rheumatologists inform them of the risk, and were open to CVD prevention care from them.
Conclusion: We identified several potentially modifiable barriers to CVD screening and management. These findings will inform the design of a clinical trial comparing the effectiveness of rheumatologist implementation of CVD guideline-based counseling, screening and prescribing statins when appropriate in patients with PsA.

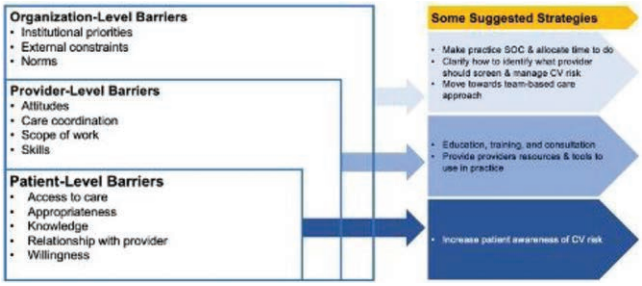


Figure 1. Barriers to CVD screening and management among patients with PsA in a rheumatology practice setting and potential strategies to address those barriers. Abbreviations: CV = cardiovascular; SOC = standard of care.

Disclosure of Interests: Alexis Ogdie Consultant of: Abbvie, Amgen, BMS, Celgene, Corrona, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, Grant/research support from: Pfizer to Penn, Novartis to Penn, Amgen to Forward/NDB, Alix Gustafson: None declared, Adina Lieberman: None declared, Jennifer Mason: None declared, April Armstrong: None declared, Nehal Mehta Consultant of: Amgen, Eli Lilly, and Leo Pharma receiving grants/other payments, Grant/research support from: AbbVie, Celgene, Janssen Pharmaceuticals, Inc, and Novartis receiving grants and/or research funding and as a principal investigator for the National Institute of Health receiving grants and/or research funding., Employee of: NNM is a full-time US government employee, Rinad Beidas Consultant of: Camden Coalition of Healthcare Providers in the past 3 years. She currently is a consultant for United Behavioral Health. She serves on the Optum Behavioral Health Clinical and Scientific Advisory Council. Dr. Beidas receives royalties from Oxford University Press., Joel Gelfand Shareholder of: Dr Gelfand is a co-patent holder of resiquimod for treatment of cutaneous T-cell lymphoma, and he is a deputy editor for the Journal of Investigative Dermatology, receiving honoraria from the Society for Investigative Dermatology., Paid instructor for: CME work related to psoriasis that was supported indirectly by Eli Lilly and Company and Ortho Dermatologics, Consultant of: Bristol-Myers Squibb, Boehringer Ingelheim, GlaxoSmithKline, Janssen Biologics, Novartis Corp, UCB (Data Safety and Monitoring Board), Sanofi, and Pfizer Inc, Grant/research support from: research grants (to the Trustees of the University of Pennsylvania) from AbbVie, Janssen, Novartis Corp, Celgene, OrthoDermatologics, and Pfizer Inc.
DOI: 10.1136/annrheumdis-2021-eular.902

POS1064 SERUM BIOMARKERS BEFORE AND AFTER A SIX MONTHS STRUCTURED WEIGHT LOSS INTERVENTION IN PATIENTS WITH PSORIATIC ARTHRITIS AND OBESITY COMPARED WITH CONTROLS

L. Torres[1], C. Jonsson[1], B. Eliasson[2], H. Forsblad-D'elia[1], A. Bilberg[3], I. Gjertsson[1], I. Larsson[4], E. Klingberg[1]. *[1]University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; *[2]Institute of Medicine, Sahlgrenska University Hospital, University of Gothenburg, Sweden, Department of Medicine, Gothenburg, Sweden*; *[3]Institute of Neuroscience and Physiology, Sahlgrenska Academy at the University of Gothenburg, Sweden, Section of Health and Rehabilitation, Physiotherapy, Gothenburg, Sweden*; *[4]Institute of Medicine, Sahlgrenska Academy at University of Gothenburg, Sweden, Department of Gastroenterology and Hepatology, Gothenburg, Sweden*

Background: Obesity is highly overrepresented in psoriatic arthritis (PsA) and associated with increased disease activity. We have previously shown in 41 patients with PsA (Caspar criteria) and obesity (here body mass index BMI ≥33 kg/m^2) that weight loss treatment including Very Low Energy Liquid Diet (VLED) resulted in a median weight loss of 18.6% and concomitantly a significant improvement in CRP and disease activity in joints, entheses and skin at six months (M6) follow up.

Objectives: To analyze serum biomarkers associated with inflammation, cartilage and bone metabolism before and after weight loss treatment in PsA patients compared with controls, without PsA or psoriasis, matched for age, sex and weight.

Methods: The weight loss treatment included VLED (640 kcal/day) during 12 or 16 weeks (depending on baseline (BL) BMI <40 or ≥40 kg/m^2), followed by a structured reintroduction of an energy restricted diet. cs/bDMARDs were held unchanged from 3 months before BL until M6. The patients were assessed with 66/68 joints counts.

Serum levels of vascular endothelial growth factor (VEGF), S100A8, S100A9, matrix metalloproteinases (MMP-3, 8 and 13), hepatocyte growth factor (HGF), B-cell activating factor (BAFF), Dickkopf (DKK)-1, sclerostin (SOST), soluble receptor activator of nuclear factor-kB ligand (RANKL), osteprotegerin (OPG) and aggrecan were measured at BL and M6 in PsA patients and controls with Magnetic Luminex Assays (R&D-systems) following the manufacturer's instructions using a Bio-Plex 200 system (BioRad). Serum cartilage oligomeric matrix protein (COMP) (R&D-systems), carboxyterminal telopeptide of type-1 collagen (CTX-1) (Immunodiagnostics systems: IDS) and osteocalcin (IDS) were measured with enzyme-linked immunosorbent assay (ELISA).

Results: Totally 41 PsA patients [age median 54 (IQR 48-62) yrs; 63 % women] and 39 controls [age 55 (46-60) yrs, 72 % women] were included. At M6 the weight-loss since BL was 18.7 (14.6-26.5) kg in the PsA patients and 22.6 (14.7-28.4) kg in the controls (p=0.546). Significant reductions in DAS28CRP [2.9 (2.1–3.7) vs. 2.4 (1.7–3.0)] and DAPSA [15.3(6.6-29.1) vs. 11.0 (2.8–17.6)] (p<0.001) were seen in the PsA patients.

At BL serum levels of the biomarkers were not significantly different in patients vs. controls.

After weight-loss significant reductions were seen in serum VEGF, S100A8, MMP-8, HGF, BAFF, COMP and DKK-1, whereas serum SOST and CTX-1 were significantly increased in both patients and controls (Table 1). The other biomarkers were not significantly changed.

Conclusion: Weight loss in patients with PsA and controls was associated with lowered serum levels of several biomarkers related to inflammation and cartilage degradation, along with increased levels of biomarkers for bone turnover.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.999

Table 1.

	PsA (N=41) BL median (IQR)	PsA (N=41) M6 median (IQR)	PsA p-value	Ctrl (N=39) BL median (IQR)	Ctrl (N=39) M6 median (IQR)	Ctrl p-value
BMI (kg/m^2)	35.2 (34.1-38.1)	29.8 (26.6-31.5)	**<0.001**	37.7 (36.7–41.5)	30.4 (27.9–33.2)	**<0.001**
CRP (mg/L)	4 (2–8.5)	2 (1–6.5)	**0.041**	4 (2–6)	2 (1–4)	**<0.001**
VEGF (pg/mL)	79.6 (55.9–113.5)	69.6 (53.1–105.3)	**0.010**	82.3 (48.0–125.9)	65.0 (42.2-85.5)	**<0.001**
S100A8 (pg/mL)	75.5 (48.0–99.5)	63.3 (42.8–93.6)	**0.021**	71.8 (40.5–101.0)	63.3 (40.3-85.7)	**0.006**
MMP-8 (pg/mL)	9975.4 (6811.8–14154.8)	9202.6 (5767.1–12049.6)	**0.017**	7494.7 (4805.2-12616.9)	7218.3 (3466.0-9785.3)	0.112
HGF (pg/mL)	327.9 (250.3–413.6)	271.3 (206.9–331.0)	**<0.001**	307.9 (239.1–348.3)	239.8 (200.3-276.0)	**<0.001**
BAFF (pg/mL)	794.4 (716.4–868.2)	674.6 (613.2–790.5)	**<0.001**	760.8 (664.1–827.3)	678.1 (603.7–719.8)	**<0.001**
COMP (pg/mL)	266.1 (209.8–366.0)	217.0 (156.0–272.0)	**0.008**	293.6 (185.2–340.5)	221.6 (163.5-300.0)	**0.018**
Dkk-1 (pg/mL)	3608.4 (3055.0–4401.3)	3382.6 (2802.5–4218.2)	**0.002**	3635.8 (3212.8-4380.6)	3480.4 (2948.9–4087.3)	**0.007**
SOST (pg/mL)	52.9 (32.5–65.4)	60.3 (37.2–85.6)	**0.014**	50.0 (30.8–79.3)	61.3(35.7–81.4)	**0.019**
CTX-1 (ng/mL)	0.27 (0.20–0.39)	0.51 (0.35–0.64)	**<0.001**	0.23 (0.16–0.34)	0.50(0.30–0.61)	**<0.001**

POS1065 CIRCULATING ENDOTHELIAL CELLS AS A MARKER OF CARDIOVASCULAR DISEASES IN PATIENTS WITH PSORIATIC ARTHRITIS

S. Smiyan[1], A. Bilukha[1], B. Koshak[1]. *[1]Ternopil State Medical University, Internal Medicine №2, Ternopil, Ukraine*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory joint disease which develops in patients with psoriasis. Mortality among patients with PsA is 1.28 times higher than population levels and in most cases it is caused by cardio-vascular diseases (CVD). Those patients have increased risk of clinical and subclinical CVD, mostly due to endothelial dysfunction (ED) and accelerated atherosclerosis. Elevated levels of circulating endothelial cells (CEC) have been described in different cardiovascular pathologies, suggesting their potential use as diagnostic biomarkers for dysfunction of endothelium.

Objectives: To identify the potential role of circulating endothelial cells as a marker of cardiovascular diseases in patients with psoriatic arthritis.

Methods: In total, ninety-four patients with PsA, who fulfilled the disease criteria (CASPAR) were examined using standard diagnostic methods (including C-reactive protein (CRP), lipid profile) and evaluation endothelium-dependent vasodilation in response to reactive hyperemia (EDVD). Circulating endothelial cells were determined in the peripheral venous blood samples by flow cytometry and counted according to a standardized protocol using a fluorescence microscope after acridine orange labeling. The control group, which were consisted from thirty healthy adults were also examined.

Results: CEC were quantified in patients with PsA (7,15 ± 0,19 cells mL^{-1}) and in the control group (4,05 ± 0,11 cells mL^{-1}). Comparing two groups of patients, endothelial circulating cell level was significantly different (p = 0.0001). Finally, we analyzed the relationship between CEC count, comorbidities, cardiovascular risk factors and EDVD in patients with PsA. Increased CEC levels were associated with obesity (r=0,62), duration of disease (r=0,65), age (r=0,67), increased CRP (r=0,76), high blood pressure (r=0,87) and decreased EDVD (r=–0,91).

Conclusion: CEC counts were significantly higher in patients with PsA, positively correlated with the main factors of CVD, and another specific marker of ED - EDVD. Elevated CEC levels were also associated with high concentrations of CRP, which plays a direct role in promoting vascular inflammation, vessel damage and clinical CVD events. In conclusion, increased CEC counts provide a direct proof of endothelial damage in patient with PsA and a clinically informative diagnostic tool for endothelial damage in pre-symptomatic CVD. As CEC are one of the most sensitive biomarker for ED, further efforts should concentrate on improving the sensitivity of its detection in order to increase diagnostic sensitivity.

REFERENCES:

[1] Maura Farinacci, Thomas Krahn, Wilfried Dinh, et al. Circulating endothelial cells as biomarker for cardiovascular diseases. Res Pract Thromb Haemost, Vol. 3, Issue, 2019, P.49-58;

[2] C. Horreau, C. Pouplard, E. Brenautet, et al. Cardiovascular morbidity and mortality in psoriasis and psoriatic arthritis: a systematic literature review. J Eur Acad Dermatol Venereol, Vol. 27, Issue 3, 2013, P.12-19;

[3] Frank Verhoeven, Clément Prati, Céline Demougeot, Daniel Wendling. Cardiovascular risk in psoriatic arthritis, a narrative review. Joint Bone Spine, Vol. 87, Issue 5, 2020, P.413-418;

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1000

POS1066 IS ENTHESITIS A SONOGRAPHIC BIOMARKER OF DISEASE SEVERITY IN PSORIATIC ARTHRITIS? THE LINK BETWEEN ULTRASOUND ENTHESEAL ABNORMALITIES AND PERIPHERAL JOINT EROSIVE DAMAGE

G. Smerilli[1], E. Cipolletta[1], G. M. Destro Castaniti[2], A. DI Matteo[1], M. DI Carlo[1], E. Moscioni[1], F. Francioso[1], W. Grassi[1], E. Filippucci[1]. *[1]Marche Polytechnic*

University, Rheumatology Unit, Department of Clinical and Molecular Sciences, "Carlo Urbani" Hospital, Jesi, Italy; [2]*University of Palermo, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, Rheumatology section, "P. Giaccone" Hospital, Palermo, Italy*

Background: Enthesitis is one of the hallmark of psoriatic arthritis (PsA). Ultrasound (US) accurately detects morphostructural abnormalities indicative of entheseal inflammation and structural damage. Interestingly, in a recent study, US-detected entheseal pathology appeared to be a potential marker of disease severity, being associated with higher radiographic score of structural damage at peripheral joint level. (1) However, a sub-analysis of the impact of each elementary finding of US enthesitis was not performed. Moreover, some US entheseal abnormalities (hypoechogenicity, thickening and calcification/enthesophyte) have been described as frequent findings in healthy subjects and patients with dysmetabolic conditions, undermining their specificity. (2) Thus, we hypothesized that their role as a sonographic biomarker of joint disease severity could be questioned.
Objectives: The main aim of the present study was to explore the association between the US elementary findings of enthesitis defined by OMERACT [i.e. hypoechogenicity, thickening, Doppler signal, calcification/enthesophyte and bone erosion at enthesis] (3) and the presence of US-detected joint bone erosions in patients with PsA.
Methods: Consecutive patients with PsA (CASPAR criteria) were included in this cross-sectional single-centre study. The scanning protocol included bilateral assessment of the main entheses of the lower limbs [plantar fascia, quadriceps, patellar (proximal and distal) and Achilles tendons]. The presence of US joint bone erosions was investigated in the following areas: 2nd and 5th metacarpophalangeal (MCP) joints, ulnar head and 5th metatarsophalangeal (MTP) joint, bilaterally, as well as the most inflamed joint at the physical examination. The US examination was carried out with a 6-18 MHz probe. Univariate and multivariate logistic analysis were performed to identify predictors of US joint bone erosions.
Results: A total of 74 PsA patients were enrolled. The mean disease duration was 7.9±8.0 years. Joint bone erosions were found in 36/75 patients (48.0%), and in 71/600 joints (11.8%), most frequently in the 5th MTP joint (in 26/75 patients, 34.7%). The univariate analysis showed that entheseal bone erosions [odds ratio (OR) 27.1, 95% confidence interval (CI) 3.3-220.2, p value <0.01] and Doppler signal (OR 3.5, 95% CI 1.3 - 9.4, p value 0.01) were associated with joint bone erosions. Only entheseal bone erosions remained significantly associated with joint bone erosions in the multivariate analysis (Table 1).

Table 1. Multivariate regression analysis: predictive value of the entheseal US findings for the presence of joint bone erosions.

	OR (95% CI)	P value
Hypoechogenicity	0.5 (0.1-3.4)	0.45
Thickening	2.2 (0.6-8.3)	0.27
Doppler signal	3.2 (0.9-10.8)	0.06
Calcification/enthesophyte	1.1 (0.1-11.2)	0.99
Entheseal bone erosion	24.2 (2.7-216.2)	**<0.01**

Conclusion: Entheseal bone erosion and, to a lesser extent, Doppler signal, were the only entheseal abnormalities correlated with the presence of US-detected joint bone erosions, representing potential sonographic biomarkers of disease severity in PsA.
REFERENCES:
[1] Polachek A, Cook R, Chandran V, Gladman DD, Eder L. The association between sonographic enthesitis and radiographic damage in psoriatic arthritis. Arthritis Res Ther 2017; 15;19:189.
[2] Balint PV, Terslev L, Aegerter P, Bruyn GAW, Chary-Valckenaere I, Gandjbakhch F, et al. Reliability of a consensus-based ultrasound definition and scoring for enthesitis in spondyloarthritis and psoriatic arthritis: An OMERACT US initiative. Ann Rheum Dis 2018; 77(12):1730-5.
[3] Di Matteo A, Filippucci E, Cipolletta E, Martire V, Jesus D, Musca A, et al. How normal is the enthesis by ultrasound in healthy subjects? Clin Exp Rheumatol 2020;38:472-8.
Disclosure of Interests: Gianluca Smerilli: None declared, Edoardo Cipolletta: None declared, Giulia Maria Destro Castaniti: None declared, Andrea Di Matteo: None declared, Marco Di Carlo: None declared, Erica Moscioni: None declared, Francesca Francioso: None declared, Walter Grassi Speakers bureau: W.G. has received speaking fees from AbbVie, Celgene, Grünenthal, Pfizer and UCB Pharma., Emilio Filippucci Speakers bureau: E.F. has received speaking fees from Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Roche, Pfizer, UCB Pharma.
DOI: 10.1136/annrheumdis-2021-eular.1159

POS1067 BASELINE VITAMIN D LEVELS AND DISEASE ACTIVITY AND RESPONSE IN PORTUGUESE PATIENTS WITH PSORIATIC ARTHRITIS UNDER BMDARD: DOES IT MAKE A DIFFERENCE?

F. Oliveira Pinheiro[1], B. M. Fernandes[1], S. Garcia[1], M. Rato[1], D. Fonseca[2], D. Santos Oliveira[1,3], A. Martins[1], F. R. Martins[4], P. Madureira[1], M. Bernardes[1,5], L. Costa[1]. [1]*Centro Hospitalar Universitário de São João, Rheumatology Department, Porto, Portugal*; [2]*Centro Hospitalar Vila Nova de Gaia/Espinho, Rheumatology Department, Vila Nova de Gaia, Portugal*; [3]*Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; [4]*Centro Hospitalar Universitário do Algarve, Rheumatology Department, Faro, Portugal*; [5]*Faculty of Medicine, University of Porto, Medicine Department, Porto, Portugal*

Background: There is growing evidence that vitamin D [25(OH)D]) plays an important role in maintaining skeletal health and modulating the immune system. Epidemiological data indicate that vitamin D deficiency is common in immune-mediated rheumatic diseases, especially in rheumatoid arthritis, but there is little data regarding its association with disease activity and response to therapy in patients with psoriatic arthritis (PsA) under bDMARD therapy.
Objectives: We aimed to assess whether 25(OH)D basal levels correlate with disease activity and clinical response to the first bDMARD, at 6 and 12 months of therapy, in a monocentric cohort of patients with PsA.
Methods: This retrospective study was carried out on PsA patients from a Rheumatology department of a tertiary hospital, fulfilling CASPAR criteria and registered in our national database (Reuma.pt), who started the first bDMARD since 2008. Demographic, clinical and laboratory criteria were evaluated at 0, 6 and 12 months of biologic therapy. Disease activity was assessed using CDAI, SDAI, DAS28(4V), BASDAI, ASDAS, DAPSA and the response was measured using the EULAR, BASDAI50, ASDAS, ASAS, ACR and PsARC responses. Correlations were made between absolute serum levels of 25(OH)D and continuous variables, as well as associations between different vitamin D cutoffs and disease activity measures and response criteria. Multiple linear and logistic regression analyses were performed to determine whether vitamin D is a predictor of disease activity and therapeutic response.
Results: We included 81 patients, 41 (50.6%) females; with a mean age of 48.0±11.7 years, a mean disease duration of 9.5±7.4 years and a mean body mass index of 28.4±5.2kg/m2. Thirteen (16.0%) were smokers. The mean 25(OH)D basal level was 25.5±13.2ng/ml, 21 (25.9%) had 25(OH)D basal levels ≥30ng/mL and 31 (38.3%) ≤20ng/mL. Sixty-two patients (76.5%) were under csDMARD therapy. Golimumab (29, 35,8%), etanercept (28, 34.6%) and adalimumab (10, 12.3%) were the most frequently prescribed bDMARDs. There were only very weak, albeit positive, correlations between 25(OH)D levels and measures of disease activity. The BASDAI50 response at 6 months was associated with higher basal 25(OH)D levels (29.5±14.5 vs 21.5±10.2ng/mL, p = 0.013); the ASAS20 (33.9±15.9 vs 24.2±12.8ng/mL; p = 0.023), ASAS40 (31.9±14.6 vs 25.0±13.8ng/mL; p = 0.023) and ASAS70 (47.0±4.2 vs 26.6±14.2; p = 0.027) responses at 12 months were associated with higher basal levels of 25(OH)D; basal 25(OH)D levels were ≥ 30ng/mL in a significantly higher proportion of patients who achieved CDAI (38.9% vs 10.5%; p = 0.027) and SDAI (38.9% vs 7.7%; p = 0.008) remission and ASDAS disease inactive (29.4% vs 7.3%; p = 0.040) at 1 year. In the regression models, basal levels of 25(OH)D were found to be predictors of good EULAR responders (OR 1.315, 1.017-1.213 95% CI; p = 0.037) at 6 months. Basal levels of 25(OH)D were not significantly different in patients who discontinued bDMARD and no significant correlations or associations were identified regarding more specific PsA activity measures, such as DAPSA and PsARC, nor were they predictive of these responses.
Conclusion: We can conclude that there is a global trend for an association between higher levels of vitamin D and lower measures of disease activity and better therapeutic responses to the first biologic. It was possible to find statistically significant associations with some disease activity measures and response criteria that, although primarily designed for other rheumatic diseases, are often used in PsA.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1255

POS1068 CARDIAC BIOMARKERS ARE ASSOCIATED WITH THE DEVELOPMENT OF CARDIOVASCULAR EVENTS IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS

K. Colaco[1,2,3], K. A. Lee[4], S. Akhtari[5], R. Winer[6], P. Welsh[7], N. Sattar[7], I. Mcinnes[8], V. Chandran[9,10], P. Harvey[5,9], R. Cook[4], D. D. Gladman[9,10], V. Piguet[1,9], L. Eder[1,9]. [1]*Women's College Hospital, Women's College Research Institute, Toronto, Canada*; [2]*University Health Network, Krembil Research Institute, Toronto, Canada*; [3]*University of Toronto, Institute of Medical Science, Toronto, Canada*; [4]*University of Waterloo, Statistics and Actuarial Science, Waterloo, Canada*; [5]*Women's College Hospital, Cardiology, Toronto, Canada*; [6]*Rambam Health Care Campus, Neurology, Haifa, Israel*; [7]*University of Glasgow, Institute of Cardiovascular & Medical Sciences, Glasgow, United Kingdom*; [8]*University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; [9]*University of Toronto, Medicine, Toronto, Canada*; [10]*University Health Network, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto, Canada*

Background: N-terminal pro-brain-type natriuretic peptide (NT-proBNP) and troponin I (TnI) are established cardiac biomarkers that predict cardiovascular events (CVEs) in the general population. While patients with psoriatic arthritis and psoriasis, collectively termed psoriatic disease (PsD), have an increased risk of developing CVEs, the use of these cardiac biomarkers to predict CV risk has not been investigated in this population.

Objectives: We aimed to evaluate the association between these cardiac biomarkers and incident CVEs, and assess their predictive value beyond the Framingham Risk Score (FRS).
Methods: A longitudinal cohort study was conducted in patients with PsD without prior history of CVEs. NT-proBNP and TnI concentrations were measured using automated clinical assays in the first available serum sample. The study outcome included any of the following CVEs occurring within the first 10 years of biomarker assessment: angina, myocardial infarction, transient ischemic attack, stroke, revascularization and CV death. Associations with incident CVEs were analyzed separately for each biomarker using Cox proportional hazards regression models first adjusted for age and sex, and subsequently for the FRS. The added value of cardiac biomarkers to improve predictive performance beyond the FRS was assessed using the area under the receiver operator characteristic curve (AUC), net reclassification index (NRI) and integrated discrimination index (IDI).
Results: A total of 1000 patients with PsD were assessed between 2002 and 2019 (mean age 49 ± 12.8 years, 44.6% female) (Table 1). During a mean follow-up of 7.1 years, 64 patients developed incident CVEs. Both TnI (Hazard Ratio (HR) 3.02, 95% Confidence Interval (CI) 1.12, 8.16) and NT-proBNP (HR 2.02; 95% CI 1.28, 3.18) predicted CVEs independently of the FRS (Figure 1). The association was stronger in males than females. Including all cardiac biomarkers and the FRS in a single model, NT-proBNP retained statistical significance (HR 1.91, 95% CI 1.23, 2.97), while TnI did not (HR 2.60, 95% CI 0.98, 6.87). When comparing the predictive performance of the base model (FRS alone, AUC 75.4) to the expanded models, there was no significant improvement in any of the predictive indices with the addition of TnI (AUC 73.5, p = 0.21; NRI 0.08, p = 0.67; IDI 0.005, p = 0.37), NT-proBNP (AUC 71.0, p = 0.35; NRI 0.20, p = 0.06; IDI 0.017, p = 0.10), or both TnI and NT-proBNP (AUC 70.0, p = 0.23; NRI 0.27, p = 0.05; IDI 0.021, p =0.05).
Conclusion: In patients with PsD, elevated NT-proBNP and TnI predict incident CVEs independent of the FRS. We did not observe a significant improvement in the performance of the predictive model when combining these cardiac biomarkers with the FRS.
REFERENCES:
[1] Eder L, Wu Y, Chandran V, et al. Incidence and predictors for cardiovascular events in patients with psoriatic arthritis. *Ann Rheum Dis* 2016;75(9):1680-6.

Table 1. Baseline characteristics of the study population (n=1000)

Variable	Mean ± SD / Frequency (%)
PsA, no. (%)	648 (64.8)
PsC, no. (%)	352 (35.2)
Age (years)	49 ± 12.8
Male sex, no. (%)	554 (55.4)
Disease duration (years)	20.2 ± 14.1
Ethnicity, Caucasian (%)	834 (83.4)
Current smoker (%)	164 (16.4)
FRS (%)	8.2 ± 8.6
Diabetes	77 (7.7)
Hypertension	274 (27.4)
BMI (kg/m^2)	28.7 ± 5.9
PASI	4.1 ± 6.3
Use of lipid-lowering medications (%)	100 (10)
Current use of DMARDs	362 (36.2)
Current use of Biologics	214 (21.4)
Current use of NSAIDs (daily use)	265 (26.5)

[1] Applicable only to patients with PsACVE, cardiovascular events; DMARD, disease-modifying antirheumatic drug; FRS, Framingham Risk Score; NSAID, non-steroidal anti-inflammatory drug; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis; PsC, psoriasis without arthritis

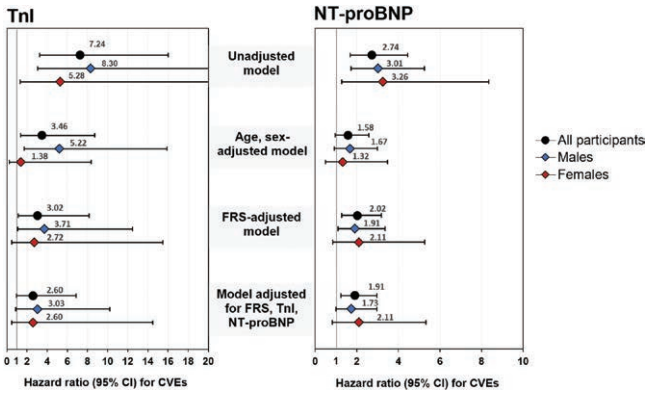


Figure 1. Hazard ratios of cardiac biomarker measures for incident cardiovascular events (n = 1000, 64 events). Error bars denote 95% confidence intervals. CI indicates confidence interval; CVEs, cardiovascular events; FRS, Framingham Risk Score; NT-proBNP, N-terminal pro-brain-type natriuretic peptide; TnI, troponin I.

Acknowledgements: Keith Colaco is supported by the Enid Walker Estate, Women's College Research Institute, Arthritis Society (TGP-19-0446), National Psoriasis Foundation (Early Career Grant) and the Edward Dunlop Foundation. Lihi Eder is supported by a Young Investigator Award from the Arthritis Society and an Early Researcher Award from the Ontario Ministry of Science and Innovation. The study was supported in part by a discovery grant from the National Psoriasis Foundation and an operating grant from the Arthritis Society (YIO-16-394).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1297

POS1069 VALIDATION OF THE DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS (DAPSA) WITH A QUICK QUANTITATIVE C-REACTIVE PROTEIN ASSAY (Q-DAPSA) IN PATIENTS WITH PSORIATIC ARTHRITIS (PSA): A PROSPECTIVE, NATIONAL, MULTICENTER STUDY

F. Proft[1], J. Schally[1], H. C. Brandt[2], J. Brandt-Juergens[3], G. R. Burmester[4], H. Haibel[1], H. Käding[1], K. Karberg[2], S. Lüders[1], B. Muche[1], M. Protopopov[1], J. Rademacher[1], V. Rios Rodriguez[1], M. Torgutalp[1], M. Verba[1], S. Zinke[5], D. Poddubnyy[1]. *[1]Charité – Universitätsmedizin Berlin, Division of Gastroenterology, Infectiology and Rheumatology, Campus Benjamin Franklin, Berlin, Germany*; *[2]Praxis für Rheumatologie und Innere Medizin, Praxis für Rheumatologie und Innere Medizin, Berlin, Germany*; *[3]Rheumatologische Schwerpunktpraxis, Rheumatologische Schwerpunktpraxis, Berlin, Germany*; *[4]Charité – Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; *[5]Rheumapraxis Berlin, Rheumapraxis Berlin, Berlin, Germany*

Background: Psoriatic arthritis (PsA) is a heterogeneous disease with multiple musculoskeletal and dermatological manifestations. Due to this multifaceted clinical appearance, international guidelines do not provide a clear recommendation for one specific score to assess disease activity in PsA [1]. The Disease Activity Index for Psoriatic Arthritis (DAPSA), a validated, unidimensional score focusing on joint involvement, is one of the recommended options [1]. However, routine determination of C-reactive protein (CRP) to calculate DAPSA values takes hours to days. In contrast, quick quantitative CRP (qCRP) tests require only a few minutes and might facilitate regular assessment of the DAPSA (as Q-DAPSA) in clinical routine.
Objectives: To validate the Q-DAPSA in a prospective, multicenter study of PsA patients. Since the Disease Activity Score 28 (DAS28) is not only used in rheumatoid arthritis, but also in PsA patients, the study also investigated the performance of a qCRP based DAS28 (DAS28-qCRP) in a PsA cohort.
Methods: The study was conducted in five centers in Berlin, Germany. Consecutive adult (≥ 18 years) PsA patients were included. In addition to a rheumatological assessment, including patient reported outcomes (PROs), routine CRP and erythrocyte sedimentation rate (ESR) were measured in the local labs. Additionally, a qCRP testing with the „QuikRead go instrument" (Aidian Oy, Finland) was performed locally at the study center (measurement range 0.5 - 200 mg/l for hematocrit concentrations of 40 – 45%). Statistical analysis included descriptive statistics, cross tabulation and weighted Cohen´s kappa comparing disease activity categories, Bland-Altman plots and intraclass correlation coefficient (ICC) for DAPSA, Q-DAPSA, DAS28-CRP and DAS28-qCRP.
Results: In this study 104 patients were included between January and October 2020 (mean age: 51.2 years, mean disease duration: 7.1 years, 49 patients (47.1%) were male). 53 patients (51.0%) were treated with a bDMARD and 37 patients (35.6%) with csDMARDs. CRP and qCRP showed mean values of 5.20 and 6.17 mg/l, respectively. With the Q-DAPSA, 103 patients (99.0%) were assigned to the same disease activity category when compared to DAPSA (Table 1). Weighted Cohen´s kappa was 0.990 (95%CI 0.970; 1.000). ICC for numerical values of DAPSA and Q-DAPSA was 1.000 (95%CI 0.999; 1.000). The agreement of Q-DAPSA and DAPSA is shown in a Bland-Altman plot (Figure 1). DAS28-CRP and -qCRP were available for 103 patients; 101 patients (98.1%)

Table 1. Disease activity categories by Q-DAPSA vs. DAPSA

		Q-DAPSA (n = 104)			
		Remission (≤ 4)	**Low Disease Activity** (> 4 and ≤ 14)	**High Disease Activity** (> 14 and ≤ 28)	**Very high Disease Activity** (> 28)
DAPSA	**Remission** (≤ 4)	**36 (34.6%)**	**1 (1.0%)**		
	Low Disease Activity (> 4 and ≤ 14)		**39 (37.5%)**		
	High Disease Activity (> 14 and ≤ 28)			**22 (21.2%)**	
	Very high Disease Activity (> 28)				**6 (5.8%)**

The fields highlighted in red indicate that disease activity categories do not match.DAPSA = Disease activity index for Psoriatic Arthritis, Q-DAPSA = DAPSA calculated based on a quick quantitative CRP

showed the same disease activity category in the DAS28-qCRP and weighted Cohen´s kappa was 0.951 (95%CI 0.886; 1.000).
Conclusion: The Q-DAPSA and DAPSA showed an almost perfect agreement on the assignment to disease activity categories (99%) with the important advantage of time. With Q-DAPSA, rheumatologists could base their clinical decision-making on a disease activity measurement by using a composite score immediately. Consequently, Q-DAPSA can be integrated in clinical routine and clinical trials and could be implemented into the treat-to-target concept in PsA patients. For rheumatologists who prefer DAS28-CRP for assessing disease activity in PsA patients, DAS28-qCRP may serve as a suitable alternative.
REFERENCES:
[1] Smolen JS, et al. Ann Rheum Dis. 2018 Jan; 77(1):3-17.

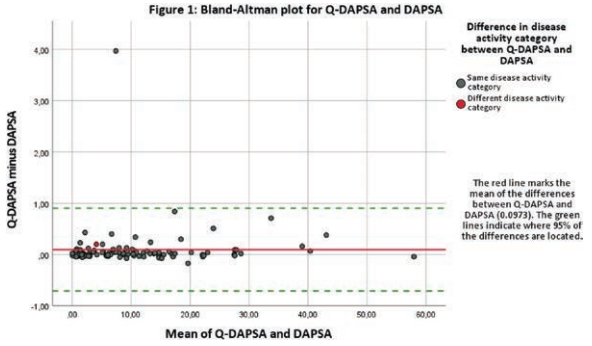


Figure 1. Bland-Altman plot for Q-DAPSA and DAPSA

Acknowledgements: The authors would like to deeply thank Braun T, Doerwald C, Deter N, Höppner C, Lackinger J, Lorenz C, Lunkwitz K, Mandt B, Sron S and Zernicke J for their practical support and coordinating the study.
Funding statement: The AQUA study was supported by an unrestricted research grant from Novartis. Testing kits were provided free of charge from Aidian Oy, Finland.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1468

POS1070 **ANXIETY IN PSORIATIC ARTHRITIS PATIENTS: RESULTS FROM THE HUR-BIO BIOLOGIC REGISTRY**

G. Ayan[1], B. Farisoğulları[1], E. Bilgin[1], E. C. Bolek[1], G. K. Yardımcı[1], E. Duran[1], Z. Özsoy[1], G. Sandal Uzun[1], L. Kılıç[1], A. Akdoğan[1], O. Karadag[1], Ş. A. Bilgen[1], S. Kiraz[1], A. İ. Ertenli[1], U. Kalyoncu[1]. [1]*Hacettepe University Medical Faculty, Department of Internal Medicine Division of Rheumatology, Ankara, Turkey*

Background: Anxiety is commonly observed, underestimated problem in patients with psoriatic arthritis (PsA). Overall rate has been reported around 20% [1]. However the data on anxiety in PsA patients requiring advanced treatment and change in response to therapy is scarce.
Objectives: Our aim was to understand the frequency of anxiety before starting biologic agents and change in the anxiety scores with the treatment.
Methods: PsA patients from the Hacettepe University biological database (HUR-BIO) were assessed for anxiety (score ≥ 4) using the patient self-reported measure of anxiety on a 0-10 numerical scale, included in the Psoriatic Arthritis Impact of Disease questionnaire (PSAID-12) [2]. The anxiety rate and scores were determined before starting biologic agents and at first visit in 6 months. Change in the scores were compared between patients according to the favourable treatment responses (Table 1). The correlation between the score-changes in anxiety and treatment response parameters was assessed by spearman correlation analysis.
Results: From 520 patients registered, 147 [mean (SD) age 43.3 (12.4) years, 70.7% female] had anxiety score registered both at baseline and first visit in 6 months. Both the frequency and mean (SD) score of anxiety decreased at first visit [63.9% vs 41.4 %, 4.8(3.4) vs 3.2 (3.1) respectively, p<0.001 for both] after a mean (SD) follow-up of 105.7 (22.2) days. There was a statistically significant difference between changes in the anxiety scores in patients with/without treatment responses in pain, PGA, BASDAI, HAQ-DI and DAS-28. A positive correlation between the change in anxiety and all treatment response parameters was observed (Table 1, Figure 1).
Conclusion: Anxiety is a more frequent problem at the time of biologic initiation compared to rates observed in general PsA population which could be related to the high disease activity. The rates are still high in 6 months under treatment, however both the frequency and score of anxiety showed a decreasing trend parallel to the treatment response.
REFERENCES:
[1] Zusman EZ, Howren AM, Park JYE,et. al (2020) Epidemiology of depression and anxiety in patients with psoriatic arthritis: A systematic review and meta-analysis. Semin Arthritis Rheum 50 (6):1481-1488.
[2] Gossec L, de Wit M, Kiltz U, Braun J, et al (2014) A patient-derived and patient-reported outcome measure for assessing psoriatic arthritis: elaboration and preliminary validation of the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire, a 13-country EULAR initiative. Ann Rheum Dis 73 (6):1012-1019.

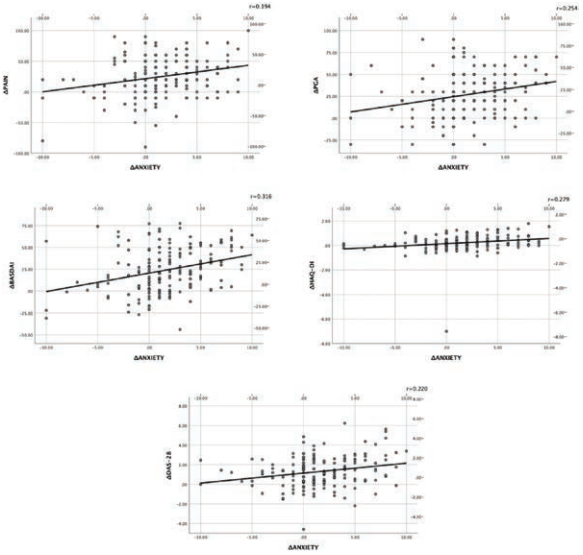


Figure 1. Correlation between the score changes

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1495

Table 1. Patient characteristics at baseline and changes in the anxiety score according to treatment response

	Total N= 147	Patients with anxiety N=94	Patients without anxiety N=53	P		
Age, mean (SD)	43.3(12.4)	43.2 (12.9)	43.5 (11.4)	0.761		
Female gender, n (%)	70.7	73.4	66	0.352		
Psoriasis duration, years$	12 (4-20)	12 (3-19)	12 (4.75-24)	0.661		
Psoriatic arthritis, duration years$	1 (0-5)	1 (0-5)	1 (0-5)	0.344		
DAS-28*	3.9 (1.3)	4 (1.3)	3.7 (1.3)	0.285		
HAQ-DI*	0.75 (0.53)	0.84 (0.53)	0.58 (0.48)	0.003		
BASDAI*	6.1 (2.1)	6.4 (1.9)	5.5 (2.1)	0.003		
CRP*	1.7 (2.3)	1.7 (2.1)	1.8 (2.5)	0.843		
Pain*	6.8 (2.3)	7.1 (1.9)	6.4 (2.8)	0.486		
PGA*	6.5 (2.1)	6.7 (1.8)	6.3 (2.5)	0.589		
PsAID-12*	6.3 (1.7)	6.8 (1)	3.1 (1.9)	0.002		
Favorable treatment response						
	Response n	ΔAnxiety score*	P		ΔAnxiety r	P
ΔPain ≥20 mm	Yes = 98 No= 49	2.2 (3.6) 0.5 (3.9)	0.017	ΔPain	0.194	0.011
ΔPGA ≥20 mm	Yes = 104 No= 43	2.3 (3.7) 0.3 (3.7)	0.002	ΔPGA	0.254	0.001
ΔBASDAI ≥20 mm	Yes = 85 No= 62	2.9 (3.4) 0.1 (3.7)	<0.001	ΔBASDAI	0.316	<0.001
ΔHAQ-DI ≥0.22	Yes = 70 No= 73	2.67 (3.2) 0.9 (4.1)	0.023	ΔHAQ-DI	0.279	<0.001
ΔDAS-28≥1.2	Yes = 75 No= 67	2.3 (3.9) 0.9 (3.5)	0.036	ΔDAS-28	0.220	0.004

$=median (IQR), *=mean (SD)SD, Standard deviation; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C-reactive protein (mg/dl); DAS-28, Disease Activity Score-28; PGA, patient global assessment; HAQ-DI, Health Assessment Questionnaire Disability Index; PsAID, Psoriatic Arthritis Impact of Disease

POS1071

DETERMINATION OF THE RELIABILITY AND VALIDITY OF THE BETY-BIOPSYCHOSOCIAL QUESTIONNAIRE IN PATIENTS WITH A DIAGNOSIS OF PSORIATIC ARTHRITIS

S. Bulut[1], E. Ünal2, J. Karakaya[3], U. Kalyoncu[4]. [1]*Hacettepe University, Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey*; [1]*Hacettepe University, Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey*; [3]*Hacettepe University, Faculty of Medicine, Department of Basic Medical Sciences, Ankara, Turkey*; [4]*Hacettepe University, Faculty of Medicine, Department of Internal Medical Sciences, Ankara, Turkey*

Background: In the literature, there is a lack of questionnaires, which is evaluate patients with psoriatic arthritis (PsA) from a biopsychosocial perspective.
Objectives: This study was planned to examine the reliability and validity of the BETY- Biopsychosocial Questionnaire (BQ) in individuals diagnosed with PsA.
Methods: Test-retest method was used to examine the reliability of the BETY-BQ. In comparing the reliability of test-retest results, ıntraclass coefficient (ICC) was checked. For the internal consistency analysis of the BETY-BQ, the total score of the responses given to the first filled scale was calculated and the Cronbach's Alpha coefficient was found. Psoriatic Arthritis Quality of Life Questionnaire (PsAQoL), Health Assessment Questionnaire (HAQ), Hospital Anxiety and Depression Scale (HADS) and Short Form-36 (SF-36) were used in the validity study of 150 individuals with PsA included in the study.
Results: Test-retest method and intraclass coefficient were examined for reliability analysis (for 30 patients). The correlation (r = 0.844, p <0.001) of the answers given to the BETY-BQ by individuals with 30 PsA after one week interval was very high. While the ICC coefficient (0.915, p <0.001) showed excellent reliability. The Cronbach's Alpha coefficient (0.940) was examined for internal consistency and the internal consistency of the scale was also found to be excellent. As a result of statistical analysis, the correlation between the scales used and the BETY-BQ was found between r = -0.432 and 0.807 (p <0.001).
Conclusion: With this study, it was concluded that the BETY-BQ is a reliable and valid assessment tool in individuals diagnosed with PsA, and is also a biopsychosocial tool that can be used to evaluate individuals with PsA.
REFERENCES:
[1] Unal E, Arin G, Karaca Nb, Kiraz S, Akdoğan A, Kalyoncu U, et al. Romatizmalı hastalar için bir yaşam kalitesi ölceginin gelistirilmesi: madde havuzunun olussturulması. Journal of Exercise Theraphy and Rehabilitation. 2017;4(2):67-75.
[2] Husni ME, Merola JF, Davin S. The psychosocial burden of psoriatic arthritis. Semin Arthritis Rheum. 2017;47(3):351-60
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1520

POS1072

ASSOCIATION OF NAIL PSORIASIS WITH WORSE DISEASE OUTCOMES IN PSORIATIC ARTHRITIS PATIENTS. DATA FROM CLINICAL PRACTICE

E. Gubar[1], Y. Korsakova[1], E. Loginova[1], S. Glukhova[2], T. Korotaeva[1], E. Nasonov[1,3], A. Lila[1,4], N. Kuznetsova[5], I. Umnova[6], V. Sorotskaya[7], I. Patrikeeva[8]. [1]*V.A. Nasonova Research Institute of Rheumatology, Spondyloarthritis and psoriatic arthritis, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Medical and Social Problems in Rheumatology, Moscow, Russian Federation*; [3]*I.M. Sechenov First Moscow State Medical University, Rheumatology, Moscow, Russian Federation*; [4]*Russian Medical Academy of Continuing Professional Education, Rheumatology, Moscow, Russian Federation*; [5]*Municipal Autonomous Institution "City Clinical Hospital No. 40", Rheumatology, Yekaterinburg, Russian Federation*; [6]*Omsk region "Regional clinical hospital", Rheumatology, Omsk, Russian Federation*; [7]*Medical Institute of the Tula State University, Rheumatology, Tula, Russian Federation*; [8]*Tyumen Regional Clinical Hospitai №1, Rheumatology, Tyumen, Russian Federation*

Background: Limited data are available regarding the burden of nail disease in psoriatic arthritis (PsA). The latest data show that nail involvement in PsA patients (pts) is associated with significantly more severe disease status (1).
Objectives: To analyze, in clinical practice, the association of nail psoriasis with disease activity, quality of life, and work productivity in PsA pts.
Methods: 588 pts (M/F–277 /311) with PsA according to CASPAR criteria were included in the study. Data were collected from 43 rheumatology clinics from different regions of the Russian Federation. Pts' age 48.6±0.5 years (yrs), disease duration 7.0±0.3 yrs. Pts underwent standard clinical examination of PsA activity. Pts were split into two groups (gr.): those with nail psoriasis – gr.1, and those without it – gr.2. Demographics, disease activity, quality of life, and work productivity were compared between pts with and without nail psoriasis using Pearson's chi-square test and Mann–Whitney U test.
Results: Gr.1 includes 312 (53.1%) cases, gr.2 – 276 (46.9%) cases. More pts in gr.1 were males (51.9% vs 44.1%, p=0.013), disabled at work (37.20% vs 26.40%, p=0.000), chronic smokers (18.9% vs 8.7%, p=0.000) and with axial PsA disease signs according to physician (35.0% vs 26.4%, p=0.025) compared to pts in gr.2. Pts in gr.1 had higher tender and swollen joint counts: 8 [4-15] vs 5 [2-12] (p=0.002) and 5 [1-9] vs 2 [0-7] (p=0.003) respectively. Gr.1 pts had higher disease activity measured by DAPSA 25 [15-39] vs 20 [12-33] (p= 0.001), higher frequency of dactylitis (24.4% vs 16.7% p=0.022) and heel enthesitis (17.0% vs 10.1% p=0.016) respectively, higher frequency of erosive radiographic arthritis of feet (45.0% vs 31.2% p=0.003) compared to gr.2 pts. Pts in gr.1 had worse skin psoriasis measured by Psoriasis Area Severity Index – 6 [2-14] vs 3 [1-6] (p=0.000). Less pts in gr.1 than in gr.2 (27.0% vs 52.0% p=0.004) achieved minimal disease activity (MDA). Pts' reported outcomes (PRO's) in gr.1 were worse than in gr.2 in regard to reduced health-related quality of life according to PsAID (4.9±2.3 vs 4.0±2.3, p=0.040) and to EQ-5D (0.56±0.19 vs 0.64 ±0.21, p=0.024) questionnaires, overall work impairment (0.0 [0.0-0.3] vs 0.0 [0.0-0.2], p=0.034) and overall activity impairment (0.4 [0.1-0.7] vs 0.3 [0.0-0.5], p=0.006) according to WPAI.
Conclusion: Nail involvement in PsA pts is associated with male gender and axial disease. PsA pts with nail involvement are more often disabled, more often are chronic smokers, have significantly worse disease status as measured by disease activity; they are more likely to have more severe (erosive) peripheral arthritis of feet, higher frequency of heel enthesitis and dactylitis, higher psoriasis disease severity, lower frequency of MDA achievement, and worse quality of life and work productivity according to PRO's. Detection of nail involvement is critical for choice of treatment approach and better outcomes.
REFERENCES:
[1] Mease PJ et al.J Rheumatol, 2020
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1576

POS1073

AXIAL PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS. SAME OR DIFFERENT? A REAL-WORLD STUDY WITH EMPHASIS ON COMORBIDITIES

G. E. Fragoulis[1], M. Pappa[1], G. Evangelatos[1], A. Iliopoulos[2], P. Sfikakis[1], M. Tektonidou[1]. [1]*National and Kapodistrian University of Athens, First Department of Propaedeutic Internal Medicine, Joint Rheumatology Program, Athens, Greece*; [2]*417 Army Shared Fund Hospital "NIMTS", Department of Rheumatology, Athens, Greece*

Background: Axial involvement affects 25-70% of psoriatic arthritis (PsA) patients, depending on the criteria used for its definition. Efforts are underway to clarify the similarities and differences between axial-PsA and ankylosing spondylitis (AS).
Objectives: We aimed to compare, in a real-world setting, axial-PsA and AS, in terms of demographic, radiologic and clinical (musculoskeletal and extra-articular) characteristics, with a focus on comorbidities.
Methods: All AS (New York criteria, n=128) and PsA patients (CASPAR criteria, n=78) with axial involvement who were regularly followed-up in the outpatients' rheumatology clinics from two tertiary hospitals (December 2018-July 2020) were included. Axial-PsA was defined when both of the following were ever present: inflammatory axial symptoms and radiological findings in X-ray or MRI of the sacroiliac joints or the spine. The following findings were considered: sacroiliitis (unilateral ≥ grade 3 or bilateral ≥ grade 2), corner lesions or squaring in the vertebrae, syndesmophytes (marginal or para-marginal) and facet joints arthritis.
Demographic, radiologic and clinical characteristics including comorbidities were compared between AS and axial-PsA. For comorbidities (Major Adverse Cardiovascular Events [MACE: combined coronary disease and cerebrovascular accidents], hypertension, diabetes mellitus, dyslipidemia, depression, osteoporosis, and malignancies), adjustments were made for relevant confounders as follows: MACE were adjusted for: age, gender, smoking, hypertension, dyslipidemia, disease duration, DM and non-steroidal anti-inflammatory drugs [NSAIDs] use; depression for: age, gender and disease duration; malignancy for: age, gender, disease duration; hypertension for: age, sex, BMI, NSAIDs use, smoking for; DM: age, sex, BMI, glucocorticoids treatment; osteoporosis for: age, sex, glucocorticoids treatment. Statistical significance is considered for p-values less than 0.05 and 0.1 in univariate and multivariate analyses, respectively.
Results: AS patients were younger (p=0.05) and were diagnosed at a younger age (p=0.002), more frequently of male gender (p=0.04), had lower BMI (p=0.006) and they were more frequently HLA-B27-positive (p=0.006). In AS patients, peripheral arthritis, dactylitis and nail involvement were less common (p=0.001 for all), in contrast to eye (p=0.001) and bowel involvement (p=0.004). Frequency of radiologic abnormalities in the spine was similar between the two groups while sacroiliitis was more often bilateral in AS and unilateral in axial-PsA (p<0.001 for both) Comorbidities, including MACE, were comparable between AS and axial-PsA, apart from depression which was more frequent in axial-PsA (Table 1. next page).

Table 1. Comorbidities. Comparison between axial-PsA and AS. OR: odds ratio, MACE: Major cardiovascular events. * adjustments are reported in the text

Comorbidities	axial-PsA (n=79)	AS (n=129)	Crude OR (95%CI)	Adjusted OR (95%CI)	p-value
MACE* n (%)	4 (5.1)	6 (4.6)	0.91 (0.25-3.34)	1.73 (0.32-9.34)	0.526
Dyslipidemia n (%)	37 (46.8)	45 (34.9)	0.61 (0.34-1.07)	NA	0.108
Hypertension* n (%)	27 (34.2)	24 (18.6)	0.44 (0.23-0.83)	1.11 (0.38-3.21)	0.843
Diabetes mellitus* n (%)	12 (15.2)	10 (7.7)	0.47 (0.19-1.14)	1.65 (0.43-6.29)	0.463
Depression* n (%)	19 (24.1)	16 (12.4)	0.44 (0.21-0.93)	0.48 (0.22-1.07)	**0.07**
Osteoporosis* n (%)	3 (3.8)	10 (7.7)	2.13 (0.57-7.98)	2.40 (0.56-10.18)	0.235
Malignancies* n (%)	3 (3.8)	3 (2.3)	0.60 (0.12-3.06)	0.87 (0.16-4.70)	0.870

Conclusion: AS and axial-PsA have certain clinical and radiologic differences. Comorbidities were comparable, while depression was more common in axial-PsA.
Disclosure of Interests: George E. Fragoulis: None declared, Maria Pappa: None declared, Gerasimos Evangelatos: None declared, Alexios Iliopoulos: None declared, Petros Sfikakis Grant/research support from: AbbVie, Pfizer, MSD, Roche, UCB, GSK, Novartis, Maria Tektonidou Grant/research support from: AbbVie, GSK, Genesis, MSD, Novartis, Pfizer, UCB.
DOI: 10.1136/annrheumdis-2021-eular.2129

POS1074 CARDIOVASCULAR RISK FACTORS IN A MEXICAN MESTIZO PATIENTS WITH PSORIATIC ARTHRITIS

S. Lugo-Perez[1], I. J. Colunga-Pedraza[2], J. R. Azpiri-López[1], D. Á. Galarza-Delgado[2], A. B. Rodriguez-Romero[2], N. Guajardo-Jauregui[2], D. E. Flores Alvarado[2], A. Cárdenas[2], O. Ilizaliturri Guerra[2]. [1]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico*; [2]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*

Background: Psoriatic Arthritis (PsA) is a chronic inflammatory arthropathy that affects 14%-30% of patients with skin and/or nail psoriasis. Patients with psoriatic arthritis (PsA) have a higher prevalence of traditional cardiovascular (CV) risk factors and an increased risk of developing cardiovascular diseases (1), such as acute myocardial infarction, cerebrovascular accident, peripheral vascular disease and heart failure. Despite the evidence patients with PsA are inadequately screened and undertreated for CV risk factors (CVRF), highlighting a gap in preventive medicine to adjust cardiovascular therapies(2).
Objectives: The aim of the study is to determine the main CVRF in Mexican Mestizo patients with a diagnosis of PsA and to compare it with healthy controls. Additionally, to assess the impact of the diagnosis of PsA on the presence on these cardiovascular comorbidities.
Methods: A cross-sectional, observational, and comparative study of ninety-six patients with PsA between 40-75 years who fulfilled CASPAR criteria 2006. Patients were matched by age and gender with non-PsA subjects. A medical history and physical exam were performed, also a blood sample was collected during the first visit. Chi square and Student´s t test were used for comparations between groups. A binary logistic regression was performed including the traditional CVRF (type 2 diabetes mellitus, hypertension, obesity, and active smoking), age and the diagnosis of PsA. A p value <0.05 was considered statistically significant.
Results: There were 58 (60.4%) women in each group with a mean of 53 years. Patients with PsA showed a higher prevalence of hypertension (HTN) compared to healthy controls (35.4% vs 19.8%, respectively, p = 0.015). Additionally, there was a significant difference in the diagnosis of dyslipidemia (42.7% vs 22.9%, p = 0.003).We found no statistically difference between the two groups in type 2 diabetes mellitus, active smoking and, obesity (Table 1. below).

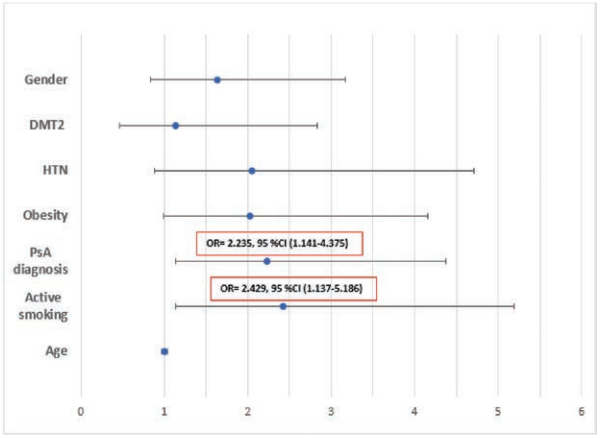
Table 1. Comparison of cardiovascular risk factors between Psoriatic Arthritis and controls.

	PsA (n=96)	Control (n=96)	p
Age, years ± SD	53.19 ± 11.13	53.34 ± 8.4	NS
Women, n (%)	58 (60.4)	58 (60.4)	NS
T2DM, n (%)	21 (21.9)	12 (12.5)	NS
HTN, n (%)	34 (35.4)	19 (19.8)	**0.015**
Active smoking, n (%)	21 (21.9)	20 (20.8)	NS
Dyslipidemia, n (%)	41 (42.7)	22 (22.9)	**0.003**
Obesity, n (%)	36 (37.5)	25 (26.0)	NS

NS, no significative; SD, standard deviation; HTN, hypertension; T2DM, type2 diabetes mellitus.

The binary logistic regression showed that the diagnosis of PsA (OR 2.235, 95% CI 1.141-4.375, p = 0.019) and active smoking (OR 2.429 95%, CI 1.137-5.186, p = 0.022) are independent risk factors for the presence of dyslipidemia.
Conclusion: Patients with PsA have a higher prevalence of HTN and dyslipidemia. The diagnosis of PsA seems to be an independent factor for the presence of dyslipidemia. It is important for rheumatologists to identify those patients who could benefit from adjust antirheumatic and cardiovascular therapies due to their impact on morbidity and mortality.
REFERENCES:
[1] Peluso R, Caso F, Tasso M, et al. Cardiovascular Risk Markers and Major Adverse Cardiovascular Events in Psoriatic Arthritis Patients. Rev Recent Clin Trials 2018;13(3):199-209. doi: 10.2174/1574887113666180314105511
[2] Takeshita J, Grewal S, Langan SM, et al. Psoriasis and comorbid diseases: Implications for management. J Am Acad Dermatol 2017;76(3):393-403. doi: 10.1016/j.jaad.2016.07.065

Figure 1. Binary logistic regression for the presence of dyslipidemia.



Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2779

POS1075 PREDICTIVE FACTORS ASSOCIATED WITH DEVELOPMENT OF PSORIATIC ARTHRITIS IN PATIENTS WITH UNDERLYING PSORIASIS

W. Y. Loo[1], F. Yahya[1], W. H. Han[2], N. A. A. Fahem[2], S. S. Yong[2], L. S. L. Pok[1], Z. Kwan[2], Y. C. Tee[1]. [1]*University of Malaya, Rheumatology Unit, Medicine, KUALA LUMPUR, Malaysia*; [2]*University of Malaya, Dermatology Unit, Medicine, KUALA LUMPUR, Malaysia*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory condition in which a delayed diagnosis will have health impacts including physical and psychological aspects. Thus, identification of risk factors and early diagnosis are crucial in clinical practice. In Malaysia, 13.7% of patients with underlying psoriasis develop PsA [1]. However, there are limited data on the risk factors in developing PsA in these patients, not just in Malaysia but also in the Southeast Asia region.
Objectives: To analyse sex, clinical features, comorbidities in patients with psoriasis and PsA, and the predictive factors of developing PsA in patients with underlying psoriasis.
Methods: A retrospective study was carried out involving patients with a physician-verified diagnosis of psoriasis who were attending the dermatology and/or rheumatology clinics at the University of Malaya Medical Centre, Kuala Lumpur between 2015 to 2020. Data were retrieved from electronic medical records. Data collected included sex, age, body mass index (BMI), duration of psoriasis, socio-demographics, comorbidities, body area affected, severity of skin involvement, presence of nail involvement and systemic therapy used in treating psoriasis. Systemic therapy is defined as methotrexate, sulfasalazine and/or acitretin used before diagnosis of PsA. Patients with psoriasis who developed PsA had information collected on tender joint count, swollen joint count and erythrocyte sedimentation rate (ESR) at their initial visit to the rheumatologist. Logistic regression analyses were performed to identify the possible risk factors of developing PsA.
Results: A total of 330 psoriasis patients which included 54.5% male and a mean age of 53 (standard deviation, SD 18.85) years were included. Eighty-three (25.0%) patients were diagnosed with PsA. Among patients with PsA, 39.8% were males with a mean age of 54 (SD 15.79) years. Majority of the PsA patients were ethnic Malay (45.8%), followed by 28.9% Chinese and 25.3% Indian. The median duration of developing PsA was at 36 (IQR 3.5 - 114) months after the

diagnosis of psoriasis. 12.3% presented with active polyarthritis at the initial diagnosis of PsA. There was a significant difference in the use of systemic therapy in females, in which there was a higher rate of systemic therapy used in female PsA patients prior to developing PsA as compared to females with psoriasis who did not develop PsA (n=24, 48% vs n=16, 16%; p < 0.001). There was no significant association between ethnicity, education level, comorbidities, BMI, body area affected and family history of psoriasis with development of PsA. The predictive factors in developing PsA are females (OR = 3.14, 95% CI 1.77,5.58), presence of nail involvement (OR = 3.72, 95% CI 1.91,7.26) and the use of systemic therapy (OR = 3.04, 95% CI 1.70,5.43), (all p values <0.001).

Conclusion: This study highlighted that female sex, presence of nail involvement and use of systemic therapy prior to PsA diagnosis are predictive risk factors in developing PsA among patients with underlying psoriasis. Further prospective studies with larger cohorts are needed to better delineate these risk factors.

REFERENCES:

[1] Mohd Affandi A, Khan I, Ngah Saaya N. Epidemiology and Clinical Features of Adult Patients with Psoriasis in Malaysia: 10-Year Review from the Malaysian Psoriasis Registry (2007-2016). Dermatology research and practice. 2018;2018:4371471.

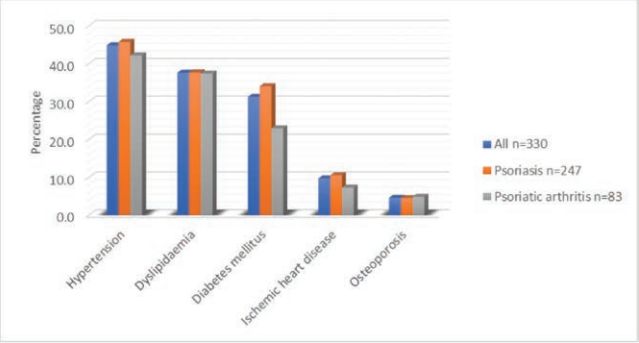


Figure 1. Comorbidities among Patients with underlying Psoriasis and Psoriatic Arthritis (n=330)

Chi-square test revealed that there was no significant difference between psoriasis and psoriatic arthritis (p > 0.05)

Disclosure of Interests: WAI YANG LOO: None declared, FARIZ YAHYA Speakers bureau: speaker for Novartis, Gilead, AbbVie, Janssen, Eli Lilly, Zuellig-Pharma and Pfizer., Consultant of: consultancy work with Novartis, Gilead, AbbVie, Eli Lilly, Zuellig-Pharma and Pfizer., Grant/research support from: research grants from Novartis, Gilead, AbbVie, Boehringer-Ingelheim and Pfizer., WINN HUI HAN: None declared, NIK AIMEE AZIZAH FAHEM: None declared, SHIN SHEN YONG: None declared, Lydia Say Lee Pok: None declared, Zhenli Kwan Speakers bureau: Novartis, Zuellig, YING CHEW TEE: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2792

POS1076 APICAL FIBROSIS AND INTERSTITIAL LUNG DISEASE IN PATIENTS WITH PSORIATIC ARTHRITIS: DO WE UNDERESTIMATE?

G. Ayan[1], E. B. Ata[2], G. Durhan[3], M. Ariyurek[3], U. Kalyoncu[1]. [1]*Hacettepe University Medical Faculty, Department of Internal Medicine Division of Rheumatology, Ankara, Turkey*; [2]*Hacettepe University Medical Faculty, Department of Internal Medicine, ANKARA, Turkey*; [3]*Hacettepe University Medical Faculty, Department of Radiology, ANKARA, Turkey*

Background: Extra-articular manifestation (EAMs) definition is not clearly defined in psoriatic arthritis (PsA). Nail involvement, enthesitis, dactylitis has been widely studied however, data are needed on pulmonary involvement in PsA.

Objectives: We aimed to understand real-life results of lung involvement in PsA patients.

Methods: From the PsA cohort followed in our outpatient clinic, patients who have been requested a chest computed tomography (CT) for any reason by any department were retrieved from medical records and included in this retrospective cross-sectional analysis. All CTs were assessed by a radiologist who is blinded to the patients` clinical history and findings were categorized as parenchymal, airway, pleural findings and lymphadenopathy (LAM). Moreover, any findings that are radiologically attributed to a specific entity such as previous tuberculosis (Tb) infection were noted. Demographic/clinic data including smoking status, concomitant lung problems, disease characteristics (duration, axial/peripheral involvement) were collected and analyzed.

Results: A total of 80/1072 (7.4 %; 65% female) PsA patients with mean (SD) age 56.1 (13.2) years were included in the study. Median (IQR) PsA duration was 23.5 (55.75) months and 36 (45%) patients had peripheral, 29 (36.3%) patients had axial involvement. For the rest of 15 (18.7 %) patients, radiographic assessment was missing. Smoking status could be retrieved in 47 patients (never=40.4%, ex-smoker= 19.1%, current smoker=40.4%). There were 14 concomitant lung problem in 12 (15%) patients. CT findings showed that 68.8% of patients had at least one lung pathology. Parenchymal findings were seen in 65% of the patients as both non-spesific changes (atelectasis, n= 35; nodules, n=24; ground glass opacity, n= 9; sequelae fibrosis, n= 9; emphysema, n= 7; consolidation, n= 5, interstitial thickening, n= 5; pulmonary cyst, n =4) and specific pathologies as apical fibrosis (AF) (n=5) and intersititial lung disease (ILD) (n=5, NSIP=3, LIP=2). AF was linked to previous Tb infection in 1 patient and radiotherapy in another (Table 1). However, there is no specific pathology in the rest of 3 (3.7%) patients that AF could be attributed to and all of them were male. Other pathologies were seen as airway findings in 28.8% patients (bronchiectasis, n= 17, bronchial wall thickness, n= 10, air trapping n= 7, centrilobular opacity, n= 4,) and pleural findings in 13.8 % of the patients (pleural plaque, n= 5, effusion, n= 3, thickness, n=3). LAM was observed in around 4% of the patients.

Table 1. Patient characteristics with apical fibrosis, interstitial lung disease

	Involvement	Gender	Age	PsA duration, months	Axial Disease (yes/no)	Smoking Status	Smoking pack-age-years	Concomitant Lung Disease (yes/no)	Linked to another problem by radiologist (yes/no)
ID-1	AF	M	58	2	No	Current	40	No	No
ID-2	AF	M	61	1	No	Current	40	No	No
ID-3	AF	M	73	122	Yes	Ex	30	No	No
ID-4	AF	F	55	1	Yes	NA	NA	No	Yes*
ID-5	AF	F	65	#	NA	Never	-	Yes€	Yes€
ID-6	NSIP	F	96	NA	NA	Never	-	No	No
ID-7	NSIP	M	69	NA	NA	Ex	15	Yes$	No
ID-8	NSIP	F	66	156	No	NA	NA	Yes$	No
ID-9	LIP	M	61	200	Yes	Never	-	No	No
ID-10	LIP	F	80	14	Yes	NA	NA	No	No

AF= Apical fibrosis; NSIP= Non-spesific interstitial pneumonia, LIP= Lymphocytic interstitial pneumonia; PsA= Psoriatic Arthritis, NA= Not available*radiotherapy sequelae; # tomography was done prior to PsA diagnosis; € previous tuberculosis infection; $ chronic obstructive pulmonary disease

Conclusion: The real-life experience of our PsA cohort showed that pulmonary findings included variable spesific, non-spesific findings. As a limitation results represent the CT findings of around 8% of our PsA cohort. Within the scope of previous reports male predominant AF and ILD come forward in PsA that requires further attention in future studies [1,2].

REFERENCES:

[1] Peluso R, Iervolino S, Vitiello M, et al (2015) Extra-articular manifestations in psoriatic arthritis patients. Clin Rheumatol 34 (4):745-753.

[2] Bargagli E, Bellisai F, Mazzei MA, et al (2020) Interstitial lung disease associated with psoriatic arthritis: a new disease entity? Intern Emerg Med.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2873

POS1077 CLINICAL AND RADIOLOGICAL FEATURES OF SEROPOSITIVE PSORIATIC ARTHRITIS

H. EL Moutaouakil[1], K. Nassar[1], S. Janani[1]. [1]*University Hospital of Ibn Rochd, Department of Rheumatology, casablanca, Morocco*

Background: Rheumatoid factor (RF) and anti-cyclic citrullinated peptides (anti-CCP) are two highly specific laboratory markers for rheumatoid arthritis. However, they can also be found in other chronic inflammatory arthritis such as psoriatic arthritis (Psa).

Objectives: The aim of our study is to analyze the different epidemiological and paraclinical characteristics of seropositive psoriatic arthritis.

Methods: Descriptive and analytical retrospective study from January 2010 to December 2020 conducted in the Department of Rheumatology of the University Hospital of Ibn Rochd, Casablanca.

Inclusion criteria: patients diagnosed with psoriatic arthritis according to the CASPAR or ASAS 2009 criteria, regardless of the immunological status (RF/anti-CCP).

The patients were then divided into two groups: seropositive (positive anti-CCP and / or positive RF) and seronegative. A univariate analytical study was performed by jamovi version 1.2.27

Results: 80 patients were enrolled. 22 patients were seropositive (Group 1) and 58 were seronegative (Group 2). In the group 1, the mean age was 51.1 years (+/- 9.45). The sex ratio M/F was 0.29, the mean age of onset was 43.5 years (+/- 10.4), the mean duration of disease was 9.55 +/- 8 years. All patients had skin involvement. Polyarticular involvement was present in all cases; axial involvement was present in 68.18% of cases and enthesitis in 68.18% of cases. All patients were HLA B 27 negative. The presence of X-ray and / or ultrasound bone

Table 1. Comparison of characteristics of seropositive and seronegative PsA patients

Items	Group 1 Seropositive patients (n=22)	Group 2 Seronegative patients (n=58)	p-value
Age (years)	51.1 +/-9.45	50.7 +/- 15.8	0.9
Sex ratio M/F	0.29	1.14	0.013
Age onset (years)	43.5 +/- 10.4	37.4+/- 16.5	0.123
Skin involvement (%)	100	50	0.009
Bone erosions (%)	81.1	56.9	<0.001
Response to treatment (%)	70.58	51.14	<0.001

erosions in addition to signs of destruction was in 81.8% of cases. The response to treatment with (corticosteroids / NSAIDs / DMARDs) was partial in 70.58%.
In group 2, the mean age was 50.7 years (+/- 15.8). The sex ratio M/F was 1.14, the mean age of onset was 37.4 years (+/- 16.5), the mean duration of disease was 13.3 years (+/- 9.5). Skin involvement was present in 50% of patients. Polyarticular involvement was present in all cases, axial involvement was present in 67.24% of cases and enthesitis in 56.9% of cases. All patients were HLA B 27 negative. The presence of X-ray and / or ultrasound bone erosions in addition to signs of destruction was in 56.9% of cases. The response to treatment with (corticosteroids / NSAIDs / DMARDs) was partial in 57.14%.
Conclusion: The presence of anti-CCP according to several studies is linked to the presence of deformities, dactylites and radiological erosions (1,2). In our series, seropositivity was accompanied by the erosive nature of the destruction, as well as a tendency to resistance to treatment.

REFERENCES:

[1] Kim KY, Lee YH. Anti-cyclic citrullinated peptide antibody in psoriatic arthritis: a meta-analysis of its frequency and association with clinical features. Z Rheumatol. mai 2020;79(4):397-403.
[2] Hagiwara S, Tsuboi H, Terasaki T, Terasaki M, Toko H, Shimizu M, et al. Association of anti-cyclic citrullinated peptide antibody with clinical features in patients with psoriatic arthritis. Modern Rheumatology. 3 mars 2020;30(2):365-72.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2958

POS1078

CURRENT REGISTRIES IN PSA DO NOT WELL REFLECT THE PROFILES OF PATIENTS WITH PsA BECAUSE THEY ORIGINATE IN SIMILAR COUNTRIES: A SYSTEMATIC LITERATURE REVIEW OF 27 REGISTRIES, OR 16183 PATIENTS

G. S. Moysidou[1], K. Aouad[1], A. Rakotozafiarison[1], B. Fautrel[1], L. Gossec[1].
[1]*Sorbonne Université – INSERM; AP-HP, Pitié Salpêtrière Hospital, Rheumatology department, Paris, France*

Background: Psoriatic arthritis (PsA) is a multidimensional inflammatory disease with a great geographic variability and a global average prevalence estimated at 133 every
100,000 subjects according to a recent systematic review and meta-analysis (1). Registries and cohorts reflect more closely real-world data than randomized controlled trials (RCTS) and may indicate ongoing interest of each country on PsA.
Objectives: The purpose of this study is to assess how recent registries and PsA related cohorts reflect its worldwide prevalence.
Methods: A systematic literature review was performed in Pubmed Medline (PROSPERO
CRD42020175745) to identify all articles reporting on either registries or longitudinal cohorts in PsA, published between 2010 and March 2020. Registries centered on drugs or not PsA-specific, trials and long term extension studies were excluded. The data collection comprised registries' and cohorts' originating countries, patient characteristics and the clinical outcome measures reported. Statistics were descriptive.
Results: Of 673 articles, 73 were relevant for analysis, corresponding to 27 registries or PsA specific cohorts, with the participation of 30 countries. The overall number of patients was 16,183 with a mean of 599 per study. Overall, 50.1% were men, weighted mean age was 50,6 years and weighted mean disease duration was 6.9 years.
Most of the registries were based in Europe (67%) or North America (26%) whereas Africa was underrepresented (Figure 1). USA was the most represented country participating in 6 registries. Mean age and mean disease duration were shorter in international registries (Table 1). Caspar diagnostic criteria were the most frequently used, mainly in the national registries (86,4%), whereas the use of diagnostic criteria was more heterogenous in the international registries.
Conclusion: Recent registries and PsA specific cohorts do not cover the worldwide spectrum of the disease.

REFERENCES:

[1] Scotti L, Franchi M, Marchesoni A, Corrao G. Prevalence and incidence of psoriatic arthritis: A systematic review and meta-analysis. Semin Arthritis Rheum. 2018 Aug;48(1):28-34

Table 1. Description of 27 ongoing PsA registries or PsA cohorts, comparing nationwide and international registries

	NATIONWIDE REGISTRIES (N=22)	INTERNATIONAL REGISTRIES (N=5)
WOMEN (%)	49,4	50,8
MEAN AGE, WEIGTHED (YEARS)	52,32	48,09
MEAN DISEASE DURATION, WEIGHTED (YEARS)	8,59	5,86
CASPAR DIAGNOSTIC CRITERIA (%)	86,4	40

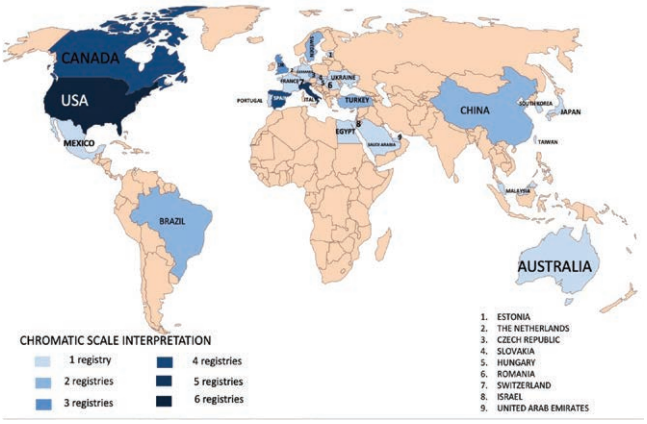


Figure 1. Geographical distribution of PsA registries

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3097

POS1079

ASSOCIATION OF C-REACTIVE PROTEIN AND NON-STEROIDAL ANTI-INFLAMMATORY DRUGS WITH CARDIOVASCULAR EVENTS IN PATIENTS WITH PSORIATIC ARTHRITIS: A TIME-DEPENDENT Cox REGRESSION ANALYSIS

S. H. M. Lam[1], H. So[1], I. T. Cheng[1], E. LI[1], P. C. Wong[1], T. K. LI[1], A. P. W. Lee[1], L. S. Tam[1]. [1]*The Chinese University of Hong Kong, Department of Medicine and Therapeutics, Sha Tin, Hong Kong (SAR)*

Background: Psoriatic arthritis (PsA) is associated with accelerated atherosclerosis due to underlying inflammation. Whether inflammatory burden and drugs used to suppress inflammation over time are associated with cardiovascular (CV) events remains unclear.

Objectives: This study aims to examine the time-varying effect of C-reactive protein (CRP) levels and the use of drugs including non-steroidal anti-inflammatory drugs (NSAIDs) on the risk of CV events independent of traditional CV risk factors in PsA patients.

Methods: A retrospective cohort analysis was performed in patients with PsA who were recruited from 2008 to 2015 and followed till the end of 2019. The outcome was occurrence of a first CV event. Framingham risk score (FRS) was used to quantify the traditional CV risk. Cox proportional hazard models with time-varying CRP levels and drugs used were analyzed to identify the risk factors for CV events in PsA patients.

Results: 200 patients with PsA (median age: 47.5[40.0 – 56.0]; male: 119 [59.5%]) were recruited (Table 1. next page). After a mean follow-up of 8.8±3.8 years, 30 (15%) patients developed a first CV event. The Kaplan-Meier survival analysis indicated a significant difference in the CV event-free survival between patients with and without CRP level >3 mg/L (Figure 1A) and an inverse relationship between time-varying NSAIDs exposure and CV event-free survival (Figure 1B). The multivariable Cox regression model showed that time-varying CRP level (HR 1.02, 95% CI 1.00 to 1.04) and NSAIDs exposure (HR 0.30, 95% CI 0.15 to 0.95) were significantly associated with CV events after adjusting for baseline FRS (HR 5.04, 95% CI 1.83 to 13.85).

Table 1. Baseline demographic and clinical characteristics, cardiovascular risk factors and treatments received.

Variables	All patients n=200 median (IQR) or n (%)	CVD -ve, n=170 median (IQR) or n (%)	CVD +ve, n=30 median (IQR) or n (%)	*p*-value	NSAID -ve, n=61 median (IQR) or n (%)	NSAID +ve, n=139 median (IQR) or n (%)	*p*-value
Male, n (%)	119 (59.5%)	100 (58.6%)	19 (63.3%)	0.228	39 (63.9%)	80 (57.6%)	0.397
Age, years	47.5 (40.0 – 56.0)	46.5 (37.7 – 54.0)	57.0 (45.3 – 65.8)	<0.001*	49.0 (44.0 – 56.5)	46.0 (38.0 – 54.8)	0.176
Disease duration, years	4.3 (1.8 – 7.9)	4.1 (1.7 – 7.0)	6.0 (2.1 – 8.6)	0.066	4.6 (1.5 – 8.7)	4.3 (1.9 – 7.3)	0.393
Diabetes, n (%)	45 (22.5%)	30 (17.6%)	15 (50.0%)	<0.001*	10 (16.4%)	35 (25.2%)	0.171
Hypertension, n (%)	68 (34.0%)	46 (27.1%)	22 (73.3%)	<0.001*	21 (34.4%)	47 (33.9%)	0.933
CRP, mg/L	4.9 (1.7 – 12.6)	4.2 (1.5 – 12.0)	11.3 (2.4 – 19.6)	0.035*	5.5 (1.7 – 15.1)	7.2 (1.4 – 15.8)	0.770
ESR, mm/hr	21 (10.0 – 38.0)	20 (9 – 35)	31 (14 – 60)	0.038*	21 (7 – 33)	21 (11 – 43)	0.291
Systolic blood pressure, mmHg	125 (115 – 140)	124 (115 – 137)	144 (129 – 160)	<0.001*	123 (118 – 137)	125 (115 – 141)	0.889
Diastolic blood pressure, mmHg	78 (70 – 85)	78 (70 – 84)	82 (72 – 90)	0.199	78 (72 – 86)	78 (70 – 85)	0.697
FRS	8.4 (4.0 – 17.0)	7.5 (3.3 – 14.0)	19.6 (13.4 – 43.0)	<0.001*	7.9 (3.5 – 15.5)	8.7 (4.2 – 17.1)	0.885
Lipid-lowering drugs, n (%)	30 (15.0%)	25 (14.7%)	5 (16.7%)	0.782	9 (14.8%)	21 (15.1%)	0.949
MTX, n (%)	99 (49.5%)	81 (47.6%)	18 (60.0%)	0.212	25 (41.0%)	74 (53.2%)	0.111
bDMARDs, n (%)	17 (8.5%)	13 (7.6%)	4 (13.3%)	0.303	6 (9.8%)	11 (7.9%)	0.654
NSAIDs, n (%)	139 (69.2%)	119 (70.0%)	20 (66.7%)	0.715	N/A	N/A	N/A
Steroid, n (%)	2 (1.0%)	2 (1.2%)	0 (0%)	1.000	1 (1.6%)	1 (0.7%)	0.518

**statistically significant at p≤ 0.05CVD+ve, patients who developed cardiovascular events during subsequent follow-up;CVD-ve, patients who did not developed cardiovascular events during subsequent follow-up;NSAIDs, nonsteroidal anti-inflammatory drugs; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FRS, Framingham Risk Score; MTX, methotrexate; bDMARDs, biological disease-modifying antirheumatic drugs.*

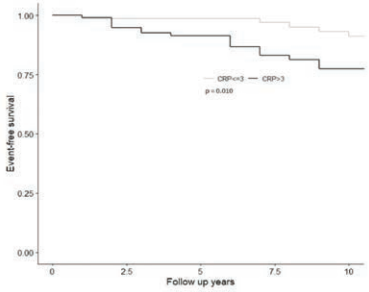


Figure 1A

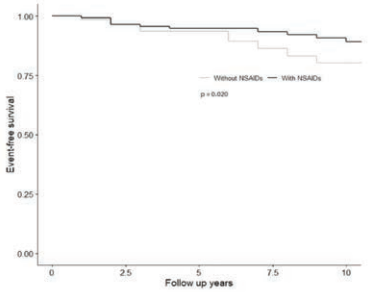


Figure 1B

Figure 1. Kaplan-Meier curves showing the cardiovascular event-free survival between patients with A) CRP≤3 mg/L and CRP>3 mg/L; B) treated with NSAIDs and without NSAIDs use during their follow-up intervals.

Conclusion: Increased inflammatory burden as reflected by elevated CRP level was associated with increased risk of CV events, while the risk was significantly reduced with NSAIDs use in PsA patients.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3118

POS1080

HYPERLIPIDEMIA IN PSORIATIC DISEASE: HIGHER PREVALENCE IN PSORIATIC ARTHRITIS AND INVERSE ASSOCIATION WITH SYSTEMIC THERAPY

R. Queiró Silva[1], E. Pardo Campo[1], S. Fernández[1], L. Arboleya Rodríguez[1], I. Zapico[1], F. Jirout[1]. *[1]Hospital Universitario Central de Asturias, Rheumatology, OVIEDO, Spain*

Background: Although the evidence that testifies to a higher prevalence of cardiometabolic risk factors in psoriatic disease is robust, there are not too many studies that have analyzed which disease traits are associated with these risk factors both in psoriasis and psoriatic arthritis[1].

Objectives: We aimed to analyze the frequency and disease-associated features of hyperlipidemia in psoriatic disease.

Methods: Cross-sectional observational study that included 290 patients with psoriatic arthritis (mean age 54 ± 12 years, 54.8 % male, psoriasis average duration 21 ± 10 years) and 310 with psoriasis alone (mean age 53 ± 11.5 years, 52.9% male, psoriasis average duration 22 ± 11 years). We first analyzed the frequency of this comorbidity and then the factors associated with it using conditional logistic regression. The significant factors in this first model were introduced in a multivariate model using a backward stepwise approach.

Results: Main disease features are depicted in Table 1. A total of 124 patients had hyperlipidemia (20.7%). Among arthritis patients, 82/290 (28.3%) had hyperlipidemia, compared with 42/310 (13.5%) of those with psoriasis alone (OR 2.5, 95%CI: 1.7–3.3, p < 0.001). Hyperlipidemia was independently associated with age [OR 1.07, 95%CI: 1.04–1.11, p < 0.001] and systemic therapy [OR 0.4, 95%CI: 0.17–0.89, p = 0.026].

Conclusion: Hyperlipidemia is common in psoriatic disease, but much more among arthritis patients. This comorbid factor seems to go in parallel with increasing age. There is an inverse association between systemic treatment and hyperlipidemia that should be endorsed with well-designed longitudinal studies.

REFERENCES:

[1] Puig L. Cardiometabolic comorbidities in psoriasis and psoriatic arthritis. Int J Mol Sci 2018; 19: 58.

Table 1. Disease characteristics of both subpopulations

Variable	PsA n = 290	Psoriasis n = 310	p-values
Age (yr ± SD)	54 ± 12	53 ± 11.5	*NS*
Age at psoriasis onset (yr ± SD)	32 ± 16	31 ± 14.2	*NS*
Age at arthritis onset (yr ±SD)	46 ± 14		*NS*
Duration of psoriasis (yr ± SD)	21 ± 10	22 ± 11	*NS*
Duration of arthritis (yr ± SD)	11 ± 7.2		*NS*
Male gender (n, %)	159 (54.8)	164 (52.9)	*NS*
Primary education (n, %)	145 (50)	148 (47.7)	*NS*
Secondary education (n, %)	79 (27.2)	87 (28.1)	*NS*
University degree (n, %)	66 (22.8)	235 (24.2)	*NS*
Plaque psoriasis (n, %)	250 (86.2)	272 (87.7)	*NS*
Nail disease (n, %)	122 (42.1)	110 (35.5)	*NS*
Psoriasis in ≥ 3 body areas (n, %)	130 (45)	155 (50)	*<0.05*
Family history of psoriasis (n, %)	130 (45)	136 (44)	*NS*
Family history of PsA (n, %)	44 (15.2)	15 (4.8)	
PASI	6.5 ± 4.3	6.8 ± 3.5	
Oligoarthritis (n, %)	122 (42.1)		
Polyarthritis (n, %)	81 (28)		
Axial disease (n, %)	17 (5.8)		
Mixed pattern (n, %)	70 (24.1)		
Dactylitis (n, %)	87 (30)		
DIP joint disease (n, %)	72 (24.8)		
Mutilating arthritis (n, %)	5 (1.7)		
Erosive disease (n, %)	58 (20)		
HAQ (mean ± SD)	0.74 ± 0.32		
*BASDAI (mean ± SD)	3.64 ± 2.12		
Pain VAS (mean ± SD)	4.09 ± 2.64		
HLA-B*27 (n, %)	52 (17.9)		
HLA-C*06 (n, %)	112 (38.6)	124 (40)	*NS*
NSAID (n, %)	72 (24.8)	47 (15.2)	*NS*
Glucocorticoids (n, %)	34 (11.7)	15 (4.8)	*NS*
MTX (n, %)	189 (65.2)	128 (41.3)	*<0.05*
Biologics (n, %)	128 (44.1)	132 (42.6)	*NS*

SD, standard deviation; PsA, psoriatic arthritis; PASI, psoriasis area and severity index; DIP, distal interphalangeal joint; HAQ, Health Assessment Questionnaire; BASDAI, bath ankylosing spondylitis disease activity index; VAS, visual analog scale; NSAID, non-steroidal anti-inflammatory drugs. MTX, methotrexate. *Only in patients with axial disease

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3170

POS1081 OSTEOPOROSIS AND INSUFFICIENCY RISK FACTORS IN PSORIATIC ARTHRITIS

M. P. Martínez-Vidal[1], V. Jovani[2], A. Alvarez de Cienfuegos[3], J. R. Noguera-Pons[4], R. Martín-Domenech[5], M. T. Pedraz-Penalva[5], P. Bernabéu[2]. [1]*Hospital Universitario de San Juan de Alicante, Rheumatology, Alicante, Spain*; [2]*Hospital General Universitario de Alicante, Rheumatology, Alicante, Spain*; [3]*Hospital Vega Baja Orihuela, Rheumatology, Orihuela, Spain*; [4]*Hospital General Universitario de Elche, Rheumatology, Elche, Spain*; [5]*Hospital General Universitario de Elda, Rheumatology, Elda, Spain*

Background: Osteoporosis (OP) has been described to be frequent in spondyloarthritis [1]. However, the specific association of psoriatic arthritis (PsA) and bone fragility remains inconclusive, with a prevalence of OP ranging from 1.4–68.8 [2, 3].
Objectives: The aim of this study was to describe the prevalence of osteopenia and OP in a representative cohort of patients with PsA
Methods: Multi-centric, cross-sectional, descriptive study of patients with clinical diagnosis of PsA. Patients were randomly selected; they were invited to participate and were included after signing informed consent until the calculated sample size was reached. Clinical and demographic characteristics were recorded, as well as several protective and risk factors for osteoporosis and insufficiency fractures. Patients were asked to undergo a hip and lumbar (L2-L4) densitometry by DXA, and lateral X-Ray of the dorsal and lumbar spine if they had not these tests available in the previous year. The prevalence of osteoporosis and the risk factors was calculated. The characteristics of the patients with OP were compared to those without by univariate analyses, and were adjusted by age and sex. Multivariate analyse by ANOVA test was done to study the association of OP and fractures with clinical characteristics of the disease. The Clinical Research Ethics Committee of the Hospital General Universitario de Alicante (ISABIAL- approval number 180264) approved the study
Results: 166 patients were included (Female 69%, male 30,1%), median age 58 (IR 51-65). Basal characteristics are shown in Table 1. Osteopenia or OP was present in 100 patients (60.2%). OP was present in 44 patients (26.5%). Among these, 9 patients (20.5%), all women ≥50 years old, had a total amount of 14 insufficiency fractures (4 vertebrae, 2 hips, 4 distal radius, 4 others). OP was present in 21.7% of the women, and 4.8% of the men. The most frequent risk factors among patients with OP were D-vitamin deficit (54.5%), sedentary life style by WHO standards (43.2%) and low calcium intake (38.6%). The most frequent protector factors in the group without osteopenia/nor OP was the intake of statins for ≥12 months. The presence of vertebral fractures was associated with female sex, sedentary lifestyle and age.
Conclusion: The prevalence of insufficiency fractures among PsA patients was very superior to that recently found in the general population in Spain (prevalence 1.83%) [4]. Fractures are associated, similar to the general population, to female sex, sedentary life and age. Inherent factors to psoriatic disease may be responsible for this increased prevalence
REFERENCES:
[1] Moltó A et al. Prevalence of comorbidities and evaluation of their screening in spondyloarthritis: results of the international cross-sectional ASAS-COMOSPA study. Ann Rheum Dis. 2016;756:1016
[2] Gulati AM et al. Bone mineral density in patients with psoriatic arthritis: data from the Nord-Trøndelag Health Study 3. RMD Open. 2017;3: e000413.
[3] Busquets N et al. Bone mineral density status and frequency of osteoporosis and clinical fractures in 155 patients with psoriatic arthritis followed in a university hospital. Reumatol Clin. 2014;10:89.
[4] Seoane-Mato D et al. Prevalence of rheumatic diseases in adult population in Spain (EPISER 2016 study): Aims and methodology. Reumatol Clin. 2019;15:90.

Table 1. Basal characteristics (n=166)

Age (years)	57,9 (SD 0,8)	Median 58 (IR 51-65)
Sex		
Male	50 (30.1%)	
Female	116 (69.9%)	
Duration of disease (years)	10.3 (SD 0.63)	Median 9 (IR 4.75-13)
Type of PsA		
Axial	15 (9%)	
Peripheral	125 (75.3%)	
Both	26 (15.7%)	
HAQ (n=142)	0.47 (SD 0.05)	Median 0.25 (IR 0-1)
BASFI (n=40)	3.7 (SD0.5)	Median 3.6 (IR 1-5.75)
cDMARD		
Never	25 (15.1%)	
Previous/actual	141 (85%)	
bDMARD		
Never	84 (50.6%)	
Previous/actual	82 (49.4%)	

PsA: psoriatic arthritisHAQ: Health Assessment QuestionnaireBASFI: Bath Ankylosing Spondylitis Functional Index cDMARDs: classical disease modifying anti-rheumatic drugs bDMARDs biological drugs

Acknowledgements: Thanks to doctors C. Fernández-Carballido, M Mínguez and G Panadero for their help recruiting candidates.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3175

POS1082 CATASTROPHIZING IN PATIENTS WITH PSORIATIC ARTHRITIS

C. Gaujoux-Viala[1,2], B. Coste[1], C. Traverson[1], E. Filhol[1,2], S. Laurent-Chabalier[3], J. Morel[4,5], B. Combe[4,5], C. Daien[4,5], C. Lukas[2,4], C. Hua[1,2]. [1]*Nîmes University Hospital, Rheumatology, Nîmes, France*; [2]*University of Montpellier, IDESP, UMR-INSERM, Montpellier, France*; [3]*Nîmes University Hospital, BESPIM, Nîmes, France*; [4]*CHU Lapeyronie, Rheumatology, Montpellier, France*; [5]*University of Montpellier, Montpellier, France*

Background: Catastrophizing is a negative cognitivo-affective response to an anxiety-provoking stimulus, especially anticipated or actual pain. It can be quickly assessed using a validated questionnaire: the Pain Catastrophizing Scale (PCS)[1]. Catastrophizing plays a role in maintaining chronic pain and is associated with several pain-related outcomes in osteoarthritis and low back pain. To our knowledge, there are no data on catastrophizing in patients with psoriatic arthritis (PsA).
Objectives: To assess the prevalence of catastrophizing and associated factors in PsA.
Methods: We performed a bi-centric observational, prospective study. All patients aged 18 or over with PsA fulfilling the 2006 CASPAR criteria were consecutively included. Sociodemographic data, information on the disease and its treatments were collected as well as questionnaires for disease activity (BASDAI), function (HAQ, BASFI), quality of life (SF12, EQ5D), anxiety and depression (HADS, GAD7), fibromyalgia (FiRST), insomnia (ISI) and catastrophizing scores (PCS). Statistical analysis included samples T-test, one-way variance analysis, Spearman's correlation coefficient, Chi^2 test, Fisher's exact test, Wilcoxon test, multivariate linear regression (considering catastrophizing as a continuous variable) and multivariate logistics regression (considering catastrophizing as a categorical variable: PCS ≥ 20 = high level catastrophizing).
Results: From September 2019 to March 2020, 85 PsA patients were included: 54.1% were women, the median age was 54.0 years and 33 patients (39.8%) were professionally active. The majority of patients (88.2%) had a disease lasting for more than 2 years. Axial involvement was found for 39 patients (45.9%), almost all patients (98.8%) had peripheral involvement, 32 patients (37.7%) had enthesitic involvement and 14 patients (16.7%) had erosions. Median DAS28 CRP was 3.12 [2.13-4.46] and the median BASDAI score was 5.50 [4.30-6.70]. The prevalence of a PCS score ≥20 was 45.9% [35.3;56.5]. The median PCS score was 16 [6-29]. In multivariate logistics regression, high-level catastrophizing was significantly associated with the HADS anxiety score (OR=1.35 [1.15-1.61]) and pain VAS (OR=1.04 [1.02-1.06]). In multivariate linear regression, catastrophizing was significantly associated with the HADS anxiety score (p= 0.004), pain VAS (p=0.001), HADS depression score (p=0.018) and insomnia score (p=0.034).
Conclusion: Almost half the patients with PsA were high catastrophizers. Catastrophizing is related to anxiety, pain, depression and insomnia. It may be interesting to detect catastrophizing in order to improve the care of our patients.
REFERENCES:
[1] Sullivan MJL. et al. Psychological Assessment. 1995;7(4):524–32
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3189

POS1083 PSORIATIC DISEASE – A HETEROGENOUS DISEASE WHO NEEDS A MULTIDISCIPLINARY CARE!

B. Santos[1], J. Antao[2], M. Loureiro[3], A. Barcelos[1]. [1]*Centro Hospitalar do Baixo Vouga, Rheumatology, Aveiro, Portugal*; [2]*University of Aveiro, Medical Statistic, Aveiro, Portugal*; [3]*Centro Hospitalar do Baixo Vouga, Dermatology, Aveiro, Portugal*

Background: Rheumatologists and Dermatologists usually manage Psoriatic Arthritis (PsA) and Psoriasis (PsO) separately, but early diagnosis and integrated management could achieve better outcomes with gains in quality of life of the patients. A multidisciplinary care is essential to achieve these goals.
Objectives: The aim of this study is to describe a model of integrated multidisciplinary approach for early diagnosis of PsA and the multidisciplinary management of PsA patients.
Methods: A retrospective study including patients that attended the multidisciplinary clinical from January 2019 to December 2020 was performed. Patients with PsO complaining articular symptoms and patients with articular symptoms with cutaneous lesions suspected to be PsO was referred to this clinical. Demographic, clinical data and disease activity measures were collected. Descriptive, Student's t and Fisher test and Odds Ratio were estimated.
Results: A total of 50 patients were referred to multidisciplinary clinical. Of these, 40 patients met criteria for psoriatic arthritis according to CASPAR criteria:

22 (55%) were male and median age was 49.5 ± 11.5 years. Family history of psoriasis was present in 19 (47.5%) and 7 (17.5%) had spondyloarthritis family history. Obesity and overweight were the comorbidities most found, 42.9% and 37.1%, respectively, followed by hypertension 25%, dyslipidaemia and depression 22.5% and metabolic syndrome 15%. Thirty-three patients (84.6%) were under topical treatment, 23 (59%) were under csDMARDs and 13 (32.5%) were under bDMARDs. After multidisciplinary clinical evaluation, treatment change was made - switch to another bDMARDs in 5 patients and bDMARD was started in 7 patients. All patients had a previous evaluation for infection risk assessment and 11 patients performed 9 months isoniazid for latent tuberculosis treatment.

Eleven patients (28.9%) presenting moderate to severe PASI. Thirty-one patients presenting prolonged disease duration (> 10 years) with cutaneous (74.2%) and articular (61.3%) involvement. Peripheral disease without axial involvement was present in 28 patients (90%) while the others (10%) had both axial and peripheral involvement. Severe or moderate articular disease activity (DAS28) was present in 52.6% of the patients. The most frequent extra-articular manifestation was dactylitis (23.3%) and enthesitis (19.4%). The average number of multidisciplinary clinical consultations for these patients was 2.

There was a statistically significant difference at the mean age, gender and disease duration > 10 years between patients with psoriatic disease with and without arthritis (p= 0.047; p=0.01 and p=0.03, respectively); there was no statistically significant differences in family history of psoriasis (p=0.711) and spondyloarthritis (p=0.174), nutritional status (p=0.732) and comorbidities such as diabetes mellitus (p=0.545), hypertension (p=0.404), dyslipidaemia (p=0.394) and depression (p=0.089).

In the remaining 10 patients screened, the osteoarthritis and/or tendonitis were responsible for the articular complaints in 6 patients and scalp seborrhoea and eczema were responsible for the cutaneous complaints in the rest.

Conclusion: Despite the small number of patients observed in our multidisciplinary clinical, we found that this kind of clinical care may facilitate the diagnosis of joint disease and offers a more comprehensive treatment approach for patients with both psoriasis and PsA.

REFERENCES:

[1] Luchetti MM, Benfaremo D, Campanati A, Molinelli E, Ciferri M, Cataldi S, Capeci W, Di Carlo M, Offidani AM, Salaffi F, Gabrielli A. Clinical outcomes and feasibility of the multidisciplinary management of patients with psoriatic arthritis: two-year clinical experience of a dermo-rheumatologic clinic. Clin Rheumatol. 2018 Oct;37(10):2741-2749. doi: 10.1007/s10067-018-4238-4

[2] Theodorakopoulou E, Dalamaga M, Katsimbri P, Boumpas DT, Papadavid E. How does the joint dermatology-rheumatology clinic benefit both patients and dermatologists? Dermatol Ther. 2020 May;33(3):e13283. doi: 10.1111/dth.13283

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3226

POS1084 COMPARISON OF NUMERICAL RATING SCALE (NRS) AND VISUAL ANALOGUE SCALE (VAS) IN THE PATIENT REPORTED OUTCOME MEASURES OF 3VAS AND 4VAS IN PSORIATIC ARTHRITIS

J. Day[1], W. Ye[2], W. Tillett[1], L. C. Coates[3]. [1]*Royal National Hospital for Rheumatic Diseases, Rheumatology, Bath, United Kingdom*; [2]*Oxford University, Rheumatology, Oxford, United Kingdom*; [3]*Oxford University, Nuffield Department of Orthopaedics, Oxford, United Kingdom*

Background: There is a recognised need for a feasible continuous composite measure in routine clinical care for psoriatic arthritis (PsA). Two multidimensional composite Visual Analogue Scales (VAS) have been proposed; the 3 and 4VAS[1], but there may be some advantages to using a numerical rating scale (NRS) over VAS in patient reported outcomes. VAS is a 100mm horizontal line, and the NRS a 21-point scale ranging from 0 to 10 in increments of 0.5. NRS are simple and faster to score, less susceptible to measurement error and may reduce the floor and ceiling effects, whereby patients avoid using the extremes of the scale. A previous study has demonstrated good agreement between VAS and NRS for the separate patient reported outcome measures in PsA, which correlate with disease severity and life impact.[2]

Objectives: To test the performance of NRS, compared with VAS, in the composite 3 and 4VAS scores.

Methods: Data were collected prospectively across three UK hospital trusts from 2018-2019, as part of a study assessing the use of NRS in patient reported outcome measures in PsA.[2] Patients completed the VAS and NRS for pain, arthritis, skin psoriasis, and global disease activity. The 3 VAS comprises of a physician global VAS, patient global VAS and patient skin VAS and the 4 VAS comprises of the physician global VAS, patient pain VAS, joint VAS and skin VAS. NRS and VAS versions of the patient reported measures were tested. Physician global scores were not available from the study data, therefore only the patient reported components are included. Agreement between the scales was assessed using the intraclass correlation coefficients (ICCs), with a two-way mixed absolute agreement model, and Bland-Altman plots. Spearman's rank correlation coefficients were used to assess dependency between scale scores and clinical parameters including tender and swollen joint count, PsAID12 and HAQDI.

Results: Data from 209 patients were analysed. 60.0% were male, with mean age of 51.7 years and median PsA duration of 7.0 years. Mean 3VAS score was 3.57 and the mean NRS-3VAS was 3.79, with ICC 0.98 (95% CI 0.96-0.98). Mean 4VAS was 3.71 and NRS-4VAS was 3.90 with ICC 0.98 (95% CI 0.97-0.98). Average NRS scores were slightly higher than VAS scores. The Bland-Altman plots comparing NRS and VAS for the patient-reported components of 3VAS and 4VAS are demonstrated in Figure 1. 64.1% patients reported a preference for NRS over VAS. Correlation of the 3/4VAS with PSAID, HAQ and joints counts are reported in Table 1. Visual representation of the NRS and VAS scales for 3VAS and 4VAS as histograms demonstrated that there is marginally less floor effect using NRS compared to VAS.

Conclusion: There is good agreement between VAS and NRS for the patient-reported components of 3VAS and 4VAS, supporting that VAS scores are reproducible as NRS scores. Both NRS and VAS versions of the 3 and 4VAS scales correlate with disease activity and life impact.[2] There may be advantages in testing the 3/4VAS as NRS moving forward.

REFERENCES:

[1] Tillett W et al. *J Rheumatol.* 2021; in press

[2] Ye W et al. *J Rheumatol*. 2020 Dec 1:jrheum.200928.

Table 1. Spearman's correlations of the 3 and 4 VAS scores with TJC, SJC, PsAID and HAQ

Patient Reported	TJC	SJC	PsAID	HAQDI without aids
3 VAS vas	0.51	0.44	0.88	0.62
4 VAS vas	0.54	0.47	0.89	0.65
3 VAS nrs	0.49	0.43	0.89	0.63
4 VAS nrs	0.53	0.46	0.92	0.67

Key: 3VAS; Patient global and skin VAS, 4 VAS: Patient pain, joint and skin VAS. 3 and 4 NRS; Numeric Rating Scale (NRS). TJC/ SJC: Tender/Swollen Joint count. PSAID: Psoriatic Arthritis Impact of Disease. HAQDI: Stanford Heath Assessment Questionnaire.

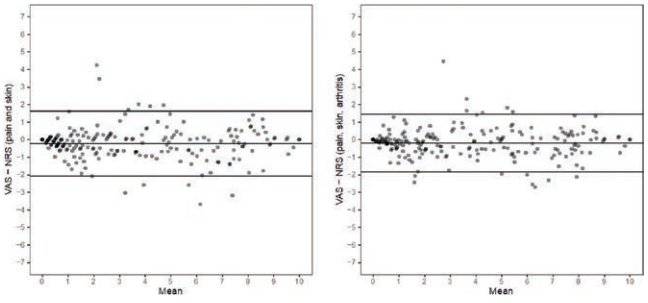


Figure 1: Bland-Altman plots comparing VAS and NRS for patient reported components of 3VAS (left) and 4VAS (right). VAS: visual analogue scale (scored 0-10); NRS: numerical rating scale (scored 0-10).

Acknowledgements: Dr Day and Dr Ye contributed equally to the development of this abstract.

Disclosure of Interests: Julia Day: None declared, Weiyu Ye: None declared, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer Inc., and UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer Inc., and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, Janssen and UCB, Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Gilead, Eli Lilly, Janssen, Medac, Novartis, Pfizer, and UCB., Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB;, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Pfizer, and Novartis.

DOI: 10.1136/annrheumdis-2021-eular.3598

POS1085 OSTEOPOROSIS IN PSORIATIC ARTHRITIS: A 5 YEAR PROSPECTIVE STUDY OF AN OUTPATIENT CLINIC COHORT

S. Brådland[1], A. Kavanaugh[2], G. Haugeberg[1,3]. [1]*Sørlandet Hospital Kristiansand, Division of Rheumatology, Dept of Internal medicine, Kristiansand, Norway*; [2]*University of California San Diego, Division of Rheumatology, Allergy, and Immunology, La Jolla, United States of America*; [3]*Norwegian University of Science and Technology, Division of Rheumatology, Trondheim, Norway*

Background: Data addressing whether patients with psoriatic arthritis (PsA) are at increased risk of osteoporosis have been inconclusive (1). Most studies have reported cross sectional data, and there is a lack of longer-term studies. We have previously reported bone density data from an outpatient PsA clinic cohort (2). Herein, we present 5-year follow up data from that same cohort.

Objectives: To explore longer-term change in bone mineral density (BMD) at femoral neck and spine (L1-4) in an outpatient PsA cohort.

Methods: 140 PsA patients were at baseline examined with dual energy x-ray absorptiometry (DXA) with measurements at femoral neck and spine (L1-4). Trained nurses performed the DXA scans. The DXA machines used at baseline (Lunar Prodigy) and at 5 year follow-up (Lunar iDXA) were stable over the measurement periods. Cross calibration using a spine phantom was performed between the two DXA machines (BMD of the old phantom in the new machine and the old phantom in the old machine, with 55 measurement over a time period of 2 weeks) had a difference of less than 1%. Demographic, disease measures and treatment data was collected at the same day or within 14 days to the date of DXA assessment. For group comparison, we used paired student t-test.

Results: After 5 years, 114 PsA patients (50.4% women) were re-examined. Baseline mean (SD) was for age 51.4 (9.4) years, BMI 28.1 (3.4) kg/m2, disease duration 9.1 (6.7) years.

Disease characteristics at baseline and follow-up presented as mean (SD) were: DAS28 3.05 (1.1) and 2.4 (0.8); CRP 4.3 (6.7) and 5.1 (12.2) mg/dl, ESR 14.9 (11.1) and 10.9 (12.9) mm/hr; mHAQ 0.40 (0.35) and 0.38 (0.37).

The proportions of patients as baseline and follow up using conventional synthetic disease modifying anti-rheumatic drugs (DMARD) were 61.4% vs. 46.5%; for biological DMARDs 37.7% vs. 48.2%; for prednisolone 5.3% vs. 10.5%, for targeted osteoporosis medication 0.9% vs. 3.5%; for calcium and vitamin-D 11.4% vs. 26.3%.

As shown in the table, no significant change in femoral neck and spine BMD and T-scores was found for the 114 patients. However for Z-scores (age and weight adjusted T-score) a significant increase was found both at femoral neck and lumbar spine. When gender was examined separately no significant reduction in bone density was found in men whereas in women a significant reduction during follow up was only found for right femoral neck BMD.

	Baseline	5 years	P value
BMD spine L1-4	1.22 (0.17)	1.23 (0.17)	0.13
T-score spine L1-4	0.21 (1.42)	0.32 (2.01)	0.42
Z-score spine L1-4	0.20 (1.32)	0.78 (2.05)	<0.001
BMD Femoral neck L	0.98 (0.14)	0.97 (0.14)	0.09
T-score Femoral neck L	-0.59 (1.15)	-0.50 (1.02)	0.14
Z-score Femoral neck L	-0.06 (1.02)	0.37 (1.04)	<0.001
BMD Femoral neck R	0.98 (0.14)	0.98 (1.16)	0.57
T-score Femoral neck R	-0.59 (1.10)	-0.52 (0.94)	0.22
Z-score Femoral neck R	-0.08 (1.02)	0.35 (0.90)	<0.001

Conclusion: No reduction in BMD at femoral neck and spine was found in our PsA outpatient clinic cohort at baseline or over 5 years follow up. Rather, we found a statistically significant increase in age adjusted bone density (Z-score) both at femoral neck and spine over time. Our data thus adds evidence that PsA patients treated in ordinary clinical practice do not seem to be at an increased risk of developing osteoporosis.

REFERENCES:

[1] Tai-li Chen, et al. Bone Mineral Density, Osteoporosis, and Fracture Risk in Adult Patients with Psoriasis and Psoriatic Arthritis: A systematic Review and Meta-Analysis of Observational Studies, J Clin Med 2020;9:3712

[2] Agnete Malm Gulati, et al. Osteoporosis in psoriatic arthritis: a cross-sectional study of an outpatient clinic population. RMD Open 2018;4:1

Acknowledgements: Research nurse Hanne Vestaby and osteoporosis nurses at -Division of Rheumatology, Kristiansand.

Disclosure of Interests: Serina Brådland: None declared, Arthur Kavanaugh: None declared, Glenn Haugeberg Grant/research support from: Unrestricted Research Grant from Pfizer Norway.

DOI: 10.1136/annrheumdis-2021-eular.4038

POS1086 DIFFERENCES IN PROINFLAMMATORY AND LIPID PROFILE BETWEEN PSORIATIC ARTHRITIS, ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS

K. Bonek[1], E. Kuca-Warnawin[2], M. Ciechomska[2], P. Głuszko[1], E. Kontny[2]. *[1]National Institute of Geriatrics, Rheumatology and Rehabilitation, Department of Rheumatology, Warszawa, Poland*; *[2]National Institute of Geriatrics, Rheumatology and Rehabilitation, Department of Pathophysiology and Immunology, Warsaw, Poland*

Background: Patients with rheumatic diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) are at increased risk of developing dyslipidaemia and premature cardiovascular disease (CVD)(1).

Objectives: To investigate the relationship between proinflammatory cytokines, microRNA, and lipid profile in patients with RA, AS, and PsA.

Methods: A group of 65 patients (RA15/ AS25/ PsA25) with high disease activity (mean DAS28 5,98 / ASDAS-CRP 3,7/ DAPSA 38,5) and 25 healthy controls (HC) were compared. Lipid profile comprised triglycerides (TG), total cholesterol(TC), low (LDL), and high-density lipoprotein (HDL). Serum concentrations of IL-6, IL-21, IL-17, TNF and osteoprotegerine (OPG) were measured by commercially available enzyme-linked immunosorbent assays. Expression of miR-233-5p,miR-92-3p,miR-485-3p,miR-10b-5p,let-7d-5p, miR-26 -a-2-3p levels in sera was normalized to miR-16a internal control. The Mann-Whitney test was applied for intergroup comparison, the correlation was assessed using Spearman's Rank test.

Results: Patients with RA revealed mixed dyslipidemia (mean values:TC196; LDL 117; HDL, 48 TG; 124 mg/dl), PsA revealed hypertriglyceridemia (TC 175; LDL 100; HDL 50; TG137 mg/dl) and in AS no specific profile was found (TC 179; LDL98; HDL55; TG103 mg/dl). Higher expression of miR-485was observed in patients with PsA (4,8-fold) and AS (5,9-fold) compared to RA and HC groups (3,1 and 1,5-fold p=0,02). Similarly, miR-26a revealed higher expression in patients with PsA (28,4-fold) and AS (21,5-fold) than in RA and HC (3,5 and 2,9-fold p<0,00). PsA patients had higher expression of miR-146b than patients with RA, AS and HC (40,9-fold vs 12,6 vs 15,7 vs 3,4-fold p=0,002) and higher miR-10b (11,7 vs 1,4 vs 4,9 vs 1,7-fold p=0,004). Patients with RA showed higher expression of let7-d than patients with PsA, AS and HC (22-fold vs 1,8 vs 2,3 vs1,9 -fold p=0,002). In PsA miR-92b expression correlated negatively with HDL levels (r=-0,62 p=0,02) and positively with fasting glucose (r=0,71 p<0,00). TG levels negatively correlated with TNF (r=-0,47 p=0,01), IL-17 (r=-0,49 p=0,01) and OPG (r=-0,51 p=0,00) serum levels. Let-7d correlated negatively with TC (r=-0,58 p=0,03). In RA IL-21 positively correlated with LDL (r=0,71 p=0,00) and TC (r=0,75 p=0,001) concentrations. TG levels correlated positively with expressions of miR-92b (r=6,9 p=0,02) and miR-26a (r=0,69 p=0,03). In AS expression of let-7d was correlated positively with HDL (r=0,41 p=0,00) and TC (r=0,45 p=0,00) levels and negatively with ASDAS-CRP (r=-0,675 p=0,02) and CRP levels (r=-0,53 p=0,01). There were no significant differences in OPG, IL-21 concentrations or miR-146b, miR-92b,miR-233 expressions.

Conclusion: Differences in proinflammatory profile in RA, PsA, and AS seem to be associated with different phenotypes of dyslipidemia. In PsA expression of miR-92b and higher levels of TNF, IL-17 and OPG are associated with altered lipid profile and hypertriglyceridemia. High activity of AS is associated with lowered expression of let-7d, possibly influencing TC and HDL levels. Therefore, measuring lipid profile in active disease might be misleading. In active RA increase of TC and LDL levels was associated with high IL-21 concentration, while hypertriglyceridemia with miR-92b and miR-26a expressions.

REFERENCES:

[1] Bonek K,et al AB0775 Peripheral joint inflammation is associated with more proatherogenic cardiovascular risk profile in patients with psoriatic arthritis. Annals of the Rheumatic Diseases 2020;79:1685-1686

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4072

Osteoarthritis

POS1087 USING LIPIDOMICS TO PREDICT PREDNISOLONE TREATMENT RESPONSE IN PATIENTS WITH INFLAMMATORY HAND OSTEOARTHRITIS: THE HOPE STUDY

M. Loef[1], T. Faquih[2], J. Von Hegedus[1], M. Ghorasaini[3], A. Ioan-Facsinay[1], F. Kroon[1], M. Giera[3], M. Kloppenburg[1,2]. *[1]Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; *[2]Leiden University Medical Center, Clinical Epidemiology, Leiden, Netherlands*; *[3]Leiden University Medical Center, Center for Proteomics and Metabolomics, Leiden, Netherlands*

Background: Lipidomics analysis has become a valuable technology for understanding patho-physiological mechanisms and may aid the identification of biomarkers of therapeutic responsiveness.

Objectives: To explore the use of lipidomics for prediction of prednisolone treatment response in patients with inflammatory hand osteoarthritis.

Methods: The Hand Osteoarthritis Prednisolone Efficacy (HOPE) study is a blinded, randomized placebo-controlled trial, that investigated the effect of prednisolone treatment in patients with painful, inflammatory hand OA, fulfilling the American College of Rheumatology criteria. The present analyses comprised only patients randomized to daily 10 mg prednisolone treatment for six weeks. Response to prednisolone treatment was defined according to the OARSI-OMERACT responder criteria at six weeks. Baseline blood samples were obtained non-fasted. Lipid species were quantified in erythrocytes with the Lipidyzer™ platform (Sciex). After pre-processing of the data, 286 lipids species were available for further analyses (nmol/mL). In addition, we used an in-house LC-MS/MS platform to analyse oxylipins in plasma, identifying 25 oxylipins (area ratios). Elastic net regularized regression was used to predict prednisolone treatment response. A 10-fold cross-validation (CV) was performed for selection of the optimal tuning parameters based on the smallest CV mean prediction error. First, a model was fit with commonly assessed patient characteristics and patient reported outcomes, measured at baseline (model 1). Second, we fitted model 2 by adding the Lipidyzer™ platform lipids to model 1. Third, we fitted model 3 by adding the oxylipins to model 1. The discriminatory

accuracy of the model was estimated by receiver operating characteristic (ROC) analyses. The area under the curve (AUC) and corresponding 95% confidence intervals (CI) were calculated using 1,000 bootstrap replications.

Results: Among the 40 patients included, 31 (78%) fulfilled the OARSI-OMERACT responder criteria. From the included general patient characteristics (Table 1), elastic net selected baseline hand function as only predictor of treatment response, with an AUC of 0.78 (95% CI 0.60;0.96) (Figure 1). In model 2, we added the 286 Lipidyzer™ platform variables to model 1. In addition to hand function, two lipids were selected: diacylglycerol(DAG)(16:0/16:0) and phosphatidylethanolamine(PE)(O-18:0/20:4), which improved the discriminatory accuracy to an AUC of 0.92 (0.83;1.02). Lastly, model 3 was fit with patient characteristics as well as oxylipins, resulting in selection of AUSCAN function and three oxylipin predictors: 9-hydroxy-octadecatrienoic acid (HOTrE), 5-hydroxy-eicosapentaenoic acid (HEPE) and 10-hydroxy-docosahexaenoic acid (HDHA), with an AUC of 0.85 (0.69;1.02).

Conclusion: The patients' lipid profile improved the discriminative accuracy of the prediction of prednisolone treatment response in patients with inflammatory hand osteoarthritis compared to prediction by commonly measured patient characteristics alone. This exploratory study suggests that lipidomics is a promising field for biomarker discovery for prediction of anti-inflammatory treatment response.

Table 1. Baseline characteristics

	All prednisolone treated n = 40	Responders n = 31 (78%)	Non-responders n = 9 (23%)
General characteristics			
Age, year	62.4 (9.3)	62.9 (9.4)	60.8 (9.4)
Sex, % women	85	84	89
BMI, kg/m^2	27.4 (4.4)	27.8 (4.2)	26.2 (5.0)
Education, % high	46	42	56
Disease duration	6.7 (7.1)	7.2 (7.4)	4.9 (5.8)
Erosive OA, %	71	74	56
Kellgren-Lawrence sum score, 0-120	35.1 (16.4)	34.1 (16.5)	37.5 (14.7)
Ultrasound synovitis sum score, 0-90	16.2 (6.6)	15.5 (6.4)	18.7 (7.2)
VAS global assessment, 0-100	52.3 (20.6)	54.2 (16.8)	45.6 (30.8)
AUSCAN pain, 0-20	11.0 (3.3)	11.3 (2.4)	10 (5.4)
AUSCAN function, 0-36	17.7 (7.6)	19.6 (6.6)	11 (7.5)

Numbers represent mean (SD) unless otherwise specified. AUSCAN = Australian/Canadian Hand Osteoarthritis Index, BMI = body mass index, VAS = visual analogue scale

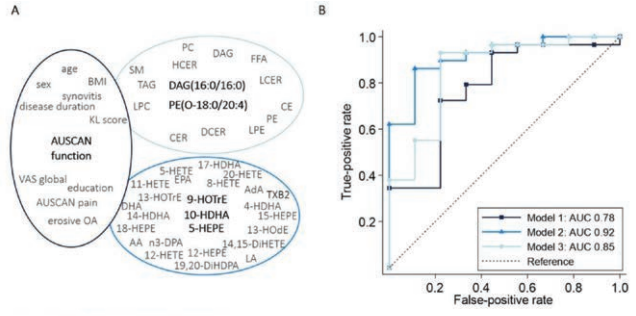


Figure 1. Prediction model characteristics

A) shows the variables included for model fitting of the three prediction models, colours correspond to the lines of the ROC curves in B). Of model 2, only the lipid classes are shown. Variables in bold font were selected in the final models. Model 1: General patient characteristics, model 2: model 1 + Lipidyzer™ platform, model 3: model 1 + oxylipin platform. Abbreviations: AUC = area under the curve, AUSCAN = Australian/Canadian Hand Osteoarthritis Index, CE = cholesteryl ester, CER = ceramide, DAG = diacylglycerol, DCER = dihydroceramide, FFA = free fatty acid, HCER = hexosylceramide, KL = Kellgren-Lawrence, LCER = lactosylceramide, (L)PC = (lyso)phosphatidylcholines , (L)PE = (lyso)phosphatidylethanolamine, OA = osteoarthritis, SM = sphingomyelin, TAG = triacylglycerol, VAS = visual analogue scale, 9-HOTrE = 9-hydroxy-octadecatrienoic acid, 5-HEPE = 5-hydroxy-eicosapentaenoic acid, 10-HDHA = 10-hydroxy-docosahexaenoic acid.

Disclosure of Interests: Marieke Loef: None declared, Tariq Faquih: None declared, Johannes von Hegedus: None declared, Mohan Ghorasaini: None declared, Andreea Ioan-Facsinay: None declared, Féline Kroon: None declared, Martin Giera Shareholder of: Pfizer, Consultant of: Boehringer Ingelheim Pharma, Margreet Kloppenburg: None declared.

DOI: 10.1136/annrheumdis-2021-eular.19

POS1088

EFFICACY OF SUBCUTANEOUS TANEZUMAB FOR THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE OR HIP: A POST-HOC SUBGROUP ANALYSIS OF PATIENTS FROM A RANDOMIZED, NSAID-CONTROLLED STUDY WITH A HISTORY OF DEPRESSION, ANXIETY, OR INSOMNIA

P. J. Mease[1], T. Mallick-Searle[2], E. Johnston[3], L. Viktrup[3], D. Menuet[4], R. Yang[5], R. J. Fountaine[6]. [1]*Swedish Medical Center & Providence St. Joseph Health and University of Washington, -, Seattle, United States of America*; [2]*Stanford Health Care, Redwood City, United States of America*; [3]*Eli Lilly and Company, -, Indianapolis, United States of America*; [4]*Pfizer SAS, Paris, France*; [5]*Pfizer Inc., New York, United States of America*; [6]*Pfizer Inc., Groton, United States of America*

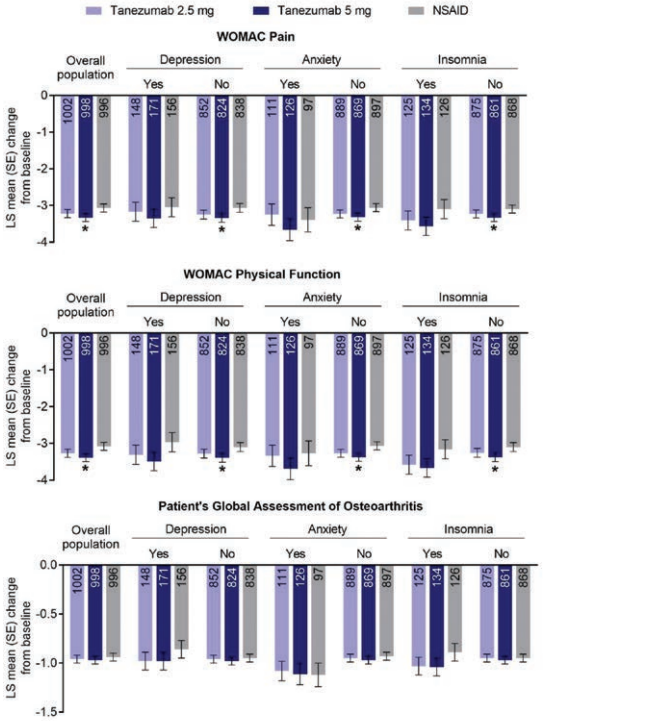
Background: Tanezumab is a monoclonal antibody directed against nerve growth factor. It is in development for the treatment of moderate to severe chronic pain associated with osteoarthritis (OA) in adult patients for whom other treatments are ineffective or not appropriate. Phase 3 clinical trials have demonstrated the efficacy of subcutaneous tanezumab versus placebo for pain and function outcomes over various timepoints. Largely similar change from baseline was demonstrated in an oral nonsteroidal anti-inflammatory drug (NSAID)-controlled study.[1,2,3,4] The efficacy of some other OA therapies can be dampened in patients with depression, anxiety, or insomnia.[5,6,7]

Objectives: A post-hoc analysis to explore the efficacy of subcutaneous tanezumab after 16 weeks treatment, as compared to oral NSAID, in patients with OA and a history of depression, anxiety, or insomnia at baseline.

Methods: Subgroup analysis of data from a randomized, double-blind, double-dummy, active-controlled phase 3 study of subcutaneous tanezumab (2.5 mg or 5 mg every 8 weeks) vs twice daily oral NSAID in patients (≥18 years) with radiographically-confirmed moderate to severe hip or knee OA (Kellgren-Lawrence grade ≥2; NCT02528188).[4] Co-primary efficacy endpoints were change from baseline to week 16 in Western Ontario and McMaster Universities OA Index (WOMAC*) Pain and Physical Function subscale scores (both ≥5/10 at randomisation; increasing score indicates increasing pain/disability), and Patient's Global Assessment of OA (PGA-OA, ≥3/5 at randomisation; increasing score indicates poorer condition). Enrolled patients had a history of inadequate pain relief with acetaminophen; inadequate pain relief with/intolerance to/contraindication to tramadol or opioids; or an unwillingness to take opioids. Patients were on a stable dose of NSAID for ≥30 days before screening. Data are presented as least squares (LS) mean change from baseline to week 16 for the whole population and for subgroups of patients with/without a history of depression, anxiety, or insomnia at baseline. Exploratory statistical analysis was conducted by analysis of covariance. P values were not adjusted for multiplicity. This exploratory post-hoc analysis was not part of the pre-specified hypothesis testing plan or included in any sample size calculations; therefore, comparisons between treatment arms or patient subgroups should be interpreted with caution.

Results: Overall, 2996 patients were randomized and received at least one dose of study treatment (subcutaneous tanezumab 2.5 mg: n=1002; subcutaneous tanezumab 5 mg: n=998; oral NSAID: n=996). In this population (comprising patients with or without a history of anxiety, depression or insomnia), all treatments were associated with notable and largely similar magnitude improvements in WOMAC Pain, WOMAC Physical Function, and PGA-OA at week 16 (Figure 1). Across treatment groups, differences in LS mean change from baseline in patients with

Figure 1: Co-primary efficacy endpoints after 16 weeks of treatment



*p<0.05 vs NSAID

LS, least squares; NSAID, nonsteroidal anti-inflammatory drug; SE, standard error; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

*©1996 Nicholas Bellamy. WOMAC® is a registered trademark of Nicholas Bellamy (CDN, EU, USA)

and without a history of depression, anxiety or insomnia ranged between 0 - 0.34 for WOMAC Pain and Physical Function and 0 - 0.19 for PGA-OA.
Conclusion: Patients with a history of depression, anxiety, or insomnia did not appear to experience dampened improvements in pain or function with tanezumab or NSAID, as compared to those without.
REFERENCES:
[1] Schnitzer T, et al. JAMA. 2019;322(1):37-48;
[2] Berenbaum F, et al. Ann Rheum Dis. 2020;79(6):800-10;
[3] Schnitzer T, et al. Semin Arthritis Rheum. 2020;50(3):387-93;
[4] Hochberg M, et al. Arthritis Rheumatol. In Press;
[5] Sharma A, et al. Open Access Rheumatol. 2016;31(8):103-13;
[6] Mallen C, et al. PLoS Med. 2017;14(4):e1002273;
[7] Campbell C, et al. Arthritis Care Res. 2015;67(10):1387-96.
Acknowledgements: Study sponsored by Pfizer and Eli Lilly and Company. Editorial support was provided by Jennifer Bodkin of Engage Scientific Solutions and funded by Pfizer and Eli Lilly and Company.
Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Eli Lilly and Company, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Galapagos, Gilead, GlaxoSmithKline, Janssen, Eli Lilly and Company, Novartis, Pfizer, Sun, UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Eli Lilly and Company, Novartis, Pfizer, Sun, UCB, Theresa Mallick-Searle Speakers bureau: Allergan, Abbvie, Eli Lilly and Company, Salix, Consultant of: Pfizer, Eli Lilly and Company, Elizabeth Johnston Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Lars Viktrup Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Dominique Menuet Employee of: Pfizer, Ruoyong Yang Employee of: Pfizer, Robert J Fountaine Shareholder of: Pfizer, Employee of: Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.166

POS1089 ASSOCIATION BETWEEN PAIN SEVERITY AND HEALTHCARE UTILIZATION IN AN OSTEOARTHRITIS POPULATION: AN 18-YEAR RETROSPECTIVE COHORT STUDY

J. Graham[1], T. Novosat[2], H. Sun[3], B. Piper[1,4], J. Boscarino[5], V. Duboski[1], M. Kern[1], E. Wright[1], R. Robinson[6], E. Casey[7], C. Beck[7], J. Hall[8], P. Schepman[9]. [1]*Geisinger, Center for Pharmacy Innovation and Outcomes, Danville, United States of America*; [2]*Geisinger, Interventional Pain, Danville, United States of America*; [3]*Geisinger, Biostatistics Core, Danville, United States of America*; [4]*Geisinger Commonwealth School of Medicine, Department of Medical Education, Scranton, United States of America*; [5]*Geisinger, Department of Population Health Sciences, Danville, United States of America*; [6]*Eli Lilly & Co., Lilly Research Labs, Indianapolis, United States of America*; [7]*Pfizer, Inc., Global Medical Affairs, New York, United States of America*; [8]*Eli Lilly & Co., Global/US Medical Affairs, Indianapolis, United States of America*; [9]*Pfizer, Inc., Global HEOR, New York, United States of America*

Background: Osteoarthritis (OA) is a common disease that varies in severity among patients. A standardized definition to classify patients into different severity levels is lacking, however, due to the disease's complex pathogenesis and presentation. Prior studies have shown associations between pain severity and higher healthcare resource utilization (HRU) and costs. We investigated an association between pain severity and higher healthcare resource utilization by examining the use of specific OA-related treatments across pain intensity levels in a large, integrated health system's OA population over an 18-year period.
Objectives: Our aim was to compare use of medications and other treatments among OA patients experiencing mild, moderate, or severe pain.
Methods: This was a retrospective study of electronic health records from 2001 to 2018 at Geisinger, an integrated health system in Pennsylvania. Patients were included with a diagnosis code for OA (ICD-9: 715.*, ICD-10 M15-19) on a problem list or encounter or an OA-specific procedure (hip or knee replacement, arthroscopy or injection). We examined pain scores (0-10 scale, with 10 being worst pain) taken after the first OA diagnosis date and defined pain episodes starting on the pain score's date and lasting for 90 days. If a new pain score was measured before 90 days elapsed, the episode was extended for an additional 90 days, with this process repeated as necessary. Each episode was categorized as mild (pain score 0-3), moderate (4-6), or severe (7-10) based on initial score, and patients could contribute multiple episodes to the analysis. Descriptive statistics were used to quantify treatment utilization during each patients' mild, moderate and severe episodes. Percentages of patients who had any use of 10 medication types (tramadol, non-tramadol opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), injectable corticosteroids, acetaminophen, salicylates, duloxetine, homeopathic medications, other topical medications, and other over-the-counter (OTC) medications were compared across pain episode types. Percentages of patients with knee or hip surgeries, spine or joint imaging procedures (x-ray, computed tomography or magnetic resonance) and consults to OA-related care (pain management, orthopedics or physical medicine and rehabilitation) were also compared. All analyses used logistic regression with p-values <0.05 considered significant.
Results: We identified 290,897 patients with OA, representing 34% of the health system population in 2018; 58% were female with mean age of 49 years and mean BMI of 30.5 kg/m2. A total of 801,144 pain episodes were defined, with 75% of patients having at least one pain score. The two most frequently occurring pain scores were 0 (17%) and 5 (13%), and pain episodes were classified as 43% mild, 32% moderate and 25% severe. Significantly higher percentages of patients used certain medication types (NSAIDs, injectable corticosteroids, non-tramadol opioid, duloxetine) in both moderate and severe pain episodes as compared to mild episodes, but other medication types were less likely to be used as pain severity increased (acetaminophen, salicylates, homeopathic medications, other OTC medications). Knee or hip surgeries, imaging, and consults to OA-related specialists were all consistently significantly more likely to occur in patients during moderate or severe pain episodes versus mild episodes (relative risk ratios of 1.76, 1.25 and 1.35 for moderate vs mild, respectively, and 2.00, 1.44 and 1.46 for severe vs mild, all p-values <0.05).
Conclusion: While pain is generally recognized to be a subjective measure that could be influenced by other unmeasured factors and can be confounded with treatment effectiveness, it is nevertheless the primary symptom of OA. It is important to understand the relationship between pain intensity and treatment utilization, and our results support an overall association between pain and utilization but provide new details on the extent to which it depends on specific utilization type.
Acknowledgements: Pfizer and Eli Lilly and Company for sponsoring this study.
Disclosure of Interests: Jove Graham Grant/research support from: I am an employee of Geisinger which received financial support from Pfizer and Eli Lilly and Company in connection with the development of this abstract, Tonia Novosat Grant/research support from: I am an employee of Geisinger which received financial support from Pfizer and Eli Lilly and Company in connection with the development of this abstract, Haiyan Sun Grant/research support from: I am an employee of Geisinger which received financial support from Pfizer and Eli Lilly and Company in connection with the development of this abstract, Brian Piper Grant/research support from: I am an employee of Geisinger which received financial support from Pfizer and Eli Lilly and Company in connection with the development of this abstract, Joseph Boscarino Grant/research support from: I am an employee of Geisinger which received financial support from Pfizer and Eli Lilly and Company in connection with the development of this abstract, Vanessa Duboski Grant/research support from: I am an employee of Geisinger which received financial support from Pfizer and Eli Lilly and Company in connection with the development of this abstract, Melissa Kern Grant/research support from: I am an employee of Geisinger which received financial support from Pfizer and Eli Lilly and Company in connection with the development of this abstract, Eric Wright Grant/research support from: I am an employee of Geisinger which received financial support from Pfizer and Eli Lilly and Company in connection with the development of this abstract, Rebecca Robinson Shareholder of: Eli Lilly & Co., Employee of: Eli Lilly & Co., Edward Casey Shareholder of: Pfizer, Inc., Paid instructor for: As an employee of Pfizer, Inc. this is part of my role., Employee of: Pfizer, Inc., Craig Beck Shareholder of: Pfizer, Inc., Employee of: Pfizer, Inc., Jerry Hall Shareholder of: Eli Lilly & Co., Employee of: Eli Lilly & Co., Patricia Schepman Shareholder of: Pfizer, Inc., Employee of: Pfizer, Inc.
DOI: 10.1136/annrheumdis-2021-eular.523

POS1090 ASSOCIATION BETWEEN ANTIBIOTIC USE AND KNEE PAIN AND FUNCTION IN OA: DATA FROM THE OSTEOARTHRITIS INITIATIVE

I. Shirinsky[1], V. Zagainova[2], V. Shirinsky[1]. [1]*Research Institute of Fundamental and Clinical Immunology, Laboratory of Clinical Immunopharmacology, Novosibirsk, Russian Federation*; [2]*Research Institute of Fundamental and Clinical Immunology, Rheumatology Unit, Novosibirsk, Russian Federation*

Background: Recently, gut dysbiosis has been linked with joint pain in osteoarthritis (OA) (1). Thus, it can be hypothesized that antibiotic use impacts symptoms of OA. To date, there have been no studies assessing association between the intake of antibiotics and clinical manifestations of knee OA.
Objectives: To evaluate association between the use of antibiotics and OA-related knee pain and function.
Methods: For the current study we used 4-year longitudinal data obtained from the Osteoarthritis Initiative (OAI) progression (n= 1390) and incidence (n = 3284) subcohorts, which are publically available at https://oai.nih.gov. The outcome variables studied were Western Ontario McMaster Osteoarthritis Index (WOMAC) pain and function subscales. To acquire information about the use of antibiotics, a medication inventory method was used. We excluded participants who used antibiotics at or 30 days prior to baseline (a "new-user" design). Antibiotic users were defined as those with at least one recorded use during first four years of the study. The participants were matched into antibiotic users/non-users pairs using genetic matching based on various demographic and clinical characteristics. The outcomes were assessed at baseline and annually until year 4. Generalized

estimating equations (GEE) were used to model the relationship between outcomes and antibiotic use by time interaction.
Results: A total of 515 new antibiotic users were matched with 515 non-users. After matching, all standardized differences of means were less than 0.05 indicating that covariates were well balanced between groups. No association between the use of antibiotic and changes in WOMAC pain and function scores was found (Table 1). No associations were also observed in multiple stratified analyses based on different duration of antibiotic use, particular classes of antibiotics, or different baseline WOMAC pain or disability levels.

Table 1. Longitudinal analysis (with treatment*time interaction) of WOMAC subcategories and antibiotics use

	β coefficient	95% CI	P value
WOMAC Pain	-0.008	(-0.08 to 0.07)	0.8
WOMAC Function	-0.014	(-0.24 to 0.21)	0.9

Conclusion: These findings do not support the effects of antibiotics on knee OA pain or disability. More research is needed on the role of microbiota and its modulation in OA.
REFERENCES:
[1] Boer, C.G., Radjabzadeh, D., Medina-Gomez, C. et al. Intestinal microbiome composition and its relation to joint pain and inflammation. Nat Commun 10, 4881 (2019). https://doi.org/10.1038/s41467-019-12873-4
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.963

POS1091 KNEE JOINT DISTRACTION RESULTS IN MRI CARTILAGE THICKNESS INCREASE UP TO TEN YEARS AFTER TREATMENT

M. Jansen[1], S. Mastbergen[1], T. D. Turmezei[2,3], J. W. Mackay[3,4], F. Lafeber[1]. *[1]UMC Utrecht, Department of Rheumatology & Clinical Immunology, Utrecht, Netherlands*; *[2]Norfolk & Norwich University Hospital, Department of Radiology, Norwich, United Kingdom*; *[3]University of East Anglia, Norwich Medical School, Norwich, United Kingdom*; *[4]University of Cambridge, Department of Radiology, Cambridge, United Kingdom*

Background: Knee joint distraction (KJD) is a joint-preserving treatment option for younger (age <65 years) knee osteoarthritis (OA) patients. It has shown clinical improvement for up to nine years after treatment. Radiographs and MRI scans have previously shown cartilage regeneration activity, especially in the first two years after treatment. However, MRIs have not been evaluated more than five years after this treatment.
Objectives: To evaluate MRI cartilage thickness up to ten years after KJD treatment.
Methods: Patients (n=20) with end-stage knee OA, indicated for total knee arthroplasty (TKA) but <60 years old, were treated with KJD. 3T MRIs with 3D spoiled gradient recalled imaging sequence with fat suppression (SPGR-fs) were acquired before and one, two, five, seven and ten years after surgical treatment. Stradview v6.0 was used for semi-automatic cartilage segmentation; wxRegSurf v18 was used for surface registration. MATLAB R2020a and the SurfStat MATLAB package were used for data analysis and visualization. For changes over time, linear mixed models were used. Two separate linear regression models were used to show the influence of baseline Kellgren-Lawrence grade and sex on the changes over time. Statistical significance was calculated with statistical parametric mapping; a p-value <0.05 was considered statistically significant. Since KJD has previously shown significant results mostly in the patients' most affected compartment (MAC), patients were separated in two groups based on whether their MAC was the medial or lateral compartment.
Results: The MAC was predominantly the medial side (medial MAC n=18; lateral n=2). The 18 patients with a medial MAC all had MRI scans at baseline, one and two years after treatment. After two years, some patients were lost to follow-up, decreasing data availability at five (n=15), seven (n=11) and ten years (n=7). Figure 1 (top) shows the average cartilage thickness at the different time points for all medial MAC patients together. One and two years after treatment the cartilage in the medial weight-bearing region was on average thicker than before treatment. While from five years after treatment the cartilage thickness gradually decreased, even at ten years the medial cartilage thickness seemed slightly higher than pre-treatment. Figure 1 (bottom) shows cartilage thickness changes compared to baseline for patients with a medial MAC. Patients with a lateral MAC showed a similar pattern, with the biggest changes showing on the lateral side. As indicated by the dark blue areas, the medial femoral cartilage thickness increase, which was up to 0.5 mm after one year and 0.6 mm after two years, was largely statistically significant at both these time points. While the medial tibia showed an increase of up to 0.5 mm at these time points as well, this was not statistically significant at two years. Surprisingly, long-term results showed areas of the lateral (less affected) compartment were significantly thicker, up to 0.7 mm, compared to pre-treatment in both the femur and tibia compared to baseline. Kellgren-Lawrence grade and sex were shown to influence the changes, albeit not statistically significantly. Patients with a higher Kellgren-Lawrence grade and male sex showed a higher short-term (one and two year) but a lower long-term (seven and ten year) cartilage thickness increase.
Conclusion: KJD treatment results in significant short-term cartilage regeneration in the most affected compartment. While after two years this initial gain in cartilage thickness is gradually lost, likely as a result of natural progression, even ten years after treatment the cartilage is thicker than before treatment. In the less affected compartment, a delayed cartilage response seems to take place, with significantly increased cartilage thickness in the long term. In conclusion, in these young OA patients indicated for TKA, KJD results in femoral and tibial cartilaginous tissue regeneration both short- and long-term and in both sides of the joint.

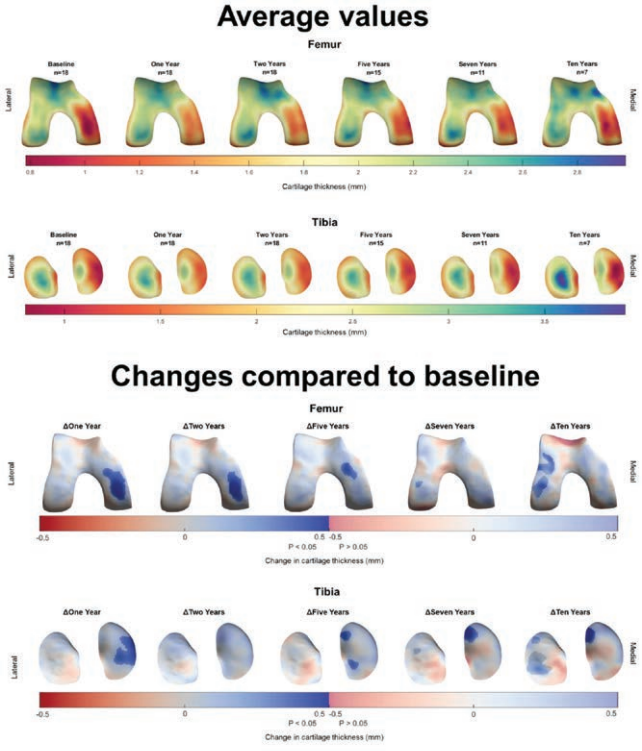


Figure 1: Top: average cartilage thickness of all patients whose medial compartment was the most affected, at baseline (n=18) and one (n=18), two (n=18), five (n=15), seven (n=11) and ten (n=7) years after treatment with knee joint distraction. The color range is based on the minimum and maximum average values of the femur (0.78-3.00) and tibia (0.80-3.92) separately. Bottom: change in cartilage thickness compared to baseline, for all patients whose medial compartment was the most affected, after one (n=18), two (n=18), five (n=15), seven (n=11) and ten (n=7) years after treatment with knee joint distraction. Statistically significant changes are indicated by the darker color map (p<0.05) while non-significant areas are shown with faded colors (p>0.05). Blue indicates an increase and red a decrease in cartilage thickness compared to baseline. All results are viewed on average right femur and tibia articular cartilage surfaces.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1321

POS1092 SUBCHONDRAL BONE NORMALIZATION AFTER KNEE JOINT DISTRACTION TREATMENT AS MEASURED WITH CT

M. Jansen[1], A. Ooms[1], T. D. Turmezei[2,3], J. W. Mackay[3,4], S. Mastbergen[1], F. Lafeber[1]. *[1]UMC Utrecht, Department of Rheumatology & Clinical Immunology, Utrecht, Netherlands*; *[2]Norfolk & Norwich University Hospital, Department of Radiology, Norwich, United Kingdom*; *[3]University of East Anglia, Norwich Medical School, Norwich, United Kingdom*; *[4]University of Cambridge, Department of Radiology, Cambridge, United Kingdom*

Background: In addition to cartilage degeneration, knee osteoarthritis (OA) causes bone changes, including cortical bone thickening, subchondral bone density decrease, and bone shape changes as a result of widening and flattening condyles and osteophyte formation. Knee joint distraction (KJD) is a joint-preserving treatment for younger (<65 years) knee OA patients that has been shown to reverse OA cartilage degradation. On radiographs, KJD showed a decrease in subchondral bone density and an increase in osteophyte formation. However, these bone changes have never been evaluated with a 3D imaging technique.
Objectives: To evaluate cortical bone thickness, subchondral trabecular bone density, and bone shape on CT scans before and one year after KJD treatment.
Methods: 19 KJD patients were included in an extended imaging protocol, undergoing a CT scan before and one year after treatment. Stradview v6.0 was used for semi-automatic tibia and femur segmentation from axial thin-slice

(0.45mm) CT scans. Cortical bone thickness (mm) and trabecular bone density (Hounsfield units, HU) were measured with an automated algorithm. Osteophytes were excluded. Afterwards, wxRegSurf v18 was used for surface registration. Registration data was used for bone shape measurements. MATLAB R2020a and the SurfStat MATLAB package were used for data analysis and visualization. Two-tailed F-tests were used to calculate changes over time. Two separate linear regression models were used to show the influence of baseline Kellgren-Lawrence grade and sex on the changes over time. Statistical significance was calculated with statistical parametric mapping; a p-value <0.05 was considered statistically significant. Bone shape changes were explored visually using vertex by vertex displacements between baseline and follow-up. Patients were separated into two groups based on whether their most affected compartment (MAC) was medial or lateral. Only patients with axial CT scans at both time points available for analysis were included for evaluation.

Results: 3 Patients did not have complete CTs and in 1 patient the imaged femur was too short, leaving 16 patients for tibial analyses and 15 patients for femoral analyses. The MAC was predominantly the medial side (medial MAC n=14; lateral n=2). Before treatment, the MAC cortical bone was compared to the rest of the joint (Figure 1). One year after treatment, MAC cortical thickness decreased, although this decrease of up to approximately 0.25 mm was not statistically significant. The trabecular bone density was also higher before treatment in the MAC, and a decrease was seen throughout the entire joint, although statistically significant only for small areas on mostly the MAC where this decrease was up to approximately 80 HU (Figure 1). Female patients and patients with a higher Kellgren-Lawrence grade showed a somewhat larger decrease in cortical bone thickness. Trabecular density decreased less for patients with a higher Kellgren-Lawrence grade, and female patients showed a higher density decrease interiorly while male patients showed a higher decrease exteriorly. None of this was statistically significant. The central areas of both compartments showed an outward shape change, while the outer ring showed inward changes.

Conclusion: MAC cortical bone thickness shows a partial decrease after KJD. Trabecular bone density decreased on both sides of the joint, likely as a direct result of the bicompartmental unloading. For both subchondral bone parameters, MAC values became more similar to the LAC, indicating (partial) subchondral bone normalization in the most affected parts of the joint. The bone shape changes may indicate a reversal of typical OA changes, although the inward difference that was seen on the outer edges may be a result of osteophyte-related changes that might have affected the bone segmentation. In conclusion, KJD treatment shows subchondral bone normalization in the first year after treatment, and longer follow-up might show whether these changes are a temporary result of joint unloading or indicate more prolonged bone changes.

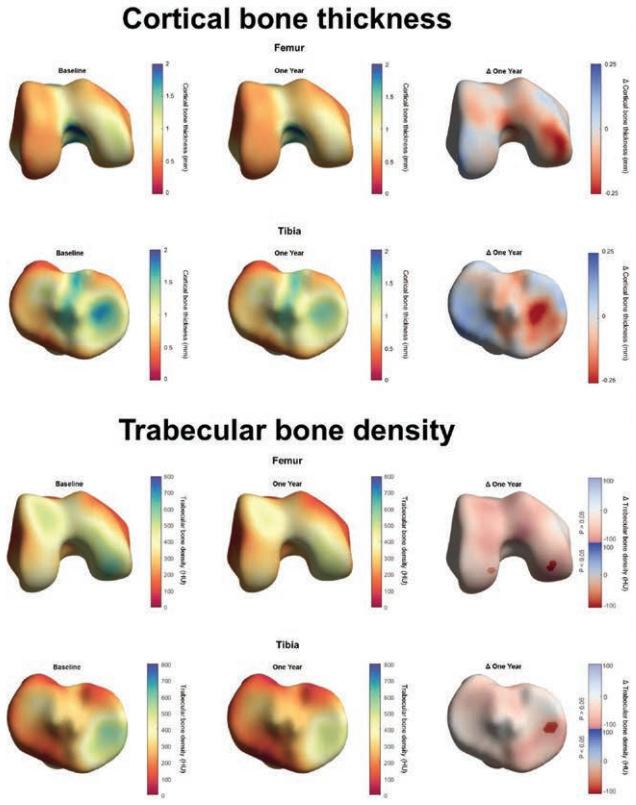


Figure 1: The average cortical bone thickness (top) and trabecular bone density (bottom) of all patients whose medial compartment was the most affected at baseline (left) and one year after treatment with knee joint distraction (mid). On the right a difference map between the two time points is shown; blue indicates an increase and red a decrease. Statistically significant changes are indicated by the darker color map (p<0.05) while non-significant areas are shown with faded colors (p>0.05) for the trabecular bone density; the cortical bone thickness did not show statistically significant differences.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1329

POS1093

KNEE AND HIP OSTEOARTHRITIS ARE ASSOCIATED WITH SUBCLINICAL AND MANIFEST ATHEROSCLEROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Barguil Macedo[1], V. M. Ostrovski Souza Santos[1], R. M. Pereira[1], R. Fuller[1].
[1]*University of Sao Paulo Faculty of Medicine, Rheumatology, Sao Paulo, Brazil*

Background: An association between osteoarthritis (OA) and atherosclerosis (AT) has long been suggested, with its plausibility based on several guessed commonalities, from shared risk factors to overlapping molecular pathways, given that both conditions represent a state of chronic low-grade inflammation. However, meta-analyses of the impact of OA on hard cardiovascular (CV) endpoints have displayed conflicting results. Those disparate results probably stemmed from the heterogeneous OA population adjoined, as it has been postulated that OA denotes not a single, but a group of diseases with particular pathogenic mechanisms. Also, CV mortality may capture just the extreme of a continuum of atheromatous burden, and miss earlier subclinical disease.

Objectives: In order to discern a more refined association between OA and AT, a systematic review and a meta-analysis of studies that focused on OA of weight-bearing joints (i.e., hip and knee) were performed, and the results stratified by clinical and subclinical AT.

Methods: A search on PubMed, Web of Science, LILACS, and SciELO from inception until August 2020, was done using the MeSH search terms "osteoarthritis", "aorta", "carotid", "intima-media thickness", "coronary artery disease", "atherosclerosis", "cardiovascular disease", and "death". To appraise the quality of the studies, we applied the NewCastle-Ottawa scale. To assess for heterogeneity, I^2 was used. A random-fixed effect model was adopted, and outliers were excluded when detected. Publication bias was ascertained qualitatively by funnel plot, and quantitatively by Egger regression test. Analyses were performed on RStudio version 1.3.1093.

Results: The search retrieved 1335 citations, of which 168 were screened for abstract reading. From those, 127 were selected for full-text reading. After exclusion of duplicates and out of scope aricles, a total of 23 studies, comprising 151,187 individuals with OA and 287,444 controls, were included on the narrative synthesis, and 17 on the meta-analysis. All but one study were deemed as of fair or good quality. Fifteen studies found a positive association between OA and AT, the remaining 8 did not reach statistical significance. Four studies subdivided the OA patients by gender, and in half of those a positive association was found exclusively on females. Thirteen studies worked with a subclinical definition of AT, 1 included both subclinical and manifest disease, and the remainder included only manifest disease. Hip and knee OA increased the risk for both subclinical AT (OR 1.15, 95% CI 1.01-1.31, Figure 1A), and CV disease (OR 1.13, 95% CI 1.05-1.22, Figure 1B), but not for CV death (OR 1.08, 95% CI 0.99-1.19).

Conclusion: Hip and knee OA are associated with AT. This may have practical implications on the management of OA patients, as a more intensive control of traditional CV risk factors may be advised.

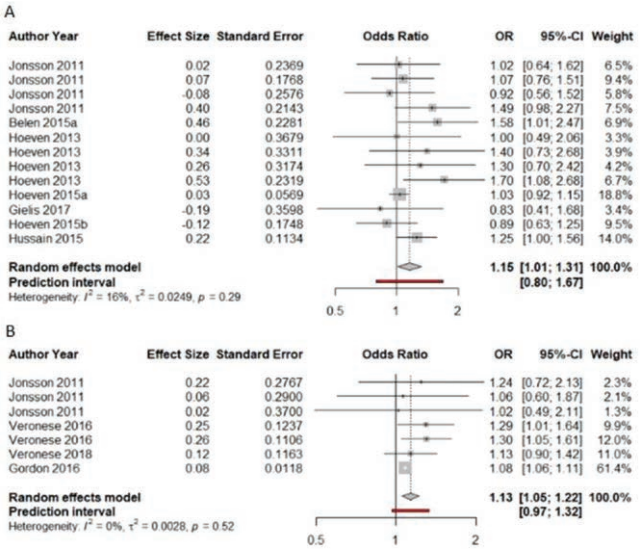


Figure 1. Forest plots showcasing the association between hip and knee OA and subclinical AT (A) and CV disease (B).

Acknowledgements: Statistical analysis was performed under the supervision of Danielle Daffre Carvalho.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1453

POS1094 SYNOVITIS IS FACTOR OF OSTEOARTHRITIS KNEE PROGRESSION IN PATIENTS WITH LESS THAN 5 YEARS OF DISEASE DURATION

L. Alekseeva[1,2], N. Kashevarova[1], E. Taskina[1], D. Kusevich[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of osteoarthritis, Moscow, Russian Federation*; [2]*Russian Medical Academy of Continuous Professional Education, Rheumatology, Moscow, Russian Federation*

Background: There are many studies about investigation of risk factors (RF) of knee osteoarthritis (OA) radiologic progression. Especially, in patients with small disease duration. At the moment, there are ambivalent of results of previous studies, lead to uncertain role of synovitis.
Objectives: The aim of study is to investigate relationship between knee OA synovitis and progression risk in patients with small disease duration during a follow-up period of 5 years.
Methods: Eligible patients had knee OA based on ACR criteria with x-ray confirmation; baseline (BL) disease duration less than 5 years. Patients were evaluated at BL and at 5-year follow-up, using the questionnaires, clinical examination, knee joints pain by visual analog scale (VAS), musculoskeletal ultrasound and X-ray. Unadjusted p-values are presented.
Results: Among 52 adults with knee OA (mean age ± standard deviation, 59.11 ± 8.95 years; 100% female) had the proportion of patients at BL 42.3% (n=22), 46.2 % (n=24), 11.5% (n=6) by disease stage 1,2 and 3, respectively. Patients were categorized into 2 groups by progression during 5 years from BL based on changes of radiological stage. After 5-years follow-up period the progression of knee OA was established in 14 patients (1 group) and in 38 patients (2 group) the progression by radiological stage was absent. BL patients' characteristics were similar across 1st and 2nd groups: mean age 58.29±7.68 vs 56.05±8.74, p>0.05; disease duration 3.43±1.34 vs 3.47±1.33, p>0.05. Individuals with knee OA progression had worse knee joints pain during walking (60.36±18.33 vs 48.71±17.81, p=0.043), higher body mass index (BMI) (34.45±4.60 vs 28.92±4.92 kg/m^2, p=0.001), higher frequency of knee synovitis by clinical examination (42.9% vs 10.5%, RR=4.07; 95%CI (1,3-12,3), p=0.01) and by musculoskeletal ultrasound (57.1% vs 18.4%, RR=3.1; 95%CI (1.38-6.96), p=0.009). At 5-years follow-up knee pain was significantly greater for 1st group (69.64±18,49 vs 55.76±12.76, p = 0.003), higher BMI (35.74±5.83 vs 30.64±4.64, p = 0.002), also higher frequency of knee synovitis by clinical examination (57.1% vs 10.5%, RR = 5.4 (95%CI 1.9-15.2), p=0.001) and by musculoskeletal ultrasound (50% vs 13.2%, RR=3.8 (95%CI 1.4-10.0), p=0.009). Spearman correlation coefficients between radiologic stage and OA progression factors were indicated: between radiologic stage and knee pain during walking (r = 0.34, p<0.05), BMI (r = 0.46, p<0.01), knee synovitis by musculoskeletal ultrasound (r = 0.41, p<0.01). Multivariate (discriminant) analysis was determined that synovitis is a significant predictor of radiographic progression (p < 0.05).
Conclusion: The proportion of patients with knee synovitis by clinical examination and musculoskeletal ultrasound data increased by 5-year follow-up from BL. Synovitis is a significant predictor of radiographic progression of knee OA in patients with small disease duration.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1577

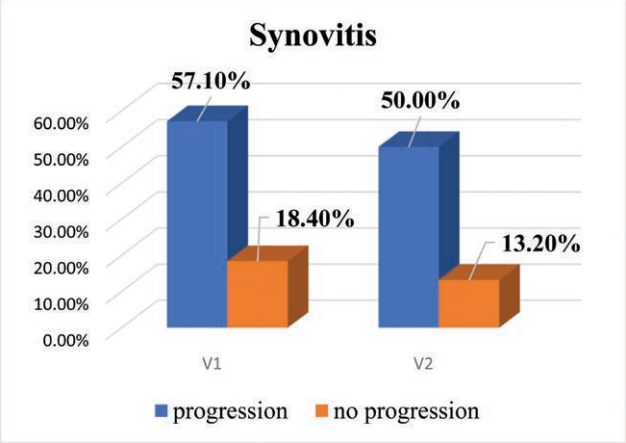


Figure 1.

POS1095 FOOD SOURCES OF DIETARY FIBRE AND RISK OF TOTAL KNEE REPLACEMENT RELATED TO SEVERE OSTEOARTHRITIS, THE SINGAPORE CHINESE HEALTH STUDY

Y.Y. Leung[1], A. Jin2, K. Tan[3], L. W. Ang[4], J. M. Yuan[5,6], W. P. Koh[2,7]. [1]*Duke-NUS Medical School, Health Services and Systems Research, Singapore, Singapore*; [1]*Duke-NUS Medical School, Health Services and Systems Research, Singapore, Singapore*; [3]*Ministry of Health, Policy, Research and Evaluation Division, Singapore, Singapore*; [4]*Ministry of Health, Public Health Group, Singapore, Singapore*; [5]*University of Pittsburgh, Division of Cancer Control and Population Sciences, UPMC Hillman Cancer Centre, Pittsburgh, United States of America*; [6]*University of Pittsburgh, Department of Epidemiology, Graduate School of Public Health, Pittsburgh, United States of America*; [7]*National University of Singapore, Saw Swee Hock School of Public Health, Singapore, Singapore*

Background: Although fibre intake was inversely associated with the risk of symptomatic knee osteoarthritis (KOA) in a US study, this association was partially confounded by lower body mass index (BMI) in those with higher fibre intake.
Objectives: We evaluated the association between fibre intake and its food sources, and the risk of total knee replacement (TKR) due to severe KOA.
Methods: We used data from the Singapore Chinese Health Study, a prospective cohort study that recruited 63,257 participants aged 45-74 years from 1993 to 1998. At baseline, we assessed diet using a validated 165-item semi-quantitative food frequency questionnaire, together with BMI and lifestyle factors. Incident TKR cases were identified via record linkage with nationwide hospital discharge database through 2017. We used multivariable Cox regression models to compute hazard ratio (HR) and the corresponding 95% confidence interval (CI) for risk of TKR.
Results: There were 2,816 cases of incident TKR due to severe KOA. Total fibre intake at baseline was not associated with risk of TKR after adjustment for confounders. Among the food sources of fibre, higher intake of legumes was associated with lower risk of TKR in dose-dependent manner; compared with those having the lowest quartile intake, HR (95% CI) was 0.86 (0.76, 0.96) for the highest quartile (*p* for trend = 0.004). This association was consistent after including BMI in the model, and homogenous across BMI categories. The consumption of other fibre sources, namely grain products, nuts and seeds, soy food, fruits and vegetables, was not associated with risk of TKR.
Conclusion: Intake of legumes, but not total fibre, was associated with a reduced risk of TKR. Further research is needed to replicate our findings, and to evaluate possible biological mechanisms that could explain the effect of dietary legumes in pathogenesis or progression of KOA.

Table 1. Hazard ratios (95% confidence intervals) for risk of total knee replacement according to intake of fibre (only shown total fibre and legumes): The Singapore Chinese Health Study (1993-2017).

Quartiles of energy-adjusted food intake	Q1	Q2	Q3	Q4	*p* for trend [1]
Total fibre					
Median, g/day	8.55	9.43	12.19	17.70	
Cases/ person-years	528/ 275,050	712/ 280,456	767/ 284,394	809/ 287,955	
Multivariate Model 1	1.00	1.08 (0.96, 1.21)	1.12 (1.00, 1.26)	1.18 (1.05, 1.32)	0.003
Multivariate Model 2	1.00	1.06 (0.95, 1.19)	1.09 (0.97, 1.22)	1.11 (0.99, 1.24)	0.088
Legumes					
Median, g/day	0.11	0.43	2.11	7.01	
Cases/ person-years	638/ 280,170	754/ 278,001	756/ 280,407	668/ 289,275	
Multivariate Model 1	1.00	0.97 (0.87, 1.09)	0.95 (0.84, 1.06)	0.84 (0.76, 0.94)	<0.001
Multivariate Model 2	1.00	0.98 (0.87, 1.09)	0.94 (0.84, 1.06)	0.86 (0.77, 0.96)	0.004
Multivariate Model 3	1.00	0.98 (0.87, 1.09)	0.95 (0.84, 1.06)	0.86 (0.76, 0.96)	0.004

[1]Linear trend was tested by assigning to participants the median value of the quartile and treating this as a continuous variable. [2] The grain products included noodles and pasta, rice, bread and pancakes, breakfast cereals, biscuits and crackers.Multivariate model 1: adjusted for age at interview, sex, year of interview, total energy intake, dialect, education levelMultivariate model 2: model 1 plus BMI, sitting duration, sleep, physical activity, smoking, history of hypertension, diabetes, coronary artery disease and stroke.Multivariate model 3: model 2 plus grain products, legumes, nuts and seeds, soy food, fruits and vegetables.Q = quartile

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1707

POS1096

THE EFFECT OF ONE DRY NEEDLING SESSION ON PAIN AND CENTRAL PAIN PROCESSING IN PATIENTS WITH KNEE OSTEOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

S. Vervullens[1], L. Meert[1], I. Baert[1], N. Delrue[2], K. Heusdens[3], A. Hallemans[1], T. Van Criekinge[1,4], R. Smeets[5,6], K. De Meulemeester[7] on behalf of MOVANT (MOvement ANTwerp) of the University of Antwerp. *[1]Antwerp University, Rehabilitation Sciences and Physiotherapy, Antwerp, Belgium*; *[2]Dry Needling Ghent, Rehabilitation Sciences, Ghent, Belgium*; *[3]University Hospital of Antwerp, Orthopedics, Antwerp, Belgium*; *[4]KULeuven, Rehabilitation Sciences, Bruges, Belgium*; *[5]Maastricht University, Rehabilitation Medicine, Maastricht, Netherlands*; *[6]University Hospital of Maastricht, Rehabilitation Medicine, Maastricht, Netherlands*; *[7]Ghent University, Rehabilitation Sciences, Ghent, Belgium*

Background: Osteoarthritis (OA) is the leading cause of chronic disability in the elderly[1,2]. Abnormal central pain processing (CPP) is present in around 30% of the knee OA patients[3] and can be partly induced by peripheral nociception through long term potentiation[4]. An attempt to resolve abnormal CPP can be to eliminate this nociception[5]. Myofascial trigger points (MTrPs) are often present in knee OA[6], can lead to nociception[7] and therefore abnormal CPP if prolonged present[8]. These are usually defined as hypersensitive tender spots within taut bands of a muscle[9]. Additionally, both MTrPs and knee OA can induce disturbed motor control, increased co-antagonist activation and modified gait pattern[10,11]. Dry needling (DN) is often used to deactivate the MTrP and thus resolve the source of nociception, which normally results in reducing pain and restoring muscle dysfunction[12]. However, studies about the effect of DN on CPP and other outcomes than pain are very limiting. Therefore, more high-quality studies concerning DN and its effects on CPP, muscle features and gait are needed[13,14].
Objectives: The aim of this randomized controlled trial is to assess the effect of one DN session compared to one sham needling (SN) session on pain (processing), muscle activity and gait in patients with knee OA.
Methods: 61 patients participated of which 31 were allocated to the DN and 30 to the SN group. Each patient underwent one treatment session. Primary outcomes were pain intensity, measured with questionnaires; and CPP, measured with quantitative sensory testing. Secondary outcomes included muscle co-activation, measured with electromyography; and spatiotemporal parameters, measured with gait analysis. Patients were assessed at baseline, 15 minutes (post 1) and 3 days after intervention (post2- only for the outcome pain). Linear mixed models was used to identify the possible differences over time between the two therapy modalities.
Results: The following significant within group differences were observed: decreased pain, stride- and step time and increased widespread pain pressure threshold and step length. A significant between group difference of the conditioned pain modulation score was found, whereas the SN group showed a decrease in difference between the pain pressure threshold scores (with and without conditioning stimulus) and the DN group remained stable. No other significant between or within group differences were detected. However, if we compared both interventions, the change over time for the visual analogue scale (VAS) behaved different in the DN ($p<0.05$, post 2 - baseline) and SN group ($p<0.05$, post 1 - baseline and post 2 - post 1).
Conclusion: One DN session has no larger effect on all outcome measurements compared to SN. Both therapies seem to be useful to improve pain and widespread pain pressure threshold in short term, however the improvement of pain differs in the groups. Although improvements in some spatiotemporal parameters were observed, it is uncertain they are of clinical relevance or related to treatment. More research is necessary to reveal the ideal number of sessions of DN to improve outcomes and to reveal the effect of DN compared to no treatment, as SN could have hide the real treatment effect.

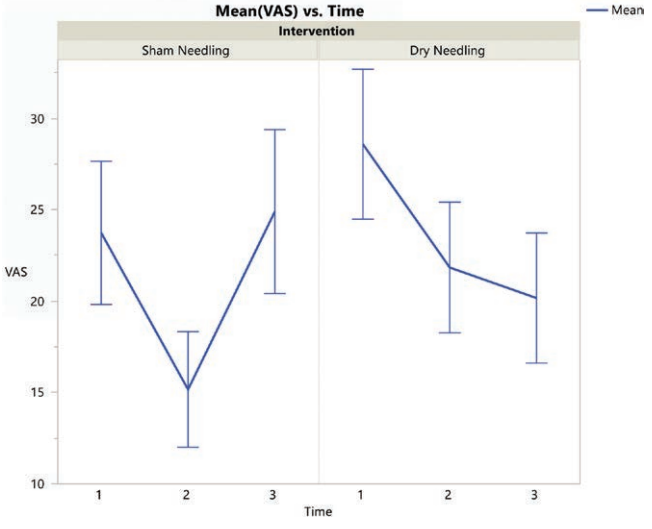


Figure 1. Mean and standard error of VAS scores over time in the DN and SN group

REFERENCES:
[1] Reginster, J. Y. *Rheumatol. Oxf.* 41 Supp 1, 3–6 (2002)
[2] Lespasio, M. J. *et al. Perm J* 21, 16–183 (2017)
[3] Lluch, E. *et al. Eur J Pain* 18, 1367–75 (2014)
[4] Mease, P. J. *et al. J. Rheumatol.* 38, 1546–1551 (2011)
[5] Nijs, J. *et al. Expert Opin Pharmacother* 15, 1671–83 (2014)
[6] Bajaj, P. *et al. J. Musculoskelet. Pain* 9, 17–33 (2001)
[7] Jafri, M. S. *Int. Sch. Res. Not.* 2014, (2014)
[8] Cagnie, B. *et al. Curr Pain Headache Rep* 17, 348 (2013)
[9] Borg-Stein, J. *et al. Arch. Phys. Med. Rehabil.* 83, S40–S47 (2002)
[10] Childs, J. D. *et al. Clin. Biomech.* 19, 44–9 (2004)
[11] Ibarra, J. M. *et al. J Pain* 12, 1282–8 (2011)
[12] Rahou-El-Bachiri, Y. *et al. J. Clin. Med.* 9, (2020)
[13] Stieven, F. F. *et al. J. Manipulative Physiol. Ther.* (2021)
[14] Dor, A. *et al. J Bodyw Mov Ther* 21, 642–647 (2017)

Acknowledgements: I like to thank and acknowledge the contribution of the other executive researchers (Lise Brosens, Ayoub El Bouchaoni, Ben Ceusters, Sven Huybrechts and Mathias Van Loon), the participated dry needling therapists, Dry Needling Ghent, Trigger and the University Hospital of Antwerp.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2108

POS1097

TREATMENT KNOWLEDGE AND PREFERENCES FOR BLACK PEOPLE WITH HIP AND KNEE OSTEOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

C. Brantner[1], D. Pearce-Fisher[1], C. Moezinia[1], H. Tornberg[1], J. Fitzgerald[2,3], M. Parks[4,5], P. Sculco[4,5], C. Kahlenberg[4], C. Mensah[1], A. Premkuar[4], N. Williams[6], M. Demetres[7], S. Goodman[8,9]. *[1]Hospital for Special Surgery, Medicine, New York, United States of America*; *[2]Ronald Reagan UCLA Medical Center, Medicine, Los Angeles, United States of America*; *[3]UCLA Santa Monica Medical Center, Medicine, Santa Monica, United States of America*; *[4]Hospital for Special Surgery, Orthopedic Surgery, New York, United States of America*; *[5]Weill Cornell Medicine, Orthopedic Surgery, New York, United States of America*; *[6]Weill Cornell Medicine, Population Health Sciences, New York, United States of America*; *[7]Weill Cornell Medicine, Information Technologies and Services - Library, New York, United States of America*; *[8]Hospital for Special Surgery, Rheumatology, New York, United States of America*; *[9]Weill Cornell Medicine, Rheumatology, New York, United States of America*

Background: Black people are less likely to undergo total joint arthroplasties, despite reporting more severe symptoms. (1) While racial disparities exist in treatment utilization for osteoarthritis, comprehensive studies of the treatment preferences of Black people have not been conducted.
Objectives: The purpose of this manuscript is to systematically review the literature and identify Black osteoarthritis patients' treatment preferences to understand how they may contribute to racial differences in the utilization of different treatment options.
Methods: Searches ran on April 8, 2019 and April 7, 2020 in the following databases: Ovid MEDLINE (ALL - 1946 to Present); Ovid EMBASE (1974 to present); and The Cochrane Library (Wiley). Using the Patient/Population-Intervention-Comparison/Comparator-Outcome (PICO) format, our population of interest was Black people with hip and/or knee osteoarthritis, our intervention was preferences and opinions about treatment options for osteoarthritis, our comparator was white people with hip and/or knee osteoarthritis, and our outcome was preferences of osteoarthritis therapies. The protocol was registered under the PROSPERO international register, and the Preferred Reporting Items of Systematic reviews and Meta-Analyses (PRISMA) guidelines were followed.
Results: Searches across the chosen databases retrieved 10,894 studies after de-duplication, 182 full text, and 31 selected for inclusion in this review. Black people were less likely to use NSAIDs or narcotic analgesics compared to white people. (Figure 1) Black people were more likely than white people to use spirituality and prayer, as well as topical treatments. Utilization of meditation, supplement/vitamin use, and hot/cold treatments was not significantly different between groups. Black people were less willing than white people to consider or undergo joint replacements, even if the procedure was needed and recommended by a physician.
Conclusion: Racial differences persist in OA care across the spectrum of options. Future interventions should focus on providing accessible information surrounding treatment options and targeting perceptions of the importance of joint health.

REFERENCES:

[1] Suarez-Almazor ME, Souchek J, Kelly PA, et al. Ethnic Variation in Knee Replacement: Patient Preferences or Uninformed Disparity? *Arch Intern Med*. 2005;165(10):1117-1124. doi:10.1001/archinte.165.10.1117

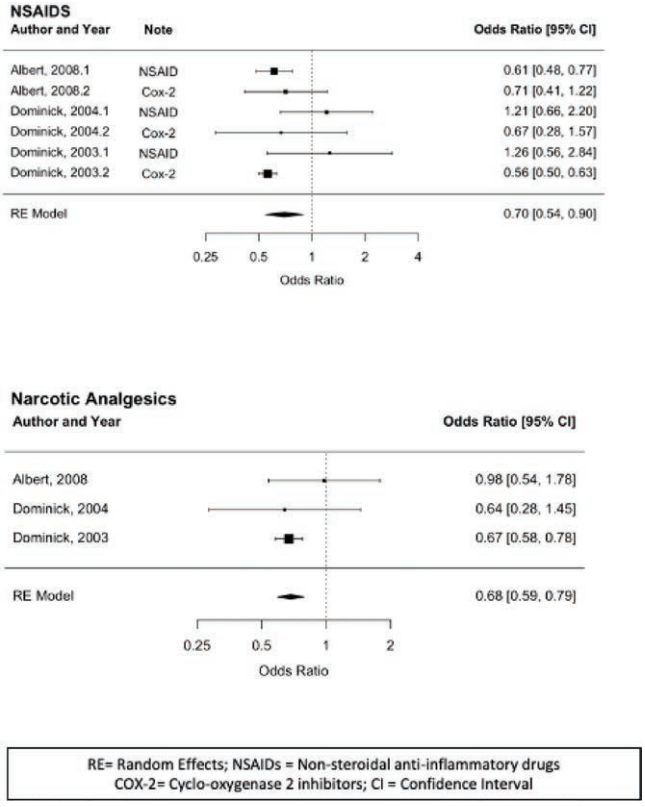


Figure 1. Meta-analysis describing the odds ratios of Black people using NSAIDs and Narcotic Analgesics compared to white people

Disclosure of Interests: Collin Brantner: None declared, Diyu Pearce-Fisher: None declared, Carine Moezinia: None declared, Haley Tornberg: None declared, John FitzGerald: None declared, Michael Parks Consultant of: Zimmer Biomet, Peter Sculco Consultant of: EOS Imaging, Intellijoint Surgical, DePuy Synthes, Lima Corporate, Cynthia Kahlenberg: None declared, Curtis Mensah: None declared, Ajay Premkuar: None declared, Nicholas Williams: None declared, Michelle Demetres: None declared, Susan Goodman Consultant of: UCB, Grant/ research support from: Novartis, Horizon Therapeutics.

DOI: 10.1136/annrheumdis-2021-eular.3136

POS1098 PREVALENT COMORBIDITIES ASSOCIATED WITH CLINICALLY DIAGNOSED OSTEOARTHRITIS: A CASE-CONTROL ANALYSIS INCLUDING 1,936,792 PEOPLE

A. Vivekanantham[1,2], D. Prieto-Alhambra[1,3], D. E. Robinson[1]. [1]*University of Oxford, Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, Oxford, United Kingdom*; [2]*Nuffield Orthopaedic Centre, Rheumatology, Oxford, United Kingdom*; [3]*Erasmus University Medical Center, Health Data Sciences, Rotterdam, Netherlands*

Background: Osteoarthritis (OA) is the most common form of arthritis and a major cause of pain and disability worldwide. Individuals with OA have increased cardiovascular morbidity and mortality, and other comorbidities are also more common amongst them than in the general population. In this study, we examined the prevalence and timing of the diagnosis of co-morbidities prior to the clinical diagnosis of OA.
Objectives: To determine the odds of comorbidities in newly diagnosed OA cases versus matched controls in the up to 10 years prior to diagnosis.
Methods: Case-control study of people registered in the Information System for Research in Primary Care (SIDIAP). SIDIAP includes primary care records covering over 80% of the population of Catalonia, Spain.
Participants with an incident diagnosis of OA, based on ICD-10-CM disease codes, were matched to up to 4 controls by age (within 2 years), gender and primary care practice. The first diagnosis date of OA used the index date, with matched controls using the same index date, to retrospectively review for comorbidities. Patients were required to have at least 3 years continuous registration prior to the index date. A total of 57 comorbidities were considered, based on prior knowledge and clinical consensus.
Descriptive statistics were used to obtain the demographic information about cases and controls. Counts of any comorbidity were calculated, and univariable and multivariable logistic regression were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) of individual comorbidities adjusted for age, gender and socio-economic status.
Results: In total, there were 455,494 OA cases and 1,481,298 matched controls. The cases and controls were similar with regards to age, gender and deprivation level.
The incident diagnosis of any comorbidity at any time prior to index date was 77% (n= 350,913) in cases versus 61% (n= 909,497) in controls.
The results from the multivariable analysis [Table 1] showed that OA patients had higher prevalence of many comorbidities up to 1 year prior to their diagnosis of OA compared to up to 10 years prior to diagnosis. They were most likely to be diagnosed with another musculoskeletal condition followed by neuro-psychiatric and metabolic and cardiovascular conditions. Conversely, patients with OA were less likely to be diagnosed with cancer up to 10 years prior to index date than matched controls.
Conclusion: Patients with OA have multiple chronic conditions. Our results found that the diagnosis of these other co-morbidities (particularly musculoskeletal and neuro-psychiatric conditions) were more likely to occur in the 1-year prior to their diagnosis of OA, compared to in the 10-year prior, except for lymphoma and solid malignancy. These results help us to further understand the relationship and timing of the development of multiple co-morbidities in patients with OA.

Table 1. Multivariable analysis at 1 year and 10 year prior to index date

Co-morbidity	Multivariable analysis 1-year prior (OR, 95% CI)	Multivariable analysis 10-year prior (OR, 95% CI)
Musculoskeletal conditions		
Ankylosing Spondylosis	**3.12 (2.41, 4.05)**	**1.27 (1.12, 1.43)**
Fibromyalgia	**4.24 (3.96, 4.54)**	**1.85 (1.80, 1.91)**
Rheumatoid Arthritis	**2.67 (2.40, 2.97)**	**1.27 (1.20, 1.34)**
Back/ neck pain	**2.41 (2.38, 2.45)**	**1.76 (1.75, 1.78)**
Neuro-psychiatric		
Anxiety	**1.69 (1.65, 1.73)**	**1.23 (1.22, 1.24)**
Depression	**1.87 (1.81, 1.93)**	**1.25 (1.24, 1.27)**
Irritable Bowel Syndrome	**1.90 (1.71, 2.11)**	**1.28 (1.22, 1.34)**
Migraine	**1.81 (1.69, 1.94)**	**1.23 (1.20, 1.27)**
Cancer		
Leukaemia	1.07 (0.88, 1.30)	0.91 (0.82, 1.00)
Lymphoma	0.84 (0.68, 1.03)	**0.90 (0.82, 0.99)**
Solid malignancy	**0.95 (0.91, 0.99)**	**0.95 (0.93, 0.97)**
Other medical conditions		
Stroke	**1.15 (1.10, 1.20)**	**0.95 (0.93, 0.97)**
Hypertension	**1.70 (1.68, 1.74)**	**1.26 (1.25, 1.28)**
Diabetes	**1.34 (1.30, 1.38)**	**1.07 (1.06, 1.09)**
Obesity	**1.96 (1.92, 2.01)**	**1.60 (1.58, 1.62)**

Disclosure of Interests: Arani Vivekanantham: None declared, Daniel Prieto-Alhambra: None declared, Danielle E Robinson Grant/research support from: Dr. Prieto-Alhambra reports grants and other from AMGEN, grants, non-financial support and other from UCB Biopharma, grants from Les Laboratoires Servier, outside the submitted work; and Janssen, on behalf of IMI-funded EHDEN and EMIF consortiums, and Synapse Management Partners have supported training programmes organised by DPA's department and open for external participants.

DOI: 10.1136/annrheumdis-2021-eular.3202

POS1099 EFFICACY OF INTRA-ARTICULAR CORTICOSTEROID INJECTIONS IN KNEE OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

A. Najm[1], A. Alunno[2], C. Weill[3], J. Gwinnutt[4], F. Berenbaum[5]. [1]*Institute of Infection, Immunity and Inflammation, College of Medical Veterinary and Life Sciences, University of Glasgow, Rheumatology, Glasgow, United Kingdom*; [2]*University of Perugia, Rheumatology Unit, Department of Medicine, Perugia, Italy*; [3]*Paris Descartes University, Bibliothèque interuniversitaire de Santé, Paris, France*; [4]*Centre for Epidemiology Versus Arthritis, Centre for Musculoskeletal Research, School of Biological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Division of Musculoskeletal and Dermatological Sciences, Manchester, United Kingdom*; [5]*Sorbonne Université, INSERM CRSA Saint-Antoine, AP-HP, Saint Antoine Hospital, Paris, France., Rheumatology, Paris, France*

Background: Knee osteoarthritis (OA) is a frequent degenerative disease representing an important health and economic burden. Symptomatic medical treatments available include intra-articular (IA) injections of corticosteroids (GC) but

their efficacy is debated. In addition, safety signals regarding cartilage damage with IA GC have been highlighted in a few studies.
Objectives: To perform a meta-analysis of studies assessing IA GC efficacy and safety in knee OA.
Methods: A systematic literature review and a meta-analysis of randomized controlled trials (RCTs) assessing the effect of GC IA injections versus other interventions (IA Hyaluronic Acid, IA placebo, IA NSAID, oral NSAID or physiotherapy) in knee OA was performed. The effect of the interventions on pain and function were extracted from the single studies and pooled and are presented as short term (<6weeks), medium term (6-24 weeks) and long term (>24 weeks) follow-up period. Standardized mean differences (SMD) are reported.
Results: Of 520 studies screened, 23 were included in the SLR and 14 subsequently included in the MA. While IA GC showed a superior effect compared to control on both pain (SMD -0.61 (95% CI -1,25, 0.03)) and function (SMD -1.02 (95% CI -2.14, 0.10)) in short term follow-up; long term follow-up analysis favored controls (IA HA, IA NSAID, physiotherapy) for both pain (SMD 0.68 (95% CI -0.11, 1.47)) and function (SMD 0.88 (95% CI -0.36, 2.12) outcomes (Figure 1). No difference was found between interventions in the medium term. Safety data were reported in 18/23 studies (n= 1936/2314 patients); and side effects were reported as follows: arthralgia (69 IA GC patients, 146 IA HA patients, and 20 saline patients); site injection pain (7 in the IA GC group, 2 in the IA saline group, 14 in the IA HA group); 16 post injection knee swelling without signs of septic arthritis in the IA GC group and 24 in the IA HA group. In one study assessing cartilage effects of GCs, the rate of cartilage loss was greater in the GC group with a reduction of cartilage thickness at 2 year compared to placebo group. No difference was observed in the progression of cartilage denudation or bone marrow lesion. On the contrary, another study showed no effect of injections on the cartilage structure.

Conclusion: We demonstrate in this work that IA GC injections reduce pain and improve function in the early phase (≤6 weeks) of treatment. In the long term (≥24 weeks), other intervention such as IA HA injections or physiotherapy seem to be more efficient, but this effect was largely driven by single studies with large effect sizes and the comparators were heterogeneous.

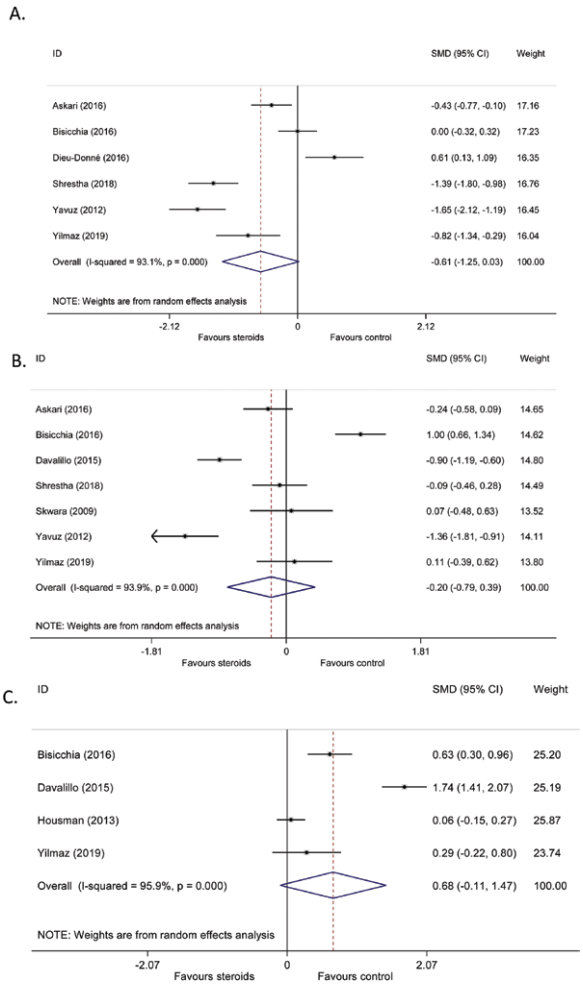


Figure 1. Knee pain outcome at short term (≤6weeks) (A), medium term (>6 & <24 weeks) (B), and long term (≥24 weeks) (C) follow up.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3291

POS1100 THE IMPACT OF CARDIOVASCULAR COMORBIDITIES ON KNEE OSTEOARTHRITIS PROGRESSION

H. Parente[1], F. Guimarães[1], D. Esperança Almeida[2], S. Azevedo[1], J. Rodrigues[1], D. Faria[1], D. Peixoto[1], J. Tavares-Costa[1], C. Afonso[1], F. Teixeira[1]. [1]*Unidade Local de Saúde do Alto Minho, Serviço de Reumatologia, Ponte de Lima, Portugal*; [2]*Hospital de Braga, Serviço de Reumatologia, Braga, Portugal*

Background: Osteoarthritis' (OA) pathophysiology is a complex and evolving subject, resulting in different phenotypes[1]. There is a known association between cardiovascular risk factors (CVRF) and OA, but its subjacent mechanism remains under-documented[2]. Pursuing this logic of direct systemic effect on joints by CV comorbidities[2], new therapeutic approaches could be reached.
Objectives: To determine the impact of CV comorbidities on knee OA, based on radiographic rate of progression and the need for total knee arthroplasty (TKA).
Methods: Cohort retrospective study among non-obese patients with primary knee OA, seen at a Portuguese hospital between 2017 and 2020. Clinical records were reviewed for sociodemographic and clinical data [age at the diagnosis, radiographic scoring through Kellgren Lawrence (KL) classification system at baseline (diagnosis) and 5 years later, KL progression and time to TKA]. CVRF such as Essential Arterial Hypertension (EHA), Dyslipidemia (DLP) and Type 2 Diabetes Mellitus (T2DM) prior to the OA diagnosis, as well as medication history were also recorded. Comparison of both cohorts, with and without the mentioned CVRF, was performed.
Results: A total of 304 patients with knee OA were eligible, 86 (28.3%) men and 218 (71.7%) women. Of those with CVRF (n=169), 121 (71.6%) were women and the mean age was 74.47±0.59 years. Among them, 129 (76.4%) had EAH, 122 (72.2%) had DLP, and 52 (30.8%) had T2DM. Five (3%) were treated with fenofibrate, 114 (67.5%) with statins, 40 (23.7%) with metformin, and 4 (2.4%) with liraglutide. Of those without CV risk factors (n=135), 97 (71.9%) were women and the mean age was 71.36±0.83 years. The presence of CVRF was associated with higher KL score (moderate to severe) at baseline [OR=2.118 (CI 95%: 1.264-3.549)] and 5 years later [OR=14.960 (CI 95%: 3.439-65.079)], faster KL progression, i.e., 2-grade worsening [OR=2.755 (CI 95%: 1.205-6.299)], and greater need for TKA [OR=3.781 (CI 95%:2.257-6.335)]. However, there was no association between the number of CVRF and progression of the KL score nor the rate of this progression, as well as between the number of CVRF and the need for TKA. EAH was associated with higher KL score at baseline [OR=1.819 (CI 95%: 1.108-2.987)] and 5 years later [OR=17.921 (CI 95%: 2.382-134.835)] but not with faster KL progression. It also associated with a greater need for TKA [OR=3.320 (CI 95%:1.197-5.750)]. DLP was associated with higher KL score at baseline [OR=1.843 (CI 95%: 1.120-3.030)] and 5 years later [OR=7.709 (CI 95%: 1.772-33.530)], as well as with faster KL progression [OR=2.560 (CI 95%: 1.249-5.246)], and greater need for TKA [OR=2.493 (CI 95%: 1.457-4.268)]. T2DM was associated with higher KL score 5 years after OA diagnosis [OR=1.103 (CI 95%: 1.059-1.148)], but not with KL score at baseline nor the occurrence of KL score progression during those first 5 years of disease or the need for TKA. Metformin, liraglutide, statins or fenofibrate use (either compounded or isolated) showed no statistically significant association with any of the following: KL score at baseline and 5 years later, occurrence of KL progression, and need for TKA. Time to TKA was not statistically different between patients with or without these medications. The number of medications used was not associated with KL progression or the need for TKA.
Conclusion: CVRF contribute globally to OA progression. Patients with EAH and DLP showed worse radiographic expression of OA features and greater need for TKA, with DLP patients having faster KL progression. The presence of more than one CVRF was not associated with an increased disease progression, and cardiovascular therapeutic medications were not associated with an overall protective role. This study highlights the importance of acting on preventive measures for CVRF, in OA management.
REFERENCES:
[1] Deveza *et al*. Clinical and experimental rheumatology vol. 37 Suppl 120,5 (2019): 64-72.
[2] Orcha *et al*. Revue du Rhumatisme vol. 87 Suppl 1 (2020): A244.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3844

POS1101

THE OMERACT KNEE INFLAMMATION MRI SCORING SYSTEM: VALIDATION OF QUANTITATIVE METHODOLOGIES AND TRI-COMPARTMENTAL OVERLAYS BY COMPARISON WITH THE MRI OSTEOARTHRITIS KNEE SCORE

W. P. Maksymowych[1,2], J. L. Jaremko[3], S. Juhl Pedersen[4,5], I. Eshed[6], U. Weber[7], A. Mcreynolds[3], S. Wichuk[1], J. Paschke[2], R. G. Lambert[3]. [1]*University of Alberta, Medicine, Edmonton, Canada*; [2]*CARE Arthritis, Rheumatology, Edmonton, Canada*; [3]*University of Alberta, Radiology and Diagnostic Imaging, Edmonton, Canada*; [4]*COPECARE, Rheumatology, Copenhagen, Denmark*; [5]*Rigshospitalet, Clinical Medicine, Glostrup, Denmark*; [6]*Sheba Medical Center, Radiology and Diagnostic Imaging, Tel Aviv, Israel*; [7]*Practice Buchsbaum, Rheumatology, Schaffhausen, Switzerland*

Background: Randomized controlled trials have targeted reducing the size of BML and degree of synovitis for the treatment of OA. We have developed the OMERACT Knee Inflammation MRI Scoring System (KIMRISS) and have recently refined it to maximize reliability and sensitivity to change. Innovations include electronic overlays for assessment of BML in 500 subregions, a web-based interface with direct online scoring, and real-time iterative calibration (RETIC) prior to reading exercises. Synovitis-effusion (S-E) is also scored on all consecutive sagittal slices on a web-based interface.
Objectives: We aimed to test the feasibility, reliability, and responsiveness of KIMRISS versus an established method, MOAKS, in two multi-reader exercises.
Methods: KIMRISS incorporates web-based graphic overlays for each of femur, tibia, and patella (range 0-500). S-E is recorded as the largest diameter perpendicular to the longest axis of this feature (range 0-100). All scores are pro-rated for a standardized number of MRI slices. In a pre-reading exercise for KIMRISS, readers scored sufficient cases in RETIC to attain scoring proficiency, pre-specified as an ICC of ≥0.80 and ≥0.70 for status and change scores of BML and S-E compared to developer reads. A new web-based scoring platform with overlays designating different subregions for scoring BML was developed for MOAKS. We compared reliability for status and change scores of BML and S-E in 2 international multi-reader exercises of baseline and one-year MRI scans from the Osteoarthritis Initiative: A. 4 expert readers and an OMERACT fellow scored 38 cases selected for MOAKS BML score ≥1. B. 7 expert readers and an OMERACT fellow scored 60 cases selected for MOAKS BML ≥3 and Kellgren-Lawrence (K-L) grade <3. Reliability was assessed by intra-class correlation coefficient (ICC) and Smallest Detectable Change (SDC), responsiveness by the standardized response mean (SRM), and feasibility using the System Usability Scale (SUS scoring range 0-100).
Results: For exercises A/B, subjects were 55.3%/ 26.7% male, mean(±SD) age 61.7(±9.1)/61.9(8.8) years, and radiographic K-L grade ≤2 in 39.4%/100%. Change was small in both exercises (<5% of scoring range for KIMRISS and MOAKS BML and S-E) with comparable responsiveness (Table 1). Despite this, ICC for change was consistently good to very good for both BML and S-E and consistently better for KIMRISS (Table 1). Mean SUS scores were 88.2 for KIMRISS and 54.3 for MOAKS.

Table 1. KIMRISS and MOAKS scores in Two International Multi-reader Exercises

Method	MRI feature	Scores mean (SD)			SDC (% of max)	P value	SRM
		Baseline	One-year Follow up	Change			
EXERCISE A							
MOAKS	**BML**	3.6 (2.9)	3.4 (2.3)	-0.2 (1.9)	1.0 (2.2%)	0.72	-0.11
	Synovitis-effusion	1.3 (0.8)	1.5 (0.8)	0.2 (0.4)	0.4 (13.3%)	0.017	0.5
KIMRISS	**BML**	15.7 (13.3)	21.2 (22.5)	5.5 (15.3)	5.6 (1.1%)	0.022	0.36
	Synovitis-effusion	21.8 (12.0)	24.3 (11.9)	2.5 (7.4)	2.8 (2.8%)	0.043	0.34
EXERCISE B							
MOAKS	**BML**	4.2 (2.6)	3.7 (2.4)	-0.5 (2.1)	1.1 (2.4%)	0.083	-0.24
	Synovitis-effusion	1.2 (0.7)	1.3 (0.8)	0.0 (0.5)	0.4 (13.3%)	0.59	0.0
KIMRISS	**BML**	18.0 (17.5)	15.9 (14.3)	-2.1 (12.3)	5.9 (1.2%)	0.19	-0.17
	Synovitis-effusion	21.8 (9.3)	22.9 (10.8)	1.1 (7.1)	2.2 (2.2%)	0.25	0.15

Intra-class Correlation Coefficients (95%CI)

Method	MRI feature	Exercise A	Exercise B
KIMRISS status	BML	0.86 (0.78-0.92)	0.80 (0.70-0.87)
KIMRISS change		0.88 (0.81-0.93)	0.72 (0.64-0.80)
MOAKS status	BML	0.71 (0.46-0.85)	0.67 (0.56-0.77)
MOAKS change		0.76 (0.64-0.85)	0.69 (0.60-0.78)
KIMRISS status	Synovitis-effusion	0.88 (0.81-0.93)	0.75 (0.52-0.86)
KIMRISS change		0.87 (0.79-0.92)	0.87 (0.82-0.91)
MOAKS status	Synovitis-effusion	0.66 (0.4-0.79)	0.65 (0.52-0.75)
MOAKS change		0.52 (0.36-0.67)	0.48 (0.37-0.60)

Conclusion: The KIMRISS method for scoring BML and Synovitis-Effusion scores highly for feasibility and demonstrates consistently high reliability when compared to MOAKS. Further validation for responsiveness is necessary in cases with greater change in MRI features than in the OAI dataset.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4052

Osteoarthritis

POS1102

TEMPORAL TRENDS AND FACTORS ASSOCIATED WITH VITAMIN D PRESCRIPTION AND INTAKE

G. Adami[1], D. Gatti[1], O. Viapiana[1], P. Olivi[2], F. Bertoldo[3], A. Fassio[1], M. Rossini[1]. [1]*University of Verona, Rheumatology Unit, Verona, Italy*; [2]*University of Verona, Orthopedic Unit, Verona, Italy*; [3]*University of Verona, Bone Metabolism and Osteoncology Unit, Verona, Italy*

Background: Vitamin D has proven skeletal effects and its administration is recommended in patients with osteoporosis by many national and international guidelines. Nevertheless, the compliance to treatment of patients with osteoporosis is scarce. Understanding the factors associated with low vitamin D intake and prescription might help design future intervention aimed to improve adherence.
Objectives: This study aims to investigate the temporal trends and factors associated with vitamin D prescription and intake.
Methods: Using a web-based fracture risk-assessment tool, we collected demographic, densitometric and clinical data of women at high risk for fractures. To determine the factors associated with low vitamin D intake we ran a multivariable logistic regression analysis. We described the public general interest in the term "vitamin D" using the Google Trends tool.
Results: 12,419 women were included in the study. 6,748 (54.4%) individuals had a prevalent fragility fracture and 8,950 (72.1%) individuals were on <800 IU of vitamin D per day and 11,434 (92.1%) were taking <1,200 IU of vitamin D per day. The factors associated with vitamin D intake were evaluated with a multivariable logistic regression analysis, which results are presented in Table 1. We found that low BMD levels, the presence of associated comorbidities and glucocorticoid utilization were associated with greater vitamin D intake. Falls were associated only with lower risk of receiving very low dose of vitamin D (<250 IU day). Smoking status was associated with lower vitamin D intake. Overall, the internet interest in vitamin D was higher during the winter season Figure 1.

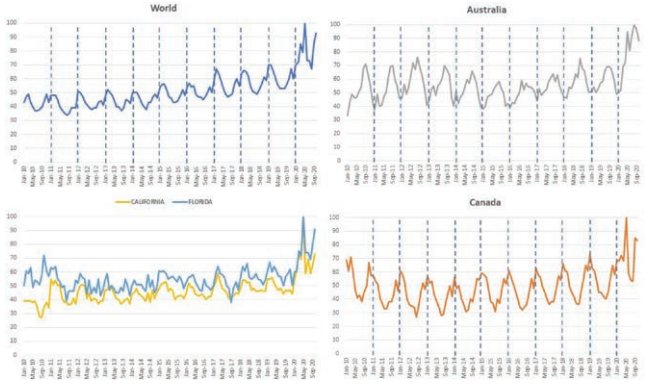


Figure 1. Google trends interest in the term "vitamin D" from January 2010 to October 2020

Conclusion: Low vitamin D intake (<800 IU day) was common in our cohort of women at high risk for fractures. The factors associated with greater vitamin D intake were: having low BMD levels, associated rheumatic diseases and glucocorticoid use. Falls were associated with lower risk of receiving very low dose of vitamin D (<250 IU day). Smoking status was associated with lower vitamin D intake.

Table 1. Binary logistic regression to predict the risk of low vitamin D intake (<800 IU/day)

>800 IU day REF		aOR (95% CI)	p value
400-800 IU day	**Age**	1.001 (0.995-1.007)	NS
	T-score	**1.422 (1.342-1.508)**	<0.001
	No comorbidities	REF	
	Rheumatoid arthritis	**0.732 (0.583-0.920)**	<0.001
	Psoriatic arthritis	**0.362 (0.218-0.607)**	<0.001
	Connective tissue disease	**0.630 (0.486-0.816)**	<0.001
	No cigarette smoking	REF	
	Cigarette smoking	1.040 (0.893-1.212)	NS
	Alcohol <3 unit day	REF	
	Alcohol ≥3 unit day	1.201 (0.660-2.187)	NS
	No glucocorticoids	REF	
	Glucocorticoids 2.5-5 mg/day	**0.688 (0.550-0.860)**	<0.001
	Glucocorticoids ≥5 mg/day	**0.739 (0.554-0.986)**	<0.001
	No falls	REF	
	Falls	0.875 (0.754-1.015)	NS
250-400 IU day	**Age**	0.994 (0.985-1.002)	NS
	T-score	**1.223 (1.117-1.339)**	<0.001
	No comorbidities	REF	
	Rheumatoid arthritis	**0.670 (0.463-0.970)**	<0.001
	Psoriatic arthritis	**0.300 (0.119-0.752)**	<0.001
	Connective tissue disease	**0.651 (0.435-0.975)**	<0.001
	No cigarette smoking	REF	
	Cigarette smoking	**1.371 (1.104-1.702)**	<0.001
	Alcohol <3 unit day	REF	
	Alcohol ≥3 unit day	1.824 (0.865-3.887)	NS
	No glucocorticoids	REF	
	Glucocorticoids 2.5-5 mg/day	0.930 (0.666-1.297)	NS
	Glucocorticoids ≥5 mg/day	0.743 (0.464-1.189)	NS
	No falls	REF	
	Falls	0.934 (0.741-1.176)	NS
<250 IU day	**Age**	**0.993 (0.988-0.998)**	<0.01
	T-score	**1.139 (1.079-1.202)**	<0.001
	No comorbidities	REF	
	Rheumatoid arthritis	**0.645 (0.522-0.795)**	<0.001
	Psoriatic arthritis	**0.553 (0.376-0.812)**	<0.001
	Connective tissue disease	**0.697 (0.558-0.871)**	<0.001
	No cigarette smoking	REF	
	Cigarette smoking	**1.339 (1.171-1.532)**	<0.001
	Alcohol <3 unit day	REF	
	Alcohol ≥3 unit day	1.267 (0.749-2.145)	NS
	No glucocorticoids	REF	
	Glucocorticoids <5 mg/day	0.964 (0.796-1.168)	NS
	Glucocorticoids ≥5 mg/day	0.946 (0.736-1.215)	NS
	No falls	REF	
	Falls	**0.615 (0.530-0.712)**	<0.001

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.217

POS1103 SLEEP DISTURBANCE AND BONE MINERAL DENSITY, RISK OF FALLS AND FRACTURE: RESULTS FROM A 10.7-YEAR PROSPECTIVE COHORT STUDY

F. Pan[1], J. Tian[1], F. Cicuttini[2], G. Jones[1]. *[1]University of Tasmania, Menzies Institute for Medical Research, Hobart, Australia*; *[2]Monash University Medical School, Department of Epidemiology and Preventive Medicine, Melbourne, Australia*

Background: Sleep problems are common in the general population and have been reported to adversely affect bone health and increase risk of falls and fracture. However, no study has investigated whether an increased risk of fracture is attributable to sleep-related low bone mineral density (BMD) and/or an increased risk of falls.
Objectives: This study, therefore, sought to describe the associations of sleep disturbance with BMD, risk of falls and fractures.
Methods: The analyses were performed in a population-based prospective cohort study with 1,099 participants (aged 50–80 years) enrolled at baseline, and 875, 768 and 563 participants traced at a mean follow-up of 2.6, 5.1 and 10.7 years, respectively. At each visit, self-reported sleep disturbance was recorded. BMD (by DXA), falls risk and fracture were measured at each visit. The short-form Physiological Profile Assessment was used to measure falls risk expressed as Z-score. Fractures were self-reported. Mixed-effects model and generalised estimating equations were used for the analyses.
Results: In multivariable analysis, there was a dose-response relationship between extent of sleep disturbance and falls risk score with the strongest association in those reporting the worst sleep disturbance (β=0.15/unit; 95%CI 0.02-0.28). The worst sleep disturbance was associated with an increased risk of any (relative risk [RR] 1.30/unit; 95%CI 1.01-1.67) and vertebral fracture (RR 2.41/unit; 95%CI 1.00-5.80) compared with those reporting no interrupted sleep. This was independent of covariates, hip BMD and falls risk. There was no statistically significant association between sleep disturbance and BMD at hip, spine or total body.
Conclusion: Sleep disturbance was independently associated with a greater falls risk score and an increased risk of fractures, suggesting that correcting sleep disturbance has the potential to reduce both falls risk and fractures.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.376

POS1104 THE DEVELOPMENT AND VALIDATION OF A RISK STRATIFICATION QUESTIONNAIRE TO SCREEN FOR MEDICATION RELATED OSTEONECROSIS OF THE JAW RISK IN OSTEOPOROTIC PATIENTS

Y. El-Miedany[1,2], M. El Gaafary[3], M. Toth[4], S. Bahlas[5], W. Hassan[6], M. H. Abu-Zaid[7] on behalf of Egyptian Academy of Bone Health and Metabolic Bone Diseases. *[1]Canterbury Christ Church University Medway Campus, Rheumatology, Gillingham, United Kingdom*; *[2]King's College London, Education, London, United Kingdom*; *[3]Faculty of Medicine, Ain Shams University, Public Health and community, Cairo, Egypt*; *[4]Darenth Valley Hospital, Medicine, Dartford, United Kingdom*; *[5]King Abdulaziz University, Rheumatology, Jeddah, Saudi Arabia*; *[6]Faculty Of Medicine - Benha University, Rheumatology and Rehabilitation, Benha, Egypt*; *[7]Faculty Of Medicine - Tanta University, Rheumatology and Rehabilitation, Tanta, Egypt*

Background: Given the gaps in knowledge that exist in relation to risk stratification for osteonecrosis of the jaw (ONJ) amongst patients treated with anti-resorptive agents, there is a high need for an evidence-based measure which would facilitate the identification of those patients at higher risk of ONJ development; particularly, most of the available advice is empirically based.
Objectives: to develop a valid self-administered questionnaire to facilitate risk stratification and risk minimisation of medication related ONJ in osteoporotic patients treated with anti-resorptive agents.
Methods: Development of ONJ risk assessment questionnaire (ONRAQ) followed 5 stages: 1. Review of the literature to Identify the risk factors associated with medication related ONJ. 2. Item pool development: a list of the main risk factors was compiled. Rare or uncommon factors were excluded. 3. A questionnaire was developed. This was based on the idea that the questions should be straight forward and as clear as possible. 4. Pre-testing of the questionnaire. 5. Validation of the questionnaire by comparing the patients answers with their medical records. Patients at risk were advised to seek dental assessment and the dental report was evaluated. The last prescription was reviewed to verify the current medications. 157 patients were invited to participate and were prospectively monitored for 5-years to assess for the incidence of medication related ONJ. Advice was given regarding how to maintain good dental hygiene to prevent dental disease and to ensure that any dental interventions that are considered necessary are carried out as conservative and preservative as possible. Comprehensibility of the model sections was also assessed.
Results: Stages 1 and 2 identified the risk factors chosen for the questionnaire. These risk factors were stratified into 4 sections: Personal, Dental and oral health, current medications and associated comorbidities. Stage 3 led to the development of the 27 items questionnaire. Personal: 3 risk factors (age, elevated BMI and smoking), Dental and oral health (11 risk factors), current medications (3 risk factors) and associated comorbidities (10 risk factors). Analysis of the answers provided by 126 patients, who completed the study, age range 58-82 years revealed that the mean time to answer the questionnaire was 1.9 + 0.153 minutes. The ONRAQ has shown a strong validity when compared to the patients' data record (range 0.89-0.97). All patients rated the questionnaire as easily comprehensible. Comprehensibility of the various questionnaire sections ranged between 96.1% and 98.2% denoting that all the questions were well understood by the great majority of patients. 11/126 (8.7%) had a dental procedure in the past 6-months, 13/126 (10.3%) were advised to stop smoking. Whereas 20/126 (20.6%) had associated comorbidities. Risk stratification led to the advice to start oral bisphosphonates/ denosumab rather than IV zoledronate for patients at moderate risk (comorbidities, personal, medication). Treatment was postponed till complete healing for those with recent history of invasive dental procedure (high risk). No ONJ was identified after 5-years of follow up.
Conclusion: Results of this questionnaire revealed that the ONRAQ is valid screening questionnaire. It can be implemented, as a risk minimisation measure, in standard practice. The questionnaire was able to identify patients at risk of developing medication related osteonecrosis of the jaw and facilitate the prospective risk management of ONJ.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.657

POS1105

EFFECTS OF CHOLECALCIFEROL AND CALCIFEDIOL IN OSTEOPOROTIC WOMEN WITH SECONDARY HYPERPARATHYROIDISM DUE TO SEVERE VITAMIN D DEFICIENCY UNDERGOING ZOLEDRONIC ACID TREATMENT: A RANDOMIZED-CONTROLLED TRIAL

G. Botticella[1], M. Pizzonia[2], B. Cossu[3], R. Bruno[3], D. Camellino[1], G. Girasole[1], A. Giusti[1], M. Pedrazzoni[1], S. Alexovits[1], F. Pleitavino[3], F. Santolini[4], A. Nencioni[2], G. Bianchi[1]. [1]*Local Health Trust 3, Division of Rheumatology, Department of Medical Specialties, Genoa, Italy*; [2]*University of Genoa, Geriatric Clinic, Department of Internal Medicine and Medical Specialties, Genoa, Italy*; [3]*Local Health Trust 3, Orthopedic and Trauma Unit, Department of Surgery, Genoa, Italy*; [4]*Policlinic San Martino Hospital, Orthopaedic and Trauma Unit, Department of Emergency, Genoa, Italy*

Background: Secondary hyperparathyroidism (sHPTH) due to vitamin D deficiency impairs the bone mineral density (BMD) response to alendronate,[1-2] but the optimal strategy for its correction in postmenopausal osteoporotic women (PMO) about to start zoledronic acid (ZOL) therapy is still unknown.

Objectives: To evaluate the effects of cholecalciferol (D3) and calcifediol (25OHD) on serum 25-OH-vitamin D (s25OHD), parathyroid hormone (PTH) and BMD in PMO presenting with sHPTH due to vitamin D deficiency.

Methods: PMO with s25OHD <20 ng/ml, sHPTH (PTH >65 pg/ml) and BMD T-score at the lumbar spine (LS), femoral neck (FN) or total hip (TH) < -2.5, or between -1 and -2.5 plus one vertebral/femoral fracture, were randomly assigned to receive a therapeutic dose of D3 (300.000 IU bolus) followed by 175 mcg/weekly of D3, or 175 mcg/weekly of 25OHD alone, 2 months before receiving a single intravenous infusion of ZOL (5 mg). BMD at the LS, FN and TH was assessed at baseline and after one year from ZOL. Serum calcium, PTH and s25OHD were measured at baseline, and 6- and 12-month after ZOL. Adverse and clinical events were ascertained by 3-and 9-month telephone interviews, and by 6- and 12-month clinical evaluation.

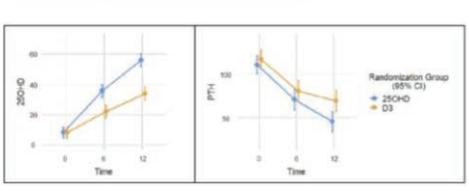
Results: 45 PMO (25OHD N=23, D3 N=22) were enrolled over one year and 32 subjects (mean age ±SD 75±10 years, range 51-91) completed the 1-year of treatment/follow-up (25OHD N=17, D3 N=15). Most PMO discontinued for protocol violation, while three deceased before study ending (25OHD N=1, D3 N=2) for reasons not related to the agents investigated. The baseline characteristics were comparable in both groups. At baseline mean s25OHD (±SE) was 8±1 ng/ml in the 25OHD group and 8±1 ng/ml in the D3 group. The corresponding figures for PTH were 111±6 pg/ml (25OHD) and 117±5 pg/ml (D3). Mean s25OHD (±SE) increased in both groups at 6- and 12-month, being significantly greater in the 25OHD group (12-month, 56±2 ng/ml) compared to the D3 group (12-month, 34±2 ng/ml, P<.001) at both time points (Figure 1). PTH (mean ±SE) decreased in both groups, being significantly lower in the 25OHD group at 12-month (25OHD 46±6 pg/ml versus D3 70±6 pg/ml, P=.007), as shown in Figure 1. BMD at the LS, FN and TH increased in both groups (with significant increases versus baseline only at the FN) without significant differences between s25OHD and D3. In PMO receiving D3 serum calcium remained stable over time, while those receiving s25OHD demonstrated a significant increase of serum calcium, with 2 PMO presenting a value close to the upper limit of the reference range at 12-month. No patient reported incident fractures or adverse events.

Conclusion: Calcifediol 175 mcg weekly appears more potent in improving s25OHD and decreasing PTH concentrations compared to cholecalciferol therapeutic dose (300'000 IU) plus 175 mcg weekly in PMO presenting with sHPTH due to severe vitamin D deficiency about to start ZOL therapy. Further studies are warranted to clarify implications on BMD improvements on the long-term of similar 25OHD and D3 regimens.

REFERENCES:

[1] Barone A et al., J Am Geriatr Soc 2007.
[2] Kincse G et al., BMC Musculoskelet Disord 2012.

Figure 1. Mean (95% confidence interval) value of 25-hydroxyvitamin D (25OHD, ng/ml) and parathyroid hormone (PTH, pg/ml) at baseline, and 6- and 12-month (Time) after zoledronic acid infusion, in patients receiving a therapeutic dose of D3 (300.000 IU bolus) followed by 175 mcg/weekly of cholecalciferol (D3, yellow line), or 175 mcg/weekly of calcifediol (25OHD, blue line).



Disclosure of Interests: Giulia Botticella: None declared, Monica Pizzonia: None declared, Barbara Cossu: None declared, Roberta Bruno: None declared, Dario Camellino Speakers bureau: AbbVie, Celgene, Janssen-Cilag, Eli Lilly, Medac, Mylan, Novartis, and Sanofi, outside the submitted work, Giuseppe Girasole Speakers bureau: Abiogen Pharma and Novartis, outside the submitted work, Andrea Giusti Speakers bureau: UCB, Amgen, Kyowa Kirin, Abiogen Pharma, and Eli Lilly, outside the submitted work, Consultant of: EffRx and Abiogen Pharma, outside the submitted work, Mario Pedrazzoni: None declared, Simona Alexovits: None declared, Franco Pleitavino: None declared, Federico Santolini: None declared, Alessio Nencioni: None declared, Gerolamo Bianchi Speakers bureau: Abbvie, Abiogen Pharma, Amgen, BMS, Celgene, Eli Lilly, GSK, Janssen-Cilag, Medac, MSD, Novartis, Pfizer, Roche, Sanofi, Genzyme, and Servier, outside the submitted work.

DOI: 10.1136/annrheumdis-2021-eular.809

POS1106

FRAX AND THE EFFECT OF TERIPARATIDE ON BONE MINERAL DENSITY IN SECONDARY OSTEOPOROSIS

S. Garcia[1], B. M. Fernandes[1], M. Rato[1], F. Oliveira Pinheiro[1], D. Fonseca[2], D. Santos Oliveira[1,3], A. Martins[1], F. R. Martins[4], G. Terroso[1], M. Bernardes[1,5], L. Costa[1]. [1]*São João Universitary Hospital Center, Rheumatology, Porto, Portugal*; [2]*Centro Hospitalar Vila Nova de Gaia/Espinho - Unit 1, Rheumatology, Vila Nova de Gaia, Portugal*; [3]*Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal*; [4]*University Hospital Center of Algarve, Faro, Rheumatology, Faro, Portugal*; [5]*Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal*

Background: Teriparatide has been shown to increase spine and hip bone mineral density (BMD) and to reduce vertebral and non-vertebral fractures. (1) It is currently not clear whether the effect of teriparatide is dependent on the baseline risk of fracture or osteoporosis (OP) type, a finding that could have an impact on our therapeutic decision.

Objectives: Investigate if there is a relationship between teriparatide effect in BMD and baseline 10-year fracture probability, assessed using FRAX®, in primary and secondary OP patients.

Methods: This is a longitudinal, retrospective study including consecutive patients with the diagnosis of OP treated with teriparatide for 24 months, with a ten-year follow-up period, at our rheumatology department. Demographic, clinical, laboratorial, BMD and occurrence of fracture data were collected. The 10-year risk of osteoporotic fracture was estimated using the fracture risk assessment tool (FRAX) v 4.1 with the Portuguese population reference. Statistical analysis was performed using the software SPSS 23.0. Correlations between continuous variables were evaluated with spearman coefficient. p<0.05 was considered statistically significant.

Results: Eighty patients (88.8% female, median age 65.00 (59; 75)) were included. Forty-nine patients (61.3%) has secondary OP, mainly of cortisonic etiology (61.2%, n=30). Before treatment, median lumbar spine BMD was 0.870 [0.767, 0.964] g/cm^2, median T-score of -2.60 (-3.30, -1.90); median total femur BMD was 0.742 [0.667, 0.863] g/cm^2, median T-score of -2.10 (-2.80, -1.30); median femoral neck BMD was 0.671 [0.611, 0.787] g/cm^2, median T-score of -2.50 [-3.20, -1.85]. Regarding fracture risk, median FRAX-based 10-year major fracture risk (with BMD) at baseline was 16% [10.0; 23], and median hip fracture risk was 7.2% [3.4; 13.8].

The median variation of BMD, after finishing teriparatide treatment, in the spine was 0.107 [0.029; 0.228]; median BMD variation in total femur was 0.013 [-0.013; 0.068] and median BMD femoral neck was 0.046 [-0.002; 0.109]. We observed a numerically superior effect, albeit without any statistical significance, of teriparatide on bone mineral density gain in secondary OP (*versus* primary OP) at lumbar spine, total femur and femoral neck.

Most patients continued anti-osteoporotic treatment with a bisphosphonate (81.2%, n=65) and, during follow-up, 17 patients had an incident fracture (8 hip fractures and 6 vertebral fractures), median of 5 [1.75, 8.25] years after ending teriparatide.

We found a discrete correlation between FRAX-based hip fracture probability and the variation of bone mineral density in total femur (Spearman's coefficient 0.248, p=0.04). There was no correlation between FRAX-based major fracture probability and and the variation of bone mineral density in the spine or femur. When we separately analyze the relationship between the variation in total hip BMD and the FRAX-based fracture risk, depending on whether it is a secondary or primary OP, we find that the correlation is stronger and only remains in secondary OP (Spearman's coefficient 0.348, p=0.03).

Conclusion: Our data suggest that teriparatide could be an important weapon in the treatment of secondary cause OP, particularly cortisonic, and in patients at high fracture risk, although further larger studies are needed to confirm these findings.

REFERENCES:

[1] Kendler DL, Marin F, Zerbini CAF, Russo LA, Greenspan SL, Zikan V, Bagur A, Malouf-Sierra J, Lakatos P, Fahrleitner-Pammer A, Lespessailles E, Minisola S, Body JJ, Geusens P, Möricke R, López-Romero P. Effects of teriparatide and risedronate on new fractures in post-menopausal women with severe osteoporosis (VERO): a multicentre, double-blind, double-dummy,

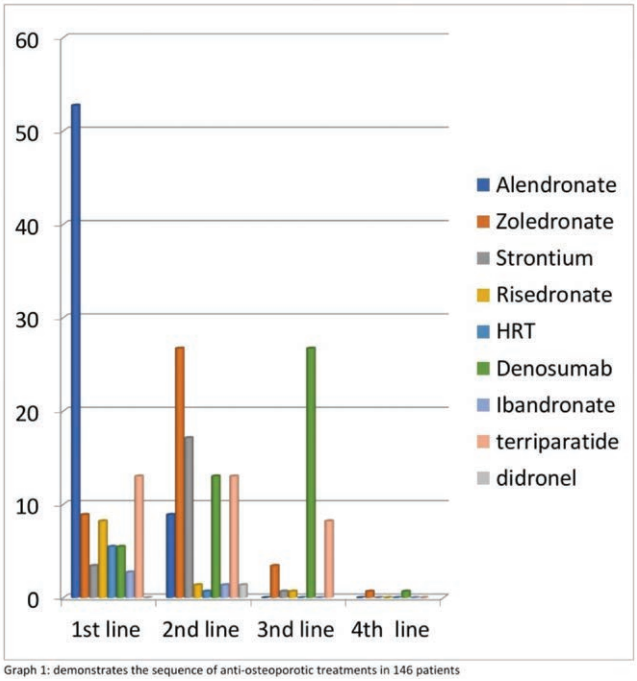
randomised controlled trial. Lancet. 2018 Jan 20;391(10117):230-240. doi: 10.1016/S0140-6736(17)32137-2.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.961

POS1107

THE EFFICACY, SAFETY AND OUTCOME AFTER 5-8 YEARS OF PARENTERAL ANTI-OSTEOPOROTIC THERAPY EVALUATED AT A DISTRICT GENERAL HOSPITAL IN THE UK

Z. Alkutobi[1], D. Laila2, T. Jones[3], A. Nandagudi2. *[1]Basildon and Thurrock University Hospitals NHS Foundation Trust, Rheumatology, Basildon, United Kingdom*; *[1]Basildon and Thurrock University Hospitals NHS Foundation Trust, Rheumatology, Basildon, United Kingdom*; *[3]Basildon and Thurrock University Hospitals NHS Foundation Trust, Internal Medicine, Basildon, United Kingdom*

Background: Parenteral anti-osteoporotic medications are frequently recommended for the management of primary and secondary osteoporosis by NICE (1) and EULAR (2) guidelines.
Objectives: This audit aimed at evaluating the efficacy, adherence and safety profile of denosumab (D), zoledronate (Z) and teriparatide (T).
Methods: The data of patients initiating D, Z and T from 2012-2021 were retrospectively reviewed using electronic medical records at Basildon hospital.
Results: We enrolled 146 patients diagnosed with low bone density and on following treatment (3-6 years D (n: 50), 4-5 years Z (n: 50) and 2 years T (n: 46). More than 92% were Caucasian females; 41.7% were above 80 years.
T group had more pronounced reduction in bone mineral density (BMD) with a mean T-score
(spine:-3.9, hip: -2.6, neck of femur: -2.7; followed by Z group (spine: -2.6, hip:-2, neck of femur: -2.5) and D group (spine: -2.3, hip:-2.2, neck of femur: -2.3).
Primary prevention was in 26% and secondary prevention in 73.9%; with the commonest fractures at the vertebrae at 40%.
Oral bisphosphonate was the first choice in 63.6% of the cases (please see graph1). Intolerance, gastric upset or inefficacies were the commonest reasons to avoid them.



Graph 1: demonstrates the sequence of anti-osteoporotic treatments in 146 patients

After the 3rd Z or 5th D, DXA scan shows improvements or stability in BMD at both hip and spinal areas in 88% and 82% respectively; compared to 69.6% after completing 2 years of T. The rate of improvement or stability plummeted after the 10th D and 5th Z (Please see Table 1).

Table 1. Monitoring BMD after courses of D, Z and T.

DXA scan: changes in BMD:	*After the 5th D*	*After the 10th D*	*After the 3rd Z*	*After the 5th Z*	*After 2 years of T*
Percentage of scanned patients	100%	90%	100%	60%	71.73%
Improved or stable BMD at spine or hip areas	82%	75.5%	88%	85.6%	69.6%
Improved or stable BMD at the spine but declined at hip area	18%	19.9%	12%	13.3%	24.2%
Declined BMD at both spine and hip areas		4.4%			6%

The course of T was stopped earlier in 28.2% of the cases due to the difficulty in taking injections or side effects including nausea, gastric upset, myalgia, insomnia, poor renal function, raised PTH, ALP and calcium. Dental issues (not osteonecrosis) were the reason to stop Z and D in 2% of each group and 8% choose to discontinue D after developing other non-related comorbidities. There were no fragility fractures during the treatment courses.
The outcome after reviewing 91.3% of those who completed or stopped the T course shows 39% commenced on D whereas 35.7% and 19% on Z and alendronate respectively leaving 7.1% on drug holiday. After completion of the 10th D, 78.5% of the reviewed patients were continued on further D injections whereas 3.5% were switched to T and 17.8% given drug holiday. For those who were reviewed after the 5th Z, 94% were switched to D and 5.8% given drug holiday.
Conclusion: D, Z and T were well tolerated and could effectively either maintain or improve the BMD at both spinal and hip sites and prevent fragility fractures and T was associated with the most pronounced soar in BMD. There were few cases of deterioration mainly at the hip area with all groups.
Prior bisphosphonate therapy did not show significant influence on the later effects of D, Z or T on BMD. After completion of the treatment for the 3 groups, only 30.87 % of the reviewed cases were advised for drug holiday and majority were switched to D as Z and T is limited to 5 and 2 years course respectively.
Heterogeneity in decision making exists due to variability in recommending these medications, patient preference and mode of administration. To optimize the adherence and effects of anti-osteoporotic medications, stratified guidelines is required for the long term use of these medications and discontinuation of D.

REFERENCES:

[1] NICE Pathway: 20 August 2019, http://pathways.nice.org.uk/pathways/osteoporosis
[2] Kanis JA et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int. 2019 Jan;30(1):3-44.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1670

POS1108

THE ACCURACY OF OSTEOPOROTIC FRACTURE RISK PREDICTION IN PATIENTS WITH RHEUMATOID ARTHRITIS USING THE PREDICTIVE MODEL DEVELOPED AT V.A. NASONOVA REASEARCH INSTITUTE OF RHEUMATOLOGY (RUSSIA) AND FRACTURE RISK ASSESSMENT TOOL (FRAX)

P. Kozhevnikova[1], P. Kovalenko[1], S. Glukhova[1], I. Dydykina[1], A. Lila[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Safety Control of Drug Therapy, Moscow, Russian Federation*

Background: FRAX is a computer-based algorithm that calculates the 10-year probability of a major osteoporotic fracture and the 10-year probability of hip fracture. However, FRAX has several limitations in assessing the risk of fracture in patients with rheumatoid arthritis (RA).
In 2013 V.A. Nasonova Reasearch Institute of Rheumatology (Russia) developed a predictive mathematical model for assessing the risk of osteoporotic fractures in RA, which includes 2 main risk factors: cumulative glucocorticoid dose (GC), decrease in BMD in the femoral neck to osteoporosis, and 2 additional factors: for patients under 65 years of age - the presence of ischemic heart disease, and for people over 65 - a history of gastric ulcer or duodenal ulcer.
Objectives: To compare accuracy of osteoporotic fracture risk prediction in patients with RA using the predictive model developed at V.A. Nasonova Reasearch Institute of Rheumatology (IR) and FRAX.
Methods: This monocentric (single-center) prospective study included 70 patients with RA, aged 40 to 80 years. The follow-up period - 8.0 ± 1.2 years; mean age at the baseline was 55.4±7.8 years old; the mean disease duration at

the baseline - 14,7±10,2 years. All patients retrospectively calculated the 10-year probability of fractures and prognostic model developed by the IR.
Results: According to the Fracture Risk Assessment Tool, 32 (46%) patients had a low risk of osteoporotic fractures, 38 (54%) had a high risk. According to the predictive model of IR 33 (47%) patients had a low risk of osteoporotic fractures, 37 (53%) had a high risk. During the follow-up period, osteoporotic fractures were occurred in 18 (26%) patients: 14 (78%) of them had a high risk of fractures according to the predictive IR model, and 13 (72%) patients - according to the Fracture Risk Assessment Tool. Positive and negative predictive value of the Fracture Risk Assessment Tool was 34% and 84%, respectively, of the predictive model of IR - 38% and 88%, respectively. Prognosis of the predictive model of IR in 73% cases coincided with assessing the 10-year probability of fracture.
Conclusion: The predictive model developed at V.A. Nasonova Reasearch Institute of Rheumatology (Russia) showed a higher sensitivity and specificity in determining the risk of osteoporotic fractures in RA patients vs FRAX algorithm.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1717

POS1109 MULTIVARIATE ANALYSIS OF RISK FACTORS FOR REDUCED BONE MINERAL DENSITY ASSESSED WITH RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS)

Z. Batalov[1], M. Nikolov[2], N. Nikolov[2]. [1]*Medical University of Plovdiv, University Hospital Kaspela, Plovdiv, Bulgaria*; [2]*UMBAL Dr. Georgi Stranski, Rheumatology, Pleven, Bulgaria*

Background: Radiofrequency echographic multi spectrometry (REMS) is an innovative radiation-free approach for the assessment of bone mineral density (BMD) at axial sites. The principle of this technology is based on the analysis of native raw unfiltered ultrasound signals, the so called radiofrequency ultrasound signals, acquired during an echographic scan of the lumbar spine and/or femoral neck. [1]. A previous published study showed a high degree of correlation between the T-score values provided by the two techniques-REMS and dual energy X-ray absorptiometry for both lumbar spine and femoral neck [2]. REMS software outputs information about BMD (g/cm2), T-scores, Z-scores [standard deviations (SD)], percentage of body fat and basal metabolic rate [BMR (kcal/daily)] [3].
Objectives: The aim of the current study is to investigate the multivariate significant risk factors for reduced BMD through REMS technology.
Methods: In this study, a total of 273 women with mean age 62 years (yrs.) ± 12 yrs. (range 25-88 yrs.) underwent REMS assessments. Subjects were divided into two groups after acquiring information about the spinal T-scores: 1st group with T-scores ≥-1 SD and 2nd group with T-scores <-1 SD. Age, weight, height, body mass index (BMI), basal metabolic rate (BMR), body fat and menopausal status were the risk factors included in the multivariate statistical analyses. Binary logistic regression was used to assess which are the significant risk factors for T-score <-1 SD. Youden's indices were calculated for selecting the cut-off points for each risk factor.
Results: 273 women had mean weight of 70.5 kg. ± 15.7 kg. (range 39.4-127 kg.), mean height 157.1 cm. ± 8.8 cm. (range 100-182 cm.) and mean body mass index (BMI) 28.6 kg/cm2 ± 6.1 kg/cm2 (range 14.9-47.5 kg/cm2). The mean body fat of the subjects was 37.8% ± 8.8% (range 9-52%) and the mean BMR was 1274.01 kcal/daily ± 163.17 kcal/daily (range 929.7-1908.4 kcal/daily). 260 women (95.2%) were attributed to postmenopausal. Age (p=0.000), BMI (p=0.015), menopause (p=0.006) and BMR (p=0.000) were the multivariate significant risk factors for T-score <-1 SD. Odds ratio for the risk factor age was 1.16, so each added year of the women's age increased the risk for T-score <-1 SD by 1.16%. Women over the age of 65 yrs. showed the highest risk for spinal T-score <-1 SD. The odds ratio of the menopause as a risk factor for spinal T-score <-1 SD was 9.54, so postmenopausal women showed about 9.5 times higher risk of T-score <-1 SD of the lumbar spine than women who still have their period. The increase of BMI by one kg/cm2 decreased the probability of spinal T-score <-1 SD by 0.15% and the increase of BMR by one kcal/daily decreased this probability by 0.02%. Women with BMI above 28.63 kg/cm2 and those with BMR >1331.75 kcal/daily were unlikely to develop spinal T-score <-1 SD.
Conclusion: In the current study, multivariate regression analysis was used to develop a specific REMS-based risk prediction model for spinal BMD, corresponding to T-score <-1 SD. Postmenopausal women over age of 65 yrs. with BMI lower than 28.63 kg/cm2 and BMR <1331.75 kcal/daily were at the highest risk for T-score <-1 SD of the lumbar spine.
REFERENCES:
[1] Pisani P, Renna MD, Conversano F, Casciaro E, Muratore M, et al. (2013) Screening and early diagnosis of osteoporosis through X-ray and ultrasound-based techniques. World J Radiol 5(11): 398-410.
[2] Kirilov N. Analysis of dual-energy x-ray absorptiometry images using computer vision methods. (2020) Trakia Journal of Sciences, Vol. 18, Suppl. 1, pp 114-117.
[3] Kirilova E, Kirilov N, Popov I, Vladeva S. (2019) Bone mineral density of lumbar spine and femoral neck assessed by novel echographic approach-Radiofrequency Echographic Multi Spectrometry (REMS). Clin. Cases Miner. Bone Metab., 16 (1), pp. 14-17.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1768

POS1110 RELIABILITY OF VERTEBRAL FRACTURE ASSESSMENT ON DUAL-ENERGY X-RAY ABSORPTIOMETRY

M. Yasmine[1], S. Mariem[1], S. Miladi[1], A. Fazaa[1], E. Fguiri[1], L. Souebni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: Vertebral Fracture Assessment (VFA) is a new feature available on modern densitometers. Yet, the assessment of vertebral fracture (VF) status has not become standard practice.
Objectives: Our study aimed to evaluate the reliability of VFA as assessed by a rheumatologist and a radiology technician.
Methods: We conducted a cross-sectional study assessing the performance of low-radiation single energy x-ray absorptiometry VFA for the detection of VF. We selected patients who were assessed for osteoporosis according to screening protocols. Bone mineral densitometry was measured using standard methods over the lumbar spine L1-L4, the total proximal femur, and results were expressed as T-scores. All VFA were independently evaluated by 2 experienced readers: a rheumatologist and a radiology technician for the identification of VF (T4-L4). VF was classified according to the Genant grading system: grade 1 for an anterior, mid or posterior reduction of 20–25% in vertebral height; grade 2 for a reduction of 25– 40% and grade 3 for a reduction of more than 40% in vertebral height. A score for the inter-rater reliability between the readers was expressed using the kappa statistic.
Results: One hundred patients were included with a mean age of 66.9 ± 9.5 years [46.7-83] years. There was a female predominance (91%). Nearly half of patients had osteopenia (48.9%), 27.7% had osteoporosis and 23.4% had a normal bone mineral density. On VFA scans, the non-visible vertebra was mostly located in the upper thoracic spine (60%). The mean number of VF was 1.2 [0-3] for both readers. According to the doctor's evaluation, 25% of patients had at least one VF, of which 75.9% had a Genant grade 1, 17.2% had a Genant 2, and 6.9% had a VF grade 3. According to the technician evaluation, at least one VF was found in 36% of patients. A grade 1 was assessed in 91.7% of cases, a grade 2 in 8.3% of patients but no VF grade 3 was assessed. A kappa score for the inter-rater reliability between the readers for VFA was 0.545 (p=0.000). The overall agreement by grade between the readers was 0.785 (p=0,000). The exclusion of non-visible vertebra resulted in a better agreement (k=0.853). Further analysis excluding vertebra T4 to D10, revealed a very good agreement (k=0.9).
Conclusion: Our study showed a low agreement between the readers on VFA and a better agreement when non-visible vertebrae were excluded. Thus, caution should be advocated when relying exclusively on this device.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1866

POS1111 DIAGNOSIS OF OSTEOPOROSIS USING RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS) AT THE LUMBAR SPINE IN PATIENTS WITH DIFFERENT BODY MASS INDEX

B. Cortet[1], E. Dennison[2], A. Diez-Perez[3], M. Locquet[4], M. Muratore[5], D. Ovejero Crespo[3], X. Nogués[3], M. L. Brandi[6,7]. [1]*University-Hospital of Lille, Department of Rheumatology and EA 4490, Lille, France*; [2]*Southampton General Hospital, University of Southampton, MRC Lifecourse Epidemiology Unit, Southapmton, United Kingdom*; [3]*IMIM (Hospital del Mar Medical Research Institute), Centro de Investigación Biomédica en Red en Fragilidad y Envejecimiento Saludable (CIBERFES), ISCIII, Musculoskeletal Research Group, Barcelona, Spain*; [4]*University of Liège, Department of Public Health, Epidemiology and Health Economics, Liège, Belgium*; [5]*Vito Fazzi Hospital, ASL-LE, O.U. of Rheumatology, Lecce, Italy*; [6]*FIRMO Foundation, Florence, Italy*; [7]*The National Observatory on Fragility Fractures, Florence, Italy*

Background: In recent years, the technology based on the analysis of raw ultrasound signals, Radiofrequency Echographic Multi Spectrometry (REMS), has been validated against Dual-energy X-ray Absorptiometry (DXA) for the diagnosis of osteoporosis and risk fracture prediction.
Objectives: The aim of this multicenter observational study was to evaluate the diagnostic performance of REMS with respect to DXA in patients with different body mass index (BMI) categories.
Methods: The inclusion criteria were: Caucasian women; age between 30 and 90 years; referral by their clinician for spinal DXA assessment; absence of significant walking impairment; signed informed consent.

Patients underwent DXA and REMS scans at the lumbar spine, according to the procedures described in Di Paola et al. [1], including an *a-posteriori* quality check of the examinations in order to guarantee the maximum reliability of the diagnostic outputs.

Three groups of patients were considered according to BMI:: underweight (BMI<18.5 kg/m^2), normal weight (BMI≥18.5 kg/m^2 and <25 kg/m^2), and overweight/obese (BMI≥25 kg/m^2). DXA and REMS BMD values were also stratified in 3 diagnostic categories: osteoporotic, osteopenic, or healthy.

The degree of correlation between DXA and REMS BMD values was quantified by calculating Pearson's correlation coefficient (*r*). The diagnostic concordance between REMS and DXA was assessed by Cohen's *K* considering the 3 diagnostic categories. REMS´s sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for discriminating patients with and without osteoporosis were also calculated using DXA outcomes as reference. The same statistics were calculated accepting a 0.3 T-score tolerance on T-score values of borderline cases [1].

Results: Overall, 4282 patients were enrolled and, after the quality check, 3501 couples of scans were included in the analyses. Of these patients, 122 (3.5%) were underweight, 1964 (56.1%) were normal weight, and 1415 (40.4%) were overweight. The results of the diagnostic performance in patients after BMI stratification are reported in Table 1.

Conclusion: We observed an excellent correlation between REMS-based diagnosis with respect to the osteoporosis diagnosis performed by DXA in patients from each BMI category. These results indicate that lumbar spine REMS analysis is a suitable and accurate diagnostic tool for patients with different BMI.

REFERENCES:

[1] Di Paola M et al. Osteoporos Int. 2019 Feb;30(2):391-402.

Table 1. Diagnostic performance of REMS with respect to DXA considered as reference for patients of different body size.

BMI categories	*r*	No tolerance					0.3 T-score tolerance				
		Sens.	Spec.	PPV	NPV	*K*	Sens.	Spec.	PPV	NPV	*K*
Underweight	0.946	97.5	91.5	86.8	98.4	0.89	98.2	93.2	89.2	99.3	0.91
Normal weight	0.946	92.6	94.4	87.0	96.9	0.85	97.5	96.7	92.3	99.0	0.93
Overweight	0.930	86.7	95.8	84.8	96.4	0.82	96.3	97.8	92.1	99.0	0.93

Abbreviations: **BMI** = body mass index; ***r*** = Pearson correlation coefficient; **Sens.** = sensitivity; **Spec.** = specificity; **PPV** = positive predictive value; **NPV** = negative predictive value; ***K*** = Cohen's K.***The authors BC, ED, ADP, ML, MM, XN, DOC are equal contributors listed in alphabetical order.***

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2337

POS1112 COMPARISON OF TWO APPROACHES IN FRACTURES RISK ASSESSMENT IN WOMEN WITH RHEUMATOID ARTHRITIS AND GLUCOCORTICOID USE

N. Grygorieva[1], V. Povoroznyuk[1]. [1]*State Institution "D. F. Chebotarev Institute of Gerontology NAMS of Ukraine", Department of Clinical Physiology and Pathology of Locomotor Apparatus, Kyiv, Ukraine*

Background: Nowadays, FRAX is the most useful tool for osteoporotic fracture risk assessment that is included in many guidelines. Rheumatoid arthritis (RA) and glucocorticoid (CG) use are two crucial factors for osteoporotic fractures included in FRAX algorithm. According to the last ACR guidelines for the treatment of GC-induced osteoporosis [1], it was recommended to divide the patients into three groups of fracture risk (high, medium and low) that have a great impact on treatment decision. Recently, we received own Ukrainian thresholds [2] for the national version of FRAX that are age-dependent and now widely used in clinical practice.

Objectives: Our study was aimed to compare two approaches (ACR-2017 and Ukrainian (2019) recommendations) in fracture risk assessment in women with RA and GC use.

Methods: We examined 195 females with RA aged 40-89 years old who took GC (at dose ≥5 mg/d for ≥3 months) due to RA. The 10-year probabilities of major osteoporotic (MOFs) and hip fractures (HFs) were calculated with and without bone mineral density (BMD) using the Ukrainian FRAX model [3]. The DXA was used to measure the lumbar spine, femoral neck and total body BMDs; T and Z scores were calculated (DISCOVERY Wi, Hologic, Inc., USA).

Results: FRAX indexes for MOFs and HFs without BMD in patients with RA and GC were (Me [25-75Q]) 12.0 [8.1-18.0] and 4.2 [1.7-7.2] %. The correspondent FRAX indexes with BMD were 13.5 [8.5-20.0] and 5.1 [1.8-8.7] %.

50 % of examined women had previous fractures and 20 % had previous vertebral fractures. BMD of the femoral neck consisted of 0.62±0.13 and L1-L4 BMD was 0.85±0.15 g/cm^2. 89 % of females had low BMD at the lumbar spine and / or femoral neck (49 % osteoporosis and 40 % osteopenia).

61 % of women required antiosteoporotic treatment according to ACR-2017 guideline (17.4 % of them a had high risk of MOF and 43.1 % moderate one) without BMD measurement and 64 % of subjects after DXA scan.

According to Ukrainian national guideline, 57 % of patients required antiosteoporotic treatment without BMD measurement and 42 % – after additional DXA examination. After BMD measurement in subjects who required the DXA scan, 78.2 % of females with RA and GC use required antiosteoporotic treatment (additionally to calcium and vitamin D, lifestyle modifications).

Conclusion: Approximately 60 % of subjects with RA and GC use required antiosteoporotic treatment without additional DXA measurement according to correspondent FRAX indexes from both guidelines. The proportion of women requiring treatment after DXA scan is slightly higher according to Ukrainian recommendations. It proves that both of them can be used effectively in daily clinical practice for fracture risk assessment in females with RA.

REFERENCES:

[1] Buckley L, Guyatt G, Fink HA, Cannon M et al. 2017 American College of Rheumatology Guideline for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis & Rheumatology, 2017;69(8), 1521–1537. DOI:10.1002/art.40137

[2] Povoroznyuk V, Grygorieva N, Kanis JA et al. Ukrainian FRAX: criteria for diagnostics and treatment of osteoporosis. Pain. Joint. Spine. 2019;9(4):7-16. DOI: 10.22141/2224-1507.9.4.2019.191921

[3] Povoroznyuk VV, Grygorieva NV, Kanis JA et al. Epidemiology of hip fracture and the development of FRAX in Ukraine. Arch Osteoporos. 2017;12(1):53. DOI: 10.1007/s11657-017-0343-2.

Disclosure of Interests: Nataliia Grygorieva Consultant of: Servier, Redis, Vladyslav Povoroznyuk: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2448

POS1113 ANTIRESORPTIVE THERAPY AFTER TERIPARATIDE DISCONTINUATION – WHEN IS THE BEST TIME TO STARTING IT?

M. Rato[1], F. Oliveira Pinheiro[1], S. Garcia[1], B. M. Fernandes[1], D. Fonseca[2], D. Santos Oliveira[1,3], A. Martins[1], F. R. Martins[4], A. Bernardo[1], R. Ferreira[1], M. Bernardes[1,5], L. Costa[1]. [1]*Centro Hospitalar Universitário de São João, Rheumatology, Porto, Portugal*; [2]*Centro Hospitalar Vila Nova de Gaia/Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; [3]*Faculdade de Medicina da Universidade do Porto - FMUP, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; [4]*Centro Hospitalar Universitário do Algarve - Faro, Rheumatology, Faro, Portugal*; [5]*Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal*

Background: Treatment with teriparatide (TPTD) is associated with reduction of fracture risk in patients with severe osteoporosis. This drug can only be used for up to 2 years. After that a treatment course with antiresorptives should be considered, in order to prevent the rebound of bone turnover observed after TPTD discontinuation. In this regard, interest in sequential osteoporosis therapy has grown in recent years but the ideal timing for starting another treatment after TPTD is not well established.

Objectives: The aim of this study is to assess if the timing of onset of antiresorptive therapy after TPTD discontinuation has implications in total hip bone mineral density (BMD) and in fracture risk.

Methods: We performed a retrospective cohort study that included patients with severe osteoporosis treated with TPTD 20mcg/day for 24 months and followed for at least 2 more years in the rheumatology department of a tertiary university hospital. For analysis, demographic and clinical data and results of dual-energy X-ray absorptiometry (DXA) after cessation of teriparatide were used. For comparison between groups Mann-Whitney U test was used.

Results: Fifty-five patients with osteoporosis, with a median age of 68 (32-85) years, were included. Forty-nine patients were female (89.1%). Nineteen patients (34.5%) had primary osteoporosis and 36 (65.5%) glucocorticoid-induced osteoporosis. The median time for initiating antiresorptive treatment was 7 (0-35) months after cessation of TPTD. Forty-three patients (78.2%) started a bisphosphonate, 6 denosumab (10.9%) and 6 patients did not receive any other treatment. The most prescribed bisphosphonate was zoledronate (69.8%). All patients received calcium and vitamin D supplementation. After completion of TPTD regimen 8 patients experienced at least one fragility fracture (14.5%). At follow-up, 37 (67.3%) of patients underwent DXA on average 30.0±15.4 months after starting antiresorptive agents. The median total hip BMD in patients who started antiresorptive therapy in the first 12 months (inclusive) after cessation of TPTD regime was 0,738 (0.587-0.993) g/cm^2 and the median total hip BMD of patients who started therapy after one year of discontinuation of TPTD was 0.683 (0.390-0.813) g/cm^2. This difference is marginally significant (p=0.067). The median time in starting antiresorptive treatment is higher in patients with new fragility fractures after TPTD than in patients without new fractures however this difference was not statistically significant (10.0 [2-35] vs 6.0 [0-35] months; p=0.393, respectively).

Conclusion: Although this study is unable to show that anti-resorptive treatment should be started in the first year after discontinuation of TPTD, it is promising since the difference between the medians in the total hip BMD values obtained until one year and after one year are marginally significant. These results can be linked to the small sample size and highlight the need for further studies in this area.

REFERENCES:

[1] Napoli N, Langdahl BL, Ljunggren Ö, Lespessailles E, Kapetanos G, Kocjan T, Nikolic T, Eiken P, Petto H, Moll T, Lindh E, Marin F. Effects of Teriparatide in Patients with Osteoporosis in Clinical Practice: 42-Month Results During and After Discontinuation of Treatment from the European Extended Forsteo® Observational Study (ExFOS). Calcif Tissue Int. 2018 Oct;103(4):359-371. doi: 10.1007/s00223-018-0437-x. Epub 2018 Jun 16. PMID: 29909449; PMCID: PMC6153867.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2964

POS1114 INFECTION RISK AMONG RHEUMATIC PATIENTS RECEIVING DENOSUMAB THERAPY: SINGLE CENTRE EXPERIENCE

K. L. Ng[1], M. Mohd Zain[1], I. S. Lau[1]. [1]*Selayang Hospital, Rheumatology, Batu Caves, Malaysia*

Background: Osteoporosis (OS) is common in rheumatic diseasas (RMD). OS fracture leads to morbidity and premature mortality. The treatment for OS is well established with good long term safety profile. Oral bisphosphonate (BIS) is recommended as initial treatment option for both postmenopausal and glucocorticoid induced OS. Denosumab (DSB), is the noninferior alternative option. Despite its efficacy, DSB was linked with elevated infection risk in non RMD. Yet, data in RMD is lacking.

Objectives: To determine the infection risk and associated factors in RMD patients receiving DSB.

Methods: This is retrospective cohort study. Data was extracted from medical database (between Jan 2010 & Dec 2018) at Selayang Hospital, Malaysia. Descriptive statistical analysis, logistic regression (LR) and cox (proportional hazard) regression [CPHR] were the analysis methods.

Results: 50 cases were analysed. 96% were female. The median age was 72.5 ± 12.7 years. The primary rheumatological disorders were rheumatoid arthritis (48%), OS (24%) and systemic lupus erythematosus (10%). 92% had ≥ 1 comorbidity including metabolic/cardiovascular diseases (74%), chronic lung diseases (CLD) (40%) and diabetes mellitus (DM) (22%). 54% had disease modifying anti rheumatic drug (DMARD) therapy; majority (59.2%) received single conventional synthetic DMARD. Only 7.4% received combination biologic DMARD therapy. 28% had received prednisolone therapy, with dose < 7.5mg OD in 78.6%.

The median age at DSB initiation was 71 ± 12.4 years. 38% had fracture history and 88% had received previous OS treatment.

In total, 13 infection episodes were recorded. The infection risk was 26% & incidence rate was 134 cases per 1000 person-years. 84.6% required hospitalisation and 38.5% were severe cases. The mortality rate was 23.1%. The mean DSB treatment duration to first infection was 15.46 ± 11.9 months.

Univariate LR showed infection risk and hospitalisation were higher with longer DSB treatment duration, OR 1.062 (95% CI: 1.010 - 1.117), p = 0.018) & OR 1.057 (95% CI: 1.003 - 1.114, p = 0.037), respectively. These risks were lower in absence of steroid use, OR 0.2 (95% CI: 0.051 - 0.784, p = 0.021) and OR 0.215 (95% CI: 0.052 - 0.889, p = 0.034), respectively. Additionally, infection risk was lower in absence of CLD, OR 0.188 (95% CI: 0.048 - 0.742, p = 0.017) and hospitalisation was lower without concomitant DM, OR 0.050 (95% CI: 0.050 — 0.950, p = 0.043). Yet, multivariate LR did not infer the above predictions, after adjustment made for age, gender, rheumatological diseases, comorbidity, DMARD therapy and steroid dosing. For severe infection and case fatality, no predictive factors were identified.

CPHR showed patients without steroid use had lower fatality risk, HR 0.077 (95% CI: 0.007 - 0.864, p = 0.038). With confounding factors (age, gender, previous infection and comorbidity), the observed difference was insignificant.

Conclusion: Risk of infection and hospitalisation could be higher in rheumatic patients receiving longer DSB treatment duration. Concomitant comorbidities (CLD and DM) might increase the risk of infection and/or hospitalisation.

REFERENCES:

[1] Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med 2009;361:756–65.

[2] Watts NB, Roux C, Modlin JF, Brown JP, Daniels A, Jackson S, Smith S, Zack DJ, Zhou L, Grauer A, Ferrari S. Infections in postmenopausal women with osteoporosis treated with denosumab or placebo: coincidence or causal association? Osteoporos Int. 2012;23(1):327–337.

[3] Prabhakaran S, Pritchard C. Comparison of infection rates in patients receiving denosumab, denosumab and biologics and biologics alone in a suburban rheumatology clinic [abstract]. Arthritis Rheumatol 2014;66 Suppl 10:S409.

[4] Bray V, Bagley A, West S, Etzel C, Kremer J, Kolfenbach J. Infection risk among patients receiving concurrent denosumab and biologic or non-biologic DMARD therapy: An analysis of the Consortium

Acknowledgements: We would like to thank the Director General of Health Malaysia for his permission for this poster presentation.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3038

POS1115 DESCRIPTIVE STUDY OF THE PERCEPTIONS AND PREVENTIVE PRACTICES OF POSTMENOPAUSAL TUNISIAN WOMEN REGARDING OSTEOPOROSIS

S. Ben Jemaa[1], Y. Mejdoub[2], H. Fourati3, J. Damak[2], S. Baklouti3. [1]*Hedi Chaker Hospital, Rheumatology, SFAX, Tunisia*; [2]*Hedi Chaker Hospital, Community Medecine, SFAX, Tunisia*; [1]*Hedi Chaker Hospital, Rheumatology, SFAX, Tunisia*

Background: Due to their serious consequences affecting quality of life, prevention of osteoporosis is considered a priority. Thus, identifying the level of knowledge is useful in developing effective interventions and in guiding public health programs to prevent osteoporosis.

Objectives: The aim of this study is to describe beliefs and practices of menopaused Tunisian women related to health and osteoporosis in order to develop effective and targeted interventions for the prevention of this disease.

Methods: A descriptive cross-sectional study was conducted among menopaused Tunisian women who consult the basic health center in the area of Sfax region in Tunisia. Data collection include socio-demographic characteristics, the “osteoporosis health belief scale” developed by Kim and his colleagues and the daily calcium intake which was calculated by a questionnaire developed by Patrice Fardellone.

Results: We have included 170 women. The mean age was 58.92 ± 9.07 years. Seventy-seven percent of women were housewives, 14.7% were active and 8.3% were retired. Seventy-five percent were married. Forty-two women (24.7%) were illiterate, sixty-three (37.1%) were at primary level and 33.5% were at secondary level. One hundred twelve women (65.3%) live in an urban environment, against 34.7% who belong to a rural environment.

The level of perception of osteoporosis was very altered in 22.9%, altered in 32.4% and moderately altered in 31.8% of women. Women’s perceptions of the benefits of physical exercise and calcium intake were moderately altered in 42.4% and 51.2%, respectively. For obstacles to the practice of physical exercise, the level of perception was altered in 43.5% of women. Regarding the obstacles to calcium intake, the perceptions of our population were altered in 32.9% of cases.

The daily intakes of calcium vary from 215 to 1444 mg per day with an average of 620.20 ± 204.523 mg / day. Only eight women (4.7%) had sufficient daily intake.

Conclusion: Our study showed that all subscale of the “osteoporosis health belief scale” were altered. Promotion programs should aim at creating a supportive physical and social environment for the adoption of safer behaviors and especially education must be targeted.

REFERENCES:

[1] Belgacem, A. Nouira, et S. Soussi, « Les perceptions des femmes tunisiennes selon le modèle des croyances liées à la santé et leurs pratiques relativement à l’ostéoporose », Pan Afr Med J, vol. 23, 2016.

[2] H. Ahmadieh, A. Basho, A. Chehade, A. Al Mallah, et A. Dakour, « Perception of peri-menopausal and postmenopausal Lebanese women on osteoporosis: A cross-sectional study », Journal of Clinical & Translational Endocrinology, vol. 14, p. 19-24, déc. 2018.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3571

POS1116 ENHANCING OSTEOPOROSIS MANAGEMENT: THE CONTRIBUTION OF FRAX® AND VFA IN TUNISIAN WOMEN

C. Daldoul[1], N. El Amri[1], S. Laataoui[1], K. Baccouche[1], H. Zegaloui[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*

Background: The FRAX® is a tool proposed by the World Health Organization (WHO) to calculate 10-year fracture risk of hip fracture and major osteoporotic fractures. The utility of this tool is to help treatment decision when it is litigious. Previous low trauma fracture represent a factor in FRAX® calculation. However, asymptomatic osteoporotic vertebral fractures (VF) identified on X-rays or Vertebral Fracture Assessment (VFA) scans are rarely included. To the best of our knowledge, there was no previous evaluation of fracture risk in Tunisian women.

Objectives: To compare hip fracture risk and major osteoporotic fractures risk using the FRAX® tool, without and with the consideration of asymptomatic VF on VFA. To evaluate the impact of FRAX® calculation and asymptomatic VF identified on VFA on osteoporosis management.
Methods: We conducted a cross-sectional study over a period of 5 months at the rheumatology department. The study included post-menopausal women without a previous diagnosis of VF referred for BMD (Bone mineral density) measurement. Each participant had a BMD assessment and a VFA scan to detect VF. The FRAX® was calculated using femoral neck BMD initially without then with consideration of VF. The change of therapeutic decision was assessed after taking into consideration FRAX® and the VFA results.
Results: The study included 210 post-menopausal women with a mean age of 61.5±8.5 years. The mean BMI was 31.04±5.52 kg/m^2. One women was a current smoker and alcohol intake was not found in our sample. Thirty-seven percent of our participants had at least one fragility fracture. A severe fragility fracture was recorded in 10.5% and a previous hip fracture was reported in 5.24%. An early menopause was found in 19.5% of our women. Twenty percent of our population were receiving corticosteroids and 8.2% of our population had rheumatoid arthritis. The mean vertebral and total hip BMD was 0.955±0.165 g/cm2 and 0.850±0.135 g/cm2 respectively. Osteoporosis and low BMD were found in respectively 50% and 34.28%. The median probability of major osteoporotic fracture for our population was 1.5% with an interquartile range from 0.9 to 2.5% without using VFA data and 1.65% with an interquartile range from 1 to 2.6% while taking into consideration VFA results and the difference was statistically significant (p<0.0001). The median probability of hip fracture for our population was 0.4% with an interquartile range from 0.1 to 0.9% without using VFA data and 0.4% with an interquartile range from 0.1 to 1% while taking into consideration VFA results and the difference was statistically significant (p<0.0001). In all patients, the FRAX® was under the threshold intervention even after including the asymptomatic VF and it did not change the therapeutic decision. The presence of asymptomatic VF on VFA changed the therapeutic decision in 15% and indicated an anti-osteoporosis drug therapy.
Conclusion: VFA scanning helped in the therapeutic decision in 15% of our population. In this evaluation, we showed that a comprehensive fracture risk pathway incorporating VFA has enhanced diagnosis of vertebral fractures and improved targeting of treatment better than FRAX® tool.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4195

POS1117 AGREEMENT BETWEEN VERTEBRAL FRACTURE ASSESSMENT AND RADIOGRAPHIC SCANS FOR THE DIAGNOSIS OF VERTEBRAL FRACTURE

C. Daldoul[1], N. El Amri[1], K. Baccouche[1], H. Zegaloui[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*

Background: Conventional radiography of thoracic and lumbar spine are considered the gold-Standard imaging for vertebral fracture (VF) identification. However, there was a growing interest in the use of vertebral fracture assessment (VFA) as a low radiation tool. In fact, the radiation dose for VFA is about 3 micro Sievert compared to 600 Sievert for lateral standard radiography. Moreover, it costs 2-times less than X-rays. However, the advantage granted by a lower radiation dose is unfortunately counterbalanced by higher noise rates and therefore lower image quality.
Objectives: The aim of this study was to investigate the diagnostic accuracy of VFA compared to lateral spine radiographs.
Methods: We conducted a cross-sectional study over a period of 5 months at the rheumatology department. The study included post-menopausal women without a previous diagnosis of VF. Each participant had a BMD assessment, a VFA scan and a lateral thoracolumbar X-rays (Rx) to detect VF. VF were identified according the Genant semi-quantitative method. The number of unreadable vertebrae were compared between VFA and Rx using a McNemar test. Cohen's kappa coefficient, the sensitivity (Se), the specificity (Sp), the positive (PPV) and negative predictive (NPV)values at each vertebral level and at the individual level were calculated with 95% confidence interval (95% CI) to analyze the agreement between VFA and Rx results.
Results: The study included 62 patients were collected. The mean age was 62.03±7.84 years. the mean body mass index (BMI) was 29.99±5.13 kg/m^2 and the mean menopausal duration was 15.7±8.28 years. Parental history of hip fracture and prior history of fragility fracture were recorded in 25.9% and 40.3% respectively. A premature menopause, Rheumatoid arthritis and use of corticosteroids were found in 12.9%, 4.8% and 19.4% respectively. A historical height loss of more than 4cm and a prospective height loss of more than 2 cm were reported in 21% and 38.7% respectively. Using VFA, 22.6% of our population had at least one VF≥ grade2 and 33.9% had at least one VF≥grade1. Using Rx, 19.4% of our population had at least one VF≥ grade2 and 25.8% had at least one VF≥grade1. Among all vertebral levels, no statistically significant difference was found while comparing the number of unreadable vertebrae on VFA and radiographs. Taking into consideration VF≥grade2, there was an almost perfect agreement between VFA and Rx (k=0.806, p<0.001); the Se, Sp, PPV and NPV of VFA were respectively 91.7% (95% CI 59.8-99.6), 94%(95% CI 82.5-98.4), 78.6% (95% CI 48.8-94.3) and 97.9%(95% CI 87.5-99.9). . Taking into consideration VF≥grade1, there was a moderate agreement between VFA and Rx (k=0580, p<0.001); the Se, Sp,PPV and NPV of VFA were respectively 81.3% (95% CI 53.7-95),82.6% (95% CI 68-91.7), 61.9% (95% CI 38.7-81) and 92.7% (95% CI 79-98.1). At the vertebral level and when including only grade 2 and 3 VF, the Se, Sp, PPV of VFA were 100% (95% CI 82.2-100), 98.9% (95% CI 97.7-99.5), 74.2% (95% CI 55.1-87.5) and 100% (95% CI 99.3-100) respectively. At the vertebral level, the Se, Sp, PPV and NPV of VFA in detection of grade≥1 VF were 65.8% (95% CI 48.6-79.9), 98.3% (95% CI 96.9-99.1), 67.6% (95% CI 50.1-81.4) and 98.1% (95% CI 96.8-99.0) respectively. The analysis by vertebral level revealed substantial to almost perfect agreement for all levels except for T4 and T6 where the test was not applicable. There was a perfect agreement for T5, T8, L3 and L4 vertebrae.
Conclusion: VFA showed a high diagnostic performance compared to Rx. One interesting finding is that the NPV of VFA is very high at the vertebral and the individual level and either grade 1 VF were took into consideration or not. This means that a normal VFA can formally rule out the presence of VF.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4206

POS1118 THE RELEVANCE OF OSTEOPOROSIS DIAGNOSIS AND TREATMENT FOR DOCTORS WORKING IN THE FIELD OF PHYSICAL AND REHABILITATION MEDICINE

L. Marchenkova[1], V. Vasileva[1]. [1]*National Medical Research Center for Rehabilitation and Balneology of Ministry of Health of Russian Federation, Rehabilitation Department for Somatic Patients, Moscow, Russian Federation*

Background: There is a high prevalence of osteoporosis (OP) among patients of the older age undergoing rehabilitation. Therefore, it is obvious that physicians working in the field of physical and rehabilitative medicine should be well oriented in this medical problem.
Objectives: to study the relevance of the problem of osteoporosis (OP) for physicians working in the field of physical and rehabilitation medicine, their awareness of the main methods of diagnosis, treatment and prevention of this disease, as well as the frequency of their use in daily clinical activities.
Methods: A cross-type study was carried out using a questionnaire survey. The study included 157 doctors (M-34, F-123) of 8 medical specialties working in 27 specialized medical institutions on the profile of "medical rehabilitation. The questionnaire for doctors consisted of 21 items of special questions.
Results: 90.45% of the surveyed doctors believed that the problem of OP is relevant for their clinical activities, 100% of the respondents indicated that the presence of OP significantly affects the rehabilitation prognosis and 95.54% - on the degree of effectiveness of medical rehabilitation. According to the respondents, patients with OP make up on average 30.0% [20.0; 50.0] (0-90) of the total flow of patients. 92.36% (145/157) of doctors indicated that they know the risk factors for OP, 98.73% (155/157) - methods for diagnosing OP, 68.79% (108/157) - methods for treating OP, 80.25 % (126/157) - methods of preventing OP, 47.13% (74/157) - what is FRAX. However, 35.01% (55/157) of the respondents considered their level of awareness of the problem sufficient for managing patients with OP. Diagnostic procedures for OP are recommended by all endocrinologists (100%) and the majority of traumatologists (72.73%), gynecologists (66.67) and cardiologists (64.28%), as well as on average half (50%) neurologists and therapists. Endocrinologists (100%), gynecologists (66.67%) and therapists (60%) are mainly involved in the treatment of OP. 32.48% (51/157) of physicians have ever referred their patients to a bone mineral density assessment.
Conclusion: Conclusion. The problem of OP is relevant for the clinical activities of specialists in physical and rehabilitation medicine, and there is the need for advanced training on the problem of OP among these specialists.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4274

POS1119 A SINGLE DOSE OF ZOLEDRONATE INDUCES MODIFICATIONS OF SERUM VEGF IN OSTEOPOROTIC POSTMENOPAUSAL WOMEN

F. Bellone[1], N. Morabito[1], A. Gaudio[2], A. Sottile[1], S. Loddo[1], F. Corica[1], A. Catalano[1]. [1]*University of Messina, Department of Clinical and Experimental Medicine, Messina, Italy*; [2]*University of Catania, Department of Clinical and Experimental Medicine, Catania, Italy*

Background: Zoledronate (Zol) is an aminobisphosphonate commonly used to treat osteoporosis and other benign and malignant skeletal diseases. Exposure to bisphosphonates has been previously associated with the risk of osteonecrosis of the jaw (BRONJ), a rare but serious side effect. In cancer patients,

the Vascular Endothelial Growth Factor (VEGF) has been advocated to take part to BRONJ pathogenesis via interfering with angiogenesis. No information is currently available on the VEGF concentrations after Zol administration for osteoporosis.

Objectives: To explore change of VEGF concentrations after Zol administration in postmenopausal women with osteoporosis.

Methods: A total of twenty-eight postmenopausal women with osteopenia or osteoporosis and at least one prevalent vertebral fracture were recruited and randomized in two groups. Eighteen women received a single i.v. dose of Zol 5 mg, while the other ten served as controls. Serum samples were collected at baseline, after 3 and 30 days, for repeated measurements of VEGF, and measurement of bone turn over markers and 25-hydroxyvitamin D (25(OH)D).

Results: VEGF levels increased significantly after 3 days in women receiving Zol; then levels decreased after 30 days compared with VEGF concentrations at both day-3 and baseline (-18% at day-30 vs. baseline, p=0.01). 25(OH)D level, a surrogate of vitamin D status, was associated with VEGF change at the end of the study (r=0.29, p=0.028), and this association was maintained also after correcting for age, BMI, time since menopause, femoral neck BMD, osteocalcin, C-terminal telopeptide of collagen type 1 and baseline levels of VEGF (β=1.7, SE=0.71, p=0.03).

Conclusion: Zol administration induced a reduction of circulating VEGF in postmenopausal women treated for osteoporosis, and vitamin D status has been showed to modulate this change. Further studies in this setting of women are needed to define whether VEGF modifications may predict the risk of BRONJ.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4312

Crystal diseases, metabolic bone diseases other than osteoporosis

POS1120 PRESENCE OF TOPHI IS ASSOCIATED WITH A RAPID DECLINE IN THE RENAL FUNCTION IN PATIENTS WITH GOUT

Y. J. Oh[1], K. W. Moon[2]. [1]*Kangwon National University Hospital, Division of Rheumatology, Department of Internal Medicine, Chuncheon, Korea, Republic of (South Korea)*; [2]*Kangwon National University Hospital, Division of Rheumatology, Department of Internal Medicine, Chuncheon, Korea, Republic of (South Korea)*

Background: Gout is the most common inflammatory arthritis resulting from a chronic deposition of MSU crystals in the joints and other soft tissues. After the process of repeated tissue damage and repair due to gout, tophi could be formed around the affected joints. Intra-articular tophi may sometimes result in bone destruction, joint deformities, and dysfunction which can adversely affect the patient's quality of life. Furthermore, early-onset tophaceous gout patients are more likely to develop renal dysfunction, however, few studies have investigated if the presence of tophi is related with the progression of renal dysfunction in gout patients.

Objectives: We aimed to compare clinical characteristics of patients with and without tophi at the time of the diagnosis of gout and investigate the effect of tophi on the renal function in gout patients.

Methods: Data of 257 patients who were first diagnosed with gout at the Kangwon National University Hospital from January 2012 to December 2018 were retrospectively studied. Patients were divided into 2 groups according to the presence of tophi at the diagnosis. We compared clinical characteristics and the progression of renal dysfunction between the two groups.

Results: Of all patients, 66 (25.5%) initially presented with tophi. Patients with tophi were older, had a longer duration of symptoms, and had a higher prevalence of multiple joint involvement than those without tophi. The decline in the eGFR was more prominent in patients with tophi than in those without (-4.8±14.5 ml/min/1.73m^2 *vs*. -0.7±11.9 ml/min/1.73m^2, respectively; *P*=0.039). In multivariate logistic regression analysis, a prolonged symptom duration (odds ratio [OR], 1.010; 95% confidence interval [CI], 1.004–1.017; *P*=0.001) and multiple joint involvement (OR, 3.027; 95% CI, 1.831–5.004; *P*<0.001) were significantly associated with increased risk of formation of tophi. The presence of tophi was significantly associated with a rapid decline in the eGFR (β=-0.141; *P*=0.035).

Conclusion: A prolonged symptom duration and multiple joint involvement were independent risk factors for tophi as the presenting symptom in gout patients. The presence of tophi was associated with a declining renal function. Therefore, an early diagnosis and active treatment are important in tophaceous gout.

REFERENCES:

[1] Bardin T, Richette P. Definition of hyperuricemia and gouty conditions. Curr Opin Rheumatol 2014;26:186-91.
[2] Liu F, Du GL, Song N, Ma YT, Li XM, Gao XM, et al. Hyperuricemia and its association with adiposity and dyslipidemia in Northwest China: results from cardiovascular risk survey in Xinjiang (CRS 2008-2012). Lipids Health Dis 2020;19:58.
[3] Dalbeth N, Merriman TR, Stamp LK. Gout. Lancet 2016;388:2039-52.
[4] Ruoff G, Edwards NL. Overview of Serum Uric Acid Treatment Targets in Gout: Why Less Than 6 mg/dL? Postgrad Med 2016;128:706-15.
[5] Bieber A, Schlesinger N, Fawaz A, Mader R. Chronic tophaceous gout as the first manifestation of gout in two cases and a review of the literature. Semin Arthritis Rheum 2018;47:843-8.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.50

POS1121 DEMOGRAPHICS, COMORBIDITIES, AND RENAL FUNCTION OF UNCONTROLLED GOUT PATIENTS WHO RECEIVED PEGLOTICASE: FINDING FROM A LARGE US CLAIMS DATABASE

C. Vesel[1], A. Morton[2], M. Francis-Sedlak[1], B. Lamoreaux[1]. [1]*Horizon Therapeutics plc, Medical Affairs, Deerfield, United States of America*; [2]*Michigan State University, School of Osteopathic Medicine, Internal Medicine, East Lansing, United States of America*

Background: NHANES data indicate that approximately 9.2 million Americans have gout,[1] with a small subset having uncontrolled disease.[2] Pegloticase is a PEGylated recombinant uricase enzyme indicated for treating uncontrolled gout that markedly reduces serum uric acid levels (sUA)[3] and resolves tophi in treatment responders.[4] Despite pegloticase availability in the US for many years, real world demographics of pegloticase users in the treatment of uncontrolled gout have not been previously reported in a population-based cohort.

Objectives: This study utilized a large US claims database to examine demographics and co-morbidities of uncontrolled gout patients treated with pegloticase. Kidney function before and after pegloticase treatment and concomitant therapy with immunomodulators were also examined.

Methods: The TriNetX Diamond database includes de-identified data from 4.3 million US patients with gout (as of September 2019), including demographics, medical diagnoses, laboratory values, procedures (e.g. infusions, surgeries), and pharmacy data. Patients who had received ≥1 pegloticase infusion were included in these analyses. The number of infusions was evaluated for a subgroup of patients who were in the database ≥3 months before and ≥2 years after the first pegloticase infusion (i.e. first infusion prior to September 2017) to ensure only complete courses of therapy were captured. In this subpopulation, kidney function before and after pegloticase therapy was examined, along with the presence of immunomodulation prescriptions (methotrexate, mycophenolate mofetil, azathioprine, leflunomide) within 60 days prior to and 14 days after the first pegloticase infusion.

Results: 1494 patients treated with pegloticase were identified. Patients were 63.1 ± 14.0 years of age (range: 23–91), mostly male (82%), and white (76%). Mean sUA prior to pegloticase was 8.7 ± 2.4 mg/dL (n=50), indicating uncontrolled gout in the identified population. The most commonly reported comorbidities were chronic kidney disease (CKD, 48%), essential hypertension (71%), type 2 diabetes (39%), and cardiovascular disease (38%), similar to pegloticase pivotal Phase 3 trial populations. In patients with pre-therapy kidney function measures (n=134), pre-treatment eGFR averaged 61.2 ± 25.7 ml/min/1.73 m^2, with 44% having Stage 3-5 CKD. In patients with complete therapy course capture and pre- and post-therapy eGFR measures (n=48), kidney function remained stable (change in eGFR: -2.9 ± 18.2 ml/min/1.73 m^2) and CKD stage remained the same or improved in 81% of patients. In 791 patients with complete treatment course capture, patients had received 8.7 ± 13.8 infusions (median: 3, IQR: 2-10). Of these, 189 (24%) patients received only 1 pegloticase infusion and 173 (22%) received ≥12 infusions. As the data cut-off for this analysis pre-dated emerging data on the use of immunomodulation as co-therapy, only 19 of 791 (2%) patients received immunomodulation co-therapy with pegloticase.

Conclusion: This relatively large group of patients with uncontrolled gout treated with pegloticase had similar patient characteristics of those studied in the phase 3 randomized clinical trials. Patients with uncontrolled gout are significantly burdened with systemic co-morbid diseases. The majority of patients had stable or improved kidney function following pegloticase treatment. As these results reflect patients initiating treatment prior to 2018, before co-treatment with immunomodulation was introduced, this cohort only included a small percentage of patients who were co-treated with an immunomodulator. Future studies using more current datasets are needed to evaluate real world outcomes in patients treated with pegloticase/immunomodulator co-therapy and to evaluate the impact of systemic co-morbid diseases.

REFERENCES:

[1] Chen-Xu M, et al. *Arthritis Rheumatol* 2019 71:991-999.
[2] Fels E, Sundy JS. *Curr Opin Rheumatol* 2008;20:198-202.
[3] Sundy J, et al. *JAMA* 2011;306:711-720.
[4] Mandell BF, et al. *Arthritis Res Ther* 2018;20:286.

Disclosure of Interests: Claudia Vesel Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Allan Morton Speakers bureau: Sanofi, Amgen, and Horizon, Megan Francis-Sedlak Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Brian LaMoreaux Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc.

DOI: 10.1136/annrheumdis-2021-eular.95

POS1122 PRELIMINARY FINDINGS OF THE PROTECT CLINICAL TRIAL: PEGLOTICASE EFFICACY AND SAFETY IN KIDNEY TRANSPLANT RECIPIENTS

A. Abdellatif[1], L. Zhao[2], P. M. Peloso[2], K. Cherny[2], B. Marder[3], J. Scandling[4], K. Saag[5]. *[1]Baylor College of Medicine, Nephrology, Houston, United States of America*; *[2]Horizon Therapeutics plc, Research and Development, Deerfield, United States of America*; *[3]Horizon Therapeutics plc, Medical Affairs, Deerfield, United States of America*; *[4]Stanford Medicine, Nephrology, Standford, United States of America*; *[5]University of Alabama, Clinical Immunology and Rheumatology, Birmingham, United States of America*

Background: The prevalence of gout is high in kidney transplant (KT) recipients (up to 13%), largely because of decreased kidney function and calcineurin inhibitor use.[1] Residual chronic kidney disease (CKD) leading to decreased urate lowering therapy clearance and drug interactions make managing gout in KT recipients challenging. Studies show that successful treatment with pegloticase, a pegylated uricase, leads to marked reductions in serum uric acid (sUA)[2] and a subsequent decrease in overall urate load and tophi burden.[3] However, pegloticase use in solid organ transplant recipients has not been systematically studied or well-characterized in the literature.[4,5]

Objectives: To examine the safety and efficacy of pegloticase in KT recipients with uncontrolled gout.

Methods: This ongoing multicenter, open-label, efficacy and safety study of pegloticase in KT recipients (NCT04087720) included patients with uncontrolled gout sUA ≥7 mg/dL, urate lowering therapy [ULT] contraindication/inefficacy, and with either visible tophi, chronic gouty arthritis, or ≥2 flares in past year, who were KT recipients (KT >1 year prior), had a functioning graft (estimated glomerular filtration rate [eGFR] ≥15 ml/min/1.73m^2), and were on a stable immunosuppressant regimen. Pegloticase (8 mg infusion) was administered biweekly for 24 weeks (12 infusions) followed by a safety visit 30 days after the last infusion and 3-month post-treatment follow up visit. The primary endpoint was proportion of patients who were serum uric acid responders during Month 6 (sUA <6 mg/dL for ≥80% of time). Change from baseline (CFB) at 24 weeks was also evaluated for sUA, renal function, and health assessment questionnaire (HAQ) disability index (DI, maximum = 3) and pain (maximum = 100).

Results: Preliminary findings of this study included 15 patients (12 male, 53.5±11.0 years of age) with uncontrolled gout (6.2±6.0 years since diagnosis) who had received a donor kidney 15.1±6.6 years earlier. At the time of analysis, 5 patients had completed the 24-week treatment period and 8 remained on therapy (last visit sUA <0.1 mg/dL in 6 patients, 1 had sUA of 7.4 mg/dL, 1 only received first infusion), and 2 had discontinued treatment (sUA rise [n=1], COVID-19 concerns [n=1]). Of the 5 patients who completed 24 weeks of therapy, all met response criteria and sUA was below detection limits (CFB: -10.2±1.3 mg/dL, baseline [BL]: 10.2±1.3 mg/dL). Patients also had less pain (HAQ-pain CFB: -33.6±22.2, BL: 35.9±22.0; n=5) and disability (HAQ-DI CFB: -0.3±0.6, BL: 0.7±0.8; n=5) at 24 weeks compared to BL. eGFR remained stable during 24 week treatment (eGFR CFB: -0.2±6.3 ml/min/1.73 m^2, BL: 40.9±14.4 ml/min/1.73 m^2; n=5). Urine albumin-to-creatinine ratio showed improvement at 24 weeks (CFB: -223±405 mg/g, BL: 664±870 mg/g; n=5). 80% of patients experienced an AE, and 4 SAEs (duodenal ulcer, cellulitis, dyspnea, skin bacterial infection) deemed unrelated to pegloticase were reported. AEs that occurred in >1 patient included gout flare, pyrexia, arthralgia, and nasal congestion. No anaphylaxis or infusion reactions occurred.

Conclusion: Initial findings suggest that pegloticase therapy is effective at reducing sUA in most KT recipients while preserving renal function. Results suggest that in the setting of profound urate lowering with pegloticase in KT patients, eGFR remains stable and patients experience clinically beneficial reductions in pain and disability with an absence of unexpected safety findings.

REFERENCES:

[1] Clive DM. *J Am Soc Nephrol* 2000;May11(5):974-9.
[2] Sundy JS, et al. *JAMA* 2011;306:711-720.
[3] Mandell BF, et al. *Arthritis Res Ther* 2018;20:286.
[4] Freyne B. *Transplant Proc* 2018;50:4099-101.
[5] Hershfield MS, et al. *Arthritis Res Ther* 2014;16:R63.

Disclosure of Interests: Abdul Abdellatif Speakers bureau: Horizon Therapeutics plc, Consultant of: Horizon Therapeutics plc, Lin Zhao Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Paul M. Peloso Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Katya Cherny Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Brad Marder Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, John Scandling Consultant of: Horizon Therapeutics plc, Kenneth Saag Consultant of: Arthrosi, Atom Bioscience, Horizon, LG Pharma, Mallinkrodt, SOBI, Takeda, Grant/research support from: Horizon, SOBI, Shanton.

DOI: 10.1136/annrheumdis-2021-eular.97

POS1123 DISORDERS OF URODYNAMICS AND PARENCHYMA CONCENTRATION FUNCTION IN PATIENTS WITH ARTERIAL HYPERTENSION AND GOUT

M. Gromova[1], V. Tsurko[2], O. Kisliak[1], A. Kashkadayeva[3], S. Averinova4. *[1]Pirogov Russian National Research Medical University (Pirogov Medical University),The Department of Faculty Therapy of the Medical Faculty, Moscow, Russian Federation*; *[2]I.M. Sechenov First Moscow State Medical University (Sechenov University),The Department of General Medical Practice of the Institute of Postgraduate Education, Moscow, Russian Federation*; *[3]N.N.Blokhin National Medical Research Center of Oncology, Laboratory of Radioisotope Diagnostics, Moscow, Russian Federation*; *[3]N.N.Blokhin National Medical Research Center of Oncology, Laboratory of Radioisotope Diagnostics, Moscow, Russian Federation*

Background: The combination of arterial hypertension and gout increases the risk of developing chronic kidney disease in patients.

Objectives: To assess urodynamics and concentration function of the renal parenchyma in patients with arterial hypertension and gout.

Methods: We examined 87 patients with arterial hypertension and gout. 83% of the patients were men with a mean age of 55.4±12.3 years. Grade I arterial hypertension was detected in 43.7% of patients, grade II was in 36.9% and grade III was in 19.3%. The duration of arterial hypertension was 8 [4; 11] years. All the patients had chronic gouty arthritis. 30% of the patients had tophi. The duration of gout was 7 [2; 10] years. Markers of renal lesions, urine sediment and GFR calculation were assessed in all the patients. All the patients were performed a modern systems analysis of nephrological conditions based on comprehensive renoscintigraphy (SENS-CRS) which allows to make an in-depth differential analysis of the renal parenchyma and thus reveals abnormalities in the upper and lower urinary tract function with a minimum of radiation exposure of 0.6 mSv per patient.

Results: Using the standard method of GFR calculation with CKD-EPI formula we found that 10 patients (11.3%) had no signs of CKD (GFR over 90 ml/min); 56 patients (64.5%) had I-II stage of CKD (GFR over 60 ml/min) 21 patients (24.2%) had III-IV stage of CKD (GFR less than 60 ml/min).

The patients were divided into two groups for a differentiated assessment of urodynamics. Group I consisted of 66 patients with a GFR of more than 60 ml/min and Group II consisted of 21 patients with a GFR of less than 60 ml/min. The comparison of the two groups revealed abnormalities in urodynamics. In Group 1 arterial blood flow in the parenchyma (A 14.5±6.8 sec) was slowing down against the background of normal venous outflow (V 17.8%±9.2%). Concentration function of the kidneys was sufficient (Gren 17.6±5.2 o.e.). The total excretion rate of labeled urine from the two kidneys decreased to D = 56.5% ± 16.1% during its transition from the cortical to the cerebral layer of the renal parenchyma. The indixes of the relative urinary stasis in the renal calyx-pelvis system exceeded the standard ones on average by 2 times (KC 4.8 ± 3.2; KP 7.0 ± 4.2), which indicated stagnant disorders in the kidneys, hidden from conventional diagnostic methods. The patients in Group II had those abnormalities even more expressed (A 12.4±4.5 sec, V 12.8%±9.4%, D 51.9%±15.4%, KC 5.0±3.3; KP 9.5±5.2).

16 patients under follow-up who had arterial hypertension with serum creatinine levels greater than 125 μmol/l were classified as a subgroup of patients at an increased risk of developing high stages of CKD. Stages I-II were previously diagnosed in the 16 patients according to the CKD-EPI formula and stage III CKD with a high risk of progression to stage IV CKD was diagnosed in one patient.

A comparative analysis of the SENS-CRS data of the patients with arterial hypertension was performed between the above-mentioned 16 patients and the remaining 71 patients. The nonparametric Mann-Whitney method was used ($p<0.05$) for the purpose. The method was established only by the indicator D (%) of the rate of elimination of the radiopharmaceutical from the renal parenchyma. However, no significant differences were found either for the calculated GFR values, or for all other parameters of complex renoscintigraphy

Conclusion: After the gout diagnosis is made and confirmed by screening, it is important that patients with gout and hypertension should be included in the nephrologic monitoring system to control risk factors associated with the development or aggravation of CKD.

The renocortical parameter D (%), used in the SENS-CRS technology, is a prognostically important preclinical marker of intrarenal congestion in the latent development of serious morphofunctional disorders in the renal parenchyma leading to the development of CKD or the aggravation of an existing stage of CKD.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.343

POS1124

IDENTIFYING POTENTIAL CLASSIFICATION CRITERIA FOR CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD): RESULTS FROM THE INITIAL PHASES

S. Tedeschi[1], T. Pascart[2], A. Latourte[3], C. Godsave[4], B. Kundaki[4], R. Naden[5], W. Taylor[6], N. Dalbeth[7], T. Neogi[8], F. Perez-Ruiz[9], A. Rosenthal[10], F. Becce[11], E. Pascual[12], M. Andrés[12], T. Bardin[3], M. Doherty[4], H. K. Ea[3], G. Filippou[13], J. Fitzgerald[14], M. Gutierrez[15], A. Iagnocco[16], T. Jansen[17], M. Kohler[18], F. Lioté[3], M. Matza[18], G. Mccarthy[19], R. Ramonda[20], A. Reginato[21], P. Richette[3], J. Singh[22], F. Sivera[23], A. So[24], L. Stamp[25], J. Yinh[18], C. Yokose[18], R. Terkeltaub[26], H. Choi[18], A. Abhishek[4]. *[1]Brigham and Women's Hospital, Rheumatology, Boston, United States of America*; *[2]Lille Catholic University, Rheumatology, Lille, France*; *[3]Hôpital Lariboisière, Rheumatology, Paris, France*; *[4]University of Nottingham, Academic Rheumatology, Nottingham, United Kingdom*; *[5]Auckland City Hospital, Medicine, Auckland, New Zealand*; *[6]University of Otago, Medicine, Wellington, New Zealand*; *[7]University of Auckland, Medicine, Auckland, New Zealand*; *[8]Boston University School of Medicine, Rheumatology, Boston, United States of America*; *[9]Cruces University Hospital, Rheumatology, Basque Country, Spain*; *[10]Medical College of Wisconsin, Rheumatology, Milwaukee, United States of America*; *[11]Lausanne University Hospital, Radiology, Lausanne, Switzerland*; *[12]Hospital General Universitario de Alicante, Rheumatology, Alicante, Spain*; *[13]Luigi Sacco University Hospital, Rheumatology, Milan, Italy*; *[14]UCLA David Geffen School of Medicine, Rheumatology, Los Angeles, United States of America*; *[15]Instituto Nacional de Rehabilitacion, Musculoskeletal and Rheumatic Disorders, Mexico City, Mexico*; *[16]Università degli Studi di Torino, Academic Rheumatology, Turin, Italy*; *[17]VieCuri Medical Center, Rheumatology, Venlo, Netherlands*; *[18]Massachusetts General Hospital, Rheumatology, Boston, United States of America*; *[19]Mater Misericordiae University Hospital, Rheumatology, Dublin, Ireland*; *[20]University of Padova, Rheumatology, Padova, Italy*; *[21]Brown University School of Medicine, Rheumatology, Providence, United States of America*; *[22]University of Alabama at Birmingham, Rheumatology, Birmingham, United States of America*; *[23]Universidad Miguel Hernandez, Rheumatology, Elche, Spain*; *[24]University Hospital of Lausanne, Musculoskeletal Medicine, Lausanne, Switzerland*; *[25]University of Otago, Medicine, Christchurch, New Zealand*; *[26]San Diego VA Healthcare Service and UCSD, Rheumatology, San Diego, United States of America*

Background: Classification criteria for calcium pyrophosphate deposition disease (CPPD) will facilitate clinical research on this common crystalline arthritis. ACR/EULAR are jointly sponsoring development of CPPD classification criteria using a multi-phase process.

Objectives: To report preliminary results from the first two phases of a four-phase process for developing CPPD classification criteria.

Methods: CPPD classification criteria development is overseen by a 12-member Steering Committee. Item generation (Phase I) included a scoping literature review of five literature databases and contributions from a 35-member Combined Expert Committee and two Patient Research Partners. Item reduction and refinement (Phase II) involved a Combined Expert Committee meeting, discussions among Clinical, Imaging, and Laboratory Advisory Groups, and an item rating exercise to assess the influence of individual items toward classification. The Steering Committee reviewed the modal rating score for each item (range -3 [strongly pushes away from CPPD] to +3 [strongly pushes toward CPPD]) to determine items to retain for future phases of criteria development.

Results: Item generation yielded 420 items (312 from the literature, 108 from experts/patients). The Advisory Groups eliminated items they agreed were unlikely to distinguish between CPPD and other forms of arthritis, yielding 127 items for the item rating exercise. Fifty-six items, most of which had a modal rating of +/- 2 or 3, were retained for future phases (see Table 1). As numerous imaging items were rated +3, the Steering Committee recommended focusing on imaging of the knee, wrist, and one additional affected joint for calcification suggestive of CPP crystal deposition.

Conclusion: The ACR/EULAR CPPD classification criteria working group has adopted both data- and expert-driven approaches, leading to 56 candidate items broadly categorized as clinical, imaging, and laboratory features. Remaining steps for criteria development include domain establishment, item weighting through a multi-criteria decision analysis exercise, threshold score determination, and criteria validation.

Table 1. Categories of items retained for future phases of classification criteria development

Age in decade at symptom onset
Acute inflammatory arthritis (e.g. knee, wrist, 1st MTP joint*)
Recurrence and pattern of joint involvement (e.g. 1 self-limited episode, >1 self-limited episode)
Physical findings (e.g. palpable subcutaneous tophus*, psoriasis*)
Co-morbidities and family history (e.g. Gitelman disease, hemochromatosis, familial CPPD)
Osteoarthritis location and features (e.g. 2nd or 3rd MCP joint, wrist)
Synovial fluid findings (e.g. CPP crystals present, CPP crystals absent on 1 occasion* or 2 occasions*, monosodium urate crystals present*)
Laboratory findings (e.g. hypomagnesemia, hyperparathyroidism, rheumatoid factor*, anti-CCP*)
Plain radiograph: calcification in regions of fibro- or hyaline cartilage+
Plain radiograph: calcification of the synovial membrane/capsule/tendon+
Conventional CT: calcification in regions of fibro- or hyaline cartilage+
Conventional CT: calcification of the synovial membrane/capsule/tendon+
Ultrasound: CPP crystal deposition in fibro- or hyaline cartilage+
Ultrasound: CPP crystal deposition in synovial membrane/capsule/tendons+
Dual-energy CT: CPP crystal deposition in fibro- or hyaline cartilage+
Dual-energy CT: CPP crystal deposition in synovial membrane/capsule/tendon+

*Potential negative predictor +Assessed in the knee, wrist, and/or 1 additional affected joint

Disclosure of Interests: Sara Tedeschi Consultant of: NGM Biopharmaceuticals, Tristan Pascart: None declared, Augustin Latourte Consultant of: Novartis, Cattleya Godsave: None declared, Burak Kundaki: None declared, Raymond Naden: None declared, William Taylor: None declared, Nicola Dalbeth Speakers bureau: Abbvie and Janssen, Consultant of: AstraZeneca, Dyve, Selecta, Horizon, Arthrosi, and Cello Health, Tuhina Neogi: None declared, Fernando Perez-Ruiz: None declared, Ann Rosenthal: None declared, Fabio Becce Consultant of: Horizon Therapeutics, Grant/research support from: Siemens Healthineers, Eliseo Pascual: None declared, Mariano Andrés: None declared, Thomas Bardin: None declared, Michael Doherty: None declared, Hang Korng Ea: None declared, Georgios Filippou: None declared, John FitzGerald: None declared, Marwin Gutierrez: None declared, Annamaria Iagnocco: None declared, Tim Jansen Speakers bureau: Abbvie, Amgen, BMS, Grunenthal, Olatec, Sanofi Genzyme, Consultant of: Abbvie, Amgen, BMS, Grunenthal, Olatec, Sanofi Genzyme, Minna Kohler Speakers bureau: Lilly, Consultant of: Novartis, Frederic Lioté: None declared, Mark Matza: None declared, Geraldine McCarthy Consultant of: PK Med, Roberta Ramonda: None declared, Anthony Reginato: None declared, Pascal Richette: None declared, Jasvinder Singh Speakers bureau: Simply Speaking, Consultant of: Crealta/Horizon, Medisys, Fidia, UBM LLC, Trio health, Medscape, WebMD, Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam associates, Focus forward, Navigant consulting, Spherix, Practice Point communications, Francisca Sivera: None declared, Alexander So: None declared, Lisa Stamp: None declared, Janeth Yinh: None declared, Chio Yokose: None declared, Robert Terkeltaub Consultant of: Sobi, Horizon Therapeutics, Astra-Zeneca, Selecta, Grant/research support from: Astra-Zeneca, Hyon Choi: None declared, Abhishek Abhishek Consultant of: NGM Biopharmaceuticals.

DOI: 10.1136/annrheumdis-2021-eular.469

POS1125

DUAL ENERGY CT HAS PROGNOSTIC VALUE IN GOUT BEYOND STANDARD CLINICAL MEASURES: A BEST EVIDENCE SYNTHESIS

S. Stauder[1], P. M. Peloso[2]. *[1]Florida State University, Medical, Tallahassee, United States of America*; *[2]Horizon Therapeutics plc, Research and Development, Deerfield, United States of America*

Background: Dual Energy CT Scan (DECT) can detect monosodium urate crystal deposits in multiple tissues. EULAR gout guidelines (Richette, 2020) recognized the value of DECT in making a clinical diagnosis when joint aspiration is difficult. DECT shows crystal deposits in almost 50% of gout patients without tophi (Dalbeth, 2017). Tophi are known to predict all-cause and cardiovascular mortality (Vincent 2017, Perez-Ruiz 2013) and it is plausible that DECT could as well. A prognostic measure should be reliable and valid. DECT validity would be evident for death, disability and distress.

Objectives: This study used a best evidence synthesis approach to synthesize the evidence for DECT as a prognostic measure in gout.

Methods: PUBMED and EMBASE were searched from initiation to December 2019; keywords (Dual Energy Computed Tomography OR DECT, gout,

tophaceous gout, chronic gout, monosodium urate crystals OR monosodium urate burden OR tophi OR monosodium urate volume OR flares OR pain OR distress OR death OR disability OR function). Human studies in English were considered. Titles, abstracts and full articles were reviewed. A manual search of secondary sources was conducted. Key gaps identified were considered throughout 2020 when reviewing emerging articles and presentations. Data extraction was conducted by both authors; data presented represents consensus.

Results: Of 344 articles, 81 titles/abstracts met screening inclusion criteria (24%) in the 2019 search; review of the full manuscript led to 41 articles selected (51%). Additionally, 3 key papers and 2 ACR 2020 presentations were identified through 2020. DECT is highly reliable with inter-class correlation coefficients >0.9. DECT has content validity. Dalbeth (2015) showed DECT and X-Rays findings correlated in tophaceous patients, r=0.70, p<0.001. Hand function correlates with DECT burden, with r^2=0.59, p=0.024 (Dalbeth 2007). Dalbeth (2017) showed DECT associated with greater flares at 3 and 12 months (p<0.01) in 152 patients. Pascart (2018) confirmed that subjects with flares had nearly doubled DECT feet volumes (0.9 vs 2.1 cm^3, p=0.05) versus those not flaring. Dalbeth (2017) showed abnormal DECT scans occurred in 47% of patients with normal uric acid (<6.0 mg/dL) without palpable tophi and in 90% with elevated uric acid and palpable tophi. DECT is very sensitive to change (Araujo 2015) with 95% volume reduction in 152 patients on pegloticase treated up to 12 months. Three studies show DECT is correlated to cardiovascular risk factor prevalence (Pascart 2020, Gamala 2018, Lee 2017). Marty-Ané reported that DECT volume predicts mortality (Marty-Ané ACR 2020). Limited evidence from 3 studies suggests that the minimum important volume for DECT is 1.0 cm^3 at feet and ankles, including Pascart 2020.

Conclusion: DECT imaging is highly reliable, has evidence for content validity and is highly sensitive to change. DECT appears to predict future gout flares, cardiovascular risk factor prevalence and mortality. Minimum important DECT volume approximates 1.0 cm^3. DECT requires further study but appears to be a relevant outcome for clinical trials and staging gout patients.

REFERENCES:

Authors	Journal, Volume, Issue	Year
Araujo, E. G., Bayat, S., et al.	*RMD Open*	2015
Dalbeth, N., Nicolaou, S., et al.	*Ann Rheum Dis*, 77(3)	2017
Dalbeth, N., Aati, O., et al.	*Ann Rheum Dis*, 74(6)	2015
Dalbeth, N., Collis, J., et al.	*Rheumatology*, 46(12)	2007
Gamala, M., Linn-Rasker, S. P., et al.	*Clinical Rheumatol*, 37(7)	2018
Lee, K., Ryu, S., et al.	*Clinical Rheumatol,* 37	2017
Marty-Ané, A., Norberciak, L., et al.	*Arthritis Rheumatol* 72 (supp 10) [abstract #0954] ACR 2020.	2020
Pascart, T., Ramon, A., et al.	*J Clin Med,* 9(5)	2020
Pascart, T., Capon, B., et al.	*Arthritis Res and Therapy*, 20(1)	2018
Perez-Ruiz, F., Martínez-Indart, L., et al.	*Ann Rheum Dis,* 73(1)	2013
Richette, P., Doherty, M., et al.	*Ann Rheum Dis*, 79(1)	2020
Vincent, Z., Gamble, G., et al.	*J Rheumatol,* 44 (3)	2017

Disclosure of Interests: Sally Stauder: None declared, Paul M. Peloso Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc.
DOI: 10.1136/annrheumdis-2021-eular.872

POS1126 PREVALENCE OF HYPOPHOSPHATASIA IN ADULT RHEUMATOLOGY PATIENTS SCREENED BY LOW LEVELS OF ALKALINE PHOSPHATASE

P. Karakostas[1], R. Dolscheid-Pommerich[2], M. Hass[3], P. Brossart[4], V. Schäfer[4].
[1]University Hospital of Bonn, Germany, Clinic of Internal Medicine III, Oncology, Hematology, Rheumatology and Clinical Immunology, Bonn, Germany; *[2]University Hospital of Bonn, Germany, Institute of Clinical Chemistry and Clinical Pharmacology, Bonn, Germany*; *[3]Center for Blood Coagulation Disorders and Transfusion Medicine Bonn, Germany, Center for Blood Coagulation Disorders and Transfusion Medicine Bonn, Germany, Bonn, Germany*; *[4]University Hospital of Bonn, Germany, Clinic of Internal Medicine III, Oncology, Hematology, Rheumatology and Clinical Immunology, Bonn, Germany*

Background: Hypophosphatasia (HPP) is a genetic disease caused by one or more mutations in the alkaline phosphatase (ALP) gene, which encodes tissue-specific ALP and affects the mineralization process. Accordingly, arthralgia, fractures, and dental abnormalities have been reported in adults, and fatal courses in children. This metabolic disorder is commonly misdiagnosed with other more prevalent bone diseases due to its low prevalence and lack of recognition (i.e. chrondrocalcinosis). However, no epidemiological studies on the prevalence of HPP in the rheumatological patient population have been available to date.

Objectives: To identify the prevalence of HPP in rheumatological patients screened for persistent low levels of ALP and association with mutations in the ALP gene.

Methods: All adult rheumatology patients were screened for pathological low levels of ALP (< 35 IU/L) between January 1, 2017 and June 30, 2019 at the Department of Rheumatology, Clinic of Internal Medicine III, University Hospital Bonn, Germany. Medical files of patients with pathological low ALP levels were then reviewed for clinical signs and symptoms as well as results of genetic testing for HPP (full sequencing using Next Generation Sequencing).

Results: In total, 2,289 rheumatology patients were screened for low ALP levels. In 60 patients (2.62 %), pathological low ALP levels were identified, while in 30 of these (1.31 %), persistent low ALP levels were detected. In 19 of the 30 patients, genetic tests for ALPL gene mutations were done. Seven out of 19 patients (36.84 %) had HPP-related symptoms (fracture, dental abnormalities) with normal bone densitometry, while four of these patients (21.05 %) had a history of fracture and three patients (15.78 %) showed dental abnormalities. In addition to the typical HPP signs and symptoms, 13 patients (68.42%) showed mutations in the ALPL gene. One of the ALP mutations was found to be a novel genetic variant, classified as pathological. Interestingly, no association with chondrocalcinosis was detected.

Conclusion: In summary, it can be concluded that HPP is an under-diagnosed condition with a higher proportion of affected rheumatologic patients than previously thought (at least 0.56 percent of rheumatologic patients vs. 0,01 percent in a spanish healthy population). If we replicate these numbers for the german population (83 million, 5 percent of whom suffer from rheumatic conditions) the yield is approximately 4.15 million. This possibly indicates that 23,240 potential cases of HPP are currently not diagnosed. Therefore, implementation of a protocol in clinical practice to prevent underdiagnosis of HPP and to treat this disease appropriately is essential.

REFERENCES:

[1] García-Fontana C, Villa-Suárez JM, Andújar-Vera F et al (2019) Epidemiological, Clinical and Genetic Study of Hypophosphatasia in A Spanish Population: Identification of Two Novel Mutations in The Alpl Gene. Sci Rep. https://doi.org/10.1038/s41598-019-46004-2

[2] Mornet E, Yvard A, Taillandier A et al (2011) A molecular-based estimation of the prevalence of hypophosphatasia in the European population. Ann Hum Genet 75:439–445. https://doi.org/10.1111/j.1469-1809.2011.00642.x

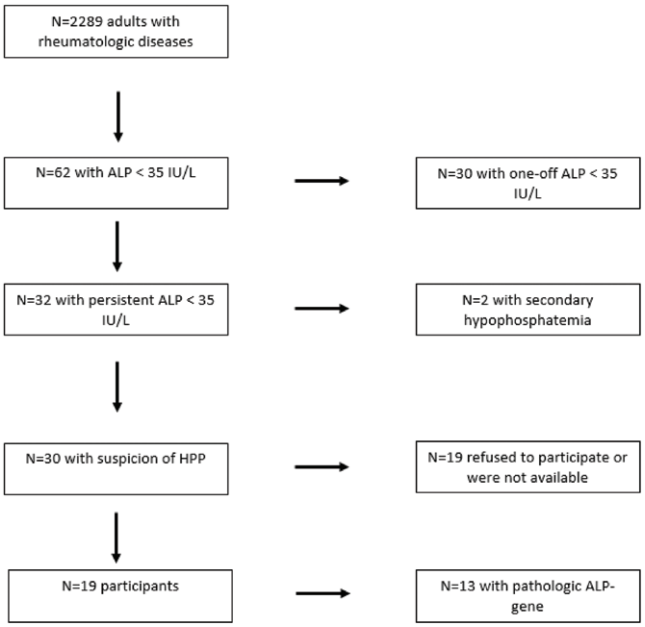


Figure 1.

Flow chart of identification of potential hypophosphatasia (HPP) patients from an adult rheumatology population. Threshold alkaline phosphatase < 35 IU/L at 37`C. ALP: alkaline phosphatase

Disclosure of Interests: Pantelis Karakostas: None declared, Ramona Dolscheid-Pommerich: None declared, Moritz Hass: None declared, Peter Brossart: None declared, Valentin Schäfer Speakers bureau: AbbVie, Novartis, BMS, Chugai, Celgene, Medac, Sanofi, Lilly, Hexal, Pfizer, Janssen, Roche, Schire, Onkowissen, Royal College London, Consultant of: Novartis, Chugai, AbbVie, Celgene, Sanofi, Lilly, Hexal, Pfizer, Amgen, BMS, Roche, Gilead, Medac, Grant/research support from: Novartis, Hexal, Lilly, Roche, Celgene, Universität Bonn.
DOI: 10.1136/annrheumdis-2021-eular.1082

POS1127

ULTRASOUND ASSESSMENT OF GOUT LESIONS IN AN ALGERIAN POPULATION WITH ASYMPTOMATIC HYPERURICEMIA

B. Bengana[1], A. Ladjouze-Rezig[2], S. Ayoub[3], N. B. Raaf[4], C. Aimeur[5], A. Boukabous[1], S. Lefkir[1]. [1]*University Hospital of Beni Messous - Algiers, Rheumatology, BeniMessous, Algeria*; [2]*Specialized hospital establishment of Benaknoune, Rheumatology, Benaknoune, Algeria*; [3]*University hospital of Beni Messous, Internal Medicine, BeniMessous, Algeria*; [4]*Hospital of Bitraria, Biochemistry, El Biar, Algeria*; [5]*University hospital of Mustapha Bacha, Radiology, Sidi Mhamed, Algeria*

Background: Hyperuricemia is a common biological abnormality, often clinically asymptomatic. However, it can announce a gout and be linked to many diseases such as metabolic syndrome, high blood pressure or kidney disease.
In fact, the majority of learned societies do not recommend any urate lowering therapy (ULT) as long as the hyperuricemia remains asymptomatic. But it turns out that part of the population with asymptomatic hyperuricemia (AH) develops a gout after a few years particularly with genetic predisposition, but also on certain risk factors that need to be confirmed.
By this way, musculoskeletal ultrasound (MUS) can detect "asymptomatic gout" by visualizing signs of urate deposits (UD) in subjects with AH.
Objectives: Our main objective is already to estimate the prevalence of specific signs of gout in Algerian population with AH and assess the factors exposing to UD.
Methods: This is a descriptive cross-sectional study from January 2017 to February 2019, with the recruitment of subjects with AH and serum urate level > 60 mg / L, who do not take any ULT and have not associated any chronic inflammatory rheumatism, where we performed a MUS of the knees, metatarsophalangeal joints MTP1, MTP2 and metacarpophalangeal joint MCP2 and MCP3 with the Achilles, patellar and quadricipital tendons.
Results: We retained 258 subjects with AH, 132 women and 126 men (sex ratio = 0.95), the mean age was 59 years, the mean body mass index (BMI) was 28.4 kg / m2, 42 patients were under diuretics, 37 patients reported being on low-dose of aspirin 100 mg daily.
The mean rate of serum urate levels was 78 ± 10 mg / L, the prevalence of UD found at the MUS was 22% (n = 58), among them 36 % (21/58) had a sign of the double contour DC on the MTP1 and 29% (17/58) on the knee, 7% (4/58) had tophi on the MTP1 and 3% (2/58) had urate aggregates. The factors reported to be linked to UD in the sample were: the male gender (p = 0.0016); the high uric acid level (p= 0.0355); BMI (p = 0.0427); taking diuretics for women (p= 0.0002).
Conclusion: Through this work, it is clear that elementary ultrasound lesions related to gout disease are common in a population with AH and concerned one fifth of subjects in our study with a higher risk in men and subjects with obesity and high uric acid level, but also in women taking diuretics. These results need to be enhanced with a randomized controlled study in order to better determine the predisposing factors for gout in any subject with AH.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1161

POS1128

COMBINATION TREATMENT OF AR882, A NEW URAT1 INHIBITOR, AND XANTHINE OXIDASE INHIBITORS ALLOPURINOL OR FEBUXOSTAT: EFFECT ON URIC ACID, HYPOXANTHINE AND XANTHINE IN PLASMA OR SERUM AND URINE

Z. Shen[1], C. Colton[1], R. Yan[1], E. Polvent[1], V. Hingorani[1], S. Yan[1], L. T. Yeh[1]. [1]*Arthrosi Therapeutics Inc, Laguna Hills, California, United States of America*

Background: Xanthine oxidase inhibitors (XOI) are commonly used as urate lowering therapy (ULT) for the treatment of gout. Allopurinol, the first-line treatment, demonstrates low response rate (< 40%), defined as serum urate (sUA) lowering effect below 6 mg/dL, in multiple large-scale clinical trials. As recommended in EULAR guidelines and other literatures, targeting sUA <5 mg/dL or even <4 mg/dL, provides a better opportunity to lower incidence of gout flare and resolution of tophi in gout patients. Febuxostat, a more potent XOI, has been classified as a second-line ULT agent due to increased cardiovascular risks in certain patient populations. For XOI intolerance and non-responders, replacing the agent with a potent URAT1 inhibitor or adding an URAT1 inhibitor onto a current treatment regimen provides opportunities to improve response rates in patients with refractory gout. AR882 is a uricosuric agent that blocks the reabsorption of uric acid in the apical side of renal tubule, hence increases excretion of uric acid into the urine. A phase 2a study has demonstrated the additive effects of AR882 in combination with allopurinol or febuxostat.
Objectives: To evaluate the effect of AR882 alone or in combination with allopurinol or febuxostat on circulating levels and urinary excretion of hypoxanthine, xanthine and uric acid. Furthermore, to elucidate the contribution of each drug towards the combination effect in sUA lowering.
Methods: Plasma, serum, and urine samples were collected from 17 patients with gout who received a once-daily dosing of AR882 50 mg, allopurinol 300 mg or febuxostat 40 mg, or in combination for one week in a phase 2a study. Samples were collected to measure hypoxanthine, xanthine and uric acid levels in plasma or serum and the amount of each excreted in the urine. Plasma C_{max} and AUC and 24-hour urine excretion amount (mg) of hypoxanthine and xanthine were calculated by non-compartmental analysis method.
Results: In monotherapy, AR882 demonstrated better sUA lowering effect (↓53%) compared to allopurinol (↓35%) or febuxostat (↓39%). Combination of AR882 and allopurinol lowered sUA by 66% while combination of AR882 and febuxostat lowered sUA by 71%. Based on the change of xanthine in plasma following combination treatments, it can be calculated that allopurinol contributed 28% of the urate lowering effect, whereas AR882 contributed 38% of the effect. Similarly, febuxostat contributed 33% of the urate lowering effect and AR882 contributed to about 36-38% of the effect when used in combination. The combination treatments significantly increased the response ratio for patients achieving sUA levels < 5 mg/dL, 4 mg/dL, and even 3 mg/dL. In the combination with allopurinol, 100%, 100%, 100%, and 44% patients achieved sUA < 6 mg/dL, < 5 mg/dL, 4 mg/dL, and 3 mg/dL, respectively. Similar results were seen with the combination of AR882 and febuxostat. Treatment with allopurinol or febuxostat alone resulted in 8 to 10-fold and 16-fold increases of xanthine exposure, respectively. The combination of AR882 and allopurinol or febuxostat showed approximately 5-8 fold or 13-fold increases in plasma xanthine, respectively. Treatment with allopurinol or febuxostat alone resulted in 2-3 fold increase in hypoxanthine exposure. Relative changes of hypoxanthine were not significantly different in the presence versus absence of AR882. Increased excretion of xanthine and hypoxanthine was also observed in urine. AR882 was well tolerated in gout patients, showing a similar safety profile to that observed in healthy volunteer studies.
Conclusion: AR882 dose alone had no effect on plasma or urine hypoxanthine and xanthine levels. AR882 contributed to a greater portion of the serum urate lowering effects when used in combination with XO inhibitors, and with 100% of patients achieving levels below 4 mg/dL when combined with allopurinol. The use of AR882 in combination with XO inhibitors may provide an option for preventing flares as well as tophi reduction in advanced patients.
Disclosure of Interests: Zancong Shen Employee of: arthrosi therapeutics, Chris Colton Employee of: Arthrosi therapeutics Inc, Rongzi Yan Employee of: Arthrosi therapeutics Inc, Elizabeth Polvent Employee of: Arthrosi therapeutics Inc, Vijay Hingorani Consultant of: Arthrosi therapeutics Inc, Shunqi Yan Employee of: Arthrosi therapeutics Inc, Li-Tain Yeh Employee of: Arthrosi therapeutics Inc.
DOI: 10.1136/annrheumdis-2021-eular.1215

POS1129

OPTIMIZATION OF DUAL ENERGY COMPUTED TOMOGRAPHY POST-PROCESSING TO REDUCE LOWER LIMB ARTIFACTS IN GOUT

B. Dubief[1], J. Avril[2], T. Pascart[3], M. Schmitt[1], R. Loffroy[2], J. F. Maillefert[1], P. Ornetti[1], A. Ramon[1]. [1]*Dijon University Hospital, Rheumatology, Dijon, France*; [2]*Dijon University Hospital, Diagnostic and Therapeutic Radiology Department, Dijon, France*; [3]*Lille Catholic Hospital, Rheumatology, Lomme, France*

Background: Dual energy computed tomography (DECT) is highly accurate for the diagnosis of gout. However, many artifacts have been described (1,2) such as nail bed, skin, beam hardening, sub-millimeter and vascular artifacts). Their presence can lead to a risk of over-diagnosis (false positives).
Objectives: Main objective of this case-control study was to determine the optimal DECT settings post-treatment parameters (ratio and attenuation coefficient (HU)) in order to reduce the frequency of lower limb artifacts in patients with suspected gout of the lower limbs.
Methods: Seventy-seven patients hospitalized for suspected gout arthritis (feet/ankles and/or knees) who received a DECT imaging were consecutively included (final diagnosis of 43 gout and 34 other rheumatic disorders). Different post-treatment settings were evaluated from the Syngovia software: an R1 (standard) setting with a ratio at 1.36 and minimum attenuation at 150 HU; an R2 setting with a ratio at 1.28 and minimum attenuation at 170 HU and an R3 setting with a ratio at 1.28 and minimum attenuation at 120 HU. The frequency of each artifact according to the 3 settings was determined. Diagnostic accuracy of R1 and R2 settings has been calculated. Correlations between artefacts and patient's clinical characteristics were obtained by performing a Spearman test.
Results: The R2 setting (170 HU, ratio=1.28) significantly reduced the presence of knee and foot/ankle artifacts compared to the standard R1 setting (85% and 94% decrease in beam hardening and clumpy artifacts in the ankle and foot, respectively ($p < 0.001$); a decrease of 71%, 60% and 88% respectively of meniscal beam hardening, beam hardening and submillimeter artifacts in the knee ($p < 0.001$). The use of R3 setting lead to a significant increase of some artifacts (clumpy artifacts, skin artifacts, beam hardening and nail beds.). In addition, our results found a positive correlation between the presence of deposits of knee menisci beam hardening chondrocalcinosis. Body mass index was

also positively correlated with the presence of knee beam hardening artifact. Compared to standard setting, the use of R2 settings decreased sensitivity (0.79 [95CI: 0.65;0.88] versus 0.90 [95CI: 0.78;0.96] and increased specificity (0.86 [95CI: 0.71;0.93) versus 0.63 [95CI: 0.47;0.77] (p<0.001).

Conclusion: Applying a ratio of 1.28 and a minimum attenuation of 170 HU (R2 settings) in DECT post-processing eliminates the majority of the artifacts located on the lower limbs, particularly the clumpy artifact and the beam hardening artifact.

REFERENCES:

[1] Neogi T, Jansen TLTA, Dalbeth N, Fransen J, Schumacher HR, Berendsen D, et al. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2015;74:1789-98.

[2] Mallinson PI, Coupal T, Reisinger C, Chou H, Munk PL, Nicolaou S, et al. Artifacts in dual-energy CT gout protocol: a review of 50 suspected cases with an artifact identification guide. AJR 2014;203:W103-109.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1275

POS1130 PHARMACOKINETICS AND SERUM URATE LOWERING EFFECTS OF AR882, A NOVEL, POTENT AND SELECTIVE URICOSURIC AGENT, IN PATIENTS WITH GOUT

Z. Shen[1], E. Polvent[1], V. Hingorani[1], A. Clouser Roche[1], C. Colton[1], R. Yan[1], S. Yan[1], L. T. Yeh[1]. [1]*Arthrosi Therapeutics Inc, Laguna Hills, California, United States of America*

Background: AR882 is a novel, potent and selective uric acid transporter 1 (URAT1) inhibitor in Phase 2 development for the treatment of hyperuricemia and gout. In Phase 1 healthy subject studies, AR882 demonstrated good dose proportionality, a long effective half-life and sustained serum urate (sUA) lowering effects, consequently making it suitable for once-daily dosing. In addition, AR882 was well tolerated following single and multiple dosing.

Objectives: This Phase 2a study evaluated the pharmacokinetics (PK), pharmacodynamics (PD), and safety of AR882 following monotherapy in patients with gout. PK and sUA lowering effects in patients with renal impairment and normal renal function were also compared.

Methods: A total of 30 adults with gout (sUA >7 mg/dL) were enrolled and 28 had post-baseline PKPD assessments performed. AR882 was administered at escalating doses of 25, 50 and 75 mg, with each dose administered once daily for 7 days. Serial blood samples were collected to measure AR882 PK and sUA levels at the end of each treatment week. Urine samples were collected for assessment of uric acid excretion. Laboratory safety tests, vital signs, and electrocardiograms were collected throughout the study.

Results: Following once daily administration in patients with gout, AR882 exposures increased dose proportionally between 25 and 75 mg. Mean sUA levels were maximally reduced from baseline (mean 8.9 mg/dL) to 5.6, 4.2 and 3.2 mg/dL at the 25-, 50- and 75-mg dose levels, respectively. The corresponding percent reductions were 36.8%, 52.7% and 61.5%. The effects were sustained throughout the entire dosing day with minimal fluctuation. In patients receiving 25 mg AR882 (N=9), 56% achieved sUA levels below 6 mg/dL. At 50 mg (N=28), 96% of patients had sUA levels below 6 mg/dL and 93% were below 5 mg/dL. At the 75 mg dose (N=8), all patients (100%) achieved levels below 5 mg/dL, and 88% were below 4 mg/dL. Among these 28 gout patients, 17 patients had normal renal function (CrCL>90 mL/min) and 11 patients had mild impairment (CrCL 60-90 mL/min). AR882 exposures were similar between patients with mild renal impairment and those with normal renal function. Both groups showed nearly identical sUA lowering effects following each 7-day dosing period. Response rates were also similar between these groups, including at the 50 and 75 mg dose levels. Consistent with its sUA lowering effects, dose-dependent increases in fractional excretion of uric acid were observed across all doses.

AR882 was well tolerated at all doses tested. All AEs were mild or moderate in severity and most were considered not related to study treatment. There were no serious AEs or AEs resulting in study drug discontinuation. There were no clinically significant laboratory or ECG abnormalities noted.

Conclusion: In patients with gout, AR882 exhibited dose proportional increases in plasma exposure and dose-dependent reductions in sUA. Nearly all patients had sUA levels below 5 mg/dL at doses ≥50 mg, and about 90% of patients had sUA levels <4 mg/dL at 75 mg dosing. Similar PK exposures and sUA lowering effects were observed in patients with mild renal impairment compared to those with normal renal function. Current data suggest that AR882 50 mg may offer improved efficacy over existing standard-of-care for gout and AR882 75 mg may have utility in the treatment of patients with severe or refractory gout disease.

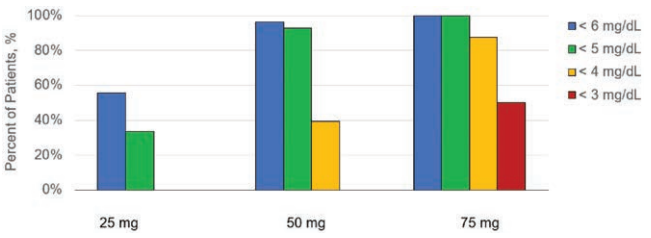


Figure 1. Percent of Patients with sUA below 6 mg/dL, 5 mg/dL, 4 mg/dL or 3 mg/dL Following Once-Daily Oral Doses of AR882.

Table 1. Mean (SD) sUA Levels Following Once-Daily Oral Doses of AR882.

Treatment	N	Time (hr), sUA (mg/dL)			
		0	6	12	24
Baseline	30	8.8 (1.1)	8.8 (1.1)	9.0 (1.0)	8.9 (1.1)
25 mg	9	6.1 (0.4)	5.6 (0.4)	5.6 (0.3)	5.8 (0.4)
50 mg	28	4.7 (0.9)	4.2 (0.9)	4.3 (0.8)	4.7 (1.0)
75 mg	8	3.7 (1.1)	3.2 (0.9)	3.2 (0.8)	3.6 (1.0)
50 mg (normal renal function)	17	4.8 (1.1)	4.3 (1.1)	4.4 (0.9)	4.8 (1.2)
50 mg (mild impairment)	11	4.5 (0.6)	4.1 (0.6)	4.3 (0.5)	4.6 (0.6)

Disclosure of Interests: Zancong Shen Employee of: Arthrosi Therapeutics Inc, Elizabeth Polvent Employee of: Arthrosi Therapeutics Inc, Vijay Hingorani Consultant of: Arthrosi Therapeutics Inc, Andrea Clouser Roche Employee of: Arthrosi Therapeutics Inc, Chris Colton Employee of: Arthrosi Therapeutics Inc, Rongzi Yan Employee of: Arthrosi Therapeutics Inc, Shunqi Yan Employee of: Arthrosi Therapeutics Inc, Li-Tain Yeh Employee of: Arthrosi Therapeutics Inc.

DOI: 10.1136/annrheumdis-2021-eular.1284

POS1131 THE INCIDENCE AND PREVALENCE OF CARDIOVASCULAR DISEASES IN GOUT: A SYSTEMATIC REVIEW AND META-ANALYSIS

P. Cox[1], S. Gupta[2], S. S. Zhao[3], D. Hughes[4]. [1]*University of Liverpool, Institute of Translational Medicine, Liverpool, United Kingdom*; [2]*University of Liverpool, School of Medicine, Liverpool, United Kingdom*; [3]*University of Liverpool, Institute of Ageing and Chronic Disease, Liverpool, United Kingdom*; [4]*University of Liverpool, Department of Health Data Science, Liverpool, United Kingdom*

Background: Gout is an inflammatory crystal arthropathy characterised by hyperuricaemia and sodium urate crystal deposition. Both gout and subclinical hyperuricaemia are associated with adverse cardiovascular outcomes. Several studies have found gout to cause an increased risk of cardiovascular disease, but the evidence is not unanimous. The conflicting evidence has made it difficult to establish the extent of the cardiovascular risk to patients with gout.

Objectives: To describe the incidence and prevalence of cardiovascular disease in gout, compare these results with non-gout controls.

Methods: PubMed, Scopus and Web of Science were systematically searched in January 2021 for studies reporting prevalence of any cardiovascular disease in a gout population. Studies with non-representative sampling, where a cohort had been used in another study, small sample size (< 100) and where gout could not be distinguished from other rheumatic conditions were excluded. Sample size, prevalence of the investigated cardiovascular disease, definition of gout and cardiovascular disease, demographic data, data source and any comparisons with non-gout controls were extracted from each study. Where prevalence data was reported in ≥3 cohorts meta-analysis was performed using random-effect models.

Results: Of the 6164 titles identified, 105 full texts were assessed for eligibility with 30 included in the review, producing a gout population of 1,125,988. Pooled prevalence estimates were calculated for six cardiovascular diseases: heart failure (8.73%; 95% confidence interval (CI), 2.85 – 23.76), cerebrovascular accident (4.27%; 95% CI, 1.83 – 9.67), myocardial infarction (2.82%; 95% CI, 1.58 – 5.01), venous thromboembolism (2.05%; 95% CI, 1.22 – 3.43), hypertension (63.94%; 95% CI, 24.51 – 90.64) and cardiovascular mortality (4.75%; 95% CI, 3.56 – 6.31). Twenty studies reported comparisons with non-gout controls, illustrating an increased risk in the gout group across all cardiovascular diseases, particularly for myocardial infarction.

Conclusion: Cardiovascular diseases are more prevalent in patients with gout and should prompt vigilance from clinicians to the need to assess and stratify cardiovascular risk. These results are in line with other studies which have shown an increased cardiovascular risk for sufferers of hyperuricaemia, highlighting the need for future research to explain this finding. There are limited studies in the

literature investigating less common cardiovascular conditions, illustrating the need for future work if a more thorough picture of prevalence is to be established.

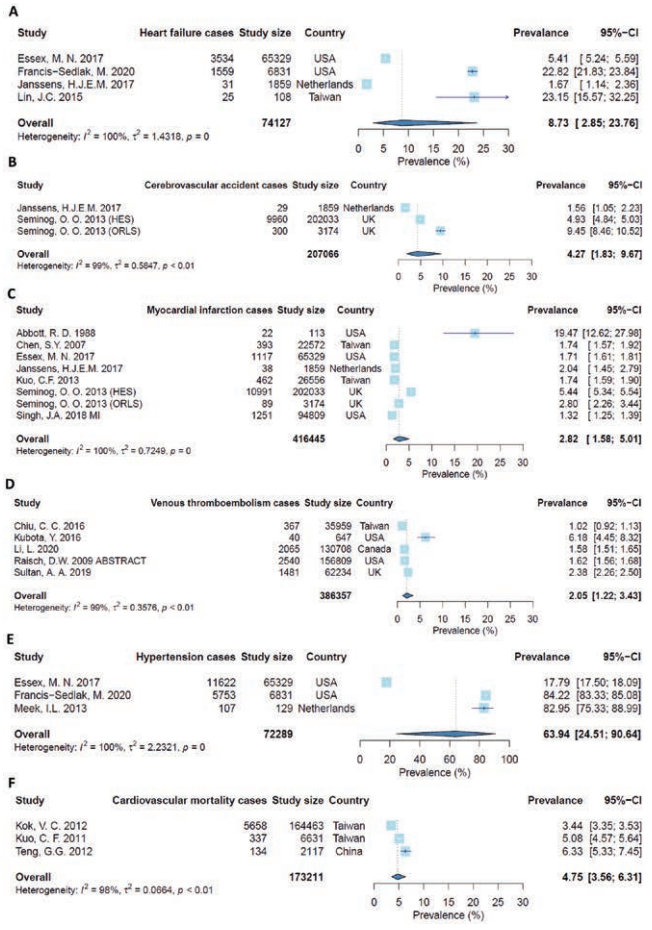


Figure 1. Forest plots of pooled prevalence of: (**A**) 8.73% for heart failure, (**B**) 4.27% for cerebrovascular accident, (**C**) 2.82% for myocardial infarction, (**D**) 2.05% for venous thromboembolism, (**E**) 63.94% for hypertension and (**F**) 4.75% for cardiovascular mortality.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1425

POS1132

DIAGNOSTIC ACCURACY OF CONVENTIONAL RADIOGRAPHY OF THE KNEE FOR CALCIUM PYROPHOSPHATE DEPOSITION DISEASE: AN ANCILLARY STUDY OF THE OMERACT ULTRASOUND – CPPD GROUP

S. Sirotti[1], F. Becce[2], L. M. Sconfienza[3], C. Pineda[4], M. Gutierrez[4], T. Serban[5], D. Maccarter[6], A. Adinolfi[7], E. Naredo[8], A. Scanu[9], C. A. Scirè[10], I. Möller[11], P. Sarzi-Puttini[1], A. Abhishek[12], H. Choi[13], N. Dalbeth[14], S. Tedeschi[15], M. A. D'agostino[16], H. Keen[17], L. Terslev[18], A. Iagnocco[19], G. Filippou[1]on behalf of OMERACT Ultrasound working group, subgroup CPPD. *[1]Sacco Hospital, Rheumatology Department, Milano, Italy*; *[2]Lausanne University Hospital, Department of Diagnostic and Interventional Radiology, Lausanne, Switzerland*; *[3]University of Milan, Department of Biomedical Sciences for Health, Milano, Italy*; *[4]National Rehabilitation Institute, Division of Musculoskeletal and Rheumatic Diseases, Ciudad de México, Mexico*; *[5]Hospital La Colletta, Rheumatology Department, Arenzano, Italy*; *[6]North Valley Hospital, Rheumatology Department, Whitefish, United States of America*; *[7]Niguarda, Rheumatology Unit, Milan, Italy*; *[8]Hospital Universitario Fundación Jiménez Díaz, Department of Rheumatology and Joint and Bone Research Unit, Madrid, Spain*; *[9]University of Padua, Department of Medicine-DIMED, Rheumatology Unit, Padova, Italy*; *[10]Società Italiana di Reumatologia, Epidemiology Research Unit, Milan, Italy*; *[11]Instituto Poal de Reumatologia, Rheumatology, Barcelona, Spain*; *[12]University of Nottingham, Academic Rheumatology, Nottingham, United Kingdom*; *[13]Massachusetts General Hospital Department of Medicine, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; *[14]The University of Auckland, Bone and Joint Research Group, Department of Medicine, Auckland, New Zealand*; *[15]Brigham And Women's Hospital, Division of Rheumatology, Inflammation and Immunity, Boston, United States of America*; *[16]Agostino Gemelli University Policlinic, Rheumatology Department, Roma, Italy*; *[17]The University of Western Australia, School of Medicine, Murdoch, Perth, Australia*; *[18]Rigshospitalet, Center for Rheumatology and Spine Diseases, København, Denmark*; *[19]University of Turin, Academic Rheumatology Centre, Department of Clinical and Biological Sciences, Torino, Italy*

Background: Conventional Radiography (CR) has been widely used in the assessment of knee chondrocalcinosis (CC) and is still considered one of the most important diagnostic methods for the diagnosis. However, there are very few studies that examine the diagnostic accuracy of CR compared to histology of the knee tissues.
Objectives: To assess the diagnostic accuracy of CR of the knee in Calcium Pyrophosphate Deposition Disease (CPPD) by using the recently created definitions for CPPD in CR of the ACR/EULAR taskforce for the new classification criteria for CPPD.
Methods: This is an ancillary study of the Criterion Validity of Ultrasound in CPPD study [1]. Consecutive patients with osteoarthritis (OA) awaiting total knee replacement were enrolled in 4 centres from Romania, Italy, USA and Mexico. All patients underwent CR of the knees taken maximum 6 months before surgery, in posterior-anterior weight baring and lateral projections. DICOM files of the radiographs were anonymised and read independently by two musculoskeletal radiologists with experience in microcrystalline arthropathies. For each patient, a dichotomic score was used (absence/presence of CC) at the level of the menisci and tibiofemoral hyaline cartilage by each reader. The definitions of the ACR/EULAR taskforce for identification of CPPD in CR were used in this study [paper in preparation]. According to these definitions CPPD in CR appears as "linear or punctate opacities in the region of fibro- or hyaline articular cartilage/synovial membrane or joint capsule/within tendons or entheses that are distinct from denser, nummular radio-opaque deposits due to basic calcium phosphate deposition". In case of disagreement a consensus decision was taken by both radiologists after discussion of the case. Menisci and the hyaline cartilage were analysed using compensated polarized light microscopy as described previously [1], patients were considered positive for CPPD if at least one of their tissue specimens revealed the presence of calcium pyrophosphate crystals. All examiners were blind to each other's findings.
Results: We enrolled 33 patients with OA (61% female, mean age 69yo). The accuracy values of CR in the various sites of the knee are indicated in Table 1. CR demonstrated to be a specific exam for identification of CPPD at the knee, but sensitivity remains low in all sites and in the overall evaluation. Identification of CPPD appears challenging and this could be due to the advanced grade of OA in our cohort of patients. Advanced degeneration, dislocation of the menisci and thinning of the hyaline cartilage in these patients is frequent and the eventual presence of calcific deposits in one of these structures could overlap with other anatomical structures making the exact localisation difficult. According to the results of the predictive values, the presence of typical deposition on CR allows a definite confirmation of the diagnosis, but a negative radiography does not exclude CPPD as testified by the low negative predictive value.

Table 1. ***Sensitivity, specificity, PPV, NPV, accuracy and AUC of CR for identification of CPPD by using the new ACR/EULAR taskforce definitions.***

	Medial meniscus	Lateral meniscus	Hyaline cartilage	Overall
Sensitivity	22%	33%	31%	42%
Specificity	100%	100%	85%	90%
Positive predictive value	100%	100%	67%	80%
Negative predictive value	56%	60%	55%	61%
Accuracy	61%	68%	58%	66%
AUC	0.6	0.7	0.6	0.7

Conclusion: CR has been extensively used for the diagnosis of OA and CPPD and has been tested previously for diagnostic accuracy. The results of our study confirm that the presence of typical CPPD calcifications, as defined by the ACR/EULAR task force, are highly specific but have low sensitivity for disease identification when using CR. Absence of CPPD on CR does not exclude the diagnosis.
REFERENCES:
[1] Filippou G, *et al.* Criterion validity of ultrasound in the identification of calcium pyrophosphate crystal deposits at the knee: an OMERACT ultrasound study. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-217998
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1437

POS1133

RELIABILITY OF CONVENTIONAL RADIOGRAPHY OF THE KNEE FOR THE ASSESSMENT OF CHONDROCALCINOSIS: AN ANCILLARY STUDY OF THE OMERACT ULTRASOUND – CPPD GROUP

S. Sirotti[1], F. Becce[2], L. M. Sconfienza[3], C. Pineda[4], M. Gutierrez[4], T. Serban[5], D. Maccarter[6], A. Adinolfi[7], E. Naredo[8], A. Scanu[9], I. Möller[10], P. Sarzi-Puttini[1], A. Abhishek[11], H. Choi[12], N. Dalbeth[13], S. Tedeschi[14], M. A. D'agostino[15], H. Keen[16], L. Terslev[17], A. Iagnocco[18], G. Filippou[1]on behalf of OMERACT Ultrasound working group, CPPD subgroup. *[1]Sacco Hospital, Rheumatology Department, Milano, Italy*; *[2]Lausanne University Hospital, Department of Diagnostic and Interventional Radiology, Lausanne, Switzerland*; *[3]University of Milan, Department of Biomedical Sciences for Health, Milano, Italy*; *[4]National Rehabilitation Institute, Division of Musculoskeletal and Rheumatic Diseases, Ciudad de México, Mexico*; *[5]Hospital La Colletta, Rheumatology Department, Arenzano, Italy*; *[6]North Valley Hospital, Rheumatology Department, Whitefish, United States of America*; *[7]Niguarda, Rheumatology Unit, Milan, Italy*; *[8]Hospital Universitario Fundación Jiménez Díaz, Department of Rheumatology and Joint and Bone Research Unit, Madrid, Spain*; *[9]University of Padua, Department of Medicine-DIMED, Rheumatology Unit, Padova, Italy*; *[10]Instituto Poal de Reumatologia, Rheumatology, Barcelona, Spain*; *[11]University of Nottingham, Academic Rheumatology, Nottingham, United Kingdom*; *[12]Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Boston, United States of America*; *[13]The University of Auckland, Bone and Joint Research Group, Department of Medicine, Faculty of Medical and Health Sciences, Auckland, New Zealand*; *[14]Brigham And Women's Hospital, Division of Rheumatology, Inflammation and Immunity, Boston, United States of America*; *[15]Agostino Gemelli University Policlinic, Rheumatology Department, Roma, Italy*; *[16]The University of Western Australia, School of Medicine, Murdoch, Perth, Australia*; *[17]Rigshospitalet, Center for Rheumatology and Spine Diseases, København, Denmark*; *[18]University of Turin, Academic Rheumatology Centre, Department of Clinical and Biological Sciences, Torino, Italy*

Background: Conventional Radiography (CR) has been widely used in the assessment of knee chondrocalcinosis (CC) and is still considered one of the most important diagnostic methods for the diagnosis. However, there are no studies on the reliability of CR for CC.

Objectives: To assess the reliability of CR of the knee in the assessment of chondrocalcinosis (CC).

Methods: This is an ancillary study of the Criterion Validity of Ultrasound in Calcium Pyrophosphate Deposition Disease (CPPD) study [1]. Consecutive patients with knee osteoarthritis (OA) that were planned for total knee replacement surgery were enrolled in 4 centres from Romania, Italy, USA and Mexico. All patients underwent CR of the knees taken maximum 6 months before surgery, in posterior-anterior weight baring and lateral projections. DICOM files of the radiographs were retrieved, anonymised and read independently by two musculoskeletal radiologists with experience in microcrystalline arthropathies. Each reader performed a second evaluation 3 weeks after the first one to calculate the inter- and intra-reader agreement. For each patient a dichotomic score was assigned (absence/presence of CC) at the level of the medial and lateral menisci, tibiofemoral hyaline cartilage, quadriceps and patella tendons, synovial membrane/joint capsule. The definitions of the ACR/EULAR taskforce for identification of CPPD in conventional radiography were used in this study [paper in preparation]. According to these definitions CPPD in CR appears as "linear or punctate opacities in the region of fibro- or hyaline articular cartilage/synovial membrane or joint capsule/within tendons or entheses that are distinct from denser, nummular radio-opaque deposits due to basic calcium phosphate deposition". Cohen's kappa was used to calculate the agreement between the two readers.

Results: We enrolled 33 patients with knee OA (60.6% female, mean age 69yo ± 8). The kappa values of the inter-reader and intra-reader agreement in the various sites of the knee are indicated in Table 1. Inter-reader agreement was substantial at the level of both menisci but only moderate or fair at the other sites of assessment. This had a negative impact on the overall evaluation of the knee joint that proved to be unreliable (k of 0.16 – none to slight agreement) if all anatomical structures are included for assessment, and moderately reliable (kappa 0.41) when both menisci and hyaline cartilage are considered. On the other hand, intra-reader kappa values were substantial or higher in all sites (except for synovial membrane/joint capsule for one reader). The striking difference of the intra-reader compared to the inter-reader kappa values, highlight a different interpretation and application of the definitions used for most of the sites with the exception of the menisci.

Table 1. ***kappa values for intra- and inter-reader agreement. Values from 0.01–0.20 are considered as none to slight agreement, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.***

	Medial meniscus	Lateral menis-cus	Hyaline cartilage	Quadriceps tendon	Patellar tendon	Capsule/ synovia	Menisci + cartilage	Entire joint
Inter-reader	0.67	0.71	0.34	0.47	NA	0.37	0.40	0.17
Intra-reader 1st assessor	0.67	0.90	0.84	0.65	NA (insufficient number of categories)	0.53	0.71	0.76
Intra-reader 2nd assessor	1	0.80	1	1	1	0.91	0.86	0.94

Conclusion: CR has been extensively used for diagnosis of OA and CPPD. The results of our study raise some concerns on the reliability of CR in identification of CPPD. Assessment of calcium crystals at the menisci level should be used for identification of CC as other sites of the knee seem to present low reliability.

REFERENCES:

[1] Filippou G *et al.* Criterion validity of ultrasound in the identification of calcium pyrophosphate crystal deposits at the knee: an OMERACT ultrasound study. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-217998

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1438

POS1134

COMPARATIVE ANALYSIS OF THE CLINICAL AND LABORATORY PROPERTIES OF GOUT, OSTEOARTHRITIS, AND CALCIUM PYROPHOSPHATE DEPOSITION DISEASE

D. Kravchenko[1], R. Bergner[2], C. Behning[3], V. Schäfer[4]. *[1]University Hospital Bonn, Department of Diagnostic and Interventional Radiology, Bonn, Germany*; *[2]Klinikum Ludwigshafen, Medical Clinic A: Clinic for Internal Medicine, Hematology, Nephrology, Infektiology and Rheumatology, Ludwigshafen, Germany*; *[3]University Hospital Bonn, Institute for Medical Biometrics, Informatics and Epidemiology (IMBIE), Bonn, Germany*; *[4]University Hospital Bonn, Clinic of Internal Medicine III, Hematology, Oncology, Rheumatology and Clinical Immunology, Bonn, Germany*

Background: The clinical differentiation between gout, osteoarthritis (OA), and calcium pyrophosphate deposition disease (CPPD) still remains a hurdle in daily practice without imaging or arthrocentesis. Although a plethora of clinical data exists, reliable predictor biomarkers for all but gout are still missing.

Objectives: To explore an association between common physical examination, ultrasound and laboratory findings and gout, OA, and CPPD, which can in turn provide reliable diagnostic predictions.

Methods: 277 patients were retrospectively analysed using ANOVA with Scheffe's post hoc tests and conditional inference trees regarding biomarkers such as age, sex, body mass index, hypertension, renal status, cumulative affected joint size, number of afflicted joints, double contour sign, intracartiliginous double contour sign, degree of vascularization on ultrasound (DoV), uric acid, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ferritin, and leucocyte count. Simple linear regressions were carried out to explore associations between increased inflammatory parameters and the above-mentioned biomarkers. Statistically significant associations were defined as p values < 0.05.

Results: The male sex was associated with gout (p value < 0.05 vs CPPD and < 0.05 vs OA). OA affected younger patients than CPPD (mean 64.5 vs 73.1 years, p < 0.05). Hypertension was correlated with gout (p < 0.05) and CPPD (p < 0.05), impaired renal status with gout when compared to OA (p < 0.05) but not compared to CPPD (p 0.21). A higher number of involved joints was associated with gout (mean 2.2 joints) compared to OA (1.0, p < 0.05) and CPPD (1.6, p 0.01). The double contour sign was not able to differentiate gout and CPPD with a sensitivity/specificity of 71%/55% for gout and 59%/39% for CPPD. The intracartilaginous double contour sign was specific for CPPD (99%) but with a low sensitivity of 26%. DoV was significantly associated with gout (vs OA, p < 0.05) and CPPD (vs OA, p < 0.05). Unsurprisingly, uric acid was associated with gout while ESR and CRP were increased in gout and CPPD, but not in OA. Some associations were statistically significant but arguably clinically unimportant. Conditional inference trees were able to exclude OA (specificity 97.5%) and CPPD (specificity 94.0%) as possible differentials based on just uric acid, CRP, hypertension,

and sex, and diagnose gout with a sensitivity of 95.1%, summarized in Figure 1. Linear regressions demonstrated an elevated CRP response in people suffering from type II diabetes, higher cumulative joint points score, number of affected joints, as well as elevated uric acid, ESR, and leucocyte count.

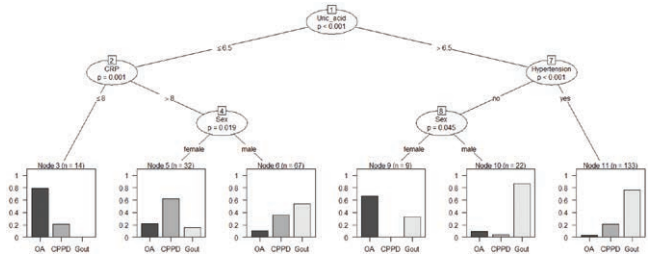


Figure 1. Conditional inference tree using unbiased recursive partitioning to reliably differentiate between gout, osteoarthritis, and calcium pyrophosphate deposition disease.

Conclusion: Gout can be reliably diagnosed, simultaneously excluding OA and CPPD as differential diagnoses by conditional inference trees using just four biomarkers. A correlation between inflammatory reaction severity based on CRP levels was found in patients suffering from type II diabetes, more or larger joint involvement and elevated uric acid levels. The double contour sign remains a questionable differentiator between gout and CPPD with a sensitivity/specificity of 71%/55% for gout and 59%/39% for CPPD, similar to findings reported by Löffler et al (1) with a sensitivity/specificity of only 64%/52% for gout.

REFERENCES:

[1] Löffler C, Sattler H, Peters L, Löffler U, Uppenkamp M, Bergner R. Distinguishing gouty arthritis from calcium pyrophosphate disease and other arthritides. J Rheumatol 2015; 42(3):513–20.

Disclosure of Interests: Dmitrij Kravchenko Shareholder of: Pfizer, Raoul Bergner: None declared, Charlotte Behning: None declared, Valentin Schäfer Speakers bureau: AbbVie, Novartis, BMS, Chugai, Celgene, Medac, Sanofi, Lilly, Hexal, Pfizer, Janssen, Roche, Schire, Onkowissen, Royal College London, Consultant of: Novartis, Chugai, AbbVie, Celgene, Sanofi, Lilly, Hexal, Pfizer, Amgen, BMS, Roche, Gilead, Medac, Grant/research support from: Novartis, Hexal, Lilly, Roche, Celgene, Universität Bonn.

DOI: 10.1136/annrheumdis-2021-eular.1855

POS1135 MONOSODIUM URATE CRYSTALS REDUCE SCHWANN CELLS VIABILITY

Y. Liu[1,2], Y. Huang[1], S. Sun[1], W. Deng[1], T. W. LI[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*; [2]*University of South China, Guangdong Second Provincial General Hospital, Guangzhou, China*

Background: The prevalence of peripheral neuropathy in patients with gout almostly reaches 25%[1]. Demyelination caused by Schwann cell (SCs) injury and apoptosis is the major pathological feature of peripheral[2]. None of study has focused on the effects of monosodium urate (MSU) crystals on SCs.

Objectives: To assess the effect of MSU crystals on SCs.

Methods: Mouse-derived Schwann cells (RSC96) are stimulated with different concentrations of MSU crystals (0mg/ml,0.25mg/ml,0.5mg/ml) and time (24h,48h,72h). The migration ability of Schwann cells is evaluated by acratch assay, the proliferation level is assessed by the cell counting kit-8 (CCK-8) assay, and the apoptosis rate is detected by flow cytometry.

Results: The acratch assay showed that the migration ability of SCs was worsened, CCK-8 assay suggested that proliferation of SCs was reduced in a dose-dependent manner (P<0.05). According to the result of flow cytometry, the survival rate of SCs at 0.5mg/ml(78.60%±2.26%) was lower than that 0.25mg/ml(87.50%±0.95%)and 0mg/ml (98.80%±0.26%)(p<0.05) at 24h. When the stimulation time increased to 72h, the survival rate at 0.5mg/ml(47.90%±11.70%) dropped significantly, which was significantly different from the other two groups(p<0.05).

Conclusion: MSU crystals can cause damage to Schwann cells. It may help to explain the reason of peripheral neuropathy in gout patients.

REFERENCES:

[1] López-López, C.O., et al., Peripheral neuropathies in rheumatic diseases: More diverse and frequent than expected. A cross-sectional study. International journal of rheumatic diseases, 2020. 23(2): p. 226-232.

[2] Liu, Y., S. Shao and H. Guo, Schwann cells apoptosis is induced by high glucose in diabetic peripheral neuropathy. Life sciences, 2020. 248: p. 117459.

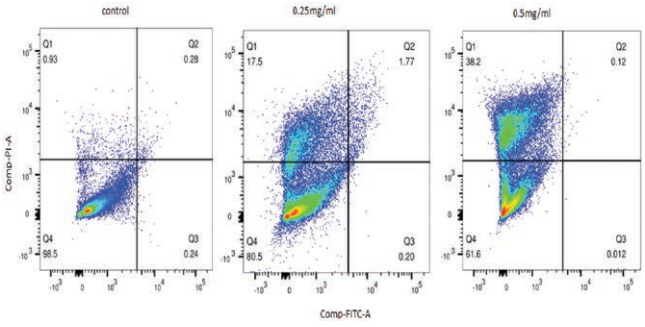


Figure 1. Flow cytometry assays of RSC96 on MSU crystals at 72h

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1989

POS1136 PHARMACOKINETICS OF PEGLOTICASE AND METHOTREXATE POLYGLUTAMATE(S) IN PATIENTS WITH UNCONTROLLED GOUT RECEIVING PEGLOTICASE AND CO-TREATMENT OF METHOTREXATE

Y. Song[1], Y. Xin[1], M. E. Weinblatt[2], J. Chamberlain[1], K. Obermeyer[3], L. Zhao[3], C. Canavan[3], P. M. Peloso[3], S. Ramanathan[1]. [1]*Horizon Therapeutics plc, Research and Development, South San Francisco, United States of America*; [2]*Brigham and Women's Hospital, Division of Rheumatology, Immunology and Allergy, Boston, United States of America*; [3]*Horizon Therapeutics plc, Research and Development, Deerfield, United States of America*

Background: In an open-label, single-arm trial in adult patients with uncontrolled gout (MIRROR open-label [OL] trial) evaluating pegloticase co-treatment with methotrexate (MTX); 78.6% patients were responders, defined as maintenance of serum uric acid <6 mg/dL for at least 80% of the time during month 6 [weeks 20, 22, and 24]. In comparison, 42% patients achieved a response during month 3 and 6 in historical Phase 3 monotherapy trials of pegloticase (C0405 and C0406)[1]. MTX co-treatment is shown to improve the pharmacokinetics (PK) of biologics by attenuating the formation of anti-drug antibodies[2].

Objectives: To determine the systemic exposures of pegloticase and methotrexate polyglutamate(s) (MTX-PGs) in uncontrolled gout patients receiving pegloticase and MTX; to evaluate the effect of MTX on the PK of pegloticase in comparison to historical pegloticase monotherapy trials (C0405 and C0406)[3, 4]; and to evaluate the immunogenicity of pegloticase in co-treatment with MTX.

Methods: In the MIRROR OL trial, MTX (15 mg/week) was given orally 4 weeks prior to the first pegloticase dose and continued weekly, in combination with pegloticase 8 mg given intravenously every 2 weeks, for a treatment duration of up to 52 weeks. Pre-infusion samples were collected to measure MTX-PGs in red blood cells. Pre- and post-infusion blood samples were obtained to measure the peak (C_{max}) and trough (C_{min}) concentrations of pegloticase at multiple visits. Anti-drug antibody blood samples were collected at multiple visits. The impact of MTX on pegloticase PK was evaluated by comparing pegloticase exposures with MTX from this trial to historical monotherapy data (C0405 and C0406)[3, 4]. The observed pegloticase concentrations with MTX were also overlaid with the 90% prediction interval based on the population PK model[5] from C0405 and C0406.

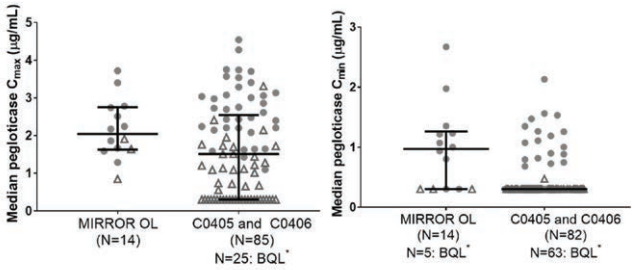
Results: Pegloticase and MTX-PG levels were determined in 14 patients. The 11 responders were generally associated with higher pegloticase exposures than the non-responders, especially C_{min} (Figure 1). Concomitant treatment of MTX resulted in fewer patients with C_{min} below quantitation limit (BQL) (5/14 [36%] with MTX vs 63/82 [77%] without MTX), and higher overall C_{min} (median: 1.03 µg/ml with MTX vs BQL without MTX); C_{max} was slightly higher (median [Q1, Q3]: 2.11 [1.65, 2.59] µg/mL with MTX vs 1.51 [BQL, 2.48] µg/mL without MTX). Pegloticase co-treatment with MTX resulted in more concentrations above the predicted median value of pegloticase, compared to monotherapy. ADA data is consistent with pegloticase PK and efficacy. Significant increase in ADA titers were only observed in 2 subjects (both were non-responders) at time corresponding to the loss of pegloticase exposure and increases in sUA levels. Concentrations of MTX-PGs were maintained during the treatment course, suggesting compliance of MTX administration. There was no apparent difference in concentrations of MTX-PGs between responders and non-responders.

Conclusion: Pegloticase 8 mg IV every 2 weeks co-treatment with MTX 15 mg weekly resulted in fewer patients with pegloticase C_{min} below the quantification

limit (BQL) and gave higher overall trough concentrations (C_{min}) compared to pegloticase monotherapy in the phase 3 studies.
Pegloticase 8 mg IV every 2 weeks co-treatment with MTX 15 mg weekly was associated with an improved response rate for pegloticase in association with improved drug levels in these patients with uncontrolled gout compared to pegloticase monotherapy in the phase 3 studies.

REFERENCES:

[1] Botson J., et al. *J Rheumatol*. 2020; doi: 10.3899/jrheum.200460
[2] Goss S. L., et al. *Clin Ther*;2018, 40 (2).
[3] Lipsky P. E., et al. *Arthritis Res Ther*;2014, 16 (2).
[4] Sundy J. S., et al. *JAMA*;2011, 306 (7).
[5] Yue C. S., et al. *ASCPT*, Atlanta, 2010.



*Data that are BQL (Below quantitation limit of 0.6 µg/mL) were imputed as 0.3 µg/mL (LLOQ/2).
Closed circles: Responders (11/14 in MIRROR OL; 36/85 in C0405 and C0406);
Open triangles: Non-responders (3/14 in MIRROR OL; 49/85 in C0405 and C0406).
Lower, middle and upper lines represent Q1, median and Q3 of data range.
Median pegloticase Cmin and Cmax were calculated based on observed values across visits.

Figure 1. Comparison of pegloticase exposures (C_{max} and C_{min}) in methotrexate co-treatment (MIRROR OL) and monotherapy trials (C0405 and C0406)

Disclosure of Interests: Yang Song Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Yan Xin Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Michael E. Weinblatt Shareholder of: Canfite, Inmedix, Lycera, Vorso, Scipher, Grant/research support from: Crescendo Bioscience, Bristol Myers Squibb, Sanofi, Eli Lilly, Amgen, Jason Chamberlain Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Katie Obermeyer Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Lin Zhao Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Colleen Canavan Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Paul M. Peloso Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Srini Ramanathan Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc.
DOI: 10.1136/annrheumdis-2021-eular.2136

POS1137 IDENTIFYING ADULT HYPOPHOSPHATASIA IN THE RHEUMATOLOGY UNIT

J. Feurstein[1,2], M. Behanova[1], J. Haschka[1,2], K. Roetzer[3,4], G. Uyanik[3,4], M. Witsch-Baumgartner[5], G. Schett[6], J. Zwerina[1,2], R. Kocijan[1,2,7]. [1]*Ludwig Boltzmann-Institute of Osteology at Hanusch Hospital of OEGK and AUVA Trauma Center Meidling, 1st Medical Department, Vienna, Austria*; [2]*Hanusch Hospital Vienna, 1st Medical Department, Vienna, Austria*; [3]*Hanusch Hospital Vienna, Center for Medical Genetics, Vienna, Austria*; [4]*Sigmund Freud University, Medical Faculty of Genetics, Vienna, Austria*; [5]*Medical University Innsbruck, Department of Medical Genetics, Molecular and Clinical Pharmacology, Division Human Genetics, Innsbruck, Austria*; [6]*Friedrich-Alexander-University Erlangen-Nuremberg and Universitatsklinikum, Department of Internal Medicine 3, Erlangen, Germany*; [7]*Sigmund Freud University, Medical Faculty of Bone Diseases, Vienna, Austria*

Background: The most frequent manifestation in adult Hypophosphatasia (HPP) is musculoskeletal pain.[1,2] The unspecific nature of its clinical presentation may prevent correct diagnosis.[3]
Objectives: Identifying adult hypophosphatasia in the rheumatology unit.
Methods: Over a period of 10 years 9,522 patients were screened in a rheumatological outpatient unit. Serum ALP levels ≤ 40 U/l were found in 524 patients. After screening for secondary causes, 73 patients were invited for clinical evaluation. Genetic testing was performed in 23 patients with suspected HPP. Logistic regression models were used to estimate the association of each clinical factor with HPP.
Results: Mutations in the *ALPL* gene were observed in 57% of genetically screened patients. Arthralgia, fractures and pain were the leading symptoms in HPP patients. Chondrocalcinosis (OR 29.12; 95% CI 2.02-1593.52) and dental disease (OR 8.33; 95% CI 0.93-143.40) were associated with HPP independent of BMI. Onset of symptoms in HPP was at 35.1 (14.3) years, with a mean duration from symptoms to diagnosis of 14.4 (8.1) years. Bone mineral density (BMD) and trabecular bone score (TBS) as well as bone turnover markers were not indicative for HPP.
Conclusion: HPP can mimic joint diseases.[4] Thus, in patients with uncertain rheumatologic complaints and low ALP, HPP should be considered as potential diagnosis.

REFERENCES:

[1] Durrough C, Colazo JM, Simmons J, et al. Characterization of physical, functional, and cognitive performance in 15 adults with hypophosphatasia. *Bone* 2021;142:115695.
[2] Seefried L, Kishnani PS, Moseley S, et al. Pharmacodynamics of asfotase alfa in adults with pediatric-onset hypophosphatasia. *Bone* 2021;142:115664.
[3] Högler W, Langman C, Gomes da Silva H, et al. Diagnostic delay is common among patients with hypophosphatasia: initial findings from a longitudinal, prospective, global registry. *BMC musculoskeletal disorders* 2019;20(1):80.
[4] Seefried L, Dahir K, Petryk A, et al. Burden of Illness in Adults With Hypophosphatasia: Data From the Global Hypophosphatasia Patient Registry. *Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research* 2020;35(11):2171-78.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2787

POS1138 SERUM URIC ACID-TO-CREATININE RATIO: A POTENTIAL MARKER FOR GOUT

Z. Huang[1], T. LI[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*

Background: Serum uric acid-to-creatinine ratio (SUA/Cr) is a useful index of renal function-normalized serum uric acid (SUA), which reflects endogenous SUA levels more precisely than SUA. SUA/Cr relates to disease activity and prognosis of several metabolic disorders, like metabolic syndrome, non-alcoholic fatty liver disease, and diabetes mellitus [1]. Besides, the urine uric acid-to-creatinine ratio is valuable for the assessment of gout [2]. However, no study focuses on the relationship between SUA/Cr and gout.
Objectives: We aimed to investigate the relationship between SUA/Cr and the features of demography, manifestations, laboratory tests, and urate-lowering therapies (ULTs) in gout patients.
Methods: This cross-sectional study was performed from December 2015 to February 2020. Medical records of gout patients who were regularly undergone follow-up were evaluated. Characteristics of gout patients, included age, gender, the duration of gout, body mass index (BMI), tophus, complications, the number of flares, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), were recorded. Complications were defined as hypertension, coronary artery diseases, diabetes, strokes, and/or metabolic diseases. Information about ULT was obtained as well. The Spearman correlation analysis was used to assess the relationship between continuous variables. The Mann-Whiney U test or Kruskal-Wallis test was employed to compare the differences of SUA/Cr between genders, ULTs, and whether patients had tophus or complications. A $P<0.05$ was considered as statistically significant.
Results: (1) Of 627 gout patients who were involved, 608 (96.97%) were male. Their median (range) of age and the duration of gout were 30.00 (51.00) years and 5.00 (30.00) years, respectively. (2) SUA/Cr negatively correlated with age ($r=-0.71$, $P<0.05$). SUA/Cr was similar between genders. (3) SUA/Cr positively correlated with BMI ($r=0.14$, $P<0.05$), while the coefficient correlation for the duration of gout and the number of flares did not reach statistically significant ($P>0.05$). SUA/Cr was significantly higher in patients with complications than the others [5.56 (9.26) vs. 4.16 (8.34), $P<0.05$], but whether patients with tophus or not shared similar SUA/Cr. (4) CRP and ESR did not associate with SUA/Cr ($P>0.05$). (5) Patients with combination therapy with xanthine oxidase inhibitor and uricosuric agent had a lower SUA/Cr compared with those who used ULTs monotherapy [3.44 (7.10) vs. 4.53 (7.91), $P<0.05$].
Conclusion: SUA/Cr relates to some features of gout, so it may be a potential marker for its assessment.

REFERENCES:

[1] Medicine (Baltimore) 2020;99(17):e19959.
[2] J Korean Med Sci 2020;35(13):e95.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2844

POS1139 COMPARISON OF THE FREQUENCY OF DETECTION OF EARLY SIGNS OF ATHEROSCLEROSIS IN PATIENTS WITH CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION DISEASE AND OSTEOARTHRITIS

M. Eliseev[1], A. Novikova[1], O. Sheliabina[1], M. Chikina[1], E. Markelova[2]. [1]*VA Nasonova Research Institute of Rheumatology, Laboratory of Microcrystalline Arthritis, Moscow, Russian Federation*; [2]*VA Nasonova Research Institute of Rheumatology, Laboratory of Systemic Rheumatic Diseases, Moscow, Russian Federation*

Background: Crystal-induced inflammation can significantly increase cardiovascular risk (CVR) and cause early development of atherosclerosis [1]. However, no studies have been performed in patients with calcium pyrophosphate crystal deposition disease (CPPD).
Objectives: To compare the presence of atherosclerosis early signs (increased thickness of the intima-media complex (CIMT)) in patients with CPPD and osteoarthritis (OA).
Methods: A cross-sectional study included 48 patients, aged 18 to 65 years, 26 patients with crystal-verified diagnosis of CPPD (McCarty criteria) (6 (23%) men and 20 (77%) women) and 22 patients with OA (7 (32%) men and 15 (68%) women). Exclusion criteria are the presence of other rheumatic diseases with symptoms of arthritis, diabetes mellitus, coronary heart disease (CHD), prior myocardial infarction, stroke or myocardial revascularization surgery, estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m2, high and very high CVR on the SCORE scale. The examination of the patients included the history taking, assessment of anthropometric parameters and the following laboratory tests: determination of serum creatinine level (eGFR according to the MDRD formula), total cholesterol (TC), high density lipoprotein cholesterol (HDL cholesterol) and low density lipoprotein cholesterol (LDL cholesterol), C-reactive protein (CRP). Doppler ultrasound of the carotid arteries with an assessment of the thickness of the intima media complex (CIMT) was made for all patients - CIMT up to 0.9 mm was taken as the norm, CIMT> 0.9 mm and <1.3 mm as increased, and CIMT>1.3 mm was regarded as an atherosclerotic plaque. Statistica 12.0 package was used for statistical data processing.
Results: The groups were completely comparable by gender, age and all laboratory parameters (see Table 1), an increase in CRP>5 mg/l was more often detected in patients with CPPD - 31% vs 14% patients with OA (p=0.16).

Table 1. Clinical characteristics of patients included in the study.

Parameters	CPPD (n=26)	OA (n=22)	p value (reliable at p<0,05)
Age, years M±SD	55.9±5.9	52.4±8.3	0.14
Gender, men/women,n (%)	6 (23)/20 (77)	7 (32)/15 (68)	0.50
Smoking, n (%)	5(19)	6(27)	0.50
Systolic blood pressure, mmHg, M±SD	134±20	127±15	0.19
Arterial hypertension, n (%)	13(50)	10(45)	0.75
Family history of CVD, n %	6(23)	7(32)	0.50
TC, mmol/L, M±SD	5.4±1.3	5.3±1.3	0.95
TC >5,0 mmol/L, n (%)	17(65)	10(45)	0.17
HDL, mmol/L M±SD	1.7±0.5	1.4±0.5	0.10
LDL, mmol/L, M±SD	2.9±1.3	3.4±1.4	0.33
Creatinine, µmol/l, M±SD	73.2±13.8	78.9±11.5	0.16
CRP, mg/l, Me [25-75th percentiles]	1.1 [0.6; 6.4]	1.2 [0.3; 2.8]	0.60
CRP ≥5 mg/l, n (%)	8 (31)	3(14)	0.16

Mean CIMT values on the right (0.76±0.22 mm vs 0.70±0.18 mm) and on the left (0.75±0.18 mm vs 0.70±0.17 mm) did not significantly differ in CPPD and OA (p=0.34 and 0.32, respectively), the maximum CIMT values on the right (0.67±0.16 mm vs 0.67±0.16 mm) and on the left (0.67±0.14 mm vs 0,66±0.16 mm) with CPPD and OA were also comparable (p=0.95 and 0.77, respectively). However, an increase in CIMT> 0.9 mm was found in 13 (50%) patients with CPPD and only 5 (23%) with OA (p=0.02). No increase in CIMT>1.3 mm was found in patients of both groups.

Conclusion: Early signs of atherosclerosis are detected in 50% of patients with CPPD without clinical signs of atherosclerosis and with low or moderate CVR according to SCORE, significantly more often than in patients with OA (23%), which can be reflection of chronic crystal-induced inflammation.
REFERENCES:
[1] Hoseini Z, Sepahvand F, Rashidi B, Sahebkar A, Masoudifar A, Mirzaei H. NLRP3 inflammasome: Its regulation and involvement in atherosclerosis. J Cell Physiol. 2018 Mar;233(3):2116-2132. doi: 10.1002/jcp.25930. Epub 2017 May 23. PMID: 28345767.
Disclosure of Interests: Maxim Eliseev Speakers bureau: Berlin Chemie Menarini Group, Novartis International AG, EGIS, Aleksandra Novikova: None declared, Olga Sheliabina: None declared, Maria Chikina: None declared, Eugenia Markelova: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3121

POS1140 RISK FACTORS FOR THE DEVELOPMENT OF DIABETES MELLITUS IN PATIENTS WITH GOUT ACCORDING TO A 6-YEAR PROSPECTIVE FOLLOW-UP STUDY

O. Sheliabina[1], M. Eliseev[1], A. Novikova[1], M. Chikina[1]. [1]*VA Nasonova Research Institute of Rheumatology, Laboratory of Microcrystalline Arthritis, Moscow, Russian Federation*

Background: Gout is often associated with diabetes mellitus (DM), but the role of serum uric acid (sUA) and urate-lowering drugs in its development in patients with gout remains controversial [1].
Objectives: To study risk factors for DM in patients with gout based on the results of long-term prospective follow-up study.
Methods: The prospective study included 444 patients with a crystal-verified diagnosis of gout, aged ≥18 years, 49 (11%) women, 395 (89%) men. Patients were followed up at the V.A. Nasonova Research Institute of Rheumatology from 2010 to January 2021, the median follow-up was 6.1 [2.8; 7.8] years. The exclusion criteria were the presence of other rheumatic diseases with symptoms of arthritis, DM. DM was diagnosed on the 1998 WHO criteria. The following parameters were considered as risk factors: gender, family history for diabetes mellitus, body mass index (BMI)>25 kg/m2 and > 30 kg/m2, waist volume ≥88 cm for women and ≥102 cm for men, alcohol consumption > 20 units per week, chronic kidney disease (CKD), intake of diuretics and glucocorticoids, and serum total cholesterol >5 mmol/l, triglycerides>2.25 mmol/l, serum C-reactive protein (CRP) level> 5 mg/l, as well as clinical manifestations of gout: subcutaneous tophi, polyarthritis (simultaneous involvement of ≥5 joints), intake of urate-lowering drugs, sUA (> 480 µmol/L,> 420 µmol/L,> 360 µmol/L,> 300 µmol/L). Statistica 12.0 package was used for statistical data processing.
Results: A total of 444 patients were included, the mean age was 51.0±12.9 years, the median follow-up was 6.1 [2.8; 7.8] years. In dynamics: 35 (8%) patients died, 6 (1%) patients were not available, 403 patients were examined (44 (11%) - women and 359 (89%) - men). 290 (72%) patients received urate-lowering therapy (263 (65%) patients used allopurinol, 27 (7%) - febuxostat). The target sUA <360 µmol/L was reached by 165 (41%) patients and <300 µmol/L - by 92 (23%) patients. All patients with sUA<300 µmol/L received urate-lowering therapy, 62 (67%) patients used allopurinol, 17 (18%) - febuxostat, 13 (14%) - uricosuric drugs. Diabetes mellitus was developed in 106 (26%) patients. The factors influencing the risk of developing diabetes were - the presence of diabetes in family history (odds ratio (OR) 2.27, 95% confidence interval (CI) 1.37; 3.76); BMI> 30 kg / m2 (OR 1.79, 95% CI 1.14; 2.80), diuretics (OR 2.32, 95% CI 1.36; 3.96) and sUA> 300 µmol / l (OR 2.89, 95% CI 1.50, 5.56).
Conclusion: The risk of developing DM in patients with gout is associated with sUA> 300 µmol/l, which may be one of the probable reasons for choosing this as a target level. Large prospective studies are needed to confirm the antidiabetic effect of urate-lowering drugs.
REFERENCES:
[1] Chang HW, Lin YW, Lin MH, Lan YC, Wang RY. Associations between urate-lowering therapy and the risk of type 2 diabetes mellitus. PLoS One. 2019 Jan 7;14(1):e0210085. doi: 10.1371/journal.pone.0210085.
Disclosure of Interests: Olga Sheliabina: None declared, Maxim Eliseev Speakers bureau: Berlin Chemie Menarini Group, Novartis International AG, EGIS, Aleksandra Novikova: None declared, Maria Chikina: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3151

POS1141

ASSESSING RELEVANT JOINTS FOR MONITORING CPPD DISEASE: A SYSTEMATIC LITERATURE REVIEW OF IMAGING TECHNIQUES BY THE OMERACT ULTRASOUND – CPPD SUBGROUP

A. Adinolfi[1], S. Sirotti[2], G. Sakellariou[3], E. Cipolletta[4], E. Filippucci[4], F. Porta[5], P. Sarzi-Puttini[2], C. A. Scirè[6], H. Keen[7], P. Mandl[8], G. Mouterde[9], C. Pineda[10], L. Terslev[11], M. A. D'agostino[12], A. Iagnocco[13], G. Filippou[2]on behalf of Omeract Ultrasound working group, subgroup CPPD. *[1]ASST Grande Ospedale Metropolitano Niguarda, Rheumatology Unit, Milan, Italy*; *[2]Luigi Sacco University Hospital, Rheumatology Department, Milan, Italy*; *[3]Istituti Clinici Scientifici Maugeri IRCCS, University of Pavia, Pavia, Italy*; *[4]Università Politecnica delle Marche, Rheumatology Unit, Department of Clinical and Molecular Sciences, Ancona, Italy*; *[5]Institute of Neurosciences, Neurosciences, Florence, Italy*; *[6]SIR Epidemiology, Research Unit, Milan, Italy*; *[7]The University of Western Australia, Medicine and Pharmacology Department, Murdoch, Perth, Australia*; *[8]Medical University Vienna, Internal Medicine 3, Division of Rheumatology, Vienna, Austria*; *[9] University of Montpellier, Rheumatology, Montpellier, France*; *[10]Instituto Nacional de Rehabilitacion, Rheumatology Department, Mexico City, Mexico*; *[11]Copenhagen University, Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark*; *[12]Università Cattolica del Sacro Cuore, Policlinico Universitario Agostino Gemelli IRCSS, Rheumatology Department, Rome, Italy*; *[13]Università degli Studi di Torino, Rheumatology Unit, Department of Clinical and Biological Sciences, Torino, Italy*

Background: Imaging has been extensively used for the Calcium Pyrophosphate Deposition Disease (CPPD) diagnosis but the prevalence of joint calcifications at imaging in CPPD patients has not been thoroughly assessed.
Objectives: This systematic literature review (SLR) is aimed to estimate the prevalence of calcium crystal deposition in peripheral joints by imaging in suspected or definite CPPD patients to establish relevant joints for CPPD monitoring
Methods: After defining PICOs, Pubmed and Embase were searched from inception to October 2020 for identifying studies that evaluated the use of Conventional Radiography (CR), Ultrasound (US), Computed Tomography (CT) and Dual Energy Computed Tomography (DECT) in detecting calcifications at peripheral joints in patients with defined or probable CPPD. Search strategies based on MeSH terms and free text were applied. Six reviewers independently screened titles and abstracts, eligible article full texts were evaluated for inclusion and data extraction.
Results: The SLR identified 1149 manuscripts. 524 papers entered in the full text evaluation and 181 articles were finally included. Considering excluded abstracts and full texts, 23 and 17 were excluded as duplicate, 156 and 9 for language, 171 and 48 for population, 171 and 20 for intervention, 57 and 117 for outcome, 47 and 70 for study type and 76 for full text unavailability. Among included, 41 papers considered patients with definite CPPD with a total population of 1239 patients, 908 cases and 331 controls and 140 papers referred to patients with suspected CPPD with a total population of 26785 patients, 2896 affected by CPPD and 23889 controls. The results about all joints are summarized in the Table 1. In patients with definite diagnosis, knee and wrist are the joints with the highest prevalence of calcifications at all imaging types, followed by hip and acromion-clavicular joint while in patients with suspected CPPD, the knee is the most prevalent followed by the wrist, hip and ankle (only sites with more than 50 patients assessed considered). The hand joints are characterized by CPPD lowest prevalence at imaging. Bilateral imaging findings varies depending on the technique used, the site and the patient's type.
Conclusion: According to the results of this SLR, knees and wrists could be the sentinel joints for CPPD detection by imaging.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3153

POS1142

INTERLEUKIN-37: ASSOCIATIONS OF PLASMA LEVELS AND GENETIC VARIANTS IN GOUT

A. Navrátilová[1,2], V. Voclonová[1], H. Hulejova[1], L. Andres Cerezo[1,2], J. Zavada[1,2], K. Pavelka[1,2], L. Šenolt[1,2], B. Stiburkova[1,3,4]. *[1]Institute of rheumatology, Department of Experimental Rheumatology, Prague, Czech Republic*; *[2]First Faculty of Medicine Charles University, Department of Rheumatology, Prague, Czech Republic*; *[3]First Faculty of Medicine Charles University, Department of Pediatrics and Adolescent Medicine, Prague, Czech Republic*; *[4]General University Hospital in Prague, Department of Pediatrics and Adolescent Medicine, Prague, Czech Republic*

Background: IL-37, recently characterized IL-1 family member, has anti-inflammatory effects by suppression of IL-1ß and other proinflammatory cytokines. In this study we investigated the effects of genetics variants in IL-37 link with IL-37 plasma levels in a cohorts of patients with hyperuricemia/gout.
Objectives: The aim of this study was to determine the association of IL-37 gene polymorphism and plasma IL-37 levels in patients with hyperuricemia and gout.
Methods: The cohorts consisted of 50 control subjects, 50 subjects of primary hyperuricemia, 50 subjects of primary gout, 28 subjects of tophaceous gout and 19 subjects of acute gout flare. The analyzed cohorts were selected from a previously reported set of 250 hyperuricemia/gout patients and 132 normouricemic subjects (1) according to the descending level of serum urate. All coding regions and intron-exon boundaries of IL-37, exon 1-5, were amplified and sequenced directly. Comparisons of presence/absence of identified variants was performed using P-values binomial test. Levels of plasma IL-37 were measured using Enzyme-Linked ImmunoSorbent Assay. All tests were performed in accordance with standards set by the institutional ethics committees, which approved the project in Prague (no.6181/2015).
Results: We identified 12 IL-37 genetic variants: five intron (rs28947188, rs2466448, rs3811045, rs3811048, rs2708944), and seven non-synonymous allelic variants (rs3811046, rs3811047, rs2708943, rs2723183, rs2723187, rs2708947, rs27231927). Minor allele frequency (MAF) of those variants in European population from ExAC databases were used for comparison. Our data showed that the rs28947188, rs3811045, rs3811046, rs3811047, rs2723187, rs2708947, and rs27231927 variants were under-represented in the Czech hyperuricemia, gout, and tophaceous gout cohort compared with the control cohort and general European population (P = 0.0082 – 0.0395).
The levels of plasma IL-37 were significantly higher in patients with tophaceous gout compared to control subjects (P 0.0329) whereas no changes were observed in subjects with primary hyperuricemia, primary gout or acute gout flare compared to control subjects. However, IL-37 was elevated in cohorts of patients with gout, tophaceous gout and acute gout flare compared to primary hyperuricemia subjects (P 0.0198, 0.0005, 0.0099; respectively).
Conclusion: Although further analyzes are needed to elucidate the role of IL-37 in the gout, our results show that genetic variants in anti-inflammatory cytokine IL-37 are probably implicated in the pathogenesis of gout.
REFERENCES:
[1] Toyoda Y, et al. Functional characterization of clinically-relevant rare variants in ABCG2 identified in a gout and hyperuricemia cohort. *Cells*. 2019 Apr 18;8(4).

Table 1. ***Definite CPPD Diagnosis***

		KNEE	*WRIST*	*HAND*	*ELBOW*	*SHOULDER*	*AC*	*HIP*	*ANKLE*	*FOOT*	*TM*
XR	Imaging positive cases/all cases	330/584 57%	214/409 52%	43/158 27%	54/212 25%	65/249 26%	37/84 44%	140/293 48%	30/255 12%	15/59 25%	0
	Cases positive bilaterally	99/146 68%	30/79 38%	0/10	4/12 33%	2/2 100%	9/17 53%	7/10 70%	7/10 70%	0	0
US	Imaging positive cases/all cases	155/252 62%	86/118 75%	4/42 9%	2/2 100%	0/30	4/30 13%	47/80 59%	30/255 12%	15/59 25%	0
	Cases positive bilaterally	83/96 86%	33/47 70%	1/ 4 25%	0	0	3/ 4 75%	29/47 62%	7/10 70%	0	0
CT	Imaging positive cases/all cases	41/50 82%	22/28 78%	0	0	0	0	0	0	0	0
	Cases positive bilaterally	27/30 90%	0	0	0	0	0	0	0	0	0
DECT	Imaging positive cases/all cases	8/10 80%	9/10 90%	1/1 100%	0	0	0	0	0	0	0
	Cases positive bilaterally	0	0	1/1 100%	0	0	0	0	0	0	0
Suspected CPPD diagnosis											
		KNEE	*WRIST*	*HAND*	*ELBOW*	*SHOULDER*	*AC*	*HIP*	*ANKLE*	*FOOT*	*TM*
XR	Imaging positive cases/all cases	1989/2442 81%	549/1024 54%	98/602 16%	29/72 40%	75/185 41%	27/31 87%	322/887 36%	56/116 48%	24/42 57%	0
	Cases positive bilaterally	611/1068 57%	209/334 63%	64/85 75%	22/23 96%	41/46 89%	0/2	94/196 48%	44/53 83%	18/19 95%	0
US	Imaging positive cases/all cases	241/261 93%	125/185 68%	2/39 5%	1/1 100%	4/12 33%	0	2/2 100%	27/78 35%	8/37 22%	0
	Cases positive bilaterally	4/9 44%	74/93 80%	0	0	0	0	0	0	0	0
CT	Imaging positive cases/all cases	0	19/23 83%	0	0	2/2 100%	0	2/2 100%	0	0	1/1 100%
	Cases positive bilaterally	0	0	0	0	0	0	0	0	0	1/1 100%
DECT	Imaging positive cases/all cases	1/1 100%	2/2 100%	0	0	0	0	0	0	0	0
	Cases positive bilaterally	1/1 100%	0	0	0	0	0	0	0	0	0

Table 1 For each joint, are summarized the ratio between positive joints and overall evaluated joints and the ratio between the joints positive bilaterally and overall joints evaluated bilaterally.AC Acromion Clavicular, TM temporo mandibular

Acknowledgements: This study was supported by the grant from the Czech Republic Ministry of Health RVO 00023728.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3217

POS1143 GOUT AND JOINT REPLACEMENTS IN THE US

G. Singh[1], M. Sehgal[2], A. Mithal[3]. [1]*Stanford University, Medicine, Palo Alto, United States of America*; [2]*University of California, Los Angeles, Computer Sciences, Los Angeles, United States of America*; [3]*Institute of Clinical Outcomes Research and Education, Epidemiology, Woodside, United States of America*

Background: Irreversible joint damage in gout has been linked to a possible increase in knee and hip joint replacements[1]. In addition, the strong association between gout and osteoarthritis[2,3] could also lead to an increased risk of joint replacements in patients with gout. Population-based data from the UK and Taiwan have shown hazard rates of 1.14 and 1.16 respectively for knee replacements in patients with gout compared to age and gender matched controls[1]. However, there is little national data in the US on clinical and economic burden of joint replacements in patients with gout.
Objectives: To evaluate total or partial hip and knee joint replacements in patients with gout in the US and to estimate their economic impact
Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. Detailed information including clinical and nonclinical data elements on each hospital stay including International Classification of Diseases (ICD)10 diagnosis and procedure codes, age, gender, length of stay, payer, charges, comorbidities etc. is available. We examined hospitalizations in patients with gout with hip and knee joint replacements in NIS 2018, the most recent year of data.
Results: In 2018, there were 914,510 hospitalizations with primary or secondary diagnosis of gout in the US. Of these 43,615 were for joint replacement surgeries (knee (24,840) and hip (18,755)). Patients with knee replacement were on an average 68.5 years old (95% confidence intervals 68.2 years -68.8 years). Patients with hip replacement were slightly older (mean age 70.3 years, 95% confidence intervals 69.8 years -70.7 years). Unlike general population statistics, men formed a majority of these joint replacements (68% for the knee and 72% for the hip). The average charge per hospitalization was $69,279 and $72,944 for knee and hip replacement respectively. The total annual national cost estimate was $3.09 billion, with government insurances (Medicare and Medicaid) responsible for 67% of knee replacement and 70% of hip replacement costs.
Conclusion: Joint replacements in gout patients have a large clinical and economic burden in the US. This calls for an increased awareness and management of associated hip and knee arthritis in patients with gout.
REFERENCES:

[1] Kuo CF, Chou IJ, See LC, et al. Urate-lowering treatment and risk of total joint replacement in patients with gout. *Rheumatology.* Dec 1 2018;57(12):2129-2139.
[2] Howard RG, Samuels J, Gyftopoulos S, et al. Presence of gout is associated with increased prevalence and severity of knee osteoarthritis among older men: results of a pilot study. *Journal of clinical rheumatology: practical reports on rheumatic & musculoskeletal diseases.* Mar 2015;21(2):63-71.
[3] Roddy E, Zhang W, Doherty M. Are joints affected by gout also affected by osteoarthritis? *Annals of the rheumatic diseases.* Oct 2007;66(10):1374-1377.

Disclosure of Interests: Gurkirpal Singh Shareholder of: Pfizer, Merck, Sanofi, Grant/research support from: Horizon, Maanek Sehgal: None declared, Alka Mithal: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3432

POS1144 SERUM URIC ACID TO CREATININE RATIO IS ASSOCIATED WITH URINARY URIC ACID EXCRETION IN PATIENTS WITH GOUT

Z. Zhong[1], Y. Huang[1], X. Huang[1], Q. Huang[1], Y. Liu[1], T. W. LI[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*

Background: Underexcretion of uric acid is the dominant mechanism leading to hyperuricemia [1] and the 24-hour urinary uric acid excretion is an important measurement. However, it is inconvenient due to accurate timing and complete collection of the specimen.
Objectives: The aim of this study was to investigate the relationship between serum uric acid to creatinine ratio (sUACR) and 24-hour urinary uric acid excretion in gout patients.
Methods: A total of 110 gout patients fulfilling 2015 ACR/EULAR classification criteria from Guangdong Second Provincial General Hospital from January 2019 to January 2021 were retrospectively enrolled in this study. Patients were divided into underexcretion group (<3600 μmol/24h) and non-underexcretion group (≥3600 μmol/24h). The correlation between sUACR and 24-hour urinary uric acid excretion was analyzed by the Pearson's correlations analysis. Receiver operation characteristic (ROC) curves were performed to assess the utility of sUACR for discriminating between underexcretion group and non-underexcretion group. Furthermore, the risk factors of uric acid underexcretion were evaluated using binary logistic regression analysis.
Results: sUACR in the underexcretion group was significantly lower than the non-underexcretion group (p=0.0001). Besides, sUACR was positively correlated with 24-hour urinary uric acid excretion (r=0.4833, p<0.0001). Furthermore, ROC suggested that the area under the curve (AUC) of sUACR was 0.728, which was higher that of serum uric acid and creatinine. The optimal cutoff point of sUACR was 5.2312, with a sensitivity and specificity of 71.9% and 67.9%. Logistic analysis results revealed that decreased sUACR (<5.2312) was an independent risk factor of underexcretion of uric acid (OR =5.510, 95% CI: 1.952-15.550, P=0.001).
Conclusion: sUACR is lower in gout patients with underexcretion of uric acid and may serve as a useful and convenient marker of assessing underexcretion of uric acid in gout patients.
REFERENCES:

[1] Perez-Ruiz F, Calabozo M, Erauskin GG, Ruibal A, Herrero-Beites AM. Renal underexcretion of uric acid is present in patients with apparent high urinary uric acid output. Arthritis Rheum 2002; 47: 610–13.

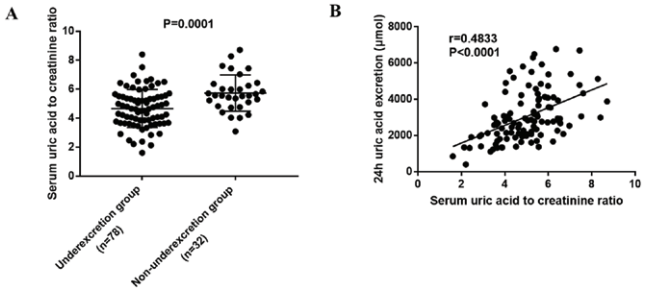


Figure 1. A. Comparison of serum uric acid to creatinine ratio between underexcretion group and non-underexcretion group. B. Correlation between serum uric acid to creatinine ratio and 24h uric acid excretion.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3497

POS1145 PREVALENCE OF CHONDROCALCINOSIS IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES – FREQUENTLY FOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS AND VICE VERSA

M. Krekeler[1], X. Baraliakos[1], S. Tsiami[1], J. Braun[1]. [1]*Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*

Background: Calcium pyrophosphate deposition disease (CPPD), also known as pseudogout, is a prominent member of the crystal deposition diseases much like gout where urate crystals are the pathogens. CPPD is differentiated from chondrocalcinosis, a radiographic finding showing joint calcification, which may or may not be relevant for the clinical picture of patients (1).
Objectives: To determine the prevalence of chondrocalcinosis in different inflammatory rheumatic diseases.
Methods: In a retrospective cross-sectional study design we reviewed the records of not established new patients presenting to our center between 1.1.2016 and 31.12.2018. Based on the availability of radiographs of hands and feet, 514 patients were identified including 181 patients with CPPD, 273 with rheumatoid arthritis (RA), 143 seropositive (52.4%) and 130 seronegative, 30 with gout and 30 with polymyalgia rheumatica (PMR). Radiographs of hands and feet were available from all patients, of the knee in 376 cases. All images were read by two experienced readers with no access to clinical data.
Results: Almost all patients had a short disease duration of < 1 year. In patients diagnosed with CPPD all radiographs showed chondrocalcinosis (93%) at some location, mostly in the hands. This was different in seronegative (36.5%) and seropositive (30.3%) RA. Chondrocalcinosis was found less frequently also in gout (18.8%) and PMR (12.5%). More data are shown in the Table 1. Radiographic chondrocalcinosis was present in more than one joint in 36.6% patients with CPPD, in 11.9% in seropositive and in 17.3% in seronegative RA. Patients with CPPD were older and had acute attacks more often than RA patients. While RA patients were more frequently on methotrexate (MTX), patients with CPPD were more often on colchicine.

Table 1. Radiographic and clinical features of the examined patients

	CPPD N=181	Seropositive RA N=142	Seronegative RA N=129	Gout N=30	PMR N=30
% women	77,8	76,2	75,3	28,1	44,1
Mean age (years)	73,8± 9,8	58,8± 13,0	58,9± 14,7	56,6± 14,7	65,7± 8,9
Symptom duration (years)	0,3±0,7	0,4± 0,7	0,4± 0,9	1.0±3,0	0,4±1,7
Chondrocalcinosis (radiography, %)	93,0	35,7	34,6	12,5	11,8
Erosions (radiography, %)	50,8	42,9	32,1	50	8,8
Clinical involvement of hands (%)	83,2	76,2	72,8	25	50
Clinical involvement of feet (%)	24,3	33,3	32,1	62,5	11,8
Clinical involvement of knee (%)	42,7	39,3	42	59,4	32,4
Symmetric arthritis (%)	64,6	67,9	74	65,6	44,1
Acute attacks, sudden onset (%)	60,5	40,5	40,7	65,6	38,2
Both diagnoses RA and CPPD in record (%)	27,6	29,7	32,1	6,25	14,7
Therapy with MTX or another csDMARD (%)	13,0	52,4	42,0	3,1	23,5
Therapy with Hydroxychloroquine (%)	7,0	4,8	7,4	0	0
Therapy with Colchicine (%)	43,8	9,5	9,9	75	5,9

Conclusion: There were a lot of similarities but also some important differences between patients with CPPD and RA with no major differences between seropositive and seronegative RA. Of interest, radiographic chondrocalcinosis was seen in more than a third of RA patients. Importantly, clinical symmetry of arthritis and involvement of hands did not differentiate between CPPD and RA, mainly the acuteness of attacks did. Co-occurrence of both diseases was frequently observed. There was no major difference between seropositive and seronegative RA.

REFERENCES:

[1] Rosenthal AM, Ryan LM. N Engl J Med. 2016

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3660

POS1146 NONCODING RNA CONTRIBUTE TO PATHOGENESIS IN PRIMARY GOUTY ARTHRITIS

Q. B. Zhang[1], Y. Q. Huang[1], F. N. Xiao[1], G. L. Jian[1], Y. P. Tang[2], F. Dai[2], J. X. Zheng[2], Y. F. Qing[2]. *[1]The Affiliated Hospital of North Sichuan Medical College, Geriatrics, Nanchong, Sichuan, China*; *[2]The Affiliated Hospital of North Sichuan Medical College, Rheumatology and Immunology, Nanchong, Sichuan, China*

Background: Gout is an arthritic disease caused by the deposition of monosodium urate crystal (MSU) in the joints, which can lead to acute inflammation and damage adjacent tissue [1].Over the past decade, noncoding RNAs (ncRNAs) have been shown to have crucial importance in health and disease[2,3]. However, studies evaluating the function of ncRNAs in gout are scarce, and current knowledge of the role of ncRNAs in gout is still limited.

Objectives: To assess the contribution of noncoding RNAs to gout and the clinical importance of these genes in primary gouty arthritis (GA).

Methods: The mRNA expression levels of noncoding RNAs (LINC00173, LINC00963, LINC01330 and miRNA-182-5p) were measured in peripheral blood mononuclear cells (PBMCs) from 60 gout patients(including 30 acute gout patients, 30 intercritical gout patients) and 40 healthy subjects. The relationship between noncoding RNA expression levels and laboratory features was analyzed in GA patients.

Results: The expression levels of LINC00173, LINC00963 and miRNA-182-5p were much lower in the AG and IG group than in the HC groups ($p<0.05$), and no significant difference was detected between AG and IG groups($P>0.05$). The expression levels of LINC01330 were much lower in the AG group than in the IG and HC groups ($p<0.05$), and no significant difference was detected between AG and IG groups($P>0.05$). In GA patients, the levels of noncoding RNAs mRNA correlated with laboratory inflammatory and metabolic indexes.

Conclusion: Altered noncoding RNAs expression suggests that noncoding RNAs is involved in the pathogenesis of GA and participates in regulating inflammation and metabolism.

REFERENCES:

[1] Xu Yi-Ting,Leng Ying-Rong,Liu Ming-Ming et al. MicroRNA and long noncoding RNA involvement in gout and prospects for treatment.[J].Int Immunopharmacol, 2020, 87: 106842.doi:10.1016/j.intimp.2020.106842

[2] Yu Yunfang,Zhang Wenda,Li Anlin et al. Association of Long Noncoding RNA Biomarkers With Clinical Immune Subtype and Prediction of Immunotherapy Response in Patients With Cancer.[J].JAMA Netw Open, 2020, 3: e202149. doi:10.1001/jamanetworkopen.2020.2149

[3] Zou Yaoyao,Xu Siqi,Xiao Youjun et al. Long noncoding RNA LERFS negatively regulates rheumatoid synovial aggression and proliferation.[J].J Clin Invest, 2018, 128: 4510-4524.doi:10.1172/JCI97965

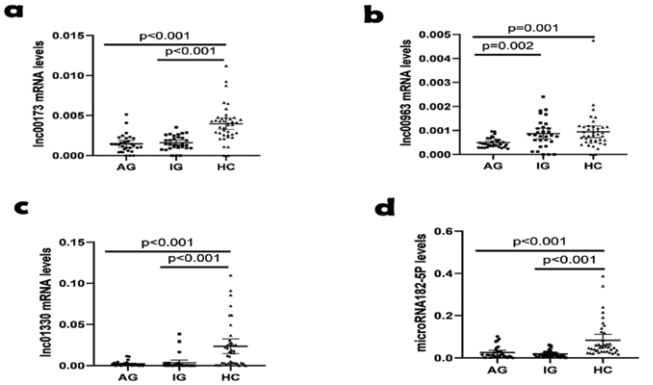


Figure 1. Relative Expression of noncoding RNAs in the PBMCs of Patients.

Disclosure of Interests: Quan-Bo Zhang Grant/research support from: the National Natural Science Foundation of China(General Program) (no.81974250) and Science and Technology Plan Project of Sichuan Province (no.2018JY0257), Yu-Qin Huang: None declared, Fan-Ni Xiao: None declared, gui-lin jian: None declared, Yi-Ping Tang: None declared, Fei Dai: None declared, Jian-Xiong Zheng: None declared, Yu-Feng Qing Grant/research support from: Science and Technology Project of Nanchong City (no.18SXHZ0522).

DOI: 10.1136/annrheumdis-2021-eular.4056

POS1147 COSTS AND FACTORS AFFECTING HEALTH SERVICE UTILISATION IN PATIENTS WITH GOUT: A LONGITUDINAL, POPULATION-LEVEL LINKED DATA STUDY IN WESTERN AUSTRALIA

E. Kelty[1], J. Nossent[2], W. Raymond[2], P. Robinson[3], C. Hill[4], C. Inderjeeth[2], D. Preen[1], H. Keen[2]on behalf of WARDER. *[1]UWA, School of Population & Global Health, Perth, Australia*; *[2]UWA, School of Medicine, Perth, Australia*; *[3]UQ, School of Medicine, Brisbane, Australia*; *[4]University of Adelaide, School of Medicine, Adelaide, Australia*

Background: Evidence suggests that gout is associated with high health care costs and that many inpatient admissions are preventable (1). Understanding the driver of health care costs will allow more targeted intervention.

Objectives: To examine factors associated with high health service utilisation and cost in patients admitted to hospital with gout, using whole-population linked hospital, WA cancer registration, Emergency Department (ED) and death data (2).

Methods: The study included patients (18 to 84 years) who had been admitted to hospital with a primary or co-diagnosis of gout for the first time between 1 Jan 02 and 31 Dec 09 Hospital costs were calculated per patient using DRG codes and ED costs were calculated from URG codes. Costs are presented in Australian dollars. Follow-up was completed at five years post their initial gout hospitalisation, at death, or at the 31th of December 2014. Both univariable and multivariable analysis was conducted for each patient characteristic. Independent variables were assessed for collinearity. Collinearity was assumed present where the correlation co-efficient was greater than 0.7.

Results: 4,379 individuals were included. In the following five years, there was 22,222 ED attendances (median cost, $1826 per patient (IQR: $433 - $4,414)), and 58,920 hospital admissions, (median cost, $25,009 per patient (IQR: $6,844 - $60,535)). 4,059 (18.3%) ED attendances and 3,834 (6.5%) hospital admissions were potentially preventable. Gout was not a major driver of events, with 341 (1.5%) ED attendances and 620 (1.1%) hospital admissions coded with a primary diagnosis of gout. In the univariable analysis (Table 1), Aboriginality and smoking were associated with an increased number of both ED attendances and hospital admissions. Increased socio-economic status was associated with a reduction in ED attendances, however, this was not reflected in hospital admissions.

Conclusion: Patients admitted to hospital with gout are highly likely to be re-admitted or attend ED in the following 5 years. Many of these contacts are preventable, but are usually driven by comorbidities rather than gout.

REFERENCES:

[1] Loh K, . Intern Med J. 2020 Mar;50(3):386.

[2] https://www.datalinkage-wa.org.au.

Table 1: Univariable incident risk ratio (95% confidence intervals) for factors associate with health service utilisation in the five years following initial gout hospitalisation.

	ED presentations			Hospital admissions		
	All presentations	PPE	Cost	All presentations	PPE	Cost
Age at 1st presentation	1.00 (1.00, 1.00)	**0.96 (0.96, 0.97)**	**1.01 (1.01, 1.02)**	1.01 (1.00, 1.01)	**1.04 (1.03, 1.04)**	**1.03 (1.02, 1.03)**
Sex (base: male)	**1.32 (1.19, 1.45)**	1.22 (0.97, 1.51)	**1.28 (1.11, 1.49)**	**1.14 (1.01, 1.28)**	**1.60 (1.36, 1.89)**	1.24 (1.08, 1.42)
Aboriginality	**3.47 (2.99, 4.03)**	**12.98 (9.80, 17.20)**	**2.34 (1.75, 2.86)**	**1.51 (1.25, 1.82)**	**1.39 (1.07, 1.80)**	1.00 (0.79, 1.25)
Socio-economic status (SES)						
- 0 to 20% (lowest SES)	Base	Base	Base	Base	Base	Base
- 21 to 40%	**0.53 (0.44, 0.65)**	**0.29 (0.21, 0.42)**	**0.68 (0.50, 0.92)**	0.90 (0.70, 1.14)	1.03 (0.74, 1.44)	0.99 (0.75, 1.31)
- 41 to 60%	**0.45 (0.38, 0.53)**	**0.10 (0.07, 0.14)**	**0.70 (0.54, 0.93)**	1.16 (0.93, 1.44)	1.06 (0.78, 1.44)	1.24 (0.96, 1.60)
- 61 to 80%	**0.37 (0.31, 0.45)**	**0.10 (0.07, 0.14)**	**0.56 (0.42, 0.75)**	1.01 (0.80, 1.26)	0.97 (0.71, 1.33)	1.07 (0.82, 1.39)
- 81 to 100% (highest SES)	**0.27 (0.23, 0.33)**	**0.02 (0.01, 0.03)**	**0.48 (0.36, 0.64)**	1.12 (0.89, 1.41)	0.85 (0.62, 1.17)	1.25 (0.96, 1.63)
Smoking (ever)	**1.79 (1.64, 1.95)**	**1.78 (1.46, 2.16)**	**1.68 (1.48, 1.92)**	**1.53 (1.38, 1.70)**	**2.12 (1.82, 2.46)**	**1.48 (1.31, 1.67)**
Comorbidities						
- CVD	**1.87 (1.71, 2.03)**	0.87 (0.72, 1.06)	**2.37 (2.09, 2.69)**	**3.06 (2.78, 3.38)**	**6.60 (5.71, 7.64)**	**2.68 (2.39, 3.01)**
- Diabetes	**1.74 (1.59, 1.92)**	**1.39 (1.12, 1.71)**	**1.83 (1.59, 2.11)**	**2.43 (2.18, 2.71)**	**4.02 (3.48, 4.64)**	**1.84 (1.62, 2.11)**

Acknowledgements: The authors wish to thank the staff at the Western Australian Data Linkage Branch and the Hospital Morbidity Data Collection, and the Death Registrations and the Emergency Department Data Collection.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4166

POS1148 RISK FACTORS FOR POLYARTICULAR GOUT FLARES—ANALYSIS OF A LONGITUDINAL ONLINE GOUT FOLLOW-UP STUDY

J. Dau[1], N. Mccormick[1], S. Stratton[1], C. Yokose[1], C. Chen[2], T. Neogi[3], D. Hunter[4], K. Saag[5], Y. Zhang[1], H. Choi[1]. [1]*Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [2]*Boston University School of Public Health, Biostatistics & Epidemiology Data Analytics Center, Boston, United States of America*; [3]*Boston University School of Medicine, Section of Rheumatology, Boston, United States of America*; [4]*University of Sydney, Institute of Bone and Joint Research, Sydney, Australia*; [5]*University of Alabama Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, United States of America*

Background: There are known and established risk factors for gout flares; however, no study has examined the factors specifically associated with a polyarticular gout flare.
Objectives: Evaluate risk factors of a polyarticular gout flare in a longitudinal study of individuals with gout.
Methods: We used data from the Boston Online Gout Study, a longitudinal internet-based case-crossover study, where gout patients with at least one flare within the past year were enrolled across the US. Participants (N=903) were followed prospectively for 1 year via the internet to collect information on gout flares and related data including number and specific joints involved, medical comorbidities, diet, exercise and medications.
A polyarticular gout flare was defined as having 3 or more joints involved during a patient-reported flare period. Individuals with at least one flare (to determine flare pattern) during follow-up were included in the analysis. Univariable associations were first assessed to determine factors were associated with polyarticular joint flares. was used to adjust for confounders. When assessing the association of each risk factor with prevalent polyarticular joint involvement, we used multivariable logistic regression, adjusting specific confounders guided by causal diagram.
Results: There were 724 participants with at least one flare with a mean and median age of 55 years. The cohort was 78% male and 89% White with a mean gout disease duration of 8.1 years (median 5). 197 (27%) had a polyarticular gout flare. In univariable analysis (Table 1), female sex, osteoarthritis, obesity, heart failure, hypertension, chronic kidney disease and gout related medication use were each associated with higher odds of polyarticular gout flare, whereas higher education, alcohol use at study enrollment and aspirin use were associated with lower odds. In multivariable analysis, obesity, osteoarthritis and heart failure remained associated with a higher odds of polyarticular gout flare, whereas education remained inversely associated.
Conclusion: In this prospective cohort of gout patients, obesity, heart failure and osteoarthritis were independently associated with higher odds for polyarticular gout flares. Female sex was also positively associated, whereas higher education was protective. The positive association with gout-related medications likely reflects residual confounding by indication. If confirmed, these findings would help identify those at risk for polyarticular flares to help improve clinical care.

Table 1. Associations with Polyarticular Gout Flare (≥ 3 joints)

Risk Factor		Univariable OR (95% CI)	Age- and Sex-Adjusted OR (95% CI)	Multivariable OR* (95% CI)
Age ≥ 55 years (vs < 55)		0.82 (0.59,1.14)	0.77 (0.56,1.08)	0.70 (0.49,1.01)
Female Sex		1.51 (1.04,2.22)	1.55 (1.03,2.32)	1.21 (0.78,1.88)
White Race (vs Non-White)		0.89 (0.54,1.48)	0.93 (0.56,1.54)	0.75 (0.44,1.28)
Education (vs High School or Less)	Some college	0.63 (0.37,1.07)	0.53 (0.37,1.07)	0.68 (0.39,1.17)
	College	0.45 (0.25,0.78)	0.46 (0.26,0.81)	0.49 (0.27,0.88)
	Post-graduate	0.42 (0.25,0.72)	0.44 (0.26,0.76)	0.48 (0.28,0.84)
Body Mass Index (kg/m^2) at Enrollment (vs < 25)	25-29.9	1.69 (0.85,3.33)	1.77 (0.89,3.51)	1.82 (0.90,3.65)
	≥ 30	2.38 (1.24,4.58)	2.30 (1.19,4.43)	2.19 (1.12,4.28)
Alcohol Use at Enrollment (vs. Non-Use)		0.60 (0.40,0.89)	0.60 (0.40,0.91)	**
Gout Duration ≥ 5 years (vs < 5)		0.85 (0.61,1.18)	0.93 (0.66,1.31)	0.95 (0.66,1.35)
Presence of Comorbidities at Enrollment (vs Absence)	Osteoarthritis	2.35 (1.45,3.81)	2.37 (1.43,3.95)	2.39 (1.42,4.04)
	Heart Failure	2.06 (1.11,3.81)	2.21 (1.17,4.17)	2.03 (1.06,3.91)
	Hypertension	1.61 (1.08,2.40)	1.69 (1.10,2.60)	**
	Chronic Kidney Disease	1.97 (1.03,3.78)	2.11 (1.09,4.11)	**
Medication Use at Enrollment (vs No Use)	Allopurinol	1.58 (1.13,2.22)	1.59 (1.13,2.23)	**
	Diuretics	1.53 (1.06,2.21)	1.59 (1.06,2.38)	**
	Oral Steroids	2.21 (1.16,4.18)	2.26 (1.19,4.31)	**
	Aspirin	0.68 (0.47,0.98)	0.72 (0.49,1.07)	**

*Mutually adjusted for the variables in this column**Not included in model

Acknowledgements: NIH P50AR060772.
Disclosure of Interests: Jonathan Dau: None declared, Natalie McCormick: None declared, Sarah Stratton: None declared, Chio Yokose: None declared, Clara Chen: None declared, Tuhina Neogi Shareholder of: Lilly, EMD Merck Serono, Novartis, Regeneron, Pfizer/Lilly, David Hunter Shareholder of: Pfizer, Lilly, Merck Serono, Kenneth Saag Consultant of: Arthrosi, Horizon Therapeutics plc, Atom Bioscience, LG Pharma, Takeda, Mallinkrodt, SOBI, Grant/research support from: Horizon Therapeutics plc, Shanton, SOBI, Yuqing Zhang: None declared, Hyon Choi Consultant of: Ironwood, Selecta, Horizon, Takeda, Kowa, Vaxart, Grant/research support from: Ironwood, Horizon.
DOI: 10.1136/annrheumdis-2021-eular.4168

POS1149 CARDIOVASCULAR RISK STATUS AND OBESITY IN GOUT COMPARED TO HEALTHY MEXICAN SUBJECTS: A CASE-CONTROLS STUDY WITH A PROPENSITY SCORE-MATCHED ANALYSIS

R. Jimenez-Soto[1], A. Sanchez Rodríguez[2], C. Moreno del Castillo[1], A. Turrent[2], P. E. Bermudez Bermejo[2], R. Burgos-Vargas[3], C. Gómez-Ruiz[3], J. Vazquez Mellado[3]. [1]*ABC Medical Center, Internal Medicine, Mexico City, Mexico*; [2]*ABC Medical Center, Rheumatology, Mexico City, Mexico*; [3]*Hospital General de Mexico, Rheumatology, Mexico City, Mexico*

Background: Atherosclerotic cardiovascular diseases (ASCVD), metabolic syndrome and hyperuricemia due to an increment in their incidence world-wide, but information regarding the 10-year estimated risk in gout vs. healthy subjects is scarce.
Objectives: To assess baseline the 10-year cardiovascular risk and high-risk status in gout patients compared to healthy controls.
Methods: Data from 494 gout paired to controls in a ratio of 1:1 matched with age, sex and body mass index (BMI) and stratified by normal (≤ 24.9 Kg/m^2), overweight (25 - 29.9 Kg/m^2) and obese (≥30 Kg/m^2). Controls were asymptomatic subjects attending a preventive clinic in Mexico City. We used the Framingham Risk Score for Coronary Heart Disease (FRS-CHD) and the 2013 American College of Cardiology/American Heart Association (2013 ACC/AHA). Additionally, high risk status was defined according to pre-defined cutoff points for FRS-CHD (≥ 20%) and ACC/AHA 2013 (≥7.5%).
Results: Data from 494 gout and 494 controls. Gout patients were male 97.4%, 47 (SD ± 13) years, mean BMI of 28.4 (SD ± 4.31) Kg/m^2. Age, sex, and BMI and subgroups were equilibrated (p=NS). Gout patients had higher 10-year estimated risk vs. controls nevertheless, only FRS-CHD reached statistically significant difference with 9.38 vs. 7.5 ± 5.74 (p<0.001); For 2013 ACC/AHA 4.94 ± 6.16 vs. 5.23 ± 6.78, (p=0.49). Further stratification by BMI groups revealed that subjects

with gout in normal and overweight categories were had higher risk vs. controls with FRS-CHD score of 8.86 ± 8.05 vs. 6.53 ± 6.41 (p=0.03) and 9.37 ± 7.72 vs. 7.89 ± 5.58 (p=0.01), respectively. No differences for 2013 ACC/AHA in global and BMI-stratified comparisons. Proportion of high-risk subjects were similar in both groups regardless of BMI category: for FRS-CHD 7.5 vs 4.7% (p=0.06) and 2013 ACC/AHA with 21.5 vs. 17.8% (p=0.14).

Conclusion: Normal BMI or overweight Mexican patients with gout may be at higher 10-year estimated cardiovascular risk compared to matched age, gender and BMI healthy controls. Obese gout subjects are at high risk with non-statistical significance scores for FRS-CHD or 2013 ACC/AHA compared to controls.

REFERENCES:

[1] Acosta-Cázares B, Escobedo-de la Peña J. High burden of cardiovascular disease risk factors in Mexico: An epidemic of ischemic heart disease that may be on its way?. American Heart Journal. 2010;160:230-6.

[2] Sánchez Rodríguez A, Moreno-Del Castillo C, Prado Anaya CA et al. ESTIMATED 10-YEAR CARDIOVASCULAR RISK WITH FRAMINGHAM RISK AND 2013 ACC/AHA IN GOUT AND HEALTHY MEXICAN SUBJECTS: A CASE-CONTROL STUDY WITH A PROPENSITY SCORE-MATCHED ANALYSIS J Clin Rheumatol: 2019;25:S1–S96.

[3] Bevis M, Blagojevic-Bucknall M, Mallen C, Hider S, Roddy E. Comorbidity cluster in people with gout: an observational cohort study with linked medial record review. Rheumatology (Oxford). 2018 Apr 17.

[4] Andrés M, Bernal JA, Sivera F, Quilis N, Carmona L, Vela P, Pascual E. Cardiovascular risk of patients with gout seen at rheumatology clinics following a structured assessment. Ann Rheum Dis. 2017;76:1263-8.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4226

POS1150

ANATOMICAL LOCATIONS AND CORRELATES OF CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITS OF THE SPINE – PATHOLOGIC EXAMINATION OF 77 SURGICAL CASES

J. Dau[1], G. Ho[2], H. Choi[1], J. Schwab[3], M. Kohler[1]. [1]*Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [2]*New York University Langone Health, Division of Rheumatology, New York City, United States of America*; [3]*Massachusetts General Hospital, Department of Orthopaedic Surgery, Boston, United States of America*

Background: Spinal involvement in calcium pyrophosphate deposition disease (CPPD) is thought to be a rare occurrence and is seen infrequently as crowned dens syndrome. Furthermore, data on anatomical locations and correlates of calcium pyrophosphate (CPP) deposits in spinal CPPD are scarce.

Objectives: To describe the anatomical locations and correlates of pathologically confirmed CPPD of the spine.

Methods: Consecutive patients with spinal CPPD were identified via retrospective chart review of individuals who underwent spine surgery for intractable chronic neck or back pain at Massachusetts General Hospital between 2009 and 2014. These deposits and surrounding anatomical structures were surgically resected and confirmed to have calcium pyrophosphate deposition upon pathologic review. We reviewed musculoskeletal imaging (CT, MRI, XR) and laboratory data from these pathologically confirmed cases.

Results: From April 2009 to August 2014, we identified 77 individuals with pathologically confirmed CPPD of the spine. The mean age was 68 years; 41 (53%) were female; mean BMI was 28.7. Calcium pyrophosphate (CPP) was grossly identified intraoperatively by the surgeon in 38 cases (50%), typically as "chalky white deposits" (Figure 1). CPP deposits were seen most frequently in the ligamentum flavum (23%) and intervertebral disc (23%), followed by other less common locations (Table 1). Imaging findings in the soft tissue or intervertebral disc suggestive of CPPD were found in 5 cases (6%), whereas findings of spinal canal narrowing, facet arthropathy, or ligamentum flavum thickening were eventually correlative with CPP deposits in pathologic specimens. Only 7 (9%) experienced a prior episode of acute CPP arthritis (pseudogout). Chondrocalcinosis on x-ray was seen in 26 cases (34%), most commonly in the wrist and/or knees. Osteoarthritis was present in all spinal imaging, and 65% had comorbid scoliosis. Laboratory abnormalities associated with secondary causes of CPPD (hypercalcemia, hypomagnesemia, hyperparathyroidism) were not seen with spinal CPPD.

Conclusion: Spinal CPPD may occur more frequently than previously perceived. The ligamentum flavum and intervertebral discs were common anatomical locations for spinal CPPD. Advanced imaging of the spine showed low sensitivity for detecting spinal CPPD. Only a small minority had typical peripheral joint involvement or imaging with peripheral joint chondrocalcinosis. Thus, without pathologic confirmation, the vast majority of cases would remain unidentified. These findings call for the need to seek pathologic confirmation to determine the robust epidemiology and also raise the potential role for preoperative CPPD treatment.

Table 1. Spinal Anatomic Locations of Pathologically Confirmed CPPD

Spinal Anatomic Location	No. of Sites (%)*
ligamentum flavum	29 (23)
Intervetebral Disc	28 (23)
Other Location	19 (15)
Posterior Elements	18 (15)
Facet	14 (11)
Synovium	8 (6)
Interspinous Ligament	3 (2)
Subarticular/Lateral Recess	2 (2)
Fibrocartilaginous Tissue	1 (1)
Inner Spine	1 (1)
Other Ligament	1 (1)

*Some patients had more than one anatomic location where CPP was isolated

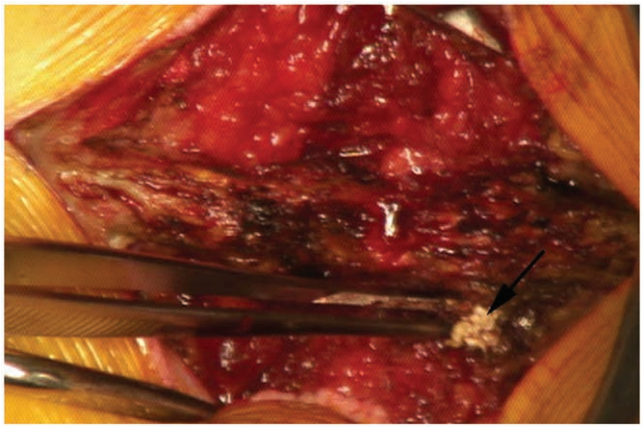


Figure 1. Gross visualization of calcium pyrophosphate deposition (black arrow)

Disclosure of Interests: Jonathan Dau: None declared, Gary Ho: None declared, Hyon Choi Consultant of: Ironwood, Selecta, Horizon, Takeda, Kowa, Vaxart, Grant/research support from: Ironwood, Horizon, Joseph Schwab: None declared, Minna Kohler Speakers bureau: Eli Lily, Consultant of: Novartis.

DOI: 10.1136/annrheumdis-2021-eular.4313

Infection-related rheumatic diseases

POS1151

IMMUNOGENICITY AND SAFETY OF 23-VALENT PNEUMOCOCCAL POLYSACCHARIDE VACCINE IN PATIENTS WITH SPONDYLOARTHRITIS.

N. Muravyeva[1], B. Belov[1], M. Baranova[1], M. Cherkasova[2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory for Studying Comorbid Infections and Monitoring the Safety of Drug Therapy, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*

Background: Currently, for the treatment of patients with spondyloarthritis (SpA), basic anti-inflammatory drugs and biological drugs are widely used to effectively control the activity of the disease. At the same time, the use of these drugs is associated with an increased risk of developing infections, some of which can be prevented by vaccination.

Objectives: The aim of the study was to evaluate the immunogenicity and safety of the 23-valent pneumococcal polysaccharide vaccine (PPV-23) in patients with SpA.

Methods: The study included 42 patients with SpA: 30 men, 12 women, age 22-60 years, disease duration 14.8±10.6 years. Ankylosing spondylitis was diagnosed in 30 patients, psoriatic spondyloarthritis – in 12 patients. Activity of diseases was assessed as high in 78% of patients (median BASDAI index was 5.3 [4.1; 6.8]). At the time of inclusion in the study, all patients received nonsteroidal anti-inflammatory drugs, 14 patients - methotrexate, 10 - sulfasalazine, 6 - glucocorticoids, 2 - leflunomide, 2 - etanercept, 2 - secukinumab. 15 patients were planned to be prescribed secukinumab, 3 – etanercept, 3 - adalimumab, 1 – golimumab. 7 patients had a history of more than 2 cases of lower respiratory tract infections, 2 patients reported a monthly exacerbation of chronic sinusitis, 1 patient – the development of otitis every 2-3 months, requiring the use of antibacterial drugs. PPV-23 was administered in the amount of 1 dose (0.5 ml) subcutaneously into the deltoid muscle against the background of anti-rheumatic therapy.

The level of antibodies to pneumococcal capsular polysaccharide was determined using the EIA PCP IgG kit (TestLine Clinical Diagnostics s.r.o., Czech Republic) before vaccination, 1, 3 and 12 months after vaccination.
Results: The dynamics of the concentration of antibodies to pneumococcal capsular polysaccharide in patients with SpA is presented in the Table 1.

Table 1. Concentration of pneumococcal antibodies, U/ml, Me [25; 75 percentile]

1 visit (initial)	2 visit (after 1 month)	3 visit (after 3 month)	4 visit (after 12 month)
80.0 [35.2; 154.0]	160.1 [73.5; 245.7] *	214.5 [103.2; 255.0] **	175.0 [120.1; 260.1] *

*p=0.01 **p=0.005

At 1, 3 and 12 months after vaccination, the concentration of antibodies to pneumococcal capsule polysaccharide was significantly higher compared to the baseline values. In 81% of patients, vaccination tolerance was good. Reactions at the injection site (pain, swelling and hyperemia of the skin up to 2 cm in diameter), resolved independently after 1-5 days, were observed in 6 patients. In 2 patients, a severe local reaction was registered in the form of pain in the arm, infiltration and hyperemia of the skin up to 8 and 15 cm in diameter, respectively, accompanied by low-grade fever in one patient for 2 days, and febrile fever in the other for 3 days. In both cases, these symptoms were completely stopped after administration of paracetamol and antihistamines. Exacerbation of SpA and the emergence of new autoimmune disorders were not detected. During the follow-up period, no patients developed lower respiratory tract infections. Patients suffering from frequent sinusitis and otitis reported the absence of these infections after vaccination.
Conclusion: The obtained data indicate satisfactory immunogenicity and good tolerability of PPV-23 in patients with SpA. Further studies are needed to better assess the immunogenicity and safety of vaccine, as well as to study of the influence of anti-rheumatic therapy on the effectiveness of immunization.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.505

POS1152 COMORBID INFECTIONS IN PATIENTS WITH SPONDYLOARTHRITIS.

M. Baranova[1], N. Muravyeva[1], B. Belov[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Department of Study Comorbid Infection and Monitoring Antirheumatic Therapy, Moscow, Russian Federation*

Background: Data on the frequency and structure of comorbid infections (CI) in spondyloarthritis (SpA) are few and contradictory.
Objectives: The aim of the study was to study the frequency and structure of CI in the inpatient population of SpA patients in the course of a one-moment retrospective study.
Methods: The study included 208 patients with SpA (121 men, 87 women, mean age 39.1±12.2 years) who were hospitalized at the V.A. Nasonova Research Institute of Rheumatology. Ankylosing spondylitis was diagnosed in 133 patients, psoriatic arthritis - in 57, spondyloarthritis associated with Crohn's disease - in 1, undifferentiated spondyloarthritis - in 17. The majority of respondents had higher education (60.6%). None of the patients consumed alcohol on a daily basis, 124 patients never smoked. The Charlson comorbidity index, equal to 0, had 98 respondents, 1 - 51, 2 - 27, 3 - 15, 4 - 10, 5 or more - 7. Most patients (n=168) received nonsteroidal anti-inflammatory drugs (NSAIDs), as well as glucocorticoids-GC (average duration of administration 239.5±65.8 months), methotrexate-MT (32.4±46.2), sulfasalazine (21.0±32.1), leflunomide (24.0±46.6), biological drugs - TNF-α inhibitors (21.5±23.3), inhibitors of interleukin (iIL)-12/23 (9.0±5.2), iIL-17 (11.0±9.3). Patients were interviewed by a research doctor with the completion of a unified questionnaire, additional data were obtained from medical documentation.
Results: Leading in the structure of CI in patients with SpA were respiratory tract infections: acute nasopharyngitis (n=168), tonsillitis (74), acute bronchitis (34), sinusitis (33), pneumonia (29, including 9 cases by the virus SARS-CoV-2), influenza (31), tuberculosis-TB (5, including 2 cases on infliximab therapy, which was the reason for withdrawal of the drug). Infectious diseases of other localization include herpes-viral infections (n=109), mycoses (51), urinary tract infections (47), conjunctivitis and blepharitis (37), otitis (25), genital infections (15), skin infections (14), intestinal infections (13), COVID-19 without lung damage (19), nervous system infections (2), bone infections (2), chronic hepatitis B (1), chronic hepatitis C (1), HIV infection (1), rubella in adulthood (1), measles in adulthood (1). 20.2% of patients reported more frequent development of CI after the onset of the of SpA: 35 of them received immunosuppressive therapy, 7 – monotherapy of NSAIDs. In SpA patients receiving immunosuppressive drugs, there was an increase in the frequency of acute nasopharyngitis (more often 3 times a year), sinusitis, acute bronchitis, pneumonia and herpes-viral infections, in particular herpes zoster. 29.8% of patients reported a more severe course of CI against the background of SpA (12 of them did not receive immunosuppressive drugs). Temporary discontinuation of therapy due to the development of CI occurred in 26.4% of patients. At the same time, in 5 patients treated with GC (including in combination with MT, n=3), the development of furunculosis was the reason for changing the treatment regimen. In one patient, MT therapy was discontinued due to the frequent development of purulent tonsillitis. Exacerbation of SpA after CI was diagnosed in 84 patients (70 of them received immunosuppressive therapy).
Conclusion: The data obtained indicate the important of the problem of CI in SpA. Further studies are needed on large samples of patients in order to find significant risk factors for CI, study their relationship with clinical characteristics and influence on the course of SpA.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.551

POS1153 EFFECTIVENESS OF SCREENING IN PATIENTS WITH RHEUMATIC DISEASE ON BIOLOGICAL THERAPY AND RISK OF ACTIVE TUBERCULOSIS

S. Abdulaziz[1], S. Attar[2], W. Bajhammoh[3], E. A. Sindi[1], D. M. Ayish[4], E. Bakhashwain[5]. *[1]King Fahad Hospital, Medicine,Division of Rheumatology, Jeddah, Saudi Arabia*; *[2]King Abdulaziz University, Medicine,Division of Rheumatology, Jeddah, Saudi Arabia*; *[3]King Fahad Hospital, Medicine,Division of Infectious Diseases, Jeddah, Saudi Arabia*; *[4]Prince Mohammed Bin Nasser Hospital, Medicine,Division of Rheumatology, Gizan, Saudi Arabia*; *[5]East Jeddah Hospital, Medicine,Division of Rheumatology, Jeddah, Saudi Arabia*

Background: Treatment with biologic therapy has been associated with a high risk of reactivation of latent tuberculosis (TB). Preventive strategies for tuberculosis remain a crucial step before initiating biologics in rheumatic disease.Treatment with biological therapy has been associated with high risk of reactivation of latent tuberculosis (TB). Prevention strategies remain a crucial step before initiating biologics.
Objectives: We aimed to assess the effectiveness of TB screening before the initiation of biologics and the risk of occurrence of active TB among patients with rheumatic diseases on biologic therapies.
The study aimed to access the effectiveness of TB screening recommendations before the initiation of biological therapy and identify the incidence of active TB among these patients.
Methods: We performed a hospital-based retrospective cohort study among rheumatic disease patients on biological therapy in two centers in Jeddah between January 2005 to December 2019. Medical files were retrospectively reviewed for demographics data, baseline screening for TB, use of prophylaxis, information on DMARDs and biological therapies, and outcomes results were collected.
Results: A total of 365 patients were included over a period of 14 years. Two hundred ninety-two (80%) had Rheumatoid arthritis (RA),13% psoriatic arthritis (PSA), 9% spondyloarthritis (SPA), 2% SLE, and 4% others. The mean age was 47.54 (±14.2), 311 (85%) were females with a mean duration of disease 8.45 years (± 6.58). Hundred forty-nine (42.3%) were on steroids. Anti TNFs were prescribed in 213 (58.4%) patients, Non Anti-TNFs 124 (36.6%) patients, and Jak inhibitors 18 (5%) patients.TB screening was done to all patients except 3 patients (data missing) before commencing biologics. Forty-four (12.1%) patients had latent TB at baseline and all received chemoprophylaxis with isoniazid before starting biologics. Four patients with active TB were identified (one with Behcet's disease and three with RA). One patient had a reactivation of latent TB and 3 patients developed de novo TB. Three out of four had an infection in the first 6 months of treatment (one on infliximab and two on rituximab) and one case after 1 year of stopping adalimumab. Two cases had pulmonary TB and two others with extrapulmonary TB (pericarditis and brain abscess each). All four patients with active TB were treated with standard anti TB medications. Three had complete resolution of their TB and one died.
Conclusion: Baseline screening has been effectively carried out in our cohort as per recommendations. Physician should be vigilant not only for reactivation of latent TB but occurrence of de novo TB in patients on biological therapy.
REFERENCES:
[1] Gardam, M. A. *et al.* Anti-tumour necrosis factor agents and tuberculosis risk: mechanisms of action and clinical management. *Lancet. Infect. Dis.* **3**, 148-155, doi:10.1016/s1473-3099(03)00545-0 (2003).
[2] Winthrop, K. L., Yamashita, S., Beekmann, S. E. & Polgreen, P. M. Mycobacterial and other serious infections in patients receiving anti-tumor necrosis factor and other newly approved biologic therapies: case finding through the Emerging Infections Network. *Clin. Infect. Dis.* **46**, 1738-1740, doi:10.1086/587989 (2008).
[3] Cantini, F., Niccoli, L. & Goletti, D. Tuberculosis risk in patients treated with non-anti-tumor necrosis factor-α (TNF-α) targeted biologics and recently licensed TNF-α inhibitors: data from clinical trials and national registries. *J. Rheumatol. Suppl.* **91**, 56-64, doi:10.3899/jrheum.140103 (2014).

Acknowledgements: We would acknowledge Dr. Noran Alhashmi, Dr. Roaa Jodah, and Dr. Lamis Ramadan for their assistance in data collection.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1617

POS1154 CHARACTERISTICS OF SURGICALLY TREATED TUBERCULOUS AND BRUCELLAR SPONDYLODISCITIS

D. Khalifa[1], N. El Fani[2], R. Moncer[2], E. Toulgui[2], W. Ouanes[2], S. Jemni3. [1]*Farhat hached hospital, rheumatology, sousse, Tunisia*; [2]*sahloul hospital, physical therapy and rehabilitation, sousse, Tunisia*; [2]*sahloul hospital, physical therapy and rehabilitation, sousse, Tunisia*

Background: Although rare in most developed countries, tuberculous and brucellar spondylodiscitis are still frequent in the mediterranean countries. Management of spondylodiscitis may require a surgical intervention in cases of spinal cord or root compression, bone destructions and deformities, unsuccessfull medical treatment or large abcesses.
Objectives: To study characteristics and outcome of surgically treated tuberculous and brucellar spondylodiscitis.
Methods: Medical records of patients who were admitted into the physical therapy and rehabilitation ward immediately post surgery of the spine were retrospectively studied. The study included records from January 2010 to December 2020.
Results: Twenty patients were diagnosed with tuberculous or brucellar spondylodiscitis for which they underwent surgery. The mean age of diagnosis was 49.7± 11.9 years. The sex ratio was 1:1. The diagnosis was delayed in 60% of the cases due to atypical presentations. Fatigue was reported in 45% of the patients, back pain in 60% of the cases, radicular pain in 15% of the cases, fever in 20% of the patients and abnormal gait in 60% of the cases. Tuberculosis was identified in 75% of cases and brucellar infection in 25% of the cases. On biology, elevated inflammatory markers were noted in 60% of the cases. Intradermal reaction for tuberculosis was positive in 9 patients while cultures allowed the diagnosis of tuberculosis in 1 patient. Wright serology test confirmed the diagnosis of brucellar infection in all 5 cases. In the remaing ones, vertebral biopsy or intraoperative samples allowed the diagnosis of the tuberculous spondylodiscitis. Cervical spine involvement was noted in 5% of cases, lumbar spine in 25% and dorsal spine in 30% of the cases. All patients recieved antibiotics and spinal immobilization. Surgery was indicated in 78.6% of cases for spinal cord decompression and in 21.4% of the cases for voluminous abcesses. Anterior approach was used in 7.1% of the cases and posterior approach in 92.9% of cases. 23.1% of the patients benifited concomitantly with spinal fusion surgery. Post operative success was immediately confirmed by recovery of normal gait in 15.4% of the patients. Complications after surgery were reported in 35.7% of the cases. They consisted in spinal instability in 60% of the cases, abcesses in 20% of the cases and the emergence of secondary articular localizations in 20% of the cases. 28.6% of the patients underwent a second surgery mainly to stabalize the spine. Before surgery, walking was impossible for 65% of the patients and 12 months after surgery only 30% of the patients couldn't walk (p=0.001). 15.8% of the patients developed later on pressure ulcers and 45% of the patients were prescribed appropriate wheelchairs.
Conclusion: Spinal surgery in tuberculous or brucellar spondylitis may be indicated if medical treatment is insufficient and especially if neurological complications occur. Surgery may be invasive with various complications but sometimes it could be the only option to treat a neurological deficit.
REFERENCES:
[1] Guerado E, Cerván AM. Surgical treatment of spondylodiscitis. An update. *Int Orthop* 2012; 36: 413–420.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1932

POS1155 INFECTIOUS RISK DURING BIOLOGIC THERAPY FOR INFLAMMATORY RHEUMATIC DISEASES: DATA FROM THE TUNISIAN BINAR REGISTRY

S. Boussaid[1], R. Ben Aissa[2], S. Kochbati[2], M. Elleuch[1], L. Abdelmoula[3], A. Laatar[4], W. Hamdi[5], I. Gharsallah[6], E. Bouagina[7], S. Baklouti[8], N. Bergaoui[9], M. Younes[10]. [1]*Rabta Hospital, Department of Rheumatology, Tunis, Tunisia*; [2]*Habib Thameur Hospital, Department of Internal Medecine, Tunis, Tunisia*; [3]*Charles Nicolle Hospital, Department of Rheumatology, Tunis, Tunisia*; [4]*Mongi Slim Hospital, Department of Rheumatology, Marsa, Tunisia*; [5]*Med Taieb Kassab Institute, Department of Rheumatology, Mannouba, Tunisia*; [6]*Military Hospital, Department of Internal Medecine, Tunis, Tunisia*; [7]*Farhat Hachad Hospital, Department of Rheumatology, Sousse, Tunisia*; [8]*Hedi Chaker Hospital, Department of Rheumatology, Sfax, Tunisia*; [9]*Fattouma Bourguiba Hospital, Department of Rheumatology, Monastir, Tunisia*; [10]*Tahar Sfar Hospital, Department of Internal Medecine, Mahdia, Tunisia*

Background: The development of biologics for the treatment of systemic rheumatic diseases increased the risk of infections. The management of this complication deserves particular attention since it remains a major cause of morbidity and mortality.
Objectives: The aim of our study was to determine infection frequency under biological treatment and consequences on the therapeutic management.
Methods: Patients included in the Biological National Registry (BINAR) from 2016 to 2020. Data related to the disease, biological agents, and infections occurring under biologic disease-modifying antirheumatic drugs (bDMARDs) were collected.
Results: The study included 298 patients with a mean age of 49.2 years [18-79] 175 patients with rheumatoid arthritis and 123 with spondyloarthritis (Axial Spondyloarthritis=48, Enteropathic Arthritis=41, Psoriatic Arthritis=34). Anti Tumor necrosis factor-alpha (Anti-TNF) agents were the most prescribed bDMARDs in 87.9% (n=263) of patients: Infliximab 20.4% (n=61),Etanercept 23.1%(n=69), Adalimumab 24.6%(n=74) and Certolizumab (n=79). No patients were treated with Golimumab. Tocilizumab and Rituximab were prescribed respectively in 10.4% (n=31) and 5% (n=15) of patients. Infections occured in 9 patients (3.1%) with a total of 13 infectious episodes 12 bacterial and a viral one. The site of infections was: respiratory (38%), urinary (15%), cutaneous (23%), ORL (8%), infective endocarditis (8%), and other (8%). The infectious agent was identified in only 3 patients. The outcomes were favorable in most cases except in one patient where there was a definitive interruption of bDMARDs. The patient was hospitalized for sepsis complicating a cutaneous infection with favorable outcomes under antibiotics within a week. The biological agent with higher risk of infections was Tocilizumab (p = 0.056), unlike Rituximab (p = 0.483) and Anti-TNF (p = 0.082). All patients who had an infectious episode were under corticosteroids.
Conclusion: Our results confirm that bDMARDs are predisposing to infections, but data from BINAR showed that most infections were trivial with no serious outcomes. Therefore, infections should be assessed in patients under bDMARDs for an early therapeutic intervention.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3000

POS1156 INFECTIONS AND OTHER ADVERSE EFFECTS WITH BIOLOGICAL THERAPIES OVER THE PAST 10 YEARS

G. Alvarez[1], A. Perez Jaen[1], A. Uribe Luna[1], M. Rexach Fumaña[1], L. Peries Reverter[2], C. Diez Vallejo[3], L. Viñas Sague[3], A. Castro Guardiola[1]. [1]*Hospital Universitario de Girona Doctor Josep Trueta, Internal Medicine, Girona, Spain*; [2]*Hospital Universitario de Girona Doctor Josep Trueta, Gastroenterology, Girona, Spain*; [3]*Hospital Universitario de Girona Doctor Josep Trueta, Pharmacology, Girona, Spain*

Background: Biological therapies have marked a difference in the treatment of many autoimmune conditions. As all treatments, they have their side effects although little evidence of long-term effects has been reported.
Objectives: Analyze retrospectively the appearance of infections that required hospitalization and other side effects in patients treated with biological therapies over the past 10 years.
Methods: Biological drugs dispensed in our center to non-cancer patients from 2008 to 2018 were reviewed. Health records were collected from our database and all statistical analyzes were performed with the SPSS program.
Results: 24 different biological drugs applied to 34 medical conditions; 847 treatments were dispensed over a total of 555 patients. The median age was 44 years with a mean duration of 3.6 years of treatment. The most commonly used drug were adalimumab (n = 280, 33%), infliximab (n = 119, 12%), etanercept (n = 97.13%), rituximab (n = 63, 7%), vedolizumab (n = 47, 5.5%) and omalizumab (n = 43.5%). The rest of the drugs were administered <30 times each (ustekinumab, golimumab, certolizumab, tocilizumab, secukinumab and abatacept), representing <4% of the total sample.
The underlying conditions included Crohn's Disease (n = 262, 31%), rheumatoid arthritis (n = 133, 16%), ulcerative colitis (n = 118, 14%), spondyloarthropathies (n = 86, 10%), psoriatic arthritis (n = 56, 7%), psoriasis (n = 49, 6%), asthma (n = 34, 4%), nephropathies (n = 19, 2%) and vasculitis (n = 13, 1.5%). The rest were pathologies with <10 cases.
During treatment, infection requiring hospitalization occurred in 10.2% (n = 86). The most frequent focus of infection was respiratory (n = 23, 27%), abdominal (n = 19, 22%), soft tissue-bone (n = 17 cases, 20%), urinary (n = 7, 8%) and tuberculosis (n = 4, 5%). No case of hepatitis reactivation was observed. At the time of hospital admission, 46% of patients were only under biological therapy, 21% had another non-corticosteroid immunosuppressant, 17% were associated with corticosteroid, and 15% had triple therapy (corticosteroids, another immunosuppressant and the biological drug). The drugs associated with more infections were: abatacept 20%, rituximab 16% and adalimumab 13%.
During the study period, 14 deaths (1.7%) were observed; being the cause cancer-related (n=5), infection (n=5), the disease itself for which was receiving biological treatment (n=2), and endocrine metabolic causes (n=2).

At the end of the review, 48% of the treatments were still in use, while 52% had stopped for various reasons: 20% ineffectiveness, 12% side effects, 12% maintained complete remission. The remaining low percentage was due to death, pregnancy, or study entry.

The side effects that led to a change in treatment was: non-immune hematological disorders in 4.1% (14% of tocilizumab, 7% of rituximab and 6% of vedolizumab), immune disorders in 3.8% (6% of secukinumab, 5% of tocilizumab and 4.5% of certolizumab), nervous system involvement in 2.4% (11.5% of golimumab,10% of abatacept, 5% of tocilizumab), debut or worsening of heart failure in 1.4% (9, 5% of tocilizumab, 2.5% of etanercept and 1.4% of adalimumab) and cancer-related in 0.7% (2% of infliximab, 1.7% of etanercept).

Conclusion: In these 10 years of follow-up and and evaluating 847 treatments, there were 10% hospitalizations due to infections (n = 86) causing death in 5 patients. In light of these results, and pending an exhaustive statistical analysis, we did not find high frequencies of serious side effects in our series. Very little long-term evidence exists on the safety of these drugs.

REFERENCES:

[1] Singh JA, Wells GA, Christensen R, et al. Adverse effects of biologics: a network meta-analysis and Cochrane overview. Cochrane Database Syst Rev. 2011;2011(2):CD008794. Published 2011 Feb 16.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3130

POS1157 CONCORDANCE BETWEEN THE QUANTIFERON-TB GOLD IN-TUBE AND TUBERCULIN TEST FOR THE DIAGNOSIS OF LATENT TUBERCULOSIS INFECTION IN PATIENTS WITH RHEUMATIC DISEASES

C. Pávez Perales[1], A. Quiles Roger[2], E. Grau García[1], M. De la Rubia Navarro[1], S. Leal Rodriguez[1], R. Gonzalez Mazario[1], J. J. Fragío Gil[1], C. Alcañiz Escandell[1], J. Ivorra Cortés[1], I. Chalmeta Verdejo[1], L. Gonzalez Puig[1], I. Martínez Cordellat[1], R. Negueroles Albuixech[1], F. M. Ortiz Sanjuan[1], J. E. Oller Rodríguez[1], E. Vicens Bernabeu[1], C. Nájera Herranz[1], I. Cánovas Olmos[1], J. A. Román Ivorra[1]. *[1]HUP La Fe, Rheumatology Department, Valencia, Spain*; *[2]UCV, Medical School, Valencia, Spain*

Background: Patients with rheumatic diseases (RD) are at higher risk of latent tuberculosis infection (LTBI) reactivation. To detect and treat it before starting treatment, especially with biological therapies, decrease the reactivation risk. Diagnosis is carried out by the tuberculin skin test (TST) or interferon-gamma release assays (IGRAs), IGRAs might be more specific and sensitive.

Objectives: We aim to analyze the concordance between QuantiFERON-TB Gold In-Tube (QTF) and TST for the diagnosis of LTBI in patients with rheumatic diseases.

Methods: A retrospective observational study was conducted including patients diagnosed with RD screened for LTBI with both TST and QTF (2014-2018). Demographical and clinical variables at screening and at follow-up were collected. The concordance between both tests has been estimated as categorical variables using Cohen´s Kappa test, considering "poor" if it is ≤ 0,20; "low" if 0,20 < k ≤ 0,40, "moderate" if 0,40 < k ≤ 0,60, "substantial" if 0,60 < k ≤ 0,80 and "optimal" if k > 0,80.

Results: 167 patients were included (57% women) with a mean age of 52±16 years. 42% of them had systemic autoimmune diseases, 22% spondyloarthropathies and 36% other RD. 2 had history of past active tuberculosis (TB). At the time of screening, 46.11% were treated with GC.

LTBI was diagnosed in 35 patients: 15 had both QTF and TST positive, 16 only QTF positive and 4 only TST positive. 12 from 31 QTF positive patients were treated with GC at the time of screening. 3 from 19 TST positive patients were treated with GC at the time of screening.

After LTBI screening 62 patients received biological treatment, 4 of them had both test positive, 6 only QTF positive and 2 only TST positive. 11 received LTBI treatment according to the hospital protocol (isoniazid for 6 to 9 months). 10 completed treatment, 1 did not because of intolerance and did not receive other treatment. 1 patient with only TST positive was considered a false positive and did not receive treatment. During follow-up no TB reactivation was reported.

23 patients with LBTI received treatment other than biological therapy during follow-up, of them 8 received LBTI treatment. There was no TB reactivation during follow up.

The Kappa concordance between QTF and TST was estimated: moderated in the whole sample, poor in the patients treated with GC at screening, and substantial when the patients treated with GC at screening were excluded. Results are shown in Table 1.

Table 1. Kappa concordance between QTF and TST.

	TOTAL SAMPLE	PATIENTS WITH GC AT LTBI SCREENING	PATIENTS WITHOUT GC AT LTBI SCREENING
Number of coincidences (p1)	147 (88.02%)	64 (83.12%)	83 (92.22%)
Number of randomly expected coincidences (p_e)	124.1 (74.28%)	62.9 (81.73%)	61.8 (68.62%)
Kappa = p1- p_e /1- p_e	**0,534**	**0,117**	**0.752**
IC 95%	(0.358-0.710)	(-0.154-0.305)	(0.579-0.926)

Conclusion: QTF seems to be the most appropriate LTBI screening test in patients with RD treated with GC. Screening and treatment of LTBI in patients with RD treated with or without biological agents was effective in reducing TB reactivation.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3157

POS1158 THE SPECTRUM OF NON-TUBERCULOUS OSTEOARTICULAR INFECTIONS IN A RHEUMATOLOGY DEPARTMENT DURING THE YEARS 2010-2020: A RETROSPECTIVE STUDY OF 102 CONSECUTIVE CASES IN A SINGLE CENTER

M. Chammakhi[1], C. Bendahmane[1], F. Kemiche[1], I. Cerf-Payrastre[1], E. Pertuiset[1]. *[1]Centre Hospitalier René Dubos, Rheumatology, Pontoise, France*

Background: osteoarticular infections (OAI) are characterized by a large variety of sites, causative microorganisms, source and route of infection, risk factors and also by the fact that several medical specialties are involved in diagnosis and treatment. These characteristics are subject to changes over the time.

Objectives: to describe the spectrum of non-tuberculous OAI in the absence of OA material, including native septic arthritis (SA) and non-postoperative SA or infectious spondylodiscitis (SPDI) during the years 2010-2020. This includes demographics, comorbidities, site of infection, causative microorganisms, source of infection, diagnosis, treatment procedures and mortality.

Methods: medical records of patients aged 18 years old or above who were diagnosed with a non-tuberculous OAI in the Department of rheumatology of our hospital during the 2010-2020 period were selected and retrospectively reviewed. OAI with the following characteristics were excluded: SA on prosthetic joints, postoperative SA or SPDI, osteomyelitis, brucellosis, Lyme disease. Only proven cases where included on the basis of an isolated pathologic organism at the site of infection and/or in the blood (with typical clinical, biological and imaging features).

Results: There were 102 consecutive patients (males 62%), aged 62.5±16.8 years, with an IMC of 25.1±5.2. Peripheral SA where observed in 52 cases, SPDI in 33 cases, non-peripheral SA in 10 cases (sacroiliitis 5, pubic symphysitis 2, sternoclavicular 2, posterior interapophyseal 1); in 7 patients, there was an association of SPDI and peripheral SA. At least two non-contiguous sites were involved in 22 patients (21.5%). The sites of the positive sample where: osteoarticular (synovial fluid, vertebral biopsy) in 47 cases; blood in 28 cases; both of them in 27 cases.

In the 102 cases, 105 microorganisms grew in culture including one Candida glabrata. The following bacteria where responsible in the other cases: 42 *Staphylococcus aureus* (including 3 cases of methicillin resistant); 7 coagulase-negative *Staphylococcus spp.;* 6 Group A *Streptococcus*; 12 group B *Streptococcus agalactiae*; 8 groups C/G *Streptococcus*; 3 group D *Streptococcus gallolyticus*; 2 *Streptococcus pneumoniae*; 1 *Neisseria gonorrhea*; 8 enterobacteria; 3 *Enterococcus faecalis;* 3 *Pseudomonas aeruginosa*; 3 *Haemophilus*; 6 others species (2 *Parvimonas micra*, 1 *aerococcus urinae*, 1 *Nesseiria bacilliformis*, 1 *bacteroides fragilis*, 1 *campylobacter fetus*).

The most frequent host risk factors were: diabetes (21%), inflammatory/auto-immune disease (10%; including 3 rheumatoid arthritis), chronic renal insufficiency

(CC<30 ml/mn) (6%), active cancer with local or general extension (6%), immunodeficiency state (SCID revealed by OAI in 2 cases). Three patients where on biological therapy.
The source of infection was known in 76 cases: skin infection in 27; urinary tract infection in 17; joint injection in 7 **cases**; dental infection in 6 cases; infected vascular material in 6 cases; abdominal infection in 5 cases; genital infection in 3 cases; ENT infection in 3 cases; pulmonary disease 2 cases.
Mean duration of symptoms ranged from 13 days for peripheral SA to 39 days for SPDI. Fever (≥38°C) was present in 52% of cases. Mean CRP was 182±128 mg/l. Blood cultures where positive in 55.5%. There was only one case of infectious endocarditis. All patients were treated with antibiotics with a mean duration of 10.2±5.6 weeks. Orthopedic surgery was proceeded in 67% of peripheral septic arthritis and in 10% of the other OAI. Six patients where admitted in the intensive care unit; 4 patients died (4.3%). Mean length of hospitalization was 28.6±15 days.
Conclusion: in the years 2010-2020, non-tuberculous OAI represents a regular cause of hospitalization in rheumatology. Iatrogenic origin accounts for 13% of cases and urinary tract infection for 17%. Staphylococcus species are involved in only 48% of cases and Streptococcal species in 30%.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3569

POS1159 **THE ROLE OF URINARY TRACT INFECTIONS AS A SOURCE OF OSTEOARTICULAR INFECTIONS IN A RHEUMATOLOGY DEPARTMENT DURING THE 2010-2020 PERIOD: A RETROSPECTIVE STUDY**

C. Bendahmane[1], M. Chammakhi[1], F. Kemiche[1], I. Cerf-Payrastre[1], E. Pertuiset[1]. [1]*Centre Hospitalier René Dubos, Rheumatology, Pontoise, France*

Background: There are several sources of infection in the pathogenesis of osteoarticular infections (OAI). Urinary tract infections (UTI) have rarely been involved whereas skin infection and Staphy*lococcus aureus* represent the classic pair.
Objectives: To describe the role of UTI as the source of infection in OAI including septic arthritis (SA) on native joints and infectious spondylodiscitis (SPDI). To compare characteristics of these cases with those of others source and those without any known source.
Methods: Medical records of patients aged 18 years old or above who were diagnosed with a non-tuberculous OAI in the department of rheumatology of our hospital during the 2010-2020 period were selected and retrospectively reviewed. The following cases were excluded: SA on prosthetic joint, OIA on surgical material, osteomyelitis, post-operative OAI, SA after joint injection, brucellosis, Lyme disease. Only proven cases where included on the basis of an isolated pathologic organism at the site of OAI infection and/or in the blood (with typical clinical, biological and imaging features). Usually the OAI was considered of urinary source if the same microorganism grew in urine and the OA/blood sample. Cases with probable urinary source were also included on the basis of the type of microorganism and a history of UTI and/or urologic surgery and/or recent antibiotic therapy.
Results: 95 consecutive cases of proven OAI were included. There were 17 cases (18%) of urinary origin. In 12 cases the same micro-organism grew in urine and OA/blood culture: 5 methicillin sensitive *Staphylococcus aureus*, 2 *Streptococcus Gallolyticus* (associated with *E. Coli* in one case), 1 *Escherichia Coli*, 1 *Klebsiella pneumoniae*, 1 *Enterococcus faecalis*, 1 *aerococcus urinae*, 1 candida glabrata. Five patients had a probable urine source. In one patient with SPDI and an history of recurrent UTI, blood culture grew *E. Coli* whereas urine culture grew *Enterococcus faecalis*. In 4 cases, urine was sterile but a sample (OA in 3, blood in 1) was positive for *E. Coli* (n=2) or *Pseudomonas aeruginosa* (n=2).
The type of OAI was: SPDI in 10 cases, peripheral SA in 4 cases, both of them in one case and pubic symphysitis in 2 cases. Blood culture was positive in 10 cases and OA sample in 9 cases. Demographics characteristics were: male 59%; age 68.7±11 years. Risk factors were: diabetes 29%; cancer treated with cytotoxic chemotherapy 2 cases; inflammatory disease 2 cases; urological disease and/or recurrent UTI in 59%; immunodeficiency 1 case. Duration of symptoms was 47.1 +/- 50.7 days. Urinary symptoms where present in 29% of patients and fever in 47%. There was no case of infectious endocarditis. Surgical intervention was realized in only one patient. No patient has been admitted in intensive care unit and no patient died. Length of hospitalization was 28±8.5 days. Duration of antibiotic therapy was 13.6±9 weeks. One patient with pubic symphysitis was not cured.
The comparison between the group of OAI with urinary source (n=17) and the groups with another primary source of infection (n=52) or no known source of infection (n=26) shows in the first one: a higher prevalence of SPDI (59% vs 34% and 19% respectively), an older age (68.7 years vs 61.9 and 59.7 respectively), a higher prevalence of diabetes or cancer, a longer duration of symptoms (47.1+/-50.7 days vs 21.9+/-29.6 and 22.5+/-25.4 respectively) and a lower mean value of CRP (156+/-135 mg/l vs 182+/-124 and 180+/-140 respectively). A UTI was detected in 76% of OAI of urinary source but also in 13% of other cases (including *E. Coli* 5 cases).
Conclusion: In the years 2010-2020, UTI was responsible for 18% of non-tuberculous OAI as we defined them in this study. A UTI does not demonstrate the responsibility of the microorganism isolated. Thoracolumbar SPDI is the main type. This relatively high frequency has not been reported before and is probably the consequence of the increasing population of aged patients with risk factors and urologic diseases. Clinicians have to be aware of it and prevention is required.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3611

POS1160 **BRUCELLAR SPONDYLODISCITIS: CLINICAL AND MAGNETIC RESONANCE IMAGING FINDINGS**

C. Daldoul[1], N. El Amri[1], S. Laataoui[1], K. Baccouch[1], H. Zegaloui[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*

Background: Osteoarticular involvement is one of the most common complications of brucellosis and it can occur in up to two thirds of patients infected. Vertebral involvement during brucellosis is considered not only as the most prevalent localization but also as the most severe one.
Objectives: The aim of the present study was to describe the clinical and the magnetic resonance imaging features of brucellar spondylodiscitis.
Methods: We conducted a retrospective study including 21 patients who have been hospitalized for spinal brucellosis from 1998 to 2019. The diagnosis of brucellosis was based on clinical symptoms, MRI findings and isolation of brucella species in blood or tissue specimens and/or a positive Wright agglutination test.
Results: Twenty-one patients were included. The mean age was 57.5 years [33-74] (13 males and 8 female). The geographical origin of the patients was rural in 76% of the cases. The median duration of symptoms progression before diagnosis was 4.5 months [1-8].The main symptom leading to seek medical care was an inflammatory back pain and it was found in all cases. It was associated with unilateral radiculopathy in 8 cases and with a bilateral radiculopathy in 1 case. The other clinical features found were fever in 17 patients, sweats in 14 cases, weight loss in 10 cases and hepatomegaly in 1 patient. The physical examination revealed tenderness on palpation in 12 cases, a motor weakness of the two lower limbs in 2 cases. Brucella agglutination test was ≥1/160 in all cases. Blood cultures were negative in all cases. The median erythrocyte sedimentation rate (ESR) and serum C-reactive protein level were 40 mm and 11 mg/dl) respectively. Spondylodiscitis was located in the lumbar dorsal and cervical spine in respectively 10, 8 and 3 cases. The most affected level was the L4-L5 level in 5 cases followed by the T10-T11 level in 3 cases. The involvement of more than 2 vertebrae was found in 4 cases. Associated sacroiliitis was found in one patient. All MRI images of the affected vertebrae showed hypo intense signal on T1 weighted image and hyper intense signal on T2 weighted image. Disc space narrowing was found in 8 cases. Vertebral body osteolysis was found in 10 cases. Epidural collection was documented in 3 cases with a size up to 5cm. Paravertebral and peri-vertebral abscesses were detected in 5 cases. Intradiscal abscesses were observed in 3 cases. Cord compression and involvement of root nerve were noted in respectively 5 and 1 cases. Biopsy was performed in 5 cases, but bacteriological examination was contributory to the diagnosis in 1 case. All patients received antibiotic treatment with a combination of two or three drugs, corticosteroids were prescribed in 5 patients and one patient underwent a surgical intervention. The evolution was good 16 in patients, three patients suffered from chronic back pain, one patient had persistent neuropathic pain and one patient had paresis.
Conclusion: Brucella spondylodicitis is still a serious public health problem in developing countries. MRI findings associated with clinical symptoms may establish the diagnosis even if bacteriological examinations are negatives
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4153

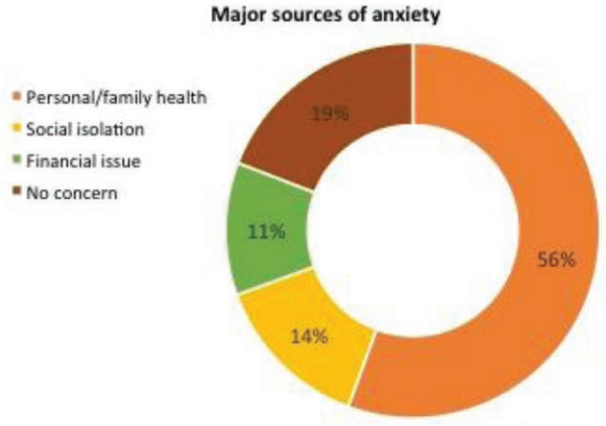
COVID-19

COVID-19

POS1161 **A CITIZEN SCIENCE APPROACH TO CAPTURE POOR MENTAL HEALTH RELATED TO COVID-19 IN RHEUMATIC PATIENTS AFTER CONFINEMENT DURING PANDEMIC IN ITALY**

F. Ingegnoli[1], M. Buoli[2], C. Posio[3], R. DI Taranto[1], A. Lo Muscio[3], E. Cumbo[1], S. Ostuzzi[4], R. Caporali[1]. [1]*Università degli Studi di Milano, Division of Clinical Rheumatology, ASST Pini, Dept. of Clinical Sciences & Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Milano, Italy*; [2]*Università degli Studi di Milano, Dept. of Pathophysiology and Transplantation, Dept. of Neurosciences and Mental Health, Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Milano, Italy, Milano, Italy*; [3]*Università degli Studi di Milano, Dept. of Pathophysiology and Transplantation, Milano, Italy*; [4]*ALOMAR, Lombard Association for Rheumatic Diseases, Milano, Italy*

Background: A considerable psychosocial burden is one of the relevant consequences of the COVID-19 pandemic. In particular, quarantine measures have been related to negative psychological effects, including symptoms of post-traumatic stress disorder, stress, anxiety, and depression (1). This rise in mental health disorders might be even worse among people more vulnerable to psychological stress such as patients suffering from chronic rheumatic diseases (RDs).
Objectives: The present Italian nationwide survey engages patients with rheumatic conditions through eleven associations of RD patients. It is conducted to establish the COVID-19 related self-reported poor mental health symptoms and to identify potential factors associated with these concerns among RDs who experienced the COVID-19 quarantine in Italy.
Methods: We collected data from May to September 2020 from RD patients living in Italy during the COVID-19 quarantine by an ad-hoc online survey. By using their mailing list and the related webpage and social network, eleven patients' associations sent a call to RD patients asking them to complete an anonymous online survey which included the Perceived Stress Scale (PSS), and the Impact Event Scale-Revised (IES-R). χ^2 tests were performed to detect statistically significant differences in both rating scale scores between groups defined by qualitative variables. Correlation analyses were realized with quantitative variables and rating scale scores. Variables significant in univariate analyses were then inserted in multivariate regression models.
Results: In total, 507 RD patients completed to the survey. 375 (73.9%) patients had inflammatory arthritis (243 rheumatoid arthritis, 76 psoriatic arthritis, 49 ankylosing spondylitis, and 7 Still's disease), and 96 (18.9%) with connective tissue diseases or systemic vasculitis. 31 (6.1%) patients had primary fibromyalgia and 5 osteoarthritis or crystal arthropathies. Self-reported major sources of anxiety are reported in the Figure 1 below.



The mean (SD) scores of the PSS-10 and the IES-R were 18.1 ± 8.1 and 29.7 ± 17.5, respectively. With regard to the IES-R subscale scores, the total sample did not show a prominence of one of the three main domains (intrusion, avoidance and hyperarousal). Higher PSS scores were significantly associated with younger age (p<0.01), female gender (p<0.01), living outside Lombardy (p=0.03), presence of overweight/obesity (p=0.01), ongoing psychopharmacotherapy (p<0.01), and anxiety for loss of incomes (p<0.01). Female gender (p<0.01) and living outside Lombardy (p=0.02) were associated also with higher IES-R scores, together with the presence of intestinal diseases (p=0.03), anxiety disorders (p<0.01), and worries about health (p<0.01).
Conclusion: This nationwide study revealed a high impact of self-reported distress, anxiety, and perceived stress among rheumatic patients after confinement during COVID-19 pandemic in Italy. Different factors were found to be predictive of poor mental health such as having female gender, younger age, living outside Lombardy, having overweight/obesity, or intestinal diseases, having a history of psychiatric symptoms (e.g. anxiety). Moreover, the lockdown experience worsened psychiatric symptoms and increased the assumption of psychopharmacotherapy in this vulnerable population. Prevention strategies focused on specific variables should be implemented to ameliorate psychological well-being of fragile patients during pandemics.
REFERENCES:
[1] Brooks SK, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. Lancet. 2020;395:912-20
Acknowledgements: We wish to thank the Lombard Association of Rheumatic Diseases (ALOMAR) for its invaluable contribution to the planning and dissemination the survey, all the Italian associations among which the National Association of People with Rheumatic and Rare Diseases (APMARR) and National Association of People with Rheumatic Diseases (ANMAR) that disseminated the survey through social media. The authors are grateful to all patients for contributing to this project.

Disclosure of Interests: Francesca Ingegnoli: None declared, Massimiliano Buoli: None declared, Cristina Posio: None declared, Raffaele Di Taranto: None declared, Alessandro Lo Muscio: None declared, Enrico Cumbo: None declared, Silvia Ostuzzi: None declared, Roberto Caporali Speakers bureau: Abbvie, Amgen, BMS, Celltrion, Galapagos, Gilead, Lilly, Pfizer, Roche, UCB, Sanofi, Fresenius Kabi, Samsung bioepis, MSD, Consultant of: Galapagos, Gilead, Lilly,Janssen, MSD.
DOI: 10.1136/annrheumdis-2021-eular.380

POS1162

PREDICTORS OF HOSPITALISATION IN PATIENTS WITH RHEUMATIC DISEASE AND COVID-19 IN IRELAND: DATA FROM THE COVID-19 GLOBAL RHEUMATOLOGY ALLIANCE PHYSICIAN-REPORTED REGISTRY

R. Conway[1,2], E. Nikiphorou[3,4], C. Demetriou[5], C. Low[6], K. Leamy[7], J. Ryan[8], R. Kavanagh[9], A. Fraser[10,11], J. Carey[12,13], P. O'connell[14], R. Flood[15], R. Mullan[2,15], D. Kane[2,15], P. Robinson[16], J. Liew[17], R. Grainger[18], G. Mccarthy[7]on behalf of COVID-19 Global Rheumatology Alliance. *[1]St. James's Hospital, Rheumatology, Dublin, Ireland*; *[2]Trinity College Dublin, Medicine, Dublin, Ireland*; *[3]King's College Hospital, Rheumatology, London, Ireland*; *[4]King's College London, Centre for Rheumatic Diseases, London, United Kingdom*; *[5]University of Nicosia Medical School, Primary Care and Population Health, Nicosia, Cyprus*; *[6]St. Vincent's University Hospital, Rheumatology, Dublin, Ireland*; *[7]Mater Misericordiae University Hospital, Rheumatology, Dublin, Ireland*; *[8]Cork University Hospital, Rheumatology, Cork, Ireland*; *[9]Galway Clinic, Rheumatology, Doughiska, Ireland*; *[10]University Hospitals Limerick, Rheumatology, Limerick, Ireland*; *[11]University of Limerick, Graduate Entry Medical School, Limerick, Ireland*; *[12]Galway University Hospitals, Rheumatology, Galway, Ireland*; *[13]National University of Ireland Galway, Medicine, Galway, Ireland*; *[14]Beaumont Hospital, Rheumatology, Dublin, Ireland*; *[15]Tallaght University Hospital, Rheumatology, Dublin, Ireland*; *[16]University of Queensland, Medicine, Brisbane, Australia*; *[17]Boston University School of Medicine, Rheumatology, Boston, United States of America*; *[18]University of Otago, Medicine, Wellington, New Zealand*

Background: There is limited data regarding the risk of hospitalisation in patients with rheumatic disease and COVID-19 in Ireland.
Objectives: We used the COVID-19 Global Rheumatology Alliance (GRA) registry data to study outcomes and their predictors.

		All significant variable model		Most parsimonious model	
	Unadjusted OR (95% CI)	Adjusted OR (95%CI)*	Adjusted p-value*	Adjusted OR (95%CI)[&]	Adjusted p-value[&]
Female	0.45 (0.20-1.02)	0.33 (0.05-2.23)		0.34 (0.09-1.36)	0.128
Age (years)	1.08 (1.05-1.11)	1.04 (0.97-1.10)	0.224	1.06 (1.01-1.10)	0.010
Inflammatory arthritis	0.11 (0.05-0.28)	0.14 (0.02-0.95)	0.044	0.09 (0.02-0.32)	<0.001
Connective Tissue Disease and Other	1.56 (0.62 - 3.92)				
No comorbidities	0.11 (0.04-0.30)	0.76 (0.09-6.58)	0.802		
Most common comorbidities					
COPD / asthma	4.77 (1.23-18.54)	3.09 (0.16-60.07)	0.456		
CVD	3.40 (1.31-8.85)	0.11 (0.01-1.88)	0.129		
Hypertension	3.71 (1.52-9.08)	0.56 (0.04-7.94)	0.668		
Obesity	0.58 (0.10-3.30)				
Number of comorbidities (Median, IQR)	3.01 (1.92-4.72)	2.99 (0.59-15.02)	0.184	1.93 (1.11-3.35)	0.020
Never Smoker	ref.		0.889		
Ever Smoker	3.17 (1.18-8.89)	1.19 (0.10-13.68)			
Medication prior to COVID-19 diagnosis					
Glucocorticoids	9.26 (1.95-43.89)	18.14 (1.13-290.81)	0.041	15.01 (1.77-127.16)	0.013
csDMARD monotherapy	0.42 (0.17-1.00)				
b/tsDMARD (monotherapy or in combination with csDMARD)	0.24 (0.10-0.58)	1.36 (0.19-9.72)	0.557		

Methods: We examined data on patients and their disease-related characteristics entered into the COVID-19 GRA provider registry from Ireland (24th March 2020 to 31st August 2020). Multivariable logistic regression was used to assess the association of demographic and clinical characteristics with hospitalisation.
Results: Of 105 patients, 47 (45.6%) were hospitalised and 10 (9.5%) died. Multivariable logistic regression analysis showed age (OR=1.06, 95%CI 1.01 to 1.10), number of comorbidities (OR=1.93, 95%CI 1.11 to 3.35), and glucocorticoid use (OR=15.01, 95%CI 1.77 to 127.16) were significantly associated with hospitalisation. A diagnosis of inflammatory arthritis was associated with a lower odds of hospitalisation (OR=0.09, 95%CI 0.02 to 0.32).
Conclusion: Increasing age, comorbidity burden, and glucocorticoid use were associated with hospitalisation, while a diagnosis of inflammatory arthritis was associated with lower odds of hospitalization.
Disclosure of Interests: Richard Conway Speakers bureau: Janssen, Roche, Sanofi, Abbvie, Elena Nikiphorou Speakers bureau: AbbVie, Eli-Lilly, Gilead, Celltrion, Pfizer, Sanofi, Christiana Demetriou: None declared, Candice Low: None declared, Kelly Leamy: None declared, John Ryan: None declared, Ronan Kavanagh: None declared, Alexander Fraser: None declared, John Carey: None declared, Paul O'Connell: None declared, Rachael Flood: None declared, Ronan Mullan: None declared, David Kane: None declared, Philip Robinson Speakers bureau: UCB, Roche, Pfizer, Gilead, Janssen, Novartis, Eli Lilly, Abbvie, Grant/research support from: Abbvie, UCB, Novartis, Janssen, Pfizer, Jean Liew Grant/research support from: Pfizer, Rebecca Grainger Speakers bureau: Pfizer, Cornerstones, Janssen, Novartis, Abbvie, Geraldine McCarthy: None declared.
DOI: 10.1136/annrheumdis-2021-eular.420

POS1163 CHARACTERISTICS AND OUTCOMES IN A REAL-WORLD COHORT OF RHEUMATOID ARTHRITIS PATIENTS WITH COVID-19

Y. Ye[1], X. Yue[1], W. Krueger[1], L. Wegrzyn[1]. [1]*AbbVie Inc., Global Epidemiology, North Chicago, United States of America*

Background: While some risk factors for severe COVID-19 outcomes have been identified for the general population and patients with rheumatic diseases (1-3), what drives these outcomes in specific rheumatic disease remains unclear. In addition, these findings need to be assessed across various observational data sources to ensure external validity.
Objectives: To describe the demographics, comorbidities, and severe COVID-19 outcomes among rheumatoid arthritis (RA) patients infected with SARS-CoV-2 in the United States.
Methods: A large nationwide electronic health record database (Optum, Inc.) in the United States, with data range between February 1, 2020 and September 17, 2020, was used to describe the demographics, comorbidities, and severe COVID-19 outcomes of RA patients with confirmed COVID-19 diagnosis (diagnosis for COVID-19 or positive PCR or antigen test). Patients with a single diagnosis of RA (ICD-10 code) before the diagnosis of COVID-19 were included. Patients missing age or sex, under 18 years of age on COVID-19 diagnosis date, or having less than 15 months of activity prior to COVID-19 diagnosis in the data source were excluded. We described demographics, comorbidities, and severe COVID-19 outcomes, including death, hospitalization, ICU admission, and acute respiratory insufficiency (ARI) identified between 14 days prior to and 30 days after COVID-19 diagnosis. Mean and standard deviation (SD) was reported for continuous variables. For categorical variables, count (N) and proportion was reported.
Results: We identified 2,948 patients diagnosed with RA and infected with SARS-CoV-2 (mean age± SD: 62 years ± 16, 77% female, 68% white). Of all identified patients, 38% were current or former smokers. For the 2,614 patients with BMI recorded, 78% were overweight or obese (mean BMI±SD: 31.2±8.3). The mean Charlson comorbidity index (CCI) was 3.6 (SD 3.2), with 87% of the study cohort having one or more comorbid condition, including hypertension (55%), type 2 diabetes (26%), COPD (20%), moderate to severe asthma (17%), coronary artery disease (17%), chronic kidney disease (13%), and heart failure (13%). Severe COVID-19 outcomes occurred in 618 (21%) patients. Among all RA patients with COVID-19, 137 patients (4.6%) experienced ARI, 484 patients (16.4%) were hospitalized (including 174 (5.9%) admitted to the ICU), and 155 patients (5.3%) died.
Conclusion: Underlying medical conditions that are known or possible risk factors of severe illness from SARS-CoV-2 infection in the general population are common in this RA cohort from a large national EHR database. However, whether patients with RA are more vulnerable to severe COVID-19 outcome than the general population requires adjustment by age and other important confounders.
REFERENCES:
[1] Gianfrancesco M, Hyrich KL, Al-Adely S, Carmona L, Danila MI, Gossec L, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis. 2020;79(7):859-66.
[2] Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020;584(7821):430-6.
[3] Gold JAW, Wong KK, Szablewski CM, Patel PR, Rossow J, da Silva J, et al. Characteristics and Clinical Outcomes of Adult Patients Hospitalized with COVID-19 - Georgia, March 2020. MMWR Morb Mortal Wkly Rep. 2020;69(18):545-50.
Disclosure of Interests: Yizhou Ye Shareholder of: AbbVie Inc. and Pfizer Inc., Employee of: AbbVie Inc., Xiaomeng Yue Employee of: AbbVie Inc., Whitney Krueger Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Lani Wegrzyn Shareholder of: AbbVie Inc., Employee of: AbbVie Inc.
DOI: 10.1136/annrheumdis-2021-eular.565

POS1164 USE OF TELEMEDICINE FOR FOLLOW-UP OF SLE PATIENTS WITH NEPHRITIS IN THE COVID-19 OUTBREAK ("TELESLE"): THE 6-MONTH RESULTS OF A RANDOMIZED CONTROLLED TRIAL

H. So[1], E. Chow[1], T. K. LI[1], S. L. Lau[1], I. T. Cheng[1], C. C. Szeto[1], L. S. Tam[1]. [1]*The Chinese University of Hong Kong, Medicine and Therapeutics, Hong Kong, Hong Kong (SAR)*

Background: Patients with lupus nephritis (LN) might be more susceptible to COVID-19 due to the underlying disease, co-morbidities and use of immunosuppressants. We hypothesized that telemedicine (TM) could be a well-accepted mode of health-care delivery minimizing the risk of exposure to the severe acute respiratory syndrome coronavirus 2 (*SARS-CoV-2*), while maintaining disease control in these patients.
Objectives: To evaluate the short-term patient satisfaction, compliance, disease control and infection risk of TM compared with standard in-person follow-up (FU) for patients with LN during COVID-19.
Methods: This was a single-center randomized-controlled study. Consecutive patients followed at the LN clinic were randomized to either TM (TM group) or standard FU (SF group) in a 1:1 ratio. Patients in the TM group received scheduled follow-ups via videoconferencing. SF group patients continued conventional in-person outpatient care. The 6-month data were compared.
Results: From June to December 2020, 122 patients were randomized (TM: 60, SF: 62) and had attended at least 2 FU visits. There were no baseline differences, including SLEDAI-2k and proportion of patients in lupus low disease activity state (LLDAS), between the 2 groups except a higher physician global assessment score (PGA) in the TM group (mean 0.67±0.69 vs 0.45±0.60, p=0.003) (Table 1). The mean FU duration was 19.8±4.5 weeks. When comparing the most recent visit, the mean waiting time between entering the clinic waiting room (virtual or real) and seeing a rheumatologist (virtual or in-person) was significantly shorter in the TM group (22.5±28.6 vs 68.9±40.7 minutes, p< 0.001) (Figure 1A). The mean overall patient satisfaction score was higher in the TM group (mean 2.19±0.61 vs 1.89±0.78, p=0.042). The results of the post-consultation satisfaction questionnaire are shown in Figure 1B. The number of visits was similar in the two groups (TM: 3.1±1.3 vs SF: 3.0±1.2, p=0.981). However, there was a trend suggesting that alternative mode of FU was requested more frequently in the TM group than the SF group (TM: 12/60, 20.0% and SF: 5/62, 8.1%; p=0.057). More patients in the TM group had hospitalization (15/60, 25.0% vs 7/62, 11.3%; p=0.049) within the FU period, which was no longer statistically significant after adjusting for the baseline PGA. The proportions of patients remained in LLDAS were similar in the 2 groups (TM: 75.0% vs SF: 74.2%, p=0.919). None of the patients had COVID-19.
Conclusion: TM resulted in better patient satisfaction and could achieve similar disease control in patients with LN in the short-term when compared to standard care.

Table 1. Baseline clinical data of the recruited patients and comparison between the telemedicine/standard follow-up groups

	Overall (n=122)	Telemedicine group (n=60)	Standard follow-up group (n=62)	P-value
Age in years	44.4±11.5	44.1±11.7	44.7±11.5	0.779
Gender: Female	111 (91.0)	55 (91.7)	56 (90.3)	0.796
Disease duration in years	15.1±9.0	16.2±8.7	14.0±9.1	0.115
Nephritis class III, IV or V	108 (88.5)	54 (90.0)	54 (87.1)	0.427
24 hour urine proteinuria in gram	0.51±0.63	0.53±0.60	0.50±0.65	0.712
Current use of prednisolone	112 (91.8)	57 (95.0)	55 (88.7)	0.323
Daily prednisolone dose in mg	5.51±4.21	5.69±4.17	5.34±4.29	0.570
Use of immunosuppressant	90 (73.8)	46 (76.7)	44 (71.0)	0.474
SLEDAI-2K	3.65±2.33	4.00±2.34	3.30±2.29	0.097
PGA	0.56±0.65	0.67±0.69	0.45±0.60	**0.003**
LLDAS	78 (63.9)	36 (60.0)	42(67.7)	0.251
Remission	0 (0)	0 (0)	0 (0)	n/a
Presence of comorbidity	87 (71.3)	40 (66.7)	47 (75.8)	0.264
SDI	0.93±1.15	1.08±1.28	0.78±0.98	0.243
HAQ-DI	0.23±0.46	0.25±0.47	0.21±0.44	0.571
HADS:	6.07±4.12	6.20±4.19	5.93±4.09	0.720
Anxiety scale	5.72±4.31	5.73±3.93	5.70±4.68	0.724
Depression scale				

Data are reported as mean ± SD or number (%). LLDAS: lupus low disease activity state; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index; HAQ-DI: Health Assessment Questionnaire Disability Index; and HADS: Hospital Anxiety and Depression Scale.

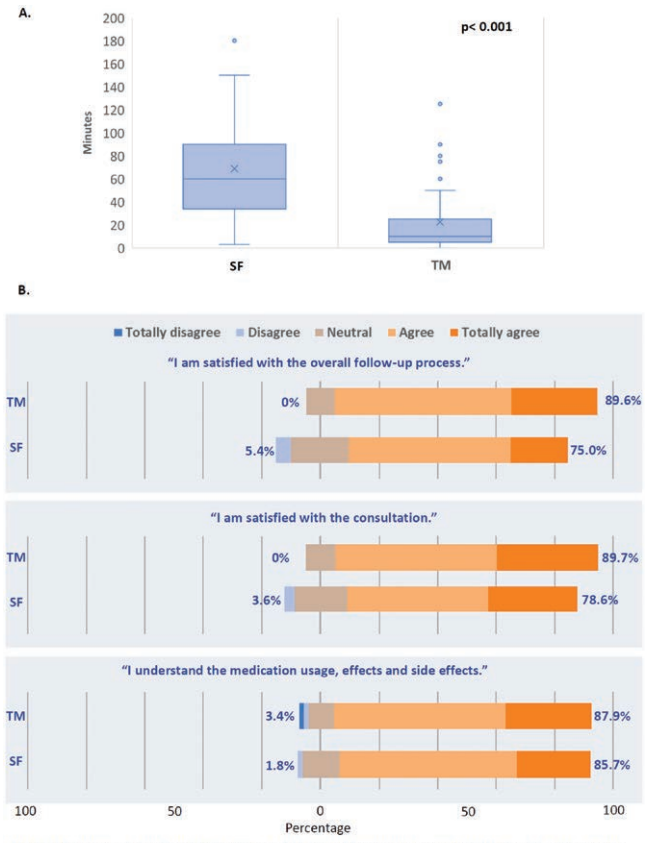


Figure 1A. Mean waiting time between entering the clinic waiting room (virtual or real) and seeing a rheumatologist. TM = Telemedicine, SF = Standard follow-up. **Figure 1B.** The results of the post-consultation satisfaction questionnaire. Response is shown as percentage with positive responses on the right. The neutral category was removed when calculating percentages.

Disclosure of Interests: Ho SO: None declared, Evelyn Chow: None declared, Tena K. Li: None declared, Sze-Lok Lau: None declared, Isaac T. Cheng: None declared, Cheuk-Chun Szeto: None declared, Lai-Shan Tam Grant/research support from: Grants from Novartis and Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.580

POS1165

LIFESTYLE AND MOOD CHANGES IN AXSPA PATIENTS DURING THE QUARANTINE PERIOD

E. Erpek[1], D. Solmaz[1], E. Durak Ediboglu[1], G. Alp[1], E. Otman Akat[1], H. Cinakli[1], G. Kabadayi[1], İ. Kurut Aysin[1], O. Bayindir[1], S. Gucenmez[1], M. Ozmen[1], S. Akar[1]. [1]*Izmir Katip Celebi University Faculty of Medicine, Rheumatology, Izmir, Turkey*

Background: On March 11, 2020, the World Health Organization declared coronavirus disease 2019 (COVID-19) as a pandemic, and mandatory quarantine was applied in Turkey between April and June 2020. With this sanction, sudden changes occurred in a routine lifestyle.
Objectives: This study aimed at evaluating physical activity changes, presence of anxiety and depression, altered eating habits and their relationship with disease activity in axial spondyloarthritis (AxSpA) patients during the quarantine period.
Methods: AxSpA patients, who were examined in the rheumatology clinic in the last year before the pandemic period and their relatives were included in this study and were contacted by phone to participate. A structured questionnaire form was performed which included the following data: questions about demographic characteristics, medication use, disease activity scales; BASDAI, BASFI, Patient acceptable symptom state (PASS), patient-reported physical activity state, Short Questionnaire to Assess Health enhancing physical activity (SQUASH), Three-Factor Eating Questionnaire (TFEQ-21), and Hospital Anxiety and Depression Scale (HADs).
Results: 204 AxSpA patients and 106 patients' relatives were contacted in the study (Figure 1). The frequency of male sex and alcohol consumption was higher in the AxSpA compared to the relatives and, other demographic features were summarized in Table 1. 30% of AxSpA patients and 37% of patient relatives were gained weight with mean 4.5±2.4 and 4.4±3.4 kilograms, respectively. Weight gain were similar male and female in AxSpA (26.2% vs 37.2%, p>0.05). However, the men in the AxSpA group gained more weight than relatives group (26.2% vs 7%, p<0.05). Weight gain group had decreased physical activity than stable group in AxSpA patients (54.8% vs 37.8%, p<0.05). We showed mild negative correlation between BASDAI and BASFI scores with SQUASH- total activity score (r:-0.15, p<0.05; r:-0.25, p<0.001, respectively). Anxiety prevalence were found slightly higher in patients group but not significantly (40.2% vs 32.1%; p>0.05). Depression were much higher in AxSpA group than relatives (43.6% vs 28%, p<0.001). Depression and anxiety were correlated with disease activity (HADs Depression vs BASDAI r:0.380, p<0.001; HADs Anxiety vs BASDAI r:0.418, p<0.001) and function (HADs Depression vs BASFI r:0.342, p<0.001; HADs Anxiety vs BASFI r:0.313, p<0.001). Among eating habits, uncontrolled and emotional eating scores were showed low correlation with anxiety (r:0.169, p<0.05; r:0.163, p<0.05, respectively).
Conclusion: One third of our patients were weight gain and approximately half of them had decreased physical activity but we did not show relation between these parameters and disease related factors in the limited period. In addition to that depression and anxiety were detected significant part of AxSpA patients and both of them were correlated with disease activity.

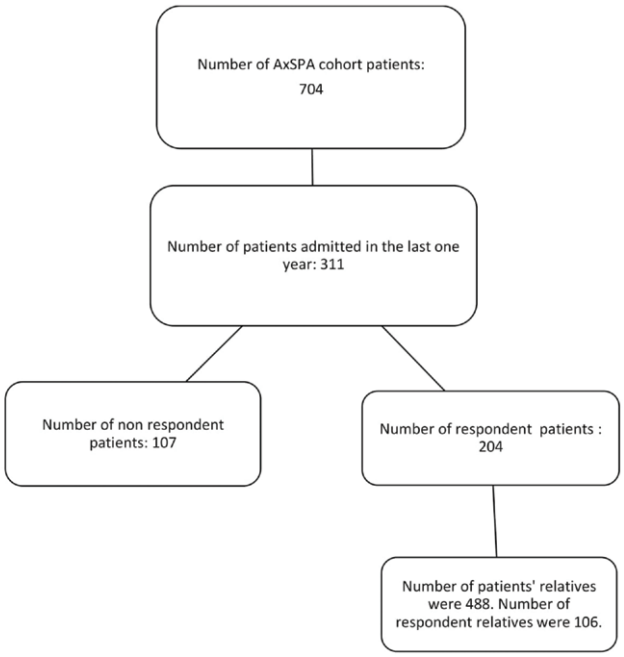


Figure 1: Flow chart of study population

Table 1. Study Population Characteristics

	AxSpa n:204	Controls n:106	p value
Age (years) mean ± SD	43.1±11.4	40.6±12.6	>0.05
Male n(%)	125(61.3)	26(24.5)	**<0.001**
Education time (years) mean ± SD	9.8±4.3	9.7±4.0	>0.05
Current smoker n(%)	77(37.7)	31(29.2)	>0.05
Alcohol consumption n(%)	60(29.4)	9(8.5)	**<0.001**
Current BMI kg/m^2 mean ± SD	26.8±4.6	26.5±4.7	>0.05
Weight gain group n(%)	62 (30.4)	40(37.7)	>0.05
Weight stable group n(%)	142 (69.6)	66(62.3)	
Current BASDAI mean ± SD	1.8±1.5	N/A	
Current BASFI mean ± SD	1.5±1.8	N/A	
Patients treated with biologic drugs n(%)	118(57.8)	N/A	
Patients treated with conventional drugs n(%)	84(41.1)	N/A	
Presence of Anxiety n(%)	82(40.2)	34(32.1)	>0.05
Presence of Depression n(%)	89(43.6)	30(28.0)	**<0.001**
TFEQ-R21emotional eating mean ± SD	5.2±3.1	5.6±2.7	**<0.05**
TFEQ-R21uncontrolled eating mean ± SD	14.7±6.3	17.5±5.4	**<0.001**
TFEQ-R21cognitive restraint mean ± SD	14.3±4.3	15±4.2	>0.05
Stable physical activity n(%)	117(57.4)	49(46.2)	>0.05
Decreased physical activity n(%)	87(42.6)	57(53.8)	

Acknowledgements: Special thanks to our clinical nurse Alev Vayni for her devoted assistance in interviewing patients to fill out the questionaire.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.592

POS1166 UNDERSTANDING PRESCRIPTION BEHAVIOR ACROSS HEALTHCARE PROFESSIONALS IN TREATING KNEE OSTEOARTHRITIS BEFORE AND DURING THE 2020 COVID-19 PANDEMIC

D. Baldock[1], E. Baynton[1], H. Hamdan[2]. [1]*Ipsos MORI, Healthcare Service Line, london, United Kingdom*; [2]*Ipsos Sdn Bhd, Healthcare Service Line, Kuala Lumpur, Malaysia*

Background: Knee Osteoarthritis (OA) treatment aims to provide symptom relief, easing joint pain and enabling mobility. The COVID-19 pandemic affected healthcare systems globally, including ways OA patients were treated.
Objectives: This study is to understand how treatment management of knee OA patients and prescribing behavior across US healthcare professionals (HCPs) was affected when COVID-19 impacted healthcare systems and regimes globally
Methods: A multi-center online medical chart review study of patients with OA was conducted between May – July 2019 & 2020 among US rheumatologists (rheums), orthopedic surgeons (orthos), primary care physicians with a focus in sports medicine (SM PCPs), and pain specialists, practicing across hospital and private practices. Recruited from a large access panel, physicians were screened for duration of practice in their specialty (3-50 years) and caseload (35 or more knee OA patients personally managed, at least 10 of which must be classified as moderate-severe). Patient charts were recorded for the next 5 eligible patients seen during the screening period. Respondents abstracted patient demographics and treatment regimes used. Descriptive statistics were used to analyse the data
Results: 275 physicians were recruited and collectively reported 1375 patients between May-Jul 2019; 260 physicians were recruited and collectively reported 1300 patients between May-Jul 2020.
Looking at treatments patients were receiving at time of reporting, oral medications, particularly NSAIDs, were widely used, regardless of the physician specialty. A directional increase of 6% in the proportion of reported patients deriving from sampled primary care SM PCPs from pre-COVID (Q219) to during COVID (Q220), whilst the same is not true for rheums, orthos, and pain specialists.

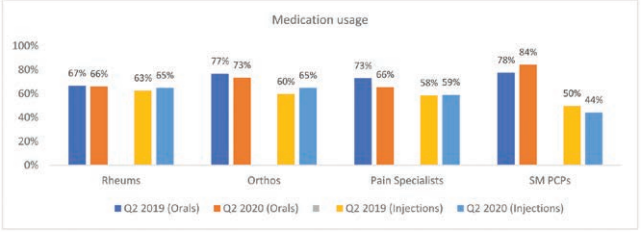


Figure 1. Medication usage in reported knee OA patients across all sampled specialties - Q2 2019 vs Q2 2020

With regards to the usage of injectable therapy, the opposite pattern is seen - higher proportions of reported patients deriving from sampled rheums, orthos & pain specialists receiving injectables vs those deriving from sampled SM PCPs. While focusing on orthos, the proportion of reported patients deriving from them who receive injectables grew by 5% in Q220 (during COVID) vs Q219 (pre-COVID) – directionally more so than other specialties. This is possibly due to limited elective surgeries during the pandemic.
Looking deeper into injectable usage amongst reported patients deriving from sampled rheums and orthos, the proportion of the total reported patient set receiving this treatment type is relatively similar across both specialties, prior to, and during the COVID-19 pandemic. However, among reported patients who received surgery, a directionally higher proportion of this reported patient cohort deriving from orthos are noted to receive injectables vs those from rheums – this is true both pre- and during the pandemic.
Conclusion: From the sample surveyed, it appears that primary care SM PCPs adopted their treatment adjustment during COVID-19 pandemic differently, by prescribing more orals, while other secondary care physicians (rheums, orthos, pain specialists) focused on injection treatment for longer pain relief. Considering movement restrictions and limited elective surgeries during the pandemic, the lack of targeted treatment options for knee OA has been made more apparent. With a burgeoning pipeline, many of which are targeted therapies, it is hopeful that knee OA treaters will be less reliant on symptom remedies and can readily offer patients' longer-acting pain relief or disease modifying options to combat joint deterioration

REFERENCES:

[1] Ipsos Osteoarthritis Therapy Monitor (May – July 2019, 275 specialists reporting on 1375 OA patients seen in consultation; May – July 2020, 260 specialists reporting on 1300 OA patients seen in consultation, data collected online. Participating physicians were primary treaters and saw a minimum number of 35 knee OA patients). Data © Ipsos 2021, all rights reserved.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.629

POS1167 REVIEW OF THE IMPACT OF COVID-19 PANDEMIC ON RHEUMATOLOGY SERVICES AT A LARGE TERTIARY CARE CENTRE IN WALES, UK

R. Asif[1], N. Elndari[2], A. Negi[1]. [1]*Cardiff and Vale University Health Board, Rheumatology, Cardiff, United Kingdom*; [2]*Cardiff and Vale University Health Board, Internal Medicine, Cardiff, United Kingdom*

Background: COVID-19 pandemic had an unprecedented impact on the delivery of patient care. Rheumatology services had to rapidly adapt to virtual consultations at the onset of the pandemic. However, providing a high quality and effective service in a virtual setting can be challenging and therefore its prudent to do a formal review and gain patient feedback to ensure that these clinics are fit for purpose.
Objectives: To evaluate the impact of first wave of COVID-19 pandemic on patients with autoimmune rheumatic conditions, assess delivery of rheumatology outpatient care and record patient feedback.
Methods: This study included patients on the Rheumatology clinic lists between 3rd and 31st August 2020. An electronic survey questionnaire was developed and the survey link was sent to patients via a text message using secure IT platform. Data was collected on patient demographics, diagnosis, comorbidities, treatments, clinical/ laboratory confirmed COVID-19 diagnosis, treatment interruption, impact on work, personal protective measures taken and views on virtual consultations.
Results: 307 patients responded with 287 complete responses. 73.1%(223) were female and 32.4% (99) were >65 years of age. Rheumatoid arthritis was the most common diagnosis 41.6%(127). Hypertension was the commonest comorbidity 21.4%(64) followed by Chronic lung disease 17.3%(52). 28.8%(85) were on Hydroxychloroquine, 26.7%(79) Methotrexate, 14.2%(42) Sulfasalazine and 13.2%(39) on Prednisolone. 22.3%(66) were on Biologics: Anti TNF 12.8%(38), Tocilizumab 3.7%(11) and Rituximab 3%(9). 52.6%(161) shielded, 16.9%(55) self-isolated and 30.3%(93) only maintained social distance. 197 patients self reported as being vulnerable but based on their treatment,only 167 patiemts met the clinically extremely vulnerable (CEV) criteria and all of those received government shielding letter.
3.6%(11) had lab confirmed COVID-19, 3.2%(10) had clinically suspected COVID-19 infection. 14.3% (43) had their treatment interrupted. 4.6%(14) were unable to work from home or maintain social distancing at work. 59.8%(182) had face-to-face consultation changed to virtual. 63.2%(189) were satisfied, 28%(84) neutral and 8.7%(26) reported dissatisfaction with their consultation. 50.5%(153) were happy to continue with virtual consultation but with an option of face to face only if necessary.For consultations post COVID-19, 59.4%(182) preferred a mixture of face to face and virtual appointments.
Conclusion: Majority of our patients seem happy with virtual consultations as long as they are assured of a face-to-face consultation if needed. A minority(8.7%) however, were dissatisfied. Some of the suggestions were,

use of video consultations and improvement in communication before the virtual appointments. Our survey also shows that our patients have adapted well to virtual consultations and many are keen to have virtual consultation in the longer term. In our survey, only 6.8%(21) patients reported definite or clinically suspected COVID-19. Possible explanations for this include strict compliance with government advice on social distancing/shielding and limited testing at the onset of the pandemic. More patients assumed themselves to be clinically CEV than those who were actually CEV based on their treatment which is not surprising because of high level of anxiety among patients due to rapidly spreading pandemic and multiple sources of information.

This feedback provides useful data which will help us to plan the delivery of rheumatology services post COVID-19 pandemic. While face-to-face patient contact is needed for comprehensive disease assessment, teaching and training, a model for the future is likely to include a combination of face-to-face and virtual consultations. This could allow a greater capacity to see new patients and reduce waiting lists. Patients with uncomplicated and stable disease could be followed up in virtual clinics. There is also a need to formally incorportate the virtual consultations into the curriculum for Rheumatology trainees.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.649

POS1168

SELF-REPORTED SARS-CoV2 TESTING AND COVID-19 DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS IN A SWISS OBSERVATIONAL COHORT

E. Papagiannoulis[1], A. Ciurea[2], D. Dan[3], A. Finckh[4,5], B. Gilbert[4,5], I. Von Loga[1], C. Melong Pianta Taleng[4,5], A. Scherer[1], K. Lauper[4,5,6]. [1]*SCQM, Statistics, Zurich, Switzerland*; [2]*Zurich University Hospital, University of Zurich, Rheumatology, Zurich, Switzerland*; [3]*CHUV, Rheumatology, Lausanne, Switzerland*; [4]*Faculty of Medicine, University of Geneva, Internal Medicine, Geneva, Switzerland*; [5]*Hôpitaux Universitaires de Genève (HUG), Rheumatology, Geneva, Switzerland*; [6]*Centre for Musculoskeletal Research, University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*

Background: Since the beginning of the pandemic in Switzerland, immunosuppressed people were strongly advised to be tested for SARS-CoV2 when symptomatic as it was conjectured that they might be more at risk for infection and/or severe disease. While patients with autoimmune diseases might be indeed more at risk of death from COVID-19[1], it remains unknown, whether there are differences in infection or complication rates between patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (AxSpA), and whether this relates to their disease or their treatment. Additionally, the prevalence of SARS-CoV2 testing in this population is not known.

Objectives: This study aimed to assess and compare the rate of COVID-19 and SARS-CoV2 testing in patients with RA, AxSpA and PsA, the potential association with their treatment and, for testing, the number of symptoms.

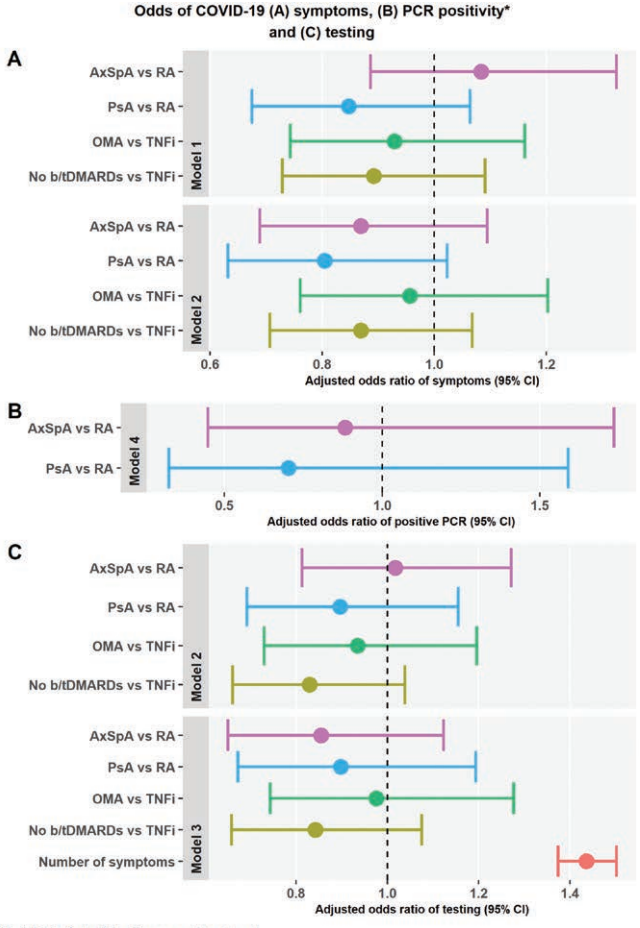
Methods: We included patients with RA, AxSpA and PsA from the Swiss Clinical Quality Management register (SCQM) using a smartphone app (mySCQM) to record information between March and December 2020. The outcomes of interest were self-reported SARS-CoV2 testing, symptoms compatible with COVID-19 during the previous month and confirmed COVID-19 through PCR nasopharyngeal swab. Outcomes were evaluated over the complete length of the aforementioned period (i.e. the outcome has been reported at least once during the period). Outcomes were compared between diseases groups, using logistic regression. We also evaluated the association of baseline treatment (TNF-inhibitors, b/tsDMARDs with other modes of action (OMA), no b/tsDMARDs) on the odds of symptoms and testing and the association of the number of symptoms (0-9) on the odds of testing. The analyses of SARS-CoV2 testing and COVID-19 symptoms were additionally adjusted for age, gender, glucocorticoids and csDMARDs. Confirmed cases were not adjusted for treatment and other covariates considering the low number of events.

Results: We included 927 patients with RA, 805 with AxSpa and 453 with PsA (Table 1). 1010 patients reported COVID-19-like symptoms (mostly fever, runny nose and cough), but only 455 of them (45%) reported being tested. 151 patients were tested without symptoms. In between March and December 2020, 7.6% of RA, 8.5% of AxSpA and 10.5% of PsA patients were tested positive for COVID-19 (p=0.678). The odds of testing, symptoms and confirmed COVID-19 were similar between diseases and not associated with treatment for testing and symptoms (Figure 1). The number of symptoms was associated with the odds of testing (OR 1.43, 95%CI 1.37-1.50 by symptom).

Table 1.

		RA	axSpA	PsA	p
n		927	805	453	
Age (mean, SD)		56.4 (13)	47.1 (12)	52.7 (11)	<0.001
Gender	female	705 (76)	403 (50)	230 (51)	<0.001
Treatment	TNFi	272 (29)	498 (62)	174 (38)	<0.001
	OMA	355 (38)	71 (9)	137 (30)	
	No b/tsDMARDs	300 (32)	236 (29)	142 (31)	
csDMARDs use		476 (51)	111 (14)	147 (33)	<0.001
Steroids use		93 (10)	11 (1)	19 (4)	<0.001
Disease duration		14.2 (10)	17.4 (11)	14.8 (12)	<0.001
Testing for COVID-19	All patients	258 (28)	231 (29)	117 (26)	0.550
	Patients with symptoms	189/427 (44)	179/392 (46)	87/191 (46)	0.911
Presence of COVID-19 symptoms		427 (46)	392 (49)	191 (42)	0.082
Positive COVID-19 test*		18/237 (8)	19/223 (9)	11/105 (11)	0.678

N, % when not specified otherwise.*Missing data on test results in 41 patientsχ2 test for categorical and t-test for continuous variables.



Model 1: Adjusted for disease and treatment
Model 2: Model 1 + adjustement for age, gender, csDMARDs (Y/N), glucorticoids (Y/N)
Model 3: Model 2 + adjustment for the numbers of symptoms (fever, cough, shortness of breath, running nose, muscle aches, headaches, fatigue, diarrhoea, sore throat)
Model 4: Adjusted for disease

***In patients with information on tests results (N=565)**

Figure 1.

Conclusion: Prevalence of COVID-19 symptoms and confirmed cases was similar between diseases, and for symptoms, was not associated with treatment. Despite strong advice from health authorities, less than 50% of patients with inflammatory rheumatic diseases and COVID-19 symptoms were tested. This proportion was not significantly different between diseases and not influenced by type of treatment. Efforts should be made to improve rates of SARS-CoV2 testing in patients with rheumatic diseases.

REFERENCES:

[1] Williamson, E. J. et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature 584, 430–436 (2020).

Acknowledgements: This study was supported by Pfizer, Sanofi, Novartis, Gilead, Biogen and Bristol-Myers Squibb.

We thank all the patients and health professionals contributing to SCQM.

Disclosure of Interests: Eleftherios Papagiannoulis: None declared, Adrian Ciurea Speakers bureau: Abbvie, Eli Lilly, MSD, Novartis, Pfizer, Diana Dan: None declared, Axel Finckh: None declared, Benoit GILBERT: None declared, Isabell von Loga Consultant of: Deloitte Consulting AG., Cathy Melong Pianta Taleng: None declared, Almut Scherer Consultant of: Pfizer, Employee of: BMS (2007-2008), Kim Lauper Consultant of: Gilead Galapagos, Grant/research support from: AbbVie. The SCQM foundation is supported by different companies https://www.scqm.ch/en/sponsoren/.

DOI: 10.1136/annrheumdis-2021-eular.683

POS1169

IMPACT OF THE COVID-19 PANDEMIC ON MORBIDITY AND MORTALITY AMONG SWEDISH PATIENTS WITH INFLAMMATORY JOINT DISEASES VERSUS THE GENERAL POPULATION

H. Bower[1], T. Frisell[1], D. DI Giuseppe[1], B. Delcoigne[1], G. M. Alenius[2], E. Baecklund[3], K. Chatzidionysiou[1], N. Feltelius[4], H. Forsblad-D'elia[5], A. Kastbom[6], L. Klareskog[1], E. Lindqvist[7], U. Lindström[5], C. Turesson[8], C. Sjowall[5], J. Askling[1]. [1]*Karolinska Institutet, Department of Medicine Solna, Division of Clinical Epidemiology, Stockholm, Sweden*; [2]*Umeå University, Rheumatology Unit, Department of Public Health and Clinical Medicine, Umeå, Sweden*; [3]*Uppsala University, Department of Medical Sciences, Uppsala, Sweden*; [4]*Swedish Medical Products Agency, Swedish Medical Products Agency, Uppsala, Sweden*; [5]*Sahlgrenska Academy, University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden*; [6]*Linköping University, Department of Biomedical and Clinical Sciences, Linköping, Sweden*; [7]*Skåne University Hospital, Lund University, Department of Clinical Sciences, Rheumatology, Lund, Sweden*; [8]*Lund University, Rheumatology, Department of Clinical Sciences, Malmö, Sweden*

Background: Studies from COVID-19 case-repositories among patients with rheumatic diseases have assessed associations (relative risks) between characteristics of the disease and adverse COVID-19 outcomes. Such designs are susceptible to bias from selection of cases reported. Few studies have assessed absolute and relative risks for COVID-19 outcomes in population-based cohorts of patients with inflammatory joint diseases, nor compared these risks to those in the general population.

Objectives: To estimate all-cause mortality, absolute and relative risks for severe COVID-19 in patients with chronic inflammatory joint diseases, compared over time and to the general population.

Methods: We updated a multi-register nationwide linkage ("ARTIS") on adults with RA, PsA, AS, SpA or JIA and population referents (matched on sex, age, and region), with data on hospitalizations, admission to intensive care (ICU), and deaths due to COVID-19. We calculated all-cause mortality March-September 2015-2020, and absolute and relative risks for COVID-19 outcomes March-September 2020. Patients were compared to population referents using hazard ratios (HR) from Cox models adjusted for comorbidities and socio-economy.

Results: We identified 110567 individuals with inflammatory joint disease (53455 with RA) in Sweden on March 1st 2020, and 484277 matched general population subjects. In all cohorts, the absolute risk of death from any cause in 2020 was higher than 2015-2019 (Figure 1), with a peak in mid-April, but the relative risks of death (vs. the general population) 2020 remained similar to HRs for 2015-2019 (HR for 2020 in Table 1).

Among all individuals with inflammatory joint disease in 2020, the risk for hospitalization, admission to ICU, and death due to COVID-19 was 0.5%, 0.04% and 0.1%, respectively (Table 1). HRs (vs. the general population) were elevated for almost all outcomes. HRs for COVID-19 related outcomes (Table 1) were higher than for non-COVID-19 outcomes; adjustment for co-morbidities and socio-economy explained much of these increases, somewhat less so for the former.

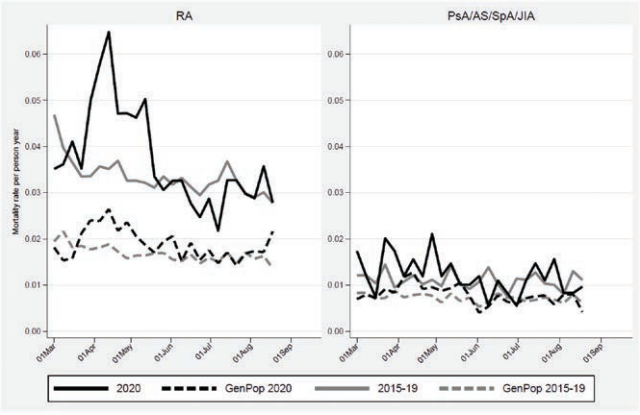


Figure 1. All-cause mortality in Swedish individuals with inflammatory joint disease and general population, March-September 2020 and the average 2015-2019

Table 1. Absolute and relative risks for COVID-19 outcomes in Swedish individuals with inflammatory joint disease compared to general population comparators March-September 2020

	Outcome	Events (risk, %)	Events (risk, %), general population	HR1*	HR2**
All					
	Hospitalization, all causes	8971 (8.1%)	24273 (5.0%)	1.65 (1.61, 1.69)	1.18 (1.15, 1.21)
	Hospitalization, COVID-19	581 (0.5%)	1443 (0.3%)	1.77 (1.61, 1.95)	1.32 (1.19, 1.46)
	ICU, COVID-19	45 (0.04%)	162 (0.03%)	1.22 (0.88, 1.70)	1.17 (0.82, 1.66)
	Death, all causes	1310 (1.2%)	3036 (0.6%)	1.90 (1.78, 2.02)	1.13 (1.05, 1.21)
	Death, COVID-19	161 (0.1%)	338 (0.07%)	2.09 (1.73, 2.52)	1.18 (0.97, 1.44)
RA					
	Hospitalization, all causes	5275 (9.9%)	13072 (5.9%)	1.71 (1.66, 1.77)	1.21 (1.17, 1.25)
	Hospitalization, COVID-19	379 (0.7%)	784 (0.4%)	2.02 (1.78, 2.28)	1.40 (1.23, 1.60)
	ICU, COVID-19	31 (0.06%)	79 (0.04%)	1.63 (1.08, 2.48)	1.53 (0.98, 2.40)
	Death, all causes	968 (1.8%)	2026 (0.9%)	1.99 (1.85, 2.15)	1.18 (1.09, 1.28)
	Death, COVID-19	134 (0.3%)	245 (0.11%)	2.28 (1.85, 2.81)	1.27 (1.02, 1.59)
PsA AS SpA JIA					
	Hospitalization, all causes	3696 (6.5%)	11201 (4.3%)	1.54 (1.48, 1.59)	1.16 (1.11, 1.20)
	Hospitalization, COVID-19	202 (0.4%)	659 (0.3%)	1.41 (1.20, 1.65)	1.20 (1.02, 1.41)
	ICU, COVID-19	14 (0.02%)	83 (0.03%)	0.78 (0.44, 1.37)	0.76 (0.43, 1.37)
	Death, all causes	342 (0.6%)	1010 (0.4%)	1.56 (1.38, 1.76)	0.98 (0.86, 1.12)
	Death, COVID-19	27 (0.05%)	93 (0.04%)	1.34 (0.87, 2.05)	0.83 (0.54, 1.28)

*HR1 unadjusted, matched (age, sex, and region) **HR2, as HR1 but adjusted for comorbidities and socio-economy

Conclusion: Risks of severe COVID-19 were increased among patients with inflammatory joint diseases, but similar increases were seen for non-COVID-19 morbidity. Co-morbidities and socio-economy explain much of this increase.

Disclosure of Interests: Hannah Bower: None declared, Thomas Frisell: None declared, Daniela Di Giuseppe: None declared, Bénédicte Delcoigne: None declared, Gerd-Marie Alenius: None declared, Eva Baecklund: None declared, Katerina Chatzidionysiou Speakers bureau: Eli Lilly, AbbVie and Pfizer, Consultant of: Eli Lilly, AbbVie and Pfizer, Nils Feltelius Employee of: Nils Feltelius is employed by the Medical Products Agency (MPA), which is a governmental body. The views in this abstract may not represent the views of the MPA, Helena Forsblad-d'Elia: None declared, Alf Kastbom Employee of: Former employee of Sanofi, Lars Klareskog: None declared, Elisabet Lindqvist: None declared, Ulf Lindström: None declared, Carl Turesson Speakers bureau: Roche, AbbVie and

Pfizer, Consultant of: Roche, Grant/research support from: Research grant from Bristol-Myers Squibb, Christopher Sjowall: None declared, Johan Askling Grant/research support from: PI for agreements between Karolinska Institutet and Abbvie, BMS, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and Sanofi for safety monitoring of anti-rheumatic therapies (ARTIS).

DOI: 10.1136/annrheumdis-2021-eular.685

POS1170

SELF-PROTECTION STRATEGIES, HEALTH BEHAVIOR AND DISEASE ACTIVITY DURING THE FIRST WAVE, RE-OPENING AND SECOND WAVE OF THE COVID-19 PANDEMIC IN >7000 DANISH PATIENTS WITH INFLAMMATORY ARTHRITIS

B. Glintborg[1], D. V. Jensen[2], S. Engel[1], L. Terslev[1], M. Pfeiffer Jensen[1], O. Hendricks[3], M. Østergaard[1], S. H. Rasmussen[1], T. Adelsten[4], K. Danebod[1], A. Colic[4], M. Kildemand[5], A. G. Loft[6], H. L. Munk[5], J. K. Pedersen[7], R. Østgård[8], C. M. Sørensen[9], N. Steen Krogh[10], J. Nørgaard Agerbo[11], C. Ziegler[11], M. L. Hetland[1]. [1]*Center for Rheumatology and Spine Diseases, Centre of Head and Orthopedics, DANBIO and Copenhagen Center for Arthritis Research (COPECARE), Copenhagen, Denmark*; [2]*Center for Rheumatology and Spine Diseases Gentofte and Herlev Hospital, Department of Rheumatology, Gentofte, Denmark*; [3]*University Hospital of Southern Denmark, Danish Hospital for Rheumatic Diseases, Sønderborg, Denmark*; [4]*Zealand University Hospital, Department of Rheumatology, Køge, Denmark*; [5]*Odense University Hospital, Department of Rheumatology, Odense, Denmark*; [6]*Aarhus University Hospital, Department of Rheumatology, Aarhus, Denmark*; [7]*Odense University Hospital and Svendborg Hospital, Department of Rheumatology, Odense, Denmark*; [8]*Silkeborg Regional Hospital, Diagnostic Center, Silkeborg, Denmark*; [9]*Horsens Regional Hospital, Department of Medicine, Horsens, Denmark*; [10]*ZiteLab Aps, Copenhagen, Denmark*; [11]*Gigtforeningen/Danish Rheumatism Association, -, Copenhagen, Denmark*

Background: The COVID-19 pandemic has caused lockdown, reduced access to face-to-face consultations, anxiety about taking immunosuppressive agents and self-isolation[1] which potentially impact rheumatic disease control negatively. However, changes in behavior including self-protection strategies during the ongoing pandemic and impact on rheumatic disease activity have only been scarcely described.

The first COVID-19 wave hit Denmark in March 2020 followed by a gradual re-opening from mid-April and the second surge began in the late autumn of 2020.

Objectives: To describe changes over time in self-protection strategies and health behavior during the first 8 months of the COVID-19 pandemic and to explore impact on self-reported disease activity and quality of life (=patient reported outcomes, PROs) in patients with inflammatory rheumatic disease (IRD) in DANBIO.

Methods: Patients were invited to answer two on-line questionnaires regarding current behavior and disease specific PROs: One in June 2020 (including also questions regarding behavior in March 2020), and one in November 2020. Responses were linked to PROs collected as part of routine care before March 2020 (=Before) in DANBIO. For each PRO, changes (=delta values) between the two timepoints were calculated in individual patients.

Results: Overall, 7,836 patients (22% of eligible patients) answered both questionnaires and were included (rheumatoid arthritis(RA): 5270(67%), psoriatic arthritis(PsA): 1217(15%), axial spondyloarthritis(AxSpA): 932(12%), other IRD: 417(5%). Patients reported highest levels of anxiety and self-protection in March with an improvement in June that was largely unchanged in November (Figure 1), e.g. proportions staying at home avoiding others as much as possible (completely or mostly agree) were 87%/49%/51% in March/June/November, respectively (Figure 1**, Panel C**).

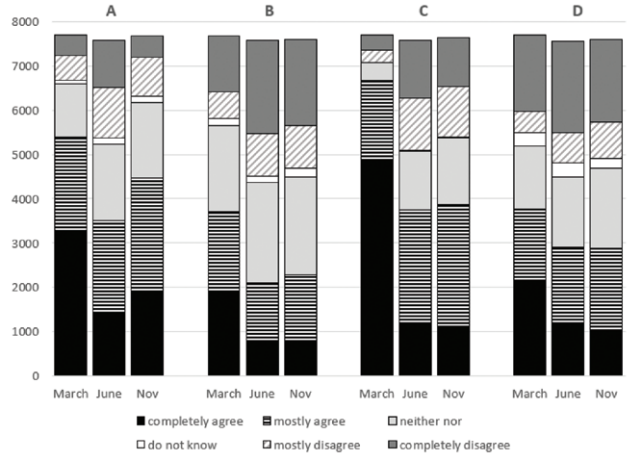
Disease activity and proportions of patients reporting acceptable symptom state remained stable at the three time points (Table 1), with all median delta values being close to zero (not shown).

Conclusion: In this large cohort of patients with inflammatory rheumatic diseases followed in the nationwide DANBIO registry, COVID-19 related self-protection strategies were highest in March 2020, but more than half of the patients also reported self-isolation in June and November. We found no negative impact of the pandemic on patient-reported outcomes, which remained largely unchanged and were similar to before the pandemic. The latter finding probably reflects that few patients reduced or withdrew from treatment due to fear of COVID-19.[1]

REFERENCES:

[1] Glintborg et al, 2021, https://rmdopen.bmj.com/content/rmdopen/7/1/e001505.full.pdf

Figure. Self-protection strategies and health behavior in March, June and November 2020



A: I consider myself at high risk of COVID-19 infection. **B:** I worry more about COVID-19 than about my rheumatic disease. **C:** I stay at home and avoid others as much as possible. **D:** My arthritis causes me to self-isolate more than others my age

Table 1. Patient reported outcomes before March, in June and in November 2020 in patients with IRD. N=7,836

	Before*	June 2020	Nov 2020
Patient VAS global, mm	30 (12-58)	28 (10-54)	29 (10-55)
Patient VAS pain, mm	27 (11-51)	28 (11-51)	29 (11-52)
HAQ	0.50 (0.13-1.0)	0.50 (0.13-1.00)	0.50 (0.13-1.00)
EQ-5D	0.80 (0.72-0.86)	0.79 (0.71-0.86)	0.80 (0.71-0.86)
PASS, yes	73%	75%	76%

Numbers are median (IQR) unless otherwise stated*Latest registration in DANBIO before March 2020Patient characteristics for RA/AxSpA/PsA/Other: female, %: 70/53/44/69. Age, years, median(IQR): 67(59-74)/62(54-69)/56(46-65)/59(50-68)Abbreviations: EQ-5D: Quality of life, 5 dimensions, HAQ: health assessment questionnaire, PASS: patient acceptable symptom state, VAS: visual analogue scale

Disclosure of Interests: Bente Glintborg Grant/research support from: AbbVie, BMS, Pfizer, Dorte Vendelbo Jensen: None declared, Sara Engel: None declared, Lene Terslev Speakers bureau: AbbVie, Janssen, Roche, Novartis, Pfizer, MSD, BMS and GE, Mogens Pfeiffer Jensen: None declared, Oliver Hendricks Grant/research support from: AbbVie, Novartis, Pfizer, Mikkel Østergaard Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB., Grant/research support from: Research grants: Abbvie, BMS, Celgene, Merck, Novartis, Simon Horskjær Rasmussen: None declared, Thomas Adelsten: None declared, Kamilla Danebod: None declared, Ada Colic: None declared, Malene Kildemand: None declared, Anne Gitte Loft Speakers bureau: AbbVie, Eli-Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Heidi Lausten Munk: None declared, Jens Kristian Pedersen: None declared, René Østgård Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Eli-Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi and UCB., Grant/research support from: Research grants: Abbvie, Christian Møller Sørensen: None declared, Niels Steen Krogh: None declared, Jette Nørgaard Agerbo: None declared, Connie Ziegler: None declared, Merete L. Hetland Grant/research support from:: AbbVie, Biogen, BMS, Celtrion, Eli Lilly Denmark A/S, Janssen Biologics B.V, Lundbeck Fonden, MSD, Pfizer, Roche, Samsung Biopis, Sandoz. MLH chairs the steering committee of the Danish Rheumatology Quality Registry (DANBIO), which receives public funding from the hospital owners and funding from pharmaceutical companies. MLH co-chairs the EuroSpA research collaboration, which generates real-world evidence of treatment of psoriatic arthritis and axial spondylorthritis based on secondary data and is partly funded by Novartis.

DOI: 10.1136/annrheumdis-2021-eular.722

POS1171

THE COVID-19 PANDEMIC PROMPTS ISOLATION AND BEHAVIORAL CHANGES IN PATIENTS WITH CHRONIC RHEUMATIC DISEASES LEADING TO REDUCED PHYSICAL ACTIVITY, INCREASED PAIN, DISEASE ACTIVITY, AND LOW SEROPREVALENCE OF SARS-COV2 ANTIBODIES

C. Ammitzbøll[1], J. B. Andersen[1], S. R. Vils[1,2], C. M. Jørgensen[1,2,3], E. M. Hauge[1,3], C. Erikstrup[3,4], S. Mikkelsen[3,4], M. K. Thomsen[5], A. Troldborg[1,2,3]. [1]*Aarhus University Hospital, Rheumatology, Aarhus, Denmark*; [2]*Aarhus University, Biomedicine, Aarhus, Denmark*; [3]*Aarhus University, Clinical Medicine, Aarhus, Denmark*; [4]*Aarhus University Hospital, Clinical Immunology, Aarhus, Denmark*; [5]*Aarhus University Hospital, Clinical Microbiology, Aarhus, Denmark*

Background: The coronavirus disease 2019 (COVID-19) pandemic has complicated the management of chronic rheumatic diseases (CRD). Patients with CRDs are immunocompromised and generally prone to infection. The fear of COVID-19 and the degree of the self-imposed shielding strategy implemented by many patients introduced new challenges for the patients. Although recommendations have been developed to manage patients with CRDs by, i.e., EULAR, strong evidence is still lacking to guide treatment decisions.

Objectives: This study aimed to assess the seroprevalence of SARS-CoV-2 antibodies in patients with CRDs and healthy controls during the first wave of the pandemic. We further evaluated the effect of the pandemic on patient behavior regarding medication, exercise, pain, and experienced disease activity. Finally, we investigated the self-perceived consequences of the pandemic and lock-down on anxiety and depression in patients with CRDs compared with healthy controls.

Methods: More than 900 participants were included in the study: 405 patients with rheumatoid arthritis or systemic lupus erythematosus and 513 blood donors. All participants had SARS-CoV-2 antibodies measured (Wantai SARS-CoV-2 total antibody ELISA; sensitivity 96.7%, specificity 99.5%) and answered a questionnaire concerning behavior, anxiety, and symptoms of depression (PHQ-9). The participants with CRD were further asked about physical activity, adherence to medication, and disease-related symptoms.

Results: CRD patients had a sixfold lower seroprevalence of SARS-CoV-2 antibodies compared to controls (p=0.03) (Figure 1). Almost 60% of patients were unable to exercise as usual, leading to increased pain in 34%, and experience of increased disease activity in 27%. Approximately 10% of patients reduced or discontinued their immunosuppressive treatments at their own initiative. Symptoms of moderate depression were present in 19% of patients compared to 6,8% of controls (p<0.001).

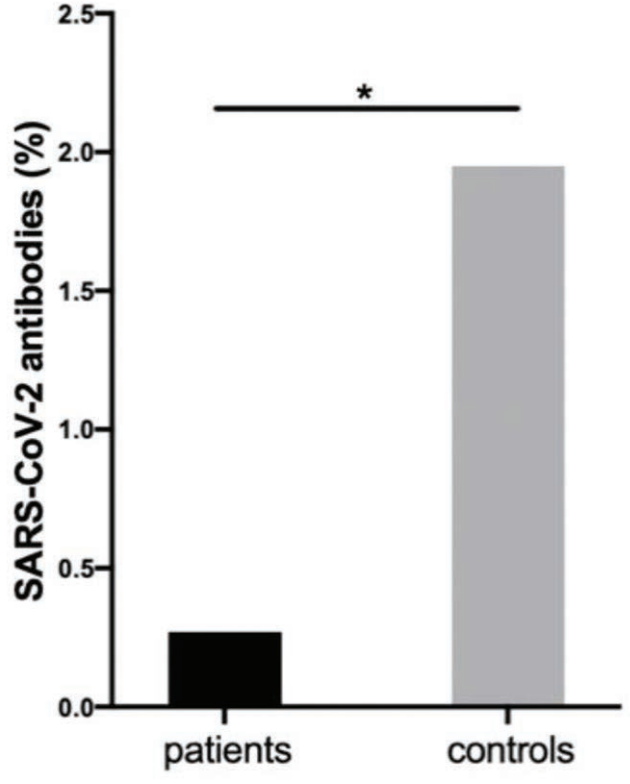


Figure 1. Presence of SARS-CoV-19 antibodies in chronic rheumatic disease patients (1/365, 0.3%) and controls (blood donors (10/513, 1.9%), *(p=0.03).

Conclusion: Low seroprevalence in patients with CRDs indicates successful mitigation of exposure to SARS-CoV-2. However, this appears to occur at the expense of physical activity and adherence to immunosuppressive treatment. Our results raise an important concern regarding the consequences of isolation for patients with CRDs. The result of physical isolation is a risk of severe mental health issues, physical inactivity, self-medication, increased pain, and increased disease activity. The long-term consequences of recommendations for patients with CRDs should be taken into account when tackling the continuing pandemic.

Table 1.

Patient characteristics	**CRD cohort**		**Blood donors**	
Patients included, n	405 (206 SLE, 199 RA)		513	
Disease duration, years (IQR)	12.9	(7.0-23.0)		
Age, years (IQR)	56.9	(43.6-66.9)	47	(33-57)
BMI, kg/m2 (IQR)	25.0	(22.1-28.6)	25.5	(23.1-28.4)
Charlson Comorbidity Index, score (IQR)	2	(1-4)		
Behavioral and mental changes due to the risk of COVID-19	**CRD cohort**		**Blood donors**	**p-value**
Washes hands more often (%)	91.6		91.4	0.92
Coughing or sneezing in the elbow (%)	83.0		84.0	0.67
Wearing face mask (%)	5.0		2.4	0.001
Restricts the use of public transport (%)	47.4		32.9	<0.001
Avoid places where many people are gathered (%)	80.7		70.0	<0.001
Stay at home (%)	51.6		35.3	<0.001
Symptoms of moderate depression, PHQ-9 >=10, (%)	19.01		6.75	<0.001
Pandemic effect on training, pain and disease activity	**CRD cohort**			
Have you been able to exercise as usually, yes (%)	41.4			
Have you been less physically active due to COVID-19, yes (%)	44.7			
Has the degree of physical activity increased the pain from your rheumatological disease? yes(%)	33.9			
Have you experienced increased disease activity during COVID-19? yes(%)	26.9			

Interquartile range (IQR), Patient Health Questionnaire-9 (PHQ-9),

Acknowledgements: This study was funded by the Danish Rheumatism Association. We are thankful for the help with creation of the questionnaire by patient research partners Lene Mandrup Thomsen, Nanna Bacci Hartz, Lene Lau og Jeanette Andersen.

Disclosure of Interests: Christian Ammitzbøll: None declared, Jakob Bøgh Andersen: None declared, Signe Risbøl Vils: None declared, Clara Mistegaard Jørgensen: None declared, Ellen-Margrethe Hauge Speakers bureau: AbbVie, Sanofi, Sobi, MSD, UCB, Grant/research support from: Roche, Norvartis, Christian Erikstrup: None declared, Susan Mikkelsen: None declared, Marianne Kragh Thomsen: None declared, Anne Troldborg: None declared.

DOI: 10.1136/annrheumdis-2021-eular.725

POS1172

COVID-19 ACROSS RHEUMATOLOGY: A BIBLIOMETRIC STUDY

B. Doskaliuk[1], R. Yatsyshyn[1], I. Stoika[1], K. Fedorovych[1], O. Drogomeretska[1], O. Hotsaniuk[1], Y. Delva[1]. [1]*Ivano-Frankivsk National Medical University, Internal medicine #1 clinical immunology and allergology, Ivano-Frankivsk, Ukraine*

Background: The Coronavirus disease 2019 (COVID-19) outbreak spread rapidly among the whole world, becoming the greatest pandemic for the decades. It triggered the enormous challenges for the global health system, forcing doctors and patients to adapt to new realities and the field of rheumatology was not an exclusion.

Objectives: The aim of this study was to analyze articles covering interconnection between COVID-19 and rheumatic diseases; to investigate the common features of papers in this category and indicate the most influential among them; to determine which rheumatic nosologies were most represented.

Methods: For retrieving of literature data, we applied the bibliometric database Scopus and conducted our search on 12th of January using following keywords: “rheumatoid arthritis” OR “systemic lupus erythematosus” OR “systemic sclerosis” OR “vasculitis” OR “myositis” OR “rheumatology” AND “COVID-19”. All selected articles were analyzed according to various aspects: type of document, authorship, journal, citations score, rheumatology field, country of origin, language, and keywords. We have built the visualizing keywords network (Figure 1) with the help of software tool VOSviewer version 1.6.15 (the minimum keyword occurrence threshold was set at 5).

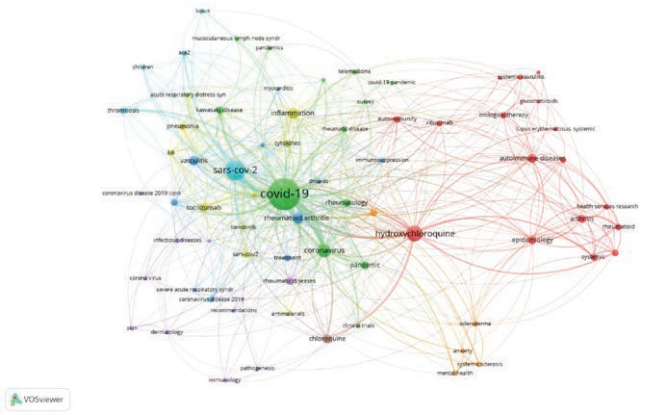


Figure 1.

Results: A total of 844 literature items were obtained. After screening of title, abstract and keywords we excluded 106 records as they were not emphasized the rheumatological perspective on COVID-19 and as a result were inapplicable for this study. The 738 retrieved articles were mostly (86.8%) open access publications. The top five journals that contributed most to the coverage of this topic were: Annals Of The Rheumatic Diseases (n=59), Clinical Rheumatology (n=41), Lancet Rheumatology (n=24), Arthritis And Rheumatology (n=20) and Rheumatology International (n=19). The origin of most studies was not surprisingly from those countries, which belong to the top ten according to the total cases of COVID-19 [1] (USA – 167; Italy – 148; UK – 76; India – 60 and Spain – 58). Most items were written in English but articles in German (n=12), Spanish (n=11), Russian (n=5) and Chinese (n=2) could also be found. Analyzed studies were designed in the form of Original Articles (41.2%), Reviews (23.7%), Letters (21.8), Notes (6.9%), Editorials (5.1%). According to the citations scores, articles of highest interest were dedicated to clinical course of COVID-19 in patients with autoimmune pathologies. The other highly cited studies were about cytokine storm and perspective usage of biological drugs for severe cases of COVID-19. Our analysis of keywords showed that the most widely discussed rheumatic disease in the view of COVID-19 was systemic lupus erythematosus (n=188), followed by vasculitis (n=132), rheumatoid arthritis (n=90), systemic sclerosis (n=32) and psoriatic arthritis (24). The liveliest discussion about disease-modifying antirheumatic drugs in COVID-19 revolved around hydroxychloroquine (n=305), corticosteroids (n=161), tocilizumab (n=83), methotrexate (n=46) and anakinra (n=34).

Conclusion: As far as we know, it is the first bibliometric overview of studies dedicated to interrelation between COVID-19 and rheumatic pathology. The high number of open access items contributes to the increase of research visibility in this emergently developing research field and facilitates the process of scientific data sharing. The conducting of bibliographic studies may provide a valuable guide through this area of knowledge.

REFERENCES:

[1] https://www.worldometers.info/coronavirus/ Accessed on January 12, 2021

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.734

POS1173 A SHORT DELAY IN ARTHRITIS CARE IS ASSOCIATED WITH HIGHER DISEASE ACTIVITY - LESSONS FROM THE CORONAVIRUS DISEASE 19 (COVID-19) PANDEMIC

A. Giollo[1], E. Bertoldo[1], C. Benini[1], O. Viapiana[1], L. Idolazzi[1], G. Adami[1], A. Fassio[1], D. Gatti[1], M. Rossini[1]. *[1]University of Verona, Rheumatology Section, Department of Medicine, Verona, Italy*

Background: Although disease activity is a significant outcome in rheumatology, few studies have investigated the relationship between routine care of rheumatic conditions and disease activity control.

Objectives: To determine the association between delay in routine care of chronic inflammatory arthritides (CIAs) and disease activity during the first wave of coronavirus disease 19 pandemic in Verona, Italy.

Methods: This study enrolled patients with an established diagnosis of rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and undifferentiated arthritis (UA). Between 01/04/2020 and 30/06/2020, participants were emailed an online questionnaire. Items comprised multiple or single-choice questions evaluating routine rheumatology care disruptions/delays and disease characteristics, treatments, comorbidities, and demographics. Compliance to anti-rheumatic medications was evaluated with I-CQR5. Disease activity was assessed with RAPID3, and active disease was defined as a RAPID3 score>1. Study period referred to the time between the last rheumatology assessment and the date of enrolment.

Results: Of 1210 patients contacted, 450 participated, of whom 219 CIAs patients were included (RA 55.3%, PsA 35.2%, AS 15.1%, UA 3.7%). One hundred twenty-five patients (57.1%) had their routine clinical assessment delayed (median days 68.4; IQR 66.8, 85.9). Patients in this group had significantly higher MDHAQ (p=0.001) and RAPID3 (p=0.031) scores, while they did not differ for disease severity, medications or compliance. Most (87.7%) reported good compliance to therapy; only 5.9% had difficulties in supplying anti-rheumatic medications, and 13.2% discontinued medications for at least four weeks for any reason. However, several patients (37.9%) reported moderate-to-high worse disease activity perception due to routine care delay, and 31.1% self-reported a disease flare (median RAPID3 score 3.8; IQR 2.0, 5.4). One hundred one patients (46.1%) had high disease activity, while only 15.1% were in remission. In logistic regression, active disease was significantly associated with delay of scheduled routine care visit, independent of disease duration, time from last rheumatology assessment, therapy with b/tsDMARDs, and compliance (Table 1, Figure 1 below).

Table 1.

Predictor	Active (n=186)	Remission (n=33)	OR	P-value	95% CI Inf.	95% CI Sup.
Routine care delay (yes vs no)	113 (60.8%)	12 (36.4%)	.030	2.459	1.091	5.543
Disease duration (years)	10 (4.0, 20.0)	10.5 (7.0, 19.8)	.695	1.007	.972	1.044
Time since last rheumatology assessment (days)	68.4 (66.8, 75.8)	71.2 (66.9, 74.9)	.854	1.002	.978	1.027
b/tsDMARDs (yes vs no)	105 (56.5%)	15 (45.5%)	.653	1.202	.538	2.687
I-CPR5 (likely low vs likely high adherent)	36 (19.4%)	10 (30.3%)	.187	.563	.240	1.321

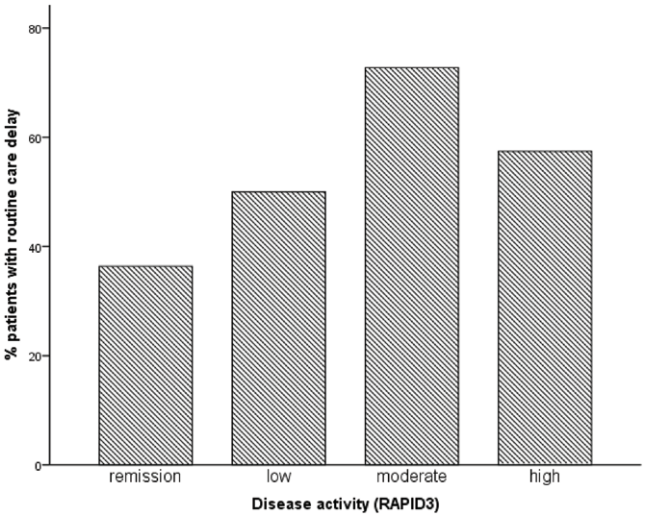


Figure 1.

Conclusion: In patients with established CIAs, a relatively short delay in routine assessment by a rheumatologist resulted in higher disease activity. Frequent rheumatology referrals appear to be a critical factor for disease activity control in CIAs.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.737

POS1174 HYPERINFLAMMATION AND CLINICAL OUTCOMES FOR PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES HOSPITALIZED FOR COVID-19: A COMPARATIVE COHORT STUDY

T. Hsu[1,2], K. D'silva[2,3], N. Serling-Boyd[2,3], J. Wang[1], A. Mueller[1,2], X. Fu[3], L. Prisco[1], L. Martin[1], K. Vanni[1], A. Zaccardelli[1], C. Cook[3], H. Choi[2,3], Y. Zhang[2,3], E. Gravallese[1,2], Z. Wallace[2,3], J. Sparks[1,2]. *[1]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, United States of America*; *[2]Harvard Medical School, Division of Rheumatology, Inflammation, and Immunity, Boston, United States of America*; *[3]Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*

Background: COVID-19 can induce a hyperinflammatory state resulting in cytokine storm, which can lead to poor outcomes. Patients with systemic rheumatic diseases may be at increased risk for respiratory failure with COVID-19. Therefore, we investigated the relationship between rheumatic disease, hyperinflammation, and clinical outcomes among hospitalized COVID-19 patients.

Objectives: To compare laboratory values, hyperinflammation, and clinical outcomes of hospitalized COVID-19 rheumatic patients and matched comparators.

Methods: We performed a comparative cohort study of patients with polymerase chain reaction (PCR)-confirmed COVID-19 requiring hospitalization between 3/1/20-7/7/20 at a large health care system. We compared each systemic rheumatic disease case to up to 5 matched (by age, sex, and date of +SARS-CoV-2 PCR) comparators without systemic rheumatic disease. We extracted laboratory values from their hospitalization to compare peaks/troughs of individual laboratory results by case status and derived the COVID-19-associated hyperinflammation score (cHIS), a composite of 6 laboratory domains (0-6, ≥2 indicating hyperinflammation), as previously developed[1]. We used multivariable logistic regression to estimate ORs for COVID-19 outcomes by hyperinflammation and case status.

Results: We identified 57 hospitalized rheumatic disease cases (mean age 67 years, 67% female) and 232 matched comparators hospitalized with PCR-confirmed COVID-19. Among cases, 26 (46%) had rheumatoid arthritis and 14 (25%) had systemic lupus erythematosus. Most cases (34, 60%) had active rheumatic disease. At baseline, 15 (27%) of cases were treated with biologic DMARDs, and 32 (56%) were using glucocorticoids. We analyzed 39,900 total laboratory results (median 85 per patient). Cases had higher peak neutrophil-to-lymphocyte ratio (9.6 vs 7.8, p=0.02), LDH (421 vs 345 U/L, p=0.04), creatinine (1.2 vs 1.0 mg/dL, p=0.01), and BUN (31 vs 23 mg/dL, p=0.03) than comparators but similar peak CRP (149 vs 116 mg/L, p=0.11, Figure 1). Cases had higher peak median cHIS (3 vs 2, p=0.01). Peak cHIS ≥2 had higher odds of intensive care unit (ICU) admission (OR 3.45, 95%CI 1.98-5.99), mechanical ventilation (OR 66.0, 95%CI 9.0-487.8), and mortality (OR 16.4, 95%CI 4.8-56.4) compared to cHIS <2 (Table 1). Cases had increased risk of ICU admission (OR 2.0, 95%CI 1.1-3.7) and mechanical ventilation (OR 2.7, 95%CI 1.4-5.2) than comparators.

Table 1. Associations of peak cHIS and systemic rheumatic disease with COVID-19 hospitalization outcomes

	Intensive care unit admission		Mechanical ventilation		Death	
	%	Adjusted OR (95%CI)	%	Adjusted OR (95%CI)	%	Adjusted OR (95%CI)
Hospitalization outcomes by hyperinflammation on cHIS[1]						
cHIS <2 (n=112)	21%	1.0 (Ref)	1%	1.0 (Ref)	3%	1.0 (Ref)
cHIS ≥2 (n=177)	48%	**3.5 (2.0-6.0)**	37%	**66.2 (9.0-487.8)**	27%	**16.4 (4.8-56.4)**
Hospitalization outcomes by rheumatic disease status						
Comparators (n=232)	30%	1.0 (Ref)	19%	1.0 (Ref)	16%	1.0 (Ref)
Rheumatic cases (n=57)	51%	**1.87 (1.03-3.40)**	39%	**2.46 (1.30-4.67)**	21%	1.32 (0.61-2.88)

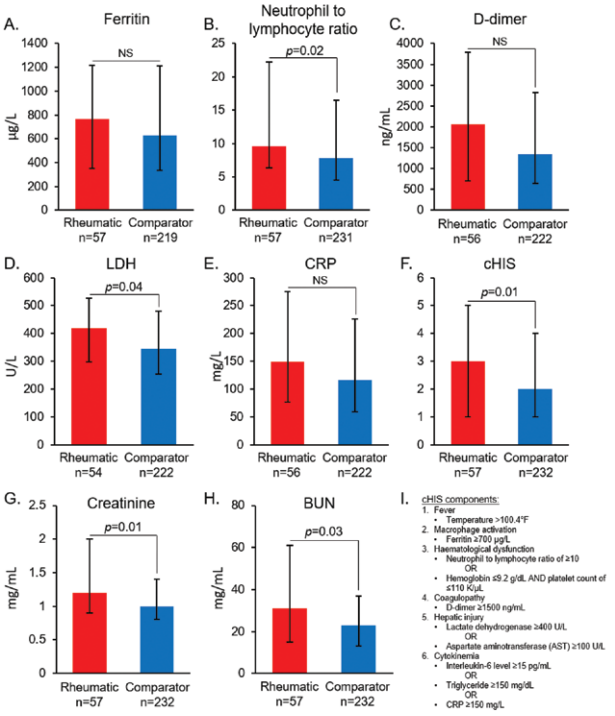
Matching factors: age, sex, and date of +PCR.[1]Adjusted for age, sex, and case status.[2]Adjusted for race, smoking, comorbidities, and body mass index.cHIS, COVID-19-associated hyperinflammation score; CI, confidence interval; OR, odds ratio; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Conclusion: Patients with systemic rheumatic disease hospitalized for COVID-19 had higher risk for hyperinflammation, kidney injury, and mechanical ventilation than non-rheumatic comparators. We validated the cHIS in our cohort, which was strongly associated with poor COVID-19 outcomes. These findings highlight that hospitalized patients with rheumatic diseases may be vulnerable to poor COVID-19 outcomes.

REFERENCES:

[1] Webb BJ et al. Clinical criteria for COVID-19-associated hyperinflammatory syndrome. Lancet Rheumatol. 2020 Dec;2(12):e754-e763.

Figure:
Median peak laboratory values and composite COVID-19-associated hyperinflammation scores (cHIS) for systemic rheumatic disease cases (n=57) and matched comparators (n=232) during hospitalization for COVID-19. Error bars indicate interquartile range. cHIS was derived from 39,900 laboratory results, and the components are listed.



Disclosure of Interests: Tiffany Hsu: None declared, Kristin D'Silva: None declared, Naomi Serling-Boyd: None declared, Jiaqi Wang: None declared, Alisa Mueller: None declared, Xiaoqing Fu: None declared, Lauren Prisco: None declared, Lily Martin: None declared, Kathleen Vanni: None declared, Alessandra Zaccardelli: None declared, Claire Cook: None declared, Hyon Choi Consultant of: Dr. Choi reports consultancy fees from Takeda, Selecta, GlaxoSmithKline, and Horizon, Grant/research support from: Dr. Choi reports research support from AstraZeneca., Yuqing Zhang: None declared, Ellen Gravallese: None declared, Zachary Wallace Consultant of: Dr. Wallace reports consulting fees from Viela Bio and MedPace., Grant/research support from: Dr. Wallace reports research support from Bristol-Myers Squibb and Principia., Jeffrey Sparks Consultant of: Dr. Sparks reports consultancy fees from Bristol-Myers Squibb, Gilead, Inova, Janssen, Optum, and Pfizer., Grant/research support from: Dr. Sparks reports research support from Amgen and Bristol-Myers Squibb.

DOI: 10.1136/annrheumdis-2021-eular.936

POS1175

ASSESSMENT OF THE COVID-19 PANDEMIC FROM THE PERSPECTIVE OF PEOPLE WITH RHEUMATIC MUSCULOSKELETAL DISEASES IN EUROPE. RESULTS FROM THE REUMAVID STUDY (PHASE 1)

M. Garrido-Cumbrera[1], H. Marzo-Ortega[2], J. Correa-Fernández[1], S. Sanz-Gómez[1], L. Christen[3], V. Navarro-Compán[4]on behalf of REUMAVID working group. [1]*Universidad de Sevilla, Health & Territory Research (HTR), Sevilla, Spain*; [2]*University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [3]*Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; [4]*Hospital Universitario La Paz, IdiPaz, Madrid, Spain*

Background: The COVID-19 pandemic is an unprecedented public health crisis affecting people worldwide, including those with rheumatic and musculoskeletal diseases (RMDs).

Objectives: REUMAVID aims to assess the impact of the COVID-19 pandemic and lockdown on the wellbeing, mental health, disease activity and function, access to health care and treatment, support services, and hopes and fears of people RMDs.
Methods: REUMAVID is an international collaboration led by the Health & Territory Research group at University of Seville, Spain, together with a multidisciplinary team including patient organization and rheumatologists. This cross-sectional study consisting of an online survey gathering data from patients with a diagnosis of 15 RMDs in Cyprus, France, Greece, Italy, Portugal, Spain and the United Kingdom. Participants are recruited by patient organizations. Data is collected in two phases: 1) during the first peak of the COVID-19 pandemic (Spring 2020), and 2) as a follow-up to the pandemic (Winter 2020). This analysis presents descriptive results of the aggregated data, summarizing continuous and categorical variables.
Results: A total of 1,800 RMD patients have participated in the first wave of the COVID-19 pandemic (from early April to mid-June 2020). The most frequent reported diagnosis were axial spondyloarthritis (37.2%), rheumatoid arthritis (29.2%) and osteoarthritis (17.2%). Mean age was 52.6±13.2, 80.1% were female, 69.6% were in a relationship or married and 48.6% had university studies. In total, 1.1% had tested positive for COVID-19, 10.8 % reported symptoms but were not tested, while 88.1% did not experience any symptoms. 46.6% reported worsening health during the pandemic. 63.9% perceived their health status to be "fair to very bad". Access to care was limited with 58.4% being unable to keep the rheumatologist appointment, of which, 35.2% were cancelled by the provider and 54.4% was attended by phone or online. 15.8% changed their medication, for which 65.5% were changed by the provider and 24.6% by own decision. Reported wellbeing and psychological health during the pandemic was poor, with 49.0% reporting poor wellbeing according to the WHO-5 scale, 57.3% marking as anxiety and 45.8% as depression in the HADS scale. During the pandemic, 24.6% smoked and 18.2% drank more than before and 54.5% were unable to exercise at home.
Conclusion: Results from the first phase of REUMAVID show disturbance of the healthcare quality, substantial changes in harmful health behaviors and an unprecedented impairment of mental health in REUMAVID participants. REUMAVID will continue to collect information in order to assess the impact of the COVID-19 pandemic in people affected by RMDs across Europe.
Acknowledgements: This study was supported by Novartis Pharma AG. We would like to thank all patients that completed the survey as well as all of the patient organisations that participated in the REUMAVID study including: the Cyprus League Against Rheumatism (CYPLAR) from Cyprus, the Association Française de Lutte Anti-Rhumatismale (AFLAR) from France, the Hellenic League Against Rheumatism (ELEANA) from Greece, the Associazione Nazionale Persone con Malattie Reumatologiche e Rare (APMARR) from Italy, the Portuguese League Against Rheumatic Diseases (LPCDR), from Portugal, the Spanish Federation of Spondyloarthritis Associations, the Spanish Patients' Forum (FEP), UNiMiD, Spanish Rheumatology League (LIRE), Andalusian Rheumatology League (LIRA), Catalonia Rheumatology League and Galician Rheumatology League from Spain, and the National Axial Spondyloarthritis Society (NASS), National Rheumatoid Arthritis (NRAS) and Arthritis Action from the United Kingdom.
Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Helena Marzo-Ortega Speakers bureau: AbbVie, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Takeda and UCB, Consultant of: AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Grant/research support from: Janssen and Novartis, José Correa-Fernández: None declared, Sergio Sanz-Gómez: None declared, Laura Christen Employee of: Novartis Pharma AG, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.956

POS1176 THE IMPACT OF COVID-19 QUARANTINE ON MENTAL HEALTH OF PATIENTS WITH FIBROMYALGIA

F. Ingegnoli[1], M. Buoli[2], C. Posio[3], R. DI Taranto[1], R. Caporali[1]. [1]*Università degli Studi di Milano, Division of Clinical Rheumatology, ASST Pini, Department of Clinical Sciences & Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Milano, Italy*; [2]*Università degli Studi di Milano, Department of Pathophysiology and Transplantation, Department of Neurosciences and Mental Health, Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Milano, Italy, Milano, Italy*; [3]*Università degli Studi di Milano,Department of Pathophysiology and Transplantation, Milano, Italy*

Background: Detrimental psychological effects, including symptoms of post-traumatic stress disorder (PTSD), stress, anxiety, and depression have been related to COVID-19 quarantine measures (1). These aspects may be particularly relevant in stress-related disorders such as fibromyalgia (FM) in which previous evidence demonstrated a causal effect of psychological stressors on chronic non-inflammatory pain of FM (2). Recent studies highlighted a significant worsening of FM symptoms after COVID-19 related lockdown period (3-4), but the levels of perceived stress and distress have not been evaluated yet.
Objectives: The aim of this study is to establish the COVID-19 related perceived stress and distress among patients with FM who experienced the COVID-19 quarantine in Italy. Data were retrieved from a larger nationwide online survey involving patients affected by different rheumatic diseases (RD).
Methods: We collected data from May to September 2020 from RD patients living in Italy during the COVID-19 quarantine by an ad-hoc online survey. Eleven associations of RD patients sent a call by using their mailing list, webpages and social network. They asked to complete an anonymous online survey which included the Perceived Stress Scale (PSS), and the Impact Event Scale-Revised (IES-R). Descriptive statistics were used to summarize results.
Results: 79 of 507 (15.6%) of RD patients who completed the survey declared to have been diagnosed FM. 77 (97.5%) were females, with a mean (± SD) age of 51.0 ± 12.4 yrs. In FM patients, the mean (SD) PSS score was 23.8 ± 8.1. In particular, 8 (10.1%) reported low, 38 (48.1%) moderate and 33 (41.8%) high PSS scores. Moreover, IES-R mean (SD) score was 38.5 ± 17.2. Among FM patients, 51 (64.6%) reported scores greater than 33, indicating the probable presence of a PTSD. With regard to the IES-R subscale scores, the total sample did not show a prominence of one of the three main domains: intrusion (13.9 ± 7.3), avoidance (11.9 ± 6.1) and hyperarousal (12.6 ± 5.9). In these FM patients, self-reported major sources of anxiety were related to personal and relatives' health (59.5%), followed by social withdrawal (21.5%) and employment loss/financial difficulties (11.4%). There was a slight increase of self-reported use of antidepressants (15 [18.9%] vs 16 [20.2%]) and anxiolytics drugs (4 [5.1%] vs 5 [6.3%]) after lockdown period.
Conclusion: These results confirm that psychosocial stress and distress were highly pervasive in FM after COVID-19 national lockdown. It is known that stressed status may exacerbate and/or precipitate later development of FM symptoms. These data support the substantial worsening of somatic burden of FM after lockdown period reported in previous studies (3-4). Coping strategies should be implemented to ameliorate psychological well-being of these patients in this stressful era.
REFERENCES:
[1] Brooks SK, et al. Lancet. 2020;395:912-20.
[2] Hung CH, et al. Ann Rheum Dis 2020;79:1644-1656.
[3] Batres-Marroquín AB, et al. J Clin Rheumatol. 2020 Epub ahead of print.
[4] Cavalli G, et al. Rheumatology 2021;60:465-467.
Acknowledgements: We wish to thank the Lombard Association of Rheumatic Diseases (ALOMAR) for its invaluable contribution to the planning and dissemination the survey, all the Italian associations among which the National Association of People with Rheumatic and Rare Diseases (APMARR) and National Association of People with Rheumatic Diseases (ANMAR) that disseminated the survey through social media. The authors are grateful to all patients for contributing to this project.
Disclosure of Interests: Francesca Ingegnoli: None declared, Massimiliano Buoli: None declared, Cristina Posio: None declared, Raffaele Di Taranto: None declared, Roberto Caporali Speakers bureau: Abbvie, Amgen, BMS, Celltrion, Galapagos, Gilead, Lilly, Pfizer, Roche, UCB, Sanofi, Fresenius Kabi, Samsung bioepis, MSD, Consultant of: Galapagos, Gilead, Lilly,Janssen, MSD.
DOI: 10.1136/annrheumdis-2021-eular.984

POS1177 REVAMPING BIOLOGIC THERAPY DURING COVID-19

S. Ahmed Narikkoottungal[1], A. Siddiqui[1], A. Constantin[1], S. Farrow[1], K. Ahmed[1]. [1]*Princess Alexandra Hospital, Department of Rheumatology, Harlow, United Kingdom*

Background: The COVID-19 pandemic has caught us all by surprise – from governments to individuals; the medical fraternity being no exception. It has affected all walks of life; with its immense contagiosity, diverse and intriguing pathogenesis and manifestations differing from other viruses. It has indeed left humanity in dark, unchartered waters; particularly in the early months of the pandemic.
Objectives: This article shares the experience, in a Rheumatology department in a District General Hospital (DGH) in the United Kingdom, of managing patients on Biologic (b) and Targeted Synthetic (ts) DMARDs, in the midst of the COVID-19 Pandemic.
Methods: All Rheumatology patients at the Princess Alexandra Hospital (PAH) in Harlow newly started on a biologic or targeted synthetic DMARD between 3rd July and 3rd Oct 2020 were identified. These patients had active inflammatory arthritis. Each patient was discussed in a dedicated Multi-Disciplinary Team (MDT) meeting and a consensus on treatment reached in-line with local and National guidelines.

Figure 1. A slide presented at the Essex Rheumatology Association (ERA) meeting explaining the process adopted at the Rheumatology Department at Harlow during the peak of COVID-19 pandemic with new b/ts DMARD patients.

Results: Of the 50 patients identified; 39 had Rheumatoid Arthritis, 6 had Ankylosing Spondylitis and 5 had Psoriatic Arthritis. Of these 50 patients, 5 patients decided against treatment during the stage of 'Enhanced Verbal Consent'. These patients were flaring recurrently and were in regular contact with the department. However, they were afraid to start new Biologic treatment because of the risks of Covid-19. The breakdown of the biologic agents used in the remaining 45 patients were as follows: Adalimumab:11, Rituximab: 10, Etanercept: 9, Tofacitinib: 11, Tocilizumab SC: 3, Tocilizumab IV: 1, Sarilumab: 2, Secukinumab: 1, Infliximab: 1, Baricitinib: 1, Apremilast: 1

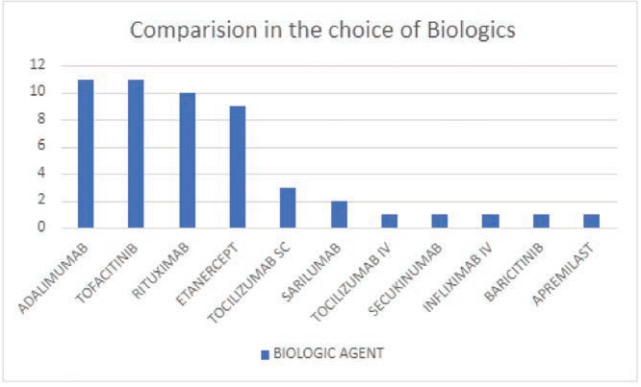


Figure 2. Breakdown of the various b/ts DMARD agents newly started in the 45 patients between 3/7/20 - 3/10/20 at PA Hospital, Harlow, UK

Conclusion: The over-riding principle that guided the Department during the COVID crisis was: *primum non nocere* (first, do no harm). The adherence to the Case Based Discussions (CBDs) positively impacted on decision making, ensuring safe initiation of Biologic DMARDs even during the height of the pandemic. This is vital to achieve early disease remission. The MDT meetings comprising Doctors, Specialist Pharmacist and Nurse Specialists ensured prompt risk stratification of individual patients. It gave patients the opportunity to be part of the decision-making - evident in the five of the fifty patients, who opted to defer the start date of their treatments. The choice of the new Biologic agent was based on the latest National COVID-19 guidelines. The agents with the shortest half-life were selected. Moreover, patients for Rituximab were given one pulsed infusion, as opposed to two infusions. Only one of the 45 patients started on a Biologic agent over this period, either was tested positive or had symptoms suggestive of COVID-19.

REFERENCES:

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7261974
[2] https://rmdopen.bmj.com/content/6/2/e001314
[3] https://www.nejm.org/doi/full/10.1056/nejmc2009567
[4] https://www.jrheum.org/content/early/2020/05/13/jrheum.200527
[5] https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-care-of-adult-patients-with-systemic-rheumatic-disease
[6] www.england.nhs.uk/clinical-guide-rheumatology-patients-v1-19-march-2020.pdf
[7] https://www.rheumatology.org.uk/practice-quality/covid-19-guidance
[8] https://www.nice.org.uk/guidance/ng167/chapter/4-Treatment-considerations
[9] https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/decision-making-and-consent

Acknowledgements: We acknowledge the whole Rheumatology Dept at Harlow for their sincere team work during the COVID-19 pandemic – Sabaa Naz (Rheumatology Pharmacist), Mona Kamal Zou (Biologics Nurse Specialist), Lily Robinson (DMARD Nurse Specialist), Mary Surendran (Osteoporosis Nurse Specialist), Janet Bell (Secretary to Dr Ahmed) and Claire Stroud (Secretary to Dr Farrow).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1008

POS1178 THE ROLE OF VIRTUAL TELEPHONE VISITS IN THE TIGHT CONTROL OF RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TARGETED THERAPIES DURING THE COVID-19 PANDEMIC

F. Ingegnoli[1], G. Cincinelli[1], A. F. Luppino[1], E. Favalli[1], R. Caporali[1]. [1]*Università degli Studi di Milano, Division of Clinical Rheumatology, ASST Pini, Department of Clinical Sciences & Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Milano, Italy*

Background: Rheumatic patients' follow-up in terms of treatment adherence, disease control achieved with treat-to-target (T2T) and tight-control strategy have been deeply influenced by nationwide mitigation strategies such as quarantine, travel restrictions, and inadequate access to routine visits, laboratory and imaging investigations. These restrictions could be potentially detrimental for patients' care, but to what extent these measures affected the T2T and tight-control approach in rheumatoid arthritis (RA) is unknown.
Objectives: This study investigated whether the adoption of telephone virtual care imposed by COVID-19 pandemic has been effective in maintaining remission in RA treated with targeted therapies and to identify factors associated with its maintenance.
Methods: This observational retrospective real-life study was conducted from November 2019 through September 2020. Clinical Disease Activity Index (CDAI) of RA patients treated with targeted therapies was analysed retrospectively before, during and after the national lockdown (LD). During LD period, rheumatologists provided virtual care by telephone to assess the clinical status to guarantee the absence of current contraindications to therapy. Then, patients could choose whether to receive home drug delivery or to maintain their face-to-face consultations. Logistic mixed effects regression models were fitted, with CDAI remission as response variable. A multivariate analysis and a parsimonious model were finally obtained by stepwise selection procedure using AIC.
Results: Data were extracted from a longitudinal observational registry, and at baseline, 502 RA patients were eligible for this study. 52 patients failed to complete their follow-up, 450 patients were included in the final analysis. During LD, 359 patients chose in-person visit, 91 patients home drug delivery and virtual visit. Our cohort did not show a statistically significant decrease in the number of patients fulfilling CDAI remission criteria all along the three periods. Among the 450 patients evaluated, the CDAI remission rate was 40.22% (N=181) and 43.78% (N=197) during pre-LD and post-LD, respectively. As for the 359 patients who choose in-person visits during LD, 43.18% (N=155) were in remission according to CDAI. The final model (step-wise selection) applied to the multivariate analysis of factors that potentially could interfere with disease control in patients with CDAI remission showed that the probability to maintain remission was associated with Caucasian ethnicity, male gender and absence of fibromyalgia (Table 1 below).

Table 1.

	Adjusted OR (95% CI)	p-value
Period (LD vs Pre-LD)	1.24 (0.83 - 1.85)	0.292
Period (Post-LD vs Pre-LD)	1.22 (0.84 - 1.77)	0.299
Gender (male vs female)	2.26 (1.15 - 4.61)	0.020
Disease duration (≥10 years vs <10 years)	0.65 (0.36 - 1.15)	0.141
Ethnicity (Hispanic/Asian vs Caucasian)	0.32 (0.12 - 0.83)	0.021
Fibromyalgia (yes vs no)	0.30 (0.11 - 0.82)	0.021

Conclusion: Telephone-based tight control strategy ensured satisfactory management of RA treated with targeted therapies during the first wave of COVID-19 pandemic. All along the three periods, we observed that the probability to be in CDAI remission was significantly associated with Caucasian ethnicity, male

gender, and absence of fibromyalgia. This temporary approach has been a feasible compensation for face-to-face visits, thus reassuring for future months before the end of pandemic.

Disclosure of Interests: Francesca Ingegnoli: None declared, Gilberto Cincinelli: None declared, Angela Flavia Luppino: None declared, Ennio Favalli Speakers bureau: AbbVie, Sanofi-Genzyme, Lilly, UCB, Pfizer, Novartis, Janssen, Paid instructor for: Roche, MSD, Consultant of: Lilly, Galapagos, Roberto Caporali Speakers bureau: Abbvie, Amgen, BMS, Celltrion, Galapagos, Gilead, Lilly, Pfizer, Roche, UCB, Sanofi, Fresenius Kabi, Samsung bioepis, MSD, Consultant of: Galapagos, Gilead, Lilly,Janssen, MSD.

DOI: 10.1136/annrheumdis-2021-eular.1104

POS1179 POST COVID ARTHRITIS; REACTIVE ARTHRITIS OR RHEUMATIC DISEASE FLARE OR BOTH

F. Fayed[1], E. Abdelkarim[1]. [1]*Alexandria University Students' Hospital, Rheumatology and immunology department, alexandria, Egypt*

Background: Reactive arthritis (ReA) is an emerging arthritis after viral infection especially respiratory and gastrointestinal related viruses. In 2020, SARS-COV2 virus is sweeping worldwide with diverse symptoms and prolonged post-Covid manifestations in which are arthralgia and myalgia are frequently present for days and even months. Interestedly, arthritis in covid era is a part of ReA or a flare of autoimmune disease, it is challenging.(1)

Objectives: Our objective was to determine the frequency of musculoskeletal symptoms with SARS-COV2 virus and after recovery as well as its relation to autoimmune diseases flares.

Methods: A Prospective study was done on 241 patients who admitted to the Rheumatology clinic from March 2020 to January 2021, complaining from new onset of musculoskeletal symptoms. Detailed history, Examination of systems including Musculoskeletal, laboratory investigation, past history of existing rheumatic disease, and history of infection with covid 19.

Results: Among 241 patients with median age 34.4, 36.92% had an existing Rheumatic disease while 63.08% are not. Moreover, 39% of patients had a post history with covid 19 within weeks. The most frequent Musculoskeletal symptoms are myalgia (74.56%), arthralgia (69.36%), and arthritis (10.78%). Furthermore, ReA (Post covid arthritis) accounted (2.07%) especially monoarthritis of Ankle (68.75%) while rheumatic diseases flares (24.48%) as well as new onset rheumatic diseases (39.68%). ($p \leq 0.001$) patients of ReA improved on NSAID and intrarticular injection of glucocorticosteroid.

Conclusion: Covid 19 is one of environmental triggers for development of rheumatic disease as well as reactive arthritis post viral infections. ReA is commonly affected the Ankle joint mainly monoarthritis and had improved on oral NSAID and intrarticular injection of Glucocorticosteroid.

REFERENCES:

[1] Schett, G., Manger, B., Simon, D. *et al.* COVID-19 revisiting inflammatory pathways of arthritis. *Nat Rev Rheumatol* **16,** 465–470 (2020).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1148

POS1180 TREATMENT COMPLIANCE OF PATIENTS WITH RHEUMATOID ARTHRITIS DURING THE FIRST WAVE OF THE SARS-CoV-2/COVID-19 PANDEMIC IN PORTUGAL: RESULTS FROM THE COVID IN RA (COVIDRA) SURVEY

F. Araujo[1], N. Gonçalves[2], A. F. Mourão[1,2]. [1]*Hospital de Sant'Ana, Rheumatology and Osteoporosis Unit, Parede, Portugal*; [2]*Hospital Egas Moniz, Department of Rheumatology, Lisboa, Portugal*

Background: The outcomes of the infection by the SARS-CoV-2 in patients with immune-mediated inflammatory diseases were largely unknown during the early days of the COVID-19 pandemic. It was hypothesized that these patients were at higher risk of morbidity and mortality due to their inherent immune dysfunction and immunosuppressive therapy. Several rheumatology societies issued recommendations urging patients not to stop their anti-rheumatic treatments.

Objectives: To assess treatment compliance of patients with rheumatoid arthritis (RA) during the first wave of the SARS-CoV-2/COVID-19 pandemic in Portugal.

Methods: The web-based survey COVIDRA (COVID in RA) was developed to assess the impact of the first wave mandatory confinement in patients with RA focusing on 5 domains: RA symptoms, attitudes towards medication, employment status, physical exercise and mental health. The questionnaire was sent to RA patients through e-mail and social media of the Portuguese Society of Rheumatology and two patient associations; and it was filled locally at two rheumatology centers in Lisbon. Recruitment took place during June and July 2020. Descriptive statistics were generated by the survey software and were afterwards transported and evaluated using appropriate biostatistics software.

Results: We obtained 441 valid questionnaires. Most respondents were female (88.4%), caucasian (93.6%), with a mean age of 58 (+/-13) years. The majority (57.6%) had longstanding disease (>10 years) and were treated with csDMARDs (63.2%) and/or bDMARDs/tsDMARDS (23,7%). Only 14% (N=61) discontinued or reduced the dosage or frequency of their RA treatment. Most of these changes were previously planned by the attending physician (27.9%). Only 11 patients (18%) discontinued their immunosuppressive medication out of fear of becoming infected with SARS-CoV-2 (corresponding to 2.5% of total responders). Another 11 patients did so because they had no prescription, couldn't go to the community/hospital pharmacy or couldn't afford the medication. Although these numbers preclude any statistical analysis, when compared to patients who persisted on their treatment, those discontinuing due to fear of contagion were younger (56.4 vs 58.5 years), all female (100 vs 86.8%), with long-lasting disease (≥ 11 years) (90.9% vs 57.5%), more frequently treated with bDMARDs (36.4 vs 23.1%) and presenting more symptoms of depression (54.5 vs 49.7%).

Conclusion: Most RA patients complied with their treatment during the first wave of the SARS-CoV-2 pandemic in Portugal. Only a minority changed their immunosuppressive treatment due to fear of SARS-CoV-2 infection. Very similar rates of immunosuppressive discontinuation due to fear of contagion were reported by other authors (such as Schmeiser *et al*, Pineda-sic *et al* and Fragoulis *et al*).

Disclosure of Interests: Filipe Araujo Speakers bureau: Pfizer, Biogen, Novartis, Menarini, Consultant of: MSD, Nuno Gonçalves: None declared, Ana Filipa Mourão: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1152

POS1181 CLINICAL COURSE OF COVID-19 IN CHILDREN WITH RHEUMATIC DISEASE UNDER BIOLOGIC THERAPY

F. Demir[1], K. Ulu[1], Ş. Çağlayan[1], T. Coşkuner[1], B. Sözeri[1]. [1]*Health Sciences University, Umraniye Training and Research Hospital, Pediatric Rheumatology, Istanbul,Turkey*

Background: Since the beginning of the COVID-19 pandemic in our country, Turkey, more than two million people have been infected and more than 20,000 people have died. Although children infected less frequently and generally have a milder findings of COVID-19, the number of patients with a more severe clinical course as multisystem inflammatory syndrome in children (MIS-C) is increasing significantly. However, it has not been shown exactly how biological disease-modifying antirheumatic drug (bDMARD)s, which we frequently use in our pediatric rheumatology practice, and/or the underlying rheumatological diseases affect the clinical course of COVID-19.

Objectives: Here, we aimed to reveal the outcome of COVID-19 infection in our patients with pediatric rheumatic disease and treated with bDMARDs.

Methods: During the period between April 1, 2020 and December 1, 2020, the patients who received bDMARDs were evaluated at the regular outpatient clinic follow-up or by telemedicine with a maximum of 3 months interval. Clinical and demographic characteristics, COVID-19 data and outcome of these patients were retrospectively collected.

Results: Out of the 436 patients treated with bDMARDs, 39 children were infected with COVID-19. The diagnosis was confirmed in 37 patients by RT-PCR (nasalpharyngeal swab) and in two by antibody test. Twenty-two (56.4%) patients were female (17 male, %43.6) and the median age of patients were 12.3 years (min-max: 1.2-20.9). The primary diagnosis of patients were as follows; 20 juvenile idiopathic arthritis (six were systemic subtype), 12 systemic autoinflammatory diseases, three vasculitis, three chronic recurrent multifocal osteomyelitis and one Sjögren's syndrome. Prior to COVID-19 infection, 13 patients (33.3%) were using canakinumab, seven were infliximab (18%), five were adalimumab (12.8%), four were etanercept 10.2%), four were tocilizumab (10.2%), three were anakinra (7.7%), two were rituximab (5.1%), and one was tofacitinib (2.6%).

Of the 39 patients, 21 had at least one COVID-19-related symptom, while 18 patients were asymptomatic. No laboratory or imaging tests was performed for asymptomatic patients and they were followed up without treatment at home isolation. Laboratory tests revealed that fourteen patients had elevated acute phase reactants, six had elevated D-dimer levels, three had lymphopenia (<1000/mm^3), and three had hyperferritinemia.

Hospitalization was required in 20 patients (51.3%) at median of 7-days (min-max: 3-17) and pediatric intensive care unit admission in one. Five patients developed MIS-C and one of these patients was followed up in the pediatric intensive care unit. Myocardial dysfunction was developed in this patient and he was died. The other four patients fully recovered with no remain morbidity.

Conclusion: Considering the literature data and the results of our study, it is not possible to say that currently used bDMARDs worse the course of COVID-19 infection. In patients with underlying risk factors for hyperinflammation, as in one of our patients, COVID-19 may cause mortality regardless of the use of bDMARDs. Whether bDMARDs does not affect the severity of the disease, but it is still not true to say that these drugs are protective. Since cessation of

bDMARDs for COVID-risk may cause exacerbation of the primary rheumatic disease, continuing with current treatments seems an appropriate approach.

REFERENCES:

[1] FELDSTEIN LR, ROSE EB, HORWITZ SM, et al: Overcoming COVID-19 Investigators; CDC COVID-19 Response Team. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *N Engl J Med* 2020; 383: 334-46.

[2] MICHELENA X, BORRELL H, LÓPEZ-CORBETO M, et al. Incidence of COVID-19 in a cohort of adult and paediatric patients with rheumatic diseases treated with targeted biologic and synthetic disease-modifying anti-rheumatic drugs. *Semin Arthritis Rheum* 2020; 50: 564-70.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1173

POS1182 MANAGEMENT OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS DURING THE COVID-19 PANDEMIC: EVIDENCE FROM THE ITALIAN EPICENTER

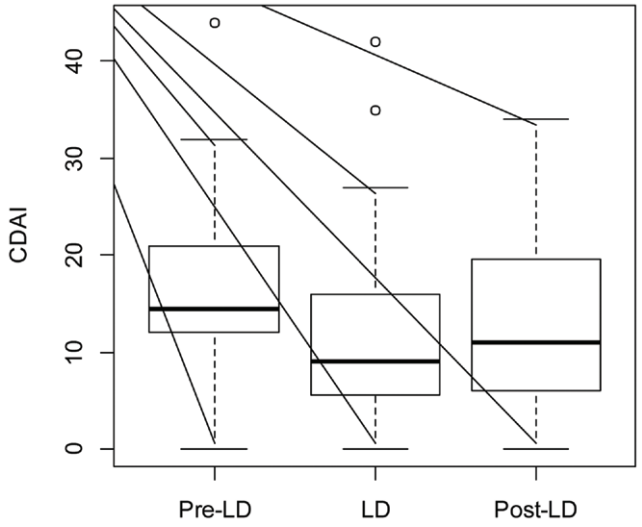
F. Ingegnoli[1], A. F. Luppino[1], G. Cincinelli[1], E. Favalli[1], R. Caporali[1]. [1]*Università degli Studi di Milano, Division of Clinical Rheumatology, ASST Pini, Department of Clinical Sciences & Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Milano, Italy*

Background: Despite significant improvement in the RA management, up to twenty percent of patients with rheumatoid arthritis (RA) have a difficult-to-treat (D2T) disease. The COVID-19 related mitigation policies, for instance quarantine, and consequent difficult access to in-person visits, laboratory and imaging investigations, adversely affected the follow up of rheumatic patients. Although pandemic-imposed limitations could have negatively influenced disease management particularly in D2T patients, to what degree these restrictions affected the treat-to target (T2T) and tight-control strategy in this subgroup of RA patients has not been investigated yet.

Objectives: To evaluate whether the switch to telehealth imposed by COVID-19 pandemic was effective in the management of D2T RA patients treated with targeted therapies.

Methods: This observational retrospective real-life study was conducted from November 2019 through September 2020. Among RA patients treated with targeted therapies, RA D2T patients according to EULAR definition (1) were identified. Clinical Disease Activity Index (CDAI) of these patients was analysed retrospectively before, during and after lockdown (LD). During LD period, patients could choose whether to receive home drug delivery or to maintain their face-to-face consultations, and in the former rheumatologists provided virtual care. To evaluate the effect of LD on the percentage of patients in remission, logistic mixed effects regression models were fitted, with CDAI remission as response variable.

Results: Data were extracted from a longitudinal observational registry, and at baseline, 52 patients treated with targeted therapies were classified as D2T RA. Among them, during pre-LD, LD, and post-LD 11.54% (N=6), 53.49% (N=23), and 46.15% (N=24) had CDAI remission/low disease activity, while 46 (88.46%), 20 (46.51%) and 28 (53.85%) had CDAI moderate/high. All the patients completed the follow-up. Median values of CDAI during pre-LD, LD, and post-LD were 14.5 [IQR 12-21], 9 [IQR 5.5-16], and 11 [IQR 6-19.2] respectively (see Figure 1 below).



Conclusion: Telephone-based tight control strategy ensured satisfactory management of D2T RA treated with targeted therapies. This temporary approach has been a feasible compensation for the decline of face-to-face visits also in this challenging group of RA patients, thus reassuring for future months before the end of pandemic.

REFERENCES:

[1] Nagy G, et al. EULAR definition of difficult-to-treat rheumatoid arthritis. Ann Rheum Dis 2021;80(1):31-35.

Disclosure of Interests: Francesca Ingegnoli: None declared, Angela Flavia Luppino: None declared, Gilberto Cincinelli: None declared, Ennio Favalli Speakers bureau: AbbVie, Sanofi-Genzyme, Lilly, UCB, Pfizer, Novartis, Janssen, Paid instructor for: Roche, MSD, Consultant of: Lilly, Galapagos, Roberto Caporali Speakers bureau: Abbvie, Amgen, BMS, Celltrion, Galapagos, Gilead, Lilly, Pfizer, Roche, UCB, Sanofi, Fresenius Kabi, Samsung bioepis, MSD, Consultant of: Galapagos, Gilead, Lilly,Janssen, MSD.

DOI: 10.1136/annrheumdis-2021-eular.1188

POS1183 OUTCOMES OF COVID-19 INFECTION AMONG CHILDREN AND YOUNG PEOPLE WITH PRE-EXISTING RHEUMATIC AND MUSCULOSKELETAL DISEASES

L. Kearsley-Fleet[1], S. Lawson-Tovey[2,3], R. E. Costello[1], A. Belot[4], F. Aeschlimann[5,6], I. Melki[5,6,7], I. Koné-Paut[8], D. Clemente[9], M. C. Pinedo Gago[10], N. Svestkova[11], N. Vinšová[11], M. Hamad Saied[12], Y. Berkun[13], N. Wulffraat[14], S. Eulert[15], C. A. Scirè[16], A. Strangfeld[15], E. Mateus[17,18], P. Machado[19,20,21], Y. Uziel[22,23], K. Hyrich[1,3]. [1]*The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [2]*The University of Manchester, Centre for Genetics and Genomics Versus Arthritis, Centre for Musculoskeletal Research, Manchester, United Kingdom*; [3]*Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, National Institute of Health Research Manchester Biomedical Research Centre, Manchester, United Kingdom*; [4]*Hospices Civils de Lyon, Pediatric Rheumatology Unit, Lyon, France*; [5]*Hôpital Necker-Enfants Malades, Pediatric Hematology-Immunology and Rheumatology Department, Reference center for Rheumatic, AutoImmune and Systemic diseases in children (RAISE) & FAI2R, Paris, France*; [6]*Paris University, Laboratory of Immunogenetics of Paediatric Autoimmunity, Imagine Institute, Paris, France*; [7]*Hôpital Robert Debre, General Pediatrics, Infectious Disease and Internal Medicine Department, Reference center for Rheumatic, AutoImmune and Systemic diseases in children (RAISE) & FAI2R, Paris, France*; [8]*University of Paris Sud Saclay, CeRéMAIA, FAI2R, AP-HP, Bicêtre Hospital, Paris, France*; [9]*Hospital Niño Jesús, Unidad de Reumatología Pediátrica, Madrid, Spain*; [10]*Hospital Universitario Cruces, Reumatología Pediátrica, Barakaldo, Spain*; [11]*Charles University and General University Hospital, Centre for Paediatric Rheumatology and Autoinflammatory Diseases, Department of Paediatrics and Inherited Metabolic Disorders, 1st Faculty of Medicine, Prague, Czech Republic*; [12]*Carmel Medical Centre, Pediatrics Rheumatology Unit, Haifa, Israel*; [13]*Hebrew University of Jerusalem, Department of Pediatrics, Hadassah-Hebrew University Medical Center, Mount Scopus, Faculty of Medicine, Jerusalem, Israel*; [14]*University Medical Center, Department of Pediatric Immunology and Rheumatology, Wilhelmina Children's Hospital, Utrecht, Netherlands*; [15]*German Rheumatism Research Center (DRFZ Berlin), Epidemiology and Health Care Research Unit, Berlin, Germany*; [16]*University of Ferrara, Rheumatology Unit, Department of Medical Sciences, Ferrara, Italy*; [17]*Portuguese League Against Rheumatic Diseases, LPCDR, Lisbon, Portugal*; [18]*European League Against Rheumatism (EULAR) Standing Committee, People with Arthritis/Rheumatism in Europe (PARE), Kilchberg, Switzerland*; [19]*University College London, Centre for Rheumatology & Department of Neuromuscular Diseases, London, United Kingdom*; [20]*University College London Hospitals National Health Service (NHS) Trust, National Institute for Health Research (NIHR) University College London Hospitals Biomedical Research Centre, London, United Kingdom*; [21]*London North West University Healthcare NHS Trust, Department of Rheumatology, Northwick Park Hospital, London, United Kingdom*; [22]*Meir Medical Center, Pediatric Rheumatology Unit, Department of Pediatrics, Kfar-Saba, Israel*; [23]*Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel*

Background: It remains unknown whether children and young people with rheumatic and musculoskeletal diseases (RMD) who acquire COVID-19 infection have a more severe COVID-19 course, due to either underlying disease or immunosuppressive treatments.

Objectives: To describe outcomes among children and young people with underlying RMD who acquire COVID-19 infection.

Methods: All children and young people <18 years of age with COVID-19 (presumptive or confirmed) reported to the EULAR COVID-19 Database, which collects details regarding RMD diagnosis and treatment, COVID infection and outcomes, between 27 March 2020 and 29 January 2021 (cutoff date for this analysis) were included. Patient characteristics and COVID-19 outcomes are presented.

Results: A total of 151 children and young people (age range 2-17 years; Table 1) have been reported to the database from 12 countries; mostly Spain (N=30), France (N=29), Israel (N=29), and Czechia (N=25). Most patients had a diagnosis of juvenile idiopathic arthritis (JIA; N=92; 61%). Other diagnoses were autoinflammatory syndrome (including TRAPS, CAPS, FMF; 12%), and systemic lupus erythematosus (4%). There were 14 (9%) hospitalisations and 1 (0.7%) death reported due to COVID-19. The most commonly reported symptoms were fever (46%), cough (34%), anosmia (19%), and headache (19%). Only 19 (13%) patients reported glucocorticoid use. DMARD therapy was used by 104 (69%) patients; 67 (44%) were on csDMARDs (methotrexate [N=54], antimalarials [N=7]), 45 (30%) on anti-TNF, 9 (6%) on IL-6 inhibitors, and 7 (5%) on IL-1 inhibitors. Among the 145 patients with hospitalisation data, patients on any DMARD therapy (cs/b/tsDMARDs) had similar odds for hospitalisation compared with those not on therapy, adjusted for age (odds ratio 0.7; 95% CI 0.2, 2.4).

		All Patients
N		151
Gender	Female	94 (62%)
	Male	56 (37%)
	Unknown	1 (<1%)
Age, years	Median (IQR)	12 (8, 15)
	Range	2 to 17
Top Rheumatology Diagnoses	Juvenile Idiopathic Arthritis (JIA)	92 (61%)
	Polyarthritis	*50 (33%)*
	Oligoarthritis	*31 (21%)*
	Systemic	*11 (7%)*
	Autoinflammatory syndrome (e.g. TRAPS, CAPS, FMF)	18 (12%) 6 (4%)
	Systemic Lupus Erythematosus	
Comorbidities	None stated	112 (74%)
	Obesity	9 (6%)
	Ocular inflammation	9 (6%)
	Asthma	3 (2%)
Required Hospitalisation	Yes	14 (9%)
	No	131 (87%)
	Missing	6 (4%)
Top 5 Symptoms Reported	Fever	69 (46%)
	Cough	51 (34%)
	Anosmia	28 (19%)
	Headache	28 (19%)
	Fatigue	23 (15%)
Deaths due to COVID-19	Yes	1 (<1%)
Treatment at onset of COVID-19 infection	Glucocorticoids	19 (13%)
	csDMARDs	67 (44%)
	Methotrexate	*54 (36%)*
	Antimalarials	*7 (5%)*
	Mycophenolate	*5 (3%)*
	bDMARDs	64 (42%)
	Anti-TNF	*45 (30%)*
	IL-6	*9 (6%)*
	IL-1	*8 (5%)*
	Any DMARD	104 (69%)

Conclusion: These initial data on outcomes of COVID-19 in paediatric RMDs are very reassuring, with less than 1 in 10 patients reporting hospitalisation. Due to the database design and inherent reporting bias, this is likely an overestimate, suggesting that overall outcomes among this population appear to be generally good, with mild infection. Increasing case reports to the database will allow further exploration of drug- and disease-specific outcomes.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1243

POS1184 AUTOIMMUNE SYSTEMIC DISEASES AND COVID-19 INFECTION

S. Monov[1], R. Shumnalieva[2], D. Monova[3]. [1]*Medical University - Sofia, Departmant of Rheumatology, Sofia, Bulgaria*; [2]*Medical University - Sofia, Department of Rheumatology, Sofia, Bulgaria*; [3]*Medical Institute, Medical University - Sofia, Department of Internal Medicine, Sofia, Bulgaria*

Background: Covid-19 infection poses a serious challenge for immune-compromised patients. This is likely due to a combination of immune dysfunction, immunosuppressive therapy and excess co-morbidities. Little is known about the impact of Coronavirus disease 2019 (COVID-19) in patients with inflammatory autoimmune systemic diseases.

Objectives: The aim of this study is to describe clinical characteristics of patients with autoimmune systemic diseases and COVID-19, and to identify baseline variables associated with a severe infection requiring hospitalization.

Methods: A telephone survey investigating the impact of COVID-19 on patients with systemic lupus erythematosus (SLE), systemic sclerosis (SSc), inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis), idiopathic inflammatory myopathies (IIM), ANCA-associated vasculitis (AAV) was administered. Data extraction included diagnosis, disease activity status, demographics, disease duration, occupational exposure, adherence to social distancing advise, therapy, comorbidities, and laboratory tests. Covid-19 was classified as definite diagnosis of Covid-19 disease: presence of symptomatic Covid-19 infection, confirmed by a nasopharyngeal SARS-CoV-2 polymerase chain reaction test. Comparisons between patients with or without hospitalization were performed.

Results: 512 patients (median age 53,4 ± 14,3 years) with autoimmune systemic diseases (234 IA, 182 SLE, 42 SSc, 31 IIM, 23 AAV) were included in the study. 89 patients (58 woman, 31 men) developed at least one symptom (fever, asthenia, chills, cough, sore throat, dyspnea, chest pain, headaches, arthralgias, myalgias, odynophagia, diarrhea, conjunctivitis, hypo-, ageusia, hypo-, anosmia) of COVID-19 and were PCR test positive. Of patients with COVID – 19 infection 54 patients were treated with methylprednisolone, 36 – with methotrexate, 34 – with hydroxychloroquine, 26- with biologics, 10 - with azathioprine, 6 - with cyclophosphamide prior to their COVID-19 illness.

Conclusion: Covid-19 is more frequent in the subgroup of patients without therapy with modifying anti-rheumatic drugs, which might play some protective role against the most harmful manifestations of Covid-19. 21 patients required hospitalization - these were more frequently men, older and with comorbidities (cardio-respiratory illness, renal diseases, diabetes mellitus). Male sex, previous coronary and lung disease, serum creatinine level, proteinuria, glucocorticoids use > 5 mg/day, were associated to hospitalization. Patients with inflammatory arthritis do not seen to be at higher risk for infection or a severe course of COVID-19.

REFERENCES:

[1] Monova, D., S. Monov. Mechanisms of kidney injury in patients with COVID-19. Nephrology, dialysis and transplantation, 2020; 26 (4): 5-15.

[2] Monova, D., S. Monov. Kidney injures in COVID-19. Nephrology, dialysis and transplantation, 2020; 26 (4): 16-34.

Disclosure of Interests: Simeon Monov Speakers bureau: AMGEN, PFIZER, NOVARTIS, ABBVIE, ROCHE, ASTRA-ZENECA, Russka Shumnalieva: None declared, Daniela Monova: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1254

POS1185 IMPACT OF LOCKDOWN DURING COVID-19 PANDEMIC ON THE ONSET OF POST-TRAUMATIC STRESS DISORDER (PTSD) IN SYSTEMIC SCLEROSIS PATIENTS: A CASE-CONTROL STUDY

D. M. Reza Beigi[1], G. Pellegrino[1], A. Lorello[1], C. Angelelli[1], K. Stefanantoni[1], F. Conti[1], V. Riccieri[1]. [1]*Sapienza University of Rome, Department of Internal Medicine, Anesthesiology and Cardiovascular Sciences, Rome, Italy*

Background: Social distancing due to COVID-19 pandemic had a major impact on the mental health of general population, with a high prevalence of post-traumatic stress disorder (PTSD) related symptoms[1, 2]. Psychological repercussions were notably found in people with chronic diseases, including systemic sclerosis (SSc) patients, where an increasing of anxiety symptoms, related also to low financial resources, emerged[3].

Objectives: To evaluate the impact of COVID-19 lockdown on the onset of PTSD in patients with SSc, firstly during the total confinement period (March-April 2020) and then at the time of less restrictive government measures, following the RT index lowering (June-July 2020)[4].

Methods: We carried out a case-control study on 57 SSc patients, according to the ACR/EULAR 2013 criteria, and on 57 healthy subjects as control group (HC), matched by sex and age. At T0 (March-April) and T1 (June-July) both populations received the "Impact of Event Scale Revised" questionnaire (IES-R) by e-mail, with a cut-off of ≥ 33 defining probable diagnosis of PTSD[5]. A multivariate analysis of possible factors influencing IES-R score, such as age, number of cohabitating people and weekly outings count, was performed in SSc patients at both times of the survey.

Results: At T0 we found a significantly greater number of SSc patients with IES-R score ≥ 33 compared to HC (26/45.6% vs 13/22.8%; median value [quartiles] 31 [19.5;42.5] vs 24 [15.5; 32]; p-value 0.046). At T1, we obtained data from 44 SSc patients and 35 HC but no significant difference was noticed (18 / 40.9% vs 8 / 23.5%; 26 [15.25; 38] vs 26.5 [20.75; 32.5]; p> 0.05). SSc patients also had significantly fewer weekly outings than HC, both at T0 (p <0.001) and T1 (p <0.001) (Table 1). The multivariate analysis performed at T0 on SSc patients showed a significant association of IES-R ≥33 score with age (p 0.025) and with a lower count of weekly outings (p 0.002). The latter data negatively correlated with an IES-R ≥33 score in SSc patients (r -0.267, p 0.004).

Conclusion: We found a significantly higher prevalence of PTSD in SSc patients compared to HC at the strictest lockdown time, turning into comparable when

government measures were less restrictive, due to the minimum RT index values recorded in Italy. Older age and lower count of weekly outings were associated with PTSD in SSc patients during the lockdown, whereas the count of weekly outings was lower than in HC during both the examined periods. The results of this study indicate that COVID-19 lockdown had a worse impact in SSc patients, where the fewer weekly outings may depend on their clinical condition and on a greater concern about their health[6]. These findings strengthen the World Scleroderma Foundation recommendations regarding care to the psychological frailty of SSc patients[7].

REFERENCES:

[1] Wang C, Brain Behav Immun. 2020.
[2] Dubey S, Psychiatr Pol. 2020.
[3] Thombs BD, J Psychosom Res. 2020 Dec.
[4] https://covid19.infn.it/grafici/?chart=italia,rt,covidstat
[5] Weiss, D. S., & Marmar, C. R. (1996). The Impact of Event Scale - Revised, Assessing. psychological trauma and PTSD (pp. 399-411).
[6] Orlandi M, *Clin Rheumatol*. 2020
[7] Matucci-Cerinic M, *Ann Rheum Dis*. 2020

Table 1. Descriptive analysis of study population: T0 (Time 0), T1 (Time 1), SD (Standard Deviation), IES-R (Impact of Event Scale-Revised).

	SSc patient group	HS group
Female:male ratio at T0	46:7	46:7
Mean age ± SD at T0	59±12.8	51±8.7
IES-R ≥33 score n°/% at T0	26/45.6%*	13/22.8%
IES-R ≥33 score n°/% at T1	18/40.9%	8/23.5%
IES-R score at T0, median value [quartiles]	31 [19.5;42.5]	24 [15.5;32]
IES-R score at T1, median value [quartiles]	26 [15.25; 38]	26.5 [20.75; 32.5]
N° of weekly outings at T0, median value [quartiles]	2 [1;3.5]	4 [2;10]**
N° of weekly outings at T1, median value [quartiles]	5 [3;6]	14 [6.75;15]**

*p<0.046; **p<0.001

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1266

POS1186

EFFECT OF SOCIO-ECONOMIC STATUS AND EDUCATIONAL LEVEL ON COVID-19 OUTCOMES IN PATIENTS WITH RHEUMATIC DISEASES FROM ARGENTINA: DATA FROM THE SAR-COVID REGISTRY

L. Sorrentino[1], J. Rebak[1], F. Maldonado[1], V. V. Castro Coello[1], A. Brigante[1], A. Hamaui[1], D. Dubinsky[1], R. Baez[2], C. Pisoni[2], C. Gobbi[2], L. Carlevaris[2], R. Tanten[2], A. K. Cogo[2], M. Delavega[2], R. Perez Alamino[2], M. A. Lazaro[2], M. Pera[2], S. I. Pineda Vidal[2], M. E. Calvo[2], D. Guaglianone[2], C. G. Alonso[2], M. Guinsburg[2], C. Retamozo[2], C. Aeschlimann[2], R. Quintana[3], K. Roberts[3], C. A. Isnardi[3], G. Pons Estel[3]on behalf of SAR-COVID Registry. *[1]Sanatorio Güemes, Department of Rheumatology, Ciudad Autónoma de Buenos Aires, Argentina*; *[2]Argentine Society of Rheumatology, On behalf of SAR-COVID Registry, Ciudad Autónoma de Buenos Aires, Argentina*; *[3]Argentine Society of Rheumatology, Research Unit - SAR-COVID Registry, Ciudad Autónoma de Buenos Aires, Argentina*

Background: SARS-CoV-2 infection can present with a broad clinical spectrum, from asymptomatic to lethal. Different risk factors have been recognized. Socio-economic status and educational level may affect access to the healthcare system and therefore COVID-19 infection outcome.

Objectives: The aim of this study was to assess the association between socio-demographic status and educational level and SARS-CoV-2 outcomes, such as hospitalization, ICU admission, need for mechanical ventilation and death, in Argentinean patients with rheumatic diseases from the SAR-COVID Registry.

Methods: We performed a cross-sectional study of consecutive adult patients with rheumatic diseases and SARS-CoV-2 infection included in the multicentric Argentinean SAR-COVID Registry. The following variables were included: gender, ethnicity, age, health insurance, educational level (under or over 12 years of education), socio-economic level according to Graffar Scale in high, medium-high, medium, medium-low, low; underlying rheumatic disease, its duration and treatment at the time of infection.

SARS-CoV-2 infection outcomes were: hospitalization, admission to ICU, mechanical ventilation requirement and death.

Statistical analysis was performed using Chi^2, Fisher, T-test, ANOVA.

Results: Five hundred and twenty-five patients were included, 422 (80.4%) were female, with a mean age of 51.3 years (SD 15.2). Most of them were caucasians (48%) or mestizos (43%) and 96.8% lived in an urban environment. Almost half of the patients (47%) were categorized as middle-class, 24% middle-high or high class, 21% middle-low or low. 48.4% of the patients were employed. Regarding educational level, 54% had more than 12 years of education.

The most prevalent rheumatic disease was Rheumatoid Arthritis (40.4%), followed by Systemic Lupus Erythematosus (14.9%), Sjögren (5.5%) and Psoriatic Arthritis (5.5%). Treatments used at the time of SARS-CoV-2 infection were corticosteroids (19%), cs-DMARDs (49%), and b- and ts-DMARDs (16%).

Overall hospitalization frequency was 35%, median hospital stay was 10 days (IQR 10 days), 11.6% were admitted to the ICU, 10% required mechanical ventilation and the global mortality was 8%.

Notably, patients with less than 12 years of education required mechanical ventilation more frequently than the more educated ones (11.9% vs. 5.6%, p=0.026) and showed a higher mortality due to COVID-19 (9% vs. 2.8%, p=0.0004).

Patients categorized as upper social classes (middle-high and high) were admitted to the hospital on a more frequent basis (74.4% of cases), when compared with middle class (64.4%) and middle-low and low class (58%) (p=0.77). Median duration of hospitalization for the aforementioned groups was 12.5 (IQR 17.3), 10 (IQR 9) and 10.5 (IQR 9.3) days respectively (p=0.60).

Patients with health insurance were found to be hospitalized more frequently in comparison to those without insurance (42.4% vs. 33.7%, p=0.14), but showed similar admission rates to the ICU (11.8% vs. 12.8%; p=0.78), need for mechanical ventilation (10.7% vs. 8.7%; p=0.70) and mortality (7.1% vs. 6.5%; p=0.99).

Caucasian patients had fewer hospital admissions when compared against other ethnicities (mestizos mostly) (26.1% vs. 43.4%; p<0.0001), but showed no statistically significant difference in need for mechanical ventilation 10.3% vs. 9.9% (p=0.99) or mortality 8.7% vs. 5.1% (p=0.15).

Conclusion: Patients with lower educational level needed twice the frequency of mechanical ventilation, and showed thrice the mortality than those with more than 12 years of education.

Albeit patients in upper social stratus and those with health insurance were admitted to the hospital in a more frequent manner, no statistically significant differences were found regarding the need for ICU, mechanical ventilation or mortality.

Caucasians were hospitalized less frequently than mestizos, but had no significant differences in the other measured outcomes.

Disclosure of Interests: Laura Sorrentino Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Jonathan Rebak Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Federico Maldonado Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Vanessa Viviana Castro Coello Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Alejandro Brigante Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Adriana Hamaui Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Diana Dubinsky Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Roberto Baez Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Cecilia Pisoni Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Carla Gobbi Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Leandro Carlevaris Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Romina Tanten Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Adriana Karina Cogo Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Maria DeLaVega Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Rodolfo Perez Alamino Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Maria Alicia Lazaro Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Mariana Pera Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Susana Isabel Pineda Vidal Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Maria Elena Calvo Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Debora Guaglianone Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Carla G Alonso Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Mara Guinsburg Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Cinthya Retamozo Grant/research support from: Unrestricted

grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Carolina Aeschlimann Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Rosana Quintana Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Karen Roberts Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Carolina Ayelen Isnardi Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Guillermo Pons Estel Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.

DOI: 10.1136/annrheumdis-2021-eular.1294

POS1187

WILLINGNESS TO GET THE COVID-19 VACCINE AMONG PATIENTS WITH RHEUMATIC DISEASES, HEALTH WORKERS AND GENERAL POPULATION

B. Yurttas[1], B. C. Poyraz[2], N. Süt[3], A. Ozdede[1], M. Oztas[1], Ö. F. Tabak[4], V. Hamuryudan[1], E. Seyahi[1]. [1]*Istanbul University- Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*; [2]*Istanbul University- Cerrahpasa, Cerrahpasa Medical Faculty, Department of Psychiatry, Division of Geropsychiatry, Istanbul, Turkey*; [3]*Trakya University Medical Faculty, Department of Biostatistics and Medical Informatics, Edirne, Turkey*; [4]*Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey*

Background: As of January 2021 the COVID-19 pandemic has been responsible for more than 2.2 million deaths worldwide (1). Potential vaccines against COVID-19 have been developed swiftly and vaccination programs were started in many countries. Turkey agreed to use inactivated vaccine candidate, 'CoronaVac' produced by Chinese biopharmaceutical company (3). Many of our patients having a rheumatic diseases (RD) call us for permission to get vaccination, while some express their concerns about the efficacy and safety issues.

Objectives: We therefore assessed the willingness to get vaccination among patients with RD compared to health workers and a sample from general population.

Methods: A web-based questionnaire study was conducted in a cross-sectional design in 3 groups of participants: 1. patients with RD, 2. hospital workers and 3. General population. The questionnaire sought socio-demographic variables, COVID-19 related risk factors, willingness to get vaccination, and concerns and thoughts about vaccine. COVID-19 related anxiety (CAS) was also evaluated through the questionnaire.

Results: We studied in total 732 (258 M/ 474 F) patients with RD, 320 (88 M/ 232 F) hospital workers and 763 (258 M/ 505 F) individuals representing general population. Patients with RD were significantly older and less educated and spent less time using social media compared to both control groups (Table 1). CAS scores were similar between the study groups. Of the patients with RD, 29.2% were willing to be vaccinated, 19% were unwilling and 51.8% were undecided. These were similar among the general population (34.6%, 23.3% and 42.1%, respectively), whereas hospital workers were significantly more willing (52.5%, 20.9% and 26.6%, respectively) ($p<0.0001$). About a third in each group thought that vaccination should be obligatory.The major concerns associated with vaccine were fear from side effects, unknown scientific results and lack of confidence. Being male, older age, working in a hospital and increased anxiety levels were found to be independently associated with willingness.

Conclusion: Only about one third of the patients with RD were willing to get vaccination, which was somewhat similar to that observed among the general population. This could be due to rushed vaccine development as well as negative news on vaccines on the social media. Our study also reveals that, after almost one year after the pandemic, about 95% in all study groups did not express dysfunctional anxiety related with COVID-19.

REFERENCES:

[1] https://covid19.who.int/

[2] https://www.bloomberg.com/news/articles/2020-12-26/turkey-signs-accord-with-biontech-for-coronavirus-vaccine

Table 1. Socio-demographic and COVID-19 associated variables, anxiety scores and willingness to get vaccination

	Patients with RD (n=732)	Hospital workers (n = 320)	General population (n =763)	P
Male/ Female, n	258/474	88/232	258/505	0.045
Age, mean ± SD, years	42.8 ± 11.6	37.0 ± 10.0	40.8 ± 12.0	<0.001
Primary/middle school education, n (%)	225 (30.7)	6 (1.9)	28 (3.7)	<0.001
≤ 1 hour daily spent using social media, n (%)	270 (36.9)	100 (31.3)	192 (25.2)	<0.0001
COVID-19 related anxiety, total score, mean ± SD	1.62 ± 3.03	1.81±2.64	1.55±2.71	0.389
COVID-19 related anxiety, cut off value of ≥ 9, n (%)	36 (5.1)	13 (4.2)	29 (4.0)	0.626
COVID-19 diagnosis in the participant (n %)				<0.0001
Yes	104 (14.2)	69 (21.6)	70 (9.2)	
No	617 (84.3)	248 (77.5)	687 (90.0)	
Unsure	11 (1.5)	3 (0.9)	6 (0.8)	
COVID-19 diagnosis among the household or close friends, n (%)				<0.0001
Yes	460 (62.8)	244 (76.3)	435 (57.0)	
No	254 (34.7)	76 (23.8)	317 (41.5)	
Unsure	18 (2.5)	0	11 (1.4)	
Presence of any comorbid disease, n (%)	304 (41.5)	67 (20.9)	181 (23.7)	<0.0001
History of psychiatric disorder, n (%)	177 (24.2)	51 (15.9)	110 (14.4)	<0.0001
Willingness to get vaccination (n %)				<0.0001
Yes	214 (29.2)	168 (52.5)	264 (34.6)	
No	139 (19.0)	67 (20.9)	178 (23.3)	
Unsure	379 (51.8)	85 (26.6)	321 (42.1)	
Do you think that vaccination should be obligatory? n (%)				0.003
Yes	216 (29.5)	113 (35.3)	207 (27.1)	
No	277 (37.8)	136 (42.5)	331 (43.4)	
Unsure	239 (32.7)	71 (22.2)	225 (29.5)	

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1435

POS1188

COVID-19 IN PATIENTS WITH RHEUMATIC DISEASES: COMPARISON OF DATA FROM THE ARGENTINE REGISTRY (SAR-COVID), WITH THE LATIN AMERICAN AND GLOBAL REGISTRY (GLOBAL RHEUMATOLOGY ALLIANCE)

A. A. Reyes[1], G. Alle[1], R. Tanten[1], M. Scolnik[1], E. Soriano[1], G. Berbotto[2], M. Haye[2], M. J. Gamba[2], R. Nieto[2], M. García[2], V. Savio[2], L. Gonzalez Lucero[2], P. Alba[2], L. Takashima[2], F. Risueño[2], L. Casalla[2], N. Cucchiaro[2], A. Bertoli[2], S. Porta[2], C. Maldini[2], R. Gallo[2], C. Goizueta[2], E. Picco[2], R. Quintana[3], K. Roberts[3], C. A. Isnardi[3], G. Pons-Estel[3]on behalf of SAR-COVID Registry. [1]*Hospital Italiano de Buenos Aires, Reumatologia, Buenos Aires, Argentina*; [2]*On behalf of SAR-COVID Registry, On behalf of SAR-COVID Registry, Buenos Aires, Argentina*; [3]*Argentine Society of Rheumatology - Research Unit - SAR-COVID Registry, Argentine Society of Rheumatology - Research Unit - SAR-COVID Registry, Buenos Aires, Argentina*

Background: SARS CoV-2 infection has recently burst onto the global scene, and the knowledge of the course of this infection in patients with rheumatic diseases receiving immunomodulatory treatment is still insufficient. The Argentine Society of Rheumatology (SAR) designed a national registry called SAR-COVID in order to get to assess our reality.

Objectives: To identify the particular characteristics of patients with rheumatic diseases and COVID-19 in Argentina (SAR-COVID Registry), and to compare them with the data reported at the Latin American and Global level (Global International Alliance Rheum-COVID Registry).

Methods: A national, multicenter, prospective and observational registry was carried out. Patients older than 18 years, with a diagnosis of rheumatic disease and SARS-CoV-2 infection by PCR or serology, were included between August 13, 2020 and January 17, 2021. Demographic data, underlying rheumatic disease (activity of the disease, current treatment), comorbidities, clinical-laboratory characteristics of the SARS-CoV-2 infection, as well as received treatments (pharmacological, oxygen therapy / ventilatory support) and outcomes (hospitalization, mortality) were recorded. The characteristics of the

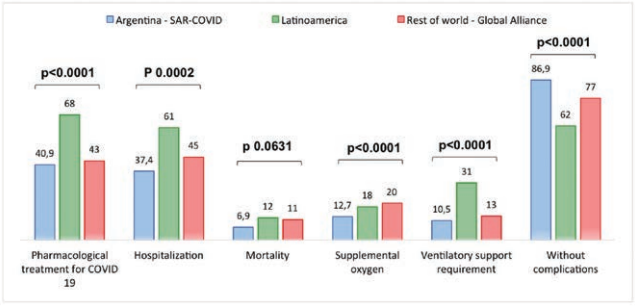
included patients were compared with the data reported at the Latin American and global level. Descriptive statistics were performed. Comparisons between groups were made using ANOVA, chi2 or Fisher's test, according to the type of variable.

Results: Four hundred sixty-five patients from Argentina, 74 patients from Latin America and 583 from the rest of the world were included, mostly women (79.6%, 73% and 71% respectively), with a mean age of 50.2 (SD 15.3), 53.5 (DE 15.6) and 55.8 (15.5), years respectively. The most frequent rheumatic diseases in the three groups were rheumatoid arthritis (43.9%, 35%, and 39%) and systemic lupus erythematosus (16.1%, 22%, and 14%) (Table 1).

In Argentina, fewer patients received specific pharmacological treatment for COVID-19 (40.9%, 68% and 43% respectively, p <0.0001), and there was a lower requirement of NIMV / IMV (Non-Invasive Mechanical Ventilation/Invasive Mechanical Ventilation) than in the rest of Latin America and the world (10.5% vs 31% vs 13%, p <0.0001).

Hospitalization was lower in Argentina than in the rest of Latin America (37.4% vs 61% p 0.0002) and of the world (37.4% vs 45% p 0.0123), and mortality was numerically lower in Argentina, but without statistically significant differences between the three groups (6.9%, 12% and 11%; p 0.6311). Most of the patients, (86.9%) did not present any complications in Argentina, with a statistically significant difference with the rest of the groups (62% and 77%, p <0.0001) (Graph 1).

Conclusion: The patients with rheumatic diseases and SARS-CoV-2 infection reported in this argentinian registry received less specific pharmacological treatment for COVID-19, presented fewer complications and required less ventilatory support, than those reported in the Latinoamerican and Global registry. However, no statistically significant differences were observed in terms of mortality.



Graph 1. Main outcomes and evolution of patients with rheumatic disease and COVID-19.

REFERENCES:

[1] Stokes, Erin K, Zambrano, Laura D, Anderson, Kayla N, et al. *Coronavirus Disease 2019 Case Surveillance - United States, January 22-May 30, 2020.* MMWR Morb Mortal Wkly Rep; 69(24): 759-765, 2020 Jun 19.

[2] Mehta P, McAuley DF, Brown M, et al. *COVID-19: consider cytokine storm síndromes and immunosuppression.* Lancet 2020;395:1033–4.

[3] Gianfrancesco M, et al. *Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry.* Ann Rheum Dis 2020;79:859–866.

[4] Manuel F. Ugarte-Gil, et al. *Characteristics associated with Covid-19 in patients with Rheumatic Disease in Latin America*. Global Rheumatology. Septiembre 2020.

Disclosure of Interests: Alvaro Andres Reyes Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Gelsomina Alle Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Romina Tanten Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Marina Scolnik Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Enrique Soriano Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Guillermo Berbotto Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Maria Haye Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", María Julieta Gamba Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Romina Nieto Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Mercedes García Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Veronica Savio Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Luciana Gonzalez Lucero Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Paula Alba Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Lorena Takashima Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", FABIAN RISUEÑO Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Luciana CASALLA Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Natalia Cucchiaro Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Ana Bertoli Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Sabrina POrta Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Carla Maldini Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Rosana Gallo Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Cecilia Goizueta Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Eugenia Picco Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Rosana Quintana Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Karen Roberts Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Carolina Ayelen Isnardi Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.", Guillermo Pons-Estel Grant/research support from: "Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data."

DOI: 10.1136/annrheumdis-2021-eular.1458

POS1189 THE IMPACT OF TELEMEDICINE AND COVID-19 ON A TERTIARY RHEUMATOLOGY SERVICE: A RETROSPECTIVE AUDIT

W. Zhu[1], T. De Silva[2], L. Eades[2], S. Morton[2], S. Ayoub[1,2], E. F. Morand[1,2], A. Antony[1,2]. [1]*Monash University, School of Clinical Sciences, Melbourne, Australia*; [2]*Monash Health, Department of Rheumatology, Melbourne, Australia*

Background: Telemedicine was widely utilised to complement face-to-face (F2F) care in 2020 during the COVID-19 pandemic, but the impact of this on patient care is poorly understood.

Objectives: To investigate the impact of telemedicine during COVID-19 on outpatient rheumatology services.

Methods: We retrospectively audited patient electronic medical records from rheumatology outpatient clinics in an urban tertiary rheumatology centre between April-May 2020 (telemedicine cohort) and April-May 2019 (comparator cohort). Differences in age, sex, primary diagnosis, medications, and proportion of new/review appointments were assessed using Mann-Whitney U and Chi-square tests. Univariate analysis was used to estimate associations between telemedicine usage and the ability to assign a diagnosis in patients without a prior rheumatological diagnosis, the frequency of changes to immunosuppression, subsequent F2F review, planned admissions or procedures, follow-up phone calls, and time to next appointment.

Results: 3,040 outpatient appointments were audited: 1,443 from 2019 and 1,597 from 2020. There was no statistically significant difference in the age, sex, proportion of new/review appointments, or frequency of immunosuppression use between the cohorts. Inflammatory arthritis (IA) was a more common diagnosis in the 2020 cohort (35.1% vs 31%, p=0.024). 96.7% (n=1,444) of patients seen in the 2020 cohort were reviewed via telemedicine. In patients without an existing rheumatological diagnosis, the odds of making a diagnosis at the appointment were significantly lower in 2020 (28.6% vs 57.4%; OR 0.30 [95% CI 0.16-0.53]; p<0.001). Clinicians were also less likely to change immunosuppressive therapy in 2020 (22.6% vs 27.4%; OR 0.78 [95% CI 0.65-0.92]; p=0.004). This was mostly driven by less de-escalation in therapy (10% vs 12.6%; OR 0.75 [95% CI 0.59-0.95]; p=0.019) as there was no statistically significant difference in the escalation or switching of immunosuppressive therapies. There was no significant difference in frequency of follow-up phone calls, however, patients seen in 2020 required earlier follow-up appointments (p<0.001). There was also no difference in unplanned rheumatological presentations but significantly fewer planned admissions and procedures in 2020 (1% vs 2.6%, p=0.002). Appointment

non-attendance reduced in 2020 to 6.5% from 10.9% in 2019 (OR 0.57 [95% CI 0.44-0.74]; p<0.001), however the odds of discharging a patient from care were significantly lower in 2020 (3.9% vs 6%; OR 0.64 [95% CI 0.46-0.89]; p=0.008), although there was no significance when patients who failed to attend were excluded. Amongst patients seen via telemedicine in 2020, a subsequent F2F appointment was required in 9.4%. The predictors of needing a F2F review were being a new patient (OR 6.28 [95% CI 4.10-9.64]; p<0.001), not having a prior rheumatological diagnosis (OR 18.43 [95% CI: 2.35-144.63]; p=0.006), or having a diagnosis of IA (OR 2.85 [95% CI: 1.40-5.80]; p=0.004) or connective tissue disease (OR 3.22 [95% CI: 1.11-9.32]; p=0.031).

Conclusion: Most patients in the 2020 cohort were seen via telemedicine. Telemedicine use during the COVID-19 pandemic was associated with reduced clinic non-attendance, but with diagnostic delay, reduced likelihood of changing existing immunosuppressive therapy, earlier requirement for review, and lower likelihood of discharge. While the effects of telemedicine cannot be differentiated from changes in practice related to other aspects of the pandemic, they suggest that telemedicine may have a negative impact on the timeliness of management of rheumatology patients.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1497

POS1190 EXPECTATIONS AND POTENTIAL CONCERNS OF PATIENTS WITH AUTOIMMUNE AND RHEUMATIC DISEASES REGARDING VACCINATION AGAINST SARS-COV-2 (COVID-19): THE WORLDWIDE ONLINE VAXICOV STUDY

R. Felten[1], M. Dubois[1], M. F. Ugarte-Gil[2], J. Fort[1], L. Pijnenburg[1], A. Chaudier[1], L. Kawka[1], C. Costecalde[1], H. Bergier[1], E. Chatelus[1], R. M. Javier[1], C. Sordet[1], J. E. Gottenberg[1], J. Sibilia[1], Y. Fuentes-Silva[3], L. Arnaud[1]. *[1]Hôpitaux Universitaires de Strasbourg, Service de Rhumatologie, Strasbourg, France*; *[2]Universidad Cientifica del Sur, Hospital Nacional Guillermo Almenara Irigoyen, School of Medicine and Rheumatology Department., Lima, Peru*; *[3]Complejo Hospitalario Universitario Ruiz y Páez, Universidad de Oriente, Ciudad Bolívar, Centro Nacional de Enfermedades Reumáticas, Division of Rheumatology, Ciudad Bolívar, Venezuela (Bolivarian Republic)*

Background: Vaccination is an important and effective tool to prevent infections in the general population as well as in patients with systemic autoimmune or inflammatory rheumatic diseases (AIIRDs) who may be at increased risk of serious infection. While the global race for vaccines against COVID-19 has already lead to first authorizations and vaccinations in some countries, multiple questions arise for access and provisions as well as for the acceptance of vaccine policies by immunocompromised patients.

Objectives: We conducted an international survey about expectations and potential concerns regarding SARS-CoV-2 vaccine in patients with AIIRDs and healthcare professionals.

Methods: The online study consisted of 57 questions which addressed determinants associated with SARS-2-CoV-2 vaccine willingness. Dissemination was ensured through social media and patient associations between December 12 and December 21, 2020.

Results: The study included 1266 patients with AIIRDs and 265 healthcare professionals from 56 countries. SARS-CoV-2 vaccine willingness was reported by 54.2% of AIIRD patients (uncertainty in 32.2% and unwillingness in 13.6%) and 74.0% of healthcare professionals. In patients, the willingness to get vaccinated increased significantly with age (p<0.0001) and was strongly associated with the fear to be infected by SARS-CoV-2 (p<0.0001) or to develop severe COVID19 (p<0.0001) but not with presence of additional comorbidities (p=0.71) or immunocompromised status (p=0.94). The most trusted healthcare professional regarding the recommendation to get vaccinated against COVID-19 was their specialist (rheumatologist, internist, etc.) for 69.9%. Vaccine unwillingness was low (7.9%) among healthcare professionals and willingness was significantly increased in those who had been vaccinated against influenza in the last 3 years (p=0.01).

Subject groups	Patients	Healthcare professionals
N	1266	265
Age (years), median [IQR25-75]	50 [40-61]	40 [32.5-53]
Female, n (%)	1141 (90.1%)	150 (56.6%)
Male, n (%)	115 (9.9%)	115 (43.4%)
Country, n (%)		
France	320 (25.3%)	159 (60%)
UK	345(27.3%)	4 (1.5%)
Chile	123 (9.7%)	4 (1.5%)
USA	114 (9.0%)	7 (2.6%)
Venezuela	43 (3.4%)	26 (9.8%)
Spain	57 (4.5%)	3 (1.1%)
Mexico	53 (4.2%)	3 (1.1%)
Argentina	45 (3.6%)	8 (3.0%)
Other*	166 (13.1%)	51 (19.2%)
Rheumatic diagnosis, n (%)	1266	-
Systemic lupus erythematosus	492 (38.9%)	-
Spondyloarthritis	176 (13.9%)	-
Rheumatoid arthritis	160 (12.6%)	-
Giant cell arteritis / Polymyalgia rheumatica	144 (11.4%)	-
Primary anti-phospholipid syndrome	64 (5.1%)	-
Inflammatory myositis	62 (4.9%)	-
Relapsing polychondritis	45 (3.6%)	-
Other**	123 (9.7%)	-
-Health professionals, n (%)	-	265
Doctor	-	203 (76.6%)
Nurse (or equivalent)	-	23 (8.7%)
Nursing assistant	-	11 (4.2%)
Other***	-	28 (10.6%)
Associated comorbidities, n (%)		
Diabetes	69 (5.5%)	6 (2.3%)
Hypertension	267 (21.1%)	24 (9.1%)
Myocardial infarction, stroke, transient stroke	60 (4.7%)	1 (0.4%)
Respiratory disease (asthma, chronic bronchitis, emphysema, etc.)	169 (13.3%)	13 (4.9%)
Renal failure	47 (3.7%)	1 (0.4%)
Obesity (BMI > 30)	228 (18.0%)	18 (6.8%)
At least one associated comorbidity, n (%)	588 (46.4%)	50 (18.9%)
Smoker, n (%)	128 (10.2%)	22 (8.3%)
Current	411 (32.7%)	51 (19.2%)
Past	719 (57.1%)	192 (72.5%)
Never		
Use of oral glucocorticoids, n (%)	551 (56.1%)	3 (1.1%)
Immunocompromised[$], n (%)	770 (60.8%)	0
On a 0 to 10 scale, median	8 (6-10)	5 (3-8)
[IQR25-75]	9 (7-10)	5 (1-8)
–Afraid to get infected by SARS-CoV-2		
–Afraid to get a severe COVID-19		
Willing to get vaccinated (Yes / uncertain / No), %	54.2 / 32.2 / 13.6	74.0 / 18.1 / 7.9
Vaccine hesitancy, n (%)	357 (28.2%)	59 (22.3%)

Conclusion: Data from this study are crucial to understand the main expectations and concerns regarding SARS-CoV-2 vaccination in patients with AIIRDs and healthcare workers and allow the identification of valuable strategies to increase vaccine coverage in those populations.

Acknowledgements: We wish to acknowledge the crucial role of the following patient associations: LupusEurope (tweeter: @LupusEurope), Agrupacion Lupus Chile (@Lupus_Chile), RarasNoInvisibles (@Noinvisibles), Lupus UK, Lupus France, SPONDYLʼASSO, Spondyl(O)action, AFL+, in the dissemination of the survey. We are indebted to Gonzalo Tobar Carrizo (@pinkycito) for the Spanish translation of the survey, all patients, families, and health professionals for their kind participation in our study. We wish to thank Ms. Sylvie Thuong for her invaluable assistance.

Disclosure of Interests: Renaud FELTEN Speakers bureau: Pfizer, Maxime Dubois: None declared, Manuel F. Ugarte-Gil Speakers bureau: Janssen and Pfizer, Jérémy Fort: None declared, Luc PIJNENBURG: None declared, Aurore Chaudier: None declared, Lou Kawka: None declared, Charlotte Costecalde: None declared, Hugo Bergier: None declared, Emmanuel Chatelus: None declared, Rose-Marie Javier: None declared, Christelle Sordet: None declared, Jacques-Eric Gottenberg Speakers bureau: Pfizer and Astra-Zeneca, Jean Sibilia Speakers bureau: Pfizer, Yurilis Fuentes-Silva: None declared, Laurent Arnaud Speakers bureau: Pfizer and Astra-Zeneca.

DOI: 10.1136/annrheumdis-2021-eular.1503

POS1191

COVID-19 STRESS: DOES IT AUGMENT PAIN IN PEOPLE WITH FIBROMYALGIA AND MIGHT PSYCHOLOGICAL FLEXIBILITY PROTECT AGAINST THIS INFLUENCE?

T. Koppert[1], J. W. G. Jacobs[2], M. Lumley[3], R. Geenen[4,5]. [1]*Leiden University - Faculty of Social Sciences, Developmental & Educational Psychology, Leiden, Netherlands*; [2]*University Medical Center Utrecht, Rheumatology & Clinical Immunology, Utrecht, Netherlands*; [3]*Wayne State University, Psychology, Detroit, United States of America*; [4]*Utrecht University, Psychology, Utrecht, Netherlands*; [5]*Altrecht, Psychosomatic Medicine, Zeist, Netherlands*

Background: Stress might augment pain in people with fibromyalgia, possibly through sensitization of the central nervous system. The COVID-19 pandemic offers a unique opportunity to examine this mechanism. If it holds, the link between COVID-19 stress and pain would be stronger in people with fibromyalgia than in people without it. Additionally, psychological flexibility might act as a resilience factor, reducing pain severity. If psychological flexibility buffers the impact of stress on pain in people with fibromyalgia, then enhancing psychological flexibility may be of value.
Objectives: To determine the association between COVID-19 stress and pain severity in people with fibromyalgia, as compared to people without fibromyalgia, and whether psychological flexibility buffers the impact of stress on pain severity.
Methods: In a repeated cross-sectional design, we analysed questionnaire data from two independent surveys. The data collection has been described in a previous study of mental well-being in people with inflammatory rheumatic diseases. [1] The current study analysed data from people with and without fibromyalgia. Data were collected before the COVID-19 pandemic (2018; fibromyalgia: n=145, no fibromyalgia: n=386) and at the first peak of the pandemic in the Netherlands (2020; fibromyalgia: n=270, no fibromyalgia: n=1259). Stress due to the pandemic, psychological flexibility, and pain were subjected to regression analyses. Two operationalisations of stress were analysed: self-reported stress levels during the peak of the pandemic in 2020, and a comparison of assessments in 2018 and 2020 (assuming higher stress levels during the pandemic peak in 2020).
Results: In regression analyses, stress during the pandemic (p<.001), having fibromyalgia (p<.001), and lower psychological flexibility (p<.001) were all associated with more severe pain, but the interactions showed that the strength of the association of stress with pain was not different in people with fibromyalgia compared to people without fibromyalgia (p=.76 and p=.28 for the two operationalization of stress, respectively). Another interaction indicated that psychological flexibility was a potential buffer against the association between self-reported stress and pain in the first operationalisation of stress (p=.04), but not in the second (p=.44). The significant but small interaction is shown in the Figure 1. It suggests that pain is higher in people with low psychological flexibility and higher stress levels during the pandemic. This effect was not specific to fibromyalgia.
Conclusion: Overall, the significant main effects show that negative states, such as stress related to the pandemic and low psychological flexibility, are associated with another negative state: pain. A small interaction effect suggests that psychological flexibility may protect against the impact of COVID-19 stress on pain, both in people with and without fibromyalgia. However, the analyses reject our hypothesis that COVID-19 stress would augment pain especially in people with fibromyalgia.
REFERENCES:
[1] Koppert TY, Jacobs JWG, Geenen R. The psychological impact of the COVID-19 pandemic on Dutch people with and without an inflammatory rheumatic disease. Rheumatology (Oxford) 2020; keaa842. doi: 10.1093/rheumatology/keaa842.
.Pain (standard deviation from the norm) as a function of low (-1 SD) and high (+1 SD) psychological flexibility and low (-1 SD) and high (-1 SD) self-reported stress levels during the first peak of the pandemic in 2020, while controlling for gender, age, education level, and number of diseases.
Disclosure of Interests: Tim Koppert: None declared, Johannes W.G. Jacobs: None declared, Mark Lumley Consultant of: Paid research consultant to Cognifisense, LLP, which studies virtual reality treatments for chronic pain., Rinie Geenen Speakers bureau: Sanofi Genzyme paid for a lecture and worshop on depression and fatigue in RA.
DOI: 10.1136/annrheumdis-2021-eular.1529

POS1192

BEHAVIOR AND FEELINGS OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DURING LOCKDOWN MEASURES FOR THE COVID-19 OUTBREAK

G. De Marchi[1], D. Azzolina[2], E. Maresio[3], D. Colatutto[4], M. Binutti[4], M. Monte[5], S. Gallipoli[6], F. Zobec[6], A. Palese[7], M. Silano[8], S. De Vita[4], D. Gregori[9], L. Quartuccio[4]. [1]*ASUFC, Rheumatology Clinic, Udine, Italy*; [2]*University of Piemonte Orientale, Statistics, Turin, Italy*; [3]*ProChild Onlus, Psychology, Trieste, Italy*; [4]*University of Udine, Rheumatology Clinic, Udine, Italy*; [5]*Associazione Malati Reumatici - Friuli Venezia Giulia, Section - Udine, Udine, Italy*; [6]*Zeta Research srl, Clinical Project Management & Quality Assurance, Trieste, Italy*; [7]*University of Udine, School of Nursing, Department of Medicine, Udine, Italy*; [8]*Istituto Superiore di Sanità, Unit of Human Nutrition and Health, Department of Food Safety Nutrition and Veterinary Public Health, Rome, Italy*; [9]*University of Padova, Unit of Biostatistics, Epidemiology and Public Health, Department of Cardiology, Thoracic and Vascular Sciences, Padova, Italy*

Background: COVID-19 is a systemic viral disease currently spreading as a pandemic. A more severe course and prognosis of COVID-19 in systemic lupus erythematosus (SLE) and vasculitis has been reported (1).
Several papers have focused on the concerns, healthcare-related behaviors and psychological impact of COVID-19 pandemic among patients with rheumatic diseases, and specifically on SLE patients, showing a trend towards remarkable psychological distress (2-4). To date, no investigation on the psychological effects of quarantine strategy on SLE patients has been carried out.
Objectives: To investigate the psychological impact of the lockdown measures adopted in Italy to contrasting the COVID-19 outbreak, on patients with SLE as compared to the general population.
Methods: Patients affected by SLE were given an online questionnaire focused on psychological impact and self-perception during the lockdown measures contrasting the COVID-19 outbreak. The survey was focused on COVID-19 concerns, emotional impact, self-perception and changes in daily living activities and relationships. Results were compared with those of PRESTO (imPact of quaRantine mEasures againST cOvid19) project, an Italian survey, which used the same questionnaire, directed to the general population, with or without chronic diseases. A propensity matching procedure has been applied to LEPRE (Lupus Erythematosus PRESTO project) cases and the PRESTO responders with a ratio of 2 versus 1.
Results: 64 patients and 1114 unselected people completed the survey. After the matching procedure, patients were compared to 128 matched adults. Missing data were below 6%. The median age among patients was 43 years (I-III interquartile range 35-54.5), 88% were female and 100% Caucasian. The SLE subjects live mainly in detached houses (38/64 vs 348/1114, p<0.0001), having access to a private garden (52/64 vs 625/1112, p<0.0001) and also owning a pet (43/64 vs 508/1114, p<0.001), in comparison with the PRESTO sample living mainly in flats. The psychological impact measured by IES-R, GHQ.12, and CEDS scores were not statistically different between patients and the general population, such as globally COVID-19 concerns and feelings. However, patients perceived more difficulty to find some free time and enjoy it (13/60 vs 48/121, p=0.01) and to be able to solve own problems (47/61 vs 71/120, p=0.02). On the contrary, patients felt more able to cope with the problem and less sad or depressed in comparison with the PRESTO group (17/61 vs 13/120, p=0.003). Moreover, patients missed playing sports/exercise less than general population (12/63 vs 46/128, p=0.02), while they felt more the distance from family and relatives (45/63 vs 42/86, p<0.0001).
Conclusion: the COVID-19 pandemic didn't unveil a greater psychological fragility of people living with SLE than the others. By contrast, a coping strategy, including the role of the family and the lifestyle, contributes to resilience of SLE in difficult scenarios such as those presented by the pandemic.
REFERENCES:
[1] Gianfrancesco M, et al. Ann Rheum Dis 2020;79:859-866.
[2] George M, et al. J Rheumatol 2020 Nov 15; doi: 10.3899/jrheum.201017.
[3] Rathi M, et al. Lupus 2020 Oct 6:961203320962855. doi: 10.1177/0961203320962855.
[4] Koppert TY, et al. Rheumatology 2020;keaa842. doi: 10.1093/rheumatology/keaa842.
Acknowledgements: We thank the PRESTO Investigators dr Corrado Lanera and dr Giulia Lorenzoni (Biostatistics, Epidemiology and Public Health, Department of Cardiology, Thoracic and Vascular Sciences, University of Padova, Italy) for their contribution.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1590

POS1193

CLINICAL FEATURES AND THE COURSE OF COVID-19 IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

A. Avanoglu Guler[1], T. Yüce İnel[2], H. Karadeniz[1], R. Bilici Salman[1], H. Satış[1], H. Küçük[1], M. A. Ozturk[1], B. Goker[1], S. Haznedaroglu[1], İ. Sari[2], T. Kasifoglu[3], A. Tufan[1]. [1]*Gazi University Faculty of Medicine Hospital, Rheumatology Department, Ankara, Turkey*; [2]*Dokuz Eylul University Faculty of Medicine Hospital, Rheumatology Department, Izmir, Turkey*; [3]*Eskisehir Osmangazi University Faculty of Medicine Hospital, Rheumatology Department, Eskisehir, Turkey*

Background: The novel coronavirus 2019 (COVID-19) has a wide range of clinical presentation from asymptomatic or mild viral infection to severe life-threating complications, including acute respiratory distress syndrome (ARDS), which develop as a result of immune system dysregulation, exaggerated immune response, and cytokine release syndrome [1]. Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disorder characterized by dysfunction

of the innate immune system and excessive production of proinflammatory cytokines, including interleukin (IL)-1β, IL-6, interferon-gamma, and tumor necrosis factor-alpha, all of which have increased in severe cases in COVID-19 [1-3].
Objectives: The aim of this study is to report clinical characteristics and outcome of FMF patients with COVID-19.
Methods: This study included 48 consecutive FMF patients who were diagnosed COVID-19 by SARS-CoV-2 nucleic acid RT-PCR in nasopharyngeal swab or sputum, or symptoms and computed tomography findings suggestive for COVID-19. Data on demographic and clinical characteristics of FMF disease, clinical course and outcome of COVID-19 were evaluated.
Results: The median age of patients was 35.5 (29-43.5) years, ranging from 18 to 87 years. The median disease duration of FMF was 10 (6-16) years. The most common presenting symptoms and signs of patients during attacks were peritonitis (85.5%), fever (81.3%), and pleuritis (48%). Twelve (25%) patients had amyloidosis. Comorbidities were present in half of patients with ankylosing spondylitis (21%) and hypertension (17%) being the most frequently seen. Two-third of patients (66%) were in remission for FMF. The median dosage of colchicine treatment for FMF was 1.5 (IQR 1) mg/day. 90% of patients continued colchicine treatment for FMF during the COVID-19 course. The baseline characteristics and treatment modalities of patients were demonstrated in Table 1. Forty-six patients presented with at least one COVID-19 symptoms. Fever (73%), myalgia/arthralgia (69%), and cough (60%) were the most common symptoms. 16 patients were admitted at hospital, 5 of them required oxygen therapy and 2 patients with amyloidosis developed ARDS and went to intensive care unit (ICU) for invasive mechanical ventilation (IMV). One patient who had been followed-up at ICU died.
Conclusion: Our FMF patients with COVID-19 have similar clinical features and outcomes as general population. Dysregulation of innate immune system in FMF might not be risk factors for COVID-19. Besides, colchicine and IL-1 inhibitors intake might have protective and preventive effects on COVID-19 progression.

Table 1. Baseline characteristics, treatment modalities and outcome of patients

Age years, median (IQR)	39.4 (15)
Gender (F/M)	25/23
FMF Disease duration, years, median (IQR)	10 (10)
Mutations*	
Monoallelic mutation, n (%)	6 (14)
Biallelic mutation, n (%)	34 (81)
Homozygous M694V mutation	18 (43)
Heterozygous M694V mutation	15 (36)
Comorbidities, n (%)	24 (50)
FMF treatment	
Colchicine 1 mg/day, n (%)	17 (35.5)
Colchicine 1.5 mg/day, n (%)	18 (37.5)
Colchicine 2 mg/day, n (%)	13 (27)
Anakinra, n (%)	12 (25)
Canakinumab, n (%)	3 (6.3)
Positive SARS-Cov-2 RT-PCR, n (%)	42 (87.5)
Interstitial pneumonia in CT scan, n (%)	15 (31.3)
COVID-19 treatment, n (%)	46 (95.8)
Outpatient treatment, n (%)	32 (66.7)
Hospitalized, not required supplemental oxygen, n (%)	9 (18.8)
Hospitalized, required supplemental oxygen, n (%)	5 (10.4)
ICU, required IMV, n (%)	2 (4.2)
Outcome	
Recovered, n (%)	47 (98)
Deceased, n (%)	1 (2)
Complications, n (%)	3 (6.3)

*42 patients were included in the analysis

REFERENCES:
[1] Tufan A, Avanoğlu Güler A, Matucci-Cerinic M. COVID-19, immune system response, hyperinflammation and repurposing antirheumatic drugs. Turkish journal of medical sciences. 2020;50:620-632.
[2] Hausmann JS. Targeting cytokines to treat autoinflammatory diseases. Clinical immunology (Orlando, Fla.). 2019;206:23-32.
[3] Tufan A, Lachmann HJ. Familial Mediterranean fever, from pathogenesis to treatment: a contemporary review. Turkish journal of medical sciences. 2020;50:1591-1610.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1649

POS1194 THE EFFECT OF SARS-COV-2 ON THE COURSE AND THE TREATMENT OF RHEUMATIC INFLAMMATORY DISEASES. EXPERIENCE FORM THE NORTHWESTERN GREECE

E. Pelechas[1], E. Kaltsonoudis[1], M. Migos[1], P. Karagianni[2], A. Kavvadias[3], P. Voulgari[1], A. Drosos[1]. [1]*University of Ioannina, School of Medicine, Greece, Internal Medicine - Division of Rheumatology, Ioannina, Greece*; [2]*University of Ioannina, School of Medicine, Greece, Laboratory Medicine, Ioannina, Greece*; [3]*University of Ioannina, School of Medicine, Greece, Gastroenterology, Ioannina, Greece*

Background: COVID-19 has been shown to significantly affect the vulnerable population [1,2]. Among them, patients suffering from inflammatory rheumatic diseases, and especially the immunosuppressed [3].
Objectives: to assess the effect of SARS-CoV-2 on the course and the treatment of rheumatic inflammatory diseases.
Methods: from February to December 2020, 46 patients with inflammatory rheumatic diseases were included (32 female) that got infected with the SARS-CoV-2. Mean age was 65 years old, 17 were smokers, 12 had arterial hypertension, 8 diabetes mellitus, and 3 hypothyroidism. Most of them had their comorbidities well-controlled and their rheumatic disease was in remission. More specifically, 24 patients had rheumatoid arthritis, 13 psoriatic arthritis, and 9 ankylosing spondylitis. All patients were under treatment with conventional synthetic (cs) and/or biological (b) disease-modifying anti-rheumatic drugs (DMARDs), while 7 of them were also on treatment with glucocorticoids (GC) (<5mg/day). Twenty-eight patients were on tumor necrosis alpha (TNF-α) inhibitors (19 as monotherapy), 4 on anti- interleukin (IL)-6 monotherapy, 3 on Janus Kinase (JAK) inhibitors plus on low dose methotrexate (MTX), and the rest (11 patients) were on a csDMARD with or without GCs.
Results: positive patients with the SARS-CoV-2, instructed to discontinue their immunosuppressive treatment, except GCs that were adjusted for their disease. Most patients (37 out of 46) had a mild disease course and their symptomatology was nothing more than a simple flu-like syndrome. Furthermore, on 9 of them olfactory dysfunction and gastrointestinal manifestations as well as low grade fever were noted but without the need of a hospital admission. On the other hand, only 5 patients needed hospitalization (2 on MTX monotherapy and 3 on combination therapy) due to dyspnea with low oxygen saturation (hypoxemia) and high fever. From those 5, 3 had a short in-hospital stay, while 2 developed pneumonia and a longer in-hospital stay was required in order to get the appropriate treatment. None of the patients did not require an intensive care unit admission. Finally, in 14 patients that got infected from February to May 2020, viral antibodies had been measured. All patients had high titres of IgG antibodies in their serum for as long as six months after their infection. Of note, none of the infected patients were smokers.
Conclusion: patients with rheumatic diseases that are in remission using low doses of GCs and DMARDs, have almost the same chances with the general population to have a serious course of their infection with the SARS-Cov-2. In addition, in these patients, the immune response appears to be adequate, both in the production and maintenance of antibodies, which appear to be maintained for at least 6 months after infection.
REFERENCES:
[1] Patel JA, Nielsen FBH, Badiani AA, Assi S, Unadkat VA, Patel B, et al. Poverty, inequality and COVID-19: the forgotten vulnerable. Public Health. 2020;183:110-111. Doi: 10.1016/j.puhe.2020.05.006.
[2] Poteat T, Millet GA, Nelson LE, Beyrer C. Understanding COVID-19 risks and vulnerabilities among black communities in America: the lethal force of syndemics. Ann Epidemiol. 2020;47:1-3. Doi: 10.1016/j.annepidem.2020.05.004.
[3] Gianfrancesco MA, Hyrich KL, Gossec L, Strangfeld A, Carmona L, Mateus EF, et al. Rheumatic disease and COVID-19: initial data from the COVID-19 Global Rheumatology Alliance provider registries. Lancet Rheumatol. 2020;2(5):e250-e253. Doi: 10.1016/S2665-9913(20)30095-3.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1691

POS1195 ASSESSING ANTIBODY STATUS FOR SARS-CoV-2 IN PEOPLE WITH CORONAVIRUS INFECTION: A TIME COURSE STUDY IN PEOPLE WITH AUTOIMMUNE CONDITIONS

K. Biddle[1], S. Koushesh[1], A. Blundell[1], D. Clark[1], S. Krishna[1], N. Sofat[1]. [1]*St George's University of London, Institute for Infection and Immunity, London, United Kingdom*

Background: With the emergence of the global coronavirus pandemic, increasing concerns have been raised about the course of SARS-CoV-2 infection in people with immune-mediated disorders.
Objectives: In this study we aimed to assess the time course of proven SARS-CoV-2 infection, development of humoral immunity with detectable antibodies to the virus and evaluate any changes in antibody titres over time.
Methods: We recruited 114 participants in total who had potential symptoms of Covid-19 infection. Participants were recruited from rheumatology or inflammatory bowel disease (IBD) clinics from their records who attended a London Teaching hospital for care. Ethical Approval was in place for the study. Age- and gender- matched control participants without any underlying rheumatological condition/IBD were recruited as a comparator group. Clinical symptoms for Covid-19 infection were assessed using the Covid-19 Rheumatology Global

Alliance assessment criteria (https://rheum-covid.org/). Information about Disease Modifying Anti-Rheumatic Drug (DMARD) drug use was also recorded. Participants' serum samples were collected for quantitative serological assessment of antibodies to SARS-CoV-2 using the Mologic Enzyme-Linked Immuno-Sorbent Assay (ELISA) IgG kit. The optical density values were plotted aganist time using a normalisation as previously described (1). A cut-off above 0 indicated positive serology.

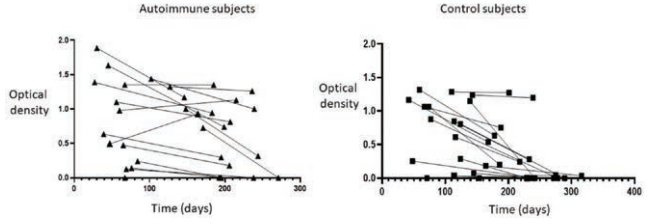
Results: A total of 114 subjects were recruited into the study. Subjects were recruited if they had suspected Covid symptoms. Of the population recruited, the total number subsequently testing positive for SARS-CoV-2 was n=59 (either on serology or PCR). The number of subjects with autoimmune conditions diagnosed with Covid-19 was 32, with 30 subjects being symptomatic (the asymptomatic 2 subjects were excluded from further analyses). Of the 30 symptomatic subjects, the average age was 56, with a female to male ratio of 19:11. The most prevalent diagnoses were RA (30%), Psoriatic Arthritis (16.7%), SLE (10%), sarcoidosis 10%), Ulcerative Colitis (10%), Crohn's disease (10%), seronegative inflammatory arthritis (6.7%), Sjogren's (3.3%) and Juvenile Idiopathic Arthritis (3.3%). The majority were on csDMARDs (60%), biologic DMARDs (20%), tacrolimus (3.3%) and the remaining 16.7% were not on DMARDs. Most subjects required treatment in hospital (56.7%), a smaller number required high dependency care (6.7%) and the rest were treated at home (36.6%). The majority required no oxygen (63.3%), with a further 30% requiring oxygen and 6.7% needed more supportive care i.e. CPAP/ventilation. We also had a matched control group (n=29) of subjects who developed SARS-CoV-2 but had no underlying autoimmune conditions. These subjects had a mean age of 55, female: male ratio 18: 11. Of these 31% had home management, 55.2% had ward level treatments and 13.8% had intensive care treatment. Of the controls, 48.3% did not require oxygen, 37.9% needed simple oxygen and 13.8% were on CPAP. A total of 35 subjects from the original study have attended for follow-up visits. Antibody titres for IgG using the Mologic ELISA detection assay were compared at two visits for the control and autoimmune group. Results showed that subjects with autoimmune conditions and those without who developed SARS-CoV-2 showed very similar antibody titres by optical density (OD) (Figure 1) and maintained antibody responses beyond 6 months in most cases.

Conclusion: Serological assays can assist in the understanding of disease severity of SAR-CoV-2 infection. They can be a useful tool for patient surveillance, especially in people who are on immunomodulatory drugs and are being seen in Rheumatology services. Future work is needed to assess the duration and potential protective nature of humoral antibody responses to SARS-CoV-2.

REFERENCES:

[1] Staines HM, Kirwan D, Clark DJ et al. Dynamics of IgG seroconversion and pathophysiology of COVID:19 infections. medRxiv preprint doi: https://doi.org/10.1101/2020.06.07.20124636.

Figure 1.



Disclosure of Interests: Kathryn Biddle: None declared, Soraya Koushesh: None declared, Anna Blundell: None declared, David Clark: None declared, Sanjeev Krishna: None declared, Nidhi Sofat Consultant of: Advisory work for Pfizer and Eli Lilly, Grant/research support from: Received grants from Bristol Myers Squibb and Pfizer for Investigator Initiated Studies.

DOI: 10.1136/annrheumdis-2021-eular.1736

POS1196 COVID-19 VACCINE WILLINGNESS IN RA? RESULTS FROM THE RA LOUVAIN BRUSSELS COHORT

T. Sokolova[1], V. Pirson[1], T. Xavier[1], E. Curraj[2], L. Bricman[1], E. Sapart[1], S. De Montjoye[1], S. Dierckx[2], A. Avramovska[1], P. Durez[1]. [1]*Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Belgium*; [2]*CHU Mont-Godinne, UCLouvain, Rheumatology, Mont-Godinne, Belgium*

Background: Over 2 million deaths from the COVID-19 disease have been reported in the world. Since no antiviral treatment is available, the vaccination is the most important option to fight the SARS-CoV-2 infection. Patients living with rheumatoid arthritis (RA) affecting the immune system or under immunosuppressive agent will be considered as a high risk population and will start the vaccination shortly. But many patients could decline the vaccine for several reasons including safety concerns.

Objectives: The aim of this study is to evaluate the proportion of patients with RA who are favourable to COVID-19 vaccination, to know the reasons to decline and to analyse the characteristics of these patients.

Methods: We included patients with RA from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 classification criteria. A simple and standard questionnaire was distributed to patients who attended rheumatology out patient and day care clinic from 14 december 20 to 14 januari 21. All patient and RA characteristics (Age, gender, education, smoking habits, disease duration, ACPA, RF, DAS28-CRP, HAQ and therapies) were collected at the same time.

Results: Data from 460 eligible RA patients were analyzed. The average age of the population is 58.21 years. 72% of the patients are women. 21% are smokers and 65% are positive for anti-citrullinated protein antibody (ACPA) with a mean DAS28-CRP of 2.39 and a mean HAQ of 0.821.

281 patients (61%) indicated they would receive the vaccine as soon as it is available. For the 179 patients (39%) who decline, the reasons for not having vaccine were no trust in the vaccine at this time (53%), fear of side effects (28%), opposition to vaccine (4%), previous SARS-CoV-2 infection (2%) and unknown (5%),

Interestingly, there were differences among RA patients not willing to receive the vaccine. Patient under the age of 50, women, low education grade, smokers, presence of RF/ACPA and treatment with a bioDMARD were less willing to receive the vaccine. No differences were observed for RA disease duration, HAQ and DAS28-CRP (see Table 1).

Table 1. Characteristics of RA population and correlation between groups.

	TOTAL n=460	VACCIN-YES n=281 (61%)	VACCIN-NO n=179 (39%)	
Age, mn	58,21 +/-0,71	60,37 ± 0,9004	**54,82 ± 1,090**	p=0.0001*
Group Age <30 yrs	25 (5%)	15 (5%)	10 (6%)	
Group Age =31-50 yrs	112 (24%)	53 (19%)	**59 (33%)**	
Group Age =51-70 yrs	209 (45%)	127 (45%)	82 (46%)	
Group Age > 70 yrs	114 (25%)	**86 (31%)**	28 (16%)	p=0.0003**
Gender, F/M, %-F	332/128 (F-72%)	193/88 (F-69%)	139/40 **(F-78%)**	p=0.043**
Educ0-1	63 (15%)	**27 (11%)**	36 (22%)	
Educ2-3	349 (85%)	222 (89%)	**127 (78%)**	p=0.003**
RA Disease duration yrs, mn	14,77 +/-0,51	15,24 +/-0,69	14,04 +/-0,73	
Smokers: YES/NO/ Ex-Smokers, %-YES	85/248/79 (21%)	42/156/52 (17%)	43/92/27 **(27%)**	p=0.018**
RF YES/NO, %	243/137 (64%)	133/94 (59%)	110/43 **(72%)**	p=0.009**
ACPA YES/NO, %	244/132 (65%)	127/93 (58%)	117/39 **(75%)**	p=0.001**
HAQ, mn	0,814+/-0,039	0,797+/-0,051	0,838+/-0,061	
DAS28-CRP, mn	2,39+/-0,05	2,35+/-0,07	2,44+/-0,09	
GC, YES/NO, %	360/86 (19%)	217/55 (20%)	143/31 (18%)	
csDMARDs (MTX), YES/NO, %	124/322 (72%)	72/200 (74%)	52/122 (70%)	
BioDMARDs, NO/YES, %	151/295 (66%)	107/165 (61%)	44/130 **(75%)**	p=0.003**

(*) - Unpaired t Test; (**) - Fisher's exact test

Conclusion: In our RA cohort, the rates of willingness to receive the vaccine are promising. Dedicated education and outreach efforts should be developed, especially in some RA subpopulation.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1779

POS1197 IN DEPTH IDENTIFICATION OF RISK FACTORS FOR SEVERE COVID-19, REQUIRING HOSPITALIZATION, IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES: RESULTS OF A DUTCH NESTED CASE CONTROL STUDY (PRELIMINARY RESULTS)

M. Opdam[1], S. Benoy[2], L. M. Verhoef[1], S. Van Bijnen[3], F. Lamers-Karnebeek[4], R. A. M. Traksel[2], P. Vos[5], A. Den Broeder[1], J. Broen[2]. [1]*Sint Maartenskliniek, Rheumatology, Ubbergen, Netherlands*; [2]*Regional Rheumatology Center, Máxima Medical Center, Rheumatology, Eindhoven, Netherlands*; [3]*Elisabeth-TweeSteden Hospital, Rheumatology, Tilburg, Netherlands*; [4]*Bernhoven, Rheumatology, Uden, Netherlands*; [5]*Amphia Hospital, Rheumatology, Breda, Netherlands*

Background: Several risk factors for severe COVID-19 have been identified[1]. An important question is whether in addition to these generic risk factors, patients with a potentially altered immune response, either by disease (inflammatory rheumatic diseases (IRDs)) or use of immunomodulatory agents (IA), carry a higher or lower risk of severe COVID-19. In addition, several other potential risk factors for severe COVID-19 have been suggested, such as vitamin D status and specific medication (NSAIDs, ACE-inhibitors)[2].

Objectives: To identify risk factors for severe COVID-19, requiring hospitalization, in patients with IRDs.
Methods: Multicenter, unmatched nested case control study in four rheumatology centers in the Netherlands. Cases are IRD patients requiring hospitalization for COVID-19 between March 1st 2020 and May 31st 2020. Control patients are IRD patients not hospitalized for COVID-19 within this period and were included in a 1:4 ratio. Patient-, disease- and treatment characteristics were extracted (still ongoing) from electronic patient files, and a questionnaire was used to collect additional data (e.g. on behavioral aspects). Potential risk factors for severe COVID-19 were analyzed using unconditional logistic regression, corrected for confounders.
Results: 77 cases and 198 controls were included. 26 case patients died as a result of COVID-19, 14 were admitted to the ICU. Crude ORs for female sex, age, BMI and presence of one or more comorbidities were 0.46 (95% CI 0.27-0.29), 1.1 (95%CI 1.0-1.1), 1.0 (95%CI 0.98-1.1) and 3.0 (95%CI 1.7-5.2) respectively. Table 1 displays corrected OR, highlighted when OR <0.5/>2.0. Corrected ORs were not significantly increased for any IRD, but a trend for gout was present. Use of hydroxychloroquine (HCQ) shows a protective effect, while use of other csDMARDs than methotrexate or HCQ leads to a higher risk of severe COVID-19. Trends were present for increased risk for rituximab (RTX), glucocorticoids and ACE inhibitors, and protective effect for IL-6R blockers.
Conclusion: The outcomes of this study are in agreement with other research regarding risk of severe COVID-19 related to IRDs and use of IA[1]. The suggested increased risk of severe COVID-19 in RTX use is of concern and should be monitored closely. Strengths of this study include low bias due to behavioral effects as only cases early in the pandemic were included, completeness of the determinants of interest and ultimately, it provides answers to a relevant and urgent question.
REFERENCES:
[1] Williamson, Elizabeth J et al. "Factors associated with COVID-19-related death using OpenSAFELY." Nature vol. 584,7821 (2020): 430-436.
[2] Rizk, John G et al. "Pharmaco-Immunomodulatory Therapy in COVID-19." Drugs vol. 80,13 (2020): 1267-1292.
[3] Rentsch, Christopher T et al. "Effect of pre-exposure use of hydroxychloroquine on COVID-19 mortality: a population-based cohort study in patients with rheumatoid arthritis or systemic lupus erythematosus using the OpenSAFELY platform." The Lancet Rheumatology vol. 3,1 (2021): e19-e27.

Table 1. Corrected ORs for several potential risk factors

Potential risk factor	Corrected OR (95% CI)
IRD	
RA*	1.38 (0.68 – 2.8)
Spondylarthritis	0.60 (0.25-1.5)
Gout	**2.8 (0.80-9.8)**
Polymyalgia	0.54 (0.18-1.6)
Systemic diseases	1.6 (0.49-5.0)
DMARDs	
csDMARDs (any)	**0.39 (0.17-0.88)**
Methotrexate	0.90 (0.46-1.7)
HCQ	**0.40 (0.16-0.98)**
Other	**2.0 (0.99-4.1)**
bDMARDs (any)	0.96 (0.43-2.2)
TNF-inhibitors	1.0 (0.43-2.6)
IL6R-blockers	**0.43 (0.044 – 4.2)**
RTX	**4.5 (0.25-79)**
tsDMARDs	0.89 (0.08-9.8)
Other	
Glucocorticoids > 10 mg/day	**2.5 (0.70-9.0)**
NSAIDs	0.82 (0.37-1.8)
ACE-inhibitors	**3.4 (1.6-7.1)**
Vitamin D sufficient	0.77 (0.40-1.5)

*incl. unspecified arthritis

Disclosure of Interests: Merel Opdam Grant/research support from: has received research grants (to the institution) from Gilead, S Benoy: None declared, L.M. Verhoef: None declared, Sandra van Bijnen: None declared, Femke Lamers-Karnebeek: None declared, R.A.M. Traksel: None declared, Petra Vos: None declared, Alfons den Broeder Grant/research support from: has received consultancy honoraria, congress invitations and research grants (to the institution) from Abbvie, Amgen, Cellgene, Roche, Biogen, Lilly, Novartis, Celltrion Sanofi, Gilead. Is coinventor on a rituximab related patent (pending)., Jasper Broen Consultant of: has received consultancy fees from Gilead and Galapagos.
DOI: 10.1136/annrheumdis-2021-eular.1853

POS1198 THE ROLE OF SOCS3 IN COLCHICINE ANTI-INFLAMMATORY EFFECT ON COVID-19 INFECTION

M. Y. Hachim[1], F. Alqutami[1], S. Hannawi[2]. [1]*Mohammed Bin Rashid University Of Medicine and Health Sciences, Basic Sciences, Dubai, United Arab Emirates*; [2]*Ministry of Health And Prevention MOHAP, Rheumatology, Dubai, United Arab Emirates*

Background: In the fight against COVID-19, the use of an old anti-gout agent which is inexpensive and easily administered (1). A meta-analysis suggests a definite benefit with the addition of colchicine in patients with COVID-19(2). It was suggested that colchicine can have efficacy for hospitalized patients with a severe course of COVID-19 and concurrent inflammatory rheumatic diseases who have a higher risk of venous thromboembolism (3). On the other hand, some reports suggested that colchicine is associated with an increased risk of infections (4). Currently, there are nine clinical trials using colchicine for COVID-19(5), nevertheless, the exact mechanism of action is not well understood.
Objectives: Using publicly available transcriptomic data profiling human cells' response to colchicine to identify core differentially expressed genes (DEGs) then examine the dynamics of the identified DEGs in different datasets of COVID-19 transcriptomics databases to suggest the possible mechanisms of action on the molecular level.
Methods: Gene Expression Omnibus was searched for human samples treated with colchicine compared to controls. GSE4090 dataset was identified where global gene expression of HUVEC (human umbilical vein endothelial cell line) cells exposed to various concentrations of colchicine (n=9) compared to controls (n=7). We reanalyzed this datset using GEO2R online tool to identify DEGs. The identified DEGs were searched in SARS-CoV-2 transcriptome datasets using metascape online tool to identify gene sets were the DEGs identified showed significant similarity.
Results: Fifty DEGs were identified in response to colchicine no matter what the concentration is used, (Figure 1A). Two gene sets (COVID323, RNA_Wilk_CD4+T-cells_patient-C2_Up [peripheral immune cells] and COVID008, RNA_Blanco-Melo_A549_Up[lung epithelial cells]) showed significant enrichment of the identified DEGs, (Figure 1B). SOCS3, ZC3H12C, CD55, GLIPR1, BACH1, PHLDA1, JUNB, NFKBIZ, and MYLIP were the shared genes between the identified DEGs, and the two gene sets with top enriched terms related to important immune-related pathways like IL-6, chemotaxis, leukocytes migration, cytokine release, and response to glucocorticoid, (Figure 1C). Only Suppressor of cytokine signaling 3 (SOCS3) was shared in the three datasets. SOCS3 expression was significantly downregulated in the HUVEC cells exposed to colchicine, (Figure 1D). Next, the normalized gene expression of SOCS3 from whole blood of 62 COVID-19 patients was compared to that of 24 healthy controls using (GSE15264) showed significant upregulation of SOCS3 in the blood of CVOID-19 patients indicating its role in COVID-19, (Figure 1E).

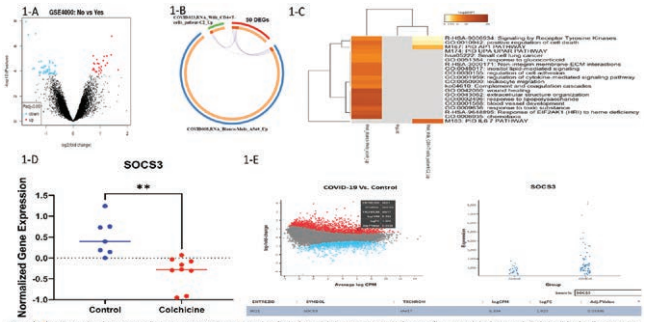


Figure (1-A): Volcano plot showing DEGs between GSE4090 dataset was identified where global gene expression of HUVEC (human umbilical vein endothelial cell line) cells exposed to various concentrations of colchicine (n=9) compared to controls (n=7). Figure (1-B):Overlap between gene lists: (a) only at the gene level, where purple curves link identical genes. The inner-circle represents gene lists, where hits are arranged along the arc. Genes that hit multiple lists are colored in dark orange, and genes unique to a list are shown in light orange. Figure (1-C): Heatmap of enriched terms across input gene lists, colored by p-values. Figure (1-D): The normalized gene expression of SOCS3 in HUVEC (human umbilical vein endothelial cell line) cells exposed to various concentrations of colchicine (n=9) compared to controls (n=7). Figure (1-E): The normalized gene expression of SOCS3 from whole blood of 62 COVID-19 patients was compared to that of 24 healthy controls using (GSE15264).

Conclusion: Our reanalysis showed that the possible beneficial effect of colchicine in COVID-19 patients might be through its direct effect on SOCS3 which is specifically upregulated in COVID-19 by IL6 and interferon (IFN)-gamma.
REFERENCES:
[1] Reyes AZ, Hu KA, Teperman J, Wampler Muskardin TL, Tardif J-C, Shah B, et al. Anti-inflammatory therapy for COVID-19 infection: the case for colchicine. Annals of the Rheumatic Diseases. 2020:annrheumdis-2020-219174.
[2] Vrachatis DA, Giannopoulos GV, Giotaki SG, Raisakis K, Kossyvakis C, Iliodromitis KE, et al. Impact of colchicine on mortality in patients with COVID-19. A meta-analysis. Hellenic Journal of Cardiology. 2021.
[3] Kow CS, Hasan SS. Colchicine as an adjunct to heparin for prophylaxis of venous thromboembolism in patients with COVID-19. Rheumatol Int. 2021:1-2.
[4] McEwan T, Robinson PC. A systematic review of the infectious complications of colchicine and the use of colchicine to treat infections. Semin Arthritis Rheum. 2020;51(1):101-12.
[5] Montealegre-Gómez G, Garavito E, Gómez-López A, Rojas-Villarraga A, Parra-Medina R. Colchicine: A potential therapeutic tool against COVID-19. Experience of 5 patients. Reumatología Clínica. 2020.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1859

POS1199 CLINICAL MANIFESTATIONS OF SARS-CoV2 INFECTIONS IN CHILDREN AND ADOLESCENTS WITH RHEUMATIC AND MUSCULUSKELETAL DISEASES – SURVEY DATA FROM GERMANY

C. Sengler[1], S. Eulert[2], M. Niewerth[2], T. Kallinich[3], H. Wittkowski[4], H. Girschick[5], J. P. Haas[6], G. Horneff[7], T. Hospach[8], J. Armann[9], J. B. Kuemmerle-Deschner[10], J. Brunner[11], M. Borte[12], R. Hühn[13], K. Minden[2], A. Klein[7]. *[1]Gernan Rheumatism Research Center Berlin, Epidemiology Unit, Berlin, Germany*; *[2]German Rheumatism Research Center Berlin, Epidemiology Unit, Berlin, Germany*; *[3]Charité – Universitätsmedizin Berlin, Department of Pediatrics, Berlin, Germany*; *[4]Universitätsklinikum Münster - UKM, Klinik für Kinder- und Jugendmedizin, Münster, Germany*; *[5]Krankenhaus im Friedrichshain, Klinik für Kinder- und Jugendmedizin, Berlin, Germany*; *[6]Deutsches Zentrum für Kinder- und Jugendrheumatologie, Kinder- und Jugendrheumatologie, Garmisch-Partenkirchen, Germany*; *[7]Allgemeine Kinder- und Jugendmedizin - Asklepios Klinik Sankt Augustin, Kinderrheumatologie, Sankt Augustin, Germany*; *[8]Olgahospital and Women's Clinic, Pädiatrie 2 - Allgemeine und spezielle Pädiatrie, Stuttgart, Germany*; *[9]University Hospital Carl Gustav Carus Dresden, Kinik und Poliklinik für Kinder- und Jugendmedizin, Dresden, Germany*; *[10]Tübingen University Hospital, Department of Pediatrics, Tübingen, Germany*; *[11]Tirol Kliniken GmbH, Department für Kinder- und Jugendheilkunde, Innsbruck, Austria*; *[12]Klinikum St. Georg, Leipzig, Klinik für Kinder- und Jugendmedizin, Leipzig, Germany*; *[13]Universitätsklinikum Halle (Saale), Klinik für Kinder- und Jugendmedizin, Halle (Saale), Germany*

Background: Although children and adolescents are less likely to develop COVID-19 and generally show milder disease courses, it is unclear what impact the SARS-CoV2 infection has on children and adolescents with rheumatic and musculoskeletal disease (RMD). Due to their underlying disease as well as therapeutic immunosuppression these patients may be at higher risk of being more severely affected by SARS-CoV2. Furthermore, SARS-CoV2 infection might trigger a flare of the underlying disease.

Objectives: To evaluate clinical characteristics and disease course of COVID-19 in children and adolescents with RMD and to analyze possible effects of SARS-CoV2 infection on the underlying disease under different therapeutic regimens.

Methods: Data from juvenile patients with RMD recorded via the SARS-CoV2 questionnaire within the National Pediatric Rheumatology Database and the registry for hospitalized children and adolescents with COVID-19 of the German Society for Pediatric Infectious Diseases were analyzed. In addition to age, sex and diagnosis, information was collected about the date and method of a positive SARS-CoV2 testing, reason for testing, on clinical manifestations, disease course, treatment and outcome of COVID-19, on drug therapy at the time of virus detection, on disease activity (NRS 0 – 10, 0 = best) of the underlying disease at the last visit before and after the SARS-CoV2 infection.

Results: From April 17th 2020 until January 25th 2021, data of 67 patients with RMD and confirmed SARS-CoV2 infection were collected. Mean age was 13.5 ± 3.9 years with equal sex distribution. The majority of patients were diagnosed with juvenile idiopathic arthritis (JIA, 64%), 12 (18%) patients had an autoinflammatory disease (FMF, CAPS, PFAPA, TRAPS) and 5 (7%) a connective tissue disease. Fifty-two patients (78%) were treated with a disease modifying antirheumatic drug (DMARD), 39% with a biological DMARD and 9% systemic glucocorticoids at the time of SARS-CoV-2 infection. Nineteen patients (28%) were tested for SARS-CoV-2 because of typical symptoms, the majority (67%) because of contact to an infected person. PCR was used most often (in 60 %).

52 patients (78%) developed symptoms of COVID-19, 15 patients remained asymptomatic. The most common symptom of COVID-19 was rhinitis (42%) and fever (38%), followed by fatigue (34%), taste/smell disorder (33%), sore throat (27%) and cough (23%).

Disease severity was graded as mild in 44 of 52 (85%) symptomatic patients, only two patients were hospitalized, one of whom required intensive care and died of cardiorespiratory failure 3 days after symptom onset. In 22 of 26 (85%) SARS-CoV2-positive patients, no relevant increase in disease activity (difference in NRS ≤ 1 before/after infection) of the underlying disease was observed 31 days after symptom onset (median, IQR 17-52 days). One patient, who had paused tocilizumab for 2 doses, experienced a flare of his seronegative polyarthritis 2 months after asymptomatic SARS-CoV-2 infection.

Conclusion: In our cohort, the clinical picture of COVID-19 in children and adolescents with RMD was similar to that of healthy peers. The majority of patients showed mild disease course with good outcome under various medications, however, one patient with a severe course of COVID-19 died. In addition, SARS-CoV2 infection does not appear to have a relevant impact on the underlying disease activity, whereas discontinuation of therapy might pose a risk of flare.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1875

POS1200 IL-6 HIGHER LEVEL AFTER TOCILIZUMAB TREATMENT AS A PREDICTOR OF NOT-SURVIVAL IN COVID19 SEVERE PNEUMONIA: THE EXPERIENCE OF THE COVIBAS-STUDY

M. Gilio[1], S. B. Morella[1], M. A. Purgatorio[2], D. Palazzo[1], M. Frontuto[1], A. Erezanu[1], G. Mastroberti[1], A. Linzalone[3], G. Pietromatera[3], A. Fineo[3], M. Onofrio[3], G. Casciano[3], G. De Stefano[2]. *[1]San Carlo Hospital, Infectious Disease, Potenza, Italy*; *[2]San Carlo Hospital and Madonna delle Grazie Hospital, Infectious Disease, Matera, Italy*; *[3] Madonna delle Grazie Hospital, Infectious Disease, Matera, Italy*

Background: Cytokine release storm is the most fearsome complication associated with worse outcomes in COVID-19 patients with severe acute respiratory failure. In COVID-19 patients, interleukin-6 (IL-6) levels are significantly elevated. Blocking IL-6 preliminarily resulted in the improvement of this hyperinflammatory state.

Objectives: To define if the serum level of IL-6 early tested after tocilizumab treatment could be useful to distinguish non-survivors from survivors in patients with severe respiratory failure due to COVID-19 pneumonia.

Methods: This prospective cohort study was conducted at two referral hospitals for management of COVID-19 in Basilicata region, Italy: San Carlo Hospital, Potenza and Madonna delle Grazie Hospital, Matera. All consecutive patients with COVID-19 confirmed by RT-PCR testing of a naso-oropharyngeal swab. The enrollement period was from the 23rd of February to the 15th of August. 37 patients between all 124 underwent tocilizumab 8 mg/kg intravenously at baseline and after 24h. All patients were tested for serum IL-6, 24 hours before and 72 hours after tocilizumab infusion. Comparisons between survivors (Sv) and nonsurvivors (NSv) were performed.

Results: 21 patients were discharged, while 16 patients died. The main clinical or laboratory differences ($p < 0.001$) between the two groups at baseline were mean diseases duration before ward admission and serum troponine levels. IL-6 was not different at baseline ($p = 0.01$), while 72 hours post-tocilizumab IL-6 serum levels were significantly higher in non-survivors than in survivors [(Sv 21.1%)vs(NSv 64%) $p < 0.001$)]. Serum IL-6 post-tocilizumab could be considered a good predictor to discriminate Sv from NSv. At multivariate stepwise analysis including disease duration at admission, baseline serum troponine levels and IL-6 post TCZ) were independent predictors of not survival

Conclusion: Our data confirm the results of Quartuccio et al. In fact the highest burden of inflammation may be revealed by IL-6 levels after tocilizumab. Therefore repeated measurement of the serum level of IL-6 early after tocilizumab could be useful to distinguish non-survivors from survivors and support the choice of deeper targeting IL-6 in COVID-19 pneumonia.

REFERENCES:

[1] Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020; 395(10229): 1033- 1034.

[2] Toniati P, Piva S, Cattalini M, et al. Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: a single center study of 100 patients in Brescia, Italy. Autoimmun Rev. 2020; 19:102568

[3] McGonagle D, Sharif K, O'Regan A, Bridgewood C. The role of cytokines including interleukin 6 in COVID19 induced pneumonia and macrophage activation syndrome-like disease. Autoimmun Rev. 2020; 19(6):102537.

[4] Chakraborty C, Sharma AR, Bhattacharya M, Sharma G, Lee SS, Agoramoorthy G. COVID19: consider IL6 receptor antagonist for the therapy of cytokine storm syndrome in SARS CoV2 infected patients. J Med Virol 2020

[5] Quartuccio L, Sonaglia A, Pecori D,et al. Higher levels of IL-6 early after tocilizumab distinguish survivors from nonsurvivors in COVID-19 pneumonia: A possible indication for deeper targeting of IL-6. J Med Virol.2020;92:2852–2856

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1902

POS1201

INCIDENCE AND OUTCOME OF COVID-19 IN ANCA-ASSOCIATED VASCULITIS: IMPACT OF COVID-19 IN PATIENTS UNDERGOING RITUXIMAB FOR MAINTENANCE

E. Treppo[1], M. Binutti[1], G. Del Frate[1], S. De Vita[1], L. Quartuccio[1]. [1]*University of Udine, Rheumatology Clinic, Udine, Italy*

Background: COVID-19 is an emerging infectious disease caused by SARS-CoV-2. Risk factors for the worst outcome in COVID-19 are pre-existing pulmonary and cardiovascular disease, while the impact of chronic immunosuppression has not yet completely been clarified (1).
Currently, there is no clinical evidence that chronically immunosuppressed rheumatic patients under biologic agent or a small molecule may have a higher risk of COVID-19 or a worse prognosis(2). However, the anti-CD20 antibody monoclonal rituximab may contribute to severe consequences, inhibiting the humoral response to SARS-CoV-2 and capacity to produce efficient antibodies against it (3,4). Rituximab is widely use in the treatment of ANCA-associated vasculitis (AAV). Nowadays, the incidence and impact of COVID-19 in AAV-patients are still unknown and, in particular, in AAV-patients who have been exposed to rituximab since the outbreak (5).
Objectives: Herein we evaluate the incidence and outcome of SARS-CoV-2 infection in our cohort of AAV-patients who had at least one visit in the year 2020.
Methods: We collected clinical data of 100 AAV-patients who had at least one visit in our Centre from February 2020 to December 2020, and we described cases of COVID-19 infection among them. The COVID-19 was proved by detection of SARS-CoV-2 RNA in nose-pharyngeal swabs. In case of infection, anti-SARS-CoV-2 IgM or IgG production was then investigated.
Results: Among 100 patients (53 females; 47 males) regularly followed, the median age was 65, and the mean (SD) duration of disease was 8.8 (6.8) years. The most frequent diagnosis was granulomatosis with polyangiitis (GPA) (56%), followed by granulomatosis eosinophilic with polyangiitis (EGPA) (31%), and microscopic polyangiitis (MPA) (13%). The mean (SD) BVASv3 at the onset of disease was 12.6 (5.6). More than half of the patients (59%) have had lung and/or ENT involvement at the onset of disease. Overall, 84% of our patients received immunosuppressive agents and 45% also received glucocorticoids (GC). Rituximab was administered in 15% of patients during the pandemic. COVID-19 was diagnosed in 2 cases (2%). Both patients have received rituximab as maintenance: the last rituximab infusion was on November 9, 2020 for patient 1 (female, 73 years old, GPA ANCA-PR3+) and was on August 17, 2020 for patient 2 (female, 74 years old, MPA ANCA-MPO+). Both patients had a BVAS 0 and negative ANCA antibodies at the time of the first positive nose-pharyngeal swab RT-PCR test, on December 24 and on November 25, respectively. Both patients were B-cell depleted and IgG levels were 455 mg/dL and 866 mg/dL, respectively. While patient 1 died due to critically ill COVID-19 pneumonia 25 days after the COVID-19 disease onset, patient 2 remained asymptomatic with nose-pharyngeal swab still positive on day 56 after the first detection. Anti-SARS-CoV-2 IgM or IgG antibodies above the cut-off (cut-off value 10 AU/mL) were absent in patient 1, while in patient 2 a low level of anti-SARS-CoV-2 IgG (39 AU/mL, cut-off value 10 AU/mL) was documented.
Conclusion: Prevalence of COVID-19 in AAV seems lower than in general population (prevalence of 29582/466700, 6.3%, in the same geographical area). Rituximab compromises the B-cells function and can lead to humoral immunodeficiency, causing the inability to produce anti-SARS-CoV-2 IgG antibodies. The timing of the last rituximab infusion and the levels of IgG can greatly affect the outcome. Patients who underwent anti-CD20 therapy are at higher risk of severe outcome in case of infection (3), and require prioritization for SARS-CoV-2 vaccination.
REFERENCES:
[1] Guilpain P, et al. Ann Rheum Dis. 2021;80(1):e10.
[2] Quartuccio L, et al. Joint Bone Spine. 2020;87(5):439–43.
[3] Benucci M, et al. Ann Rheum Dis. 2020; Aug 4:annrheumdis-2020-218590.
[4] Tepasse P-R, et al. Br J Haematol. 2020;190(2):185–8.
[5] Kant S, et al. J Nephrol. 2020; J Nephrol. 2020 Oct 8:1-6.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2015

POS1202

EXPERIENCE WITH COVID-19 IN GERMAN PAEDIATRIC RHEUMATOLOGY CENTRES

A. Klein[1], D. Windschall[2], W. Emminger[3], R. Berendes[4], J. Kuemmerle-Deschner[5], R. Trauzeddel[6], C. Rietschel[7], A. Kühn[8], M. Hufnagel[9], M. Sailer-Hoeck[10], T. Hospach[11], M. Haller[12], S. Mrusek[13], C. Sengler[14], K. Minden[14], G. Horneff[1]. [1]*Asklepios Klinik Sankt Augustin, Pediatric Rheumatology, Sankt Augustin, Germany*; [2]*St.Josef-Stift, Pediatric Rheumatology, Sendemhorst, Germany*; [3]*Universitätsklinik, Pediatrics, Wien, Austria*; [4]*Kinderkrankenhaus St. Marien, Pediatric Rheumatology, Landshut, Germany*; [5]*Universitätskinderklinik, Pediatric Rheumatology, Tübingen, Germany*; [6]*Helios Klinikum Berlin Buch, Pediatric Rheumatology, Berlin, Germany*; [7]*Clementine Kinderhospital, Pediatric Rheumatology, Frankfurt, Germany*; [8]*Universitätsklinik, Pediatrics, Halle, Germany*; [9]*Universitätsklinikum, Pediatric Infectiology and Rheumatology, Freiburg, Germany*; [10]*Universitätsklinik, Pediatrics, Innsbruck, Austria*; [11]*Olgahospital, Pediatric Rheumatology, Stuttgart, Germany*; [12]*practice, Pediatrics, Gundelfingen, Germany*; [13]*Practice, Pediatrics, Baden-Baden, Germany*; [14]*Gernan Rheumatism Research Center Berlin, Epidemiology Unit, Berlin, Germany*

Background: COVID-19 is a major challenge worldwide. Although the risk for a severe disease course is low among children with COVID-19, symptoms may be exacerbated by underlying disease and/or immunosuppressive medication. We analysed clinical data from COVID-19 cases in among pediatric patients with juvenile idiopathic arthritis (JIA) in Germany reported to the BIKER registry.
Objectives: This is an analysis of clinical data for 56 COVID-19 cases reported to the German BIKER registry from 29 German pediatric rheumatology centers and clinics from February 2020 to January 2021.
Methods: The major task of the German BIKER (Biologics in Paediatric Rheumatology) Registry is surveillance of biologics used in pediatric rheumatology patients. Following the start of the COVID-19 pandemic in Germany, a survey was established to proactively interview all participating centers regarding the occurrence, presentation and outcome of SARS-CoV-2-infected children with rheumatic diseases. Initially, the interviews were conducted in weekly intervals, later bi-weekly.
A standardized Adverse Event of Special Interest form was developed requesting biographic data, pre-treatment, current medication, data on clinical presentation, course, treatment and outcome of COVID-19 pediatric rheumatology patients.
Results: In all, 56 patients with JIA and SARS-CoV-2 infection were reported (Table 1). Of these patients, 71% were 12 or more years old.

Table 1. Patient characteristics. COVID-19 positive patients.

	JIA patients, n=56 n (%)
Age	
0-5 years / 6-11years / 12-18years	3 (5.4) / 13 (23.2) / 40 (71.4)
JIA category	
• Systemic JIA	5 (8.9)
• Oligoarthritis JIA	9 (16)
• Polyarticular JIA	32 (57)
• Enthesitis-related JIA	2 (3.6)
• Psoriatic JIA	1 (1.8)
• Unknown	7 (12.5)
Uveitis (concomitant)	4 (7.1)
Treatment	
• DMARD / MTX	23/ 22 (41/39)
• Biologics	29 (52)
• TNF inhibitors	20 (36)
• Tocilizumab	5 (8.9)
• Abatacept	1 (1.8)
• Anakinra	1 (1.8)
• Ustekinumab	1 (1.8)
• JAK inhibitors	1 (1.8)
• Steroids	5 (8.9)
Asymptomatic	13 (23.2)
Hospitalized/ICU/Ventilation/Death	1/1/1/1 (1.8)

At the time of infection, 41% of the patients received conventional DMARDs and 52% received biologics (Table 1). Forty-four patients (79%) received either a conventional DMARD or a biologic. Most patients had a polyarticular course of their JIA (57%).
In 49 of the 56 cases (88%) COVID-19 was detected directly by PCR (n=46), by antigen test only (n=1) or an undisclosed method (n= 2). Six patients had detectable SARS-CoV2 antibodies and reported to have had typical symptoms. One patient tested negative but developed typical symptoms at approximately the same time a positive SARS-CoV-2 test was returned for a family member.
Symptoms were reported in 43 of the 56 patients (77%): fever n=15, rhinitis n=14, cough n=12, headache n=10, loss of sense of taste and/or smell n=9, pharyngitis n=8, fatigue n=5, musculoskeletal pain n=5, GI symptoms n=2 (abdominal pain n=1, diarrhoea n=1), dizziness n=3, encephalitis/seizure/respiratory failure/death n=1. Thirteen patients (23%) were asymptomatic.
A 3½ -year-old female patient initially diagnosed with systemic JIA developed intracranial oedema and respiratory failure. Her SARS-CoV2 PCR test was positive and pulmonary imaging displayed typical changes in lung texture. Before her SARS-CoV-2 infection, the patient was treated with methotrexate and low-dose steroids. Unfortunately, she died three days following hospital admission. Genetic testing revealed an inborn immunodeficiency. Except for this one patient, all other cases were treated as outpatients and no deaths were reported.
Conclusion: Apart from one patient with an inborn immunodeficiency who died from her COVID-19 infection, no case of hospitalization or severe COVID-19 was

reported in our cohort of JIA patients. At the time of COVID-19 diagnosis, nearly 80% of patients in our cohort had been treated with conventional DMARD and/or biologics. This seemed not to have a negative effect on severity or outcome of SARS-CoV2 infection.

Acknowledgements: Thanks also for contributing Reports for this analysis to: Normi Brück, Frank Dressler, Ivan Foeldvari, Tilman Geikowski, Hermann Girschick, Johannes-Peter Haas, Tilmann Kallinich, Bernd-Ulrich Keck, Eggert Lilienthal, Anna-Hedrich Müller, Ulrich Neudorf, Nils Onken, Peggy Rühmer.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2045

POS1203 EFFECT OF THE COVID19 PANDEMIC ON RHEUMATOLOGIST PRESCRIPTION BEHAVIOUR OF NEW ADVANCED THERAPY: DATA OF THE TARDIS-RA REGISTRY, A NATIONWIDE BELGIAN BIOLOGIC REGISTRY

D. De Cock[1], P. Durez[2], V. Badot[3], R. Westhovens[1,4], P. Verschueren[1,4]. [1]*KU Leuven, Skeletal Biology and Engineering Research Centre, Leuven, Belgium*; [2]*Cliniques universitaires Saint-Luc, Rheumatology, Brussels, Belgium*; [3]*CHU-UVC Brugmann, Division of Rheumatology, Brussels, Belgium*; [4]*University Hospitals Leuven, Rheumatology, Leuven, Belgium*

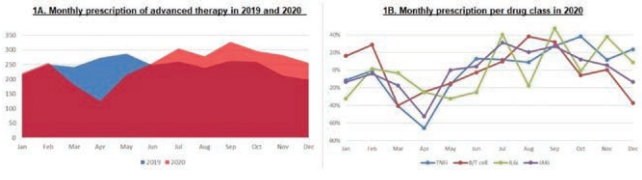
Background: Belgium suffered considerably from the COVID19 pandemic with high hospitalisation rates during 2 periods: a first wave in March and April 2020, and a second starting from October until the end of 2020. Measures of lowering social interaction were taken throughout 2020 and intensified during the first and second wave when needed. This pandemic could have influenced the access to care and advanced therapies for patients with Rheumatoid Arthritis (RA). In the electronic platform "Tool for Administrative Reimbursement Drug Information Sharing" (TARDIS), data from all Belgian RA patients on biologic and targeted therapy are collected during the submission of a request for initiation and prolongation of reimbursement for these drugs.

Objectives: to investigate the effect of the COVID19 pandemic on the monthly prescription behaviour of a new advanced therapy in 2020 by comparing it to 2019.

Methods: Patients were selected for this analysis if they started a new TNFi, B/T cell therapy, IL6 inhibitors or tsDMARD therapy in the TARDIS registry in 2019 or in 2020. Rheumatologists request reimbursement via the online TARDIS tool, which is considered here as a new drug prescription. Prescription behaviour was compared between 2019 and 2020, between bionaive and bioexperienced patients, and between the different drug classes

Results: In 2019, 2949 patients were prescribed any new advanced therapy, including 1153 TNFi, 469 B/T cell therapy, 436 IL6 inhibitors and 891 tsDMARDs. In 2020, 2998 patients were prescribed any new advanced therapy including 1233 TNFi, 382 B/T cell therapy, 496 IL6 inhibitors and 887 tsDMARDs.

On a monthly basis, on average 246 and 250 new advanced therapies were prescribed in 2019 and 2020 respectively. Monthly deviations from this average in 2019 ranged from -19% to +16%. Monthly deviations from this average in 2020 ranged from -50% to +30%. Figure 1A shows the monthly prescription of new advanced therapies in 2019 and 2020.



For bionaive and bioexperienced patients, the same trend can be noted. Monthly deviations in bionaive patients in 2020 ranged from -60% to +38%, compared to -18% to +21% in 2019. Monthly deviations in bioexperienced patients ranged from -40% to +25%, compared to -19% to +17% in 2019.

Comparison per drug class in 2020 show similar trends. IL6 inhibitors show a slightly different timeline than other drugs classes with other periods of less or more prescriptions changes compared to the other drugs classes. See Figure 1B.

Conclusion: The COVID19 pandemic did affect reimbursement requests for patients starting new advanced therapies in March and April 2020, especially for bionaive patients. The latter half of 2020 was apparently used to catch up with reimbursement requests for patients in need for advanced therapies resulting in similar total numbers of patients treated with advanced therapy in 2019 and 2020. The choice for a particular drug type was not clearly influenced by the pandemic. IL6 inhibitor use did seem to be affected differently by the pandemic, yet caution is warranted as these relatively large differences in proportional changes parallel small differences in actual drug numbers.

In sum, the observed effect of the pandemic on initiating advanced therapy during the first wave corresponds with Belgian governmental measures that restricted non-essential care which was less observed in the latter half of 2020.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2049

POS1204 LOW POSITIVITY RATE IN ANTIBODY SARS-COV2 TESTS IN PATIENTS WITH RHEUMATIC DISEASES TREATED WITH RITUXIMAB. A CASE CONTROL STUDY OF A HIGH IMPACT SARS-COV2 INFECTION AREA.

A. García Fernández[1], P. Morán Álvarez[1], J. Bachiller-Corral[1], M. Vázquez Díaz[1]. [1]*Hospital Universitario Ramón y Cajal, Rheumatology, Madrid, Spain*

Background: Diagnosis of previous SARS-COV2 infection may be challenging in immunocompromised patients.

Objectives: To analyze positivity rate to SARS-COV2 antibody tests (SC2AT) in patients diagnosed of rheumatic diseases (RMD) treated with Rituximab.

Methods: We conducted a case-control study of patients diagnosed of RMD followed in a referral hospital in Madrid, Spain. Positivity rate to IgG-SC2AT were analyzed in Rituximab-treated patients (RTX) compared with patients treated with TNF inhibitors (TNFi) and/or conventional DMARDs (cDMARDs) (N-RTX).

We included patients that received Rituximab in the previous year to a confirmed SARS-COV2 infection (defined as a positive polymerase chain reaction test (PCR) and/or compatible chest Xray), to a suspected SARS-COV2 infection (2 or more symptoms) or to SC2AT determination. Patients with RMD treated with other biological DMARDs (bDMARDs) rather than Rituximab or TNFi were excluded.

Results: We included 152 patients with RMD who underwent a SC2AT. Main characteristics are reported in Table 1.

Table 1. Main characteristics. AS, axial spondylitis; bDMARDs, biological disease-modifying anti-rheumatic drugs; cDMARDs, conventional DMARDs; COPD, Chronic obstructive pulmonary disease; CVD, Cardiovascular disease; IMM, immune-mediated myositis; JIA, Juvenile Idiopathic arthritis; PsoA, Psoriatic Arthritis; RA, Rheumatoid Arthrtis; SLE, Systemic Lupus Erythematosus; SSc, Systemic Sclerosis; SSj, Sjogren Syndrome.

	Rituximab (RTX)	Non-Rituximab (N-RTX)	p value
Patients, n (%)	48 (31.6)	104 (68.4)	
Age, years, median (IQR)	65 (54-72)	60 (47-71.8)	p= 0.190
Female, n (%)	38 (79.2)	74 (71.2)	p=0.297
Diagnosis, n (%)			p=0.2
- RA	20 (41.7)	42 (40.4)	
- SSj	4 (8.3)	6 (5.8)	
- RA SSj	3 (6.3)	0 (0)	
- SLE	4 (8.3)	8 (7.7)	
- Vasculitis	7 (14.6)	13 (12.5)	
- IMM	1 (2.1)	4 (3.8)	
- JIA	2 (4.2)	3 (2.9)	
- SSc	7 (14.6)	15 (14.4)	
- AS	0 (0)	4 (3.8)	
- PSoA	0 (0)	5 (4.8)	
- Others[a]	0 (0)	4 (3.8)	
Comorbidities, n (%)			
- Hypertension	18 (37.5)	34 (32.7)	p=0.561
- Diabetes	5 (10.4)	10 (9.6)	p=0.878
- Dyslipidemia	18 (37.5)	30 (28.8)	p=0.286
- COPD/asthma	6 (12.5)	4 (3.8)	p=0.049*
- CVD	11 (35.4)	25 (24)	p=0.831
Interstitial lung disease, n (%)	17 (35.4)	8 (7.7)	p<0.0001*
Corticosteroids use, n (%)	26 (54.2)	33 (31.7)	p=0.008*
cDMARDs use, n (%)	27 (56.3)	73 (70.2)	p=0.092
bDMARDs, n (%)			-
- None	0 (0)	83 (79.8)	
- TNF inhibitors	0 (0)	21 (20.2)	
- Rituximab	48 (100)	0 (0)	
Previous positive PCR, n (%)	8 (16.7)	20 (19.2)	p=0.191
- Time from positive PCR to SC2AT, days, mean ±SD	47.4 (38.7)	65.1 (49)	p=0.368
Previous symptoms, n (%)			
- Time from symptom onset to SC2AT, days, mean ±SD	13 (27.1) 130.3 ±91.1	36 (34.6) 93.5 ±72.6	p=0.356 p=0.15
COVID, n (%)			p=0.183
- Non suspected	35 (72.9)	66 (63.5)	
- Suspected	3 (6.3)	18 (17.3)	
- Confirmed	10 (20.8)[b]	20 (19.2)	

[a]Including gout, polymyalgia rheumatica.[b]Two patients had negative PCR but compatible symptoms and chest X-Ray.

Among RTX and N-RTX, 4/48 (8.3%) and 35/104 (33.7%) showed a positive IgG-SC2AT, respectively. Four out of 104 (38.5%) N-RTX tested positive without previous symptoms. No asymptomatic infection was diagnosed among RTX.
Univariable analysis showed a lower rate of positivity to SC2AT in confirmed and suspected infection among RTX [Positive IgG-SC2AT in confirmed infection: RTX 4/10 (40%), N-RTX 16/20 (80%); p=0.045. Positive IgG-SC2AT in suspected infection: RTX 0/3 (0%), N-RTX 15/18 (83.3%); p=0.015].
A logistic binary regression identified previous symptoms [OR 61.2, 95CI(13.3-280.6) p=0.0001], male sex [OR 4.8, 95CI(1.3-17.8) p=0.02], non-rituximab treatment [OR 19.7, 95CI(3.6-106.3) p=0.001] as independent factors associated with a higher probability of positive IgG-SC2AT. Age, previous PCR status, corticosteroid and cDMARD use showed no statistical significance. This model accounted for 47.6% of positive cases.
Conclusion: RTX had a lower rate of positivity to IgG-SC2AT compared to N-RTX. Previous symptoms, male sex and non-RTX treatment were independently associated with higher probability of positive IgG-SC2AT.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2082

POS1205 THE IMPACT OF COVID-19 ON PATIENT MANAGEMENT AND PRESCRIBING STRATEGY ACROSS THE EU AND US: A REAL-WORLD SURVEY OF RHEUMATOLOGISTS, DERMATOLOGISTS, AND GASTROENTEROLOGISTS

E. Holdsworth[1], R. Lukanova[1], M. Hughes[1], J. Hall[1], J. Austin[1], G. Taylor-Stokes[1], J. Piercy[1]. [1]*Adelphi Real World, Real World Evidence, Bollington, United Kingdom*

Background: The COVID-19 pandemic is expected to have impacted patient management on a global level. However, the degree of impact on patient management and prescribing strategy in the fields of rheumatology, dermatology and gastroenterology is unclear.
Objectives: Assess the impact of COVID-19 on patient management and prescribing strategy across the EU and US, as described by rheumatologists, dermatologists, and gastroenterologists.
Methods: Data were drawn from physician surveys in France, Germany, Italy, Spain, UK and US between July and December 2020. Physicians completed an online or telephone survey assessing how COVID-19 has impacted type and frequency of consultations; choice and prescription of medication.
Results: 847 physicians took part; 355 rheumatologists, 200 dermatologists (Germany, Spain, UK, and US only), and 282 gastroenterologists. As a result of COVID-19, most physicians stated they have moved at least some patients to video or telephone consultations (70% rheumatologists; 55% dermatologists; 60% gastroenterologists) and reduced overall frequency of consultations with patients (59% rheumatologists; 64% dermatologists; 51% gastroenterologists) (Table 1).
35% of rheumatologists, 22% of dermatologists, and 14% of gastroenterologists described COVID-19 as changing the way they choose and prescribe medication, with differences observed between countries (Figure 1). Of those who stated they have made medication changes, rheumatologists stated changing medication to self-administration (62%) and not starting new patients on an advanced therapy (biologic DMARD or targeted synthetic DMARD) (58%) as most frequent. Dermatologists stated changes include changing treatment to more COVID-appropriate treatment (71%) and prescribing repeat prescriptions more regularly without consultation (56%). Gastroenterologists stated changes include changing medication to self-administration (55%) and prescribing a longer course of medication (48%).
Comparing across countries, for all specialties, the greatest changes were observed in the UK followed by Spain, with least changes in Germany and Italy.
Conclusion: There have been changes in the process of how healthcare is delivered, although treatment prescription was impacted to a lesser extent than consultation type and frequency. This varies across geographies, which may be due to differences in reported prevalence of COVID-19. Differences are also observed across specialities, which may be due to guidance received from specialty bodies. It is unknown what the long-term impact of changes in the management of patients due to COVID-19 will be on patient outcomes, satisfaction, engagement and adherence, and further research is needed.

Table 1. Rheumatologist, Dermatologist, and Gastroenterologist described impact on patient management, by country

	Global	France	Germany	Italy	Spain	UK	US
	(n=847)	(n=90)	(n=168)	(n=122)	(n=161)	(n=133)	(n=163)
Rheumatologists	n=365	n=50	n=58	n=59	n=57	n=50	n=81
Moving to video/telephone consultation	70%	70%	36%	47%	86%	94%	84%
Fewer visits for individual patients (reduced visiting schedule)	59%	80%	0%	41%	96%	76%	65%
Dermatologists	**n=200**	**-**	**n=50**	**-**	**n=50**	**n=50**	**n=50**
Moving to video/telephone consultation	55%	-	40%	-	58%	66%	56%
Fewer visits for individual patients (reduced visiting schedule)	64%	-	60%	-	54%	72%	72%
Gastroenterologists	**n=282**	**n=40**	**n=60**	**n=63**	**n=54**	**n=33**	**n=32**
Moving to video/telephone consultation	60%	63%	18%	54%	83%	100%	69%
Fewer visits for individual patients (reduced visiting schedule)	51%	35%	43%	51%	43%	79%	69%

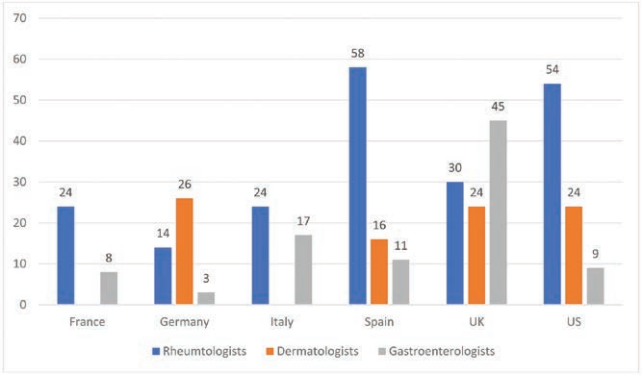


Figure 1. Proportion of rheumatologists, dermatologists, and gastroenterologists reporting changing the way they choose and prescribe medication as a result of COVID-19

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2103

POS1206 SEROPREVALENCE OF SARS-CoV-2 ANTIBODIES IN AUTOIMMUNE INFLAMMATORY RHEUMATOLOGIC PATIENTS

T. Eviatar[1,2], D. Levartovsky[1,2], V. Furer[1,2], A. Polachek[1,2], O. Elalouf[1,2], M. Zisapel[1,2], T. Halperin[1,3], D. Turner[1,4], D. Paran[1,2], S. Pel[1,2], S. Nevo[1,2], O. Elkayam[1,2]. [1]*Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv-Yafo, Israel*; [2]*Tel Aviv Sourasky Medical Center, Rheumatology Department, Tel Aviv, Israel*; [3]*Tel Aviv Sourasky Medical Center, Immunology Department, Tel Aviv, Israel*; [4]*Tel Aviv Sourasky Medical Center, Infectious Disease Department, Tel Aviv, Israel*

Background: Immune responses in AIIRD patients may be reduced and influenced by immunosuppressive treatments[1].The effect of immunosuppression on the mounting of SARS-CoV-2 antibodies in AIIRD is not clear.
Objectives: To assess the prevalence of SARS-CoV-2 antibodies in AIIRD patients and to define clinical factors affecting this prevalence.
Methods: Consecutive consenting AIIRD patients from the Rheumatologic department in Tel Aviv Medical Center participated in the study.
Patients answered a questionnaire and were tested for SARS-CoV-2 antibodies. A two stage antibody testing was done in order to increase specificity.
Results: The study included 560 AIIRD patients (229 RA, 149 PsA, 84 SLE, 55 vasculitidies, 40 SpA, 3 other CTD), of them 26 patients were found to have SARS-CoV-2 IgG antibodies (4.6%) (Table 1). This was more than double than a

previous prevalence in the same clinic population studied after the first wave of the pandemic in Israel, which was 2.07% (accepted for publication).

A lower rate of immunosuppression was found for positive SARS-CoV-2 IgG patients compared to negative serology patients (Table 1, p=0.009). There was also a trend for the subgroup of patients on biologic DMARDS (26.92% vs. 47% respectively, p=0.06).

Positive SARS-CoV-2 PCR test was reported and confirmed in 36 patients, of them 14 (38.89%) had negative serology. Patients who did not have antibodies had numerically more than double rates of glucocorticoids and bDMARDs treatment. The time between positive PCR test to positive serology test was significantly shorter (mean±standart deviation 75.57±40.44 days) than the time between positive PCR to negative serology test (130.79±86.47 (p=0.04) (Table 1 and Figure 1) suggesting a fading of the antibody response with time.

Conclusion: The prevalence of SARS-CoV-2 IgG was 4.6% in a population of AIIRD patients from a single tertiary medical center in Israel. SARS-CoV-2 seroprevalence tended to be low among AIIRD patients on immunosuppressive treatment, including in patients with a confirmed history of positive SARS-CoV-2 PCR, similar to other studies [3].

As in individuals without AIIRD, the mounting of SARS-CoV-2 IgG seems to fade with time.

Larger studies are needed to confirm the potential effect of immunosuppression on the antibody response in AIIRDs.

Table 1. ***Demographic and clinical characteristics of patients with negative and positive SARS-CoV-2 IgG, and in the subgroup with positive SARS-CoV-2 PCR test***

	Total population (n=560)			Positive PCR population (n=36)		
	Negative IgG(n=534)	**Positive IgG(n=26)**	*P*	**Negative IgG(n=14)**	**Positive IgG(n=22)**	*P*
Female n (%)	360 (67.42)	22 (84.62)	0.08	10 (71.43)	18 (81.82)	0.68
Age median (95% CI)	57 (54.95-57.58)	52.5 (46.55-58.6)	0.23	42 (35.46-53.11)	52.5 (47.62-60.65)	0.06
No. of comorbidities mean±STD (95%CI)	0.88±1.15 (0.78-0.98)	0.92±1.2 (0.44-1.41)	0.86	0.79±1.12 (0.14-1.43)	0.96±1.3 (0.4-1.51)	0.68
AIIRD treatments n(%)						
Total immunosuppression	401 (75.09)	13 (50)	**0.009**	11 (78.57)	12 (54.54)	0.175
GC	113 (21.16)	3 (11.54)	0.32	5 (35.71)	3 (13.64)	0.32
csDMARDS	257 (48.13)	13 (50)	1	7 (50)	13 (59.09)	0.73
bDMARDS	251 (47)	7 (26.92)	0.06	9 (64.29)	7 (31.82)	0.09
Anti CD-20	36 (6.74)	0	0.4	1 (7.14)	0	0.39

SARS-CoV-2, severe acute respiratory syndrome-coronavirus-2; IgG, immunoglobulin G; PCR, polymerase chain reaction; n, number; 95%CI, 95% confidence interval; GC, glucocorticoids; csDMARDS, conventional synthetic disease modifying antirheumatic drugs; bDMARDS, biologic disease modifying antirheumatic drugs.

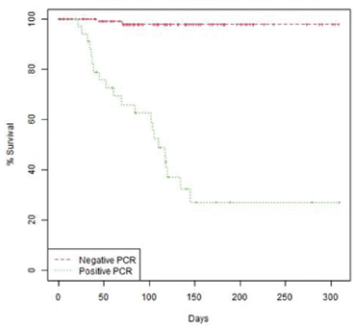


Figure 1. *Kaplan-Meier plot of SARS-CoV-2 IgG survival in days from SARS-CoV-2 PCR test*
There were 160 negative SARS-CoV-2 PCR tests with 2 positive serologies among them, and 35 positive SARS-CoV-2 PCR tests with 21 positive serologies among them (for 3 patients time between PCR test and serology was unknown). The median survival of SARS-CoV-2 serology in PCR positive patients was 110 days and was not applicable to PCR negative patients (p<0.0001).

REFERENCES:

[1] V. Furer *et al.*, "Incidence and prevalence of vaccine preventable infections in adult patients with autoimmune inflammatory rheumatic diseases (AIIRD): a systemic literature review informing the 2019 update of the EULAR recommendations for vaccination in adult patients wit," *RMD Open*, vol. 5, no. 2, p. e001041, Sep. 2019.

[2] D. Simon *et al.*, "Patients with immune-mediated inflammatory diseases receiving cytokine inhibitors have low prevalence of SARS-CoV-2 seroconversion," *Nat. Commun.*, vol. 11, no. 1, pp. 1–7, 2020.

Acknowledgements: This study was performed in collaboration with the Israeli Ministry of Health.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2107

POS1207

REAL WORLD POPULATION-BASED ASSESSMENT OF COVID-19 OUTCOMES AMONG RHEUMATOID ARTHRITIS PATIENTS USING BIOLOGIC OR SYNTHETIC DMARDs

L. Wegrzyn[1], K. Winthrop[2], S. Kim[3], Y. Ye[1], C. Huisingh[1], W. Krueger[1], A. Maniccia[4], R. Kilpatrick[1]. [1]*AbbVie, Global Epidemiology, Pharmacovigilance, & Patient Safety, North Chicago, United States of America*; [2]*Oregon Health & Science University, Division of Infectious Diseases, Portland, United States of America*; [3]*Brigham and Women's Hospital/Harvard Medical School, Division of Rheumatology, Inflammation, and Immunity, Boston, United States of America*; [4]*AbbVie, Medical Affairs, North Chicago, United States of America*

Background: While some risk factors for severe COVID have been identified for patients with rheumatic diseases,[1] few studies have investigated whether outcomes differ based on the type of rheumatoid arthritis (RA) treatment. Most existing reports have been limited to individual centers or voluntary reporting registries.[2,3]

Objectives: To compare the occurrence of hospitalizations following COVID-19 diagnosis among patients with RA treated with various classes of DMARDs.

Methods: A cohort of patients with confirmed COVID-19 (ICD10 diagnosis code or positive PCR or antigen test result) were identified within a large US electronic health record (EHR) dataset (Optum, Inc.) during the time period Feb 1, 2020 through Oct 14, 2020. From these, we identified RA patients (ICD10 RA diagnosis code) with treatment (most recent of JAK inhibitor [JAKi], biologic [bDMARD] or conventional synthetic [csDMARD] only) within the 12 months prior to COVID-19 diagnosis (i.e., index). The primary outcome was any hospitalization on or within 30 days after COVID-19 diagnosis. Multivariable logistic regression models compared users of JAKi's to non-TNFi bDMARDs and csDMARDs (separately), as well as users of TNFi's to non-TNFi bDMARDS and csDMARDs (separately), and were adjusted for age, gender, index month and baseline corticosteroid use. Sensitivity analyses included restriction of prevalent treatment use to within 180 days prior to COVID-19 diagnosis and restriction of csDMARDs to a group without hydroxychloroquine or chloroquine.

Results: The study included 910 RA patients on DMARD treatment who were diagnosed with COVID-19 (mean age ± SD: 61±15, 80% female, 62% white. Of those, 26% (n=240) were hospitalized on or within 30 days after COVID-19 diagnosis. The proportion of patients hospitalized was highest in non-TNFi bDMARD users (37/87; 43%), followed by csDMARDs users (161/581; 28%) and lowest in JAKi (13/68; 19%) and TNFi users (29/174; 17%). In multivariable-adjusted models, no differences in risk of hospitalization were found comparing JAKi users to csDMARD users (aOR=0.71; 95% CI 0.37-1.36) or TNFi users to csDMARD users (aOR=0.67; 95%CI 0.43-1.06). Compared to non-TNFi bDMARD users, JAKi use and TNFi use was associated with reduced risk of hospitalization (JAKi aOR=0.32; 95%CI 0.14-0.71; TNFi aOR=0.34; 95%CI 0.18-0.62). Age and corticosteroid use were positively associated with 30-day hospitalization in all models. Results of sensitivity analyses were consistent with the main findings.

Conclusion: In this study, roughly a quarter of RA patients with recent DMARD treatment were hospitalized within 30 days after COVID diagnosis. Patients treated with JAKi and TNFi therapies experienced the lowest risk of hospitalization, with risk of hospitalization significantly lower than non-TNFi bDMARDs. However, recent therapy recorded in the EHR may not reflect exposure at time of COVID-19 diagnosis and small sample size per treatment may limit interpretation.

REFERENCES:

[1] Hyrich KL, Machado PM. *Nat Rev Rheumatol* 2020;1-2. doi:10.1038/s41584-020-00562-2

[2] Gianfrancesco MA, et al. *Lancet Rheumatol* 2020;2(5):e250-e253. doi:10.1016/S2665-9913(20)30095-3

[3] Veenstra J, et al. *J Am Acad Dermatol* 2020;83(6):1696-1703.

Acknowledgements: Jonathan Johnson of Optum, Inc. provided dataset guidance and conducted data analyses. AbbVie funded this study, contributed to its design, participated in data collection, analysis, and interpretation of the data, and in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship.

Disclosure of Interests: Lani Wegrzyn Shareholder of: AbbVie, Employee of: AbbVie, Kevin Winthrop Consultant of: Pfizer, AbbVie, UCB, Eli Lilly & Company, Galapagos, GSK, Roche, Gilead, BMS, Regeneron, Sanofi, AstraZeneca, Novartis, Grant/research support from: BMS, Pfizer, Seoyoung Kim Grant/research support from: institutional research grants from Pfizer, AbbVie, Roche, BMS for unrelated studies, Yizhou Ye Shareholder of: AbbVie, Employee of: AbbVie, Carrie Huisingh Shareholder of: AbbVie, Employee of: AbbVie, Whitney Krueger Shareholder of: AbbVie, Employee of: AbbVie, anna maniccia Shareholder of: AbbVie, Employee of: AbbVie, Ryan Kilpatrick Shareholder of: AbbVie, Employee of: AbbVie.

DOI: 10.1136/annrheumdis-2021-eular.2206

POS1208

EPIDEMIOLOGY AND OUTCOMES OF PATIENTS WITH RHEUMATIC DISEASES AND SARS-CoV-2 INFECTION: DATA FROM THE ARGENTINEAN SAR-COVID REGISTRY

C. A. Isnardi[1], R. Quintana[1], K. Roberts[1], V. V. Castro Coello[2], A. A. Reyes[2], Y. Tissera[2], M. Cosatti[2], R. Rojas Tessel[2], J. Scafati[2], T. Barbich[2], M. S. Gálvez Elkin[2], G. F. Rodriguez Gil[2], S. Moyano[2], M. L. Werner[2], J. Rebak[2], J. Morbiducci[2], V. Martire[2], M. S. Castaño[2], C. Dieguez[2], G. C. Subils[2], G. Pons-Estel[1]on behalf of SAR-COVID Registry. *[1]Argentina Society of Rheumatology, Research Unit, AAQ, Argentina*; *[2]On behalf of SAR-COVID Registry, Rheumatology, Ciudad Autónoma de Buenos Aires, Argentina*

Background: In the last time, many papers about SARS-CoV-2 have been published in the world. However, data from latinamerican patients is still scarce. In order to assess the impact of SARS-CoV-2 infection in patients with rheumatic diseases in our country and contribute to the global knowledge about the effect of immunosuppressive therapies in this group, the Argentine Society of Rheumatology has developed the National Registry of Patients with Rheumatic Diseases and COVID-19 (SAR-COVID).

Objectives: The aim of this study was to evaluate clinical characteristics and outcomes of SARS-CoV-2 infection in patients with rheumatic diseases, treated or not with immunomodulators and/or immunosuppressants.

Methods: SAR-COVID is a national, multicenter, prospective and observational registry, in which patients, ≥18 years of age, with a diagnosis of a rheumatic disease who had SARS-CoV-2 infection (PCR or positive serology) are consecutively included between August 13, 2020 and January 17, 2021. Sociodemographic data, comorbidities, underlying rheumatic disease and treatment, clinical characteristics, complications, laboratory and treatment of the SARS-CoV-2 infection were recorded. Hospitalization, mechanical ventilation requirements and death were assessed to evaluate COVID-19 outcome. Statistical analysis: Descriptive analysis. Chi^2 or Fischer test and T test or Mann-Whitney U test or ANOVA, as appropriate. Multiple logistic regression.

Results: A total of 525 patients were included, 80.4% were female, with a median age of 52 years (IQR 40-62). Comorbidities were reported in half of them (53.3%). The most frequent rheumatological diseases were rheumatoid arthritis (40.4%) and systemic lupus erythematosus (14.9%). At the time of the infection, most of them were in remission or in minimal/low disease activity (68.2%) and 72.9% were receiving immunosuppressive or immunomodulatory treatment.

Symptoms were present in 96% of the patients, the most frequent being fever (56.2%), cough (46.7%) and headache (39.2%). During infection, 35.1% received some pharmacological treatment, dexamethasone (20%) the most frequently used. One third (35.1%) of the patients were hospitalized, 11.6% were admitted to the ICU, 10.1% needed mechanical ventilation and 6.9% died due to COVID-19. Complications were reported in 12.4%, being acute respiratory distress syndrome the most prevalent (8.8%).

Patients over 65 years of age were more frequently hospitalized, admitted to the ICU, needed mechanical ventilation and died due to COVID-19 (50% vs 31.4%, 22% vs 9%, 16.3% vs 5.2%, 14% vs 5%, respectively; p<0.001 in all cases). Similar results were seen in patients with vasculitis (57.7% vs 33.9%, 46.2 vs 9.8%, 34.6% vs 6 %; 30.8% vs 5.6%, respectively; p< 0.001 in all cases) and those with moderate/high disease activity (55.7% vs 26.5%, 21.3 vs 7.8%, 17.2% vs 4.2 %; 17.2% vs 4.2 %, respectively; p< 0.001 in all cases). Patients with APS were more frequently admitted to the ICU (29.4% vs 11%, p= 0.037). The presence of comorbidities was associated with higher hospitalization (46% vs 22.6%, p<0.001), admission to the ICU (17.2% vs 5.9%, p<0.001) and mechanical ventilation (10.2% vs 4.6%, p= 0.028). Immunosuppressive treatment was not associated with worse outcomes.

Conclusion: In this cohort of patients with a wide distribution of rheumatic diseases, we have found clinical characteristics similar to those reported by other international cohorts. Compared with national data, the mortality reported in these patients is higher. However, it should be noted that these are early data collected during isolation and that there may be an underreporting of asymptomatic patients or with mild symptoms who do not attend the rheumatologist.

Older patients, those with comorbidities, with vasculitis and with higher disease activity showed poor COVID-19 outcomes.

Disclosure of Interests: Carolina Ayelen Isnardi Speakers bureau: Janssen, BMS, Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Rosana Quintana Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Karen Roberts Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Vanessa Viviana Castro Coello Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Alvaro Andres Reyes Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Yohana Tissera Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Micaela Cosatti Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Romina Rojas Tessel Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Julia Scafati Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Tatiana Barbich Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., María Soledad Gálvez Elkin Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Gustavo Fabian Rodriguez Gil Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Sebastian Moyano Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Marina Laura Werner Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Jonathan Rebak Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Julieta Morbiducci Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Victoria Martire Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., María Sol Castaño Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Carolina Dieguez Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Gisela Constanza Subils Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data., Guillermo Pons-Estel Grant/research support from: Unrestricted grants: Pfizer, Abbvie, Elea Phoenix. None of them have access to patient data.

DOI: 10.1136/annrheumdis-2021-eular.2250

POS1209

SUCCESSFUL TREATMENT OF SEVERE COVID-19 PNEUMONIA AND CYTOKINE RELEASE WITH SIMULTANEOUS TOCILIZUMAB AND ANAKINRA WITH ONE-MONTH FOLLOW-UP

H. Haibel[1], J. L. Vahldiek[2], S. Angermair[3], M. Schumann[4], B. Siegmund[5], D. Poddubnyy[1], T. Schneider[6]. *[1]Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Rheumatology, Berlin, Germany*; *[2]Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Radiology, Berlin, Germany*; *[3]Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Anestesiology and Surgical Intensive Care, Berlin, Germany*; *[4]Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Gastroenterology, Berlin, Germany*; *[5]Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Gastroenterology, Infectiology and Rheumatology, Berlin, Germany*; *[6]Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Infectiology, Berlin, Germany*

Background: Severe and life threating COVID-19 pneumonia is often characterized by local and systemic immune-mediated hyperinflammation At the early disease stage activated monocytes are migrating to the lung and cause the typical opac infiltrates, which lead to an reduction of oxygen uptake. These pathophysiological observations and the fact that corticosteroids are so far the only drug, which has shown significant improvement, was the rationale use this combination anti-inflammatory drugs in severe Covid-19 disease. Interleukin (IL)-6 and IL-1 blockade alone, respectively showed contradictory results in severe COVID-19 pneumonia that might be related to the differences is patient populations (early vs. late stage) and to the fact that blockade of just one cytokine might be not sufficient against the cytokine storm.

Objectives: Here we report results of an open-label treatment with a combination of an IL-6 receptor blocker tocilizumab and an IL-1 receptor antagonist anakinra in patients with early (up to 10 days since symptom onset) severe COVID-19 pneumonia with evidence of cytokine release.

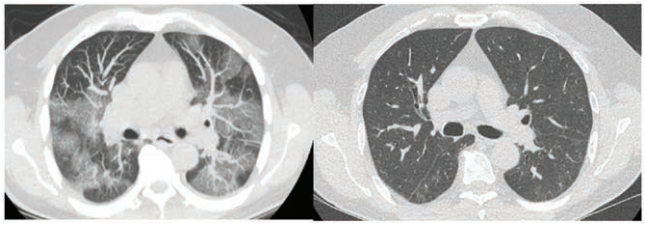
Methods: Adult patients with, according to World Health Organisation criteria, severe to critical COVID-19 infection associated pneumonia and cytokine release, requiring oxygen supplementation and evidence of rapid deterioration and decrease of oxygen saturation to ≤ 95% hospitalized between May 2020 and December 2020 were treated with tocilizumab 8 mg/ kg up to 800 mg intravenously and anakinra 100 to 300 mg for 3 to 5 days, starting at the same day. We excluded patients with a symptom duration of > 10 days, patients with evidence of bacterial infection, indicated by an elevated procalcitonin serum level, patients with severe pre-existing lung disease such as severe COPD or heart failure of > II according to the NYHA classification and patients > 80 years. Laboratory parameters and chest CT were performed on initial presentation and one month after treatment. A semi-quantitative CT score was calculated based on the extent of lobar pneumonia involvement (0:0%; 1, < 5%; 2:5-25%; 3:26-50%; 4:51-75%; 5, > 75%; range 0-5; global score 0-25) for each time point.

Results: 15 patients with severe to critical COVID-19 pneumonia and signs of cytokine release, mean age 55 (range 31-79) years, all male, with a mean

symptom duration of 6 (range 4-10) days were treated. Mean oxygen saturation was 86% (range 76-95%) before initiating therapy. Mean ferritin was 1297 µg/l (range 347 – 2734), mean IL-6 112 ng/L (range 2.2 – 607.4) and CRP 82.4 mg/L (range 36.4 – 125). In all patients we were able to prevent them from intubation and mechanic ventilation, none of our patients died. Fife patients did not need to be referred to the intensive care unit at all, while 9 patients received noninvasive ventilation and high-flow nasal oxygen support. All patients showed typical imaging features of COVID-19 pneumonia at baseline (BL) according to the Radiological Society of North America (RSNA) chest CT classification system. The mean of the global chest CT severity score at BL was 13 (range 7-20) and decreased to 6 (range 0-16) within 1 month which corresponded to a mean reduction of 58%. Chronic fibrotic pulmonary changes were not seen in any patient at BL and after 1 month mild changes were observed in 6 patients. One patient experienced lower abdominal pain, urinary tract infection, gastrointestinal bleeding due to antrum ulcers Forrest III, in another patient atrial fibrillation, urinary tract infection and apoplexy were observed.

Conclusion: In our case series, all patients treated with the combination tocilizumab and anakinra recovered fast and sustained without major infectious side effects, indicating that early interruption of cytocine release might be very effective and safe in preventing patients from mechanical ventilation, death and long-term damage.

Image 1: Chest CT of a patient with active COVID-19 infection before and one month after treatment with a combination of tocilizumab and anakinra



Disclosure of Interests: Hildrun Haibel Speakers bureau: Abbive, Novartis, Janssen, Pfizer, Roche, Consultant of: Janssen, Novartis, Roche, Janis Lucas Vahldiek: None declared, Stefan Angermair: None declared, Michael Schumann: None declared, Britta Siegmund Speakers bureau: Abbvie, CED Service GmbH, Falk, Ferring, Janssen, Novartis and Takeda as a representative of Charité – Universitätsmedizin Berlin, Consultant of: Abbvie, Arena, BMS, Boehringer, Celgene, Falk, Janssen, Lilly, Pfizer, Prometheus, Takeda representative of Charité – Universitätsmedizin Berlin, Grant/research support from: Pfizer, Denis Poddubnyy Speakers bureau: AbbVie, Bristol-Myers Squibb, Lilly, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Biocad, Gilead, GlaxoSmithKline, Eli Lilly, MSD, Novartis, Pfizer, Samsung Bioepis, and UCB, Grant/research support from: AbbVie, Eli Lilly, MSD, Novartis, and Pfizer, Thomas Schneider: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2289

POS1210 PREVALENCE OF COVID-19 AMONG PATIENTS WITH RHEUMATIC DISEASES: AN OBSERVATIONAL SURVEY DURING THE TWO WAVES IN ITALY

S. Fasano[1], I. Pantano[1], D. Mauro[1], D. Capocotta[2], D. Iacono[1], E. Gaggiano[1], M. D. Pasquale[1], G. Rozza[1], C. DI Vico[1], A. Ruggiero[1], E. Tirri[2], F. Ciccia[1].
[1]University of Campania L. Vanvitelli, Rheumatology Unit, Department of Precision Medicine, Naples, Italy; *[2]Ospedale S. Giovanni Bosco, U.O.S.D. di Reumatologia, Naples, Italy*

Background: The new coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19) is a source of concern for the management of patients suffering from rheumatic and musculoskeletal diseases (RMDs) treated with immunomodulatory therapies (1).

Objectives: We aimed to analyze the prevalence of SARS-CoV-2 infection in patients with RMDs living in Italy.

Methods: During the first wave (March-May 2020) and during the second wave (October-December 2020) of COVID-19, we conducted a survey to investigate the incidence of SARS-CoV-2 infection in patients with RMDs followed at the Rheumatology Unit of the University of Campania, Italy. The demographic data, medication use, the frequency of respiratory symptoms and the incidence of COVID-19 confirmed by nasopharyngeal swab were collected with questionnaires administered by phone. The prevalence of COVID-19 of our cohort was compared to that of the general population (2).

Results: During the first wave, we collected data from 900 patients with RMDs (Table 1): 320 patients with rheumatoid arthritis (RA), 295 patients with spondyloarthropathies (SpA), 283 patients with systemic lupus erythematosus (SLE), 2 patients with vasculitis. 546 (60%) were treated with bDMARD/tsDMARDs. Overall, a total of 11/900 (1%) cases were tested for COVID-19 due to compatible symptoms. 2 (0.2%) adult patients treated with bDMARDs were registered as swab test positive by PCR for COVID-19. 2 patients without confirmed COVID-19 developed pneumonia that required admission to hospital. No deaths occurred among the patients with confirmed COVID-19.

During the second wave, data were collected from 470 patients who accepted to take part of the study (Table 1). 49 presented with symptoms that were compatible with COVID-19. 139 patients were tested whereas 30 patients (6%) had a swab confirmation of SARS-CoV-2 infection. Among them, 16 (53%) were treated with bDMARDs and a patient was treated with tofacitinib. we found no increase in COVID-19 prevalence in patients treated with bDMARD/tsDMARDs (p>0.05). A patient with SLE developed pneumonia that required admission to hospital and died.

Lacking distinct prevalence data between first and second waves, we found no differences in total COVID-19 prevalence between general population living in Campania (215.752/5.802.000; 3.7%) and patients with RMDs (32/900; 3.5%). However, we had a significant increase in COVID-19 prevalence in our cohort during the second wave compared to the first. Nevertheless, no increase in mortality or hospitalization was recorded, confirming the safety of immunomodulatory therapies in patients with RMDs.

Conclusion: In this cohort of patients with RMDs in a geographical region with a high prevalence of COVID-19, the risk of SARS-CoV-2 infection does not appear different from that observed in the general population.

REFERENCES:

[1] Wang L., Wang Y., Ye D. Int J Antimicrob Agents. 2020:105948.
[2] http://www.protezionecivile.gov.it/ (accessed 28.01.21)

Table 1. Demographics and clinical characteristics of 900 patients with rheumatic diseases during the COVID-19 Pandemic.

	First wave	Second wave
Women, n	660 (73 %)	366(77%)
Age, years, median (range)	56 (54-57)	53 (51-55)
Rheumatoid Arthritis	320 (35.5%)	143 (30%)
Spondyloarthritis	295 (32%)	110 (23%)
Systemic Lupus Erythematosus	283 (31%)	217 (46 %)
Vasculitis	2 (0.2%)	1 (0.2%)
Prior ILD	56 (6%)	22 (4.6%)
Smokers	220 (24%)	118 (25%)
Hydroxychloroquine	215 (23%)	155 (32%)
Steroids	337 (37%)	194 (41%)
Prednisone equivalent dose, median (range)	5 (0-75)	5 (0-50)
bDMARD/tsDMARDs	546 (60%)	247 (52%)
csDMARDS	387 (43%)	185 (39%)
Angiotensin-converting enzyme (ACE) inhibitors	178 (19.8%)	101 (21%)
Angiotensin II receptor blockers(ARBs)	153 (17%)	61 (13%)
Fever	64 (7%)	30 (6.3%)
Cough	83 (9%)	36 (7%)
Shortness of breath	34 (3%)	15 (3%)
Sore throat	32 (3%)	11 (2.3%)
Rhinorrhoea	36 (3%)	11 (2.3%)
Headache	5 (0.5%)	2 (0.4%)
Anosmia	10 (1%)	24 (5%)
Myalgia	2 (0.2%)	1 (0.2%)
Gastrointestinal symptoms	24 (2.6%)	3 (0.6%)
Pneumonia	2 (0.2%)	2 (0.4%)
Admission to hospital	2 (0.2%)	9 (1.9%)
Swab confirmation of SARS-CoV-2 infection	2	30

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2297

POS1211 IDENTIFICATION OF COMMON FUNCTIONAL PATHWAYS IN PATIENTS WITH LUPUS AND COVID-19 BY TIME-SERIES ANALYSIS

Y. LI[1,2,3], S. X. Zhang[1,2,3], J. Qiao[1,2,3], Q. Wang[4,5], S. Song[1,2,3], R. Zhao[1,2,3], Y. Zhang[1,2,3], T. Cheng[1,2,3], M. J. Chang[1,2,3], G. Y. Liu[1], J. Luo[1], P. F. He[5], X. LI[1,2,3]. *[1]The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; *[2]Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; *[3]Ministry of Education, Key laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; *[4]Shanxi Medical University, Basic Medical College, Taiyuan, China*; *[5]Shanxi Medical University, Medical Data Sciences, Taiyuan, China*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by abnormal activity of the immune system, producing the autoantibodies directed against nuclear and cytoplasmic antigens[1]. Infection is known as one of the common trigger factors for SLE. Coronavirus disease in 2019 (COVID-19), a severe acute respiratory syndrome, is now spreading rapidly throughout the world[2].Though previous studies have addressed the susceptibility of lupus patients to the virus but how patients with SLE deal with COVID-19 is unclear up until now.

Objectives: To clarify the common pathogenesis of SLE and COVID-19, and find the appropriate treatment for Lupus and prevent COVID-19.
Methods: The transcription profile of SLE (GSE38351) and COVID-19 (GSE161778) were obtained from the Gene Expression Omnibus database (GEO). R package was used to find differentially expressed genes (DEGs) between lupus patients and HCs. After background adjustment and other pre-procession, DEGs were extracted from the peripheral blood of patients with COVID-19 at three different disease progression(moderate, severe and remission status). The Short Time-series Expression Miner (STEM) was used to cluster and compare average DEGs with coherent changes. The different expression patterns of time-series genes (TSGs) were also compared among these patients. GO and KEGG pathway enrichment analysis of TSGs and DEGs were performed by Metascape.
Results: Compared with HC, patients with SLE expressed 977 DEGs, which were mainly associated with defense response to virus, Epstein-Barr virus infection and response to interferon-γ(INF-γ) (Figure 1a). As for COVID-19 patients, there were 1584 DEGs obtained when compared with those of HCs ($P < 0.05$) (Figure 1b). Gene landscapes suggested the signatures of COVID-19 patients gradually changed during the disease progression, and gradually converge to HCs signatures. Time-series genes in the three stage of disease had different expression patterns and functions. A total of 959 TSGs in profile 3 showed a stable-stable-decreasing expression trend and significantly associated with INF signaling pathway (Figure 1c,1d). Interestingly, patients with SLE and COVID-19 shared common pathways such as INF-γ related functional pathway.
Conclusion: INF-γ is an important common node of SLE and COVID-19. Controlling the production of INF-γ not only has therapeutic effect on SLE patients, but also may prevent COVID-19.
REFERENCES:
[1] Tsokos GC. Systemic lupus erythematosus. N Engl J Med 2011;365(22):2110-21. doi: 10.1056/NEJMra1100359 [published Online First: 2011/12/02]
[2] Wan DY, Luo XY, Dong W, et al. Current practice and potential strategy in diagnosing COVID-19. Eur Rev Med Pharmacol Sci 2020;24(8):4548-53. doi: 10.26355/eurrev_202004_21039 [published Online First: 2020/05/07]

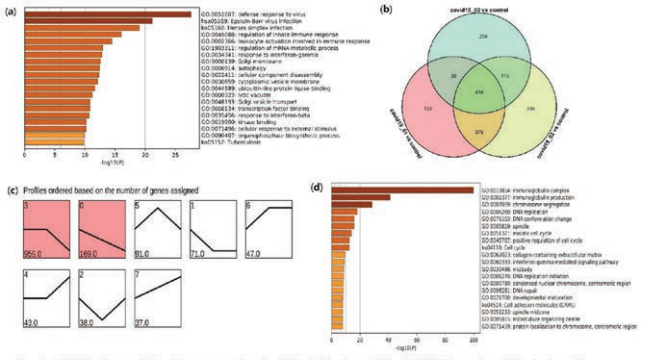


Figure 1: (a) KEGG pathway and GO enrichment were performed on DEGs of SLE patients and HCs. (b) VENN diagram showe DEGs of patients with COVID-19 and HCs. Among them, covid19-01 represents moderate patients, covid19-02 represents severe patients, covid19-03 represents remission patients, and control represents HCs. (c) Expression patterns of time-series genes in COVID-19 and HCs. The colored profiles represent significant profiles. Colored in red represented statistically significant (P<0.05). (d) KEGG pathway and GO enrichment results of the significant stable-stable-decreasing expression trend TSGs.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2384

POS1212 SARS-CoV-2 INFECTION AMONG PATIENTS WITH BEHÇET'S SYNDROME

I. Mattioli[1], A. Bettiol[1], M. L. Urban[1], E. Silvestri[1], D. Malandrino[1], A. Palermo[1], F. Fagni[1], D. Prisco[1], G. Emmi[1]. [1]*University Hospital Careggi, Department of Experimental and Clinical Medicine, Florence, Italy*

Background: Studies on SARS-Cov-2 in Behçet's syndrome (BS) patients are limited to two small case series from European centres.[1,2]
Objectives: We aimed to assess the prevalence of SARS-CoV-2 infection among Italian BS patients referring to Careggi University Hospital (Florence, Italy) and to evaluate the possible association between BS disease activity and treatment and the risk of Sars-CoV-2 infection among patients with BS.
Methods: A survey was conducted among 335 subjects diagnosed with BS and followed at Careggi University Hospital. Moreover, we conducted a case-control study. Cases were described in term of SARS-CoV-2 manifestation and prognosis, changes in disease activity, and in pharmacological therapies. Sars-CoV-2 negative controls matched 1:3 by sex, age and disease duration ± 5 years were randomly selected.
Results: Out of 335 BS patients, 12 declared to have/have had SARS-CoV-2 infection (3.6%). Eight were females (median age of 40 years), with a median duration of BS disease of 6 years; five had active disease. Nine patients reported fever, 9 myalgia/arthralgia, 5 gastrointestinal symptoms, 5 anosmia/ageusia, 5 cough, 3 headache, 3 fatigue, 2 breathlessness, panic attacks and dizziness (one each). Before infection, patients were treated with corticosteroids, colchicine, hydroxychloroquine (HCQ), traditional DMARDs [azathioprine (n patients = 4), methotrexate (n=1)], and biologics DMARDs [adalimumab (n=6), infliximab (n=2), secukinumab (n=1), and canakinumab (n=1)]. Therapy was suspended for a median time of 33 days in 9patients and resumed after a median time of 5 days from negativation. Regarding SARS-CoV-2 treatment, most patients started or increased corticosteroids, whereas heparin and antipyretic drugs were used in 4 and 5 patients, respectively. Cases were comparable to controls in terms of disease manifestations, activity, and immunomodulating therapy, with the only exception of corticosteroids, whose daily dose was significantly higher in cases (Table 1).
Conclusion: Prevalence of SARS-CoV-2 infection among Italian BS patients is 3.6%, similarly to the Italian general population (4.2%). Disease activity at time of infection was not associated with an increased risk of SARS-CoV-2 infection. Most patients interrupted biologic DMARDs. However, use of DMARDs, seemed not to be associated with an increased risk of SARS-CoV-2 infection, while higher doses of corticosteroids resulted to be more common among patients with SARS-CoV-2 infection as compared to controls. No patient required hospitalization or died. Our experience shows encouraging data about BS patients who do not appear be at greater risk of SARS-CoV-2 infection or complications than the general population.
REFERENCES:
[1] Espinosa et al. COVID-19 and Behçet's disease: clinical case series. Ann Rheum Dis. 2020
[2] Yurttaş et al. Characteristics and outcomes of Behçet's syndrome patients with Coronavirus Disease 2019: a case series of 10 patients. IEM. 2020
[3] http://www.salute.gov.it

Table 1. Features of SARS-CoV-2+ cases and matched controls

	12 SARS-CoV-2+ CASES PRE-INFECTION	12 SARS-CoV-2+ CASES POST-INFECTION	36 CONTROLS	p-value*
Female sex	8 (66.7%)		24 (66.7%)	Matching variable
Median age	40 (IQR 31-45)		40 (IQR 32-44)	Matching variable
Median disease duration	6 (IQR 5-9)		6 (IQR 3-8)	Matching variable
Active disease (BDCAF≥1)	5 (41.7%)	4 had disease relapse	24 (66.7%)	0.176
Immunomodulating therapy				
Corticosteroids –	8 (66.7%)	8 (66.7%)	12 (33.3%)	0.088
Median dosage (IQR)	5 (IQR 0-12.5)	6 (IQR 0-15)	0 (IQR 0-2.5)	0.010
Colchicine	2 (16.7%)	Continued	11 (30.6%)	0.469
HCQ	1 (8.3%)	Continued	1 (2.8%)	0.441
Traditional DMARDs	5 (41.7%)	1 interrupted	8 (22.2%)	0.263
Biologic DMARDs	10 (83.3%)	8 interrupted	27 (75%)	0.705
Disease involvement				
Mucocutaneous	5 (41.7%)		12 (33.3%)	0.731
Articular	5 (41.7%)	4 worsened	17 (47.2%)	1.000
Ocular	0		2 (5.6%)	n.a.
Vascular	0		0	n.a.
Neurological	3 (25%)		8 (22.2%)	1.000
Gastrointestinal	2 (16.7%)	1 worsened	6 (16.7%)	1.000

**p-value from Fisher exact test for unpaired data between first columns vs third columns*

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2387

POS1213 IMPACT OF THE COVID-19 PANDEMIC AND LOCKDOWN ON WELLBEING ON PATIENTS WITH RHEUMATIC DISEASES. RESULTS FROM THE REUMAVID STUDY (PHASE 1)

M. Garrido-Cumbrera[1], H. Marzo-Ortega[2,3], L. Christen[4], L. Carmona[5], J. Correa-Fernández[1], S. Sanz-Gómez[1], P. Plazuelo-Ramos[6], L. Grange[7,8], D. Webb[9], S. Irwin[10], C. Jacklin[11], S. Makri[12], E. Mateus[13,14], S. Mingolla[15], K. Antonopoulou[16], V. Navarro-Compán[17]on behalf of REUMAVID working group. [1]*Universidad de Sevilla, Health & Territory Research (HTR), Sevilla, Spain*; [2]*University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [3]*Leeds Teaching Hospitals Trust, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*; [4]*Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; [5]*Institute for Musculoskeletal Health, InMusc, Madrid, Spain*; [6]*Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; [7]*French League Against*

Rheumatism (AFLAR), Management, Grenoble, France; [8]*Centre Hospitalier Universitaire de Grenoble, Rheumatology, Grenoble, France*; [9]*National Axial Spondyloarthritis Society (NASS), Management, London, United Kingdom*; [10]*Arthritis Action, Management, London, United Kingdom*; [11]*National Rheumatoid Arthritis Society (NRAS), Management, London, United Kingdom*; [12]*Cyprus League Against Rheumatism (CYPLAR), Management, Nicosia, Cyprus*; [13]*Liga Portuguesa Contra as Doenças Reumáticas (LPCDR), Management, Lisbon, Portugal*; [14]*NOVA Medical School, Comprehensive Health Research Centre (CHRC), Lisbon, Portugal*; [15]*Italian National Association of People with Rheumatic and Rare Diseases (APMARR), Communication, Bari, Italy*; [16]*Hellenic League Againts Rheumatism (ELEANA), Management, Athens, Greece*; [17]*Hospital Universitario La Paz, IdiPaz, Madrid, Spain*

Background: The COVID-19 pandemic has impacted the wellbeing of patients with Rheumatic and Musculoskeletal Diseases (RMDs).
Objectives: The aim is to assess emotional well-being and its associated factors in patients with RMDs during the first wave of the COVID-19 pandemic.
Methods: REUMAVID is an international collaboration led by the Health & Territory Research group at the University of Seville, together with a multidisciplinary team including patient organisations and rheumatologists. This cross-sectional study consisting of an online survey gathering data from patients with a diagnosis of 15 RMDs in Cyprus, France, Greece, Italy, Portugal, Spain, and the United Kingdom. 1,800 participants were recruited by patient organisations. Data was collected between April and July 2020. Participants were divided into two groups: 1) Participants with poor wellbeing (World Health Organization-Five Wellbeing Index (WHO-5) ≤ 50), 2) Participants with good wellbeing (WHO-5 >50). The Mann-Whitney and χ^2 tests were used to analyse possible relations between sociodemographic characteristics, lifestyle, and outdoor contact with wellbeing during the first wave of the COVID-19 pandemic. Univariate and multivariate binary logistic regression was used to determine the impact of the independent variables associated with poor wellbeing.
Results: 1,777 patients with 15 different RMDs were included. The mean age was 52.7, 80.2% female, 48.7% had a university degree, and 69.7% were married or in a relationship. The most frequent diagnoses were inflammatory arthritis (75.4%). 49.0% reported poor wellbeing. 57.7% of patients who belonged to a patient organisation reported good wellbeing (vs 46.3% who did not, p<0.001). Those who reported poor wellbeing had higher disease activity (51.4% vs 41.3%, p<0.001), a higher risk of anxiety (54.3% vs 41.7%, p<0.001) and depression (57.0% vs 42.1%, p<0.001), and poorer self-perceived health (53.0% vs 41.8%, p<0.001), compared to those who did not. A higher proportion of those who engaged in physical activity presented good wellbeing (54.0% vs 46.5%, p=0.012). 57.4% of the patients who were unable to attend their appointment with their rheumatologist reported poor wellbeing, compared to 48.2% who did attend (p=0.027). Patients who did not walk outside (56.2%) or who lacked elements in their home to facilitate outside contact (63.3%) experienced poor wellbeing (p<0.001). The factors associated with poor wellbeing were lack of elements in the home enabling contact with the outside world (OR=2.10), not belonging to a patient organisation (OR=1.51), risk of depression (OR=1.49), and not walking outside (OR=1.36) during the COVID-19 pandemic (Table 1).
Conclusion: Almost half of the patients with RMDs reported poor emotional wellbeing during the first wave of the COVID-19 pandemic. The lack of elements in the home that facilitate outdoor contact, not belonging to a patient organisation, the presence of anxiety, and not walking outside during the pandemic increase the probability of poor emotional well-being. These results highlight the importance of environmental factors and the role of patient organisations in addressing the effects of the pandemic and its containment measures.

Table 1. Logistic regression for poor wellbeing WHO-5 (N=1,104)

	Univariate logistic analysis		Multivariate logistic analysis	
	OR	95% CI[1]	OR	95% CI[1]
Patient organisation. Non-member	1.57	**1.30, 1.89**	1.51	**1.18, 1.93**
Disease activity (VAS ≥ 4)	1.50	**1.21, 1.86**	1.16	0.85, 1.56
Risk of anxiety (HADs, 0-21)	1.67	**1.38, 2.02**	1.20	0.92, 1.58
Risk of depression (HADs, 0-21)	1.83	**1.51, 2.21**	1.49	**1.12, 1.99**
Self-reported health. Fair to very bad	1.58	**1.30, 1.91**	1.26	0.94, 1.68
Change in health status. Worse	1.27	**1.06, 1.53**	1.05	0.80, 1.38
Physical activity. No	1.35	**1.07, 1.71**	1.08	0.83, 1.40
Talked with rheumatologist during the pandemic. No	1.45	**1.04, 2.03**	1.04	0.68, 1.61
Walk outside during COVID-19 pandemic. No	1.47	**1.19, 1.83**	1.36	**1.02, 1.81**
Element in home with outdoor contact. No	1.93	**1.42, 2.62**	2.10	**1.41, 3.15**

[1]95% CI for test H_0: OR = 1

Acknowledgements: This study was supported by Novartis Pharma AG. We would like to thank all patients that completed the survey as well as all of the patient organisations that participated in the REUMAVID study including: the Cyprus League Against Rheumatism (CYPLAR) from Cyprus, the Association Française de Lutte Anti-Rhumatismale (AFLAR) from France, the Hellenic League Against Rheumatism (ELEANA) from Greece, the Associazione Nazionale Persone con Malattie Reumatologiche e Rare (APMARR) from Italy, the Portuguese League Against Rheumatic Diseases (LPCDR), from Portugal, the Spanish Federation of Spondyloarthritis Associations (CEADE), the Spanish Patients' Forum (FEP), UNiMiD, Spanish Rheumatology League (LIRE), Andalusian Rheumatology League (LIRA), Catalonia Rheumatology League and Galician Rheumatology League from Spain, and the National Axial Spondyloarthritis Society (NASS), National Rheumatoid Arthritis (NRAS) and Arthritis Action from the United Kingdom.
Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Helena Marzo-Ortega Speakers bureau: AbbVie, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Takeda and UCB., Consultant of: AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Laura Christen Employee of: Novartis Pharma AG, Loreto Carmona: None declared, José Correa-Fernández: None declared, Sergio Sanz-Gómez: None declared, Pedro Plazuelo-Ramos: None declared, LAURENT GRANGE: None declared, Dale Webb Grant/research support from: AbbVie, Biogen, Janssen, Lilly, Novartis and UCB., Shantel Irwin: None declared, Clare Jacklin Grant/research support from: has received grant funding from Abbvie, Amgen, Biogen, Eli Lilly, Gilead, Janssen, Pfizer, Roche, Sanofi & UCB, Souzi Makri Grant/research support from: Novartis, GSK and Bayer., Elsa Mateus Grant/research support from: Lilly Portugal, Sanofi, AbbVie, Novartis, Grünenthal S.A., MSD, Celgene, Medac, Janssen-Cilag, Pharmakern, GAfPA., Serena Mingolla: None declared, KATY ANTONOPOULOU: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.2396

POS1214 THE DYNAMICS OF INFLAMMATORY MARKERS IN COVID-19 PATIENTS TREATED WITH LEVILIMAB

N. Lomakin[1], B. Bakirov[2], G. Musaev[3], D. Protsenko[4], O. Moiseeva[5], E. Pasechnik[6], V. Popov[7], E. Smolyarchuk[8], I. Gordeev[9], M. Gilyarov[10], D. Fomina[11], V. Mazurov[12], M. Morozova[13], E. Dokukina[14], D. Bogdan[14], A. Lutskii[13], A. Zinkina-Orihan[13], I. Linkova[13], A. Seleznev[13]. [1]*Central Clinical Hospital of Presidential Affairs Department, Intensive Care and Emergency Cardiology, Moscow, Russian Federation*; [2]*Bashkir State Medical University, Department of Hospital Therapy No. 2, Ufa, Russian Federation*; [3]*Republican Clinical Hospital, Acting Chief Physician, Makhachkala, Russian Federation*; [4]*Municipal Clinical Hospital No. 40, Chief Physician, Moscow, Russian Federation*; [5]*V.A. Almazov National Medical Research Center, Research Department of Non-Coronary Heart Diseases, Saint-Petersburg, Russian Federation*; [6]*Regional Clinical Hospital, Department of Hematology, Kaluga, Russian Federation*; [7]*N.A. Semashko Railroad Clinical Hospital, Clinical Pharmacology Unit, Moscow, Russian Federation*; [8]*I.M. Sechenov First Moscow State Medical University, Center for Clinical Studies of Medicinal Products, Moscow, Russian Federation*; [9]*O.M. Filatov City Clinical Hospital No. 15, University Clinic of Internal Diseases, Moscow, Russian Federation*; [10]*N.I. Pirogov Municipal Clinical Hospital No. 1, Deputy Chief Physician for Therapy, Moscow, Russian Federation*; [11]*Municipal Clinical Hospital No. 52, Center of Allergology and Immunology, Moscow, Russian Federation*; [12]*North-Western State Medical University n.a. I.I. Mechnikov, Department of Therapy and Rheumatology of Temporary Disability and Medical Care Quality Expertise named after E. E. Eichwald, Saint-Petersburg, Russian Federation*; [13]*BIOCAD, Clinical Development, Saint-Petersburg, Russian Federation*; [14]*BIOCAD, Clinical Research, Saint-Petersburg, Russian Federation*

Background: Levilimab (LVL) is a novel anti-IL6Rmonoclonal antibody against IL6Rα. Cytokine release syndrome plays the key role in the pathogenesis of a range of life-threatening conditions including the acute respiratory distress syndrome in severely ill COVID-19 patients. Thus, the use of LVL could be considered as anti-cytokine therapy with a potency to prevent the complications and progression of respiratory failure in COVID-19.
Objectives: We analyzed the changes in the serum concentrations of inflammatory markers (Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and IL-6) in patients treated with LVL or placebo as part of a phase III multicenter randomized double-blind placebo-controlled adaptive-design CORONA clinical study aimed to evaluate the efficacy and safety of LVL in subjects with severe COVID-19 (NCT04397562).
Methods: A total of 217 patients were enrolled in the study, 206 patients were randomized, and 204 patients received the investigational product (IP, LVL or placebo).
Study included men and non-pregnant women aged ≥18 years, hospitalized for severe COVID-19 pneumonia, receiving standard therapy according to the national guidelines. Patients with acute respiratory failure with the need in invasive respiratory support, septic shock, multiple organ failure or life expectancy

less than 24 hours could not participate in the study. The use of other monoclonal antibodies and glucocorticoids for the treatment of COVID-19 were not allowed. Subjects were stratified according to the CRP level (CRP ≤ 7 mg/L; CRP > 7 mg/L) and then randomized (1:1) into 2 groups to receive LVL 324 mg or placebo. LVL/placebo were administered as a single subcutaneous injection, investigator and patients were unaware of the received therapy.

Among secondary endpoints of the study changes from baseline in ESR, CRP and IL-6 concentrations were assessed. CRP level and ESR were measured before the IP administration and on Days 3, 5, 7, 14, 21, 29 and 30. Blood samples for the measurement of IL-6 concentration were obtained before the IP administration and then every day for 2 weeks after administration.

Results: We observed the pronounced decrease of ESR in LVL group compared to Placebo group. The difference was statistically significant on Days 3 and 7: the median ESR change from baseline was -3 mm/h and +3 mm/h on Day 3, -11 mm/h and -3.1 mm/h on Day 7, in LVL and Placebo groups, respectively (p=0.0319 and p=0.0110, Days 3 and 7). The statistically significant difference in the change of CRP level was detected between the groups on Day 3: -26.6±41.9 mg/L and -19.2±58.2 mg/L in LVL and Placebo groups, respectively (p=0.0241). Numerically the same dynamics of ESR and CRP was observed over entire study period.

The dynamics of IL-6 serum concentrations in LVL and Placebo groups was strikingly different. After LVL administration we detected the rapid significant increase in IL-6 concentration due to IL-6 receptors inhibition. Maximum change from baseline was observed on Day 3 (+91.9±117.7 pg/mL), on Day 14 the value was +31.9±62.7 pg/mL.

In the Placebo group, the IL-6 concentration increased slightly until Day 4 (+5,1±76,5 pg/mL), and then decreased significantly (-39.2±55.1 pg/mL on Day 14) due to clinical improvement in this group.

Conclusion: The significant differences in the dynamics of ESR, CRP and IL-6 after LVL administration compared to placebo confirmed the pharmacodynamic effect and its potency to prevent the excessive release of inflammatory substances in severely ill COVID-19 patients.

REFERENCES:

[1] Xu X, Han M, Li T, Sun W, Wang D, Fu B, Zhou Y, Zheng X, Yang Y, Li X, Zhang X, Pan A, Wei H. Effective treatment of severe COVID-19 patients with tocilizumab. Proc Natl Acad Sci U S A. 2020 May 19;117(20):10970-10975. doi: 10.1073/pnas.2005615117. Epub 2020 Apr 29. PMID: 32350134; PMCID: PMC7245089.

Acknowledgements: We thank all contributors to the CORONA study.

Disclosure of Interests: Nikita Lomakin: None declared, Bulat Bakirov: None declared, Gaziiavdibir Musaev: None declared, Denis Protsenko: None declared, Olga Moiseeva: None declared, Elena Pasechnik: None declared, Vladimir Popov: None declared, Elena Smolyarchuk: None declared, Ivan Gordeev: None declared, Michail Gilyarov: None declared, Daria Fomina: None declared, V Mazurov: None declared, Maria Morozova Employee of: JSC BIOCAD, Ekaterina Dokukina Employee of: JSC BIOCAD, Dmitrii Bogdan Employee of: JSC BIOCAD, Anton Lutskii Employee of: JSC BIOCAD, Arina Zinkina-Orihan Employee of: JSC BIOCAD, Iulia Linkova Employee of: JSC BIOCAD, Anton Seleznev Employee of: JSC BIOCAD.

DOI: 10.1136/annrheumdis-2021-eular.2509

POS1215 INFLUENCE OF CONFINEMENT CARRIED OUT BY PATIENTS WITH AUTOIMMUNE AND IMMUNE-MEDIATED INFLAMMATORY DISEASE WITH BIOLOGICAL TREATMENT ON COVID-19 INFECTION

J. Font-Urgelles[1], S. Mínguez[1], B. Rodríguez-Diez[1], L. Creus-Vila[2], M. Esquius Rafat[2], X. Fusta Novell[2], J. Llao Guardia[3], E. Sainz Arnau[3], M. Lopez de Recalde-Martorell[1], A. Arnau Bartes[4], M. Sallés Lizarzaburu[1]. *[1]Althaia, Xarxa Assistencial Universitària de Manresa, Rheumatology, Manresa, Spain*; *[2]Althaia, Xarxa Assistencial Universitària de Manresa, Dermatology, Manresa, Spain*; *[3]Althaia, Xarxa Assistencial Universitària de Manresa, Gastroenterology, Manresa, Spain*; *[4]Althaia, Xarxa Assistencial Universitària de Manresa, Research department, Manresa, Spain*

Background: The disease caused by SARS-CoV-2 is a potentially serious infection. The autoimmune and immune-mediated inflammatory disease (AI/IMID) itself, its activity, the immunosuppression and the presence of comorbidities are associated with an increased risk of serious infections. At this moment the literature shows a similar risk of infection and severity compared to the general population. Some reports noted that these patients might adopt stricter measures of self-care protection than general population which could contribute to an incidence of infection lower than expected.

Objectives: To assess the incidence and clinical presentation of SARS-CoV-2 infection in our cohort of patients with AI/IMID treated with biological agents (BA) or Janus Kinasa (JAK) inhibitors. To analyse the association of the incidence and the type of confinement between the AI/IMID group and the general population.

Methods: A case-control study nested within a retrospective observational study was conducted from March 13th until April 23th, 2020 in Althaia, Xarxa Assistencial Universitària de Manresa. Subjects: cohort of AI/IMID patients followed by Rheumatology (inflammatory arthritis), Dermatology (psoriasis) and Digestology (inflammatory bowel disease) treated with BA/JAK inhibitors. Controls were selected from our Primary Care Centers. Main outcome: Type of confinement: strict: <1 outing / week with safety measures (SM), regular (2-3 outings with SM), lax (> 3 outings or face-to-face work with SM) and without confinement (without SM). Secondary outcome: SARS-CoV-2 infection: confirmed (PCR and/or positive serology), probable (severe illness requiring admission without PCR/serology or mild moderate with epidemiological contact) and possible (mild infection without microbiological check nor epidemiological contact); as well as severity according to the WHO.

Results: 367 patients and 193 controls were included. 45.2% of patients were men, with a mean age of 52 (SD 14.6). 47.4% were patients with rheumatologic disease, 25.3% from dermatology and 27.2% from digestive. 95.6% received a BA (66.6% anti-TNF and 33.4% non-anti-TNF) and the remaining 4.4% received JAK inhibitors. 43.3% patients had at least a risk factor compared to 37.8% in the control group (p=0.761). The Table 1 shows the incidence of COVID divided into confirmed and cumulative cases (confirmed and possible), with no significant differences. One patient (0.3%) in the case group and 3 patients (1.6%) in the control group required hospital admission (p=0.121). In relation to the type of confinement we had significant differences (p=0.013) within the AI/IMID group versus the control group in lax confinement. There were no differences in the incidence of COVID between the different confinement types.

Table 1.

	Case (n=367)	Control (n=193)	p-value	
SARS-CoV-2 infection				
Cumulative COVID	10.1 (7.2-13.6)	13.5 (9.0-19.1)	0.228	
Confirmed COVID	3.3 (1.7-5.6)	5.7 (2.9-10.0)	0.169	
Probable	2.2 (0.9-4.2)	3.1 (1.1-6.6)	0.572	
Possible	4.6 (2.7-7.3)	4.7 (2.1-8.7)	0.987	
Type of confinement				**OR (95% CI)**
Strict	59.1 (53.8-64.2)	50.3 (43.0-57.5)	0.059	1.40 (0.99-1.99)
Regular	15.4 (11.8-19.5)	14.4 (9.9-203)	0.813	1.06 (0.65-1.73)
Lax	25.0 (20.6-29.4)	34.7 (28.0-41.9)	**0.013**	**0.62 (0.42-0.91)**
No confinement	0.5 (0.1-1.9)	0.5 (0.01-0.03)	1.000	1.05 (0.09-11.7)

CI: confidence interval; OR: Odds ratio

Conclusion: The incidence of COVID-19 infection in our cohort is similar to that reported in other series of AI/IMID patients and in general population, both for confirmed cases (3.3% vs 5.7%) as well as for cumulative cases (10.1% vs 13.5%). None of our patients developed a severe form of the infection. We observed that strict confinement was predominant in both groups, being higher in the AI/IMID patients (59.1% vs 50.3%). Furthermore, lax confinement was more frequent in the control group. Although the difference was not statistically significant, the incidence of infection was higher in the control group, especially in the subjects who performed lax confinement.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2576

POS1216 SYMPTOM RATES, ATTITUDES AND MEDICATION ADHERENCE OF RHEUMATIC AND MUSCULOSKELETAL DISEASE PATIENTS DURING THE SARS-CoV2 PANDEMIC

K. Murray[1], S. Quinn[2], M. Turk[1], A. O'rourke[3], E. Molloy[1], L. O'neill[1], A. B. Mongey[1], U. Fearon[4], D. Veale[1]. *[1]Saint Vincent's University Hospital, Rheumatology, Dublin 4, Ireland*; *[2]Saint Vincent's University Hospital, Radiology, Dublin, Ireland*; *[3]St James' University Hospital, Infectious Diseases, Dublin, Ireland*; *[4]Trinity College, Trinity Biomedical Sciences Institute, Dublin 2, Ireland*

Background: SARS-CoV2 has caused over two million deaths globally. The relationship between rheumatic and musculoskeletal disease (RMDs), immunosuppressive medications and COVID-19 is unclear.

Objectives: This study explores the rates of COVID-19 symptoms and positive tests, DMARD adherence and attitudes to virtual clinics. amongst RMD patients.

Methods: An online population survey was disseminated via the Arthritis Ireland website and social media channels.

Results: There were 1381 respondents with RMD, 74.8% were on immunosuppressive medication. COVID-19 symptoms were reported by 3.7% of respondents of which 0.46% tested positive, no different from the general population at that timepoint. The frequency of COVID-19 symptoms was higher for respondents with spondyloarthropathy [odds ratio (OR) 2.06, 95% CI: 1.14, 3.70] and lower in those on immunosuppressive medication (OR 0.48, 95% CI: 0.27, 0.88), and

those compliant with health authority (HSE) guidance (OR 0.47, 95% CI: 0.25, 0.89). Adherence to RMD medications was reported in 84.1%, with 57.1% using health authority guidelines for information on medication use. Importantly, adherence rates were higher amongst those who cited guidelines (89.3% vs 79.9%, P <0.001), and conversely lower in those with COVID-19 symptoms (64.0% vs 85.1%, P =0.009). Finally, the use of virtual clinics was supported by 70.4% of respondents.

Conclusion: The rate of COVID-19 positivity in RMD patients was similar to the general population. COVID-19 symptoms were lower amongst respondents on immunosuppressive medication and those adherent to medication guidelines. Respondents were supportive of HSE advice and virtual rheumatology clinics.

Disclosure of Interests: Kieran Murray Grant/research support from: Bresnihan Molloy and Newman fellowships, Sean Quinn: None declared, Matthew Turk: None declared, Anna O'Rourke: None declared, Eamonn Molloy: None declared, Lorraine O'Neill: None declared, Anne Barbara Mongey: None declared, Ursula Fearon: None declared, Douglas Veale: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2579

POS1217 THE PATTERN OF COVID 19 PANDEMIC AMONG PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES (AIIRD)

F. Kharouf[1], T. Eviatar[2], M. Braun[3], E. Pokroy-Shapira[4], M. Brodavka[5], N. Agmon-Levin[6], K. Toledano[7], S. Oren[4], M. Lidar[5], Y. Tavor[7], M. Amit Vazina[8], F. Sabbah[9], G. Breuer[10], A. Dagan[11], D. Zisman[12], D. Markovits[7], T. Reitblat[13], S. Giryes[7], D. Mevorach[1], D. Paran[2], O. Elkayam[2], A. Balbir-Gurman[7], Y. Braun-Moscovici[7]. *[1]Hadassah Medical Center, Hebrew University of Jerusalem, Rheumatology, Jerusalem, Israel*; *[2]Tel Aviv Medical Center, Sackler School of Medicine, Tel Aviv University, Rheumatology, Tel Aviv-Yafo, Israel*; *[3]Hadassah Medical Center, Hebrew University of Jerusalem, Faculty of Medicine, Jerusalem, Israel*; *[4]Beilinson Hospital, Sackler School of Medicine, Tel Aviv University, Rheumatology, Petach Tikva, Israel*; *[5]Sheba Medical Center, Sackler School of Medicine, Tel Aviv University, Rheumatology, Tel Hashomer, Israel*; *[6]Sheba Medical Center, Sackler School of Medicine, Tel Aviv University, Allergy and Clinical Immunology Unit, Tel Hashomer, Israel*; *[7]Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion-Israeli Institute of Technology, Rheumatology, Haifa, Israel*; *[8]Shamir Medical Center, Sackler School of Medicine, Tel Aviv University, Rheumatology Unit, Beer Yaakov, Israel*; *[9]Padeh Poriya, Rheumatology, Tiberias, Israel*; *[10]Shaare Zedek Medical Center, Hebrew University of Jerusalem, Rheumatology, Jerusalem, Israel*; *[11]Assuta Ashdod Medical Center, Ben Gurion University of the Negev, Rheumatology, Ashdod, Israel*; *[12]Carmel Medical Center, Rappaport Faculty of Medicine, Technion-Israeli Institute of Technology, Rheumatology, Haifa, Israel*; *[13]Barzilai Medical Center, Ben Gurion University of the Negev, Rheumatology, Ashkelon, Israel*

Background: The epidemiology of COVID19 among patients with AIIRD may be influenced by a dysregulated immune system, immunosuppressive therapies and behavioral patterns. Data regarding the epidemiology of COVID19 among patients with AIIRD is scarce.

Objectives: To assess the pattern of COVID19 pandemic among patients with AIIRD compared to the general population in Israel

Methods: At the beginning of the COVID-19 pandemic, we established a national registry of patients with AIIRD, diagnosed with COVID-19, based on voluntary reporting by the treating rheumatologist. All the members of the Israeli Society of Rheumatology were encouraged to participate and repeatedly reminded to report any new cases. Rheumatology centers from 11 hospitals from the Northern and Central part of Israel participated in this study. The registry included demographic data, AIIRD diagnosis and duration, systemic organ involvement, co-morbidities, treatment (conventional synthetic disease modifying drugs (csDMARDs), biologic/targeted (b/ts) DMARDs, corticosteroids use, dose and treatment duration, date of COVID19 diagnosis, severity of the viral disease and complications, duration of hospitalization, if required, treatment for COVID 19, laboratory results and outcome. The diagnosis of COVID 19 was made by a positive SARS CoV2 PCR. The indications for SARS CoV2 PCR testing in Israel comprise clinical symptoms or exposure to a confirmed close contact. Severe illness was defined by SpO_2 <94% in room air, respiratory rate of >30 breaths/min, PaO_2/FiO_2 <300 mm Hg, or lung infiltrates >50% on chest imaging.

The epidemiological data regarding the number of COVID19 confirmed patients, the number of severe cases and the rate of mortality among the general population per day and per week, were extracted from the data dashboard of the Israeli Ministry of Health. We analyzed data from 02.2020 to 15.01.2021.

Results: During the study period we experienced 3 waves of COVID 19 pandemic. The governmental management of COVID19 spread, at the beginning of the pandemic, included inforcement of severe travel restrictions and social distancing, followed eventually by a preventive lockdown, in spite of the relatively low number of cases. Easing of the restrictions, lifting the travel ban, opening of the commerce and schools led to 2 much more severe waves, which triggered 2 new lockdowns. Up to January 2021, 549763 Israelis had confirmed COVID19, 30% of whom had severe disease, 0.84% died (30% of the patients with severe disease). We identified 190 AIIRD patients (mean(SD) age 52(18), 30% males) who had confirmed COVID19. The weekly incidence curve of patients with rheumatic diseases correlated with the curve of the general population (Figure 1).

Sixty-one % of the patients with AIIRD received csDMARDs, 41% were on b/tsDMARDs, 39% on chronic corticosteroids, 12% on ≥10mg prednisone. Forty-seven% of patients required hospitalization, 20% had severe COVID19. Sixteen patients (42% of patients with severe COVID19) (mean(SD), median age 64.7(15.4),67)) died (systemic sclerosis-4 patients, rheumatoid arthritis – 6, systemic lupus erythematosus – 2, antiphospholipid syndrome-2, granulomatous polyangiitis -1, polymyalgia rheumatica-1). The AIIRD was active in 56% of them, 50% received csDMARDs, none of them were on b/tsDMARDs, 31% received chronic prednisone>10 mg. All patients who died had at least 2 comorbidities.

Conclusion: The pattern of spread of COVID19 in AIIRD patients is similar to the general population despite repeated mass media alerts for enhanced social distancing for elderly and immune suppressed patients. The disease tends to be more severe with enhanced mortality, especially in those with active AIIRD disease and organ involvement (lungs, heart, renal), older age and co-morbidities. A reporting bias cannot be excluded.

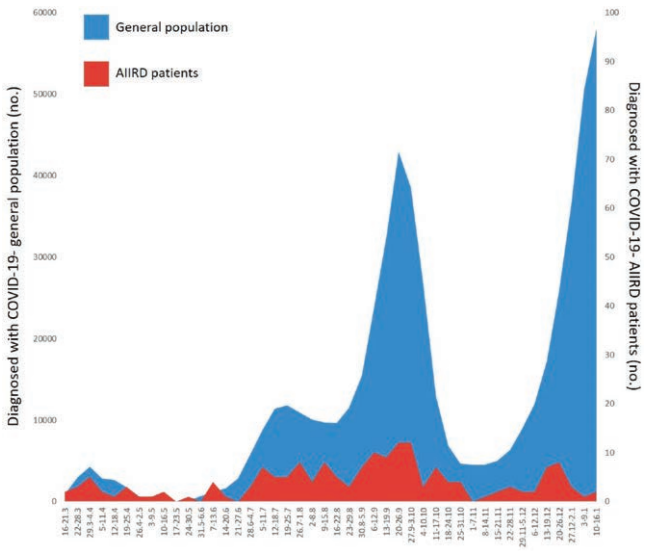


Figure 1.

Acknowledgements: Both first authors contributed equally to the manuscript.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2581

POS1218 SAFETY AND EFFICACY OF ANAKINRA IN SEVERE SARS-COV2 INFECTION (COVID19) AT A TERTIARY HOSPITAL

O. Rusinovich[1], A. Mora[2], E. Muñez[3], L. Delgado Tellez de Cepeda[3], N. De la Torre[1], M. Pavía[1], J. Sanz[1], M. Espinosa[2], J. L. Andréu Sánchez[1], J. Campos Esteban[1]. *[1]Hospital Universitario Puerta de Hierro Majadahonda, Rheumatology, Majadahonda, Spain*; *[2]Hospital Universitario Puerta de Hierro Majadahonda, Internal Medicine, Majadahonda, Spain*; *[3]Hospital Universitario Puerta de Hierro Majadahonda, Pharmacy, Majadahonda, Spain*

Background: SARS-CoV-2 virus is a novel coronavirus that causes COVID-19 disease, which in its most severe form produces life-threatening atypical pneumonia and ARDS. Coronaviruses induce dysregulation of the immune system resulting in a cytokine storm syndrome with activation of the macrophage mediated mainly by IL-1 and IL-6. Although there is no specific treatment to date, researchers have explored novel approaches through targeting both IL-6 and IL-1. Anakinra is a recombinant human IL-1 receptor antagonist that prevents IL-1β and IL-1α binding and therefore blocks signal transduction. Its high bioavailability, rapid action, relatively short half-life and good safety profile make it a promising drug.

Objectives: Analyse the experience of administering Anakinra for severe forms of COVID19 in patients hospitalised at a tertiary hospital.

Methods: Retrospective single-center study in which all patients admitted for COVID-19 and treated with Anakinra from April 1st to the end of the 1st wave

(July 2020) were included. Medical records were reviewed to collect demographic, clinical and lab test data, using Brescia-COVID respiratory severity scale, SaFi, CRP, Ferritin, LDH and lymphocytes. Variables were assessed at baseline, 72h and 7 days after treatment initiation. Descriptive statistical analysis was performed, including a sub-analysis of patients who received anakinra as the only biological treatment.

Results: 54 patients were included, of which 37 male (68.5%) with a median age of 69.5 years (36-94). Comorbidities were lung disease 14 pts (25.9%), cardiovascular disease 39 pts (72.2%), Diabetes Mellitus 11 pts (20.4%), kidney disease and rheumatic disease each in 6 pts (11.1%), and immunosuppression 13 pts (24.1%). Each patient received a mean of 4.85 doses of anakinra (± 3.96). Other therapies included low-dose steroids (70.3%); high-dose steroids: 1mg/kg (87%), bolus (24%), Tocilizumab (57.4%), Infliximab (24.1%), Lopinavir/Ritonavir (48%), Hydroxychloroquine (94.4%), and Azithromycin (79.6%). Mortality was 22% overall, 75% due to COVID19, 8.3% due to infectious complications and 16.7% due to non-infectious complications. In the group receiving Anakinra as only biological drug, mortality accounted for 17.9% of patients, 75% due to COVID19 and 25% to non-infectious complications. No adverse effects related to anakinra were observed.

	General group (n=54)			Group receiving anakinra as only biological drug (n=23)			P
	Baseline	After 72h	After 7d	Baseline	After 72h	After 7d	
Brescia-COVID Mean(SD)	1.65 (0.95) Values: 0: 11.1% 1: 31.5% 2: 42.6% 3: 53.7% 4: 3.7%	1.63 (1.13) Values: 0: 16.7% 1: 27.8% 2: 38.9% 3: 7.4% 4: 9.3%	1.73 (1.19) Values: 0: 7.9 % 1: 52.6% 2: 18.4% 3: 7.9% 4: 13.2%	1.09 (0.8) Values: 0: 26.1% 1: 47.8% 2: 21.7% 3:4.34% 4: 0%	0.91 (0.88) Values: 0: 39.1% 1: 34.8% 2: 21.7% 3: 4.34% 4: 0%	1.09 (0.8) Values: 0: 8.7 % 1: 82.6% 2: 8.7% 3: 0% 4: 0%	NS
SaFi Mean (SD)	222.60 (115.2) Values: >300: 25.9% 201-299 : 14.8% <201: 59.3%	240.51 (117.6) Values: >300: 24.5 % 201-299: 26.4% <201: 49%	250.95 (102.6) Values: >300: 34.2 % 201-299: 34.2% <201: 31.6%	306.35 (124.7) Values: >300: 56,52% 201-299: 17.39% <201: 26.1%	316.04 (129.8) Values: >300: 52.2 % 201-299: 21.7% <201: 26.1%	300.36 (135.4) Values: >300: 45.46 % 201-299: 27.27% <201: 27.27%	NS
Lymphocytes, 10^3/microL Mean (SD)	1.07 (1.5)	5.16 (3.05)	1.15 (2.49)	0.88 (0.56)	1.25 (0.79)	1.15. (2.4)	NS
Ferritine, ng/ml Mean (SD)	1098.4 (944.8)	1080.23 (873.9)	1069.19 (989.42)	1112.76 (621.80)	903.25 (385.49)	704.14 (261.86)	NS
C-reactive protein, mg/L Mean (SD)	38.78 (37.58)	21.46 (20.17)	7 (6)	50 (6.38)	34.67 (23.3)	19.96 (28.92)	NS
LDH, U/L Mean (SD)	387.64 (163.1)	394.98 (209.32)	374.26 (157.63)	326.38 (111.66)	308 (116.59)	355 (151.96)	NS
Respiratory improvement*	N/A	20.37%	51.85%	N/A	30.43%	69.5%	.007
Lab test improvement**	N/A	51.85%	77.78%	N/A	60.87%	78.2%	NS

* SaFi normalised or increased 100 mmHg or more** Improvement of 2 or more analytic variables

Conclusion: Anakinra in severe SARS-CoV-2 infection offers respiratory improvement and partial lab tests improvement. No adverse effects were observed.

Acknowledgements: We wish to acknowledge Puerta de Hierro Majadahonda COVID19 task force and all the patients and staff affected by the pandemic.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2590

POS1219 SARS-COV-2 VACCINE HESITANCY AMONG PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES: A MESSAGE FOR RHEUMATOLOGISTS

R. Priori[1,2], G. Pellegrino[1], S. Colafrancesco[1], C. Alessandri[1], F. Ceccarelli[1], M. DI Franco[1], V. Riccieri[1], R. Scrivo[1], A. Sili Scavalli[1], F. R. Spinelli[1], F. Conti[1]. [1]*Sapienza University of Rome, Department of Clinical Internal, Anesthesiological and Cardiovascular Sciences, Rome, Italy*; [2]*Saint Camillus International University of Health Sciences, Saint Camillus International University of Health Sciences, Rome, Italy*

Background: Conflicting results have been published regarding the risk of infection with SARS-CoV-2 and development of severe COVID-19 among patients affected by rheumatic musculoskeletal diseases (RMDs). [1-4] Taking into account the lack of effective drugs to treat the COVID-19 and despite the burdensome and costly lockdown measures adopted to counteract the spread of SARS-CoV-2, effective and safe vaccines appear reasonably to be the best strategy for fighting the virus. [6] Before vaccines availability, several reports showed that a non-negligible proportion of subjects, among the general population or within specific categories, would have refused vaccination against COVID-19 once possible;[6, 7] data on vaccination hesitation among patients with RMD are not available yet.

Objectives: This study aimed to evaluate the attitude of patients with RMDs to vaccination against SARS-CoV-2 and explore the factors which may influence it.

Methods: During the first weeks of Europe vaccination campaign, we proposed an online survey to Italian adult patients with RMDs followed up in the Rheumatology Unit. All patients fulfilled the most recent classification criteria for each disease. HCs were recruited using a "best friend" system. The informed consent was collected for all participants. The questionnaires included the following items: demographic features, presence of comorbidities, educational level, and ongoing therapy. The individual's perception of the COVID-19 vaccination, as well as the willingness to receive a COVID-19 vaccination with targeted questions was properly assessed.

For the statistical analyses, Mann-Whitney and Chi-square tests were used. To account for baseline clinical differences among RMD-patients and controls, multivariable logistic regression analysis was used; covariates were selected according to a clinical criterion. The hypothesis that willingness for COVID-19 vaccine varied in specific subgroups of patients was tested using interaction terms at logistic regression analysis. All statistical tests were performed using the RStudio graphical interface and all tests were two-sided with a significance level set at p<0.05.

Results: We provided an online survey to 830 adult RMD-patients and 370 healthy controls (HCs). Overall, 626 RMD-patients and 345 HCs completed the survey. Patients with RMDs were less willing to receive a COVID-19 vaccination compared to HCs (Odds Ratio (OR) 0.24, 95% CI 0.17 – 0.34, p<0.0001) despite they perceived themselves as at higher risk both to get infected (OR 11.3, 95% CI 8 – 15.9, p<0.0001) and develop a severe COVID-19 (OR 11.06, 95% CI 7.8 – 15.6, p<0.0001) and even if they had been vaccinated for influenza and pneumococcus more frequently than controls (OR 1.60 95% CI 1.18 – 2.16, p=0.002; OR 2.23, 95% CI 1.34 – 3.73, p=0.002). However, our results reveal that RMD-patients are more willing to change their minds if properly informed by the rheumatologist (OR 3.08, 95% CI 2.19 – 4.34, p<0.0001) in comparison to controls.

Conclusion: The results of our study indicate for the first time that patients with RMDs are less willing to receive COVID-19 vaccination compared to the general population, despite perceiving themselves as at higher risk of getting infected with SARS-CoV-2 and develop severe COVID-19. However, our data underscored a meaningful aspect: patients with RMDs may change their attitude to COVID-19 vaccination if properly informed about risks and benefits by their trusted specialist.

The results of this study encourage the entire rheumatologist community to become more committed to patient education, increasing their willingness to COVID-19 vaccine, which is the most promising strategy to protect them from the virus.

References: 1]Favalli EG et al. *Arthritis Rheumatol*, 2020

[2] Fredi M, et al. *Lancet Rheumatol*, 2020.

[3] Giardina F et al. Rheumatol Int 2021.

[4] Pellegrino G et al. Clin Rheumatol 2020.

[5] Frederiksen LSF, et al. *Front Immunol,* 2020.

[6] La Vecchia C et al. *Med Lav* 2020.

[7] Qiao S, et al. medRxiv 2020.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2622

POS1220 PREGNANT AND POSTPARTUM WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES AND COVID-19: A CASE SERIES

R. A. Rodriguez Chavez[1], C. M. Skinner Taylor[1], L. Pérez Barbosa[1], G. Figueroa-Parra[1], J. E. Compeán-Villegas[1], L. G. Espinosa Banuelos[1], R. Moyeda Martinez[1], A. Y. Lujano Negrete[1], A. Cárdenas[1], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Rheumatology Service, Monterrey, Mexico*

Background: Pregnant women represent a high-risk population during the COVID-19 pandemic. The main cause of maternal deaths in Mexico during 2020 was COVID-19 with 191 (21.2%) deaths registered until December 2020. The age group most affected was 30 to 34 years. Women during their third trimester and during puerperium were the most affected. Information regarding pregnant and postpartum women with autoimmune rheumatic diseases remains scarce.

Objectives: The aim of this study was to describe a COVID-19 case series from a clinic of pregnancy and rheumatic diseases.

Methods: We conducted a descriptive, retrospective study in patients from the clinic of pregnancy and rheumatic diseases of the University Hospital "Dr. Jose Eleuterio Gonzalez" in Monterrey, Mexico. Pregnant patients with RD and documented COVID-19 between March and November 2020 were included. Demographic and clinical features were obtained. Results are shown in descriptive statistics.

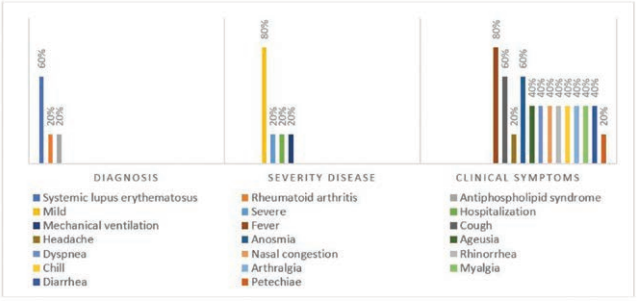
Results: From the 18 women with autoimmune rheumatic disease in follow-up during this period, 2 (11.1%) pregnant women, 2 (11.1%) postpartum women, and 1(5.5%) post-miscarriage woman developed COVID-19. The mean age was 28 ± 6.3 years, 3 (60%) had systemic lupus erythematosus, 1 (20%) had rheumatoid arthritis, and 1 (20%) had the antiphospholipid syndrome. Clinical features and treatments are shown in Graphic 1 and Table 1. The most frequent symptoms were fever (80%), cough (60%) and anosmia (60%). Four (80%) had mild symptoms, and 1 (20%) had severe symptoms requiring intensive care unit admission and mechanical ventilation. Three (60%) referred history of contact with a person who had COVID-19. All the patients were using hydroxychloroquine and prednisone. No patient in our study died.

Conclusion: From our population, a total of 27.8% presented COVID-19. Most of our patients had a mild course of SARS-CoV-2 infection consistent with data from the general population. Additionally, none of our patients had risk factors such as hypertension, diabetes, chronic kidney disease or lung disease. Nonetheless, pregnant women remain a vulnerable population. Prevention measures must continue worldwide to avoid additional COVID-19 morbidity and mortality.

REFERENCES:

[1] Gob.mx. 2021. *INFORME SEMANAL DE NOTIFICACIÓN INMEDIATA DE MUERTE MATERNA*. [online] Available at: <https://www.gob.mx/cms/uploads/attachment/file/601780/MM_2020_SE51.pdf> [Accessed 10 January 2021].

[2] Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *JAMA.* 2020;323(16):1612–1614. doi:10.1001/jama.2020.4326



Graphic 1. Diagnosis, severity disease and clinical symptoms of pregnant rheumatic disease patients with COVID-19

Table 1. Features, preventive measures, and treatments of pregnant rheumatic disease patients with COVID-19

	N=5
Age, years, mean (SD)	28 (6.36)
Obesity, n (%)	2 (40)
Current occupation, n (%)	
Employee	3 (60)
Student	1 (20)
Housewife	1 (20)
Positive PCR test, n (%)	5 (100)
Prevention measures, n (%)	
Social Distancing	2 (40)
Quarantine	3 (60)
Contact with a person who had COVID-19	3 (60)
Treatments used before disease, n (%)	
Prednisone	5 (100)
Hydroxychloroquine	5 (100)
Sulfasalazine	2 (40)
Azathioprine	1 (20)
Methotrexate*	1 (20)
Rheumatic treatment during disease, n (%)	
Continued	3 (60)
Suspended	2 (40)

PCR: polymerase chain reaction, *Methotrexate was used during conception and suspended immediately after the pregnancy detection.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2641

POS1221

SARS-COV2 SEROLOGY SCREENING IN SPONDYLOARTHRITIS PATIENTS IN NORTH-EASTERN ITALY: A PILOT STUDY

A. Ortolan[1], C. Cosma[2], M. Lorenzin[1], G. Cozzi[1], A. Doria[1], M. Plebani[2], R. Ramonda[1]. [1]*University of Padova, Rheumatology Unit, Department of Medicine DIMED, Padova, Italy*; [2]*University of Padova, Department of Laboratory Medicine, Department of Medicine DIMED, Padova, Italy*

Background: Serology could help defining the real extent of Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV2) diffusion in the population, especially in individuals considered at higher risk of SARS-CoV2 infection (COVID-19), such as Spondiloarthritis (SpA) patients undergoing immunosuppressive therapy or health care workers (HCW). In fact, COVID-19 detection is complicated by the fact that many patients can be asymptomatic. In these cases, it has also been suggested that a weaker immune response might be elicited.
In this context, the role of anti-cytokine targeted therapy –commonly used as treatment in SpA- is uncertain, as it is not clear whether it is detrimental or protective towards severe disease forms.

Objectives: The aim of the study was to explore the potential role of serology in detecting previous contact with SARS-CoV2 in SpA patients and HCW, and compare the frequency of positive findings with a control population.

Methods: Consecutive patients affected by axial or peripheral SpA, classified according to Assessment of SpondyloArthritis international Society (ASAS) criteria and undergoing cytokine-targeted therapy, as well as HCW and controls from the pre-COVID-19 era (control group, 2015) were recruited. In SpA patients, disease activity was assessed by Ankylosing Spondylitis Disease Activity Score (ASDAS) and Disease Activity Score on 28-joint-count (DAS28).
Sera from all patients were analysed through chemiluminescent analytical system (CLIA) for the presence of IgG and IgM anti-SARS-CoV2. Patients with a positive serological test (either IgM or IgG) additionally underwent real time Polymerase Chain Reaction (RT-PCR) in nasopharyngeal swabs in order to test for active infection. In SpA patients, serology was repeated after 3 months. Data across the 3 groups were compared by ANOVA or Chi-square, while comparison between 2 groups were conducted by Wilcoxon signed rank test or Chi-Square, for continuous and categorical data respectively. $P \leq 0.05$ were considered as significant.

Results: A total of 396 patients were recruited: 200 SpA, 95 HCW and 101 healthy controls. SpA patients were mostly (54%) males, with mean age 49.6 ±14.7 years, and all were treated with anti-TNFα (78%), anti-IL-17 (9%) and anti-IL-23 drugs (7%), or small molecules (6%). Their disease activity level was moderate-low as assessed by ASDAS (1.95 ±0.98) and DAS28 (2.33 ±2.02). Among HCW and controls, 35% and 62% were male, with mean age 46.7 ±12.9 and 50.6±10.6 respectively.
Positive serology (IgM or IgG, or both) was found in 12.5% SpA patients, 8.4% HCW, 0% controls (p=0.001). Among these, IgM titres were higher in the SpA group than in HCW (2.76±2.94 versus 0.80±0.67 KU/L, p= 0.016), while IgG mean titres were lower in the SpA group than in HCW (0.88±3.18 KU/L versus 1.05±0.88, p= 0.035). SpA patients with positive serology more frequently reported COVID-19 like symptoms than those with negative serology (20% vs 4%, p=0.009) and 2 had COVID-19 as confirmed by RT-PCR, none with a severe disease course. None of the HCW reported symptoms or tested positive by RT-PCR. In the SpA patients, at 3 months, the mean IgM titre decreased from 2.76±2.93 to 2.38±2.95 (p=0.001), while the IgG titres decreased from 0.89±3.25 to 0.31±0.87 (p=ns). Interestingly, the IgM or IgG titer at a single-patient level did not seem to change much in terms of absolute value (Figure 1), except in one patient, with documented COVID-19 (positive RT-PCR), in whom IgG level even decreased at 3 months.

Conclusion: Serology revealed that exposure to COVID-19 in SpA patients, as well as HCW, was higher than expected based on reported symptoms. Targeted anti-cytokine therapy could act as a protective factor for a severe disease course in SpA patients. However, in this population, IgG and IgM titres did not change in a clinically significant manner at 3 months, and patient did not seem to develop an immune profile consistent with durable response. This result could be due to a weaker immune response in mild infections, but further studies are warranted to clarify the pathophysiology beyond these observations.

Figure. Levels of IgM and IgG anti-Severe Acute Respiratory Syndrome-coronavirus 2 (SARS-CoV2) at baseline and 3 months in spondyloarthritis patients

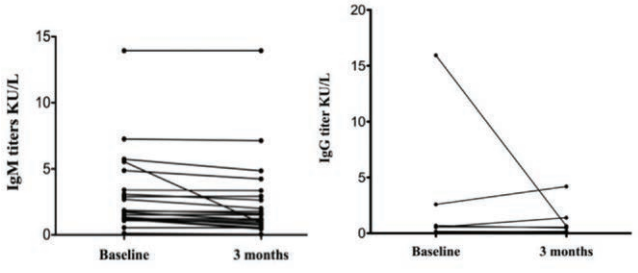


Figure 1.

Disclosure of Interests: Augusta Ortolan: None declared, Chiara Cosma: None declared, Mariagrazia Lorenzin: None declared, Giacomo Cozzi: None declared, Andrea Doria Speakers bureau: Novartis, Abbvie, Pfizer, MSD, Janssen, Glaxosmithkline, Mario Plebani: None declared, Roberta Ramonda Speakers bureau: Novartis, Abbvie, Pfizer, MSD, Janssen
DOI: 10.1136/annrheumdis-2021-eular.2681

POS1222

FACTORS ASSOCIATED WITH USE OF TELEMEDICINE FOR FOLLOW-UP OF LUPUS NEPHRITIS IN THE COVID-19 OUTBREAK

H. So[1], E. Chow[1], T. K. LI[1], I. T. Cheng[1], S. L. Lau[1], C. C. Szeto[1], L. S. Tam[1]. [1]*The Chinese University of Hong Kong, Medicine and Therapeutics, Hong Kong, Hong Kong (SAR)*

Background: It is important to weigh the potential risk of exposure to the severe acute respiratory syndrome coronavirus 2 (*SARS-CoV-2*) during a doctor visits against the risk of missing disease controls in patients with lupus nephritis during the COVID-19. Telemedicine (TM) follow-up is a reasonable option. Despite the recent exponential increase in application worldwide, there is no study examining the clinical factors associated with the patients' choice of TM use in lupus nephritis.
Objectives: In this study, we aimed to examine the clinical variables associated with a higher preference for TM follow-up in patients with lupus nephritis.
Methods: Consecutive patients followed at the lupus nephritis clinic were contacted for their preferred mode of follow-up. The demographic, socioeconomic and clinical data of the first 140 patients opted for TM and 140 patients preferred to continue standard in-person follow-up were collected and compared.
Results: The mean age of the 280 recruited patients was 45.6 ± 11.8 years. The mean disease duration was 15.0 ± 9.2 years. The majority of them had lupus nephritis class III, IV or V (88.2%) and were on prednisolone (90%). Three quarters of the patients (67.1%) were on immunosuppressants. The mean SLEDAI-2k was 4.06 ± 2.54, physician global assessment (PGA) 0.46 ± 0.62 and SLICC/ACR damage index 1.11 ± 1.36. A significant proportion of the patients (72.1%) had one or more comorbidities. It was found that patients with higher PGA and family monthly income (> USD3,800) preferred TM, while fulltime employees preferred in-person follow-up (Table 1). These predictors remained significant after controlling for age in the multivariate analysis with odd ratios for PGA 1.05 (95% CI 1.01-1.09), family income >USD3,800 1.90 (95% CI 1.24-3.79) and fulltime employment 0.53 (95% CI 0.32-0.88). PGA was noted to be positively correlated with the perceptions that TM reduces (r=0.13, p=0.036) and routine visit increases (r=0.12, p=0.04) the risk of COVID-19 during the outbreak.
Conclusion: When choosing the mode of care delivery between TM and clinic visit, the patient's disease activity as well as employment and economic status appeared to be important.

Table 1. Demographic, socio-economic and disease data of the recruited lupus nephritis patients with comparison between the telemedicine/standard follow-up groups

	Overall (n=280)	Telemedicine group (n=140)	Standard follow-up group (n=140)	P-value
Age in years	45.6±11.8	44.6±11.4	46.6±12.1	0.159
Gender: Female	256 (91.4)	127 (90.7)	129 (92.1)	0.669
Ever presence of rash	170 (60.8)	87 (62.1)	82 (58.6)	0.527
Ever presence of joint pain	174 (62.1)	92 (65.7)	82 (58.6)	0.247
Disease duration in months	15.8±9.5	15.0±9.3	16.5±9.6	0.176
24 hour urine proteinuria in gram	0.45±0.60	0.50±0.63	0.40±0.57	0.176
Daily prednisolone dose in mg	8.82±6.1	5.28±4.46	6.35±7.37	0.143
Use of immunosuppressant	188 (67.1)	96 (68.6)	92 (65.7)	0.611
SLEDAI-2K	3.39±2.35	3.51±2.28	3.26±2.41	0.366
PGA	0.46±0.62	0.54±0.63	0.38±0.59	**0.025**
LLDAS	196 (70)	92 (0.66)	104 (74.3)	0.160
Presence of comorbidity	202 (72.1)	100 (71.4)	102 (72.9)	0.790
SDI	0.97±1.23	0.95±1.21	1.00±1.26	0.732
HAQ-DI	0.20±0.40	0.23±0.45	0.18±0.34	0.300
HADS: Anxiety scale	5.93±3.98	5.86±4.06	6.00±3.91	0.776
Depression scale	5.57±3.91	5.56±4.25	5.59±3.54	0.954
Education level: tertiary or above	122 (43.6)	63 (45.0)	59 (42.1)	0.746
Fulltime employment	127 (45.4)	56 (40.0)	71 (50.7)	**0.041**
Occupation: professionals	36 (12.9)	22 (15.7)	14 (10.0)	0.181
Monthly family income > USD3,800	84 (30.0)	51 (36.4)	33 (23.6)	**0.028**

Data are reported as mean ± SD or number (%). HAQ-DI: Health Assessment Questionnaire Disability Index; *HADS:* Hospital Anxiety and Depression Scale; PGA: physician global assessment; LLDAS: lupus low disease activity state and SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index.

Disclosure of Interests: Ho SO: None declared, Evelyn Chow: None declared, Tena K. Li: None declared, Isaac T. Cheng: None declared, Sze-Lok Lau: None declared, Cheuk-Chun Szeto: None declared, Lai-Shan Tam Grant/research support from: Grants from Novartis and Pfizer
DOI: 10.1136/annrheumdis-2021-eular.2751

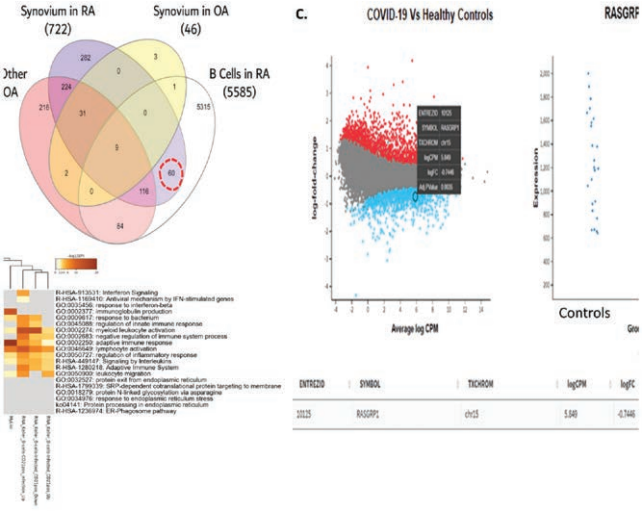
POS1223

RAS GUANYL RELEASING PROTEIN 1 (RASGRP1) IN PERIPHERAL B CELLS LINKS RA TO COVID-19

S. Hannawi[1], F. Alqutami[2], M. Y. Hachim[2]. [1]*Ministry of Health and Prevention MOHAP, Rheumatology, Dubai, United Arab Emirates*; [2]*Mohammed Bin Rashid University of Medicine and Health Sciences, Basic Sciences, Dubai, United Arab Emirates*

Background: Changes in the B cell subpopulations is a hallmark of the antiviral response against SARS-CoV-2 and is associated with COVID-19 severity (1). Recently our group showed common derangement observed in rheumatoid arthritis (RA) and COVID-19 (2). In RA, synovium attracts potentially autoreactive—B cells and plasma cells that play a central role in RA pathogenesis (3). We were interested to know the similarity in B cell's transcriptomic changes specific to RA and COVID-19.
Objectives: Identify similar upregulated genes in synovium and B cells in RA and at the same time are differentially expressed in B cells infected with SARS-CoV-2 or from COVID-19 patients.
Methods: RNAseq dataset (GSE89408) of (218) samples isolated from joint synovial biopsies from subjects with and without rheumatoid arthritis were retrieved from GEO online database. Differentially expressed genes (DRGs) specific to RA were identified after exclusion of those upregulated in Osteoarthritis or other joint condition samples in the same dataset. The RA specific genes were intersected with DEGs between B cells from healthy versus RA as extracted from (GSE110999) dataset. The shortlisted genes specifically upregulated in B cells of RA were identified and were explored in B cells COVID-19 transcriptome datasets using (https://metascape.org/COVID).
Results: 60 genes were found to be specifically upregulated in RA synovium and B cells and are changed in B cells infected with SARS-CoV-2 or from COVID-19 patients, Figure (1-A). Those genes were involved in interferon signaling, antiviral and immune cell activation. RASGRP1 was common between B cells of RA and COVID-19 and might play a role in the pathogenesis of both, Figure (1-B). RASGRP1 controls ERK/MAPK kinase cascade needed in B-/T-cell differentiation and development. It is vital to protect against viral infection and the autoimmune associated proliferation of activated T-cells like RA (4). We checked its level in another dataset (GSE152641) of the whole blood RNASeq of 62 COVID-19 patients and 24 healthy controls. RASGRP1 was significantly down in COVID-19 compared to healthy control, Figure (1-C).
Conclusion: SARS-CoV-2 impair B and T's cells' immune response through its action on RASGRP1 and that can be a novel mechanistic explanation of how the virus decreases immune cells and impair the B cell's humoral immunity.
REFERENCES:

[1] Sosa-Hernández VA, Torres-Ruíz J, Cervantes-Díaz R, Romero-Ramírez S, Páez-Franco JC, Meza-Sánchez DE, et al. B Cell Subsets as Severity-Associated Signatures in COVID-19 Patients. Frontiers in Immunology. 2020;11(3244).
[2] Hachim MY, Hachim IY, Naeem KB, Hannawi H, Al Salmi I, Hannawi S. C-C chemokine receptor type 5 links COVID-19, rheumatoid arthritis, and Hydroxychloroquine: in silico analysis. Translational Medicine Communications. 2020;5(1):14.
[3] Doorenspleet ME, Klarenbeek PL, de Hair MJ, van Schaik BD, Esveldt RE, van Kampen AH, et al. Rheumatoid arthritis synovial tissue harbours dominant B-cell and plasma-cell clones associated with autoreactivity. Ann Rheum Dis. 2014;73(4):756-62.
[4] Molineros JE, Singh B, Terao C, Okada Y, Kaplan J, McDaniel B, et al. Mechanistic Characterization of RASGRP1 Variants Identifies an hnRNP-K-Regulated Transcriptional Enhancer Contributing to SLE Susceptibility. Frontiers in Immunology. 2019;10(1066).



The B cells markers upregulated in B cells infected with SARS-CoV-2 and are specifically DEGs in B cells and) Venn diagram showing shared DEGs in synovium and B cells in RA generated by http://www.interactivenn.ne the RA and COVID-19 DEGs genes as generated by (https://metascape.org/COVID). (C) Normalized gen n whole blood of 62 COVID-19 patients and 24 healthy controls

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2809

POS1224

RHEUMATIC MANIFESTATIONS IN COVID-19 PATIENTS - SINGLE-CENTER EXPERIENCE AMIDST THE PANDEMIC

S. Bogdanova-Petrova[1,2], T. Georgiev[1,2], G. Gerganov[2,3], S. Hristova[2,4], S. Dimitrov[1,2], T. Shivacheva[1,2]. [1]*Medical University - Varna, First Department of Internal Medicine, Varna, Bulgaria*; [2]*St. Marina's Hospital, Rheumatology Clinic, Varna, Bulgaria*; [3]*Medical University - Varna, Department of Propedeutics of Internal Medicine, Varna, Bulgaria*; [4]*Medical University - Varna, Department of General Medicine and Clinical Laboratory, Varna, Bulgaria*

Background: Recently evolved from a monochromic flu-like disease to a polysyndromic "spectrum of disease", our understanding of coronavirus disease 2019 (COVID-19) is still far from being complete [1]. Hyperinflammation involving not only the lungs but also the musculoskeletal system, skin, cardiovascular, genitourinary systems is immune-mediated resembling the flares of a full-blown rheumatic disease [2,3].

Objectives: To describe the prevalence and type of rheumatic manifestations in a cohort of COVID-19 patients hospitalized in the COVID-19 rheumatology department in University Hospital St. Marina, Varna, Bulgaria.

Methods: In the present single-center cohort study, a retrospective database analysis was performed among all COVID-19 patients hospitalized from 1 Dec 2020 to 22 Jan 2021. All 243 patients (age 19 - 93 years) were treated for moderate or severe SARS-CoV-2 infection confirmed by laboratory tests, including positive polymerase chain reaction (PCR) test, and imaging modality. Inpatient treatment included antibiotics, dexamethasone, anticoagulants, and antiviral drug remdesevir (optional). Detailed disease history and clinical examination were carried out by a fully certified rheumatologist and/or specialist in internal medicine.

Results: Among all 243 COVID-19 patients, those with prominent self-reported myalgia and arthralgia were 26% (n = 63) and 21.3 (n = 52), respectively. We had 4 (1.6%) cases of newly developed cutaneous vasculitis and 2 (0.8%) cases of severe Raynaud's phenomenon after SARS-CoV-2 infection onset. Two patients experienced severe muscle weakness, had elevated creatine phosphokinase, and were diagnosed with inflammatory myopathy secondary to COVID-19. Lupus-like syndrome was observed in 2 (0.8%) patients.

Conclusion: Rheumatic manifestations are part of the heterogeneous spectrum of COVID-19 disease. Amidst the COVID-19 crisis, each newly onset rheumatic manifestation warrants exclusion of SARS-CoV-2 infection. Therefore, a rheumatologist should be a part of a multidisciplinary approach towards the COVID-19 treatment.

REFERENCES:

[1] Misra DP, Agarwal V, Gasparyan AY, Zimba O. Rheumatologists' perspective on coronavirus disease 19 (COVID-19) and potential therapeutic targets. Clin Rheumatol. 2020;39(7):2055-2062

[2] Georgiev T, Angelov AK. Complexities of diagnosis and management of COVID-19 in autoimmune diseases: Potential benefits and detriments of immunosuppression. World J Clin Cases. 2020;8(17):3669-3678

[3] Ciaffi J, Meliconi R, Ruscitti P, Berardicurti O, Giacomelli R, Ursini F. Rheumatic manifestations of COVID-19: a systematic review and meta-analysis. BMC rheumatology. 2020 Dec;4(1):1-5.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2836

POS1225

INFLUENCE OF COLCHICINE PRESCRIPTION IN COVID19-RELATED HOSPITAL ADMISSIONS: A SURVIVAL ANALYSIS

M. P. Álvarez[1], A. Madrid García[1,2], I. Perez-Sancristobal[1], J. I. Colomer[1], L. León[1], J. A. Jover[1], B. Fernandez[1], L. Abasolo[1], L. Rodriguez Rodriguez[1]. [1]*Health Research Institute (IdISSC), Hospital Clínico San Carlos, Rheumatology Department, Madrid, Spain*; [2]*Escuela Técnica Superior de Ingenieros de Telecomunicación (ETSIT), Universidad Politécnica de Madrid, Madrid, Spain*

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), triggers the innate immune system, leading in severe cases, an excessive immune response, which can lead to high levels of pro-inflammatory cytokines promoting a "cytokine storm".

To modulate this exaggerated inflammatory response, several clinical trials with already approved and well-known therapeutic agents that inhibit the inflammatory response, are being carried out. However, none of these drugs seems to achieve the desired results when treating COVID19.

Colchicine, a drug often used in the management of patients with Rheumatic and Musculoskeletal diseases (RMDs), is one of the several drugs that are being currently tested for efficacy in COVID19 due to its anti-inflammatory effects.

Objectives: To analyze association between colchicine prescription and COVID19-related hospital admissions in patients with Rheumatic and Musculoskeletal diseases (RMDs).

Methods: Patients attending a rheumatology outpatient clinic from a tertiary care center in Madrid, Spain, from 1st September 2019 to 29th February 2020 were included.

Patients were assigned as exposed or unexposed based on whether they were prescribed with colchicine in their last visit to the clinic during the 6 months before the start of the observation period. Treatment changes during the observation period were also considered. The primary outcome was COVID19-related hospital admissions occurring between March 1st and May 20th, 2020. Secondary outcome included COVID19-related mortality. Several weighting techniques for data balancing, based and non-based on the propensity score, followed by Cox regressions were performed to estimate the association of colchicine prescription on both outcomes.

Results: 9,379 patients entered in the study, with 406 and 9,002 exposed and unexposed follow-up periods, respectively. Generalized Boosted Models (GBM) and Empirical Balancing Calibration Weighting (EBCW) methods showed the best balance for COVID19-related hospital admissions. Colchicine prescription did not show a statistically significant association after covariable balancing (p-value = 0.195 and 0.059 for GBM and EBCW, respectively). Regarding mortality, the low number of events prevented a success variable balancing and analysis.

Conclusion: Colchicine prescription does not play a significant protective or risk role in RMD patients regarding COVID19-related hospital admissions. Our observations could support the maintenance of colchicine prescription in those patients already being treated, as it is not associated with a worse prognosis.

REFERENCES:

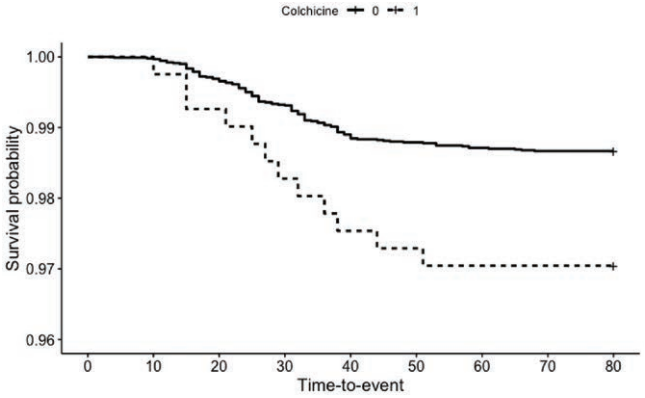
[1] Fernandez-Gutierrez B. COVID-19 with Pulmonary Involvement. An Autoimmune Disease of Known Cause. *Reumatol Clin* 2020; 16: 253–254.

[2] Coperchini F, Chiovato L, Croce L, et al. The cytokine storm in COVID-19: An overview of the involvement of the chemokine/chemokine-receptor system. *Cytokine Growth Factor Rev* 2020; 53: 25–32.

[3] Shaffer L. 15 drugs being tested to treat COVID-19 and how they would work. *Nat Med*. Epub ahead of print 15 May 2020. DOI: 10.1038/d41591-020-00019-9.

[4] Fernandez-Gutierrez B, Leon L, Madrid A, et al. Hospital admissions in inflammatory rheumatic diseases during the COVID-19 pandemic: incidence and role of disease modifying agents. *medRxiv* 2020; 2020.05.21.20108696.

[5] Freites Nuñez DD, Leon L, Mucientes A, et al. Risk factors for hospital admissions related to COVID-19 in patients with autoimmune inflammatory rheumatic diseases. *Ann Rheum Dis* 2020; 1–7.



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2845

POS1226

THE COURSE OF CORONAVIRUS DISEASE 2019 (COVID-19) IN PATIENTS WITH SJOGREN'S SYNDROME TREATED WITH ANTI-CD20 MONOCLONAL ANTIBODY (RITUXIMAB)

E. Sokol[1], A. Torgashina[1], B. Chalcev[1], J. Khvan[1], O. Golovina[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Intensive Care of Rheumatic Diseases, Moscow, Russian Federation*

Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19) raised concern for the outcomes in people with different rheumatic diseases and management of these patients. There was an anxiety that biologic therapies, especially anti-B-cell depletion strategies, could lead to more severe disease course and lack of protective antibodies formation.

Information about the course of COVID-19 in patients with certain rheumatic diseases is still lacking.
Objectives: To examine clinical course of COVID-19 in patients with Sjogren's syndrome treated with anti-CD20 monoclonal antibody (rituximab).
Methods: Single center observational study. Diagnosis of SjS was based on ECR/EULAR 2016 criteria. COVID-19 diagnosis was based on positive PCR test even without clinical symptoms and/or typical clinical features (CT signs, fever and anosmia). Rituximab was administrated in two 1000 mg infusions 14 days apart for the 1st course, then 500 mg every 6 months.
Results: 19 patients were included, 18 women and 1 man. Median age was 55 years (29-70 years), and median rituximab treatment duration was 24 months (1-48 months). Five patients had concomitant RA (2 patients), SLAE (1 pt), Systemic sclerosis (2 patients). Patients with RA took baricitinib and methotrexate as well. 3 patients had MALT-lymphoma anamnesis (24, 38 and 24 months before the diagnosis of COVID-19). Only 3 patients had chronic ischemic heart disease and/or arterial hypertension. 12 patients were PCR positive, 6 negative and in 1 the test was not done. 11 patients had full and 4 partial B-cell depletion in peripheral blood. Five patients had <20% lung involvement on CT, 2 patients – 20-40% and 4 patients – 40-60%. Three patients with 40-60% lung involvement required hospitalization due to marked shortness of breath and long febrile period, 2 of them received anti-IL6 treatment and neither of them required mechanical lung ventilation (either non-invasive or invasive). Seventeen patients were treated at home and recovered in 10-24 days. Anti-SARS-CoV-2 IgG were measured in 9 patients, 6 (66.7%) of them were positive.
Conclusion: It seems that neither SjS itself nor anti-CD20 therapy predisposes patients to severe course of COVID-19. Presumably risk factors such as age, diabetes or anamnesis of cardiovascular diseases have far more significant impact on COVID-19 severity. Data hints that anti-CD20 therapy might negatively affect the formation of specific anti-SARS-CoV-2 humoral immunity, but further investigation is required to determine that with any degree of certainty.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2933

POS1227 IMPACT OF A PRE-EXISTING INTERSTITIAL LUNG DISEASE ON SEVERITY OF COVID-19 IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

P. A. Juge[1], E. Hachulla[2], C. Richez[3], E. Drumez[4], A. Duhamel[4], R. Borie[5], P. Dieudé[1]. [1]*Bichat-Claude Bernard Hospital, Rheumatology, Paris, France*; [2]*Chu De Lille, Internal Medecine, Lille, France*; [3]*Hospital Center University De Bordeaux, Rheumatology, Bordeaux, France*; [4]*Chu De Lille, Biostatistic, Lille, France*; [5]*Bichat-Claude Bernard Hospital, Pulmonology, Paris, France*

Background: COVID19 due to SARS-CoV-2 infection implies an important anti-viral immune response leading to a major inflammatory syndrome with increased pro-inflammatory cytokine levels (*i.e*. the cytokine storm paradigm). The impact of a preexisting interstitial lung disease (ILD) on the morbi-mortality of COVID-19 is unclear. An increased mortality rate has been identified in studies that included a limited number of patients with ILD from various etiologies. To date, no studies have investigated the severity of COVID-19 in patients with preexisting ILD in a large population of rheumatic and musculoskeletal diseases (RMD-ILD). Since March 18th, 2020, the French RMD COVID19 dataset (NCT04353609) includes patients with an RMD and SARS-Cov-2 infection.
Objectives: To assess the impact of a preexisting ILD on COVID-19 morbi-mortality within the French RMD COVID-19 dataset.
Methods: Patients from the French RMD COVID-19 dataset were included in the analysis. COVID-19 diagnosis was established by a positive SARS-CoV-2 PCR test and/or typical symptoms or chest CT scans pattern during the period of the pandemic. Baseline phenotypic characteristics of the RMD including pre-existing ILD prior to the SARS-CoV-2 infection were collected. COVID-19 evolution was characterized as benign (ambulatory care), moderate (hospitalization outside intensive care unit [ICU]) and severe (hospitalization in ICU). Association between the ILD status and the severity and mortality rate of COVID-19 was assessed using multivariable logistic regression adjusted on sex, age, body mass index and diabetes.
Results: By June 26, 2020, 897 patients were included. Pre-existing ILD was reported in 27 patients (3%): 11 patients with systemic sclerosis, 8 with rheumatoid arthritis, 2 with auto-immune myositis, 2 with mixed connective tissue disease and 4 with other RMD. Among these 27 patients (11 male, mean age 63.1 ± 16.4 y/o, 56.5% having a usual interstitial pneumonia HRCT pattern), 22 had severe infection. Death related to COVID-19, was observed in 58 patients with RMD without ILD (7.1%) and in 10 patients with RMD-ILD (37%). Having a preexisting ILD was found to be independently associated with an increased risk of severe COVID-19 (adjusted OR=7.6 [2.9 – 20.2], P<0.001) and an increased mortality rate (adjusted OR=12.3 [3.8 – 39.2], P<0.001).
Conclusion: In RMD patients with SARS-CoV-2 infection, preexisting ILD was associated with an increased risk to severe COVID-19 and related mortality. Our findings suggest that RMD-ILD patients should be prioritized for COVID-19 vaccination according to the high morbi-mortality rate during SARS-CoV-2 infection.
Disclosure of Interests: Pierre-Antoine Juge Consultant of: BMS, Eric Hachulla Consultant of: Actelion, Bayer, GSK and Pfizer, Grant/research support from: Actelion, Bayer, GSK and Pfizer, Christophe Richez: None declared, Elodie Drumez: None declared, Alain Duhamel: None declared, Raphael Borie: None declared, Philippe Dieudé: None declared
DOI: 10.1136/annrheumdis-2021-eular.2934

POS1228 THE ROLE OF CHEST CT IN UNDERSTANDING INTERSTITIAL LUNG DISEASE (ILD): SYSTEMIC SCLEROSIS (SSC). VERSUS COVID-19

M. Orlandi[1,1], N. Landini[2], G. Sambataro[3], C. Nardi[4], C. Bruni[1], S. Bellando-Randone[1], C. Denton[5], F. Luppi[6], B. Ruaro[7], S. Tomassetti[1], E. Cavigli[8], F. Melchiorre[9], S. Palmucci[10], S. Guiducci[1], A. Moggi Pignone[1], Y. Allanore[11], A. Bartoloni[1], M. Confalonieri[12], G. Cortese[13], L. Dagna[14], F. De Cobelli[15], A. De Paulis[16], S. Harari[17], D. Khanna[18], M. Kuwana[19], V. Miele[8], G. Taliani[20], M. Hughes[21], C. Vanchieri[22], S. Colagrande[2], M. Matucci-Cerinic[23]. [1]*University of Florence, Department of Experimental and Clinical Medicine, Florence, Italy*; [2]*University of Florence, Department of Experimental and Clinical Biomedical Sciences, Radiodiagnostic Unit n. 2, Florence, Italy*; [3]*University of Catania, Dept. of Clinical and Experimental Medicine, Catania, Italy*; [4]*University of Florence, Department of Experimental and Clinical Biomedical Sciences, Radiodiagnostic Unit n. 2, Florence, Italy*; [5]*Centre Head and Professor of Experimental Rheumatology, Experimental Rheumatology, London, United Kingdom*; [6] *University of Milano-Bicocca, S. Gerardo Hospital, Respiratory Unit, Monza, Italy*; [7]*University Hospital of Cattinara, Department of Pulmonology, Trieste, Italy*; [8]*AOUC Careggi, SOD Radiodiagnostica Emergenza-Urgenza, Florence, Italy*; [9]*Sant'Andrea Hospital Vercelli, Department of Radiology, Vercelli, Italy*; [10]*University of Catania, Department of Medical Surgical Sciences and Advanced Technologies, Catania, Italy*; [11], *Descartes University, APHP, Cochin Hospital, Department of Rheumatology A, Paris, Italy*; [12]*University Hospital of Cattinara, Department of Pulmonology, Trieste, Italy*; [13]*OSPEDALE MARIA VITTORIA e AMEDEO DI SAVOIA, S.C. RADIOLOGIA, Torino, Italy*; [14]*IRCCS San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milano, Italy*; [15]*RCCS San Raffaele Scientific Institute, Department of Radiology I, Milano, Italy*; [16]*University of Naples Federico II, Department of Translational Medical Sciences, Naples, Italy*; [17]*Ospedale San Giuseppe MultiMedica, IRCCS, Department of Pulmonology, Milan, Italy*; [18] *University of Michigan, Ann Arbor, MI, Department of Medicine, Michigan, United States of America*; [19]*Nippon Medical School Graduate School of Medicine, Department of Allergy and Rheumatology, Tokyo, Japan*; [20] *Sapienza University, Rome, Department of Translational and Precision Medicine, Rome, Italy*; [21]*Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK, United Kingdom*; [22] *University of Catania, Dept. Of Clinical and Experimental Medicine, Catania, Italy*; [23]*University of Florence, Dept. Of Clinical and Experimental Medicine, Florence, Italy*

Background: COVID-19 pandemic is a global emergency which may overlap on the clinical and radiological scenario of ILD in SSc. In clinical practice, the striking similarities observed at computed tomography (CT) between the diseases make it difficult to distinguish a COVID-19 superinfection from a progression of SSc-ILD.
Objectives: The aim of our study was to identify the main CT features that may help distinguishing SSc-ILD from COVID-19 pneumonia.
Methods: 22 international readers were included and divided in the radiologist group (RAD) and non-radiologist group (nRAD). The RAD group included non-chest RAD and chest-RAD. A total of 99 patients, 52 with COVID-19 and 47 with SSc-ILD, were included in the study.
Results: Fibrosis inside focal ground glass opacities (GGO) in the upper lobes; fibrosis in the lower lobe GGO; reticulations in lower lobes (especially if bilateral and symmetrical or associated with signs of fibrosis) were the CT parameters most frequently associated with SSc-ILD. The CT parameters most frequently associated with COVID- 19 pneumonia were: consolidation (CONS) in the lower lobes, CONS with peripheral (both central/peripheral or patchy distributions), anterior and posterior CONS and rounded-shaped GGOs in the lower lobes. After multivariate analysis, the presence of CONS in the lower lobes (p <0.0001) and signs of fibrosis in GGO in the lower lobes (p <0.0001) remained independently associated with COVID-19 pneumonia or SSc-ILD, respectively. These two variables were combined in a predictive score which resulted positively associated with the COVID-19 diagnosis, with 96.1% sensitivity and 83.3% specificity: 3 different risk class for COVID-19 pneumonia may be identified: high risk for COVID-19 pneumonia (5-9 points); probable overlap COVID-19 pneumonia in SSc-ILD (4 points); low risk for COVID-19 pneumonia (0-3 points).
Conclusion: The CT differential diagnosis between COVID-19 Pneumonia and SSc-ILD is possible and may be fostered in practice by the use of a

radiological score. In the case where an overlap of both diseases is suspected, the presence of consolidation in the lower lobes may suggest a COVID-19 pneumonia while the presence of fibrosis inside GGO may indicate a SSc-ILD.

REFERENCES:

[1] Orlandi M, Landini N, Bruni C, et al. Infection or autoimmunity? The clinical challenge of interstitial lung disease in systemic sclerosis during COVID 19 pandemic. J Rheumatol. 2020 Dec 1: jrheum.200832
[2] Simpson S, Kay FU, Abbara S, et al. Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA [published online ahead of print, 2020 Apr 28]. J Thorac Imaging. 2020;10.1097/RTI.0000000000000524.
[3] Cheng C, Li C, Zhao T, et al. COVID-19 with rheumatic diseases: a report of 5 cases. Clin Rheumatol. 2020;39(7):2025-2029.
[4] Mariano RZ, Rio APTD, Reis F. Covid-19 overlapping with systemic sclerosis. Rev Soc Bras Med Trop. 2020 Sep 21;53:e20200450.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2967

POS1229 ANTI-MDA5 AND ANTISYNTHETASE ANTIBODIES SCREENING IN SEVERE SARS-COV-2 PNEUMONIA. BE AWARE OF FALSE POSITIVE RESULTS

A. Gil-Vila[1], J. Perurena-Prieto[2], C. Nolla-Fontana[1], O. Orozco-Galvez[1], M. Miarons-Font[3], A. Guillén del Castillo[1], A. Pacheco-Reyes[4], E. Trallero-Araguás[5], M. Hernandez-Gonzalez[2], A. Selva-O'callaghan[1]. *[1]Vall d'Hebron University Hospital, Internal Medicine, Barcelona, Spain*; *[2]Vall d'Hebron University Hospital, Immunology, Barcelona, Spain*; *[3]Vall d'Hebron University Hospital, Pharmacology, Barcelona, Spain*; *[4]Vall d'Hebron University Hospital, Intensive Care Medicine, Barcelona, Spain*; *[5]Vall d'Hebron University Hospital, Rheumatology, Barcelona, Spain*

Background: Several reports have shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection may trigger a vigorous immune response that could lead to the appearance of various autoantibodies such as antinuclear antibodies, antiphospholipid antibodies or anti-neutrophil cytoplasmic antibodies, among others. Moreover, the pulmonary involvement in SARS-CoV-2 may resemble that of patients with anti-MDA5 positive syndrome or acute form of antisynthetase syndrome.

Objectives: Our aim was to analyse the presence of anti-MDA5 and other myositis-specific autoantibodies such as the antisynthetase antibodies in patients diagnosed with severe acute respiratory syndrome caused by SARS-CoV-2.

Methods: Retrospective observational study performed in a tertiary care center. We included 28 patients admitted to the intensive care unit with severe acute respiratory syndrome, 14 at the onset of the disease (group A) and 14 after 30 days of being treated in an intensive care unit (group B). Chest CT was performed at the admission. We analyzed the presence of anti-MDA5 and antisynthetase antibodies by immunoblot (Euroimmune®) and in those who were positive we performed a confirmatory test by immunoprecipitation.

Results: All chest CT showed bilateral ground glass pattern. Three out of 14 patients of group A (12 males, 86%, mean ± SD age 67.1 ± 12.2) were positive for antisynthetase antibodies (2 anti-PL7, 1 anti-Jo1), and 6 out of 14 patients of the group B (6 males, 48%, mean ± SD age 68.7 ± 8.1) were positive to antisynthetase antibodies (2 anti-PL7, 2 anti-PL-12, 1 anti-EJ, 1 anti-OJ+PL7). Immunoblots also show positivity for other myositis-specific or associated antibodies, such as anti-TIF1g, anti-PM75, anti-SAE and anti-SRP. All of these results found by immunoblotting were negative by immunoprecipitation. None of the 28 patients were positive for anti-MDA5 antibodies.

Conclusion: Severe SARS-CoV-2 pneumonia is characterized by ground glass pattern in chest CT, as it is found in anti-MDA5 or antisynthetase syndrome. The positivity of several myositis related autoantibodies showed in immunoblot appears to be more related to the vigorous immune response producing polyclonal immunoglobulins than triggering a real myositis-associated interstitial lung disease. Clinicians must be aware about these false positive results in patients with severe COVID-19 acute respiratory syndrome.

REFERENCES:

[1] Xu Q. MDA5 should be detected in severe COVID-19 patients. Med Hypotheses. 2020; 143:109890.
[2] Giannini M, Ohana M, Nespola B, Zanframundo G, Geny B, Meyer A. Similarities between COVID-19 and anti-MDA5 syndrome: what can we learn for better care? Eur Respir J. 2020; 56:2001618.
[3] Vlachoyiannopoulos PG, Magira E, Alexopoulos H, Jahaj E, Theophilopoulou K, Kotanidou A, Tzioufas AG. Autoantibodies related to systemic autoimmune rheumatic diseases in severely ill patients with COVID-19. Ann Rheum Dis. 2020 Dec;79(12):1661-1663

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3019

POS1230 OUTCOME FOLLOWING COVID-19 INFECTION IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS

A. Antovic[1], B. Lövström[2], A. Hugelius[3], O. Borjesson[3], A. Bruchfeld[4], I. Gunnarsson[1]. *[1]Karolinska Institutet, Department of Medicine, Division of Rheumatology, Unit of Rheumatology, Karolinska University Hospital, Stockholm, Sweden*; *[2]Karolinska University Hospital, Unit of Rheumatology, Stockhom, Sweden*; *[3]Karolinska University Hospital, Unit of Rheumatology, Stockholm, Sweden*; *[4]Linköping University, Department of Health, Medicine and Caring Sciences, Linköping, Sweden*

Background: Patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) require immunosuppressive therapy for disease control and reduction of disease relapse and may be at risk for complications during Sars-CoV-2 (COVID-19) infection.

Objectives: To analyze the consequences of COVID-19 in a large cohort of AAV patients regarding occurrence, need of hospitalization, treatment at the intensive care units (ICU), or death.

Methods: Data were retrieved from March 2020 to mid-January 2021 from medical records from the AAV cohort (n=233). Patients diagnosed with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) or eosinophilic granulomatosis with polyangiitis (EGPA) were included. Data included age, gender, diagnosis, ongoing immunosuppressive medication at onset of COVID-19 or at last follow-up in non-COVID individuals. Renal involvement (ever) and estimated glomerular filtration rate (eGFR) were included. COVID-19 was confirmed either by a positive PCR test in the upper airways or by serology. Severe COVID-19 was defined as need of non-invasive ventilation, ICU care, and/or death.

Results: The cohort comprised of 172 patients with GPA, 50 with MPA and 11 with EGPA. There were 121 females (52%). During the study period, 20 patients (8.6%) were diagnosed with COVID-19. The median age at data retrieval in all patients was 68 years (21-93), in the COVID-19 group 63 (29-93) and 68.5 (21-90) years in the non-COVID patients.

Fourty-three patients in all (18%) were hospitalized during the study period of which 11 (4.7%) due to COVID-19 infection. In all, 8 deaths occurred of which 3 were related to COVID-19.

At data retrieval, 110 (47%) patients were on prednisolone treatment, 10/20 (50%) in the COVID-19 group and 100 (47%) in the non-COVID-19 group (p=0.5), with significantly higher doses in COVID-19 patients (p<0.001). In patients hospitalized with COVID-19, 6/11 (54.5%) were on prednisolone, median dose 5 mg/day (0-50). In the total group 112 (48%) were on disease modifying anti-rheumatic drugs (DMARD) and 64 (27.5%) on rituximab as maintenance therapy. Eight patients were on induction treatment with either cyclophosphamide or rituximab.

Of the 20 COVID-19 cases, 8 had severe COVID-19. Of these, 2 were inactive without immunosuppressive treatment, 4 had stable disease with prednisolone (5-7.5 mg/day) in combination with DMARDs, and 2 were active treated with high dose prednisolone (25-50 mg/day) in combination with cyclophosphamide and rituximab (n=1) or rituximab (n=1).

A higher proportion of patients had active AAV (p=0.03) in the severe COVID-19 then in the non-COVID group (10/213 patients).

In the group with the severe COVID-19, 1/8 (12%) patient had rituximab as maintenance therapy, compared to 61/213 (28.6%) in the group of non-COVID-19 patients (p=0.5).

Renal involvement (ever) was present in 144 patients (62%), in 6 patients (30%) with COVID- 19, from which 5 (62%) were in the group of severe COVID-19 patients. Median eGFR did not differ between severe COVID-19 and remaining patients with renal involvement independently of COVID-19 infection.

Conclusion: We found a high rate of severe COVID-19 infection in our cohort of AAV patients which indicates risk for serious complications, especially in patients with active disease and intense immunosuppressive therapy. Maintenance therapy with rituximab did not seem to increase the risk for severe COVID-19. The findings stress the need for continued shielding and early vaccination in AAV patients.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3020

POS1231 COVID-19 INFECTION IN RHEUMATIC IMMUNE-MEDIATED INFLAMMATORY DISEASES. EPIDEMIOLOGICAL STUDY IN A SINGLE UNIVERSITY HOSPITAL

D. Martínez-López[1], D. Prieto-Peña[1], L. Sanchez-Bilbao[1], A. Herrero-Morant[1], C. Álvarez-Reguera[1], M. Trigueros-Vazquez[1], M. A. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*

Background: Immune-mediated inflammatory diseases (IMID) have an increased risk of infections due to the disease itself, and/or immunosuppressive therapy. Risk of COVID-19 infection in the different rheumatic IMID (R-IMID) remains controversial.
Objectives: To assess the epidemiology and comorbidities of COVID-19 in R-IMID from a Single-University hospital.
Methods: Cross-sectional study in a Single-University hospital. We included all consecutive patients with a diagnosis of a R-IMID and a positive test for COVID-19 up to November 6th, 2020. Medical records of 11,199 patients that suffered COVID-19 in our region, and 6891 with R-IMID from our hospital were reviewed. Incidence data in the different underlying R-IMID were calculated for patients with follow-up in our hospital. Confirmed infection was defined if the patient had a positive nasopharyngeal swab for SARS-CoV-2.
Results: We included 147 patients from our region (96 women/51 men), mean age 60±18 years. Underlying R-IMID were: Rheumatoid arthritis (RA) (n=36, 24.5%), Axial spondyloarthritis/Psoriatic arthritis (SpA/PsA) (n=54, 36.7%), Polymyalgia Rheumatica (PMR) (n=16, 10.9%), systemic lupus erythematosus (SLE) (n=10, 6.8%), sarcoidosis (n=5, 3.4%), Sjögren's syndrome (SS) (n=4, 2.7%), giant cell arteritis (GCA) (n=3, 2%), Behçet's disease (n=3. 2%), ANCA-vasculitis (n=2, 1.4%) and systemic sclerosis (SSc) (n=1, 0.7%).
Main comorbidities were hypertension (n=65, 44.2%), dyslipidemia (n=64, 43.5%), age higher than 65 years old (n=55, 37.4%), obesity (n=35, 23.8%), coronary vascular disease (n=27, 18.4%), diabetes mellitus (n=22, 15%), chronic obstructive pulmonary disease (n=15, 10.2%) and chronic kidney disease (n=15, 10.2%).
Total cumulative COVID-19 incidence in all patients from our region was 1.9% (11,199 /582,905). From 147 patients with COVID-19 from our region, 115 (76 women/39 men; mean age, 59±18 years) were followed in our hospital. In the latter, the global cumulative incidence in R-IMID was 1.7% (115/6891), ranging from 1.3% in Systemic Scleroderma (SSc) and Giant Cell Arteritis (GCA) up to 5.3% in Behcet's disease (Table 1 **and** Figure 1**).**

Table 1. Incidence and relative risk of COVID-19 in patients with different R-IMID in a Single-University hospital

R-IMID	Total cumulative incidence in our hospital(%)	Relative risk (95% confidence interval)
Global population 582,905 inhabitants	1.9	-
Global R-IMID 6,891 patients	1.7	0.9 (0.7-1)
Behçet's disease	5.3	2.7 (0.9-8.2)
ANCA-vasculitis	3.5	1.8 (0.4-7.1)
PMR	2.8	1.4 (0.8-2.6)
SS	2.6	1.4 (0.5-3.6)
SLE	2.3	1.2 (0.6-2.3)
Sarcoidosis	2.3	1.2 (0.3-4.7)
SpA/PsA	2.2	1.1 (0.8-1.5)
RA	1.6	0.8 (0.6-1.2)
GCA	1.3	0.7 (0.2-2.8)
SSc	1.3	0.7 (0.1-4.6)

GCA: Giant cell arteritis, PsA: Psoriatic arthritis, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, SpA: Axial spondyloarthritis, SSc: Systemic scleroderma.

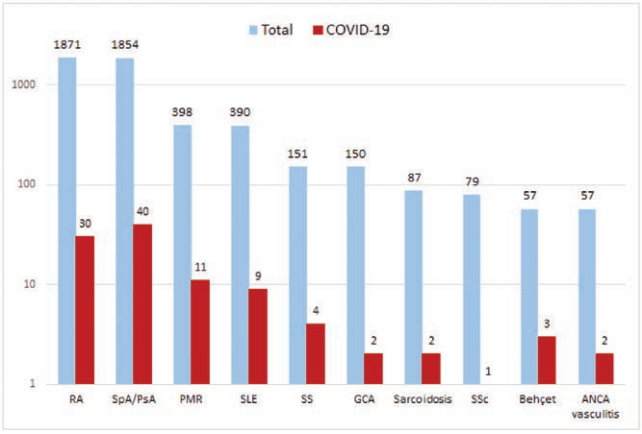


Figure 1. Number of patients with COVID-19 in different R-IMID in a Single-University hospital. Data are presented on a logarithmic scale.

In addition, Relative Risk (RR) in different R-IMID compared to the general population was calculated (Table 1**).** Although RR did not reach statistical significance in any R-IMID, most R-IMID showed a tendency to a higher risk, with the exception of RA, GCA and SSc.
Conclusion: In our series, the total cumulative incidence of COVID-19 in R-IMID was similar to the general population. Higher RR, without statistical significance, was observed in Behçet's disease, ANCA-vasculitis and Polymyalgia Rheumatica. GCA: Giant cell arteritis, PsA: Psoriatic arthritis, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, SpA: Axial spondyloarthritis, SSc: Systemic scleroderma.
Disclosure of Interests: David Martínez-López: None declared, Diana Prieto-Peña Grant/research support from: UCB Pharma, Roche, Sanofi, Pfizer, Abbvie, Lilly, Lara Sanchez-Bilbao: None declared, Alba Herrero-Morant: None declared, Carmen Álvarez-Reguera: None declared, Martin Trigueros-Vazquez: None declared, Miguel A González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi and MSD., Consultant of: Abbvie, Pfizer, Roche, Sanofi and MSD., Grant/research support from: Abbvie, MSD, Jansen, Roche, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Grant/research support from: Abbvie, MSD and Roche
DOI: 10.1136/annrheumdis-2021-eular.3039

POS1232 COVID-19 IN PATIENTS WITH SYSTEMIC SCLEROSIS: ONE RHEUMATOLOGY CENTER EXPERIENCE

M. Starovoytova[1], O. Desinova[1], L. P. Ananyeva[1], O. Koneva[1], L. Garzanova[1], O. Ovsyannikova[1], R. Shayakhmetova[1], V. Babak[1], T. Beketova[1]. [1]*VA Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*

Background: Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) virus infection or COVID-19 is a serious problem for patients with systemic autoimmune diseases Given the serious complications, including acute lung injury, patients with systemic sclerosis (SSc), especially SSs associated with interstitial lung disease (ILD), may represent a high risk group for infection and the development of severe COVID-19.
Objectives: We present an analysis of the COVID-19 course and outcomes in 110 SSc pts.
Methods: The study included 147 patients with SSc. The information was clarified by means of telephone survey after 10 months of the pandemic (December 2020). Covid-19 was diagnosed when confirmed by positive oral /nasopharyngeal swab, in the presence of positive antibodies and/or characteristic symptoms, and data from chest computed tomography (CT). 110 pts (77%) out of 147 patients in the SSc registry, gave the necessary information. COVID-19 was diagnosed in 59 pts (53 %). 42 pts (71%) had SSc-ILD. Pts mean age was 54.96 (s.d.11, min 31, max 79), 83% women (49 women and 10 men). 38 pts (65%) had a limited form of SSc, 15 (26%) pts had diffuse form SSc, 6% had overlap (SSc-polymyositis (PM) and SSc had rheumatoid arthritis (RA) and 3% had visceral form of SSc). All patients received low-dose prednisone, and more than half of the pts received immunosuppressive therapy. Rituximab therapy was performed in 24 pts (41%).
Results: Almost all patients had positive swab from the oral cavity/nasopharynx. And only in 4 (7%) pts nasopharyngeal swabs were negative, in these patients specific antibodies and characteristic CT changes were detected. Chest CT was performed in 51 (86%) pts. Novel coronavirus pneumonia developed in the vast majority of pts - in 46 (78 %) pts. CT1 (up to 25% of lung lesions) had 10 (17%) pts, CT2 (25-50%) – 21(36%) pts, CT 3 (50-75%) – 15(25%) pts. In 5 (8.5%) pts no changes were detected on CT. The course of COVID-19 was mild and moderate (20 (34%) pts and 18 (31%) pts respectively), severe course was observed in 21 (35%) pts, including fatal in 12 (20%) pts. Among the deceased pts, only 1 patient with SSc-PM had not had ILD, but 7 patients had been treated with rituximab.
Conclusion: SSc SARS-CoV-2-infected patients may be at risk of severe disease and mortality due to the frequent presence of ILD and the frequent use of immunosuppressive, including biological, therapy.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3086

POS1233 USE OF BARICITINIB AND TOCILIZUMAB FOR THE TREATMENT OF MODERATE TO SEVERE COVID-19 IN HOSPITALIZED PATIENTS

D. X. Xibille Friedmann[1], S. M. Carrillo Vazquez[2]. [1]*Hospital General de Cuernavaca, Internal Medicine, Cuernavaca, Mexico*; [2]*Hospital Regional 1 de Octubre, Rheumatology, Mexico City, Mexico*

Background: SARS-CoV2 infection and COVID-19 associated pneumonia are associated to a dysregulated inflammatory response known as cytokine storm and the use of cytokine inhibitors, especially those targeting IL-6, has been

proposed as a therapeutic alternative in these patients. Janus Kinase (JAK) inhibitors in combination to the antiviral Remdesivir have shown evidence of reducing recovery time and accelerating improvement in clinical status among patients with COVID-19, notably among those receiving high-flow oxygen or non-invasive ventilation[1].

Objectives: To describe the outcomes associated with the use of Tocilizumab (TCZ) and Baricitinib (Bari) in patients hospitalized for COVID-19.

Methods: Descriptive study nested in a cohort. Patients from the General Hospital of Cuernavaca who were hospitalized due to COVID-19 associated pneumonia and/or respiratory failure requiring supplemental oxygen or invasive/non-invasive assisted mechanical ventilation (AMV) were analyzed. All patients had a positive RT-PCR upon hospital admission, sampled under standardized conditions. The clinical and demographic data of the patients upon hospitalization were obtained from the instrument on a specific platform (SISVER) used on a national basis. Severe disease was considered as the need for any type of AMV. TCZ was used at 400-600 mg in two infusions (baseline and at 72 hours), Bari at 4 mg daily for 14 days. The outcomes were the need for AMV, death, or discharge. A p≤ 0.05 was considered statistically significant.

Results: Data from 404 SARS-CoV2 positive patients were analyzed. 269 (65.9%) were men. The mean age of the patients was 57.5 years (18-94; SD 15.3). 59.6% of the patients had one or more comorbidities (Diabetes and Hypertension in most cases [31.8%]). 22.8% of the patients had a history of current or previous smoking. Mean hospital stay was 7.4 days (1-36; SD 5.9). 15.9% of the patients required invasive or non-invasive AMV. 11 patients were treated with TCZ and 30 patients received treatment with Baricitinib. 5 of the 11 patients with TCZ required AMV (all but one were intubated), but only 6 of the 30 (20%) with Bari required AMV (all except one received CPAP). The use of Baricitinib was correlated with a reduction in the use of AMV (p 0.01). 6 patients with TCZ were discharged due to improvement and 5 died. In the case of Bari, 19 improved and were discharged and 11 died, significantly correlating with lower mortality (p 0.05). The use TCZ was not associated with a reduced hospitalization (50% remained hospitalized for more than 10 days) but patients receiving Baricitinib had significantly shorter hospital stays (86.6% had a hospital stay of less than 10 days) than those receiving TCZ (p<0.0001).

Conclusion: The patients that were treated with Baricitinib and required AMV most often improved with non-invasive CPAP while the majority of the patients under AMV receiving TCZ were treated with an invasive mode, although this was due in part to the fact that TCZ can be employed intravenously and is more practical for intubated patients in whom oral drug administration is limited. Baricitinib was significantly associated with a better outcome (hospital discharge due to improvement) and a significantly shorter hospital stay.

REFERENCES:

[1] Kalil, A.C.; Patterson, T.F.; Mehta, A.K.; Tomashek, K.M.; Wolfe, C.R.; Ghazaryan, V.; Marconi, V.C.; Ruiz-Palacios, G.M.; Hsieh, L.; Kline, S.; et al. Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19. N. Engl. J. Med. 2020.

Acknowledgements: Thanks to B. Flores and M. Hernandez for their help with data collection.

Disclosure of Interests: Daniel Xavier Xibille Friedmann Speakers bureau: Lilly, Abbvie, Paid instructor for: Lilly, Abbvie, Consultant of: Pfizer, Lilly, Sandra Miriam Carrillo Vazquez Speakers bureau: Roche, Novartis, Paid instructor for: Roche, Janssen, Consultant of: Roche, Janssen

DOI: 10.1136/annrheumdis-2021-eular.3122

POS1234 IMPACT OF THE CHANGE IN ADMINISTRATION ROUTE OF TOCILIZUMAB AND ABATACEPT, DUE TO THE COVID-19 LOCKDOWN ON DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

L. Diebold[1], T. Wirth[1], V. Pradel[2], N. Balandraud[1], E. Fockens[1], C. Paris[1], S. Trijau[1], P. Lafforgue[1], T. Pham[1]. *[1]APHM, Rheumatology Department, Marseille, France*; *[2]APHM, Public Health Department, Marseille, France*

Background: Among therapeutics used to treat rheumatoid arthritis (RA), Tocilizumab (TCZ) and Abatacept (ABA) are both biologic agents that can be delivered subcutaneously (SC) or intravenously (IV). During the first COVID-19 lockdown in France, all patients treated with IV TCZ or IV ABA were offered the option to switch to SC administration.

Objectives: The primary aim was to assess the impact of changing the route of administration on the disease activity. The second aim was to assess whether the return to IV route at the patient's request was associated with disease activity variation, flares, anxiety, depression and low physical activity during the lockdown.

Methods: We conducted a prospective monocentric observational study. Eligibility criteria: Adult ≥ 18 years old, RA treated with IV TCZ or IV ABA with a stable dose ≥3 months, change in administration route (from IV to SC) between March 16, 2020, and April 17, 2020. The following data were collected at baseline and 6 months later (M6): demographics, RA characteristics, treatment, history of previous SC treatment, disease activity (DAS28), self-administered questionnaires on flares, RA life repercussions, physical activity, anxiety and depression (FLARE, RAID, Ricci &Gagnon, HAD).

The primary outcome was the proportion of patients with a DAS28 variation>1.2 at M6. Analyses: Chi2-test for quantitative variables and Mann-Whitney test for qualitative variables. Factors associated with return to IV route identification was performed with univariate and multivariate analysis.

Results: Among the 84 patients who were offered to switch their treatment route of administration, 13 refused to change their treatment. Among the 71 who switched (48 TCZ, 23 ABA), 58 had a M6 follow-up visit (13 lost of follow-up) and DAS28 was available for 49 patients at M6. Main baseline characteristics: female 81%, mean age 62.7, mean disease duration: 16.0, ACPA positive: 72.4%, mean DAS28: 2.01, previously treated with SC TCZ or ABA: 17%.

At M6, the mean DAS28 variation was 0.18 ± 0.15. Ten (12.2%) patients had a DAS28 worsening>1.2 (ABA: 5/17 [29.4%] and TCZ: 5/32 [15.6%], p= 0.152) and 19 patients (32.8%) had a DAS28 worsening>0.6 (ABA: 11/17 [64.7%] and TCZ: 8/32 [25.0%], p= 0.007).

At M6, 41 patients (77.4%) were back to IV route (26 TCZ, 15 ABA) at their request. The proportion of patients with a DAS28 worsening>1.2 and>0.6 in the groups return to IV versus SC maintenance were 22.5%, 42.5% versus 11.1% and 22.2% (p=0.4), respectively. The univariate analysis identified the following factors associated with the return to IV route: HAD depression score (12 vs 41, p=0.009), HAS anxiety score (12 vs 41, p=0.047) and corticosteroid use (70% vs 100%, p=0.021), in the SC maintenance vs return to IV, respectively.

Conclusion: The change of administration route of TCZ and ABA during the first COVID-19 lockdown was infrequently associated with a worsening of RA disease. However, the great majority of the patients (77.4%) request to return to IV route, even without disease activity worsening. This nocebo effect was associated with higher anxiety and depression scores.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3126

POS1235 ASSESSMENT OF RISK FACTORS FOR HOSPITALIZATION OF AUTOIMMUNE AND RHEUMATIC DISEASE PATIENTS WITH COVID-19 – A SINGLE CENTRE OBSERVATIONAL STUDY

J. M N[1], P. Dekate[2], S. Vontari[1], R. Dudam3. *[1]Hyderabad Rheumatology Center, Clinical Pharmacology, Hyderabad, India*; *[2]Hyderabad Rheumatology Center, Rheumatology, Hyderabad, India*; *[2]Hyderabad Rheumatology Center, Rheumatology, Hyderabad, India*

Background: Most of the patients suffering from autoimmune and rheumatic diseases (AIRD) are on immunomodulator or immunosuppressive therapies and they are susceptible to infections including COVID19.

Objectives: To assess the risk factors for hospitalization with COVID-19 in patients with AIRD

Methods: A single centre retrospective observational study including patients with AIRD who had contracted COVID-19. Data was collected from all patients attending our clinic from September 2020 to January 2021. Patients with COVID-19 were divided into hospitalized and non-hospitalized groups. Clinical, demographic, ongoing medications, comorbidities and post COVID flare data were collected and analysed using crosstabs-chi square and Mann-Whitney U test.

Results: 520 patients with AIRD were screened over the study duration, of which 52 patients who had contracted COVID-19 were included in the study. Amongst them, 19 patients (36.5%) required hospitalization. The common symptoms in the hospitalized patients over non-hospitalized were fever (63.2% vs 57.6), fatigue (42.1% vs 21.2%), headache (36.8% vs 18.2%), abdominal pain (26.3% vs 6.1%), myalgias (36.8 vs 18.2%) and dyspnea (31.6% vs 18.2%). The most common rheumatic conditions seen in both the groups were RA (42.1% vs 30.3%), SPA (26.3% vs 36.4%), and SLE with other CTD's (15.8% vs 24.2%). 6 patients (11.5%) required ICU stay, 3 patients (5.7%) were ventilated, and 2 (3.8%) patients died.

Patients requiring hospitalization were aged >50 years (p=0.018), had DM type II (p=0.003), HTN (p=0.035), multimorbidity (p=0.021), and a higher CORAD score (p<0.001). Usage of CsDMARDS, bDMARDS, TsDMARDS, corticosteroids did not show a significant difference between both the groups. Patients with >2 years of disease duration required hospitalization in comparison to <2 years of duration but this was not statistically significant.

84.2% of hospitalized and 69.7% of non-hospitalized patients stopped anti-rheumatic treatment and disease flare was seen in 47.4% and 39.4% patients respectively.

Conclusion: The rheumatic disease and their medications did not increase the risk of COVID-19 hospitalization in this study. However, higher age, DM II, HTN, and high CORAD score were found to be associated with hospitalization in AIRD patients. The findings of this study are limited by a small sample size.

Table 1. Demographic and Rheumatic disease specific data of COVID-19 patients

		All patients (n=52)	Hospitalized (n=19)	Non-hospitalized (n=33)	p-value
Age – n (%)		45.73 (10.829)	50.53 (10.905)	42.97 (9.923)	**0.018**
Gender (Male/Female)		21 (40.4)/ 31 (59.6)	7 (36.8) / 12 (63.2)	14 (42.4)/ 19 (57.6)	0.462
BMI – n (%)	Normal	27 (51.9)	8 (42.1)	19 (57.6)	0.528
	Pre-obese	19 (36.5)	8 (42.1)	11 (33.3)	
	Obesity	6 (11.5)	3 (15.8)	3 (9.1)	
Disease – n (%)	RA	18(34.6)	8(42.1)	10(30.3)	0.287
	SPA	17(32.7)	5(26.3)	12(36.4)	0.335
	SLE and other CTD'S	11(21.2)	3(15.8)	8(24.2)	0.364
	Others	6(11.5)	3(15.8)	3(9.1)	0.380
Comorbidities -n (%)	DM2	12(23.1)	9(47.4)	3.(9.1)	**0.003**
	HTN	13(25)	8(42.1)	5(15.2)	**0.035**
	CKD	2 (3.8)	2 (10.5)	0 (0)	0.129
	Hypothyroidism	12 (23.1)	4 (21.1)	8 (24.2)	0.537
	Multimorbidity	8(15.4)	6(31.6)	2(6.1)	**0.021**

		All patients (n=52)	Hospitalized (n=19)	Non-hospitalized (n=33)	p-value
Duration – n (%)	>2 years	14(26.9)	3(15.8)	11(33.3)	0.147
	>2 years	38(73.1)	16(84.2)	22(66.7)	
Corticosteroids – n (%)	No steroids	18(34.6)	5(26.3)	13(39.4)	0.294
	Low dose steroids	33(63.5)	13(68.4)	20(60.6)	
	Moderate dose steroids	1(1.9)	1(5.3)	0(0.0)	
DMARDS (CS) – n (%)	MTX	25 (48.1)	8 (42.1)	17 (51.5)	0.358
	HCQ	13 (25)	5 (26.3)	8 (24.2)	0.560
	LEF	4 (7.7)	3 (15.8)	1 (3)	0.132
	SSZ	10 (19.2)	6 (31.6)	4 (12.1)	0.090
	Azathioprine	2 (3.8)	2 (10.5)	0 (0)	
	Iguratimod	3 (5.8)	1 (5.3)	2 (6.1)	0.129
	Combination	13 (25.0)	6 (31.6)	7 (21.2)	0.701
DMARDS(B) – n (%)	Adalimumab	1 (20.0)	0 (0)	1 (25.0)	0.659
	Etanercept	1 (20.0)	0 (0)	1 (25.0)	
	Rituximab	3 (60.0)	1 (100.0)	2 (50.0)	
CO RADS -n (%)	0	11 (21.2)	0 (0)	11 (33.3)	**<0.001**
	1	9 (17.3)	0 (0)	9 (27.3)	
	2	3 (5.8)	0 (0)	3 (9.1)	
	3	3 (5.8)	2 (10.5)	1 (3)	
	4	11 (21.2)	7 (36.8)	4 (12.1)	
	5	15 (28.8)	10 (52.6)	5 (15.2)	

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3137

POS1236 IMPACT OF COVID-19 ON INITIATION AND RENEWAL OF BIOTHERAPIES AND TARGETED SYNTHETIC TREATMENTS

P. Richette[1], M. Allez[2], V. Descamps[3], L. Perra[4], S. Pilet[5], M. Maravic[6].
[1]Lariboisiere Hospital, Rheumatology, France, France; *[2]St Louis Hospital, Gastroenterology, Paris, France*; *[3]Bichat Hospital, Dermatology, Paris, France*; *[4]IQVIA, Ai & Data engine, Courbevoie, France*; *[5]IQVIA, Analytic solutions, Courbevoie, France*; *[6]IQVIA, Real World Solutions, Courbevoie, France*

Background: During the epidemic's peak of COVID-19, scientific societies published recommendations on biotherapy and targeted synthetic treatment (B/TST) use in patients with chronic articular inflammatory diseases, inflammatory bowel diseases, and psoriasis.
Objectives: The objective was to evaluate the impact of COVID-19 in France on initiation and renewal of B/TST.
Methods: LRx contains all anonymized medication dispenses prescribed in outpatient care in a representative panel of French retails pharmacies, including data of near 40 million patients. The impact of B/TST initiation and renewal were studied using 2019 as reference and dispense deliveries data of pharmacies with regular flew in order to perform the comparison. B/TST considered were abatacept, anti-TNF, anti-IL6, anti-IL17, anti-IL12/23 or anti-IL23, JAK inhibitors (JAKi) and other classes such as aprelimast, aminosalicylates (AS), hydroxychloroquine (HCQ), and methotrexate (MTX). A treatment initiated was defined as a treatment not delivered in the past 12 months, and conversely for a treatment renewal. Results were presented as raw one and expressed in percentage of patients having at least one B/TST delivery in each therapeutic classes of interest in 2020 compared to 2019 used as reference year (period from week 12 to week 19 considered and corresponding to the lockdown period in France).
Results: During the lockdown period, a decrease in initiation was observed for patients treated with: abatacept (405 in 2019 vs 227 in 2020: -44%, p<0.001), anti-TNF (1156 vs 1058, -31%, p<0.001), anti-IL17 (415 vs 206, -50%, p<0.001), anti-IL12-23 (395 vs 339, -12%, p=0.16), JAKi (289 vs 174, -39%, p=0.006), contrasting with an increase for Tociliumab (117 vs 445, +152%, p=0,01). We found a decrease of 7% (2171 vs 2015, p=0,35), 44% (405 vs 227, p<0.001), 30% (3430 vs 2390, p p<0.001) of AS, aprelimast and MTX initiation, respectively, and an increase of 173% (1708 vs 4671, p=0.11) of HCQ initiation. No decrease for the renewal of B/TST was observed
Conclusion: During the epidemic's peak, initiation of AS, MTX, biotherapies (except for tocilizumab), and JAKi dramatically decreased without impacting their renewal. Two treatments were mainly initiated, tocilizumab probably due to a switch from intravenous to subcutaneous injection and HCQ in relation to its presumably effect on COVID-19. Overall, recommendations from scientific societies have been followed.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3146

POS1237 ALGORITHM IDENTIFYING CHRONIC INFLAMMATORY DISEASES TREATED BY BIOTHERAPY AND/OR TARGETED SYNTHETIC TREATMENTS IN OUTPATIENT CARE IN FRANCE: FEASIBILITY, PRELIMINARY RESULTS, AND IMPACT OF COVID-19

P. Richette[1], M. Allez[2], V. Descamps[3], L. Perra[4], S. Pilet[5], M. Maravic[6].
[1]Lariboisiere Hospital, Rheumatology, Paris, France; *[2]St Louis Hospital, Gastroenterology, Paris, France*; *[3]Bichat Hospital, Dermatology, Paris, France*; *[4]IQVIA, Ai & Data engine, Courbevoie, France*; *[5]IQVIA, Analytic Solutions, Courbevoie, France*; *[6]IQVIA, Real World Solutions, Courbevoie, France*

Background: Discriminating chronic inflammatory diseases under biotherapy and/or targeted synthetic treatments (B/TST) using medico-administrative databases are challenging but required for medico-economic analyses focusing on these diseases.
Objectives: The objective was to evaluate the feasibility of using a medication dispense data in order to identify patients with chronic inflammatory diseases under B/TST in outpatient care setting and evaluate the impact of COVID-19 in France
Methods: LRx contains all anonymized medication dispenses prescribed in outpatient care in a representative panel of French retails pharmacies, including data of near 40 million patients. Patients having at least one B/TST delivered in 2019 were selected. An algorithm was constructed using different steps, including a machine learning step by transfer learning applied in patient classified as having a rheumatologic condition in order to differentiate rheumatoid arthritis (RA) from spondyloarthritis (SA). We numbered 190,640 patients, of which 87.8% were classified in one of the following diseases: RA, SA, psoriatic arthritis (PA), psoriasis, inflammatory bowel diseases (IBD) (extrapolated data to France). Descriptive analysis was performed. The impact of COVID-19 on biotherapy initiation was evaluated during the lockdown period (W2-W19 2020) in these different conditions.
Results: Among the 167,468 patients under B/TST, 20.7%, 18.4%, 6.5%, 37.9% and 16.5% were considered as having a psoriasis, IBD, PA, RA, and SA, respectively. Female patients were more frequent in RA and PA (> 60%); younger (< 20 years) and older patients (74 years) were found in patients with IBD (5.7%) and RA (12.6%), respectively. Contrasting with IBD, SA, and RA patients were mainly under anti-TNF treatment (> 90% for IBD and SA, 73.5% for RA), psoriasis and PA patients received a range of broadly well-balanced of B/TST. Among the immunosuppressant, methotrexate was mostly prescribed in RA (58.4%), PA (34.1%), and psoriasis (14.1%), and azathioprine in IBD (19.9%). Oral corticosteroid delivered at least 4 times in 2019 were mostly found to be associated with a RA condition (28%). A significant decrease of biotherapy initiation was observed during the lockdown in France in patients with IBD (-20%, p=0.03) and psoriasis (-54%, p<0.0001), not significant decrease in patients with SA (-6%) and increase in RA patients (+23%).
Conclusion: The algorithm was able to identify patients with chronic inflammatory diseases under B/TST delivered in outpatient care and will allow to follow-up its management and study the COVID-19 impact on biotherapy initiation. An external validation needs to be performed
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3165

POS1238 ANTIPHOSPHOLIPID ANTIBODIES AND COVID-19: TREND OVER TIME

S. Mancuso[1], S. Truglia[1], A. Capozzi[2], F. Pasquali[1], S. Recalchi[2], G. Riitano[2], F. R. Spinelli[1], M. Sorice[2], R. Misasi[2], C. Alessandri[1], C. M. Mastroianni[3], F. Conti[1]. *[1]Sapienza University of Rome, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Rome, Italy*; *[2]Sapienza University of Rome, Dipartimento di Medicina Sperimentale, Rome, Italy*; *[3]Sapienza University of Rome, Dipartimento di Sanità Pubblica e Malattie infettive, Rome, Italy*

Background: Since the beginning of the SARS-CoV-2 outbreak, antiphospholipid antibodies (aPL), a known thrombotic risk factor, have been studied in COVID-19 patients, in whom thromboembolic events have been associated with poor prognosis. To date, the pathogenetic role of aPL and the trend over time is still unknown.

Objectives: Aim of the study was to investigate whether aPL positivity was correlated with thrombosis in COVID-19 patients and whether it was a transient or persistent.

Methods: We included all consecutive COVID-19 patients hospitalized at Policlinico Umberto I, Sapienza University of Rome from April 1, 2020 to June 7, 2020. In these patients, serum levels of anti-cardiolipin (aCL) IgM, IgG, IgA, anti-β2glycoprotein I (aβ2GPI) IgM, IgG were measured by enzyme-linked immunosorbent assay (ELISA) and Lupus Anticoagulant (LA) was detected with coagulatory tests in patients not in treatment with anticoagulant drugs.

Results: Five out of 73 (6.8%) patients resulted positive for aCL IgM, 3 of them also tested positive for aβ2GPI IgM. aCL IgA were tested positive in 14 out of 46 patients (30.4%). Overall 18 patients resulted positive for at least one test. Seven (9.6%) patients developed thrombotic events during hospitalization, 3 of them resulting positive for aPL (Table 1. below).

We observed that patients showing double positivity for aCL IgM and aβ2GPI IgM had a likelihood positive ratio of 6.3 for thrombotic events (p=0.012) and a likelihood positive ratio of 4.9 for increased D-dimer levels (p=0.027). aCL IgA, the most prevalent aPL in this cohort, was not associated with thrombosis. Of the 18 aPL positive patients, 5 died, 3 were lost to follow-up, and 10 were tested on a second occasion at least 12 weeks, two patients confirmed positivity without clinical signs suggestive of APS.

Conclusion: These results suggest that double positivity for aCL and aβ2GPI IgM increases the risk of thrombosis in COVID-19 patients, unlike aCL IgA. APL positivity may be persistent and it is advisable to monitor it over time.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3199

POS1239 POSITIVE IMPACT OF THE FIRST LOCKDOWN IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATISM

C. Gaujoux-Viala[1,2], C. Traverson[1], E. Filhol[1,2], C. Daien[3,4], S. Laurent-Chabalier[5], B. Combe[3,4], C. Lukas[2,3], J. Morel[3,4], C. Hua[1,2]. *[1]Nîmes University Hospital, Rheumatology, Nîmes, France*; *[2]University of Montpellier, IDESP, UMR-INSERM, Montpellier, France*; *[3]CHU Lapeyronie, Rheumatology, Montpellier, France*; *[4]University of Montpellier, -, Montpellier, France*; *[5]Nîmes University Hospital, BESPIM, Nîmes, France*

Background: Since the beginning of 2020, the COVID-19 pandemic has caused a considerable amount of fear, worry and concern in the general population and among certain groups such as the elderly, healthcare providers and people with pre-existing conditions in particular. Our patients suffering from chronic inflammatory rheumatism (CIR), a group of autoimmune pathologies treated by immunosuppressant medication, are particularly concerned. Actions taken – particularly quarantine and its effects on the normal activities, habits or livelihoods of many people – also have a significant impact. There is little information on the impact of the lockdown in patients with CIR with data measured prospectively, in a standardized way, before and during the first lockdown period.

Objectives: The objective of this ancillary study was to evaluate the psychological impact of the first lockdown period (anxiety, depression, sleep disorders, catastrophizing...) as well as the evolution of disease activity in patients suffering from CIR.

Methods: At two French university hospitals, adult patients with rheumatoid arthritis (RA) according to the ACR-EULAR 2010 criteria, spondyloarthritis (SpA) fulfilling the ASAS 2009 criteria and psoriatic arthritis (PsA) according to the Caspar 2006 criteria were consecutively included in the Catastrophism in Chronic Inflammatory Rheumatism (CRIC) study from September 2019. Sociodemographic data, information on the disease and its treatments were collected as well as questionnaires on disease activity (DAS28, CDAI, BASDAI), function (HAQ), quality of life (SF12, EQ5D), anxiety and depression (HADS, GAD7), insomnia (ISI) and catastrophizing scores (PCS). These data were collected prospectively at baseline, 3, 6 and 12 months.

In this ancillary study, data from patients with an assessment before and during lockdown were analyzed. Statistical analyses were descriptive with a paired Student's T-test.

Results: In all, 140 patients (49 RA, 69 SpA and 22 PsA) were evaluated before and during lockdown. The median age was 53.5 [44-63] years and 60.7% were women; 74 patients (53.2%) were professionally active and 102

Table 1. Clinical and demographic features of the 7 Covid-19 patients that presented thrombotic events

Features	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age - yr	67	78	83	43	70	74	95
Sex	female	female	female	male	male	female	male
Medical History	Malignancy, Hypertension	Stroke	Chronic obstructive pulmonary disease	No medical history	Chronic obstructive pulmonary disease, Hypertension	Malignancy,	Hypertension
Initial findings							
Signs and symptoms	Dyspnea	Dyspnea	Dyspnea	Fever, ageusia/ anosmia, chest pain	Fever, cough	Dyspnea	Dyspnea
HRCT chest: Bilateral ground glass opacity	yes	yes	yes	yes	yes	yes	yes
Baseline laboratory values							
Lymphocyte count, cells x 10^6/L	220	210	2330	1580	1680	600	1390
Lactate dehydrogenase, U/L	223	321	199	227	226	349	199
Ferritin mcg/L	614	317	213	387	462	2455	197
D-dimer mcg/L	730	1213	2912	282	688	1298	1097
PaO2:FIO2, mm Hg	132	120	442	534	348	493	314
Anticoagulant therapy at the time of the thrombotic event	Therapeutic dosage	Prophylactic dosage	Prophylactic dosage	Not administered	Therapeutic dosage	Therapeutic dosage	Therapeutic dosage
Thrombotic events	Stroke	Pulmonary embolism	Peripheral venous thrombosis	Myocardial infarction	Pulmonary embolism	Myocardial infarction, peripheral arterial thrombosis, peripheral venous thrombosis	Peripheral venous thrombosis
Antiphospholipid antibodies	negative	Anti-cardiolipin IgM low title, anti-β2glicoprotein I IgM low title	negative	negative	negative	Anti-cardiolipin IgM low title, anti-β2glicoprotein I IgM low title	Anti-cardiolipin IgA low title
Outcome	Exitus	Exitus	Suicide	Discharged	Discharged	Discharged	Exitus
Antiphospholipid antibodies tested after at least 12 weeks	NP	NP	NP	NP	NP	Negative	NP

(72.9%) were living as couples. The majority of patients (92.9 %) had a disease lasting more than 2 years. Concerning treatments, 63 (45%) were treated by bDMARD monotherapy, 40 (28.5%) by bDMARD+ csDMARD, 17 (12.1%) by csDMARD monotherapy and 2 patients by tsDMARD; 90.7% were not taking any corticosteroids and 8.6% were taking ≤5 mg/d; 30% were on NSAIDs.

When comparing before and during lockdown, pain, tender joint count, swollen joint count, disease activity (CDAI, BASDAI) and function (HAQ, SF12 physical component) were similar. However, there was a significant improvement in psychological status, anxiety (HADS, GAD7), the mental component of SF12, catastrophizing and overall quality of life (EQ5D) (see Table 1 below).

Conclusion: There are very few prospective, standardized data on the impact of lockdown in patients with CIR with an assessment before and during the first lockdown period. In patients with CIR, the first lockdown period had no impact on the activity of the disease and was well experienced psychologically with less anxiety and an improvement in quality of life.

Table 1.

Outcome (*N*) **140 CIR: 49 RA, 69 SpA, 22 PsA**	Before lockdown Mean (SD)	During lockdown Mean (SD)	**Mean change (SD)**	*P*
Pain VAS *(138)*	39.4 (25.3)	39.4 (25.0)	-0.28 (27.1)	NS
TJC *(57)*	4.0 (6.8)	4.7 (4.4)	0.7 (5.9)	NS
SJC *(56)*	1.0 (2.6)	1.6 (1.7)	0.5 (2.4)	NS
CDAI *(36)*	11.7 (1.4)	12.3 (7.5)	1.2 (8.7)	NS
BASDAI *(84)*	4.7 (1.9)	4.9 (2.0)	0.14 (1.4)	NS
HAQ *(135)*	0.72 (0.57)	0.72 (0.53)	0.03 (0.33)	NS
SF12 mental *(136)*	**32.7 (8.7)**	**36.2 (8.4)**	**3.46 (8.01)**	**<0.0001**
GAD-7 (anxiety) *(135)*	**7.7 (5.5)**	**5.0 (5.3)**	**-1.73 (0.40)**	**<0.0001**
HADS anxiety *(137)*	**8.5 (3.9)**	**7.8 (3.9)**	**-0.64 (2.91)**	**0.0113**
EQ5D *(139)*	**0.55 (0.31)**	**0.61 (0.29)**	**0.06 (0.24)**	**0.0078**
PCS (catastrophizing) *(137)*	**18.9 (13.3)**	**15.9 (11.1)**	**-3.10 (9.60)**	**0.0003**

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3203

POS1240 HYDROXYCHLOROQUINE CARDIOTOXICITY: A CASE-CONTROL STUDY COMPARING PATIENTS WITH COVID19 AND PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

S. Mancuso[1], F. R. Spinelli[1], L. Agati[2], M. R. Ciardi[3], F. Natalucci[1], E. Molteni[1], S. Truglia[1], V. Riccieri[1], R. Priori[1], C. M. Mastroianni[3], F. Conti[1]. [1]*Sapienza University of Rome, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Rome, Italy*; [2]*Sapienza University of Rome, Dipartimento di Scienze Cardiovascolari e Respiratorie, Rome, Italy*; [3]*Sapienza University of Rome, Dipartimento di Sanità Pubblica e Malattie infettive, Rome, Italy*

Background: Antimalarials have been associated with QT prolongation in COVID19 patients but are generally safe in patients with rheumatologic disease.

Objectives: Aim of the study was to compare the prevalence of QTc prolongation between COVID19 and Systemic Lupus Erythematosus (SLE) patients treated with hydroxychloroquine (HCQ).

Methods: We included consecutive patients with SARS-CoV-2 infection confirmed by nasopharyngeal swab and patients taking HCQ for SLE. A prolonged QTc was defined as an increase in QTc intervals >60 ms (compared with baseline) or as a QTc of ≥500 ms.

Results: We enrolled 58 COVID19 patients (median age 70.5 years, IQR 25). HCQ, without or with azithromycin, was given to 26 (44.8%) and 15 patients (25.9%), respectively; 17 (29.3%) had not received either drug. The median baseline QTc was 432 (IQR 36) and prolonged QTc was observed in 15 (26%) patients (12 QTc≥500 ms and 3 patients ΔQTc>60 ms). We didn't find significant differences in QTc prolongation among the three treatment groups. Baseline QTc (OR 111.5) and D-dimer (OR 78.3) were independently associated to QTc prolongation.

Compared to the 50 SLE patients (median age of 38.5 years, IQR 22), chronically treated with HCQ, patients with COVID19 showed significantly longer QTc ($p < 0.001$) (Table 1).

Conclusion: This is the first study demonstrating that, differently from COVID19 patients, patients with SLE are not susceptible to HCQ-induced long QT syndrome and arrhythmia. The combined arrhythmogenic effect of SARS-CoV-2 infection and HCQ could account for the excess of QTc prolongation and fatal arrhythmias described in patients with COVID19.

Table 1. Difference in clinical and demographic features between Systemic Lupus Erythematosus and COVID19 patients.

Demographic Features	**SLE patients**	**Covid-19 patients**	**p-Value**
N°	50	58	
Female	43	23	< 0.001
Age (years)	45 (17)	70.5 (25)	< 0.001
Comorbidities N %			
Hypertension	15 (30)	24 (48)	0.2
Cardiovascular diseses	8 (16)	13 (22.4)	0.4
COPD	1 (2)	9 (15.5)	0.016
Thyroid disease	8 (16)	8 (13.8)	0.75
Chronic kidney disease	4 (8)	5 (8.6)	0.91
Population characteristics Median (IQR)			
HCQ (mg/die)	400 (125)	400	< 0.001
HCQ Time (days)	3255 (5790)	7	< 0.001
QTc (ms)	432 (36.25)	395 (80)	< 0.001
SLEDAI-2K	0 (4)	-	-
SDI	0	-	-

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3228

POS1241 THE IMPACT OF THE COVID-19 PANDEMIC ON PHYSICAL FUNCTIONING AND MENTAL WELLBEING IN 824 PATIENTS WITH RHEUMATIC DISEASE OVER 8 MONTHS: PHYSICAL FUNCTIONING DECLINES

N. Cleaton[1], S. Raizada2, T. Sheeran[1], J. Bateman[1]. [1]*The Royal Wolverhampton Trust, Rheumatology, Wolverhampton, United Kingdom*; [1]*The Royal Wolverhampton Trust, Rheumatology, Wolverhampton, United Kingdom*

Background: Worldwide the detrimental consequences of the COVID-19 pandemic on physical and psychological health have been recognised. Social distancing and isolation measures have negatively impacted physical functioning (PF) and mental health (MH), and are known to have reduced physical activity (PA) generally within the population. A significant proportion of patients with autoimmune rheumatic disease (ARD) are considered 'clinically extremely vulnerable' (CEV), at high risk from COVID19 and been advised to follow stricter social distancing precautions than the general population. Evidence in ARD patients highlights the importance of PA in maintaining physical and psychological wellbeing. Prior to the pandemic limitations in both PF and MH in patients with ARD were recognised and early in the pandemic MH was noted to be impacted by distancing measures in this population.

Objectives: This is an interim report of a research study (clinicaltrials.gov NCT04542031) exploring the impact of the COVID19 pandemic on the physical and psychological wellbeing of patients with rheumatic disease, to inform guidelines and target service provision as the pandemic continues.

Methods: We distributed two web-based surveys, eight months apart during the first (April-2020) and second wave (December-2020) of the pandemic. Surveys were communicated via a linked mobile-phone SMS message, to all rheumatology patients with a validated mobile number under follow-up at the Royal Wolverhampton Trust. We assessed patients using the Short Form-12 version 2 made up of mental (MCS) and physical component scores (PCS). For each survey, data were collected 4-weeks following distribution; comparative analysis was conducted using SPSS version-27.

Results: Initial surveys were sent to 7911 active follow up patients; 1694/7911 (21.4%) responded and consented for further follow up, of which 1636 were linked to a validated mobile number. 899/1636 (55.0%) responded to the second survey and 824/899 (91.7%) responses were linked across both surveys. These 824 patients were predominately female (69.5%), aged 61 years and 76.3% had an ARD; 388/824 patients were CEV, 436 were in the comparator group. For the CEV group, scores remained significantly lower than the comparator for PCS (survey 1: 36.40 vs 39.61 [P<0.001], survey 2: 36.11 vs 38.66 [P<0.001]) and MCS (41.61 vs 43.44 P<0.001; 41.19 vs 43.60 [P<0.001]); there was no deterioration in CEV scores. In the comparator group, while MCS did not differ in patients with ARD, PCS significantly decreased (1.39; 95% CI: 0.69, 2.08; P<0.001); PCS in the non-inflammatory group did not significantly change (-0.23, P=0.65).

Conclusion: These preliminary data suggest that while the physical and mental health of CEV patients is significantly lower in this cohort, surprisingly, neither aspects of health have been worsened by the impacts of the pandemic over an 8-month period. However, the physical functioning of patients with ARD significantly decreased in this time, which may reflect the reduction in PA faced by society, and reduced contact with secondary care services. These data suggest services need to adapt to provide additional support to patients with ARD to maintain physical functioning during the pandemic. Further work exploring the

evolving pattern of the physical and psychological responses to the pandemic is ongoing.

Acknowledgements: We would like to thank the Hibbs Lupus Trust.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3246

POS1242 FACTORS ASSOCIATED WITH MORTALITY IN PATIENTS WITH RHEUMATIC DISEASES AND COVID-19 IN MEXICO

D. Alpizar-Rodriguez[1], F. Irazoque-Palazuelos[2], T. S. Rodriguez-Reyne[3], E. Zamora[4], D. X. Xibille Friedmann[5], A. Castillo Ortiz[6], M. U. Martínez-Martínez[7], B. E. Zazueta[8], S. Duran Barragan[9], M. Rull-Gabayet[3], M. Vázquez-Del Mercado Espinosa[10], J. F. Moctezuma-Ríos[11], A. Barragán-Garfías[12], E. Martin-Nares[3], D. Cervantes-Rosete[3], D. Vega-Morales[13], M. Aguiar Castellanos[6], G. Reyes[14], M. Macias[15], L. V. Maya-Piña[12], F. Cobos-Villanueva[12], J. E. Navarro-Zarza[16], A. Sanchez-Rodriguez[12], M. D. P. Cruz-Domínguez[12], X. Jimenez Jimenez[12], O. Marquez[17], A. Martínez[12], A. Vargas Guerrero[12], L. Andrade[12], C. F. Pacheco Tena[18]on behalf of Mexican Study group of COVID-19 in Rheumatic diseases. *[1]Colegio Mexicano de Reumatología, Research Unit, Mexico City, Mexico*; *[2]Centro de Investigación y Tratamiento Reumatológico S.C., Rheumatology, Mexico City, Mexico*; *[3]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran, Immunology and Rheumatology, Mexico City, Mexico*; *[4]Centro Médico de Pensiones, Rheumatology, Merida, Mexico*; *[5]Servicios de Salud de Morelos, Departamento de Investigación y Capacitación,, Cuernavaca, Mexico*; *[6]Private Practice, Rheumatology, Merida, Mexico*; *[7]Instituto Mexicano del Seguro Social, Internal Medicine, Rioverde, Mexico*; *[8]Private Practice, Rheumatology, Mexicali, Mexico*; *[9]Clínica de Investigación en Reumatología y Obesidad, Rheumatology, Guadalajara, Mexico*; *[10]Hospital Civil de Guadalajara "Juan I. Menchaca", Rheumatology, Guadalajara, Mexico*; *[11]Hospital General de México 'Dr. Eduardo Liceaga', Rheumatology, Mexico City, Mexico*; *[12]Private Practice, Rheumatology, Mexico City, Mexico*; *[13]Private Practice, Rheumatology, Monterrey, Mexico*; *[14]Private Practice, Rheumatology, Chihuahua, Mexico*; *[15]Private Practice, Rheumatology, Veracruz, Mexico*; *[16]Private Practice, Rheumatology, Chilpancingo, Mexico*; *[17]Private Practice, Rheumatology, Campeche, Mexico*; *[18]Facultad de Medicina y Ciencias Biomédicas, Rheumatology, Chihuahua, Mexico*

Background: As of the 25th of January 2021, more than 150 thousand deaths as consequence of COVID-19 have been reported in Mexico [1]. Advanced age, male gender and comorbidities have been described as risk factors for severe disease and mortality in general population [2]. COVID-19 mortality in Mexican patients with rheumatic and musculoskeletal diseases (RMDs) is unknown.

Objectives: To describe characteristics of Mexican patients with RMDs and COVID-19, and to analyse factors associated with mortality.

Methods: The Global Rheumatology Alliance COVID-19 (GRA) physician reported registry, is an international effort to collect information on COVID19 in adult patients with RMDs. GRA is an observational registry. The first patient from Mexico was registered on April 17, 2020. All Mexican patients registered in GRA until October 30, 2020 were included in this analysis. The association of mortality with demographic and clinical variables was estimated using logistic regression analysis.

Results: A total of 323 patients were registered, with a median age of 52 (IQR 41-61) years old, 166 (51.4%) patients lived in Mexico City. The most frequent RMDs were rheumatoid arthritis, 149 (46.1%) and systemic lupus erythematosus, 24 (19.8%). Over a third of patients with RMDs and COVID-19 (119 (36.8%)) were hospitalized, and 43 (13.3%) died. Table 1 shows clinical and demographic characteristics. In the univariable analysis, the absence of comorbidities was a protective factor, OR 0.3 (95% CI 0.1-0.6). Factors associated with mortality at COVID-19 diagnosis were age over 65 years old, having type 2 diabetes, chronic renal insufficiency, treatment at COVID-19 diagnosis with corticosteroids or with CD20 inhibitors. In the multivariable adjusted analysis, these factors remained independently associated with mortality. No associations with other treatments or comorbidities at COVID-19 diagnosis were found.

Conclusion: Mexican patients with RMDs and COVID-19 in the GRA physician reported registry had a mortality of 13.3%. Factors associated with mortality were those described in the general population, such as older age and being on corticosteroids and CD20 inhibitors treatment at COVID-19 diagnosis.

Table 1. Clinical and demographic characteristics of patients with rheumatic diseases and COVID-19 in Mexico and mortality.

Characteristics at COVID-19 diagnosis	Total N=323	Death 43 (13.3)	Survivors 280 (86.7)	Univariable OR (95% CI)	Multivariable OR (95% CI)
Women, n(%)	268 (82.9)	33 (76.7)	235 (83.9)	0.6 (0.3-1.4)	0.5 (0.2-1.3)
Age >65 years old, n(%)	62 (19.2)	18 (41.9)	44 (15.7)	**3.9 (1.9-7.7)**	**3.9 (1.9-8.3)**
RMDs* n(%)					-
Rheumatoid arthritis	149 (46.1)	23 (53.5)	126 (45.0)	1.6 (0.7-3.7)	-
Systemic Lupus Erythemathosus	64 (19.8)	10 (23.3)	54 (19.3)	1.6 (0.6-4.3)	-
Spondyloarthritis (axial and others)	33 (10.2)	2 (4.7)	31 (11.1)	0.1 (0.1-2.8)	-
Others	77 (23.8)	8 (18.6)	69 (24.6)	1	-
Moderate/High disease activity[1], n(%)	57 (18.6)	7 (17.9)	50 (18.7)	1.0 (0.4-2.5)	-
None comorbidities, n(%)	136 (42.1)	8 (18.6)	128 (45.7)	**0.3 (0.1-0.6)**	**-**
Hypertension*, n(%)	88 (27.2)	12 (27.9)	76 (27.1)	1.0 (0.5-2.1)	-
Type 2 Diabetes*, n(%)	49 (15.2)	13 (30.2)	36 (12.9)	**2.9 (1.4-6.1)**	**2.4 (1.1-5.4)**
Obesity*, n(%)	21 (6.5)	3 (6.9)	18 (6.4)	1.1 (0.3-3.9)	-
Chronic obstructive pulmonary disease*, n(%)	15 (4.6)	1 (2.3)	14 (5.0)	0.5 (0.1-3.5)	-
Chronic renal insufficiency*, n(%)	17 (5.2)	6 (13.9)	11 (3.9)	**3.9 (1.4-11.4)**	**3.4 (1.1-10.4)**
Cardiovascular diseases*, n(%)	14 (4.3)	2 (4.7)	12 (4.3)	1.1 (0.2-5.0)	-
Corticosteroids*, n(%)	171 (52.9)	30 (69.7)	141 (50.3)	**2.3 (1.1-4.5)**	**3.0 (1.4-6.5)**
CsDMARD*, n(%)	247 (76.5)	33 (16.3)	214 (76.4)	1.0 (0.5- 2.2)	-
CD20 inhibitor*, n(%)	21 (6.5)	7 (16.3)	14 (5.0)	**3.7 (1.4-9.9)**	**4.9 (1.7-14.5)**

*Overlapped, [1] 307 patients.

REFERENCES:
[1] WHO. Coronavirus disease (COVID-19) pandemic. https://www.who.int/emergencies/diseases/novel-coronavirus-2019. (accessed 26 January, 2021).
[2] Zhou F, et al. Lancet 2020;**395**(10229):1054-62.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3342

POS1243 TELEMEDICINE AND MANAGEMENT OF THE PATIENT AFFECTED BY GIANT CELL ARTERITIS DURING THE COVID-19 PANDEMIC - TELEMACOV

S. Parisi[1], M. C. Ditto[1], A. Laganà[1], C. L. Peroni[1], E. Fusaro[1]. *[1]AOU Città della Salute e della Scienza di Torino, Rheumatology Unit, Turin, Italy*

Background: Giant cell arteritis (GCA) is the most common primary systemic vasculitis in western countries with the highest incidence among persons 70–79 years of age. Treatment has been with glucocorticoids (GCs) alone for many decades but recently Tocilizumab (TCZ) has demonstrated efficacy in reducing GC dose and flare rates in patients with GCA. Therefore, both early diagnosis and regular monitoring are necessary for the correct management of GCA. The COVID-19 pandemic has led to decisions by the governments of the countries involved, aimed above all at reducing the contagion. This has also led to reductions in health activities, limiting them to those of urgency by reducing or canceling checkups involving the risk of a time gap which for the GCA meant the interruption of clinical monitoring and therapeutic adjustment. At the same time, the pandemic situation has stimulated remote monitoring activities, through telephone contacts or video calls carried out by the rheumatologist. EULAR identified a minimal data set aimed at research and for clinical use, which includes the main clinical and instrumental data to be taken into consideration in monitoring the patient. For many data a clinical examination is not necessary but an interview is sufficient. We activated the TELEMACOV protocol (TELEmedicine and Management of the patient affected by giant cell arteritis during the COVid-19 pandemic) monitoring the follow-up of patients affected by GCA through telemedicine tools in order to maintain an effective and risk-free follow-up in a pathology with a high risk of relapse.

Objectives: The purpose of the study is to evaluate the effectiveness of telemedicine in the follow-up of the patient with GCA.

Methods: We evaluated patients (pts) with a clinical diagnosis of GCA (received in previous periods) who were admitted to the our Rheumatology Unit. They were monitored monthly by telephone from 9 March to 9 June 2020 (during lockdown). All patients were asked questions divided according to the sub-groups listed below:
- Onset of new symptoms or their recurrence
- Exams carried out
- Current therapy
- Satisfaction of telephone call

Results: We performed 148 remote monitoring visits in 37 pts. The cohort was mainly composed by female (77,8%) and had a mean age of 71,85 ± 9,25 years. They were affected by GCA, with a mean duration of 5,3±2,3 months. The characteristics of these pts and the course of the disease are reported in Table 1. Pts treated with TCZ reduced their GC dose more than patients treated with GC alone (p: 0.032). Only one patient (treated with GC alone) had an ocular flare with the need to increase the dosage of the GC with good response and rapid

improvement. Furthermore, all patients considered this type of monitoring very satisfactory according to the Likert scale (1-5) with mean 4,4±0,2.

Conclusion: Our study has shown how telemedicine can be well used in pts with GCA as a possible alternative, for a limited period, to traditional visits, especially in a fragile population such as the elderly and more exposed to the risk of SARS-COV2 infection.

REFERENCES:

[1] Ehlers L et al. Ann Rheum Dis 2019 Sep;78(9):1160-1166
[2] Wagner E et al. Prim Care. 2012 Jun;39(2):241-59.

Table 1. Disease course and remote monitoring

Parameters	Baseline (at diagnosis)		Pre-lock down		First Interview		Second Interview	
Patients treated with only GC (19 pts)								
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
ESR	74,08	23,95	13,02	8,2	12,75	6,42	9,84	6,63
CRP mg/l	47,4	42,2	1,01	1,1	1,55	2,29	1,56	2,24
Hgb mg/dl	11,6	2,6	13,2	2,24	12,75	3,19	13,58	2,12
PGA (1-10)	7,55	2,05	2,71	1,79	2,24	1,59	2,15	1,04
EGA (1-10)	6,99	1,85	2,19	1,42	1,97	1,13	1,43	0,97
GC mg	52,72	18,3	10,1	6,95	7,6	4,51	6,67	3,1
Patients treated with GC and TCZ (18 pt)								
ESR	74,56	36,58	11,3	3,85	9,89	4,71	3,37	4,4
CRP mg/l	47,8	41,7	1,13	0,65	1,58	0,85	1,62	0,73
Hgb mg/dl	11,36	3,88	12,98	4,91	12,43	4,3	13,25	5,15
PGA (1-10)	7,14	3,11	2,47	2,15	1,89	0,4	1,93	0,72
EGA (1-10)	6,93	2,72	0,95	0,73	0,68	0,43	0,41	0,72
GC mg	51,76	18,85	8,04	4,38	5,88	3,92	4,16	4,32

PGA: Patient Global Assessment EGA: Evaluator Global Assessment;

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3357

POS1244

PRELIMINARY RESULTS OF LONG-TERM FOLLOW-UP OF THE HEALTH STATUS OF PATIENTS USING CSDMARDS AND B/TSDMARDS FOR RHEUMATIC DISEASES DURING THE COVID-19 PANDEMIC

F. Unlu Ozkan[1], K. Sari[1], I. Aktas[1]. [1]*University of Health Sciences Fatih Sultan Mehmet Training and Research Hospital, Physical Medicine and Rehabilitation, Istanbul, Turkey*

Background: Since its inception, the COVID-19 outbreak has been carefully monitored both by the patients using DMARDs and their physicians. There is no data that patients with rheumatic and musculoskeletal diseases (RMD) are at a higher risk of contracting COVID-19 disease than those without RMD (1). COVID-19-related death in people with RMD has been associated with older age, male gender, concomitant cardiovascular and pulmonary diseases, moderate/high disease activity, and certain treatments (rituximab (RTX), sulfasalazine (SSZ) and some immunosuppressants) (2).

Objectives: To determine the conditions of getting and being affected poorly by COVID-19 and related factors of RMD patients followed in our outpatient clinic.

Methods: 160 patients over 18 years of age who applied to our outpatient clinic between July 2020-January 2021; who used DMARDs for rheumatic diseases and agreed to participate were included in the study. The patients's demographic data, RMDs, csDMARDs and b/tsDMARDs usage, comorbid diseases and smoking status were recorded. The data of the patients on COVID-19 disease between March 2020 and January 2021 were questioned at each visit.

Table 1. Patient characteristics

	All Patients n=160	COVID-19 Patients n=24
Male	61 (38%)	6 (25%)
Female	99 (62%)	18 (75%)
Mean age	49.5	49.5
Ever smoker	88 (55%)	8 (33,3%)
Obesity	51 (32%)	9 (37,5%)
Hypertension (HT)	46 (29%)	7 (29%)
Diabetes (DM)	22 (14%)	2 (8%)
Cardiovascular disease (CVD)	26 (16%)	5 (20%)
Chronic lung disease (CLD)	12 (7,5%)	4 (16%)
SpA	71 (44,3%)	9 (37,5%)
RA	71 (44,3%)	14 (58,3%)
PsA	14 (8,8%)	1 (4,2%)
SLE	2 (1,25%)	-
PMR	2 (1,25%)	-
cDMARD only	82 (51,2%)	14 (58,3%)
b/tsDMARD only	55 (34,4%)	8 (33.3%)
Combined DMARD	23 (14,4%)	2 (8.4%)

The rate of getting COVID-19 infection was 15% in all patients. This rate was 18% in all obese patients, 19% in those with at least one comorbid disease (HT, DM, CVD, CLD), and 22% in those who were obese and had at least one comorbid disease. 16% of non-smokers and 9% of those who ever smoked got COVID-19. Among patients over the age of 65 (n=17), 2 patients (%12) had COVID-19. Treatments of RMDs of patients with COVID-19 were as follows: bDMARD=8 [(Etanercept(ETN) n=2, adalimumab (ADA) n=2, certolizumab pegol (CTZ) n=1, infliximab (IFX) n=1, golimumab (GOL) n=1, RTX n=1)], csDMARD=14 [(methotrexate (MTX) n=4, leflunomid (LEF) n=4, SSZ n=3, HCQ n=2, MTX+SSZ+HCQ n=1)], combined=2 [tofacitinib (TOF)+MTX n=1, TCZ+LEF n=1)], none of them was using glucocorticoids. Overall 17% of patients using csDMARD, 14,5% of patients using b/tsDMARD as monotherapy and 9% of patients using combination treatment had COVID-19. Of the patients using HCQ (n=14), 3 (21%) were diagnosed with COVID-19 disease. 18 of the patients received COVID-19 treatment at home, 6 were hospitalized and 1 of them (RA patient, LEF user) needed intensive care unit. None of them died.

Results: Patient characteristics are presented in Table 1. 57 (36%) of all patients had COVID-19 PCR test, 23 (14%) were positive, and 1 patient was diagnosed with COVID-19 because the CT findings were positive, although the PCR test was negative.

Conclusion: Preliminary results regarding the health status associated with COVID-19 of our patients with RMD are presented. Biologic drugs seems not to increase COVID-19 but final results will be presented after the completion of statistical analysis of all data.

REFERENCES:

[1] Landewé RB, Machado PM, Kroon F, et al. EULAR provisional recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2. Ann Rheum Dis. 2020;79(7):851-858. doi:10.1136/annrheumdis-2020-217877
[2] Strangfeld A, Schäfer M, Gianfrancesco MA, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry [published online ahead of print, 2021 Jan 27]. Ann Rheum Dis. 2021;annrheumdis-2020-219498. doi:10.1136/annrheumdis-2020-219498

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3445

POS1245

MORTALITY OF COVID-19 IN PATIENTS WITH RHEUMATIC DISEASES: COMPARISON TO THE GENERAL POPULATION IN MÉXICO

M. U. Martínez-Martínez[1], F. Irazoque-Palazuelos[2], T. S. Rodriguez-Reyne[3], E. Zamora[4], A. Castillo Ortiz[5], B. E. Zazueta[6], S. Duran Barragan[7], M. Rull-Gabayet[3], J. F. Moctezuma-Ríos[8], X. Jimenez Jimenez[9], E. Martin-Nares[3], D. Cervantes-Rosete[3], D. Vega-Morales[10], D. X. Xibille Friedmann[11], A. Barragán-Garfías[9], E. Alvarez Hernandez[8], M. Vázquez-Del Mercado Espinosa[12], C. F. Pacheco Tena[13], D. Alpizar-Rodriguez[14]on behalf of Mexican Study group of COVID-19 in Rheumatic diseases. [1]*Instituto Mexicano del Seguro Social, Internal Medicine, Rioverde, Mexico*; [2]*Centro de Investigación y Tratamiento Reumatológico S.C., Rheumatology, Mexico City, Mexico*; [3]*Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran, Immunology and Rheumatology, Mexico City, Mexico*; [4]*Centro Médico de Pensiones, Rheumatology, Merida, Mexico*; [5]*Private Practice, Rheumatology, Merida, Mexico*; [6]*Private Practice, Rheumatology, Mexicali, Mexico*; [7]*Clínica de Investigación en Reumatología y Obesidad, Rheumatology, Guadalajara, Mexico*; [8]*Hospital General de México 'Dr. Eduardo Liceaga', Rheumatology, Mexico City, Mexico*; [9]*Private Practice, Rheumatology, Mexico City, Mexico*; [10]*Private Practice, Rheumatology, Monterrey, Mexico*; [11]*Servicios de Salud de Morelos, Departamento de Investigación y Capacitación, Cuernavaca, Mexico*; [12]*Hospital Civil de Guadalajara "Juan I. Menchaca", Rheumatology, Guadalajara, Mexico*; [13]*Facultad de Medicina y Ciencias Biomédicas, Rheumatology, Chihuahua, Mexico*; [14]*Colegio Mexicano de Reumatología, Research Unit, Mexico City, Mexico*

Background: COVID-19 outcomes in Mexican patients with rheumatic diseases (RDs) in comparison to general population patients are unknown.

Objectives: To compare mortality and hospitalization of COVID-19 patients with RDs and those without.

Methods: We included for this study all the Mexican patients with RDs and COVID-19 registered from April 17th to October 30th, 2020 in the COVID-19 Global Rheumatology Alliance registry. We compare clinical and demographic characteristics of patients with RDs and COVID-19 to patients with COVID-19 that were selected randomly from the Mexican Epidemiology database (1:3). A logistic regression analysis was performed to adjust for confusion variables.

Results: We included 322 patients with COVID-19 and RDs and 969 controls without RDs. Table 1 shows the demographic characteristics and comorbidities of both groups. Bivariate analysis showed that patients with RDs had higher mortality, were older, and were more frequently hospitalized. Comorbidities, such as diabetes, hypertension, cardiovascular and renal diseases were also more frequent in patients with RDs. In the multivariate analysis, having a RD was no longer associated with mortality (Figure 1).

Table 1. Comparison of patients with COVID-19 with and without RDs

	COVID-19 patients without RDs	COVID-19 patients with RDs	p-value
N	969	323	
Age (mean (SD))	42.6 (17.4)	51.2 (13.9)	<0.001
Sex = Male (%)	455 (47.0)	55 (17.0)	<0.001
Deceased = Yes (%)	55 (5.7)	43 (13.3)	<0.001
Hospitalization = Hospitalized (%)	164 (16.9)	152 (47.1)	<0.001
Intubation = Yes (%)	27 (2.8)	32 (11.8)	<0.001
COPD_Asthma = Yes (%)	37 (3.8)	15 (4.6)	0.522
Diabetes = Yes (%)	114 (11.8)	49 (15.2)	0.116
Obesity = Yes (%)	128 (13.3)	21 (6.5)	0.001
Hypertension = Yes (%)	152 (15.8)	88 (27.2)	<0.001
Cardiovascular disease = Yes (%)	19 (2.0)	14 (4.3)	0.02
CRF = Yes (%)	22 (2.3)	17 (5.3)	0.007
Pregnancy = Yes (%)	5 (0.5)	2 (0.6)	0.827
Smoker = Yes (%)	86 (8.9)	10 (3.1)	0.001

Abbreviations: RDs, rheumatic diseases; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure.

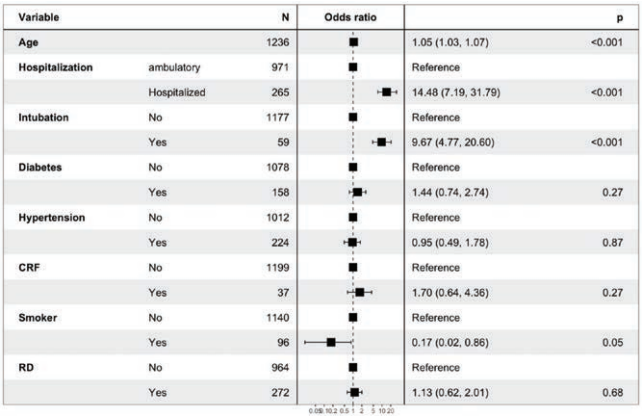


Figure 1. Multivariate analysis of mortality

Conclusion: Patients with RDs had higher comorbidities, hospitalizations, and mortality than the general population in the bivariate analysis. However, adjusted multivariate analysis showed that the odds for mortality were not increased because of having a RD. These findings suggest that the increased mortality of Mexican patients with RDs may be explained by the higher frequency of comorbidities in this population.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3447

POS1246

COVID-19 IN ITALIAN PATIENTS WITH RHEUMATIC AUTOIMMUNE SYSTEMIC DISEASES: RESULTS OF A NATIONWIDE SURVEY STUDY

C. Ferri[1], D. Giuggioli[2], V. Raimondo[3], L. Dagna[4], V. Riccieri[5], E. Zanatta[6], S. Guiducci[7], A. Tavoni[8], R. Foti[9], G. Cuomo[10], R. De Angelis[11], F. Cozzi[12], G. Murdaca[13], I. Cavazzana[14], N. Romeo[15], V. Codullo[16], F. Ingegnoli[17], R. Pellegrini[18], G. Varcasia[19], A. Della Rossa[20], M. De Santis[21], G. Abignano[22], M. Colaci[23], M. Caminiti[24], M. L'andolina[25], E. Lubrano[26], A. Spinella[2], F. Lumetti[2], G. De Luca[4], S. Bellando Randone[7], E. Visalli[9], S. Bilia[8], F. Masini[10], G. Pellegrino[5], E. Pigatto[12], E. Generali[21], F. Franceschini[14], G. Pagano Mariano[24], S. Barsotti[20], G. Pettiti[15], G. Zanframundo[16], R. Brittelli[27], V. Aiello[27], D. Scorpiniti[27], T. Ferrari[19], R. Caminiti[27], C. Campochiaro[4], P. Gigliotti[28], R. Cecchetti[29], D. Olivo[30], F. Ursini[31], V. Brusi[31], R. Meliconi[31], F. Caso[32], R. Scarpa[32], S. D'angelo[22], F. Iannone[33], M. Matucci-Cerinic[7], A. Doria[6], M. Miccoli[34], S. R. Paparo[35], F. Ragusa[34], G. Elia[34], S. M. Ferrari[34], P. Fallahi[36], A. Antonelli[37]. *[1]Rheumatology Unit, University of Modena & RE., School of Medicine, Modena, Italy; Rheumatology Clinic 'Madonna dello Scoglio' Cotronei, Crotone, Italy, Rheumatology Department, Modena; Cotronei, Italy*; *[2]Rheumatology Unit, University of Modena & RE., School of Medicine, Modena, Italy, Rheumatology Department, Modena, Italy*; *[3]Rheumatology Clinic 'Madonna dello Scoglio' Cotronei, Rheumatology Department, Cotronei, Italy*; *[4]Ospedale S. Raffaele, Milano, Italy, Rheumatology Department, Milano, Italy*; *[5]Rheumatology, Sapienza-University of Rome, Italy, Rheumatology Department, Roma, Italy*; *[6]Rheumatology, University of Padova, Italy, Rheumatology Department, Padova, Italy*; *[7]Rheumatology, University of Florence, Italy, Rheumatology Department, Firenze, Italy*; *[8]Clinical Immunology, University of Pisa, Pisa, Italy, Immunology, Pisa, Italy*; *[9]AOU Policlinico Vittorio Emanuele, Catania, Italy, Rheumatology Department, Catania, Italy*; *[10]University of Campania, Luigi Vanvitelli, Napoli, Italy, Rheumatology Department, Napoli, Italy*; *[11]Rheumatology Clinic, Marche Polytechnic University, Ancona. Italy, Dpt Clinical & Molecular Sciences, Ancona, Italy*; *[12]Ospedale "Villa Salus" Mestre, Italy, Rheumatology Department, Mestre, Italy*; *[13]Ospedale Policlinico S. Martino-University of Genova, Italy, Rheumatology Department, Genova, Italy*; *[14]Rheumatology, Spedali Civili di Brescia, Italy, Rheumatology Department, Brescia, Italy*; *[15]ASO S. Croce e Carle, Cuneo, Italy, Rheumatology Department, Cuneo, Italy*; *[16]Rheumatology, Policlinico San Matteo, Pavia, Italy, Rheumatology Department, Pavia, Italy*; *[17]Rheumatology, University of Milano, Italy, Rheumatology Department, Milano, Italy*; *[18]U.O.C. Medicina Interna "M.Valentini" P.O. Annunziata Cosenza, Italy, Medicine, Cosenza, Italy*; *[19]U.O.S. Reumatologia, Ospedale Castrovillari, Cosenza, Italy, Rheumatology Department, Castrovillari, Italy*; *[20]Rheumatology, University of Pisa, Pisa, Italy, Rheumatology Department, Pisa, Italy*; *[21]Istituto Clinico Humanitas, Rozzano, Milano, Italy, Rheumatology Department, Milano, Italy*; *[22]AOR San Carlo di Potenza, Potenza, Italy, Rheumatology Department, Potenza, Italy*; *[23]Rheumatology, University of Catania, Catania Italy, Rheumatology Department, Catania, Italy*; *[24]UOD Reumatologia- Grande Ospedale Metropolitano, Reggio Calabria, Italy, Rheumatology Department, Reggio Calabria, Italy*; *[25]Rheumatology Outpatient Clinic, ASP- Vibo Valentia–Tropea Hospital, Italy, Rheumatology Department, Tropea, Italy*; *[26]Rheumatology, Università del Molise, Campobasso, Italy, Rheumatology Department, Campobasso, Italy*; *[27]Rheumatology Clinic 'Madonna dello Scoglio' Cotronei, Crotone, Italy, Rheumatology Department, Cotronei, Italy*; *[28]U.O.T. Specialistica Ambulatoriale ASP 201, Cosenza, Italy, Rheumatology Department, Cosenza, Italy*; *[29]Ospedale di Portoferraio, Livorno, Italy, Rheumatology Department, Livorno, Italy*; *[30]Rheumatology Outpatient Clinic, San Giovanni di Dio Hospital, Crotone, Italy, Rheumatology Department, Crotone, Italy*; *[31]University of Bologna, Rizzoli Orthopaedic Institute Bologna, Bologna, Italy, Rheumatology Department, Bologna, Italy*; *[32]Rheumatology Unit, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy, Rheumatology Department, Napoli, Italy*; *[33]UO Reumatologia – DETO, Università di Bari, Italy, Rheumatology Department, Bari, Italy*; *[34]University of Pisa, School of Medicine, Pisa, Italy, Department of Clinical and Experimental Medicine, Pisa, Italy*; *[35] University of Pisa, School of Medicine, Pisa, Italy, Department of Translational Research & New Technologies in Medicine and Surgery, Pisa, Italy*; *[36]University of Pisa, School of Medicine, Pisa, Italy, Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy*; *[37]University of Pisa, School of Medicine, Pisa, Italy, Clinical and Experimental Medicine, Pisa, Italy*

Background: SARS-CoV-2 infection poses a serious challenge for patients with rheumatic autoimmune systemic diseases (ASD), characterized by marked immune-system dysregulation and frequent visceral organ involvement.
Objectives: To evaluate the impact of Covid-19 pandemic in a large series of Italian patients with ASD.
Methods: Our multicenter telephone survey (8-week period, March-April 2020) included a large series of 2,994 patients (584 M, 2,410 F, mean age 58.9±13.4SD years) with ASD followed at 34 tertiary referral centers of 14 regions of northern, central, and southern Italian macro areas, characterized by different prevalence of SARS-CoV-2 infection. According to currently used criteria, Covid-19 was classified as *definite* Covid-19 (signs or symptoms of Covid-19 confirmed by positive oral/nasopharyngeal swabs at PCR testing) or *highly suspected* Covid-19 (signs or symptoms highly suggestive of Covid-19, but not confirmed by PCR testing due to limited availability of virological tests in that period). The results were analyzed performing the Odds Ratio by Java-Stat 2-way Contingency Table Analysis.
Results: The main findings of the survey study revealed a significantly increased prevalence of Covid-19 in:
a.the whole series of ASD patients (*definite* Covid-19: 22/2994, 0.73%; p=0.0007; *definite* Covid-19 plus *highly suspected* Covid-19: 74/2,994, 2.47%; p<0.0001) when compared to Italian general population of Covid-19 infected individuals (349/100000 = 0.34%; data from Italian Superior Institute of Health; https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-national-surveillance-system).
b.the subgroup of patients with connective tissue diseases or systemic vasculitis (n = 1,901) compared to the subgroup of inflammatory arthritis (n = 1,093), namely rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis (*definite* Covid-19: 19/1,901, 0.99%, vs 3/1,093, 0.27%; p=0.036; *definite* Covid-19 plus *highly suspected* Covid-19: 69/1,901, 3.6%, vs 5/1,093, 0.45%; p<0.0001)
c.the subgroup of patients with pre-existing interstitial lung involvement (n = 526) compared to those without (n = 2,468) (*definite* Covid-19: 10/526, 1.90%, vs 12/2,468, 0.48%; p=0.0015; *definite* Covid-19 plus *highly suspected* Covid-19: 33/526, 6.27%, vs 41/2,468, 1.66%; p<0.0001).

Of interest, the prevalence of Covid-19 did not correlate with presence/absence of different comorbidities, mainly diabetes, cardio-vascular and/or renal disorders, as well as of ongoing treatments with biological DMARDs; while patients treated with conventional DMARDs showed a significantly lower prevalence of Covid-19 compared to those without. Covid-19 was more frequently observed in the patients' populations from northern and central compared to southern Italian macro area with lower diffusion of pandemic. Clinical manifestations of Covid-19, observed in 74 patients, were generally mild or moderate; 4/9 individuals requiring hospital admission died for severe pneumonia.

Conclusion: The prevalence of Covid-19 observed in ASD patients during the first wave of pandemic was significantly higher than that observed in Italian general population; moreover, the actual prevalence of Covid-19 might be underestimated due to the high number of mild variants as well as the possible clinical overlapping between these two conditions. Patients with ASD should be invariably regarded as 'frail patients' during the pandemic course, considering the risk of worse outcome in the acute phase of Covid-19, as well as the potential long-term effects of viral infection.

The statistically significant association of Covid-19 with connective tissue diseases/systemic vasculitis, as well as with pre-existing interstitial lung involvement, suggests the presence of distinct clinico-pathological ASD subsets, characterized by markedly different patients' vulnerability to SARS-CoV-2 infection.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3493

POS1247 CLINICAL FEATURES AND OUTCOMES OF COVID-19 IN PATIENTS WITH IGG4-RELATED DISEASE. A COLLABORATIVE EUROPEAN MULTI-CENTRE STUDY

G. A. Ramirez[1,2], M. Lanzillotta[1,2], M. Ebbo[3,4], A. Fernandez-Codina[5,6,7,8], G. Mancuso[1,2], F. Martínez-Valle[9,10], O. Orozco-Galvez[9,10], N. Schleinitz[3,4], L. Dagna[1,2], E. L. Culver[11,12], E. Della Torre[1,2]. *[1]IRCCS Ospedale San Raffaele, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy*; *[2]Università Vita-Salute San Raffaele, Immunology, Milan, Italy*; *[3]CHU de Marseille - Hôpital de la Timone, Département de Médecine Interne, Marseille, France*; *[4]Aix-Marseille University, Internal Medicine, Marseille, France*; *[5]Windsor Regional Hospital, General Internal Medicine, Windsor, Canada*; *[6]Saint Joseph's Health Care London, Rheumatology, London, Canada*; *[7]University of Western Ontario, Rheumatology, London, Canada*; *[8]Hospital Clinic i Provincial, Emergency Department, Barcelona, Spain*; *[9]Universitat Autònoma de Barcelona, Autoimmune Diseases Research Lab., Barcelona, Spain*; *[10]Vall d'Hebrón Hospital, Systemic Diseases Unit, Internal Medicine Service, Barcelona, Spain*; *[11]Oxford University Hospitals NHS Foundation Trust, Hepatology, Oxford, United Kingdom*; *[12]University of Oxford, Translational Gastroenterology Unit, Oxford, United Kingdom*

Background: Coronavirus disease 2019 (COVID-19) is a pandemic-spread systemic infectious disease with prominent respiratory manifestations and significant associated morbidity and mortality. Elderly people are most significantly affected with mortality ranging from 2.4% (age 60-69) to 19.6% (age>80) in European Countries. The prevalence of COVID-19 and of its complications in patients with immune-mediated disorders, remains unclear. The frequency and impact of COVID-19 on patients with IgG4-related diease (IgG4-RD), many of whom are on concurrent immunosuppression has not been addressed.

Objectives: To assess the epidemiological and clinical relevance of COVID-19 in patients with IgG4-RD.

Methods: This is a multi-centre retrospective observational study of IgG4-RD patients from France, Italy, Spain and the United Kingdom. Demographics, comorbidities, IgG4-RD features, current and past treatment along with COVID-19-suggestive symptoms and COVID-19 diagnoses from February 2020 to January 2021 were recorded by means of direct or phone interviews. Patients with reverse-transcriptase polymerase chain reaction-confirmed (cCOVID) or presumed COVID-19 based on clinical, serological or imaging features (pCOVID) were pooled for analysis (totCOVID) and compared to patients who were not diagnosed with COVID-19. Inter-group comparison of categorical and quantitative variables were performed by using the chi-square test with Fisher's correction and the Mann-Whitney's test respectively. Data are expressed as median (interquartile range) unless otherwise specified.

Results: A total of 305 patients [71% males, median age 64 (54-74) years] were studied. Pancreato-biliary disease was the most frequently observed IgG4-RD phenotype (39%). Fifty-one percent of patients were taking corticosteroids at time of interview and 30% were on biological or conventional immunosuppressants. Thirty-two totCOVID cases (23 cCOVID, nine pCOVID) were identified: 11/32 were hospitalised, two needed intensive care and four (13%; 3/4 aged >80 years) died. Having one or more infected family members was a risk factor for COVID-19 in patients with IgG4-RD (OR=19.9; p<0.001). No other demographic, clinical or treatment features associated with COVID-19. In particular there was no association between adverse outcomes with COVID-19 and higher doses of steroids (>20mg) or rituximab administration.

Conclusion: The prevalence and course of COVID-19 in IgG4-RD patients are similar to those of the general population of the same age, with no evident impact of disease- or treatment-related factors to the basal infectious risk. Effective public health countermeasures might be beneficial for patients with IgG4RD.

REFERENCES:

[1] European Centre for Disease Prevention and Control (ECDC): https://covid19-surveillance-report.ecdc.europa.eu/
[2] Yang H, Ann Rheum Dis, 2021

Disclosure of Interests: Giuseppe Alvise Ramirez: None declared, Marco Lanzillotta: None declared, Mikael Ebbo: None declared, Andreu Fernandez-Codina Consultant of: consulting fees from Atheneum Consulting, Gaia Mancuso: None declared, Fernando Martínez-Valle: None declared, Olimpia Orozco-Galvez: None declared, Nicolas Schleinitz: None declared, Lorenzo Dagna Consultant of: Abbvie, Amgen, Biogen, BristolMyers Squibb, Celltrion, Galapagos, GlaxoSmithKline, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI, Grant/research support from: The Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR) received unresctricted research/educational grants from Abbvie, Bristol-Myers Squibb, Celgene, GlaxoSmithKline,Janssen, Merk Sharp & Dohme, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi Genzyme, and SOBI, Emma L. Culver: None declared, Emanuel Della Torre: None declared
DOI: 10.1136/annrheumdis-2021-eular.3513

POS1248 SAFETY PROFILE OF PFIZER-BIONTECH COVID-19 VACCINE IN PATIENTS WITH RHEUMATIC DISEASES: PRELIMINARY ASSESSMENT

G. Cuomo[1], M. Atteno[2], C. Naclerio[3], L. E. Adinolfi[4], C. Romano[4]. *[1]University of Campania Studies "Luigi Vanvitelli", Precision of Medicine, Napoli, Italy*; *[2]Azienda Ospedaliera di Rilievo Nazionale San Giuseppe Moscati, Internal Medicine, Avellino, Italy*; *[3]P.O. Scarlato, UO. Dipartiemntale di Reumatologia, Scafati, Italy*; *[4]University of Campania Studies "Luigi Vanvitelli", Department of Medical and Surgical Sciences, Napoli, Italy*

Background: Efficacious vaccines are urgently needed to contain the ongoing coronavirus disease 2019 (Covid-19) pandemic of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On December 11, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for Pfizer-BioNTech COVID-19 vaccine to prevent COVID-19, administered as 2 doses separated by 21 days (1)

On December 27, 2020, Italy started use of Pfizer-BioNTech COVID-19 vaccine and initial doses were reserved for health care personnel

Objectives: The primary end points were the safety of each administered dose in patients with Rheumatic diseases (RD's)

Methods: In this multicenter, observational study, we interviewed by phone 27 patients with rheumatic diseases (RDs) and 30 healthy subjects receiving the Pfizer-BioNTech vaccine (0.3 ml i.m. in two doses 21 days apart, time 0 and 3 weeks).

Results: As of 30 January 2021, 57 subjects (27 patients and 30 healthy subjects) were interviewed. The epidemiological and clinical features of the 27 patients are reported in Table 1. Among the whole population, 35 subjects (16 patients and 19 healthy subjects) complained of an adverse event after the first vaccine dose, with symptom onset occurring within 1 day of vaccination. All adverse events (100%) were classified as nonserious and included: injection site pain (17), fatigue (5), headache (16), fever (3), tachycardia (2), and paresthesia (2).

After 21 days, 6 patients and 11 healthy subjects received the second vaccine dose. Fifteen (5 patients and 10 healthy subjects) of them (88%) reported adverse events, again categorized as nonserious. Specifically, injection site pain (7), fatigue (10), headache (10), fever (10), paresthesia (1), cutaneous vasculitis (1), itchy and scratchy throat (1), diarrhea (4), lymph node enlargement (1) were recorded. No differences were noted between patients with RDs and healthy subjects in terms of adverse events.

Conclusion: This preliminary study shows that the Pfizer-BioNTech COVID-19 vaccine is as safe in patients with RDs as in healthy subjects. Whether patients with RDs will develop protective titers of anti-SARS-CoV-2 antibodies as compared to healthy subjects will be evaluated in further, ongoing studies.

REFERENCES:

[1] Dooling K et al. MMWR Morb Mortal Wkly Rep 2020; 69:1857

Table 1.

Table 1

Epidemiological and clinical features	Patients (27)	Healthy control (30)
Age (m±sd)	48.7±11	49.1±10
F/M	21/6	20/10
Comorbidity		
Hypertension	4	5
Obesity	2	3
Diabetes	1	1
Rheumatic disease		
Psoriatic arthritis / Spondylo-arthritis	10/3	
Rheumatoid arthritis	6	
Systemic sclerosis / Sjogren syndrome/SLE	5/1/2	
Therapy		
TNF-i	5	
Small molecules	3	
Anti-IL17	3	
OH-clorochine	5	
Methotrexate /Mycophenolate	4/1	
Anti-il 12/23	2	
Anti-IL 6 /CTLA4–Ig	1/1	
No therapy	2	

Acknowledgements: I thank the Italian League of Systemic Sclerosis for launching a survey for ssc patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3529

POS1249 MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN DURING THE COVID-19 PANDEMIC IN TURKEY: FIRST REPORT FROM THE EASTERN MEDITERRANEAN

Y. Ozsurekci[1], S. Gürlevik[1], S. Kesici[2], U. Kaya Akca[3], P. D. Oygar[1], K. Aykac[4], D. Karacanoglu[2], O. Sarıtas Nakip[2], S. Ilbay[1], B. Katlan[2], A. B. Cengiz[1], Ö. Basaran[3], B. C. Cura Yayla[4], J. Karakaya[5], Y. Bilginer[3], B. Bayrakci[2], M. Ceyhan[1], S. Özen[3]. [1]*Hacettepe University School of Medicine, Department of Pediatric Infectious Diseases, Ankara, Turkey*; [2]*Hacettepe University School of Medicine, Department of Pediatrics, Division of Pediatric Intensive Care Unit, Ankara, Turkey*; [3]*Hacettepe University School of Medicine, Department of Pediatrics, Division of Pediatric Rheumatology, Ankara, Turkey*; [4]*University of Health Science Ankara Training and Research Hospital, Department of Pediatric Infectious Diseases, Ankara, Turkey*; [5]*Hacettepe University School of Medicine, Department of Bioistatistics, Ankara, Turkey*

Background: The severity of COVID-19 symptoms can range from mild to severe. Severe COVID-19 cases with excessive hyperinflammation have many overlap features with multisystem inflammatory syndrome in children (MIS-C).
Objectives: We aimed to describe the typical clinical and laboratory features and treatment of children diagnosed with MIS-C and to understand the differences as compared to severe/critical pediatric cases with COVID-19 in an eastern Mediterranean country.
Methods: Children (aged <18 years) who diagnosed with MIS-C and severe/critical pediatric cases with COVID-19, were admitted to hospital between 26 March and 3 November 2020 were enrolled in the study.
Results: A total of 52 patients, 22 patients diagnosed with COVID-19 with severe/critical disease course and 30 patients diagnosed with MIS-C. Although severe COVID-19 cases and cases with MIS-C share many clinical and laboratory features, MIS-C cases had longer fever duration and higher rate of the existence of rash, conjunctival injection, peripheral edema, abdominal pain, altered mental status, and myalgia than in severe cases (p<0.001 for each). Of all, 53.3% of MIS-C cases had the evidence of myocardial involvement as compared to severe cases (27.2%). Additionally, C-reactive protein (CRP) and white blood cell (WBC) are the independent predictors for the diagnosis of MIS-C, particularly in the existence of conjunctival injection and rash. Corticosteroids, intravenous immunoglobulin (IVIG), and biologic immunomodulatory treatments were mainly used in MIS-C cases rather than cases with severe disease course. There were only 3 deaths among 52 patients, one of whom had Burkitt lymphoma and the two cases with severe COVID-19 of late referral.
Conclusion: Differences between clinical presentations, acute phase responses, organ involvements, and management strategies indicate that MIS-C might be a distinct immunopathogenic disease as compared to pediatric COVID-19. Conjunctival injection and higher CRP and low WBC count seem good diagnostic parameters for MIS-C cases.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3572

POS1250 VITAMIN D DEFICIENCY IS MAINLY ASSOCIATED WITH SEVERE LUNG INVOLVEMENT, LONGER DISEASE DURATION AND RISK OF DEATH IN ELDERLY COVID-19 PATIENTS

A. Sulli[1], E. Gotelli[1], A. Casabella[1], M. Grosso[2], C. Schenone[1], C. Pizzorni[1], S. Paolino[1], E. Alessandri[1], V. Smith[3], M. Cutolo[1]. [1]*Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic Hospital, Genova, Italy*; [2]*Pneumology Unit, IRCCS San Martino Polyclinic Hospital, Genova, Italy*; [3]*Department of Rheumatology, Ghent University Hospital, Department of Internal Medicine, VIB Inflammation Research Centre Ghent University, Ghent, Belgium*

Background: Vitamin D regulates the innate and adaptive immune system responses and low vitamin D levels have been associated with the increased risk of respiratory tract infections (1). Vitamin D deficiency has been recently reported to interfere with the prognosis of COVID-19 (2,3).
Objectives: The aim of this study was to correlate the 25OH-vitamin D serum levels with lung involvement and disease severity, in a cohort of elderly patients hospitalized for SARS-CoV-2 infection.
Methods: Sixty-five COVID-19 patients (mean age 76±13 years) and sixty-five sex- and age-matched control subjects (CNT) were included in the study. Respiratory parameters (PaO_2, SO_2, $PaCO_2$, PaO_2/FiO_2), clinical and laboratory parameters (including 25OH-vitamin D, D-dimer, C-reactive protein) and type of radiological pulmonary involvement were collected at hospital admission. Statistical analysis was performed by non-parametric tests.
Results: Vitamin D sufficiency (>30 ng/ml), insufficiency (between 20 and 30 ng/ml), deficiency (between 10 and 20 ng/ml) and severe deficiency (<10 ng/ml) were observed respectively in 11, 11, 21 and 57 % of COVID-19 patients. Vitamin D serum levels were found significantly lower in COVID-19 patients than in CNT (median 8 vs 16 ng/ml, p=0.001). A statistically significant positive correlation was observed between vitamin D serum levels and SO_2 (p=0.05), PaO_2 (p=0.03), PaO_2/FiO_2 (p=0.02). A statistically significant negative correlation was found between vitamin D serum levels and severity of radiologic pulmonary involvement: vitamin D was significantly lower in COVID-19 patients with either diffuse/severe interstitial lung involvement (p=0.05) or multiple lung consolidations (p=0.0001) than in those with mild radiological lung involvement. Significantly lower vitamin D serum levels were found in COVID-19 patients who died during hospitalization, compared to those who survived (median 3 vs 8 ng/ml, p=0.05). Finally, a statistically significant negative correlation was found between vitamin D serum levels and D-dimer (p=0.04), C-reactive protein (p=0.04) and disease duration (p=0.05).
Conclusion: This study confirms that severe vitamin D deficiency is associated with more severe lung involvement, longer disease duration and risk of death in elderly COVID-19 patients.
REFERENCES:
[1] Cutolo M, et al. RMD Open. 2020; 6(3):e001454.
[2] Bilezikian JP, et al. Eur J Endocrinol. 2020; 183(5):R133-R147.
[3] Weir EK, et al. Clin Med (Lond). 2020; 20:e107-e108.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3576

POS1251 ROLE OF SYSTEMIC AUTOINMUNE CONDITIONS IN HOSPITAL ADMISSIONS RELATED TO COVID-19

I. Perez-Sancristobal[1], L. Lopez Pedraza[2], M. P. Álvarez Hernandez[1], J. I. Colomer[3], A. Madrid García[2], B. Fernandez[1], C. Martinez Prada[1], L. Rodriguez Rodriguez[2], A. Mucientes[2], L. León[2], L. Abasolo[2]. [1]*Hospital Clínico San Carlos, Reumathology, Madrid, Spain*; [2]*Instituto de Investigación Sanitaria del Hospital Clínico San Carlos, Reumathology, Madrid, Spain*; [3]*Fundación para la Investigación Biomedica, Reumathology, Madrid, Spain*

Background: The COVID-19 pandemic continues worldwide and has had a strong impact on public health, quality of life and economy of the general population. To date, the number of infections and deaths are still increasing. From the beginning of the pandemic, efforts were intensified to identify risk factors for development of the severe form of COVID-19. In this sense underlying medical comorbidities have been shown to have a worse prognosis in these patients.

Objectives: In patients with rheumatic and musculoskeletal diseases (RMDs) and infected with Covid – 19, we aim to investigate the role of systemic autoimmune conditions compared to other type of RMDs in severity of COVID-19 in terms of hospital admissions.

Methods: An observational longitudinal study was conducted during the epidemic peak in Madrid (1stMar to 20thMay2020). All patients attended at the rheumatology outpatient clinic of a tertiary hospital with a diagnosis of RMDs and Covid-19 infection were included (according to a medical diagnosis or confirmed with a positive SARS-CoV-2 PCR diagnostic test). All patients were included since the time of COVID-19 diagnosis. Main variable: hospital admission related to Covid -19 infection. Independent variable: type of RMD including: autoimmune (systemic autoimmune conditions and inflammatory joint disease (IJD)) and non-autoimmune (mechanical diseases, and inflammatory diseases (microcrystalline arthritis and tendonitis)). Covariates: sociodemographic, clinical and therapy used. Statistical analysis: description of the sociodemographic, clinical and treatment characteristics of the patients. A multivariate logistic regression adjusted by age, sex and comorbidities was used to evaluate the risk of the different types of RMDs in hospital admissions related to Covid-19. The results were expressed as OR with its corresponding confidence interval (95% CI).

Results: 406 patients were included with RMDs and Covid- 19 infection. 69.21% were women with a mean age at diagnosis of 60 ± 15.26 years. The evolution time from the diagnosis of RMD was 8 ± 8.38 years. 26% had comorbidity at baseline. 25% were chronically on corticoids prior to the infection. Of the 406 patients, 244 (60.09%) had non-autoimmune RMD (157 mechanic, 87 inflammatory) and 162 (39.9%) (106 (65.43%) IJD, 56 (34.56%) systemic autoimmune condition) had autoimmune RMD. 36% of all patients were admitted (31% from not autoimmune RMDs and 43% from autoimmune RMD (p = 0,013). The risk of hospital admission in autoimmune RMD compared to non-autoimmune RMD was higher (OR: 1.68; [1.11-2.54], p=0.013), being the risk of systemic autoimmune condition compared to both IJD and non-autoimmune RMD higher (OR IJD: 0.41 [0.21-0.51], p=0.01; OR non-autoimmune: 0.33; [0.18-0.61]; p=0.000). After adjusting by confounders, autoimmune RMD had higher risk of hospital admissions compared to the rest (OR: 1.75; [1.04-2.95]; p=0.03), and specifically systemic autoimmune condition had higher risk compared to IJD (OR of IJD 0.33; [0.14-.076]; p=0.009) and compared to non–autoimmune (OR non autoimmune 0.28; [0.13-0.59], p=0.001). Advanced age (OR: 1.10; [1.07-1.12], p<0.001), male (OR 0.58; [0.33-1.02], p=0.06), and more number of comorbidities (OR 1.39; [1.02-1.90] p=0.03) also increased the risk of hospitalization related to COVID-19.

Conclusion: One third of the RMD patients infected with COVID-19 required hospital admission. This study shows that patients with autoimmune and specifically with systemic autoimmune conditions have a higher risk of hospitalization related to COVID-19. We also show that advanced age, male sex and a higher number of comorbidities can contribute to worsen the prognosis of the COVID-19 disease.

REFERENCES:

[1] Jorge A, et al. Temporal trends in severe COVID-19 outcomes in patients with rheumatic disease: a cohort study. *Lancet Rheumatol*. Ahead of print 2021.

[2] Hyrich KL, Machado PM. Rheumatic disease and COVID-19: epidemiology and outcomes. *Nature Reviews Rheumatology* 2020; 17: 71–72.

[3] Bonfá E, et al. How COVID-19 is changing rheumatology clinical practice. *Nat Rev Rheumatol* 2021; 17: 11–15.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3676

POS1252

COVID-19 IN PATIENTS WITH RHEUMATIC DISEASES ON CHRONIC USE OF HYDROXYCHLOROQUINE IN A LARGE BRAZILIAN COHORT – A 24-WEEK PROSPECTIVE STUDY

G. Salviato Pileggi[1], G. Ferreira[2], A. P. Gomides[3], E. Reis Neto[4], M. Abreu[5], C. Albuquerque[3], N. Araújo[6], A. B. Bacchiega[1], D. Bianchi[7], B. Bica[8], E. Bonfa[9], E. Borba[9], D. Brito[10], A. Duarte[11], M. Peixoto Gu e Silva de Souza[12], K. Wagner Poti Gomes[13], A. Maria Kakehasi[2], R. Cavalheiro Do Espírito Santo[14], P. Realle[15], E. Klumb[16], C. C. Lanna[2], C. Marques[11], O. Monticielo[14], L. Mota[3], G. Munhoz[17], E. Paiva[18], H. Pereira[19], J. R. Provenza[20], S. Ribeiro[19], L. Rocha Jr[21], C. Sampaio[22], V. Sampaio[23], E. Sato[4], T. Laroca Skare[24], V. De Souza[15], V. Valim[25], M. Lacerda[23], R. Xavier[14], M. Pinheiro[26]. *[1]Faculdade de Medicina de Barretos (FACISB), Education & Research Institute Cancer Hospital Barretos, Barretos-SP, Brazil, Rheumatology, Barretos-SP, Brazil*; *[2]Hospital das Clínicas, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte-MG, Brazil, Rheumatology, Belo Horizonte-MG, Brazil*; *[3]Hospital Universitário de Brasília da Universidade de Brasília, EBSERH (HUB-UnB), Brasília-DF, Brazil, Rheumatology, Brasília-DF, Brazil*; *[4]Universidade Federal de São Paulo (UNIFESP/EPM), Rheumatology, São Paulo-SP, Brazil*; *[5]Universidade Federal do Rio de Janeiro (UFRJ), Rheumatology, Rio de Janeiro-RJ, Brazil*; *[6]Hospital do Servidor Público Estadual, Instituto de Assistência Médica ao Servidor Público Estadual (IAMSPE), São Paulo-SP, Brazil, Rheumatology, São Paulo-SP, Brazil*; *[7]Santa Casa de Misericórdia do Rio de Janeiro (HGSCMRJ), Rio de Janeiro-RJ, Brazil, Rheumatology, Rio de Janeiro-RJ, Brazil*; *[8]Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro-RJ, Brazil, Rheumatology, Rio de Janeiro-RJ, Brazil*; *[9]Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo-SP, Brazil, Rheumatology, São Paulo-SP, Brazil*; *[10]Hospital Universitário Lauro Wanderley, Universidade Federal da Paraíba (UFPB), João Pessoa-PB, Brazil, Rheumatology, João Pessoa-PB, Brazil*; *[11]Hospital das Clínicas da Universidade Federal de Pernambuco (UFPE), Recife-PE, Brazil, Rheumatology, Recife-PE, Brazil*; *[12]Santa Casa de Misericórdia de Belo Horizonte, Belo Horizonte-MG, Brazil, Rheumatology, Belo Horizonte-MG, Brazil*; *[13]Hospital Geral de Fortaleza (HGF), Fortaleza-CE, Brazil, Rheumatology, Fortaleza-CE, Brazil*; *[14]Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre-RS, Brazil, Rheumatology, Porto Alegre-RS, Brazil*; *[15]Hospital Universitário da Universidade Federal de Juiz de Fora (UFJF), Juiz de Fora-MG, Brazil, Rheumatology, Juiz de Fora-MG, Brazil*; *[16]Hospital Universitário Pedro Ernesto, Universidade do Estado do Rio de Janeiro (UERJ), Rio de Janeiro-RJ, Brazil, Rheumatology, Rio de Janeiro-RJ, Brazil*; *[17]Irmandade da Santa Casa de Misericórdia de São Paulo (ISCMSP), São Paulo-SP, Brazil, Rheumatology, São Paulo-SP, Brazil*; *[18]Universidade Federal do Paraná (UFPR), Curitiba-PR, Brazil, Rheumatology, Curitiba-PR, Brazil*; *[19]Hospital Universitário Getúlio Vargas Universidade Federal do Amazonas, Manaus-AM, Brazil, Rheumatology, Manaus-AM, Brazil*; *[20]Pontifícia Universidade Católica de Campinas (PUC-CAMP), Campinas-SP, Brazil, Rheumatology, Campinas-SP, Brazil*; *[21]Instituto de Medicina Integral Professor Fernando Figueira (IMIP/ PE), Recife-PE, Brazil, Rheumatology, Recife-PE, Brazil*; *[22]Instituto de Ensino e Pesquisa no Sírio Libanês, São Paulo-SP, Brazil, RedCap, São Paulo-SP, Brazil*; *[23]Instituto Leônidas & Maria Deane, Fiocruz, Manaus-AM, Brazil, Epidemiology, Manaus-AM, Brazil*; *[24]Hospital Universitário Evangélico Mackenzie (HUEM), Curitiba-PR, Brazil, Rheumatology, Curitiba-PR, Brazil*; *[25]Hospital Universitário Cassiano Antonio de Moraes, Universidade Federal do Espírito Santo, Vitória-ES, Brazil, Rheumatology, Vitória-ES, Brazil*; *[26]Universidade Federal de São Paulo (UNIFESP/EPM), Rheumatology, São Paulo, Brazil*

Background: The role of chronic use of hydroxychloroquine (HCQ) in rheumatic disease (RD) patients during the SARS-CoV-2 pandemic is still subject of discussion.

Objectives: To compare the occurrence of COVID-19 and its outcomes between RD patients on HCQ use with individuals from the same household not taking the drug during community viral transmission in an observational prospective multicenter study in Brazil.

Methods: Participants were enrolled and monitored through 24-week (From March 29th to Sep 30th, 2020) regularly scheduled phone calls performed by trained medical professionals. Epidemiological and demographic data, as well as RD disease activity status and current treatment data, specific information about COVID-19, hospitalization, need for intensive care, and death was recorded in both groups and stored in the Research Electronic Data Capture (REDCap) database. COVID-19 was defined according to the Brazilian Ministry of Health (BMH) criteria. The statistical analysis was performed using IBM-SPSS v.20.0 software. Group comparisons were made using the Man-Whitney, Chi-Square and Fisher Exact Test, as well as multivariate regression models adjusted to confounders. Survival curves were performed using Kaplan-Meier analysis.

Results: A total of 10,427 participants mean age (SD) of 44.04 (14.98) years were enrolled, including 6004 (57.6%) rheumatic disease patients, of whom 70.8% had systemic lupus erythematosus (SLE), 6.7% rheumatoid arthritis (RA), 4% primary Sjögren's syndrome (pSS), 1.8% mixed connective tissue disease (DMTC), 1% systemic sclerosis (SSc) and others (15.9), including overlap syndromes. In total, 1,132 (10.8%) participants fulfilled criteria for COVID-19, being 6.7% RD patients and 4.1% controls (p=0.002). A recent influenza vaccination had a protective role (p<0.001). Moderate and severe COVID-19 included the need for hospitalization, intensive care, mechanical ventilation or death. Infection severity was not different between groups (p=0.391) (Table 1). After adjustments for multiple confounders, the main risk factors significantly associated with COVID-19 were higher education level (OR=1.29 95%CI 1.05-1.59), being healthcare professionals (OR=1.91; 95%CI 1.45-2.53), presence of two comorbidities (OR=1.31; 95%CI 1.01-1.66) and three or more comorbidities associated (OR=1.69; 95%CI 1.23-2.32). Interestingly, age >=65 years (OR=0.20; 95%CI 0.11-0.34) was negatively associated. Regarding RD, the risk factors associated with COVID-19 diagnosys were SLE (OR= 2.37; 95%CI 1.92-293), SSc (OR=2.25; 95%CI 1.05-4.83) and rituximab use (OR=1.92; 95%CI 1.13-3.26). In addition, age >=65 years (OR=5.47; 95%CI 1.7-19.4) and heart disease (OR=2.60; 95%CI 1.06-6.38) were associated with hospitalization. Seven female RD patients died, six with SLE and one with pSS, and the presence of two or more comorbidities were associated with higher mortality rate.

Conclusion: Chronic HCQ use did not prevent COVID-19 in RD compared to their household cohabitants. Health care profession, presence of comorbidities LES, SSc and rituximab were identified as main risk factors for COVID-19 and aging and heart disease as higher risk for hospitalization. Our data suggest these outcomes could be considered to manage them in clinical practice.

Table 1. Frequency and severity of COVID-19 in patients with rheumatic diseases on chronic use of hydroxychloroquine compared to their household controls

			Groups		
		Total	Patients		P
COVID-19 outcomes		(%)	(%)	Controls (%)	
Diagnosis	No	9256 (89.1)	5300 (88.3)	3956 (90.2)	0.002
	Yes	1132 (10.9)	704 (11.7)	428 (9.8)	
Severity	Mild	1059 (93.6)	662 (94.0)	397 (92.8)	0.391
	Moderate	52 (4.6)	32 (4.5)	20 (4.7)	
	Severe	21 (1.9)	10 (1.4)	11 (2.6)	

HCQ: hydroxychloroquine.Moderate and severe COVID-19 included the need for any of the following: hospitalization, intensive care, mechanical ventilation or death.

Acknowledgements: To the Brazilian Society of Rheumatology for technical support and rapid nationwide mobilization.
To all the 395 interviewers (medical students and physicians) who collaborated in the study and the participants
To CNPq (Number 403442/2020-6)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3727

POS1253 MORTALITY RATE RELATED TO COVID - 19 IN RHEUMATIC AND MUSCULOSKELETAL DISEASES (RMDS)

D. Freites[1], I. Perez-Sancristobal[1], L. Lopez Pedraza[2], M. P. Álvarez Hernandez[1], I. Hernandez[1], J. I. Colomer[3], A. Madrid García[2], B. Fernandez[1], C. Vadillo[1], L. Rodriguez Rodriguez[2], A. Mucientes[2], L. León[3], L. Abasolo[2]. *[1]Hospital Clínico San Carlos, Reumathology, Madrid, Spain*; *[2]Instituto de Investigación Sanitaria del Hospital Clínico San Carlos, Reumathology, Madrid, Spain*; *[3]Fundación para la Investigación Biomedica, Reumathology, Madrid, Spain*

Background: Spain has been one of the countries most impacted by the COVID-19 pandemic. Among Spanish patients, 56,799 deaths have been reported. Although we have been in this situation of pandemic for a year, studies that show risk mortality rates in patients with rheumatic diseases continue to be scarce.
Objectives: In patients with rheumatic and musculoskeletal diseases (RMDs) and infected with Covid – 19, a) we want to assess the mortality rate (MR) related to COVID-19; and b) to analyze the role of RMDs in mortality risk.
Methods: An observational longitudinal study was conducted during the epidemic peak in Madrid (1stMar to 20thMay2020). All patients attended at the rheumatology outpatient clinic of a tertiary hospital with a diagnosis of RMDs and SARS - CoV 2 infection were included (according to a medical diagnosis or confirmed with a positive SARS-CoV-2 PCR diagnostic test). All patients were included since the time of COVID-19 diagnosis. Main outcome: death related to COVID-19 infection. Independent variable: type of RMDs including: autoimmune (systemic autoimmune conditions (SAC) and inflammatory joint disease (IJD)) and non–autoimmune (mechanical diseases and inflammatory diseases (microcrystalline arthritis and tendonitis)). Covariates: sociodemographic, comorbidities, chronic use of corticoids prior to COVID-19 infection. Survival techniques were used to estimate the MR related to COVID-19, given per 1,000 persons-month with a 95% confidence interval [CI]. The time of observation comprised the elapsed time between the date of COVID-19 diagnosis of infection until the date of patient's death, or end of study. Cox multiple regression analysis was run to examine the effect of autoimmune RMDs compared to non-autoimmune RMDs on mortality risk adjusted by sex, age and comorbidities. Results were expressed by Hazard Ratio (HR) and [CI].
Results: 406 patients were included with RMD and Covid – 19 infection with a total follow-up 642.5 patients-month. 69.21% were women with a mean age at diagnosis of 60 ± 15.26 years. The evolution time from the diagnosis of rheumatic disease was 8 ± 8.38 years. 26% had comorbidity at baseline. 25% were chronically on corticoids prior to the infection. Of the 406 patients, 244 (60.09%) had non-autoimmune RMD (157 mechanic, 87 inflammatory) and 162 (39.9%) (106 (65.43%) IJD, 56 (34.56%) systemic condition) had autoimmune RMD. Of the 406 patients, 45 (11%) died during the follow-up, being 12± 14 days the mean time from infection to death (P50: 6[2-12] and a maximum of 60 days). MR was estimated in 70.03 [52.28-93.79] per 1,000 persons-month. MR was higher for men (MR 105[68-163]) than for women (MR 55 [37.2-81.6]) and in older people (MR <60: 4.4, [0.6-31.7]; MR 60-75 years: 38.7[17.3-86.2]; MR >75Years: 486 [354-1668]). The HR of mortality in autoimmune RMDs compared to non-autoimmune RMDs did not achieved statistical significance (HR: 1.39 [0.77-2.5], p=0.27). After adjusting for confounders, we did not find higher risk of mortality among the different types of RMDs (HR autoimmune vs non-autoinmunes: HR: 1.12 [0.6-2.02], p=0.7; HR IJD vs SAC; 1.5 [0.6-3.6], p=0.34; HR non-autoimmune vs SAC: 1.1 [0.5-2.5], P=0.7). Age (HR: 1.12; [1.10-1.15], p<0.001), and the presence of comorbidities (HR: 2.05; [1.08-3.89], p=0.027) increased the Mortality risk.
Conclusion: In patients with RMD and COVID-19 infection, we found a mortality rate of 7 per 100 persons-month. This study shows that the mortality risk related to COVID-19 is similar between autoimmune and non-autoimmune diseases after adjusting by confounders. We also found that age and comorbidities are risk factors for mortality related to COVID-19 infection.
REFERENCES:
[1] Jorge A, et al. Temporal trends in severe COVID-19 outcomes in patients with rheumatic disease: a cohort study. *Lancet Rheumatol*. Epub ahead of print 2021..
[2] Bonfá E, et al. How COVID-19 is changing rheumatology clinical practice. *Nat Rev Rheumatol* 2021; 17: 11–15.
[3] Hyrich KL, Machado PM. Rheumatic disease and COVID-19: epidemiology and outcomes. *Nature Reviews Rheumatology* 2020; 17: 71–72.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3731

POS1254 INCIDENCE AND OUTCOME OF COVID-19 IN ROUTINE RHEUMATOLOGY CARE: DATA FROM A SINGLE OUTPATIENT CENTER IN GERMANY

S. G. Werner[1], P. Höhenrieder[2], R. Chatelain[2,3], H. E. Langer[1]. *[1]RHIO (Rheumatology, Immunology, Osteology) Düsseldorf, RHIO Reasearch Institute, Düsseldorf, Germany*; *[2]University of Witten-Herdecke, Faculty of Health, Witten, Germany*; *[3]Evangelical Hospital Düsseldorf, Departement of Dermatology, Düsseldorf, Germany*

Background: Coronavirus SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) and its associated disease COVID-19 (Corona Virus Disease 2019) has become a worldwide pandemic since its first cases in December 2019 in Wuhan Province in China. Until now little is known about the incidence and the course of the disease in a routine setting of rheumatology outpatient care.
Objectives: Aim of the study was to identify cases with COVID-19, to analyse course and outcome of the disease and the potential role of antirheumatic medication.
Methods: On the occasion of a routine follow-up examination all consecutive patients of our rheumatology outpatient center were questioned about the history of established COVID-19, about typical symptoms or about contacts with patients in the period from March to the end of December 2020. Diagnostic work-up (results of PCR or antibody testing, imaging) was documented. Antibody ELISA-tests (IgG, IgA, IgM, Euroimmun) were performed in patients reporting typical signs and symptoms. Course and outcome of COVID-19 were divided in 5 groups (mild, moderate, severe, most severe, and lethal).
Results: About 2.000 patients were screened. Positive findings for SARS-CoV-2 confirmed by PCR or serological testing were detected in n=33/2000 (1.65%) patients (n=14/33 (43%) rheumatoid arthritis (RA), n=8/33 (24%) psoriatic arthritis (PsA), n=7/33 (21%) spondyloarthritis (SpA), n=4/33 (12%) other diseases).
No patient died and no patient required intensive care or invasive mechanical ventilation. N=2/33 patients (6%) suffered a severe course with hospitalization, one of these required intermittent oxygen administration. Both patients had no ongoing therapy with disease modifying antirheumatic drugs (DMARDs). One patient suffered from SpA, one patient from RA. Both patients had relevant comorbidities with chronic lung disease and breast cancer.
Symptoms were absent or mild in n=21/33 (64%) patients, moderate in n=10/33 (30%). N=22/31 (71%) of patients with absent, mild or moderate symptoms were treated at least with one DMARD.
Conclusion: For an at-risk population, the incidence of COVID-19 was unexpectedly low. Overall, patients had a mild course despite immunosuppressive therapy. This finding is consistent with published data from a single university

center (1) and other university outpatient clinics (2). Possibly DMARD-therapy may protect against the occurrence of cytokine storm and vasculitic complications, which lead to severe courses and lethal outcomes in some of the patients. The data support the recommendation not to discontinue DMARDs for fear of COVID-19.

REFERENCES:

[1] Simon D et al. Patients with immune-mediated inflammatory diseases receiving cytokine inhibitors have low prevalence of SARS-CoV-2 seroconversion. Nat Commun. 2020 Jul 24;11(1):3774. doi: 10.1038/s41467-020-17703-6. PMID: 32709909; PMCID: PMC7382482.

[2] Gianfrancesco M et al. COVID-19 Global Rheumatology Alliance. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis. 2020 Jul;79(7):859-866. doi: 10.1136/annrheumdis-2020-217871. Epub 2020 May 29. PMID: 32471903; PMCID: PMC7299648.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3822

POS1255 REACTOGENICITY OF SARS-COV-2 VACCINES IN PATIENTS WITH AUTOIMMUNE AND INFLAMMATORY DISEASE

M. Yang[1], P. Katz[1], D. Paez[1], A. Carvidi[1], M. Matloubian[1], M. Nakamura[1], L. S. Gensler[1]. *[1]University of California, San Francisco, Division of Rheumatology, San Francisco, United States of America*

Background: Patients with autoimmune disease often require immunosuppressive medications that may increase their risk of developing severe illness from COVID-19. The importance of immunization in this population is particularly high. While the studied vaccines show efficacy in the general population, nothing is known regarding the immune response or safety profile in patients with autoimmune disease and those taking immunomodulatory medications.

Objectives: To assess the safety profile and degree of adverse events from SARS-CoV-2 vaccines in patients with autoimmune and inflammatory disease.

Methods: This study is part of a larger prospective observational study examining the immunogenicity and safety profile of the SARS-CoV-2 vaccine in patients with immune-mediated diseases taking immunomodulatory medications. Adults with an immune-mediated disease scheduled to receive either a Pfizer or Moderna SARS-COV-2 vaccine were enrolled in this study. Subjects participated in 3 study visits (pre-vaccine, dose 1 (D1) and dose 2 (D2)) where blood, for immunologic assays, and clinical data were collected. Assessments of adverse events (AE), including local and systemic symptoms and validated degree of AE severity were solicited within 7 days of receiving each vaccine dose.

Results: To date, 70 patients with autoimmune and inflammatory disease have been enrolled. Demographic and clinical characteristics are shown in Table 1. Distribution of current immunomodulatory medications included prednisone 18.6%, conventional synthetic DMARD 55.7%, targeted synthetic DMARD 4.3%, and biologic DMARD 68.5%. Almost all participants experienced an adverse event following vaccination (D1 96%, D2 100%). Following D1 AEs were generally mild (76.5%) whereas following D2 a large portion of patients experienced AEs that were moderate (47.8%) and severe (30.5%). Injection site pain was the most common AE following both doses followed by arthralgias (D1 21.6%, D2 78.2%), fever (D1 21.6%, D2 70%) and fatigue (D1 21.6%, D2 65.2%) (Figure 1).

Table 1. Demographic and Clinical Characteristics of Participants

Parameter N (%)	N=70
Age [years], mean (SD)	
Age group	48.3 ± 16.4
< 65	53 (75.7)
65+	17 (24.3)
Gender	
Female	48 (68.6)
Male	20 (38.5)
Other	2 (2.9)
Race	
White	47 (67.1)
Asian	14 (20.0)
Hispanic	8 (11.4)
Black	1 (1.4)
BMI [kg/m2], mean (SD)	25.0 ± 5.4
Immunologic Diagnosis	
Rheumatoid Arthritis	21 (30.0)
Spondyloarthritis*	21 (30.0)
Systemic Lupus Erythematous	8 (11.4)
Connective Tissue Disease, Other‡	12 (17.1)
Vasculitis	3 (4.2)
Inflammatory Bowel Disease	7 (10.0)
Autoinflammatory Syndrome	5 (7.1)
Multiple Sclerosis	2 (2.9)
IgG4 Related Disease	2 (2.9)
Disease Duration [years], mean (SD)	9.0 ± 5
Medications	
Prednisone	13 (18.6)
DMARDs	
Hydroxychloroquine	16 (22.9)
Methotrexate	15 (21.4)
Sulfasalazine	6 (8.6)
Tofacitinib	3 (4.3)
Azathioprine	2 (2.9)
Biologics	
TNF inhibitor	33 (47.1)
Rituximab	7 (10)
Abatacept	6 (8.6)
IL-23 inhibitor	2 (2.9)

* Spondyloarthritis includes Axial Spondyloarthritis and Psoriatic Arthritis. ‡ Other Connective Tissue Disease includes scleroderma, Sjogren's syndrome, polymyositis, and UCTD.

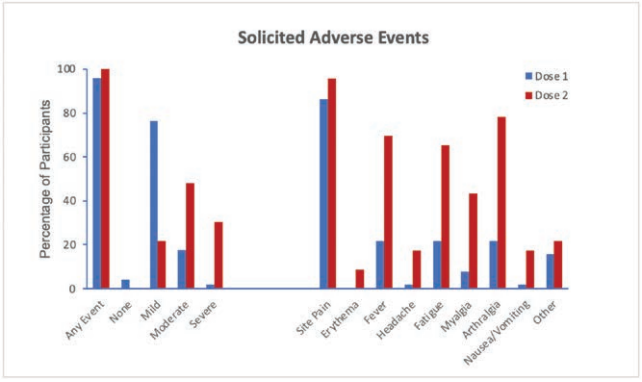


Figure 1. Solicited Local and Systemic Adverse Events. Percentage of participants who had endorsed an adverse event within 7 days of first or second dose of SARS-CoV-2 Vaccine. 'Other' symptoms included chills, blurry vision, brain fog and dizziness.

Conclusion: Patients with autoimmune and inflammatory disease experience a significant burden of adverse events following SARS-CoV-2 vaccination with both frequency and severity appearing greater than that of the reported results from the vaccine clinical trials. Several of the endorsed AEs such as fever, fatigue and arthralgias can also be commonly seen in rheumatologic diseases, mimicking flares. While SARS-CoV-2 immunization is crucial in patients with autoimmune diseases, this study demonstrates the importance of understanding the AEs experienced by this patient population to better inform patients of possible expected side effects of SARS-CoV-2 vaccination and further management in the future.

Disclosure of Interests: Monica Yang: None declared, Patti Katz: None declared, Diana Paez: None declared, Alexander Carvidi: None declared, Mehrdad Matloubian: None declared, Mary Nakamura: None declared, Lianne S. Gensler Consultant of: AbbVie, Eli Lilly, Gilead, GSK, and Novartis, Grant/research support from: Pfizer and UCB

DOI: 10.1136/annrheumdis-2021-eular.3834

POS1256 SINGLE DOSE TOCILIZUMAB PHARMACOKINETICS IN GLUCOCORTICOID PRE-TREATED COVID-19 PATIENTS DURING CYTOKINE STORM SYNDROME HYPERINFLAMMATORY EPISODE: LESS IS MORE

N. Boone[1], S. Ramiro[2], D. J. Moes[3], R. Mostard[4], C. Magro Checa[2], C. Van Dongen[2], M. Gronenschild[4], E. Van Haren[4], J. Buijs[5], R. Peeters[2], D. Wong[1], R. B. M. Landewé[2,6]on behalf of COVID-19 Study group Zuyderland Medical Centre. *[1]Zuyderland Medisch Centrum Sittard-Geleen, Clinical Pharmacy, Pharmacology and Toxicology, Geleen, Netherlands*; *[2]Zuyderland MC, Rheumatology, Heerlen, Netherlands*; *[3]Leiden University Medical Center (LUMC), Clinical Pharmacy, Pharmacology and Toxicology, Leiden, Netherlands*; *[4]Zuyderland MC, Pulmonology, Heerlen, Netherlands*; *[5]Zuyderland Medisch Centrum, Internal Medicine, Brunssum, Netherlands*; *[6]Amsterdam UMC, locatie AMC, Amsterdam Rheumatology & Clinical Immunology Center, Amsterdam, Netherlands*

Background: The cytokine storm syndrome (CSS) associated with COVID-19 pneumonia occurs in up to 20% of the admitted patients causing high morbidity and mortality [1]. In the COVID High-intensity Immunosuppression in Cytokine storm syndrome (CHIC) study [1] we reported that CSS patients, who despite high-dose methylprednisolone (MP) treatment still showed severe respiratory deterioration, received subsequent single dose tocilizumab (TCZ) treatment. Our clinical experience with TCZ, every 4 weeks in RA, where a pre-dose serum concentration of > 1 µg/ml is sufficient to block all interleukin (IL)-6 receptors and thereby induce and maintain clinical remission, prompted further investigation of TCZ pharmacokinetics in patients with COVID-19 CSS [1,2].

Objectives: In this pharmacokinetic study we investigated the clinical-pharmacokinetic rationale for a single TCZ dose in a subset of COVID19 induced CSS patients.

Methods: Patients with COVID-19-associated CSS, defined as rapid respiratory deterioration plus at least two biomarker elevations (C-reactive protein (CRP) >100 mg/L; ferritin >900 µg/L; D-dimers >1500 µg/L), received per protocol high-dose intravenous MP for 5 consecutive days. If the respiratory condition had not improved sufficiently, TCZ (8 mg/kg, max. 800 mg) single infusion was added on or after day 2[1]. TCZ serum samples were drawn at TCZ day 1, 3 and 10 to assess TCZ serum concentrations with a validated ELISA-method. A nonlinear-mixed effects model was developed based on all concentration time data to characterise TCZ pharmacokinetics (NONMEM). Subsequently individual pharmacokinetic parameters (AUC0-inf, Cmax, time above 1 µg/ml) were estimated and TCZ concentration-time observations were plotted against the individual predicted concentrations to visualize the complete TCZ concentration-time curve.

Results: In total, 34 patients with COVID19 induced CSS still showing clinical deterioration upon MP treatment received TCZ per protocol [mean (SD) age: 62 (12) years, 22% female, baseline mean (SD) bodyweight: 87 (17) kg, CRP: 108 (833) mmol/L, ferritin: 1653 (911) µg/L, D-dimers 4462 (7272) µg/L]. TCZ clearance was described by a homogeneous population-kinetics model yielding 87 serum samples. TCZ serum concentrations followed a biphasic course [Distribution volume 5.0 L (3.3-7.3), Area Under the Curve$_{0-\infty}$ 1st dose (682 (397-913) mg/L*days), Cmax 137 mg/L (88 – 199), half-life (linear) 3.5 days (2.3-4.1)]. In all patients, TCZ serum concentrations remained above the theoretical maximum IL-6 receptor occupancy concentration of 1 µg/ml for at least 12 days, depicted in Figure 1.

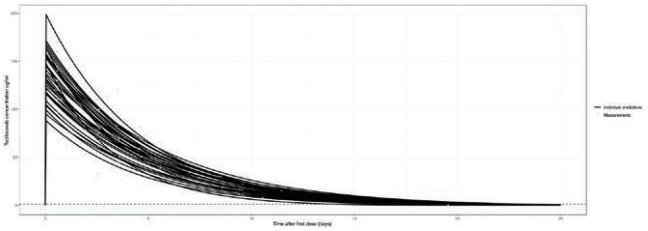


Figure 1. Predicted concentration-time profiles after single dose tocilizumab in 34 methylprednisolone pretreated patients with COVID-19 induced cytokine storm syndrome. Dashed line: maximum IL-6 receptor occupancy concentration 1 µg/ml

Conclusion: Based on our study results on the pharmacokinetics of TCZ in patients with severe COVID-19 induced CSS we conclude that the clearance of TCZ is faster compared to RA-patients at steady state. However, our observations indicate that a single dose of tocilizumab in CSS-patients is enough to cover IL-6 mediated hyperinflammation. Restricting TCZ to a single dosage can prevent overtreatment, drug shortage and saves costs, while still maintaining efficacy, as most patients will have overcome their hyperinflammatory period of the CSS after 10-14 days.

REFERENCES:

[1] Ramiro S. Mostard R.L.M. et al. Historically controlled comparison of glucocorticoids with or without tocilizumab versus supportive care only in patients with COVID-19-associated cytokine storm syndrome: results of the CHIC study. Ann Rheum Dis 2020;79(9):1143-1151.

[2] Nishimoto N, Terao K et al. Mechanisms and pathologic significances in increase in serum interleukin-6 (IL-6) and soluble IL-6 receptor after administration of an anti IL-6 receptor antibody, tocilizumab, in patients with rheumatoid arthritis and Castleman disease. *Blood*. 2008;112:3959-3964.

Acknowledgements: The authors are grateful to all patients, nurses and physicians who participated in this study.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3836

POS1257

HYPOGAMMAGLOBULINEMIA IS A SIGNIFICANT RISK FACTOR FOR MORTALITY IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS AND COVID-19

B. Ince[1], M. Bektas[1], N. Koca[1], B. F. Agargun[2], S. Zaralı[2], D. Y. Guzey[3], Y. Yalçınkaya[1], B. Artim-Esen[1], A. Gül[1], M. Inanc[1]. *[1]Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*; *[2]Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Istanbul, Turkey*; *[3]Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey*

Background: The negative impact of COVID-19 in patients with ANCA associated vasculitis (AAV) and patients on rituximab (RTX) treatment have been reported (1). Risk factors for severe course of COVID-19 and increased mortality in these patients are unclear.

Objectives: To evaluate the course of COVID-19 in our AAV cohort and identifying risk factors for mortality.

Methods: Patients with AAV who were classified according to CHCC and whose scheduled last visit were after December 2019 were screened and evaluated for COVID-19 either by phone call or in the clinic. Records of patients with a history of hospital admission due to COVID-19 were evaluated. Cumulative clinical findings and treatment history were noted. Hypogammaglobulinemia (hIgG) was defined as IgG level below 700 mg/dl. All inpatients with a diagnosis of COVID-19 were screened for hIgG and IVIG was administered if necessary.

Results: Eighty-nine patients (47.2% female, mean age 56 + 12.5 (28-81)) were included into the study. The diagnosis was GPA in 56 (62.9%) and MPA in 33 (37.1%) patients. Mean follow up time was 91 + 53.4 (26-272) months. Anti-PR3 and anti-MPO were positive in 46 (51.7%) and 32 (35.9%) patients, respectively. Lower respiratory tract (LRT) involvement was present in 72 (80.9%) and 10 patients had a history of diffuse alveolar haemorrhage (DAH). Sixty-one patients (68.2%) had a history of rapidly progressive glomerulonephritis (RPGN) and 21 (23.6%) had peripheral nervous system (PNS) involvement.

Fifteen (16.9%) patients had COVID-19; 14 of them were PCR positive, one patient had symptoms and thorax CT findings compatible with COVID-19. Pulmonary infiltrates were observed in 13 patients (86.7%); 9 (60%) had severe pneumonia. Twelve patients (85.7%) were hospitalized, 6 patients (42.9%) needed ICU admission and 5 patients (35.7%) died. Tocilizumab and anakinra for hyperinflammation during COVID-19 were used in 1 (6.7%) and 4 (26.7%) patients, respectively.

Four out of five deceased patients (3 on RTX treatment, 1 with renal transplant) were in remission at the time of COVID-19. COVID-19 was detected in a patient with disease flare and DAH, during treatment with high dose steroids and plasmapheresis. hIgG was detected in all deceased patients from COVID-19 during hospital admission (mean IgG: 495±113.2 mg/dL).

Table 1. Comparison of risk factors for CI and mortality in patients with AAV

	COVID-19 (n=15)	Non-infected (n=74)	p	OR	Death (n=5)	Survive (n=10)	p2	OR2
Age	53.4±11.9	56.6±12.6	NS		51.2±12.6	54.6±12.1	NS	
Sex (female)	6	35	NS		4	2	0.036	14 (0.9-207)
LRT Involvement	14	58	NS		5	9	NS	
DAH	4	6	0.038	4.1 (1-16.9)	1	3	NS	
RPGN	15	46	0.004	8.5 (1-68.4)	5	7	NS	
PNS involvement	3	18	NS		3	0	0.005	9 (1.4 - 57)
RTX treatment	10	33	NS		3	7	NS	
hIgG in outpatient visits	6	7	0.02	6.3 (1.8-23.3)	4	2	0.02	16 (1.5-234)
hIgG during hospitalization due to CI	-	-	-	-	5	4	0.025	2.5 (1.2-5.4)
Flares≥1	7	25	NS		4	3	NS	
Chronic Renal Insufficiency	7	22	NS		4	3	NS	

Symptomatic COVID-19 was more frequent in patients with a history of DAH, RPGN and hIgG. hIgG during the follow-up was significantly associated with COVID-19 in multivariable analysis (p=0.01, OR=20,6 %95 CI (2-210). Comparison of patients who died of COVID-19 and survived showed that female sex, PNS involvement and hIgG during the clinical course and hospital admission were risk factors for increased mortality (Table 1). Age, smoking, treatments, history of flares or serious infections, remission status and chronic renal insufficiency did not differ between groups.

Conclusion: The frequency and mortality from COVID-19 is found to be high in our AAV cohort compared to previous reports (1). Patients with serious lung or renal involvement are prone to symptomatic COVID-19. Previously reported severe outcomes on RTX therapy might be related to consequent hIgG. High dose IVIG treatment may not be sufficient in improving survival in AAV patients with severe COVID-19 and hIgG.

REFERENCES:

[1] Severity of COVID-19 and survival in patients with rheumatic and inflammatory diseases: data from the French RMD COVID-19 cohort of 694 patients. 2020:annrheumdis-2020-218310.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3880

POS1258 MISSING THE WINDOW OF OPPORTUNITY: EARLY ARTHRITIS CLINICS IN TIMES OF COVID-19

B. D'onofrio[1,2], L. De Stefano[1,2], B. L. Palermo[1,2], B. Xoxi[1], A. Manzo[1,2], C. Montecucco[1,2], S. Bugatti[1,2]. [1]*IRCCS Policlinico San Matteo Foundation, Division of Rheumatology, Pavia, Italy*; [2]*University of Pavia, Department of Internal Medicine and Therapeutics, Pavia, Italy*

Background: The outcomes of patients with chronic inflammatory arthritis (IA), such as rheumatoid arthritis (RA), have dramatically improved over the past 20 years. Earlier identification of IA and prompter treatment institution have been key advancements, promoted by the constitution of Early Arthritis Clinics (EAC) and the development of more sensitive classification criteria for RA. The outbreak of new COronaVIrus Disease 2019 (COVID-19) has quickly become a global health emergency and has forced a rearrangement in the management of other non-COVID-19 diseases. The impact of the lock-down of the healthcare systems on chronic inflammatory diseases such as RA is expected to be significant but is at present unknown.

Objectives: To assess the effects of the lock-down imposed by the COVID-19 pandemic on the referral and clinical presentation of patients with new-onset RA.

Methods: Data were retrieved from the Pavia EAC inception cohort, established in 2005 for the early identification of patients with new-onset IA. Referral criteria to the EAC include: ≥3 swollen joints (SJ) and/or <3 SJ and positive squeeze test and/or <3 SJ and morning stiffness >30 min. Demographic and clinical characteristics of the patients are assessed at baseline and regularly over follow-up. At 31 Dec 2020, the Pavia EAC collects information on 2.508 patients. For this study, baseline characteristics of the patients referred in the semester following the COVID-19 lock-down (Jul-Dec 2020) were compared with: (i) patients referred in the semester immediately preceding the lock-down (Jul-Dec 2019); (ii) patients referred in the semester following the publication of the 2010 RA classification criteria (Jan-Jun 2011); (iii) patients referred in the semester preceding the publication of the 2010 criteria (Jul-Dec 2009).

Results: In the semester following the lock-down imposed by the COVID-19 pandemic, there was a decrease in the referral of patients with new-onset suspected IA compared with previous periods (n=71 vs n=91 in the semester before the lock-down, n=96 in the first semester of 2011, n=101 in the second semester of 2009). Furthermore, fewer of the referred patients fulfilled RA criteria at presentation (36.6% vs 44.3%, 46.5% and 42.9% in the other semesters). Among patients with RA, more were autoantibody-positive (72% vs 50%, 49.1% and 52.2%). There was a trend for increased diagnostic delay in the overall cohort of RA after the COVID-19 lock-down (Figure 1A). The delay was particularly longer in autoantibody-positive patients, returning to the values seen before the introduction of the 2010 RA criteria (Figure 1B). In contrast, the few autoantibody-negative patients were referred earlier (Figure 1C). Disease activity at presentation was significantly higher in RA patients presenting after the lock-down compared with the progressive trend for reduction observed over the previous years, irrespective of the autoantibody status (Figure 1D-F). Such increase was determined by an inversion of the trend towards lower levels of objective parameters of inflammation, such as the swollen joint count (Figure 1G-I) and acute phase reactants, and a further increase in the secular trend towards worsening of patient-derived measures, such as the tender joint count and patient global assessment (Figure 1J-L).

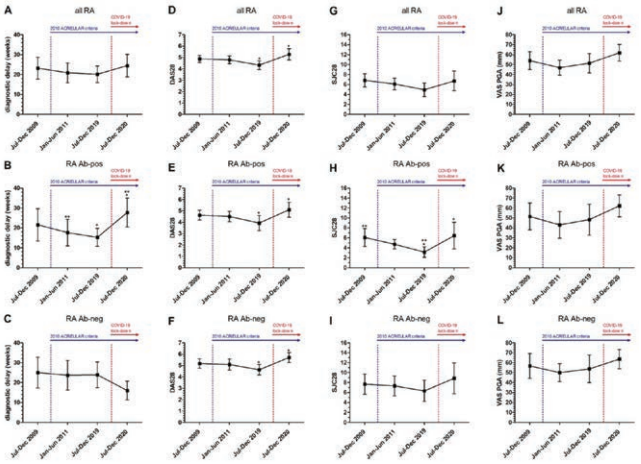


Figure 1. Effects of COVID-19 lock-down on new-onset RA at presentation.

Conclusion: The COVID-19 pandemic is posing unprecedented challenges in the management of patients suffering from chronic diseases. RA has returned to be diagnosed outside the window of opportunity, with a significantly higher inflammatory burden at presentation. The many benefits of early diagnosis, which have dramatically changed the outcomes of autoantibody-positive RA, are at risk of vanishing in short times. Equally important, autoantibody-negative RA is at risk of further under-diagnosis and under-treatment.

Disclosure of Interests: Bernardo D'Onofrio: None declared, Ludovico De Stefano: None declared, Bianca Lucia Palermo: None declared, Blerina Xoxi: None declared, Antonio Manzo: None declared, Carlomaurizio Montecucco Speakers bureau: BMS, Lilly, Sanofi, Pfizer, Galapagos, Roche, Novartis, Serena Bugatti Speakers bureau: BMS, Lilly, Sanofi, Pfizer, Galapagos

DOI: 10.1136/annrheumdis-2021-eular.3893

POS1259 FAVOURABLE SHORT-TERM COURSE OF COVID-19 IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER USING BIOLOGIC AGENTS

N. Aliyeva[1], B. Ç. Yalçın Dulundu[1], S. Amikishiyev[1], S. Aghamuradov[1], M. Bektaş[1], B. Ince[1], N. Koca[1], Y. Yalçınkaya[1], B. Artim-Esen[1], M. Inanc[1], A. Gül[1]. [1]*İstanbul Medical Faculty, Rheumatology, İstanbul, Turkey*

Background: COVID-19 runs a variable course resulting in acute respiratory distress syndrome and death in a subset of patients. The entry of SARS-CoV-2 into the cell stimulates innate immunity including NLRP3 inflammasome and lead to development of adaptive immunity later. Hyperinflammatory response with the release of proinflammatory cytokines including IL-1β and IL-6 results in cytokine storm in some patients with a worse outcome. Colchicine acts on NLRP3 inflammasome and inhibits and IL-1 mediated inflammatory attacks in gout and familial Mediterranean fever (FMF) patients. Patients with inadequate response to colchicine may benefit from anti-IL-1 biologic agents such as anakinra and canakinumab. Recently, favourable effects of anakinra have been observed in COVID-19 patients with findings of cytokine storm.

Objectives: We aimed to evaluate the impact of COVID-19 among refractory FMF patients followed-up in tertiary referral with the treatment of biologic agents and also document the course of COVID-19 in these patients.

Methods: We searched out database of FMF patients to identify those using biologic agents (anti-IL-1, anti-IL-6 or anti-TNF) for colchicine-refractory FMF. We interviewed the patients using a standard questionnaire by phone call for symptomatic COVID-19 and evaluated those patients who described findings of COVID-19 further by their hospital records or inviting them to the hospital for additional investigations.

Results: We identified 183 patients and contacted 106 of them by phone in May-October 2020. A history of symptomatic COVID-19 was documented in 7 FMF patients who were on a biologic agent. Six were on anti-IL-1 and one was on anti-TNF, and one of the patients was not taking his biologic agents for 1 year. All of 7 patients had a favourable outcome. All but 1 patient followed at home and none of them developed findings of cytokine storm, thromboembolism and secondary bacterial infection. Hospitalized patient did not require intensive care unit (ICU) support or mechanical ventilation, and he was not given additional anti-inflammatory medications.

Conclusion: This series of refractory FMF patients with potentially higher inflammatory characteristics showed COVID-19 did not result in a worse outcome in those patients during the first phase of the pandemic, and none developed findings of cytokine storm. Observations in these patients supports further that biologic agents blocking IL-1 and possibly TNF may contribute to the uneventful course of COVID-19 by preventing the development of hyperinflammatory response. Data collection from a larger group of patients, especially those with amyloidosis, will clarify the protective effects of colchicine and contribution of anti-IL-1 treatments on the favourable disease course during the second phase of the pandemic.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age (years)	45	48	39	53	32	37	31
MEFV variants	Unknown	M694V /M680I	Unknown	M694V/ M694V	M694V/ M694V	M694V/ M694V	M694V/ M694V
Amyloidosis	No	No	No	No	No	No	No
Biologic agents	Anakinra 100mg/ day	Not taken for 1 year	Adalimu- mab	Canakinumab 150mg/ month	Anakinra 100mg/ day	Canakinumab 150mg/ month	Anakinra 100mg/ day
Prednisone (mg/day)	5	No	No	No	No	No	No
Colchicine (mg/day)	2	1,5	1,5	1,5	1,5	2,0	2,0
RT-PCR positivity	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Chest CT signs	Yes	Yes	Not done	Not done	Not done	Not done	Not done
Hospitalisation	No	No	No	Yes	No	No	No
Antiviral therapy	Oseltamivir	Oseltamivir	No	Favipravir	Favipravir	Favipravir	Favipravir
HCQ use	Yes	Yes	Yes	Yes	No	No	No
New FMF attack during COVID-19	No	No	No	No	No	No	No

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3903

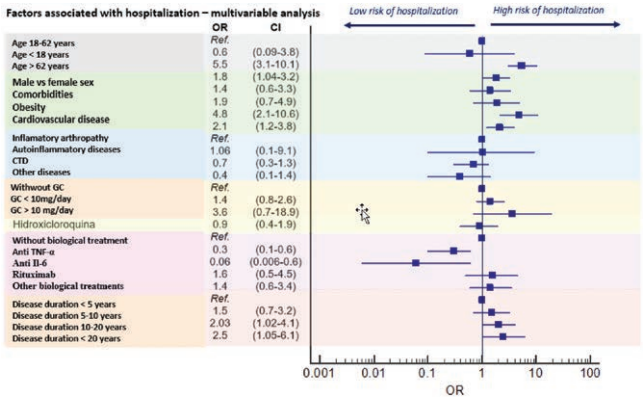
POS1260

FACTORS ASSOCIATED WITH SEVERE SARS-COV-2 INFECTION IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES IN MADRID: RESULTS FROM REUMA-COVID SORCOM REGISTRY

A. Boteanu[1], A. García Fernández[1], N. De la Torre[2], M. Pavia Pascual[2], O. Sanchez Pernaute[3], S. Recuero Diaz[3], S. Perez Esteban[3], G. Bonilla[4], L. Nuño[4], J. J. Sanmartin Martinez[5], C. Bonilla Gonzalez-Leganá[6], D. Clemente Garulo[7], L. Lojo Oliveira[8], J. M. Rodríguez Herredia[9], J. Bachiller-Corral[1]on behalf of REUMA-COVID SORCOM. [1]*H. U. Ramón y Cajal, Rheumatology, Madrid, Spain*; [2]*H.U. Puerta de Hierro, Rheumatology, Madrid, Spain*; [3]*H.U Fundación Jiménez Diaz, Rheumatology, Madrid, Spain*; [4]*H.U La Paz, Rheumatology, Madrid, Spain*; [5]*H.U Severo Ochoa, Rheumatology, Madrid, Spain*; [6]*H.U del Tajo, Rheumatology, Madrid, Spain*; [7]*H.U. Niño Jesus, Rheumatology, Madrid, Spain*; [8]*H.U Infanta Leonor, Rheumatology, Madrid, Spain*; [9]*H.U. Getafe, Rheumatology, Madrid, Spain*

Background: Patients with inflammatory rheumatic diseases (IRD) infected with SARS-CoV-2 may be at risk to develop a severe course of COVID-19 due to the immune dysregulation or the influence of immunomodulating drugs on the course of the infection. For a better understanding of SARS-CoV-2 infections in patients with IRD and due to the high incidence of COVID-19 in Madrid from the beginning of this pandemic infection in Spain, the Society of Rheumatology from Madrid (SORCOM) established a registry (REUMA-COVID SORCOM) shortly after the beginning of the pandemic in Spain.

Objectives: To determine factors associated with severity of infection with SARS-CoV-2 in patients with inflammatory rheumatic diseases in Madrid
Methods: The REUMA-COVID SORCOM registry is a multicenter, retrospective, observational cohort study conducted in Madrid, a SORCOM initiative. All rheumatology departments from Madrid were invited to participate. The study includes patients with IRD presenting with a confirmed or highly suspected diagnosis of COVID-19 between March 1, 2020, and November 10, 2020. We consider severe infection death or need of hospitalization. Inclusion criteria was having an IRD and at least 1 of the following 4 criteria: (1) a biologically confirmed COVID-19 diagnosis based on a positive result of a SARS-CoV-2 polymerase chain reaction (PCR) test on a nasopharyngeal swab; (2) Detection of IgM or IgG anti SARS-CoV2 in a symptomatic or asymptomatic patients (3)typical thoracic computed tomography (CT) abnormalities (ground-glass opacities) in epidemic areas; (4) COVID19–typical symptoms in an epidemic zone of COVID-19.
Results: As of November 10, 2020, 417 patients with IRD were included in the REUMA-COVID SORCOM registry. 5 patients were discharged for incomplete data. Of 412 patients (mean age 57 years, 87.4% Caucasian race, 66.3% female) 174 need hospitalization (42.2%) and 33 patients died (18.4% mortality in hospitalized patients). 82.3% had comorbidities. 234 (56.8%) patients were classified as inflammatory arthropathy, 133 (32.3%) had connective tissue diseases (CTD). 41.1% of the patients had a large history of IRD (> 10 years). 10.4% of patients had previously pulmonary involvement. The study includes 143 patients taking Methotrexate, 89 patients taking anti-TNFα therapy and 27 Rituximab. In the univariant analysis, no differences were seen in the severity of COVID-19 infection in patients taking methotrexate. 63% of the all patients taking Rituximab included in the registry need hospitalization and 22% of them died. Hypertension, COPD or cardiovascular disease was associated with hospitalization.
Independent factors associated with COVID-19 hospitalization in the multivariate analysis was: age (>62 years), male sex, IMC >30, previous cardiovascular comorbidities and the IRD disease duration (> 10 years). Independent factors associated with COVID-19 related death was: age (> 62 years), having a CTD diagnose, pulmonary involvement before infection and chronical GC treatment.
Conclusion: Patients with IRD represent a population of particular interest in the pandemic context because the baseline immunological alteration and the treated with immunosuppressants agents they receive, comorbidities and the well-known risk of severe infection. Older age, male sex, cardiovascular comorbidities were factors associated with high risk of hospitalization in IRD patients. CTD diseases, previously pulmonary involvement and chronical GC treatment with more than 10mg/day were associated with high risk of death. Neither anti TNF-α treatment nor Methotrexate were risk factor for hospitalization or death COVID-19 related in IRD patients.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3973

POS1261

DISEASE ACTIVITY AND PAIN LEVELS ARE NOT INFLUENCED BY THE CURRENT COVID19 PANDEMIC IN PATIENTS WITH RHEUMATIC DISEASES IN GERMANY – DATA FROM THE GERMAN COVID-19 PATIENT SURVEY

R. Hasseli[1], U. Müller-Ladner[1], T. Schmeiser[2], H. M. Lorenz[3], A. Krause[4], H. Schulze-Koops[5], A. Pfeil[6], A. Regierer[7], J. Richter[8], A. Strangfeld[7], R. Voll[9], C. Specker[10], B. F. Hoyer[11]. [1]*Justus-Liebig-Universität Giessen, Campus Kerckhoff, Giessen, Germany*; [2]*Rheumatologie im Veedel, na, Cologne, Germany*; [3]*Universitätsklinikum Heidelberg, Rheumatology, Heidelberg, Germany*; [4]*Immanuel Krankenhaus Berlin, 4Klinik für Innere Medizin, Abteilung Rheumatologie, Klinische Immunologie und Osteologie, Berlin, Germany*; [5]*Ludwig-Maximilians-Universität München, Sektion Rheumatologie und Klinische Immunologie, Medizinische Klinik IV, Munich, Germany*; [6]*Universitätsklinikum Jena, Rheumatology, Jena, Germany*; [7]*DRFZ, Epidemiology, Berlin, Germany*; [8]*Universitätsklinikum Düsseldorf, Rheumatology, Düsseldorf, Germany*; [9]*Universitätsklinikum Freiburg, Rheumatology and Clinical Immunology, Freiburg, Germany*; [10]*Kliniken Essen-Mitte, 10Klinik für Rheumatologie & Klinische Immunologie, Essen, Germany*; [11]*Universitätsklinikum Schleswig-Holstein, Campus Kiel, Rheumatology and Clinical Immunology, Kiel, Germany*

Background: The current pandemic constitutes an entirely new situation for patients as well as physicians. The insecurity of the early phase, shutdowns, increasing infection rate and appearing SARS-CoV2 mutations have created a situation that makes live difficult especially for chronic diseases i.e. patients with rheumatic and musculoskeletal diseases (RMD) and their treating physicians. The psychosocial burden that is created by this special situation is completely unknown and is estimated to be higher in patients than in the general population.
Objectives: In order to measure the impact on our patients, the German COVID19-Rheuma patient survey was set up in April 2020, during Germany's first shut down.
Methods: The German COVID19-Rheuma patient survey is a patient reported longitudinal online survey where patients with RMD who registered between April and July 2020 are asked on a monthly base using an online survey on social, personal, medical factors, whether a COVID19 infection occurred, isolation measures were changed and scores regarding stress and anxiety are recorded. Between April and July 2020, 637 patients registered and completed a first survey. Up to January 2021, about 400 patients are still enrolled.
Here we present an interim analysis of the first 6 months regarding patients that were enrolled in April and May during the first shut-down. This first analysis compares the situation in the first lockdown to July, a phase with very low infection numbers in Germany, and to November, the beginning of the second lockdown.
Results: 150 patients (87% female) were enrolled in April/early May 2020. Mean age was 48 years (range 11-89). The majority of patients suffered from rheumatoid arthritis (51%), followed by psoriatic arthritis (17%), other spondyloarthropathies (10%) and connective tissue diseases (10%).
The majority of patients received antirheumatic therapies: 32% glucocorticoids (GC), 31% cDMARDs, 21% TNF inhibitors, 7% Jak inhibitors, and 9% other biologicals. Of the patients treated with GC, 25% were on GC monotherapy.
In the first lockdown, 26% of patients were working remotely and 24% were self-isolating (doubles included). Additionally, 48% were using masks that were not mandatory at that time and 41% were using disinfection in a regular manner. The rates for remote work and self-isolation did not change significantly over time while the mask use increased to 98% with the official obligation to do so. The use of disinfectants increased to 88% in November.
Regarding disease activity, no change in patient global assessment could be observed over time (4.3 ± 2.5 vs. 4.0 ±2.6 and 4.0 ± 2.5). Self-reported pain was also stable over time as were sleep disturbances. While 48.2% of patients who were receiving physiotherapy paused in April, only 10 and 14% did so in July and November, respectively. 11% of the patients paused their medication in the first lockdown, whereas only 2.75% did so in July and 3.4% in November. Contact with the treating rheumatologist was maintained over time in the majority of cases.
Conclusion: While in the beginning of the pandemic the insecurity was considerable and the concern that the fear for infection would lead to inadequately treated patients with RMDs, we here show for the first time that on the one hand our patients were timely in taking adequate measures to keep themselves safe (e.g. self-isolating, mask use) and adapted to the clinical situation in not pausing their medication. Altogether, in this alert cohort, the pandemic did not lead to an increase of patient-reported disease activity in the first six months.
Acknowledgements: Thanks goes to all patients who participated in the study.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4002

POS1262

A COHORT STUDY OF COVID-19 RELATED MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN AND ADOLESCENTS FROM MULTIPLE TERTIARY CARE CENTRES IN SOUTH INDIA

A. Tiwari[1], A. Rauf[2], S. Kesavan[3], M. Kappanayil[4], S. Sivadas[5], S. Balan[1], P. Chickermane[1]. [1]*Amrita Institute of Medical Sciences, Rheumatology and Clinical Immunology, Kochi, India*; [2]*Baby Memorial Hospital, Pediatric Intensivist, Kozhikode, India*; [3]*Amrita Institute of Medical Scinces, Pediatric Pulmonology and Intensive Care, Kochi, India*; [4]*Amrita Institute of Medical Sciences, Pediatric Cardiology, Kochi, India*; [5]*Amrita Institute of Medical Sciences, Pediatrics, Kochi, India*

Background: After the peak of COVID 19 pandemic, a surge of cases with multi-system involvement and hyperinflammatory state was reported in children, at multiple tertiary care centers across the world. (1) This COVID-19 associated multisystem inflammatory syndrome in children and adolescents is also known as multisystem inflammatory syndrome in children (MIS-C). There is a paucity of literature of clinical profile of MIS-C patients from India.
Objectives: To study the clinical manifestations and treatment outcomes of COVID-19 related multisystem inflammatory syndrome in children (MIS-C) and adolescents.
Methods: It was a cohort study including cases defnied as per the case definitions of MIS-C by World Health Organisation (WHO) or Centre for Disease Control and Prevention(CDC).(2)The clinical parameters, laboratory parameters (including inflammatory markers, D dimer and NT ProBNP), electrocardiogram, 2D echocardiogram, course in hospital, and immediate outcomes were noted.

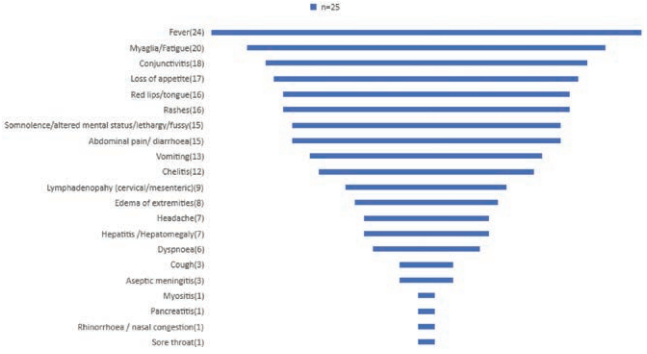


Figure 1. Frequency of clinical features in our MIS-C cohort patients

Table 1. Clinical characteristics of MIS-C patients (n)=25

Clinical Phenotypes:	
Incomplete/ Atypical Kawasaki Disease (KD)	18 (72%)
Macrophage activation syndrome (MAS)	11 (44%)
Unexplained Shock	13 (52%)
Fever with gastrointestinal symptoms	17 (68%)
Fever with neurological symptoms	9 (36%)
Fever with respiratory symptoms	5 (20%)
COVID chronology:	
MISC with acute COVID 19 with MAS	1 (4%)
MISC with acute COVID 19 with incomplete/atypical KD	1 (4%)
COVID 19 tests:	
COVID 19 RTPCR positive	2 (8%)
COVID 19 RTPCR negative	23 (92%)
COVID 19 IgG positive	20 (80%)
COVID 19 IgM positive	6 (24%)
COVID 19 IgG and IgM both positive	2 (8%)
COVID 19 IgG and IgM not done	4 (16%)
Other laboratory investigations	
(Peak/ trough values):	
Anaemia	20 (80%)
Leukopenia	2 (8%)
Thrombocytopenia	6 (24%)
Pancytopenia	2 (8%)
Positive CRP	23 (92%)
High Procalcitonin	9 (36%)
High ferritin	10 (40%)
High D- dimer	17 (68%)
High NT ProBNP	23 (92%)
Hypoalbuminemia	14 (56%)
Sterile pyuria	7 (28%)
Proteinuria	4 (16%)
Cardiac assessment:	
Abnormal Electrocardiogram (ECG)	5 (20%)
Abnormal Echocardiography	15 (60%)
Coronary dilation/prominence/non-tapering	9 (36%)
Coronary aneurysm	1 (4%)
LAD Z score (Mean±SD)	2.12 ± 1.11
Decreased Ejection fraction (EF)	5 (20%)
Systolic Dysfunction	5 (20%)
Pericardial effusion	9 (36%)
Global/septal hypokinesia	4 (16%)
Mitral Valve regurgitation	3 (12%)
Complete heart block	1 (4%)

Results: Twenty five patients (male-14) with a mean age of 6.22 ±4.25 years and a mean body mass index of 16.21 ±3.36 kg/m^2 were enrolled on the study. Average length of hospital stay was 8.12±5.76 days. Associated comorbidities were present in 4 of our patients (16%). Figure 1 shows the frequency of clinical features in our study patients. Table 1 shows the clinical, laboratory, imaging findings, disease course and outcomes.

Twenty patients (80%) had severe illness requiring intensive care. Fourteen patients (56%) required inotropic support, 8 patients (32%) required supplemental oxygen, 5 patients (20%) required mechanical ventilation and 2 patients (8%) expired. A total of 23 patients (92%) received pulse steroids followed by oral/iv steroids, 22 patients (88%) received IVIG (2g/kg) and 3 patients (12%) required anticoagulation.

Conclusion: Our MIS-C cohort had varied clinical manifestations ranging from the mild cutaneous and gastrointestinal symptoms to fatal multiorgan dysfunctions. In contrast to western cohorts, our study cohort had higher number of patients from younger age group and lower BMI.

REFERENCES:

[1] Ahmed M, Advani S, Moreira A, Zoretic S, Martinez J, Chorath K et al. Multisystem inflammatory syndrome in children: A systematic review. EClinicalMedicine. 2020;26:100527.

[2] Jiang L, Tang K, Levin M, Irfan O, Morris S, Wilson K et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. The Lancet Infectious Diseases. 2020;20(11):e276-e288.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4034

POS1263 COVID-19 FROM THE PATIENTS'S P ERSPECTIVE: PRELIMINARY RESULTS OF ONLINE SURVEY

D. Karateev[1], P. Pchelnikova[2], E. Luchikhina[1], T. Boboshko[3]. [1]*Moscow Regional Research and Clinical Institute n.a. M.F. Vladimirsky (MONIKI), Moscow Regional Rheumatology Center and Department of Rheumatology, Moscow, Russian Federation*; [2]*EULAR Standing Committee of People with Arthritis/Rheumatism in Europe, PARE, Zurich, Switzerland*; [3]*Russian Rheumatology Association "Nadezhda", Moscow Branch, Moscow, Russian Federation*

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as COVID-19, is now in the spotlight of the medical community. Obtaining the most complete data on COVID-19 in the rheumatic diseases (RD) is an urgent task, and the data received directly from patients seems to be is extremely important.

Objectives: To study the factors, associated with the possibility of COVID-19 in patients with RDs.

Methods: We conduct COVID-19 Russian rheumatology patient experience survey to create a registry of "Patient's Opinion on Covid-19 in Rheumatic Diseases (POPCORD)". This ongoing project is based on the data collected directly from Russian-speaking patients with different RDs who fill out a special questionnaire via the https://revmo-covid.ru/. The questionnaire was developed by the national patient organization – Russian Rheumatology Association "Nadezhda" in collaboration with Moscow regional rheumatology center and department of rheumatology of Moscow Regional Research and clinical institute n.a. M.F. Vladimirsky (MONIKI). The anonymous questionnaire includes information on whether the patient had COVID-19, as well as information on rheumatic disease, its treatment, and information on social distancing and compliance with other anti-epidemic measures.

Results: At the moment, 1050 patients (92% from Russia, 8% from other countries) completed the survey, including residents of 74 regions of Russia, most of them from Moscow (20%), Moscow region (8%) and St. Petersburg (8%). In total, there were 93% females, with mean age 40,28±11,26 (M±SD, median 38 [32;48]), BMI 24,52±5,38 (median 23,42 [21;27]), disease duration 7,91±8,46 (median 5,00 [2;11]). The main diagnoses reported: rheumatoid arthritis (49%), ankylosing spondylitis (14%), systemic lupus erythematosus (13%), psoriatic arthritis (6%), Sjogren's disease (5%), systemic sclerosis (3%), other (10%). 344 (31,8%) patients reported COVID-19 or suspected SASR-CoV-2 viral pneumonia. Relatives or physicians reported 3 cases of death related to COVID-19. The most important results of the survey presented in Table 1.

Table 1. Main results of the patients survey, n=1050.

Item	Results (n, %)		
	No COVID-19/ pneumonia reported (n=716)	*COVID-19/ pneumonia (n=334)*	*p, chi-square*
Smoking status			0,003
• Current smoker	118, 16,5%	25, 7,5%	
• Never smoke	359, 50,1%	199, 59,6%	
• Quit smoking	239, 33,4%	110, 32,9%	
Vaccination during last 3 years against Influenza, Pneumococcus and others			0,265
• No	531, 74,2%	236, 70,7%	
• Yes	185, 25,8%	98, 29,3%	
Social distancing			0,003
• I avoid crowds and large gatherings of people	412, 57,5%	172, 51,5%	
• Self-isolation	219, 30,6%	96, 28,7%	
• No social distancing	85, 11,9%	66, 19,9%	
Hygiene			0,031
• wearing a mask, hand washing/ using a sanitizer, gloves etc.	705, 98,5%	321, 96,1%	
• nothing	11, 1,5%	13, 3,9%	
Withdrawal of anti-rheumatic medication last weeks for fear of infection			<0,001
• Yes	124, 17,3%	104, 31,1%	
• No	592, 82,7%	230, 68,9%	
Possible contacts with COVID-19 infected persons			<0,001
• Yes	203, 28,4%	205, 61,4%	
• No	299, 41,8%	65, 19,5%	
• Don't know	214, 29,9%	64, 19,1%	

Conclusion: According to patient-reported data, lack of adherence to social distancing and hygienic measures, higher possibility of contacts with infected persons, as well as withdrawal of anti-rheumatic medication for fear of infection and smoking status were the factors, significantly associated with the possibility of COVID-19/viral pneumonia in patients with rheumatic diseases.

Acknowledgements: Dr Anna S Misiyuk from V.A. Nasonova Institute of Rheumatology, Moscow, Russia.

The COVID-19 Russian patient experience survey is conducted on behalf of Russian Rheumatology Association "Nadezhda". The project was partially granted by BIOCAD.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4046

POS1264 IMMUNE-MEDIATED DISEASES (IMID) AND CORONAVIRUS DISEASE 2019 (COVID-19): RESULTS FROM AN OBSERVATIONAL RETROSPECTIVE MULTICENTER STUDY

R. Dos-Santos[1], C. Calviño[2], I. Bastón[2], R. Ferreiro[2], F. Montero[3], C. Gonzalez[3], I. Marín-Jiménez[4], M. Barreiro-de-Acosta[2], E. Perez-Pampín[1]. [1]*Clinical University Hospital in Santiago de Compostela, Rheumatology Department, Santiago de Compostela, Spain*; [2]*Clinical University Hospital in Santiago de Compostela, Gastroenterology Department, Santiago de Compostela, Spain*; [3]*Gregorio Marañón Hospital, Rheumatology Department, Madrid, Spain*; [4]*Gregorio Marañón Hospital, Gastroenterology Department, Madrid, Spain*

Background: The novel coronavirus emerged in 2019 in Wuhan has caused a global pandemic of coronavirus disease (COVID-19). Immune-mediated diseases (IMID), as inflammatory arthritis or inflammatory bowel disease (IBD), have some special implications due to their pathogenesis and treatments. Some treatments employed in IMID are now being used in the treatment of severe COVID-19. There still exists controversy about IMID behavior and its complications.[1, 2]

Objectives: To assess COVID-19 severity in IMID patients and its prognosis predictors.

Methods: An observational retrospective multicenter study was performed in two Spanish Hospitals (Clinical University Hospital in Santiago de Compostela

and Gregorio Marañón Hospital). Patients were selected if they were diagnosed of an IMID (rheumatoid arthritis, psoriatic arthritis, espondyloarthritis, ulcerative colitis and Crohn's disease) and had COVID-19 infection between February and April 2020.
Demographic, clinical, analytical and treatment data were collected. Logistic regression was used to evaluate potential predictors.
Stata 15.1 was used to perform statistical analysis.
Results: 91 patients were recruited. 55 suffered from a rheumatic disease and 36 suffer IBD. Baseline characteristics are shown in Table 1.
Univariable analysis reached age, comorbidity, female gender, flu vaccine, arthropathy, basal classical synthetic anti-rheumatic drugs (csDMARD), pneumonia and basal C-reactive protein (CRP) as potential predictors of non-severe (absence of death, respiratory insufficiency, intensive care unit admission or sepsis) COVID-19 disease ($p < 0.2$). After multivariable analysis, only female gender (OR 4.60 [CI95% 1.00, 21.2] p=0.050), lower age (OR 0.94 [CI95% 0.88, 1.00] p=0.042) and lower basal levels of CRP (OR 0.87 [CI95% 0.77, 0.97] p=0.010) were predictors for non-severe disease ($p < 0.005$).
Mean time of healing (symptoms solved in outpatient and hospital discharge in admitted) from COVID-19 was 13.8 days (SD 16.3). Univariable analysis showed arthropathy, COVID-19 symptomatic and basal glucocorticoids (GC) dose as potential predictors of higher time-to-healing from COVID-19 disease ($p < 0.2$). After multivariable analysis, only lower GC basal dose predicts higher time-to-healing (OR -1.83 [CI95% -2.81, -0.84] p=0.001).
11 patients deceased because of COVID-19. Univariable analysis reached age, basal csDMARD, pneumonia and basal CRP as potential predictors of COVID-19 mortality ($p < 0.2$). After multivariable analysis, only higher age was a predictor for mortality (OR 1.14 [CI95% 1.04,1.25] p=0.006).
Conclusion: IMID patients showed similar predictors of mortality than general population involving COVID-19. Immune-modulating agents did not seem to overshadow the prognosis of COVID-19 infection. Female gender, lower age and lower basal CRP could select a cohort of "good" prognosis patients with mild COVID-19 disease as well higher age points out the worst prognosis. Even that, each case should be individiualized.
REFERENCES:
[1] Ceribelli A, et al. Recommendations for coronavirus infection in rheumatic diseases treated with biologic therapy. J Autoimmun. 2020;109:102442.
[2] Micaela F, et al. COVID-19 in patients with rheumatic diseases in northern Italy: a single-centre observational and case-control study. Lancet Rheumatol 2020;2:e549-56.

Table 1. baseline characteristics between non-severe and severe COVID-19 patients.

Variables	Non-severe (67)	Severe (24)	p-value
Age, mean (SD)	56.8 (14.6)	70.2 (13.7)	0.000
Female, n (%)	38 (63.3)	10 (41.7)	0.070
HLA-B27 +, n (%)	9 (17.7)	2 (10.0)	0.423
Disease evolution (years), median (IQR)	12.5 (5;24)	14 (9;20)	0.891
Comorbidity, n (%)	35 (59.3)	21 (87.5)	0.013
Flu vaccine, n (%)	51 (85.0)	23 (95.8)	0.166
Basal GC, n (%)	18 (30.0)	12 (50.0)	0.084
csDMARD, n (%)	32 (47.8)	16 (66.7)	0.111
b/tsDMARD, n (%)	35 (52.2)	11 (45.8)	0.590
COVID-19 symptoms, n (%)	55 (93.2)	24 (100)	0.191
Pneumonia, n (%)	31 (51.7)	21 (87.5)	0.002
Admission, n (%)	30 (50.0)	23 (95.8)	0.000
CRP, median (IQR)	3.5 (2;9)	10.0 (3;20)	0.005

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4059

POS1265 CHALLENGES OF EGYPTIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DURING COVID-19 PANDEMIC

S. Tharwat[1], S. Zohdy[2]. [1]*Mansoura University, Internal Medicine, Rheumatology & Immunology, Mansoura, Egypt*; [2]*Faculty of Medicine, Horus University, Internal Medicine Department, Mansoura, Egypt*

Background: Coronavirus disease 2019 (COVID-19) pandemic in Egypt is part of worldwide COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. The current COVID-19 pandemic has contributed to substantial deterioration to healthcare systems worldwide [2].Systemic lupus erythematosus (SLE) patients may have several barriers as medications access during the pandemic.
Objectives: The aim of this study was to assess the tremendous challenges faced by the Egyptian SLE patients during COVID-19 pandemic either in the drug shortage, hospitalization or COVID-19 infection through a questionnaire-based study.
Methods: This questionnaire-based study was carried out on 200 patients with SLE from Egypt. The questionnaire provided covered socioeconomic status, lupus disease data, knowledge about COVID-19 infection and medical and family history of COVID-19 infection.
Results: The mean age of the participants was 30.1 years (with SD 8.4). Among the participants,180 (90 %) were females and 172 (86%) were from urban areas. Corticosteroids and mycophenolate mofetil and antimalarials were the most used medications (87%,87% and 70 % respectively). 140/200 (70 %) of the participants reported difficulty in obtaining medications during COVID-19 pandemic particularly antimalarials (60%). Lupus disease activity was affected by the drug shortage in half of the participants. Twenty-eight (14%) patients lost their jobs while 26 patients (13%) reported that their work was severely impacted by the crisis. Among the precautions taken for prophylaxis against infection wearing protective masks (74%) and using disinfectants of the hands several times per day (67%) were the most reported measures. Forty patients (20%) had to stop or reduce taking NSAIDs to guard against COVID-19 infection while 10 patients (5%) had to start taking antimalarials as a prophylaxis. Among 34 patients (17%) who needed hospitalization,26 (76%) were mainly due to lupus activity and 24 (71%) of them found difficulty on hospital admission because of COVID-19 pandemics. About 40 % of the participants reported that they had at least one close relative had confirmed COVID-19 infection. In addition, thirty-two patients (16%) had confirmed COVID-19 infection. Most of them became clinically free after treatment. However, about half of them had lupus flare and had to change the medications used for treatment of lupus.
Figure 1 shows the differences between males and females in response to the questionnaire. 58.6% of females versus 20 % of males would use telemedicine for remote contact with the rheumatologist. Most of females were more keen than males to wear the masks (76.7% versus 50 % respectively).
Conclusion: The current COVID-19 pandemic has negative impact on the healthcare provided to SLE patients in Egypt. Patients with SLE faced shortage their medications especially antimalarials.
REFERENCES:
[1] Today, E.J.R.o., Egypt announces first Coronavirus infection. 2020. **28**(02): p. 2020.
[2] Rathi, M., et al., Impact of the COVID-19 pandemic on patients with systemic lupus erythematosus: Observations from an Indian inception cohort. 2021. **30**(1): p. 158-164.

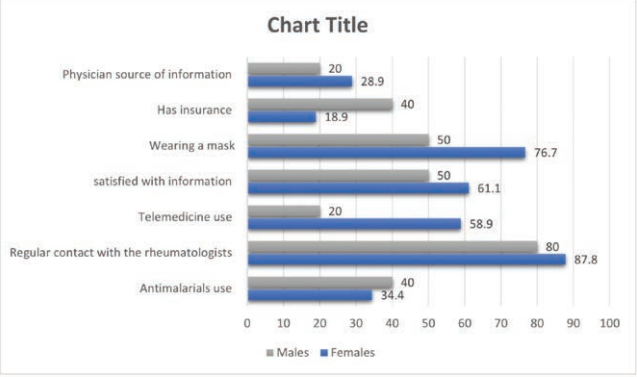


Figure 1. The frequency of the response to questionnaire in Egyptian lupus patients by gender

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4064

POS1266 COVID-19 IN PATIENTS WITH RHEUMATIC DISEASES: SURVEY-BASED ASSESSMENT OF THE RISK OF HOSPITALIZATION

D. Karateev[1], P. Pchelnikova[2], E. Luchikhina[1], T. Boboshko[3]. [1]*Moscow Regional Research and Clinical Institute n.a. M.F. Vladimirsky (MONIKI), Moscow Regional Rheumatology Center and Department of Rheumatology, Moscow, Russian Federation*; [2]*EULAR Standing Committee of People with Arthritis/ Rheumatism in Europe, PARE, Zurich, Switzerland*; [3]*Russian Rheumatology Association "Nadezhda", Moscow Branch, Moscow, Russian Federation*

Background: Prognosis of the need for in-hospital treatment in patients suffered with COVID-19 is crucial to optimize the use of medical resources. Risk factors of hospitalization due to COVID-19 are not sufficiently studied in patients with rheumatic diseases (RD).
Objectives: To reveal factors associated with the risk of hospitalization of patients with RD due to SARS-CoV-2 (COVID-19) infection.

Methods: We analyzed data based on the preliminary results of the patients registry from the ongoing project "Patient's Opinion on Covid-19 in Rheumatic Diseases (POPCORD)". The registry contains data collected directly from Russian-speaking patients with different RD who completed a special questionnaire, located on the website https://revmo-covid.ru/. The questionnaire includes information on whether the patient had COVID-19 and related information, as well as information on rheumatic disease and its treatment.
Results: 1050 patients (92% from Russian Federation, 8% from other locations) completed the survey - 93% females, mean age 40,28±11,26 (M±SD, median 38 [32;48]), BMI 24,52±5,38 (median 23,42 [21;27]), disease duration 7,91±8,46 (median 5,00 [2;11]). Diagnoses reported: rheumatoid arthritis (49%), ankylosing spondylitis (14%), systemic lupus erythematosus (13%), psoriatic arthritis (6%), Sjogren's disease (5%), systemic sclerosis (3%), other (10%). 51% of respondents indicated concomitant conditions: arterial hypertension (19%), obesity (15%), kidney disease (11%), cardiovascular disease (7%), liver disease (6%), IBD (5%), other lung diseases, including ILD (5%). 96% of patients reported constant intake of antirheumatic drugs: steroids (37%), NSAIDs (46%), hydroxychloroquine (22%), csDMARDs (66%), bDMARDs (17%), tsDMARDs (2%). 344 (31,8%) patients reported COVID-19 or suspected SASR-CoV2 viral pneumonia, 282 (84,4%) were treated as outpatients, 52 (15,6%) were hospitalized. Relatives or physicians reported 3 cases of death related to COVID-19 (0,9% of total mortality, 5,8% of in-hospital mortality). Table 1 contains odds ratios for the main factors, related to hospitalization, based on the results of the survey. Analysis of the survey participants' parameters (patients' characteristics, treatments etc.) did not reveal any significant variables, related to increased risk of hospitalization. No increased risk related to any groups of anti-rheumatic drugs or any particular medications was found either. Risk of hospitalization was significantly lower in patients with ankylosing spondylitis.

Table 1. Factors, related to hospitalization due to COVID-19 in patients with RD.

Factor	*OR [95% CI]*	*p*
Age ≥50 y.o.	2,12 [1,14;3,94]	0,99
Age ≥65 y.o.	9,04 [2,10;38,98]	1,00
Female	1,73 [0,70;4,25]	0,92
Body mass index ≥35	2,09 [0,71;6,10]	0,88
Current smoking	0,47 [0,11;2,06]	0,24
Smoking in the past	1,43 [0,83;2,48]	0,92
Diagnosis of ankylosing spondylitis	0,25 [0,06;1,05]	0,02
Comorbid conditions:		
• Diabetes mellitus	3,39 [1,07;10,77]	0,99
• Cardiovascular disease	1,91 [0,72;5,08]	0,94
• Asthma	5,42 [1,07;27,61]	0,99
• COPD	0,42 [0,05;3,26]	0,34
• Kidney disease	1,57 [0,71;3,50]	0,91
• Liver disease	0,90 [0,26;3,18]	0,57
• Neurological disorders	5,42 [0,75;39,36]	0,99
• No concomitant conditions	0,70 [0,40;1,25]	0,14
Therapy:		
• Oral steroids	1,37 [0,82;2,29]	0,91
• NSAIDs	1,12 [0,67;1,87]	0,72
• Traditional DMARDs	1,39 [0,89;2,17]	0,94
• Biologic DMARDs	1,15 [0,55;2,43]	0,72
• Targeted synthetic DMARDs (JAK-inhibitors, apremilast)	3,25 [0,75;14,03]	0,97
Level of concern about COVID-19:		
• Low level / no concern about COVID-19	0,57 [0,28;1,17]	0,08
• Medium level of concern	0,60 [0,28;1,28]	0,12
• High level of concern	1,69 [1,03;2,76]	0,99

Conclusion: Survey of patients with RD did not show significantly increased risk for hospitalization due to COVID-19 in relation with specific diagnosis, any anti-rheumatic medications, as well as comorbid conditions and main patient characteristics. Diagnosis of ankylosing spondylitis related to significantly lower risk of hospitalization.
Acknowledgements: Dr Anna S Misiyuk from V.A. Nasonova Institute of Rheumatology, Moscow, Russia.
The COVID-19 Russian patient experience survey is conducted on behalf of Russian Rheumatology Association "Nadezhda". The project was partially granted by BIOCAD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4065

POS1267 CLINICAL COURSE OF NEW SARS-COV-2 INFECTION IN CHILDREN WITH RHEUMATIC DISEASES: RETROSPECTIVE STUDY OF SINGLE PEDIATRIC RHEUMATOLOGY CENTER

I. Nikishina[1], Z. Kolkhidova[1], V. Matkava[1], A. Shapovalenko[1], S. Arsenyeva[1], M. Kaleda[1], E. Fedorov[1], S. Salugina[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Pediatric Department, Moscow, Russian Federation*

Background: About one year ago at the beginning of the new SARS-CoV-2 infection pandemic, it was expected, that rheumatic disease (RD) and immunosuppressive therapy could predispose to a more severe course of the Covid-19 infection. At that time, it was unspeakable how this infection would occur in children with RB in compare to adults. Now it's time to draw preliminary conclusions.
Objectives: to analyze all features of COVID19 infection in children with RD
Methods: The retrospective single center study of all patients with pediatric RD who had the COVID19 infection up to the end of January 2021. It was analyzed all variety of clinical manifestations, changing in therapy at the time of COVID-19 and after it, the dynamics of the RD and consequences of the new viral disease.
Results: The study included 66 patients under the age of 18 with various RS, including autoinflammatory disease (AIDs). The diagnostic distribution, sex ratio, age and previous therapy present in the Table 1. There were patients treated with DMARDS (methotrexate -47, hydroxychloroquine -3, mycophenolate mofetil -2, colchicine -1), NSAID monotherapy -6, systemic steroids -10; 29 patients recived Biologics, including combination with methotrexate. None of our patients had a severe course of the COVID-19, none of 66 patients was hospitalized for emergency indications in the intensive care unit or in other specialized departments. The diagnosis of Covid-19 infection was based on different evidences: positive PCR in 15 (23%) cases, high levels of immunoglobulins G and M - in 64 (97%) and 7 (11%) respectively, viral pneumonia was confirmed by CT in 2 (10%) cases. A manifest clinical picture presented just in 21 (32 %) of patients, the others were carried the disease asymptomatically. Among the clinical manifestations of SARS-CoV-2 that were observed in our patients were the following: fever, as the most frequent symptom - 19 (90%), rhinitis - 12 (57%), anosmia - 10 (48%), sore throat - 3 (14%), arthralgia/myalgia in 4 (19%), rash - 1 (5%) case, cough - 4 (19%) cases. it is important to note that until July 2020, only 4 patients were registered, and in the next 6 months – 62. The treatment against Covid-19 in our patients with clinical symptoms included: NSAID monotherapy -4 (19%), Systemic steroids -2 (10%), Hydroxychloroquine -2(10%), Antibiotics-5 (24%).

Table 1. Clinical characteristics of children with RD according to presence of symptoms of Covid-19

Parameter		Covid-19 symptomatic course (n=21)	Covid-19 asymptomatic course (n=45)	p-values
Sex ratio (F/M)		9/12	30/15	ns
Duration of RD (Me. Years)		4 (2;6)	4 (2;7)	ns
Age	Me	15 (13; 17)	11 (8;13.5)	**<0,001**
(years)	<10 yrs	1	19	**<0,05**
	>10 yrs	20	26	**<0,001**
Covid-19 evidences	IgG Covid-19 +	19	45	ns
	IgM Covid-19 +	3	4	ns
	PCR Covid-19 +	11	0	ns
Diagnosis of RD	JIA non-systemic	14	31	ns
	sJIA	1	3	ns
	SLE	4	1	ns
	JDM	1	1	ns
	Scleroderma		6	ns
	AIDs (CAPS, FMF, FOP)	1	3	ns
Previous therapy	NSAID monotherapy	3	6	ns
	DMARDs	16	33	ns
	Systemic steroids	4	7	ns
	TNF-inhibitors	5	12	ns
	Abatacept	1	3	ns
	IL6-inhibitors (Tocilizumab, Sarilumab)	0	2	ns
	JAK-kinase inhibitors	1	2	ns
Worsening/flare of RD after Covid-19 infection		5	0	p<0,05

Conclusion: Our study suggests that the presence of RD and immunosuppression therapy does not lead to an increased frequency or severe course of Covid-19 infection in children. The final conclusion will be drawn as the data accumulates.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4101

POS1268 COVID-19 VACCINE HESITANCY AMONG RHEUMATOLOGY PATIENTS RECEIVING INFLUENZA VACCINE

V. Valerio[1], H. C. Shen[2], E. Field[1], E. G. Mcdonald[3], A. Turner[4], S. Bernatsky[3], M. Hudson[5], I. Colmegna[3]. *[1]The Research Institute of the McGill University Health Care Centre, Medicine, Montreal, Canada*; *[2]University of Montreal, Medicine, Montreal, Canada*; *[3]McGill University Health Care Centre, Medicine, Montreal, Canada*; *[4]McGill University Health Care Centre, Nursing, Montreal, Canada*; *[5]Jewish General Hospital, Medicine, Montreal, Canada*

Background: Adults with rheumatic diseases are a COVID-19 vulnerable population with potential increased risk for severe infection. COVID-19 vaccines are a key strategy to ending the pandemic. Unfortunately, fears about vaccines, some of which are propagated by misinformation, are common and may prevent or inappropriately delay vaccination. *Refusal or uncertainty to get a vaccine despite its availability* is known as vaccine hesitancy.
Objectives: This study aims at defining causes of COVID-19 vaccine hesitancy among rheumatology patients.
Methods: Between November and December 2020, a cross-sectional survey was completed by rheumatology patients presenting to a large Canadian tertiary-care center for influenza immunization. COVID-19 risk factors, previous COVID-19 infection, the likelihood of getting a future COVID-19 vaccine (scale 0-10), and contextual, individual, and vaccine-specific potential determinants of vaccine hesitancy were assessed. Patients were classified into 5 groups based on how likely they were to get a future COVID-19 vaccine (0= not likely at all; 2.5= unlikely; 5= intermediate; 7.5= likely; 10= highly likely). A machine learning approach (XgBoost) was used to fit univariate models for a multi-class correlation.
Results: 157 rheumatology patients completed the survey. Most were females (n=112, 71%) with a mean age of 54.6 (standard deviation 17.9). The majority (73%) had tertiary-education, and 46% were employed at the time of the survey. The most common rheumatology diagnoses were rheumatoid arthritis (n=90, 58%), systemic lupus erythematosus/vasculitis (n=41, 26%) and spondyloarthropathies (n=39, 25%). Most patients were on immunosuppressors (n=93, 59%). Only half (n=85, 54%) were highly likely to accept a future COVID vaccine, 17% (n=26) likely, 19% (n=30) intermediate, 6% (n=10) unlikely, and 4% (n=6) not likely at all. One hundred thirty-five patients (86%) previously received the flu vaccine, whereas 6% (n=10) previously rejected it. Only three patients were previously diagnosed with COVID-19 (2%) one of whom was hospitalized. Eighty-seven patients (56%) considered that the COVID-19 vaccine should be mandatory, and 101 (65%) that they should receive it. Most respondents were somewhat concerned about receiving a future COVID-19 vaccine (n=116, 76%) despite that 65% believed that vaccines benefits outweighed their risks. Almost all, (n=145, 96%) believed that governmental decisions about vaccines are in the best interest of the population, while less than half (n=70, 45%) were confident that pharmaceutical companies would provide safe and effective vaccines. One hundred participants (65%) denied feeling social pressure to get the vaccine, and 55% (n=81) were willing to pay for the vaccine. Feeling social pressure about getting a COVID-19 vaccine, having severe concerns about receiving a future COVID-19 vaccine, distrust in pharmaceutical companies, lower education, and doubts of whether vaccines benefits outweigh their risks, were negatively associated with COVID vaccine acceptance.
Conclusion: Forty six percent of rheumatology patients being immunized against influenza showed at least some hesitancy towards COVID-19 vaccination. Multiple contextual, individual, and vaccine-related factors may contribute. Targeted educational strategies, including producing and communicating data on vaccine safety, may help promote vaccine uptake in this potentially vulnerable population.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4150

Spine, mechanical musculoskeletal problems, local soft tissue disorders

POS1269 **THE UTILITY OF ULTRASOUND TO PREDICT PATIENT OUTCOMES IN SHOULDER PAIN: A PROSPECTIVE OBSERVATIONAL STUDY OF 500 PATIENTS**

G. Tran[1,2,3], S. Kingsbury[1,2], E. Hensor[1,2], P. G. Conaghan[1,2]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine, Chapel Allerton Hospital, Leeds, United Kingdom*; [2]*National Institute for Health Research Leeds Biomedical Research Centre, Chapel Allerton Hospital, Leeds, United Kingdom*; [3]*Harrogate and District NHS Foundation Trust, Department of Rheumatology, Harrogate, United Kingdom*

Background: Shoulder pain is common and persistent, with a large socioeconomic burden. Ultrasound (US) scans are used for diagnosing and managing shoulder pain, but the extent to which it informs management and improves outcomes is unknown. A recent retrospective study identified groups with different patterns of US pathologies.
Objectives: To confirm the existence of US-based groups of shoulder pain and determine if US-detected pathology (grouped or individual) predicts outcomes in the context of usual care. Response to local steroid injection was also evaluated.
Methods: This was a 6 month, prospective, single centred, community based, observational cohort study. Inclusion: shoulder pain, ≥18 years, first shoulder US. Exclusion: shoulder surgery, inflammatory arthritis, steroid/physiotherapy in prior 6 weeks. Standardised reporting for 10 US pathologies was employed. Latent class analysis (LCA) identified pathology-based groups. Multiple linear regression analysis explored associations between baseline pathologies, subsequent treatment and 6-month Shoulder Pain and Disability Index (SPADI). Growth mixture modelling (GMM) identified groups with common trajectories of change.
Results: Of 500 patients (mean age 53.6; 52% female), 330 completed follow-up. LCA identified 4 groups: bursitis without acromioclavicular joint degeneration (ACJD) (group 1), bursitis with ACJD (group 2), rotator cuff tear (group 3), no bursitis/tear (group 4). SPADI was higher at baseline for tears (55.1 vs. 49.7-51.3) (overall p=0.005), but groups did not differ at 6 months (p=0.379) (Table 1). No individual pathologies predicted 6-month outcomes. Response to baseline injection at week 2 did not differ between groups (p=0.423). GMM found 4 trajectories; the majority of patients followed trajectory 1 (little change), irrespective of US pathology group (79%, 77%, 87%, 70% of US groups 1-4 respectively) (Figure 1).
Conclusion: This is the largest prospective study involving US of symptomatic shoulders, and the first to investigate groups with distinct patterns of US pathologies in predicting outcome. US-based classification of pathology (as groups or individually) did not predict 6-month outcomes with current treatments and there were no differences in short-term response to steroids between groups. The role of routine diagnostic US for shoulder pain needs consideration; it may be useful if evidence-based therapies for specific pathologies are established.

Table 1. Predictors of SPADI score at 6 months

Baseline characteristic	Coefficient* (95% CI), p-value
Pathology group:Bursitis w/o ACJ degeneration (group 1)	Reference
Bursitis with ACJ degeneration (group 2)	0.08 (-5.15, 5.32), p=0.975
RC tear (group 3)	5.01 (-1.48, 11.50), p=0.130
No bursitis, no RC tear (group 4)	1.98 (-4.00, 7.96), p=0.516
Injection at scan	4.87 (0.40, 9.34), p=0.033
Age, years	-0.01 (-0.17, 0.15), p=0.898
Female	-1.51 (-5.42, 2.40), p=0.448
Symptom duration, months	0.00 (-0.04, 0.05), p=0.879
Uses arms to rise from chair	2.65 (-1.50, 6.81), p=0.210
Physiotherapy before baseline	-0.23 (-4.78, 4.31), p=0.920
1 injection before baseline	2.35 (-2.87, 7.56), p=0.377
≥2 injections before baseline	6.53 (-2.50, 15.57), p=0.156
Total SPADI	0.62 (0.35, 0.89), p<0.001
Shoulder activity score	-0.59 (-1.15, -0.04), p=0.037
P-SEQ score	-0.20 (-0.46, 0.07), p=0.141
Brief IPQ score	0.19 (-0.16, 0.54), p=0.298
HADS score	0.01 (-0.38, 0.41), p=0.947
Constant**	35.44 (29.50, 41.38), p<0.001

*Interpreted as unit difference in Rasch-transformed SPADI score per 1 additional unit of the independent variable **Estimated SPADI at 26 weeks in patients in the reference category for all categorical variables and with mean values for continuous covariates. ACJ=acromioclavicular joint; HADS=hospital anxiety and depression scale; IPQ=illness perception questionnaire; P-SEQ=pain self-efficacy questionnaire; RC=rotator cuff; SPADI=shoulder pain and disability index

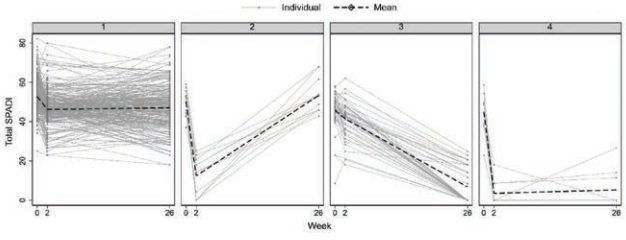


Figure 1. Trajectories of total SPADI over time by the pathology groups found and response to injections

Acknowledgements: This research was funded by the National Institute for Health Research (NIHR) Leeds Biomedical Research Centre (BRC) and by a NIHR Doctoral Research Fellowship (GT; DRF-2016-09-159). The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care. This study was also part-funded through the Arthritis Research UK Leeds Experimental Osteoarthritis Treatment Centre (20083).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.292

POS1270 **MUSCULOSKELETAL MANIFESTATIONS IN A COHORT OF 234 INFLAMMATORY BOWEL DISEASE PATIENTS**

B. M. Fernandes[1], M. Bernardes[1], D. R. Gonçalves[2], F. Magro[3], L. Costa[1]. [1]*Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*;

[2]*Centro Hospitalar Entre Douro e Vouga, Rheumatology, Santa Maria da Feira, Portugal*; [3]*Centro Hospitalar Universitário São João, Gastroenterology, Porto, Portugal*

Background: Musculoskeletal symptoms represent the most common extraintestinal manifestations of inflammatory bowel disease (IBD) and a major cause of impaired quality of life in these patients. Spondyloarthritis (SpA) is classically associated with IBD, but other rheumatic manifestations may occur.
Objectives: To characterize musculoskeletal symptoms and rheumatic diseases in an IBD cohort.
Methods: Retrospective monocentric descriptive study including all the patients with IBD consecutively reffered from Gastroenterology to the Rheumatology Department between January of 2013 and December 2020 in a tertiary university hospital. Demographic and clinical data and musculoskeletal symptoms were collected at the time of the first visit in the Rheumatology outpatient center and the rheumatic diseases diagnosed during the entire follow-up were registered.
Results: A total of 234 patients were included, 136 (58.1%) females, 20 (8.5%) smokers. At the first Rheumatology consultation the mean age was 43.6 (±13.7) years and the mean IBD duration was 11.7 (±9.7) years. Concerning IBD: 172 (73.5%) had Crohn's disease and 62 (26.5%) had ulcerative colitis; azathioprine (39.7%), infliximab (28.2%) and mesalazine (26.5%) were the most frequently used drugs; eleven patients (4.7%) were taking glucocorticoids and 106 (45.3%) had already been treated with glucocorticoids.
Regarding musculoskeletal symptoms: 76 (32.5%) patients had peripheral symptoms and 98 (41.9%) had axial symptoms (Table 1).

Table 1. Characterization of peripheral and axial musculoskeletal symptoms in patients with Inflammatory Bowel Disease.

		N (%)
Peripheral symptoms	**No**	158 (67.5%)
	Arthritis / "inflammatory" joint pain	24 (10.3%)
	"Mixed" rhythm joint pain	15 (6.4%)
	"Mechanical" joint pain	29 (12.4%)
	Enthesopathy	8 (3.4%)
Axial symptoms	No	136 (58.1%)
	"Inflammatory" back pain	46 (19.7%)
	"Mixed" rhythm back pain	35 (14.9%)
	"Mechanical" back pain	17 (7.3%)
Total		234 (100%)

Twenty-six (11.1%) patients had radiographic sacroiliitis, 14 (6.0%) had sacroiliitis in computed tomography and 9 (3.8%) in magnetic resonance. Forty-four (18.8%) patients fulfilled *Assessment of SpondyloArthritis international Society* (ASAS) criteria for axial SpA and 5 (2.1%) for peripheral SpA. Also of note, 16 (6.8%) patients had a previous diagnosis of psoriasis and 5 (2.1%) had uveitis in the past.
Concerning other rheumatic diagnosis, we observed: osteoarthritis in 64 (27.3%), osteoporosis in 16 (6.9%), diffuse idiopathic skeletal hyperostosis in 6 (2.6%), systemic lupus erythematosus in 4 (1.7%), rotator cuff tendinopathy in 2 (0.9%), rheumatoid arthritis, gout, calcium pyrophosphate deposition disease, fibromyalgia, drug-induced lupus, osteitis condensans ilii, Dupuytren's contracture and avascular necrosis of the femoral head in 1 (0.4%), each.
Conclusion: Our results demonstrate a high prevalence of musculoskeletal symptoms and rheumatic diseases in patients with IBD. These diagnoses are not limited to the group of SpA and osteoporosis, emphasizing the importance of rheumatologists being alert to other rheumatic diagnoses in patients with IBD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.490

POS1271 PREVALENCE OF JOINT EFFUSION, HYPERPERFUSION AND ENTHESITIS IN YOUNG HEALTHY INDIVIDUALS

J. K. Schreiner[1], D. Scheicht[2], P. Karakostas[1], C. Behning[3], P. Preuss[4], P. Brossart[1], V. Schäfer[1]. [1]*University Hospital Bonn, Clinic of Internal Medicine III, Oncology, Hematology, Rheumatology and Clinical Immunology, Bonn, Germany*; [2]*Porz am Rhein Hospital, Department for Rheumatology, Cologne, Germany*; [3]*University Hospital Bonn, Department of Medical Biometry, Informatics and Epidemiology, Bonn, Germany*; [4]*University of Bonn, University Sport, Bonn, Germany*

Background: The European League Against Rheumatism (EULAR) recommends using ultrasound (US) in patients with rheumatoid arthritis and psoriatic arthritis in diagnosis (1). In addition, US examination is crucial for detecting enthesitis in the above mentioned rheumatic diseases. However, abnormal findings on US may also occur in healthy individuals as indicated by recent studies focusing on small joints like metacarpophalangeal joint, metatarsophalangeal joint or the elbow. (2,3)
Ultrasound assessment of large joints in healthy individuals has not been extensively studied so far, causing a lack of information concerning normal values in musculoskeletal US examination.
Objectives: The purpose of this study was to determine the prevalence of joint effusion, hyperperfusion of the synovia and enthesitis in large and medium-sized joints of healthy individuals.
Methods: Ultrasound assessment of shoulder, elbow, wrist, hip, knee and ankle joints as well as corresponding entheseal sites including the Achilles tendon and the plantar aponeurosis was performed in healthy individuals below the age of 30 years. Additionally, participants filled out a survey on their physical activity level, underwent a bioelectrical impedance analysis (BIA) and conducted a supervised weight training to determine their training volume. Prevalence of US findings was calculated, and a binary logistic regression model was applied to determine the association between the present findings and sex, age, handedness, hours of sports activity per week, BMI, amount of skeletal muscle mass (SMM) or training volume of strength training.
Results: We included 51 healthy individuals with a mean age of 23.7 years, 52.9% were female with a mean BMI of 22.5 kg/m^2. Ultrasound examination detected joint effusion in one joint in 25.5% (n=13), 29.4% (n=15) showed effusion in two of twelve examined joints. Joint effusion in three, four and five joints was detected in 9.8% (n=5), 3.9% (n=2) and 3.9% (n=2) of the cases, respectively. In 27.5% (n=14) of the individuals no joint effusion was observed. The most frequently affected joint was the elbow joint. Synovial hyperperfusion was not detected in any participant. Enthesitis was observed in one, two and three examined entheseal sites in 19.5% (n=10), 5.9% (n=3) and 2% (n=1), respectively. In 72% (n=37) of the examined individuals no pathology of the entheseal sites was found. Hyperperfusion presented to be the most frequent pathology observed in enthesitis (23%), followed by calcification (6%).
Binary logistic regression model demonstrated a significant association between reported hours of sports activity per week and the prevalence of effusion in the knee (p = 0.017). The odds of joint effusion in the knee increased with the hours of sports activity by 34.1% (Exp(B)= 1.341, 95%-CI(1.054, 1.705)). Additionally, the odds of enthesitis in any entheseal site increased with BMI (p= 0.015, Exp(B) = 1.407, 95%-CI(1.068, 1.852).
Binary logistic regression model did not show any significant association between sex, age, handedness, amount of SMM or training volume of strength training and the prevalence of joint effusion or enthesis pathology in the examined participants.
Conclusion: Joint effusion in large and mid-sized joints as well as enthesitis are not only detected in patients with rheumatic diseases but also in healthy individuals. Hours of sports activity and BMI have a significant association with the findings and should be considered during ultrasound examination.
REFERENCES:
[1] Colebatch AN, Edwards CJ, Østergaard M, van der Heijde D, Balint PV, D'Agostino M-A, u. a. EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. Ann Rheum Dis. Juni 2013;72(6):804–14.
[2] Padovano I, Costantino F, Breban M, D'Agostino MA. Prevalence of ultrasound synovial inflammatory findings in healthy subjects. Ann Rheum Dis. Oktober 2016;75(10):1819–23.
[3] Schäfer VS, Recker F, Vossen D, Ge I, Matuschek E, Hartung W. Prevalence of Elbow Joint Arthritis and Enthesitis in Rheumatoid Arthritis. 2020;11.
Disclosure of Interests: Julia Konstanze Schreiner: None declared, Dennis Scheicht: None declared, Pantelis Karakostas: None declared, Charlotte Behning: None declared, Peter Preuss: None declared, Peter Brossart: None declared, Valentin Schäfer Speakers bureau: AbbVie, Novartis, BMS, Chugai, Celgene, Medac, Sanofi, Lilly, Hexal, Pfizer, Janssen, Roche, Schire, Onkowissen, Royal College London, Consultant of: Novartis, Chugai, AbbVie, Celgene, Sanofi, Lilly, Hexal, Pfizer, Amgen, BMS, Roche, Gilead, Medac, Grant/research support from: Novartis, Hexal, Lilly, Roche, Celgene, Universität Bonn
DOI: 10.1136/annrheumdis-2021-eular.1010

POS1272 DIFFERENCES IN RANGE OF MOTION AND MECHANICAL MUSCLE CHARACTERISTICS AMONG INFLAMMATORY AND MECHANICAL SPINAL PAIN: A CASE-CONTROL STUDY

S. Alcaraz-Clariana[1], L. García-Luque[1], I. C. Aranda-Valera[2], M. L. Ladehesa Pineda[2], C. López-Medina[2], C. Gonzalez-Navas[3], F. Alburquerque Sendin[1], D. P. Rodrigues-de-Sousa[1], C. Garrido-González[1], J. L. Garrido-Castro[3], E. Collantes Estevez[2]on behalf of CASTRO. [1]*University of Cordoba, Medicine, Nursing and Physiotherapy Faculty, Cordoba, Spain*; [2]*Hospital Universitario Reina Sofia, Rheumatology, Córdoba, Spain*; [3]*Maimónides Biomedical Research Institute of Córdoba, Motion Analysis Lab, Cordoba, Spain*

Background: The spinal range of motion (ROM) and the mechanical muscle properties (MMPs) at rest are defined as relevant clinical factors in inflammatory (i.e. axial Spondyloarthritis -axSpA) and mechanical spinal pain (i.e. Mechanical

Neck pain -NP- or Mechanical Low Back pain -LBP-). Nevertheless, there is not enough evidence regarding if ROM and MMPs are different in both types of spinal pain.

Objectives: To identify differences between axSpA patients and NP or LBP subjects, in cervical and lumbar ROMs and MMPs at rest.

Methods: Subjects with axSpA and with NP or LBP composed the Inflammatory pain Group (IG) and the Mechanical pain Group (MG), respectively. For the analysis of the spinal mobility, two Inertial Measurement Units (IMU) were used. For both spinal regions (cervical and lumbar - Figure 1A,B) 3 repetitions of flexion-extension, lateral-flexion, and rotation were executed separately[1]. A record of the MMPs using a hand myotonometer was made in both lumbar (muscular belly of the erector spinal – Figure 1D) and cervical (the semispinalis capitis muscles at C4 - Figure 1C) spine in prone position with both arms along the body. The MMPs recorded in this study included: frequency (tone), stiffness, decrement (elasticity), relaxation and creep (viscosity). The order of assessments (right/left) was randomized. Since no side-to-side differences in either group were observed, the mean of both sides was considered. Student-t tests were used to compare the groups, and Cohen-d effect size index was estimated as a measure of the size of difference. P<0.05 was considered statistically significant.

Results: 61 subjects in IG (42% women, age 41±12 years, BMI 25±3) and 66 in MG (51% women, age 38±13 years, BMI 25±3) participated in this study. No significant differences were identified in sociodemographic data between both groups. Table 1 shows ROM and MMPs between groups. All lumbar ROMs were significantly lower in the IG, with the different between means achieving the minimum clinical important difference (>8º) for flexion-extension and lateroflexion. On the contrary, the cervical ROMs were not different between groups, and showed the highest variability, probably related to compensatory mechanisms due to lumbar ROMs restrictions. The IG showed greater Lumbar stiffness than the MG with large effect size (d=0.94). No other difference in MMPs was identified in this region (p>0.05). Regarding the cervical region, all MMPs showed differences between groups. Thus, tone, stiffness and elasticity were higher in the IG, while relaxation and viscosity were lower. In all cases, except for decrement, the effect size was from moderate to large (0.6<d<0.8).

	IG (n=61)	MG (n=66)	p-value	Cohen-d
Lumbar flexion- extension (°)	62.7 ± 20.2	70.8 ± 17.9	0.019 *	0.42
Lumbar rotation (°)	25.6 ± 8.3	30.1 ± 10.1	0.007 *	0.48
Lumbar lateral-flexion (°)	46.6 ± 12.3	54.8 ± 10.8	<0.001 *	0.70
Cervical flexion- extension (°)	96.5 ± 21.6	96.2 ± 18.8	0.941	0.01
Cervical rotation (°)	130.9 ± 27.3	131.9 ± 25.6	0.817	0.01
Cervical lateral-flexion (°)	66.4 ± 21.5	71.6 ± 15.6	0.122	0.27
Lumbar tone (Hz)	15.32 ± 3.40	14.52 ± 1.93	0.129	0.29
Lumbar stiffness (N/m)	330.85 ± 56.93	272.48 ± 65.59	0.001 *	0.94
Lumbar decrement	1.33 ± 0.41	1.29 ± 0.32	0.480	0.10)
Lumbar relaxation (ms)	19.11 ± 7.58	20.23 ± 4.29	0.312	0.18
Lumbar creep	1.16 ± 0.43	1.21 ± 0.22	0.519	0.14
Cervical tone (Hz)	17.27 ± 1.93	16.17 ± 1.84	0.001 *	0.58
Cervical stiffness (N/m)	313.93 ± 54.17	282.61 ± 50.07	0.001 *	0.59
Cervical decrement	1.34 ± 0.23	1.42 ± 0.18	0.020 *	0.39
Cervical relaxation (ms)	16.66 ± 2.52	18.49 ± 2.74	<0.001 *	0.69
Cervical creep	1.02 ± 0.14	1.13 ± 0.14	<0.001 *	0.80

Conclusion: AxSpA patients present lower lumbar ROMs than NP and LBP subjects. Further, posterior cervical MMPs of axSpA are more rigid and less viscoelastic than those of NP and LBP subjects. ROMs and MMPs show a different behavior pattern in cervical and lumbar regions when spinal pain from different origin is assessed.

REFERENCES:

[1] Measuring Spinal Mobility Using an Inertial Measurement Unit System: A Validation Study in Axial Spondyloarthritis. Diagnostics 10(6):426

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1036

POS1273 A CHANGE IN A REHABILITATION MODEL INCREASES WORK CAPACITY AT 36 MONTHS IN LOW BACK PAIN

M. Norberg[1]. [1]*Lavey Medical Center, Rehabilitation, Lavey-les-Bains, Switzerland*

Background: In chronic low back pain, the most expensive patients are them with long-standing sick-leave of more than 6 months. Several studies have showed the importance of rehabilitation models working with kinesiophobia (fear of movement). One possibility of treating chronic low back pain is a multidisciplinary rehabilitation program.

Objectives: The aim of this study was to analyze the impact of a change in a rehabilitation program for chronic lumbar pain by introducing a progressive exposure procedure to decrease apprehension associated with low back pain. We studied its impact on work capacity after 3 years, compared to our classic program.

Methods: We have compared the results of 1004 of our patients that have accomplished a multi-disciplinary program and that have been followed over 12 months. They were divided in two groups: one before the implantation of PHODA (PHOto of Daily Activity: photos showing activites) associated with occupational training and work exposure. Then a second one including 200 patients that followed the new program. The program contained physical training, occupational tasks developed on the basis of the apprehension following a cogntivo-comportemental approach.

We have analyzed the evolution of apprehension according to different questionnaires (FABQ, Tampa scale (TSK) and PACT (evaluating the subjective work capacity)), the Phoda results and the official work capacity at beginning of the program and after 36 months.

Results: We saw a clear increase in the global work capacity at 12 months after completing the program: passing from 40 to 79% (p < 0.01) in the old program comparing to the new one with an increase of 86% (p< 0.01). These results were confirmed at 36 months, with stabilized results. In parallel there was an increase in the subjective sensation of physical capacity (Pact), but less in the new program. This increase was correlated with a decrease in fear-avoidance according to the Fabq, and in the TSK

Conclusion: In chronic low back, a multidisciplinary rehabilitation program, gives a global work capacity of 79%. This capacity could be increased on focalising on patient's apprehensions with gradual exposure according the fear-avoidance model developed by Waddell and explored by Vlayen. The correlation were confirmed on the psychological part, with less apprehension and less anxiety. Finally, the SF 36 showed an increase in body confidence as an important factor in these functional restoration programs.

REFERENCES:

[1] Waddell G et al. Low back pain, fear-avoidance beliefs and disability: With the development of a Fear-Avoidance Beliefs (FAB) questionnaire. Pain 1993;52:157-68

[2] Vlaeyen JWS et al. Graded exposure in vivo in the treatment of pain-related fear: a replicated single-case experimental design in four patients with chronic low back pain. Behaviour Res Therapy 2001;39(2):151–66

[3] Waddell G et al. Low back pain, fear-avoidance beliefs and disability: With the development of a Fear-Avoidance Beliefs (FAB) questionnaire. Pain 1993;52:157-68

[4] Vlaeyen JWS et al. Graded exposure in vivo in the treatment of pain-related fear: a replicated single-case experimental design in four patients with chronic low back pain. Behaviour Res Therapy 2001;39(2):151–66

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1816

POS1274 THERAPEUTIC MANAGEMENT OF RHEUMATOLOGISTS VERSUS OTORHINOLARYNGOLOGISTS OF CERVICOGENIC DIZZINESS

M. Yasmine[1], K. Maatallah[1], H. Ferjani[1], W. Triki[1], D. Ben Nsib[1], D. Kaffel[1], W. Hamdi[1]. [1]*Kassab Institute of Orthopedics, Rheumatology, Tunis, Tunisia*

Background: The treatment of patients presenting with cervicogenic dizziness (CGD) may be challenging. Indeed, there is no consensual treatment approach for CGD, nor is there no gold-standard assessment for diagnosis.

Objectives: Our study aimed to assess the management of CGD by rheumatologists versus otorhinolaryngologists.

Methods: We conducted a cross-sectional study including Tunisian doctors dealing with CGD. Rheumatologists (RTO) and otorhinolaryngologists (ORL) were invited to answer a questionnaire via google form about CGD daily management. Outcomes of interest were treatment modalities.

Results: The study included 30 RTO and 32 ORL. Most of the doctors (RTO, vs ORL) were females (88.3%, vs 56.3%), aged between 35 and 45 (43.3%, vs 62.5%), and worked at a private practice (33.3%, vs 59.4%). The number of patients diagnosed with CGD by RTO was as follows: 1-2 per year (33.3%), 1-2 per month (18.8%), 1-2 per week (20%), less than one patient a year (10%) and none in 3.3% of cases. The number of patients diagnosed with CGD by ORL was as follows: 1-2 per year (50%), 1-2 per month (33.3%), 1-2 per week (6.2%), less than one patient a year (15.7%) and none (9.4%). Most patients presenting with CGD were females in both groups (93.1%, vs 82.8% respectively) with a mean

age between 36 and 65 (79.3%, vs 82.1%). Most of the respondents declared treating patients with CGD (93.1%, vs 79.1%). Regarding treatment modalities, physical therapy was the most prescribed in both specialties (81.5% and 48.3%, respectively). Only RTO (18.5%) prescribed manual therapy. Concerning medical treatment, anti-inflammatory were the most prescribed drugs in both groups (92.6, and 34.5%, respectively). Sixty-seven percent of RTO prescribed anti-vertigo medication. Interestingly, it was the least prescribed drug by ORL (6.9%). Only RTO (59.3%) prescribed Muscle relaxants.

Conclusion: Despite the disparities in the management of CGD, physical therapy remains the first prescribed treatment by Tunisian doctors. Further studies are needed to establish a consensus to treat CGD.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2230

POS1275 PERITENON THICKENING IS ASSOCIATED WITH THE INTENSITY OF MANUAL SPORTS ACTIVITY

C. Guillén-Astete[1], P. Zurita-Prada[2], C. Urrego-Laurín[1], N. García-Montes[3], H. García-López[2]. [1]*Hospital Ramón y Cajal, Rheumatology, Madrid, Spain*; [2]*University Hospital Moncloa, Rheumatology, Madrid, Spain*; [3]*Hospital Ramón y Cajal, Emergency, Madrid, Spain*

Background: Peritenon enlargement has been considered as a specific ultrasound finding associated with psoriatic arthritis based on studies in patients. Recent observations in athletes have demonstrated the existence of this finding although its relationship with the type of physical activity performed has not been determined.

Objectives: To determine to what extent manual physical activity is associated with the prevalence of peritenon thickening in the fingers of healthy athletic subjects.

Methods: Thirty-five healthy young male volunteers were recruited from a local sports centre in the community of Madrid. All of them performed sports activities with their hands for more than 12 hours a week.A digital dynamometer was used to determine the flexion strength of the fingers of the dominant hand. A single observer performed an ultrasound scan of this hand to determine the presence or absence of a hypoechoic image surrounding the extensor digitorum tendon of the 2nd, 3rd, 4th and 5th fingers, according to previous definitions. Mean flexion strengths were compared with the number of positive ultrasound findings.

Results: Fifteen volunteers (mean age 24.3 years, BMI 24.4) did not present peritenon enlargement (42.8%). The mean ± standard deviation of the fingers flexor strength according to the number of peritenon enlargement detected were 43.5 ± 6.2, 49.2 ± 3.8, 53.2 ± 1.64 and 63.0 ± 4.83 Kg for volunteers with none, 1, 2, 3 and 4 peritenon enlargements, respectively. (ANOVA P<0.001; Pearson's coefficient 0.827, P<0.001). Correlation between BMI, body fat percentage or training hours per week and the number of peritenon enlargement detected was not demonstrated.

Conclusion: Peritenon enlargement, also knew as peritenon tendon inflammation, is detectable by ultrasound scan in healthy subjects and it seems to be associated to the physical activity intensity, indirectly measured by the flexor strength of the fingers.

REFERENCES:

[1] Gutierrez et al. Ann Rheum Dis. 2011;70:1111-4
[2] Zabotti et al. Clin Exp Rheumatol. 2016;34:459-65
[3] Husic et al. Ann Rheum Dis. 2014;73:1529-36

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2740

POS1276 LONG TERM OUTCOME OF MULTIPLE ULTRASOUND GUIDED SUPRASCAPULAR NERVE BLOCK IN TREATMENT OF FROZEN SHOULDER IN DIABETIC PATIENTS

M. A. Mortada[1], R. Hassan[1], Y. A. Amer[1]. [1]*Faculty of Medicine, Zagazig University, Rheumatology and Rehabilitation, zagazig, Egypt*

Background: Frozen shoulder is prevalent among diabetic patients, and usually has aggressive course, with more tendency to be bilateral and resistant to treatment. Suprascapular nerve block (SSNB) is used with increasing frequency by anesthetists and rheumatologists in the management of frozen shoulder. We previously introduced a protocol of nine injections for SSNB with better short term outcome than single SSNB injection (1). Long term outcome of SSNB in management of frozen shoulder is still not detected.

Objectives: To evaluate the long term effect of multiple (nine) ultrasound guided supra-scapular nerve block in treatment of diabetic frozen shoulder.

Methods: A retrospective cohort study followed up 40 diabetic patients who received a course of ultrasound guided multiple supra-scapular nerve block (9 injections) on 2014. In this study we retrospectively assessed the patients from previously recorded data at a mean duration of 6 years after completing the 9 injection course SSNB clinically by measuring the shoulder active range of motion (using a goniometer in three planes: abduction, internal, and external rotation). Visual analogue scale and Functional assessment by shoulder pain and disability index (SPADI).

Results: Thirty four patients (85% of original cohort) completed the long term follow up.

The patients were 19 (55.9%) females, 60.6 y mean age, and the mean of disease duration was 85.6 months. The majority of patients (33 patients 97.05%) continues improvement and gained within normal complete range of motions in all directions and excellent grades of shoulder function (Table 1).

Table 1.

Clinical Parameters	At base line	At 4 months	Last follow up at (72months±4)	**P value
SPADI pain score (100)	(68.8 ± 0.5)a	(10.3 ± 7.4)b	(0.9±1.9)c	0.00*
SPADI disability score (100)	(69.2 ± 7.7)a	(6.25 ± 2.25)b	(0.4±0.8)c	0.00*
SPADI total (100)	(69.1 ± 8.5)a	(8.15 ± 5.4)b	(1.1±0.9)c	0.00*
Patient global assessment (100)	(90.2 ± 8.2)a	(8.2 ± 4.2)b	(0.4±2.1)c	0.00*
Night pain (100)	(55.4±10.2)a	(10.3 ± 4.9)b	(2.3±1.1)c	0.00*
Abduction (180°)	(77.5 ± 4.7)a	(170.3 ± 10.3)b	(174.2±6.2)b	0.00*
External rotation (100 °)	(46 ± 12.6)a	(80.1 ± 10.2)b	(86.4±10.3)b	0.00*
Internal rotation (70 °)	(34.5 ± 2.4)a	(55.4 ± 10.1)b	(60.2±9.5)b	0.00*

* P <0.05 there was a statistical significant difference**•A,b,c**--- the alphabet of different symbols ---means a significant statistical difference between groups**SPADI:** shoulder pain and disability index

Conclusion: The multiple injection courses for supra-scapular nerve block has an excellent long term efficacy as treatment of diabetic frozen shoulder. This method should be the treatment of choice in patients of diabetic frozen shoulder who do not respond to physiotherapy.

REFERENCES:

[1] Mortada, M. A., Ezzeldin, N., Abbas, S. F., Ammar, H. A. & Salama, N. A. Multiple versus single ultrasound guided suprascapular nerve block in treatment of frozen shoulder in diabetic patients. J. Back Musculoskelet. Rehabil. 30, 537–542 (2017).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2951

POS1277 NON-CONTIGUOUS MULTIFOCAL SPONDYLODISCITIS: A CASE SERIES AND REVIEW OF LITERATURE

A. Feki[1], I. Sellami[2], R. Akrout[1], S. Ben Jemaa[1], A. Hriz[1], M. Ezzeddine[1], M. H. Kallel[1], H. Fourati[1], S. Baklouti[1]. [1]*Hedi Chaker Hospital, Rheumatology, Sfax, Tunisia*; [2]*Hedi Chaker Hospital, Occupational Medicine, Sfax, Tunisia*

Background: Spondylodiscitis is an infective process of the disc and the two adjacent vertebrae. It is quite a rare disease accounting for 2–7% of all cases of septic osteomyelitis. These spinal infections touch commonly a single level, the lumbar spine being the most affected. Non-contiguous spine level involvement is seldom reported in the literature. This last group is for the most part imputable to granulomatous organisms [1,2].

Objectives: Study the clinical, microbiological, radiological, therapeutic and evolutional characteristics of non-contiguous multi-levels spondylodiscitis.

Methods: We conducted a retrospective descriptive study over twenty-one years in the Department of Rheumatology. The diagnosis of spondylodiscitis was based on combination of clinical, biological and radiological arguments.

Results: Eight patients had non-contiguous multi-levels infectious spondylodiscitis. There were 6 men and 2 women. The mean age was 53.3±26.2 years. The mean delay from onset of symptoms to diagnosis was 134.6±77.6 days. Back pain was the most common symptom. All patients had spinal syndrome. The Signs of spinal cord compression were observed in 3 patients. C-reactive protein levels were elevated in 6 patients (mean: 56 ± 30.8 mg/L). Plain radiography, performed in all cases, showed pathological pictures in 7 patients. Magnetic resonance imaging was performed in 6 patients. Vertebral levels affected were thoracic / lumbar in 6 cases, cervical/thoracic in 1 case and cervical/lumbar in 1 case. The paravertebral abscess was associated to the disc involvement in 3 cases. Epiduritis was associated in 3 cases. Pathogens were isolated in all cases. Tuberculosis was the most common cause. The leading causative agents in non-tuberculosis spondylodiscitis were staphylococcus aureus, brucella and streptococcus B. Two microorganisms combined were found in two cases (mycobacterium tuberculosis associated to Escherichia coli in one case and mycobacterium tuberculosis associated to Brucella in another). Medical treatment was adapted to the microbial culture and the sensitivity profile of the etiological agent.

After therapy, 7 patients had regression of symptoms and 1 patient had a permanent neurological impairment.

Conclusion: Multilevel spondylodiscitis involving non-contiguous spine segments is rare. Although atypical organisms are generally held to be responsible, the common bacteria such as Streptococcus B or Staphylococcus aureus should not be overlooked.

REFERENCES:

[1] Zimmerli W. Clinical practice.Vertebral osteomyelitis. N Engl J Med 2010 Mar;362(11):1022–9.

[2] Cottle L, Riordan T. Infectious spondylodiscitis. J Infect 2008; 56(June (6)):401–12.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3190

POS1278 THE PREVALENCE AND CLINICAL SIGNIFICANCE OF ULTRASONOGRAPHIC FINDINGS OF DISTAL MEDIAL HAMSTRING TENDONS IN PATIENTS WITH POSTEROMEDIAL KNEE PAIN

H. Saad[1], Y. Gazar[1], S. Ghanem[1], A. Maaty[2,3]. [1]*Al-Azhar University, Cairo, Egypt, Rheumatology and Rehabilitation, Cairo, Egypt*; [2]*Faculty of Medicine, Suez Canal University, Ismailia, Egypt, Physical Medicine, Rheumatology, and Rehabilitation, Ismailia, Egypt*; [3]*Armed Forces Center of Health Rehabilitation, Taif, Saudi Arabia, Physical Medicine and Rehabilitation, Taif, Saudi Arabia*

Background: Periarticular abnormalities are common ultrasonographic (U/S) findings in individuals with knee pain. Incidental U/S observations, including thickening of the distal hamstring tendons, require explanations for their clinical importance. Tendon thickness may be a good indicator of tendinopathy and tendon dysfunction. Also, it is uncertain whether these tendon changes are correlated with knee pain or not?

Objectives: The aim of this study was to determine U/S findings of distal medial hamstring tendons in patients with posteromedial (PM) knee pain and assess the diagnostic values of tendon thickness in predicting tendinopathy.

Methods: We studied distal medial hamstring tendons (semimembranosus [SM] and semitendinosus [ST]) of 104 patients (104 knees) with non-traumatic unilateral PM knee pain and 118 healthy controls (236 knees). U/S evaluations included tendon thickness, echogenicity, the presence of intrasubstance tears, calcification, and vascularity.

Results: The mean age (standard deviation) of the patients and control groups were 51.7 (10.4) years and 49.8 (9.9) years, respectively. The mean visual analogue scale (VAS) for pain among patients was 5.1 and 58.6% of them located the pain at medial joint line. The studied patients had significantly higher mean SM thickness (7.17 mm *vs.* 5.46 mm, respectively) and ST thickness (3.93 mm *vs.* 3.45 mm, respectively) than the controls. U/S abnormalities among patients were hypoechogenicity (62.5%), intrasubstance tears (31.7%), loss of fibrillar pattern (23.1%), Baker cyst (20.2%), calcification (18.3%), Anserine bursitis (11.5%), and neovascularization (6.7%). We found significant correlations between tendon thickness and VAS (r=0.752, p=0.004), and pain location (r=0.680, p=0.008). SM thickness had higher accuracy to predict tendinopathy than ST thickness (80.6% *vs.* 68.9%, respectively).

Table 1. Diagnostic values of tendon thickness in predicting tendinopathy.

Tendons	Cutoff	Sensitivity	Specificity	+PV	-PV	Accuracy	AUC
SM	>6.6	70.2	89.8	85.7	76.8	80.6	0.835
ST	>3.7	56.7	79.6	71.1	67.6	68.9	0.696

SM: semimembranosus, ST: semitendinosus, +PV: positive predictive value, -PV: negative predictive value, AUC: area under curve.

Conclusion: U/S changes are frequently present in patients with PM knee pain. Tendon thickness is an accurate predictor of tendinopathy. These findings suggest that U/S screening of all individuals with PM knee pain is a useful tool for improving patients' outcomes and decreasing tendon-related disability.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3233

POS1279 ADVERSE DRUG REACTIONS IN TUBERCULOSIS AND MANAGEMENT

R. Grassa[1], N. El Amri[1], S. Lataoui[1], O. Jomaa[1], H. Zeglaoui[1], K. Baccouche[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumathology, Sousse, Tunisia*

Background: Around 10 million people worldwide contract tuberculosis (TB) every year. According to the World Health Organization (WHO), approximately one-quarter of the world's population is latently infected with Mycobacterium tuberculosis. Its treatment is extremely long and patients may experience a variety of adverse reactions.

Objectives: The aim of this study was to assess the different adverse drug reactions (ADR's) in patients treated with first-line anti-tubercular drugs.

Methods: This retrospective study included 45 cases of TB followed in the Rheumatology department of Farhat Hached hospital in Sousse, Tunisia, over a period of 22 years (1998-2020).

Results: The mean age was 52.2 ± 17.72 years [14-95 years]. These were 19 men (42.2%) and 26 women (57.8%).The different locations of tuberculosis were as follows: pulmonary for 5 patients (11.1%), spinal for 26 patients (57.8%), articular for one patient (2.2%), urinary for two (4.4%), and multifocal for 8 patients (17.8%). An anti-tuberculosis treatment (based on quadrytherapy: Rifadine(R), Isoniazide(I), Pyrazinamide (Z) and Ethambutol (E)during 2 months, followed by biotherapy based on (R)and (I) was prescribed for an average duration of 10.85 months [6-24 months]. ADR's were observed in 53.33% of patients. Abdominal pain and nausea were detected in 5 cases (11.1%). Hepatic cytolyse was noticed in 8 cases (17.8%) under (R). Cholestatic hepatitis occurred in 9 cases (20%) under (R). Asymptomatic Hyperuricemia was detected in 15 cases (33.3%) with (E). Two cases of toxiderma were detected: the first under (E) and the second under (E) + (Z). Ethambutol was responsible for a case of DRESS syndrome and a case of drug-induced hepatitis. One case of hemolytic anemia had occurred under (R). A sensorineural hearing loss was noted under streptomycin in one case. No fatal side effects were observed. These ADR's were reversible in all cases.

Conclusion: The treatment of TB can cause a variety of ADRs'. Early recognition by active surveillance and appropriate management of these ADRs' might improve adherence and treatment success.

REFERENCES:

[1] Prasad, R., Singh, A., & Gupta, N. Adverse drug reactions in tuberculosis and management. Indian Journal of Tuberculosis, 66(4), 520–532 (2019).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3273

POS1280 SPINAL LOCATION OF TUBERCULOSIS: WHAT HAS CHANGED OVER THE LAST YEARS?

S. Boussaid[1], M. Mrabet[1], S. Jemmali[1], H. Sahli[1], H. Ajlani[1], E. Cheour[1], S. Rekik[1], M. Elleuch[1]. [1]*Rabta Hospital, Rheumatology, Tunis, Tunisia*

Background: Tuberculosis (TB) is no longer a disease limited to developing nations and is still a major cause of significant morbidity and mortality worldwide. It can affect the different parts of the spine.

Objectives: The aim of this study was to determine the preferred spinal location of TB.

Methods: We conduct a retrospective and descriptive study in a single rheumatology department. Data were collected from observations of patients hospitalized in the past 20 years (2000-2020) who have been diagnosed with tuberculous spondylodiscitis (TS).

Results: Fifty-two patients were included (37F/15M). Their mean age was 55.21 years ± 17.79 [19-91]. TS was more frequently unifocal (75%) than multifocal (25%). Lumbar spine involvement was the most common (57.7%) and more frequent in women (63.3%) but with no statistically significant difference (p = 0.2). Other localizations were described such as: dorso-lumbar (21.2%), dorsal (15.4%), lumbosacral (3.8%) and cervical (1.9%). Lumbar pain was present in 34 patients (65.4%) and 29 patients (55.8%) suffered from segmental lumbar stiffness. Imaging was contributive by showing the vertebral location using standard X-rays, computed tomography and magnetic resonance imaging. Disc pinch, erosion of vertebral plateaus and vertebral collapse were the major signs (82.7%, 65.4% and 67.3%, respectively).

Conclusion: TS is a rare but serious clinical condition which may lead to severe deformity and early or late neurological complications. Spinal involvement is often unifocal and mostly diagnosed with lumbar pain or stiffness. Multifocal forms, touching several parts of the spine, however remain rare. Our findings remain consistent with those of the literature.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3365

POS1281 HOW DOES OBESITY INFLUENCE THE FEATURES OF KNEE OSTEOARTHRITIS?

H. Hachfi[1], D. Khalifa[1], M. Brahem[1], N. Ben Chekaya[1], M. Younes[1]. [1]*Taher Sfar Hospital, Rheumatology, Mahdia, Tunisia*

Background: Knee osteoarthritis and obesity are both major health problems. It is now admitted that the prevalence of knee osteoarthritis gets higher with obesity and that weight loss helps knee function and allows patients to avoid surgery.

Objectives: The aim of this study was to study the influence of obesity on knee osteoarthritis features.

Methods: A cross-sectional study was conducted in the university hospital Taher Sfar of Tunisia over a period of 6 months. Patients who had knee osteoarthritis confirmed by radiographs were included. Sociodemographic, clinical, radiological and therapeutic data were collected from medical records and visits. Obesity was

defined by a body mass index (BMI) ≥30. Functional impairment was assessed by the Womac index and Lequesne index.
Results: The study included 186 patients. There were 31 males and 155 femmes. The mean age was 60±10 years. The percentage of obese patients was 53,8%. The mean age was similar in both groups obese and non obese. There were more women in the obese group compared to the non obese group (p=0.0001), more patients who had diabetes mellitus and dyslipidemia (p=0.002). Non-obese patients had a shorter duration of symptoms with no statistical significance (p=0.151). Obese patients had more involvement of both knees (p<0.0001). Obesity did not have an impact on pain severity. Severity of radiological images (p=0,0001) were more frequent in obese patients. Functional impairment was similar in both groups. However, the percentage of patients having a very important functional impairment with Lequesne index was higher in obese patients (p<0.029). Obese patients also needed more physical therapy sessions (p=0.035).
Conclusion: Knee osteoarthritis in obese patients is characterized with the femlae gender predominance, bilateral knee involvement, and a more severe images on radiographs. Thus the need for better control of weight and the importance of physical activity.
REFERENCES:
[1] Coggon D, Reading I, Croft P, et al. Knee osteoarthritis and obesity. *Int J Obes Relat Metab Disord J Int Assoc Study Obes* 2001; 25: 622–627.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3602

POS1282 VERIFICATION OF MANIFESTATIONS OF SARCOPENIA IN OBESE PATIENTS WITH THREE METHODS FOR BODY COMPOSITION ASSESSMENT

V. Vasileva[1], L. Marchenkova2, V. Sergeev2. [1]*National Medical Center for Rehabilitation and Balneology, Department of Somatic Rehabilitation, Reproductive Health and Active Longevity, Moscow, Russian Federation*; [1]*National Medical Center for Rehabilitation and Balneology, Department of Somatic Rehabilitation, Reproductive Health and Active Longevity, Moscow, Russian Federation*

Background: With new technologies for body composition assessment determining changes learn, muscle and fat mass. Prevention of sarcopenic obesity is timely detection of decrease.
Objectives: Aim of the study was to compare the effectiveness of three methods of body composition assessment such as bioimpedans analysis (BIA), air-replacement bodyplatismography (BodPod) and Dual X-ray absorptiometry Total body program (DXA Total Body) in the verification of reducing of skeletal muscle mass as sign of sarcopenic obesity in obese patients.
Methods: The study group included 95 patients aged 21-69 y.o. (average age 53,9±11,05 years) with BMI≥30.0 kg/m2. The control group included 37 patients aged 37-69 y.o (average age 50,73±10,6 years) of the same age without obesity with BMI 20.0-29.9 kg/m2. Body composition was tested using BIA, BodPod and DXA with calculating fat, lean and skeletal muscles mass (kg) and % in all the patients.
Results: According to BIA the groups differ only in fat mass (FM) 42.75 (4.8;6.3) vs. 33.15 (28.4;35.5) kg; p=0.036 and did not differ (p>0.05) in lean (LM), skeletal muscle mass (SMM) and in % of FM and SMM. According to BodPod analyses groups differed in the FM 3.4 [36.81;69.94] vs 31.02 [23.22;38] kg, p=0.007, % FM 45.4 [42.1;53.8] vs 37.7 [28.6;41.1], p=0.003 and % LM - 54.6 [46.2;57.9] vs 62.3 [58.9;71.4], p=0.003, but had statistically equivalent values of LM 55 [49.48;67.77] vs 40.36 [33.12;49.06] kg, p=0.19. According to DXA Total Body analyses statistically significant differences (p<0.05) have been identified between the groups in FM and % FM of the hands, feet, trunk, total body (p>0.05), but not in LM and % LM (p>0.05) (Table 1).

Table 1. Effectiveness of three methods for body composition assessment

INDICATORS	STUDY GROUP	CONTROL GROUP	p
Weight (kg)	106 [96;122]	80 [77;81]	0.00251
BMI (kg/m2)	37.6 [104;124]	26.8 [24;30]	0.000000
Bod Pod			
% fat mass	45.4 [42.1;53.8]	37.7 [28.6;41.1]	0.003424
% lean mass	54.6 [46.2;57.9]	62.3 [58.9;71.4]	0.003424
fat mass (kg)	43.4 [36.81;69.935]	31.016 [23.223;38.004]	0.006836
lean mass (kg)	55.002 [49.48;67.77]	40.359 [33.122;49.058]	0.185377
BIA			
fat mass (kg)	42.75 [4.8;6.3]	33.150 [28.4;35.5]	0.035771
lean mass (kg)	59.5 [53.95;71.05]	54.850 [49.9;62.6]	0.458312
skeletal muscle mass (kg)	27.9 [23.9;33.2]	25.6 [22;29.3]	0.701678
skeletal muscle mass (%)	45.3 [43.3;47.7]	47.1 [42.3;48.1]	0.415687
DXA Total Body			
total body lean mass (g)	97276 [86062; 109154]	62628 [57839; 85068]	0.602523
total body fat mass (g)	47030 [39300; 56729]	25652 [22164; 36396]	0.009796
total body muscle mass (g)	49861 [42793; 57088]	36426 [32273; 43341]	0.973711

Conclusion: From methods of body composition assessment, air-replacement bodyplatismography (BodPod) is the most sensitive in the verification of skeletal muscle mass reduction in obese patients. This method shows that patients with obesity have a significantly reduced muscle mass compared with normal weight or overweight subjects.

REFERENCES:
[1] L. A. Marchenkova, V. A. Vasileva, Motor and balance function disorders and possibilities of their correction in patients with obesity and metabolic syndrome // Lechashchiy vrach. 2019. № 4. S. 68.
[2] P. Corbeil, M. Simoheau, D. Rancourt, A. Tremblay, N. Teasdale, Increased risk for falling associated with obesity: mathematical modeling of postural control // IEEE Transactions on Neural Systems and Rechabilitation Enqineering. 2001; 9 (2): 126-136.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3629

POS1283 SPONDILODISCITIS WITHOUT DOCUMENTED GERM: WHAT THERAPEUTIC MANAGEMENT?

R. Grassa[1], N. El Amri[1], K. Baccouche[1], S. Lataoui[1], H. Zeglaoui[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumathology, Sousse, Tunisia*

Background: Spondylodiscitis (SD) is an infectious inflammation that affects the vertebrae, vertebral discs and adjacent structures. It may have a bacterial or non-bacterial etiology. Although analysis has improved and identification of pathogens is highly pursued, in one third of cases, no organism can be identified.
Objectives: The objective of our work is to describe the epidemiological, clinical and evolutionary profile of SD with no germ identified and management.
Methods: This is a retrospective study including 37 cases of SD with no germ identified, collected in the Rheumatology Department of Farhat Hached hospital in Sousse, Tunisia over a period of 22 years (1998-2020).
Results: The mean age was 59.7 years [18-97 years]. These were 21 men (56.76 %) and 16 women (43.24 %).Spinal pain was the major symptom. The lumbar location was the most frequent in 56.76% of cases. It was a multifocal localization in 21.62%. The imaging allowed the detection of para abscesses -vertebral in 43.24%. An epiduritis was objectified in 54.05%.CT-guided biopsy was performed in 59.46% and it was not conclusive. A bacteriological survey was carried out and came back negative. Spondylodiscitis was presumed to be tubercular and staphylococcal in respectively 62.16 % and 18.92 %. The tuberculosis origin was retained in view of the chronic evolution, the multi-stage damage in the radiological assessment. While staphylococcal SD was retained due to the presence of cutaneous lesion and subacute evolution. Large-spectrum antibiotic therapy was initiated in the other cases.One case was initially considered to be staphylococcal but with epidural and soft tissue extension tuberculosis was then considered to be the cause. The evolution after initiation of adequate antibiotic treatment was interspersed with neurological complications in one case of tuberculosis SD.
Conclusion: Our results show a higher frequency of presumed tuberculosis SD considering the endemicity of our country and the improvement under anti tuberculosis treatment.
REFERENCES:
[1] Cornett, C. A., and al. Bacterial Spine Infections in Adults. Journal of the American Academy of Orthopaedic Surgeons, 24(1), 11–18.(2016)
[2] Lener, S., and al Management of spinal infection: a review of the literature. Acta Neurochirurgica, 160(3), 487–496.(2018)
[3] Homagk, L., and al SponDT (Spondylodiscitis Diagnosis and Treatment): spondylodiscitis scoring system. Journal of Orthopaedic Surgery and Research, 14(1).(2019)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3649

POS1284 FASCIAL ULTRASOUND: THE CONTEXT FOR DRY NEEDLING TRIGGER POINTS IN TREATMENT OF MYOFASCIAL PAIN, POSTURAL IMBALANCE

R. Bubnov[1], L. Kalika[2]. [1]*Clinical Hospital "Pheophania", Ultrasound, Kyiv, Ukraine*; [2]*NYDNRehab: Physical Therapy Clinic & Chiropractic NYC, Rehabilitation, New York, United States of America*

Background: Muscles and fascia are the major source of pain in rheumatic diseases. Dry needling under ultrasound guidance (DN-US) is a crucial therapeutic approach to treat muscle pain [1,2], the definition `myo-fascial` calls for searching trigger points (TrPs) in fascia to improve the treatment effectiveness.
Objectives: Aim was to evaluate the relevance of fascial ultrasound for DN-US in myo-fascial pain.
Methods: We included 36 patients (21 females, 20-69 years old) with myofascial pain different localisations (low back, limbs, shoulder, neck pain), postural imbalance; did DN-US protocol according to R. Bubnov [1]: trigger points were identified according, fine (28G) steel needle DN-US was applied. Additionally considered fascial structures for detecting areas of abnormalities (hypervascularity, heterogeinity, hypomotility, adhesions) aka `trigger points` and potental nerve compression/irritation and did precise DN-US where appropriate.
Results: In all patients movement restored and pain decreaed after muscles DN; in 30 patients additionally we detected and did successful DN-US the

major fascial points as follows: thoracolumbar fascia, sacroiliac joint, pelvis ligaments, rotator cuff; potential nerve compressions (e.g., arcade of Frochse, soleus arcade); nerve sheath surrounding nerves (sciatic nerve, brachial plexus) and vessels (thoracic outlet syndrome), smaller fascia, joint capsule thickening. We detected higher rates of motility, improvement postural balance and pain decrease, fewer sessions needed in patients after extensive protocol.

Conclusion: Fascia dry needling is accessible and effective method for myo-fascial pain treatment, may provide additional mechanical benefit and help to maintain treatment effect. Affected fascia can be considered as relevant trigger points, specific ultrasound symptoms should be validated.

REFERENCES:

[1] Bubnov R Trigger Points Dry Needling Under Ultrasound Guidance for Low Back Pain Therapy. Comparative Study. Annals of the Rheumatic Diseases2015;74:624. http://dx.doi.org/10.1136/annrheumdis-2015-eular.2323

[2] Bubnov R, Kalika L, Babenko L. Dynamic ultrasound for multilevel evaluation of motion and posture in lower extremity and spine. Annals of the Rheumatic Diseases 2018;77:1699. http://dx.doi.org/10.1136/annrheumdis-2018-eular.3949

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3843

POS1285 FOOT DISORDERS AND FALLS RISK IN OLDER PERSONS

N. Fani[1], E. Toulgui[1], D. Khalifa[2], S. Mtaoua[3], W. Ouanes[1], S. Jemni[1]. *[1]Hôpital Sahloul, Physical Medicine and Rehabilitation, Sousse, Tunisia*; *[2]Hospital Farhat Hached, Rhumatologie, Sousse, Tunisia*; *[3]Hospital Ibn El Jazzar, Physical Medicine and Rehabilitation, Kairouan, Tunisia*

Background: Falls are major problems in older people, leading to serious morbidity and mortality. Many studies have identified intrinsic and extrinsic fall risk factors in order to develop preventive strategies and guidelines. There are few reports which studied the impacts of aging feet on falls [1].

Objectives: The present study aimed to explore foot musculoskeletal disorders and their relationship to falls in a healthy aging population.

Methods: This was a cross-sectional descriptive study involving the patients aged 65 years and over who were independent in self-care and walking followed at the physical medicine and rehabilitation department of the university hospital of sousse over 3 months. The analysed data focused on the epidemiological and clinical characteristics.Trained physicians evaluated health status, foot problems, and fall(s) history of all subjects. Walking performance was assessed using the 'Timed Get Up & Go' test and the unipedal stance test was used for the assessment of balance. Footprints were taken from the standing position. Associated factors of foot disorders and falls were analyzed.

Results: There were 45 subjects: 18 men, 27 women with a mean age of 69.6 [65-86] years. Foot deformities presented in 87% and were a significantly associated with walking performance or falls (p=0.01, p=0.02). The most common foot musculoskeletal disorder were Halux valgus 31%, followed by Mallet toe 15%. Arch of foot classified by physical examination revealed that pes planus was presented in 35% of cases. There was a significant correlation between BMI and an arch index (p=0.04). Foot problems remained significantly associated with impaired timed up and go test and the unipedal stance test. The causes of pain were plantar fasciitis, hallux valgus, callus, metatarsalgia, and inappropriate footwear. Falls were reported in 33.3 of patients. Falls were significantly associated with Hallux valgus, mallet toe and pain (p<0.05).

Conclusion: Independent of the influence of age, gender, common conditions; foot problems have a significant impact on the ability to perform functional tasks integral to independent living.

REFERENCES:

[1] Menz HB, Lord SR: Foot problems, functional impairment, and falls in older people. J Am Podiatr Med Assoc 1999;89:458– 467. 3 Americ

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3918

POS1286 SHORT-TERM AND MID-TERM EFFICACY OF CAUDAL EPIDURAL STEROID INJECTIONS IN THE MANAGEMENT OF DEGENERATIVE SCIATICA

D. Khalifa[1], N. El Fani[1], R. Moncer[1], E. Toulgui[1], W. Ouanes[1], S. Jemni[1]. *[1]Sahloul Hospital, Physical Therapy and Rehabilitation, Sousse, Tunisia*

Background: Epidural steroid injections are largely used in the management of osteoarthritis-related sciatica. Three possible sites of injection are possible: the caudal through the sacral hiatus, the interlaminar and the transforaminal site. The caudal technique is known to be the most simple one. However, doubts still persist about this infiltration's efficacy.

Objectives: The aim of this work was to study the short-term and mid-term efficacy of caudal epidural steroid injections in patients suffering from sciatica related to a degenerative etiology and to study the determining factors of its efficacy.

Methods: A retroscpective, descriptive and monocentric study was conducted in Sahloul university hospital of Tunisia. Medical records of patients who suffered from sciatica due to disc herniation or spinal stenosis were analysed. Only patients who benefited from at least one caudal epidural steroid injection were included. Other etiologies were ruled out by CT-scan or MRI and laboratory tests. Efficacy of the injection was evaluated by the visual analog scale of pain (VAS) at the first week post infiltration, 3 months and 6 months later. The infiltration was considered effective if the difference of pain scoe by VAS was ≥50% compared to baseline's score. The presence of anxiety and depression was also tracked down with the hospital anxiety and depression scale. Data was collected and analysed using the statistical tool SPSS.20.

Results: Twenty-five patients were included. They were 7 males and 18 females. The mean age at diagnosis was 51.88± 15.28 years. Eleven patients had another osteoarthritis site. Five patients had previous back surgery: 2 dissectomies, 1 arthrodesis, and 2 laminectomies. Median duration of sciatica was 30 months. Sciatica was bilateral in 41.7% of the cases, impulsive during efforts in 52% of the cases and with claudication in 92% of the cases. The median VAS score at baseline was 7 out of 10 (min=4; max=9). All patients had tried medical treatment using NSAIDS and painkillers, and physical therapy before prescribing the infiltration. The technique was similar in all patients: Lidocaine 1% was first injected at a median volume of 5ml, followed by corticosteroids and finally a saline solution (median volume of 20ml). The median number of epidural caudal injections was 3 injections (min=1; max=3). The caudal epidural steroid injections were effective in 60% of the patients at the first week, 56% in the cases at 3 months and 56% of the cases at 6 months. Factors associated with efficacy of the injection at the first week were greater total volume injected (p=0.001), and greater saline solution volumes (p=0.016). At 3 months, factors significantly associated with efficacy of the infiltration were having unilateral pain (p=0.05), a positive straight leg raise test sign (p=0.028), a lower anxiety score (0.014) and a lower depression (0.000) score. At 6 months, factors associated with efficacy were not having cervical osteoarthritis (p=0.03), unilateral pain (p=0.05), low anxiety (p=0.014) and low depression (p=0.001) scores and a higher number of steroid injections (p=0.05).

Conclusion: Caudal epidural steroid injections seem effective on the short-term and this efficacy is maintained till the mid-term. Greater volumes may help with pain by possible adhesiolyse-like mechanisms and having unilateral pain, positive straight leg raise sign, a higher number of injections, no anxiety or depression and no other osteoarthritis sites makes the infiltration more effective.

REFERENCES:

[1] Dincer U, Kiralp MZ, Cakar E, Yasar E, Dursan H. Caudal epidural injection versus non-steroidal anti-inflammatory drugs in the treatment of low back pain accompanied with radicular pain. Joint Bone Spine. 2007;5.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3967

POS1287 ANXIETY, DEPRESSION, FIBROMYALGIA SYNDROME AND PAIN INTENSITY IN PATIENTS WITH LOW BACK PAIN

R. Dhahri[1], A. Dghaies[1], M. Slouma[1], L. Metoui[1], I. Gharsallah[1], I. Dorgham[2], R. Ayari[2], Y. Mallat[2], K. Amri[2]. *[1]The Military Hospital of Tunis, Rheumatology, Tunis, Tunisia*; *[2]The Military Hospital of Tunis, Traumatology-Orthopedic Department, Tunis, Tunisia*

Background: Common low back pain (LBP) is a common health problem affecting 50 to 80% of working age adults resulting in significant personal, social and occupational impairment. Chronic pain has a negative impact on quality of life and psychological well-being.

Objectives: The aim of this study was to examine the relationship between anxiety, depression and pain intensity in patients with low back pain in a population made of military agents.

Methods: It was an analytical cross-sectional study including 50 patients with at least three months of LBP, in the department of rheumatology and orthopedics at the Military Hospital of Tunis between January 1st and March 31, 2020. All patients had a standardized clinical assessment. Patients completed the «hospital anxiety and depression scale» (HADS) and the «Fibromyalgia Rapid Screening Tool» (FIRST) to evaluate psychological impact of chronic LBP. Pain intensity was assessed using a visual analog scale (VAS).

Results: The mean age of the patients was 41.9 ± 8.4 years and the sex ratio was 4.5. LBP duration was 66.4 months. The mean lumbar visual analog scale (VAS) was 4.5 ± 1.9, and the root VAS was 2.6 ± 2.5. Neuropathic pain was found in 26% of patients. Abnormal level of anxiety and depression were found in 58% and 62% of the patients respectively. Out of them 20% and 26% were borderline abnormal for anxiety and depression respectively, while 38% (16.4%) and 36% were certainly abnormal for anxiety and depression respectively. Twelve percent of the patients had fibromyalgia syndrome associated with LBP as they had a FIRST score ≥5. Positive correlations were found between lumbar VAS and HAD anxiety/depression scores (r = 0.35; p<0.01/ r = 0.3; p = 0.04). Positive correlations were also found between root VAS and HAD anxiety/depression (R= 0.38;

P<0.01/ R=0.29; P=0.03). There was positive correlations between Fibromyalgia syndrome (FIRST scale) and lumbar VAS (r= 0.42; p=0.01) and root VAS (R= 0.29; P<0.01).
Conclusion: The results of this study showed that anxiety, depression and fibromyalgia syndrome are not only frequent with patient suffering from chronic LBP but they are also correlated to the pain intensity. As a consequence, assessment of and intervention in anxiety, depression symptoms and fibromyalgia syndrome is crucial in the provision of pain-relief nursing treatment in patients with low back pain.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4086

POS1288 TUBERCULOUS SPONDYLODISCITIS IN ELDERLY: EPIDEMIOLOGY, CLINICAL, FEATURES, TREATMENT AND OUTCOMES

M. Mrabet[1], S. Boussaid[1], S. Jemmali[1], H. Sahli[1], H. Ajlani[1], E. Cheour[1], S. Rekik[1], M. Elleuch[1]. [1]*Rabta Hospital, Rheumatology, Tunis, Tunisia*

Background: Tuberculosis is still endemic all over the world. The incidence of tuberculous spondylodiscitis (TS) is steadily increasing. Clinical features and outcomes of this affection are various and depending on various parameters, including age.
Objectives: Our objective was to explore the differences in presentation and the results of further investigations and the prognosis of TS between young and elderly subjects.
Methods: We conduct a retrospective and descriptive study in a single rheumatology department. Data were collected from files of patients hospitalized in the past 20 years (2000-2020) who have been diagnosed with TS. We carried out a comparative study concerning the clinical biological, imaging features and outcomes between young subjects and subjects aged over 65 years.
Results: Fifty-two cases of TS were collected (37F/15M). The mean age of the population was 55.21 years ± 17.79 [19-91]. Thirty-three patients (69.2%) were classified as young versus 16 elderly patients (30.8%), with female predominance in both groups (69.4% and 75% respectively, p = 0.57). Young subjects was more frequently vaccinated (88.9%) by Bacillus Calmette–Guérin (BCG) (p < 0.001). A delayed diagnosis was noted in both groups (p = 0.24). Lumbar spine involvement was the most common (57.7%). In the two age ranges, the onset of the disease was progressive (p = 0.22), characterized by segmental spine stiffness (p = 0.57) and lumbar pain with general signs (p = 0.27), such as: impaired general condition, fever, night sweats and weight loss. Biological inflammatory syndrome and normochrome normocytic anemia were encountered in both cases (p = 0.08 and p = 0.2, respectively). Standard X-rays and Computed tomography were more performed in young subjects (94.4% and 69.4%, respectively; p < 0.001), unlike magnetic resonance imaging which was more common in elderly subjects but with no statistically significant difference (p = 0.22). Disc pinch, erosion of vertebral plateaus and vertebral collapse were the major signs (82.7%, 65.4% and 67.3%, respectively). Clinical, biological and imaging arguments contributed to positive diagnosis in both groups (p = 0.24). Common medical treatment was anti-tuberculosis: Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E) and physical treatment such as immobilization witch was more common in the eldery (56.3%, p = 0.16). The evolution of the disease was characterized by a clear improvement of young subjects during the second week of treatment (p < 0.001). A more frequent clinical improvement in older subjects was during the fourth week but with no statistically significant difference (p = 0.13). The occurrence of immediate complications was more frequent in the elderly (p = 0.23) with a predominance for drug complications (56.3%) such as: hepatic cytolysis (12.5%), hyperuricemia (18.8%) and major intolerance to anti-tuberculosis (18.8%).
Conclusion: TS is a frequent condition that needs to be treated rapidly. the clinical presentation of TS in the elderly is less noisy which leads to more frequent complications and mortality.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4129

POS1289 CHRONIC LOW BACK PAIN: THERAPEUTIC STRATEGIES AND CLINICAL OUTCOMES IN A MILITARY POPULATION

R. Dhahri[1], A. Dghaies[1], M. Slouma[1], L. Metoui[1], I. Gharsallah[1], I. Dorgham[2], Y. Mallat[2], R. Ayari[2], K. Amri[2]. [1]*Military Hospital of Tunis, Rheumatology, Tunis, Tunisia*; [2]*Military Hospital of Tunis, Orthopedics, Tunis, Tunisia*

Background: Low back pain is an extremely common patient complaint. Most cases resolve quickly after the acute episode. However, a significant number of patients develop chronic low back pain; a persistent disabling condition. Patients suffer from unremitting pain and often become functionally impaired.
Objectives: The aim of this study is to describe the characteristics of chronic LBP, physical examination abnormalities, treatment strategies and the impact of LBP on the professional life of the patients.
Methods: It was a an analytical cross-sectional study including 50 patients with at least three months of LBP, in the department of rheumatology and orthopedics at the Military Hospital of Tunis between January 1st and March 31, 2020. All patients had a standardized investigation and clinical assessment.
Results: The study included 80% of active military serving members and 20% of administrative officers. The mean age of the patients was 41.9 ± 8.4 years and the sex ratio was 4.5. Four patients were suffering from diabetes; two patients were suffering from high blood pressure. All the patients were suffering from chronic LBP lasting for an average of 66.4 months. LBP was associated with radicular pain in 78% of the cases. It was a unilateral radicular pain in 72% of the cases and bilateral in 28% of the cases. The main triggering factors were: carrying heavy loads in 98% of the cases, standing or sitting for long periods in 90% and 76% of the cases, tremors in 74% of the cases. Neuropathic pain was found in 26% of patients. Physical examination showed paravertebral muscle tenderness in 66% of the cases and slack abdominal muscles in 56% of the cases. Assessement of range of flexion of the lumbar spine showed: fingertip to floor test was 18 ±12.2 cm [054cm], schober test was +3.8±1.2cm [16cm]. The extension of lumbar spine was painful in 80% of the cases. A trigger point was found in 28% of the cases. Lasegue sign was positive in 18% of the cases. Leri's test was positive in 8% of the cases. Required treatments during the last episode of LBP were: Paracetamol (62%), nonsteroidal antiinflammatory drugs (26%), tramadol (4%), myorelaxant (4%) and pregabalin (2%). Half of the patients needed functional rehabilitation. Forty percent of the patients reported improvement; 46% of them reported improvement then recurrence of the pain, 8% of them reported no improvement and 4% reported worsening of the symptoms. Thirty six percent of the patients needed an average of 21 days of leave and 35% of them needed exemption from work for LBP problems. One patient needed an outplacement from his original work and one patient needed an early retirement.
Conclusion: Chronic low back pain can cause significant functional disability, and commonly becomes frustrating for both patients and physicians to cope with and treat. There is still no consensus on the best way to manage chronic low back pain, and clinical guidelines are scarce. A combination of pharmacological agents and non-pharmacological methods is the most appropriate therapeutic regimen.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4149

POS1290 CYTOKINE BIOMARKERS IN COMMON LOW BACK PAIN

R. Dhahri[1], A. Dghaies[1], M. Slouma[1], L. Metoui[1], I. Gharsallah[1], I. Dorgham[2], R. Ayari[2], Y. Mallat[2], K. Amri[2], A. Tezeghdenti[3], W. Dkhili[3], R. Kochkar[3], E. Ghazouani[3]. [1]*Military Hospital of Tunis, Rheumatology, Tunis, Tunisia*; [2]*Military Hospital of Tunis, Orthopedics, Tunis, Tunisia*; [3]*The Military Hospital of Tunis, Immunology, Tunis, Tunisia*

Background: Common low back pain (LBP) is a common health problem affecting 50 to 80% of working age adults. It is one of the common and costly health problems in Tunisia. Actually, the role of the immune response and inflammatory cytokines in the pathogenesis of chronic pain has been of growing interest.
Objectives: The aim of this study was to assess whether pro and anti-inflammatory cytokines could be detected in serum in patients with LBP compared with healthy subjects and whether they could be related to pain severity and to clinical findings.
Methods: It was a an analytical cross-sectional study including 50 patients with at least three months of LBP, in the department of rheumatology, orthopedics and immunology at the Military Hospital of Tunis between January 1st and March 31, 2020. All patients had a standardized clinical assessment.
Levels of serum cytokines IL-6, IL-8, IL-1β and TNF- α, were measured using the chimiluminescence technique. Serum concentration of IL-10 was assayed by the enzyme-linked immunosorbent assay technique (ELISA). The normal levels of cytokines were determined in 50 healthy controls.
Results: The mean age of the patients was 41.9 ± 8.4 years and the sex ratio was 4.5. LBP duration was 66.4 months. The mean lumbar visual analog scale (VAS) was 4.5 ± 1.9, and the root VAS was 2.6 ± 2.5. Neuropathic pain was found in 26% of patients. The average BMI was 27 ± 3.7 kg/m^2. Only serum level of IL-8 was significantly higher in subjects with LBP compared to healthy controls (p <10-3). IL-1β was indetectable in both patients and controls. Positive correlations were found between IL-8 levels and anxiety/functional scores (r = 0.3; p = 0.02/ r = 0.3; p = 0.04). IL-6 was positively correlated with BMI, and negatively correlated with the Schober test. No correlations were found between serum levels of IL-6, IL-8, IL-10, TNF-α and pain intensity (VAS), neuropathic pain (DN4), fibromyalgia (FIRST), depression (HAD) and various radiological data.
Conclusion: Interleukin-8 is a biomarker of common low back pain and correlate with anxiety and functional disability. These results suggest that IL-8 may be a therapeutic target to reduce chronic back pain and reduce the social and profession impact.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4205

POS1291

PROFILE OF LUMBAR SPINE DEGENERATIVE PATHOLOGY IN RHEUMATOLOGIC CONSULTATION IN NORTHEN TOGO

P. Houzou[1], V. E. S. Koffi-Tessio[2], E. Fianyo[2], K. Tagbor[2], K. Kakpovi[3], O. Onianikitan[2], M. Mijiyaw[2]. [1]*University of Kara, Rheumatology, Kara, Togo*; [2]*University of Lomé, Rheumatology, Lomé, Togo*; [3]*University of Lomé, Rheumatology, Kara, Togo*

Background: Degenerative spine pathology is a common reason for consultation in rheumatology. The lumbar spine is the first seat.
Objectives: To determine the epidemiological and semiological profile of degenerative lumbar spine damage in Kara.
Methods: It was a cross-sectional study based on patient records who had consulted for a degenerative lumbar spine pathology in the rheumatology department of the CHU-Kara (Northen Togo) over a three-year period.
Results: Of the 1,767 patients examined during the study period, 745 (42.16%) suffered from a degenerative pathology of lumbar spine. They were 285 men (38.3%), and 460 women (61.7%) H/F ratio of 0.62. Traders (30%), civil servants (12.5%), teachers (9.5%), and housewives (8.7%) were the most affected occupational categories. The average age of patients at the consultation was 50.6 ± 12.3 years, and the average duration of disease progression was 4.3 years ± 1.8 years. The clinical forms of degenerative lumbar spine damage were: common low back pain (194 cases; 26.04%), common lomboradiculalgia by probable disco-radicular conflict (457 cases; 61.34%) and the narrowed lumbar canal (94 cases; 12.62%). Common low back pain was acute in 56.7% of cases. The path of radiculalgia during the probable herniated disc was truncated in 19.2% of cases, L5 in 46.4% of cases, S1 in 32.9% of cases, and L4 in 2.7% of cases. The walking perimeter was less than 500 meters in 48% of patients with narrowed lumbar canal. Signs of degenerative disc disease (536 cases), spondylolisthesis (102 cases) and isthmic lysis (37 cases) were the main radiological lesions observed.
Conclusion: Degenerative damage to lumbar spine is dominated in North Togo by common lomboradiculalgia by probable herniated disc.
REFERENCES:

[1] Mijiyawa M, Oniankitan O, Kolani B, Koriko T. La lombalgie en consultation hospitalière à Lomé (Togo). Rev Rhum 2000;67:914-20.
[2] Louw QA, Morris LD, Grimmer-Somers K. The prevalence of low back pain in Africa: a systematic review. BMC Musculoskelet Disord 2007;8:105.
[3] Morris LD, Daniels KJ, Ganguli B, Louw QA. An update on the prevalence of low back pain in Africa: a systematic review and meta-analyses. BMC Musculoskelet Disord 2018;19:196.
[4] Ouédraogo D-D, Ntsiba H, Tiendrébéogo Zabsonré J, Tiéno H, Bokossa LIF, Kaboré F, et al. Clinical spectrum of rheumatologic diseases in a department of rheumatology in Ouagadougou (Burkina Faso). Clin Rheumatol 2014;33:385-9.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4234

Paediatric rheumatology

POS1292

REAL-WORLD EFFECTIVENESS OF ETANERCEPT AND ADALIMUMAB IN CHILDREN AND YOUNG PEOPLE WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) WITHOUT UVEITIS

L. Kearsley-Fleet[1], E. Baildam[2], M. Beresford[2,3], H. Foster[4,5], T. Southwood[6], W. Thomson[7,8], K. Hyrich[1,8]on behalf of BCRD and BSPAR-ETN study groups. [1]*The University of Manchester, Manchester Academic Health Science Centre, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [2]*Alder Hey Children's NHS Foundation Trust, Clinical Academic Department of Paediatric Rheumatology, Liverpool, United Kingdom*; [3]*University of Liverpool, Institute of Life Course and Medical Sciences, Liverpool, United Kingdom*; [4]*Newcastle University, Population Health Institute, Newcastle Upon Tyne, United Kingdom*; [5]*Great North Children's Hospital, Paediatric Rheumatology, Newcastle Upon Tyne, United Kingdom*; [6]*University of Birmingham and Birmingham Children's Hospital, Institute of Child Health, Birmingham, United Kingdom*; [7]*The University of Manchester, Centre for Genetics and Genomics Versus Arthritis, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, Manchester, United Kingdom*; [8]*Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, National Institute of Health Research Manchester Biomedical Research Centre, Manchester, United Kingdom*

Background: Biologic therapies have revolutionised treatment pathways and outcomes for patients with juvenile idiopathic arthritis (JIA). Although there is a choice of approved TNF inhibitors available as a first biologic, there lacks data to inform treatment choices in clinical practice.
Objectives: To compare short-term outcomes on etanercept and adalimumab in children and young people with JIA without uveitis, including drug survival, arthritis disease activity and function ability at 1 year.
Methods: All patients starting a first biologic (etanercept/adalimumab including biosimilars) from 2010 in the UK JIA biologic registers (BCRD and BSPAR ETN) were included. Those with systemic JIA or with any history of uveitis were excluded. Data were collected at start of therapy, 6 months, 1 year, and then annually, including patient demographic, disease activity and drug therapy. In this analysis, drug survival and arthritis disease activity / function ability at 1 year (range 3-15 months) were investigated; comparing between therapies using logistic / linear regression, adjusted for propensity deciles.
Results: There were 550 patients with outcome data available (to 30 Sept 2020); 384 etanercept, 166 adalimumab. At registration, 68% female, median age 12 years old (IQR 8-14), median disease duration 1 year (IQR 1-4), 72% on concomitant methotrexate. Disease activity was similar between both therapies at baseline and one year. At one year, 70% were still on biologic therapy; most stopping therapy for ineffectiveness (45%), adverse events (31%), or patient / family choice (15%). Inactive disease and minimal disease activity was achieved in 26% and 46% respectively, 48% achieved a minimally clinical important improvement in their functional ability (CHAQ improvement >0.13).

	All Patients	Adalimumab	Etanercept
N	**550**	**166**	**384**
Females	68%	59%	71%
Age (years), median (IQR)	12 (8-14)	12 (10-14)	11 (8-14)
Disease duration (years), median (IQR)	1 (1-4)	1 (0-3)	1 (1-4)
ILAR			
Persistent oligo	9%	6%	11%
Extended oligo	20%	14%	23%
RF negative	37%	32%	39%
RF positive	11%	11%	12%
Psoriatic	5%	8%	4%
Enthesitis-related	16%	27%	11%
Undifferentiated	1%	2%	1%
Concomitant oral steroids	16%	20%	15%
Concomitant methotrexate	72%	84%	66%
Follow-up time, years			
Median (IQR)	2.5 (1.4-3.8)	2.1 (1.2-3.1)	3.0 (1.6-4.0)
Min-Max	0.4 - 8.2	0.4 - 7.3	0.4 - 8.2
Drug Survival			
Still on drug at one year	70%	67%	71%
Still on drug at two years	47%	50%	46%
CHAQ			
Baseline, mean (SE)	0.9 (0.04)	0.8 (0.06)	1.0 (0.04)
One Year, mean (SE)	0.7 (0.03)	0.5 (0.06)	0.7 (0.04)
Change, mean (SE)	-0.2 (0.04)	-0.2 (0.06)	-0.2 (0.04)
Regression coef (95% CI)	-	-0.09 (-0.2, 0.04)	Ref
PD Adjusted coef (95% CI)	-	-0.08 (-0.2, 0.07)	Ref
MCID (CHAQ)			
Proportion achieved	48%	48%	48%
OR (95% CI)	-	1.0 (0.6, 1.5)	Ref
PD Adjusted OR (95% CI)	-	1.2 (0.8, 1.9)	Ref
JADAS			
Baseline, mean (SE)	14 (0.4)	14 (0.7)	14 (0.4)
One Year, mean (SE)	5 (0.3)	4 (0.5)	6 (0.3)
Change, mean (SE)	-9 (0.4)	-9 (0.7)	-8 (0.5)
Regression coef (95% CI)	-	-1.1 (-2.3, -0.01)*	Ref
PD Adjusted coef (95% CI)	-	-1.0 (-2.8, 0.8)	Ref
Inactive Disease (JADAS<1)			
Proportion achieved	26%	32%	24%
OR (95% CI)	-	1.5 (1.0, 2.4)	Ref
PD Adjusted OR (95% CI)	-	1.5 (0.9, 2.4)	Ref
Minimal Disease Activity (MDA) [excludes enthesitis-related JIA]			
	N=473	N=121	N=352
Proportion achieved	46%	49%	45%
OR (95% CI)	-	1.2 (0.8, 1.9)	Ref
PD Adjusted OR (95% CI)	-	1.2 (0.8, 2.0)	Ref

*Childhood Health Assessment Questionnaire (CHAQ), confidence interval (CI), International League Against Rheumatism (ILAR), interquartile range (IQR), odds ratio (OR), propensity decile (PD), rheumatoid factor (RF), standard error (SE). *p<0.05*

Conclusion: This is the first comparative effectiveness analysis of adalimumab and etanercept within UK children receiving TNFi therapies for JIA. Despite large patient numbers, there was no evidence of difference between adalimumab and etanercept regarding arthritis disease control or treatment persistence. For children without uveitis, both adalimumab and etanercept can be considered as effective treatment options for children and young people with JIA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.186

POS1293

RISK FACTORS OF NON-PROTECTIVE LEVELS OF ANTIBODIES TO VACCINES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

N. Lybimova[1], I. Fridman[2], O. Goleva[3], S. Kharit4, M. Kostik[5,6]. [1]*Almazov National Medical Research Centre, Saint Petersburg, Russian Federation, Department of Pediatrics and Medical Rehabilitation N 1,*

Saint Petersburg, Russian Federation; [2]*Pediatric Research and Clinical Center for Infection Diseases, Saint-Petersburg, Russia, Prevention of Infectious Diseases and Immunodeficiency States, Saint Petersburg, Russian Federation*; [3]*Pediatric Research and Clinical Center for Infection Diseases, Saint-Petersburg, Russia, Department of Virology and Molecular Biological Research Methods, Saint Petersburg, Russian Federation*; [2]*Pediatric Research and Clinical Center for Infection Diseases, Saint-Petersburg, Russia, Prevention of Infectious Diseases and Immunodeficiency States, Saint Petersburg, Russian Federation*; [5]*Saint Petersburg State Pediatric Medical University, Hospital Pediatry, Saint-Petersburg, Russian Federation*; [6]*Almazov National Medical Research Centre, Autoimmune and Autoinflammatory Diseases, Saint-Petersburg, Russian Federation*

Background: Immunosuppressive drugs, decreased vaccine coverage, aberrant immunity might be factors of low anti-vaccine antibodies in JIA patients.
Objectives: The study aimed to evaluate risk factors of non-protective levels of antibodies against measles, mumps, rubella, hepatitis B and diphtheria in JIA patients.
Methods: A prospective study included 170 children diagnosed with JIA aged 2 to 17 years, who received routine vaccinations against measles, rubella, mumps, diphtheria and hepatitis B. In all patients, the levels of post-vaccination antibodies (IgG) for measles, rubella, mumps, hepatitis B and diphtheria measured with ELISA.
Results: Protective level of antibodies were 50% against hepatitis B, 52% diphtheria, 58% measles, 80% mumps, 98%rubella. The best coverage for MMR had patients with enthesytis-related arthritis85%, compare to oligoarthritis70%, polyarthritis69%, systemic arthritis63%. Diphtheria coverage was 50%, 51%, 46%, 63%, respectively. Incomplete MMR vaccination had 39%patients, treated with biologics, 22%with methotrexate and 14%with NSAID(p=0.025), and 61%, 46%, 36% for diphtheria (p=0.021). Incomplete vaccination was a risk factor of non-protective level of antibodies against measles (HR=2.03[95%CI: 1.02; 4.0], p=0.042), parotitis (HR=6.25[95%CI: 2.13; 17.9], p=0.0008) and diphtheria (HR=2.39[95%CI:1.18; 4.85], p=0.016) vaccines. The lowest probability of having a protective level of antibodies was observed in systemic arthritis compared to oligoarthritis (p=0.008) and polyarthritis (p=0.005). JIA patients, with non-protective levels of antibodies against measles, had more extended methotrexate treatment (2.8 [1.3; 6.4] vs 2.2 [0.9; 3.9] years, p<0.05) and increased applying of the biologics (76% vs 52%, p<0.05). Patients treated with biologics had the lowest probability of having protective levels of antibodies against measles, mumps, hepatitis B, and diphtheria than MTX and NSAID. Patients with non-protective antibodies had lower vaccine coverage against mumps (56% vs 67%, p<0.05) and diphtheria (38% vs 61%, p<0.01), longer duration of methotrexate 3.3 [1.4; 6.7] vs 1.8 [1.0; 2.9] years, p<0.01) and biologic treatment 3.1 [1.1; 5.4] vs 0.9 [0.0; 1.9] years, p<0.05) compare to patients with protective levels. The main risk factors to have non-protective levels of antibodies against specific vaccines are in Table 1 below.
Conclusion: Children with JIA may have lower anti-vaccine antibodies levels and required routine check, especially in children with incomplete vaccination, biologics, systemic arthritis and long-term methotrexate treatment. Funding statement:
Footnotes: CI confidence interval, GCS glucocorticosteroids, HR hazard ratio, MTX methotrexate, na not applicable, soJIA systemic onset of juvenile idiopathic arthritis.
* Data were not calculated due to a small number of patients with a non-protective level of antibodies against rubella and no patients with incomplete vaccination against hepatitis
This work was supported by the Russian Foundation for Basic Research (grant № 18-515-57001).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.503

Table 1.

Parameters	Measles		Parotitis		Rubella		Diphtheria		Hepatitis B	
	HR (95%CI)	p	HR (95%CI)	p	HR (95%CI)	p	HR (95%CI)	p	HR (95%CI)	P
soJIA, yes	1.84 (0.84; 4.03)	0.128	1.43 (0.53; 3.95)	0.492	0.99 (0.05; 18.6)	0.995	2.04 (0.91;4.59)	0.08	2.52 (1.27; 5.0)	0.008
GCS, yes	1.54 (0.91; 2.61)	0.104	0.31 (0.45;1.84)	0.799	0.736 (0.11; 4.88)	0.736	1.89 (1.1; 3.24)	0.02	1.34 (0.77; 2.32)	0.295
MTX, yes	0.86 (0.39; 1.88)	0.703	1.55 (0.49; 4.88)	0.453	1.53 (0.08; 28.64)	0.776	2.02 (0.71; 5.76)	0.187	0.6 (0.31; 1.15)	0.122
Biologics, yes	2.02 (1.22; 3.32)	0.006	1.76 (0.98; 3.15)	0.057	2.26 (0.5; 9.87)	0.293	1.67 (0.99; 2.8)	0.053	1.2 (0.75; 1.92)	0.453
>1 biologics, consequent, yes	1.57 (1.13; 2.2)	0.007	1.4 (0.93; 2.09)	0.104	1.82 (0.71; 4.7)	0.213	1.4 (0.98; 2.0)	0.062	1.11 (0.78; 1.58)	0.572
Incomplete vaccination, yes	2.02 (1.02; 4.0)	0.042	6.25 (2.13; 17.9)	0.00008	na*	na*	2.39 (1.18; 4.85)	0.016	na*	na*

POS1294

EFFECT OF EMOTIONAL TRIGGERS ON THE FREQUENCY OF PFAPA ATTACKS - A MULTICENTER STUDY

Y. Levinsky[1,2], Y. Butbul[3], M. Gafner[2], M. Broide[2], S. Kagan[2], R. Tal[1], M. Natur[4], K. Kaidar[4], N. Dagan[4], G. Amarilyo[4,5], L. Harel[1,5]. [1]*Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel*; [2]*Schneider Children's Medical Center of Israel, Pediatrics, Petach Tikva, Israel*; [3] *Technion - Israel Institute of Technology, Haifa, Israel, Pediatric Rheumatology Service, Ruth Rappaport Children's Hospital, Rambam Health Care Campus, Haifa, Israel, Haifa, Israel*; [4]*Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel*; [5]*Schneider Children's Medical Center of Israel, Pediatric Rheumatology Clinic, Petah Tikva, Israel*

Background: The fact that mental state may serve as a trigger for attacks of periodic fever diseases is known in Familial Mediterranean fever (FMF). There is a lack of information regarding the role of emotional triggers for PFAPA attacks.
Objectives: To examine whether emotional distress may trigger PFAPA attacks.
Methods: Enrolled were patients with active PFAPA, from two Israeli medical centers. Researchers contacted their parents by phone in two occasions: a. within the two weeks of returning to school after the first COCID-19 lockdown; b. during the summer vacation (i.e., non-stressful period). Parents were asked regarding the occurrence of PFAPA attacks within the two weeks preceding the calls. The relative stress levels of the two periods were validated by an emotional distress scale questionnaire. Differences between occurrences of attacks during these two periods of time were recorded.
Results: One-hundred and six pediatric patients enrolled in the study. Mean age was 7.37± 2.9. In the stressful period, 41 (38.7%) reported at least one attack during the preceding 2 weeks, compared to 24 (22.6%) in the non-stressful period (p = 0.017). Scores for the mean emotional distress questionnaire were higher in the stressful period compared to the non-stressful period (35.6± 8.1 vs. 32.1± 7.7, respectively, P = 0.047).
Conclusion: This study shows that during a period of stress for children there were more PFAPA attacks compared to a relaxed period. These findings indicate that mental factors such as stress or excitement may be triggers for PFAPA attacks.

Table 1. Attacks status during prior 2 weeks during stressful or non-stressful event

Outcome	First call (May 2020)	Second call (August 2020)	P-value
Pediatric emotional distress score (PEDS), mean (±SD)	35.6 (±8.1)	32.1 (±7.7)	0.047
Any attacks during last 2 week, n (%)	41 (39.8%)	24 (24.2%)	0.017
Number of attacks			0.04
One, n (%)	27 (25.5%)	19 (17.9%)	
Two, n (%)	14 (13.2%)	5 (4.7%)	

REFERENCES:

[1] Marshall GS, Edwards KM, Butler J, Lawton AR. Syndrome of periodic fever, pharyngitis, and aphthous stomatitis. J Pediatr. 1987;110(1):43-46. doi:10.1016/S0022-3476(87)80285-8
[2] Feder HM, Salazar JC. A clinical review of 105 patients with PFAPA (a periodic fever syndrome). *Acta Paediatr Int J Paediatr*. 2010;99(2):178-184. doi:10.1111/j.1651-2227.2009.01554.x
[3] Hall, J, Lindorff A. Children's Transition to School: Relationships Between Preschool Attendance, Cortisol Patterns, and Effortful Control. The Educational and Developmental Psychologist. *Educ Dev Psychol*. 2017;34(1):1-18
[4] Stokes SJ, Saylor CF, Swenson CC, Daugherty TK. A comparison of children's behaviors following three types of stressors. *Child Psychiatry Hum Dev.* 1995;26(2):113-123. doi:10.1007/BF02353235
[5] Førsvoll J, Kristoffersen EK, Øymar K. The immunology of the periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis syndrome; what

can the tonsils reveal. A literature review. *Int J Pediatr Otorhinolaryngol*. 2020;130. doi:10.1016/j.ijporl.2019.109795
[6] Gidron Y, Berkovitch M, Press J. Psychosocial correlates of incidence of attacks in children with Familial Mediterranean Fever. *J Behav Med*. 2003;26(2):95-104. doi:10.1023/A:1023038504481
[7] Makay B, Emiroğlu N, Ünsal E. Depression and anxiety in children and adolescents with familial Mediterranean fever. *Clin Rheumatol*. 2010;29(4):375-379. doi:10.1007/s10067-009-1330-9
[8] Kraszewska-Głomba B, Matkowska-Kocjan A, Szenborn L. The Pathogenesis of Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Cervical Adenitis Syndrome: A Review of Current Research. *Mediators Inflamm* 2015;2015:563876. doi:10.1155/2015/563876
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.706

POS1295

PERFORMANCE OF 2019 EULAR/ACR CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN A PEDIATRIC POPULATION – A MULTICENTER STUDY

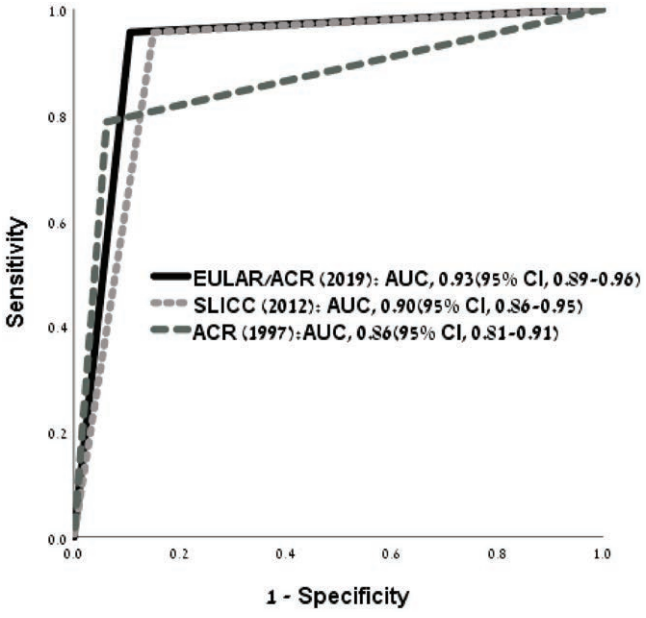
Y. Levinsky[1,2], M. Broide[1], S. Kagan[1], O. Goldberg[1], O. Scheuerman[1], R. Tal[3], I. Tirosh[4], Y. Butbul[5], L. Harel[2,3], G. Amarilyo[2,3]. *[1]Schneider Children's Medical Center of Israel, Pediatrics, Petach Tikva, Israel*; *[2] Tel Aviv University, Tel Aviv, Israel, Sackler Faculty of Medicine, Tel Aviv, Israel*; *[3]Schneider Children's Medical Center of Israel, Pediatric Rheumatology Unit, Petach Tikva, Israel*; *[4]Sheba Medical Center, Tel Hashomer, Pediatric Rheumatology Service, Edmond and Lily Safra Children's Hospital, Ramat Gan, Israel*; *[5]Rambam Health Care Campus, Haifa, Israel, Pediatric Rheumatology Service, Ruth Rappaport Children's Hospital, Haifa, Israel*

Background: The "European League Against Rheumatism" and "American College of Rheumatology" 2019 (EULAR/ACR-19) criteria for the diagnosis of Systemic Lupus Erythematosus (SLE) were recently published, with the stated goal of maintaining the level of sensitivity and raising the level of specificity for classification of SLE in adults.
Objectives: We aimed to examine the function of the new EULAR/ACR-19 criteria in a population of children and compare them to the SLICC-12 and ACR-97 criteria.
Methods: In this multicenter study the charts of jSLE patients from three tertiary medical centers were reviewed and compared to patients with non-jSLE diagnosis. Pediatric rheumatologists, blinded to the original diagnosis, reviewed and diagnosed all cases. Pediatric patients' clinical and laboratory data were retrospectively extracted and then examined with regard to how they met the new and old criteria.
Results: Included were 225 patients (112 jSLE, 113 non-SLE). When applied to juvenile SLE classification, the sensitivity of the new EULAR/ACR-19 criteria was 0.96 (0.9-.0.99) and the specificity was 0.89 (0.82-0.94). These were comparable to the Systemic Lupus International Collaborating Clinics (SLICC) criteria. The sensitivity of the EULAR/ACR-19 criteria improves over time and was 0.83 twelve months following disease onset, reaching 0.96 after longer than 24 months.
Conclusion: Among a cohort of jSLE patients, sensitivity of the new EULAR/ACR-19 criteria was found to be high and specificity may have improved slightly compared to the SLICC-12 criteria. We support the use of the new classification criteria for pediatric patients in future jSLE studies, but it should be noted that its specificity is lower than for adults.

	ACR-97	SLICC-12	EULAR/ ACR-19
Sensitivity (95% CI)	0.79 (0.70-0.86)	0.96 (0.9-0.99)	0.96 (0.9-.0.99)
Specificity (95% CI)	0.94 (0.88-0.97)	0.85 (0.77-0.91)	0.89 (0.82-0.94)
Accuracy (95% CI)	0.86 (0.81-0.9)	0.9 (0.86-0.94)	0.92 (0.88-.0.96)
Positive Likelihood Ratio (95% CI)	12.7(6.1-26.2)	6.35(4.1-9.9)	9.0 (5.3-15.4)
Negative Likelihood Ratio (95% CI)	0.23(0.16-0.33)	0.05(0.02-0.12)	0.05(0.02-0.12)
Diagnostic odds ratio (95% CI)	55.5(22.80-135.0)	120.85(43.0-340.0)	180.1(61.3-529.4)

REFERENCES:

[1] Smith EMD, Lythgoe H, Midgley A, Beresford MW, Hedrich CM. Juvenile-onset systemic lupus erythematosus: Update on clinical presentation, pathophysiology and treatment options. Clin Immunol 2019 published on December 2019. doi: 10.1016/j.clim.2019.108274
[2] Massias JS, Smith EMD, Al-Abadi E, Armon K, Bailey K, Ciurtin C, et al. Clinical and laboratory characteristics in juvenile-onset systemic lupus erythematosus across age groups. Lupus 2020;29(5):474–81.
[3] Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997 Sep;40(9):1725
[4] Petri M, Orbai AM, Alarcõn GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012 Aug;64(8):2677-86
[5] Hartman EAR, van Royen-Kerkhof A, Jacobs JWG, Welsing PMJ, Fritsch-Stork RDE. Performance of the 2012 Systemic Lupus International Collaborating Clinics classification criteria versus the 1997 American College of Rheumatology classification criteria in adult and juvenile systemic lupus erythematosus. A systematic review and meta-an. Autoimmun Rev. 2018;17(3):316–22.
[6] Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheumatol 2019;71(9):1400–12.
Disclosure of Interests: None declared



DOI: 10.1136/annrheumdis-2021-eular.708

POS1296

JIA PATIENTS DO NOT HAVE MORE OSTEOPOROSIS THAN HEALTHY AGE AND SEX-MATCHED CONTROLS BUT LOWER BONE MASS DENSITY IS FOUND AT TOTAL HIP AND CORTICAL COMPARTMENT

M. Lopez Corbeto[1], M. Barcelo Bru[2], E. Moreno Ruzafa[1], M. Pasqual Pastor[2]. *[1]Vall d'Hebron University Hospital, Pediatric Rheumatology, Barcelona, Spain*; *[2]Vall d'Hebron University Hospital, Rheumatology, Barcelona, Spain*

Background: Achievement of a normal peak bone mass is an especially important consideration in young adults with juvenile idiopathic arthritis (JIA), because interference with attainment of peak bone mass may not be repaired later in life. It has been suggested that children with JIA cortical appendicular skeletal bone is more affected by disease activity than axial trabecular bone. To evaluate bone mineral density (BMD) DXA measurements are widely used. Although, DXA is limited to two-dimensional evaluation of integral BMD and cannot differentiate between trabecular and cortical bone compartments. Alternatively, 3D-DXA analysis is a new method based on DXA scans of proximal femur that provides accurate estimates of trabecular and cortical volumetric BMD.
Objectives: The aim of the study was to analyze the trabecular and cortical bone using 3D-DXA in young adults with JIA compared to age-matched healthy controls.
Methods: This cross-sectional study was aimed to analyze the differences in 3D-DXA proximal femur compartments. The patients were recruited from the specialized transitional unit of the Vall d'Hebron University Hospital. JIA patients older than 18 yo without previous bisphosphonates intake were included. Age and sex-matched healthy controls were selected. DXA scans (Lunar Prodigy, General Electric Medical Systems, v.15) were acquired. OP was defined according to the WHO criteria. The 3D-DXA software was used to assess in 3D the trabecular density and cortical thickness from DXA scans as reported previously

[1]. The 3D-DXA and DXA measurements were compared using Student's *t* test. Categorical variables were compared using Chi-squared test. All hypothesis tests with p value lower than 5% were considered significant.

Results: Forty-six patients and 46 age and sex-matched controls were evaluated. The mean time of disease's duration was 7.37 years, and the most frequent JIA subtype was Oligoarticular ANA positive. More than 21% of the patients had an active disease. OP was present in 5 patients and 1 control. Despite not finding significant differences in the prevalence of osteoporosis, JIA patients had lower aBMD at total hip by DXA and lower cortical sBMD by 3D-DXA than controls (Table 1).

Table 1. Comparison of DXA and 3D-DXA measurements between JIA and healthy controls

Variable	JIA patients (n=46)	Healthy controls (n=46)	*P value*
DXA			
Lumbar aBMD (g/cm^2), mean ± sd	1.097 ± 0.02	1.155 ± 0.02	0.042
Right femoral neck aBMD (g/cm^2), mean ± sd	0.930 ± 0.02	1.014 ± 0.01	0.041
Right total hip aBMD (g/cm^2), mean ± sd	0.932 ± 0.02	1.001 ± 0.01	**0.008**
Lumbar T-score, mean ± sd	-0.716 ± 0.16	-0.212 ± 0.16	0.037
Right femoral neck T-score, mean ± sd	-0.563 ± 0.17	0.087 ± 0.12	0.036
Right total hip T-score, mean ± sd	-0.721 ± 0.18	-0.12 ± 0.13	0.008
3D-DXA			
Trabecular vBMD (mg/cm^3), mean ± sd	180.44 ± 5.54	194.57 ± 5.11	0.064
Cortical sBMD (mg/cm^2), mean ± sd	147.23 ± 3.41	161.52 ± 2.89	**0.002**
Osteoporosis (WHO definition)			
Yes, n (%)	5 (10.87)	1 (2.17)	0.091
No, n (%)	41 (89.13)	45 (97.83)	

DXA dual-energy X-ray absorptiometry, *sd* standard deviation, *aBMD* areal bone mineral density, *3D-DXA* three-dimensional dual-energy X-ray absorptiometry, *vBMD* volumetric bone mineral density, *sBMD* superficial cortical bone mineral density

Conclusion: JIA patients do not have more OP than controls in our cohort but there are differences in BMD in the different locations and greater involvement of the cortical bone in JIA.

REFERENCES:

[1] Brance ML, et al. Trabecular and cortical bone involvement in rheumatoid arthritis by DXA and DXA-based 3D modelling. Osteoporos Int, 2020 Sep 24.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.742

POS1297 HOW HLA B27 PREVALENCE IN THE POPULATION INFLUENCE ON FEATURES OF JUVENILE IDIOPATHIC ARTHRITIS: DATA FROM SAKHA REPUBLIC (YAKUTIA)

F. Vinokurova[1], L. Sorokina[2], V. Argunova[3], P. Sleptsova[3], T. Bourtseva[4,5], V. Chasnyk[2], M. Kostik[2]. [1]*Yakut Science Center of Complex Medical Problems, Laboratory of Immunological Researches, Yakutsk, Russian Federation*; [2]*Saint-Petersburg State Pediatric Medical University, Department of Hospital Pediatrics, St. Petersburg, Russian Federation*; [3]*Republic Hospital № 1 - National Center of Medicine, Pediatric Center, Department of Cardio-Rheumatology, Yakutsk, Russian Federation*; [4]*North-Eastern Federal University (NEFU), Department of Pediatrics and Pediatric Surgery of Medical Institute NEFU, Yakutsk, Russian Federation*; [5]*Yakut Science Center of Complex Medical Problems, Laboratory of Children Health Monitoring and Medical and Environmental Research, Yakutsk, Russian Federation*

Background: Sakha Republic (Yakutia) - SR(Y) is a bid arctic region of Russia with high proportion of aboriginals - Yakutians (50%), intra-national marriages, increased level of inbreeding and high distribution of HLAB27 among aboriginals – 33%, according the epidemiological studies. The main type of arthritis is ankylosing spondylitis in adults and enthesytis-related arthritis (ERA) of juvenile idiopathic arthritis (JIA) in children. The pattern of arthritis distribution in adults and children in SR(Y) is differ from Caucasians and similar to Native Americans.

Objectives: Our study aimed to evaluate the features of JIA in aboriginals of SR(Y), associated with high prevalence of HLAB27 antigen.

Methods: In the retrospective study we included 144 Yakutians who were admitted in the rheumatology department of Yakutsk in 2007-2016 years and 753 JIA patients Caucasian origin in Saint-Petersburg in the same years. We evaluated routine clinical and laboratorial features. HLA B27 was evaluated according the clinical judgement of the attending physicians.

Results: ERA is a main JIA category in Yakutians. The main features the male predominance, higher onset age, high inflammatory activity, lower number of active joints, high incidence of hip and sacroiliac joints involvement, lower levels of psoriasis and uveitis. Yakutians have rare the involvement of cervical spine (6% vs 14%, p=0.0000001), TMJ (1% vs 6%, p=0.027), elbow (8% vs 16%, p=0.012), wrist (18% vs 28%, p=0.017), MCP (7% vs 21%, p=0.00005), PIP (8% vs 25%, p=0.00005). The treatment rates of methotrexate and biologics were similar between groups, but in Yakutians the biologics were administered earlier, because methotrexate failed and often was ineffective. The cumulative probability to receive biologics was higher in Yakutians compare to Caucasians: HR=3.4 [2.6; 4.4], p=0.000001 (Figure 1). The main biologic in Yakutians was etanercept (49/70; 70%). Yakutians received corticosteroids and cyclosporine A rarely, due to low incidence of systemic onset JIA and oligoarthritis with uveitis. It was observed, that the HLA B27 as a risk factors had different significance in Yakutians and Caucasians. HLA B27 presence increased the risk of ERA OR=2.72 (1.3; 5.6) p=0.01 in Yakutians and OR=69.2 (29.5; 162.3), p=0.00001 for Caucasians; for biologic administration: 0,86 (0,4; 1,8), p=0.529 and 2,45 (1,5; 4,0), p=0.0003, respectively.

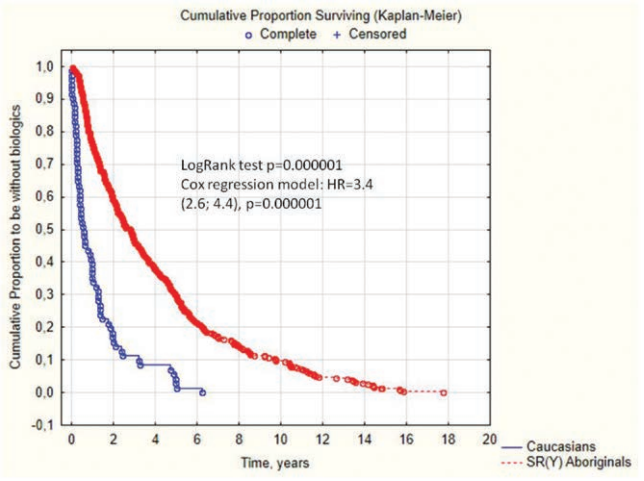


Figure 1. Cumulative probability to leave without biologics between Yakutian and Caucasian JIA patients.

Conclusion: High distribution of HLA B27 antigene in Yakutians, lead to different pattern of JIA categories distributions and patient's management.

This work was supported by the Project of the Ministry of Science and Higher Education of the Russian Federation (basic part of funding to M.K. Ammosov North-Eastern Federal University #FSRG-2020-0016) and by the RFBR grant #18-05-600035_Arctika.

Table 1. Differences between Yakutian and Caucasian JIA patients.

JIA features	Yakutians, n=144 (%)	Caucasians, n=723 (%)	p
Gender, boys, n (%)	85 (59.0)	279 (38.6)	0.000006
Onset age, years	10.6 (6.0; 13.4)	6.0 (3.0; 10.3)	0.0000001
JIA categories, n (%)			
Oligoarthritis	36 (25.0)	188 (26.0)	0.0000001
Poly, RF (-)	21 (14.6)	248 (34.3)	
Poly, RF (+)	1 (0.7)	22 (3.0)	
Systemic onset	4 (2.8)	53 (7.3)	
ERA	76 (52.8)	171 (23.7)	
Psoriatic arthritis	6 (4.2)	41 (5.7)	
Active joints	4.0 (3.0; 6.0)	6.0 (3.0; 12.0)	0.0000001
Uveitis, n (%)	16 (11.1)	114/503 (22.7)	0.002
Psoriasis, n(%)	3/143 (2.1)	46/719 (6.4)	0.043
Hip involvement	50 (34.7)	146 (20.2)	0.0001
Sacroiliitis	46 (31.9)	69 (9.6)	0.0000001
HLA B27, n (%)	76/131 (58.0)	105/301 (34.8)	0.00001
ANA, n (%)	4/46 (8.7)	204/444 (46.0)	0.00001
RF, n (%)	3/141 (2.1)	22/403 (5.5)	0.104
Biologics, primary, n (%)	70/144 (48.6)	347 (48.0)	0.892
Time before first biologics, years	0.6 (0.3; 1.4)	2.6 (1.0; 5.4)	0.0000001

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.810

POS1298 COMPARISON OF FMF CLINICAL FEATURES BETWEEN TURKISH AND CRIMEAN TATAR CHILDREN

O. Zhogova[1], U. Kaya Akca[2], E. Suspitsin[3,4], E. Sag[2], V. Nizhnik[3], A. Tumakova[3], S. Ivanoskiy[1], N. Lagunova[1], Y. Bilginer[2], S. Özen[2], M. Kostik[3,5]. [1]*Crimean Federal University named after V.I. Vernadsky, Pediatry, Simferopol, Russian Federation*; [2]*Hacettepe University, Department of Pediatric Rheumatology, Faculty of Medicine, Ankara, Turkey*; [3]*Saint Petersburg State Pediatric Medical University, Hospital Pediatry, Saint-Petersburg, Russian Federation*; [4]*N.N. Petrov National Research Center of Oncology, Molecular Diagnostics, Saint-Petersburg, Russian Federation*; [5]*Almazov National Medical Research Centre,*

Autoimmune and Autoinflammatory Diseases, Saint-Petersburg, Russian Federation

Background: Crimean Tatars is an ethnic group in Russia. The presence of familial Mediterranean fever (FMF) has been recognized since 2016.

Objectives: The study aimed to evaluate the prevalence and clinical features as well as genetic aspects of FMF in children of Crimean Tatar (CT) origin and compare them with a cohort from Turkey.

Methods: This retrospective study included all FMF cases in patients of CT origin (n=18) diagnosed in Children's Regional Hospital in Simferopol since 2016. We included 40 consecutive FMF cases between February-March 2020, diagnosed and followed at Hacettepe University, Ankara, Turkey. All children were less than 18 years old at the time of inclusion. The diagnosis of FMF was based on the EULAR criteria (2019). We excluded other autoinflammatory diseases and any doubtful cases. For assessment of MEFV alleles prevalence 127 healthy unrelated CT adults from different parts of Crimea peninsula were included. Sanger sequencing of MEFV exons 2 and 10 was performed in all the patients and controls.

Results: FMF in CT was diagnosed with nearly 5 year-delay, despite the earlier age at onset. CT children had more frequent and prolonged fever, joint involvement (arthritis and arthralgia) and erysipeloid rash compared to Turkish, who had more attacks with chest pain and abdominal pain which last longer. (Table 1) CT had higher white blood cell count, C-reactive protein, erythrocyte sedimentation rate and lower hemoglobin. It might be explained by the fact that the majority of Crimean Tatars were admitted to the clinic during an attack, which was not always the case with Turkish children. Distribution of MEFV pathogenic alleles p.M694V, p.M680I, p.V726A in CT children was 81%, 9.5% and 9.5%, respectively, while in Turks it was 68.6%, 14.3% and 12.9%. Among the CT patients, proportion of homozygotes, compound-heterozygotes and heterozygotes were 11%, 6% and 83%, and among Turkish patients were 45%; 30%; and 25%, respectively. MEFV pathogenic variants were detected in 10.2% of healthy CT donors: 7.1% individuals had p.M694V, 1.6% - p.M680I, 1.6% - p.V726A. Comorbid diseases including IgA vasculitis, sacroiliitis, JIA, autoimmune hepatitis and inflammatory bowel disease were reported in 5.6% of CT and 10% of Turks. The colchicine treatment rate and regimen were similar, but CT received biologics more frequently (44%) than Turks (22.5%).

Conclusion: CT is an ethnic group with a significant number of MEFV mutation carriers assuming the expected prevalence of FMF to be as high as 1:385. Thus, any periodic fever in CT patients should be considered as a sign of possible FMF. The clinical course of FMF has some peculiarities in CT patients.

This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001).

Table 1. Comparative data of FMF patients with Turkish and Crimean Tatar origin

FMF features	Turkish (n=40)	Crimean Tatars (n=18)	p
Family history of FMF, n (%)	16 (40)	9 (50)	0.477
Consanguinity, n (%)	8 (20)	6 (33)	0.272
Onset age, years	3.3 (2; 5)	1.3 (0; 4)	0.040
Age at FMF diagnosis, years	4.7 (3; 8)	9.6 (4; 14)	0.005
Diagnosis delay, years	0.9 (0; 2)	5.5 (2; 10)	0.00001
Fever, n (%)	33 (83)	18 (100)	0.058
Episode duration, days	2.0 (2; 3)	3.0 (3; 6)	0.000003
Fever duration, hours	48.0 (48; 72)	72.0 (72; 120)	0.000002
Chest pain, n (%)	12 (30)	1 (6)	0.039
Chest pain duration, hours	48.0 (24; 72)	0.0 (0; 0)	0.000001
Abdominal pain, n (%)	30 (75)	9 (50)	0.061
Abdominal pain duration, hours	48.0 (24; 48)	24.0 (24; 24)	0.043
Arthritis, n (%)	10 (25)	16 (89)	0.000006
Arthralgia, n (%)	19 (48)	17 (94)	0.0007
Erysipeloid rash, n (%)	0 (0)	9 (50)	0.000001

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.817

POS1299 RISK FACTORS OF TOTAL HIP ARTHROPLASTY IN JUVENILE ARTHRITIS WITH HIP INVOLVEMENT

L. Sorokina[1], I. Avrusin[1], R. Raupov[1], N. Garipova[2], M. Gharabaghtsyan[3], S. Khrypov[4], E. Isupova[1], E. Gaidar[1], I. Chikova[1], M. Dubko[1], V. Masalova[1], T. Likhacheva[1], L. Snegireva[1], M. Kostik[1,5]. [1]*Saint-Petersburg State Pediatric Medical University, Department of Hospital Pediatrics, St. Petersburg, Russian Federation*; [2]*Almazov National Medical Research Centre, Pediatric Department, St. Petersburg, Russian Federation*; [3]*Institute of Child and Adolescent Health (ICAH) with the Arabkir Medical Center, Pediatric Department, Yerevan, Armenia*; [4]*Saint-Petersburg Clinical Research-Practical Center for Specialized Healthcare (Oncology), Surgical Department, St. Petersburg, Russian Federation*; [5]*Almazov National Medical Research Centre, Autoimmune and Autoinflammatory Diseases, St. Petersburg, Russian Federation*

Background: Hip osteoarthritis (HOA) is a severe outcome of juvenile idiopathic arthritis (JIA) itself and also can be result of corticosteroid (CS) treatment, if it was used. Total hip arthroplasty (THA) is the last step in JIA treatment and indicates ineffectiveness of conservative treatment.

Objectives: We aimed to evaluate risk factors which lead to THA in JIA patients with HOA.

Methods: 753 patients aged 2-17 years were included in our retrospective study during the last 10 years. Diagnosis was made according to ILAR criteria. Clinical, laboratory and radial examinations were evaluated. Diagnosis of HOA was made on MRI, CT and planar radiograms and confirmed by morphological examination of removed femoral heads.

Results: Total 153/753 (20.3%) patients with JIA had hip involvement. HOA developed in 48/153 (31.4%) of JIA patients and 16/48 (33.3%) of them had THA was undergone. Prevalence of HOA and THA (%) in JIA subtypes: in polyarticular (5/32 (15.6%) and 8/16 (50%), systemic (6/32 (18.7%) and 5/16 (31.2%)), enthesitis-related (19/32 (59.4%) and 3/16 (18.8%)) and psoriatic (2/32 (6.7%) and 0/16) subtypes respectively, p=0,0000001. Patients who underwent THA initially had higher level of inflammation: elevated ESR (33 vs 5 mm/h, p=0.002) and CRP (14.7 vs 1.9 mg/l, p=0.03), more active joint, and especially involvement of joints of upper limbs: elbows (p=0.004) and proximal interphalangeal joints (p=0.001), arthritis of subtalar joint (p=0.02). Delayed biologic treatment (7.5 vs 3.4 years, p=0.043) and delayed achievement of remission (9.2 vs 5.6 years, p=0.047) were main predictors of THA. Patients with HOA without biologics had increased cumulative probability of THA: HR=1.99 (1.01; 3.98), p=0.049 (Figure 1). Patients with THA received corticosteroids (93.7 vs 50%, p=0.003) more often including high dose pulse-therapy regimes, but differences in the cumulative doses were not observed (5000 vs 4500 mg, p=0.54) between groups, CS administration was independent risk factor of HOA and THA.

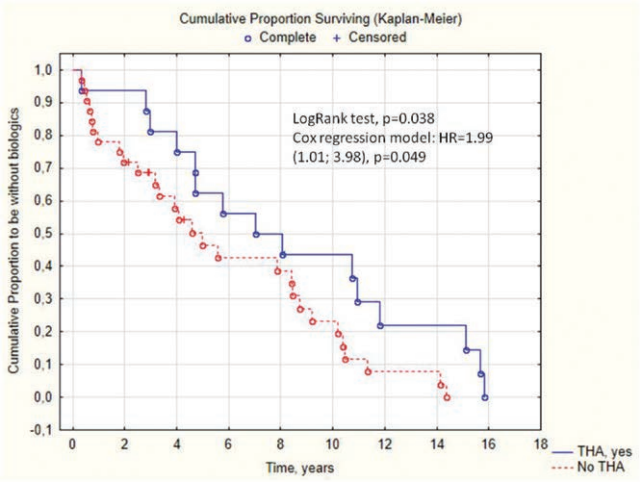


Figure 1. Cumulative probability of THA in JIA patients with hip osteoarthritis.

Conclusion: the main risk factors of THA are systemic and polyarticular course because of their activity, systemic CS and delayed biologic treatment. Corticosteroids should be avoided in those group of patients because of risk of avascular pathway HOA formation.

This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001).

Table 1. The features of JIA patients with hip osteoarthritis depending on

JIA features	THA, (n=16)	HOA without THA, (n=32)	p
Time to THA, years	5.2 (3.6; 10.2)	4.6 (2.2; 8.7)	0.4
Onset age, years	7.95 (3.5; 11.1)	8.3 (4.3; 13.1)	0.5
JIA duration, years	8.5 (6.5; 13.2)	5.43 (2.8; 11.1)	0.07
Polyarticular JIA, n (%)	8 (50.0)	5 (15.6)	0.037
Systemic JIA, n (%)	5 (31.3)	6 (7.0)	0.037
ANA, n (%)	3/8 (37.5)	5/16 (31.3)	0.760
HLA B27, n (%)	3/6 (50)	9/19 (47.4)	0.911
RF, n (%)	0/9 (0)	1/15 (6.7)	0.429
Uveitis, n (%)	1/16 (6.3)	3/24 (12.5)	0.519
ESR, mm/h	33 (13; 54)	5 (3; 27)	0.002
CRP, mg/l	14.7 (2.9; 72.3)	1.9 (0.3; 12.7)	0.03
Active joints, n	21.5 (8.5; 52.5)	9 (5; 16)	0.02
Elbows, n (%)	11 (68.7)	8 (25.0)	0.004
Proximal interphalangeal joints, n (%)	10 (62.5)	5 (15.6)	0.001
Subtalar, n(%)	4 (25.0)	1 (3.1)	0.02
Pulse-therapy GCS, n(%)	11 (68.7)	10 (31.3)	0.014
Cumulative GCS dose, mg	5000 (3000; 14000)	4500 (500; 20000)	0.54
Time to biologic, years	7.6 (4.3; 11.4)	3.4 (1.9; 8.6)	0.04
Achievement of remission, years	9.2 (6.6; 15.4)	5.6 (3.3; 11.4)	0.047

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.857

POS1300

PAIN IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS TREATED TO TARGET: 24 MONTH RESULTS FROM A RANDOMISED TRIAL

K. Spekking[1], P. De Boer[1], S. A. Bergstra[2], J. M. Van den Berg[3], D. Schonenberg-Meinema[3], L. W. A. Van Suijlekom-Smit[4], M. Van Rossum[5,6], Y. Koopman-Keemink[7], R. Ten Cate[1], C. Allaart[2], D. M. C. Brinkman[1], P. C. E. Hissink Muller[1]. [1]*Leiden University Medical Center, Department of Pediatric Rheumatology, Leiden, Netherlands*; [2]*Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; [3]*Emma Children's Hospital, Amsterdam University Medical Centers, Department of Pediatric, Immunology, Rheumatology and Infectious Diseases, Amsterdam, Netherlands*; [4]*Sophia Children's Hospital Erasmus Medical Center, Department of Pediatrics/ Pediatric Rheumatology, Rotterdam, Netherlands*; [5]*Emma Children's Hospital, Amsterdam University Medical Centers, Department of Pediatrics, Amsterdam, Netherlands*; [6]*Amsterdam Rheumatology and Immunology Center | Reade, Department of Pediatric Rheumatology, Amsterdam, Netherlands*; [7]*Hagaziekenhuis Juliana Children's Hospital, Department of Pediatrics, the Hague, Netherlands*

Background: Juvenile Idiopathic Arthritis (JIA) is the most common auto-immune disease in children and pain is a common symptom. Despite treatment advances in recent years, pain often persists when the disease is inactive. Treating JIA to target has been widely recommended[1], but effectiveness in pain reduction has not been proven yet[2].
Objectives: To compare pain scores over two years in three treatment arms in JIA patients that were treated to target and to identify baseline characteristics predicting unfavorable pain outcomes.
Methods: DMARD naïve children who participated in the BeSt for kids study[3] with oligoarticular JIA, RF negative polyarticular JIA and juvenile psoriatic arthritis were included. Patient were treated to target aimed at inactive disease according to 1 of 3 different treatment groups; 1) initial sequential DMARD monotherapy 2) initial methotrexate (MTX) with prednisolone bridging or 3) initial MTX with etanercept. Pain intensity was measured using a 100 mm Visual Analogue Scale during 24 months of follow up with 3-monthly intervals. Potential differences in VAS pain scores over time between treatment arms were compared using linear mixed models with random intercept and random slope for visits clustered within patients. A similar multivariable mixed model was used to assess the ability of several baseline characteristics to predict the chance of high pain levels during follow-up.
Results: 92 patients were randomized into the three treatment groups. Overall, pain scores over time reduced from mean 55.3 (SD 21.7) at baseline to 19.5 (SD 25.3) after 24 months. When comparing pain over time per arm, pain scores decreased significantly over time β -1.37 (95% CI -1.726; -1.022). No significant difference was found in pain over time between treatment groups (interaction term treatment arm*time (months) β (95% CI) arm 1 0.13 (-0.36; 0.62) and arm 2 0.37 (-0.12; 0.86) compared to arm 3), Figure 1. Correction for sex and symptom duration as possible confounders yielded similar results. Multiple baseline characteristics demonstrated a significant predictive value for pain over time: VAS pain (scale 0-100) with β 0.44 (95% CI 0.25; 0.65), VAS physician (scale 0-100) with β -0.34 (-0.55; -0.06), number of active joints with β 0.77 (0.19; 1.34), Child Health Questionnaire Physical summary Score with β -0.42 (-0.72; -0.11) and Psychosocial summary Score β -0.42 (-0.77; -0.06). Symptom duration, VAS patient/parent and NSAID use were no significant predictors, Table 1.
Conclusion: Treatment to target seems effective in pain reduction in non-systemic JIA patients irrespective of initial treatment strategy. Several baseline predictors for pain over time were identified, which could serve as an initial indication for non-systemic JIA-patients with a high risk of pain despite a strict treat-to-target strategy.

REFERENCES:

[1] Ravelli A, Consolaro A, Horneff G, et al. Treating juvenile idiopathic arthritis to target: recommendations of an international task force. Ann Rheum Dis. 2018;77(6):819–828.
[2] Schoemaker, C.G., Swart, J.F. & Wulffraat, N.M. Treating juvenile idiopathic arthritis to target: what is the optimal target definition to reach all goals?. Pediatr Rheumatol. 18, 34 (2020)
[3] Hissink Muller P, Brinkman DMC, Schonenberg-Meinema D, et al. Treat to target (drug-free) inactive disease in DMARD-naive juvenile idiopathic arthritis: 24-month clinical outcomes of a three-armed randomised trial. Ann Rheum Dis. 2019 Jan;78(1):51-59.

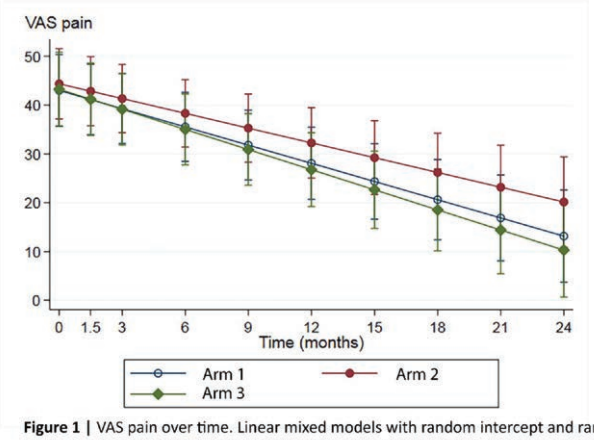


Figure 1 | VAS pain over time. Linear mixed models with random intercept and random slope for visits clustered within patients. VAS pain measured on a 100mm scale. Error bars indicate 95% confidence intervals.

Table 1. Baseline Characteristics

	β	p-value	95% Confidence Interval
VAS Pain	0.45	0.000	0.25 to 0.65
VAS Physician	-0.31	0.014	-0.55 to -0.06
VAS Patient/parent	-0.02	0.873	-0.21 to 0.18
No. of active joints	0.77	0.009	0.19 to 1.34
PhS*	-0.42	0.008	-0.72 to -0.11
PsS**	-0.42	0.022	-0.77 to -0.06
Symptom duration (mo.)	8.09	0.118	-2.08 to 18.26
NSAID use	-1.30	0.791	-10.91 to 8.31

VAS Pain, **VAS** physician and VAS patient/parent was measures on a 100mm scale.*PhS= Physical Summary Score of the Child Health Questionnaire Parent form 50 (scale 0-100).**PsS= Psychosocial Summary Score of the CHQ-PF50 (scale 0-100).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.988

POS1301

DRUG SURVIVAL OF BIOLOGICS WITH RESPECT TO COMBINATION WITH METHOTREXATE IN TREATMENT OF POLYARTICULAR JIA

G. Horneff[1], D. Windschall[2], K. Minden[3], T. Hospach[4], F. Dressler[5], F. Weller-Heinemann[6], B. Huegle[7], I. Foeldvari[8], A. Klein[1]on behalf of BIKER registry. [1]*Asklepios Clinic, Paediatics, Sankt Augustin, Germany*; [2]*St. Josef Stift, Paediatric Rheumatology, Sendenhorst, Germany*; [3]*Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), ein Institut der Leibniz-Gemeinschaft, Epidemiology, Berlin, Germany*; [4]*Klinikum Stuttgart - Olga Hospital / Women's Hospital, Paediatrics, Stuttgart, Germany*; [5]*MHH Kinderklinik Station 61b, Paediatrics, Hannover, Germany*; [6]*Prof Hess Childrens Hospital, Paediatrics, Bremen, Germany*; [7]*Deutsche Zentrum, Kinder- und Jugendrheumatologie, Garmisch-Partenkirchen, Germany*; [8]*Zentrum, Kinderheumatologie, Hamburg, Germany*

Background: In polyarticular juvenile idiopathic arthritis (pJIA) biologic therapies are often combined with methotrexate (MTX). This combination was shown to increase efficacy in adult rheumatoid arthritis patients. MTX may also have a protective effect on the formation of anti-drug antibodies and thus may prolong drug survival. In pJIA, there are few and sometimes controversial data available.
Objectives: To compare the effect of combination treatment with MTX on discontinuation due to inefficacy and on drug survival discontinuation of biologics approved for first line treatment of pJIA.
Methods: Patients from the German BIKER registry with their first treatment course with Adalimumab, Etanercept, Golimumab or Tocilizumab were selected. Rates of ineffectiveness-related withdrawal were analysed and compared using $\chi 2$-test, Wald-test and Kaplan-Meier analysis of patients receiving biologic monotherapy or concomitant methotrexate. Cases were censored if MTX was discontinued before the biologic.
Results: 2173 pJIA patients were identified who for the first time received a biologic. Etanercept (ETA) was by far the most frequently used biologic for first line biologic treatment in pJIA (77%) followed by Adalimumab (ADA, 16%). Patients on Golimumab (GOL) received most frequently a combination with MTX (86.5%), while patients on Tocilizumab (TOC) had the lowest rate of combination treatment (53%).
ETA/ADA/GOL/TOC was given as monotherapy in 500(30%)/89(26%)/5(13.5%)/46(47%) and combined with MTX in 1179 (70%)/259(74%)/32(86.5%)/51(53

%) cases. More patients with rheumatoid-factor negative (54 vs 50%; p=0.04) and rheumatoid-factor positive pJIA (13 vs 10%, p=0.04) received combination with MTX, while more patients in the monotherapy cohort had extended oligoarthritis (40 vs 32%, p<0.001). Patients with MTX had a shorter disease duration (4 vs 5.5years, p<0.001) and received concomitant steroid more often (34 vs 24%), p<0.001). There was no statistical difference regarding disease activity parameters (active joint count, patient assessment and physician assessment of disease activity, ESR, CRP, CHAQ-DI, JADAS10). Discontinuation due to ineffectiveness was reported for ETA/ADA/GOL/TOC in 20%/18%/14%/28% of patients, respectively in 3.7/4.9/6/10.5 patients/100 treatment years. Thus discontinuation due to inefficacy was reported less frequently with ETA compared to ADA (p=0.046) and TOC (p<0.001) and with ADA compared to TOC (p<0.001).

Patients on ETA and ADA had a slightly, but not statistically significant lower rate of withdrawal for ineffectiveness if on methotrexate (Figure 1). There was no difference regarding baseline disease activity parameters in patients with ETA/ADA monotherapy compared with combination with MTX, apart from patients with ETA+MTX receiving more often systemic steroids at baseline (36vs 24%,p<0-001). For both GOL and TOC treatment, no baseline differences in disease activity between cohorts with monotherapy and MTX combination could be shown. The combination with MTX led to significantly lower rates of discontinuation due to inefficacy (p<0.05) with GOL and TOC (Figure 1).

Conclusion: Patients with pJIA mostly were treated with a combination of the biologic and MTX rather than with biologic monotherapy. Treatment was discontinued due to lack of efficacy in 14% to 28%. No statistically significant effect of combination treatment with MTX versus monotherapy could be observed regarding the rate of treatment failures in patients treated with ETA or ADA. However, combination treatment with MTX significantly prolonged the survival of GOL and TOC in patients with polyarticular JIA. The results are limited by low patient numbers in the GOL cohort and possible bias by JIA category.

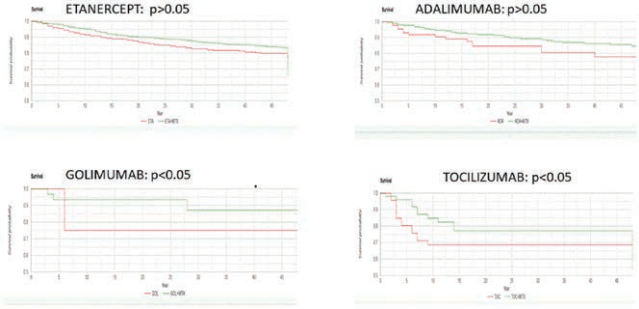


Figure 1. Kaplan Meier plot of drug survival in patients with monotherapy or with combination with MTX of the indicated biologic

Disclosure of Interests: Gerd Horneff Speakers bureau: MSD, Grant/research support from: Pfizer, Roche, Chugai, MSD, Daniel Windschall: None declared, Kirsten Minden Speakers bureau: Pfizer, Abbvie, Grant/research support from: Pfizer, Toni Hospach: None declared, Frank Dressler: None declared, Frank Weller-Heinemann: None declared, Boris Huegle: None declared, Ivan Foeldvari Speakers bureau: Pfizer, Ariane Klein: None declared

DOI: 10.1136/annrheumdis-2021-eular.995

POS1302 THE MUSCULOSKELETAL SYSTEM MANIFESTATIONS IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

F. Demir[1], S. Canbek[2], B. Sözeri[1]. [1]*Health Sciences University, Umraniye Training and Research Hospital, Pediatric Rheumatology, Istanbul, Turkey*; [2]*Health Sciences University, Umraniye Training and Research Hospital, Medical Genetics, Istanbul, Turkey*

Background: Familial Mediterranean fever (FMF) is a monogenic inherited periodic fever syndrome presenting with episodes of self-limiting fever and inflammation of serosal membranes. The attacks emerge with arthritis were defined as one of the major diagnostic criteria besides involvement of serosal membranes. Non-specific musculoskeletal findings such as myalgia, arthralgia, transient synovitis, and more rare manifestations like protracted febrile myalgia can also be seen in FMF patients attacks

Objectives: We aim to reveal the frequency and genotype association of musculoskeletal manifestations in children with FMF.

Methods: The patients diagnosed with FMF between January 1, 2017 and June 1, 2019, and followed for at least 6 months in our pediatric rheumatology clinic were included in the study. Musculoskeletal manifestations of patients were enrolled. The patients were grouped according to the "Mediterranean Fever" (MEFV) gene variants. Musculoskeletal manifestations of the patients were compared between the groups

Results: The study group included 634 children with FMF (336 female and 298 male, F/M: 1.13/1). The clinical manifestations of patients in attack period were as follows: 99% of the patients had fever, 87.3% had abdominal pain, 20.7% had chest pain, 11.3% had vomiting, 10.7% had erysipelas like erythema, and 9.3% had headache. The musculoskeletal symptoms were accompanied by 58.6% (n: 372) of the patients during the attack period. The most common musculoskeletal manifestation was found as arthralgia (32.6%, n: 206). Also, the other musculosceletal manifestations were found as follows during attacks; arthritis in 23.7% (n: 150), myalgia in 20.5% (n: 130), exertional calf pain in 6.5% (n: 41), and protracted febrile myalgia in 1% (n: 7) of the patients. It was observed that the musculoskeletal manifestations were significantly higher in patients with homozygous M694V variant in exon-10 (p=0.017). Also, it was found that the musculoskeletal manifestations are more common in the attack periods of patients carrying the M694V variant in at least one allele (p = 0.019).

Conclusion: It was determined that the musculoskeletal manifestations were seen as an attack symptom in more than half of FMF patients. Also, homozygous and compound heterozygous *MEFV* mutations including M694V variant found as a risk factor for emerge of musculoskeletal manifestations. In children with unexplained and recurrent musculoskeletal symptoms, especially in ethnicities with the high frequency of FMF, analysis of *MEFV* gene can help reveal the underlying cause.

REFERENCES:

[1] Brik R, Shinawi M, Kasinetz L, Gershoni-Baruch R. The musculoskeletal manifestations of familial Mediterranean fever in children genetically diagnosed with the disease. Arthritis Rheum 2001;44:1416-9.

[2] Jarjour RA, Dodaki R. Arthritis patterns in familial Mediterranean fever patients and association with M694V mutation. Mol Biol Rep 2011;38:2033-6.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1169

POS1303 EXPERIENCE WITH ADALIMUMAB BIOSIMILAR USE IN CLINICAL PRACTICE: DATA FROM THE GERMAN BIKER-REGISTRY

G. Horneff[1], F. Dressler[2], M. Rühlmann[3], T. Geikowski[4], S. Mrusek[5], A. Klein[1]. [1]*Asklepios Clinic Sankt Augustin, General Paediatrics, Sankt Augustin, Germany*; [2]*MHH, Paediatrics, Hannover, Germany*; [3]*Office, Paedaitrics, Goettingen, Germany*; [4]*Office, Paediatrics, Bad Honnef, Germany*; [5]*Office, Paediatrics, Baden-Baden, Germany*

Background: In 2017, Adalimumab Biosimilars became approved. Comparative studies to the originator have been performed in adult patients with rheumatoid arthritis, ankylosing spondylitis and psoriasis and extrapolation led to approval for juvenile idiopathic arthritis (JIA).

Objectives: So far there is limited experience with biosimilars in JIA: The large national data base of the BIKER-registry was used to describe experience with Adalimumab biosimilars in clinical practice

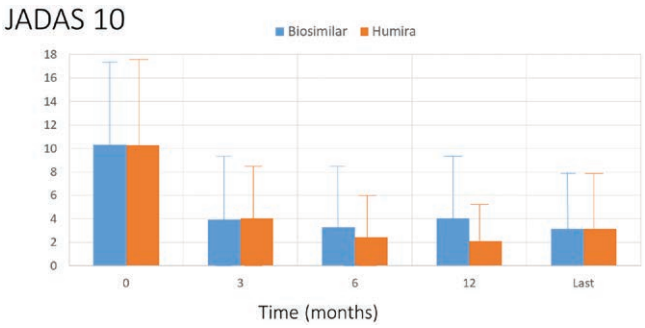
Methods: This retrospective analysis used data of the German BIKER-registry. The data basis war screened for patients exposed to Adalimumab. Subcohorts with initiation of treatment after 2017, use of the originator and of biosimilars were built. The course of JADAS10, Physician global assessment VAS 0–100-mm, Parent/patient global assessment VAS 0–100-cm, Active joint count 0-71, truncated at 10, ESR and CHAQ-DI was analyzed. Descriptive statistics was used for demographic, clinical data, drug exposure, adverse events (AEs) and events of special interest (ESI).

Results: Until 31.10.2020, 1173 JIA patients were reported to have received Adalimumab. 352 treatments have been started after January 1, 2017. A biosimilar was used first line in 44 patients. Further 55 patients switched for the originator to a biosimilar. 2 patient switched from a biosimilar to the originator. 3 patients switched to a second biosimilar while 5 patients who switched from the originator to a biosimilar reswitched back to the originator.

After 2017, 33 pediatric rheumatology centres reported initiation of Adalimumab treatment. 17 have used a biosimilar. 15 centres have swichted at least 1 patient from the originator to a biosimilar and 14 have used first line a biosimilar in at least 1 patient. In a single centre, initiation of a biosimilar was used more frequently (8 versus 7).

The patients' characteristics and disease activity parameters were brightly comparable. The JIA category rheumatoid factor (RF) negative polyarthritis was less frequent in the biosimilar first cohort while RF positive polyarthritis and psoriatic arthritis was more frequent. In patients with idiopathic uveitis the originator was used more often. In the switching cohort, more patients had RF negative polyarthritis, persistent oligoarthritis but less had psoriatic arthritis and no had RF positive polyarthritis.

No difference in disease activity parameters between patients receiving the originator or biosimilars were noted, neither at baseline, during the course of treatment nor at last observation upon treatment (Figure 1). At the time of switching, 46 (92%) had JADAS minimal disease activity (MDA) and 30 (69%) were in JASDAS remission. At last observation, those numbers were comparable with 42 (86%) with JADAS MDA and 28 (57%) with JADAS remission.
In total, 45 adverse events (AE) were reported in 45 patients upon biosimilar treatment. 26 patients had 1, 12 patients had 2 and 6 patients reported 3 and 1 reported 4 events. Adverse event of special interest were Infection associated leukopenia (n=1), COVID 19 infection (n=1), Uveitis flare (n=8), other disease deterioration (arthritis flare) (n=20), injection site reaction n=2. A single serious AE was reported. A 16 year old female adolescent was admitted for unexpected CK elevation. In 10 patients, Adalimumab was discontinued, in 2 it was temporarily paused.
Conclusion: This article is the first attempt to present a large sample of data on JIA patients exposed to Adalimumab biosimilars. Since approval of Adalimumab-Biosimilars, limited experience from clinical practice is available. Biosimilars are used in a minority of patients and by a minority of centers although no difference in efficacy or safety was noted from our analysis.



Disclosure of Interests: Gerd Horneff Speakers bureau: Novartis, MSD, Sobi, Grant/research support from: MSD, Roche, Frank Dressler: None declared, Michael Rühlmann: None declared, Tilmann Geikowski: None declared, Sonja Mrusek: None declared, Ariane Klein: None declared
DOI: 10.1136/annrheumdis-2021-eular.1433

POS1304 JUVENILE SYSTEMIC SCLEROSIS (JSSC) PATIENTS WITH OVERLAP CHARACTERISTICS DO NOT HAVE MILD DISEASE. RESULTS FROM THE JSSC INCEPTION COHORT. WWW.JUVENILE-SCLERODERMA.COM

I. Foeldvari[1], J. Klotsche[2], O. Kasapcopur[3], A. Adrovic[3], K. Torok[3], M. T. Terreri[3], A. P. Sakamoto[3], B. Feldman[3], V. Stanevicha[3], J. Anton[3], F. R. Sztajnbok[3], R. Khubchandani[3], E. Alexeeva[3], M. Katsikas[3], S. Sawhney[3], V. Smith[3], S. Appenzeller[3], T. Avcin[3], M. Kostik[3], T. Lehman[3], E. Marrani[3], D. Schonenberg[3], W. A. Sifuentes-Giraldo[3], N. Vasquez-Canizares[3], M. Janarthanan[3], M. Moll[3], D. Nemcova[3], A. Patwardhan[3], M. J. Santos[3], C. Battagliotti[3], L. Berntson[3], B. Bica[3], J. Brunner[3], R. Cimaz[3], P. Costa Reis[3], D. Eleftheriou[3], L. Harel[3], G. Horneff[3], S. Johnson[3], D. Kaiser[3], T. Kallinich[3], D. Lazarevic[3], K. Minden[2], S. Nielsen[3], F. Nuruzzaman[3], S. Opsahl Hetlevik[3], Y. Uziel[3], N. Helmus[1]. *[1]Hamburg Centre for Pediatric and Adolescence Rheumatology, Schön Klinik Hamburg Eilbek, Hamburg, Germany*; *[2]German Rheumatism Research Center, German Rheumatism Research Center, Berlin, Germany*; *[3]JSSC Collaborative Group, Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, Germany*

Background: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of around 3 in 1, 000,000 children. It is known that in pediatric jSSc cohorts, there are a significant number of patients with overlap features, such as arthritis and myositis. However, the disease burden between those with and without overlap features in jSSc has not been defined.
Objectives: Compare the clinical phenotype between children with and without overlap features in the juvenile systemic scleroderma inception cohort (jSScC).
Methods: A cross-sectional study was performed using baseline visit data. Demographic, organ system evaluation, autoantibody profile, treatment, and patient and physician reported outcome variables were extracted from jSScC. Comparison between patients with and without overlap features was performed using chi-square test and Mann Whitney U-test.
Results: At the time of data extraction, 175 jSSc patients were enrolled in the cohort, 81% were Caucasian and 81% female. Mean disease duration was 3.1 year (±2.7). Mean age at Raynaud´s onset was 10 years (±3.8) and mean age of first non-Raynaud´s was 10.2 years (±3.8). Overlap features occurred 17% (n=30) of the cohort, 12.5% in the diffuse cutaneous (dc) jSSc and in 30% in the limited cutaneous (lc) jSSc. Significant differences in clinical characteristics were found between those patients with compared to without overlap characteristics. Patients with overlap features presented more frequently with Gottron papules (p=0.007), swollen joints (p=0.019), muscle weakness (p=0.003), and lung involvement documented by decreased DLCO < 80% (p=0.06) and/or abnormal high resolution computed tomography (p=0.049). Anti-PM/Scl autoantibodies were also more common in this group (p=0.001). Significantly more patients without overlap features had Raynaud´s (p=0.006). Physician Global Assessment of disease activity was significantly higher in patients with overlap features (41 vs 34; p=0.041). (Table 1.)

Table 1. Demographic and clinical characteristics of jSSc patients with and without overlap features.

	Whole Cohort N=175	Patients without overlap N=145	Patients with overlap N=30	P value
Female to Male Ratio	4.3:1 (142/33)	4:1 (116/29)	6.5:1 (26/4)	0.395
Cutaneous subtype				
Diffuse subtype (N)	73% (128)	112	16	
Limited subtype (N)	27% (47)	33	17	
Mean disease duration (years)	3.1 (± 2.7)	3.2 (± 2.8)	3.1 (± 2.2)	0.291
Mean age of onset of Raynaud´s (years)	10.0 (± 3.8) 17 non-Raynaud	10.0 (± 3.8) 10 non-Raynaud	10.0 (± 3.7) 7 non-Raynaud	0.931
Mean age of onset of non-Raynaud´s (years)	10.2 (± 3.8)	10.2 (± 3.9)	9.8 (± 3.7)	
Disease modifying drugs (N)	88% (154)	89% (129)	83% (25)	0.388
Raynaud´s phenomenon	90% (158)	93% (135)	77% (23)	0.006
Anti-PMScl	18% (12/68)	9% (5/53)	47% (7/15)	0.001
Gottron Papules (N)	27% (46/171)	23% (33/144)	48% (13/27)	0.007
DLCO <80% (N)	44% (39/88)	39% (28/71)	65% (11/17)	0.06
Abnormal findings in HRCT (N)	44% (59/133)	40% (43/107)	62% (16/26)	0.049
Proportion of patients with swollen joints	18% (32)	14% (21)	37% (11)	0.019
Muscle Weakness (N)	21% (31/149)	16% (20/123)	42% (11/26)	0.003
Physician global disease activity (0-100) min -max	35 (0-90) n=141	34 (0-90) n=114	41 (0-80) n=27	0.041

Conclusion: Results from this large international cohort of jSSc patients demonstrate significant differences between patients with and without overlap features. Patients with overlap have significantly more interstitial lung disease and more physician rated disease activity and should not be considered to have more "mild disease".
Supported by the "Joachim Herz Stiftung"
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1613

POS1305 TREATMENT RESPONSE TO TUMOR NECROSIS FACTOR INHIBITORS IN ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS: DATA FROM THE NOR-DMARD STUDY

I. Bardan[1], K. M. Fagerli[2], J. Sexton[2], G. Bakland[3], P. Mielnik[4], L. M. Paucar Loli[5], T. K. Kvien[1,2], E. Kristianslund[2], A. B. Aga[2,6]. *[1]University of Oslo, Faculty of Medicine, Oslo, Norway*; *[2]Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway*; *[3]University Hospital Northern Norway, Department of Rheumatology, Oslo, Norway*; *[4]Helse Førde, Section for Rheumatology, Department for Neurology, Rheumatology and Physical Medicine, Førde, Norway*; *[5]Lillehammer Hospital for Rheumatic Diseases, Department of Rheumatology, Lillehammer, Norway*; *[6]Oslo University Hospital, Department of Rheumatology, Oslo, Norway*

Background: Juvenile idiopathic arthritis (JIA) can cause considerable pain and disability in childhood and adulthood. Studies exploring the efficacy of medications in adult JIA patients are limited, although tumor necrosis factor inhibitors (TNFi) have been increasingly used in this patient group.
Objectives: To explore the efficacy of TNFi ± comedication on disease activity in adult JIA patients, compared to a weighted rheumatoid arthritis (RA) cohort.
Methods: Data from NOR-DMARD, a longitudinal observational study including patients > 18 years starting or switching DMARD treatment, was used [1]. Patients with a clinical JIA diagnosis, or patients with other inflammatory joint diseases diagnosed before 16 years were identified from the study population. RA patients were included for comparative purposes.
Disease activity measurements and remission rates among patients starting treatment with TNFi ± comedication were collected at baseline, 3 and 6 months.

Changes in disease activity and absolute remission rates after 3 and 6 months were calculated. Remission rates and change in disease activity from baseline were compared between JIA patients and a weighted RA cohort with weights based on age and gender, using linear and logistic regression for continuous and categorical variables, respectively.

Results: 281 JIA patients (68.9% female, mean (SD) age 32.1 (11.1) years, mean (SD) diagnosis duration 23.5 (12.2) years) and 1374 RA patients (71.6% female, mean (SD) age 52.7 (14.5) years, mean (SD) diagnosis duration 9.5 (10.0) years) were included in the analyses. Age, gender distribution and disease duration differed significantly between cohorts.

Both groups had a significant improvement across all disease activity measures after 3 months (Table 1), which was maintained after 6 months across all measures except MHAQ. The RA group had a significantly greater 3- and 6-month improvement in SJC28. Both groups had an overall 6-month increase in absolute remission rates. The JIA group had a significantly higher 3-month DAS28 remission rate (Figure 1). This difference was not significant after 6 months, as remission rates from 3 to 6 months in the JIA group declined across all measures.

Table 1.

	Baseline			Change to 3 months			Change to 6 months		
	JIA*	RA*	Diff.§	JIA*	RA*	Diff.§	JIA*	RA*	Diff.§
ESR, mm/h	18.7 (18.9)	25.5 (22.0)	1.3 (-2.3 to 4.9)	-7.4 (15.8)	-7.6 (16.6)	-0.3 (-4.4 to 3.8)	-7.4 (16.8)	-8.5 (18.2)	0.0 (-5.7 to 5.7)
SJC28	2.5 (3.6)	5.5 (5.4)	1.6 (1.3 to 2.0)	-1.4 (3.4)	-3.1 (4.7)	-1.0 (-1.7 to -0.3)	-1.6 (3.2)	-3.5 (5.1)	-1.0 (-1.9 to -0.1)
TJC 28	4.0 (5.6)	6.6 (6.4)	1.3 (0.4 to 2.3)	-1.8 (3.9)	-3.1 (5.9)	-0.6 (-1.4 to 0.2)	-1.8 (3.9)	-3.9 (6.2)	-1.0 (-2.0 to 0.1)
DAS28	3.6 (1.4)	4.5 (1.6)	0.3 (0.1 to 0.6)	-1.2 (1.3)	-1.2 (1.4)	-0.0 (-0.3 to 0.3)	-1.2 (1.3)	-1.5 (1.4)	-0.2 (-0.6 to 0.2)
SDAI	16.8 (10.6)	23.1 (14.3)	2.4 (0.3 to 4.5)	-7.7 (9.9)	-10.9 (12.7)	-2.0 (-4.2 to 0.2)	-7.9 (8.6)	-13.2 (13.6)	-2.8 (-5.8 to 0.2)
PGA	51.4 (26.3)	49.9 (25.5)	-4.0 (-8.5 to 0.5)	-20.6 (26.7)	-17.0 (26.7)	2.7 (-2.2 to 7.6)	-21.6 (25.3)	-19.1 (28.7)	3.4 (-3.0 to 9.8)
MHAQ	0.6 (0.5)	0.7 (0.5)	0.0 (-0.1 to 0.1)	-0.24 (0.42)	-0.22 (0.42)	0.0(-0.1 to 0.1)	-0.23 (0.40)	-0.25 (0.45)	0.0 (-0.1 to 0.1)

*Mean (SD)§ Weighted group difference, RA coefficient (95 % confidence interval)

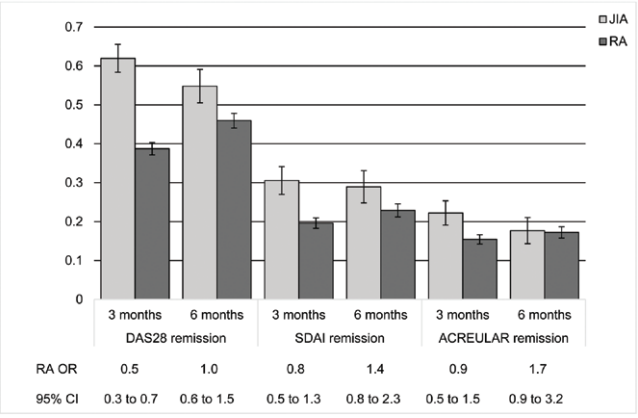


Figure 1. Mean 3- and 6-month remission rates with error bars (SE)

Conclusion: TNFi was equally effective in reducing disease activity in the JIA and RA cohort after 3 and 6 months, and in inducing remission after 6 months. Absolute remission rates in the JIA group declined from 3 to 6 months across all measures, and studies with longer duration are needed to explore the long-term efficacy of TNFi in the patient groups.

REFERENCES:

[1] Kvien, T.K., et al., A Norwegian DMARD register: prescriptions of DMARDs and biological agents to patients with inflammatory rheumatic diseases. Clin Exp Rheumatol, 2005. **23**(5 Suppl 39): p. S188-94.

Disclosure of Interests: Imane Bardan: None declared, Karen Minde Fagerli: None declared, Joe Sexton: None declared, Gunnstein Bakland Speakers bureau: Abbvie, Consultant of: UCB, Pfizer, Novartis, Pawel Mielnik: None declared, Liz Marina Paucar Loli: None declared, Tore K. Kvien Speakers bureau: Fees for speaking: Amgen, Celltrion, Egis, Evapharma, Ewopharma, Hikma, Oktal, Sandoz, Sanofi, Consultant of: Fees for consulting: AbbVie, Amgen, Biogen, Celltrion, Eli Lilly, Gliead, Mylan, Novartis, Pfizer, Sandoz, Sanofi, Grant/research support from: Received research funding to Diakonhjemmet Hospital from Abbvie, Amgen, BMS, MSD, Pfizer and UCB, Eirik kristianslund: None declared, Anna-Birgitte Aga Grant/research support from: Dr. Aga reports personal fees from Abbvie, Eli Lilly, Novartis and Pfizer, outside the submitted work

DOI: 10.1136/annrheumdis-2021-eular.1708

POS1306 TREATMENT STRATEGIES IN CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CMRO) OR CHRONIC NON-BACTERIAL OSTEOMYELITIS (CNO): SYSTEMATIC REVIEW AND META-ANALYSIS

R. Dos-Santos[1], C. Gomez-Vieites[1], D. Fernández Fernández[1], I. González Fernández[1], A. Souto Vilas[1], E. Perez-Pampín[1], A. Mera Varela[1]. [1]*Clinical University Hospital in Santiago de Compostela, Rheumatology Department, Santiago de Compostela, Spain*

Background: Glucocorticoids (GC), bisphosphonates (BP), non-steroidal anti-inflammatory drugs (NSAID) and classical synthetic or biological disease-modifying antirheumatic drugs (cs/bDMARD) have been employed in the treatment of chronic recurrent multifocal osteomyelitis (CRMO) or chronic non-bacterial osteomyelitis (CNO).[1, 2] This one is a rare bone childhood illness and none treatment guidelines have been carried out till present.[3]

Objectives: To asses which treatment schedule employed in CRMO had the best response rates and try to expose a treatment recommendation.

Methods: A systematic literature review was made using Medline, Embase, Cochrane library and the Web of Science databases. The search strategy focused on synonyms of CRMO. A prevalence meta-analysis was performed to evaluate each treatment response. Stata 15.1 was used to perform statistical analysis.

Results: The search identified 1883 articles, of which 43 were finally selected. Complete response rate reached with NSAIDs was acceptable [50% (CI95% 40-60)]. Lower response rates were reached by GC treatment [44% (CI95% 25-63)] or csDMARD [38% (CI95% 28-48)]. The best complete response rates were reached by bDMARD and BP treatments [69% (CI95% 56-82) and 73% (CI95% 62-84), respectively].

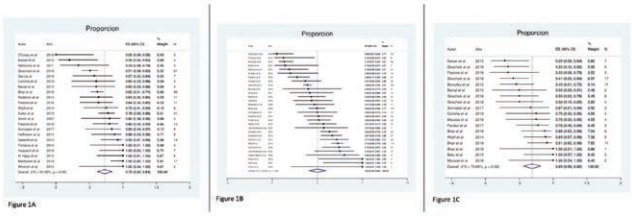
Conclusion: This review and meta-analysis supports, taking into account its remission rates and its risk-benefit profile, NSAIDs as potential first-line agents in CRMO treatment. bDMARD and BP have reached the higher remission rates, turning into helpful treatment alternatives. There is not any treatment guidelines driving CRMO patients, but this analysis could help to select a suitable agent for each patient. Decision-making should be individualized.

REFERENCES:

[1] Wipff J, Costantino F, Lemelle I, *et al*. A large national cohort of French patients with chronic recurrent multifocal osteitis. Arthritis & Rheumatol. 2014;67(4):1128-1137.

[2] Zhao Y, Wu E Y, Oliver M S, et al. Consensus treatment plans for chronic non-bacterial osteomielitis refractory to nonsteroideal anti-inflammatory drugs and/or with active spinal lesions. Arthritis Care Res. 2018;70(8):1228-1237.

[3] Menashe SJ, Aboughalia H, Zhao Y, *et al*. The many faces of pediatric chronic recurrent multifocal osteomyelitis (CRMO): a practical location- and case-based approach to differenciate CRMO from its mimics. J Magn Reson Imaging. 2020;e27299.



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1890

POS1307 ULTRASOUND-DETECTED TENOSYNOVITIS IN ANKLES WITH CLINICALLY ACTIVE DISEASE OF CHILDREN WITH NEW-ONSET JUVENILE IDIOPATHIC ARTHRITIS DOES NOT AFFECT THE CHANCE TO ACHIEVE DISEASE REMISSION

S. Lanni[1], O. De Lucia[2], S. Orsi[1], S. Costi[2,3], G. Beretta[1], T. Giani[4,5], G. Filocamo[1], C. V. Agostoni[1,3], R. Cimaz[3,6]on behalf of PRAGMA (Pediatric Rheumatology Associated Group of the Milan Area). [1]*Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milano, Italy, Paediatrics, Milano, Italy*; [2]*Clinical Rheumatology Unit, ASST Centro Traumatologico Ortopedico G. Pini-CTO, Milano, Italy, Department of Rheumatology and Medical Sciences, Milano, Italy*; [3]*University of Milano,*

Italy, Department of Clinical Sciences and Community Health, Milano, Italy; [4]*AOU Meyer, Florence, Italy, Paediatrics, Firenze, Italy*; [5]*University of Siena, Siena, Italy, Department of Medical Biotechnology, Siena, Italy*; [6]*Pediatric Rheumatology Unit, ASST Centro Traumatologico Ortopedico G. Pini-CTO, Milano, Italy, Department of Rheumatology and Medical Sciences, Milano, Italy*

Background: The ankle is one of the most commonly affected sites in juvenile idiopathic arthritis (JIA). This region has a complex anatomical structure owing to the presence of multiple joint recesses and surrounding tendons. While the prognostic value of ultrasound (US)-detected arthritis has been investigated in recent studies, the role of tenosynovitis in JIA remains still unexplored.
Objectives: To investigate: 1) US features of ankle involvement in JIA at disease onset; 2) the predictive value of US-detected tenosynovitis in ankles with clinically active disease of children with new-onset JIA.
Methods: The clinical charts of all consecutive patients with new-onset JIA between May 2018 and January 2020 at study centres (Policlinico and G.Pini Hospitals of Milan) and with clinically active ankle disease among the joints affected were reviewed retrospectively. Data on ankle US assessment were retrieved and patients were then stratified as follows: 1) patients with detection on US of isolated arthritis in at least one of the joint recesses of the ankle region; 2) patients with detection on US of tenosynovitis in at least one of the tendon compartments of the ankle irrespective of the presence of concomitant arthritis. For each of these two categories, estimation of patients who were able to achieve clinical disease remission at 12 months since disease onset was evaluated.
Results: Twenty-seven new-onset JIA patients were found to have clinical involvement of the ankle among the joints affected. Nine of them (33.3%) showed on US isolated arthritis of the ankle, whereas US-detected tenosynovitis was found in 18 (66.7%) patients. The amount of patients who were able to achieve disease remission at 12-months was the same (66.7%) for both patients with and without US-detected tenosynovitis in the ankle (12/18 and 6/9 patients, respectively). In patients with US-detected tenosynovitis and clinical disease remission at 12 months, the lateral tendon compartment (LTC) was the tendon site more frequently affected by pathology (75.0%). Patients with US-detected tenosynovitis that did not achieve clinical disease remission at follow-up had the highest frequency of tendon pathology on US in the medial tendon compartment (MTC) (83.3%). The anterior tendon compartment was the less frequently affected tendon compartment of the ankle in all patients (33.3% in both patients with and without clinical remission of disease at the 12-months follow-up visit).
Conclusion: US-detected tenosynovitis of the ankle is a common finding in patients with new-onset JIA with clinically ankle disease activity and is more frequent than the detection on US of isolated arthritis. The MTC and LTC are the tendon compartments more commonly affected on US. The detection on US of tenosynovitis at disease onset in ankles with clinical disease activity did not seem to affect the change to achieve the overall clinical disease remission compared to patients without tendon pathology but with joint disease in the ankle region.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1931

POS1308 PREDICTORS OF DISEASE PROGRESSION IN A MONOCENTRIC COHORT OF 100 PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

C. Chighizola[1,2], I. Pontikaki[2], S. Costi[1,2], G. Armentaro[1,2], M. Gattinara[2], T. Giani[3], R. Cimaz[1,2,4]. [1]*University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy*; [2]*ASST G. Pini & CTO, Pediatric Rheumatology Unit, Milan, Italy*; [3]*Azienda Ospedaliero Universitaria Meyer, Rheumatology, Florence, Italy*; [4]*University of Milan, RECAP_RD, Milan, Italy*

Background: Childhood-onset systemic lupus erythematosus (cSLE) accounts for 10-20% of overall cases, usually presenting in early adolescence. SLE in children is characterized by a severe clinical course.
Objectives: This study describes the evolution of clinical manifestations of cSLE, with the aims of i) identifying biomarkers predictive of disease progression and ii) assessing the effects of treatment on disease course.
Methods: Laboratory and clinical data of cSLE patients followed in our Paediatric Rheumatology Unit were retrospectively collected at diagnosis and during follow-up. Continuous data were expressed as median (interquartile range [IQR]) and categorical data as percentages. The association between categorical variables was assessed by chi-squared test, the correlation between variables was tested by Pearson's test. Univariate linear regression analyses were performed to investigate the relationship between the rate of new disease manifestations at follow-up and candidate predictors. Statistical analysis was performed using GraphPadPrism v6. P values <0.05 were regarded statistically significant.
Results: One-hundred patients (89% of female gender) with cSLE were included in this study, with a median age at disease onset of 13 years (10.5-15). Clinical details are presented in Table 1. Complement levels were reduced in 71 patients (C3 in 62 and C4 in 65). At a median follow-up of 118 months (57-239), the disease progressed in 93 patients, with a median of two new manifestations per patient (1-3). No correlation emerged between the number of new disease manifestations and both age at diagnosis and disease duration. Among serological biomarkers, a reduction in complement fractions at diagnosis emerged as the only predictor of new clinical manifestations due to cSLE (p=0.013 for low C3 and p=0.0004 for low C4). Among the several different pharmacological tools, hydroxychloroquine (HCQ, p=0.021, 95% confidence interval (CI) 0.0084-0.1007), azathioprine (AZA, p=0.0217, 95%CI 0.013-0.1703) and cyclophosphamide (CTX, p=0.0305, 95%CI 0.013-0.170) were identified as protective.
At follow-up, patients most commonly developed new haematological and cutaneous involvements, which were diagnosed in 43 and 11 patients, respectively. A trend towards statistical significance emerged for low C4 levels to predict new haematological involvement at follow-up (p=0.064, chi-squared: 3.42). Differently, positivity for antibodies against dsDNA emerged as the only predictor of the onset of cutaneous manifestations during follow-up (p=0.022, chi-squared: 7.62). Low C3 levels approached statistical significance in the prediction of skin involvement (p=0.058, chi-squared 5.68).
Conclusion: According to the data from our monocentric cohort of 100 patients, complement and anti-dsDNA antibodies are the most accurate tools to predict disease progression in cSLE. HCQ, AZA and CTX reduce the rate of disease progression.

Table 1. Clinical manifestations, laboratory features and treatment details of recruited patients at diagnosis.

	Number of patients
Skin manifestations	44
Haematological involvement	51
Lupus nephritis	16
Musculoskeletal involvement	72
Serositis	14
Neuropsychiatric involvement	6
Anti-nuclear antibodies	90
Anti-Ro antibodies	11
Anti-Sm antibodies	13
Anti-dsDNA antibodies	67
Anti-phospholipid antibodies	29
Hydroxychloroquine	89
Azathioprine	40
Cyclophosphosphamide	29
Micophenolate mofetil	13
Cyclosporine	15
Rituximab	1
Belimumab	2
Steroids	91

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2051

POS1309 PREVALENCE AND CORRELATES OF UNDERWEIGHT, OVERWEIGHT AND OBESITY AMONG PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA): EVIDENCE FROM THE NATIONAL PAEDIATRIC RHEUMATOLOGIC DATABASE (NPRD)

F. Milatz[1], J. Klotsche[1], M. Niewerth[1], J. Hörstermann[1], D. Windschall[2], F. Weller-Heinemann[3], F. Dressler[4], R. Berendes[5], J. P. Haas[6], G. Horneff[7,8], K. Minden[1,9]. [1]*German Rheumatism Research Centre, Epidemiology and Health Care Research, Berlin, Germany*; [2]*Northwest German Center for Rheumatology, Clinic of Paediatric and Adolescent Rheumatology, St.-Josef-Stift, Sendenhorst, Germany*; [3]*Klinikum Bremen-Mitte, Prof.-Hess-Kinderklinik, Bremen, Germany*; [4]*Children's Hospital, Medical School Hannover, Department of Paediatric Pneumology, Allergology and Neonatology, Hannover, Germany*; [5]*Kinderkrankenhaus St. Marien, Paediatric Rheumatology, Landshut, Germany*; [6]*German Center for Paediatric and Adolescent Rheumatology, Centre for Pain Therapy of Young People, Garmisch-Partenkirchen, Germany*; [7]*Sankt Augustin Asklepios Children's Hospital, Division of Paediatric Rheumatology, Sankt Augustin, Germany*; [8]*University Hospital of Cologne, Department of Paediatric and Adolescent Medicine, Cologne, Germany*; [9]*Charité University*

Medicine Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany

Background: In patients with JIA, growth impairment and variance in body composition are well-known long-term complications that may be associated with prolonged drug therapy (e.g. glucocorticoids) as well as impaired physical and psychosocial well-being. An increased accumulation of body fat represents a significant risk factor for metabolic abnormalities and a modifiable variable for a number of comorbidities. Recently, evidence has emerged in favour of the potential negative influence of overweight on the course of the disease and treatment response [1].

Objectives: The study aimed a) to estimate the prevalence of underweight, overweight and obesity in children and adolescents with JIA compared to the general population, and b) to investigate correlates of patients' weight status.

Methods: A cross-sectional analysis of physicians' recorded body weights and heights of patients with JIA enrolled in the NPRD in the year 2019 was performed. Underweight (BMI <10th), overweight (BMI >90th) and obesity (BMI >97th) were defined according to age- and sex-specific percentiles used in the German reference system. For comparison with data from the general population [2], sex- and age-matched pairs of 3-17-year-old patients and controls were generated. A multinomial logistic regression analysis was performed to examine the association between weight status and patients' clinical and self-reported outcomes.

Results: In total, data from 6.515 children and adolescents with JIA (age 11.2 ± 4.1 years, disease duration 4.9 ± 3.8 years, 67% girls, 40% persistent oligoarthritis) were included. Of these, 3.334 (age 5.9 ± 2.1 years, 52.5% girls) could be considered for matched-pair analysis. Compared with the general population, patients underweight, overweight and obesity rates were 10.6% (vs. 8.1%), 8.8% (vs. 8.5%) and 6.1% (vs. 5.7%), respectively. No significant sex differences were found in either group. Largest difference in prevalence was registered for underweight, specifically in the age group 3-6 years (12.9% patients vs. 5.9% controls). Similar to the general population, higher rates of overweight were observed in adolescent patients than in affected children (19.1% age group 11-13 vs. 8.4% age group 3-6). While the highest underweight prevalence was registered in patients with RF+ polyarthritis (16%), patients with Enthesitis-related arthritis (22%), psoriatic arthritis (21%) and systemic JIA (20%) showed the highest overweight rates (including obesity). Younger age (OR = 0.51, 95% CI = 0.31-0.83), more frequent physical activity (OR = 0.92, 95% CI = 0.85-0.99) and high parental vocational education (OR = 0.39, 95% CI = 0.18-0.80) were independently associated with a lower likelihood of being overweight/obese.

Conclusion: The overall prevalence of underweight, overweight and obesity in children and adolescents with JIA is comparable to that found in the general population. Behavioural health promotion, including regular physical activity, as part of the treatment strategy in JIA should preventively already begin at preschool age and necessarily be made accessible to patients of all educational levels.

REFERENCES:

[1] Giani T et al. The influence of overweight and obesity on treatment response in juvenile idiopathic arthritis. Front Pharmacol 2019;10:637.

[2] Schienkiewitz A et al. BMI among children and adolescents: prevalences and distribution considering underweight and extreme obesity. Bundesgesundheitsbl 2019;62:1225–1234.

Acknowledgements: The National Paediatric Rheumatological Database has been funded by AbbVie, Chugai, Novartis and GSK.

Disclosure of Interests: Florian Milatz: None declared, Jens Klotsche: None declared, Martina Niewerth: None declared, Jana Hörstermann: None declared, Daniel Windschall: None declared, Frank Weller-Heinemann Speakers bureau: Pfizer, AbbVie, SOBI, Roche and Novartis., Frank Dressler: None declared, Rainer Berendes: None declared, Johannes-Peter Haas: None declared, Gerd Horneff: None declared, Kirsten Minden Speakers bureau: Pfizer, AbbVie, Consultant of: Novartis

DOI: 10.1136/annrheumdis-2021-eular.2058

POS1310 CANAKINUMAB IS A RESCUE TREATMENT FOR MACROPHAGE ACTIVATION SYNDROME IN PATIENTS WITH SYSTEMIC ONSET JUVENILE IDIOPATHIC ARTHRITIS: SINGLE CENTER EXPERIENCE

M. Kostik[1], E. Isupova[1], I. Chikova[1], T. Likhacheva[1], V. Masalova[1], L. Snegireva[1], M. Dubko[1], E. Gaidar[1], M. Kaneva[1], T. Kornishina[1], O. Kalashnikova[1], V. Chasnyk[1]. *[1]Saint Petersburg State Pediatric Medical University, Hospital Pediatry, Saint-Petersburg, Russian Federation*

Background: Macrophage activation syndrome (MAS) is a severe life-threatening complication of the systemic-onset juvenile idiopathic arthritis (soJIA). The treatment options included high-dose of the corticosteroids (CS), cyclosporine A (CsA), intravenous immunoglobulin (IVIG) and biologics, predominantly IL-1 antagonist – anakinra. In Russia anakinra has not approved yet, so canakinumab (CAN) is a single anti-IL-1 option, available in Russia.

Objectives: To evaluate the safety and efficacy of canakinumab in patients with severe MAS in soJIA, who failed the previous treatment.

Methods: In the retrospective case series study were included 9 soJIA patients (4 boys and 5 girls) with severe MAS, resistant to combination of high-dose CS, IVIG and CsA.

Results: All patients had a MAS during the onset of JIA. The main clinical features of disease onset included: fever 9 (100%), active arthritis 5 (56%), pleuritis 7 (78%), pericarditis – 5 (56%), peritonitis 2 (22%), rash 6 (67%), hepatomegaly 9 (100%), splenomegaly 9 (100%), lymphadenopathy 7 (78%), bleeding 4 (44%), CNS involvement – 3 (33%). Initial treatment included high doses CS 8 (89%), oral CS 9 (100%), methotrexate 5 (56%), tocilizumab 4 (44%), and canakinumab 5 (56%), CsA 4 (44%), IVIG 6 (67%). TCZ was discontinued due to infusion reaction (n=2), TCZ inefficacy (n=3) and presence of MAS in all patients (n=5). In children whom TCZ was switched on CAN we used the standard dose of CAN 4 mg/kg, but if MAS occurred on the CAN we temporally increased the doses since 8 to 25 mg/kg (300 mg). In all cases MAS episodes were successfully resolved during CAN treatment. In 5 (56%) MAS had repeated course during the CAN which lead to temporally increasing the doses of CAN (pt3, pt5, pt8, pt 9) or required to increase immunosupression with abatacept or tofacitinib. Three patients with repeated MAS developed interstitial lung disease (ILD). Two patients who successfully resolved MAS after CAN had relapses of arthritis and switched CAN to TCZ.

ID	Sex	JIA onset, y	Repeated MAS	Initial bio-logic	MAS on CAN	Experience of increased CAN doses	Outcomes	Current treatment
1	F	7.7	N	TCZ	N	N	Remission	CAN
2	F	11.5	N	CAN	N	N	soJIA flare, ILD	TCZ
3	F	7.9	Y	CAN	Y	Y	Remission	CAN
4	F	3.4	N	TCZ	N	Y	Remission, ILD	CAN, CS, MMF
5	M	0.8	Y	TCZ	Y	Y	Remission, ILD	CAN, abatacept, CsA, CS
6	M	14.2	Y	CAN	N	N	Remission	TCZ
7	M	1.1	Y	CAN	N	N	Remission	N
8	M	1.3	N	CAN	Y	Y	Remission	CAN every 12 months
9	F	9.1	N	TCZ	Y	Y	Minimal disease activity	CAN, tofacitinib

Footnotes: CAN – canakinumab, CS – corticosteroids, CsA – cyclosporine A, ID – identification, ILD – interstitial lung disease, F – females, M – males, N- no, TCZ – tocilizumab, Y – yes.

Conclusion: Canakinumab is an effective rescue treatment either soJIA either MAS. In patients with MAS developed on CAN required the temporal increasing of the doses.

Funding statement: This work was supported by the Russian Foundation for Basic Research (grant № 18-515-57001).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2141

POS1311 SCLERODERMA PATTERN IN NAILFOLD CAPILLARIES OF (CHILDHOOD-ONSET) SYSTEMIC LUPUS ERYTHEMATOSUS: LESSONS FROM LONGITUDINAL FOLLOW-UP

D. Schonenberg-Meinema[1], S. Bergkamp[1], A. Nassar-Sheikh Rashid[1], M. Gruppen[1], A. E. Hak[2], P. C. E. Hissink Muller[3], M. Middelkamp[4], M. Van Onna[2], T. Kuijpers[5], V. Smith[6], J. M. Van den Berg[1]on behalf of EULAR study group on Microcirculation in Rheumatic Diseases. *[1]Amsterdam UMC, locatie AMC, Pediatric Immunology, Rheumatology and Infectious Diseases, Amsterdam, Netherlands*; *[2]Amsterdam UMC, locatie AMC, Amsterdam Rheumatology and Immunology Centre, Department of Rheumatology and Clinical Immunology, Amsterdam, Netherlands*; *[3]Leiden University Medical Center (LUMC), Department of Pediatric Rheumatology, Leiden, Netherlands*; *[4]Amsterdam UMC, locatie AMC, Department of Dermatology, Amsterdam, Netherlands*; *[5]Amsterdam UMC, locatie AMC, Department of Pediatric Immunology, Rheumatology and Infectious diseases, Amsterdam,*

Netherlands; [6]*Ghent University Hospital, Department of Rheumatology, Gent, Belgium*

Background: It has been suggested that a capillary scleroderma pattern in patients with systemic lupus erythematosus (SLE)-patients predisposes for clinical signs of systemic sclerosis (SSc) or overlap disease (1). However, this was previously shown not to be the case in a cross-sectional study in childhood-onset SLE (cSLE) (2).
Objectives: To assess if nailfold capillary patterns in cSLE change over time and if a capillary scleroderma pattern is associated with prospective development of clinical SSc-features, higher SLE disease activity or –damage.
Methods: Prospective clinical and capillaroscopy data were used from a longitudinal cohort of cSLE patients. Patients with a disease onset before the age of 18 years and diagnosis according to SLICC 2012 criteria were included. Disease activity was defined by SLEDAI score and disease damage by the SLICC damage index. Nailfold images from eight fingers (excluding thumbs) were obtained by videocapillaroscopy. A scleroderma pattern was defined according to the 'fast track algorithm' (3). An abnormal capillary pattern that did not match the criteria for a scleroderma pattern was defined as 'microangiopathy'.
Results: Our longitudinal study cohort consisted of n=53 cSLE patients with a median disease onset of 14 years (IQR 12.5-15.5 years) and a median SLEDAI score at diagnosis of 11 (IQR 8-15.5). Clinical follow-up data were available from 0.5-16 years after disease onset. Median disease duration at first capillaroscopy was 17 months (IQR 5.5-51.5 months) and 17/53 (32.1%) of patients had Raynaud's phenomenon. In total, n=9 (17%) showed a scleroderma pattern (at some point in time), n=37 (70%) had microangiopathy and n=7 (13%) showed a normal capillary pattern. N=27 patients had follow up with capillaroscopy (1-7 times over 1-5 years). In most patients (23/27) we did not observe any change in capillary pattern during follow-up. Two patients showed changes from microangiopathy to a scleroderma pattern, one patient from a scleroderma pattern to microangiopathy and one patient from microangiopathy to a normal pattern. Raynaud's phenomenon was equally distributed among patients with different capillaroscopy patterns (p=0.487), as was median SLEDAI score at diagnosis (p=0.285). Follow-up patients with a capillary scleroderma pattern did not show any clinical features for SSc over time (follow-up over 1-5 years, Table 1 below. Patients with a capillary scleroderma pattern showed significantly more disease damage (Chi-square, p=0.008), also indicated by a survival analysis for disease damage (Figure 1, p=0.042).
Conclusion: Our study indicates that a capillary scleroderma pattern in cSLE correlates with disease damage but not with clinical SSc features during follow-up period.
REFERENCES:

[1] S. Pavlov-Dolijanovic et al. Is there a difference in systemic lupus erythematosus with and without Raynaud's phenomenon? Rheum Int 2013;33: 859–865
[2] D. Schonenberg-Meinema et al. Nailfold capillary abnormalities in childhood-onset systemic lupus erythematosus. *Revised manuscript after review re-submitted to Lupus in January 2021*
[3] V. Smith et al. Fast track algorithm. Autoimm Rev 2019 Nov;18(11): 102394

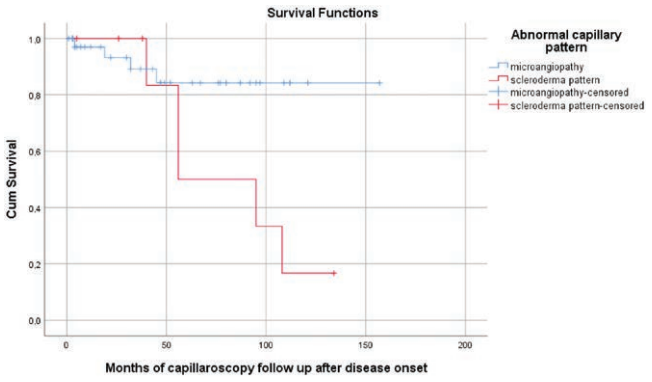


Figure 1. Occurrence of disease damage (with survival as 'no damage') in cSLE patients with microangiopathy (blue) and a capillary scleroderma pattern (red)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2195

POS1312 DRUG SURVIVAL FOR IL-6 INHIBITOR TOCILIZUMAB: DATA FROM A SINGLE-CENTER OBSERVATION

E. Krekhova[1,2], E. Alexeeva[1,2], T. Dvoryakovskaya[1,2], K. Isaeva[1], R. Denisova[1], O. Lomakina[1], A. Mamutova[1], A. Chomakhidze[1], A. Fetisova[1], M. Gautier[1], I. Kriulin[1,2], I. Tsulukiya[1]. [1]*National Medical Research Center of Children's Health, Rheumatology, Moscow, Russian Federation*; [2]*Sechenov First Moscow State Medical University, Pediatric, Moscow, Russian Federation*

Background: The efficacy of tocilizumab for treatment patients with systemic juvenile idiopathic arthritis (sJIA) was demonstrated before. We want to describe tocilizumab drug survival based on data from a single-center observation.
Objectives: To analyze the drug survival of tocilizumab in patients with sJIA treated at the National Medical Research Center of Children`s health, Moscow, Russia.
Methods: Medical records from sJIA patients treated with tocilizumab (TOC) were analyzed retrospectively from the National Medical Research Center of Children`s health, Moscow, Russia.
Results: One hundred ninety-two patients presenting with sJIA were included in this observation, with a median age at treatment initiation of 7,2 (interquartile range, IQR 3,9-10,8) years and a median disease duration of 1,9 (IQR 0,4-5,9) years. All patients had been bio-naive. TOC therapy was highly effective in patients with sJIA. At 6 month of follow-up 148/172 (86%) patients achieved inactive disease according the criteria C. Wallace, disease activity persisted in 24/172 (14%) patients. At 1 year of medication 139/150 (92%) patients had inactive disease. We analyzed the reason of TOC withdrawal retrospectively. A total of 82/192 drug withdrawals were performed. TOC was discontinued due to primary ineffectiveness in 4 patients, due to secondary ineffectiveness in 39 patients. 33 patients achieved drug-free remission.

Table 1. Clinical characteristics of cSLE-patients (n=9/53) with a nailfold capillary scleroderma pattern

	Butterfly rash	Photosensitive rash	Lupus nephritis	Autoimmune cytopenia	Positive Coombs	Low C3/C4	Serositis	Damage	Type of auto-antibodies	Follow-up in years
1	+	+	-	+	+	+	-	+	ANA, Anti-ds-DNA, anti-Sm, anti-RNP, anti-Ro52, anti-SS-A	5
2	+	+	-	+	+	+	-	+	ANA, Anti-ds-DNA, anti-Sm, anti-RNP, anti-SS-A	5
3	-	+	+	+	+	+	+	+	ANA, Anti-ds-DNA, anti-Sm, anti-RNP, anti-SS-A	10
4	-	+	+	-	+	+	+	+	ANA, Anti-ds-DNA, anti-Sm, anti-RNP, anti-Ro52, anti-SS-A	9
5	-	+	-	-	+	-	+	-	ANA	1 (lost)
6	-	+	+	+	+	+	+	-	ANA, Anti-ds-DNA, anti-c1q	3
7	-	-	-	+	-	-	-	-	ANA, Anti-ds-DNA, anti-Sm, anti-RNP	1
8	+	+	-	+	-	-	-	-	ANA	9
9	-	+	+	+	+	+	+	+	ANA, Anti-ds-DNA, anti-RNP, anti-SS-A	8

Six patients developed side effects that required discontinuation of TOC therapy (4 patients had allergic reactions, 1 patient developed tuberculosis, 1 patient had severe neutropenia). 47/82 patients were switched on other biologic drug: on canakinumab (31), on TNF-inhibitors (11), on rituximab (5). In summary, TOC was canceled in 49/192 (25%) patients due to ineffectiveness or AEs in our cohort.
Conclusion: These results demonstrated that TOC is highly effective as the first biologic drug in patients with sJIA. Our observations have shown a good tolerability and survival of the IL-6 inhibitor TOC in patients with sJIA treated in a real-world clinical setting.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2255

POS1313 PSYCHIATRIC DISORDERS IN JUVENILE IDIOPATHIC ARTHRITIS - A POPULATION-BASED COHORT STUDY

B. Delcoigne[1], A. Horne[2,3], S. Omarsdottir[3,4], J. Reutfors[1], J. Askling[1].
[1]Karolinska Institutet of Medecine, Division of Clinical Epidemiology, Stockholm, Sweden; *[2]Karolinska Institutet, Department of Women's and Children's Health, Stockholm, Sweden*; *[3]Karolinska University Hospital, Pediatric Rheumatology Unit, Theme of Children's Health, Stockholm, Sweden*; *[4]Pediatric Rheumatology Registry, Pediatric Rheumatology Registry, Stockholm, Sweden*

Background: Juvenile idiopathic arthritis (JIA) may have substantial consequences for quality of life, for instance due to chronic pain, restriction of activities, concern about physical appearance, and treatment protocols that may limit interactions with peers. However, it remains unclear whether children and adolescents with JIA sow a higher incidence of psychiatric disorders compared with the general population.
Objectives: To examine the incidence of psychiatric disorders during childhood in JIA patients in Sweden relative to general population controls.
Methods: We performed a register- and population-based cohort study including new-onset JIA patients aged 0 to 17 years 1st January 2012 through 31st December 2017. Incident JIA patients were followed-up from the date of their 2nd JIA diagnosis. At this date, five sex-age-region matched individuals were sampled from the general population. Nine psychiatric disorders were defined with ICD-10 codes and associated drugs (ATC codes): psychotic disorders (ICD-10: F20-29; ATC: N05A), mood and anxiety disorders (F30-F43; N05B, N06A, R06AD01, R06AD02, N03AX16), sleeping disorders (F51; N05C, N03AE01), eating and personality disorders (F50, F60-61, F69), neuropsychiatric disorders (F70-F79, F84, F90; N06BA, C02AC02), substance misuse (F10-F19; N07B), suicide attempts (X60-X84, Y10-34) and death by suicide or substance abuse, and all these combined. The follow-up stopped at date of first outcome, migration, death, 18th birthday or end of the study period, whichever occurred first. Incidence rates were calculated and compared by Cox regression analyses, adjusted for age, sex, calendar year, patient's and family's history of psychiatric disorder, country of birth, parents' education level, and comorbidities (IBD, obesity and celiac disease). In sensitivity analyses, we (1.) excluded children with a history of a psychiatric diagnosis at start of follow-up, and (2.) defined the psychiatric disorders based on ICD-10 codes only.
Results: We identified 2224 JIA patients (64% girls, mean age: 9.8 years) and 10,264 matched controls. In the JIA cohort, 309 patients developed a psychiatric disorder (all outcomes combined) during 4998 person-years (pyrs), which corresponded to a crude incidence rate (IR) of 6.2 per 100 pyrs (95% confidence interval (CI): 5.5-6.9). The corresponding crude IR for the general population matched controls was 3.6 (3.4-3.9). Comparing these incidence rates resulted in a sex-age adjusted hazard ratio (HR) of 1.66 (95% CI: 1.46-1.89) and a fully adjusted HR of 1.68 (1.47-1.91). Considering specific outcomes, the IRs per 100 pyrs in the JIA population ranged from 0.1 (suicide attempt) to 3.7 (mood and anxiety disorders) (Table 1). No death from suicide was recorded. There was an overlap across the seven outcomes: among all individuals diagnosed with at least one of the psychiatric outcomes during follow-up, 58% were diagnosed with one outcome only, 25% with two and 19% with three or more outcome conditions. The Cox analyses of the 7 outcome groups demonstrated four statistically significant increased risks for psychotic, mood and anxiety, sleeping and neuropsychiatric disorders (Figure 1). The three latter outcomes were correlated to each other (with Cramer's V coefficient between 0.3 and 0.5). The sensitivity analyses did not substantially modify these findings.
Conclusion: The burden of psychiatric illness in individuals with JIA is increased compared to the general population.

Table 1. Risk of psychiatric disorders in JIA patients and general population controls.

Disorders	N events JIA	N events controls	IR JIA (95% CI)	IR controls (95% CI)
All combined	309	918	6.2 (5.5-6.9)	3.6 (3.4-3.9)
Psychotic	25	44	0.5 (0.3-0.7)	0.2 (0.1-0.2)
Mood	194	534	3.7 (3.2-4.3)	2.0 (1.9-2.2)
Sleeping	148	348	2.8 (2.4-3.3)	1.3 (1.2-1.5)
Neuropsychiatric	126	442	2.4 (2.0-2.8)	1.7 (1.5-1.9)
Eating	13	55	0.2 (0.1-0.4)	0.2 (0.2-0.3)
Substance misuse	14	49	0.3 (0.2-0.4)	0.2 (0.1-0.2)
Suicide attempt	7	55	0.1 (0.1-0.3)	0.2 (0.2-0.3)

IR: crude incidence rate per 100 person-years; CI: confidence interval[1] adjustment: see text.

Figure:
Comparisons of risks for several psychiatric disorders in juvenile idiopathic arthritis patients versus general population: Hazards ratio and 95% confidence intervals (with general population as reference)

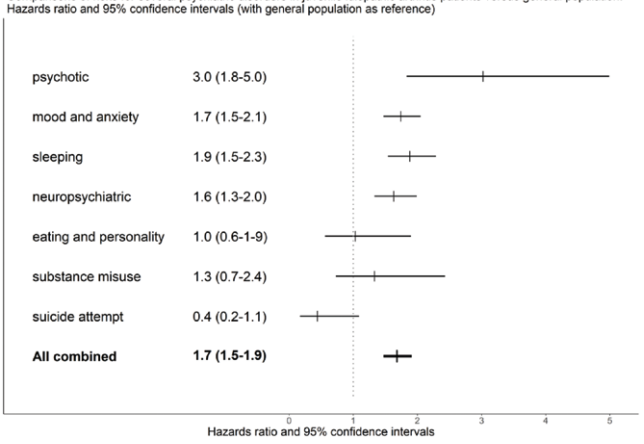


Figure 1.

Disclosure of Interests: Bénédicte Delcoigne: None declared, AnnaCarin Horne Consultant of: SOBI and Novartis, Soley Omarsdottir: None declared, Johan Reutfors: None declared, Johan Askling Consultant of: Abbvie, Astra-Zeneca, BMS, Eli Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB. These entities have entered into agreements with Karolinska Institutet with JA as principal investigator, mainly in the context of safety monitoring of biologics via the ARTIS national safety monitoring system
DOI: 10.1136/annrheumdis-2021-eular.2821

POS1314 JUVENILE IDIOPATHIC ARTHRITIS IN THE CONTEXT OF THE CORONAVIRUS DISEASE 19 PANDEMIC: IMPACT ON THE DECREASE IN TREATMENT AND THE RETURN TO SCHOOL

B. Quéré[1], I. Lemelle[2], A. Lohse[3], P. Pillet[4], J. Molimard[4], O. Richer[4], C. Sordet[5], V. Despert[6], L. Rossi-Semerano[7], C. Borocco[7], I. Koné-Paut[7], E. Gervais[8], D. Guellec[1], V. Devauchelle-Pensec[9]. *[1]Hospital La Cavale Blanche, Rheumatology, Brest, France*; *[2]CHRU de Nancy - Hôpitaux de Brabois, Paediatric Onco-Haematology, Vandœuvre-lès-Nancy, France*; *[3]Hospital Nord Franche-Comté, Rheumatology, Trévenans, France*; *[4]Hôpital Pellegrin Bordeaux, Paediatrics, Rheumatology and Paediatric Internal Medicine, Bordeaux, France*; *[5]Hôpital de la Robertsau - Hôpitaux Universitaires de Strasbourg, Rheumatology, Strasbourg, France*; *[6]South Hospital, Paediatric, Rennes, France*; *[7]Bicetre Hospital AP-HP, Paediatric Rheumatology, Le Kremlin-Bicêtre, France*; *[8]Poitiers University Hospital, Rheumatology, Poitiers, France*; *[9]Hospital La Cavale Blanche, Rheumatology, Brest, France*

Background: The SARS-CoV-2 pandemic has induced an exceptional sanitary crisis, potentially having an impact on treatment continuation, for juvenile idiopathic arthritis (JIA) patients receiving immunosuppressive therapies. In France, after the first lockdown from March to May 2020, many parents and children were then also concerned about whether reopening plans for school could ensure the safety of students, despite data concerning children with COVID-19 seem reassuring, and very few of them develop severe forms of the disease (1, 2, 3).
Objectives: Our objectives were to evaluate the impact of the COVID-19 pandemic on the therapeutic management of JIA, the frequency of returning to school after the first lockdown period and the prevalence of SARS-CoV-2 infection at the time of the survey.
Methods: JIA patients under 18 years of age, usually treated with disease-modifying anti-rheumatic drugs (DMARDs) were prospectively included during their outpatient visit and completed a standardized questionnaire. Data regarding the general characteristics of the participants, medical history, SARS-CoV-2 infection, characteristics of JIA subtypes and treatment modifications were collected.
Results: A total of 173 patients from 8 different expert centers were included between May and August 2020. Their mean age was 11.6 years (± 4.1 years), and most of them 31.2% (54/173) had a rheumatoid factor-negative polyarticular JIA. Fifty percent (86/172) were treated with methotrexate, and 72.5% (124/171) were treated with bDMARDs. DMARD treatment modification in relation to the pandemic was observed in 4.0% (7/173) of participants, our results reflect good adherence of the patient/parents to their immunosuppressive treatments. 49.1% (81/165) of the patients did not return to school due to a personal/parental decision in 69.9% (55/81) of cases, due to anxiety of the patient/parents regarding COVID-19. Two patients were diagnosed positive for SARS-CoV-2 infection.

Conclusion: This study suggests that JIA patients treated with DMARDs continued their treatment during the pandemic. In contrast, parents' reluctance was a major obstacle for returning to school. Therefore, more solidified school reopening strategies should be developed.

REFERENCES:

[1] Filocamo G, et al. "Absence of severe complications from SARS-CoV-2 infection in children with rheumatic diseases treated with biologic drugs." J Rheumatol. 25 avr 2020;

[2] Tagarro A, et al. "Screening and Severity of Coronavirus Disease 2019 (COVID-19) in Children in Madrid, Spain." JAMA Pediatr. 8 avr 2020;

[3] Lu X, et al. « SARS-CoV-2 Infection in Children". N Engl J Med. 23 avr 2020;382(17):1663-5.

Acknowledgements: We would like to thank all the participants involved in this clinical research and six medical students who helped completing the forms: Margaux Blondel, Alice Bonnod, Marie Desval, Béatrice Dordain, Gabrielle Fagnet, and Madouc De Saint Martin Pernot.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2838

POS1315 USEFULNESS OF SYNOVIAL BIOPSY IN THE DIFFERENTIAL DIAGNOSIS AND AS POSSIBLE PREDICTOR OF RESPONSE TO TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS

S. Costi[1], F. Pregnolato[2], A. Parafioriti[3], E. Armiraglio[3], T. Giani[4,5], R. Cimaz[6,7]. *[1]University of Milan, Rheumatology, Milan, Italy*; *[2]Auxologico Italiano, Experimental Laboratory of Immunological and Rheumatologic Researches, Milan, Italy*; *[3]ASST G.Pini-CTO, Pathological Anatomy, Milan, Italy*; *[4]Meyer Children's Hospital, Pediatric Rheumatology, Florence, Italy*; *[5]University of Siena, Department of Medical Biotechnology, Siena, Italy*; *[6]University of Milan, Department of Clinical Sciences and Community Health, and Research Center for Adult and Pediatric Rheumatic Diseases, Milan, Italy*; *[7]ASST G.Pini-CTO, Pediatric Rheumatology, Milan, Italy*

Background: While synovial biopsy is an invasive procedure and is not required for the diagnosis of juvenile idiopathic arthritis (JIA), it may be useful in doubtful cases.

Objectives: Aims of the study were i.to verify the role of synovial biopsy in the differential diagnosis of JIA and ii. to review the pathology slides in order to evaluate possible associations of a histologic pattern with response to treatment.

Methods: We reviewed data from medical records of patients under the age of 18 years who underwent a synovial biopsy requested by our Pediatric Rheumatology Unit over the last 10 years. We collected information on demographic, clinical, laboratory, radiological, histopathological characteristics, as well as treatment response (in particular, remission at the last visit and number of examination, number of biologic drugs used). Among variables in the histologic score, number of layers in the synovial lining and inflammatory infiltrate (0-5) were compared to clinical status at last visit. Potential differences in variables between responders and non responders were assessed by unpaired t-test or non-parametric Mann-Whitney test, as appropriate.

Results: We identified 64 patients (40F, 24M) with a median age at disease onset of 9 years (range 1-15) and a median follow-up time of 161 months (range 8-1160). We recognized two groups of interest: patients with a known JIA diagnosis (28/64) and patients with unknown diagnosis (36/64) at the moment of synovial biopsy. In the group with known JIA, most underwent the procedure during orthopedic surgery, and in all cases the histology was consistent with JIA. Among the unknown diagnosis group, in 19 cases results were consistent with a chronic synovitis, while among the other 17 histology could lead to a diagnosis of other conditions in 6 cases (foreign body and villonodular synovitis n=2 each, sarcoidosis and osteochondromatosis n=1 each). In the remaining 11 the final diagnoses were varied (mostly genetic forms eg skeletal dysplasia, CACP, Thiemann disease).

Between the two groups we identified 46 patients with a definite JIA diagnosis. At the last follow-up visit 29 of them were in clinical remission, albeit on medication. The remaining 17 had a severe course of disease, with persistent activity and use of at least two biologic drugs. In 26 cases we could evaluate the correlation between status at last visit and number of layers/inflammatory infiltrate, but no statistical significant correlation was found.

Conclusion: Despite its limited use nowadays, synovial biopsy may still be a useful tool in patients whose diagnosis is unclear. In our study, while it confirmed the suspicion in most cases, in other instances it allowed the diagnosis of rare conditions that would have been otherwise missed. No association between disease course and histological features in a small JIA cohort was found. We are currently expanding the study with a larger series.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2989

POS1316 VISUAL FUNCTION AND QUALITY OF LIFE: PRELIMINARY RESULTS FROM A PIVOTAL CROSS-SECTIONAL STUDY ON ONE HUNDRED PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED AND IDIOPATHIC UVEITIS

G. B. Beretta[1], F. Minoia[1], L. Marelli[2], C. Mapelli[3], G. Leone[3], T. Giani[4], P. Nucci[2,5], E. Miserocchi[6], R. Cimaz[7,8]on behalf of Pediatric Rheumatology Associated Group of the Milan Area. *[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Pediatric Rheumatology, Milan, Italy*; *[2]Ospedale San Giuseppe, IRCCS Multimedica, Ophthalmology, Milan, Italy*; *[3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Ophthalmology, Milan, Italy*; *[4]Università degli Studi di Siena, Pediatric Rheumatology, Siena, Italy*; *[5] Università degli Studi di Milano, Ophthalmology, Milan, Italy*; *[6]IRCCS Ospedale San Raffaele, Ophthalmology, Milan, Italy*; *[7]ASST Gaetano Pini-CTO, Milan, Italy, Pediatric Rheumatology, Milan, Italy*; *[8]Università degli Studi di Milano, Pediatric Rheumatology, Milan, Italy*

Background: Juvenile idiopathic arthritis (JIA) is the main cause of chronic uveitis in childhood and JIA associated uveitis (JIA-U) is the most common extraarticular complication of JIA. Despite continuous improvement in its management, pediatric uveitis still represents a serious condition with potential sight-threatening complications and a significant impact on quality of life (QoL).

Objectives: To evaluate visual function (VF) and QoL in children with JIA-U and idiopathic uveitis

Methods: A cross-sectional study was conducted in two tertiary Pediatric Rheumatology Centres, enrolling all patients seen with JIA-U, JIA without uveitis and idiopathic uveitis. VF was assessed by a translated form of the available EYE-Q, adapted for cross-cultural feasibility into a 10-question tool, while QoL was evaluated by the Italian version of the Pediatric Rheumatology Quality of Life scale part of the Juvenile Arthritis Multidimensional Report (JAMAR), shortened for feasibility to a 8-question tool. JAMAR section on treatment compliance and school attendance was also included. Parents, and patients when appropriate, were asked to complete each patient/parent-reporting outcome measure, answering on a 4-point Likert scale, with a total score ranging from 0 to 72 (worst condition). Medical charts were reviewed regarding JIA and uveitis features and outcome. Quantitative and qualitative variables were compared by means of Mann-Whitney U test or chi-square/Fisher exact test, as appropriate; correlations among quantitative non-parametric variables were evaluated by Spearman's test.

Results: We herein describe results from the first 100 patients enrolled (76% female), with a median age at study time of 12.8 (9.0-17.6) years. Forty-nine had JIA-U, 37 JIA without uveitis and 14 idiopathic uveitis. Uveitis was active in 14/63 patients (22.2%), with a median of uveitis duration of 9.0 years (3.6-14.8). Almost all children with uveitis were on systemic treatment (58/63, 92%) at the time of interview; 54.0% of patients presented an ocular damage, with 8.0% having a best corrected visual acuity (BCVA) < 4/10. Total score, VF and QoL scores resulted significantly higher in JIA-U patients compared to JIA without uveitis, while no differences were noticed among children with uveitis with or without JIA (Table 1). School absence was reported more frequently in JIA-U compared to JIA only (32.7% vs 10.8%, p 0.0211). VF was significantly worse in patients with ocular damage and BCVA < 4/10 (p 0.0351 and 0.0123, respectively). In patients with uveitis, VF and QoL showed a significant correlation (r 0.50, p <0.0001) especially in patients with idiopathic uveitis (r 0.74, p <0.0001).

Conclusion: Visual function is a crucial component of QoL in children with uveitis and it correlates with ocular damage. Since eye involvement significantly affect QoL in patients with JIA, a specific tool widely validated and cross-cultural adapted is highly demanded in the clinical care of JIA-U patients.

REFERENCES:

[1] Angeles-Han ST et al. The importance of visual function in the quality of life of children with uveitis. J AAPOS, 2010. Filocamo et al. A New Approach to Clinical Care of Juvenile Idiopathic Arthritis: The Juvenile Arthritis Multidimensional Assessment Report. J Rheumatol, 2011.

Table 1.

	JIA-U n = 49	Idiopathic uveitis n = 14	JIA n = 37	p-value*	p-value#
Total score	5.0 (3.0-11.0)	4.5(2-9.8)	2.0(0-4.0)	0.5739	**<0.0001**
VF score	2.0 (0-3.0)	1.0(0-3.0)	0(0-0)	0.9098	**<0.0001**
QoL score	3.0(2.0-6.0)	3.5(2.0-4.8)	2.0(0-4.0)	0.5611	**0.0005**

Numbers are medians (IQR). * JIA-U vs idiopathic uveitis; #JIA-U vs JIA

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2994

POS1317 PREDICTIVE FACTORS FOR RESPONSE TO TREATMENT IN A LONG-TERM COHORT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED UVEITIS

L. Marelli[1], F. Minoia[2], G. Beretta[2], C. Mapelli[3], G. Leone[3], G. Cincinelli[4], T. Giani[5], P. Nucci[6], R. Cimaz[4,6], E. Miserocchi[7]. *[1]Ospedale San Giuseppe, IRCCS Multimedica, Ophthalmology, Milan, Italy*; *[2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Pediatric Rheumatology, Milan, Italy*; *[3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Ophthalmology, Milan, Italy*; *[4]ASST Gaetano Pini CTO, Pediatric Rheumatology, Milan, Italy*; *[5]Università degli Studi di Siena, Pediatric Rheumatology, Siena, Italy*; *[6]Università degli Studi di Milano, Dipartimento di Scienze Cliniche e di Comunità, Milan, Italy*; *[7]IRCCS Ospedale San Raffaele, Ophthalmology, Milan, Italy*

Background: Uveitis is the main extraarticular complication of juvenile idiopathic arthritis (JIA) with still a significant impact on JIA morbidity, despite continuous improvement in systemic treatment. Although antinuclear antibody positivity and early onset of JIA have been associated with a high risk of uveitis onset, so far no clinical features have been widely recognized as predictive factors for JIA-associated uveitis (JIA-U) response to treatment.
Objectives: To investigate clinical features associated with response to systemic treatment in a long-term cohort of patients with JIA-U
Methods: Clinical records of patients with JIA-U were retrospectively reviewed with regard to clinical features, therapeutic choices and outcome. Clinical and laboratory variables were compared by means of Mann-Whitney U test or chi-square/Fisher exact test, as appropriate.
Results: Data from 164 JIA-U patients were analysed (81.7% female), with a median follow up of 12.1 years (7.1-17.3). Median age at JIA and uveitis onset was 2.6 (1.6-4.8) and 4.8 (2.9 – 7.0) years, respectively. Monotherapy with a conventional disease-modifying antirheumatic drug (DMARD) was used in 25.0% of patients, while 111 patients (67.7%) received at least one biologic DMARD (bDMARDs). Compared to patients responsive to DMARDs, children requiring a bDMARDs for uveitis had a lower median age at both JIA (2.4 vs 4.3 years, p 0.0234) and uveitis onset (4.1 vs 6.2 years, p 0.0023). Despite no differences in ocular damage at onset and median disease duration, patients not responsive to conventional DMARDs showed a higher frequency of ocular damage at the last visit (66.2% vs 33.3%, p 0.011). Children requiring more than one bDMARD for uveitis presented a more frequent polyarticular course (87.0% vs 20.2%, p 0.0022), a longer disease duration (median follow-up: 14.2 vs 10.4 years, p 0.0397) and a higher frequency of visual loss (best corrected visual acuity < 4/10: 23.3% vs 6.3%, p 0.0069).
Conclusion: JIA-U patients with a lack of response to conventional DMARDs were significantly younger both at JIA and uveitis onset. Severe JIA-U requiring more than one bDMARDs was associated with polyarticular JIA course and longer disease duration. Children resistant to conventional treatment need prompt recognition and additional strategies to improve long-term outcome.
REFERENCES:
[1] Heiligenhaus et al. Predictive factors and biomarkers for the 2-year outcome of uveitis in juvenile idiopathic arthritis. Rheumatology 2019.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3006

POS1318 A NATIONWIDE COHORT STUDY ON CLINICAL AND LABORATORY MANIFESTATIONS IN CHILDREN WITH MULTISYSTEM INFLAMMATORY SYNDROME (MIS-C)

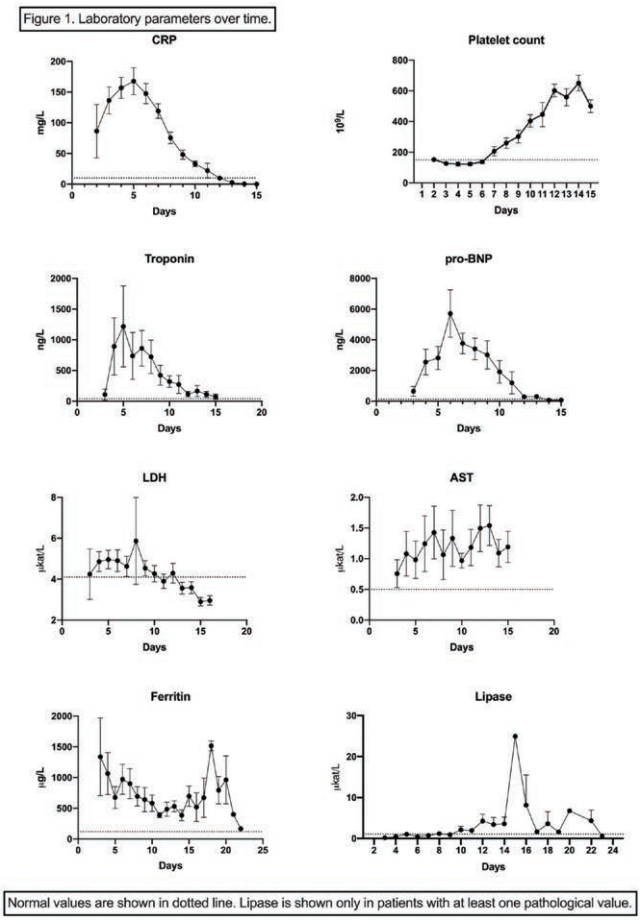
M. Zajc Avramovic[1,2], K. Vincek[3], G. Mlakar[4], N. Emersic[1], T. Plankar Srovin[3], T. Avsic-Zupanc[5], A. Ihan[5], T. Avcin[1,2]. *[1]University Medical Center Ljubljana, Children's Hospital, Department for Allergology, Rheumatology and Clinical Immunology, Ljubljana, Slovenia*; *[2]University of Ljubljana, Faculty of Medicine, Pediatrics, Ljubljana, Slovenia*; *[3]University Medical Center Ljubljana, Clinic of Infectious Diseases, Ljubljana, Slovenia*; *[4]University Medical Center Ljubljana, Children's Hospital, Department for Cardiology, Ljubljana, Slovenia*; *[5]University of Ljubljana, Faculty of Medicine, Institute of Microbiology and Immunology, Ljubljana, Slovenia*

Background: Multisystem inflammatory syndrome in children (MIS-C) was recognized during the 2020 pandemic of SARS-CoV-2. Because of the relative rarity current knowledge is limited, especially in the European Caucasian population.
Objectives: To report the epidemiology, clinical and laboratory characteristics of patients with MIS-C in a nationwide cohort study in Slovenia.
Methods: This is a nationwide prospective cohort study of all consecutive patients with MIS-C, admitted from the beginning of epidemics to 31st December 2020 to University Medical Centre Ljubljana, Slovenia, the only tertiary care pediatric rheumatology center in the country. The inclusion criteria were meeting the CDC criteria for MIS-C. Infection with SARS-CoV-2 was confirmed in all patients by positive antibodies for SARS-CoV-2. Data were collected from the patients' medical records. Data on the COVID-19 epidemics in Slovenia were collected from National Institute of Public Health. Population data were provided by the Statistical Office of the Republic of Slovenia.
Results: Twenty-three patients with MIS-C were diagnosed nationwide in Slovenia, all of them in the second wave of epidemics from 14th September to 31st December 2020. All patients were Caucasian and the estimated prevalence of MIS-C was 5.8/100 000 persons younger than 19 years of age. Detailed analyses were available in 20 patients of which 14 were boys (70 %), median age was 12.4 years (4 months to 17.7 years). Two patients (10 %) were treated in the intensive care unit and none of the patients died. Troponin was elevated in 15/20 (75 %) patients during the disease course, and 7/15 (47 %) of these had normal troponin level at admission. The serum level of troponin closely followed the serum level of CRP. Six out of 20 (30 %) patients had elevated pancreatic enzymes in the second week of the disease after treatment was already given,and one patient developed asymptomatic acute pancreatitis with serum lipase level reaching the maximum of 25μkat/L. All patients had elevated levels of D-dimer with no signs of thrombosis. Five patients (5/20; 25 %) had pleural effusions and five patients (5/20, 25 %) had ascites. Half of the patients (10/20; 50 %) had hepatosplenomegaly and eight (8/20; 40 %) had mesenterial lymphadenopathy. Three patients (3/20; 15 %) had radiologic signs of cholecystitis. Two patients had thickened lung parenchyma. All patients received IVIG and systemic glucocorticosteroids. Because of resistant or organ threatening disease 4 patients (4/20, 20%) received high dose methylprednisolone pulse therapy. Biologic therapy with anakinra was started in 2 patients. Nineteen patients (19/20, 95%) received acetylsalicylic acid and prophylactic anticoagulation was prescribed in 15/20 (75%) of patients.
The mean follow up was 50 days (14 – 122). At the last follow-up visit all patients had normal laboratory parameters of inflammation, troponin, pro-BNP, d-dimer values and normal heart function.

Table 1. Clinical characteristics.

	n *(%)*
Fever n *(%)*	20 (100)
Fever duration (days) [min; max]	*5.9 [4; 8]*
Headache	8 (40)
Lymphadenopathy	15 (75)
Chest pain	6 (30)
Tachycardia	16 (80)
Gastrointestinal involvement	19 (95)
• Abdominal pain	16 (80)
• Vomiting	11 (55)
• Diarrhoea	9 (45)
• Loss of apetite	18 (90)
Cough	7 (35)
Skin and mucous involvement	14 (70)
• Rash	12 (60)
• Palmar/plantar oedema	3 (15)
• Lip and mouth changes	12 (60)
• Bilateral conjunctivitis	14 (70)
Myocarditis	19 (95)

Conclusion. A very high incidence of MIS-C, estimated 5.8/100 000 persons under the age of 19 with a predominantly cardiac involvement but very good outcome was noted in European Caucasian population in a nationwide cohort study in Slovenia. Attention to newly described pancreatic involvement should be raised.



Conclusion: A very high incidence of MIS-C, estimated 5.8/100 000 persons under the age of 19 with a predominantly cardiac involvement but very good outcome was noted in European Caucasian population in a nationwide cohort study in Slovenia. Attention to newly described pancreatic involvement should be raised.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3022

POS1319 RAYNAUD'S PHENOMENON IN A SINGLE CENTER COHORT OF TURKISH CHILDREN

Ş. Çağlayan[1], F. Demir[1], B. Sancar[1], K. Ulu[1], T. Coşkuner[1], B. Sözeri[1]. [1]*Health Sciences University, Umraniye Traning and Research Hospita, Pediatric Rheumatology, Istanbul, Turkey*

Background: Raynaud's phenomenon (RF) is a vasospastic condition characterized by episodic color changes of blanching, cyanosis, and hyperemia of the extremities of the body

Objectives: We aim to examine the clinical presentation, capillaroscopic findings and disease associations of Raynaud's phenomenon (RP) in pediatric patients

Methods: We retrospectively enrolled a single-center cohort of 247 consecutive pediatric patients with RP admitted to Umraniye Training and Research Hospital, Pediatric Rheumatology Clinic, Istanbul, Turkey, since 2016. Medical records were analyzed for clinical presentation, disease associations, and physical examination and laboratory findings.

Results: We reported 247 patients (152 female, 95 male) with RP. Their mean age at disease onset was 14.5±2.55 years and median age at diagnosis was 15.4± 2.21 years. In patients with secondary RP syndrome (10.9%), the age of complaint was found to be lower than others (p=0.03). Although most patients have affected upper extremity (hand and fingers), lower extremity (toes) involvement was also detected in 50 (20%) patients. In both the patients with primary and secondary RP, main triggering factor was found as cold exposure. Biphasic (53.6%) color changes were more seen in primary RP, although triphasic (51.8%) color changes were more in patients with secondary RP (p=0.00). The presence of antinuclear antibodies and abnormal nailfold capillaries were more seen in patients with secondary RP (28% vs 74% and 35.3% vs 66.7, respectively p=0.00). Digital ulcer was detected 5.2% of patients (mostly secondary). Out of 247, 31 patients were treated with low-dose aspirin, 47 with calcium blockers, 25 with low-dose aspirin and calcium blockers, 16 with iloprost and/or bosentan, while the remaining 140 did not receive any drug.

Conclusion: Similar to adults, RP is more common in girls without an underlying disease. In patients with secondary RP, the symptoms. It has been shown that in patients with secondary RP, symptoms begin at a younger age and the ANA positivity and abnormal nailfold capillaries correlate.

REFERENCES:

[1] Jones G, et al. Arthritis Rheum 2003;48:3518–352
[2] Garner R et al. BMJ Open. 2015; 5(3): e006389
[3] Nigrovic PA et al. Pediatrics 2003, 111 (4) 715-721

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3076

POS1320 DIFFERENCES IN CLINICAL MANIFESTATION AND DISEASE ACTIVITY OF PEDIATRIC BEHÇET DISEASE: A CROSS-SECTIONAL COHORT COMPARISON BETWEEN TURKEY AND UNITED STATES

E. Demirkaya[1], M. Romano[1], C. Swearingen[2], O. Kasapcopur[3], B. Makay[4], S. Özen[5], Y. Yazici[6]. [1]*Schulich School of Medicine & Dentistry, University of Western Ontario, Paediatric Rheumatology, LONDON, Canada*; [2]*NYU Hospital for Joint Disease, Rheumatology, New YorK, United States of America*; [3]*Istanbul University-Cerrahpasa, Paediatric Rheumatology, Instanbul, Turkey*; [4]*Dokuz Eylul University, Paediatric Rheumatology, Izmir, Turkey*; [5]*Hacettepe University, Ankara, Paediatric Rheumatology, Ankara, Turkey*; [6]*New York University School of Medicine, Rheumatology, New YorK, United States of America*

Background: Behçet disease (BD) is a systemic inflammatory disease which is rare in children. It is also known a higher prevalence along the ancient Silk Road and the eastern Mediterranean, especially in Turkey. Despite the presence of diagnostic criteria, the diagnosis of pediatric BD is still difficult due to atypical findings and the heterogeneity of the disease. While descriptive cohort studies in pediatric BD exist, direct comparison studies of clinical manifestations and disease activity between patients from different countries are scarce.

Objectives: We aimed to compare the main clinical features and activity of pediatric BD patients from Turkey versus United States (US).

Methods: The BD was diagnosed before 18 years of age and based on expert opinion. Disease activity was assessed with Physician Global Assessment (PhGA), Parents/Patient Global Assessment (PWPGA) and Behçet's Syndrome Activity Scale (BSAS) were administered to patients from both countries.

Results: A total of 161 patients were included (61 from Turkey; 100 from US). Males were more prevalent among patients from Turkey than among patients from US (63.9% vs. 32%, respectively, $p < 0.001$). Disease duration at the diagnosis was significantly longer in US p=0.002). Oral aphthosis was the most common symptom in both groups (96.7% for Turkey and 73% for US), however a significant difference was found (p<0.001). Genital ulcers were documented in 47% of US patients and in 41.4% of Turkish patients (p=0.5). There were significant difference between two groups with regards to the ocular involvement: uveitis and posterior uveitis were more frequently in Turkish patients (p=<0.001 respectively) while retinal vasculitis was no seen in US patients (p<0.001). Erythema nodosum occurred more frequently in Turkish group (p<0.001). The pathergy test was reported as positive in 22 (37.3%) patients in Turkey and 2 (2.3%) in USA in our study (p<0.001). Gastrointestinal and neurological involvement did not differ between cohorts. The rate of colchicine and oral steroids was similar. Azathioprine, cyclosporine and methotrexate usage was more frequent in Turkey (p=0.005, p=0.007, p=0.033, respectively) and infliximab was administered just in the US cohort ($p = 0.002$). PhGA and BSAS scores were higher in patients from Turkey (p=0.003 and p=0.017 respectively) and no significant differences were seen in PWPGA scores.

Conclusion: Disease activity and clinical features seem to be different between the two countries which may be linked to the environmental factors, referral patterns and immune system responses in the expression of this disease. The diagnosis of BD in the US was based on both fulfilling the ISBD criteria and in cases when criteria were not met, based on treating physician assessment, which can explain some of the differences in disease presentation. In addition, there were differences in regard to clinical practice and treatment patterns between two countries. Increasing knowledge about heterogeneity of BD will improve the ability of diagnosis, development of new diagnostic criteria, and management of BD.

REFERENCES:

[1] *Butbul Aviel Y et al, Semin Arthritis Rheum. 2020*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3132

POS1321 MENTAL HEALTH SCREENING IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

S. Eulert[1], M. Niewerth[1], J. Hörstermann[1], C. Sengler[1], D. Windschall[2], T. Kallinich[3], J. Grulich-Henn[4], F. Weller-Heinemann[5], I. Foeldvari[6], S. Hansmann[7], H. Baumeister[8], R. Holl[9], D. Staab[3], K. Minden[1,3].
[1]Deutsches Rheuma-Forschungszentrum, Programmbereich Epidemiologie, Berlin, Germany; *[2]St. Josef-Stift Sendenhorst, Abt. für Kinder- und Jugendrheumatologie, Sendenhorst, Germany*; *[3]Charité - Universitatsmedizin Berlin, Klinik für Pädiatrie mit Schwerpunkt Pneumologie und Immunologie, Berlin, Germany*; *[4]Universitätsklinikum Heidelberg, Zentrum für Kinder- und Jugendmedizin, Heidelberg, Germany*; *[5]Klinikum Bremen-Mitte, Prof.-Hess-Kinderklinik, Bremen, Germany*; *[6]Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg, Germany*; *[7]Universitätsklinikum Tübingen, Klinik für Kinderheilkunde und Jugendmedizin, arcT, Tübingen, Germany*; *[8]Universität Ulm, Institut für Psychologie und Pädagogik, Ulm, Germany*; *[9]Universität Ulm, ZIBMT, Institut für Epidemiologie und med. Biometrie, Ulm, Germany*

Background: Mental disorders often begin in the vulnerable phase of adolescence and young adulthood. Young people with chronic diseases are particularly at risk. Early recognition of mental health problems is necessary in order to be able to support those affected in a timely and adequate manner. By implementing a web-based generic screening tool for mental health in routine care, patients with juvenile idiopathic arthritis (JIA) and mental health conditions can be identified and provided with targeted treatment.
Objectives: To investigate the prevalence of mental health conditions in young people with JIA in routine rheumatology care.
Methods: Mental health screening is implemented as an add-on module to the National Paediatric Rheumatology Database (NPRD). The current data was gathered over a period of 24 months. Patients complete the screening tool which includes the Patient Health Questionnaire[1] (PHQ-9, score 0-27) and the Generalized Anxiety Disorder scale[2] (GAD-7, score 0-21) via a web-based questionnaire. The cut-off for critical values in PHQ-9 and GAD-7 were defined as values ≥ 10. Simultaneously, other data, such as sociodemographic data, disease activity (cJADAS10, score 0-30), functional status (CHAQ, score 0-3) were collected as well.
Results: The analysis included 245 patients (75% female) with a mean age of 15.7 years and a mean disease duration of 8.8 years. 38.8% of the patients had oligoarthritis (18.0% OA, persistent/20.8% OA, extended) and 23.3% RF negative polyarthritis. At the time of documentation 49 patients (30.6%) had an inactive disease (cJADAS10 ≤ 1) and 120 (49.4%) no functional limitations (CHAQ = 0). In total, 53 patients (21.6%) had screening values in either GAD-7 or PHD-9 ≥10. Patients with critical mental health screening values showed higher disease activity and more frequent functional limitations than inconspicuous patients (cJADAS10 (mean ± SD): 9.3 ± 6 vs. 4.9 ± 4.9; CHAQ: 0.66 ± 0.6 vs. 0.21 ± 0.42). When compared to males, females were significantly more likely to report either depression or anxiety symptoms (11.7% vs. 24.9%, p = 0.031).
17.6% of all patients with valid items for these data reported to receive psychological support, meaning psychotherapeutic support (14.5%) and/or drug therapy (8.6%). Among those with a critical mental health screening score, 38.7% received psychological support (psychotherapeutic support (35.5%) and/or drug therapy (16.1%)).
Conclusion: Every fifth young person with JIA reported mental health problems, however, not even every second of them stated to receive psychological support. The results show that screening for mental health problems during routine adolescent rheumatology care is necessary to provide appropriate and targeted support services to young people with a high burden of illness.
REFERENCES:
[1] Löwe B, Unützer J, Callahan CM, Perkins AJ, Kroenke K. Monitoring depression treatment outcomes with the patient health questionnaire-9. Med Care. 2004 Dec;42(12):1194-201.
[2] Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006 May 22; 166(10):1092-7.
[3] The screening data were collected as part of COACH (Conditions in Adolescents: Implementation and Evaluation of Patient-centred Collaborative Healthcare), a project supported by the Federal Ministry of Education and Research (FKZ: 01GL1740F).
Disclosure of Interests: Sascha Eulert: None declared, Martina Niewerth: None declared, Jana Hörstermann: None declared, Claudia Sengler: None declared, Daniel Windschall: None declared, Tilmann Kallinich: None declared, Jürgen Grulich-Henn: None declared, Frank Weller-Heinemann Consultant of: Pfizer, Abbvie, Sobi, Roche, Novartis, Ivan Foeldvari Consultant of: Gilead, Novartis, Pfizer, Hexal, BMS, Sanofi, MEDAC, Sandra Hansmann: None declared, Harald Baumeister: None declared, Reinhard Holl: None declared, Doris Staab: None declared, Kirsten Minden: None declared
DOI: 10.1136/annrheumdis-2021-eular.3249

POS1322 A DATA SCIENCE EVALUATION OF THE JUVENILE ARTHRITIS MULTIDIMENSIONAL ASSESSMENT REPORT (JAMAR) QUESTIONNAIRE FOR IMPROVING MANAGEMENT OF JIA PATIENTS

H. Quesada-Masachs[1], M. Faloutsos[1], M. López- Corbetó[2], S. Ghose[3], S. Marsal[4], E. Quesada-Masachs[2]. *[1]University of California Riverside, Computer Science & Engineering, Riverside, United States of America*; *[2]Hospital Universitari Vall d'Hebron, Rheumatology, Pediatric Rheumatology Unit, Barcelona, Spain*; *[3]University of California Berkeley, University of California Berkeley, Berkeley, United States of America*; *[4]Hospital Universitari Vall d'Hebron, Rheumatology, Barcelona, Spain*

Background: The Juvenile Arthritis Multidimensional Assessment Report (JAMAR) is a questionnaire developed to comprehensively assess Juvenile Idiopathic Arthritis (JIA) patients. Despite being translated into 54 languages, there is still limited literature about it. The length of the questionnaire could have been influencing its clinical practicality.
Objectives: The purpose of this study is to answer the following questions:
a)"Which are the most informative questions?";
b)"How well do the collected data correlate with other clinical variables?";
c)"Are there discrepancies between the perceptions of patients and parents?";
Methods: We included 71 children with JIA according to ILAR criteria, all of them receiving treatment and we followed them up for a year. JAMAR questionnaires were answered by both children and parents at baseline, 6 and 12 months. Also, a thorough clinical examination was performed in every visit: all the joints were clinically assessed for swelling, tenderness, and limited range of motion, and Juvenile Arthritis Disease Activity Score (JADAS), disease activity state, parents and patients assessment through Visual Analogue Scale (VAS), physician's VAS, Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) were recorded. We applied state of the art machine learning methods in order to find the most relevant questions in JAMAR. Additionally, we utilized tensor decomposition to identify relevant patient clusters. Furthermore, we correlated these critical questions with clinical and biological parameters recorded. We have compared the discordance rate between patients vs parents responses in 5 of JAMAR parameters as previously reported [1]. We explored the relation between discordance and demographic and clinical variables.
Results: A total of 374 JAMAR questionnaires are analyzed with our Machine Learning algorithms. First, we identify a small group of questions as the most relevant for patients and parents. The identified questions exhibit better correlations with the JADAS scores than the non-relevant ones. Second, 96% of the pairs (child-parent) are discordant for at least one item, but the differences are small and VAS well being is the only score with a statistically significant difference ($P < 0.0001$). We observe a higher rate of activity in the patients exhibiting discordant evaluations with their parents. In addition, the observation patient-parent agreement in Juvenile Arthritis Functionality Scale (JAFS) is better than Pediatric Rheumatology Quality of Life Scale (PRQL).
Conclusion: In this study, we revisited the JAMAR questionnaire by applying modern data mining techniques in a longitudinal dataset. Our results suggest that a small number of questions in the JAMAR questionnaire provide significant information and correlate well with the JADAS scores. We argue that this reduced set of questions could make the data collection easier by trading off the number of questions for frequency and ease of self-reported data collection.
REFERENCES:
[1] Vanoni F, et al. The difference of disease perception by juvenile idiopathic arthritis patients and their parents: analysis of the JAMAR questionnaire. *Pediatr Rheumatol Online J*. 2016;14(1):2.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3319

POS1323 SACROILIAC JOINT MRI ABNORMALITIES IN JUVENILE SPONDYLOARTHRITIS: AN UPDATE OF DEFINITIONS AND SCORING OF THE OMERACT JUVENILE IDIOPATHIC ARTHRITIS MRI SCORE

T. M. Otobo[1,2,3], N. Herregods[4], J. L. Jaremko[5], R. G. Lambert[5], I. Sudoł-Szopińska[6], A. B. Meyers[7], E. Kirkhus[8], P. Weiss[9], S. M. Tse[10], S. Appenzeller[11], P. G. Conaghan[12], D. G. Rumsey[13], J. Stimec[1], L. Jans[4], M. Van Rossum[14], N. Tzaribachev[15], J. Carrino[16], O. Papakonstantinou[17], M. Tolend[1,2,3], R. Moineddin[18], N. Haroon[19,20], W. P. Maksymowych[21], A. S. Doria[1,3,22]on behalf of Outcome Measure in Rheumatology Juvenile Idiopathic Arthritis MRI - Sacroiliac Joint Special Interest Group (OMERACT JAMRI-SIJ). *[1]Hospital for Sick Children, Diagnostic Imaging, Toronto, Canada*; *[2]University of Toronto, Institute of Medical Science, Toronto, Canada*; *[3]Hospital for Sick Children Research Institute, Translational Medicine, Toronto, Canada*; *[4]Prinses Elisabeth Children's Hospital / Ghent University Hospital, Radiology and Nuclear Medicine, Ghent, Belgium*; *[5]University of Alberta, Radiology and Diagnostic Imaging, Edmonton, Canada*; *[6]National Institute of Geriatrics, Rheumatology and Rehabilitation, Radiology, Warsaw, Poland*; *[7]Cincinnati Children's Hospital Medical Center, Radiology, Cincinnati, United States of America*; *[8]Oslo University Hospital, Radiology, Oslo, Norway*; *[9]Children's Hospital of Philadelphia and*

Center for Clinical Epidemiology and Biostatistics, Department of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Rheumatology, Philadelphia, United States of America; [10]*The Hospital for Sick Children, Rheumatology, Toronto, Canada*; [11]*School of Medical Sciences - University of Campinas, Rheumatology, Campinas, Brazil*; [12]*Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, and NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Rheumatology, Leeds, United Kingdom*; [13]*University of Alberta, Rheumatology, Edmonton, Canada*; [14]*Amsterdam Rheumatology and Immunology Center | Reade and Emma Children's Hospital Amsterdam University Medical Centers, Rheumatology, Amsterdam, Netherlands*; [15]*PRI, Achtern Dieck 7, Rheumatology, Bad Bramstedt, Germany*; [16]*Hospital for Special Surgery, Radiology, New York, United States of America*; [17]*National and Kapodistrian University of Athens, Radiology, Athina, Greece*; [18]*University of Toronto - St. George Campus, Family Medicine, Toronto, Canada*; [19]*University of Toronto - St. George Campus, Medicine, Toronto, Canada*; [20]*Krembil Research Institute, Schroeder Arthritis Institute, Toronto, Canada*; [21]*University of Alberta, Medicine, Edmonton, Canada*; [22]*University of Toronto - St. George Campus, Diagnostic Imaging, Toronto, Canada*

Background: Preliminary definitions for SIJ lesions in the OMERACT Juvenile Idiopathic Arthritis Magnetic Resonance Imaging score has been reported[1]. Investigators identified the need to revise the JAMRIS-SIJ item definitions.
Objectives: To update the JAMRIS-SIJ definitions and scoring method.
Methods: The OMERACT JAMRI working group was convened to discuss the performance of the score in a reliability exercise using 30 patients. Twenty investigators (12 radiologists, 8 rheumatologists) decided which definitions and scoring methods to be revised, retained or added.
Results: The revised JAMRI-SIJ is in the Table 1.

Table 1. Revised OMERACT JAMRIS-SIJ.

Component	Definition	Segmentation/ slice	Score range/ slice
Bone Marrow Edema (BME)	An ill-defined area of high bone marrow signal intensity within the subchondral bone in the ilium or sacrum on fluid sensitive images	4 quadrants/ SIJ	0-8
BME Intensity	Presence of hyperintensity of the marrow on fluid sensitive images using the signal of the presacral veins or cerebrospinal fluid as reference	1 score/SIJ	0-2
BME Depth	Continuing increased signal on fluid sensitive images of depth ≥ 5mm/ ≥ 1cm from the articular surface using the signal of the presacral veins or cerebrospinal fluid as reference	1 score/SIJ	0-2
Osteitis	An ill-defined area of high bone marrow signal intensity within the subchondral bone in the ilium or sacrum on contrast enhanced T1 weighted sequences	4 quadrants/ SIJ	0-8
Capsulitis	Increased signal on fluid sensitive or contrast enhanced T1 weighted sequences involving the superior portion of the SIJ capsule	superior halves/SIJ	0-2
Joint space fluid	High signal intensity equivalent to the CSF on fluid sensitive sequences within the joint space of the cartilaginous portion of the SIJ	halves/SIJ	0-4
Joint space enhancement	Increased signal intensity on contrast enhanced T1 weighted sequences within the joint space of the cartilaginous portion of the SIJ	halves/SIJ	0-4
Inflammation in erosion cavity	Increased signal intensity on fluid sensitive or contrast enhanced T1 weighted sequences in an erosion cavity of the cartilaginous portion of the SIJ	halves/SIJ	0-4
Enthesitis	Increased signal intensity in bone marrow and/or adjacent soft tissue on fluid sensitive or contrast enhanced T1 weighted sequences at sites where ligaments and tendons attach to a bone excluding retroarticular enthesitis	Score per case	0-1
Damage Domain			
Sclerosis	A substantially wider than normal area of very low bone marrow signal intensity within the subchondral bone in the ilium or sacrum on a non-fat suppressed sequence, preferably a non-fat suppressed T1 weighted sequence. This feature must also be present on all other sequences, as available	4 quadrants/ SIJ	0-8
Erosion	A focal loss of the low signal of cortical bone at the osteochondral interface and adjacent marrow matrix on T1 weighted images	4 quadrants/ SIJ	0-8
Fat metaplasia lesion	Homogeneous increased signal intensity within the subchondral bone marrow on T1weighted images	4 quadrants/ SIJ	0-8
Backfill	A high signal on non-contrast enhanced T1 weighted sequences in a typical location for an erosion, with signal intensity greater than normal bone marrow, clearly demarcated from adjacent bone marrow by an irregular band of low signal reflecting sclerosis at the border of the original erosion	halves/SIJ	0-4
Ankylosis	Presence of signal equivalent to regional bone marrow continuously bridging a portion of the joint space between the iliac and sacral bones	halves/SIJ	0-4

Statement of overarching consideration for all definitions: "[…] in comparison to physiological changes normally seen on MRI examinations of age- and sex-matched children, and visible in 2 planes wherever available."

Conclusion: Revised JAMRIS-SIJ has been developed. Validation steps are underway.

REFERENCES:

[1] Otobo TM, et al. Preliminary Definitions for Sacroiliac Joint Pathologies in the OMERACT Juvenile Idiopathic Arthritis Magnetic Resonance Imaging Score (OMERACT JAMRIS-SIJ). The Journal of rheumatology. 2019;46(9):1192-7.

Acknowledgements: The authors acknowledge The Hospital for SickKids Research Trainee Competition (RESTRACOMP) and Queen Elizabeth II/Edward Dunlop Foundation Scholarship In Science and Technology (QEII-GSST) at the University of Toronto for funding provided to Dr. Tarimobo M. Otobo. The authors also acknowledge Prof. Dr. Desiree van der Heijde for providing expert commentary.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3321

POS1324 TREATMENT OF UVEITIS ASSOCIATED WITH JUVENILE IDIOPATHIC ARTHRITIS: A SEVEN YEARS' SINGLE-CENTRE EXPERIENCE

E. Gaidar[1], A. Kononov[2], E. Isupova[2], M. Kostik[3], O. Kalashnikova[4], T. Nikitina[5], E. Sinelnikova[4], V. Chasnyk[4]. [1]*Saint-Petersburg State Pediatric Medical University, Hospital Pediatrics, Sankt-Peterburg, Russian Federation*; [2]*Saint-Petersburg State Pediatric Medical University, Hospital Pediatrics, Sankt-Peterburg, Russian Federation*; [3]*Saint-Petersburg State Pediatric Medical University, Hospital Pediatrics, Sankt-Peterburg, Russian Federation*; [4]*Saint-Petersburg State Pediatric Medical University, Hospital Pediatrics, Sankt-Peterburg, Russian Federation*; [5]*Saint-Petersburg State Pediatric Medical University, Ophthalmology, Sankt-Peterburg, Russian Federation*

Background: Uveitis (U) is one of the most common extra-articular manifestation of juvenile idiopathic arthritis (JIA). It is usually revealed in 10-20% of children with JIA, often asymptomatic and sometimes the onset of U precedes the onset of arthritis. Being inappropriately treated, U leads to vision loss in up to 20% of children. Despite the efforts of the Standardization of Uveitis Nomenclature (SUN) Working Group and the European initiative Single Hub and Access point for pediatric Rheumatology in Europe (SHARE) which optimized management of JIA-associated U [1], the actual treatment is mostly based on physicians' experience. Initial treatment typically includes topical glucocorticoids (G) or systemic immunosuppressive therapy if topical G don't work. Methotrexate (MTX) is the first-line systemic immunosuppressive agent, followed by tumor necrosis factor inhibitors (TNFi) [1,2].
Objectives: To provide treatment recommendations for JIA-associated U based on monitoring of 221 patients during 7 years.
Methods: Data collected during 2240 hospitalisations of 221 patients aged 3 - 17 years treated at the State Pediatric Medical University in years 2014 - 2020 were analyzed. U and JIA were diagnosed according to the SUN and ACR recommendations. Initial treatment of U included topical G or non-steroidal anti-inflammatory drugs (NSAIDs). Treatment of JIA included systemic NSAIDs, cytostatics (MTX, Cyclosporine or Cyclophosphamide) and biologics: Adalimumab (Ada), Infliximab (Inf), Etanercept (Eta), Abatacept (Aba), Tocilizumab (Toc), Golimumab (Gol). Statistical analysis included traditional Descriptive Statistics, Spearman Rank Order Correlation (SROC) and Multivariate Exploratory Techniques [Statistica for Windows, Statsoft].
Results: Of all patients with JIA-associated U the proportion of those treated with biologics during the monitoring increased from 60 to 70% (of them, Ada 79 - 93%, Inf 7 - 1%, Eta 5 - 1%, Aba 7 - 3%, Toc 7 - 0%, Gol 0 - 3%). Of all children in whom U was diagnosed later than arthritis 36% were treated with systemic NSAIDs, 25% - with cytostatics (MTX - 84%, Cyclosporine - 8%, Cyclophosphamide - 8%), 23% - with systemic G, 6% - with biologics (Eta - 83%, Toc - 17%). Of patients in whom U and arthritis were diagnosed simultaneously, 95% were treated with cytostatics (MTX - 95%, Cyclosporine - 15%), 93% - with topical G, 91% - with topical NSAIDs, 81% - with systemic G, 60% - with systemic NSAIDs. Efficacy of treatment in terms of SROK showed evidence of steady improvement already after 1 month of therapy with TNFi or with MTX (increase of r during the first year from 0.37 to 0,62, $p<0.02$; from 0.37 to 0.55, $p<0.05$ respectively), though r was never higher than 0.84 during the first 3 years of treatment. Topical NSAIDs and G were less effective: improvement was revealed after 3 months of treatment, it was not so steady and r was never higher than 0.35. Systemic NSAID's were not effective at all.
Conclusion: 1. The likelihood of improvement of U treated with TNFi (Eta excepted) after one month, after 1 and after 3 years of therapy was 37%, 62% and 84% respectively. For MTX this likelihood was 37% after 1 month and 55% after 3 months.
2. TNFi (Eta excepted) in treatment of JIA prevents the onset of U, thereby supposing its early administration.

3. Eta neither prevents nor treats U.
4. Topical NSAIDs and G can hardly be recommended as a reliable means for treatment of U without TNFi and MTX.
5. Systemic NSAIDs neither prevent nor treat JIA-associated U.

REFERENCES:

[1] Constantin T, Foeldvari I, Anton J, et al. Consensus-based recommendations for the management of uveitis associated with juvenile idiopathic arthritis: the SHARE initiative Ann Rheum Dis 2018;77:1107–1117
[2] Angeles-Han ST, Ringold S, Beukelman T, Lovell D et al., 2018 American College of Rheumatology/Arthritis Foundation Guideline for the Screening, Monitoring, and Treatment of Juvenile Idiopathic Arthritis-Associated Uveitis. Arthritis Care Res (Hoboken). 2019 June; 71(6): 703–716

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3327

POS1325 COMPARISON OF THREE DIFFERENT ALGORITHMS FOR THE TREATMENT OF CHILDREN WITH POLYARTICULAR JIA: THE FIRST YEAR AFTER DIAGNOSIS

K. Minden[1,2], T. Schwarz[3], F. Dressler[4], I. Foeldvari[5], J. P. Haas[6], G. Horneff[7], T. Hospach[8], J. Kümmerle-Deschner[9], K. Moenkemoeller[10], F. Weller-Heinemann[11], K. Tenbrock[12], M. Niewerth[1], C. Sengler[1], D. Foell[13], J. Klotsche[1]. *[1]Deutsches Rheuma-Forschungszentrum Berlin, Epidemiology, Berlin, Germany*; *[2]Charité Universitätsmedizin Berlin, Paediatric Rheumatology, Berlin, Germany*; *[3]St-Josef-Stift Sendenhorst, Paediatric Rheumatology, Sendenhorst, Germany*; *[4]MHH, Kinderklinik, Hannover, Germany*; *[5]Hamburg Center for Pediatric and Adolescent Rheumatology, Pediatric and Adolescent Rheumatology, Hamburg, Germany*; *[6]Deutsches Zentrum für Kinder- und Jugendrheumatologie, Kinder- und Jugendrheumatologie, Garmisch-Partenkirchen, Germany*; *[7]Asklepios Kinderklinik, Paediatric Rheumatology, St. Augustin, Germany*; *[8]Olgahospital Stuttgart, Paediatric Rheumatology, Stuttgart, Germany*; *[9]Universitätskinderklinik Tübingen, Paediatric Rheumatology, Tübingen,*; *[10]Kinderkrankenhaus Amsterdamer Straße, Paediatric Rheumatology, Köln, Germany*; *[11]Klinikum Bremen Mitte, Prof. Hess Kinderklinik, Bremen, Germany*; *[12]Universitätsklinikum Aachen, Kinder- und Jugendmedizin, Aachen, Germany*; *[13]Universitätsklinikum Münster, Klinik für Pädiatrische Rheumatologie und Immunologie, Münster, Germany*

Background: Various treatment strategies are used for children with newly diagnosed polyarticular JIA. MTX is usually prescribed, sometimes in combination with high-dose intravenous glucocorticoid pulses (HDGC) or multiple intra-articular GC injections (IAGC). These different approaches were considered in the German consensus-based treatment protocols for polyarticular JIA[1], they were also the leading therapies in patients with rheumatoid factor-negative polyarthritis (RF- PA) included in the JIA inception cohort ICON.

Objectives: To compare the effectiveness of three different treatment strategies in nearly DMARD-naïve patients with RF- PA.

Methods: Patients with RF- PA who were included in the ICON cohort and received one of the following treatments within the first three months were considered for the analysis: Group 1: MTX + IAGC in >4 joints, Group 2: MTX + HDGC, Group 3: MTX, no IAGC in >4 joints, no HDGC. Propensity score-adjusted group differences in outcomes after one and two years were analysed by linear and logistic regression analyses.

Results: The analysis included data from 150 patients (79% female, mean age 6.7±4.8 years) enrolled in ICON 1.6±1.9 months after the diagnosis of RF- PA, of whom 52 were in Group 1, 54 in Group 2 and 44 in Group 3. Disease activity did not differ significantly between the groups at treatment start (cJADAS-10 16.7±4.7, 15.8±5.7, 15.9±6.5, respectively).

Of the total group, at 1- and 2-year follow-up (FU), 60.9%/60.1% and 52.3%/58.8% of patients had inactive disease (cJADAS ≤1/Wallace criteria[2]), 21.3% and 35.6% were in remission off drug[2], and mean cJADAS-10 scores were 2.6±3.9 and 3.0±3.5, respectively. 60.5% and 67.0% had no functional limitations (CHAQ=0).

Patients in Group 1 more often had an inactive disease (according to Wallace[2]) at the 1-year FU and tended to have inactive disease more often at 2-year FU than patients in Group 3 (78.1% vs. 45.2%, p=0.025; 73.3 vs. 49.1%, p=0.075, respectively). Group 2 patients (inactive disease in 56.1% and 53.4% at 1- and 2-year FU) did not differ significantly from either Group 1 or Group 3. In addition, Group 1 patients had a significantly better quality of life than patients of Group 2 at the 2-year FU (mean PedsQL 4.0 total score 90.4±9.3 vs. 83.8±11.2, p=0.031). At that time, Group 3 patients had a mean PedsQL 4.0 total score of 85.0±14.6, which was not significantly different from either Group 1 or 2.

On the other hand, Group 1 patients tended to develop new uveitis more frequently within the first two years of treatment than patients in Groups 2 and 3 (13% vs. 2.2% and 3.6%, p=0.101 and 0.131, respectively). At the 2-year FU, patients in Group 1 also had a significantly lower mean height SDS than patients of Group 3 (-0.3±1.1 vs. 0.2±1.1, p=0.038). Mean height SDS was lowest (-0.5±0.8) in patients in Group 2 and significantly lower than in Group 3 (0.019). Mean body mass index SDS also differed significantly between the groups at 2-year follow-up. The mean BMI SDS was highest in Group 1 patients (0.2±0.8), differing significantly from Group 2 (-0.3±0.7, p=0.014) and Group 3 (-0.4±1.1, p=0.023).

There were no significant differences in inactive disease (according to cJADAS) and functional status (CHAQ) between the three groups at 1- and 2-year FU. Over time, treatments were very different in the three groups. In Group 3, biologics were used significantly more often over time than in group 1 (54.0% vs. 18.3%, p=0.014), and Group 2 patients received bDMARDs in 36.1%.

Conclusion: While patients with numerous early joint injections seem to achieve inactive disease more frequently and earlier, they have a slightly smaller body height and tend to develop uveitis slightly more often than patients with more intensive DMARD therapy. However, the differences are small between the groups. Further comparative effectiveness studies with higher patient numbers are needed to identify particularly effective and safe treatment strategies.

REFERENCES:

[1] Horneff et al. Pediatric Rheumatology 2017;15:78.
[2] Wallace et al. Arthritis Care Res (Hoboken) 2011;63:929-36.

Acknowledgements: The ICON study is funded by a research grant of the Federal ministry of education and research (BMBF, FKZ 01ER0812, FKZ 01ER1504A-C).

Disclosure of Interests: Kirsten Minden Speakers bureau: Pfizer, Abbvie, Consultant of: Novartis, Tobias Schwarz: None declared, Frank Dressler: None declared, Ivan Foeldvari Consultant of: Gilead, Novartis, Pfizer, Hexal, BMS, Sanofi, MEDAC, Johannes-Peter Haas: None declared, Gerd Horneff Speakers bureau: Pfizer, Consultant of: Novartis, Toni Hospach Consultant of: Novartis, Jasmin Kümmerle-Deschner: None declared, Kirsten Moenkemoeller: None declared, Frank Weller-Heinemann Speakers bureau: Pfizer, AbbVie, SOBI, Roche, Novartis, Klaus Tenbrock: None declared, Martina Niewerth: None declared, Claudia Sengler: None declared, Dirk Foell: None declared, Jens Klotsche: None declared

DOI: 10.1136/annrheumdis-2021-eular.3448

POS1326 FAMILIAL PERIODIC FEVER, APHTHOUS STOMATITIS, PHARYNGITIS AND ADENITIS (PFAPA)SYNDROME; IS IT A SEPARATE DISEASE?

Y. Butbul[1]. *[1]1The Ruth and Bruce Rappaport Faculty of Medicine,Technion - Israel Institute of Technology, Haifa, Israel, Pediatric Rheumatology unit, Haifa, Israel*

Background: Periodic fever, aphthous stomatitis, pharyngitis, and adenitis syndrome (PFAPA) is the most common periodic fever syndrome in the pediatric population. Unlike other periodic fever syndromes, the pathogenesis and genetics of PFAPA is unknown. Until recently, PFAPA was believed to be a sporadic disease, yet family clustering has been widely observed and current research indicates that heredity is likely.

Objectives: To identify demographic and clinical differences between patients with PFAPA who have a positive family history (FH+) compared to those with PFAPA with no family history (FH-) that can reveal if heritable and sporadic subtypes of this disorder exist.

Methods: In a database comprising demographic and clinical data of 273 pediatric PFAPA patients treated at two tertiary centers in Israel, 31(14.3%) of patients were PFAPA FH+. Data from patients with FH+ for PFAPA was compared to data from those with FH- of the disorder. Furthermore, family members (FMs) of those with FH+ were contacted via telephone for more demography and clinical details.

Results: FH+ group had more headaches (32% vs.2%; p= 0.016), myalgia (56% vs. 19%; p= 0.001), higher carrier frequency of M694V mutation (54% vs. 25%; p=0.053), greater family history of FMF (30% vs. 15%; p=0.096) and better outcomes with colchicine (82% vs. 52%; p=0.096) compared to those with FH-. FMs displayed almost identical characteristics to the FH+ group except for greater arthralgia during flares (64% vs. 23%; p=0.008) and compared to the FH- group, more oral aphthae (68% vs. 43%; p=0.002), myalgia/arthralgia (64% vs. 19%/16%; p<0.0001), and higher rates of FH of FMF (45% vs.15%; p=0.003).

Conclusion: Our findings suggest that FH+ had probably different subset of disease with higher frequency of family history of FMF arthralgia, myalgia and better response to colchicine. Colchicine prophylaxis for PFAPA should be considered in FH+.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3458

POS1327 DO JIA PATIENTS RESPONSE TO RE-TREATMENT AFTER A FLARE DURING TAPERING OF BDMARDS? A DESCRIPTIVE STUDY

A. García Fernández[1], A. Briones-Figueroa[1], L. Calvo Sanz[1], Á. Andreu-Suárez[1], A. Boteanu[1]. [1]*Hospital Universitario Ramón y Cajal, Rheumatology, Madrid, Spain*

Background: Tapering and withdrawal of biological DMARDs (bDMARDs) is often attempted in Juvenile Idiopathic Arthritis (JIA) patients but data about response to re-treatment after an unsuccessful tapering are scarce.
Objectives: Our aim is to assess response to re-treatment after a disease flare during tapering or withdrawal of bDMARDs and to describe re-treatment strategies.
Methods: A retrospective, descriptive study was conducted in a cohort of JIA patients followed up in a referral hospital and who had received bDMARDs between 2000 and 2019. All JIA patients with at least one flare during tapering or withdrawal were included. Response to re-treatment was defined as achieving Wallace criteria for remission for 6 months.
Results: A total of 142 flares during tapering or withdrawal were identified and included. In 3/142 (2.1%) patients bDMARDS were not re-started after a flare, 1 due to patient refusal, 2 due to unplanned pregnancy. Main characteristics according to tapering strategies are reported in Table 1.

Table 1. Main characteristics according to tapering strategies. Apso, Psoriatic Arthritis; ERA, Enthesitis related Arthritis; OligE, Oligoarticular Extended; OligP, oligoarticular persistent; Poly RF+, polyarticular rheumatoid factor positive; PolyRF-, polyarticular rheumatoid factor negative; sJIA, Systemic JIA; Und, Undifferenciated.

	Tapering	Withdrawal
Cases, n (%)	80 (57.5)	59 (42.4)
Female, n (%)	57 (71.3)	36 (61)
Age at diagnosis,years, median (IQR)	5 (2-11)	4 (2-11)
Age at start of tapering or withdrawal, years, median (IQR)	17 (11-25)	16 (8-29)
Categories, n (%)		
OligP	19 (23.8)	12 (20.3)
OligE	15 (18.8)	13 (22)
sJIA	10 (12.5)	11 (18.6)
ERA	12 (15)	8 (13.6)
Apso	7 (8.8)	6 (10.2)
Poly RF+	9 (11.3)	4 (6.8)
Poly RF-	7 (8.8)	3 (5.1)
Und	1 (1.3)	2 (3.4)
Uveitis, n (%)	24 (30)	16 (27.1)
Laboratory values, n (%)		
- RF	15 (18.8)	5 (8.5)
- ANA	45 (56.3)	33 (55.9)
cDMARDs at start of tapering, n (%)	40 (50)	20 (33.9)
bDMARD target, n (%)		
- TNF inhibitors	63 (78.8)	45 (76.3)
- IL6-blockers	14 (17.5)	5 (8.5)
- IL1-blockers	2 (2.5)	7 (11.9)
- Rituximab	1 (1.3)	2 (3.4)
Line of bDMARD, n (%)		
- First	50 (62.5)	45 (76.3)
- Second	18 (22.5)	10 (16.9)
- Third	5 (6.3)	2 (3.4)
- Forth	6 (7.5)	2 (3.4)
- Fifth	1 (1.3)	0 (0)
Time in bDMARD treatment, months median (IQR)	28.4 (13.3-52.5)	28.2 (13.9-44.6)
Remission prior tapering or withdrawal,months median (IQR)	8 (6-12)	8 (6-12)

Fifty-nine out of 80 (73.8%) tapering cases were on remission at 6 months (6m) and 42/80 (52.5%) at 12 months (12m). Regarding dosage schedule adjustments, interval widening was the most frequent in 70/80 (87.5%) followed by combined strategy in 7/80 (8.8%) and lower dosage in 3/80 (3.8%). Median remaining dosage administrated was 54.9% IQR(50-75). Median time to flare was 14.9 months IQR (5.6-24.7). Median time to re-start of bDMARDs was 0 months min-max(0-13).
After withdrawal of bDMARDs 23/59 (39%)cases at 6m and 14/59 (23.7%) cases at 12m were on remission. Median time to flare was 4.7 months IQR (2.8-11.4). Median time to re-start of bDMARDs was 1 month min-max (1-6).
Most frequent re-treatment strategies were re-start of standard dosage [tapering 42/80 (52.5%), withdrawal 34/59 (57.6%)], re-start of previous effective dosage [tapering 28/80 (35%), withdrawal 11/59 (18.6%)], change of bDMARD [tapering 6/80 (7.5%), withdrawal 6/59 (10.2), re-start of bDMARD and cDMARD [tapering 4/80 (5%), withdrawal 6/59 (10.2)] and re-start of cDMARD [tapering 0/80 (0), withdrawal 1/59 (1.7%)].
Overall response to re-treatment was 75/80 (93.8%) and 53/58 (91.4%) among tapering and withdrawal, respectively. In 12/139 (8.6%) patients bDMARD was changed, achieving remission in 11/12 (91.7%) cases. No factors were associated with response to re-treatment and there were no differences between re-treatment strategies and re-achieving remission (p=0.596).
Conclusion: Response to re-treatment was high (92.7%), no risk factors were identified. Most frequent retreatment strategy was re-start of standard bDMARD dosage in 76/139 (54.7%) followed up by restart of previous effective bDMARD dosage in 39/139 (28.1%).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3525

POS1328 HAVE THE CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS AN EXCESS OF ADIPOSITY?

G. Diaz-Cordobes[1], S. Aguado Henche[2], L. Martín Pedraz[3], R. Galindo Zavala[3], N. Mena-Vázquez[4], E. Núñez Cuadros[3]. [1]*Instituto de Investigación Biomédica de Málaga (IBIMA). Hospital Regional Universitario de Malaga. Universidad de Malaga, Reumatología, Málaga, Spain*; [2]*Universidad de Alcalá. Facultad de Medicina, Departamento de Anatomía y Embriología Humana, Madrid, Spain*; [3]*Hospital Materno Infantil. Hospital Regional Universitario de Mälaga, Pediatria., Málaga, Spain*; [4]*Instituto de Investigación Biomédica de Málaga (IBIMA). Hospital Regional Universitario de Malaga. Universidad de Malaga, Reumatología, Màlaga, Spain*

Background: In recent years, several studies show contradictory results regarding body composition in juvenile idiopathic arthritis. Adiposity in Rheumatoid Arthritis and Psoriasic Arthritis has been associated to inflammatory activity, but it is not clear what happens in JIA.
Objectives: To describe the body composition and anthropometric parameters of patients with JIA compared with healthy controls and analyze associated risk factors in JIA patients.
Methods: Observational cross-sectional study in spanish children aged 4-15 years with JIA compared with healthy controls matched for age and sex. We recorded epidemiological variablesanthropometric parameters, clinical data and validated physical activity questionnaires. Body composition was measured using dual-energy x-ray absorptiometry (DXA), and included total mass (kg), fat mass (g), lean mass (g), and lean mass and android and gynoid fat mass. The fat mass index (FMI) was defined as fat mass (kg)/height squared (m^2) and fat-free mass index (FFMI) as fat-free mass (kg)/height squared (m^2). Descriptive, bivariete and two multivariate models were constructed to identify factors associated with obesity and fat mass in JIA patients.
Results: We analyze 160 subjects: 80 patients with JIA and 80 healthy controls. The baseline characteristics of both groups are shown in Table 1. No differences were found between both groups in BMI (p=0.936), fat mass (p = 0.449), lean mass (p = 0.793) and in fat and lean mass of legs, arms and trunk, or in physical activity questionnaire (p = 0.582). The factors associated with obesity in patients with JIA were: time with biological drug (OR [95% CI] = 1.12 [1.01-1.04]; p = 0.042) and sedentary lifestyle (OR [95% CI] = 3.50 [1.18-7.35]; p = 0.023); while the factors associated with the fat mass index were: age (ß [95% CI] = 0.30 [0.16-1.41]; p= 0.014), inflammatory activity (JDAS) (ß [95% CI] = 0.44 [0.16-1.08]; p= 0.009) and physical activity (ß [95% CI] = -0.22 [-0.10,-0.28]; p = 0.031).

Table 1. Baseline characteristics of patients with JIA and controls

Variable	JIA (n=80)	Controls (n=80)	P-value
Sex, girls n (%)	56 (70.0)	57 (71.3)	0.862
Age, mean (SD)	10.7 (3.2)	10.2 (3.2)	0.893
Disease duration (years) JIA, mean (SD)	6.5 (3.7)		
JIA subtype			
Systemic, n (%)	9 (11.3)		
Oligoarticular persistent, n (%)	38 (47.5)		
Oligoarticular extended, n (%)	13 (16.3)		
Rheumatoid Factor-positive polyarticular, n (%)	1 (1.3)		
Rheumatoid Factor-negative polyarticular, n (%)	19(23.8)		
CRP (mg/l), mean (SD)	4,8 (9,5)		
ESR (mm/h), mean (SD)	8.8 (7,3)		
JADAS27, mean (SD)	2 (4.0)		
CHAQ, mean (SD)	0.17 (0.4)		
Treatment			
DMARDs (synthetic), n (%)	42 (52.5)		
DMARDs (biological), n (%)	24 (30.0)		
Anti IL-1, n (%)	4 (16.7)		
Anti IL-6, n (%)	2 (8.3)		
Anti TNF-α, n (%)	18 (75.0)		
Treatment duration			
DMARDs synthetic, (months), mean (±SD)	51 (37.5)		
DMARDs biological, (months), mean (±SD)	19.7 (28.4)		
DMARDs total (months), mean (±SD)	55.8 (38.0)		
Cumulative corticoisteroids dose, median (range)	11.3 (0.12-870)		

Abreviaturas; JIA: juvenile idhipathic arthritis; SD: standart deviation; CRP: C-reactive protein; VSG:erytrocyte sedimentation rate; JADAS27: Juvenile Arthritis Disease Activity Score; CHAQ: Childhood Health Assessment; DMARD: disease-modifyng anti-rheumatic drug.

Conclusion: Children with JIA have adiposity similar to healthy controls. Inflammatory activity measured by JDAS is associated with fat mass but not to anthropometric measurements such as body mass index (BMI).

REFERENCES:

[1] Grönlund et al Juvenile idiopathic arthritis patients with low inflammatory activity have increased adiposity. Scand J Rheumatol 2014.
[2] Giani et al. The Influence of Overweight and Obesity on Treatment Response in Juvenile Idiopathic Arthritis. Front Pharmacol 2019
[3] Wiech et al. Body composition and phase angle as an indicator of nutritional status in children with juvenile idiopathic arthritis. Pediatric Rheumatology 2018
[4] Alvarez-Nemegyei et al. Association between Overweight/Obesity and Clinical Activity in rheumatoid arthritis. Reumatol Clin 2020

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3750

POS1329 A COHORT STUDY ON THE RISK OF DEVELOPING OBSTRUCTIVE SLEEP APNEA, TEMPOROMANDIBULAR JOINT DISORDERS AND CRANIOFACIAL DEFORMITIES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

K. S. K. MA[1], L. T. Wang[2]. *[1]National Taiwan University,Taipei,Taiwan, ROC, Department of Life Science,Taipei,Taiwan, Republic of China*; *[2] National Taiwan University Hospital, Department of Obstetrics & Gynecology,Taipei,Taiwan, Republic of China*

Background: Juvenile Idiopathic Arthritis (JIA), an autoimmune disease, has been proposed to be comorbid with obstructive sleep apnea (OSA).

Objectives: We aimed at identifying the relationship between JIA and OSA.

Methods: We performed a cohort study including JIA and OSA patients from 1999 to 2013. A total of 2791 patients diagnosed with OSA after JIA onset were recruited, which 11,164 eligible individuals without JIA history were selected as matched-controls. A Cox proportional hazard model was developed to estimate the risk of OSA in JIA patients. A cumulative probability model was adopted to assess the time-dependent effect of JIA on OSA development, implying the casual link of the association. To identify whether JIA patients have higher risks for developing temporomandibular joint (TMJ) disorders, craniofacial anomalies and deformities than non-JIA individuals, subgroup analyses was conducted. Finally, Ingenuity Systems Pathway Analysis (IPA) was conducted to identify underlying mechanisms of the above disease correlation among peripheral blood mononuclear cells (PBMCs) from rheumatic factor (RF)-positive and RF-negative JIA patients, and subcutaneous fat tissues from OSA patients, using p-value visualization for RNA-seq analyses.

Results: The Cox proportional hazard model showed that JIA patients were more likely to have OSA than non-JIA individuals (adjusted hazard ratio =1.949, 95% CI =1.264–3.005). The incidence of developing OSA was particularly high among patients who developed JIA aged 18-30 years old (aHR= 2.034, 95% CI=1.305-3.169) and males (aHR=1.82, 95% CI=1.121-2.954). The risk of developing OSA increased within 0-36 months (aHR = 2.216, 95% CI = 1.001 – 4.907) and over 60 months (aHR = 2.558, 95% CI = 1.346 – 4.860) of follow-up duration after JIA onset. Subgroup analyses showed that JIA patients were more likely to have TMJ disorders (relative risk = 2.047, 95% CI = 1.446-2.898) and to receive treatment for craniofacial deformities (RR = 1.722, 95% CI = 1.38-2.148) than non-JIA controls. IPA analyses suggested that the underlying mechanisms involved activation of antigen presentation pathway followed by antigen presentation to CD4+ and CD8+ T lymphocytes, as well as B cell development.

Conclusion: Our findings identified high risks of developing OSA, TMJ disorders, and craniofacial deformities following JIA onset, which the underlying mechanisms may involve both cellular and humoral immunity.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3961

POS1330 SAFETY OF ANAKINRA IN PATIENTS WITH CRYOPYRIN ASSOCIATED PERIODIC SYNDROMES (CAPS) USING A GRADUATED PRE-FILLED SYRINGE

R. Papa[1,2], G. Giancane[2,3], H. J. Lachmann[4], P. Brogan[5], E. Legger[6], D. Lindqvist[7], S. Cederholm[7], F. Bagnasco[8], N. Ruperto[9], M. Gattorno[1]on behalf of Paediatric Rheumatology International Trials Organisation (PRINTO) and Eurofever registry. *[1]IRCCS Istituto Giannina Gaslini, UOSD Centro Malattie Autoinfiammatorie e Immunodeficienze, Genoa, Italy*; *[2]Università degli Studi di Genova, Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DiNOGMI), Genoa, Italy*; *[3]IRCCS Istituto Giannina Gaslini, Clinica Pediatrica e Reumatologia, Genoa, Italy*; *[4]Royal Free Campus, National Amyloidosis Centre, London, United Kingdom*; *[5]UCL Institute of Child Health, Great Ormond Street Hospital, Infection, Inflammation and Rheumatology Unit, London, United Kingdom*; *[6]Beatrix Kinderkliniek, University Medical Center, Department of Pediatric Rheumatology, Groningen, Netherlands*; *[7]Sobi, Stockholm, Sweden*; *[8]IRCCS Istituto Giannina Gaslini, Servizio di Epidemiologia e Biostatistica, Genoa, Italy*; *[9]IRCCS Istituto Giannina Gaslini, Clinica Pediatrica e Reumatologia, PRINTO, Genoa, Italy*

Background: Cryopyrin associated periodic syndromes (CAPS) are a group of ultra-rare autoinflammatory diseases caused by mutations in the *NLRP3* gene, leading to overproduction of IL-1β. CAPS includes the following subdiagnoses: familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS) and chronic infantile neurological cutaneous articular syndrome/neonatal-onset multisystem inflammatory disease (CINCA/NOMID), where FCAS is the mildest form of CAPS and CINCA/NOMID the most severe. A graduated pre-filled syringe of the IL-1 receptor antagonist anakinra was introduced to meet the need of smaller and varying doses when treating children with CAPS.

Objectives: To evaluate the safety of anakinra in CAPS patients using the novel pre-filled syringe.

Methods: Investigators managing patients with CAPS treated with anakinra were identified via the Eurofever registry. Follow-up data of at least 3 years for each patient were prospectively collected and analyzed (EUPAS6366). The primary study endpoints were the occurrence of adverse events (AEs) with focus on serious infections, malignancies, injection site reactions, allergic reactions and medication errors, including re-use of the syringe. Secondary endpoints included dose at specific time points, discontinuations, and switch to other IL-1 blocking treatment.

Results: 12 patients with CAPS were included in the study, 8 with MWS, 2 with FCAS and 2 with CINCA/NOMID. The majority were male (75%) and white (83.3%). At baseline, all but one patient were already using the graduated pre-filled syringe with anakinra. 5 patients required a median dose of 2 to 3 mg/kg/day and 6 patients below 2 mg/kg/day. During a total of 26.1 patient years of treatment, there were 7 AEs with rate of 26.8 (95% CI 4.2-169.6) per 100 patient years. All AEs were infections from 1 patient with CINCA/NOMID and were considered unrelated to anakinra by the investigator. Two of the AEs were considered serious as hospitalization was required (1 tonsillitis and 1 urinary tract infection). No AEs were severe, 6 of the AEs were of moderate severity and 1 was of mild severity. In total, 6 patients discontinued anakinra permanently, 2 during the first year of treatment, 3 during the second year and 1 after the third year of follow-up. The reasons for discontinuation included switch to canakinumab (4 patients), switch to canakinumab and inefficacy (1 patient) and non-compliance (1 patient). The remaining 5 patients continued anakira until the end of the study. 1 patient discontinued anakinra temporarily during the second year of treatment due to non-compliance. No deaths, malignancies, injection site reactions, allergic reactions or medication errors, including re-use of the pre-filled syringe, were observed.

Table 1. Study results

Patients	12 (100)
Gender, M:F	9:3 (75:25)
Ethnicity, white:black	10:2 (83.3:16.7)
Age at baseline, median (range), years	25.3 (1.4-54.9)
Age at disease onset, median (range), years	2.5 (0-29.5)
Age at diagnosis, median (range), years	24.4 (0.6-54.6)
Disease duration, median (range), years	15.5 (1.4-51.3)
Patients already using anakinra at baseline	11 (91.7)
Patients with history of other IL-1 blocking treatments at baseline	3 (25)
Anakinra dose at baseline, median (range), mg/kg/day	1.7 (1.1-2.5)
Anakinra dose during follow-up years 1:2:3:>3, median (range), mg/kg/day	1.6:1.6:2.6:1.4 (1.1-3.9:1-4.4:1.7-3.7:1-3.2)
Patients with AEs	1 (8.3)
Patients with permanent discontinuation of anakinra	6 (50)
Patients with continuation of anakinra until the end of the study	5 (41.7)
Patients with temporary discontinuation of anakinra	1 (8.3)
Total duration of anakinra exposure, median (range), years	1.3 (0.5-7)
Any AE	7 (100)
Urinary tract infection	1 (14.3)
Upper respiratory tract infection	1 (14.3)
Tonsillitis	5 (71.4)

Results are shown as number (%) unless stated otherwise.

Conclusion: The results of the present study confirm the safety profile of anakinra treatment in CAPS patients using the graduated pre-filled syringe. No new safety findings were identified.

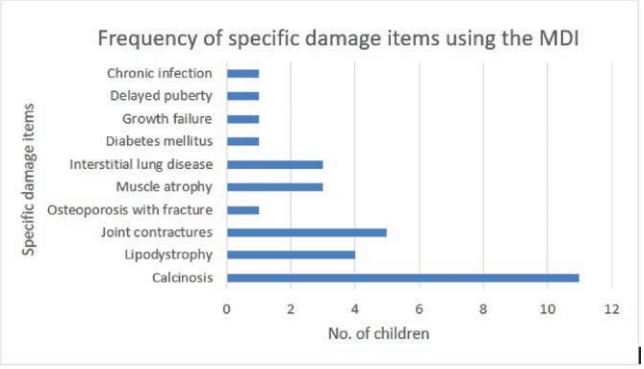
Disclosure of Interests: Riccardo Papa: None declared, Gabriella Giancane: None declared, Helen J. Lachmann: None declared, Paul Brogan: None declared, Elizabeth Legger: None declared, Daniel Lindqvist Shareholder of: Sobi employee and holder of Sobi shares, Speakers bureau: Sobi employee and holder of Sobi shares, Paid instructor for: Sobi employee and holder of Sobi shares, Consultant of: Sobi employee and holder of Sobi shares, Grant/research support from: Sobi employee and holder of Sobi shares, Employee of: Sobi employee and holder of Sobi shares, Susanna Cederholm Shareholder

of: Sobi employee and holder of Sobi shares, Speakers bureau: Sobi employee and holder of Sobi shares, Paid instructor for: Sobi employee and holder of Sobi shares, Consultant of: Sobi employee and holder of Sobi shares, Grant/ research support from: Sobi employee and holder of Sobi shares, Employee of: Sobi employee and holder of Sobi shares, Francesca Bagnasco: None declared, Nicolino Ruperto: None declared, Marco Gattorno: None declared
DOI: 10.1136/annrheumdis-2021-eular.3995

POS1331 LONG-TERM OUTCOME IN CHILDREN WITH JUVENILE DERMATOMYOSITIS FROM SOUTHERN INDIA

P. R. Chickermane[1], M. Kuriakose2, A. Tiwari2, A. Shahul2, S. Balan2. [1]*Amrita Institute of Medical Sciences, Clinical Immunology and Rheumatology, Kochi, India*; [1]*Amrita Institute of Medical Sciences, Clinical Immunology and Rheumatology, Kochi, India*

Background: There is paucity of data regarding long-term outcome and cumulative damage in children with juvenile dermatomyositis (JDM) from the Indian subcontinent.
Objectives: To assess the long-term outcome and cumulative damage in children with JDM receiving treatment at a tertiary hospital in southern India.
Methods: Retrospective review of records and cross-sectional assessment of outcome and damage in 29 patients with JDM at a tertiary hospital in Kochi, India. The disease course was categorized as monocyclic, polycyclic and chronic progressive. Cumulative damage was assessed using the IMACS myositis damage index (MDI).
Results: Twenty-nine patients (male-16) diagnosed with definite or probable juvenile dermatomyositis based on the Bohan and Peter criteria and having a minimum follow-up period of 3 years each were enrolled. Of these, 20 children were diagnosed and initiated on treatment at our institute (inceptional) and 9 were diagnosed elsewhere and referred to our centre for further management (non-inceptional). The mean age at disease onset was 7.01 ± 3.34 years (range 1.0 to 13.5 years). The median interval from onset to diagnosis was 3 months (range- 3 weeks to 8.75 years). Delayed diagnosis defined as interval from onset to diagnosis exceeding 6 months was noted in case of 8 children. Among patients in the non-inceptional group, six were considered to have not received standard of care treatment prior to referral to our centre. Standard of care treatment was defined as initiation of a treatment regimen comprising of a combination of glucocorticoids with an immunosuppressive agent within 4 weeks of diagnosis. A total of 11 children had a delayed diagnosis and/or had not received standard of care treatment prior to referral.
At our centre, all patients received oral steroids and subcutaneous methotrexate as standard therapy. Pulse steroids were used to induce remission in 12 patients and as a rescue for relapses in 2 patients. Intravenous immunoglobulin was used in 10 children with severe myositis, oropharyngeal weakness, refractory cutaneous disease including calcinosis and concomitant infection, where affordable with good results. Hydroxychloroquine was added in 15 patients with dominant cutaneous manifestations. Mycophenolate mofetil, azathioprine and tacrolimus were used in patients refractory or intolerant to methotrexate. Cyclophosphamide and rituximab were used in 4 patients each with refractory disease and extra-muscular manifestations such as interstitial lung disease. Seven patients with refractory calcinosis received pamidronate infusions.



The total follow-up duration was 121.06 patient-years. A monocyclic course was observed in 11/29 (37.9%), chronic progressive course in 16/29 (55.2%) and polycyclic course in 2/29(6.9 %). Nearly half of the patients (14/29) had damage in at least one organ using the MDI (MDI ≥1). 38% of the patients (11/29) had at least one sign of cutaneous damage, the most common being calcinosis (n=11) and lipodystrophy (n=4). This was followed by skeletal damage (n=6, joint contractures-5, osteoporosis with fracture-1), muscle and pulmonary (pulmonary fibrosis) damage in 3 patients each, endocrine damage in 2 patients (diabetes mellitus-1, growth failure and delayed development of secondary sexual characteristics-1) and chronic infection in one patient. All patients with damage in at least one organ had a chronic progressive course, indicating damage accrual. Delayed diagnosis and lack of standard of care treatment prior to referral (i.e., longer duration of untreated/ sub-optimally treated disease) were associated with an increased risk of cumulative damage ($p< 0.05$).
Conclusion: Nearly half of the patients had damage in at least one organ using the MDI. Cutaneous damage was the most common, followed by skeletal, muscle, pulmonary and endocrine damage. Longer duration of untreated/ sub-optimally treated disease significantly increases the risk of cumulative damage, highlighting the need for an early diagnosis and referral to pediatric rheumatology services.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4010

POS1332 ETANERCEPT-ASSOCIATED NEW ONSET UVEITIS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS UNDER BIOLOGICAL THERAPY: SINGLE CENTER EXPERIENCE

I. Nikishina[1], S. Arsenyeva[1], M. Kaleda[1], O. Kostareva[1], A. Shapovalenko[1], E. Denisova[2], A. Panova[1,2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Pediatric Department, Moscow, Russian Federation*; [2]*Helmgoltz Moscow Research Institute of Eye Diseases, Pediatric Department, Moscow, Russian Federation*

Background: Biological agents (BA), especially TNF inhibitors, are high efficacy options for current therapy for patients (pts) with juvenile idiopathic arthritis (JIA). They are successfully used not only for the arthritis but also for JIA-associated uveitis, however, development of uveitis *de novo* in pts treated with BA is a well-established paradoxical phenomenon.
Objectives: to evaluate the frequency of new onset (*no*-) uveitis, occurring under BA therapy in JIA pts, to establish clinical features, which may be associated with development of such effects.
Methods: retrospective cohort study involved all JIA pts (1136) who were treated with BA in our clinic from 2004 to 2020. All cases of *no*-uveitis were collected for the describing of their clinical features in disease onset and course, activity level, JIA category, exposure to Methotrexate (MTX) and BA, presence of ANA, HLA B27.
Results: among of 1136 pts treated with different BA we identified 36 (3.3%) pts (19 female/17 male) with *no*-uveitis under BA. Mostly during etanercept (ETA) therapy (34 cases from 488 ETA courses, 7%), 1/166 - in abatacept (ABA) and 1/372 - in adalimumab (ADA). 30 pts (83%) with *no*-uveitis developed it on the 1st line of BA treatment (29 ETA vs 1 ADA). 4pts (11%) developed *no*-uveitis on 2 nd line (3 ETA vs 1 ABA). 2 pts (6%) on third line (all ETA, both pts had also psoriasis). There are no cases of *no*-uveitis under other BA. Frequency of *no*-uveitis was much higher in ETA group. ETA exposure was 26.8±28.8 months (mo). It means there are no "safe" period of therapy from paradoxical phenomenon of no-uveitis. JIA subtypes were as follows: RF-neg polyarthritis 9 (25%), persistent oligoarthritis 3 (8%), extended oligoarthritis 21 (59%), enthesitis-related arthritis (ERA) - 3 (8%). Average age at JIA onset was 4.6±3.9 yrs. 20/36 patients had high laboratory activity (CRP 54±23 mg/l; ESR 41±19 mm/h) and severe arthritis before BA initiation. However most of pts (25/36) achieved 90-100% ACRpedi-response by the uveitis development. 23/36 pts were ANA-positive, 17/36 pts had HLAB27, including 7 pts who had the both features. Uveitis was occurred earlier in ANA plus HLAB27 positive pts (mean exposure - 15.3 mo) than in only ANA-positive or HLAB27-positive pts (27.7 mo and 27.6 mo accordingly). 29/36 (81%) of pts received methotrexate (MTX) in mean dosage 11.5 mg/m^2/week. There are no differences in time of uveitis development depending of MTX. In all cases of *no*-uveitis BA was switched.
Conclusion: Our study suggested that new onset of uveitis is rare adverse event during BA therapy in JIA. Uveitis can develop despite the excellent effect of therapy on joint manifestation. The most typical development of *no*-uveitis is under ETA therapy, especially in the predisposed cases (certain variants of JIA, ANF positivity, HLAB27 presence) and in patients with very high disease activity at the time of the start of biological therapy.
Disclosure of Interests: Irina Nikishina Speakers bureau: Novartis, MSD, Pfizer, Abbvie, Hofman la Roche, Svetlana Arsenyeva: None declared, Maria Kaleda Speakers bureau: Novartis, Roche, MSD, Olga Kostareva: None declared, Anna Shapovalenko: None declared, Ekaterina Denisova: None declared, Anna Panova: None declared
DOI: 10.1136/annrheumdis-2021-eular.4135

POS1333 ANKLE ARTHRITIS IN JUVENILE IDIOPATHIC ARTHRITIS: DON'T MISS TENOSYNOVITIS. CLINICAL AND SONOGRAPHIC FEATURES OF ANKLE TENOSYNOVITIS IN JIA

S. Pastore[1], S. Della Paolera[1], A. Zabotti[2,3], A. Tommasini[1,4], A. Taddio[1,4]. [1]*IRCCS Burlo Garofolo, Pediatric Department, Trieste, Italy*; [2]*Azienda Sanitaria*

Universitaria Friuli Centrale, Rheumatology Clinic, Udine, Italy; [3]*University of Udine, Department of Medical and Biological Sciences, Udine, Italy*; [4]*University of Trieste, Department of Medicine, Surgery and Health Sciences, Trieste, Italy*

Background: Tenosynovitis can occur in patients with Juvenile Idiopathic Arthritis (JIA) and may be clinically difficult to distinguish from joint synovitis. The role of musculoskeletal ultrasound (msk-US) is still discussed in the management of JIA but recent studies supported the utility of msk-US especially in detection of tenosynovitis. There is no consensus treatment for tenosynovitis in children with JIA and almost all studies focused on tendon sheath injection with glucocorticoids.
Objectives: The aims of the study were: i) to define the prevalence of tenosynovitis of the ankle in JIA patients and ankle swelling; ii) to describe the clinical characteristics of patient with tenosynovitis and to analyze different response to treatment.
Methods: We conducted an observational cross-sectional study of a group of patients with JIA followed at the Rheumatology Service of the Maternal and Child Institute "Burlo Garofolo" of Trieste. We enrolled all the patients who reported a swelling of the ankle at least once during the follow-up period and, among these patients, we included only those who underwent msk-US. Based on both clinical and sonographic examination, we identified patients with tenosynovitis and we described their demographical and clinical characteristics as well as the therapeutic approach undertaken in this group of patients.
Results: On December 31st 2019, 56 swollen ankles of 48 patients were assessed with msk-US: 22 ankles showed sonographic signs of synovitis (39%), 16 ankles of both synovitis and tenosynovitis (28%), 14 ankles of tenosynovitis only (25%). Overall, tenosynovitis was detected on twenty-seven (56%) out of 48 children with at least a swollen ankle. The majority of patient were females (70%) and the most affected tendon was the tibialis posterior (66%). Twenty-five patients with tenosynovitis (92%) achieved clinical and radiological remission: seven out of 26 patients (26%) treated with methotrexate achieved clinical and radiological remission without the addition of other therapies; fifteen out of seventeen patients (88%) treated with a biological drug responded to the therapy, of which eleven (73%) were in combination therapy with methotrexate.
Conclusion: We observed that more than 50% of the patients with a swelling of the ankle presented a tenosynovitis and among these patients about 50% did not show sonographic sign of synovitis. Msk-US was decisive in order to identify tenosynovitis and to characterize ankle swelling in JIA patients. Among patients with tenosynovitis biological therapy alone or in association with immunomodulating therapy showed effectiveness in inducing disease remission.
REFERENCES:
[1] Peters SE, Laxer RM et al. Ultrasound-guided steroid tendon sheath injections in juvenile idiopathic arthritis: a 10-year single-center retrospective study. Pediatr Rheumatol Online J. 2017 Apr 11;15(1):22.
[2] Lanni S, Bovis F et al. Delineating the Application of Ultrasound in Detecting Synovial Abnormalities of the Subtalar Joint in Juvenile Idiopathic Arthritis. Arthritis Care Res (Hoboken). 2016 Sep;68(9):1346-53.
[3] Cimaz R, Giani T et al. What is the real role of ultrasound in the management of juvenile idiopathic arthritis? Ann Rheum Dis. 2020 Apr;79(4):437-439. doi: 10.1136/annrheumdis-2019-216358
[4] Lanni S, Marafon DP et al. Comparison between clinical and ultrasound assessment of the ankle region in juvenile idiopathic arthritis. Arthritis Care Res (Hoboken). 2020 Apr 27.
[5] Laurell L, Court-Payen M et al. Ultrasonography and color Doppler in juvenile idiopathic arthritis: diagnosis and follow-up of ultrasound-guided steroid injection in the ankle region. A descriptive interventional study. Pediatr Rheumatol Online J. 2011 Jan 29;9(1):4.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4272

POS1334 **RHEUMATOLOGY PATIENT ATTENDANCE TO THE PAEDIATRIC EMERGENCY DEPARTMENT**

M. Al-Attar[1]. [1]*Paediatric Emergency Department, Royal Manchester Children's Hospital, Manchester, United Kingdom*

Background: A large proportion of patients present to the paediatric emergency department (PED) with non-urgent problems [1]. With growing pressures on services, there is a need to reduce unnecessary attendances. Children with rheumatological conditions may attend PED with flares of their condition or unrelated presentations. These patients may be immunosuppressed due to steroid, disease-modifying or biologic therapy; PED attendance may therefore pose a serious infection risk.
Objectives: To evaluate why children with rheumatological conditions attend the PED and whether these attendances are avoidable.
Methods: This study was run in Royal Manchester Children's Hospital, a UK hospital with a PED and tertiary paediatric rheumatology services. Patients under rheumatology who attend PED are usually seen directly. A dataset of all patients referred directly to paediatric rheumatology between 01/01/19 and 31/12/19 was obtained from electronic records (n=59). The age, sex and reason for attendence were collected, as well whether they were admitted/discharged. Further data on management was collected from discharge letters for those with joint pain/swelling.
Results: This cohort had 36 females and 23 males, with an average age of 11.9 years (range 1-18). 28 were discharged (47.5%) and 30 were admitted (50.8%). One patient left before being seen. The average waiting time was 3.97 hours.
Table 1 summarises reasons for attendance to PED and final outcome. The most common reason for attendance was joint pain/swelling (n=14, 23.7%). Of these, nine were discharged with advice on analgesia or steroid dosing and for early review in clinic. There was no documentation on whether there had been any attempt to access the available rheumatology helpline prior to attending PED.
Non-rheumatology-related reasons for attendance are also shown in Table 1, and notably include 20 patients with infections, 75% of whom were admitted to hospital. Chicken pox was the second most common reason for attendance (n=5, 8.5%); all patients attending with chicken pox or shingles (n=6) were admitted.

Table 1. Reasons for attendance to PED and final outcome

Reason for attendance	Number admitted	Number discharged
Joint pain/swelling	5	9
Chicken pox	5	0
Viral URTI	1	4
Rash	0	4
Pneumonia	3	0
SLE flare	3	0
Influenza A	2	0
GPA flare	2	0
Asked to attend due to blood results from clinic	2	0
Drug reaction	0	2
Minor injury	0	2
Shingles	1	0
Oral herpes simplex	1	1
Orbital inflammation	1	0
Urinary tract infection	1	0
Dysphagia	1	0
Gastroenteritis	1	0
Cerebral infarcts	1	0
Constipation	0	1
Chest pain	0	1
Abdominal pain	0	1
Enlarged lymph node	0	1
Picking up prescription	0	1
Unresponsive episode	0	1

Conclusion: Our study shows that attendance to PED with joint pain/swelling is usually avoidable in patients known to paediatric rheumatology services. Appropriate alternative services are needed to reduce hospital attendances; nurse-led helplines are beneficial, but still face some challenges in both availability and accessibility [2]. It is also important that patients and parents are given action plans for acute flares, which would ideally involve early clinic review rather than PED attendance. Our data also showed that patients are spending a long time waiting in PED, which needs to be avoided particularly in the context of immunosuppression. This is especially poignant now in light of the Covid-19 pandemic. Direct referral to rheumatology with non-rheumatological problems likely reflects a desire for specialist advice in the context of complex conditions and medications, for example with regards to infections whilst on immunosuppressive medications, or uncertainty about whether new symptoms are related to the underlying condition. Expansion of helpline services and new approaches such as remote consultations should be explored.
REFERENCES:
[1] Poku BA et al. Reducing repeat paediatric emergency department attendance for non-urgent care: a systematic review of the effectiveness of interventions. Emerg Med J. 2019 Jul;36(7):435-442.
[2] Palmer et al. Rheumatology helpline: challenges in the biologic therapy era. Br. J. Nurs. 2011 20:12, 728-732
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4325

Other orphan diseases

POS1335 **CLINICAL CHARACTERISTICS OF THE PULMONARY ARTERY INVOLVEMENT IN PATIENTS WITH BEHÇET'S SYNDROME: A SINGLE-CENTRE EXPERIENCE OF 61 PATIENTS**

D. Sahin Eroglu[1], M. Torgutalp[1], S. Baysal[2], A. Colaklar[3], S. Sezer[1], M. E. Yayla[1], C. Uzun[3], T. M. Turgay[1], G. Kınıklı[1], A. Ates[1]. [1]*Ankara University Faculty of Medicine, Department of Internal Medicine, Division of*

Rheumatology, Ankara, Turkey; [2]*Ankara University Faculty of Medicine, Department of Internal Medicine, Ankara, Turkey*; [3]*Ankara University Faculty of Medicine, Department of Radiology, Ankara, Turkey*

Background: Behçet's Syndrome (BS) is a vasculitis of unknown origin. Vascular involvement, so-called vascular Behçet's syndrome (VBS), may involve blood vessels of all sizes belonging to both venous and arterial system, with pulmonary artery involvement (PAI) being the most frequent form of arterial involvement. PAI in BS occurs in the form of aneurysms or thrombosis, and results in significant mortality.

Objectives: To report the clinical characteristics of PAI in patients with BS and to define the predictors of relapses.

Methods: We performed a retrospective analysis of BS patients with PAI who fulfilled international study group criteria. Among 460 patients with VBS, 66 were diagnosed with PAI. For final analyses, 61 patients with PAI, who had at least 2 follow-up visits (72.1% male, mean age at BS diagnosis 29.34 (SD 10.1) years), were included. The data of the patients were recorded. Relapse was defined as the reoccurrence of vascular event at any vascular structure. Factors associated with relapse were assessed by logistic regression analysis.

Results: There were not any differences considering demographic and clinical features of the patients with and without PAI in VBS group except for that intracardiac thrombosis was more common in the patients with PAI than the patients without (19.7% vs 0.3%, respectively) (Figure 1). Among 61 patients with PAI, 50 (82.0%) had isolated pulmonary artery thrombosis (PAT), whereas 11 (18.0%) had pulmonary artery aneurysm (PAA) with or without PAT. The characteristics of 61 patients with PAI were shown in Table 1. A total of 37 relapses occurred in 24 (39.3%) patients during follow-up a median of 65.9 (IQR 20.1-109.0) months. To define the factors associated with relapses, the patients with isolated PAT were analysed. In multivariable logistic regression analysis, older age at BS diagnosis and anticoagulation usage seemed to be protective, even though they could not reach statistical significance (OR: 0.92 95% CI 0.86-1.02, OR: 0.34 95% CI 0.09-1.33, respectively).

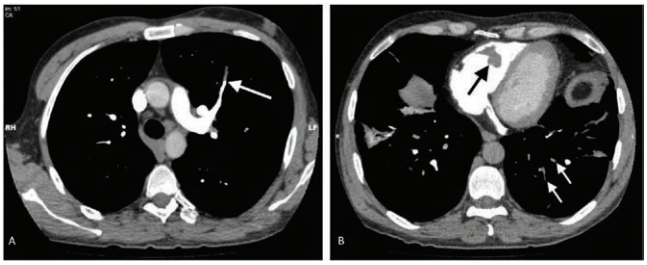


Figure 1. A) Axial CT image shows thrombus formation in the left upper lobe pulmonary artery branch. **B)** Giant thrombus is seen in the right ventricle (black arrow). Note the thrombus formation in the left lower lobe pulmonary artery branches (white arrows).

Table 1. Characteristics of the patients with pulmonary artery involvement

	All n= 61	Isolated PAT n= 50	PAA n= 11
Sex (male), n (%)	44 (72.1)	35 (70.0)	9 (81.8)
Age at diagnosis of BS, years (SD)	29.3 (10.1)	28.8 (10.4)	31.9 (8.0)
Age at diagnosis of PAI, years (SD)	36.3 (12.83)	36.7 (13.8)	34.7 (6.7)
Symptoms, n (%)			
Dyspnea	28 (45.9)	23 (46.0)	5 (45.5)
Hemoptysis	26 (42.6)	19 (38.0)	7 (63.6)
Vascular event before PAI, n (%)	21 (34.4)	20 (40.0)	1 (9.1)
Other vascular events at PAI, n (%)	33 (54.1)	28 (56.0)	5 (45.5)
Thrombophlebitis, n (%)	7 (21.2)	6 (21.4)	1 (20.0)
Upper and/or lower extremity DVT, n (%)	20 (60.6)	16 (57.1)	4 (80.0)
SVCS, n (%)	1 (3.0)	1 (3.6)	0 (0)
IVCS, n (%)	3 (9.1)	1 (3.6)	2 (40.0)
Intracranial thrombosis, n (%)	4 (12.1)	4 (14.3)	0 (0)
Intracardiac thrombosis, n (%)	8 (24.2)	7 (25.0)	1 (20.0)
Arterial event other than PAI, n (%)	4 (12.1)	3 (10.7)	1 (20.0)
Relapse, n (%)	24 (39.3)	20 (40.0)	4 (36.4)
Time to the first relapse, median (IQR), month	49.8 (13.2-102.6)	54.1 (24.4-117.9)	3.9 (1.7-67.9)
Death, n (%)	2 (3.3)	0 (0)	2 (18.2)

BS= Behçet Syndrome, PAI= pulmonary artery involvement, PAT= pulmonary artery thrombosis, PAA= pulmonary artery aneurysm, DVT= deep vein thrombosis, SVCS= superior vena cava syndrome, IVCS= inferior vena cava syndrome

Conclusion: Our results indicate that there is a higher frequency of intracardiac thrombosis in BS patients with PAI and an increasing current trend of PAT in patients with PAI. In addition, there might be a possible efficacy of anticoagulation usage in preventing relapses, which needs confirmation with further studies.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.411

POS1336

RETROPERITONEAL FIBROSIS IN ERDHEIM-CHESTER DISEASE HAS UNIQUE PRESENTING AND PROGNOSTIC FEATURES: A SINGLE CENTRE RETROSPECTIVE COMPARATIVE COHORT STUDY

A. Tomelleri[1], C. Campochiaro[1], M. Lanzillotta[1], G. De Luca[1], G. Cavalli[1], E. Della Torre[1], L. Dagna[1]. [1]*IRCCS San Raffaele Hospital, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy*

Background: Erdheim-Chester disease (ECD) is a multisystemic non-Langerhans cell histiocytosis. Retroperitoneal fibrosis (RPF) is a common ECD feature, found in up to 60% of patients. Besides ECD, RPF differential diagnosis includes other clinical entities of rheumatological interest, such as idiopathic RPF and IgG4-related disease (IgG4-RD). Since ECD management does not include glucocorticoids and mainly relies on the use of anti-neoplastic small molecules, a prompt diagnosis is critical.

Objectives: To characterize the main differential clinical, radiologic and prognostic features of a monocentric cohort of patients with RPF. To provide practical learning points useful to recognize ECD among patients with RPF.

Methods: Medical records of ECD patients with radiologic signs of RPF and of patients with non ECD-related RPF followed up at our Rheumatology Clinic were retrospectively reviewed. Final diagnosis relied either on analysis of histologic samples or on fulfilment of appropriate classification criteria. Main clinical, radiologic and laboratory features at diagnosis and long-term outcomes were evaluated and compared between the two groups. Non parametric tests were used for comparison.

Results: 31 (41%) ECD and 45 (59%) non-ECD patients (IgG4-RD, n=28; idiopathic RPF, n=11; peri-aortitis with large-vessel involvement, n=6) were included. All but one (97%) ECD patients and 56% non-ECD patients had a biopsy-proven diagnosis. ECD patients were younger at disease onset (51±14 vs 59±10 years, P=0.024) and diagnosed with a greater delay (48 [IQR, 13-92] vs 4 [IQR, 2-7] months, P<0.001). In the majority of ECD patients (84%), RPF was clinically silent and was disclosed in the context of the diagnostic work-up; conversely, 82% non-ECD patients had at least one RPF-related symptom (mainly, abdominal pain, n=19, and low-back pain, n=16). At diagnosis, C-reactive protein (50±34 vs 33±31 mg/L, P=0.052) and serum creatinine (1.31±0.53 vs 1.34±0.79, P=0.76) levels were not statistically different. In all ECD patients, fibrotic tissue surrounded both kidneys symmetrically, involving the ureters in half of the cases (Table 1); signs of hydronephrosis were present in 55% of patients (mostly bilaterally, 77%). In the non-ECD group, kidneys were rarely affected, and ureteral involvement was mostly asymmetric; hence, hydronephrosis incidence was similar (76%), but more frequently monolateral (65%). In non-ECD patients, fibrotic tissue more frequently involved inferior vena cava and iliac arteries. FDG uptake by RPF was disclosed in 39/40 (98%) non-ECD and 5/12 (42%) ECD patients who underwent a PET before therapy start (P<0.001). Ureteral stenting was required by a similar fraction of patients (ECD, 29%; non-ECD, 38%, P=0.47), but it was bilateral in 100% of ECD vs 29% of non-ECD patients (P<0.001). No differences in the rate of chronic kidney failure was found (26% vs 18%, P=0.41), but only ECD patients progressed to a terminal stage requiring hemodialysis (13% vs 0%, P=0.025).

Table 1.

	ECD patients (n=31)	Non-ECD patients (n=45)	*P-value*
Left kidney	30 (97%)	4 (9%)	<0.001
Right kidney	31 (100%)	6 (13%)	<0.001
Left ureter	16 (52%)	16 (36%)	0.24
Right ureter	16 (52%)	24 (53%)	1
Abdominal aorta	21 (68%)	40 (89%)	0.04
Inferior vena cava	5 (16%)	29 (64%)	<0.001
Left iliac artery	10 (32%)	27 (60%)	0.02
Right iliac artery	10 (32%)	29 (64%)	0.001
Left renal artery	9 (29%)	6 (13%)	0.14
Right renal artery	6 (19%)	4 (9%)	0.3
Mesenteric artery	8 (26%)	4 (9%)	0.06
Celiac trunk	7 (23%)	3 (7%)	0.08

Conclusion: Our retrospective study suggests that ECD-related RPF has a significantly worse renal prognosis than non ECD-related RPF. A complete baseline work-up including a critical evaluation of the extension of the fibrotic tissue and the sites involved is fundamental to avoid patients' misdiagnosis and mistreatment.

REFERENCES:

[1] Campochiaro C, Tomelleri A, Cavalli, G, et al. Erdheim-Chester disease. Eur J Intern Med (2015)
[2] Lanzillotta M, Mancuso G, Della-Torre E. Advances in the diagnosis and management of IgG4 related disease. BMJ (2020)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.550

POS1337 BEHÇET`S DISEASE AND COURSE OF PREGNANCY - RESULTS FROM THE NATIONWIDE PREGNANCY REGISTER REVNATUS

H. S. Koksvik[1], B. Jakobsen[1], H. Bjørngaard[1], C. Skorpen[2,3], M. Wallenius[1,2]. [1]*St. Olavs Hospital, Trondheim University Hospital, Norwegian National Advisory Unit on Pregnancy and Rheumatic Diseases, Trondheim, Norway*; [2]*NTNU, Department of Neuromedicine and Movement Science, Trondheim, Norway*; [3]*Alesund Hospital, Department of Rheumatology, Alesund, Norway*

Background: Behçets disease (BD) is a complex and multisystemic disorder of unknown etiology. It is characterized by recurrent oral and genital ulcers and inflammatory eye involvement. It can also affect the cardiovascular, pulmonary and skeletal system. BD is commonly diagnosed in women in reproductive age. Pregnancy outcomes are reported in previous studies with discrepancies in the rate of pregnancy-related complications.
Objectives: To describe the course of pregnancy in patients with BD.
Methods: We prospectively collected data on pregnancy outcome in women with BD through the nationwide Norwegian registry on pregnancy and rheumatic diseases (RevNatus) from 2016-2020. All women were diagnosed with ICD-10 code M35.2. 13 pregnancies in 11 women were recorded. One women had two pregnancies including one twin birth.
Results: Median age at conception was 30 years (range 25-32), with median disease duration 7 years (range 1-15). There were no serious organ manifestations. Tnf-alpha-inhibitors were used in 2nd trimester in 3 pregnancies. All pregnancies resulted in live births with median gestational age at delivery of 38 weeks (range 36-41). No preeclampsia or HELLP were recorded.

Table 1. Pregnancy outcome in 13 BD pregnancies

Patient #	Pregnancy #	Medication at 2.nd trimester	Oral or genital ulcers during pregnancy	Disease activity during pregnancy	CRP value at 2nd trimester	Gestational age at delivery, week	Mode of delivery	Birth weight, gram
A	1	Azathioprine Colchicine LMWH	no	persistent*	13	38	SVD	3475
B	2	Adalimumab Colchicine LDPrednisolon	yes	persistent *	4	40	SVD	3215
C	3	no	yes	persistent*	5	41	SVD	3355
D	4	Adalimumab LDPrednisolon	yes	persistent*	23	36	SVD	1940
E	5	Etanercept ASA	no		2	41	SVD	3410
	6a (twin)	Etanercept ASA	no		5	37	Elective Sectio	2400
	6b (twin)							2410
F	7	LDPrednisolon	yes	flare**	15	38	SVD	3180
	8	Adalimumab LDPrednisolon	yes	flare**	4	37	Acute Sectio	3049
G	9	no	no	remission***	1	41	SVD	3150
H	10	LDPrednisolon	yes	persistent *	10	38	SVD	2480
I	11	ASA	no	persistent*	3	39	SVD	3410
J	12	no	yes	persistent*	1	37	SVD	3115
K	13	Ciklosporine	no	remission***	3	37	SVD	3130

SVD = spontaneous vaginal delivery, ASA = acetylsalicylic acid, LDPrednisolon = Low dose Prednisolon <10 mg/day, *= persistent throughout pregnancy, **= flare once during pregnancy, ***= remission throughout pregnancy

Conclusion: Pregnancies in women with BD in this cohort were uncomplicated. We did not reveal any serious events, and they all resulted in live births. However, BD is a very heterogeneous disease, and the women in our cohort did not have any serious organ manifestations. Larger cohorts representing the heterogeneity are needed to study the course and outcome of pregnancies in BD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.666

POS1338 INCIDENCE, PREVALENCE, AND MORTALITY OF CHRONIC PERIAORTITIS: A POPULATION-BASED STUDY

U. Ghaffar[1], K. J. Warrington[1], S. Duong[2], C. S. Crowson[1,2], M. Burke[1], B. Viers[3], A. Potretzke[3], H. Bjarnason[4], M. Koster[1]. [1]*Mayo Clinic College of Medicine and Science, Rheumatology, Rochester, United States of America*; [2]*Mayo Clinic School of Health Sciences, Biomedical Statistics and Informatics, Rochester, United States of America*; [3]*Mayo Clinic College of Medicine and Science, Urology, Rochester, United States of America*; [4]*Mayo Clinic College of Medicine and Science, Vascular and Interventional Radiology, Rochester, United States of America*

Background: Chronic periaortitis is an inflammatory condition that typically involves the infrarenal portion of the abdominal aorta. Few studies are available to outline the epidemiology of this rare condition. To date, no epidemiologic studies on periaoritis have been performed in North America.
Objectives: To evaluate the epidemiology, presentation and outcomes of patients with chronic periaortitis from 1998 through 2018.
Methods: An inception cohort of patients with incident chronic periaortitis from January 1, 1998 through December 31, 2018, in Olmsted County, Minnesota, USA, was identified based on comprehensive individual medical record review utilizing the Rochester Epidemiology Project medical record linkage system. Inclusion required radiographic and/or histologic confirmation of periarterial soft tissue thickening around at least part of the infra-renal abdominal aorta or the common iliac arteries. Data were collected on demographic characteristics, clinical presentation, renal and radiographic outcomes, and mortality. Incidence rates were age and sex adjusted to the 2010 United States white population.
Results: Eleven incident cases of chronic periaortitis were identified during the study period. Mean±SD age at diagnosis was 61.8±13.4 years. The cohort included 9 men (82%) and 2 women (18%). The most common presenting symptom was pain with 55% (6/11) reporting abdominopelvic-pelvic pain, 36% (4/11) back pain, and 18% (2/11) flank pain. Obstructive uropathy was present in 73% (8/11) subjects: 3 (27%) unilateral left, 1 (9%) unilateral right, and 4 (36%) bilateral. Mean creatinine at presentation was 2.7±3.4 mg/dL. Ureteral stenting was required at diagnosis in seven patients: unilateral left in 2, unilateral right in 1 and bilateral in 4. All 11 patients received glucocorticoids with a median (IQR) dose of 40 (30, 60) mg/day. Additional non-glucocorticoid therapeutics were used in 10 patients.
Renal function stage at last follow up declined in 2 patients, remained the same in 3 patients and improved in 6 patients. Mean creatinine at last follow-up was 1.2±0.2 mg/dL. Among the seven patients requiring baseline indwelling ureteral stent placement only two required ongoing ureteral stenting at last follow up. None of the four patients without ureteral stenting at diagnosis progressed to require stenting during the follow-up period. No patient underwent ureterolysis surgery in this cohort. Periarterial soft tissue thickening at last follow up had increased in thickness in 1 (9%), was unchanged in 2 (18%), decreased in size but did not resolve in 6 (55%), and fully resolved in 18%.
Age- and sex-adjusted incidence rates per 100,000 population were 0.26 for females, 1.56 for males and 0.87 overall. Overall prevalence on January 1, 2015 was 8.98 per 100,000 population. Median (IQR) length of follow-up was 10.1 (2.5, 13.8) years. Overall mortality was similar to the expected age, sex, and calendar estimates of the Minnesota population with standardized mortality ratio (95% CI) for the entire cohort 2.07 (0.67, 4.84).
Conclusion: This study reports the first epidemiologic data on chronic periaortitis in the United States. In this cohort of patients with chronic periaortitis, men were approximately 4 times more commonly affected than women. Mortality was not increased compared to the general population.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.698

POS1339 MORE FREQUENT AND EARLIER HIP INVOLVEMENT IN SPONDYLOARTHRITIS ASSOCIATED WITH FAMILIAL MEDITERRANEAN FEVER

M. Bektaş[1], S. Sarı[1], C. Cetin[1], B. Ç. Yalçın Dulundu[1], N. Koca[1], B. Ince[1], Y. Yalçınkaya[1], B. Artim-Esen[1], M. Inanc[1], M. L. Ocal[1], A. Gül[1]. [1]*Istanbul Faculty of Medicine, Internal Medicine, Rheumatology Division, Istanbul, Turkey*

Background: Familial Mediterranean fever (FMF) is a hereditary autoinflammatory disorder caused by the *MEFV* gene variants. Although association between FMF and spondyloarthritis (SpA) has previously been reported, clinical and laboratory features of patients with FMF and SpA have not been defined in detail.
Objectives: We aimed to evaluate clinical and laboratory characteristics, disease outcome and biologic responses of patients with FMF+SpA compared to patients with only SpA who were followed-up in our tertiary referral center.
Methods: Database of FMF Clinic was screened for FMF patients with coexistent SpA and 113 patients were identified fulfilling Tel Hashomer and ASAS criteria for FMF and SpA, respectively. A group of patients with SpA without FMF matched for age, gender and disease duration were selected as the control group.
Results: Thirteen patients were excluded because of missing data, and 100 patients (F/M: 52/48) were included into the analysis. Mean follow-up time was 93.6 ± 77 (range[r]: 3-324) months and mean patient age was 43.3 ± 12 (r: 20-87) years. Mean age of onset for FMF was 12.5 ± 8 (r: 1-36) and for SpA was 25 ± 11 (r: 7-72) years. SpA findings was classified as axial in 35.4%, axial and peripheral in 47.9% and only peripheral in 16.7% in FMF+SpA group. Half (49%) of the

patients had hip involvement (70% bilaterally), and 21.5% of them needed total hip joint replacement (TJR), which were significantly more frequent compared to control group. Two exon 10 MEFV variants were found in 69.4%, and most (69.8%) had homozygous M694V. Hip involvement was more frequent in patients with two exon 10 variants (p=0.036; OR=4.4) compared to those with one variant; and TJR was more frequent in those with homozygous M694V compared to other exon 10 variants (p=0.001; OR=10). Radiographic sacroiliitis was less frequent in patients with homozygous M694V (p=0.019; OR=5.48). HLA-B27 positivity was not associated with hip or axial involvement in patients with FMF+SpA.
Biologics were used in 60 patients (anti-TNF in 43, secukinumab in 1, and tocilizumab in 2). Anti-IL-1 drugs were used in 23 patients for refractory FMF. In 9 patients, anti-TNF and anti-IL-1 drugs were tried for refractory joint involvement: 5 switched to anti-TNFs from anti-IL-1, 4 patients switched to anti-IL-1 from anti-TNFs. Biologic DMARD requirement was more frequent in patients with two exon 10 variants (p=0.006; OR=7.4), especially in those with homozygous M694V (p=0.006; OR=7.6). Although anti-IL-1 usage did not differ among MEFV variants, anti-TNF was used more frequently in patients with homozygous M694V (p=0.007; OR=7.2). FMF+SpA patients had higher serum CRP and developed amyloidosis more frequently than those patients with SpA.

Table 1. Comparison of clinical and laboratory findings between the patients with FMF+SpA and SpA control

	FMF + SpA (n=100)	SpA (n=217)	P value
Age (years)*	43.3 ± 12	43.4 ± 11	0.6
Sex (n, %)			
Male	48	104 (47.9)	0.99
Female	52	113 (52.1)	
Duration of SpA (monnths)*	181.6 ± 108	180.2 ± 112	0.8
Age onset of SpA (years)*	25.1±11	28.4±8	0.008
Peripheral arthritis (n, %)	35/80 (43.8)	79/212 (37.3)	0.3
HLA-B27 positivity (n, %)	6/21 (28.6)	105/139 (75.5)	<0.001 (OR=18.9)
CRP (mg/dL)*	26.7 ± 25**	18.96±29	0.001
ESR (mm/hour)*	39.7 ± 27	39.4 ± 28	0.8
Hip involvement (n, %)	47/96 (49)	23/118 (19.5)	<0.001 (OR=20.9)
TJR (n, %)	20/93 (21.5)	8/205 (3.9)	<0.001 (OR=23.3)
Fulfilling mNY criteria (n, %)	52/81 (64.2)	164/199 (82.4)	0.001 (OR=10.8)
Biologic DMARD (n, %)	60	68/214 (31.8)	<0.001 (OR=22.5)
Anti-TNF (n, %)	46	68/214 (31.8)	0.015 (OR=5.96)
Amyloidosis (n, %)	16	5/205 (2.4)	<0.001 (OR=19.3)

* mean±standard deviation, **during the attack-free period

Conclusion: In this group of FMF+SpA patients, hip involvement and need for TJR were more frequent and associated with penetrant MEFV variants rather than HLA-B27 positivity. These patients had higher inflammatory response and risk of developing amyloidosis, and they needed biologics more frequently compared to SpA group. More severe disease course in FMF+SpA patients requires further attention and analysis in larger cohorts.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.716

POS1340 MULTICENTER STUDY OF 71 PATIENTS WITH REFRACTORY UVEITIS RELATED TO IMMUNE-MEDIATED INFLAMMATORY DISEASES ON CERTOLIZUMAB PEGOL TREATMENT

J. L. Martín-Varillas[1], V. Calvo-Río[2], L. Sanchez-Bilbao[2], I. González-Mazón[2], A. Adan[3], I. Hernanz Rodríguez[3], A. Gallego[4], E. Beltrán[5], S. Castro[6], P. Fanlo[7], A. García Martos[8], I. Torre-Salaberri[9], M. Cordero-Coma[10], J. De Dios-Jiménez Aberásturi[11], Á. García-Aparicio[12], M. Hernández-Garfella[13], A. Sanchez-Andrade[14], A. García-Valle[15], O. Maiz[16], R. Miguélez[17], S. Rodríguez Montero[18], A. Urruticoechea-Arana[19], R. Veroz Gonzalez[20], A. Conesa[21], C. Fernández-Carballido[22], V. Jovani[23], O. Martínez González[24], P. Moya[25], S. Romero-Yuste[26], P. Rubio Muñoz[27], E. Peña Sainz-Pardo[28], M. A. González-Gay[2], J. L. Hernández[2], R. Blanco[2]. *[1]Hospital Sierrallana, Rheumatology, Torrelavega, Spain*; *[2]H. U. Marqués de Valdecilla, Rheumatology, Santander, Spain*; *[3]H. Clinic, Ophthalmology, Barcelona, Spain*; *[4]H.U. de Badajoz, Rheumatology, Badajoz, Spain*; *[5]H. del Mar, Rheumatology, Barcelona, Spain*; *[6]H. U. Joan XXIII, Rheumatology, Tarragona, Spain*; *[7]C.H. de Navarra, Internal Medicine, Navarra, Spain*; *[8]H. U. del Tajo, Rheumatology, Madrid, Spain*; *[9]H. Basurto, Rheumatology, Bilbao, Spain*; *[10]C.A.U. de León, Ophthalmology, León, Spain*; *[11]H. U. de Álava, Rheumatology, Vitoria, Spain*; *[12]C.H.U. de Toledo, Rheumatology, Toledo, Spain*; *[13]H.G.U. de Valencia, Ophthalmology, Valencia, Spain*; *[14]H. Lucus Augusti, Rheumatology, Lugo, Spain*; *[15]C.A.U. de Palencia, Rheumatology, Palencia, Spain*; *[16]H.U. Donostia, Rheumatology, San Sebastian, Spain*; *[17]H. Móstoles, Rheumatology, Madrid, Spain*; *[18]H.U. Virgen de Valme, Rheumatology, Sevilla, Spain*; *[19]H. Can Misses, Rheumatology, Ibiza, Spain*; *[20]H. Merida, Rheumatology, Mérida, Spain*; *[21]H.G.U. de Castellón, Rheumatology, Castellón, Spain*; *[22]H. San Juan, Rheumatology, Alicante, Spain*; *[23]H.G.U. de Alicante, Rheumatology, Alicante, Spain*; *[24]H.C.U. de Salamanca, Rheumatology, Salamanca, Spain*; *[25]H. Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*; *[26]C.H.U. de Pontevedra, Rheumatology, Pontevedra, Spain*; *[27]H. de l'Esperit Sant, Rheumatology, Barcelona, Spain*; *[28]H.U. 12 de Octubre, Pediatrics, Madrid, Spain*

Background: Prognosis of non-infectious refractory uveitis has improved markedly with biologic therapy (BT) **(1-5)**. Most data are with monoclonal anti-TNF drugs, especially Adalimumab (ADA) and Infliximab (IFX). However, there is not enough evidence for the use of Certolizumab Pegol (CZP).
Objectives: To evaluate the efficacy and safety of CZP in refractory uveitis secondary to Immune-Mediated Inflammatory Diseases (IMID).
Methods: Multicenter study of 71 patients with uveitis due to IMID refractory to glucocorticoids and conventional immunosuppressants. Efficacy was assessed with the following ocular parameters: best corrected visual acuity (BCVA), anterior chamber cells, vitritis, macular thickness and presence of retinal vasculitis. These outcomes were compared between baseline, 1st week, 1st and 6th month, and 1st and 2nd year. Statistical analysis was performed with IBM SPSS Statistics v.23.
Results: 71 patients/100 affected eyes (29 men/42 women) with mean age of 40.0±11.3 years were studied. Underlying IMIDs were: spondyloarthritis (n=38), Behçet (10), psoriatic arthritis (8), Crohn disease (3), sarcoidosis (2), JIA (1), reactive arthritis (1), rheumatoid arthritis (1), relapsing polychondritis (1), TINU (1), pars planitis (1), Birdshot (1) and idiopathic uveitis (3). Uveitis pattern was anterior (n=55), posterior (6), panuveitis (6) and intermediate (4).
Prior to CZP, patients had received: methotrexate (37), sulfasalazine (26), azathioprine (14), cyclosporine (10), leflunomide (3), mycophenolate mofetil (3) and cyclophosphamide (1). Previous BT was administered in 48 (67.6%) patients, with a mean of 1.4±1.3 drugs per patient as follows: ADA (n=56), IFX (27), golimumab (14), tocilizumab (5) and etanercept (3). Pregnancy was the reason for prescribing CZP in 19 patients. CZP was administered in monotherapy (n=39) or combined with conventional immunosuppressants (n=32).
After a mean follow-up of 27.1±21.1 months, most of the ocular variables showed a rapid and significantly improvement (Table 1). A decrease in the median number [IQR] of flares of uveitis before and after CZP, (3 [1-4] vs. 0 [0-1], p<0.001) was observed. CZP was discontinued in 15 patients due to remission (n=2), ocular insufficient response (2) and incomplete response of extraocular manifestations (11). No serious adverse events were reported.
Conclusion: CZP seems to be effective and safe in patients with refractory uveitis due to IMID.
REFERENCES:
[1] Martín-Varillas JL, et al. Ophthalmology 2018; 125:1444-1451. doi: 10.1016/j.ophtha.2018.02.020.
[2] Atienza-Mateo B, et al. Arthritis Rheumatol 2019; 71:2081-2089. doi: 10.1002/art.41026.
[3] Santos-Gómez M, et al. Clin Exp Rheumatol 2016; 34(6 Suppl 102):S34-S40. PMID: 27054359
[4] Vegas-Revenga N, et al. Am J Ophthalmol 2019; 200:85-94. doi: 10.1016/j.ajo.2018.12.019
[5] Calvo-Río V, et al. Clin Exp Rheumatol. 2014; 32 (4 Suppl 84):S54-7. PMID: 25005576

Table 1.

	Baseline	1st week	1st Month	6th Month	1st year	2nd year
BCVA (mean±SD)	0.68±0.27	0.72±0.27*	0.79±0.25*	0.84±0.24*	0.85±0.25*	0.87±0.22*
Improvement in AC Cells, n (%)*Patients with AC cells at baseline (n=48)*	-	21 (43.7)	30 (62.5)*	41 (85.4)*	48 (100)*	48 (100)*
Improvement in Vitritis, n (%) *Patients with vitritis at baseline (n=13)*	-	3 (23.1)	8 (61.5)*	11 (84.6)*	13 (100)*	13 (100)*
OCT (μ) (mean±SD)	292.5±47.7	294±47.4	286.7±41.9*	274.7±38.7*	272.8±38.9*	266.31±36.2*
Choroiditis; affected eyes, n, (%)	3 (4.2)	3 (4.2)	2 (2.8)	2 (2.8)	1 (1.4)	0 (0)
Retinal Vasculitis; affected eyes, n, (%)	2 (2.8)	0 (0)	1 (1.4)	0 (0)	0 (0)	0 (0)

p<0.001

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1233

POS1341

TOCILIZUMAB FOR THE TREATMENT OF IMMUNE-RELATED ADVERSE EVENTS TO IMMUNE CHECKPOINT INHIBITORS: A CASE SERIES

C. Campochiaro[1], N. Farina[1], A. Tomelleri[1], G. De Luca[1], G. Cavalli[1], C. Lazzari[2], R. Ferrara[3], M. Garassino[3], V. Gregorc[2], L. Dagna[1]. [1]*IRCCS San Raffaele Hospital, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy*; [2]*IRCCS San Raffaele Hospital, Department of Oncology, Division of Experimental Medicine, Milan, Italy*; [3] *Fondazione IRCCS Istituto Nazionale dei Tumori, Medical Oncology Department, Milan, Italy*

Background: Immune checkpoint inhibitors (ICI) are pharmacological agents effectively used in the treatment of several malignant tumors. The hyperactivation of the immune system induced by ICI may trigger an inflammatory involvement of healthy tissues, a phenomenon referred to as immune-related adverse event (irAE). No clinical trials are available to guide the management of irAEs. Observational data suggest tocilizumab might be effective in severe cases of irAEs, but data are scant. The possibility of continuing ICI treatment despite the development of irAE and the subsequent initiation of tocilizumab has never been evaluated.
Objectives: To evaluate the efficacy and safety of tocilizumab, as monotherapy or alongside the continuation of ICI treatment, in the management of irAEs.
Methods: We retrospectively identified patients who developed irAEs and were referred to our specialized Clinic between May 2018 and December 2020. Among these patients, we identified those who had been treated with tocilizumab and collected information about their oncologic history and outcome, ICI therapy and irAEs.
Results: Thirty-nine patients were referred to our outpatient Clinic following the development of irAEs. Five of them were treated with tocilizumab. Disease and demographic features are reported in Table 1. At irAEs onset all patients were treated with glucocorticoids. A steroid-sparing agent was started to permit an adequate prednisone tapering without the irAE relapsing. Before tocilizumab start, two patients were treated with methotrexate monotherapy, one with anakinra monotherapy, and one with methotrexate and anakinra combination therapy. A significant therapeutic effect was confirmed in all patients and no significant adverse reactions were reported. ICI therapy was permanently discontinued in two patients. In the other three cases, cancer immunotherapy was safely continued alongside tocilizumab without further irAEs occurring. Only one patient experienced tumor progression two years after ICI suspension and subsequently died despite the improvement of his myocardial inflammatory involvement.
Conclusion: In our cohort, tocilizumab proved to be an effective and safe therapy for the management of irAEs.
Our case series also supports the possibility of maintaining ICI while introducing tocilizumab for irAE treatment. This combined approach might represent a suitable therapeutic option to guarantee a significant anti-inflammatory activity without losing the oncologic response.

REFERENCES:

[1] Kostine M *et al*, Ann Rheum Dis, 2021;80:36-48.

Table 1. Clinical characteristics of patients who developed irAEs secondary to ICI therapy and who received tocilizumab.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age at irAE onset (years)	69	52	72	57	75
Sex	Male	Male	Male	Female	Female
Neoplastic histology	NSCLC	NSCLC	NSCLC	NSCLC	Pleural mesothelioma
ICI treatment	Nivolumab	Nivolumab	Pembrolizumab	Pembrolizumab	Pembrolizumab
irAE	Myocarditis	Arthritis Cutaneous vasculitis	Arthritis	Arthritis	Large vessel vasculitis
ICI discontinuation due to irAE	Yes	No	No	No	Yes
PDN initial dose (mg daily)	50	37.5	25	25	37.5
DMARD therapy *	T16: ANK T20: TCZ T26: TCZ + MMF	T5: MTX T6: MTX + ANK T11: MTX + TCZ	T3: MTX T11: MTX + TCZ	T4: MTX T6: MTX + TCZ	T3: TCZ
irAE outcome	Improvement	Low disease activity	Low disease activity	Remission	Remission
Follow-up length (months)	50	47	57	25	26
Since oncologic diagnosis	10	25	2	5	8
Since TCZ start					
Oncological outcome	Progressive disease and death	Complete response	Stable disease	Stable disease	Complete response

* Treatment chronology is referred to as a *T* followed by the number of months since irAE onset. ANK, anakinra; ICI, immune checkpoint inhibitor; irAE, immune-related adverse events; DMARD, disease modifying anti-rheumatic drug; MTX, methotrexate; NSCLC, non-small cell lung cancer; PDN, prednisone; TCZ, tocilizumab.

Disclosure of Interests: Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Nicola Farina: None declared, Alessandro Tomelleri: None declared, Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, MSD, Pfizer, Giulio Cavalli Speakers bureau: SOBI, Chiara Lazzari: None declared, Roberto Ferrara: None declared, Marina Garassino: None declared, Vanesa Gregorc: None declared, Lorenzo Dagna Speakers bureau: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, SOBI, Celgene Janssen, MSD, MP
DOI: 10.1136/annrheumdis-2021-eular.1253

POS1342

CHEMOPROPHYLAXIS IN LATENT TUBERCULOSIS ASSOCIATED WITH RHEUMATIC IMMUNE-MEDIATED DISEASES. STUDY OF 240 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL

D. Martínez-López[1], J. Rueda-Gotor[1], J. Osorio-Chavez[1], C. Álvarez-Reguera[1], V. Portilla[1], M. A. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*

Background: Tuberculosis (TB) may be increased with biologic therapy (BT). Diagnosis and treatment of latent TB infection (LTBI) is the best strategy to prevent TB. In Rheumatic Immune-Mediated Diseases (R-IMID) and LTBI, chemoprophylaxis must be used before BT. The drugs more frequently used are Isoniazid (INH), Rifampicin (RIF) and Fluoroquinolones (FQ). These drugs may be associated with side-effects, especially hepatotoxicity.
Objectives: To assess, in a single University Hospital, **a)** used chemoprophylactic drugs and, **b)** adverse events with these drugs.
Methods: We included all consecutive patients in the last five years (2016-2020) with a diagnosis of R-IMID and a positive LTBI test (positive tuberculin skin test and/or interferon-γ–release assay), who received chemoprophylaxis prior to BT. Dose of chemoprophylactic drugs were **a)** INH (5 mg/kg/d, maximum, 300 mg; for 9 months with vitamin B6), **b)** RIF (10 mg/kg/d, maximum, 600 mg for 4 months) and **c)** FQ levofloxacin (500 mg/day for 9 months).
In all patients analytic controls that included liver enzymes were performed at the 1st and 3rd month and then at a variable time.
Results: 240 patients were analyzed (165 women/ 75 men), mean age of 56±11 years. The underlying R-IMID of patients receiving chemoprophylaxis were rheumatoid arthritis (n=74, 30.8%), axial spondyloarthritis (n=59, 24.6%), psoriatic arthritis (n=62, 25.8%), conectivopathies (n=17, 7.1%), vasculitis (n=12, 5%), sarcoidosis (n=2, 0.8%), Behçet's disease (n=1, 0.4%), inflammatory myopathies (n=1, 0.4%) and other (n=12, 5%).
At the onset of chemoprophylaxis they were taking: Prednisone in 61 patients (24 of them above 10 mg/day) and the following conventional DMARD, methotrexate (n=109, 45.4%), hydroxychloroquine (n=20, 8.3%), sulfasalazine (n=11, 4.6%), leflunomide (n=4, 1.7%) and azathioprine (n=2, 0.8%).
The first-line chemoprophylactic drug was INH in 232 (96.7%) patients and RIF in the remaining 8 (3.3%). Due to adverse events, second-line therapy was used in 18 (RIF, n=17 and Levofloxacin, n=1) patients previously treated with INH.
Adverse events were more frequent with INH, being observed in 55 patients (23.7%) out of 232. (Table 1 next page, Figure 1 below). By contrast, only 1 out of 25 (4%) receiving RIF presented an adverse event, which was hepatotoxicity, requiring suspension of RIF. No adverse events were described in the only patient receiving levofloxacin.

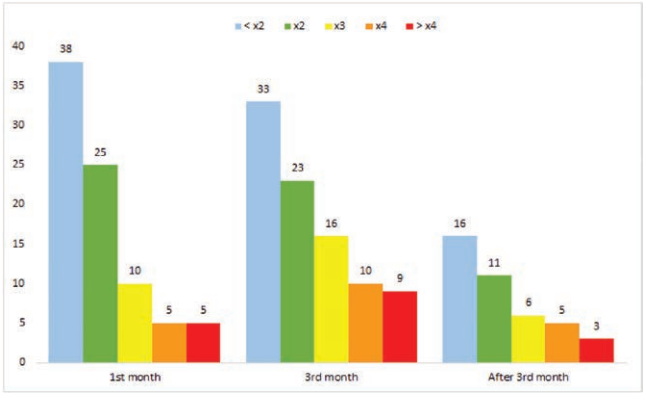


Figure 1. Liver enzyme elevation over baseline in patients in treatment with isoniazid.* Patients with higher liver enzyme elevation are included in the previous groups.

Conclusion: INH is the most used first-line treatment for LTBI. RIF was mainly used as second-line therapy if an adverse event with INH was observed. Treatment was generally well tolerated and most adverse events did not require the withdrawal of the treatment. Hepatotoxicity was the most frequent adverse event with INH and the most frequent cause of treatment withdrawal.

Table 1. Adverse events with isoniazid at months 1 and 3 and after month 3

	Month 1 (n=232)			Month 3 (n=222)			After month 3 (n=214)		
Adverse events, n (%)	Total	Requiring switching	Requiring suspension	Total	Requiring switching	Requiring suspension	Total	Requiring switching	Requiring suspension
Hepatotoxicity	38 (16.4)	6 (2.6)	0	33 (14.9)	5(2.3)	2 (0.9)	16 (7.5)	2 (0.9)	0
Gastrointestinal side effects	4 (1.3)	3 (1.3)	1 (0.4)	3 (1.5)	0	3 (1.5)	2 (0.9)	0	1 (0.5)
Cutaneous toxicity	2 (0.9)	1 (0.4)	0	0	0	0	0	0	0
Dizziness	1 (0.4)	1 (0.4)	0	0	0	0	0	0	0
Total	44 (19)	11 (4.7)	1 (0.4)	36 (16.2)	5 (2.3)	5(2.2)	18 (8.4)	2 (0.9)	1 (0.5)

Disclosure of Interests: David Martínez-López: None declared, Javier Rueda-Gotor: None declared, Joy Osorio-Chavez: None declared, Carmen Álvarez-Reguera: None declared, Virginia Portilla: None declared, Miguel A González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi and MSD, Consultant of: Abbvie, Pfizer, Roche, Sanofi and MSD, Grant/research support from: Abbvie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Grant/research support from: Abbvie, MSD, Roche

DOI: 10.1136/annrheumdis-2021-eular.1446

POS1343 ABNORMAL ELECTROCHEMICAL SKIN CONDUCTANCE VALUES IN PATIENTS WITH AA AMYLOIDOSIS

S. Deshayes[1], R. Bourguiba[2], J. P. Haymann[3], L. S. F. Lea.Savey@aphp.Fr>;[2], A. Aouba[1], G. Grateau[2], S. Georgin-Lavialle[2]. *[1]CHU de Caen Normandie, Internal Medicine, Caen, France*; *[2]Hôpital Tenon, Internal Medicine, Paris, France*; *[3]Hôpital Tenon, Physiology, Paris, France*

Background: Clinical manifestations are scarce in AA amyloidosis (AAA) and, contrary to other types of amyloidosis, involvement of the peripheral nervous system was rarely reported in AAA. However, the usual absence of hypertension despite chronic renal failure and the digestive involvement may be secondary to dysautonomia, but the autonomic nervous system has rarely been studied in AAA (1). Measure of the electrochemical skin conductance (ESC) is a simple and reproducible method to evaluate the function of eccrine sweat glands, which are innervated by small non-myelinated C fibers, and patients with AL and hereditary transthyretin amyloidoses show decreased ESC values (2,3).
Objectives: To evaluate ESC values by Sudoscan in patients with AAA.
Methods: Patients diagnosed as having AAA based on positive immunohistochemistry with an anti-serum amyloid A antibody followed at the national reference center for AAA in Tenon Hospital between July, 2017 and September, 2020, were routinely assessed for ESC with FDA approved Sudoscan (Impeto Medical, Paris, France). An ESC value above 60 microSiemens (µS) or 70 µS were considered normal for hands or feet, respectively. Categorical variables are reported as percentages and continuous variables are expressed as means±standard deviation. Correlations between age, body mass index (BMI), hemoglobin levels, C-reactive protein levels, estimated glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration equation (defined as 0 for dialysis patients) and ESC values were calculated using the nonparametric Spearman test. GraphPad Prism Version 7 software (GraphPad Software, San Diego, California, USA) was used for statistical analyses. A p-value <0.05 was considered as statistically significant.
Results: Overall, 32 patients (16 women) were included, with a mean age of 57.4±13.6 years and a mean BMI of 25.2±6.8 kg/m^2. Six (19%) had diabetes mellitus, and 5 (16%) had a kidney transplantation. The main causes of AAA were: monogenic autoinflammatory diseases (n=11, 34%, including 9 patients with familial Mediterranean fever), chronic and/or recurrent infections (n=5, 16%), obesity (n=3, 9%) and undefined (n=3, 9%). The mean hands' ESC values was normal at 65.5±21.1 µS, although 8 (25%) patients had ESC values below 60 µS, including 2 diabetic patients. In contrast, the mean feet's ESC values was abnormal at 62.7±23.7 µS, including half of the patients with ESC values below 70 µS (2 diabetic patients). Eight patients had abnormal ESC values only for feet, and 1 had abnormal values only for hands. Apart from a significant correlation between feet and hands' ESC values (p<0.0001), only the estimated glomerular filtration rate was significantly associated with hands' ESC values (p<0.01).
Conclusion: To our knowledge, this is the first study to assess ESC in AAA. Feet's ESC values were moderately impaired in half of the patients with AAA. Therefore, this study reinforces the previously reported alterations in the autonomic nervous system in patients with AAA that should probably be searched for in these patients. In addition, the identification of an alteration of the ESC values cannot allow to distinguish the type of amyloidosis.

REFERENCES:

[1] Nussinovitch U, Volovitz B, Nussinovitch M, Lidar M, Feld O, Nussinovitch N, et al. Abnormal heart rate variability in AA amyloidosis of familial Mediterranean fever. Amyloid 2011;18:206–10.
[2] Montcuquet A, Duchesne M, Roussellet O, Jaccard A, Magy L. Electrochemical skin conductance values suggest frequent subclinical autonomic involvement in patients with AL amyloidosis. Amyloid 2020;27:215–6.
[3] Fortanier E, Delmont E, Verschueren A, Attarian S. Quantitative sudomotor test helps differentiate transthyretin familial amyloid polyneuropathy from chronic inflammatory demyelinating polyneuropathy. Clin Neurophysiol 2020;131:1129–33.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1459

POS1344 EVALUATING THE MULTIVISCERAL INVOLVEMENT ON ADULT-ONSET STILL'S DISEASE TO RETRIEVE IMAGING-BASED DIFFERENCES IN PATIENTS WITH AND WITHOUT MACROPHAGE ACTIVATION SYNDROME; RESULTS FROM A SINGLE-CENTRE OBSERVATIONAL STUDY

I. DI Cola[1], F. Bruno[1], O. Berardicurti[1], R. Monti[1], A. Conforti[1], A. DI Sibio[1], V. Pavlych[1], F. Sensini[1], C. Masciocchi[1], A. Barile[1], P. Cipriani[1], P. Ruscitti[1]. *[1]University of L'Aquila, Department of Biotechnological and Applied Clinical Sciences, L'Aquila, Italy*

Background: Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder usually affecting young adults, burdened by life-threatening complications, mainly macrophage activation syndrome (MAS), a secondary form of hemophagocytic lymphohistiocytosis [1]. In this context, the importance of an accurate assessment of AOSD is suggested to promptly recognise the multivisceral involvement of the disease which is associated with life-threatening complications. The assessment of the most aggressive subsets of the disease could guide the clinicians when to apply additional resources but avoiding unnecessary expenditures in patients with a less severe clinical picture.
Objectives: In this study, we aimed at describing the multivisceral involvement of the disease to retrieve imaging-based differences in AOSD patients with and without MAS.
Methods: The present evaluation has been designed as a cross-sectional study to descriptively compare the multivisceral involvement in AOSD patients with and without MAS. Patients admitted to our Institution, who underwent a total body CT scan, were selected from our historical cohort and assessed. Clinical and CT scan characteristics of AOSD patients with and without MAS were compared. Clinical and CT scan characteristics of AOSD patients with and without MAS were analysed by parametric or non-parametric t tests for all continuous variables, and chi squared test was used for categorical ones, as appropriate. Furthermore, possible correlations among radiological outcomes with laboratory markers and systemic score were estimated by using a point-biserial coefficient correlation.
Results: This study evaluated 39 AOSD patients (men 64.1%), mean age of 48.8±16.6 years). Out of those, 14 patients (35.9%) were complicated by MAS. These patients showed higher values of ferritin [AOSD: 770.0 (1306.5) ng/mL vs MAS: 2926.3 (4918.5) ng/mL p=0.003] and systemic score (AOSD: 4.6±1.4 vs MAS: 6.9±1.7, p<0.0001). AOSD patients with MAS presented a higher prevalence of lung disease than others (AOSD: 56.0% vs MAS 85.7% p=0.048). Lung disease correlated with the systemic score (coefficient 0.491, p=0.003). AOSD patients with MAS were more frequently characterised by hepatomegaly (AOSD: 12.0% vs MAS: 50.0% p=0.019) and splenomegaly (AOSD: 16.0% vs MAS 50.0% p=0.033), respectively, than others. Hepatomegaly correlated with CRP (coefficient 0.421, p=0.016), ferritin (coefficient 0.397, p=0.020), and systemic score (coefficient 0.391, p=0.022). Furthermore, the presence of splenomegaly correlated with the systemic score (coefficient 0.439, p=0.009). CT scan features of abdominal effusions were more frequently observed in AOSD patients with MAS than those without this complication (AOSD: 12.0% vs 57.1% p=0.007).

Finally, a higher percentage of AOSD patients with MAS showed a significant lymph node enlargement, either mediastinal or abdominal, than others on CT scan (AOSD: 36.0% vs MAS 71.4% p=0.048). The presence of lymphadenomegaly correlated with the systemic score (coefficient 0.368, p=0.032).
Conclusion: Our findings showed a higher prevalence of multiorgan involvement in AOSD patients with MAS, suggesting imaging-based differences, although other studies are needed to fully assess this issue. Pulmonary disease, hepatomegaly, splenomegaly, lymph nodes enlargement, and abdominal effusions were associated with these more aggressive patients.
REFERENCES:
[1] Giacomelli R, Ruscitti P, Shoenfeld Y. A comprehensive review on adult onset Still's disease. J Autoimmun. 2018 Sep;93:24-36.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1600

POS1345 PULMONARY ARTERY PSEUDOANEURYSMS IN BEHCET'S DISEASE

O. Jomaa[1], O. Berriche[1], S. Arfa[1], A. Fraj[1], W. Romdhane[1], M. Belkhiri[1], M. Hermassi[1], R. Makhloufi[1]. [1]*University Hospital Tahar Sfar Mahdia, Tunisia, Internal Medicine Department, Mahdia, Tunisia*

Background: Pulmonary artery pseudoaneurysms (PAP) is a serious complication of Behcet's Disease (BD).
Objectives: The aim of this work is to analyze, through 4 observations, the clinical, para-clinical and therapeutic aspects of PAP.
Methods: Matériels et méthodes:
Retrospective study including 4 cases of PAA among 150 patients who satisfied the criteria of the International Study Group on BD, followed in the Internal Medicine and Radiology Departments at Tahar Sfar Hospital Mahdia TUNISIA.
Results: Résultats:
Four men, with an average age of 27 years (20-34). PAPs were inaugural, and multiple (>3) in 3 cases and associated with pulmonary embolism in 2 cases. Hemoptysis was the main clinical symptom. All patients were treated with high-dose corticosteroid therapy combined with monthly boluses of cyclophosphamide in addition to colchicine. Two patients had undergone arterial embolization. Surgery was indicated for 2 patients, one of whom died after surgery as a result of massive hemoptysis. The others had a favorable outcome.
Conclusion: PAP severity justifies the necessity of early diagnosis and management. The thoracic angio-CT is the imaging of choice for diagnosis. The treatment is based on a corticosteroid therapy and immunosuppressive association with possibly a selective embolization.
DOI: 10.2214/ajr.172.3.10063870
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1667

POS1346 CLINICAL ASSOCIATIONS OF ANTI-RO52 ANTIBODIES IN PATIENTS WITH SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES

D. Prieto-Peña[1], B. Atienza-Mateo[1], M. A. González-Gay[1], R. Blanco[1], M. Lopez-Hoyos[2]. [1]*Hospital Universitario Marques de Valdecilla, IDIVAL, Rheumatology, Santander, Spain*; [2]*Hospital Universitario Marques de Valdecilla, IDIVAL, Immunology, Santander, Spain*

Background: Anti-SSA/Ro antibodies (Abs) can target Ro60 and Ro52 antigens. The presence of anti-Ro60 Abs has been widely described in patients with systemic autoimmune rheumatic diseases (SARDs). However, the clinical implication of anti-Ro52 Abs for the diagnosis and management of SARDs remains unclear.
Objectives: To assess the clinical associations of anti-Ro52 antibodies in patients with high clinical suspicion of SARDs.
Methods: We retrieved the clinical records of all patients with positive anti-Ro52 Abs tested in our hospital between November 2017 and September 2020. Patients were divided into 3 groups: 1) anti-Ro52+Ro60+2) antiRo52+Ro60-3) antiRo52+Ro60+ with other Abs. A comparative study between groups was performed.
Results: 57 patients (43 women/14 men; mean age 62.1±13.6 years) with antiRo52+ Abs were identified. Final diagnosis were: undifferentiated connective tissue disease (UCTD) (n=13), anti-synthetase/overlap myositis (n=12), Sjögren's syndrome (n=7), interstitial pneumonia with autoimmune features (IPAF) (n=6), scleroderma (n=4), systemic lupus erythematosus (n=2), dermatomyositis (n=2), other systemic inflammatory diseases (n=3). In 8 (14%) patients the diagnosis of inflammatory diseases was finally ruled out. 27 patients were classified in the Ro52+Ro60+ group, 11 in the Ro52+Ro60- group and 19 Ro52+ with other Abs. Patients with Ro52+Ro60- were younger and more often women than patients with Ro52+Ro60+.Interstitial lung disease (ILD) was less frequent in patients with Ro52+Ro60-(Table 1**).** Isolated Ro52 Abs were more frequently associated with UCTD, while IPAF was more commonly found in patients with anti-Ro52+Ro60+ Abs (Table 1 **and** Figure 1).

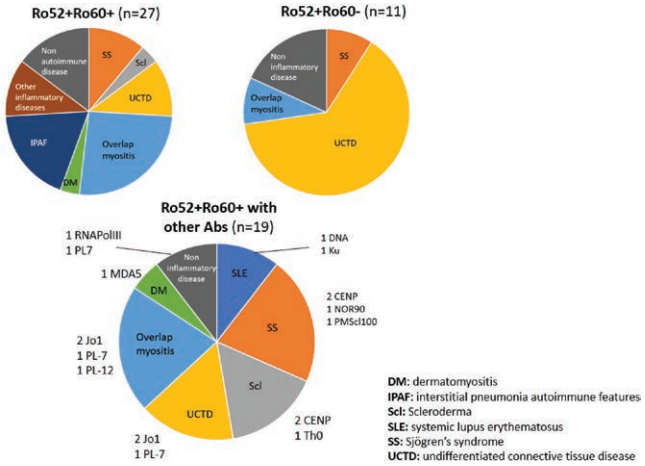


Figure 1.

Conclusion: Anti Ro52 Abs determination has clinical implications in the diagnosis of SARDs.

Table 1.

	Anti-Ro52+Ro60+ (n=27)	Anti-Ro52+Ro60- (n=11)	Anti-Ro52+Ro60+ with other Abs (n=19)
Age (years), mean ± SD	65.7 ± 10.0	53.8 ± 18.0*	61.7 ± 13.6
Sex (females), n (%)	19 (70.4)	10 (90.9) *	14 (73.7)
Clinical manifestations at anti-Ro52 determination, n (%)			
Arthralgias/arthritis	18 (66.7)	7 (63.6)	14 (73.7)
Raynaud's phenomenon	9 (33.3)	4 (36.4)	9 (47.4)
Myopathy	4 (14.8)	1 (9.1)	2 (10.5)
Final diagnosis, n (%)			
Systemic lupus erythematosus	0 (0)	0 (0)	2 (10.5)
Sjögren's syndrome	3 (11.1)	1 (9.1)	4 (21.1)
Scleroderma	1 (3.7)	0	3 (15.8)
Undifferentiated connective tissue disease	3 (11.1)	7 (63.6) **	3 (15.8)
Overlap myositis	7 (25.9)	1 (9.1)	4 (21.1)
Dermatomyositis	1 (3.7)	0	1 (5.3)
IPAF	5 (18.5) **	0	0
Other systemic inflammatory diseases	3 (11.1)	0	0
Non inflammatory disease	4 (14.8)	2 (18.2)	2 (10.5)
Comorbidities, n (%)			
ILD	11 (40.7)	1 (9.1) **	7 (36.8)
Malignancy	5 (18.5)	1 (9.1)	0 (0.0)

*** p< 0.05** (Ro52+Ro60+ *vs* Ro52+Ro60-)
**** p< 0.05** (Ro52+Ro60+ *vs* Ro52+**Ro60**- *vs* Ro52+Ro60+ with other Abs)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1729

POS1347 IMPACT OF CANAKINUMAB AND ANAKINRA ON PATIENT-REPORTED OUTCOMES IN ADULT-ONSET STILL'S DISEASE PATIENTS

N. Farina[1], C. Campochiaro[1], A. Tomelleri[1], G. De Luca[1], G. Cavalli[1], E. Baldissera[1], L. Dagna[1]. [1]*IRCCS San Raffaele Hospital, Milan, Italy, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy*

Background: Adult-onset still's disease (AOSD) is a rare systemic inflammatory disease. Interleukin-1 (IL1) blockade has shown to be crucial for the management of refractory AOSD patients. The IL1 inhibitors anakinra and canakinumab are both effectively used in clinical practice for the management of AOSD. No data are available on the impact of these therapies on patient-reported outcomes (PROs).
Objectives: To assess the impact of ANK and CNK therapies on PROs of AOSD patients.
Methods: Medical records of AOSD patients followed up at our Institution who had been treated with both ANK and CNK were identified. Disease features were retrospectively collected. All patients were initially treated with ANK and

subsequently with CNK. At the moment of CNK introduction and at their latest visit while on CNK, patients were asked to fill a questionnaire investigating their experience with either ANK or CNK. The questionnaire included 4 different domains that were assessed through means of Visual Analogue Scales (VAS) ranging from 0 to 10. The following domains were considered: injection-related pain, satisfaction with the frequency of administration, concern for drug-related adverse events including infections, and overall drug tolerability. VAS values for each of the domains were compared between ANK and CNK with Mann-Whitney U test.

Results: Ten AOSD patients treated with both ANK and CNK were included in the analysis. Disease characteristics are shown in Table 1 below. ANK was discontinued due to inefficacy in 6 patients and due to adverse reactions in 4. As shown in Figure 1, CNK overall tolerability significantly exceeded ANK one (p=0.021). Only 1 AOSD patient reported a greater tolerability with ANK compared to CNK because she felt more comfortable with pre-filled syringes. The reasons for higher CNK tolerability were the lower pain at injection site (median 1, IQR 1-1 vs median 4.5, IQR 1.25-7; p=0.015) and the greater level of satisfaction with the frequency of administration (median 10, IQR 9.25-10 vs median 3.5, IQR 2.25-4.75, p<0.001). The concern for drug-related adverse events was not significantly different between ANK and CNK (p=0.549) and overall low among AOSD patients. CNK led to a satisfying control of systemic inflammation and steroid-sparing effect in most of patients and it was discontinued in only one case (*Patient 5*), due to ineffective disease control.

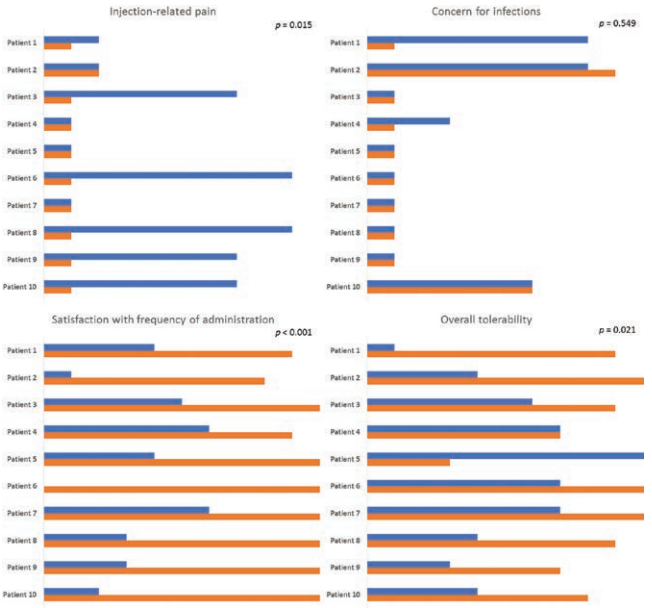


Figure 1. Comparative tolerability of anakinra (blue line) and canakinumab (orange line) in our study population, expressed as Visual Analogue Scale values (range from 1 to 10). Reported p-values refer to the comparative analysis between the two drugs.

Conclusion: In our cohort of AOSD patients, CNK proved not only to be effective in controlling systemic inflammation in ANK refractory cases, but its use was associated with greater patients' satisfaction and tolerability.

REFERENCES:

[1] Kluetz *et al*, Value Health, 2018;21(6):742-747.

Disclosure of Interests: Nicola Farina: None declared, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Alessandro Tomelleri: None declared, Giacomo De Luca Speakers bureau: SOBI, Novartis, Celgene, MSD, Pfizer, Giulio Cavalli Speakers bureau: SOBI, Elena Baldissera Speakers bureau: Novartis, Pfizer, Roche, Alpha Sigma, Sanofi, Lorenzo Dagna Speakers bureau: Abbvie, Amgen, Biogen, BMS, Celltrion, Novartis, Pfizer, Roche, SG, SOBI, Celgene Janssen, MSD, MP

DOI: 10.1136/annrheumdis-2021-eular.1751

POS1348 MORTALITY AND ITS RELATED FACTORS IN PATIENTS WITH IGG4-RELATED DISEASE: A JAPANESE SINGLE-CENTER STUDY

I. Mizushima[1], H. Kawahara[1], T. Yoshinobu[1], S. Shin[1], R. Hoshiba[1], R. Nishioka[1], T. Zoshima[1], S. Hara[1], Y. Suzuki[1], K. Ito[1], M. Kawano[1]. [1]*Kanazawa University Hospital, Rheumatology, Kanazawa, Japan*

Background: In recent years, IgG4-related disease (IgG4-RD) has become a widely recognized disorder. However, mortality and its related factors in this disease are not well known.

Objectives: This study aimed to clarify mortality and its related factors in patients with IgG4-RD.

Methods: We retrospectively reviewed the medical records of patients with IgG4-RD diagnosed by experts based on fulfillment of the Japanese comprehensive diagnostic criteria and/or the 2019 ACR/EULAR classification criteria for IgG4-RD at a single center in Japan. Using the collected data, we calculated the crude mortality rate and the standardized mortality ratio (SMR) using national Japan mortality statistics and investigated the cause of death. We performed Cox regression analyses to assess mortality-related factors.

Results: A total of 179 patients with IgG4-RD were included: 124 were male (69.3%); the median age was 68 years (interquartile range [IQR] 60-75 years); and the median follow-up from diagnosis was 47 months (IQR 17-84). Ten patients (5.6%) in our cohort died during the follow-up period. Five died of malignancy, one of respiratory failure, two of infectious pneumonia, one of sudden cardiac event, and one of suspected aortic aneurysmal rupture. The crude mortality rate was 11.1 per 1,000 person-years. According to national Japan mortality statistics, 11.6 age- and sex-matched deaths were expected to occur within the follow-up period, resulting in a SMR of 0.86 (95% confidence interval [CI] 0.41-1.59). Univariate Cox regression analyses indicated that the number of affected organs at diagnosis (hazard ratio [HR] 1.45, 95% CI 1.02-2.05), serum creatinine levels at diagnosis (HR 1.82, 95% CI 1.06-3.12), and the presence of malignancy during the clinical course (HR 3.93, 95% CI 1.10-14.02) had a significant impact on the time to death, whereas the other factors including age at diagnosis and serum C-reactive protein and IgG4 levels at diagnosis did not.

Conclusion: Our findings suggest that the mortality rate of patients with IgG4-RD does not significantly differ from that of the Japanese general

Table 1. Clinical and treatment characteristics of study population.

	Sex and age (years)	Disease duration (months)	Disease manifestations	Sequential biologic therapies	Steroid dosage variation (mg/day)*	ESR variation (mm/hour)*	CRP variation (mg/L)*
Patient 1	Male, 70	22	Arthritis, Fever Rash	TCZ, ANK, CNK	25 → 5	120 → 13	55 → 1
Patient 2	Female, 72	11	Arthritis, Fever Rash	TCZ, ANK, CNK	5 → 0	60 → 24	265 → 6
Patient 3	Male, 32	48	Fever, Rash	ANK, CNK	15 → 0	29 → 11	27 → 1
Patient 4	Male, 71	12	Fever	ANK, CNK	20 → 5	120 → 2	180 → 1
Patient 5	Female, 58	72	Fever	ANK, CNK	0 → 5	27 → 36	5 → 83
Patient 6	Female, 48	5	Arthritis, Fever Rash	ANK, CNK	10 → 0	8 → 10	2 → 1
Patient 7	Female, 74	180	Arthritis, Fever, Rash, MAS	ETN, ANK, CNK	5 → 5	33 → 1	1 → 25
Patient 8	Male, 78	180	Arthritis, Fever Rash, Myocarditis Pleuropericarditis	ANK, CNK	40 → 20	46 → 10	58 → 40
Patient 9	Male, 22	144	Arthritis, Fever	ETN, TCZ, ANK, CNK	20 → 10	86 → 94	135 → 1
Patient 10	Male, 43	24	Arthritis, Fever Rash	ANK, CNK	15 → 5	15 → 10	4 → 1

* Before and after canakinumab start.

ANK, anakinra; CNK, canakinumab; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ETN, etanercept; MAS, macrophage activation syndrome; MTX, methotrexate; PDN, prednisone; TCZ, tocilizumab.

population. Multi-organ involvement and renal dysfunction at diagnosis as well as malignancy during the clinical course may be associated with higher mortality. An appropriate clinical evaluation for the early detection of these risk factors is required at first diagnosis and during long-term follow-up.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1798

POS1349 THE JOINT INVOLVEMENT IN ADULT ONSET STILL'S DISEASE IS CHARACTERISED BY A PECULIAR MAGNETIC RESONANCE IMAGING AND A SPECIFIC TRANSCRIPTOMIC PROFILE

P. Ruscitti[1], A. Barile[1], O. Berardicurti[1], S. Iafrate[1], P. DI Benedetto[1], A. Vitale[2], F. Caso[3], L. Costa[3], F. Bruno[1], F. Ursini[4], L. Navarini[5], F. Sensini[1], R. Scarpa[3], B. Frediani[2], L. Cantarini[2], C. Masciocchi[1], R. Giacomelli[5], P. Cipriani[1]. [1]*University of L'Aquila, Department of Biotechnological and Applied Clinical Sciences, L'Aquila, Italy*; [2]*University of Siena, Research Center of Systemic Autoinflammatory Diseases and Behçet's Disease Clinic, Department of Medical Sciences, Surgery and Neurosciences, Siena, Italy*; [3]*University Federico II of Naples, Department of Clinical Medicine and Surgery, School of Medicine, Naples, Italy*; [4]*IRRCS Istituto Ortopedico Rizzoli, Bologna, Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy*; [5]*University of Campus Bio-Medico of Rome, Unit of Allergology, Immunology, Rheumatology, Department of Medicine, Rome, Italy*

Background: Adult onset Still's disease (AOSD) is a rare systemic autoinflammatory disease and joint involvement is one of its clinical manifestations [1]. Arthritis, either oligoarthritis or bilateral symmetrical rheumatoid arthritis-like polyarthritis, is another common clinical feature of AOSD, with a migrating pattern at the beginning and becoming stable over the time [1].

Objectives: The aims of the study were to assess joint involvement in AOSD by using magnetic resonance imaging (MRI), to describe main patterns of involvement, and associated clinical characteristics, and to evaluate the global transcriptomic profile of synovial tissues in AOSD to elucidate possible pathogenic pathways involved with.

Methods: AOSD patients, who underwent to magnetic resonance imaging (MRI) exam on joints, were assessed to describe patterns of joint involvement and associated clinical characteristics. Some synovial tissues were collected for RNA-sequencing purposes.

Results: In this study, 31 patients with AOSD (mean age 42.3 ± 15.2 years, 54.8% male gender), who underwent to at least one MRI exam on joints, were assessed. The most common MRI finding was the presence of synovitis on 60.5%, mainly in peripheral affected joints. MRI revealed a mild to moderate proliferative synovitis, as thickening of the synovial membrane, with low to intermediate signal intensity on T1-weighted images and intermediate to high signal intensity on T2-fat saturated weighted and STIR images, suggesting the presence of a hyperplastic than of a hypertrophied synovial tissue. Bone oedema and bone erosions were reported on 34.9% and 25.6% MRI exams, respectively. In all patients but one, bone erosions were synchronous with bone oedema, overlapping completely the locations. Assessing clinical characteristics in patients with MRI-erosions, a higher prevalence of splenomegaly, a more frequent chronic disease course, lower levels of erythrocyte sedimentation rate and ferritin was observed.

Assessing the synovial tissues of some AOSD patients, a moderate perivascular mononuclear infiltrate in the sub-lining stroma of hip synovial tissues was observed, whereas the lining cells were relatively unremarkable. In addition, interleukin (IL)-1β, IL-6, TNF, and heavy ferritin subunit (FeH) were found on AOSD synovial tissues.

An RNA-sequencing analysis assessed the global transcriptomic profile of synovial tissues on AOSD patients and matched-controls. Assessing IL-1 pathway, we found an increased expression of *il1a*, *il1b*, *il1rap*, *il1r1*, *il18r1*, and *Il18bp* on AOSD tissues when compared with controls. In IL-6 pathway, we found an increased expression of *il6* and *il6st*/*gp130* on AOSD synovial tissues whereas an increased expression of *il6r* was shown on the controls. Among genes involved in TNF pathway, *tnf*, *traf1*, *traf2*, *tnfaip3* and *tnfrsf1a* resulted to be more expressed in AOSD synovial tissues than in controls. Finally, *fth1* and *ftl* were more expressed in AOSD patients than controls, when we explored the iron uptake and transport pathway.

Conclusion: A peculiar MRI pattern of joint involvement in AOSD was reported; the most common finding was the presence of synovitis, characterised by intermediate to high signal intensity on T2-fat-saturated weighted and STIR images. Bone erosions and bone oedema were also observed. This MRI pattern was associated with a hyper-activation of IL-1, IL-6, and TNF pathways together with a hyper-expression of ferritin genes on AOSD synovial tissues.

REFERENCES:

[1] Giacomelli R, Ruscitti P, Shoenfeld Y. A comprehensive review on adult onset Still's disease. *J Autoimmun.* 2018;93:24-36.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1844

POS1350 FAMILIAL MEDITERRANEAN FEVER DURING PREGNANCY: A 26 CASE SERIES WITH 38 PREGNANCIES

Y. Karabulut[1]. [1]*Private Yıldırım Doruk Hospital, Division of Rheumatology, Bursa, Turkey*

Background: Familial Mediterranean Fever (FMF) is an autoinflammatory disease characterized by recurrent attacks with autosomal recessive inheritance. FMF usually occurs in young age; most patients (90%) begin to suffer from their first attack before 20 years of age. Pregnancy can occur frequently during the course of the disease, as women of reproductive age are affected by the disease.

Objectives: In this study, it was aimed to retrospectively examine the demographic, genetic, and clinical features (frequency of attacks during pregnancy, duration of attacks, treatment of attacks) of 26 cases who were followed up with a diagnosis of FMF in the last five years and experienced pregnancy.

Methods: A total of twenty-six female FMF cases experienced pregnancy and diagnosed or followed up in our rheumatology center between 2015-2020 were included in the study. All patients were diagnosed according to Tel-Heshomer criteria. All data and follow-up visit records of the patients were retrospectively recorded by the rheumatologist. Patients were followed up by an obstetrician working in the same center during pregnancy. The demographic and genetic characteristics of the patients, the treatment used, the duration and characteristics of the attack during pregnancy, and the treatment they received during the attack were recorded retrospectively. Data processing and analysis conducted with SPSS 22 for Windows.

Results: During the follow-up period, a total of 38 pregnancies were observed in 26 female cases. When the genetic mutation tests of all patients were examined, 61% were M694, 15% were V726, 11% were M680I positive and compound mutation was detected in 42% of the patients. The mean age of the patients was 30±7.8, the disease duration was 9.8± 5.4 years, the follow-up period was 38±14 months, the attack frequency during pregnancy was 3.6± 1.7 and the attack duration was 14± 9.8 hours. Considering the clinical features, fever was seen in 92.3%, abdominal pain 96.1%, chest pain 88.4%, arthritis 11.5% and other symptoms seen in 26% during attacks of pregnant FMF patients. All patients used 1 gram of colchicine regularly throughout pregnancy. Steroids were used in 11.5% of patients and non-steroid anti-inflammatory drugs in 53.8% of patients during the attack. Anakinra was used in 11.5% of the cases except for the first trimester following a written consent obtained from the patients.

In 10.5% of 38 pregnancies, spontaneous abortion was observed in the early period, 7.8% of pregnancies resulted in preterm delivery before 32 weeks. In addition, 81.5% of pregnancy completed the planned period and resulted in a healthy birth. Cesarean section was performed in 4 patients and normal delivery procedure in 27 patients. Major malformation-anomaly was not observed in any baby. When patients using colchicine (73%) irregularly and less than 1 gram (26.9%) before pregnancy were compared in terms of attack frequency and duration, the group using regular medication had significantly fewer and shorter attacks ($p<0.05$).

Three colchicine resistant patients with M694 homozygous mutation became pregnant under anakinra treatment. A total of five pregnancies were followed in three cases. No medication was used in these patients in the first trimester. As of the second trimester, 100mg/day for 3 days of anakinra was administered in these patients after obtaining an informed consent. In this patient group, no obstetric problem was observed during and after pregnancy, and healthy deliveries were realized.

Conclusion: Pregnancy is common in FMF patients of reproductive age. Disease and relapse treatment during pregnancy is still a problem due to the limited number of medications that can be used for treatment. Further studies required to verify safety of Anakinra in refractory FMF cases. There is a need to develop options for the prevention and treatment of attacks during pregnancy.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1878

POS1351 CAUSES OF HOSPITALIZATION IN BEHÇET SYNDROME

Y. Ozguler[1,2], G. Hatemi[1,2], A. S. Pala[3], S. N. Esatoglu[1,2], S. Ugurlu[1,2], E. Seyahi[1,2], M. Melikoglu[1,2], I. Fresko[1,2], H. Ozdogan[1], S. Yurdakul[1,2], H. Yazici[1,2], V. Hamuryudan[1,2]. [1]*Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*; [2]*Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Behcet Disease Center, Istanbul, Turkey*; [3]*Prof. Dr. Cemil Taşcıoğlu City Hospital, Department of Internal Medicine, Istanbul, Turkey*

Background: The causes of hospitalization may provide important information on the course of diseases and treatment-related adverse effects.
Objectives: We aimed to determine the causes and outcome of hospitalizations among patients with Behçet Syndrome (BS) in a dedicated center.
Methods: We surveyed hospitalization records in our clinic between January 2002 and December 2019 and identified those with a diagnosis of BS. The records of these patients were reviewed for demographic and clinical features, causes of hospitalization and outcome. We divided hospitalization causes into 2 as being BS related (organ involvement or deterioration) and non-BS related (treatment complication or others).
Results: Three-hundred and thirty BS patients (75% men, mean age 37.7 ±11.4 SD years) were hospitalized for a total of 456 times during 18 years. The mean disease duration was 10.8± 8.8 SD years. Two-hundred and ninety-one (64%) patients were using immunosuppressives (IS) with or without corticosteroids (CSs) and 72 (16%) of them were under biologic treatment at the time of hospitalization. The mean duration of hospitalization was 12.7±10.7 SD days. The reasons for hospitalization were directly related to BS in 259 patients (57%) and non-related to BS in 191 (42%). Six patients were hospitalized for both BS and non-BS related reasons at the same time. The most common reasons were vascular involvement (n=169, 64%) for BS related reasons and infections (n=64, 32%) for non-BS related reasons (Table 1). Patients hospitalized for BS related causes were younger (35.2±10.6 vs 41.1±11.7, p<0.001), had short mean disease duration (8.5±7.5 vs. 13.6±9.4 years, p<0.001), stayed shorter in the hospital (11.6±8.6 vs 14.0±12.9 days p=0.03) and had less frequent IS±CSs use (59% vs 70%, p=0.02) compared to those with non-BS related hospitalizations. There were no differences between the groups regarding gender distribution (203 M/62 F vs. 143 M/54 F) and use of biologic agents (15% vs 17%). Three patients died during hospitalization. The reasons were malignancy, infection and right heart failure due to pulmonary artery thrombosis and pulmonary hypertension, respectively.
Conclusion: Vascular involvement is the leading cause of hospitalization among BS patients, followed by infections. The predominance of men among hospitalized patients underlines the relatively severe course of BS in men. The retrospective design and inclusion of patients who were hospitalized only in the rheumatology unit are limitations of this study.

Table 1. Distributions of BS related and non-BS related reasons of hospitalizations

	BS patients hospitalized with BS related reasons (n of pts=195, n of hospitalizations=265)*	BS patients hospitalized with non-BS related reasons (n of pts=170, n of hospitalizations=197)*
Causes of hospitalizations (per hospitalization)	Vascular inv. (n=169, 64 %)	Infection (n=64, 32%)
	Pulmonary artery inv. (n=64, 24 %)	*Pneumonia (n=17, 8%)*
	Deep vein thrombosis (n=39, 15 %)	*Tuberculosis (n=8, 4%)*
	Budd-Chiari synd. (n=24, 9%)	*Urinary tract inf (n=7, 4%)*
	Vena cava inf. thrombosis (n=19, 7 %)	*Gastroenteritis (n=4, 2%)*
	Peripheral artery inv. (n=15, 6 %)	*Osteomyelitis (n=3, 2%)*
	Vena cava sup. thrombosis (n=14, 5 %)	*Septic arthritis (n=3, 2%)*
	Aorta inv. (n=14, 5%)	*Aspergillosis (n=2, 1%)*
	Coronary artery inv. (n=4, 2 %)	*Nocardia (n=1, 1%)*
	Neurologic inv. (n=50, 19 %)	*Salmonella (n=1, 1%)*
	Parenchymal inv. (n=37, 14%)	*Others (n=18, 9%)*
	Dural sinus thrombosis (n=13, 5%)	Drug side effects other than infections (n=29, 15 %)
		Interferon (n=10, 5%)
		Azathioprine (n=7, 4%)
		Cyclosporine (n=5, 3%)
		Steroid (n=3, 2%)
		TNF antagonists (n=3, 2%)
		IVIG (n=1, 1%)
	GI inv. (n=18, 7%)	Additional rheumatologic diseases (n=17, 9%)
	Joint inv. (n=12, 5%)	Renal disease (n=16, 8 %)
	Mucocutaneous inv. (n=10, 4%)	Cardiovascular dis. (n=12, 6%)
	Eye inv. (n=8, 3%)	Avascular necrosis (n=4, 2%)
	Others (n=8, 3%)	Malignancy (n=11, 6%)
		Others (n=40, 20%)

*Some patients were hospitalized more than one times and for both BS related and non-BS related reasons at different time and had more than one type of BS related and/or non-BS related reasons.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1987

POS1352 ANTIINFLAMMATORY, ANTIOXIDANT AND ANTI-ATHEROSCLEROTIC EFFECTS OF A COMBINATION OF NATURAL SUPPLEMENTS ON PATIENTS WITH FMF RELATED AA AMYLOIDOSIS: A NON-RANDOMIZED 24 WEEKS OPEN LABEL INTERVENTIONAL STUDY

M. Romano[1], F. Garcia-Bournissen[2], D. Piskin[2], R. Cimaz[3], M. Yilmaz[4], E. Demirkaya[1]. [1]*Schulich School of Medicine & Dentistry, University of Western Ontario, Paediatric Rheumatology, London, Canada*; [2]*Western University, London, Ontario, Canada, Paediatrics, London, Canada*; [3]*University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy*; [4]*Epigenetic Health Solutions, Unit of Nephrology, Ankara, Turkey*

Background: Few studies have focused on Familial Mediterranean Fever (FMF)-related AA amyloidosis and cardiovascular disease event risk. Systemic inflammation stimulates the development and progression of atherosclerosis which is accelerated by vascular endothelial inflammation and enhanced oxidative stress. Excessive reactive oxygen species (ROS) generation has been reported in FMF, which correlated with attack severity. ROS may also be involved in amyloid formation, and in the pathogenesis of progressive renal injury.
Objectives: In this non-randomized, 24 weeks open label interventional study, we aimed to evaluate the effect of a combination of natural products on parameters related to inflammation, endothelial dysfunction and oxidative stress in a cohort of FMF patients with AA amyloidosis.
Methods: Morinda citrifolia (anti-atherosclerotic liquid- AAL), omega-3 (anti-inflammatory capsules- AIC) and extract with Alaskan blueberry (anti-oxidant liquid- AOL) were given to patients with FMF related AA amyloidosis. We included patients with biopsy proven AA amyloidosis, older than 18 years who have normal estimated glomerular filtration rate (eGFR) and proteinuria [>3500mg/day]. Flow-mediated dilatation (FMD), asymmetric dimethylarginine (ADMA), hs-CRP, serum PTX3, Carotis intima media thickness (CIMT), malondialdehyde (MDA), Cu/Zn-superoxide dismutase (Cu/Zn-SOD), glutathione peroxidase (GSH-Px) levels were studied in baseline and after 24 weeks.
Results: 67 FMF-related amyloidosis [52 male (77.6%); median recruitment age 36 years (range 21-66)] were enrolled. M694V mutation was the most common mutation found (74%), with 50.7% of the patients in homozygosity. All patients were treated with colchicine, and most of them (83.6%) has been on colchicine treatment at the time of enrollment. Serum ADMA, MDA, PTX3, hsCRP, cholesterol, and proteinuria were significantly decreased compared to baseline, while CuZn-SOD, GSH-Px and FMD levels were significantly increased following AAL, AIC and AOL therapies (Table 1). The change of the inflammatory markers PTX3, and hsCRP were negatively correlated with the change in FMD and positively correlated with the change of proteinuria, ADMA, MDA, cholesterol and CIMT.
Conclusion: 24 weeks of AAL, AIC and AOL combined supplementation was significantly associated with reduction in serum inflammatory markers (PTX3 and hsCRP), improved endothelial functions (FMD, ADMA), and oxidative state (MDA). Our findings highlight the link among the three pathogenetic mechanisms including inflammation, endothelial function and oxidative status in progression of atherosclerosis and renal injury in patients with FMF related AA amyloidosis. Efficient control of these three mechanisms can have long term benefits from the cardiovascular and renal perspective of the patients with AA amyloidosis.

REFERENCES:

[1] Romano M et al. Sci Rep, 2020
[2] Yilmaz M et al. Sci Rep, 2020

Table 1. Comparison of clinical and laboratory characteristics at the baseline and after 24 weeks of AAL, AIC and AOL supplementation

	Baseline	24th week	Delta	
	Mean (SD)	Mean (SD)	Mean (SD)	p
Total Cholesterol (mg/dl)	221.2 (60.3)	155.8 (35.4**)	-65.3 (55.5)	<0.001
eGFR (ml/min/ 1.73 m2)	110.2 (12.8)	104.1 (11.2**)	-6.1 (11.9)	<0.001
Malondialdehyde (MDA) (nmol/ml)	4.2 (1.8)	1.8 (0.5**)	-2.2 (1.8)	<0.001
CuZn-SOD (U/ml)	431.5 (154.7)	538.1 (146.4**)	159.7 (211.8)	<0.001
GSH-Px (U/ml)	47.8 (13.2)	74.1 (20.3**)	26.3 (21.1)	<0.001
ADMA (µmol/l)	4.5 (2.6)	1.3 (0.6**)	-3.2 (2.5)	<0.001
FMD (%)	5.0 (0.7)	6.4 (0.8**)	1.3 (0.9)	<0.001
CIMT (mm)	0.9 (0.2)	0.7 (0.1)	-0.2 (0.2)	<0.001
Proteinuria (mg/24h)	6855.3 (3116.9)	4079.9 (2359.6)	-2775.3 (2874.5)	<0.001
hs-CRP (mg/l)	25.5 (4.4-48.0)	3.0 (1.0-9.1)*	-20.8 (11.2)	<0.001
PTX3 (ng/ml)	13.4 (2.3-67.0)	2.3 (0.4-14.5)*	-17.5(17.5)	<0.001

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2144

POS1353 SERUM PROTEOMICS REVEALS INSULIN-LIKE GROWTH FACTOR BINDING PROTEINS-1 AS BIOMARKERS FOR IDIOPATHIC MULTICENTRIC CASTLEMAN'S DISEASE

R. Sumiyoshi[1], T. Koga[1], A. Kawakami[1]. [1]*Nagasaki University Graduate School of Biomedical Sciences, Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki, Japan*

Background: Castleman's disease (CD) is a lymphoproliferative disorder[1] and presents as two distinct clinical entities: the localized form, unicentric CD (UCD) and the multicentric form, multicentric CD (MCD)[2]. MCD without human herpesvirus-8 (HHV-8) infection is defined idiopathic MCD (iMCD)[3] and most MCDs in Japan are iMCDs. TAFRO syndrome is a group of disease that present with T: thrombocytopenia, A: anasarca, F: fever, R: reticulin fibrosis/renal dysfunction, O: organomegaly[4]. iMCD-TAFRO is present in the TAFRO syndrome and it is thought that pathology of lymph node biopsy shows an MCD-like appearance, and some clinical features overlap with MCD[5]. That do not belong to any of the above categories is classified as iMCD-not otherwise specified (iMCD-NOS). No biomarkers stratifying iMCD-NOS and iMCD-TAFRO have been identified, and no biomarkers defining treatment response have been identified for iMCD.
Objectives: We will identify biomarkers that discriminate iMCD-NOS and iMCD-TAFRO or predict the treatment responsiveness.
Methods: We performed a comprehensive analysis of serum proteins using the L-Series Human Antibody Array L-507 on the 4 iMCD-NOS and 2 iMCD-TAFRO patients from which pre- and post-tocilizumab treatment samples were obtained. An analysis by L-507 identified insulin-like growth factor binding proteins-1 (IGFBP-1) as a protein with a high rate of reduction post treatment. Sera from 28 healthy controls, 8 patients with iMCD-NOS, and 6 patients with iMCD-TAFRO were used to validate IGFBP-1 by ELISA. The mean ages of healthy controls, iMCD-NOS, and iMCD-TAFRO used in the validation ELISA were 50, 56, and 47 years, respectively, with no significant differences among the groups. The ratio of male to female was almost 1:1.
Results: The 4 patients who responded well to treatment with tocilizumab all had a high rate of IGFBP-1 reduction by L-507 serum protein arrays. In ELISA, serum IGFBP-1 was significantly higher (p=0.0016) before the introduction of treatment in iMCD patients than healthy controls. In addition, serum IGFBP-1 level of iMCD-TAFRO was significantly higher than iMCD-NOS (p=0.024). Furthermore, post-treatment serum IGFBP-1 was decreased in many cases.
Conclusion: Serum IGFBP-1 may play a particularly important role in the pathogenesis of iMCD-TAFRO and may be useful in discriminating between iMCD-NOS and iMCD-TAFRO. In the future, we will accumulate more cases, compare it with other inflammatory diseases, and examine the difference in response to treatment.
REFERENCES:
[1] CASTLEMAN, et al. 1954. CASE records of the Massachusetts General Hospital Weekly Clinicopathological Exercises: Case 40011. N Engl J Med, 250, 26-30.
[2] WATERSTON, et al. 2004. Fifty years of multicentric Castleman's disease. Acta Oncol, 43, 698-704.
[3] FAJGENBAUM D, et al. 2014. HHV-8-negative, idiopathic multicentric castleman disease (iMCD): A description of clinical features and therapeutic options through a systematic literature review. Blood (ASH Annual Meeting Abstracts), 124, 4861.
[5] TAKAI K, et al. 2010. Thrombocytopenia with mild bone marrow fibrosis accompanied by fever, pleural effusion, ascites and hepatosplenomegaly [in Japanese]. Rinsho Ketsueki, 51, 320-325.
[6] IWAKI N, et al. 2016. Clinicopathologic analysis of TAFRO syndrome demonstrates a distinct subtype of HHV-8-negative multicentric Castleman disease. Am J Hematol, 91, 220-226.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2246

POS1354 GENDER DIFFERENCES IN CLINICAL FEATURES AND BURDEN IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: PRELIMINARY REPORT

M. T. Duruöz[1], A. Ozer[1], H. H. Gezer[1], M. Alkan Melikoglu[2], S. Hizmetli[3], H. S. Baklacioglu[4], N. Sahin[5], N. Öz[1], D. Erdem Gürsoy[6], D. Altıntaş[7], P. Oba[8], S. Acer Kasman[1]. [1]*Marmara University School of Medicine, PMR Department, Rheumatology Division, İstanbul, Turkey*; [2]*Ataturk University School of Medicine, PMR Department, Rheumatology Division, Erzurum, Turkey*; [3]*Cumhuriyet University School of Medicine, PMR Department, Rheumatology Division, Sivas, Turkey*; [4]*Samsun Training and Research Hospital, Rheumatology Clinic, Samsun, Turkey*; [5]*Balikesir University School of Medicine, PMR Department, Balıkesir, Turkey*; [6] *Adıyaman Training and Research Hospital, Rheumatology Clinic, Adıyaman, Turkey*; [7]*Ataturk University School of Medicine, PMR Department, Erzurum, Turkey*; [8] *Cumhuriyet University School of Medicine, PMR Department, Sivas, Turkey*

Background: Familial Mediterranean fever (FMF) is the most common hereditary auto-inflammatory disease, which is more common in groups in the Mediterranean basin, characterized by recurrent attacks of febrile peritonitis, pleuritis and arthritis.
Objectives: The aim of this study is to investigate the gender differences in clinical and demographic features in patients with familial Mediterranean fever (FMF).
Methods: Patients with FMF diagnosed according to Tel-Hashomer criteria were included in this multi-center study. Data about age, sex, disease duration, symptom duration, age at diagnosis, comorbid diseases and medications were noted. All patients were screen with Hospital Anxiety and Depression Scale (HADS), Health Assessment Questionnaires (HAQ), Short Form 36 (SF-36). The severity of FMF was assessed by the PRASS scoring system.
Results: Of the 286 patients, 199 (69,6%) were female with the mean age 36,2(SD:12.32) years and 87 (30,4%) were male with the mean age 32,9(SD:12,6) years (p=0,017). Age of diagnosis in male patients was lower than in females (p=0,008). The most common genetic mutation in both genders was M694V gene mutation. Homozygous M694V positivity was higher in males (31,79% vs 17,4%). More than 90% of patients were receiving colchicine,10 (3,5%) patients were receiving anakinra and 5(1,75%) patients were receiving canakinumab. Among the patients regularly taking colchicine, 86.2% were females and 86% were males (p=0,981). There were no differences between male and females in terms of clinical findings, frequency and duration of attacks, presence of colchicine resistance, and the presence of amyloidosis (p>0.05). ESR was detected higher in female group (p=0,011). Headache (p=0,001), migraine (p=0,031), and concomitant diseases (p=0,017) were also more common in females than males. Anxiety and depression scores were higher in females (p<0,05). The PRASS activity scores were similar between genders (p>0,05). All parameters of SF-36 were higher in male patients, while HAQ score was higher in females (p<0,05).
Conclusion: Although clinical findings, disease severity and treatment compliance are similar in both genders, males are diagnosed with FMF earlier than females, but findings such as anxiety, depression, migraine, and headache are more common in female patients.
REFERENCES:
[1] Doğan HO, Koca Y, Erden G, Karaaslan Y, Bozat H. Evaluating MEFV mutation frequency in Turkish familial Mediterranean fever suspected patients and gender correlation: a retrospective study. Mol Biol Rep. 2012 May;39(5):6193-6.

Table 1. Demographic and clinical features between female and male FMF patients.

	Female (n:199)	Male (n:87)	*P*
Demographic features, mean (SD)			
Age	36,2 (12.32)	32,9 (12,6)	**0,017**
BMI	26,87(5,73)	25,79(5,28)	0,177
Educational level, years	8,77(4,36)	12,08(3,23)	**0,000**
Age at diagnosis	28 (13,31)	23,7 (13,42)	**0,008**
Age at onset of disease	19,2 (12,6)	17 (10,6)	0,265
Clinical features, n (%)			
Fever	166 (83,4)	77 (88,5)	0,268
Abdominal pain	180 (90,5)	78 (89,7)	0,835
Chest pain	62 (31,2)	20 (23)	0,160
Erysipelas like erythema	12 (6)	4 (4)	0,628
Arthritis	46 (23,1)	24 (24)	0,419
Arthralgia	102 (51,3)	42 (48,3)	0,643
Myalgia	101 (50,8)	47 (54)	0,611
MEVF mutations, n (%)			
M694V/M694V	24 (12.3)	19 (22)	**0.047**
*M694V h*eterozygous	38 (19,5)	14 (16,3)	0.523
M694V/any	25 (12,8)	15 (17,4)	0.307
PRASS disease severity, n (%)			0,813
Mild	99(49,7)	46(52,9)	
Moderate	88(44,2)	35(40,2)	
Severe	12(6)	6(6,9)	
ESR, mm/hour, mean (SD)	23,77(16,27)	18,25(18,41)	**0,011**
HAQ, mean (SD)	0,49 (0,63)	0,16 (0,43)	**0,000**
HAD, mean (SD)			
Anxiety	8,4 (4,4)	6,7 (3,44)	**0,003**
Depression	7,1 (4,27)	5,7 (3,81)	**0,006**
SF-36, mean (SD)			
Physical functioning	63,56 (23,81)	79,93 (19,32)	**0,000**
Physical role limitation	45,78 (40,95)	61,41 (39,14)	**0,003**
Emotional role limitation	47,36 (42,04)	66,20 (40,69)	**0,020**
Energy/fatigue	42,50 (20,64)	53,64 (19,82)	**0,000**
Emotional well-being	51,61 (18,47)	58,74 (18,30)	**0,003**
Social functioning	57,06 (23,09)	70,52 (23,82)	**0,000**
Pain	51,66 (24,05)	65,72 (24,51)	**0,000**
General health	39,53 (20,01)	52,46 (23,83)	**0,000**

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2317

POS1355 THE REMITTING SERONEGATIVE SYMMETRICAL SYNOVITIS WITH PITTING EDEMA SYNDROME (RS3PE): REVIEW OF TEN YEARS AT A REFERENCE HOSPITAL

S. Garcia Perez[1], J. L. Modesto Dos Santos[2], J. Mendizabal[1], M. López I Gómez[1], G. Sada[1], J. Restrepo Vélez[1], J. I. Elejalde[2], L. Garrido Courel[1], V. Aldasoro[1], I. Paniagua Zudaire[1], R. Gutierrez[1], L. Horcada[1], F. J. Anniccherico[2], N. Del Val del Amo[1], M. C. Fito Manteca[1], J. Sanchez Alvarez[2]. *[1]Complejo Hospitalario de Navarra (CHN), Rheumatology, Pamplona, Spain*; *[2]Complejo Hospitalario de Navarra (CHN), Internal Medicine, Pamplona, Spain*

Background: The Remitting Seronegative Symmetrical Synovitis with Pitting Edema Syndrome (RS3PE) is a rare rheumatological disease, considered a benign process.
Objectives: This study aims to describe its clinical features and serological markers, and also to analyze its possible association with neoplasms.
Methods: An observational retrospective study was performed to assess demographic and clinical characteristics of patients diagnosed from RS3PE at a reference hospital amongst the Rheumatology and Internal Medicine departments, from 2010 to 2021.
Results: Twenty-seven patients were included, with a mean age of 82.74 y.o. (IC95% 80.45-85.04; range 66 to 93), and a 51.85% proportion of males. Only 22.22% were from rural areas.
All patients presented bilateral hand edema although some associated feet edema (40.74%) or morning stiffness (70.37%). Blood tests demonstrated anemia in 44.44% of patients. Inflammatory markers were elevated, such as C-Reactive Protein (29.23 mg/L, IC95% 18.17-40.29), erythrocyte-sedimentation rate (33.74 mm/hour, IC95% 24.22-43.26) and fibrinogen (531.6 mg/dL, IC95% 482.91-580.30). Only a few patients presented any autoimmune serological marker such as antinuclear antibodies (18.18%) or rheumatoid factor (8.70%).
X-ray screening was realized to 22 patients. 14 showed of osteoarthritis radiologic presentation, 4 had radiological findings of chondrocalcinosis and one of them presented both. Only one patient had bone erosion.
Malignancy screening was performed at diagnosis in only 29.63% of patients (all negative). During follow-up only two tumors were detected (mean accumulated follow-up: 40.37 months, IC95% 26.70-54.04; range 1 to 122) and there were adenocarcinoma primary neoplasms.
All but one patient received low-dose corticosteroids, with a good and rapid response in all cases. Three patients received treatment with methotrexate (2) or leflunomide (1).
Conclusion: RS3PE must be contemplated in elderly patients presenting with bilateral hand pitting edema and articular symptoms. No specific biomarkers have been described, but inflammatory reaction is often found in the absence of rheumatoid arthritis biomarkers. Rapid response to corticosteroids is prevalent. Only two neoplasms were detected during follow-up.
REFERENCES:
[1] Paira S, Graf C, Roverano S, Rossini J. Remitting seronegative symmetrical synovitis with pitting oedema: a study of 12 cases. Clin Rheumatol. 2002 May;21(2):146-9. doi: 10.1007/pl00011218. PMID: 12086166.
[2] Cobeta García JC, Martínez Burgui J. RS3PE syndrome or benign edematous polysynovitis in the elderly. Study of 8 cases. Rev Clin Esp. 1999 Dec;199(12):785-9. Spanish. PMID: 10687410.
[3] Moreno Obregón F, Del Castillo Madrigal M, Díaz Narváez F, Pérez Delgado FJ. RS3PE syndrome with positive rheumatoid factor. Reumatol Clin. 2019 Nov-Dec;15(6):e168-e169. English, Spanish. doi: 10.1016/j.reuma.2017.11.009. Epub 2017 Dec 15. PMID: 29254743
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2646

POS1356 PERSISTENCE OF TFH CELLS AFTER RITUXIMAB IS ASSOCIATED WITH IGG4-RELATED DISEASE RELAPSE

G. Mancuso[1,2], T. Jofra[3], M. Lanzillotta[4], J. Gerosa[3], G. DI Colo[2], L. Dagna[2], G. Fousteri[3], E. Della Torre[2]. *[1]Università Vita-Salute San Raffaele, Allergologia ed Immunologia clinica, Milano, Italy*; *[2]Ospedale San Raffaele, Immunologia, Reumatologia, Allergologia e Malattie Rare, Milano, Italy*; *[3]Università Vita-Salute San Raffaele, Diabetes Research Institute (DRI), Milano, Italy*; *[4]Università Vita-Salute San Raffaele, Internal medicine, Milano, Italy*

Background: Clinical improvement after B-cell depletion with rituxmab suggests a prominent pathogenic role of B-lymphcytes in IgG4-related disease (IgG4-RD). IgG4-RD, however, relapses in most cases together with re-expansion of clonally divergent plasmablasts indicating that treatment with rituximab does not completely abrogates T follicular helper (Tfh)-cells dependent germinal center reactions leading to de-novo plasmablast differentiation.
Objectives: In the present work we aim to study the effects of B-cell depletion therapy with rituximab on circulating Tfh cells and on the levels of CXCL13 - a chemotactic factor for B-lymphocytes produced by Tfh cells - in patients with IgG4-RD.
Methods: Thirty patients with IgG4-RD, diagnosed according to the "Consensus Statement on the Pathology of IgG4-RD" and fulfilling the "2019 ACR/EULAR Classification Criteria" were included in the present study. Ten patients with relapsing disease were treated with the anti-CD20 monoclonal antibody rituximab (two 1g infuxions 15 days apart). Peripheral blood mononuclear cells and serum were collected before rituximab and three months after infusion. Tfh cells subsets in the peripheral blood were measured by flow cytometry and CXCL13 plasma levels were measured by ELISA assay.
Results: No changes in total Tfh cells and Tfh cells subsets were observed three months after rituximab neither in absolute counts nor in percentage of CD4+ T cells. In particular, no difference in Tfh1, Tfh2, Tfh17, T follicular regulatory and highly functional Tfh cells counts was observed before and after treatment. The serum level of CXCL13 was significantly higher in active untreated IgG4-RD patients compared to healthy controls (151.94 pg/ml vs 66.98 pg/ml, p value = 0.0026), but was not affected by rituximab treatment (p value = 0.41).
Conclusion: In relapsing patients with IgG4-RD rituximab does not affect circulating Tfh cells numbers and serum levels of CXCL13. Persistence of Tfh cells after rituximab and reconstitution of germinal center reactions likely drives IgG4-RD flare.
REFERENCES:
[1] Lanzillotta M, Mancuso G, Della-Torre E. Advances in the diagnosis and management of IgG4 related disease. BMJ. 2020 Jun 16;369:m1067. doi: 10.1136/bmj.m1067. PMID: 32546500.
[2] Lanzillotta M, Della-Torre E, Stone JH. Roles of Plasmablasts and B Cells in IgG4-Related Disease: Implications for Therapy and Early Treatment Outcomes. Curr Top Microbiol Immunol. 2017;401:85-92. doi: 10.1007/82_2016_58. PMID: 28091934.
[3] Campochiaro C, Ramirez GA, Bozzolo EP, Lanzillotta M, Berti A, Baldissera E, Dagna L, Praderio L, Scotti R, Tresoldi M, Roveri L, Mariani A, Balzano G, Castoldi R, Doglioni C, Sabbadini MG, Della-Torre E. IgG4-related disease in Italy: clinical features and outcomes of a large cohort of patients. Scand J Rheumatol. 2016;45(2):135-45. doi: 10.3109/03009742.2015.1055796. Epub 2015 Sep 23. PMID: 26398142.
[4] Mattoo H, Mahajan VS, Della-Torre E, Sekigami Y, Carruthers M, Wallace ZS, Deshpande V, Stone JH, Pillai S. De novo oligoclonal expansions of circulating plasmablasts in active and relapsing IgG4-related disease. J Allergy Clin Immunol. 2014 Sep;134(3):679-87. doi: 10.1016/j.jaci.2014.03.034. Epub 2014 May 6. PMID: 24815737; PMCID: PMC4149918.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2715

POS1357 OCULAR SCLERAL PATHOLOGY. UNDERLYING DISEASES AND SYSTEMIC TREATMENT. STUDY OF 175 PATIENTS FROM A SINGLE UNIVERSITY CENTER

L. Sanchez-Bilbao[1], V. Calvo-Río[1], J. L. Martín-Varillas[2], C. Álvarez-Reguera[1], A. Herrero-Morant[1], I. González-Mazón[1], R. Demetrio-Pablo[3], M. A. González-Gay[1], R. Blanco[1]. *[1]H.U. Marqués de Valdecilla, Rheumatology, Santander, Spain*; *[2]H.Sierrallana, Rheumatology, Torrelavega, Spain*; *[3]H.U. Marqués de Valdecilla, Ophthalmology, Santander, Spain*

Background: Ocular scleral pathology (OSP) includes episcleritis and scleritis. Episcleritis is generally a benign disease with a self-limited course, while scleritis is a more severe ocular condition. In some severe and refractory cases systemic therapy may be required.
Objectives: In a wide series with OSP our aim was to assess **a)** underlying diseases and **b)** systemic treatment.
Methods: Study of unselected all consecutive patients studied in a single University Hospital during the last ten years with**: a)** episcleritis and **b)** scleritis diagnosed by clinical features and slit-lamp (Watson and Hayreh criteria). Best corrected visual acuity (BCVA) and intraocular pressure (IOP) were measured at diagnosis and after systemic treatment.
Results: We studied 175 patients (106 women/ 69 men) /212 affected eyes with OSP (episcleritis=135; scleritis=40); mean age 48.9±14.2 years.
OSP was unilateral in 138 (78.9%), recurrent in 74 (42.9%) and chronic in 21 (12%). Most of them were idiopathic (n=81, 46.3%) while associated with IMID were 43.4% (Table 1). The most important underlying IMID were spondyloarthritis and inflammatory bowel disease, without significant differences between scleritis and episcleritis. Granulomatosis with polyangiits and systemic lupus erythematosus were more frequent in scleritis, not reaching statistical significance.
Regarding treatment, topical treatment was used in all patients. 41.1% received systemic treatment, including systemic glucocorticoids, cDMARDS and

bDMARDs. Systemic glucocorticoids and Methotrexate were used more frequently in scleritis (Table 1). The main indication for biologic therapy was related to underlying IMID in both groups, but 7 bDMARDs in scleritis were indicated for systemic and ocular compromise.
BVCA and IOP improved significantly after systemic treatment in scleritis (Figure 1).

Table 1. Underlying diseases and systemic treatment.

	Overall (n =175)	Episcleritis (n=135)	Scleritis (n=40)	p
Age (years), mean ± SD	48.9 ± 14.2	47.8 ± 14.3	52.6 ± 13.9	0.061
Sex (women), n (%)	106 (60.6)	81 (60)	25 (62.5)	0.920
UNDERLYING DISEASE				
-Idiopathic, n (%)	81 (46.3)	65 (48.1)	16 (40)	0.364
-Infectious, n (%)	11 (6.3)	7 (5.2)	4 (10)	0.276
-IMID, n (%)	76 (43.4)	57 (42.2)	19 (47.5)	0.563
◦Spondyloarthritis	21 (12)	17 (12.6)	4 (10)	0.787
◦Crohn's disease	16 (9.1)	14 (10.4)	2 (5)	0.469
◦Rheumatoid Arthritis	14 (8)	12 (8.9)	2 (5)	0.740
◦Granulomatosis with polyangiits	7 (4)	3 (2.2)	4 (10)	0.080
◦Relapsing polychondritis	6 (3.4)	4 (3)	2 (5)	0.621
◦Systemic lupus erythematosus	5 (2.9)	2 (1.5)	3 (7.5)	0.079
◦Ulcerative colitis	3 (1.7)	2 (1.5)	1 (2.5)	0.796
SYSTEMIC TREATMENT	72 (41.1)	37 (27.4)	35 (87.5)	**0.000***
-Systemic glucocorticoids, n (%)	72 (41.1)	37 (27.4)	35 (87.5)	**0.000***
-Methotrexate, n (%)	39 (22.3)	17 (12.6)	22 (55)	**0.000***
-Non-methotrexatecDMARD, n (%)	35 (20)	24 (17.8)	11 (27.5)	0.177
-TNFibDMARD, n (%)	27 (15.4)	19 (14.1)	8 (20)	0.362
-Non-TNFibDMARD, n (%)	8 (4.6)	5 (3.7)	3 (7.5)	0.386

*p<0,05*p<0,05

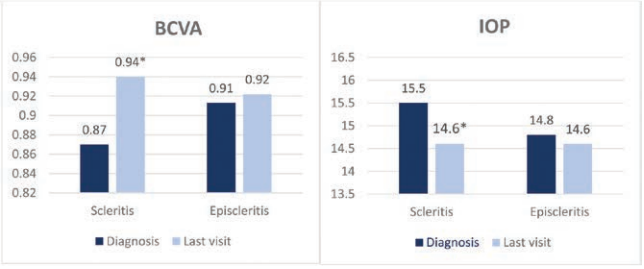


Figure 1. BVCA and IOP at diagnosis and last visit.

Conclusion: OSP is a relatively frequent entity. It is necessary to exclude an underlying systemic disease to establish correct systemic treatment.
Disclosure of Interests: Lara Sanchez-Bilbao: None declared, Vanesa Calvo-Río Speakers bureau: AbbVie, Lilly, Celgene, Grünenthal and UCB Pharma., Grant/research support from: MSD and Roche, José Luis Martín-Varillas: None declared, Carmen Álvarez-Reguera: None declared, Alba Herrero-Morant: None declared, Iñigo González-Mazón: None declared, Rosalía Demetrio-Pablo: None declared, Miguel A González-Gay Speakers bureau: AbbVie, Pfizer, Roche, Sanofi, Celgene and MSD. Ricardo, Grant/research support from: AbbVie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD., Grant/research support from: AbbVie, MSD and Roche
DOI: 10.1136/annrheumdis-2021-eular.2731

POS1358 THE EFFECTS AND SAFETY OF APREMILAST AND CYTOKINE EXPRESSION IN BEHCET'S DISEASE PATIENTS

Y. Ushio[1], R. Wakiya[1], K. Ueeda[1], T. Kameda[1], S. Nakashima[1], H. Shimada[1], M. Mahmoud Fahmy Mansour[1], M. Kato[1], T. Miyagi[1], K. Sugihara[1], R. Senba[1], M. Mizusaki[1], H. Dobashi[1]. *[1]Kagawa University, Division of Hematology, Rheumatology and Respiratory Medicine, Takamatsu, Japan*

Background: Apremilast, the small-molecule phosphodiesterase (PDE) -4 inhibitor, was approved for the treatment of recurrent oral ulcers associated with Behcet's disease (BD) in Japan from September 2019, following the success of the phase 3 RELIEF study (1). However, the efficacy of apremilast on domains other than oral ulcers in BD patients is unclear. On the other hand, it has been reported that apremilast may decrease the production of proinflammatory cytokine and increase the production of anti-inflammatory mediators in psoriasis (PS) and psoriatic arthritis (PsA) (2).
Objectives: To evaluate the effects and safty of apremilast on clinical symptoms and the changing of serum cytokine expression.
Methods: BD patients who had treated with apremilast for active oral ulcers were included in the study. We investigated the improvement rate of oral and genital ulcers, skin lesions, arthritis. In addition, serum cytokines (IFN-γ, IL-10, IL-8, and TNF-α) before and after apremilast treatment were measured using a multiplex immunoassay (Luminex Assay, R&D Systems).
Results: Fourteen patients (3 males and 11 females) were enrolled in this study. The mean age was 46.6 ± 13.0 years and the mean duration of disease was 10.2 ± 8.8 years. All patients had active oral ulcers, five had genital ulcers, six had skin lesions, and four had arthritis. Three months after the treatment with apremilast, oral ulcers improved in 13 patients (92.9%). The improvement rates of genital ulcers, skin lesions and arthritis were 60%, 25% and 25%, respectively. Changes in serum cytokines were different from those previously reported in PS. Adverse events were gastrointestinal symptoms such as nausea and diarrhea in 6 patients and sensorineural deafness in 1 patient. Medication was reduced in 2 patients, and discontinued in 1 patient due to nausea and diarrhea.
Conclusion: Apremilast is useful not only for oral ulcers, but also for other lesions in BD patients. The effect of apremilast for other domain such as genital ulcers, skin lesions, arthritis was not comparable to that of active oral ulcers. Additionally, BD may have different cytokine profile from PS and PsA.
REFERENCES:
[1] Hatemi G, Mahr A, Ishigatsubo Y, et al. Trial of Apremilast for Oral Ulcers in Behcet's Syndrome. N Engl J Med. 2019;381(20):1918-28
[2] Schafer P. Apremilast mechanism of action and application to psoriasis and psoriatic arthritis. Biochem Pharmacol. 2012;83(12):1583-1590
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2772

POS1359 REGIONAL DIFFERENCES IN DISEASE CHARACTERISTICS OF FAMILIAL MEDITERRANEAN FEVER IN TURKEY: PRELIMINARY REPORT

M. T. Duruöz[1], H. H. Gezer[1], M. Alkan Melikoglu[2], S. Hizmetli[3], H. S. Baklacioglu[4], N. Sahin[5], A. Ozer[1], N. Öz[1], D. Erdem Gürsoy[6], D. Altıntaş[7], P. Oba[8], S. Acer Kasman[1]. *[1]Marmara University School of Medicine, PMR Department, Rheumatology Division, Istanbul, Turkey*; *[2]Ataturk University School of Medicine, PMR Department, Rheumatology Division, Erzurum, Turkey*; *[3]Cumhuriyet University School of Medicine, PMR Department, Rheumatology Division, Sivas, Turkey*; *[4]Samsun Training and Research Hospital, Rheumatology Clinic, Samsun, Turkey*; *[5]Balıkesir University School of Medicine, PMR Department, Balıkesir, Turkey*; *[6]Adıyaman Training and Research Hospital, Rheumatology Clinic, Adıyaman, Turkey*; *[7]Ataturk University School of Medicine, PMR Department, Erzurum, Turkey*; *[8]Cumhuriyet University School of Medicine, PMR Department, Sivas, Turkey*

Background: Familial Mediterranean fever (FMF) is a hereditary autoinflammatory disease accompanied by recurrent attacks of fever and serositis. It is prevalent among Mediterranean populations, mainly Turks, Armenians; Jews and Arabs. As genetic factors are variable in the population, environmental factors can also affect phenotypic characteristics.
Objectives: This study aimed to determine the geographic differences in disease characteristics and burden in patients with FMF in Turkey.
Methods: Patients diagnosed with FMF according to the Tel-Hashomer criteria were included in this multi-center study. Patients were included from the different regions of Turkey. Demographic features and clinic characteristics of the patients including disease duration, medications, comorbid conditions, attack characteristics, amyloidosis, acute phase reactants, FMF gene mutations, arthritis, sacroiliitis, and febrile myalgia were recorded. PRASS disease activity score, FMF-QoL, HAD, and HAQ were assessed. Patients from different parts of Turkey were divided into 3 groups the Central Anatolia, Western, and Eastern. Disease activity, characteristics and burden were also investigated among 3 distinct geographic regions.
Results: A total of 281 patients with FMF (195 women, 86 men) were enrolled in this study. The mean age of the patients was 34.9 (SD:12.3) years. While the patients in the eastern areas of Turkey were diagnosed earlier age (*p<0.001*), the patients in the western area had a longer diagnostic delay time (*p<0.001*). Patients enrolled from western regions tended to have higher ESR and PRASS scores than those from eastern and central Anatolian regions, but attack numbers per 6 months were similar among the regions. The highest proportion of patients who were M694V/M694V homozygous patients were in western, and then eastern and central Anatolia (19.5%, 18%, and 5.4%). While fever and arthritis were more common in the eastern, pleuritis and sacroiliitis were more common in the central anatolia. Peritonitis and erysipelas like erythema rates were similar among the regions. The majority of patients were receiving colchicine treatment in all three regions. FMF-QoL scores were highest in the eastern and lowest in the western (*p=0.006*). Patients enrolled in the central Anatolia region experienced more functional disability than those from the western and eastern regions (p=0.009). Anxiety and depression scores were similar between groups (p=0.385 vs p=0.549).
Conclusion: These findings suggest that patients with FMF have diversity concerning the age at diagnosis, diagnostic delay time, disease activity, quality of

life, and functional disability among the 3 regions. In the genotypic analysis, the M694V mutation is the most common pathogenic mutation in all regions. Regional genetic and environmental varieties may explain the areal differences. These relationships can occur more clearly in larger patient populations.

REFERENCES:

[1] Ureten K,et al. Demographic, clinical and mutational characteristics of Turkish familial Mediterranean fever patients: results of a single center in Central Anatolia. *Rheumatol Int*. 2010;30(7):911-915.

Table 1. Clinical and demographic characteristics of patients by geographic region

	Western, n=107	Central, n=74	Eastern, n=100	*p*
Age	37.7 (12.5)	36 (12.6)	31.2 (10.9)	**<0.001**
Sex, female	79 (73.8%)	58 (78.4%)	58 (%58)	**0.007**
Age at the symptom onset, year	16.8 (11.3)	20.4 (13.2)	18.5 (11)	0.229
Age at the diagnosis, year	29.6 (13.4)	27.7 (13.3)	22.1 (12.1)	**<0.001**
Diagnostic delay time, year	12.3 (12.9)	7.3 (10.5)	3.6 (5.3)	**<0.001**
ESR, mm/hr	26.8 (18.9)	15.5 (12)	13.1 (13.1)	**0.003**
PRASS		41 (55.4%)		0.577
Low	50 (46.7%)	28 (37.8%)	51 (51%)	
Moderate	48 (44.9%)		45 (45%)	
High	9 (8.4%)	5 (6.8%)	4 (4%)	
Fever	83 (77.6%)	60 (81.1%)	96 (96%)	**0.001**
Peritonitis	98 (91.6%)	64 (86.55)	92 (92%)	0.412
Pleuritis	35 (32.7%)	27 (36.5%)	18 (18%)	**0.013**
Arthritis	18 (16.8)	16 (21.6)	36 (36%)	**0.005**
Sacroiliitis	8 (7.5%)	14 (18.9%)	1 (1%)	**0.000**
Erysipelas like erythema	2 (1.9%)	7 (9.5%)	7 (7%)	0.075

Data are presented as mean (SD), median (min-max), and n (%)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2894

POS1360 MONOGENIC AUTO-INFLAMMATORY DISEASES IN ADULTS IN THE PRACTICE OF A RHEUMATOLOGIST

S. Salugina[1], E. Fedorov[1], T. Dubinina[2], S. Palshina[3]. [1]*V.A.Nasonova Research Institute of Rheumatology, Pediatric Department, Moscow, Russian Federation*; [2]*V.A.Nasonova Research Institute of Rheumatology, Laboratory of Medical and Social Problems of Rheumatology, Moscow, Russian Federation*; [3]*V.A.Nasonova Research Institute of Rheumatology, Laboratory of Intensive Therapy Methods, Moscow, Russian Federation*

Background: The group of the most common monogenic auto-inflammatory diseases (mAIDs) includes FMF, TRAPS, HIDS, CAPS. Descriptions of these diseases are widely presented in the literature, but they are not well covered among adults. MAIDs in the adult rheumatological practice are found: 1) in pts with the onset and diagnostics of the disease in their childhood; 2) in pts with juvenile onset, but diagnostics of the disease in their adulthood; 3) in pts with the onset of the disease in adulthood. Adult specialists, in contrast to pediatricians, are not very well aware of the clinical and laboratory picture, course, age characteristics, approaches to treatment, consequences of mAID, which leads to late diagnostics and untimely prescription of targeted therapy, development of complications (amyloidosis) and damage to organs, life quality impairment.

Objectives: To characterize adult patients with mAIDs in the practice of a rheumatologist.

Methods: Within the period from 2009 to 2020, 123 patients with mAIDs (FMF-53, CAPS-44, TRAPS-21, HIDS-5) were diagnosed, of which 50 were adults. All pts underwent a standard rheumatological examination, including ESR, CRP, ophthalmological and other instrumental examinations, audiogram, if required. Molecular genetic analysis of genes MEFV, TNFRSF1A, MVK, NLRP3 was performed in all pts. All but one patient with CAPS (CINCA / NOMID) showed feature genetic mutations.

Results: The study included 50 pts aged 18 to 66 years, 35 women, 15 men. The age of onset was from 0 to 53 years, in 88% of cases the onset of the disease was noted in childhood, 6 pts debuted at the age over 18 years (4 with FMF - 23-35 years; 2 CAPS - 51 and 53 years). As of the time of inclusion into the study, the duration of the disease ranged from 6 months to 59 years. All patients had fever, skin rashes were present in the majority (72%) of pts with CAPS (urticaria), TRAPS (erythematous and anulyariform) and HIDS (spotted), in half of pts with FMF (erysipeloid erythema). Articular manifestations were present in the majority of pts (80%), oligoarthritis in 38%, mainly in pts with CAPS (35%) and FMF (47.8%). Polyarthritis occurred in 18% of pts. Ophthalmic changes (32%) in the form of conjunctivitis and/or uveitis were more common in patients with CAPS (65%), sensorineural deafness only in pts with CAPS (40%), stomatitis in 16% in pts, more often in case of CAPS (35%). Family history is aggravated in almost half of pts. All pts showed an increase in ESR and CRP performance. Colchicine treatment was used mainly in patients with FMF. Glucocorticoids (GC) and biological agents (IL-1 inhibitors) were more often received by pts with CAPS (55% and 60%).

Table 1. Clinical and demographic characteristics of adult patients with mAIDs

AIDs	FMF (23)	CAPS (20)	TRAPS (5)	HIDS (2)	N (%)
Fever	23(100)	20 (100)	5 (100)	2 (100)	50 (100)
Rash	11(47,8)	18 (90)	5 (100)	2 (100)	36 (72)
Joints	17 (73,9)	16 (80)	5 (100)	2 (100)	40(80)
eye symptoms	1(4,3)	13 (65)	2 (40)	-	16(32)
Sensorineural hearing loss	-	8 (40)	-	-	
Family history	11(47,8)	8 (40)	3 (60)	-	22 (44)
Colchicine	23	1	2	-	26 (52)
Steroids	3	11	3	2	19 (38)
Biological therapy	5	12	3	1	21 (42)
Etanercept	2	-	1	-	3 (6)
Adalimumab	1	1	-	-	2 (4)
Tocilizumab	1	2	-	1	4 (8)
Canakinumab	1	7	2	-	10 (20)
Anakinra	1	5	-	-	6 (12)

Conclusion: The study of the peculiarities of the course of mAIDs in adults, increase in the awareness of adult rheumatologists about these diseases will improve and speed up diagnostics, develop approaches to treatment and management algorithms in order to improve the prognosis and quality of patients' life.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2996

POS1361 EVALUATION OF PATIENTS WITH (SUSPECTED) BEHÇET SYNDROME; DIAGNOSTIC VALUE OF PATHERGY TESTING AND OPHTHALMOLOGIC EXAMINATION

G. Duttenhofer[1], I. Visman[1], F. Kerstens[1], G. Piskin[2], F. Turkstra[1]. [1]*Reade, Rheumatology, Amsterdam, Netherlands*; [2]*BovenIJ ziekenhuis, Dermatology, Amsterdam, Netherlands*

Background: Behçet syndrome (BS) is a multisystem vasculitis of unknown etiology. A positive pathergy test (PT) is part of the ISG criteria for the classification of BS [1]. The added value of PT in the diagnostic workup is unknown. Also, it is unknown whether real time assessment of the pathergy reaction after 48 hours by a physician can be replaced by patient assessment.

The diagnostic value of routine eye examination in patients with suspected BS is unclear.

Objectives: Assess the diagnostic value of PT and ophthalmologic examination in (suspected) BS patients. Examine the correlation between physician and patient assessment of PT results.

Methods: This prospective cohort study in (suspected) BS patients was conducted from 2009 to 2020.

At baseline, patients were classified as "true" (≥3 criteria), "probable" (2 criteria) or "no" (0-1 criteria) BS according to ISG criteria and were referred to a dermatologist and/or ophthalmologist for PT and/or eye examination. The percentage of positive PT and eye examination in each group was assessed and the percentage of patients with a changed classification (probable to true BS) was determined.

PT results were scored by both patients and physicians.

Results: Baseline characteristics are reported in Table 1. Figure 1 displays the flowchart of diagnostic value of PT.

Table 1. Baseline characteristics of (suspected) BS patients.

	All patients n=153	ISG +[1] n=59	ISG+ after FU[2] n=11	ISG –[3] n=83	P-value (+ vs -)
Age (mean ± SD[4] years)	39.5 (12)	41.8 (11.6)	33.6 (7.5)	38.5 (12.6)	0.294
Male n (%)	47 (30.7)	16 (27.1)	4 (36.4)	27 (32.5)	0.360
HLA-B51+ n/n (%)	8/18 (44.4)	5/7 (71.4)	1/3 (33.3)	2/8 (25)	0.070
Ethnicity: endemic[5] n (%)	82 (53.6)	38 (64.4)	6 (54.5)	38 (45.8)	0.114
Oral aphthae n (%)	145 (94.8)	59 (100)	11 (100)	75 (90.4)	**0.008**
Genital ulcers n (%)	82 (53.6)	50 (84.7)	8 (72.7)	24 (28.9)	**0.000**
Skin n (%)	71 (46.4)	51 (86.4)	1 (9.1)	19 (22.9)	**0.000**
Pathergy + n/n (%)	23/58 (39.7)	17/33 (51.5)	2/3 (66.7)	4/22 (18.1)	**0.000**
Eye n (%)	28 (18.3)	17 (28.8)	1 (9.1)	10 (12)	**0.035**
Superficial thrombophlebitis n (%)	15 (9.8)	11 (18.6)	1 (9.1)	3 (3.6)	**0.018**
Vascular n (%)	11 (7.2)	5 (8.5)	1 (9.1)	5 (6)	0.360
Venous n (%)	10 (6.5)	5 (8.5)	1 (9.1)	4 (4.8)	
Arterial n (%)	2 (1.3)	1 (1.7)	0	1 (1.2)	
Neurological n (%)	5 (3.3)	3 (5.2)	0	2 (2.4)	0.433
Arthritis n (%)	40 (26.1)	20 (33.9)	2 (18.2)	18 (21.7)	0.197
Gastro- intestinal n (%)	6 (3.9)	3 (5.1)	0	3 (3.6)	1.00
Epididymitis n (% of males)	5 (10.6)	5 (31.3)	0	0	**0.002**

1.patients fulfilling the ISG criteria at enrollment2.patients who fulfilled the ISG criteria during FU3.patients did not fulfill the ISG criteria after FU4.standard deviation5.Turkey, Asia, Middle and Far Eastern, Arabic countries and Northern Africa

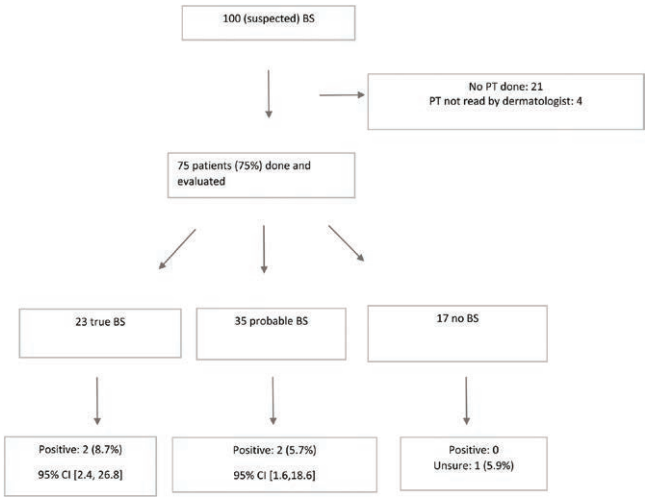


Figure 1. Flowchart of the results of PT in (suspected) BS patients

In 22 patients with two ISG criteria, grade I uveitis was diagnosed in 1 patient (4.5%, 95% CI [0.8,21.8]) and retinal vasculitis in 1 patient (4.5%, 95% CI [0.8,21.8]). He had shortly experienced photophobia 3 months earlier. Both patients (9%, 95% CI [2.5,27.8]) changed from "probable" to "true" BS, the latter also had a positive PT.

47 patients assessed the results of their own PT. The dermatologist scored PT as positive in one patient. This patient scored the results as unsure on all six PT points. In 46 patients, the dermatologist scored PT as negative, a total of 26 patients (56.5%, 95% CI [42.2,69.7]) scored their results negative as well.

Conclusion: The added diagnostic value of PT in patients fulfilling 2 features of the ISG criteria was limited in our study, i.e. 5.7% 95% CI [1.6,18.6]. Furthermore, half of patients scored their true negative PT result as negative. The added diagnostic value of routine eye examination in probable BS patients was limited in our study.

REFERENCES:

[1] Criteria for diagnosis of Behcet's disease. International Study Group for Behcet's Disease. Lancet 1990;335(8697):1078–8

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3047

POS1362 NEUROSARCOIDOSIS. STUDY OF 30 PATIENTS FROM A SERIES OF 384 SYSTEMIC SARCOIDOSIS FROM A TERTIARY UNIVERSITY HOSPITAL

A. Herrero-Morant[1], L. Sanchez-Bilbao[1], I. González-Mazón[1], D. Martínez-López[1], J. L. Martín-Varillas[2], R. Fernández-Ramón[1], M. Á. González-Gay[1], R. Blanco[1]. *[1]Hospital Universitario Marqués de Valdecilla, Rheumatology and Ophtalmology, Santander, Spain*; *[2]Hospital de Sierrallana, Rheumatology, Torrelavega, Spain*

Background: Neurosarcoidosis is a serious and infrequent complication of sarcoidosis. Data on Biologic Therapy (BT) efficacy is scarce.

Objectives: To assess in neurosarcoidosis a) its prevalence and associations of clinical clusters and b) efficacy and safety of BT.

Methods: Study of neurosarcoidosis from a large cohort (n=384) of all consecutive patients diagnosed with sarcoidosis from January 1, 1999 to December 31, 2019 in a single University hospital.

Results: 30 (19 women/ 11 men) out of 384 (7.8%) patients had neurosarcoidosis. Mean age at diagnosis was 41.8±15.8 years. Clusters of clinical associations were lungs (n=23, 76.7%) and joints (n=15, 50.0%) (Figure 1). The underlying neurological manifestations were chronic headache (n=13, 43.4%), peripheral neuropathy (n=6, 20.0%), cranial neuropathy (n=5, 16.7%), spinal cord abnormalities (n=3, 10.0%) and aseptic meningitis (n=3, 10.0%). 26 (86.7%) patients received oral corticosteroids (mean maximum dose 50±19.2mg) and 7 (23.3%) iv corticosteroids. In addition, 18 (60.0%) patients received conventional immunosuppressants and 12 (40.0%) BT. 4 (13.3%) did not have any treatment. Table 1 shows the main clinical features and treatment.

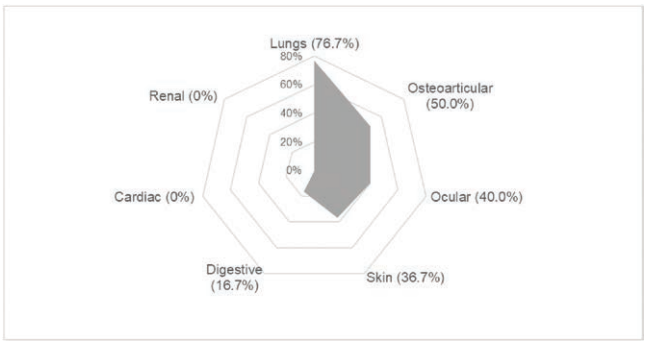


Figure 1. Clusters of clinical associations in neurosarcoidosis

12 patients received treatment with 14 BT. Monoclonal anti-TNFα (n=10, 83.3%) was the most used BT. 10 (83.3%) patients treated with BT achieved clinical remission. No serious adverse effects were observed.

Conclusion: Neurosarcoidosis was observed in 7.8% of systemic sarcoidosis. Most patients treated with BT, especially monoclonal anti-TNFα, achieved clinical remission.

Table 1. Main clinical features and treatment of 30 patients with neurosarcoidosis.

	n (%)	Conventional immunosuppressant, n (%)	monoclonal anti-TNFα, n (%)	Etarnecept, n (%)	Tocilizumab, n (%)	Secukinumab, n (%)	Rituximab, n (%)
Chronic headache	13 (43.4)	5 (38.5)	2 (15.4)	0 (0)	0	1 (7.7)	1 (7.7)
Peripheral neuropathy	6 (20.0)	4 (66.7)	3 (50.0)	1 (16.7)	0	0	0
Cranial neuropathy	5 (16.7)	4 (80.0)	3 (60.0)	0	0	0	0
Spinal cord abnormalities	3 (10.0)	1 (33.3)	1 (33.3)	0	0	0	0
Aseptic meningitis	3 (10.0)	2 (66.7)	2 (66.7)	0	1 (33.3)	0	0

Disclosure of Interests: Alba Herrero-Morant: None declared, Lara Sanchez-Bilbao: None declared, Iñigo González-Mazón: None declared, David Martínez-López: None declared, José Luis Martín-Varillas Grant/research support from: AbbVie, Pfizer, Lilly, Janssen, and Celgene, Raúl Fernández-Ramón: None declared, Miguel Á. González-Gay Speakers bureau: AbbVie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Grant/research support from: AbbVie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, Sanofi, Lilly and MSD, Grant/research support from: AbbVie, MSD, and Roche

DOI: 10.1136/annrheumdis-2021-eular.3052

POS1363 CHONDROCALCINOSIS AS PREDICTOR OF DEVELOPMENT OF PRIMARY HYPERPARATHYROIDISM: RESULTS OF THE FOLLOW-UP OBSERVATION

A. Novikova[1], M. Eliseev[1], O. Sheliabina[1], M. Chikina[1]. *[1]VA Nasonova Research Institute of Rheumatology, Laboratory of Microcrystalline Arthritis, Moscow, Russian Federation*

Background: The association between chondrocalcinosis and primary hyperparathyroidism (PHPT) is known, but chondrocalcinosis is considered as a late complication of PHPT.

Objectives: To investigate whether calcium pyrophosphate crystal deposition is an early clinical sign of PHPT.

Methods: The prospective study included 113 patients aged ≥18 years, 42 (37.2%) men and 71 (62.8%) women, with a crystal-verified diagnosis of calcium pyrophosphate crystal deposition disease (CPPD) (McCarty criteria). Exclusion criteria were the presence of other rheumatic diseases with symptoms of arthritis, the presence of hyperparathyroidism (HPT). Patients were examined at their enrollment and over time, the median follow-up was 3.86 [2.07; 8.36] years. The examination of the patients included assessment of anthropometric parameters, information about the affected joints and the time of onset of symptoms.

Table 1. Results of patients with PHPT at screening and in dynamics.

	Crystals of calcium pyrophosphate in synovial fluid	Chondrocalcinosis by ultrasound	Chondrocalcinosis by X-ray	Convulsions	ECG changes (shortening of the QT interval)	Arthralgias / arthritis	PTH, pg/ml (15,0-65,0)	Ca, μmol/l (2.10-2.62)	Ca^{++}, μmol/l (1.10-1.33)	vitamin D (25-OH), ng/ml (30-100)
	screening / dynamics									
Patient A.	yes/yes	yes/yes	not/yes	not/not	not/not	yes/yes	61.6/96.2	2.73/2.67	1.37/1.24	-/31
Patient B.	yes/yes	yes/yes	yes/yes	not/yes	not/yes	yes/yes	40.7/252	2.63/2.56	1.34/1.77	19.1/14.2
Patient C.	yes/yes	yes/yes	not/yes	not/not	not/not	yes/yes	26.6/102.4	2.60/2.65	1.25/1.26	-/40

Laboratory tests included determination of the following in blood serum: creatinine (with estimating glomerular filtration rate (eGFR) according to the MDRD formula), total and ionized calcium (Ca and Ca^{++}), phosphorus (P), parathyroid hormone (PTH), vitamin D (25-OH); ultrasound and X-ray investigations of the target joints (hands, knee joints) were made for all patients. Scintigraphy and ultrasound of the parathyroid glands were performed if medically required. Statistica 12.0 package was used for statistical data processing.

Results: 113 patients were examined, the average age was 58.4±12.4 years. 10 patients were excluded due to diagnosed HPT at screening. 41 patients dropped out of observation: 5 - died, 36 were not available for dynamic examination. 62 patients were examined in dynamics, 4 (6.5%) of those had HPT. In 1 (1.6%) case, HPT was associated with chronic renal failure, 3 (4.8) patients were diagnosed PHPT. The results of the examination of patients who developed PHPT during screening and in dynamics are presented in Table 1 above.

In all three patients, chondrocalcinosis was revealed by ultrasound and Crystals of calcium pyrophosphate in synovial fluid during the screening examination, in one patient chondrocalcinosis was revealed by X-ray. In two out of three cases, the level of serum Ca and Ca^{++} was minimally increased at a normal level of PTH, no other disorders of calcium metabolism were observed during the screening.

Interestingly, the first clinical manifestation of HPT in all patients was damage of the musculoskeletal system - mainly arthralgia, as well as arthritis of large and small joints. Moreover, all patients had a different CPPD phenotype: patient A - asymptomatic chondrocalcinosis, patient B - chronic arthritis (pseudo-rheumatoid form) and patient C - chronic arthritis (pseudosteoarthritis).

Conclusion: The deposition of calcium pyrophosphate crystals may be an early predictor of the development of PHPT and precedes other manifestations.

Disclosure of Interests: Aleksandra Novikova: None declared, Maxim Eliseev Speakers bureau: Berlin Chemie Menarini Group, Novartis International AG, EGIS, Olga Sheliabina: None declared, Maria Chikina: None declared

DOI: 10.1136/annrheumdis-2021-eular.3096

POS1364 MUSCULOSKELETAL VARIANT OF FAMILIAL MEDITERRANEAN FEVER MAY HAVE MORE SEVERE DISEASE

M. E. Tezcan[1], R. Mercan[2], Ö. Volkan[1], N. Şen[1], S. Yilmaz-Oner[1]. [1]*Kartal Dr. Lütfi Kırdar Şehir Hastanesi, Rheumatology, Istanbul, Turkey*; [2]*Tekirdağ Namık Kemal Üniversitesi, Rheumatology, Tekirdag, Turkey*

Background: Familial Mediterranean fever (FMF) is one of the prototypes of auto inflammatory diseases. Besides recurrent serositis, some patients also have musculoskeletal involvement similar to spondyloarthropathies (SpA) (1). These patients usually have more severe disease (2). In addition, some experts think FMF can be considered a variant of SpA.

Objectives: There is handful of studies in literature that evaluated the disease severity, FMF complications and treatment variations in FMF patients with individual musculoskeletal features separately (3). However, these patients can be considered as musculoskeletal/SpA variants of FMF. Here, we evaluated the validity of hypothesis: "The patients with any of musculoskeletal symptoms or SpA variant of FMF have more severe disease."

Methods: We included 218 FMF patients who met Modified Tel- Hashomer criteria. We divided the patients according to suffering from any of the musculoskeletal symptoms (arthritis, enthesitis, arthralgia/myalgia, sacroiliitis,standing myalgia).Here, arthritis, enthesitis were diagnosed with physical examination according to appropriate methods. Standing myalgia diagnosis was depending upon patients' history. Lastly, sacroiliitis was demonstrated in radiological screening. The patients with any of the musculoskeletal symptoms were considered musculoskeletal variants of FMF. In this study we compare disease characteristics and treatment differences between the groups. We used Mann-Whitney-U or chi-square tests where appropriate.

Results: There were 126 (57.7%) patients in the musculoskeletal group. FMF patients in both groups had similar demographic and disease characteristics except musculoskeletal signs. Musculoskeletal variant group had higher The International Severity Score for FMF (ISSF) (p<0.001); more frequent (p=0.009), intense (p=0.009) and longer attacks (p=0.001) than the others. Also, patients with musculoskeletal variant received higher colchicine dose (p=0.006).

Table 1. Demographic, disease and treatment characteristics of the patients

	Musculoskeletal variant n=126	Non-musculoskeletal group n=92	p
Gender (M/F)	45/81	34/58	0.85
Disease duration(year)	9.6±7.3	8.3±6.9	0.08
Fever (%)	81 (64.3)	53 (57.6)	0.37
Abdominal pain (%)	106 (84.1)	83 (90.2)	0.19
Plevritis (%)	46 (36.5)	28 (30.4)	0.35
Number of attack region	1.7±0.8	1.3±0.5	**<0.001**
Attack frequency (/year)	3.4±5.0	2.1±3.5	**0.009**
Attack duration (day)	1.6±1.7	0.9±1.5	**0,001**
Attack VAS score (0-100)	33.3±32.7	23.1±31.5	**0,009**
ISSF score	1.6±1.3	0.6±0.9	**<0.001**
Exon 10 homozygote (%)	33 (26.2)	19 (20.7)	0.42
Amyloidosis (%)	6 (4.8)	2 (2.2)	0.47
Colchicine dose (mg/day)	1.4±04	1.2±0.4	**0.006**
Il-1 blocker (%)	1 (0.8)	2 (2.2)	0.57

M: Male; F: Female; ISSF: The International **Severity** Score for FMF; VAS: Visual analog score. All continuous variables shown as mean±SD. p<0.05 is significant.

Conclusion: We showed that FMF patients with musculoskeletal signs have more severe disease and received higher colchicine dose as compared to non-musculoskeletal group and can be considered as the SpA variant of FMF or a distinct variant of SpA.

REFERENCES:

[1] Atas N, Armagan B, Bodakci E, et al. Familial Mediterranean fever is associated with a wide spectrum of inflammatory disorders: results from a large cohort study. Rheumatol Int 2020; 40:41-48.

[2] Sen N, Yilmaz M, Mercan R, et al. Enthesitis may be one of the signs of severe disease in familial Mediterranean fever. Clin Rheumatol 2020

[3] Eshed I, Rosman Y, Livneh A, et al. Exertional leg pain in familial Mediterranean fever: a manifestation of an underlying enthesopathy and a marker of more severe disease. Arthritis Rheumatol 2014; 66:3221-6.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3100

POS1365 ANNALYSIS OF PRO-INFLAMMATORY BIOMARKERS IN A POLYMYALGIA RHEUMATICA COHORT DURING THE ACUTE ONSET OF THE DISEASE

F. M. Ortiz Sanjuan[1], E. Grau García[1], C. Riesco Barcena[1], A. V. Huaylla Quispe[1], C. Pávez Perales[1], S. Leal Rodriguez[1], M. De la Rubia Navarro[1], I. Martínez Cordellat[1], C. Nájera Herranz[1], R. Negueroles Albuixech[1], J. E. Oller Rodríguez[1], E. Vicens Bernabeu[1], C. Alcañiz Escandell[1], I. Cánovas Olmos[1], I. Chalmeta Verdejo[1], J. J. Fragío Gil[1], L. Gonzalez Puig[1], J. Ivorra Cortés[1], J. A. Román Ivorra[1]. [1]*HUP La Fe, Rheumatology Department, Valencia, Spain*

Background: Polymyalgia Rheumatica (PMR) is a common inflammatory disease found in elderly patients and results in a high burden of long-term CS-based therapies. Most patients diagnosed with PMR have a good evolution following the introduction of medium-dose glucocorticoid treatment. However, the need to maintain corticosteroid treatment for an extended period (around 12-15 months) is often the norm in standard clinical practice. Activation of Th-17 lymphocytes with the consequent action of pro-inflammatory cytokines such as IL-1, IL-6, IL-17, or IL-23 is well known in the acute phase of this disease and treated by glucocorticoids or IL-6 blockers satisfactorily. However, activation of Th-1 lymphocytes appears to play a leading role in a chronic phase of the disease through the activation of INF-gamma and IL-12.

Objectives: Our aim was to assess proinflammatory biomarkers in a cohort of patients with PMR during the acute onset of the disease and its possibly relationship with corticosteroid dose.

Methods: Prospective study of a wide and unselected series of patients classified as PMR following 2012 ACR/EULAR classification criteria for PMR. Patient evaluations were performed at baseline and at 3 and 6 months after initiation of corticosteroid therapy. Serum levels of the proinflammatory biomarkers interleukin-6 (IL-6), interleukin-8 (IL-8), CXC motif ligand 10 chemokine (CXCL10), CXC motif ligand 9 chemokine (CXCL9), CXC motif ligand 2 chemokine (CXCL2) and

CC motif ligand 2 chemokine (CCL2) were measured in PMR patients and in healthy controls.
Results: A total of 25 patients with PMR were studied (32% men; 68% women). The mean age was 72.72 ±9.32 years (range 65-79). We also included 35 healthy controls. In reference to laboratory parameters and proinflammatory biomarkers at the onset of PMR, the mean values (± standard deviation) were as follows: C reactive protein (CRP): 28.4±26.6 mg/dL; erythrocyte sedimentation rate (ESR): 54.3±21.3 mm/h; haemoglobin: 12.6±1.6 g/dL; IL-6: 17.6±30.1 pg/mL; IL-8: 10.1±6.9 pg/mL; CXCL10: 259.4±290.7 pg/mL; CXCL9:5175±4396.8 pg/mL;, CXCL2: 25.9±12.5 pg/mL; CCL2: 471.3±152.9 pg/mL.
IL-6, IL-8 and CXCL9 levels were significantly increased in PMR patients comparing with the healthy control group.
The Health Assessment Questionnaire (HAQ) performed at the onset of the PMR yielded a mean value of 1.6±0.6. The mean dose of prednisone employed at the onset of PMR was 14.8±5.6 mg/day.
After 6 months, the mean dose of prednisone employed was 6.7±3.9 mg/day, the median [range] value for CRP was 3.1 [1.75-7.2] mg/dl and the mean value for ESR was 22±14 mm/h. Regarding relationship between proinflammatory biomarkers studied and doses of prednisone employed, no differences were observed.
Regarding pain perception and disability, we observed higher visual analogic scale values (VAS) in association with higher IL-6 levels (P=0.03) and higher HAQ values in association with higher IL-6 and CXCL2 values.
After 6 months, our patients showed an excellent evolution, and no complications were observed.
Conclusion: During the acute onset of PMR, IL-6, IL-8 and CXCL9 levels were significantly increased in our population of PMR patients. No differences were observed between proinflammatory biomarkers studied and doses of prednisone employed.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3114

POS1366 THE RELATIONSHIP OF MAST CELL ACTIVATION SYNDROME AND HYPERMOBILE EHLERS-DANLOS SYNDROME IN HOSPITALIZED PATIENTS IN THE UNITED STATES

K. Mathias[1], A. Mantha[2], L. Mathias[3], D. Arkfeld[3]. [1]*University of Chicago, Internal Medicine, Chicago, United States of America*; [2]*USC Keck School of Medicine, Internal Medicine, Los Angeles, United States of America*; [3]*USC Keck School of Medicine, Rheumatology, Los Angeles, United States of America*

Background: Patients with hypermobile Ehlers-Danlos syndrome (hEDS) often report symptoms of cutaneous flushing, pruritis, vomiting, diarrhea and anaphylactoid responses to environmental, food, and mechanical stimuli. There is a growing body of literature investigating the possible link between disorders of mast cell regulation including mast cell activation syndrome (MCAS) and connective tissue disorders including hEDS. The evidence for such a relationship, however, remains limited[1].
Objectives: We aimed to evaluate the association between hEDS and MCAS among hospitalized patients using a nationally representative cohort.
Methods: Hospitalized patients with a diagnosis of hEDS or MCAS were identified in the 2016-2018 National Inpatient Sample (NIS) using the International Classification of Diseases 10 system (ICD-10). The NIS is an all-payer inpatient database that estimates over 37 million annual U.S. hospitalizations and is maintained by the Healthcare Cost and Utilization Project. The primary outcomes were prevalence of EDS and MCAS among hospitalized patients. Secondary outcomes included cause of admission, mortality, length of stay, and cost of care. Multivariate hierarchical regression analysis was using adjusting for demographics, hospital factors, and comorbid conditions.
Results: Among 37,665 patients identified in this study, 35,115 (95.9%) patients had hEDS and 3,630 (9.6%) patients had MCAS. 1080 patients had concomitant diagnosis of hEDS (3.1%) and MCAS (29.8%), of whom 555 (51.4%) were diagnosed in 2018 compared with 100 (9.3%) patients in 2016 (P<0.001). The mean age of patients with both conditions was significantly lower than those diagnosed with hEDS (29.5 vs 36.6 years, P<0.001) or MCAS (29.5 vs 39.8 years, P<0.001) alone. Those with comorbid hEDS and MCAS were more likely female (95.8% vs 84.5%, P<0.001), had private insurance (67.6% vs 52.4%, P<0.001) and were among the highest income quartile (47.4% vs 31.9%, P<0.001). There were no significant differences in mortality or overall comorbidity burden. Patients with hEDS and MCAS had higher adjusted hospitalization charges ($64,445 vs $54,782, β=0.15, P<0.05) and longer adjusted lengths of stay (6.4 vs 4.9 days, IRR 1.35, P<0.001).
Conclusion: Nearly 1 in 3 patients diagnosed with MCAS have comorbid diagnosis of hEDS. This association appeared to increase over time with the increasing diagnosis of MCAS. Social determinants of disease such as health insurance status and income appeared to be associated with the identification of the overlap syndrome. These findings merit further investigation into the co-occurrence of these disease entities and development of consistent clinical diagnostic criteria.
REFERENCES:
[1] Kohn A, Chang C. The Relationship Between Hypermobile Ehlers-Danlos Syndrome (hEDS), Postural Orthostatic Tachycardia Syndrome (POTS), and Mast Cell Activation Syndrome (MCAS). *Clin Rev Allergy Immunol*. 2020;58(3):273-297. doi:10.1007/s12016-019-08755-8
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3177

POS1367 PROCALCITONIN IN RHEUMATOLOGY

K. Erraoui[1], K. Nassar[2], S. Janani[1]. [1]*CHU Ibn Rochd, Department of Rheumatology, Casablanca, Morocco*; [2]*CHU Ibn Rochd, Department of Rheumatology, Casablanca, Morocco*

Background: The differentiation between infection and aseptic inflammation is difficult and often a challenge in the daily practice of rheumatology.Procalcitonin (PCT) is a preferred marker for bacterial infections that allows the rheumatologist to make an early diagnosis, choose an appropriate antibiotic therapy for bacterial infection, and avoid unnecessary antibiotic therapy for inflammation.
Objectives: To study the levels of PCT in various inflammatory states observed in a rheumatology department, and to assess its possible discriminating role in the differentiation of bacterial infection from other inflammatory processes.
Methods: This is a preliminary monocentric retrospective study conducted from January 2018 to December 2020 in our rheumatology department. The inclusion criteria were all patients hospitalized in rheumatology for a rheumatic or autoimmune disease or a bone and joint infection.PCT samples from patients were analyzed along with general signs (fever/chills) and with routine assessment (blood count including white blood cell count(WBC), erythrocyte sedimentation rate (ESR)and C reactive protein(CRP)) in patients admitted to hospitalfor a fever or a biological inflammatory syndrome, or both, with a laboratory cut-off value of 0.5 ng/ml.
Results: 20 patients were included. Their mean age was 46.1 (extremes 19 – 66) and the with sex ratio was 1. Three patients had a history of autoimmune disease, 2 of neoplasia, 1 with chronic terminal kidney failure and hemodialysis, and 4 patients took antibiotics before hospitalization. The mean PCT was 100.01ng/ml (extremes 0.01-200), and Sensitivity at 57.44% and specificity at 100%, PPV: 100%, NPV: 81.25%.
The patients were divided according to their final diagnosis into 3 groups: bacterial or fungal infection; inflammatory abacterian disease (autoimmune or rheumatic flare, neoplasia, metabolic, reactive arthritis); infection + inflammatory abacterian disease. Group 1 included 4 patients, their mean PCT was 6.92ng/ml (0.16-26.80),mean CRP was 131.725 mg/L, and mean ESR was 50 mm,

	Group 1(n=4)	Group 2(n=13)	Group 3(n=3)
Mean age	45	46.77	44.67
Sex ratio M/F	2/2	8/5	0/3
Reason for hospitalization	Phlegmon of the left shoulder and inflammatory gonalgia in a feverish context 25% Multiple vertebral fractures 25% Acute monoarthritis of the left knee 25% Pain in the left hip with functional impairment 25%	Inflammatory polyarthralgia15.38% Inflammatory back pain 23.07% Activity of his autoimmune 15.38% disease Chronic hip pain 7.69% Acute febrile polyarthralgia 30.77% Biarthritis 7.69%	Acute febrile polyarthralgia 66.67% Flare of polymyalgia rheumatica 33.33%
History	Neoplasia 25%	Autoimmune disease 23.07%	End-stage chronic renal disease with hemodialysis 33.33%
PCT indication	Suspected septic arthritis 75% Exploration of inflammatory syndrome 25%	Suspicion of arthritis 46.15% Exploration of inflammatory syndrome 53.85%	Suspicion of sepsis 33.33% Exploration of inflammatory syndrome 66.67%
Mean PCT value (ng/ml)	6.92	0.025	66.88
fever/chills	75%	30.77%	33.33%
Biological parameters	25%	30.77 %	33.33%
Hyperleukocytosis	50	84.38	107.33
ESR (mm)	131.725	132.25	560
CRP (mg/L)			

and 25% had hyperleukocytosis.2 patients had already taken antibiotics before admission. Group 2 included 13 patients, their mean PCT was 0.025 ng/mL (0.01-0.13), mean CRP was 132.25mg/L, mean ESR was 84.38mm, and 30.77% of them had hyperleukocytosis. Group 3 included 3 patients, their mean PCT was 66.88 ng/mL (0.02-200), mean CRP was 560 mg/L, mean ESR was 107.33 mm, and 33.33% had hyperleucocytosis. The patient with the highest PCT was admitted for a sepsis with uremic encephalopathy that improved after hemodialysis. A control PCT was made in 2 patients with infection who received antibiotics,showing a decrease or negativation compared to the initial value of PCT.

Conclusion: Our study showed that PCT levels only increased significantly in bacterial infections. The PCT values were more discriminating than the level of WBC and CRP in differentiating a bacterial infection from another inflammatory process, hence the value of using this marker in case diagnosis doubt.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3191

POS1368 ANTI-IL-1 THERAPIES IN COLCHICINE-RESISTANT OR İNTOLERANT PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: SINGLE CENTER EXPERIENCE

M. E. Derin[1], B. Karakaş[2], B. Karataş[2], N. Çabuk Çelik[2], İ. Yalçın[2], A. Şahin[2]. [1]*Sivas Numune Hospital, Internal Medicine – Rheumatology, Sivas, Turkey*; [2]*Sivas Cumhuriyet University, Internal Medicine – Rheumatology, Sivas, Turkey*

Background: Familial Mediterranean Fever (FMF) is a hereditary auto-inflammatory disease characterized by recurrent fever and serosal inflammation (1). The goal of FMF treatment is to prevent the attacks and to minimize subclinical inflammation between attacks The main treatment of FMF is colchicine however anti-interleukin-1 treatments are recommended in colchicine resistant and/or intolerant FMF patients (2).

Objectives: The aim of this study is to evaluate the efficacy of anti-interleukin-1 (anti-IL-1) agents in 81 FMF patients with resistant/intolareted to colchicine or complicated with amyloidosis.

Methods: Between January 2014 and December 2020, eighty-one patients who were diagnosed as FMF according to the criteria of Tel-Hashomer that following-up at Cumhuriyet University Medical Faculty Rheumatology-Internal Medicine Department were included in to the study.

Results: 45 (55.6%) male and 36 (44.4%) female were included in the study. The median age of the patients was 25 years (min:17-max: 60) and the median age at diagnosis was 15 years (min 3-max 46). 44 patients (54.3%) used Anakinra (100 mg/day), and 27 (45.7%) canakinumab (150mg/8month) were used. 49 cases were resistant to colchicine,16 were intolerant to colchicine, 16 (20%) cases were comlicated with amyloidosis. 10 patients had renal transplantation. MEFV gene mutations are shown in Table 1. Median duration of anti-IL-1 agent use was 24 month (min:4-max 52). 9 patients were resistant to anakinra, 18 patients had side effects which anakinra related. After a median follow up 12 months overall clinical response was %95 (frequency of attacks <1/6months). median proteinuria decreased from 3500 mg /day to median 1500 mg /day (p: 0.04) (Table 2). IL-6 treatment was started in 4 patients because of ineffective canakinumab. Five pregnant patients were followed up with anakinra during pregnancy and there were no problems.

Conclusion: Anti-interleukin-1 agents are effectively and safely in the treatment of FMF patients. There are still unanswered questions in FMF treatment such as other factors affecting the frequency of attacks, colchicine resistance is not defined precisely and the importance of some mutations. The effect of anti IL-1 agents on FMF patients with amyloidosis is not clearly. According to our experience, these treatments are effective in patients with glomerular filtration rate> 60 ml/min. For answers to these and similar questions, Large and long follow-up studies are needed for long-term effects.

REFERENCES:

[1] Özen S, Batu ED, Demir S., Familial Mediterranean Fever: Recent Developments in Pathogenesis and New Recommendations for Management. Front Immunol. 2017 Mar 23;8:253. doi: 10.3389/fimmu.2017.00253. eCollection 2017.

[2] Seza Özen ve ark. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis. 2016 Apr;75(4):644-51.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3257

POS1369 ADULT-ONSET STILL'S DISEASE: A SINGLE-CENTER EXPERIENCE

B. Egeli[1], S. Ugurlu[2]. [1]*Boston Children's Hospital, Immunology, Boston, United States of America*; [2]*Istanbul University-Cerrahpasa, Internal Medicine, Istanbul, Turkey*

Background: Adult-Onset Still's disease (AOSD) is an autoinflammatory condition characterized by fever, rash, and arthritis. The diagnosis of AOSD is made by excluding common causes of fever of unknown origin which are infections, malignancies, autoimmune conditions and medication adverse effects. As it is a diagnostic challenge, further data on highlighting clinical and laboratory findings are necessary on guiding clinicians.

Objectives: Our main objective is to present our single tertiary center experience of patients diagnosed with AOSD.

Methods: This retrospective study was conducted at a tertiary rheumatology center. Patients were diagnosed with AOSD using Yamaguchi's criteria and followed between 2007 and 2020. Demographic, clinical and laboratory information was retrieved from the patient chars. Treatment-related and prognostic information were also noted with additional information from phone call interviews.

Results: The study includes 69 patients (23 M, 46 F). The mean age of diagnosis was 33.86±14.3. The presenting signs and symptoms of the patients are shown in Figure 1. The laboratory findings supporting the diagnosis at initial encounter are summarized in Table 1. The mean corticosteroid dose at initial diagnosis was 29.7±18 mg. In addition to corticosteroid treatment these patients were followed with different glucocorticoid-sparing agents. Methotrexate was the choice of treatment in 54 patients with the mean dose of 14.5±3.43 mg. Eight patients were treated with leflunomide, seven with anti-TNF agents, seven with tocilizumab, nineteen with anakinra and four with canakinumab.

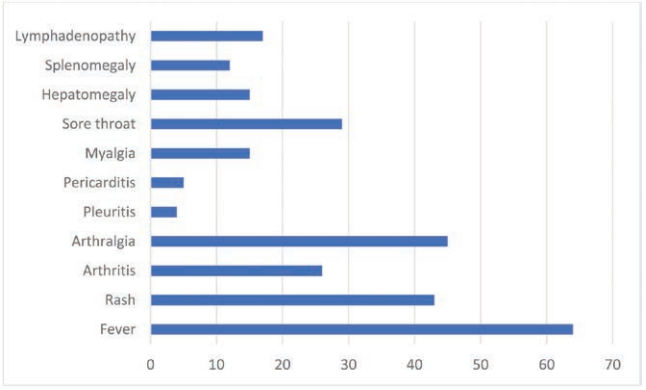


Figure 1. The presenting signs and symptoms of the patients

Conclusion: In conclusion, the most common presenting symptoms in our AOSD cohort were fever and salmon-colored rash. In the differential diagnosis of fever of unknown origin especially with rash, AOSD should be considered. Corticosteroid was the main treatment modality. In patients who are unresponsive to conventional immunosuppressive treatment, biologic agents can be an alternative.

Table 1. The laboratory findings at initial encounter

	Mean ± Standard Deviation
Ferritin (ng/mL)	3179.46±6503.56
ESR (mm/h)	77.43±28.47
CRP (mg/L)	102.29±70.39
Leukocyte Count (cells/L)	13147.3±4640.9
ESR (mm/h)	80±28.48
CRP (mg/L)	105.15±54.67
Leukocyte Count (cells/L)	12427.14±6530.43

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3280

POS1370 HYDROXYCLOROQUINE-INDUCED ATRIOVENTRICULAR BLOCK IN IMMUNE-MEDIATED DISEASES. SINGLE UNIVERSITY CENTER STUDY OF 293 PATIENTS

A. Herrero-Morant[1], A. Margarida-de Castro[1], R. Pérez-Barquín[1], J. Zubiaur-Zamacola[1], M. Á. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology and Cardiology, Santander, Spain*

Background: Hydroxychloroquine (HCQ) is an extensively used drug in immune-mediated diseases (IMID). Despite its general safety, HCQ can cause serious toxicity such as heart conduction disorders. Atrioventricular block (AVB)

is an underrecognized adverse effect that can potentially cause significant morbidity and mortality.
Objectives: To study incidence, presentation, and characteristics of HCQ-induced AVB in IMID.
Methods: Open-label single center study of 293 patients with IMID treated with HCQ for at least 3 months. Electrocardiograms were analyzed at baseline and during HCQ treatment. In addition, a comparative study between patients with and without AVB was conducted.
Results: We studied 293 patients (270 women/ 23 men; mean age 59.7±14.7 years). Underlying IMID were Systemic Lupus Erythematosus (SLE) (n=109, 40.6%); undifferentiated connective-tissue disease (n=70, 23.9%), Sjögren's syndrome (SS) (n=70, 23.9%), antiphospholipid syndrome (n=31,10.6%) and other IMID (n=13, 4.4%). HCQ was used for 4.1±3.5 years.
After 11.8±8.9 years of follow-up (HCQ mean cumulative dose: 979.7±272.1 g). AVB was observed in 19 out of 293 (6.5%) patients: 16 (84.2%) were first-degree AVB and 3 (15.8%) complete AVB. 4 (21.2%) patients with AVB were treated with a permanent pacemaker.
Presentation of atrioventricular block according to hydroxychloroquine incidence rate and treatment duration is shown in Figure 1. Most of AVB happened in the first 40 months, regardless of HCQ cumulative dose.

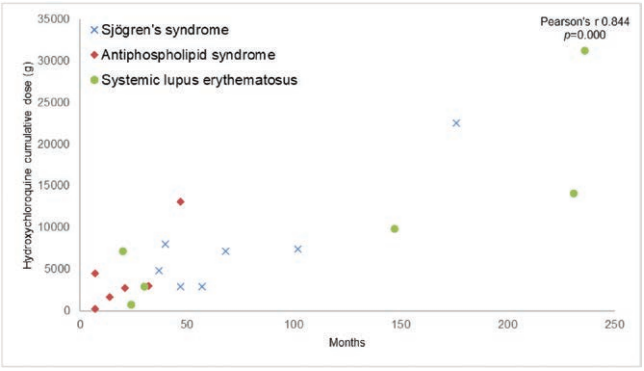


Figure 1. Presentation of atrioventricular block according to hydroxychloroquine incidence rate and treatment duration.

A comparative study between patients with and without AVB was performed (Table 1). Patients with AVB were older (p=0.014) and had a higher incidence of diabetes mellitus (p=0.033). HCQ cumulative dose and duration of IMID were similar in both groups (p>0.05).
Other HCQ adverse effects were retinopathy (n=16, 5.4%), gastrointestinal alterations (n=14, 4.8%), cutaneous alterations (n=14, 4.8%), allergic reactions (n=4, 1.4%) and myopathy (n=1, 0.3%).
Conclusion: AVB was observed in 6.5% of patients with IMID treated with HCQ. Most AVB were first-degree AVB. HCQ increased the risk of developing an AVB in patients with IMID regardless of HCQ cumulative dose or underlying disease duration. Older patients with diabetes mellitus had a higher risk of developing an AVB.

Table 1. Comparative study between patients with and without AVB.

	with AVB	without AVB	
	n= 19	n = 274	*p*
General features at HCQ onset			
Age, years mean±SD	57.4±14.5	46.4±16.8	**0.014**
Female, n (%)	17(89.5)	239(87.4)	0.877
Hypertension, n (%)	14 (73.7)	149 (54.4)	0.118
Dyslipemia, n (%)	11 (58.9)	117 (42.7)	0.265
Diabetes Mellitus, n (%)	5 (26.3)	24 (8.7)	**0.033**
Renal impairment, n (%)	5 (26.3)	29 (10.7)	0.073
Ischemic cardiopathy, n (%)	2 (10.5)	11 (3.9)	0.228
CRP, mg/dL median [IQR]	0.3 [0.1-0.5]	0.4 [0.3-0.8]	0.343
ESR, mm/h median [IQR]	17.0 [15.0-22.3]	13.0 [7.0-29.5]	0.206
Data at last visit (11.8±8.9 years of follow-up)			
IMID duration, years mean±SD	11.8±8.9	14.3±10.3	0.288
# Use of other cardiotoxic drugs, n (%)	2 (10.5)	11 (4.0)	0.723
HCQ cumulative dose, g mean±SD	813.2±206.0	996.3±266.9	0.527

(beta blockers, calcium channel blockers, tricyclic drugs, other AVB inducers)

Disclosure of Interests: Alba Herrero-Morant: None declared, Adrián Margarida-de Castro: None declared, Raquel Pérez-Barquín: None declared, Jon Zubiaur-Zamacola: None declared, Miguel Á. González-Gay Speakers bureau: AbbVie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Grant/research support from: AbbVie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, Sanofi, Lilly and MSD, Grant/research support from: AbbVie, MSD, and Roche
DOI: 10.1136/annrheumdis-2021-eular.3295

POS1371 BIOLOGICAL THERAPY IN REFRACTORY NEUROBEHÇET'S DISEASE. MULTICENTER STUDY OF 42 PATIENTS

A. Herrero-Morant[1], J. L. Martín-Varillas[2], S. Castañeda[3], I. González-Mazón[1], O. Maiz[4], A. Blanco[4], J. Sánchez[5], N. Ortego[6], E. Raya[6], A. Olive[7], A. Brandy-Garcia[7], Á. Prior-Español[7], C. Moriano[8], E. Diez Alvarez[8], R. Melero[9], J. Graña[10], Á. Seijas-López[10], A. Urruticoechea-Arana[11], A. Ramos Calvo[12], C. Delgado Beltrán[13], M. Loredo Martínez[13], E. Salgado-Pérez[14], F. Sivera[15], I. Torre-Salaberri[16], J. Narváez[17], J. L. Andréu Sánchez[18], O. Martínez González[19], R. Gómez de la Torre[20], S. Fernández[21], S. Romero-Yuste[22], G. Espinosa[23], M. Á. González-Gay[1], R. Blanco[1]. *[1]Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*; *[2]Hospital de Sierrallana, Rheumatology, Torrelavega, Spain*; *[3]Hospital Universitario La Princesa, Rheumatology, Madrid, Spain*; *[4]Hospital Universitario de Donostia, Rheumatology and Ophtalmology, San Sebastián, Spain*; *[5]Hospital 12 de octubre, Rheumatology, Madrid, Spain*; *[6]Hospital San Cecilio, Rheumatology and Internal Medicine, Granada, Spain*; *[7]Hospital Universitario Germans Trias i Pujol, Rheumatology, Barcelona, Spain*; *[8]Hospital de León, Rheumatology, León, Spain*; *[9]Complejo Hospitalario de Vigo, Rheumatology, Vigo, Spain*; *[10]Hospital Universitario de A Coruña, Rheumatology, A Coruña, Spain*; *[11]Hospital Can Misses, Rheumatology, Ibiza, Spain*; *[12]Complejo Hospitalario de Soria, Rheumatology, Soria, Spain*; *[13]Hospital Clínico Lozano Blesa, Rheumatology, Zaragoza, Spain*; *[14]Complejo Hospitalario Universitario de Ourense, Rheumatology, Ourense, Spain*; *[15]Hospital General Universitario de Elda, Rheumatology, Elda, Spain*; *[16]Hospital de Basurto, Rheumatology, Bilbao, Spain*; *[17]Hospital Bellvitge, Rheumatology, Barcelona, Spain*; *[18]Hospital Universitario Puerta de Hierro, Rheumatology, Madrid, Spain*; *[19]Hospital Clínico Universitario de Salamanca, Rheumatology, Salamanca, Spain*; *[20]Hospital Universitario Central de Asturias, Internal Medicine, Oviedo, Spain*; *[21]Hospital Universitario de Cabueñes, Rheumatology, Gijón, Spain*; *[22]Complejo Hospitalario Universitario de Pontevedra, Rheumatology, Pontevedra, Spain*; *[23]Hospital Clínic de Barcelona, Internal Medicine, Barcelona, Spain*

Background: Neuro-Behçet's disease (NBD) is a severe complication of Behcet's disease (BD). Despite well-established therapies with glucocorticoids and conventional immunosuppressants (cIS), a significant proportion of patients are refractory.
Objectives: To assess efficacy and safety of biologic therapy (BT) in NBD refractory to glucocorticoids and at least one cIS.
Methods: Open-label multicenter study of refractory NBD from 23 different referral Spanish Hospitals. Main outcome was neurological response. Secondarily, analytical efficacy was measured by Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and Hemoglobin (Hb) at baseline, 6 months, 1 year and 2 years.
Results: We studied 42 patients (21 women/ 21 men; mean age 40.4±10.8 years). HLA B51 was positive in 15 out of 37 (40.5%) patients tested. Non-neurological manifestations were oral ulcers (n=41, 97.6%), genital ulcers (n=31, 73.8%), skin lesions (n=28, 66.7%), arthralgia (n=27, 64.3%), uveitis (n=21, 50.0%), arthritis (n=9, 21.4%), venous thrombosis (n=9, 21.4%) and arterial thrombosis (n=4, 9.5%). The underlying neurologic manifestation were parenchymal (n=34, 81.0 %) and non-parenchymal (n=17, 40.5%) involvement (Table 1). The first BT used was infliximab (n=20), adalimumab (n=13), golimumab (n=3), tocilizumab (n=3) and etanercept (n=2).
After 58.2±51.4 months since initiation of BT, neurological response was complete (n=27; 64.3%), or partial (n=11, 26.1%) (Figure 1). Only 4 (9.5%) patients did not respond. After 6 months of BT, ESR improved from.31.5±25.6 to 15.3±11.9 mm/h (p=0.005), CRP from 1.4 [0.2-12.8] to 0.3[0.1-3] mg/dL (p= 0.002) and Hb from 13.1±1.6 to 13.8±1.3 g/dL (p=0.005).

Table 1. Neurologic manifestation of 42 patients with refractory neurobehçet's disease treated with biologic therapy.

Parenchymal subtype, n (%)	**34 (81.0)**
-Hemiparesis	8 (19.1)
-Polineuropathy	8 (19.1)
-Encephalopathy	6 (14.3)
-Cognitive impairments	4 (9.5)
-Optic neuropathy	4 (9.5)
-Ophtalmoparesis	4 (9.5)
-Other cranial nerve involvement	3 (7.1)
-Hemihypoesthesia	3 (7.1)
-Cerebellar dysphasia	1 (2.4)
-Cerebellar involvement	1 (2.4)
-Non-steroidal psicosis	1 (2.4)
Non-parenchymal subtype, n (%)	**17 (40.5)**
-Aseptic meningitis	12(28.6)
-Thrombosis	4 (9.5)
-Intracranial hypertension	1 (2.4)

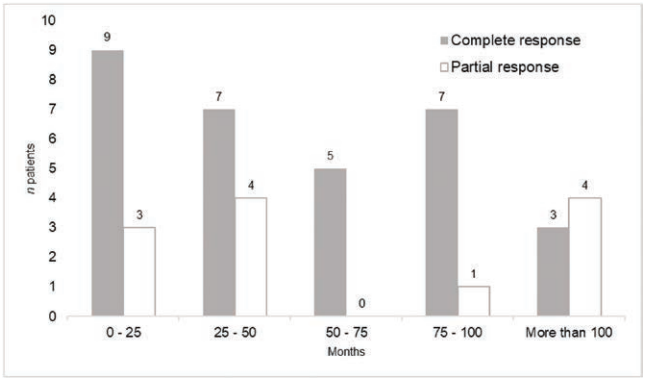


Figure 1. Neurological clinical response to biological therapy.

Primary failure was observed in 16 (38.1%) patients due to inefficacy (n=11, 68.8%) or adverse effects (n=5, 31.3%). Similarly, causes of secondary failure (n=6, 14.3%) were inefficacy (n=5, 83.3%) and adverse effects (n=1, 16.7%). No serious adverse effects were observed.

Conclusion: BT, especially monoclonal anti-TNF drugs, seems to be effective and safe in refractory NBD.

Disclosure of Interests: Alba Herrero-Morant: None declared, José Luis Martín-Varillas Grant/research support from: AbbVie, Pfizer, Lilly, Janssen, and Celgene, Santos Castañeda: None declared, Iñigo González-Mazón: None declared, Olga Maiz: None declared, Ana Blanco Speakers bureau: AbbVie, Julio Sánchez: None declared, Norberto Ortego: None declared, Enrique Raya Speakers bureau: MSD, Grant/research support from: AbbVie, Alejandro Olive: None declared, Anahy Brandy-Garcia: None declared, Águeda Prior-Español: None declared, Clara Moriano: None declared, Elvira Diez Alvarez: None declared, Rafael Melero: None declared, Jenaro Graña: None declared, Álvaro Seijas-López: None declared, ANA URRUTICOECHEA-ARANA: None declared, Angel Ramos Calvo: None declared, Concepción Delgado Beltrán: None declared, Marta Loredo Martínez: None declared, Eva Salgado-Pérez: None declared, Francisca Sivera: None declared, Ignacio Torre-Salaberri: None declared, J. Narváez Speakers bureau: Bristol-Myers Squibb, José Luis Andréu Sánchez: None declared, Olga Martínez González: None declared, Ricardo Gómez de la Torre: None declared, Sabela Fernández: None declared, Susana Romero-Yuste: None declared, Gerard Espinosa: None declared, Miguel Á. González-Gay Speakers bureau: AbbVie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Grant/research support from: AbbVie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, Sanofi, Lilly and MSD, Grant/research support from: AbbVie, MSD, and Roche

DOI: 10.1136/annrheumdis-2021-eular.3407

POS1372 EVALUATION OF E148Q AND CONCOMITANT AA AMYLOIDOSIS SECONDARY TO FAMILIAL MEDITERRANEAN FEVER AFTER ADJUSTED CLINICAL-DEMOGRAPHIC CHARACTERISTICS

Z. S. Arici[1], M. Romano[2], D. Piskin[3], F. Guzel[4], M. Yilmaz[5], E. Demirkaya[2]. *[1]Sanliurfa Training and Research Hospital, Paediatric Rheumatology, Sanliurfa, Turkey*; *[2]Schulich School of Medicine & Dentistry, University of Western Ontario, Paediatric Rheumatology, London, Canada*; *[3]Lawson Health Research Institute, Pediatrics, London, Canada*; *[4]Gentera Biotechnology, Biotechnology, Istanbul, Turkey*; *[5]Epigenetic Health Solutions, Unit of Nephrology, Ankara, Turkey*

Background: Amyloid A (AA) amyloidosis, previously known as secondary or reactive amyloidosis, is a long-recognized severe complication of some chronic inflammatory diseases. The pathogenesis and risk factors for amyloidosis in Familial Mediterranean Fever (FMF) remain partially understood (1). The development of AA amyloidosis is dependent on ethnicity and country of residence (2). In the pre-colchicine era, renal AA-amyloidosis was largely reported patients of Turkish (67%) and Sephardic Jewish ancestry (26.5%) (2,3). Currently it's well known that the MEFV M694V variant associated with high risk of amyloidosis however, mutations on exon 2, specifically E148Q variant remained controversial.

Objectives: To evaluate the E148Q mutation variant and concomitant AA Amyloidosis secondary to FMF after adjusted clinical-demographic characteristics.

Methods: Patients were recruited from the renal unit at Epigenetic Health Center outpatient clinic in Turkey between September 2003 and February 2020. Patients who had biopsy confirmed FMF related AA amyloidosis were included the study. Tel-Hashomer criteria were applied in the diagnosis of FMF. The clinical characteristics of FMF patients and medication history were recorded by the physician at the time of registry entry. All patients had detailed baseline assessment of clinical features, renal functions, genetic testing, histopathological diagnosis of amyloidosis, and treatment received. We performed multiple comparisons according to the age of diagnosis, demographic features, disease phenotype, allele frequency, type of mutation and mortality. Statistical analysis was performed with Statistical Package of Social Science (SPSS) for Windows, version 15.0 (SPSS Inc, Chicago, IL).

Results: Our registry consists of 195 patients with a diagnosis of AA amyloidosis. Complete information on 169 patients (lost to follow up, n=26) were included. The median age was 36 (19-49) years; male/female ratio was 1.6 (104/65). The median follow-up duration was 15.0 years (4-17 years). There were 101 patients diagnosed with FMF <18 years of age and 68 patients diagnosed ≥18 years of age. All participants developed renal amyloidosis before the age of 32 years. Family history of FMF was documented in 56 patients (33.1%) and family history of amyloidosis was present in 41 patients (24.3%). The three most common clinical symptoms were fever (84,6%), abdominal pain (71.6%) and arthritis (66.9%). During the follow-up, 5 patients started dialysis treatment and 9 patients had kidney transplantation. The most common allele frequency across patients was M694V (60.6%), E148Q (21.4%) and M680I (10.3%). The most frequent mutations were M694V/M694V (63.3%), M694V/E148Q (20.8%) and E148Q/E148Q (15.8%). During the follow up period, 15 patients (10 male, 5 female) died. In those that died, the mutations in 14 had M694V/M694Vand one demonstrated E148Q/E148Q.

Conclusion: Patients with FMF related AA amyloidosis have an increased risk for mortality. This study confirmed the association between M694V and FMF-associated AA amyloidosis, which has been reported in many studies. Close clinical follow-up and further evaluation of patients with the E148Q mutation is warranted specifically if residing in FMF endemic areas. The possible relationship between E148Q and AA amyloidosis need to be confirmed in other cohorts.

REFERENCES:

[1] Erer B, Demirkaya E, Ozen S, Kallinich T. What is the best acute phase reactant for familial Mediterranean fever follow-up and its role in the prediction of complications? A systematic review. Rheumatology international. 2016;36(4):483-7.

[2] Touitou I, Sarkisian T, Medlej-Hashim M, Tunca M, Livneh A, Cattan D, et al. Country as the primary risk factor for renal amyloidosis in familial Mediterranean fever. Arthritis and rheumatism. 2007;56(5):1706-12.

[3] Pras M, Bronshpigel N, Zemer D, Gafni J. Variable incidence of amyloidosis in familial Mediterranean fever among different ethnic groups. Johns Hopkins Med J. 1982;150(1):22-6.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3420

POS1373 DEFINING EAR CHONDRITIS: DATA FROM 685 PATIENTS WITH RELAPSING POLYCHONDRITIS

M. Ferrada[1], N. Costedoat-Chalumeau[2], G. Moulis[3], N. Linn[4], E. Rose[1], P. Grayson[1]. *[1]NIH, NIAMS, Bethesda, United States of America*; *[2]APHP, Université de Paris, Paris, France*; *[3]Toulouse University Hospital, Department of Internal Medicine, Toulouse, France*; *[4]Relapsing Polychondritis Foundation, Relapsing Polychondritis Foundation, New York, United States of America*

Background: Ear chondritis is often considered the pathognomonic feature of relapsing polychondritis (RP). Although painful redness and swelling of the pinna and a resultant cauliflower ear are universally recognized as chondritis, the complete spectrum of symptoms associated with ear chondritis have not been well described.

Objectives: The study objective was to seek patient input to help characterize ear chondritis An online survey was administered in English or Spanish to participants with self-reported RP.
Methods: Participants were asked questions about their ear pain, including quality, location, duration, aggravating/alleviating factors, timing of onset and duration. Participants were included who reported age ≥ 18 years, a diagnosis of RP confirmed by a physician, and sufficient symptoms to meet McAdams or Damiani's diagnostic criteria. Participants were categorized as having "typical ear chondritis" if they reported ear pain localized to the pinna with associated redness and swelling. Atypical presentations of ear chondritis were also considered.
Results: A total of 685 participants from five continents completed the survey. Among them, 659 met inclusion criteria for subsequent analysis. Most participants were female (n=574; 87%), white (n=548; 83%) and from the United States (n=484;74%). The median age was 50 years (interquartile range = 41-58). In total, 593 (90%) patients reported ear pain, 227 (38%) had "typical ear chondritis", and 98 (16%) had cauliflower ear.
Ear pain was most commonly described as burning (n=334, 56%) or throbbing (n=295, 50%). The most common location of pain was the pinna (n=373, 63%). Participants reported ear redness (n=454, 60%) and swelling (n=405, 62%). Some patients experienced only ear redness without swelling (n=286, 48%) or only ear swelling without redness (n=71, 12%). The most common aggravating factors were minor trauma (n=371, 62%) and stress (n=358, 60%). The most common alleviating factor was avoidance of touching the ear (n=374, 63%). Pain was most frequently reported during the daytime (n=355, 60%) and most likely to occur in either ear at different times (n=310, 52%). Onset could be gradual (n=198, 33%) or sudden (n=155, 26%). Pain typically lasted a few hours (n=175, 30%) or 2-3 days (n=130, 22%). The majority of patients who had pinna pain also had pain in other parts of the ear (e.g. mastoid process, inner ear, whole ear) at some point (n=394, 67%). In patients with cauliflower ear, the most common location of pain was the pinna (n=57, 58%) followed by pain inside the ear (n=53, 54%). Most participants reported at least two different types of pain (n=420, 64%).
Conclusion: Ear chondritis in patients with RP has a wide range of clinical presentations and characteristics beyond the typical triad of redness, swelling, and pain localized to the pinna. The description of pain often significantly varies within the same patient. Knowledge of the various distinct characteristics of ear involvement in RP may help physicians recognize and monitor the disease more effectively.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3440

POS1374 RHEUMATOLOGIC DISEASES AS PRESENTATIONS OF PRIMARY IMMUNODEFICIENCY DISEASES

S. Kudryashov[1], L. Karzakova[1], N. Zhuravleva[1], I. Sidorov[1], T. Lutkova[1].
[1]*Federal State Budgetary Educational Institution of Higher Education "The Chuvash State University named after I.N. Ulyanov", Department of Internal Medicine, Cheboksary, Russian Federation*

Background: Primary immunodeficiency diseases (PID) occur on average with a frequency of 1: 100 000 of the population. In accordance with the classification of PIDS of the International Union of Immunological Societies (IUIS) 9 different groups of innate errors of immunity are distinguished [1]. The polymorphism of the clinical picture, difficulties in recognizing PID cause their late diagnosis and the associated development of irreversible organ damage, complications and high mortality. According to the traditional view, the clinical marker of PID is an infectious syndrome. However, in some cases, PID is detected as a rheumatologic disease.
Objectives: The aim of the study is to analyze the frequency of rheumatologic diseases in adult patients with PID living in one of the subjects of Russia –Chuvashia.
Methods: The material of the study was patient data obtained during a retrospective analysis of 49 outpatient records included in the Republican Register of PID. Diagnosis of various forms of PIDS was carried out in accordance with the criteria developed by the IUIS [1].
Results: During the period from 1993 to January 2020, 49 cases of PID were registered in the adult population of Chuvashia. According to the frequency of PID, common variable immunodeficiency (CVID) is the most common in Chuvashia (26 people). In the second place there is selective IgA deficiency (10 people); in third place there are X-linked agammaglobulinemia (4 people) and hereditary angioedema (4 people). The remaining forms of PID account for 5 cases: 2 cases of Louis-Bar syndrome, 1 case of DiGeorge syndrome, 1 case of Wiskott-Aldrich syndrome and 1 case of Hyper IgE syndrome. The main symptom of PID in 35 (71.4%) patients was heightened susceptibility to infection. In 14 (28.6%) patients, the clinical picture was dominated by non-infectious presentations (autoimmune, lymphoproliferative and oncological diseases). In 9 patients (18.3%), it was manifested by rheumatologic diseases (rheumatoid arthritis, psoriatic arthritis, scleroderma-like syndrome). These symptoms were more characteristic of CVID. With selective IgA deficiency and X-linked agammaglobulinemia, rheumatic symptoms were observed only in isolated cases. CVID debuted in 2 cases as rheumatoid arthritis, resulting in the delay in the diagnosis of an average of 5.2 years. Only the detailed immunological and genetic study made it possible to diagnose PID and prescribe adequate treatment – replacement immunoglobulin therapy. This treatment reduced the frequency of infectious manifestations of the disease and it did not significantly improve the course of rheumatological diseases. Therefore, the use of methotrexate and targeted therapy was continued.
Conclusion: In the clinical picture of PID, rheumatic symptoms predominate in 28.6% of cases, which requires a thorough immunological and genetic examination of patients with rheumatic diseases in order to diagnose PID in a timely manner.
REFERENCES:
[1] Picard C, Bobby Gaspar H, Al-Herz W, et al. *J Clin Immunol*. 2018;38(1):96-128.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3526

POS1375 THE EFFECT OF M694V HOMOZYGOSITY ON THE CAROTID INTIMA-MEDIA THICKNESS AND FLOW MEDIATED DILATATION IN PATIENTS WITH FMF RELATED AMYLOIDOSIS

S. Sahin[1], M. Romano[2], F. Guzel[3], O. Kasapcopur[1], D. Piskin[4], I. Yilmaz[5], E. Demirkaya[6]. [1]*Istanbul University-Cerrahpasa, Cerrahpasa School of Medicine, Department of Pediatric Rheumatology, Istanbul, Turkey*; [2]*Schulich School of Medicine & Dentistry, University of Western Ontario, Department of Paediatrics, Division of Paediatric Rheumatology, London, Canada*; [3]*Gentera Biotechnology, Biotechnology, Istanbul, Turkey*; [4]*Schulich School of Medicine & Dentistry, University of Western Ontario, Department of Epidemiology and Biostatistics, London, Canada*; [5]*Epigenetic Health Solutions, Unit of Nephrology, Ankara, Turkey*; [6]*Schulich School of Medicine & Dentistry, University of Western Ontario, Department of Paediatrics, Division of Paediatric Rheumatology and Department of Epidemiology and Biostatistics, London, Canada*

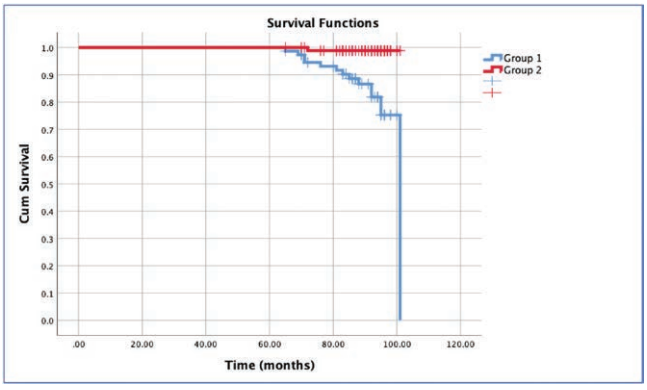
Background: There are limited data in FMF associated AA amyloidosis patients regarding the vascular abnormalities including atherosclerosis and endothelial dysfunction, all of which are contributors of cardiovascular disease (CVD) risk. And, this risk assessment for future CV events have not yet been evaluated between FMF amyloidosis patients with different genotypes.
Objectives: We aimed to compare early markers of endothelial dysfunction and atherosclerosis, mortality and other disease characteristics in FMF-related amyloidosis patients with a homozygous M694V genotype and in patients with other genotypes with this cross-sectional comparative study.
Methods: For this purpose, patients with FMF-related amyloidosis were assigned according to the *MEFV* gene mutation to one of the two groups. **Group 1:** Patients homozygous for M694V (which is the most common genotype associated with the most severe clinical phenotype in FMF) **Group 2:** Patients homozygous (other than M694V) or compound heterozygous (including M694V) for other *MEFV* variants. Potential confounders were controlled by excluding the patients with untreated hypertension, diabetes mellitus, obesity, smoking, previous history of CVD low glomerular filtration rate (eGFR <70 mL/min). Flow-mediated dilatation (FMD), pentraxin-3 (PTX3) as early markers of endothelial dysfunction and carotid intima-media thickness (cIMT), fibroblast Growth Factor 23 (FGF23) as an indicator of atherosclerotic vascular disease, all of which are non-invasive tests that are also used to identify subjects at increased risk for future CV events were measured in these 2 groups.
Results: We analyzed demographic, clinical, genetic, survival data and these non-invasive markers of endothelial dysfunction (FMD and PTX3) and atherosclerosis (cIMT and FGF23) in 76 FMF amyloidosis patients with homozygous M694V mutations (Group 1) and 93 FMF amyloidosis patients with two pathogenic mutations apart from M694V homozygosity (Group 2) (Table 1). Brachial artery FMD was significantly lower in Group 1 when compared with Group 2 subjects (6.0 vs. 6.5%, p<0.001). cIMT, FGF23 and PTX3 levels were higher in Group 1 when compared with Group 2 (cIMT: 0.84 vs. 0.67 mm, p<0.001; FGF23: 52.4 vs. 38.0 pg/dL, p=0.01; PTX3: 14.0 vs. 3.2 ng/mL, p<0.001). Time to develop amyloidosis was similar in patients homozygous for M694V (median 10.0 years, 95%CI: 8.99-11.0) and in Group 2 (median 10.0 years, 95%CI: 8.97-11.0) (p>0.05). Mortality rate was significantly higher in Group 1 compared to Group 2 (18.4% vs. 1.1%, p<0.001) over a median of 7.8 years of follow-up. FMF amyloidosis patients homozygous for M694V had reduced survival (mean survival: 97 months, 95%CI: 94.9 to 101.0 months) as compared to Group 2 (mean survival: 100.7 months, 95%CI: 100.0 to 101.3 months) (p<0.001) (Figure 1). The proportion of the clinical manifestations including fever, serositis, erysipelas-like

erythema, all of which are associated with an FMF attack did not differ between two groups (p>0.05) apart from arthritis (76.3% in Group 1 and 59.1% in Group 2, p<0.05) (Table 1).

Conclusion: In patients with FMF related amyloidosis, M694V homozygosity is associated with lower FMD values and higher cIMT, FGF23 and PTX3 levels. In summary, the data demonstrate that a genotype-phenotype association exists in terms of endothelial dysfunction and atherosclerosis in FMF patients with amyloidosis.

Table 1.

	Group 1 (n=76)	Group 2 (n=93)	Total (n=169)	p
Clinical Findings	**n (%)**	**n (%)**	**n (%)**	
Dialysis	2 (2.6)	3 (3.2)	5 (3.0)	1.00*
Kidney transplantation	5 (6.6)	4 (4.3)	9 (5.3)	0.73*
Kidney biopsy	68 (89.5)	85 (91.4)	153 (90.5)	0.67
	Median	**Median**	**Median**	
	(Min-max)	**(Min-max)**	**(Min-max)**	
Age (years)	36.5 (19.0-49.0)	35.0 (22.0-49.0)	36.0 (19.0-49.0)	0.16
Age of amyloidosis (years)	20.0 (13.0-31.0)	20.0 (15.0-26.0)	20.0 (13.0-31.0)	0.86
BMI (kg/m^2)	26.0 (21.0-32.0)	27.0 (19.0-32.0)	26.6 (29.0-32.0)	0.89
HOMA	2.2 (1.2-7.3)	2.4 (1.1-8.4)	2.4 (1.1-8.4)	0.40
Proteinuria (g/24h)	7.6	4,6	5.4	**<0.001**



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3582

POS1376

UVEITIS IN 1449 PATIENTS WITH INFLAMMATORY BOWEL DISEASE. STUDY FROM A SINGLE UNIVERSITY CENTER

L. Sanchez-Bilbao[1], M. J. García-García[2], D. Martínez-López[1], M. Rivero-Tirado[2], B. Castro[2], I. González-Mazón[1], J. Crespo[2], M. A. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*; [2]*Hospital Universitario Marqués de Valdecilla, Gastroenterology, Santander, Spain*

Background: Inflammatory bowel disease (IBD), which includes Crohn's disease (CD), and Ulcerative colitis (UC) are related to Spondyloarthritis (SpA). Ocular manifestations (OM) are well-stablished in axial SpA but not in IBD. It has been classically reported that whereas uveitis with axial SpA is predominantly anterior, unilateral, acute, and non-recurrent; in IBD it is bilateral, posterior, insidious, and chronic **(1).**

Objectives: In a large unselected series of IBD, our aim was to assess **a)** epidemiology and clinical features of uveitis associated to IBD, **b)** to compare patients who developed uveitis and those who did not, and **c)** its relationship with biological treatment used in IBD.

Methods: Study of all consecutive patients from a single University Hospital during the last 40 years with**: a)** IBD (CD and UC), and **b)** uveitis according to Standarization Uveitis Nomenclature (SUN) Working Group. Demographic features, clinical findings, occurrence of other extraintestinal manifestations and treatment were recorded.

Results: We studied 1449 (714 women/735 men) patients with IBD, mean age of 55.2±15.9 years.

Uveitis was present in 23 (1.6 %) (38 eyes) of 1448 IBD patients. The most common pattern of uveitis was typically anterior (n=18; 78.3%), unilateral (n=19; 82.6%), acute (n=19; 82.6%), and non-recurrent (n=12; 52.2%).

The comparative study between patients with and without uveitis showed a significant predominance of women (Table 1) in patients with uveitis, as well as erythema nodosum, hidradenitis suppurativa and joint involvement.

Regarding IBD severity, in terms of surgical interventions, and conventional and biological immunosuppressive treatments, there were no significant differences.

Conclusion: Although uveitis is more infrequent in IBD than in axial SpA, it is also anterior, unilateral, acute, and non-recurrent in contrast with published data from selected series. Patients with uveitis do not seem to represent more severe phenotype of IBD.

REFERENCES:

[1] Lyons & Rosenbaum JT. Arch Ophthalmol 1997; 115:61-4.

Table 1. General features of 1448 patients with IBD with and without uveitis.

	Overall	Uveitis	Non uveitis	p
	(n=1449)	(n=23)	(n=1426)	
Main general features				
Age, years, mean±SD	55.2±15.9	49.1±14.6	55.2±15.9	0.8
Sex, women/men, n, (% of women)	714 / 735 (49.3)	17 / 6 (73.9)	697 / 729 (48.9)	**0.02***
IBD duration, years, mean±SD	13.2 ± 9.7	17.4 ± 10.2	13.1 ± 8.9	0.08
IBD Severity				
Surgical Interventions, n (%)	289 (19.9)	2 (8.7)	284 (19.9)	0.7
Conventional Immunosuppressive drugs, n (%)	878 (60.6)	14 (60.9)	863 (60.5)	0.5
Biological Therapy, n (%)	384 (26.5)	7 (30.4)	378 (26.5))	0.9
TNFi monoclonal antibodies	384 (26.5)	7 (30.4)	378 (26.5)	0.9
Ustekinumab	27 (1.9)	1 (4.3)	27 (1.9)	0.5
Other	23 (1.6)	1 (4.3)	22 (1.6)	0.3
Extraintestinal manifestations				
Cutaneous manifestations, n (%) (TOTAL)	125 (8.6)	9 (39.1)	121 (8.7)	0.1
Erythema nodosum, n (%)	26 (1.8)	6 (26.1)	24 (1.7)	**0.009***
Pyoderma gangrenosum, n (%)	13 (0.9)	1 (4.3)	13 (0.9)	0.7
Hidradenitis suppurativa, n (%)	2 (0.1)	1 (4.3)	1 (0.1)	**0.0001***
Joint involvement, n (%) (TOTAL)	131 (9)	10 (43.5)	121 (8.5)	**0.0001***
Axial pattern, n (%)	65 (4.5)	4 (17.4)	58 (4.1)	**0.0001***
Peripheral pattern, n (%)	64 (4.4)	4 (17.4)	63 (4.4)	0.9

Disclosure of Interests: Lara Sanchez-Bilbao: None declared, María José García-García: None declared, David Martínez-López: None declared, Montserrat Rivero-Tirado: None declared, Beatriz Castro: None declared, Iñigo González-Mazón: None declared, Javier Crespo: None declared, Miguel A González-Gay Speakers bureau: AbbVie, Pfizer, Roche, Sanofi, Celgene and MSD., Grant/research support from: AbbVie, MSD, Jansen and Roche,, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD., Grant/research support from: AbbVie, MSD and Roche

DOI: 10.1136/annrheumdis-2021-eular.3610

POS1377

SOME PARAMETERS OF ENDOTHELIAL FUNCTION IN PATIENTS WITH IDIOPATHIC AVASCLAR NECROSIS

K. Gudkevich[1], N. Martusevitch[2], E. Dashkevich[3]. [1]*Minsk City Clinical Hospital No.6, Rheumatology, Minsk, Belarus*; [2]*Belarusian State Medical University, Cardiology and Internal Diseases, Minsk, Belarus*; [3]*Minsk City Clinical Hospital No.10, Central Hormonal Laboratory, Minsk, Belarus*

Background: Avascular necrosis (AN) is a disease, which is the result of blood flow disturbance and necrosis of the bone tissue. It affects predominantly men of working age and steadily progresses to secondary osteoarthritis. AN is a multifactorial disease. In the context of vascular hypothesis it is of particular interest to evaluate homocysteine and its metabolism in patients with AN.

Objectives: The aim of the present study was to evaluate some parameters of endothelial function in patients with AN of the femoral head or femoral condyles in order to determine possible treatment and prevention options.

Methods: We included 53 patients with AN of the femoral head or femoral condyles into the study. The patients were aged 49 (35-62) years, 58,49% (n=31) were male. The inclusion criteria was diagnosis of AN confirmed by X-Ray, CT or MRI. The exclusion criteria were: traumatic AN, Legg-Calve-Pertes disease, connective tissue systemic diseases. We recruited 51 patients into the control group. The groups were comparable by age and gender. In order to analyse engothelial function in the groups we investigated the following serum parameters: homocysteine, vitamin B12, folate. In order to analyse the data obtained we used non-parametric statistics.

Results: We determined a higher level of homocysteine in patients with AN (12,15 (7,55-14,60) vs. 8,18 (6,57-10,70) mcmol/l in the control group, p=0,04). Also we observed almost equal levels of vitamin B12 in patients with AN an in the control group (531,95 (340,80-793,55) vs. 532,75 (417,60-669,7) pg/ml, p=0,99). The level of folate was lower in the study group (5,66 (3,83-6,83) vs. 6,99 (5,02-10,38) ng/ml, p=0,01).

Conclusion: The data obtained show that homocysteine level in patients with AN is higher. This can be a consequence of folate deficiency, which takes part in homocysteine metabolism. Therefore, homocysteine metabolism disturbances can lead to endothelial dysfunction, which results in cardiovascular events in the heart, brain, kidneys [1] as well as in the bone, according to the study results. Folate supplement is the possible way of AN treatment and prevention.

REFERENCES:

[1] Nowroozpoor A, Gutterman D, Safdar B. Is microvascular dysfunction a systemic disorder with common biomarkers found in the heart, brain, and kidneys? - A scoping review. Microvasc Res. 2021 Mar;134:104123. doi: 10.1016/j.mvr.2020.104123. Epub 2020 Dec 15. PMID: 33333140.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3699

POS1378 COMPARISON OF DEMOGRAPHIC AND CLINICAL FEATURES OF FAMILIAL MEDITERRANEAN FEVER PATIENTS AND PATIENTS WITH AXIAL SPONDYLOARTHRITIS ACCOMPANYING FAMILIAL MEDITERRANEAN FEVER

M. Kiracı[1], E. Bilgin[2], E. Duran[2], B. Farisoğulları[2], E. C. Bolek[2], G. K. Yardımcı[2], Z. Özsoy[2], G. Ayan[2], G. Sandal Uzun[2], B. Balci Peynircioglu[3], O. Karadag[2], A. Akdoğan[2], Ş. A. Bilgen[2], S. Kiraz[2], A. İ. Ertenli[2], U. Kalyoncu[2], L. Kılıç[2]. *[1]Hacettepe University, Internal Medicine, Ankara, Turkey*; *[2]Hacettepe University, Internal Medicine, Rheumatology, Ankara, Turkey*; *[3]Hacettepe University, Medical Biology, Ankara, Turkey*

Background: The rate of co-occurrence of Familial Mediterranean Fever (FMF) and axial spondyloarthritis (axSpA) in adults is reported ranging from 0.5% to 7.5%. The clinical implications of this co-occurrence in the course of FMF is still a research question.

Objectives: To compare of demographic and clinical features of patients with FMF and FMF+axSpA.

Methods: A total of 9630 FMF patients was detected according to the ICD-10 code (E85.0) of FMF in Hacettepe University Hospital database. 241 of these patients also had axSpA according to the ICD-10 code (M45). FMF diagnosis was confirmed by Tel-Hashomer criteria. AxSpA was diagnosis was confirmed by either presence of sacroiliitis on sacroiliac radiography according to the Modified New York Criteria (mNY) or presence of active sacroiliitis according to ASAS criteria on magnetic resonance imaging. 136 patients were confirmed according to these criterias as having FMF+axSpA. As a control group, 231 consequent FMF patients without axSpA recorded on the "FMF in Central Anatolia (FiCA) database" and followed up at our center were included in the analysis. Demographic and clinical features of those patients in both groups were compared. p<0.05 was considered as statistically significant, correction for multiple comparisons was not performed.

Results: 136 patients were included in FMF+axSpA group and 231 patients were included in FMF group. 114 (83.8%) patients in FMF+axSpA group had radiographic sacroiliitis according to mNY criteria; median cervical mSASSS was 0 (available for 49 patients, min-max, 0-36), median lumber mSASSS was 4 (available for 121 patients, min-max, 0-36), 33 (27%) patients had cervical or lumber syndesmophyte. Twenty-six (19.1%) of these patients had radiologically documented inflammatory hip disease 12 (8.8%) of these patients underwent total hip replacement. Female gender was more prevalent in FMF+axSpA group (53.7% vs 32.5%, p<0.001). Age at FMF symptom onset and diagnosis were earlier in FMF patients; however, symptom and disease durations were longer in FMF+axSpA group in our study cohort (Table 1). Frequency of FMF signs and symptoms were comparable except the rate of pleuritis was higher in FMF patients compared to FMF+axSpA group (p=0.003). Amyloidosis was more prevalent in FMF+axSpA group (6.6% vs. 1.7%, p=0.014). Results of MEFV gene analysis were available for 273 patients. Although presence of M694V mutation (either in 1 allele or 2 alleles) was comparable in 2 groups, homozygous M694V mutation was more prevalent in FMF+axSpA group (39.8% vs. 28.9%, p=0.02).

Conclusion: The coexistence of spondyloarthritis in FMF patients appears to be associated with the increased prevalence of amyloidosis. The inflammatory burden of a second disease and the increased prevalence of the homozygous M694V mutation may explain this risk.

Table 1. Comparison of demographic and clinical features of two groups.

	FMF+AxSpA (n=136, 37.1%)	FMF (n=231, 62.9%)	p
Female, n(%)	73 (53.7)	75 (32.5)	<0.001
Age at FMF symptom onset, years med (IQR)	12 (5-20)	10 (6-18)	0.046
Symptom duration, years, med (IQR)	24 (18-32)	20 (14-29)	0.007
Age at FMF diagnosis, years, med (IQR)	24 (13-33)	20 (11-30)	0.10
Duration after diagnosis, years, med (IQR)	16 (10-22)	13 (7-17)	<0.001
FMF signs and symptoms, n(%)			
-Fever	128 (94.1)	204 (88.3)	0.067
-Abdominal pain	123 (90.4)	217 (93.9)	0.21
-Pleuritis	31 (22.8)	87 (37.7)	0.003
-Pericarditis	3 (2.2)	2 (1.0)	0.34
-Arthritis	64 (47.1)	92 (39.8)	0.17
-Erysipelas	24 (17.6)	38 (16.5)	0.77
-Febrile myalgia	9 (6.6)	13 (5.6)	0.70
Inflammatory back pain, n(%)	92 (67.6)	26 (11.3)	<0.001
Inflammatory bowel disease, n(%)	6 (4.4)	4 (1.7)	0.12
FMF family history, n(%)			
-Any degree	66 (48.5)	137 (59.8)	0.04
-First degree	48 (35.8)	97 (42.0)	0.24
-Second degree	25 (18.7)	86 (37.2)	<0.001
Number of attacks at recent year, med (min-max)	1 (0-12)	1 (0-10)	0.13
Amyloidosis	9 (6.6)	4 (1.7)	0.014
M694V status (N=273)			
-Present (one or two allels)	91 (80.5)	120 (75.0)	0.28
-Two allels	45 (39.8)	43 (28.9)	0.02

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3738

POS1379 LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF) - INTERIM ANALYSIS OF THE RELIANCE REGISTRY

J. Henes[1], J. B. Kuemmerle-Deschner[2], T. Kallinich[3], F. Dressler[4], F. Weller-Heinemann[5], B. Kortus-Goetze[6], I. Foeldvari[7], G. Horneff[8], M. Hufnagel[9], F. Meier[10,11], J. Weber-Arden[12], N. Blank[13]. *[1]University Hospital Tuebingen, Department of Internal Medicine II, Rheumatology, Tuebingen, Germany*; *[2]University Hospital Tuebingen, Department of Pediatrics, Division of Pediatric Rheumatology, Tuebingen, Germany*; *[3]Charité University Medicine Berlin, Department of Pediatrics, Division of Pulmonology, Immunology and Critical Care Medicine, Berlin, Germany*; *[4]Hannover Medical School, Division of Pediatric Pneumology, Allergology and Neonatology, Hannover, Germany*; *[5]Klinikum Bremen-Mitte, Prof. Hess Kinderklinik, Bremen, Germany*; *[6]University of Marburg, Division of Nephrology, Marburg, Germany*; *[7]Centre for Pediatric and Adolescence Rheumatology Hamburg, Centre for Pediatric and Adolescence Rheumatology Hamburg, Hamburg, Germany*; *[8]Asklepios Clinic Sankt Augustin, Asklepios Clinic Sankt Augustin, Sankt Augustin, Germany*; *[9]University Hospital Medical Center, Medical Faculty, University of Freiburg, Division of Pediatric Infectious Diseases and Rheumatology, Department of Pediatrics and Adolescent Medicine, Freiburg, Germany*; *[10]University Hospital Frankfurt, Goethe University, Division of Rheumatology, Frankfurt am Main, Germany*; *[11]Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Project Group Translational Medicine and Pharmacology TMP, Frankfurt am Main, Germany*; *[12]Novartis Pharma GmbH, Novartis Pharma GmbH, Nuernberg, Germany*; *[13]University Hospital Heidelberg, Rheumatology, Heidelberg, Germany*

Background: Familial Mediterranean Fever (FMF) is characterized by recurrent attacks of fever and serositis as well as elevated inflammatory markers. FMF treatment goals according to EULAR are to control acute attacks and subclinical inflammation and to improve patients´ quality of life[1]. In a phase 3 pivotal study (*CLUSTER* study), FMF patients treated with the interleukin-1β inhibitor canakinumab met all these goals[2].

Objectives: The present study explores the long-term efficacy and safety of canakinumab (CAN) in routine clinical practice in pediatric (age ≥2 years) and adult FMF patients.

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a three-year follow-up period. Patients with clinically confirmed diagnosis of FMF who routinely receive CAN were enrolled in order to evaluate effectiveness and safety of CAN under standard clinical practice conditions. Disease activity and remission by physicians´ assessment, disease activity, fatigue and impact on social life by patients' assessment, inflammatory markers and AIDAI (Auto-Inflammatory Diseases Activity Index) score were recorded at baseline and were assessed at 6-monthly intervals within the three-year observation period of the study.

Table 1. Baseline characteristics and third interim analysis data of patients with FMF

Baseline			6 months		12 months		18 months		
								Number of patients, N	54
All patients | patients without prior CAN therapy									
11	35	7	27	5	16	3	Number (%*) of patients in disease remission (physician assessment)	18 (48.6)	1 (20.0)
19 (73.1)	3 (75.0)	13 (65.0)	1 (50.0)	8 (61.5)	1 (100.0)	Physician Global Assessment, percentage* of absent/ mild-moderate/severe rating	43/38/11	0/40/60	65/27/0
50/50/0	55/35/0	0/50/0	46/46/0	0/100/0	Patient assessment of current disease activity; 0–10, median (min; max)	3.0 (0; 10)	7.0 (0; 10)	2.5 (0; 7)	2.0 (0; 5)
2.0 (0; 7)	2.0 (0; 2)	2.0 (0; 6)	0.5 (0; 1)	Patient assessment of current fatigue; 0–10, median (min; max)	5.0 (0; 10)	5.0 (0; 9)	3.5 (0; 10)	3.0 (1; 6)	3.0 (0; 10)
0.0 (0; 4)	3.0 (0; 7)	0.5 (0; 1)	Number (%*) of patients without impairment of social life by the disease	19 (46.3)	3 (37.5)	18 (66.7)	3 (75.0)	14 (66.7)	4 (80.0)
5 (55.6)	2 (66.7)	CRP, median (mg/dl)	0.2	1.1	0.2	0.1	0.2	0.0	0.1
0.5	SAA, median (mg/dl)	0.7	6.8	0.8	0.4	0.8	0.6	0.6	0.7
ESR, median (mm/h)	9.0	18.5	6.0	5.0	5.5	4.0	8.0	5.0	**SAE**
Number of events					**Incidence rate per 100 patient years**				Total
11					16.23			Arthritis	5
7.38				SARS-CoV-2 infection		2			2.95
Familial Mediterranean Fever			1			1.48			Intestinal Hemorrhage
1					1.48			Pyrexia	1
1.48				Tonsillectomy (SADR)		1			1.48

*not reported for all patientsCRP, c-reactive protein; ESR, erythrocyte sedimentation rate; n. a., not annotated; SAA, serum amyloid A; SADR, serious adverse drug reaction; SAE, serious adverse event

Results: This interim analysis of FMF patients (N=54) enrolled by December 2020 includes baseline as well as 6-, 12- and 18-month data. Mean age in this cohort was 25 years (4–56 years) and the proportion of female patients was 46 % (N=25). At baseline, median duration of prior CAN treatment was 2.0 years (0–6 years).

While physician ratings report around 62% of patients in disease remission, 52% with absent and 34% with mild-moderate disease activity, patient-reported disease activity decreased from moderate (PPA 3.0) to low (PPA 2.0) during the observation period. A decrease was observed regarding disease activity parameters, in particular in patients without prior CAN therapy (Table 1, Figure 1). A total of 11 serious adverse events was reported, of which one case of tonsillectomy was classified as drug-related.

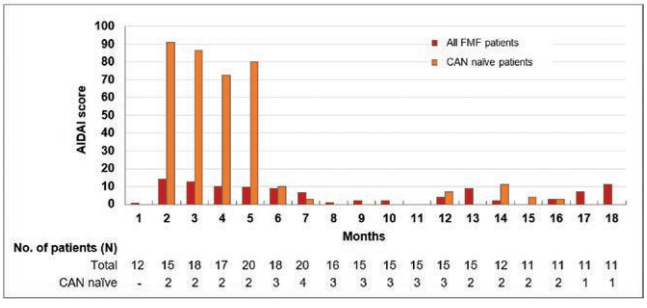
Conclusion: Interim data of FMF patients from the RELIANCE study, the longest running real-life CAN registry, confirm efficacy and safety of long-term CAN treatment.

REFERENCES:

[1] Ozen S, et al. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis 2016;75:644–651. doi:10.1136/annrheumdis-2015-208690

[2] De Benedetti F, et al. Canakinumab for the treatment of autoinflammatory recurrent fever syndromes. N Engl J Med 2018;378:1908–19.

Figure 1: Median AIDAI score (0-390) of the FMF main group (N = 54, at baseline) and the FMF subgroup without prior CAN therapy (N=11) within 18 months



Disclosure of Interests: Jörg Henes Consultant of: Novartis, AbbVie, Sobi, Roche, Janssen, Boehringer-Ingelheim, Grant/research support from: Novartis, Roche, J. B. Kuemmerle-Deschner Consultant of: Novartis, AbbVie, Sobi, Grant/research support from: Novartis, AbbVie, Sobi, Tilmann Kallinich Consultant of: Sobi, Novartis, Roche, Grant/research support from: Novartis, Frank Dressler Consultant of: Abbvie, Mylan, Novartis, Pfizer, Grant/research support from: Novartis, Frank Weller-Heinemann: None declared, Birgit Kortus-Goetze Consultant of: Novartis, Ivan Foeldvari Consultant of: Novartis, Gerd Horneff Speakers bureau: bbVie, Bayer, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Grant/research support from: AbbVie, Chugai, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Markus Hufnagel Grant/research support from: Novartis, Florian Meier Speakers bureau: Novartis, Julia Weber-Arden Employee of: Novartis, Norbert Blank Consultant of: Novartis, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Actelion, UCB, Boehringer-Ingelheim, Roche, Grant/research support from: Novartis, Sobi

DOI: 10.1136/annrheumdis-2021-eular.3756

POS1380

LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH TRAPS (TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME) - INTERIM ANALYSIS OF THE RELIANCE REGISTRY

N. Blank[1], J. Henes[2], T. Kallinich[3], P. Oommen[4], C. Schuetz[5], M. Borte[6], J. Weber-Arden[7], J. B. Kuemmerle-Deschner[8]. [1] *University Hospital Heidelberg, Rheumatology, Heidelberg, Germany*; [2]*University Hospital Tuebingen, Department of Internal Medicine II, Rheumatology, Tuebingen, Germany*; [3]*Charité University Medicine Berlin, Department of Pediatrics, Division of Pulmonology, Immunology and Critical Care Medicine, Berlin, Germany*; [4]*Heinrich-Heine-University Düsseldorf, Clinic of Pediatric Hematology, Oncology and Clinical Immunology, Duesseldorf, Germany*; [5]*Medizinische Fakultät Carl Gustav Carus, Technische Universität Dresden, Pediatrics, Dresden, Germany*; [6]*Hospital St. Georg gGmbH Leipzig, ImmunoDeficiencyCenter Leipzig (IDCL), Leipzig, Germany*; [7]*Novartis Pharma GmbH, Novartis Pharma GmbH, Nuernberg, Germany*; [8]*University Hospital Tuebingen, Department of Pediatrics, Division of Pediatric Rheumatology, Tuebingen, Germany*

Table 1. Baseline characteristics and interim analysis data of patients with TRAPS

	Baseline	6 months	12 months	18 months	Number of patients, N
16	13	10	6	Median age, years (min; max)	23 (3; 43)
17 (3; 43)	16 (4; 38)	25 (4; 43)	Females (%)	11 (69)	9 (69)
7 (70)	3 (50)	Median duration of prior CAN therapy at baseline, years (min; max)	1.0 (0; 4)	1.0 (0; 4)	1.0 (0; 4)
1.5 (0; 2)	Number (%) of patients in disease remission (physician assessment)	9 (60.0)	9 (81.8)	7 (77.8)	4 (80.0)
Physician Global Assessment, percentage of absent/mild-moderate/severe rating	40 / 53 / 0	82 / 9 / 0	44 / 44 / 11	80 / 20 / 0	Patient assessment of current disease activity; 0–10, median (min; max)
1.5 (0; 5)	1.0 (0; 4)	1.0 (0; 6)	0.0 (0; 3)	Patient assessment of current fatigue; 0–10, median (min; max)	2.0 (0; 8)
1.0 (0; 7)	2,5 (0; 8)	4.0 (0; 7)	Number (%) of patients without impairment of social life by the disease	4 (50)	5 (63)
2 (33)	3 (60)	Number (%) of patients with days absent from work/school during last 6 months	8 (50)	5 (39)	5 (56)
3 (50)	CRP, median (mg/dl)	0.1	0.1	0.1	0.0
SAA, median (mg/dl)	0.5	0.4	0.4	0.3	ESR, median (mm/h)
7.0	5.0	5.0	5.0	**SAE**	**Number of events**
Incidence rate per 100 patient years			Total	3	
14.7		Circulatory collapse (non fatal)		1	4.9
Dizziness	1			4.9	Headache
1		4.9			

CRP, c-reactive protein; **ESR**, erythrocyte sedimentation rate; SAA, serum amyloid A; SAE, serious adverse event

Background: Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is a rare autoinflammatory condition characterized by severe systemic and organ inflammation. In a phase 3 pivotal trial (*CLUSTER* study), TRAPS patients have been successfully treated with the interleukin-1β inhibitor canakinumab. 45% of patients reached clinical remission after 16 weeks (primary endpoint)[1]. Canakinumab has been approved and applied for the treatment of TRAPS patients since 2017[2].

Objectives: The present study explores the long-term efficacy and safety of canakinumab under routine clinical practice conditions in pediatric (age ≥2 years) and adult TRAPS patients.

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up period. Patients with clinically confirmed diagnoses of TRAPS, CAPS, FMF or HIDS/MKD who routinely receive canakinumab are enrolled in order to evaluate efficacy and safety of canakinumab under standard clinical practice conditions. Disease activity and remission by physician assessment, disease activity and fatigue by patient assessment, days absent from school/work due to study indication, inflammatory markers, and AIDAI (Auto-Inflammatory Diseases Activity Index) score were assessed at baseline and at 6-monthly intervals.

Results: The interim analysis of TRAPS patients enrolled by December 2020 includes baseline (N=16, including 1 patient with atypical TRAPS) and preliminary 18-month data. Mean age in this cohort was 23 years (3–43 years) and the median duration of prior CAN treatment was 1.0 year (0–4 years).

Physician assessment indicated 60-80% remission and laboratory parameters were within normal range. Disease control by patient assessment showed no major changes regarding the analyzed parameters (Table 1, Figure 1). Of the three serious adverse events reported none was classified as drug-related.

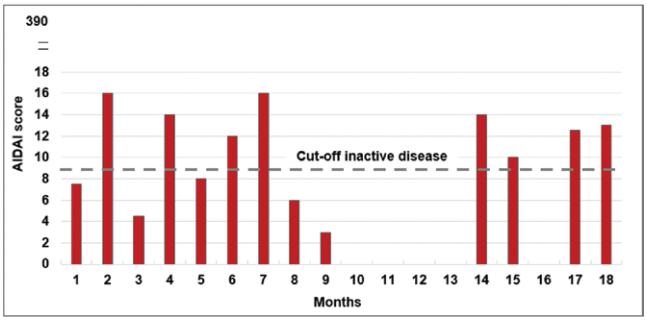
Conclusion: Preliminary analysis of 18 month interim data of TRAPS patients treated with CAN available from the RELIANCE study indicate stable efficacy and safety of CAN long-term treatment.

REFERENCES:

[1] De Benedetti F, et al. Canakinumab for the treatment of autoinflammatory recurrent fever syndromes. N Engl J Med 2018;378:1908–19.

[2] Ilaris, INN-canakinumab (europa.eu)

Figure 1: Median AIDAI score (0-390) of the TRAPS patients (N = 16 at baseline) within 18 months



Disclosure of Interests: Norbert Blank Consultant of: Novartis, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Actelion, UCB, Boehringer-Ingelheim, Roche, Grant/research support from: Novartis, Sobi, Jörg Henes Consultant of: Novartis, AbbVie, Sobi, Roche, Janssen, Boehringer-Ingelheim, Grant/research support from: Novartis, Roche, Tilmann Kallinich Consultant of: Sobi, Novartis, Roche, Grant/research support from: Novartis, Prasad Oommen Grant/research support from: Novartis, Catharina Schuetz: None declared, Michael Borte Grant/research support from: Pfizer, Shire, Julia Weber-Arden Employee of: Novartis, J. B. Kuemmerle-Deschner Consultant of: Novartis, AbbVie, Sobi, Grant/research support from: Novartis, AbbVie, Sobi

DOI: 10.1136/annrheumdis-2021-eular.3808

POS1381 BIOLOGIC TREATMENT OF ADULT-ONSET STILL'S DISEASE: A SINGLE CENTER EXPERIENCE

B. Yurttas[1], B. Egeli[2], G. Guzelant Ozkose[1], S. Ugurlu[1]. [1]*Istanbul University-Cerrahpasa, Rheumatology, Istanbul, Turkey*; [2]*Boston Children's Hospital, Immunology, Boston, United States of America*

Background: Even though corticosteroids and cDMARDs are effective for inducing remission in patients with Adult-Onset Still Disease (AOSD), relapse is common. Hence, maintaining the clinical stability is challenging. Almost all of the patients face side effects because of high dose steroid treatment. Biological DMARDs have been reported to be effective in refractory patients.
Objectives: We aimed to evaluate the patients' outcomes who were diagnosed with AOSD and treated with at least one bDMARDs in our tertiary center.
Methods: Patients with AOSD who were followed in our clinic between 2007 and 2020 were screened retrospectively. For the diagnosis of AOSD, all of the patients fulfilled Yamaguchi criteria. The demographic characteristics, baseline and post-treatment clinical findings and outcomes were reported.
Results: Twenty-eight patients (21 F, 7 M) were screened (Figure 1). The mean disease duration of the first bDMARD was 21,76 ± 28,05 months (mean ± SD). The mean duration of bDMARD treatment was 37,04 ± 30,75 months. The reasons for starting a bDMARD were systemic symptoms (%80) and chronic arthritis (%20). All of the patients used methotrexate (MTX) except one. This patient had macrophage activation syndrome during diagnosis and was treated with cyclosporine. All of the patients were treated with corticosteroids (34,28 ± 26,70 mg/d) and a cDMARD at initiation (22 of them MTX, 1 of them azathioprine, 2 of them cyclosporine and 1 of them IVIg). Anakinra was the most preferred biologic as a first-line treatment modality (TNF inhibitors=5, tocilizumab=4). The main reason for switching was loss of efficacy (8/22). Tocilizumab was the most used agent in 2nd line and canakinumab was in 3rd line. Twenty-two patients were in remission at last visit. Also, 15 patients were steroid-free, 14 patients were MTX-free. Patient global visual analogue scale, acute phase reactants and daily steroid dose were reduced significantly at last visit compared to the initial visit (Table 1).

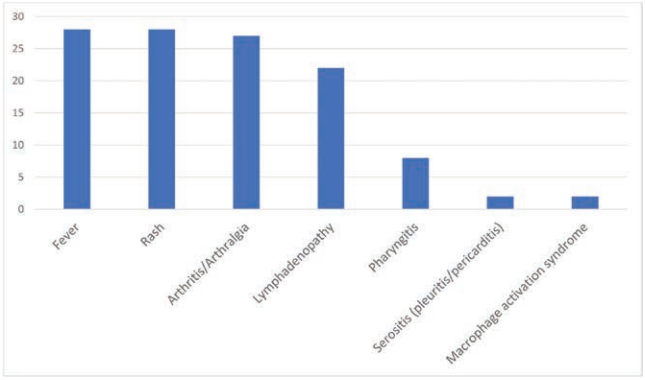


Figure 1. Presenting signs and the symptoms of the patients

Table 1. Comparison of important laboratory findings and the mean steroid dose

Clinical finding	At initiation of bDMARD mean ± SD	At the last visit mean ± SD
PG-VAS	9.8 ± 0.8	2.3 ± 2.3
ESR (mm/h)	34,28 ± 33,95	18.82 ± 11.60
CRP (mg/l)	70,76 ± 67,80	13.44 ± 27.33
Ferritin (ng/mL)	1662 ± 1239	275.7 ± 381.4
Daily steroid dose (prednisolone, mg/d)	34.28 ± 26.70	5.60 ± 8.60

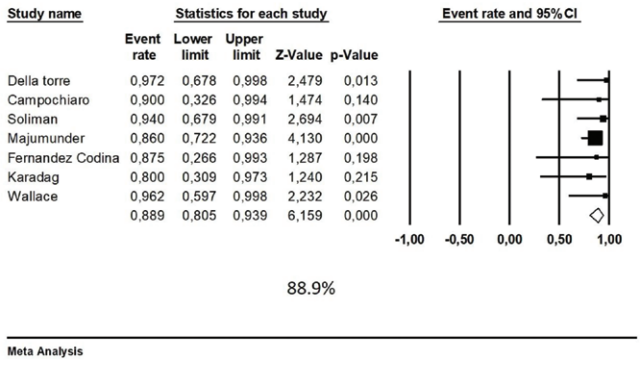
bDMARD treatment was terminated in 5 patients due to complete remission (n=2) and side effects (1 of them pneumonia, 1 of them EBER (+) Hodgkin Lymphoma and 1 of them tuberculosis). Six patients experienced local injection site reaction, none of them stopped treatment. Also, one patient died while she was in remission under anakinra treatment with an unknown cause.
Conclusion: The most common presenting symptoms in our cohort were fever and salmon-colored rash. Tocilizumab is an alternative treatment modality in cases with chronic arthritis and IL-1 inhibitors are an alternative for systemic course of disease. bDMARDs, especially IL-1 inhibitors are highly effective for refractory patients with AOSD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3968

POS1382 RITUXIMAB FOR INDUCTION OF REMISSION IN TYPE 1 AUTOIMMUNE PANCREATITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Lanzillotta[1], G. Capurso[2], Z. Wallace[3], O. Karadag[4], L. Dagna5, E. Della Torre5. [1]*San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy*; [2]*San Raffaele Scientific Institute, PancreatoBiliary Endoscopy and EUS Division, Milan, Italy*; [3]*Massachusetts General Hospital, Clinical Epidemiology Unit, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [4]*Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; [1]*San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy*

Background: Type I autoimmune pancreatitis (AIP) is a rare form of pancreatitis that belongs to the IgG4-related disease (IgG4-RD) spectrum (1). Autoimmune pancreatitis responds brilliantly to glucocorticoids, but iatrogenic toxicity associated with prolonged steroid therapy represents a relevant clinical concern in the long-term (2). B cell depletion therapy proved to be effective in inducing IgG4-RD remission, yet most evidence are derived from small and heterogenous cohorts.
Objectives: We performed a systematic review and meta-analysis to estimate the remission rate following rituximab-based induction treatment.
Methods: Two reviewers searched MEDLINE, SCOPUS, and EMBASE until December 2020 to identify studies on remission rate and relapse rate of Type I AIP after induction of remission with rituximab. Studies involving three or more patients were included, including the most recent or most numerous cohorts in case of duplicates This study was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Pooled effects were calculated using a random-effects model and expressed in terms of pooled remission, relapse and adverse effects (AEs) rates.
Results: Seven cohort studies met inclusion criteria for the meta-analysis for a total of 101 patients. Reasons for rituximab administration were relapsing disease (63.5%), new diagnosis (18.5%) or glucorticoids intolerance (17.9%). The median follow-up time was 18.5 months. The pooled rate of complete response at 6 months from induction of remission was 88.9% (95% CI 80.5%-93.9%) without heterogeneity (I^2=0%) (Figure 1). The median time to relapse was 9.75 months. The pooled estimate of relapse rate was 21% (95% CI 10.5%-40.3%) with moderate heterogeneity (I^2=51%), being 35.9% (95% CI 17.3%-60.1%) in the 4 studies with rate of other organs involvement (OOI)>80% and as low as 10.1% (4.8%-20.3%) in the others. The pooled estimate of rituximab-related AEs was 25% (95% CI 8.8%53%) with substantial heterogeneity (I^2=73.6%). There was no publication bias.
Conclusion: Treatment of type I AIP with rituximab is associated with high remission rate, a higher relapse rate in presence of OOI and limited AEs. Randomized controlled trials with adequate power are needed to confirm these findings.
REFERENCES:
[1] Lanzillotta M, Mancuso G, Della-Torre E. Advances in the diagnosis and management of IgG4 related disease. BMJ. 2020;369:m1067
[2] Lanzillotta M, Vinge-Holmquist O, Overbeek KA, et al. PrescrAIP: A Pan-European Study on Current Treatment Regimens of Auto-Immune Pancreatitis. Front Med (Lausanne). 2020;7:408

Fig.1 Pooled rate of complete response



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3993

POS1383 THE ASSOCIATION BETWEEN BARIATRIC SURGERY AND DUPUYTREN DISEASE: A COHORT STUDY FROM SWEDISH NATIONWIDE HEALTHCARE REGISTRIES

T. Burkard[1], J. Lane[2], D. Holmberg[3], A. M. Burden[1,4], D. Furniss[2]. [1]*ETH Zurich, Department of Chemistry and Applied Biosciences, Zurich, Switzerland*; [2]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology, and*

Musculoskeletal Sciences, Oxford, United Kingdom; [3]*Karolinska Institutet and Karolinska University Hospital, Department of Molecular medicine and Surgery, Stockholm, Sweden*; [4]*Maastricht University Medical Center+, 4 Department of Clinical Pharmacy and Toxicology, Maastricht, Netherlands*

Background: Dupuytren disease (DD) is multifactorial, with several genetic and environmental risk factors contributing to disease susceptibility. High body mass index, however, was suggested to be protective of DD.[1] The impact of weight loss among obese patients on DD has not been assessed to date.
Objectives: To assess the association between bariatric surgery and DD in a secondary care setting.
Methods: We performed a propensity score (PS)-matched cohort study using data from Swedish nationwide healthcare registries (patient registry [secondary care], causes of death registry, prescribed drug registry). Patients aged 30-79 years who underwent bariatric surgery between 2006 and 2019 were matched to up to 2 obese bariatric surgery-free patients (called unexposed patients) based on their PS. PS-matching was carried out in risk set sampling to reduce selection bias, within 4 sequential cohort entry blocks to account for time trend biases. The outcome DD was defined as a diagnosis of DD in secondary care or partial or total fasciotomy of wrist or hand. After a 1-year run-in period, patients were followed in an "as-treated" approach. We applied Cox proportional hazard regression to calculate hazard ratios (HR) with 95% confidence intervals (CIs) of incident DD among bariatric surgery patients when compared to obese unexposed patients overall, and in subgroups of age, sex, bariatric surgery type, and by duration of follow-up.
Results: A total of 34 959 bariatric surgery patients were PS-matched to 54 769 obese unexposed patients. A total of 71.6% of bariatric surgery patients were women. Bariatric surgery patients had a mean age of 45.5 years and a mean follow-up of 6.9 years. All patient characteristics in obese unexposed patients were highly similar. We observed 126 and 136 severe DD cases among bariatric surgery and obese unexposed patients, respectively. The risk of DD was significantly increased in bariatric surgery patients compared to obese unexposed patients (HR = 1.30, 95% CI 1.02-1.65). The risk of DD was higher in women (HR = 1.36, 95% CI 1.00-1.84) than in men (HR = 1.05, 95% CI 0.70-1.58). Age did not modify the risk of DD among bariatric surgery patients compared to obese unexposed patients. Malabsorptive bariatric surgery yielded an increased risk of DD when compared to obese unexposed patients (HR = 1.33, 95% CI 1.04-1.71), while restrictive bariatric surgery yielded a null result. The risk of DD increased with duration of follow-up (>5 years of follow-up: HR = 1.63, 95% CI 1.14-2.34, null result in earlier follow-up).
Conclusion: Our results suggest that substantial weight loss is associated with a latent increased risk of severe DD in an obese population. This observation further strengthens current evidence that high body mass index is protective against DD. The latency of risk increase of DD after bariatric surgery may suggest that slowly adapting metabolic changes may be part of the mechanism of DD emergence.
REFERENCES:
[1] Hacquebord JH, Chiu VY, Harness NG. The Risk of Dupuytren Surgery in Obese Individuals. J Hand Surg Am. 2017, 42: 149–55.
Acknowledgements: We thank Prof. Dr. Jesper Lagergren (Karolinksa Institutet, Stockholm, Sweden) for hosting Dr. Theresa Burkard for a research stay at the Upper Gastrointestinal Surgery Group and making the data available for use. Furthermore, we thank Dr. Giola Santoni (Karolinksa Institutet, Stockholm, Sweden) for her technical support.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4067

POS1384 DIFFERENT CLINICAL CHARACTERISTICS OF IGG4-RRD PATIENTS AND NON-IGG4-RRD PATIENTS: A LARGE CHINESE COHORT STUDY

Z. Wang[1], L. Jiaxi[1], Y. Liu[1]. [1]*Peking University People's Hospital, Department of Rheumatology and Immunology, Beijing, China*

Background: IgG4-related disease (IgG4-RD) is an autoimmune disorder and frequently involve multiple organs. The respiratory tract is one of the most frequently involved sites.
Objectives: This study aimed to compare the demographic and clinical characteristics of IgG4-related respiratory disease (IgG4-RRD) and non-IgG4-RRD patients in a large cohort.
Methods: We carried out a retrospective study of 452 cases of IgG4-RD (104 IgG4-RRD patients and 348 non-IgG4-RRD patients) diagnosed at Peking University People's Hospital between 2003 and 2020.
Results: IgG4-RRD patients had an elder age of disease onset and diagnosis. Multiorgan involvement and hypocomplementemia were more common in IgG4-RRD. Besides, the level of ESR, eosinophilia, IgG and IgG4 were higher in IgG4-RRD patients. In IgG4-RRD group, salivary gland, lacrimal gland, lymph nodes, biliary system and kidney were more commonly involved than those in the non-IgG4-RRD group. Also, more numbers of organ involvement and biliary involvement were independent risk factors for the development of respiratory involvement in IgG4-RD patients.
Conclusion: Our study revealed demographic, clinical, laboratory and imaging features of IgG4-RRD patients and the underlying differences in pathogenesis between the two phenotypes, which have important implications for the diagnosis and treatment of the disease.
REFERENCES:
[1] Morales AT, Cignarella AG, Jabeen IS, Barkin JS, Mirsaeidi M. An update on IgG4-related lung disease. European journal of internal medicine. 2019;66:18-24.
[2] Stone JH, Zen Y, Deshpande V. IgG4-related disease. The New England journal of medicine. 2012;366(6):539-51.
[3] Vasaitis L. IgG4-related disease: A relatively new concept for clinicians. European journal of internal medicine. 2016;27:1-9.
[4] Matsui S, Yamamoto H, Minamoto S, Waseda Y, Mishima M, Kubo K. Proposed diagnostic criteria for IgG4-related respiratory disease. Respiratory investigation. 2016;54(2):130-2.
[5] Cao L, Chen YB, Zhao DH, Shi WF, Meng S, Xie LX. Pulmonary function tests findings and their diagnostic value in patients with IgG4-related disease. Journal of thoracic disease. 2017;9(3):547-54.
[6] Wallace ZS, Perugino C, Matza M, Deshpande V, Sharma A, Stone JH. Immunoglobulin G4-related Disease. Clinics in chest medicine. 2019;40(3):583-97.
[7]Matsui S. IgG4-related respiratory disease. Modern rheumatology. 2019;29(2):251-6.
[8] Johansson SG, Hourihane JO, Bousquet J, Bruijnzeel-Koomen C, Dreborg S, Haahtela T, et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy. 2001;56(9):813-24.
[9] Fei Y, Shi J, Lin W, Chen Y, Feng R, Wu Q, et al. Intrathoracic Involvements of Immunoglobulin G4-Related Sclerosing Disease. Medicine. 2015;94(50):e2150.
[10] Wallace ZS, Deshpande V, Mattoo H, Mahajan VS, Kulikova M, Pillai S, et al. IgG4-Related Disease: Clinical and Laboratory Features in One Hundred Twenty-Five Patients. Arthritis & rheumatology (Hoboken, NJ). 2015;67(9):2466-75.
[11] Yamada K, Yamamoto M, Saeki T, Mizushima I, Matsui S, Fujisawa Y, et al. New clues to the nature of immunoglobulin G4-related disease: a retrospective Japanese multicenter study of baseline clinical features of 334 cases. Arthritis research & therapy. 2017;19(1):262.
[12] Borges T, Silva S. IgG4-related disease: How to place it in the spectrum of immune-mediated and rheumatologic disorders? Modern rheumatology. 2020;30(4):609-16.
[13] Liu Y, Xue M, Wang Z, Zeng Q, Ren L, Zhang Y, et al. Salivary gland involvement disparities in clinical characteristics of IgG4-related disease: a retrospective study of 428 patients. Rheumatology (Oxford, England). 2020;59(3):634-40.
[14] Matsui S, Taki H, Shinoda K, Suzuki K, Hayashi R, Tobe K, et al. Respiratory involvement in IgG4-related Mikulicz's disease. Modern rheumatology. 2012;22(1):31-9.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4277

POS1385 AUTOIMMUNE DISEASES ASSOCIATED WITH CHRONIC LIVER DISEASES

N. Trad[1], G. Mohamed[2], B. Ben Slimen[1], K. Boughoula[2], S. Bizid[1], H. Ben Abdallah[2], R. Bouali[1], M. N. Abdelli[2]. [1]*Military Hospital of Tunis, Gastroenterology, Tunis, Tunisia*; [2]*Military Hospital of Tunis, Gastroenterology, Tunis, Tunisia*

Background: Chronic liver diseases whatever their etiologies could be associated with immunological disturbances.
Objectives: Our aim was to evaluate the prevalence and the characteristics of autoimmune diseases associated with chronic liver diseases.
Methods: We performed a retrospective analysis of data from consecutive patients followed in our department for chronic liver diseases recruited from January 2010 to December 2019. Demographic, clinical, and paraclinical data were collected.
Results: A total of 224 patients were included. The mean age was 61.02 ±13.2 years and the sex-ratio was 1.6. The main etiology of chronic liver diseases was viral infection C (32.1%) followed by viral infection B (22.8%) and non-alcoholic steatohepatitis (21.4%). The prevalence of autoimmune chronic liver diseases was 7.58%: autoimmune hepatitis (AIH) in four cases, primary biliary cholangitis (PBC) in huit cases, primary sclerosing cholangitis (PSC) in three cases and overlap syndrome (AIH-PBC) in two cases. Autoimmune diseases were noted in 31 cases (13.9%): autoimmune hemolytic anemia in 15 cases, autoimmune thyroiditis in 12 cases, one case of psoriasis, one case of CREST syndrome, one case of Sjögren's syndrome and one case of autoimmune thrombocytopenia. Autoimmune pathologies were more associated with autoimmune chronic liver disease than other causes of chronic liver disease (47% vs 11.1%, p <0.001). Autoimmune pathologies were not statistically associated with female gender (p = 0.085) or young age (p = 0.483).
Conclusion: In our study, the prevalence of autoimmune diseases during chronic liver diseases was 13.9%. This prevalence was higher in the case of autoimmune chronic liver diseases (47%), which would underline the importance of systematic screening for clinical and biological immune manifestations in those patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4288

Diagnostics and imaging procedures

POS1386 ANGIOGRAPHIC CHARACTERISTICS OF VASCULOPATHY IN PATIENTS WITH CONNECTIVE TISSUE DISEASES

J. Yeo[1], E. A. Park[2,3], E. B. Lee[1,4], Y. W. Song[1,4], J. K. Park[1,4]. [1]*Seoul National University Hospital, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*; [2]*Seoul National University Hospital, Department of Radiology, Seoul, Korea, Rep. of (South Korea)*; [3]*Seoul National University College of Medicine, Department of Radiology, Seoul, Korea, Rep. of (South Korea)*; [4]*Seoul National University College of Medicine, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)*

Background: Vasculopathies are a heterogeneous group of morphologically and pathogenetically distinct vascular diseases. They include both non-inflammatory and inflammatory vasculopathies. Patients with connective tissue disease (CTD), including systemic sclerosis (SSc), dermatomyositis (DM), and polymyositis (PM), can develop a non-thrombotic proliferative vasculopathy (NTPV), a distinctive disease entity characterized by vascular wall proliferation without overt evidence of vascular inflammation and intraluminal thrombosis.
Objectives: This study aimed to analyze the angiographic features of NTPV in patients with CTD, including SSc, DM, and PM in comparison to polyarteritis nodosa (PAN).
Methods: Angiograms of 47 extremities (24 upper and 23 lower extremities) of 11 patients with CTD (6 SSc, 4 DM, and 1 PM), and 12 patients with PAN who presented with critical digital ischemia between January 2001 and May 2020 were analyzed. The degree and pattern of stenosis, occlusion, aneurysms, and neovascularization in proximal arteries (defined as arteries above the wrist and ankle) and distal arteries (defined as those at or below the wrist and ankle) were compared between CTD-vasculopathy and PAN.
Results: Diffuse narrowing was significantly more frequent (66.1% vs. 38.0%; p=0.001), whereas multifocal stenosis was significantly less frequent (6.5% vs. 26.8%, p=0.002) in the CTD group than in the PAN group. All patients with CTD and 72.0% with PAN had diffuse narrowing in the distal arteries (p =0.010). Tapered occlusion was more frequent than abrupt occlusion in patients with CTD (43.5% vs. 11.3%). Abrupt occlusion (11.3% vs. 29.6%, p=0.010) and aneurysm formation (1.6% vs. 11.3%; p=0.037) were significantly less frequent in the CTD than in the PAN group. After 1 year, three patients (27.3%) in the CTD group and seven (58.3%) in the PAN group showed improvements in digital ischemia. Moreover, four patients (36.4%) in the CTD group and two (16.7%) in the PAN group underwent auto- or surgical amputation.
Conclusion: Patients with CTD-vasculopathy exhibit more frequently diffuse smooth narrowing, tapered occlusion and delayed distal blood flow on conventional angiograms and worse outcomes than with PAN patients. Larger studies are needed to confirm the current findings.

REFERENCES:

[1] Kahaleh MB. Vascular involvement in systemic sclerosis (SSc). Clin Exp Rheumatol. 2004;22(3 Suppl 33):S19-23.
[2] Lee JS, Kim H, Lee EB, Song YW, Park JK. Nonthrombotic proliferative vasculopathy associated with antiphospholipid antibodies: A case report and literature review. Mod Rheumatol. 2019;29(2):388-92.

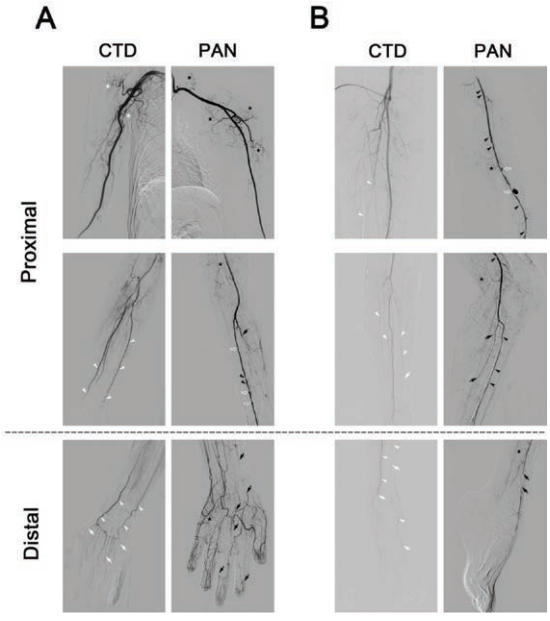


Figure 1. Angiographic features of CTD-vasculopathy and PAN. Arteries in the (A) upper extremities and (B) lower extremities of patients with CTD-vasculopathy and PAN. Diffuse narrowing is indicated by white arrowheads; tapered occlusion by white arrows; multifocal stenosis by black arrowheads; abrupt occlusion by black arrows; aneurysmal changes by empty arrows; grade 2 tortuosity by white stars; and grade 3 tortuosity by black stars. CTD, connective tissue disease; PAN, polyarteritis nodosa.

Table 1. Comparison of angiographic parameters between CTD-vasculopathy and PAN.

	CTD (upper 14, lower 8)	PAN (upper 10, lower 15)	*p*-value
Total number of images	62	71	
Shoulder/elbow/wrist and hand	11/14/14	8/10/10	
Femoral/knee/ankle and foot	7/8/8	13/15/15	
Stenosis			
Diffuse narrowing	41/62 (66.1%)	27/71 (38.0%)	**0.001**
Focal stenosis	13/62 (21.0%)	10/71 (14.1%)	0.295
Multifocal stenosis	4/62 (6.5%)	19/71 (26.8%)	**0.002**
Occlusion			
Tapered occlusion	27/62 (43.5%)	23/71 (32.4%)	0.185
Abrupt occlusion	7/62 (11.3%)	21/71 (29.6%)	**0.010**
Aneurysm	1/62 (1.6%)	8/71 (11.3%)	**0.037**
Neovascularization in muscular branch			
Tortuosity			
Grade 1	45/62 (72.6%)	30/68 (39.1%)	**0.002**
Grade 2	11/62 (17.7%)	14/68 (23.9%)	
Grade 3	6/62 (9.7%)	24/68 (37.0%)	

Tortuosity grade 1, normal; grade 2, mild to moderate; grade 3, severe (hypertortuosity). CTD, connective tissue disease; PAN, polyarteritis nodosa.

Disclosure of Interests: Jina Yeo: None declared, Eun-Ah Park: None declared, Eun Bong Lee Consultant of: Pfizer, Grant/research support from: GC Pharma and Handok Inc., Yeong Wook Song: None declared, Jin Kyun Park: None declared
DOI: 10.1136/annrheumdis-2021-eular.245

POS1387 QUANTIFICATION OF BONE MARROW EDEMA BY MRI OF THE SACROILIAC JOINTS IN PATIENTS DIAGNOSED WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE ESPERANZA COHORT

R. Almodovar[1], P. Zarco-Montejo[1], A. Bueno[2], C. Garcia-Monco[2], E. De Miguel[3], C. Tornero[3], M. Moreno Martinez Losa[4], J. Gratacos-Masmitja[4], R. Mazzucchelli[1]. [1]*Hospital Universitario Fundación Alcorcón, Rheumatology Unit, Alcorcón, Spain*; [2]*Hospital Universitario Fundación Alcorcón, Radiology Department, Alcorcón, Spain*; [3]*Hospital Universitario La Paz, Rheumatology Unit, Madrid, Spain*; [4]*Hospital Universitario Parc Taulí, Rheumatology Unit, Sabadell. Barcelona, Spain*

Background: The present study analyzes the added value of quantification by MRI of SI joints by comparing it to the standard interpretation with ASAS criteria for the classification of patients with axSpA of recent onset and a six-year follow-up.
Objectives: To evaluate if the quantification of bone marrow edema (BME) of the sacroiliac (SI) joints by magnetic resonance imaging (MRI) improves capacity for axial spondyloarthritis (axSpA) classification in comparison to the assessment of sacroiliitis by means of ASAS classification criteria.
Methods: Prospective study from the ESPeranza cohort involving 66 subjects with an available MRI of the SI joints at baseline. This subgroup includes patients with axSpA (n=28), peripheral spondyloarthritis (n=10) and a group with other diagnoses that were not spondyloarthritis (n=28). Measures of diagnostic usefulness (area under the curve (AUC), sensitivity, specificity, Youden's J statistic, LR+ and LR-) were calculated for MRI of the SI joints according to ASAS criteria and for MRI quantified by means of SCAISS (Spanish tool for semi-automatic quantification of sacroiliac inflammation by MRI in spondyloarthritis). This analysis was stratified in patients who were HLA-B27 positive and negative.
Results: Out of a total of 66 MRI of the SI joints, 20 (30.3%) were positive according to ASAS criteria. Out of these 20 subjects, 18 patients with final diagnosis of axSpA had a positive MRI, and 2 patients did not have axSpA. Out of the 66 patients of the cohort, 23 (34.8%) patients were HLA-B27 positive and 42 (63,6%) were negative. AUC value with bone marrow edema (BME) quantification was 0.919 (CI95% 0.799-1) for HLA-B27 positive patients and 0.884 (CI95% 0.764-1) for HLA-B27 negative patients. A SCAISS cutoff point of 80 units obtained a specificity of 94.4% and LR+ 7.5, while assessment by ASAS criteria showed a specificity value of 90% and LR+ 6.4.
Conclusion: For patients with suspected axSpA, quantification of BME improves the predictive capacity of MRI of the SI joints, for both HLA-B27 positive and negative patients.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.315

POS1388 ULTRASOUND FOR PANNICULITIS

A. Potapova[1], O. Egorova[1], O. Alekseeva[1], A. Volkov[1], S. Radenska-Lopovok[2]. *[1]V.A. Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*; *[2]I.M. Sechenov First Moscow State Medical University (Sechenov University), Pathomorphology, Moscow, Russian Federation*

Background: Ultrasound (US) is a non-invasive and safe imaging method that allows in vivo differentiation of the morphological structures of subcutaneous fat (SCF) tissue in in normal and pathology.
Objectives: Reveal features of ultrasound changes in SCF in panniculitis (Pn).
Methods: 57 patients (f – 45, m - 12) aged 18 - 67 years with an initial diagnosis of erythema nodosum and a disease duration of 3.6 ± 1.4 years were examined. In addition to the general clinical examination, a computed tomography of the chest organs and a pathomorphological examination of a skin biopsy from the site of the node were performed. Ultrasound was performed on a MyLabTwice apparatus (ESAOTE, Italy) using a multi-frequency linear transducer (10-18 MHz) with the PD technique, the parameters of which were adapted for recording low-speed flows (PRF 300-600 Hz, low filter, dynamic range - 20-40 dB), the presence of vascularization was assessed not only in the affected area, but also on the contralateral side using high-energy Doppler.
Results: 33 patients were diagnosed with septal Pn (SPn), 24 - lobular Pn (LPn). In all cases, the diagnosis was verified by histological examination. Ultrasound made it possible to assess the thickness, echoicity and vascularization of the SCF. In 35 patients, significant thickening of the SCF was revealed (as compared to the contralateral side), of which in 14 cases with SPn, in 21 - with LPn. Significant diffuse thickening of the SCF with the contralateral side was observed in 18 patients, incl. in 12 (66%) patients with LPn. Limited thickening was more typical for SPn (73%). A significant increase in the echoicity of the SCF was noted in all forms of Pn. A "lobular" echo pattern with an anechogenic environment was observed in 25 patients, of which 18 (72%) had LPn. An increase in vascularization compared to the contralateral side was recorded in 30 cases (SPn-17, LPn-13).
Conclusion: The obtained preliminary results indicate the important role of ultrasound in assessing the depth and prevalence of the inflammatory process at Pn. To clarify the diagnostic value of this method, further studies are needed on a larger sample of patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.663

POS1389 IDIOPATHIC, RHEUMATOID ARTHRITIS AND DIABETES MELLITUS ASSOCIATED CARPAL TUNNEL SYNDROME: EVALUATION OF THE DEPTH OF THE CARPAL TUNNEL BY ULTRASONOGRAPHY

A. Elsaman[1], Y. Alzahrani[2], H. Alzahrani[2], A. Radwan[1]. *[1]Sohag University Hospital, Rheumatology and Rehabilitation, Sohag, Egypt*; *[2]Armed Forces Specialized Center for Health Rehabilitation, Altaif, Kingdom of Saudi Arabia, Rehabilitation Depatment, Taif, Saudi Arabia*

Background: The depth of the carpal tunnel is a relatively new sonographic parameter for evaluation of carpal tunnel syndrome (CTS). It showed a sensitivity and specificity comparable to cross-sectional area measurement. So far it is not clear how the depth can changes with different types of CTS [1, 2].
Objectives: is to assess the depth in 3 different types of CTS including idiopathic, rheumatoid arthritis, and diabetes mellitus associated CTS and to compare it with other sonographic and electro-physiologic scales.
Methods: We included a total number of 360 participants; including 289 with CTS (60 idiopathic, 106 diabetes associated, and 123 rheumatoid arthritis associated CTS), all fulfilled the criteria for electro-physiologic diagnosis according to the American Association of Electro Diagnostic Medicine; along with 71 non-CTS cases (20 healthy controls, 20 RA and 31 diabetic patients). Median nerve cross-sectional area (CSA); flattening ratio (FR); and depth of the carpal tunnel (DCT) were measured for all participants.
Results: We found the mean age 35.6±9.48 years. The female-to-male ratio was 47:13. The sensitivities for CSA, FR and DCT were 74.7%, 68.9%, and 75.1%; respectively, and the specificities were 91.6%, 63.4% and 87.3%; respectively. DCT was the best sonographic parameter with rheumatoid arthritis associated CTS (giving an accuracy of 88.6%) and CSA was the best in the other two types (giving an accuracy of 87.5% for idiopathic CTS and 83.4% for diabetes associated CTS). Table 1 summarizes the sensitivity statistics among each of the three groups and all over the study participants.
Conclusion: The depth of the CTS showed the best accuracy in rheumatoid arthritis associated CTS followed by idiopathic CTS and finally diabetes mellitus associated CTS.
REFERENCES:

[1] Elsaman AM, Thabit MN, Radwan AR, Ohrndorf S. Idiopathic Carpal Tunnel Syndrome: Evaluation of the Depth of the Carpal Tunnel by Ultrasonography. Ultrasound in medicine & biology 2015; 41: 2827-35.
[2] AM E, Hamed A, Borai A, Radwan A. Carpal tunnel syndrome in rheumatoid arthritis patients: evaluation of the depth by ultrasonography.
[3] Elsaman AM, Thabit MN, Radwan AR, Ohrndorf S. Idiopathic Carpal Tunnel Syndrome: Evaluation of the Depth of the Carpal Tunnel by Ultrasonography. Ultrasound in medicine & biology 2015; 41: 2827-35.

Table 1. Sensitivity statistics for different US measures for CTS

		Idiopathic	RA	Diabetic	All
Number of the CTS cases		60	123	106	289
Number of the controls		20	20	31	71
CSA	Sensitivity	80%	70.7%	76.4%	74.7%
	Specificity	95%	90%	90.3%	91.6%
	Accuracy	87.5%	80.4%	83.4%	83.1%
FR	Sensitivity	75%	61.8%	73.6%	68.9%
	Specificity	60%	65%	64.5%	63.4%
	Accuracy	67.5%	63.4%	69.1%	66.1%
DCT	Sensitivity	75%	82.1%	67%	75.1%
	Specificity	85%	95%	83.9%	87.3%
	Accuracy	80%	88.6%	75.4%	81.2%

CSA: cross sectional area, FR: flattening ratio, DCT: Depth of the carpal tunnel

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.717

POS1390 COMPARISON OF CAROTID SUBCLINICAL ATHEROSCLEROSIS AND STRUCTURAL DAMAGE IN AXIAL SPONDYLITIS WITH AND WITHOUT CONCOMITANT ANTERIOR UVEITIS. A MULTICENTER STUDY WITH 886 PATIENTS

I. González-Mazón[1], J. Rueda-Gotor[1], I. Ferraz-Amaro[2], L. Sanchez-Bilbao[1], F. Genre[3], V. Calvo-Río[1], S. Remuzgo-Martínez[3], V. Pulito-Cueto[3], A. Corrales[1], L. Lera-Gómez[3], V. Portilla[1], V. Hernández-Hernández[4], J. C. Quevedo-Abeledo[5], C. Rodríguez-Lozano[5], C. López-Medina[6], M. L. Ladehesa Pineda[6], S. Castañeda[7], E. F. Vicente-Rabaneda[7], C. Fernández-Carballido[8], M. P. Martínez-Vidal[8], D. Castro-Corredor[9], J. Anino-Fernández[9], D. Peiteado[10], M. L. García Vivar[11], E. Galindez[11], E. Montes Pérez[12], R. Demetrio-Pablo[13], C. Fernández-Díaz[1], R. Blanco[1], M. A. González-Gay[1,3]. *[1]Universitary Hospital Marques de Valdecilla, Rheumatology, Santander, Spain*; *[2]Hospital Universitario de Canarias, Rheumatology, Santander, Spain*; *[3]IDIVAL, Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Santander, Spain*; *[4]Hospital Universitario de Canarias,, Rheumatology, Tenerife, Spain*; *[5]Hospital Universitario de Gran Canaria Dr. Negrín, Rheumatology, Las Palmas, Spain*; *[6]Reina Sofia Hospital, Rheumatology, Cordoba, Spain*; *[7]Hospital de La Princesa, Rheumatology, Madrid, Spain*; *[8]Hospital Universitario San Juan de Alicante, Rheumatology, Alicante, Spain*; *[9]Hospital General Universitario de Ciudad Real, Rheumatology, Ciudad Real, Spain*; *[10]Hospital Universitario La Paz-IdiPaz, Rheumatology, Madrid, Spain*; *[11]Hospital Universitario Basurto, Rheumatology, Bilbao, Spain*; *[12]Diagnóstico Médico Cantabria, DMC, Santander, Spain*; *[13]Universitary Hospital Marques de Valdecilla, Ophtalmology, Santander, Spain*

Background: Anterior uveitis (AU) is one of the most frequent extra articular manifestations of axial spondyloarthritis (axSpA), present in around 25% of patients. As with axSpA, AU has also been associated with the development of accelerated atherosclerosis[1]. If the presence of AU confers an increased cardiovascular (CV) risk or specific disease-related features to patients with axSpA remains unclear.
Objectives: To compare the atherosclerotic burden, CV events, CV risk factors and disease related factors including structural damage in axSpA patients with and without AU.
Methods: Cross-sectional analysis of the AtheSpAin cohort, a Spanish multicenter cohort designed for the study of atherosclerosis in axSpA, comparing axSpA patients with and without concomitant uveitis. Background information on CV and disease-related factors was reviewed. Data on CV risk and disease status at the time of the study were also obtained, including the structural damage assessed by the presence of syndesmophytes, the severity of the sacroiliitis (defined as grade 3 or 4 according to New York criteria), and the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Carotid ultrasound (US) was performed in all patients at the time of the study, including measurement of carotid intima-media wall thickness (cIMT) and plaque detection according to the Mannhein consensus criteria.
Results: A set of 886 axSpA patients were included. 709 (80.0%) of them had no history of concomitant AU, which was present in the remaining 177 (20.0%). The group with AU was older (50 ± 11 vs 48 ± 13 years, p=0.05), had a higher proportion of patients with AS (90.1% vs 76.3%, p=0.00) (Table 1) and a longer disease duration 13(7-23) vs 7(2-16) years, p=0.00]. The prevalence of HLA-B27 was higher in AU patients (82% vs 67%).
Remarkably, structural damage showed interesting differences between both groups (Table 1). AU patients had a higher prevalence of severe sacroiliits (69% vs 49%, p=0.00), which remained significant after adjustment for age, disease duration and AS/nr-axSpA ratio. Furthermore, a non-significant trend towards a

higher prevalence of syndesmophytes (44% vs 36%, p=0.06) and hip involvement (20% vs 15%, p=0.09) was observed in the group of AU.
Regarding CV risk features, no differences were observed in the prevalence of CV risk factors and events (Table 1). Patients with AU showed a higher cIMT in the crude analysis (665 ± 156 mm vs 640 ± 142 mm, p = 0.047), but no significant differences were observed after adjustment by age and sex (p=0.6). Prevalence of carotid plaques was comparable in both groups (32% Vs 32%, p=0.84).

Table 1.

	axSpA without uveitis (n=709)	axSpA with uveitis (n=177)	p	P (adjusted model)
Men/Women, n	477/232	122/55	0.68	
Mean age (years) ±SD at the time of study	48 ± 13	50 ± 11	**0.049**	
AS/nr-AxSpa	541/168	160/17	**0.000**	
History of CV risk factors, n (%)				
Current smoker	247 (35)	50 (28)	0.096	
Obesitty				
Dyslipemia	233 (33)	63 (36)	0.48	
Hypertension	188 (27)	50 (28)	0.63	
Diabetes Mellitus	50 (7)	14 (8)	0.69	
Chronic Kidney Disease	18 (3)	4 (2)	0.99	
History of cardiovascular events, n (%)	29 (4)	12 (7)	0.13	
Structural damage at the time of study				
Presence of syndesmophytes, n (%)	253 (36)	77 (44)	0.063	
mSASSS	5 (1-15)	6 (0-16)	0.31	
Severe sacroiliitis (grade 3,4), n (%)	348 (49)	122 (69)	**0.000**	0.000*
Carotid US data at the time of study				
Carotid plaques, n (%)	225 (32)	57 (32)	0.84	
IMT (mm)	640 ± 142	665 ± 156	**0.047**	0.6**
IMT >= 0.900 mm	36 (5)	10 (6)	0.72	

*: adjusted by age, disease duration and AS/nr-axSpA ratio
**: adjusted by age and sex
Abbreviations: AS = ankylosing spondylitis. AxSpA= axial spondylitis. CV = cardiovascular. IMT = intima-media wall thickness. Nr-axSpA = no-radiographic axial spondylitis.

Conclusion: The presence of AU does not confer additional CV risk to axSpA patients, although it is associated with a more severe structural damage in our series.
REFERENCES:
[1] Conkar S, Güven Yılmaz S, Koska İÖ, Berdeli A, Mir S. Evaluation of development of subclinical atherosclerosis in children with uveitis. Clin Rheumatol. 2018 May;37(5):1305-1308.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.909

POS1391 MEASURING SUBCLINICAL INFLAMMATION IN HAND AND FOREFOOT IN PATIENTS WITH ARTHRALGIA USING 1.5T OR 3.0T MRI: DOES FIELD STRENGTH MATTER?

D. Krijbolder[1], M. Verstappen[1], F. Wouters[1], L. R. Lard[2], P. D. De Buck[3], J. Veris-van Dieren[4], M. Reijnierse[5], H. Bloem[5], A. Van der Helm - van Mil[1,6]. *[1]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; *[2]LangeLand Ziekenhuis, Department of Rheumatology, Zoetermeer, Netherlands*; *[3]Haaglanden Medical Center, Department of Rheumatology, Den Haag, Netherlands*; *[4]Reumazorg Zuid West Nederland, Department of Rheumatology, Goes, Netherlands*; *[5]Leiden University Medical Center, Department of Radiology, Leiden, Netherlands*; *[6]Erasmus Medical Center, Department of Rheumatology, Rotterdam, Netherlands*

Background: Magnetic resonance imaging (MRI) of small joints sensitively detects inflammation. MRI-detected subclinical inflammation, and tenosynovitis in particular, has been shown predictive for RA development in patients with arthralgia. These scientific data are mostly acquired on 1.0T-1.5T MRI scanners. However, 3.0T MRI is nowadays increasingly used in practice. Evidence on the comparability of these field strengths is scarce and it has never been studied in arthralgia where subclinical inflammation is subtle. Moreover, comparisons never included tenosynovitis, which is, of all imaging features, the strongest predictor for progression to RA.
Objectives: To determine if there is a difference between 1.5T and 3.0T MRI in detecting subclinical inflammation in arthralgia patients.
Methods: 2968 locations (joints, bones or tendon sheaths) in hands and forefeet of 28 arthralgia patients were imaged on both 1.5T and 3.0T MRI. Two independent readers scored for erosions, osteitis, synovitis (according to RAMRIS) and tenosynovitis (as described by Haavaardsholm et al.). Scores were also summed as total inflammation (osteitis, synovitis and tenosynovitis) and total RAMRIS (erosions, osteitis, synovitis and tenosynovitis) scores. Interreader reliability (comparing both readers) and field strength agreement (comparing 1.5T and 3.0T) was assessed with interclass correlation coefficients (ICCs). Next, field strength agreement was assessed after dichotomization into presence or absence of inflammation. Analyses were performed on patient- and location-level.
Results: ICCs between readers were excellent (>0.90). Comparing 1.5 and 3.0T revealed excellent ICCs of 0.90 (95% confidence interval 0.78-0.95) for the total inflammation score and 0.90 (0.78-0.95) for the total RAMRIS score. ICCs for individual inflammation features were: tenosynovitis: 0.87 (0.74-0.94), synovitis 0.65 (0.24-0.84) and osteitis 0.96 (0.91-0.98). The field strength agreement on dichotomized scores was 83% for the total inflammation score and 89% for the total RAMRIS score. Of the individual features, agreement for tenosynovitis was the highest (89%). Analyses on location- level showed similar results.
Conclusion: Agreement of subclinical inflammation scores on 1.5T and 3.0T were good to excellent, in particular for tenosynovitis. This suggests that scientific evidence on predictive power of MRI in arthralgia patients, obtained on 1.5T, can be generalized to 3.0T when this field strength would be used for diagnostic purposes in daily practice.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1417

POS1392 ECHOCARDIOGRAPHIC FINDINGS IN PSORIATIC ARTHRITIS, RHEUMATOID ARTHRITIS AND CONTROLS

A. B. Rodriguez-Romero[1], J. R. Azpiri-López[2], I. J. Colunga-Pedraza[1], D. Á. Galarza-Delgado[1], N. Guajardo-Jauregui[1], S. Lugo-Perez[2], A. Cárdenas[1], H. Azpiri-Diaz[2], O. A. Cepeda-Ayala[2]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology Service, Monterrey, Mexico*; *[2]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology Service, Monterrey, Mexico*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy associated with cardiovascular abnormalities (1). The echocardiography is a non-invasive tool useful in the detection of cardiac abnormalities, which may be the only manifestation of cardiac involvement preceding a global dysfunction. However, echocardiographic differences between PsA patients, rheumatoid arthritis (RA) patients, and controls have not yet been well described.
Objectives: To analyze the echocardiographic parameters in PsA patients and to compare them with RA patients and controls.
Methods: This cross-sectional, observational and comparative study, included thirty-six patients (nineteen in each group), aged 40-75 years, with PsA and RA who fulfilled the CASPAR (Classification criteria for Psoriatic Arthritis) and ACR/EULAR 2010 classification criteria, respectively, matched by age, gender and comorbidities with nineteen healthy controls. Exclusion criteria were a poor echocardiographic window, patients with a previous atherosclerotic cardiovascular disease (ischemic heart disease, cerebrovascular accident or peripheral arterial disease), and pregnancy. Transthoracic echocardiogram was performed and reviewed by 2 board-certified cardiologists, in all study subjects. Comparisons were done with X2, Kruskall Wallis or ANOVA.
Results: There were not differences in the demographic characteristics between groups (Table 1). When comparing echocardiographic findings a statistically significant difference was found in the prevalence of diastolic dysfunction, being more prevalent in PsA and RA patients compared with controls (52.6% vs 52.6% vs 5.3%, p=0.002), likewise the presence of mild mitral valve regurgitation was higher (84.2% vs 53.6% vs 10.5%, p=0.001) and mild pulmonary valve regurgitation (68.4% vs 10.5% vs 0%, p=0.001). Prevalence of abnormal left ventricular geometry was higher in PsA and RA patients than controls (68.4% vs 63.2% vs 21.1%, p=0.006).

Table 1. Comparison of demographic characteristics and echocardiographic findings between patients with PsA, RA and controls.

	PsA (n=19)	RA (n=19)	Controls (n=19)	*p*
Age, years ± SD	54.7 ± 7.7	55.4 ± 9.9	55.3 ± 5.9	NS
Female, n (%)	11 (57.9)	11 (57.9)	11 (57.9)	NS
Diabetes Mellitus	4 (21.1)	3 (15.8)	2 (10.5)	NS
Hypertension	10 (52.6)	8 (42.1)	7 (36.8)	NS
Dyslipidemia	10 (52.6)	4 (21.1)	7 (36.8)	NS
Active smoking	4 (21.1)	2 (10.5)	5 (26.3)	NS
Disease duration, years (p25-p75)	6 (4-14)	7 (5-18)	-	NS
DAS28-CRP, mean ± SD	2.2 ± 0.8	3.1 ± .8	-	**0.003**
Echocardiographic findigs				
Diastolic dysfunction, n (%)	10 (52.6)	10 (52.6)	1 (5.3)	**0.002**
LV mass index, g/m^2 (p25-p75)	78.9 (55.9-86.9)	73.7 (61.0-85.7)	69.5 (52.0-98.7)	**NS**
LVEF, ± mean SD	62.3 ± 6.1	59.7 ± 8.6	62.9 ± 6.1	NS
TAPSE, cm ± SD	21.8 ± 2.7	22.4 ± 2.7	23.7 ± 3.1	NS
Mild aortic regurgitation, n (%)	5 (26.3)	4 (21.1)	1 (5.3)	NS
Mild mitral regurgitation, n (%)	16 (84.2)	10 (52.6)	2 (10.5)	**<0.001**
Mild pulmonary regurgitation, n (%)	13 (68.4)	2 (10.5)	0 (0)	**<0.001**
Mild tricuspid regurgitation, n (%)	15 (83.3)	13 (76.5)	11 (57.9)	NS
LV geometry alterations, n (%)	13 (68.4)	12 (63.2)	4 (21.1)	**0.006**
Concentric remodeling, n (%)	12 (63.2)	10 (52.6)	4 (21.1)	**0.025**

NS, non-significant; DAS28-CRP, disease activity score using 28 joints and C reactive protein; LV, left ventricular; LVEF, left ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion.

Conclusion: This study shows the high prevalence of echocardiographic alterations in PsA patients compared to the general population, of the same magnitude as patients with RA. We emphasize the value of an echocardiogram for a complete cardiovascular evaluation and early detection of cardiac abnormalities in these patients.

REFERENCES:

[1] Shang Q, Tam LS, Yip GW, et al. High prevalence of subclinical left ventricular dysfunction in patients with psoriatic arthritis. J Rheumatol 2011;38(7):1363-70. doi: 10.3899/jrheum.101136

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1439

POS1393 QUANTITATIVE AUTOFLUORESCENCE FINDINGS IN PATIENTS UNDERGOING HYDROXYCHLOROQUINE TREATMENT

S. Parrulli[1], M. Cozzi[1], M. Airaldi[1], F. Romano[1], F. Viola[2], P. Sarzi-Puttini[3], G. Staurenghi[1], A. Invernizzi[1,4]. *[1]Sacco Hospital, University of Milan, Eye Clinic, Department of Biomedical and Clinical Science "Luigi Sacco", Milan, Italy*; *[2]University of Milan, IRCCS-Ca Granda Fondazione Ospedale Maggiore Policlinico, Ophthalmological Unit, Department of Clinical Sciences and Community Health, Milan, Italy*; *[3]ASST Fatebenefratelli L.Sacco University Hospital, Rheumatology Unit, Milan, Italy*; *[4]Sydney Medical School, The University of Sydney, Save Sight Institute, Discipline of Ophthalmology, Sydney, Australia*

Background: Hydroxychloroquine (HCQ) is a relatively safe and effective drug widely used as primary or adjunctive treatment for several rheumatological and dermatological disorders[1]. HCQ modulates immune response through several mechanisms and has a tropism for pigmented ocular tissues, particularly retinal pigment epithelium (RPE)[2]. Its accumulation within RPE cells can lead to sight threatening retinal toxicity, with bull's eye maculopathy (BEM) representing its advanced phenotype. [3] Quantitative Auto-Fluorescence (qAF) is an imaging modality that allows the measurement of retinal auto-fluorescence following short-wavelength light (488nm) excitation of retinal fluorophores (lipofuscin). [4] Two recent studies have focused on qAF values in patients treated with HCQ [5,6]. In both cases qAF was increased in eyes with BEM. Furthermore, Reichel et al.[6] were able to detect increased values of qAF in patients without BEM as early as 6 months after the start of HCQ treatment using an experimental imaging analysis procedure.

Objectives: To measure quantitative autofluorescence (qAF) in patients under treatment with hydroxychloroquine (HCQ) with no apparent signs of retinal toxicity and to compare it with that of untreated subjects.

Methods: Consecutive patients at risk for the development of HCQ retinal toxicity (duration of treatment >5 years or daily HCQ dose >5 mg/kg of actual body weight (ABW) and/or renal insufficiency)[7] but no alterations on Spectral Domain - Optical Coherence Tomography, Short-Wavelength Autofluorescence and 10-2 Visual Field examination were recruited. Healthy subject matched by age and sex were also enrolled in the study. All subjects underwent qAF measurements in one eye. Images were analyzed using the conventional qAF grid by Delori calculating the qAF of 8 sectors of the intermediate ring and the mean of those values (qAF_8).

Results: Thirty-nine patients treated with HCQ (38 females, mean age 52,1 ± 8,6 years) and 39 untreated subjects (38 females, mean age 51,2 ± 8,6 years). In both HCQ patients and untreated subjects, qAF_8 was positively correlated with age (p=0.004) (Figure 1). Although HCQ patients showed a higher mean qAF_8 compared to untreated subjects (294,7 ±65,3 vs 268,9 ± 57,5), the difference was not significant (p=0.068). HCQ patients showed significantly higher mean qAF values in the inferior-temporal, inferior and inferior-nasal sectors of the intermediate ring of qAF grid compared to untreated subjects (all p<0.05).

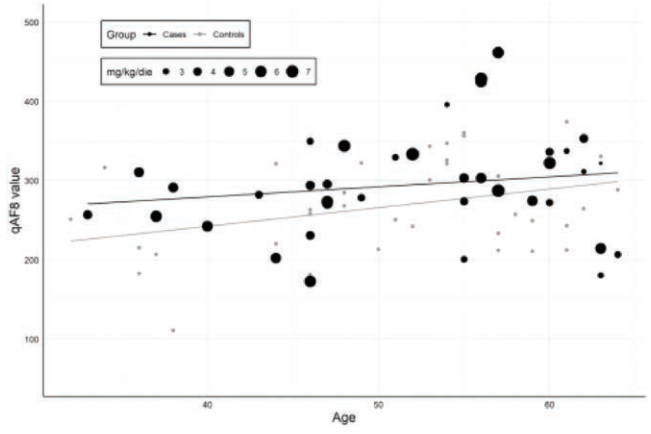


Figure 1. Visual representation of a model predicting the standardized qAF values as influenced by age and HCQ daily dose/ABW, calculated for a treatment duration of 15 years.

Conclusion: These results suggest a possible preclinical increase of qAF values in inferior parafoveal sectors probably induced by HCQ exposure. Further studies are required to improve our understanding of preclinical stages of HCQ retinopathy and the possible role of qAF in the HCQ toxicity screening.

REFERENCES:

[1] Haładyj, E., Sikora, M., Felis-Giemza, A. & Olesińska, M. Antimalarials - are they effective and safe in rheumatic diseases? *Reumatologia* **56**, 164–173 (2018).
[2]Rosenthal, A. R., Kolb, H., Bergsma, D., Huxsoll, D. & Hopkins, J. L. Chloroquine retinopathy in the rhesus monkey. *Invest. Ophthalmol. Vis. Sci.* **17**, 1158–1175 (1978).
[3] Modi, Y. S. & Singh, R. P. Bull's-Eye Maculopathy Associated with Hydroxychloroquine. *N. Engl. J. Med.* **380**, 1656 (2019).
[4] Sparrow, J. R., Duncker, T., Schuerch, K., Paavo, M. & de Carvalho, J. R. L. J. Lessons learned from quantitative fundus autofluorescence. *Prog. Retin. Eye Res.* **74**, 100774 (2020).
[5] Greenstein, V. C. *et al.* Quantitative Fundus Autofluorescence in HCQ Retinopathy. *Invest. Ophthalmol. Vis. Sci.* **61**, 41 (2020).
[6] Reichel, C. *et al.* Quantitative Fundus Autofluorescence in Systemic Chloroquine/Hydroxychloroquine Therapy. *Transl. Vis. Sci. Technol.* **9**, 42 (2020).
[7] Yusuf, I. H., Sharma, S., Luqmani, R. & Downes, S. M. Hydroxychloroquine retinopathy. *Eye (Lond).* **31**, 828–845 (2017).

Disclosure of Interests: Salvatore Parrulli: None declared, Mariano Cozzi Grant/research support from: Bayer, Nidek, Zeiss, Matteo Airaldi: None declared, Francesco Romano: None declared, Francesco Viola: None declared, Piercarlo Sarzi-Puttini: None declared, Giovanni Staurenghi Grant/research support from: Heidelberg Engineering (C), QuantelMedical (C), Centervue (C), Carl Zeiss Meditec (C), Alcon (C), Allergan (C), Bayer (C), Boheringer (C), Genentech (C), GSK (C),Novartis (C), and Roche (C), Optos (F), Optovue (F) and Centervue (F), Alessandro Invernizzi Grant/research support from: Novartis (C), Bayer (C)

DOI: 10.1136/annrheumdis-2021-eular.2022

POS1394 ACCURACY AND PERFORMANCE OF A HANDHELD ULTRASOUND DEVICE TO ASSESS ARTICULAR AND PERIARTICULAR PATHOLOGIES IN PATIENTS WITH INFLAMMATORY ARTHRITIS

G. Corte[1,2], S. Bayat[1,2], K. Tascilar[1,2], L. Valor[1,2], L. Schuster[1,2], J. Knitza[1,2], G. Schett[1,2], A. Kleyer[1,2], D. Simon[1,2]on behalf of https://www.medizin3.uk-erlangen.de/en/research/research-main-focus/digital-rheumatology-and-experimental-imaging/. *[1]Friedrich-Alexander-Universität (FAU) and Universitätsklinikum Erlangen, Internal Medicine 3, Rheumatology and Immunology, Erlangen, Germany*; *[2]Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Deutsches Zentrum Immuntherapie, Erlangen, Germany*

Background: Handheld ultrasound (HHUS) devices have increasingly found their way into clinical practice due to several advantages (e.g. portability, significantly lower purchase cost). However, there is no evidence to date on the accuracy and performance of HHUS in patients with inflammatory arthritis (IA).

Objectives: To assess accuracy and performance of a new HHUS machine in comparison to a conventional cart-based sonographic machine in patients with IA.

Methods: Consecutive IA patients of our outpatient clinic with at least one tender and swollen joint in the 66/68 joint count were enrolled. US was performed on clinically affected joints with corresponding tendons/entheses using a cart-based sonographic device ("Samsung HS40") and a HHUS device ("Butterfly iQ") in standard scan positions. One blinded reader scored all images for the presence of following pathologic findings: erosions, bony enlargement, synovial hyperthrophy, joint effusion, bursitis, tenosynovitis and enthesitis. In addition, synovitis was graded (B Mode and power Doppler (PD)) by the 4-level EULAR-OMERACT scale [1]. To avoid bias by the blinded reader, who otherwise would have been tempted to identify pathological findings for each examined joint, we also included 67 joints of two healthy volunteers into the evaluation. We calculated the overall concordance and the concordance by type of joint and type of pathological finding between the two devices (percentage of observation pairs in which the same rating was given by both devices). The Cohen's kappa coefficient (κ) with 95% bootstrap confidence intervals was used to assess the agreement between the two US devices. We also measured the time required for the US examination of one joint with both devices.

Results: 32 patients (20 rheumatoid arthritis, 10 psoriatic arthritis, 1 gouty arthritis, 1 systemic lupus erythematosus) were included in this study. Mean age of patients was 58.2±13.7 years, 63% were females. In total 186 joints were examined. The overall raw concordance in B-mode between the two devices was 97 %, with an overall κappa for agreement of 0.90, 95% CI (0.89, 0.94). No significant differences were found in relation to type of joint or pathological finding examined. The PD-mode of the HHUS device did not detect any PD-signal, whereas the cart-based device detected a PD-signal in 61 joints (33%). The portable device did not offer any time saving compared to the cart-based device (mean time in seconds per examined region: 47 seconds for the HHUS device versus 46.3 seconds for the cart-based device).

Conclusion: The HHUS device "Butterfly iQ" has been shown to be accurate in the assessment of structural joint damage and inflammation in patients with IA,

but only in B-mode. Significant improvements are still needed to reliable demonstrate blood flow detection by PD mode.

REFERENCES:

[1] D'Agostino, M.A., et al., RMD Open, 2017. 3(1): p. e000428.

Table 1. Concordance between a handheld and a conventional cart-based US device in B-mode

	Agreement by site		
	N joints (%)	Concordance (%)	Kappa 95%CI
Overall	186	97	0.90 (0.89 to 0.94)
Wrist	32 (17.2)	96	0.86 (0.77 to 0.93)
Finger/toe joint (MCP, PIP, DIP, MTP)	114 (61.3)	97	0.92 (0.88 to 0.95)
Elbows	11 (5.9)	95	0.87 (0.75 to 0.97)
Shoulder	4 (2.2)	100	1.00 (NA to NA) *
Knee	20 (10.7)	98	0.96 (0.90 to 1.00)
Ankle	5 (2.7)	100	1.00 (NA to NA) *
Agreement by pathological finding			
Joint effusion		95	0.81 (0.68 to 0.92)
Synovitis		94	0.87 (0.79 to 0.93)
Synovitis OMERACT grade (0– 3)		90	0.84 (0.76 to 0.91)
Bone enlargement		98	0.88 (0.71 to 1.00)
Erosion		98	0.89 (0.77 to 0.89)
Tenosynovitis		98	0.83 (0.61 to 0.96)
Entheseopathy		100	1.00 (NA to NA) *
Bursitis		97	0.90 (0.89 to 0.94)

** unreliable kappa statistics because of small number of shoulders/ankles examined and small number of entheseopathies*

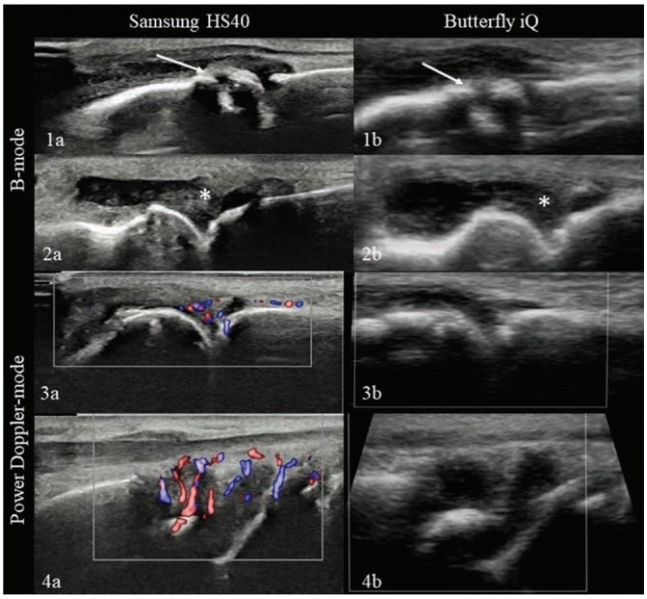


Figure 1. Pathological US findings in MCP joints (1, 2, 3) and wrist (4) depicted by the two different ultrasound devices

B-mode erosive (arrow) and synovial (asterisk) changes could be detected by both devices (1-2), while PD changes of different grades only by the conventional US device (3-4).

Acknowledgements: This study was supported by the Deutsche Forschungsgemeinschaft (DFG- FOR2886 PANDORA and the CRC1181). Additional funding was received by the Bundesministerium für Bildung und Forschung (BMBF; project METARTHROS, MASCARA), the H2020 GA 810316 - 4D-Nanoscope ERC Synergy Project, the IMI funded project RTCure, the Emerging Fields Initiative MIRACLE of the Friedrich-Alexander-Universität Erlangen-Nürnberg, the Else Kröner-Memorial Scholarship (DS, no. 2019_EKMS.27) and Innovationsfond Lehre / FAU Erlangen-Nürnberg 2019.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2163

POS1395

ASSESSMENT OF MICROVASCULAR INVOLVEMENT IN LUPUS NEPHRITIS PATIENTS BY RETINAL OCT-ANGIOGRAPHY AND KIDNEY BIOPSIES

S. Ferrigno[1], P. Conigliaro[1], C. Giannini[2], C. Nesi[2], G. L. Fonti[1], M. Cesareo[2], R. Perricone[1]. [1]*University of Rome Tor Vergata, Rheumatology, Allergology and Clinical Immunology, Department of "Medicina dei Sistemi", Rome, Italy*; [2]*University of Rome Tor Vergata, Ophthalmology Unit, Department of Experimental Medicine and Surgery, Rome, Italy*

Background: Lupus Nephritis (LN) and retinopathy are organ-threatening manifestation of Systemic Lupus Erythematosus (SLE) and both share common pathophysiology represented by microvascular damage. Optical coherence tomography angiography (OCTA) is a recent non-invasive technique showing retinal vascular damage.

Objectives: To analyze retinal microvascular alterations in SLE-LN patients and investigate correlations between ocular and renal involvement.

Methods: We recruited SLE-LN patients and healthy controls (HC), age and sex -matched. Patients underwent rheumatological evaluation, including clinical, laboratory, kidney function and kidney biopsies examination.

Patients and HC underwent a complete ophthalmological evaluation including eye definition color retinography and OCTA whole image, parafovea and fovea vessel density assessment of superficial and deep retinal capillary plexus. Parafovea and fovea thickness, fovea avascular zone (FAZ) area and perimeter were detected.

Statistical analysis was performed using: $\chi 2$ test, unpaired t-test, Mann Whitney U test, Pearson or Spearman rank correlation and ROC curve analysis.

Results: 48 eyes of 24 SLE-LN patients and 44 eyes of 21 HC were evaluated. Table 1 shows demographic, clinical, laboratory and histological parameters.

Figure 1 shows results of OCTA data and relative AUC curves and ROC analysis. Analysis of OCTA data showed a significative reduction of vessel density in SLE-LN compared to HC regarding the following parameters: superficial whole en face, parafovea and fovea density (Figure 1A-C), deep whole en face and deep fovea density, (Figure 1D-E), parafovea and fovea thickness (Figure 1F-G), FAZ area and perimeter (Figure 1H-I).

OCTA data were correlated with demographic, clinical and histologic features of patients showing negative correlation between: SLE duration and both superficial (p=0.03; r=-0.3) and deep (p= 0.004; r=-0.4) whole en face density; LN duration and superficial whole en face (p=0,05; r=-0.4) and parafovea (p=0.007; r=-0.4) density, deep whole en face (p=0.004; r=-0.4) and fovea (p=0.01; r=-0.4) density and parafovea thickness (p=0.004; r=-0.3); SLEDAI-2K and both superficial and deep fovea density (p<0.0001, r=-0.6 and p=0.0, r=-0.4 respectively); BUN and superficial whole en face density (p=0.003; r=-0.5) and parafovea (p=0.004; r=-0.4) density and deep fovea density (p=0.03; r=-0.3); serum creatinine and deep whole en face density (p=0.004; r=-0.4).

Positive correlation was found between LN duration and FAZ area (p= 0.01; r= 0.4); creatinine clearance and both deep whole en face (p=0.05; r= 0.3) and fovea (p=0.0007; r= 0.5) density.

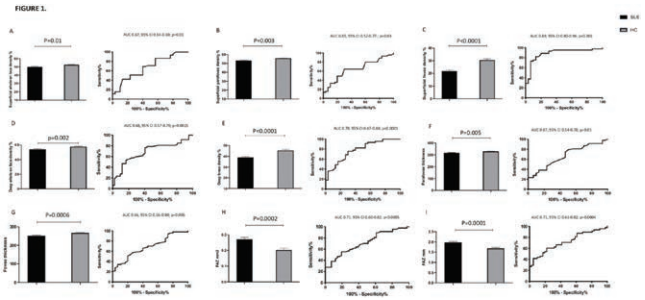
OCTA data analysis showed a reduction in superficial (p=0.02) and deep (p=0.009) whole en face density in patients with LN-vascular lesions assessed by kidney biopsy. In this group, patients with intimal hyalinosis showed a reduction in deep whole en face density (p=0.04) compared to those without intimal hyalinosis.

Conclusion: Preliminary results suggest a correlation between retinal microvascular alterations and kidney function and histologic lesions encouraging the use of OCTA measurement as a potential biomarker of systemic vascular involvement.

Table 1.

	SLE	HC	P value
	N=24	N=21	
Age (years)	44.4±13.8	38.3±10.4	ns
Female (n/%)	21/87.5	17/81	ns
BCVA (logMAR)	0.01± 0.05	0.0 ± 0.1	ns
Disease duration (months)	177.6± 126.6	/	
LN duration (months)	108 ± 97	/	
SLEDAI-2K	6.8±5	/	
Creatininemia (mg/dl)	0.9±0.3	/	
BUN (mg/dl)	39,6±17.6	/	
Creatinine clearance (ml/min)	99.2±53.7	/	
Proteinuria (mg/24h)	432.8±524.5	/	
GMN class III-IV (n/%)	19/77.7	/	
GMN class III-V (n/%)	5/22.2	/	
Kidney biopsy active lesions (n/%)	15/62.5	/	
Kidney biopsy chronic lesions (n/%)	15/62.5	/	
Kidney biopsy vascular lesions (n/%)	8/33.3	/	
Kidney biopsy intimal hyalinosis (n/%)	7/29	/	
Moderate stage lupus retinopathy (n/%)	20/83.3	/	
Severe stage lupus retinopathy (n/%)	3/12.5	/	

BCVA: best-corrected visual acuity, SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000, BUN: blood urea nitrogen; GMN: glomerulonephritis



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2637

POS1396 DAMAGE PROGRESSION OF FINGER JOINT CARTILAGE EVALUATED BY ULTRASOUND AND X-RAY IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

T. Ogura[1], A. Hirata[1], Y. Inoue[1], T. Kagtagiri[1], Y. Takakura[1], H. Kameda[1]. [1]*Toho University, Division of Rheumatology, Department of Internal medicine, Tokyo, Japan*

Background: Cartilage damage in RA has been evaluated by joint space narrowing (JSN) in X-ray, while it is not a direct evaluation of cartilage. Previously we have confirmed the usefulness of the direct imaging of finger joint cartilage by ultrasound (US) in patients with RA [1].
Objectives: We aimed to examine the temporal changes of US cartilage thickness in RA patients.
Methods: We enrolled 53 RA patients in whom the cartilage thickness of finger joints was measured by US and had radiographs of both hands at baseline and 1-year later. The cartilage of metacapophalangeal and proximal interphalangeal joints of 2nd to 5th fingers were bilaterally visualized at the middle portion from a longitudinal dorsal view. Cartilage thickness was measured from the base of the cartilage to the interface artefact at the cartilage surface by static images. In addition, the JSN of the corresponding joints was scored using a hand X-ray by van der Heijde-modified Sharp method. Continuous variables from the two groups were analyzed using the Mann-Whitney U test or Wilcoxon signed-rank test. The relationships among the continuous variables were assessed using the Spearman's rank correlation coefficient.
Results: The median age of the patients was 68 years and the median disease duration was 6.3 years. The sum of total cartilage thickness from 16 joints per patient ranged from 3.1 to 9.1mm (median 6.5mm) at baseline, and it was significantly correlated with total JSN score of the same joints (ρ=-0.63, p<0.001). The cartilage thickness was inversely correlated with disease duration (rho=-0.40, p=0.003), but not associated with age nor height. The decrease in cartilage thickness over 1 year was evident in patients with persistent moderate to high disease activity by the DAS28-CRP (n=10; median -6.2%) as compared with other patients (n=43; median -1.2%, p=0.004 versus active patients).
Conclusion: This pilot study demonstrated the progression of cartilage damage by sustained RA activity, supporting the validity and usefulness of joint cartilage thickness evaluation by ultrasound in patients with RA.
REFERENCES:
[1] Ogura T, et al. Arthritis Care Res 2019 Oct 25.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2784

POS1397 HYDROXYCHLOROQUINE INDUCED RETINAL TOXICITY IN PATIENTS WITH RHEUMATIC DISEASES

R. Maheshwari[1], R. Sankaralingam2, S. Chinnadurai2, J. Antony2, B. Chilukuri2, M. Mani2. [1]*Sri Ramachandra Institute of Higher Education and Research, Clinical Immunology and Rheumatology, Chennai, India*; [1]*Sri Ramachandra Institute of Higher Education and Research, Clinical Immunology and Rheumatology, Chennai, India*

Background: Retinal toxicity from hydroxychloroquine (HCQ) is rare, but the vision loss maybe irreversible and could have medicolegal consequences.
Objectives: To determine the prevalence and assess the predictors of retinal toxicity due to HCQ in patients with rheumatic diseases. There is paucity of literature on retinal toxicity due to HCQ in rheumatic diseases.
Methods: A retrospective observational study was conducted in the Department of Clinical Immnuology and Rheumatology, Sri Ramachandra Institute of Higher Education and Research,Chennai, India from November 2018-May 2020, on patients taking HCQ for more than 6 months. All patients underwent ophthalmological screening at baseline and every 6 months, and thereafter by modern day screening methods-Humphrey Visual Field (HVF)10-2, Spectral Domain Optical Coherence Tomography(SD-OCT), except for patients with evidence of suspected retinal toxicity at baseline.Fundus autofluorescence (FAF) was done in feasible patients.
Results: 9 out of 743(1.2%) patients were identified to have retinal toxicity, detected via fundus examination (n=9), SD-OCT (n=8/9), HVF 10-2 (n=6/9), FAF (n=1/9). 55.5% (n=5/9) had Rheumatoid Arthritis(RA) and 44.4% (n=4/9) had Systemic Lupus Erythematosus(SLE) as their primary diagnosis. 77.7% (n=7/9) were females. The mean age was 47.5 years (20-72 years).75%(n=3/4) of SLE patients were below 30 years of age. The average daily and cumulative dose of HCQ in these 9 patients were 244mg (200-400mg) and 311.22g(73-730g) respectively, whereas the mean recommended dose as per real body weight was 287.2mg/day. Average duration of HCQ consumption was 3.6 years (1-10 years). Only 11.1% (n=1/9) had presented with visual complaints of black floaters.
Conclusion: The asymptomatic nature of this irreversible toxicity, warrants frequent screening.Retinal toxicity was not age-related.Toxicity was manifested at low daily and cumulative doses.Screening should be done atleast every 6 months by fundus examination.Objective tests like HVF and SD-OCT should be done annually, especially in patients with underlying rheumatic diseases.The early manifestation of retinal toxicity in young SLE patients could have a genetic association and needs further evaluation.

Table 1. SALIENT FEATURES OF THE 9 PATIENTS PRESENTING WITH RETINAL TOXICITY DUE TO HCQ

					Dose				Detection Method Used			
Sl. No	Age	Gender	Weight (Kg)	Primary Diagnosis	Recommended Dose (mg/Day)	Received Dose (mg/Day)	Cumulative Dose (grams)	Duration (Years)	FUNDUS EXAM.	SD-OCT	HVF 10-2	F AF
1	47	F	58	SLE	290	400	438	3	RPE Changes	Thinning/Photoreceptor Loss	Defects seen	-
2	20	F	46	SLE	230	200	146	2	Multiple Small Drusens In Paramacular Area	Multiple Drusens	Normal	Perifoveal autofluorescence spots-drusens
3	23	F	50	SLE	250	400	146	1	RPE Changes	RPE Disruptions	Defects seen	-
4	30	F	55	SLE	275	200	73	1	Normal	Normal	Paracentral Scotoma	-
5	50	F	49	RA	245	200	511	7	Early Bull's Eye Maculopathy	RPE Atrophy	Defects seen	-
6	72	F	60	RA	300	200	730	10	RPE Atrophy FR Absent	RPE Atrophy	General reduction in sensitivity	-
7	65	M	57.4	RA	287	200	146	2	RPE Changes	RPE Disruptions & Thinning Noted	Defects seen	-
8	62	F	70	RA	350	200	219	3	Chorioretinal Atrophy	Altered RPE Membrane	Defects seen	-
9	59	M	71.6	RA	358	200	292	4	RPE Changes	RPE Disruptions	Normal	-

F:Female; M:Male; SLE:Systemic Lupus Erythematosus; RA: Rheumatoid Arthritis, FUNDUS EXAM.: Fundus Examination; SD-OCT:Spectral Domain-Optical Coherence Tomography, HVF 10-2:Humphrey Visual Field 10-2; FAF: Fundus Autofluorescence, RPE:Retinal Pigment Epithelium; FR:Foveal Reflex

REFERENCES:
[1] Mortada A Abozaid et al. hydoxychloroquine retinopathy in a ohort of patients from upper Egypt.Journal of Egyptioan Ophthalmological Society 2017;110:110-113
[2] Roy AN,Samala V,Kumar YA,Fatima SS.Assessing the risk of retinopathy in Indian patients using hydroxychloroquine for rheumatic and musculoskeletal Diseases:A Retrospective Observational Study.Indian J Rheumatol 2020.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2922

POS1398 RHEUMATOLOGICAL PATIENTS PERFORMING BLOOD SELF-SAMPLING FOR DMARD THERAPY SAFETY: A PROOF OF CONCEPT STUDY COMPARING WITH VENOUS BLOOD SAMPLES

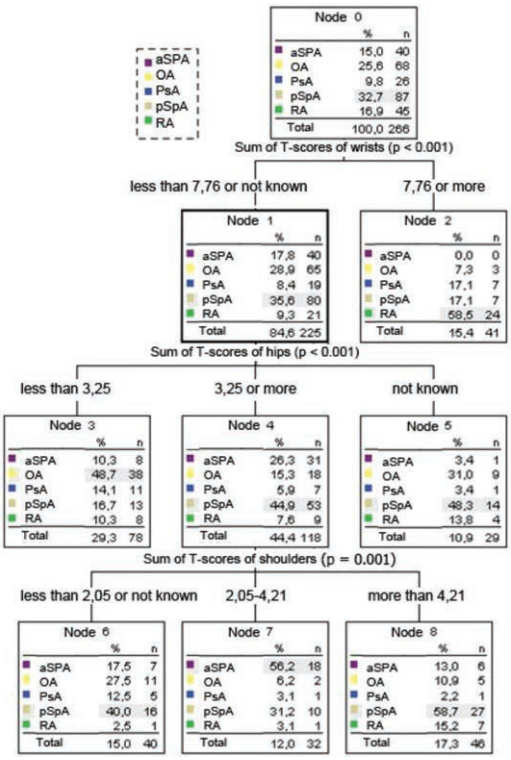
S. A. Just[1,2], P. Toftegaard[1], U. Jakobsen[3], T. R. Larsen[2,3]. [1]*Svendborg Hospital - Odense University Hospital, Section of Rheumatology, Department of Medicine, Svendborg, Denmark*; [2]*University of Southern Denmark, Department of Clinical Research, Odense, Denmark*; [3]*Svendborg Hospital - Odense University Hospital, Department of Biochemistry, Svendborg, Denmark*

Background: Regular blood sampling is a requirement for rheumatological patients receiving csDMARD, bDMARD or tsDMARD therapies (1). The frequent blood sampling affects the patient's life as they use a substantial amount of time at hospitals or by the general practitioner. Often visits are time-consuming with transport, waiting time, and for some patient's costly long travels. Giving patients the option of taking the blood samples themself in their own home, as part of a patient-centred monitoring approach, could provide the patient much higher degree of independence. Further, it may increase the quality of life, cause higher compliance with taking the control samples and possibly reduce health care costs.
Objectives: 1. To investigate if rheumatological patients can take capillary blood samples and describe patient-reported outcomes (PRO) about the procedure. 2. Compare the venous and capillary samples' results. 3. Test if the laboratory automated analysis equipment can handle the small capillary samples.
Methods: 21 rheumatological patients, underwent capillary and venous blood sampling at up to 4 occasions (1-2 months between). Instructions were available on a pictogram. PRO data were assessed by questionnaires. The patient performed blood extraction to the capillary samples from a finger after using a device making a small incision (2 mm depth and 3 mm width). Two capillary tubes (one Microtainer K2-EDTA and one Microtainer lithium heparin with gel) were filled with a total volume of approximately 1.0 mL blood. A phlebotomist took the venous sample. Blood samples were analyzed for alanine aminotransferase (ALAT), albumin, alkaline phosphatase (ALP), calcium, C-reactive protein (CRP), creatinine, potassium, lactate dehydrogenase (LDH), urate, hemolysis index, erythrocyte corpuscular volume (MCV), haemoglobin, leukocytes, differential count and platelets.
Results: A total of 53 paired capillary (C) and venous (V) samples were taken. The average perceived pain of the procedure of C sampling was VAS: 10.3 (SD:14.4) (0-100) versus V sampling VAS: 8.5 (SD:11.7). 90% of patients would accept it as a future form of blood sampling.
Differences in blood samples (C versus V) were: CRP (-3.4%); Hemoglobin (-1.4%); Creatinine (-4.4%), ALAT (-2.9%), neutrophils (1.43%), platelets (-16.9%). The index of hemolysis was on average 128.9 mg/dL (SD: 203) in C versus 6.7 mg/dL (SD: 4.6) in V. Results was evaluated by a rheumatologist, and 92.5% of capillary samples could be used to evaluate the safety of DMARD treatment based on the most critical samples for this: ALAT, creatinine, neutrophils and platelets (1). The 7.5 % not accepted were all due to aggregated platelets leading to low platelet count. There was hemolysis in 18% of the samples, but the analysis results could be used despite this.
Conclusion: In the majority of rheumatological patients, capillary self-sampling is well tolerated.
We show that it is possible to extract the needed results from the capillary samples to evaluate DMARD treatment safety, despite higher hemolysis index. Using capillary samples taken at home could be a central instrument in future rheumatological patient-centred monitoring.
REFERENCES:
[1] Rigby WFC et al. Review of Routine Laboratory Monitoring for Patients with Rheumatoid Arthritis Receiving Biologic or Nonbiologic DMARDs. *Int J Rheumatol*. 2017
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2927

POS1399 ALGORITHM FOR DIFFERENTIAL DIAGNOSIS OF ARTHROPATHIES USING OSTEOSCINTIGRAPHY

E. Prokhorova[1], E. Zhilyaev[2], G. Zhilyaev[3]. [1]*Main Hospital of Police, Nuclear Imaging, Moscow, Russian Federation*; [2]*JSC European Medical Center, Medical Administration, Moscow, Russian Federation*; [3]*Moscow State University of Medicine and Dentistry named after A.I. Evdokimov, Student, Moscow, Russian Federation*

Background: Joint bone scintigraphy is a promising method for diagnosing of inflammatory joint diseases. However, its scintigraphic semiotics remains to be developed.
Objectives: To develop an algorithm for the differential diagnosis of the most common arthropathies based on quantitative osteoscintigraphy.
Methods: This single-center study included inpatients with clinical diagnoses of rheumatoid arthritis (RA), axial spondyloarthritis (including ankylosing spondylitis - aSPA), peripheral spondyloarthritis (including reactive arthritis - pSpA), psoriatic arthritis (PsA), and osteoarthritis (OA) established by a rheumatologist and meeting the relevant criteria, Three hours after the injection of pyrophosphate, labeled with Tc-99m, scintigraphy of the skeletal bones was carried out according to the "whole body" program. The joint / bone accumulation ratio (AR) was calculated as the ratios of counts in relevant areas. All AR were recalculated into T-score for each joint based on data from control group. The CHAID algorithm for classification trees constructing was used. The significance of the division in the nodes was estimated with Bonferroni adjustment.
Results: 266 patients were included in the study aged 46.6±14.3 years, men - 134 (50.4%). aSPA was diagnosed in 40 patients, pSpA in 87, RA in 45, OA in 68, PsA in 26. 2279 joints were analyzed. A classification tree for differential diagnosis of arthropathies has been built (Pict.). Key indicators for identifying subgroups in the algorithm: AR in the wrist, knee and hip joints.
At the first step of the classification tree, the sum of the T-scores of the wrist joints is determined. If this amount exceeds 7.76 (node 2), the most likely diagnosis is RA (58.5% of patients in the subgroup of this node). Patients with the sum of the T-scores in the wrist joints less than 7.76 (node 1), in turn, were divided depending on the sum of the T-scores of hip joints. Those with this value less than 3.25 (node 3), mainly suffered from OA (48.7%), less often in this subgroup were diagnosed pSpA (16.7%) and PsA (14.1%). Patients in whom the sum of the T-score in the hips was more than 3.245 (node 4) were further subdivided depending on the sum of the T-scores in the shoulder joints. If it was more than 4.21 (node 8), then pSpA was most likely (58.7%). If the sum of the T-scores of the shoulder joints was in the range from 2.05 to 4.21 (node 7), then these are mainly patients with spondyloarthritides (56.2% with aSPA and 31.2% with pSpA) and a small number of patients (10%) with PsA. In the subgroup with the sum of T-scores of the shoulder joints <2.05 (node 6), patients with PSA (40%) prevailed, with a significant proportion of persons with OA (27.5%). Thus, out of the final branches formed by the tree (node 2, 3, nodes 6-8), four correspond to certain diseases (node 2 - PA, node 3 - OA, node 7 - aSPA, node 8 - pSpA). Node 6 includes patients with various diseases with a predominance of PsA. The level of significance of differences between the formed groups at all branch points of the tree is p = 0.001 or less (Bonferroni adjusted). In the training sample, 51.5% of observations are correctly classified. According to cross-validation data, the expected rate of correct classifications in real application of the algorithm is 38.0%.
Conclusion: An algorithm for the differential diagnosis of the most common inflammatory diseases of the joints has been developed, which makes it possible to use the data of quantitative osteoscintigraphy in the process of diagnosing arthritis.



Acknowledgements: MD. PhD Constantin V. Kushnir, Main hospital of police.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2931

POS1400 A SYSTEMATIC REVIEW OF INTERNATIONAL GUIDELINES REGARDING THE ROLE OF RADIOGRAPHY IN THE DIAGNOSIS OF OSTEOARTHRITIS

C. Henry-Blake[1], K. Treadwell[1], S. Parmar[1], J. Higgs[1], M. Marshall[1], J. Edwards[1], G. Peat[1]. *[1]Keele University, Department of Primary, Community and Social Care, Keele, United Kingdom*

Background: A substantial proportion of primary care osteoarthritis (OA) consultations are associated with an X-ray request [(1,2)]. Uncertainty exists regarding the ability of radiography to improve a clinical OA diagnosis, and the over-use of radiography may lead to inappropriate referrals due to severe radiographic features that do not correlate with patients' symptoms. Additionally, there are cost implications of unnecessarily imaging such a prevalent disease. As evidence questions the utility of routine radiography in OA, the extent to which radiography is supported by international guidelines is unknown.
Objectives: To undertake a systematic review and narrative synthesis of UK and international guideline recommendations on the role of radiography in the diagnosis of OA.
Methods: A systematic search of eleven electronic databases (including EMBASE, MEDLINE CINAHL, Epistemonikos and Guideline Central) and the websites of nine professional organisations (including NICE, Royal College of Radiologists (RCR), EULAR, and the American College of Radiology (ACR)) identified the most recent evidence-based guidelines produced by professional organisations on the role of imaging in OA. Guidelines not addressing the role of radiography in the diagnosis of OA were excluded, as were non-English and spinal OA guidelines. Each title was screened by one reviewer whilst each abstract and full text underwent dual screening. A single reviewer, using a standard proforma, undertook data extraction. Each guideline was independently appraised by two reviewers using the AGREE II tool. A narrative synthesis of the nature and consistency of OA radiographic recommendations was performed.
Results: 18 evidence-based OA guidelines published between 1998-2019 were included. These guidelines considered OA at any joint (n=8), or at the knee (n=3), hip (n=2), hand (n=2), wrist (n=1), foot (n=1), and ankle (n=1). Seven guidelines were produced by European organisations; four guidelines were produced by EULAR. Guidelines were targeted at general practitioners (n=11), radiologists (n=7), rheumatologist (n=4) and orthopaedic surgeons (n=3). Using the AGREE II tool, the identified guidelines scored highly on rigour of development (mean score 69%) but poorly on applicability (32%). All 18 guidelines recommended X-rays as the first-line modality, where imaging was indicated. A clinical diagnosis of OA without radiographic confirmation was recommended by all eleven guidelines produced by organisations represented general practitioners, with seven guidelines justifying this due to a poor correlation between radiographic features and clinical symptoms. Only three guidelines explicitly discouraged the routine use of radiography for the diagnosis of OA and only two guidelines reassured practitioners of a low probability of missing serious pathology when not routinely requesting radiographs. Guidelines produced by organisations representing radiologists were more supportive of radiography. The ACR recommended radiographic confirmation in patients suspected to have OA at the hand, wrist, hip, knee, ankle, and foot. Conversely, the RCR recommended radiographic confirmation in patients suspected to have OA at the hand, feet, and hip, but not the knee.
Conclusion: Differences in guideline recommendations on the utility of radiography in OA appear related to country/region, professional organisation, and joint. The use and utility of radiography in OA may need to be reviewed in light of a shift towards remote consultations, a change that has been accelerated by COVID-19 in many countries.
REFERENCES:
[1] Yu D, Jordan K, Bedson J, Englund M, Blyth F, Turkiewicz A et al. Population trends in the incidence and initial management of osteoarthritis: age-period-cohort analysis of the Clinical Practice Research Datalink, 1992–2013. Rheumatology. 2017;56(11):1902-1917.
[2] Brand C, Harrison C, Tropea J, Hinman R, Britt H, Bennell K. Management of Osteoarthritis in General Practice in Australia. Arthritis Care & Research. 2014;66(4):551-558
Acknowledgements: JJE is funded by an Academic Clinical Lectureship from the National Institute for Health Research (NIHR) for this research project (CL-2016-10-003). The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR, NHS or the UK Department of Health and Social Care.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3117

POS1401 ASSESSMENT OF INTERREADER RELIABILITY IN SCORING PATIENTS WITH HAND OSTEOARTHRITIS AND PSORIATIC ARTHRITIS BY FLUORESCENCE OPTICAL IMAGING

B. Drude[1], Ø. Maugesten[2], S. G. Werner[3], G. R. Burmester[1], J. Berger[4], I. K. Haugen[2], S. Ohrndorf[1]. *[1]Charité Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; *[2]Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway*; *[3]RHIO (Rheumatology, Immunology, Osteology) Duesseldorf, RHIO Research Institute, Duesseldorf, Germany*; *[4]Xiralite GmbH, Head Development and Produktion, Berlin, Germany*

Background: Fluorescence Optical Imaging (FOI) utilises the fluorophore indocyanine green (ICG) to reflect enhanced microcirculation in hand and finger joints due to inflammation.
Objectives: We wanted to assess the interreader reliability of FOI enhancement in patients with hand osteoarthritis (OA) and psoriatic arthritis (PsA). Furthermore, predefined typical morphologic patterns were included to determine the ability of FOI to discriminate between both diagnoses.
Methods: An atlas with example images of grade 0-3 in different joint groups and typical morphologic patterns ('streaky signals'[1], 'green/blue nail sign'[2], 'Werner sign'[3,4], and 'Bishop's crozier sign') of PsA and hand OA was created. Two readers scored all joints in both hands (30 in total) of 20 cases with hand OA and PsA. The cases were randomly mixed and both readers were blinded to diagnosis. Each joint was rated on a semiquantitative scale from 0 to 3 in five different images (PrimaVista Mode (PVM), phase 1, 2 (first and middle image), and 3) during the FOI sequence according to the scoring method FOIAS (fluorescence optical imaging activity score) [1,3]. Interreader reliability on scoring joint enhancement was calculated using linear weighted Cohen's kappa (κ). Agreement on diagnosis (hand OA vs. PsA) and different morphologic patterns was assessed by calculating (regular) Cohen's kappa.
Results: Overall agreement on scoring joint enhancement (all phases) was substantial (κ = 0.75), with greatest consensus in phase 2 first (κ = 0.75) and lowest agreement in phase 1 (κ = 0.46). Reliability varied in different joint groups (wrist, MCP, (P)IP, DIP), with almost perfect overall agreement on PIP joint affection (κ = 0.81), substantial agreement on wrist (κ = 0.69) and DIP joint affection (κ = 0.63), and moderate agreement on MCP joint affection (κ = 0.49) across all phases. Consensus on morphologic patterns showed overall fair agreement (κ = 0.37) with a similar kappa value on the ability to discriminate between both diagnoses (κ = 0.3).
Conclusion: Joint enhancement in FOI can be reliably assessed using a predefined scoring method. The ability of FOI to differentiate between hand OA and PsA seems to be limited. Clearer definition and more training might be needed to better agree on morphologic patterns in FOI.
REFERENCES:
[1] Glimm AM, Werner SG, Burmester GR, et al. Ann Rheum Dis. 2016 Mar;75(3):566-570
[2] Wiemann O, Werner SG, Langer HE, et al. J Dtsch Dermatol Ges. 2019 Feb;17(2):138-148
[3] Werner SG, Langer HE, Ohrndorf S, et al. Ann Rheum Dis. 2012 Apr;71(4):504-510
[4] Zeidler H 2019. Fluoreszenzoptische Bildgebung. In: Zeidler H, Michel BA. *Differenzialdiagnose rheumatischer Erkrankungen* 5. Aufl. Springer, Heidelberg, S. 88-89
Disclosure of Interests: Benedict Drude: None declared, Øystein Maugesten: None declared, Stephanie Gabriele Werner: None declared, Gerd Rüdiger Burmester: None declared, Jörn Berger Employee of: Xiralite GmbH, Ida K. Haugen: None declared, Sarah Ohrndorf: None declared
DOI: 10.1136/annrheumdis-2021-eular.3145

POS1402 HIGHER PREVALENCE OF SUBCLINICAL ATHEROSCLEROSIS IN PSORIATIC ARTHRITIS PATIENTS

S. Lugo-Perez[1], I. J. Colunga-Pedraza[2], D. Á. Galarza-Delgado[2], J. R. Azpiri-López[1], A. B. Rodriguez-Romero[2], N. Guajardo-Jauregui[2], D. E. Flores Alvarado[2], A. Cárdenas[2], A. C. Garza Acosta[3], O. Ilizaliturri Guerra[2], G. García-Arellano[2]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico*; *[2]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*; *[3]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Radiology, Monterrey, Mexico*

Background: Psoriatic arthritis (PsA) patients have a higher risk of developing a cardiovascular (CV) event than the general population due to an increased prevalence of traditional CV risk factors and to disease characteristics such as disease duration and activity. The carotid ultrasound (US) is a non-invasive diagnostic tool that can detect the presence of subclinical atherosclerosis which is directly associated with the risk of developing a CV event.
Objectives: The aim of this study is to compare the prevalence of subclinical atherosclerosis detected by carotid US in PsA patients and controls.

Methods: This is a cross-sectional, observational, and comparative study. A total of seventy-five PsA patients aged 40-75 years old, who fulfilled the 2006 CASPAR criteria and seventy-five matched controls by age (±5 years), gender and comorbidities were recruited for this study. Patients with history of a previous CV event and pregnant women were excluded from this study. A high-resolution B mode carotid US was performed in all study subjects by a certified radiologist. Subclinical atherosclerosis was defined as the presence of a carotid plaque (CP) or an increased carotid intima media thickness (cIMT). The presence of CP was defined as a cIMT ≥1.2mm or a focal narrowing ≥0.5mm in the surrounding lumen. An increased cIMT was considered as a value ≥0.8mm. Distribution was evaluated with the Kolmogorov-Smirnov test. Comparisons were done with $\chi 2$ test for qualitative variables and Student´s t test and Mann-Whitney's U test for quantitative variables. A *p* value <0.05 was considered statistically significant.

Results: There were no differences when comparing the demographic characteristics between both groups (Table 1). When comparing the carotid US findings, a statistically significant difference was found in the prevalence of CP, which was higher in the PsA group (44.0% vs 26.7%, *p*=0.026), in the presence of unilateral CP (25.3% vs 10.7%, *p*=0.019) and in the presence of subclinical atherosclerosis (52.0% vs 34.7%, *p*=0.032) (Figure 1).

Conclusion: The prevalence of subclinical atherosclerosis was higher in PsA patients than controls, and this could be attributed to an increase in the inflammatory burden of these patients. The carotid US should be considered as part of the CV evaluation in all PsA patients, identifying those who would benefit from an opportune treatment preventing the development of a CV event.

REFERENCES:

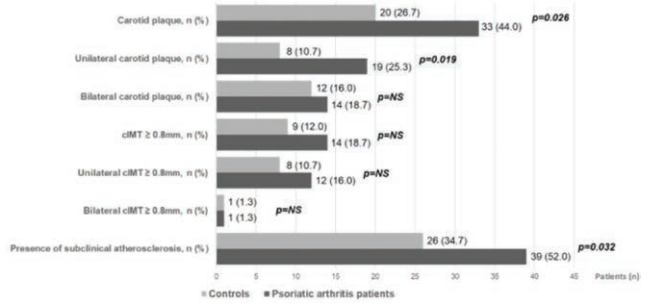
[1] Yim KM, Armstrong AW. Updates on cardiovascular comorbidities associated with psoriatic diseases: epidemiology and mechanisms. Rheumatol Int. 2017;37(1):97–105.

Table 1. Demographic and clinical characteristics of psoriatic arthritis patients and controls.

	PsA (n=75)	Controls (n=75)	*p*
Age years, mean ± DE	53.89 ± 10.59	54.25 ± 7.08	NS
Female gender, n (%)	43 (57.3)	43 (57.3)	NS
T2DM, n (%)	16 (21.3)	15 (20.0)	NS
HTN, n (%)	28 (37.3)	21 (28.0)	NS
Dyslipidemia, n (%)	33 (44.0)	28 (37.3)	NS
Obesity, n (%)	31 (41.3)	32 (42.7)	NS
Active smoking, n (%)	14 (18.7)	18 (24.0)	NS
BMI kg/m^2, median (p25-p75)	29.32 (26.23-32.03)	28.9 (25.4-33.5)	NS
Disease duration years, median (p25-p75)	5.0 (3.0-10.0)	-	-
DAPSA, median (p25-p75)	12.6 (5.3-22.9)	-	-
Glucocorticoids, n (%)	10 (13.3)	-	-
MTX, n (%)	51 (68.0)	-	-
bDMARD, n (%)	28 (37.3)	-	-

PsA, psoriatic arthritis; NS, not significant; T2DM, type 2 diabetes mellitus; HTN, hypertension; BMI, body mass index; DAPSA, disease activity for psoriatic arthritis; MTX, methotrexate; bDMARD, biological disease modifying antirheumatic drug.

Figure 1. Carotid ultrasound findings in psoriatic arthritis patients and controls.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3188

POS1403 RADIOSYNOVECTOMY IN A CLINICAL SETTING: AN UNDEREXPLOITED TOOL AT OUR DISPOSAL

L. R. Caballero Motta[1], A. M. Anzola Alfaro[1], J. Molina Collada[1], I. Janta[1], Y. K. Henao[2], R. Perez Pascual[2], F. J. López-Longo[1], J. M. Alvaro Gracia[1], J. C. Nieto González[1]. [1]*Gregorio Marañón Hospital, Rheumatology, Madrid, Spain*; [2]*Gregorio Marañón Hospital, Nuclear Medicin, Madrid, Spain*

Background: Radiosynovectomy (RS) is a useful for treating inflammatory arthritis that fail conventional treatments. The main isotope used is Yttrium-90 on large joints as knees, whereas Erbium-169 and Renium-186 are more common in small and medium sized joints respectively.

RS is a safe procedure since the isotopes cannot escape the synovial capsule or be absorbed into circulation. It is, however, lethal against cells within the inflamed joint. The most common rheumatic disease treated with RS is rheumatoid arthritis (RA), followed by axial spondyloarthritis (SpA) and idiopathic juvenile arthritis (JIA). It has also been used on persistent synovitis after joint replacements, pigmented villonodular synovitis (PVNS) and undifferentiated arthritis.

Objectives: To describe the experience in RS of a tertiary rheumatology center and compare patients with and without clinical response to treatment in the following 12 months.

Methods: Observational retrospective study between May 31st 2013 and October 31st 2019. We collected demographic variables, data about the disease of the patient, the joints affected, isotope utilized, presence of Baker's cyst, systemic treatment received, need of additional infiltrations (before and after), complications and any changes in medication up to a year after the procedure.

All the RS were performed ambulatory and the radioisotope infiltration was guided by ultrasound, with 40mg of triamcinolone infiltrated after.

SPSS v23 was used for statistical analysis; with Chi2 for qualitative variables and Student's T distribution for quantitative variables.

Results: We evaluated 67 joints in 49 patients in total. All of them were refractory to conventional treatment. 44 patients (65.7%) were women, median of 53.4 years of age (IQ 43.4-67.1).

The median disease duration was 12.5 years and RS seemed to fare better the longer the patient had the disease (median of 13.5 years vs 6.5 years p<0.001).

The joints infiltrated where 46 (68.6%) knees, 14 (20.9%) wrists and 7 (15.2%) elbows. Out of the knees, 16 (34.8%) belonged to RA patients with effective response in 14 (87,5%). 100% of elbows had an effective response, of them 6 (85.7%) had RA. However, even when 9 (64.2%) wrists also had RA as diagnosis, only 3 (21.4%) were effective.

Of the PVNS, 6 out of 8 (75%) had no clinical response, as shown in Table 1.

Table 1. RS response compared to clinical diagnosis.

	TOTAL	EFFECTIVE	INEFFECTIVE	p
	67 (100%)	46 (68.6%)	21 (31.3%)	
Inflammatory Arthritides	52 (77.6)	**39 (75%)**	13 (25%)	<0.0001
(RA + PsA + SpA + sJIA), (%)				
RA (%)	30 (44.7)	**22 (73.3)**	8 (26.6)	<0.001
RA *positive ACPA/FR*	21 (70)	**15 (71.4)**	6 (28.6)	<0.0001
Psoriasic arthritis (PsA) (%)	6 (9)	4 (66.6)	2 (33.3)	0.42
SpA (%)	10 (14.9)	8 (80)	2 (20)	0.45
sJIA (%)	6 (9)	5 (83.3)	1 (16.6)	0.55
PVNS (%)	8 (11.9)	2 (25)	**6 (75)**	<0.001
Inespecific monoarthritis (%)	3 (4.4)	3 (100)	0 (0)	0.23
OA + Calcium Pyrophosphate Deposition (CPPD) (%)	4 (5.9)	2 (50)	2 (50)	0.33

Intra articular corticosteroids were needed before RS, with no differences in effective and ineffective joints; however after RS it was significantly lower in effective joints in the first six months (0% vs 43% p<0.0001) and remained so in the following 6 months (0% vs 19% p<0.0001)Only 13 (28%) patients with effective RS needed to change systemic treatment compared to 10 (43%) of those ineffective (p<0.0001). None of the patients with RS had any complication after the procedure during follow up.

Conclusion: Our study showed that knees were the main joint infiltrated and they had an overall good response to treatment, especially if the diagnosis was RA.

Patients with effective procedures needed leest treatment changes and significantly less corticosteroids infiltrations.

In our study, RS in PVNS was significantly less effective than in inflammatory arthritis (25% vs 75% p<0.0001) and RA seemed to have the best response overall.

REFERENCES:

[1] Liepe K. Efficacy of radiosynovectomy in rheumatoid arthritis. Rheumatol Int. 2012 Oct; 32(10):3219-24.

[2] Ćwikła JB, Żbikowski P, Kwiatkowska B, Buscombe JR, Sudoł-Szopińska I. Radiosynovectomy in rheumatic diseases. J Ultrason. 2014 Sep; 14(58):241-51.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3250

POS1404 ECHOCARDIOGRAPHIC FINDINGS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AND ITS RELATION TO ANTIBODIES TITERS

A. B. Rodriguez-Romero[1], J. R. Azpiri-López[2], I. J. Colunga-Pedraza[1], D. Á. Galarza-Delgado[1], S. Lugo-Perez[2], N. Guajardo-Jauregui[1], A. Cárdenas[1], H. Azpiri-Diaz[2], O. A. Cepeda-Ayala[2]. [1]*Hospital Universitario "Dr. José Eleuterio*

González", Universidad Autónoma de Nuevo León, Rheumatology Service, Monterrey, Mexico; [2]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology Service, Monterrey, Mexico*

Background: Systemic lupus erythematosus (SLE) is a chronic and autoimmune disease characterized by systemic involvement. Patients with SLE have accelerated atherosclerosis, resulting in an up to nine-fold increased risk of cardiovascular disease, compared to the general population (1), being the leading cause of death for these patients. Speckle tracking echocardiography (STE) is an accurate technique to estimate myocardial function and deformation.
Objectives: This study aims to determine the association between echocardiographic findings and the presence of antibodies in SLE patients.
Methods: This was a cross-sectional and observational study. A total of forty-three patients ≥18 years with a diagnosis of SLE according to EULAR/ACR 2019 criteria were included for this study. Those with a history of cardiovascular disease (myocardial infarction, cerebrovascular accident, or peripheral arterial disease) and pregnancy were excluded. Transthoracic echocardiogram was performed and reviewed by 2 board-certified cardiologists, in all study subjects. Blood samples obtained from all patients were analyzed for the following: anti-nuclear antibodies (ANA), anti, SSA/Ro, SSB/La antibodies, anti-cardiolipin antibodies (IgA, IgM, IgG), and complement levels. Distribution was evaluated with the Kolmogorov-Smirnov test. Correlations between numerical variables were done using Spearman's rho, considering two-tailed p-values <0.05 as statistically significant.
Results: The 39 female patients (90.7%) and 4 male patients (9.3%) had a mean age of 35.5 ± 12.0 years and a median disease duration of 72 months (14-132). At the time of inclusion, 90.7% of the patients were being treated with glucocorticoids and antimalarials. Concerning traditional cardiovascular risk factors; 20.9% of the patients had hypertension, 7.0% had dyslipidemia, 2.3% had diabetes mellitus and 18.6% were active smokers. Correlations between echocardiographic findings and antibodies are shown in Table 1. We found a moderate positive correlation between global circumferential strain and IgA anticardiolipin antibody (r=0.507, p=0.002), a low positive correlation in left ventricular ejection fraction with anti-Ro (r=0.397, p=0.012) and anti-La (r=0.397, p=0.012) and a low positive correlation between TAPSE and C3 levels (r=0.396, p=0.013).
Conclusion: There is an association between anticardiolipin antibody titers, anti-Ro, and anti-La with echocardiographic alterations. All SLE patients especially those who had positive antibodies should be screened for the presence of structural cardiac abnormalities. STE can be helpful as a noninvasive diagnostic tool, that could result in earlier treatment and prognosis.
REFERENCES:
[1] Hesselvig JH, Ahlehoff O, Dreyer L, et al. Cutaneous lupus erythematosus and systemic lupus erythematosus are associated with clinically significant cardiovascular risk: a Danish nationwide cohort study. Lupus 2017;26(1):48-53. doi: 10.1177/0961203316651739

Table 1. Spearman rho correlations between antibody titers and echocardiographic findings.

Variables	GLS, mean ± SD -19.11 ± 3.33	LVEF, mean ± SD 57.43 ± 7.17	TAPSE, mean ± SD 22.23 ± 3.24
ANA, median (p25-p75) 640 (160-2550)	NS	NS	NS
IgA Anti-Cardiolipin, median (p25-p75) 2 (2-3)	**0.507****	NS	NS
IgM Anti-Cardiolipin, median (p25-p75) 2 (2-4)	NS	NS	NS
IgG Anti-Cardiolipin, median (p25-p75) 4 (3-6)	NS	NS	NS
Anti-Ro, median (p25-p75) 17 (2-80)	NS	**0.326***	NS
Anti-La, median (p25-p75) 3 (2-5.5)	NS	**0.397***	NS
C3, mean ± SD 91.41 ± 37.38	NS	NS	**0.396***

**Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level. NS, not significant; GLS, global circumferential strain; LVEF, left ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3399

POS1405 OPTICAL SPECTRAL TRANSMISSION (HANDSCAN) IN PATIENTS WITH PSORIATIC ARTHRITIS: FIRST DATA ON DIAGNOSTIC VALUE AND ASSOCIATIONS WITH CLINICAL AND ULTRASOUND DISEASE ACTIVITY MARKERS

K. Triantafyllias[1], S. Liverakos[2], C. Noack[3], A. Schwarting[1,2]. [1]*ACURA Clinics, Rheumatology, Bad Kreuznach, Germany*; [2]*Johannes Gutenberg University Medical Center, Internal Medicine I, Deparmtnet of Rheumatology and Clinical Immunology, Mainz, Germany*; [3]*University of Mannheim, Graduate School of Economics and Social Sciences, Mannheim, Germany*

Background: Valid assessment of disease activity leads to improvement of long-term outcomes in patients with inflammatory arthritis (1). Optical spectral transmission (OST) is a modern diagnostic tool able to assess the blood-specific absorption of light transmitted through a tissue, promising quantification of inflammation in the finger and wrist joints of patients with rheumatoid arthritis (RA) (commercial device: HandScan – Demcon/Hemics, The Netherlands) (2). Even though an increasing number of studies have evaluated diagnostic value of this new technology in RA patients (2,3), no data exist regarding psoriatic arthritis (PsA).
Objectives: To examine for the first time the diagnostic value of OST in detecting inflammation in patients with PsA and to evaluate its relationship with disease activity markers and various epidemiological and anthropometric patient characteristics.
Methods: OST-Measurements were performed in a group of PsA patients and a group of healthy controls. The difference between OST in the two groups was statistically examined and relationships of OST with clinical (tender / swollen joint counts, disease activity on a visual analogue scale) and serological disease activity markers were evaluated. Moreover, joint ultrasound (US) examinations were performed in a subgroup of PsA patients and OST associations with a Power Doppler- and a Grey Scale-US score were examined. Finally, relationships of OST with various anthropometric and epidemiologic parameters (BMI, handsize, gender, age) were assessed.
Results: We recruited 49 PsA patients [65.3% female; mean age 53.3 years (± 11.8 SD)] and 114 control subjects [77.2% female; mean age 46 years (± 12.8 SD)]. OST was statistically significantly higher in the patient group, compared to the control group [14.95 (12.04 - 17.18, IQR) vs. 10.31 (7.84 – 13.79, IQR); p<0.001]. OST correlated moderately-strongly with both examined US scores (Power Doppler-score: r = 0.5; p = 0.026 and Grey Scale-score: r = 0.52; p = 0.028). Moreover, OST showed a moderate, statistically significant association with C-reactive protein (CRP) (r = 0,298; p = 0,037). Finally, males had significantly higher OST values than females and OST associated moderately-weakly with body mass index (BMI) in the control group (rho = 0.24; p< 0.001).
Conclusion: This is the first report of a possible diagnostic value of OST in patients with PsA. OST correlated with ultrasound and serological activity markers and may thus prove to be a useful tool of disease activity assessment, next to well established diagnostic modalities, such as the joint US. Correlations of OST with patient characteristics implicate the need to take also anthropometric and epidemiological patient characteristics into account when interprenting OST results in order to avoid confounding.
REFERENCES:
[1] Katchamart W, et al. Systematic monitoring of disease activity using an outcome measure improves outcomes in rheumatoid arthritis. J Rheumatol 2010;37:1411–1415.
[2] Triantafyllias, et al. Diagnostic value of optical spectral transmission in rheumatoid arthritis: associations with clinical characteristics and comparison with joint ultrasonography. J Rheumatol 2020 1;47(9):1314-1322.
[3] Onna M Van, et al. Assessment of disease activity in patients with rheumatoid arthritis using optical spectral transmission measurements, a non-invasive imaging technique. Ann Rheum Dis 2016;75:511–518.
Disclosure of Interests: Konstantinos Triantafyllias Speakers bureau: Pfizer, Novartis, Janssen, Chugai, Stefanie Liverakos: None declared, Claudia Noack: None declared, Andreas Schwarting: None declared
DOI: 10.1136/annrheumdis-2021-eular.3670

POS1406 DEVELOPMENT OF A DIAGNOSTIC ALGORITHM FOR THE DIFFERENTIAL DIAGNOSIS OF INTERSTITIAL LUNG DISEASE: PRELIMINARY DATA FROM A MULTICENTER RETROSPECTIVE CASE-CONTROL STUDY

B. Maranini[1], T. Chiodin[1], C. A. Scirè[1], M. Govoni[1], E. Lucioni[2], S. Chiarello[2], F. Scabbia[2], I. Marchi[3], G. Zanframundo[4], L. Cavagna[4], E. Bellis[4], M. Silva[5], G. Tringali[5], A. Carnevale[2]. [1]*Rheumatology Unit, University of Ferrara and Azienda Ospedaliero-Universitaria S. Anna, Department of Medical Sciences, Ferrara, Italy*; [2]*Radiology Unit, Azienda Ospedaliero-Universitaria S. Anna, Department of Radiology, Ferrara, Italy*; [3]*Pneumology Unit, University of Ferrara and Azienda Ospedaliero-Universitaria S. Anna, Department of Medical Sciences, Ferrara, Italy*; [4]*University and IRCCS Policlinico S. Matteo Foundation of Pavia, Department of Rheumatology, Pavia, Italy*; [5]*Department of Medicine and Surgery (DiMeC), University of Parma, Scienze Radiologiche, Parma, Italy*

Background: Interstitial lung diseases (ILDs) represent a heterogeneous group of disorders with different treatment and prognosis. ILD may be the presenting or

the dominant manifestation of a connective tissue disease (CTD). Multidisciplinary team (MDT) discussion is currently the diagnostic standard. However, there is no consensus on how MDT diagnosis is validated and on the core elements of discussion.

Objectives: To explore the performance of a diagnostic algorithm for the differential diagnosis of ILD based on clinical, serological and radiological data, supporting clinician decision-making.

Methods: In this retrospective study, analysis was performed on clinical, serological and radiological features at diagnosis and 1-year follow-up in 71 patients, including 41 with CTD-ILD and 30 with idiopathic interstitial pneumonias (IIPs). In order to identify robust hallmarks, we conducted the Receiver Operating Characteristic (ROC) curve analyses in logistic regression, to discriminate significantly different features between CTD-ILD and non-CTD-ILD groups.

Results: Out of 71 patients 46% were women, with a mean age of 66±11 years. History of smoking (8.8% current and 39.8% former smokers), was more associated with IIPs. 54% of patients had dyspnea on exertion and 39% dry cough, both more frequently associated with IIPs (p = 0.016). Among radiological features, NSIP pattern was more frequent in CTD-ILD, while UIP was associated with IIP. Lung fibrosis extent was greater in IIP (p = 0.063), in which CT is generally performed in symptomatic patients at diagnosis and rarely for screening purpose. Baseline features with good performance (OR p-value ≤ 0.05) were eligible as potential candidate discriminators: age, sex, smoking habit, rheumatological signs and symptoms, autoantibodies, ILD patterns were selected, to build a multivariate model with high discrimination accuracy (AUC 0.971). The model has a sensitivity of 100% and specificity of 89.7%. The most relevant correlations between population features and CTD-ILD are presented in Table 1.

Table 1. Correlation analysis of the most significant discriminative features.

Features	Odds ratio	P value	Area under ROC curve
Sex (female)	3.29	0.019*	0.643
Age	0.91	0.001*	0.736
Smoke	0.12	<0.001*	0.738
Respiratory symptoms (dyspnea and/or dry cough)	0.26	0.016*	0.644
Rheumatological symptoms (any)	28.8	<0.001*	0.839
• Raynaud's phenomenon	15.04	0.011	0.654
• Cutaneous manifestations	8.16	0.053	0.593
Autoantibodies (ANA, ENA, RF, ACPA, myositis-specific antibodies or aPL) positivity	33.68	<0.001*	0.792
Lung function test			
• Forced vital capacity (%FVC)	0.97	0.175	0.638
• Diffusing capacity of carbon monoxide (%DLCO)	0.96	0.072	0.665
High-resolution computed tomography (HRCT) imaging			
• Honeycombing	0.34	0.068	0.593
• Emphysema	0.14	0.005*	0.647
• Extent of lung involvement (%)	0.97	0.063	0.668
HRCT pattern			
• NSIP vs UIP	3	0.033*	0.625

Abbreviations: ANA, antinuclear antibody; ENA, extractable nuclear antigen; RF, rheumatoid factor; ACPA, anti-citrullinated peptide antibody; aPL, antiphospholipid antibody; NSIP, non-specific interstitial pneumonia; UIP, usual interstitial pneumonia.

Conclusion: Our study shows that the most important variables in the differential diagnosis between CTD-ILD versus IIPs include, as expected, autoimmune features (rheumatological symptoms and serological data). Questionnaire tool containing these specific hallmarks may be relevant during MDT discussion, limiting the number of misdiagnosed CTD-ILDs and potentially avoiding further unnecessary investigations. However, only prospective cohort studies of early onset ILD are needed to fully validate the relative importance of clinical, serological, functional and radiological data.

REFERENCES:

[1] Furini F. et al, The Role of the Multidisciplinary Evaluation of Interstitial Lung Diseases: Systematic Literature Review of the Current Evidence and Future Perspectives. Front Med (Lausanne). 2019; 6: 246.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3760

POS1407

COMPARISON OF CAROTID SUBCLINICAL ATHEROSCLEROSIS AND STRUCTURAL DAMAGE IN AXIAL SPONDYLITIS WITH AND WITHOUT CONCOMITANT INFLAMMATORY BOWEL DISEASE. A MULTICENTER STUDY WITH 886 PATIENTS. . A MULTICENTER STUDY WITH 886 PATIENTS

I. González-Mazón[1], J. Rueda-Gotor[1], I. Ferraz-Amaro[2], L. Sanchez-Bilbao[1], F. Genre[3], V. Calvo-Río[1], S. Remuzgo-Martínez[3], V. Pulito-Cueto[3], A. Corrales[1], L. Lera-Gómez[3], V. Portilla[1], V. Hernández-Hernández[2], J. C. Quevedo-Abeledo[4], C. Rodríguez-Lozano[4], C. López-Medina[5], M. L. Ladehesa Pineda[5], S. Castañeda[6], N. Garcia-Castañeda[6], C. Fernández-Carballido[7], M. P. Martínez-Vidal[7], D. Castro-Corredor[8], J. Anino-Fernández[8], D. Peiteado[9], C. Plasencia[9], M. L. García Vivar[10], E. Galindez[10], E. Montes Pérez[11], C. Fernández-Díaz[1], R. Blanco[1], M. A. González-Gay[1,3].

[1]Universitary Hospital Marques de Valdecilla, Rheumatology, Santander, Spain; *[2]Hospital Universitario de Canarias, Rheumatology, Tenerife, Spain*; *[3]IDIVAL, Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Santander, Spain*; *[4]Hospital Universitario de Gran Canaria Dr. Negrín, Rheumatology, Santander, Spain*; *[5]Reina Sofia Hospital, Rheumatology, Cordoba, Spain*; *[6]Hospital de La Princesa, Rheumatology, Santander, Spain*; *[7]Hospital Universitario San Juan de Alicante, Rheumatology, Santander, Spain*; *[8]Hospital General Universitario de Ciudad Real, Ciudad Real, Santander, Spain*; *[9]Hospital Universitario La Paz-IdiPaz, Rheumatology, Santander, Spain*; *[10]Hospital Universitario Basurto, Rheumatology, Santander, Spain*; *[11]Diagnóstico Médico Cantabria, DMC, Santander, Spain*

Background: The prevalence of inflammatory bowel disease (IBD) in ankylosing spondylitis (AS) has been reported to range between 6%-15%. As occurs with axial spondyloarthrtitis (axSpA), patients with IBD have an increased risk of cardiovascular (CV) events because of a process of accelerated atherosclerosis[1]. However, it is unknown whether the presence of IBD confers an increased cardiovascular CV risk in patients with axSpA.

Objectives: To compare the atherosclerotic burden, CV events, CV risk factors and disease related factors including structural damage in axSpA patients with and without IBD.

Methods: Cross-sectional analysis of the AtheSpAin cohort, a Spanish multicenter cohort designed for the study of atherosclerosis in axSpA, comparing axSpA patients with and without concomitant IBD. Background information on CV and disease-related factors was reviewed. Data on CV risk and disease status at the time of the study were also obtained, including the structural damage assessed by the presence of syndesmophytes, the severity of the sacroiliitis (defined as grade 3 or 4 according to New York criteria), and the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Carotid ultrasound (US) was performed in all patients at the time of the study, including measurement of carotid intima-media wall thickness (cIMT) and plaque detection according to the Mannhein consensus criteria.

Results: A set of 886 axSpA patients were included. 829 (93.6%) of them had no concomitant IBD, which was present in 57 (6.4%) patients. Age, sex and AS/nr-axSpA ratio were comparable in both groups (Table 1. next page). Patients with IBD were characterised by a lower prevalence of HLA B27 (46% vs 72%, p=0.01) and a higher presence of concomitant psoriasis (21% vs 10%, p=0.01) Regarding peripheral disease (history of synovitis, enthesitis, dactylitis) and hip involvement, no differences were found between both groups. There were either no differences in the structural damage found in patients with and without IBD (Table 1. next page). With respect to the management of the disease, prednisone (21% vs 13%, p = 0.03), DMARDs (54% vs 35%, p = 0.01) and anti-TNFα therapy (54% vs 31%, p = 0.00) were more commonly used in the group with IBD, while treatment with NSAIDs was more frequent in patients without IBD (81% vs 70%, p = 0.04). Regarding CV risk features, smoking was more frequent in patients without IBD (34% vs 21%, p = 0.045) (Table 1. next page). No differences were observed neither in the lipid profile or blood pressure at the time of the study, nor in the prevalence of CV events (5% vs 4%, p=0.99) (Table 1) and the subclinical atherogenic burden assessed both by the presence of carotid plaques (31% vs 37%, p=0.45) and the cIMT (645 ± 147 mm vs 636 ± 112 mm, p = 0.64) (Table 1. next page).

Conclusion: The presence of IBD does not confer additional CV risk to axSpA. In our series, patients with axSpA and IBD showed a lower frequency of HLA B27 and a higher prevalence of psoriasis.

Table 1.

	axSpA without IBD (n=829)	axSpA with IBD (n=57)	p
Men/Women, n	272/557	15/42	0.33
Mean age (years) ±SD at the time of study	49 ± 13	49 ± 10	0.99
AS/nr-AxSpa	656/173	45/12	0.97
History of CV risk factors			
Current smoker	285 (34)	12 (21)	**0.045**
Obesitty			
Dyslipemia	280 (34)	16 (28)	0.42
Hypertension	223 (27)	16 (28)	0.79
Diabetes Mellitus	60 (7)	4 (7)	0.99
Chronic Kidney Disease	20 (2)	2 (4)	0.65
History of cardiovascular events, n (%)	40 (5)	2 (4)	0.99
Structural damage at the time of study			
Presence of syndesmophytes, n (%)	307 (37%)	23 (49%)	0.66
mSASSS	5 (1-15)	6 (3-23)	0.64
Severe sacroiliitis (grade 3,4), n (%)	436 (53)	34 (60)	0.42
CV data at the time of study			
Carotid plaques	261 (31)	21 (37)	0.45
IMT (mm)	645 ± 147	636 ± 112	0.64
IMT >= 0.9 mm	46 (6)	0 (0)	0.066

Abbreviations: AS = ankylosing spondylitis. AxSpA= axial spondylitis. CV = cardiovascular. IBD = Inflammatory bowel disease. IMT = intima-media wall thickness. Nr-axSpA = no-radiographic axial spondylitis.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3802

POS1408 REPRODUCIBILITY OF A NEW AUTOMATIC SYSTEM (CAPILLARY.IO) IN THE ANALYSIS OF NAILFOLD CAPILLAROSCOPY IMAGES

B. Gracia Tello[1,2], E. Ramos[3], C. P. Simeón-Aznar[4], V. Fonollosa Pla[4], A. Guillén-Del-Castillo[4], A. Selva-O'callaghan[4], L. Sáez-Comet[5], E. Martínez Robles[6], J. J. Rios[6], G. Espinosa[7], J. A. Todolí Parra[8], J. L. Callejas-Rubio[9], N. Ortego[9], B. Marí-Alfonso[10], M. Freire[11], P. Fanlo[12]. *[1]Hospital Clínico Universitario Lozano Blesa, Zaragoza. Spain, Internal Medicine, Zaragoza, Spain*; *[2]Zaragoza, Instituto de investigación Sanitaria de Aragón (ISSA), Zaragoza, Spain*; *[3]Zaragoza, Computer Science Graduate by University of Zaragoza, Zaragoza, Spain*; *[4]Hospital Universitari Vall d'Hebron, Unit of Autoimmune Diseases, Department of Internal Medicine, Barcelona, Spain*; *[5]Hospital Universitario Miguel Servet, Department of Internal Medicine, Zaragoza, Spain*; *[6]Hospital General Universitario La Paz, Department of Internal Medicine, Madrid, Spain*; *[7]Hospital Clínic, Department of Internal Medicine, Unit of Autoimmune Diseases, Barcelona, Spain*; *[8]Hospital La Fe, Department of Internal Medicine, Valencia, Spain*; *[9]Hospital Universitario Virgen de las Nieves, Unit of Autoimmune Diseases, Department of Internal Medicine, Granada, Spain*; *[10]Hospital Universitario Parc Taulí, Department of Internal Medicine, Sabadell, Spain*; *[11]Complejo Hospitalario Universitario de Santiago, Department of Internal Medicine, Santiago de Compostela, Spain*; *[12]Complejo Hospitalario de Navarra, Pamplona, Department of Internal Medicine, Pamplona, Spain*

Background: Nailfold Capillaroscopy is a simple, inexpensive and non-invasive technique that allows microvascular damage to be observed, gaining recent importance in the diagnosis, monitoring and prognosis of many diseases with microangiopathy. However, the variability in the results interpretation has led to the development of new computerized systems that allow the automatic analysis of capillaroscopic images.

Objectives: to compare the degree of agreement between the automatic system Capillary.io and a gold standard obtained from the agreement of 9 expert capillaroscopists and to know the degree of the interobserver reliability To demonstrate the validity of the system to detect normal and enlarged capillaries, hemorrhages, megacapillaries, ramifications and tortuosities.

Methods: a cross-sectional study was performed in which 300 random and anonymous nailfold capillaroscopic images (1165 capillaries) were analyzed by 9 experienced observers. The degree of interobserver agreement was calculated from the 5 users. Likewise, the system performed an automatic assessment of the images and their agreement with the gold standard was calculated (interobserver agreement greater than 5, 6, 7, 8 and 9 successively). The validity of the program for each variable was also analyzed using sensitivity and specificity, positive and negative predictive values, and likelihood ratios, as well as their degree of agreement using the weighted kappa statistic (95% CI, p <0.05). The programs used for statistical calculations were SPSS 22.0 and EPIDAT 3.0.

Results: the degree of interobserver agreement was 76.5% for the agreement of 5 or more observers, progressively decreasing to 15.4% for the 9 observers. Capillary.io obtained higher levels of agreement, reaching 97.7% for the 9 observers. Statistically significant results were obtained in the automated detection of all the morphological alterations analyzed Capillary.io presented a sensitivity (S) of 79.82% and a specificity (E) of 82% in the recognition of normal capillaries. The automatized system was able to recognize enlarged capillaries with a sensitivity of 86.97% and a specificity of 81.38%. Megacapillaries were detected with 89.41% sensitivity and 78.75% specificity. Similarly, the system was able to detect tortuosities (S 66.94%; E 67.71%), ramifications (S 54.34%; E 58.61%) and hemorrhages (S 71.36; E 73.97%).

Conclusion: Capillary.io demonstrated a high degree of agreement with the gold standard, stronger with greater consensus among observers. It was able to detect with great sensitivity and specificity hemorrhages and megacapillaries, very relevant alterations in microangiopathies.

REFERENCES:

[1] Roldán LMC, Franco CJV, Navas MAM. Capillaroscopy in systemic sclerosis: A narrative literature review. Rev Colomb Reumatol; 2016; 23: 250-8.

[2] Ingegnoli F, Gualtierotti R, Lubatti C, Bertolazzi C, Gutierrez M, Boracchi P, et al. Nailfold capillary patterns in healthy subjects: A real issue in capillaroscopy. Microvasc Res. 2013;90:90-5.

[3] Cutolo M, Pizzorni C, Secchi ME, Sulli A. Capillaroscopy. Best Pract Res Clin Rheumatol. 2008; 22:1093-108.

[4] Tavakol ME, Fatemi A, Karbalaie A, Emrani Z, Erlandsson BE. Nailfold Capillaroscopy in Rheumatic Diseases: Which Parameters Should Be Evaluated? BioMed Res Int. 2015; 2015: 974530.

[5] Smith V, Herrick AL, Ingegnoli F, Damjanov N, De Angelis R, Denton CP, et al. Standardisation of nailfold capillaroscopy for the assessment of patients with Raynaud's phenomenon and systemic sclerosis. Autoimmunity Reviews. 2020; 19: 102458.

Disclosure of Interests: Borja Gracia Tello Shareholder of: Co-founder and shareholder of Capillary.io., Eduardo Ramos Shareholder of: Co-founder and shareholder of Capillary.io., Carmen Pilar Simeón-Aznar: None declared, Vicent Fonollosa Pla: None declared, Alfredo Guillén-Del-Castillo: None declared, Albert Selva-O'Callaghan: None declared, Luis Sáez-Comet: None declared, Elena Martínez Robles: None declared, Juan José Rios: None declared, Gerard Espinosa: None declared, Jose Antonio Todolí Parra: None declared, Jose Luis Callejas-Rubio: None declared, Norberto Ortego: None declared, Begoña Marí-Alfonso: None declared, Mayka Freire: None declared, Patricia Fanlo: None declared
DOI: 10.1136/annrheumdis-2021-eular.4063

POS1409 AUTOMATED DETECTION OF SCLERODERMIFORM PATTERNS USING CAPILLARY.IO

E. Ramos[1], A. Guillén-Del-Castillo[2], C. P. Simeón-Aznar[2], B. Gracia Tello[3,4], V. Fonollosa Pla[2], A. Selva-O'callaghan[2], L. Sáez-Comet[5], E. Martínez Robles[6], J. J. Rios[6], G. Espinosa[7], J. A. Todolí Parra[8], J. L. Callejas-Rubio[9], N. Ortego[9], B. Marí-Alfonso[10], M. Freire[11], P. Fanlo[12]. *[1]Zaragoza, Computer Science Graduate by University of Zaragoza, Zaragoza, Spain*; *[2]Hospital Universitario Vall d'Hebron, Unit of Autoimmune Diseases, Department of Internal Medicine, Barcelona, Spain*; *[3]Hospital Clinico Universitario Lozano Blesa, Department of Internal Medicine, Zaragoza, Spain*; *[4]Zaragoza, Instituto de Investigación Sanitaria de Aragón (ISSA), Zaragoza, Spain*; *[5]Hospital Universitario Miguel Servet, Department of Internal Medicine, Zaragoza, Spain*; *[6]Hospital General Universitario La Paz, Department of Internal Medicine, Madrid, Spain*; *[7]Hospital Clínic, Department of Internal Medicine, Unit of Autoimmune Diseases, Barcelona, Spain*; *[8]Hospital La Fe, Department of Internal Medicine, Valencia, Spain*; *[9]Hospital Universitario Virgen de las Nieves, Unit of Autoimmune Diseases, Department of Internal Medicine, Granada, Spain*; *[10]Hospital Universitario Parc Taul, Department of Internal Medicine, Sabadell, Spain*; *[11]Complejo Hospitalario Universitario de Santiago, Department of Internal Medicine, Santiago de Compostela, Spain*; *[12]Complejo Hospitalario de Navarra, Department of Internal Medicine, Pamplona, Spain*

Background: A nailfold capillaroscopy procedure is a non-invasive, low-cost, and well-established examination that can be used to diagnose several rheumatic autoimmune diseases and support the necessary follow-up of patients. While the clinical implications of the technique are known, a rigorous and in-depth examination of nailfold capillaries remains as one of the major challenges to produce new advances in research and diagnosis, due to practical limitations for analysing the whole nailfold area of each patient. The difference between the different patterns established by Maricq and Cutolo makes it possible to predict the evolution that the patient will present. We introduce Capillary.io, an automatic image reading system able to recognize capillaries in images obtained with any microscope, generate automatic measurements of each capillary and take advantage of this information to report capillary morphology and patterns.

Objectives: to determine the ability to detect active and early sclerodermiform patterns of Capillary.io.

Methods: Forty-nine complete capillaroscopies, reported by expert capillaroscopists according to the different patterns manually (gold standard), were compared with the pattern detection capability of Capillary.io. A scoring system based on the algorithm of the Spanish Capillaroscopy Study Group (GREC) was performed and interpreted by capillary.io for the global interpretation of each of the capillaroscopies analyzed.
Results: Overall, 37 of the 49 capillaroscopies reported agreed with the diagnosed pattern (75.51%). Separately, the early pattern presented a concordance of 77.27% and the active pattern of 74.07%. In reference to the findings detected by the Capillary.io system, the mean overall density was 5.01 capillaries/mm in the group with the active pattern compared to 6.46 capillaries/mm in the early pattern. The density of dilations and megacapillaries was 2.81/mm and 1.21/mm in the active pattern group versus 4.69/mm and 0.4/mm in the early pattern group. Global diameters were greater in the active pattern group with an apical mean of 37.3 μm compared to 28.5 μm in the early pattern subgroup.
Conclusion: Capillary.io is a simple, easy-to-learn web system for interpreting capillaroscopic images of nail folds. It can be a very useful tool to standardize the interpretation of capillaroscopic images, not only individually for each capillary, but also jointly through the detection of different patterns.
REFERENCES:
[1] Chen K, Wang J, Pang J, Cao Y, Xiong Y, Li X, et al. MMDetection: Open MMLab Detection Toolbox and Benchmark. arXiv preprint arXiv:190607155 2019;.
[2] Cutolo M, Pizzorni C, Sulli A. Nailfold videocapillaroscopy assessment of microvascular damage in systemic sclerosis - Reply. The Journal of Rheumatology 2000 11;27:2722–2723.
[3] Cutolo M, Trombetta AC, Melsens K, Pizzorni C, Sulli A, Ruaro B, et al. Automated assessment of absolute nailfold capillary number on videocapillaroscopic images: Proof of principle and validation in systemic sclerosis. Microcirculation 2018 May;25(4):e12447.
[4] Smith V, Vanhaecke A, Herrick AL, Distler O, Guerra MG, Denton CP, et al. Fast track algorithm: How to differentiate a "scleroderma pattern" from a "non-scleroderma pattern". Autoimmu- nity Reviews 2019 nov;18(11):102394.
[5] Tavakol ME, Fatemi A, Karbalaie A, Emrani Z, Erlandsson BE. Nailfold Capillaroscopy in Rheumatic Diseases: Which Parameters Should Be Evaluated? BioMed Research International 2015;2015:1–17.
Disclosure of Interests: Eduardo Ramos Shareholder of: Co-founder and shareholder of Capillary.io, Alfredo Guillén-Del-Castillo: None declared, Carmen Pilar Simeón-Aznar: None declared, Borja Gracia Tello Shareholder of: Co-founder and shareholder of Capillary.io, Vicent Fonollosa Pla: None declared, Albert Selva-O'Callaghan: None declared, Luis Sáez-Comet: None declared, Elena Martínez Robles: None declared, Juan José Rios: None declared, Gerard Espinosa: None declared, Jose Antonio Todolí Parra: None declared, Jose Luis Callejas-Rubio: None declared, Norberto Ortego: None declared, Begoña Marí-Alfonso: None declared, Mayka Freire: None declared, Patricia Fanlo: None declared
DOI: 10.1136/annrheumdis-2021-eular.4112

POS1410

FLUORESCENCE OPTICAL IMAGING (FOI) DETECTS SUBCLINICAL INFLAMMATION IN HANDS OF PATIENTS DIAGNOSED WITH FIBROMYALGIA SYNDROME AND OTHER RHEUMATIC DISEASES

P. Welker[1], J. Ferl[2], S. Ohrndorf[3], A. Briel[4], V. Failli[5]. [1]*Charité, Functional Anatomy, Berlin, Germany*; [2]*Medical Faculty University Hospital Magdeburg, Clinical Chemistry and Pathobiochemistry, Magdeburg, Germany*; [3]*Charité, Rheumatology and Clinical Imunology, Berlin, Germany*; [4]*nanoPET GmbH, Pharma, Berlin, Germany*; [5]*Xiralite, GmbH, Berlin, Germany*

Background: Myalgias are a common symptom of infections and diseases of the rheumatic type but can also occur in the case of physical overstress or as an undesirable drug side effect. Anamnesis, clinical examination and determination of specific laboratory parameters are usually helpful for diagnosis, but do not always lead to correct results. Particularly, differentiation between the diagnoses of fibromyalgia syndrome (FMS), polymyalgia rheumatica (PMR), and other myalgic diseases of the rheumatic type is often difficult. FOI are playing an increasingly role as quantifiable and sensitive diagnostic imaging methods. After injecting a fluorescent dye, the signal intensity enables visualization of the microcirculation. This can be used for the differential diagnosis of inflammatory, degenerative, muscular and connective tissue-associated diseases.
Objectives: The present work investigates the potential of this method for the detection of subclinical inflammatory processes to differentiate between FMS and various rheumatic diseases which are accompanied by myalgia.
Methods: Analyses of subjects without clinical symptoms (n = 59) were compared with patients with a clinical diagnosis of FMS (n = 63), PMR (n = 5), or polymyalgia as a consequence of other diseases (PM, n = 6), Sjogren's syndrome (SS, n = 20), and erosive rheumatoid arthritis (RA, n = 162). The FMS patients were stratified according to primary (n = 31) and secondary (n = 32) pathology. FOI signal intensity (SI) was defined by ratio of areas with SI in patients and controls. Clinical and FOI examinations were carried out under the conditions of standard outpatient rheumatological care. The laboratory parameters were created in certified medical laboratories.
Results: Only 21% of all patients diagnosed with FMS are seropositive for rheumatic factors. Secondary FMS have higher values than primary FMS (26 versus 13%). In contrast, 79% of the patients with RA, 75% of the SS patients, and 100% of the patients with PMR are seropositive. On average, both the CRP values and the ESR of FMS patients were in the normal range, whereas in the other cohort the mean values were significantly increased. X-ray examinations showed erosions in all patients with RA and in 80% with PMR, whereas this was only the case in less than 15% of FMS and SS patients. However, in nearly 80% of patients both with primary and secondary FMS, increased SI value as a sign of inflammation could be detected by FOI. While in patients with RA or PMR an accumulation of the dye in the metacarpophalangeal joints can be detected in an early phase of the FOI examination, in the FMS or SS patients signal increases can be detected in the later phases in the area of connective tissue, tendons and muscles (Figure 1).
Conclusion: The examination with FOI gives more precise information on the localization and extent of an inflammation in the hands and can thus make an important contribution to differential diagnosis and optimization of therapy. The present work demonstrates a high potential in the detection and localization of subclinical inflammatory processes which cannot be detected in FMS patients with other methods, often leading to a psychosomatic diagnosis. In future, there will a requirement for diagnostic technologies that can be used widely and are suitable for interlinking therapy with diagnostics more closely than before.

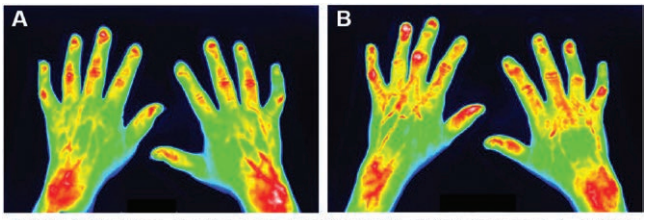


Figure 1: Examples of FOI images in patients with clinical diagnosed: A. primary FMS or, B. secondary FMS as an accompanying syndrome of RA. Analysis of intermediate/late phase (P2/3) of fluorescence dye (indocyanine green) distribution.

Disclosure of Interests: Pia Welker Employee of: nanoPET GmbH, Josefine Ferl: None declared, Sarah Ohrndorf: None declared, Andreas Briel Shareholder of: Xiralite GmbH, nanoPET GmbH, Vieri Failli Employee of: Xiralite GmbH
DOI: 10.1136/annrheumdis-2021-eular.4268

Public health, health services research, and health economics

POS1411 EARLY IDENTIFICATION OF AXIAL SPONDYLOARTHRITIS IN A MULTI-ETHNIC ASIAN POPULATION

L. Xiang[1,2], W. Fong[1,2,3], A. Low[1,2,3], Y. Y. Leung[1,2,3], M. Gandhi[4,5,6], X. Xin[7], E. Uy[1], L. Hamilton[8], J. Thumboo[1,2,3]. *[1]Singapore General Hospital, Department of Rheumatology and Immunology, Singapore, Singapore*; *[2]National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore*; *[3]Duke-NUS Medical School, NA, Singapore, Singapore*; *[4]Duke-NUS Medical School, Centre for Quantitative Medicine, Singapore, Singapore*; *[5]Singapore Clinical Research Institute, Biostatistics, Singapore, Singapore*; *[6]Tampere University, The Center for Child Health Research, Tampere, Finland*; *[7]Singapore General Hospital, Academic Clinical Program for Medicine, Singapore, Singapore*; *[8]Norfolk and Norwich University Hospitals NHS Foundation Trust, Department of Rheumatology, Norforlk, United Kingdom*

Background: To facilitate earlier diagnosis of spondyloarthritis (SpA), we have previously cross-culturally adapted a self-administered screening questionnaire.
Objectives: We aimed to improve the sensitivity of this questionnaire as a screening tool by comparing various scoring methods.
Methods: Subjects newly referred to a rheumatology clinic self-administered the questionnaire before seeing a rheumatologist. Identification of axial SpA by the questionnaire using original scoring (Method A) and scoring based on Assessment of SpondyloArthritis International Society (ASAS) inflammatory back pain (IBP) criteria (Method B), ASAS referral criteria (Method C), ASAS classification criteria (Method D) and a combination of ASAS referral and classification criteria (Method E) were compared to classification by the ASAS classification criteria and diagnosis by rheumatologist. Since Methods B-E were based on SpA features, we compared self-reported vs rheumatologist-documented features in subjects with axial SpA.
Results: Of 1418 subjects (age: 54 ± 14 years, female: 73%), 39 were classified as axial SpA cases by classification criteria. Methods A-E yielded sensitivities of 39%, 72%, 67%, 49% and 85%, respectively, among patients newly referred to the rheumatology clinic (Table 1). Rheumatologist-documented clinical SpA features exceeded self-report for IBP (62 vs 44%) and uveitis (15 vs 5%). The reverse was true for arthritis (21 vs 80%), enthesitis (28 vs 33%), dactylitis (3 vs 18%), good response to NSAIDs (33 vs 41%) and family history for SpA (5 vs 10%).

Table 1. Performance of the five scoring methods for the cross-culturally adapted Hamilton axial SpA questionnaire.

Scoring method	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)
Method A	38.5	93.7	14.7	98.2
	(23.4 – 55.4)	(92.3 – 94.9)	(8.5 – 23.1)	(97.3 – 98.8)
Method B	71.8	73.1	7.0	98.9
	(55.1 – 85.0)	(70.7 – 75.4)	(4.7 – 10.0)	(98.1 – 99.5)
Method C	66.7	77.8	7.8	98.8
	(49.8 – 80.9)	(75.5 – 80.0)	(5.2 – 11.3)	(98.0 – 99.4)
Method D	48.7	74.9	5.2	98.1
	(32.4 – 65.2)	(72.5 – 77.2)	(3.2 – 8.0)	(97.1 – 98.8)
Method E	84.6	37.2	3.7	98.8
	(69.5 – 94.1)	(34.6 – 39.8)	(2.5 – 5.1)	(97.5 – 99.6)

Method A: the original scoring defined by the questionnaire developers; Method B: a scoring based on the ASAS IBP criteria; Method C: a scoring based on the ASAS referral criteria; Method D: a scoring based on the ASAS classification criteria for axial and peripheral SpA; Method E: a scoring based on a combination of the ASAS referral and classification criteria.

Conclusion: A self-administered questionnaire scored based on a combination of ASAS referral and classification criteria achieved high sensitivity in identifying axial SpA in subjects referred to a rheumatology clinic. This supports its evaluation as a screening tool for axial SpA in the general population.

REFERENCES:

[1] Xiang L, Teo EPS, Low AHL, Leung YY, Fong W, Xin X, et al. Cross-cultural adaptation of the Hamilton axial spondyloarthritis questionnaire and development of a Chinese version in a multi-ethnic Asian population. Int J Rheum Dis. 2019;22(9):1652-60.
[2] Sieper J, Rudwaleit M, Baraliakos X, Brandt J, Braun J, Burgos-Vargas R, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. Annals of the rheumatic diseases. 2009;68 Suppl 2:ii1-44.
[3] Poddubnyy D, van Tubergen A, Landewe R, Sieper J, van der Heijde D. Development of an ASAS-endorsed recommendation for the early referral of patients with a suspicion of axial spondyloarthritis. Annals of the rheumatic diseases. 2015;74(8):1483-7.
[4] Rudwaleit M, van der Heijde D, Landewe R, Akkoc N, Brandt J, Chou CT, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Annals of the rheumatic diseases. 2011;70(1):25-31.

Acknowledgements: This work was supported by a Health Services Research Grant (HSRG) from the Singapore Ministry of Health National Medical Research Council [grant number: NMRC/HSRG/0075/2017].
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.449

POS1412 IDENTIFYING HIGH-COST DRUGS FOR RARE RHEUMATIC DISEASES IN ROUTINELY COLLECTED NHS DATA. RESULTS FROM A PILOT STUDY OF RITUXIMAB USE IN VASCULITIS USING DATA FROM THE NATIONAL DISEASE REGISTRATION SERVICE AND THE REGISTRATION OF COMPLEX RARE DISEASES-EXEMPLARS IN RHEUMATOLOGY (RECORDER) PROJECT

C. Godsave[1], M. Chakravorty[2], M. Rutter[2,3,4], P. Lanyon[2,3,4,5], J. Aston[4], M. Bythell[4], S. Stevens[4], F. Pearce[2,3,4,5]. *[1]Royal Derby Hospital, Rheumatology, Derby, United Kingdom*; *[2]Nottingham University Hospitals NHS Trust, Rheumatology, Nottingham, United Kingdom*; *[3]University of Nottingham, Division of Epidemiology and Public Health, Nottingham, United Kingdom*; *[4]Public Health England, National Congenital Anomaly and Rare Disease Registration Service, London, United Kingdom*; *[5]National Institute for Health Research (NIHR), Nottingham Biomedical Research Centre, Nottingham, United Kingdom*

Background: Understanding real-world usage of high-cost drugs is crucial to support planning, adoption of innovation and reduce unwarranted variation in treatment. Hospital Episode Statistics (HES) contain diagnoses (coded by ICD-10) and procedures/treatments (coded by OPCS) for all daycase or inpatient care in England. However, OPCS codes are not specific for individual drugs, for example X921 (cytokine inhibitors band 1) includes rituximab (RTX) and 15 other drugs.
Objectives: We aimed to validate the accurate identification of patients treated with RTX for ANCA-associated vasculitis (AAV) using HES data.
Methods: We used data from the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) at Public Health England and their legal permissions (CAG 10-02(d)/2015). We extracted records from HES of all patients treated at two hospitals during financial year 2018/19 who ever had a coded diagnosis of granulomatosis with polyangiitis (GPA, M313), eosinophilic granulomatosis with polyangiitis (EGPA, M301), microscopic polyangiitis (MPA, M317), polyarteritis nodosa (PAN, M300) or arteritis unspecified (I776). Where people had multiple diagnoses of vasculitis, the most specific was considered their diagnosis. Enabled by data sharing agreements, we reviewed hospital records of those patients to validate diagnoses and whether X921 reliably identified RTX. We report the positive predictive value and sensitivity of the coding for X921 and GPA/EGPA/MPA for identifying people with AAV who are treated with RTX.
Results: At Trust 1 records ever coded with GPA/EGPA/MPA identified 74 people, 69 of whom had AAV confirmed in their medical notes. Among these 74 patients there were 59 episodes coded with X921 procedure codes, of which 56 correctly identified a RTX infusion given for AAV. A total of 64 RTX infusions were given to people with AAV – 3 missed infusions were X921 procedures in patients who had coded diagnoses of PAN or I776 but never GPA/EGPA/MPA and 5 infusions were not coded as X921.
The same analysis at Trust 2 identified 46 people, 44 of whom had AAV confirmed in their medical notes. Among patients identified with AAV there were 17 episodes coded as X921, of which 15 correctly identified a RTX infusion. A total of 23 infusions were given to people with AAV: 4 infusions were X921 procedures in patients who had coded diagnoses of PAN or I776 but never GPA/EGPA/MPA, and 4 infusions were not coded as X921.

Table 1. Summary of Positive Predictive Values (PPV) applying our algorithm to identify AAV diagnoses and RTX use

	Trust 1	Trust 2	Combined
Diagnosis of AAV and coded as AAV	69	44	113
AAV coded	74	46	120
Diagnosis of AAV under any code	73	55	128
PPV AAV ascertainment (95% CI)	93.2% (84.9-97.8)	95.7% (85.2-99.5)	94.2% (88.4-97.6)
Sensitivity of AAV ascertainment (95% CI)	94.5% (86.8-98.5)	80.0% (67.0-89.6)	88.3% (81.4-93.3)
RTX given in people coded as AAV	56	15	71
RTX coded in people coded as AAV	59	17	76
RTX given for AAV under any diagnostic or procedure code	64	23	87
PPV RTX ascertainment (95% CI)	94.9% (85.9-98.9)	88.2% (63.6-98.5)	93.4% (85.3-97.8)
Sensitivity of RTX ascertainment (95% CI)	87.5% (76.8-94.4)	65.2% (42.7-83.6)	81.6% (71.9-89.1)

Conclusion: HES data identified patients treated with RTX for AAV with a PPV of 93.4% (85.3-97.8) and sensitivity of 81.6% (71.9-89.1). This demonstrates the utility of national data to identify people receiving RTX for AAV. The RECORDER project, within the National Disease Registration Service plans to conduct real-world studies of the high-cost drug RTX, given for AAV, across the whole of England, and assess whether geography, demographics or socioeconomic factors influence frequency of prescription of this, and potentially other, high-cost drugs in line with the NHS long term plan.

REFERENCES:

[1] Ward-Platt M, Stevens S, Miller N. I18 The national congenital anomaly and rare disease registration service (NCARDRS): The first year

Acknowledgements: I have no acknowledgements to declare.

Disclosure of Interests: Cattleya Godsave: None declared, Mithun Chakravorty: None declared, Megan Rutter: None declared, Peter Lanyon Grant/research support from: P.C.L. is a recipients of a grant from Vifor Pharma. Vifor Pharma had no influence on the design, conduct or interpretation of this study., Jeanette Aston: None declared, Mary Bythell: None declared, Sarah Stevens: None declared, Fiona Pearce Grant/research support from: I have received a research grant from Vifor Pharma

DOI: 10.1136/annrheumdis-2021-eular.1591

POS1413 INTERVAL BETWEEN SYMPTOM ONSET AND DIAGNOSIS AMONG PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES IN A MULTI-ETHNIC ASIAN POPULATION

L. Xiang[1,2], A. Low[1,2,3], Y. Y. Leung[1,2,3], W. Fong[1,2,3], M. Gandhi[3,4], S. Yoon[3], T. C. Lau[2,5], D. R. Koh[2,5], J. Thumboo[1,2,3]. [1]*Singapore General Hospital, Department of Rheumatology and Immunology, Singapore, Singapore*; [2]*National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore*; [3]*Duke-NUS Medical School, NA, Singapore, Singapore*; [4]*Singapore Clinical Research Institute, Biostatistics, Singapore, Singapore*; [5]*National University Hospital, Department of Medicine, Singapore, Singapore*

Background: The interval between symptom onset and diagnosis can often be longer than is ideal in autoimmune rheumatic diseases (ARDs).

Objectives: We aimed to characterise this interval among patients newly diagnosed with ARDs in a multi-ethnic Asian population and to identify factors associated with a longer interval.

Methods: We used Scott's model of pathways to treatment to characterise the interval between symptom onset and diagnosis into 4 intervals: #1 between symptom onset and first seeking medical attention, #2 between first medical attention and rheumatology referral, #3 between rheumatology referral and first rheumatology assessment, and #4 between first rheumatology assessment and diagnosis. Linear regression models were used to identify factors associated with a longer the overall interval between symptom onset and diagnosis and Interval #1.

Results: Among 259 patients (age: 51±15 years, female: 71%, most common three ARDs: rheumatoid arthritis (n = 75), axial spondyloarthritis (n = 40) and psoriatic arthritis (n = 35)), the median overall interval was 11.5 months. Interval #1 (median = 4.9 months) was significantly longer than the other intervals (Table 1). Patients with axial spondyloarthritis had a significantly longer overall interval (median = 38.7 months) and Interval #1 (median = 26.6 months) compared to patients with RA (median = 7.6 and 3.5 months, respectively), PsA (median = 7.0 and 2.6 months, respectively) and the other ARDs. Gender was the only patient-related factor significantly associated with the overall interval (reference = male, coefficient = -15.3, p = 0.033) in regression models.

Conclusion: A longer than ideal interval between symptom onset and diagnosis was observed among patients with ARDs. This was primarily due to a relatively long interval between symptom onset and first seeking medical attention, and highlights the importance of interventions targeting patients prior to first medical attention in reducing the duration between symptom onset and diagnosis.

REFERENCES:

[1] Scott SE, Walter FM, Webster A, Sutton S, Emery J. The model of pathways to treatment: conceptualization and integration with existing theory. Br J Health Psychol. 2013;18(1):45-65.

Table 1. Interval between symptom onset and diagnosis

	Overall interval, months, median (lower and upper quartiles)†	Interval #1, months, median (lower and upper quartiles)	Interval #2, months, median (lower and upper quartiles)	Interval #3, months, median (lower and upper quartiles)	Interval #4, months, median (lower and upper quartiles)
Overall	11.5	4.9	0.3	1.5	0.0
(n = 259)	(4.7 – 36.0)	(1.0 – 24.0)	(0.0 – 3.9)	(0.8 – 1.8)	(0.0 – 1.2)
RA	7.6	3.5	0.2	1.3	0.0
(n = 75)	(3.1 – 14.8)	(1.3 – 11.6)	(0.0 – 2.5)	(0.6 – 1.6)	(0.0 – 0.2)
AxSpA	38.7	26.6	1.6	1.6	0.0
(n = 40)	(9.6 – 66.7)	(4.2 – 56.1)	(0.0 – 7.6)	(1.2 – 2.3)	(0.0 – 2.0)
PsA	7.0	2.6	0.5	1.6	0.0
(n = 35)	(3.0 – 28.4)	(0.2 – 11.3)	(0.2 – 3.9)	(0.6 – 1.7)	(0.0 – 0.0)
Seronegative IA	12.0	6.4	0.1	1.4	0.0
(n = 21)	(4.7 – 22.8)	(1.9 – 34.4)	(0.0 – 4.6)	(1.3 – 1.5)	(0.0 – 0.8)
SjS	14.2	4.6	0.3	1.6	0.8
(n = 27)	(6.0 – 48.0)	(0.6 – 19.0)	(0.0 – 3.9)	(0.9 – 1.9)	(0.0 – 2.3)
UCTD	15.7	2.2	0.8	1.6	1.2
(n = 27)	(5.1 – 39.8)	(0.7 – 24.0)	(0.1 – 8.1)	(0.5 – 1.8)	(0.0 – 2.1)
Other ARDs	8.1	6.3	0.2	1.5	0.3
(n = 34)	(5.3 – 36.0)	(0.9 – 31.7)	(0.0 – 1.1)	(1.2 – 1.8)	(0.0 – 1.1)

Overall interval and Intervals #1-4: refer to abstract for definitions; RA: rheumatoid arthritis; axSpA: axial spondyloarthritis; PsA: psoriatic arthritis; IA: inflammatory arthritis; SjS: Sjögren's syndrome; UCTD: undifferentiated connective tissue disease; other ARDs: systemic lupus erythematosus, systemic sclerosis, idiopathic inflammatory myopathies, palindromic rheumatism and overlap syndromes.†Intervals #1-4 did not sum to the overall interval mainly due to the fact that Intervals #1-4 might not available for all patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1713

POS1414 RHEUMATOID ARTHRITIS AND INTERSTITIAL LUNG DISEASE: PREVALENCE AND DRUG PRESCRIPTIONS IN GERMAN CLAIMS DATA

K. Albrecht[1], A. Strangfeld[1], U. Marschall[2], J. Callhoff[1]. [1]*German Rheumatism Research Centre, Epidemiology, Berlin, Germany*; [2]*BARMER Institute for Health System Research, Department Medicine and Health Services Research, Berlin, Germany*

Background: Persons with rheumatoid arthritis (RA) have an increased risk of interstitial lung disease (ILD). ILD is a serious extraarticular manifestation in RA with a significantly increased mortality but without evidence-based drug therapy (1).

Objectives: The aim of this analysis was to investigate the frequency of ILD diagnosis in RA using claims data and to identify the medications prescribed.

Methods: Data from a large German statutory health insurance fund were used to identify persons with one inpatient or two outpatient diagnoses of RA (ICD-10: M05, M06) and ILD (J84.1, J84.8, J84.9 and M05.1+J99.0) in 2019. Specialist care by rheumatologists and/or pulmonologists was identified using physician specialty numbers. Drug prescriptions of glucocorticoids, conventional synthetic disease modifying antirheumatic drugs (csDMARDs: methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, mycophenolate), biologic (b) DMARDs (abatacept, rituximab, TNF inhibitors, tocilizumab) or targeted synthetic (ts) DMARDs (tofacitinib) were identified by ATC codes. Prescriptions were included if a person received at least one prescription of the respective drug in 2019.

Results: Among 7,479,000 persons over 18 years of age and insured in 2019 a total of 2.0% (n=148,000) had a diagnosis of RA and 1.1% (n=1,600) of those had an additional diagnosis of ILD. The majority of persons with RA+ILD

diagnosis was older than 70 years (59%), mean age was 72 years, 68% were female and 41% had a diagnosis of serpositive RA (M05). 4 out of 5 patients were in rheumatologist or pulmonologist care (36% both, 22% only rheumatologist, 22% only pulmonologist). In total, 67% received glucocorticoids, 49% csDMARDs and 19% bDMARDs and 1.8% tofacitinib. TNF inhibitors were the most frequently prescribed bDMARDs followed by abatacept and tocilizumab. Persons without specialized care received considerably less DMARD therapy (Table 1). Nintedanib was prescribed to 14 patients, pirfenidon to 10 patients, all of them were in specialist care.

Table 1. Demographics and treatment of persons with RA and ILD diagnosis, numbers are percentages unless indicated otherwise.

Variable	Not treated by rheumatologist or pulmonologist	Treated by rheumatologist and/or pulmonologist	All
N (%)	326 (20%)	1274 (80%)	1,600 (100%)
Age, mean years (std)	75 (10)	72 (10)	72 (10)
<70 years	35	43	41
70 to 80 years	31	39	37
>80 years	35	18	22
Female sex	67	69	68
Glucocorticoids	49	72	67
csDMARDs	**24**	**56**	**49**
MTX	13	30	27
Leflunomide	4.9	10	8.9
(Hydroxy-)chloroquine	2.8	9.0	7.8
Mycophenolate	1.2	2.2	2.0
Sulfasalazine	2.1	3.8	3.4
bDMARDs	**7**	**22**	**19**
TNF-alpha Inhibitors	3.4	9.0	7.9
Abatacept	2.1	5.6	4.9
Tocilizumab	1.2	3.6	3.1
Rituximab	0.9	2.9	2.5
Tofacitinib	1.5	1.9	1.8

Conclusion: ILD was diagnosed in one of 100 persons with RA diagnosis. Specialist care is necessary to provide disease-specific therapies. While methotrexate is the most commonly used DMARD, the bDMARD prescription is heterogeneous.

REFERENCES:

[1] Hyldgaard C, Ellingsen T, Hilberg O, Bendstrup E. Rheumatoid Arthritis-Associated Interstitial Lung Disease: Clinical Characteristics and Predictors of Mortality. Respiration. 2019;98(5):455-460.

Acknowledgements: The study was supported by the German Federal Ministry of Education and Research within the network TARISMA [01EC1902A].

Disclosure of Interests: Katinka Albrecht: None declared, Anja Strangfeld: None declared, Ursula Marschall Employee of: Employee of the BARMER statutory health insurance fund, Johanna Callhoff: None declared

DOI: 10.1136/annrheumdis-2021-eular.2355

POS1415 SOCIO-ECONOMIC IMPACT OF SJÖGREN'S SYNDROME IN WESTERN SWITZERLAND: A CROSS-SECTIONAL STUDY

K. Cunha Rodrigues[1], A. Grosjean[2], T. Hügle[1], A. Dumusc[1]. *[1]University Hospital Lausanne, Rheumatology, Lausanne, Switzerland*; *[2]Sjögren's Patients Association for Western Switzerland, (ARSYS), Vevey, Switzerland*

Background: Several studies investigated the socio-economic impact of Sjögren's syndrome (SS) showing an increased risk of work disability and a reduced health-related quality of life. SS is also associated with increased direct and indirect healthcare costs. There are no published data about Switzerland, a country with high resources and easy access to healthcare except dental care, which is rarely reimbursed.

Objectives: To evaluate the professional and economic impact of SS in patients living in Western Switzerland.

Methods: Cross-sectional survey-based study conducted in December 2020, during the pandemic. Patients suffering from SS and living in Western Switzerland (Geneva and Lausanne region) were invited by the regional association of patients with SS to complete a survey assessing the socio-economic impact of SS.

Results: Among the 86 patients who were contacted, 55 (64%) completed the survey. Participants were predominantly female (95%) with a mean (SD) age of 54.2 (12.3). Mean (SD) EULAR SS Patient Reported Index (ESSPRI) was 6.5 (1.6), assessing pain, fatigue and dryness.

In the working age population (under 65, n=39), 64% of the participants reported to be employed, 88% of whom working part-time. They reported to work 23.3 (10.1) hours per week (mean, SD). 60% reported SS-related work incapacity periods during the past year. 72% of participants had to reduce their working hours and 27% had to change careers due to their medical condition. 16% benefited from an adaptation of their workstation to their health status.

In terms of work disability, 27% of the participants depended on disability insurance pension, of whom 38% received a full pension. 16% of the participants applied for a disability pension and were waiting for an administrative decision. A minority of participants (11%) reported to receive a minimum subsistence allowance from the local social service.

Participants estimated to pay 2752 CHF (3000) per year (median, IQR) out of their own pocket (Swiss monthly median wage: 6500 CHF) for health care not covered by health insurances. 95% of the patients had to pay for dental medicine costs, at least partially. Public health insurance contributed to dental costs for 44% of the patients and private health insurance for 28% of them. 22% of the patients reported to limit dental care for financial reasons.

Conclusion: Two-thirds of the patients with SS remained in active employment, but the majority of them working in part-time, with a substantial loss of income. One third of the patients are work disabled and depend on a disability pension. Dental care was not reimbursed in half of the patients by their health insurance, leading to dental care access restriction for 20% of the patients with SS. Despite a relatively high wage level in Switzerland, SS represents a substantial financial burden for most of the patients.

REFERENCES:

[1] Mandl T, Jørgensen TS, Skougaard M, Olsson P, Kristensen LE. Work Disability in Newly Diagnosed Patients with Primary Sjögren Syndrome. J Rheumatol. 2017 Feb;44(2):209-215.

[2] Meijer JM, Meiners PM, Huddleston Slater JJ, Spijkervet FK, Kallenberg CG, Vissink A, Bootsma H. Health-related quality of life, employment and disability in patients with Sjogren's syndrome. Rheumatology. 2009 Sep;48(9):1077-82.

[3] Westhoff G, Dörner T, Zink A. Fatigue and depression predict physician visits and work disability in women with primary Sjögren's syndrome: results from a cohort study. Rheumatology. 2012 Feb;51(2):262-9.

[4] Miyamoto ST, Valim V, Fisher BA. Health-related quality of life and costs in Sjögren's syndrome. Rheumatology. 2019 Feb 15:key370. doi: 10.1093/rheumatology/key370. Epub ahead of print.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2721

POS1416 THE IMPACT OF NON-PERSISTENCE ON RESOURCE UTILIZATION COSTS IN IMMUNE-MEDIATED RHEUMATIC DISEASES

N. Carballo[1], E. Garcia-Alzorriz Morral[2], O. Ferrández-Quirante[1], C. Perez-Garcia[3], M. E. Navarrete-Rouco[1], X. Duran[4], J. Monfort[3], F. Cots[2], S. Grau[1]. *[1]Hospital del Mar, Pharmacy Department, Barcelona, Spain*; *[2]Hospital del Mar, Management Control Department, Barcelona, Spain*; *[3]Hospital del Mar, Rheumatology Department, Barcelona, Spain*; *[4] Institute Hospital del Mar for Medical Research (IMIM), Methodology and Biostatistics Support Unit, Barcelona, Spain*

Background: Rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) are chronic progressive immune-mediated rheumatic diseases (IMRD) that can cause a progressive disability and joint deformation and thus can impact in healthcare resource utilization (HCRU) and costs.

Objectives: To describe the HCRU and treatment costs in IMRD patients initiating subcutaneous tumour necrosis factor-alpha inhibitors (SC-TNFi) therapy, based on treatment persistence.

Methods: Retrospective cohort study including all naïve patients initiating SC-TNFi therapy for IMRD from 2015-2018 in a tertiary university hospital.

Patients were divided into two cohorts: persistent and non-persistent. Treatment persistence was estimated as the duration of time from SC-TNFi therapy initiation to discontinuation during one year of follow-up.

SC-TNFi therapy and HCRU costs (outpatient care, rheumatology specialized outpatient care, inpatient care, emergency care, laboratory testing and other non- biological therapies) were calculated one year before and after initiation of SC-TNFi and compared between persistence and non-persistence groups.

Results: 110 patients were identified.

Baseline characteristics: Non-persistent cohort (n=25) versus Persistent cohort (n=85): median age 48.6(12.7) vs 47.3(15.4) (p=0.692). Female (n=12;48%) vs (n=49;57.6%) (p=0.493). Race: Caucasian (n=22;88%), Asiatic (n=3;12%), Other (n=0;0%) vs Caucasian (n=75;88.2%), Asiatic (n=5;5.9%), Other (n=5;5.9%) (p=0.351).IMRD: RA (n=14;56%),PsA (n=2;8%), AS (n=4;16%), other spondyloarthropathy (n=5;20%) vs RA (n=34;40%),PsA (n=11;12.9%), AS (n=24;28.3%), other spondyloarthropathy (n=16;18.8%) (p=0.470). SC-TNFi therapy: adalimumab (n=4;16%), etanercept commercial (n=4;16%), etanercept biosimilar1 (n=5;20%), etanercept biosimilar2 (n=5;20%), golimumab (n=5;20%), certolizumab (n=2;8%) vs adalimumab (n=22;25.9%), etanercept commercial (n=11;12.9%), etanercept biosimilar1 (n=7;8.3%), etanercept biosimilar2 (n=10;11.8%), golimumab (n=24;28.2%), certolizumab (n=11;12.9%) (p=0.398).

Overall cost of SC-TNFi treatment: Non-persistent 11218.81€ (6444.32), persistent 10470.19€ (3465.48); p= 0.658.

Table 1. HCRU costs

	Non-persistent(n=25)	Persistent(n=85)	Total(n=110)	P
HCRU costs 12 months prior to SC-TNFi initiation,€(SD)				
Outpatient care	243.48(828.86)	87.17(293.61)	122.70(471.20)	0.204
Rheumatology outpatient care	216.39(169.88)	174.79(101.06)	184.24(120.55)	0.224
Inpatient care	500.41(1542.93)	170.34(846.47)	245.36(1046.74)	0.571
Emergency care	37.77(66.00)	39.30(83.16)	38.95(79.31)	0.850
Laboratory testing	376.12(195.59)	388.20(207.07)	385.46(203.70)	0.458
Other non-biological therapies	10.77(39.83)	36.79(250.55)	30.88(221.01)	0.803
Total	1384.94(1816.17)	896.60(1247.60)	1007.59(1402.87)	0.299
HCRU costs 12 months post SC-TNFi initiation,€(SD)				
Outpatient care	106.11 (172.85)	76.67 (112.90)	83.36 (128.67)	0.682
Rheumatology outpatient care	327.29(170.10)	195.58(100.05)	225.52(130.99)	**<0.001**
Inpatient care	89.35(446.77)	80.86(466.54)	82.79(460.11)	0.969
Emergency care	89.14(171.89)	36.06(106.23)	48.12(125.31)	0.198
Laboratory testing	182.14(128.62)	146.86(141.48)	154.88(138.89)	0.061
Other non-biological therapies	3859.80(4043.86)	25.89(116.05)	897.24(2493.21)	**<0.001**
Total	4653.84(4269.61)	561.93(682.14)	1491.91(2709.23)	**<0.001**

Conclusion: - Non-persistence was observed in less than a quarter of the patients.
- No differences in the costs of SC-TNFi treatment were observed between the persistent and non-persistent groups, leading us to believe that persistence may not be associated with SC-TNFi costs offsets for patients with IMRD.
- During the period post SC-TNFi initiation, the costs of rheumatologic outpatient care and treatment with other non-biological therapies as well as total costs were statistically significantly lower in the persistent cohort. These results suggest that persistence may be associated with HCRU cost savings for IMRD patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3510

POS1417 DO SOCIAL FACTORS IMPACT ON BIOLOGICS COSTS IN RHEUMATOID ARTHRITIS? RESULTS FROM THE MOROCCAN RBSMR REGISTRY

S. Farih[1], H. Rkain[1,2], S. Fellous[1], S. Ahid[3], R. Abouqal[4], T. Latifa[1], I. Hmamouchi[5,6], L. Achemlal[7], I. El Bouchti[8], A. EL Maghraoui[9], I. Ghozlani[10], H. Hassikou[11], T. Harzy[12], I. Linda[13], O. Mkinsi[14], R. Niamane[15], R. Bahiri[16], F. Allali[1]. *[1] El Ayachi Hospital, Ibn Sina University Hospital, Department of Rheumatology B, Salé, Morocco*; *[2]Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Physiology Laboratory, Rabat, Morocco*; *[3]Mohammed V University, Research Team of Pharmacoeconomics & Pharmacoepidemiology, Rabat, Morocco*; *[4]Faculty of Medicine and Pharmacy, Mohammed V University, Laboratory of Biostatistical, Clinical and Epidemiological Research, Rabat, Morocco*; *[5]Faculty of Medicine and Pharmacy, Mohammed V University, Laboratory of Biostatistical, Clinical and Epidemiological Research, Rabat, Morocco*; *[6]Provincial Hospital of Temara, Department of Rheumatology, Temara, Morocco*; *[7]Military Hospital Mohammed V, Ibn Sina University Hospital, Department of Rheumatology, Rabat, Morocco*; *[8]Arrazi University Hospital, Department of Rheumatology, Marrakech, Morocco*; *[9]Private Medical Office, Private Medical Office, Rabat, Morocco*; *[10]Department of Rheumatology, University Hospital, Agadir, Morocco*; *[11]Military Hospital Moulay Ismail, Hassan II University Hospital, Department of Rheumatology, Meknès, Morocco*; *[12] Hassan II University Hospital, Department of Rheumatology, Fes, Morocco*; *[13]Mohammed VI University Hospital, Department of Rheumatology, Oujda, Morocco*; *[14] Ibn Rochd University Hospital, Department of Rheumatology, Casablanca, Morocco*; *[15] Military Hospital Avicenne, Mohammed VI University Hospital, Department of Rheumatology, Marrakech, Morocco*; *[16]El Ayachi Hospital, Ibn Sina University Hospital, Department of Rheumatology A, Salé, Morocco*

Background:
Objectives: The aim of this study was to estimate the annual direct cost of biologics in rheumatoid arthritis and to evaluate the impact of social factors on biological use and costs.
Methods: Patients in the Moroccan register of biologicals (RBSMR) with available 1-year data were included. Variables related to socio-economic status, disease and biological were collected. Direct costs included prices of biologics, costs of infusions, and subcutaneous injections. Biological use and costs were compared based on social factors.
Results: Our study included 197 patients (female sex of 86.8%, mean age of 52.3 ± 11 years). Patients were on one of the following therapies: Rituximab (n=132), Tocilizumab (n=37) or TNF-blockers (n=28). 44.2% of included patients have the RAMED medical assistance (health insurance scheme for the economically underprivileged). Illiteracy was noted in 45.7% of cases. Median one-year direct costs per patient were €1,665 [€1,472 - €9,879].
There was no statistically significant difference in costs between men and women (p>0.05), between illiterate and literate (p>0.05). There was a statistically significant difference in costs between patients with the RAMED medical assistance scheme and other health insurances (p<0.01).
Conclusion: This study showed that Moroccan RA patients had equal access to biologics regardless of their gender or level of education. Indeed, the insurance system influence the costs of biologics. Accessibility of those expensive treatments in a developing country seems be explained by efforts of the Moroccan ministry of health who has allocated a substantial budget for biologic DMARDs for patients with RAMED in the tertiary structures in our country.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4225

Epidemiology, risk factors for disease or disease progression

POS1418 REALIZING EARLY RECOGNITION OF ARTHRITIS IN TIMES OF INCREASED TELEMEDICINE: THE VALUE OF PATIENT-REPORTED SWOLLEN JOINTS

C. Rogier[1], B. Van Dijk[2], E. Brouwer[3], P. De Jong[1], A. Van der Helm - van Mil[1,2]. *[1]Erasmus MC, Department of Rheumatology, Rotterdam, Netherlands*; *[2]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*; *[3]University Medical Center Groningen, Department of Rheumatology, Groningen, Netherlands*

Background: Early diagnosis and management of patients with inflammatory arthritis(IA) are critical to improve long-term patient-outcomes. Assessment of joint swelling at joint examination is the reference of IA-identification; early access clinics are constructed to promote this early recognition of IA. However, due to the COVID-19 pandemic the face-to-face capacity of such services is severely reduced. The accuracy of patient-reported swelling in comparison to joint examination has been extensively evaluated in established RA (ρ 0.31-0.67), but not in patients suspected for IA.[1]
Objectives: To promote evidence based care in the era of telemedicine, we determined the accuracy of patient-reported joint swelling for actual presence of IA in persons suspected of IA by general practitioners(GP).
Methods: Data from two Dutch Early Arthritis *Recognition* Clinics were studied. These are screening clinics (1.5-lines-setting) where GPs send patients in case of doubt on IA. At this clinic patients were asked to mark the presence of swollen joints on a mannequin with 52 joints. For this study the DIP joints and the metatarsal joints were excluded and, therefore, a total of 42 joints were assessed for self-reported joint swelling. Clinically apparent IA of ≥1 joint determined by the physician was the reference to calculate sensitivity, specificity, positive and negative likelihood ratios (LR+,LR-), and positive and negative predictive values (PPV, NPV) on patient-level. Pearson correlation coefficients(ρ) were determined. Predictive values depend on the prevalence of a disease in a population. Because the prevalence of IA in a 1.5-lines-setting will differ from a primary care setting, post-test probabilities of IA were estimated for two lower prior-test probabilities as example, namely 20% (estimated probability in patients GPs belief IA is likely) and 2% (prior-test probability with less preselection by GPs), using likelihood ratios and nomograms.
Results: A total of 1637 consecutive patients were studied. Median symptom duration was 13 weeks. 76% of patients marked ≥1swollen joint at the mannequin. 41% of patients had ≥1swollen joint at examination by rheumatologists. ρ was 0.20(patient-level)-0.26(joint-level).
The sensitivity of patients-reported joint swelling was high, 87%, indicating that the majority of patients with IA had marked swelling on the mannequin. However the specificity was 31%, indicating that 69% of persons without IA had also done so. The LR+ was 1.25; the LR- 0.43. The PPV was 46%, the NPV 77%. Thus the PPV increased hardly (from 41% to 46%) and the NPV somewhat (from 59% to 77%). Also in settings with prior-test probabilities of 20% and 2%, estimated PPVs (from respectively 20% and 2% to 24% and 2%) and NPVs (from respectively 80% and 98% to 90% and 99%) hardly increased.
Conclusion: Patient-reported joint swelling had little value in distinguishing patients with/without IA for different prior-test probabilities, and is less valuable in comparison to self-reported flare detection in established RA.
REFERENCES:
[1] Barton JL, Criswell LA, Kaiser R, et al. Systematic review and metaanalysis of patient self-report versus trained assessor joint counts in rheumatoid arthritis. *J Rheumatol* 2009;36:2635-2641.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.235

POS1419

PREDICTIVE FACTORS FOR PULMONARY PROGRESSION IN PATIENTS WITH CONNECTIVE TISSUE DISEASE AND INTERSTITIAL LUNG DISEASE

Y. H. Chiu[1,2], J. Spierings[1], P. De Jong[3], F. Mohamed Hoesein[3], J. M. Van Laar[1], M. Voortman[4]. *[1]University Medical Centre Utrecht, Department of Rheumatology and Clinical Immunology, Utrecht, Netherlands*; *[2]National Defense Medical Center, Division of Rheumatology/Immunology/Allergy, Taipei, Taiwan, Republic of China*; *[3]University Medical Centre Utrecht, Department of Radiology, Utrecht, Netherlands*; *[4]University Medical Centre Utrecht, Department of Heart and Lung, Utrecht, Netherlands*

Background: Interstitial lung disease (ILD) is associated with decreased quality of life and higher mortality risk in patients with connective tissue disease (CTD). Outcome and treatment response to immunosuppressive therapies is unpredictable, and therefore the management of CTD-ILD can be challenging.
Objectives: Our study aimed to identify clinical and imaging factors that are predictive for outcome in patients with CTD-ILD.
Methods: We performed a retrospective cohort study in patients with CTD-ILD who were treated in our centre between 2004 and 2018. Clinical, biochemical data as well as pulmonary function test (PFT) and high-resolution computed tomography (HRCT) results were recorded. Two experienced chest radiologists independently and blindly reviewed the HRCT's. When the two chest radiologists assessed the ILD pattern differently, a diagnosis was made by consultation of a third expert. The ILD patterns were classified as fibrotic or inflammatory. Overall survival and progressive fibrosing interstitial lung disease (PF-ILD, defined as a significant decline of PFT and HRCT) after two years of treatment were assessed using a Kaplan-Meier plot. Multivariable Cox regression was including for treatment, comorbidity, and age as variables. Factors with a p value < 0.2 in the univariate analysis were included in the multivariate analysis. The correlation between the variation of serum markers and PFT over-time was evaluated with Spearman's Rho.
Results: In total, 150 patients with CTD-ILD were included, of which 53 (35.3%) had systemic sclerosis, 19 (12.7%) Sjogren's syndrome, 29 (19.3%) inflammatory myopathy, 24 (16%) rheumatoid arthritis, 5 (3.3%) systemic lupus erythematosus, 4 (2.7%) mixed connective tissue disease, and 16 (10.7%) undifferentiated connective tissue disease patients. Median disease duration of CTD was 14 months (IQR 2–73) in patients with CTD diagnosis before ILD onset. The median follow-up duration was 40 months (IQR 27.3–60.8). Thirty (20%) deaths occurred, in which the cause of death was a pulmonary infection in 6 (4%) patients and a respiratory failure due to ILD in 10 (6.7%) patients. PF-ILD occurred in 82 (54.7%) patients, which was associated with poor overall survival (HR 3.03, 95%CI 1.15–7.98) (Figure 1). Age, smoking, and steroid usage were associated with increased mortality risk as well (Table 1). There was no dose-related effect of smoking on mortality.

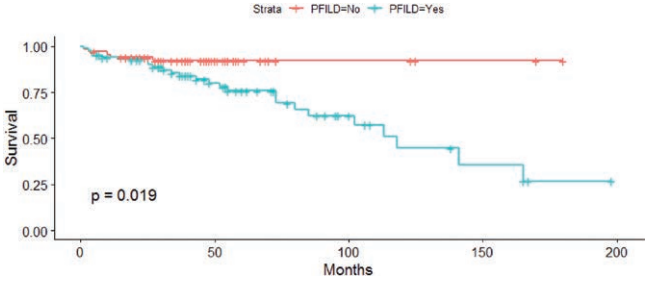


Figure 1. The Kaplan-Meier plot for progressive fibrosing interstitial lung diseases (PF-ILD). PF-ILF was defined as pulmonary function decline or high-resolution computed tomography progression after two years of treatment.

Inflammatory patterns on baseline HRCT were correlated with a lower risk of FVC decline than fibrotic patterns (OR 0.24, 95%CI 0.09–0.64). The increase in CA15.3 level was associated with the decline in FVC (Rho -0.308, p=0.037). Besides, the elevation in CRP was associated with the reduction in FVC (Rho -0.302, p=0.006) and DLCO (Rho -0.268, p=0.019).
Conclusion: Our study identified several factors associated with outcomes. Age, smoking, and steroid treatment increased the risk of mortality in patient with CTD-ILD. Inflammatory HRCT pattern at baseline revealed a better pulmonary outcome than a fibrotic pattern. The patients having PF-ILD after two years of treatment showed a higher mortality risk.

Table 1. Multivariable Cox-regression for the clinical risk of mortality.

Clinical factor	Crude HR (95%CI)	P	Adjusted HR (95%CI)	p
Age	1.11 (1.06–1.15)	$1.7*10^{-6}$	1.12 (1.07–1.17)	$3.54*10^{-6}$
Smoking	1.64 (0.79–3.43)	0.187	2.53 (1.11–5.78)	0.028
Congestive heart failure	1.86 (0.75–4.58)	0.179	1.17 (0.47–2.91)	0.737
MMF	0.55 (0.23–1.35)	0.195	0.73 (0.29–1.85)	0.512
Steroid	4.37 (1.67–11.45)	0.003	4.96 (1.84–13.40)	0.002

MMF, mycophenolate mofetil; HR, hazard ratio.

Acknowledgements: We want to thank Marieke Vianen for the support in data management, Lieke Wintermans and Lisa Hessels for collecting the clinical data.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.261

POS1420

RISK OF SERIOUS INFECTIONS IN OFFSPRING EXPOSED IN UTERO TO USTEKINUMAB OR VEDOLIZUMAB

J. Gorodensky[1], S. Bernatsky[1,2], W. Afif[3], Y. St-Pierre[2], K. Filion[1,4], E. Vinet[1,2]. *[1]McGill University, Epidemiology, Montréal, Canada*; *[2]Research Institute of the McGill University Health Centre, CORE, Montréal, Canada*; *[3]McGill University, Gastroenterology and Hepatology, Montreal, Canada*; *[4]Lady Davis Institure for Medical Research, Center for Clinical Epidemiology, Montreal, Canada*

Background: Ustekinumab, an IL-12/23 inhibitor, is indicated in adult patients with inflammatory bowel disease (IBD), psoriasis (PsO), and psoriatic arthritis (PsA) and vedolizumab, an $\alpha_4\beta_7$ receptor antagonist is indicated in IBD only. Both are monoclonal antibodies harbouring an Fc portion, which are actively transported across the placenta, often reaching higher fetal than maternal levels. As fetuses could be exposed to therapeutic or supra-therapeutic levels of these drugs, there are concerns that these agents could cause immunosuppression after birth. However, evidence is lacking.
Objectives: We compared the risk of serious infections in offspring exposed to ustekinumab, vedolizumab, tumour necrosis factor inhibitors (TNFi), and non-biologic immunosupressives versus offspring unexposed during pregnancy among women with IBD, PsO and/or PsA.
Methods: We conducted a retrospective cohort study using the US MarketScan database, an employment insurance database. We included live births (01/2011-12/2018) among women with PsO, PsA, and/or IBD. Drug exposure was defined as ≥1 filled prescrip tion or infusion procedure code during pregnancy. In offspring, we evaluated serious infections within the first year of life as any single inpatient infection code. We performed multivariate analyses using logistic regression, adjusting for maternal age, co-morbidities, corticosteroid use, concomitant drug use, and preterm birth.
Results: We included 16,115 offspring born to 7,612 women with PsO/PsA, 8,315 with IBD, and 188 with PsO/PsA and IBD. A total of 52 offspring were exposed to ustekinumab, 43 to vedolizumab (including 7 to both TNFi and vedolizumab),1,578 to TNFi, 1,857 to non-biologic immunosuppressives alone, and 12,585 unexposed to any drug. The percentage of serious infections in offspring exposed to ustekinumab was 3.9% (95% CI 0.5-13.9), versus 2.7% (95% CI 1.9-3.6) for TNFi, 2.3% (95% CI 0.06-13.0) for vedolizumab and 2.6 (95% CI 2.3-2.8) for those unexposed to any drug, though all estimates had wide, overlapping confidence intervals. Compared to children unexposed to any drug, there was a potential trend for increased risk with ustekinumab (OR 1.54, 0.37-6.45), but CIs were wide and included the null. For those exposed to vedolizumab (OR 0.82, 0.15-5.91) or TNFi (OR 0.98, 0.68-1.40) there was no clear excess risk.
Conclusion: In a large cohort, we did not detect a clear excess risk for offspring exposed in-utero to, vedolizumab or anti-TNF's, compared to unexposed patients; there was a signal for more events with ustekinumab, but confidence intervals were wide. Ongoing caution, as well as more research on short and long-term effects, is warranted for biologics actively transported across the placenta
Disclosure of Interests: Jonah Gorodensky: None declared, Sasha Bernatsky: None declared, Waqqas Afif Consultant of: Abbvie, Amgen, Arena Pharmaceuticals, Dynacare, Janssen, Merck, Novartis, Pfizer, Sandoz, Takeda, Yvan St-Pierre: None declared, Kristian Filion: None declared, Evelyne Vinet: None declared
DOI: 10.1136/annrheumdis-2021-eular.691

POS1421

HIGHER SERUM URIC ACID IS ASSOCIATED WITH INCREASED RISK OF OBESITY IN CHINESE ADULTS: A LONGITUDINAL DATA ANALYSIS

J. Zeng[1], W. R. Lawrence[2], J. Yang[3]. *[1]Department of Ultrasonography, Institute of Ultrasound in Musculoskeletal Sports Medicine, Guangdong Second Provincial General Hospital, Guangzhou, China, Department of*

Ultrasonography, Guangzhou, China; [2]*Department of Epidemiology and Biostatistics, School of Public Health, University at Albany, State University of New York, One University Place, Rensselaer, New York., Department of Epidemiology and Biostatistics, New York, United States of America*; [3]*Institute for Environmental and Climate Research, Jinan University, Guangzhou, 511443, China, Jinan University, Guangzhou, China*

Background: Hyperuricemia has been reported to be significantly associated with risk of obesity. However, previous studies on the association between serum uric acid (SUA) and body mass index (BMI) yielded conflicting results.
Objectives: The present study examined the relationship between SUA and obesity among Chinese adults.
Methods: Data were collected at Guangdong Second Provincial General Hospital in Guangzhou City, China between January 2010 and December 2018. Participants with ≥2 medical checkup times were included in our analyses. Logistic regression model (LRM) was performed for data at baseline. For all participants, generalized estimation equation (GEE) model was used to assess the association between SUA and obesity, where the data were repeatedly measured over the nine-year study period. We calculated the cut-off values for SUA of obesity using the receiver operating characteristic curves (ROC) technique.
Results: A total of 15,959 participants (10,023 males and 5,936females) were included in this study, with an average age of 37.38 years (SD: 13.27) and average SUA of 367.05 μmol/L (SD: 97.97) at baseline, respectively. Finally, 1078 participants developed obesity over the 9-year period. The prevalence of obesity was approximately 14.2% for high SUA level. In logistic regression analysis at baseline, we observed a positive association between SUA and risk of obesity: OR=1.84 (95% CI: 1.77,1.90) for per-SD increase in SUA. Considering repeated measures over 9-year for all participants in the GEE model, the per-SD OR was 1.85 (95% CI:1.77,1.91) for SUA and the increased risk of obesity were greater for male (OR=1.45) and elderly participants (OR=1.01). The SUA cutoff points for risk of obesity using ROC curves were approximately consistent with the international standard.
Conclusion: Our study observed higher SUA level was associated with increased risk of obesity. More high-quality research is needed to further support these findings.

REFERENCES:

[1] Nagahama S, Kashino I, Hu H, Nanri A, Kurotani K, Kuwahara K *et al.* Haemoglobin A1c and hearing impairment: longitudinal analysis using a large occupational health check-up data of Japan. *BMJ open* 2018; **8**(9): e023220.
[2] Kim YJ, Park H. Improving Prediction of High-Cost Health Care Users with Medical Check-Up Data. *Big data* 2019; **7**(3): 163-175.
[3] Ishizaka N, Ishizaka Y, Toda A, Tani M, Koike K, Yamakado M *et al.* Changes in waist circumference and body mass index in relation to changes in serum uric acid in Japanese individuals. *The Journal of rheumatology* 2010; **37**(2): 410-6.

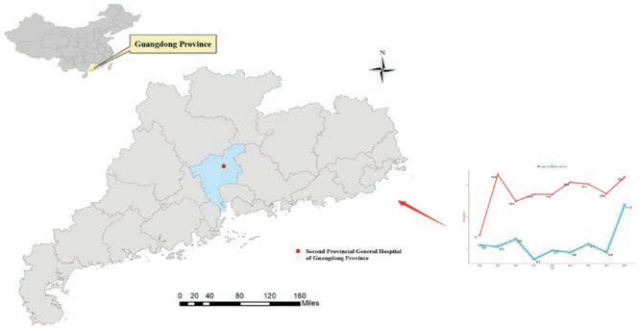


Figure 1. Location of Guangdong Second Provincial General Hospital (Guangzhou, Guangdong, China) and the prevalence of obesity by different years stratified by baseline SUA.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.752

POS1422 CORRELATES OF TESTING POSITIVE FOR SARS-COV-2 IN PATIENTS WITH RHEUMATIC AD MUSCULOSKELETAL DISEASES

N. Singh[1,2], I. Huang[2], M. Singleton[2], A. Bays[2], J. Sabo[2], S. Chung[2], G. Gardner[2], J. Schaeffer[2], K. Wysham[2], J. Andrews[2], R. Patel[2], J. Simard[3], J. Liew[4]. [1]*University of Washington, Rheumatology, Bellevue*; [2]*1959 NE Pacific St, Internal Medicine, Seattle, United States of America*; [3]*450 Serra Mall, Internal Medicine, Stanford, United States of America*; [4]*233 Bay State Rd, Internal Medicine, Boston, United States of America*

Background: Many studies on COVID-19 outcomes in patients with RMD have either restricted to COVID positive RMD patients or compared them to the general clinic population as a comparator. Given heterogeneity in behaviors and risks, clinical characteristics associated with a positive diagnosis among patients with RMD seeking testing for Sars-CoV-2 remain less well studied.
Objectives: Among patients with RMD receiving a Sars-CoV-2 PCR test, we aimed to identify RMD-related factors associated with a positive test result.
Methods: Among patients seen at least once in the University of Washington (UW) rheumatology clinics between March 2018 to March 2020, we reviewed electronic medical records to identify patients undergoing Sars-CoV-2 PCR testing from March 1 through October 31, 2020. Patients with RMD were categorized into two groups: those who tested positive for Sars-CoV-2 and those who tested negative. We randomly selected patients from the negative group in a 2:1 ratio for further data abstraction. Student's *t*-test and Chi-squared tests were used to compare continuous and categorical variables, respectively, between the groups. To determine the correlates of testing positive for Sars-CoV-2, specifically RMD medication use and disease activity, we constructed different multivariable logistic regression models adjusted for age, sex, race/ethnicity, presence of comorbidities, body mass index, and smoking.
Results: A total of 2768 RMD patients underwent SARS-CoV-2 PCR testing within the UW system, of whom 43 (1.5%) were positive at least once. Three patients with incomplete information were excluded. Patients who tested positive had higher prevalence of end stage renal disease (ESRD)/chronic kidney disease (CKD) (24% versus 11%), had higher rates of active disease (24% versus 20%), were older (>55 years) (mean age 57.3 versus 54.8 years), male (63% versus 55%), non-white race/ethnicity (32% versus 26%), and higher prevalence of multiple comorbidities (42% versus 31%) (Table 1). In the multivariable models, neither RMD medication use (versus no use, Table 1) nor high disease activity (vs low disease activity/remission) were statistically significantly associated with COVID-19 positivity. Among the 41 COVID-19 positive patients, a majority recovered without specific treatments, although approximately one third of the positive patients were hospitalized and three deaths were observed.
Conclusion: In this study, patients who tested positive did not differ in many ways from those who tested negative.

Table 1. Baseline characteristics of the patients prior to COVID testing

Variables	All (N=126)	COVID Positive (N=41)	COVID Negative (N=85)	P value
Age in years – mean (SD)	55.6 (15.3)	57.3 (16.3)	54.8 (14.9)	0.40
Sex				0.39
Male	73 (57.9)	26 (63.4)	47 (55.3)	
Female	53 (42.1)	15 (36.6)	38 (44.7)	
Race				0.39
White	89 (71.2)	26 (63.4)	63 (74.1)	
Other race	35 (28.2)	13 (31.7)	22 (25.9)	
Missing	2 (1.6)	2 (4.9)	0 (0.0)	
Rheumatic disease				0.64
OA/Crystal/Fibromyalgia	37 (29.4)	11 (26.8)	26 (30.6)	
RA/SpA	32 (25.4)	9 (22.0)	23 (27.1)	
All others	57 (45.2)	21 (51.2)	36 (42.3)	
Rheumatic disease activity				0.57
Active	27 (21.4)	10 (24.4)	17 (20.0)	
Not active	99 (78.6)	31 (75.6)	68 (80.0)	
Co-morbidities				
Diabetes mellitus (%)	25 (19.8)	9 (22.0)	16 (18.8)	0.68
Hypertension	48 (38.1)	20 (48.8)	28 (32.9)	0.09
Cardiovascular disease	23 (18.3)	9 (22.0)	14 (16.5)	0.46
Lung disease	25 (19.8)	10 (24.4)	15 (17.7)	0.37
Cancer	10 (7.9)	3 (7.3)	7 (8.2)	0.86
ESRD/CKD	19 (15.1)	10 (24.4)	9 (10.6)	**0.04***

BMI: Body mass index; SD: Standard deviation; OA: Osteoarthritis; Crystal: Crystalline diseases; RA: Rheumatoid arthritis; SpA: Spondyloarthritis

Acknowledgements: The work in this study was supported by grant UL1 TR002319 to Dr Singh from the Institute of Translational Health Sciences of the University of Washington.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.858

POS1423 LIFESTYLE HABITS IN PATIENTS WITH RHEUMATOID ARTHRITIS – A CROSS SECTIONAL STUDY ON TWO SCANDINAVIAN COHORTS

J. K. Karstensen[1,2,3], J. Primdahl[1,2,4], M. Andersson[5,6], J. Reffstrup Christensen[7,8], A. Bremander[1,2,3,5,6]. [1]*Department of Regional Health Research, University of Southern Denmark, Odense, Denmark*; [2]*Danish Hospital for Rheumatic Diseases, University Hospital of Southern Denmark, Sønderborg, Denmark*; [3]*The DANBIO Registry, Danish Hospital for Rheumatic Diseases, Sønderborg, Denmark*; [4]*Hospital of Southern Jutland, University Hospital*

of Southern Denmark, Aabenraa, Denmark; [5]*Section of Rheumatology, Department of Clinical Sciences Lund, Lund University, Lund, Denmark*; [6]*Spenshult, Research and Development Centre, Halmstad, Sweden*; [7]*Research Initiative for Activity Studies and Occupational Therapy, Research Unit of General Practice, Department of Public Health, University of Southern Denmark, Odense, Denmark*; [8]*Research Unit of User Perspectives, Department of Public Health, University of Southern Denmark, Odense, Denmark*

Background: In people with rheumatoid arthritis (RA), modifiable lifestyle factors such as smoking, being overweight/obese, alcohol overuse and physical inactivity may not only affect treatment response and quality of life, but can also increase the risk for cardio-vascular diseases and other comorbidities (1,2). Evidence and EULAR guidelines (3) support lifestyle changes in patients with RA. If a patient need to change several habits, the challenge may seem overwhelming and substantial support will be needed. There is little information concerning the prevalence of a combined number of unhealthy lifestyle (UL) factors in people with RA.
Objectives: I) To study the prevalence of unhealthy lifestyle factors in two Scandinavian RA cohorts. II) To study the association between disease impact and two or more unhealthy lifestyle factors.
Methods: Patients diagnosed with RA who participated in a cardiovascular screening consultation at a specialist clinic during 2016-2018 and responded to four lifestyle questions, constituted the Danish cohort (data retrieved from the national registry DANBIO). Patients with RA belonging to the BARFOT cohort, and who in a 2017 survey responded to four lifestyle questions, constituted the Swedish cohort. Lifestyle information was dichotomized as present tobacco use or not, BMI <25 kg/m2 vs. ≥25 kg/m2, alcohol overuse or not, and health enhancing physical activity (≥ 150 minutes/week) or less. The combined number of UL factors (0, 1, 2, 3, 4) were calculated. Crude logistic regression analyses were performed to determine the association between disease impact and two or more UL factors (controlled for age, gender and disease duration). Independent factors (disease impact) were pain (NRS 0-10, best to worst), fatigue (NRS 0-10, best to worst), function (HAQ, 0-3, best to worst) and quality of life (EQ-5D-3L 0-1, worst to best).
Results: The 566 included Danish patients had a mean age of 61.82 (SD 11.13) years, a disease duration of mean 12.40 (SD 10.95) years, and 72% were women. The 995 Swedish patients had a mean age of 66.38 (SD 12.90) years, a disease duration of mean 15.55 (SD 3.85) years, and 72% were women. 95% of the Danish patients and 82% of the Swedish patients reported at least one UL factor, while 66% and 47% respectively reported two or more (Figure 1). The most common ones were overweight/obesity and physical inactivity in both cohorts. Male gender OR 1.86 95% CI [1.21-2.85] and shorter disease duration OR 0.97 95% CI [0.95-0.99] were associated with two or more UL factors in the Danish cohort. In the Swedish cohort, male gender OR 1.42 95% CI [1.07 – 1.89], worse pain OR 1.10 95% CI [1.04 – 1.15], fatigue OR 1.09 95% CI [1.04 – 1.15], function OR 1.64 95% CI [1.28 – 2.10], and worse quality of life OR 0.35 95% CI [0.20 – 0.60] were associated with two or more UL factors.
Conclusion: Every other patient with RA had two or more UL factors in both the Danish and Swedish cohort, and more often they were men. The combined number of UL factors was not necessarily associated with disease impact. The findings are important for health professionals working with lifestyle interventions in patients with RA.

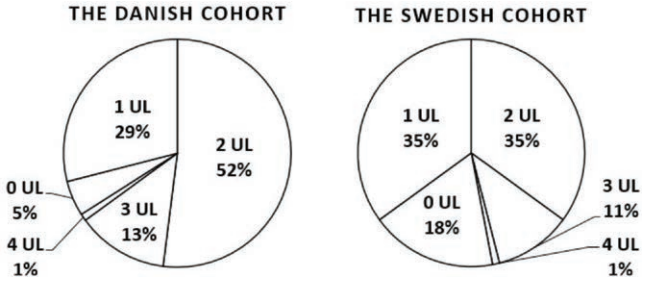


Figure 1. The combined number of unhealthy lifestyle (UL) factors in two Scandinavian RA cohorts.

REFERENCES:

[1] Smolen JS, Landewé RBM, Bijlsma JWJ, Burmester GR, Dougados M, Kerschbaumer A, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Ann Rheum Dis. 2020;79(6):685-99.
[2] Lindhardsen J, Ahlehoff O, Gislason GH, Madsen OR, Olesen JB, Torp-Pedersen C, et al. The risk of myocardial infarction in rheumatoid arthritis and diabetes mellitus: a Danish nationwide cohort study. Ann Rheum Dis. 2011;70(6):929-34.
[3] Agca R, Heslinga SC, Rollefstad S, Heslinga M, McInnes IB, Peters MJ, et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Ann Rheum Dis. 2017;76(1):17-28.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1378

POS1424 PREGNANCY COURSE IN A COHORT OF WOMEN WITH MYOSITIS - RESULTS FROM REVNATUS

B. Jakobsen[1], H. Bjørngaard[1], H. S. Koksvik[1], T. T. Pedersen[1], M. Wallenius[1,2]. [1]*St. Olavs Hospital, Trondheim University Hospital, Norwegian National Advisory Unit on Pregancy and Rheumatic Diseases, Trondheim, Norway*; [2]*Norwegian University of Science and Technology, Department of Neuromedicine and Movement Science, Trondheim, Norway*

Background: Myositis is a rare autoimmune disease characterized by proximal and symmetrical muscle weakness and inflammatory infiltrates on muscle biopsy, and may affect women in reproductive age. Only few reports exist on pregnancy outcomes in women with myositis. Well-controlled disease at time of conception seems to give better outcome for the mother and the fetus (1). Inflammatory active disease before and during pregnancy has been associated with preterm birth and infant small for gestational age (1).
Objectives: To describe the course of pregnancy in patients with myositis.
Methods: We prospectively collected data on pregnancy in women with myositis in the nationwide Norwegian quality registry - RevNatus. ICD-10 codes: ICD-10 M33.0 (5), M33.1 (2), M33.2 (1), M33.9 (3). Eleven pregnancies in ten women with a known pregnancy outcome from 2016 – 2020 were included.
Results: Median disease duration was 10 years (range 3-26), and median age at conception was 29 years (range 25-43). Five women had juvenile myositis. Two pregnancies ended in spontaneous abortions, one in 1st trimester and one in 2nd trimester. Nine pregnancies ended with live birth at median pregnancy week 39 (range 35-41) and a median birth weight of 3355 gram (range 2580-4750). None of the women experienced preeclampsia or HELLP. Three women was positive for ANA. Median CRP in second trimester was three (range 0-7). Among nine women with live births, seven were in remission, and two women had persistent disease in second trimester, defined by rheumatologist. Seven women used DMARDs in pregnancy, and two women used prednisolone 5 mg throughout pregnancy.

Patient #	Pregnancy #	Maternal age at conception	Disease duration years	Medication during pregnancy	Disease activity 2nd trimester	Gestational age at delivery	Infant birth weight (gram)	Delivery mode
A	1	29	25	none	Remission	38	3355	Standard vaginal delivery
B	2	34	7	azathioprine	Persistent	39	3725	Standard vaginal delivery
C	3	29	15	azathioprine				Spontaneous abortion week 7
D	4	35	3	ciclosporin prednisolone 5mg	Persistent	40	3000	Standard vaginal delivery
E	5	28	13	none	Remission	37	2765	Operational vaginal delivery
F	6	25	10	azathioprine hydroxy-chloroquine	Remission	41	4085	Standard vaginal delivery
F	7	27	13	azathioprine hydroxy-chloroquine	Remission	41	3815	Standard vaginal delivery
G	8	36	13	prednisolone 5mg				Spontaneous abortion > week 12
H	9	29	9	azathioprine	Remission	35	2580	Standard vaginal delivery
I	10	43	5	azathioprine prednisolone 5mg	Remission	37	3140	Sectio
J	11	36	28	none	Remission	41	4750	Acute sectio

Conclusion: We did not observe disease flare during pregnancy and no serious adverse outcomes in the pregnancies ending with live births. However, data are sparse, and larger cohorts are necessary to evaluate possible risk factors.

References: 1. Munira S, Christopher-Stine L. Pregnancy in myositis and scleroderma. Best Pract Res Clin Obstet Gynaecol. 2020 Apr;64:59-67. doi: 10.1016/j.bpobgyn.2019.10.004. Epub 2019 Oct 18. PMID: 31928915.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1539

POS1425 ANTIBODIES TO PORPHYROMONAS GINGIVALIS ASSOCIATE WITH THE PRESENCE OF RHEUMATOID ARTHRITIS-RELATED AUTOANTIBODIES IN PATIENTS WITH PERIODONTITIS

C. De Vries[1], G. Ruacho[1], N. Sippl[1], B. A. Potempa[2], L. Ryden[3], J. S. Potempa[2], B. Klinge[4], E. Svenungsson[1], K. Lundberg[1]. *[1]Karolinska Institute, Department of Medicine, Division of Rheumatology, Stockholm, Sweden*; *[2]University of Louisville, Department of Oral Immunology & Infectious Diseases, Louisville, United States of America*; *[3]Nya Karolinska, Department of Medicine, Stockholm, Sweden*; *[4]Huddinge Hospital, Department of Dental Medicine, Division of Oral Diseases, Huddinge, Sweden*

Background: Epidemiologic studies have demonstrated a link between periodontitis (PD) and rheumatoid arthritis (RA), specifically RA characterized by anti-citrullinated protein antibodies (ACPA). The keystone pathogen driving PD, *Porphyromonas gingivalis (Pg),* is the only pathogen known to express peptidylarginine deiminase (PAD), a citrullinating enzyme. Hence, *Pg* has been proposed to be involved in triggering the ACPA response, by generating citrullinated antigens in an inflammatory milieu(1). Another major virulence factor of *Pg* is arginine gingipain B (RgpB), a proteinase which cleaves proteins so that *P.*PAD can access the site where citrullination takes place. We have previously shown elevated anti-RgpB IgG levels in ACPA+ RA patients, even before clinical onset(2, 3), and we hypothesize that anti-RgpB IgG could serve as a serological marker to identify PD patients with increased risk of developing ACPA+ RA.
Objectives: Based on this hypothesis, we set out to investigate whether anti-RgpB IgG was associated with PD, PD severity, autoimmunity in general, and the ACPA response in particular.
Methods: Anti-RgpB IgG, as well as RA- and systemic lupus erythematosus (SLE)-related autoantibodies targeting cyclic citrullinated peptide(s) (CCP2), rheumatoid factor (RF), dsDNA, cardiolipin, and β2 glycoprotein, were measured by ELISA in serum samples from the ParoKrank study, which is a well-characterized cohort of 805 patients with a first myocardial infarction and 805 matched controls, where periodontal status has been determined by dentists(4). In this study, individuals with PD (n=941) were compared to individuals without PD (n=557).
Results: We detected significantly elevated (p<0,0001) anti-RgpB IgG levels in PD compared to non-PD individuals, with highest levels recorded in severe PD. Anti-RgpB IgG levels were significantly increased in PD patients positive for CCP2 and/or RF (n=50), when compared to PD patients negative for CCP2 and RF (n=507), p<0,05, and when compared to non-PD individuals positive for CCP2 and/or RF (n=62), p < 0,05. Notably, these differences were not seen for SLE-related autoantibodies. In addition, anti-RgpB IgG levels were significantly elevated amongst MI patients versus controls (p < 0,05), supporting the previous finding that PD is more common among MI patients(4).
Conclusion: Our data demonstrates a specific association between severe PD, elevated anti-RgpB IgG levels and RA-related autoantibodies, supporting a role for *Pg* in linking PD to ACPA+ RA. Further investigation will be needed to confirm whether anti-RgpB IgG can be used as a serological marker to identify PD patients with increased risk of developing ACPA+ RA.
REFERENCES:

[1] Rosenstein ED, Greenwald RA, Kushner LJ, Weissmann G. Hypothesis: the humoral immune response to oral bacteria provides a stimulus for the development of rheumatoid arthritis. Inflammation. 2004;28(6):311-8.
[2] Kharlamova N, Jiang X, Sherina N, Potempa B, Israelsson L, Quirke AM, et al. Antibodies to Porphyromonas gingivalis Indicate Interaction Between Oral Infection, Smoking, and Risk Genes in Rheumatoid Arthritis Etiology. Arthritis Rheumatol. 2016;68(3):604-13.
[3] Johansson L, Sherina N, Kharlamova N, Potempa B, Larsson B, Israelsson L, et al. Concentration of antibodies against Porphyromonas gingivalis is increased before the onset of symptoms of rheumatoid arthritis. Arthritis Res Ther. 2016;18(1):201.
[4] Rydén L, Buhlin K, Ekstrand E, Faire Ud, Gustafsson A, Holmer J, et al. Periodontitis Increases the Risk of a First Myocardial Infarction. Circulation. 2016;133(6):576-83.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1580

POS1426 PATIENTS WITH IMMUNE MEDIATED INFLAMMATORY DISEASES ARE OVERREPRESENTED IN LOW-FREQUENCY VIRAL SYMPTOM CLUSTERS

K. Tascilar[1,2], D. Simon[1,2], G. Krönke[1,2], A. Kleyer[1,2], A. Ramming[1,2], R. Atreya[2,3], M. Tenbusch[4], K. Überla[4], C. Berking[2,5], M. Sticherling[2,5], M. F. Neurath[2,3], G. Schett[1,2]. *[1]Friedrich Alexander University of Erlangen Nuremberg and Universitätsklinikum Erlangen, Department of Medicine-3, Rheumatology and Immunology, Erlangen, Germany*; *[2]Friedrich Alexander University of Erlangen Nuremberg and Universitätsklinikum Erlangen, Deutsches Zentrum für Immuntherapie, Erlangen, Germany*; *[3]Friedrich Alexander University of Erlangen Nuremberg and Universitätsklinikum Erlangen, Department of Medicine-1, Gastroenterology, Pneumology and Endorcrinology, Erlangen, Germany*; *[4]Friedrich Alexander University of Erlangen Nuremberg and Universitätsklinikum Erlangen, Institute of Clinical and Molecular Virology, Erlangen, Germany*; *[5]Friedrich Alexander University of Erlangen Nuremberg and Universitätsklinikum Erlangen, Department of Dermatology, Erlangen, Germany*

Background: Viral respiratory infections are common in the general population and result in a spectrum of outcomes ranging from effective viral clearance with no symptoms, to a maladaptive immune response that can result in severe symptomatic disease and death. Although patients with immune-mediated inflammatory diseases (IMID) are considered susceptible to poor outcomes from infectious syndromes, it is not known whether IMID patients are overall more prone to manifest common viral infection symptoms.
Objectives: To explore frequency patterns of common viral infection symptoms in IMID patients.
Methods: We previously recruited patients with IMIDs and individuals with no IMIDs for a seroprevalence study between February 1st and April 30th 2020 (1). Participants were questioned for the presence of eleven common viral disease symptoms. We clustered these data using an unsupervised binary data clustering algorithm (2) into 6 symptom clusters based on symptom frequency. Three major clusters (broadly symptomatic, intermediately symptomatic and oligo-/asymptomatic) and 2 sub-clusters (higher and lower frequency) for each major cluster. In addition, qualitative symptom clustering was done. We estimated standardized residuals to quantify the over/underrepresentation of IMID diagnosis frequencies in each subject cluster. We used Poisson regression to compare symptom counts by diagnosis.
Results: We analyzed 1909 participants (757 with IMIDs; 1152 non-IMID controls; Table 1). Within each major subject cluster (Figure 1A), IMID patients showed the highest positive deviation from the expected frequencies in lower frequency sub-clusters while non IMID controls showed the highest positive deviations in the higher frequency sub-clusters (Figure 1B). Inflammatory bowel disease and psoriasis were remarkably overrepresented in the lower frequency sub-cluster of the broadly-symptomatic cluster while RA was overrepresented in the lower frequency sub-clusters of intermediate and oligo-/asymptomatic clusters. X axis of Figure 1A presents qualitative symptom clusters. Regression analysis shows that RA patients among other IMIDs reported overall less symptoms (RR= 0.69, 95%CI, 0.58 - 0.80) compared to non-IMID controls.

Table 1. Participant characteristics and distribution of IMID diagnoses across subject clusters.

		Clusters					
		Broad Symptomatic		Intermediate Symptomatic		Oligo-Asymptomatic	
	Overall	Higher	Lower	Higher	Lower	Higher	Lower
N	1909	101	85	412	259	283	769
Age, years, mean (SD)	45.4 (15.2)	42.4 (13.3)	47.3 (15.2)	42.4 (12.9)	50.4 (15.5)	41.8 (14.9)	46.8 (15.9)
Male	1080 (56.6)	42 (41.6)	38 (44.7)	196 (47.6)	137 (52.9)	178 (62.9)	489 (63.6)
Diagnosis, n(%)							
No-IMID	1152 (60.3)	72 (71.3)	44 (51.8)	280 (68.0)	112 (43.2)	207 (73.1)	437 (56.8)
RA	226 (11.8)	7 (6.9)	5 (5.9)	29 (7.0)	56 (21.6)	17 (6.0)	112 (14.6)
IBD	178 (9.3)	5 (5.0)	15 (17.6)	46 (11.2)	29 (11.2)	19 (6.7)	64 (8.3)
SpA	142 (7.4)	7 (6.9)	5 (5.9)	23 (5.6)	25 (9.7)	14 (4.9)	68 (8.8)
Psoriasis	89 (4.7)	4 (4.0)	9 (10.6)	14 (3.4)	8 (3.1)	13 (4.6)	41 (5.3)
Other	122 (6.4)	6 (5.9)	7 (8.2)	20 (4.9)	29 (11.2)	13 (4.6)	47 (6.1)
Symptom count/ patient, mean (SD)	1.2 (1.7)	6.0 (1.3)	3.9 (1.1)	2.2 (1.0)	1.5 (0.6)	0.5 (0.5)	0.0 (0.0)

IBD, inflammatory bowel disease.

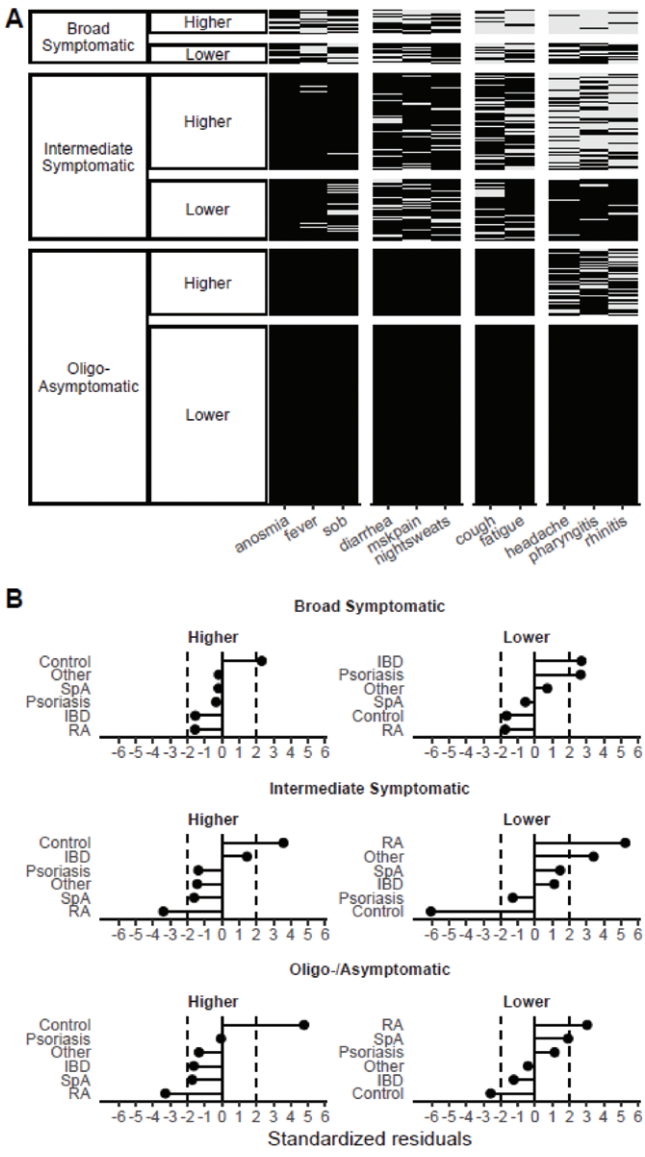


Figure 1. A) distribution of common viral respiratory disease symptoms across patient and symptom clusters. B) Standardized residuals indicating deviation from expected frequencies of IMID diagnoses across patient clusters. sob: shortness of breath, mskpain: musculoskeletal pain

Conclusion: This analysis shows that symptoms of common respiratory viral infections are less frequent in RA patients and to a lesser extent in other IMID patient. As major clusters in this analysis can also be considered to represent exposure categories, these data suggest that IMIDs or their treatments may mitigate common respiratory viral infection symptoms.

REFERENCES:

[1] Simon D. et al. Nat Commun (2020) 11, 3774
[2] Bhatia P. et al. J. Stat. Softw (2017) 76(9)

Acknowledgements: This study was supported by the Deutsche Forschungsgemeinschaft (DFG- FOR2886 PANDORA and the CRC1181), the Bundesministerium für Bildung und Forschung (BMBF; project MASCARA), the H2020 GA 810316 - 4D-Nanoscope ERC Synergy Project, the IMI funded project RTCure, the Emerging Fields Initiative MIRACLE of the Friedrich-Alexander-Universität Erlangen-Nürnberg as well as the Schreiber Stiftung gemeinnützige Gesellschaft mbH.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1598

POS1427 NATIONAL BURDEN OF RHEUMATOID ARTHRITIS IN CANADA 1990-2017: FINDINGS FROM THE GLOBAL BURDEN OF DISEASE STUDY 2017

N. Hassen[1], D. Lacaille[1], A. Xu[1], S. Sidi[1], A. Alandejani[1], M. Mansourian[2], N. Sarrazadegan[1], J. Kopec[1]. [1]*The University of British Columbia, Faculty of Medicine, Vancouver, Canada*; [2]*Isfahan University of Medical Sciences, Isfahan, Iran (Islamic Republic of)*

Background: According to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017, over 120,000 individuals currently have rheumatoid arthritis (RA) in Canada, yet a study that evaluates the combined effect of RA on the longevity and quality of life in the country is lacking.

Objectives: The objectives of this study are three: 1) to describe burden of RA levels and trends from 1990-2017 using GBD data, 2) to describe age and sex differences, and 3) to compare Canada RA burden to other countries.

Methods: We obtained publicly available data from GBD Study 2017 from the Institute for Health Metrics and Evaluation interactive visualization tool (http://vizhub.healthdata.org/gbd-compare). Disease burden indicators include prevalence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs). Estimates were presented as non age-standardized and age-standardized rates per 100,000 population. GBD estimated prevalence using published literature, survey data, patient records, and health insurance claims, and mortality using cause of death ensemble modelling technique. YLLs measure premature death calculated as the sum of each death multiplied by the standard life expectancy at each age. YLDs measure amount of time in a year an individual lives with a short- or long-term health condition, calculated by combining prevalence with disability weights for each age/sex/year. DALYs were calculated as the sum of YLLs and YLDs. DALYs for Canada were compared to DALYs of countries with similar socio-demographic index (SDI) values. SDI combines income per capita, average educational attainment, and fertility rates. Data were analysed by DisMod-MR 2.1, a Bayesian meta-regression tool.

Results: In Canada, RA mortality (mortality and YLLs) improved over time, with a steeper decline after the year 2002. However, the population burden of quality of life (YLDs and DALYs) increased due to increasing prevalence. The disease burden was higher in females (prevalence, mortality, YLLs, YLDs, DALYs), and DALY rates were higher among older populations. Compared to other countries, Canada had greater improvement in mortality and YLLs over time and had a lower age-standardized DALYs rate compared to countries of similar SDI values. A weak association was found between global age-standardized DALYs and SDI (R^2 = 0.0138).

Conclusion: RA is a major public health challenge. Canada fares better than other countries with regards to national RA burden. Early identification and management are critical to reducing the overall burden of RA in Canada, especially in women. More data from multiple provincial RA databases would increase the accuracy of our estimates for Canada.

REFERENCES:

[1] Cross M, Smith E, Hoy D, et al. The global burden of rheumatoid arthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis. 2014;73(7):1316-1322. doi:10.1136/annrheumdis-2013-204627
[2] Myasoedova E, Davis JM 3rd, Crowson CS, Gabriel SE. Epidemiology of rheumatoid arthritis: rheumatoid arthritis and mortality. Curr Rheumatol Rep. 2010;12(5):379-385. doi:10.1007/s11926-010-0117-y
[3] Safiri S, Kolahi AA, Hoy D, et al. Global, regional and national burden of rheumatoid arthritis 1990-2017: a systematic analysis of the Global Burden of Disease study 2017. Ann Rheum Dis. 2019;78(11):1463-1471. doi:10.1136/annrheumdis-2019-215920

Acknowledgements: Nejat Hassen is supported by a grant from the Canadian Institute of Health Research. Dr. Diane Lacaille is supported by the Mary Pack Chair in Arthritis Research from the University of British Columbia and The Arthritis Society of Canada.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1927

POS1428 VALIDATION OF ANCA-ASSOCIATED VASCULITIS AS THE CAUSE OF END-STAGE RENAL DISEASE IN THE UNITED STATES RENAL DATA SYSTEM

C. Cook[1], H. Choi[1,2], Z. Wallace[1,2]. [1]*Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [2]*Harvard, Medical School, Boston, United States of America*

Background: Glomerulonephritis and other renal manifestations are common in ANCA-associated vasculitis (AAV). Renal involvement in AAV is associated with adverse outcomes, including end-stage renal disease (ESRD) in up to 25% of patients (1). The United States Renal Data System (USRDS), a national registry of ESRD patients, represents a unique nationwide data source for studying AAV patients with ESRD. Prior research has assessed how often patients with ESRD attributed to AAV have biopsy-proven glomerulonephritis in USRDS (2), but the validity of the diagnosis of AAV as the cause of ESRD in the USRDS remains unknown.

Objectives: We aim to validate the diagnosis of AAV as the primary cause of ESRD listed in USRDS.

Methods: We identified all patients in the Mass General Brigham (MGB) healthcare system with a billing code for advanced chronic kidney disease or end-stage renal disease or procedure code for dialysis or renal transplantation. We identified all MGB patients fulfilling these criteria to records in the USRDS by name, sex, date of birth, and social security number. From this cohort of patients, we identified those with AAV or related diagnoses listed as the primary disease causing ESRD (ICD9: 446.0, 446.4 or ICD10: M31.3X, M31.7). Two authors reviewed medical records to collect information on whether or not a physician had diagnosed AAV, details of AAV history, renal and non-renal biopsies, and antineutrophil cytoplasmic antibody (ANCA) tests. Discrepancies were resolved through consensus. Details regarding initial ESRD onset date were obtained from the USRDS. To calculate the positive predictive value (PPV) for AAV as the primary cause of ESRD a definite physician diagnosis of AAV (a diagnosis confirmed by two physicians based on available data) in the MGB medical record was used as the gold standard. To calculate sensitivity, we linked the Partners (MGB) AAV Cohort to USRDS records using the same methods. A diagnosis code of AAV as the cause of ESRD was considered a true positive and a diagnosis code for other types of nephritis was considered a false negative.

Results: We identified 89 USRDS records linked to MGB medical records in which the primary cause of ESRD was attributed to AAV. Of these, 85 were confirmed to be true cases of AAV after medical record review (PPV=96%) (Table 1). Among the cases classified as AAV, 84 (99%) had a positive ANCA test, which was predominantly MPO/P-ANCA (47, 55%); 36 (42%) had a renal biopsy, all of which were supportive of the diagnosis. The majority of cases were identified as AAV by ICD9 or 10 codes for Wegener's granulomatosis (446.4 or M313.1). Within the Partners (MGB) AAV cohort linked to USRDS records, 33 (55%) of 60 identified cases had AAV listed as the cause of ESRD; in the remainder, ESRD was attributed to non-specific nephritis codes.

Table 1. AAV and non-AAV patients in the USRDS with ESRD due to AAV (N=89)

	Physician-Diagnosed AAV (N=85)
ANCA type n (%)	84 (98.8)
MPO/P-ANCA+	47 (55.3)
PR3/C-ANCA+	33 (38.8)
Renal biopsy n (%)	36 (42.4)
Pauci-Immune Glomerulonephritis n (%)	16 (44%)
Non-renal biopsy n (%)	
Yes	10 (11.8)
No	74 (87.1)
Years from AAV diagnosis to ESRD median [IQR]	1 [0, 6]
Principal diagnosis code (ICD9/ICD10) n (%)	
Wegener's granulomatosis (446.4, 446.4B, or M313.1)	81 (95.3)

Conclusion: We found that the diagnosis of AAV as the primary cause of ESRD in the USRD had a high PPV, suggesting accurate classification of ESRD due to AAV in the USRDS, but that sensitivity was moderate. These findings support the past and future use of the USRDS for research with ESRD attributed to AAV.

REFERENCES:

[1] Moiseev S, Novikov P, Jayne D, Mukhin N. End-stage renal disease in ANCA-associated vasculitis. Nephrol Dial Transplant. 2017;32(2):248-53.

[2] Layton JB, Hogan SL, Jennette CE, Kenderes B, Krisher J, Jennette JC, et al. Discrepancy between Medical Evidence Form 2728 and renal biopsy for glomerular diseases. Clin J Am Soc Nephrol. 2010;5(11):2046-52.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2138

POS1429

ORAL DYSBIOSIS REFLECTS THE IMMUNOLOGICAL ALTERATION OF RA REGARDING TO HLA DRB1*SE, ACPA AND CIGARETTE SMOKING: NAGASAKI ISLAND STUDY

Y. Tsuji[1], M. Tamai[2], S. Morimoto[3], D. Sasaki[2], S.Y. Kawashiri[1], K. Yanagihara[2], K. Aoyagi[4], T. Maeda[1], F. Matsuda[5], A. Kawakami[4], T. Saito[6]. *[1]Nagasaki University, Department of Community Medicine, Graduate School of Biomedical Sciences, Nagasaki, Japan*; *[2]Nagasaki University, Department of Laboratory Medicine, Nagasaki, Japan*; *[3]Nagasaki University, Department of Public Health, Graduate School of Biomedical Sciences, Nagasaki, Japan*; *[4]Nagasaki University, Department of Immunology and Rheumatology, Nagasaki, Japan*; *[5]Kyoto University, Center for Genomic Medicine, Kyoto, Japan*; *[6]Nagasaki University, Department of Oral Health, Medical and Dental Sciences, Nagasaki, Japan*

Background: Anti-citrullinated protein antibody (ACPA) production is observed in several organs even prior to the onset of rheumatoid arthritis (RA), and oral mucosa is considered to be one of the important tissues. Saliva is considered to reflect the oral microbiota(oralMB) including periodontal disease. A gene-environment interaction between cigarette smoking and shared epitope genes in HLA-DRB1*shared epitope (SE) provides a high risk of ACPA-positive RA. However, the interaction of HLA-DRB1*SE, ACPA, cigarette smoking and oralMB of RA patients remains to be elucidated.

Objectives: We investigated that the difference of oralMB among RA patients and healthy subjects(HS) regarding to ACPA, HLA-DRB1*SE and cigarette smoking.

Methods: The Nagasaki Island Study, which had started in 2014 collaborating with Goto City, Nagasaki Prefecture, Japan, is intended for research of the preclinical stage of RA, including ACPA, HLA genotype screening, oralMB and lifestyle habit. Both of blood and salivary samples were obtained from 1422 subjects out of 4276 participants in this study from 2016 to 2018. ACPA positivity was 1.7 % in total 4276 subjects. At this point, we selected 291 subjects, who were ACPA positive non-RA HS(n=22) and patients with RA (n=33, 11 subjects were ACPA positive and 22 ACPA negative, respectively) as the case, age and gender matched ACPA negative non-RA HS (n=236) as the control. In RA subjects, current smoker was n=1(3.0%) and ever smoker was n=8(24.2%). In HS, current smoker was n=29(11.2%) and ever smoker was n=55(21.3%). ACPA was measured by ELISA, and HLA genotyping was quantified by next-generation sequencing (Ref.1). The operational taxonomic unit (OTU) analysis using 16S rRNA gene sequencing were performed. The richness of microbial diversity within subject (α-diversity) was scaled via Shannon entropy. The dissimilarity between microbial community composition was calculated using Bray-Curtis distance as a scale, and differences between groups (β-diversity) were tested by permutational multivariate analysis of variance (PERMANOVA). In addition, UniFrac distance calculated in consideration of the distance on the phylogenetic tree were performed.

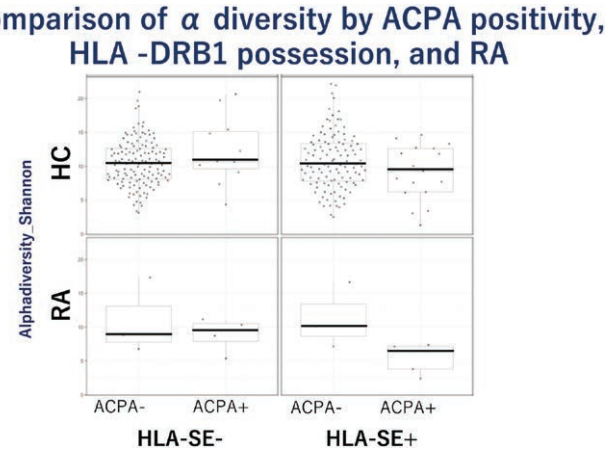
Results: Median age 71 y.o., % Female 58.4 %. Among RA and non-RA subjects, not α-diversity but β-diversity was statistically smaller significantly in RA (p=0.022). In the HS, there was no decrease in α-diversity between the ACPA-positive and HLA-DRB1*SE-positive groups, but in the ACPA-positive group, there was a decrease in α-diversity in the HLA-DRB1*SE-positive group. When we compared α-diversity stratified by the presence or absence of three factors (RA, ACPA, and HLA-DRB1*SE), the RA group with ACPA and HLA-DRB1*SE positive tended to have the lowest diversity (Figure 1 lower right). RA subjects, presence of HLA-DRB1*SE did not show the difference but the tendency of lower α-diversity (p=0.29).

Conclusion: HS with ACPA-positive HLA-DRB1*SE tended to show lower α-diversity than ACPA-positive HS and HLA-DRB1*SE positive HS. Furthermore, RA subjects with ACPA-positive HLA-DRB1*SE showed lower α-diversity than HS with ACPA-positive HLA-DRB1*SE.

Our study suggested that the oral dysbiosis may reflect the immunological status of patients with RA. Because of the small number of ACPA-positive patients, stratification by smoking history was difficult. Further examination is needed to clarify the gene-environment interaction and microbiome.

REFERENCES:

[1] Kawaguchi S, et al. Methods Mol Biol 2018;1802: 22.



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2270

POS1430

EPIDEMIOLOGY OF LUPUS NEPHRITIS IN BRAZIL: FINDINGS FROM THE MACUNAÍMA STUDY - A NATIONWIDE MULTICENTRIC STUDY

M. Abreu[1,2], O. Monticielo[3], V. Fernandes[4], A. Cristovão Maiorano[2], F. Dos Santos Beserra[2], F. Lamarao[5], N. David[5], B. De Veras[5], B. Bica[1], D. Sávio Nunes de Lima[6], M. Maria Das Chagas Medeiros[7]. [1]*Universidade Federal do Rio de Janeiro, Faculdade de Medicina, Rio de Janeiro, Brazil*; [2]*Universidade Federal do Rio de Janeiro, Laboratório Para Pesquisa em Desfechos Centrados no Paciente, Rio de Janeiro, Brazil*; [3]*Universidade Federal do Rio Grande do Sul, Serviço de Reumatologia do Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil*; [4]*Universidade de Cuiabá, Department of Medicine, Cuiabá, Brazil*; [5]*GlaxoSmithKline, Medical Department, Rio de Janeiro, Brazil*; [6]*Universidade Federal do Amazonas, Serviço de Reumatologia do Hospital Universitário Getúlio Vargas, Manaus, Brazil*; [7]*Universidade Federal do Ceará, Faculdade de Medicina, Fortaleza, Brazil*

Background: Lupus nephritis (LN) is one of the most serious organic manifestations of systemic lupus erythematosus (SLE). Ethnicity can contribute to disparities in the prevalence and disease activity of LN.
Objectives: To assess the prevalence of LN in Brazilian patients with SLE and to determine factors associated with LN activity across the country.
Methods: This cross-sectional study (GSK Study 207353) was carried out through face-to-face interviews and review of medical records (12-month study period). Adult patients with SLE (American College of Rheumatology [ACR] criteria, 1997) were included. Five SLE reference teaching centres were selected: North (NO), Northeast (NE), Midwest (CO), Southeast (SE), and South (SU). Patients with another disease whose morbidity surpassed SLE were excluded. LN was defined as reported in the medical record or history of confirmed renal biopsy; disease activity by pre-defined changes in SLE Disease Activity Index (SLEDAI) or the patient's kidney disease during the study. Activity was assessed during (T0), 6 months before (T6), and 12 months before (T12) the interview. Systemic Lupus International Collaborating Clinics/ACR Damage Index score mapped damage accrual. Two pairings were performed, aiming to discriminate factors associated with LN and its activity, respectively. Matching technique was used to select similar individuals based on propensity scores, obtained from a logistic regression model. A bootstrapping method explored characteristic variables associated with the risk of progressing to LN.
Results: Overall, 300 Brazilian patients with SLE were included in the study. Two groups were paired: LN group (N=150) and non-LN group (N = 141). The prevalence of LN in the paired sample (N=291) was 51.5%, with a disparity between centres (p<0.001; Figure 1A). Most patients were female (LN: 92.7%; non-LN: 94.3%) and the mean (standard deviation [SD]) age for the LN and non-LN groups was 39.46 (11.86) and 43.96 (12.18), respectively. History of serositis was associated with the presence of LN (42 [28.0%] vs 21 [14.9%] non-LN; p=0.010). Type IV histological class predominated in both groups, with no disparity between centres. Social disparities were noted between groups. Non-active workers prevailed among the LN group (115 [76.7%] vs 98 [69.5%] for non-LN, p=0.024).
When pairing for disease activity at T12, 73 (50.3%) patients with LN (N=145) had active disease. There was regional disparity in terms of disease activity (Figure 1B), with a predominance of active LN in the NO (28 [68.3%]) and SU (16 [55.2%], p=0.026). Type IV histological class was the component most associated with active LN (active: 32 [43.8%]; non-active: 11 [15.3%], p<0.001). Variation in SLEDAI during the study period discriminated between active and non-active LN. The mean (SD) SLEDAI score at T12 was substantially higher in those with active LN compared with non-active LN (7.18 [4.83] vs 2.47 [4.63], p<0.001). As for the pattern of care, corticosteroids users prevailed in those with active LN (62 [84.9%] vs 45 [62.5%] for non-active LN, p=0.004). There was no disparity in the use of immunosuppressants, with the exception of cyclophosphamide use, noted among 16 (21.9%) patients with active LN and 6 (8.3%) patients with non-active LN (p=0.041). Psychotropic or anticonvulsant use was higher in patients with non-active LN (32 [44.4%] vs 17 [23.3%] patients with active LN, p=0.012). Consultation with a neurologist was verified in 15 (20.8%) patients with non-active LN and 6 (8.2%) with active LN (p=0.055). Hospitalisation occurred in 17 patients with non-active (23.6%) and active (23.3%) LN.
Conclusion: Disparities in the prevalence of LN and its activity were evident between the regions across Brazil, highlighting differences in clinical factors, regional factors, and patterns of care.
Funding: GSK

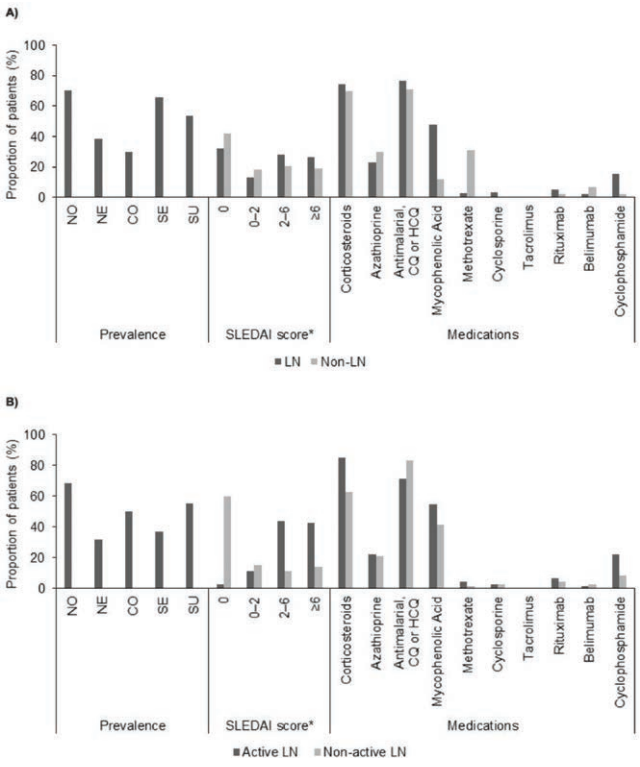


Figure 1. Prevalence of A) LN among regional centres, comparing them to disease activity profile and prescriptive practice, and B) Active and non-active LN according to prescriptive practiceCQ, chloroquine; HCQ, hydroxychloroquine*At T12

Acknowledgements: Medical writing assistance was provided by Helen Taylor, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.
Disclosure of Interests: Mirhelen Abreu Grant/research support from: GSK, Amgen, Biogen, Libbs, Odirlei Monticielo Speakers bureau: GSK, AbbVie, UCB, Roche, Novartis, Consultant of: GSK, AbbVie, Janssen, Vander Fernandes Speakers bureau: Janssen, Novartis, Roche, AbbVie, Pfizer, Grant/research support from: Novartis, GSK, Pfizer, Alexandre Cristovão Maiorano: None declared, Fernando dos Santos Beserra: None declared, Flavia Lamarao Employee of: GSK, Nathalie David Shareholder of: GSK, Employee of: GSK, Bruna de Veras Employee of: GSK, Blanca Bica: None declared, Domingos Sávio Nunes de Lima Grant/research support from: GSK, Marta Maria das Chagas Medeiros: None declared
DOI: 10.1136/annrheumdis-2021-eular.2336

POS1431

THE ASSOCIATION OF CLINICAL AND STRUCTURAL KNEE OSTEOARTHRITIS WITH PHYSICAL ACTIVITY IN THE MIDDLE-AGED POPULATION: THE NEO STUDY

S. Terpstra[1], J. Van der Velde[2], R. De Mutsert[2], D. Schiphof[3], M. Reijnierse[4], F. Rosendaal5, M. Kloppenburg5,6, M. Loef6. [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [2]*Leiden University Medical Center, Clinical Epidemiology, Leiden, Netherlands*; [3]*Erasmus Medical Center, General Practice, Rotterdam, Netherlands*; [4]*Leiden University Medical Center, Radiology, Leiden, Netherlands*; [2]*Leiden University Medical Center, Clinical Epidemiology, Leiden, Netherlands*; [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*

Background: Lack of physical activity in individuals with knee OA has shown to be associated with increased cardiovascular risk and mortality. Consequently, physical activity is a potential target for interventions in knee OA. However, most of the available studies concerning physical activity in individuals with knee OA were performed in relatively old populations with an inactive lifestyle. It is unclear

how previous results can be generalized to other populations with different lifestyle and physical activity habits.

Objectives: To investigate if knee OA is associated with lower physical activity in a general middle-aged Dutch population. Furthermore, to investigate the association of physical activity with patient reported outcomes such as knee pain and function, and health-related quality of life in individuals with knee OA.

Methods: We used cross-sectional data from the Netherlands Epidemiology of Obesity (NEO) study, in which participants aged 45-65 years were included. Clinical knee OA was defined using the ACR criteria. Structural knee OA was defined on MRI using the modified criteria by Hunter et al. in a random subset of 1,285 individuals of our study population.

We assessed knee pain and function with the Knee injury and Osteoarthritis Score (KOOS), and health-related quality of life (HRQoL) with the Short Form (SF)-36. Physical activity (in Metabolic Equivalent of Task (MET) hours per week) was assessed using the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH).

We used linear regression analyses to investigate 1) the association of knee OA with physical activity, and 2) of physical activity with knee pain, function, and HRQoL in participants with clinical knee OA. All analyses were adjusted for age, sex, body mass index (BMI), ethnicity, educational level and comorbidities. To account for possible information bias, we performed a sensitivity analysis to assess the association between clinical knee OA and physical activity measured by an accelerometer in a random subset of 15% of the study population.

Results: Of 6,212 participants, we observed clinical knee OA in 14%, and structural knee OA in 12%. The general population characteristics and median physical activity of our study population are presented in Table 1. In comparison to participants without knee OA, participants with clinical knee OA had on average 9.60 (95% CI 3.70;15.50) MET hours per week more total physical activity (Figure 1). Structural knee OA was associated with 3.97 (-7.82; 15.76) MET hours per week more physical activity, compared with no structural knee OA.

Sensitivity analysis showed a weak positive association of clinical knee OA with physical activity measured by an accelerometer: 2.37 (-6.05; 10.80) MET hours per week more physical activity in participants with clinical knee OA, compared with participants without clinical knee OA.

In the subpopulation of participants with clinical knee OA, physical activity was not associated with knee pain, function or HRQoL.

Conclusion: Knee OA was not associated with lower physical activity in this middle-aged Dutch population. This contrasts previous findings and warrants caution when generalizing physical activity outcomes to other populations. Furthermore, it stresses the need of more insight in the barriers and facilitators of physical activity in the middle-aged population.

Table 1. Characteristics of the NEO study population

	All n = 6,214	No clinical knee OA 86%	Clinical knee OA 14%
General population characteristics			
Age (year)	55.7 (6.0)	55.4 (6.1)	57.5 (5.0)
Sex (% women)	55	54	67
BMI (kg/m^2)	26.3 (4.4)	26.1 (4.3)	27.6 (5.1)
Comorbidities (% present)	24	23	32
Physical activity			
Total^ (MET-hours per week)	118.8 (76.8;155.0)	118.4 (76.6;154.4)	123.5 (77.8;157.2)

Numbers represent mean (SD) or percentages. ^median (25th, 75th percentiles). Abbreviations: OA = osteoarthritis. BMI = Body Mass Index. MET = Metabolic Equivalent of Task.

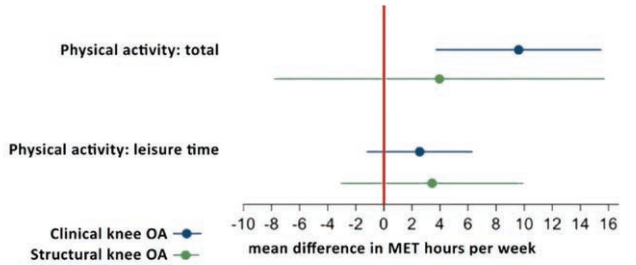


Figure 1. Association of clinical and structural knee OA with physical activity

Figure 1: the association of clinical and structural knee osteoarthritis with physical activity adjusted for age, sex, body mass index, ethnicity, educational level and comorbidities. Reference: participants without knee osteoarthritis. The dots represent the means, and the blue and green lines represent the 95% confidence interval around the means. Abbreviations: OA = osteoarthritis. MET = Metabolic Equivalent of Task.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2363

POS1432

SHORT-TERM RISK OF OSTEOPOROSIS IN ADULTS TREATED WITH CORTICOSTEROIDS: AN OBSERVATIONAL STUDY

E. Berni[1], P. Ambery[2], S. Adamsson Eryd[3], S. Jenkins-Jones[1], M. Brown[4], C. Astbury[5], P. Hunt[6], C. Currie[1,7]. [1]*Pharmatelligence, Epidemiology, Cardiff, United Kingdom*; [2]*AstraZeneca, Late-Stage Development, Cardiovascular, Renal and Metabolism, BioPharmaceuticals R&D, Gothenburg, Sweden*; [3]*AstraZeneca, BioPharmaceuticals Medical, CVRM Evidence, Gothenburg, Sweden*; [4]*AstraZeneca, Research and Early Development, Respiratory & Immunology, BioPharmaceuticals R&D, Boston, United States of America*; [5]*AstraZeneca, Research and Early Development, Respiratory & Immunology, BioPharmaceuticals R&D, Cambridge, United Kingdom*; [6]*AstraZeneca, BioPharmaceuticals Medical, CVRM Evidence, Gaithersburg, United States of America*; [7]*Cardiff University, School of Medicine, Cardiff, United Kingdom*

Background: Exposure to corticosteroids is recognised to increase the risk of osteoporosis.

Objectives: Our aim was to evaluate patients' short-term absolute risk of osteoporosis over the course of their first continuous exposure to corticosteroids.

Methods: This was an observational study using UK data from the Clinical Practice Research Datalink. Adult patients were selected if exposed to systemic corticosteroids for any condition and had no prior osteoporosis. Non-exposed adults matched on age, sex, and disease burden were selected from the general population. Patients were followed from their first exposure to corticosteroid to the earlier of 90 days following the end of continuous prescribing or for a maximum of three years. Cohorts were categorised by age (18-42 years, 43-67 and 68-92 years), BMI (underweight, normal overweight, obese and obese+) and gender. Absolute risk rates were calculated for each of these categories.

Results: In total, 573,056 exposed patients were matched 1:1 to non-exposed controls. Mean age was 52 years; 57% were female. The mean and median days' supply were 50.9 and 13 days, respectively. Underweight females aged 68-92 years exposed to corticosteroids had the highest absolute risk of osteoporosis (70.9 per 1000 patient years (PKPY)); in matched non-exposed controls this was 26.6 PKPY. Generally, following their first continuous exposure to corticosteroids, patients taking steroids had greater risk of osteoporosis compared with those in the same age, sex and BMI category never exposed to corticosteroids.

Conclusion: Whilst it is understood that exposure to corticosteroids increases the risk of osteoporosis, there are large differences in risk in accordance with age, sex and BMI. Alternatives to corticosteroids are urgently needed.

		Male					Female				
		Steroid-exposed		Never exposed			Steroid-exposed		Never exposed		
Age group	BMI group	Patients	Absolute rate (per 1,000 patient years)	Patients	Absolute rate (per 1,000 patient years)	*p*-value	Patients	Absolute rate (per 1,000 patient years)	Patients	Absolute rate (per 1,000 patient years)	*p*-value
18-42	1: Underweight	1,242	2.0	1,195	0.0	0.5661	3,079	4.5	3,486	0.9	0.1361
	2: Normal	18,798	2.2	19,638	0.0	<0.0001	42,234	0.9	47,340	0.1	0.0049
	3: Overweight	16,536	2.6	15,114	0.0	0.0001	24,893	0.5	24,009	0.1	0.2382
	4: Obese +	10,311	0.6	8,453	0.0	0.2874	26,600	0.6	20,320	0.3	0.4614
43-67	1: Underweight	1,254	27.4	683	0.0	0.0040	2,420	30.9	1,990	18.5	0.1141
	2: Normal	27,037	8.6	26,569	2.0	<0.0001	45,467	15.9	50,423	6.1	<0.0001
	3: Overweight	42,428	4.3	43,872	0.7	<0.0001	42,620	10.8	43,253	4.1	<0.0001
	4: Obese +	31,478	2.5	30,852	0.8	0.0007	45,339	6.0	39,876	2.4	<0.0001
68-92	1: Underweight	936	30.3	432	10.3	0.1505	1,532	70.9	1,239	26.6	0.0003
	2: Normal	15,891	11.3	15,021	4.5	<0.0001	18,308	42.3	18,717	18.6	<0.0001
	3: Overweight	21,371	7.3	23,137	1.8	<0.0001	19,149	26.2	19,760	12.9	<0.0001
	4: Obese +	11,216	5.6	11,396	1.9	0.0021	14,453	20.0	13,614	8.7	<0.0001

Disclosure of Interests: Ellen Berni Consultant of: Employed by Pharmatelligence, which carries out consultancy work for AstraZeneca and other pharmaceutical companies., Philip Ambery Shareholder of: AstraZeneca, Employee of: AstraZeneca, Samuel Adamsson Eryd Shareholder of: AstraZeneca, Employee of: AstraZeneca, Sara Jenkins-Jones Consultant of: Employed by Pharmatelligence, which carries out consultancy work for AstraZeneca and other pharmaceutical companies., Mary Brown Shareholder of: AstraZeneca, Employee of: AstraZeneca, Carol Astbury Shareholder of: AstraZeneca, Employee of: AstraZeneca, Phillip Hunt Shareholder of: AstraZeneca, Employee of: AstraZeneca, Craig Currie Consultant of: Director of Pharmatelligence, which carries out consultancy work for AstraZeneca and other pharmaceutical companies

DOI: 10.1136/annrheumdis-2021-eular.2424

POS1433 IMPACT OF RHEUMATOID ARTHRITIS ON STRESS: A SYSTEMATIC SCOPING REVIEW

C. Vervloesem[1], D. De Cock[1], A. Van Breda[1], D. Bertrand[1], M. Doumen[1,2], S. Pazmino[1], R. Westhovens[1,2], P. Verschueren[1,2]. *[1]KU Leuven, Skeletal Biology and Engineering Research Centre, Leuven, Belgium*; *[2]University Hospitals Leuven, Rheumatology, Leuven, Belgium*

Background: The literature about the impact of Rheumatoid Arthritis (RA) on mental health is mostly focused on depression and anxiety. Yet, patients can experience stress without depressed mood or anxiety.
Objectives: To examine the impact of RA on psychological stress excluding depression and anxiety focusing on 3 questions: 1) What is the stress level of RA patients compared to a control group? 2) Which types of stress do RA patients experience? 3) Which are risk factors to develop stress as an RA patient?
Methods: Four scientific databases, EMBASE, PubMed (including MEDLINE), Web of Science Core Collection and Cochrane Library, were systematically searched from inception until 19/04/2020. Eligible studies included psychological stress in RA patients as outcome. Two reviewers (CV&AVB) independently screened titles and abstracts, and later full texts for eligibility. Full-text screening excluded studies without a separate RA population, with a focus on only anxiety and/or depression or not answering at least 1/3 research questions. Quality was appraised by MINORS/AXIS tools.
Results: From 11 115 potentially relevant studies, 16 studies met the inclusion criteria (Table 1). Remarkably, 13 different stress measurement instruments were picked-up in this review. Work stress and interpersonal stress seem more prevalent in RA patients compared to healthy controls. Stress at disease onset was more prevalent in RA compared to osteoarthritis. Psychological stress was higher in patients with chronic pain compared to RA. Role stress, social stress and work stress were induced by RA. More disability, more pain, less social support, lower income, younger age and personality factors like excessive worrying, pessimism, and sensitivity to anxiety, seem to increase the risk for increased stress levels.
Conclusion: This scoping review is to our knowledge the first to address the heterogeneity of measurement tools and definitions of stress in RA research. It provides the basis for further research, which is needed to predict different stress trajectories and respond to these with patient-centered interventions.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2702

Table 1. Included Studies

First Author	Year	Country	Population	Age Mean ±SD	Stress Instrument	Quality Assessment
Bugajska	2010	Poland	N=437 Polish N=137 German	>50y (71%) >50y (38%)	SF36v2	AXIS: 16/20
Coty	2017	USA	N=80	54y ±12y	RCQW	AXIS: 17/20
Cunha	2016	Portugal	N=80	58y	DASS-21	AXIS: 10/20
Goulia	2015	Greece	N=168	55y ±13y	SCL-90R	MINORS: 11/16
Latman	1996	USA	RA, N=128 OA, N=79	56y 63y	SRRS	AXIS: 20/20
Mancuso	2006	USA	RA, N=122 HC, N=122	49y ±12y 49y ±12y	DUSOCS	MINORS: 20/24
Nyklicek	2015	The Netherlands	N=201	57y ±12y	PSS	MINORS: 13/16
Persson	2005	Sweden	N=158	52y	SCL-90R	MINORS: 12/16
Rahim	2018	Malaysia	N=189	52y ±11y	DASS-21	AXIS: 17/20
Rice	2017	Canada	RA, N=226 CP, N=229	58y ±15y 45y ±12y	DASS-21	AXIS: 17/20
Rice	2016	Canada	RA, N=163 CP, N=167	56y ±13y 45y ±11y	DASS-21	AXIS: 18/20
Richter	2018	Germany	RA, N=163 HC, N=167	48y ±10y 43y ±10y	ERI	AXIS: 17/20
Smith	2002	USA	RA, N=93 OA, N=82 HC, N=80	RA, 62y OA, 65y HC, 62y	1 question probing stress	MINORS: 17/24
Treharne	2007	UK	N=134	55y	PSS	MINORS: 11/16
Turner-Cobb	1998	UK	RA, N=13 CP, N=24	42y ±8y 39y ±4y	LEI/HUS	MINORS: 17/24
Zautra	1997	USA	N=41	55y ±10y	ISLE	MINORS: 12/16

POS1434 WHICH PROGNOSTIC FACTORS MIGHT PREDICT THE NEED FOR TREATMENT ADAPTATION IN EARLY RHEUMATOID ARTHRITIS? A COMPARISON OF MACHINE LEARNING, SURVIVAL ANALYSIS AND REGRESSION METHODS

G. Verhavert[1,2], T. Verdonck[2], S. Pazmino[1], V. Stouten[1], D. Bertrand[1], M. Doumen[1], R. Westhovens[1,3], P. Verschueren[1,3], D. De Cock[1]. *[1]KU Leuven, Skeletal Biology and Engineering Research Center, Leuven, Belgium*; *[2]KU Leuven, Department of Mathematics, Leuven, Belgium*; *[3]University Hospitals Leuven, Rheumatology, Leuven, Belgium*

Background: Current EULAR guidelines recommend treating RA early, intensively and to-target. A data-driven tool for planning the optimal moment for subsequent visits might adapt visit schedules more to the patient's needs, without losing treatment quality.
Objectives: To determine the optimal statistical model and clinical factors to predict the time to a treatment adaptation in early RA patients.
Methods: This study included 379 patients from the treat-to-target Care in Rheumatoid Arthritis (CareRA) trial. The CareRA protocol included 2 predefined treatment adaptation steps for patients not reaching low disease activity (DAS-28CRP<3.2). The 1st adaptation was an MTX dose increase and the second one was adding/increasing the dose of a 2nd csDMARD. Three predictive models (Cox Proportional Hazards, Linear Multi-Task Regression and Random Survival Forest) were trained and validated to predicting time until these 2 adaptations. Factor selection for these models was performed by applying Cox Proportional Hazards with LASSO penalty to each set of demographic and clinical variables recorded at baseline, w4 and w8. Models used these factors at these 3 time points to predict future treatment adaptations. Model performance was estimated by the Uno Concordance Index with five-fold cross-validation. Missing data were imputed by interpolation or mean score.
Results: Factors selected to predict the first per protocol change included TJC, SJC, HAQ, CRP, pain and morning stiffness>15min. Factors selected to predict the second per protocol change included TJC, SJC, PGA, PhGA. Uno Concordance indices showed similar scores per different statistical model but higher scores at w4 and w8 compared to baseline indicating a better predictive performance (Table 1. next page).

Table 1. ***Uno Concordance Scores. Format 'mean (min-max)'.***

		Baseline	Week 4	Week 8
Cox Proportional Hazards	Change 1	0.63 (0.59-0.69)	0.72 (0.68-0.80)	0.75 (0.69-0.82)
	Change 2	0.58 (0.50-0.66)	0.75 (0.65-0.87)	0.78 (0.65-0.93)
Linear Multi-Task Regression	Change 1	0.65 (0.62-0.68)	0.72 (0.68-0.78)	0.75 (0.69-0.79)
	Change 2	0.58 (0.51-0.68)	0.72 (0.67-0.82)	0.77 (0.68-0.89)
Random Survival Forest	Change 1	0.64 (0.58-0.67)	0.71 (0.66-0.78)	0.76 (0.68-0.80)
	Change 2	0.56 (0.50-0.68)	0.72 (0.60-0.82)	0.77 (0.64-0.92)

Conclusion: Our data-driven approach identified predictive clinical factors with a high face validity including joint counts, functionality scores and global health indicators. The different model approaches did not seem to increase the predictive capacity performance. However, our results underline that not so much the baseline disease status but rather the early response to initial treatment reflected in the selected predictive factors can be used for prediction of the need for further treatment adaptation. These models will have to be enriched with patient reported outcomes to further improve predictive performance.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2717

POS1435 CLINICAL CHARACTERIZATION AND PREDICTIVE FACTORS FOR PROGRESSION IN A COHORT OF ILD PATIENTS WITH FEATURES OF AUTOIMMUNITY: ARE IPAF CRITERIA SUFFICIENT?

F. Bozzao[1], P. Tomietto[2], E. Baratella[3,4], F. Giudici[4], M. Kodric[5], R. Della Porta[5], I. Prearo[6], S. M. G. Pirronello[7], F. Fischetti[2,4], M. Confalonieri[4,5], B. Fabris[4,8]on behalf of ILD multidisciplinary unit of the "Azienda sanitaria universitaria Giuliano Isontina" (Trieste). *[1]Azienda ULSS 2 Marca Trevigiana, Internal Medicine, Treviso, Italy*; *[2]Azienda Sanitaria Universitaria Giuliano Isontina, Internal Medicine - Rheumatology Unit, Trieste, Italy*; *[3]Azienda Sanitaria Universitaria Giuliano Isontina, Radiology, Trieste, Italy*; *[4]University of Trieste, Medicine, Surgery and Health Sciences, Trieste, Italy*; *[5]Azienda Sanitaria Universitaria Giuliano Isontina, Pneumology, Trieste, Italy*; *[6]University Hospital, LMU Munich, Vascular Medicine, Munich, Germany*; *[7]Azienda Ospedaliera Cannizzaro, Emergency Medicine, Catania, Italy*; *[8]Azienda Sanitaria Universitaria Giuliano Isontina, Internal Medicine, Trieste, Italy*

Background: It is unknown whether patients with interstitial lung disease (ILD) and only some features of autoimmunity have a different natural history from those with a defined connective tissue disease (CTD-ILD). The classification criteria for "ILD with autoimmune features" (IPAF) may not be able to characterize all these patients, especially those with a usual interstitial pneumonia (UIP) pattern [1].

Objectives: To determine clinical characteristics and predictive factors for progression in a cohort of ILD patients with features of autoimmunity, through the application of classification criteria for IPAF and specific CTD, whenever possible.

Methods: We retrospectively selected a cohort of consecutive patients with ILD as onset manifestation and features of autoimmunity (at least 1 autoantibody and/or 1 clinical sign/symptom), evaluated by our multidisciplinary unit from March 2009 to March 2020. All the final diagnoses were revised according to the latest CTD and IPAF criteria. Patients were followed up for 33 (16.5-69.5) months.

Results: Of the 101 patients enrolled (67.4±10.9 yrs, F/M ratio 65/36), 53 (52.5%) and 37 (36.6%) respectively satisfied the CTD and IPAF criteria. Eleven patients (10.9%) did not satisfy IPAF criteria because of only 1 item (clinical or serologic) within the IPAF domains and a UIP pattern; we defined this group as "autoimmune" UIP (AI-UIP). All the 8 patients initially classified as undifferentiated CTD had sufficient IPAF criteria. Among the IPAF patients (68.2±10.1 years, F/M ratio 20/17), the most common findings were: Nonspecific interstitial pneumonia pattern (56.8%), antinuclear antibodies positivity (43.2%) and arthritis (24.3%). The combination of a positive morphologic and serologic domain was the most common to reach the diagnosis (48.6%). Some IPAF patients had features not included in IPAF criteria, such as non-anti-synthetase myositis-specific antibodies (21.6%), objective sicca syndrome (13.5%) and anti-myeloperoxidase antibodies (2.7%). Over a median of 17 months, 2 IPAF patients (5.4%) developed a definite UIP pattern, while 4 (10.8%) a specific CTD. Comparing the IPAF, CTD-ILD and AI-UIP groups, no statistically significant differences were found in the mean age, sex distribution, smoking habits and mean duration of the disease. However, IPAF patients had a significantly higher prevalence of arterial hypertension and left-sided heart failure and a lower predominance of UIP pattern as expected (10.8% vs. 32.1% vs. 100%, $p<0.01$). Although no differences were found at the diagnosis, at 1 year the proportion of IPAF patients with radiological progression of the fibrosis and/or functional deterioration (defined by a decline in FVC of ≥ 10% and/or DLCO of ≥ 15% predicted) was lower to that of CTD-ILD and AI-UIP (17.1% vs. 31.4% vs. 63.6%, p 0.01). Fewer IPAF patients needed oxygen support (8.6% vs. 31.4% vs. 36.4, p 0.02). Considering the overall 101 patients, having an IPAF and a UIP pattern respectively predicted a slower (OR: 0.37, p 0.04) and a faster (OR: 3.56, p 0.01) ILD progression at the multivariate analysis.

Conclusion: In our cohort, IPAF criteria were useful to identify a subset of patients with a slower ILD progression and a possible evolution to CTD (10-15% of cases) [2]. These criteria do not characterize all the patients with a UIP pattern and limited features of autoimmunity, which seem to have a worse prognosis, independently from the final diagnosis. Further studies are needed to clarify if the prognosis of AI-UIP is different from that of idiopathic pulmonary fibrosis.

REFERENCES:

[1] Graney, *et al. Ann Am Thorac Soc* 2019;16(5):525-33.
[2] Sebastiani, *et al. Biomedicines* 2021,9,17.

DISCLOSURE OF INTERESTS:NONE DECLARED
DOI: 10.1136/annrheumdis-2021-eular.2899

POS1436 EPIDEMIOLOGY OF LATENT TUBERCULOSIS INFECTION IN PATIENTS WITH RHEUMATIC IMMUNE-MEDIATED DISEASES. SINGLE UNIVERSITY STUDY OF 1117 PATIENTS

D. Martínez-López[1], J. Osorio-Chavez[2], C. Álvarez-Reguera[3], V. Portilla[3], M. A. González-Gay[3], R. Blanco[3]. *[1]Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander (SPAIN), Spain*; *[2]Hospital Universitario Marqués de Valdecilla, Pulmonology, Santander (SPAIN), Spain*; *[3]Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*

Background: Patients with rheumatologic immune-mediated diseases (R-IMID) with Latent tuberculosis infection (LTBI) requiring biologic therapy (BT) are at an increased risk of active tuberculosis (TB). Screening of LTBI with tuberculin skin test (TST) and/or Interferon (IFN)-γ release assays (IGRA) is recommended before starting of BT.

Objectives: In patients with R-IMID previously to BT our aim was to assess **a)** prevalence of LTBI, **b)** importance of using a booster test in negative TST and **c)** to compare TST with the IGRA test.

Methods: Cross-sectional single University Hospital study including all patients diagnosed with R-IMID who underwent a TST and/or IGRA in the last five years (2016-2020).

TST was performed by a subcutaneous injection of 0.1 ml of purified protein derivative (PPD) with a reading after 72 hours. TST was considered positive with an induration of more than 5 mm of diameter. If the first TST was negative, a new TST (Booster) was performed between 1 and 2 weeks after the first TST.

LTBI was diagnosed by a positive IGRA and/or TST and absence of active TB (Chest radiograph). Diagnosis with IGRA vs TST was compared (Cohen's kappa coefficient).

Results: We included 1117 patients (741 women/376 men), mean age 53±15 years with LTBI. Chest radiograph was normal in most of the patients, only 39 patients (3.5%) presented signs of previous TB infection, mostly granuloma. Total LTBI prevalence was 31.7% (354/1117). LTBI prevalence in different underlying R-IMID ranges from 35% in vasculitis up to 26.5% in conectivopathies (Figure 1**).**

Booster was positive in 66 patients (7.7%) out of 859 patients with a negative simple TST. Results of TST (+booster) and IGRA tests are shown in Table 1. TST (+booster) was positive in 187 patients (22.9%) out of 817 with a negative or indeterminate IGRA test. IGRA test was positive in 30 (3.8%) out of 793 patients with a negative TST (+booster). Cohen's Kappa coefficient between TST (+booster) and IGRA (QFT-plus), was 0.381.

Conclusion: LTBI is frequent between patients with R-IMID. Booster after negative simple TST may be useful, since it can detect false negatives for LTBI. IGRA and TST(+booster) show a low grade of agreement. Therefore, performing both tests before BT may be recommendable.

Table 1. Results of TST (+booster) and IGRA test

		IGRA (QFT-Plus)				
		Positive	**Negative**	**Indeterminate**	**Unavailable**	**Total**
TST (+Booster)	**Positive**	89	142	45	48	324
	Negative	30	500	130	133	793
	Total	119	642	175	181	1117

* Cohen's kappa coefficient: 0.381

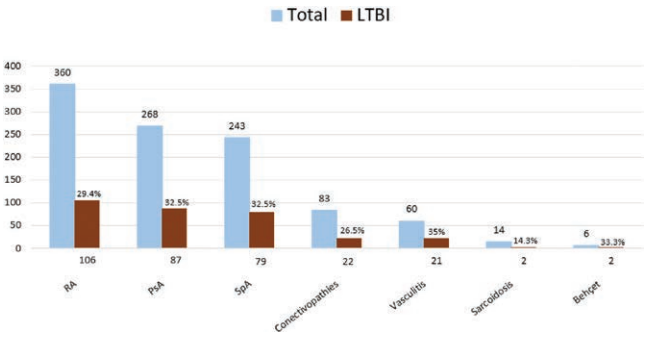


Figure 1. Prevalence of LTBI in different underlying R-IMID

LTBI: Latent tuberculosis infection, PsA: Psoriatic arthritis, RA: Rheumatoid arthritis, SpA: Axial spondyloarthritis.
Diagnosis of LTBI: Positive TST(+booster) and/or IGRA test.
Disclosure of Interests: David Martínez-López: None declared, Joy Osorio-Chavez: None declared, Carmen Álvarez-Reguera: None declared, Virginia Portilla: None declared, Miguel A González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi and MSD, Consultant of: Abbvie, Pfizer, Roche, Sanofi and MSD, Grant/research support from: Abbvie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Grant/research support from: Abbvie, MSD, and Roche
DOI: 10.1136/annrheumdis-2021-eular.2900

POS1437 LATENT TUBERCULOSIS INFECTION IN RHEUMATIC DISEASES: A REAL-LIFE STUDY OF THREE APULIAN CENTRES. DATA FROM BIOPURE REGISTRY

M. Fornaro[1], D. Goletti[2], A. Abbruzzese[1], M. G. Anelli[1], A. Semeraro[3], N. Maruotti[4], F. P. Cantatore[4], F. Cacciapaglia[1], F. Iannone[1]on behalf of BIOlogic aPUlian REgistry (BIOPURE). [1]*Rheumatology Unit, Department of Emergence and Transplantation (DETO), University of Bari, Bari, Italy*; [2]*Translational Research Unit, Department of Epidemiology and Preclinical Research, National Institute for Infectious Diseases, L. Spallanzani, Roma, Italy*; [3]*Rheumatology Unit, ASL Taranto, Taranto, Italy*; [4]*UOC Reumatologia Universitaria, University of Foggia, Foggia, Italy*

Background: Latent tuberculous infection (LTBI) is very common in the world and screening for it is essential before starting treatment with biotechnological drugs
Objectives: The aims of our study were to assess the prevalence in Apulia of LTBI among patients affected with rheumatic disease and to record the cases of tuberculosis (TB) infection among patients treated with biologic agents.
Methods: We analysed data of patients included in BIOPURE registry from 2008 to 2018, who underwent Quantiferon (QTF) test as routinely screening for biologic treatment. Demographic and clinical data were recorded at the time of the first QTF assessment and this time point was considered the "baseline" of the study. Data regarding further QTF tests performed during follow-up was also acquired by electronic charts. Prophylaxis administration and bDMARD treatments were recorded for patients with positive QTF test. All tuberculosis infections were recorded during the entire time of follow-up.
Results: Three thousand thirty-five patients (female 67.2%, mean age 52 ± 18.3 years) were included in these study, 2692 patients (88.7%) had inflammatory arthritis (28.2% rheumatoid arthritis, 33% psoriatic arthritis and 27.4% spondyloarthritis), 129 (4.2%) patients had connective tissue disease, whereas 214 (7.1%) patients were affected by others rheumatic diseases. The prevalence of LTBI was 10.7% (326 patients) at baseline. Comparisons between positive and negative patients for QTF are reported in Table 1. We acquired data of LTBI prophylaxis of 284 patients; 235 out 265 patients treated with isoniazid completed the treatment, whereas 19 out 19 patients treated with rifampicin completed the prophylaxis regimen. The main cause of isoniazid withdrawal was hypertransaminasemia, but 8 patients then completed prophylaxis with rifampicin. During the entire follow-up (42.6±30.5 months), we recorded 5 (0.02%) cases of primary TB infection in patients on anti-TNFα agents treatment, which had baseline screening negative for LTBI. Data and outcome of these patients are reported in Table 2. The mean time of follow-up of patients on bDMARDs treatment with positive QTF at baseline was 52.7±35.2 months. bDMARD treatment regimens are reported in Table 3. No case of TB reactivation was found among patients with positive baseline QTF. Moreover, of 1563 (51.5%) patients who repeated QTF during follow-up, 62 (4%) of them showed a change in the test result. We observed a change to a positive state in 36 patients with previous negative QTF test, whereas 26 patients with previous positive QTF showed a shift to a negative test during follow-up.
Conclusion: Our study shows a prevalence of LTBI of 10.7% in Apulian patients affected with rheumatic disease. bDMARDs therapy appears to be safe in patients with positive QTF test treated according to current recommendations[1]. However, cases of primary TB infections, especially in patients receiving anti-TNFα drugs, have been observed.
REFERENCES:
[1] Cantini F, et al, Guidance for the management of patients with latent tuberculosis infection requiring biologic therapy in rheumatology and dermatology clinical practice, Autoimmun Rev (2015).

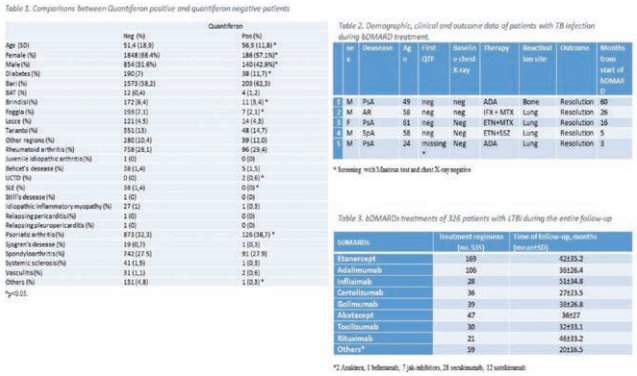


Table 1. Comparisons between Quantiferon positive and quantiferon negative patients

	Quantiferon	
	Neg (%)	Pos (%)
Age (SD)	51,4 (18,9)	56,9 (11,8) *
Female (%)	1848 (68.4%)	186 (57.1%)*
Male (%)	854 (31.6%)	140 (42.9%)*
Diabetes (%)	190 (7)	38 (11,7) *
Bari (%)	1573 (58,2)	209 (62,3)
BAT (%)	12 (0,4)	4 (1,2)
Brindisi (%)	172 (6,4)	11 (3,4) *
Foggia (%)	193 (7,1)	7 (2,1)*
Lecce (%)	121 (4,5)	14 (4,3)
Taranto (%)	551 (13)	48 (14,7)
Other regions (%)	280 (10,4)	39 (12,0)
Rheumatoid arthritis (%)	758 (28,1)	96 (29,4)
Juvenile idiopathic arthritis (%)	1 (0)	0 (0)
Behcet's desease (%)	38 (1,4)	5 (1,5)
UCTD (%)	0 (0)	2 (0,6) *
SLE (%)	38 (1,4)	0 (0) *
Still's desease (%)	1 (0)	0 (0)
Idiopathic inflammatory myopathy (%)	27 (1)	1 (0,3)
Relapsing pericarditis (%)	1 (0)	0 (0)
Relapsing pleuropericarditis (%)	1 (0)	0 (0)
Psoriatic arthritis (%)	873 (32,3)	126 (38,7) *
Sjogren's desease (%)	19 (0,7)	1 (0,3)
Spondyloarthritis (%)	742 (27,5)	91 (27,9)
Systemic sclerosis (%)	41 (1,5)	1 (0,3)
Vasculitis (%)	31 (1,1)	2 (0,6)
Others (%)	181 (4,8)	1 (0,3) *

*p<0.05.

Table 2. Demographic, clinical and outcome data of patients with TB infection during bDMARD treatment.

	se x	Deasease	Ag e	First QTF	Baselin e chest X-ray	Therapy	Reactivat ion site	Outcome	Months from start of bDMAR D
1	M	PsA	49	neg	neg	ADA	Bone	Resolution	60
2	M	AR	58	neg	neg	IFX + MTX	Lung	Resolution	26
3	F	PsA	61	neg	Neg	ETN+MTX	Lung	Resolution	16
4	M	SpA	58	neg	Neg	ETN+SSZ	Lung	Resolution	5
5	M	PsA	24	missing *	Neg	ADA	Lung	Resolution	3

* Screening with Mantoux test and chest X-ray negative

Table 3. bDMARDs treatments of 326 patients with LTBI during the entire follow-up

bDMARDs	Treatment regimens (no. 326)	Time of follow-up, months (mean±SD)
Etanercept	169	42±35.2
Adalimumab	106	36±26.4
Infliximab	28	51±34.8
Certolizumab	36	27±23.5
Golimumab	39	39±26.8
Abatacept	47	36±27
Tocilizumab	30	32±33.1
Rituximab	21	46±33.2
Others*	59	20±16.5

*2 Anakinra, 1 belimumab, 7 jak-inhibitors, 28 secukinumab, 12 ustekinumab

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2932

POS1438 EARLY FACTORS ASSOCIATED WITH THE INITIATION OF TREATMENT WITH BIOLOGICS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS – RESULTS FROM A SINGLE CENTRE RETROSPECTIVE COHORT STUDY

E. Costa[1,2], L. Lages[3], D. Esperança Almeida[1,2], A. M. Gomes Correia[1], M. Cerqueira[1], J. Silva[1], A. R. Ribeiro[1], J. Redondo Costa[1], J. Neves[1]. [1]*Hospital de Braga, Rheumatology, Braga, Portugal*; [2]*Unidade Local de Saúde do Alto Minho, Rheumatology, Ponte de Lima, Portugal*; [3]*University of Minho, School of Medicine, Braga, Portugal*

Background: Axial Spondyloarthritis (axSpA) refers to a group of rheumatic diseases that mainly affect the axial skeleton. Treatment with Biological Disease Modifying Anti-Rheumatic Drug (bDMARDs) is indicated when low disease activity is not achieved with Non-Steroid Anti-inflammatory Drugs. Some studies reported that some clinical and socio-demographic were associated with biologics initiation[1,2]. However, early factors associated with the initiation of bDMARDs have not been extensively studied.
The authors speculate that certain features early in disease presentation may be associated with future need for treatment with bDMARDs in patients with axSpA.
Objectives: To study a population of patients with axSpA and determine whether the presence of certain factors at diagnosis is associated with a later need for biological treatment.
Methods: A single centre retrospective study was conducted comprising patients fulfilling the ASAS criteria for axSpA that attended the Rheumatology Outpatient Clinic from January to December 2019. Patients with psoriatic arthritis and enteropathic spondyloarthritis were excluded. All data, except regarding use of bDMARD, refers to the two initial appointments. Between group comparisons were performed through independent sample t-test or Chi-Square as applicable. Logistic Multivariate Regression was performed to understand which factors independently contributed to the use of bDMARDs.
Results: One hundred and fifty patients were included, and 52 patients (34,7%) were under biological treatment. In comparison to the group that was not under treatment with bDMARDs, these were significantly more likely to be *hard-workers* (57,8% *vs* 29,7%; p =,003), to have had elevated C-Reactive Protein (81,6% *vs* 48,9%; p <,001), to have had a grade of sacroiliitis greater than 2 (67,4% *vs* 29,5%; p <,001) and to have history of enthesitis, (32,7% *vs* 13,3%; p =,006). No differences between groups were found in sex, age, HLA-B27 positivity, state of employment, diagnostic delay, smoking status, history of dactylitis and history of uveitis. In multivariate regression analysis, only the *hard-worker* type and the highest grade of sacroiliitis were found to be independently associated with the use of bDMARDs as presented in Table 1. Although not statistically significant, a trend to association was found between elevated CRP at diagnosis and use of bDMARDs.

Table 1. Multivariate logistic regression of variables associated with initiation of bDMARDs.

		B	*S.E.*	*Wald*	*OR*	*95% CI*	*p*
Worker type[a]	Non-hard				ref.		
	Hard	1,127	,509	4,890	3.09	1.14 – 8.37	.027*
HLA-B27	Negative				ref.		
	Positive	1,153	,670	2,962	3.17	0.85 – 11.77	.085
CRP[a]	Normal				ref.		
	Elevated	1,003	,529	3,591	2.73	0.97 – 7.69	.058
Grade of Sacroiliitis[a]	≤2				ref.		
	>2	1,485	,489	9,226	4.41	1.69 – 11.50	.002*
History of Enthesitis[a]	No				ref.		
	Yes	,299	,574	,272	1.35	0.44 – 4.15	.602

[a]At the time of diagnosis; ref. - reference*S.E.* – Standard Error; *OR* – Odds Ratio; *CI* – Confidence Interval

Conclusion: In our study, the performance of work associated with greater biomechanical stress and the presence of greater structural damage at diagnosis were shown to be associated with the latter use of bDMARDs. The authors highlight the importance of recognizing these factors that seem to relate to more aggressive disease, with more structural damage, thus suggesting a need for a tighter control management strategy in these patients accordingly current guidelines. More studies still needed to better depict the influence of certain early clinical and patient related variables in management of axSpA patients.

REFERENCES:

[1] Png WY, Kwan YH, Lee YX, *et al.* Factors Associated with Initiation of Biologics in Patients With Axial Spondyloarthritis in an Urban Asian City: A PRESPOND Study. *J Clin Rheumatol*. 2019 Mar;25(2):59-64.

[2] Inman R, Garrido-Cumbrera M, Chan J*, et al* SAT0629-HPR FACTORS ASSOCIATED WITH USE OF BIOLOGICAL THERAPIES FOR AXIAL SPONDYLOARTHRITIS IN CANADA. RESULTS FROM THE IMAS SURVEY. *Annals of the Rheumatic Diseases* 2020;**79:**1274-1275.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2952

POS1439 A MULTI-PREDICTOR MODEL TO PREDICT RISK OF SCLERODERMA RENAL CRISIS IN SYSTEMIC SCLEROSIS

D. Xu[1], R. Mu[1]. [1]*Peking University Third Hopsital, Department of Rheumatology and Immunology, Beijing, China*

Background: Scleroderma renal crisis (SRC) is a life-threatening syndrome. The early identification of patients at risk is essential for timely treatment to improve the outcome[1].

Objectives: We aimed to provide a personalized tool to predict risk of SRC in systemic sclerosis (SSc).

Methods: We tried to set up a SRC prediction model based on the PKUPH-SSc cohort of 302 SSc patients. The least absolute shrinkage and selection operator (Lasso) regression was used to optimize disease features. Multivariable logistic regression analysis was applied to build a SRC prediction model incorporating the features of SSc selected in the Lasso regression. Then, a multi-predictor nomogram combining clinical characteristics was constructed and evaluated by discrimination and calibration.

Results: A multi-predictor nomogram for evaluating the risk of SRC was successfully developed. In the nomogram, four easily available predictors were contained including disease duration <2 years, cardiac involvement, anemia and corticosteroid >15mg/d exposure. The nomogram displayed good discrimination with an area under the curve (AUC) of 0.843 (95% CI: 0.797-0.882) and good calibration.

Conclusion: The multi-predictor nomogram for SRC could be reliably and conveniently used to predict the individual risk of SRC in SSc patients, and be a step towards more personalized medicine.

REFERENCES:

[1]Woodworth TG, Suliman YA, Li W, Furst DE, Clements P (2016) Scleroderma renal crisis and renal involvement in systemic sclerosis. Nat Rev Nephrol 12 (11):678-91.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3613

POS1440 ASSOCIATION BETWEEN SERUM URATE AND INFLAMMATORY MARKERS IN YOUNG ADULTS: CROSS-SECTIONAL FINDINGS FROM A BIRTH COHORT

T. Loyola Correa[1], I. Oliveira de Oliveira[2]. [1]*Universidade Federal de Pelotas, Faculty of Medicine, Pelotas, Brazil*; [2]*Universidade Federal de Pelotas, Postgraduate Program in Epidemiology, Pelotas, Brazil*

Background: Uric acid is the end product of purine metabolism and an abruptly increase or decrease on its serum concentrations can form free urate crystals and precipitate a gout attack. Serum urate (SU) has been positively and independently associated with cardiometabolic diseases in observational studies, but causal roles remain unclear.[1] In addition, inflammatory markers are deeply associated with cardiometabolic diseases, such as essential hypertension and type 2 diabetes mellitus.[2] However, little has been published about the association of SU and subclinical inflammation.

Objectives: To assess the associations of SU with interleukin 6 (IL-6), C-reactive protein (CRP), and adiponectin at 22-year-old individuals belonging to the 1993 birth cohort of Pelotas (Brazil).

Methods: During 1993, all live born babies in the city were invited to take part in a prospective study and sub-samples of this cohort were followed-up since then. At the 22-year follow-up, interviews and clinical measurements were performed and non-fasting blood samples were drawn from the participants. SU was evaluated by enzymatic-colorimetric assay; IL-6 and adiponectin, by immunoassay; and CRP by immunoturbidimetric assay. The co-variables taken into consideration were skin color; asset index at 22 years; cardiometabolic risk factors (body mass index, systolic and diastolic blood pressure); presence of cardiometabolic diseases (hypertension, diabetes and dyslipidemia); and behavioral variables (alcohol use disorder, smoking status and physical inactivity). Exposition variables were categorized into tertiles. Sex-stratified linear regressions have been performed using STATA 13 and p<0.05 was considered statistically significant.

Results: The sample was composed by 1657 (46.3%) men and 1921 (53.7%) women of 22 years old. The median (25-75 IQR) for IL-6 (pg/mL) was higher in women than in men [1.26 (0.85; 2.02) *vs.* 1.07 (0.76; 1.69)]; the same was observed for CRP (mg/dL) [1.6 (0.6; 4.1) *vs.* 0.6 (0.3; 1.4)]. The mean (95%CI) for adiponectin (µg/mL) was also higher in women [10.72 (10.50; 10.94) *vs.* 7.97 (7.78; 8.16)]. As expected, the mean (±SD) for SU (mg/dL) was higher in men (5.2±1.2 *vs.* 3.9±1.1). In adjusted analysis, IL-6 was positively associated with SU only in women; p=0.018 (Table 1). CRP was positively associated with SU in crude and adjusted analyses for both sexes; p=0.002 (Table 1). In addition, higher adiponectin was independently associated with lower concentrations of SU for men (p<0.001) and women (p=0.013) (Table 1).

Conclusion: The increase of SU is associated with IL-6 and CRP increasing and adiponectin decreasing since early adult age.

REFERENCES:

[1] Mortada I. Curr Hypertens Rep. 2017;19(9):69.

[2] Pouvreau C et al. J Inflamm Res. 2018;19(11):61-68.

Table 1. Mean SU concentrations (mg/dL) according to physiological markers' tertiles

		Men				Women			
		Crude		Adjusted		Crude		Adjusted	
Physiological marker	Tertile	Mean	CI95%	Mean	CI95%	Mean	CI95%	Mean	CI95%
			p<0.001		*p=0.12*		***p<0.001***		***p=0.018***
IL-6	1	5.01	(4.91; 5.12)	5.16	(5.06; 5.26)	3.67	(3.58; 3.77)	3.85	(3.76; 3.95)
	2	5.29	(5.19; 5.40)	5.30	(5.19; 5.40)	3.81	(3.72; 3.90)	3.88	(3.79; 3.97)
	3	5.46	(5.35; 5.58)	5.30	(5.18; 5.42)	4.23	(4.14; 4.31)	4.03	(3.94; 4.12)
			p<0.001		***p=0.002***		***p<0.001***		***p=0.002***
CRP	1	5.01	(4.93; 5.09)	5.14	(5.05; 5.22)	3.57	(3.47; 3.66)	3.77	(3.67; 3.87)
	2	5.37	(5.26; 5.47)	5.31	(5.20; 5.41)	3.89	(3.80; 3.98)	3.95	(3.86; 4.03)
	3	5.62	(5.48; 5.75)	5.42	(5.28; 5.56)	4.13	(4.06; 4.20)	3.99	(3.92; 4.06)
			p<0.001		***p<0.001***		***p<0.001***		***p=0.013***
Adiponectin	1	5.45	(5.37; 5.54)	5.36	(5.27; 5.45)	4.26	(4.16; 4.36)	4.06	(3.95; 4.16)
	2	5.09	(4.99; 5.20)	5.19	(5.09; 5.30)	3.93	(3.84; 4.01)	3.91	(3.83; 3.99)
	3	4.97	(4.84; 5.09)	5.07	(4.94; 5.19)	3.75	(3.67; 3.82)	3.86	(3.79; 3.93)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3790

POS1441

SYMPTOMS CHARACTERISTICS OF SEROPOSITIVE INDIVIDUALS AT-RISK FOR DEVELOPING RHEUMATOID ARTHRITIS ARE VERSATILE AND COMPARABLE TO THOSE IN PEOPLE WITH EARLY RHEUMATOID ARTHRITIS

P. Studenic[1,2], A. Circiumaru[1,3], D. Aletaha[2], K. Chatzidionysiou[1,4], A. Hensvold[1,3], A. Catrina[1,4]. [1]*Karolinska Institute, Department of Medicine (Solna), Division of Rheumatology, Stockholm, Sweden*; [2]*Medical University of Vienna, Department of Internal Medicine 3, Division of Rheumatology, Wien, Austria*; [3]*Academic Specialist Center - Stockholm Health Care Services, Center for Rheumatology, Stockholm, Sweden*; [4]*Karolinska University Hospital, Rheumatology Unit, Stockholm, Sweden*

Background: The symptom burden of typical rheumatoid arthritis (RA) symptoms in those at risk for developing RA - positive for anti-citrullinated peptide antibodies (ACPA) and musculoskeletal complaints - has not been explored.
Objectives: To evaluate patient-reported symptoms in individuals at-risk to develop RA in comparison to people with newly diagnosed, early seropositive RA.
Methods: Two datasources from the region of Stockholm were used: The RISK RA cohort follows up ACPA positive individuals with arthralgia, but without signs of joint inflammation in a structured program over 3 years. The baseline visit of this cohort was used. Patients with early seropositive (ACPA and/or rheumatoid factor positive) RA (symptom duration of 12 months maximum) reported in the Swedish Rheumatology Quality Register (SRQ) at their closest visit to their diagnosis date before receiving DMARD treatment have been identified. At-risk individuals were matched 1:3 by sex and age using the nearest neighbour method utilizing Mahalanobis distance, corrected for sample bias and exact matches on sex. Effect estimates of being at-risk compared to early RA for pain, patient global (GH), fatigue (all visual analogue scales), health assessment questionnaire (HAQ), TJC28 and the EuroQol-5D (EQ5D; range: 0-1) have been derived. Propensity score matching was used as sensitivity analyses.
Results: A total of 223 individuals at risk for developing RA were compared to 820 matched early RA patients. The summary of distribution of variables and effect estimates of differences between at-risk and early RA individuals are shown in the Figure 1. At-risk individuals show 24mm of lower pain scores than early RA. This difference is even less (-17mm, 95%CI: -24 to -11) when the estimate is additionally matched for the number of tender joints. The TJC28 was on average 5.4 joints lower than in early RA patients. People at-risk show 22mm lower GH scores (rate themselves better) and 17mm lower fatigue scores than early RA patients. Fatigue was scored highest (mean:35mm, 95%CI: 30 to 29) among the three VAS. HAQ was on average lower by 0.6 points in at-risk individuals and EQ5D showed 0.24 higher index-values, outlining a better health status. Still the mean EQ5D in at-risk individuals was only 0.74 (95%CI: 0.71 to 0.77), which is lower than average values of an age-matched general population (0.92 to 0.96). Sensitivity analyses revealed similar results.

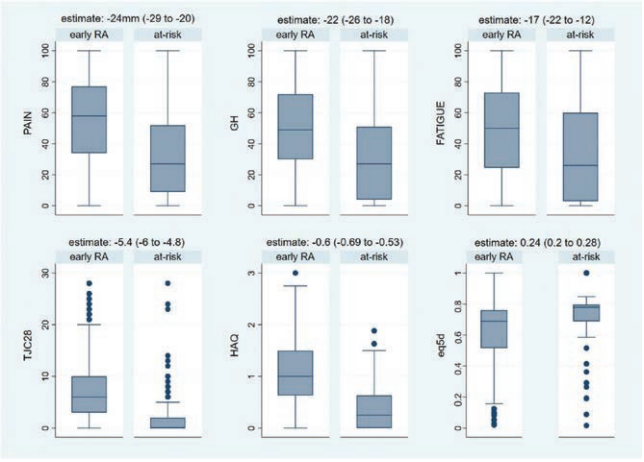


Figure 1. Boxplots of pain, global health, fatigue, TJC28, EQ5D and HAQ, separately displayed for people with early seropositive RA and individuals at-risk. Population effect estimates (all p<0.001) comparing at-risk to early RA are provided for every pair, with 95% confidence interval in brackets.

Conclusion: Not surprisingly, individuals at risk for RA report less symptom burden then early diagnosed RA patients. However, these differences only range around minimal clinically important differences and for fatigue even below, which stresses the need for medical attention and management strategies for symptomatic at-risk individuals.

Acknowledgements: This study was supported through the New Horizon Fellowship and the FOREUM research fellowship grant and is part of the Innovative Medicines Initiative Joint Undertaking under grant agreement no 777357 (RTCure).
Hensvold AH and Catrina IA contributed equally.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3884

Validation of outcome measures and biomarkers

POS1442

THE SUBGROUP OF ACPA-NEGATIVE RHEUMATOID ARTHRITIS PATIENTS ACHIEVING SUSTAINED DMARD-FREE REMISSION IS CHARACTERIZED BY A DIFFERENT RESPONSE IN SEROLOGICAL MARKERS WITHIN THE FIRST YEAR OF DMARD-INITIATION

M. Verstappen[1], A. Van der Helm - van Mil[1,2]. [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [2]*Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands*

Background: Whilst ~40% of ACPA-negative RA-patients achieve sustained DMARD-free remission (SDFR; the sustained absence of synovitis after DMARD-cessation), the biological pathways involved in SDFR-development are incompletely understood. Previously, high baseline levels of MMP-3, SAA and CRP were found in ACPA-negative RA-patients achieving SDFR. Differences in biomarker levels might reflect distinct underlying biological pathways leading towards disease resolution in this subgroup of ACPA-negative RA-patients. Subsequently, the course of specific biomarkers after treatment-initiation could attain more insight in the understanding of SDFR-development in ACPA-negative RA.
Objectives: We explored whether the response of specific biomarkers after treatment-initiation could increase the understanding of SDFR-development in ACPA-negative RA.
Methods: One-hundred-thirty-one consecutive ACPA-negative RA-patients were studied on SDFR-development during (median) 7.2-years follow-up. Twelve biomarkers (SAA/CRP/MMP-1/MMP-3/resistin/leptin/IL-6/TNF-R1/YKL-40/EGF/VEGF/VCAM-1) were measured at diagnosis and 1-, and 2-years after DMARD-initiation and compared between patients achieving and not achieving SDFR. To extend on previous findings on baseline levels, correlations between baseline levels and change in levels within year-1 were determined using spearman's rho (ρ).
Results: RA-patients that achieved SDFR (n=63) were characterized by a stronger decline in MMP-1, MMP-3, SAA and CRP in the first 12-months after DMARD-start, compared to RA-patients not achieving SDFR. MMP-1 and MMP-3 declined 1.30-times (95%CI; 1.08-1.57) and 1.44-times (95%CI; 1.00-2.06) stronger in SDFR-patients. In SAA and CRP, this decline was 2.12-times (95%CI; 1.08-4.14) and 2.24-times (95%CI; 1.16-4.35) stronger. Baseline levels of MMP-3, SAA and CRP and strongly correlated with decline in 12-months; ρ -0.6991, ρ -0.9205 respectively ρ -0.9008. RA-patients with high baseline levels characterized the subgroup with the strongest decline in biomarker levels in the first year after DMARD-initiation.
Conclusion: The subgroup ACPA-negative RA-patients achieving SDFR are characterized by higher baseline levels and a stronger serological response of MMP-3, SAA and CRP after DMARD-initiation. Because MMP-3 and SAA are expressed by fibroblast-like synoviocytes, these cells may differ in RA-patients achieving disease resolution; molecular studies on synovial tissue could be a next step.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.246

POS1443

RELATIONSHIP BETWEEN FIBRINOGEN TO ALBUMIN RATIO AND DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

M. Liu[1], Y. Huang[1], Z. Huang[1], Q. Huang[1], T. W. Li[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*

Background: Systemic lupus erythematosus (SLE) is a systemic inflammatory autoimmune disease characterized by excessive production of immune complexes and proinflammatory cytokine. Low complement, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been used as inflammatory biomarkers to assess the disease activity of SLE. Recently, the fibrinogen to albumin ratio (FAR) has emerged as an effective indicator to reflect the systemic inflammation in many diseases. However, the role of FAR in SLE has been scarcely studied.
Objectives: This study was to investigate the association between FAR and SLE Disease Activity Index 2000 (SLEDAI-2K) in SLE.

Methods: This retrospective study included 74 SLE patients and 79 age- and sex-matched healthy subjects. According to the SLEDAI-2K score, SLE patients were divided into Group 1 with a score ≤ 9 (patients with mild disease activity, *N* = 41) and Group 2 with a score > 9 (patients with moderate to severe disease activity, *N* = 33). Neutrophil, lymphocyte, monocyte, platelet, albumin, fibrinogen, NLR, PLR, monocyte to lymphocyte ratio (MLR), FAR, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complement 3 (C3), complement 4 (C4) and SLEDAI-2K were collected. Receiver operation characteristic (ROC) curves were conducted to discriminate SLE patients from healthy controls and SLE patients with different disease activity. Correlations between the inflammatory markers and SLEDAI-2K were analyzed.
Results: FAR, NLR, PLR, MLR and fibrinogen in SLE patients were higher compared to those of the healthy controls ($P < 0.05$), while albumin was lower ($P < 0.05$). Patients in Group 2 had higher levels of FAR, NLR, PLR, fibrinogen and CRP than those in Group 1 ($P < 0.05$) except MLR ($P = 0.579$) and ESR ($P = 0.130$), albumin and C3 were lower ($P < 0.05$). Furthermore, FAR were higher in SLE patients with nephritis than those without nephritis ($P = 0.009$). The ROC curve for differentiating SLE patients from healthy individuals showed that the area under curve (AUC) of FAR (0.801, 95%CI: 0.728 - 0.874) and albumin (0.833, 95%CI: 0.764-0.903) were higher than NLR (0.798, 95%CI: 0.725 - 0.871), PLR (0.680, 95%CI: 0.588 - 0.771), MLR (0.785, 95%CI: 0.712 - 0.859) and fibrinogen (0.645, 95%CI: 0.556 - 0.733). Besides, the ROC curve for predicting the disease activity of SLE patients indicated that the AUC of FAR (0.911, 95%CI: 0. 842 - 0.980) was higher than NLR (0.697, 95%CI: 0.574 - 0.821), PLR (0.695, 95%CI: 0.571 - 0.820), MLR (0.553, 95%CI: 0.415 - 0.691), fibrinogen (0.718, 95%CI: 0.590 - 0.847), CRP (0.672, 95%CI: 0.540 - 0.803), ESR (0.640, 95%CI: 0.510 - 0.770), C3 (0.644, 95%CI: 0.515 - 0.773), C4 (0.544, 95%CI: 0.407 - 0.681) and albumin (0.894, 95%CI: 0.819 - 0.969). FAR was positively correlated with SLEDAI-2K ($r = 0.682$, $P < 0.001$), yielding a highest relevance than other inflammatory parameters.
Conclusion: FAR was significantly elevated in SLE patients compared with healthy subjects and related with the disease activity of SLE. FAR might be a useful inflammatory index to evaluate disease activity in patients with SLE.
REFERENCES:
[1] Liu M, Huang Y, Huang Z, Zhong Z, Deng W, Huang Z, et al. The role of fibrinogen to albumin ratio in ankylosing spondylitis: Correlation with disease activity. Clin Chim Acta. 2020 Jun; 505:136-140.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1406

POS1444 ADOPTION OF DIGITAL MANIKINS TO SELF-REPORT PAIN: A SYSTEMATIC REVIEW

S. Mustafa Ali[1], R. Lee[1], A. Chiarotto[2], J. Mcbeth[1], S. Van der Veer[3], W. Dixon[1]. [1]*University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; [2]*Erasmus University Medical Centre, Department of General Practice, Rotterdam, Netherlands*; [3]*University of Manchester, Centre for Health Informatics, Manchester, United Kingdom*

Background: Chronic pain is common in rheumatic and musculoskeletal conditions, and a major driver of disability worldwide. Knowledge gaps exist with respect to correct estimates of chronic pain [1], what causes it and how best to manage it [2]. To address this, researchers need validated methods to measure pain in large, representative populations. Though many authors have recognised the potential benefits of paper-based and digital pain manikins [3]–[5], it is unknown to what extent studies have adopted digital manikins as a data collection tool.
Objectives: The objective of our review was to identify and characterise published studies that have used digital pain manikins as a data collection tool.
Methods: We systematically searched six electronic databases, including Medline, CINAHL, Embase, Scopus, IEEE Xplore digital library, ACM Digital Library, on 3-4 of November 2020 by using a pre-defined search strategy. We included a study in our review if it used a digital manikin for self-reporting any pain aspect (e.g., intensity, type) by people suffering from pain, and if its full text was published in English. We conducted this review by following the PRISMA reporting guidelines and conducted a descriptive synthesis of findings, including manikin-derived outcome measures.
Results: Our search yielded 4,685 unique studies. After full text screening of 705 articles, we included 14 studies in our review. Most articles were excluded because they used either paper-based manikins or didn't include enough details to determine that the manikin was digital (n=386). The majority of included studies were published in Europe (n=11). Most studies collected data on a manikin once (n=11); from people with pain conditions (n=9); and in clinical settings (n=9). There was only one study that collected digital pain manikin data in a large sized (i.e., ~20,000) population-based survey.
In most studies participants shaded any painful area on manikin (n=9) and did not enable participants to record location-specific pain aspects (n=11). None of the manikins enabled participants to record location-specific pain intensity. Pain distribution (i.e. number or percentage of pre-defined body areas or locations experiencing pain) and pain extent (i.e. number or percentage of shaded pixels) were commonly used manikin-derived outcome measures. In six studies, a heat map was used to summarise the extent of pain across the population.
Conclusion: Digital pain manikins have been available since the 1990s but their adoption in research has been slow. Few manikins enabled location-specific pain recording suggesting that the digital nature of the manikin is not yet fully utilised. Future development of a validated digital pain manikin supporting self-reporting of the location and intensity of pain, usable across any device and screen size, may increase uptake and value.
REFERENCES:
[1] S. E. E. Mills, K. P. Nicolson, and B. H. Smith, "Chronic pain: a review of its epidemiology and associated factors in population-based studies," *Br. J. Anaesth.*, vol. 123, no. 2, pp. e273–e283, Aug. 2019.
[2] D. B. Reuben *et al.*, "National Institutes of Health Pathways to Prevention Workshop: The Role of Opioids in the Treatment of Chronic Pain," *Ann. Intern. Med.*, vol. 162, no. 4, p. 295, Feb. 2015.
[3] R. Waller, P. Manuel, and L. Williamson, "The Swindon Foot and Ankle Questionnaire: Is a Picture Worth a Thousand Words?," *ISRN Rheumatol.*, vol. 2012, pp. 1–8, 2012.
[4] M. Barbero *et al.*, "Clinical Significance and Diagnostic Value of Pain Extent Extracted from Pain Drawings: A Scoping Review," *Diagnostics*, vol. 10, no. 8, p. 604, Aug. 2020.
[5] S. M. Ali, W. J. Lau, J. McBeth, W. G. Dixon, and S. N. van der Veer, "Digital manikins to self-report pain on a smartphone: A systematic review of mobile apps," *Eur. J. Pain*, vol. 25, no. 2, pp. 327–338, Feb. 2021.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2679

POS1445 RETINOL BINDING PROTEIN 4 AS AN ACUTE PHASE REACTANT AND BIOMARKER IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER AND AMYLOIDOSIS COMPARED TO INFECTIONS

N. Koca[1], R. Deniz[1], M. Erdugan[1], Y. Yalçınkaya[1], B. Artim-Esen[1], M. L. Ocal[1], M. Inanc[1], A. Gül[1]. [1]*Istanbul Faculty of Medicine, Istanbul University, Division of Rheumatology, Department of Internal Medicine, Istanbul, Turkey*

Background: Retinol binding protein 4 (RBP4) is a plasma retinol transporter that transports retinol from liver to periphery. RBP4 has been studied as a biomarker in metabolic and neoplastic conditions, however its association with inflammation is not clear. Serum amyloid A (SAA), another retinol binding protein, has been known as a sensitive biomarker of inflammation in familial Mediterranean fever (FMF) and other autoinflammatory disorders. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and SAA are commonly used as acute phase reactants, but they are not successful in differentiating non-infectious inflammatory conditions from infections.
Objectives: We aimed to evaluate the potential of serum RBP4 as a biomarker of acute phase response and to determine its performance in differentiation of inflammation of patients with FMF and AA amyloidosis from infections.
Methods: A total of 169 participants in 5 groups, consisting of FMF (n = 60), FMF with AA amyloidosis (n = 58), non-FMF AA amyloidosis (n = 23), infections (n = 10, 3 pneumonia, 3 sepsis, 1 pyelonephritis, 1 fungal infection, 1 cellulitis, 1 disseminated zoster), and healthy controls (HC) (n = 18), were included and evaluated cross sectionally. Hemogram and serum CRP, ESR, SAA, ferritin, creatinine, AST, ALT, albumin levels were recorded from the patient charts. FMF and FMF + amyloidosis patients were evaluated during attack-free period. Serum RBP4 levels were investigated by ELISA (Elabscience, USA). Mean values and relative changes compared to healthy controls were evaluated for SAA, CRP, RBP4 levels in all groups.
Results: Serum RBP4 level was found to be higher in FMF group compared to the patients with infection ($p = 0.002$) and HC ($p < 0.001$) as well as in patients with amyloidosis. Compared to HC, 47%, 28% and 27% increase was observed in mean RBP4 levels in FMF, FMF + amyloidosis and non-FMF amyloidosis patients, despite no significant change in patients with infections. However, CRP and SAA elevations were much more prominent in patients with infections (58 and 134 times, respectively) compared to the patients with FMF (13 and 35 times, respectively), FMF + amyloidosis and non-FMF amyloidosis (Table 1). There was no significant difference in RBP4 levels between FMF, FMF-amyloidosis and non-FMF amyloidosis groups. CRP, ESR, ferritin and SAA levels were higher in the infection group compared to HCs.

Table 1. Demographic features and laboratory findings of the participants

Variables	FMF (n=60)	FMF-Amyloidosis (n=58)	Non-FMF-AA Amyloidosis (n=23)	Infection (n=10)	Healthy control (n=18)
Female/Male	46/14	33/25	8/15	3/7	8/10
Age (SD)*	38±13	43±11	53±13	65±15	33±9
	(18-74)	(21-69)			
Creatinine (mg/dL)*	0,8±0,2	1,7±1,7	2,0±1,6	1,7±1,0	0,7±0,2
Albumin(mg/dL)*	4,7±0,4	4,3±0,6	3,3±0,9	3,0±0,9	4,8±0,2
Ferritin (ng/mL)*	70±94	245±315	139±168	554±38	83±72
RBP4 (ng/mL)*	772±183	671±214	666±256	512±204	524±117
RBP4 (median)	770	653	645	487	498
	(434-1142)	(227-1259)	(331-1214)	(226-876)	(566-738)
CRP (mg/L)*	16±47,1	12,8±32,8	25,7±36,4	69±36,8	1,2±1,2
SAA (mg/dL)*	10,3±31,4	5,0±13,9	7,1±14,1	40,2±18,5	0,3±0,1
ESR*	15±13	19±16	41±29	45±42	7±5
Relative RBP4 increase	1,47±0,35	1,28±0,41	1,27±0,49	0,98±0,39	
Relative CRP increase	13,4±39,2	10,6±27,3	21,4±30,3	57,7±30,6	
Relative SAA increase	34,5±104,8	16,0±45,7	23,7±47,1	133,9±61,7	

*mean, RBP4 (Retinol Binding Protein 4), C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Serum Amyloid A (SAA).

Conclusion: This preliminary study showed that RBP4 levels may be increased about 1.5 times in FMF and to lesser extent in AA amyloidosis patients despite no significant change during acute phase response of different infections. Patients with infections show strong CRP and SAA response, and the differential response of RBP4 in FMF patients warrants further analysis in larger group of patients with different clinical characteristics.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3692

Rehabilitation

POS1446

ANTHROPOMETRIC MEASUREMENTS IN UPPER EXTREMITY REHABILITATION OF PATIENTS WITH RHEUMATIC DISEASES

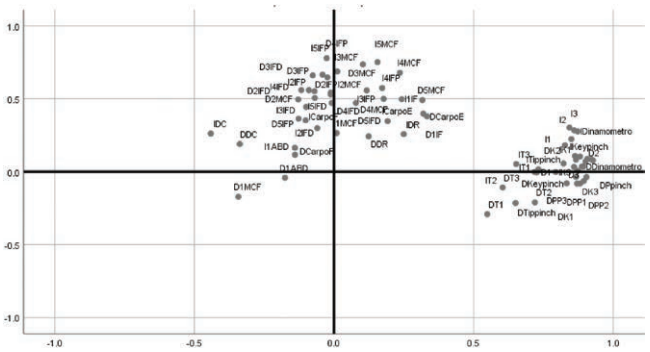
P. Herrera-Sandate[1], D. Vega-Morales[1], A. L. De-Leon-Ibarra[1], P. Valdes-Torres[2], L. A. Chavez-Alvarez[1], I. D. J. Hernandez-Galarza[1], R. Pineda-Sic[1], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Rheumatology Service, Monterrey, Mexico*; [2]*Hospital Universitario Dr. José Eleuterio González, Sports Medicine and Physical Rehabilitation Department, Monterrey, Mexico*

Background: The chronic nature of rheumatic diseases has a negative impact in quality of life. Pain and loss of function in the upper extremity cause a progressive difficulty to perform daily activities, often requiring integral physical rehabilitation programs. Anthropometric measurements habitually take prolonged periods of time, given the extensive nature of physical examination in rheumatic patients. It is unknown which factors are most efficient to better reflect the functional status of the rheumatic patient.

Objectives: Determine the most efficient anthropometric measurements in the upper extremity to assess the functional status of rheumatic patients in rehabilitation programs.

Methods: Thirty-six patients were recruited from Rheumatology consultation of University Hospital "Dr. José Eleuterio González" in Monterrey, Mexico. Patients had a complete physical examination by a board-certified rheumatologist, which referred patients to Physical Rehabilitation consultation if necessary. A cross-sectional study was carried out in these patients with Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire (1), measurement of ranges of motion (ROM) and hand strength with the Mathiowetz protocol (2). Analysis was performed through Principal Components Analysis including Total Variance Explained (TVE), Rotated Component Matrix (RCM) and dendrograms.

Results: From the total of patients, 34 (94.4%) were women with a mean age of 34 years (SD 11.33). The most common diagnosis was rheumatoid arthritis (47.2%) followed by osteoarthritis (8.3%). The mean disability score in DASH was 29.3% (DE 23.36). The TVE analysis found that 3 elements explained 48.6% of the total variance, and 13 elements explained 89.4%. RCM correlations among hand strength parameters ranged from 0.51 to 0.93, whereas ROM correlation values were below 0.4. Graph 1 depicts data dispersion for ROM, grip strength and pinch gauge by dynamometer.



Graph 1. Two main clusters are observed in the RCM plot of the data. In the center and superior to the x axis, a conglomeration corresponding to ROM is shown, consisting of radial and ulnar deviation; flexion, extension, abduction and adduction in carpal bones, metacarpophalangeal joints, and proximal and distal interphalangeal joints of the five fingers of both hands, accordingly. To the right and across the x axis, another cluster depicts the grip strength and tip, key, and lateral pinch gauge of the fingers according to the Mathiowetz protocol. Closeness of data points portray a higher similarity among variances in the second cluster.

Conclusion: Hand strength is the most efficient parameter to assess the functional status of the upper extremity in rheumatic patients in rehabilitation programs.

REFERENCES:

[1] Arreguín Reyes, R., López López, C. O., Alvarez Hernández, E., Medrano Ramírez, G., Montes Castillo, M., & Vázquez-Mellado, J. (2012). Evaluation of hand function in rheumatic disease. Validation and usefulness of the Spanish version AUSCAN, m-SACRAH and Cochin questionnaires. Reumatologia clinica, 8(5), 250–254. https://doi.org/10.1016/j.reuma.2012.03.005

[2] Mathiowetz, V., Kashman, N., Volland, G., Weber, K., Dowe, M., & Rogers, S. (1985). Grip and pinch strength: normative data for adults. Archives of physical medicine and rehabilitation, 66(2), 69–74.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1301

POS1447

LOW-INTENSITY PULSED ELECTROMAGNETIC FIELDS IMPROVE PHYSICAL PERFORMANCE IN A DOSE-DEPENDENT MANNER: AN OBSERVATIONAL STUDY IN OLDER ADULTS WITH RHEUMATIC DISEASES

M. Giovale[1], G. Tramontano[1], R. Galli[1], S. Rando[1], A. Giusti[1], L. Bandi[1], F. Russo[1], S. Rampoldi[2], L. C. Bottaro[3], G. Bianchi[1]. [1]*Local Health Trust 3, Rheumatology Unit, Department of Medical Specialties, Genoa, Italy*; [2]*THS Therapeutic Solutions, Department of Engineering, Milano, Italy*; [3]*Local Health Trust 3, Executive Board, Genoa, Italy*

Background: Low-intensity pulsed electromagnetic fields (PEMF) have been shown to improve gait parameters in frail older adults.[1] Furthermore, the continuous exposure to PEMF (up to 1 year) have been demonstrated to produce progressive improvements in self-selected gait speed in older adults at risk of falling.[2]

Objectives: To investigate the effects of two different treatment regimens of PEMF on physical performances in older adults presenting with rheumatoid arthritis (RA), osteoarthritis (OA) or severe osteoporosis (OP).

Methods: Older adults presenting with RA, OA or OP, at increased risk of falls, evaluated in our Falls Prevention Clinic, were considered for a prospective observational study investigating the effects of PEMF on physical performances. PEMF were supplied by the THS 280 E device (THS-Therapeutic Solutions Srl, Milan, Italy). It provides a new therapeutic approach, named TEPS (Triple Energy Postural Stabilization), that represents an evolution of physical therapy.[1,2] On the basis of the physician judgment, PEMF were administered following an intensive protocol, every 45 days (PEMF-45), or a standard validated protocol[1,2], every 60 days (PEMF-60). All subjects were assessed at baseline and every 3 months with the following tests: 4 meters gait speed test [4MGS, seconds (sec)], timed up and go test (TUG, sec), chair stand test (CST, sec), short physical performance battery (SPPB, score), and hand grip strength (HGS) by hand dynamometer (Kg). Demographic, anthropometric and clinical characteristics, including pharmacological treatments and functional status were evaluated at baseline. Clinical and adverse events were assessed every 45 or 60 days after PEMF administration.

Results: Overall, 94 patients were enrolled between January and December 2020. Of these, 43 subjects (N=33 PEMF-45, N=11 PEMF-60) with a valid 6-month follow-up assessment were considered for the current analysis. The two groups were comparable regarding the main baseline characteristics, and similar

% of patients presented with RA, OA or OP. Mean age (±SE) was 78±7 in PEMF-45 and 77±7 in PEMF-60. As expected, all physical performance tests improved significantly from baseline to 6 months in both groups. Mean (±SE) 4MGS increased significantly more in PEMF-45 (from 3.24±0.12 sec to 2.83±0.18 sec) compared to PEMF-60 (from 3.22±0.21 sec to 3.02±0.30 sec, p=.018). Likewise, mean (±SE) CST improved more in PEMF-45 (from 12.4±0.9 sec to 8.7±0.4 sec) compared to PEMF-60 (from 11.1±1.5 sec to 9.8±0.7 sec, p=.002). No significant difference between groups was found for the other tests, although a trend toward better results in PEMF-45 was manifest: SPPB improved by 6.4% in PEMF-45 and by 3.0% in PEMF-60, and TUG decreased by 7.8% in PEMF-45 and by 6.1% in PEMF-60. During the 6 months observation period no adverse event was observed.

Conclusion: Preliminary results of our ongoing prospective observational study suggest that a more frequent administration of PEMF produces greater improvements in some but not all physical performance parameters compared to a standard validated regimen[1,2].

REFERENCES:

[1] Giusti A et al., Geriatr Gerontol Int 2013. [2]Giusti A et al., J Am Geriatr Soc 2014.

Disclosure of Interests: Massimo Giovale: None declared, Giuseppina Tramontano: None declared, Rossana Galli: None declared, Simone Rando: None declared, Andrea Giusti Speakers bureau: UCB, Amgen, Kyowa Kirin, Abiogen Pharma, and Eli Lilly, outside the submitted work, Consultant of: EffRx and Abiogen Pharma, outside the submitted work, Lorenzo Bandi: None declared, Francesca Russo: None declared, Stefano Rampoldi Employee of: THS Therapeutic Solutions SRL, Luigi Carlo Bottaro: None declared, Gerolamo Bianchi Speakers bureau: Abbvie, Abiogen Pharma, Amgen, BMS, Celgene, Eli Lilly, GSK, Janssen-Cilag, Medac, MSD, Novartis, Pfizer, Roche, Sanofi, Genzyme and Servier, outside the submitted work

DOI: 10.1136/annrheumdis-2021-eular.2383

Education

POS1448 EVIDENCE BASED PRACTICE: WHAT IS THE EVIDENCE THAT BRITISH SOCIETY FOR RHEUMATOLOGY GUIDELINES ARE EVIDENCE BASED?

M. Lee[1], G. Reynolds[2], M. Yates[3], J. Galloway[3]. [1]*Mohammed Bin Rashid University Of Medicine and Health Sciences, Rheumatology, Dubai, United Arab Emirates*; [2]*Newcastle University, Translational and Clinical Research Institute, Newcastle, United Kingdom*; [3]*King's College London, Rheumatology, London, United Kingdom*

Background: Clinical practice guidelines are designed to ensure that patients are treated according to best evidence, with the goal of optimizing clinical outcomes and reducing unwarranted variation in care. They compile, rate and translate the data available into recommendations that form the basis of evidence-based practice for most clinicians. Despite their importance, the evidence base informing different guidelines varies in quality. A recent study of American College of Rheumatology (ACR) Practice Guidelines demonstrated only 17 of 35 class I (strong benefit to harm ratio) recommendations were supported by level A evidence (high quality randomized controlled trails or meta-analyses)[1].

Objectives: To review the evidence supporting the British Society for Rheumatology (BSR) guidelines.

Methods: Thirteen sets of guidelines that were available on the BSR website as of October 16th 2019 were reviewed (https://www.rheumatology.org.uk/practice-quality/guidelines). A range of methodologies (including Grading of Recommendations Assessment, Development and Evaluation (GRADE), Scottish Intercollegiate Guidelines Network (SIGN), EULAR and Royal College of Physicians (RCP) recommendations) were used to assess the quality of evidence and strength of recommendation. For comparability between guidelines the level of evidence was converted to a score between I (highest quality) and IV (lowest quality) and the strength of recommendation was converted to a rating between A and D. The polymyalgia rheumatica guideline was not assessed due to unclear methodology and lack of level of evidence for all recommendations.

Results: Of the 12 BSR guidelines assessed, there were 554 recommendations in total. The number of recommendations per guideline ranged between 13 and 80. Across all assessed guidelines, 94 recommendations (17.0%) were classified as level I, 161 (29.1%) as level 2 and 299 (54.0%) as level 3 or 4. These figures are similar to those reported in the ACR guidelines (23%, 19% and 58% respectively)[1]. The proportion of level I evidence varied from 46.2% (Axial Spondyloarthropathy guideline) to 0% (Hot Swollen Joint guideline).

Conclusion: Over half of all BSR guideline recommendations have level of supporting evidence of III/IV. A wide range of methodologies are used to generate BSR guidelines (GRADE, SIGN, RCP / EULAR). This makes it challenging for readers unfamiliar with these approaches to interpret evidence and hinders comparisons between guidelines. A standardized methodology for future guideline development would overcome these barriers.

REFERENCES:

[1] Duarte-Garcia A, Zamore R & Wong JB. The Evidence Basis for the American College of Rheumatology Practice Guidelines. JAMA Intern Med, 2018 Jan 1;178(1):146-148.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.822

POS1449 SEGMENTED SHORT-FORMAT ONLINE EDUCATION SIGNIFICANTLY INCREASES PREDICTION, PROGNOSIS, AND MANAGEMENT OF FIBROSING INTERSTITIAL LUNG DISEASE ASSOCIATED WITH CONNECTIVE TISSUE DISEASE

C. Rohani-Montez[1], M. Calle[1], C. Allen[1], T. Maher[2], V. Smith[3], J. Jacob[4], G. Riemekasten[5], M. Kolb[6]. [1]*Medscape Education Global, Medscape Education Global, London, United Kingdom*; [2]*Keck Medicine of USC, Clinical Medicine, Los Angeles, United States of America*; [3]*Ghent University Hospital, Department of Rheumatology, Gent, Belgium*; [4]*University College London, UCL Respiratory, CMIC UCL, London, United Kingdom*; [5]*University Medical Center Schleswig-Holstein, Department of Rheumatology and Clinical Immunology, Lubuck, Germany*; [6]*McMaster University, Division of Respirology, Department of Medicine, Hamilton, Canada*

Background: Identifying fibrosing interstitial lung disease (ILD) at the earliest opportunity remains one of the most urgent challenges for the effective management of this potentially rapidly progressive and burdensome condition, which is frequently associated with several connective tissue diseases (CTDs). However, knowledge on how to identify early hallmarks and predictors of fibrosing ILD, as well as knowing which steps to take next is frequently lacking in clinical practice.

Objectives: This study was conducted to determine whether online independent medical education could improve rheumatologists' and pulmonologists' knowledge and competence in identifying and managing progressive fibrosing ILDs earlier in the disease course.

Methods: Rheumatologists and pulmonologists participated in five ~10-min presentations about the early identification of fibrosing ILD in patients with or without CTDs and completed all pre- and post-questions.[1] The effects of the education on knowledge and competence were assessed using a 3-question, repeated pairs, pre-assessment/post-assessment study design. For all questions combined, the chi-square test assessed differences from pre- to post-assessment. P values <.05 are statistically significant. The activity launched on October 9, 2020, and data were collected through December 18, 2020.

Results: Overall significant improvements were seen after participation for both rheumatologists (average correct response rate of 28% at pre-assessment vs 74% at post-assessment; P<.001, representing a 165% relative percentage change [RPC]; N=39), and pulmonologists (average correct response rate of 39% at pre-assessment vs 67% at post-assessment; P<.001, representing a 72% RPC; N=102). Specifically, significant improvements were observed in clinicians' knowledge of predictors of fibrosing ILD in patients with CTD, as well as competence in selecting the right HRCT parameters to assess prognosis and select a treatment approach to reduce the risk of disease progression (Figure 1).

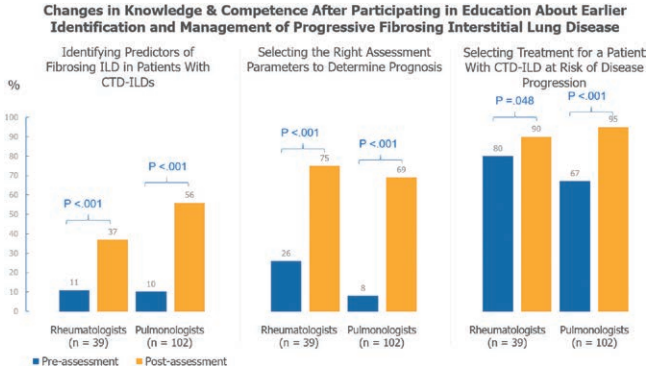


Figure 1.

After participating in the activity, 59% of rheumatologists and 50% of pulmonologists had measurable improved confidence related to identifying early disease progression in patients with progressive fibrosing ILDs.

Given the very low rates of correct responses at baseline regarding predictors of fibrosing ILD and assessing prognosis, it will be important to continue to reinforce these learnings in ongoing educational programs.

Conclusion: This study demonstrates the success of segmented online education in improving rheumatologists' and pulmonologists' knowledge and competence in evaluating risk and prognosis of fibrosing ILD and managing patients with CTD-ILDs. This could lead to earlier changes in therapeutic approach for those with signs of progression and result in improved overall outcomes for these patients.

REFERENCES:

[1]Kolb M, Maher T, Smith V, Jacob J, Rimekasten G. Catching and Managing Progressive Fibrosing Interstitial Lung Disease Progression Earlier. Launched: Oct 9, 2020. Data as of Dec 18, 2020. Available at www.medscape.org/viewarticle/938826

Disclosure of Interests: Christy Rohani-Montez: None declared, Marinella Calle: None declared, Chris Allen: None declared, Toby Maher Speakers bureau: Astra Zeneca, Bayer, Blade Therapeutics, Boehringer Ingelheim, Bristol-Myers Squibb, Galapagos, Galecto, GlaxoSmithKline R&D, Indalo, IQVIA, Pliant, Respivant, Roche and Theravance, Consultant of: Astra Zeneca, Bayer, Blade Therapeutics, Boehringer Ingelheim, Bristol-Myers Squibb, Galapagos, Galecto, GlaxoSmithKline R&D, Indalo, IQVIA, Pliant, Respivant, Roche and Theravance, Grant/research support from: Astra Zeneca and GlaxoSmithKline R&D, Vanessa Smith Speakers bureau: Boehringer-Ingelheim Pharma GmbH&Co and Janssen-Cilag NV, Consultant of: Boehringer-Ingelheim Pharma GmbH&Co, Grant/research support from: Research Foundation - Flanders (FWO), Belgian Fund for Scientific Research in Rheumatic diseases (FWRO), Boehringer-Ingelheim, Pharma GmbH&Co, and Janssen-Cilag NV, Joseph Jacob Speakers bureau: Boehringer-Ingelheim; Roche, Consultant of: Boehringer-Ingelheim, Grant/research support from: GlaxoSmith-Kline, Gabriela Riemekasten Speakers bureau: AbbVie; Actelion; Boehringer-Ingelheim, Consultant of: Actelion; CellTrend; Janssen, Grant/research support from: AbbVie; Actelion, Martin Kolb Speakers bureau: AstraZeneca; Boehringer-Ingelheim; Novartis; Roche, Consultant of: AbbVie Inc.; Algernon Pharma; AstraZeneca;, Boehringer-Ingelheim; Cipla; Covance; EPG Health; Galapagos NV; Gilead; GlaxoSmithKline; Indalo; MitoImmune Therapeutics Inc; Novartis; Pieris; Prometic (now Liminal Biosciences); Roche; Third Pole Inc.; TwoXAR Inc., Grant/research support from: Boehringer-Ingelheim; GlaxoSmithKline; Novartis; Prometic; Roche; Avalyn

DOI: 10.1136/annrheumdis-2021-eular.1510

POS1450 PATIENTS' SAFETY SKILLS ASSESSMENT WITH BIOLOGICS AND JAK INHIBITORS: UPDATE OF THE BIOSECURE QUESTIONNAIRE

C. Beauvais[1], V. Gaud-Listrat[2], J. Sellam[3], F. Fayet[4], M. Beranger[5], N. Deparis[6], M. Antignac[7], C. Sordet[8], M. Rodere[4], L. Gossec[9]on behalf of On the behalf of the therapeutic patient education section of the French Rheumatology Society. *[1]Centre Hospitalier Universitaire Saint Antoine, Sorbonne Université, Rheumatology Department, Paris, France*; *[2]Cochin Hospital, Rheumatology Department, Paris, France*; *[3]Hospital Saint-Antoine Ap-Hp, Rheumatology Department, Paris, France*; *[4]Centre Hospitalier Universitaire Gabriel Montpied, Rheumatology Department, Clermont-Ferrand, France*; *[5]Centre Hospitalier Universitaire Orléans, Rheumatology Department, Orleans, France*; *[6]Association Nationale de Défense Contre l'Arthrite Rhumatoïde, ANDAR, Paris, France*; *[7]Centre Hospitalier Universitaire Saint Antoine, Sorbonne Université APHP, Pharmacy Department, Paris, France*; *[8]Hôpitaux Universitaires de Strasbourg, Rheumatology Department, Strasbourg, France*; *[9]Sorbonne Université, Hopital Pitié Salpetrière, Rheumatology Department, Paris, France*

Background: Biologic disease-modifying anti-rheumatic drug (bDMARDs) and JAK inhibitors (JAKi) may lead to an increased risk of infections, which could be prevented by enhancing patients' safety skills (ref). We developed a self-administered questionnaire (BioSecure1, ref) in 2013 to assess the patients' safety skills (Table 1). Following the appearance of new bDMARDs and JAKi and new information on safety, this questionnaire needed updating.

Table 1. Nine domains of core safety skills and number of corresponding questions in BioSecure questionnaires.

Domain of competence	BioSecure1	BioSecure2
General knowledge	4	2
Dealing with infectious symptoms and fever	10	11
Dealing with other infectious symptoms	4	4
Dealing with injuries, preventing infectious complications, vaccinations	8	8
Dental hygiene, preventing infectious complications, information to share with the dentist	2	2
Planning surgery, information to share with the surgeon/ anesthesiologist	7	7
Planning child conception	2	1
Communication: who to contact?	2	2
Subcutaneous treatments: cold chain/cold storage, subcutaneous injection techniques	3	0

Objectives: To update the BioSecure questionnaire assessing patients' safety skills

Methods: Four steps by a 10 participants multidisciplinary steering committee. Step1: critical analysis of content and formulations of BioSecure1 on the basis of i) the participants' own experience of the questionnaire use in current practice (5/10 participants) or research (6/10 participants) ii) assessment of BioSecure1 consistency with current guidelines for management of targeted drugs. Step2: development of a first updated version by a core group of 10 persons. Step3: comments by an extended panel of rheumatology teams interested in therapeutic patient education (TPE). Step4: testing of the final version (Biosecure2) by ten patients through cognitive debriefing.

Results: In total, 10 rheumatologists, 6 rheumatology nurses, 1 pharmacist and 1 patient from a patient association participated. Inadequate formulations were reported regarding some situations for which recommendations had the most shifted since Biosecure1 development such as planning pregnancy, remission management and prevention measures before surgery. Features of some infectious conditions were clarified; barriers measures against infection and complications such as sigmoiditis and Herpes Zoster infection were added. BioSecure2 continues to assess the 9 domains of core safety skills (Table 1). The questionnaire was shortened to 50 items (mean filling in time is 10 minutes) with a good understanding and scoring was simplified (mean scoring time 3.5 minutes).

Conclusion: BioSecure2 represents an updated outcome measure to evaluate the patient's skills to prevent adverse events with targeted therapies. This questionnaire can be useful in the context of patient-health professional communication, and as a tool to measure TPE on safety issues.

REFERENCES:

[1] Gossec et al, Joint Bone Spine. 2013;80:471–476

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1628

POS1451 DEVELOPING A TOOL TO MEASURE THE LEARNING CURVE: ENTHESITIS ULTRASOUND IN PSORIASIS ARTHRITIS

S. Brådland[1], P. Andel[1,2,3], A. Diamandopoulos[4,5], G. Haugeberg[1,6]. *[1]Hospital of Southern Norway, Department of Rheumatology, Kristiansand, Norway*; *[2]Østfold Hospital Trust, Department of Cardiology, Kalnes, Norway*; *[3]University of Oslo, Department of Clinical Medicine, Oslo, Norway*; *[4]Akershus University Hospital, Department of Rheumatology, Oslo, Norway*; *[5]Martina Hansens Hospital, Department of Rheumatology, Bærum, Norway*; *[6]Norwegian University of Science and Technology, Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, Trondheim, Norway*

Background: Enthesitis is defined as inflammation of the tendon inserting the bone encompassing the adjacent trabecular bone network, the fascia and surrounding soft tissues as the cartilage, the bursa and the fat pad. In enthesitis clinical examination alone is a method with significant limitations in terms of diagnostic accuracy and does not correlate strongly with imaging diagnostics (1,2).

Ultrasound (US) is a widely used imaging technique in Rheumatology. But while learning curricula and standardization for joint US are available, other US techniques as vascular-, enthesis- or serosa-US gets usually less attention in rheumatologic US curricula. Though both OMERACT (4) and GRAPPA (3) have recently published qualitative and semi quantitative criteria in enthesitis US, few publications explicitly address the learning curves in these particular domain.

Objectives: To describe the development of a tool to measure the learning curve for enthesitis US.

Methods: 3237 US images of 561 enthesis were obtained by one experienced ultrasonographer (PMA) in B- and color Doppler (CD) mode in longstanding psoriasis arthritis patients of different disease activity. Due to duplicity and poorer image quality 2115 images were eliminated. The remaining fully anonymized 1122 images (561 enthesis) were afterward implemented in a random multiple choice algorithm presenting a B-mode and a CD image of the same enthesis at the same time without timely limitation. Rating follows qualitative GRAPPA criteria as well as semiquantitative OMERACT criteria (3, 4). The enthesitis scoring application was than written in.NET/ C#, TypeScript and ReactJS and is hosted in Azure Cloud platform. The scoring is stored in a database allowing extraction to SPSS for statistical analysis.

Results: The interface of the functional program is shown in image 1 (Screenshot). In a next step the program will be presented to different raters of different ultrasound experience (>10 years, 5-10 years, 1-5 years, <1 years). The program will be presented a multitude of times in different order to every rater to adjust for inter-rater reliability. Correlation between raters will be given to depict a learning curve on enthesitis ultrasound assuming the rater with the highest experience as gold standard.

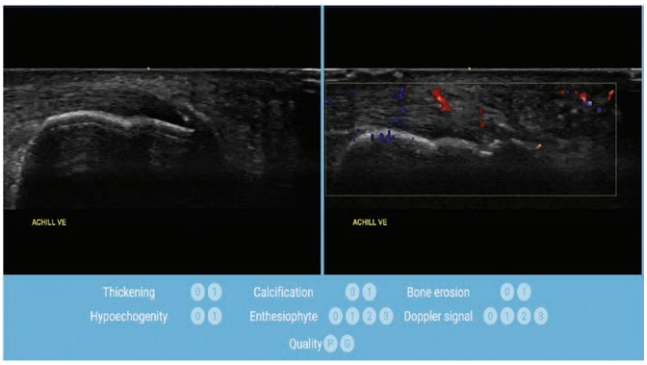


Image 1. Screenshot of grafical user interface of the scoring program.

Conclusion: In this presentation we outline the successful development of a tool to measure the learning curve in enthesitis. We hypothesize that knowledge about the learning curve and inter-rater reliability in enthesitis US obtained by our tool might contribute to future US curricula, structured reporting and deep learning algorithms.

REFERENCES:

[1] Achilles enthesitis defined by ultrasound is not associated with clinical enthesitis in patients with psoriatic arthritis, Brigitte Michelsen et al. RMD Open 2017;3
[2] Ultrasonographic evaluation in psoriatic arthritis is of major importance in evaluating disease activity Brigitte Michelsen et al. Annals of the Rheumatic Diseases 12(2108-2113)
[3] Development of a Preliminary Ultrasonographic Enthesitis Score in Psoriatic Arthritis -GRAPPA Ultrasound Working Group, Stephanie Tom et al. The Journal of Rheumatology; 4(384-390)
[4] Reliability of a consensus-based ultrasound definition and scoring for enthesitis in spondyloarthritis and psoriatic arthritis: an OMERACT US initiative, Peter V Balint et al. Annals of the Rheumatic Diseases, 12(1730-1735)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4096

Educational cases

POS1452 DE NOVO LUPUS NEPHRITIS FOLLOWING THE INTRODUCTION OF BELIMUMAB

J. Pinnell[1], S. Tosounidou[1]. [1]*Birmingham City Hospital, Rheumatology, Birmingham, United Kingdom*

Background: Belimumab inhibits the activity of the soluble cytokine BLyS (B lymphocyte stimulator) and is recommended for use in moderate refractory systemic lupus erythematosus (SLE). A recent randomised controlled trial reported that Belimumab improves the outcomes for patients with lupus nephritis when used with standard therapy.

Objectives: We present two cases of lupus nephritis that developed in SLE patients without pre-existing renal disease shortly after commencing treatment with Belimumab.

Methods: Both patients are Afro-Caribbean females with similar immunological profiles, including ANA, dsDNA, anti-Sm, anti- Ro and anti-RNP antibodies. The first was 59 years old with a long standing diagnosis of SLE since 1996 that had required previous Cyclophosphamide for neuropsychiatric lupus. She was most recently taking Hydroxychloroquine, Mycophenolate and Prednisolone having previously failed with Azathioprine twice. Belimumab was commenced in February 2020 due to worsening arthritis, mouth ulcers, pleuritis and systemic features associated with a significant rise in her dsDNA and low complement. Her SLEDAI score was 13. After six months of treatment she developed proteinuria for the first time. Her urine protein creatinine ratio (uPCR) was measured at 205mg/mmol and a subsequent renal biopsy revealed features of active Class IV and V lupus nephritis. Belimumab was changed to Rituximab. Mycophenolate was stopped due to persistent neutropenia and Tacrolimus was introduced instead. After 5 months treatment her uPCR is now 33mg/mmol.

The second patient was 37 years old with a recent diagnosis of SLE in 2018. She presented with inflammatory arthritis, oral and nasal ulcers, and cytopenia. She responded poorly to Azathioprine and was intolerant of Mycophenolate. Her most recent treatment was Hydroxychloroquine and Prednisolone. She was commenced on Belimumab in February 2020 due to active mucocutaneous and musculoskeletal features of lupus with a SLEDAI score of 12. The mucocutaneous features of lupus responded well but she developed proteinuria seven months later, and by November 2020 her uPCR was 149mg/mmol. Belimumab was switched to Rituximab and initially her uPCR continued to rise but it has now fallen to 43mg/mmol.

Results: The occurrence of new lupus nephritis soon after the initiation of Belimumab monotherapy has been reported previously and our cases raise further concerns. A prospective observational study recently reported significantly increased rates of new lupus nephritis developing in patients receiving Belimumab in addition to standard care compared to those receiving standard treatment. An association between Belimumab and the development of de novo lupus nephritis has not yet been conclusively established but it would create a significant challenge in how Belimumab is used and consented for in SLE, especially if it becomes more widely used to treat lupus nephritis. The mechanism by which Belimumab may increase the risk of, or trigger, lupus nephritis is currently unclear but may result from increased activity in BLyS associated pathways following the blockade of the BLyS pathway.

Conclusion: These two cases raise questions about the role of using Belimumab in patients at risk of developing lupus nephritis. We therefore recommend caution in its use and recommend active monitoring of renal parameters especially in patients with poor clinical and serological response to Belimumab.

REFERENCES:

[1] Furie R, Rovin BH, Houssiau F, et al. Two-year, randomized, controlled trial of belimumab in lupus nephritis. N Engl J Med. 2020; 383(12):1117-28
[2] Sjöwall C, Cöster L. Belimumab may not prevent lupus nephritis in serologically active patients with ongoing non-renal disease activity. Scand J Rheumatol. 2014; 43(5):428-30
[3] Staveri C, Karokis D, Liossis SN. New onset of lupus nephritis in two patients with SLE shortly after initiation of treatment with belimumab. Semin Arthritis Rheum. 2017; 46(6):788-790
[4] Parodis I, Vital EM, Hassan SU, et al. De novo lupus nephritis during treatment with belimumab. Rheumatology. 2020; keaa796

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.67

POS1453 OVERLAPPING FEATURES OF RELAPSING POLYCHONDRITIS AND SWEET'S SYNDROME: COULD THIS BE VEXAS (VACUOLES, UBIQUITIN A1E MUTATION, X-LINKED, AUTOINFLAMMATORY, SOMATIC) SYNDROME?

A. Vivekanantham[1,2], M. Kesavan[3], J. Evans[4], R. N. Matin[5], I. Elliott[6], R. Luqmani[1,2]. [1]*Oxford University Hospitals NHS Foundation Trust, Nuffield Orthopaedic Centre, Rheumatology, Oxford, United Kingdom*; [2]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Botnar Research Centre, Oxford, United Kingdom*; [3]*Oxford University Hospitals NHS Foundation Trust, Churchill Hospital, Haematology, Oxford, United Kingdom*; [4]*Oxford University Hospitals NHS Foundation Trust, Churchill Hospital, Haematology, Oxford, United Kingdom*; [5]*Oxford University Hospitals NHS Foundation Trust, Churchill Hospital, Dermatology, Oxford, United Kingdom*; [6]*Oxford University Hospitals NHS Foundation Trust, John Radcliffe Hospital, Infectious Diseases, Oxford, United Kingdom*

Background: An 83-year-old male presented to the infectious diseases team with intermittent fevers associated with tension headaches, malaise and fatigue for two years, with recent worsening. He had noted a progressive decline in his mobility over the past year following replacement of his right knee for osteoarthritis. His past medical history included atopic eczema, malaria and bilateral cataract extractions.

On examination, he had a widespread non-scaly annular urticated rash. He had persistently raised inflammatory markers (CRP 40mg/L, ESR 82mm/hour), normocytic anaemia (Hb 102 g/L, MCV 101.9 fL), lymphopenia (0.70 x10^9/L), fluctuating eosinophilia (0.88-1.25 x10^9/L) and a mildly elevated lactate dehydrogenase (243IU/L). A thorough work up for pyrexia of unknown origin showed no evidence of infection/ vasculitis/ immune pathology. The only positive finding was prior exposure to schistosomiasis, treated with a single dose of praziquantel. An echocardiogram and serial PET-CT scans were normal. Given the deterioration in mobility since the right knee replacement, an MRI knee was performed, and cobalt/ chromium levels to look for allergic responses to the prosthesis, but these tests did not reveal any findings of significance.

An initial haematology work-up did not identify an abnormality of concern (screening for a myeloproliferative neoplasm including BCR-ABL studies were negative and mast cell tryptase was not elevated). Due to a worsening skin rash, he was reviewed by dermatology where a skin biopsy showed features of superficial neutrophilic dermatosis which can be observed with Sweet's syndrome. However, it was felt that this was an unlikely explanation for the persistent systemic symptoms. He proceeded to a bone marrow biopsy which showed reactive features including vacuolation of myeloid precursors with normal cytogenics.

During follow up appointments, the patient described new recurrent violaceous patches with episodes of inflammation of the pinna of the ear, suggesting a diagnosis of relapsing polychondritis and so the patient was started on high dose prednisolone (80mg per day [1mg per kg]) and referred for rheumatological assessment. He had an excellent response to prednisolone (fever, ear swelling and rash subsided). The overlapping features of relapsing polychondritis and Sweet's syndrome in an elderly man suggested a diagnosis of VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory and somatic) syndrome. The prednisolone dose was rapidly reduced to 10mg per day and the patient was commenced on methotrexate, as a steroid-sparing agent. Further blood tests have been sent for genetic analysis for VEXAS syndrome but results are pending.

Objectives: N/A

Methods: N/A

Results: N/A

Conclusion: VEXAS syndrome is a newly identified genetically defined syndrome, described by Beck et al in October 2020 consisting of somatic mutations in the *UBA1* gene, affecting bone marrow stem cells. In a study of 25 patients with this mutation, diagnostic/ classification criteria for relapsing polychondritis (n=15), Sweet's syndrome (n=8), polyarteritis nodosa (n=3) or giant cell arteritis (n=1) were met and patients often had severe refractory disease with overlapping systemic inflammatory and haematologic features. Features of VEXAS include the presence of vacuoles in myeloid cells, somatic mutations in the UBA1 (ubiquitin-activating enzyme) gene, X-linkage (therefore only occurring in males), in older people with autoinflammatory syndromes. Although VEXAS syndrome is a relatively rare condition, it was a relevant consideration in this case.

REFERENCES:

[1] Beck et al. Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease. N Engl J Med 2020; 383:2628-2638. DOI: 10.1056/NEJMoa2026834

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3219

HPR Measuring health (development and measurement properties of PROs, tests, devices)

POS1454-HPR AESTHETIC IMPAIRMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS: A CASE CONTROL STUDY USING A SEMI-QUANTITATIVE SCALE FOR BODY IMAGE ASSESSMENT

M. M. Farhat[1,2,3], P. Guerreschi[4], S. Morell-Dubois[1,2,3], V. Deken[5], J. Labreuche[5], S. Sanges[1,2,3], V. Sobanski[1,2,3], E. Hachulla[1,2,3], O. Cottencin[6], D. Launay[1,2,3].
[1]Lille Unversity, U1286 - INFINITE - Institute for Translational Research in Inflammation, Lille, France; *[2]INSERM, Haut-de-France, Lille, France*; *[3]CHU Lille, Service de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Autoimmunes Systémiques Rares du Nord et Nord-Ouest de France (CeRAINO), Lille, France*; *[4]CHU Lille, Plastic Surgery Department, Competence Center for Clefts and CranioFacial Malformations, Lille, France*; *[5]CHU Lille, EA2694 - Santé Publique: Epidémiologie et Qualité des Soins, Lille, France*; *[6]CHU Lille, U-1172, LiNC; Department of Psychiatry and Addiction, Lille, France*

Background: Systemic sclerosis (SSc) is a fibrotic autoimmune disease characterized by dermatological involvement. Skin involvement can alter appearance, which can have a psychological impact(1). Assessment of body image could be central in optimizing care. Yet, data are scarce(2).

Objectives: The main objective of our study was to assess aesthetic impairment measured on a visual aesthetic scale (AES) (3) in patients with SSc compared to a group of healthy subjects. Secondary objectives were to assess associations between aesthetic impairment and standardized questionnaires for aesthetic impairment as well as clinical, biological, psychological/quality of life, and functional parameters of SSc.

Methods: The "Sclero-esthet" study is a descriptive single-center study of two populations: patients with SSc, included in a referral center for systemic and autoimmune diseases at Lille Hospital, France, and healthy controls.

Results: This study, from January 2017 to October 2017, included 88 patients (69 [78.4%] women) with a median age of 52 years (range: 43 to 59) and 88 controls (49 [55.7%] women) with a median age of 45 years (range: 32 to 55). Perception of physical changes assessed using the AES was greater in cases than in controls (3.7 ± 0.3 vs 2.8 ± 0.3, p=0.028), with statistical correlation with ASWAP. SSc patients with anxiety or depressive symptoms had significantly higher AES scores. Cases presented poorer quality of life than controls.

Conclusion: The AES appears to be a good tool to evaluate aesthetic impairment. Correlations found with psychological and quality of life parameters support the need to improve patient management in this field.

REFERENCES:

[1] Cash TF. Body image: past, present, and future. Body Image 2004;1(1):1–5.
[2] Benrud-Larson LM, Heinberg LJ, Boling C, Reed J, White B, Wigley FM. Body image dissatisfaction among women with scleroderma: extent and relationship to psychosocial function. Health Psychol mars. 2003;22(2):130–9.
[3] Nguyen C, Ranque B, Baubet T, Bérezné A, Mestre-Stanislas C, Rannou F, et al. Clinical, Functional and Health-Related Quality of Life Correlates of Clinically Significant Symptoms of Anxiety and Depression in Patients with Systemic Sclerosis: A Cross-Sectional Survey. PLoS ONE 2014;9(2).
[4] Heinberg LJ, Kudel I, White B, Kwan A, Medley K, Wigley F. Assessing body image in patients with systemic sclerosis (scleroderma): Validation of the Adapted Satisfaction with Appearance Scale. Body Image 2007;4(1):79–86.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.334

POS1455-HPR RELATIONSHIP BETWEEN PSYCHOLOGICAL FACTORS AND MEASURES OF RHEUMATOID ARTHRITIS ACTIVITY

Y. Olyunin[1], V. Rybakova[2], E. Likhacheva[3], E. Nasonov[4,5]. *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Early Arthritis, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Outpatient Department, Moscow, Russian Federation*; *[3]Institute of Psychology and Pedagogy, Russian New University, Department of General Psychology and Labor Psychology, Moscow, Russian Federation*; *[4]V.A. Nasonova Research Institute of Rheumatology, Scientific Supervisor, Moscow, Russian Federation*; *[5]I.M. Sechenov First Moscow State Medical University, Ministry of Health of Russia (Sechenov University), Department of Therapy and Occupational Diseases, Moscow, Russian Federation*

Background: The patient-reported outcomes are important components of quantitative methods of rheumatoid arthritis (RA) activity assessment which are used to choose the appropriate drug therapy. The value of these parameters can be significantly affected not only by the inflammatory process, but also by the psychological characteristics of the patient and, in particular, by hardiness [1].

Objectives: To study the relationship between psychological factors and signs of RA activity.

Methods: Patients with RA who met the EULAR/ACR 2010 criteria, and observed at the V. A. Nasonova Research Institute of Rheumatology were included. Clinical examination was performed including patient global assessment (PGA), physician global assessment (PhGA), pain measurement on a visual analog scale, tender joint count (TJC), swollen joint count (SJC). The functional status was determined by HAQ, the quality of life – by SF-36 EQ-5D, the nature of pain – by painDETECT, the presence of anxiety and depression – by HADS. Patients also completed Hardiness Survey questionnaire to assess hardiness (HDS) and 3 components of the HDS – commitment (CMT), control (CT) and challenge (CLN). Disease activity was evaluated with DAS28, CDAI, and RAPID3. All patients signed informed consent to participate in the study. Analysis of the data was performed using Spearman's rank test, Fisher exact test, qui-square and t-tests.

Results: 85 patients with RA were included. There were 69 women and 16 men. Mean age was 56.7±13.1 years, disease duration – 7.6±2.7 years. 72 patients were positive for rheumatoid factor, 75 – for anti-cyclic citrullinated peptide antibody. CDAI showed high activity in 15, moderate – in 37, low – in 30, and remission in 3 patients, DAS 28 – in 10, 55, 12, and 8, and RAPID3 – in 24, 25, 15, and 21, respectively. 24 patients had subclinically or clinically expressed anxiety and 15 –subclinically or clinically expressed depression (≥8 according to HADS). In 31 patients, the painDETECT questionnaire revealed possible or probable neuropathic pain. Mean HDS was 84.8±21.7, CMT – 38.9±9.2, CT – 29.4±8.6, CLN – 17.3±7.1. These values were comparable with the corresponding population data for this age group. There was a significant inverse correlation between HDS and RA activity measures, including SJC, TJC, DAS28 ($p<0.05$), pain, PGA, PhGA, CDAI, RAPID3, and HAQ ($p<0.01$). In addition, HDS and all its components positively correlated with quality of life, assessed by SF-36 and EQ-5D ($p<0.01$). In patients with subclinically and clinically expressed anxiety and depression, HDS, CMT, and CT were significantly lower than in patients without anxiety and depression ($p<0.01$), while the values of CLN in these groups did not differ significantly.

Conclusion: The results of the present study suggest that low HDS may be one of the significant factors determining RA activity level because it does not allow patients to adapt adequately to a stressful situation produced by the disease.

REFERENCES:

[1] Maddi SR. Am Psychol. 2008 Sep;63(6):563-4.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.760

POS1456-HPR THE SERUM IRON LEVEL MIGHT BE USEFUL IN DETERMINING THE SEVERITY OF MALNUTRITION IN PATIENTS WITH RHEUMATOID ARTHRITIS

Y. Matsumoto[1,2], Y. Sugioka[3], M. Tada[4], T. Okano[5], K. Mamoto[5], K. Inui[6], D. Habu[2], T. Koike[1,3]. [1]*Shirahama Foundation for Health and Welfare, Search Institute for Bone and Arthritis Disease, Shirahama, Japan*; [2]*Osaka City University Graduate School of Human Life Science, Medical Nutrition, Osaka, Japan*; [3]*Osaka City University Medical School, Center for Senile Degenerative Disorders, Osaka, Japan*; [4]*Osaka City General Hospital, Orthopaedic Surgery, Osaka, Japan*; [5]*Osaka City University Medical School, Orthopaedic Surgery, Osaka, Japan*; [6]*Osaka Saiseikai Nakatsu Hospital, Orthopaedic Surgery, Osaka, Japan*

Background: The Global Leadership Initiative on Malnutrition (GLIM) criteria, the first international criteria for diagnosis of malnutrition, was released in 2018 [1]. Patients with rheumatoid arthritis (RA) are thought to be prone to malnutrition due to decreased food intake and increased muscle catabolism caused by chronic inflammation or pain. However, there has been no report to assess the nutritional status of RA patients in accordance with the GLIM criteria. In addition, commonly used blood nutrient indicators such as albumin might not be appropriate as nutritional indicators for RA because these values are affected by inflammation.

Objectives: This study aims to examine the rates of malnutrition in RA patients according to GLIM criteria, and the relationship between blood nutrient indicators and the severity of malnutrition.

Methods: In this study, we conducted a cross-sectional survey of 135 female RA patients in 2020. According to the GLIM criteria, patients were considered to be malnourished if patients had one of the following phenotypic: (1) low body mass index, (2) non-volitional weight loss, (3) reduced muscle mass, and one of the following etiologic: (1) reduced food intake or assimilation, (2) disease burden/inflammatory condition. Reduced muscle mass was evaluated by measuring calf circumference, and inflammatory condition was evaluated by Disease Activity Score (DAS) 28. In accordance with the GLIM criteria, the severity of malnutrition was judged as three levels: no problem, moderate, and severe malnutrition. Albumin, transthyretin, transferrin, retinol binding protein, zinc, iron, ceruloplasmin, and total cholesterol were assessed as blood nutrition indicators. Also grip strength was assessed. We compared each nutritional indicator among the three groups according to the severity of malnutrition using age-adjusted analysis of covariance, and examined the relationship between each nutritional indicator and the severity of malnutrition using receiver operating characteristic (ROC) analysis.

Results: In RA patients, 20% were classified as severe malnutrition, and 40% were moderate or more. Serum iron levels were significantly lower in the severe malnutrition group compared to the no problem group ($p = 0.001$). In ROC analysis, serum iron, zinc, albumin, and grip strength (area under curve; AUC; 0.680, 0.696, 0.636, 0.790, respectively) were significant parameters for classification of moderate and severe malnutrition. Serum iron and grip strength (AUC for respective parameters were 0.741, 0.747) were significant parameters for classification of severe malnutrition.

Conclusion: Evaluation based on the GLIM criteria showed that about 40% of RA patients were under moderate or severe malnutrition. It was suggested that serum iron and grip strength might be useful to predict the severity of malnutrition.

REFERENCES:

[1] Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition – A consensus report from the global clinical nutrition community. Clinical Nutrition 2019; 38: 1-9.

Acknowledgements: We thank to Tomoko Nakatsuka, and the Center for Drug & Food Clinical Evaluation, Osaka City University Hospital, for management and collection of the study data. We also thank to study participants.

Disclosure of Interests: Yoshinari Matsumoto Grant/research support from: Yamada Research Grant, Yuko Sugioka: None declared, Masahiro Tada: None declared, Tadasi Okano Speakers bureau: AbbVie, Asahikasei, Astellas Pharma Inc, Ayumi Pharmaceutical, Bristol-Myers Squibb, Chugai Pharmaceutical, Daiich Sankyo, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, Novartis Pharma, Ono Pharmaceutical, Pfizer, Sanofi, Takeda Pharmaceutical, Teijin Pharma and UCB, Grant/research support from: AbbVie, Eisai, Mitsubishi Tanabe Pharma Corporation and Nipponkayaku, Kenji Mamoto: None declared, Kentaro Inui Speakers bureau: Daiichi Sankyo Co. Ltd., Mitsubishi Tanabe Pharma, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Takeda Pharmaceutical Co. Ltd., Ono Pharmaceutical Co. Ltd., Abbvie GK, Pfizer Inc., Eisai Co., Ltd., Chugai Pharmaceutical Co., Ltd, Grant/research support from: anssen Pharmaceutical K.K., Astellas Pharma Inc., Sanofi K.K., Abbvie GK, Takeda Pharmaceutical Co. Ltd., QOL RD Co. Ltd., Mitsubishi Tanabe Pharma, Ono Pharmaceutical Co. Ltd., Eisai Co., Ltd., Daiki Habu: None declared, Tatsuya Koike Speakers bureau: AbbVie, Astellas Pharma Inc, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB, Grant/research support from: AbbVie, Astellas Pharma Inc, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB

DOI: 10.1136/annrheumdis-2021-eular.947

POS1457-HPR GASTROINTESTINAL SYMPTOMS AND RHEUMATIC DISEASES: TWO SIDES OF THE SAME COIN

R. Spagnuolo[1], F. S. Iaquinta[2], S. Naty[3], R. D. Grembiale[3], P. Doldo[1]. [1]*University "Magna Graecia" of Catanzaro - AOU Mater Domini - Gastroenterology Unit, Department of Experimental and Clinical Medicine, Catanzaro, Italy*; [2]*University "Magna Graecia" of Catanzaro, Rheumatology Research Unit, Department of Health Sciences, Catanzaro, Italy*; [3]*University "Magna Graecia" of Catanzaro, Rheumatology Research Unit, Department of Health Sciences, Catanzaro, Italy*

Background: Patients with Rheumatic Diseases (RD) often show different symptoms besides the osteoarticular ones. Healthcare workers can evaluate the impact of specific symptoms on RD patients' quality of life in order to improve global management.

Objectives: The aim of this study was to assess the presence of gastrointestinal symptoms in RD patients through Patients Reported Outcomes.

Methods: We carried out a cross-sectional study of 101 RD patients compared with 202 healthy volunteers. Healthcare workers invited patients and volunteers to complete questionnaires on gastrointestinal symptoms, through seven domains (belly pain, constipation, diarrhea, disrupted swallowing, gas and bloating, nausea and vomiting, gastroesophageal reflux) of the Patient-Reported Outcomes Measurement Information System (PROMIS®).

Results: Among 101 RD patients, 34 (33.6%) had a diagnosis of Rheumatoid Arthritis, 23 (22.7%) had a diagnosis of Psoriatic Arthritis, 12 (11.8%) had axial spondyloarthritis; 18 (17.8%) had Systemic Sclerosis, 8 (7.9%) were classified as Connectivitis (i.e.Lupus, Sjögren Syndrome), and finally 6 (5.9%) had vasculitis. Median disease duration was 7±5 years and just under half (45.5%) of RD patients had active disease according to specific disease activity index. As shown in Table 1, no significant differences were found between patients and controls with regard to demographic and anthropometric characteristics except for sex, since males were 25.7% (n=26) in RD patients and 125 (61,8%) in healthy volunteers. In our study, Patients reported significantly greater gastrointestinal symptoms than healthy controls. More specifically, as shown in Figure 1A, median T score for belly pain, constipation, diarrhea and disrupted swallowing were significantly higher in the RD patients than in healthy controls (50.2 ± 14 vs 41.7 ± 12 $p<0.001$; 51.5 ± 10 vs 42.2 ± 9 $p <0.001$; 45.3 ± 8 vs 42 ± 5 $p <0.001$; 51.1 ± 10 vs 44.6 ± 7 $p <0.001$) respectively. Moreover, also regarding others domains (gas and bloating, nausea and vomiting and gastroesophageal reflux), patients reported a median T score worse than healthy controls (Figure 1B).

Table 1.

	Patients (N= 101)	Healthy (N= 202)	*p*
Demographic and Anthropometric			
Age (years)	60±13	54.2 ±15	ns
Gender n male (%)	26 (25,7)	125 (61,8)	<0,001
BMI (Kg/m2)	26,4±4	25,5±4	ns
Smoke n (%)	51(50,5)	97(48)	ns
Physical Activity (%)	27(26,7)	62(30,7)	ns
Rheumatoid Arthritis	34(33,6)	-	
Psoriatic Arthritis	23(22,7)	-	
Spondyloarthritis	12(11,8)	-	
Systemic Sclerosis	18(17,8)	-	
Connectivitis	8(7,9)	-	
Vasculitis	6(5,9)	-	
Disease duration (years)	7±5	-	
Disease Activity n yes (%)	46(45,5)	-	
Medications n (% patients)		-	
NSAID	11(10,9)	-	
Steroids	26(25,7)	-	
Biological Treatment	54(53,5)	-	
Methotrexate	34(33,7)	-	

Continuous variables are shown as mean ± standard deviation. Categorical variables are presented as number and proportion. The overall p-value was calculated by the Mann–Whitney non-parametric test for independent samples and by Chi-square test as appropriate.

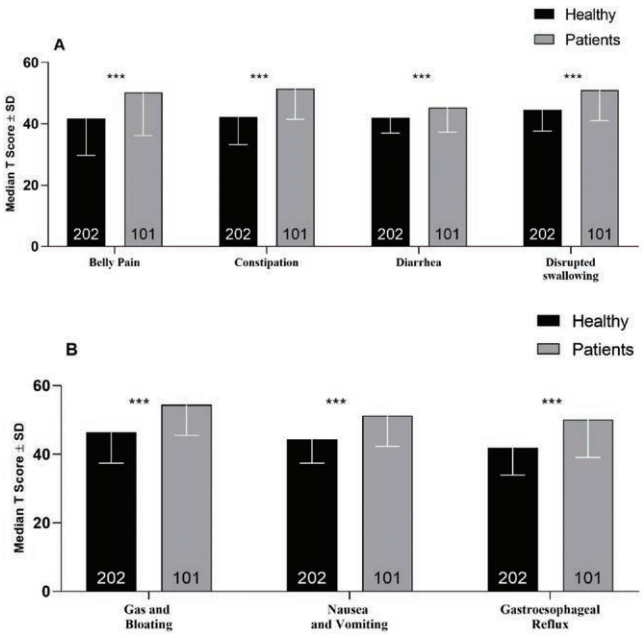


Figure 1. Median T Score stratified by study group. Data are shown as mean and standard deviation. The overall p-value was calculated by the Mann–Whitney non-parametric test for independent samples.

Conclusion: Firstly, this study highlights the need to investigate further the association between Rheumatic Diseases and gastrointestinal symptoms as potential patterns of underlying diseases and, secondly, the need to adopt validated questionnaires in clinical practice that can help healthcare professionals to detect underestimated symptoms.

REFERENCES:

[1] P. T. Kröner, O. A. Tolaymat, A. W. Bowman, A. Abril, e B. E. Lacy, «Gastrointestinal Manifestations of Rheumatological Diseases», Am. J. Gastroenterol., vol. 114, n. 9, pagg. 1441–1454, 2019.

[2] J. P. Witter, «The Promise of Patient-Reported Outcomes Measurement Information System-Turning Theory into Reality: A Uniform Approach to Patient-Reported Outcomes Across Rheumatic Diseases», Rheum. Dis. Clin. North Am., vol. 42, n. 2, pagg. 377–394, 2016

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1040

POS1458-HPR

DIGITAL RHEUMATOLOGY IN THE ERA OF COVID-19: RESULTS OF A NATIONAL PATIENT AND PHYSICIAN SURVEY

A. Kernder[1,2], H. Morf[2,3], P. Klemm[2,4], D. Vossen[2,5], M. Meyer[2,6], I. Haase[2,7], J. Mucke[1,2], A. Kleyer[2,3], P. Sewerin[1,2], G. Bendzuck[8], S. Eis[8], J. Knitza[2,3], M. Krusche[2,9]. *[1]Heinrich-Heine-University Düsseldorf, Department of Rheumatology & Hiller-Research Unit Rheumatology, Düsseldorf, Germany*; *[2]German Society for Rheumatology (Working Group Young Rheumatology), Rheumatology, Berlin, Germany*; *[3]Friedrich-Alexander University Erlangen-Nürnberg, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany*; *[4]Department of Rheumatology, Immunology, Osteology and Physical Medicine, Department of Rheumatology, Immunology, Osteology and Physical Medicine, Bad Nauheim, Germany*; *[5]St. Elisabeth Hospital, Rheinisches Rheumazentrum Meerbusch, Rheumatology, Meerbusch, Germany*; *[6]Universitätsklinikum Hamburg-Eppendorf, Rheumatology, Hamburg, Germany*; *[7]Department of Rheumatology & Hiller-Research Unit Rheumatology, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany*; *[8]German League against Rheumatism, German League against Rheumatism, Bonn, Germany*; *[9]Charité- Universitätsmedizin, Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*

Background: Digital health applications (DHAs) are gaining influence and promise great potential for the monitoring and management of rheumatic and musculoskeletal diseases (RMDs).

Objectives: To analyse the impact of the COVID-19 pandemic on RMD patients' and rheumatologists' usage, preferences, and perception of digital health applications (DHAs) in Germany.

Methods: A web-based national survey was developed by the Working Group Young Rheumatology of the German Society for Rheumatology and the German League against Rheumatism. The prospective survey was distributed via social media, QR-code, and email. Descriptive statistics were calculated, and regression analyses were performed to show correlations.

Results: We analysed the responses of 299 patients and 129 rheumatologists. Most patients (74%) and rheumatologists (76%) believed that DHAs are useful in the management of RMDs and felt confident in their own usage thereof (90%; 86%). 38% of patients and 71% of rheumatologists reported that their attitude had changed positively towards DHAs and that their usage had increased due to COVID-19 (29%; 48%).

Usage and recommendation of DHAs for both groups are shown in Figure 1:

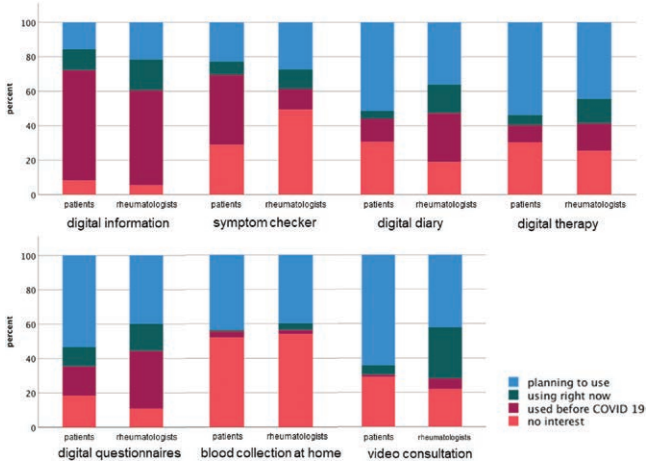


Figure 1. Usage or recommendation of digital health applications. Patients and rheumatologists were asked to indicate the specific digital health applications (DHAs) they used or were recommended.

The majority in both groups agreed on implementing virtual visits for follow-up appointments in stable disease conditions. The most reported advantages of DHAs were usage independent of time and place (76.6%; 77.5%). The main barriers were a lack of information on suitable, available DHAs (58.5%; 41.9%), poor usability (42.1% of patients) and a lack of evidence supporting the effectiveness of DHAs (23.2% of rheumatologists) (Table 1).

Table 1. Advantages and Barriers of DHA, n (%).

Advantages			Barriers		
	Patients	Rheumatologists		Patients	Rheumatologists
Location-Independence	229 (76.6)	100 (77.5)	Too little information	175 (58.5)	54 (41.9)
Time-independence	223 (74.6)	94 (72.9)	Too little evidence of benefits	36 (12.0)	30 (23.3)
Detailed documentation	97 (32.4)	47 (36.4)	Poor quality of current apps	47 (15.7)	29 (22.5)
Cost saving	95 (31.8)	37 (28.7)	Concerns about data protection	52 (17.4)	25 (19.4)
More information	88 (29.4)	38 (29.5)	Lack of usability	126 (42.1)	17 (13.2)
Independence of doctors+	36 (12.0)	-	Lack of accessibility	4 (1.3)	-
More flexibility	107 (36.8)	77 (59.7)	High costs	4 (1.3)	23 (17.8)
Preparation for discussion+	46 (15.4)	-	No suitable equipment	17 (5.7)	11 (8.5)
No advantages at all	18 (6.0)	1 (0.8)	Lack of user competence	9 (3.0)	-
			No Need	39 (13.0)	12 (9.3)

Patients and rheumatologists were asked about the advantages and barriers of DHAs. Multiple answers were allowed. Patients had two additional potential advantages and potential barriers to choose from*.

Only a minority (<10% in both groups) believed that digitalisation has a negative impact on the patient-doctor relationship.

Conclusion: The COVID-19 pandemic instigated an increase in patients' and rheumatologists' acceptance and usage of DHAs, possibly introducing a permanent paradigm shift in the management of RMDs.

Acknowledgements: The authors thank the following persons and societies for their great effort, distributing the online survey: P.Aries, A.Hueber, E.Feist, C.Fiehn, P.Korsten, I.Kötter, F.Mühlensiepen, A.Pfeil, M.Rudwaleit, M.Welcker, S.Zinke, Deutsche Vereinigung Morbus Bechterew e.V., Deutsche Rheuma-Liga Bundesverband e. V., Sklerodermie Selbsthilfe e.V.

Disclosure of Interests: Anna Kernder: None declared, Harriet Morf: None declared, Philipp Klemm: None declared, Diana Vossen Speakers bureau: Novartis, Abbvie, Amgen, Consultant of: Abbvie Deutschland GmbH & Co. KG, Bristol-Myer Squibb, Celgene GmbH, Gilead Sciences Inc., Lilly Deutschland GmbH, Medac GmbH, Novartis Pharma GmbH, Pfizer Deutschland GmbH, UCB Pharma GmbH, Grant/research support from: Pfizer, Abbvie, Marco Meyer Consultant of: Medac, Isabell Haase Speakers bureau: Medac, Consultant of: Medac, Grant/research support from: UCB, Abbvie, BMS, Johanna Mucke Speakers bureau: AbbVie Deutschland GmbH & Co. KG, Amgen, Bristol-Myers Squibb, Chugai Pharma Germany GmbH, Celgene GmbH, Gilead Sciences Inc., GlaxoSmithKline, Janssen-Cilag GmbH, Lilly Deutschland GmbH, Novartis Pharma GmbH, Pfizer Deutschland GmbH and UCB Pharma GmbH., Consultant of: AbbVie Deutschland GmbH & Co. KG, Amgen, Bristol-Myers Squibb, Chugai Pharma Germany GmbH, Celgene GmbH, Gilead Sciences Inc., GlaxoSmithKline, Janssen-Cilag GmbH, Lilly Deutschland GmbH, Novartis Pharma GmbH, Pfizer Deutschland GmbH and UCB Pharma GmbH., Arnd Kleyer Shareholder of: yes, Speakers bureau: Lilly, Novartis, Consultant of: Abbvie, Lilly, Novartis BMS, Gilead,Janssen, Grant/research support from: Lilly, Novartis, Gilead,, Philipp Sewerin Consultant of: AbbVie, Amgen, Axiom Health, Biogen, Bristol-Myers Squibb, Celgene, Chugai Pharma Marketing Ltd./Chugai Europe, Deutscher Psoriasis-Bund, Fresenius Kabi, Gilead Sciences, Hexal Pharma, Janssen-Cilag, Johnson & Johnson, Lilly, Medi-login, Mediri GmbH, Novartis Pharma, Onkowissen GmbH, Pfizer, Roche Pharma, Rheumazentrum Rhein-Ruhr, Sanofi-Genzyme, Swedish Orphan Biovitrum, and UCB, Grant/research support from: AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Bundesministerium fuer Bildung und Forschung (BMBF), Deutsche Forschungsgesellschaft (DFG), Deutscher Psoriasis-Bund, Fresenius Kabi, Gilead Sciences, Hexal Pharma, Janssen-Cilag, Lilly, Novartis Pharma, Pfizer, Rheumazentrum Rhein-Ruhr, Roche Pharma, Sanofi-Genzyme, and UCB, Gerlinde Bendzuck: None declared, Sabine Eis: None declared, Johannes Knitza Consultant of: Abbvie, Novartis, Lilly, Medac, BMS, Sanofi, Amgen, Gilead, UCB, ABATON, GSK, Grant/research support from: Novartis, UCB, Thermofisher, Sanofi, Martin Krusche Speakers bureau: Lilly, Medac, Novartis, Roche/Chugai, Consultant of: Abbvie, Lilly, Gilead, Medac, Novartis, Sobi, BMS, Amgen, GSK, Grant/research support from: Sanofi

DOI: 10.1136/annrheumdis-2021-eular.1328

POS1459-HPR IDENTIFYING MEANINGFUL CHANGE IN THE RA FLARE QUESTIONNAIRE SCORES IN RHEUMATOID ARTHRITIS

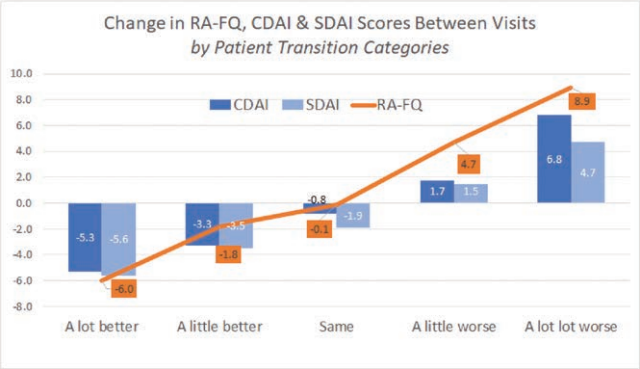
S. J. Bartlett[1,2], C. Bingham[2], O. Schieir[3], M. F. Valois[4], G. Hazlewood[5], J. Pope[6], C. Thorne[7], D. Tin[7], C. Hitchon[8], L. Bessette[9], G. Boire[10], E. Keystone[11], V. Bykerk[12]on behalf of CATCH Investigators. [1]*McGill University, Clinical Epidemiology & Rheumatology, Montreal, Canada*; [2]*Johns Hopkins Medicine, Rheumatology, Baltimore, United States of America*; [3]*Montreal, Canada*; [4]*McGill University, Clinical Epidemiology, Montreal, Canada*; [5]*University of Calgary, Rheumatology, Calgary, Canada*; [6]*St. Joseph's Hospital, Rheumatology, London, Canada*; [7]*The Arthritis Program,., Newmarket, Canada*; [8]*University of Manitoba, Rheumatology, Winnipeg, Canada*; [9]*Centre de l'ostéoporose et de rhumatologie de Québec, Rhumatologie, Quebec City, Canada*; [10]*University of Sherbrooke, Rheumatology, Sherbrooke, Canada*; [11]*Mt. Sinai Hospital, Rheumatology, Toronto, Canada*; [12]*Hospital for Special Surgery, Rheumatology, New York, United States of America*

Background: The RA-FQ is a patient-reported measure of current disease activity in RA that can be used to identify disease flares. The RA-FQ queries pain, physical function, fatigue, stiffness, and participation and yields a score from 0-50. We previously reported on reliability, validity, and responsiveness.

Objectives: To identify changes in RA-FQ that represent minimal and meaningful improvement or worsening from the perspective of people with RA, treating rheumatologists, and in relation to disease activity indices. We hypothesized that

Methods: Data were from adults with early RA (sx <1 year) enrolled in the Canadian Early Arthritis Cohort, a prospective study of real-world patients treated across Canada. Participants completed the RA-FQ, Patient Global, and RA transition item since last visit (a little vs. a lot better or worse or same) between consecutive 3- and 6-month visits. Rheumatologists recorded joint counts, MD Global, and change in RA. We compared mean change across improvement and worsening using patient anchors and disease activity indicators.

Results: The 808 adults were mostly white (84%) women (71%) with a mean (SD) age of 55 (15) and moderate-high CDAI level (85%) at enrollment. Most (79%) reported their RA had changed; 59% were better and 20% worse. Patients who were *a lot worse* had a mean increase of 8.9 points whereas those who rated themselves as *a lot better* had a -6.0 decrease on the RA-FQ (Figure 1). Minimal worsening and improvement were associated with 4.7 and -1.8 change in RA-FQ scores, respectively, while patients who rated their RA unchanged had stable RA-FQ scores (Table 1).



Similar changes were evident in CDAI, SDAI, and DAS indices (Table 1). Larger differences were observed with patient vs. physician global scores and tender vs. swollen joints. Across measures, the change associated with worsening was greater than for improvement. Results supported all prespecified hypotheses ab.

Table 1. Change in RA-FQ scores between visits by patient rating of RA status.

	A Lot Better (N=346; 43%)			A Little Better (N=132; 16%)			The Same (N=174; 21%)			A Little Worse (N=94; 12%)			A Lot Worse (N=62; 8%)		
Domain	Δ	95% CI	SD	Δ	95% CI	SD	Δ	95% CI	SD	Δ	95% CI	SD	Δ	95% CI	SD
RA-FQ Total (0-50)	-6.0	(-7.1, -4.9)	10.3	-1.8	(-3.2, -0.3)	8.4	-0.1	(-1.3, 1.1)	8.1	4.7	(2.9, 6.6)	9.1	8.9	(5.1, 12.7)	15.0
Pain	-1.2	(-1.4, -0.9)	2.4	-0.4	(-0.8, 0.0)	2.3	0.0	(-0.2, 0.3)	1.8	1.3	(0.8, 1.7)	2.2	2.0	(1.2, 2.9)	3.3
Physical Function	-1.3	(-1.6, -1.1)	2.4	-0.3	(-0.6, 0.1)	2.1	0.0	(-0.3, 0.3)	2.1	0.9	(0.4, 1.4)	2.4	1.8	(0.8, 2.7)	3.7
Fatigue	-1.1	(-1.4, -0.8)	2.6	-0.4	(-0.7, 0.0)	1.9	0.0	(-0.3, 0.3)	2.1	0.7	(0.3, 1.1)	2.1	1.3	(0.5, 2.1)	3.2
Stiffness	-1.1	(-1.4, -0.9)	2.4	-0.4	(-0.7, 0.0)	2.0	-0.1	(-0.4, 0.2)	2.0	1.1	(0.6, 1.5)	2.2	1.8	(1.0, 2.7)	3.3
Participation	-1.2	(-1.5, -1.0)	2.5	-0.1	(-0.5, 0.3)	2.1	-0.1	(-0.4, 0.2)	2.2	0.8	(0.4, 1.3)	2.2	2.0	(1.1, 2.8)	3.4
Disease Activity															
CDAI*	-5.3	(-6.3, -4.3)	9.1	-3.3	(-5.4, -1.3)	11.5	-0.8	(-2.0, 0.5)	8.1	1.7	(-0.1, 3.5)	8.8	6.8	(3.7, 9.8)	12.0
SDAI	-5.6	(-6.8, -4.4)	9.2	-3.5	(-6.1, -0.9)	12.2	-1.9	(-3.6, -0.2)	8.9	1.5	(-0.7, 3.7)	9.2	4.7	(1.0, 8.4)	12.2
DAS28-CRP	-0.7	(-0.8, -0.6)	1.01	-0.5	(-0.7, -0.2)	1.2	-0.2	(-0.4, 0.0)	1.0	0.3	(0.1, 0.5)	1.0	0.5	(0.2, 0.9)	1.2
Patient Global (0-10)	-1.3	(-1.5, -1.0)	2.7	-0.5	(-0.9, -0.1)	2.1	-0.1	(-0.4, 0.2)	2.1	1.3	(0.8, 1.8)	2.4	2.9	(2.1, 3.6)	3.1
MD Global (0-10)	-1.2	(-1.4, -1.0)	1.9	-0.7	(-1.1, -0.3)	-0.1	-0.1	(-0.4, 0.2)	1.9	0.1	(-0.3, 0.5)	2.8	0.7	(0.0, 1.5)	2.8
Swollen Joints (28)	-1.4	(-1.7, 1.0)	3.2	-1.0	(-1.8, -0.2)	4.6	-0.4	(-0.9, 0.0)	3.0	0.0	(-0.7, 0.7)	3.4	1.3	(0.2, 2.5)	4.6
Tender Joints (28)	-1.5	(-1.9, -1.1)	3.9	-1.3	(-2.2, -0.3)	5.5	0.0	(-0.7, 0.6)	4.3	0.3	(-0.7, 1.2)	4.5	2.2	(0.8, 3.5)	5.4

Conclusion: In this large cohort of adults with ERA, the RA-FQ was responsive to change and generally distinguish between minimal and meaningful improvement and worsening. These data add to a growing evidence demonstrating robust psychometric properties of the RA-FQ and offer

initial guidance about the amount of change associated with improvement or worsening, supporting its use in RA care, research and decision-making.

Acknowledgements: The CATCH study was designed and implemented by the investigators and financially supported through unrestricted research grants from: Amgen and Pfizer Canada - Founding sponsors since January 2007; AbbVie Corporation and Hoffmann-LaRoche since 2011; Medexus Inc. since 2013;, Merck Canada since 2017, Sandoz Canada, Biopharmaceuticals since 2019,Gilead Sciences Canada since 2020 and Fresenius Kabi Canada Ltd. since 2021. Previously funded by Janssen Biotech from 2011-2016, UCB Canada and Bristol-Myers Squibb Canada from 2011-2018, Sanofi Genzyme from 2016-2017, and Eli Lilly Canada from 2016-2020.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1663

POS1460-HPR MYRA TOUCH FOR DISEASE ACTIVITY EVALUATION IN RHEUMATOID ARTHRITIS: A COMPARISON OF PATIENT-REPORTED OUTCOMES WITH PHYSICIAN'S ASSESSMENT

L. H. Eow[1], J. Yew[1], K. H. Lee2, S. Selvadurai2, S. M. Liau2, N. Mohd Noor2, A. Mohd2, Y. L. Loh2, S. C. Gun2. *[1]Hospital Tuanku Ja'afar, Medical Department, Seremban, Malaysia*; *[1]Hospital Tuanku Ja'afar, Medical Department, Seremban, Malaysia*

Background: Patient-reported outcomes (PROs) have become an essential component of patients' assessment in the management of Rheumatoid Arthritis(RA).They have been reported to be at least as informative if not more than physician assessed outcomes.

MyRA Touch was pioneered by the Rheumatology Unit of Hospital Tuanku Jaa'far in Seremban Malaysia in March 2018,to engage and empower all RA patients on their own disease activity monitoring. It is an electronic platform, designed to enhanced the application of electronic patient reported outcomes (ePROs) among RA patients where they examine and record their own painful and/or swollen joints for DAS28 calculation and report their health assessment through Routine Assessment of Patient Index Data with 3 Measures (RAPID 3).MyRA Touch is an applications (App) that is user friendly and available in four major spoken languages (English, Chinese, Malay and Tamil) with an animated version for patients who are illiterate.

Objectives: The objectives of this study are to determine the correlation between:

I)Patient-reported and physician reported DAS28 ESR/CRP

II)RAPID3 and Clinical Disease activity Index (CDAI)

III)RAPID3 and DAS28 ESR/CRP assessed by physician and patient

IV)RAPID3 and inflammatory markers ESR/CRP.

Methods: This was a cross-sectional study carried out in the Rheumatology Unit of Hospital Tuanku Jaa'far. All data entered through MyRA Touch App from April 2018 till April 2020 was analysed.

Results: There were a total of 562 patients who entered the data in the App, 87.9% were women. The ethnic compositions of the study subjects comprised of Indians (36.7%) followed by the Malays (34.7%),Chinese (26.3%) and other ethnics (2.3%). About half of patients (59.8%) were in the 51-70 age group whereas 22.9%,1.8% and 15.5% were in the 31-50,18-30 and above 70 age groups respectively. The majority of our patients (96%) were literate. A total of 54.3% of them received secondary education, 27% primary, 12.2% tertiary and 6.6% did not receive any formal education.

There was a high level of correlation between DAS28 ESR/CRP performed by patient and DAS28 ESR/CRP assessed by physician, (r=0.808 for DAS28 ESR and r=0.804 for DAS28 CRP). RAPID3 also showed high level of correlation with CDAI and DAS28 CRP assessed by patient (r=0.700 and r=0.718 respectively). There was a moderate correlation between DAS28 ESR/CRP done by physician with RAPID3 (r=0.656 and r=0.696 respectively).RAPID3 demonstrated little correlation with inflammatory markers ESR and CRP (r=0.141 and r=0.171 respectively).

Conclusion: PROs via DAS 28 (ESR/CRP) and RAPID3 showed moderate to high correlation with disease activity assessed by physician. We can empower patients to perform their own disease assessment by using the MyRA Touch App before seeing their physician and the information provided in the App, can help to reduced consultation time. During the COVID-19 pandemic, telemedicine is very much encouraged. By using the MyRA Touch, patients can assess their own tender and swollen joint count on a homunculus, evaluate their own physical function, health and pain using the RAPID3 parameters. The information obtained from the PROs in the MyRA touch App enables the physician to make a more comprehensive virtual assessment of the patient's condition which helps in treatment decision making. In conclusion, MyRA Touch is an useful tool for disease activity measurement by patient.

REFERENCES:

[1] Jenny AA, Diana BC, Omar JC, et al. Usefulness of Patients-Reported Outcomes in Rheumatoid Arthritis Focus Group. Hindawi Publishing Corporation Arthritis, vol 2012,Article ID935187.

[2] Ana MO, Clifton OB. Patient Reported Outcomes in Rheumatoid Arthritis Clinical Trials. Curr Rheumato Rep.2015 April;17(4):501.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1813

POS1461-HPR THE DEVELOPMENT OF A NOVEL EPRO DELIVERY SYSTEM TO MEASURE PATIENT QUALITY OF LIFE IN ROUTINE CLINICAL CARE: AN ANALYSIS OF 5 YEARS OF EXPERIENCE

K. Tymms[1,2], T. Smith[1], C. Deakin[1], T. Freeman[3], D. Hoffman[3], D. Segelov[3], H. Griffiths[1,4], S. Ciciriello[1,5], P. Youssef[1,6], D. Mathers[1,7], C. Osullivan[1], G. Littlejohn[1,8]. *[1]OPAL Rheumatology, Ltd, Sydney, Australia*; *[2]Canberra Rheumatology, Canberra, Australia*; *[3]Software 4 Specialists (S4S), Pty Ltd, Sydney, Australia*; *[4]Barwon Rheumatology, Services, Geelong, Australia*; *[5]Dept. of Rheumatology, Royal Melbourne Hospital, Melbourne, Australia*; *[6]Dept. of Rheumatology, Royal Prince Alfred Hospital, Sydney, Australia*; *[7]Georgetown Arthritis, Georgetown, Australia*; *[8]Dept. of Medicine, Monash University, Clayton, Australia*

Background: Registry studies and clinical trials are increasingly incorporating patient reported outcomes (PROs) to measure the full burden of disease and better measure the efficacy and value of medicines; however, the burden of paper-based surveys, time constraints, and privacy concerns impede the widespread use of PROs in routine clinical care.

Objectives: To develop a simple and secure technological solution to incorporate validated PROs into routine clinical care for patients with rheumatic diseases, and to assess the patient response to functional assessment of chronic illness therapy fatigue (FACIT-F), patient health questionnaire-2 (PHQ-2), and healthcare resource utilization (HCRU) questionnaires delivered using this ePRO method.

Methods: A novel ePRO questionnaire delivery system was developed by Software4Specialists in partnership with OPAL Rheumatology. Validated PRO questionnaires were sent from the patient's electronic medical record (Audit4, Software4Specialists) and delivered to the patient's email address at time intervals specified by the rheumatologist (defaults to quarterly) or completed in the clinic waiting room prior to the consultation using a tablet or the patient's smart phone (in-practice). Completed questionnaires were encrypted and returned directly to the patient's Audit4 electronic medical record held on the clinician's server for review at the next clinical consultation. The link to the PRO questionnaire expired within 28 days if the questionnaire was not completed, and the questionnaires were automatically cancelled if 2 consecutive links expired. This technology was made available to up to 111 rheumatologists located in 42 clinics in 6 states/territories in Australia, and the use of this technology to furnish the clinical consultation was voluntary for clinicians and patients. Deidentified clinical data was extracted from the servers of participating rheumatologists and aggregated across all sites.[1] Data collected between April 2016-Dec 2020 was analysed descriptively.

Results: Between April 2016-Dec 2020, 99,505 FACIT-F, PHQ-2 and HCRU questionnaires have been delivered to 5,784 patients from 39 of 42 contributing clinics (93%). 85% of questionnaires were delivered via email and 15% in-practice. Overall, 85% of patients completed at least one questionnaire, and of all questionnaires sent, 73% were completed. These rates have remained consistent over time. The completion rates were higher when questionnaires were delivered to patients in-practice compared to email (96% vs 69%). Females were more likely to engage with the questionnaires than males (87% vs 81%), and older patients were slightly more likely to complete all questionnaires delivered. 69% of questionnaires sent via email were completed on the day they were delivered and 94% were completed within 7 days. The median (IQR) number of questionnaires completed per patient was 3 (1,7) and the median (IQR) time since the first questionnaire was completed was 13 months (5,26).

Conclusion: The novel Audit4 ePRO delivery system is an effective tool for incorporating PROs into routine clinical care to capture data directly from the patient on the impact of their condition on their quality of life. The data generated provides a unique opportunity to understand the full burden of disease for patients in the real-world setting and the impact of interventions.

REFERENCES:
[1] Littlejohn GO, Tymms KE, Smith T, Griffiths HT. Using big data from real-world Australian rheumatology encounters to enhance clinical care and research. Clin Exp Rheum 2020:38(5): 874 -880.
Acknowledgements: The authors acknowledge the members of OPAL Rheumatology Ltd and their patients for providing clinical data for this study, and Software4Specialists Pty Ltd for providing the Audit4 platform.
Disclosure of Interests: Kathleen Tymms: None declared, Tegan Smith: None declared, Claire Deakin: None declared, Tim Freeman: None declared, David Hoffman: None declared, Dana Segelov: None declared, Hedley Griffiths Consultant of: AbbVie, Gilead, Novartis and Lilly., Sabina Ciciriello: None declared, Peter Youssef: None declared, David Mathers: None declared, Catherine OSullivan: None declared, Geoff Littlejohn Consultant of: Over the last 5 years Geoffrey Littlejohn has received educational grants and consulting fees from AbbVie, Bristol Myers Squibb, Eli Lilly, Gilead, Novartis, Pfizer, Janssen, Sandoz, Sanofi and Seqirus
DOI: 10.1136/annrheumdis-2021-eular.2253

POS1462-HPR VALIDITY AND PSYCHOMETRIC CHARACTERISTICS OF THE PSORIATIC ARTHRITIS QUALITY OF LIFE (PSAQOL) QUESTIONNAIRE IN TURKISH POPULATION

M. T. Duruöz[1], K. Nas[2], S. Acer Kasman[1], E. Uzun[3], H. H. Gezer[1]. *[1]Marmara University, School of Medicine, Physical Medicine and Rehabilitation Department, Rheumatology Division, Istanbul, Turkey*; *[2]Sakarya University School of Medicine, Division of Rheumatology and Immunology, Department of Physical Medicine and Rehabilitation, Sakarya, Turkey*; *[3]Sakarya University School of Medicine, Department of Physical Medicine and Rehabilitation, Sakarya, Turkey*

Background: Psoriatic Arthritis Quality of Life (PsAQoL) questionnaire was developed to measure quality of life (QoL) in patients with psoriatic arthritis (PsA) (1).
Objectives: The aim of the study was to assess validity and psychometric properties of the PsAQoL questionnaire.
Methods: The translation-back translation method by a bilingual panel was used to translate the original PsAQoL into Turkish (2). Face and content validities were evaluated via cognitive debriefing interviews with 10 PsA patients. Then, patients with PsA according to CASPAR criteria were recruited to assess feasibility, missing data, floor and ceiling effect, reliability, and construct validity. Reliability was assessed by internal consistency. Construct validity was investigated by convergent and divergent validity by assessing the PsAQoL's relations with QoL and non-QoL parameters. For this purpose, demographics, clinical characteristics (shown in Table 1), survey data including PsAQoL, Short form 36, visual analog scales for pain and fatigue, Health Assessment Questionnaire, and Hospital Anxiety and Depression Scale results were recorded.
Results: One hundred and sixty-two patients were recruited and 74 of them had axial PsA. Cognitive debriefing showed the Turkish version of PsAQoL to be clear, understandable, and relevant. It was easy to complete and calculate, with the 3 minutes and 20 seconds, respectively. The Cronbach's alpha coefficient for internal consistency was 0.930. The questionnaire presented no floor or ceiling effect (<15% for both) and no missing data. PsAQoL showed good correlations with the QoL scales indicating its convergent validity and moderate to non-significant correlations with the non-QoL parameters supporting its divergent validity (Table 1).

Table 1. Spearman's correlation coefficients of PsAQoL with the other parameters for construct validity

Convergent			Divergent		
SF-36 subscales	**Rho**	**Clinical Parameters**	**Rho**	**Surveys**	**Rho**
Physical component	-0.744**	Age	0.150	BASDAI (n:74)	0.355**
Mental component	-0.731**	Disease duration	0.014	VAS Pain	0.408**
Physical functioning	-0.629**	Tender joint count	0.262**	VAS Fatigue	0.447**
Physical role limitations	-0.640**	Swollen joint count	0.170*	HAQ	0.533**
Emotional role limitations	-0.576**	MASES	0.152	HADS Anxiety	0.535**
Vitality	-0.657**	PASI	-0.032	HADS Depression	0.517**
Emotional well-being	-0.590**	DAPSA	0.409**		
Social functioning	-0.591**	DAS28	0.322**		
Pain	-0.535**	BASMI (n: 61)	0.032		
General health	-0.536**				

*** p<0.001, *p: 0.001-0.049.PsAQoL: Psoriatic Arthritis Quality of Life, SF-36: Short Form 36, MASES: Maastricht Ankylosing Spondylitis Enthesitis Score, PASI: Psoriasis Area Severity Index, DAPSA: Disease Activity in PSoriatic Arthritis, DAS28: Disease Activity Score 28, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, VAS: Visual analog scale, HAQ: Health Assessment Questionnaire, HADS: Hospital Anxiety and Depression Scale.*

Conclusion: The Turkish version of the PsAQoL is a valid and disease-specific instrument with good psychometric characteristics to assess PsA-specific QoL.
REFERENCES:
[1] McKenna SP, Doward LC, Whalley D, Tennant A, Emery P, Veale DJ. Development of the PsAQoL: a quality of life instrument specific to psoriatic arthritis. Ann Rheum Dis. 2004;63(2):162-169.
[2] Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine (Phila Pa 1976). 2000;25(24):3186-3191.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3311

POS1463-HPR IMPACT OF COVID-19 PANDEMIC ON DISEASE ACTIVITY AND EMOTIONAL WELL-BEING AMONG RHEUMATOID ARTHRITIS PATIENTS: A TELEMEDICINE STUDY

B. Lucchino[1], C. Iannuccelli[1], C. Gioia[1], G. Dolcini[1], M. DI Franco[1]. *[1]Sapienza University of Rome, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Rome, Italy*

Background: By the beginning of March 2020, the pandemic of the novel coronavirus disease (COVID-19) imposed severe lockdown measures opposing the viral spread, limiting non-COVID patients' access to hospitals. Previous reports suggest that Rheumatoid Arthritis (RA) patients may experience a worsening of self-reported disease activity following natural disasters. Moreover, RA patients are at increased risk of mood disorders, such as depression and anxiety. An increase of depressive symptoms, anxiety and suicidal rate has been recently reported as result of the lockdown in response to COVID-19.
Objectives: Aims of this study were to investigate the impact of the lockdown measures on disease activity and emotional well-being among patients affected by RA, through a telemedicine approach.
Methods: Patients followed in the "Early Arthritis Clinic" of our hospital were invited to participate to an online survey. They were asked also to invite their best friend (BF), matched for age and sex, to participate the survey, as control group. Moreover, clinical records from the same "Early Arthritis Clinic" cohort were used as pre-pandemic group. The online survey included demographic questions and, for RA patients, the evaluation of perceived pain (P-VAS) and disease activity (DA-VAS) on a scale of 1-10 as well as Rheumatoid Arthritis Disease Activity Index-5 (RADAI-5), a validated self-reported disease activity measure. Both RA patients and BF responded also to validated, psychometric scales for stress vulnerability (Stress Vulnerability Scale-SVS), resilience (Resilience Scale-RS), depression (Zung's depression questionnaire-Zung-D) and anxiety (Zung's anxiety questionnaire-Zung-A) evaluation.
Results: The cohort was composed by 76 RA patients who answered the survey, 32 BF and 170 RA patients from historical cohort. There were no differences in demographic characteristics, SVS, RS, Zung-D and Zung-A between RA patients and BF. RADAI-5 correlated positively with SVS (r=0,29;p=0,01), P-VAS (r=0,8;p<0,0001) and DA-VAS (r=0,8;p<0,0001) and negatively with RS (r=-0,23;p=0,04). Patients with higher disease activity showed higher classes of Zung-D (p=0,03) and SVS (p=0,006), and lower classes of RS(p=0,001). P-VAS was the only significant predictor of RADAI-5 (β=0,83;CI=0,53-0,76;p<0,001), and the concordance between RADAI-5, P-VAS and DA-VAS was high (K=0,94;p<0,001). Compared with the historical cohort, RA patients involved in the survey showed higher frequencies of moderate and elevated disease activity classes (p<0,001;Figure 1) despite there were no differences in P-VAS and DA-VAS.
Conclusion: These results suggest that lockdown did not affect differently emotional well-being of RA patients compared to healthy subjects. RA patients with elevated disease activity report higher stress and depressive symptoms, and SVS and RS may be useful to identify patients at higher risk. The higher self-reported disease activity measured through RADAI-5 may be the result of an overestimation of disease severity by patients, which depends mostly from pain. This should be considered in the assessment of disease activity through telemedicine.

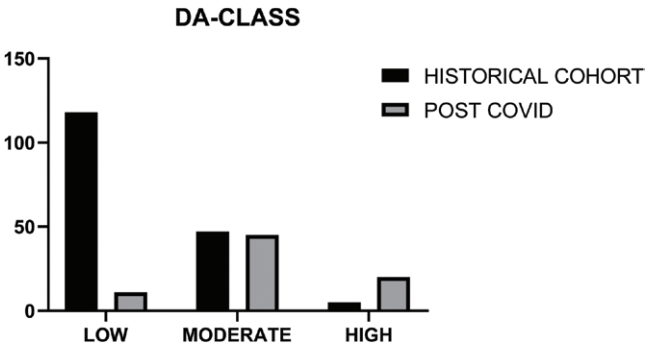


Figure 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3479

POS1464-HPR **ASSESSMENT OF EMOTIONAL WELL-BEING IN RHEUMATIC PATIENTS DURING COVID-19 LOCKDOWN THROUGH A WEB-BASED SURVEY APPROACH**

C. Iannuccelli[1], B. Lucchino[1], C. Gioia[1], A. Gattamelata[1], F. Giardina[1], M. Dl Franco[1], R. Priori[1], F. Conti[1]. [1]*Sapienza University of Rome, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Rome, Italy*

Background: The severe measures of lockdown imposed in Italy to limit the SARS coronavirus 2 disease (COVID-19) spread caused an increase of reported anxiety, depression and suicidal rate among general population. Patients affected by rheumatic disorders feature an increased risk of mood disorders for the chronic course of the disease itself and for the related disability.
Objectives: Aim of this study was to investigate the impact of COVID-19 lockdown on emotional well-being of a large cohort of rheumatic patients through a telemedicine approach.
Methods: Patients in follow-up in rheumatologic out-patient clinics of our hospital were invited to participate to an online survey. They were asked also to invite their best friend, matched for age and sex, to participate the survey, as control group. The online survey included demographic questions and validated, psychometric scales for stress vulnerability (Stress Vulnerability Scale-SVS), resilience (Resilience Scale-RS), depression (Zung's depression questionnaire-Zung-D) and anxiety (Zung's anxiety questionnaire-Zung-A) evaluation.
Results: The cohort was composed by 484 subjects (84,1% F, 15,9% M). The number of subjects and the frequency of various diagnosis are shown in Table 1. According to the psychometric scales, 55,5% and 43,3% of subject showed respectively an increased stress vulnerability and a reduced resiliency. Moreover, 64% and 40,5% of the enrolled subjects reported respectively anxiety and depressive symptoms worthy of psychiatric attention. There was a significant different distribution of scores for SVS (p<0,0001), Zung-A (p<0,0001) and Zung-D (p<0,0001) among the various diagnosis. In comparison with controls, higher scores of SVS were present in connective tissue diseases (CTD) (p=0,007), Sjogren's Syndrome (SSJ) (p=0,0029) and fibromyalgia (FM) (p<0,0001) patients, higher scores of Zung-A were present in SSJ (p=0,006) and FM (p<0,0001) patients and higher scores of Zung-D were present in FM (p<0,0001) patients (Figure 1). Ordinal regression analysis showed that higher classes of anxiety were independently predicted by the Tension (β=0,32;CI=0,13-0,52;p=0,003) and Demoralization (β=0,22;CI=0,04-0,44;p=0,046) components of SVS and by the Zung-D score (β=0,09;CI=0,05-0,1;p<0,001), while higher classes of depression were independently predicted by SVS total (β=0,17;CI=0,03-0,30;p=0,012), by its subcomponent Demoralization (β=0,22;CI=0,01-0,43;p=0,038), by a lower absolute RS score (β=-0,083;CI=-0,1--0,06;p<0,001) and by the Zung-A score (β=0,11;CI=0,06-0,15;p<0,001). In both cases, a specific diagnosis was not associated to a higher risk of advanced anxiety and depression classes.
Conclusion: Rheumatic patients developed a high frequency of anxiety and depressive symptoms following COVID-19 lockdown, of which a large part should be referred for specialist attention according to their severity. There was a large variability of the symptoms reported among the various diagnosis. CTD, SSJ and FM patients were the most susceptible to the development of anxiety, depression and stress vulnerability. The application of psycometric scales through a telemedicine approach represents a useful tool to identify patients with higher levels of anxiety and depression.

Table 1.

DIAGNOSIS

	Frequency	Percent
Controls	45	9,3
RA	82	16,9
PSA	21	4,3
UA	4	0,8
SPA	7	1,4
CTD	70	14,5
FM	79	16,3
Myositis	8	1,7
Behcet's	11	2,3
Vasculitis	16	3,3
APS	6	1,2
Other AID	13	2,7
SSJ	122	25,2
Total	484	100

RA: Rheumatoid Arthritis, PSA: Psoriatic Arthritis; UA: Undifferentiated Arthritis; SPA: Spondyloarthritis; CTD: Connective tissues diseases (including Systemic Lupus Erythematosus, Scleroderma, Undifferentiated Connettivitis, Mixed Connettivitis); FM: Fibromyalgia; APS: Anti-phospholipid syndrome; Other AID: Other autoimmune/inflammatory disorders (including Adult-onset Still disease, IgG4 related disease); SSJ: Sjogren Syndrome

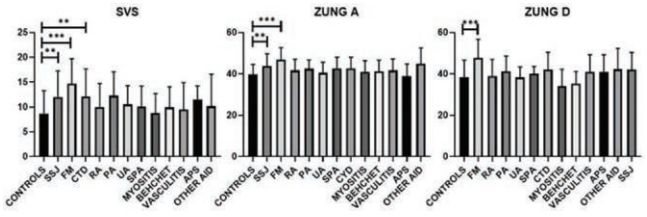


Figure 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3488

HPR Epidemiology and public health (including prevention)

POS1465-HPR **THE RELATIONSHIP BETWEEN SEDENTARY BEHAVIOR AND SLEEP IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY**

N. Kelly[1], E. Hawkins[1], H. O'leary[2], K. Quinn[3], G. Murphy[4], L. Larkin[5]. [1]*University of Limerick, School of Allied Health, Limerick, Ireland*; [2]*University Hospital Kerry, Physiotherapy, Kerry, Ireland*; [3]*Cork University Hospital, Physiotherapy, Cork, Ireland*; [4]*Cork University Hospital, Rheumatology, Cork, Ireland*; [5]*University of Limerick, School of Allied Health and Health Research Institute, Limerick, Ireland*

Background: Rheumatoid arthritis (RA) is a chronic, autoimmune inflammatory condition that affects 0.5% of the adult population worldwide (1). Sedentary behavior (SB) is any waking behavior characterized by an energy expenditure of ≤1.5 METs (metabolic equivalent) and a sitting or reclining posture, e.g. computer use (2) and has a negative impact on health in the RA population (3). Sleep is an important health behavior, but sleep quality is an issue for people living with RA (4, 5). Poor sleep quality is associated with low levels of physical activity in RA (4) however the association between SB and sleep in people who have RA has not been examined previously.
Objectives: The aim of this study was to investigate the relationship between SB and sleep in people who have RA.
Methods: A cross-sectional study was conducted. Patients were recruited from rheumatology clinics in a large acute public hospital serving a mix of urban and rural populations. Inclusion criteria were diagnosis of RA by a rheumatologist according to the American College of Rheumatology criteria age ≥ 18 and ≤ 80 years; ability to mobilize independently or aided by a stick; and to understand written and spoken English. Demographic data on age, gender, disease duration

and medication were recorded. Pain and fatigue were measured by the Visual Analogue Scale (VAS), anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS), and sleep quality was assessed using the Pittsburgh Sleep Quality Index. SB was measured using the ActivPAL4™ activity monitor, over a 7-day wear period. Descriptive statistics were calculated to describe participant characteristics. Relationships between clinical characteristics and SB were examined using Pearson's correlation coefficients and regression analyses.

Results: N=76 participants enrolled in the study with valid data provided by N=72 participants. Mean age of participants was 61.5years (SD10.6) and the majority 63% (n = 47) were female. Participant mean disease duration was 17.8years (SD10.9). Mean SB time was 533.7 (SD100.1) minutes (8.9 hours per day/59.9% of waking hours). Mean sleep quality score was 7.2 (SD5.0) (Table 1). Correlation analysis and regression analysis found no significant correlation between sleep quality and SB variables. Regression analysis demonstrated positive statistical associations for SB time and body mass index (p-value=0.03846, R^2 = 0.05143), SB time and pain VAS (p-value=0.009261, R^2 = 0.07987), SB time and HADS (p-value = 0.009721, R^2 = 0.08097) and SB time and HADSD (p-value = 0.01932, R^2 = 0.0643).

Conclusion: We found high levels of sedentary behavior and poor sleep quality in people who have RA, however no statistically significant relationship was found in this study. Future research should further explore the complex associations between sedentary behavior and sleep quality in people who have RA.

REFERENCES:

[1] Carmona L, et al. Rheumatoid arthritis. *Best Pract Res Clin Rheumatol* 2010;24:733–745.

[2] Anon. Letter to the editor: standardized use of the terms "sedentary" and "sedentary behaviours". *Appl Physiol Nutr Metab = Physiol Appl Nutr Metab* 2012;37:540–542.

[3] Fenton, S.A.M. et al. Sedentary behaviour is associated with increased long-term cardiovascular risk in patients with rheumatoid arthritis independently of moderate-to-vigorous physical activity. *BMC Musculoskelet Disord* 18, 131 (2017).

[4] McKenna S, et al. Sleep and physical activity: a cross-sectional objective profile of people with rheumatoid arthritis. *Rheumatol Int.* 2018 May;38(5):845-853.

[5] Grabovac, I., et al. 2018. Sleep quality in patients with rheumatoid arthritis and associations with pain, disability, disease duration, and activity. *Journal of clinical medicine*, 7(10)336.

Table 1. Sleep quality in people who have RA

Sleep variable	
Bed Time N(%)	
before 10pm	13(18%)
10pm-12pm	43 (60%)
after 12pm	16 (22%)
Hours Sleep mean(SD)	6.56 (1.54)
Fall Asleep minutes mean(SD)	33.3(27.7)
Night Waking N(%)	45(63%)
Self-Rate Sleep mean(SD)	2.74 (0.90)
Hours Sleep mean(SD)	6.56 (1.54)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.641

POS1466-HPR IMPACT OF COVID-19 PANDEMIC ON ADHERENCE BEHAVIOR OF LATIN-AMERICAN PATIENTS WITH RHEUMATIC DISEASES

I. A. Moreno-Arquieta[1], G. G. Sánchez Mendieta[1], D. E. Flores Alvarado[1], J. A. Esquivel Valerio[1], D. Á. Galarza-Delgado[1]. [1]*Dr. José Eleuterio González (Gonzalitos) 235, Rheumatology, Monterrey, Mexico*

Background: One of the greatest challenges of the COVID-19 pandemic for rheumatologists concerns the patient's adherence to treatment (1). The impact of poor adherence on the effectiveness of chronic disease treatment is severe in terms of poorer health outcomes and increased health care costs (2). Information regarding covid-19 on adherence behavior in Latin-American is scarce.

Objectives: The aim of this study is to describe impact of COVID-19 outbreak on adherence behavior in Latin-American population with rheumatic diseases.

Methods: We carried out a descriptive, cross-sectional, self-report study through voluntary telephonic survey, to determine adherence behaviors during the COVID-19 pandemic, from September 9th, 2020 to November 19th, 2020, for consecutive patients of the outpatient rheumatology clinic in the Hospital Universitario (Monterrey, Nuevo Leon, Mexico), which serves a resource limited population that lack access to health insurance, from five neighboring states. A 17-items survey was designed. Baseline demographics that were collected included age, sex, rheumatologic diagnosis, current medications and patient perception of disease control. Patients were asked if they continued follow-up care, last prescribed therapy and reasons. Also, the survey assessed whether patients had any issues with medication supply and where they were obtaining information about covid-19 (could choose as many options as applicable). Transferred to SPSS for analysis for descriptive statistics.

Results: A total of 150 patients were called, the survey response rate was 54.6% (n=82), with a mean completion time of 10 minutes. The mean +/- SD age of the participants was 52 +/- 15.9 years, and 95% were female. The most common self-reported diagnoses were rheumatoid arthritis (RA) (13.4%) and systemic lupus erythematosus (SLE) (13.4%) [Table 1]. Patient perception of disease control was primary good 37.8% and regular 35.4%.

Patients that continued their follow-up with their rheumatologist (on the clinic face-to-face, electronically or telehealth) or in another clinic were 26.9%, the majority were nonadherent 73%. Persistence to treatment was 82.9%, the main reason to discontinue therapy was lack of prescriptions or medical advice 8.5% and overall 58.5% had trouble finding their medicine.

Information regarding covid-19 was mainly obtained by television (health secretary conference) 90.2%, and the least directly from their doctor 4.8%.

Table 1. Survey Results

		N (%)
Age, mean +/- SD years 52 +/- 15.9		
Female/ Male	78 (95.1) / 4 (4.9)	
Diagnoses	RA	50(61)
	SLE	11(13.4)
	Osteoarthritis	10(12.2)
	Other	11(13.4)
Disease Control during covid-19	Excellent	8 (9.8)
	Good	31 (37.8)
	Regular	29 (35.4)
	Bad	14 (17.1)
Continued follow-up		22 (26.9)
(face-to-face, telehealth, other)		
Continued last prescribed treatment		68 (82.9)
Reasons to discontinue treatment	Lack of prescriptions/ medical advice	7 (8.5)
	Lack of availability	6(7.3)
	Economic disadvantage	3 (3.6)
	Fear of getting sick of COVID-19	2(2.4)
"Trouble" finding medicine		48 (58.5)
COVID-19 information	Television (Health Secretary conference)	74 (90.2)
	Social network	27 (32.9)
	Newspaper/ magazines	14 (17)
	Internet	9 (10.9)
	From a doctor	4 (4.8)

Conclusion: Patients continue their therapeutic regimen, still many of them have trouble finding their medications, which affects the disease control. Also, despite having a poor disease control (majority between regular and bad) they are not continuing their follow-up care, more objective studies are needed to determine a specific cause.

REFERENCES:

[1] Pineda-Sic RA, Galarza-Delgado DA, Serna-Pena G, et al. Ann Rheum Dis Epub ahead of print: [20-06-2020]. doi:10.1136/ annrheumdis-2020-218198

[2] Anghel, L. A., Farcaş, A. M., & Oprean, R. N. (2018). Medication adherence and persistence in patients with autoimmune rheumatic diseases: a narrative review. Patient preference and adherence, 12, 1151–1166. https://doi.org/10.2147/PPA.S165101

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2773

POS1467-HPR SEVERE RESPIRATORY INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS WITH BIOLOGIC THERAPY. COMPARATIVE STUDY BETWEEN VACCINATED AND NON VACCINATED PATIENTS

L. Domínguez[1], P. Rodriguez Cundin[2], T. Dierssen-Sotos[3], V. Calvo-Río[1], N. Vegas-Revenga[1], A. Corrales[1], N. Palmou-Fontana[1], D. Prieto-Peña[1], M. Calderón-Goercke[1], M. A. González-Gay[1], R. Blanco[1]. [1]*HUMV,*

Rheumatology, Santander, Spain; [2]*HUMV, Preventive Medicine, Santander, Spain*; [3]*University of Cantabria, Santander, Spain*

Background: Rheumatoid arthritis (RA) patients are at increased risk of severe infections due to the disease itself, and the immunosuppressive treatment. Vaccination programs are designed to decrease the risk of infections.
Objectives: In patients with RA treated with biologic therapy (BT) our aim was to assess a) the incidence of severe respiratory infections and b) to compare the risk between vaccinated and non vaccinated patients.
Methods: Observational study of 431 patients diagnosed with RA that iniciated BT. One group of patients participated in a vaccination program from October 2011 to October 2016 (Group 1). The other group was not included in the vaccination program (Group 2). The follow-up was made until June 2017 with a minimum follow-up period of 8 months and a maximum of 5.5 years.
Information on severe respiratory infections, defined as those that required hospitalization or at least one dose of intravenous antibiotic treatment at the emergency room, was retrieved from the hospital medical records.
Results: We studied 431 patients (335 women/96 men); mean age 63.4±13.7 years. In the vaccination program *(group 1)* were included 299 (69.37%) patients and in the *group 2* 132 patients (30.63%). The main features of both groups are summarized in Table 1**.**
During the follow-up, we registered 299 hospital admissions due to severe respiratory infections in both groups (incidence density 9.9 (95% CI: 6.9-13.6).
In group 1, vaccinated patients, this incidence density was reduced to 7.1 (95% CI: 4.1-11.6). Figure 1**.**
The vaccination program reduced the general incidence of severe respiratory infection in 44%.
Conclusion: RA patients with BT included in the vaccination program present a lower incidence of severe respiratory infections compared with non vaccinated patients.

Table 1. Main general features at BT onset

	Group 1 Vaccination program N=299	Group 2 Non vaccination program N=132	p
Age (years) mean±SD	61.32±13.04	67.97±14.17	0.32
Women, n (%)	231 (77.3%)	105 (79.5%)	0.59
Duration of RA (months) mean±SD	73.24±10.4	112.62±60.2	
Positive RF/ Positive ACPA, n (%)	177(59.2)/172 (57.52%)	93(70.5%)98 (74.24%)	0.02/0,01
Erosive disease, n (%)	116 (38.8%)	70 (53%)	0.06
Vasculitis, n (%)	15 (5%)	2 (1.5%)	0.08
Interstitial lung disease n (%)	12 (4%)	7 (5.3%)	0.54
Subcutaneous nodules n (%)	16 (5.4%)	6 (4.5%)	0.72
Corticosteroids	299 (100%)	132 (100%)	1
Number of conventional DMARDs, mean±SD	1.66±0.89	2.03±1.05	0.3

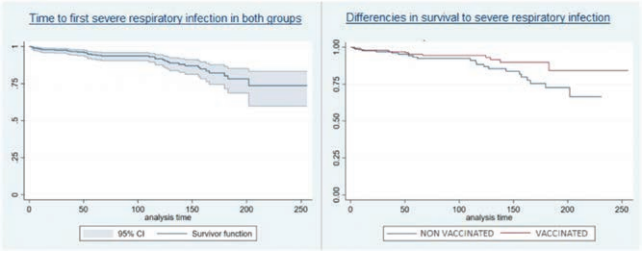


Figure 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3180

POS1468-HPR **THE IMPACT OF COVID-19 ON RHEUMATOLOGY HEALTH CARE WORKERS AND THEIR SCIENTIFIC OUTPUT: HEAVY LIES THE CROWN ON FEMALE RHEUMATOLOGISTS**

C. Kirchler[1], M. R. Andrews[2], E. Mosor[2], K. Thaler[3], T. Stamm[2], R. Fritsch-Stork[1,3,4], C. Duftner[5]. [1]*School of Medicine, Sigmund Freud University Vienna, Austria, Rheumatology, Vienna, Austria*; [2]*Medical University of Vienna, Section for Outcomes Research, Center for Medical Statistics, Informatics, and Intelligent Systems, Vienna, Austria*; [3]*Hanusch Hospital of the Austrian Health Insurance Fund, 1st Medical Department of Internal Medicine, Vienna, Austria*; [4]*Ludwig Boltzmann Institute of Osteology, Hanusch Hospital and AUVA Trauma Center Meidling, Vienna, Austria*; [5]*Medical University Innsbruck, Clinical Division of Internal Medicine II, Innsbruck, Austria*

Background: COVID-19 has changed daily practice in medicine and affected teaching as well as research activities of medical personnel. Meanwhile, the pandemic´s impact on private life and responsibilities for dependents also affected health care workers in rheumatology.
Objectives: To examine the adaptability of clinician-researchers in rheumatology in a time of crisis focusing on academic output in the first six months of the COVID-19 pandemic and to investigate the professional and private burden experienced by health care workers in rheumatology.
Methods: A systematic search in PubMed, medRxiv and bioRxiv for reports of rheumatic diseases *and* COVID-19/SARS-CoV-2 submitted (or published) from January 1 to June 30 2020 was carried out. As comparison, publications from April 6 to 13 2019 of the same rheumatic diseases *without* COVID-19 were analysed in terms of author characteristics and journal metrics. Additionally, a questionnaire was circulated via EULAR countries rheumatology societies and individual working group members. The participants were asked to answer 43 questions regarding their family situation, professional background, research output, changes in work and private responsibilities during the pandemic as well as the burden experienced. Responses were collected using an online survey tool and data analyses performed with SPSS Statistics 25; missing variable analysis was performed, excluding records with >15% missing responses. Descriptive and summary statistics were calculated for the entire dataset and split by gender.
Results: Whereas the overall number of publications and authors was equal between 2020 and 2019, the portion of female first authors of review articles and original studies decreased substantially in the first phase of the pandemic (Table 1). The numerical contribution of female authors in highly ranked journals (impact factor>6) was comparable in 2019 and 2020, however, the percentage of female first authors dropped from 50% to 32% (P=0.07).

Table 1. Author and journal metrics of publications

	Authors		
	2019 (%)	2020 (%)	
Proportion female	**N=1386**	**N=1361**	**P-value**
overall	46,8	41.1	n.s.
first authorships			
all publications	46,8	35,3	0.021
reviews	56,7	30	n.s.
original studies	46,2	18,2	0.004
other reports*	42,6	39,9	n.s.
last authorships			
all publications	34,7	27,9	n.s.
reviews	33,3	15	n.s.
original studies	32,1	30,3	n.s.
other reports*	40,7	29,1	n.s.

*other reports: letters/editorials/case reports

In the survey, a total dataset was available for N=180 responders. On average, female respondents (52.5%) were younger, more likely to live alone (19,1% vs 10,5%) and have no caring responsibilities (51.1% vs. 36.3%) than male respondents.

Male doctors were more often tenure-track/tenured or chairmen (31.4% vs 12.8% female) and worked less often part-time (9,3% vs. 19.1%). Unpaid overtime hours of all participants were striking with 46.3/44,2% (female/male) reporting to accumulate >10 hours/ week.
Regarding gender differences in scientific output, male respondents more frequently revealed >20 publications as first (57,6% vs. 26,9%) or last authors (34.1% vs. 10,1%). Similarly, 44,7% of male respondents reported a last author publication during COVID-19 vs. 26,4% of female respondents.
While female and male respondents reported similar experience of burden during the pandemic, more female respondents reported increased family care as a major source of this (38,2% vs. 22,2%). Both genders would like to see increased support from superiors and official institutions.

Conclusion: In a time of acute crisis, the adaptability of scientifically active female health care workers in rheumatology is lower than that of their male counterparts. This is reflected in a lower scientific output, especially as first or last authors. However, the burden experienced in the current pandemic is similar between the genders.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3586

POS1469-HPR **THE ASSESSMENT OF FRACTURE RISK AND OSTEOPOROSIS RATE AMONG PATIENTS OVER 50 YEARS OLD UNDERGOING MEDICAL REHABILITATION**

L. Marchenkova[1]. [1]*National Medical Research Center for Rehabilitation and Balneology of Ministry of Health of Russian Federation, Rehabilitation Department for Somatic Patients, Moscow, Russian Federation*

Background: Taking a course of physical rehabilitation creates the prerequisites for falls and injuries in patients at high risk of fractures. Data on fracture risk and prevalence of osteoporosis in older patients starting medical rehabilitation can change the approach of doctors to the development of rehabilitation programs and the management of such patients.

Objectives: To assess the prevalence of osteoporosis, individual risk factors for osteoporosis as well as the proportion of people with high risk of osteoporotic low-energy fractures among patients over 50 years old undergoing treatment according to the "medical rehabilitation" profile.

Methods: The study group comprised of 600 patients (426 women and 174 men) aged 50 to 84 years, average age 64.25 ± 10.17 years, undergoing treatment in a rehabilitation department. This was a cross-sectional study in the form of unified questionnaire, including data concerning age, weight, height, BMI, clinical and rehabilitation diagnosis, anamnesis of the main disease, anamnesis vitae, presence of osteoporosis diagnosis in the anamnesis, its treatment, osteoporosis risk factors estimation. An assessment of 10-year probability of osteoporotic fractures was carried out using Russian model of online FRAX® calculator.

Results: 41.8% patients in the study sample had osteoporosis risk factors, including 31.2% of subjects had 3 risk factors or more. 38.0% patients showed a high fracture risk according to the FRAX calculator. 34.1% had a diagnosis of osteoporosis, and 45.8% already had osteoporotic fractures. Among those who did not undergo densitometry examination, 69.9% had a history of low-traumatic fractures, and only 58.5% of patients with an established diagnosis of osteoporosis and 26.8% of those at high risk of fractures received effective therapy for osteoporosis.

Conclusion: Population of patients over 50 years old undergoing rehabilitation is characterized by high frequency of osteoporosis and probability of fractures, and insufficient quality of osteoporosis verification and anti-osteoporotic therapy administration at the same time.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4258

HPR Interventions (educational, physical, social and psychological)

POS1470-HPR **BARRIERS AND FACILITATORS OF A NEW MODEL OF STRATIFIED EXERCISE THERAPY IN KNEE OSTEOARTHRITIS: A QUALITATIVE STUDY**

J. Knoop[1], W. Van Berkel-de Joode[1], H. Brandt[1], J. Dekker[2], R. Ostelo[1]. [1]*Vrije Universiteit Amsterdam, Health Sciences, Amsterdam, Netherlands*; [2]*Amsterdam UMC (VUmc), Department of Rehabilitation, Amsterdam, Netherlands*

Background: We have developed a model of stratified exercise therapy, in which three knee osteoarthritis (OA) subgroups (i.e., 'high muscle strength subgroup', 'low muscle strength subgroup' and 'obesity subgroup') can be distinguished and provided a subgroup-specific intervention. Currently, the (cost-)effectiveness of this model compared to usual exercise therapy is tested in a large-scaled randomized controlled trial (OCTOPuS-study [1]). Alongside this trial, we performed a qualitative study to explore perceived barriers and facilitators of the application of this model in primary care.

Objectives: To explore barriers and facilitators of the application of this model in primary care, as perceived by patients, physiotherapists and dieticians.

Methods: Qualitative data were collected through semi-structured interviews in a random sample of 15 patients (5 from each subgroup), 11 physiotherapists and 5 dieticians, from the experimental arm of the OCTUPuS trial. A thematic analysis of the data was performed.

Results: We identified 14 themes in 5 categories. In general, patients and therapists were positive about the added value and applicability of the model, although some physiotherapists would prefer more flexibility. Regarding the 'high muscle strength subgroup', both patients and physiotherapists reported mixed feelings on the low number of supervised sessions, with some perceiving this low number as advantageous for stimulating the patient's own responsibility, whereas others as hindering an optimally guided treatment. Regarding the 'obesity subgroup', dieticians and physiotherapists acknowledged the added value of the combined intervention, but both were disappointed by the lack of interdisciplinary collaboration. Moreover, those patients in this subgroup already following a diet restriction, therefore not perceiving any added value of the diet intervention.

Conclusion: This qualitative study revealed relevant barriers and facilitators of our new model of stratified exercise therapy, which will help us interpreting the upcoming results on its (cost-) effectiveness [1]. If proven to be (cost-)effective, implementation strategies should specifically focus on guidance of patients from the 'high muscle strength subgroup' within only a few sessions, collaboration between physiotherapist and dietician in the 'obesity subgroup', and adequate use of booster sessions after the supervised period to optimize treatment adherence.

REFERENCES:

[1] Knoop J, Dekker J, van der Leeden M, de Rooij M, Peter WFH, van Bodegom-Vos L, van Dongen JM, Lopuhäa N, Bennell KL, Lems WF, van der Esch M, Vliet Vlieland TPM, Ostelo RWJG. Stratified exercise therapy compared with usual care by physical therapists in patients with knee osteoarthritis: A randomized controlled trial protocol (OCTOPuS study). Physiother Res Int. 2020 Apr;25(2):e1819. doi: 10.1002/pri.1819. Epub 2019 Nov 28.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1508

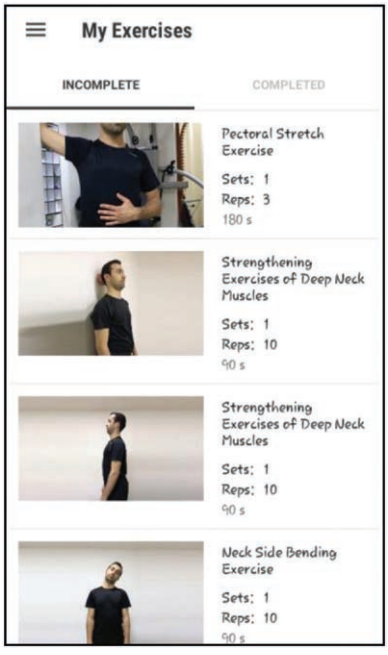
POS1471-HPR **EVALUATION OF THE EFFECTIVENESS OF MOBILE APP-BASED EXERCISES PROGRAMME IN PATIENTS WITH NECK PAIN: THE RANDOMIZED CONTROLLED TRIAL**

L. Beyaztaş[1], E. Tonga[1]. [1]*Marmara University Faculty of Health Sciences, Physical Therapy and Rehabilitation, İstanbul, Turkey*

Background: Mobile health applications are frequently used to increase exercise adherence in patients with musculoskeletal problems. However, the usability of these health mobile applications mostly has not been proven. In our previous study, the usability of the mobile app, which includes postural correction and neck spinal stabilization exercises, has been proven. (M.U-NeckExercise application)
Objectives: The aim of this study is to evaluate the effectiveness of the mobile application-based home exercise program for patients with chronic neck pain.
Methods: 60 people with chronic neck pain were participated in the our study. They were randomized into two groups. The first group (n:30) received home exercises via the novel mobile app, and the second group (n:30) received the same home exercises via the brochure. The exercise program consisted of neck and thoracic postural correction and neck spinal stabilization exercises. Participants has been requested to do the exercises 3 days in a week for 6 weeks. Participants' pain levels were assessed by using the Visual Analogue Scale (VAS), their neck-related functional limitations were evaluated by Neck Pain and Disability Index (BADI). Exercise adherence was meausered with a ratio of total participated sessions compared with the target defined by patient activation monitor and exercise adherance questionnaire. Targeted participation were %60 of total sessions.
Results: In both groups, the improvement in VAS and BADI scores was statistically significant ($p<0.05$). It was found that the pain parameters of VAS score decreased statistically more in the mobile application-based exercise group ($p<0.05$). While there was no statistically significant difference between the groups in the BADI score, the effect size results was higher in the mobile app group (effect size= 0.411). Our exercise commitment target in the mobile app group was an average of 10.5 sessions. The target session number has been reached 11.25 sessions.
Conclusion: It has been observed that the mobile application-based exercise program is effective in reducing pain and increasing exercise adherence in people with chronic neck pain. The findings support M.U-NeckExercise-App could be recommended to health professionals for exercise prescription in patients with cronic neck pain.
REFERENCES:

[1] Tonga E, Can M, Polat MG (2019). "SAT0730-HPR development and design of smartphone application for postural alignment of cervical and thoracic spine for young adults." Annals of the Rheumatic Diseases, 78,2.
[2]Voth, E. C., Oelke, N. D., & Jung, M. E. (2016). A theory-based exercise app to enhance exercise adherence: a pilot study. JMIR mHealth and uHealth, 4(2), e62.

Variable	*Group*	*X±SS*	*z*	*p*
Post-Exercise VAS Value (0-10 cm)	Mobile app Brochure	2,90±2,04 4,63±1,69	*-3,272*	****0,001**
Post-Exercise BADI Value	Mobile app Brochure	38,86±12,38 32,23±12,35	*0,031*	**0,861**



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2204

POS1472-HPR **CLINICIANS' PERSPECTIVES ON PSYCHOLOGICAL DISTRESS AND MEETING PATIENTS' SUPPORT NEEDS IN RHEUMATOLOGY CARE SETTINGS**

C. Silverthorne[1,2], J. Daniels[3], M. Thompson[1], J. Robson[1,2], M. Ndosi[1,2], C. Swales[2], K. Wilkins[2], E. Dures[1,2]. [1]*University of the West of England, Faculty of Health and Applied Sciences, Bristol, United Kingdom*; [2]*University Hospitals Bristol and Weston NHS Foundation Trust, Academic Rheumatology, Bristol, United Kingdom*; [3]*University of Bath, Department of Psychology, Bath, United Kingdom*

Background: People with inflammatory rheumatic diseases (IRDs) face challenges that include fluctuations in pain, fatigue and flares of disease activity, complex medical regimens, and decisions about when to seek clinical help with symptoms [1,2]. Evidence suggests levels of anxiety and depression are higher in people with IRDs compared to the general population [3]. Rheumatology teams report that psychologically distressed patients can have additional support needs and require more time. Patients' concerns include health-related anxiety and difficulty accepting the diagnosis. This group can have poor outcomes and poor adherence to treatments. However, little is currently known about optimal ways to meet these patients' support needs.
Objectives: To understand rheumatology clinicians' perspectives on psychological distress in care settings with the long-term aim to develop a proposed model/pathway of support.
Methods: Telephone interviews were conducted with members of UK rheumatology teams who have clinical experience with patients experiencing distress. The semi-structured interviews explored both 'what happens now' (current clinical practice) and 'what should happen' (acceptable models of future psychological support provision). The semi-structured format provided flexibility to probe more deeply and develop new lines of enquiry based on participants' responses.
Results: Fourteen interviews were conducted with rheumatology clinicians including 2 consultants, 4 nurses, 1 physiotherapist, 4 occupational therapists, 2 clinical psychologists and 1 podiatrist. Inductive thematic analysis was used to analyse the data. Two main themes represent the data (Table 1).

Table 1.

Main Theme	Sub-themes
1. 'No one shoe fits all' – the many manifestations of distress in patients. 'I pick up on distress as increased emotion…tearfulness and sadness I suppose, but also frustration, anger...A lot of helplessness comments'	1. 'Distress can be quite emotive and quite obvious, but then it can also hide away' 2. 'They're [patients] trying to manage their own conditions, but they're also trying to manage life'
2. 'If Rheumatology could be interwoven with psychological principles' – the need to attend to the psychological impact of IRDs, alongside the physical impact. 'The physical and mental health side of things are so closely linked because one affects the other…after a while they [patients] don't really know what's affecting what'	1. 'Prioritising physical health…sometimes the stress gets not thought about' 2. 'Make best use of everyone in the team to work with patients who are struggling' 3. 'For the psychological side of things we don't measure anything about that at all'

Conclusion: Distress can be obvious or hidden and cause issues for both patient and clinician. It can lead to poor engagement with care provision. Clinicians differ in their perceptions of distress and in their thresholds for dealing with distress and have described the inconsistency of support offered for distressed patients. They described the powerful link between physical and mental distress, the vicious cycle that can develop, and the benefits of incorporating a psychological approach to treatment. This study suggests psychological support should be embedded within the team as it is felt there is a need for speciality understanding and for patients' emotional wellbeing to consistently be given equal priority to their physical wellbeing.
REFERENCES:

[1] Gettings L. Psychological well-being in rheumatoid arthritis: a review of the literature. *Musculoskeletal care* 2010;8(2):99-106. doi: 10.1002/msc.171 [published Online First: 2010/03/17]
[2] Homer D. Addressing psychological and social issues of rheumatoid arthritis within the consultation: a case report. *Musculoskeletal care* 2005;3(1):54-9. doi: 10.1002/msc.26 [published Online First: 2006/10/17]
[3] Isik A, Koca SS, Ozturk A, et al. Anxiety and depression in patients with rheumatoid arthritis. *Clinical rheumatology* 2007;26(6):872-8. doi: 10.1007/s10067-006-0407-y [published Online First: 2006/08/31]

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2429

POS1473-HPR **SELF- AND SHARED-MANAGEMENT INTERVENTIONS FOR CHILDREN, YOUNG PEOPLE, AND FAMILIES LIVING WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES: AN INTEGRATIVE REVIEW**

S. Stones[1] on behalf of iSMART Research Group. [1]*University of Leeds, School of Healthcare, Leeds, United Kingdom*

Background: Self-management refers to the manner in which individuals manage the symptoms, treatment, physical and psychosocial impact of long-term conditions (LTCs). The importance of equipping children and young people living with LTCs, like rheumatic and musculoskeletal diseases (RMDs) with the capacity to self-manage is increasingly recognised in the literature, and in conversation. In addition, there is a strong case to support families who assume a shared-management role for their child. However, there is a limited understanding of interventions designed to improve self- and shared-management capacity in this population, prompting for a review of the literature, across multiple study designs.
Objectives: The aim of this integrative review was to identify and describe interventions promoting self-management of RMDs by children and young people, and shared-management of RMDs by families.
Methods: The integrative review followed a six-stage process [1]. Studies published since 2010 were identified through a search of eight bibliographic databases. Studies reporting on any paediatric-onset RMD were included, as were those in multiple condition areas where RMDs were included in the analysis. Twenty-six articles met the inclusion criteria: 24 research articles reporting on 17 interventions, and two review articles containing a further four research articles. The methodological quality of included articles was assessed using the Mixed Methods Appraisal Tool, and a thematic synthesis was undertaken.
Results: Most study participants were CYP and families living with JIA. A minority of studies included CYP and families living with other RMDs, as well as chronic pain, type 1 diabetes mellitus, epilepsy, sleeping disorder, and cancer. Around half of the articles reported a specific theory and/or model or framework guiding the intervention. Interventions tended to be focussed at either CYP or families, with few designed to span the lifecourse from birth to young adulthood, while supporting all members of the family unit. Intervention types included: decisional aids; comic educational book; family retreat weekend; internet- and group-based cognitive behavioural programme; internet-based peer mentoring intervention; internet-based self-guided self-management intervention with weekly social support; internet-based electronic patient-reported outcome platform; smartphone applications; telenursing intervention; therapeutic recreational camp; therapeutic family nursing conversations; transition programme/clinic; and video games-based task-orientated activity training.
Conclusion: This integrative review identified a range of interventions that have been evaluated to promote self- and shared management of RMDs by CYP and their families. There is a noticeable lack of emphasis on targeting the whole lifecourse for CYP, as well as supporting both CYP and families as they manage their RMD. Further work is needed to explore the underlying mechanisms which dictate how self- and shared-management interventions influence outcomes for CYP and families, under differing contexts, since this was overlooked by the majority of included studies.
REFERENCES:
[1] De Souza et al. Integrative review: What is it? How to do it? *Einstein (São Paulo)* 2010; 8(1): 102-106.
Acknowledgements: This work formed part of a PhD study funded by the University of Leeds.
Disclosure of Interests: Simon Stones Speakers bureau: Janssen, Consultant of: Envision Pharma Group
DOI: 10.1136/annrheumdis-2021-eular.3824

HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

POS1474-HPR **PERSONAL EXPERIENCES WITH DIAGNOSTIC DELAY AMONG AXIAL SPONDYLOARTHRITIS PATIENTS – A QUALITATIVE STUDY**

C. Dubé[1], K. Lapane[1], K. Ferrucci[1,2], A. Beccia[1], S. Khan[1], E. Yi[3], J. Kay[1,4,5], K. A. Kuhn[6], A. Ogdie[7], S. H. Liu[1]. [1]*University of Massachusetts Medical School, Population and Quantitative Health Sciences, Worcester, United States of America*; [2]*University of Massachusetts Medical School, Clinical and Population Health Research Program, Graduate School of Biomedical Sciences, Worcester, United States of America*; [3]*Novartis Pharmaceuticals Corporation, HE&OR and Medical Access, East Hanover, United States of America*; [4]*University of Massachusetts Medical School, Division of Rheumatology, Department of Medicine, Worcester, United States of America*; [5]*UMass Memorial Medical Center, Rheumatology Center, Worcester, United States of America*; [6]*University of Colorado School of Medicine, Department of Medicine, Denver, United States of America*; [7]*University of Pennsylvania Perelman School of Medicine, Epidemiology and Biostatistics, Center for Clinical Epidemiology and Biostatistics, Philadelphia, United States of America*

Background: The estimated prevalence of axial Spondyloarthritis (axSpA) in the U.S. is 0.4 to 1.3 percent. Undiagnosed axSpA patients suffer from symptoms on average 7 to 10 years, which can also contribute to psychological suffering and healthcare burden due to the prolonged search for diagnosis and treatment.
Objectives: To explore the experiences of diagnostic delay of axSpA patients as part of the SpondyloArthritis Screening and Early Detection (SpA-SED) Study.
Methods: We conducted exploratory semi-structured patient focus groups. English-speaking participants ≥18 years of age with a rheumatologist-verified clinical diagnosis of axSpA were recruited from three rheumatology practices in Massachusetts, Colorado, and Pennsylvania. Six focus groups were conducted with 26 total participants (16 men, 10 women, age range 21-76 years). Discussions ranged from 1.33 to 2.13 hours. Verbatim transcripts were deidentified, cleaned and coded using NVivo qualitative software. A coding list was generated and summary themes were constructed.
Results: Participants described meandering and frustrating journeys in search of a diagnosis. When doctors gave up, it was experienced by patients as profoundly negative. Intermittent axSpA symptoms confused some physicians and caused some patients to either delay seeking medical care (e.g., sporadic flare-up) or use dramatic language to convey the magnitude of the impact on their symptoms. Patients explained their experiences where physicians presumed that patients were trying to obtain narcotics or were "imagining/exaggerating" symptoms. Early symptom stories fell into five areas of importance for patients: pain, stiffness and lack of mobility, impact on sleep, impact on daily life, and changes with weather. Tenacity on the part of the patient and/or their family, patient research and confidence to challenge their physicians were important. Self-advocacy was challenging but necessary and particularly difficult when patients were sick. During the typically lengthy time that participants waited to be diagnosed, they experienced frustration and mental suffering due to lack of answers and/or not being heard, believed, or taken seriously. Some participants described the fatigue they experienced after trying without success to obtain a diagnosis or receive treatment. Early administration of a definitive diagnostic test or screening tools for axSpA would have alleviated both physical and emotional suffering for these participants.
Conclusion: Overall, participants expressed satisfaction with physicians who sought to understand them and believed them, took them seriously, and did not give up even with long delays. Patients with axSpA described significant suffering prior to diagnosis which could have been prevented and treated. Further research is needed with axSpA patients who are early in their diagnostic journey to determine best practices to support patients and reduce diagnostic delay.
Disclosure of Interests: Catherine Dubé Grant/research support from: Novartis, as personnel on such studies, Kate Lapane: None declared, Katarina Ferrucci: None declared, Ariel Beccia: None declared, Sara Khan: None declared, Esther Yi Employee of: Novartis Pharmaceuticals, Jonathan Kay Consultant of: AbbVie, Inc.; Boehringer Ingelheim GmbH; Celltrion Healthcare Co. Ltd.; Jubilant Radiopharma; Merck & Co.,Inc.; Pfizer Inc.; Samsung Bioepis; Sandoz Inc.; Scipher Medicine; UCB, Inc., Grant/research support from: (paid to UMass Medical School) Gilead Sciences Inc.; Novartis Pharmaceuticals Corp.; Pfizer Inc., Kristine A. Kuhn Consultant of: UCB, Eli Lilly, Novartis, Grant/research support from: Pfizer, Alexis Ogdie Consultant of: Abbvie, Amgen, BMS, Celgene, Corrona, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, Grant/research support from: Pfizer to Penn, Novartis to Penn, Amgen to Forward/NDB, Shao-Hsien Liu Grant/research support from: Novartis
DOI: 10.1136/annrheumdis-2021-eular.612

POS1475-HPR **EFFECT OF ARGENTINE TANGO PRACTICE ON TOTAL PHYSICAL ACTIVITY TIME IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATISM: A PILOT STUDY**

N. Darmant[1], F. Fayet[1], C. Lambert[2], B. Pereira[2], M. Rodere[1], A. Fan[1], M. Soubrier[1], M. Duclos[3]. [1]*CHU Gabriel-Montpied, Rhumatologie, Clermont-Ferrand, France*; [2]*CHU Gabriel-Montpied, Biostatistics Unit, Clermont-Ferrand, France*; [3]*CHU Gabriel-Montpied, Sports Medicine, Clermont-Ferrand, France*

Background: Most patients with chronic inflammatory rheumatism (CIR) have a physical activity (PA) level below recommendations [1,2]. Currently, adapted structures offer a range of activities supervised by adapted physical activity educators. To the best of our knowledge, Argentinean tango is not yet offered in these structures.
Objectives: The objective of this pilot study was to study the effect of 24 consecutive sessions of Argentinean tango on the total PA level in patients with CIR, including rheumatoid arthritis (RA) and spondyloarthritis (AS).
Methods: In this controlled, randomized, open-label, clinical trial with two parallel arms, patients were required to attend two tango sessions per week,

48 sessions from 0 (M0) to 6 months (M6) for the intervention group (IG) and 24 sessions from 3 months (M3) to M6 for the control group (CG). Total PA time was measured at M3 using the Global Physical Activity Questionnaire (GPAQ) [3].

Results: A total of 27 patients (23 women) were included, including 15 with RA and 12 with AS. Mean age was 59 ± 12 years, and median disease duration was 10 years (IQR: 3-19). The majority of patients had background treatment (conventional and/or biological). At M3, 22 patients could be evaluated (11 GC patients and 11 GI patients), as 3 patients were lost to follow-up and 2 were unable to come in due to health or professional reasons. The 11 GI patients attended a median of 16 sessions (IQR: 8-22), i.e., approximately one session per week. At M3, the total PA time was not increased, regardless of the measurement method, GPAQ questionnaire (effect size and 95% confidence interval (CI): 0.03 [-0.60; 0.67], p=0.91) or accelerometer (effect size and 95% CI: 0.43 [-0.37; 1.24], p=0.26), and regardless of the intensity of the PA. No significant change was found for sedentary time, disease activity, fatigue, or anxiety. However, improvements were found in body appreciation as assessed by the Body Appreciation Scale 2 questionnaire (p=0.016), balance (p=0.053), wrist bending angle (p=0.092), and shoulder amplitude (p=0.093). The few participants in this study is explained by the geographic distance of the classes and their homes, the lack of availability of patients in professional activity, fatigue, or not liking dance (mainly among men).

Conclusion: The results of this pilot study suggest that one Argentinean tango session per week in CIR patients is more achievable than two sessions as originally planned. As the practice of classes in hospitals is constrained due to geographic distance, the sessions could be offered in adapted structures. Nevertheless, our pilot study shows that the Argentinean tango is beneficial for body appreciation in patients with CIR. A qualitative study is needed to better understand these effects.

REFERENCES:

[1] Haute Autorité de Santé (2007). Rheumatoid arthritis: therapeutic aspects excluding drugs and surgery - medico-social and organizational aspects. Professional recommendations service - Medical-economic evaluation and public health service.

[2] Haute Autorité de Santé (2008). Spondylarthritis: guide - long-term condition. Good Professional Practices Department - Communication Department.

[3] Cleland CL, Hunter RF, Kee F, Cupples ME, Sallis JF, Tully MA. (2014 Dec). Validity of the global physical activity questionnaire (GPAQ) in assessing levels and change in moderate-vigorous physical activity and sedentary behaviour. BMC Public Health. 10;14:1255. doi: 10.1186/1471-2458-14-1255.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.690

POS1476-HPR THE NEED FOR INFORMATION AMONG PATIENTS WITH ANCA ASSOCIATED VASCULITIS DIFFERS BETWEEN GROUPS

S. Brolin[1], B. Lövström[1], E. Welin[2], I. Gunnarsson[1,3], S. Pettersson[1]. [1]*Karolinska University Hospital, Department of Gastroenterology, Dermatology and Rheumatology, Stockholm, Sweden*; [2]*Örebro University, School of Health Sciences, Örebro, Sweden*; [3]*Karolinska Institutet, Rheumatology, Stockholm, Sweden*

Background: Being diagnosed with ANCA associated vasculitis (AAV) can be a frightening experience and means facing changes that involves adapting to new situations1. Patients that are provided adequate information are better equipped to make well informed decisions regarding their care and stay compliant to the treatment plan. In order to provide adequate patient-centered information at the appropriate time and to identify those who may need extra support, the information needs must be explored2. There have been several studies on the information needs of rheumatological patients, although very few studies for patients with AAV.

Objectives: The aim of this study was to explore what information patients with AAV need from their rheumatological team and how it differs between groups (gender, disease duration).

Methods: Men and women over 18 years were included through a consecutive sample from a Rheumatology or Nephrology Clinic at Karolinska University Hospital in Sweden during 2008-2019. Patients with all forms of AAV (GPA, MPA and EGPA), that had the Rheumatology clinic as primary contact, were included.

The participants were given Educational Needs Assessment Tool (ENAT) that measures the patient's information needs3. The initial question, 'Do you need information right now about something that can help you with your rheumatic disease?' is answered yes/no. ENAT then includes 7 domains (Managing pain, Movement, Feelings, Disease process, Treatments, Self-help measures and Support systems) each containing 4-7 items (4-point Likert scale, 'not at all important = 0' to 'extremely important = 3'). The total sum is divided by the maximum score and gives the percentage response of maximum score (0-100%), 0% meaning no information need and 100% highest information need. The responses are presented as "mean % of the domain score". Independent-sample t-test was used to compare the mean between groups. One way ANOVA was used to compare the mean domain score between the different diagnoses and age groups.

Results: 178 individuals completed the questionnaire, equally divided by gender. Age ranged from 18-85, median 61. 33,7% had been diagnosed within 2 years.

The mean total score was 56,8 % of the highest possible score (0-100%). The highest information need was found in the domains 'Disease process' (78,1%), 'Self-help measures' (68,5%) and 'Treatments' (63,6%) whereas lesser need for information was found in the domains 'Managing pain' (47,5%), 'Support systems' (46,5%) and 'Movement' (41,1%). The domain 'Feelings' was scored as moderate (55,5%).

Those who acknowledge a present information need also scored significantly higher overall in all the domains. Disease duration and gender showed significantly affect the information need. Highest scores were found among women with a disease duration < 2 years with significant difference in 3/7 domains. Age, disease activity, diagnosis and social status did not affect the ENAT scores.

Conclusion: Even though only 38% of participants stated a current need for information, the results indicate that there are certain areas that patients with AAV consider important to receive more information about. Special consideration needs to be taken to women with short disease duration since they were shown to have a significantly higher need for information.

REFERENCES:

[1] Mooney, J., et al. (2013). 'In one ear and out the other - it's a lot to take in': a qualitative study exploring the informational needs of patients with ANCA-associated vasculitis. Musculoskeletal Care, 11(1)

[2] Ntatsaki, E., et al. (2014). BSR and BHPR guideline for the management of adults with ANCA-associated vasculitis. Rheumatology (Oxford), 53(12)

[3] Hardware, B., et al. (2004). Towards the development of a tool to assess educational needs in patients with arthritis. Clinical Effectiveness in Nursing, 8(2)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.765

POS1477-HPR GOUT PATIENTS IN REMISSION, AND THEIR PERSPECTIVES ON URATE LOWERING THERAPY TREATMENT STOP OR CONTINUATION STRATEGIES

I. R. Peeters[1,2], S. A. C. Wanten[1,2], L. M. Verhoef[1], A. Den Broeder[1,2], N. Van Herwaarden[1,2], M. Flendrie[1]. [1]*Sint Maartenskliniek, Rheumatology, Nijmegen, Netherlands*; [2]*Radboud University Medical Center, Rheumatology, Nijmegen, Netherlands*

Background: Urate lowering therapies (ULT) are used to reduce hyperuricemia in gout patients (1). When gout remission is reached, patients often ask if ULT should be continued lifelong (treat to target strategy, T2T), or if tapering or stopping (a treat to symptom approach, T2S) can be attempted. In fact, although current rheumatology guidelines (1,2) suggest continuation, conclusive evidence for this is absent. Since ULT therapy adherence also remains suboptimal, exploring gout patients' beliefs on different long term ULT treatment strategies is of great value.

Objectives: To identify cognitions and emotions on ULT treatment strategies (T2T continuation and T2S cessation) of gout patients in remission with current or previous ULT use.

Methods: Purposive sampling (3) was used to recruit patients from a general practice and a rheumatology department (Nijmegen, the Netherlands), with a clinical diagnosis of gout, current or previous ULT use and remission according to adapted (without serum urate criterion) preliminary gout remission criteria(4). Semi-structured interviews were conducted by two interviewers and audio-records were fully transcribed. Inductive thematic analysis (5) was used to analyse and interpret our data using the ATLAS.ti. software.

Results: From a total of 18 patients (16 male/2 female), 14 patients were treated by a rheumatologist (10 currently using ULT, 1 intermittent and 3 previously) and 4 were treated by a general practitioner (all currently using ULT). Patients were satisfied with a T2T strategy, due to the absence of flares, a feeling of certainty and the reassurance of serum urate monitoring. Reluctance towards medication was reported, the importance of indefinite ULT use was questioned and its chronic use was addressed as a drawback. Reducing medication use by a T2S strategy was assessed positively and this strategy was considered less burdensome. A wish for and the willingness to follow a T2S approach was expressed. Fear and concerns of flaring after ULT cessation were expressed and were deemed both acceptable and unacceptable. See Table 1 for a schematic overview of the results.

Table 1. ***Overview of patients' perspectives on ULT treatment strategies***

Motivation for a T2T strategy	Drawbacks of a T2T strategy
1. Being free of flares	1. Resistance to (any) medication use
2. Acceptance of and contentment with chronic ULT use	2. Side effects of ULT
3. Feels secure due to regular SU monitoring	3. Possibly detrimental to healthcare costs
4. No desire for change	
Motivation for a T2S strategy	**Drawbacks of a T2S strategy**
1. Doubt if chronic ULT use is necessary	1. Fear and insecurities on
a. Possible restorative capacity of the body	a. Flaring and not being able to function
b. Curious to effects of ULT cessation	b. Joint damage
2. Being free of ULT side effects	2. Feels uncontrolled
3. Long term damage ULT unknown	3. Hassle with visits, blood tests and medication adjustments when a flare occurs.
4. Less burdensome for patient and body	
5. Wish for minimization of (any) medication use	

Conclusion: This study provides an overview of perspectives on ULT treatment strategies of gout patients in remission. These results must be considered in developing educational material for patients and in future research on gout management, particularly in designing randomised clinical trials on this subject.

REFERENCES:

[1] Richette P et al. Ann Rheum Dis. 2017;76(1):29-42.
[2] FitzGerald JD et al. Arthritis Care Res (Hoboken). 2020;72(6):744-60.
[3] Pope C et al. Qual Saf Health Care. 2002;11(2):148-52.
[4] de Lautour H et al. Arthritis Care Res (Hoboken). 2016;68(5):667-72.
[5] Pope C et al. Bmj. 2000;320(7227):114-6.

Acknowledgements: We would like to thank dr. Erik Bischoff for his cooperation and help in including primary care patients from his general practice UGC Heyendael, Nijmegen the Netherlands.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.890

POS1478-HPR NURSE LED REMOTE MANAGEMENT OF OSTEOPOROSIS – DO PATIENTS APPROVE?

J. Begum[1], J. Fourmy[1], M. K. Nisar[1]. [1]*Luton and Dunstable University Hospital, Rheumatology, Luton, United Kingdom*

Background: Specialist services are heavily reliant on consultant delivered models however lack of sufficient consultant appointments pose a significant operational challenge. Clinical nurse specialists (CNSs) are highly trained and can fill this gap whilst maintaining a high standard of care.
Objectives: We designed an innovative proof-of-concept osteoporosis service with patients only consulting a metabolic bone CNS and a consultant providing remote oversight. The aim of the project was to improve the efficiency of the service by eliminating consultant appointments and reducing unnecessary hospital visits whilst continuing to deliver high-quality care.
Methods: A new pathway was implemented where a consultant rheumatologist and a CNS virtually triaged women over the age of 65 into the service. A dedicated proforma provided the template for the CNS to undertake new patient telephone consultation. Relevant investigations were requested during the telephone clinic and treatment related information was despatched to help with shared decision making. All patients were then reviewed in a consultant-CNS virtual MDT. Appropriate parenteral treatment option was agreed and confirmed to each individual. The CNS worked through a safety checklist and provided further advice and support to the patient as necessary. We surveyed 100 consecutive patients to gain their feedback regarding the service using a ten-item questionnaire employing binary and Likert scale options.
Results: The questionnaire was posted to 100 patients. Mean age of participants was 77.2 years (65-92). 75 returned the survey. 67 (89%) were happy with the waiting time and seventy (93%) found thirty-minute appointment acceptable. 66 (88%) were happy with the phone consultation and agreed that the care plan was adequately explained. 73 (97%) were happy for the CNS review in future and would recommend the service. 67 (89%) were satisfied with the overall service. Though most (95%) were able to take the call maintaining privacy, eleven (15%) participants would've found physical appointment more convenient. When asked which medium they would prefer for future reviews, only fifty (66%) patients would keep telephone as their choice. Sixteen (21%) would prefer face to face consultation, seven (9%) a combination of the two and only two would choose online option.
Conclusion: To our knowledge, this is the first successful example of an innovative service wholly provided by CNSs. Most patients were satisfied with this model of care and would highly recommend it. They were happy to be reviewed by CNS in the future. However a significant minority did not like the remote element and a higher proportion would choose physical review in future if offered. Interestingly, telephone consultation still scored substantially higher than online platform despite being physically visible in the latter. This is intriguing as most remote services strive for online consultations assuming its preference to phone. Our study suggests against this notion certainly in older patient group. Overall, a nurse-delivered osteoporosis treatment pathway is highly effective, safe and provides an innovative solution though remote consultations may not be the optimal delivery model.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1072

POS1479-HPR PATIENTS' PERCEPTIONS OF PERSON-CENTRED CARE IN EARLY RA: A QUALITATIVE STUDY

E. Landgren[1,2,3], A. Bremander[1,3,4,5], E. Lindqvist[1,2], M. Nylander[3,6], I. Larsson[1,3,7]. [1]*Lunds University, Department of Clinical Sciences, Section of Rheumatology, Lund, Sweden*; [2]*Skåne University Hospital, Department of Rheumatology, Lund, Sweden*; [3]*Spenshult Research and Development Centre, Halmstad, Sweden*; [4]*University of Southern Denmark, Department of Regional Health Research, Odense, Denmark*; [5]*University Hospital of Southern Denmark, Danish Hospital for Rheumatic Diseases, Sonderborg, Denmark*; [6]*Swedish Rheumatism Association, Stockholm, Sweden*; [7]*Halmstad University, School of Health and Welfare, Halmstad, Sweden*

Background: Data on patients' experience can identify strengths and weaknesses with given care, why a person-centred care will improve health care quality. In rheumatology care, most research on patient preferences for and experiences of RA care is performed in patients with established RA and less often in patients with early RA. In the early course of RA patients often struggle to manage their new life situation with a chronic disease and its treatment. Expectations and experiences of health care may change over time why it is important to understand how newly diagnosed patients perceive person-centred care.
Objectives: To explore patients' perceptions of person-centred care early in the RA disease course within the framework of person-centred care.
Methods: In this qualitative study 31 patients with early RA from four rheumatology specialist outpatient clinics were interviewed. An abductive qualitative content analysis was conducted based on the framework of McCormack and McCance (2006, 2016). The four constructs; prerequisites, care environment, person-centred processes, and person-centred outcomes constituted the four categories in the deductive part of the study. An inductive analysis revealed eleven sub-categories exploring the content of person-centred care for patients with early RA.
Results: For patients with early RA person-centred care was described as; *1. Prerequisites* were to be treated with respect, to meet dedicated healthcare professionals, and to meet professional competence. *2. The care environment* was to have access to a multidisciplinary team, to have access to health care, and a supportive organization. *3. Person-centred processes* were to be listened to, to be supported, and to be involved in decision-making. *4. The person-centred outcomes* were to be satisfied with received health care and to achieve optimal health.
Conclusion: A true person-centred care is important to patients early in the RA disease course, supporting the relevance to implement person-centred approach at all stages in the health care system. This study contributes to information about how to further develop person-centredness in rheumatology care also early in the disease course.

REFERENCES:

[1] McCormack, B., & McCance, T. V. (2006). Development of a framework for person-centred nursing. *J Adv Nurs, 56*(5), 472-479. doi:10.1111/j.1365-2648.2006.04042.x
[2] McCormack, B., & McCance, T. V. (2016). *Person-centred practice in nursing and health care: theory and practice* (2nd edition ed.): John Wiley & Sons.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1240

POS1480-HPR IMPLEMENTATION OF TELEMEDICINE IN RHEUMATOLOGY: VIRTUAL CONSULTATION AS A TOOL FOR DIRECT COMMUNICATION WITH PRIMARY CARE

I. Garcia Hernandez[1], D. V. Mendoza Mendoza[1], P. Muñoz Reinoso[1], J. J. Pérez Venegas[1]. [1]*Hospital Universitario Virgen Macarena, Rheumatology, Sevilla, Spain*

Background: Virtual consultation is defined as the provision of a healthcare service when there is a distance between the subjects and information and communication technologies are used to carry out the consultation. This tool has been successfully implemented in different specialties. It is useful for providing quick solutions, improving the overload of the medical care and for the early detection of inflammatory diseases[1]. In our centre, virtual consultation from Primary Care (PC) to Hospital Care (HC) has been implemented.
Objectives: The main objective is to describe our experience with the use of virtual consultation and its value as a new modality of specialised medical care.

The second aim is to identify the most frequent reasons for consultation and diagnoses, to assess the concordance between the two and to analyse the trend over time of the number of virtual consultations and their relationship with the different waves of the COVID 19 pandemic.

Methods: Retrospective observational study. The virtual consultations made from PC (47 centres) to Rheumatology during 2020 were analysed. They were carried out through a computer programme, using the "Andalusian Health Service Virtual Consultation Platform" tool. A specific agenda was established for virtual consultations. The reason for the referral and the rheumatologist's diagnosis were collected. The response given to the PC was divided into four models: NON-TRIBUTARY (not related to the speciality), DISCHARGE (a diagnosis and therapeutic response is concluded), APPOINTMENT FOR CONSULTATION and FOLLOW-UP (new contact is requested, completing the information). The reasons for consultation, diagnoses, time and type of response were analysed.

Results: 47 virtual consultations were carried out. 54.5% (n 298) were closed as DISCHARGE. 27.4% (n 150) were APPOINTMENT FOR CONSULTATION, and 17.7% (n 97) indicated FOLLOW-UP. Only 0.4% (n 2) were NOT TRIBUTARY.

The average response time was 2 days 15 hours and 56 min.

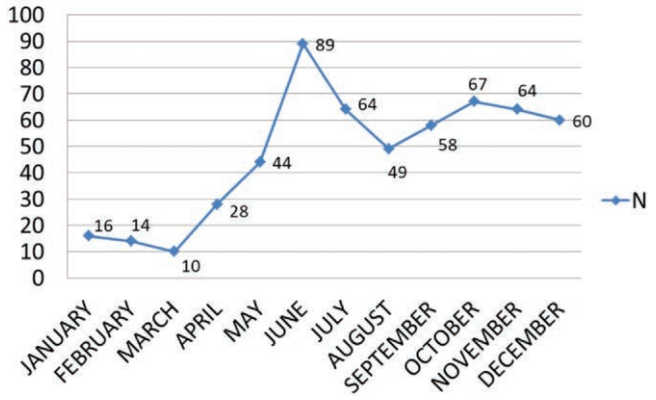
The most frequent reason for consultation was polyarthralgias (26.7%, n 146) and after the rheumatologist's assessment a diagnosis was established in 89% of them. Inflammatory arthropathy accounted for 30.8% (n 45), osteoarthritis for 19.9% (n 29), fibromyalgia for 12.3% (n 18), polymyalgia rheumatica (PMR) for 6.9% (n 10), osteoporosis for 2.7% (n 4) and connective tissue disease for 2.1% (n 3).

Another frequent reason for consultation was osteoporosis (13.5% n 74), of which 85.1% (n 63) had a confirmed diagnosis and/or need for revision.

A diagnosis could be made via telematics in 89.6% of the consultations. 15.5% were osteoporosis (n 85), 14.9% osteoarthritis (n 81), 10.5% soft tissue injuries, 8.8% mechanical/nonspecific pain (n 47), 7.1% rheumatoid arthritis (n 39), 6.5% fibromyalgia (n 34), 6.2% connective tissue disease (n 34), 5.7% PMR (n 31), 4.9% suspected spondyloarthritis (n 26), 4.2% psoriatic arthritis (n 23) and 4.2% microcrystalline arthritis (n 23).

27.4% (n 150) of the virtual consultations were required for assessment in a face-to-face appointment. We analysed the distribution over time (Figure 1). In the COVID 19 confinement phase (14 March - 21 June), the number of consultations increased, peaking in June, a behaviour that has persisted in the other mobility phases (October/November).

Figure 1. ANNUAL PROGRESS OF VIRTUAL CONSULTATIONS TO RHEUMATOLOGY



Conclusion: More than half of the virtual consultations carried out were resolved without face-to-face assessment, with a diagnosis being established in almost 90%. It is an effective tool for rapid access to Rheumatology, detecting pathology requiring preferential attention, with a face-to-face appointment, as well as for the early diagnosis of inflammatory arthropathy, which was detected in a quarter of the consultations, as well as for the diagnosis and follow-up of osteoporosis. Virtual consultation facilitates a quick response, playing an even more relevant role in the current SARS CoV-2 pandemic situation.

REFERENCES:

[1] B. Tejera, S. Bustabad. A new form of communication between rheumatology and primary care: The virtual consultation. Reum Clin., 12 (2016), pp 11-14

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1443

POS1481-HPR SEXUAL EXPERIENCE IN MALE PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS FROM A CROSS-SECTIONAL STUDY OF 113 PATIENTS

L. Hu[1], D. Gao[1], Y. MA[1], Y. Wang[1], X. Ji[1], F. Huang[1]. *[1]Chinese PLA General Hospital, Rheumatology, Beijing, China*

Background: The expression and experience of sexuality is a key part of an individual self-identity[1], so it is essential for both healthy individuals and patients. Patients with ankylosing spondylitis (AS) may be susceptible to sexual issues due to disease activity, dysfunction and comorbid emotional problems. However, sexuality, especially sexual experience, are rarely paid attention in patients with AS.

Objectives: Our study aims to assess sexual experience in male patients with AS, and analyze the factors affecting sexual experience.

Methods: This is a cross-sectional study. A total of 113 patients with AS and 46 healthy people were investigated, matched according to age and body mass index. The Sexual Experience Questionnaire is used to assess male sexual experience. Linear regression analysis is used to explore the contributions of clinical variables to worse sexual experience.

Results: There is a significant difference in the total sexual experience score between AS patients and healthy controls (41.92±8.83 vs 46.98±8.10, *P*=0.0013). Also, patients with AS have a worse score in all dimensions of sexual experience, including erectile function, individual satisfaction and couple satisfaction, comparing to healthy people. In the regression model after controlling for the effects of age, disease duration and body mass index, disease activity (BASDAI), function (BASFI), mobility (BASMI, chest expansion and finger-floor distance), health index (ASAS HI), sleep quality (PSQI) and psychological status (HADS, HADS-A and HADS-D) are significant determinants of sexual experience, including erectile function (except for chest expansion), individual satisfaction (except for BASMI) and couple satisfaction (except for BASMI). See Table 1 for details.

Table 1. Multivariable regression analysis of association between sexual experience and clinical outcomes

Independent	Sexual experience total score		Erectile function		Individual satisfaction		Couple satisfaction	
	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*
Pain total	-0.09 (-0.25,0.28 0.07)		-0.27 (-0.58, 0.073 0.03)		-0.51 (-0.91, 0.014 -0.10		-0.15 (-0.32, 0.077 0.02)	
BASDAI	1.35 (-2.24, 0.003 -0.45)		-0.42 (-0.75, 0.014 -0.09)		-0.72 (-1.16, 0.001 -0.28)		-0.21 (-0.40, 0.028 -0.02)	
BASFI	-1.80 (-2.59, <0.001 -1.01)		-0.62 (-0.91, <0.001 -0.32)		-0.89 (-1.28, <0.001 -0.50)		-0.30 (-0.47, 0.001 -0.13)	
BASMI	-1.04 (-2.01, 0.036 -0.07)		-0.47 (-0.82, 0.008 -0.12)		-0.48 (-0.96, 0.051 0.001)		-0.09 (-0.29, 0.413 0.12)	
Chest expansion	1.60 (0.24, 2.96)	0.021	0.50 (-0.004,0.052 0.99)		0.74 (0.07, 1.42)	0.032	0.36 (0.08, 0.64)	0.011
Finger-floor distance	-0.20 (-0.33,0.003 -0.07)		-0.07 (-0.11, 0.009 -0.02)		-0.10 (-0.17, 0.003 -0.03)		-0.04 (-0.06, 0.011 -0.01)	
ASAS HI	-1.27 (-1.64, <0.001 -0.91)		-0.42 (-0.55, <0.001 -0.28)		-0.62 (-0.80, <0.001 -0.43)		-0.24 (-0.32, <0.001 -0.16)	
PSQI	-0.60 (-1.11, 0.021 -0.09)		-0.19 (-0.38, 0.045 -0.004)		-0.28 (-0.54, 0.03 -0.03)		-0.13 (-0.23, 0.019 -0.02)	
HADS	-0.53 (-0.76,<0.001 -0.29)		-0.18 (-0.27, <0.001 -0.09)		-0.24 (-0.36, <0.001 -0.13)		-0.10 (-0.15, <0.001 -0.05)	
HADS-A	-0.86 (-1.30, <0.001 -0.42)		-0.28 (-0.44, 0.001 -0.12)		-0.42 (-0.63, <0.001 -0.20)		-0.17 (-0.26, <0.001 -0.07)	
HADS-D	-0.99 (-1.45, <0.001 -0.53)		-0.35 (-0.52, <0.001 -0.19)		-0.44 (-0.67, <0.001 -0.21)		-0.20 (-0.29, <0.001 -0.10)	

Conclusion: Worse sexual experience is associated with increased disease activity, decreased function, poor mobility, decreased health index, poor sleep quality and psychological status. Therefore, special attention to worse sexual experience in patients with AS is essential to assess disease-related suffering and develop new patient management strategies.

REFERENCES:

[1] Hill J, Bird H, Thorpe R. Effects of rheumatoid arthritis on sexual activity and relationships. Rheumatology (Oxford), 2003. 42(2):280-6.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1470

POS1482-HPR PAIN CATASTROPHIZING IS ASSOCIATED WITH RESIDUAL PAIN AFTER REACHING IMPROVED CONDITIONS OF SWOLLEN/TENDER JOINTS AND SERUM C-REACTIVE PROTEIN LEVEL

T. Yoshida[1,2], M. Hashimoto[3], K. Murakami[4], K. Murata[3,5], K. Nishitani[3,5], R. Watanabe[3], T. Koyama[1], R. Uehara[1], M. Tanaka[3], H. Ito[3,5], S. Matsuda6. *[1]Kyoto Prefectural University of Medicine, Department of Epidemiology for Community Health and Medicine, Kyoto, Japan*; *[2]Kyoto Prefectural University of Medicine, Department of Nursing, Kyoto, Japan*; *[3]Graduate School of Medicine, Kyoto University, Department of Advanced Medicine for Rheumatic Diseases, Kyoto, Japan*; *[4]Graduate School of Medicine, Kyoto University, Department of Rheumatology and Clinical Immunology, Kyoto, Japan*; *[5]Graduate School of Medicine, Kyoto University, Department of Orthopaedic Surgery, Kyoto, Japan*; *[5]Graduate School of Medicine, Kyoto University, Department of Orthopaedic Surgery, Kyoto, Japan*

Background: It has long been recognized that immune-mediated inflammatory diseases, such as rheumatoid arthritis (RA), are prone to coexist with depression due to the effects of cytokines, and that these two illnesses lead to an elevation in patients' pain. However, we often encounter patients with RA who suffer from residual pain despite an improvement in disease activity and inflammation. The specific psychological factors associated with residual pain have not yet been clarified. In addition to the traditional psychological factors, such as depression and anxiety, we focused on pain catastrophizing due to the distortion of pain perception and explored its association with residual pain.
Objectives: To examine whether psychological factors, such as pain catastrophizing, depression, and anxiety, are associated with self-reported pain visual analogue scale (pain-VAS) scores in RA patients with 1 or less on 28joints- swollen/tender counts (SJC/TJC) and CRP.
Methods: This was a cross-sectional study of 290 RA outpatients (85% of whom were women) with scores of less than 1 on SJC, TJC, and CRP, with a median (IQR) age of 66 (57–73) years. The participants completed questionnaires, including pain VAS (0–100 mm), Pain Catastrophizing Scale (PCS, 0–52 scale), and Hospital Depression and Anxiety Scale (HADS, 0–42 scale). Using linear regression analyses, we analysed whether PC (PCS ≥30), depression (HADS-D ≥11), and anxiety (HADS-A ≥11) (independent variables) were associated with pain VAS scores (dependent variable). After univariate regression analysis, multivariate analysis adjusted for confounding factors was performed.
Results: Patients reported a wide range of pain severity with a median (range) pain VAS score of 9 (0–96mm). The prevalence of anxiety and depression were 5.5% and 5.9%, respectively. Meanwhile, 24.1% of the patients experienced pain catastrophizing. Pain catastrophizing was associated with pain VAS scores in univariate and multivariate analyses (Table 1). The presence of anxiety and depression was not associated with pain VAS scores in any model. Multivariate analysis of other covariates showed that age, disease duration, and presence of SJC/TJC of joints other than the 28 joints were positively correlated with pain VAS scores.

Table 1. Univariate and multivariate regression analysis for independent variables associated with pain-VAS scores

		Univariate	Multivariate	
independent variables			Model 1*	Model 2**
Pain catastrophizing	Estimate	3.7	4.1	3.6
	95%CI	0.7 to 6.6	1.1 to 7.0	0.5 to 6.6
	p-value	0.015	0.006	0.021
Anxiety	Estimate	3.7	4.4	0.5
	95%CI	-1.9 to 9.2	-1.0 to 9.9	-3.5 to 7.9
	p value	0.198	0.108	0.453
Depression	Estimate	3.5	4.2	3.9
	95%CI	-1.9 to 8.9	-1.1 to 9.5	-1.9 to 8.7
	p-value	0.204	0.119	0.210

The covariates in multivariate analysis are as follows: age, sex, body mass index, disease duration, Steinbrocker's Stage, prednisolone dosage, biologic agents use, and presence of swollen joint counts/tender joint counts of joints other than the 28 joints. *Model 1: each psychological independent variable and the above covariates.**Model 2: all psychological independent variables and the above covariates.

Conclusion: Pain catastrophizing was associated with pain VAS scores in RA patients with 1 or less on 28joints-SJC/TJC and CRP, emphasising that residual pain in the patients should be treated in a biopsychosocial framework focussing on pain catastrophizing.
Disclosure of Interests: Tamami Yoshida: None declared, Motomu Hashimoto Speakers bureau: Mitsubishi Tanabe Pharma Corporation; Bristol-Myers Squibb; Eisai Co., Ltd.; and Eli Lilly and Company., Grant/research support from: Mitsubishi Tanabe Pharma Corporation; Bristol-Myers Squibb; Eisai Co., Ltd.; and Eli Lilly and Company., Kosaku Murakami Speakers bureau: Eisai Co., Ltd.; Chugai Pharmaceutical Co., Ltd.; Pfizer Inc.; Bristol-Myers Squibb; Mitsubishi Tanabe Pharma Co; UCB Japan Co., Ltd.; Daiichi Sankyo Co., Ltd.; and Astellas Pharma Inc., Consultant of: Eisai Co., Ltd.; Chugai Pharmaceutical Co., Ltd.; Pfizer Inc.; Bristol-Myers Squibb; Mitsubishi Tanabe Pharma Co; UCB Japan Co., Ltd.; Daiichi Sankyo Co., Ltd.; and Astellas Pharma Inc., Koichi Murata Speakers bureau: Eisai Co., Ltd. and Astellas Pharma Inc., Consultant of: Eisai Co., Ltd. and Astellas Pharma Inc., Kohei Nishitani Grant/research support from: Asahi-Kasei Pharma., Ryu Watanabe Speakers bureau: Mitsubishi Tanabe Pharma Co; Pfizer Inc.; Sanofi S.A.; AbbVie GK; Asahi Kasei Pharma; Eisai Co., Ltd.; Eli Lilly and Company; Bristol-Myers Squibb; and Janssen Pharmaceutical K.K., Teruhide Koyama: None declared, Ritei Uehara: None declared, Masao Tanaka Speakers bureau: AbbVie GK, Asahi Kasei Pharma., Astellas Pharma Inc., Ayumi Pharmaceutical Co., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Novartis Pharma K.K., Pfizer Inc., Taisyo Pharma., Ltd., UCB Japan Co., Ltd., Grant/research support from: AbbVie GK, Asahi Kasei Pharma., Astellas Pharma Inc., Ayumi Pharmaceutical Co., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Novartis Pharma K.K., Pfizer Inc., Taisyo Pharma., Ltd., UCB Japan Co., Ltd., Hiromu Ito Grant/research support from: Bristol-Myers Squibb, Eisai Co, Taisyo Pharma., and Mochida., Shuichi Matsuda: None declared
DOI: 10.1136/annrheumdis-2021-eular.1723

POS1483-HPR A QUANTITATIVE ASSESSMENT OF THE LIKELIHOOD THAT PATIENTS WITH RHEUMATOID ARTHRITIS WILL COMMUNICATE INFORMATION ABOUT RHEUMATOID ARTHRITIS RISK TO RELATIVES

I. Wells[1], P. Nightingale[2], G. Simons[1], C. Mallen[3], K. Raza[1], M. Falahee[1].
[1]*Rheumatology Research Group, University of Birmingham, Birmingham, United Kingdom*; [2]*Institute of Translational Medicine, Queen Elizabeth Hospital, Birmingham, United Kingdom*; [3]*Primary Care Centre Versus Arthritis, School of Medicine, David Weatherall Building, Keele University, Keele, United Kingdom*

Background: First-degree relatives (FDRs) of patients with rheumatoid arthritis (RA) are at increased risk of RA and are being recruited to studies of predictive and preventive approaches. Access to FDRs is usually via the proband with RA. Qualitative investigations have shown that communication of RA risk to FDRs is a complex and selective process. However, quantitative data are needed to develop a robust understanding of this process and its determinants to develop effective communication strategies and support for RA patients and their relatives.
Objectives: To identify predictors of the RA patients' reported likelihood of communicating RA risk information to their FDRs.
Methods: Patients with RA were invited to anonymously complete a survey assessing patient characteristics including age, gender, duration of RA, information seeking and decision making preferences (Autonomy Preference Index[1]), interest in FDRs taking a predictive test for RA, dispositional openness, and the general functioning subscale of the McMaster Family Assessment Device[2]. Reported likelihood of communicating RA risk to each of the patients' FDRs was assessed using a Likert scale ranging from extremely unlikely (0) to extremely likely (4). The median score across all FDRs was calculated for each patient. The association between patient characteristics and the median score was examined using univariate approaches.
Results: Surveys were completed by 482 patients (median age 65 years, 72% female). Most patients reported being likely to communicate RA risk to their FDRs (median score=3). Those who reported their likelihood of communicating RA risk to both children and siblings were more likely to communicate risk to children than siblings (p<0.001). No significant difference was found for FDRs' gender, or patients' gender, on reported likelihood to communicate about RA risk (p=0.32 and p=0.87, respectively). Patients who were older and who had had RA for longer were less likely to communicate about RA risk with their relatives. Patients who had higher interest in their FDRs taking a predictive test for RA, information seeking preferences, openness to communicate, and family functioning were more likely to communicate about risk (Table 1).

Table 1. Descriptive statistics and Spearman's rank-order correlations for the association between patients' characteristics and their median reported likelihood of communicating to their FDRs about RA risk

Patient characteristics	Descriptive statistics	Association with median likelihood to communicate risk to relatives	
		Test statistic	P value
Age; median (IQR)	65 (55-72)	-0.19	<0.001*
RA duration; median (IQR)	10 (4-20)	-0.18	0.001*
Autonomy preferences			
Information seeking; median (IQR)	84 (75-97)	0.26	<0.001*
Decision making; median (IQR)	54 (42-67)	0.09	0.048
Interest in children taking a test; median (IQR)	3 (2-3)	0.44	<0.001*
Interest in siblings taking a test; median (IQR)	2 (2-3)	0.44	<0.001*
Openness; median (IQR)	2 (1-3)	0.13	0.004*
Family functioning; median (IQR)	2 (2-3)	0.23	<0.001*

* p values significant at the Bonferroni adjusted value of 0.006.

Conclusion: Respondents were willing to communicate RA risk to their FDRs, and were more likely to communicate about risk to their children than their siblings. Factors including information seeking preferences, dispositional openness, interest in FDRs taking a predictive test, and family functioning were associated with increased likelihood of communicating RA risk information to FDRs. Patients' age and RA duration were associated with decreased likelihood. These findings increase understanding of communication about RA risk in families, and

will inform the development of informational approaches to support family communication and access to FDRs.

REFERENCES:

[1] Ende et al. Journal of General Internal Medicine. 1989; 4(1): 23-30.

[2] Epstein et al. Journal of Marital and Family therapy.1983; 9(2): 171-180.

Acknowledgements: This work was supported by Versus Arthritis; Grant reference: 21560 and Riksbankens Jubileumsfond (The Swedish Foundation for Humanities and Social Sciences); Grant reference: M13-0260:1 'Mind the Risk'.

Disclosure of Interests: Imogen Wells: None declared, Peter Nightingale: None declared, Gwenda Simons: None declared, Christian Mallen Grant/research support from: Keele School of Medicine have received funding to support BMS recruit to a non-pharmacological atrial fibrillation trial., Karim Raza Grant/ research support from: KR reports grants from Abbvie and Pfizer, and personal fees from Abbvie, Pfizer, Sanofi, Lilly, Bristol Myers Squibb, UCB, Janssen, and Roche Chugai, all outside the submitted work., M. Falahee: None declared

DOI: 10.1136/annrheumdis-2021-eular.1749

POS1484-HPR THE ASSOCIATION OF STIGMA WITH DISEASE VARIABLES IN PATIENTS WITH FIBROMYALGIA (FM)

M. Offenbächer[1], L. Toussaint[2], M. Weigl[3], J. Dezutter[4], N. Kohls[5], M. Vallejo[6], J. Rivera[7], F. Sirois[8], J. Hirsch[9]. *[1]Gasteiner Heilstollen, Medical Department, Bad Gastein, Austria*; *[2]Luther College, Psychology, Decorah, United States of America*; *[3]University Hospital, Department of Orthopaedics, Physical Medicine and Rehabilitation, München, Germany*; *[4]University of Leuven, School Psychology and Development in Context, Leuven, Belgium*; *[5]Coburg University of Applied Sciences, Health Promotion, Coburg, Germany*; *[6]UNED, Psychology, Madrid, Spain*; *[7]Gregorio Marañón Hospital, Rheumatology, Madrid, Spain*; *[8]The University of Sheffield, Psychology, Sheffield, United Kingdom*; *[9]East Tennessee State University, Psychology, Johnson City, United States of America*

Background: Stigma, defined as social devaluation of an individual, can be an important stressor for chronic pain patients [1]. Not every condition is stigmatized. A relevant factor for illness stigmatization seems to be whether the cause is mental-behavioural or physical. Chronic pain is often regarded as an imaginary illness or caused by psychological problems [2]. Sources of stigma for chronic pain patients are perceived negative attitudes from family members, the general public, and physicians [1]..

Objectives: To assess perceived stigma and the associations with disease variables in a cohort of patients with FM.

Methods: We invited 18 FM self-help groups in Germany to participate anonymously in our survey, and we sent the survey battery to 192 potential participants via postal mail. To measure perceived stigma, we used the Chronic Pain Stigma Scale (CPSS) developed by Reed [3], which has 30 items and 3 subscales (public, physicians, family). We also assessed sociodemographic characteristics, disease related variables (e.g., pain, stress, depression, anxiety), and other health-related factors, including health related quality of life [Healthy Days Core Module (CDC HDQOL-4)], disease specific impact (FIQ), fear avoidance belief questionnaire (physical activity subscale) (FABQ-PA), pain catastrophizing scale (PCS) and pain self-efficacy questionnaire (PSEQ).

Results: In total 162 FM patients participated (=84% response rate). Their mean age was 58 years (SD=10), 84% (N=135) were female. Highest level of education was: Elementary School 29%, Junior High School 35%, High School 15%, College 12%, and other 10%. Duration of chronic pain was 18.2 years (SD=12.0). There was no significant gender difference in the stigma subscales, nor was there an association with duration of chronic pain. Table 1 presents the significant Pearson correlations.

Table 1. Correlations of CPSS stigma subscales with health variables. *<.05; **<.01; ns=not significant.

	CPSS-public	CPSS-physician	CPSS-family
Regional pain scale	ns	.19*	.20*
VAS pain today	ns	ns	Ns
FIQ	.20*	.16*	.22**
HADS-anxiety	.37*	.20*	.24*
HADS-depression	.41**	.16*	.25**
CDC-HDQOL-4			
General health	.19*	.18*	.22**
Physical health	.19*	ns	ns
Mental health	.20*	ns	.21*
Impairment	.24*	ns	ns
Perceived stress scale	.44**	.24**	.37**
FABQ-PA	ns	-.17*	ns
PCS	.21*	ns	ns
PSEQ	.19*	ns	.18*

Conclusion: Perceived stigma in our FM patient cohort has an important impact on a variety of different disease variables including mental and general health, physical functioning, and on pain coping. Stigmatizing attitudes perceived from the general public exhibited the greatest association with most variables in our chronic pain patients. Perceived stigma from physicians and the family were also related to negative disease consequences in our FM patients. To conclude, we assert that assessing and addressing multi-source perceived stigmatization in routine clinical care may improve the management and wellbeing of patients with FM.

REFERENCES:

[1] Waugh OC, Byrne DG, Nicholas MK. Internalized stigma in people living with chronic pain. J Pain 2014;15(5):550 e1-10.

[2] Werner A, Isaksen LW, Malterud K. 'I am not the kind of woman who complains of everything': illness stories on self and shame in women with chronic pain. Soc Sci Med 2004;59(5): 1035-45

[3]Reed P. Chronic pain stigma: developement of the Chronic Pain Stigma Scale. 2005.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1974

POS1485-HPR PATIENTS' PERSPECTIVE ON CONTINUATION VERSUS TEMPORARY INTERRUPTION OF IMMUNOMODULATORY AGENTS DURING INFECTIONS IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES: AN INTERVIEW STUDY

M. Opdam[1], L. M. Verhoef[1], J. Vriezekolk[1], B. Van den Bemt[2,3], A. Den Broeder[1]. *[1]Sint Maartenskliniek, Rheumatology, Ubbergen, Netherlands*; *[2]Sint Maartenskliniek, Pharmacy, Ubbergen, Netherlands*; *[3]Radboud University Medical Center, Pharmacy, Nijmegen, Netherlands*

Background: Immune mediated inflammatory diseases (IMIDs) like rheumatoid arthritis (RA) are often treated with immunomodulatory agents (IA). Infection risks appear to be slightly increased in IMID patients using IA[1]. However, it remains uncertain whether it is best to continue or temporary interrupt IA in case of an infection For this decision, it is essential to know patient's perceptions about both strategies. Unfortunately, little is known about the patients' perceptions on this topic.

Objectives: To explore the patients' perspectives on continuation and temporary interruption of IA in case of an infection and assess possible barriers and facilitators.

Methods: Semi-structured interviews were conducted in IMID patients using IA. Patients were recruited from the rheumatology, dermatology and gastroenterology departments of two hospitals in the Netherlands. Purposive sampling was used to select a diverse patient population. Semi-structured interviews were performed until data saturation was reached and analyzed using inductive thematic analysis.

Results: 19 patients with 6 different IMIDs and 17 different IA were interviewed. The majority was female, mean age 51 years and mean disease duration 17 years. Four had experienced a severe infection (requiring hospitalization). 15 patients indicated that they would prefer to continue their IA in case of an infection, however, for most patients this would depend on the infection severity. Several facilitators and barriers were identified (Table 1). Patients mentioned disease flare as a barrier for temporary interruption. Beliefs about susceptibility to infections form barriers and facilitators for both temporary interruption and continuation. Patients also mentioned that they would follow their physician's advice on continuation/temporary interruption.

Table 1. Identified barriers and facilitators

Temporary interruption	
Barriers	Disease flare and its impact
	Loss of IA effects or increased side effects after restarting
	Long duration of interruption
	Belief: IA has no/a positive effect on infection (risk)
	Belief: not more susceptible for infections
	Practical barriers
	Not aware of possibility of interruption
	Not following physician's advice
Facilitators	More severe and/or longer lasting infection
	Interactions with medication needed for infection
	Positive effect of interruption on immune system
	Short duration of interruption
	Belief: more susceptible for infections
	Belief: IA has a negative effect on infection (risk)
	Concerned about infections
	Current stable disease
	Physician's advice
	Long duration of IA effects
	Wish to taper/stop IA in general
	Negative impact of infection on daily activities
Continuation	
Barriers	Belief: more susceptible for infections
	Belief: IA has a negative effect on infection (risk)
	Negative previous experiences during infection
	Loss of IA effects after long use
	Interactions with medication needed for infection
Facilitators	Belief: not more susceptible for infections
	Belief: IA has no/a positive effect on infection (risk)
	Not concerned about infections
	IA needed to control IMID
	Mild infection
	Positive previous experiences with continuation
	Physician's advice

Conclusion: Interviewed patients seemed to prefer continuation of IA during an infection if possible. The concern of disease flare might form a barrier for temporary interruption, this is in line with a previous study, showing that RA patients fear disease flare after dose reduction [2].

REFERENCES:

[1] Singh JA, Cameron C, Noorbaloochi S, Cullis T, Tucker M, Christensen R, et al. Risk of serious infection in biological treatment of patients with rheumatoid arthritis: a systematic review and meta-analysis. Lancet. 2015;386(9990):258-65.

[2]Verhoef LM, Selten EMH, Vriezekolk JE, de Jong AJL, van den Hoogen FHJ, den Broeder AA, et al. The patient perspective on biologic DMARD dose reduction in rheumatoid arthritis: a mixed methods study. Rheumatology. 2018;57(11):1947-55.

Disclosure of Interests: Merel Opdam Grant/research support from: has received research grants (to the institution) from Gilead, L.M. Verhoef: None declared, Johanna Vriezekolk: None declared, Bart van den Bemt: None declared, Alfons den Broeder Grant/research support from: has received consultancy honoraria, congress invitations and research grants (to the institution) from Abbvie, Amgen, Cellgene, Roche, Biogen, Lilly, Novartis, Celltrion Sanofi, Gilead. Is coinventor on a rituximab related patent (pending)

DOI: 10.1136/annrheumdis-2021-eular.2280

POS1486-HPR DAILY ACTIVITY IMPAIRMENT IS MEDIATED BY BOTH ORAL DRYNESS AND ORAL HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

Y. Yenisoy[1], A. Kapusuz[1], E. N. Çakır[1], K. Abacar[2], İ. Tatlı[3], F. Türe-Özdemir[3], M. Yay[4], Ü. Karaçaylı[5], N. Inanc[2], H. Direskeneli[2], G. Mumcu[6]. [1]*Marmara University, Institute of Health Sciences, Istanbul, Turkey*; [2]*Marmara University, Division of Rheumatology, Istanbul, Turkey*; [3]*Marmara University, Department of Hematology and Immunology, Istanbul, Turkey*; [4]*Mimar Sinan Fine Arts University, Department of Statistics, Istanbul, Turkey*; [5]*Health Sciences University, Department of Oral and Dental Surgery, Ankara, Turkey*; [6]*Marmara University, Department of Health Management, Istanbul, Turkey*

Background: Both oral functions and oral health-related quality of life (OHRQoL) are poorly affected by low salivary flow rate in patients with primary Sjögren's syndrome (pSS).

Objectives: The aim of the study was to evaluate the effects of oral dryness and OHRQoL on daily life in patients with primary Sjögren's syndrome (pSS).

Methods: In this cross-sectional study, 86 patients with pSS (M/F: 5/81; mean age: 52.4 ± 11.6 years) were included. The data were collected by clinical examination and a questionnaire regarding patient-reported outcome measures (PROMs). Patient filled PROMs regarding Oral Health Impact Profile-14 (OHIP-14) for OHRQoL, Work Productivity and Activity Impairment scale (WPAI) for Daily life and the EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI) for their symptoms. Unstimulated whole saliva flow rates (U-WSFR) of patients were calculated as ml/min. Increases in PROMs and decreases in U-WSFR reflected poor conditions. After preliminary analysis, a mediation analysis was used to evaluate the relations among variables.

Results: WPAI-Daily activity impairment score was higher in patients with low U-WSFR (≤0,1 ml/min) than the others (67±29,8 vs 52,5±28,6) (p=0.042). Both U-WSFR (0,43±0,57 ml/min) and ESSPRI-Dryness score (6.31 ± 2.71) were correlated with scores of OHIP-14 (25,96±17,13)(r:- 0,38 p=0.000; r: 0,37 p=0.000) and WPAI-Daily activity impairment (57,96±29,71)(r: -0,36 p=0.004; r: 0,53 p=0.000). Moreover, scores of ESSPRI-Pain (5,16±3,12) and ESSPRI-Fatigue (5,41±2,97) were also related to WPAI-Daily activity impairment score (r: 0,41 p=0.001; r:0,49 p=0.000, respectively).

In the mediation analysis, WPAI-Daily activity impairment score (57.9 ± 29.7) was directly mediated by ESSPRI-Dryness score (p=0.0010) and indirectly mediated by OHIP-14 score (25.9 ± 17.1) (p=0.0357). After mediation analysis, a bootstrap analysis with 5000 replications was applied to estimate the mediation effect to generate 95% CI. Percentile bootstrap of OHIP-14 score was found to be an effective mediator for Daily activity impairment based on 5000 bootstrap samples.

Conclusion: Both oral dryness and poor OHRQoL in patients with pSS affected daily activity impairment. Therefore, the patients' needs for improving oral health were critical components of treatment plans to improve the daily activity of SjS patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3013

HPR Service developments, innovation and economics in healthcare

POS1487-HPR NEXT-GENERATION ONLINE TELEMEDICINE SYSTEM UTILIZING MIXED REALITY FOR RHEUMATOID ARTHRITIS

S. Y. Kawashiri[1], F. Nonaka[2], S. Chiba[3], T. Honda[4], T. Nakajima[4], T. Ishikawa[3], A. Kawakami[5]. [1]*Nagasaki University Graduate School of Medical Sciences, Departments of Community Medicine, Nagasaki, Japan*; [2]*Nagasaki University Graduate School of Medical Sciences, Department of Island and Community Medicine, Nagasaki, Japan*; [3]*Microsoft Japan Co., Ltd., N/A, Tokyo, Japan*; [4]*Rocket Studio, Inc., N/A, Tokyo, Japan*; [5]*Nagasaki University Graduate School of Medical Sciences, Departments of Immunology and Rheumatology, Nagasaki, Japan*

Background: Telemedicine can be performed using a conventional videophone or web conferencing system. Then, joint lesions can only be observed and inferred from two-dimensional images, and it is difficult to perform accurate joint assessments, which is essential for the management of rheumatoid arthritis (RA).

Objectives: To develop the next-generation online telemedicine system utilizing mixed reality for RA.

Methods: We have developed a system that can assess joints accurately in three-dimensions images in real-time, using Azure Kinect DK (depth sensor)/ HoloLens 2 (headset), which are mixed reality technologies, and Teams (online interview/chat) provided by Microsoft. Furthermore, by applying artificial intelligence (AI), we plan to implement additionally to this system 1) a function to quickly catch and automatically evaluate the patient's anxiety and changes in facial expressions at the time of examination, 2) a function to record dialogue with the patient in chronological order, 3) a function to support the detection of swollen joints, and 4) function to automatically analyze the questionnaire.

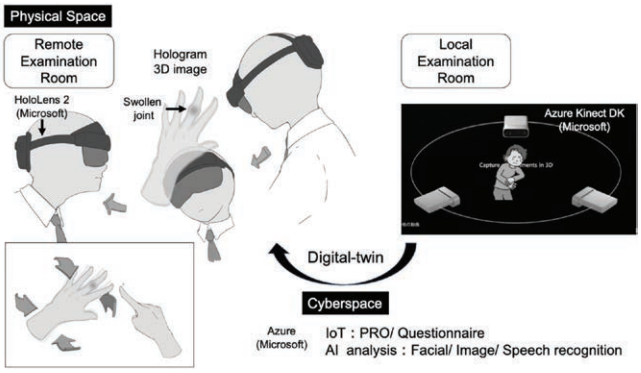
Results: This system remotely connects a rheumatologist in the Nagasaki University Hospital (Nagasaki City, urban area) and a patient with RA and a non- rheumatologist in the Goto Central Hospital (Goto Island, rural area). A three-dimensional hologram of the patient's hand projected in front of a rheumatologist. Using this system, we are able to evaluate joints more accurately than using a conventional videophone or web conferencing system.

Conclusion: It is expected that this system will enable remote medical care specializing in rheumatology, which is standardized at a high level even in areas without rheumatologists such as remote islands and remote areas. This system remotely connects Nagasaki City and Goto Island, but due to the performance of the system, it is not limited to these areas and it is possible to connect rheumatologists to any area that can be connected to the network. It is also effective for the purpose of avoiding the risk of infection during long-distance hospital visits under the epidemic of COVID-19 infection.

REFERENCES:

[1] Mov Disord. 2020;35:1719-1720.

Figure



Disclosure of Interests: Shin-ya Kawashiri Speakers bureau: Speaker fees from AbbVie, Asahi Kasei, Astellas, Chugai, Eisai, Eli Lilly, Mitsubishi Tanabe, Novartis, and ONO., Grant/research support from: Research grants from Pfizer., Fumiaki Nonaka: None declared, Shinji Chiba: None declared, Tomoyuki Honda: None declared, Tomohiko Nakajima: None declared, Tomoyuki Ishikawa: None declared, Atsushi Kawakami Speakers bureau: Speaker fees from AbbVie, Actelion, Asahi Kasei, Astellas, Boehringer Ingelheim, Celltrion, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, GSK, Janssen, Kowa, MedPeer, Mitsubishi Tanabe, Novartis, ONO, Pfizer, Taisho, and Takeda., Grant/research support from: Grants and research support from AbbVie, Actelion, Asahi Kasei, Astellas, AYUMI, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, Kyowa Hakko Kirin, MSD, Neopharma, Novartis, ONO, Sanofi, Taisho, Takeda Science Foundation, and Teijin

DOI: 10.1136/annrheumdis-2021-eular.1029

POS1488-HPR CAN A SPECIALIST NURSE LEAD A COMPREHENSIVE OSTEOPOROSIS SERVICE WITH REMOTE SUPERVISION – AN INNOVATIVE CONCEPT

D. Masieh[1], J. Begum[1], J. Fourmy[1], M. K. Nisar[1]. [1]*Luton and Dunstable University Hospital, Rheumatology, Luton, United Kingdom*

Background: Specialist services traditionally rely on a consultant to lead a multidisciplinary team and provide patient facing activities. However, demand

outstrips the limited expertise available and therefore significant delays occur in treatment pathways. There is an urgent need to expand the skill set of the employed workforce and think 'outside the box'. A service run by clinical nurse specialists (CNS) can be an effective solution. CNS are already an integral part of multidisciplinary teams caring for a diverse range of patients including those with chronic conditions such as osteoporosis.

Objectives: We designed an innovative osteoporosis service with patients consulting only a metabolic bone CNS with a consultant rheumatologist providing remote oversight. The aim of the project was to improve the efficiency of the service by eliminating consultant appointments and reducing unnecessary hospital visits while continuing to deliver a high-quality and safe service.

Methods: A new pathway was implemented where a consultant rheumatologist and a CNS virtually triaged post menopausal women over the age of 65 into the service. A dedicated proforma provided the template for the CNS to undertake new patient telephone consultation. Relevant investigations were requested during the telephone clinic and treatment related information was despatched to help with shared decision making. All patients were then reviewed in a Rheumatologist-CNS virtual MDT. An appropriate parenteral treatment option was agreed and confirmed to each individual. The CNS worked through a safety checklist and provided further advice and support to the patient as necessary. Using the database, we compared the timelines for the patient journey to the conventional pathway, obtained the number of consultant follow-up appointments saved by implementing this service, and calculated total savings.

Results: In the pilot phase, 116 patients were triaged into the new service. The patient cohort was a combination of new referrals and patients taken from the consultants' waiting lists. The mean age of the participants was 78 years (65-93). The median time: from referral to virtual triage was 20 days (0-308); from triage to new patient CNS telephone consultation was 20 days (0-137); and from virtual MDT to treatment authorisation was zero days (0-331 days). 45 patients had anabolic therapy commenced via home care. The remainder had anti resorptive therapy. No patient requested face-to-face review. Only one patient fed back that they would've preferred to see the consultant once. 116 new patient consultant appointments were saved and the median delay in treatment commencement was reduced from 84 to 38 days.

Conclusion: To our knowledge, this is the first successful example of an innovative service wholly provided by CNS for commencing parenteral anti-osteoporotic therapy with only remote consultant supervision. Our service redesign has significantly improved the efficiency of the parenteral osteoporosis pathway with reduction in treatment delay and a more streamlined patient journey. A nurse-delivered osteoporosis treatment pathway is highly effective, safe and provides an innovative solution to address thinly stretched health care resources for people with chronic conditions.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1069

POS1489-HPR TELEMEDICINE CONSULTATIONS IN RHEUMATOLOGY: IDENTIFIED PROBLEMS OF NEW TECHNOLOGY

Y. Livshits[1], O. Teplyakova[1], A. Sarapulova[1]. [1]*Ural State Medical University, All Patient Department, Yekaterinburg, Russian Federation*

Background: Telemedicine counseling (TMC) has gained rapid development during the COVID-19 pandemic. The prospect of using this technology in rheumatology was based on the possibility of getting maximum information about the patient during the survey, examination and interpretation of laboratory and instrumental data, that is excepting direct contact with the patient. Several rheumatological clinics have reported on the success of using TMC. However, there is very little data of the difficulties that can be encountered when organizing this process.

Objectives: To characterize the identified problems during TMC in rheumatology, to suggest potential directions for their elimination.

Methods: Since June 2021, on the basis of the Medical Association "New Hospital", Yekaterinburg, Russian Federation, 76 TMCs have been performed on the profile of rheumatology in patients aged 29 to 71 years. Of these, 13 applied to the primary TMC, the other patients were preliminarily examined in person. The consultation included the preliminary acquaintance with the examination results, a 20-minute video communication and writing of a conclusion. After each TMC, a survey was conducted between the doctor and the patient, including the identified deficiencies in counseling. The frequency of identified problems is presented as an absolute indicator and as a percentage of the total number of TMCs performed.

Results: We noted a high degree of patient satisfaction: 74 (97.4%) responded that they received answers to all. However, according to the doctor, the following groups of problems were identified.

[1] Technical problems in 29 (38.2%): most often there were various problems with the Internet, but there were also registered: the end of the charge on the patient's tablet, the patient was not registered in the electronic queue. Elimination of these violations depends on the work of IT-specialists, but each consulting physician should be prepared for an immediate transition to an alternative form of communication (for example - telephone).

[2] Lack of objective examination, leading to the impossibility of correct remote diagnosis - 8 (10.5%). This problem was identified due to the inability to establish the presence or absence of arthritis during the initial diagnosis (6 cases) and to clarify the nature of the rash (2 cases). All patients are invited for a face-to-face consultation.

[3] The need to write prescriptions for psychotropic drugs - 12 (15.8%), which under the conditions of national legislation cannot be done in the TMC regime.

[4] The time spent directly on remote communication with the patient was 17.2 minutes (from 8 to 31), however, taking into account the study data and writing the conclusion, the total time was 40.7 minutes (from 21 to 73). Thus, it turned out that the average time for remote and face-to-face consultations is the same, while TMC's payment is only about 50% of the face-to-face consultation. This situation reduces the doctor's interest in carrying out TMC. The solution to the problem is associated with reducing the time for the documentation process through technical improvements. In addition, of the 9 patients in whom the TMC process lasted 60 minutes or more, 5 were diagnosed with fibromyalgia. It is possible that with a previously established diagnosis of fibromyalgia, only face-to-face counseling should be recommended to patients.

Conclusion: The TMC system is promising, however, there are a number of problems that need to be improved, since they can reduce the doctor's interest in using this technology.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1183

HPR Professional education, training and competencies

POS1490-HPR "WHERE DOES IT HURT?": IDENTIFYING PAIN CONTENT AND ITS CONTEXT WITHIN PAEDIATRIC AND ADOLESCENT RHEUMATOLOGY TRAINING

R. Lee[1,2], J. Mcdonagh[1,2,3], M. Connelly[4], S. Peters[5], L. Cordingley[6]. [1]*Centre for Epidemiology Versus Arthritis, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom*; [2]*NIHR Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, Manchester, United Kingdom*; [3]*Department of Paediatric and Adolescent Rheumatology, Royal Manchester Children's Hospital, Manchester University NHS Foundation Trust, Manchester, United Kingdom*; [4]*Division of Developmental and Behavioral Sciences, Section of Psychology, Children's Mercy Kansas City, Kansas City, United States of America*; [5]*Manchester Centre for Health Psychology, Division of Psychology and Mental Health, University of Manchester, Manchester, United Kingdom*; [6]*Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom*

Background: Complex pain symptoms present across a wide spectrum of long-term musculoskeletal conditions in paediatric rheumatology. Pain training should therefore be part of a core curriculum for the professionals working in this speciality, but it is unclear to what extent this is the case currently.

Objectives: To identify the extent of pain-specific content included in the training of healthcare professionals in paediatric and adolescent rheumatology in the UK.

Methods: A systematic search of documental data using key internet search engines was conducted using combinations of the following terms: 'training', 'curriculum', 'competency', 'paediatric', 'adolescent' and 'rheumatology'. A targeted search of online content from the main professional organisations followed; doctors (Royal College of Paediatric and Child Health [RCPCH]), nurses (Royal College of Nursing [RCN]), physiotherapists (Chartered Society of Physiotherapy), occupational therapists (Royal College of Occupational Therapists) and psychologists (British Psychological Society). Documents from professional learned societies such as The British Society of Paediatric and Adolescent Rheumatology (BSPAR) and The Scottish Paediatric and Adolescent Rheumatology Network (SPARN) were also included. Document search strategies were designed by the authors in partnership with healthcare professionals. Data were extracted and analysed following a summative content analysis. Pain-related terms were quantified. Latent content was interpreted qualitatively to explore the context in which pain-related phrases were presented.

Results: Nine documents were identified. Pain-related terms represented 0.17% of all words across texts (used 55 times in total). Most pain terms were found in documents aimed at doctors (n=40, 72.7%). Of the pain terms used, most were used in the context of referring to specific pain syndromes such as chronic regional pain, generalized idiopathic pain and pain amplification. Content around

the assessment and management of pain was vague and no detail was given as to how health professionals should perform these tasks. There was no reference to pain intensity, location or emotion. There were several problematic conceptual issues in the way pain was presented, with pain mostly portrayed either in the context of inflammatory or non-inflammatory pain and rarely in the context of both. Musculoskeletal pain was also positioned as a 'somatic' symptom, potentially conveying an interpretation of pain as being psychologically mediated.
Conclusion: Training for healthcare professionals in paediatric rheumatology would benefit from updates informed by contemporary pain theories and evidence-based practices. This is key to ensuring that children and young people with chronic pain receive effective pain care from tertiary care services focused on treating musculoskeletal disease.

Table 1. Documents and pain terms identified

Profession	*Title*	*Organisations, year.*	*% of document covered by pain terms*
Doctors	Generic syllabus level 1.	RCPCH, 2018.	**0.14%**
Doctors	Generic syllabus level 2.	RCPCH, 2018.	**0.14%**
Doctors	Generic syllabus level 3.	RCPCH, 2018.	**0.06%**
Doctors	Paediatric rheumatology level 3.	RCPCH, 2018.	**0.48%**
Doctors	Competencies for the special interest module in paediatric rheumatology	RCPCH, 2014.	**0.43%**
Nurses	Competencies for rheumatology nurses.	RCN, 2020.	**0.05%**
Nurses	Competencies for clinical nurse specialists/ advanced nurse practitioners.	BSPAR, 2014.	**0.29%**
Nurses	Role of the paediatric rheumatology nurse.	SPARN, 2016.	**0%**
Allied Health Professionals (AHPs)	Competencies for AHPs	BSPAR, 2019.	**0.73%**

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.210

POS1491-HPR MENTAL HEALTH OUTCOMES AMONG HEALTH CARE WORKERS DURING THE CORONAVIRUS-19 PANDEMIC

O. Hamdi[1], M. Sellami[1], S. Miladi[1], A. Fazaa[1], L. Souabni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunisia, Tunisia*

Background: The coronavirus-19 (COVID-19) pandemic is having negative effects on societies' mental health, particularly health care workers who are exposed to tremendous psychological stress.
Objectives: To assess the magnitude of mental health outcomes among health care workers treating patients exposed to COVID-19.
Methods: This cross-sectional study collected demographic data and mental health measurements from health workers in different hospitals using an online questionnaire. Participants were also asked to complete the 9-item Patient Health Questionnaire (PHQ-9), the 7-item Insomnia Severity Index (ISI), and the 7-item Generalized Anxiety Disorder scale (GAD-7). The total scores of these measurement tools were interpreted as follows: PHQ-9 normal (0-4), mild (5-9), moderate (10-14), and severe (15-21) depression; ISI normal (0-7), mild (8-14), moderate (15-21), and severe (22-28) insomnia; GAD-7 normal (0-4), mild (5-9), moderate (10-14), and severe (15-21) anxiety.
Results: A total of 155 health care workers with a mean age of 31.3 ± 25 years [26-45] and a sex-ratio of 0.3 completed the online questionnaire. All participants were directly engaged in diagnosing, treating, or caring for patients with or suspected to have COVID-19. Participants were divided into two groups: 79% medical (61% doctors in training and 18% hospital doctors) and 21% paramedical staff. Twenty-two participants (14.2%) had a chronic disease and 21(13.5%) had a history of depression. Nineteen (12.2%) of the participants were infected with COVID-19, 4 of whom contracted the infection in the hospital (50% during October 2020). A statement to the department of occupational medicine was made in 70% of cases. Ninety-one percent of the participants were fit for treating patients with COVID-19. The mean number of nightshifts in the COVID unit per month was 5.3. The mean number of hours of work in the COVID unit was 5 hours per day, 36 hours per week, and 62 hours per month. An increase in workload compared to the pre-epidemic was noted in 62.9% of cases. Thirteen percent of participants experienced the same anxiety level as the first time of taking care of COVID patients while 65% were rather at ease compared to the first time. Forty-seven percent of participants felt the need for psychological support and 16.7% of whom had consulted a psychiatrist. Participants were diagnosed with depression (9 cases), anxiety (13 cases), and burn-out (3 cases). The prescribed treatment was: antidepressants (5 cases), anxiolytic (10 cases), and psychotherapy (12 cases). Mild depression was detected in 13% of cases, moderate depression in 4% of cases, and severe depression in 2% of cases. Mild insomnia was detected in 41% of cases, moderate insomnia in 14% of cases, and severe insomnia in 9% of cases. As for anxiety, 33% of participants suffered from mild anxiety, 14% moderate anxiety, and 5% severe anxiety.
Conclusion: Participants reported experiencing psychological burden and a high rate of anxiety, depression, and insomnia. It is important to protect health care workers and to promote mental well-being to survive this pandemic.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.783

POS1492-HPR EVALUATION OF A VIRTUAL REALITY-BASED APPLICATION TO EDUCATE HEALTHCARE PROFESSIONALS AND MEDICAL STUDENTS ABOUT INFLAMMATORY ARTHRITIS

P. Klemm[1], A. Kleyer[2], K. Tascilar[2], L. Schuster[2], T. Meinderink[2], F. Steiger[2], U. Lange[1], U. Müller-Ladner[1], J. Knitza[2], P. Sewerin[3], J. Mucke[3], A. Pfeil[4], G. Schett[2], F. Hartmann[2], A. Hueber[5], D. Simon[2]. [1]*Justus-Liebig University Gießen, Campus Kerckhoff, Department of Rheumatology, Immunology, Osteology and Physical Medicine, Gießen, Germany*; [2]*Universitätsklinikum Erlangen, Department of Internal Medicine 3, Rheumatology and Immunology, Erlangen, Germany, Erlangen, Germany*; [3]*Heinrich Heine University Düsseldorf, Department and Hiller Research Unit for Rheumatology, Düsseldorf, Germany*; [4]*Jena University Hospital - Friedrich Schiller University, Department of Internal Medicine 3, Jena, Germany*; [5]*Sozialstiftung Bamberg, Sektion Rheumatologie, Bamberg, Germany*

Background: Inflammatory arthritides (IA), such as rheumatoid arthritis or psoriatic arthritis, are disorders that can be difficult to comprehend for health professionals and students in terms of the heterogeneity of clinical symptoms and pathologies. New didactic approaches using innovative technologies such as Virtual Reality (VR) applications could be helpful to demonstrate disease manifestations as well as joint pathologies in a more comprehensive way. However, the potential of using a VR education concept in IA has not yet been evaluated.
Objectives: We evaluated the feasibility of a VR application to educate healthcare professionals and medical students about IA.
Methods: We developed a VR application using IA patients data as well as two- and three-dimensional visualized pathological joints from X-ray and computed tomography generated images (1). This VR application (called Rheumality) allows the user to interact with representative arthritic joint and bone pathologies of IA patients (Figure 1 A, B). In a consensus meeting an online questionnaire was designed to collect basic demographic data (age, sex), profession of the participants, and their feedback on the general impression, knowledge gain and potential areas of application of the VR application. The VR application was subsequently tested and evaluated by healthcare professionals (physicians, researchers, and other healthcare professionals) and medical students at predefined events (two annual rheumatology conferences and academic teaching seminars at two sites in Germany).
Results: 125 individuals participated in this study (56% female, 43% male, 1% non-binary). 59% of the participants were between 18-30 years of age, 18% between 31-40, 10% between 41-50, 8% between 51-60 and 5% were between 61-70. Of the participants, 50 were physicians, five researchers and four other health care professionals, the remaining were medical students (66). The participants rated the application as excellent (Figure 1 C, D), the mean rating of the VR application was 9.0/10 (SD 1.2) and many participants would recommend the use of the application, with a mean recommendation score of 3.2/4 (SD 1.1). A large majority stated that the presentation of pathological bone formation improves the understanding of the disease (120 out of 125 (96%)).
Conclusion: The data show that IA-targeting innovative teaching approaches based on VR technology are feasible. The use of VR applications enables a disease-specific knowledge visualization and may add a new educational pillar to conventional educational approaches.
REFERENCES:
[1] Kleyer A et al. *Z Rheumatol* 78, 112–115 (2019)

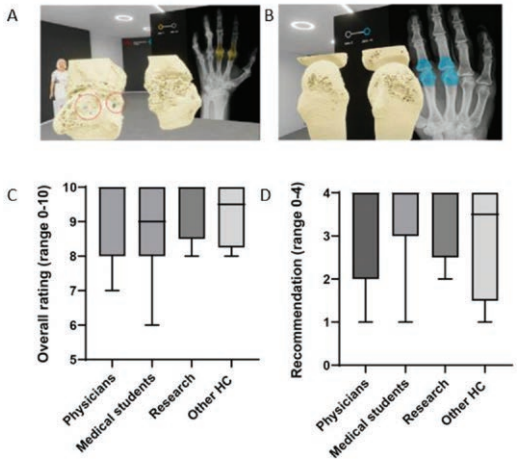


Figure 1. Illustration of the VR application and evaluation results

Two- and three-dimensional visualized pathological joints from X-ray and computed tomography generated images in a patient with long-standing (inadequately treated) RA (A) and a patient with early RA (B). Overall rating (range 0-10) on the VR application divided into four different professional subgroups (C); recommendations of VR application in the four different professional subgroups (D). HC, health care professionals; Boxplot explanation: Crossbars represent medians, whiskers represent 5-95 percentiles (points below the whiskers are drawn as individual points), box always extends from the 25th to 75th percentiles (hinges of the plot).

Disclosure of Interests: Philipp Klemm Consultant of: Lilly Deutschland GmbH, Arnd Kleyer Speakers bureau: Lilly Deutschland GmbH, Consultant of: Lilly Deutschland GmbH, Grant/research support from: Lilly Deutschland GmbH, Koray Tascilar: None declared, Louis Schuster: None declared, Timo Meinderink: None declared, Florian Steiger: None declared, Uwe Lange: None declared, Ulf Müller-Ladner: None declared, Johannes Knitza Speakers bureau: Lilly Deutschland GmbH, Philipp Sewerin Speakers bureau: Lilly Deutschland GmbH, Paid instructor for: Lilly Deutschland GmbH, Johanna Mucke Consultant of: Lilly Deutschland GmbH, Alexander Pfeil Speakers bureau: Lilly Deutschland GmbH, Paid instructor for: Lilly Deutschland GmbH, Consultant of: Lilly Deutschland GmbH, Georg Schett: None declared, Fabian Hartmann Consultant of: Lilly Deutschland GmbH, Axel Hueber Consultant of: Lilly Deutschland GmbH, Grant/research support from: Lilly Deutschland GmbH, David Simon Speakers bureau: Lilly Deutschland GmbH, Paid instructor for: Lilly Deutschland GmbH, Consultant of: Lilly Deutschland GmbH, Grant/research support from: Lilly Deutschland GmbH

DOI: 10.1136/annrheumdis-2021-eular.1452

POS1493-HPR **IMPACT OF THE EULAR HCP CORE COMPETENCIES ON RHEUMATOLOGY PHYSIOTHERAPISTS IN THE UK: SURVEY RESULTS**

W. J. Gregory[1,2], S. Burchett[3], C. Mccrum[4,5]. [1]*Salford Royal NHS Foundation Trust, Rheumatology Directorate, Manchester, United Kingdom*; [2]*Manchester Metropolitan University, Department of Health Professionals; Faculty of Health, Psychology and Social Care, Manchester, United Kingdom*; [3]*East Sussex Healthcare NHS Trust, Information Management and Performance, Hastings, United Kingdom*; [4]*East Sussex Healthcare NHS Trust, Physiotherapy Department, Hastings, United Kingdom*; [5]*University Of Brighton, Research Centre for Healthcare Professionals, Brighton, United Kingdom*

Background: A European Alliance of Associations for Rheumatology (EULAR) initiative in 2019 saw the first-ever publication of Core Competencies for Health Care Professionals (HCPs) working in Rheumatology (Edelaar et al 2019). This document sets the tone for how HCPs in Rheumatology should be working. One of the listed research agenda items created as a part of this project was to define discipline-specific competencies related to each of the HCPs unique roles in the multidisciplinary team.

Objectives: In response to this call for discipline-specific application, a recent national survey of physiotherapists working in rheumatology in the UK included a section looking at the comfort these clinicians feel in the day-to-day application of these Core Competencies.

Methods: In late 2019, an internet-based survey was emailed, and shared via other digital platforms, aiming to target all UK-based rheumatology physiotherapists. Other areas were covered and have been published (Gregory, Burchett and McCrum 2021), but there are unpublished data from Question 8 on this survey which involved listing the EULAR HCP Core Competencies and asking responders to rate on a 5-point Likert scale their comfort with these statements in relation to their day-to-day practice.

Results: Ninety-seven UK-based physiotherapists working at least some of their job in rheumatology completed the survey. Overall the EULAR HACP core competency statements with the highest scores were statements 2 and 5; those statements with the lowest comfort response were statements 4 and 6.

Statement 2 relates to assessment and statement 5 to non-pharmacological management; it is in line with the traditional physiotherapy job role that these are the two areas identified by survey responders as their strongest areas.

Statement 4 relates to pharmacological management, and as this is not a formal part of expected specialist rheumatology physiotherapist job role at banding levels below band 8, this result was lower level of comfort probably to be expected.

Statement 6 relates to patient education and whilst this is clearly a big part of the physiotherapist role, we expect the lower score here represents respondents awareness that broader disease education may sit better with other members of the rheumatology multi-disciplinary team.

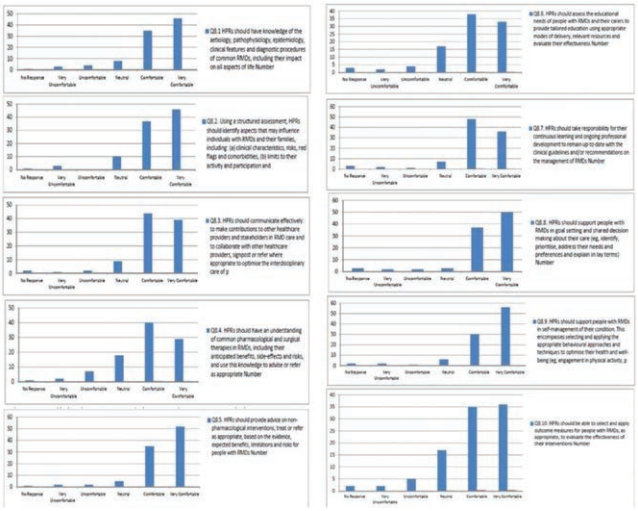
Conclusion: Written for all HCPs, the competency statements do show less comfort on this survey of physiotherapists with regards to less profession-specific statements, namely medication management and disease education. Team working means these areas will be picked up by other rheumatology HCPs.

Generally there is a good amount of familiarity with and comfort in application of these new core competencies. An alternative conclusion is that the EULAR working group creating the competencies achieved a strong understanding of the HCP roles and the competencies are hence seen to fit well in this survey. As per the concluding statements of the 2019 EULAR core competencies document, there does remain a requirement to work on profession specific competencies in rheumatology.

REFERENCES:

[1] Edelaar L, Nikiphorou E, Fragoulis GE, *et al.* 2019 EULAR recommendations for the generic core competences of health professionals in rheumatology. *Annals of the Rheumatic Diseases* 2020;**79:**53-60.

[2] Gregory, W.J., Burchett, S. and McCrum, C. (2021), National survey of the current clinical practices of the UK rheumatology physiotherapists: A short report. Musculoskeletal Care. https://doi.org/10.1002/msc.1516



Disclosure of Interests: William J. Gregory Speakers bureau: Speaker fees from Novartis and Abbvie., Consultant of: Advisory boards for Pfizer and Novartis., Sharon Burchett: None declared, Carol McCrum Speakers bureau: Speaker fees from Novartis

DOI: 10.1136/annrheumdis-2021-eular.2808

HPR Interdisciplinary research

POS1494-HPR **THE COLLABORATION OF RHEUMATOLOGY-DERMATOLOGY IN THE EVALUATION OF RHEUMATIC DISEASES PATIENTS: EXPERIENCE IN A UNIVERSITY HOSPITAL**

G. Figueroa-Parra[1], A. Moreno-Salinas[1], C. M. Gamboa-Alonso[1], M. A. Villarreal-Alarcón[1], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Servicio de Reumatología, Monterrey, Mexico*

Background: Dermatological manifestations are not rare in patients with rheumatic diseases (RD). Multidisciplinary management and direct interaction between these disciplines are essential. According to Dermatology-Rheumatology clinics, most diagnoses evaluated are systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), with dermatitis being the most common manifestation. It is important to be aware that skin problems in RD patients are not always related to the underlying condition(1). Nowadays, there is significant evidence to support the manifold advantages of the joint dermatology-rheumatology clinics, including improved quality of care for patients and multidisciplinary training for new physicians(2). This ongoing trend is intended to highlight the important interaction between specialties that treat overlapping conditions, and it has been incorporated in academic health centers to give a comprehensive approach to patients.

Objectives: Our purpose was to describe the collaboration between the Rheumatology and Dermatology services during the evaluation of RD patients.

Methods: An observational, retrospective study was performed in the Rheumatology Service of the University Hospital “Dr. Jose Eleuterio Gonzalez” in Monterrey, Mexico, between March 2019 and February 2020. All the patients with a Rheumatology or Dermatology consultation requested were included (hospitalized and outpatients). Demographic (age, gender, baseline diagnosis), the reason for consultation, specialty requested, type of treatment, final diagnoses, and agreement in final diagnosis were registered. Results are shown in descriptive statistics.

Results: One hundred and seventy-four patients were included, 142 (81.6%) patients from the outpatient clinic and 32 (18.4%) patients hospitalized. The mean age was 45.1 (SD±15.8) years, 135 (77.6%) were females, 54 (31%) patients were under initial diagnosis evaluation, 30 (17.2%) had RA, 25 (14.4%) patients had SLE, 15 (8.6%) patients had psoriatic arthritis, 12 (6.9%) patients had systemic sclerosis, 6 (3.4%) patients had dermatomyositis. The main reasons for consultation in hospitalized patients were acute lupus (15.6%), subacute lupus (12.5%), purpura (12.5%), cutaneous vasculitis (9.4%), urticarial dermatitis (9.4%), dermatomyositis (6.3%) and others (34.3%). The consultation requested was: 156 (89.7%) to Dermatology and 18 (10.3%) to Rheumatology. The type of treatment prescribed was topic/local in 37 (21.3%) patients, systemic in 25 (14.4%) and both in 92 (52.9%) patients. The final diagnoses were related to the underlying disease in 102 (77%) patients and unrelated in 40 (23%) patients. The agreement between initial clinical suspicion and final diagnoses reached 75.9% between Rheumatology and Dermatology services. Figure 1.

Conclusion: The collaboration between Rheumatology and Dermatology services are very important. Most of the patients were under initial evaluation. All the rheumatologists and dermatologists should be aware of the interdependence from both specialties to give the best quality of care to the patients.

REFERENCES:

[1] Samycia M, McCourt C, Shojania K, Au S. Experiences From a Combined Dermatology and Rheumatology Clinic: A Retrospective Review. J Cutan Med Surg. 2016;20(5):486-489. doi:10.1177/1203475416649138.

[2] Theodorakopoulou E, Dalamaga M, Katsimbri P, Boumpas DT, Papadavid E. How does the joint dermatology-rheumatology clinic benefit both patients and dermatologists?. Dermatol Ther. 2020;33(3):e13283. doi:10.1111/dth.13283

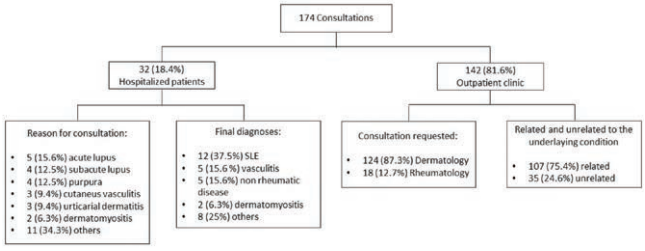


Figure 1.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2767

POS1495-HPR THE EXPERIENCE OF A RHEUMATOLOGY UNIT DURING THE COVID19 LOCKDOWN: TELEMEDICINE ALLOWS A SAFE FOLLOW UP OF PATIENTS WITH RHEUMATIC DISEASES

K. El Aoufy[1,2], M. R. Melis[1,2], S. Bellando Randone[1,2], J. Blagojevic[1,2], F. Bartoli[1,2], G. Fiori[1,2], F. Nacci[1,2], M. L. Conforti[1,2], L. Cometi[1,2], C. Bruni[1,2], A. Moggi Pignone[1,3], L. Rasero[4], S. Guiducci[1,2], M. Matucci-Cerinic[1,2].
[1]University of Florence, Clinical and Experimental Medicine, Florence, Italy; *[2]Careggi University Hospital, Department of Geriatric Medicine, Division of Rheumatology, Firenze, Italy*; *[3]Careggi University Hospital, of Emergency Medicine, Division of Internal Medicine, Firenze, Italy*; *[4]University of Florence, Departement of Health Science, Florence, Italy*

Background: In March this year, most of the routine activities were cancelled during the streaming of the pandemic in Italy. This prompted a pragmatic reorganization of the traditional care model of nursing and medicine, to quickly give an efficient clinical response. During the first phase of the pandemic, outpatient visits dropped by more than 60%, forcefully shifting to telemedicine to assure continuity of care despite the lockdown.

Objectives: The **aim** of the present work was to describe the strategy adopted during and immediately after the lockdown to assure the follow up of patients and the maintenance of their treatment in an outpatient "virtual" *telemedicine clinic* dedicated to RDs.

Methods: the patient flow to a rheumatology division during the lockdown was evaluated retrospectively from March to September 2020 in accordance with local restrictions, and three periods are described.

Results: 653/913 (71.5%), 542/542 (100%) and 1.048/1.048 (100%) infusion activities scheduled were performed at the centre for daily infusion and pre-infusion assessment, respectively during the 1st, 2nd and 3rd period. In the outpatient clinic during the 1st period, 96.96% of the cases was shifted to Telemedicine, which decreased to 52.45% in the 2nd period; while in the 3rd period, 97.6% of the performances were carried out at the clinic. Diagnostic procedures, such as ultrasound, capillaroscopy, and joint injection were generally postponed during the 1st period, reduced drastically during the 2nd and performed regularly during 3rd period. Ulcer treatment and the Clinical Trial Unit never stopped their activity. The flow of the activity of the outpatient clinic and the day hospital is represented as monthly trends in graph 1 (See Graph 1).

Conclusion: Our data show the feasibility of Telemedicine in a lockdown condition. Shifting stable patients to Telemedicine has the potentiality to minimize the risk of contagion and allow continuity of care. In the future, the use of Telemedicine for specific clinical uses might assure patient assistance also in non-pandemic conditions.

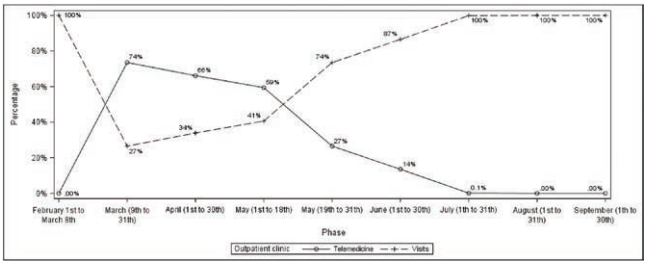
REFERENCES:

[1] Rawaf S, Allen LN, Stigler FL et al. Lessons on the COVID-19 pandemic, for and by primary care professionals worldwide. Eur J Gen Pract. 2020 Dec;26(1):129-133. doi: 10.1080/13814788.2020.1820479. PMID: 32985278.

[2] McDougall JA, Ferucci ED, Glover J, et al. Telerheumatology: A Systematic Review. Arthritis Care Res (Hoboken). 2017 Oct;69(10):1546-1557. doi: 10.1002/acr.23153. Epub 2017 Aug 22. PMID: 27863164; PMCID: PMC5436947.

[3] Romão VC, Cordeiro I, Macieira C, Oliveira-Ramos F, Romeu JC, Rosa CM, Saavedra MJ, Saraiva F, Vieira-Sousa E, Fonseca JE. Rheumatology practice amidst the COVID-19 pandemic: a pragmatic view. RMD Open. 2020 Jun;6(2):e001314. doi: 10.1136/rmdopen-2020-001314. PMID: 32584782; PMCID: PMC7425193.

Characters from table content including title and footnotes:



Graph 1. *Monthly trend for telemedicine and visits during the SARS Cov2 emergency*

Acknowledgements: The project (Telereuma) has been supported by an unrestricted grant of Biogen, BMS, and Novartis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3023

POS1496-HPR IS NUTRITIONAL FOLLOW-UP IN PATIENTS LIVING WITH RHEUMATOID ARTHRITIS BETTER WITH TELECONSULTATION? - EXPERIENCE BEFORE AND AFTER PANDEMIC

I. Mozo[1], M. Marquez[2], O. Valencia[3]. *[1]Fundación Santa Fé de Bogotá, Centro de Cuidado Clínico en Artritis Reumatoide, Bogotá, Colombia*; *[2]Fundación Santa Fé de Bogotá, Nutrition, Bogotá, Colombia*; *[3]Fundación Santa Fé de Bogotá, Research, Bogotá, Colombia*

Background: Nutritional follow-up as part of the integral attention for patients living with rheumatoid arthritis (RA) has been limited due to the COVID-19 pandemic. It made necessary to implement a remote monitoring for the care of the patients and to evaluate the outcomes of the changes in the care model.

Objectives: To identify the effects of the telemonitoring intervention within the pandemic scenario and the outcomes of the traditional face-to-face nutrition consultation.

Methods: A retrospective analysis of health records and the administrative data base of the patient's follow-up, between 2019 and 2020, was developed at the arthritis specialized center of the Santa Fe de Bogotá Foundation in Bogotá, Colombia. The outcomes measured include the number of visits per year and the proportion of patients who attend their nutritional follow-up by telemonitoring in 2020 vs patients attending to face-to-face nutrition consultation. Differences in the Body Max Index (BMI) and the changes based on eating habits, defined by the quality of food consumption per day, were also measured.

Results: A total of 212 patients from 2020 and 179 from 2019 were analyzed; An increase of 61.5% in the number of consultations, using nutritional telemonitoring per year, was identified in 2020 (n=412) compared to 2019 (n=255). In patients followed from 2019 to 2020, 13% (10/77) experienced an increase of more than 2 units of their BMI, while 22% (17/77) showed a decrease; in 2% of patients was not possible to evaluate their current weight; in the same way, 49% (103/212) in 2020 showed a positive change in their feeding habits compared with a 12% (21/179) in 2019. 135 new patients were recruited for nutritional telemonitoring 2020.

Conclusion: Nutritional telemonitoring to follow-up patients with RA has increased considerably in terms of consultations per year and changes in the feeding habits. However, more evaluation is required for this model.

REFERENCES:
[1] Melanie J Martin, Nora Ng, Laura Blackler, Toby Garrood, P227 Remote monitoring of patients with RA: a user-centred design approach, *Rheumatology*, Volume 59, Issue Supplement_2, April 2020, keaa111.221, https://doi.org/10.1093/rheumatology/keaa111.221
[2] Principio del formulario
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4118

Patient information and education

POS1497-PARE POST-TRIAL SURVEY OF PARTICIPANTS OF A PHASE 3 CLINICAL TRIAL IN SSC-ILD

I. Galetti[1,2], E. Brown[1,3], A. Kennedy[2], R. J. Riggs[4], A. Roennow[5], M. Sauvé[6], J. Welling[7], H. Finnern[8], A. Gilbert[9], M. Gahlemann[10], W. Sauter[11]. [1]*Gruppo Italiano per la Lotta alla Sclerodermia, n/a, Milan, Italy*; [2]*FESCA aisbl, n/a, Saint Maur, Belgium*; [3]*Scleroderma and Raynaud's UK, n/a, London, United Kingdom*; [4]*Scleroderma Foundation, Inc, n/a, Danvers, United States of America*; [5]*Sklerodermiforeningen, n/a, Rødovre, Denmark*; [6]*Scleroderma Canada, n/a, Hamilton, Canada*; [7]*Nationale Vereniging Voorlupus, APS, Sclerodermie en MCTD, n/a, UTRECHT, Netherlands*; [8]*Boehringer Ingelheim International GmbH, n/a, Ingelheim, Germany*; [9]*AK Gilbert Ltd, n/a, Brighton, United Kingdom*; [10]*Boehringer Ingelheim Schweiz GmbH, n/a, Basel, Switzerland*; [11]*Boehringer Ingelheim International GmbH, n/a, Biberach, Germany*

Background: The SENSCIS® trial (2015–18) was a large clinical trial (n=576) investigating the efficacy and safety of nintedanib in patients with systemic sclerosis-associated interstitial lung disease.1 The clinical research sponsors (CRS) collaborated with the scleroderma patient community advisory board (CAB) regarding the design, implementation and conduct of the trial.2 As part of this collaboration, the CRS and CAB developed a post-trial survey for SENSCIS® participants. The use of the developed patient-centric materials was optional for the sites.
Objectives: The objectives of the SENSCIS® post-trial survey were to gain experience in collecting real-world information and trial satisfaction data from patients to inform and improve future patient centric clinical research.
Methods: SENSCIS® trial participants who were involved in the extension trial SENSCIS®-ON completed a post-trial survey covering nine multiple-choice questions about three main topics:

[1] Recruitment – Where do patients usually search for clinical trials and how did they become aware of SENSCIS®?
[2] Motivation & Retention – What motivated patients to start and continue participation in SENSCIS®?
[3] Challenges & Wishes – What were the challenges during trial participation and how can future clinical trials be improved regarding patient centricity?

Results: A total of 125 participants completed all survey questions. Participants could select more than one option. A total of 51 patients reported that they are usually not actively looking for trials. For those actively searching, the most common sources to learn about trials were specialists/general practitioners (GPs) (46 patients) and internet search engines (20 patients), followed by patient organisations (12 patients). Of note, 78 patients would pay attention to printed materials, such as a card/flyer/poster in a doctor's office and get in touch with a trial/study site. Back in 2015–2017, during recruitment for the SENSCIS® trial, the majority of the patients who answered the survey were made aware via their specialist/GP (116 patients), whereas 5 were made aware via patient organisations and 4 via the internet.
The most frequent motivations to join the trial were 'hope to receive an improved therapy' (98 patients), to help other patients (64 patients), and on the recommendation of their specialist/GP (81 patients). Similarly, the most liked aspects of the trial were the 'opportunity to receive an improved therapy' (92 patients) and 'to support the development of an improved therapy for my illness' (90 patients). More than half of patients reported 'continuous observation of general health' (72 patients) and 'advice from GPs/specialists' (71 patients) as motivation to stay in the trial (Figure 1).
'Concerns about side effects' (72 patients) and 'not knowing whether the trial medication will work for me' (63 patients) were reported as the least liked aspects of the trial. Travel to the site was reported as a challenge by 21 patients.
To improve clinical trials, patients requested more patient-friendly information (50 patients) and multiple formats of information material (46 patients). Finally, 48 patients expressed the desire to communicate with other trial participants.
Conclusion: The SENSCIS® post-trial survey is a unique approach to receive real-world feedback from trial participants, and these pilot data will help improve future clinical trials and communication. The results highlight the importance of reaching patients who may not be actively looking for clinical trials.

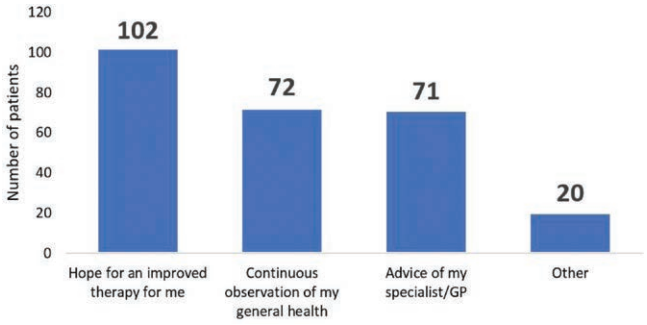


Figure 1. Motivation to stay in the SENSCIS® trial[1,2]

[1]More than one option could be selected.
[2]Data collected on 9th January 2021

REFERENCES:
[1] Distler O et al. *N Engl J Med*. 2019 Jun 27;380(26):2518-2528. doi: 10.1056/NEJMoa1903076.
[2] Roennow A et al. *BMJ Open*. 2020 Dec 16;10(12):e039473. doi: 10.1136/bmjopen-2020-039473.
Acknowledgements: Sue Farrington (Federation of European Scleroderma Associations [FESCA] Belgium), Luke Evnin (Scleroderma Research Foundation, United States), Beatriz Garcia (Asociacion Espanola de Esclerodermia, Spain), Catarina Leite (Associacao Portuguesa de Doentes com Esclerodermia, Portugal), Alison Zheng (Chinese Organisation for Scleroderma), Matea Perković Popović (Hrvatska udruga oboljelih od sklerodermije, Croatia), Tina Ampudia (Asociacion Mexicana de Orientacion Apoyo y Lucha Contra la Esclerodermia, AC, Mexico), Stephanie Munoz (Norsk Revmatikerforbund, Diagnosegruppen for Systemisk Sklerose, Norway), Monica Holmner (Reumatikerförbundet Riksföreningen för systemisk skleros, Sweden).
Disclosure of Interests: Ilaria Galetti: None declared, EDITH BROWN: None declared, Ann Kennedy Consultant of: I have been a member of the CAB (Community Patient Advisory Board) described in the accompanying abstract under discussion. My patient organisation has been paid for its participation in the CAB., Grant/research support from: It is not myself personally, but FESCA (Federation of European Scleroderma Associations) aisbl., that has received project grants for awareness raising and education. I was President of this Federation., Robert J Riggs: None declared, Annelise Roennow: None declared, Maureen Sauvé: None declared, Joep Welling Speakers bureau: BI MIDI and BI International, Sanofi, Henrik Finnern Employee of: I am employee of Boehringer Ingelheim International GmbH, Annie Gilbert Consultant of: I am a paid consultant for Bohringer Ingelheim since 2016, Martina Gahlemann Employee of: I am employed by Boehringer Ingelheim (Schweiz) GmbH, Basel, Switzerland, Wiebke Sauter Employee of: I am employer of Boehringer-Ingelheim
DOI: 10.1136/annrheumdis-2021-eular.1847

Building patient led organisations

POS1498-PARE LAUNCHING A NEW RELAPSING POLYCHONDRITIS ("RP") PROGRAM

N. Linn[1]. [1]*Relapsing Polychondritis Foundation, Rare Diseases, New York, United States of America*

Background: In 2011, I was diagnosed with relapsing polychondritis ("RP"), a debilitating and sometimes fatal rheumatic disease that is characterized by inflammation of cartilage and other tissues. The disease affects multiple organs, particularly cartilaginous structures such as the ears, nose, airways, and joints as well as eyes, skin, heart valves and brain. The cause of RP remains unknown and there currently is no cure for the disease.
As a patient, I had the opportunity to be evaluated by an incredible team of multidisciplinary expert medical professionals. While interacting with these experts, it was evident that there were tremendous unmet needs in the areas of diagnosis and treatments. As a retired Registered Nurse, it was clear that targeted research initiatives would be required to combat RP.
Objectives: After diagnosis, I realized that I could focus on my specific case or combat RP more broadly and help others. I decided to live my life with the purpose of helping others.
Methods: While fighting RP, I met many highly skilled, collaborative research scientists, especially at annual gatherings of rheumatology professionals.
In 2017 in San Diego, I participated in an RP study group that received a tremendous response from participating clinicians, clinical and basic scientist researchers, patients, and patient advocacy groups.

In 2018 in Chicago, I helped organize the RP Foundation's reception, co-hosted an event with the University of Michigan Division of Rheumatology, participated on a podcast of a news source dedicated to the rheumatology field, and facilitated two exhibitor booths at a prominent rheumatology conference.
In 2019 in Atlanta, I participated in an RP investigator meeting, which provided an update on a classification criteria project, introduced a new project to modify the disease activity index, and summarized RP-related projects.
With knowledge gleaned at these sessions, my husband and I collaborated with the RP Foundation to provide a substantial gift in 2020 to establish the Penn RP Fund, which will support a unique partnership between the University of Pennsylvania and the National Institutes of Health sponsored Vasculitis Clinical Research Consortium.
Results: Living with the purpose of helping other patients continues to improve the quality of my life. It affords me the ability to be excited about the extraordinary advances in patient care and cutting-edge research.
Participating in these conferences has provided exceptional opportunities to learn and collaborate with highly skilled research scientists. Further, I was able to build relationships with these scientists, which played a key role in the launch of the Penn RP Program.
This program will allow researchers to pursue important projects, including the development of a world-class referral center to examine the impact of the microbiome on RP disease activity. Additionally, patients with RP will have the opportunity to be evaluated by multiple subspecialties in a coordinated patient-centered manner.
Conclusion: The RP Foundation, University of Pennsylvania, and the Vasculitis Clinical Research Consortium (VCRC) Created a Powerhouse Healthcare Coalition. The Penn RP program will significantly improve the quality of my life and other RP patients for years to come.

Nancy Linn

RELAPSING POLYCHONDRITIS FOUNDATION

Penn
UNIVERSITY of PENNSYLVANIA

VASCULITIS CLINICAL RESEARCH CONSORTIUM

RACE FOR RP

The Relapsing Polychondritis Foundation formed a powerhouse healthcare coalition with the University of Pennsylvania and the NIH sponsored Vasculitis Clinical Research Consortium

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3890

Arthritis research

POS1499-PARE **PATIENT PERSPECTIVES OF BIOLOGIC TREATMENTS FOR AXIAL SPONDYLOARTHRITIS: SATISFACTION, WEAR-OFF BETWEEN DOSES, AND USE OF SUPPLEMENTAL MEDICATIONS**

W. B. Nowell[1], K. Gavigan[1], T. Hunter[2], W. Malatestinic[3], R. Bolce[3], J. Lisse[3], C. Himelein[3], J. Curtis[4], J. A. Walsh[5,6]. [1]*Global Healthy Living Foundation, Patient-Centered Research, Upper Nyack, United States of America*; [2]*Eli Lilly and Company, Global Patient Outcomes and Real World Evidence, Indianapolis, United States of America*; [3]*Eli Lilly and Company, Medical Affairs, Indianapolis, United States of America*; [4]*University of Alabama at Birmingham, Rheumatology, Birmingham, United States of America*; [5]*University of Utah, Rheumatology, Salt Lake City, United States of America*; [6]*George E. Wahlen Veterans Affairs Medical Center, Rheumatology, Salt Lake City, United States of America*

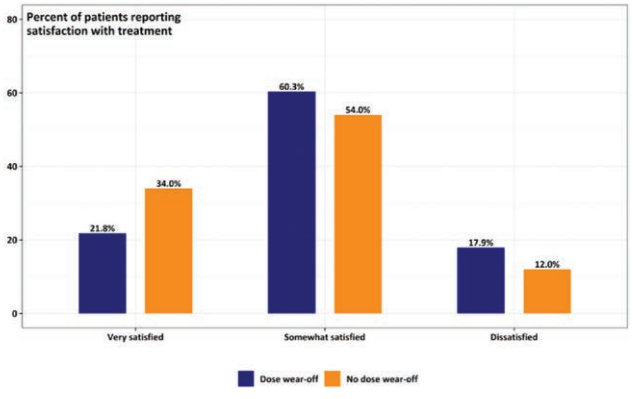
Background: Biologic disease-modifying antirheumatic drug (bDMARD) therapy has been shown to be effective in the treatment of axial spondyloarthritis (axSpA).[1,2] Little is understood about patients' experience of axSpA treatment from their own perspective.
Objectives: To characterize patient experiences and perspectives with bDMARD treatments for axSpA, including satisfaction, and use of supplementary treatments when wear-off between doses is perceived among those currently treated with bDMARD therapy.
Methods: Adult US participants (pts) within the ArthritisPower registry with physician-diagnosed axSpA were invited to complete electronic PRO measures, such as the BASDAI (0-10 scale, score ≥4 indicates suboptimal disease control), and an online survey about their perspectives of treatment. Analysis compared pt characteristics and treatment satisfaction by whether or not pt reported wear-off between bDMARD doses.
Results: 128 pts with axSpA and on bDMARD therapy met inclusion criteria of whom 82.8% were female, with mean age of 47 years. Mean BASDAI scores indicated poor disease control (6.4, SD 1.8), worse for those perceiving wear-off between doses compared with those who did not [6.8 (1.6) vs. 5.9 (2.0), p=0.01]. A majority of pts on a bDMARD reported being somewhat (57.8%) or very satisfied (26.6%) with their current axSpA treatment, and about 53.1% were satisfied with how well it controls axSpA-related pain. However, 60.9% (n=78) of pts reported that their current bDMARD typically wears off before the next dose. Treatment satisfaction was lower for pts experiencing wear-off compared to pts without wear-off (highly satisfied: 21.8% vs. 34%; somewhat satisfied: 60.3% vs. 54%; dissatisfied: 17.9% vs. 12%). 82.1% (n=64) of pts reporting wear-off used additional medications or supplements when that happened, chiefly NSAIDs (68.8%, n=44), muscle relaxers (42.2%, n=27) and/or opioids (37.5%, n=24). Among the 20 pts not satisfied with current axSpA treatment, side effects (6/20, 30.0%), or worry about risk of side effects (2/20, 10%) were the main reasons.
Conclusion: In a predominantly female sample of bDMARD-treated axSpA patients with high disease activity, most expressed satisfaction with treatment. However, most experienced wear-off between doses and took supplementary medications, including opioids, to manage.
REFERENCES:
[1] Dubash S, et al. Ther Adv Chronic Dis. 2018;9(3):77–8.
[2] Van Der Heijde D, et al. Ann Rheum Dis. 2017;76(6):978–91.

Table 1. Demographic and clinical characteristics by wear-off between bDMARD doses (n=128)

	Pts currently on bDMARD (N=128)	Wear-off between bDMARD oses (N=78)	No wear-off / Not sure (N=50)	p-value
	Number or mean (% or SD)			
Age	46.9 (10.3)	46.1 (9.2)	48.2 (11.8)	0.25
Female	106 (82.8)	69 (88.5)	37(74.0)	0.03
White	115 (89.8)	70 (89.7)	45 (90.0)	0.96
Body Mass Index	30.9 (7.8)	31.2 (8.5)	30.4 (6.6)	0.57
Current Medications, addition to bDMARD				
Conventional Synthetic DMARD (e.g. methotrexate, sulfasalazine)	17 (13.3)	15 (19.2)	2 (4.0)	0.01
Prescription NSAID	59 (46.1)	39 (50.0)	20 (40.0)	0.27
Other prescription medication¥	70 (54.7)	44 (56.4)	26 (52.0)	0.62
Noticed improvement in symptoms related to axSpA since starting current bDMARD	80 (62.5)	51 (65.4)	29 (58.0)	0.40
Noticed improvement in symptoms NOT related to axSpA since starting current bDMARD	40 (31.3)	22 (28.2)	18 (36.0)	0.35
BASDAI‡	6.4 (1.8)	6.8 (1.6)	5.9 (2.0)	0.01
PROMIS Pain Interference £	65.3 (5.7)	66.0 (5.1)	64.3 (6.4)	0.09
PROMIS Physical Function £	36.7 (5.6)	36.1 (5.3)	37.7 (5.8)	0.11
PROMIS Sleep Disturbance £	59.8 (8.5)	61.2 (7.7)	57.6 (9.3)	0.02

* Statistical significance between groups of pts who experienced wear-off between bDMARD or not, $p < 0.05$ ¥ Other prescription medications: muscle relaxers, nerve pain medications or anti-depressants, and opioids ‡ BASDAI is scored on a 0-10 scale with score ≥4 indicating suboptimal control of disease £ PROMIS measures use T-score metric in which 50 is mean, 10 is standard deviation (SD), of US population; higher T-score = more of concept measured

Figure 1. Satisfaction with axSpA treatment by wear-off between bDMARD doses (n=128)



Acknowledgements: This study was sponsored by Eli Lilly and Company. We thank the patients who participated in this study.

Disclosure of Interests: W. Benjamin Nowell Grant/research support from: Full-time employee of Global Healthy Living Foundation, an independent nonprofit research organization, which received funding pursuant to a contract from Eli Lilly to conduct the study that is the subject of this abstract; Principal Investigator for studies with grant support from AbbVie, Amgen and Eli Lilly, Kelly Gavigan Grant/research support from: Full-time employee of Global Healthy Living Foundation, an independent nonprofit research organization, which received funding pursuant to a contract from Eli Lilly to conduct the study that is the subject of this abstract, Theresa Hunter Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, William Malatestinic Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Rebecca Bolce Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jeffrey Lisse Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Carol Himelein Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jeffrey Curtis Consultant of: AbbVie, Amgen, BMS, Corrona, Eli Lilly, Janssen, Myriad, Pfizer, Roche, Regeneron, Radius, UCB, Grant/research support from: AbbVie, Amgen, BMS, Corrona, Eli Lilly, Janssen, Myriad, Pfizer, Roche, Regeneron, Radius, UCB, Jessica A. Walsh Consultant of: AbbVie, Amgen, Eli Lilly and Company, Janssen, Merck, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Merck, Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1876

Publication Only

Genomics, genetic basis of disease and functional genomics

AB0001 INTERFERON SIGNATURE IN CHILDREN WITH CHRONIC NON-BACTERIAL OSTEOMYELITIS AND IT'S DYNAMIC AFTER BISPHOSPHONATES TREATMENT

M. Kostik[1], R. Raupov[1], R. Mulkidzhan[2], A. Kosmin[2], E. Suspitsin[1,2]. [1]*Saint-Petersburg State Pediatric Medical University, Hospital Pediatry, Sankt-Peterburg, Russian Federation*; [2]*N.N.Petrov Institute of Oncology, Molecular Diagnostics, Saint-Petersburg, Russian Federation*

Background: Chronic non-bacterial osteomyelitis (CNO) is an immune-mediated chronic inflammatory bone disease which predominantly affects children and adolescents. The pathogenesis of CNO related to imbalance between pro-inflammatory and anti-inflammatory cytokines. Interferon-I mediated pathway is associated with pathogenesis of different pediatric rheumatic diseases, such as juvenile systemic lupus erythematosus (jSLE), juvenile dermatomyositis (JDM), systemic onset of juvenile idiopathic arthritis (soJIA), and, most of all, with macrophage activation syndrome. The data on interferon-I- regulated pathway in CNO is absent. NSAIDs, non-biologic and biologic anti-inflammatory drugs and bisphosphonates (BF) are treatment options for patients with CNO. The main adverse event of BF is a flu-like syndrome probably caused by the excessive cytokine release stimulated by BF.
Objectives: The aim of our study was to evaluate activity of Interferon-I mediated pathway in CNO patients and it's dynamics after BF treatment.
Methods: This prospective study included children with CNO requiring BF treatment (n=9), patients with soJIA (n=8), JDM (n=11) and jSLE (n=40) and healthy controls (HC, n=21). The activity of Interferon-I mediated pathway was assessed using interferon I score (IFN1 score). The score represented the median expression of 5 IFN1-regulated genes (IFI44L, IFI44, IFIT3, LY6E, MX1) measured by quantitative real-time PCR. Patients with CNO were treated with standard 3-day regimen (1 mg/kg/day). We measured interferon score before pamidronate (Day 0, n=9) and after (Day 3, n=7).
Results: Median interferon score was 1.09 (0.96; 1.67) in CNO patients, 1.95 (1.3; 5.75) in soJIA, 7.6 (1.78; 29.0) in JDM and 16.9 (2.55; 40.3) in jSLE and 0.95 (0.82; 1.17) in HC (p=0.00001). Where were no difference in the IFN1 score between CNO and HC (p=0.222). In 6/7 CNO patients interferon score increased after pamidronate (p=0.015). The median interferon score after pamidronate increased and became 3.06 (0.87; 4,9, p=0.043); this may possibly explain the development of BF-related flu-like symptoms (cytokine release syndrome).
Conclusion: While interferon I-regulated pathway is not directly associated with CNO pathogenesis, BF likely activates interferon-I-regulated pathway and thus could be a possible cause of flu-like syndrome.
This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.508

AB0002 ASSOCIATION OF C1Q GENETIC POLYMORPHISMS WITH SUSCEPTIBILITY TO RHEUMATOID ARTHRITIS IN BULGARIAN COHORT

M. Kosturkova[1], G. Mihaylova[2], M. Radanova[2]. [1]*Varna Medical University, Propedeutics of Internal Diseases, Varna*; [2]*Varna Medical University, Biochemistry, Molecular Medicine and Nutrigenomics, Varna, Bulgaria*

Background: Complement is strongly implicated in the pathogenesis of autoimmune diseases like systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Its component C1q plays a dualistic role, triggering the inflammatory cascade on one hand and directing the clearance of immune complexes on the other. Homozygous genetic deficiency of C1q is strongly associated with SLE and SLE-like phenotype as almost 90% of C1q deficient individuals develop SLE or similar disease. Nevertheless, there are few and inconsistent studies exploring the single nucleotide polymorphisms (SNPs) of the C1q gene cluster in relation to the pathogenesis of SLE and RA.
Objectives: The aim of the study was to evaluate the possible association of five SNPs – rs292001, rs172378, rs294179, rs665691 and rs682658 in complement C1q gene cluster with susceptibility to SLE and RA in Bulgarian cohort.
Methods: Fifty patients with SLE, sixty-one patients with RA and sixty-seven healthy controls were genotyped for the five SNPs by TaqMan allelic discrimination assay.
Results: Frequency of genotypes and alleles of rs294179, rs665691 and rs682658 SNPs was similar between patients with SLE, RA and healthy controls. For rs172378 SNP, the minor G allele (OR = 2.73; 95% CI, 1.59-4.67, p=0.0003) and GG genotype (OR = 5.12; 95% CI, 1.60-16.49, p=0.006) were associated with susceptibility to RA. In our cohort in accordance with others, AA rs292001 SNP genotype was associated with increased risk for RA (OR = 3.32; 95% CI, 1.19-9.20, p=0.021). For SLE patients, AA rs292001 SNP genotype was low presented and did not associate with disease.
Conclusion: GG genotype of rs172378 SNP in C1q gene cluster could be considered as a new risk factor for RA.
REFERENCES:
[1] Diane Scott et al (2016). The paradoxical roles of C1q and C3 in autoimmunity. Immunobiology, 719-25. doi:10.1016/j.imbio.2015.05.001.
[2] Giles JL et al (2015). Functional analysis of a complement polymorphism (rs17611) associated with rheumatoid arthritis. J Immunol., 3029-34. doi:10.4049/jimmunol.1402956.
[3] Holers, V. M. (2018). Complement in the Initiation and Evolution of Rheumatoid Arthritis. Frontiers in immunology, 1057. doi:10.3389/fimmu.2018.01057.
[4] Lintner, K. E. (2016). Early Components of the Complement Classical Activation Pathway in Human Systemic Autoimmune Diseases. Frontiers in immunology, 36. doi:10.3389/fimmu.2016.00036.
[5] Lu, J. &. (2017). C1 Complex: An Adaptable Proteolytic Module for Complement and Non-Complement Functions. Frontiers in immunology, 592. doi:10.3389/fimmu.2017.00592.
[6] Manderson, A. P. (2004). The role of complement in the development of systemic lupus erythematosus. Annual review of immunology, 431-456. doi:10.1146/annurev.immunol.22.012703.104549.
[7] Martens, H. A. (2009). Analysis of C1q polymorphisms suggests association with systemic lupus erythematosus, serum C1q and CH50 levels and disease severity. Annals of the rheumatic diseases, 715–720. doi:10.1136/ard.2007.085688.
[8] Namjou B, G.-M. C. (2009). Evaluation of C1q genomic region in minority racial groups of lupus. Genes Immun., 517-24. doi:10.1038/gene.2009.33.
[9] Radanova M et al(2015). Association of rs172378 C1q gene cluster polymorphism with lupus nephritis in Bulgarian patients. Lupus, 280-9. doi:10.1177/0961203314555173.
[10] Rafiq S et al (2010). Assessing association of common variation in the C1Q gene cluster with systemic lupus erythematosus. Clin Exp Immunol., 284-9. doi:10.1111/j.1365-2249.2010.04185.x.
[11] Schejbel L et al (2011). Molecular basis of hereditary C1q deficiency-revisited: identification of several novel disease-causing mutations. Genes Immun., 626-634.
[12] Trouw LA et al (2013). Genetic variants in the region of the C1q genes are associated with rheumatoid arthritis. Clin Exp Immunol., 76-83. doi:10.1111/cei.12097.
[13] Trouw L. A. (2017). The complement system as a potential therapeutic target in rheumatic disease. Nature reviews. Rheumatology, 538–547. doi:10.1038/nrrheum.2017.125.
[14] Walport M. J. (2002). Complement and systemic lupus erythematosus. Arthritis research, S279–S293. doi:10.1186/ar586.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.989

AB0003 HLA-ALLELES IN SUSCEPTIBILITY TO SYSTEMIC AND OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS IN THE BELARUSIAN POPULATION

H. Yatskiu[1], A. Sukalo[2], R. Goncharova[1]. [1]*Institute of Genetics and Cytology of NAS of Belarus, Laboratory of Molecular Basis of Genomic Stability, Minsk, Belarus*; [2]*Belarusian State Medical University, 1st Department of Pediatric Diseases, Minsk, Belarus*

Background: Juvenile idiopathic arthritis (JIA) is a complex trait, the most common rheumatic disease in children. Considering clinical heterogeneity of the disease, the genetic background of particular JIA subtypes may also vary significantly.
Objectives: This work was aimed to reveal characteristic patterns of HLA associations within 11 loci for two clinically different forms of JIA in the Belarusian population.
Methods: 24 patients diagnosed with systemic JIA, 24 patients with oligoarticular JIA and 24 healthy controls were included into the study. The JIA patients were divided into subgroups according to IIAR classification criteria. High-throughput HLA typing was performed using TruSight HLA v2 Sequencing Panel (Illumina) on MiSeq system. Sample analysis was performed using Assign TruSight HLA v2.0 software.
Results: *DQA1**05:01:01 and *DQB1**02:01:01 alleles showed protective effect against both systemic (p = 0.007; OR=0.08; 95% CI=[0.009–0.65] and p = 0.01; OR=0.09; 95% CI=[0.01–0.83]) and oliarticular JIA

(p = 0.026; OR=0.16; 95% CI=[0.03–0.79] and p = 0.046; OR=0.2; 95% CI=[0.04–1.00], while for *DRB1**03:01 negative association was revealed only for systemic JIA (p = 0.03; OR=0.11; 95% CI=[0.01–0.88]). At the same time the *DQB1**04:02:01 (p=0.026; OR=5.88; 95% CI=[1.20–28.72]) and *DRB1**08:01:01 (p=0.07; OR=3.94; 95% CI=[1.01–15.39]) allele frequencies were significantly higher in patients with oligoarthritis but not systemic JIA when compared with controls.

Conclusion: High-throughput HLA typing revealed distinct HLA-alleles associated with different JIA subtypes in the Belarusian population as well as some alleles protective both for oligoartricular and systemic JIA.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1346

AB0004 THE ASSOCIATION OF THE RARE RS35667974 IFIH1 GENE POLYMORPHISM WITH SIX AUTOIMMUNE DISEASES: STRUCTURAL BIOLOGICAL INSIGHTS

M. Zervou[1], A. Andreou[2], G. Goulielmos[1], E. Eliopoulos[2]. [1]*University of Crete, Heraklion, Greece, Section of Molecular Pathology and Human Genetics, Department of Internal Medicine, School of Medicine, Heraklion, Greece*; [2]*Agricultural University of Athens, Department of Biotechnology, Athens, Greece*

Background: Genome wide association studies (GWAS) have successfully identified novel autoimmune disease-associated loci, with many of them shared by multiple disease-associated pathways but much of the genetics and pathophysiological mechanisms remain still obscure. Considering that most of the potential causal variants are still unknown, many studies showed that the missense variant rs35667974 at interferon induced with helicase C domain 1 (*IFIH1*) gene is protective for type 1 diabetes (T1D), psoriasis (PS) and psoriatic arthritis (PsA), while it was found to be also associated with ankylosing spondylitis (AS), Crohn's disease (CD) and ulcerative colitis (UC). *IFIH1* gene encodes a cytoplasmic RNA helicase that recognizes viral RNA and is involved in innate immunity through recognition of viral RNA [1].

Objectives: To investigate the role of the rare rs35667974 variant of *IFIH1* gene, which resides in exon 14 and changes a conserved isoleucine at position #923 to valine in T1D, PS, PsA, AS, CD and UC [2-4] as well as the mechanism that may affect the function in the protein structure.

Methods: Evolutionary analysis revealed heavily conserved sequence elements among species, indicating structural/functional importance of the mutation at position #923. *In silico* mutagenesis and three-dimensional (3D) homology modeling was used to localize the polymorphism under study on the IFIH1 protein. The mutant was constructed using molecular modeling with the program Maestro (Schrodinger, LLC) [5]. Molecular mechanics/dynamics studies were applied to validate structural/functional changes caused by the Ile923V substitution. All figures depicting 3D models were generated using the PyMOL molecular-graphics system V.2.2 [6].

Results: Evolutionary and **s**tructural analysis revealed that the position of residue Ile923 is located on a protein loop (921-927) directly interacting with mRNA both to the phosphoribose chain and the base pairs. Mutation of Ile to Val at position #923 will directly affect the said interaction with mRNA [7] (Figure 1). Moreover, it has been reported that pre-mRNA or mRNA levels did not correlate with Ile923Val, suggesting that, Ile923Val did not alter the expression of *IFIH1* in a major way [7].

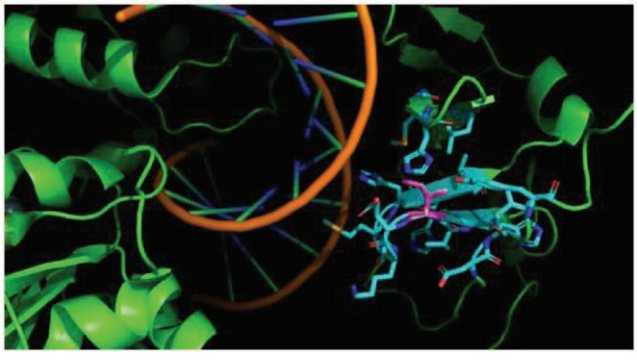


Figure 1. Structural representation of the interferon-induced helicase C domain-containing protein 1 [Homo sapiens] structure (4GL2 from Protein Data Bank) (in green) bound to the double stranded RNA (in orange-yellow). The location of the mutation (I923V) is highlighted in pink. The proximity of the aminoacid 923 to the nucleotide is apparent.

Conclusion: This study represents a comprehensive evaluation of the role of the shared rs35667974 variant of autoimmune locus *IFIH1*, reported to lead to a loss of function phenotype and, as a consequence, reduced levels of IFIH1 protein and activity that protect against autoimmunity. Structural analysis of rare shared genetic susceptibility or protection loci may provide insight to our understanding of the pathophysiology of autoimmune diseases and the research findings may affect the better management of the diseases under study.

REFERENCES:

[1] Nejentsev S *et al*. (2009). Science 324:387–389.
[2] Smyth DJ *et al*. (2006). Nat Genet. 38: 617–619.
[3] Li Y *et al*. (2010). J Invest Dermatol 130:2768–2772.
[4] Ellinghaus D *et al*. (2016). Nat Genet 48:510–518.
[5] Schrödinger Release 2017-1: Maestro, Schrödinger, LLC, New York, NY, 2017.
[6] Schrödinger LLC: The PyMOL Molecular Graphics System 2016 version 2.2.
[7] Wu B *et al*. (2013). Cell 152:276-289[8] Downes K *et al*. (2010). PLoS One 5:e12646.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1388

AB0005 IDENTIFICATION OF KEY GENES AND PATHWAYS FOR PSORIASIS BASED ON GEO DATABASES BY BIOINFORMATICS ANALYSIS

X. Sun[1], S. X. Zhang[2,3,4], S. Song[2,3,4], T. Kong[1], C. Zheng[1], L. Cheng[1], S. Feng[5], G. Shi[6], X. Li[2,3,4], P. F. He[7], Q. Yu[1,7]. [1]*Shanxi Medical University, School of Management, Taiyuan, China*; [2]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [3]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [4]*Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [5]*Shanxi Medical University, School of Humanities and Social Science, Taiyuan, China*; [6]*Shanxi Medical University, Basic Medical College, Taiyuan, China*; [7] *Shanxi Medical University, Institute of Medical Data Sciences, Taiyuan, China*

Background: Psoriasis is an immune-mediated, genetic disease manifesting in the skin or joints or both, and also has a strong genetic predisposition and autoimmune pathogenic traits[1]. The hallmark of psoriasis is sustained inflammation that leads to uncontrolled keratinocyte proliferation and dysfunctional differentiation. And it's also a chronic relapsing disease, which often necessitates a long-term therapy[2].

Objectives: To investigate the molecular mechanisms of psoriasis and find the potential gene targets for diagnosis and treating psoriasis.

Methods: Total 334 gene expression data of patients with psoriasis research (GSE13355 GSE14905 and GSE30999) were obtained from the Gene Expression Omnibus database. After data preprocessing and screening of differentially expressed genes (DEGs) by R software. Online toll Metascape[3] was used to analyze Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis of DEGs. Interactions of proteins encoded by DEGs were discovered by Protein-protein interaction network (PPI) using STRING online software. Cytoscape software was utilized to visualize PPI and the degree of each DEGs was obtained by analyzing the topological structure of the PPI network.

Results: A total of 611 DEGs were found to be differentially expressed in psoriasis. GO analysis revealed that up-regulated DEGs were mostly associated with defense and response to external stimulus while down-regulated DEGs were mostly associated with metabolism and synthesis of lipids. KEGG enrichment analysis suggested they were mainly enriched in IL-17 signaling, Toll-like receptor signaling and PPAR signaling pathways, Cytokine-cytokine receptor interaction and lipid metabolism. In addition, top 9 key genes (CXCL10, OASL, IFIT1, IFIT3, RSAD2, MX1, OAS1, IFI44 and OAS2) were identified through Cytoscape.

Conclusion: DEGs of psoriasis may play an essential role in disease development and may be potential pathogeneses of psoriasis.

REFERENCES:

[1] Boehncke WH, Schon MP. Psoriasis. *Lancet* 2015;386(9997):983-94. doi: 10.1016/S0140-6736(14)61909-7 [published Online First: 2015/05/31].
[2] Zhang YJ, Sun YZ, Gao XH, et al. Integrated bioinformatic analysis of differentially expressed genes and signaling pathways in plaque psoriasis. *Mol Med Rep* 2019;20(1):225-35. doi: 10.3892/mmr.2019.10241 [published Online First: 2019/05/23].
[3] Zhou Y, Zhou B, Pache L, et al. Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. *Nat Commun* 2019;10(1):1523. doi: 10.1038/s41467-019-09234-6 [published Online First: 2019/04/05].

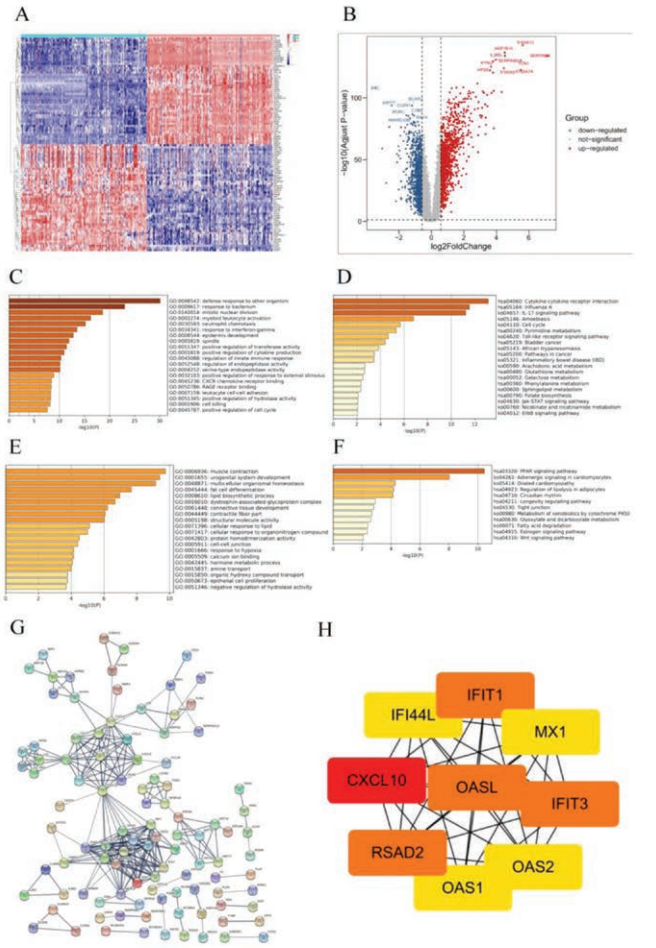


Figure 1: **(A)**Heatmap of DEGs: The red and blue colors represent up-regulation and down-regulation, respectively.**(B)**Volcano map of gene expression: The horizontal axis is log2 FC, the vertical axis is log10 adj.P.Val . Each dot represents a gene, blue indicates low expression genes, red indicates high. **(C,D,E,F)**Visualization GO enrichment analysis and KEGG pathway enrichment analysis. **(G,H)**PPI network and hub gene identification: Top 9 hub genes in the PPI network were screened by Cytoscape plugin Cytohubba based on their degree value (high degree value) to yellow (low degree value).

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1773

AB0006 GENETIC RISK PROFILE FOR PSORIATIC ARTHRITIS PREDISPOSITION IN ITALIAN PATIENTS

M. S. Chimenti[1], C. Ciccacci[2], G. De Benedittis[3], A. Latini[3], P. Conigliaro[1], G. L. Fonti[1], P. Triggianese[1], P. Borgiani[3], R. Perricone[1]. [1]*University of Rome Tor Vergata, Rheumatology, Allergology and Clinical Immunology, Rome, Italy*; [2]*UniCamillus - Saint Camillus International University of Health Sciences, Genetics Unit, Rome, Italy*; [3]*University of Rome Tor Vergata, Genetics Unit, Rome, Italy*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory joint disease typically associated with psoriasis and classified in the group of spondyloarthritis (1). The pathogenesis is based on an interplay of different genes interacting with several environmental factors including stress, trauma, infections, triggering an inflammatory response related to the activation of innate and acquired immunity in different tissues and organs (2). However, the risk for the development of PsA is not clearly understood.
Objectives: The aim of this study was to evaluate, in a cohort of Italian PsA out-patients of the Rheumatology Unit of the University of Rome Tor Vergata, the association of genetic variants in candidate genes for PSA susceptibility and their possible contribute in the modulation of clinical and laboratory features.
Methods: The genes were selected according to previous studies describing these genes as involved in susceptibility to rheumatoid arthritis (RA) (3), since a common genetic background can be shared between these diseases. Nine SNPs (single nucleotide polymorphism) in eight candidate genes were analysed: STAT4 (rs7574865), TRAF3IP2 (rs33980500), TNFAIP3 (rs6920220 and rs2230926), MIR146A (rs2910164), PSORS1C1 (rs2233945), IL-10 (rs1800872), HCP5 (rs3099844) and ERAP1 (rs27524). Polymorphisms were analysed in 163 consecutive PsA out-patients and 198 healthy controls (HC). Genotyping was performed by allelic discrimination by TaqMan assay. Alleles frequencies differences between cases and controls or between phenotypic groups were compared using Pearson's χ 2 test.
Results: We have observed an association between PSA susceptibility and the variant alleles of STAT4 [OR= 1.60 (1.15-2.21), P= 0.005], TRAF3IP2 [OR= 1.65 (1.01-2.65), P= 0.04], ERAP1 [OR= 1.40 (1.05-1.85), P= 0.02] and TNFAIP3 (rs6920220) [OR= 1.75 (1.19-2.57), P= 0.004]. On the contrary, the variant allele of IL-10 polymorphism seems to play a protective role [OR= 0.74 (1.05-1.85), P= 0.05]. Moreover, in order to define a genetic risk profile, we have counted the total number of risk alleles in each subject, considering as risk alleles the allelic variant of rs7574865 (STAT4), rs33980500 (TRAF3IP2), rs6920220 (TNFAIP3) and rs27524 (ERAP1) SNPs. Then, we have compared the risk allele number distribution between patients and HC (Fig.1). Classes with 3 or more risk alleles are significantly more represented in patients than in HC (OR= 2.03, P=0.004). The risk to develop the disease increases significantly in subjects with at least four risk alleles (OR= 2.96, P=0.002).

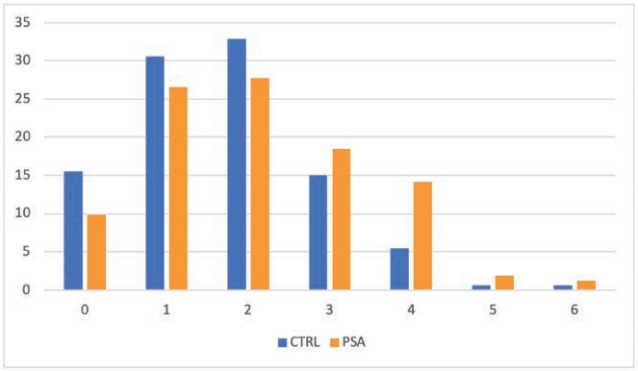


Figure 1. Number of risk alleles in patients and controls: rs7574865 (STAT4), rs33980500 (TRAF3IP2), rs6920220 (TNFAIP3) and rs27524 (ERAP1) SNPs.

Conclusion: We confirm the associations between five SNPs, already studied in RA, and PSA susceptibility, suggesting a common inflammatory pathway in chronic inflammatory rheumatological diseases. Moreover, we show how the genotyping of only few associated SNPs could help to define a genetic risk profile for PSA development.
REFERENCES:
[1] Calabresi E, et al. One year in review 2019: psoriatic arthritis. Clin Exp Rheumatol. 2020;38:1046-55.
[2] Chimenti MS, Triggianese P, De Martino E, Conigliaro P, Fonti GL, Sunzini F, Caso F, Perricone C, Costa L, Perricone R. An update on pathogenesis of psoriatic arthritis and potential therapeutic targets. Expert Rev Clin Immunol. 2019 Aug;15(8):823-836.
[3] Ciccacci C, et al. Polymorphisms in STAT-4, IL-10, PSORS1C1, PTPN2 and MIR146A genes are associated differently with prognostic factors in Italian patients affected by rheumatoid arthritis. Clin Exp Immunol. 2016;186:157-63.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1976

AB0007 STAT4 RS7574865 G/T POLYMORPHISM AS MARKER OF PREDISPOSITION TO SYSTEMIC LUPUS ERYTHEMATOSUS WITH JUVENILE ONSET

M. Kaleda[1], M. Krylov[2], I. Nikishina[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Pediatric Department, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Genetic Department, Moscow, Russian Federation*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with a significant genetic predisposition. Recent studies have identified STAT4 (signal transducers and transcription activators 4) as a susceptibility gene for SLE.
Objectives: To investigate the hypothesis of the association of STAT4 rs7574865 G/T polymorphism with the predisposition to SLE in children and its relationship with some of SLE manifestations.

Methods: The case-control pilot study included 143 children (39 with SLE and 103 healthy unrelated volunteers as a control group). Diagnosis of SLE was based on 2012 SLICC criteria. STAT4 rs7574865 G/T polymorphism was investigated using allele-specific real-time polymerase chain reaction (RT-PCR).
Results: The group of pts with SLE consisted of 29 girls and 10 boys, with an average age of 11.8±3.7 years (from 3 to 17 years) and an average disease duration of 4.1±2.4 years. 79.5% pts had acute cutaneous lupus at the onset, 46.1% - nonscarring alopecia, 71.8% - arthritis, 23.1% - oral and nasal ulcers, 23.1% - serositis, 43.6% - renal involvement, 35.9% –neuropsychiatric disorders. Leucopenia/lymphopenia was found in 71.8% of pts, thrombocytopenia – in 23,1%. ANA were detected in 100% pts, anti-dsDNA – in 79.5%, anti-Sm – in 31.6%, antiphospholipid antibodies - in 7,3%, hypocomplementemia – in 61.5%, positive direct Coombs test – in 35.9 %. Macrophage activation syndrome at the onset was documented in 15.4 % of pts. The distribution of rs7574865 genotypes in the control group showed no significant deviations from the Hardy-Weinberg equilibrium. The distribution of genotype frequencies among pts had statistically significant differences compared to the control (χ2=12.95, p=0.0015): GG-30.8% and 63.1% (p=0.001), GT-56.4% and 33.0% (p=0.018), TT-12.8% and 3.9% (p=0.114), GT+TT - 69.2% and 36.9% (p=0.0005). The frequency of the mutant STAT 4 allele T (polymorphism), was significantly higher in the SLE group than in the control group (41% and 20.4%, respectively; p=0.0007). We identified an association of the T allele with some clinical, laboratory, and immunological disorders in SLE: arthritis (OR 3.9, p=0.0002), acute cutaneous lupus (OR 2.47, p=0.003), nonscarring alopecia (OR 3.12, p=0.002), renal involvement (OR 2.42, p=0.022), leucopenia (OR 2.72, p=0.003), thrombocytopenia (OR 4.88, p=0.002), anti-dsDNA (OR 2.82, p=0.0006), hypocomplementemia (OR 2.34, p=0.012), positive direct Coombs test (OR 3.38, p=0.002).
Conclusion: Our pilot study confirmed that the STAT4 rs7574865 G/T polymorphism was associated with the risk of SLE in children and some of SLE manifestations.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2142

AB0008 APPLYING WHOLE EXOME SEQUENCING TO FAMILIAL ANTIPHOSPHOLIPID SYNDROME: NEW PLAYERS IN A RARE DISEASE?

A. Barinotti[1], M. Radin[1], I. Cecchi[1], S. G. Foddai[1], E. Rubini[1], D. Roccatello[1], S. Sciascia[1], E. Menegatti[1]. [1]*University of Turin, Clinical and Biological Sciences, Turin, Italy*

Background: Antiphospholipid Syndrome (APS) is an autoimmune disease whose precise aetiology is still unknown, but the high heterogeneity of its manifestations and clinical course is presumably due to the occurrence of different mechanisms and alterations at different levels and pathways [1]. The first genetic studies in APS focused primarily on the human leukocytes antigen system region, but more recent data highlighted a role of other genes in APS susceptibility, primarily those involved in the immune response and in the haemostatic process.
Objectives: We aimed to deepen the investigation of APS genetic background starting from a case of familial APS, analysing two siblings with thrombotic APS (Table 1), both triple positive for antiphospholipid antibodies (aPL).

Table 1. ***Main clinical and laboratory characteristics of the patients included in the study.***

Patient	Age	aPL Profile	Relevant Clinical History
1 (F)	51	Triple positive (LA, aCL IgG, aβ2GPI IgG)	Two episodes of ischemic stroke, one episode of CAPS (renal thrombotic microangiopathy, visual impairment, ischemic stroke)
2 (M)	47	Triple positive (LA, aCL IgG, aβ2GPI IgG)	Three episodes of deep vein thrombosis, regardless ongoing well conducted therapy vitamin k antagonist and additional retinal vein thrombosis

LA: lupus anticoagulant; aCL: anti-cardiolipin antibodies; aβ2GPI: anti- β2 glycoprotein I antibodies; CAPS: catastrophic APS.

Methods: Genomic DNA was extracted from peripheral blood and the samples underwent Whole Exome Sequencing (WES). Sequencing was done on a 100X coverage, and reads have been aligned to the human reference genome (GRCh37/hg19 assembly) using the Burrows–Wheeler Alignment tool (BWA). The mean sequencing depth on target regions was 170X for patient 1, 205X for patient 2, moreover, 99.50% of the targeted bases had at least 10X coverage for all the three donors. The resulting single nucleotide polymorphisms (SNPs) have been analysed through a step-by-step process based on their frequency population (using Genome Aggregation Database), their predicted effects on the protein (using VarSome) and a literature research about the genes carrying them. Moreover, genes previously associated with a pro-thrombotic tendency and with APS have been analysed in the two patients.
Results: Starting from more than 120000 SNPs for each patients, the analysis led to reduce the list of SNPs of interest to 27 missense mutations. The complete literature research regarding the genes carrying these mutations allowed to further reduce the number of selected genes, focusing on those that exert a role potentially involved in APS pathogenesis and development. In particular, these genes (*PLA2G6*, *HSPG2*, *BCL3*, *ZFAT*, *ATP2B2*, *CRTC3* and *ADCY3*) take part in the immune response and the vascular homeostasis. The list of the DNA missense variants of interest found in our cases of familial APS is resumed in Figure 2.

GENE	FULL NAME	SNP	CHR	COORDINATE	TRANSCRIPT	VARIANT EFFECT
CROCC	Ciliary rootlet coiled-coil / Rootletin	rs144279934 (A/T)	1	17270657	NM_014675.3	Missense variant (p.Gln624Leu)
HSPG2	**Heparan sulfate proteoglycan 2**	**rs766963773 (C/T)**	**1**	**22207015**	**NM_005529.5**	**Missense variant (p.Arg679His)**
KIF14	Kinesin family member 14	rs375895990 (C/T)	1	200573057	NM_014875.2	Missense variant (p.Arg598Gln)
ADCY3	**Adenylate cyclase 3**	**rs754839662 (C/T)**	**2**	**25050928**	**NM_004036.3**	**Missense variant (p.Val759Met)**
GRM7	Glutamate metabotropic receptor 7	rs1480175679 (A/C)	3	7494339	NM_181874.2	Missense variant (p.Lys697Thr)
SRGAP3	SLIT-ROBO Rho GTPase activating protein 3	rs76113478 (C/T)	3	9146461	NM_014850.3	Missense variant (p.Arg1086Gln)
ATP2B2	**ATPase plasma membrane Ca2+ transporting 2**	**rs751257556 (G/A)**	**3**	**10382352**	**NM_001001331.2**	**Missense variant (p.Ala985Val)**
OXNAD1	Oxidoreductase NAD binding domain containing 1	rs1456591626 (T/G) rs1159857217 (T/A) rs1390159575 (C/G)	3	16343175 16343176 16343177	NM_138381.3	Missense variant (p.Phe159Gln)
PDZD2	PDZ domain containing 2	rs1345334581 (C/G)	5	32098731	NM_178140.2	Missense variant (p.Pro2737Ala)
FAT2	FAT atypical cadherin 2	rs761199516 (C/A)	5	150945648	NM_001447.2	Missense variant (p.Ala4995er)
OR2F1	Olfactory receptor family 2 subfamily F member 1	rs777034277 (T/C)	7	143657370	NM_012369.2	Missense variant (p.Phe103Leu)
ZFAT	**Zinc finger and AT-hook domain containing**	**rs748139099 (G/A)**	**8**	**135596174**	**NM_020863.3**	**Missense variant (p.Arg930Cys)**
IFNA17	Interferon alpha 17	c.358A>T	9	21227855	NM_021268.3	Missense variant (p.Tyr119Phe)
ZNF462	Zinc finger protein 462	c.226A>T	9	109686419	NM_021224.4	Missense variant (p.Asn76Tyr)
MRPL48	Mitochondrial ribosomal protein L48	rs745995390 (G/T)	11	73555903	NM_016055.5	Missense variant (p.Asp85Tyr)
LTBP2	Latent transforming growth factor beta binding protein 2	rs1310944162 (G/A)	14	74995323	NM_000428.2	Missense variant (p.Ala744Val)
CRTC3	**CREB regulated transcription coactivator 3**	**c.163C>T**	**15**	**91083301**	**NM_022769.4**	**Missense variant (p.Leu55Phe)**
USP32	Ubiquitin specific peptidase 32	c.1169T>C	17	58313569	NM_032582.3	Missense variant (p.Leu390Pro)
IMPA2	Inositol monophosphatase 2	rs1423846345 (T/C)	18	12009980	NM_014214.2	Missense variant (p.Val110Ala)
MUC16	Mucin 16	rs200972932 (C/T)	19	9067504	NM_024690.2	Missense variant (p.Gln6648Lys)
CC2D1A	Coiled-coil and C2 domain containing 1A	c.791G>T	19	14028928	NM_017721.4	Missense variant (p.Arg265Leu)
MAP3K10	Mitogen-activated protein kinase kinase kinase 10	c.358G>A	19	46698296	NM_002446.3	Missense variant (p.Gln120Lys)
BCL3	**BCL3 transcription coactivator**	**rs747655476 (C/A)**	**19**	**45262063**	**NM_005178.4**	**Missense variant (p.Thr381Asn)**
MCM8	Minichromosome maintenance 8 homologous recombination repair factor	rs768426546 (G/A)	20	5953350	NM_001281521.1	Missense variant (p.Arg451His)
PLA2G6	**Phospholipase A2 group VI**	**rs780423461 (C/G)**	**22**	**38528920**	**NM_003560.2**	**Missense variant (p.Cys332Ser)**

Figure 2. List of DNA missense variants of interest found in patient 1 and 2.Genes potentially involved in APS pathogenesis and development are highlighted in bold.

No mutations on genes known to be associated with a pro-thrombotic state (*F5*, *F2*, *MTHFR*, *F13A1*, *PROC*, *PROS1*, *FGB* and *SERPINE1*), or on genes previously associated with APS (*B2GPI*, *PF4V1*, *SELP*, *TLR2*, *TLR4*, *GP Ia*, *GP1BA*, *F2R*, *F2RL1*, *TFPI*, *F3*, *VEGFA*, *FLT1*, and *TNF*) have been found in the WES analysis.
Conclusion: To some extent, this can be seen as a proof of concept of the complexity of APS. Efforts to interpret the genetic risk factors involved in the heterogeneous clinical features of the syndrome, for instance, the integration of WES and network-based approaches might help to identify and stratify patients at risk of developing APS.
REFERENCES:
[1] Iuliano A, Galeazzi M, Sebastiani GD. Antiphospholipid syndrome's genetic and epigenetic aspects. Autoimmun Rev. 2019;18(9).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2499

AB0009 ASSOCIATION OF STAT4 RS7574865, RUNX1 RS9979383, IL6 RS1800795, IL6R RS2228145, IL6R RS4845618 WITH SYSTEMIC LUPUS ERYTHEMATOSUS SUSCEPTIBILITY AND SOME LUPUS MANIFESTATIONS IN BELARUSIAN POPULATION

N. Dostanko[1], V. Yagur[1], R. Goncharova[2], E. Siniauskaya[2], T. Zybalova[1]. [1]*Belarusian State Medical University, 2-nd Department of Internal Medicine, Minsk, Belarus*; [2]*National Academy of Sciences of Belarus, Institute of Genetics and Cytology, Minsk, Belarus*

Background: Systemic lupus erythematosus (SLE) has a significant genetic predisposition. Many genetic variants of susceptibility to SLE have been published and analyzed, but the clinical and functional significance of the various genotypes has not yet been clearly defined [1].
Objectives: To estimate the association between some of non-HLA gene polymorphisms such as STAT4 rs7574865, RUNX1 rs9979383, IL6 rs1800795, IL6R rs2228145, IL6R rs4845618 and susceptibility to SLE in Belarusian population as well as some disease manifestations.
Methods: We examined 383 healthy blood donors and 54 SLE patients (18-72 years old, median age 35) classified according to the 1997 American College of Rheumatology (ACR) revised classification criteria [2]. Deoxyribonucleic acid was extracted from peripheral blood samples by phenol-chloroform method. Genotyping was performed by real-time PCR with fluorescent probes. Differences of distribution of all the single nucleotide polymorphism (SNP) genotypes and their associations with secondary antiphospholipid syndrom (APS) and lupus arthritis were analyzed using Pearson χ^2 (χ^2) and two-way Fisher exact test (F, $p_{2\text{-}t}$). Diagnostic odds ratio (dOR), likelihood ratio of positive (LR^+) and negative (LR^-) tests and corresponding 95% confidence intervals (CI) were also calculated.
Results: We revealed significant difference in STAT4 rs7574865 genotypes in SLE patients and healthy donors (χ^2=8,27, p=0,016) with significant increase of TT genotype frequency in SLE patients vs healthy donors (χ^2=6.83 p=0.009; $p_{2\text{-}t}$ =0.020; dOR=3.78 ($CI_{95\%}$ 1.36-10.55); LR^+ =3.44 ($CI_{95\%}$ 1.35-8.71); LR^- =0.91

($CI_{95\%}$ 0.83-0.98)). Lupus arthritis was more common in risk TT-genotype SLE carriers than in other SLE patients (χ^2=5.902 p=0.015; $p_{2\text{-}t}$ =0.027).
We revealed significant increase of CT genotype (RUNX1 rs9979383) in healthy donors vs SLE patients (χ^2=4.14; p=0.042; dOR=0.53 ($CI_{95\%}$ 0.29-0.98); LR^+ =0.69 ($CI_{95\%}$ 0.45-0.99); LR^- =1.3 ($CI_{95\%}$ 1.01-1,56)). Lupus arthritis was more common in SLE CT-genotype carriers than in other SLE patients (χ^2=4.66 p=0.031; $p_{2\text{-}t}$ =0.058).
Significant differences in IL6 rs1800795, IL6R rs2228145 and IL6R rs4845618 genotypes distribution between studied groups were not found (χ^2, p=0.427, p=0.559 and p=0.407, correspondingly) but GG-genotype (IL6 rs1800795) carriership in SLE patients was associated with increased APS frequency (χ^2=4.45, p=0.035; dOR=0.19 ($CI_{95\%}$ 0.04-0.9); LR^+ =0.28 ($CI_{95\%}$ 0.07-0.93); LR^- =1.41 ($CI_{95\%}$ 1.03-1.64).
Conclusion: Our data suggest the susceptibility to SLE in TT genotype of STAT4 rs7574865 polymorphism, protective role of CT genotype of RUNX1 rs9979383 for SLE and association between GG-genotype of IL6 rs1800795 and APS in SLE patients in Belarusian population. Lupus arthritis was associated with TT genotype of STAT4 rs7574865 and CT genotype of RUNX1 rs9979383.
REFERENCES:
[1] Chen L, Morris DL, Vyse TJ. Genetic advances in systemic lupus erythematosus: an update. Curr Opin Rheumatol 2017;29:423–33.
[2] Hochberg MC. Updating the American College of Rheumatology Revised Criteria for the classification of Systemic Lupus Erythematosus. Arthritis Rheum 1997;40:1725.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2523

AB0010 ASSOCIATION OF SAA1 GENE POLYMORPHISM -13T/C (RS12218) WITH ANKYLOSING SPONDYLITIS IN RUSSIAN POPULATION

I. Guseva[1], K. Sakharova[2], M. Krylov[1], E. Samarkina[1], S. Erdes[2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Spondyloarthritis, Moscow, Russian Federation*

Background: Ankylosing spondylitis is a chronic systemic inflammatory disease. Inflammation and high levels of serum amyloid A (SAA) protein are predisposing factors for secondary AA amyloidosis. The role of *SAA1* gene polymorphisms in AS is not well understood.
Objectives: To investigate the association of *SAA1* gene polymorphism -13T/C (rs12218) with ankylosing spondylitis and to evaluate the influence of this polymorphism on SAA protein concentration.
Methods: 123 AS patients (72 males, 51 females; age - M (SD) 37.51 (12.77) years; disease duration - 14.28 (11.22) years; BASDAI – 5.59 (1.13); B27-positive - 111 (90.2%) pts) and 95 gender, age matched healthy individuals (control group) were included in this study. *SAA1* gene polymorphism -13T/C was genotyped using allele-specific RT-PCR assay. SAA protein concentration was measured using nephelometry in AS patients.
Results: The distribution of genotypes TT, TC and CC differed statistically between AS and control groups (24.4%, 56.1%, 19.5% and 41.1%, 44.2%, 14.7% respectively, χ^2=6.9, p=0.03).
The presence of the C allele was associated with the development of AS (OR=1.55 [CI 1.04-2.33], p=0.03). The *SAA1* -13T/C polymorphism tended to be associated with SAA protein value in AS patients: TT+TC genotypes -13.8 mg/l [4.2; 91.0], CC genotype -7.8 mg/l [1.6; 29.6], p=0.07. ESR, CRP and BASDAI values did not correlated with *SAA1* - 13T/C polymorphism (p=0.6, p=0.4, p=0.4 respectively).
Conclusion: The results of our study demonstrated for the first time that *SAA1* gene polymorphism -13T/C (rs12218) is associated with susceptibility to AS. It is also shown that this polymorphism can affect the SAA protein level. Our findings need to be verified in AS patients with high levels of SAA protein in various ethnic and population groups.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2998

AB0011 EXPRESSION PROFILE AND POTENTIAL FUNCTION OF CIRCRNAS IN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH PRIMARY GOUT

Y. F. Qing[1], F. Dai[1], Q. B. Zhang[2], Y. P. Tang[1], Z. R. Dong[1], Y. X. He[1], Y. Jiang[1], Y. Q. Huang[2], J. Zheng[1]. [1]*Institute of Rheumatology and Immunology, Affiliated Hospital of North Sichuan Medical College, Department of Rheumatology and Immunology, Affiliated Hospital of North Sichuan Medical College, Nanchong, China*; [2]*Institute of Rheumatology and Immunology, Affiliated Hospital of North Sichuan Medical College, Department of Geriatrics, Affiliated Hospital of North Sichuan Medical College, Nanchong, China*

Background: Autophagy is a phenomenon of "self-phagocytosis" in eukaryotic cells, which maintains cell homeostasis by transporting intracellular materials to lysosomes for degradation and recycling. In recent years, studies have shown that autophagy may be involved in the pathogenesis of rheumatoid arthritis(RA) [1], but its specific mechanism is still unclear.
Objectives: The expression levels of autophagy-related genes(ATG) unc-51-like kinase 1(ULK1), ATG13, ATG17, microtubule associated protein 1 light chain 3 (LC3), and P62 in peripheral blood mononuclear cells (PBMC) of patients with RA were detected, and their role and clinical significance in the pathogenesis of RA were explored.
Methods: Real-time fluorescent quantitative PCR was performed to detect the expression levels of ULK1, ATG13, ATG17, LC3, and P62 in PBMCs of 50 RA patients, 50 healthy controls (HC), and 25 moderate to severe RA patients before and after treatment. Then, t test, χ2 test, Mann-Whitney U test, Pearson test were used for statistical analysis.
Results: 1.The levels of hsCRP, white blood cell(WBC), neutrophils(GR), platelet(PLT) and plateletcrit(PCT) in RA group were higher than those in HC group (P <0.05). Lymphocytes (LY), red blood cell(RBC), hemoglobin(HGB), hematocrit(HCT), mean corpuscular hemoglobin(MCH), mean red blood cell volume(MCV) and mean red blood cell hemoglobin concentration(MCHC) in RA group were lower than those in HC group (P <0.05). 2.The expressions of ULK1, ATG17, and LC3 in RA group were higher than those in HC group, while the expressions of P62 was lower than those in HC group(P<0.05) (Figure 1). The correlation analysis suggested that ATG17 was positively correlated with tender joint count (TJC), swollen joint count (SJC), and health assessment questionnaire (HAQ) (P<0.05); ULK1 and HAQ were negatively correlated (P<0.05).3. Compared with before treatment with TNFi, ATG17, HAQ, DAS-28, ESR, hsCRP, WBC, GR, PLT and PCT were significantly reduced after treatment (P<0.05); the expressions of RBC, HCT, MCV and MCH were significantly increased after treatment,(P<0.05); ULK1, ATG13, LC3, P62 and other related clinical and laboratory indicators were not significantly different before and after treatment with TNFi (P>0.05).

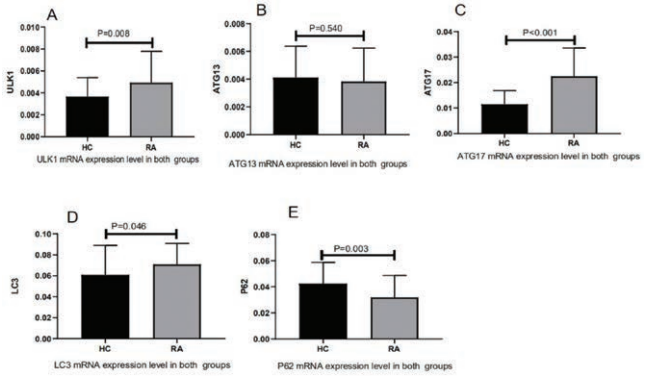


Figure 1. The expression levels of ATGs in HC and RA groups.

Conclusion: There is abnormal expression of autophagy genes in the peripheral blood of RA patients. ULK1, ATG17, LC3 and P62 may be related to the pathogenesis of RA, among them, ATG17 may regulate the pathogenesis of RA by participating in the TNF-α pathway.
REFERENCES:
[1] Rockel Jason S,Kapoor Mohit,Autophagy: controlling cell fate in rheumatic diseases.[J].Nat Rev Rheumatol, 2016, 12: 517-31.
Disclosure of Interests: Yu-Feng Qing Grant/research support from: Science and Technology Project of Nanchong City (no.18SXHZ0522), Fei Dai: None declared, Quan-Bo Zhang Grant/research support from: the National Natural Science Foundation of China(General Program) (no.81974250), and Science and Technology Plan Project of Sichuan Province (no.2018JY0257), Yi-Ping Tang: None declared, Zeng-Rong Dong: None declared, Yi-Xi He: None declared, Yi Jiang: None declared, Yu-Qin Huang: None declared, Jianxiong Zheng: None declared
DOI: 10.1136/annrheumdis-2021-eular.3081

AB0012 THE EFFECTS OF COMMON THERAPEUTICS ON AIRE METHYLATION STATUS AND THE LEVELS OF IL-16, IL-1B, AND IFN-Γ IN LPS-INDUCED MACROPHAGE CELLS CAN SULPHASALAZINE'S INFLUENCE ON METHYLATION STATUS OF AIRE EXPLAIN ITS AUTOIMMUNE SIDE EFFECTS?

Z. B. Çelik[1], C. Gunaydin[2], A. K. Cengiz[3]. [1]*19 Mayis University Medical Faculty, Medical Biology, Samsun, Turkey*; [2]*19 Mayis University Medical Faculty, Pharmacology, Samsun, Turkey*; [3]*19 Mayis University Medical Faculty, Physical Medicine and Rehabilitation-Rheumatology, Samsun, Turkey*

Background: The autoimmune regulator gene (*AIRE*) has very important role in self-tolerance. Estrogen induced hypermethylation of *AIRE* promoter was put forward as one of the reasons for susceptibility to autoimmunity in females. [1] Sulphasalazine is a commonly used drug in rheumatology and is known to be responsible for various autoimmune side effects.
Objectives: We aimed to investigate the effects of commonly used treatments on the methylation status of *AIRE* and levels of interleukin-16 (IL16), interleukin-1β (IL1β), and interferon-γ (IFNγ), in lipopolysaccharides (LPS)-induced RAW264.7 macrophage cells which mimic inflammatory state in rheumatoid arthritis in vitro.[2]
Methods: RAW264.7 cells were stimulated by LPS (1μ/mL). Cell viability test was performed to determine drug concentrations. Following drug treatments, cell media was isolated for the determination of IL16, IL1β, and IFNγ levels by ELISA. Also, the cells detached by trypsin-EDTA were used for DNA isolation and bisulfite modification. Then, the promoter methylation status of AIRE was analyzed with methylation-specific PCR and agarose jel electrophoresis.
Results: Our results demonstrated that the *AIRE* promoter is highly methylated in absence of any inflammatory stimulus.LPS treatment changed methylation status to unmethylated form. Leflunomide(LEF), sulfasalazine(SLZ) and methotrexate(MTX) significantly altered methylation status as the methylated (p=0.041,p<0.001,p<0.001, respectively). Surprisingly, SLZ treatment caused significantly more methylation in AIRE promoter than other drugs (p<0.001,-Fig 1A). Analysis of IL16, IL1β and IFNγ levels demonstrated that LPS caused potent increase in all three cytokines (p<0.001, Fig 1B-D). LEF and SLZ significantly prevented LPS-induced increase in these cytokines (p=0.025, p<0.001 for IL-16, p<0.001 for IL-1β and IFNγ, Fig 1B-D). Although MTX exacerbated LPS-induced increase in IL16 levels, it inhibited LPS induced increase in IL1β and IFNγ levels (p<0.001, Fig 1B-D).

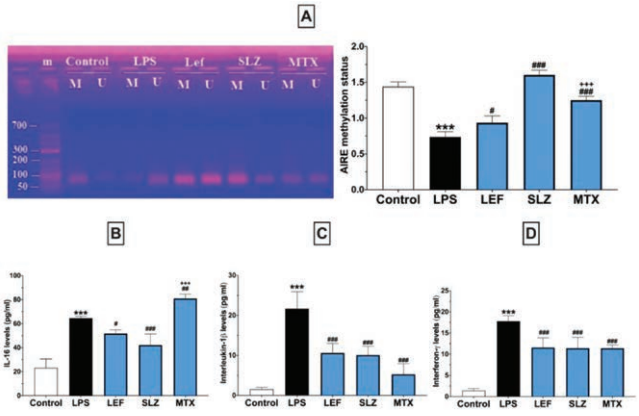


Figure 1. PCR gel image. All data expressed as mean±SD. ***p<0.001 versus control, ###p<0.001, #p<0.05 versus LPS, +++p<0.001 versus sulfasalazine.

Conclusion: Our results suggest that although LEF,SLZ and MTX potently suppresses LPS-induced inflammatory cytokines, they affect *AIRE* methylation differently.Changes in the methylation status of *AIRE* are important for autoimmunity. Relative increase in methylation of *AIRE* promoter by SLZ usage can be responsible for its autoimmune side effects, like drug induced lupus or hypersensitivity reactions, which are not common in MTX and LEF usage.
IL16 is a key regulator of biological properties of CD4+T cells, it also regulates migration of CD4+CD25+Treg cells.[3] MTX treatment was shown to increase Treg cells in early rheumatoid arthritis patients. LEF and SLZ's effect on Treg cells was shown to be different from that of MTX.[4] Our results demonstrated that MTX exacerbated LPS-induced increase in IL16 levels in contrary to LEF and SLZ. This difference may also be responsible for the different effect of these medications on Treg functions.
The different effect of commonly used disease modifying drugs on IL16 levels and methylation of *AIRE* promoter is interesting and deserves attention.
REFERENCES:
[1] Berrih-Aknin, Le Panse R, Dragin N. AIRE:a missing link to explain female susceptibility to autoimmune diseases. Ann.N.Y.Acad.Sci, 2018;1412(1):21-32.
[2] Lin Y-Y, Jean Y-H, Lee H-P et al. Excavatolide B attenuates rheumatoid arthritis through the inhibition of osteoclastogenesis. Marine Drugs, 2017; 15(1):9.
[3] Skundric DS, Cruikshank WW, Montgomery PC et al. Emerging role of IL-16 in cytokine-mediated regulation of multiple sclerosis. Cytokine, 2015;75(2):234-248.
[4] Oh JS, Kim Y-G, Lee SG et al. The effect of various disease modifying anti-rheumatic drugs on suppressive function of CD4+CD25+ regulatory Tcells. Rhematol Int. 2013;33:381-388.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3335

AB0013 ASSOCIATION BETWEEN STAT4 POLYMORPHISM AND MANIFESTATIONS OF SLE

V. Agarwal[1], S. Kakati[1], P. Debbaruah[2]. [1]*Assam Medical College and Hospital, Medicine, Dibrugarh, India*; [2]*Assam Medical College and Hospital, Anatomy, Dibrugarh, India*

Background: SNP rs7574865, located within the third intron of STAT4 gene at chromosome 2, has been associated with susceptibility to SLE among different ethnic groups.[1,2] Interestingly, we recently have documented an association between this gene and susceptibility to systemic lupus erythematosus (SLE) in Indian population.[3]
Objectives: To determine whether the STAT4 (rs7574865) SNP is associated with clinical and immunological manifestations in SLE.
Methods: The study was carried out on 100 unrelated SLE (SLICC criteria 2012) patients from North-East India. Genotyping of STAT4 rs7574865 SNP was done using Taqman probe and Real-Time Polymerase chain reaction. An association study was performed between the alleles and genotypes of STAT4 rs7574865 with the clinical and immunological manifestations included in the SLE SLICC classification criteria. For all analysis, the statistical significance was fixed at 5% level of significance ($p < 0.05$).
Results: The mean duration of illness was 2.69±2.55 years. Cases and Controls remained in Hardy-Weinberg equilibrium.The occurrence of Photosensitivity and hyperpigmentation was significantly higher in TT genotype group (97.22% and 77.77%, respectively) with p <0.001 in each case.SLE patients with nephritis (Albuminuria >500mg/24 hours) and elevated serum creatinine were both significantly higher in TT genotype group as compared to GT and GG (p< 0.001 and p=0.001 respectively).The Anti-dsDNA antibody was significantly associated with TT genotype (p <0.001).
Conclusion: Our study provides evidence regarding the association between STAT4 rs7574865 gene polymorphism is risk factor for cutaneous manifestations, Lupus nephritis and Anti ds-DNA positivity in SLE. So, our findings reinforce the need for further association studies including prospective studies with larger subjects in order to replicate such findings.
REFERENCES:
[1] Graham RR, Ph D, Hom G, Ph D, Behrens TW, Bakker PIW De, et al. and the Risk of Rheumatoid Arthritis and Systemic Lupus Erythematosus. N Engl J Med. 2007;357(10):977–86.
[2] Yuan H, Feng JB, Pan HF, Qiu LX, Li LH, Zhang N, et al. A meta-analysis of the association of STAT4 polymorphism with systemic lupus erythematosus. Mod Rheumatol. 2010;20(3):257–62.
[3] Gupta V, Kumar S, Pratap A, Singh R, Kumari R, Kumar S, et al. Association of ITGAM, TNFSF4, TNFAIP3 and STAT4 gene polymorphisms with risk of systemic lupus erythematosus in a North Indian population. Lupus. 2018;27(12):1973–9.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3470

AB0014 METHOTREXATE - IMPLICATIONS OF PHARMACOGENETICS IN THE TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS

R. Pinheiro Torres[1,2], F. Pimentel Dos Santos[1,2,3], J. Branco[1,2,3]. [1]*Hospital Egas Moniz, Rheumatology, Lisboa, Portugal*; [2]*CEDOC, Rheumatology, Lisboa, Portugal*; [3]*Nova Medical School, Rheumatology, Lisboa, Portugal*

Background: Methotrexate (MTX) is an anti-folate drug with anti-proliferative and anti-inflammatory effects. MTX proved to be the most highly effective, fast-acting disease modifying anti-rheumatic drug (DMARD), being widely used for the treatment of rheumatoid arthritis (RA) (1).
Objectives: This review aims to describe the main genetic variants identified concerning proteins that play a role in methotrexate's kinetics and efficiency profile.
Methods: A literature review was conducted since January of 2000 until December 2020, by searching the PubMed and Embase bibliographic databases, employing the following MeSH terms: methotrexate, pharmacogenetics, pharmacokinetics and rheumatoid arthritis. The search was limited to articles in English language. Two independent reviewers screened the titles and abstracts followed by a full-text review to assess papers regarding their eligibility. A total of 48 articles matched the research criteria and were analysed.
Results: Genetic variants of four main proteins, with different functions, have been consistently described.
Reduced folate carrier 1 (RFC1), a constitutively expressed folate transport protein that has high affinity for MTX is responsible, almost exclusively, for the transport of folate and MTX into the cell. The most commonly studied variant of the gene is the 80G > A variant (rs1051266), mapped within exon 2, on chromosome 21. It seems to improve RA responses to MTX, clinical efficacy with long disease remission (2).

ABC transporters are involved in the eflux of MTX from cells. An increased expression and function of these transporters should decrease MTX concentrations in target cells, resulting in lack of therapeutic response. *ABCB1 3435* C/T (rs1045642) is a high frequency polymorphism, significantly associated with RA good responses, symptom remission and reduced adverse events, due to MTX treatment (3).
Thymidylate synthase (TYMS) is involved in thymidine synthesis. MTX decreases TYMS activity by inhibition and decreasing the access to tetrahydrofolate (THF) cofactors (1). The most common genetic variant of the TYMS gene consists of a 28 bp tandem repeat (rs34743033), with double and triple number of repeats (2R and 3R). The 3R allele genotype was associated with decreased efficacy and increased toxicity (4).
The 5,10-methylenetetrahydrofolate reductase (MTHFR) enzyme is indirectly inhibited by MTX. The most common SNPs of the MTHFR gene are C677T (rs1801133) and A1298C (rs1801131). Both are associated with a decreased efficacy and an increased toxicity of MTX (5).
Conclusion: MTX response is affected by many gene variants; the effect of each variant separately is likely to be small. Additionally, gene-gene interaction, enhancing the potential role of linkage disequilibrium. This shows the emerging need for a better gene characterization and to improve the knowledge about variants distribution according to ethnicity, to explain different responses to MTX at an individual level.
REFERENCES:

[1] Song, G. et al. Association of the MTHFR C677T and A1298C polymorphisms with methotrexate toxicity in rheumatoid arthritis: a meta-analysis. *Clin Rheumatol* **33,** 1715–1724 (2014).
[2] Hayashi H. et al. A single nucleotide polymorphism of reduced folate carrier 1 predicts methotrexate efficacy in Japanese patients with rheumatoid arthritis. Drug Metab Pharmacokinet. 2013;28(2):164-8.
[3] Zhu H. et al. Pharmacogenetics and pharmacogenomics for rheumatoid arthritis responsiveness to methotrexate treatment: the 2013 update. Pharmacogenomics. 2014 Mar;15(4):551-66.
[4] Owen SA. et al. Genetic polymorphisms in key methotrexate pathway genes are associated with response to treatment in rheumatoid arthritis patients. Pharm J. 2013;13:227–34.
[5] Hughes LB. et al. Racial or ethnic differences in allele frequencies of single-nucleotide polymorphisms in the methylenetetrahydrofolate reductase gene and their influence on response to methotrexate in rheumatoid arthritis. Ann Rheum Dis. 2006;65:1213–8.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3749

AB0015 **STUDY OF VDR AND VDBP GENES AS CANDIDATE SUSCEPTIBILITY GENES FOR THE DEVELOPMENT OF IMMUNE-MEDIATED DISEASES IN THE PARAGUAYAN POPULATION**

I. Acosta-Colman[1], M. Vazquez[1], S. Cabrera-Villalba[1], A. Ayala-Lugo[2], M. E. Acosta[2], I. Arevalo de Guillen[2], V. Jolie[2], M. Duarte[1], V. Valinotti[1], R. Contreras[3], G. Avila[1], T. Martinez[4], A. Juliá[5], S. Marsal[5]. [1]*Hospital de Clinicas, Universidad Nacional de Asuncion, Rheumatology, Asunción, Paraguay*; [2]*Insituto de Investigaciones en Ciencias de la Salud, UNA, Asunción, Paraguay*; [3]*Hospital de Clinicas, Universidad Nacional de Asuncion, Dermatology, Asunción, Paraguay*; [4]*Laboratorio Curie, Laboratorio Curie, Asunción, Paraguay*; [5]*Hospital General Vall d'Hebron, Vall d'Hebron Institut de Recerca, Barcelona, Spain*

Background: Immune Mediated Inflammatory Diseases (IMIDs) are complex diseases that are believed to have a strong interaction between the genome and the environment as part of their aetiology. In studies using the candidate gene strategy, genetic variation in a gene where functionality has been associated with the pathophysiology of the disease under study is being analyzed. In the last decade, polymorphisms of the vitamin D receptor (VDR) and VDBP genes have been more emphatically studied in IMIDs in different populations, but the results reported have not yet been conclusive.
Objectives: To identify an association between vitamin D receptor (VDR) and vitamin D-binding protein (VDBP) gene polymorphisms, and IMIDs in Paraguayan patients.
Methods: Association study of VDR (SNPs rs731236, rs7975232, rs2228570) and VDBP (rs4588) gene polymorphisms with susceptibility to IMIDs in Paraguayan population. A total of 399 patients with IMIDs (i.e. Systemic Lupus Erythematosus (SLE), Scleroderma (ES), Rheumatoid Arthritis (RA), and Cutaneous Psoriasis (CPS) and 100 hypernormal controls (HC) from the same population were included in this study. Genotyping was performed using Taqman real-time PCR-based technology (Life Technologies, USA). Statistical analysis was performed using Rv3.0.1 statistical language software (www.R-project.org). A p value ≤ 0.05 was used for statistical significance.
Results: A total of 399 individuals, 100 controls and 299 patients (99 RA, 100 SLE, 50 ES, and 50 PSO) were included. Seventy-six percent were female and 24% were male. The mean age was 43.7±14 years. Four SNPs were genotyped: rs731236, rs7975232, rs2228570, rs4588. The HWE test was not statistically significant for any of the 4 SNPs considered (P>0.05), confirming the quality of genotyping and the absence of technical bias. (Table 1).

Table 1. Genotyping of SNPs of the VDR and VDBP gene in Paraguayan population with IMIDs.

SNP	IMID	Minor Allele	Major Allele	MAF Control	MAF Case	OR	IC.L	IC.H	p allelic	P.Genetic
rs731236	SLE	G	A	0.5	0.4	0.64	0.42	0.97	0.035	0.08
rs731236	RA	G	A	0.5	0.41	0.69	0.46	1.05	0.071	0.12
rs731236	SS	G	A	0.5	0.42	0.71	0.42	1.18	0.18	0.37
rs731236	CPS	G	A	0.5	0.38	0.6	0.36	1.01	**0.049**	**0.042**
rs2228570	SLE	A	G	0.36	0.38	1.14	0.74	1.74	0.6	0.45
rs2228570	RA	A	G	0.36	0.31	0.83	0.53	1.28	0.4	0.56
rs2228570	SS	A	G	0.36	0.36	1.02	0.6	1.73	1	0.057
rs2228570	CPS	A	G	0.36	0.39	1.16	0.68	1.96	0.61	0.83
rs7975232	SLE	C	A	0.36	0.32	0.82	0.53	1.26	0.4	0.072
rs7975232	RA	C	A	0.36	0.29	0.72	0.46	1.12	0.14	0.064
rs7975232	SS	C	A	0.36	0.22	0.49	0.27	0.88	**0.012**	**0.0064**
rs7975232	CPS	C	A	0.36	0.41	1.21	0.72	2.03	**0.45**	**0.016**
rs4588	SLE	T	G	0.23	0.27	1.24	0.77	2	0.42	0.48
rs4588	RA	T	G	0.23	0.22	0.93	0.56	1.53	0.81	0.84
rs4588	SS	T	G	0.23	0.21	0.89	0.47	1.65	0.77	0.76
rs4588	CPS	T	G	0.23	0.29	1.37	0.76	2.43	0.26	0.53

Conclusion: There is evidence of nominal association between VDR SNPs: rs731236 (in SLE and CPS), and rs7975232 (in SS and CPS) and the presence of IMIDs disease in Paraguayan patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4299

Adaptive immunity (T cells and B cells) in rheumatic diseases

AB0016 **THE IMPACT OF IL-17A THERAPY ON IGG SIALYLATION IN HUMANS**

R. Pfeifle[1,2], J. Kittler[1], M. Wuhrer[3], G. Schett[1], G. Krönke[1]. [1]*University Hospital Erlangen, Department of Internal Medicine 3 and Institute of Clinical Immunology, Erlangen, Germany*; [2]*Friedrich-Alexander University, Nikolaus-Fiebiger Center of Molecular Medicine, Erlangen, Germany*; [3]*Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*

Background: Rheumatoid arthritis (RA) is characterized by autoreactive B- and T cells. Autoantibodies are a hallmark of RA and contribute to synovial inflammation. We have recently demonstrated that Th17 cells suppress the enzyme ST6 a-galactoside b-2,6-sialyltransferase (ST6GAL1) in developing plasma cells. Thereby, Th17 cells regulate the degree of autoantibody sialylation leading to the increased inflammatory activity of autoantibodies. These events correlate with the onset of RA, arguing for a crucial role of the IL-23/Th17 axis during the transition of asymptomatic autoimmunity into active RA. Therefore, treatment against the IL-23/TH17-axis might present an attractive therapeutic approach to halt or delay RA's onset. However, the effects of Th17 cytokines like IL-17 on IgG glycosylation in humans are so far poorly studied.
Objectives: To explore whether anti-IL17A treatment can inhibit pro-inflammatory IgG glycosylation patterns in humans.
Methods: Total IgG from patient cohorts suffering from psoriatic arthritis (PsA) treated with Secukinumab (anti-IL-17 blockade, n=26) or Ustekinumab (anti-IL12/23 blockade, n=14) was compared with patients treated with anti-TNFa blockade as a control (n=20). The cohorts were age- and sex-matched and included patients being on therapy for at least six months. Total IgG was isolated using Protein G columns, and IgG glycopeptides of IgG1, IgG2, and IgG4 were analyzed using the LC-MS technique. The effect of IL-17 depletion on IgG glycosylation was analyzed in psoriatic arthritis patients who have been treated with secukinumab for at least six months. Furthermore, in a longitudinal approach, IgG1, IgG2, and IgG4 glycosylation were analyzed from samples, isolated before the beginning of anti-IL-17 blockade and after at least six months of therapy (n=16).
Results: Cross-sectional comparison of cohorts treated with Ustekinumab, Sekukinumab, and anti-TNFa therapy did not show any significant differences in sialylation, galactosylation, or fucosylation of IgG1 and IgG2. IgG4 from anti-TNFa treated patients displayed a small increase of sialylation when compared to the Ustekinumab treated cohort.
Longitudinal analyses, however, showed that IL-17A blockade during Secukinumab therapy caused a significant increase of sialic acid-rich IgG glycoforms on IgG1, IgG2 IgG4 patients, while the galactosylation, fucosylation remained unaffected.
Conclusion: This data indicates that IL-17A blockade specifically affects IgG sialylation, while other Fc-glycan modifications remain unaltered. This data confirms our recent findings in mice, where cytokines of the IL-23/Th17 axis specifically induce the production of hypo-sialylated, proinflammatory autoantibodies in

rheumatoid arthritis (RA) [2]. Therefore, neutralizing IL-17 might be a therapeutic option during the asymptomatic autoimmune prodromal phase in autoimmune diseases like RA, where TH17 cytokines orchestrate the emergence of a pro-inflammatory autoantibody response and the transition into active RA.

REFERENCES:

[1] McInnes IB, G. Schett, The pathogenesis of rheumatoid arthritis. N Engl J Med 2011; 365: 2205-19.

[2] Pfeifle R et al, Regulation of autoantibody activity by the IL-23-Th17 axis determines the onset of autoimmune disease. Nat Immunol. 2017, Jan;18(1):104-113.

Disclosure of Interests: Rene Pfeifle Grant/research support from: Novartis AG., Julia Kittler: None declared, Manfred Wuhrer: None declared, Georg Schett: None declared, Gerhard Krönke Grant/research support from: Novartis AG

DOI: 10.1136/annrheumdis-2021-eular.1087

AB0017 IMMUNE CHARACTERISTICS OF PERIPHERAL BLOOD IN SECONDARY SJOGREN'S SYNDROME PATIENTS WITH RHEUMATOID ARTHRITIS

R. Su[1], Y. Y. Wang[1], C. Wang[1]. [1]*The Second Hospital of Shanxi Medical University, Rheumatology, Taiyuan, China*

Background: Secondary Sjogren's Syndrome (sSS) is diagnosed when symptoms of SS coexist with other systemic connective tissue disease, often secondary to rheumatoid arthritis(RA).The occurrence of SS secondary with RA will worsen the course of disease and increase the high incidence and mortality of RA. At present, the immune characteristics of peripheral blood of sSS with RA are not clear.

Objectives: To observe the difference of immune Immune characteristics in peripheral blood between sSS secondary to RA, primary Sjogren's syndrome(pSS) and RA patients.

Methods: 20 sSS with RA patients, 20 pSS paients and 20 RA pateints hospitalized in ShanXi medical university the second Hospital were enrolled. The percentage and absolute numbers of lymphocyte phenotypes and CD4+ T subsets in peripheral blood were examined by flow cytometry.

Results: As for the percentage and absolute number of total T, B, NK, CD4+T,CD8+ T and the ratio of CD4 + T to CD8+ T cells, there was no significant difference between the sSS with RA, RA, and SS group. There was also no statistical difference in the percentage of CD4+T subsets(Th1,Th2,Th17 and Treg) between the three groups. But the ratio of Th17 and Treg in sSS with RA group was increased than pSS group.About comparison of absolute number of CD4+T subsets, there was no statistical difference among the three groups except that the Th1 cells in RA group was significantly higher than SS group.

Conclusion: Elevated Th17/Treg may be an immunological feature that differentiates sSS with RA patients from pSS patients. In addition, in general, peripheral blood of patients with RA and SS have similar immune characteristics.

REFERENCES:

[1] Wei W,Ahmad S S, Chi S. From Molecular Mechanism to the Etiology of Sjogren Syndrome.Curr Pharm Des. 2018;24(35):4177-4185.

[2] Hajiabbasi A, Masooleh I S,Alizadeh Y, Secondary Sjogren's Syndrome in 83 Patients With Rheumatoid Arthritis.Acta Med Iran.2016;54(7):448-53.

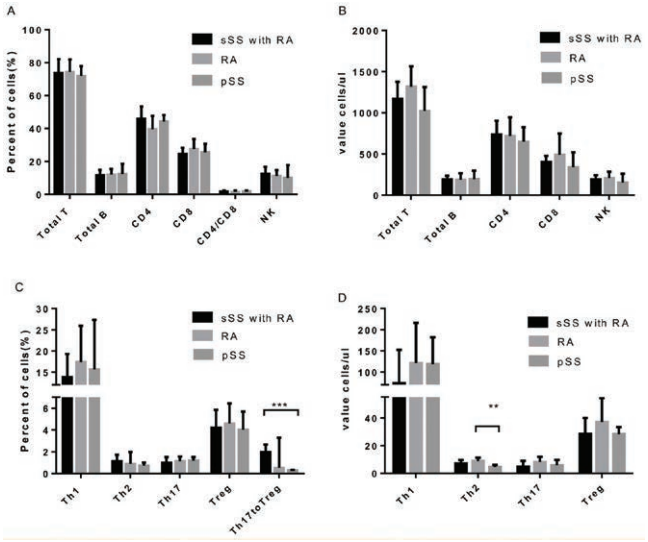


Figure 1. The comparsion about the lymphocyte phenotypes and CD4+ T subsets in peripheral blood of sSS with RA(n=20), pSS(n=20) and RA patients(n=20).(*p<0.05,**p<0.001,*p<0.0001)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1158

AB0018 ACCUMULATION OF FUNCTIONALLY MATURE CD1C+ DENDRITIC CELLS CONTRIBUTES TO SYNOVIAL INFLAMMATION IN INFLAMMATORY ARTHRITIS

M. Canavan[1,2], V. Marzaioli[1,2], V. Bhargava[3], S. Nagpal[3], P. Gallagher[4], C. Hurson[4], R. Mullan[5], D. Veale[2], U. Fearon[1,2]. [1]*Trinity College Dublin, Molecular Rheumatology, Dublin, Ireland*; [2]*St Vincent's University Hospital, Centre for Arthritis and Rheumatic Diseases, Dublin, Ireland*; [3]*Janssen Research and Development, Immunology and Discovery Sciences, Pennsylvania, United States of America*; [4]*St Vincent's University Hospital, Department of Rheumatology, Dublin, Ireland*; [5]*Adelaide and Meath Hospital, Department of Rheumatology, Dublin, Ireland*

Background: Myeloid Dendritic Cells (DC) are potent antigen presenting cells that can be subdivided into CD141 and CD1c$^+$ DC. We have previously reported an unacknowledged role for CD141$^+$DC in the IA synovium. However, the identification and function of CD1c$^+$ DC in the IA synovium has yet to be fully elucidated.

Objectives: To investigate if CD1c$^+$DC reside in the IA synovium and ascertain if they represent a unique population, distinct from peripheral CD1c$^+$DC and if they contribute to synovial inflammation.

Methods: Synovial tissue (ST) biopsies and synovial fluid mononuclear cells (SFMC) were obtained via arthroscopy and healthy control (HC) ST was obtained during ACL surgery. Synovial tissue single cells suspensions were generated following enzymatic and mechanical digestion. Single cell analysis of synovial tissue cell suspensions, along with PBMC and SFMC was performed by multicolour flow cytometry. CD1c$^+$DC were sorted from IA synovial fluid and peripheral blood and bulk RNA sequencing was performed. CD1c$^+$DC functionality and maturation was assessed using OVA DQ phagocytosis assays, multiplex ELISA and DC: T cell cocultures.

Results: Within the circulation the frequency of CD1c$^+$DC are significantly decreased in IA peripheral blood compared to HC ($p<0.01$) in addition to expressing significantly higher levels of the maturation markers CD80 ($p<0.01$) and CD40 ($p=0.08$). IA peripheral blood DC also express significantly higher levels of CXCR3 ($p<0.01$) and CCR7 ($p<0.05$) compared to HC - suggestive of DC migration from the periphery to the synovium. Following RNA-seq analysis, IPA and differentially expressed gene (DEG) analysis revealed an enrichment in genes involved in DC maturation, TLR signalling and chemokine signalling in IA peripheral blood compared to HC. In support of the hypothesis that DC migrate and accumulate in the IA synovium, CD1c$^+$ DC were identified in IA ST and were significantly enriched compared to IA peripheral blood ($p<0.01$). IA ST CD1c$^+$DC express significantly higher levels of the activation marker CD80 compared to IA peripheral blood ($p<0.05$) or HC ST ($p<0.05$). Upon examination of IA synovial fluid, we report similar findings to ST, whereby CD1c$^+$DC are enriched in synovial fluid compared to PB ($p<0.001$). Moreover, RNA sequencing and PCA analysis of synovial versus blood CD1c$^+$DC revealed distinct transcriptional variation between both sites. Functionally, synovial CD1c$^+$DC express higher levels of the maturation markers CD80, CD83, CD40, PD-L1 and BTLA (all $p<0.05$) and have distinct coexpression of these maturation markers which is unique to the synovium. Synovial CD1c$^+$DC are less phagocytic compared to peripheral blood DC, have decreased production of MMP1 and MMP9 and importantly are still capable of additional activation *in-vitro*. Finally, synovial CD1c$^+$DC induce the proinflammatory cytokines TNFα, GMCSF, IL-17a and IFNγ from CD4$^+$ T-cells in allogeneic DC: T cells cocultures.

Conclusion: Mature circulatory CD1c$^+$DC migrate and accumulate in the IA synovium. Synovial DC are present in the IA synovium in a mature state, have distinct tissue specific characteristics and can induce proinflammatory CD4$^+$T cell responses.

Acknowledgements: We would like to thank all the patients who contributed to this study

Disclosure of Interests: Mary Canavan: None declared, Viviana Marzaioli: None declared, Vipul Bhargava Employee of: Janssen Research and Development, Sunil Nagpal Employee of: Janssen Research and Development, Phil Gallagher: None declared, Conor Hurson: None declared, Ronan Mullan: None declared, Douglas Veale Speakers bureau: Abbvie, Janssen, Novartis, Pfizer, MSD, UCB, Consultant of: Abbvie, Janssen, Novartis, Pfizer, MSD, UCB, Grant/research support from: Pfizer, Janssen, AbbVie, UCB, Ursula Fearon Speakers bureau: Abbvie, Grant/research support from: Pfizer, Janssen, Abbvie, UCB

DOI: 10.1136/annrheumdis-2021-eular.1584

AB0019 TREATMENT OF AUTOIMMUNE AND INFLAMMATORY SKIN DISEASES USING SKIN-TARGETING BIFUNCTIONAL ANTIBODIES: A LOCALIZED IMMUNOMODULATION APPROACH

S. Borthakur[1], P. Mande[2], D. Rios[2], P. Halvey[2], A. Boisvert[1], M. Rowe[2], A. Agrawal[1], M. Borah[2], M. Cianci[2], J. L. Viney[2], K. Kis-Toth[2], K. L. Otipoby[2], I. Mascanfroni[2], N. Higginson-Scott[1]. [1]*Pandion Therapeutics Inc., Biotherapeutics, Watertown, United States of America*; [2]*Pandion Therapeutics Inc., Immunology, Watertown, United States of America*

Background: Current treatment approaches for autoimmune conditions comprise primarily of systemic immunosuppressants or cytokine blockade. The concentration of therapeutic molecules to the tissues that are the sites of autoimmune and inflammatory diseases is a promising approach with the potential to induce therapeutic benefit and avert risks associated with systemic immunotherapies. Pandion Therapeutics is developing a bifunctional antibody platform that can drive localized immune modulation by combining a "tether antibody" that targets a tissue of choice and "an effector end" that activates specific regulatory immune pathways to restore immune-homeostasis.
Objectives: Here we report the engineering of a skin-tethered PD-1 agonist and a skin-tethered CD39 that inhibit T cell activation and function and deplete local ATP, respectively, modulating different arms of the immune system in a tissue specific manner.
Methods: Biophysical assays were performed to characterize Skin-tethered immune effectors for drug-like properties and *in vitro* and *in vivo* assays for target binding, cellular activity and tissue specific-localization. Moreover, these bifunctionals were tested in pathway-relevant preclinical models such as Vitiligo and Contact Hypersensitivity.
Results: Biophysical characterization of the bifunctional molecules showed desired drug like properties including specificity, stability, and manufacturability. The skin tethered bifunctionals showed effector activity in *in vitro* assays and selectively localized to the skin. Skin localization strikingly correlated with a tether-dependent efficacy compared to a non-tether control.
Conclusion: We believe that this therapeutic approach has the potential to drive the resolution of cutaneous inflammation, providing an opportunity for developing new targeted therapies for autoimmune and inflammatory skin diseases.
Disclosure of Interests: Susmita Borthakur Shareholder of: Pandion Therapeutics Inc., Employee of: Pandion therapeutics Inc., Purvi Mande: None declared, Daniel Rios: None declared, Patrick Halvey: None declared, Angela Boisvert: None declared, MIchael Rowe: None declared, Anisha Agrawal: None declared, Minasri Borah: None declared, Mike Cianci: None declared, Joanne L. Viney Shareholder of: Pandion therapeutics Inc., Consultant of: Harpoon, Finch, Quench, HotSpot, Employee of: Pandion Therapeutics Inc., Katalin Kis-Toth: None declared, Kevin L. Otipoby Shareholder of: Pandion Therapeutics Inc., Employee of: Pandion Therapeutics Inc., Ivan Mascanfroni: None declared, Nathan Higginson-Scott Shareholder of: Pandion Therapeutics Inc., Consultant of: Mediar Tx, Employee of: Pandion Therapeutics Inc.
DOI: 10.1136/annrheumdis-2021-eular.1665

AB0020 ACPA ILLUSTRATING THE IMPACT OF IGG FAB-GLYCOSYLATION ON TRANSPLACENTAL TRANSFER OF ANTIBODIES AND THEIR BINDING TO THE NEONATAL FC-RECEPTOR (FCRN)

M. Volkov[1], K. Van Schie[1], A. Bondt[2], T. Kissel[1], M. Brinkhaus[3], A. Bentlage[3], C. Koeleman[4], S. De Taeye[3], R. Dolhain[5], M. Wuhrer[4], R. Toes[1], G. Vidarsson[3], D. Van der Woude[1]. [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [2]*Utrecht University, Biomolecular Mass Spectrometry and Proteomics, Utrecht, Netherlands*; [3]*Sanquin Research, Immunoglobulin Research, Amsterdam, Netherlands*; [4]*Leiden University Medical Center, Center for Proteomics and Metabolomics, Leiden, Netherlands*; [5]*Erasmus Medical Center, Rheumatology, Rotterdam, Netherlands*

Background: Fc neonatal receptor (FcRn) is crucial for IgG half-life and transplacental transport. Different sites of IgG carry glycans which may affect binding to FcRn. While the effect of Fc-glycans has been investigated, the impact of Fab-glycosylation (~14% IgG) on IgG-FcRn interaction remains unclear. Anti-citrullinated protein antibodies (ACPA) of rheumatoid arthritis patients exhibit remarkably high Fab-glycosylation (~90%). This makes ACPA an ideal model to investigate how Fab-glycosylation influences IgG-FcRn interaction.
Objectives: To investigate the potential impact of IgG Fab-glycosylation on IgG transplacental transfer and interaction with FcRn.
Methods: To investigate transplacental transport of ACPA and total IgG, serum of ACPA-positive RA patients (mothers) as well as of healthy mothers and their respective newborns was analyzed. IgG Fab- and Fc-glycosylation was investigated with liquid chromatography and mass-spectrometry. Furthemore, ACPA monoclonal IgG were produced and glycoengineered to acquire several variants of the same monoclonal antibody differing only in their glycosylation profile. These glycovariants were then used to investigate the impact of Fab-glycans on the affinity of IgG for FcRn. Surface plasmon resonance (SPR) and affinity chromatography were implemented.
Results: When measured in mothers' serum and cord blood samples, Fab-glycosylation of IgG antibodies was ~20% lower in newborns compared to their mothers, which was observed for ACPA IgG, non-ACPA IgG in RA patients and total IgG of healthy controls (Figure 1). This may indicate that transplacental transfer of Fab-glycosylated antibodies is impaired. SPR results suggested that presence of Fab-glycans slightly lowered the affinity of IgG for FcRn. However, presence of Fab-glycans did not have a significant effect on the results of FcRn affinity chromatography. Together, these results suggest that Fab-glycans may impair association of IgG with FcRn, while dissociation likely stays intact.
Conclusion: Our results suggest that Fab-glycans inhibit IgG-FcRn binding which negatively affects the transplacental transfer of Fab-glycosylated IgG. The impact of Fab-glycosylation on IgG half-life requires further investigation.

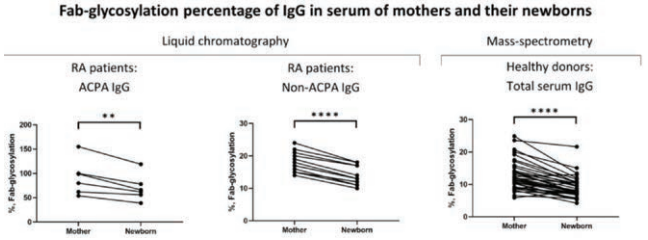


Figure 1.

Disclosure of Interests: Mikhail Volkov: None declared, Karin van Schie: None declared, Albert Bondt: None declared, Theresa Kissel: None declared, Maximilian Brinkhaus Grant/research support from: argenx, Arthur Bentlage: None declared, Carolien Koeleman: None declared, Steven de Taeye Grant/research support from: Genmab, Radboud Dolhain: None declared, Manfred Wuhrer: None declared, Rene Toes: None declared, Gestur Vidarsson: None declared, Diane van der Woude: None declared
DOI: 10.1136/annrheumdis-2021-eular.1727

AB0021 CHARACTERISATION OF AGE-ASSOCIATED B CELLS IN EARLY, DRUG NAÏVE RHEUMATOID ARTHRITIS

G. Vidal-Pedrola[1], N. Naamane[1], D. Scheel-Toellner[2], A. Pratt[1], A. Mellor[1], J. D. Isaacs[1], A. E. Anderson[1]. [1]*Newcastle University, Translational and Clinical Research Institute, Newcastle upon Tyne, United Kingdom*; [2]*University of Birmingham, Centre for Translational Inflammation Research, Birmingham, United Kingdom*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease of immune dysregulation affecting the joints. While T cells play a recognised role in disease pathogenesis, the presence of autoantibodies years before the clinical onset of disease, and the efficacy of the B cell-depleting therapy rituximab, highlight a pathogenic role for these functionally diverse lymphocytes. A novel subset, termed age-associated B cells (ABCs), are described as $CD19^{high}$ $CD21^{-}$ $CD11c^{+}$, with a high proportion expressing the transcription factor T-bet; they are elevated in murine models of autoimmunity and produce autoantibodies characteristic of autoimmune disease. A detailed characterisation of ABCs in early, drug naïve RA has not yet been conducted.
Objectives: We aimed to characterise peripheral blood (PB) and synovial fluid (SF) ABCs in patients suffering from early drug naïve RA. As a secondary objective we sought to determine whether this population differs between RA patients and age-matched early psoriatic arthritis (PsA; disease controls) and healthy controls.
Methods: Newly presenting early RA and other inflammatory arthritis patients, naïve to immunomodulatory treatment, were recruited from the Newcastle Early Arthritis Clinic. Patients with established RA (≥1 year duration on treatment and age-matched healthy controls were recruited in parallel. B cell subsets (naïve ($CD19^{+}IgD^{+}CD27^{-}$), switched memory ($CD19^{+}IgD^{-}CD27^{+}$) and ABC ($CD19^{+}CD21^{-}CD11c^{+}$)) in PB and SF were characterised by flow cytometry. FACS sorted PB B cell subset gene expression profiles were assessed using a customised NanoString nCounter Human Immunology v2 Panel.
Results: Transcriptionally, ABC differed from both naïve and switched memory B cells. In keeping with published studies ABCs had an activated memory phenotype, exemplified by elevated expression of CD69, CD80, and CD86, as well as Ki67, HLA-DR, IgG and T-bet. Interestingly, ABC had high expression of the Fc Receptor Like (FcRL) family (FcRL1-5), and an inflammatory homing profile (high levels of CXCR3 and low levels of CXCR4 and CXCR5). We found no difference in the proportion of PB ABC between RA patients and control groups, and no association of ABC frequencies with age. Focussing on RA ABCs specifically, we observed elevated ABC frequencies in females, but no association with disease activity. In keeping with their chemokine receptor profile, cross-sectional analysis also demonstrated ABC enrichment in SF compared to PB, with SF frequencies higher in established than early disease. The transcriptome of ABCs from early RA patients differed from both age-matched disease controls and healthy donors (Figure 1 next page).
Conclusion: These data demonstrate that ABCs have a unique, activated, class-switched proliferative phenotype that is transcriptionally distinct from switched memory and naïve B cells. Interestingly, at the transcriptome level early RA ABCs differ to their counterparts in health and other inflammatory arthritides, suggesting they may differ functionally and contribute to pathogenesis. Of note,

their high expression of MHC class II (HLA-DR) and co-stimulatory (CD80 and CD86) molecules suggests an important antigen-presentation function of ABC, which together with their unique FcRL family expression pattern, warrants further functional characterisation.

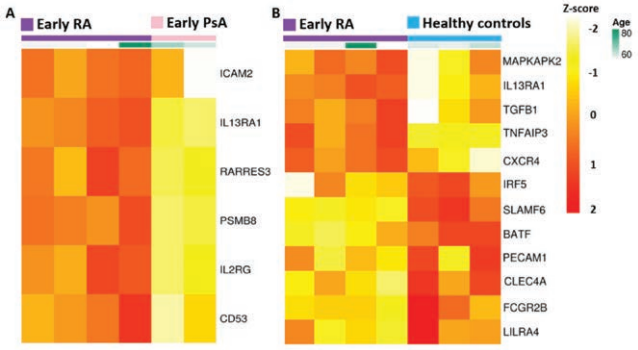


Figure 1. Differential gene expression in ABCs from early RA patients compared to early PsA patients (A) and healthy controls (B). A NanoString nCounter Technologies chip was used to assess gene expression. Raw counts were normalised to the housekeeping genes. Sample quality was then assessed using the arrayQualityMetrics package. Gene expression profiles between different donor groups was assessed using the DESeq2 R package. In both hierarchical clustering heatmaps gene expression intensities were log2 transformed and their z-scores are displayed as colours ranging from yellow (low expression) to red (high expression) as shown in the key.

Disclosure of Interests: Gemma Vidal-Pedrola: None declared, Najib Naamane: None declared, Dagmar Scheel-Toellner: None declared, Arthur Pratt Grant/research support from: GSK, Pfizer and Janssen, Andrew Mellor: None declared, John D Isaacs Speakers bureau: Abbvie, Gilead, Roche, UC, Consultant of: Abbvie, Gilead, Roche, UC, Grant/research support from: Pfizer, GSK and Janssen, Amy E. Anderson Grant/research support from: Pfizer, GSK and Janssen

DOI: 10.1136/annrheumdis-2021-eular.2010

AB0022 AUTOREACTIVE B CELLS IN RHEUMATOID ARTHRITIS DISPLAY AN ACTIVATED PHENOTYPE OF RECENT ANTIGEN EXPOSURE

N. Blomberg[1], H. Kristyanto[1], T. Huizinga[1], R. Toes[1], H. U. Scherer[1]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*

Background: Rheumatoid arthritis, in particular ACPA+ RA, is characterized by frequent disease flares and poor chances to achieve DMARD-free sustained remission. Recently, we have shown that ACPA-expressing memory B cells (MBC) remain in a persistently activated state throughout disease, even in patients in DMARD-induced clinical remission.(1) The reasons why the ACPA B cell response is continuously activated are unknown, as well as why the response does not revert to a resting, 'quiescent' state. We hypothesized that continuous antigen exposure in germinal centres drives ACPA B cell activation, leading to a 'recent germinal centre emigrant' phenotype of these cells in the circulation.

Objectives: To understand whether the activated phenotype of ACPA-expressing B cells could be induced by recent antigen exposure, to thereby discern the processes of immune activation that remain active in patients even in clinical remission and to argue whether these processes could be targets for therapeutic intervention.

Methods: ACPA-expressing B cells were identified in peripheral blood of RA patients by flow cytometry during different stages of disease and characterized by a panel of activation- and germinal centre related markers (CD80, CD86, CD32, CD95, Ki-67). In addition, three healthy donors received a TT booster vaccination. TT-specific MBC were identified in blood at different timepoints (before vaccination and up to 22 weeks after vaccination) and analysed phenotypically over time.

Results: The majority of ACPA-expressing B cells strongly expressed CD95 and the co-stimulatory marker CD80. A part was also positive for the proliferation marker Ki-67 (on average 30%), and most cells downregulated the inhibitory marker CD32. TT-specific MBC adopted a comparable phenotype after booster vaccination, but most markers returned to the pre-vaccination expression level gradually over time. These effects were antigen-dependent because the phenotype of TT-negative B cells remained unchanged. The phenotypic composition of the proliferating ACPA-positive B cell pool most closely corresponded to a stimulation history of 1-2 weeks after antigen exposure. Notably, none of the Ki-67 negative ACPA-specific MBC showed phenotypic quiescence, indicating either a short life-time (in circulation) after antigen encounter or persistent additional factors of activation.

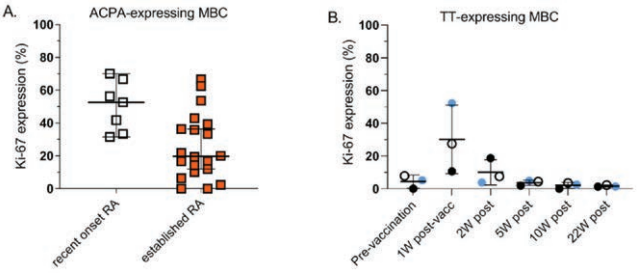


Figure 1. Ki-67 expression on ACPA-specific MBC in RA (A) and on TT-specific MBC in 3 healthy donors before and after booster vaccination (B).

Conclusion: ACPA-expressing MBC phenotypically resemble TT-specific MBC after recent (1-2 weeks) booster vaccination, reflecting the phenotype of recent germinal centre emigrants, and remain activated, whereas TT-specific MBC lose this marker profile over time. These observations suggest that ACPA-expressing MBC either home to tissue or survive shortly in the circulation, or that additional factors drive or program these cells to persistent activation. Transcriptomic profiling and analysis of the homing marker profile may help to answer these questions. Furthermore, it will be important to understand the association of persistent activation of ACPA-expressing B cells in clinical remission and the risk for disease flares upon treatment discontinuation.

REFERENCES:

[1] Kristyanto H, Blomberg NJ, Slot LM, van der Voort EIH, Kerkman PF, Bakker A, et al. Persistently activated, proliferative memory autoreactive B cells promote inflammation in rheumatoid arthritis. Sci Transl Med. 2020;12(570).

Disclosure of Interests: Nienke Blomberg: None declared, Hendy Kristyanto: None declared, Thomas Huizinga Grant/research support from: Gilead, Rene Toes: None declared, Hans Ulrich Scherer Grant/research support from: Pfizer, Lilly, Sanofi, BMS

DOI: 10.1136/annrheumdis-2021-eular.2050

AB0023 DENDRITIC CELLS AS A PROMINENT MARKERS OF AUTOIMMUNE DISEASES

M. Korolev[1], Y. Kurochkina[1], N. Banshhikova[1], V. Omelchenko[1], A. Akimova[1], E. Letyagina[1], O. Poveschenko[2]. [1]*Research Institute of Clinical and Experimental Lymphology - Branch of the Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Science, Rheumatology, Novosibirsk, Russian Federation*; [2]*Research Institute of Clinical and Experimental Lymphology - Branch of the Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Science, Cells Technologies, Novosibirsk, Russian Federation*

Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of different autoimmune diseases. It is clear nowadays the role of DCs in rheumatoid arthritis (RA) but not well investigated in Axial spondylitis (AxSpA). DCs are a heterogeneous population and can be divided into groups: myeloid (mDCs) and plasmacytoid (pDCs). DCs can induce both immune response and tolerance.

Objectives: To investigate the subpopulations of peripheral blood myeloid and plasmacytoid DCs in patients with early stage of RA (duration of illness up to 12 months) and AS.

Methods: The study include sixty five patients with early forms of diseases including 55 patients with RA and 10 patients with AxSpA. Diagnosis RA was established according ACR/EULAR criteria (2010). Diagnosis AxSpA was established according ASAS criteria. All patients received conventional synthetic DMARDs. Thirty patients with osteoarthritis (OA) used as a control group. Analysis of the content of the B-lymphocytes, myeloid and plasmacytoid DCs was carried out by flow cytometry. B-lymphocytes, subtypes of peripheral blood DCs were characterized by the following phenotypes: myeloid DCs (CD3-CD14-CD19-HLA-DR + CD11c + CD123-), plasmacytoid DCs (CD3-CD14-CD19-HLA-DR + CD11c-CD123 +), B-lymphocytes (CD19 +). Analyses were performed before treatment and after 3 and 6 months.

Results: Patients with early RA are characterized by significant evaluation of the population of myeloid DCs in comparison of patients with osteoarthritis (25.3% vs 21.5, p=0.005). Furthermore, the difference was found in the number of cells with the phenotype B-lymphocytes: 5.7% vs 3.1%, p = 0.0007). No significant differences were observed in the number of plasmocytoid DCs. After 3 and 6 month of observation we detected reducing amount of myeloid DCs 26.7% vs 20.1% vs 16.4% respectively. Disease activity according to DAS28 droped to low (4.32 to3.06, p=0.03). Patients with AxSpA are characterized a lower mDCs levels in compared with RA (19.3% vs 26.7, p=0.07). After 6 month of investigation we detected decreasing mDCs (19.3% to 14.2%, p=0.05). The percent of pDCs were constant and did not differ from the level of healthy donors.

Conclusion: The data obtained indicate that early form of rheumatic diseases namely rheumatoid arthritis and axial spondylitis have the common features such as the dominance of mDCs and their decreasing in reduction of activity of disease.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2293

AB0024

IN VITRO CHARACTERIZATION OF CENERIMOD, A POTENT AND SELECTIVE SPHINGOSINE 1-PHOSPHATE RECEPTOR 1 (S1P1) MODULATOR IN PREVENTING MIGRATION OF NON-ACTIVATED AND ACTIVATED PRIMARY HUMAN B CELLS IN THE PRESENCE OR ABSENCE OF GLUCOCORTICOIDS

L. Schlicher[1], P. Kulig[1], M. Murphy[1], M. Keller[1]. [1]*Idorsia Pharmaceuticals Ltd, Immunology, Basel, Switzerland*

Background: Cenerimod is a potent, selective, and orally active sphingosine 1-phosphate receptor 1 ($S1P_1$) modulator that is currently being evaluated in a Phase 2b study in patients with systemic lupus erythematosus (SLE) (NCT03742037). $S1P_1$ receptor modulators sequester circulating lymphocytes within lymph nodes, thereby reducing pathogenic autoimmune cells (including B lymphocytes) in the blood stream and in inflamed tissues. Extensive clinical experience has become available for the nonselective S1P receptor modulator fingolimod in relapsing forms of multiple sclerosis, supporting this therapeutic concept for the treatment of autoimmune disorders.
Objectives: Although the effect of S1P-receptor modulators in reducing peripheral B cells is well documented[1,2], the role of the $S1P_1$ receptor on this cell type is only incompletely understood. In this study, the mode of action of cenerimod on primary human B cells was investigated in a series of *in vitro* experiments, including $S1P_1$ receptor cell surface expression and chemotaxis towards S1P. Moreover, $S1P_1$ expression following B cell activation *in vitro* was studied. As glucocorticoids (GC) are frequently used in the treatment of patients with autoimmune disorders including SLE, the potential influence of GC on the mode of action of cenerimod was evaluated.
Methods: Primary human B lymphocytes from healthy donors were isolated from whole blood. In one set of experiments, cells were treated with different concentrations of cenerimod to measure $S1P_1$ receptor internalization by flow cytometry. In a second set of experiments, isolated B cells were activated using different stimuli or left untreated. Cells were then analysed for $S1P_1$ and CD69 cell surface expression and tested in a novel real-time S1P-mediated migration assay. In addition, the effect of physiological concentrations of GCs (prednisolone and prednisone) on cenerimod activity in preventing S1P mediated migration was tested.
Results: *In vitro,* cenerimod led to a dose-dependent internalization of the $S1P_1$ receptor on primary human B lymphocytes. Cenerimod also blocked migration of nonactivated and activated B lymphocytes towards S1P in a concentration-dependent manner, which is in line with the retention of lymphocytes in the lymph node and the reduction of circulating lymphocytes observed in the clinical setting. Upon B cell activation, which was monitored by CD69 upregulation, a simultaneous downregulation of $S1P_1$ expression was detected, leading to less efficient S1P-directed cell migration. Importantly, physiological concentrations of GC did not affect the inhibitory activity of cenerimod on B cell migration.
Conclusion: These results show that cenerimod, by modulating $S1P_1$, blocks B lymphocyte migration towards its natural chemoattractant S1P and demonstrate compatibility of cenerimod with GC. These results are consistent with results of comparable experiments done previously using primary human T lymphocytes.
REFERENCES:
[1] Nakamura M et al., Mult Scler. 2014 Sep; 20(10):1371-80.
[2] Strasser DS et al., RMD Open 2020;6:e001261.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2482

AB0025

CITRULLINATED-PEPTIDE SPECIFIC CD4+ T CELL RESPONSES IN RHEUMATOID ARHRITIS

J. Swift[1], J. Stanway[1], I. Nicorescu[1], C. Hilkens[1], F. Stevenaert[2], A. Anderson[1], A. Pratt[1], J. D. Isaacs[1]. [1]*Newcastle University, Translational and Clinical Research Institute, Newcastle-upon-Tyne, United Kingdom*; [2]*Janssen Pharmaceutica, Immunosciences, Beerse, Belgium*

Background: CD4+ T cells reacting to post-translationally modified, citrullinated self-antigens are thought to play a central role in the pathogenesis of rheumatoid arthritis (RA)[1]. This is evidenced by a strong HLA class II association, the success of therapeutic co-stimulation blockade and the detection of autoantigen specific T-cells using HLA class II multimers[2]. These cells may represent a target for antigen-specific, tolerogenic therapies and their in-depth phenotyping may provide the means by which to monitor such treatment.
Objectives: To identify the citrullinated-peptide (cit-peptide) induced cytokine repertoire of antigen-specific memory CD4+ T cells in both healthy controls (HCs) and ACPA positive RA patients using intracellular cytokine staining and flow cytometry. Of note, the HLA-types of both HCs and RA patients were not known.
Methods: Cryopreserved peripheral blood mononuclear cells (PBMC) from both HCs (n = 8) and RA patients (n = 13) with both early (untreated) and established disease were thawed and labelled with a proliferation tracking dye (PTD). Labelled PBMC were then either incubated alone or with a pool of cit-peptides for 9-days, followed by a 5-hour restimulation with PMA and ionomycin, where cytokine secretion was blocked for the final 4-hours using brefeldin-A. Cells were then harvested, permeabilised and stained for T cell surface markers and intracellular cytokines including IFN-γ, IL-4, IL-21 and IL-17. Stained cells were immediately acquired using a BD Fortessa X20, where antigen-specific CD4+ T cells were identified as the viable CD45RO+ (memory) CD4+ T cell population that had proliferated (PTDlow) in response to the cit-peptides. Stimulation indices (SI) were calculated as the percentage of proliferated memory CD4+ T cells in the stimulated wells divided by the percentage in the unstimulated conditions, and cit-peptide responders were defined as those with an SI > 2.0. Net cytokine production was measured by subtracting the percentage cytokine production from unstimulated CD4+ CD45RO+ PTDlow cells, from those stimulated with the cit-peptides.
Results: Comparable proliferative responses were observed in both donor groups in response to stimulation with the cit-peptide pool, where 37 % of HCs and 31 % of RA patients responded with an SI > 2.0 (Fig. 1A). While little cytokine production was observed in the cit-peptide responding HC T cells, for responding RA donors, cit-peptide responsive CD4+ memory T cells were predominantly IFN-γ and IL-21 producing (Fig. 1B and 1C). In contrast, these donors did not produce significant levels of either IL-17 or IL-4 (Fig. 1D and 1E).
Conclusion: Cit-peptides were able to induce proliferation in both HCs and RA memory CD4+ T cells which, amongst the RA donors only, were of a Th1/Tfh subtype. In contrast, and while based only on a small sample, cit-peptides did not induce either IL-17 or IL-4 production in either donor group, suggesting a lack of Th17/Th2 responses. Not all donors responded to the peptide pool, possibly reflecting the limited number of pooled cit-peptides or to a lack of confirmed HLA-DRB1*04:01 positive donors, as peptides were selected for their specificity on this basis. Future work will therefore include HLA-typing, as well as the inclusion of additional citrullinated-epitopes to demonstrate autoreactivity in a wider cross-section of patients. Further phenotyping of the cit-peptide specific T cells will be performed, and future plans will be to study the assay data alongside clinical outcomes to assess its value for immune monitoring.
REFERENCES:
[1] Malmström, V *et al* Nat Rev Immunol. 2017; 17(1):60-75.
[2] Gerstner, C *et al* BMC Immunol. 2020; 21(27):1-14.
Disclosure of Interests: Jessica Swift: None declared, James Stanway: None declared, Ioana Nicorescu: None declared, Catharien Hilkens: None declared, Frederik Stevenaert Employee of: Janssen, Amy Anderson Grant/research support from: Pfizer, GSK and Janssen, Arthur Pratt Grant/research support from: Pfizer, GSK and Janssen, John D Isaacs Speakers bureau: Abbvie, Gilead, Roche, UC, Consultant of: Abbvie, Gilead, Roche, UC, Grant/research support from: Pfizer, GSK and Janssen

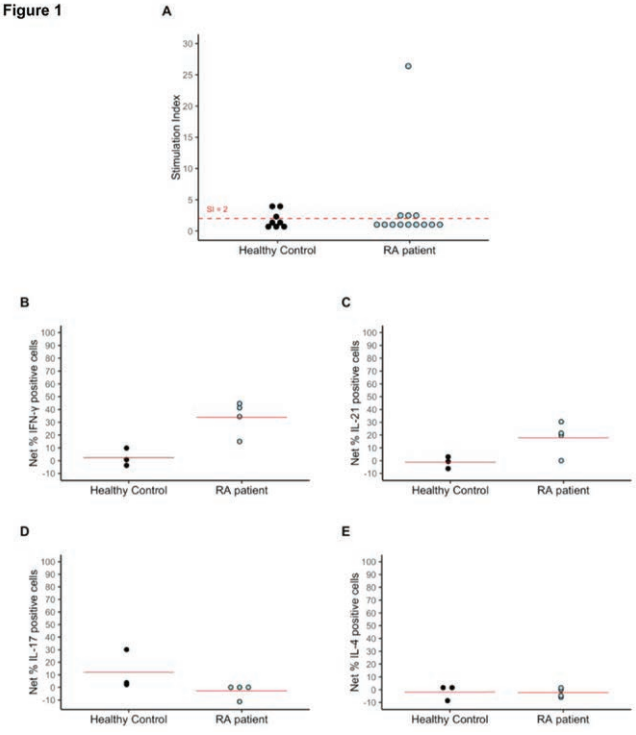


Figure 1. Citrullinated-peptide specific memory CD4+ T cell proliferation (A) and net % cytokine production of IFN-γ (B), IL-21 (C), IL-17 (D) and IL-4 (E) positive cells.
DOI: 10.1136/annrheumdis-2021-eular.2652

AB0026

DECREASE OF ANGIOGENIC T CELLS IN CONNECTIVE TISSUE DISEASE-ASSOCIATED INTERSTITIAL LUNG DISEASE

V. Pulito-Cueto[1], S. Remuzgo Martinez[1], F. Genre[1], B. Atienza-Mateo[1,2,3], V. M. Mora-Cuesta[1,4], D. Iturbe-Fernández[1,4], L. Lera-Gómez[1], R. Pérez-Fernández[1],

P. Alonso Lecue[1,4], J. Rodriguez Carrio[5], D. Prieto-Peña[1,3], V. Portilla[1,3], R. Blanco[1,3], A. Corrales[1,3], J. M. Cifrián-Martínez[1,4,6], R. López-Mejías[1], M. A. González-Gay[1,3,6,7]. *[1]IDIVAL, Research Group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, Santander, Spain*; *[2]Hospital Universitario Marqués de Valdecilla, `López Albo´ Post-Residency Programme, Santander, Spain*; *[3]Hospital Universitario Marqués de Valdecilla, Department of Rheumatology, Santander, Spain*; *[4]Hospital Universitario Marqués de Valdecilla, Department of Pneumology, Santander, Spain*; *[5]Faculty of Medicine, Universidad de Oviedo, Deparment of Functional Biology, Immunology Area, Oviedo, Spain*; *[6]Universidad de Cantabria, School of Medicine, Santander, Spain*; *[7]Faculty of Health Sciences, University of the Witwatersrand, Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Johannesburg, South Africa*

Background: Interstitial lung disease (ILD) is one of the most significant complications of connective tissue diseases (CTD), leading to an increase of the morbidity and mortality in patients with CTD [1]. A specific T cell subset termed angiogenic T cells (TAng), that promote endothelial repair and revascularization, have been involved in the pathogenesis of CTD [2-4]. However, to the best of our knowledge, no information regarding the role of TAng in CTD-ILD$^+$ is available.
Objectives: To study, for the first time, the potential role of TAng related to vascular damage in CTD-ILD$^+$.
Methods: Peripheral venous blood was collected from 40 patients with CTD-ILD$^+$ and three comparative groups: 44 CTD-ILD$^-$ patients, 21 idiopathic pulmonary fibrosis (IPF) patients and 20 healthy controls (HC). All subjects were recruited from the Rheumatology and Pneumology departments of Hospital Universitario Marqués de Valdecilla, Santander, Spain. Quantification of TAng was performed by flow cytometry. TAng were considered as triple-positive for CD3, CD31 and CXCR4.
Results: Patients with CTD-ILD$^+$ exhibited a significantly lower TAng frequency than CTD-ILD$^-$ patients ($p<0.001$). Similar results were obtained when patients with CTD-ILD$^+$ were compared with HC ($p=0.004$) although no difference was observed between CTD-ILD$^+$ and IPF. In addition, a significant increase of TAng frequency was shown in patients with CTD-ILD$^-$ in relation to IPF patients ($p<0.001$), while no difference was observed between CTD-ILD$^-$ and HC.
Conclusion: Our results reveal a decrease of TAng frequency related to vascular damage in CTD-ILD$^+$. Furthermore, we disclose that the presence of ILD is associated with lower TAng frequency.
REFERENCES:
[1] Expert Rev Clin Immunol 2018;14(1):69-82.
[2] Circulation 2007;116(15):1671-82.
[3] Ann Rheum Dis 2015 74(5):921-7.
[4] PLoS One 2017;12(8):e0183102.
Acknowledgements: Personal funds, VP-C: PREVAL18/01 (IDIVAL); SR-M: RD16/0012/0009 (ISCIII-ERDF); LL-G: INNVAL20/06 (IDIVAL); RP-F: START PROJECT (FOREUM); RL-M: Miguel Servet type I CP16/00033 (ISCIII-ESF).
Disclosure of Interests: Verónica Pulito-Cueto: None declared, Sara Remuzgo Martinez: None declared, Fernanda Genre: None declared, Belén Atienza-Mateo: None declared, Victor Manuel Mora-Cuesta: None declared, David Iturbe-Fernández: None declared, Leticia Lera-Gómez: None declared, Raquel Pérez-Fernández: None declared, Pilar Alonso Lecue: None declared, Javier Rodriguez Carrio: None declared, Diana Prieto-Peña: None declared, Virginia Portilla: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD and Roche, Alfonso Corrales: None declared, Jose Manuel Cifrián-Martínez: None declared, Raquel López-Mejías: None declared, Miguel A González-Gay Speakers bureau: Pfizer, Abbvie, MSD, Grant/research support from: Pfizer, Abbvie, MSD
DOI: 10.1136/annrheumdis-2021-eular.2676

AB0027 INCREASED CIRCULATING CD39+FOXP3+CD4+ TREG CELLS IN EARLY RHEUMATOID ARTHRITIS FACILITATE THE ANTIINFLAMMATORY ACTION OF METHOTREXATE

L. Nuño[1], A. Villalva[1], M. Novella-Navarro[1], I. Monjo[1], D. Peiteado[1], S. García-Carazo[1], A. Puig-Kröger[2], A. Balsa[1], M. E. Miranda-Carus[1]. *[1]Hospital Universitario La Paz, Rheumatology, Madrid, Spain*; *[2]Gregorio Marañón Hospital, Immunology, Madrid, Spain*

Background: Methotrexate (MTX) remains the first line of treatment in Rheumatoid Arthritis (RA)[1,2]. Inhibition of AICAR transformylase by MTX results in augmented release of adenine nucleotides to the extracellular space[1]; these are rapidly hydrolysed by the combined action of ectonucleotidases CD39 and CD79 rendering the antiinflammatory agent adenosine[1]. CD39, the rate-limiting enzyme in this cascade, is highly expressed by a subset of human FoxP3+CD4+ regulatory T cells (Treg39+)[2-4] and MTX may act synergistically with Tregs in the control of inflammation.
Objectives: To study the expression of CD39 on circulating Treg cells of untreated early Rheumatoid Arthritis (ERA) patients and its relation with the ex vivo effect of MTX.
Methods: Peripheral blood was drawn from 22 DMARD- and steroid- naïve ERA patients with a disease duration < 24 weeks, 15 longstanding RA patients (LRA, disease duration > 2 years) and 37 age and gender-matched healthy controls (HC). LRA patients were receiving low-dose weekly MTX and were naïve for biologicals. 10 ERA patients who had achieved remission 12 months after initiating MTX donated blood for a second time (ERA-R). The frequency of Treg and Treg cell subsets was assessed by flow cytometry. CD4+CD25+CD127- (total T reg), CD4+CD27+CD127-CD39+ Treg (Treg39+) and CD4+CD25-CD39- responder T (Tresp39-) cells were isolated by Ficoll-Hypaque, followed by sorting. The suppressor potency of Tregs was assessed in cocultures of isolated Tregs with Tresp, established at different Treg/Tresp ratios. Proliferation was determined by CFSE dilution; cytokine secretion was measured by ELISA of culture supernatants.
Results: As previously described[5], ERA but not LRA patients demonstrated a superior frequency of circulating Treg (CD4+CD25+CD127-FoxP3+) cells. In addition, the proportion of Tregs that expressed CD39 (Treg39+) was significantly increased in ERA but not LRA. Total ERA Tregs were significantly more potent suppressors of proliferation, TNFα and IFNγ secretion when compared with HC or LRA Tregs, and this difference was partially and significantly abrogated in the presence of adenosine deaminase, or the adenosine A2A receptor (A2AR) antagonists DMPX (3,7-dimethyl-1-propargylxanthine) or ZM 241385, but not in the presence of the adenosine A1 receptor antagonist DPCPX (8-cyclopentyl-dipropylxanthine). When MTX was added to the culture medium, the suppressor potency of total Tregs was further enhanced in all 3 groups of patients, and this enhancement was significantly higher in ERA total Treg/Tresp39- cocultures as compared with HC or LRA total Treg/Tresp39- cocultures. The effect of MTX was also partially and significantly abrogated by adenosine deaminase, DMPX or ZM 241385 but not by DPCPX. We then tested the suppressor potency of isolated Treg39+ together with the enhancer effect of MTX on this potency, and observed that there were no longer differences among ERA, LRA and HC; this further suggests that the differences observed in assays using total Tregs can be attributable to the increased Treg39+ proportions present in ERA. The frequency and function of ERA-R Treg cells were not different from HC or LRA Tregs.
Conclusion: The suppressor action of CD39+Tregs is mediated at least in part by adenosine trough A2AR ligation, and the superior suppressive potency of total ERA Tregs is associated with their higher proportion of TregCD39+ cells as compared with HC or LRA. In addition, the augmented suppressor effect observed in the presence of MTX is partly mediated by an increased adenosine production acting on A2AR and is more marked in ERA patients reflecting again their higher proportion of Treg39+ cells. This indicates that MTX cooperates with Treg39+ cells in the control of inflammation.
REFERENCES:
[1] Montesinos MC, et al. Arthritis Rheum. 2007.
[2] Peres RS, et al. Proc Natl Acad Sci U S A. 2015.
[3] Deaglio S, et al. J Exp Med. 2007.
[4] Borsellino G, et al. Blood. 2007.
[5] Benito-Miguel M, et al. J Immunol. 2009.
Acknowledgements: FIS PI 20/00141; FIS RD16/0012/0012; Fondo Europeo de Desarrollo Regional (FEDER), unrestricted research grant from Gebro Pharma
Disclosure of Interests: Laura Nuño: None declared, Alejandro Villalva: None declared, Marta Novella-Navarro: None declared, Irene Monjo: None declared, Diana Peiteado: None declared, Sara García-Carazo: None declared, Amaya Puig-Kröger: None declared, Alejandro Balsa Grant/research support from: BMS, Gebro Pharma, Maria-Eugenia Miranda-Carus Grant/research support from: BMS, Gebro Pharma
DOI: 10.1136/annrheumdis-2021-eular.2680

AB0028 EXPRESSION OF FATTY ACID TRANSPORTERS AND FREE FATTY ACID UPTAKE IN CD8+ T CELLS IN AUTOIMMUNE ARTHRITIS PATIENTS

S. Keck[1], F. V. Kraus[1], H. M. Lorenz[1], M. Souto-Carneiro[1]. *[1]University Hospital Heidelberg, Department of Rheumatology, Heidelberg, Germany*

Background: RA CD8+ T cells (CD8s) have been shown to vastly contribute to tissue damage and RA disease activity by presenting and maintaining an active effector phenotype promoting autoinflammation. In order to meet their high metabolic requirements RA CD8s alter not only their glycolytic and glutaminolytic profiles, but also rely on increased lipid metabolism characterized by increased free fatty acid (FFA) uptake and lipid biosynthesis.
Objectives: In order to classify the importance of lipid metabolism in RA CD8s in terms of initiation and perpetuation of effector functions and therefore exploring potential novel therapy targeting points or biomarkers additional investigations have to been made. By analysing FFA uptake and the expression of free fatty acid transporters (FAT) upon TCR-stimulation in RA, PsA, SpA patients and healthy controls (HC), we aimed to further characterize the importance of RA CD8s´ lipid metabolism.
Methods: Blood samples from 23 RA patients, 22 SpA patients, 20 PsA patients and 7 HC recruited at Heidelberg University Hospital were processed via negative magnetic separation selection to obtain purified CD8s. CD8s were cultured for 72 hours in [1,6-13C] glucose containing medium in the presence of anti-CD3 and anti-CD28. FFA uptake was measured by Palmitate-Bodipy 488 staining (ThermoFisher), the expression of FAT CD36, FABP4 and GPR84 besides CD69, CD36, CD45RA, CD3 and CD8 were assessed by FACS analysis.

Ethic approval NR: S-096/2016.
Results: The intake of the FFA palmitate by CD8s was higher in all patients groups than in HC ($p < 0,05$). In all three diseases´ stimulated CD8s, unlike in the HC group, the expression of GPR84 was inversely correlating to the expression of CD69 (Spearman $r < -0,62$). In patient´s stimulated CD8s the expression of GPR84 tended to be lower in RA and PSA effector memory (EM) CD8s. In RA and HC the expression of FABP4 tended to be lower in the naive CD8+ subset when compared to the effector subset. HC naive and effector CD8+ subsets had a higher expression of CD36 than in the patient groups. In RA and SPA patients the expression of FAT correlated with clinical variables. In RA DAS28 and CRP inversely correlated with CD36 (MFI), and disease duration with FABP4 as well. In SPA CRP and BASDAI inversely correlated with FABP4 while disease duration had a negative correlation with CD36 (MFI). GPR84 (MFI) had an inverted relationship to BASDAI. While the BMI was directly correlated with the expression of CD36 in RA, this relationship was inverted in SPA.
Conclusion: A high free fatty acid uptake seems to characterize autoimmune arthritis CD8+ T cells. The gain of effector functions appears to be connected to changes in the expression of different fatty acid transporters on the surface of CD8+ T cells. The correlation between the expression of fatty acid transporters and clinical parameters (specially disease activity scores) in RA and SPA suggests that they could potentially be used as biomarkers for disease activity and progression.
Acknowledgements: We thank all the individuals involved in the study for their participation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3069

Innate immunity in rheumatic diseases

AB0029 THE METABOLIC HIERARCHY OF IMMUNE PROCESSES IN HUMAN MONOCYTES

P. L. Krauß[1], F. Buttgereit[1], T. Gaber[1], M. Pfeiffenberger[1], Y. Chen[1], T. Buttgereit[2]. [1]*Charite Universitaetsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany*; [2]*Charite Universitaetsmedizin Berlin, Dermatology, Venerology, and Allergology, Berlin, Germany*

Background: At sites of inflammation, monocytes carry out specific immunological functions while facing challenging bioenergetic restrictions.
Objectives: Here, we investigated the potential of human monocytes to adapt under conditions of reduced energy supply by gradually inhibiting oxidative phosphorylation (OXPHOS) under glucose free conditions.
Methods: We modelled this reduced energy supply with myxothiazol, an inhibitor of mitochondrial respiration, at 0, 2 and 4 pmol/10^6 cells to decrease mitochondrial ATP production for 0%, 25% and 66% under glucose free conditions. For the three energy levels, we assessed (i) phagocytosis of FITC-labelled *E.coli* using flow cytometry, (i) production of reactive oxygen species (ROS) through NADPH oxidase (NOX) as determined by VAS2870-sensitive OCR using a Clark-type electrode, (iii) ATP generation and steady state level using a Clark-type electrode and luminometric assessment (iv) expression of surface activation markers CD16, CD80, CD11b, HLA-DR and (v) production of the inflammatory cytokines IL-1β, IL-6 and TNF-α using flow cytometry in peripheral blood-derived human monocytes with and without LPS-stimulation.
Results: As a prerequisite for our study, we demonstrate that human monocytes survived strong inhibition of mitochondrial respiration without any sign of apoptosis as determined by flow cytometry. As a result of the inhibition of OXPHOS, we demonstrate a reduction of VAS2870-sensitive OCR (ROS production through NOX), ATPase-dependent OCR and ATP steady-state levels. Focusing on immune function, we observed that phagocytosis and the production of IL-6 were the least sensitive to reduced energy supply while surface expression of CD11b, HLA-DR, production of TNF-α and IL-1β were most affected by inhibition of OXPHOS.
Conclusion: Our data demonstrate an energy-dependent hierarchy of immune functions in monocytes, which may represent a potential therapeutic target in monocyte-mediated inflammatory diseases.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.794

AB0030 BETA BOSWELLIC ACID BLOCKS INNATE IMMUNE RESPONSES IN MULTIPLE OA JOINT CELLS

E. Franco-Trepat[1], A. Lois-Iglesias[1], A. Alonso-Pérez[1], M. Guillán-Fresco[1], M. López-Fagúndez[1], J. P. Cerón-Carrasco[2], A. Pazos-Pérez[1], A. Crespo-Golmar[1], A. Jorge-Mora[1], S. Belén Bravo[3], R. Gómez[1]. [1]*Institute IDIS, Musculoskeletal Pathology Group, Santiago de Compostela, Spain*; [2]*Universidad Católica de Murcia (UCAM), Bioinformatics and High Performance Computing (BIO-HPC), Murcia, Spain*; [3]*Institute IDIS, Proteomics Unit, Santiago de Compostela, Spain*

Background: Osteoarthritis (OA) incidence has skyrocketed in the last decade and yet a definitive treatment has still to be found. This worldwide disease is depriving our society from their life quality and has become a grave economic burden. Research on anti-inflammatory tools has been done on traditional Asian medicine. Boswellic acid is a plant-derived molecule from the *Boswellia* species that has shown to prevent cartilage loss in an OA mouse model[1]. However, the specific mechanism of action is still unclear. The activation of innate immune receptors, such Toll-like receptor 4 (TLR4) has been involved in chondrocyte-mediated inflammatory responses and OA development. Although, boswellic acid has shown an inhibitory effect on TLR4-mediated inflammatory responses little is known about its role on TLR4-mediated chondrocyte inflammatory and catabolic responses.
Objectives: Determine the ability of beta boswellic acid (BBA) to block TLR4-mediated innate immune responses in chondrocytes and synoviocytes.
Methods: *In silico*
The binding affinity of beta boswellic acid (BBA) to TLR4 complex signalling was determined by optimized docking algorithm in the BIO-HPC Research Group facilities.
In vitro
Cellular proteome and secretome profiling (LC-MALDI/TOFF) was used to study inflammatory pathways induced by the agonist of TLR4 (LPS [100ng/ml]) and IL1R (IL1β [0.1ng/ml]). The effect of BBA on TLR4-mediated innate immune responses was determined by RT-PCR, Western Blot and ELISA in primary human OA chondrocytes (hOC), murine ATDC5 chondrocytes, human synoviocytes (SW982) and primary human osteoblasts (hOB). Cell viability was tested using the methyl-thiazolyl-tetrazolium (MTT) reagent. Nitric oxide production in cell culture media was assessed by Griess reaction. Green Malachite Assay was used to semi-quantify the whole phosphoproteome.
Ethics
This study was approved by the CEIC (CAEIG 2014/310).
Results: Cellular proteome and secretome profiling validated the activation of TLR4 and IL1R signalling by LPS and IL1β ligands and revealed an enrichment in innate immune responses (NF-Kβ, NLRP3, MMPs, Interleukins, etc).
Non-toxic doses of BBA [0.5-1000nM] prevented the activation of TLR4 in multiple articular joint cells and inhibited TLR4 & IL1R-dependant innate immune responses at the mRNA and protein level such as inflammatory factors IL6, NOS2, COX2, LCN2, MMP1, -3, -9, -13 and ADAMTS4, among others. Furthermore, NF-Kβ/IKBα and NLRP3/PYCARD/IL1β axis were also severely inhibited after BBA treatment. Moreover, these results were validated by in silico docking analysis that showed BBA interacted with TLR4/NF-Kβ.
Conclusion: We prove that BBA inhibit TLR4 & IL1R -dependent innate immune responses in multiple human joint cells (Figure 1). We show that NF-Kβ & NLRP3 signalling, both associated to OA, are blocked (mRNA and protein) after BBA treatment (Figure 1).
Our data support previous studies showing the prevention of cartilage loss in an OA animal models by BBA might come from its ability to inhibit TLR4 signalling. In the clinical practice of rheumatologists, *Boswellia Serrata* could be a useful nutraceutical to manage OA inflammation due to its content in BBA.

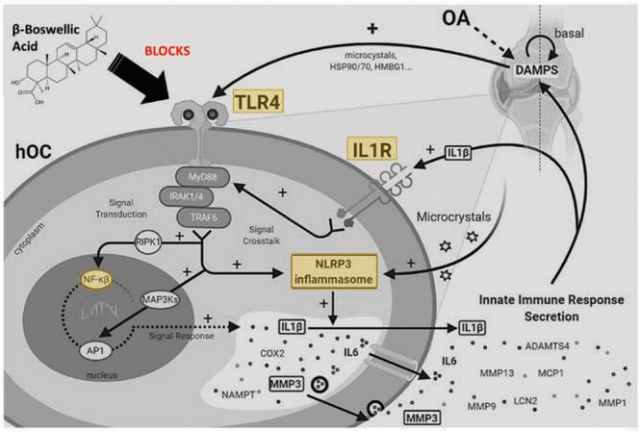


Figure 1.

REFERENCES:
[1] Wang, Q.; Pan, X.; Wong, H.H.; Wagner, C.A.; Lahey, L.J.; Robinson, W.H.; Sokolove, J. Oral and topical boswellic acid attenuates mouse osteoarthritis. *Osteoarthr. Cartil.* **2014**, *22*, 128–132, doi:10.1016/j.joca.2013.10.012.
Acknowledgements: Eloi Franco-Trepat and Ana Lois-Iglesias contributed equally to this work.
This research has been funded by the non-profit FER (Fundación Española de Reumatologia /Spanish Foundation of Rheumatology) through the project "Búsqueda de nuevos fármacos bloqueantes de la inflamación asociada a TLR4 en condrocitos humanos artrósicos".
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1889

AB0031

METABOLIC ADAPTATION OF HUMAN NEUTROPHILS TO GLUCOSE DEPRIVATION IS IMPAIRED WITH INCREASING AGE

M. Pfeiffenberger[1,2], P. L. Krauß[1,2], T. Buttgereit[3], Y. Chen[1], A. Damerau[1,2], T. Gaber[1,2], F. Buttgereit[1,2]. [1]*Charité Universitaetsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany*; [2]*German Rheumatism Research Center, Rheumatism Research, Berlin, Germany*; [3]*Charité Universitaetsmedizin Berlin, Venerology and Allergology, Berlin, Germany*

Background: Age-related impairment of classical neutrophil functions is well described (Fortin, McDonald et al. 2008). However, experimental evidence for age-related alterations of neutrophil metabolic adaptation towards nutrient deprivation -a feature of neutrophil battlefields- remains elusive. Moreover, age-related differences in neutrophil metabolic adaptation may contribute to age-related pathologies such as atherosclerosis, cancer, and autoimmune diseases including rheumatoid arthritis.
Objectives: Therefore, we hypothesized that metabolic adaptation of human neutrophils to glucose deprivation is impaired with increasing age.
Methods: We isolated human peripheral CD15+ neutrophils from four healthy young donors (mean age: 23.4 ± 2.7) and four healthy donors with a mean age of 58.7 ± 2.4. First, we analyzed the survival of neutrophils either stimulated with PMA or left untreated and subsequently incubated for 0 h and 6 h under varying glucose concentrations (0, 0.5, 1, 5, and 10 mM). To address this, we used 7-AAD staining and flow cytometry. Using Seahorse™ technology, we determined basal respiration, ATP-bound respiration, and maximal and spare capacity.
Results: We show that neutrophils (purity > 95%) survived for 6 hours *in vitro*, independent of treatment with PMA or concentrations of glucose in the culture medium. With negligible differences between the various concentrations of glucose used, the percentage of living cells after 6 h was 95% ± 2.5 without PMA and 75% ± 4.7 with PMA stimulation. No differences were uncovered in this respect between the two age groups. However, Seahorse™ technology revealed significant differences in basal, maximal, and spare respiratory capacity. Briefly, OCR (pmol/min/cell count) with respect to basal, maximal and reserve respiratory capacity was lower in the elderly donors compared to the young donors. For instance, with a concentration of 5 mM glucose, the basal respiration (OCR) was 17 ± 0.7 in elderly donors compared to 22.5 ± 1 in young donors, while the maximal respiration was 25 ± 0.8 in elderly and 41 ± 0.6 in the young donor group. Interestingly, these differences were independent of glucose concentration in the medium.
Conclusion: Our data show that basal metabolic parameters differ between neutrophils from young and older donors. Further experiments are needed to understand in detail the mechanisms and effects of age-related differences in metabolism on neutrophil functions.

REFERENCES:

[1] Fortin, C. F., P. P. McDonald, O. Lesur and T. Fülöp, Jr. (2008). "Aging and neutrophils: there is still much to do." Rejuvenation Res **11**(5): 873-882.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2018

AB0032

DIFFERENTIAL IMPACT OF BIOLOGICS AND GLUCOCORTICOIDS ON TNF SECRETION AND CD14+CD16+ MONOCYTES PERCENTAGE IN CULTURE DERIVED FROM SYNOVIAL FLUIDS OF PATIENTS WITH PSORIATIC ARTHRITIS-IN VITRO RESEARCH

S. Gertel[1], A. Polachek[1], V. Furer[1], D. Levartovsky[1], R. Tzemach[1], K. Meridor[1], D. Caspi[1], O. Elkayam[1]. [1]*Tel Aviv Sourasky Medical Center, Department of Rheumatology and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*

Background: Inflammatory joint diseases, such as psoriatic arthritis (PsA), are frequently treated by biologics. Assessment of treatment efficacy is based upon change in clinical activity scores and in tender and swollen joint counts. Although the response to these agents may be attributed to their central anti-inflammatory effects, synovial response may be operating in parallel. The potential beneficial role of intra-articular injection of tumor necrosis factor (TNF) blockers compared to glucocorticoids (GCs) in reducing synovitis was shown by means of clinical and instrumental validated measures (1). The inflamed synovial fluid is rich in mononuclear cells, however, the different mode of action of the in vitro response of these cells to drugs may contribute to the understanding of cellular response to therapeutic agents in central as opposed to peripheral compartments.
Objectives: To evaluate the effect of biologics used in the management of PsA on synovial fluid mononuclear cells (SFMCs) in vitro, and to compare their modes of action to GCs that are used to locally alleviate synovial inflammation.
Methods: SFMCs were obtained from PsA patients (n=11) during therapeutic knee arthrocentesis. The cells were cultured in vitro for 7 days in the presence of biologics (adalimumab, infliximab, secukinumab and ustekinumab, 10ug/ml) and GCs (betamethasone and methylprednisolone, 1 ug/ml and 10ug/ml) or medium as control. Levels of the secreted TNF were measured by ELISA. Changes in %$CD14^+CD16^+$ monocytes were analyzed by flow cytometry.
Results: Both TNF inhibitors (adalimumab $p<0.01$, infliximab $p=0.0003$) and GCs (betamethasone and methylprednisolone at 1ug/ml $p<0.01$ and at 10ug/ml $p<0.04$) significantly reduced TNF levels in cultured media derived from SFMCs of PsA patients (n=8) compared to medium. None of the other biologics reduced TNF levels in culture (Fig. 1A). Additionally, %$CD14^+CD16^+$ SFMCs derived from PsA patients (n=11) were significantly reduced by TNF inhibitors ($p=0.0003$) compared to medium, however, other biologics and GCs did not display similar activity (Fig. 1B).

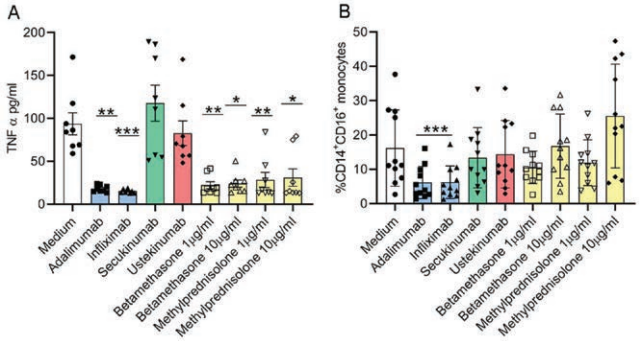


Figure 1. Both TNF inhibitors and GCs block TNF secretion but exhibit different activity on inflammatory $CD14^+CD16^+$ monocytes derived from SFMCs of PsA patients. SFMCs were co-cultured for 7 days in the presence of adalimumab, infliximab, secukinumab and ustekinumab at 10ug/ml or with betamethasone and methylprednisolone at 1ug/ml and 10ug/ml. Medium alone was used as a control. (A) Culture supernatants were analyzed for TNF levels by ELISA (n=8). (B) Cells were analyzed for %$CD14^+CD16^+$ monocytes by flow cytometry (n=11). All *p* values were calculated by the non-parametric one-way ANOVA Kruskal-Wallis test and Dunn's multiple comparison test, *$p<0.04$, **$p<0.01$ and ***$p=0.0003$.

Conclusion: Our data demonstrated marked activity mediated by TNF inhibitors in comparison with other biologics tested for their ability to suppress TNF secretion and inflammatory $CD14^+CD16^+$ monocytes. In contrast, GCs suppressed TNF secretion but did not significantly change the proportion of inflammatory $CD14^+CD16^+$ monocytes. These findings suggest an additional mechanism of action exerted directly by TNF inhibitors on synovial monocytes and which differs from that of GCs. These results warrant further studies of the therapeutic potential of local peripheral activity of TNF inhibitors for clinical application.

REFERENCE:

[1] Carubbi F, Zugaro L, Cipriani P, Conchiglia A, Gregori L, Danniballe C, et al. Safety and efficacy of intra-articular anti-tumor necrosis factor alpha agents compared to corticosteroids in a treat-to-target strategy in patients with inflammatory arthritis and monoarthritis flare. Int J Immunopathol Pharmacol. 2016;29:252-66.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2064

AB0033

MACROPHAGE ACTIVATION IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS (PRELIMINARY DATA)

E. Gerasimova[1], T. Popkova[1], T. Kirichenko[2], A . Markin[2], Y. Markina[2], D. Gerasimova[3], A. Bogatyreva[2], A. Orekhov[2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Systemic Rheumatic Diseases, Moscow, Russian Federation*; [2]*Research Institute of Human Morphology, Laboratory of Cellular and Molecular Pathology of the Cardiovascular System, Moscow, Russian Federation*; [3]*I.M. Sechenov First Moscow State Medical University (Sechenov University), Department of Pharmaceutical Economics, Moscow, Russian Federation*

Background: The study of the ability of monocytes to activate associated with the clinical activity of immunological markers of inflammation in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) will provide important and fundamentally new information on the involvement of these cells in the development of autoimmune rheumatic diseases (ARDs).
Objectives: To study macrophage activation in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients (pts).
Methods: A total of 21 active ARDs pts (11 RA, 10 SLE) were enrolled in the study (median age was 55[44; 63] years; disease duration was 8 [2; 14] months). There are 11 pts with early RA (disease duration was ≤12 months), moderate to high activity (DAS28 was 6.1[4.9;6.7]; SDAI was 25(22;31); ACCP was positive in 73% and RF in 87% cases) and 10 pts with active SLE (SLADAI-2K was 7 [6;8])

in the study. All early RA pts and 4 SLE pts were not treated with glucocorticoids and disease-modifying antirheumatic drugs. Six SLE pts received low-dose glucocorticoids and hydroxychloroquine.
All pts were assessed for macrophage activation and laboratory data: ESR, RF, ACCP, CRP, ANA, anti-dsDNA. Isolation of monocytes was carried out according to the standard procedure for obtaining a leukocyte fraction in a Ficoll gradient and subsequent selection of CD14 + cells using magnetic separation. After isolation, the cells were cultured in X-Vivo medium. To assess the degree of monocyte activation, cells were stimulated by the addition of LPS. The value of monocyte activation was expressed as a ratio of the level of secretion of proinflammatory cytokines by monocytes cultured with and without LPS addition. Secretion levels were determined by ELISA. The belonging of the isolated cells to CD14 + monocytes was additionally confirmed by flow cytometry.
Results: Macrophage activation was 2.6 (2.0;5.4) and 4.8 (2.8;7.3) in RA and SLE pts, respectively (p>0.05). In RA and SLE pts macrophage activation was independent of age, sex, body mass index, traditional risk factors (arterial hypertension, overweight, smoking, family history of cardiovascular diseases), RA activity scores (DAS28, SDAI), and SLADAI-2K. No association was found between macrophage activation and levels of ESR, RF, ACCP, CRP, ANA, and anti-dsDNA.
Conclusion: No differences in macrophage activation were found in RA and SLE pts. Macrophage activation was independent of age, sex, traditional risk factors, and ARD-related parameters. A study on a larger number of pts will clarify the link between macrophage activation and autoimmune disorders.
This work was supported by the Russian Science Foundation (Grant № 21-15-00225).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2285

AB0034 **PD-1 AGONISM INHIBITS ACTIVATION OF PLASMACYTOID DENDRITIC CELLS**

I. Banerjee[1], L. Edwards[1], P. Halvey[1], S. Alioto[1], D. Cluckley[1], C. Mitchell[1], C. Cox[1], E. Lurier[1], M. Cianci[1], S. Bengeri[1], S. Borthakur[1], K. Kis-Toth[1], N. Higginson-Scott[1], J. Viney[1], K. L. Otipoby[1]. [1]*Pandion Therapeutics, Immunology, Watertown MA, United States of America*

Background: T cell function is regulated by complex signaling networks of interconnected activators and inhibitors. Blockade of inhibitory receptors such as programmed death-1 (PD-1) has emerged as a novel treatment for multiple forms of cancer. One of the most common adverse events associated with blockade of the endogenous PD-1/PD-L1 pathway is the induction of autoimmune pathology in multiple tissues, demonstrating that PD-1 activation is necessary for normal immune homeostasis in humans (Kostine, et al., 2018). Given this body of clinical data, we sought to develop a PD-1 agonist antibody as a therapeutic approach to restore immune homeostasis in patients living with autoimmune diseases. PD-1 expression and function has been primarily described on T cells (Ishida, et al., 1992), with additional data available from several other immune cell populations (Ohaegbulam, et al., 2015).
Objectives: To study the effect of PD-1 agonism on plasmacytoid dendritic cell (pDC) function.
Methods: Human PBMCs stimulated with or without toll-like receptor (TLR)-9 agonist, CpG were analyzed by flow cytometry for PD-1 expression on immune cell subsets. To assess the impact of PD-1 agonist on pDC function human PBMCs were activated by CpG in the presence or absence of PD-1 agonist. Type-I interferon (IFN) levels were quantified using ELISA from culture supernatants. The expression of interferon stimulated genes was analyzed by qPCR as a measure of type-I IFN activation.
Results: We have discovered that TLR9 activation can induce PD-1 expression on plasmacytoid dendritic cells, which has not been previously reported. Further, we have demonstrated that PD-1 agonism inhibits TLR9-mediated activation and the effector functions of plasmacytoid dendritic cells.
Conclusion: These data suggest the potential of PD-1 as a target for regulating diseases with pathology generated by type-I IFN.
REFERENCES:
[1] Ishida, Y., Agata, Y., Shihibahara, K., & Honjo, T. (1992). Induced expression of PD-1, a novel member of the immunoglobulin gene superfamily, upon programmed cell death. *EMBO J.*, 11(11):3887-95.
[2] Kostine, M., Rouxel, L., Barnetche, T., Veillon, R., Martin, F., Dutriaux, C., . . . Schaeverbeke, T. (2018). Rheumatic disorders associated with immune checkpoint inhibitors in patients with cancer-clinical aspects and relationship with tumour response: a single-centre prospective cohort study. *Annual Rheumatic Disease*, 77(3):393-398.
[3] Ohaegbulam, K. C., Assal, A., Lazar-Molnar, E., Yao, Y., & Zang, X. (2015). Human cancer immunotherapy with antibodies to the PD-1 and PD-L1 pathway. *Trends in Molecular Medicine*, 21(1); 24-33.
Disclosure of Interests: Ishita Banerjee Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Lindsay Edwards Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Patrick Halvey Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Salvatore Alioto Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, David Cluckley Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Caitlin Mitchell Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Christopher Cox Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Emily Lurier Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Michael Cianci Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Soumya Bengeri Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Susmita Borthakur Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Katalin Kis-Toth Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Nathan Higginson-Scott Shareholder of: Pandion Therapeutics, Consultant of: Biotech Companies, Employee of: Pandion Therapeutics, Jo Viney Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Kevin L. Otipoby Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics
DOI: 10.1136/annrheumdis-2021-eular.2682

Osteo arthritis, aetiology, pathology and animal models

AB0035 **A REVIEW OF THE CLINICAL AND ECONOMIC BURDEN OF OSTEOARTHRITIS PAIN BY SEVERITY IN THE UNITED STATES**

A. Sadosky[1], P. Schepman[2], S. Thakkar[2], R. Robinson[3], C. Beck[4]. [1]*Apperture LLC, HEOR, Westerly, United States of America*; [2]*Pfizer Inc, PHI, New York, United States of America*; [3]*Eli Lilly and Company, Global Patient Outcomes & Real World Evidence, Indianapolis, United States of America*; [4]*Pfizer Inc, Medical Affairs, Tadworth, United Kingdom*

Background: The development of new therapies to treat symptomatic osteoarthritis (OA) often requires targeting patient subgroups such as mild and/or moderate and/or severe. Multiple assessments for pain are used in clinical and research settings, yet to quantify patient burden with increasing pain severity it is important to understand the potential variability in outcomes based on definitions of severity used[1].
Objectives: The objective of this study was to examine studies in the published literature that report the burden of OA pain by severity to assess similarities and/or differences across study methodologies and outcomes.
Methods: A targeted literature review of PubMed and Google Scholar was conducted January 2021 and included search terms: osteoarthritis, severity, United States (US), burden, quality of life, medication/treatment, and healthcare resource utilization. The search was limited to the English language, full-text articles, and no restriction on publication date. Results included a recent study of the burden of symptomatic OA pain respondents by severity level in the US[2,3]. Over 100 publication titles were reviewed. Comparison of findings was descriptive in nature.
Results: Nine publications were identified representing 7 unique studies, 6 being patient and/or healthcare provider surveys. Two studies focused on OA severity: the remaining 5 stratified patients by pain severity, and all but 2 of the 5 identified and confirmed pain as OA-related. Pain measures included numeric rating scales (generic 0-10, Western Ontario and McMaster Universities Arthritis Index [WOMAC] NRS 3.1), visual analog scales (generic 0-100, Short-Form McGill Pain Questionnaire Visual Analog Scale [SF-MPQ-VAS]) or Pain Interference with Activities (PIA) scale derived from the 12-Item Short Form Health Survey [SF-12v2] developed for the Medical Outcomes Study, with recall periods varying from 48 hours to 7 days to 4 weeks. Only one study exclusively assessed symptomatic patients only i.e., patients with pain scores of 0 were excluded; the remainder compared cohorts of no/mild pain with increasing severity cohorts. Four of the 7 studies examined pairwise differences among mild, moderate, and severe patients (1 study vs. a non-OA cohort); 2 compared no/mild vs. moderate-to-severe OA pain and 1 study compared mild to moderate-to-severe OA pain. For most outcomes examined like clinical comorbidities, quality of life, and healthcare resource utilization, increasing burden was observed with increasing OA and/or pain severity despite study variability.
Conclusion: Pain severity levels represent an important and distinguishing factor that contributes to health outcomes in OA patients in the US. Considerable heterogeneity across studies may impact how OA pain is defined, perceived by patients, and treated. Selecting appropriate OA pain severity assessments, including cut-points, may contribute to the successful monitoring of outcomes or comparisons of therapies to manage symptomatic OA pain, especially those that target specific pain severity subgroups.
REFERENCES:
[1] Hawker GA, Mian S, Kendzerska T et al. Arthritis Care and Research. 2011; 63(11):S240-S252.
[2] Schepman P, Robinson RL, Thakkar S, et al. International Society of Pharmacoeconomics and Outcomes Research (ISPOR) Virtual Annual Meeting; May 2020.
[3] Schepman P, Thakkar S, Robinson RL, et al. PAINWeek 2020 Virtual Meeting; September 2020.

Disclosure of Interests: Alesia Sadosky Shareholder of: Own stock in Pfizer Inc, Consultant of: I am an employee with the consulting firm Apperture Health, Employee of: I am retired from Pfizer Inc, Patricia Schepman Shareholder of: Owns shares in Pfizer Inc, Employee of: Employee of Pfizer Inc, Sheena Thakkar Shareholder of: Owns shares of Pfizer Inc, Employee of: Employee of Pfizer Inc, Rebecca Robinson Shareholder of: Owns shares of Eli Lilly and Company, Employee of: Employee of Eli Lilly and Company, Craig Beck Shareholder of: Owns shares of Pfizer Inc, Employee of: Employee of Pfizer Inc
DOI: 10.1136/annrheumdis-2021-eular.534

AB0036 APPA (APOCYNIN AND PAEONOL) REDUCES ROS PRODUCTION AND SENESCENCE IN HUMAN ARTICULAR CHONDROCYTES

M. Fernandez-Moreno[1], N. Larkins[2], A. Reynolds[2], T. Hermida Gómez[1,3], F. J. Blanco[1]. *[1] Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). CICA-INIBIC., Servicio de Reumatología., A Coruña, Spain*; *[2]AKL Research & Development, Stevenage Bioscience, Stevenage SG1 2FX., United Kingdom*; *[3]Centro de Investigación Biomédica en Red, Bioingenieria, Biomatereial y Nanomedicina, (CIBER-BBN)., Madrid, Spain*

Background: Disease modification is not yet possible for osteoarthritis (OA). Mitochondrial ROS and pro-inflammatory cytokines are involved in the pathogenesis of OA and are potential therapeutic targets. APPA, a combination of apocynin (AP) and paeonol (PA), has the potential capacity to modulate synthesis of pro-inflammatory stimuli.
Objectives: To investigate the anti-inflammatory effect of APPA in human articular chondrocytes and cartilage.
Methods: Tissue and chondrocytes from human OA cartilage were isolated. The effect of APPA on chondrocyte viability was analyzed using MTT. IL-1β 10 ng/mL and LPS 10 ng/mL were used as pro-inflammatory stimuli. ROS production was evaluated by flow cytometry using DCFH-DA and MitoSoxRed. The percentage of senescent cells was evaluated through the quantification of Fluorescein di-β-D-galactopyranoside (FDG) by flow cytometry. The effect of APPA on gene expression of pro-inflammatory cytokines (IL-8 and TNF-α) and enzymes degrading cartilage (MMP-13 and MMP-3) were analyzed in chondrocyte and cartilage by RT-PCR. Quantification of Toluidine Blue (TB) staining in cartilage was performed to evaluate proteoglycans content using software ImageJ/Fiji. Release of Glycosaminoglycan (GAGs) into the supernatant was quantified using BlyscanTM Glycosaminoglycan assay. Statistical analyses were performed with GraphPad Prism v6.
Results: *Chondrocytes*, incubated in presence of APPA 10 µg/mL for 24 h had viability >85%, reduced cytoplasmic ROS (p=0.028) and mitochondrial anion superoxide production induced by LPS 10 ng/mL (p=0.057). Chondrocytes incubated in presence of APPA 10 µg/mL for 2 hours contained significantly fewer senescent cells (p=0.0079). APPA significantly reduced the gene expression induced by IL-1β 10 ng/mL in chondrocytes of *IL-8*, *TNF-α*, *MMP-13* and *MMP-3*. *Cartilage* incubated with APPA 60 and 100 µg/mL for 48 h showed decreased the *MMP-3* gene expression induced by IL-1β (p=0.021 and p<0.0001 respectively). Quantification of TB showed that APPA 60 and 100 µg/mL during 48h increased the proteoglycans in intermedial layer, which had been decreased through the incubation with IL-1β (p=0.0018 and p=0.018 respectively). Quantification of release GAGs into the supernatant decreased significantly when the cartilage explants were incubated for 48h in presence of APPA 100 µg/mL (p=0.028).
Conclusion: APPA has a clear anti-inflammatory effect on human articular chondrocytes, and could reduce extracellular matrix degradation of cartilage. This could be mediated by the capacity to modulate ROS production and reduce senescence.
Disclosure of Interests: Mercedes Fernandez-Moreno: None declared, Nicholas Larkins Shareholder of: I am a shareholder in AKL Research and Development Ltd, Alan Reynolds Shareholder of: I have share options in AKL Research and Development Ltd, Speakers bureau: I have not been a paid speaker for a pharma company - at least not since 2008 whichI think is outside the scope of this, Consultant of: The last time I was a paid consultant was in 2017 when I acted as a consultant for Avillion and Norgine, Employee of: I am also an employee of AKL Research and Development Ltd, Tamara Hermida Gómez: None declared, Francisco J. Blanco Speakers bureau: Lilly
Pfizer
Sanofi
Galapagos, Consultant of: Lilly
Pfizer
Sanofi
Galapagos, Grant/research support from: Lilly
MSD
Merck Serono
Pfizer
Pierre-Fabra
Roche
Sanofi
Servier
UCB
Abbvie
Amgen
Bioiberica
Bristol Mayer
Celgene
Celltrion
Cellerix
Grunenthal
Gebro Pharma
AKL Research and Development Ltd
DOI: 10.1136/annrheumdis-2021-eular.2027

AB0037 UNDIFFERENTIATED ARTHRITIS

O. Jomaa[1], J. Mahbouba[1], S. Zrour[1], I. Bejia[1], M. Touzi[1], N. Bergaoui[1]. *[1]University Hospital Fattouma Bourguiba Monastir, TUNISIA, Rheumatology Department, Monastir, Tunisia*

Background: Early recognition and treatment of inflammatory arthritis is imperative for the further course of the disease.
Objectives: This study aims to determine the evolution of undifferentiated arthritis observed in rheumatology.
Methods: Retrospective descriptive study which collects patients files identified as undifferentiated Arthritis and followed in the Rheumatology Department at Fattouma Bourguiba Hospital Monastir TUNISIA over a period of 15 years (2005, 2019). Epidemiological, clinical, paraclinical, and evolutionary data were collected and analyzed.
Results: 99 files were analyzed. The average age was 42.06±15.56; they were 42 males and 57 females with an average body mass index of 27±6.1 Kg/m2. The reason leading to consultation was, polyarthritis (37), oligoarthritis (27), mono-arthritis (21), and polyarthralgia (15). The median time to visit was 60 days [15 days, 3 months]. The median number of painful joints and swollen joints was 4 [2, 8], and 2 [1, 4] respectively. The mean duration of morning derusting was 34.8 ±24.4 minutes. Extra-articular manifestations were: a dry syndrome (22), a rheumatoid nodule (2), and serosal damage (1). Anemia (52 patients), leukopenia (6 patients), and lymphopenia (13 patients) were found in the blood cell count with a biological inflammatory syndrome in most patients (72/99). The immunology results showed: positive anti-nuclear antibodies (15/99), positive Anti-Citrullinated Protein Antibodies (9/99) and positive rheumatoid factor (8/99). 31 patients had standard radiological signs represented mainly by joint pinching and erosions. A joint puncture was done in 36/99 revealing inflammatory fluid in most cases. After an average follow-up of 1047 days [365, 1460]. undifferentiated arthritis was classified as rheumatoid arthritis (RA) (23), spondyloarthritis (SpA) (10), connective tissue disease (11), Crystalline Arthritis (5), and paraneoplastic arthritis (2). One patient had self resolution of symptoms and 38 remain undifferentiated.we found that the more the patients were seropositive, the more likely to develop Rheumatoid Arthritis (p=0.001), the more there was disorder in the blood cell count, the more the evolution was towards connective tissue disease (0.01), The more male patients were, the more likely to develop SpA (p=0.04). The patients management was mainly based on: analgesics (94), systemic corticosteroids (57) with a mean dose of 10.89± 5.8 mg/day. The use of Methotrexate and antimalarial drugs was noted in 18 and 15 patients respectively.
Conclusion: Follow-up of patients with undifferentiated arthritis leads to a definite inflammatory rheumatism diagnosis in 61.6% of cases. Our data indicate that seropositive patients with chronic symptoms carry an increased risk of developing Rheumatoid Arthritis (P=0,001). Clinical, biological and genetic data can help the health care provider to predict future outcomes.
REFERENCES:
[1] DOI: 10.1007/s00132-018-3539-2.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2309

AB0038 CIRCULATING MICRORNAS IN HAND OSTEOARTHRITIS

A. Pekacova[1,2], J. Baloun[1], O. Sleglova[1,2], O. Růžičková[1,2], J. Vencovský[1,2], K. Pavelka[1,2], L. Šenolt[1,2]. *[1]Institute of Rheumatology, Department of Rheumatology, Prague, Czech Republic*; *[2]First Faculty of Medicine Charles University, Department of Rheumatology, Prague, Czech Republic*

Background: microRNAs (miRNAs) are small non-coding RNAs that can ignite the degradation of mRNAs or inhibit the protein translation and are therefore essential for several physiological and pathological functions. miRNAs can regulate up to 60 % of human mRNA, including genes related to cartilage development, homeostasis, and OA pathology. For example, miR-9 inhibits matrix metalloproteinase 13

or miR-140 expression level correlates with the disease progression of knee OA (Zhang et al.; Chao et al.). Under certain circumstances, miRNAs can be released into the body fluids and easily be detected in the blood samples. Therefore, miRNAs are hot candidates as biomarkers for early diagnosis or structural progression of OA.

Objectives: The aim of this study was to evaluate circulating miRNAs in patients with hand osteoarthritis (HOA) and healthy individuals. Simultaneously, we studied specific miRNAs in order to differentiate between erosive and non-erosive subsets of the disease.

Methods: Eight patients with HOA (erosive: n=4, 3 females, mean age=63.7±7 yrs; non-erosive: n=4, 3 females, mean age= 62.4±6 yrs) and 4 healthy controls (3 females, mean age=63.5±7 yrs) were included in this study. Firstly, Advance TaqMan low-density assay (TLDA) was performed for the purpose of miRNA high-throughput screening. Differently expressed miRNAs were further verified by real-time qPCR on the validation cohort in 31 patients with hand OA (19 females, mean age=66.2±7 yrs, erosive: n=9, non-erosive: n=10, healthy controls: n=12).

Results: TLDA profiling displayed 346 circulating miRNAs in plasma of patients with HOA and healthy controls. We demonstrated 40 differently expressed circulating miRNAs in patients with HOA compared with healthy controls. Using a real-time qPCR, we verified increased expression levels of 10 circulating miRNAs in patients with HOA compared with healthy controls, e.g. miR-191-5p (3.4 fold), miR-151a-3p (3.4 fold) or miR-222-3p (2.4 fold). We did not find any specific miRNA, which could distinct erosive from a non-erosive subset of the disease.

Conclusion: Extensive profiling of circulating miRNAs revealed several miRNAs that can be associated with HOA and can help to better understand OA pathogenesis.

REFERENCES:

[1] Chao, Yu, et al. "Expression of MiR-140 and MiR-199 in Synovia and Its Correlation with the Progression of Knee Osteoarthritis." *Medical Science Monitor*, vol. 26, 2020, pp. 1–6, doi:10.12659/MSM.918174.

[2] Zhang, Hongxin, et al. "Downregulation of MicroRNA-9 Increases Matrix Metalloproteinase-13 Expression Levels and Facilitates Osteoarthritis Onset." *Molecular Medicine Reports*, vol. 17, no. 3, 2018, pp. 3708–14, doi:10.3892/mmr.2017.8340.

Acknowledgements: Supported by AZV NV18-01-00542, MHCR No. 023728

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2327

AB0039 AGRIN REPAIRS BONE AND CARTILAGE IN VIVO

S. Eldridge[1], A. Barawi[1], H. Wang[2], A. Roelofs[2], M. Kaneva[1], Z. Guan[1], H. Lydon[3], B. Thomas[1], A. S. Thorup[1], B. F. Fernandez[1], S. Caxaria[1], D. Strachan[1], A. Ali[1], K. Shanmuganathan[1], C. Pitzalis[1], J. Whiteford[4], F. Henson[3], A. Mccaskie[5], C. De Bari[2], F. Dell'accio[1]. [1]*The William Harvey Research Institute, Experimental Medicine and Rheumatology, London, United Kingdom*; [2]*University of Aberdeen, Aberdeen Centre for Arthritis and Musculoskeletal Health, AB25 2ZD, United Kingdom*; [3]*University of Cambridge, Department of Veterinary Medicine, Cambridge, United Kingdom*; [4]*The William Harvey Research Institute, Centre for Microvascular Research, London, United Kingdom*; [5]*University of Cambridge, Department of Surgery, Cambridge, United Kingdom*

Background: Cartilage defects in the joints are reported in 61% of all arthroscopies[1&2]. The size of the cartilage repair market is estimated to be $2.195 million by 2025[3]. Cartilage defects can evolve into osteoarthritis, in which abnormal load results in cartilage breakdown, joint pain and reduced mobility. Osteoarthritis is the leading cause of permanent disability and absenteeism and affects up to 1/3 of the people over 60yrs. In western countries osteoarthritis costs 1.5-2% of the GDP[4]. Joint replacement with a prosthesis restores some degree of independence but in up to 20% of patients it does not meet expectations [5] and has a limited life span. There is no pharmacological intervention that arrests or reverts the course of osteoarthritis, despite the desperate need.

We previously published that agrin plays an important role in cartilage homeostasis[6]. The addition of agrin to chondrocytes *in vivo* resulted in enhanced cartilage formation, suggesting a potential role for agrin in cartilage repair.

Objectives: Investigate the potential of agrin for use in cartilage repair.

Methods: Critical size osteochondral defects were generated in mice and sheep and injected intraarticularly with type I collagen gel containing agrin or vehicle. Animals were monitored for 8 weeks or 6 months respectively. MicroCT, histological analysis, qPCR, linage tracking, reporter assays, chondrogenesis assay, immunohistochemistry were performed.

Results: A single intraarticular administration of agrin induced regeneration of critical-size osteochondral defects in mice, restoring the tissue architecture and bone-cartilage interface. Agrin stem cells to the site of injury and, through simultaneous activation of CREB and suppression of canonical WNT signalling, induced GDF5 expression and differentiation into stable articular chondrocytes, forming stable articular cartilage. In sheep, agrin treatment resulted in regeneration of bone and cartilage, which promoted increased ambulatory activity.

Conclusion: Agrin orchestrates repair morphogenesis at the joint surface by modulating multiple signalling pathways, supporting the therapeutic use of agrin for joint surface regeneration.

REFERENCES:

[1] Curl, W. W. et al. Cartilage injuries: a review of 31,516 knee arthroscopies. Arthrosc. J. Arthrosc. Relat. Surg. Off. Publ. Arthrosc. Assoc. N. Am. Int. Arthrosc. Assoc. 13, 456–460 (1997).

[2] Hjelle, K., Solheim, E., Strand, T., Muri, R. & Brittberg, M. Articular cartilage defects in 1,000 knee arthroscopies. Arthrosc. J. Arthrosc. Relat. Surg. Off. Publ. Arthrosc. Assoc. N. Am. Int. Arthrosc. Assoc. 18, 730–734 (2002).

[3] Cartilage Repair Market Size, Share, Industry Analysis 2018-2025 | AMR. Allied Market Research https://www.alliedmarketresearch.com/cartilage-repair-market.

[4] Hiligsmann, M. et al. Health economics in the field of osteoarthritis: an expert's consensus paper from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Semin. Arthritis Rheum. 43, 303–313 (2013).

[5] Dieppe, P., Lim, K. & Lohmander, S. Who should have knee joint replacement surgery for osteoarthritis? Int. J. Rheum. Dis. 14, 175–180 (2011).

[6] Eldridge, S., et al. Agrin mediates chondrocyte homeostasis and requires both LRP4 and α-dystroglycan to enhance cartilage formation in vitro and in vivo. Annals of the rheumatic diseases 75 (6), 1228-1235 (2016).

Acknowledgements: We thank the technical staff in the ARM Lab and Staff at the University of Aberdeen's Animal Facility and Microscopy and Histology Facility for support. Funding: We gratefully acknowledge funding support of this work by the MRC (MR/L022893/1, MR/N010973/1,and MR/P026362/1), Versus Arthritis (19667, 21515, 20886, and 21621), Rosetrees Trust (A1205), the Medical College of St Bartholomew's Hospital Trust, and the William Harvey Research Foundation.

Disclosure of Interests: Suzanne Eldridge: None declared, Aida Barawi: None declared, Hui Wang: None declared, Anke Roelofs: None declared, Magdalena Kaneva: None declared, Zeyu Guan: None declared, Helen Lydon: None declared, Bethan Thomas: None declared, Anne-Sophie Thorup: None declared, Beatriz F Fernandez: None declared, Sara Caxaria: None declared, Danielle Strachan: None declared, Ahmed Ali: None declared, Kanatheepan Shanmuganathan: None declared, Costantino Pitzalis: None declared, James Whiteford: None declared, Fran Henson: None declared, Andrew McCaskie: None declared, Cosimo De Bari: None declared, Francesco Dell'Accio Consultant of: F.D. has received consultancy fees from Samumed and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2584

AB0040 PYRUVATE DEHYDROGENASE KINASES AS A POTENTIAL TARGET IN THE TREATMENT OF OSTEOARTHRITIS TO UNLEASH THE METABOLIC FLOW?

A. Damerau[1,2], M. Kirchner[3], M. Pfeiffenberger[1,2], A. Lang[1,2], F. Buttgereit[1,2], T. Gaber[1,2]. [1]*Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; [2]*German Rheumatism Research Centre (DRFZ) Berlin, a Leibniz Institute, Berlin, Germany, Rheumatism Research, Berlin, Germany*; [3]*Berlin Institute of Health (BIH) and Max-Delbrück-Centrum für Molekulare Medizin (MDC), Proteomics Core Facility, Berlin, Germany*

Background: While osteoarthritis (OA) is the most common joint disease worldwide, rheumatoid arthritis (RA) represents the most common type of autoimmune arthritis. In both diseases, fibroblast-like synoviocytes (FLS), which maintain the structural and dynamic integrity of the joint, have been identified as key drivers of cartilage degradation. FLS can be divided into two major populations. The destructive phenotype which is restricted to the THY1- FLS of the synovial lining promotes bone erosion, while THY1+ FLS of the sublining layer drives synovitis. The FLS phenotype is shaped by glucose metabolism, which promotes disease progression in patients with synovitis. However, profound knowledge about the contribution of FLS to pathogenic mechanisms in cartilage degradation is limited.

Objectives: Here, we present the phenotypic features of FLS obtained from patients with OA (OA-FLS) compared to bone marrow-derived mesenchymal stromal cells (MSC) on transcriptomic, proteomic and metabolic levels with the aims (i) to identify novel targets for the development of disease-modifying osteoarthritis drugs and (ii) to distinguish both cell types.

Methods: To this end, we comprehensively compared human bone marrow-derived MSC with OA-FLS isolated from human knee joint sections. MSC and OA-FLS were characterized in detail according to their multipotency, surface marker pattern, cell viability, proliferation rate, morphology and expression of fibroblast- and metabolic-related markers using flow cytometry, immunofluorescence and Seahorse™. More in-depth, selected gene and protein expression patterns were analyzed using qPCR and mass spectrometry.

Results: We observed a similar phenotype of OA-FLS and MSC with regard to the minimal criteria that define a MSC phenotype. In-depth comparison of

OA-FLS and MSC on proteome level revealed 598 differentially expressed proteins. We observed no differences in the expression of classical fibroblast markers such as vimentin, tenascin C and decorin as confirmed on RNA level. Remarkably, fibronectin, which is mainly produced by fibroblasts, is significantly lower expressed at both protein and RNA levels in OA-FLS together with collagen type 1 and CD106. Conversely, CD9, CD54 and fibroblast-specific protein-1 were expressed significantly higher in FLS at both levels, while hyaluronan synthase 1-3 remained unchanged. Of note, in terms of mitochondrial function, human OA-FLS show a significantly lower basal respiration and ATP production than MSC, but a comparable spare respiratory capacity and cellular mitochondrial dehydrogenase activity (NADH amount) per cell. Additionally, we identified the pyruvate dehydrogenase kinase (PDK) 3 to be highly expressed in OA-FLS, while the expression of mitochondrial ATP synthase subunits, electron transport chain complexes and glycolytic enzymes was comparable with MSC. Finally, inhibition of PDK by using DCA resulted in a significant increase in oxygen consumption rate and ATP production in OA-FLS. Thus, our data newly suggest, that PDKs may play a crucial role in the pathogenesis of OA and possibly RA.
Conclusion: Our data provide evidence that, although the classical fibroblast markers do not discriminate between MSC and FLS, the latter demonstrate a significantly higher expression of PDKs, known to inhibit the pyruvate entry into the TCA cycle which finally limits the mitochondrial ATP production. Therefore, shifting the metabolism of FLS from glycolysis to mitochondrial respiration via inhibition of PDKs might be a novel approach in OA for the development of disease-modifying osteoarthritis drugs in order to unleash the metabolic flow.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2829

AB0041

TO ESTIMATE THE PREVALENCE OF ACETABULAR OSSIFICATIONS IN THE ADULT POPULATION WITH ASYMPTOMATIC, MORPHOLOGICALLY NORMAL HIPS AT CT AND TO DETERMINE WHETHER THE PRESENCE OF LABRAL OSSIFICATIONS IS ASSOCIATED WITH PATIENT-RELATED OR HIP-RELATED PARAMETERS

C. Valente[1], L. Haefliger[2], J. Favre[2], P. Omoumi[2]. [1]*CHV, Radiology, Versailles, France*; [2]*CHUV, Radiology, Lausanne, Switzerland*

Background: In clinical practice, ossifications adjoining the acetabular rim are frequently seen in healthy-appearing hip joints, at all ages. The origin of these acetabular rim ossifications (ARO) is unclear. While ARO have been described by some authors as variants that may mimic marginal acetabular osteophytes, others have hypothesized that ARO may be the cause or the consequence of femoroacetabular impingement. Overall, the literature on ARO is limited, in particular in the healthy population, and their characteristics and origin not fully understood.
Objectives: To estimate the prevalence of acetabular rim ossifications in the adult population with asymptomatic, morphologically normal hips at CT and to determine whether the presence of these ossifications is associated with patient-, or hip-related parameters.
Methods: We prospectively included all patients undergoing thoracoabdominal CT over a 3-month period. After exclusion of patients with a clinical history of hip pathology and/or with signs of osteoarthritis on CT, we included a total of 150 hips from 75 patients. We analyzed the presence and the size of ossifications around the acetabular rim. The relationships between the size of acetabular rim ossifications and patient-related (sex, age, BMI), or hip-related parameters (joint space width, and cam- and pincer-type femoroacetabular impingement morphology) were tested using multiple regression analysis.
Results: The prevalence of acetabular rim ossifications in this population of asymptomatic, non-osteoarthritic hips was 96% (95%CI=[80.1;100.0]). The presence of ossifications and their size were correlated between right and left hips (Spearman coefficient=0.64 (95%CI=[0.46;0.79]),p<0.05)).The size of acetabular rim ossifications was significantly associated with age (p<0.0001) but not with BMI (p=0.35), gender (p=0.05), joint space width (p≥0.53 for all locations) or any of the qualitative or quantitative parameters associated with femoroacetabular morphology (p≥0.34).
Conclusion: Acetabular rim ossifications are highly prevalent in asymptomatic, non-osteoarthritic adult hips at all ages. Their size is not correlated with any patient-, or hip-related parameters except for the age. These findings suggest that ossifications at the acetabular rim, when present in isolation, should not be considered as signs of osteoarthritis or femoroacetabular impingement morphology.
REFERENCES:
[1] J. W. T. Byrd, K. S. Jones, C. R. Freema. Surgical Outcome of Pincer Femoroacetabular Impingement With and Without Labral Ossification. *Arthroscopy* 2016; 32: 1022–1029.
[2] P. D. Byers, C. A. Contepomi, and T. A. Farkas. A post mortem study of the hip joint. Including the prevalence of the features of the right side. *Annals of Rheumatic Diseases 1970*; 29: 15–31.
[3] S. Ninomiya, A. Shimabukuro, T. Tanabe, Y. T. Kim, Y. Tachibana. Ossification of the acetabular labrum. *Journal of Orthopaedics Science* 2001; 5: 511–514.

Table 1. Association between the average severity size of ossifications and patient-related, and hip-related parameters

		Regression coefficient	p- value
Patient-related parameters	BMI	0.02	0.35
	Age	0.04	<0.001
	Gender	-0.43	0.05
Joint space width	Apical	0.17	0.53
	Supero-medial	0.17	0.65
	Supero-lateral	0.06	0.82
Cam morphotype parameters	Angle alpha 45	0.00	0.81
	Offset	0.09	0.34
Pincer morphotype parameters	Acetabular version angle	-0.01	0.83
	Lateral center-edge angle	0.02	0.56
	Acetabular index	0.03	0.53
	Crossover sign	0.26	0.41
	Posterior wall sign	-0.25	0.47

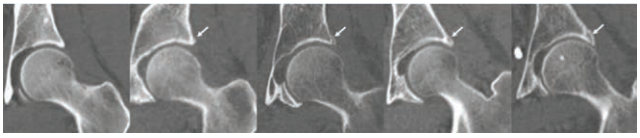


Figure 1. Coronal reformats of CT examinations showing different sizes of labral ossifications in the posterosuperior quadrant (arrows). (a) No labral ossification, (b-c-d-e) Increasingly large labral ossification from left to right. Two lines are visible at the location of the ossification, formed by the contour of the acetabular rim and of the ossification (double line-sign).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3216

Rheumatoid arthritis - aetiology, pathogenesis and animal models

AB0042

THREE HEMATOLOGIC/IMMUNE SYSTEM-SPECIFIC EXPRESSED GENES ARE CONSIDERED AS THE POTENTIAL BIOMARKERS FOR THE DIAGNOSIS OF EARLY RHEUMATOID ARTHRITIS THROUGH BIOINFORMATICS ANALYSIS

Q. Cheng[1], X. Chen[1], H. Wu[1], Y. Du[1]. [1]*The Second Affiliated Hospital of Zhejiang University School of Medicine, Rheumatology, Hangzhou, China*

Background: Rheumatoid arthritis (RA) is a common chronic autoimmune connective tissue disease that mainly involves the joints. The incidence of RA is 5 to 10 per 1000 people[1]. Early diagnosis and treatment of RA can effectively prevent disease progression, joint damage, and other complications in 90% of patients[2]. At present, serum biomarkers used in the diagnosis of established RA are rheumatoid factor and anti-cyclic citrullinated peptide antibody[3]. However, early RA especially serum RF and anti-CCP antibody-negative is difficult to diagnose due to the lack of effective biomarkers. Therefore, it is vital to identify new and effective biomarkers for the early diagnosis and treatment of RA.
Objectives: This study aimed to identify new biomarkers and mechanisms for RA disease progression at the transcriptome level through a combination of microarray and bioinformatics analyses.
Methods: Microarray datasets for synovial tissue in RA or osteoarthritis (OA) were downloaded from the Gene Expression Omnibus (GEO) database, and differentially expressed genes (DEGs) were identified by R software. Tissue/organ-specific genes were recognized by BioGPS. Enrichment analyses were performed and protein-protein interaction (PPI) networks were constructed to understand the functions and enriched pathways of DEGs and to identify hub genes. Cytoscape was used to construct the co-expressed network and competitive endogenous RNA (ceRNA) networks. Biomarkers with high diagnostic value for the early diagnosis of RA were validated by GEO datasets. The ggpubr package was used to perform statistical analyses with Student's t-test.
Results: A total of 275 DEGs were identified between 16 RA samples and 10 OA samples from the datasets GSE77298 and GSE82107. Among these DEGs, 71 tissue/organ-specific expressed genes were recognized. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis indicated that DEGs are mostly enriched in immune response, immune-related biological process, immune system, and cytokine signal pathways. Fifteen hub genes and gene cluster modules were identified by Cytoscape. Eight haematologic/immune system-specific expressed hub genes were verified by GEO datasets. GZMA, PRC1, and TTK may be biomarkers for diagnosis of early RA through combined the analysis of the verification results and the receiver operating characteristic (ROC) curve. NEAT1-miR-212-3p/miR-132-3p/miR-129-5p-TTK, XIST-miR-25-3p/miR-129-5p-GZMA,

and TTK_hsa_circ_0077158- miR-212-3p/miR-132-3p/miR-129-5p-TTK might be potential RNA regulatory pathways to regulate the disease progression of early RA.

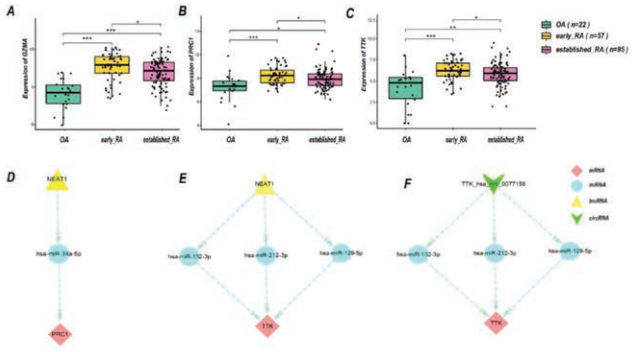
Conclusion: This work identified three haematologic/immune system-specific expressed genes, namely, GZMA, PRC1, and TTK, as potential biomarkers for the early diagnosis and treatment of RA and provided insight into the mechanisms of disease development in RA at the transcriptome level. In addition, we proposed that NEAT1-miR-212-3p/miR-132-3p/miR-129-5p-TTK, XIST-miR-25-3p/miR-129-5p-GZMA, and TTK_hsa_circ_0077158-miR-212-3p/miR-132-3p/miR-129-5p-TTK are potential RNA regulatory pathways that control disease progression in early RA.

REFERENCES:

[1] Smolen JS, Aletaha D, McInnes IB: **Rheumatoid arthritis.** *Lancet* 2016, **388:**2023-2038.

[2] Aletaha D, Smolen JS: **Diagnosis and Management of Rheumatoid Arthritis: A Review.** *Jama* 2018, **320:**1360-1372.

[3] Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, 3rd, Birnbaum NS, Burmester GR, Bykerk VP, Cohen MD, et al: **2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative.** *Arthritis Rheum* 2010, **62:**2569-2581.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.135

AB0043 EFFECT OF ANTI-INFLAMMATORY MEDICATION ON INTERACTION OF SYNOVIAL FIBROBLASTS WITH MACROPHAGES IN RHEUMATOID ARTHRITIS

M. Schmeller[1], M. Diller[1], R. Hasseli[1], A. Knothe[1], S. Rehart[2], I. Tarner[1], W. Hermann[1], U. Lange[1], U. Müller-Ladner[1], E. Neumann[1]. [1]*Justus Liebig University Giessen, Campus Kerckhoff, Department of Rheumatology and Clinical Immunology, Bad Nauheim, Germany*; [2]*Agaplesion Markus Hospital, Department of Orthopaedics and Trauma Surgery, Frankfurt, Germany*

Background: One of the key mechanisms in the pathogenesis of rheumatoid arthritis (RA) is the interaction of macrophages and synovial fibroblasts during joint inflammation. Increased synergistic proinflammatory activity of both cell types leads to the release of high levels of proinflammatory cytokines, especially of interleukin-6 (IL-6), and of matrix degrading enzymes. If this mechanism is uncontrolled, progressive destruction of articular cartilage and bone will take place.

In active disease, immediate anti-inflammatory treatment with glucocorticoids is usually replaced by disease-modifying anti-rheumatic drugs (DMARDS), especially by methotrexate (MTX) and biologics such as TNF-α- or IL-6-inhibitors. This led to great improvements in prognosis and outcome for RA patients. However, about 40% of patients experience no remission or suffer from side effects of medication. To optimize established substances and to develop new treatment strategies, it is necessary to understand the mechanisms underlying the limited therapeutic effects.

Objectives: Evaluation of the effect of prednisolone, MTX, adalimumab, tocilizumab on IL-6 secretion by RA synovial fibroblasts (RASF) and macrophages.

Methods: RA synovium was used for RASF isolation. Peripheral blood mononuclear cells (PBMCs) were isolated from blood of healthy donors and RA patients by using Ficoll© medium followed by density gradient centrifugation. Mononuclear cells were seeded on six well plates (6x10^6/well) and incubated for one week. Then they were stimulated with Interferon-γ (20 ng/ml) and LPS (50 ng/ml) for 48h to initiate differentiation into proinflammatory M1 macrophages. The M1 macrophages were co-cultured with RASF (100.000/well) and different treatments added (prednisolone: 10, 25, 50, 75, 100 nM, 1 µM; adalimumab: 100, 500 µg/ml; tocilizumab: 1, 5 µg/ml; MTX: 0,5, 1, 5, 10, 100 nM, 1µM). After 24h culture supernatants were collected and IL-6- and TNFα-ELISAs were performed.

Results: IL-6 concentrations of untreated controls were comparable, regardless whether M1 macrophages from healthy donors or RA-patients were used for co-culture. Prednisolone reduced co-culture-induced IL-6 up to 56% ($p<0.001$) in co-culture of RASF and M1 macrophages of healthy donors and up to 60% ($p<0.001$) in co-culture of RASF and RA M1 macrophages. Adalimumab reduced IL-6 up to 28% ($p<0.05$) in M1 of healthy donors and up to 45% ($p<0.01$) in RA M1 macrophage co-cultures. A minor reduction by 10-20% of IL-6 was observed with tocilizumab and no significant effect could be achieved after treatment with MTX.

Conclusion: Prednisolone and adalimumab clearly decrease but do not eliminate proinflammatory synergistic activity of RASF and M1 macrophages. These results confirm the clinical observation, that there is a large number of RA-patients that independent of anti-inflammatory treatment still suffer from low-level joint inflammation.

The synergistic proinflammatory activity of M1 macrophages and RASF seems to be a complex and multifactorial mechanism that is difficult to eliminate by a single treatment substance. Since it is one of the key mechanisms in RA pathogenesis, there is a critical need to investigate how therapy effects could be optimized. This study confirmed RASFs as one of the leading effector cells of increased synergistic proinflammatory activity, thus underlining their promising role as a treatment target in rheumatoid arthritis.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.247

AB0044 ENDOTHELIAL CELL AND RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLAST MIGRATION AND ADHESION ARE ALTERED BY ACTIVIN/FOLLISTATIN

H. M. Scholz[1], I. Aykara[1], K. Frommer[1], S. Rehart[2], U. Müller-Ladner[1], E. Neumann[1]. [1]*Kerckhoff-Klinik GmbH, Rheumatologie und Klinische Immunologie, Bad Nauheim, Germany*; [2]*Agaplesion Markus Krankenhaus, Klinik für Orthopädie und Unfallchirurgie, Frankfurt am Main, Germany*

Background: Activin A and follistatin belong to an anti-inflammatory auto-regulatory cycle. Patients with rheumatoid arthritis (RA) have increased activin A levels in the synovial fluid and tissue. During inflammation, activin A is released systemically, then inducing its antagonist follistatin. This negative feedback is active in different cell types but not RA synovial fibroblasts (SF). Fibroblasts interact with endothelial cells in inflamed tissues inducing angiogenesis.

Objectives: Evaluation of the role of activin A and follistatin on RASF and endothelial cell interactions.

Methods: RA synovium was used for RASF isolation, HUVEC were commercially obtained. RASF and HUVEC were stimulated in mono- and coculture. Direct: RASF together with HUVEC; indirect: inserts with HUVEC separated by a membrane from RASF. Stimuli: activin A 15ng/ml, follistatin 500ng/ml, IL-1β 1ng/ml. Proliferation was analyzed by BrdU assay. RASF were Calcein-AM stained. Cells were transferred to 24-well plates after 18h stimulation. After adhesion for 1h, non-adherent cells were removed by shaking 3x for 5 min. Afterwards, fluorescent cells were quantified. For the flow-adhesion assay, HUVEC were cultured on rattail collagen coated capillary slides. HUVEC and RASF were stimulated for 4h with TNFα, TNFα+activin A or TNFα+follistatin. After stimulation, 2x10^6 RASF were resuspended in 20ml medium and sent through the capillaries. Two 1min videos were recorded (18.4ml/h, 30.5ml/h). Settings: TNFα-stimulated RASF on HUVEC stimulated wit TNFα or activin A+TNFα or follistatin+ TNFα. For migration assays, 2% FCS medium with 1x10^5 cells were placed in inserts (8µm membrane) into wells with 10% FCS (control: 2%FCS vs. 2%FCS) and stimulated with, IL-1, IL-1+activinA and IL-1+follistatin. After 16h, migrated cells were quantified. For scratch-assay 4x10^5 cells were cultured overnight, then cells were scratched and stimulated, afterwards 3 pictures per scratch were taken at start, after 10h and every 1.5h. Cells migrating into the scratch area were quantified.

Results: IL-1 induced activin A in RASF and HUVEC in all settings. IL-1-induced activin A release was reduced by follistatin in HUVEC monoculture and both cocultures compared to IL-1 alone but not in RASF monoculture. IL-1-induced IL-6 release was reduced by activin A in HUVEC and indirect coculture but not in RASF monoculture and direct coculture. Follistatin did not alter IL-6 responses. IL-1 induced VEGF in RASF but not in HUVEC and was not altered by activin A. Short-term adhesion showed no significant influence of activin A or follistatin (n=4). Flow adhesion assay showed reduced adherence/rolling of RASF on HUVEC stimulated with TNFα and activin A (n=4). Migration assays showed that IL-1 decreased migration but without significant difference between the induced effects mediated by IL-1+activinA and IL-1+follistatin (n=4). Scratch assay showed increased migration in dicrect coculture with greater difference between stimulated and unstimulated cells in RASF monoculture and indirect coculture (n=4). Proliferation was not altered by activin A or follistatin.

Conclusion: In direct and indirect coculture of HUVEC with RASF the effect on HUVEC was dominant leading to reduced IL-1-induced activin A release. However, the IL-1-induced IL-6 release in RASF or HUVECs was decreased by activin A in HUVEC monoculture and indirect coculture but not during cell-contact between both cell types. The direct interaction of RASF with HUVEC seems to prevent the reducing activin A effect on IL-6 release in HUVECs. Activin A seems to not to have an impact on short-term cell adhesion but first observations show, that activin A alters selectin-mediated adhesion under flow conditions. The migration assay shows that IL-1-induced effects on cell migration were enhanced by activin

A and follistatin. Migration assay shows that IL-1-induced decrease on migration more prominent in indirect coculture and RASF monoculture than in direct coculture although in gap migration in the scratch assay was highest in direct coculture.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.271

AB0045 THE RELATIONSHIP BETWEEN CD14 AND VIMENTIN-POSITIVE SYNOVIAL DENDRITIC-SHAPED CELLS AND SYNOVITIS IN RHEUMATOID ARTHRITIS

R. Kurose[1,2], T. Satoh[3], K. Murakami[4], A. Kurose[5], Y. I. Satoh[6], Y. Ishibashi[2], K. Ishida[7], K. Ogasawara[7], A. Morikawa[8], T. Sawai[9]. [1]*Hirosaki Memorial Hospital, Orthopedic Surgery, Hirosaki, Japan*; [2]*Hirosaki University, Orthopedic Surgery, Hirosaki, Japan*; [3]*Iwate Medical University, Pathology, Morioka, Japan*; [4]*Iwate Medical University, Orthopaedic Surgery, Morioka, Japan*; [5]*Hirosaki University, Pathology, Hirosaki, Japan*; [6]*Iwate Medical University, Medical Education, Morioka, Japan*; [7]*Iwate Medical University, Technical Support Center, Morioka, Japan*; [8]*Hitachi High-Technologies Corporation, Electron Microscope Application Group, Hitachinaka, Japan*; [9]*Tohoku University, Pathology, Sendai, Japan*

Background: Inflammation in rheumatoid arthritis (RA) is caused by multiple cell types, including infiltrating inflammatory cells, such as lymphocytes, neutrophils, macrophages, and spindle-shaped fibroblasts. Especially, we are focusing on fibroblast-like synoviocytes (FLSs). In our previous study, we have reported that FLSs were positive for multiple markers including CD14, CD68 and HLA-DR, and were dendritic-shaped cells constituting nursing phenomenon between lymph or plasma cells. In addition, in our recent study, we found that CD14+FLSs were positive for vimentin (VIM), which is a marker for mesenchymal cells. There are still many issues to be discussed regarding CD14+VIM+ cells.
Objectives: To investigate the relationship between CD14+VIM+ cells and the degree of synovitis in rheumatoid arthritis.
Methods: Synovial tissues collected from RA patients who underwent joint surgeries were prepared for this study. First, the proportions of CD14+ cells in RA synovial tissue and control were analyzed using flow cytometry and the concentrations of inflammatory cytokines released by CD14+ cells in RA synovial tissue and control were examined by ELISA. Next, the proportions of CD14+VIM+ cells in RA synovial tissue and control were examined immunohistologically and then we analyzed the results using image analysis software. Also, we statistically analyzed the relationship between the proportion of CD14+VIM+ cells, the degree of synovitis, and clinical data.
Results: Results of flow cytometry showed that CD14+ cells were frequently observed in RA synovial tissue than control. Cultured CD14+ cells released more inflammatory cytokines than cultured CD14- cells. Also, results of immunohistological staining showed that many CD14+VIM+ cells were observed in RA synovial tissue than in control. The proportion of CD14+VIM+ cells was correlated with Krenn synovitis score. High proportion cases significantly showed high level of CRP and MMP-3.
Conclusion: CD14+VIM+ cells might be involved in the mechanism of chronic immunological inflammation in RA and the proportion of these cells might influence the clinical data.

REFERENCES:

[1] Ochi T, Yoshikawa H, Toyosaki-Maeda T, Lipsky PE. Mesenchymal stromal cells. Nurse-like cells reside in thesynovial tissue and bone marrow in rheumatoid arthritis. Arthritis Research&Therapy 2007; 9(1): 201.
[2] Ochi T, Sawai T, Murakami K, Kamataki A, Uzuki M, Tomita T, et al. Nurse-like cells in rheumatoid arthritis: Formation of survival niches cooperating between the cell types. Mod Rheum 2018; 29: 1-5.
[3] Krenn V, Morawietz L, Burmester GR, Kinne RW, Muller-Ladner U, Muller B, Haupl T. Synovitis score: discrimination between chronic low-grade and high-grade synovitis. Histopathology 2006; 49: 358-64.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.428

AB0046 THE EXPRESSION AND CLINICAL SIGNIFICANCE OF TAM RECEPTOR TYROSINE KINASE ON MONOCYTE SUBSETS IN RHEUMATOID ARTHRITIS

J. Xue[1], L. Xu[1], F. Hu[1], Y. Su[1]. [1]*Peking University People's Hospital, Department of Rheumatology and Immunology, Beijing, China*

Background: The TAM receptor tyrosine kinases (Tyro3/Axl/Mer TK) are a subfamily of receptor tyrosine kinases, the role of which in autoimmune diseases such as systemic lupus erythematosus has been well explored, while their functions in rheumatoid arthritis (RA) remain largely unknown [1].
Objectives: The study aimed to investigate the expression and clinical significance of Tyro3, Axl and MerTK on monocyte subsets in rheumatoid arthritis (RA).
Methods: The expression of Tyro3, Axl and MerTK on CD14+ monocytes, nonclassical monocytes (NCM, $CD14^{+}CD16^{++}$), intermediate monocytes (IM, $CD14^{++}CD16^{+}$), and classical monocytes (CM, $CD14^{++}CD16^{-}$) were evaluated in peripheral blood of RA by flow cytometry and qPCR. And the correlation between the expression of Tyro3TK and MerTK on NCM, IM, and CM with RA patient clinical feature were further analyzed.
Results: The results revealed that the expression of Tyro3TK on CD14+ monocytes was significantly upregulated in RA patients ($F = 9.18$, $P < 0.0001$), while there was no significant difference of the expression MerTK on HC, OA, and RA, and the expression of AxlTK was minimal (Fig 1). The expression of Tyro3TK on CM was significantly upregulated in RA patients as compared with HC and osteoarthritis (OA) patients ($P < 0.05$, Fig 2-3), and positively correlated with the disease manifestations, such as swollen joint count (SJC), tender joint count (TJC) and the disease activity score (Fig 4).

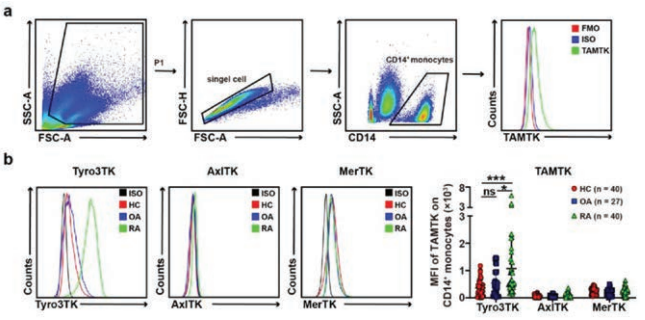


Figure 1. The expression of Tyro3, Axl and MerTK on CD14+ monocytes is increased in RA. (a) Gating strategy for flow cytometry of Tyro3, Axl and MerTK on CD14+ monocytes. **(b)** The expression of Tyro3, Axl and MerTK on CD14+ monocytes were compared between HC (n = 40), OA (n = 27), and RA patients (n = 40). **P* < 0.05, ***P* < 0.01, ns, not significant.

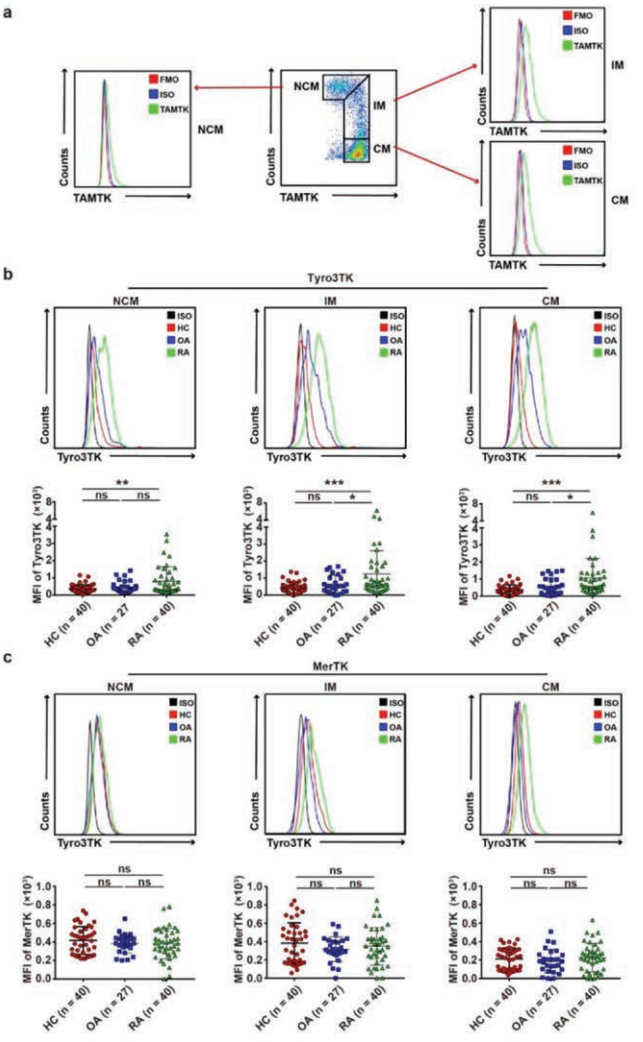


Figure 2. The expression of Tyro3TK on IM and CM were increased in RA. (a) Gating strategy for flow cytometry of TAMTK on monocyte subsets. The expression of **(b)** Tyro3TK and **(c)** MerTK on NCM, IM, and CM were compared between HC (n = 40), OA (n = 27), and RA patients (n = 40). *P < 0.05, ***P* < 0.01, ****P* < 0.001, ns, not significant.

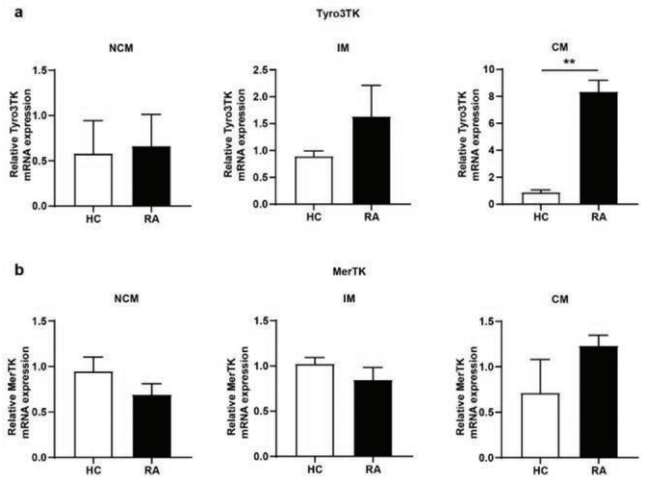


Figure 3. The mRNA expression of Tyro3TK on CM is increased in RA. (a) The mRNA expression of Tyro3TK on NCM, IM, and CM in HC (n = 3) and RA (n = 3) patients. **(b)** The mRNA expression of MerTK on NCM, IM, and CM in HC (n = 3) and RA (n = 3) patients. $^{**}P < 0.01$.

Conclusion: These findings indicate that Tyro3TK on CM was elevated in RA patients and correlated positively with disease activity, which may serves as an important participant in RA pathogenesis.

REFERENCES:

[1] Rothlin CV, Lemke G, TAM receptor signaling and autoimmune disease. Curr Opin Immunol, 2010. 22(6): p. 740-6.

Footnotes: The study was supported by grants from the National Natural Science Foundation of China (81671609 and 81871290 to Dr. Y. Su, 82001718 to Dr. L. Xu), the Beijing Science and Technology Planning Project (Z191100006619111 to Dr. Y. Su), the Beijing Municipal Natural Science Foundation (7194329 to Dr. L. Xu).

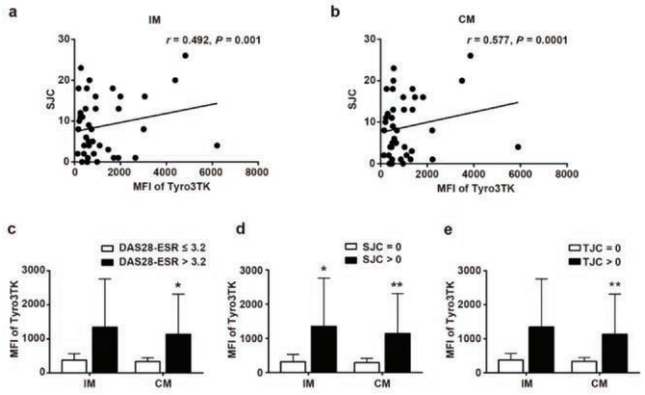


Figure 4. Correlation analysis of Tyro3TK on IM and CM with RA patient clinical manifestations. The associations of Tyro3TK on IM (r = 0.492, $^{*}P = 0.001$) **(a)** and CM (r = 0.577, $^{*}P = 0.0001$) **(b)** with RA patient swollen joint counts (SJC) were analyzed, respectively. The expression of Tyro3TK on IM and CM were also compared between different RA patient groups: **(c)** RA with high disease activity (DAS28-ESR > 3.2) and non-high disease activity (DAS28-ESR ≤ 3.2), **(d)** RA with and without swollen joints, (e) tender joints. $^{*}P < 0.05$, $^{**}P < 0.01$.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.636

AB0047

CLINICAL AND RADIOLOGICAL CHARACTERISTICS AND TREATMENTS OF A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS AND DIFFUSE INTERSTICIAL PULMONARY DISEASE FOLLOWED AT THE VIRGEN MACARENA UNIVERSITY HOSPITAL

P. Muñoz Reinoso[1], F. J. Toyos Sáenz de Miera[1], D. Ruiz-Montesinos[1], I. García Hernández[1], P. Guerrero Zamora[2], J. J. Pérez Venegas[1]. *[1]Hospital Universitario Virgen Macarena, Reumatología, Sevilla, Spain*; *[2]Hospital Universitario Virgen Macarena, Neumología, Sevilla, Spain*

Background: Diffuse interstitial lung disease (ILD) is an extra-articular manifestation of rheumatoid arthritis (RA)[1,2]. The most common pattern is the usual interstitial pneumonia (UIP), conditioning a worse prognosis[3].

Objectives: To describe epidemiological, clinical, and radiological characteristics and treatment used in a cohort of patients diagnosed with RA and ILD.

Methods: Retrospective descriptive study, including patients with a diagnosis of RA and ILD, reviewed in the Rheumatology and Pneumology consultations of the Virgen Macarena University Hospital, from 2010 to 2019. Data obtained from medical records are analyzed. SPSS statistical software is used.

Results: 26 patients were included, 18 women (69.2%). Median age at diagnosis of ILD was 62 years (53-73). Twelve patients (46.6%) used to smoke. The mean time from RA diagnosis to ILD diagnosis was 79 months (8-264). The RF was positive in 91.3% cases (21) and 87% of them (20) were ACPA positive. Fourteen patients (53.8%) had erosions and 3 (11.5%) had an associated Sjögren's Syndrome. When ILD was diagnosed, the RA activity by DAS28PCR was moderate (3.28; 2.34-3.28) and 13 patients (54.1%) suffered from dyspnea. The mean value of FVC and DLCO in the first assessment was 84% (63-108) and 71.7% (64-86), respectively. The most frequent radiological pattern of ILD was NINE in 15 patients (57.7%), 6 of them (23.1%) had UIP and 5 (19.3%) presented other patterns. Prior to ILD diagnosis, 24 (92.3%) patients received oral glucocorticoids, 18 (69.2%) cases started treatment with c-DMARD and 11 (42.3%) of them with b-DMARD; the most widely used were methotrexate (MTX) in 17 patients (65.4%) and anti-TNFα in 10 (38.5%). After diagnosis, treatment was changed to 12 patients (46.6%); the most used DMARD was leflunomide, in 11 (42.3%), MTX was maintained in 7 patients (26.9%); the number of anti-TNFα used decreased to 4 cases (15.4%), using instead drugs such as rituximab 5 (19.2%), abatacept 3 (11.5%), baricitinib 2 (7.7%) and anti-IL6 2 (7, 7%). During follow-up, 11 cases (57.9%) remained radiologically stable. A slight deterioration in DLCO was observed (66%; 51-80) and there was one death due to lung disease (UIP).

Conclusion: In this study, the most frequent radiological pattern was NINE. Half of the patients used to smoke. At the diagnosis of ILD (at ILD diagnosis), dyspnea was the most relevant clinical symptom, with a slight deterioration in the? respiratory function tests. This represented a change in the therapeutic strategy.

REFERENCES:

[1] Olson AL, Swigris JJ, Sprunger DB, et al. Rheumatoid arthritis-interstitial lung disease-associated mortality. Am J Respir Crit Care Med. 2011;183:372-78.
[2] Fragoulis GE, Nikiphorou E, Larsen J, Korsten P and Conway R. Methotrexate-Associated Pneumonitis and Rheumatoid Arthritis-Interstitial Lung Disease: Current Concepts for the Diagnosis and Treatment. Front. Med. 2019;6:238.
[3] Tanaka N, Kim JS, Newell JD, et al. Rheumatoid arthritis-related lung diseases: CT findings. Radiology. 2004;232:81-91.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1413

AB0048

ENZYMATIC PATTERN OF CIRCULATING PRO- AND ANTIOXIDANT ENZYMES IN RHEUMATOID ARTHRITIS PATIENTS

S. Bedina[1], E. Mozgovaya[1], A. Trofimenko[1], S. Spitsina[1], M. Mamus[1]. *[1]Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky, Clinical Biochemistry Lab, Volgograd, Russian Federation*

Background: Rheumatoid arthritis (RA) is an autoimmune rheumatic disease of unknown etiology characterized by chronic erosive arthritis and systemic organ involvement resulting in early disability and shorter life expectancy. Neutrophils are suggested to play a substantial role in the induction and promotion of autoimmune inflammation in RA. This ability can be based on newly discovered feature of neutrophils to release neutrophil extracellular traps (NETs) during specific type cell death called NETosis. Hyperproduction of reactive oxygen species (ROS) is one of the factors promoting NETs production. With this background, the study of pro- and antioxidant enzymatic activities in RA patients can be of great interest.

Objectives: To assess plasma activities of essential prooxidant and antioxidant enzymes in RA patients.

Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles. 71 RA patients (46 women and 25 men) were enrolled in the study. The diagnosis was verified using ACR/EULAR criteria (2010). RA activity was measured using the Disease Activity Score of 28 joints (DAS28). 30 healthy persons comprise control group. Plasma xanthine oxidase (XO; EC 1.17.3.2), xanthine dehydrogenase (XDH; EC 1.17.1.4) and superoxide dismutase (SOD; EC 1.15.1.1) activities were measured using spectrophotometric technique. XO and XDG activities were expressed as nmol/ml/min, SOD activity – as units of action. Statistical analysis was performed using Statistica 6.0 software package. Differences were considered significant when p<0.05. Reference ranges were calculated as means ±2SD.

Results: Mean age of patients was 43.2±3.6 years, mean RA duration was 11.9±2.6 years. 24 (33.8%) RA patients had low disease activity, and 6 (8.5%) patients had high one. Extra-articular manifestations were found in 30 (42.2%) patients. 30% of them had cardiovascular involvement, 23.3% – pulmonary lesions, and 23.3% had renal involvement. Reference ranges for XO, XDG, and SOD activities were 2.28-5.12 nmol/min/ml, 3,96-7,24 nmol/min/ml, and 3,13-6,58 units, respectively. We examined activities of these enzymes in circulation

of RA patients with different patterns of clinical manifestations as well as relationship between RA activity and XO, XDG, and SOD activities. RA patients had increased both mean XO and mean SOD activities ($p<0.001$ for both enzymes). XO activity reached its highest values at maximum disease activity and overt extra-articular involvements, while SOD activity did it in moderate and high disease activities as well as in patients with joint manifestations. XDG activity was increased in low disease activity ($p<0.001$) and solely joint lesions ($p=0.011$), while moderate or high disease activities ($p=0.008$) and extra-articular involvements ($p=0.025$) were characterized by decreased activity of this enzyme.

Conclusion: We have revealed substantial multidirectional changes of plasma XO and XDG activities in RA. Plasma enzymatic pattern in RA patients is characterized by activation of both oxidant and antioxidant metabolic pathways. Activities of XO and SOD were positively correlated with RA activity, while XDG activity was negative correlated with RA activity. The differences between selective articular RA type and RA form with extraarticular manifestations were also revealed. Changes in oxidant and antioxidant enzyme activities can be connected with anticitrulline autoimmunity in RA via production of citrulline-rich neutrophil extracellular traps, thus enhancing rheumatoid autoimmunity.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1754

AB0049 RELATIONSHIP OF RHEUMATOID FACTOR AND XANTHINE OXIDOREDUCTASE ENZYMATIC CONSTITUENTS IN SEVERAL BLOOD COMPARTMENTS OF RHEUMATOID ARTHRITIC PATIENTS

S. Bedina[1], A. Trofimenko[1], E. Mozgovaya[1], M. Mamus[1], S. Spitsina[1].
[1]*Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky, Clinical Biochemistry Lab, Volgograd, Russian Federation*

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by the presence of rheumatoid factor (RF) and anticitrulline autoantibodies. Recent evidences suggest that impairment of neutrophil extracellular traps (NETs) could exert substantial influence on RA pathogenesis. The production of NETs depends heavily on the ROS generation. One of its mechanisms is xanthine oxidoreductase (XOR) mediated degradation of purine metabolites. Analysis of pro-oxidant activity of the enzymatic complex XOR and its constituents, xanthine oxidase (XO) and xanthine dehydrogenase (XDG), is an issue of considerable interest in this context.

Objectives: Evaluation of XO and XDG activities in RF-positive and RF-negative RA using both plasma and lysed lymphocyte samples.

Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles. Diagnosis of RA had been verified using ACR/EULAR 2010 criteria. Enzymatic activities in plasma and lymphocytes were measured spectrophotometrically and expressed as nmol/min/ml. Enzymatic activities in lymphocytes were also normalized to 1×107 cells/ml. Statistical tests were selected in line with common guidelines. Differences were considered significant when $p<0.05$. Reference ranges were calculated as means ±2SD.

Results: 75 adult RA patients (52 females and 23 males, mean age 43.9±0.97 years, mean disease duration 8.5±0.3 years) from the rheumatology unit of Volgograd Clinical Emergency Hospital #25 as well as 35 healthy controls were included in the study. RF-positive RA and RF-negative RA were observed in 49 (65.3%) and 26 (34.7%) patients, respectively. Reference ranges for plasma and lymphocyte XO activities were 2.60-3.96 and 14.2-27.8 nmol/min/ml, respectively. Similar ranges for XDG activities were 4.49-5.93 and 22.5-40.7 nmol/min/ml, respectively. Enzymatic profile of RA patients is characterized by significantly increased XO activity in plasma and decreased XO and XDG activities in lymphocytes ($p<0.001$). XO activity is increased ($p<0.001$), XDG activity is decreased ($p<0.001$) in blood plasma of patients with RF-negative RA, while the activity of both enzymes is decreased in lymphocytes ($p<0.001$). XO activity ($p<0.001$) and XDG activity ($p<0.05$) is increased in blood plasma, XO activity and XDG activity are decreased ($p<0.001$) in lymphocytes of patients with RF-positive RA. Plasma XO and XDG activities are also higher, and lymphocyte XO and XDG activities are lower in patients with RF-positive RA than in patients with RF-negative RA ($p<0.001$).

Conclusion: Our study revealed the relationship between enzyme parameters and rheumatoid factor presence. More pronounced changes in the enzyme activities were observed in patients with RF-positive RA. These results demonstrate that activation of the xanthine oxidase/xanthine dehydrogenase enzyme complex is an substantial factor of induction and continuation of the autoimmune rheumatoid inflammation.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1756

AB0050 A NOVEL METHOD FOR ISOLATION OF EXOSOMES FROM SYNOVIAL FLUID

Y. Liu[1,2], Y. Huang[1], Q. Huang[1], S. Sun[1], Z. Ji[1], W. Deng[1], T. W. LI[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*; [2]*University of South China, Guangdong Second Provincial General Hospital, Guangzhou, China*

Background: Exosomes in synovial fluid (SF) has a close relationship with the pathogenesis of rheumatiod arthritis. As a complex biological fluid, SF presents challenges for exosomes isolation using standard methods, such as Exoquick™ kit and ultracentrifugation.

Objectives: The study aims to compared the quality of exosomes separated by Exoquick™ kit (TM), Exoquick™ kit+Exoquick™ kit (TM-TC), ultracentrifugation (UC) and TM-TC+UC(TM-TC-UC) from SF.

Methods: Exosomes was separated by TM, TM-TC, UC and TM-TC-UC respectively. The size and concentrations of exosomes were detected by high sensitivity flow cytometry for nanoparticle analysis. Total protein and RNA were extracted from exosomes. SDS-PAGE was used to detect the protein distribution of exosomes. Western blot was used to examine the level of albumin and exosomes marker (TSG101 and CD81).

Results: There was no statistic difference in the diameters of exosomes separated by the four methods. The concentrations of exosomes in TM, TM-TC, TM-TC-UC and UC were (5.65±0.93), (3.02±1.19), (1.67±0.25) and (4.61±0.73) $*10^9$Particles/mL. The protein concentrations of exosomes separated by the four methods were consistent with the concentrations of exosomes. SDS-PAGE showed that the protein distribution of exosomes separated by the four methods were different. Low levels of albumin were detected in TM-TC and TM-TC-UC, while high levels of albumin in TM and UC. Total RNA concentrations from exosomes in TM-TC was higher than other groups.

Conclusion: TM-TC can be used to obtain higher quality exosomes from SF for the study of exosome-enriched components.

REFERENCES:

[1] Helwa I, et al, A Comparative Study of Serum Exosome Isolation Using Differential Ultracentrifugation and Three Commercial Reagents. PloS one, 2017. 12(1): p. e0170628-e0170628.

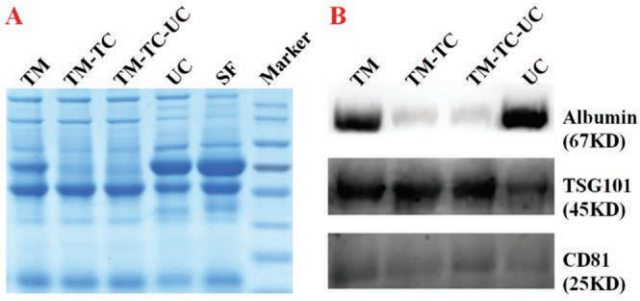


Figure 1. A: SDS-PAGE showed the protein distribution of exosomes; **B**: the detection of albumin, TSG101 and CD81 by western blot.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1996

AB0051 THE EFFECTS OF NON-INVASIVE VAGUS NERVE STIMULATION ON IMMUNOLOGICAL RESPONSES AND PATIENT REPORTED OUTCOME MEASURES OF FATIGUE IN PATIENTS WITH CHRONIC FATIGUE SYNDROME, FIBROMYALGIA, AND RHEUMATOID ARTHRITIS

E. Traianos[1], B. Dibnah[2], D. Lendrem[3], Y. Clark[4], V. Macrae[4], V. Slater[4], K. Wood[1], D. Storey[1], B. Simon[5], J. Blake[5], J. Tarn[3], W. F. Ng[3,4]. [1]*Newcastle University, FMS Professional Services, Newcastle upon Tyne, United Kingdom*; [2]*University of Glasgow, Institute of Molecular Cell & Systems Biology, Glasgow, United Kingdom*; [3]*Newcastle University, Translational & Clinical Research, Newcastle upon Tyne, United Kingdom*; [4]*National Institute for Health Research (NIHR), Newcastle Biomedical Research Centre (BRC), Newcastle upon Tyne, United Kingdom*; [5]*electroCore, Inc., NJ, United States of America*

Background: Fatigue is reported as a common symptom among autoimmune and other chronic diseases such as fibromyalgia (FM), a long-term condition with uncertain pathophysiology. Previous studies from our group suggest that non-invasive vagus nerve stimulation (nVNS) may contribute to the improvement of patient reported outcome measures (PROMs) of fatigue in patients with primary Sjögren's Syndrome (1).

Objectives: This follow-up study uses the gammaCore device (electroCore) to assess the effect of nVNS on PROMs of fatigue and immune responses in chronic fatigue syndrome (CFS), FM and rheumatoid arthritis (RA).

Methods: The study included thirteen CFS, fourteen FM and fifteen RA patients who used the gammaCore nVNS device twice daily over a 26-day period. Pre- and post- nVNS bloods were drawn at baseline and final visits. Whole blood

samples were stimulated with 2ng/mL lipopolysaccharide (LPS) and the IL-6 and TNF-α cytokine concentrations were quantified at 24 hours. In addition, the epidermal growth factor (EGF), IFN-γ, IL-6, IP-10, MIP-1α, and TNF-α levels were measured in 'pre-nVNS' serum and flow cytometric profiles of whole blood immune cells were analysed. The patient reported outcome measures (PROMs) recorded at each visit were the Visual Analogue Scale (VAS) (0-100cm) of abnormal fatigue, Hospital Anxiety and Depression (HAD) Scale, Orthostatic Grading Scale, Epworth Sleepiness Scale (daytime sleepiness), and Profile of fatigue (PRO-F) for Physical and Mental fatigue. Paired t-tests were performed to assess for changes in PROMs, cytokine levels, and cell subset distribution and associations of cytokine response with PROMs were investigated by correlation analyses.
Results: Eleven CFS, twelve FM and fourteen RA patients completed the study. There was a significant reduction in daytime sleepiness in CFS (p =0.0321) and FM (p =0.0294) patients between the final and baseline visits and a significant reduction in HAD depression (p =0.0413) in FM (Fig.1). Improvement in VAS for abnormal fatigue, HAD-Anxiety, HAD-Depression, PRO-F Physical and Mental fatigue was observed in all three groups over the study period with a reduction in VAS fatigue in 64% of CFS, 67% of FM and 62% of RA patients. There were no significant changes in the immune cell subsets or in cytokine response. Finally, higher baseline pre-nVNS supernatant IL-6 levels were predictive of an improvement in VAS fatigue (p =0.0006), Daytime Sleepiness (p =0.0466) and PRO-F Physical fatigue (p =0.0196) in RA, while higher baseline TNF-α levels were predictive of an improvement in VAS fatigue (p =0.0003), Daytime Sleepiness (p =0.0380), Orthostatic (p =0.0281) and PRO-F Physical fatigue (p =0.0007) in FM.
Conclusion: Our findings suggest that nVNS may contribute to the improvement of PROMs of fatigue in CFS, FM and RA. NVNS led to significant reductions in daytime sleepiness in CFS and FM, and depression in FM. Further studies and a larger sample size are needed to investigate the potential effects of nVNS on diseases characterised by persistent fatigue.
REFERENCES:

[1] Tarn J, Legg S, Mitchell S, Simon B, Ng WF. The Effects of Noninvasive Vagus Nerve Stimulation on Fatigue and Immune Responses in Patients With Primary Sjögren's Syndrome. Neuromodulation Technol Neural Interface. 2018;22(5):580–5.

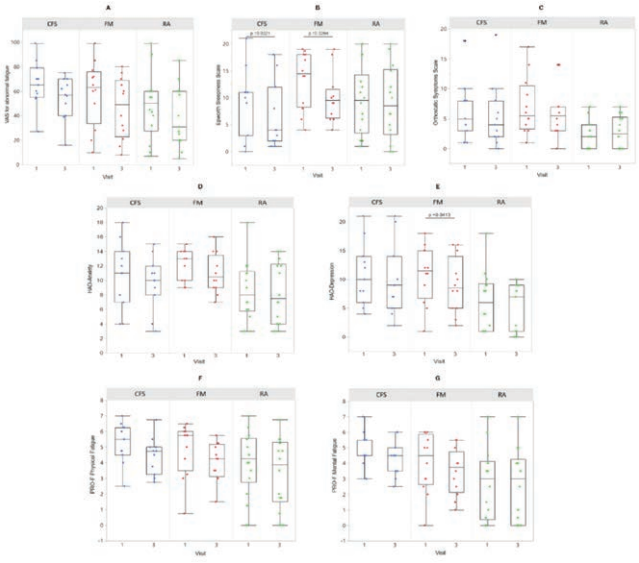


Figure 1. VAS for abnormal fatigue and PROMs recorded at baseline and final visits in patients with chronic fatigue syndrome (CFS), fibromyalgia (FM) and rheumatoid arthritis (RA). Boxplots show the median, upper, and lower quartiles for PROMs at visit 1 and visit 3 in each disease group. Paired-t tests revealed a significant reduction in daytime sleepiness in CFS and FM (B), and a significant reduction in HAD depression in FM (E). Improvement trends were observed in VAS for abnormal fatigue, HAD-Anxiety, HAD-Depression, PRO-F Physical fatigue and PRO-F Mental fatigue in all three groups over the 26-day study period.

Acknowledgements: This study received infrastructural support from the National Institute of Health Research (NIHR) Newcastle Biomedical Research Centre at Newcastle Hospitals Foundation Trust and Newcastle University.
Disclosure of Interests: Emmanuella Traianos: None declared, Bethany Dibnah: None declared, Dennis Lendrem: None declared, Yasmin Clark: None declared, Victoria Macrae: None declared, Victoria Slater: None declared, Karl Wood: None declared, David Storey: None declared, Bruce Simon Shareholder of: Bruce Simon is an employee and shareholder of electroCore., Employee of: electroCore, Inc., Justyna Blake Shareholder of: Justyna Blake is an employee of electroCore, and receives stock ownership., Employee of: electroCore, Inc., Jessica Tarn: None declared, Wan Fai Ng: None declared
DOI: 10.1136/annrheumdis-2021-eular.1999

AB0052 **INFLAMMATORY PROTEOMIC SIGNATURE RELATED TO DECREASED FERTILITY IN WOMEN WITH RHEUMATOID ARTHRITIS**

M. Bongenaar[1], H. T. Smeele[1], E. Lubberts[1], R. Dolhain[1]. [1]*Erasmus University Medical Centre, Department of Rheumatology, Rotterdam, Netherlands*

Background: Fertility issues are common in women with rheumatoid arthritis (RA). Decreased fertility in these patients is associated with high disease activity and the use of certain medication [1]. However, immunological mechanisms behind this phenomenon remain unresolved.
Objectives: This study aims to identify inflammation-related proteins associated with decreased fertility in women with rheumatoid arthritis and a wish to conceive.
Methods: Patients were derived from the PARA-study, a prospective cohort on RA and pregnancy. High-multiplex immunoassay technology with qPCR readout (Olink Proteomics, Uppsala, Sweden) was used to assess 92 inflammation-related proteins in serum obtained before pregnancy of 186 women with RA and a wish to conceive. Measured protein levels were imputed into multivariable cox regression models with time to pregnancy (TTP) as dependent variable. This model was corrected for known confounders age, nulliparity, NSAID use, prednisone use and past methotrexate use [2].
Results: Our analyses show prolonged TTP to be associated with increased expression of pro-inflammatory cytokines (TNF, IL-6, IL-18), chemokines (CCL23, CCL19, CXCL10, MCP-3, CXCL9) and T cell stimulating factors (TNFRSF9, CDCP-1). Furthermore, increased factors associated with angiogenesis (VEGF-A) and bone and collagen damage (RANKL, MMP-1) were found. Lastly, decreased fertility is associated with increased immune regulatory factors (IL-10, IL10RB, PD-L1). After false discovery rate (FDR) correction for multiple testing, IL-10, CCL23, MCP-3 and CDCP-1 remained statistically significant (adjusted P<0.05). Results are depicted in table 1.
Conclusion: This study shows a pro-inflammatory proteomic signature, including a counterbalance of increased immune regulatory proteins, to be associated with prolonged TTP. These findings provide more insight into the immunological pathways involved in fertility in RA patients.
REFERENCES:

[1] Smeele HTW, Dolhain R. Current perspectives on fertility, pregnancy and childbirth in patients with Rheumatoid Arthritis. Semin Arthritis Rheum. 2019;49(3S):S32-S5.
[2] Brouwer J, Hazes JM, Laven JS, Dolhain RJ. Fertility in women with rheumatoid arthritis: influence of disease activity and medication. Ann Rheum Dis. 2015;74(10):1836-41.

Table 1. Significant multivariable cox regression results with time to pregnancy as dependent variable, corrected for age, nulliparity, NSAID use, prednisone use and past MTX use. HR = hazard ratio, FDR = false discovery rate.

Protein	HR	P	P FDR adjusted	Function
IL-10	0,64	0,001	0,026	Immune regulatory
CCL23	0,51	0,001	0,026	T cell/monocyte migration
MCP-3	0,74	0,001	0,026	Monocyte migration
CDCP1	0,56	0,002	0,039	T cell migration
CCL19	0,77	0,005	0,077	DC/T cell/B cell migration
TNFRSF9	0,63	0,007	0,090	T cell costimulator
VEGF-A	0,7	0,014	0,154	Angiogenesis
CXCL10	0,82	0,021	0,185	T cell/monocyte/NK/DC migration
RANKL	0,76	0,022	0,185	Osteoclast activation, DC survival
IL-6	0,88	0,024	0,185	Pro-inflammatory cytokine, stimulation of acute phase response
PD-L1	0,55	0,027	0,189	Immune suppression
IL-18	0,7	0,035	0,193	Type 1 response activator
IL-7	0,69	0,038	0,208	Lymphocyte maturation
IL-10RB	0,48	0,039	0,208	IL-10 receptor
MMP-1	0,73	0,045	0,208	Collagen breakdown
TNF	0,44	0,048	0,208	Pro-inflammatory cytokine, necrosis
CXCL9	0,26	0,049	0,208	Th1 polarization

Acknowledgements: The authors are grateful to all patients who participated in the PARA study. Additionally, they thank Yaël de Man, Fleur van de Geijn, Esther Gasthuis, Florentien de Steenwinkel, Jenny Brouwer and all laboratory workers and research assistants for their contribution to the data collection.
Disclosure of Interests: Margot Bongenaar: None declared, Hieronymus TW Smeele: None declared, Erik Lubberts Grant/research support from: CHDR, Galapagos, Radboud Dolhain Speakers bureau: Yes, for UCB, Roche, Abbvie, Genzyme, Novartis, Consultant of: Yes, Galapagos, Grant/research support from: Yes, UCB
DOI: 10.1136/annrheumdis-2021-eular.2063

AB0053

THE ROLE OF ANGIOPOIETIN-LIKE PROTEINS TYPES 3 AND 4 IN THE DEVELOPMENT OF RENAL DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

V. Aleksandrov[1,2], L. Shilova[1], A. Aleksandrov[1,2]. [1]*Volgograd State Medical University, Department of Hospital Therapy, Volgograd, Russian Federation*; [2]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», Department of Clinical and Laboratory Diagnostics, Volgograd, Russian Federation*

Background: Rheumatoid arthritis (RA) often contributes to the development of kidney disease. Angiopoietin-like proteins can be target markers for studying cardiorenal complications of RA [1].

Objectives: Assessment of the correlation of serum concentrations of angiopoietin-like proteins types 3 and 4 (ANGPTL 3 and 4) with the progression of renal dysfunction in RA patients.

Methods: 114 patients with reliable RA (90.4% of women, 9.6% of men) aged 21 to 80 years (mean age 55.4 ± 11.2 years old), disease duration - 11.18 ± 9.03 years, positive for rheumatoid factor (RF-IgM) - 63.2%, positive for anti-citrullinated protein antibody (ACPA) - 59.7%) were examined. The laboratory examination included the determination of serum concentrations of angiopoietin-like protein type 3 (Human Angiopoietin-like Protein 3 ELISA, Bio Vendor, Czech Republic) and type 4 (RayBio Human ANGPTL4 ELISA Kit; RayBiotech, USA). To assess renal function in RA patients we used the calculated glomerular filtration rate (GFR) according to the CKD-EPI formula [2], taking into account the height and weight of a particular patient without indexing by body surface area. GFR values <60 ml / min / 1.73 m2 were regarded as a certain decrease, and GFR values from 60 to 89 ml / min / 1.73 m2 - as a slight decrease in global kidney function.

Results: The concentration of ANGPTL3 in the blood serum of RA patients (n = 158) was 641.9 ± 224.5 ng / ml, and that of ANGPTL4 (n = 158) - 3.15 [0.77; 12.1] ng / ml. 74.7% (n = 118) were considered positive for the presence of ANGPTL3; 49.4% (n = 78) of RA patients were recognized as positive for the presence of ANGPTL4. The average glomerular filtration rate in RA patients was 74.0 ± 18.6 ml / min. More than a half of the examined RA patients had GFR ranging from 89 to 60 ml / min / 1.73 m2 (C1 - 21.5%; C2 - 58.9%; C3 - 19.6%). No sharp reduce of renal function (GFR <30 ml / min / 1.73 m2) corresponding to CKD C4-5 stages was recorded. Negative correlations of average strength were found between GFR and the level of ANGPTL 3 (r = -0.32, p <0.001) and ANGPTL 4 (rS = -0.31, p <0.001), as well as with age (rS = -0.28, p <0.001), the duration of RA (rS = -0.22, p = 0.005) and blood pressure increase (rS = -0.25, p = 0.001). On the basis of GFR measurements, patients were divided into three groups: group I - optimal renal function (> 90 ml / min); group II - a slight decrease in renal function (89-60 ml / min); group III - reduced renal function (<59 ml / min).

Table 1. Content of ANGPTL 3 and 4 in RA patients with different GFR, ng / ml

	Group I (n=34)	Group II (n=93)	Group III (n=31)
ANGPTL 3	533,4±161,7 [I-III]	650,0±223,9	733,2±244,1
ANGPTL 4	0,77 [0,28;3,6] [I-II, I-III]	3,3 [0,93;12,1]	6,48 [1,52;19,3]

Note: upper case indicates intergroup differences at p <0.05.

There was a significant difference in the content of ANGPTL3 in patients of the first group and the patients of the third group (H-test = 6.55, p = 0.032) and ANGPTL4 in the group of patients with normal renal function (group I) and groups of RA patients with decreased GFR (group I- II: H-test = 10.7, p = 0.001; groups I-III: H-test = 20.1, p <0.001). ANGPTL4 indices also had intergroup differences (groups II-III: H-test = 7.2, p = 0.007) with GFR less than 90 ml / min.

Conclusion: Chronic rheumatoid inflammation potentiates the development of renal dysfunction according to our data in 78.5% of patients. It is also accompanied by an increase in the content of ANGPTL types 3 and 4 in the blood of RA patients. A better understanding of the actions and mechanisms of ANGPTL may be of paramount importance for the development of effective ways of treatment for cardiorenal complications in RA.

REFERENCES:

[1] Aleksandrov A., Aleksandrov V., Shilova L. Study of the role of angiopoietin-like protein type 4 in metabolic disorders caused by inflammation in rheumatoid arthritis. Ann Rheum Dis. 2020;79(s1):1341. doi: 10.1136/annrheumdis-2020-eular.4558.

[2] KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3:1–150.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2275

AB0054

IS TEA CONSUMPTION ASSOCIATED WITH RISK OF RHEUMATOID ARTHRITIS?

H. Westerlind[1], I. Palmqvist[1], S. Saevarsdottir[1,2], L. Alfredsson[3], L. Klareskog[1], D. DI Giuseppe[1]. [1]*Karolinska Institute, Department of Medicine Solna, Stockholm, Sweden*; [2]*School of Health Sciences, University of Iceland, Faculty of Medicine, Reykjavik, Iceland*; [3]*Karolinska Institute, Institute of Environmental Medicine, Stockholm, Sweden*

Background: Only few studies have looked at the association between tea consumption and risk of rheumatoid arthritis (RA) with inconclusive results.

Objectives: To estimate the association between tea consumption and risk of RA in a large population-based case-control study.

Methods: We used data from the Swedish Epidemiological Investigation of RA (EIRA), a population-based case-control study including incident RA cases with 2 controls randomly matched from the general population, based on age, sex and residential area at the date of diagnosis. All participants filled in a comprehensive questionnaire on lifestyle factors, including a 124-item food frequency questionnaire (FFQ). Data from October 2005 - May 2018 was used.

Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated using conditional logistic regression, overall and stratified by anti-citrullinated protein antibody (ACPA) and smoking status. We adjusted for smoking status, coffee and alcohol consumption, educational level and BMI. The dose-response trend of the association between tea consumption and risk of rheumatoid arthritis was estimated using restricted cubic spline with knots at 0, 0.29, and 2.29 cups per day. Missing tea values (44.8%) were imputed based on the zero-consumption assumption. A sensitivity analysis was performed to evaluate the influence of the assumption on the main result, with 70% of the missing randomly imputed as no consumption, and the remaining 30% randomly assigned to the other categories (10% per category).

Results: We included 2237 cases and 4661 controls. Controls were more likely to drink ≥2 tea cups/day compared to RA cases (22.1% vs. 19.7%).

The crude odds of developing RA was 22% lower (OR=0.78, 95% CI: 0.66-0.92) among those who consumed ≥2 tea cups/day compared to those who drank <1 cup/day (irregular drinkers). After adjustment for covariates, the inverse association was less pronounced and only borderline significant (OR=0.85, 95% CI: 0.71-1.01). A similar OR was observed among non-tea consumer (OR=0.82, 95% CI: 0.70-0.95). The odds of developing ACPA positive RA (but not ACPA negative) was statistically significant lower among participants drinking >=2 cups/day compared to irregular tea drinkers (OR=0.76, 95% CI: 0.62-0.94). In analyses stratified by smoking, an inverse association between tea intake and RA was found only among current smokers (OR=0.58, 95% CI: 0.37-0.92), while no association was found in never smoker. The sensitivity analysis showed results similar to the main analysis, although the OR in the no consumption category was not significant (OR=0.88, 95% CI: 0.76-1.02) while the OR in the highest category was statistically significant (OR=0.85, 95% CI: 0.73-0.99).

	Overall tea consumption			
	0 cups/day	**<1 cup/day**	**1-2 cups/day**	**>=2 cups/day**
Overall				
Number	955/1941	453/847	388/845	441/1028
OR crude*	0.89 (0.77-1.03)	Ref	0.84 (0.71-1.00)	**0.78 (0.66-0.92)**
OR adjusted±	**0.82 (0.70-0.95)**	Ref	0.87 (0.73-1.04)	0.85 (0.71-1.01)
ACPA positive				
Number	637/1156	321/527	268/501	277/630
OR adjusted	**0.81 (0.67-0.97)**	Ref	0.88 (0.71-1.09)	**0.76 (0.62-0.94)**
ACPA negative				
Number	312/571	129/221	119/251	162/288
OR adjusted	0.87 (0.66-1.14)	Ref	0.87 (0.63-1.19)	1.07 (0.78-1.46)
Never smokers				
Number	290/859	164/436	142/433	213/563
OR adjusted	0.90 (0.72-1.14)	Ref	0.88 (0.68-1.15)	1.04 (0.81-1.33)
Current smokers				
Number	296/371	89/96	59/78	59/99
OR adjusted	0.81 (0.57-1.14)	Ref	0.83 (0.52-1.31)	**0.58 (0.37-0.92)**

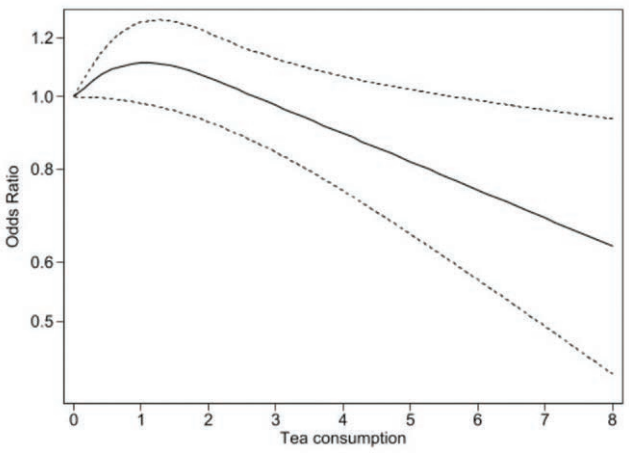


Figure 1. Dose-response odds ratio for risk of rheumatoid arthritis (RA) by tea consumption.

Conclusion: In this large population-based case-control study, high tea consumption, as well as no consumption, was associated with a decreased risk to develop ACPA positive, but not negative, RA, when compared to irregular tea drinking (<1 cup/day). The inverse association between high tea consumption and RA was lowest in analyses restricted to current smokers.
Disclosure of Interests: Helga Westerlind: None declared, Ida Palmqvist: None declared, Saedis Saevarsdottir Employee of: part-time employee of deCODE genetics, Lars Alfredsson: None declared, Lars Klareskog: None declared, Daniela Di Giuseppe: None declared
DOI: 10.1136/annrheumdis-2021-eular.2423

AB0055 AUTOIMMUNE RESPONSE AGAINST THE SHARED EPITOPE SEQUENCE IN RHEUMATOID ARTHRITIS

E. Graell[1], J. F. Delgado de la Poza[2], A. D. Gomez Centeno[1], M. Garcia Manrique de Lara[1], M. J. Amengual Guedan[2], E. Nuez Zaragoza[2], M. Aliste Fernandez[2], S. Rodriguez Navarro[2], M. Arevalo Salaet[1], S. Garcia-Cirera[1], M. Rusiñol[1], E. Costa Moya[1], C. Orellana[1], J. Calvet Fontova[1], M. Moreno Martinez-Losa[1], E. Casado[1], C. Galisteo[1], N. Navarro[1], M. Llop Vilaltella[1], J. Gratacos Masmitja[1]. [1]*Hospital de Sabadell, Rheumatology, Sabadell, Spain*; [2]*Hospital de Sabadell, Inmunology, Sabadell, Spain*

Background: Rheumatoid Arthritis (RA) is a systemic autoimmune disease, associated with hiperproduction of autoantibodies (AAb), in which the most specific are the AAb against citrullinated peptides (ACPA). RA is influenced by genetic factors, specifically, there is a strong genetic association with the shared epitope (SE), a five amino acid sequence motif in positions 70–74 of HLA-DRβ1 chains encoded by HLA-DRB1 alleles: QKRAA, QRRAA and RRRAA.
The present study aims to analyze whether SE-peptides (SE-p) can be a target of the autoimmune response in RA.
Objectives: To analyze the presence of AAb against the unmodified (*Un*) SE-p, citrullinated (*Cit*) SE-p and carbamylated (*Car*) SE-p.
Methods: Sera from consecutive 117 RA patients and 21 psoriasic arthritis (PsA) from our outpatient clinic were collected by venopunture. Also 138 sera from blood donors were obtained as healthy controls (HC). All participants signed the informed consent.
We perfomed a homemade ELISA test using a sequence of 15 aminoacid peptides from positions 65-79 of HLA-DRB1 containing the 3 different SE sequences, in the *Un*, *Cit* and *Car* SE-p, synthesized in a linear and cycled form. We established a 90% of specificity using a ROC curve obtained from HC and PsA for each ELISA test.
HLA-DRB1 polymorphism was performed using a HLA-DRB1 sequence specific oligonucleotide typing kit (Lifecodes) in 95 RA and in 15 PsA.
ACPA and RF were determined with commercial assays (Inova Diagnostics and Binding Site, respectively).
Results: The overall sensitivity of the different SE-p AAb tests ranged from 5.1-21.4%.
RRRAA SE polymorphism was associated with AAb against cycled CitCitCitAA SE-p (p=0.025), QKRAA polymorphism was almost significantly associated with AAb against cycled QKCitAA SE-p (p=0.067), whereas there was no association between QRRAA polymorphism and AAb against cycled QCitCitAA SE-p (p=0.690). On the other hand, there was no association between SE polymorphisms and AAb to any other peptide used in the ELISA test.
Significant differences were observed in the presence of AAb against lineal RRRAA, lineal CitCitCitAA and cycled CitCitCitAA SE-p when comparing RA vs. HC patients (p=0.022, 0.044, 0.022, respectively). Moreover, there also were significant differences in the presence of AAb against cycled CitCitCitAA SE-p between RA and PsA patients (sensitivity 21.4%, specificity 100%; p=0.014).
It must be highlighted that cycled CitCitCitAA SE-p AAb were detected in 20.0% of RA patient sera that were negative for RF and ACPA.
There was no association between RF or ACPA with the presence of any SE-p AAb.
Conclusion: RA patients have autoantibodies against the Shared Epitope (SE). The cycled CitCitCitAA SE peptide (SE-p) shows the best performance among all the peptides tested and could identify patients seronegative for ACPA and RF, both analyzed by commercial assays.
Additional studies must be performed to verify the diagnostic and utility of these new autoantibodies against SE-p in RA.
Acknowledgements: This work was granted by the 2018 call of the "Fundación Española de Reumatologia" and the 2017 call grant "Fundació Parc Taulí".
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2470

AB0056 TNFR2 PROMOTES INFLAMMATORY PROGRAMS IN FIBROBLAST-LIKE SYNOVIOCYTES

T. Suto[1], K. Von Dalwigk[1], A. Platzer[1], B. Niederreiter[1], T. M. Karonitsch[1]. [1]*Medical University of Vienna, Division of Rheumatology, Vienna, Austria*

Background: TNF-mediated fibroblast-like synoviocyte (FLS) activation is important for inflammation and joint destruction in rheumatoid arthritis (RA). The role of TNF-receptor 1 (TNFR1) in FLS activation has thoroughly been characterized. The functions of TNFR2 are, however, largely unknown.
Objectives: To investigate the contribution of TNFR2 to the TNF-mediated activation of FLS.
Methods: RA-FLS were transfected with TNFR2-targeting siRNA pools and transcriptional changes were determined by RNA-seq. QPCR, ELISA and immunoblotting were used to confirm the RNA-seq results and to gain insights into the pathways that regulate TNFR2-mediated changes in FLS.
Results: TNF stimulation of FLS resulted in a strong upregulation of proinflammatory cytokines, chemokines, tissue-degrading enzymes and other genes that are associated with synovial inflammation in RA. Silencing of TNFR2 markedly diminished the TNF-response of RA-FLS. Especially, "interferon"-stimulated-genes (ISGs) including putative master regulators of joint inflammation, such as the CXCR3 chemokines CXCL9, CXCL10 and CXCL11 were affected by the knockdown of TNFR2. Consistently, immunoblots showed that TNFR2 was required for the TNF-induced phosphorylation of the transcription factor STAT1, which is known to mediate the transcription of ISGs, such as CXCR3 chemokines.
Conclusion: TNFR2 regulates proinflammatory gene expression in RA-FLS via STAT1 and thereby contributes to the detrimental effects of TNF in synovial joint inflammation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2500

AB0057 IN VITRO EFFECT OF CTLA4-IGG ON M1-M2 SHIFT OF MACROPHAGES FROM RHEUMATOID ARTHRITIS PATIENTS

S. Tardito[1], S. Soldano[1], E. Gotelli[1], P. Montagna[1], S. Paolino[1], V. Smith[2,3,4], M. Cutolo[1]. [1]*University of Genova, IRCCS San Martino Polyclinic Hospital, Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, Genoa, Italy*; [2]*Ghent University Hospital, Department of Rheumatology, Ghent, Belgium*; [3]*Ghent University, Department of Internal Medicine, Ghent, Belgium*; [4]*VIB Inflammation Research Center (IRC), Unit for Molecular Immunology and Inflammation, Ghent, Belgium*

Background: Among the cells involved in the inflammatory process of rheumatoid arthritis (RA) [1], macrophages play a key role through their capacity to polarize into "classically" or "alternatively" activated phenotypes (M1 or M2) and making macrophages important players for the inflammatory cascade or for the anti-inflammatory reaction, respectively [2]. CTLA4-Ig fusion protein (abatacept) has been shown to contribute to macrophage shift from M1 to M2 [3].
Objectives: We aimed to investigate the effects of abatacept to induce the polarization from the pro-inflammatory M1 phenotype into the anti-inflammatory M2 phenotype in cultured human macrophages obtained from RA patients' and healthy subjects'(HS) circulating monocytes.
Methods: Cultured monocytes were isolated from peripheral blood mononuclear cells (PBMCs) of three early RA patients and ten HS, after signing informed consent and Ethics Committee approval. Cells were treated with phorbol myristate acetate (PMA) [5ng/ml] for 24 hours (hrs) to induce their differentiation into monocyte-derived macrophages (MDMs). Therefore, cultured HS MDMs were stimulated with lipopolysaccharides [LPS, 1mg/mL] for 4hrs [4] in order to induce their polarization into a pro-inflammatory M1 phenotype and then treated or not with abatacept at the concentrations of 100mg/mL and 500mg/mL for 3, 12, 24 and 48hrs. Cultured RA MDMs, were directly treated with abatacept as previous described. Cultured HS and RA MDMs without any pro-inflammatory stimuli and abatacept treatment were used as respective control.
The transition of MDMs from M1 to M2 phenotype was evaluated through gene expression and protein synthesis of M2 macrophage markers, namely scavenger receptors (CD163 and CD204), and mannose receptor-1 (CD206) by quantitative real-time polymerase chain reaction (PCR) and by Western blotting. The statistical analysis evaluation was carried out by GraphPad Prism 8 analysis software using the Wilcoxon non-parametric t-test. Any p-value lower than 0.05 was considered as statistically significant. Results were indicated as median±standard deviation (SD).
Results: In cultured RA MDMs (three cases), abatacept upregulated the gene expression of all investigated M2 markers, specifically after 12hrs of treatment with the concentration of 100mg/mL. In these cells, abatacept upregulated only the CD204 protein synthesis with more evidence at 24hrs of treatment and with the 500mg/mL concentration. In cultured HS MDMs (ten cases), abatacept upregulated the gene expression of M2 markers, significantly for that of CD206 [at 3hrs with 100mg/mL concentration, p= 0.0312] and CD163 [at 12hrs with 500mg/mL concentration, p= 0.0312]. Moreover, in these cells, abatacept significantly upregulated the protein synthesis of CD206 [at 48hrs with 500mg/mL concentration, p= 0.0195] and CD204 [at 24hrs with 100mg/mL concentration, p= 0.0156; both at 24 and 48hrs with 500mg/mL concentration, p= 0.0234].

Conclusion: Preliminary data seem to indicate that abatacept can promote the in vitro shift from the M1 into the M2 macrophage phenotype, by upregulating specific markers (CD163, CD204, CD206) in cultured M1-MDMs from RA patients and in M1 macrophages induced from HS.

REFERENCES:

[1] McInnes IB, et al. N Engl J Med 2011;365:2205–19.
[2] Fujii M, et al. Biochem Biophys Res Commun. 2013;438(1):103-9.
[3] Cutolo M, et al. Arthritis Res Ther. 2009;11:R176.
[4] Pelegrin P., Surprenant, A. EMBO J. 2009 Jul 22; 28(14): 2114–2127.

Disclosure of Interests: Samuele Tardito: None declared, Stefano Soldano: None declared, Emanuele Gotelli: None declared, Paola Montagna: None declared, Sabrina Paolino: None declared, Vanessa Smith: None declared, Maurizio Cutolo Grant/research support from: I received grant/research support from Bristol-Myers Squibb, Boehringer, Celgene.

DOI: 10.1136/annrheumdis-2021-eular.2524

AB0058 ASSOCIATION BETWEEN HLA-DRB1*04:01, RHEUMATOID NODULES AND PARTICULAR EPITOPES OF CITRULLINATED FIBRIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

G. Larid[1], M. Pancarte[2], G. Offer[2], C. Clavel[2,3], M. Martin[4], V. Pradel[5], I. Auger[4], P. Lafforgue[1], G. Serre[2], J. Roudier[1,4], N. Balandraud[1,4]. [1]*AP-HM, Rheumatology, Marseille, France*; [2]*UDEAR, Toulouse 2 University, INSERM U1056, Toulouse, France*; [3]*Centre Hospitalier Universitaire (CHU) de Toulouse, Institut Fédératif de Biologie, Laboratory of Cell Biology and Cytology, Toulouse, France*; [4]*Aix-Marseille-University, INSERM UMRs1097 Arthrites Auto Immunes, Marseille, France*; [5]*AP-HM, Public Health Laboratory, Marseille, France*

Background: Rheumatoid arthritis (RA) is associated with HLA-DRB1 genes encoding the shared epitope (SE), a 5 amino acid motive. RA is usually preceded by the emergence of anti-citrullinated protein antibodies (ACPAs) detected by anti-CCP2 tests. Citrullin is a neutral amino acid resulting from post translational modification of arginin by Peptidyl Arginyl Deiminases (PADs). ACPAs recognize epitopes from citrullinated human fibrinogen (Fib-cit) and can be specifically detected by the AhFibA assay. Five peptides derived from Fib-cit together represent almost all of the epitopes recognized by patients with ACPA-positive RA: β60–74cit, α36–50cit, α621–635cit, α501–515cit and α171–185cit. As RA is a pleiomorphic disease, whose evolution is difficult to predict, the use of antibody fine specificity as a marker of clinical phenotypes has become a major challenge.

Objectives: Our objective was to study whether clinical characteristics and HLA-DRB1 genetic background were associated with a specific reactivity against these epitopes.

Methods: 184 ACPA positive RA patients fulfilling the 2010 ACR/EULAR criteria were studied. Patients characteristics, including HLA-DRB1 genotype, were collected from their medical files. Anti-CCP2, AhFibA, Rheumatoid Factors (RF), and antibodies against the five major Fib-cit peptides were analyzed using ELISA assays.

Results: Anti-CCP2 and AhFibA titres were strongly correlated (rs: 0.7037; $p = 5.69x10^{-29}$, Pearson's). Anti-α505-515cit antibodies were associated with HLA-DRB1*04:01 (OR = 5.52 [2.00 – 13.64]; p = 0.0003). High level anti-α505-515cit antibodies were significantly associated with rheumatoid nodules (OR = 2.71 [1.00 – 7.16], p= 0.044). Anti α501–515cit antibodies were associated with RF (OR=2.31 [1.10 – 4.78], p= 0.026).

Conclusion: Immune complexes containing anti-α501–515cit antibodies and rheumatoid factors might be involved in the development of rheumatoid nodules on the HLA-DRB1*04:01 background. These findings highlight the role played by the HLA-DRB1*04:01 molecule and its rapid intracellular route into the lysosomes, enabling original antigen processing. Finally, purifying these epitope specific antibodies might be a new therapeutic opportunity for rheumatoid nodules.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2568

AB0059 STUDY OF THE ANTI-INFLAMMATORY EFFECT OF CINNAMOMUM VERUM IN RATS

R. Dhouibi[1], A. Hanène[1], S. Ben Youssef[2], M. Ben Salem[3], R. Marrakchi[4], S. Charfi[5], S. Hammami[1], K. Ksouda[1]. [1]*Medecine School of Sfax, Pharmacology Department, Sfax, Tunisia*; [2]*University of Sfax, Higher Institute of Biotechnology of Sfa, Sfax, Tunisia*; [3]*University of Sfax, Laboratory of Biochimie, Hedi Chaker Hospital Sfax, Sfax, Tunisia*; [4]*Hedi Chaker Hopital, Laboratory of Biochimie, Sfax, Tunisia*; [5]*Habib Bourguiba Hopital, Laboratory of Histology, Sfax, Tunisia*

Background: Inflammatory response is a common physiological response that protects the host of many harmful stimuli such as toxins, local injuries and pathogens. Today, non-steroidal anti-inflammatory drugs are the most commonly prescribed for the treatment of many inflammatory treatments. However, long term administration of these NSAIDs causes many adverse effects, including gastrointestinal ulcers and bleeding and kidney damage. Therefore, the need for new anti-inflammatory drugs with fewer side effects is required.

Objectives: The aim of our study was to evaluate the anti-inflammatory activity of *Cinnamomum verum* (*C. Verum*) on rats while testing the dose effect and the typical effect of the solvent.

Methods: The edema was induced by injection of carrageenan solution (CARR) in paw of rats according to the method of Winter et al, 1963. The measurements of volumes of right hind paw of each rat were taken before induction of edema and each 1 h, 2 h, 3 h, 4 h and 5 h after the injection of carrageenan. 7 groups of 6 rats received, one hour before the injection of the carrageenan, different treatment: G1= witness, G2=CARR + saline solution, G3= CARR+ Acetylsalicylic acid, G4= CARR + *C. verum*- MeOH 100, G5= CARR + *C. verum*- MeOH 300, G6= CARR + CARR + *C. verum*- EtOH 100 and G7= CARR + *C.verum*- EtOH 300.

Results: For this test, the volume of edema increases with time, this increase is greater in the group treated with saline solution than with the extracts of *C.Verum* and with Acetylsalicylic acid. The extracts of *C. Verum* administered intraperitoneally one hour before the injection of the carrageenan, reduced the edema in the third hour after.

Conclusion: The interesting anti-inflammatory activity of *Cinnamomum verum* recorded in this work may at least in part support its popular use in traditional medicine [1, 2].

REFERENCES:

[1] Mirza Muhammad Fahd Qadir, Attya Bhatti, Muhammad Usman Ashraf, Mansur Abdullah Sandhu, Sidrah Anjum, Peter John. Immunomodulatory and therapeutic role of Cinnamomum verum extracts in collagen-induced arthritic BALB/c mice. Inflammopharmacology 2018 Feb;26(1):157-170.
[2] Heping Cao, Joseph F Urban Jr, Richard A Anderson. Cinnamon polyphenol extract affects immune responses by regulating anti- and proinflammatory and glucose transporter gene expression in mouse macrophages. J Nutr 2008 May;138(5):833-40.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2948

AB0060 INCREASED AGE/AUTOIMMUNE-ASSOCIATED B CELLS IN RA AND CLINICAL IMPLICATIONS

Y. QIN[1], **Z. CHEN[1].** [1]*THE FIRST AFFILIATED HOSPITAL OF USTC, RHEUMATOLOGY AND IMMUNOLOGY, HEFEI, CHINA*

Background: Age/Autoimmune-associated B cells (ABCs) are an emerging B cell subset that accumulate in aged and autoimmune-prone mice. Expansion of human ABCs has been observed in patients with autoimmune diseases like SLE and correlated with disease activity. However, it is less known whether ABCs contribute to the pathogenesis of RA.

Objectives: The aim of this work was to explore the role of ABCs in RA.

Methods: 83 RA patients who met the 2010 ACR classification criteria for RA, 42 sex and age matched healthy control (HC), 35 Spondyloarthritis (SpA) and 31 Osteoarthritis (OA) patients were enrolled and blood samples were collected. The proportion of circulating ABCs was detected by flow cytometry and association with clinical and laboratory parameters were analyzed. Expression of characteristic proteins and inflammatory cytokines on ABCs were examined by quantitative real-time PCR.

Results: The proportion of ABCs, defined as $CD19^+CD27^-IgD^-CD21^-CD11c^+$, was significantly elevated in RA patients, compared with HC, SpA and OA patients. The frequency of ABCs was higher in patients with high disease activity (DAS28>3.2) compared with remission and low disease activity (DAS28<3.2). There was a positive correlation of ABCs with SJC, TJC, DAS28 whereas no association with RF and anti-CCP titer were observed. In addition, increased mRNA expression levels of T-bet, IL-21, MAF and IL-17 were noted on ABCs compared with $CD19^+CD27^-CD11c^-$ B cells.

Conclusion: ABCs were expanded in RA patients and associated with active disease status. It might contribute to RA development by production of IL-17.

REFERENCES:

[1] Cancro, M.P., Age-Associated B Cells. Annu Rev Immunol, 2020. 38(315-340).
[2] F. Zhang, K. Wei, K. Slowikowski et al., Defining inflammatory cell states in rheumatoid arthritis joint synovial tissues by integrating single-cell transcriptomics and mass cytometry. Nat Immunol 2019, 20, 928-942.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3026

AB0061

ALTERATIONS OF XANTHINE OXIDOREDUCTASE ACTIVITY IN RED BLOOD CELLS AFTER GLUCOCORTICOID TREATMENT IN RHEUMATOID ARTHRITIS

E. Mozgovaya[1], S. Bedina[1], A. Trofimenko[1], M. Mamus[1], S. Spitsina[1], I. Zborovskaya[1]. [1]*Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky, Clinical Biochemistry Lab, Volgograd, Russian Federation*

Background: According to modern concepts, rheumatoid arthritis (RA) refers to severe autoimmune rheumatic diseases. The activation of free radical oxidation processes is essential in the development of this disease [1]. Xanthine oxidoreductase is a significant reactive oxygen species source [2]. Despite the great advances in the treatment of rheumatoid arthritis (RA) associated with the introduction of innovative drugs and especially the improvement of the strategy for their use into clinical practice, glucocorticoids still remain an important component of RA pharmacotherapy in actual clinical practice.
Objectives: to evaluate the changes in activities of xanthine oxidoreductase interconvertible forms (xanthine oxidase, EC 1.17.3.2 and xanthine dehydrogenase, EC 1.17.1.4) in lysed red blood cells of RA patients in relation with glucocorticoid treatment.
Methods: 47 RA patients with verified RA and 30 healthy controls were enrolled in the study. The diagnosis was verified using the 2010 ACR/EULAR criteria 2010. All patients have moderate DAS28 scores. RA patients were randomized into 2 groups comparable in gender, age and the principal clinical manifestations. Methylprednisolone (Metipred, Orion Corp.), average dose 30 mg/day, and betamethasone (Diprospan, Schering-Plough), single dose7 mg, were administered intramuscularly in the respective groups. Xanthine oxidase (XO) and xanthine dehydrogenase (XDG) activities were measured in lysed red blood cells by spectrophotometric method as previously described [3]. The changes of these enzymes activities were studied in RA patients before and after the injection of glucocorticoids. Statistical comparison tests were selected in according to common guidelines, differences were considered significant when $p<0.05$. Central tendencies were expressed as means±SEM.
Results: Mean age of patients in methylprednisolone group was 41.8±1.05 years, and mean RA duration (± SEM) was 7.9±0.21 years. Mean age of patients in diprospan group was 40.9±1.07 years, and mean RA duration was 8.0±0.33 years. Significant decreases of XO activity and increase of XDG activity were observed in lysed red blood cells of RA patients just after the injection of each glucocorticoid drug. Changes of the enzymatic activities in lysed red blood cells were more pronounced in methylprednisolone group. However enzymatic activity did not reach the level of healthy controls. As described previously, decreased XO activity and increased XDG activity were observed in plasma of RA patients just after the injection of the average therapeutic doses of glucocorticoids, as well as in lysed lymphocytes just after the injection of methylprednisolone [4].
Conclusion: Treatment with methylprednisolone and betamethasone can affect the balance of XO/XDG activity and increase the antioxidant potential of the blood. This effect can exert beneficial influence on autoimmune inflammation in RA.
REFERENCES:

[1] Mateen S., et al. Increased reactive oxygen species formation and oxidative stress in rheumatoid arthritis. PLoS ONE 2016;11(4):e0152925.
[2] Çimen M.Y., et al. Oxidant/antioxidant status of the erythrocytes from patients with rheumatoid arthritis. Clin Rheumatol 2000;19(4):275-277.
[3] Zborovskaya I.A., et al. Influence of analgetics on plasma and lymphocytic activity of the purine metabolism enzymes in rheumatoid arthritis patients. Russian Journal of Pain 2018;3:47.
[4] Mozgovaya E.E., et al. Xanthinoxidase and xanthine dehydrogenase activities in rheumatoid arthritis after glucocorticoid treatment. Osteoporosis International 2019;30(2):S433-434.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3168

AB0062

TIME COURSE OF INTESTINAL PERMEABILITY AND BACTERIAL TRANSLOCATION IN THE MODEL OF ADJUVANT-INDUCED ARTHRITIS

S. Hecquet[1], P. Totoson[2], H. Martin[2], C. Peyronnel[2], M. Tournier[2], P. Saas[3], J. P. Pais-De-Barros[4], D. Wendling[1], C. Demougeot[2], F. Verhoeven[1]. [1]*Centre hospitalier régional universitaire de Besançon, Rheumatology, Besançon, France*; [2]*EA4267 PEPITE LAB, Physiology, Besançon, France*; [3]*UMR 1098, Interactions Hôte Greffon Tumeur, Besançon, France*; [4]*UMR 1231, Plateforme de lipidomique, Dijon, France*

Background: Intestinal inflammation, dysbiosis, intestinal permeability (IP) and bacterial translocation (BT) have been identified in patients with spondyloarthritis but the time at which they appear and their contribution to the pathogenesis of the disease is still a matter of debate.
Objectives: To investigate the time-course of intestinal inflammation, IP and BT in a rat model of reactive arthritis, a subgroup of SpA, the adjuvant-induced arthritis model.
Methods: Adjuvant-induced arthritis (AIA) was induced in 6-week-old male Lewis rats by an injection at the base of the tail of *Mycobacterium butyricum* with incomplete Freund's adjuvant (Day (D) 0). Control rats received saline using the same procedure. Body weights and a clinical arthritis score were daily assessed. A group of AIA and control rats (n=15 per group) were euthanized at three different times of arthritis: D4 for the pre-arthritic phase (AIA-preclinical), D11 for the onset of arthritis (AIA-onset) and D28 for the acute phase (AIA-acute). In each group (AIA and control, n=15 per group)), IP was assessed by measuring plasma levels of zonulin (ELISA) and ileal mRNA expression of zonulin and occludin (RT-qPCR), BT was studied by measuring bacterial endotoxins (or LPS, by $LCMS^2$ method), soluble CD-14 (sCD14, ELISA) and ileal mRNA expression of TLR-4, and intestinal inflammation was assessed by measuring ileal mRNA expression of IL-8, IL-33, IL-17, IL-23p19 and TNF-α (RT-qPCR). Joint damage was assessed by the determination of a clinical and radiographic score of hind paws.
Results: Body weights of AIA rats decreased from D4 to D28 as compared to controls, in parallel to the development of a severe clinical and radiographic arthritic disease from D11 and D28. Compared to control rats, AIA induced an increase in plasma zonulin levels at D4, D11 but not at D28. Ileal mRNA zonulin overexpression occurred at D11 while occludin was unchanged. As early as Day 4 (preclinical phase), mRNA of IL-8, IL-33 and IL-17 were overexpressed in ileum from AIA. At Day 11 (onset), overexpression of IL-8 persisted and mRNA of TNF-α and IL-23p19 increased in AIA. Neither LPS levels nor ileal mRNA expression of TLR-4 were changed by arthritis whatever the phase of arthritis. By contrast, blood levels of sCD-14 was significantly increased in the AIA group at all stages of arthritis. No correlation was found between clinical and radiographic arthritis scores and zonulin or LPS levels. Conversely, a negative correlation was observed between intestinal IL-8 mRNA expression and arthritis score ($r=-0.3$, $p=0.02$).
Conclusion: In an animal model of SpA, intestinal inflammation and increased intestinal permeability occur prior to joint inflammation, suggesting a role of these disorders in the pathogenesis of this disease.
Acknowledgements: I would like to thank the Société Française de Rhumatologie for its support in this work.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3207

AB0063

DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: A BIOMARKER SCREENING PILOT STUDY

J. Baloun[1], A. Pekacova[2,3], H. Mann[1,2], J. Vencovský[1,2], K. Pavelka[1,2], L. Šenolt[2,3]. [1]*Institute of Rheumatology, Department of Rheumatology, Prague, Czech Republic*; [2]*1st Faculty of Medicine, Charles University, Department of Rheumatology, Prague, Czech Republic*; [3]*Institute of Rheumatology, Department of Experimental Rheumatology, Prague, Czech Republic*

Background: Despite modern therapeutic approaches, many patients with rheumatoid arthritis (RA) remain symptomatic after several cycles of treatment and may become so called Difficult-To-Treat (D2T)1. D2T RA is a multifactorial condition in which different factors may be major determinants of the persistence of signs and symptoms, which is seldom caused by drug resistance only2. Discovering new biomarkers is necessary to develop tailored therapies that will be effective in an individual patient at each stage of the disease.
Objectives: The primary aim of this pilot study was to validate a target proteomic technique for the proteome profiling of the two cohorts of RA patients and controls. Moreover, we searched for potential plasma biomarker(s) predicting D2T RA.
Methods: Seven RA patients with persistent remission on biological therapy in two consecutive examinations 12 wks apart (mean age 59.6±14 yrs), seven D2T RA patients fulfilling proposed EULAR definition of D2T RA1 (mean age 59.3±13 yrs), and six healthy controls (mean age 58.8±15 yrs) were included in this study. All subjects were females and their samples were collected before starting biological therapy. We employed Thermo Orbitrap Fusion paired with nano-flow UHPLC Dionex Ultimate 3000. Prior to quantification, 125 plasma proteins were modified by Peptiquant Plus Human kit to increase the sensitivity. Data were analysed by ANOVA and Tukey`s posthoc test with false-discovery-rate adjustment.
Results: The target proteome profiling reliably quantified 92 from 125 labelled proteins. Our follow-up statistical analysis revealed ten plasma proteins, which significantly differed among groups. Notably, we found significantly different plasma levels of paraoxonase/arylesterase 1 (PON1), an esterase with an antioxidant characteristic preventing lipid peroxidation[3], between RA patients and controls and between RA patients with persistent remission and D2T RA patients.

Conclusion: Using target proteome profiling technique, we demonstrated PON1 as a potential biomarker of D2T RA. However, these results have to be validated on a larger cohort.

REFERENCES:

[1] Nagy G, Roodenrijs NMT, Welsing PMJ, et al. EULAR definition of difficult-To-Treat rheumatoid arthritis. Annals of the Rheumatic Diseases 2021;80:31-5.
[2] de Hair MJH, Jacobs JWG, Schoneveld JLM, van Laar JM. Difficult-to-treat rheumatoid arthritis: an area of unmet clinical need. Rheumatology (Oxford, England) 2018 Jul 1;57(7):1135-1144.
[3] Isik A, Koca SS, Ustundag B, Celik H, Yildirim A. Paraoxonase and arylesterase levels in rheumatoid arthritis. Clinical Rheumatology 2007;26:342-8.

Acknowledgements: This research was supported by MHCR No. 023728 and authors thank Proteomics Service Laboratory, Faculty of Science, Charles University for performing the LC–MS/MS analysis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3290

AB0064 EVALUATION OF QUALITY OF LIFE IN RHEUMATOID ARTHRITIS USING SF-36 AND HAQ SCALES

M. Brahem[1], M. Hassayoun[1,1], H. Hachfi[1], R. Sarraj[1], M. Ardhaoui[1], A. Ben Salem[1], S. Abdellatif[1], R. Ben Tekaya[1], Y. Mohamed[1]. *[1]Taher Sfar Hospital, Rheumatology, Mahdia, Tunisia*

Background: The assessment of health-related quality-of-life (HRQoL) in rheumatoid arthritis (RA) is becoming a common tool in clinical practice. The medical outcomes survey short form 36 (SF- 36) is one of the most widely used tools for measuring HRQoL in RA as well as the HAQ scale.
Objectives: The aim of our study is to evaluate the impact of the RA in the quality of life (QoL) of our patients using the SF-36 and the HAQ questionnaires.
Methods: This is a cross-sectional study during a period of the year 2020, including 70 patients followed in the department of Rheumatology in Mahdia, Tunisia. All patients were diagnosed with RA based in ACR 1987/EULAR 2010. We evaluated for each patient, the mean global scale and the eight domains of SF-36 (physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), a social functioning (SF), role emotional (RE) and mental health (MH)), scored from 0 (worst) to 100 (best).
Results: Our study included 70 patients (59 females/11males) with an age ranged from 21 to 76 years. The mean age was 54 ± 12 years. The mean duration of the disease was 11 ± 10 years [1-40]. The mean number of tender joints was 9.7 ±9.4 and swollen joints were 4.2 ±6.1. The mean disease activity score (DAS28) was 4.6 ±1.9 [1.2-8.4]. The mean HAQ score was 1.5±1.3, 47.1% of patients had specific joint deformations, 82.9% had radiologic involvement and 31.4% had osteoporosis. The biologic analysis showed that the mean ESR was 46.7 ± 30.5 and the CRP was 15.8 ±23.3. Rheumatoid factors were positive in 42.9% of cases, the ACPA were positive in 50% of cases. 84.3% of RA patients were treated by methotrexate, 4.3% were treated by salazopyrin and 11.4% were treated by biologic treatments.
The SF-36 global score was 50.4 ± 26.3 [15.3-92.8]. 46 patients (65.7% of cases) had impaired QoL (SF-36<66.7). The means of different domains (PF, RP, BP, GH, VT, SF, RE, MH) were respectively 51; 41.4; 51.4; 50; 51.2; 57.7; 41.9; 59.2. The most severely impacted domains were the RP and RE.
Our study showed a significant correlation between the SF-36 global score and the number of tender joints (p=0.002), the DAS28 (p=0.017) and the HAQ(p=0.000).
Conclusion: Our study showed that 65.7% of RA patients presented impaired QoL (SF-36<66.7), which is associated with high disease activity. So it's important to jugulate the disease, in order to ameliorate the quality of life of our patients.

REFERENCES:

[1] Matcham, F., Scott, IC, Rayner, L., Hotopf, M., Kingsley, GH, Norton, S.,… Steer, S. (2014). *L'impact de la polyarthrite rhumatoïde sur la qualité de vie évalué à l'aide du SF-36: une revue systématique et une méta-analyse. Séminaires sur l'arthrite et les rhumatismes, 44 (2), 123-130.* doi: 10.1016 / j.semarthrit.2014.05.001.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3309

AB0065 HGF/C-MET SIGNALING PROMOTE ANGIOGENESIS THROUGH CXCL16 IN RHEUMATOID ARTHRITIS

M. Hosonuma[1,2,3,4], T. Isozaki[2], H. Furuya[2], Y. Yamazaki[5], Y. Ikari[2], S. Nishimi[2], S. Ishii[2], A. Maeoka[2], T. Tokunaga[2], K. Wakabayashi[2], N. Konishi[2], S. Fukuse[2], K. Ishikawa[6], N. Sakai[7], K. Inagaki[6], T. Kasama[2]. *[1]Clinical Research Institute for Clinical Pharmacology & Therapeutics, Showa University, Department of Clinical Immuno Oncology, Tokyo, Japan*; *[2]Showa University, Division of Rheumatology, Department of Medicine, Tokyo, Japan*; *[3]Showa University, Division of Medical Oncology, Department of Medicine, Tokyo, Japan*; *[4]Showa University, Department of Pharmacology, School of Medicine, Tokyo, Japan*; *[5]Showa University School of Pharmacy, Division of Toxicology, Department of Pharmacology, Toxicology and Therapeutics, Tokyo, Japan*; *[6]Showa University School of Medicine, Department of Orthopaedic Surgery, Tokyo, Japan*; *[7]Showa University, Department of Pharmacology, School of Dentistry, Tokyo, Japan*

Background: Hepatocyte growth factor (HGF) binds to the receptor tyrosine kinase c-Met and is a multifunctional cytokine that promotes processes such as cell proliferation, survival, differentiation, migration and angiogenesis [1]. We previously reported that HGF is produced by inflammation in the RA synovium, and activates monocyte migration to the synovium and promotes bone destruction through its own chemotactic effect and enhanced chemokine production in the synovium [2].
Objectives: Therefore, we next aimed to determine the role of HGF in RA angiogenesis.
Methods: The expression of HGF / c-Met in the serum and synovial tissues (STs) of RA patients and controls and human umbilical vein endothelial cells (HUVECs) was evaluated by ELISA and immunostaining. The effect of HGF/c-Met signaling on the promotion of CXCL16 production from HUVECs and RA fibroblast-like synoviocytes (FLSs) was determined by ELISA. To examine the role of HGF in angiogenesis, we performed in vitro Matrigel assays using HUVECs treated with HGF.
Results: HGF in serum in treatment-naive RA patients was significantly higher than that in controls and HGF in serum in treatment-resistant RA showed a significant positive correlation with CXCL16. c-Met were expressed on vascular endothelial cells of RA STs and HUVECs. Stimulation of HUVECs with HGF dose-dependently increased CXCL16 production. c-Met signal inhibition by SU11274 suppressed TNF-α stimulation-enhanced CXCL16 production by RA FLSs in a dose-dependent manner. Furthermore, HGF induced HUVEC tube formation by 1.8-fold.
Conclusion: HGF is produced by inflammation in the RA synovium, and activates angiogenesis through its own potent angiogenic effect and enhanced production of CXCL16 in the synovium. These results indicate that a strategy targeting c-Met signalling may be important for resolving treatment-resistant RA.

REFERENCES:

[1] Nakamura T, Nishizawa T, Hagiya M, et al. Molecular cloning and expression of human hepatocyte growth factor. Nature. 1989 Nov 23;342(6248):440-3.
[2] Hosonuma M, Sakai N, Furuya H, et al. Inhibition of hepatocyte growth factor/c-Met signalling abrogates joint destruction by suppressing monocyte migration in rheumatoid arthritis. Rheumatology (Oxford). 2021 Jan 5;60(1):408-419.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3491

AB0066 MECHANISMS OF TOTAL SAPONINS OF PANAX JAPONICUS MITIGATES COLLAGEN-INDUCED ARTHRITIS

Z. Feng[1], X. Guo[1], J. Ji[1], X. Hou[2], Y. Luo[1], X. Fu[1]. *[1] Medical College of China Three Gorges University, Third-Grade Pharmacological Laboratory on Chinese Medicine Approved by State Administration of Traditional Chinese Medicine, Yichang, China*; *[2] Medical College of China Three Gorges University, Institute of Rheumatology, The First College of Clinical Medical Sciences, Yichang, China*

Background: Total saponins of *Panax japonicus* (TSPJ) are extracted from *Panax japonicus (T.Nees) C.A.Mey* and have achieved a good therapeutic effect in the treatment of rheumatoid arthritis (RA). Unfortunately, the mechanism of TSPJ acting on RA is not clear.
Objectives: To investigate the potential mechanisms and key targets of TSPJ on RA.
Methods: The raw data were downloaded from the Gene Expression Omnibus (GEO) database, and the RStudio3.6.1 software was used to identify differentially expressed genes (DEGs). The potential targets of active compounds from TSPJ were predicted by the Pharmmapper and SwissTargetPrediction databases. Based on the overlapping genes, we used Cytoscape 3.7.2 software to construct a protein-protein interactions (PPI) network and to determine the mechanisms of the treatment by Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis. Collagen-induced arthritis (CIA) model was established and treated with different doses of TSPJ. Arthritis index (AI) and histology score were used to evaluate the symptoms of CIA. The levels of vascular endothelial growth factor (VEGF), hypoxia-inducible factor 1 (HIF-1), IL-1β, and IL-17A tested by enzyme linked immunosorbent assay and real time-quantitative Polymerase Chain Reaction.

Results: A total of 2670 DEGs and 371 TSPJ targets were obtained, including 52 overlapping genes. 41 genes had protein interactions that are used to build the PPI network. The results of the KEGG enrichment analysis included VEGF and HIF-1 signaling pathway. Seven negative correlation genes and 16 positive correlation genes were obtained by correlational analysis of DEGs in VEGF and HIF-1 signaling pathway. SRC proto-oncogene, nonreceptor tyrosine kinase (SRC), and the signal transducer and the activator of transcription 3 (STAT 3) had a higher value of degree in PPI and showed a significant correlation in the pathways; they were regarded as key targets. Compared with the CIA model group, TSPJ significantly decreased the AI and histology scores. Moreover, the expression of VEGF-A, HIF-1α, IL-1β, and IL-17A in serum or spleens significantly reduced in a dose-dependent.

Conclusion: Present study show that SRC and STAT 3 may be the key targets of TSPJ acting on the VEGF and HIF-1 signaling pathways, thus inhibiting angiogenesis and improving RA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3496

AB0067 RHEUMATOID ARTHRITIS IS DRIVEN NOT ONLY BY INFLAMMATION BUT ALSO BY FIBROGENESIS

A. C. Bay-Jensen[1], S. F. Madsen[1,2], K. Gehring[3], K. Musa[3], M. Karsdal[1]. [1]*Nordic Bioscience, ImmunoScience, Herlev, Denmark*; [2]*University of Copenhagen, Department of Biomedical Sciences, Copenhagen, Denmark*; [3]*Nordic Bioscience, Clinical Laboratory, H, Denmark*

Background: Rheumatoid arthritis (RA) is a chronic, autoimmune disease characterized by inflammation of the synovium, cartilage and bone leading to joint swelling, tenderness, and dysfunction. The destruction of the joint tissue involves degradation of the extracellular matrix (ECM). The ECM consist of collagens and other connective proteins[1]. Studies have shown that elevated levels of collagen metabolites, such as those of type I, II, III and VI, are highly elevated in RA, correlated to disease activity and modulated in response to, for example tocilizumab[2], baricitinib[3] and methotrexate[4]. However, little is known about the formation of collagen, fibroblast activity, the fibrotic component of RA and how this influence likelihood of response to treatment.

Objectives: We investigated the level of active fibrogenesis in a population of moderate to severe RA patients (in contrast healthy controls) by assessing blood-levels of PRO-C3 and PRO-C6 (type III and VI collagen formation markers), which have been reported to be associated with the degree and extent of fibrosis5.

Methods: PRO-C3 and PRO-C6 was measured in serum of 166 RA patients (age; 54 (20-82), 83 % females, 91% white) at baseline and week 16 after treatment with an anti-IL6 receptor antibody in combination with MTX, as well as in serum of 77 donors (age; 42 (20-69), 51 % females, 66% white). Marker data was LN transformed. A general linear model was used when comparing groups.

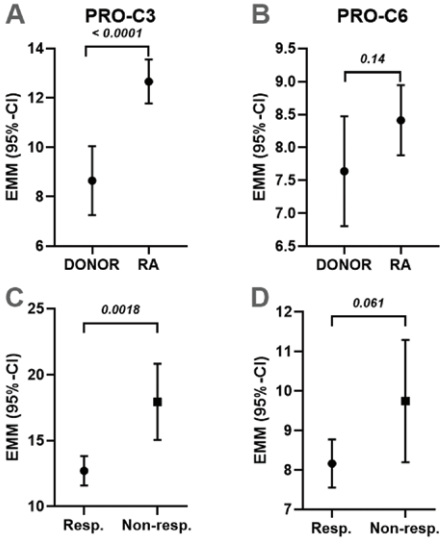


Fig. Difference in active fibrogenesis assessed by serum PRO-C3 and PRO-C6 between donors and RA patients at baseline (A,B) and between resp. and non-resp. at week 16 (C,D). Data is shown as back-transformed estimated marginal means (EMM) with 95%-CI adjusted for age, gender, and race (all), and BMI, disease duration and baseline marker level (C,D).

Results: The serum fibrogenesis marker PRO-C3, but not PRO-C6, was significantly elevated in RA compared to donors (2.1 vs. 2.4 ≈ 30% difference, p<0.0001, fig. 1A). None of the markers were correlated with disease measures such as DAS28, CRP, VASpain. None of the markers were modulated significantly in response to treatment. Interestingly, PRO-C3 levels were significantly higher at in non-responders (resp.) at week 16 compared to resp. (2.8 vs. 2.4 ≈ 40% difference, p=0.0018, fig. 1C). Similar trend was observed for PRO-C6 (2.2 vs. 2.0 ≈ 20% difference, p=0.061 fig. 1D).

Conclusion: Active fibrosis, with activated fibroblasts, may play an unseen role in RA. Patients will elevated levels of the fibrosis markers PRO-C3 and PRO-C6 were less likely to respond to an anti-IL6R. This may also give clue why such treatment are less efficacious in diseases with a clear fibrotic component.

REFERENCES:

[1] **Karsdal** et al. Rheumatoid arthritis: A case for personalized health care? ACR 2014; 66: 1273–80.
[2] **Bay-Jensen** et al. Effect of tocilizumab combined with methotrexate on circulating biomarkers of synovium, cartilage, and bone in the LITHE study. SAR 2014; 43: 470–8.
[3] **Thudium** et al. The Janus kinase 1/2 inhibitor baricitinib reduces biomarkers of joint destruction in moderate to severe rheumatoid arthritis. ART 2020; 22.
[4] **Drobinski** et al. Connective tissue remodeling is differently modulated by tocilizumab versus methotrexate monotherapy in patients with early rheumatoid arthritis: the AMBITION study. ART 2021; 23.
[5] **Karsdal** et al. Profiling and targeting connective tissue remodeling in autoimmunity - A novel paradigm for diagnosing and treating chronic diseases. AutoRev 2021; 20.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3619

AB0068 B- AND T- LYMPHOCYTE SUBSETS IN PATIENTS WITH EARLY AND PROGRESSED RHEUMATOID ARTHRITIS

A. Martynova[1], T. Popkova[1], A. Aleksankin[1], E. Gerasimova[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases, Moscow, Russian Federation*

Background: Role of B- and T- lymphocytes is well established in pathogenesis of rheumatoid arthritis (RA). Self-containing activation of B-cells in ectopic germinative centers is followed by auto-activation of T-lymphocytes while T-cells themselves are antigen-presenting cells for B-lymphocytes [1-2]. As these processes continue with the duration of RA, different subsets of B- and T-cell might be prevalent at different stages of RA.

Objectives: Evaluate differences in dynamics of B- and T- cell subsets in early and progressed RA.

Methods: 53 patients with diagnosed RA(ACR/EULAR 2010 criteria) were included in research in October 2019 - May 2020. Age median 54,2 [47; 62] yrs. 2 groups were formed: 1st (n = 27 pts., 25 female and 2 male) with early arthritis, median duration of RA 6 [5; 12] months prior to therapy, mediane DAS28-CRP - 5,8 [5,15-6,2]; and 2nd group (n=26 pts., 22 female and 4 male) - patients with progressed RA, duration of RA 84 [24; 121] months, on DMARDs (methotrexate 20 [15; 20] mg/week or leflunomide 20 mg/day), mediane DAS28-CRP - 6,31 [5,64-6,88]. Control group included 29 individuals (23 female and 6 male), age median 58,5 [53; 62] yrs. Blood of all patients underwent standart flow cytometry with T- and B-cell immunotyping.

Results: B and C-cells subsets were studied. B-cells subsets are presented in table 1 below.

Conclusion: As disease activity was high in both groups, therefore therapy was ineffective, and results could be interpreted as natural progression of RA, resulting mainly in dynamics of switched B-memory cells, transitioning B-cells and plasmoblasts. These subsets might be indicating disease development patterns but further research is required.

REFERENCES:

[1] Weyand, C. M., &Goronzy, J. J. Ectopic germinal center formation in rheumatoid synovitis. Annals of the New York Academy of Sciences, 2003, 987, 140–149.
[2] Shi K., HayashidaK. Lymphoid Chemokine B Cell-Attracting Chemokine-1 (CXCL13) Is Expressed in Germinal Center of Ectopic Lymphoid Follicles Within the Synovium of Chronic Arthritis Patients. J Immunol 2001; 166:650-655.

B-cell subsets	1 group (n=27)		2 group (n=26)		Control group (n=29)	
	Cells, 10^9/л	Persentage, %	Cells, 10^9/л	Persentage, %	Cells, 10^9/л	Persentage, %
B-cell [CD19+]	0,144 [0,1; 0,21]	9,1 [7,5-10,9]	0,105 [0,1-0,2] **	8,35 [6-10,2]	0,2 [0,1–0,2]	8,5 [7,2–11,0]
B-memory cell [CD19+CD27+]	0,003 [0,00166; 0,0044]	2,1 [1,6-3,1]	0,0015 [0,001-0,003] *	1,25 [0,9-1,7] *,**	0,003 [0,001–0,007]	2,2 [1,1–3,0]
Switched B-cells [CD19+CD27+IgD-]	0,0187 [0,0133-0,0289]	16 [9,3-18,4]	0,01 [0,005-0,02]	6,8 [3,6-11,6] *,**	0,02 [0,01–0,04]	12,8 [9,3–17,0]
Non-switched B-cells [CD19+CD27+IgD+]	0,0073 [0,00619-0,0122]	5,9 [3,6-9,7]	0,009 [0,006-0,01]	7,45 [5,1-11,4]**	0,01 [0,005–0,02]	7,4 [3,7–11,1]
Double negative D-cells [CD19+CD27-IgD-]	0,021 [0,011-0,028]	14 [9,6-19,5]	0,02 [0,01-0,03]	15,05 [11,9-18,1]	0,02 [0,01–0,02]	13,3 [7,1–19,3]
Naive B-cells [CD19+CD27-IgD+]	0,076 [0,063-0,13]	61,6 [52,9-68,8]	0,095 [0,07-0,1]	70,85 [62,5-75,6] **	0,1 [0,06–0,1]	64,7 [57,6–72,4]
Transitioning B-cells [CD19+CD38++CD10+IgD+CD27-]	0,000424 [0,000162-0,000624]*,**	0,2 [0,1-0,4]	0 [0-0,0001]	0 [0-0,1]	0,0001 [0–0,0003]	0,1 [0–0,1]
Plasmoblasts [CD19+CD38+++CD27+IgD-CD20-]	0,00071 [0,00023-0,00129]*,**	0,4 [0,3-0,8]*, **	0,0003 [0,00007-0,0004]	0,15 [0,1-0,3]	0,0002 [0,0001– 0,0004]	0,1 [0,1–0,2]
Plasmocytes [CD19+CD38+]	0,000262 [0,000106-0,000414]*, **	0,1 [0,1-0,3]	0,0001 [0-0,0002]	0,1 [0-0,1]	0,0001 [0,00-0,0002]	0,1 [0,05-0,1]

Data presented as median and interquartile range. * - differences to control group were observed, p<0,05. ** - differences between pts. goups were observed, p<0,05.No significant difference between T-cell subsets was found.In comparison with healthy individuals, pts. with early RA had increased levels of switched B-memory cells, transitioning B-cells and plasmoblasts, the opposite was observed in progressed RA pts with addition of decrease in B-memory cells.

Acknowledgments: The reported study was funded by RFBR, project 19-315-90090
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3816

AB0069

ANTIBODIES AGAINST PHOSPHORYLCHOLINE AS PROTECTION MARKERS IN AUTOIMMUNITY, ATHEROSCLEROSIS, CARDIOVASCULAR DISEASE AND CHRONIC INFLAMMATION – IMPLICATIONS FOR TREATMENT

J. Frostegård[1]. [1]*Karolinska Institutet, IMM, Stockholm, Sweden*

Background: Autoimmunity, atherosclerosis and cardiovascular disease (CVD) are chronic inflammatory conditions and represent a major part of global burden of morbidity and also mortality. The immune system plays an important role in these conditions. Further, the risk of CVD and atherosclerosis is raised in several autoimmune conditions, where SLE is an important example. Its major cause, atherosclerosis (where activated immune competent cells producing cytokines are abundant), for example, active and passive immunization can influence the degree of atherosclerosis in animal experiments, but no treatment developed to specifically ameliorate inflammation is presently available. The cause of the chronic inflammation and immune activation in atherosclerosis has not been fully defined, and there are different, non-mutually exclusive and potentially synergistic possibilities including oxidized LDL (oxLDL) heat shock proteins (HSP) and infections. We focused on the lipid moiety in OxLDL, especially phosphorylcholine (PC) which is a small hapten, immunogenic when exposed and reported that OxLDL´s immunological effects is to some extent caused by PC. Antibodies against PC (anti-PC) are abundant, about 5-10% of circulating IgM is IgM anti-PC.
This is thus a theranostic concept, combining novel risk markers with possible underlying mechanisms and potentially immunization to raise anti-PC.
Objectives: We reported that anti-PC, especially IgM (and Ig1) anti-PC is negatively associated with atherosclerosis progress, CVD (including both MI and stroke) in different populations, and also with autoimmune diseases, especially systemic rheumatic diseases as SLE. Potential mechanisms include anti-inflammatory effects, inhibition of uptake of OxLDL in the vascular wall, promotion of T regulatory cells, inhibition of cell death, and increased clearance of dead cells.
Methods: We have used a combination of experimental and translational/clinical studies.
Results: Based on our findings, we have proposed a novel hypothesis which is a development of the hygiene/old friends-hypothesis, namely that low exposure to microorganisms as nematodes, parasites and some bacteria which from an evolutionary point of view has been with humanity for millions of years, leads to low levels of the antibodies described and a lack of ability to prevent autoimmune conditions. Indeed, individuals from Kitava, New Guinea leading a traditional life as hunter-gatherers and horticulturalists appear not to have CVD or rheumatic disease, but strikingly high anti-PC levels.
Conclusion: anti-PC could be a novel factor protecting against rheumatic disease.
Disclosure of Interests: Johan Frostegård Shareholder of: I am named as inventor on patents related to antibodies against phosphorylcholine, Grant/research support from: From Amgen, related to PCSK9 and inflammation, unrelated to this topic
DOI: 10.1136/annrheumdis-2021-eular.4317

Spondyloarthritis - aetiology, pathogenesis and animal models

AB0070

ROLE OF VASPIN IN ATHEROSCLEROTIC DISEASE AND CARDIOVASCULAR RISK IN AXIAL SPONDYLOARTHRITIS

J. Rueda-Gotor[1], R. López-Mejías[1], S. Remuzgo-Martínez[1], V. Pulito Cueto[1], A. Corrales[1], L. Lera-Gómez[1], V. Portilla[1], I. González-Mazón[1], R. Blanco[1], R. Expósito[2], C. Mata[2], J. Llorca[3], V. Hernández-Hernández[4], C. Rodríguez-Lozano[5], N. Barbarroja Puerto[6], R. Ortega Castro[6], N. García Castañeda[7], C. Fernández-Carballido[8], M. P. Martínez-Vidal[9], D. Castro-Corredor[10], J. Anino-Fernández[10], D. Peiteado[11], C. Plasencia[11], E. Galindez[12], M. L. García Vivar[12], O. Gualillo[13], J. C. Quevedo-Abeledo[5], S. Castañeda[7], I. Ferraz-Amaro[4], M. A. González-Gay[1,14,15], F. Genre[1]. [1]*IDIVAL, Hospital Universitario Marqués de Valdecilla, Research Group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Diseases of the Musculoskeletal System, Santander, Spain*; [2]*Hospital Comarcal de Laredo, Rheumatology Department, Laredo, Spain*; [3]*University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), School of Medicine, Santander, Spain*; [4]*Hospital Universitario de Canarias, Rheumatology Division, Santa Cruz de Tenerife, Spain*; [5]*Hospital Universitario de Gran Canaria Dr. Negrín, Rheumatology Department, Las Palmas de Gran Canaria, Spain*; [6]*Hospital Reina Sofía, Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC), University of Cordoba, Rheumatology Department, Córdoba, Spain*; [7]*Hospital de La Princesa, IIS-Princesa, Rheumatology Department, Madrid, Spain*; [8]*Hospital Universitario de San Juan, Rheumatology Department, Alicante, Spain*; [9]*Hospital General Universitario de Alicante, Rheumatology Department, Alicante, Spain*; [10]*Hospital General Universitario de Ciudad Real, Rheumatology Department, Ciudad Real, Spain*; [11]*Hospital Universitario La Paz-IdiPaz, Rheumatology Department, Madrid, Spain*; [12]*Hospital Universitario Basurto, Rheumatology Department, Bilbao, Spain*; [13]*SERGAS*

and IDIS, NEIRID Lab, Research Laboratory 9, Santiago University Clinical Hospital, Santiago de Compostela, Spain; *[14]University of Cantabria, School of Medicine, Santander, Spain*; *[15]University of the Witwatersrand, Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, Johannesburg, South Africa*

Background: Vaspin is a novel anti-inflammatory adipokine associated with cardiovascular (CV) disease and inflammation in chronic inflammatory conditions different from axial spondyloarthritis (axSpA).[1] Given the high incidence of CV disease (mainly due to accelerated atherosclerosis) exhibited by axSpA patients,[2] we wondered if vaspin could also be a key molecule in this process. However, data on the role of vaspin regarding atherosclerotic disease in the context of axSpA is scarce.[3]
Objectives: To evaluate the implication of vaspin, at the genetic and serological level, in subclinical atherosclerosis and CV risk in axSpA.
Methods: 510 patients who fulfilled the ASAS criteria for axSpA[4] were included in this study. Carotid ultrasound (US) was performed to evaluate the presence of subclinical atherosclerosis. Three *vaspin* gene variants (rs2236242 T/A, rs7159023 G/A and rs35262691 T/C) were genotyped by TaqMan probes. Serum vaspin levels were assessed by Enzyme-Linked ImmunoSorbent Assay. Analysis was performed using a statistical software.
Results: Serum vaspin levels were significantly higher in female patients than in males and also in obese patients when compared to those with normal weight (p<0.05). At the genetic level, we disclosed that the minor allele of rs2236242 (A) was associated with lower serum vaspin levels in axSpA, while the rs7159023 minor allele (A) was linked to higher serum levels (p<0.05). When the three polymorphisms assessed were combined conforming haplotypes, we disclosed that the TGC haplotype related to high serum levels of vaspin (p=0.01). However, no statistically significant association was observed between vaspin and markers of subclinical atherosclerosis, both at the genetic and serological level.
Conclusion: Our results revealed that vaspin is linked to CV risk factors that may influence on the atherosclerotic process in axSpA. Additionally, we disclosed that serum vaspin concentration is genetically modulated in a large cohort of patients with axSpA.
REFERENCES:
[1] Adv Exp Med Biol. 2019;1111:159-88.
[2] Front Med (Lausanne). 2018;5:62.
[3] Braz J Med Biol Res. 2016;49(7):e5231.
[4] Ann Rheum Dis. 2009;68(2):ii1-44.
Acknowledgements: Personal funds: RL-M: Miguel Servet type I CP16/00033 (ISCIII-ESF); SR-M: RD16/0012/0009 (ISCIII-ERDF); VP-C: PREVAL18/01 (IDIVAL); LL-G: INNVAL20/06 (IDIVAL).
Disclosure of Interests: Javier Rueda-Gotor: None declared, Raquel López-Mejías: None declared, Sara Remuzgo-Martínez: None declared, Verónica Pulito Cueto: None declared, Alfonso Corrales: None declared, Leticia Lera-Gómez: None declared, Virginia Portilla: None declared, Iñigo González-Mazón: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD and Roche, Rosa Expósito: None declared, Cristina Mata: None declared, Javier Llorca: None declared, Vanessa Hernández-Hernández: None declared, Carlos Rodríguez-Lozano: None declared, Nuria Barbarroja Puerto: None declared, Rafaela Ortega Castro: None declared, Noelia García Castañeda: None declared, Cristina Fernández-Carballido: None declared, Maria Paz Martínez-Vidal: None declared, David Castro-Corredor: None declared, Joaquín Anino-Fernández: None declared, Diana Peiteado: None declared, Chamaida Plasencia: None declared, E Galindez: None declared, María L. García Vivar: None declared, Oreste Gualillo: None declared, Juan Carlos Quevedo-Abeledo: None declared, Santos Castañeda: None declared, Iván Ferraz-Amaro: None declared, Miguel A González-Gay Speakers bureau: Pfizer, Abbvie, MSD, Grant/research support from: Pfizer, Abbvie, MSD, Fernanda Genre: None declared
DOI: 10.1136/annrheumdis-2021-eular.839

AB0071 RELATIONSHIP BETWEEN PRO-INFLAMMATORY CYTOKINE AND ATHEROGENIC INDEXES IN AXIAL RADIOGRAPHIC SPONDYLOARTHRITIS

K. Ben Ali[1], M. Slouma[1], L. Kharrat[1], A. Tezeghdenti[2], R. Dhahri[1], E. Ghazouani[2], I. Gharsallah[1], L. Metoui[1], B. Louzir[1]. *[1]The Military Hospital of Tunis, Rheumatology, Tunis, Tunisia*; *[2]The Military Hospital of Tunis, Immunology, Tunis, Tunisia*

Background: The cardiovascular burden in inflammatory rheumatic diseases is well recognized. This burden has been reported in spondyloarthritis. Atherogenic indexes are known with their role of predicting cardiovascular risk.
Objectives: The aim of our study was to determine the relation between pro-inflammatory cytokines and atherogenic indexes in spondyloarthritis.
Methods: We performed a cross sectional study including 38 patients with spondyloarthritis according to ASAS criteria. For each patient we measured interleukin (IL)1, IL6, IL17, IL23 and tumor necrosis factor (TNF) alpha, total Cholesterol (CT), Triglycerides (TG), High density lipoprotein Cholesterol (HDLc) and Low density lipoprotein cholesterol (LDLc). We also calculated the following ratios: CT/HDLc, TG/HDLc, LDLc/HDLc, and LogTG/HDLc.
Disease activity was measured using ASDAS (Ankylosing Spondylitis Disease Activity Score) and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index). Statistical analysis was performed using IBM SPSS Statistics 25.
Results: The mean age were 45.4±12.5 years. There were 33 Male (sex ratio were 6.6).
The mean C-reactive protein(CRP) were 29.6 ±40.34mg/L, mean erythrocyte sedimentation rate(ESR) were 41±33.9mm.
The mean ASDASCRP, BASDAI were 2.8±1.24, 3.7±2.12, respectively.
Active disease were noted in 68 % of patients using ASDASCRP score.
The mean IL1, IL6, IL17, IL23, TNF alpha were 11.6 ±25pg/ml, 15.4±45.9pg/ml, 84.6±77.9pg/ml, 15.3±15.26pg/ml, 25.3± 47.9pg/ml respectively.
The mean CT,HDLc,LDLc, TG were 4.47±0.93mmol/l, 1.09±0.3mmol/L, 2.77±0.78mmol/L, 1.29±0.54mmol/L respectively.
The mean CT/HDLc, TG/HDLc, LDL/HDLc, LogTG/HDLc were 4.28±1.26, 1.22±0.6, 2.7±1.06, 0.03±0.23, respectively.
Correlations were found between TG/HDLC ratio and IL1 (p<0.01, r=0.515), IL6(p<0.05; r=0.407), Log TG/HDLc and IL1 (p< 0.05, r=0.369), and IL6(p<0.05; r=0.333)
However, no correlations were noted between atherogenic indexes and IL7, IL17, IL23, TNFalpha.
Conclusion: Our study showed a correlations between atherogenic indexes and both IL1 and IL6.
These findings suggests that serum IL-6 and IL1 levels in spondyloarthritis contribute to the development of cardiovascular disease atherosclerosis.
REFERENCES:
[1] Lau et al. Role of Adipokines in Cardiovascular Disease. Circ J. 2017; 81(7): 920-8.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1281

AB0072 SERUM AMYLOID A PROTEIN (SAA) IN ANKYLOSING SPONDYLITIS AND THE RELATIONSHIP WITH SYSTEMIC INFLAMMATION

K. Sakharova[1], M. Cherkasova[1], S. Erdes[1]. *[1]V.A. Nasonova Scientific Research Institute of Rheumatology, Spondyloarthritis and PsA, Moscow, Russian Federation*

Background: Serum amyloid A protein (SAA) likely has a critical role in control and possibly propagation of the primordial acute phase response and is the precursor of AA amyloid fibrils. Prolonged elevations in SAA are the major inciting factor for AA amyloidosis developing in chronic inflammatory diseases. In Russia 2-4% of patients with ankylosing spondylitis (AS) have secondary (AA) amyloidosis.
Objectives: To study the level of SAA in AS its relationship with indicators of disease activity.
Methods: 124 patients with AS (according to mNYC 1984) 70 men, 54 women, of whom HLA B 27 positive 91.1% mean age 38.1 (± 12.9), age at the onset of the disease 23.5 (± 9.9) consecutively admitted to the clinic of the Research Institute rheumatology from February to November 2020. In addition to the standard examination (the median CRP 6.7 mg/l [1.4; 24.9], ESR 13 mm/h [7; 27], SAA was studied in all patients by the nephelometric method.
Results: The median SAA in 124 patients was 12.5 mg/l [4;71.6]. Among them, 31% had normal SAA level (<5 mg/l), and 69 % - more than 5 mg/l. In 21 (17.5 %) cases, the level of SAA was increased at normal CRP levels, and only in 2 cases an increase in the level of CRP at normal SAA levels; 50 patients (40.3 %) with normal ESR had elevated SAA levels, and 7 (5.6%) - ESR exceeded the upper limits of the norm with normal SAA levels. Comparison of the average values of the levels of SAA, CRP, ESR in men and women did not reveal significant differences between them. The SAA level was weakly correlated with ESR (r = 0.2; p=0.002) and BASDAI (r=0.3; p=0.002), moderately with ASDAS-CRP (r=0.5; r<0.0001), but showed a strong association with CRP (r = 0.80; p<0.00001). Patients with elevated SAA levels (>5 mg/l) had a shorter disease duration (10 and 12 year; p<0.0004), higher ASDAS-CRP (2.9 and 2.4; p<0.003), blood CRP level (14.6 and 1.3; p<0.00001), and significantly more peripheral arthritis (60% and 39%; p<0.05) than patients with normal indicators.
Conclusion: The level of SAA correlates well with indicators of AS activity, especially with the level of CRP, and can be used as an alternative indicator of disease activity.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1782

AB0073

INTESTINAL PERMEABILITY IN SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW OF THE LITERATURE

S. Hecquet[1], P. Totoson[2], H. Martin[2], C. Prati[1], D. Wendling[1], C. Demougeot[2], F. Verhoeven[1]. [1]*Centre hospitalier régional universitaire de Besançon, Rheumatology, Besançon, France*; [2]*EA4267 PEPITE LAB, Physiology, Besançon, France*

Background: Growing evidence argue for a role of the gut in the pathophysiology of various chronic rheumatic diseases such as spondyloarthritis (SpA). This so-called "gut-joint axis" involves dysbiosis, bacterial translocation, intestinal inflammation and increase in intestinal permeability. Recent data from clinical and basic research suggested that the integrity of the intestinal barrier might be a key determinant in translating autoimmunity to inflammation, making intestinal permeability a potential marker or a target for future therapies.
Objectives: To analyse the available data on intestinal permeability in SpA patients and the effects of drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) on intestinal permeability.
Methods: A systematic review was conducted. Without date restriction, the following databases were searched through September 1, 2020: Medline, Embase and Cochrane. Studies with patients with SpA assessing the intestinal permeability were selected. Some of the included studies have assessed the effect of NSAIDs on intestinal permeability.
Results: A total of 12 studies were included in the final analysis. The 12 studies involved a total of 268 SpA patients, including 240 ankylosing spondylitis (AS). Among the studies included, four studies used the lactulose/mannitol test, four studies used the 51Cr-ethylenediaminetetraacetic test and two studies used the polyethylene glycols test. Nine of the 12 studies reported increased intestinal permeability regardless on the method used for intestinal permeability evaluation. Four studies evaluated the link between disease activity, assessed by CRP and ESR levels, and intestinal permeability and showed no correlation between increased intestinal permeability and markers of disease activity in AS patients. As regards the effects of NSAIDs on intestinal permeability, data are controversial. Two studies, including one evaluating indomethacin, did not show any influence of NSAIDs in AS patients, one study showed an increase in intestinal permeability under NSAIDs in only 60% of the patients, another study reported increased intestinal permeability. When comparing the effect of NSAIDs in patients with AS to healthy subjects, one study reported a comparable NSAIDs-induced increase in intestinal permeability in both groups.
Conclusion: The results of our review suggest that increased intestinal permeability is present in SpA patients even in the absence of NSAIDs use and regardless of the method used to assess intestinal permeability. The effects of NSAIDs on intestinal permeability in SpA patients is more controversial and further studies are needed to clarify them.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3254

AB0074

NO DIFFERENCE BETWEEN THE SEROLOGIES OF DENTAL GERMS AND THE PHENOTYPES OF SPONDYLOARTHRITIS WITHIN THE DESIR COHORT

T. Neel[1], A. Tournadre[2], M. Paul[3], M. Norman[3], S. Paul[4], H. Marotte[1]. [1]*CHU, Rhumatology, Saint-Etienne, France*; [2]*CHU, Rhumatology, Clermont-Ferrand, France*; [3]*SAINBIOSE INSERM U1059, Research, Saint-Etienne, France*; [4]*GIMAP EA3064, Immunology, Saint-Etienne, France*

Background: Porphyromonas gingivalis (PG) and Prevotella Intermedia (PI) are two oral pathogens involved in the pathophysiology of chronic periodontopathies. Several studies have determined a role of these periodontal pathologies in the pathophysiology of rheumatoid arthritis (1) while the link with spondyloarthritis is not clearly established with currently contradictory studies (2,3,4).
Objectives: The purpose of this work is to investigate a link between spondylarthritis and the presence of chronic periodontopathy evaluated by PG and IP serologies.
Methods: The positivity and quantity of anti-PG and anti-PI antibodies were determined by ELISA method in patients from the DESIR cohort with one of the spondyloarthritis phenotypes compared to patients with common low back pain (n=50) (population control). Patients with spondyloarthritis were classified according to the following phenotypes (diagnosis chosen at 3 years in the DESIR cohort): axial spondylarthritis (n=126), psoriatic rheumatism (n=101), spondyloarthritis associated with chronic inflammatory bowel disease (n=36), undifferentiated spondylitis (n=241), reactive arthritis (n=2), SAPHO (acronym for Synovite, Acne, Pustulose, Hyperostosis and Osteitis. Correlations between patients' serological status, and smoking status, body mass index and age were sought.
Results: According to the general characteristics, the control group was significantly older than the axial spondylarthritis (p<0.001), and the psoriatic rheumatism group had a higher body mass index than the control population (p<0.05). The positivity and concentration of anti-PG and anti-PI antibodies were similar between different groups of spondyloarthritis compared to the control group. However, the subgroups "reactive arthritis" and "SAPHO" could not be analyzed due to insufficient staffing. Smoking status and body mass index were not related to antibody concentrations, however there was a statistical correlation between anti-PG antibody concentrations and age. After adjusting on age, there was no difference between the axial spondylarthritis and control groups.
Conclusion: Our results therefore suggest the absence of a link between periodontal germs involved in chronic periodontopathies and spondyloarthritis, provided that the two phenotypes involving germs in their pathophysiology could not be analyzed. Our results from a population of beginner spondylitis are therefore not in favour of the involvement of oral flora in the pathophysiology of spondyloarthritis, as is the case in rheumatoid arthritis (1). The associations found previously could therefore be favoured by a systemic inflammatory phenomenon. In conclusion, our study suggests no link between chronic periodontopathy and the occurrence of spondyloarthritis. However, the effect of chronic periodontopathy on the evolution of spondylarthritis remains to be explored.
REFERENCES:
[1] Detert J, Pischon N, Burmester GR, Buttgereit F. The association between rheumatoid arthritis and periodontal disease. Arthritis Res Ther. 2010;12(5):218.
[2] Ratz T, Dean LE, Atzeni F, Reeks C, Macfarlane GJ, Macfarlane TV. A possible link between ankylosing spondylitis and periodontitis: a systematic review and meta-analysis. Rheumatology. 2015;54(3):500-10.
[3] Pischon N, Pischon T, Gülmez E, Kröger J, Purucker P, Kleber B-M, et al. Periodontal disease in patients with ankylosing spondylitis. Ann Rheum Dis. janv 2010;69(01):34-8.
[4] Sezer U, Erciyas K, Pehlivan Y, Üstün K, Tarakçıoğlu M, Şenyurt SZ, et al. Serum cytokine levels and periodontal parameters in ankylosing spondylitis: Ankylosing spondylitis and periodontal diseases. J Periodontal Res. juin 2012;47(3):396-401.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3258

AB0075

HSA_CIRC_0012732, HSA_CIRC_0008961, HSA_CIRC_0405239 AND HSA_CIRC_0068784 MIGHT BE INVOLVED IN THE PATHOGENESIS AND DEVELOPMENT OF ANKYLOSING SPONDYLITIS

Y. P. Tang[1], Y. F. Qing[1], Z. R. Dong[1], F. Dai[1], J. Zheng[1], Y. Jiang[1], Y. X. He[1], Q. B. Zhang[2]. [1]*Institute of Rheumatology and Immunology, Affiliated Hospital of North Sichuan Medical College, Department of Rheumatology and Immunology, Affiliated Hospital of North Sichuan Medical College, Nanchong, China*; [2]*Institute of Rheumatology and Immunology, Affiliated Hospital of North Sichuan Medical College, Department of Geriatrics, Affiliated Hospital of North Sichuan Medical College, Nanchong, China*

Background: CircRNAs have been found to be involved in the occurrence and development of many rheumatic diseases[1-2]. Are circRNAs involved in the pathogenesis of ankylosing spondylitis (AS)? How do these circRNAs participate in the pathogenesis of AS? This all needs further study.
Objectives: This study is to clarify the expression levels of hsa_circ_0012732, hsa_circ_0008961, hsa_circ_0405239 and hsa_circ_0068784 in the peripheral blood of AS patients, and to explore whether these circRNAs are involved in the pathogenesis of AS.
Methods: To collected 60 cases of AS (30 cases of active AS (ASA): BASDA> 6 or 6> BASDAI> 4, ESR> 22mm / h or 6> BASDAI> 4, hsCRP> 9mg / L; 30 cases of stable AS (ASS): BASDAI <4) and 30 health control (HC) peripheral blood samples, related clinical and laboratory indicators. The relative expression levels of hsa_circ_0012732, hsa_circ_0008961, hsa_circ_0405239 and hsa_circ_0068784 in each group were detected by real-time quantitative polymerase chain reaction (qPCR). The relationships between the 4 circRNAs and clinical and laboratory indicators were explored by correlation analysis.
Results: 1. The qPCR results suggested that the expression of hsa_circ_0012732 between the ASA and ASS groups was statistically significant (p<0.05), and the expression of hsa_circ_0008961 was statistically significant between the ASA and HC groups (p<0.05). Howeverthere was no statistical significance among other groups (p>0.05)Figure 1. Similarly, the expression level of hsa_circ_0405239 was not statistically significant among the groups (p>0.05), and the same was true for hsa_circ_0068784 (p>0.05).
2. Correlation analysis results (Figure 2) showed that hsa_circ_0012732 is positively correlated with lymphocyte count (LY), mean corpusular volume (MCV), albumin (ALB), and negatively correlated with Bath ankylosing spondylitis disease activity index (BASDAI), Bath ankylosing spondylitis functional index (BASFI), high sensitivity C-reactive protein (hsCRP), Globulin (GLOB) (p<0.05); hsa_circ_0008961 is negatively correlated with platelet (PLT) (p<0.05); hsa_circ_0405239 is negatively correlated with BASDAI and BASFI; hsa_circ_0068784 was negatively correlated with BASDAI (p<0.05); and there was no statistically significant (p>0.05) between these 4 circRNAs and other indicators.

Conclusion: Hsa_circ_0012732, hsa_circ_0008961, hsa_circ_0405239 and hsa_circ_0068784 may be related to the pathogenesis of AS. Among them, hsa_circ_0012732 may be involved in AS inflammation and has the potential to participate in the judgment of disease activity.

REFERENCES:

[1] LS, K., et al., The biogenesis, biology and characterization of circular RNAs. 2019. 20(11): p. 675-691.

[2] J, W., et al., Non-coding RNAs in Rheumatoid Arthritis: From Bench to Bedside. 2019. 10: p. 3129.

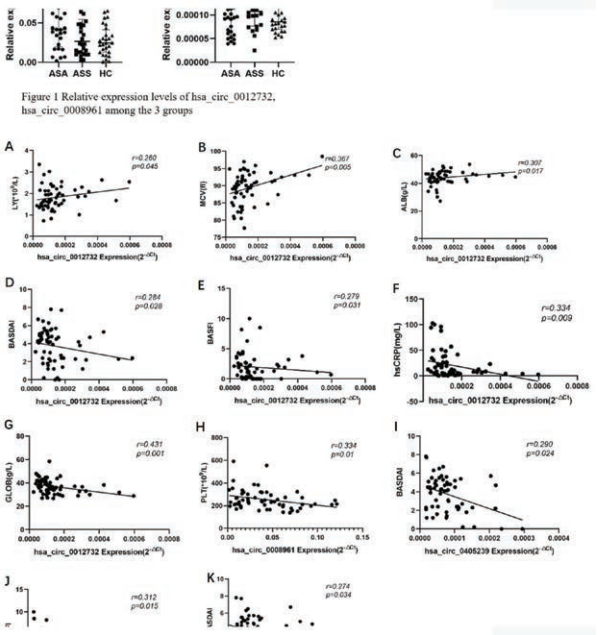


Figure 1 Relative expression levels of hsa_circ_0012732, hsa_circ_0008961 among the 3 groups

Disclosure of Interests: Yi-Ping Tang Grant/research support from: Science and Technology Project of Nanchong City (18SXHZ0522)., Yu-Feng Qing: None declared, Zeng-Rong Dong: None declared, Fei Dai: None declared, Jianxiong Zheng: None declared, Yi Jiang: None declared, Yi-Xi He: None declared, Quan-Bo Zhang Grant/research support from: National Natural Science Foundation of China(General Program) (81974250); Science and Technology Plan Project of Sichuan Province (2018JY0257)

DOI: 10.1136/annrheumdis-2021-eular.3412

AB0076

THE ROLE OF MACROPHAGE MIGRATION INHIBITORY FACTOR IN ACTIVITY AND PROGRESSION OF ANKYLOSING SPONDYLITIS

Y. Gazar[1], M. Hanafy[1], M. Elrefi[2]. *[1]Faculty of Medicine, AL-Azhar university, Rheumatology and Rehabilitation, cairo, Egypt*; *[2]Military Hospitals, Rheumatology, cairo, Egypt*

Background: Ankylosing Spondylitis (AS) is a chronic inflammatory form of arthritis that predominantly affects the axial joints and has a global prevalence of 1%. Disease progression is marked by osteoproliferation and bone fusion in the axial joints, causing considerable loss of mobility. Migration Inhibitory Factor (MIF) is a potent pro-inflammatory cytokine implicated in several diseases. Elevated serum MIF levels have been reported in AS the role of MIF in bone formation has been a subject of controversy.

Objectives: Detection the level of Migration Inhibitory Factor in Ankylosing Spondylitis patients and correlate the level with disease activity and progression.

Methods: This cross-sectional case-control study were concluded upon 70 randomly selected people from internal medicine department in Kobry El-kobba Military Hospital and from rheumatology and rehabilitation department in EL-Hussein university hospital. The population study were divided into two groups: Group A: (50) Patients with Ankylosing Spondylitis (AS) who met the European Spondyloarthropathy Study Group (ESSG) criteria for AS (30) and Group B: (20) Healthy controls. Serum MIF by ELISA were measured. X-rays cervical &lumbosacral vertebrae (dorsal, lateral) views were obtained. m-SASS score (based on radiographic findings to detect progression) were assessed. MSK U/S on Tendo Achilles affected in AS patients were done.

Results: the mean age of all patients was (38.2 ± 8.4) years. Regarding gender of the patients, the majority (65.7%) of patients were males, while (34.3%) were females. (88%) of AS patients had cervical erosion or sclerosis, (46%) had dorsal erosion or sclerosis, (92%) had lumbosacral erosion or sclerosis, with m-SASS score of (11 ± 6.1). Regarding musculoskeletal U/S, (72%) had evidence of inflammation and erosion. Highly significant increase in ESR, CRP and MIF levels in A group; compared to control B group; with highly significant statistical difference ($p < 0.01$). the increase in smoking, ESR and MIF level; had an independent effect on increasing the probability of progression occurrence; with significant statistical difference ($p < 0.05$ respectively). MIF level at a cutoff point (>51) predicted patients with progression, with fair accuracy (74%), sensitivity= 53% and specificity= 94% ($p = 0.0056$).

Conclusion: MIF ply an important role in the pathogenesis of Ankylosing Spondylitis and has a link between chronic inflammation, new bone formation and disease progression and can be used as indicator for activity and disease progression.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3421

SLE, Sjögren's and APS - aetiology, pathogenesis and animal models

AB0077

ASSOCIATION BETWEEN VITAMIN D RECEPTOR GENE POLYMORPHISMS AND SYSTEMIC LUPUS ERYTHEMATOSUS IN MALTESE PATIENTS

R. Magro[1], J. A. Grech Meli[2], J. Debattista3, N. Aquilina[4], K. Gatt5, A. Borg6, C. Scerri[2]. *[1]Mater Dei Hospital, Rheumatology, Msida, Malta*; *[2]University of Malta, Faculty of Medicine and Surgery, Msida, Malta*; *[2]University of Malta, Faculty of Medicine and Surgery, Msida, Malta*; *[4]Mater Dei Hospital, Medicine, Msida, Malta*; *[4]Mater Dei Hospital, Medicine, Msida, Malta*; *[1]Mater Dei Hospital, Rheumatology, Msida, Malta*

Background: Vitamin D deficiency is highly prevalent in patients with systemic lupus erythematosus (SLE). Vitamin D acts through the vitamin D receptor (VDR) that is present in most cells, and it can regulate the transcription of over 200 genes. The expression of vitamin D receptors by a variety of cells belonging to the innate and adaptive immune systems has created interest with regards to the role of vitamin D in the pathogenesis of SLE. Several polymorphisms of the VDR gene have been described, namely BsmI, ApaI, TaqI and FokI. A number of VDR gene polymorphism genotypes have been associated with increased risk of SLE mostly in Asians and Africans.[1]

Objectives: The aim of this study was to establish whether an association was present between VDR gene polymorphisms and SLE susceptibility in a cohort of SLE patients living in Malta. A further aim was to assess the relationship between these VDR gene polymorphisms and SLE disease characteristics.

Methods: 59 SLE patients living in Malta and attending Rheumatology clinic at Mater Dei Hospital were recruited for the study after providing informed consent. The patients were over the age of 18 years and fulfilled the SLICC classification criteria for SLE. The patients were interviewed and blood samples were taken. RNA extraction was performed from whole blood. QuantiGene Plex technology was used to measure the expression of 12 interferon (IFN) signature genes in the extracted RNA. 93 cord blood samples obtained from individuals living in Malta were used as a control. DNA extraction was carried out from the blood samples obtained from the patients and controls. The VDR gene was screened and the regions containing the VDR polymorphisms were amplified for each patient. The amplified regions were then digested with their respective restriction enzymes in order to view the patient's genotype via restriction fragment length polymorphism. Statistical analysis, including odds ratio (OR), was carried out to gauge the significance in the association of these polymorphisms with SLE.

Results: 94.9% of SLE patients were female and they had a mean age of 44.5 years. All the patients were of Caucasian ethnicity. 13.6% had vitamin D deficiency (serum 25-hydroxyvitamin D <20ng/ml) and 25.4% were vitamin D insufficient (serum 25-hydroxyvitamin D 20-29ng/ml). The results showed that when ApaI polymorphism was present as a homozygote for the variant allele there was a significant decrease in SLE prevalence (OR=0.39, CI 0.17-0.87, p=0.02). The results were also analysed by placing the polymorphs into haplotypes. The haplotype containing all wild-type alleles for the VDR gene and the haplotype containing all wild-type alleles with the variant allele for FokI had an increased prevalence of SLE (OR= 1.95, CI 1.12-3.38, p=0.01 and OR= 2.36, CI 1.13-4.91, p=0.02 respectively). The patients who were homozygous for the variant allele for BsmI had a significantly higher SLE disease activity index-2K (SLEDAI-2K) (mean 5.00) compared to those that were heterozygous (mean 2.66; p=0.010). No significant difference was noted in damage, IFN signature gene expression, organ manifestation and autoantibody profile between the different genotypes for the 4 VDR polymorphisms. SLE patients who were homozygous variant for the ApaI or TaqI polymorphisms had an increased prevalence of fibromyalgia (OR=7.50, CI 1.47-38.16, p=0.02 and OR=12.00, CI 1.80-80.05, p=0.02 respectively).

Conclusion: The study showed that in the Maltese population the presence of the VDR gene polymorphism haplotype containing all wild-type alleles and the haplotype containing all wild-type alleles with the variant allele for FokI are associated with an increased risk of SLE. Moreover the homozygous variant genotype for BsmI was associated with a higher SLE disease activity. The homozygous

variant genotype for ApaI and TaqI was associated with a higher risk of fibromyalgia in SLE patients.

REFERENCES:

[1] Zhou TB, Jiang ZP, Lin ZJ, Su N. Association of vitamin D receptor gene polymorphism with the risk of systemic lupus erythematosus. J Recept Signal Transduct Res. 2015;35(1):8-14.

Acknowledgements: The Faculty of Medicine and Surgery, University of Malta provided funding for this research.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.770

AB0078 LIPID IMMOBILIZATION AS A METHOD TO OBTAIN ANTIGENIC NANO-OBJECTS

O. Rusanova[1], O. Emelyanova[1,2], N. Emelyanov[2]. [1]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», 1, Волгоград, Russian Federation*; [2]*Federal State Budgetary Educational Institution of Higher Education «Volgoorad State Medical University» of the Ministry of Healthcare of the Russian Federation, 2, Волгоград, Russian Federation*

Objectives: Objective of the study is to research the effect of emulsion polymerization on active sites of cardiolipin antigen determinant in antiphospholipid syndrome (APS) in patients with systemic lupus erythematosus (SLE).

Methods: Having integrated antigen nanoobjects we developed immobilized magnetocontrollable antigen nanosystems and put them to an evaluation test. The nanosystems are polyacrylamide granules with a built in antigen. To obtain stable immobilized multi–use biopharmaceuticals with targeted properties (shape, particle diameter, pore size, density) we used a modified version of emulsion polymerization method using polyacrylamide carrier gel. This method permitted a greater sorptive capacity, preserving the antigen in maximum native state, and opened up the possibility of controllable modification of nanoobjects. Cardiolipin was used as the antigen in question.

Results: Following the method described above we performed sorption of anticardiolipin antibodies from blood plasma of SLE patients who showed clinical presentations of antiphospholipid syndrome. Blood serum from 10 apparently healthy individuals served as control. The level of cardiolipin antibodies was determined before and after sorption by indirect solid phase immunoenzyme method. In the eluate we estimated total protein by Lowry method. In vitro testing showed that the obtained antigen nanosystems based on immobilized cardiolipin could effectively remove cardiolipin antibodies from whole blood of SLE patients with clinical presentations of APS to achieve the values of healthy individuals (before sorption cardiolipin antibodies 0.328 ± 0.028; after sorption 0.059 ± 0.017; p<0.001; sorption capacity 8.00 ± 0.390 mg/ml).

Conclusion: The method of emulsion polymerization with consideration to hydrophobic and hydrophilic properties of lipid molecules permits obtaining and modifying biomolecules with certain properties, in a controlled fashion.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1075

AB0079 ENDOTHELIAL FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: IMPACT OF CAFFEINE CONSUMPTION ON ENDOTHELIAL PROGENITOR CELLS

V. Orefice[1], F. Ceccarelli[1], C. Barbati[1], E. Putro[1], C. Pirone[1], F. R. Spinelli[1], C. Alessandri[1], F. Conti[1]. [1]*Lupus Clinic, Sapienza University of Rome, Department of Clinical Internal, Anesthesiological and Cardiovascular Sciences, Rome, Italy*

Background: As widely demonstrated, circulating endothelial progenitor cells (EPCs) could be considered biomarkers of endothelial dysfunction. Their frequency and function varied in systemic lupus erythematosus (SLE) patients, with a significant association with subclinical atherosclerosis[1]. Caffeine, one of the most widely consumed products in the world, seems to interact with multiple components of the immune system by acting as a non-specific phosphodiesterase inhibitor[2]. In terms of cardiovascular disease (CVD), data from the literature showed a U-shaped association between habitual coffee intake and CVD[3]. In this view, Spyridopoulos et al. demonstrated a significant improvement in mature endothelial cells and EPCs migration in relation to coffee consumption in coronary artery disease both in mouse models and in patients[4]. Finally, caffeine seems to play a positive effect on SLE disease activity status, as demonstrated by the inverse association between its intake and SLE Disease Activity Index 2000 (SLEDAI-2K) and the serum levels of inflammatory cytokines[5]. At the best of our knowledge, there are no data about the effect of caffeine on cardiovascular risk in SLE patients.

Objectives: The aim of this study was to evaluate the possible role of caffeine intake on endothelial function in SLE patients, by evaluating its effect on circulating EPCs.

Methods: We performed a cross-sectional study enrolling SLE patients, fulfilling the revised 1997 ACR criteria. According with the protocol study, we excluded patients with history of smoking, CVD, chronic kidney failure, dyslipidaemia, and/or diabetes. At recruitment, the clinical and laboratory data were collected and disease activity was assessed using the SLEDAI-2k. Caffeine intake was evaluated using a 7-day food frequency questionnaire, previously employed in SLE cohort[5]. At the end of questionnaire filling, blood samples were collected. EPCs were isolated from peripheral blood mononuclear cells (PBMC) by a flow cytometry analysis and they were defined as early EPCs CD34+KDR+CD133+ cells and late EPCs CD34+KDR+CD133-, expressed as a percentage within the lymphocyte gate.

Results: We enrolled 19 patients (F:M 18:1, median age 45 years, IQR 15; median disease duration 240 months, IQR 168). In this cohort, we observed a mean±SD SLEDAI-2k value of 1.3±3.3 and the most frequent disease-related feature was joint involvement (73.7%). Concerning treatment at the time of enrolment, the majority of patients were receiving treatment with hydroxychloroquine (78.9%) and seven with glucocorticoids (36.8%). The median intake of caffeine was 163 mg/day (IQR 138) and we used this value as cut-off to categorize SLE patients in 2 groups: group 1 (N=10, caffeine intake ≤ 163 mg/day) and group 2 (N=9, caffeine intake > 163 mg/day). Patients with less intake of caffeine showed a significantly more frequent history of lupus nephritis (p=0.03), haematological manifestations (p=0.0003) and anti-dsDNA positivity (p=0.0003). Moving on EPCs, a positive correlation between caffeine intake and EPCs percentage was observed (p=0.04, r=0.4) (Figure 1A). Moreover, patients with more caffeine intake showed higher levels of early EPCs (p=0.02) (Figure 1B).

Conclusion: This is the first report analysing the impact of caffeine on EPCs frequency in SLE patients. We found a positive correlation between its intake and both early and late EPCs percentage, suggesting a caffeine influence on endothelial function in SLE patients. Nonetheless, these results support the possible impact of dietary habits on autoimmune diseases.

REFERENCES:

[1] Westerweel et al. *Ann Rheum Dis* 2007.

[2] Aronsen et al. *Europ Joul of Pharm* 2014.

[3] Ding et al. *Circulation* 2015.

[4] Spyridopoulos et al. *Art.Thromb Vasc Biol.* 2008.

[5] Orefice et al. *Lupus* 2020.

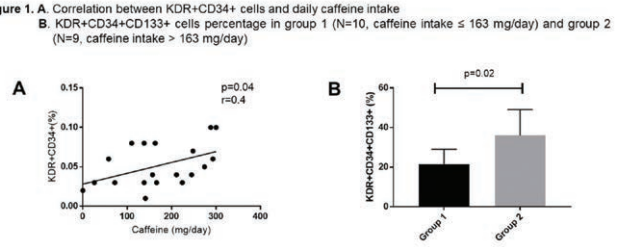


Figure 1. A. Correlation between KDR+CD34+ cells and daily caffeine intake
B. KDR+CD34+CD133+ cells percentage in group 1 (N=10, caffeine intake ≤ 163 mg/day) and group 2 (N=9, caffeine intake > 163 mg/day)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1224

AB0080 ALTERED CONCENTRATIONS OF DIFFERENT SMALL EXTRACELLULAR VESICLE POPULATIONS IN PLASMA OF PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

U. Stok[1,2], A. Shephard[3], S. Cucnik[1,2], S. Sodin-Šemrl[1,4], P. Zigon[1,4]. [1]*University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia*; [2]*University of Ljubljana, Faculty of Pharmacy, Ljubljana, Slovenia*; [3]*Nanoview Biosciences, Research and Development, Malvern, United Kingdom*; [4]*University of Primorska, Faculty of Mathematics, Natural Sciences and Information Technologies, Koper, Slovenia*

Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by thrombosis, obstetric complications, and the presence of antiphospholipid antibodies (aPL) that cause endothelial injury and thrombophilia [1]. Extracellular vesicles (EVs) are involved in various thrombotic disorders [2], including APS [3, 4], and therefore may influence the prothrombotic status of APS patients. One of the hallmarks of activated endothelium is the expression of adhesion molecules, such as ICAM-1 (CD54) and E-selectin (CD62E), that play a key function in the interactions with leukocytes and platelets.

Objectives: To determine the level of total tetraspanin (CD81/CD63/CD9)-positive vesicles and specific EV populations (CD54- and CD62E-positive EVs) in plasma from APS patients.

Methods: Whole blood was collected from 4 APS patients and 3 healthy blood donors (HBDs) and processed to obtain platelet-depleted plasma. The size and concentration of EVs were determined using ExoView platform (NanoView

Biosciences, MA, USA). In brief, EVs were captured and immobilized on ExoView Tetraspanin chips using the capture antibodies CD81, CD63, and CD9. Size was determined using SP-IRIS technology. Concentration measurements were performed with fluorescently labeled detection antibodies, specifically tetraspanins (CD81/CD63/CD9) for total EVs and CD54 and CD62E for specific EV populations.

Results: Analysis of EVs size confirmed the presence of small EVs (sEVs, < 70 nm) in both study groups. The size of EVs did not vary significantly between study groups (mean size ± SD in APS vs. HBD; CD81 (63.1 ± 1.5 nm vs. 66.6 ± 10.6 nm), CD63 (63.3 ± 1.64 nm vs. 69.2 ± 13.2 nm), and CD9 capture spot (61.8 ± 1.18 nm vs. 64.1 ± 7.64 nm)). The levels of total EVs (tetraspanin-positive) were increased 1.7-fold, 1.4-fold, and 2.2-fold for CD81, CD63, and CD9 capture spots, respectively, in APS patients compared to HBDs (Figure 1A). In addition, CD54- and CD62E-positive EVs represented a small population (< 2 %) of the total EVs (Figure 1B). The levels of CD54 were increased 2.9-fold, 3.0-fold, and 2.5-fold on CD81, CD63, and CD9 capture spots, respectively, and similarly, the levels of CD62E were increased 2.2-fold, 2.7-fold, and 2.0-fold on CD81, CD63, and CD9 capture spots, respectively, in APS patients compared to HBDs (Figure 1A).

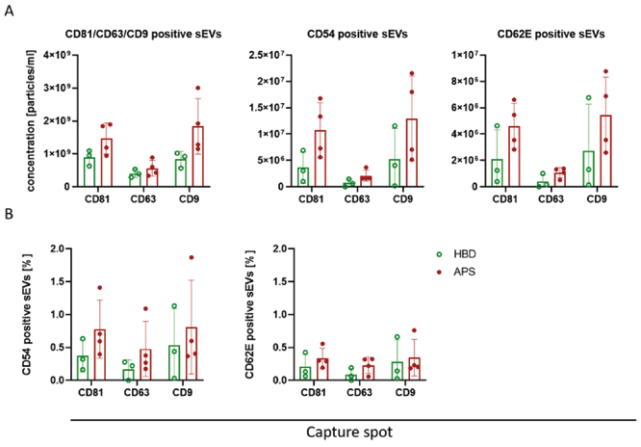


Figure 1. Concentration of tetraspanin- (CD81/CD63/CD9), CD54- and CD62- positive sEVs in APS patients and HBDs.

Conclusion: Higher levels of sEVs and increased percentage of CD54- and CD62E-positive sEVs in plasma of APS patients could indicate an altered and activated endothelium in those patients.

REFERENCES:

[1] Miyakis S. *Journal of thrombosis and haemostasis*. **2006**.
[2] Zara M. *Int J Mol Sci*. **2019**.
[3] Chaturvedi S. *Semin Thromb Hemost*. **2018**.
[4] Stok U. *Cells*. **2020**.
[5] Oggero S. *Front Pharmacol*. **2019**.

Disclosure of Interests: Ula Stok: None declared, Alex Shephard Employee of: NanoView Biosciences., Sasa Cucnik: None declared, Snežna Sodin-Šemrl: None declared, Polona Zigon: None declared
DOI: 10.1136/annrheumdis-2021-eular.1371

AB0081 ENDOTHELIAL MARKERS WITH DYSREGULATION IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC LITERATURE REVIEW

S. Bergkamp[1], M. J. Wahadat[2], V. Smith[3,4,5], S. Kamphuis[2], J. M. Van den Berg[1], D. Schonenberg-Meinema[1]. *[1]Amsterdam UMC, Paediatric Rheumatology, Amsterdam, Netherlands*; *[2]Erasmus MC, Paediatric Rheumatology, Rotterdam, Netherlands*; *[3]Ghent University, Internal Medicine, Gent, Belgium*; *[4]Ghent University Hospital, Rheumatology, Gent, Belgium*; *[5]VIB Inflammation Research Centre (IRC), Unit for Molecular Immunology and Inflammation, Ghent, Belgium*

Background: Systemic lupus erythematosus (SLE) is a severe, lifelong autoimmune disease known for its multisystem organ involvement. SLE patients are known to be at risk for premature atherosclerosis at a relatively young age (1). Endothelial dysregulation is one of the pathophysiologic mechanisms that can lead to the higher risk for cardiovascular disease in SLE (2). Multiple endothelial markers with dysregulation in SLE have been described so far, of which some are associated with disease activity.

Objectives: To report a systematic literature review regarding endothelial markers that are dysregulated in SLE and search for associations with disease activity.

Methods: The search was performed according to the Preferred Reporting Items for Systematic review and Meta-analysis Protocols (PRISMA-P) 2015 (3). In July 2020, the search terms were used in Embase, MEDLINE, Web of Science, Google Scholar and Cochrane. Inclusion criteria were 1) published studies after the year 2000 that reported measurements of endothelial cell markers in serum and/or plasma of SLE patients (diagnosed according to ACR/SLICC criteria), 2) English language peer reviewed articles and 3) disease activity measurement (i.e. SLEDAI, BILAG, SLAM, ECLAM or PGA). Exclusion criteria were 1) case reports or editorials, 2) studies performed in animals and 3) studies with microRNA/cytokine biomarkers. There was no minimum count for study population. The screening process is shown in figure 1.

Results: From 1892 hits, we identified 110 eligible articles. Table 1 shows an overview of the most frequently studied endothelial markers. These identified endothelial markers are involved in endothelial cell (EC) activation, EC apoptosis, disturbed angiogenesis, defective vascular tone control, immune dysregulation and coagulopathy. In most studies, dysregulation of the endothelial marker was associated with disease activity. The majority of the studies had a cross-sectional design, longitudinal data on endothelial markers in SLE are scarce.

Conclusion: We identified multiple endothelial markers that are dysregulated in SLE and this dysregulation was often associated with disease activity in cross-sectional studies. Our future plan is to test the identified endothelial markers in (longitudinally collected) samples of (childhood onset) SLE patients, disease- and healthy controls. This will be a next step in unravelling the pathophysiology of premature atherosclerosis and cardiovascular events in SLE-patients in young adulthood.

Table 1.

Endothelial marker	Articles (no. of studies)	Significant correlation with SLEDAI (no. of studies)			Studies with control groups (no. of studies)		Longitudinal data (no. of studies)
		Yes	No	Unknown	Healthy controls	Diseased controls	
VCAM-1	26	20	1	5	23	3	8
VEGF	22	13	5	4	20	2	2
ICAM-1	18	11	5	2	17	3	4
Thrombomodulin	17	10	5	2	13	2	2
E-Selectin	13	6	5	2	10	2	1
MCP-1	8	6	2	0	7	1	2
P-Selectin	6	3	2	1	6	1	1
IP-10	6	5	1	0	5	0	1
Pentraxin-3	5	5	0	0	5	1	2
vWF	5	4	1	0	5	0	2
Neopterin	3	2	1	0	2	0	2
Fas	3	0	2	1	2	0	1
Angiopoeietin-2	3	3	0	0	2	1	-
Endothelin-1	3	1	2	0	3	0	-
PAI-1	3	1	1	1	2	0	-
Adrenomedullin	3	2	0	1	2	0	-
TWEAK	3	1	1	1	1	2	-
PECAM-1	3	1	1	1	3	0	-

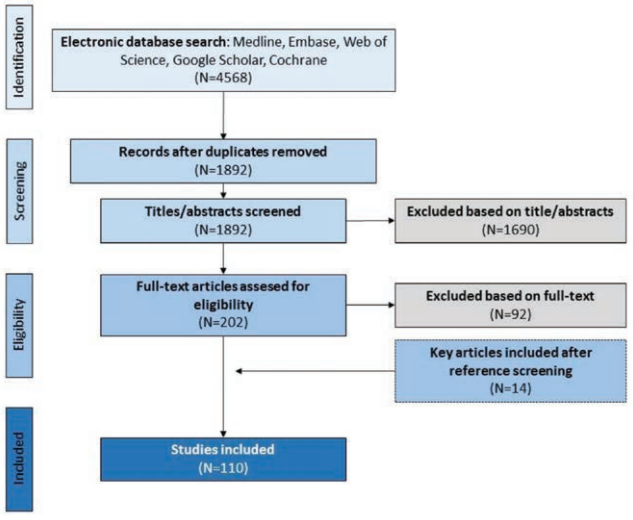


Figure 1.

REFERENCES:

[1] Vavlukis M, Pop-Gjorceva D, Poposka L, Sandevska E, Kedev S. Myocardial Infarction in Systemic Lupus Erythematosus - the Sex Specific Risk Profile. Curr Pharm Des. 2020 Dec 9.

[2] Westerweel PE, Luyten RK, Koomans HA, Derksen RH, Verhaar MC. Premature atherosclerotic cardiovascular disease in systemic lupus erythematosus. Arthritis Rheum. 2007 May;56(5):1384-96.
[3] Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;350:g7647.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2008

AB0082 PERSISTENT LOW COMPLEMENT LEVELS AND INTERFERON GENE UPREGULATION ARE PREDICTIVE FOR DISEASE PROGRESSION IN PATIENTS WITH INCOMPLETE SYSTEMIC LUPUS ERYTHEMATOSUS

W. Lambers[1], J. Westra[2], S. Arends[2], B. Doornbos- van der Meer[2], B. Horvath[3], H. Bootsma[2], K. De Leeuw[2]. [1]*University Medical Centre Groningen, Rheumatology/Clinical Immunology, Groningen, Netherlands*; [2]*University Medical Center Groningen, Rheumatology/Clinical Immunology, Groningen, Netherlands*; [3]*University Medical Center Groningen, Dermatology, Groningen, Netherlands*

Background: A subgroup of lupus patients present with mild symptoms and immunologic features, while they do not meet classification criteria for SLE. This disease state can be referred to as "incomplete systemic lupus erythematosus" (iSLE). Up to 55% of iSLE patients progress to SLE. Furthermore, previous research has shown that iSLE might overlap with early primary Sjögren's disease (pSS).(1) Unfortunately, there are no predictive markers available for progression to classifiable disease. Type-I interferon (IFN) plays an important role in disease initiation of both SLE and pSS.(2,3) Myxovirus-resistance protein A (MxA) is a GTP-ase that has previously be demonstrated to correlate strongly with IFN-type I expression. Furthermore, interferon-inducible chemokines IFN-γ induced protein 10 (IP-10), and B-cell activating factor (BAFF), that are both inducible by IFN, are of interest, because it is demonstrated that these proteins are increased prior to the diagnosis of SLE.(4)
Objectives: To find predictive markers that identify patients with incomplete systemic lupus erythematosus (iSLE) who are at the highest risk to progress to classifiable systemic lupus erythematosus (SLE) or primary Sjögren's syndrome (pSS).
Methods: Patients with iSLE (ANA ≥ 1:80, ≥ 1 clinical SLICC criterion, but not fulfilling the criteria, and disease manifestation <5 years) were included in a longitudinal observational study. Every half year, clinical status was evaluated and regular immunological serologic assessment was performed. Annually, interferon (IFN)-gene expression was determined by RT-PCR in whole blood using 14 genes. These genes represented 3 IFN-related modules. Some genes were mainly inducible by IFN-type I, others by IFN-type II. Furthermore, IFN-related mediators Myxovirus resistance protein A (MxA), interferon-gamma-induced protein 10 (IP-10) and B-cell activating factor (BAFF) were measured.
Results: Of 38 included iSLE patients, 6 had developed SLE and 1 develop pSS (18%) after median follow up of 36 months. The 7 patients who developed SLE/pSS were all women, and were younger at baseline than those who remained having iSLE (median 26 years, IQR 20-29 vs. median 42 years, IQR 30-56, p=0.0009). Over time, these patients had significantly lower complement 3 (p<0.0001) and complement 4 levels (p=0.005), higher IFN-gene expression (p=0.007), and lower neutrophil counts (p=0.033) (see Figure 1.). No difference was found between IFN-type I and IFN-type II inducible genes. Levels of MxA, IP-10 and BAFF did not differ between patients who remained iSLE and who progressed to SLE/pSS.

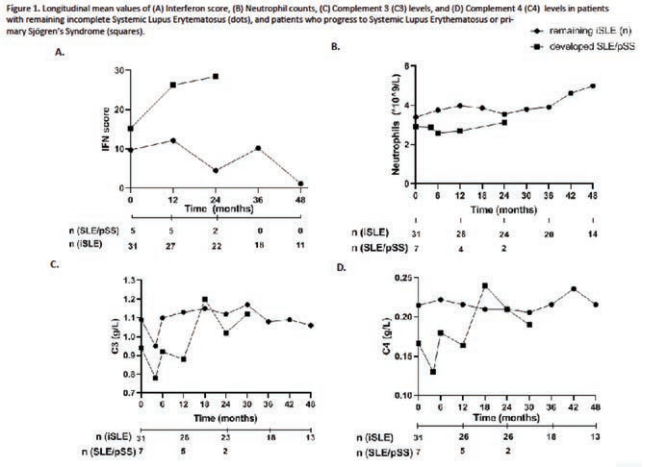


Figure 1.

Conclusion: Gender, age at diagnosis, persistent low complement levels, and high IFN-gene expression can help to identify iSLE patients at the highest risk of progressing to classifiable disease.

REFERENCES:

[1] Md Yusof MY, et al. Prediction of autoimmune connective tissue disease in an at-risk cohort: Prognostic value of a novel two-score system for interferon status. Ann Rheum Dis. 2018;1–8.
[2] Yao Y, et al. Type I interferons in Sjögren's syndrome. Autoimmun Rev. 2013;12(5):558–66.
[3] Crow MK. Type I Interferon in the Pathogenesis of Lupus. J Immunol [Internet]. 2014;192(12):5459–68.
[4] Lu R, et al. Dysregulation of innate and adaptive serum mediators precedes systemic lupus erythematosus classification and improves prognostic accuracy of autoantibodies. J Autoimmun. 2016;74:182–93.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2306

AB0083 SIGNALING OF PSGL-1 IN HUMAN NEUTROPHILS MIGHT CONTROL NET GENERATION AND APOPTOSIS AND MIGHT BE ALTERED IN SLE PATIENTS

A. Muñoz-Callejas[1], E. González Sánchez[1], E. F. Vicente-Rabaneda[2], J. Garcia Perez[3], S. Castañeda[2], A. Urzainqui[1]. [1]*Instituto de Investigación Sanitaria-Hospital de la Princesa, Inmunologia, Madrid, Spain*; [2]*Hospital de la Princesa, Reumatologia, Madrid, Spain*; [3]*Hospital de la Princesa, Neumologia, Madrid, Spain*

Background: Neutrophil extracellular traps (NETs) are extracellular chromatin fibers decorated with neutrophil antimicrobial proteins and histones, which are formed by neutrophils to trap invading pathogens and facilitate their removal. Excessive presence of NETs has been reported in autoimmune diseases like Systemic Lupus Erythematosus (SLE) and has been related with disease pathogenesis [1]. Our previous work showed that P-selectin KO mice develop an autoimmune syndrome similar to human lupus and that patients with cutaneous lupus have reduced expression of P-selectin in skin vessels [2]. Although it has been reported that P-selectin might induce NET generation in mouse neutrophils [3], there are no studies performed with human neutrophils.
Objectives: 1)To analyze the contribution of PSGL-1/P-Selectin interaction to control the generation of NETs by human neutrophils from healthy donors and patients with SLE.
2)To study the implication of PSGL-1/P-Selectin interaction in the control of other types of neutrophil death.
Methods: Human neutrophils were isolated from healthy donors and patients with SLE. After incubation *in* vitro with BSA or P-Selectin in rolling-like conditions (60 rpm shaking at 37^{0}C) for 10 min, neutrophils were left to adhere for 1 hour. Then, NETs were labeled with Sytox Green and quantified by fluorimetry and by flow cytometry (FACSCanto II, BD Biosciences). For quantification of necrosis and apoptosis, cells were labeled with propidium iodide and annexing V and analyzed by flow cytometry. Data were analyzed with two-sided Student, two-sided Mann-Whitney U or two-sided Wilcoxon signed rank test using GraphPad Prism software (Version 8.0.1, La Jolla, CA). Results were considered significant at P<.05.
Results: Our results show that rolling on BSA, compared to adhesion, induces NET generation and apoptosis of neutrophils isolated from blood of healthy donors. Rolling on P-selectin reduces apoptosis of neutrophils and increase the percentage of NET events, although reducing NET intensity. Comparing to healthy donors, neutrophils from active SLE patients generate NETs with higher intensity in adhesion and do not respond to P-Selectin.
Conclusion: The interaction of PSGL-1 with P-Selectin preserves neutrophil death from apoptosis and controls NET generation. Our results suggest that this control might be altered in patients with active SLE.

REFERENCES:

[1] Fousert, E., Toes, R., & Desai, J. (2020). Neutrophil extracellular traps (NETs) take the central stage in driving autoimmune responses. *Cells*, *9*(4), 915.
[2] González-Tajuelo, R., Silván, J., Pérez-Frías, A., De La Fuente-fernández, M., Tejedor, R., Espartero-Santos, M. & Urzainqui, A. (2017). P-Selectin preserves immune tolerance in mice and is reduced in human cutaneous lupus. *Scientific reports*, *7*(1), 1-12.
[3] Etulain, J., Martinod, K., Wong, S. L., Cifuni, S. M., Schattner, M., & Wagner, D. D. (2015). P-selectin promotes neutrophil extracellular trap formation in mice. *Blood*, *126*(2), 242-246.

Disclosure of Interests: None declared

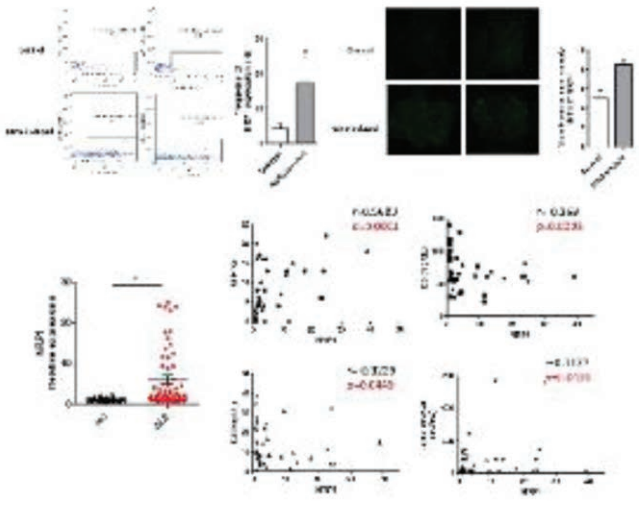
DOI: 10.1136/annrheumdis-2021-eular.2508

AB0084

INCREASED LEVEL OF NEUROPILIN-1 IN CD4+ T CELL AND ITS CORRELATION WITH DISEASE ACTIVITY OF SYSTEMIC LUPUS ERYTHEMATOSUS

Y. J. Choi[1], E. K. Lee[1], M. S. Lee[2], C. H. Lee[2], C. H. Chung[2], W. H. Yoo[1]. [1]*Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Internal Medicine, Jeonju, Korea, Rep. of (South Korea)*; [2]*Wonkwang University Hospital, Internal Medicine, Iksan, Korea, Rep. of (South Korea)*

Background: Semaphorin has been found as a neuronal guidance molecule, but has recently been called "immune semaphorin", as their critical role in immune cell activation, differentiation and migration has been revealed. In particular, class 4 semaphorin has been shown to contribute to lymphocyte activation and immune homeostasis.
Objectives: This study was aimed to investigate the expression of neuropilin-1 (NRP-1), the receptor of class 4 semaphorin, in the murine mouse model of systemic lupus erythematosus (SLE) and the patients with SLE and the correlation between the expression of NRP-1 and disease activity of SLE.
Methods: The expression of NRP-1 was measured in T cells in spleen and renal tissue in control mouse and TLR-7 agonist-induced lupus mouse by flow cytometry, PCR, and immunofluorescence (IF). CD4+ T cells from human peripheral blood were isolated to investigate the expression of NRP-1 in healthy control and the patients with SLE (n=40).
Results: The frequency of NRP-1 positivity in CD4+ T cells in spleen was significantly higher in lupus mouse group (median [interquartile range]: 15.34 [14.84] %) compared to vehicle mouse group (4.0 [2.77]%). The quantitative analysis of fluorescense intensity in kidney stained for NRP-1 revealed the increased level in lupus group compared to vehicle group. The CD4+ T cells from peripheral blood mononuclear cells in the patients with lupus also showed significantly higher frequency of NRP-1 positive CD4+ T cells than those from healthy controls. Comparing the correlation of the expression of NRP-1 and disease activity with SLEDAI, C3, C4, and anti-DNA antibodies, the significant correlation between NRP-1 and disease activity markers were confirmed.
Conclusion: Our results demonstrate that higher expression of NRP-1 in CD4+ T cells and its significant correlation with disease activity of SLE. These results indicate that pathologic contribution of NRP-1 in the pathogenesis of SLE and potential of targeting NRP-1 for the treatment of SLE.
REFERENCES:
[1] Nishide M, Kumanogoh A. The role of semaphorins in immune responses and autoimmune rheumatic diseases. Nat Rev Rheumatol. 2018 Jan;14(1):19-31.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3388

AB0085

ANTI-MULLERIAN HORMONE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Z. Alekberova[1], R. Goloeva[1], M. Cherkasova[1], A. Lila[1]. [1]*VA Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases, Moscow, Russian Federation*

Background: Anti-Mullerian hormone (AMH) is one of the key parameters for assessing reproductive function and ovarian reserve. The level of AMH correlates with the residual follicular pool in women of reproductive age.
Objectives: To assess AMH levels in SLE female patients of child-bearing potential, and analyze the relationship between AMH levels and disease severity, as well as relationship between serum AMH levels and different therapeutic regimens.
Methods: The study group included 12 women with SLE aged 20-40 years, and the control group - 15 age-matching healthy women. SLE diagnosis was established based on the EULAR/ACR classification criteria, 2019. The SLEDAI 2K was used to evaluate disease activity, and the SLICC index – to evaluate damage. AMH levels was measured using ELISA. AMH reference values ranged within 1.0-10.6 ng / ml. Values <1.0 were interpreted as a decreased ovarian reserve.
Results: SLE patients' mean age was 33.5 [29;38] years, and control group subjects' - 32.0 [26;35] years. Mean disease duration was 11.5 [2.8;18] years. Acute, subacute and chronic SLE was established in 33%, 17%, and 50%, respectively. Disease activity according to SLEDAI 2K was low in 25%, moderate – in 33%, and high – in 42% of pts. The SLICC damage baseline evaluation: no damage – 17%, low – 50%, medium – 16.5%, high-16.5%.
Mean AMH level was 3.5 ng/ml in SLE pts, and 3.1 ng/ml - in the control group, showing no statistical difference. A decrease in ovarian reserve (AMH less than 1.0 ng / ml) was significantly more common in SLE pts - 42% vs 13% in the control group. No correlation was found between AMH levels and the SLICC damage index, AMH and SLEDAI 2K, as well as AMH and SLE duration or clinical course. Detailed analysis showed that all pts with reduced ovarian function had CP included into their therapeutic regimens; the only exclusion within this subgroup – i.e., normal AMH level-6 ng/ml and preserved ovarian function - was documented in a patient who received a cumulative CP dose of 5.6 g. In all other patients a cumulative CP dose was higher, i.e.: 7.2 g, 7.8 g, 10.6 g, and 18.4 g – 1 patient per each dose value. Three pts with low AMH levels within 0.1 -0.3 ng/ml were 39 years old, while AMH reference values in 33-39y age group are 0.77-5.24 ng / ml. Analysis of gynecological history indicate that episodes of menstrual disorders were significantly more often reported in SLE pts (50% vs 20% in controls, p=0.001), similarly, gynecological diseases were also documented in 50% of SLE pts (chronic salpyngo-oophoritis, colpitis, endometriosis and uterine endometrioma, subserous uterine myoma, cervical dysplasia, cervical erosion), meanwhile low AMH was found only in 4 SLE pts; there was only 1 subject with gynecological condition – teratoma of the ovaries – in the control group (favorable outcome – surgical removal, preserved fertility and two births after surgery).
Conclusion: Ovarian reserve was significantly more often reduced in women with SLE compared to healthy controls. CP therapy negatively affects ovarian function, and most likely in a dose-dependent manner. In this study, 4 out of 5 patients with reduced ovarian function had gynecological diseases additionally compromising the ovarian reserve. Further studies are needed to clarify potential contribution of both - autoimmune inflammation and SLE therapy – into development of gynecological diseases and loss of fertility.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3402

AB0086

PREGNANCY OUTCOMES IN SYSTEMIC LUPUS ERYTEMATOSUS (SLE)

Z. Alekberova[1], R. Goloeva[1], T. Popkova[1]. [1]*V A Nasonova Research Institute of Rheumatology, systemic rheumatic disease, Moscow, Russian Federation*

Background: There's no doubt that SLE has negative effect not only on the course of pregnancy, but also on maternal and fetal outcomes.
Objectives: To clarify pregnancy outcomes in patients with SLE by means of retrospective analysis.
Methods: The study group included 12 women with SLE aged 20-40 years, and the control group - 15 age-matching healthy women. SLE diagnosis was established based on the EULAR/ACR classification criteria, 2019. The SLEDAI 2K was used to evaluate disease activity, and the SLICC index – to evaluate damage. Completed by all women issue-specific questionnaire covered clinical symptoms of SLE and details of obstetric history (characteristics of menstrual and reproductive function, presence of genital and extragenital pathology, previous pregnancies outcomes; previous intrauterine interventions, a history of coagulopathy).
Results: SLE patients' mean age was 33.5 [29;38] years, and control group subjects' - 32.0 [26;35] years. Mean disease duration was 11.5 [2.8;18] years. Acute, subacute and chronic SLE was established in 33%, 17%, and 50%, respectively. Disease activity according to SLEDAI 2K was low in 25%, moderate – in 33%, and high – in 42% of pts. The SLICC damage baseline evaluation: no damage – 17%, low – 50%, medium – 16.5%, high-16.5%. Past pregnancies were documented in 7 out of 12 SLE patients and 6 healthy subjects from the control group. Spontaneous vaginal delivery of a full-term baby was documented in both groups. Unfavorable pregnancy outcomes were significantly more frequent in SLE pts (31% vs 13% in the control group, p= 0.001). Two SLE pts after cyclophosphane therapy (10.6 and 18.4 g cumulative dose) and low AMH levels (< 1 ng/ml) failed to become pregnant, although never used contraception.

Table 1. Pregnancy outcomes

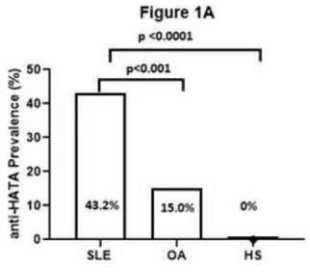
Pregnancy, n	SLE, n=16	Control, n=15	*p*
Birth	9 (56,3%)	13 (87%)	0,00
Abortion	2 (12,5%)	0	0,00
Unfavorable pregnancy outcome	5 (31,2%)	2 (13%)	0,00
Missed miscarriage	4 (25%)	0	0,00
Spontaneous abortion	1 (6%)	2 (13%)	ns

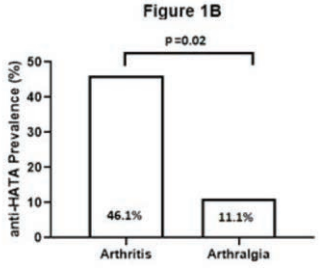
Analysis of gynecological history indicate that episodes of menstrual disorders were significantly more often reported in SLE pts (50% vs 20% in controls, *p*=0.001), similarly, gynecological diseases were also documented in 50% of SLE pts (chronic salpyngo-oophoritis, colpitis, endometriosis and uterine endometrioma, subserous uterine myoma, cervical dysplasia, cervical erosion), meanwhile low AMH was found only in 4 SLE pts; there was only 1 subject with gynecological condition – teratoma of the ovaries – in the control group (favorable outcome – surgical removal, preserved fertility and two births after surgery).
Conclusion: The incidence of unfavorable pregnancy outcomes is significantly higher in patients with SLE compared to the control group of healthy women.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3424

AB0087 AUTOANTIBODIES DIRECTED AGAINST HOMOCYSTEINYLATED ALPHA 1 ANTITRYPSIN AS A POTENTIAL NEW BIOMARKER FOR ARTHRITIS IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS

F. Natalucci[1,1], F. Ceccarelli[1], T. Colasanti[1], G. Olivieri[1], A. I. Celia[1], C. Barbati[1], M. Speziali[1], F. Ucci[1], C. Pirone[1], C. Ciancarella[1], F. R. Spinelli[1], C. Alessandri[1], F. Conti[1]. [1]*Policlinico Umberto I, Sapienza University of Rome, Department of Clinical, Internal Medicine, Anesthesiology and Cardiovascular Sciences, Rome, Italy*

Background: Joint involvement represents one of the most frequent features in patients affected by Systemic Lupus Erythematosus (SLE). This manifestation is characterized by a great heterogeneity in phenotype and severity: the application of more sensitive imaging techniques identified an erosive damage in about 25% of patients (1). This damage has been associated with autoantibodies, such as anti-citrullinated (ACPA) and anti-carbamylated proteins (antiCarP), previously identified in patients Rheumatoid Arthritis (RA) patients. Recently, homocysteinylated alpha 1 antitrypsin (Hcy-1A1AT) has been identified as a new antigenic target of autoantibodies in seronegative RA patients: in detail, anti-homocysteinylated alpha 1 antitrypsin (anti – HATA) antibodies have been identified in 75.7% of patients (2).
Objectives: In the present study, we aimed at determining the prevalence of anti – HATA in a cohort of SLE patients.
Methods: We evaluated patients affected by SLE according to the 1997 ACR criteria. Demographic, clinical, and laboratory data were collected in a standardized computerized electronically filled form. Each subject underwent peripheral blood sample collection. Hcy-A1AT was obtained by in vitro modification of native A1AT and used as antigens by ELISA to test the presence of anti–HATA in sera obtained from enrolled subjects. Finally, we investigated the presence of ACPA and Rheumatoid Factor (RF) commercial ELISA kits and of anti-CarP (home-made ELISA) by a home-made ELISA in SLE patients' sera. As control, we enrolled 40 patients affected by Osteoarthritis (OA) and 41 healthy subjects (HS).
Results: The present analysis included 88 SLE patients (M/F 6/82 median age 47 years (IQR 17), median disease duration 156 months (IQR 180). Joint involvement was observed in 75 SLE patients (85.2%): in detail, 65 patients referred arthritis and the remaining 10 inflammatory arthralgias. We identified the presence of anti–HATA IgG in 38 SLE patients (43.2%). This prevalence was significantly higher in comparison with OA and HS subjects [15.0% (p<0.001) and 0% (p<0.0001), respectively; Figure 1A]. Focusing on the SLE cohort, no differences were observed between patients with and without joint involvement in anti–HATA IgG prevalence (41.3% versus 34.7%, respectively; p=0.34). However considering SLE patients according to the presence of arthralgia and arthritis, the prevalence of anti-HATA was significantly higher in patients with arthritis in comparison with those patients with arthralgias (46.1% versus 11.1%, p=0.02; figure 1B). Finally, no significant association between anti-HATA and the other tested autoantibodies (RF, ACPA, anti-CarP) was found.





Conclusion: We evaluated the prevalence of anti-HATA in a cohort of SLE patients. The prevalence of these autoantibodies was significantly higher in SLE patients than in OA patients and in HS. The association with arthritis suggests a possible role for anti-HATA as biomarkers of SLE-related joint involvement.
REFERENCES:
[1] Ceccarelli F. Perricone C. Cipriano E. et al. Joint involvement in systemic lupus erythematosus: From pathogenesis to clinical assessment. Seminar in Arthritis and Rheumatism, 47(1), 53 – 64.
[2] Colasanti T. Sabatinelli D. Mancone et al. Homocysteinylated alpha 1 antitrypsin as an antigenic target of autoantibodies in seronegative rheumatoid arthritis patients. Journal of Autoimmunity 2020 Sep;113:102470.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3688

AB0088 QUALITY OF LIFE IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES DIFFERS ACCORDING TO ANTIPHOSPHOLIPID SYNDROME DAMAGE INDEX (DIAPS)

S. G. Foddai[1,2], M. Radin[1,2], A. Barinotti[1,2], I. Cecchi[1,2], E. Rubini[1,2], S. Sciascia[1,2], D. Roccatello[1,2]. [1]*Turin, Università di Torino, Turin, Italy*; [2]*Turin, Center of Research of Immunopathology and Rare Diseases - Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, Turin, Italy*

Background: Antiphospholipid syndrome (APS) is a rare autoimmune disorder that mainly affects young individuals. Due to the potentially devasting effects of some of its clinical manifestations, such as ischemic stroke and thrombotic microangiopathy, APS can have a deep negative impact on the quality of life (QoL) of the affected patients due to damage accrual (2).
To capture the full consequences of the disease, including both thrombotic and extra-criteria APS specific features, the antiphospholipid syndrome (APS) damage index (DIAPS), a 37-item score, was conceived.
Objectives: The aim of this study was to validate the DIAPS in a cohort of antiphospholipid antibodies (aPL) positive subjects, comparing it to the risk stratification score for the development of clinical manifestations of APS (Global APS Score -GAPSS) and QoL questionnaires filled out by APS patients.
Methods: This retrospective study included a total of 84 consecutive persistent aPL positive patients who attended the San Giovanni Bosco Hospital (Turin, Italy). Patients were then divided based on their diagnosis in 3 groups: primary APS (PAPS), secondary APS (SAPS) and aPL positive patients without clinical manifestations of APS, according to Miyakis criteria (1). Demographic, clinical and laboratory characteristics, were retrieved from electronic medical records and are summarized in Table 1. DIAPS was calculated as previously reported by adding together all points corresponding to the clinical manifestations of the patients (3).
Results: A total of consecutive 84 patients were enrolled in the study: 39 primary APS patients (PAPS), 28 secondary APS patients (SAPS) and 17 aPL positive patients without APS-related clinical manifestations. APS patients had significantly higher levels of DIAPS when compared to aPL asymptomatic patients (mean DIAPS 2.6 ±1.8 vs. 1.5 ±1.9, respectively; p<0.05). Moreover, SAPS patients had significantly higher levels of DIAPS when compared to PAPS patients (mean DIAPS 3.1 ±1.9 vs. 2.2 ±1.7, respectively; p<0.05). When comparing GAPSS and DIAPS levels in all the patients, we found a significantly positive correlation between these two scores (mean GAPSS 11.9 ±5.2 and mean DIAPS 2.4 ±1.9; Pearson 0.241; p<0.05). Finally, when applying the SF-12 score to our cohort, the mean physical component score and mental component score were lower than the average population (39.3 ±11.3 and 42.3 ±8, respectively) and we observed a negative correlation trend between DIAPS and both PCS and MCS (Pearson -0.133 and -0.183).

Table 1. Clinical and laboratory characteristics of the patients

	PAPS (n=39)	SAPS (n=28)	aPL asymptomatic (n=17)
Anagraphic			
Mean age (S.D.) at data collection	50.6±13.7	47.4±12.1	48.6±11.3
Sex (females), n	29 (74.4%)	29 (74.4%)	29 (74.4%)
Secondary diagnosis, n	N/A	SLE 24 (85.7%) SSJ 1 (3.6%) UCTD 1 (3.6%) MCTD 2 (7.1%)	SLE 8 (45.1%)
Clinical manifestations of APS			
Thrombosis, n	30 (76.9%)	26 (92.9%)	N/A
Arterial thrombosis, n	20 (51.3%)	14 (50%)	N/A
Venous thrombosis, n	17 (43.6%)	15 (53.6%)	N/A
Pregnancy morbidity, n	11 (28.2%)	4 (14.3%)	N/A
aPL profile at diagnosis			
LA, n	31 (79.5%)	23 (82.1%)	12 (70.6%)
aCL (IgG/M), n	22 (56.4%)	18 (64.3%)	10 (58.9%)
Anti-β2GPI (IgG/M), n	18 (46.2.%)	16 (57.1%)	3 (17.6%)
aPS/PT (IgG/M), n	23 (59%)	21 (75%)	8 (47.1%)

Conclusion: The DIAPS might be a valid score system for the assessment of APS-related damage and QoL.

REFERENCES:

[1] Miyakis S, Lockshin MD, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295–306.
[2] Grika EP, Ziakas PD, et al. Morbidity, mortality, and organ damage in patients with antiphospholipid syndrome. J Rheumatol 2012;39:516–523.
[3] Amigo MC, Goycochea-Robles M V. et al. Development and initial validation of a damage index (DIAPS) in patients with thrombotic antiphospholipid syndrome (APS). Lupus 2015;24:927–934.

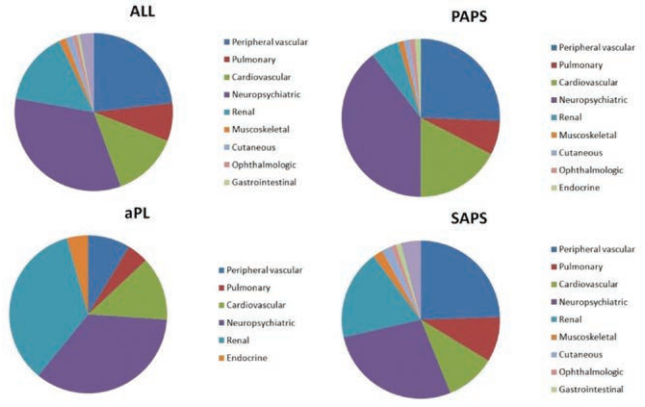


Figure 1. Relative involvement of the organ domains included in the DIAPS according to diagnosis

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4295

Systemic sclerosis, myositis and related syndromes - aetiology, pathogenesis and animal models

AB0089

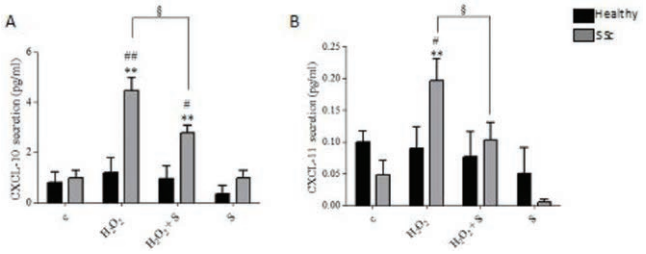
SILDENAFIL COUNTERACTS THE ACTIVATION OF CXCR3/CXCL10, -11 AXIS IN SCLERODERMA FIBROBLASTS EXPOSED TO REACTIVE OXYGEN SPECIES

C. Antinozzi[1], I. Dimauro[1], P. Sgrò[1], D. Caporossi[1], F. Del Galdo[2,3], L. DI Luigi[1]. *[1]University of Rome Foro Italico, Movement, Human and Health Sciences, Rome, Italy*; *[2]University of Leeds, Institute of Rheumatic and Musculoskeletal Diseases, Leeds, United Kingdom*; *[3]NIHR Biomedical Research Centre, University of Leeds, Leeds, United Kingdom*

Background: Oxidative stress associated with vascular damage represents one the major contributor in the pathogenesis of systemic sclerosis (SSc) [1]. Indeed, different studies demonstrated that excessive free radicals production can contribute to the activation of fibrotic process in the skin and visceral organs [1]. CXCL10 and CXCL11, together with their receptor CXCR3, are involved in vascular damage and in fibrosis [2]. Furthermore, these chemokines have been proposed as biomarkers of vascular damage progression and severe SSc prognosis [3].
Emerging evidences highlight the beneficial effects of the phosphodiesterase type 5 (PDE5) inhibitor, sildenafil, to protect different cell types from reactive oxygen species (ROS)-induced DNA damage, *in vitro* [3]. This effect has been linked to modulation of CXCL10 concentration in different pathological conditions [4,5].
Objectives: Here we set out to investigate the effects of sildenafil, in modulating the CXCR3/CXCL10, -11 inflammatory axis in dermal fibroblasts exposed to oxidative stress, *in vitro*.
Methods: Human dermal fibroblasts isolated by SSc skin biopsies were treated for 24h with 100µM of hydrogen peroxide (H_2O_2), in the presence or not of sildenafil (1µM). Dermal fibrobalsts from healthy skin were used as controls. CXCL10 and CXCL11 were evaluated in cell medium by luminex technology assay; expression of chemokine receptor (CXCR)3 and peroxisome proliferator-activated receptor (PPARγ) (a regulator of CXCL10,-11 mRNA) was evaluated by western blot assay.
Results: As showed in figure 1, SSc fibroblasts (grey bar) showed similar basal levels of CXCL10 (A) and CXCL11 (B) to healthy controls (black bar). H_2O_2 induced a significant increase of both chemokines only in SSc fibroblasts (by 4.6 fold for CXCL10 and by 4.2 fold for CXCL11) (*P<0.05 and **P<0.01 *vs.* c; #P<0.05 *vs*. healthy controls). Sildenal pre-incubation reduced by approximatively 50% the effects of H_2O_2 on chemokines release (Figure 1A and B) (§P<0.05 vs. H_2O_2), and reduced the expression of CXCR3 and PPARγ induced by hydrogen peroxyde exposure (data not shown).
Conclusion: *In vitro* study on dermal fibroblasts support clinical studies to determine the efficacy of sildenafil in the preventing tissue damage and fibrosis in SSc, by reducing the pro-inflammatory activation induced by oxidative stress.

REFERENCES:

[1] Di Luigi L, Sgrò P, Duranti G, Sabatini S, Caporossi D, Del Galdo F, Dimauro I, Antinozzi C. Sildenafil Reduces Expression and Release of IL-6 and IL-8 Induced by Reactive Oxygen Species in Systemic Sclerosis Fibroblasts. Int J Mol Sci. 2020 Apr 30;21(9):3161. doi: 10.3390/ijms21093161. PMID: 32365773; PMCID: PMC7246497.
[2] Koper OM, Kamińska J, Sawicki K, Kemona H. CXCL9, CXCL10, CXCL11, and their receptor (CXCR3) in neuroinflammation and neurodegeneration. Adv Clin Exp Med. 2018 Jun;27(6):849-856. doi: 10.17219/acem/68846. PMID: 29893515.
[3] Crescioli C, Corinaldesi C, Riccieri V, Raparelli V, Vasile M, Del Galdo F, Valesini G, Lenzi A, Basili S, Antinozzi C. Association of circulating CXCL10 and CXCL11 with systemic sclerosis. Ann Rheum Dis. 2018 Dec;77(12):1845-1846. doi: 10.1136/annrheumdis-2018-213257. Epub 2018 May 14. PMID: 29760155; PMCID: PMC6241615.
[4] Giannattasio S, Corinaldesi C, Colletti M, Di Luigi L, Antinozzi C, Filardi T, Scolletta S, Basili S, Lenzi A, Morano S, Crescioli C. The phosphodiesterase 5 inhibitor sildenafil decreases the proinflammatory chemokine IL-8 in diabetic cardiomyopathy: in vivo and in vitro evidence. J Endocrinol Invest. 2019 Jun;42(6):715-725. doi: 10.1007/s40618-018-0977-y. Epub 2018 Nov 10. PMID: 30415310; PMCID: PMC6531405.
[5] You N, Li J, Huang X, Wu K, Tang Y, Wang L, Li H, Mi N, Zheng L. COMMD7 activates CXCL10 production by regulating NF-κB and the production of reactive oxygen species. Mol Med Rep. 2018 May;17(5):6784-6788. doi: 10.3892/mmr.2018.8706. Epub 2018 Mar 8. PMID: 29532873.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.459

AB0090

THE BIOCHEMICAL BASIS OF ANIMAL MODEL OF SYSTEMIC SCLEROSIS

B. Doskaliuk[1], L. Zaiats[1], R. Yatsyshyn[2]. *[1]Ivano-Frankivsk National Medical University, Pathophysiology, Ivano-Frankivsk, Ukraine*; *[2]Ivano-Frankivsk National Medical University, Internal Medicine #1 Clinical Immunology and Allergology, Ivano-Frankivsk, Ukraine*

Background: Systemic sclerosis (SSc) is a heterogeneous autoimmune pathology, which detailed pathogenetic mechanisms of initiation and progression still require further investigations. It could be achieved with implementation of reliable experimental modeling techniques.
Objectives: This study was aimed to determine the state of oxidant/antioxidant system, dysregulation of collagen synthesis in laboratory animals and evaluate effectiveness of the considered model of SSc induction.
Methods: Thirty adult Wistar rats (220-240 g) were included in the study. The experimental group consisted of 20 animals, which received 3 subcutaneous injections of 0.5 ml of 5% sodium hypochlorite solution (NaClO) with an active chlorine concentration of 190 g / dm^3 for 6 consecutive weeks. The control group consisted of 10 rats injected with isotonic solution according to the previously described scheme.
Results: The level of catalase in the experimental group was lower than in the control 9.69 ± 0.67 g / l and 11.1 ± 0.87 g / l respectively (p = 0.002). Protein oxidative modification (POM) products were higher in the experimental group (0.0722 ± 0.023 vs 0.0527 ± 0.023, p = 0.014). Malondialdehyde (MDA) was also higher in the experimental group compared to the control (4.30 ± 0.26 and 3.85 ± 0.23, respectively, p = 0.010). The concentration of oxyproline in the serum of laboratory animals subjected to repeated administration of NaClO was significantly higher compared to the control group (34.03 ± 5.01 and 33.23 ± 2.40, p = 0.020).
Conclusion: As a result of the use of NaClO for the reproduction of SSc in laboratory animals, there is a violation of oxidative-antioxidant homeostasis and increased fibrotic processes. These changes are comparable with those in SSc patients, which makes this modeling technique a promising tool for a detailed investigation of SSc pathogenesis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.732

AB0091

INHIBITION OF AUTOPHAGY PREVENTS PROGRESSION OF FIBROSIS IN MURINE MODELS OF SYSTEMIC SCLEROSIS

A. Zehender[1], Y. N. Li[1], N. Y. Lin[1], A. H. Györfi[1], A. Soare[1], C. Bergmann[1], A. Ramming[1], G. Schett[1], J. H. W. Distler[1]. [1]*Medicine 3 of the University Clinic Erlangen, Medizin 3, Erlangen, Germany*

Background: Autophagy is catabolic process allowing cells to degrade unnecessary or dysfunctional cellular organelles. Failure of appropriate regulation of autophagy, however, can severely perturb tissue homeostasis. Recent studies demonstrate that autophagy is activated in several fibrotic diseases such as liver fibrosis, renal interstitial fibrosis, cardiac fibrosis.
Objectives: The objective of this work was to characterize the activation of autophagy in systemic sclerosis (SSc) and to decipher its role in the pathogenesis of SSc.
Methods: Activation of autophagy in skin samples of patients and murine models of SSc was assessed by co-staining of LC3B and P62 with the lysosomal marker LAMP2. The role of the autophagy was investigated in the model of bleomycin-induced dermal fibrosis. Beclin1 was overexpressed using adenovirus encoding for *Beclin1*. To knockdown *Atg7 in vivo* was achieved by subcutaneous injections of *Atg7* siRNA or non-targeting siRNA. *In vivo*, 3-methyladenine (3-MA) was administered i.p. in a concentration of 15 mg/kg ones daily. Protein expression was measured by Western blot. Target genes were analyzed by qPCR. To monitor the autophagic flux, we generated adenoviral vectors encoding for tandem fluorescent-tagged *LC3* (mRFP-EGFP-LC3).
Results: In the present study, we demonstrate that autophagy is activated in fibroblasts in SSc skin and also in experimental fibrosis models as compared to respective non-fibrotic control tissue with enhanced activity in *in vivo* and *in vitro* autophagy reporter studies. The aberrant activation of autophagy had profound stimulatory effects on fibroblasts. Activation of autophagy by forced expression of BECLIN1 promoted fibroblast-to-myofibroblast transition and stimulated the collagen release by cultured human fibroblasts and induced fibrosis in murine model. Nevertheless, inhibition of autophagy can deactivate myofibroblasts and induce regression of tissue fibrosis. Knockdown of *ATG7* or *BECLIN1* in human fibroblasts reduced the expression of αSMA and the number of stress fibers in myofibroblasts, indicating re-differentiation of myofibroblasts into resting fibroblasts upon inhibition of autophagy. Similar results were obtained with the autophagy inhibitors CQ and 3-MA. *In vivo*, siRNA mediated knockdown of *Atg7* effectively prevented progression of fibrosis in a model of established bleomycin-induced skin fibrosis. Inactivation of autophagy decreased dermal thickness, myofibroblast counts and hydroxyproline content to below pretreatment levels, indicating regression of bleomycin-induced skin fibrosis. In addition, treatment of mice with the autophagy inhibitor 3-MA ameliorated bleomycin-induced skin fibrosis.
Conclusion: We demonstrate that autophagy activity is enhanced in fibroblasts of SSc patients and in murine models of SSc. The increased activation of autophagy induces fibroblast-to-myofibroblast transition and promotes fibrotic tissue remodeling. However, inhibition of autophagy can deactivate myofibroblasts and induce regression of tissue fibrosis.
REFERENCES:
[1] Wynn, T. Cellular and molecular mechanisms of fibrosis. J Pathol 214, 199-210 (2008).
[2] Klionsky DJ, Abeliovich H, Agostinis P, *et al*. Guidelines for the use and interpretation of assays for monitoring autophagy in higher eukaryotes. Autophagy 4, 151-175 (2008).
[3] Wang, CW & Klionsky, DJ. The molecular mechanism of autophagy. Mol Med 9, 65-76 (2003).
[4] Hernández-Gea V, Ghiassi-Nejad Z, Rozenfeld R, *et al*. Autophagy releases lipid that promotes fibrogenesis by activated hepatic stellate cells in mice and in human tissues. Gastroenterology 142, 938-946 (2012).
Disclosure of Interests: Ariella Zehender: None declared, Yi-Nan Li: None declared, Neng-Yu Lin: None declared, Andrea-Hermina Györfi: None declared, Alina Soare: None declared, Christina Bergmann: None declared, Andreas Ramming: None declared, Georg Schett: None declared, Jörg H.W. Distler Consultant of: Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB., Grant/research support from: Anamar, Active Biotech, Array Biopharma, aTyr, BMS, Bayer Pharma, Boehringer Ingel-heim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB., Employee of: stock owner of 4D Science and Scientific head of FibroCure
DOI: 10.1136/annrheumdis-2021-eular.819

AB0092

ANTISYNTHETASE SYNDROME: CLINICAL PROFILE, SEROLOGIC AND TREATMENTS USED IN A COHORT OF PATIENTS FOLLOWED AT THE VIRGEN MACARENA HOSPITAL

P. Muñoz Reinoso[1], I. García Hernández[1], M. Ferrer Galván[2], F. J. Toyos Sáenz de Miera[1], L. Fernández de la Fuente Bursón[1], J. J. Pérez Venegas[1]. [1]*Hospital Universitario Virgen Macarena, Reumatología, Sevilla, Spain*; [2]*Hospital Universitario Virgen Macarena, Neumología, Sevilla, Spain*

Background: The antisynthetase syndrome (SAS) is characterized by the presence of antisynthetase antibodies, anti-JO1, PL7 y PL12 are the most common; and the classic triad of myositis, arthritis, and diffuse interstitial lung disease (ILD)[1]. Most patients present incomplete forms and the severity of the ILD determines the prognosis of the disease[2].
Objectives: to analyze epidemiological, clinical and serological characteristics and treatments used in a cohort of patients with SAS.
Methods: descriptive study of review of medical records. Data were collected from 15 patients with SAS followed in the Rheumatology and Pneumology consultations of the Virgen Macarena Hospital (Seville) in the last 10 years. The analysis was carried out using the R software.
Results: 15 patients were included, 8 men and 7 women. The median age was 56 years (33-77). Seven patients (47%) used to smoke. Four patients (27%) met the classical triad. All of them presented ILD and 8 patients (53%) had arthritis and / or myositis. Five (33%) had mechanic's hands and six of them (40%) presented Raynaud. Seven (47%) suffered from dyspnea before the SAS diagnosis. The median diagnostic delay was 1 month (0-43). Seven (47%) patients had anti-JO1, 1 (7%) anti-PL7, 2 (13%) anti-PL12 and 2 (13%) patients anti-Ro52. Radiological patterns detected by HRCT were: 5 (33%) NINE, 4 (37%) NIU and 6 (40%) others. The initial treatment included mostly (66%) glucocorticoids (GC) and one or more cFAME. In maintenance, mycophenolate was used in 7 patients (47%), cyclosporine 5 (33%), cyclophosphamide in 3 cases (20%), azathioprine in 3 patients (20%) and methotrexate in 3 of them (20%). Four (37%) patients required a combination of DMARDs and 2 cases needed (13%) biological therapy, Rituximab and Tocilizumab. Changes in the mean value of the initial respiratory function tests (FVC1 and DLCO1) and during follow-up (FVC2 and DLCO2) were not relevant (FVC1 81.5% [42-110], FVC2 81% [59-115]; DLCO1 83% [10-112], DLCO2 80.5% [47-108]). Nine patients (60%) remained clinically stable and 3 patients (20%) progressed radiologically. Four patients died from ILD progression.
Conclusion: In this study, the incomplete diagnosis of SAS predominated. The most detected antibody was anti-JO1. ILD is present in all cases, with NINE being the most frequent pattern so multidisciplinary management is necessary. Most used treatments were GC and FAMES combined, some cases required biological therapy.
REFERENCES:
[1] Irazoque F, et al. Epidemiology, etiology and classification. Reumatol Clin. 2009;5:2-5.
[2] Johnson C, et al. Clinical and pathologic differences in interstitial lung disease based on antisynthetase antibody type. Respir Med. 2014; 108(10):1542-8.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1427

AB0093

CLINICAL AND SEROLOGICAL CHARACTERISTICS OF SYSTEMIC SCLEROSIS: EXPERIENCE FROM A TERTIARY CARE CENTER IN PAKISTAN

S. Asif[1,2,2], M. Haroon[1], A. Khan2, M. Faiq[1]. [1]*Fatima Memorial Hospital, Lahore, Rheumatology, Lahore, Pakistan*; [1]*Fatima Memorial Hospital, Lahore, Rheumatology, Lahore, Pakistan*

Background: Systemic sclerosis (SS) is less studied Connective tissue disease in our population. It is characterized by different manifestations which if left undiagnosed and untreated lead to serious complications. The hallmark of this disease is fibrosis of various organs including skin and also involving pulmonary, gastrointestinal and cardiovascular system. We aim to evaluate the clinical and serological characteristics of SS in our population. In addition, we evaluated the prevalence of Fibromyalgia and Depression in patients with SS.
Objectives: We aimed to determine Clinical and Serological Characteristics of Systemic Sclerosis visiting our department of Rheumatology, Fatima Memorial hospital, Lahore.
Methods: It is a cross-sectional study of 38 patients visiting outdoor and indoor in Rheumatology department of Fatima Memorial Hospital from September 2019 to January 2020. All systemic sclerosis patients with age 16 years or above were included in this study. After taking informed consent, we filled the performas to record all the required information. We evaluated the clinical, serological and radiological features of Systemic Sclerosis.
Results: A total of 38 patients were included in the study with mean age was 34.47 ± 1.53 years. Female gender comprised of 32(84.2%), with male to female ratio of 1:5.3. Thirty-four (89.5%) had developed Raynaud phenomenon and sclerodactyly was found in 34(89.5%), digital ulcers in 25 (65.8%), and tendon friction rub in 12 (31.6%) patients. Skin tightness proximal to elbow was present in 9 (23.7%). Microstomia (decreased mouth opening) was present in 32(84.2%) patients. Twenty-eight (73.7%) patients had arthritis.Respiratory symptoms comprised of shortness of breath in 36(94.7%), palpitation in 24 (63.2%) and chest

pain in 7(18.4%). Gastrointestinal (GI) symptoms comprised of regurgitation in 31 (81.5%) and dysphagia in 14 (36.8%). Interstitial lung disease was present in 30 (78.9%) patients, with higher prevalence in diffuse scleroderma (100%) than in limited scleroderma (70%) (p=0.01). Pulmonary hypertension was present in 18 patients, with significantly higher prevalence in diffuse disease (57.1%), that was secondary to interstitial lung disease and in limited disease it was found in (11.8%) (p<0.01). Thirty (78.9%) patients were found to have restricted disease on pulmonary function tests.

Obstetric history showed a higher prevalence of primary infertility in at least 6 (15.8%) patients, with significantly higher prevalence in limited systemic sclerosis disease as compared to diffuse disease (23.5% vs 9.5%, and p=0.05). Fibromyalgia diagnosed as per ACR criteria was present in 7 (18.4%) patients, and depression assessed by Hospital Anxiety and depression (HADS) score was present in 10 (26.3%) patients.

Anti nucleic acid antibody (ANA) was found positive in 30 (78.9%) patients. Anti Scl-70 antibodies were in 24 (63.2%) patients, with significant association with diffuse disease (85% vs 35.3% and p<0.01), while anti centromere antibodies were present in 20 (52.6%) patients; significantly higher in limited disease (94.2% vs 19.0%, and p<0.01).

Conclusion: Scleroderma is a very important, autoimmune multisystem disease. It has female preponderence. Raynaud phenomenon is the most initial clinical feature followed by other manifestations of variable course and disease severity. Interstitial lung disease and pulmonary hypertension were the most important complication found in our patients which has poor prognosis. So, It is imperative to early diagnose and treat the disease manifesations to prevent future complications.

Keywords: Scleroderma, Systemic sclerosis.

DISCLOSURE OF INTEREST:

Sadia Asif: None declared, Muhammad Haroon: None declared, Dr Asadullah Khan: None declared, Dr. Muhammad Faiq: None declareDOI: 10.1136/annrheumdis-2021-eular.1635

AB0094 INCREASE OF ENDOTHELIAL PROGENITOR CELLS IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

V. Pulito-Cueto[1], S. Remuzgo Martinez[1], F. Genre[1], B. Atienza-Mateo[1,2,3], V. M. Mora-Cuesta[1,4], D. Iturbe-Fernández[1,4], L. Lera-Gómez[1], R. Pérez-Fernández[1], D. Prieto-Peña[1,3], V. Portilla[1,3], R. Blanco[1,3], A. Corrales[1,3], J. M. Cifrián-Martínez[1,4,5], R. López-Mejías[1], M. A. González-Gay[1,3,5,6]. *[1]IDIVAL, Research Group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, Santander, Spain*; *[2]Hospital Universitario Marqués de Valdecilla, `López Albo´ Post-Residency Programme, Santander, Spain*; *[3]Hospital Universitario Marqués de Valdecilla, Department of Rheumatology, Santander, Spain*; *[4]Hospital Universitario Marqués de Valdecilla, Department of Pneumology, Santander, Spain*; *[5]Universidad de Cantabria, School of Medicine, Santander, Spain*; *[6]Faculty of Health Sciences, University of the Witwatersrand, Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Johannesburg, South Africa*

Background: Endothelial progenitor cells (EPC), involved in vasculogenesis and endothelial tissue repair, have been described as relevant players in vascular and connective tissue diseases [1-2]. In this regard, a previous study of our group disclosed that the degree of EPC frequency may help to identify the presence of interstitial lung disease (ILD) in rheumatoid arthritis patients [3]. Given that ILD is the main cause of mortality in patients with systemic sclerosis (SSc) [1, 4-6], the understanding of the role of EPC in the mechanism of SSc-ILD$^+$ vasculopathy is crucial.

Objectives: To assess the potential role of EPC on vascular dysfunction associated with the presence of ILD in patients with SSc.

Methods: Peripheral venous blood was collected from a total of 39 patients with SSc, 20 with ILD (SSc-ILD$^+$) and 19 without ILD (SSc-ILD$^-$). All subjects were recruited from the Rheumatology and Pneumology departments of Hospital Universitario Marqués de Valdecilla, Santander, Spain. Quantification of EPC was analyzed by flow cytometry. EPC were considered as CD34$^+$, CD45^{Low}, CD309$^+$ and CD133$^+$.

Results: Statistically significant differences in EPC frequency between patients with SSc-ILD$^+$ and patients with SSc-ILD$^-$ were disclosed. Specifically, an increase of EPC frequency was observed in SSc-ILD$^+$ patients when compared to patients with SSc-ILD$^-$ (mean ± standard deviation: 0.033 ± 0.012 *versus* 0.021 ± 0.017, respectively, p=0.012).

Conclusion: Our results suggest a potential role of EPC on vascular damage associated with the manifestation of ILD in patients with SSc.

REFERENCES:

[1] Eur J Rheumatol 2020;7(Suppl 3):S139-S146.
[2] Arthritis Rheum 2009;60(11):3168-79.
[3] J Clin Med 2020;9(12):4098.
[4] Ann Rheum Dis 2007;66(7):940-4.
[5] Rheumatology (Oxford) 2010;49(12):2375-80.
[6] Eur Respir Rev 2015;24(135):102-14.

Acknowledgements: Personal funds, VP-C: PREVAL18/01 (IDIVAL); SR-M: RD16/0012/0009 (ISCIII-ERDF); LL-G: INNVAL20/06 (IDIVAL); RP-F: START PROJECT (FOREUM); RL-M: Miguel Servet type I CP16/00033 (ISCIII-ESF).

Disclosure of Interests: Verónica Pulito-Cueto: None declared, Sara Remuzgo Martinez: None declared, Fernanda Genre: None declared, Belén Atienza-Mateo: None declared, Victor Manuel Mora-Cuesta: None declared, David Iturbe-Fernández: None declared, Leticia Lera-Gómez: None declared, Raquel Pérez-Fernández: None declared, Diana Prieto-Peña: None declared, Virginia Portilla: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD and Roche, Alfonso Corrales: None declared, Jose Manuel Cifrián-Martínez: None declared, Raquel López-Mejías: None declared, Miguel A González-Gay Speakers bureau: Pfizer, Abbvie, MSD, Grant/research support from: Pfizer, Abbvie, MSD

DOI: 10.1136/annrheumdis-2021-eular.2350

AB0095 EXPRESSION AND PATHOGENIC ROLES OF INTEGRIN FAMILY GENE IN SYSTEMIC SCLEROSIS

D. Xu[1], T. Li[1], R. Mu[1]. *[1]Peking University Third Hopsital, Department of Rheumatology and Immunology, Beijing, China*

Background: Emerging evidence have shown that some integrin members are associated with inflammation and fibrosis in systemic sclerosis (SSc) patients[1-2]. However, the expression patterns and pathogenic significance of the whole integrin family in SSc are still unclear.

Objectives: This study aimed at evaluating the integrin family gene expression in skin lesion from SSc patients and exploring its potential pathogenic mechanism.

Methods: We utilized the public datasets of SSc skin tissue from Gene Expression Omnibus (GEO) database to analyze the expression and clinical significance of integrin family genes in SSc. In addition, functional enrichment and pathway analysis were also conducted.

Results: Compared with healthy controls, ITGA5, ITGA7, ITGA8, ITGB2, ITGB5, ITGAE and ITGB3BP were abnormally overexpressed in the skin of SSc. Further analysis indicated that ITGA5, ITGA7, ITGA8, ITGB2 and ITGB5 were positively correlated with modified Rodnan skin thickness score (mRSS), while ITGAE and ITGB3BP were negatively correlated with mRSS in SSc. Increased ITGB5 expression was associated with positive of anti-centromere antibody (ACA). Functional enrichment and pathway analysis showed that integrin members had multiple functions in SSc. Among them, ITGA5, ITGB2 and ITGB5 might synergistically promote SSc through affecting extracellular matrix (ECM) turn over, ECM-receptor interaction, focal adhesion and leukocyte trans-endothelial migration. ITGA5 and ITGB5 also affected angiogenesis and endothelial cell function. In addition, ITGA5 was uniquely enriched for actin organization, ITGB5 was uniquely enriched for TGF-β signaling, and ITGB2 was uniquely associated with immune cells activation.

Conclusion: Our results implied that integrins, especially ITGA5, ITGB5, ITGB2 participated in the process of inflammation, vasculopathy and fibrosis in SSc. Together, they might render important therapeutic targets for SSc.

REFERENCES:

[1] Brown M, O'Reilly S. The immunopathogenesis of fibrosis in systemic sclerosis. Clin Exp Immunol. 2019;195(3):310-321.
[2] Gerber, E.E., et al., Integrin-modulating therapy prevents fibrosis and autoimmunity in mouse models of scleroderma. Nature, 2013. 503(7474): p. 126-30.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3646

Vasculitis - aetiology, pathogenesis and animal models

AB0096 IGA VASCULITIS AND IGA NEPHROPATHY SHARE A SIMILAR IL17A ASSOCIATION PATTERN

D. Prieto-Peña[1], F. Genre[1], S. Remuzgo Martinez[1], V. Pulito-Cueto[1], B. Atienza-Mateo[1,2], B. Sevilla[3], J. Llorca[4], N. Ortego[5], L. Lera-Gómez[1], M. Leonardo[6], A. Peñalba[6], L. Martín-Penagos[7], J. A. Miranda-Filloy[8], J. Narváez[9], L. Caminal Montero[10], P. Collado[11], A. Fernandez-Nebro[12], G. Díaz-Cordoves[12], S. Cigarrán[13], J. Calviño[14], C. Cobelo[14], J. Sanchez Perez[15], D. De Argila[15], E. Rubio-Romero[16], M. Leon Luque[16], J. M. Blanco-Madrigal[17], E. Galindez[17], J. Martin Ibanez[18], S. Castañeda[19], R. Blanco[1], M. A. González-Gay[1,20,21], R. López-Mejías[1]. *[1]Research Group on Genetic Epidemiology and*

Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain; *[2]López Albo´ Post-Residency Programme, Hospital Universitario Marqués de Valdecilla, Santander, Spain*; *[3]Hospital Universitario San Cecilio, Division of Pediatrics, Granada, Spain*; *[4]Department of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Santander, Spain*; *[5]Hospital Universitario San Cecilio, Systemic Autoimmune Diseases Unit, Granada, Spain*; *[6]Hospital Universitario Marqués de Valdecilla, Division of Pediatrics, Santander, Spain*; *[7]Hospital Universitario Marqués de Valdecilla, Division of Nephrology, Santander, Spain*; *[8]Hospital Universitario Lucus Augusti, Division of Rheumatology, Lugo, Spain*; *[9]Hospital Universitario de Bellvitge, Division of Rheumatology, Barcelona, Spain*; *[10]Hospital Universitario Central de Asturias, Division of Rheumatology, Oviedo, Spain*; *[11]Hospital Universitario Severo Ochoa, Division of Rheumatology, Madrid, Spain*; *[12]Hospital Regional Universitario Carlos Haya, Division of Rheumatology, Málaga, Spain*; *[13]Hospital da Costa Burela, Division of Nephrology, Lugo, Spain*; *[14]Hospital Universitario Lucus Augusti, Division of Nephrology, Lugo, Spain*; *[15]Hospital Universitario de La Princesa, Dermatology Department, Madrid, Spain*; *[16]Hospital Universitario Virgen del Rocío, Division of Rheumatology, Sevilla, Spain*; *[17]Hospital Universitario de Basurto, Division of Rheumatology, Bilbao, Spain*; *[18]Instituto de Parasitología y Biomedicina 'López-Neyra', CSIC, PTS Granada, Granada, Spain*; *[19]Hospital Universitario de La Princesa, IIS-Princesa, Division of Rheumatology, Madrid, Spain*; *[20]University of Cantabria, School of Medicine, Santander, Spain*; *[21]University of the Witwatersrand, Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, Johannesburg, South Africa*

Background: IgA vasculitis (IgAV) and IgA nephropathy (IgAN) are inflammatory conditions that share pathogenic and molecular mechanisms [1] and may represent different outcomes of a continuous spectrum of disease [2]. *Interleukin (IL)17A* has been identified as a common genetic risk *locus* for several immune-mediated diseases [3, 4].

Objectives: To determine whether IgAV and IgAN exhibit a different *IL17A* association pattern.

Methods: Five *IL17A* tag polymorphisms (rs4711998, rs8193036, rs3819024, rs2275913 and rs7747909) were genotyped in 388 Caucasian patients with IgAV, 99 patients with IgAN and 1,003 sex and ethnically matched healthy controls.

Results: No statistically significant differences between patients with IgAV and healthy controls and between patients with IgAN and healthy controls were observed when each *IL17A* genetic variant was analyzed independently (Table 1). Similarly, IgAV patients exhibited similar genotype and allele *IL17A* frequencies than those with IgAN (Table 1). Moreover, no genotype or allele differences between IgAV patients who developed nephritis and patients with IgAN were detected. Furthermore, haplotype frequencies were similar in patients with IgAV, IgAV and nephritis and those with IgAN.

Table 1. Genotype and allele frequencies of *IL17A* gene in patients with IgA vasculitis, patients with IgA nephropathy and healthy controls.

Polymorphism	Change	Data set	1/1	1/2	2/2	1	2
rs4711998	G/A	IgAV	53.4 (207)	38.9 (151)	7.7 (30)	72.8 (565)	27.2 (211)
		IgAN	49.0 (48)	42.9 (42)	8.2 (8)	70.4 (138)	29.6 (58)
		Controls	52.7 (529)	41.2 (413)	6.1 (61)	73.3 (1471)	26.7 (535)
rs8193036	T/C	IgAV	57.0 (221)	38.4 (149)	4.6 (18)	76.2 (591)	23.8 (185)
		IgAN	64.3 (63)	31.6 (31)	4.1 (4)	80.1 (157)	19.9 (39)
		Controls	60.3 (605)	35.2 (353)	4.5 (45)	77.9 (1563)	22.1 (443)
rs3819024	A/G	IgAV	44.1 (171)	43.3 (168)	12.6 (49)	65.7 (510)	34.3 (266)
		IgAN	39.4 (39)	54.5 (54)	6.1 (6)	66.7 (132)	33.3 (66)
		Controls	45.6 (457)	44.6 (447)	9.9 (99)	67.8 (1361)	32.2 (645)
rs2275913	G/A	IgAV	44.6 (172)	43.3 (167)	12.2 (47)	66.2 (511)	33.8 (261)
		IgAN	39.8 (39)	53.1 (52)	7.1 (7)	66.3 (130)	33.7 (66)
		Controls	44.8 (449)	44.2 (443)	11.1 (111)	66.8 (1341)	33.2 (665)
rs7747909	G/A	IgAV	53.9 (209)	39.4 (153)	6.7 (26)	73.6 (571)	26.4 (205)
		IgAN	41.1 (39)	54.7 (52)	4.2 (4)	68.4 (130)	31.6 (60)
		Controls	53.0 (532)	39.4 (395)	7.6 (76)	72.7 (1459)	27.3 (547)

Conclusion: Our results revealed that IgAV and IgAN share a similar *IL17A* association pattern.

REFERENCES:

[1] N Engl J Med 2013;368:2402-14.
[2] Am J Kidney Dis 1988;12:373-7.
[3] Ann Rheum Dis 2014;73:1742-5.
[4] Mediators Inflamm 2018;2018:1395823.

Acknowledgements: This study was supported by European Union FEDER funds and "Fondo de Investigaciones Sanitarias" (grant PI18/00042) from 'Instituto de Salud Carlos III' (ISCIII, Health Ministry, Spain). DP-P is a recipient of a Río Hortega programme fellowship from the ISCIII, co-funded by the European Social Fund (ESF, `Investing in your future´) [grant number CM20/00006]; SR-M is supported by funds of the RETICS Program co-funded by the European Regional Development Fund (ERDF) [grant number RD16/0012/0009]; VP-C is supported by a pre-doctoral grant from IDIVAL [grant number PREVAL 18/01]; BA-M is a recipient of a `López Albo´ Post-Residency Programme funded by Servicio Cántabro de Salud; LL-G is supported by funds of IDIVAL [grant number INNVAL20/06]; RL-M is a recipient of a Miguel Servet type I programme fellowship from the ISCIII, co-funded by the European Social Fund (ESF, `Investing in your future´) [grant number CP16/00033].

Disclosure of Interests: Diana Prieto-Peña: None declared, Fernanda Genre: None declared, Sara Remuzgo Martinez: None declared, Verónica Pulito-Cueto: None declared, Belén Atienza-Mateo: None declared, Belén Sevilla: None declared, Javier Llorca: None declared, Norberto Ortego: None declared, Leticia Lera-Gómez: None declared, Maite Leonardo: None declared, Ana Peñalba: None declared, Luis Martín-Penagos: None declared, Jose Alberto Miranda-Filloy: None declared, J. Narváez: None declared, LUIS CAMINAL MONTERO: None declared, PAZ COLLADO: None declared, Antonio Fernandez-Nebro: None declared, Gisela Díaz-Cordoves: None declared, Secundino Cigarrán: None declared, Jesús Calviño: None declared, Carmen Cobelo: None declared, Javier Sanchez Perez: None declared, Diego de Argila: None declared, Esteban Rubio-Romero: None declared, MANUEL LEON LUQUE: None declared, Juan María Blanco-Madrigal: None declared, E. Galindez: None declared, Javier Martin Ibanez: None declared, Santos Castañeda: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD and Roche, Miguel A González-Gay Speakers bureau: Pfizer, Abbvie, MSD, Grant/research support from: Pfizer, Abbvie, MSD, Raquel López-Mejías: None declared

DOI: 10.1136/annrheumdis-2021-eular.766

AB0097

DIAGNOSTIC ACCURACY OF SERUM MARKERS IN LARGE VESSEL VASCULITIS AND CORRELATION WITH PET IMAGING

R. Bilici Salman[1], H. Satış2, A. Avanoglu Guler3, H. Karadeniz3, H. Küçük[1], S. Haznedaroglu[1], A. Tufan[1], B. Goker[1], U. O. Akdemir[4], L. O. Atay[4], H. Paşaoğlu[5], M. A. Ozturk[1]. *[1]Gazi University School of Medicine, Rheumatology, Ankara, Turkey*; *[1]Gazi University School of Medicine, Rheumatology, Ankara, Turkey*; *[1]Gazi University School of Medicine, Rheumatology, Ankara, Turkey*; *[4]Gazi University School of Medicine, Nuclear Medicine, Ankara, Turkey*; *[5]Gazi University School of Medicine, Biochemistry, Ankara, Turkey*

Background: The onset of symptoms in large-vessel vasculitis (LVV) tends to be subacute, which often leads to a delay in diagnosis, during which time vascular disease may start and progress to become symptomatic. PET/CT has been recognised since the 2003s as a promising tool in evaluating of LVV. There is no gold standard diagnostic laboratory tests for this patient group, novel markers for active LVV is needed.

Objectives: to investigate the association between vascular inflammation, as detected by PET imaging and interleukin-6 (IL-6), pentraxin3 (PTX3), and B-cell-activating-factor (BAFF) in subjects with LVV.

Methods: The study included 67 patients patients with newly diagnosed GCA (n= 27) or TA (n=9) and healthy control (n= 31) who had been referred to the Rheumatology Unit at Gazi University, between December 2017 and August 2020. PET images obtained from an 29 patients (22 with GCA and 7 with TA) who had not received any corticosteroid treatment prior to PET imaging and blood sampling. IL-6, PTX3, and BAFF levels were determined quantitatively by enzyme-linked immunosorbent assay (ELISA) kits.

Results: 36 patients with LVV (20 females,16 males; age 64,5±16,6) and 31 HC (14 females,17 males; age37,1±9,6) were analysed. Serum levels of IL-6,PTX3, BAFF, ESR and CRP are increased in patients with newly diagnosed LVV compared with those in control subjects. In a ROC analysis, serum IL-6 provided excellent discrimination of newly diagnosed LVV patients from HC, as indicated by AUCs>0.90. Serum BAFF also accurately distinguished newly diagnosed LVV patients from HC with AUCs>0.80. Serum PTX3 did not provide an AUC>0.80. In this study, we correlate vascular inflammation, as detected by PET imaging in newly diagnosed LVV patients, with the ESR, CRP. PTX3, IL-6 and BAFF. As a result, none of these markers has been associated with vascular inflammation as measured using PET.

Conclusion: In conclusion, our study shows that serum levels of PTX3, IL-6 and BAFF are increased in most LVV patients. The diagnostic value of BAFF and IL-6, both separately and in combination, should be further evaluated in larger cohorts of LVV patients, as well as in patients with infections or other inflammatory conditions. However, none of these markers has been associated with vascular inflammation as measured using PET.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3719

AB0098 **ASSOCIATED FACTORS IN ONE-YEAR MORTALITY IN PATIENTS WITH SMALL VESSEL SYSTEMIC VASCULITIS**

E. M. Escudero Tepale[1], M. A. Saavedra[1], D. Miranda[1], Z. Castro[1], M. J. R. Arriga Torres[2]. [1]*Hospital La Raza Puerta 4, Reumatología, Ciudad de México, Mexico*; [2]*Hospital De Cardiologia Hospital siglo XXI, Cardiología, Mexico City, Mexico*

Background: The highest mortality rates in patients with small vessel systemic vasculitis occur within the first year after the diagnosis, however associated factors have been scarcely studied in our population.
Objectives: To identify mortality associated factors at the time of diagnosis in patients with small vessel systemic vasculitis.
Methods: Retrospective cohort (2009-2020) involving 81 patients diagnosed with systemic small vessel vasculitis. Demographic, clinical and biochemical parameters were studied as potential factors associated with one-year mortality.
Results: Of the total of patients (n=81), 36 (44.4%) had generalized granulomatosis with polyangiitis, 32 (39.5%) had localized granulomatosis with polyangiitis and 5 (6.2%) had early systemic granulomatosis with polyangiitis, 7 (8.6%) had microscopic polyangiitis and 1 (1.25%) had eosinophilic granulomatosis with polyangiitis. Twenty-two deaths (27%) were observed, 14 of them (63.6%) happened within the first year of diagnosis. The leading cause of death was infection (64%). Patients who died within the first year of diagnosis had a higher frequency of hypoalbuminemia (p=0.05) and also presented hemoglobin lower than 10.8 g/dL (p=0.035) in comparison with those who died after the first year of diagnosis. Remission induction treatment did not differ between both groups.
Conclusion: Our study suggests that hypoalbuminemia and anemia are factors associated with a higher mortality within the first year after the diagnosis in patients with systemic small vessel vasculitis which contrast with previously reported data. The study design and the reduced number of patients are two major limitations of the study.
REFERENCES:
[1] Flossmann O, Berden A, Groot K, et al. Long-term patient survival in ANCA-associated vasculitis. Ann Rheum Dis. 2011;70:488-94.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4207

Rheumatoid arthritis - prognosis, predictors and outcome

AB0099 **IN VIVO BONE MICROARCHITECTURE ANALYSIS IN A PSORIATIC ARTHRITIC PATIENT BEFORE AND AFTER ANTI-TNFA TREATMENT**

E. Soldati[1,2,3], L. Escoffier[4], S. Gabrie[5], J. P. Mattei[1,4], S. Camilleri[5], D. Bendahan[1], S. Guis[1,4]. [1]*AixMarseille University, CNRS, CRMBM-CEMEREM, UMR CNRS 7339, Marseille, France*; [2]*Aix-Marseille University, CNRS, IUSTI, UMR CNRS 7343, Marseille, France*; [3]*Aix-Marseille University, CNRS, ISM, UMR CNRS 7287, Marseille, France*; [4]*Aix-Marseille University, Service de Rhumatologie, AP-HM, Marseille, France*; [5]*Institut Fresnel, Aix-Marseille Université, Service de Médecine Nucléaire, AP-HM, CNRS UMR 7249, Marseille, France*

Background: In psoriatic arthritis (PA), a systemic inflammatory phenomenon, mainly mediated by TNFα, is characterized by a bone loss due to osteoclastic stimulation. Anti-TNFα treatment should inhibit this phenomenon having a role on systemic bone loss. Ultra-high field MRI (UHF MRI) may be a tool of choice for the quantification of bone microarchitecture (BM) *in vivo*.
Objectives: The purpose of the present study was to quantify BM using UHF MRI in a PA patient and to follow up changes related to anti-TNFα treatment.
Methods: An 18 years-old untreated PA patient with knee arthritis and 7 gender-matched healthy controls [21.6±0.8 years] were scanned using a gradient echo sequence at UHF MRI (TR/TE = 15/4.36ms). After a year of Adalimumab treatment, the patient underwent a second UHF MRI. BM analysis was performed on sagittal planes in regions corresponding to tendon insertion: proximal and distal patellar, and posterior tibial. A PET-FNa imaging was also performed before and after treatment. BM was characterized using the bone volume fraction (BVF), the trabecular thickness (TbTh) and the spacing (TbSp) and number of trabeculae (TbN). Student T-test was used for the statistical analysis and a p-value < 0.01 was considered as significative.
Results: PET-FNa recorded before the treatment illustrated hypermetabolic areas which resumed after the treatment while the patient was in remission. The BM parameters are shown in figure 1. The BM parameters quantified before the treatment were very different as compared to controls. BVF was significatively lower (-33±23%), TbSp and TbN were significatively distinct (-27±3% and +27±9%) for all ROIs but proximal patellar, while TbTh was in the normal range (-2±2%). After 1 year of treatment, BM parameters were significantly improved. BVF was no longer different than controls (-8±6%). Similarly, TbSp and TbN were in the normal range (+13±12% and -15±10%) for all ROIs but posterior tibial. TbTh (-5±3%) was only significantly decreased for the distal patella.

		Healthy	P. before treatment	P. after treatment
Proximal Patella	BVF	0.393±0.008	0.339±0.018 *	0.401±0.010
	TbTh	0.254±0.013	0.254±0.022	0.266±0.014
	TbSp	0.364±0.032	0.477±0.058	0.365±0.008
	TbN	1.550±0.074	1.301±0.136	1.493±0.073
Distal Patella	BVF	0.355±0.035	0.222±0.064 *	0.328±0.027
	TbTh	0.261±0.010	0.250±0.015	0.285±0.004 *
	TbSp	0.469±0.117	0.651±0.057 *	0.532±0.064
	TbN	1.366±0.114	0.994±0.090 *	1.116±0.083
Posterior Tibia	BVF	0.381±0.009	0.307±0.016 *	0.335±0.018
	TbTh	0.258±0.008	0.260±0.009	0.267±0.012
	TbSp	0.426±0.060	0.594±0.012 *	0.570±0.016 *
	TbN	1.468±0.073	1.185±0.047 *	1.241±0.029 *

Table 1. Data are presented as mean ± SD. "P." refers as patient. BVF: Bone volume fraction, TbTh: Trabecular Thickness, TbSp: Trabecular Space, TbN: Trabecular number. * indicates a statistically significant difference (p < 0.01) with the Healthy reference values.
Conclusion: Our results illustrated knee microstructure alterations in a PA patient and a normalization after a year of treatment. The abnormalities initially observed were not only localized in the hypermetabolic regions identified by PET-FNa, suggesting that the bone loss was global and not related to inflammatory sites.
Using UHF MRI, we highlighted and quantified *in vivo* BM anomalies in a patient with an inflammatory rheumatism together with the reversibility after one year of treatment.
Acknowledgements: All the authors declare no conflict of interest.
ES has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skodowska-Curie grant agreement No713750. Also, it has been carried out with the financial support of the Regional Council of Provence- Alpes-Côte d'Azur and with the financial support of the A*MIDEX (n° ANR- 11-IDEX-0001-02), funded by the "Investissements d'Avenir" project funded by the French Government, managed by the French National Research Agency (ANR). edgements to declare.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.47

AB0100 **EVALUATION OF PGA LEVEL FOR CLINICAL REMISSION WITH BOOLEAN CRITERIA, 10MM OR 20MM?**

I. Yoshii[1]. [1]*Yoshii Hospital, Rheumatology and Musculoskeletal Medicine, Shimanto City, Japan*

Background: Patient's global assessment (PGA) is one important component of Boolean composite criteria for remission in treat with rheumatoid arthritis (RA). However, PGA no more than 10mm is sometimes obstacle to attain clinical remission. In recent few years, one opinion that PGA no more than 20mm may be comparable as no more than 10mm.
Objectives: The aim of this study is to analyze how difference of these PGA level affect disease activity and daily activities in living, and evaluate which is optimal for the remission with Boolean remission criteria from real world setting.
Methods: RA patients who were followed up for more than three years in the institute were picked up in the study. Each patient was monitored with tenderness joint count (TJC), swollen joint count (SJC), PGA, evaluator's global assessment (EGA), serum C-reactive protein level (CRP), calculated disease activity score with simplified disease activity index(SDAI), Health Assessment Questionnaire Disability Index (HAQ-DI), and pain score using visual analog scale (PS-VAS) every consulted time from the first encounter (Baseline). Patients were classified according to achievement of Boolean remission criteria. Group 1: a patient group who attained Boolean remission wih TJC≦1, SJC≦1, CRP≦1mg/dl, and PGA≦1 (G-1), Group 2: a patient group who could not attained the Boolean remission used in the G-1 evaluation, but could attained another Boolean remission with TJC≦1, SJC≦1, CRP≦1mg/dl, and PGA≦2 (G-2), and Group 3: a patient group who could not attain Boolean remission for neither criterion.
Mean values of measured parameters at Baseline and after the Baseline were compared statistically with Student T-test. Mean values of the same parameters in the G-1 and G-2 at the time of attain Boolean remission for each criteria, mean values of each of these parameters thereafter, and changes of these parameters were compared statistically with Student T-test.
Results: A total of 438 patients 385 in the G-1 group, 16 in the G-2 group, and 37 in the G-3 group, were recruited. In parameters at Baseline, level of TJC, SJC, PGA, EGA, SDAI, and HAQ-DI in the G-1 was significantly lower than in the G-3, whereas no significant differences in any parameters demonstrated between in the G-2 and G-3. Level of HAQ-DI, and PS-VAS after Baseline in the G-1 was

lower than in the G-3, whereas no significant difference of these parameters after Baseline demonstrated between in the G-2 and G-3. TJC, SJC, PGA, and EGA demonstrated significant less level in the G-1 than in the other two groups. The mean SDAI score at the time of first achievement of Boolean remission in the G-1 and G-2 were 1.08 and 2.57, respectively. The mean value of SDAI score after remission in the G-1 and G-2 were 3.35 and 6.44, respectively. These values and PS-VAS including change of the SDAI score demonstrated significant difference between the two groups (p<0.01), whereas HAQ-DI in the two groups demonstrated no significant difference.

Conclusion: These results suggested that setting PGA as no more than 10mm should be reasonable for the evaluation of clinical remission with the Boolean criteria.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.288

AB0101 THE IMPACT OF TIME SPAN TO ACHIEVE BOOLEAN REMISSION FOR MAINTAINING DISEASE ACTIVITY AFTER ACQUISITION IN RHEUMATOID ARTHRITIS PATIENT

I. Yoshii[1]. [1]*Yoshii Hospital, Rheumatology and Musculoskeletal Medicine, Shimanto City, Japan*

Background: Boolean remission criteria is one most popular and stringent criteria in treating patient with rheumatoid arthritis (RA), because it may guarantees a stable clinical course after attaining remission.

Objectives: Impact of time span from initiation to achieving Boolean remission on maintaining disease activity, daily activities, and quality of life after attaining Boolean remission was investigated from daily clinical practice data.

Methods: 685 patients with RA since August 2010 under the T2T strategy were treated. They were monitored for their TJC, SJC, PGA, EGA, CRP, and disease activity indices such as CDAI, SDAI, DAS28, and Boolean criteria at every visit. HAQ-DI score, pain score using visual analog scale (PS-VAS), and EQ-5D were also monitored, and the quality of life score (QOLS) calculated from EQ-5D was determined at every visit from the time of diagnosis (baseline).

Of 685 patients, 465 patients had achieved Boolean remission >1 times, and were consecutively followed up for >3 years. These patients were enrolled in the study. Time span from the first visit to first Boolean remission was calculated. The relationship between the time span and each of background parameters, and the relationship between the time span and each of the mean values of the SDAI score, HAQ score, PS-VAS, SHS, and QOLS at the first Boolean remission and thereafter was evaluated statistically.

Patients were subsequently divided into the G ≤ 6 and G > 6 groups based on the achievement of first Boolean remission within two groups: time span G ≤ 6 months and G > 6 months. The two groups were compared with regard to the SDAI score, HAQ score, PS-VAS, SHS, and QOLS at first visit and at the time of first Boolean remission, and the mean values of these parameters after remission were evaluated statistically. Moreover, changes of these parameters and the mean Boolean remission rate after the first remission, and SDAI remission rate at the first Boolean remission to thereafter were compared between the two groups statistically.

Results: Out of 465 patients, females comprised 343 (73.7%), and the mean age was 67.8 years (range, from 21–95 years). The mean disease duration at first visit was 6.1 years (range, from 1 months–45 years). The mean follow up length was 88.1 months (range: 36–122 months; median: 85 months) and mean time span from the first visit to the first Boolean remission was 8.1 months. The mean SDAI score, HAQ score, PS-VAS, and the QOLS at first visit were 13.3, 0.467, 33.2, and 0.834, respectively. Among the study parameters, PS-VAS and QOLS were significantly correlated with the time span. For parameters at the first Boolean remission, HAQ-DI score, PS-VAS, and QOLS demonstrated significant correlation with the time span, whereas SDAI, HAQ-DI score, PS-VAS, SHS, and QOLS after the Boolean remission demonstrated significant correlation with the time span.

The comparison between the G ≤ 6 and the G > 6 groups revealed that the disease duration, HAQ score, and PS-VAS at baseline in the G > 6 were significantly higher than that in the G ≤ 6 group, and QOLS in the G ≤ 6 group was significantly higher than that in the G > 6 group at baseline. Similarly, the HAQ score and PS-VAS at the first Boolean remission in the G > 6 group were significantly higher than that in the G ≤ 6 group, whereas QOLS in the G ≤ 6 group demonstrated no significant difference compared with that in the G > 6 group.

The mean value of the SDAI score after the first Boolean remission in the G > 6 group was significantly higher than that in the G ≤ 6 group. Similarly, the SDAI score, HAQ score, and PS-VAS after the first Boolean remission in the G > 6 group were also significantly higher than those in the G ≤ 6 group, and the mean value of the QOLS in the G ≤ 6 group were significantly higher than that in the G > 6 group. The Boolean remission rate and SDAI remission rate after the first Boolean remission were significantly higher in the G ≤ 6 group than those in the G > 6 group.

Conclusion: Attaining Boolean remission ≤ 6 months for RA has significant benefit for more stable disease control, that leads good maintenance of ADL.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.297

AB0102 EVALUATOR'S GLOBAL ASSESSMENT REFLECTS DISEASE ACTIVITY BUT NOT LINEARLY CORRELATES WITH DAILY ACTIVITY OR QUALITY OF LIFE COMPARED TO PATIENT' GLOBAL ASSESSMENT

I. Yoshii[1]. [1]*Yoshii Hopital, Rheumatology and Musculoskeletal Medicine, Shimanto City, Japan*

Background: Evaluator's global assessment (EGA) is the one component of indexed disease activity evaluation assessed by the rheumatologist for treatment of rheumatoid arthritis (RA). It does not included in the Boolean remission criteria nor 28-joints disease activity score (DAS28), however it is widely recognized among rheumatologist as an only comprehensive and objective assessment parameter.

Objectives: The aim of this study is to evaluate how EGA correlates with other components and the influence of EGA on disease activity and daily activity, and quality of life.

Methods: A total of 24,075 times of monitoring out of 683 RA patients who were followed up for more than three consecutive years was performed. Contents of monitoring included tenderness joint count (TJC), swollen joint count (SJC), patient's global assessment (PGA), EGA, C-reactive protein (CRP), and calculated values of DAS28, SDAI, composite index of Boolean evaluation, pain score with visual analog scale (PS-VAS), Health Assessment Questionnaire Disability Index (HAQ-DI), and quality of life score (QOLS) calculated from Euro-QOL questionnaire with 5th dimensions. Each measurement was classified with the EGA score divided by one increment from zero to ten. Mean values of DAS28, CDAI, SDAI, remission rate of these indices and Boolean remission rate, and mean values of PS-VAS, HAQ-DI, and QOLS were statistically evaluated. Results were compared to the results that was analyzed in according to the PGA score substituted with the EGA score.

Moreover, EGA at the time of Boolean remission of the patients who achieved Boolean remission at least once during treating were picked up. Patients were classified according to the EGA level with 0.5 increment from zero. Mean value of TJC, SJC, PGA, EGA, SDAI, Boolean remission rate, HAQ-DI, and PS-VAS after attaining Boolean remission were compared statistically.

Results: Number of measures counted 15424, 2001, 3688, 1731, 664, 293, 144, 88, 29, 2, and 11 for each level of EGA. The EGA score tended to concentrate more in zero to two in comparing to the PGA score. Mean DAS28, CDAI, and SDAI demonstrated significant increase as the EGA level increased, and remission rate of the all indices including Boolean demonstrated significant decrease as the EGA level increases (p<0.01%). CDAI, SDAI, and Boolean remission rate demonstrated zero percent from two. Mean value of PS-VAS and HAQ-DI score demonstrated also significant decrease as the EGA level increases, and QOLS demonstrated significant decrease as the EGA level increases (p<0.01%). However, these tendency showed more irregular compared to that analyzed with the PGA score. Correlation coefficients with regarding to the EGA score was always less than that with regarding to the PGA score.

In the patients who achieved Boolean remission, EGA levels were divided with 294 with zero (G-0) and 118 with 0.5 (G-.5), whereas 71 could not achieve Boolean remission. Average TJC (p<0.05), SJC (p<0.001), EGA (p<0.001), CRP (p<0.05), and SDAI (p<0.01) level in the G-0 group demonstrated significant less than in the G-.5 group, whereas PGA, Boolean remission rate, HAQ-DI, and PS-VAS demonstrated no significant difference in between the two groups.

Conclusion: It is more reliable to estimate daily activity and quality of life from the PGA score than to estimate from the EGA score. EGA correlates with SJC and CRP more strongly than with TJC and CRP. EGA does not reflect HAQ-DI and PS-VAS.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.320

AB0103 THE ACCURACY OF ADMINISTRATIVE HEALTH DATA FOR IDENTIFYING PATIENTS WITH RHEUMATOID ARTHRITIS: A VALIDATION STUDY USING MEDICAL RECORDS IN WESTERN AUSTRALIA

K. Almutairi[1], J. Nossent[1], D. Preen[2], H. Keen[1], K. Roger[3], C. Inderjeeth[1]. [1]*The University of Western Australia, School of Medicine, Perth, Australia*; [2]*University of Western Australia, School of Population and Global Health, Perth, Australia*; [3]*Sir Charles Gairdner Hospital, General Medicine, Perth, Australia*

Background: The use of large administrative health datasets is increasingly important in Rheumatology for disease trends and outcome research (1). We established the West Australian Rheumatic Disease Epidemiological Registry

containing longitudinal health data for over 10000 patients with Rheumatoid Arthritis (RA) in Western Australia (WA). Accuracy of coding for RA is essential to validity of the datasets.

Objectives: Investigate the diagnostic accuracy of International Classification of Diseases (ICD) based discharge codes for RA at WA's largest tertiary hospital.

Methods: Medical records for RA patients randomly selected from the hospital discharge database with ICD 10 codes (M05.00–M06.99) from 2008–2020 were retrospectively reviewed. Rheumatologist reported diagnosis and ACR/EULAR classification were used as gold standards to determine positive predictive value (PPV) with 95% Confidence Interval (CI) for RA primary diagnostic codes.

Results: Medical chart review was completed for 87 patients (mean age 64.7 years, 67% female). Total of 80 (92%) patients had specialist confirmed RA diagnoses, while seven patients (8%) had alternate clinical diagnoses providing a PPV of 93.5% (95%CI: 89.9 to 95.86). Overall, 69 out 87 patients (79.3%) fulfilled ACR/EULAR classification criteria based on RA primary diagnostic codes with a PPV of 80.5% (95%CI: 76.81 to 83.7). A combination of a diagnostic RA code with biologic infusion codes in two or more codes increased the PPV to 97.9%.

Conclusion: Hospital discharge diagnostic codes in WA identify RA patients with a high degree of accuracy. Combining a primary diagnostic code for RA with biological infusion codes can further increase the PPV.

REFERENCES:

[1] Hanly et al. The use of administrative health care databases to identify patients with rheumatoid arthritis. Open Access Rheumatol 2015; 7: 69–75.

Table 1. Accuracy measures of different algorithms for random sample of rheumatoid arthritis (RA) patients with one or more RA codes.

	Rheumatologist-reported diagnosis				ACR/EULAR classification criteria			
Administrative data	SN	SP	PPV	NPV	SN	SP	PPV	NPV
One or more RA primary codes	90%	28.5%	93.5%	7.6%	89.8%	16.6%	80.5%	30%
One or more RA biological infusion codes	25%	71.4%	90.9%	7.7%	20.3%	55.5%	63.6%	15.3%
Two or more RA codes including biological codes	60%	85.7%	97.9%	15.8%	56.5%	44.4%	79.6%	21%

RA=Rheumatoid Arthritis, SN=Sensitivity, SP=Specificity, PPV= Positive predictive value, NPV= Negative predictive value.

Acknowledgements: Khalid Almutairi was supported by an Australian Government research training Program PhD Scholarship at the University of Western Australia.

Disclosure of Interests: Khalid Almutairi: None declared, Johannes Nossent Speakers bureau: Janssen, David Preen: None declared, Helen Keen Speakers bureau: Pfizer Australia, Abbvie Australia, Katrina Roger: None declared, Charles Inderjeeth Speakers bureau: Eli Lilly

DOI: 10.1136/annrheumdis-2021-eular.335

AB0104 CONCORDANCE BETWEEN THE PHYSICIAN'S AND THE PATIENT'S ASSESSMENT OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: RESULTS OF THE AUTODAS-MEAC STUDY AT ONE YEAR

N. Ziade[1,2], S. Al Emadi[3], M. Abu Jbara[4], S. Saad[5,6], L. Kibbi[7], G. Merheb[8,9], H. Badsha[10], G. Harifi[10], E. Alam[11], A. Ayko[12], B. Zorkany[13], A. Daher[14], H. Halabi[15], M. Mashaleh[16], B. Masri[17], J. Messaykeh[18], K. Mroue'[19], N. Salloum[20], T. Arayssi[21] on behalf of AUTODAS-MEAC. [1]*Saint-Joseph University, Rheumatology, Beirut, Lebanon*; [2]*Hotel-Dieu de France, Rheumatology, Beirut, Lebanon*; [3]*Hamad Medical Corporation, Rheumatology, Doha, Qatar*; [4]*Al-Bashir Hospital, Rheumatology, Amman, Jordan*; [5]*Assiut University, Rheumatology, Assiut, Egypt*; [6]*King Hamad University Hospital, Rheumatology, Bahrain, Bahrain*; [7]*Specialized Medical Center, Rheumatology, Riyadh, Saudi Arabia*; [8]*Holy-Spirit University, Rheumatology, Kaslik, Lebanon*; [9]*Notre-Dame des Secours, Rheumatology, Jbeil, Lebanon*; [10]*Dr Humeira Badsha Medical Center, Rheumatology, Dubai, United Arab Emirates*; [11]*Levant Hospital, Rheumatology, Beirut, Lebanon*; [12]*Heartbeat Clinic, Rheumatology, Beirut, Lebanon*; [13]*Cairo University, Rheumatology, Cairo, Egypt*; [14]*Saint-Joseph University, Family Medicine, Beirut, Lebanon*; [15]*King Faisal Specialist Hospital, Rheumatology, Jeddah, Saudi Arabia*; [16]*King Hussein Medical Center, Rheumatology, Amman, Jordan*; [17]*Jordan Hospital, Rheumatology, Amman, Jordan*; [18]*Al Monla Hospital, Rheumatology, Tripoli, Lebanon*; [19]*AL Zahraa Hospital, Rheumatology, Beirut, Lebanon*; [20]*ZClinic, Rheumatology, Beirut, Lebanon*; [21]*Weill Cornell Medicine, Rheumatology, Doha, Qatar*

Background: Involving the patients with rheumatoid arthritis (RA) in the assessment of their disease may increase their adherence to treatment, improve the disease outcomes and facilitate the application of telehealth. We previously reported an excellent concordance between the Disease Activity Score (DAS-28) performed by physicians and patients at the baseline visit of this prospective study (1).

Objectives: To evaluate the persistence of the concordance between the physician' and the patient's assessment of disease activity in RA using DAS-28 after one year.

Methods: At the baseline visit, patients with RA from 7 Middle Eastern Arab Countries (MEAC) were briefed about DAS-28 by their rheumatologist during a routine consultation and given smartphone access to a video in Arabic language explaining the performance of DAS-28. At 3, 6 and 12 months (± 3 months), the patients were asked to self-report DAS-28, blinded to the physician's assessment. Concordance between the continuous DAS-28 at each visit was calculated using paired t-test numerically and the Bland-Altman method graphically. Agreement between physician- and patient-DAS categories (remission, low-, moderate- and high disease activity) was calculated at each visit using weighted kappa for category comparison. Weighted kappa of the different agreements were compared over time using their respective confidence intervals (CIs). Predictive factors of positive concordance between physician and patient-DAS were identified using binary logistic regression.

Results: The study included 428 patients over a period of three years (2018 to 2020). The mean age of participants was 49.8 years, 82.5% were females, 44.3% had a university degree and the mean disease duration was 11.4 years.

At baseline, the average patient-DAS was higher (4.06 (±1.52)) than the physician-DAS (3.97 (±1.52)). The mean difference was -0.09 [95%CI -0.14; -0.04] and most of the pairs were within the limit of agreement in the Bland-Altman graph, indicating a good concordance, particularly in cases of remission.

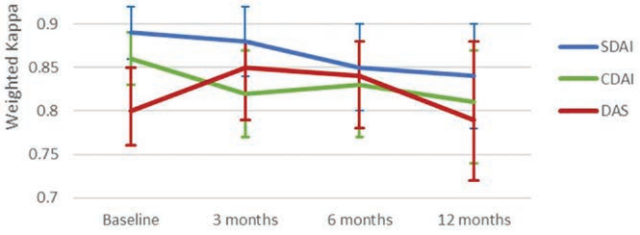
During the study follow-up, 299 patients consulted for visit 2 (69.9% of the total population), 232 for visit 3 (54.2%) and 199 for visit 4 (46.5%). The weighted kappa was 0.80 [95%CI 0.76;0.85] at visit 1 and 0.79 [95%CI 0.72;0.88] at visit 4 (Figure 1 showing kappa for DAS-28, CDAI and SDAI as well). A minor numerical decrease in kappa was observed over time; however, the CIs were overlapping over the four visits and the agreement was considered stable, remaining in the excellent range. At visit 4, a positive concordance between the physician- and the patient-DAS was associated with the profession (lower in blue collar, p=0.001), the educational level (higher in high school and university, p=0.034) and the baseline physician's DAS (higher in high disease activity, p=0.46).

Conclusion: The agreement between the DAS-28 performed by the physician and by the patient was excellent at baseline and remained stable over one year. A positive concordance was associated with the profession, the educational level and the level of disease activity. The present study can help the rheumatologist make informed decisions about the patients who may be suitable for a remote evaluation of their disease activity, that can be of particular interest in the context of the COVID-19 pandemic.

REFERENCES:

[1] Ziade N, Saad S, al Mashaleh M, et al. Perceptions of Patients with Rheumatoid Arthritis about Self-Assessment of Disease Activity after Watching an Educational Video: Qualitative Pilot Results from the Auto-DAS in Middle Eastern Arab Countries Study [abstract]. Arthritis Rheumatol. 2018; 70 (suppl 10).

Figure 1. Agreement betweent physicians and patients in disease activity scoring over time



Acknowledgements: The authors would like to acknowledge the patients for participating in the study and the assistants/ students/ nurses who assisted in the data collection: Dr. Fatima Abdul Majeed Al Hawaj, M. Atef Ahmed, M. Mohammad Alhusamiah, Ms Raquel De Guzman, Ms Lina Razzouk.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.646

AB0105

A SYSTEMATIC REVIEW OF THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE FOR THE DIAGNOSIS AND TREATMENT IN RHEUMATOID ARTHRITIS

D. Abdelhafiz[1], M. Bukhari[2]. [1]*Lancaster, Lancaster Medical School, Lancaster, United Kingdom*; [2]*University Hospitals of Morecambe Bay NHS Trust, Rheumatology, Lancaster, United Kingdom*

Background: Biomarkers are important tools that can be used in the diagnosis and monitoring of rheumatoid arthritis (RA). The multi-biomarker disease activity (MBDA) score has shown a clinical value in the overall management of patients with RA.
Objectives: To systematically explore the role of MBDA score for diagnosis and treatment of RA.
Methods: A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations. Key words used included: 'Rheumatoid Arthritis', 'Biomarkers', 'Diagnosis', 'Treatment', 'Outcome', 'Response to treatment', 'Disease Activity', and 'MBDA' The literature search included papers published in 2020 and in the English language.
Results: This literature search has yielded 5 studies that investigated the impact of MBDA score on the diagnosis, treatment or disease progression of RA and have reported clear and clinically validated diagnostic or therapeutic effects. The first study prospectively investigated 130 patients with RA, and has shown that the MBDA score moderately correlated with disease activity at baseline (r = 0.36 for adjusted MBDA score, r = 0.44 for unadjusted MBDA score) and at 16 weeks follow up (r = 0.20 for adjusted MBDA, r = 0.30 unadjusted MBDA) but did not predict treatment response to methotrexate. There was also moderate correlation between MBDA scores and erythrocyte sedimentation rate (ESR) at baseline (r = 0.54 and 0.59) and week 16 (r = 0.42 and 0.51). The second was a cross-sectional study, which included 104 patients (50% female) and demonstrated that adjusted and unadjusted MBDA score correlated similarly with clinical disease activity. Adjustment for leptin reduced the influence of adiposity, particularly among women but significantly estimated higher disease activity in thin men and women. However, MBDA score predicted disease activity and response to tofacitinib treatment, measured by musculoskeletal ultrasound score (MSUS), in RA patients as demonstrated by the third prospective study that included 25 patients (all $p < 0.05$). Correlation was found between baseline MSUS and MBDA score, and with 12-week changes in clinical disease activity ($r = 0.45–0.62$, $p < 0.05$). Regression analysis showed associations between baseline MBDA score and 6-week (all $p < 0.05$) and 12-week change in change in clinical disease activity ($p = 0.03$). The fourth prospective study which included 92 patients with RA, showed that MBDA could predict response to treatment of methotrexate with or without prednisolone. The improvement was faster in the first month of treatment followed by gradual improvement over the following 6 months. Changes from baseline to 12 months for disease activity and MBDA score showed a significant correlation for methotrexate and prednisolone ($r = 0.57$, $p = 0.002$), methotrexate and placebo ($r = 0.57$, $p = 0.001$) and for all groups ($r = 0.56$, $p < 0.001$). The final prospective study which included 148 patients, showed that MBDA predicted remission in RA and could differentiate between small differences in disease activity (low disease activity vs remission states). Baseline MBDA score discriminated baseline remission, area under the curve (AUC) 0.68-0.75, and intermittent/sustained remission (AUC 0.65-0.74). MBDA also predicted long term remission after one year.
Conclusion: MBDA appears to be a useful tool in day-to-day clinical practice that can be used in the diagnosis, monitoring of treatment and prediction of outcomes of patients with RA. MBDA correlated well with disease activity and response to treatment. It is also a good predictor of long-term disease remission.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.677

AB0106

ASSOCIATED FACTORS FOR PRESENTING WITH MODERATE TO HIGH DISEASE ACTIVITY ON THE FIRST RHEUMATOLOGY VISIT IN AN OUTPATIENT CLINIC-BASED COHORT OF COLOMBIAN RA PATIENTS: A REAL-WORLD CROSS-SECTIONAL STUDY

K. Maldonado-Cañón[1,2], P. Coral Alvarado[2,3], P. A. Mendez Patarroyo[2,3], E. Bermúdez[2], G. Quintana Lopez[1,2,3]on behalf of Reumavance Research Group. [1]*School of Medicine - National University of Colombia, Reumavance Research Group. Internal Medicine Department, Bogotá, Colombia*; [2]*Fundacion Santa Fe de Bogota University Hospital, Reumavance Research Group. Internal Medicine Department, Bogotá, Colombia*; [3] *School of Medicine - Universidad de Los Andes, Reumavance Research Group. Internal Medicine Department, Bogota, Colombia*

Background: Rheumatoid arthritis (RA) is characterized by autoantibody formation and expansion such as the rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPA), and antinuclear antibodies (ANA). Autoantibody identification has been considered as crucial not only for the diagnosis but also for its eventual association with the disease activity, to the extent of playing a pivotal role as a poor prognostic factor among patients[1].
Objectives: Our aim was to assess the eventual association between certain clinical-epidemiological factors and presenting with moderate to high disease activity on the first rheumatology visit in an outpatient clinic-based cohort of Colombian RA patients.
Methods: We conducted a cross-sectional analytic study utilizing the database of an outpatient clinic based in the Rheumatology Department at *Fundación Santa Fe de Bogotá University Hospital*. Data were collected from May 2013 until Sep. 2020 and included age, gender, autoimmune- and non-autoimmune comorbidities, family history of autoimmunity (including RA), smoking and alcoholism personal history, previous DMARD and oral steroid use, nutritional status, disease duration defined as established or early RA (disease duration of ≤1 year before starting a DMARD), autoantibody profile information (RF, ACPA, and ANA), and disease activity, assessed by the DAS28- ESR. Multiple logistic regression with backward selection was performed to build the final fitted model.
Results: Data from a total of 1229 patients were included in the analysis. Our population was primarily female (n=938, 76,3%), the majority had an initial diagnosis of established RA (n=952 (77,5%), and presentation on the first consultation with moderate to high disease activity was seen on 65,2% of the cases (n=801). Being male and having an autoimmune comorbidity were statistically significant associated protective factors whereas strongly positive RF and ACPA levels, positive high ANA titres, and established RA were recognized as risk factors after adjustment for the effects of possible confounders such as age, smoking status, previous DMARD use, and family history of RA. Table 1 provides the complete results obtained from the multiple logistic regression model.

Table 1. Multiple logistic regression analysis's results.

	OR (95% CI)	p-value
Male	**0,52 (0,39 – 0,69)**	**< 0,0001**
Age	0,99 (0,99 – 1)	0,24
Autoimmune Comorbidities	**0,41 (0,21 – 0,80)**	**0,009**
Family History of RA	0,85 (0,61 – 1,14)	0,26
Current Smoking	1,26 (0,78 – 2,07)	0,29
History of Smoking	1,26 (0,81 – 2)	0,30
Previous DMARD use	0,91 (0,70 – 1,18)	0,45
RF strong titers i.e., > 80 U/ml	**1,56 (1,21 – 2,02)**	**0,0007**
ACPA strong titers i.e., > 80 U/ml	**1,59 (1,19 – 2,11)**	**0,0016**
ANA low positive titers i.e., < 1:640 dil.	0,94 (0,72 – 1,12)	0,67
ANA strong titers i.e., > 1:640 dil.	**1,98 (1,23 – 3,27)**	**0,0063**
Disease duration (established RA)	**1,41 (1,05 – 1,90)**	**0,0277**

Bold values indicate statistically significant.

Conclusion: These findings have significant implications for the understanding of the disease activity evaluated on the first contact of a RA patient with a rheumatologist. Our data supports the consideration of being male as a protective factor; however, suggest that autoimmune comorbidities could also condition a lower disease activity for such scenarios, which may be explained by the fact that such patients were referred from- and already being treated by- other practitioners. Additionally, our research provides insights for the consideration of high ANA titers as a potentially poor prognosis factor to be identified as early as on the first visit. ANA's use on daily practice is an intriguing matter which could be usefully explored in further research with distinct methodological approaches.
REFERENCES:
[1] Smolen JS, Landewé RBM, Bijlsma JWJ, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Annals of the Rheumatic Diseases 2020;79:685-699.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.806

AB0107

CHANGES IN EXTRACELLULAR MATRIX BIOMARKER C3M CORRELATE WITH ABATACEPT RESPONSE IN SEROPOSITIVE EARLY RA

S. L. Bridges[1], J. Buckner[2], M. A. Maldonado[3], V. Bykerk[4], N. Ray[5], S. Mukherjee[6], N. Ohtsuka[7]. [1]*Hospital for Special Surgery, Department of Medicine, New York, United States of America*; [2]*Benaroya Research Institute at Virginia Mason, Center for Translational Immunology, Seattle, United States of America*; [3]*Bristol Myers Squibb, Clinical R&D, Immunoscience, Princeton, United States of America*; [4]*Hospital for Special Surgery, Rheumatology, New York, United States of America*; [5]*Bristol Myers Squibb, Global Drug*

Development, Princeton, United States of America; [6]*Bristol Myers Squibb (at the time of analysis), Translational Medicine, Princeton, United States of America*; [7]*Bristol Myers Squibb, Japan Translational Medicine, Research and Development, Tokyo, Japan*

Background: Effective biomarkers are needed to guide RA treatment selection, and the importance of evaluating synovial tissue is increasingly recognised.[1] Markers of extracellular matrix (ECM) turnover (e.g. C3M, a marker of interstitial tissue degradation)[2] may have clinical utility as disease-relevant and surrogate biomarkers of synovial joint pathophysiology.
Objectives: To evaluate baseline (BL) correlations of ECM biomarkers with disease activity and the predictive value of ECM biomarkers in patients (pts) with seropositive early RA in the exploratory head-to-head Early AMPLE study (NCT02557100), and to explore the impact of shared epitope (SE) status.
Methods: Biologic-naive, MTX-inadequate responder adults with early (≤12 months' duration), active, moderate-to-severe RA were enrolled if they were anti-cyclic citrullinated peptide 2+ and RF+. Pts were randomised 1:1 to receive SC abatacept (ABA) 125 mg weekly or SC adalimumab (ADA) 40 mg every 2 weeks (wks) for 24 wks (single-blind period). Linear correlations between levels of ECM serum biomarkers (Nordic Biosciences) and disease activity (DAS28 [CRP], SDAI) at BL and change from BL (CfB) at Wk 24 were assessed in the overall population and by SE status (+/–); early (Wk 4) changes in biomarkers were also assessed.
Results: For SE+ (n=61) and SE– (n=18) pts at BL, mean (SD) DAS28 (CRP) was 5.3 (1.2) and 5.0 (1.0), and SDAI was 35.9 (16.2) and 34.0 (13.8), respectively. At BL in the overall population, significant medium correlations between C1M, C3M and C4M and disease activity were seen (Table 1). Correlations were generally higher in SE+ vs SE– pts, with C1M highly correlated with DAS28 (CRP) in SE+; correlations between C1M, C3M and C4M and disease activity were all significant in SE+ but not SE– pts. At Wk 24, overall CfB in C3M showed higher correlation with CfB in disease activity in pts receiving ABA (n=36; DAS28 [CRP]: 0.66 [p<0.0001]; SDAI: 0.53 [p=0.0009]) vs ADA (n=32; DAS28 [CRP]: 0.33 [p=0.0644]; SDAI: 0.39 [p=0.0267]); this was more pronounced in SE+ pts (ABA, n=27; DAS28 [CRP]: 0.70 [p=0.0001]; SDAI: 0.63 [p=0.0005] vs ADA, n=25; DAS28 [CRP]: 0.33 [p=0.1120]; SDAI: 0.41 [p=0.0445]). Changes at Wk 4 in C3M showed higher correlation with response to ABA vs ADA (Figure 1). Correlations between CfB (at Wks 4 and 24) in other biomarkers and response were generally similar between treatment groups.

Table 1. BL correlation of ECM biomarkers with BL disease activity

	Overall (N=77)		SE+ (n=60)		SE– (n=17)	
	DAS28 (CRP)	SDAI	DAS28 (CRP)	SDAI	DAS28 (CRP)	SDAI
CRPM	0.26 0.0207	0.20 0.0777	0.20 0.1324	0.12 0.3583	0.41 0.0981	0.41 0.1001
Osteocalcin	0.24 0.0380	0.23 0.0416	0.23 0.0763	0.20 0.1293	0.28 0.2818	0.33 0.1890
CTX-1	0.23 0.0440	0.20 0.0844	0.21 0.1104	0.17 0.1932	0.26 0.3089	0.28 0.2703
C1M	0.54[a] 0.0000	0.34[a] 0.0028	0.60[b] 0.0000	0.38[b] 0.0029	0.34 0.1822	0.26 0.3216
C2M	–0.05 0.6774	0.00 0.9759	–0.06 0.6565	0.01 0.9567	–0.02 0.9441	0.01 0.9813
C3M	0.44 0.0001	0.30 0.0080	0.47 0.0001	0.30 0.0199	0.33 0.1943	0.31 0.2301
C4M	0.39 0.0004	0.32 0.0049	0.47 0.0001	0.36 0.0047	0.10 0.7012	0.11 0.6767

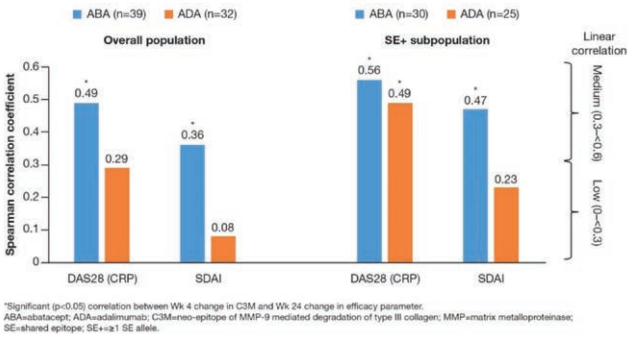
Data are Spearman correlation coefficient, p value. Linear correlations by shading: light grey, low (0–<0.3); medium grey, medium (0.3–<0.6); dark grey, high (0.6–1). Pts with missing SE allele data not included.[a]n=75.[b]n=58.C1M, C2M, C3M, C4M=MMP-mediated degradation products of collagen type I, II, III and IV, respectively; CRPM=neo-epitope of MMP-mediated degradation of CRP; CTX-1=neo-epitope of cathepsin-mediated degradation of type I collagen; MMP=matrix metalloproteinase; SE–=0 SE alleles; SE+=≥1 SE allele.

Conclusion: Significant BL correlation between C1M, C3M and C4M and disease activity was seen and was generally numerically higher in SE+ vs SE– pts. Early (Wk 4) change in C3M and later (Wk 24) treatment response were more highly correlated in pts receiving abatacept vs adalimumab. The predictive value of ECM biomarkers for treatment response warrants study in a larger population.

REFERENCES:

[1] Ouboussad L, et al. *Front Med (Lausanne)* 2019;6:45.
[2] Gudmann NS, et al. *Clin Exp Rheumatol* 2018;36:462–470.

Figure 1. Correlation between early changes in C3M and Wk 24 changes in efficacy parameters in the overall population and SE+ subpopulation



*Significant (p<0.05) correlation between Wk 4 change in C3M and Wk 24 change in efficacy parameter.
ABA=abatacept; ADA=adalimumab; C3M=neo-epitope of MMP-9 mediated degradation of type III collagen; MMP=matrix metalloproteinase; SE=shared epitope; SE+=≥1 SE allele.

Acknowledgements: Professional medical writing and editorial assistance was provided by Joanna Wright at Caudex and was funded by Bristol Myers Squibb.
Disclosure of Interests: S. Louis Bridges Grant/research support from: Bristol Myers Squibb, Jane Buckner Consultant of: Bristol Myers Squibb, Grant/research support from: Bristol Myers Squibb, Janssen, Michael A Maldonado Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Vivian Bykerk Consultant of: Grants from Amgen, Bristol Myers Squibb, Novartis, and UCB (given to institution); grants from the NIH, PCORI, and CIHR (given to institutions with whom she is affiliated); and personal fees from Amgen, Bristol Myers Squibb, Gilead, Pfizer, Regeneron, Roche, Sanofi Aventis, and UCB outside the submitted work., Grant/research support from: Grants from Amgen, Bristol Myers Squibb, Novartis, and UCB (given to institution); grants from the NIH, PCORI, and CIHR (given to institutions with whom she is affiliated); and personal fees from Amgen, Bristol Myers Squibb, Gilead, Pfizer, Regeneron, Roche, Sanofi Aventis, and UCB outside the submitted work., Neelanjana Ray Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Sumanta Mukherjee Shareholder of: Bristol Myers Squibb, GlaxoSmithKline, Employee of: Bristol Myers Squibb, GlaxoSmithKline, Nobuhisa Ohtsuka Employee of: Bristol Myers Squibb
DOI: 10.1136/annrheumdis-2021-eular.873

AB0108 USING RNA SEQUENCING TO IDENTIFY GENE EXPRESSION SIGNATURES ASSOCIATED WITH RESPONSE TO ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS

H. H. Chen[1], W. C. Chao[2], J. R. Wang[3], T. M. Ko[3]. [1]*Taichung Veterans General Hospital, Department of Medical Research, Taichung, Taiwan, Republic of China*; [2]*Taichung Veterans General Hospital, Department of Critical Care Medicine, Taichung, Taiwan, Republic of China*; [3]*National Chiao Tung University, Department of Biological Science and Technology, Hsinchu, Taiwan, Republic of China*

Background: Rheumatoid arthritis (RA) is a common chronic autoimmune disease. Abatacept (CTLA4-immunoglobulin) is one of the biological disease-modifying antirheumatic drug (bDMARD) for RA patients with indequate response to methotrexate. Recently, Yokoyama-Kokuryo et al. compared gene expression levels between abatacept responders and non-responders in RA patients using a microarray and found that type I IFN score and expression levels of nine genes may be used as a biomarker to predict response to abatacept. However, little study used RNA sequencing (RNA-seq) to identify whole blood gene expression signatures to predict therapeutic response to abatacept.
Objectives: The aim of this study is to identify gene expression signatures to predict therapeutic responses to abatacept in RA patients using RNA-seq.
Methods: This study is a single-center, prospective study. We used a PAX gene Blood RNA kit to collect whole blood at baseline and 4 weeks after abatacept treatment from RA patients. We also measured DAS28, physician global assessment, HAQ, ESR, CRP at baseline and 12 week to calculate EULAR response at 12 week. Patients with good EULAR response were defined as responders and those with moderate or no EULAR response were defined as non-responders.
Results: We finally conducted RNA-seq for whole blood from 7 RA patients initiating abatacept therapy. Of the 7 RA patients, one was non-responder and 6 were responders. We first use DESeq2 to analyze the differentially expressed genes of non-responder and responder before taking the drug. We used hierarchical clustering and PCA to evaluate the overall similarity of the samples, and group the patient data, and find that the nonresponder can be distinguished from responders. Subsequently, we analyzed the differentially expressed genes of the two groups of non-responder and responder patients before taking the drug. Before treatment, we found that 72 genes had a higher expression in the non-responder,

and 23 genes had a higher expression level in responders. Figure 1 showed the top 20 DEG Heatmap between the non-responder and responders.
Using these two sets of genes for GO analysis, we found that most of the pathways in the non-responder are related to immune response and cytokine production, and most of the pathways in the responders are related to antigen processing and MHC class II.

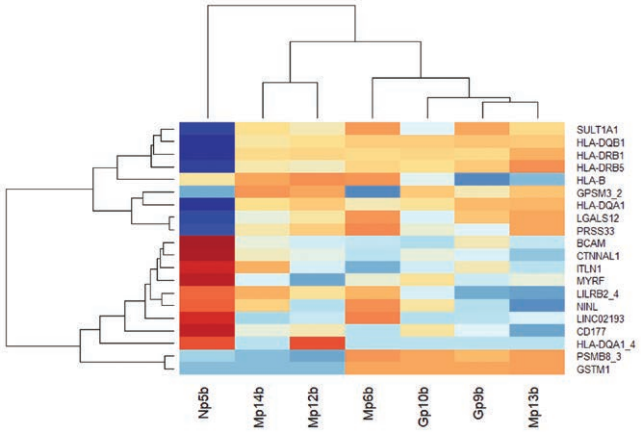


Figure 1. Top 20 DEG Heatmap between non-responder and responders

Conclusion: The study showed that most of the pathways in RA patients with no EULAR response to abatacept are related to immune response and cytokine production; while most of the pathways in RA patients with moderate/good response to abatacept are related to antigen processing and MHC class II.

REFERENCES:

[1] Yokoyama-Kokuyo W, Yamazaki H, Takeuchi T, et al. Identification of molecules associated with response to abatacept in patients with rheumatoid arthritis. Arthritis Research & Therapy. 2020;22:46.

Disclosure of Interests: Hsin-Hua Chen Grant/research support from: This is an investigator-sponsored trial with Bristol-Myers Squibb who provides funding support., Wen-Cheng Chao: None declared, Jing-Rong Wang: None declared, Tai-Ming Ko: None declared
DOI: 10.1136/annrheumdis-2021-eular.896

AB0109 VALIDATION OF SEPARATE PATIENT-REPORTED, CLINICAL AND LABORATORY FACTOR SCORES AS REPRESENTATION OF DISEASE BURDEN IN A POPULATION WITH ESTABLISHED RHEUMATOID ARTHRITIS

S. Pazmino[1], A. Lovik[2], D. De Cock[1], V. Stouten[1], D. Bertrand[1], J. Joly[3], M. Doumen[1], R. Westhovens[1,3], P. Verschueren[1,3]on behalf of TapERA study group. [1]*Katholieke Universiteit Leuven, Skeletal Biology and Engineering Research Centre, Department of Development and Regeneration, Leuven, Belgium*; [2]*Katholieke Universiteit Leuven, I-Biostat, Leuven, Belgium*; [3]*UZ Gasthuisberg Campus, Department of Rheumatology, Leuven, Belgium*

Background: Rheumatoid arthritis (RA) can cause important bio-psychosocial burden. When exploring disease burden evolution in the 2-year Care in early RA (CareRA) trial, 3 factor scores were extracted via exploratory factor analysis (EFA).[1] EFA uncovers the fact that multiple observed variables have similar patterns of responses because they are all associated with a latent, not directly observable, variable.
Objectives: To validate in a population with established RA, the 3 factors scores and their individual components originally extracted in CareRA.
Methods: Patients with established RA in sustained remission under treatment with etanercept (≥1 year) were enrolled in the TapERA (Tapering Etanercept in RA) trial between 2012 and 2014. Patients completed the Flare Assessment in RA (FLARE-RA) questionnaire.[2]
Components of disease activity scores (swollen/tender joint count, physician and patient global health assessment, CRP and ESR), as well as pain (question 2) and fatigue evaluation (question 8), from the FLARE-RA questionnaire, and HAQ were recorded at every visit (v=5).
Missingness on previously mentioned variables was handled with multiple imputation (100 imputations). Pain and fatigue were re-scaled from their original Likert scale of 1-6 to 0-100 to match CareRA data. Next, timepoint clustering was removed with multiple outputation (1000x) and each of the 100 000 datasets was analyzed by EFA with principal component extraction and oblimin rotation. The analyses were combined after re-ordering the factors by maximizing factor congruence.
Results: Sixty-six patients with a mean disease duration of 14.8 years (SD 9.03), mean age of 55.21 years (SD12.87), 96% (63/66) positive to RF or ACPA, 77% (51/66) with erosions and 68% (45/66) female were included in this analysis.
Table 1 provides the results of the EFAs from CareRA and TapERA. The factor structure and factor components remained the same in both datasets. The factor loadings, indicating how strongly a variable relates to its factor (correlation between observed and latent score), were also comparable. The HAQ, however; did have a stronger factor loading in TapERA (0.57 vs 0.92).

Table 1. Results from the exploratory factor analyses in CareRA and TapERA

Variable	CareRA			TapERA		
	PRF	CF	LF	PRF	CF	LF
Fatigue	0.90			0.80		
PaGH	0.87			0.81		
Pain	0.86			0.75		
HAQ	0.57			0.92		
SJC28		0.92			0.82	
TJC28		0.89			0.84	
PhGH		0.76			0.60	
CRP			0.87			0.85
ESR			0.78			0.82

Factor loadings presented (correlation between the observed score and the latent factor). Cross-loadings were negligible (<0.3) -not presented. The factor order is by % of variance explained.PRF: patient-reported factor, CF: clinical factor, LF: laboratory factor, PaGH: patient's global health assessment, HAQ: health assessment questionnaire, SJC28: 28 swollen joint count, TJC28: 28 tender joint count, PhGH: physician's global health assessment, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate

Conclusion: The latent factor structure for disease burden originally found in CareRA was successfully validated in the TapERA dataset, underlining the robustness of the PRF, CF and LF scores. HAQ seems to take "greater importance" on established RA. However, deviations in factor loadings (e.g., HAQ) could be attributed to differences between study populations (e.g., early vs. established RA, sample size). Apart from traditional clinical and laboratory factors, patient-reported pain, fatigue, functionality and overall well-being determine disease burden, both in early and established RA. Using these factor scores could facilitate detection and management of patient's unmet needs.

REFERENCES:

[1] Pazmino, et al. Does Including Pain, Fatigue, and Physical Function When Assessing Patients with Early Rheumatoid Arthritis Provide a Comprehensive Picture of Disease Burden? J Rheumatology 2020 Nov.
[2] Berthelot JM, et al. A tool to identify recent or present rheumatoid arthritis flare from both patient and physician perspectives: the 'FLARE' instrument. Annals Rheumatic Diseases. 2012.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.915

AB0110 DETERMINING THE AMOUNT OF COPPER–CONTAINING PROTEIN, ITS BIOCHEMICAL AND IMMUNOLOGIC ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS

O. Rusanova[1], A. Trofimenko[1], N. Emelyanov[2], O. Emelyanova[1]. [1]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», 1, Волгоград, Russian Federation*; [2]*Federal State Budgetary Educational Institution of Higher Education «Volgoorad State Medical University» of the Ministry of Healthcare of the Russian Federation, 2, Волгоград, Russian Federation*

Background: Production of antibodies to ceruloplasmin (CP) in rheumatoid arthritis is an issue that has not been studied well enough. It was not by chance that this copper–containing alpha 2-glycorpoteid of blood plasma showing multienzymatic properties was chosen as an object of investigation. Data on the content and activity of CP in the blood of rheumatoid arthritis patients are contradictory, which has to do with different approaches to selection of patients and different measuring methods.
Objectives: Improving diagnosis of rheumatoid arthritis by determination of antibodies to CP as well as its amount and enzymatic activity.

Methods: We studied the serum from 30 apparently healthy individuals, and 108 rheumatoid arthritis patients. Antibodies to CP were determined by enzyme immunoassay using immobilized granulated antigen preparations (modification by Gontar et al, 2002). The amount of CP was determined by enzyme immunoassay according to the method of I.S. Kuzmina et al (1991) using commercial diagnostic agent manufactured by Mechnikov Research Institute for Vaccines and Sera.
Results: Enzyme immunoassay showed a mean level of CP antibodies in donor sera of 0,020±0,006 optical density units. The level of normal values of specific antibodies determined as M±2σ included an extinction value in the range 0 – 0,086. The mean value of oxidase activity and the amount of CP in healthy people was 716±26,3 and 921±32 ng/ml, correspondingly. In the process of study we revealed a reliable increase in CP antibody count, the activity and amount of CP in patients with rheumatoid arthritis while in all cases the parameters under study correlated with the degree of disease activity ($p<0,05$): at activity degree I CP antibodies were 0,098±0,011; CP activity was 954±48,1; CP amount was 1292±73,4. At activity degree II CP antibodies were 0,138±0,007; CP activity was 1163±39,6; CP amount was 1763±69,3. At activity degree III, CP antibodies were 0,182±0,015; CP activity was 1368±89,5; CP amount was 1794±102,8. After a course of hospital treatment was completed, we noted a reliable decrease in the activity and amount of CP (at degree I of rheumatoid arthritis activity $p<0,001$, at degree II of rheumatoid arthritis activity $p<0,01$for both parameters; at degree III, $p<0,05$) compared with baseline findings. A decrease in CP antibodies shows decelerated dynamics, especially in patients with pronounced disease activity, which indicates severe disorders in the immunity that cannot be cured completely within 30 – 40 days of hospital treatment course.
Conclusion: Determination of CP antibodies, as well as quantitative content of CP and its oxidase activity can serve as indicators of the activity of rheumatoid arthritis, as well as an accessory criterion of the effectiveness of administered therapy.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.948

AB0111 FAMILIAL RHEUMATOID ARTHRITIS WITH LATE ONSET (50 YEARS AND OLDER) IN CLINICAL PRACTICE ACCORDING TO THE ALL-RUSSIAN ARTHRITIS REGISTER (OREL)

A. Satybaldyev[1], O. Rumyantseva[2], N. Demidova[2], E. Gerasimova[1], E. Strebkova[3], J. Murtazalieva[4], E. Koltsova[4], M. Nikolenko[4], G. Lukina[4], E. Zhilyaev[4], E. Nasonov[5]. *[1]V A Nasonova Research Institute of Rheumatology, Department of Early Arthritis, Moscow, Russian Federation*; *[2]V A Nasonova Research Institute of Rheumatology, Clinical Department, Moscow, Russian Federation*; *[3]V A Nasonova Research Institute of Rheumatology, Osteoarthritis Laboratory, Moscow, Russian Federation*; *[4]Moscow Research and Practical Center, Moscow Healthcare Department Clinical Moscow, Moscow, Russian Federation*; *[5]V A Nasonova Research Institute of Rheumatology, Scientifical Department, Moscow, Russian Federation*

Background: Relatives of the 1st degree of relationship (RFDR) of a patient with rheumatoid arthritis (RA) have the higher risk for the development of RA, associated with a 2-5 fold increase.
Objectives: Clinical characteristics of probands with RA onset at an older age (50 yrs and older) and their RFDR, which had RA, other rheumatic diseases (RD) and other autoimmune diseases (AID).
Methods: 2766 RA pts with onset of the disease at the age of 50 yrs and older, residents of Moscow and the Moscow region, were included in the Russian register of arthritis OREL in the period from 01.06.2012 to 31.12.2018. 67 probands with RA (2.4%) had RFDRs with RA, other RDs, other AIDs (86 RFDRs in total). Disease activity (by DAS-28), X-ray stage - (by modified Steinbrocker), functional disorders (by functional class - FC), immunological characteristics (RF, ACPA), etc., characterizing the clinical manifestations of RA were evaluated in accordance with the requirements of the current national working RA classification. RFDRs were divided into groups depending on relation to proband father, mother and siblings with RA, RFDRs withr other RD and RFDR with other AID; serological affiliation to RF and ACPA; association with concordant and discordant RFDR, as well as on number of RFDRs (1 and 2 or more).
Results: 67 probands with RA were investigated: 9 men, 58 women, average age in debut (m ± δ) 58.78 ± 6.23 yrs; the average age at the time of the last study was 68.8 ± 6.38 yrs, average duration of RA was 10.14 ± 5.69 yrs. 6 (9%) probands had FC1, 45 (69%) - FC2, 13 (20%) - FC3, 1 (2%) - FC4, 2 - without data; 34 (53%) had high activity, 23 (36%) -medium, 6 (9%) - minimal, 1 (2%) - remission, 3 without data; RF-positive (RF+) - 77.6%, ACPA-positive (ACPA+) - 71.7%. 19 probands (32%) had 1-2a X-ray stage, 27 (46%) - stage 2b, 10(17%) - stage 3, 3 (5%) - stage 4, 8 - without data. 61 (91%) had advanced clinical stage, 6 (9%) - late. Among 86 RFDRs (67 - RF+, 19 - RF-) 10 had father with RA (8 RF+ probands, 2 - RF-), 2 - father with other RDs (all RF+), 10 - mother with RA (all RF+), 7 - mother with other RDs (4 - RF+, 3 - RF-), 26 - siblings with RA (20 - RF+, 6 - RF-), 11 - siblings with other RDs (9 - RF+, 2 - RF-), 20 - RFDR with other AIDs (14 - RF+, 6 - RF-). Probands with concordant RFDRs had more pronounced changes: high activity (56% versus 32%), X-ray erosive stages (67% versus 60%) and stages III and IV (32% versus 6%); FC3 and FC4 (23% versus 12%) and a tendency towards more frequent development of the late clinical stage (11% versus 2%). Comparison of clinical signs in probands with 1 RFDR (49 cases) and probands with 2 or more RFDRs (17 cases) showed a significant predominance of high inflammatory activity (61% versus 41%), erosive arthritis (77% versus 57%), and a tendency to development of a late clinical stage (10% versus 6%) in probands with 1 RFDR. In probands with RF-positive RA, the predominance becomes more significant: high inflammatory activity (69% versus 43%), erosive arthritis (90% versus 54%), late clinical stage (13% versus 7%), and a tendency to severe functional impairment - FC3 and FC4 (22% vs. 15%). ACPA-positive probands showed the same tendency as RF-positive.
Conclusion: The clinical picture of probands with RFDRs with RA, other RDs, other AIDs is generally characterized by more pronounced changes in probands with RA who have RFDRs with concordant diseases in the form of more often high inflammatory activity, less often moderate, erosive arthritis, more frequent development of advanced 3 and 4 X-ray stages (every fifth). Also, more pronounced changes develop in probands with RA who have only 1 RFDR compared to probands with 2 or more RPSRs. In this group, the differences are even more pronounced in the case of RF-positive probands. In cases with ACPA-positive probands, the same trends persist. Careful interview of a proband with RA about the presence of RFDRs with RA, other RDs and other AIDs will make it possible to predict its course more correctly and facilitate planning of rational therapy.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.962

AB0112 TNF INHIBITOR MONOTHERAPY IN RHEUMATOID ARTHRITIS: IS THERE REALLY A DIFFERENCE IN COMPARISON WITH COMBINATION THERAPY WITH CSDMARDS IN REAL-LIFE?

B. M. Fernandes[1], S. Garcia[1], F. Oliveira Pinheiro[1], M. Rato[1], D. Fonseca[2], D. Santos Oliveira[1,3], A. Martins[1], F. R. Martins[4], M. Bernardes[1,5], L. Costa[1]. *[1]Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*; *[2]Centro Hospitalar Vila Nova de Gaia/Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; *[3]Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; *[4]Centro Hospitalar Universitário do Algarve, Rheumatology, Faro, Portugal*; *[5]Faculty of Medicine, University of Porto, Departamento de Medicina, Porto, Portugal*

Background: In Rheumatoid Arthritis (RA), tumor necrosis factor inhibitors (TNFi) in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) has shown advantages concerning efficacy and immunogenicity in comparison with monotherapy. However, in clinical practice, up to 40% of patients under biological DMARDs (bDMARDs) are on monotherapy.
Objectives: To compare the efficacy outcomes of TNFi in monotherapy and in combination therapy in a RA monocentric cohort.
Methods: Retrospective, cross-sectional study including all the RA patients under TNFi followed at our Rheumatology Department and registered in the national database. Demographic, clinical and laboratorial data and disease activity measures were collected at the last visit of 2019 from each patient. Mann-Whitney U and chi-square tests were used to the comparison analysis between the two groups (continuous and categorical variables, respectively).
Results: A total of 144 patients were included: 84% were females; at the last visit of 2019, the mean age was 56.3±10.9 years and the mean disease duration was 18.3±10.2 years; 73.6% were positive for rheumatoid factor (RF), 81.9% for anti-citrullinated protein autoantibodies (ACPA) and 45.1% had erosive disease. There were no statistically significant differences in these variables between the monotherapy and the combination therapy groups (table 1).

Table 1. Demographic and disease-related variables in the monotherapy and the combination therapy group.

	Monotherapy (n=31)	Combination therapy (n=113)
Age - mean±SD	59.1±14.0 years	55.5±9.8 years
Disease duration - mean±SD	20.5±11.2 years	17.7±9.7 years
RF positive - n (%)	20 (60.4%)	86 (76.8%)
ACPA positive - n (%)	25 (80.6%)	93 (85.3%)
Erosive disease - n (%)	15 (48.4%)	50 (44.6%)

Thirty-one patients (21.5%) were under monotherapy with TNFi and etanercept was the most frequent TNFi in both groups (54.8% vs 50.0%; monotherapy and combination therapy groups, respectively). At the start of the first bDMARD, the monotherapy group had a higher disease activity score 28 - 4 variables (DAS 28 4V; 6.083±0.930 vs 5.605±1.043, p=0.039) and a higher simple disease activity score (SDAI; 36.12±11.77 vs 28.76±9.98, p=0.035); also, in the monotherapy group more patients had already started the bDMARD in monotherapy (22.6% vs 2.7%, p<0.001), less patients were under (38.7% vs 73.2%, p=0.001) or had already been treated with (77.4% vs 93.8%, p=0.007) methotrexate, in comparison with the combination group therapy.

At the last visit of 2019, the monotherapy group had a higher mean years of duration of iTNF treatment (5.5±5.8 vs 3.4±4.5, p=0.048), a higher mean patient global assessment - visual analogue scale (PGA-VAS; 49±18 vs 39±25, p=0.023), a higher mean prednisolone equivalent dose in mg/day (7.6±6.3 vs 5.6±3.2, p=0.045) and a lower proportion of American College of Rheumatology 50 and 70 responses (ACR 50: 12.9% vs 17.0%, p=0.023; ACR 70: 3.2% vs 10.7%, p=0.045) in comparison with the combination therapy group.

Conclusion: In line with the literature, our real-life results demonstrate some direct (higher PGA-VAS and lower ACR 50 and 70 responses) and indirect (higher current prednisolone equivalent dose) data that suggest that patients with TNFi monotherapy may have a worst disease activity control in comparison with combination therapy.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.994

AB0113

ANTI-CARBAMYLATED PROTEIN ANTIBODIES POSITIVITY AND DISEASE ACTIVITY IN HISPANIC PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS: AN OBSERVATIONAL STUDY

D. Vega-Morales[1], M. A. Garza Elizondo[1], L. A. Trouw[2], K. I. González Márquez[1], E. Torres-Lopez[3], M. Eguia Bernal[1], S. A. Loredo Alanis[1], T. S. Gracia-Arechiga[1], B. R. Vázquez Fuentes[1], D. D. Castañeda Martínez[1], M. M. Castañeda-Martínez[1], C. V. Solis[1], A. Mendiola-Jimenez[1], M. C. Salinas-Carmona[3], P. Herrera-Sandate[1], A. Cárdenas[1], G. E. Rodriguez-Sanchez[1], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Rheumatology Service, Monterrey, Mexico*; [2]*Leiden University Medical Center (LUMC), Department of Immunohematology and Bloodtransfusion, Leiden, Netherlands*; [3]*Hospital Universitario Dr. José Eleuterio González, Immunology Department, Monterrey, Mexico*

Background: Clinically relevant anti-carbamylated (anti-CarP) antibodies are detected in up to 45% of rheumatoid arthritis (RA) patients and are associated with severe radiological progression, higher disease activity, and significantly more disability when studied in early phases of arthritis.

Objectives: We aimed to determine the prevalence of anti-CarP antibodies in Mexican Hispanics with established RA and to assess their relationship with disease activity.

Methods: A cohort study was conducted in 278 patients with established RA during an 18-month follow-up. We measured IgG/IgM/IgA rheumatoid factor (RF), IgG anticitrullinated protein antibodies (ACPA) and IgG/IgM/IgA anti-CarP antibodies using enzyme-linked immunosorbent assay (ELISA). For disease activity, we performed the 28-joint disease activity score with erythrocyte sedimentation rate (DAS28-ESR). Repeated measures one-way ANOVA was used to test the association between anti-CarP IgG antibody status and longitudinal DAS28-ESR scores. Patients were evaluated at baseline and at 6, 12, and 18 months during follow-up.

Results: Anti-CarP IgG antibodies were positive in 47.8% of patients and, accounting for all isotypes, in 9.5% of patients with negative RF and ACPA. Triple antibody positivity was present in 42.6% of patients in our sample. Anti-CarP IgG antibody positivity did not show statistically significant differences in mean DAS28-ESR when compared to anti-CarP IgG antibody negative patients at baseline, 6, 12 or 18 months.

Conclusion: Anti-CarP IgG antibodies are present in almost 50% of RA patients and, accounting for all isotypes, in 9% of RF and ACPA negative patients. Anti-CarP IgG antibody positivity was not associated to a higher disease activity measured by DAS28-ESR in Hispanic patients with established RA.

References: Shi J, Knevel R, Suwannalai P, Van Der Linden MP, Janssen GMC, Van Veelen PA, et al. Autoantibodies recognizing carbamylated proteins are present in sera of patients with rheumatoid arthritis and predict joint damage. Proc Natl Acad Sci U S A. 2011;108:17372–17377.

Table 1. Anti-CarP antibody status by isotype in a cohort of 278 patients with established RA.

	Mean (SD)	Antibody positivity, n (%)	95% CI
RF IgA[a]	266.9 (460.5)	155 (58.9)	53.0 to 64.9
RF IgM[a]	406.8 (611.9)	188 (71.5)	66.0 to 77.0
RF IgG[a]	36.1 (249.6)	44 (16.7)	12.2 to 21.3
ACPA IgG[a]	191.01 (411.1)	144 (54.8)	48.7 to 60.8
Anti-CarP IgA[b]	212.9 (464.2)	74 (26.6)	21.4 to 31.8
Anti-CarP IgM[b]	381.6 (762)	89 (32)	26.5 to 37.5
Anti-CarP IgG[b]	227.5 (402.5)	133 (47.8)	41.9 to 53.8

[a]Data were available for 263 patients. Units are RU/mL. [b]Data were available for 278 patients. Units are AU/mL. RF, rheumatoid factor; ACPA, anticitrullinated protein antibodies; Anti-CarP, anti-carbamylated protein antibodies; IgG, immunoglobulin; SD, standard deviation; 95% CI, 95% confidence intervals.

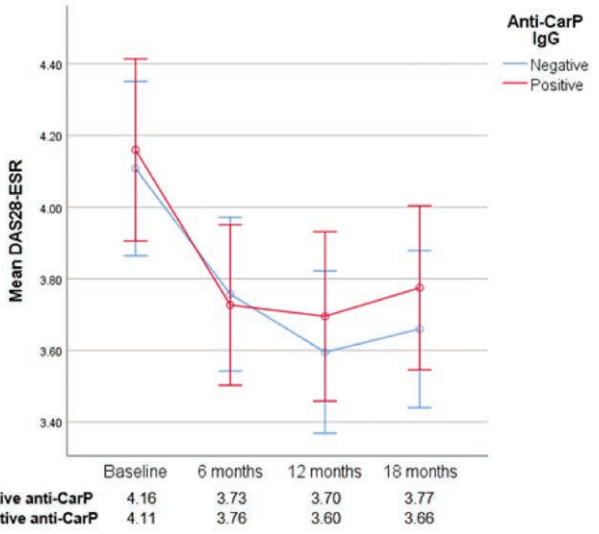


Figure 1. Mean DAS28-ESR scores over an 18-month follow-up by anti-CarP antibody status with error bars corresponding to 95% CI. With the non-sphericity assumed by Greenhouse-Geisser analysis, a non-significant statistical difference was found among groups in the repeated measures one-way ANOVA (p = 0.829). DAS28-ESR, 28-joint disease activity score with erythrocyte sedimentation rate; Anti-CarP, anti-carbamylated protein antibodies; Ig, immunoglobulin.

Figure 1.

Disclosure of Interests: David Vega-Morales Grant/research support from: This research was funded as an Investigator Initiated Study by UCB (IIS-2015-104068). The sponsor did not have any role in the design or outcomes of this study., Mario Alberto Garza Elizondo: None declared, Leendert A Trouw: None declared, Karina Itzel González Márquez: None declared, Ernesto Torres-Lopez: None declared, Myriam Eguia Bernal: None declared, SALVADOR AZAHEL LOREDO ALANIS: None declared, Tayde Sarahi Gracia-Arechiga: None declared, Brenda Roxana Vázquez Fuentes: None declared, Diana Daniela Castañeda Martínez: None declared, Martha Mariana Castañeda-Martínez: None declared, Cesar Vidal Solis: None declared, Andres Mendiola-Jimenez: None declared, Mario Cesar Salinas-Carmona: None declared, Pablo Herrera-Sandate: None declared,

Alberto Cárdenas: None declared, Gerardo Eugenio Rodriguez-Sanchez: None declared, Dionicio Ángel Galarza-Delgado: None declared
DOI: 10.1136/annrheumdis-2021-eular.1289

AB0114 INVESTIGATION OF THE EFFECTS OF EXERCISE ON MIRNA EXPRESSIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Z. B. Özcan[1], F. S. Karaahmetoğlu[2], M. Z. Çıracı[3], H. H. Pençe[4], M. Vural[5], E. I. Üstün[5], A. Kural[6], S. Kuraş[4], B. Erdoğan[4]. *[1]Hamidiye Faculty of Health Sciences, Medical Biochemistry, Istanbul, Turkey*; *[2]Hamidiye Faculty of Health Sciences, Physical Therapy and Rehabilitation, Istanbul, Turkey*; *[3]Sakarya University Education and Research Hospital, Department of Biochemistry, Sakarya, Turkey*; *[4]Istanbul Hamidiye Faculty of Health Sciences, Medical Biochemistry, Istanbul, Turkey*; *[5]Istanbul SBU Dr. Sadi Konuk Education and Research Hospital, Physical Medicine and Rehabilitation, Istanbul, Turkey*; *[6]Istanbul SBU Dr. Sadi Konuk Education and Research Hospital, Department of Biochemistry, Istanbul, Turkey*

Background: The goal of treatment for patients with RA is achieve to remission, or at least a state of low disease activity. Exercise is recommended for patients with RA in addition to drug therapy. It has been found to be effective in greatly improving functionality and reducing cardiovascular risk without exacerbating disease activity. Therefore, it is recommended that all RA patients should be encouraged to include aerobic and resistant exercise training as part of their routine treatment (1).
miRNAs(miRNA) are known to protect the pathophysiological process specific to RA. miRNA-146a is one of the miRNAs extensively studied in RA, its expression was found to be higher in the synovial fluid and synovial tissue of RA patients compared to healthy individuals (2).
Many studies have found that miRNA-146a, along with miRNA-16 and miRNA155 may be related to disease pathology. It has also been found that high levels of miRNA-16 expression correlate with active disease and low levels of expression with inactive disease. It has been found that the increased level of miRNA-155 causes a problem in the modulation of arthritis It has been found that the expression level of miRNA-145 is increased in peripheral blood mononuclear cells of RA patients and synovium supporting osteoclastogenesis (3,4,5).
Objectives: It is aimed to investigate the effect of exercise on microRNA expressions in patients with rheumatoid arthritis (RA).
Methods: 30 patients and 30 healthy controls aged 18-60 years who met the 2010 ACR / EULAR RA criteria were included in the study. A program consisting of strengthening and stretching exercises 2 days a week was applied to the study group for 8 weeks. One day a week, 30 minutes of mild moderate walking was requested. Of the cases at the beginning and at the end of the treatment; 5-10 cc peripheral blood samples were taken into one EDTA tube. Then Numeric Rating Scale (NRS) was used for pain, 28-joint Disease Activity Score (DAS28) was used to calculate disease activity, Health Assessment Questionnaire (HAQ) was used to assess general health and Short Form-36 (SF-36) was used to evaluate quality of life. 5-10 cc peripheral blood samples were taken to only 1 EDTA tube of the control group. In the samples taken, gene expressions of miRNA-146a, miRNA-155, miRNA-16, miRNA-145 were determined by real-time PZR method.
Results: There was a significant difference in DAS28, SF-36, NRS, HAQ scales before and after treatment in the RA group of patients (p 0.05). The expression level of MiRNA-146a does not differ significantly before and after treatment (p> 0.05). However, these two groups differ significantly with the control group (p 0.05). No significant difference was observed in the miRNA-155 and miRNA-16 expression levels in the pretreatment, posttreatment, and control groups (p> 0.05).
Conclusion: Exercise therapy has a good effect on pain, disease activity, quality of life and general health in patients with RA. It has been found that exercise can affect vii some of the miRNAs involved in disease pathogenesis. However, more comprehensive studies are needed.
REFERENCES:

[1] Cooney JK, Law RJ, Matschke V, Lemmey AB, Moore JP, Ahmad Y, et al. Benefits of exercise in rheumatoid arthritis. Journal of Aging Research. 2011. p. 14.
[2] Abou-Zeid A, Saad M, Soliman E. MicroRNA 146a expression in rheumatoid arthritis: Association with tumor necrosis factor-alpha and disease activity. Genet Test Mol Biomarkers. 2011;15(11):807–12.
[3] Murata K, Yoshitomi H, Tanida S, Ishikawa M, Nishitani K, Ito H, et al. Plasma and synovial fluid microRNAs as potential biomarkers of rheumatoid arthritis and osteoarthritis. Arthritis Res Ther. 2010;12(3):86.
[4] Pauley KM, Satoh M, Chan AL, Bubb MR, Reeves WH, Chan EKL. Upregulated miR-146a expression in peripheral blood mononuclear cells from rheumatoid arthritis patients. Arthritis Res Ther. 2008;10(4):101.
[5] Evangelatos G, Fragoulis GE, Koulouri V, Lambrou GI. Micrornas in rheumatoid arthritis: From pathogenesis to clinical impact. Autoimmun Rev. 2019;18(11):102391.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1369

AB0115 COMPARISON OF ULTRASOUND FINDINGS BETWEEN TNF INHIBITORS AND NON-TNF INHIBITORS AT FIRST BIOLOGICS IN PATIENTS WITH RHEUMATOID ARTHRITIS

T. Okano[1], T. Koike[2,3], K. Inui[4], K. Mamoto[1], Y. Yamada[1], K. Mandai[4], S. Anno[1], H. Nakamura[1] on behalf of Team RA. *[1]Osaka City University Graduate School of Medicine, Department of Orthopedic Surgery, Osaka, Japan*; *[2]Osaka City University Graduate School of Medicine, Center for Senile Degenerative Disorders (CSDD), Osaka, Japan*; *[3]Shirahama Foundation for Health and Welfare, Search Institute for Bone and Arthritis Disease (SINBAD), Shirahama, Japan*; *[4]Osaka Saiseikai Nakatsu Hospital, Department of Orthopedic Surgery, Osaka, Japan*

Background: In rheumatoid arthritis (RA), biologics treatment is one of the effective treatment options. Usually, there is no difference in therapeutic effect regardless of which biologics is used, but the effect for joint synovitis is unknown. Recently, ultrasound (US) has played a role of sensitive imaging modality in the diagnosis and follow-up of patients with RA.
Objectives: The aim of this study was to compare the improvement of US findings between TNF inhibitors and non-TNF inhibitors at first biologics in patients with RA.
Methods: Fifty-four RA patients who started the first biologics from September 2016 to December 2018 were included in this longitudinal study (SPEEDY study, UMIN000028260). All the patients were performed clinical examination, blood test and US examination at baseline, 4, 12, 24, 36 and 52 weeks. A US examination was performed at the bilateral first to fifth metacarpophalangeal (MCP) joints, first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) joints, wrist joints (three part of radial, medial and ulnar) and first to fifth metatarsophalangeal (MTP) joints, by using HI VISION Ascendus (Hitachi Medical Corporation, Japan) with a multifrequency linear transducer (18-6 MHz). The gray scale (GS) and power Doppler (PD) findings were assessed by the semi-quantitative method (0-3). GS score and PD score (both 0-108 points) were defined as the sum of each score. The change of disease activity and US findings were compared between TNF group and non-TNF group.
Results: Among 54 cases, 32 patients were used TNF inhibitor and 22 were non-TNF inhibitor. Age and duration of RA were significantly higher in the non-TNF group, and MTX dose was significantly lower in the non-TNF group. The baseline inflammatory markers tended to be higher in the non-TNF group and the disease activity was also higher in the non-TNF group. However, the US findings showed no significant difference in both GS and PD between two groups at baseline. US improvement ratio was no difference between TNF group and non-TNF group at 4, 12, 24, 36 and 52 weeks in both GS and PD score. Regardless of the type of biologics, patients with long-term disease duration tended to have poor improvement in US synovial fingings.

Table 1. Baseline patient and disease characteristics

	TNF (n=32)	non-TNF (n=22)	P value
Female patients, n (%)	21 (65.6)	16 (72.7)	0.767
Age (years)	63.5±15.4	71.0±9.0	0.030
Disease duration (years)	6.5±8.2	13.0±11.7	0.032
CRP (mg/dl)	1.8±2.5	3.0±3.2	0.170
DAS28-ESR	5.0±1.4	5.8±1.2	0.022
GS score	26.1±18.8	31.8±21.1	0.313
PD score	17.6±11.4	23.1±14.6	0.150

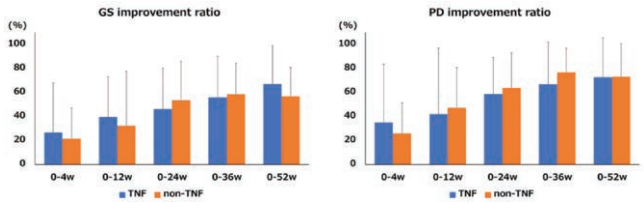


Figure 1. GS and PD improvement ratio at 4, 12, 24, 36 and 52 weeks

Conclusion: There was no difference in the US findings improvement between patients with TNF inhibitor and non-TNF inhibitor at first biologics in patients with RA.

REFERENCES:

[1] Grassi W, Okano T, Di Geso L, Filippucci E. Imaging in rheumatoid arthritis: options, uses and optimization. Expert Rev Clin Immunol. 2015;11:1131-46.

[2] Nishino A, Kawashiri SY, Koga T, et al. Ultrasonographic Efficacy of Biologic andTargeted Synthetic Disease-ModifyingAntirheumatic Drug Therapy in RheumatoidArthritis From a Multicenter RheumatoidArthritis Ultrasound Prospective Cohort in Japan. Arthritis Care Res (Hoboken). 2018;70:1719-26.

Acknowledgements: We wish to thank Atsuko Kamiyama, Tomoko Nakatsuka for clinical assistant, Setsuko Takeda, Emi Yamashita, Yuko Yoshida, Rika Morinaka, Hatsue Ueda and Tomomi Iwahashi for their special efforts as a sonographer and collecting data.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1377

AB0116 THE EFFECTS OF DISEASE MODIFYING ANTI-RHEUMATIC DRUGS ON PATIENT REPORTED OUTCOMES; PRELIMINARY RESULTS OF A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

M. Van den Dikkenberg, Msc[1], N. Luurssen-Masurel[2], M. Kuijper[1], M. R. Kok[1], P. De Jong[2], J. Hazes[2], D. Lopes Barreto[1], A. Weel[1,3]. *[1]Maasstad Hospital, Rheumatology, Rotterdam, Netherlands*; *[2]Erasmus MC, Rheumatology, Rotterdam, Netherlands*; *[3]Erasmus School of Health Policy & Management, Health Technology Assessment, Rotterdam, Netherlands*

Background: The need to involve patient reported outcomes (PROs) in the management of rheumatoid arthritis (RA) increases, since PROs quantify patient relevant outcomes. Although PROs have been incorporated in the core-outcome sets in clinical trials, knowledge about the treatment effects on these PROs is scarce. Therefore, we performed a systematic review on the effects of disease modifying anti-rheumatic drugs (DMARDs), of any type, on relevant PRO domains mentioned in the ICHOM standard set. This might support rheumatologists and RA patients during treatment decisions.

Objectives: To get insight in the treatment effects of DMARDs of any type on three PRO domains that matter to patients (pain, activity limitations and fatigue).

Methods: A systematic review was performed in Embase, Medline, Web of Science, Cochrane and Google Scholar. Included were all studies that were published before August 2019 and showed DMARD treatment effects in RA on PROs that are part of the ICHOM standard set. Three Bayesian network meta-analyses were performed for the PRO domains pain, activity limitations and fatigue. Preliminary results of DMARDs (in)directly compared to placebo were visualized by forest plots using R.

Results: The search strategy yielded n=5974 articles. After selection was performed by 2 independent researchers, n=70 individual articles representing n=53 studies were extracted, over the three PRO domains; pain (n=31), activity limitations (n=41) and fatigue (n=21). In all RCTs, PROs were only reported as secondary or tertiary endpoints. In figure 1, we show the effects on PROs for any type of DMARD investigated compared to placebo. Overall, DMARDs show a greater reduction in pain (standardized mean difference (SMD); -0.97 – -0.22) and most of them in activity limitations (SMD; -0.81 – 0.56). In fatigue, this clear direction is lacking (SMD; -0.86 – 3.5). csDMARDs and anti-TNF seem to perform slightly, but nog significantly, worse than other bDMARDs and tsDMARDs in the first two domains.

Conclusion: Within in this systematic review we report a reduction for DMARDs of any type on the domains of pain and activity limitations compared to placebo. However, results are still preliminary and should be interpreted with care. A more comprehensive network analysis might give a more definitive answer which DMARD performs best.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1578

AB0117 CARDIOVASCULAR MORBIMORTALITY IN RHEUMATOID ARTHRITIS: A 5 YEAR FOLLOW-UP STUDY

A. B. Rodriguez-Romero[1], D. Á. Galarza-Delgado[1], I. J. Colunga-Pedraza[1], J. R. Azpiri-López[2], N. Guajardo-Jauregui[1], S. Lugo-Perez[2], A. Cárdenas[1]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology Service, Monterrey, Mexico*; *[2]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology Service, Monterrey, Mexico*

Background: Rheumatoid arthritis (RA) is characterized by elevated cardiovascular morbimortality. RA patients have a higher risk to develop cardiovascular comorbidities when compared to the general population, being the main cause of mortality in these patients. Cardiovascular risk factors (CVRF) are well known, but their management is not optimal, increasing the risk of having a major heart disease (1).

Objectives: To assess the prevalence of the main causes of morbimortality and development of CVRF in RA patients during a five-year follow-up period.

Methods: A longitudinal and prospective study of a RA cohort from 2014-2019 was performed in a Cardio Rheumatology outpatient clinic at the University Hospital "Dr. Jose E. Gonzalez", UANL. Patients aged 40-75 years with RA according to ACR/EULAR 2010 criteria were recruited. At both visits, demographic, clinical variables, and lipid profile were recorded. Outcomes included the development of cardiovascular comorbidity: hypertension, diabetes mellitus (DM), dyslipidemia, myocardial infarction, stroke. Survival probabilities and outcomes cumulative frequencies were calculated according to the Kaplan-Meier lifetime analysis method. Descriptive analysis: frequencies (%), mean (SD), or median (q25-q75). Comparisons with McNemar and Student's t test.

Results: A follow-up was done in a total of 92 patients. During the follow-up, 9 patients (9.8%) died, 3 died of cardiovascular death (one myocardial infarction and two strokes). The mean age of death was 67.2 ± 10.5 years. CVRF at baseline (T0) and after five years (T5) are shown in table 1. Of the remain 83 patients, 11 patients (13.3%) developed hypertension (p=0.001), 8 (9.6%) patients developed DM (p=0.031). The number of patients with dyslipidemia decreased significantly to 14 (16.9%) (p=0.031), 4 (4.8%) developed a stroke. A survival probability of 95.7% was found at the five-year follow-up from the time of entry into the cardio rheumatology clinic (Figure 1 next page) and a 30.1% probability of developing cardiovascular comorbidity.

Conclusion: This long-term study provides updated information on RA morbimortality characteristics in our population. Patients with RA still develop significant cardiovascular comorbidities despite current treatment. In this cohort, hypertension and DM became more prevalent, and a 96% cardiovascular death-free survival was found. Is imperative to increase the effort in determining optimal markers and therapeutic measures to continue with the prevention of these comorbidities.

REFERENCES:

[1] Semb AG, Ikdahl E, Wibetoe G, et al. Atherosclerotic cardiovascular disease prevention in rheumatoid arthritis. Nat Rev Rheumatol 2020;16(7):361-79. doi: 10.1038/s41584-020-0428-y.

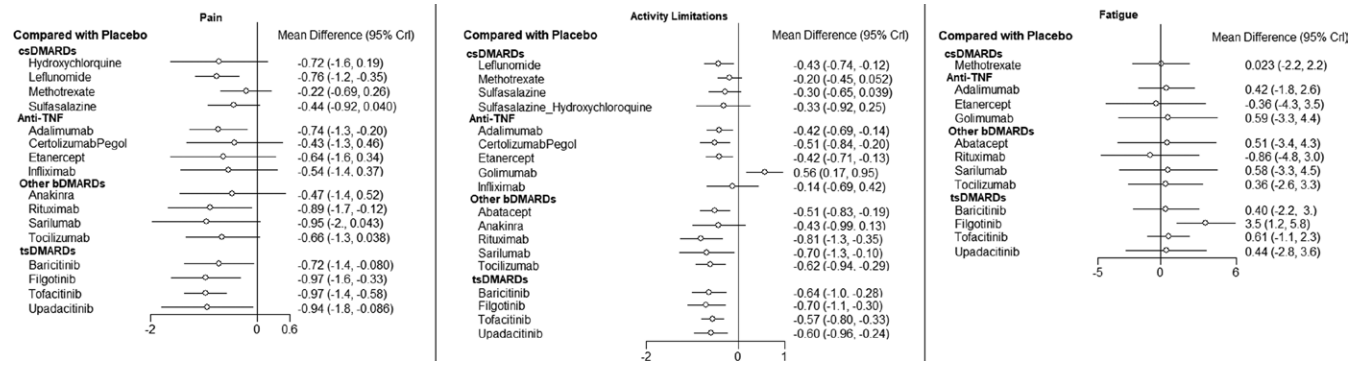


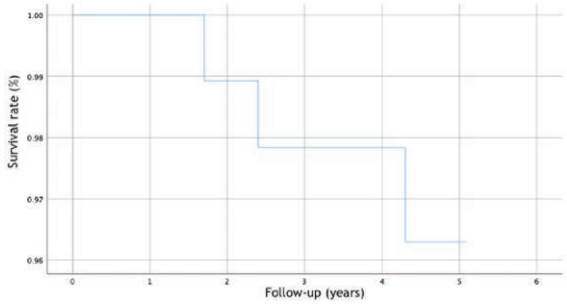
Figure 1.

Table 1. Demographic and clinical characteristics at the time of inclusion and at 5 years.

	T0 (n=83)	T5 (n=83)	*p*
Age years, mean ± SD	56.0 ± 8.9		-
Female, n (%)	75 (90.4)		-
Disease duration years median (q25-q75)	10.4 (4.4-15.7)		-
CVRF, n (%)			
Hypertension	27 (32.5)	38 (45.8)	**0.001**
Dyslipidemia	25 (30.1)	16 (19.3)	**0.041**
DM	6 (7.2)	14 (16.9)	**0.008**
Active smoking	8 (9.6)	6 (7.2)	NS
Overweight/Obesity	67 (81.7)	63 (81.9)	NS
Stroke	0	4 (4.8)	-
Clinical characteristics			
BMI kg/m^2, mean ± SD	28.1 ± 4.1	28.5± 4.3	NS
SBP mmHg, mean ± SD	123.7 ± 18.4	126.9± 16.8	NS
Total cholesterol mg/dl, mean ± SD	180.8 ± 29.0	173.9± 34.2	NS
Triglycerides mg/dl, mean ± SD	136.1 ± 56.1	146.1± 64.2	NS
HDL-C mg/dl, mean ± SD	55.2 ± 16.3	55.1± 15.9	NS
Statins, n (%)	9 (10.8)	13(15.7)	NS
Methotrexate, n (%)	71 (85.5)	63 (75.9)	**0.039**
Glucocorticoids, n (%)	49 (59)	40 (48.2)	NS

NS, non-significant; CVRF, cardiovascular risk factors; DM, diabetes mellitus; BMI, body mass index; SBP, systolic blood pressure; HDL-C, high density lipoprotein cholesterol.

Figure 1. Kaplan-Meier survival curve showing 96% probability of remaining alive at 5 years.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1601

AB0118

REMISSION OF ANXIETY AND DEPRESSIVE DISORDERS IMPROVES HAQ TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

A. Abramkin[1], T. Lisitsyna[1], D. Veltishchev[2], O. Seravina[2], O. Kovalevskaya[2], S. Glukhova[1], E. Nasonov[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Vascular Rheumatology, Moscow, Russian Federation; [2]Moscow Research Institute of Psychiatry, Serbsky NMRC PN MoH, Stress Disorders, Moscow, Russian Federation*

Background: Anxiety and depressive disorders (ADD) significantly affect disease activity and functional disability in rheumatoid arthritis (RA) patients. Psychopharmacotherapy (PPT) of ADD attempts to improve RA disease activity and lower progression of functional limitations.
Objectives: To determine factors associated with HAQ treatment response in antidepressants-treated RA-patients at five years endpoint.
Methods: 128 RA-patients (pts) were enrolled, 86% were women with a mean age of 47,4±11,3 (M±SD) yrs. All patients met the full ACR/EULAR 2010 criteria for RA. Functional limitations were assessed using Health Assessment Questionnaire (HAQ), mean HAQ was 1,42±0,78 at baseline. 69,4% RA-pts were already taking prednisone (9 [5; 10] mg/day (Me (25%; 75%)), 84,4% - cDMARDs, 7,8% - bDMARDs (anti-TNF-α – 6,3%, rituximab – 1,6%). ADD were diagnosed by psychiatrist in 123 (96,1%) of RA-pts in accordance with ICD-10 in semi-structured interview. Severity of depression and anxiety was evaluated with Montgomery–Asberg Depression Rating Scale (MADRS) and Hamilton Anxiety Rating Scale (HAM-A). RA-pts with ADD were divided into the following treatment groups: 1 – cDMARDs (n=39), 2 – cDMARDs + PPT (sertraline or mianserine) (n=43), 3 – cDMARDs + bDMARDs (n=32), 4 – cDMARDs + bDMARDs + PPT (sertraline or mianserine) (n=9). Biologics treatment duration varied from 1 to 6 years, antidepressants – from 6 to 96 weeks. Baseline HAQ scores were 1,39±0,75, 1,42±0,9, 1,58±0,76 and 1,38±0,83 in groups 1-4, respectively. At 5-yrs endpoint in 83 RA-pts differences between baseline and endpoint HAQ scores (Δ HAQ = endpoint HAQ – baseline HAQ) were assessed as HAQ treatment response with minimal clinically important difference (MCID) (Δ HAQ ≥ 0,22). HAQ response rates were 4,2%, 65,5%, 47,6% and 76,7% in groups 1-4, respectively, with the lowest response rate in group 1 (p<0,0001). Logistic regression analysis was conducted to determine factors associated with RA remission rate.
Results: By univariate logistic regression, anxiety and depressive symptoms remission at 5-yrs endpoint, baseline HAQ and major depression, lower baseline age, BMI and DAS28, no minor depression and cardiovascular diseases at baseline were significantly (p≤0,2) associated with HAQ treatment response (table 1). These variables were subjected to multivariate stepwise logistic regression. Only remission of anxiety and depressive symptoms at 5-yrs endpoint (OR 6,6 (95%CI 1,78 – 24,43), p=0,005), higher baseline HAQ (OR 2,61 (95%CI 1,12 – 6,11), p=0,027) and lower baseline BMI (OR 0,9 (95%CI 0,85 – 0,96), p=0,001) were independently associated with HAQ treatment response at 5-years follow-up.

Table 1. Factors associated with RA remission at 5 years (univariate logistic regression).

Factor	p	OR	95%CI low	95%CI up
Anxiety and depressive symptoms remission at 5-yrs endpoint	0,007	5,0	1,561	16,016
Baseline HAQ	0,01	2,657	1,264	5,588
Baseline major depression	0,142	2,082	0,782	5,542
Baseline age	0,098	0,992	0,982	1,002
Body mass index (BMI)	0,048	0,981	0,963	1,0
Baseline minor depression	0,167	0,563	0,249	1,273
Cardiovascular diseases	0,1	0,417	0,147	1,183
Baseline DAS28	0,008	0,077	1,071	2,096

Conclusion: higher HAQ and lower BMI at baseline and remission of anxiety and depressive symptoms at 5-yrs endpoint are independently associated with HAQ treatment response (MCID) at 5-years follow-up.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1658

AB0119

DISCORDANCE OF RAPID3 AND CDAI IN RHEUMATOID ARTHRITIS

L. A. Ramrattan[1], Z. Vaghaiwalla[1], S. Singh[1], K. Ramsubeik[1], M. Thway[1], G. Kaeley[1]. *[1]University of Florida, Rheumatology, Jacksonville, United States of America*

Background: The Clinical Disease Activity Index (CDAI) and the Routine Assessment of Patient Index Data 3 (RAPID3) ascertain rheumatoid arthritis (RA) disease activity and inform treatment decisions. The CDAI has provider and patient components, whilst the RAPID3 only has patient driven measures. During the COVID-19 pandemic, telemedicine visits relied on RAPID3 as a clinical outcome measure and subsequently was incorporated into all clinical visits in addition to the CDAI. On an ad-hoc basis, discrepancies were noted for the disease activity level generated by these two measures. The purpose of this retrospective study was to formally analyze the relationship between these measures.
Objectives: To determine the concordance of the outcome measures RAPID3 with CDAI in patients with established RA as a quality improvement project.
Methods: This is a retrospective study of 49 patients that fulfilled the American College of Rheumatology 2010 criteria for Rheumatoid Arthritis. IRB approval was obtained. The medical records of patients seen between June to October 2020 at the rheumatology department at UF health were reviewed. Data collected included age, gender, race, number of years with RA, Rheumatoid factor (RF) and anti-citrullinated protein antibody (CCP Ab) positivity, disease modifying treatments, ESR and CRP as well as CDAI and RAPID3 scores as calculated by clinic staff. The charts were reviewed by the authors and RAPID3 scores were verified.

Table 1. Patient Population

Age	35-90 years
Race	African American-13 Caucasian-10 Hispanic-3 Not Hispanic=13
RF Positive	35/49 (71)%
CCP Ab	37/49 (75%)
Both RF and CCP Ab Positive	32/49 (65%)
Patients on monotherapy	14/48 (29%)
Patients on dual therapy	29/48 (60%)
Patients on triple therapy	5/48 (10)
Antirheumatic Drugs used	Plaquenil, methotrexate, leflunomide, etanercept, adalimumab, infliximab, tofacitinib, upadacitinib, rituximab
CDAI and RAPID3 Concordance	18/49 (37%)
RAPID 3 Higher than CDAI	22/49 (45%)
RAPID 3 lower than CDAI	7/49 (14%)
Incorrect Calculation of RAPID3 by clinic staff	11/42 (26%)

Results: The population ranged from 35- 90 years and duration of RA from 1- 30 years. CCP Ab was present in 75% of patients and RF in 71%. Patients were on DMARDs either monontherapy (29%), dual therapy (60%) or triple therapy (10%). Antirheumatic medications used were plaquenil, methotrexate, leflunomide, etanercept, adalimumab, infliximab, tofacitinib, upadacitinib and rituximab. ESR range was 2-110 and CRP 0.2-83.1. The CDAI and RAPID3 concordance was found to be 37% with RAPID3 being higher in 45% of patients. RAPID3 was lower only in 14% of patients. There was incorrect calculation of the RAPID3 26% of the time by clinic staff. Table 1 summarizes this data. Figure 1 shows RAPID3 and CDAI compared in scatterplots.

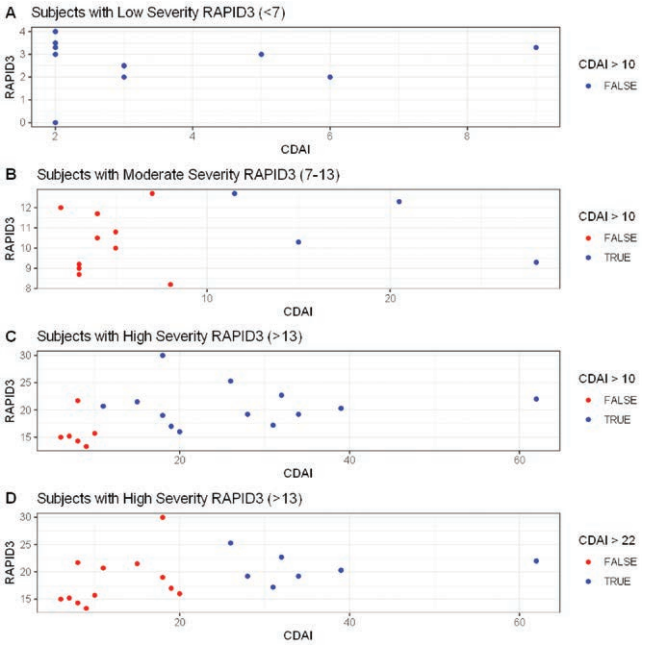


Figure 1. Scatterplots of three RAPID3 strata. Red dots represent discordant subjects when compared to CDAI.Note: Panel C demonstrates the subjects that were in low disease activity in red that had a high severity RAPID3 score

Conclusion: This study shows that RAPID3 may overestimate disease activity level for patients above low disease activity. Treatment escalation based on RAPID3 in discordant patients may be inappropriate. When making treatment decisions, a measure that includes objective physical examination and provider judgment is desirable.

REFERENCES:

[1] Kumar, B. S., Suneetha, P., Mohan, A., Kumar, D. P. & Sarma, K. V. S. Comparison of Disease Activity Score in 28 joints with ESR (DAS28), Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire Disability Index (HAQ-DI) & Routine Assessment of Patient Index Data with 3 measures (RAPID3) for assessing disease activity in patients with rheumatoid arthritis at initial presentation. *Indian J Med Res* **146**, S57–S62 (2017).

[2] Pincus, T., Swearingen, C. J., Bergman, M. & Yazici, Y. RAPID3 (Routine Assessment of Patient Index Data 3), a Rheumatoid Arthritis Index Without Formal Joint Counts for Routine Care: Proposed Severity Categories Compared to Disease Activity Score and Clinical Disease Activity Index Categories. *The Journal of Rheumatology* **35**, 2136–2147 (2008).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1682

AB0120

IDENTIFYING CORE VARIABLES TO DEVELOP A SEVERITY INDEX IN RHEUMATOID ARTHRITIS: A NATIONWIDE DELPHI CONSENSUS

S. C. Rodriguez-García[1], E. Toledano Martinez[2], M. J. García de Yébenes[3], L. Carmona[3], I. González-Álvaro[1]. [1]*Hospital de La Princesa, Rheumatology, Madrid, Spain*; [2]*Hospital Clinico Universitario San Carlos, Rheumatology, Madrid, Spain*; [3]*Instituto de Salud Musculoesquelética (InMusc), Research Unit, Madrid, Spain*

Background: Early interventions during the "window of opportunity" have been shown to improve clinical outcomes in rheumatoid arthritis (RA). However, intensive treatment can induce toxicity so identifying patients most likely to benefit from it is of great importance. Hence, tools for guiding therapeutic decisions in early disease stages are needed.

Objectives: To identify core variables to develop a RA severity index according to an expert panel.

Methods: An expert panel was prompted to analyze relevant variables to define a "severity" construct, specified as "early severe disease", able to classify patients with data collected on the first 2 years of the disease. They were also asked to identify potential modifying factors and external criteria to evaluate criterion validity.

An anonymous nationwide 2-round Delphi survey was applied to look for consensus about: (1) the priority of inclusion of each variable, (2) the feasibility to obtain them from usual sources (e.g., medical records) and (3) their definition. Each item was rated on a 10-point (priority) or 5-point (feasibility and definition) Likert scales were 0=complete disagreement and 5-10=complete agreement.

After the 1st round, any item rated from 5 to 10 in priority and 3 to 5 for feasibility by at least 70% of responders was included in the final variable list. Items not reaching at least 20% consensus were discarded. The remaining ones would be voted again in the 2nd round and adopted if they reached at least 50% consensus or else discarded.

Results: The task force identified 17 variables to define the "severity" construct (Table 1). Socio-economic status, knowledge of their own disease, type or work adherence to treatment, among others were proposed modifying factors. Rheumatoid factor or anti-citrullinated peptide antibody seropositivity as predictive factors The physician global assessment and the "burden of treatment" (lines of treatment, number and dose of DMARDs and cumulative steroid dose received) were proposed for evaluating criterion validity.

A total of 61 stakeholders from across Spain took the survey, 56% were female and had 19.8 years of average experience after training. All variables were included after 1st round. Nonetheless, definitions were submitted for a 2nd round after rephrasing, including comments received on the survey. The final list was reduced to 15 items after merging 3 of the initial variables into a new one called "refractoriness"(Table 1).

Conclusion: The consensus process resulted in a list of variables and modifying factors deemed of relevance for the severity construct as we defined it. These items will be used to develop a severity index to guide treatment decisions in early disease stages.

Table 1. Variables proposed for the severity construct.

N	Initially proposed variables	N	Final variables after Delphi
1	Polyarthritis	1	Polyarthritis
2	Big joint involvement	2	Big joint involvement
3	High disease activity at 2 years of follow-up	3	High disease activity at 2 years of follow-up
4	Maintained disease activity in the first 2 years	4	Maintained disease activity in the first 2 years
5	Acute phase reactants persistently elevated	5	Acute phase reactants persistently elevated
6	Extra-articular manifestations	6	Extra-articular manifestations
7	Failure to reach remission	7	Failure to reach remission
8	Need for aggressive therapy in the first 2 years	*8*	Need for aggressive therapy in the first 2 years
9	Presence of erosions at diagnosis	9	Presence of erosions by at diagnosis
10	Number of erosions at 2 years of follow-up	10	Number of erosions at 2 years of follow-up
11	Lack of improvement in the HAQ-DI	11	Lack of improvement in the HAQ-DI
12	Need for prosthetic surgery	12	Need for prosthetic surgery
13	Hospital Admissions	13	Hospital Admissions
14	Cortico-dependence	14	Cortico-dependence
15	MTX withdrawal due to loss of efficacy	15	*Refractoriness*
16	Completely absent response to MTX		
17	Number of drugs with lack of efficacy		

Underlined variables on the left were merged into a new variable called "Refractoriness". HAQ-DI: Health Assessment Questionnaire-Disability Index

Disclosure of Interests: Sebastián C Rodriguez-García Speakers bureau: Roche, Sanofi, MSD, UCB-Pharma, Bristol-Myers-Squibb, Novartis, janssen, Consultant of: Bristol-Myers-Squibb, Galapagos, ESTHER TOLEDANO MARTINEZ: None declared, María Jesús García de Yébenes: None declared, Loreto Carmona Grant/research support from: Novartis Farmacéutica, SA, Pfizer, S.L.U., Merck Sharp & Dohme España, S.A., Roche Farma, S.A, Sanofi Aventis, AbbVie Spain, S.L.U., and Laboratorios Gebro Pharma, SA, Isidoro González-Álvaro Speakers bureau: Abbvie, MSD, Roche, Lilly, Paid instructor for: Lilly, Consultant of: Lilly, Sanofi, Grant/research support from: Roche

DOI: 10.1136/annrheumdis-2021-eular.1821

AB0121 DOES CIGARETTE SMOKING INFLUENCE DISEASE ACTIVITY IN SEROPOSITIVE (ACPA POSITIVE) PATIENTS WITH EARLY RHEUMATOID ARTHRITIS?

N. Papadopoulos[1], N. Koletsos[2], D. Pantelidis[1], L. Mentesidou[3], V. Galanopoulou[1]. [1]*Papageorgiou General Hospital, Rheumatology Unit, Thessaloniki, Greece*; [2]*Papageorgiou General Hospital, Aristotle University of Thessaloniki, ESH Hypertension Excellence Center, 3rd Department of Internal Medicine, Thessaloniki, Greece*; [3]*Panagiotis and Aglaia Kyriakou Children's Hospital, First Department of Pediatrics, Athens, Greece*

Background: Many studies revealed that cigarette smoking is correlated with more active and severe Rheumatoid Arthritis (RA), mainly through the presence of positive RF or ACPA [1].
Objectives: To investigate the influence of cigarette smoking, in disease activity, in a cohort of Greek patients with ACPA positive early RA.
Methods: From January 2000 until December 2019, 137 patients with seropositive early RA (disease duration ≤ 3 months), and under the age of 75 years old, were diagnosed and subsequently were followed-up as outpatients in Rheumatology Unit of our hospital. All of them were treated by the same therapeutic protocol, were followed-up every 3 months and had at least one visit during 2019. Demographic, therapeutic, clinical and laboratory parameters were evaluated at the time of diagnosis and in every follow-up. At the end of the study we re-evaluated the above parameters, dividing patients in smokers and non smokers.
Analysis were performed using Student's t-test and non-parametric Mann-Whitney was used to estimate differences between mean values. Pearson's and Spearman's correlations were used, based on the variable's normality of distribution with the "Enter" method was used to identify the statistically significant predicting factors of DAS28/associations with DAS28.
Results: Mean age of our cohort were 57±10.2 years and 76.6% were females. From 137 patients 55 were current smokers.
Univariable analysis at the time of diagnosis revealed, that current smokers presented with more tender ($p<0.001$), more swollen joints ($p<0.001$) and higher levels of CRP ($p<0.001$). Also current smokers presented with higher disease activity measuring by DAS-28 4v, than non smokers (6.2±1.0 vs 5.6±0.9 respective, $p<0.001$). At the end of the study there were not found differences between the two groups.
Multivariable analysis revealed that high DAS-28 was correlated with the intensity of smoking ($p=0.049$).
Concerning the presence of extra-articular manifestations, smokers were presented more often with rheumatoid nodes ($p=0.026$).
Conclusion: Current smokers presented with more active disease at the time of diagnosis and have more often rheumatoid nodes. After the establishment of treatment there were no differences in disease activity between smokers and non smokers.
REFERENCES:
[1] Papadopoulos NG et al, Clin Exp Rheum 2005;23:861-66.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1991

AB0122 THE NORA PROJECT - PREDICTION OF THERAPY RESPONSE IN RHEUMATOID ARTHRITIS

L. Mathsson-Alm[1], I. Gehring[2], M. Poorafshar[1], J. Rönnelid[3], J. Askling[4], E. Haavardsholm[5], H. Berner Hammer[5]on behalf of NORA consortium. [1]*Thermo Fisher Scientific, Research and Development, Uppsala, Sweden*; [2]*Thermo Fisher Scientific, Research and Development, Freiburg, Germany*; [3]*Uppsala University, Department of Immunology, Genetics and Pathology, Uppsala, Sweden*; [4]*Karolinska Institutet, Department of Medicine Solna, Stockholm, Sweden*; [5]*Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway*

Background: Personalized medicine in Rheumatoid arthritis (RA) especially regarding therapy response is still in early stages. The Nordic RA (NORA) project is aiming to improve the prediction of therapy outcome by combining established serologic marker with new markers, genetic information and patient-derived data.
Objectives: As an initial step in the project the aim was to select clinically characterized patient cohorts and evaluate if changes or patterns in serological markers could predict therapy response and/or disease progress.
Methods: The ARCTIC (**A**iming for **R**emission in rheumatoid arthritis: a randomised trial examining the benefit of ultrasound in a **C**linical **TI**ght **C**ontrol regimen) study [1] was designed to compare two tight control treatment strategies for early Rheumatoid arthritis and was used as a first cohort. Plasma samples (n=1622) from 224 RA patients from the ARCTIC study were included and taken at baseline and 3, 4, 6, 8, 10, 12, 14, 16, 20, and 24 months from trial start, and analyzed for the presence of EliA™ RF (IgM, IgA, IgG), anti-CCP (IgG, IgA) and anti-RA33 (IgM, IgA, IgG) autoantibodies, as well as Calprotectin using the EliA instrument platform (Phadia AB, Uppsala, Sweden). In addition, a custom-made multiplex chip (Thermo Fisher Scientific, Sweden) [2] was used for measurement of anti-IgG antibodies against RA-specific antigens (citrullinated, acetylated and carbamylated), and established CTD-markers (Connective Tissue Disease), e.g. Ro52/60 and dsDNA. The citrullinated peptides on the multiplex chip were both multiple as well as single citrullinated at different positions within the peptide sequence. Additionally, we included an ELISA to measure antibodies against native human collagen II [3].
Results: The different single assays in the baseline samples varied between 7 – 80% positive test results, e.g. anti-CCP IgG 80%. For some patients we could see changes in levels for anti-CCP, RF and anti-RA33 in the follow up samples, which varied from negative to more than 3-10xULN (Upper Limit of Normal). For anti-CCP IgG we found 9 patients (4%), who changed from negative to positive (patient 1-5) or from positive to negative (patient 6-8), while patient 9 had a peak at visit 6 (=12 months) and declined afterwards (figure 1). In addition, the above mentioned 9 patients showed clear changes in signal strength for the markers included on the multiplex chip and followed a similar pattern as the anti-CCP IgG signal. Different antibody patterns against single citrullinated peptides were observed and number of ACPA-positive peptides correlated with IgG anti-CCP levels.

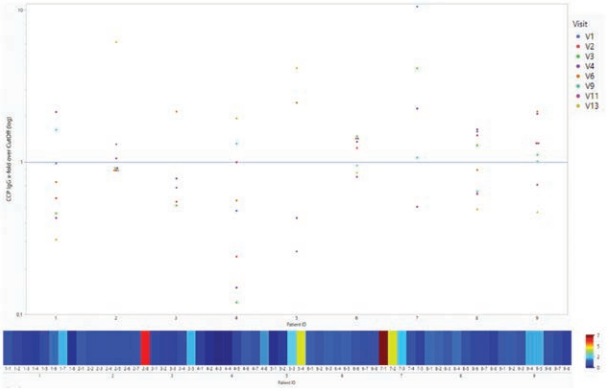


Figure 1. Anti-CCP IgG value normalised to cutoff (blue line) for patient 1 to 9. The heatmap visualizes the change over time in anti-CCP IgG signal with dark blue showing negative results and orange/red showing results >5xULN.

Anti-Collagen II antibodies (anti-CII) were detected in 15% of the baseline samples and in most cases declined over time. Two patients showed low baseline anti-CII levels that increased in the follow up samples. The changes in serological markers and the different reactivity patterns could possibly correlate with clinical outcome and define subgroups of patients with different response to therapy.
Results could be repeated in RA patients from the NOR-VEAC [4] cohort. At baseline 73% of the 106 RA patients had a positive anti-CCP IgG result and 11 patients (10%) showed a significant change of anti-CCP IgG level over time.
Conclusion: Different response patterns and changes in serological antibody levels over the first 24 months after RA diagnosis could possibly reveal subgroups of patients with different prognosis and response to treatment. Further evaluations in additional treatment cohorts and correlation with clinical data are ongoing.
REFERENCES:
[1] Haavardsholm et al., BMJ 2016;354:i4205.
[2] Hansson et al. Arthritis Research & Therapy 2012, 14:R201.
[3] Manivel et al Ann Rheum Dis. 2017 Sep;76(9):1529-1536.
[4] Mjaavatten et al., Arthritis Research & Therapy 2009, **11**:R146.
Acknowledgements: The NORA project is a NordForsk funded project.
Disclosure of Interests: Linda Mathsson-Alm Employee of: Employee of Thermo Fisher Scientific, Isabel Gehring Employee of: Employee of Thermo Fisher Scientific, Maryam Poorafshar Employee of: Employee of Thermo Fisher Scientific, Johan Rönnelid: None declared, Johan Askling Grant/research support from: Research grants from Abbvie, Astra-Zeneca, BMS, Eli Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB, mainly in the context of safety monitoring (ARTIS), Espen Haavardsholm: None declared, Hilde Berner Hammer: None declared
DOI: 10.1136/annrheumdis-2021-eular.2024

AB0123 ANXIETY AND DEPRESSION DURING RHEUMATOID ARTHRITIS

L. Ben Ammar[1], S. Rekik[1], S. Boussaid[1], S. Jemmali[1], E. Cheour[2], H. Sahli[1], M. Elleuch[1]. [1]*La Rabta Hospital, Rheumatology, Tunis, Tunisia*; [2]*La Rabta Hospital, Department of Pain Management, Tunis, Tunisia*

Background: Although the management of rheumatoid arthritis (RA) has been booming since the advent of biological treatments, the consequences of this disease remain multiple, both physical and psychological.

Objectives: The aim of our work was to investigate the factors influencing anxiety and depression in RA.
Methods: This was a cross-sectional study of 49 RA patients. We used the Hospital Anxiety and Depression scale (HAD) to assess anxiety disorders.
Results: We included 24 women and 5 men with an average age of 54.1 years. Sixty-nine percent of patients were unemployed and 81% had health insurance coverage. RA had been evolving for an average of 11.43 ± 7.32 years and the mean time to diagnosis was 2.35 years. It was erosive in 93.8% of cases. An atlanto-axial dislocation was found in 4.1% of cases and coxitis in 8.2% of cases. Eighty-three percent of patients were on cs-DMARDs and 14.2% were on biotherapy. Most patients had low active disease (53%) with a mean DAS28CRP score of 2.74 ± 0.81. Twelve percent of patients had a probable anxiety and 18% had a probable depression.
A long delay in diagnosis was associated with a higher risk of anxiety disorders. Working patients had a lower risk of depression while patients from rural areas had a higher risk. The risk of anxiety and depression disorders was associated with increased VAS pain, EGP, and DAS28. In the multivariate study, EGP was the independent risk factor for the development of anxiety and depression disorders.
Conclusion: Anxiety and depression disorders are a frequent yet underestimated consequence in RA. Appropriate care in psychiatry is required as soon as the diagnosis is announced.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2066

AB0124 STRUCTURAL DAMAGE IN THE FOOT IN RHEUMATOID ARTHRITIS: DON'T MISS THE OTHER METATARSOPHALANGEAL JOINTS

M. Yasmine[1], H. Ferjani[1], D. Kaffel[1], K. Maatallah[1], S. Rahmouni[1], W. Hamdi[1]. [1]*Kassab Institute of Orthopedics, Rheumatology, Tunis, Tunisia*

Background: The foot involvement in rheumatoid arthritis (RA) affects the functionality and the quality of life in patients. Despite this, the clinicians do not give enough care to the foot in RA patients, especially if asymptomatic, resulting in joint damage, deformity, and disability. The distribution of erosions of the other MTP joints (excluding the 5th) has not previously been studied.
Objectives: This study aimed to investigate the distribution of erosions in MTP joints and their clinical implications.
Methods: We conducted a retrospective study including patients with RA according to the American college of rheumatology/ the European league against rheumatism classification criteria. Sociodemographic data, as well as disease activity related characteristics, were recorded.
Posterior–anterior radiographs of the hands and feet of each patient were assessed for erosions.
All patients were assessed by Ultrasonography (US) of the hands. US erosions were scored 0-3 according to Szkudlarek [1]. We divided patients into two groups (G1 without MTPs erosions and G2 with MTPs erosions).
Results: We enrolled forty-two females and eleven males in our studies. The mean age was 58.6 years ±12.7 [23-77], and the mean disease duration was 8.4 years [1-47]. Rheumatoid factor or cyclic citrullinated peptide antibodies (Anti-CCP) were positive in 62.3% of cases. The mean DAS28ESR score was 5.1±1.16 [2.5-7.7]. Half of the patients had the active disease (52.8%). Hand erosions evaluated with plain radiographs and the US were found in 43.1% and 50.9% of cases, respectively. The distribution of foot erosions (15.1%) was at follows: 5th right MTP (7.5%), the 5th right IPP (2%), the 1st left MTP (2%), 3th left MTP (3.8%), 4th left MTP (5.7%) and the 5th left MTP (9.4%). Erosions on MTPs with the exclusion of the 5th MTP were present in 9.4% of cases. The presence of MTPs erosion was more frequent in males (p=0.01) but was not associated with age (p=0.6) or disease duration (p=0.2). Seropositivity was similar between the two groups (p=0.06). Similarly, the inflammatory markers (ESR and CRP), as well as DAS28 ESR, did not differ between the two groups (p>0.05). MTPs erosion was not associated with the presence of hand erosions on a plain radiograph (p=0.445). However, MTPs erosion was significantly more frequent in patients with less erosive hands-on US (p=0.034).
Conclusion: Our study showed that screening of other MTPs (excluding the 5th) is mandatory in RA diagnosis. Interestingly, in our result, MTPs erosion is more frequent in males with less erosive hands.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2227

AB0125 CLINICAL CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS WITH IGG4-RELATED SYNOVITIS

L. F. Chen[1], X. Zhang[1], C. Chen[1], J. D. Ma[1], Y. Mo[1], J. Lin[1], Y. Y. Zou[1], D. H. Zheng[1], L. Dai[1]. [1]*Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Rheumatology, Guangzhou, China*

Background: Elevated serum IgG4 (sIgG4) and IgG4+ plasma cell tissue infiltration are outstanding features of IgG4-related disease (IgG4-RD). However, elevated IgG4 is not specific for IgG4-RD. Our previous study reported elevated sIgG4 in 46% of rheumatoid arthritis (RA) patients (*Mediators Inflamm 2014*). Whether synovium from RA patients show similar characteristics of IgG4-RD and how about the clinical characteristics of RA patients with IgG4-related synovitis have not been reported yet.
Objectives: To explore the serum and synovial IgG4 level and their correlation with disease indicators in RA.
Methods: Active RA patients who underwent needle synovial biopsy with qualified synovium tissue were recruited. Demographic and clinical data were collected simultaneously. Synovium tissue were stained with H&E for Krenn synovitis score and immunohistochemistry for positive cell densities of CD20, CD38, IgG and IgG4. Serum IgG4 level was detected by immunonephelometry.
Results: Among 96 RA patients recruited, 74 (77.1%) were female, the median age was 55.0 (46.0~61.0) years, disease duration was 42.0 (12.0~120.0) months and SDAI was 31.2 (22.1~42.8).
The median sIgG4 was 1.38 (0.86~2.42) g/L and 49(51.0%) patients had elevated sIgG4. Compared with those with normal sIgG4, RA patients with elevated sIgG4 had significantly higher levels of PrGA [7 (5~8) vs. 6 (4~7)], ESR [90 (64~116) mm/h vs. 61 (38~75) mm/h], CRP [46.20 (17.20~74.20) mg/L vs. 18.90 (9.46~49.20) mg/L], DAS28-ESR [6.3 (5.6~7.4) vs. 5.7 (4.7~6.4)], SDAI [34.2 (25.3~48.8) vs. 27.8 (18.9~35.9)] and HAQ-DI [1.70 (0.61~2.28) vs. 0.88 (0.40~1.75), all $P<0.05$]. Meanwhile, they also showed significantly higher synovial counts of CD38+ plasma cells [1240(559~2290) /mm^2 vs. 1020(354~1777) /mm^2], IgG4+ plasma cells [106 (39~249) /mm^2 vs. 68 (3~123) /mm^2], and higher ratio of IgG4+/IgG+ plasma cells [26.3 (15.5~38.0) % vs. 15.2 (0.9~24.7) %, all $P<0.05$].
The median IgG4+ plasma cells count was 83 (10~192) /mm^2 and median ratio of IgG4+/IgG+ plasma cells was 19.1 (8.4~31.5)%. Both of them correlated positively with ESR, CRP and sIgG4 (r=0.216~0.394, all $P<0.05$). There were 46 (47.9%) patients with IgG4+ plasma cells >10/HPF, who had significant higher ESR [86 (50~109) mm/h vs. 65 (40~84) mm/h] and CRP [43.35 (16.93~77.85) mg/L vs. 26.15 (9.54~52.53) mg/L, both $P<0.05$] than those with IgG4+ plasma cells ≤10/HPF. There were 13 (13.5%) patients with the ratio of IgG4+/IgG+ plasma cells >40%, and 11 (11.5%) patients with both IgG4+ plasma cells >10/HPF and IgG4+/IgG+ plasma cells ratio >40% (IgG4-related synovitis). RA patients with IgG4-related synovitis had significant higher ESR than the others [106 (53~125) mm/h vs. 69 (41~91) mm/h, $P<0.05$].
There were 10 (10.4%) patients showing elevated sIgG4 and IgG4-related synovitis. Four patients completed 1-year follow-up and all of them achieved remission at 6th month (SDAI≤3.3, Figure 1). Only one patient had radiographic progression at 12th month.

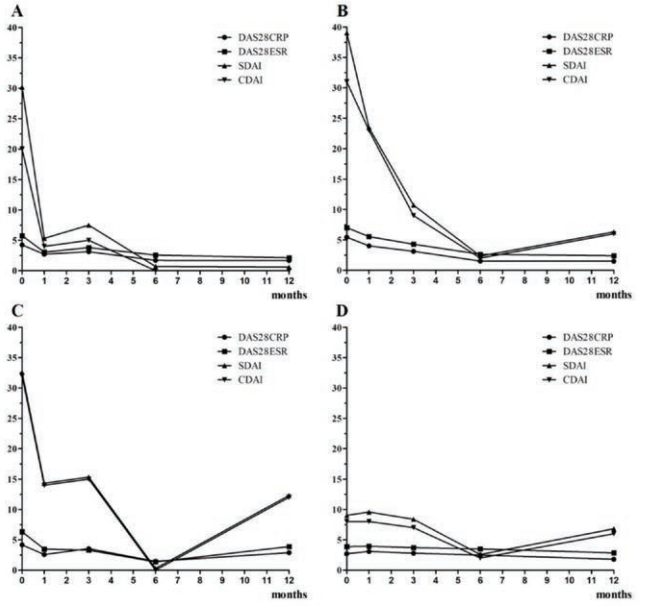


Figure 1. Dynamic disease activity of 4 RA patients with elevated sIgG4 and IgG4-related synovitis during 1-year follow-up.

Conclusion: IgG4-related synovitis can be found in RA patients. Their clinical significance in disease characteristics and outcomes are worth further study.
Acknowledgements: This work was supported by National Natural Science Foundation of China (no. 81971527, 81801606 and 81801605), Guangdong Natural Science Foundation (no. 2018A030313541 and 2018A030313690), Guangdong Medical Scientific Research Foundation (no. A2018062), Guangdong Basic and Applied Basic Research Foundation (no. 2019A1515011928 and 2020A1515110061), and Science and Technology Program of Guangzhou (no. 201904010088).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2245

AB0126 METHOTREXATE MAINTENANCE THERAPY DURING THE TARGETED THERAPY ERA IN RHEUMATOID ARTHRITIS

S. Abdellaoui[1], S. Lefkir[1]. [1]*Issad Hassani Beni Messous Hospital, Rheumatology, Algiers, Algeria*

Background: The persistence with methotrexate (MTX) at 1 year or 5 years in rheumatoid arthritis (RA) is very variable and intolerance remains the main cause of discontinuation of treatment. Changes in treatment with the strategy of adding "add-on" to a targeted therapy when the conventional DMARD becomes insufficient to optimally control the disease may decrease the maintenance MTX therapy rates, particularly for biologics with a Marketing Authorization as monotherapy.
Objectives: The main objective of this study was to determine the rate of maintenance at 1 year of the combination therapy with different biologics, to compare the evaluation scores in patients receiving treatment as monotherapy (biological only) versus combination therapy with methotrexate and to analyze predictive factors for MTX maintenance therapy.
Methods: We performed a descriptive study of 56 patients with RA meeting the criteria of the ACR 2010. Statistical analysis SPSS.20 Software.
Results: These were 56 patients: 93% women and 7% men, mean age 46.74 years with an average duration of the disease of 14.74 years. 71.42% of patients were under corticosteroids taken for a period of 13 years with an average dose of 5.04 mg / day. BMI was highin 23.80% of patients, 30.95% had at least one associated comorbidity. The RF was positive in 61.90% and ACPA positive in 78.57% of cases. 47.62% were under MTX taken for 6.55 years with a dose of 13.03 mg / week on average: 68.75% by oral intake and 31.25% by subcutaneous intake with an average duration of setting before the switch of 8 years. 28 patients were on rituximab, 19 patients on tocilizumab and 9 patients on TNFi. 88.09% did not havenot received from bDMARD before. The mean ESR was 36.57 mm H1 and CRP was 8.56 mg / L. DAS28 at baseline was 6.81 and the current DAS 28 was 2.95 and the HAQ was 1.11. The rate of MTX maintenance therapy at 1 year was 36.84%, with rituximab, 64.28% with tocilizumab and 88% with TNFi. The comparison between the combination therapy with MTX and monotherapy groups showed a significant difference for the number of tender joints NTJ (3.5 vs 2.61), however, no significant difference concerning DAS28 value (2.98 vs 3.06), number of swollen joints NSJ (0.29 vs 0.22) and HAQ (1.09 vs 1.15). Regarding predictive factors of MTX maintenance therapy: Significant correlation was found with a high DAS 28 at baseline, however no correlation concerning the positivity of ACPA, duration of the disease, NTJ, NSJ, ESR, HAQ and the high dose of MTX. Reduction in persistence has found a significant correlation with non-naive RA of ≥ 1 bDMARD, disease activity score, type of biotherapy (antiTNF / rituximab vs Tocilizumab), young age, however no influence was found with a high BMI, HAQ, the presence of comorbidities or the withdrawal of corticosteroids. The increase in the persistence of combination therapy was associated with male gender and RF seropositivity only.
Conclusion: Drug persistence is an important aspect of treatment effectiveness. For rheumatologists, knowledge of the factors that predict whether to maintain the combination therapy with methotrexate, increase or reduce the persistence is of great interest when choosing a new treatment to initiate in patients with RA.
REFERENCES:
[1] Lavielle.M and Dougados.M. Targeted therapies in rheumatoid arthritis: Combination with conventional synthetic disease modifying antirheumatic drugs or monotherapy? Jone Bone Spine 2018;85:3-9.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2346

AB0127 COMBINATION THERAPY WITH METHOTREXATE AND QUALITY OF LIFE IN RHEUMATOID ARTHRITIS

S. Abdellaoui[1], S. Lefkir[1]. [1]*Issad Hassani Beni Messous Hospital, Rheumatology, Algiers, Algeria*

Background: The level of quality of life in patients with rheumatoid arthritis (RA) is often overlooked. These patients suffer from an often-precarious quality of life resulting in pain, joint destruction and fatigue.
Objectives: The main objective of this study was to compare the level of quality of life in patients with RA receiving treatment with disease-modifying anti-rheumatic drugs (DMARDs): monotherapy (biological only) versus combination therapy with methotrexate.
Methods: We performed a descriptive study of 56 patients with RA meeting the criteria of the ACR 2010. The SPSS.20 software was used for statistical analyses.
Results: These were 56 patients: 93% women and 7% men, mean age 46.74 years with an average duration of the disease of 14.74 years. 28 patients were on rituximab, 19 patients on tocilizumab and 9 patients on TNFi. The mean HAQ was 1.11. 52.38% of patients were on biological alone as monotherapy. The Compliance Questionnaire Rheumatology score (CQR19) was 55.15 / 100, the RAID (Rheumatoid Arthritis Impact of Disease) score was 3.08 / 10, the SF36 of 56.01 / 100, the AIMS score of 2.10 / 10 for social activity, 2.44 / 10 for pain, 3.32 / 10 for depression and 4.06 for physical activity.
The comparison between the 2 groups (Combination therapy vs monotherapy) did not find any significant difference in terms of quality of life parameters: An SF-36 score> 55 was found in 56% in patients on combination therapy vs. 44% on monotherapy, the RAID score was 3.02 vs. 3.12, AIMS social activity 2.08 vs 2.13, AIMS pain 2.33 vs 2.59, AIMS activity physics of 4 vs 4.11.
Conclusion: Our study did not demonstrate any superiority of the combination with methotrexate in improving quality of life. The use of biotherapy in patients with RA has been shown to be an important pharmacological strategy for the overall management of the disease.
REFERENCES:
[1] Lavielle.M and Dougados.M. Targeted therapies in rheumatoid arthritis: Combination with conventional synthetic disease modifying antirheumatic drugs or monotherapy? Jone Bone Spine 2018; 85:3-9.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2453

AB0128 CONSTRUCTION OF THE VETERANS AFFAIRS NATIONAL RHEUMATOID ARTHRITIS DATABASE (VANRAD)

A. Joseph[1,2], J. Yanagida[2], X. Huang[1,2], P. Ranganathan[1,2], M. Laurie[3], H. Xian[2,4], S. Eisen[1,2]. [1]*Washington University School of Medicine, Rheumatology, Saint Louis, Missouri, United States of America*; [2]*VA St. Louis Health Care System, Rheumatology, Saint Louis, Missouri, United States of America*; [3]*Bristol Myers Squibb, Health Economics & Outcomes Research, Lawrence Township, United States of America*; [4]*Saint Louis University College for Public Health & Social Justice, Epidemiology & Biostatics, Saint Louis, Missouri, United States of America*

Background: The Department of Veterans Affairs (DVA) provides comprehensive medical care at minimal or no cost to 9 million veterans annually through 170 medical centers and 1074 outpatient clinics across the United States. In 1999, the DVA established a national, fully integrated electronic health record (EHR), which now includes approximately 24 million veterans. However, few studies have used VA EHR data to examine the validity of diagnoses of rheumatoid arthritis (RA).
Objectives: Develop a validated, national database (VANRAD) of patients with RA who received VA care since International Classification of Diseases, tenth revision (ICD-10) coding was introduced in 2015. The database will provide infrastructure for retrospective and prospective research to address the 'real-world' care of patients with RA.
Methods: Patients with the following criteria were identified from the VA EHR as of October 2, 2020: (a) ≥1 ICD-10 diagnosis code of RA; (b) treatment with ≥1 disease-modifying anti-rheumatic drug (DMARD); (c) ≥2 VA rheumatology clinic visits; and (d) ≥1 rheumatoid factor (RF) or anti-cyclic citrullinated peptide (aCCP) antibody test result. From this group, 553 EHRs were randomly selected for review. The 'gold standard' for the diagnosis of RA was the treating rheumatologist's diagnosis, documented in the EHR.
Results: 27,482 patients met eligibility criteria. Sociodemographic characteristics were: 85.6% male, mean age of 69.7 years (y) (SD=10.9 y; range=21.9 y to 100.5 y), 76.4% white, 17.0% African American; and mean VA care duration 14.1 y (SD=5.3 y, range=0.04 y to 20.0 y).
For patients with ≥1 RF or aCCP test, the positive predictive value (PPV) for RA ranged from 65.3% (aCCP-/RF-) to 95.8% (aCCP+/RF+); rheumatologists' likelihood of a 'possible' diagnosis was higher if the aCCP test result was negative or not available (Table 1). Excluding patients with a second rheumatologic diagnosis did not improve PPV results (data not shown).

Table 1. Proportion of patients with a valid RA diagnosis[1] as a function of RF and aCCP laboratory results

Test Result	aCCP			
	Not Available (0)[2]	Negative (-)	Positive (+)	Total
Rheumatoid Factor	Not Available (0) (N = 1253)[3]	N 427 RA[4] 89.7% Poss[5] RA 5.9%	N 1,159 RA 98.2% Poss RA 0.0%	N 1,586 RA 93.5% Poss RA 3.2%
	Negative (-) N 810 RA 86.3% Poss RA 3.9%	N 5,308 RA 65.3% Poss RA 11.9%	N 2,005 RA 94.5% Poss RA 0.0%	N 8,123 RA 80.7% Poss RA 5.8%
	Positive (+) N 2,229 RA 94.6% Poss RA 0.0%	N 2,566 RA 78.0% Poss RA 8.5%	N 12,978 RA 95.8% Poss RA 2.1%	N 17,773 RA 87.6% Poss RA 4.3%
	Total N 3,039 RA 90.7% Poss RA 1.9%	N 8.301 RA 76.1% Poss RA 9.2%	N 16,142 RA 95.9% Poss RA 0.5%	N 27,482 RA 85.9% Poss RA 4.7%

[1]Diagnosis given by the treating rheumatologist.[2]No test results available or test results available but without normal range values.[3]1,253 patients without available or interpretable RF or aCCP excluded from initial cohort.[4]Percent of 553 charts reviewed confirmed as RA.[5]Poss RA = Possible RA. Patients met our inclusion criteria but the treating rheumatologist never made definitive diagnosis of RA or alternative diagnosis (from 553 charts reviewed).

The percentage of RA-confirmed patients with one test not available, whose complementary test was negative (RF0/aCCP- or RF-/aCCP0), was greater than of patients for whom both tests were negative (RF-/aCCP-). This suggests our data extraction methods may be incomplete or that unidentified bias may be present and warrants further study.

Conclusion: Our methodology for constructing an RA database by selecting patients with ≥2 rheumatology clinic visits, ≥1 ICD-10 diagnosis of RA, and treatment with ≥1 DMARD, has high positive predictive value for RA. Positive RF and aCCP test results were strong predictors of rheumatologists' diagnostic certainty for an RA diagnosis. Thus, the VANRAD database and the associated EHR provide opportunity for a wide range of retrospective observational and prospective longitudinal studies based on 'real-world' patient care.

REFERENCES:

[1] Ng B, et al. *Arthritis Care Res* 2012;64:1490-6; Hanly JG, et al. *Open Access Rheumatol* 2015;7:69-75.

Acknowledgements: This study was sponsored by Bristol Myers Squibb.

Disclosure of Interests: Amy Joseph Speakers bureau: Speakers bureau in the distant past., Grant/research support from: Bristol Myers Squibb, Jodi Yanagida: None declared, Xinliang Huang: None declared, Prabha Ranganathan: None declared, Melissa Laurie Shareholder of: Bristol-Myers Squibb, Employee of: I am currently employed by Bristol Myers Squibb., Hong Xian Grant/research support from: Bristol Myers Squibb Co., Seth Eisen Grant/research support from: The effort presented in this Abstract was supported with funds provided by Bristol-Meyers Squibb.

DOI: 10.1136/annrheumdis-2021-eular.2519

AB0129 IL-6R GENETIC VARIANTS AS PREDICTORS OF CLINICAL RESPONSE TO TOCILIZUMAB IN RHEUMATOID ARTHRITIS PATIENTS

L. Sainz Comas[1], P. Riera[2], P. Moya[1], S. Bernal[3], A. Lasa[3], S. Jeria Navarro[1], D. Lobo Prat[1], H. Codes[1], I. Castellví[1], C. Díaz-Torné[1], A. Laiz[1], B. Magallares[1], A. M. Millán Arciniegas[1], H. Park[1], H. Corominas[1]. [1]*Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*; [2]*Hospital de la Santa Creu i Sant Pau, Pharmacy/Genetics, Barcelona, Spain*; [3]*Hospital de la Santa Creu i Sant Pau, Genetics, Barcelona, Spain*

Background: Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory autoimmune disease of unknown etiology. Tocilizumab (TCZ) is a first-line biological disease-modifying anti-rheumatic drug (bDMARD) which inhibits Interleukin 6 (IL-6) pathway through blockade of its receptor. At present, there is a lack of evidence to recommend the treatment of one bDMARD over another.(1) Seeking for genetic biomarkers to predict response to treatment could be key towards a personalized treatment strategy in rheumatology.(2)

Objectives: We aimed to evaluate whether functional single nucleotide polymorphisms (SNPs) in the *IL6R* gene could predict response and/or toxicity to TZC in Caucasian patients diagnosed with RA.

Methods: Retrospective analytical preliminar study of a cohort of 31 patients diagnosed with RA (ACR/EULAR 2010 criteria) who received treatment with TCZ within the last 10 years. Epidemiological, clinical and laboratory data were collected. DNA was extracted from EDTA blood samples. Three SNPs in the IL-6 receptor gene (rs12083537, rs2228145, rs4329505) were genotyped by real-time PCR with TaqMan probes. The associations between polymorphisms and clinicopathological features were evaluated using parametric tests. Efficacy was assessed as the difference of DAS-28 CRP at 6 months. The toxicities recorded were hepatotoxicity, infections, hypersensibility, gastrointestinal, hematological and dyslipidemia.

Results: The 31 DNA samples from patients included were mainly female (83.9%) and had a mean age at diagnosis of 46.8 years. The mean duration of treatment was 51.3 months and, previously to initiate TCZ, they received a mean of 2,6 csDMARD and 1,7 bDMARD.

The more frequent adverse effects were hypertransaminasemia (22.6%) and neutropenia (32.3%). Most relevant epidemiologic and clinical data is shown in Table 1.

Table 1. ***Clinical characteristics. RA=Rheumatoid Arthritis. CCP= anti-Cyclic Citrullinated Peptides. RF=Rheumatoid factor. csDMARDs= conventional synthetic Disease-modifying antirheumatic drug. bDMARD= biological Disease-modifying antirheumatic drug. BMI=Body Mass Index. Sc=subcutaneous. Ev=endovenous. DAS28= Disease Activity Score in 28 joints***

Sex (n=31), n (% women/men)	26/5 (83,9%/16,1%)
Age at diagnosis (n=31), years +- SD	46,8+- 12,8
Erosive RA (n=31), n(%)	14 (45,2%)
Anti-CCP positive (n=31), n(%)	23 (74,2%)
UI+- SD	259,7 +- 137,3
RF positive (n=31), n (%)	21 (67,7%)
UI+-SD	189,4+- 114
Previous csDMARD (n=31), nº+-SD	2,6 +-1,3
Previous bDMARD (n=31), nº+- SD	1,7 +- 1,4
BMI (n=29), mean +- SD	29,3+- 5,1
Duration of treatment (n=31), months +-SD	51,3 +- 36,3
-Active treatment (n=12)	-80,9+- 18,3
-Finished treatment (n=19)	-32,6+- 32,2
Route of administration (n=31), n (%) sc/ev	11/20 (35,5/64,5)
Basal DAS28 (n=30), mean+- SD	5,3 +- 1,1
DAS28 reduction at 6 months (n=28), mean+-SD	2,9 +-1,1

The univariate analyses showed that the rs2228145 variant was statistically associated with differences in DAS28 reduction at 6 months (p=0.042). Regarding efficacy, we also found a trend with the SNP rs4329505 (p=0.173), which could achieve statistical significance with the projected inclusion of more patients. No associations were found regarding adverse effects.

Conclusion: The rs2228145 polymorphisms in the *IL6R* gene may be considered as a pharmacogenetic biomarker of TCZ response in RA patients. More studies are required in order to investigate the clinical use of pharmacogenetic biomarkers in rheumatic diseases.

REFERENCES:

[1] Smolen, Josef S., Robert B., et al. 2020. "EULAR Recommendations for the Management of Rheumatoid Arthritis with Synthetic and Biological Disease-Modifying Antirheumatic Drugs: 2019 Update." *Annals of the Rheumatic Diseases* 79 (6): 685–99.

[2] Tarnowski, Maciej, Agnieszka Paradowska-Gorycka, et al. 2016. "The Effect of Gene Polymorphisms on Patient Responses to Rheumatoid Arthritis Therapy." *Expert Opinion on Drug Metabolism & Toxicology* 12 (1): 41–55.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2615

AB0130 QUESTIONING THE USEFULNESS OF CDAI AS A MEASURE OF DISEASE ACTIVITY IN A TREAT TO TARGET PROGRAMME

C. Lally[1], I. Ali[1], C. Silke[1], B. Whelan[1], M. O'sullivan[1]. [1]*Manorhamilton, Rheumatology, Manorhamilton, Ireland*

Background: Rheumatoid arthritis (RA) is a chronic autoimmune condition which if not treated can lead to joint destruction and long term disability. In RA, the concept of T2T is recommended as the appropriate method to manage early arthritis [1]. It has shown promising results to achieve clinical **remission** (CR) or **low disease activity** (LDA) [2].

Objectives: The objective of this study was to investigate the potential to achieve remission or LDA according to the Clinical Disease Activity Index (CDAI) for RA, during treatment with Disease-Modifying Anti-Rheumatic Drugs (DMARDs) and Biologics, and the factors that affect the remission/LDA outcome.

Methods: We performed an observational prospective study on patients' data available from our Early Arthritis Cohort. All patients with newly diagnosed RA who met the American College of Rheumatology (ACR) criteria were enrolled. Patients are managed by an Advanced Nurse Practitioner (ANP) with consultant supervision. To assess their response to treatment, we used the Clinical Disease Activity Index[3]. Analysis was performed using SPSS.

Results: Out of a total of 459 patients, 353 completed the programme. 217 patients (61.5%) were female and (136) 38.5 % were male. Mean age was 53.98 (SD 14.66). 195 patients were on monotherapy, 40 on combination DMARDs and

115 were on Biologics/Janus Kinase Inhibitors (JAK-Inh). Remission-rates in the monotherapy and combination DMARDs groups were approximately 60%, whilst the remission rate in the Biologics/JAK-Inh group was 41.7%. Amongst female patients 15.9% had erosions on X-ray at the time of diagnosis whilst the equivalent figure for male patients was 29.6%.

Conclusion: An association between male gender and the likelihood of erosions on X-Ray was observed. In addition an association between final medication and outcome was observed. An increased likelihood of non-remission was noted in patients that required escalation to Biologics/JAKs. A possible explanation for the lower levels of remission seen throughout the groups is the difficulty in achieving remission under the CDAI score as compared to DAS-28.

REFERENCES:

[1] Smolen JS, Breedveld FC, Burmester GR, Bykerk V, Dougados M, Emery P, et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. Annals of the Rheumatic Diseases. 2016;75(1):3.

[2] Scott IC, Ibrahim F, Panayi G, Cope AP, Garrood T, Vincent A, Scott DL, Kirkham B; TITRATE Programme Investigators. The frequency of remission and low disease activity in patients with rheumatoid arthritis, and their ability to identify people with low disability and normal quality of life. Semin Arthritis Rheum. 2019 Aug;49(1):20-26. doi: 10.1016/j.semarthrit.2018.12.006. Epub 2018 Dec 28. PMID: 30685064.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2629

AB0131 DIFFERENCES IN CLINICAL PARAMETERS AND LABORATORY DATA OF RHEUMATOID ARTHRITIS PATIENTS IN REMISSION OR WITH LOW DISEASE ACTIVITY TREATED WITH BIOLOGIC AGENTS OR JANUS KINASE INHIBITORS

Y. Hirano[1], J. Hasegawa[1], H. Kosugiyama[2], D. Kihira[2], K. Hattori[2]. [1]*Toyohashi Municipal Hospital, Rheumatology,Toyohashi, Japan*; [2]*Nagoya University Graduate School of Medicine, Orthopaedic Surgery and Rheumatology, Nagoya, Japan*

Background: There are four kinds of drugs for rheumatoid arthritis (RA) patients who are refractory or intolerant to methotrexate (MTX) or other conventional synthetic disease-modifying anti-rheumatic drugs, namely, tumor necrosis factor inhibitors (TNFi), inteleukin-6 inhibitors (IL-6i), abatacept (ABT) and Janus kinase inhibitors (JAKi). Although these drugs have distinct mechanism of action (MOA) to reduce disease activity of RA, the effects of these drugs of reducing disease activity or inhibiting joint damage are similar according past clinical trials. However, their different MOA may induce different change in body of RA patients. If there are some differences in body of RA patients treated different drugs which have different MOA, some differences may appear in clinical parameters and laboratory data we clinician are able to know in daily clinical practice.

Objectives: This retrospective cross-sectional study assessed differences in clinical parameters and laboratory data in RA patients who met the treatment goal with biologic agents (BIO) or JAKi.

Methods: Data from the Toyohashi RA database (TRAD) was used. The TRAD is a collection of single-center retrospective data. Participants were BIO- or JAK-treated RA patients with clinical disease activity remission (REM) or low disease activity (LDA) [clinical disease activity index (CDAI) ≤ 10]categorized by BIO treatment with TNFi (reference), IL-6i, or ABT, and JAKi treatment. Clinical parameters [tender joint counts (TJ), swollen joint counts (SJ), patient's global assessment (PtGA), patient's pain assessment (PainVAS), physician's global assessment (PhGA) and modified health assessment questionnaire (mHAQ)] and laboratory data [C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), matrix metalloprotease-3 (MMP-3), white blood cell counts (WBC), hemoglobin (Hb), platelet cell counts (PLT), neutrophils counts (Neut), lymphocyte counts (Lymph) and estimated glomerular filtration rate (eGFR)] were investigated in cross-sectional manner. They are statistically compared using the Dunnett test.

Results: 171 TNFi, 71 IL-6i, 50 ABT, and 18 JAKi cases are categorized in REM or LDA. Patients' characteristics (means) are as follows (TNFi/IL-6i/ABT/JAKi). Age (63.1/63.7/72.4/60.6; years old), RA duration (17.0/12.7/18.2/11.3; years), %female (83.0/71.8/88.0/83.3), %rheumatoid factor positive (81.9/80.3/90.0/88.9), %anti-cyclic citrullinated peptide antibody (84.6/74.6/97.9/73.3), %prednisolone (PSL) concomitant (3.5/4.2/18.0/11.1) and %MTX concomitant (77.2/15.5/26.0/83.3). Parameters with statistical significance (means) were: TNFi/IL-6i-ESR 34.5/14.0 mm/hr, MMP-3 47.5/71.9 ng/mL, WBC 6124/5404 /μL, Lymph 2112/1646 μL; TNFi/ABT-TJ 0.4/1.0, PtGA 13.3/20.0 mm, PainVAS 15.7/21.6 mm, PhGA 7.4/11.1 mm, CRP 0.1/0.4 mg/dL, ESR 34.5/44.2 mm/hr, MMP-3: 47.5/72.9 ng/mL, Lymph 2112/1816 μL, Neut 3364/4233 μL, eGFR 75.4/65.3 mL/min/1.73m^2; and TNFi/JAKi-PLT 21.7/29.3 104/μL, Lymph 2112/1326 μL.

Conclusion: Although differences of rates of administering concomitant PSL or MTX should be considered, clinical parameter and laboratory data differences result from differences in the targeted cytokine between TNFi and IL-6i, differences in patient characteristics between TNFi and ABT, and differences in the MOA between TNFi and JAKi.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2771

AB0132 THE STUDY OF SUBCLINICAL SYNOVITIS DETECTED BY ULTRASONOGRAPHY AND MRI IN RA PATIENTS AFTER REACHING CLINICAL REMISSION ON PATIENT'S SUBJECTIVE SYMPTOMS

M. Nawata[1,2], K. Someya[1,2], T. Aritomi[1,2], M. Funada[2], K. Nakamura[3], S. Kazuyoshi[1,2], Y. Tanaka[2]. [1]*Tobata General Hospital, Department of Clinical Immunology and Rheumatology, Kitakyushu, Japan*; [2]*School of Medicine, University of Occupational and Environmental Health, Japan,The First Department of Internal Medicine, Kitakyushu, Japan*; [3]*Tobata General Hospital, Department of Radiology, Kitakyushu, Japan*

Background: The goal of treatment in rheumatoid arthritis (RA) is to achieve remission. There is the patient with residual symptoms in the Japanese RA patient who achieved clinical remission. There are not many studies to examine the relation between everyday life, social activity and evaluation of disease activities using high-sensitivity image examinations (musculoskeletal ultrasound (MSKUS) and MRI).

Objectives: To examine the relationship between subjective residual symptoms and imaging examinations in RA patients who have achieved clinical remission.

Methods: 30 RA patients who achieved SDAI remission during RA treatment. Age, sex, disease duration, physical findings, serological markers, disease activity, HAQ, EQ-5D-5L, FACIT-F, Patient Reported Outcomes (PROs), EGA and medications were evaluated. 44 joints were assessed by MSKUS with gray scale (GS) and power doppler (PD) and contrast-enhanced bilateral joint MRI scoring with OMERACT-RAMRIS scoring.

Results: 1. The mean SDAI of the 30 RA patients was 1.3. 2.In the analysis of the presence or absence of subjective residual symptoms that led to remission of SDAI (Table 1).

Table 1.

	Subjective residual symptoms/presence (**N=17**)	Subjective residual symptoms/ absence (**N=13**)	Univariate analysis **p value**	Multivariate logistic analysis **p value**
TJC	0.0±0.0	0.3±0.5	0.0173	
HAQ	0.4±0.4	0.05±0.1	0.0095	0.00181
EQ5D-5L	0.8±0.1	0.9±0.0	0.0001	
FACIT-F	14.5±9.8	4.6±4.3	0.0233	
Morning stiffness (min)	256.5±564.8	0.0±0.0	0.0210	
Pain (VAS) (mm)	9.2±9.5	0.9±1.5	0.0044	0.0455
PGA (mm)	7.7±9.0	0.5±1.1	0.0013	

(1). In the univariate analysis, the number of tender joints, HAQ, EQ-5D-5L, FACIT-F, morning stiffness, and pain VAS were extracted with significant differences. (2). In multivariate logistic analysis, HAQ and pain VAS were extracted as independent factors with significant differences. 3.In univariate analysis of the association between HAQ and pain VAS extracted in multivariate logistic analysis and imaging examinations (MSKUS/MRI), MRI-synovitis was extracted with a significant difference in HAQ.

Conclusion: 1. It was suggested that Pain VAS and HAQ due to RA could be identified in patients reaching SDAI remission. 2. In patients reaching SDAI remission, Pain VAS ≤10 or HAQ ≤0.5 suggested that subjective residual symptoms may be eliminated. 3. HAQ ≤ 0.5 suggests that synovitis is less likely to be detected on MRI. 4. In patients who have reached SDAI remission, little residual inflammation was observed on US, suggesting that induction of remission is important not only to prevent joint destruction, but also to improve and maintain long-term QoL.

Disclosure of Interests: MASAO NAWATA Grant/research support from: I have received research funding from Eli Lilly Japan K.K., Kazuki Someya: None declared, Takafumi Aritomi: None declared, Masashi funada: None declared, Katsumi Nakamura: None declared, SAITO KAZUYOSHI Grant/research support from: I have received research funding from Eli Lilly Japan K.K., Yoshiya Tanaka Speakers bureau: I have received speaking fees from Abbvie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD, and Santen, Consultant of: I have received consulting fees from Abbvie, Daiichi-Sankyo, Chugai, Takeda, Mitsubishi-Tanabe, Bristol-Myers, Astellas, Eisai, Janssen, Pfizer, Asahi-kasei, Eli Lilly, GlaxoSmithKline, UCB, Teijin, MSD, and Santen, Grant/research support from: I have received research grants from Mitsubishi-Tanabe, Takeda, Chugai, Astellas, Eisai, Taisho-Toyama, Kyowa-Kirin, Abbvie, and Bristol-Myers

DOI: 10.1136/annrheumdis-2021-eular.2830

AB0133

LATE-ONSET AND BONE LOSS IN RHEUMATOID ARTHRITIS: WHAT FACTORS SHOULD WE CONSIDER?

K. Maatallah[1], M. Yasmine[1], H. Ferjani[1], W. Triki[1], D. Ben Nsib[1], D. Kaffel[1], W. Hamdi[1]. [1]*Kassab Institute of Orthopedics, Rheumatology, Tunis, Tunisia*

Background: Rheumatoid arthritis (RA) is an inflammatory rheumatism that causes alterations in bone components through the increased production of pro-inflammatory cytokines. Besides traditional risk factors of osteoporosis (OP), elderly RA patients are at higher risk of progressive decline in bone mineral density resulting from the disease.
Objectives: This study aimed to determine factors associated with bone loss in late-onset RA patients.
Methods: A cross-sectional study including patients with RA (according to ACR/EULAR classification criteria) in whom disease onset was after age 65 years. Sociodemographic data, daily calcium intake, and menopausal state were recorded. The characteristics of the disease were transcribed, including inflammatory markers (erythrocyte sedimentation rate (ESR) and C- reactive protein (CRP)), the disease activity assessed by Disease Activity Score 28 (DAS28), seropositivity for anti-cyclic citrullinated peptide antibody (ACPA) and rheumatoid factor (RF), and treatment modalities (cumulative dose of corticosteroids and Methotrexate). Bone mineral density (BMD) was assessed by Dual-energy X-ray absorptiometry. The risk of hip fracture (HF) and major osteoporotic fracture (MOF) after ten years were assessed using the fracture risk assessment tool (FRAX). Patients were divided into two groups (G1 with bone mineral loss (BML) and G2 without BML). Statistical analysis was performed using Kruskal-Wallis Test and chi-square. The level of significance was fixed for $p< 0.05$.
Results: The study included 58 late-onset RA patients with a female predominance (sex ratio M/F=0.3). The mean age was 71.6 ± 5.9 years [65-85], and the mean disease duration was 3.1 ±2.9 years [0-15]. The mean calcium intake was 416.4± 168.6 mg per day [168-1043]. The mean BMD was 1.5 g/cm^2[0.1-28.3] at the vertebral site and 0.7±0.2 g/cm [-0.1,1.2] at the femoral site. Bone loss was found in 55.2% of cases and was significantly associated with age (p=0.022) and longer disease duration (p=0.015). Similarly, there was a positive correlation between CRP and BML (p=0.023). However, bone loss was not correlated to sex (p=0.865), RF and ACPA positivity (p=0.9, p=0.1 respectively), or to coxitis (p=1). Similarly, disease activity, body mass index, and calcium intake were comparable between the two groups (p=0.311, p=0.179, p=0.099, respectively). G1 had a higher incidence of fractures without reaching a statistically significant correlation (63.2% in G1 and 51.3% in G2, p=0.393). Also, G1 had a higher risk of MOF (p=0.003) but not with a higher risk of HP (p=0.127). Regarding treatment modalities, the BML was significantly correlated to non-steroidal anti-inflammatory drug (NSAIDs) intake (85.7% in G1 and 37.8% in G2, p=0.001), but was not correlated to the cumulative dose of corticosteroids (p=0.384) and Methotrexate (p=0.054).
Conclusion: Our study showed that age, disease duration, NSAIDs, and inflammation were risk factors for a bone mineral loss in late-onset RA. Screening for these factors would be useful as part of an ideal form of fracture risk management.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2878

AB0134

RELATIONSHIP BETWEEN INFLAMMATORY RATIOS AND RADIOGRAPHIC JOINT DAMAGE IN RHEUMATOID ARTHRITIS

F. Maatoug[1,2], M. Slouma[1,2], R. Dhahri[1,2], O. Beskri[1,2], I. Gharsallah[1,2], L. Metoui[1,2], B. Louzir[2,3]. [1]*Military Hospital of Tunis, Department of Rheumatology, Tunis, Tunisia*; [2]*University of Tunis El Manar, Faculty of Medicine of Tunis, Tunis, Tunisia*; [3]*Military Hospital of Tunis, Department of Internal Medicine, Tunis, Tunisia*

Background: The tight control strategy is recommended in rheumatoid arthritis to tailor treatment for patients. This strategy requires regular monitoring of both disease activity and structural damage. However, radiographic assessement cannot be performed frequently and the modified Sharp score is rarely evaluated in current practice. Besides, no biomarker was able to mirror structural damage (1).
Objectives: Our study aimed to assess the relationship between the modified Sharp score and the inflammatory ratios (platelet to lymphocyte ratio (PLR), neutrophil to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), fibrinogen to albumin ratio (FAR) and CRP to albumin ratio (CAR)).
Methods: We performed a cross-sectional study including 53 patients with rheumatoid arthritis (RA). A cell blood count, fibrinogen and an albumin blood test were measured for each patient. Inflammatory ratios were also measured (PLR, NLR, LMR, FAR, and CAR). Modified Sharp score and its components (erosion score and joint space narrowing score) were evaluated using the radiograph of hand and foot.
Patients with infectious or hematological diseases were excluded from the study. Statistical analysis was performed using SPSS (Statistical Package for Social Sciences).
Results: Of the 53 patients, 39 were female (Sex Ratio: 2.8). The mean age was 53.9 ± 12.7 years. The mean disease duration was 10.1 ± 8.2 years.The average age of the onset of the disease was 43.8±13.5 years.
The mean DAS 28-ESR score was 4.64 ± 1.23. Forty three patients had a score higher than 3.2 (patients with moderate or high disease activity).
The mean values of PLR, NLR, LMR, FAR and CAR were 161.62 ± 86.59, 2.84 ± 2.39, 4.99 ± 3.23, 0.12 ± 0.06 and 1.15 ± 1.38.
The mean scores of joint erosion and joint space narrowing were respectively 12.76 ± 15.05 and 33.57 ± 25.80. The mean modified Sharp score was 46.33 ± 37.74.
There was a positive correlation between modified Sharp score and following ratios: PLR (r: 0.501; $p <10^{-3}$), NLR (r: 0.302; p:0.031), FAR (r: 0.300; p:0.030), CAR (r:0.286; p:0.042).
Moreover, a positive correlation between joint space narrowing score and these ratios was identified: PLR (r: 0.558; $p <10^{-3}$), NLR (r: 0.428; p:0.002), FAR (r: 0.371; p:0.007), CAR (r:0.387; p:0.005).
Joint erosion score correlated with PLR (r: 0.299; p:0.033).
No correlation was found between LMR and radiographic score.
Conclusion: Our study showed that the modified Sharp score correlated with PLR, NLR, FAR and CAR in patients with RA. This finding suggests that these ratios could be used as inexpensive and reliable markers to reflect radiographic joint damage. Longitudinal studies are necessary to confirm our results.
REFERENCES:
[1] Syversen SW, Landewe R, Van Der Heijde D, Bathon JM, Boers M, Bykerk VP, et al. Testing of the OMERACT 8 draft validation criteria for a soluble biomarker reflecting structural damage in rheumatoid arthritis: a systematic literature search on 5 candidate biomarkers. J Rheumatol. 2009;36(8):1769-84.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2879

AB0135

A VERY EARLY CLINICAL RESPONSE TO TOFACITINIB IS ASSOCIATED WITH LOW RHEUMATOID ARTHRITIS ACTIVITY AFTER 3 AND 6 MONTHS

A. Karateev[1], A. Lila[1], E. Nasonov[1], V. Mazurov[2], D. Chakieva[2], A. Dadalova[2], A. Dyo[3], A. Baranov[4], N. Lapkina[4], E. Koltsova[5], N. Kiryukhina[6], D. Murtazalieva[7], I. Shchendrigin[8], T. Rasevich[9], A. Davydova[10], I. Semizarova[11], I. Shafieva[12], I. Bashkova[13], D. Bobrikova[14], I. Kushnir[15], E. Kalinina[16], T. Salnikova[17], V. Sorotskaya[18], R. Samigullina19, I. Marusenko[20], O. Semagina[21], I. Vinogradova[22], D. Kretchikova[23], M. Semchenkova[24]. [1]*V.A. Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*; [2]*Mechnikov North-Western State Medical University, Rheumatology, St-Petersburg, Russian Federation*; [3]*Mechnikov North-Western State Medical University, Rheumatology, St-Petersburg, Russian Federation*; [4]*Yaroslavl State Medical University, Rheumatology, Yaroslavl, Russian Federation*; [5]*Scientific and Research Institute of Health Care Organization, Rheumatology, Moscow, Russian Federation*; [6]*National Medical and Surgical Center named after N.I. Pirogov" of the Ministry of Healthcare of the Russian Federation, Rheumatology, Moscow, Russian Federation*; [7]*Moscow Clinical Scientific and Practical Centre named after Loginov A.S., Rheumatology, Moscow, Russian Federation*; [8]*Stavropol Regional Clinical Hospital, Rheumatology, Stavropol, Russian Federation*; [9]*Astrakhan Region Alexandro-Mariinsky Regional Clinical Hospital, Rheumatology, Astrakhan, Russian Federation*; [10]*Regional Clinical Hospital №1 named. prof. S.V. Ochapovskogo, Rheumatology, Krasnodar, Russian Federation*; [11]*Regional Clinical Hospital, Rheumatology, Krasnodar, Russian Federation*; [12]*Samara State Medical University of the Ministry of Health of the Russian Federation, Rheumatology, Samara, Russian Federation*; [13]*Advisory Polyclinic Chuvash State University named after I. N. Ulyanov, 428003, Chuvash Republic - Chuvashia, Cheboksary, Russian Federation, Moskovsky Avenue, 9, Rheumatology, Cheboksary, Russian Federation*; [14]*Regional Clinical Hospital No. 1, Rheumatology, Tyumen', Russian Federation*; [15]*Kemerovo Regional Clinical Hospital, Rheumatology, Kemerovo, Russian Federation*; [16]*Volgograd State Medical University, Rheumatology, Volgograd, Russian Federation*; [17]*Regional Clinical Hospital, Rheumatology, Tula, Russian Federation*; [18]*Tula State Medical University, Rheumatology, Tula, Russian Federation*; [3]*Mechnikov North-Western State Medical University, Rheumatology, St-Petersburg, Russian Federation*; [20]*Petrozavodsk State Medical University, Rheumatology, Petrozavodsk, Russian Federation*; [21]*Regional Clinical Hospital, Rheumatology, Samara, Russian Federation*; [22]*Regional Clinical Hospital, Rheumatology, Ulyanovsk, Russian Federation*; [23]*Smolensk State Medical University, Rheumatology, Smolensk, Russian Federation*; [24]*Medical Clinical Centre, Rheumatology, Smolensk, Russian Federation*

Background: JAK inhibitors block intracellular signaling pathways responsible for the synthesis of cytokines and mediators involved in the development of chronic pain and central sensitization (CS). This determines a very rapid clinical response to JAK inhibitors. However, it is not clear how the significant pain reduction in the first weeks of therapy is associated with the achievement of low rheumatoid arthritis (RA) activity.
Objectives: to assess the relationship between the early clinical response to tofacitinib and the decrease in RA activity after 3 and 6 months.

Methods: Study group included 88 patients with RA, their age was 53±11,5, 79.3% of women, 89.8% of RF "+," DAS28 5.2±1.2, receiving DMARDs (methotrexate 59.5% and leflunomide 19.8%), who were administered with tofacitinib 5mg 2 times a day due to inefficacy or intolerance of biological DMARDs. There were assessed the pain severity using Brief pain inventory (BPI) questionnaire, the presence of neuropathic pain component (NPC) using PainDETECT questionnaire and signs of CS using Central Sensitisation Inventory (CSI) questionnaire at early time after tofacitinib administration, RA activity using DAS28 after 3 and 6 months.
Results: The mean pain severity at baseline was 5.3±2.0 according to the visual analogue scale (VAS 0-10), 51.1% of patients had signs of central sensitization (CSI ≥ 40), 15.9% had NPC (PainDETECT ≥18). 7 days after tofacitinib intake there was statistically reliable reduction of pain severity – up to 4.1±1.8 ($p<0.05$) and CS – CSI from 40.4±13.5 to 36.5±12.5 (p=0.01). After 28 days, the effect was higher: the pain level (VAS) was 2.8±1.6 (p=0.000), PainDETECT decreased from 11.8±5.6 to 6.8±3.1 (p=0.000), CSI – to 31.6±13.9 (p=0.000). DAS28 after 3 and 6 months was 3.7±1.3 and 3.6±1.2. The number of patients with pain decrease of ≥50% after 28 days of therapy was 59.9%. Low RA activity after 3 months. (DAS28 ≤3.2) was achieved in 64.4% of patients. There was a clear correlation between the number of patients with significant pain reduction at 28 days and the number of patients with low RA activity after 3 and 6 months (r_S=0.548, p=0.000; r_S=0.790, p=0.000). Six patients withdrew from the study due to inefficacy or social reasons. There were no serious adverse reactions.
Conclusion: The application of JAK inhibitor tofacitinib allows to reach a fast analgesic effect and reduce CS signs. An early clinical response to tofacitinib (pain relief) predicts a decrease in RA activity after 3 and 6 months of the therapy. Limitation: Open-label observatory study.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2902

AB0136 ASSESSING THE RELATIONSHIP AMONG OBESITY, GENETIC POLYMORPHISM, AND CLINICAL PARAMETERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Yoshida[1], S. Hatachi[1], S. Takahashi[1], N. Amano[1], M. Katayama[1], M. Sibata[2], T. Saito[2], S. Kumagai[1,2]. [1]*Shinko Hospital, Center for Rheumatic Diseases, Kobe, Japan*; [2]*Shinko Institute for Medical Research, Kobe, Japan*

Background: Several study suggested body mass index(BMI) may influence development of rheumatoid arthritis(RA). There are conflicting reports concerning the impact of high BMI on development of RA, but several reports of obese on drug resistance and functional impairment. The relationship of genetic polymorphism on obesity is unclear in RA.
Objectives: To examine the relationship among BMI, genetic polymorphism of obesity, disease activity of RA, laboratory parameters, and therapeutic agent of RA.
Methods: We have carried out a retrospective observational study by systematically analyzing medical records of total 289 patients diagnosed with RA in Shinko Hospital between March 2016 and December 2019. We also conducted genotyping single nucleotide polymorphisms (SNPs) including FTO (rs1558902 and rs9939609), UCP1 (rs1800592), ADR2(rs1042713) and ADR3(rs4994) after informed consent. Obesity was defined as BMI over than 25 and patients were divided between obese ("Ob") and non-obese ("non-Ob"). These SNPs, DAS-28CRP, laboratory parameters, methotrexate dose, use of biological DMARDs were compared between Ob and non-Ob patients.
Results: Of these 289 patients, 82.7% was female, mean age was 61.9 years and BMI was 22.4. Univariate logistic regression showed differences ($p<0.1$) between Ob and non Ob groups in UCP1 gene mutation(63.6% vs 78%, P=0.018), DAS(2.24 vs 1.99, P=0.033),triglyceride abnormality(23.8% vs 9.3%, P=0.021), HDL(56 vs 71, P=0.00009), HbA1c abnormality(26.5% vs 12.1%, P=0.019),γGTP(32 vs 21, P=0.00037), ALP (253 vs 230, P=0.0058), ALT (26.5 vs 20, P=0.029),and MTX dose(6 vs 8, P=0.066). Multivariate logistic regression showed that Ob group was significantly associated with HDL(OR=0.976, 95%CI 0.958 to 0.995), UCP1 gene mutation(OR=0.446, 95%CI 0.202 to 0.984), γGTP(OR=2.321, 95%CI 1.269 to 4.245), and MTX dose(OR=0.866, 0.784 to 0.957).
Conclusion: Obesity in patients with RA had significant positive correlation with γGTP, and negative correlation with HDL, UCP gene mutation and MTX dose.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2962

AB0137 THE ASSOCIATION BETWEEN AUTOANTIBODY LEVELS AND THE OUTCOMES OF ANTI-TUMOUR NECROSIS FACTOR ALPHA TREATMENT IN RHEUMATOID ARTHRITIS - A RETROSPECTIVE COHORT STUDY WITH TWO YEARS FOLLOW-UP

D. Santos Oliveira[1,2], A. Martins[1], F. R. Martins[3], M. Rato[1], F. Oliveira Pinheiro[1], D. Fonseca[4], S. Garcia[1], B. M. Fernandes[1], C. Vaz[1,2,5], M. Bernardes[1,5], L. Costa[1]. [1]*Centro Hospitalar Universitário de São João, Rheumatology Department, Porto, Portugal*; [2]*Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; [3]*Centro Hospitalar Universitário do Algarve, Rheumatology Department, Faro, Portugal*; [4]*Centro Hospitalar Vila Nova de Gaia / Espinho, Rheumatology Department, Vila Nova de Gaia, Portugal*; [5]*Faculty of Medicine, University of Porto, Department of Medicine, Porto, Portugal*

Background: In rheumatoid arthritis (RA), autoantibodies namely anticitrullinated protein antibodies (Anti-CCP) have prognostic value, independently predicting radiologic progression. However, the evidence is still controversial about how the autoantibody levels change over time and their role in treatments outcomes and in monitoring disease activity in RA.
Objectives: This study aimed to characterize the changes of autoantibodies levels (rheumatoid factor (RF) and Anti-CCP) over time and to explore the association between these autoantibodies and the outcomes of the first anti-tumour necrosis factor alfa (anti-TNF-α) therapy as first biologic agent in RA.
Methods: An observational retrospective cohort study was conducted with two years of follow-up. Patients with diagnosis of RA according to American College of Rheumatology (ACR) criteria and registered on Rheumatic Diseases Portuguese Register (Reuma.pt) who started their first anti-TNFα agent (as first biologic) between 2003 and 2018 were included. Patients with positive RA (>30 UI/mL) and/or positive Anti-CCP (>10 U/mL) at their first visit were included. Demographic, clinical and laboratory data were obtained by consulting Reuma.pt. Disease Activity Score for 28 joints [DAS28(3v); DAS28(4v); DAS28(3v; C-Reactive Protein (CRP)), DAS28(4v; CRP), delta DAS28(4v)], Health Assessment Questionnaire (HAQ), delta HAQ, Anti-CCP and RF levels were assessed at baseline, 12 and 24 months. Continuous variables are presented with mean, standard deviation, median, quartile 1 and quartile 3. Categorical variables are presented with absolute and relative frequencies. To examine the differences between Anti-CCP and RF levels at baseline, 12 months and 24 months the Wilcoxon test for paired samples was performed. In order to correlate the Anti-CCP and RF levels with DAS28 variables, delta DAS28(4v), HAQ and delta HAQ at baseline, 12 months and 24 months, a correlation coefficient, Spearman's coefficient, was used.
Results: A total of 116 patients (mean age of 50.2±10.4 years old; 85.3% female) with RA were included with a median disease duration of 10.5 [5-18.5] years and a follow-up time of 8 [5-14] years. About 49% of patients were FR and Anti-CCP positivity, 38% only FR positivity and 13% only Anti-CCP positivity. At baseline, 64 (55.2%) patients had an erosive disease and 50 (43.1%) had extra-articular manifestations. Compared to the baseline (160[74.8-496]), FR levels decreased significantly at 12 months (121[49.1-321.8]) and 24 months (107.5[43.3-332]) with a p=0.017 and p=0.029, respectively. There were no differences in Anti-CCP levels over time. No correlation was found between FR/Anti-CCP levels and different DAS28 variables, DAS28(4v) delta, HAQ, and HAQ delta at 12 months and 24 months.
Conclusion: We found that in patients with RA treated with a first anti-TNF-α agent as first biologic, FR levels decreased at 12 months and 24 months follow-up. However, our study failed to demonstrate a correlation between autoantibodies levels and disease activity (DAS28 variables and delta DAS28(4v)), HAQ and delta HAQ. In fact, previous research demonstrated that there is an association between autoantibodies levels and disease activity in RA, nonetheless not being static and increasing with signs of inflammation at baseline. So, further research with large samples is needed to explore this correlation considering the adjustment for confounding inflammatory variables, such as number of swollen or tender joints and morning stiffness.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3218

AB0138 A MOLECULAR SIGNATURE RESPONSE CLASSIFIER STRATIFIES SEROPOSITIVE RHEUMATOID ARTHRITIS PATIENTS BASED ON THEIR LIKELIHOOD OF INADEQUATE RESPONSE TO TNF INHIBITOR THERAPIES

S. Cohen[1], V. Strand[2], E. Connolly-Strong[3], J. Withers[3], L. Zhang[3], T. Mellors[3], V. Akmaev[3]. [1]*Metroplex Clinical Research Center, Rheumatology, Dallas, United States of America*; [2]*Stanford University, Division of Immunology/Rheumatology, Palo Alto, United States of America*; [3]*Scipher Medicine Corporation, Science and Technology, Waltham, United States of America*

Background: There is an urgent need for precision medicine in targeted therapy selection for the treatment of rheumatoid arthritis (RA). TNF inhibitor (TNFi) therapies are the most prescribed targeted therapy for RA patients, yet the majority of patients fail to achieve a clinically meaningful response using this medication class. A blood-based molecular signature test evaluates RNA and clinical metrics to stratify RA patients based on their likelihood of having an inadequate response to TNFi therapies.[1] Patients unlikely to respond to TNFi therapies can be directed to a different treatment option such as a JAK inhibitor, thus reducing the time needed to identify an effective therapy, improving confidence in and adherence to treatment, and increasing the patients' chance of reaching treat-to-target goals.

Objectives: High-titers of anti-cyclic citrillunated protein (anti-CCP) have been independently associated with reduced response to TNFi therapy;[2] thus, we evaluated the ability of a blood-based molecular signature response classifier (MSRC) test to stratify RA patients by their likelihood of inadequate response to TNFi therapies – regardless of their positive or negative anti-CCP status.
Methods: A subset of patients enrolled in the Network-04 prospective observational trial evaluating the ability of a molecular signature response classifier to stratify patients were subdivided into two groups based upon whether they were positive (N = 72) or negative (N = 74) for anti-CCP. The odds of inadequate response to TNFi therapies were calculated based on whether or not a patient had a molecular signature of non-response to TNFi therapy at baseline before the start of treatment. Odds ratios and confidence intervals were calculated[3,4] to represent the strength of association between detecting the molecular signature of non-response and the patient's failure to achieve ACR50 at 6 months.
Results: The odds that a patient with a molecular signature of non-response failed to meet ACR50 criteria at 6 months was approximately three times greater than among those patients who lacked the signal (Table 1). No significant difference in odds ratios was observed between patients who were positive or negative for anti-CCP.

Table 1. The odds of patients with a molecular signature of non-response failing to achieve an ACR50 response 6 months after TNF inhibitor therapy initiation

	Odds ratio (95% confidence interval)
Anti-CCP positive	3.5 (1.3-9.7)
Anti-CCP negative	3.1 (1.2-8.3)

Conclusion: The MSRC test evaluates RA disease biology and accurately stratifies patients based on their likelihood of having an inadequate response to TNFi therapies, regardless of being negative or positive for anti-CCP autoantibodies. Rheumatologists can use the results of the MSRC test to inform targeted therapy selection for RA patients, instead of their anti-CCP serostatus, eliminating the variability inherent to the anti-CCP measurement and its inability to consistently predict TNFi therapy incompatibility. With the MSRC test, providers can rely on a more predictable and accurate assessment of TNFi therapy success or failure when coordinating patient management.
REFERENCES:
[1] Mellors, T. *et al.* Clinical Validation of a Blood-Based Predictive Test for Stratification of Response to Tumor Necrosis Factor Inhibitor Therapies in Rheumatoid Arthritis Patients. *Network and Systems Medicine* **3**, 91-104, doi:10.1089/nsm.2020.0007 (2020).
[2] Braun-Moscovici, Y. *et al.* Anti-cyclic citrullinated protein antibodies as a predictor of response to anti-tumor necrosis factor-alpha therapy in patients with rheumatoid arthritis. *J Rheumatol* **33**, 497-500 (2006).
[3] Szumilas, M. Explaining odds ratios. *J Can Acad Child Adolesc Psychiatry* **19**, 227-229 (2010).
[4] Sperandei, S. Understanding logistic regression analysis. *Biochem Med (Zagreb)* **24**, 12-18, doi:10.11613/BM.2014.003 (2014).
Disclosure of Interests: Stanley Cohen: None declared, Vibeke Strand Consultant of: Abbvie, Amgen, Arena, BMS, Boehringer Ingelheim, Celltrion, Galapagos, Genentech/Roche, Gilead, GSK, Ichnos, Inmedix, Janssen,Kiniksa, Lilly,Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Setpoint, UCB, Erin Connolly-Strong Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Johanna Withers Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Lixia Zhang Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Ted Mellors Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Viatcheslav Akmaev Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation
DOI: 10.1136/annrheumdis-2021-eular.3307

AB0139 RHEUMATOID ARTHRITIS AND SLEEP QUALITY

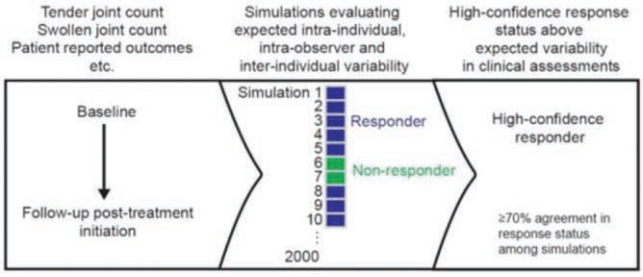
S. Rekik[1], L. Ben Ammar[1], S. Boussaid[1], S. Jemmali[1], E. Cheour[2], H. Sahli[1], M. Elleuch[1]. [1]*La Rabta Hospital, Rheumatology, Tunis, Tunisia*; [2]*La Rabta Hospital, Department of Pain Management, Tunis, Tunisia*

Background: Consequences of rheumatoid arthritis (RA) are many and varied: physical, psycho-affective and financial.
Objectives: The objective of our study is to evaluate the impact of RA on sleep quality.
Methods: We conducted a cross-sectional study including 49 RA patients. An evaluation of sleep quality using the MOS-Sleep Scale was performed.
Results: The mean age of patients was 54.1 years, with a female predominance (89.8%). The mean duration of RA was 11.43 ± 7.32 years with a mean time to diagnosis of 2.35 years. Rheumatoid factor was positive in 77.6% of cases. A atlanto-axial dislocation was found in 4.1% of cases and coxitis in 8.2% of cases. All patients were on symptomatic treatment, 57.1% of whom were on corticosteroid therapy. 83.67% of patients were on cs-DMARDs and 14.2% were on biologics. At inclusion, sleep was optimal in 63.2% of cases and the mean Sleep Problem Index was 26.19 ± 22.77. The index of sleep problems was higher in older subjects and in those with long diagnostic delays. The presence of co-morbidities and atlanto-axial dislocation and/or coxitis was associated with impaired sleep quality. Also, VAS pain and EGP were associated with an increase in the sleep problem index. In the multivariate study, EGP, the presence of co-morbidities and atlanto-axial dislocation and/or coxitis were the independent factors affecting sleep quality.
Conclusion: The impact of RA on the patient's quality of life and especially the quality of sleep is confirmed by several studies in the literature. A global management of the patient is necessary in order to adapt well to his disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3310

AB0140 A HIGH-CONFIDENCE DEFINITION OF THERAPEUTIC RESPONSE IN RHEUMATOID ARTHRITIS USING A MONTE CARLO SIMULATION APPROACH

V. Strand[1], S. Cohen[2], L. Zhang[3], T. Mellors[3], A. Jones[3], J. Withers[3], V. Akmaev[3]. [1]*Stanford University, Division of Immunology/Rheumatology, Palo Alto, United States of America*; [2]*Metroplex Clinical Research Center, Dallas, TX, Rheumatology, Dallas, United States of America*; [3]*Scipher Medicine Corporation, Science and Technology, Waltham, United States of America*

Background: Therapy choice and therapy change depend on the ability to accurately assess patients' disease activity. The clinical assessments used to evaluate treatment response in rheumatoid arthritis have inherent variability, normally considered as measurement error, intra-observer variability or within subject variability. Each contribute to variability in deriving response status as defined by composite measures such as the ACR or EULAR criteria, particularly when a one-time observed measurement lies near the boundary defining response or non-response. To select an optimal therapeutic strategy in the burgeoning age of precision medicine in rheumatology, achieve the lowest disease activity and maximize long-term health outcomes for each patient, improved treatment response definitions are needed.
Objectives: Develop a high-confidence definition of treatment response and non-response in rheumatoid arthritis that exceeds the expected variability of subcomponents in the composite response criteria.
Methods: A Monte Carlo simulation approach was used to assess ACR50 and EULAR response outcomes in 100 rheumatoid arthritis patients who had been treated for 6 months with a TNF inhibitor therapy. Monte Carlo simulations were run with 2000 iterations implemented with measurement variability derived for each clinical assessment: tender joint count, swollen joint count, Health Assessment Questionnaire disability index (HAQ-DI), patient pain assessment, patient global assessment, physician global assessment, serum C-reactive protein level (CRP) and disease activity score 28-joint count with CRP.[1-3] Each iteration of the Monte Carlo simulation generated one outcome with a value of 0 or 1 indicating non-responder or responder, respectively.
Results: A fidelity score, calculated separately for ACR50 and EULAR response, was defined as an aggregated score from 2000 iterations reported as a fraction that ranges from 0 to 1. The fidelity score depicted a spectrum of response covering strong non-responders, inconclusive statuses and strong responders. A fidelity score around 0.5 typified a response status with extreme variability and inconclusive clinical response to treatment. High-fidelity scores were defined as >0.7 or <0.3 for responders and non-responders, respectively, meaning that the simulated clinical response status label among all simulations agreed at least 70% of the time. High-confidence true responders were considered as those patients with high-fidelity outcomes in both ACR50 and EULAR outcomes.
Conclusion: A definition of response to treatment should exceed the expected variability of the clinical assessments used in the composite measure of therapeutic response. By defining high-confidence responders and non-responders, the true impact of therapeutic efficacy can be determined, thus forging a path to development of better treatment options and advanced precision medicine tools in rheumatoid arthritis.
REFERENCES:
[1] Cheung, P. P., Gossec, L., Mak, A. & March, L. Reliability of joint count assessment in rheumatoid arthritis: a systematic literature review. *Semin Arthritis Rheum* **43**, 721-729, doi:10.1016/j.semarthrit.2013.11.003 (2014).
[2] Uhlig, T., Kvien, T. K. & Pincus, T. Test-retest reliability of disease activity core set measures and indices in rheumatoid arthritis. *Ann Rheum Dis* **68**, 972-975, doi:10.1136/ard.2008.097345 (2009).
[3] Maska, L., Anderson, J. & Michaud, K. Measures of functional status and quality of life in rheumatoid arthritis: Health Assessment Questionnaire Disability Index (HAQ), Modified Health Assessment Questionnaire (MHAQ), Multidimensional Health Assessment Questionnaire (MDHAQ), Health Assessment Questionnaire II (HAQ-II), Improved Health Assessment Questionnaire (Improved HAQ), and Rheumatoid Arthritis Quality of Life (RAQoL). *Arthritis Care Res (Hoboken)* **63 Suppl 11**, S4-13, doi:10.1002/acr.20620 (2011).



Disclosure of Interests: Vibeke Strand Consultant of: Abbvie, Amgen, Arena, BMS, Boehringer Ingelheim, Celltrion, Galapagos, Genentech/Roche, Gilead, GSK, Ichnos, Inmedix, Janssen, Kiniksa, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Setpoint, UCB, Stanley Cohen: None declared, Lixia Zhang Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Ted Mellors Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Alex Jones Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Johanna Withers Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation, Viatcheslav Akmaev Shareholder of: Scipher Medicine Corporation, Employee of: Scipher Medicine Corporation
DOI: 10.1136/annrheumdis-2021-eular.3341

AB0141 THE DYNAMICAL TRAJECTORY OF GLUCOCORTICOIDS TAPERING AND DISCONTINUATION IN RHEUMATOID ARTHRITIS PATIENTS COMMENCING GLUCOCORTICOIDS WITH CSDMARDS: A REAL-WORLD DATA FROM 2009 TO 2020

W. Xie[1], H. Huang[1], Z. Zhang[1]. [1]*Peking University First Hospital, Department of Rheumatology and Clinical Immunology, Beijing, China*

Background: Glucocorticoids (GC) are currently recommended as bridging therapy in combination with csDMARDs in rheumatoid arthritis (RA) and should be tapered as rapidly as clinically feasible for safety concerns about their long-term use [1-3].
Objectives: To unravel the dynamical trajectory and characteristics of GCs tapering and discontinuation in RA patients commencing GCs with concomitant csDMARDs.
Methods: We used data from longitudinal real-world TARRA (Treat-to-TARget in RA) cohort in Peking University First Hospital. RA patient who started GCs and contaminant csDMARDs therapy over 1-year follow-up were included. The changes in GCs dose and disease activity in the context of csDMARDs were evaluated. GCs discontinuation rate was analyzed using Kaplan-Meier analysis. The relapse profiles within 6 months after GCs discontinuation were also analyzed.
Results: A total of 207 RA patients were included. During a median follow-up duration of 38.6 months, 124 (59.9%) patients discontinued GC. The median oral prednisolone dose of 10 (5-10) mg/d at initiation was reduced by 50% in the first 6 months and then more slowly reduced, finally to zero by 48 months. The cumulative probability of GCs discontinuation was 26.6% at year 1, 48.0% at year 2, 58.6% at year 3, with calculated median time of 27 months (Figure 1). Of the 124 patients who discontinued GCs, add of other csDMARDs or increment of current csDMARDs was required in 29.0% of them. Approximately half of 124 patients were in clinical remission at the time point of GCs discontinuation. Within 6 months after GCs withdrawal, 79.1% (91/115) of participants maintained relapse-free.

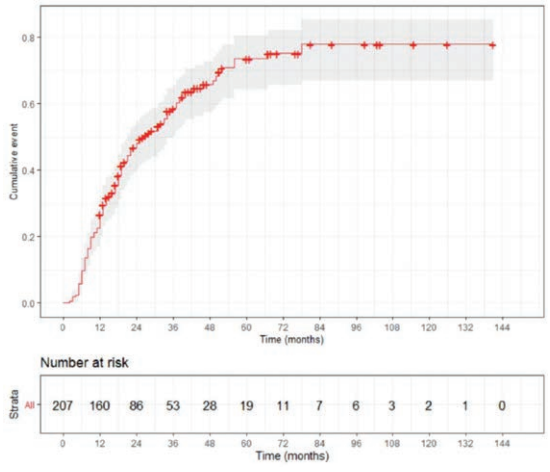


Figure 1. Kaplan-Meier curve with cumulative probability of glucocorticoids discontinuation in RA patients who start glucocorticoids with concomitant csDMARDs during the follow-up period. csDMARDs: conventional synthetic disease modifying antirheumatic drugs.

Conclusion: In RA patients commencing GCs in addition to csDMARDs, GCs are feasibly discontinued with favorable control of disease activity in real-life setting, mostly without short-term flare. Adding targeted therapies are sometimes required to attain GCs discontinuation within the time frame of 3 months in current guidelines.
REFERENCES:

[1] Hoes JN, Jacobs JW, Buttgereit F, Bijlsma JW. Current view of glucocorticoid co-therapy with DMARDs in rheumatoid arthritis. Nat Rev Rheumatol. 2010 Dec;6(12):693-702. doi: 10.1038/nrrheum.2010.179.
[2] Smolen JS, Landewé RBM, Bijlsma JWJ, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Ann Rheum Dis. 2020 Jun;79(6):685-699. doi: 10.1136/annrheumdis-2019-216655.
[3] Conn DL. The Story Behind the Use of Glucocorticoids in the Treatment of Rheumatoid Arthritis. Semin Arthritis Rheum. 2020 Dec 17;51(1):15-19. doi: 10.1016/j.semarthrit.2020.09.016.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3414

AB0142 SOCIOECONOMIC STATUS (SES) AND MEDICATION USE IN RHEUMATOID ARTHRITIS (RA): A SCOPING REVIEW

O. Russell[1], S. Lester[1], R. Black[1,2,3], C. Hill[1,2,3]. [1]*The University of Adelaide, Adelaide Medical School, Adelaide, Australia*; [2]*Royal Adelaide Hospital, Rheumatology Unit, Adelaide, Australia*; [3]*The Queen Elizabeth Hospital, Rheumatology Unit, Woodville South, Australia*

Background: Socioeconomic status (SES) influences disease outcomes in rheumatoid arthritis (RA) patients. (1, 2) Differences in medication use could partly explain this association. (3) A scoping review was used to identify research conducted on this topic and determine what knowledge gaps remain.
Objectives: To determine what research has been conducted on this topic, how this research has defined SES and medication use, and establish what knowledge gaps remain.
Methods: MEDLINE, EMBASE and PsychInfo were searched from their inception until May 2019 for studies which assessed SES and medication use as outcome variables. Studies were included if they measured medication use and incorporated an SES measure as a comparator variable.
SES was defined using any of the "PROGRESS" framework variables (4) including patients' stated gender, age, educational attainment, employment, occupational class, personal income, marital status, health insurance coverage, area- (neighbourhood) level SES, or patients' stated race and/or ethnicity. Medication use was broadly defined as either prescription or dispensation of a medicine, medication adherence, or delays in treatment. Data was extracted on studies' primary objectives, measurement of specific SES measures, patients' medication use, and whether studies assessed for differences in patients' medication use according to SES variables.
Results: 1464 studies were identified by this search from which 74 studies were selected for inclusion, including 52 published articles. Studies' publication year ranged from 1994-2019, and originated from 20 countries; most commonly from the USA.
Studies measured a median of 4 SES variables (IQR 3-6), with educational achievement, area level SES and race/ethnicity the most frequently recorded.
Likelihood of disease modifying antirheumatic drug (DMARD) prescription was the most frequent primary objective recorded.
96% of studies reported on patients' use of DMARDs, with glucocorticoids and analgesics being reported in fewer studies (51% and 23% respectively.)
Most included studies found at least one SES measure to be significantly associated with differences in patients' medication use. In some studies, however, this result was not necessarily drawn from the primary outcome and therefore may not have been adjusted for covariates.
70% of published studies measuring patients' income (n=14 of 20) and 58% of those that measured race/ethnicity (n=14 of 24) documented significant differences in patients' medication use according to these SES variables, although the direction of this effect – whether it led to 'greater' or 'lesser' medication use – varied between studies.
Conclusion: Multiple definitions of SES are used in studies of medication use in RA patients. Despite this, most identified studies found evidence of a difference in medication use by patient groups that differed by an SES variable, although how medication use differed was found to vary between studies. This latter observation may relate to contextual factors pertaining to differences in countries' healthcare systems. Further prospective studies with clearly defined SES and medication use measures may help confirm the apparent association between SES and differences in medication use.
REFERENCES:

[1] Jacobi CE, Mol GD, Boshuizen HC, Rupp I, Dinant HJ, Van Den Bos GA. Impact of socioeconomic status on the course of rheumatoid arthritis and on related use of health care services. Arthritis Rheum. 2003;49(4):567-73.
[2] ERAS Study Group. Socioeconomic deprivation and rheumatoid disease: what lessons for the health service? ERAS Study Group. Early Rheumatoid Arthritis Study. Annals of the rheumatic diseases. 2000;59(10):794-9.

[3] Verstappen SMM. The impact of socio-economic status in rheumatoid arthritis. Rheumatology (Oxford). 2017;56(7):1051-2.
[4] O'Neill J, Tabish H, Welch V, Petticrew M, Pottie K, Clarke M, et al. Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. J Clin Epidemiol. 2014;67(1):56-64.
Acknowledgements: This research was supported by an Australian Government Research Training Program Scholarship.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3439

AB0143 THE EFFECT OF RHEUMATOID ARTHRITIS AND SPONDILOARTHRITIS ON PREGNANCY: A LONGITUDINAL RETROSPECTIVE COHORT STUDY

F. Pistillo[1], A. La Rosa[2], P. De Sandre[3], E. Fracassi[1], G. Scanelli[3], A. Carletto[1], A. Hoxha[3]. *[1]University of Verona, Rheumatology Unit, Verona, Italy*; *[2]San Bortolo Hospital, Department of Obstetrics and Gynecology, Vicenza, Italy*; *[3]San Bortolo Hospital, Department of Medicine, Vicenza, Italy*

Background: Many patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA) are in their childbearing years. Concerns exist regarding the interplay between the rheumatic diseases and the pregnancy (1).
Objectives: Actually, there are contradictory data regarding the pregnancy outcome in patients with RA and SpA (2). Thus, we performed this longitudinal retrospective study to evaluate the effect of RA and SpA on pregnancy outcome.
Methods: The data of 78 pregnancies of 60 women followed from April 2017 to December 2020 at pregnancy clinic of Internal Medicine Unit, San Bortolo Hospital, Vicenza and Rheumatology Unit, University of Verona were reviewed. Fifty (64.1%) women were affected by RA and 28 (35.9%) by SpA. Information regarding demographic data, disease activity, drug exposure and maternal/foetal outcomes were collected in an electronic database. Details concerning pregnancy complications and congenital malformation were also collected. We compared pregnancy and foetal/neonatal outcome, medication use and disease activity between women affected by RA and SpA. Moreover, we evaluated the effect of disease activity on pregnancy outcome.
Results: Overall, there were 70 (86.4%) live births, 10 (12.3%) miscarriages and 1 (1.2%) foetal death. There were three twin pregnancies. Even there was a higher rate of glucocorticoids and bDMARDs use in RA than in SpA group, respectively 40% *vs* 21% and 70% *vs* 57,1%, there were no statistical differences regarding drug exposure at conception. Moreover, there were no differences concerning disease activity at conception. Still, a higher rate of glucocorticoids and bDMARDs, respectively 26% *vs* 10.7% and 46% *vs* 39.3% were used in RA than in SpA patients during pregnancy. Furthermore, we did not find any statistical differences regarding maternal and foetal/neonatal outcome between pregnancies in the RA and those in the SpA groups. There were four (4.9%), congenital malformation, two (3.8%) in RA group and two (6.9%) in SpA group. About one-third of patients 24 (30.7%) presented a moderate disease activity at conception as evaluated by DAS28PCR and BASDAI. However, there were no significant differences, on maternal and foetal/neonatal outcome in patients with moderate activity disease with respect of those in clinical remission.
Conclusion: Even a higher rate of glucocorticoids and bDMARDs were used in RA than in SpA patients, there was no differences on pregnancy outcome between them.
REFERENCES:
[1] Ostensen M. Nat Rev Rheumatol. 2017;13:485-493. doi: 10.1038/nrrheum.2017.102.
[2] Polachek et al. J Rheumatol 2020;47:161-163. doi: 10.3899/jrheum.190631.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3486

AB0144 PREDICTIVE FACTORS OF SUSTAINED CLINICAL REMISSION IN RHEUMATOID ARTHRITIS

R. Fakhfakh[1], N. El Amri[1], K. Baccouche[1], H. Zeglaoui[1], E. Bouajina[1]. *[1]Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*

Background: Sustained remission (SR) is an ultimate treatment goal in the management of patients with rheumatoid arthritis (RA) (1) and is associated with better RA prognosis, reflected by the quality of life, physical function and radiographic progression (2).
Objectives: To investigate the prevalence and predictors of SR in RA patients.
Methods: A longitudinal prospective study of patients with RA. At the inclusion, the patients were in remission DAS28 ESR≤ 2.6 for at least 6 months. A B-mode and power doppler (PD) ultrasound of 42 joints and 20 tendons was performed. Synovial hypertrophy (SH) and tenosynovitis in B-mode and PD were defined and scored from 0 to 3 using the OMERACT. The CDAI, SDAI, Boolean remission criteria, the health assessment questionnaire (HAQ) and the radiological Sharp score were calculated. Then, the $DAS28_{\text{erythrocyte sedimentation rate (ESR)}}$ was evaluated at 6 and 12 months. SR was defined as the persistence of a $DAS28_{ESR}$≤2.6 at 6 or 12 months without any change in RA therapy during the follow-up. Unstable remission (UR) was defined either as $DAS28_{ESR}$ > 2.6 at 6 or 12 months or an increase in RA therapy because of a relapse during the follow-up.
Results: At baseline, thirty-seven patients were included. At 6 and 12 months, 28 and 24 patients completed follow-up, respectively. In decreasing order, Boolean remission (92.2%), $DAS28_{ESR}$remission (85.7%), SDAI remission (85%) and CDAI remission (83.3%) achieved SR at 6 months. At 12 months, SR was found in 100% in Boolean remission, 87.5% in SDAI remission, 86.7% in CDAI remission and in 79.7% in $DAS28_{ESR}$ remission. At 6 months, only the ESR (17mm/1h in SR versus 32mm/1h in UR, p=0.04) was associated with SR. The disease duration, remission duration, swollen and tender joints, $DAS28_{ESR}$, HAQ, rheumatoid factor, radiological Sharp score and ultrasound parameters weren't associated with SR. At 12 months, the squeeze test (15% in SR vs 80% in UR, P=0.01), the ESR (15mm/1h in SR versus 30mm/1h in UR, p=0.03), the Boolean remission (61.1% in SR versus 0% in UR, p=0.04) and the $DAS28_{ESR}$ (mean: 1.8 in SR versus 2.5 in UR, P=0.01) were associated with SR. However, no association was found with radiological Sharp score and ultrasound parameters. On multivariate analysis, the ESR (OR=1.13, CI95%=1.01-1.2, p=0.03) and the Squeeze test (OR=21.3, CI95%=1.7-263, p=0.01) were predictors of SR, at 12 months.
Conclusion: At 6 and 12 months, 79.7%-85.7% of patients in $DAS28_{ESR}$ remission achieved sustained remission, respectively. Boolean and $DAS28_{ESR}$ remission were associated with SR. Unlike $DAS28_{ESR,}$ Boolean remission seems to reflect more the SR. The squeeze test and the ESR were predictors' factor. However, the radiological and the ultrasound parameters didn't show any association.
REFERENCES:
[1] Ajeganova S, Huizinga T. Sustained remission in rheumatoid arthritis: latest evidence and clinical considerations. Ther Adv Musculoskelet Dis. 2017;9(10):249-62.
[2] Xie W, Li J, Zhang X, Sun X, Zhang Z. Sustained clinical remission of rheumatoid arthritis and its predictive factors in an unselected adult Chinese population from 2009 to 2018. Int J Rheum Dis. 2019;22(9):1670-8.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3555

AB0145 SMARTPHONE- AND SMARTWATCH-ACQUIRED DAILY STEPS, ACTIVITY, AND BAROMETRIC PRESSURES ASSOCIATED WITH SUBJECTIVE MEASURES OF RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY FOR RA DIGITAL PHENOTYPING

K. Izumi[1,2,3], D. Moriwaki[3,4,5], T. Toda[5,6], M. Higashida-Konishi[2], M. Koyama[2], H. Oshima[2], Y. Okano[2], Y. Kaneko[1], S. Ko[3,5], T. Takeuchi[1]. *[1]Keio University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan*; *[2]National Hospital Organization Tokyo Medical Center, Division of Connective Tissue Diseases, Tokyo, Japan*; *[3]Keio University School of Medicine, Medical AI Center, Tokyo, Japan*; *[4]CyberAgent, Inc., AI Division, Tokyo, Japan*; *[5]Keio University School of Medicine, Department of Systems Medicine, Tokyo, Japan*; *[6]AI Shift, Inc., Machine Learning Engineering, Tokyo, Japan*

Background: Symptoms in patients with rheumatoid arthritis (RA) are potentially influenced by exercise load and meteorological change, and often vary from day to day, especially in unstable condition of RA. Patients with RA not infrequently experience worsening of joint symptoms when the load on the joint, such as walking and doing housework, exceeds a moderate range. However, the worsening of joint symptoms is often not observed in the midst of the loading of the joint, but often becomes apparent after a few hours or days.
Objectives: To elucidate the relationship between smartphone- and smartwatch-acquired daily objective data (barometric pressures, steps, and activity) and daily subjective patient reported outcomes of RA.
Methods: A smartphone (iPhone 8) and a wristband-type smartwatch (Fitbit Versa 2) were lent to each patient for free. A mobile app was developed and installed into the smartphones to collect patients' daily subjective RA symptoms including Pt-P-VAS (patient-pain-visual analogue scale), Pt-G-VAS (pt-general-VAS), PtTJCount(68)(patient self-determined tender joint count among 68 joints), PtTJCount(28), PtSJCount(66)(patient self-determined swollen joint count among 66 joints), PtSJCount(28). Also, the smartwatch data and physicians' assessment were collected from the same subject. Physicians' and patients' assessment of TJC, SJC, and G-VAS was independently performed without seeing each other's assessment. We conducted a simple linear regression analysis with outcome variables of Pt-P-VAS, Pt-G-VAS, PtTJCount(68), PtTJCount(28), PtSJCount(66), and PtSJCount(28). The independent variables included smartphone-acquired daily steps and barometric pressure of the reported day and the previous day, and smartwatch-acquired minutes of "lightly active (1-3 METs equivalent)", "fairly active(3-6 METs equivalent)", and "very active(>6 METs equivalent)" of the reported day and previous day. We defined low barometric pressure as below 1000 hPa. The level of activity was measured by the smartwatch. Patients were blinded to daily barometric pressure data and their daily active time when the patients answered daily symptom questions on the smartphones.

Results: A total of five patients were enrolled. At baseline, mean (± standard deviation (SD)) age was 50.8±14.8 years; all patients were females; mean disease duration was 6.6±4.9 years; mean SDAI was 18.6±25.5; mean DAS28-CRP was 3.23±1.85; mean morning stiffness was 134±116 min; mean HAQ-DI was 0.7±0.9. Mean observation period was 77.8 days. Because of the missing data, the sample size (N) for the regression analysis varies with the outcomes: Pt-P-VAS and Pt-G-VAS are 250 while PtTJCount and PtSJCount are 260.
The table 1 showed that the patients' assessment of TJC, SCJ, and G-VAS was correlated well with the physicians' assessment.

Table 1.

Evaluation item	Correlation between physicians and patients (ρ)
Tender Joint Count (68)	0.909
Tender Joint Count(28)	0.913
Swollen Joint Count(66)	0.896
Swollen Joint Count(28)	0.890
General VAS	0.688

The figure 1 showed the change associated with one SD increment in each independent variable with 90% confidence intervals. Low barometric pressure was associated with bad health conditions (high Pt-G-VAS, Pt-P-VAS, and SJCount). Moreover, longer very active time in the previous day ("veryactive_1" in the Figure 1) was associated with bad health condition (high SJCount). Many steps were associated with good health conditions (low Pt-G-VAS, Pt-P-VAS, and SJCount).

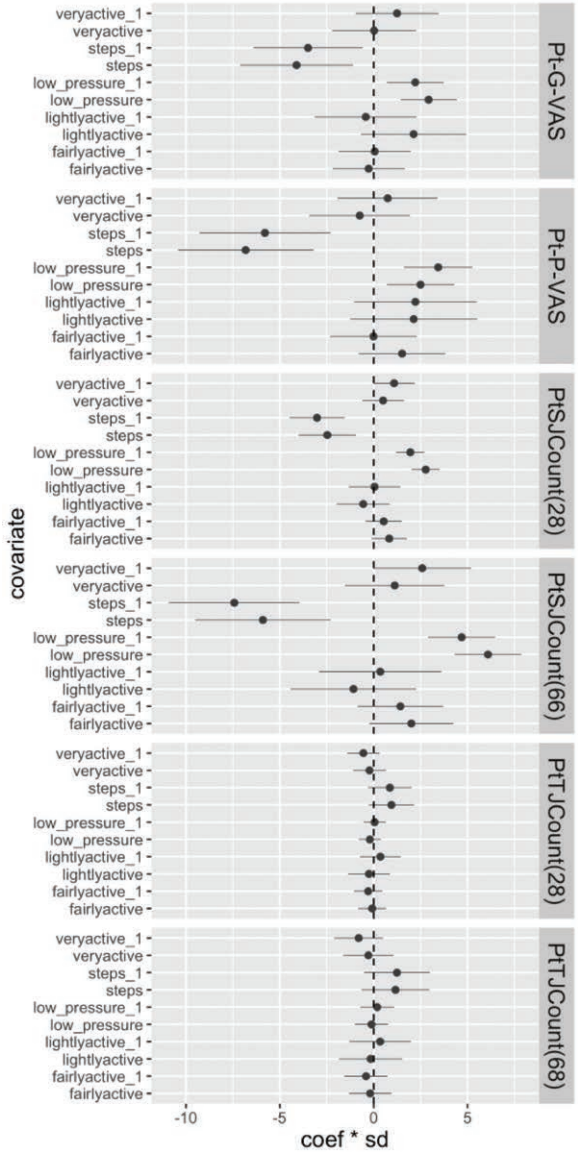


Figure 1.

Conclusion: High barometric pressure was associated with good health conditions, and longer very active time in the previous day was associated with bad health condition. Barometric pressure data and physical activity data acquired by mobile digital devices may predict the change in RA symptoms. Further investigation in larger patient numbers is warranted.
Acknowledgements: The authors would like to thank Harumi Kondo for her assistance.
Disclosure of Interests: Keisuke Izumi Speakers bureau: Abbvie, Asahi Kasei Pharma, Bristol Myers Squibb, Chugai Pharmaceutical, Eli-Lily, Mochida Pharmaceutical, Ono Pharmaceutical, Grant/research support from: Abbvie, Asahi Kasei Pharma, Daisuke Moriwaki Employee of: CyberAgent, Inc., Takamichi Toda Employee of: AI Shift, Inc., Misako Higashida-Konishi: None declared, Manami Koyama: None declared, Hisaji Oshima: None declared, yutaka okano Speakers bureau: Asahi Kasei Pharma, Yuko Kaneko Speakers bureau: AbbVie, Astellas, Ayumi, Bristol–Myers Squibb, Chugai, Eisai, Eli Lilly, Hisamitsu, Jansen, Kissei, Kirin, Novartis, Pfizer, Sanofi, Takeda, Taisho, Tanabe-Mitsubishi, and UCB, Shigeru Ko: None declared, Tsutomu Takeuchi Speakers bureau: Abbott Japan Co, Ltd, Bristol–Myers KK, Chugai Pharmaceutical Co, Ltd, Eisai Co, Ltd, Janssen Pharmaceutical KK, Mitsubishi Tanabe Pharma Co, Pfizer Japan Inc, Takeda Pharmaceutical Co, Ltd, Astellas Pharma and Daiichi Sankyo Co, Ltd., Consultant of: Astra Zeneca KK, Eli Lilly Japan KK, Novartis Pharma KK, Mitsubishi Tanabe Pharma Co, Asahi Kasei Medical KK, Abbvie GK and Daiichi Sankyo Co, Ltd., Grant/research support from: Abbott Japan Co, Ltd, Astellas Pharma, Bristol-Myers KK, Chugai Pharmaceutical Co, Ltd, Daiichi Sankyo Co, Ltd, Eisai Co, Ltd, Janssen Pharmaceutical KK, Mitsubishi Tanabe Pharma Co, Pfizer Japan Inc, Sanofi–Aventis KK, Santen Pharmaceutical Co, Ltd, Takeda Pharmaceutical Co, Ltd, Teijin Pharma Ltd, Abbvie GK, Asahikasei Pharma Corp and Taisho Toyama Pharmaceutical Co, Ltd.
DOI: 10.1136/annrheumdis-2021-eular.3730

AB0146

HAND AND WRIST ACTIVE RANGE OF MOTIONS AND CONTRIBUTING FACTORS IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY

M. He[1], W. Zhou[1], J. Guo[1], J. Liu[1], C. Dong[1], R. Zhao[1], Z. Gu[1]. [1]*Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*

Background: Patients with rheumatoid arthritis (RA) usually impaired range of motions (ROMs), especially hand and wrist active ROMs (AROMs), thus influencing their ability to perform daily activities and health-related quality of life (HR-QoL). However, little is known about the potential factors of reduced hand and wrist AROMs and their relations to quality of life in Chinese RA patients.
Objectives: To explore the contributing factors of hand and wrist AROMs and their associations with HR-QoL and functional limitation in Chinese RA population.
Methods: In this cross-sectional study, 108 patients were enrolled from Affiliated Hospital of Nantong University between November 2018 and July 2019. We measured all the participants' AROMs with different directions of the hand and wrist in both sides, including volar flexion, ulnar deviation, radial deviation and radial deviation of the wrist joint, the first metacarpophalangeal (MCP1) flexion, interphalangeal (IP) flexion, volar abduction, radial abduction and thumb opposition (cm) in the thumb, average flexion, hypertension and abduction of the MCP2-5, average proximal interphalangeal (PIP) 2-5 and distal interphalangeal (DIP) 2-5 flexions, total active range of motion (TAM) of the second to the fifth fingers (TAM2-TAM5). Their sociodemographic, physical, psychological, disease-related data, acute phase reactants, laboratory indicators, drug usage and HR-QoL were examined as well. Statistical analysis used Pearson's and Spearman's correlation analysis, univariate and multivariate linear regression analyses.
Results: In univariate analyses, we found that living in rural area, longer disease duration, comorbidity, hospitalization, more swollen joints, higher disease activity, pain level, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), red blood cell count and glucocorticoids usage were associated with most of the decreased hand and wrist AROMs ($P \leq 0.050$), while higher education and annual income were related to most of the increased hand and wrist AROMs ($P \leq 0.048$). In multivariate analyses, higher disease duration ($P \leq 0.023$) and higher disease activity ($P \leq 0.033$) were corelated with most of the decreased hand and wrist AROMs. Interestingly, the psychological factor, anxiety, was only positively associated with thumb opposition in both univariate and multivariate analyses ($P \leq 0.001$). Additionally, most of the declined hand and wrist AROMs were associated with functional impairment and poor HR-QoL, especially in physical components ($P < 0.05$).
Conclusion: Various factors, especially longer disease duration and higher disease activity, were related to decreased hand and wrist AROMs, and thus causing functional impairment and poor HR-QoL in RA patients. Clinical physicians and medical faculties should pay more attention to disease activity and disease-related symptoms of these patients in order to maintain their activity of daily living (ADL) ability and improve HR-QoL.

REFERENCES:
[1] Rheumatoid arthritis. Nat Rev Dis Primers. 2018;4:18002.
[2] Zhang L, Cao H, Zhang Q, Fu T, Yin R, Xia Y, et al. Motion analysis of the wrist joints in Chinese rheumatoid arthritis patients: a cross-sectional study. BMC Musculoskelet Disord. 2018;19(1):270.
Acknowledgements: This work was funded by Postgraduate Research & Practice Innovation Program of Jiangsu Province (Grant/Award number: KYCX19_2071), National Natural Science Foundation of China (Grant/Award number: 81871278, Science and technology Project of Jiangsu Province (Grant/Award number: BE2018671)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3763

AB0147 OLDER AGE AT ONSET AND NOT DISEASE ACTIVITY IS ASSOCIATED WITH FUNCTIONAL DISABILITY AT RA DIAGNOSIS: RESULTS FROM AN EARLY ARTHRITIS COHORT

A. R. Prata[1], M. Sousa[1], H. Assunção[1], L. Saraiva[1], M. Luis[1], L. Brites[1], F. Campos Costa[1], J. Dinis de Freitas[1], T. Santiago[1], J. A. P. Da Silva[1], C. Duarte[1]. [1]*Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal*

Background: Rheumatoid Arthritis (RA) is a chronic inflammatory arthropathy that potentially leads to loss of function and disability early in the disease course. (1) Optimizing physical function is one of the primary goals of RA treatment (2). Several demographic, psychosocial and clinical factors may influence the impact of RA upon physical capacity, and understanding their relative contribution to disability at disease diagnosis is key to an effective treatment approach.
Objectives: To evaluate functional disability at the time of disease diagnosis and identify its demographic and clinical correlates in an early RA cohort.
Methods: We conducted a cross-sectional study based on a Rheumatology centre early arthritis cohort. Consecutive patients with early RA – less than 12 months duration– fulfilling ACR/EULAR 2010 and/or ACR 1987 RA classification criteria, were included. Variables were collected from patients' registries at the first rheumatology appointment after symptom's onset. Functional disability was assessed using the *Health Assessment Questionnaire- Disability Index* (HAQ-DI) (range 0 to 3, higher values indicating greater disability). Independent *t*-test, one way-ANOVA and Pearson's correlation coefficient were performed to evaluate differences between groups. Variables with p<0.1 were included in a stepwise multiple linear regression analysis to assess the independent association of variables with the HAQ-DI at baseline.
Results: We included 71 patients (63.4% female, mean age 57.2 ±2.01 years). Mean HAQ-DI score was 1.42±0.08. Sociodemographic and clinical variables are described in Table 1. There was a significant difference in HAQ-DI scores between rheumatoid factor (RF) positive (mean 1.24±0.11) and RF negative (1.61±0.113) patients. HAQ-DI was positively weakly correlated with age (r=0.48; p<0.001), CDAI (r=0.43; p=0.038), SDAI (r=0.49; p=0.015), and moderately with DAS28-3V (r=0.60; p<0.001) and DAS28-3V-CRP (r=0.60; p<0.001). The number of tender (r=0.35; p=0.024) and swollen joints (r=0.42; p= 0.005), ESR (r=0.46; p=0.001), CRP (r=0.35; p=0.018), HADS-depression (r=0.46; p=0.023) and educational level (r= -0.48; p=0.002) were also associated with HAQ-DI in univariate analyses. After multivariate regression analysis, age at disease diagnosis (β= 0.022 [95 CI 0.010 to 0.034]; p= 0.001) was the only independent predictor of HAQ-DI (R^2= 0.46, p=0.001).

Table 1. Patients' baseline sociodemographic and clinical characteristics.

Age at diagnosis (years), mean (SD)	57.2±2.01
Educational level (years), mean (SD)	7.37±0.59
Employment: full-time, %	42.4
Employment: partial-time, %	3.00
Employment: retired, %	48.4
Employment: absenteeism in the last month, %	1.50
Unemployed, %	4.50
Disease duration at presentation (weeks), mean (SD)	20.4±1.70
Morning stiffness >30 minutes, %	83.0
RF positivity, %	47.9
ACPA positivity, %	53.5
Fibromyalgia, %	6.60
DAS28-3V, mean (SD)	4.72±0.17
CDAI, mean (SD)	29.2±2.28
SDAI, mean (SD)	32.4±2.42
PtGA, mean (SD)	66.8±3.73
PhGA, mean (SD)	54.7±3.08
Pain intensity (VAS), mean (SD)	67.7±3.75
EQ-5D score, mean (SD)	0.26±0.039
HADS-depression, mean (SD)	7.17±0.87

Legend: ACPA- anti-citrullinated protein antibodies; ESR- erythrocyte sedimentation rate; CRP- c-reactive protein; DAS- disease activity score; CDAI- clinical disease activity score; SDAI-simplified disease activity score; PtGA/ PhGA – patient's/physician's global assessment of general health; VAS- visual analogic scale; EQ-5D- EuroQoL 5-Dimensional Descriptive System; HADS-Hospital Anxiety and Depression Scale.

Conclusion: Older age at disease onset is associated with greater functional impairment at diagnosis, assessed by HAQ-DI, in this cohort of early RA patients, irrespective of disease activity and other clinical variables. This result suggests that older newly diagnosed RA patients may deserve special attention regarding physical function.
REFERENCES:
[1] Wolfe F et al. Arthritis Res Ther. 2010; 12(2): R35.
[2] Smolen JS et al. Ann Rheum Dis. 2010; 69:631-637.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3855

AB0148 CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS WITH HIP INVOLVEMENT

H. Hajji[1], K. Maatallah[1], H. Ferjani[1], W. Triki[1], D. Ben Nessib[1], D. Ameni[1], D. Kaffel[1], W. Hamdi[1]. [1]*Kassab Institute, Tunis;, Rheumatology, Tunis, Tunisia*

Background: Rheumatoid arthritis (RA) is an autoimmune inflammatory disease that affects both small and large joints. Hip involvement is an evolutionary turning point in RA and significantly alters the patient's quality of life.
Objectives: This study aimed to assess characteristics of RA patients with hip involvement.
Methods: It was a cross-sectional study, including patients with RA (according to 2010 ACR/European League Against Rheumatism (EULAR) criteria). We divided patients into two groups: G0 patients without hip involvement, G1 patients with hip involvement. Hip involvement was defined with a limited movement during examination with abnormalities on standard radiographs. We collected the following data: age, the disease activity score (DAS28), the inflammatory biomarkers C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR), Rheumatoid Factor (RF), and Anti Citrullinated Peptides Antibodies (ACPA), and SHARP score (A scoring system used to assess the radiological changes in patients with RA. It describes erosions and narrowing of the joint space of 27 small joints of the hands, including the carpal bones and feet).
Results: Among the 224 patients included, 25had hip involvement (11%). The male / female sex-ratio was higher in G1 (0.66 vs 0.22, p=0.017).Patients in G1 were younger at disease onset (44,16±16,11 years vs 51.9±13.9 years, p= 0.022) and had a longer disease duration (12,28 ± 11,49 years vs 6,2010 ± 6,45 years, p=0.02). They had also higher HAQ(1,7692 vs 1,3054, p=0.05).SHARP score was higher in G1 (176.32 vs. 106.88, p=0.011). Atlantoaxial subluxation was more common in G1 (32% vs 14%,p=0.035).When comparing the groups we did not find any significant difference regarding age (56.12 ± 11.88 years vs 58,24±12,26 years, p=0.341), disease activity (DAS28-ESR:5.41 vs. 5.65, p=0.380; DAS28-CRP: 5.19 vs. 5.51, p=0.290), ESR (53.88 vs. 46.95, p=0.237), CRP:23,8894 vs 22,89, p=0.975), and in the serological profile (RF; G1:68% vs G0: 70.8%, p=0.817, ACPA; G1: 60% vs G0:69%, p=0.366).
Conclusion: Patients with hip involvement were commonly male, were younger at disease onset and had more functional impairment based on the HAQ score. C1-C2 dislocation wasalso more common in this group.The SHARP score was also significantly higher in G1, which shows a severe and destructive disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3963

AB0149 CHARACTERISATION OF RHEUMATOID ARTHRITIS PROGRESSION IN AN EARLY UNDIFFERENTIATED ARTHRITIS COHORT

M. Novella-Navarro[1], J. L. Cabrera-Alarcón[2], A. Martínez-Feito[3], L. Nuño[1], C. Plasencia[1], M. Juarez[4], D. Peiteado[1], A. Villalva[1], A. Balsa[1]. [1]*Hospital Universitario La Paz, Rheumatology, Madrid, Spain*; [2]*CNIC, Bioinformatics, Madrid, Spain*; [3]*Hospital Universitario La Paz, Immunology, Madrid, Spain*; [4]*Universidad Autonoma de Madrid, Medicine, Madrid, Spain*

Background: Since the publication of 2010 ACR/ELUAR classification criteria for Rheumatoid Arthritis (RA), identification of patients with RA at early stages of the disease has improved. Nevertheless, up to 56% of patients are diagnosed with undifferentiated arthritis (UA) at the first visit to Rheumatology Departments, of which about 20-30% will progress to RA. For this reason, Early Arthritis Clinics (EAC) have been progressively implemented in Rheumatology departments in order to identify and have a tight follow-up of these patients.
Objectives: a) To analyze the progression rate from UA to RA in a cohort of EAC. b) To identify differences in clinical features at baseline that characterize the progression to RA of these patients.
Methods: Prospective study from a cohort of EAC between 2010 and 2018. Patients diagnosed with UA at first consultation were included and with

a follow-up of 2-years. Final diagnosis was assessed at the end of study period defining two groups: RA progression (RA-group) *vs* no progression (non-RA-group).Baseline characteristics were recorded for both groups: sex, age, smoking habit, duration of symptoms, morning stiffness, tender joint count (TJC), swollen joint count (SJC), Rheumatoid Factor (RF), Anti-Citrullinated-Peptide-Antibodies (ACPA), DAS-28, erythrocyte sedimentation rate (ESR), C-Reactive Protein (CRP), Pain visual analogue scale (VAS). Differences in sociodemographic, clinical and serological features between groups were analyzed using T-test, chi-square test and U-Mann Whitney depending on the nature of variables.

Results: A total of 228 patients with UA were included, of which 54 (23,3%) progressed to RA (patients characteristics are shown in table 1). Regarding serological characterization, we found that in our cohort, 44.4% of patients who developed RA had FR and ACPA positivity, 13% RF positive, 7.4% ACPA positive. In contrast 35% patients were seronegative. From non-RA group, 73% of patients were seronegative, 18% RF positive, 4.5% ACPA positive and 4.5% double positive.

Table 1.

Variable	Total (n=228)	RA (n=54)	Non-RA (n=174)	p-value
Female sex n(%)	165 (71.7)	42 (77.8)	121 (69.5)	0.31*
Age (mean SD)	51.47 (16.46)	52.9 (16.15)	51.26 (16.61)	0.53§
Smoking habit n (%)				0.12*
-smokers	49 (21.2)	14 (25.9)	33 (19)	
-exsmokers	52 (22.5)	15 (27.8)	37 (21.3)	
-non-smokers	113 (48.9)	19 (35.2)	93 (53.4)	
Duration of symptoms (weeks) (median IQR)	8 (4-19)	12 (8-24)	8 (4-16)	**0.006¶**
Morning stiffnes >60min n (%)	53 (22.9)	15 (27.8)	38 (21.8)	0.26*
Patient health assessment (meadian IQR)	39 (16-68)	58 (22-75)	34 (14-64)	**0.01¶**
Pain (VAS) (median IQR)	45 (18-68.2)	54 (30-71)	39 (14.5-67.5)	**0.02¶**
Tender Joint Count (median IQR)	2 (1-6)	4 (1-9)	2 (1-6)	**0.04¶**
Swollen Joint Count (median IQR)	2 (1-4)	3 (1-6)	2 (1-4)	**0.01¶**
Baseline DAS28 (mean SD)	3.97 (1.39)	4.44 (1.54)	3.82 (1.33)	**0.006§**
HAQ (median IQR)	0.75 (0.25-1.5)	1.12 (0.37-1.56)	0.62 (0.12-1.37)	0.06¶
CRP(mean SD)	2.2 (8.01)	1.39 (3.25)	2.3 (8.9)	0.44§
ESR (mean SD)	23.74 (19.5)	24.62 (16.22)	22.8 (19.3)	0.54§
RF n (%)	70 (30.3)	31 (57.4)	39 (22.4)	**<0.001***
ACPA n (%)	44 (19)	28 (51.9)	16 (9.2)	**<0.001***

No differences between age at onset, sex an smoking habit were found. Duration of symptoms until first visit to Rheumatology Department was longer RA-group. Regarding joint involvement, TCJ and SCJ were higher in RA-group at baseline and also VAS pain and patients´global health assessment.

Conclusion: One out of four patients diagnosed with early UA are at risk of RA development within the following 2 years. This fact implies that these patients benefit from EAC in order to have a tight control of the disease and have the chance of starting treatment as soon as possible.

References: Combe B et al. 2016 update of the EULAR recommendations for the management of early arthritis. Ann Rheum Dis 2017;76:948-959.

van Steenbergen HW et al. Preventing progression from arthralgia to arthritis: targeting the right patients. Nat Rev Rheumatol. 2018 Jan;14(1):32-41.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4107

AB0150 **ACPA-STATUS AND RHEUMATOID ARTHRITIS: MUCH MORE TO BE REVEALED!**

K. Maatallah[1], S. Miri[1], H. Ferjani[1], D. Ben Nsib[1], W. Triki[1], A. Dallegi[1], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab Institute of Orthopedics, Rhumatology, Manouba,Tunisia*

Background: Anti-citrullinated protein antibodies (ACPA) are commonly associated with Rheumatoid arthritis (RA). RA is, therefore, classified as immunopositive or immunonegative, with disparate mechanisms in predisposition.

Objectives: Our study aimed to determine the baseline characteristics and differences of ACPA-positive and ACPA-negative RA.

Methods: We conducted a cross-sectional study including 224 patients with RA. All patients fulfilled the 2010 American College of Rheumatology/European League Against Rheumatism RA classification criteria. The patients were divided according to their ACPA status into two groups: ACPA-positive group (G1) and ACPA-negative group (G2). We compared clinical, radiological, and *laboratory findings* between the two groups, as well as extra-articular manifestations, comorbidities including fractures and osteoporosis. The Fracture Risk Assessment Tool (FRAX) was used to estimate the 10-year probability of major osteoporotic fracture (MOF) and also hip fracture (FH).

Results: Of the 224 patients, 31.6% were negative for ACPA (n=71). Female predominance was found in both groups with a sex ratio of 0.25 (p=0.203). ACPA-negative subjects were younger (57±11 versus 59±12 years) (p= 0.305).

The initial presentation of RA was different between the two groups without reaching statistical significance. In the ACPA-negative group, alteration of general condition was more frequent (16.9% in G2 versus 13.7% in G1) (p=0.533), with a tendency to oligo-articular onset (18.5% in G2 versus 6.7% in G1) (p=0.737). ACPA-positivity was more associated with an acute start of symptoms (10.4% in G1 versus 8.4% in G2) (p=0.639)

There was no significant difference in the mean DAS28-VS (5.2±1.1 in G2 versus 5.5±1.3 in G1) and DAS28-CRP levels (5±1 in G2 versus 5.3±1.2 in G1) (p=0.069 and p=0.098 respectively).

ACPA-positive RA was, however, significantly associated with more structural joint damage: erosions (55.9±53 in G1 versus 78±36 in G2, p=0.01), joint space narrowing (50.4±45.5 in G1 versus 33.1±36.6 in G2, p=0.003), Sharp/van der Heijde radiographic score (126.6 ±103.2 in G1 versus 88.8±81.5 in G2, p=0.004). ACPA-positive RA patients had more atlantoaxial dislocation: 20.2% in G1 versus 7% in G2 (p=0.012). There was no significant difference in hip involvement (9.8% in G1 versus 14% G2) (p=0.344).

There were no significant differences in extra-articular manifestations between the two groups: Rheumatoid nodules (10.4% in G1 versus 18.3% in G2) (p=0.891), Sjögren's syndrome (16.3% in G1 versus 16.9% in G2)(p=0.715), amyloidosis (0.6% in G1) (p=1), pulmonary fibrosis (5.8% in G1 versus 4.2% in G2) (p=0.757), neurological signs (4.5% in in G1 versus 5.6% in G2) (p=0.733), anaemia (5.8% in G1 versus 1.4% in G2) (p=0.175).

When analyzing comorbidities, no significant differences were found: diabetes (10.4% in G1 versus 18.3% in G2) (p=0.103), cardiovascular diseases (19.6% in G1) (p=1), neurological diseases (0.06% in G1 versus 1.4% in G2) (p=0.534), dysthyroidism (2.6% in G1 versus 5.6% in G2) (p=0.267), dyslipidemia (3.2% in G1 versus 4.2% in G2) (p=0.711), cancer (1.3% in G1) (p=1). There were neither significant differences in the prevalence of fracture (21.5% in G1 versus 18.3% in G2) (p=0.574), and osteoporosis (23.6% in G1 versus 29.5% in G2) (p=0.347), between the two groups. However, ACPA-positive patients presented with a significantly higher FRAX score of MOF (2±2.8 in G1 versus 1.2±1 in G2) (p=0.006), and FRAX score of FH (0,9±1.8 in G1 versus 0.3±0.5 in G2) (p=0.003).

Conclusion: ACPA status appears to influence both the clinical presentation and radiological progression of RA patients. ACPA-positive patients present with an acute start of symptoms, with more structural damages and atlantoaxial dislocation. Comorbidities, including osteoporosis, does not seem affected by ACPA status. However, regardless of osteoporosis, ACPA-positivity is associated with a higher probability of major osteoporotic and hip fractures. Further research is needed to clarify this relationship.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4146

Rheumatoid arthritis - comorbidity and clinical aspects

AB0151 FOLLOW-UP IN A MULTIDISCIPLINARY UNIT IMPROVES PREGNANCY OUTCOME IN INFLAMMATORY ARTHROPATIES ON BIOLOGICAL THERAPY

O. Ibarguengoitia[1], I. Calvo[1], D. Montero[2], L. Vega[2], C. García[2], O. Fernandez[2], I. Torre[2], A. R. Inchaurbe[2], C. E. Perez[2], J. M. Blanco[2], E. Cuende[2], E. Galindez[2], I. Gorostiza[3], J. Oraa[4], M. L. García Vivar[2], M. E. Ruiz[2].
[1]Galdakao University Hospital, Rheumatology, Galdakao, Spain; *[2]Basurto University Hospital, Rheumatology, Bilbao, Spain*; *[3]Basurto University Hospital, Investigation Unit, Bilbao, Spain*; *[4]Basurto University Hospital, Obstetrics and Gynecology, Bilbao, Spain*

Background: Women with inflammatory arthropaties have fertility problems and complications during pregnancy and frequently biological therapy (BT) is required for the disease control.
Objectives: To evaluate pregnancy in women with inflammatory arthropaties in a multidisciplinary unit composed of Rheumatologists and Obstetricians: describe disease evolution, complications and treatment used (including BT).
Methods: Retrospective and descriptive study of the evolution of pregnancy in patients with
inflammatory diseases (Rheumatoid Arthritis (RA), Spondyloarthritis (SpA) and Juvenile Idiopathic Arthritis (JIA)) and follow-up in a multidisciplinary unit for more than 15 years (until December 2020). Demographics, maternal disease, time until conception, previous abortions and presence of antibodies were collected. In addition, during follow-up, treatment, abortions, Caesarean sections (C-section), preterm births, disease activity and maternal/fetal complications were collected.
Results: We registered 41 pregnancies (32 women): 20 RA (62.5%), 9 SpA (28.1%) and 3 JIA (9.4%). Maternal average age at diagnosis was 27.1±6.6 years and average age at childbirth/abortion was 34.9±5.1 years.
It took an average time of 9.6±8.5 months to conceive. 9.8% received fertility treatment with in vitro fertilization techniques.
AntiRo antibodies were registered in 7.3% of patients and 34.1% had at least 1 antiphospholipid antibody.
At the time of gestational desire/gestation 17 women (12 RA, 4 SpA, 2 JIA) were receiving BT: 7 certolizumab (CZP), 7 adalimumab (ADA), 3 etanercept (ETN). 1 patient was being treated with baricitinib. Due to pregnancy, ADA was changed to CZP in 3 women and BT was stopped in 6 cases (3 ETN, 2 ADA, 1 CZP) as well as baricitinib. In 2 cases, ADA was stopped at week 17 of pregnancy (medical indication). Pregnancy was completed with BT (CZP) in 9 cases.
9 abortions were registered prior to follow-up in the unit (0.28 abortions/mother) and 3 during follow-up (0.09 abortions/mother): 2 of them in women with CZP.
C-section was performed in 26.8% of cases.
Preterm birth (<37 weeks) happened in 9.7% (n: 4) of the pregnancies: 1 case in a woman with CZP.
A total of 17 different fetal/maternal complications were registered during follow-up: 6 in the BT group (35.3%) compared to 11 (64.7%) in the group without BT, being Intrauterine Growth Restriction (IUGR) more frequent among women with BT. Infections were not more common in patients with BT. Complications are listed in Table 1.

Table 1.

COMPLICATIONS	WITH BT (n, %) n: 11	WITHOUT BT (n, %) n: 30
IUGR	3 (27.3%)	1 (3.3%)
LOW BIRTH WEIGHT	2 (18.2%)	2 (6.6%)
INFECTION	1 (9.1%)	4 (13.3%)
CHOLESTASIS	0 (0%)	2 (6.6%)
PREECLAMPSIA	0 (0%)	1 (3.3%)
DIABETES MELLITUS	0 (0%)	1 (3.3%)
HIGH BLOOD PRESSURE	0 (0%)	0 (0%)
NEPHROPATY	0 (0%)	0 (0%)
NEONATAL LUPUS	0 (0%)	0 (0%)
HEART BLOCK	(0%)	0 (0%)
MALFORMATION	0 (0%)	0 (0%)
HELLP SYNDROME	0/0%)	0 (0%)
TOTAL	6 (54.6%)	11 (36.4%)

Regarding concomitant treatment, low dose prednisone was used in 48.8% of pregnancies, hydroxychloroquine in 51.2%, sulfasalazine in 9.8% and acetylsalicylic acid in 51.2%. We didn´t find differences in the use of these treatments between the two groups.
Median DAS28 among RA patients and available data was under 2.6 throughout pregnancy as well as previously and posteriorly. No differences in median DAS28 were found between women with BT and without BT. SpA patients had BASDAI lower than 4 in both groups during pregnancy and previously.
Conclusion: In our series, as described in the literature, women with inflammatory arthropaties are older and are more likely to have preterm births compared to general population. Fewer abortions were registered during follow-up in the multidisciplinary unit. Appropriate disease control was maintained during pregnancy, also previously and afterwards. We registered more IUGR and low birth weight among women with BT but given the low number of patients with BT no statistically significant conclusions about complications can be drawn. Therefore, more studies among pregnant women with BT are necessary.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.715

AB0152 PROSPECTIVE ANALYSIS OF OBSTRUCTIVE SLEEP APNEA IN NEWLY DIAGNOSED PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND PERIPHERAL SPONDYLOARTHRITIS – A SCREENING STUDY

D. Dejcman[1], D. Skowasch[2], C. Pizarro[2], P. Karakostas[1], P. Brossart[1], V. Schäfer[1]. *[1]University Hospital Bonn, Department of Internal Medicine III - Oncology, Hematology, Rheumatology and Stem Cell Transplantation, Bonn, Germany*; *[2]University Hospital Bonn, Department of Internal Medicine II - Cardiology, Angiology and Pulmonary Care, Bonn, Germany*

Background: An increased prevalence of obstructive sleep apnea (OSA) in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and partially in peripheral spondylarthritis (pSpA) has been noted and described for nearly two decades. Until now, there is no study yet on the occurrence of OSA in patients with these entities at the point of first diagnosis. Identifying and treating OSA could prove pivotal in improving cardiovascular risk and quality of life. Furthermore, clinicians require insights into whom to screen.
Objectives: To assess the prevalence of OSA in early RA, PsA and pSpA and strategies for targeted screening.
Methods: We performed a prospective study on patients with first diagnosis of RA, PsA or pSpA, who were screened for day sleepiness (assessed by the Epworth sleepiness scale) and tested for obstructive sleep disorders by out-of-center sleep apnea polygraphy (employing Embletta® MPR-PG devices) at the University Hospital of Bonn, Germany. Findings were assessed by three physicians, always including an attending physician responsible for the certified sleep laboratory.
Results: A total of 22 patients with RA (52.38%), 15 with PsA (35.7%), and 5 (11.9%) with pSpA were included. Day sleepiness screening was unremarkable (ESS <10) in 29 (69%) patients and suspicious for a sleep disorder (ESS≥10) in 13 patients (31%). Subsequent sleep studies of five patients (11.9%) were suspicious for severe sleep apnea (AHI >15/h), eight (19.1%) for low-to-moderate sleep apnea (AHI 5-15/h) and 29 (69.1%) were unremarkable (AHI <5). Of the eight low-to-moderate results, none were symptomatic as in ESS ≥10, resulting in a total of five (11.9%) guideline-confirming referrals for inpatient polysomnography/ventilation therapy. In comparison with the PsA/pSpA group, a diagnosis of RA had no significant relationship with ESS results (p≈0.23), nor AHI results ≥5/h (p≈0.14). The male cohort yielded more pathological sleep studies, but the result was not significant (16% vs. ~5.9%, p≈0.32). Higher ESS scores (≥10) were not predictive for findings which require a referral (p≈0.37). Increased BMI (≥25 kg/m^2) was not associated with an AHI > 5/h (p≈0.63).
Conclusion: From the point of screening, a number needed to screen of 8.4 (6.25 in the male, 17 in the female group), speaks in favor of overall cost-efficient screening for OSA in newly diagnosed male patients with arthritis diseases. A different study design, comparing early vs. established arthritis cohorts is necessary to assess the role of disease duration in the possible development of OSA.
REFERENCES:
[1] Chung W-S, Lin C-L. Sleep disorders associated with risk of rheumatoid arthritis. Sleep Breath [Internet]. 2018 Dec 10 [cited 2018 Dec 11];22(4):1083–91. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29428977.
[2] Vakil M, Park S, Broder A. The complex associations between obstructive sleep apnea and auto-immune disorders: A review. Med Hypotheses [Internet]. 2018;110:138–43. Available from: https://doi.org/10.1016/j.mehy.2017.12.004.
[3] Wali S, Mustafa M, Manzar D, Bawazir Y, Attar S, Fathaldin O, et al. Prevalence of obstructive sleep apnea in patients with rheumatoid arthritis. J Clin Sleep Med. 2020.

Table 1. Patient characteristics

	Total (n=42)	RA (n=22)	PsA (n=15)	pSpA (n=5)
Age				
Median (IQR)	49 (36-61)	58 (39-64)	43 (30-55)	39 (39-46)
Sex				
Male	25 (59.5%)	15 (68.2%)	6 (40%)	4 (80%)
Female	17 (40.5%)	7 (31.8%)	9 (60%)	1 (20%)
Obesity by BMI (<25/≥25)				
Normal weight/ Underweight	19 (45.2%)	10 (45.5%)	7 (46.6%)	2 (40%)
Overweight/ Obesity	23 (54.8%)	12 (55.5%)	8 (53.3%)	3 (60%)
ESS Score				
<10	29 (69%)	17 (77.3%)	8 (53.3%)	4 (80%)
≥10	13 (31%)	5 (22.7%)	7 (46.7%)	1 (20%)
AHI				
<5/h	29 (69%)	13 (59.1%)	12 (80%)	4 (80%)
5-15/h	8 (19.1%)	6 (27.3%)	1 (6.7%)	1 (20%)
>15/h	5 (11.9%)	3 (13.6%)	2 (13.3%)	0 (0%)

RA – rheumatoid arthritis, PsA – psoriatic arthritis, pSpA – peripheral spondyloarthritis, IQR – interquartile range, BMI – body mass index, ESS – Epworth Sleepiness Scale, AHI – Apnea/ Hypopnea Index

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1074

AB0153 REAL LIFE SEVERE INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS ON TREATMENT WITH BIOLOGICAL THERAPY AND JAKI

L. Vega[1], I. Calvo[2], O. Ibarguengoitia[2], D. Montero[1], C. García[1], J. M. Blanco[1], M. E. Ruiz[1], A. R. Inchaurbe[1], I. Torre[1], C. E. Perez[1], O. Fernandez[1], E. Cuande[1], M. R. Exposito-Molinero[1], I. Gorostiza[3], M. L. García Vivar[1], E. Galindez[1]. [1]*Basurto University Hospital, Rheumatology Unit, Bilbao, Spain*; [2]*Galdakao University Hospital, Rheumatology Unit, Galdakao, Spain*; [3]*Basurto University Hospital, Investigation Unit, Bilbao, Spain*

Background: Infections are one of the main complications among patients with rheumatoid arthritis (RA) with immunosuppressive treatment. The differences between treatments and the influence of other factors is unclear.

Objectives: To evaluate the frequency and factors associated with serious infections in patients with RA treated with biological therapy (BT) and JAKi and the differences between treatments.

Methods: Descriptive and retrospective study (January 2015-December 2020) of patients with RA treated with BT (TNFi, non-TNFi) and JAKi (tofacitinib, bariticinib, upadacitinib) in a single center. Severe infection was considered a life-threatening infection or one that required hospitalization and intravenous treatment. Epidemiological variables, clinical characteristics, Charlson comorbidity index, type of BT or JAKi and concomitant treatment were collected.

For the analysis frequencies and percentages are used in qualitative variables and mean ± SD in the quantitative ones. Statistical analysis was performed with IBM SPSS v 23.

Results: We registered 257 patients (84.4% women) mean aged 56.1±13.4 years. RF was positive in 86.8%, anti-CCP in 75.9% and 16.5 % presented extra-articular manifestations (nodulosis 9.7%, intersticial lung disease 4.3%, other 1.5%). At the start of the study, 157 (61.1%) patients were with TNFi, 80 (31.1%) with non-TNFi and 20 (7.8%) with JAKi. Conventional synthetic DMARDs (csDMARDs) were used in 86% of cases (methotrexate 71.1%, leflunomide 21.2%, other 7.7%).

During the study, 162 (63%) patients continued with the same treatment and in 95 (37%) it was changed at least once. 3 patients discontinued the treatment. At the end of the study, 126 (49%) patients were with TNFi, 81 (31.5%) with non-TNFi and 47 (18.3%) with JAKi.

Severe infection was developed in 28 (10.9%) patients (13 respiratory, 5 urinary, 5 cellulitis, 4 sepsis, 1 osteomyelitis) among them 2 patients had severe infection and herpes zoster at the same time and 3 developed a second infection. 14 (50%) patients were with TNFi, 8 (28.6%) with non-TNFi and 6 (21.4%) with JAKi. Table 1

The inflammatory activity of RA was mild at the time of infection (DAS28: 2.6±1.1). The median time until infection was: TNFi 45.25 [4.9-202.3] months, non- TNFi 19.14 [4.9-72.5] months and JAKi 17.63 [1.1-29.2] months.

The Charlson index, concomitant use of glucocorticoids (GCC) at lower doses than 10mg/d, chronic obstructive pulmonary disease (COPD), diabetes (DM), moderate-severe renal insufficiency, congestive heart failure (CHF) and peripheral vascular disease were statistically significantly associated with infection. Table 1.

TABLE 1. CHARACTERISTICS OF PATIENTS WITH INFECTION VS. WITHOUT INFECTION

	INFECTION		
	YES n:28	**NO** n:229	**p**
FEMALE, n (%)	22 (78.6)	195 (85.2)	0.406
AGE years, (mean±SD)	57.7 ± 13.9	55.9 ± 13.4	0.507
AGE ≥ 65 n (%)	10 (35.7)	68 (29.7)	0.513
RF +, n (%)	25 (89.3)	198 (86.5)	0.677
ANTI-CCP +, n (%)	21 (75)	174 (75.1)	1.00
ILD, n (%)	1 (3.5)	10 (4.3)	0.809
ALCOHOL, n (%)	3 (10.7)	17 (7.4)	0.465
SMOKER, n (%)	10 (35.7)	60 (26.2)	0.244
COPD, n (%)	7 (25)	24 (10.5)	**0.026***
DM, n (%)	7 (25)	19 (8.3)	**0.013***
CHF, n (%)	4 (14.3)	1 (0.4)	**0.001***
RENAL INSUFFICIENCY, n (%)	3 (10.7)	2 (0.9)	**0.010***
PERIPHERAL VASCULAR DISEASE, n (%)	9 (32.1)	22 (9.6)	**0.002***
CHARLSON INDEX (mean±SD)	1.64 ± 2.1	0.63 ± 1.2	**0.001***
TNFi, n (%) NON-TNFi n (%) JAKi, n (%)	14 (50)	112 (48.9)	
	8 (28.6)	73 (31.9)	
	6 (21.4)	41 (17.9)	
csDMARDs, n (%)	22 (78.6)	159 (69.4)	**0.317**
GCC dose <10mg/d, n (%)	17 (60.8)	111 (48.5)	**0.007***

Conclusion: In our study, 10.9% of patients with RA treated with BT or JAKi developed severe infection during 5 years of follow-up. Concomitant GCC therapy and comorbidity increased the risk of presenting this complication.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1141

AB0154 USAGE OF THE SARC-F QUESTIONNAIRE FOR SARCOPENIA SCREENING IN PATIENTS WITH RHEUMATOID ARTHRITIS

O. Dobrovolskaya[1], N. Toroptsova[1], O. Nikitinskaya[1], A. Efremova[1], N. Demin[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Department of Osteoporosis, Moscow, Russian Federation*

Background: Sarcopenia, characterized by low muscle strength and low muscle quantity or quality and associated with increased risks of falling and mortality. The prevalence of sarcopenia is 37% among patients with RA [1]. However, in clinical practice settings, sarcopenia among RA patients remains underdiagnosed. The SARC-F questionnaire [2] was recommended by the European Working Group on Sarcopenia in Older People (EWGSOP) before performing muscle strength tests and assessment muscle mass.
Objectives: To evaluate the diagnostic value of the SARC-F questionnaire for the screening of sarcopenia (SP) in women with rheumatoid arthritis (RA).
Methods: 83 women (average age 59±8 years) with RA without aseptic bone necrosis, joint replacement and severe comorbidities were recruited. All patients were interviewed with the SARC-F questionnaire. The summation score ≥ 4 corresponded to cut-off for suspected sarcopenia. Sarcopenia was evaluated using the European Working Group on Sarcopenia in Older People (EWGSOP2), which included dual-energy X-ray absorptiometry (DXA), handgrip strength or chair stand test, and gait speed. The sensitivity, specificity, positive and negative prognostic values of the SARC-F questionnaire were estimated.
Results: Confirmed SP was diagnosed in 20 (24%) RA patients, who had low muscle strength and mass. When conventional cut-off point (≥4) for SARC-F questionnaire was applied, only 30% of the patients with SP met this condition (sensitivity 30%, 95% confidence interval [95% CI] 13% to 54%), and 41% of the patients without SP did not meet this condition (specificity 41%, 95% CI 29% to 54%). Positive and negative prognostic values were 14% (95% CI 6% to 29%) and 65% (95% CI 48% to 79%), respectively.
Conclusion: The SARC-F questionnaire alone is not adequate for screening of SP in RA patient. It is necessary to develop other simple screening methods that can easily be carried out in real clinical practice to identify individuals with possible SP for further diagnostic tests.
REFERENCES:
[1] Torii M, Hashimoto M, Hanai A, et al. Prevalence and factors associated with sarcopenia in patients with rheumatoid arthritis. Modern Rheumatology, 2018;29(4):589-595. doi:10.1080/14397595.2018.1510565.
[2] Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16-31. doi:10.1093/ageing/afy169.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1303

AB0155

COMPARATIVE ANALYSES OF SEROLOGICAL BIOMARKERS AND DISEASE CHARACTERISTICS BETWEEN ELDERLY ONSET RHEUMATOID ARTHRITIS (EORA) AND YOUNGER ONSET RHEUMATOID ARTHRITIS (YORA)

S. Rajalingham[1], S. S. Shaharir[1], H. Mahadzir[1]. [1]*Universiti Kebangsaan Malaysia, Medicine, CHERAS, Malaysia*

Background: Several studies have reported differences in disease characteristics between elderly onset RA (EORA: age of onset > 60 years) and younger-onset RA (YORA). However, the findings across the studies have been rather inconsistent owing partially to the genetic variation across the populations studied. While a few studies have looked into the clinical aspects of EORA, there is a profound lack of comparative data on serological findings between EORA and YORA. Seropositive RA is known to be associated with more aggressive disease and the titres of the autoantibodies may predict the disease activity and the severity of radiographic progression.

Objectives: The main aim of this study was to compare the levels of the autoantibodies namely anti–CCP (cyclic citrulinated peptide), IgA, IgM, IgG rheumatoid factors(RF) and disease characteristics between the EORA and YORA groups.

Methods: We consecutively recruited a total of 151 female RA patients who were tested for IgA RF, IgG RF, IgM RF and anti CCP antibodies. Participants were aged above 18 years and met the 2010 ACR/EULAR RA criteria. Data on the disease characteristics (age at onset, disease activity at onset, disease duration and medications)were obtained by reviewing the medical records of the subjects. Subjects were divided into 2 groups i.e EORA and YORA based on age at onset of RA. All subjects were assessed for the severity of radiographic joint damage and functional disability based on Modified Sharp Score (MSS) and Health-assessment questionnaire-disability index (HAQ- DI), respectively. The EULAR response criteria was used to determine the subjects' response to disease-modifying anti-rheumatic drugs.

Results: The EORA group had 69 patients whereas the YORA group had 82 patients. The mean anti-CCP and IgA RF levels were significantly higher in the YORA group with p values of 0.002 and 0.035, respectively. The YORA group had significantly more severe disease at onset (p value for DAS 28 at onset was 0.009) with worse radiographic joint damage (p value for MSS was 0.006). In parallel with these findings, the YORA group had significantly higher ESR and CRP at onset with higher frequency of subjects requiring advanced therapies. The differences in frequency of RF positivity, disease duration, number of DMARDs, prednisolone dose and HAQ-Di scores between the groups did not reach statistical significance.

Conclusion: EORA is characterized by lower levels of anti-CCP and IgA autoantibodies with less aggressive disease as compared to YORA.

REFERENCES:

[1] Calvo-Alen J, Corrales A, et al.Clinical rheumatology 2005;24:485-9.
[2] Huscher D, Sengler C, Ochs W, et al. Clinical and experimental rheumatology 2013;31:256-62.
[3] Mueller RB, Kaegi T, et al. Rheumatology 2014;53:671-7.

Table 1. Comparison of disease characteristics between EORA and YORA

Parameter	EORA (n=69)	YORA(n=82)	p value
Age (years)*	67.19± 2.49	31.93± 5.10	**<0.050**
Disease duration (years)*	8.06±5.04	8.70± 3.63	0.365
DAS28 at onset*	3.29± 1.37	3.96± 1.68	**0.009**
RF positive at onset	47 (68.11)	62 (75.61)	0.306
Anti CCP titre*	84.52±117.97	151.14±138.02	**0.002**
IgA RF titre*	24.15±39.54	43.14±64.82	**0.035**
IgM RF titre*	68.58±97.65	72.74±93.28	0.789
IgG RF titre*	64.36±66.01	70.88±69.58	0.558
ESR at onset(mm/hr)*	54.20± 20.50	67.04± 23.60	**0.001**
CRP at onset(mmol/L)*	1.33± 1.37	3.79± 8.11	**0.019**
No. of DMARDS			
1	45 (65.21)	41 (50.00)	
2	16 (23.19)	32 (39.02)	0.106
3	8 (11.59)	9 (10.98)	
On biologics & tsDMARD	12 (17.39)	35 (42.68)	**0.008**
Prednisolone dose (mg)*	2.83 ± 3.32	2.77 ± 3.02	0.920
Treatment Response			
Good	50 (72.46)	54 (65.86)	0.487
Moderate	15 (21.74)	19 (23.17)	
None	4 (5.80)	9 (10.98)	
MSS*	10.04±12.79	17.49±19.04	**0.006**
HAQ-DI*	1.47±0.87	1.58±0.71	0.397

Data presented as either counts (percentages) or mean ± SD*

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1305

AB0156

INCIDENCE OF CERVICAL SPINE INVOLVEMENT IN RHEUMATOID ARTHRITIS, RESULTS FROM A SINGLE CENTRE OBSERVATIONAL STUDY

A. Conforti[1], F. Bruno[1], O. Berardicurti[1], V. Pavlych[1], I. DI Cola[1], F. Sensini[1], A. Barile[1], C. Masciocchi[1], P. Cipriani[1], P. Ruscitti[1]. [1]*University of L'Aquila, Department of Biotechnological and Applied Clinical Sciences, L'Aquila, Italy*

Background: Rheumatoid arthritis (RA) manifests as a chronic, symmetrical articular disease; any synovial joint may be involved and the cervical spine is another possible affected site [1,2]. Although the cervical spine involvement is a very severe complication of RA, the exact incidence of cervical spine abnormalities in RA is not fully elucidated yet.

Objectives: In this work, we aimed at evaluating the incidence of a cervical spine involvement and associated clinical characteristics in patients with RA in a single centre observational study.

Methods: In this study, we performed a retrospective analysis of prospectively followed-up patients with RA attending our Rheumatologic Clinic, University of L'Aquila, L'Aquila, Italy, between January 2010 and December 2020. Patients who met the diagnostic criteria of 1987 ACR and/or ACR/EULAR 2010 criteria were assessed. Each patient was investigated for cervical spine involvement occurrence, particularly the atlas-axis cervical involvement. Instrumental imaging evaluation of the cervical spine was performed in all patients with clinical suspicion of involvement, by both MRI and CT examinations. MRI examinations were performed on a 1.5 Tesla scanner, acquiring T1, T2, and STIR sequences on sagittal, coronal and axial planes. CT examinations were performed on a multidetector 320-row CT scanner (Aquilion One,Toshiba) acquired with a thin collimation; soft tissue or bone algorithms were applied for image data reconstruction and analysis.

Incident cases of cervical spine involvement were reported as incidence proportion and incidence rate per 1000 person-years at risk.

Results: In this evaluation, 347 consecutive patients, (mostly female 87.6%, mean age of 66.1 ± 11.3 years) attending our Rheumatologic Clinic, were studied. The incidence proportion of cervical spine involvement was 2.0% [0.6 – 3.4%], occurring in 7 out of 347 patients, and identified by both MRI and CT scan. Considering over 1623 person-years, an incidence rate of 4.0 × 1000 [3.0 – 5.0] person-years was also estimated. All our patients with cervical spine involvement were characterised by female gender, rheumatoid factor, ACPA, fulfilment of ACR 1987 classificative criteria, and poorly controlled disease activity. Smoking habit and extra-articular manifestations were also frequently reported. Glucocorticoids, methotrexate, and infliximab were mainly administered in these patients. This therapeutic strategy resulted in a complete resolution of the inflammatory synovitis in all but one patient. The latter developed a cervical spinal instability resulting in neurological progression and required a subsequent surgical management.

Conclusion: The cervical spine involvement is an uncommon but serious manifestation of RA, since possibly causing severe neurologic damage. A poorly controlled inflammatory process would be an important risk factor for developing a cervical spine involvement in RA, thus, a proper management is required, from an early accurate recognition to a timely therapeutic strategy. MRI could provide a useful clinical tool to early evaluate the cervical spine involvement in RA. Finally, considering the low incidence, further studies are needed to fully estimate the exact incidence of this manifestation, mostly in poorly symptomatic patients.

REFERENCES:

[1] Shlobin NA, Dahdaleh NS. Cervical spine manifestations of rheumatoid arthritis: a review. Neurosurg Rev. 2020 Oct 10. Neurosurg Rev. 2020 Oct 10. doi: 10.1007/s10143-020-01412-1.
[2] Kothe, R.Rheumatoid instability in the cervical spine: Diagnostic and therapeutic strategies. Orthopade. 2018 Jun;47(6):489-495.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1572

AB0157

PREVALENCE OF SARCOPENIA AND CLINICAL IMPLICATIONS IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS PATIENTS

R. Ekici[1], A. Erden[2], B. Özdemir[2], S. C. Güven[2], B. Armagan[2], Ö. Karakaş[2], K. Gok[2], A. Omma[2], O. Küçükşahin[2], S. Erten[2]. [1]*Ankara Şehir Hastanesi, Internal Medicine, Ankara, Turkey*; [2]*Ankara Şehir Hastanesi, Rheumatology, Ankara, Turkey*

Background: The aim of this study is to determine the frequency of sarcopenia at the time of diagnosis in RA patients, evaluate the effects of sarcopenia on RA disease activity, prognosis and examine the factors that may be associated with sarcopenia.

Objectives: To determine the frequency of sarcopenia at the time of diagnosis in rheumatoid arthritis (RA) patients, assessing disease activity and factors that may be associated with sarcopenia and observe effects of treatment on sarcopenia.

Methods: A prospective study was conducted on RA patients with newly diagnosed. Patients were evaluated twice, at the time of diagnosis and three months after the initiation of treatment. Demographic data, anthropometric measurements, disease activity scores and sarcopenia status were recorded. Sarcopenia was evaluated with grip strength and bioelectric impedance. The results were also compared with healthy volunteers.
Results: Hand grip strength (p<0.001), skeletal muscle mass (p=0.009) and skeletal muscle mass index (p=0.032) were found to be reduced in RA patients compared to the control group. The frequency of sarcopenia in RA at onset of diagnosis was found to be 31.5%. There was a significant decrease in the rate of sarcopenia after three months of treatment (31.5% versus 8.7%; p=0.046).
Conclusion: Sarcopenia was found in approximately one third of the patients with newly diagnosed RA in our study. With treatment, sarcopenia improved significantly. RA patients should be evaluated in terms of sarcopenia besides evaluating joint and extra-articular findings at the time of diagnosis. Early detection and treatment planning may improve the quality of life.

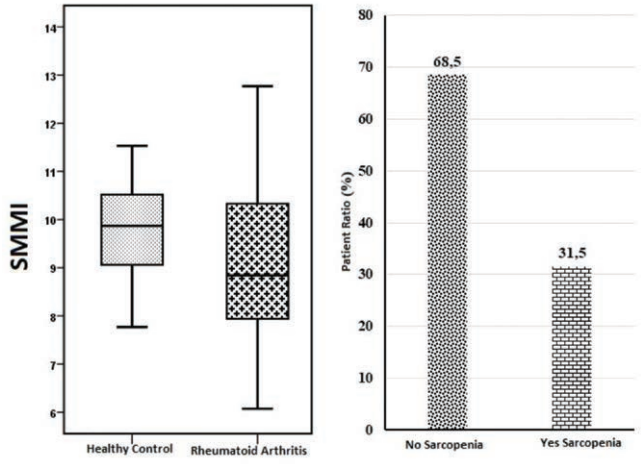


Figure 1. Distribution of skeletal muscle mass index (SMMI) and prevalence of sarcopenia in RA and control groups

Table 1. Demographics, clinical features, anthropometric measurements and disease activity scores of sarcopenic and non-sarcopenic RA patients

	RA without sarcopenia n=37	RA with sarcopenia n=17	p
Age, mean (SD), years	47,3 (12,8)	58,0 (16)	0,011*
Gender, female, n (%)	27 (73)	9 (52,9)	0,215
Marital status, married, n (%)	34 (91,9)	13 (76,5)	0,258
Tobacco consumption, n (%)			
Active smoker	10 (27)	5 (29,4)	0,086
Ex-smoker	8 (21,6)	8 (47,1)	
Never smoker	19 (51,4)	4 (23,5)	
Alcohol consumption, n (%)			
Active drinker	2 (5,4)	2 (11,8)	0,244
Ex-drinker	0 (0,0)	1 (5,9)	
Never drinker	35 (94,6)	14 (82,4)	
Occupation, n (%)			
Worker	15 (40,5)	12 (70,6)	0,060
Height, mean (SD), meter	1,6 (0,1)	1,6 (0,1)	0,664
Weight, mean (SD), kg	80,6 (17,7)	65,3 (8,6)	<0,001*
BMI, mean (SD), kg/m^2	31,4 (7,3)	24,9 (3,2)	<0,001*
Obese, n (%)	20 (54,1)	2 (11,8)	0,006*
Waist circumference, mean (SD), cm	97,1 (14,2)	89,3 (12,8)	0,058
Hip circumference, mean (SD), cm	108,1 (12,7)	96,6 (5,1)	0,001*
Calf circumference, mean (SD), cm	35,4 (5,1)	29,6 (4,0)	<0,001*
Triceps skin thickness, median (min-max), mm	22 (8-36)	15 (6-31)	0,022*
Loss of muscle strength, n (%)			
Right	10 (27,0)	9 (52,9)	0,076
Left	12 (32,4)	10 (58,8)	0,081
Dominant hand, right, n (%)	33 (89,2)	13 (76,5)	0,418
SMM, mean (SD)	25,1 (5,8)	21,9 (4,7)	0,049*
SMMI, mean (SD)	9,6 (1,5)	8,2 (1,2)	<0,001*
DAS 28 - CRP, median (min-max)	4,4 (1,7-6,5)	4,4 (2,4-6,3)	0,860
SDAI, median (min-max)	36,1 (8,8-113)	31,1 (17,1-113)	0,668
CDAI, median (min-max)	23 (0-48)	23 (6-39)	0,993
PrGA, median (min-max)	6 (0-9)	5 (2-10)	0,627
PtGA, median (min-max)	8 (0-10)	7 (4-10)	0,666
Presence of morning stiffness, n (%)	32 (86,5)	14 (82,4)	0,999
Swollen joint count, median (min-max)	2 (0-10)	4 (0-9)	0,423
Tender joint count, median (min-max)	6 (0-20)	7 (0-18)	0,911

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1874

AB0158 COMPARISON OF CLINICAL EXAMINATION AND ULTRASOUND OF HAND AND WRIST JOINTS IN RHEUMATOID ARTHRITIS

S. Bouden[1], B. D. Siwar[1], A. Ben Tekaya[1], O. Saidane[1], R. Tekaya[1], I. Mahmoud[1], L. Abdelmoula[1]. [1]*Charles Nicolle Hospital, Department of Rheumatology, Tunis, Tunisia*

Background: Ultrasound (US) is an accessible and non-invasive tool to assess joint involvement in rheumatoid arthritis (RA). It is used for diagnostic and prognosis purposes and for following of RA patients by evaluating the disease activity and therefore the response to treatment.
Objectives: This study investigates agreement between US of hand and wrist findings and the clinical examination and biological inflammatory parameters in RA patients.
Methods: We performed a cross sectional study including patients responding to the ACR/EULAR 2010 criteria for RA diagnosis. We collected US findings assessing synovitis and doppler signal in wrist, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) articulations, and concomitant clinical examination assessing synovitis and pain in the same joints along with C reactive protein (CRP) levels and disease activity score (DAS28). The power Doppler US score (PDUS) from 6 simplified synovial sites (wrists, bilateral second and third MCP joints) was calculated [1].
Results: Forty-three patients were included with 91.7% of women. The mean age was 62±12.95 years old. The mean age at diagnosis was 52±14.79 years with a mean disease evolution of 8±8.57 years. Rheumatoid factor and anti-citrullinated antibodies were positive in respectively 78% and 83.9% of cases.
The mean disease activity (DAS28) was 1,52 with levels ranging from 1.5 to 7.33. Right wrist was the articulation in which US synovitis was most frequently detected (60.5% of patients), followed by the left wrist (53.5%). Power doppler signal was detected as frequently in the right as in the left wrist articulations (41.9%). Subsequently, clinical synovitis was most frequently detected in right and left wrist with 39,5% and 41,5% respectively. These joints were the most frequently painful, in 51.2% and 48.8% at right and left respectively.
US synovitis of the first interphalangeal joint was found in only 2.3% and 4.7% in the right and left hand respectively, with positive power doppler signal in 2.3% of the patients in the same articulations.
The overall agreement between US and clinical examination in detecting synovitis of wrist, MCP and PIP joints was of 67.3%. It was of 71.4% in wrists, 54.7% in MCP joints and 87% in PIP joints. This suggests the presence of infra-clinical synovitis. All sites combined, US synovitis were correlated to clinical synovitis (p=0.03).
A positive correlation was found between PDUS from 6 simplified joint sites and CRP levels (p value of 0.02). No correlation was found with disease activity score (DAS28).
Conclusion: US of hands and wrist articulations is more performant than clinical examination in detecting synovitis. The most frequently involved joints with clinical and US synovitis, pain and positive power doppler signal were the wrist joints. CRP level is predictive of the presence of a high simplified power doppler score which is related to clinical activity of the disease as reported by Kawashiri et al. [1].
REFERENCES:
[1] Kawashiri S, Kawakami A, Iwamoto N, Fujikawa K, Satoh K, Tamai M, et al. The power Doppler ultrasonography score from 24 synovial sites or 6 simplified synovial sites, including the metacarpophalangeal joints, reflects the clinical disease activity and level of serum biomarkers in patients with rheumatoid arthritis. Rheumatology (Oxford). mai 2011;50(5):962-5.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1922

AB0159 DIASTOLIC DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Cabrera-Villalba[1], V. Valinotti[1], L. Roman[1], A. Paats[1], P. DE Abreu Trigueros[2], M. Duarte[1], T. Martinez[3], I. Acosta-Colman[1], G. Avila[1], O. Centurion[4]. [1]*Clinicas Hospital, Universidad Nacional de Asuncion, Rheumatology, San Lorenzo, Paraguay*; [2]*Sociedad Paraguaya de Reumatología, Rheumatology, Asunción, Paraguay*; [3]*Asunción, Laboratorio Curie, Asunción, Paraguay*; [4]*Clinicas Hospital, Universidad Nacional de Asuncion, Cardiovascular Medicine, Asunción, Paraguay*

Background: Rheumatoid arthritis (RA) presents with an elevated incidence of congestive heart failure disease, which has a strong association with diastolic dysfunction, defined by left ventricular delayed relaxation pattern assessed by echocardiography.(1,2)
Objectives: To describe the frequency of left ventricular delayed relaxation pattern in patients with RA, and the relationship with its clinical and serological characteristics, as well as with traditional and non-traditional cardiovascular risk factors.

Methods: Descriptive, cross sectional, prospective study, in a Paraguayan cohort of patients with RA. This study had two phases: the first one, included a standardized questionnaire according to the variables included in the Cardiovascular Risk project (PINV15-0346), from the Consejo Nacional de Ciencias y Tecnología (CONACYT), and physical examination; the second one included laboratory sample collection performed by a specialized laboratory for serum biomarkers measurement for cardiovascular risk prediction (i.e endothelin, alpha-TNF, E-selectin, t-PA, VCAM, PAI-1 and high sensitivity-CRP levels) and echocardiographic assessment with a Doppler 7 GE USA equipment at a private facility. All patients signed informed consent. SPSS Statistics v23 was used for data analysis. Quantitative variables were presented as means and qualitative variables as frequencies. Chi square test was performed for comparisons between dichotomous variables. A p value ≤ 0.05 was used for statistical significance.

Results: 100 patients were included, 87% women, with a mean age of 51.36 ± 11.03 years, mean disease duration of 130.9 ± 102.64 months. 84.4% had positive ACPA. 43.3% had bone erosions, with an average of DAS 28-ESR 3.42 ± 1.1. 60% of patients presented with echocardiographic left ventricular delayed relaxation pattern. Regarding traditional CV risk factors, the same ones presented more frequently HBP (40% vs 19.4%, p = 0.037), DM2 (11.7% vs 0%, p = 0.036), obesity (38.3% vs 16.7%, p = 0.025), altered glycemia (27.1% vs 6.5%, p = 0.02), altered HbA1C (50.8% vs 22.6%, p = 0.01), higher mean weight (75.9 ± 17.62 p = 0.02), higher Framingham index high (20% vs 3.2%, p = 0.03). Regarding to clinical parameters, a higher frequency of erosions was found (55.8% vs 22.2%, p = 0.004), without other significant differences for disease activity, seropositivity or disease duration. As for serum biomarkers, higher levels of fibrinogen (639.71 ± 189.84, p = 0.04), homocysteine (11.74 ± 7.81, p = 0.05) and VCAM (519, 16 ± 203.68, p = 0.02) were found.

Conclusion: We found a high frequency of diastolic dysfunction in patients with RA. They presented a significant association with traditional CV risk factors, erosions, and fibrinogen, homocysteine, and VCAM biomarkers. Adequate control of cardiovascular risk factors and echocardiographic assessment of these patients is essential in order to avoid the progression of heart functional damage.

REFERENCES:

[1] Aslam F, Bandeali SJ, Khan NA, Alam M. Diastolic Dysfunction in Rheumatoid Arthritis: A Meta-Analysis and Systematic Review. Arthritis Care & Research. 2013;65(4):534-43.

[2] Liang KP, Myasoedova E, Crowson CS, Davis JM, Roger VL, Karon BL, et al. Increased prevalence of diastolic dysfunction in rheumatoid arthritis. Annals of the Rheumatic Diseases. 1 de septiembre de 2010;69(9):1665-70.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1935

AB0160 HIGH NUMBER OF CONCOMITANT MEDICATIONS AND COMORBIDITIES AT BASELINE IN THE GLUCOCORTICOID LOW-DOSE OUTCOME IN RHEUMATOID ARTHRITIS (GLORIA) STUDY: AN OLDER POPULATION WITH RHEUMATOID ARTHRITIS

M. Boers[1,2], L. Hartman[1,2], D. Opris-Belinski[3], R. Bos[4], M. R. Kok[5], J. A. P. Da Silva[6], E. N. Griep[7], R. Klaasen[8], C. Allaart[9], P. Baudoin[10], H. Raterman[11], Z. Szekanecz[12], F. Buttgereit[13], P. Masaryk[14], T. Klausch[1], S. Paolino[15], A. Schilder[4], W. Lems[2], M. Cutolo[15]. *[1]Amsterdam UMC, Vrije Universiteit, Epidemiology & Data Science, Amsterdam, Netherlands*; *[2]Amsterdam UMC, location VUmc, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands*; *[3]Carol Davila University of Medicine and Pharmacy, Department of Internal Medicine and Rheumatology, Bucharest, Romania*; *[4]Medical Center Leeuwarden, Department of Rheumatology, Leeuwarden, Netherlands*; *[5]Maasstad Hospital, Department of Rheumatology and Clinical immunology, Rotterdam, Netherlands*; *[6]Faculdade de Medicina e Hospitais da Universidade de Coimbra, Department of Rheumatology, Coimbra, Portugal*; *[7]Antonius Hospital, Department of Rheumatology, Sneek, Netherlands*; *[8]Meander Medical Center, Department of Rheumatology, Amersfoort, Netherlands*; *[9]Leids University Medical Center, Department of Rheumatology, Leiden, Netherlands*; *[10]Reumazorg Flevoland, Department of Rheumatology, Lelystad, Netherlands*; *[11]Northwest Clinics, Department of Rheumatology, Alkmaar, Netherlands*; *[12]Institute of Medicine, University of Debrecen, Department of Rheumatology, Debrecen, Hungary*; *[13]Charité – University Medicine Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; *[14]National Institute for Rheumatic Diseases, Rheumatology, Piešťany, Slovakia (Slovak Republic)*; *[15]University of Genoa, Department of Rheumatology, Genoa, Italy*

Background: Treatment with low-dose glucocorticoids (GCs) (≤7.5 mg prednisolone) in combination with standard care is highly effective in rheumatoid arthritis (RA), but despite 70 years of clinical experience, evidence-based information on its balance of benefit and harm is incomplete. This leads to an ongoing debate, with under- and over-use of GCs as result. The GLORIA pragmatic trial was developed to assess harm, benefit and costs of low-dose GCs added to the standard treatment of older RA patients.

Objectives: The objective of this abstract is to document the baseline status and frequency of comorbid conditions in the GLORIA study population. The results of the unblinded data will be submitted as late-breaking abstract.

Methods: This double-blind, randomized, placebo-controlled, multicenter trial (1) was open for patients with RA according to the 1987 or 2010 (2) criteria, age ≥65 years, and disease activity score of 28 joints (DAS28) of ≥2.6. Patients were recruited from rheumatology clinics in Germany, Hungary, Italy, The Netherlands, Portugal, Romania and Slovakia. Eligible patients were randomized to two years of treatment with daily 5 mg prednisolone or matching placebo. All other medication was allowed, except for GCs. The presented data are blinded because the database is not closed yet.

Results: The population consists of 451 patients with mean disease duration 10.6 (Q1-Q3: 3-15) years. The majority (70%) is female, mean age is 72.5 (Q1-Q3: 68-76, range: 65-88) years, 66% were positive for rheumatoid factor and 56% for ACPA. Patients had a mean of 4.3 (SD 2.8) comorbidities besides RA (3.4 active) and therefore used multiple concomitant medications (3.9 (SD 3.4)) (Table 1). The most common comorbidities (provisional data of 161 patients with complete coding) in this older population are: vascular disorders (58%), musculoskeletal and connective tissue disorders (57%) and a history of surgical and medical procedures (45%). Patients were most frequently on beta blocking agents (22%, mainly metoprolol) and HMG CoA reductase inhibitors (20%, mainly simvastatin). Most patients also have an extensive history of anti-rheumatic treatment. At the start of the trial most patients (82%) were on cDMARD treatment; 15% were on bDMARDs/tsDMARDs. Almost half of the patients previously had been treated with GCs, with a mean duration of 3.4 years and a mean last dose of 4.6 mg/day.

Conclusion: The baseline data shows that we have an older study population who have relatively many other comorbidities next to RA and who are almost all treated with multiple concomitant medications in addition to the study medication. Therefore, we expect to report a high adverse event rate. Research among older patients is urgently needed, but the frailty of this population as represented by the multiple comorbidities and concomitant medications have to be taken into account in the analyses and interpretation of the results.

REFERENCES:

[1] Hartman L, Rasch LA, Klausch T, Bijlsma HWJ, Christensen R, Smulders YM, et al. Harm, benefit and costs associated with low-dose glucocorticoids added to the treatment strategies for rheumatoid arthritis in elderly patients (GLORIA trial): study protocol for a randomised controlled trial. Trials. 2018;19:67.

[2] Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010;62:2569-81.

Table 1. Comorbidities and concomitant medications at baseline in the GLORIA trial.

	Mean	SD	Range
Comorbidities	4.3	2.8	0-15
Active	3.4		
Past	1.9		
Concomitant medications (count)	3.9	3.4	0-15
Beta blocking agents (%)	22		
HMG CoA reductase inhibitors (%)	20		
Platelet aggregation inhibitors (%)	16		
ACE inhibitors (%)	12		
Angiotensin II antagonists (%)	11		
DAS28	4.52	1.05	
DAS28CRP	4.06	0.97	
HAQ (0-3)	1.2	0.7	
RA treatment	**Current (%)**		**Previous (%)**
cDMARD	84		92
bDMARD/tsDMARD	15		22
NSAID	51		29
Glucocorticoids	0		49

Acknowledgements: The GLORIA project is funded by the European Union's Horizon 2020 research and innovation programme under the topic ''Personalizing Health and Care", grant agreement No 634886.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2013

AB0161 THE IMPACT OF BIOLOGICAL AGENTS ON CARDIOVASCULAR RISK FACTORS OF PATIENTS DIAGNOSED WITH RHEUMATOID ARTHRITIS

G. Papamichail[1], T. Markatseli[2], A. Georgiadis[2], V. Xydis[3], C. Milionis[4], A. Drosos[2], P. Voulgari[5]. *[1]Internal Medicine, University of Ioannina, Greece, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece, Ioannina, Greece*; *[2]Rheumatology Clinic, University of*

Ioannina, Ioannina, Greece, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece, Ioannina, Greece; [3]*Radiology, University of Ioannina, Greece, Department of Radiology, Medical School, University of Ioannina, Ioannina, Greece, Ioannina, Greece*; [4]*Internal Medicine, University of Ioannina, Greece, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece, Ioannina, Greece*; [5]*Rheumatology Clinic, University of Ioannina, Ioannina, Greece, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece, Ioannina, Greece*

Background: The risk of cardiovascular disease in patients with rheumatoid arthritis (RA) is 1.5-2 fold higher than in people of the same age and sex of the general population.[1,2,3] This marked risk is attributed to the systemic chronic inflammation which is characteristic of the disease.
Objectives: The aim of this study is to evaluate cardiovascular risk factors and early atherosclerosis in rheumatoid arthritis patients, treated with biological agents.
Methods: This is a prospective, observational study. Thirty-five patients treated with synthetic DMARDs with no previous history of a cardiovascular event included. We compared total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides (TGs), Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB) and Lipoprotein A (LpA), the titer of autoantibodies against oxidised LDL(anti-oxLDL), systolic blood pressure, inflammatory markes as C-reactive protein (CRP) and erythrocytes sedimentation rate (ESR) between baseline and after 6 months of biological agents initiation. An ultrasonographic measurement of intima-media thickness (IMT) of carotids was also performed by an experienced sonographer at baseline and after one-year follow-up.
Results: As regards the demographic characteristics of patients, the mean (SD) age was 54(14) years, disease duration 4,3(1.4) years, 22.9% were smokers and 68,6% were women. Anti-TNF was administered in 71,4% of patients while the rest non anti-TNF was given as treatment. Six months after treatment initiation, patients presented with a significant increase in mean (SD) HDL[69(19)vs58(15)] and ApoA1[177(34)vs162(31)] levels (p value <0,001) with a simultaneous significant reduction of mean (SD) systolic blood pressure [128(12)vs136(14)] and the titer of anti-oxLDL[0,132(0,042)vs0,190(0,056)]. IMT was also reduced after one-year reassessment [0,8(0,3) mm vs 0,9(0,3)mm, (p value <0,001 for all comparisons)].
Conclusion: Biological agents administration was accompanied by an improved lipid profile in a six-month period and a significant reduction of IMT, confirming that RA patients are prone to early atherosclerosis and probably biological agents initiation correlates strongly with cardiovascular risk reduction.
REFERENCES:
[1] Avina-Zubieta JA, Choi HK, Sadatsafavi M, Etminan M, Esdaile JM, Lacaille D. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. Arthritis and rheumatism. 2008 Dec 15;59(12):1690–1697.
[2] Avina-Zubieta JA, Thomas J, Sadatsafavi M, Lehman AJ, Lacaille D. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Annals of the rheumatic diseases. 2012 Sep;71(9):1524–1529.
[3] Solomon DH, Karlson EW, Rimm EB, Cannuscio CC, Mandl LA, Manson JE, et al. Cardiovascular morbidity and mortality in women diagnosed with rheumatoid arthritis. Circulation. 2003 Mar 11;107(9):1303–1307.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2287

AB0162 OCULAR MANIFESTATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

D. Monova[1], S. Monov[2], R. Shumnalieva[2], D. Dimova[3], M. Sotirova[4]. [1]*Medical Institute, Medical University - Sofia, Department of Internal Medicine, Sofia, Bulgaria*; [2]*Medical University - Sofia, Departmant of Rheumatology, Sofia, Bulgaria*; [3]*Medical Insitute-MVR, Department of Ophtalmology, Sofia, Bulgaria*; [4]*Medical Institute, Department of Ophtalmology, Sofia, Bulgaria*

Background: Rheumatoid arthritis (RA) is the most common systemic autoimmune disease and is associated with a number of extra-articular organ manifestations, including ocular complications.
Objectives: The aim of this study is to evaluate the frequency and characteristics of ocular manifestation in patients with rheumatoid arthritis (RA).
Methods: The study involved 87 patients with RA. All the study subjects underwent complete ophthalmological examination involving visual acuity assessment, examination of anterior and posterior eye segments, Schirmer's test, diameter and mobility of pupils, as well as eyeball mobility assessment of intraocular pressure. Data regarding age, gender, disease duration, age at diagnosis, systemic corticosteroid use, blood pressure, ocular symptoms and detailed ophthalmic history were recorded. The presence of rheumatoid factor in serum was evaluated by standard test methods based on principle of agglutination. All patients were seropositive.
Results: 87 patients (26 male, 59 female, mean age 45,6 ± 13,1 years; mean disease duration 7,4 ± 6,2 years) with RA were enrolled in this study. 31 (35,63 %) of them had no ocular symptoms. Among the patients with ocular symptoms, 39 (69,64 %) complained of decreased vision, 33 (58,93 %) - of dry eye, 32 (57,14 %) - of burning, 29 (51,78 %) -photophobia, 28 (50 %) - of gritty sensation, 27 (48,21 %) - of itching, 18 (32,14 %) - of redness, 13 (23,21 %) - of ocular pain, 3 (5,36 %) - of floaters. Ophthalmological examination revealed higher incidence of the following abnormalities in the study group: myopic astigmatism - in 10 (5,74 %) eyes, vascular abnormalities within fundus - in 22 (12,64 %) eyes, increased intraocular pressure (> 21 mm Hg) - in 11 (6,32 %) eyes. Mean IOP values were 17,34 ± 5,12 mm Hg. In 48 eyes Schirmer's test results were below 10 mm, and in 18 eyes - below 5 mm. Keratoconjunctivitis sicca was present in 31 (35,63 %) of all patients. Episcleritis was diagnosed in 4 patients (4,6 %), scleritis – in 3 (3,45 %). Retinal vasculitis was present in 2 (2,3 %) patients and involves veins and arteries peripheral branches. Lens opacity was found in 13 (14,94 %) patients (21 eyes), mostly in the form of posterior subcapsular cataract (in 16 eyes) and nuclear cataract (in 5 eyes). The mean age of patients with cataracts was 52,3 ± 14,2 years. 13 of the patients with cataracts were either currently taking or had previously taken systemic corticosteroids.
Conclusion: In patients with RA numerous abnormalities within the vision of organ may be found. Ocular symptoms are relatively common complications of RA, and may result in irreversible changes in the organ of vision. Regular ophthalmological examinations are essential among the patients with RA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2823

AB0163 ELECTROCARDIOGRAPHIC MANIFESTATIONS IN PATIENTS WITH SEROPOSITIVE RHEUMATOID ARTHRITIS

S. Spitsina[1,2], E. Mozgovaya[1], A. Trofimenko[1], S. Bedina[1], M. Mamus[1]. [1]*Federal State Budgetary Institution "Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky", Clinical Biochemical Laboratory, Volgograd, Russian Federation*; [2]*Federal State Budgetary Educational Institution of Higher Education "Volgograd State Medical University" of the Ministry of Healthcare of the Russian Federation, Department of Hospital Therapy, Volgograd, Russian Federation*

Background: Cardiovascular disease in rheumatoid arthritis (RA) is more common than in general population. Particular attention should be paid to cardiac dysfunction, as their timely diagnosis strongly affects the general outcome.
Objectives: To assess the prevalence of arrhythmias and conduction disorders in patients with seropositive RA without clinical manifestations of coronary artery disease, as well as to determine their relationship with activity and duration of RA.
Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles. 48 patients with seropositive RA were included in the study. The exclusion criteria were: age over 60 years; obesity; congenital heart defects; coronary artery disease; peripheral atherosclerosis; thyroid disease; diabetes mellitus. All patients were assessed using general physical, laboratory and instrumental survey including CBC, blood chemistry panel, as well as ECG. RA diagnosis was verified using the 2010 ACR / EULAR classification criteria. Central tendencies were expressed as mean ±SD.
Results: All the included persons were women. Their average age was 50.50 ± 7.22 years, and average duration of the disease was 8.13 ± 2.34 years. All patients had articular form (without systemic manifestations) of moderate and high activity. The patients were treated with basic and NSAIDs therapy; no glucocorticoids were applied at the time of the examination. Using 12-lead ECG arrhythmias and conduction disorders were revealed in 27 (56.25%) of RA patients. Sinus rhythm deviations had the highest (31.25%) prevalence for all arrhythmias, comprising sinus tachycardias (18.75%), sinus bradycardias (6.25%), and sinus arrhythmias (6.25%). Premature beats were registered in 12.5% cases, being supraventricular and ventricular ones in equal proportions. We have found left anterior bundle branch block in 6 (12.5%) of patients. Despite absence of any angina symptoms, 9 (18.75%) of patients had myocardial repolarization disturbances, either as ST depression deeper than 0.1 mV or as negative T wave appearance, which were quite similar to silent myocardial ischemia manifestations. All the patients with these two features had RA history of more than 10 years. There was no relationship between the prevalence of the manifestations and radiographic stage of RA.
Conclusion: Arrhythmias and conduction disorders are quite frequent finding in seropositive RA (56.25% and 18.75%, respectively). Their incidence and severity do not coincide exactly with the radiographic progression in joints, while their prevalence generally increases with disease duration.
These data highlight the importance of additional Holter ECG monitoring in RA for revelation and treatment of silent life-threatening cardiovascular complications.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2895

AB0164 THE EFFECT OF RHEUMATOID ARTHRITIS ON FEMALE FERTILITY

S. Ben Jemaa[1], G. Mouna2, A. Hriz2, A. Feki2, H. Fourati2, S. Baklouti2. *[1]Hedi Chaker Hospital, Rheumatology, SFAX,Tunisia*; *[1]Hedi Chaker Hospital, Rheumatology, SFAX,Tunisia*

Background: Infertility is a disease of the reproductive system defined by the failure to achieve clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. Although rheumatoid arthritis (RA) tends to have a late onset, the disease also occurs during child-bearing years and may interfere with procreation.
Objectives: The aim of this study was to compare fertility rates in women with RA with birth-year-matched references from the general population.
Methods: This is a case-control study. Menopausal married women who were diagnosed in the department of Rheumatology at Hedi Chaker Hospital before the age of forty were recruited into this study as cases and apparently healthy age matched married women were recruited as controls. Demographic, clinical, immunological, radiological and therapeutic data were collected from each case using the medical record of patient. Data obtained included age, age of RA onset, duration of RA, extra-articular manifestations, Rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (ACPA), the presence of erosions on radiographs of hands and feet and the therapy.
Rheumatoid arthritis and controls women were asked to state their menstrual regularity, age at menarche, age at menopause, gestity, parity, number of living children, time to first pregnancy, presence of primary or secondary infertility, the interpregnancy interval, presence of miscarriage or in utero foetal death (IUFD) or preterm delivery and their number.
Results: The mean ages of the cases and controls was 54 ± 8,11 years [39, 69]. The median duration since onset of RA in the patients was 22,5 ± 10,53 years [1, 47]. The mean age of onset of the disease was 31,4 ± 6,3 [18, 39] years. Forty-nine percent (49%) of patient had extra-articular manifestations: ocular sicca syndrome in 43,8% of cases, pulmonary fibrosis in 5,3% of cases and rheumatoid nodules in 1,8 % of cases. Rheumatoid factor (RF) was present in 61,4% of cases while anti-CCP anti-body was present in 59,6% of cases.
Erosive polyarthritis was found in 80,7% of patients. The mean rate of RF was 319,7 ± 462,4 UI/ml and the mean rate of anti-CCP was 185,8 ± 264.
Women with RA had a statistically significant mean time to pregnancy longer than the control group. Primary infertility was seen in 15 (26,3%) patients and 2 (3,5%) controls, whereas secondary infertility was seen in 31 (54,5%) patients and 2 (3,5 %) controls. The patients were significantly more likely to have primary and secondary infertility. There were no significant differences in the age at menarche, the number of children, the gestity and the parity between the two groups. The age at menopause was statistically significant lower in the group patients than controls.
Conclusion: Our study showed that RA women are more likely to have reduced fertility than general population. Although this study cannot definitively address the issue of impaired fertility among women with RA, the results are suggestive enough to warrant further research into the link between RA and fertility that takes women's childbearing choices into account.
REFERENCES:

[1] Clowse ME, Chakravarty E, Costenbader KH, Chambers C, Michaud K. Effects of infertility, pregnancy loss, and patient concerns on family size of women with rheumatoid arthritis and systemic lupus erythematosus. Arthritis Care Res 2012; 64: 668-74.
[2] Brouwer J, Hazes JM, Laven JS, Dolhain RJ. Fertility in women with rheumatoid arthritis: influence of disease activity and medication. Ann Rheum Dis 2015; 74: 1836-41.
[3] Pope JE, Bellamy N, Stevens A. The lack of associations between rheumatoid arthritis and both nulliparity and infertility. Semin Arthritis Rheum 1999; 28:34250.
[4] Akintayo RO, Aworinde O, Ojo O, Akintayo FC, Akinlade OM, Awodun RO, Isa SO. Is rheumatoid arthritis an innocent bystander in female reproductive problems? A comparative study of fertility in Nigerian women with and without rheumatoid arthritis. Eur J Rheumatol 2018; 5(3): 179-83.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3055

AB0165 CENTRAL SENSITIZATION IN RHEUMATOID ARTHRITIS

E. Filatova[1], E. Pogozheva[1], V. Amirdzhanova[1], A. Karateev[1], A. Lila[1]. *[1]VA Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*

Background: Central Sensitization (CS) is a proposed physiological phenomenon in which dysregulation in the central nervous system causes neuronal dysregulation and hyperexcitability, resulting in hypersensitivity to both noxious and non-noxious stimuli. The term Central Sensitivity Syndrome (CSS) describes a group of medically indistinct (or nonspecific) disorders, such as fibromyalgia (FM) (1, 2).
The prevalence of FM has been estimated at 2-7% in general population, but 10-30% patients with several rheumatic diseases fulfill the FM criteria, which suggests that they have not only nociceptive pain, but signs of CS or nocyplastic pain. (3)
Objectives: to identify the signs of central sensitization (CS) in patients with rheumatoid arthritis (RA) with the central sensitization inventory (CSI).
Methods: We examined 43 RA patients (mean age 45.5 [29.0; 53.0] years) with chronic pain. The patients underwent rheumatological examinations; CS was diagnosed using the CSI(4).; inflammation severity (DAS28 index), pain intensity (VAS), affective disorders (HADS), and quality of life (EQ-5D) were assessed.
Results: We recruited 36 women and 7 men, mostly with moderate and high disease activity according to the DAS28 index.
Using the CSI subclinical CS was found in 9 patients (20.9%), mild in 7 (16.3%), moderate in 8 (18.6%), severe in 16 (37.2%), and extremely severe sensitization in 3 (6.7%). Thus, 62.5% of patients with RA had had clinically significant CS (CS>40 points according to the CSI questionnaire).
Patients with the presence of CS were characterized by more severe anxiety (10.0 [7.0; 11.0] vs 5.0 [3.0; 6.0], p=0.001) and lower quality of life (0.52 [-0.02; 0.52] vs 0.52 [0.52; 0.69], p= 0.02).
The CSI tests not only pain but also other diseases associated with CS. Comorbid disorders associated with CS were found in patients with RA: 34.9% had cognitive impairment, 39.5% had signs of depression.
Conclusion: Central sensitization was detected in 62.5% of patients with RA using the CSI questionnaire. CS is associated with anxiety and depression and negatively affects the patients' quality of life. Chronic pain in RA can be of a mixed nature: nociceptive and neoplastic, which must be taken into account in the selection of personalized therapy.
REFERENCES:

[1] Wolfe F. Fibromyalgianess. Arthritis Rheum. 2009; 61: 715-6.
[2] Martins Rocha T, Pimenta S, Bernardo A, et al. Determinants of non-nociceptive pain in Rheumatoid Arthritis. Acta Reumatol Port. 2018 Oct-Dec;43(4):291-303.
[3] Halioglu S, Carlioglu A., Akdeniz D., Karaaslan Y., Kosar A. Fibromyalgia in patients user rheumatic patients with several rheumatic diseases: prevalence and relationship with disease activity. Reumatol. Int. 2014 Sep; 34(90:1275-80 doi:10.1007/s00296-014-2972.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3074

AB0166 MORTALITY AND COMORBIDITIES IN A COHORT OF PACIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS

J. Calvo Gutierrez[1], B. Rodríguez Jiménez[2], M. L. Ladehesa Pineda[1], M. Rojas-Giménez[1], R. Ortega Castro[1], A. Escudero Contreras[1]. *[1]Reina Sofía University Hospital, Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), Rheumatology, Córdoba, Spain*; *[2]Reina Sofia University Hospital, Medicine University of Cordoba, Medicine, Córdoba, Spain*

Background: Patients diagnosed with Rheumatoid Arthritis (RA) have an increased risk of comorbidities and secondary mortality, in a large extent due to cardiovascular events.
Objectives: To identify the frequency of comorbidity, mortality and variables related to its increase in a cohort of patients with rheumatoid arthritis established (RAE).
Methods: Controlled cross-sectional observational study of a cohort of 188 patients with RAE a 10 year follow-up (5 years if not complete this period).
Results: 62.8% were women, mean age of patients at the time of inclusion was high 73.3 (+/-13.8) years and mean duration of disease was 12,8 (+/-6,99) years. Regarding CV risk factors, 26.6% smoked, 60.6% hypertension and 52.1 % diabetic. Regarding comorbidities, the most frequent were serious infections (45.2%), CVD (35.1%), Osteoporosis (31.9%), Depression (31.9%) and Kidney disease (26.6%). During follow-up, an improvement was observed inflammatory parameters and activity levels (p <0.001) Table 1. Mortality was associated to CVD and severe infection, and depression to lower mortality (p 0.05). Overall mortality was 32.4%. A logistic regression was performed in the group of patients with time greater evolution 10 years of our cohort, to be able to better represent the influence of disease carrying with her for longer, whose results are shown in Table 2. Analysand survival, men, CVD, severe infections, and Positive Rheumatoid Factor were associated with higher mortality, while treatment with Methotrexate was associated with increased

survival. Among the causes of death, the most frequent were infections, CVD and solid cancer.

Conclusion: -The incidence of comorbidities in our cohort is similar to that described in the literature.

-Relationship between mortality and CVD and severe infection is demonstrated.

-The mortality rate observed is higher than that described in the literature, which be influenced by the advanced age of the patients in the cohort and high time evolution of RA.

REFERENCES:

[1] Lee YK, Ahn GY, Lee J, Shin JM, Lee TH, Park DJ, Song YJ, Kim MK, Bae SC. Excess mortality persists in patients with rheumatoid arthritis. Int J Rheum Dis. 2021 Jan 19. doi: 10.1111/1756-185X.14058. Epub ahead of print. PMID: 33463890.

[2] Mikuls, T. R. (2003). Co-morbidity in rheumatoid arthritis. Best Practice & Research Clinical Rheumatology, 17(5), 729-752.

[3] Naz, S. M., & Symmons, D. P. M. (2007). Mortality in established rheumatoid arthritis. Best Practice & Research Clinical Rheumatology, 21(5), 871-883.

Table 1. Student's t test for paired data.

Variables	Basal	10 year	P
DAS28	5,25 (15,08)	2,89 (1,06)	0,036
VAS	38,61 (36,45)	26,93 (24,97)	<0,001
HAQ	1,04 (0,79)	0,88 (0,87)	NS
TJC	4,96 (5,38)	1,40 (2,57)	<0,001
SJC	3,55 (3,69)	0,72 (2,11)	<0,001
ESR (mm/h)	31,47 (21,19)	25,86 (18,47)	<0,001
CRP (mg/L)	15,24 (16,13)	9,41 (21,02)	0,001
Hemoglobin (mg/dL)	13,44 (7,92)	13,52 (7,64)	NS
Glucose (mg/dL)	102,26(35,97)	103,83 (37, 98)	NS
Cholesterol (mg/dL)	203,56 (46,11)	195,65 (38,12)	0,042
LDL (mg/dL)	123,91 (40,69)	119,58 (33,89)	NS
HDL (mg/dL)	56,73 (19,07)	54,84 (20,38)	NS
Triglycerides (mg/dL)	110,85 (60,77)	113,44 (55,61)	NS

Table 2. Logistic regression model. Hosmer-Lemeshow Chi square 9.035 Gl 7 p 0.25. Likelihood ratio test Chi square 64.658 Gl 5 p <0.001. NS, Not significant.

Variable	Univariate analysis OR (IC 95%)	p	Multiivariate analysis FINAL MODELO OR (IC 95%)	P
Dyslipidemia	1,02 (0,47-2,23)	0,965		
HT	4,73 (1,79-12,48)	0,002		
DM	1,42 (0,59-3,44)	0,438		
CV disease	11,25 (4,45-28,44)	< 0,001	12,33 (3.89-39,04)	< 0,001
Hyperuricemia	3,27 (1,39-7,65)	0,006		
Thyroid disease	0,56 (0,15-2,11)	0,393		
Interstitial lung disease	2,48 (0,77-7,99)	0,127	7,37 (1,48-36,84)	0,015
Osteoporosis	2,38 (1,07-5,29)	0,033		
Renal disease	8,25 (3,41-19,97)	< 0,001	4,14 (1,34-12,80)	0,014
Depressión	0,32 (0,12-0,84)	0,021	0,20 (0,06-0,74)	0,015
Solyd CA	1,12 (0,44-2,87)	0,809		
Hematologic CA	<0,001 (NS)	0,999		
Amyloidosis	2,65 (0,16-43,52)	0,496		
Severe infecction	6,22 (2,53-15,29)	< 0,001	5,59 (1,66-18,79)	0,005
COVID-19 infection	1,31 (0,12-14,91)	0,828		

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3082

AB0167 PECULIARITIES OF INTERACTION OF CHRONIC INFLAMMATION AND DEPRESSION IN RHEUMATOID ARTHRITIS

A. Aleksandrov[1], N. Aleksandrova[1]. [1]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», Department of Clinical and Laboratory Diagnostics, Volgograd, Russian Federation*

Background: In patients with rheumatoid arthritis (RA), a high prevalence of depression and anxiety is observed, and the severity of these conditions depends on the degree of vitamin D deficiency. The role of the main mediator, with the help of which psychological and physical stress factors can contribute to the development of depression and systemic diseases, has been attributed to inflammation in recent years.

Objectives: to assess the dependence of depressive disorders on vitamin D deficiency and the level of pro-inflammatory cytokines in patients with RA.

Methods: 88 women with a reliable diagnosis of RA (mean age 54.2 ± 12.0 years old, disease duration 9.0 [3.5; 16.0] years) were under observation. Beck's depression inventory (BDI-II) was used to assess the presence of depressive symptoms. ELISA test was used to measure serum cytokines (IL-1, IL-6) and serum 25(OH)D levels.

Results: The presence of depression was found in 66% of patients with RA. An insufficient level of 25(OH)D (<30 ng / ml) was determined in 89.8% of cases. In RA patients with no signs of depression, the level of 25(OH)D showed maximum values and significantly differed from that in the groups of patients with moderate ($p = 0.028$) and severe depression ($p < 0.001$). A negative correlation ($r = -0.38$, $n = 88$, $p < 0.05$) was established between the level of 25(OH)D and the severity of depression. A positive relationship was also found between 25(OH)D and ESR ($r = 0.29$, $n = 73$, $p < 0.05$) and a negative relationship with the number of painful joints ($r = -0.29$, $n = 76$, $p < 0.05$). Probably, vitamin D is indirectly involved in inflammatory processes in joints and in central sensitization, which provokes chronic pain and psychological disorders in patients with RA.

The level of IL-6 in patients with RA with moderate and severe depression (n=18; 14.6 ± 6.7 pg/ml) significantly exceeded the parameters of patients with RA without depressive disorders (n=30; 9.8 ± 3.7; $p = 0.003$). There was also a tendency to increase IL-6 in the group of patients with moderate and severe depression compared with patients with mild depression ($p = 0.06$). IL-1β values significantly increased with the progression of depression (without depression – mild depression, $p = 0.034$; mild – moderate, $p < 0.001$; moderate – severe depression, $p = 0.044$). A positive correlation of average severity was revealed between the degree of depression (according to BDI-II) and the dose of glucocorticoids (GC) at the time of the study ($r = 0.33$, $p = 0.002$). An increase in the GC dose in the short term can aggravate depressive disorders in RA patients (Table 1).

Table 1. Indicators of levels of depression and IL-1β depending on the dose of GC

	Group I (n=26), without GC	Group II (n=45), GC <10 mg / day	Group III (n=17), GC ≥10 mg / day
Depression level according to BDI-II, points (Me [P25; P75])	8,5[5;16]	14[9;17]	19[14;29] $^{*III-I}$
IL-1β level, pg / ml (M ± SD)	4,57 ± 1,83 $^{*I-II}$	6,04 ± 3,27	6,52 ± 5,16

* - intergroup differences are reliable, $p < 0.05$

Patients who used GC in a daily dose of ≥10 mg / day (group III) had a higher degree of depression compared to patients with RA from group I ($z = -2.98$; $p = 0.003$). In patients with RA in the first group, the level of IL-1β was significantly higher ($p_{I-II} = 0.039$) than in patients with GC prescription in minimal doses (up to 10 mg / day) (Table 1). Glucocorticoid hormones suppress pro-inflammatory cytokines. As a rule, this effect is not observed in patients with depression. This fact may indicate a violation of homeostatic mechanisms. IL-1β is thought to be the first step in the pro-inflammatory response to psychological stress and is capable of inducing a subsequent cascade of other inflammatory cytokine responses.

Conclusion: Restoring the normal level of 25(OH)D in the blood serum of patients with RA can positively affect psychological indicators by reducing the severity of depression and manifestations of pain. The activation of pro-inflammatory cytokines during stress and depression suggests that suppression of the inflammatory response can also reduce the symptoms of depression in RA patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3087

AB0168 BODY MASS INDEX IS ASSOCIATED WITH SIGNIFICANT ECHOCARDIOGRAPHIC ABNORMALITIES IN RHEUMATOID ARTHRITIS

S. Hannawi[1], K. Naeem[2], H. Hannawi[3]. [1]*Ministry of Health and Prevention-UAE, Rheumatology, Dubai, United Arab Emirates*; [2]*Ministry of Health and Prevention-UAE, Internal Medicine, Dubai, United Arab Emirates*; [3]*Ministry of Health and Prevention-UAE, Research, Dubai, United Arab Emirates*

Background: Overweight/obesity is associated with a high incidence of chronic autoimmune diseases such as rheumatoid arthritis (RA). In RA, obesity represents an increasingly prevalent comorbidity even at its first presentation, with more than 60% of patients with RA classified as overweight or obese by the body mass index (BMI ≥25 kg/m^2). On the other hand, RA is related with excess

cardiovascular disease (CVD) mortality, which accounts for over 50% of premature deaths in RA. Obesity contributes to the development of inflammation *via* changes in metabolism and function of adipose tissue and it appears to coexist with other CVD risk factors such as hypertension, insulin resistance and dyslipidemia.

Objectives: For the first time, this study looks at the effect of the BMI on echocardiography parameters in established RA cases.

Methods: A cross section study was carried out to recruit patients meeting the 2010 ACR/EULAR criteria during 2019. Standard trans-thoracic echocardiography examination was performed by a specialist cardio-sonographer who was blinded to the status of the participants. The echocardiography parameters studied included left ventricular dimensions, wall geometry, systolic and diastolic parameters, ejection fraction, right ventricular size and function, valve structure and function, aortic root dimensions, pulmonary pressures and pericardium. Anthropometric measurements of BMI were carried out as weight in kilograms divided by the square of height in meters (kg/m^2). Data was analysed using the BMI as the explanatory variable and repeating the simple linear regression analysis using the echocardiography parameters as outcome variables. P value of <0.05 was considered significant.

Results: During the one-year period, 44 RA patients were recruited, of which 91% (40) were female and 4 (9 %) male. The mean (SD) of age was 50±13 years (Min 28, Max 72). The mean (SD) of BMI was 30.887 ± 6.348 Kg/m^2 (Min 21, Max 44.38). As per BMI classification of obesity, only 11% patients were found to have normal BMI. Echocardiography revealed that 14% patients had aortic regurgitation, 2% had aortic stenosis, 2% had mitral stenosis, and 7% had tricuspid regurgitation.

Using BMI as an explanatory variable, with echocardiography parameters as outcome variables, it was found that BMI contributed positively in a linear manner to the Interventricular Septal thickness in diastole (mm) (p=0.004, CI: 0.048-0.227), LV End Diastolic Diameter (mm) (p=0.033, CI: 0.033-0.722), LV mass (g) (0.04, CI: 0.022-6.339), Early Diastolic Velocity, E, by PW mitral inflow measurement (cm/s) (p=0.02, CI: 0.150-1.933), E/E' ratio by Tissue Doppler study (p=0.01, CI: 0.025-0.225), and to Right Ventricle function measured by Tricuspid Annular Plane Systolic Excursion (TAPSE) (mm) (p=0.02, CI: 0.035-0.346).

Conclusion: Obesity and Inflammation overlap syndrome may interplay to produce various cardiovascular abnormalities. Body Mass Index is shown to be associated with significant echocardiographic abnormalities including left ventricular dimension, diastolic parameters and right ventricular function. In view of the complex interrelation between obesity, rheumatoid arthritis and cardiovascular disease, measuring Body Mass Index might help predict adverse cardiovascular events in rheumatoid arthritis patients.

REFERENCES:

[1] Body mass index and the risk of rheumatoid arthritis: a systematic review and dose-response meta-analysis. Qin B, Yang M, Fu H, Ma N, Wei T, Tang Q, Hu Z, Liang Y, Yang Z, Zhong R. Arthritis Res Ther. 2015; 17(1): 86. doi: 10.1186/s13075-015-0601-x.

[2] Cardiac eccentric remodeling in patients with rheumatoid arthritis. Pascale V, Finelli R, Giannotti R, Coscioni E, Izzo R, Rozza F, Caputo D, Moscato P, Iaccarino G, Ciccarelli M. Sci Rep. 2018; 8: 5867. doi: 10.1038/s41598-018-24323-0.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3125

AB0169 INTEREST OF THE ECHOCARDIOGRAPHY IN SCREENING OF CARDIAC INVOLVEMENT IN RHEUMATOID ARTHRITIS PATIENTS

M. Brahem[1], H. Ibn Hadj Amor[2], R. Sarraj[1], R. Rouabhia[2], E. Hmaier[2], H. Hachfi[1], A. Ben Salem[1], S. Abdellatif[1], R. Ben Tekaya[1], Y. Mohamed[1]. *[1]Taher Sfar Hospital, Rheumatology, Mahdia, Tunisia*; *[2]Taher Sfar Hospital, Cardiology, Mahdia, Tunisia*

Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory disease which usually affects peripheral joints.Extra-articular manifestations can occur during the course of this disease and even before the onset of arthritis, such as cardiac impairment that is a common cause of mortality in RA.

Objectives: The aim of our study is to identify the prevalence of cardiac manifestations in RA using the echocardiography exam and to elaborate its associated factors.

Methods: This is a cross-sectional study including consecutive RA's patients which consulted the rheumatology department in Taher Sfar hospital. The diagnosis of RA was elaborate according to ACR/EULAR 2010 criteria. The epidemiological, clinical and biological data were collected from patients' records. Echocardiography was performed by a trained cardiologist in the same hospital, using the transthoracic approach.

Results: Our study included 67 patients: 63 women (94%) and 4 men (6%), with an average age of 52.55 years [21-75 years] and mean disease duration of 11.85 years [10-40]. Joints deformities were present in 37 cases (55.2%) and radiographic joint damage in 49 cases (73.1%). 34 (50.7%) of the patients had an ESR greater than 30 mm/hour and 24 (35.8%) had a CRP greater than 6mg/L. The mean DAS28-CRP was 3.35 [1.24-6.7] and the mean DAS28-ESR was 4 [1.4-7.35]. Cardiac symptomatology was present in 22 cases (32.8%), dominated by dyspnea on effort in 22 cases (32.8%), dyspnea at rest in 4 cases (6%), chest pain in 8 cases (11.9%)and palpitation in 2 cases (3%). The echocardiography abnormalities were found in 44 cases. Valve damage was detected in 35 patients (52.2%), of which only 2 were significant. Valvular abnormalities were dominated by mitral valve regurgitation and mitral valve thickening in 11 cases (16.4%) each, aortic valve regurgitation in 6 cases (9%),aortic valve thickening in 2 cases (3%), aortic valve stenosis in 3 cases (4.5%),aortic valve calcification in 12 cases (17. 9%) aortic valve nodule in 1 case (1.5%), pulmonary insufficiency in 10 cases (14.9%) and tricuspid insufficiency in 25 cases (37.3%).Pericarditis was found in 2 cases (3%), pulmonary arterial hypertension (PAH) in 5 cases (7,5%) and Left ventricular hypertrophy in 14 cases (20,9%). The study of E/A and E/E' ratios revealed diastolic dysfunction in 23 cases (34.3%).The mean of longitudinal global strain measure was -17,83 [-21,9 to -10] and it revealed systolic dysfunction in 18 cases (26.86%). Cardiac impairment detected by echocardiography did not appear to be associated with the age (p=0.39) or the disease duration (p=0.62) nor the importance of biological inflammation(p=0.1). However, joints deformities and RA activity (DAS28) were significant predictors of cardiac involvement (p=0.01; p=0.03).

Conclusion: Our study shows that cardiac impairment in RA was often asymptomatic and was correlated with the disease activity. The echocardiography with the strain measure represents an excellent tool for its detection in early stages.

REFERENCES:

[1] Guedes C, Bianchi-Fior P, Cormier B, Barthelemy B, Rat AC, Boissier MC. Cardiac manifestations of rheumatoid arthritis: A case-control transesophageal echocardiography study in 30 patients. Arthritis Care Res. 2001;45(2):129–35.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3128

AB0170 RHEUMATOID ARTHRITIS ASSOCIATED LUNG DISEASE: EXPERIENCE IN A BIOLOGICAL THERAPY UNIT

L. Vega[1], I. Calvo[2], O. Ibarguengoitia[2], D. Montero[1], C. García[1], E. Galindez[1], J. M. Blanco[1], A. R. Intxaurbe[1], I. Torre[1], C. E. Perez[1], O. Fernandez[1], E. Cuande[1], M. R. Exposito-Molinero[1], E. Guerrero[3], M. L. García Vivar[1], M. E. Ruiz[1]. *[1]Basurto University Hospital, Rheumatology Unit, Bilbao, Spain*; *[2]Galdakao University Hospital, Rheumatology Unit, Galdakao, Spain*; *[3]Alto Deba Hospital, Rheumatology Unit, Arrasate, Spain*

Background: Rheumatoid arthritis (RA) associated lung disease is a relatively frequent extra articular disease manifestation, with a prevalence between 5% and 30%. The rather wide range of estimated prevalence is a result of differences in study designs and studied populations, as well as lacking diagnostic and classification criteria for lung disease in patients with RA.

Objectives: To evaluate the prevalence of RA associated lung disease in patients with biological therapy (BT), as well as its severity, treatment changes and possible associated factors.

Methods: Review of clinical records of 257 patients with RA treated with BT (TNFi, non-TNFi) between January 2015 to December 2020 in a single center. Patients with preexisting lung disease for other causes (asthma, smoking) have been excluded. RA diagnosis was performed according to ACR 2010 classification criteria. Epidemiological variables, clinical characteristics, type of pulmonary involvement, evolution, type of BT, changes in treatment and concomitant treatment were collected. For the analysis frequencies and percentages are used in qualitative variables, and mean ± SD in the quantitative ones. Statistical analysis was performed with IBM SPSS v 23.

Results: We registered 21 patients (85.7% women) mean aged 70.3±11.9 years. 52.4% were never smokers. RF was positive in 100% and 20 patients were anti-CCP positive. Erosive disease was present in 13 (61.9%) patients.

At the time of lung disease diagnosis, 15 patients (66.7%) were receiving TNFi (Etanercept 7, Adalimumab 6, Infliximab 1, Golimumab 1), 2 were with non-TNFi (Rituximab) and 4 had never received BT previously. Symptoms (cough and/or dyspnea) were reported in 10 (47.6%) patients. The median time of treatment with BT until lung disease diagnosis was 33 [15.5-95.5] months. Conventional synthetic DMARDs (csDMARDs) were used in 85.7% of cases (methotrexate 72.2%, leflunomide 22.2%, other 5.6%). The inflammatory activity was mild (DAS28: 3.22±1.6). The median time until lung disease diagnosis was 104 [56.2-156] months.

After the lung disease diagnosis, BT was only modified in 1 patient. In the 4 patients who had not previously received BT, non-TNFi was started (Rituximab 2, Abatacept 1, Tocilizumab 1). csDMARD was discontinued in 1 patient.

Interstitial lung disease (ILD) was the most frequent pulmonary involvement (16 patients, 76.2%): 8 usual interstitial pneumonia (UIP), 6 non-specific interstitial

pneumonia (NSIP), 1 organising pneumonia (OP) and 1 lymphocytic interstitial pneumonia (LIP). Other pulmonary manifestations observed in our patients were: nodular lung disease (2 patients) and small airways disease (bronchiectasis 2, obliterative bronchiolitis 1). Chest x-ray was normal in almost half of the patients (42.9%). Gold standard image diagnostic technique was high resolution CT.

In respiratory function tests (PFTs) at diagnosis, only 4 patients (19%) had a FVC<80% and 4 (19%) a DLCO<60%. In the following 2 years, in 2 patients the FVC worsened > 10% and in 5 there was a worsening of the DLCO > 15%. In 3 (14.3%) patients PFTs were never performed and in 7 (43.7%) were not repeated after the diagnosis.

We haven´t found association between different types of pulmonary involvement and the variables analysed.

Conclusion: In our series, prevalence of RA associated lung disease is similar to that described in the literature. Lung involvement is asymptomatic and chest X-ray is normal in most RA patients. High resolution CT is the gold standard for diagnosis.

ILD was the most frequent pulmonary involvement. Although in most patients the diagnosis of lung disease did not imply a BT change, it had an influence on the type of BT chosen for those who started treatment. Maintenance of csDMARD was not associated with a worsening of lung disease.

Screening and treatment protocols for lung disease in patients with RA in clinical practice are needed.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3178

AB0171 ACHILLES ENTHESITIS AND PLANTAR FASCIITIS IN RHEUMATOID ARTHRITIS PATIENTS: IMPACT OF BODY MASS INDEX

K. Maatallah[1], H. Boussaa[1], H. Riahi[2], H. Ferjani[1], M. Habechi[1], W. Triki[1], D. Ben Nessib[1], M. Bouaziz[2], D. Kaffel[1], W. Hamdi[1]. *[1]Mohamed Kassab Institute of Orthopedics, Rheumatology, La Manouba,Tunisia*; *[2]Mohamed Kassab Institute of Orthopedics, Radiology, La Manouba,Tunisia*

Background: Enthesitis is known as a hallmark of spondyloarthitis. However, the growing use of ultrasonography (US) increased our opportunity to encounter enthesitis in rheumatoid arthritis (RA). The involvement of Achilles tendon and the plantar fascia is not rare in RA patients.

Objectives: The aims of this study were to determine the prevalence of Achilles enthesitis and plantar fasciitis in RA patients, and to identify association with clinical data.

Methods: We conducted a cross-sectional study including patients with RA (ACR/EULAR 2010). Demographic and clinical data were collected. Three groups were defined according to the BMI: normal (BMI<25kg/m^2), overweight (BMI≥25kg/m^2) and obese (BMI≥30kg/m^2). US examination of Achilles tendon and plantar aponeurosis was performed by a blinded radiologist experienced in musculoskeletal US using a Philips HD11 device with a high-frequency linear transducer. Enthesitis was defined as hypoechoic and/or thickened insertion of the tendon close to the bone (within 2 mm from the bony cortex) which exhibits Doppler signal if active and that may show erosions, enthesophytes or calcifications as sign of structural damage. A p-value <0.05 was considered significant.

Results: Sixty-two feet were examined in 31 RA patients (25 women and six men) with a mean age of 54.8±10.8 years old [32-70]. The mean disease duration was 8.5±7.2 years [1-37]. Rheumatoid Factor (RF) and Anti-Citrullinated Peptides Antibodies (ACPA) were positive in 61.3% and 83.8% of cases. The mean DAS28 ESR was 3.8±1.5 [0.6-7].

The mean BMI was 27.7±5.4 kg/m^2 [18.3-45.8]. Obesity was noted in 22.7 % of patients and overweight in 45.5% of patients. Clinical examination revealed pes planus valgus (PPV) in 55.6% of cases and pes cavus varus (PCV) in 18.5% of cases. Heel US revealed Achilles enthesitis in 79.6% of cases. The following elementary lesions were noted in the enthesis: thickness (24.1%), hypoechogenicity (37%), erosions (9.3%), enthésophytes (75.9%), and Doppler signal (3.7%). Plantar fasciitis was noted in 81.5% of cases. The following elementary lesions were found in the insertion of plantar aponeurosis: thickness (75.9%), hypoechogenicity (77.8%), erosions (16.7%), enthesophytes (13%), calcifications (1.9%), and Doppler signal (1.9%).

An association was noted between BMI and Achilles enthesitis (p=0.002). This association was not found with plantar fasciitis (p=0.224).

Achilles enthesitis was also associated with PCV (p=0.007) while plantar fasciitis was associated with PPV (p=0.039).

Conclusion: Achilles enthesitis and plantar fasciitis are common in RA patients. These lesions seem to be associated with BMI and foot deformities rather than the inflammatory process.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3194

AB0172 ELDERLY ONSET RHEUMATOID ARTHRITIS (EORA): WHAT TO EXPECT IN REAL LIFE

I. Coman[1], I. Elisei[2], V. Bojinca[1,2], D. Mazilu[1,2], S. Daia[1,2], I. Saulescu[1,2], C. L. Constantinescu[1,2], M. Abobului[1,2], A. Borangiu[1,2], M. M. Negru[1,2], C. Cobilinschi[1,2], M. Duna[1], D. Predeteanu[1], D. Opris-Belinski[1,2], L. Groseanu[1,2], F. Berghea[1,2], A. Balanescu[1,2], R. Ionescu[1,2]. *[1]Saint Mary Hospital, Rheumatology, Bucureşti, Romania*; *[2]Carol Davila University of Medicine and Pharmacy, Medicine, Bucureşti, Romania*

Background: The term elderly onset of rheumatoid arthritis (EORA) refers to patients with rheumatoid arthritis (RA) onset after the age of 60. Data published in the literature suggest a special clinical pattern and different prognostic factors in this class of patients.

Objectives: To analyze prospectively a cohort of patients diagnosed with EORA, their disease particularities, comorbidities and treatment.

Methods: This cohort included consecutive EORA patients, diagnosed and treated in "Sfanta Maria" Clinical Hospital, Bucharest, Romania. The study was conducted for 2 years. Demographic, clinical and laboratory data was obtained. Disease activity was assessed using Disease Activity Score of 28 joints with erythrocyte sedimentation rate (DAS28-ESR). The patients were monitored using disease activity, treatment schedule modifications and possible adverse reactions.

Results: The cohort included 110 patients (88 females, 22 males). Their mean age at the beginning of disease manifestations was 70.14 years and the mean age at the diagnosis was 70.85 years. There was no statistical difference regarding the patient's residential area (urban/rural) and the period between the appearance of clinical signs and the moment of diagnosis confirmation. A great proportion of patients (77 patients, 70%) had seropositive RA, ACPA being found in 84% of the patients with seropositive RA. The mean DAS28-ESR at the diagnosis was 4.44(±1.54). A proportion of 40% of the patients had moderate disease activity, 35 patients (32.73%) - high disease activity, 11 patients (10%) - low disease activity and unexpectedly there were 19 patients (17.27%) in remission at the moment of RA diagnosis. Joint distribution was analyzed: 61.82% patients had large joint involvement, 91.82% - small joint involvement and 53.64 % had mixed joint pattern involvement. A negative significant correlation was found between the small joint involvement pattern and the body mass index (BMI) (p=0.028, R=-0.21). The mean BMI at the diagnosis was 25.81±5.358. Ninety five patients (86,36%) had at least one cardiovascular comorbidity. Hypertension was found in 70% of the patients. Only 4.55% of the patients had rheumatoid nodules and a similar proportion (4.55) had Sjogren syndrome associated. Pulmonary fibrosis was found in only 2 patients. At the moment of diagnosis 50% of patients had anemia, 36.36% had osteoporosis, 25.46% of the patients - hepatic disease, 11.82% - chronic kidney failure and 6.36% were found with a neoplasia. The main conventional synthetic disease modifying drug (csDMARD) that was recommended was methotrexate (81.8%). The second most used csDMARD was hydroxichroloquine (42 patients, 38,18%). The proportion of patients with monotherapy (50%) was similar to that with csDMARD combination (49.09%). During the follow up period only 8 patients (7.27%) had biologic therapy (4 patients - an anti TNF drug). Non steroid anti-inflammatory drugs were used in 46.63%. Cortisone therapy was used for more than 3 months in 80% of the patients. In patients with biologic therapy chronic glucocorticoids were stopped. At least one infection was documented in 20.91% of patients: 2 patients out of 6 patients (33.33%) with biologic DMARD, 14.81% of the patients with csDMARD combination and 21.81% of the patients with csDMARD monotherapy. csDMARD therapy was well tolerated with only 23.63% adverse reactions.

Conclusion: Compared to the data published in the literature, in our cohort the rate female:male was higher (4:1). A distinct feature was the high proportion of patients with seropositive RA. The joint pattern seems to be influenced by BMI: small joint pattern is less found in patients with higher BMI. As expected, the patients with EORA had multiple cardiovascular comorbidities. Arterial hypertension was the most frequent. Caution is needed in choosing treatment regarding comorbidities and the risk of infection in these patients.

REFERENCES:

[1] Villa-Blanco JI, Calvo-Alén J. Elderly onset rheumatoid arthritis: differential diagnosis and choice of first-line and subsequent therapy. Drugs Aging. 2009;26(9):739-50.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3223

AB0173 **FACTORS ASSOCIATED WITH FATIGUE AND PERSISTENT FATIGUE IN RHEUMATOID ARTHRITIS**

A. Fazaa[1], H. Boussaa[1], K. Ouenniche[1], S. Miladi[1], M. Sellami[1], L. Souabni[1], S. Chekili[1], S. Kassab[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim University Hospital, Rheumatology, Sidi Daoud, Tunisia*

Background: Fatigue is a common and debilitating symptom in patients with rheumatoid arthritis (RA). Fatigue in RA is poorly understood and appears to be multifactorial. Interactions between three factors were suggested: 'personal', 'disease processes', and 'cognitive, behavioural'.
Objectives: The aim of this study was to determine factors associated with fatigue and persistent fatigue in RA.
Methods: We conducted a longitudinal study including patients with RA (ACR/EULAR 2010). Patients with other acute or chronic diseases that may induce fatigue (such as cancer, infection or depression) were excluded. Patients were evaluated at inclusion (T0) and 12 months later (T12). Demographic and disease-related data were collected: age, gender, professional status, physical activity, disease duration, Rheumatoid Factor (RF), Anti-citrullinated peptides antibodies (ACPA), pain Visual Analog Scale (VAS), Erythrocyte Sedimentation Rate (ESR), C Protein Reactive (CRP), Disease Activity Score 28 (DAS28), and Health Assessment Questionnaire (HAQ). Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) which is a short 13-item questionnaire validated in RA. The score FACIT-F ranges between 0 and 52. Fatigue was considered mild if the FACIT-F score was ≥40, moderate if 20≤FACIT-F<40 and severe if 0≤FACIT-F<20. We defined 'persistent fatigue' as reported fatigue at T0 and T12. A p value inferior to 0.05 was considered significant.
Results: We included 100 patients (84 women and 16 men) with a mean age of 49.5±10 years old [18-65]. Among them, 25% were professionally active and 15% had a regular physical activity. At inclusion, the mean disease duration was 87.3 months [1-360]. RF and ACPA were positive in 75% and 72.6% of cases respectively. The mean pain VAS was 49 cm [0-100]. The mean levels of ESR and CRP were 38.1 mm [10-120] and 10.8 mg/l [2-61] respectively. The mean DAS28 ESR was 3.68 [1.90-8.33] and the mean HAQ score was 0.90 [0-2.75].
The mean FACIT-F score was 27.1 [0-51] at T0. Fifty-seven percent of patients had moderate fatigue and 26% had severe fatigue. At T12, the mean FACIT-F score was 33.4 [5-50]. Persistent severe fatigue was noted in 17% of patients.
A significant negative correlation was noted between FACIT-F score at T0 and the following variables: age (r=-0,258, p=0.01), pain VAS (r=-0,605, p<0.001), ESR (r=-0,621, p<0.001), DAS28 ESR (r=-0.744, p<0.001), and HAQ (r=-0.634, p<0.001).
A significant negative correlation was noted between FACIT-F score at T12 and the following variables: age (r=-0,229, p=0.022), disease duration (r=-0,296, p=0.003), pain VAS (r=-0,754, p<0.001), ESR (r=-0,405, p<0.001), CRP (r=-0,468, p<0.001), DAS28 ESR (r=-0.744, p<0.001), and HAQ (r=-0.678, p<0.001). Fatigue and persistent fatigue were not associated with gender, professional status, physical activity, and immunological profile.
Multivariable analysis showed that DAS28 ESR (OR=-0.157, 95% CI [-4.614;-0.153], p=0.036) and HAQ (OR=-0.563, 95% CI [-6.916;-2.995], p<0.001) were independently associated with persistent fatigue.
Conclusion: Fatigue is a frequent and complex symptom in RA. Higher disease activity and greater disability are suggested as predictors of persistent fatigue.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3329

AB0174 **FATIGUE IN RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY**

A. Fazaa[1], H. Boussaa[1], K. Ouenniche[1], S. Miladi[1], M. Sellami[1], L. Souabni[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim University Hospital, Rheumatology, Sidi Daoud, Tunisia*

Background: Fatigue is a common symptom in many chronic inflammatory diseases, including rheumatoid arthritis (RA). It is considered one of the most frustrating, uncontrollable, and overwhelming symptoms. However, most of rheumatologists do not assess fatigue despite its clinical significance and its impact on patients' lives.
Objectives: The aims of this study were to determine whether RA patients express more fatigue than healthy controls, and to analyze its correlation with disease activity.
Methods: We conducted a cross-sectional study including patients with RA (ACR/EULAR 2010) and healthy controls matched for sex and age. Patients with other acute or chronic diseases that may induce fatigue (such as cancer, infection or depression) were excluded. Demographic data and the following clinical parameters were collected: pain Visual Analog Scale (VAS), Global Patient Assessment (GPA), tender joint count (TJC) and swollen joint count (SJC), Erythrocyte Sedimentation Rate (ESR), C Protein Reactive (CRP), Disease Activity Score 28 (DAS28), and Health Assessment Questionnaire (HAQ). Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) which is a short 13-item questionnaire validated in RA. The score FACIT-F ranges between 0 and 52. Fatigue was considered mild if the FACIT-F score was ≥40, moderate if 20≤FACIT-F<40 and severe if 0≤FACIT-F<20. A p value inferior to 0.05 was considered significant.
Results: We included 100 RA patients (84 women and 16 men) with a mean age of 49.5±10 years old [18-65]. The mean disease duration was 87.3 months [1-360]. The mean pain VAS was 49 cm [0-100] and the mean GPA was 47.8 cm [0-100]. The mean TJC and SJC were 5.3 [0-36] and 1 [0-9] respectively. The mean levels of ESR and CRP were 38.1 mm [10-120] and 10.8 mg/l [2-61] respectively. The mean DAS28 ESR was 3.68 [1.90-8.33] and the mean HAQ score was 0.90 [0-2.75].
Thirty-nine healthy controls were enrolled including 35 women and 4 men with a mean age of 51.2 years old [30-64].
The mean FACIT-F score was 27.1 [0-51] in RA patients versus 46.2 [0-52] in healthy controls (p<0.001). Among RA patients, 57% had moderate fatigue and 26% had severe fatigue.
A significant negative correlation was noted between the FACIT-F score and the following parameters in RA patients: TJC (r=-0.568, p<0.001), SJC (r=-0.274, p<0.001), pain VAS (r=-0.605, p<0.001), GPA (r=-0.658, p<0.001), ESR (r=-0.405, p<0.001), CRP (r=-0.149, p<0.001), DAS28 (r=-0.837, p<0.001) and HAQ (r=-0.634, p<0.001).
Conclusion: Fatigue was significantly more observed in RA patients. This symptom was correlated with disease activity and disability. It is important to recognize and manage fatigue in order to improve patients' quality of life.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3339

AB0175 **OPTIMAL ASSESSMENT OF FATIGUE IN RHEUMATOID ARTHRITIS: VISUAL ANALOG SCALE VERSUS FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY – FATIGUE**

A. Fazaa[1], H. Boussaa[1], K. Ouenniche[1], S. Miladi[1], M. Sellami[1], L. Souabni[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim University Hospital, Rheumatology, Sidi Daoud, Tunisia*

Background: Fatigue is an important outcome for patients with rheumatoid arthritis (RA). As recommended by the European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) task force in 2008, fatigue should be measured in all RA clinical trials whenever possible. Despite these recommendations, it is largely ignored and rarely assessed in clinical practice.
Objectives: The aim of this study was to compare the scales being used to measure fatigue in RA.
Methods: We conducted a cross-sectional study including patients with RA (ACR/EULAR 2010). Patients with other acute or chronic diseases that may induce fatigue (such as cancer, infection or depression) were excluded. Demographic and disease-related data were collected. Fatigue was assessed using two scores. The fatigue Visual Analog Scale (VAS) ranging between 0 and 100 cm. Fatigue was considered mild if the fatigue VAS was <20 cm, moderate if 20≤VAS<50 and severe if VAS>50 cm. The Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) which is a short 13-item questionnaire validated in RA. The score FACIT-F ranges between 0 and 52. Fatigue was considered mild if the FACIT-F score was ≥40, moderate if 20≤FACIT-F<40 and severe if 0≤FACIT-F<20. We used Cohen's kappa (κ) to determine the agreement between fatigue VAS and FACIT-F. The κ result was interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement. A p value inferior to 0.05 was considered significant.
Results: We included 100 RA patients (84 women and 16 men) with a mean age of 49.5±10 years old [18-65]. The mean disease duration was 87.3 months [1-360]. RF and ACPA were positive in 75% and 72.6% of cases respectively. The mean pain VAS was 49 cm [0-100]. The mean numbers of tender and swollen joints were 5.3 [0-36] and 1 [0-9] respectively. The mean levels of ESR and CRP were 38.1 mm [10-120] and 10.8 mg/l [2-61] respectively. The mean DAS28 ESR was 3.68 [1.90-8.33].
The mean fatigue VAS was 49.1 cm [5-100]. Fatigue was mild in 9% of patients, moderate in 31% of patients, and severe in 60% of patients.
The mean FACIT-F score was 27.1 [0-51]. Fatigue was mild in 26% of patients, moderate in 57% of patients and severe in 17% of patients.
A fair agreement was noted between the two scores (κ=0.303, p<0.001).
The fatigue VAS and FACIT-F were both correlated with the following variables: pain VAS (r=0.685, p<0.001 and r=-0.605, p<0.001), ESR (r=0.384, p<0.001 and r=-0.405, p<0.001), and DAS28 ESR (r=0.684, p<0.001 and r=-0.744, p<0.001).

Conclusion: The fatigue VAS and FACIT-F are easy, brief and valid measures for monitoring this symptom and its effects on patients with RA. A fair agreement was noted between the two scores.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3346

AB0176 PATHOLOGICAL PHENOTYPES OF BODY COMPOSITION IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Feklistov[1], N. Toroptsova[1], O. Nikitinskaya[1], A. Efremova[1], N. Demin[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Osteoporosis, Moscow, Russian Federation*

Background: Inflammation, decreased physical activity, hormonal disorders, and the use of glucocorticoids lead to changes in the composition of the body in rheumatoid arthritis (RA). Various combinations of decreased muscle and bone mass and increased adipose tissue have led to the release of various pathological phenotypes of the composition of the body.
Objectives: To determine the frequency of pathological phenotypes of body composition in patients with RA.
Methods: The study included 79 women with RA, with a median age of 60 y.o. [55; 65]. 92% of the women were postmenopausal. The median duration of the disease was 9 years [3; 11]. Basic anti-inflammatory therapy was received by 81% of patients. Methotrexate was used most often as the basic therapy – in 52% of cases. 49% of patients were treated with glucocorticoid drugs. All patients underwent dual-energy X-ray absorptiometry. The mineral density of the tissues was determined in the standard measurement areas - the spine and the proximal thigh, and the content of muscle and adipose tissue was analyzed. We calculated appendicular muscle mass (AMM), which is the sum of upper and lower limb muscle mass and appendicular muscle index (AMI), the ratio of appendicular muscle mass to the square of height. AMM< 15 kg, AMI < 6 kg / m2 corresponds to sarcopenia.
Results: The average AMM was 17.8±3.0 kg. 18% patients had AMM <15 kg / m2. The average AMI was 6.8±1.0 kg / m2. 25% patients had AMI < 6 kg/m2. The average body mass index (BMI) was 27.6±4.8 kg/m2. 37% patients were overweight (25≤ BMI <29.9 kg/m2), 28% of women had a BMI corresponding to obesity. The average fat content was 28.2 kg. 71% of women had an obesity, according to X-ray absorptiometry, which is 2.5 times higher than the number of cases of obesity detected by BMI. A decrease a bone mineral density (BMD) was found in 73% of women, including osteoporosis in 25%. The most frequent phenotype was osteopenic obesity (Table 1), which was detected in almost 40% of patients. Isolated osteoporosis (16.5%) and obesity (17.7%) and osteosarcopenic obesity (16.5%) were found with approximately the same frequency. Osteosarcopenia was found in 9% of patients. In 4%, no changes in the compositional composition of the human body were detected.

Table 1. Pathological phenotypes of body composition

Pathological phenotypes of body composition	n=79
Osteoporosis, n (%)	13 (16,5)
Obesity, n (%)	14 (17,7)
Osteosarcopenia, n (%)	7 (8,9)
Osteopenic obesity, n (%)	29 (36,7)
Osteosarcopenic obesity, n (%)	13 (16,5)

Conclusion: The overall frequency of pathological phenotypes of body composition was high and amounted to 96.2% in women with RA. The most common pathological phenotype was an osteopenic obesity characterized by a decrease in BMD and an increase in fat mass.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3381

AB0177 ANXIETY-DEPRESSIVE SPECTRUM IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDILITIS

M. Letaeva[1], M. Koroleva[1], J. Averkieva[1], O. Malyshenko[1], T. Raskina[1]. [1]*Kemerovo State Medical University, Department of Propedeutics of Internal Medicine, Kemerovo, Russian Federation*

Objectives: to assess the frequency of occurrence of the anxiety-depressive spectrum in patients with rheumatoid arthritis and ankylosing spondylitis.
Methods: A survey was conducted of 44 patients aged from 21 to 57 years (average age - 42.3 ± 6.7 years), who were treated at GAUZ KO OKGVV. All patients had a verified diagnosis of RA and AS according to the ACR criteria and received treatment with basic drugs. The control group consisted of 40 people comparable in age and sex, without concomitant pathology of RA and AS.
The depression screening card, the subjective well-being scale, and the hospital anxiety and depression scale (HADS) were used to assess and detect anxiety-depressive syndrome. The assessment of the condition is carried out over the last 2 weeks, which corresponds to the temporary diagnostic criterion for depression.
The Depression Screening Scale is a 35-item self-questionnaire that assesses 7 categories of signs: sleep and appetite disorders, anxiety, emotional instability, cognitive impairment, loss of self, guilt, and suicidal tendencies. A total score of 65 and above indicates a high likelihood of depression.
The Subjective Well-Being Scale is a psychodiagnostic screening tool for measuring the emotional component of subjective well-being or emotional comfort.
Hospital Anxiety and Depression Scale Zigmond A.S., Snaith R.P. was developed for the primary detection of depression and anxiety in a general medical practice. The HADS scale consists of 14 statements with 4 possible answers and includes two parts: anxiety and depression. The sum of points of 8 or more is regarded as "subclinically expressed anxiety / depression", 11 or more points - "clinically expressed anxiety / depression".
Results: According to the results of the depression screening questionnaire, 34 (77.3%) patients with RA and AS showed signs of depression, while in the control group only 6 (15%) patients tested positive for the presence of depressive disorders. According to the data obtained when assessing the scale of well-being in the main group, 26 (59.1%) patients showed signs of emotional discomfort (the indicator was 80% or more), in the control group - in 6 (15%). Using the hospital scale of anxiety and depression HADS, anxiety-depressive syndrome was detected in 36 (81.8%) patients with RA and AS: 16 (44.4%) patients had anxiety, 20 (55.6%) - depression, of them, subclinically expressed anxiety and depression were observed in 10 (27.7%) and 12 (33.3%) people, respectively. Anxiety-depressive syndrome in the control group, according to the HADS questionnaire, was detected only in 8 (20%) patients, of whom 4 (10%) patients had subclinical anxiety and 4 (10%) had signs of depression. No clinically pronounced anxiety and depression were registered in the control group.
Conclusion: In most patients with rheumatoid arthritis and ankylosing spondylitis, anxiety-depressive disorders have been identified, which can directly affect both the course of the disease itself and the development of various complications. Timely diagnosis of mental disorders and close cooperation of rheumatologists, psychiatrists and psychologists in the selection of adequate therapy can improve the course and prognosis of the disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3444

AB0178 COMORBIDITIES IN RHEUMATOID ARTHRITIS: DO THEY INTERFERE WITH MYOCARDIAL FUNCTION?

R. Dhahri[1], W. Lahmar[1], Y. Ben Abderrazek[1], M. Slouma[1], B. Louzir[2], L. Metoui[1], I. Gharsallah[1], H. Mahfoudhi[3], C. Chourabi[3], W. Fehri[3]. [1]*Military Hospital of Instruction of Tunis, Department of Rheumatology, Tunis, Tunisia*; [2]*Military Hospital of Instruction of Tunis, Department of Internal Medicine, Tunis, Tunisia*; [3]*Military Hospital of Instruction of Tunis, Department of Cardiology, Tunis, Tunisia*

Background: Patients with rheumatoid arthritis are at increased risk for cardiovascular disease (CVD).The early myocardial dysfunction in RA patients may be detectable sooner using speckle-tracking echocariodgraphy to evaluate ventricular strain especially the global longitudinal strain (GLS), this has provided more comprehensive information on ventricular dysfunction in these patients.

Objectives: In the present study, we evaluated comorbidities that interfered the most with the GLS in rheumatoid arthritis patients.

Methods: The study population was comprised of a case group (36 patients with rheumatoid arthritis with no history of CVD and normal LVEF in the outpatient population of the Rheumatology department in the military hospital of Tunis) and a matched control group (individuals without a history of rheumatoid arthritis or cardiac abnormalities referred for clinical check-ups). In both groups, 2D and 3D echocardiographic examinations were performed by a single cardiologist to assess cardiac functional parameters.

Results: Anemia (36%) was found to be the most common comorbidity followed by diabetes mellitus (25%), arterial hypertension (17%) and dyslipidemia (17%).

Myocardial deformation study revealed that rheumatoid arthritis patients had a significantly worse global longitudinal strain than healthy controls (18.99±2.81% vs 20.42±1.33%; P=.015). Moreover, a third of the rheumatoid arthritis patients (and no healthy controls) exhibited subclinical left ventricular systolic dysfunction (GLS<18%).

Anemia (r=–0.368, P=.027), Age (r=–0.365, P=.029), Diabetes mellitus (r=–0.540, P=.001) and E/A (r=0.351, P=.036) were significantly correlated with

GLS in our univariate study. Receiver operating characteristic curve analysis revealed hemoglobin as the best predictor for subclinical LVSD (AUC=0.752, 95% CI: 0.577-0.927, *P*=.02) when compared to Age and E/A.

Conclusion: This prospective comparative study highlighted the diabetes mellitus and anemia burden on myocardial dysfunction in RA patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3650

AB0179 INFLUENCE OF AINFLUENCE OF ANTI-CITRULLINATED PROTEIN/PEPTIDE ANTIBODIES (ACPAS)ON ARTICULAR MANIFESTATIONS, DISEASE ACTIVITY AND STRUCTURAL SEVERITY IN ALGERIAN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

F. Rahal[1], N. Brahumi[2], A. Ladjouze-Rezig[2], S. Lefkir[1]. [1]*Beni Messous University Hospital Center, Rheumatology, Algiers, Algeria*; [2]*Ben Aknoun Hospital Center, Rheumatology, Algiers, Algeria*

Background: Anti-citrullinated protein/peptide antibodies (ACPA) are highly specific and sensitive markers for rheumatoid arthritis (RA). There are also suggested to have a more severe rheumatoid arthritis.

Objectives: The aim of this study was to assess the influence of ACPA on disease activity, radiological severity, and functional disability in Algerian patient with early rheumatoid arthritis (RA).

Methods: Consecutive early RA patients (symptom duration ≤24 months) recruited were included in the descriptive, longitudinal, prospective study. Demographic, biological, immunological and radiographic data were collected at the time of inclusion in the study. Disease activity as determined by the Disease Activity Score 28-CPR (DAS28- CPR: 4 variables), functional handicap as calculated by Heath Assessment Score (HAQ), and bone and joint damage as evaluated by Sharp-Van der Heijde (SVDH) erosion and narrowing score.

Results: One hundred and sixty-one patients with RA were recruited. Patients mean age 43.71±14 years and mean symptom duration at inclusion was 10.48±7 months. Small and larges were affected in 64,3%. The mean ESR was 23,53±15,2 mm/1st hour, and the mean CRP level was 19,42±39.8 mg/l. Rheumatoid Factors (RFs) and Anti-Citrullinated Protein Antibodies (ACPAs) were present in 74% and 88% of patients, respectively. The presence of ACPAs was significantly associated with DAS28 (p=0,004) and HAQ (p=0,002). There was no significant difference in inflammatory markers and radiographic SVDH score between patients with and without ACPAs. Stepwise regression analysis showed that the presence of ACPAs was independently associated with localization when RA affected smalls and larges joint in the same time (OR=5,24; IC 95% 1,224-22,483; p=0,026).

Conclusion: These data show that in patients with early RA, ACPAs positivity was significantly associated with articular manifestations, activity disease and functional handicap, but not with structural damage.

REFERENCES:

[1] Nikiphorou E, Norton S, Young A, et al. Association between rheumatoid arthritis disease activity, progression of functional limitation and long-term risk of orthopaedic surgery: combined analysis of two prospective cohorts supports EULAR treat to target DAS thresholds. *Ann Rheum Dis*. 2016;75(12):2080-2086. doi:10.1136/annrheumdis-2015-208669.

[2] Karimifar M, Salesi M, Farajzadegan Z. The association of anti-CCP1 antibodies with disease activity score 28 (DAS-28) in rheumatoid arthritis. *Adv Biomed Res*. 2012;1:30. doi:10.4103/2277-9175.98156.

[3] Boman A, Brink M, Lundquist A, et al. Antibodies against citrullinated peptides are associated with clinical and radiological outcomes in patients with early rheumatoid arthritis: a prospective longitudinal inception cohort study. *RMD Open*. 2019;5(2):e000946. Published 2019 Sep 3. doi:10.1136/rmdopen-2019-000946.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3657

AB0180 A MULTICENTER SELF-CONTROLLED CASE SERIES STUDY INVESTIGATING THE PREVENTIVE EFFECT OF SULFASALAZINE AGAINST PNEUMOCYSTIS PNEUMONIA

T. Nunokawa[1], T. Kakutani[1], N. Chinen[1], K. Shimada[2], M. Kimura[3], M. Tateishi[3], F. Chen[4], K. Setoguchi[4], M. Sugihara[5]. [1]*Tama Nambu Chiiki Hospital, Department of Rheumatic Diseases, Tokyo, Japan*; [2]*Tokyo Metropolitan Tama Medical Center, Department of Rheumatic Diseases, Tokyo, Japan*; [3]*Tokyo Metropolitan Ohtsuka Hospital, Department of Rheumatology, Tokyo, Japan*; [4]*Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Department of Rheumatology, Tokyo, Japan*; [5]*Tama-Hokubu Medical Center, Department of Rheumatic Diseases, Tokyo, Japan*

Background: An animal study revealed that sulfasalazine (SSZ) enhances *Pneumocystis* clearance from the lung by accelerating macrophage activity.[1] Although the preventive effect of SSZ on *Pneumocystis* pneumonia (PCP) in patients with rheumatoid arthritis (RA) is reported in case-control studies, some important confounders might remain unmeasured and distort the results. [2-3]. The self-controlled case series (SCCS) method involves only cases and controls fixed confounders automatically.[4]

Objectives: To evaluate the prophylactic effect of SSZ against PCP in patients with RA, controlling unmeasurable confounders by the SCCS method.

Methods: A retrospective study was conducted at five hospitals. Patients with RA who developed PCP between 2003 and 2019 were included. PCP was defined by the following criteria: (1) detection of *Pneumocystis jirovecii* in respiratory specimens by polymerase chain reaction; (2) clinical manifestations (pyrexia, dry cough, dyspnea, or hypoxia); (3) diffuse interstitial infiltrate on chest imaging; (4) absence of prophylaxis for PCP. Incidence rate ratio (IRR) for *Pneumocystis* pneumonia associated with sulfasalazine use was calculated by conditional Poisson regression.

Results: We identified 48 episodes of PCP in 47 cases. Of these, 15 (31.9%) died. Thirty received SSZ in certain periods of their observations (Table 1). While 46 episodes of PCP developed in the period of 168.9 person-years without SSZ use, only one episode of PCP developed in the period of 103.7 person-years with SSZ use. SSZ use had a decreased risk of PJP (adjusted IRR 0.007, 95% CI <0.001-0.067) after adjusted for age group, the use of glucocorticoid, methotrexate, and tacrolimus, and the use of biologic agent or janus kinase inhibitor (Table 2).

Table 1. Characteristic of the 47 patients enrolled in the study.

Male/female, n (%)	14 (29.8)/33 (70.2)
Observational period (years), median (IQR)	72.0 (66.3-79.1)
Lung disease, n (%)	4.7 (1.4-9.5)
Use of sulfasalazine, n (%)	23 (48.9)
Outcome of PCP, death, n (%)	30 (63.8)
Age at the onset of PCP (years), median (IQR)	15 (31.9)

PCP, *Pneumocystis* pneumonia; IQR, interquartile range.

Table 2. Unadjusted and adjusted incidence rate ratio for *Pneumocystis* pneumonia associated with sulfasalazine use.

	Observation length (years)	Episodes of PCP, n (%)	Unadjusted IRR 95% CI)	Adjusted IRR[a] (% CI)
Use of SSZ	103.7	1 (2.1)	0.010 (0.001-0.092)	0.007 (<0.001-0.067)
No use of SSZ	168.9	47 (97.9)	reference	reference

IRR, incidence rate ratio; PCP, *Pneumocystis* pneumonia; SSZ, sulfasalazine.

Conclusion: Our study demonstrated the preventive effect of SSZ against PCP with confounders controlled by the SCCS.

REFERENCES:

[1] Wang, J., *et al.* Immune modulation with sulfasalazine attenuates immunopathogenesis but enhances macrophage- mediated fungal clearance during pneumocystis pneumonia. *PLoS Pathog.* 2010;19;6(8):e1001058.

[2] Nunokawa, T. *et al.* Prophylactic effect of sulfasalazine against Pneumocystis pneumonia in patients with rheumatoid arthritis: A nested case-control study. *Semin. Arthritis Rheum.* 2019;48(4):573-578.

[3] Nunokawa, T., *et al.* Effect of Sulfasalazine Use on the Presence of Pneumocystis Organisms in the Lung among Patients with Rheumatoid Arthritis: A Test-Negative Design Case-Control Study with PCR Tests. *Mod. Rheumatol.* 2019;29(3):436-440.

[4] Petersen, I., *et al.* Self controlled case series methods : an alternative to standard epidemiological study designs. BMJ. 2016;12;354:i4515.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3734

AB0181

EXPLORING THE ROLE OF IL-6 BLOCKADE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHTITIS AND CHRONIC PERIODONTITIS

C. Ancuta[1,2], E. Ancuta[3], R. Chirieac[4], O. Tanculescu[5], C. Iordache[6]. [1]*University of Medicine and Pharmacy "GRIGORE T. POPA" IASI, Rheumatology, IASI, Romania*; [2]*Clinical Rehabilitation Hospital, Rheumatology 2, IASI, Romania*; [3]*"Elena Doamna" Clinical Hospital, Research, IASI, Romania*; [4]*Sanocare Medical and Research Center, Rheumatology, IASI, Romania*; [5]*University of Medicine and Pharmacy "GRIGORE T. POPA" IASI, Department of Odontology-Periodontology, Fixed Prosthodontics, Faculty of Dental Medicine, IASI, Romania*; [6]*University of Medicine and Pharmacy "GRIGORE T. POPA" IASI, Implantology, Removable Dentures, Dental Technology Department, Faculty of Dentistry, IASI, Romania*

Background: Recent data have renewed the interest in common pathobiologic pathways in autoimmune rheumatic conditions and periodontal disease, especially on dual impact of innovative anti-rheumatic drugs in modulating both inflammatory and immune articular as well as periodontal damage. Although consistent data about TNF inhibitors and chronic periodontitis are already published, the influence of IL-6 blockade.

Objectives: We aimed to explore the influence of weekly subcutaneously IL-6 receptor inhibitor tocilizumab on periodontal health in a local cohort of patients with rheumatoid arthritis (RA) and chronic periodontitis (PD).

Methods: We performed a prospective longitudinal 6 months study in 68 patients with moderate-to-severe RA starting tocilizumab (TCZ) in accordance to local recommendations. Extensive rheumatologic (clinical activity, inflammatory, serological biomarkers) and dental (plaque index PI, gingival index GI, bleeding on probing BOP, pocket probing depth PPD, clinical attachment level CAL) assessments were done. Changes in RA activity and periodontal status were reassessed after 3 and 6 months.

Results: 51 RA and concomitant t of 68 patients in our initial cohort were finally analyzed. Aggressive periodontal disease was reported particularly in disease subsets with excessive inflammatory (serum C reactive protein level) and serologic biomarkers (anti-citrullinated peptide antibodies ACPA). Furthermore, significant correlations between periodontal status, clinical disease activity and ACPA levels were also demonstrated ($p<0.05$). We also noticed consistent improvement was noticed in both RA-related parameters sand periodontal inflammation (GI and sites with bleeding of probing) after only 3 months ($p < 0.05$), while PPD improved after 6 months; overall, CAL presented only slight changes without statistical any significance as well as teeth count and plaque levels ($p > 0.05$).

Conclusion: IL-6 inhibition is able to improve periodontal outcomes in patients with RA and concomitant PD, essentially related to dramatic decrease in serum inflammatory mediators.

REFERENCES:

[1] de Molon Scaf, R., Rossa, C.; Thurlings, R.M.; Cirelli, J.A.; Koenders, M.I. Linkage of Periodontitis and Rheumatoid Arthritis: Current Evidence and Potential Biological Interactions, *Int. J. Mol. Sci*. **2019,** 20, 4541.

[2] Genco, R.J.; Sanz, M. Clinical and public health implications of periodontal and systemic diseases: An overview. *Periodont. 2000* **2020**, 83 (1), 08 May.

[3] Rinaudo-Gaujous, M.; Blasco-Baque, V.; Miossec, P. et al. Infliximab induced a dissociated response of severe periodontal biomarkers in rheumatoid arthritis patients. *J Clin Med* **2019**. 8, 751.

[4] Eezammuddeen, N.N.; Vaithilingam, R.D.; Mohamad Hassan, N.H.; Bartold, IL-6 inhibition is able to improve periodontal outcomes in patients with RA and concomitant PD, essentially related to dramatic decrease in serum inflammatory mediators.

Disclosure of Interests: CODRINA ANCUTA Speakers bureau: ABBVIE, PFIZER, UCB, NOVARTIS, LILLY, SANDOZ, Consultant of: ABBVIE, PFIZER, UCB, NOVARTIS, LILLY, SANDOZ, EUGEN ANCUTA: None declared, Rodica Chirieac Speakers bureau: ABBVIE, PFIZER, UCB, NOVARTIS, LILLY, SANDOZ, OANA TANCULESCU: None declared, CRISTINA IORDACHE: None declared

DOI: 10.1136/annrheumdis-2021-eular.3737

AB0182

HEMOGLOBIN RATE AS A PREDICTOR OF SUBCLINICAL LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN RHEUMATOID ARTHRITIS

Y. Ben Abderrazek[1], R. Dhahri[1], W. Lahmar[1], M. Slouma[1], B. Louzir[2], L. Metoui[1], I. Gharsallah[1], H. Mahfoudhi[3], C. Chourabi[3], W. Fehri[3]. [1]*Military Hospital of Instruction of Tunis, Department of Rheumatology, Tunis, Tunisia*; [2]*Military Hospital of Instruction of Tunis, Department of Internal Medicine, Tunis, Tunisia*; [3]*Military Hospital of Instruction of Tunis, Department of Cardiology, Tunis, Tunisia*

Background: The role of rheumatoid arthritis as an ischemic heart disease and heart failure risk factor is well acknowledged even if the physiopathological pathways are still debated. The effect of anemia on myocardial deformation has already been established and a hemoglobin level below 9g/dL was associated with a significantly lower global longitudinal strain (GLS) patients with no history of CVD or chronic inflammatory diseases.[1]

Objectives: In the present study, we looked into the effect of anemia and hemoglobin on the myocardial impairement in RA patients.

Methods: We conducted a monocentric cross-sectional study between march 2019 and september 2019 on 36 RA patients without any history of cardiovascular disease and non-altered left ventricular ejection fraction in the outpatient population of the rheumatology department of the military hospital of Tunis matched with 36 healthy control subjects. Both groups underwent conventional echocardiography and STE to measure GLS; subclinical left ventricular systolic dysfunction was defined as a GLS > −18%, and a complete blood cell count; anemia was defined as Hemoglobin levels < 12 g/dL for women and < 13 g/dL for men.

Results: Myocardial deformation study revealed that rheumatoid arthritis patients had a significantly worse GLS than healthy controls (18.99±2.81% vs 20.42±1.33%; *P*=.015). We also observed that third of the RA patients had subclinical left ventricular systolic dysfunction.

In our report 36% of RA patients were anemic. In our univariate analysis anemia was found to be significantly correlated with GLS (r=–0.368, *P*=.027) and hemoglobin was found to be the best predictor of subclinical LVSD in our ROC curve analysis (AUC=0.752, 95% CI: 0.577-0.927, *P*=.02). In our multivariate analysis anemia was the only factor that was independently related to subclinical LVSD (OR: 11.39, 95% CI: 1.57-82.89, *P*=.016).

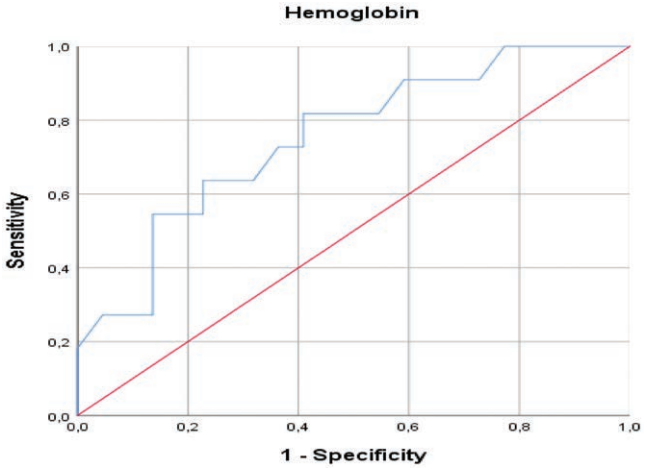


Figure 1. ***ROC curve analysis for Hemoglobin as a predictor of subclinical left ventricular systolic dysfunction***

Conclusion: To our knowledge, this is the first study to look into the relationship between GLS and anemia among RA patients, and now it is safe to say that anemia is yet another added burden on the myocardial function in RA patients that needs to be taken into account when discussing therapeutic action.

REFERENCES:

[1] Zhou Q, Shen J, Liu Y, Luo R, Tan B, Li G. Assessment of left ventricular systolic function in patients with iron deficiency anemia by three-dimensional speckle-tracking echocardiography. Anatol J Cardiol. 2017;18(3):194–9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3741

AB0183

T-CELL LARGE GRANULAR LYMPHOCYTE LEUKEMIA IN PATIENTS WITH FELTY'S SYNDROME

V. Vasiliev[1], V. Gorodetskiy[2], B. Chalcev[2], S. Palshina[3], E. Sokol[2], A. Torgashina[2], J. Khvan[2]. [1]*MEDSI, Department of Rheumatic Diseases, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Intensive Care of Rheumatic Diseases, Moscow, Russian Federation*; [3]*Clinic of Heart and Joint Diseases, Department of Rheumatic Diseases, Moscow, Russian Federation*

Background: Felty's syndrome (FS) is a rare subtype of seropositive rheumatoid arthritis (RA) and is characterized by neutropenia and splenomegaly. Some researchers suggest that FS and T-cell large granular leukemia (T-LGLL) may have common pathogenetic relationships [1].

Objectives: to characterize the clinical and laboratory manifestations of FS, to evaluate the frequency of T-LGLL and Sjogren's syndrome (SS) in this group of patients with RA, neutropenia and splenomegaly (pts).

Methods: We observed 18 pts with ACCP-positive (100%) and RF-positive (94.5%) RA diagnosed according to ACR 2010 criteria, who also had neutropenia and hepatosplenomegaly. All 18 pts underwent T-LGLL diagnostics using blood smears and phenotyping of peripheral lymphocytes for the presence of granular lymphocytes, determination of T-cell clonality using the rearrangement of the γ-chain of the T-cell receptor of lymphocytes by PCR, histological/

immunohistochemical study of bone marrow biopsy specimens for the presence of LGL invasion studies, as well as the study of 4 spleens after splenectomy. SS was diagnosed in 8 out of 18 pts (44.5%) according ACR 2016 criteria.

Results: Twelve (66.6%) of 18 pts with RA, neutropenia and splenomegaly were diagnosed with T-LGLL, the patients were divided in 2 groups: FS (6 pts) and RA+T-LGL (12 pts). Pts with FS debuted with arthritis of small hand joints, extremely rarely with extra-articular manifestations, mainly at a young age (36.5±3.9 years), and developed neutropenia after 10 years of RA. Pts with T-LGLL debuted at a younger age (39,5±4,5 and 51,5+7,8 years, respectively), had a longer course of RA before the development of neutropenia (14.3±3.3 and 5±1.5 years, respectively, p=0.03), and more often had extra-articular manifestations at the onset of the disease. RA activity did not differ between groups and in most cases was characterized by a mild course of articular syndrome. Though the course of RA+T-LGLL group was characterized by low (50%) and moderate (33%) DAS28-CRP activity and active synovitis in only 41.5% of pts, severe joint deformities (stage III and IV) developed in 58.5% of pts. Pts with T-LGLL showed a higher incidence of hepatomegaly (75% and 16.5%, respectively, p=0.02) and more severe neutropenia (p=0.02). The development of severe leukopenia ($<1x10^9$) and massive hepatosplenomegaly was observed only in pts with T-LGLL, which required splenectomy in 4 cases. SS was more often detected in the FS group than in the RA+T-LGLL group (83.5% and 25%, respectively, p = 0.02).

Conclusion: Clinical and laboratory manifestations of FS and T-LGLL are extremely close, therefore, pts who are diagnosed with FS should be examined to exclude T-LGLL.

REFERENCES:

[1] Liu, Xin, and Thomas P Loughran Jr. "The spectrum of large granular lymphocyte leukemia and Felty's syndrome." *Current opinion in hematology* vol. 18,4 (2011): 254-9. doi:10.1097/MOH.0b013e32834760fb.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3874

AB0184 SCREENING FOR DEPRESSION IN A GROUP OF TUNISIAN PATIENTS WITH RHEUMATOID ARTHRITIS

M. Sellami[1], S. Kammoun[1], S. Miladi[1], A. Fazaa[1], L. Souabni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: Depression is thought to be common comorbidity in patients with rheumatoid arthritis (RA), which is one of the most frequent chronic inflammatory diseases.

Objectives: This study aimed to screen for depression in RA patients, and study its relation to social and clinical parameters, as well as disease activity.

Methods: Single-center cross-sectional study, involving patients with RA, according to ACR/EULAR criteria 2010, using the original Beck Depression Inventory (BDI) as a screening tool for depression: measures of 0–9 indicated that a patient was not depressed, 10–18 indicated mild to moderate depression, 19–29 indicated moderate to severe depression and 30–63 indicated severe depression.

Results: Sixty-five patients were included (57 F / 8M). The average age was 55 years [23-73]. The mean duration of the disease was 11.75 years [1-25]. Half of the patients had precarious socioeconomic conditions and no social security. Forty-two patients were unemployed. Seventeen percent of them experienced grief by losing a close family member. Both rheumatoid factor and anti-citrullinated peptides antibodies were positive in 83.1 % of cases. RA was erosive in 78.5% of cases, and deformed in 21.5 % of cases. Almost half of the patients (52.3 %) were followed for at least another chronic disease. Forty-eight percent of patients were on Methotrexate with an average weekly dose of 15.3 mg/week [10-22.5], 10% on Leflunomide, 10% on Sulfasalazine, and 45% on biotherapy. The analysis of BDI scores showed that 64.6 % of patients suffered from depression: mild to moderate in 35.4 % of cases, moderate to severe in 21.5% of cases and severe in 7.7% of cases. Depression was significantly associated with precarious socioeconomic conditions (p=0.018). A correlation between the BDI score and the Disease Activity Score (DAS28) as well as the Health Assessment Questionnaire was noted (p = 0.045 and p = 0.02, respectively). There were no statistically significant associations with the other studied data.

Conclusion: Depression was frequent among RA patients. Our study suggests that better control of the disease may reduce the incidence of depression within this group of patients.

REFERENCES:

[1] Beck, A.T., Ward, C., & Mendelson, M. (1961). "Beck Depression Inventory (BDI)." Archives of General Psychiatry, 4, 561-571.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3965

AB0185 ULTRASOUND IN INFLAMMATORY ARTHRALGIA: SHOULD WE ALWAYS SCAN?

K. López Gloria[1], I. Castrejon[1], J. C. Nieto González[1], J. Rivera[1], J. Martínez-Barrio[1], B. Serrano-Benavente[1], L. Trives Folguera[1], J. M. Alvaro-Gracia[1], J. Molina Collada[1]. [1]*Hospital Universitario Gregorio Marañón, Rheumatology, Madrid, Spain*

Background: Patients with inflammatory arthralgia (IA) are considered to be at increased risk for progression to RA. Ultrasound (US) has shown high sensitivity to detect synovitis compared with physical examination. Thus, US is recommended to identify subclinical synovitis in patients without clinical signs of inflammation.

Objectives: To determine the frequency and pattern of US detected active inflammation in patients with IA and investigate factors contributing to predict this outcome.

Methods: An US clinic is scheduled in an academic center running twice every week. A retrospective analysis of our US unit cohort during a period of 12 months was undertaken. Patients with IA and no previous diagnosis of inflammatory arthropathies were included for analysis. Inclusion criteria of IA definition included: severe symptoms presenting in the morning, duration of morning stiffness ≥60 min, symptoms predominantly located in MCP joints and absence of clinically detected synovitis by the referral rheumatologist. The following routinely collected variables were included in the analysis: demographics, clinical features and laboratory tests. Patients underwent bilateral US examination of hands and/or feet according to the European League Against Rheumatism (EULAR) guidelines. The presence of synovitis and tenosynovitis was assessed on a semi quantitative scale (0–3) for Grey Scale(GS)/Power Doppler(PD). Active inflammation was defined as PD synovitis and/or tenosynovitis >1 at any location. First, differences between groups were tested using chi-squared/Fisher and Student-t tests in the univariate analysis. Second, multivariate logistic regression models were employed to investigate the association between possible predictive factors of US active inflammation.

Results: A total of 110 patients were included in the analysis. Mean age was 53.6±15.6 years, 80 (72.7%) were females, and mean symptoms duration was 11.7±9.9 months (Table1). A total of 76 (69.1%) patients presented with a polyarticular arthralgia pattern. US active inflammation were present in 38 (34.5%) patients (28.2% showed PD synovitis and 19.1% PD tenosynovitis). Hands were most commonly involved with PD synovitis at wrists in 18.2% and at MCP in 14.5% of patients. For PD tenosynovitis, the flexor MCP 2-5 (4.5%) and 6th extensor tenosynovitis (5.5 %) were the most frequent affected locations. Only 9 (8.2%) patients had erosions in hands and/or feet at baseline examination. In the univariate analysis, the higher ESR values, the shorter time from symptoms onset and the presence of ACPA were significantly associated with the presence of US active inflammation (p<0.001, p=0.035 and p=0.01, respectively). In the multivariate analysis, only ACPA and ESR values (OR=1,0003; 95%CI 1,000-1,006 and OR=1.054; 95%CI 1.016-1.094), remained significantly associated with the detection of US active inflammation.

Conclusion: US features of active inflammation are found in 1 over 3 patients with IA being PD synovitis the most common finding, specially at the wrists and MCP joints. Higher ESR and ACPA values are significantly associated with the presence of US active inflammation. Thus, we strongly recommend the use of PD US to detect subclinical inflammation in at-risk patients with IA with no sign of inflammation on clinical examination, especially those with high ESR and ACPA values.

Table 1. Baseline characteristics of patients with IA

		Total n= 110	US inflammatory findings n= 38 (34.5%)	Non-US inflammatory findings n=72 (65.5%)	p
Age		53.6 ± 15.6	57.2±16.2	51.6±13.4	0.071
Sex	Female	80 (72.7%)	26 (68.4%)	54 (75%)	0.461
Smoking	Non smoker	45 (51.7%)	12 (44.4%)	33 (55%)	0.412
n= 87	Smoker	34 (39.1%)	11 (40.7%)	23 (38.3%)	
	Former smoker	8 (9.2%)	4 (14.8%)	4 (6.7%)	
Extension	Monoarticular	12 (10.9%)	6 (15.8%)	6 (8.3%)	0.176
	Oligoarticular	22 (20%)	10 (26.3%)	12 (16.7%)	
	Polyarticular	76 (69.1%)	22 (57.9%)	54 (75%)	
Time (months) from symptoms onset		11.7 ± 9.9	9.1±8.1	13±10.5	**0.035**
ESR (mm/h) n=45		24.7 ± 18.2	33.1±21.8	20.3 ±14.4	**<0.001**
RF (IU/mL) n=53		39.1 ± 230.5	28.5±56	45.1±286.1	0.647
ACPA (IU/mL) n=56		98.1 ± 331.2	209.4±488.4	26±125.2	**0.01**

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3996

AB0186 AT WHAT LEVEL SHOULD WE MEASURE INTIMA-MEDIA THICKNESS IN RHEUMATOID ARTHRITIS?

L. Nacef[1], H. Ferjani[2], H. Riahi[3], K. Maatallah[2], Y. Mabrouk[2], E. Labbene[3], D. Kaffel[2], W. Hamdi[2], M. Bouaziz[3]. [1]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Tunis, Tunisia*; [2]*Mohamed*

Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Manouba, Tunisia; [3]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Radiology, Manouba, Tunisia*

Background: Rheumatoid arthritis (RA) is chronic inflammatory rheumatism characterized by an independent cardiovascular (CV) risk. The screening of carotid intima-media thickness (IMT) in the common carotid artery appears to be a marker of atherosclerosis and is used as a specific tool for CV risk assessment.
Objectives: The main of this study was to determine the most associated US sites with CV risk in RA.
Methods: The present study is a prospective study conducted on Tunisian RA patients in rheumatology department of Mohamed Kassab University Hospital (March and December 2020). The characteristics of the patients and those of the disease were collected. The measurement of cIMTwas done using high-resolution B-mode carotid US with a Philips machine with the patient in supine position, according to AmericanSociety of Echocardiography guidelines.The carotid bulb below itsbifurcation and the internal and external carotid arteries were evaluated bilaterally with gray scale, spectral and color Doppler ultra-sonography using proprietary software for carotid arterymeasurements.IMT was measured using the two inner layers of the commoncarotid artery and an increased IMT was defined as ≥0.9 mm. The CV risk at 10 years was calculated by the SCORE index.
Results: Forty-seven patients were collected, of which 78.7% were women. The mean age was 52.5 ±11.06 years. The rheumatoid factor (RF) was positive in 57.8% of cases, and anti-citrullinated peptide antibodies (ACPA) were positive in 62.2% of cases. RA was erosive in 81.6% of cases. Hypertension (hypertension) was present in 14.9% of patients and diabetes in 12.8% of patients. Nine patients were active smokers. The mean IMT in the left common carotid (LCC) was 0.069 ±0.015, in the left internal carotid (LIC) was 0.069 ±0.015, in the left external carotid (LEC) was 0.060 ±0.023. The mean IMT was 0.068 ±0.01 in the right common carotid (RCC), 0.062 ±0.02 in the right internal carotid (RIC), and 0.060 ±0.016 in the right external carotid (REC). The mean SCORE index of CV risk was 2±2.81 [0-11.6]. CV risk was significantly associated with the IMTs for LIC (p=0.029; r=0.374), LEC (p=0.04; r=0.480), and REC (p=0.016; r=0.408). No association was found between the IMT in the LCC (p=0,361; r=0,162), neither in the RCC (p=0,438; r=0,140) nor the RIC (p=0,670; r=0,077).
Conclusion: In our study, IMT is strongly associated with score index, especially in carotid bifurcation. However, IMT measured in common carotid does not reflect a cardiovascular risk at 10-years.
REFERENCES:
[1] S. Gunter and al. Arterial wave reflection and subclinical atherosclerosis in rheumatoid arthritis. Clinical and Experimental Rheumatology 2018; 36: Clinical *E.xperimental.*
[2] Aslan and al. Assessment of local carotid stiffness in seronegative and seropositive rheumatoid arthritis. SCANDINAVIAN CARDIOVASCULAR JOURNAL, 2017.
[3] Martin I. Wah-Suarez and al, Carotid ultrasound findings in rheumatoid arthritis and control subjects: A case-control study. Int J Rheum Dis. 2018;1–7.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4004

AB0187 PREVALENCE, RISK FACTORS, AND TREATMENT MODALITIES OF ATLANTOAXIAL DISLOCATION IN RHEUMATOID ARTHRITIS

K. Maatallah[1], S. Miri[1], H. Ferjani[1], D. Ben Nsib[1], W. Triki[1], A. Dallegi[1], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab Institute of Orthopedics, Rhumatology, Manouba, Tunisia*

Background: Cervical spine involvement is common in patients with rheumatoid arthritis (RA). The most common abnormality is atlantoaxial dislocation (AAD). It may lead to severe neurological symptoms and even death. Currently, there is a lack of consensus on the best approach to treatment.
Objectives: We investigated the prevalence of and risk factors for AAD in patients with RA, as well as its relationship to treatment modalities.
Methods: We conducted a cross-sectional study including 224 patients with RA. All patients fulfilled the 2010 American College of Rheumatology/European League Against Rheumatism RA classification criteria. Radiographs of the cervical spine included lateral views taken in flexion, extension, neutral position of the neck, anteroposterior and odontoid projection view. Patients were divided into two groups: (G1) a group with AAD and (G2) without ADD. We compared clinical, radiological, and *laboratory findings* between the two groups, as well as the treatments used: Steroid therapy, classic and biologic disease-modifying anti-rheumatic drugs (*DMARDs*). Structural joint damage was assessed with the Sharp/van der Heijde radiographic method. Functional impairment was assessed using the Health Assessment Questionnaire (HAQ). We used Statistical Package for Social Sciences (SPSS) 22.0 to analyze the results. The level of statistical significance was set at 0.05.
Results: ADD was present in 16% of the cases (n=36). Female predominance was noted, with a sex ratio of 0.25 (p=0.530). The mean age was 58±12 years, with no significant difference between groups (p=0.146). The mean disease duration was significantly higher in G1 (11.5 ± 10.5 years versus 5.9 ± 6.3, p=0.004). A noticeable relationship between AAD and immunopositivity was found: rheumatoid factor (RF) was present in 86.1% of the cases in G1 versus 67.5% in G2 (p=0.025). Anti-citrullinated protein antibodies (ACPA) were present in 86.1% of the cases in G1 versus 64.8% in G2 (p=0.012). We found a significant difference between AAD and disease activity assessed by DAS28-VS (5.8±1.3 in G1 versus 5.3±1.6 in G2,p=0.027). AAD was significantly associated with more structural joint damage: erosions (121.1±60.9 in G1 versus 61.8±56.5 in G2,$p<10^{-3}$), joints space narrowing (77.4±47.4 in G1 versus 38.7±40 in G2, $p<10^{-3}$), Sharp/van der Heijde radiographic score (190.2±103.1 in G1 versus 100.1±90.6 in G2, $p<10^{-3}$). Hip involvement was more frequent in G1 (22.2% versus 9.4% in G2, p=0.038).
HAQ score was higher in G1 (1.8±0.7 versus 1.2±1, p=0.002).
Seventy-five percent of patients in G1 had received methotrexate versus 82.3% in G2 (p=0.301). The mean duration of methotrexate therapy was longer in G1 (24.6±23.5 versus 18±24 months, p=0.015). G1 patients received a higher mean dose and cumulative dose of methotrexate: 13.2±3.5 g/week versus 11.8±4.4 g/week (p=0.048), and 6.5±6.8 versus 4.8±8.5 (p=0.025), respectively.
Thirty-five percent of patients in G1 had received corticosteroids versus 25% in G2 (p=0.217). Patients in G1 had a significantly longer duration of steroid therapy: 17.8+20.2 versus 13.3+24.3 months (p=0.22). The mean dose of corti*costeroids was similar between the two groups: 6.9±4.3 mg/day versus 5.7±4.6 mg/day (p=0.132). The total* cumulative dose was significantly higher in G1: 6.5±6.8 *mg/day* versus 4.8±8.5 *mg/day (p=0.025).*There was no significant difference in using other DMARDs: Sulfasalazine (p=0.182) and leflunomide (p=0.276).
No significant difference was observed with patients under biologic DMARDs: 24.1% in G1 versus 17% in G2 (p=0.725).
Conclusion: Cervical spine involvement is common in RA and may be asymptomatic. Immunopositive patients seem to have more frequently ADD, as well as those with high disease activity and severe structural joint damage. The treatment modalities do not appear to be affected by AAD; however, patients with ADD seem to have higher cumulative doses of corticosteroids and methotrexate. Given the cross-sectional nature of our study, it is difficult to confirm the connection between the two. Further studies are needed.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4108

AB0188 DO PATIENT-REPORTED OUTCOMES IN RHEUMATOID ARTHRITIS REFLECT DISEASE ACTIVITY?

K. Ben Abdelghani[1], H. Boussaa[1], S. Miladi[1], M. Sellami[1], L. Souabni[1], S. Kassab[1], S. Chekili[1], A. Fazaa[1], A. Laatar[1]. [1]*Mongi Slim University Hospital, Rheumatology, La Marsa, Tunisia*

Background: Patient-reported outcomes (PROs) reflect the patient's perspective and are used in rheumatoid arthritis (RA) routine clinical practice. However, PROs may be associated with other aspects of health, such as psychological distress or comorbidities, which leads to situations of discordance with objective RA assessments.
Objectives: The aim of this study was to determine whether PROs were associated with objective assessment of disease activity.
Methods: We conducted a cross-sectional study including patients with RA (ACR/EULAR 2010). Demographic data were collected. The following PROs were assessed: number of nocturnal awakenings, morning stiffness duration, estimation of spontaneous pain and fatigue by Visual Analog Scale (VAS), and global patient assessment (GPA). In addition, patients rated their current satisfaction with their disease state according to the Austrian school mark system (PATSAT: 1=excellent, 2=good, 3=average, 4=moderate (fair), 5=unsatisfactory). Disease activity was assessed using the 28-joint disease activity score with erythrocyte sedimentation rate (DAS28 ESR) and C reactive protein (DAS28 CRP). We used Cohen's kappa (κ) to determine the agreement between PATSAT and DAS28 ESR. The κ result was interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement. A p-value inferior to 0.05 was considered significant.
Results: We included 54 patients (45 women and nine men) with a mean age of 55±11 years old [23-69]. The mean disease duration was 9.9±5.9 years [0-20]. The mean number of nocturnal awakenings was 1.1 [0-4] and the mean morning stiffness duration was 25.1 minutes [0-120]. The mean GPA was 5.3±2.2 cm [0-10]. The mean pain VAS was 5.4±2.2 cm [0-10] and the mean fatigue VAS was 4±2.5 cm [0-8]. None of the patients described his disease state as 'excellent'. It was considered 'good' in 23.1% of cases, 'average' in 36.5% of cases, and 'moderate' to 'unsatisfactory' in 40.4% of cases.

The mean ESR and CRP were 46.3±29.3 mm [5-120] and 15.8 mg/l [0.6-100] respectively. The mean DAS28 ESR was 4.68±1.35 [1.50-7.16] and the mean DAS28 CRP was 3.9±1.1 [1.02-6.05].
A significant positive correlation was noted between both DAS28 ESR and DAS28 CRP and, number of nocturnal awakenings (r=0.385, p=0.013 and r=0.448, p=0.002), morning stiffness duration (r=0.495, p=0.001 and r=0.617, p<0.001), GPA (r=0.485, p<0.001 and r=0.530, p<0.001), and pain VAS (r=0.594, p<0.001 and r=0.598, p<0.001). No correlation was found between the two scores and fatigue VAS.
No significant agreement was noted between PATSAT and DAS28 ESR (κ=0.077, p=0.478).
Conclusion: PROs showed moderate to strong correlation with disease activity scores. The timely and effective use of PROs could encourage physicians to focus more on the impact of RA on patients and how patients are feeling. This in turn would facilitate shared decision making between patients and physicians.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4123

AB0189 LIPOPROTEIN ABNORMALITIES IN RHEUMATOID ARTHRITIS PATIENTS

L. Nacef[1], Y. Besbes[2], Y. Mabrouk[1], H. Ferjani[1], K. Maatallah[3], D. Kaffel[3], S. Besbes[2], W. Hamdi[1]. [1]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Manouba, Tunisia*; [2]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Biology, Tunis, Tunisia*; [3]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Tunis, Tunisia*

Background: The lipid paradox is termed the decreased cholesterol level in rheumatoid arthritis (RA). Nevertheless, the apolipoprotein levels are usually higher than a healthy person and are predictors of cardiovascular events.
Objectives: We aimed to describe lipid abnormalities in RA patients and to look for predictor factors of these changes.
Methods: The prospective study was carried out on patients with RA who met the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria. These patients were followed in the rheumatology department of the Kassab Institute.
We collected the socio-demographic data, biological and immunological parameters.
The lipid assessment included: a measurement of total cholesterol (TC), HDL, LDL, and triglycerides (TG). Lipoproteins APOA1 and APOB were measured. All data were collected after patient consent.
Results: Of the 47 patients recruited, 78.7% were female. The mean age was 52.5 ±11.06 [32-76]. The average RA progressed from 86.25 ±63 months [5-288] and was erosive in 81.6% of cases. The rheumatoid factor (RF) was positive in 57.8% of patients, and citrullinated antipeptide antibodies (ACPA) were present in 62.2%. Eight patients had a previous CV history.
Mean TC was 4.42 ±1.3 [1.2-7.58], mean HDL was 1.38 ±0.73 [0.18-4.10], mean LDL was 2.55 ±1.16 [0.24-5.54]. The mean TG value was 1.28 ±0.6 [0.24-5.54]. TC elevation was found in 9.1% of cases, HDL in 21.3% of cases, LDL in 5.5% of cases, and TG in 16.4% of cases. Mean APOB/APOA1 ratio was 0.67 ±0.18 [0,46-1,11]. LDL elevation was associated to a high DAS28 (p=0.06, r=0.512). APOA1 was associated to a low DAS28 (p=0.04, r=-0.642).
The mean value of APO A1 was 1.36 ±0.21 [0.84-1.81], that of APOB was 0.90 ±0.22 [0.58-1.40]. APOA1 values were lower in patients with high-level LDL (p=0.767). The APOB value was associated with lipid disturbance without significant correlation (p=0.291).
Conclusion: Lipid test abnormalities can be found in RA patients outside of any known CV risk factors. APOA1 seems to have a protective effect. Screening and treatment of these abnormalities can prevent CV risk.
REFERENCES:
[1] Miguel Bernardes and al. Coronary artery calcium score in female rheumatoid arthritis patients: Associations with apolipoproteins and disease biomarkers. *Int J Rheum Dis.* 2019;00:1–16.
[2] Anna So dergren and al. Biomarkers associated with cardiovascular disease in patients with early rheumatoid arthritis. PLOS ONE. August 5, 2019.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4152

AB0190 LIVER INVOLVEMENT IN RHEUMATOID ARTHRITIS

A. Ben Tekaya[1], B. D. Siwar[1], S. Bouden[1], O. Saidane[1], R. Tekaya[1], I. Mahmoud[1], L. Abdelmoula[1]. [1]*Charles Nicolle Hospital, Department of Rheumatology, Tunis, Tunisia*

Background: Rheumatoid arthritis (RA) can be associated to extra-articular manifestations and comorbidities, including hepatic disturbances. It can be related to an underlying viral, metabolic or immune disease, or to a medical treatment toxicity [1].
Objectives: We aim to study liver involvement in a group of RA patients.
Methods: We performed a cross sectional study in 249 RA patients responding to the ACR/EULAR 2010 criteria for RA diagnosis. Hepatic enzymes, B and C hepatitis viruses screening tests, abdominal ultrasonography, biliary tract MRIs, fibrotests and fibroscans if available were collected and analysed.
Results: Two hundred and forty-nine patients were included with 83.8% of women. The mean age was 59±11.67 years. The mean age at diagnosis was 47±14.9 years with a mean disease evolution of 11±8.83 years.
The mean disease activity (DAS28) was 4,66 with levels ranging from 0.12 to 7.78.
Liver abnormalities were found in 68 patients (27.3%).
Viral disease represented 32.3% of liver abnormalities and was found in 8.8% of the total number of patients. Positive anti-HBc antibodies with negative HBs antigen were found in 8.4% of the patients, no viral reactivation with conventional or biological disease-modifying anti-rheumatic drugs was noted.
Besides, 4 of the 249 patients had positive HCV antibodies tests; one of them had a reactivation of a hepatitis C infection after treatment with leflunomide, one had a chronic C hepatitis with chronic liver disease, one had an old B and C hepatitis infection and the last one had an associated liver nodule for which an exploration was triggered. One patient had post hepatitis C cirrhosis associated with a hepatocellular carcinoma treated with surgery and an association of ledipasvir and sofosbuvir with a negative serology.
Medical treatment toxicity was responsible for 25% of liver abnormalities. Paracetamol caused both hepatic cholestasis and cytolysis in 5 patients, and isolated cholestasis in 2 patients. NSAIDs caused both hepatic cholestasis and cytolysis in 2 patients, and isolated cholestasis in one patient. Methotrexate was responsible for isolated cholestasis in 2 patients, isolated hepatic cytolysis in one patient and both cholestasis and cytolysis in one patient. An interaction between methotrexate and fluconazole caused one case of hepatic cholestasis and cytolysis. Treatment of a latent tuberculosis with isoniazid and rifampicin was responsible for cholestasis in one patient.
Immune hepatic disease was present in 3 patients: 2 patients had a primary biliary cholangitis that manifested with a cholestasis and one patient had an auto-immune hepatitis that manifested with cytolysis and cholestasis.
The prevalence of hepatic steatosis was of 4.8%, assessed with ultrasonography or microscopic examination of a liver biopsy. Hepatic enzymes test was normal in 2%, showed isolated cholestasis in 2% and both cholestasis and hepatic cytolysis in 0.8% of the patients.
One patient had a secondary hemochromatosis to multiple transfusions for sickle cell anaemia, causing cholestasis and cytolysis.
No aetiology was found for hepatic cholestasis and/or cytolysis in 7.2% of patients.
Conclusion: Liver involvement in RA is common and has different aspects. A careful monitoring of liver enzymes tests is crucial to detect hepatic disease and prevent its evolution to a chronic liver disease and cirrhosis. On the other hand, screening for viral hepatitis B and C is necessary to prevent an aggravation of a chronic infection and a reactivation of a latent one [2].
REFERENCES:
[1] Sellami M, Saidane O, Mahmoud I, Tekaya AB, Tekaya R, Abdelmoula L. Etiological Features of Liver Involvement in Rheumatoid Arthritis. Curr Rheumatol Rev. 2020;16(4):332-6.
[2] Karadağ Ö, Kaşifoğlu T, Özer B, Kaymakoğlu S, Kuş Y, İnanç M, et al. Viral hepatitis screening guideline before biological drug use in rheumatic patients. Eur J Rheumatol. mars 2016;3(1):25-8.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4179

AB0191 ON WHICH FACTOR TO ACT TO REDUCE CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS?

L. Nacef[1], H. Ferjani[1], H. Riahi[2], Y. Mabrouk[1], E. Labbene[2], K. Maatallah[1], D. Kaffel[1], M. Bouaziz[3], W. Hamdi[4]. [1]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Manouba, Tunisia*; [2]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Radiology, Tunis, Tunisia*; [3]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Radiology, Manouba, Tunisia*; [4]*Mohamed Taieb Kassab Institute of Orthopedic Surgery and Traumatology, Rheumatolgy, Tunis, Tunisia*

Background: Patients with rheumatoid arthritis (RA) are at higher cardiovascular risk (CVR) than the general population due to chronic inflammation. Several factors, both modifiable and non-modifiable, can increase this risk. Intima-media thickness (IMT) was considered as a marker for atherosclerosis.
Objectives: This study aimed to identify predictor factors of increasing IMT.
Methods: The prospective study was carried out on patients with RA who met the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria. These patients were followed in the

rheumatology department of the Kassab Institute. The socio-demographic data, biological and immunological parameters were collected.
Framingham's score quantified the cardiovascular risk at 10-years. Carotid Ultrasonography (US) using a high resolution B mode carotid measured intima-media thickness (IMT) as a subclinical marker of atherosclerosis. Carotid US was performed in the supine position, according to American Society of Echocardiography guidelines. IMT was measured in the left (LCC) and right (RCC) common carotid arteries, the left (LIC) and right (RIC) internal carotid arteries, and the left (LEC) and right (RIC) internal carotid arteries. An increased IMT was defined as ≥0.9 mm.
We analyzed data by the SPSS statistical package. A p-value <0.05 was considered significant.
Results: Of the 47 patients surveyed, 78.7% were female. The mean age was 52.5 ±11.06 [32-76]. The duration disease was 86.25 ±63 months [5-288] and was erosive in 81.6% of cases. The rheumatoid factor (RF) was positive in 57.8% of patients, and citrullinated antipeptide antibodies (ACPA) were present in 62.2%. Eight patients had a previous CV history (hypertension, diabetes or dyslipidemia) and 16.4% were active smokers. Among women, 43.6% were postmenopausal. ITM was significantly higher in men at LIC (0.037) and LEC (0.025). Older age was associated with increased ITM in LIC (p=0.046; r=0.295), LEC (p=0.05; r=0.412), RCC (p=0.034; r=0.317), and REC (p=0.009; r=0.382). The ITM for LCC, LIC, LEC, RCC, RIC, and REC was higher in postmenopausal women, with no significant difference (p=0.782, p=0.208, p=0.877, r=0.734, p=0.808, p=0.437, respectively).
Among the modifiable factors, active smoking was associated with a higher ITM at the REC level (p=0.047). However, weight was not associated with an increased ITM (LCC: p=0.092; LIC: p=0.985; LEC: p=0.952; RCC: p=0.744; RIC: p=0.210; REC: p=0.510). In our study, there was no significant association between DAS28 disease activity or inflammatory marks and ITM (LCC: p=0.784; LIC: p=0.316; LEC: p=0.420; RCC: p=0.784; RIC: p=0.484; REC: p=0.754).
Conclusion: In our study, the non-modifiable factors associated with increased ITM were advanced age and male gender. The modifiable factor impacting ITM was primarily active smoking. Surprisingly, disease activity and biological inflammation did not influence ITM.
REFERENCES:
[1] S. Gunter and al. Arterial wave reflection and subclinical atherosclerosis in rheumatoid arthritis. Clinical and experimental rheumatology 2018; 36: clinical e.*xperimental.*
[2] Aslan and al. Assessment of local carotid stiffness in seronegative and seropositive rheumatoid Arthritis. Scandinavian cardiovascular journal, 2017.
[3] Martin i. Wah-suarez and al, carotid ultrasound findings in rheumatoid arthritis and control subjects: a case-control study. Int j rheum dis. 2018;1–7.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4183

AB0192 EVALUATION OF TEMPOROMANDIBULAR JOINT INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

M. Brahem[1], A. Ben Salem[1], H. Hachfi[1], R. Sarraj[1], S. Abedallatif[1], R. Tekaya[1], C. Baccouche[2], Y. Mohamed[1]. [1]*Tahar Sfar Hospital, Rheumatology, Mahdia, Tunisia*; [2]*Tahar Sfar Hospital, Dentistry, Mahdia, Tunisia*

Background: Rheumatoid Arthritis (RA) is the most common chronic inflammatory disease usually involves peripheral joints with a symmetric distribution. The temporomandibular joint (TMJ) is seldom joint to be affected first in the disease course.
Objectives: The Aim of our study is to describe and to assess the prevalence of temporomandibular joint (TMJ)disorders in patients with Rheumatoid arthritis (RA).
Methods: A cross sectional study including RA patients, which consulted or were hospitalized in Rheumatology department in Taher Sfar Hospital of Mahdia Tunisia, during a period of 10 months. The diagnosis of the RA was secured by the ACR/EULAR 2010, Rheumatoid Arthritis Classification Criteria. The clinical TMJ examination was performed by a trained dentist in the same hospital. We assessed TMJ pain with VAS (visual analog scale) which varies from 0 to 10. The following key parameters were evaluated: The pain on the TMJs by bilateral palpation; The TMJ sounds (clicking or crepitus) during opening closing of the mandible; dysfunction and movement alterations. Clinical and sociodemographic parameters were also determined.
Results: Our study included 51 patients with an average age of 51.11 years ±12.4 [21-74years]. 50patients (92.6%of cases) were women and 8 patients (14.8%) were diabetic. Only one patient was a smoker. The mean duration of RA was 10.7 years 7.7± [10months-35years]. Rheumatoid factor (RF) was positive in 25 Patients (46.3%of cases). Anti-citrullinated peptide antibody (ACPA) was positive in 32 patients (59.3 %).41patients (75.4%) had radiological impairments and 28 (51.9%) had specific deformations of RA. The average disease activity score (DAS28-VS) and (DAS28-CRP) were respectively 4.1±1.5 [1.4-7.3] and 3.4±1.5 [1.24-6.71]. TMJ pain was present in 29 patients (56.9 %) which67.7% appeared before ten years. 5 patients (16.7%) had VAS more than 7 that mean a severe pain. TMJ involvement was bilateral in 64.3% and unilateral in 35.7 %. Functional difficulties were detected in 22 patients (44.9 %). TMJ examination had also revealed a limitation of mouth opening in 11 patients (21.2 %), a movement alteration in 13 patients (27.79 %), a clicking in joint mobility in 13 patients (81.3 %) and joint crepitus in 1 patient (6.3%). Disease duration was associated with TMJ pain(p=0.05) and mobility alterations (p=0.04). Functional difficulties of the TMJ were correlated with DAS28 (p=0.02). In our study we found also that duration of corticosteroid therapy had in impact on TMJ pain (p=0.01), functional difficulties (p=0.01) and movements alterations (p=0.004).
Conclusion: TMJ is very rare to be affected in the early phase of the disease, thus patient may develop signs and symptoms in the course of time. Our study showed the frequency of TMJ disorders and the most important factors were the activity of RA and the duration of the disease course.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4194

AB0193 PRESENCE OF SUBLINICAL SYNOVITIS IN A ESTABLISHED RHEUMATOID ARTHRITIS COHORT

E. Rojas[1], V. Valinotti[1], M. Vazquez[1], L. Roman[1], M. Maidana[2], J. Ramirez[3], S. Cabrera-Villalba[1]. [1]*Clinicas Hospital, Universidad Nacional de Asuncion, Rheumatology, Asunción, Paraguay*; [2]*Maria Auxiliadora Center of Sonographic Studies, Ultrasonography, Asunción, Paraguay*; [3]*Hospital Clínic Barcelona, Rheumatology, Barcelona, Spain*

Background: Some studies prove that a significant percentage of patients with rheumatoid arthritis (RA) in sustained clinical remission has radiological progression or joint damage, and the presence of residual activity objectified by imaging studies such as ultrasonography could be related to a relapse or flare of RA.(1,2)
Objectives: To determine the presence of subclinical synovitis measured by ultrasonography in patients with RA on sustained clinical remission from the Rheumatology service at Hospital de Clínicas, San Lorenzo, Paraguay.
Materials and Methods: Prospective, cross sectional, descriptive study, in RA patients meeting ACR/EULAR 2010 criteria, older than 18 years, on sustained clinical remission (≥6 months), measured by ESR-DAS28 (<2,6), doing follow-ups on our service. A healthy control group was included. All groups signed informed consent. Synovial hypertrophy (SH) and intraarticular vascularization grades on Power Doppler (PD) mode were determined according to EULAR recommendations and OMERACT 7 group definitions. Clinical data were obtained from the service's registries.
SPSS 23rd version was used for data analysis. Quantitative variables were presented as means and qualitative as frequencies. Chi square test was performed for comparisons between dichotomous variables and t Student for continuous. For comparisons between variables the Spearman's rank correlation coefficient was performed, and p≤0.05 for statistical significance. Factors predicting subclinical synovitis were analyzed with Odds Ratio (OR) CI 95%.
Results: From 147 patients, 31 (21%) met remission criteria; 87.1% women, mean age 51.9±14.8 years. Mean disease duration was 9,06±10,81 years. 64,5% were RF and ACPA positive and 25,9% had erosions.
Ultrasonograms were made in 20 joints of both hands: radiocarpals (RC), metacarpophalangeals (MCP) and proximal interphalangeals (PIP). 12 patients (38.7%) presented subclinical synovitis (SH≥2+PD), more frequently on RC (29% right, 22.6% left), and MCP (9.7% on 2RMCP, 9.7% 4LMCP). These patients had greater CDAI (3.9±1.37 vs 2.89±1.15, p=0.03), HAQ (0.14±0.29 vs 0.00±0.00, p=0.04), CRP (9.90±7.46 vs 4.74±2.30, p=0.00) RF levels (502.67±275.66 vs 200.92±158.43, p=0,00), greater prednisone (16.5% vs 3.2%, p=0.04), and methotrexate use (20.16±5.54 vs 17.50±3.98, p=0.01). None of the healthy controls presented subclinical synovitis.
In binary logistic regression CRP levels, RF titers and methotrexate doses were associated to subclinical synovitis. This association is not found in multivariate logistic regression. Negative association was found between subclinical synovitis and two csDMARDs use.
Conclusion: This is the first study of its type in Paraguayan patients, which clearly evidenced that an important part of RA patients in clinical remission still presented subclinical synovitis (HS≥2 + PD). It was associated with CRP, RF and methotrexate dose.
REFERENCES:
[1] Płaza M, Nowakowska-Płaza A, Pracoń G, Sudoł-Szopińska I. Role of ultrasonography in the diagnosis of rheumatic diseases in light of ACR/EULAR guidelines. J Ultrason. marzo de 2016;16(64):55-64.
[2] Foltz V, Gandjbakhch F, Etchepare F, Rosenberg C, Tanguy ML, Rozenberg S, et al. Power Doppler ultrasound, but not low-field magnetic resonance imaging, predicts relapse and radiographic disease progression in rheumatoid arthritis patients with low levels of disease activity. Arthritis & Rheumatism. 2012;64(1):67-76.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4208

AB0194 **ASSOCIATION OF MALNUTRITION WITH QUALITY OF LIFE IN ELDERLY RA PATIENTS**

W. Tański[1], J. Wójciga[2], N. Świątoniowska-Lonc[3], B. Jankowska-Polańska[3,4]. *[1]4th Military Teaching Hospital, Department of Internal Medicine, Wrocław, Poland*; *[2]Wroclaw Medical University, Student Research Club at the Division of Nursing in Internal, Wroclaw, Poland*; *[3]Wroclaw Medical University, Department of Clinical Nursing, Wroclaw, Poland*; *[4]4th Military Teaching Hospital, Research and Development Department, Wrocław, Poland*

Background: Rheumatoid arthritis (RA) is a progressive joint condition that leads to joints destruction and complications in the internal organs and significantly affects the a patient's functional ability. Elderly patients with RA complain of pain, mood and sleep disturbances, fatigue, and insomnia in addition to weakness, decreased appetite and weight loss. Chronic use of medications results in the risk of comorbidities and decreased physical functioning. All this together significantly contributes to a negative assessment of quality of life (QoL).
Objectives: Due to the chronic nature of RA and the high risk of malnutrition in this group of patients, an attempt was made to assess the QoL, activities of daily living and severity of frailty syndrome according to the results of the MNA questionnaire in a group of elderly patients with RA.
Methods: The study included 98 patients (age over 60 years) with a diagnosis of RA according to ARA. Standardized tools were used in the study: the WHO-QOL-BREF to assess quality of life, the Edmonton Frailty Scale to assess frailty syndrome, MNA to assess nutritional status and MMSE to assess cognitive function. Medical data were taken from the hospital records.
Results: Patients significantly differed in the extent of limitations in basic (ADL) and advanced activities of daily living (IADL) according to their nutritional status. The higher the level of malnutrition, the greater the limitations of undertaken activities. In addition, an adverse effect of reduced body weight on the occurrence of cognitive dysfunction was observed (33.33% of malnourished patients were diagnosed with dementia vs. 1.79% in normal weight patients). Similarly, frailty syndrome or vulnerability to frailty syndrome was associated with malnourished patients (33.3% mild, 16.67% moderate, and 16.67% severe frailty syndrome). Malnourished patients had significantly lower QoL scores in all domains of the WHOQOL-BREF questionnaire compared to normal weight patients and multivariate analysis of the effect of selected variables on QoL in the domains of the WHOQOL-BREF questionnaire showed that a significant independent determinant of lower QoL in all domains was the presence of frailty syndrome, respectively: Perception of QoL (R=-0. 069), Self-perception of health (R=-0.172), Physical domain (R=-0.425), Psychological domain (R=-0.432), Social domain (R=-0.415), Environmental domain (R=-0.317). Malnutrition was a significant independent determinant of QoL in the self-perception of health domain (R=-0.08). Additionally, in the regression analysis, a positive effect of male gender was observed on the assessment of QoL in the psychological (R=1.414) and environmental (R=1.123) domains.

Table 5. Comparative analysis of quality of life in terms of each domain of the WHOQOL-BREF questionnaire according to nutritional status.

	MNA			
WHOQOL BREF	Malnutrition (Mean±SD)	Risk of malnutrition (Mean±SD)	Normal nutrition (Mean±SD)	p
Perception of quality of life	3,33±1,03	3,33±0,68	3,68±0,58	0,029
Self-perception of health	2,67±0,82	2,47±0,84	3,14±0,98	0,004
Physical health	10,83±3,49	11,31±2,39	12,68±2,27	0,02
Psychological domain	12,5±3,89	13,28±2,73	14,45±2,24	0,056
Social domain	12,33± 2,86	12,67±2,93	14,29±2,61	0,007
Environmental domain	13,83±2,86	13,22±2,28	13,96±2,17	0,34

Conclusion: Malnourished people have a lower quality of life than people of normal weight. Malnutrition is a factor that negatively affects daily functioning, cognitive functioning, and the severity of frailty syndrome. A significant independent determinant of reduced quality of life across all domains of the WHOQOL-BREF questionnaire is frailty syndrome.

REFERENCES:

[1] Marcora SM, Chester KR, Mittal G et al. Randomizedphase 2 trial of anti-tumor necrosisfactortherapy for cachexia in patients with earlyrheumatoidarthritis. Am J ClinNutr 2006;84:1463–72. 24 .
[2] Kremers HM, Nicola PJ, Crowson CS, et al. Prognosticimportance of low body mass index in relation to cardiovascularmortality in rheumatoidarthritis. ArthritisRheum. 2004;50:3450–7.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4297

Rheumatoid arthritis - biological DMARDs

AB0195 **PHARMACOKINETIC AND PHARMACODYNAMIC EVALUATION OF A PROPOSED BIOSIMILAR MSB11456 VERSUS BOTH THE US-LICENSED AND EU-APPROVED TOCILIZUMAB: RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP, SINGLE-DOSE TRIAL IN HEALTHY ADULTS**

C. Schwabe[1], C. Wynne[2], A. Illes[3], M. Ullmann[3], E. Vincent[3], V. Ghori[3], C. Petit-Frere[3], A. S. Racault[3], I. Morin[3]. *[1]Auckland Clinical Studies Ltd, Auckland, New Zealand*; *[2]Christchurch Clinical Studies Trust Ltd, Christchurch, New Zealand*; *[3]Biosimilars, Fresenius Kabi SwissBioSim, Eysins, Switzerland*

Background: Tocilizumab, a biologic disease-modifying antirheumatic drug, is a recombinant humanized monoclonal immunoglobulin G1 antibody against the interleukin-6 receptor (IL-6R). MSB11456 is a proposed biosimilar to the US-licensed tocilizumab and EU-approved tocilizumab. Prior to initiation of its clinical development program, MSB11456 was considered highly similar to the reference products based on extensive *in vitro* pharmacological testing and functional activity assays.
Objectives: This double-blind, parallel-group phase I study (NCT03282851) assessed the pharmacokinetic (PK) and pharmacodynamic (PD) equivalence of MSB11456 to US-licensed and EU-approved tocilizumab and provided data on the similarity of safety profiles and immunogenicity of MSB11456 and the reference products in healthy adult subjects.
Methods: Healthy adult volunteers were randomized to receive a single 162 mg subcutaneous injection of MSB11456, US-licensed tocilizumab, or EU-approved tocilizumab. Samples for PK/PD and immunogenicity analysis were taken predose, up to 29 days postdose, and at the end of study visit (day 48). Primary endpoint PK parameters were natural log transformed and analyzed using analysis of covariance (ANCOVA) methods; results were then transformed back to the original scale. Secondary PD analysis measured serum soluble IL-6R and serum C reactive protein (sCRP) parameters, and data were analyzed using a method similar to that for PK data. Safety data were collected throughout the study and analyzed descriptively.
Results: 685 subjects were randomized and treated. Results of the primary PK analysis demonstrated bioequivalence between MSB11456 and both US-licensed and EU-approved tocilizumab, as well as between the reference products, since all corresponding 90% confidence intervals (CIs) for the geometric least squares mean (LSM) ratios were within the predefined 80.00% to 125.00% equivalence margin (Table 1). PD analyses also demonstrated equivalence of MSB11456 and both US-licensed and EU-approved tocilizumab, as well as between the reference products. Safety, tolerability and immunogenicity were also comparable between treatments. The incidence of tocilizumab-specific neutralizing antibodies was low (<3% for all three products).
Conclusion: PK and PD equivalence of MSB11456, US-licensed tocilizumab, and EU-approved tocilizumab were demonstrated with comparable immunogenicity, safety, and tolerability for the three products. This study adds to the totality of evidence in support of MSB11456 as a proposed biosimilar to tocilizumab.

Table 1. Results of primary PK analysis

Parameter	Treatment	n	Ratio of geometric LSMs (%)	90% CI of ratio
MSB11456 vs US-licensed tocilizumab				
$AUC_{0-\infty}$	MSB11456	194	106.16	96.80, 116.43
	US-licensed tocilizumab	190		
AUC_{0-t}	MSB11456	230	104.15	93.58, 115.90
	US-licensed tocilizumab	226		
C_{max}	MSB11456	230	104.45	95.05, 114.77
	US-licensed tocilizumab	226		
MSB11456 vs EU-tocilizumab				
$AUC_{0-\infty}$	MSB11456	194	104.03	94.96, 113.96
	EU-approved tocilizumab	200		
AUC_{0-t}	MSB11456	230	94.78	85.15, 105.50
	EU-approved tocilizumab	224		
C_{max}	MSB11456	230	94.83	86.28, 104.22
	EU-approved tocilizumab	224		
US-licensed vs EU-approved tocilizumab				
$AUC_{0-\infty}$	US-licensed tocilizumab	190	97.99	89.40, 107.41
	EU-approved tocilizumab	200		
AUC_{0-t}	US-licensed tocilizumab	226	91.01	81.71, 101.36
	EU-approved tocilizumab	224		
C_{max}	US-licensed tocilizumab	226	90.79	82.57, 99.84
	EU-approved tocilizumab	224		

AUC, area under the serum concentration-time curve (μg·h/mL); $AUC_{0-\infty}$, AUC from time zero to infinity; AUC_{0-t}, AUC from time zero to the time of the last quantifiable concentration; C_{max}, maximum concentration (μg/mL)

Acknowledgements: Medical writing support was provided by Caroline Spencer and Dr Sue Chambers (Rx Communications, Mold, UK), funded by Fresenius Kabi SwissBioSim.
Disclosure of Interests: Christian Schwabe: None declared, Chris Wynne: None declared, Andras Illes Employee of: Fresenius Kabi SwissBioSim, Martin Ullmann Employee of: Fresenius Kabi SwissBioSim, Emmanuelle Vincent Employee of: Fresenius Kabi SwissBioSim, Vishal Ghori Employee of: Fresenius Kabi SwissBioSim, Corinne Petit-Frere Employee of: Biosimilars, Fresenius Kabi SwissBioSim, Anne-Sophie Racault Employee of: Fresenius Kabi SwissBioSim, Isabelle Morin Employee of: Former employee of Fresenius Kabi SwissBioSim
DOI: 10.1136/annrheumdis-2021-eular.74

AB0196 SURVIVAL ANALYSIS OF TIME TO FIRST ADVERSE DRUG REACTION AND DRUG SURVIVAL IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ADALIMUMAB AND ETANERCEPT

M. Nguyen[1], K. Velthuis[1], J. Scholl[1], J. Jansen[1], L. Kosse[1], P. Ten Klooster[2,3], N. Jessurun[1], H. Vonkeman[3,4]. *[1]Netherlands Pharmacovigilance Centre Lareb, Research Department, 's-Hertogenbosch, Netherlands*; *[2]Transparency in Healthcare B.V., Hengelo, Netherlands*; *[3]University of Twente, Department of Psychology, Health & Technology, Enschede, Netherlands*; *[4]Medisch Spectrum Twente, Department of Rheumatology and Clinical Immunology, Enschede, Netherlands*

Background: Treatment of rheumatoid arthritis (RA) with biologic disease-modifying antirheumatic drugs (bDMARDs) has been common practice in the last two decades. However, differences in patients experiencing adverse drug reactions (ADRs) between individual bDMARDs, such as adalimumab (ADA) and etanercept (ETN), during first time treatment has not been studied yet in real-world settings.
Objectives: To compare proportions of RA patients experiencing ADRs as well as survival to first ADR and drug survival during treatment with ADA and ETN.
Methods: Retrospective single centre cohort study including adult patients with RA, treated with either ADA or ETN between 1 January 2003 and 30 April 2020. The proportions of patients experiencing an ADR were compared by assessing the percentage of patients, treated with either ADA or ETN, experiencing at least one ADR during their first time treatment. Survival to first ADR and drug survival were assessed by calculating time between start of treatment and first ADR and start of treatment and discontinuation of treatment respectively. Stop and restart of treatment within 90 days was considered as continuous use. Differences in proportions were statistically tested using Fisher's Exact Test. Differences in drug survival between ADA and ETN were tested by Kaplan-Meier analysis and Log Rank tests.
Results: A total of 422 patients were included in this study (ADA 259, ETN 163). For 93 patients (21.2%) an ADR was registered during first time treatment. The proportion of patients experiencing at least one ADR during their first time treatment was 22.7% for ADA and 20.2% for ETN (p=0.628). Survival time to first ADR did not differ significantly between ADA and ETN (median survival ADA 10.34 years (95% CI [7.62-13.06], median survival ETN not reached, p=0.109, figure 1A). Median drug survival was 1.75 years for ADA (95 CI [1.38-2.11]) and 2.68 years for ETN (95% CI [1.73-3.64]). Drug survival differed significantly (p<0.001, figure 1B).

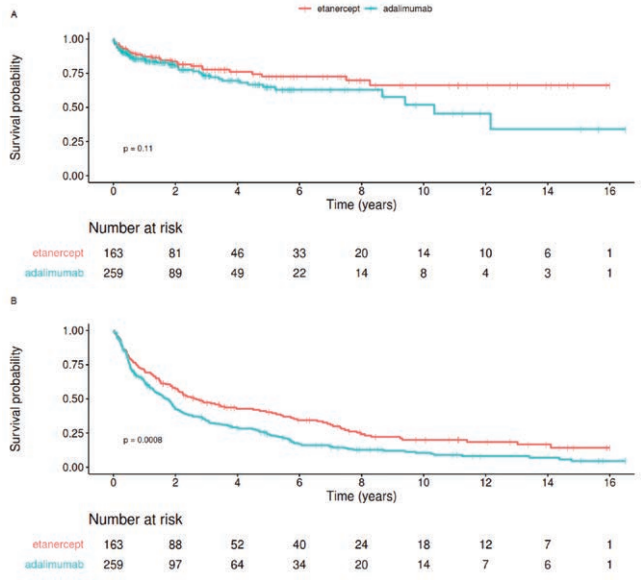


Figure 1. Kaplan-Meier survival curves for adalimumab and etanercept with (a) survival to first ADR and (b) drug survival.

Conclusion: Neither the proportion of patients experiencing ADRs nor survival to first ADR during first time treatment with ADA and ETN differed significantly. Drug survival of first time drug treatment of ADA was significantly lower compared to drug survival of first time drug treatment of ETN.
Disclosure of Interests: My Nguyen: None declared, Kimberly Velthuis: None declared, Joep Scholl: None declared, Jurriaan Jansen: None declared, Leanne Kosse: None declared, Peter ten Klooster: None declared, Naomi Jessurun: None declared, Harald Vonkeman Consultant of: BMS, Celgene, Celltrion, Galapagos, Gilead, Janssen-Cilag, Lilly, Novartis, Pfizer, Sanofi-Genzyme, Grant/research support from: Abbvie
DOI: 10.1136/annrheumdis-2021-eular.179

AB0197 EFFICACY AND SAFETY OF HLX01 COMBINED WITH METHOTREXATE IN CHINESE PATIENTS WITH MODERATELY TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS WHO HAD INADEQUATE RESPONSES TO METHOTREXATE: RESULTS OF A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 STUDY

X. Zeng[1], J. Liu[2], X. Liu[3], L. Wu[4], Y. Liu[5], X. Liao[6], H. Liu[7], J. Hu[8], X. Lu[9], L. Chen[10], J. Xu[11], Z. Jiang[12], F. Lu[13], H. Wu[14], L. Sun[15], M. Wang[16], X. Yu[17], Q. Wang[18]. *[1]Peking Union Medical College Hospital, Department of Rheumatology, Beijing, China*; *[2]Jiujiang NO.1 People's Hospital, Department of Rheumatology, Jiujiang, China*; *[3]First Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; *[4]People's Hospital of Xinjiang Uygur Autonomous Region, Department of Rheumatology, Urumchi, China*; *[5]West China Hospital of Sichuan University, Department of Rheumatology, Chengdu, China*; *[6]Chenzhou First People's Hospital, Department of Nephrology, Chenzhou, China*; *[7]Qilu Hospital of Shandong University, Department of Rheumatology, Ji'nan, China*; *[8]Jiangxi Pingxiang People's Hospital, Department of Rheumatology, Pingxiang, China*; *[9]China-Japan Friendship Hospital, Department of Rheumatology, Beijing, China*; *[10]The First Affiliated Hospital of Bengbu Medical College, Department of Rheumatology, Bengbu, China*; *[11]First Affiliated Hospital of Kunming Medical University, Department of Rheumatology, Kunming, China*; *[12]The First Hospital of Jilin University, Department of Rheumatology, Changchun, China*; *[13]The First Affiliated Hospital of Baotou Medical College, Inner Mongolia University of Science and Technology, Department of Rheumatology, Baotou, China*; *[14]The Second Affiliated Hospital Zhejiang University School of Medicine, Department of Rheumatology, Hangzhou, China*; *[15]Nanjing Drum Tower Hospital, Department of Rheumatology, Nanjing, China*; *[16]Zhongda Hospital Southeast University, Department of Rheumatology, Nanjing, China*; *[17]Cangzhou Hospital of Integrated TCM-WM · Hebei, Department of Rheumatology, Cangzhou, China*; *[18]Shanghai Henlius Biotech, Inc., Global Product Development, Shanghai, China*

Background: Rituximab is an effective therapy for rheumatoid arthritis (RA) patients with inadequate responses to methotrexate (MTX)[1, 2]. However, it has not been registered or approved in China for the treatment of RA by far. HLX01, an approved rituximab biosimilar (demonstrated in Chinese patients with diffuse large B-cell lymphoma)[3], is thus evaluated in this study for the benefits of Chinese RA patients.
Objectives: This study aimed to evaluate the efficacy and safety of HLX01 plus MTX versus placebo plus MTX in Chinese patients with active RA who had inadequate responses to MTX.
Methods: This was a randomised, double-blind, placebo-controlled phase 3 study conducted in China (NCT03522415). Eligible patients were randomised 2:1 to receive intravenous infusion of 2×1000 mg HLX01 or placebo on day 1 and day 15. Patients with inadequate responses at week 16 and 20 were allowed to receive rescue treatments. Patients were retreated with or switched to receive (if initially assigned to placebo) 2×1000 mg rituximab at the first day of week 24 and 26. The primary endpoint of this study was the American College of Rheumatology criteria (ACR) 20 response at week 24. Secondary efficacy endpoints were evaluated at week 12, 24, 36 and 48. The safety, pharmacokinetics, pharmacodynamics and immunogenicity of HLX01 were observed and analyzed throughout the study.
Results: Between May 28, 2018 and Sep 11, 2020, a total of 275 patients (ITT set) were randomised and 263 patients without major protocol deviations were included in per-protocol set (PPS). At week 24, HLX01 showed statistically superior efficacy (p <0.001) to placebo (ACR20: 60.7% vs 35.9% in ITT set, 60.3% vs 37.1% in PPS). Secondary efficacy endpoints were also significantly improved in HLX01 group compared with placebo (Table 1). The overall incidence of serious treatment emergent adverse events (TEAEs), adverse drug reactions (ADRs), and TEAEs leading to drug discontinuation were similar among treatment groups, with the most common TEAE been upper respiratory tract infection before (18.1% vs 18.5%) or after (13.0% vs 12.3%) week 24. Serum concentrations, immunogenicity and pharmacodynamics were similar between HLX01 and placebo groups.

Table 1. Results of secondary efficacy endpoints at week 12, 24, 36 and 48 in ITT set.

	Secondary efficacy endpoints									
	ACR20 (%)		ACR50 (%)		ACR70 (%)		DAS28-CRP (mean)		HAQ-DI (mean)	
Duration	HLX01	Placebo	HLX01	Placebo	HLX01	Placebo	HLX01	Placebo	HLX01	Placebo
Baseline							5.49	5.43	1.40	1.45
Week 12	48.1	32.6	21.9	10.9	4.4	5.4	3.89	4.47	1.02	1.22
Week 24	60.7	35.9	36.6	18.5	15.3	12.0	3.39	4.37	0.87	1.22
Week 36	60.1	48.9	46.4	31.5	32.2	17.4	2.88	3.51	0.71	0.97
Week 48	73.8	62.0	55.2	40.2	39.9	27.2	2.82	3.51	0.72	1.03

Conclusion: Comparing with placebo plus MTX, HLX01 plus MTX showed significantly improved clinical outcomes and comparable safety profiles in Chinese patients with moderately to severely active RA who had inadequate responses to MTX, demonstrating HLX01 in combination with MTX as a well-tolerated, safe and efficient treatment option.

REFERENCES:

[1] Emery P, Deodhar A, Rigby WF, et al. Efficacy and safety of different doses and retreatment of rituximab: a randomised, placebo-controlled trial in patients who are biological naive with active rheumatoid arthritis and an inadequate response to methotrexate (Study Evaluating Rituximab's Efficacy in MTX iNadequate rEsponders (SERENE)). *Ann Rheum Dis*. Sep 2010;69(9):1629-35. doi:10.1136/ard.2009.119933.

[2] Rubbert-Roth A, Tak PP, Zerbini C, et al. Efficacy and safety of various repeat treatment dosing regimens of rituximab in patients with active rheumatoid arthritis: results of a Phase III randomized study (MIRROR). *Rheumatology (Oxford)*. Sep 2010;49(9):1683-93. doi:10.1093/rheumatology/keq116.

[3] Shi Y, Song Y, Qin Y, et al. A phase 3 study of rituximab biosimilar HLX01 in patients with diffuse large B-cell lymphoma. *J Hematol Oncol*. Apr 16 2020;13(1):38. doi:10.1186/s13045-020-00871-9.

Acknowledgements: The authors would like to thank participants in this study and their families. They would also like to acknowledge other investigators and staff at all clinical sites and the members of the Independent Data Monitoring Committee.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.282

AB0198

EFFICACY AND SAFETY AFTER TRANSITION FROM REFERENCE ADALIMUMAB TO CT-P17 (ADALIMUMAB BIOSIMILAR: 100 MG/ML) IN COMPARISON WITH THE MAINTAINED TREATMENT (CT-P17 OR REFERENCE ADALIMUMAB) IN PATIENTS WITH MODERATE-TO-SEVERE ACTIVE RHEUMATOID ARTHRITIS: 1-YEAR RESULT

D. Furst[1], E. Keystone[2], J. Kay[3], J. Jaworski[4], R. Wojciechowski[5], P. Wiland[6], A. Dudek[7], M. Krogulec[8], S. Jeka[9], A. Zielinska[10], J. Trefler[11], K. Bartnicka-Masłowska[12], M. Krajewska-Wlodarczyk[13], P. Klimiuk[14], S. J. Lee[15], S. H. Kim[16], Y. Bae[16], G. Yang[16], J. Yoo[16], T. Kim[17]. *[1]University of California, Rheumatology, Los Angeles, United States of America*; *[2]University of Toronto, Medicine, Toronto, Canada*; *[3]University of Massachusetts Medical School, Medicine and Population & Quantitative Health Sciences, Worcester, United States of America*; *[4]Reumatika Centrum Reumatologii, Reumatika Centrum Reumatologii, Warsaw, Poland*; *[5]University Hospital No 2 in Bydgoszcz, Rheumatology and Connective Tissue Diseases, Bydgoszcz, Poland*; *[6]Wroclaw Medical University, Rheumatology and Internal Diseases, Wrocław, Poland*; *[7]Centrum Medyczne AMED, Reumatologia, Warsaw, Poland*; *[8]Reumatology Clinic NZOZ Lecznica MAK-MED, Rheumatology, Nadarzyn, Poland*; *[9]Nasz Lekarz Przychodnie Medyczne, Not applicable, Toruń, Poland*; *[10]Medycyna Kliniczna, Not applicable, Warszawa, Poland*; *[11]Reuma Centrum, Rheumatology, Warsaw, Poland*; *[12]Centrum Medyczne AMED, Oddział w Łodzi, Lodz, Poland*; *[13]University of Warmia and Mazury in Olsztyn, Rheumatology, Olsztyn, Poland*; *[14]Medical University of Bialystok, Rheumatology and Internal Diseases, Bialystok, Poland*; *[15]Celltrion, Inc, Clinical Development Division, Incheon, Korea, Rep. of (South Korea)*; *[16]Celltrion, Inc, Clinical Planning, Incheon, Korea, Rep. of (South Korea)*; *[17]Celltrion, Inc, Biometrics, Incheon, Korea, Rep. of (South Korea)*

Background: Therapeutic equivalence of CT-P17 to reference adalimumab (ref-adalimumab) has been shown in patients with moderate-to-severe active rheumatoid arthritis (RA) through primary 24-week results [1]. Here, efficacy, pharmacokinetics (PK), safety and immunogenicity results up to 52-week, including transition data from ref-adalimumab to CT-P17 are presented.

Objectives: To evaluate efficacy, PK, safety and immunogenicity when switched from ref-adalimumab to CT-P17 compared to maintaining CT-P17 or ref-adalimumab.

Methods: In this study, 648 moderate-to-severe active RA patients despite methotrexate treatment were randomized (1:1) to either CT-P17 or ref-adalimumab and treated with doses of 40 mg every 2 weeks up to Week 24. Prior to dosing at Week 26, 608 patients were randomized again to either maintaining their treatments or being switched from ref-adalimumab to CT-P17. Efficacy, PK, safety, and immunogenicity were assessed up to Week 52.

Results: After the second randomization, 303 patients continued with CT-P17, 153 patients continued with ref-adalimumab and 151 patients switched from ref-adalimumab to CT-P17 treatments, up to Week 48. Demographics and baseline characteristics were similar among the 3 groups. Sustained and comparable efficacy in terms of ACR20/50/70 response rates was achieved not only in the maintenance groups (CT-P17 or ref-adalimumab) but also in the switched from ref-adalimumab to CT-P17 group up to Week 52 (Figure 1).

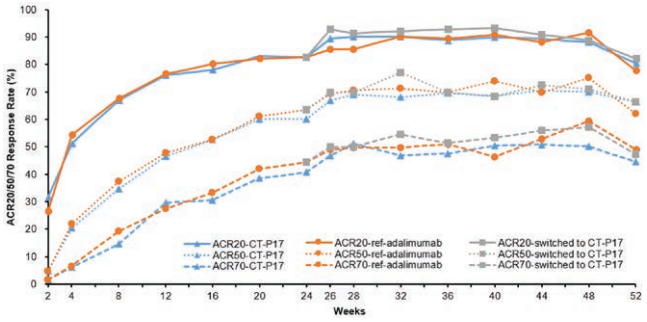


Figure 1. ACR 20/50/70 Response Rates up to 1 YearAbbreviation: ref-adalimumab, reference adalimumab.Note. There were patients who could not visit the study site due to COVID-19 pandemic and were counted as nonresponder for ACR response at Week 52.

In terms of PK, mean trough serum concentration (Ctrough) were maintained after Week 24 in all 3 groups. The observed mean Ctrough were within the reported therapeutic ranges of ref-adalimumab trough levels in RA patients (5-8 μg/mL).

The safety profile after transition was comparable among the 3 groups (Table 1). The most common treatment-emergent adverse events (TEAEs) was neutropenia. Similar proportions of patients in all 3 groups experienced at least 1 TEAE: injection site reactions, hypersensitivity/allergic reactions and infections. One malignancy (basal cell carcinoma; unrelated) was reported in the ref-adalimumab maintenance group. Safety data accumulated over 1 year also showed comparable results among the 3 groups. Anti-drug antibody (ADA) and neutralizing antibody (NAb) results were similar among the 3 groups. At Week 52, the proportions of patients who had ADA/NAbs were 28.4%/24.8% patients in CT-P17 maintenance, 27.0%/24.3% patients in ref-adalimumab maintenance and 28.3%/26.3% patients in switched to CT-P17 groups.

Conclusion: Single transition from ref-adalimumab to CT-P17 was efficacious and safe without increase in immunogenicity. Also, efficacy, PK, safety and immunogenicity profiles were comparable between CT-P17 and ref-adalimumab up to Week 52.

REFERENCES:

[1] J Kay et al, 2020. Poster Presented at ACR Convergence 2020.

Table 1. Overview of TEAEs from Weeks 26 to 52 (Safety Population – second random subset)

	Second Randomization		
Patients, n (%)	CT-P17 Maintenance (N=303)	Ref-ada Maintenance (N=152)	Switched to CT-P17 (N=152)
≥1 TEAE	121 (39.9)	69 (45.4)	73 (48.0)
≥1 TESAE	6 (2.0)	3 (2.0)	5 (3.3)
≥1 TEAE leading to study drug discontinuation	3 (1.0)	2 (1.3)	5 (3.3)
≥1 TEAE classified as hypersensitivity/ allergic reactions	2 (0.7)	1 (0.7)	0 (0)
≥1 TEAE classified as injection site reactions	1 (0.3)	4 (2.6)	1 (0.7)
≥1 TEAE classified as infection	54 (17.8)	41 (27.0)	28 (18.4)
≥1 TEAE classified as malignancy	0 (0)	1 (0.7)	0 (0)

Abbreviations: Ref-ada, reference adalimumab; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

Disclosure of Interests: Daniel Furst Speakers bureau: CME, Consultant of: Amgen, Corbus, Galapagos, Horizon, Kadmon, Pfizer, Talaris, Grant/research support from: Corbus, CSL Behring, Galapagos, Gilead, GSK, Horizon, Kadmon, Novartis, Pfizer, Roche/Genetech, Talaris, Edward Keystone Speakers bureau: Amgen, AbbVie, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Novartis, Pfizer Pharmaceuticals, Sanofi Genzyme, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb Company, Celltrion Inc., Myriad Autoimmune, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc., Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepis, Grant/research support from: Amgen, Merck, Pfizer Pharmaceuticals, PuraPharm, Jonathan Kay Consultant of: AbbVie, Inc., Boehringer Ingelheim GmbH, Celltrion Healthcare Co. Ltd., Jubilant Radiopharma, Merck & Co., Inc., Pfizer Inc., Samsung Bioepis, Sandoz Inc., Scipher Medicine, UCB, Inc., Grant/research support from: Paid to the University of Massachusetts Medical School: Gilead Sciences Inc., Novartis Pharmaceuticals Corp., Pfizer Inc., Janusz Jaworski: None declared, Rafal Wojciechowski: None declared, Piotr Wiland Speakers bureau: Eli Lilly, Sanofi Aventis, Novartis, Sandoz, Consultant of: Eli Lilly, Novartis, Sandoz, Anna Dudek: None declared, Marek Krogulec: None declared, Sławomir Jeka Speakers bureau: Novartis, Pfizer, Roche, Lilly, Teva, MSD, Abbvie, Sandoz, Egis, Medac, Consultant of: Novartis, Pfizer, Roche, Lilly, Teva, MSD, Abbvie, Sandoz, Egis, Medac, Agnieszka Zielinska: None declared, Jakub Trefler: None declared, Katarzyna Bartnicka-Masłowska: None declared, Magdalena Krajewska-Wlodarczyk Speakers bureau: Abbvie, Eli Lilly, Novartis, Roche, Piotr Klimiuk: None declared, Sang Joon Lee Employee of: Celltrion, Inc., Sung Hyun Kim Employee of: Celltrion, Inc., YunJu Bae Employee of: Celltrion, Inc., GoEun Yang Employee of: Celltrion, Inc., JaeKyoung Yoo Employee of: Celltrion, Inc., TaeKyung Kim Employee of: Celltrion, Inc.
DOI: 10.1136/annrheumdis-2021-eular.325

AB0199 PLACEBO AND NOCEBO RESPONSES IN RANDOMIZED CONTROLLED TRIALS OF NON-TUMOR NECROSIS FACTOR BIOLOGICS AND JANUS KINASE INHIBITORS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS SHOWING INSUFFICIENT RESPONSE TO TUMOR NECROSIS FACTOR INHIBITORS: A META-ANALYSIS

Y. H. Lee[1], G. G. Song[2]. [1]*Korea University, Rheumatology, Seoul, Korea, Rep. of (South Korea)*; [2]*Korea University Guro Hospital, Rheumatology, Seoul, Korea, Rep. of (South Korea)*

Background: Placebo and nocebo responses have important consequences for the development of pharmaceutical drugs and the design of randomized controlled trials (RCTs). They can lead to the incorrect measurement of treatment-related efficacy and adverse effects (AEs).

Objectives: The goal of this study was to evaluate the frequency and magnitude of placebo and nocebo responses in placebo-controlled RCTs of non-tumor necrosis factor (TNF) biologics and Janus kinase (JAK) inhibitors in patients with rheumatoid arthritis (RA) showing an insufficient response to TNF inhibitors.

Methods: We performed a meta-analysis on the rates of placebo response, AEs, severe AEs (SAEs), and withdrawal owing to AEs in placebo-controlled randomized clinical trials (RCTs) of non-TNF biologics and JAK inhibitors in patients with RA showing an insufficient response to TNF inhibitors.

Results: Nine RCTs contained a total of 3,442 patients (1,840 experimental subjects and 1,602 controls). The pooled incidence of an ACR20 response rate in placebo-treated patients was 22.1% (95% CI 16.4–29.1%) and 27.9% (95% CI 24.5–31.6%) in RCTs of non-TNF inhibitors and JAK inhibitors, respectively. A strong negative correlation was observed between drug efficacies (ACR20 response) and AE rates in the placebo arm, indicating that the greater the placebo response, the weaker the nocebo response (r = -0.762, P = 0.017). A strong positive correlation was observed between drug efficacies (ACR20 response) in the placebo and active comparator, indicating that the greater the placebo response, the greater the treatment response (r = 0.737, P = 0.003). The pooled estimate in placebo-treated patients with at least one AE was 71.8% (95% CI 57.4–82.7%) and 58.7% (95% CI 52.8–64.3%) in RCTs of non-TNF inhibitors and JAK inhibitors, respectively. The pooled estimate in placebo-treated patients who withdrew from treatment owing to an AE was 3.8% (95% CI 2.7–5.3%) and 4.0% (95% CI 2.7–6.0%) in RCTs of non-TNF inhibitors and JAK inhibitors, respectively. A strong positive correlation was observed between AE rates in the placebo and active arms, indicating that the greater the nocebo response, the stronger the AE rate in the active arm (r = 0.855, P = 0.003).

Conclusion: The frequency of the placebo and nocebo responses was 22.1% vs. 27.9% and 71.8% vs. 58.7% in placebo-controlled RCTs of non-TNF inhibitors and JAK inhibitors for RA, respectively, and the greater the placebo response, the weaker the nocebo response and the greater the efficacy.

REFERENCES:

[1] Mitsikostas DD, Chalarakis NG, Mantonakis LI, Delicha EM, Sfikakis PP. Nocebo in fibromyalgia: meta-analysis of placebo-controlled clinical trials and implications for practice. Eur J Neurol 2012;19:672-80.

[2] Kravvariti E, Kitas GD, Mitsikostas DD, Sfikakis PP. Nocebos in rheumatology: emerging concepts and their implications for clinical practice. Nat Rev Rheumatol 2018;14:727-40.

[3] Colloca L, Barsky AJ. Placebo and Nocebo Effects. N Engl J Med 2020;382:554-61.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.661

AB0200 TRENDS IN THE CHOICE OF FIRST BIOLOGIC AND TARGETED SYNTHETIC DMARD IN RHEUMATOID ARTHRITIS PATIENTS: 20-YEARS JOURNEY OF HUR-BIO REAL-LIFE REGISTRY

A. İ. Ertenli[1], U. Kalyoncu[1], O. Karadag[1], L. Kılıç[1], A. Akdoğan[1], I. Dogan[1], Ş. A. Bilgen[1], E. Bilgin[1], E. Duran[1], Y. Maraş[2], B. Kıcasık[3], A. Erden[2], B. Armagan[2], A. Sarı[4], E. C. Bolek[1], B. Farisoğulları[1], G. K. Yardımcı[1], Z. Özsoy[1], G. Ayan[1], M. Çalgüneri[1], S. Kiraz[1]. [1]*Hacettepe University, Internal Medicine, Rheumatology, Ankara, Turkey*; [2]*Ankara City Hospital, Internal Medicine, Rheumatology, Ankara, Turkey*; [3]*Medical Park Hospital, Internal Medicine, Rheumatology, Gaziantep, Turkey*; [4]*Yenimahalle Education and Research Hospital, Internal Medicine, Rheumatology, Ankara, Turkey*

Background: In the last 20 years, there have been extraordinary improvements and practice-changing developments in the management of rheumatoid arthritis (RA). Exploring the pathogenetic mechanisms first enabled clinicians to use anti-tumor necrosis factor (TNF) alpha agents, then drugs targeting different molecules. Parallel to these developments, treatment guidelines have been changed accordingly. Meanwhile, how these developments have been reflected into the real-word practice is a question of interest.

Objectives: In this study, we aimed to explore the first biologic agent trends of our 20-years of single-center experience.

Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a single center biological disease modifying anti-rheumatic drug (DMARD) registry since 2005. Patients who were started biologics before 2005 were registered retrospectively. In brief; demographic data, treatment-related data (including adverse events) and disease-related data of RA patients have been recorded in HUR-BIO. Until the end of the 2020, 21 different rheumatologists contributed to the development of HUR-BIO. In this study, distribution of the first-line biologic agents was calculated according to 5-year periods starting from the 2001. Also, demographic and serologic data of RA patients were reported.

Results: A total of 2080 RA patients was registered in HUR-BIO by the end of 2020. Of these patients, 79.5% was female. Mean age at the starting of bDMARD was 53.3 ± 17.8 years. Rate of rheumatoid factor and anti-cyclic citrullinated peptide positivity was 67.6% and 61.0%, respectively. 65 (3.2%), 335 (16.1%), 858 (41.2%) and 822 (39.5%) patients were prescribed with their first bDMARD in 2001-2005, 2006-2010, 2011-2015 and 2016-2020, respectively. There was a trend towards the increasing prescription of non-Anti-TNF bDMARDs over time.

Table 1. Distribution of first biologic DMARDs in RA patients according to 5-years periods

	2001-2005	2006-2010	2011-2015	2016-2020	Total
Adalimumab	15 (23.1)	111 (33.0)	187 (21.8)	153 (18.6)	466 (22.4)
Etanercept	30 (46.2)	154 (45.8)	229 (26.7)	54 (6.6)	467 (22.4)
İnfliximab	20 (30.8)	58 (17.3)	64 (7.5)	7 (0.9)	149 (7.1)
Golimumab	0	0	37 (4.3)	43 (5.2)	80 (3.8)
Certolizumab	0	0	37 (4.3)	68 (8.3)	105 (5.0)
Anti-TNF	65 (100)	323 (96.4)	554 (64.5)	325 (39.5)	1267 (60.9)
Tofacitinib	0	0	6 (0.7)	212 (25.8)	218 (10.5)
Tocilizumab	0	0	9 (1.0)	102 (12.4)	111 (5.3)
Rituximab	0	12 (3.6)	136 (15.8)	84 (10.2)	232 (11.1)
Abatacept	0	0	153 (17.8)	99 (12.0)	252 (12.1)
Non-Anti-TNF	0	12 (3.6)	304 (35.5)	497 (60.5)	813 (39.1)
Total	65 (100)	335 (100)	858 (100)	822 (100)	2080 (100)

***Approval years of drugs in Turkey**; Infliximab: 2003, etanercept:2004, adalimumab: 2005, golimumab: 2013, certolizumab: 2014, abatacept: 2010, tocilizumab: 2013, rituximab:2009, tofacitinib: 2015,*

Conclusion: Real-life practice in RA seems consistent with treatment guidelines. Use of non-Anti-TNF bDMARDs becoming more frequent year-by-year. Jak kinase inhibitor has rised through the last 5 years. Next decade may be the years of Jak kinases inhibitors.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.693

AB0201 CHANGES IN THE PRESCRIPTION PATTERNS OF THE SECOND-LINE BIOLOGIC AND TARGETED SYNTHETIC DMARD IN RHEUMATOID ARTHRITIS PATIENTS: 20-YEARS JOURNEY OF HUR-BIO REAL-LIFE REGISTRY

S. Kiraz[1], U. Kalyoncu[1], O. Karadag[1], L. Kılıç[1], A. Akdoğan[1], I. Dogan[1], Ş. A. Bilgen[1], E. Bilgin[1], E. C. Bolek[1], B. Kıcasık[2], Y. Maraş[3], A. Erden[3], B. Armagan[3], A. Sarı[4], E. Duran[1], B. Farisoğulları[1], G. K. Yardımcı[1], Z. Özsoy[1],

G. Ayan[1], M. Çalgüneri[1], A. İ. Ertenli[1]. [1]*Hacettepe University, Internal Medicine, Rheumatology, Ankara, Turkey*; [2]*Medical Park Hospital, Internal Medicine, Rheumatology, Gaziantep, Turkey*; [3]*Ankara City Hospital, Internal Medicine, Rheumatology, Ankara, Turkey*; [4]*Yenimahalle Education and Research Hospital, Internal Medicine, Rheumatology, Ankara, Turkey*

Background: In the last 20 years, anti-tumor necrosis factor (TNF) alpha agents re-designed the management of rheumatoid arthritis (RA). Despite this, unmet needs in the management of RA brought several drugs targeting different molecules and cytokines. It is still a research question that how did these developments changed daily-practice in RA patients who are intolerant/unresponsive to the first biological disease modifying anti-rheumatic drugs (bDMARD).
Objectives: In this study, we aimed to explore the second biologic agent trends of our 20-years of single-center experience.
Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a single center biological disease modifying anti-rheumatic drug (DMARD) registry since 2005. Patients who were started biologics before 2005 were registered retrospectively. Until the end of the 2020, 21 different rheumatologists contributed to the development of HUR-BIO. Distribution of the second-line biological agents (switch from first-line biological agent because of either adverse events or unresponsiveness) was calculated according to 5-year periods starting from the 2001. Also, demographic and serologic data of RA patients were reported.
Results: A total of 776 (776/2080, 37.3%) RA patients, who was prescribed a second biological agent, was registered in HUR-BIO by the end of 2020. Of these patients, 83.7% was female. Mean age at the starting of bDMARD was 53.1 ± 13.3 years. Rate of rheumatoid factor and anti-cyclic citrullinated peptid positivity was 69.1% and 60.5%, respectively. Distribution of first-line bDMARDs was as follows: adalimumab 194 (24.9%), etanercept 209 (26.9%), infliximab 105 (13.5%), golimumab 39 (5.0%), certolizumab 35 (4.5%), abatacept 78 (10.0%), rituximab 46 (5.9%), tofacitinib 37 (4.7%), tocilizumab 33 (4.2%). 11 (1.4%), 85 (11.0%), 282 (36.3%) and 398 (51.3%) patients were prescribed with their second bDMARD in 2001-2005, 2006-2010, 2011-2015 and 2016-2020, respectively. There was a trend towards the increasing prescription of non-Anti-TNF bDMARDs as second-line over time.

Table 1. Distribution of second biologic DMARDs in RA patients according to 5-years periods

	2001-2005	2006-2010	2011-2015	2016-2020	Total
Adalimumab	3 (27.3)	15 (17.6)	69 (23.9)	77 (18.9)	164 (20.8)
Etanercept	8 (72.7)	35 (41.2)	49 (17.0)	41 (10.1)	133 (16.8)
İnfliximab	0	12 (14.1)	13 (4.5)	25 (6.2)	50 (5.4)
Golimumab	0	0	19 (6.6)	8 (2.0)	27 (3.4)
Certolizumab	0	0	2 (0.7)	26 (6.4)	28 (3.5)
Anti-TNF	11 (100)	62 (72.9)	152 (53.9)	177 (44.5)	402 (51.8)
Tofacitinib	0	0	4 (1.4)	73 (17.9)	77 (9.7)
Tocilizumab	0	0	12 (4.2)	81(19.9)	93 (11.7)
Rituximab	0	22 (25.9)	53 (18.3)	32 (7.8)	107 (13.5)
Abatacept	0	1 (1.2)	61 (21.1)	35 (8.6)	97 (12.2)
Non-Anti-TNF	0	23 (27.1)	130 (46.1)	221 (55.5)	374 (48.2)
Total	11 (100)	85 (100)	282 (100)	398 (100)	776 (100)

***Approval years of drugs in Turkey**; Infliximab: 2003, etanercept:2004, adalimumab: 2005, golimumab: 2013, certolizumab: 2014, abatacept: 2010, tocilizumab: 2013, rituximab:2009, tofacitinib: 2015*

Conclusion: As the choice of second-line biologic and targeted synthetic DMARD, non-Anti-TNF bDMARDs, especially tofacitinib and tocilizumab becoming more frequent year-by-year. Despite that, anti-TNF agents as a group are still highly-prescribed options as second-line bDMARD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.694

AB0202

IMPROVEMENT IN CLINICAL DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES AFTER 6 MONTHS OF TREATMENT WITH ABATACEPT, STRATIFIED BY LINE OF THERAPY, IN PATIENTS WITH RA: RESULTS FROM A LARGE, US, NATIONAL OBSERVATIONAL STUDY

L. Harrold[1], K. Wittstock[2], S. Kelly[2], S. H. Park[3], X. Han[3], Y. Shan[1], C. Roberts-Toler[1], N. Middaugh[1], V. Khaychuk[4]on behalf of Corrona. [1]*Corrona, LLC, Epidemiology & Biostatistics Department, Waltham, United States of America*; [2]*Bristol Myers Squibb, Immunology US Medical, Princeton, United States of America*; [3]*Bristol Myers Squibb, WW HEOR US Market, Princeton, United States of America*; [4]*Bristol Myers Squibb, US Medical Immunology and Fibrosis, Princeton, United States of America*

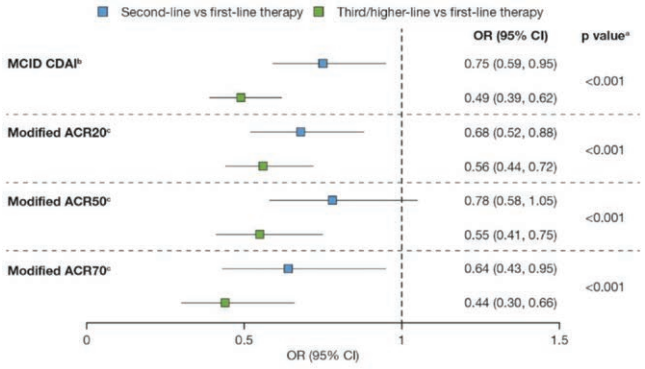
Background: RA is more responsive to treatment in the early stages of disease, and early treatment may lead to better long-term outcomes.[1,2] Data on the effectiveness of specific drugs as first or later lines of therapy will help inform treatment sequencing.
Objectives: Data from patients enrolled in the Corrona RA Registry were used to compare the effectiveness of abatacept across lines of therapy overall (primary cohort) and in a subset of patients who were anti-citrullinated protein antibody positive (ACPA+).
Methods: Patients with RA who initiated abatacept (January 2006 to October 2020), had 6 months' follow-up (within 4–9 months of starting abatacept), had baseline (BL) and follow-up CDAI scores available, and had BL CDAI >2.8 were included. Outcomes were compared for first-, second- and third or higher-line therapy: 0, 1 or ≥2 prior biologic DMARDs or Janus kinase inhibitors, respectively. Continuous outcomes included change from BL to 6 months in mean CDAI and patient-reported pain, fatigue, and HAQ. Binary outcomes included rate of achieving minimal clinically important difference (MCID) in CDAI or modified ACR20/50/70 at 6 months. Continuous and binary outcomes were analysed using multiple linear and logistic regression, respectively. The models included line of therapy, age, sex, disease duration, work status, SC nodules, history of hypertension and depression, BL CDAI, BL patient-reported pain and BL fatigue. Additional subgroup analyses were carried out in patients with moderate/high disease activity (CDAI >10) at BL.
Results: In total, 2876 patients (2327 with BL CDAI >10; 890 ACPA+) were included; 442, 911, and 1523 patients initiated first-, second- or third/higher-line abatacept, respectively. Compared with patients on second/third/higher-line abatacept therapy, those on first-line abatacept were significantly older, had shorter disease duration, and had lower BL CDAI, pain and fatigue (all p<0.001). In adjusted analyses, patients receiving abatacept as earlier lines of therapy had significantly greater improvement from BL in mean CDAI and in patient-reported fatigue and HAQ (Table 1). There was no significant difference between lines of therapy in change in patient-reported pain. Patients receiving first-line abatacept had significantly higher odds of achieving a MCID in CDAI or modified ACR20/50/70 response (Figure 1). Similar patterns were seen when the sample was limited to patients with moderate/high disease activity or in patients who were ACPA+.
Conclusion: There were significant differences in improvement in clinical disease activity and patient-reported outcomes across lines of therapy. Better treatment responses were observed with earlier lines of abatacept therapy in the overall population, in patients who were ACPA+ and in those with moderate/high BL disease activity.
REFERENCES:
[1] Harrold LR, et al. *Clin Rheumatol* 2017;36:1215–1220.
[2] Monti S, et al. *RMD Open* 2015;1(Suppl 1):e000057.

Table 1. Adjusted mean change in CDAI and patient-reported outcomes from BL to 6 months after initiation of abatacept by line of therapy (primary cohort)

Adjusted outcome, mean change (SE)	First-line (n=440)	Second-line (n=898)	Third/higher-line (n=1515)	p value[a]
CDAI	–7.96 (0.33)	–7.49 (0.27)	–5.74 (0.19)	<0.001
Patient-reported pain (VAS 0–100)	–9.43 (0.69)	–7.98 (0.47)	–7.70 (0.35)	0.074
Patient-reported fatigue (VAS 0–100)	–7.49 (0.71)	–5.87 (0.51)	–4.81 (0.36)	0.002
Patient-reported HAQ	–0.16 (0.01)	–0.12 (0.01)	–0.08 (0.01)	<0.001

[a]Estimated by multiple linear regression model adjusted for age, sex, disease duration, work status, SC nodules, history of hypertension and depression, BL CDAI, BL patient-reported pain and BL fatigue (factors that were identified *a priori* based on clinical experience or that differed significantly by line of therapy); p values reflect ANOVA overall test of differences across lines of therapy.VAS=visual analogue scale.

Figure 1. Adjusted odds ratio of achieving MCID CDAI or modified ACR20/50/70 at 6 months after initiation of abatacept by line of therapy (primary cohort)



[a]Estimated by multiple logistic regression analysis adjusted for age, sex, disease duration, work status, SC nodules, history of hypertension and depression, BL CDAI, BL patient-reported pain and BL fatigue (factors that were selected a priori based on clinical experience or differed significantly by line of therapy); p values reflect overall difference across lines of therapy.
[b]Reduction in CDAI score of 2 if BL disease activity was low (CDAI score ≤10); of 6 if BL disease activity was moderate (CDAI score >10 and ≤22); and of 11 if BL disease activity was high (CDAI score >22).
[c]Modified ACR criteria is based on 2 out of 4 measures (not using ESR or CRP).
Modified ACR20/50/70=20/50/70% improvement in modified ACR criteria; MCID=minimal clinically important difference; OR=odds ratio.

Acknowledgements: Professional medical writing and editorial assistance was provided by Claire Line, PhD, at Caudex and was funded by Bristol Myers Squibb. The poster was a collaborative effort between Corrona and Bristol Myers Squibb, with financial support provided by Bristol Myers Squibb. This study was sponsored by Corrona, LLC. Corrona is supported through contracted subscriptions with multiple pharmaceutical companies.

Disclosure of Interests: Leslie Harrold Consultant of: AbbVie, Bristol Myers Squibb, Genentech/Roche, Grant/research support from: Pfizer, Keith Wittstock Employee of: Bristol Myers Squibb, Sheila Kelly Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Sang Hee Park Employee of: Bristol Myers Squibb, Xue Han Employee of: Bristol Myers Squibb, Ying Shan: None declared, Carla Roberts-Toler: None declared, Nicole Middaugh: None declared, Vadim Khaychuk Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.701

AB0203 EFFECT OF DOSE ESCALATION OF SUBCUTANEOUS TOCILIZUMAB ON DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A RANDOMIZED CONTROLLED TRIAL

N. Singer[1], S. Mohan[2], J. Han[3], M. Edwardes[4], M. Michalska[2]. [1]*Case Western Reserve University and The MetroHealth System, Rheumatology, Cleveland, United States of America*; [2]*Genentech, Inc., Immunology, South San Francisco, United States of America*; [3]*Genentech, Inc., Biometrics, South San Francisco, United States of America*; [4]*Everest Clinical Research, Statistical Sciences, Markham, Canada*

Background: In patients with RA, subcutaneous tocilizumab (TCZ-SC) is administered every 2 weeks (q2w) or every week (qw), based on the patient's weight and clinical response.

Objectives: To compare the effects on disease activity at week 24, when the dosing schedule of TCZ-SC was escalated from q2w to qw, in patients who did not achieve LDA (DAS28-ESR > 3.2) at week 12 in COMP-ACT with patients who, despite not achieving LDA, continued TCZ-SC qw in SUMMACTA and q2w in BREVACTA.

Methods: US patients in COMP-ACT who weighed < 100 kg at baseline and who received TCZ-SC 162 mg q2w + methotrexate escalated to qw if they did not achieve LDA at week 12. DAS28-ESR remission (< 2.6) and LDA (≤ 3.2), CDAI remission (≤ 2.8) and LDA (≤ 10) and SDAI remission (≤ 3.3) and LDA (≤ 11) at week 24 were compared between patients who switched from q2w to qw and North American patients in SUMMACTA who initiated TCZ qw + csDMARDs and continued a qw dose (baseline body weight < 100 kg and DAS28 > 3.2 at week 12). A secondary analysis compared COMP-ACT patients who escalated from q2w to qw with all SUMMACTA patients who continued a qw dose and all BREVACTA patients who initiated a TCZ-SC q2w dose + csDMARDs and continued a q2w dose (baseline body weight < 100 kg and DAS28 > 3.2 at week 12). DAS28 was standardized to DAS28-ESR, and comparisons were calculated using a mixed model with repeated-measures logistic regression, including the following covariates: CDAI, SDAI and/or DAS28 at the reference visit (week 12), as well as study baseline values of CDAI, SDAI and/or DAS28, baseline age, sex, TNFi use prior to the study (yes or no) and weight category.

Results: A total of 328 US patients in COMP-ACT did not achieve LDA at week 12 and escalated from q2w to qw TCZ-SC. In SUMMACTA, 285 patients did not achieve LDA at week 12 and continued TCZ-SC qw, of whom 71 were from North America. Baseline demographic and clinical characteristics were comparable between patients in COMP-ACT and North American patients in SUMMACTA. A significantly higher proportion of patients in COMP-ACT achieved DAS28-ESR, CDAI and SDAI remission and LDA 12 weeks after TCZ dose escalation (week 24) than North American SUMMACTA patients (Table 1). Similar results were seen when the proportion of patients who achieved DAS28 remission and LDA was compared at week 24 between patients in COMP-ACT and patients from all geographic regions who did not escalate dosing in SUMMACTA and BREVACTA (N=196).

Conclusion: US patients with RA who did not achieve LDA and escalated from q2w to qw TCZ-SC at week 12 in COMP-ACT had better disease activity outcomes at week 24 than North American patients who did not achieve LDA and continued qw dosing in SUMMACTA. These results provide some evidence that escalation from q2w to qw has more effect than expected without dose change for patients who do not achieve LDA by week 12.

Table 1. Comparison at Week 24 of Clinical Response After Week 12 Dose Escalation or Continuation Between Patients Who Did Not Achieve LDA at Week 12

	All COMP-ACT (N = 328)	North American SUMMACTA (n = 71)	All SUMMACTA (N = 285)	All BREVACTA (N = 196)
DAS28-ESR remission, n (%)	66 (20.1)	7 (9.9)	44 (15.4)	36 (18.4)
Adjusted OR (95% CI)	Ref	5.76 (1.92, 17.32)	3.29 (2.11, 5.12)	2.35 (1.44, 3.84)
P value	Ref	0.0018	< 0.0001	0.0006
DAS28-ESR LDA, n (%)	122 (37.2)	17 (23.9)	90 (31.6)	60 (30.6)
Adjusted OR (95% CI)	Ref	3.36 (1.61, 7.00)	2.81 (1.97, 4.01)	2.24 (1.50, 3.33)
P value	Ref	0.0012	< 0.0001	< 0.0001
CDAI remission, n (%)	12 (3.7)	2 (2.8)	13 (4.6)	11 (5.6)
Adjusted OR (95% CI)	Ref	4.50 (1.32, 15.32)	2.93 (1.37, 6.27)	1.45 (0.69, 3.05)
P value	Ref	0.0161	0.0056	0.3325
CDAI LDA, n (%)	80 (24.4)	11 (15.5)	81 (28.4)	66 (33.7)
Adjusted OR (95% CI)	Ref	4.19 (1.88, 9.35)	2.35 (1.63, 3.39)	1.32 (0.88, 1.97)
P value	Ref	0.0005	< 0.0001	0.1825
SDAI remission, n (%)	16 (4.9)	2 (2.8)	15 (5.3)	11 (5.6)
Adjusted OR (95% CI)	Ref	5.23 (1.44, 19.01)	3.23 (1.54, 6.76)	1.64 (0.81, 3.30)
P value	Ref	0.0120	0.0019	0.1670
SDAI LDA, n (%)	89 (27.1)	11 (15.5)	91 (31.9)	72 (36.7)
Adjusted OR (95% CI)	Ref	4.68 (2.20, 9.99)	2.20 (1.56, 3.11)	1.47 (0.99, 2.17)
P value	Ref	< 0.0001	< 0.0001	0.0540

Acknowledgements: This study was funded by Genentech, Inc. Support for third-party writing assistance, furnished by Health Interactions, Inc., was provided by Genentech, Inc.

Disclosure of Interests: Nora Singer Grant/research support from: Genentech/Roche, Merck and Pfizer, Shalini Mohan Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Jian Han Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Michael Edwardes Employee of: Everest Clinical Research, Margaret Michalska Shareholder of: Genentech, Inc., Employee of: Genentech, Inc.

DOI: 10.1136/annrheumdis-2021-eular.795

AB0204 THE PROPER STUDY: INTERIM ANALYSIS OF A PAN-EU REAL-WORLD STUDY OF SB5 BIOSIMILAR FOLLOWING TRANSITION FROM REFERENCE ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS, OR PSORIATIC ARTHRITIS

U. Müller-Ladner[1], K. Gaffney[2], D. Jadon[3], U. Freudensprung[4], J. Addison[5]. [1]*Kerckhoff Klinik, Justus Liebig Universität Gießen, Abteilung für Rheumatologie und Klinische Immunologie, Bad Nauheim, Germany*; [2]*NHS Foundation Trust, Norfolk and Norwich University Hospital, Norwich, United Kingdom*; [3]*NHS Foundation Trust, Cambridge University Hospitals, Cambridge, United Kingdom*; [4]*Biogen GmbH, Medical Data Science and Analytics, Biosimilars, Baar, Switzerland*; [5]*Biogen IDEC, Clinical Research, Biosimilars, Maidenhead, United Kingdom*

	RA (N=201)		axSpA (N=134)		PsA (N=169)	
	Mean (SD)	**Q1, Q3**	**Mean (SD)**	**Q1, Q3**	**Mean (SD)**	**Q1, Q3**
Age at SB5 initiation (years)	60.2 (11.7)	53, 68	50.5 (13.6)	38, 61	53.0 (12.2)	43, 62
Duration of disease (years)	13.5 (11.7)	4.5, 20	18.7 (13.2)	9, 25	12.7 (9.9)	4, 20
	n	**%**	**n**	**%**	**n**	**%**
Women	144	71.6	41	30.6	77	45.6
SB5 Dosing regimen:	149	74.1	120	89.6	156	92.3
Baseline 40 mg Q2W						
Week 48 40mg Q2W	69	77.5	67	85.9	98	92.5
Baseline Other*	52	25.9	14	10.4	13	7.7
Week 48 Other*	20	22.4	11	14.1	8	7.5
Disease Score					**Tender Joint**	**Swollen Joint**
(paired patients)	**DAS28**	**FFbH**	**BASDAI**		**Count**	**Count**
Baseline, n, mean (95% CI)	69 2.5 (2.3–2.7)	22 73.9 (65.6–82.1)	42	2.8 (2.3–3.4)	49 1.8 (0.1–3.0)	49 0.6 (0.2–0.9)
Week 48, n, mean (95% CI)	69 2.6 (2.3–2.8)	22 72.1 (64.0–80.2)	42	3.0 (2.4–3.7)	49 1.9 (0.5–3.3)	49 0.6 (0.1–1.1)
Patient diagnosed with COVID-19 at any time on-study, n (%)						
No	142	95.3	96	88.1	140	98.6
Yes	3	2.0	1	0.9	1	0.7
Unknown	4	2.7	12	11.0	1	0.7
Imraldi regimen stopped or changed due to COVID-19, regardless of diagnosis, n (%)						
No	130	98.5	106	97.2	134	100
Yes	2	1.5	3	2.8	0	0

SD standard deviation; Q1 1st quartile, Q3 3rd quartile; CI Confidence Interval*Other includes all other reported doses and/or dosing intervals: 40mg QW, 80mg Q2W, and unspecified frequency-DAS28 Disease Activity Score 28; FFbH Hanover Functional Ability Questionnaire; BASDAI Bath Ankylosing Spondylitis Disease Activity Index

Background: SB5, a biosimilar to reference adalimumab (ADL), received EU marketing authorisation in August 2017, based on the totality of evidence from pre-clinical and clinical Phase I and III studies that demonstrated bioequivalence, similar efficacy, and comparable safety and immunogenicity to the reference. This real-world study provides data on outcomes of the transition from reference to biosimilar ADL outside the controlled, randomised, clinical trial setting.

Objectives: To evaluate candidate predictors of persistence on SB5 in EU patients (pts) across multiple indications.

Methods: This ongoing observational study enrolled 1000 pts with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), psoriatic arthritis (PsA), ulcerative colitis, or Crohn's disease who initiated SB5 as part of routine clinical practice following a minimum of 16 weeks' treatment with reference ADL, at clinics in Belgium, Germany, Ireland, Italy, Spain, and the UK. Data are captured from clinic records retrospectively for the 24 weeks prior to transition, and prospectively and/or retrospectively for 48 weeks following transition. Primary outcome measures include baseline clinical characteristics, disease activity scores and clinical management over time; data on COVID-19 infection has recently been captured. This interim analysis (IA) provides an overview of baseline characteristics, disease scores and dose regimen up to 48 weeks post-initiation of SB5, and COVID-19 infection reported to date, in subjects with RA, axSpA, or PsA enrolled at 35 specialist sites and followed up to the data extract date of 18th December 2020.

Results: Of the 504 pts included in this IA, 201 have RA, 169 have PsA, and 134 axSpA. At time of data extract, 216 pts had completed 48 weeks on SB5, 73 pts had discontinued SB5, and 8 had discontinued the study.

Conclusion: This IA provides a first insight into clinical management of pts over 48 weeks, in a contemporary cohort of EU pts with established RA, axSpA and PsA, switched from reference to biosimilar ADL SB5 in clinical practice. The majority of pts showed no meaningful difference in disease score or dose regimen of SB5 by Week 48 post-transition. As of data extract date, the proportion of pts with a known positive COVID-19 test was low (1.3%) and a small minority (1.3%) had SB5 treatment changed or interrupted as a result of the COVID-19 pandemic. With follow-up of pts ongoing to Q4 2021, the study will continue to provide pertinent information about clinical outcomes of transition from reference to biosimilar ADL in real-world practice and in indications not investigated in controlled studies.

Acknowledgements: Statistical services gave been provided by FGK Clinical Research GmbH, Munich, Germany. Data management services were provided by Worldwide Clinical trial, Research Triangle Park, NC, USA; funding was provided by Biogen International GmbH.

Disclosure of Interests: Ulf Müller-Ladner Consultant of: Biogen, Grant/research support from: Biogen, Karl Gaffney Consultant of: AbbVie, Celgene, Gilead, Lilly, MSD, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Celgene, Gilead, Lilly, MSD, Novartis, Pfizer, and UCB, Deepak Jadon Consultant of: AbbVie, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Oxford University Press, Pfizer, Roche, Sandoz, UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Oxford University Press, Pfizer, Roche, Sandoz, UCB, Ulrich Freudensprung Shareholder of: Biogen, Employee of: Biogen, Janet Addison Shareholder of: Biogen, Employee of: Biogen

DOI: 10.1136/annrheumdis-2021-eular.844

AB0205

A NOVEL METHOD FOR PREDICTING 1-YEAR RETENTION OF ABATACEPT USING MACHINE LEARNING TECHNIQUES: DIRECTIONALITY AND IMPORTANCE OF PREDICTORS

R. Alten[1], C. Behar[2], C. Boileau[3], P. Merckaert[4], E. Afari[5], V. Vannier-Moreau[6], S. Connolly[7], A. Najm[8], P. A. Juge[9], A. Rai[10], Y. Elbez[11], K. Lozenski[12].

[1]Schlosspark-Klinik University, Department of Internal Medicine, Rheumatology, Berlin, Germany; *[2]Tulsy, Co-founder, Paris, France*; *[3]Excelya, N/A, Boulogne-Billancourt, France*; *[4]Data Revenue GmbH, Machine Learning Engineering Department, Berlin, Germany*; *[5]Private Practice, N/A, Brunoy, France*; *[6]Bristol Myers Squibb, Medical Affairs, France, Rueil-Malmaison, France*; *[7]Bristol Myers Squibb, Global Drug Development, Princeton, United States of America*; *[8]University of Glasgow, Institute of Infection, Immunity and Inflammation, College of Medical Veterinary and Life Sciences, Glasgow, United Kingdom*; *[9]Université de Paris, AP-HP, Hôpital Bichat Claude-Bernard, Department of Rheumatology, Paris, France*; *[10]Bristol Myers Squibb, Global Biometrics and Data Science, Princeton, United States of America*; *[11]Deepscover, Biostatistics, Puteaux, France*; *[12]Bristol Myers Squibb, Immunology and Fibrosis, Princeton, United States of America*

Background: In the ACTION (NCT02109666) study, multivariable Cox proportional hazards regression models showed that the predictors of 1-year retention to abatacept treatment were: patient global pain assessment, country, reason for stopping last biologic, number of prior biologic treatments, abatacept monotherapy, RF/anti-cyclic citrullinated peptide (CCP) status, previous neoplasms, psychiatric disorders and cardiac disorders.[1] Machine learning techniques, using the gradient-boosting model, subsequently identified additional predictors of abatacept retention in patients with moderate-to-severe RA enrolled in ACTION; however, the analysis did not show the directionality of the predictors.[2]

Objectives: To improve the clinical interpretability of the machine learning model in terms of directionality and the importance of each variable in predicting retention.

Methods: Previous analyses using the gradient-boosting model to identify predictors of abatacept retention at 1 year in the ACTION study have been described.[2] This analysis used SHapley Additive exPlanations (SHAP), a mathematical framework, to show how a particular predictor value influences prediction in the context of all other predictors. Higher SHAP values indicate a higher likelihood of retention. The contribution of every variable in the model's prediction (with the exception of country variables) was computed for each data point to capture individual variable impact. This enabled interpretation for level of importance and directionality at a patient level.

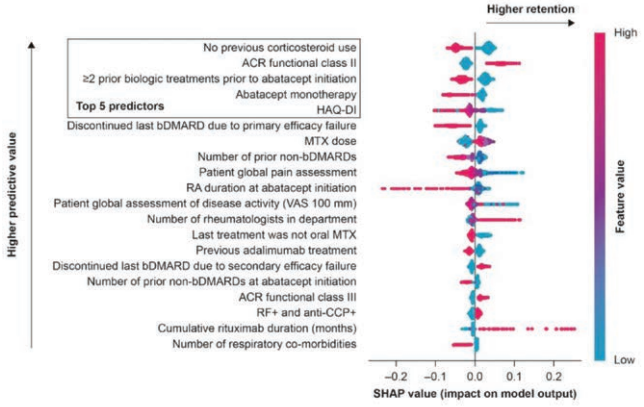
Results: Using data from 2350 patients enrolled in ACTION (May 2008 to December 2013), the mean retention rate at 1 year was 59.3% (n=1393). Overall variable importance is shown in Figure 1. After removal of country variables, the top five baseline predictors of retention were: no previous corticosteroid use, ACR functional class II, ≥2 prior biologic treatments prior to abatacept initiation, abatacept monotherapy and HAQ-DI. In terms of directionality, no previous corticosteroid use, ≥2 prior biologic treatments prior to abatacept initiation, abatacept monotherapy and a higher HAQ-DI score at baseline were associated with a lower likelihood of retention; ACR functional class II was associated with a higher likelihood of retention.

Conclusion: The gradient-boosting model previously identified predictors of abatacept retention from ACTION;[2] the addition of SHAP in this analysis has provided information on the importance and directionality of those predictors. The most important predictor of abatacept retention was no previous corticosteroid use, which was associated with lower retention. The models and predictors identified could be further refined by using additional datasets from clinical trials. Machine learning offers an innovative and complementary approach to biostatistics and could be used to identify treatment response predictors at an individual patient level, leading to a more personalised treatment approach.

REFERENCES:

[1] Alten R, et al. *RMD Open* 2017;3:e000538.
[2] Alten R, et al. Presented at the virtual ACR Convergence 2020; 5–9 November 2020. Poster number 1745.

Figure 1. Overall variable importance in ACTION, using SHAP



Colours indicate the value of the variable: pink represents higher and blue represents lower. The bulges in the plot indicate mo patients with that value; each dot represents a single patient. Higher SHAP values indicate a higher likelihood of retention. bDMARD=biologic DMARD; CCP=cyclic citrullinated peptide; SHAP=SHapley Additive exPlanations.

Acknowledgements: This study was supported by Bristol Myers Squibb. Professional medical writing and editorial assistance was provided by Claire Line, PhD, at Caudex and was funded by Bristol Myers Squibb.

Disclosure of Interests: Rieke Alten Speakers bureau: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Consultant of: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Grant/research support from: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Claire Behar Shareholder of: I have not invested directly in pharmaceutical companies producing drugs/devices for use in rheumatology however I may have shares via the funds linked to my life insurance., Consultant of: Bristol Myers Squibb, Christine Boileau Consultant of: AstraZeneca, Bristol Myers Squibb, Nanobiotix, Pierre Merckaert Consultant of: Bristol Myers Squibb, Ebenezer Afari Consultant of: Bristol Myers Squibb, Virginie Vannier-Moreau Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Sean Connolly Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Aurelie Najm Speakers bureau: Bristol Myers Squibb, Consultant of: Bristol Myers Squibb, Pierre-Antoine Juge Consultant of: Bristol Myers Squibb, Angshu Rai Shareholder of: Amgen Inc, Consultant of: Amgen Inc, Employee of: Amgen Inc, Bristol Myers Squibb, Yedid Elbez Consultant of: Bristol Myers Squibb, Karissa Lozenski Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.868

AB0206 DESCRIPTION AND FOLLOW-UP OF RHEUMATOID ARTHRITIS PATIENTS WHO STOPPED B/TSDMARD THERAPY, STRATIFIED BY CESSATION REASON

T. Burkard[1], E. Vallejo-Yagüe[1], T. Hügle[2], A. Finckh[3], A. M. Burden[1,4]. [1]*ETH Zurich, Department of Chemistry and Applied Biosciences, Zurich, Switzerland*; [2]*Lausanne University Hospital, Department of Rheumatology, Lausanne, Switzerland*; [3]*University Hospitals Geneva, Division of Rheumatology, Geneva, Switzerland*; [4]*Maastricht University Medical Center+, Department of Clinical Pharmacy and Toxicology, Maastricht, Netherlands*

Background: Biologic or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARD) may be stopped for several reasons such as non-response, adverse events, remission, or other reasons (e.g. major surgery). Understanding the reasons and consequences of b/tsDMARD therapy cessation may contribute towards therapy decision guidance. Moreover, identifying patient characteristics leading to the re-start of b/tsDMARD therapy may guide decision-making as to which patients should remain on continuous b/tsDMARD therapy versus who may potentially stop b/tsDMARD therapy.

Objectives: To describe and follow rheumatoid arthritis (RA) patients who stopped b/tsDMARD therapy, stratified by cessation reason.

Methods: We conducted a descriptive cohort study among adult RA patients in the longitudinal Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) between 1997 and 2019. RA patients who stopped their first b/tsDMARD therapy were eligible, with therapy stop date defining cohort entry. We followed all eligible patients from cohort entry until b/tsDMARD re-start (the outcome) or censoring due to end of patient record. All analyses were carried out stratified by cessation reason (non-response, adverse events, remission, other reasons, unknown reasons). We described patient characteristics (demographics, lifestyle factors, clinical information, other medication use, relevant comorbidities) at cohort entry. Furthermore, we estimated Kaplan Meier curves to describe differences in cumulative incidences of b/tsDMARD re-start. Finally, we assessed patient characteristics at b/tsDMARD re-start and compared them with those at cohort entry.

Results: Among 2559 eligible RA patients, the majority stopped their b/tsDMARD due to non-response (982, 38%), followed by adverse events (475, 19%), other reasons (445, 17%), unknown reasons (444, 17%), and remission (213, 8%). Mean age at b/tsDMARD stop was around 56.2 years except in patients who stopped due to remission (mean age of 58.1 years). The majority of patients were women (78%), stopping due to an adverse event had the highest proportion of women (84%), stopping due to remission had the lowest proportion of women (70%). Compared to patients who stopped b/tsDMARD therapy due to non-response or adverse events, patients who stopped due to remission were generally more physically active, better educated, less likely to have a family history of rheumatic diseases, and had shorter median disease duration. A total of 2086 patients (82%) re-started b/tsDMARD therapy during follow-up. Of these, the majority did so after stopping due to non-response (94%), followed by adverse events (82%), unknown reasons (79%), other reasons (74%), and remission (47%). The median cumulative incidence of re-starting b/tsDMARD therapy was shortest after non-response (30 days), followed by unknown reasons (31 days), adverse events (94 days), other reasons (212 days), and remission (1597 days). The population who stopped b/tsDMARD therapy due to remission or other reasons yielded increased RA disease activity and an increase in proportions of women, cardiac diseases, degenerative joint disease, other auto-immune diseases, and of patients with family history of rheumatic diseases at the date of b/tsDMARD re-start. However, among patients who stopped b/tsDMARD therapy due to non-response or adverse events, patient characteristics at b/tsDMARD re-start were unchanged compared to those at b/tsDMARD stop.

Conclusion: Observed differences in patient characteristics at b/tsDMARD stop may yield insight into why the patient was not responding, had an adverse event, or achieved remission. Observed changes in patient characteristics from the date of b/tsDMARD stop to re-start identified which ones may lead to a worsening of RA activity in the absence of b/tsDMARD therapy.

Acknowledgements: We would like to thank Dr. Almut Scherer, Monika Hebeisen, and Eleftherios Papagiannoulis from SCQM for providing the data and answering questions thereto. A list of rheumatology offices and hospitals that are contributing to the SCQM registries can be found on www.scqm.ch/institutions. The SCQM is financially supported by pharmaceutical industries and donors. A list of financial supporters can be found on www.scqm.ch/sponsors.

Disclosure of Interests: Theresa Burkard: None declared, Enriqueta Vallejo-Yagüe: None declared, Thomas Hügle Consultant of: Pfizer, Abbvie, Novartis, Grant/research support from: GSK, Jansen, Pfizer, Abbvie, Novartis, Roche, MSD, Sanofi, BMS, Eli Lilly, UCB, Axel Finckh Speakers bureau: Pfizer, Eli-Lilly, Paid instructor for: Pfizer, Eli-Lilly, Consultant of: Pfizer, BMS, Novartis, Grant/research support from: AbbVie, AB2Bio, BMS, Gilead, Pfizer, Viatris, Andrea Michelle Burden: None declared

DOI: 10.1136/annrheumdis-2021-eular.898

AB0207 ANALYSIS OF ABATACEPT TREATMENT RETENTION AND EFFICACY ACCORDING TO DISEASE DURATION AND TREATMENT LINE IN A REAL-WORLD SETTING

R. Alten[1], X. Mariette[2], R. M. Flipo[3], R. Caporali[4,5], M. H. Buch[6,7], Y. Patel[8], R. Sanmartí[9], S. Marsal[10], M. T. Nurmohamed[11], H. Griffiths[12], P. Peichl[13], B. Bannert[14], A. Forster[15], M. Chartier[16], Y. Elbez[17], C. Rauch[18], V. Khaychuk[19], K. Lozenski[20]. [1]*Schlosspark-Klinik University, Department of Internal Medicine, Rheumatology, Berlin, Germany*; [2]*Université Paris-Saclay, AP-HP, Hospital Bicêtre, Department of Rheumatology, Paris, France*; [3]*Centre Hospitalier Universitaire de France, Department of Rheumatology, Lille, France*; [4]*University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy*; [5]*G. Pini Hospital, Clinical Rheumatology Unit, Milan, Italy*; [6]*University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [7]*University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; [8]*Hull Royal Infirmary, Department of Rheumatology, Hull, United Kingdom*; [9]*Hospital Clinic de Barcelona,*

Rheumatology Department, Barcelona, Spain; [10]*Hospital Universitari Vall d'Hebron, Rheumatology, Barcelona, Spain*; [11]*ARC Amsterdam University Hospitals – VU University Medical & Reade, Department of Rheumatology, Amsterdam, Netherlands*; [12]*University Hospital Geelong, Barwon Rheumatology Service, Geelong, Australia*; [13]*Evangelical Hospital, Department of Internal Medicine, Vienna, Austria*; [14]*Universitätsspital Basel, Rheumatologische Universitätsklinik, Basel, Switzerland*; [15]*Schulthess Klinik, Department of Rheumatology, Zürich, Switzerland*; [16]*Bristol Myers Squibb, Non-Registrational Data Generation, Rueil-Malmaison, France*; [17]*Deepscover, Biostatistics, Puteaux, France*; [18]*Bristol Myers Squibb, Medical Immunology & Fibrosis, Munich, Germany*; [19]*Bristol Myers Squibb, US Medical Immunology and Fibrosis, Princeton, United States of America*; [20]*Bristol Myers Squibb, Immunology and Fibrosis, Princeton, United States of America*

Background: Longer disease duration and greater number of prior DMARDs have been associated with lower treatment efficacy in patients with RA.[1] Abatacept is a biologic (b)DMARD for treatment of moderate-to-severe RA and is available in SC formulation, which may offer convenience benefits with efficacy similar to IV administration.[2] ASCORE (Abatacept SubCutaneOus in Routine Clinical PracticE; NCT02090556) was a 2-year, observational, prospective, multicentre study of SC abatacept for treatment of RA in routine clinical practice.[3]

Objectives: This *post hoc* analysis was conducted to determine if retention and efficacy of abatacept were impacted by disease duration and/or treatment line.

Methods: Eligible patients, aged ≥18 years, with active moderate-to-severe RA (ACR/EULAR 2010 criteria) who were IV abatacept-naive and initiated SC abatacept 125 mg once weekly, were enrolled into two cohorts: bDMARD-naive patients and those with ≥1 prior bDMARD treatment failure. This *post hoc* analysis evaluated abatacept retention using Kaplan-Meier estimates, as well as disease activity scores (DAS28 [ESR]), CDAI and SDAI in patients with disease duration of ≤2, 3–5, 6–10 or >10 years, and in patients taking abatacept as first-line or ≥ second-line treatment.

Results: Table 1 shows baseline (BL) characteristics. Mean age increased with disease duration; other characteristics were comparable across groups. Retention proportions (95% CIs) at Month 24 were 0.50 (0.4, 0.5), 0.47 (0.4, 0.5), 0.51 (0.5, 0.5) and 0.46 (0.4, 0.5) in the ≤2, 3–5, 6–10 and >10 years' duration groups, respectively. Proportion of patients (95% CI) with ≤2 years' duration retaining treatment at Month 24 were 0.51 (0.4, 0.6) among those using abatacept as first-line treatment and 0.44 (0.3, 0.6) among those using abatacept as a ≥ second-line treatment (Figure 1). Proportions (95% CI) at Month 24 were 0.51 (0.5, 0.6), 0.57 (0.5, 0.6) and 0.52 (0.5, 0.6) in first-line patients and 0.43 (0.4, 0.5), 0.48 (0.4, 0.5) and 0.44 (0.4, 0.5) in ≥ second-line patients in the 3–5, 6–10 and >10 years' duration groups, respectively. Mean (SE) changes from BL in DAS28 (ESR) at Month 24 were –2.12 (0.205), –1.86 (0.151), –2.07 (0.140) and –2.05 (0.115) in the ≤2, 3–5, 6–10 and >10 years' duration groups, respectively; respective mean (SE) changes in CDAI were –18.74 (1.604), –15.60 (1.099), –18.50 (1.038) and –17.68 (0.850); and respective mean (SE) changes in SDAI were –19.10 (1.873), –15.72 (1.345), –19.54 (1.103) and –17.07 (0.939).

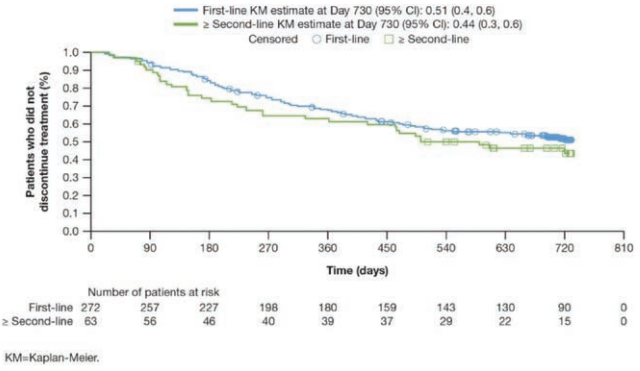
Conclusion: In this *post hoc* analysis of the real-world ASCORE trial, patients with RA receiving abatacept in clinical practice as first-line therapy had better retention versus those receiving it as a ≥ second-line treatment, regardless of disease duration at BL. Retention rates were similar across disease duration subgroups. Improvements in disease activity were seen in all duration subgroups, without consistently greater or lesser improvement seen with longer disease duration.

Table 1. BL characteristics (n=2872)

	RA disease duration, years			
	≤2 (n=338)	3–5 (n=655)	6–10 (n=686)	>10 (n=1193)
Age, years				
n	338	655	686	1193
Mean (SD)	55.2 (12.8)	55.6 (12.7)	56.9 (13.0)	59.9 (12.2)
Weight, kg				
n	327	629	665	1150
Mean (SD)	75.3 (18.1)	76.4 (19.0)	74.7 (17.4)	72.9 (16.0)
DAS28 (ESR)				
n	247	439	441	743
Mean (SD)	5.2 (1.3)	4.9 (1.3)	5 (1.2)	5.1 (1.3)
DAS28 (CRP)				
n	267	460	467	799
Mean (SD)	4.7 (1.2)	4.6 (1.2)	4.7 (1.1)	4.7 (1.2)
CDAI				
n	269	477	474	805
Mean (SD)	26.9 (12.7)	25.3 (12.2)	26.8 (12.4)	26.6 (12.2)
SDAI				
n	255	448	445	749
Mean (SD)	28.3 (13.3)	26.8 (12.9)	27.9 (12.6)	28.0 (12.7)
RF status, n (%)				
RF+	159 (47.0)	342 (52.2)	345 (50.3)	597 (50.0)
RF–	103 (30.5)	152 (23.2)	158 (23.0)	215 (18.0)
Anti-CCP status, n (%)				
Anti-CCP+	165 (48.8)	332 (50.7)	333 (48.5)	516 (43.3)
Anti-CCP–	89 (26.3)	126 (19.2)	137 (20.0)	175 (14.7)

Patients with missing duration of disease are excluded.CCP=cyclic citrullinated peptide.

Figure 1. Treatment retention over 2 years among patients with RA with ≤2 years' disease duration



KM=Kaplan-Meier.

Acknowledgements: Professional medical writing and editorial assistance was provided by Rob Coover, MPH, at Caudex and was funded by Bristol Myers Squibb. This study was funded by Bristol Myers Squibb.

Disclosure of Interests: Rieke Alten Speakers bureau: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Consultant of: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Grant/research support from: AbbVie, Bristol Myers Squibb, Gilead, Janssen, Lilly, Pfizer, Xavier Mariette Consultant of: Bristol Myers Squibb, Galapagos, Gilead, GlaxoSmithKline, Janssen, Pfizer, UCB, Rene-Marc Flipo Speakers bureau: AbbVie, Bristol Myers Squibb, Janssen, Lilly, Medac, Merck Sharp & Dohme, Novartis, Pfizer, Roche-Chugai, Grant/research support from: Amgen, Janssen, Novartis, Pfizer, Roberto Caporali Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celltrion, Fresenius Kabi, Galapagos, Gilead, Lilly, Merck Sharp & Dohme, Pfizer, Roche,

REFERENCES:

[1] Aletaha D, et al. *Ann Rheum Dis* 2019;78:1609–1615.

[2] Genovese MC, et al. *Arthritis Rheumatol* 2011;63:2854–2864.

[3] Alten R, et al. *Ann Rheum Dis* 2019;78(suppl 2):A1639.

Samsung Bioepis, Sanofi, UCB, Consultant of: Galapagos, Gilead, Janssen, Lilly, Merck Sharp & Dohme, Maya H Buch Speakers bureau: AbbVie, Consultant of: AbbVie, Eli Lilly, Gilead, Merck Serono, Pfizer, Roche, Sanofi, Grant/research support from: Gilead, Pfizer, Roche, UCB, Yusuf Patel: None declared, Raimón Sanmartí Speakers bureau: AbbVie, Bristol Myers Squibb, Gebro, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, Consultant of: AbbVie, Bristol Myers Squibb, Gebro, Lilly, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, Grant/research support from: Bristol Myers Squibb, Merck Sharp & Dohme, Pfizer, Sara Marsal Speakers bureau: Bristol Myers Squibb, Celgene, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol Myers Squibb, Celgene, Galapagos, Merck Sharp & Dohme, Pfizer, Roche, Sanofi, UCB, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Sanofi, UCB, M.T. Nurmohamed Speakers bureau: AbbVie, Bristol Myers Squibb, Eli Lilly, Roche, Sanofi, Consultant of: AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Merck Sharp & Dohme, Mundipharma, Novartis, Pfizer, Roche, Sanofi, Hedley Griffiths Consultant of: AbbVie, Gilead, Janssen, Novartis, Peter Peichl: None declared, Bettina Bannert: None declared, Adrian Forster: None declared, Melanie Chartier Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Yedid Elbez Consultant of: Bristol Myers Squibb, Christiane Rauch Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Vadim Khaychuk Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Karissa Lozenski Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.955

AB0208

DO LOW CONCENTRATIONS OF CITRATE IN AN ADALIMUMAB FORMULATION IMPACT THE INCIDENCE AND/OR INTENSITY OF INJECTION SITE PAIN? DATA FROM PHASE I AND III STUDIES ASSESSING THE LOCAL TOLERANCE OF GP2017 (ADALIMUMAB BIOSIMILAR, SDZ-ADL) IN HEALTHY VOLUNTEERS, RHEUMATOID ARTHRITIS, AND PSORIASIS PATIENTS

P. Wiland[1], A. Blauvelt[2], L. Lemke[3], O. Von Richter[3], A. Balfour[4], F. Furlan[5], N. Gaylis[6]. [1]*Medical University, Department of Rheumatology and Internal Medicine, Wroclaw, Poland*; [2]*Oregon Medical Research Center, Research Excellence & Personalized Patient Care, Portland, United States of America*; [3]*Hexal AG (A Sandoz company), Clinical Development Biopharmaceuticals, Holzkirchen, Germany*; [4]*Hexal AG (A Sandoz company), Clinical Development Biostatistics, Holzkirchen, Germany*; [5]*Hexal AG (A Sandoz company), Global Medical Affairs, Holzkirchen, Germany*; [6]*Arthritis and Rheumatic Disease Specialties, 21097 NE 27th Court Suite 200, Aventura, United States of America*

Background: Adalimumab (ADL) is typically self-administered every 2 weeks (W) as a subcutaneous (s.c.) injection by patients (pts) for diverse indications, including rheumatoid arthritis (RA), psoriatic arthritis (PsA), and psoriasis (PsO). Conflicting evaluations of local tolerance to formulations containing citrate buffer have created insecurities among health care professionals and pts.[1,2]

Objectives: To evaluate local tolerance of SDZ-ADL (GP2017), a biosimilar ADL with low citrate concentration (1.2 mM),[3] in 466 healthy volunteers (HV) and 408 pts (RA: 177 and PsO: 231 including PsA: 52) from four phase I pharmacokinetic (PK) and two phase III confirmatory studies.

Methods: HV evaluated their injection site pain (ISP) using a Visual Analogue Scale (VAS) of 0–100 mm. HV received a single 40 mg/0.8 mL s.c. injection and pts received SDZ-ADL every 2W during 48–51W duration of study. Injection site reactions (ISR) as well as adverse events (AEs) were assessed by investigators during the clinical studies. Details of study designs have been reported previously.[4–7]

Results: Overall, 456 (97.9%) HV experienced no ISR. Ten HV experienced ISR. These were mostly of mild intensity; only 1 (0.2%) had an ISR of moderate intensity. 96.6% of HV experienced no pain (VAS score 0–4 mm)[8] at 1-hour post-dose (Figure 1). In the phase III studies, a low number of ISR/ISP events were observed, which decreased during the course of study. Detailed results are provided in Table 1. No ISR/ISP led to treatment or study discontinuation in any study.

Conclusion: The proportion of HV and pts experiencing ISR and ISP after administration of SDZ-ADL was low, with no events leading to treatment or study discontinuation. These results call into question the clinical impact of citrate and its concentration in ADL formulations on the incidence and intensity of ISP.

REFERENCES:

[1] Nash et al. *Rheumatol Ther*. 2016;3:257–70.
[2] NHS. Regional medicines optimisation committee briefing, best value biologicals: adalimumab update 6. July 2019. https://www.sps.nhs.uk/wp-content/uploads/2019/07/Adalimumab-RMOC-Briefing-6.pdf.
[3] https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761071lbl.pdf.
[4] Blauvelt A, et al. *Br J Dermatol*. 2018;179:623–31.
[5] Wiland P, et al. *BioDrugs* 2020;34:809–23.
[6] Richter OV, et al. *Expert Opin Biol Ther*. 2019;19:1057–64.
[7] Richter OV, et al. *Expert Opin Biol Ther*. 2019;19:1075–83.
[8] Hawker GA, et al. *Arthritis Care Res*. 2011;63:240–52.

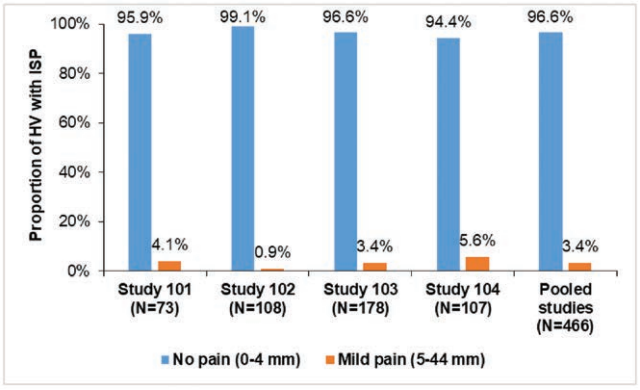


Figure 1. Proportion of HV with ISP in phase I PK studies

Table 1. ISP and ISR results from phase I PK and phase III confirmatory studies

Phase I PK studies					
Study	**101 (N=73)**	**102 (N=108)**	**103 (N=178)**	**104 (N=107)**	**Pooled studies (N=466)**
VAS scores (mm) at 1-hour post-dose					
Mean (SD)	0.89 (2.07)	0.07 (0.52)	1.03 (1.71)	1.03 (2.49)	0.79 (1.84)
Median	0	0	1	0	0
ISR scores at 1-hour post-dose, n (%)					
None	73 (100)	106 (98.2)	178 (100)	99 (92.5)	456 (97.9)
Mild	0 (0)	1 (0.9)	0 (0)	8 (7.5)	9 (1.9)
Moderate	0 (0)	1 (0.9)	0 (0)	0 (0)	1 (0.2)
Phase III confirmatory studies					
	ADACCESS[5]* (PsO and PsA pts)			**ADMYRA[6]* (RA pts)**	
	W0–17 (N=231)	W0–51 (N=168; including pts re-randomised to continue SDZ-ADL after W17)		W0–24 (N=177)	W0–48 (N=177; all pts continued SDZ-ADL after W24)
Dosage	Induction 80 mg W0, then 40 mg EoW s.c.	40 mg EoW s.c.		40 mg EoW s.c.	40 mg EoW s.c.
Study duration, W	17	51		24	48
AEs - ISR, n (%), events	15 (6.5), 34	9 (5.4), 26		7 (4.0), 11	7 (4.0), 12
Mild	14 (6.1), 30	9 (5.4), 26		7 (4.0), 11	7 (4.0), 12
Moderate	1 (0.4), 4	0		0	0
AEs - ISP (reported as ISR), n (%)	3 (1.3)	1 (0.6)		2 (1.1)	2 (1.1)

*ADACCESS and ADMYRA were switch studies, therefore, only pts exposed to SDZ-ADL throughout the study period are included here. EoW, every other week, N, number of HV or pts

Disclosure of Interests: Piotr Wiland Speakers bureau: Celltrion, Celgene, Eli Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis, Consultant of: Celltrion, Celgene, Eli Lilly, Novartis, Pfizer, Sandoz, Sanofi-Aventis, Andrew Blauvelt Speakers bureau: AbbVie, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Evommune, Forte, Galderma, Incyte, Janssen, Leo, Novartis, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun

Pharma, and UCB Pharma., Consultant of: AbbVie, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Evommune, Forte, Galderma, Incyte, Janssen, Leo, Novartis, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma., Lena Lemke Employee of: Hexal AG, Oliver von Richter Employee of: Hexal AG, Alison Balfour Employee of: Hexal AG, Fabricio Furlan Employee of: Hexal AG, Norman Gaylis: None declared

DOI: 10.1136/annrheumdis-2021-eular.1045

AB0209 SERIOUS INFECTIOUS COMPLICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS

E. Aronova[1], G. Gridneva[1], A. Kudryavtseva[1], G. Lukina[2]. [1]*VA Nasonova Research Institute of Rheumatology, Moscow, Moscow, Russian Federation*; [2]*Moscow Clinical Scientific Center named after Loginov A. S., Moscow, Moscow, Russian Federation*

Objectives: To study infectious complications of therapy with biologics, analyze the frequency of withdrawal of bDMARDs due to infectious complications.
Methods: The ambispective analysis included data on 505 cases of prescribing biologics with different mechanism of action in 188 patients with rheumatoid arthritis (160 women, 28 men).
Results: Patients in the study group received from 2 to 5 bDMARDs, mediana (25% -75%) 2 (2-3). Biologics were discontinued 326 times, of which due to the development of serious adverse reactions - 70 times, of which due to the development of infectious complications - 16 times (5% of all cases of discontinuations, 29% of all serious adverse reactions). During treatment with the first bDMARD, infectious complications that required discontinuation of the drug developed in 5.3% of cases (N = 10), with the second bDMARD - in 5.2% of cases (N = 4), no statistical differences were found between these groups. On the background of treatment with the third bDMARD, infectious complications led to the withdrawal of treatment in 14.3% of cases (N = 1), in the fourth - 0%, and in the fifth - 33.4% of cases (N = 1). There was no correlation between the number of sequentially prescribed biologics and the incidence of infectious complications. Most often, serious infections developed during treatment with drugs of the TNF-α inhibitor group (infliximab, etanercept, adalimumab, golimumab, certolizumab pegol) and tofacitinib. Out of 16 cases of infectious complications, 5 were associated with tuberculosis infection.
Conclusion: Infectious complications make up a significant proportion (29%) of all serious adverse reactions leading to the discontinuations of biologics in patients with rheumatoid arthritis. The frequency of discontinuation of bDMARDs due to infectious complications was about 5% and did not change during treatment with both the first and second biologics. It is necessary to remain alert about tuberculosis infection and examine patients before prescribing and during treatment with bDMARDs.
Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1078

AB0210 COMPARISON OF EFFICACY AND SAFETY OF BIOSIMILAR RITUXIMAB AND ORIGINATOR RITUXIMAB IN REAL CLINICAL PRACTICE

D. Kusevich[1], Y. Olyunin[2], E. Nasonov[3,4]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Osteoarthritis, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Early Arthritis, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Scientific Supervisor, Moscow, Russian Federation*; [4]*I.M. Sechenov First Moscow State Medical University, Ministry of Health of Russia (Sechenov University), Department of Therapy and Occupational Diseases, Moscow, Russian Federation*

Background: Due to the expiration of many originator biologics patents, their biosimilars (BS) have appeared and were put into clinical practice. The introduction of such drugs reduces the cost of treatment and thereby increases its availability. BS rituximab (RTX) Acellbia was developed by the Russian company "BIOCAD". Its effectiveness and safety have been proven in two clinical trials. It was licensed in Russia for the treatment of rheumatoid arthritis (RA) in 2017.
Objectives: To compare efficacy and safety of BSRTX and originator RTX (ORTX) in real clinical practice.
Methods: RA patients fulfilling the EULAR/ACR 2010 criteria and followed-up at the V. A. Nasonova Research Institute of Rheumatology were included. All of them had previously received methotrexate without effect. They were divided into 4 groups. The first and second groups included patients who had not previously received biologics. Treatment with BSRTX was started in the first group, ORTX was administered in the second group. The third and fourth groups included patients who received ORTX with significant improvement. Patients of the third group were switched to BSRTX, in the fourth group treatment with ORTX was continued. ORTX and BSRTX were administered twice 500 mg over 2 weeks. The indication for repeated administration of ORTX and BSRTX was an exacerbation of RA. Patients were examined before the first or regular administration of ORTX or BSRTX and before the planned repeat course of treatment with these drugs. RA activity was evaluated with the DAS28. Adverse events (AE) were recorded. Data were tested for normality using the Kolmogorov-Smirnov test. Continuous variables are presented as mean ±SD if they obey normal distribution, and as median [quartile interval] if they were not consistent with normal distribution. Mann–Whitney U test was used for comparison between groups.
Results: 127 patients with RA were included. 66 patients had not previously received biologics. BSRTX was started in 35 of them and ORTX – in 31. 61 patients already received ORTHX with clinical improvement. 31 of them were switched to BSRTX, and 30 continued therapy with ORTX. The median interval between the baseline examination and the assessment before the second treatment course in the BSRTX group was 6 [5; 13] months, in the ORTX group – 7 [7; 11] months. In group 1 median DAS28 during follow-up decreased from 5,8 [5,2; 6,9] to 3,9 [3,1; 4,5], in group 2 – from 5,7 [5,2; 6,0] to 4,1 [3,8; 4,6], respectively. These changes were comparable in both groups. The mean duration of the interval between infusion of BSRTX or ORTX and repeated examination – 11,3±8,2 and 10,1±4,8 months, respectively. These differences are not significant. In group 3 median DAS28 at the baseline examination was 5,1 [3,9; 5,9], at the second one – 4,3 [3,8; 5,3], in group 4 – 4,6 [3,7; 5,4] and 4,2 [3,5; 5,2] respectively. These values did not differ significantly. The frequency and nature of adverse events during treatment with ORTX and BSRTX did not significantly differ. We did not observe serious AE and unexpected AE.
Conclusion: The results of the present study show that efficacy and safety of BSRTX and ORTX were comparable when they were used as the first biologics and when switching from ORTX to BSRTX. BSRTX can be used in routine clinical practice for the treatment of RA.Disclosure of Interests:
None declared

DOI: 10.1136/annrheumdis-2021-eular.1091

AB0211 SWITCHING FROM ETANERCEPT ORIGINAL TO ETANERCEPT BIOSIMILAR: LONG TERM FOLLOW UP

G. Sada[1], M. C. Laíño Piñeiro[1], V. Aldasoro[1], J. Mendizabal[1], M. Lopez[1], S. Garcia Perez[1], L. Garrido Courel[1], N. Del-Val[1], L. Horcada[1], R. Gutiérrez Polo[1], I. Paniagua Zudaire[1], C. Fito-Manteca[1]on behalf of Complejo Hospitalario de NavarraServicio de Reumatología. [1]*Complejo Hospitalario de Navarra, Rheumatology, Pamplona, Spain*

Background: Biosimilar drugs has supposed a huge savings in our health systems and there are data that conclude that they work as original molecules when we making these switchings. There are limited studies that analize these patients across the time (1-3).
Objectives: Long term follow up of patients after switching from original etanercept to biosimilar drug.
Methods: We reviewed 187 patients who started Etanercept original in Rheumatology department at Navarra Hospital Complex and their switch to Etanercept biosimilar with a follow-up of 18 months.
Results: The switch was performed in 176 patients with rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PsA).
At 18 months of follow-up 26,1% discontinued treatment; 13% at 6 months, 9,1% at 12 months and 4% patients at 18 months. The median time in etanercept original drug before switching was 52 months.
There were 46 withdrawal patients with etanercept biosimilar: 34 inefficacy, 3 skin reaction, 2 malignancies (lymphoma and GIST), 1 injection site reaction, 1 headache, 1 diarrhea, 1 recurrent urinary infection, 1 heart failure and 2 deaths. 25 patients returned to Etanercept original but 3 did not achieve good response; all of them in RA group.
Conclusion: In our series 50 % of withdrawal happened at 6 months of follow-up. 73,9% had a good response with etanercept biosimilar at 18 months. The main reason to stop biosimilar drug was inefficacy.
Longer-term follow-up and greater number of patients are necessary to ratify these data.
REFERENCES:

[1] Selmi C, et al. BENEFIT: real-world effectiveness of SB4 after transition from reference etanercept in rheumatoid arthritis and axial spondyloarthritis. Clin Exp Rheumatol. 2020 Jun 30. Epub ahead of print.
[2] Glintborg B, et al. To switch or not to switch: results of a nationwide guideline of mandatory switching from originator to biosimilar etanercept. One-year treatment outcomes in 2061 patients with inflammatory arthritis from the DANBIO registry. Ann Rheum Dis. 2019 Feb;78(2):192-200.
[3] Tweehuysen L, et al. Open-Label, Non-Mandatory Transitioning From Originator Etanercept to Biosimilar SB4: Six-Month Results From a Controlled Cohort Study. Arthritis Rheumatol. 2018 Sep;70(9):1408-1418.

Table 1.

	WITHDRAWAL (months)	BACK TO ENBREL (n)	CONTINUEENBREL (n)	TIME TO SWITCH (months)	REASON FOR WITHDRAWAL			
					Inefficacy	A.event*	Cancer	Death
RA	22	11	8	53	14	5	2	1
PsA	16	6	6	53,5	15	0	0	1
SpA	8	8	8	45	5	3	0	0
TOTAL	46	25	22	52	34	8	2	2

*Infections (1), Heart failure (1), skin reaction (3), injection point reaction (1)
RA: rheumatoid arthritis; PsA: psoriatic artrhritis; SpA: spondyloarthritis

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1162

AB0212 NON-ADHERENCE IN RHEUMATOLOGIC IMMUNE-MEDIATED DISEASES

A. Rodríguez-Alarcón[1], N. Carballo[1], L. Río[1], C. Pérez[2], E. González-Colominas[1], X. Duran[3], J. Monfort[2], S. Grau-Cerrato[1], O. Ferrández-Quirante[1]. [1]*Hospital del Mar, Pharmacy, Barcelona, Spain*; [2]*Hospital del Mar, Rheumatology, Barcelona, Spain*; [3]*IMIM - Hospital del Mar, Statistics, Barcelona, Spain*

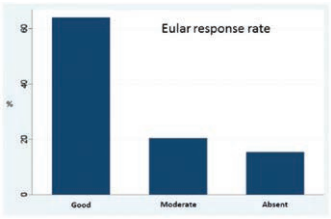
Background: Patient adherence is a key determinant of treatment success in rheumatologic immune-mediated diseases. Available data about adherence to biological treatments and factors associated to non-adherence is limited in Spain. Moreover, no studies compare adherence between subcutaneous and oral drugs.
Objectives: To evaluate non-adherence to prescribed subcutaneous biologicals and oral drugs in patients with rheumatologic immune-mediated diseases and to assess possible predictor factors associated to treatment non-adherence.
Methods: Retrospective observational study including all patients with oral and subcutaneous treatment for rheumatologic immune-mediated diseases from 2017 to 2019 in the outpatient pharmaceutical care area from a tertiary university hospital. Non-adherence was evaluated by reviewing all scheduled drug-dispensing visits in the computerized application. We considered non-adherent every time that a patient missed at least one drug administration.
Data collected: demographic, total patients and patient-treatments, total dispensing visits and route of administration for drug dispensed in every visit.
We classified patients in adherent and non-adherent considering dispensing visits. Non-adherent group: number of dispensing visits, reasons for non-adherence, number of missed administrations per patient and drug and predictor factors for non-adherence.
Results: 783 patients included: 52.4(13.7) years; 427(54.5%) female; 164 (20.9%) smoker; 697 (89%) Caucasian.
A total of 79 (10.1%) of 783 patients received more than one treatment.
869 patient-treatments: 294 adalimumab (33.8%), 236 etanercept (27.2%), 78 golimumab (8.9%), 47 apremilast (5.4%), 39 certolizumab (4.5%), 34 secukinumab (3.9%), 30 tocilizumab (3.5%).
9,197 dispensing visits. Route of administration: 6,406 subcutaneous (93.2%), 374 oral (6.8%).
Non-adherence analysis: 2417 (26.3%) dispensing visits, reasons for non-adherence/ dispensing visits: 92 unjustified (97.5%), 33 infection (1.4%), 18 (surgery) 0.7%, 3 pregnancy (0.1%), 6 others (0.3%).
Number of missed administrations/patient treatment: 675 patients missed at least one administration (77.7%).Mean 2.5 (±12.9) missed administrations.
Number of missed administrations/drug: 9.9 baricitinib (±20.8), 15.8 tofacitinib (±31.2), 25.4 apremilast (±53.2).
Predictor factors for non-adherence: ethnicity (p=0.015), treatment with golimumab (p=0.006), and tocilizumab (p=0.036). Age (p=0.072).
Conclusion: - Non-adherence to the prescribed drug occurred in 77.7% of patients with rheumatologic immune-mediated diseases
- Demographic factors such as ethnicity as well as golimumab and tocilizumab treatment, despite their different frequency of administration, were predictors for non-adherence
- Route of administration did not influence non-adherence.

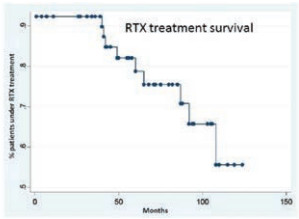
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1304

AB0213 SAVING GLUCOCORTICOIDS AFTER RITUXIMAB TREATMENT IN PATIENTS WITH REUMATOID ARTHRITIS. ANALYSIS OF A COMMON CLINICAL PRACTICE COHORT

G. Jurado Quijano[1], L. Fernández de la Fuente Bursón[1], B. Hernández-Cruz[1], P. Muñoz Reinoso[1], V. Merino Bohóquez[2], J. J. Pérez Venegas[1]. [1]*Hospital Universitario Virgen Macarena, UGC Reumatología, Sevilla, Spain*; [2]*Hospital Universitario Virgen Macarena, UGC Farmacia Hospitalaria, Sevilla, Spain*

Background: Rituximab (RTX) is a monoclonal antibody against the CD20 B cell antigen that has been used successfully in recent years for the treatment of rheumatoid arthritis (RA). It is an effective drug that reaches survival rates of 60% at 5 years of treatment as reflected in the British experience. However, survival in Spanish patients is unknown.
Objectives: To study the survival of RTX treatment and the characteristics of patients with RA treated with the drug since its commercialization in Spain.
Methods: Observational, retrospective and analytical study of a cohort of patients with RA treated with at least one dose of RTX. We reviewed the medical records of all patients with RA from January 2007 to June 2017. A total of 178 previous defined variables were collected, highlighting data about treatment (use of RTX, associated conventional synthetic disease modifying drugs [FAMEsc], doses of corticosteroids [GC] used) and activity indices. Descriptive statistics were performed (median and the 25th and 75th percentiles are shown). The comparative analysis was done with χ^2 and U of Mann Whitney for categorical variables and paired sign rank test or Student's t for continuous. Survival Kaplan Mayer curves were constructed. The study was carried out in accordance with the standards of our Clinical Research Ethics Committee.
Results: A total of 54 patients were analyzed. 74% (n = 40) of them were women, the age was 61.2 years (51.0 - 67.4). 74% (n = 40) presented some type of relevant comorbidity. Its RA was FR + in 96% (n = 52) and ACCP + in 78% (n = 42) of the cases, with an evolution time of 9.3 years (3.5-19, 2), and with radiographic erosions in up to 63% (n = 34). At the time of the start of the RTX, 100% of the patients (n = 54) received some FAMEsc, and 33 (61%) were treated with prednisone; the daily dose of prednisone was 9 (6-12) mg. The baseline DAS28-VSG was 5 (4.1 - 6.0). The duration of the follow-up was 56.6 (29.3-92.1) months. Patients received a mean of 5 (1-6) cycles of RTX at a dose of 1000 mg on days 0 and 15 in most cases. The final DAS28-VSG was 2.6 (2.1 - 4.0), p = 0.00001 compared to baseline. The delta between baseline and final DAS was -2.36 (-0.55 - -3.1). At the end of the RTX treatment, the EULAR response rate





was good in 64% (n = 25), reaching remission in 17 (31%) of the patients, and moderate response in 21% (n = 8) of them (Figure 1). Only 2 (4%) patients were treated with GCC at the end of the follow-up, p<0,00001 compared to baseline. The daily dose of PDN at the end of follow-up was 6 mg in a case and 12 mg in the other, p=00001 compared to baseline. At the end of the follow-up 24%of the patients (n = 13) changed or discontinued the drug: 9 changed due to secondary failure, 2 suspended due to adverse events, 1 due to death due to prior neoplastic process and 1 due to complete disease remission. Survival at 1, 2, 3, 4, 5, 6 and 7 years was 92%, 92%, 82% 78%, 75%, 75% and 65% respectively; with a mean survival rate of 90 months (Figure 1).

Conclusion: The results of our analysis show that patients with RA undergoing RTX treatment have adequate control of disease activity and drug survival rates, like published data. RTX treatment allowed stopped GCC treatment in 31 cases (90%).

REFERENCES:

[1] Oldroyd AGS, et al. Rheumatology (Oxford). 2018 Jun 1;57(6):1089-1096.

Disclosure of Interests: Gonzalo Jurado Quijano: None declared, Lola Fernández de la Fuente Bursón: None declared, Blanca Hernández-Cruz Speakers bureau: Sociedad Española de Reumatología, Abbvie, Roche, Bristol, MSD, Lilly, Pfizer, Amgen, Sanofi, Consultant of: Abbvie, Lilly, Sanofi, STADA, UCB, Amgen, Grant/research support from: Fundación para la Investigación Sevilla, Junta de Andalucía, Fundación Andaluza de Reumatología, Paloma Muñoz Reinoso: None declared, Vicente Merino Bohóquez: None declared, José Javier Pérez Venegas: None declared

DOI: 10.1136/annrheumdis-2021-eular.1362

AB0214

SURVIVAL, EFFICACY AND SAFETY OF GOLIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS: DATA FROM AN ARGENTINEAN COHORT

C. A. Isnardi[1], E. E. Civit De Garignani[2], A. García Ciccarelli[2], J. Sanchez Alcover[2], R. Garcia Salinas[3], S. Magri[3], E. Albiero[4], C. Gobbi[4], E. Velozo[5], E. Soriano[6], M. Brom[6], J. Zacariaz[6], I. Strusberg[7], M. Baravalle[7], S. Castaños[7], L. Morales[7], S. Paira[8], R. Calvo[8], A. Ortiz[8], R. Perez Alamino[9], H. Maldonado Ficco[10], G. Citera[1]. [1]*Psychophysical Rehabilitation Institute, Rheumatology, DQG, Argentina*; [2]*Hospital El Carmen, Rheumatology, Godoy Cruz, Argentina*; [3]*Hospital Italiano La Plata, Rheumatology, La Plata, Argentina*; [4]*Sanatorio Allende, Rheumatology, Córdoba, Argentina*; [5]*Sanatorio Adventista del Plata, Rheumatology, Libertador San Martín, Argentina*; [6]*Hospital Italiano de Buenos Aires, Rheumatology, Ciudad de Buenos Aires, Argentina*; [7]*Instituto Strusberg, Rheumatology, Córdoba, Argentina*; [8]*Hospital Provincial Dr. José María Cullen, Rheumatology, Santa Fe, Argentina*; [9]*Hospital Dr. Nicolás Avellaneda, Rheumatology, San Miguel de Tucumán, Argentina*; [10]*Nuevo Hospital Río Cuarto "San Antonio de Padua", Rheumatology, Río Cuarto, Argentina*

Background: Golimumab is a human monoclonal antibody directed against TNFα in its soluble and transmembrane forms. It can be used subcutaneously or intravenously and has shown efficacy for use in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS).

Objectives: The aim of this study was to evaluate the efficacy, safety, and cumulative survival of golimumab in patients with RA, PsA and AS from different rheumatology centers in Argentina.

Methods: We performed a longitudinal study of consecutive adults with RA (ACR/EULAR 2010 criteria), PsA (CASPAR criteria) and AS (ASAS 2009 criteria), who have started treatment with subcutaneous or intravenous golimumab according to medical indication in each center. Data was obtained by review of medical records. Sociodemographic and clinical data, musculoskeletal manifestations, comorbidities, previous treatments were recorded. In reference to golimumab treatment, start date, route of administration and concomitant treatments were identified. Disease activity was assessed using DAS28 for RA patients, DAPSA and MDA for PsA and BASDAI for AS. The presence of adverse events (AE) was recorded. If golimumab was stopped, date and cause was documented. Patients were followed up until golimumab discontinuation, loss of follow-up, or study completion (November 30, 2020). *Statistical analysis:* Chi^2 test or Fischer exact test and T test or Mann Whitney and ANOVA or Kruskal Wallis, as

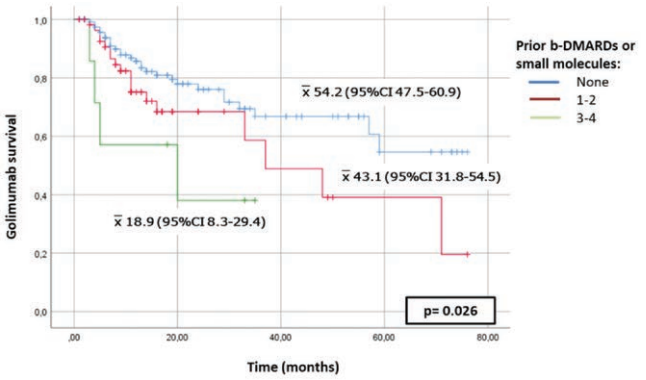


Figure 1. Golimumab survival according to prior b-DMARD o small molecule treatment.

appropriate. The incidence of EA was assessed in events every 100 patient/year. Kaplan-Meier curves and log Rank analysis. Cox proportional regression.

Results: One hundred eighty two patients were included, 116 with a diagnosis of RA, 30 with PsA and 36 with AS. Most of them (70.9%) were female with a median (m) age of 55 years (IQR 43.8-64) and m disease duration of 7 years (IQR 4-12.7) at treatment initiation. Al least one prior biological DMARD or a small molecule was received by 63 patients (34.6%). The most frequent indication cause was conventional DMARD failure. In 94.8% of the patients Golimumab was administered subcutaneously, and in 80.8% in association with conventional DMARDs, the most frequently used was methotrexate. Total follow-up was 318.1 patients/year.

Golimumab treatment showed clinical improvement in all three groups of patients. In RA patients DAS28 significantly decreased during the first 12 months of follow-up, m 5.9 (IQR 4.9-6.6) at baseline, 3.8 (IQR 2.6-4.6) at 6 months and 2.8 (IQR 2.1-3.6) at 12 months, p <0.0001. In PsA, m DAPSA-ESR value was 32.2 (IQR 24.2-47.7), 10.1 (IQR 5.8-18.3) and 11.2 (IQR 3.4-24) at baseline, 6 and 12 months, respectably (p <0.0001). In AS, m BASDAI was 6.2 (IQR 4.8-7.3), 2.8 (IQR 1.7-4.1) and 2.2 (IQR 1.1-3.2), at baseline, 6 and 12 months respectively (p <0.0001).

The incidence of adverse events was 6.6 per 100 patients/year, being infections the most frequents ones. During follow-up, 50 patients (27.5%) discontinued golimumab, the most frequent cause was treatment failure (68%), followed by lack of health insurance (16%) and adverse events (10%). Golimumab persistence was 79% and 57.6% at 12 and 24 months, respectively. Treatment survival was 50.2 months (95% CI 44.4-55.9). Patients who had received prior treatment with biological DMARDs or small molecules showed lower survival (Figure 1). In the multivariate analysis, adjusting for age, sex and disease duration, those patients showed twice the risk of suspending treatment (HR 2.01, 95% CI 1.1-3.7).

Conclusion: Golimumab treatment in real life patients in Argentina has shown good efficacy and safety. Drug survival was over 4 years and almost 80% were still using golimumab after one year. Prior treatment with other b-DMARDs o small molecules was associated with lower treatment survival.

Disclosure of Interests: Carolina Ayelen Isnardi Speakers bureau: Bristol Myers Squibb, Janssen, Grant/research support from: Pfizer, Emma Estela Civit De Garignani Speakers bureau: Abbvie, Novartis, Agustín García Ciccarelli Speakers bureau: Janssen, Novartis, Consultant of: Novartis, Grant/research support from: Janssen, Novartis, Jimena Sanchez Alcover: None declared, Rodrigo Garcia Salinas Speakers bureau: Abbvie, AMGEN, Bristol-Myers Squibb, Eli Lilly, GSK, Janssen Cilag, Montpellier-UCB, Novartis, Roche – Genentech, Sanofi, Merck Serono., Sebastian Magri Speakers bureau: Abbvie, AMGEN, Bristol-Myers Squibb, Eli Lilly, GSK, Janssen Cilag, Montpellier-UCB, Novartis, Roche – Genentech, Sanofi, Merck Serono., Eduardo Albiero Consultant of: Janssen, Carla Gobbi Speakers bureau: Pfizer, Consultant of: Pfizer, Janssen, Edson Velozo Speakers bureau: Janssen, Novartis, Pfizer, Consultant of: Abbvie, Janssen, Novartis, Grant/research support from: Janssen, Novartis, Pfizer, Enrique Soriano Speakers bureau: AbbVie, Novartis, Bristol MS, Novartis, Eli Lilly, Genzyme, Pfizer, Amgen, and Roche, Consultant of: Novartis, AbbVie, Pfizer, Eli Lilly, Sanofi, Sandoz, Amgen., Grant/research support from: Roche, Novartis, AbbVie, Glaxo Smith Kline, BMS, Martín Brom: None declared, Johana Zacariaz Grant/research support from: Bristol Myers Squibb, Ingrid Strusberg Speakers bureau: Gema Biotech SAU, BMS, Abbvie, Consultant of: Gema Biotech SAU, Abbvie, Janssen, Grant/research support from: Abbvie, Lilly, Galápagos, Servier, GSK, Merck Serono, Marcos BARAVALLE Speakers bureau: Montepellier, Consultant of: Abbvie, Janssen, Grant/research support from: Abbvie, Lilly, Galápagos, Servier, GSK, Merck Serono, Sol Castaños Speakers bureau: Abbvie, Lilly, Galápagos, Servier, GSK, Merck Serono, Liliana Morales Speakers bureau: Lilly, Consultant of: Janssen, Grant/research support from: Abbvie, Lilly, Galápagos,

Servier, GSK, Merck Serono, Sergio Paira: None declared, Romina Calvo: None declared, Alberto Ortiz: None declared, Rodolfo Perez Alamino Speakers bureau: Pfizer, Abbvie, Amgen, Bristol-Myers-Squibb, Lilly, Janssen, Novartis, Hernan Maldonado Ficco Speakers bureau: Pfizer, Abbvie, Jansen, Novartis, Bago, Bristol, Eli Lilly., Consultant of: Pfizer, Abbvie, Novartis, Jansen, Bago, Eli Lilly., Gustavo Citera Speakers bureau: Abbvie, BMS, Lilly, Jansen, Gema, Pfizer, Roche, Grant/research support from: Pfizer

DOI: 10.1136/annrheumdis-2021-eular.1399

AB0215 COMPARISON BETWEEN RITUXIMAB ORIGINATOR THERAPY AND ITS BIOSIMILAR IN THE INCIDENCE OF LATE-ONSET NEUTROPENIA IN ADULT PATIENTS WITH RHEUMATOID ARTHRITIS AND OTHER AUTOIMMUNE DISEASES

M. M. Ahmad[1], E. Mcrorie[1]. [1]*Western General Hospital, Rheumatology, Edinburgh, United Kingdom*

Background: Late-onset neutropenia (LON) occurs when the absolute neutrophil count drops below 1.5 × 10(9)/L four weeks after Rituximab infusion.[1] It is a condition recognised more in haematological malignancy patients treated with Rituximab with a reported prevalence of 8% or higher.[2] LON was reported in 6.5% of rheumatological patients[1], while a French registry found a prevalence of 1.3% in rheumatoid arthritis patients.[3]

Almost all patients receiving Rituximab originator therapy at our Rheumatology department were switched to its biosimilar starting from November 2017. Our haematology team observed LON cases in their patients after this period.

Objectives: We wanted to establish whether there is increased LON occurrence with the biosimilar than the originator therapy, requiring specific monitoring.

Methods: This is a cross-sectional retrospective review of 12 months period before and after switching to the biosimilar of all patients who received Rituximab for the first time. We reviewed the patients' blood monitoring for up to 12 months after receiving Rituximab. We used a proforma to collect the age, sex, diagnosis, date of the first infusion, use of other DMARDs, LON occurrence within 12 months after the infusion and neutropenia within the 12 months before it in addition to the frequency of the blood monitoring after the infusion.

Results: For the originator, between 1/1/2016 and 31/12/2016, 142 patients received Rituximab, 47 (33.09%) of them were given the treatment for the first time. Their median age was 62 years, 28 (59.5%) were females. The most common diagnosis was rheumatoid arthritis 38 (80.8%), and 35 (74.4%) patients were on other disease-modifying agents (DMARDs). Two patients (4.2%) developed LON. In both patients, this occurred during admission for septic arthritis whilst on antibiotics, and both had Grade 2: ≥1,000– < 1,500/mm3 neutropenia.

For the Biosimilar cohort, between 1/4/2019 and 31/3/2020, 161 patients received Rituximab, 36 (22.3%) of them were given the treatment for the first time. Their median age was 59 years, 27 (75%) of them were females. The most common diagnosis was rheumatoid arthritis 25 (69.4%), and 26 (72.2%) were on other DMARDs. One patient (2.77%) developed grade 2 LON one month after Rituximab. Another patient with known autoimmune neutropenia was excluded. In all the Three patients with LON in both groups, neutrophil count recovered in less than a month, and they had normal IgG before the infusion.

The frequency of blood monitoring after Rituximab infusion was done 1-3 monthly in 32 (68%) patients and 23 (63.8%) patients in the originator and biosimilar groups, respectively.

Four (8.5%) patients and three (8.3%) patients in the originator and biosimilar groups respectively had a frequency of blood monitoring done less than six-monthly.

Conclusion: In our patients' cohort, LON incidence following switching to the Rituximab biosimilar was not higher than the originator therapy.

REFERENCES:

[1] Monaco, W. E., Jones, J. D. & Rigby, W. F. C. Rituximab associated late-onset neutropenia-a rheumatology case series and review of the literature. *Clin Rheumatol* **35**, 2457–2462 (2016).

[2] Dunleavy, K., Tay, K. & Wilson, W. H. Rituximab-Associated Neutropenia. *Seminars in Hematology* **47**, 180–186 (2010).

[3] Salmon, J. H. *et al.* Late-onset neutropenia after treatment with Rituximab for rheumatoid arthritis and other autoimmune diseases: data from the AutoImmunity and Rituximab registry. *RMD Open* **1**, e000034 (2015).

Acknowledgements: The authors would like to thank pharmacist Christine Hay for her help in providing the Rituximab databases.

Disclosure of Interests: Mostafa Meshaal Ahmad: None declared, Euan McRorie Speakers bureau: I have spoken at meetings sponsored by Roche several years ago, Consultant of: I have sat on advisory boards for Roche several years ago., Grant/research support from: I was the local investigator for the ORBIT study, published in the Lancet in 2016.

DOI: 10.1136/annrheumdis-2021-eular.1544

AB0216 LONG-TERM RESULTS OF T2T THERAPY INITIATED AT THE ONSET OF RHEUMATOID ARTHRITIS (DATA FROM OREL REGISTRY)

V. Rybakova[1], A. Avdeeva[2], Y. Olyunin[2], E. Nasonov[3,4]. [1]*V.A. Nasonova Research Institute of Rheumatology, Outpatient Department, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Early Arthritis, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Scientific S, Moscow, Russian Federation*; [4]*I.M. Sechenov First Moscow State Medical University, Ministry of Health of Russia (Sechenov University), Department of Therapy and Occupational Diseases, Moscow, Russian Federation*

Background: Current guidelines for the treatment of rheumatoid arthritis (RA) recommend early administration of methotrexate (MTX) and addition of a biologic if MTX monotherapy does not provide remission or low activity of the disease. Efficacy of this strategy in real clinical practice was assessed using data from the Russian RA registry OREL.

Objectives: To analyze long-term results of intensive treatment initiated at RA onset in real clinical practice.

Methods: 141 RA patients with disease duration less than 3 years (29 men, 112 women) were included. 112 were positive for rheumatoid factor and 119 – for anti-cyclic citrullinated peptide antibody. Subcutaneous MTX was initiated at 10-15 mg per week with further dose escalation up to 20-30 mg per week. Therapy was adjusted every 3 months. If MTX monotherapy did not allow to achieve treatment target of remission or low disease activity, biologics were added.

Results: Median DAS 28 at baseline was 5,31 [4,79; 6,14]. Initiation of treatment resulted in steady decrease of disease activity ($p<0.05$, table1). After 1 year of follow-up 33.8% of patients received MTX monotherapy, 33.8% – MTX in combination with tumor necrosis factor alpha inhibitors, 22.0% – MTX +abatacept, 0.55% – MTX+ tocilizumab, 0.47% – MTX + rituximab. Low disease activity was achieved in 16.3% patients, and remission - in 45.8%. After 6 years median age of patients was 58 [49; 66] years, disease duration – 84 [79; 89] months, low disease activity was documented in 21.3%, and remission – in 7.8% of cases (fig. 1). 7% of patients were able to maintain remission without any treatment. Biologics were discontinued in 15 patients after achieving remission or low disease activity, and synthetic DMARDs – in 5 patients having remission.

Conclusion: Intensive therapy initiated at RA onset demonstrates high effectiveness, allowing 61.5% of patients to achieve low disease activity or remission within 12 months, and to maintain these results after 6 years of treatment in 29.2%. Adherence to this strategy allowed to discontinue biologics in 15 patients and synthetic DMARDs in 5 patients after achieving treatment target.

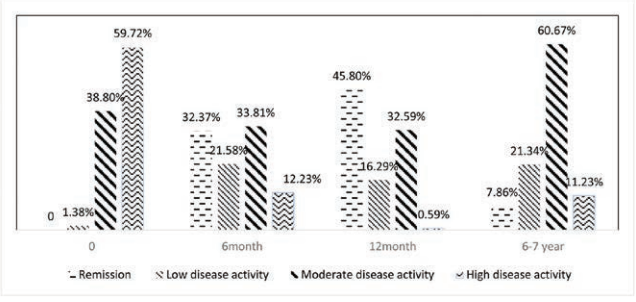


Figure 1. Changes of the disease activity during follow-up

Table 1. Changes of the main inflammatory activity measures, Me [25th; 75th percentile]

Parametres	0	12 months	6 years
DAS28	5,31 [4,79; 6,14]	2,85 [2; 3,90] *	4,008 [3,4; 4,59] *
SDAI	28,27 [18,79; 40,73]	5,67 [2; 11,98] *	15,06 [9,32; 21] *
CDAI	25 [17; 36]	5 [1,7; 11] *	15 [9; 21] *
ESR (mm/hr)	32 [19; 50]	16 [8; 30] *	16 [10; 25] *
CRP (mg/l)	26,55 [6,4; 45,30]	3,85 [1,5; 11,3]*	2,2 [0,9; 4,9] *

* p<0.05 in all cases.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1552

AB0217

NON MEDICAL SWITCH FROM ETANERCEPT ORIGINATOR TO BIOSIMILAR GP2015 IN PATIENTS WITH CHRONIC INFLAMMATORY ARTHROPATHIES

M. Colaci[1], M. L. Aprile[1], A. La Rosa[2], A. DI Maggio[2], L. Malatino[1].
[1]Rheumatology Centre, Ospedale Cannizzaro, Clinical and Experimental Medicine, University of Catania, Catania, Italy; *[2]Servizio di Farmacia Ospedaliera, Ospedale Cannizzaro, Catania, Italy*

Background: In the last decades, new biologic drugs were introduced for the treatment of chronic inflammatory arthropathies, progressively leading to a relevant increase of medical costs. However, the introduction of biosimilars (biologic molecules similar to branded drugs with expired patent) permitted to optimize the financial resources. The non-medical switch (NMS) is the switch from a biologic originator to a biosimilar agent for economic reasons only, on the basis of the substantial equivalence as regards efficacy and safety between originator and biosimilar drugs.
In literature, several evidences from clinical trials and registry studies showed that the switch from etanercept originator to biosimilar SB4 was safe [1]. Instead no sufficient data may be found regarding the biosimilar GP2015.
Objectives: We aimed to evaluate efficacy, safety, and retention rate in a series of patients with chronic arthritis treated with etanercept originator who underwent to NMS towards the ETN biosimilar GP2015.
Methods: From March to June 2020, all patient referred in our Centre affected by rheumatoid arthritis (RA), psoriatic arthritis (PA) and axial spondyloarthritis (axSpA) treated with etanercept originator and in remission/low disease activity for at least 6 months underwent to NMS. Data on disease activity (DAS28-PCR/CDAI/SDAI; DAPSA; BASDAI), eventual adverse events and causes of withdrawal of therapy were collected at 2, 4 and 6 months after the switch.
Results: We recruited 71 consecutive patients (M/F: 24/47; mean age 55,8± 11,1 years; 39 RA; 15 PA; 17 axSpA; mean duration therapy 7.3±3.8 years). Disease activity was unchanged for almost all patients after 6 months from the switch (median ΔDAS28-PCR/CDAI/SDAI: 0,1/0/0,5; median ΔDAPSA: 0; median ΔBASDAI: 0) Moreover, the 6-month retention rate was 97.2%. Only 2 patients (2.8%) switched back to the originator due to loss of efficacy in one case and adverse events in the second case (paraesthesia, headache, dizziness and worsening of arthralgia).
Conclusion: Our study confirmed that the NMS from ETN originator to GP2015 represents a safe practice that maintains the efficacy of the current treatment.
REFERENCES:
[1] Glintborg B, AG, Omerovic E, et Al. *To switch or not to switch: results of a nationwide guideline of mandatory switching from originator to biosimilar etanercept. One-year treatment outcomes in 2061 patients with inflammatory arthritis from the DANBIO registry.* Ann Rheum Dis 2019; **78**:192–200.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1557

AB0218

NON MEDICAL SWITCH FROM ADALIMUMAB ORIGINATOR TO THE BIOSIMILAR GP2017 IN PATIENTS AFFECTED BY CHRONIC ARTHRITIS

M. Colaci[1], M. L. Aprile[1], A. La Rosa[2], A. DI Maggio[2], L. Malatino[1].
[1]Rheumatology Centre, Ospedale Cannizzaro, Clinical and Experimental Medicine, University of Catania, Catania, Italy; *[2]Servizio di Farmacia Ospedaliera, Ospedale Cannizzaro, Catania, Italy*

Background: The non-medical switch (NMS) from originator drugs to biosimilars is a possible strategy adopted by rheumatologists in order to control the expansion of pharmaceutic costs for the treatment fo patients affected by chronic arthritis. To date, few real life data on the switch from adalimumab (ADA) originator to its biosimilars are available.
Objectives: We aimed to evaluate efficacy and safety in a single-Centre cohort of patients affected by chronic arthritis who switched from ADA originator to the biosimilar GP2017.
Methods: Patients affected by rheumatoid arthritis (RA), psoriatic arthritis (PA) and axial spondyloarthritis (axSpA) already on therapy with ADA originator in remission or low disease activity for at least 6 months were switched to GP2017 (March- June 2020). Data on disease activity (DAS28-PCR/CDAI/SDAI; DAPSA; BASDAI), eventual adverse events and causes of withdrawal of therapy were collected at 2, 4 and 6 months after the switch.
Results: 88 patients were enrolled (M/F 36/52; mean age 55.8 ± 12 years; 25 RA, 32 PA, 31 axSpA, mean duration of therapy 6.3 ± 3.8 years). No statistically significant difference was observed in median DAS28-PCR/CDAI/SDAI values at the baseline and after 6 months [1.03 (0.96-3.43) vs. 1.21 (0-3.7) / 0 (0-15) vs. 0 (0-17) / 0 (0-15) vs. 0.5 (0-17.5)], DAPSA [0 (0-12.2) vs. 0 (0-15)] and BASDAI [0 (0-4.3) vs. 0 (0-6.4)]. The retention rate was 93.2%. 6/88 patients (6.8%) switched back to the originator. The causes of discontinuation were: disease reactivation in a single case (1.1%), subjective reasons/ nocebo effect in 5/88 cases (5.7%), including: general malaise and transient increased of blood pressure (n.1), dizziness, paraesthesia, arthralgia, headache (n.1), itch *sine materia* (n.1) and subjective worsening without objective disease flare (n.2).
Conclusion: This is the first real life study showing that the NMS from ADA originator to GP2017 represents a safe practice that maintains the efficacy of the current treatment. However, a few cases of switchback were described, mainly attributed to nocebo effect [1].
REFERENCES:
[1] Fleischmann R, Jairath V, Mysler E et al. *Nonmedical Switching From Originators to Biosimilars: Does the Nocebo Effect Explain Treatment Failures and Adverse Events in Rheumatology and Gastroenterology?* Rheumatol Ther 7: 35–64 (2020).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1563

AB0219

EXPLORING LONG-TERM DRUG EFFECTIVENESS AND DRUG SURVIVAL FOR RITUXIMAB REFERENCE DRUG IN TREATMENT OF RHEUMATOID ARTHRITIS PATIENTS IN ORDINARY OUTPATIENT CLINIC

K. Łosińska[1], M. Wilk[1], A. H. Pripp[2], M. Korkosz[1,3], G. Haugeberg[4,5].
[1]University Hospital, Division of Rheumatology and Immunology, Cracow, Poland; *[2]Oslo University Hospital, Oslo Centre of Biostatistics and Epidemiology, Oslo, Norway*; *[3]Jagiellonian University Medical College, Department of Rheumatology, Cracow, Poland*; *[4]Sorlandet Hospital, Division of Rheumatology, Department of Medicine, Kristiansand, Norway*; *[5]NTNU, Norwegian University of Science and Technology, Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, Trondheim, Norway*

Background: In randomized controlled trials (RCTs) rituximab (RTX) has been shown to effectively suppress inflammation and reduce structural joint damage in rheumatoid arthritis (RA) patients [1]. There is a lack of RA data on RTX effectiveness and drug survival when used in real life practice.
Objectives: To explore long-term drug effectiveness and drug survival for RTX used to treat RA patients in ordinary clinical practice.
Methods: The study population included RA patients treated between 2006 and 2020 with RTX at an outpatient clinic in Norway. Patients were monitored using recommended measures for disease activity and patient reported outcomes (PROs). Drug effectiveness was assessed with random intercept linear mixed models. Drug survival was described using Kaplan-Meier survival analysis. Baseline predictors of drug survival were assessed with multivariable Cox proportional hazard models.
Results: In database a total of 246 RA patients (females 74.8%) were identified to have been treated with RTX. At baseline mean (SD) age was 59.1 (13.5) years, disease duration 13.0 (10.2) years, RF positive 88.8%, ACPA positive 92.1%. Majority of patients had first cycle RTX dosage of 2000 mg (82.9%). At baseline patients currently using conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) were 51.5% (methotrexate 39.4%), prednisolone 73.6% and a total of 17.1% were biologic DMARDs (bDMARDs) naïve. In table 1 mean (SE) values for disease activity and PROs are shown for baseline and subsequent years after baseline for 5 years follow up.

Table 1. Changes in disease activity and PROs at baseline and subsequent 1-year periods

	Baseline N=246	1 year N=246	2 year N=204	3 year N=163	4 year N=130	5 year N=111
CRP (mg/L)	23.1 (2.1)	21.3 (1.6)	11.7 (0.9)	8.6 (1.4)	6.2 (0.7)	6.7 (0.9)
ESR (mm/hr)	32.1 (1.4)	31.1 (1.3)	22.3 (1.1)	17.6 (1.2)	14.3 (1.0)	13.6 (1.2)
SJC28 (0-28)	6.3 (0.4)	5.4 (0.3)	3.2 (0.3)	2.2 (0.2)	1.6 (0.2)	1.5 (0.2)
TJC28 (0-28)	7.1 (0.4)	6.6 (0.3)	3.6 (0.3)	2.6 (0.3)	2.2 (0.3)	1.8 (0.3)
DAS28	4.9 (0.1)	4.7 (0.1)	3.6 (0.1)	3.1 (0.1)	2.8 (0.1)	2.7 (0.1)
CDAI	22.9 (0.9)	20.7 (0.7)	12.3 (0.7)	9.4 (0.7)	8.5 (0.6)	7.7 (0.7)
PGA (0-100mm)	57.2 (1.7)	53.7 (1.4)	38.1 (1.6)	33.7 (1.9)	35.0 (2.1)	32.8 (2.2)
MHAQ (0-3)	1.0 (0.0)	0.9 (0.0)	0.7 (0.0)	0.6 (0.0)	0.5 (0.0)	0.5 (0.0)

During follow up all disease activity and PRO measures improved significantly ($p < 0.001$). Least improvement was seen in first year and a more substantial improvement progressed since second year. Percentage of patients with no, moderate and good treatment response defined according to EULAR response criteria [2] is shown in figure 1.

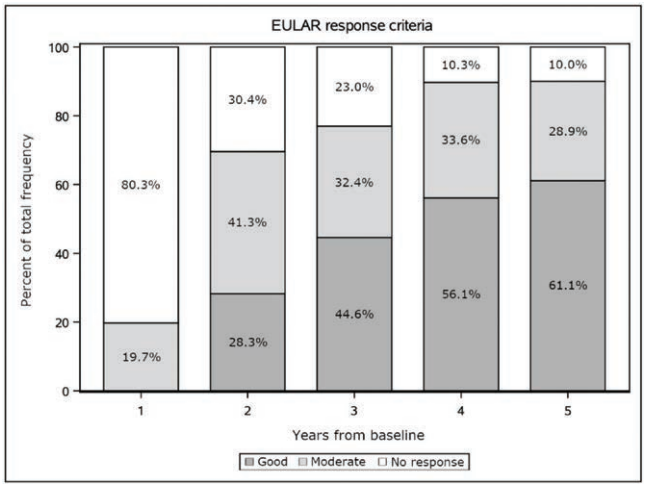


Figure 1. No, moderate and good response to RTX treatment

No significant difference during the 5-year follow-up was found regarding previous use of bDMARD or not and for concomitant use of csDMARDs or not for variables listed in the table 1.

Drug survival for the RTX was 83% (95CI 77-87%) after 1 year, 66% (95CI 60-72%) after 2 years, 53% (95CI 46-59%) after 3 years, 46% (95CI 39-52%) after 4 years and 34% (95CI 28-40%) after 5 years of follow up.

No significant difference in drug survival was found between bDMARD naïve and previous users of bDMARDs or between concomitant and non-concomitant users of csDMARDs. RF positive patients had a better drug survival.

In prediction analysis RF positive status, high baseline DAS28, low baseline CRP, previous bDMARDs use, short disease duration and low MHAQ were found to be independently associated with better drug survival.

Conclusion: Our real life data shows that RTX treated RA patients had a satisfactory treatment response and drug survival declines rather linearly over time. However, a significant treatment response was achieved primary in the second year indicating that at least 2 twin infusions should be given before identifying treatment failure.

REFERENCES:

[1] Mok CC. Rituximab for the treatment of rheumatoid arthritis: An update. Drug Des Devel Ther 2013;8:87-100.

[2] Fransen J, van Riel PL. The Disease Activity Score and the EULAR response criteria. Rheum Dis Clin North Am. 2009;35:745-viii.

Acknowledgements: Nurses and doctors from Division of Rheumatology at Sørlandet Hospital in Kristiansand, Norway contributed to data collection.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1661

AB0220 ANTI-CITRULLINATED PROTEIN ANTIBODY (ACPA) POSITIVITY IS ASSOCIATED WITH REDUCED WITHDRAWAL RATES OF ABATACEPT IN RHEUMATOID ARTHRITIS BUT ONLY IN PATIENTS WHO ARE ANTI-NUCLEAR ANTIBODY (ANA) NEGATIVE

J. Kimpton[1], M. Shipa[2], E. Hawkins[2], S. A. Yeoh[2], M. Greenwood[3], M. Ehrenstein[2]. *[1]University College London, Centre for Clinical Pharmacology and Therapeutics, London, United Kingdom*; *[2]University College London, Centre for Rheumatology, London, United Kingdom*; *[3]University College London Hospital, Pharmacy Department, London, United Kingdom*

Background: Abatacept, a selective inhibitor of T cell co-stimulation, is often used as a second-line biologic disease-modifying anti-rheumatic drug (bDMARD) after the failure of tumour necrosis factor inhibitor (TNFi) in Rheumatoid Arthritis (RA). However, in comparison to TNFi very few survival analyses of abatacept have been reported.[1,2]

Objectives: To investigate predictors of abatacept discontinuation due to either inefficacy or adverse events in RA patients over 5-years.

Methods: A retrospective observational analysis was conducted on a tertiary hospital dataset of RA (according to 2010 ACR/EULAR criteria) patients who started abatacept (either intravenous or subcutaneous). Time to abatacept discontinuation over 5-years was estimated using Kaplan-Meier survival analyses. A multivariate cox-regression model to predict abatacept discontinuation was chosen by elastic net regularisation.

Results: A total of 112 patients with RA [81% female, mean age 58.1 (SD 13.5) years] commenced abatacept therapy during the study period. 88 (78.6%) patients received intravenous abatacept, 14 (15.9%) of whom switched to subcutaneous injection, and 24 (21.4%) were initially treated with subcutaneous abatacept, 2 (8.3%) of whom switched to intravenous. More than half of the patients (65/112) were treated with at least one concomitant conventional synthetic DMARD (csDMARD). Methotrexate was the most commonly used (n = 37) csDMARD, followed by hydroxychloroquine (n = 23), sulfasalazine (n= 15), and leflunomide (n = 7). 42 (37.5%) patients were treated with glucocorticoids (either oral, intra-articular, or intramuscular injection) during the time they were treated with abatacept. Abatacept was most commonly used as 4th (n = 29) and 3rd line (n = 24) bDMARD but 19 patients received abatacept as their first line bDMARD. 75 (67%) patients were rheumatoid factor (RF) positive and 73 (65.2%) were anti-citrullinated protein antibody (ACPA) positive. Anti-nuclear antibody (ANA) was positive in 32 patients. Abatacept was discontinued in 54 patients (48.2%); 19 (35.2%) due to an adverse event and 35 (64.8%) due to loss of efficacy. Overall, the median time to discontinuation of abatacept was 3.8 years.

Multivariate cox regression (variables chosen by the elastic net and adjusted by whether or not abatacept was used as first-line therapy) showed that ACPA positivity was associated with a reduced risk of abatacept discontinuation with a hazard ratio (HR) of 0.40 (95% CI 0.18 to 0.85, p=0.02, N. of events 16/47) compared to ACPA negative patients (N. of events 15/23), but only if ANA was negative. In contrast, ACPA positivity did not reveal any retention benefit over ACPA negative patients, if they were ANA positive.

ACPA positive patients without positive ANA increased the time-to-discontinuation of abatacept predominantly after 3-months (unadjusted log-rank p=0.02), compared to ACPA, and ANA negative patients (Figure 1). Adding csDMARDs with abatacept, reduced the risk of discontinuation of abatacept by 59% (95% CI 24% to 77%, p = 0.004, N. of events 26/65) compared to monotherapy (N. of events 28/47).

Conclusion: Our data suggests patients who are ACPA positive and ANA negative are more likely to remain on abatacept therapy. Concomitant csDMARD use also acts as a positive predictor of abatacept treatment retention.

REFERENCES:

[1] Cagnotto G, et al. Arthritis Res Ther. 2020;22(1):15.

[2] Alten R, et al. Clin Rheumatol. 2019;38(5):1413-1424.

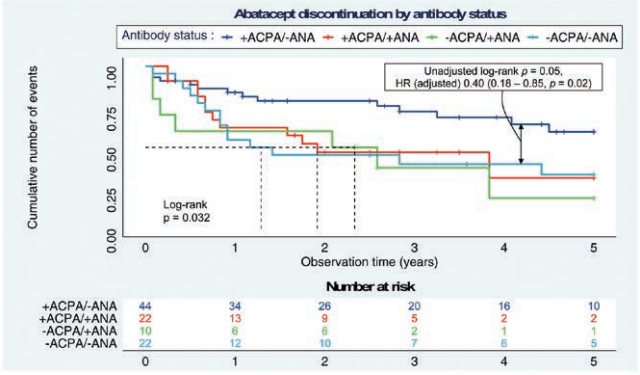


Figure 1. Kaplan-Meier survival curve of retention of abatacept, stratified by *Anti-citrullinated protein antibody (ACPA) and antinuclear antibody (ANA).*
+ACPA/-ANA = ACPA positive and ANA negative, +ACPA/+ANA = ACPA positive and ANA positive, -ACPA/-ANA = ACPA negative and ANA negative, -ACPA/+ANA = ACPA negative and ANA positive, HR = Hazard ratio.

Acknowledgements: I have no acknowledgements to declare.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1848

AB0221 CURRENT IMPLEMENTATION OF TREAT-TO-TARGET APPROACH IN RHEUMATOID ARTHRITIS TREATMENT: THE PERSPECTIVE OF CHINESE RHEUMATOLOGISTS

J. L. Zhao[1], X. Liu[2], L. Zhan[2], H. Tang[2], J. Li[2], M. Liu[2], E. Holdsworth[3], Y. Zhao[1]. *[1]Peking Union Medical College Hospital, Department of Rheumatology, Beijing, China*; *[2]Eli Lilly and Company, Medical, Shanghai, China*; *[3]Adelphi Real World, Rheumatology, Manchester, United Kingdom*

Background: Treat-to-target (T2T) approach is recommended as a standard management strategy in rheumatoid arthritis (RA) treatment by Chinese guideline for diagnosis and treatment of RA[1]. However, there is little known about its current implementation in China.

Objectives: This study aimed to evaluate the implementation and achievement of T2T approach and explore their associated factors in Chinese RA cohort.
Methods: A comprehensive cross-sectional survey of rheumatologists and their RA patients was conducted in China. Data were collected during May-Aug 2019 via physician-completed patient record forms. 60 rheumatologists provided data on demographic, clinical characteristics, treatments, and T2T approach implementation for 600 RA patients. Two logistic regressions were used to evaluate factors associated with T2T approach implementation and T2T goal achievement, respectively. Patients with missing data were not included in the models.
Results: 600 patients were included in this study (48.8±11.7 years, 70.3% female). 39.0% (N=234) of 600 patients were being treated with T2T approach, and 64.9% (N=366) of 564 patients had achieved T2T goal. Patients with longer disease duration (>2 years diagnosis) (odds ratio (OR) [95%CI]=1.61 [1.05, 2.49], vs. diagnosis ≤2 years), higher pain score (OR [95%CI]=1.26 [1.04, 1.51]), or receiving advanced therapy (OR [95%CI]=6.91 [3.64, 13.13]) were more likely to use T2T. Patients with BMI >23.9kg/m^2 (OR [95%CI]=2.83 [1.59, 5.04], vs. BMI≤23.9kg/m^2), or who worked full-time (OR [95%CI]=2.12 [1.26, 3.57]) were more likely to achieve T2T goal, while patients with more pain (OR [95%CI]=0.77 [0.64, 0.92]) were less likely to achieve T2T goal.
Conclusion: Low implementation of T2T approach is observed in Chinese RA treatment. Longer disease duration, more pain, and receiving advanced therapy are associated with higher probability of T2T use, while higher BMI, full-time work and less pain are associated with higher probability of T2T goal achievement. Standard diagnosis and treatment according to guidelines may improve T2T approach implementation.
REFERENCES:
[1] Association, C.R., 2018 Chinese guideline for the diagnosis and treatment of rheumatoid arthritis. Zhonghua nei ke za zhi, 2018. 57(4): p. 242.
Disclosure of Interests: Jiu-liang Zhao: None declared, Xin Liu Employee of: Eli Lilly and Company, Lujing Zhan Employee of: Eli Lilly and Company, Hongyu Tang Employee of: Eli Lilly and Company (Intern), Jinnan Li Employee of: Eli Lilly and Company, Mengru Liu Employee of: Eli Lilly and Company, Elizabeth Holdsworth Consultant of: Eli Lilly and Company, Employee of: Adelphi Real World, Yan Zhao: None declared
DOI: 10.1136/annrheumdis-2021-eular.1960

AB0222 COMPARISON OF SELF-INJECTION DEVICES FOR ADMINISTERING ANTI-TUMOR NECROSIS FACTOR AGENTS USING THE ORIGINAL QUESTIONNAIRE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Y. Hirano[1], J. Hasegawa[1]. [1]*Toyohashi Municipal Hospital, Rheumatology, Toyohashi, Japan*

Background: Self-injection of biological agents has become a general practice in the treatment of rheumatoid arthritis (RA). Self-injectable biological agents differ in shape, needle thickness, drug fluid volume, and so on. These differences may affect patients' evaluations of self-injection devices. Five kinds of anti-tumor necrosis factor (TNF) agents can be administered by self-injection in clinical practice in Japan. Information on patients' evaluations of self-injection devices is important in choosing the agent for the treatment of RA among several agents with the same mechanism of action.
Objectives: The aim of this retrospective cross-sectional study was to compare patient evaluations of anti-TNF self-injection devices in the treatment of RA.
Methods: RA patients in whom etanercept (ETN) pen 50 mg (Embrel Pen) was switched to ETN biosimilar (BS) 50 mg (ETN-BS [MA]), adalimumab (ADA) syringe 40 mg (Humira syringe) was switched to ADA pen 40 mg (Humira pen), golimumab (GLM) syringe 50 mg (Simponi syringe) was switched to GLM auto-injector (Simponi AI), and certolizumab pegol (CZP) syringe (Cimzia syringe) was switched to CZP autoclicks (Cimzia AC) were asked to answer an originally developed questionnaire (Toyohashi Self-injection Assessment Questionnaire [T-SAQ]; Table 1) before and after switching agents. T-SAQ included 18 questions. A score of 0 indicated "best" and 4 indicated "worst" for each question, with a highest possible score of 72. The patients' characteristics and T-SAQ scores before and after switching agents were investigated. A statistical analysis of the difference in T-SAQ score between before and after switching was performed using the Wilcoxon signed-rank test. A P value < 0.05 was considered significant.
Results: The patients were divided into groups according to the agents they received with switching as follows: switchers from ETN pen to ETN-BS, n = 32; switchers from ADA syringe to ADA pen, n = 28; switchers from GLM syringe to GLM-AI, n = 25; and switchers from CZP syringe to CZP-AC, n = 10. The total T-SAQ scores were as follows, respectively: ETN pen and ETN-BS, 23.5 and 19.0; ADA syringe and ADA pen, 25.8 and 14.9; GLM syringe and GLM-AI, 23.8 and 17.4; and CZP syringe and CZP-AC, 30.6 and 18.8. The total T-SAQ was significantly improved after switching to the pen devices in all the switching groups. In the switchers from ETN pen to ETN-BS, the scores for questions 5, 10, 11, 12, 16, 17, and 18 were significantly improved after switching. The total T-SAQ scores were significantly improved for questions 1, 2, 3, 4, 5, 7, 11, 12, 13, 15, 16, and 17 in the switchers from ADA syringe to ADA pen, for questions 1, 2, 5, 7, 10, 16, and 17 in the switchers from GLM syringe to GLM-AI, and for questions of 1, 2, 3, 4, 5, 7, 11, and 15 in the switchers from CZP syringe to GLM-AC.
Conclusion: The pen devices were favorably assessed by the RA patients in whom syringe devices were switched to pen devices for the same agent. The total T-SAQ score improved in the RA patients in whom ETN pen was switched to ETN-BS probably because the thickness of the needle was thinner in the ETN-BS than in the ETN pen. The total T-SAQ score for the ADA pen was lowest probably because the thinnest needle was used (29 gauge) and the amount of drug fluid is smallest (0.4ml). The total T-SAQ score for the CZP syringe was the lowest probably because the thickest needle was used (25 gauge).

Table 1. Toyohashi Self-injection Assessment Questionnaire (T-SAQ)

Q	Score	0	1	2	3	4
1	Ease to use	Excellent	Very Good	Fair	Poor	Unacceptable
2	Ease of learning how to use	Very easy	easy	Fair	Difficult	Very Difficult
3	Ease of abandoning	Very easy	easy	Fair	Difficult	Very Difficult
4	Ease of injection	Very easy	easy	Fair	Difficult	Very Difficult
5	Ease of holding the device	Excellent	Very Good	Fair	Poor	Unacceptable
6	Occurrence of injection fluid leak	Never	Almost not	Fair	Sometimes	Always
7	Time of injection	Very short	Short	Fair	Long	Very Long
8	Burden on leisure or travel	Very small	Small	Fair	Big	Very big
9	Burden on household affairs or child-rearing	Very small	Small	Fair	Big	Very big
10	Burden on work (only for those working)	Very small	Small	Fair	Big	Very big
11	Strain or anxiety from injection	Very small	Small	Fair	Big	Very big
12	Strain or anxiety from needle	Very small	Small	Fair	Big	Very big
13	Disgust with or anxiety from self-injection	Very small	Small	Fair	Big	Very big
14	Needlestick accident	Never	Almost not	Sometimes	Often	Always
15	External appearance	Excellent	Very Good	Fair	Poor	Unacceptable
16	Pain from pricking with the needle	None	Very mild	Moderate	Severe	Very severe
17	Pain during drug injection	None	Very mild	Moderate	Severe	Very severe
18	Pain after injection	None	Very mild	Moderate	Severe	Very severe

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2252

AB0223 MODIFIED DOSE RITUXIMAB BIOSIMILAR IN RHEUMATOID ARTHRITIS COMPARING B-CELL DEPLETION EFFECT AND DISEASE ACTIVITY SCORES

S. Bandyopadhyay[1]. [1]*Apollo Gleneagles Hospital, Internal Medicine, Kolkata, India*

Background: In emerging economies self-funding patients opt for less costly options, influencing both compliance and maintenance of treatment for chronic illness. Studies comparing originator rituximab 1000mgx2 and 500mgx2 doses in Rheumatoid arthritis (RA) have yielded interesting results[1]. Evidence of B cell depletion, measured by CD19 count, maybe a marker for disease improvement[2]. However effect of different dose of biosimilar Rituximab (bRTX) on B cell depletion and disease activity needs exploration.
Objectives: To determine correlation of CD19 count defining B cell depletion and disease activity with different dosages of bRTX treatment.
Methods: Between April 2019 and March 2020, all RA patients with DMARD failure were screened for eligibility of biologics as routine clinical practice. Depending on individual choice, after full consent, patients received either 1000mgx2 or 500mgx2 bRTX. All patients had CD19 count before and 12 months after the first dose. Effectiveness of bRTX 1000 mg×2 and 500 mg×2 was assessed by DAS28 and EULAR response. Comparative adjusted analysis was performed by analysis of variance (ANOVA).
Results: Out of 468 eligible patient, 84 opted for biologic. Of which 27 patients consented for bRTX (17 female, mean age 39.5 years).13 patients opted for 1000mg×2 and 14 for 500mg×2 dose. 74% (20/27) patients were on concomitant methotrexate and 26% on hydroxychloroquine (7/27). Both doses led to significant reduction in ESR, CRP, and DAS28-ESR at 12 months (p<0.001) (Table 1).

Table 1. RA outcome-measurement scores at 12 months post biosimilar Rituximab therapy.

Variable	Baseline		12 months	
	RTX 1000mg x 2(n=13)	RTX 500mg x 2(n=14)	RTX 1000mg x 2(n=13)	RTX 500mg x 2(n=14)
ESR*	53.9±23.9	57.1±24.7	23.9±2.9	24.1±4.7
CRP*	6.1±3.9	6.9±2.9	2.1±0.9	2.3±0.9
DAS28-ESR*	6.1±0.3	6.1±0.2	4.0±0.4	4.1±0.2
CD 19+ Count*# (10^5/L)	1191.6±308.4	1155±289.6	128.8±90.4	139±90.6

* p<0.0001 as compared to 12 mos vs baseline; # p<0.0001 as compared amongst group

At the end of 12 months, compared to 1000mg, CD19 count was higher in 500mg group (p=0.25). Percentage of patients achieving EULAR moderate or no response was higher in 500mg group (37%vs29%, p=0.205), both complete and incomplete B cell depletion, but patients achieving good response was same in both groups (14.8%vs18.5%, p = 0.25). (Figure 1).

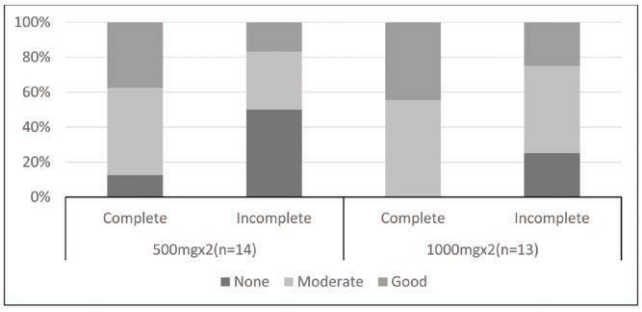


Figure 1. EULAR Response at 12 months

Conclusion: Low dose bRTX is effective in DMARD refractory RA patients with similar improvements as regular dose, although CD19 depletion was less in low dose group. A larger study to establish radiographic regression with CD19 depletion and disease activity score can help in further strengthening the use of lower dose bRTX in RA leading to significant economic advantage.

REFERENCES:

[1] Chatzidionysiou K, Lie E, Nasonov E, Lukina G,et al. Rheumatic Diseases Portuguese Register. Effectiveness of two different doses of rituximab for the treatment of rheumatoid arthritis in an international cohort: data from the CERERRA collaboration. Arthritis Res Ther. 2016 Feb 16;18:50.

[2] Vital EM, Rawstron AC, Dass S, Henshaw K, Madden J, Emery P, McGonagle D. Reduced-dose rituximab in rheumatoid arthritis: efficacy depends on degree of B cell depletion. Arthritis Rheum. 2011 Mar;63(3):603-8.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2281

AB0224 SUSTAINABLE LOW DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: REAL-WORLD EXPERIENCE WITH TOCILIZUMAB

T. Shivacheva[1], T. Georgiev[1], S. Hristova[1], S. Dimitrov[1], S. Bogdanova-Petrova[1], G. Gerganov[2]. *[1]medical University "Prof. Dr. P. Stoyanov"- Varna, UMHAT "St. Marina", First Department of Internal Diseases, Clinic of Rheumatology, Varna, Bulgaria; [2]medical University "Prof. Dr. P. Stoyanov"- Varna, UMHAT "St.Marina", Department of Propaedeutics of Internal Medicine, Varna, Bulgaria*

Background: Sustainability, the ability of drugs to maintain remission or low disease activity (LDA) in patients with rheumatoid arthritis (RA), plays a crucial role for the prevention of structural damage to joints and thus, preserving patients' functional capacity, health-related quality of life and general sense of well-being. Therefore, studying the sustainable effectiveness of tocilizumab (TCZ) as a monotherapy or combined with methotrexate (MTX) is important (1).

Objectives: We aimed to examine to what extend TCZ, alone or combined with MTX, could achieve and further sustain LDA in patients with long-standing RA in the light of current, strictly index-based definitions of LDA and to compare the two versions of DAS28 in patients in real clinical practice

Methods: 85 RA patients treated with TCZ for at least eighteen months were consecutively enrolled in the present single-center, retrospective cohort study. All participants met the 1987 ACR classification criteria and attended the rheumatology department of University Hospital "St. Marina" Varna in an outpatient setting. Patients receiving pre-filled syringe contained 162 mg TCZ once weekly subcutaneously. Real-world data were extracted and analyzed from patient's full medical file. For each visit, disease activity score 28 with ESR and CRP (DAS28-ESR and DAS28-CRP) and simple disease activity index (SDAI) were calculated simultaneously according to generally adopted formulas. A twelve-month result was determined for sustained LDA at each of the patient's three visits (at 6-month intervals), according to DAS28 and SDAI. Descriptive statistics, Chi square test, Cochran´s Q test, kappa statistic were used, a binary logistics model was compiled to study the impact. Significance level of $p < 0.05$.

Results: Two hundred fifty-five patient visits were analyzed. The mean durations of RA and treatment with TCZ were 12.6 (±9.6) years and 3.64 (±1.8) years, respectively. The mean age of patients was 60.3 years (37-87 years), 80% were women, 24.7% were obese, 65.9% have concomitant hypertension. 61.2% of patients are treated with combination therapy TCZ with MTX.

Of all patients, these with a sustained 12-month LDA were 41.2%, 28.2% or 23.5% depending on the studied index (DAS28-CRP, SDAI, or DAS28-ESR, respectively).

A 12-month SDAI LDA was found in a significantly small proportion of patients (28.2%, p = 0.001). The DAS28 ESR determined a proportion similar to SDAI (23.5%, p> 0.05), while according to the DAS28 CRP, patients with a sustained 12-month LDA were significantly more (41.2% p = 0.005). A moderate level of agreement was found between the assessments of SDAI and the two variants of DAC28 when determining 12-month results of Tocilizumab treatment (DAS28-ESR k = 0.511, p <0.001 and DAC28-CRP k = 0.618, p <0.001). No relationship was found between the combination of TCZ with MTX and the patients' chance of a sustained 12-month LDA, regardless of which index the result was measured.

Patients with hypertension were significantly less likely to have sustained 12-month LDA according to SDAI and DAS 28 ESR (OR 0.135, 95% CI 0.048-0.386; OR 0.313, 95% CI 0.111-0.882, respectively), but not according to DAS28 CRP.

Conclusion: Sustained 12- month LDA with TCZ in patients with long-term RA remains uncommon in daily clinical practice. Co-administration of MTX is not associated with an increased likelihood of achieving a sustained LDA in the analysis of long-term responses. Patients with concomitant hypertension are less likely to be in a sustained 12-month LDA, according to SDAI and DAS28-ESR. The results according to DAS28 ESR, but not according to DAS28CRP are comparable to those of SDAI when measuring long-term results of treatment with TCZ.

REFERENCES:

[1] Hamann PDH, Pauling JD, McHugh N, Shaddick G, Hyrich K; BSR-BR-RA Contributors Group. Predictors, demographics and frequency of sustained remission and low disease activity in anti-tumour necrosis factor-treated rheumatoid arthritis patients. Rheumatology (Oxford). 2019 Dec 1;58(12):2162-2169.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2335

AB0225 TUMOR NECROSIS FACTOR ALPHA (TNF-α) INHIBITORS IN PATIENTS WITH REFRACTORY RHEUMATOID ARTHRITIS: REASONS FOR WITHDRAWAL

V. Sygyrta[1], E. Aronova[1], A. Lila[1], S. Glukhova[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Antirheumatic Drugs Safety Monitoring Laboratories, Moscow, Russian Federation*

Background: Refractory rheumatoid arthritis (RRA) is a subtype of rheumatoid arthritis (RA), in which the sequential administration of optimal methotrexate doses in combination with glucocorticoids, and at least - two biologic disease-modifying antirheumatic drugs (bDMARDs) with different mechanisms of action during 18-24 months does not lead to a significant decrease in the inflammatory activity of RA.

Objectives: to determine the reasons for the withdrawal of TNF-α inhibitors in patients with RRA.

Methods: The retrospective study included data of 95 RRA patients (80 females, 80.8%), aged 23 to 80 years (mean age 57 years), treated with TNF-α inhibitors. Mean RA duration was 11.9±7.6 years. All patients were divided into 6 groups depending on the number of the lines of therapy received. A total of 154 cases of TNF-α were studied.

Results: Infliximab (INF) was most often prescribed as the first line of therapy - 40 prescriptions. The reasons for the withdrawal of INF as the first bDMARDs were: insufficient effectiveness (IE) - 20 cases (50% of appointments), administrative reasons (AdmR) - 13 cases (32.5% of appointments), adverse reactions (AR) - 6 cases (15% of appointments), remission - 1 case (2.5% of appointments). In the 2nd line of therapy, INF was prescribed in only 3 cases, the drug was canceled in all cases due to IE. In 3 lines of therapy, INF was prescribed in 4 cases, the reasons for withdrawal in these cases were IE (50%, 2 cases) and AR (50%, 2 cases).

Etanercept (ETC) was prescribed as the first line of therapy in 10 cases. The most common reason for withdrawal was IE in 5 cases (50% of appointments), AR - 4 cases (40%), AdmR - 1 case (10%). ETC was prescribed as a 2 line in 15 cases, the reasons for withdrawal then were: IE - 11 cases (73.3%), AR - 1 case (6.7%), AdmR - 3 cases (20%). ETC was prescribed as a 3-line therapy in 20 cases. The reasons for withdrawal were as follows: IE - 8 cases (40%), AR - 4 cases (20%), AdmR - 8 cases (40%). As a drug of 4 lines of therapy, ETC was prescribed 1 time and was canceled due to the development of AR. As the 5th line, ETC was appointed in 1 case and was canceled due to IE. ETC was assigned as line 6 in 1 case. The reason for the withdrawal was AR.

Adalimumab (ADA) was prescribed as the first line of therapy in 19 cases, the reasons for withdrawal were: IE - 14 cases (73.7%), AR - 2 cases (10.5%), AdmR - 3 (15.8%). On line 2, ADA made 20 appointments, the reasons for withdrawal were: IE - 13 (65%), AR - 3 (15%), AdmR - 4 (20%). ADA was prescribed as

line 3 in 8 cases, the reasons for withdrawal were: IE - 6 (75%), AR - 1 (12.5%), AdmR - 1 (12.5%). As a 4-line drug, ADA was prescribed in 4 cases and was canceled in all cases due to IE. On line 5, ADA was assigned 1 time and was discontinuation due to IE.

Golimumab (GLM). He was appointed as the first line in 5 cases. The reasons for withdrawal were: IE - 1 case (20%), AdmR - 4 appointments (80%). As a 2-line drug, GLM was prescribed once and was canceled due to AdmR. The drug was not prescribed for the 3rd and 4th lines. As a 5-line therapy, it was prescribed once and was canceled due to IE.

When assessing the frequency of drug withdrawal due to IE or AR, no significant differences were found between the lines of therapy. Discontinuation rates were also not statistically different in the study groups.

Conclusion: The most common reason for the withdrawal of TNF-α in patients with RRA is IE. With an increase in the lines of TNF-α therapy, remission as a reason for withdrawal was not identified. As a result of the increase in the number of sequentially prescribed bDMARDs, the frequency of discontinuation of TNF-α in connection with IE did not decrease. A significant reason for cancellation is AdmR, to which we attributed the absence of the drug in the pharmacy network, financial reasons limiting the continuation o

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2347

AB0226 EVALUATION OF RITUXIMAB EFFICACY WITH VARIOUS COMPOSITE MEASURES OF INFLAMMATORY ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Y. Olyunin[1], D. Kusevich[2], E. Nasonov[3,4]. *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Early Arthritis, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Osteoarthritis, Moscow, Russian Federation*; *[3]V.A. Nasonova Research Institute of Rheumatology, Scientific Supervisor, Moscow, Russian Federation*; *[4]I.M. Sechenov First Moscow State Medical University, Ministry of Health of Russia (Sechenov University), Department of Therapy and Occupational Diseases, Moscow, Russian Federation*

Background: Disease modifying anti-rheumatic drugs (DMARD) can provide an unbalanced effect on individual components of the inflammatory process, which in some cases leads to an insufficiently correct assessment of the patient's status when using composite activity indices [1].

Objectives: To compare the results of the rituximab (RTX) efficacy assessment in patients with rheumatoid arthritis (RA) using different composite indices of disease activity.

Methods: Patients with active RA observed in 23 medical centers of the Russian Federation were included. They were randomized into 2 groups in a 2:1 ratio. In the main group methotrexate (MTX) was prescribed at 15 mg per week and RTX infusions 600 mg on days 1 and 15. Patients in the control group received MTX 15 mg per week and placebo on days 1 and 15. If after 15 weeks 20% reduction of tender joint count (TJC) and swollen joint count (SJC) was not achieved, another DMARD was prescribed.

Results: 159 RA patients (131 women and 18 men) were included. The mean age of patients was 51.4±11.8 years, the median duration of RA – 2.8 [0.6; 5.8] years. At baseline DAS28, SDAI and CDAI in all cases assessed disease activity as high. 6 months after RTX administration DAS28 showed remission in 9%, low, moderate and high activity activity in 7%, 47% and 37% of cases, SDAI – in 7%, 12%, 34% and 47%, CDAI – in 7%, 11%, 30% and 52%, respectively. In the control group remission, low, moderate and high activity by DAS28 were revealed in 2%, 2%, 38% and 58%, by SDAI – in 2%, 4%, 35%, 59%, by CDAI – in 2%, 6%, 29%, 63% of patients respectively. After 6 months, in patients achieved the treatment target (remission or low activity) according to DAS28, SJC in 12 cases was 0, in 3 – 1 and in 1 – 2. TJC was 0 in 9 cases and in 7 patients ranged from 1 to 14. The level of C-reactive protein (CRP) in 14 cases was within the normal range and in 2 – increased. Erythrocyte sedimentation rate (ESR) was normal in all cases. SDAI after 6 months showed the target activity in 18 patients treated with RTX. In 12 of them the SJC was 0, in 4 – 1 and in 2 – 2. In 9 cases TJC was 0, in the rest patients it varied from 2 to 5. The level of CRP was normal in 15 patients, ESR – in all patients. CDAI met the target activity in 17 patients. In 12 of them, SJC was 0, in 3 – 1, in 2 – 2. The level of CRP was normal in 14, ESR – in all patients.

Conclusion: Assessment of RTX efficacy with DAS28, SDAI, and CDAI in RA provided comparable number of patients who achieved remission or low disease activity 6 months after administration of the drug. The groups of patients who reached this target level of activity by DAS28, SDAI, and CDAI did not have significant differences in the values of main measures characterizing residual inflammatory activity, including SJC, TJC, ESR, and CRP.

REFERENCES:

[1] Bastida C, Soy D, Ruiz-Esquide V, Sanmartí R, et al. Br J Clin Pharmacol. 2019 Aug;85(8):1710-1718.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2354

AB0227 SAFETY AND EFFECTIVENESS OF ADALIMUMAB REFERENCE PRODUCT AND BIOSIMILAR IN PATIENTS WITH INFLAMMATORY ARTHROPATHIES

W. G. Rojas Zuleta[1], O. J. Felipe Díaz[1], C. Orozco Gonzalez[2], J. Barbosa Camacho[2], C. L. Giraldo Herrera[1], J. G. Ballesteros[1], J. H. Donado Gómez[2], N. Duque Zapata[2]on behalf of Medicarte Research Group. *[1]Medicarte SAS, Rheumatology, Medellin, Colombia*; *[2]Medicarte SAS, Research, Medellin, Colombia*

Background: Biological therapy revolutionized the treatment and prognosis of inflammatory arthropathies; however, its high cost has an economic impact on health system and limits its access. Biosimilars are products with similar molecular structure, equivalent efficacy, and comparable safety and immunogenicity, which arise as a necessity to reduce costs. Although, their long-term safety is still to be confirmed[1].

Objectives: Our aim is to compare the safety and effectiveness between adalimumab reference product and biosimilar in patients with inflammatory arthropathies.

Methods: Cohort study of 92 patients with ankylosing spondylitis (AS), rheumatoid arthritis (RA) and psoriatic arthritis (PsA) in a specialized multicenter health institution in Colombia. Ratio of incidence rates (IR) for Adverse Drug Reactions (ADR) and therapeutic failure (TF) is estimated among patients exposed to reference product and biosimilar. 95% confidence interval (CI) for the ratio is also calculated. ADR and TF Incidences in both groups were calculated using the Kaplan Meier curve.

Results: Between October 2019 and October of 2020, 92 patients started adalimumab, 64% (n = 59) reference product and 36% (n = 33) biosimilar (18 naive and 15 switch). 41.3% of patients had a diagnosis of RA, 35% AS and 24% PAs. Additionally, 62% were women, with median age of 53 years (Interquartile Range (IQR): 41-62); disease evolution time of 9 years (IQR: 5-20); and treatment time of 0.8 years (IQR: 0.4-1.04). No statistically significant differences were found according to the drug between diagnosis, evolution time, or disease activity. Of all patients 21 presented ADR; 11 events with reference product (IR 0.18 per 100 person-years), and 10 with biosimilar (IR 0.30 per 100 person-years), IR ratio of 0.61 (95%CI 0.26-1.44; p-value = 0.36). From ADR reactions, 35% were infections, 13% skin disorders and 7.4% hepatobiliary disorders; all were classified as non-serious ADR. 5 TF events were presented, 3 with reference product (IR 0.05 per 100 person-years) and 2 with biosimilar (IR 0.06 per 100 person-years); IR ratio of 0.83 (95% CI 0.09-10.04; p value= 1.00). There was no statistically significant between reference product and biosimilar in time of ADR presentation (Log Rank Test 0.74; p= 0.39) or on TF (Log Rank Test 0.55; p= 0.45).

Conclusion: Results shown that analyzed biosimilar is a safe product with a similar rate of ADR and without differences in effectiveness evaluated by TF, although 95% CIs are imprecise. This suggests that use of biosimilars in a real-life setting could be safe and with similar effectiveness, which is correlated with other studies carried out in RA and is an appropriate measure to reduce treatment costs in patients with inflammatory arthropathy.

REFERENCES:

[1]Cohen, S. B. *et al.* Long-term safety, efficacy, and immunogenicity of adalimumab biosimilar BI 695501 and adalimumab reference product in patients with moderately-to-severely active rheumatoid arthritis: results from a phase 3b extension study (VOLTAIRE-RAext). *Expert Opin. Biol.Ther.* **19**, 1097–1105 (2019).

Acknowledgements: To Medicarte for the support

Disclosure of Interests: Wilmer Gerardo Rojas Zuleta Speakers bureau: Pfizer, Jannsen Cilag, Novartis, Bristol Myers Squibb, Biopass, Amgen, Paid instructor for: Pfizer, Jannsen Cilag, Novartis, Bristol Myers Squibb, Biopass, Amgen, Oscar Jair Felipe Díaz Speakers bureau: Amgen, Jannsen Cilag, Bristol Myers Squibb, Novartis, Ely-Lilly, Catalina Orozco Gonzalez: None declared, Jhyld Barbosa Camacho: None declared, Claudia Lucía Giraldo Herrera Speakers bureau: Jannsen Cilag, Bristol Myers Squib, Amgen, Pfizer, Novartis, Roche, Paid instructor for: Jannsen Cilag, Bristol Myers Squib, Amgen, Pfizer, Novartis, Roche, Jesús G Ballesteros Speakers bureau: Bristol Myers, Pfizar, Amgen, Jannsen Cilag, Paid instructor for: Bristol Myers, Pfizar, Amgen, Jannsen Cilag, Jorge Hernando Donado Gómez: None declared, Natalia Duque Zapata: None declared

DOI: 10.1136/annrheumdis-2021-eular.2592

AB0228 LONG-TERM EFFECTIVENESS, DRUG SURVIVAL OF BIOLOGIC THERAPIES IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS AND PREDICTIVE FACTORS OF DRUG DISCONTINUATION DUE TO DISEASE REMISSION

K. Preedeekanit[1], A. Koolvisoot[2]. *[1]Faculty of Medicine Siriraj Hospital, Mahidol University, Department of Medicine, Bangkok, Thailand*; *[2]Faculty of Medicine*

Table 1. Effectiveness, Drug Survival and Causes of Biologic Discontinuation in RA and SpA

RA % (87 cases)

Biologics	Total % (N)	5-year Remission rate %	5-year Drug survival rate %	Discontinuation % (N 53 cases)					
				Total % (53)	Remission	Inadequate response	Side effect	Non-adherence/ Refer	Death
Etanercept	49.4 (43)	23.9	33.6	50.9(27)	14.8(4)	44.4(12)	22.2(6)	11.1(3)	7.4(2)*
Infliximab	5.7 (5)		36	5.7 (3)	0(0)	33.3(1)	33.3(1)	33.3(1)	(0)
Rituximab	44.8 (39)		40.7	43.4 (23)	56.5(13)	17.4(4)	4.3(1)	13.0(3)	8.7(2)
SpA %(49 cases)									
Biologics	Total % (N)	5-year Remission rate %	Drug survival rate %	Discontinuation % (N 23 cases)					
				Total % (23)	Remission	Inadequate response	Side effect	Non-adherence/ Refer	Death
Etanercept	83.6 (41)	66.7	50.3	78.3(18)	22.2(4)	22.2(4)	33.3(6)	22.2(4)	0(0)
Infliximab	16.4 (8)		0	21.7 (5)	20(1)	20(1)	40(2)	20(1)	0(0)

**Cause of death: sudden cardiac death (1), intraabdominal infection (1)*
Cause of death: pneumonia (1), Lung cancer (1)

Siriraj Hospital, Mahidol University, Division of Rheumatology, Department of Medicine, Bangkok, Thailand

Background: Rheumatoid arthritis (RA) and spondyloarthropathies (SpA) are chronic rheumatic diseases that can progress to disability if left uncontrolled. Biologic therapies can induce remission in patients with inadequate response or intolerance to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs). Due to the safety and economic concern, updated treatment recommendations now consider biologics discontinuation in patients with persistent remission. However, available data are still limited.
Objectives: To evaluate the biologics effectivenss, drug survival, rate of discontinuation in real-life practice and to identify predictors of biologics discontinuation due to remission in RA and SpA.
Methods: A total of 87 patients with RA and 49 patients with SpA, starting biologics between January 2005 and October 2020, were recruited from the Rheumatic Disease Prior Authorization (RDPA) registry of Siriraj hospital. Baseline data were recorded. Time-dependent rates in achieving remission were calculated. Cumulative probability of biologics discontinuation and predictive factors of drug discontinuation due to remission were analyzed.
Results: The biologics used in RA patients were Etanercept (49.4%), Rituximab (44.8%), and Infliximab (5.7%). The 1- and 5- year remission rates were 8.5% and 23.9%, respectively. Drug survival rates were 33.6% for Etanercept, 40.7% for Rituximab, and 36% for Infliximab at five years. The main reasons for drug discontinuation were disease remission (32.1%), inadequate response (32.1%), and side effects (15.1%). Rituximab had the highest discontinuation rate due to remission (56.4%). There was no predictive factor for biologics discontinuation due to remission.
SpA patients were treated with Etanercept (83.6%) and Infliximab (16.4%). The 1- and 5- year remission rates were 67.4% and 66.7%, respectively. Drug survival rates were 50.3% for Etanercept and 0% for Infliximab at five years. Biologics withdrawal due to side effects occurred in 16%, inadequate response in 10%, and disease remission in 10% of patients. The predictive factor for biologics discontinuation due to remission was disease duration < 5 years (Hazard ratio 6.92, 95%CI 1.10, 43.29)
Conclusion: Biologic therapies are effective in patients with active RA and SpA despite csDMARDs treatment. The highest drug survival rates are Rituximab in RA and Etanercept in SpA. Infliximab has the shortest drug retention rate in SpA. Drug discontinuation due to remission is more successful in RA patients, particularly in the Rituximab group. The best predictor for biologics discontinuation due to remission in SpA is the disease duration of fewer than five years.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2776

AB0229

A NATIONAL, MULTICENTER, SECONDARY DATA USE STUDY EVALUATING EFFICACY AND RETENTION OF FIRST-LINE BIOLOGIC TREATMENT WITH TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-LIFE SETTING FROM TURKBIO REGISTRY

A. Yazici[1], Ö. Özdemir Işık[1], E. Dalkılıç[2], S. S. Koca[3], Y. Pehlivan[2], S. Şenel[4], N. Inanc[5], S. Akar[6], S. Yılmaz[7], Ö. Soysal Gündüz[8], A. Cefle[1], F. Onen[9].
[1]Kocaeli University Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, Kocaeli, Turkey; *[2]Uludağ University Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, Bursa, Turkey*; *[3]Fırat University Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, Elazığ, Turkey*; *[4]Erciyes University Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, Kayseri, Turkey*; *[5]Marmara University Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, İstanbul, Turkey*; *[6]Katip Çelebi University Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, İzmir, Turkey*; *[7]Selçuk University Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, Konya, Turkey*; *[8]Celal Bayar University Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, Manisa, Turkey*; *[9]Dokuz Eylül University Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, İzmir, Turkey*

Background: Tocilizumab (TCZ) is a human anti-interleukin (IL)-6 receptor antibody approved in Turkey for the treatment of rheumatoid arthritis (RA).
Objectives: In this study our purpose was to describe the disease activity, quality of life (QoL), and retention rate in RA patients who were prescribed TCZ as first-line biologic treatment in a real-world setting.
Methods: Anonymized patient registry of TURKBIO was used based in a national, multicenter, and retrospective context. We conducted a search in the registry between years 2013 and 2020 and included adult RA patients who were prescribed with TCZ as their first-line biologic treatment with a post-TCZ follow-up of at least 6 months. CDAI, DAS28-(ESR), and HAQ-DI scores in 6, 12, and 24 months were obtained. Pairwise comparison was carried out for survey scores across baseline and timepoints. Subgroup analysis for route of TCZ administration was performed. EULAR response criteria were used for response evaluation. Retention of TCZ was evaluated by Kaplan-Meier analysis.
Results: Overall,130 patients with a mean RA duration of14 years were included in the study. 87.7% of the patients were female and mean age was53 (SD; 15.0). Median duration of follow-up was 18.5 months. Majority (90.8%) of patients were given tocilizumab via intravenous route at baseline. Number of patients with ongoing TCZ treatment and follow-up at 6, 12, and 24 months were 121 (93%), 85 (65%), and 46 (35%), respectively. Remission rates at 6, 12, and 24 months per CDAI (<2.8) and DAS28-(ESR) (<2.6) scores were 61.5%, 44.6%, 30%, and 54.6%, 40.8%, 27.7%, respectively. CDAI, DAS28-(ESR) and HAQ-DI survey scores significantly improved at 6, 12 and 26 months, respectively (p<0.001) (Table 1) in both IV and SC TCZ subgroups. At 6, 12 and 24months 74.8%, 82.5% and 86.4% of patients achieved a EULAR good response respectively. Twenty-three patients (17.6%) discontinued TCZ at 24 months. Of these, 19 patients discontinued due to unsatisfactory response. Retention rates of TCZ at 6, 12, and 24 months were 93%, 84.3%, and 72.2%, respectively (Figure 1).
Conclusion: TCZ as a first-line biologic treatment was found to be clinically effective in this real-world study with a high retention rate. These results are in line with the results gathered from previous TCZ controlled and real-life studies in which TCZ was found clinically safe and effective.

REFERENCES:

[1] Haraoui B, Casado G, Czirjak L, Taylor A, Dong L, Button P, Luder Y, Caporali R. Tocilizumab Patterns of Use, Effectiveness, and Safety in Patients with Rheumatoid Arthritis: Final Results from a Set of Multi-National Non-Interventional Studies. Rheumatol Ther. 2019 Jun;6(2):231-243.
[2] Favalli EG, Raimondo MG, Becciolini A, Crotti C, Biggioggero M, Caporali R. The management of first-line biologic therapy failures in rheumatoid arthritis: Current practice and future perspectives. Autoimmun Rev. 2017 Dec;16(12):1185-1195.
[3] Haraoui B, Jamal S, Ahluwalia V, Fung D, Manchanda T, Khraishi M. Real-World Tocilizumab Use in Patients with Rheumatoid Arthritis in Canada: 12-Month Results from an Observational, Noninterventional Study. Rheumatol Ther. 2018 Dec; 5(2): 551–565.

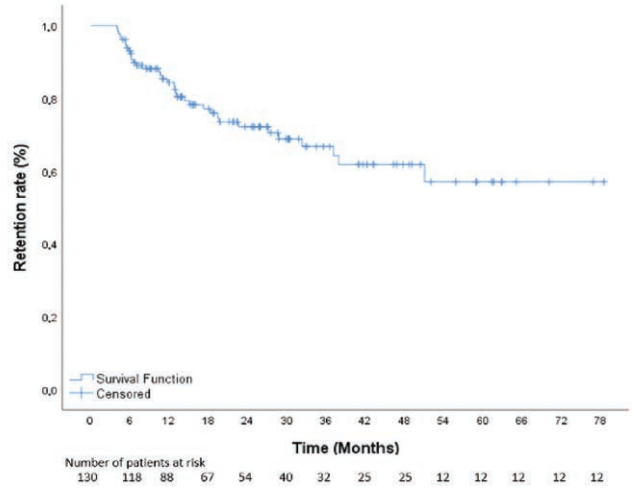
Table 1. Pairwise CDAI, DAS28-(ESR) and HAQ-DI scores at baseline, 6-, 12- and 24-month.

Survey	Pair	N	Median (min-max)	p value*
CDAI	Baseline	113	19,5 (0-47)	<0.001
	6 months		2 (1-24,5)	
	Baseline	74	20,1 (8,4-47)	<0.001
	12 months		1,8 (1-5,2)	
	Baseline	41	17,2 (9-38)	<0.001
	24 months		1,7 (1,2-3,7)	
DAS28-(ESR)	Baseline	112	5,2 (3,3-7,2)	<0.001
	6 months		2,2 (0,3-6,7)	
	Baseline	78	5,3 (3,4-7,2)	<0.001
	12 months		2 (0-5,2)	
	Baseline	41	5,2 (3,4-6,9)	<0.001
	24 months		1,8 (0-3,6)	
HAQ-DI	Baseline	118	0,95 (0-2,875)	<0.001
	6 months		0,5 (0-2)	
	Baseline	81	1 (0-3)	<0.001
	12 months		0,25 (0-2,5)	
	Baseline	43	0,875 (0-2,125)	<0.001
	24 months		0 (0-1,13)	

**Wilcoxon Signed Rank Test*

Disclosure of Interests: Ayten Yazici Speakers bureau: PFIZER, AbbVie, NOVARTIS, Özlem Özdemir Işık: None declared, Ediz Dalkılıç Speakers bureau: AbbVie, UCB Pharma, PFIZER, Roche, MSD, NOVARTIS, Süleyman Serdar Koca Speakers bureau: MSD, NOVARTIS, GILEAD, PFIZER, ABDI IBRAHIM, UCB Pharma, AMGEN, SANOFİ, Yavuz Pehlivan Speakers bureau: PFIZER, NOVARTIS, MSD, CELLTRION, Consultant of: PFIZER, Soner Şenel: None declared, Nevsun Inanc Speakers bureau: NOVARTIS, PFIZER, ABDI IBRAHIM, JANNSEN, Paid instructor for: NOVARTIS, PFIZER, ABDI IBRAHIM, JANNSEN, Consultant of: NOVARTIS, PFIZER, ABDI IBRAHIM, JANNSEN, Grant/research support from: NOVARTIS, PFIZER, ABDI IBRAHIM, JANNSEN, Servet Akar Speakers bureau: LILLY, MSD, NOVARTIS, GILEAD, PFIZER, ABDI IBRAHIM, JANNSEN, UCB Pharma, AMGEN, Paid instructor for: LILLY, NOVARTIS, GILEAD, PFIZER, ABDI IBRAHIM, UCB, AMGEN, Grant/research support from: PFIZER, Sema Yılmaz: None declared, Özgül Soysal Gündüz: None declared, Ayse Cefle Speakers bureau: UCB Pharma, PFIZER, MSD, AbbVie, AMGEN, NOVARTIS, Fatos Onen Speakers bureau: AbbVie, LILLY, MSD, NOVARTIS, GILEAD, PFIZER, ABDI IBRAHIM, JANNSEN, UCB Pharma, AMGEN, İbrahim Etem-MENARINI, Paid instructor for: AbbVie, LILLY, NOVARTIS, GILEAD, PFIZER, ABDI IBRAHIM, UCB Pharma, AMGEN, İbrahim Etem-MENARINI, Grant/research support from: PFIZER

Figure 1. Kaplan-Meier analysis of TCZ retention.



DOI: 10.1136/annrheumdis-2021-eular.2928

AB0230 **OPTIMIZED TREATMENT OF BIOLOGICAL DISEASE MODIFYING DRUGS IN ROUTINE CLINICAL PRACTICE: SURVIVAL STUDY ANDANALYSIS OF PATIENT CHARACTERISTICS**

A. De Diego Sola[1], N. Alcorta Lorenzo[1], C. A. Egües[1], L. M. Lopez Dominguez[1], O. Maiz-Alonso[1], J. J. Cancio Fanlo[1], E. Uriarte Isacelaya[1], M. B. Irastorza Larburu[2], M. A. Aranguren Redondo[2], J. M. Belzunegui Otano[1]. [1]*Hospital Universitario Donostia, Rheumatology Service, San Sebastian, Spain*; [2]*Hospital Universitario Donostia, Pharmacology Service, San Sebastian, Spain*

Background: Biological disease modifying drugs (bDMARD) has allowed a targeted approach to rheumatoid arthritis (RA). Once sustained remission is achieved, the use of bDMARDs at lower doses than indicated in data sheets is considered (optimized treatment, OT). Studies show that 33-64.2% of patients on OT lose remission in the first 6 months. Still, it is a feasible practice in selected patients.

Objectives: We aimed to describe demographic, clinical, analytical and therapeutic characteristics of RA patients on OT in our hospital. Secondly, we wanted to study the survival of OT and to compare patients with survival longer or shorter to one year.

Methods: We did a retrospective review of the medical records of RA patients who began OT between January 2014 and December 2018. We included patients on Abatacept(ABA), anti-TNF drugs and Tocilizumab (TCZ). We defined the end of OT as the restart of the usual dose. Continuous variables are described with mean and standard deviation (SD) and qualitative variables are shown in absolute value and percentage. We divided the sample into patients with OT survival greater than or equal to one year and patients with OT survival less than one year, after which the characteristics of both populations were compared. Categorical variables were analyzed using Pearsons chi and quantitative variables using Student's t-test. Survival analysis was performed using a Kaplan-Meier estimator.

Results: We identified 234 RA patients on bDMARD at our hospital, of which 53 (22.6%) had been optimized between January 2014 and December 2018: 39 (73.6%) with anti-TNF, 7 (13.2) with ABA and 7 (13.2%) with TCZ. Their characteristics are shown in table 1. It is worth mentioning the rate of monotherapy (43.3%)and the low number of bDMARD prior to optimization (median 0.71, SD 0.97). The median survival of OT was 33.8 months and thirty-nine patients (73.6%) maintained OT for at least one year (95%confidence interval, 0.59 to 0.83). When comparing patients with survival greater/equal versus shorter to one year (table 2), the only variable showing significant differences was the presence of erosions at beginning of OT (28 patients in the >1 year group vs 7 in the < 1 year group; p=0.012). Although the difference is not significant (p = 0.07), patients with a survival of less than one year had more time between the debut of disease and the beginning of the first conventional synthetic DMARD (csDMARD).

Table 1. Characteristics of the sample (N=53)

Female	40 (75.47%)
Age at diagnosis (years)	49.54 (11.68)
Active smoker	15 (33.33%)
ACPA positive	36 (67.92%)
mRF positive	44 (83.02%)
Nodules	11 (20.75%)
Extra-articular disease	11 (20.75%)
Erosions*	35 (74.47%)
Monotherapy at optimization	23 (43.4%)
bDMARD* previous to OT	0.71 (0.97)
Optimized bDMARD	
• ETN	20 (37.74%)
• ADA	16 (30.19%)
• ABA	7 (13.21%)
• TCZ	7 (13.21%)
• GOL	2 (3.77%)
• CZB	1 (1.89%)
DAS28 at	
• Diagnosis	4.88 (1.25)
• Beginning – 1st sDMARD	4.62 (1.6)
• Beginning – 1st bDMARD	4.98 (1.06)
• Beginning – opt bDMARD	4.67 (1.17)
• Optimization	1.88 (0.65)
Months from diagnosis to introduction of 1st sDMARD*	19.67 (35.01)
Months from disease debut to low activity*	38.75 (30.34)
Months in low activity until start of OT	23.73 (22.47)

ACPA: anti-citrullinated protein antibodies; mRF: monoclonal rheumatoid factor; Erosions: presence of erosions at Optimization; bDMARD: biological DMARD; ETN: Etanercept; ADA: Adalimumab; ABA:Abatacept; TCZ:Tocilizumab; GOL:Golimumab; CZB:Certolizumab; Opt bDMARD: bDMARD optimized; csDMARD: conventional synthetic DMARD; Low activity: DAS28 < 3.2

Conclusion: OT is a therapeutic option from which some patients could benefit. Maintenance of OT may be related to early start of DMARDs. More studies are needed to define the characteristics of patients who can safely benefit from OT.

REFERENCES:
[1] Henaux S et al. Risk of losing remission, low disease activity or radiographic progression in case of bDMARD discontinuation or tapering in rheumatoid arthritis: systematic analysis of the literature and meta-analysis. Ann Rheum Dis 2018;77:515–522.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3045

AB0231 OUTCOMES IN RHEUMATOID ARTHRITIS PATIENTS UNDER TOCILIZUMAB AS FIRST BDMARD: A REAL-LIFE MONOCENTRIC COHORT STUDY

F. R. Martins[1], A. Martins[2], D. Santos Oliveira[2,3], D. Fonseca[4], M. Rato[2], F. Oliveira Pinheiro[2], S. Garcia[2], B. M. Fernandes[2], L. Costa[2], M. Bernardes[2]. *[1]Centro Hospitalar Universitário do Algarve - Faro, Rheumathology, Faro, Portugal; [2]Centro Hospitalar Universitário São João, Rheumathology, Porto, Portugal; [3]Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal; [4]C. H. Vila Nova de Gaia/ Espinho, Rheumathology, Vila Nova de Gaia, Portugal*

Background: Rheumatoid arthritis (RA) is one of the most frequent systemic inflammatory rheumatic diseases, being constantly assessed regarding new disease activity monitoring tools and new therapeutic targets and therapies. Tocilizumab (TCZ) is one of the latest biological disease-modifying antirheumatic drugs (bDMARDs) approved for RA's treatment, usually as a second line agent in daily clinical practice.
Objectives: Evaluate the different disease and patient reported outcomes in patients undergoing treatment with tocilizumab as the first biologic therapy.
Methods: All patients with a definite RA diagnosis who had undergone treatment with TCZ as the first biologic therapy at a tertiary hospital's rheumatology department were included in this analysis. Diverse socio-demographic data, as well as disease and patient related outcomes were assessed at baseline, 6 and 12 months of treatment with TCZ, and posteriorly extracted from the Portuguese register of rheumatic diseases (Reuma.PT). Statistical analysis included non-parametric tests such as Wilcoxon test and univariate analysis using linear and logistic regression models.
Results: Fifty-one patients were included, 88.2% females, with a median age at introduction of TCZ of 53.5 +/- 10.4 years; mainly seropositive for either rheumatoid factor (66%) or anti citrullinated peptide antibody (ACPA; 68%), with an erosive disease (75.6%) and concomitantly treated with a conventional synthetic disease modifying anti-rheumatic drug (csDMARD) (70.5%). During follow-up there was a statistically significant reduction at 6 and 12 months of TCZ treatment regarding DAS28 (4 variables) (4v) and DAS28(4V)-CRP scores ($p < 0.001$), SDAI ($p < 0.001$), CDAI ($p < 0.001$), 68/66 tender and swollen joint counts (TJC/SJC) ($p < 0.001$), ESR and CRP ($p < 0.001$), patient and physician VAS ($p < 0.001$) and HAQ score ($p = 0.01$ at 6 months and $p < 0.001$ at 12 months). Rheumatoid factor and ACPA serum levels weren't statistically different at 6 and 12 months of treatment with TCZ compared to the initial assessment, as well as the ACR responders at the same 6 months versus those at 12 months. A majority of patients showed good EULAR response at 6 (52.6%) and 12 (56.3%) months, as well as moderate to high mean improvement in ACR core set measures at 6 (53.3±22.7) and 12 (54.3±25.2) months. Assessment of subsequent therapeutic maintenance showed that 75% of patients remained under tocilizumab with an average treatment duration of 48.8±37.7 months. Reasons for switch ranged from adverse effects (63.6%) to primary failure (18.2%) and secondary failure (18.2%). There was a significant reduction in DAS28(4V), DAS28(4V)-CRP, CDAI, SDAI, TJC and SJC, ESR, CRP, patient and physician VAS and HAQ scores between 6 and 12 months of therapy ($p < 0,001$). ACR and EULAR responses didn't differ significantly between assessments at 6 and 12 months. In the absence of a representative number of RA patients on TCZ monotherapy, it wasn't possible to draw conclusions about the need to use combined therapy with a csDMARD for better clinically significant response.
A higher degree of ACR response at 6 months was associated with higher serum rheumatoid factor levels (OR 1.13, $p < 0.05$) at baseline, while a lower degree of response was seen with higher TJC ($p = 0.05$) and HAQ score ($p < 0.01$). ACR response at 12 months was lower in patients with erosive disease at baseline ($p < 0.05$). Regarding EULAR response criteria at 6 months, there was a negative association with higher TJC ($p < 0.05$), while at 12 months the negative trend was associated with ESR levels ($p < 0.05$) and HAQ scores ($p < 0.05$) at baseline.
Conclusion: There seems to be evidence of good therapeutic response to TCZ in bDMARD naïve RA patients assessed at 6 months from baseline, without evidence of significant improvement of response measures further down the line. Basal serum rheumatoid factor levels, TJC, HAQ scores and the presence of erosive disease may have some predictive value on the therapeutic response. Further studies comparing TCZ as the first bDMARD in naïve RA patients against TNF inhibitors are needed.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3110

AB0232 PREVALENCE OF INFECTIONS UNDER BIOTHERAPY DURING RHEUMATOID ARTHRITIS

K. Baccouche[1], R. Grassa[1], S. Lataoui[1], O. Jomaa[1], N. El Amri[1], H. Zeglaoui[1], E. Bouajina[1]. *[1]Farhat Hached Hospital, Rheumathology, Sousse, Tunisia*

Background: Biologic therapies are emerging as a significant therapeutic option for many with debilitating inflammatory and autoimmune conditions including rheumatoid arthritis (RA).These biological agents are highly effective in RA. Potential complications are dominated by infections.
Objectives: To evaluate the different infections occurred under biotherapy.
Methods: This is a descriptive retrospective study including patients under biotherapy, hospitalized between 2000-2016 in the Rheumatology Department of Farhat Hached hospital in Sousse,Tunisia. We evaluated for each patient the different infections that have occurred, specifying the different types of biotherapy received.
Results: Sixty one patients are included (54 women and 7 men).The average age is 55.33 years ±11.51 [34-81 years].We found 47 infections in 40 patients (65.57%) with at least one infection under biotherapy: 41 women and 6 men with a mean age at 57.72 years [34-81 years]. Infections occurred under anti IL6 in 46.32%, Infliximab in 31.58%, anti CD20 in 11.58%, Etanercept in 7.37% and under Certolizumab in 3.16%. The infection was bacterial in 68.42%: 28 pulmonary infections, 8 oto rhino laryngology infections, 14 urinary infections, 2 soft tissue abscess, 13 cutaneous infections, 02 ocular infections. A viral origin of the infection was noted in 12.63% of cases. As for mycosis infections they represent 18.75% of the etiologies identified. The treatment was medical in 100% of cases and the evolution was favorable in all patients without resorting to the definitive discontinuation of biotherapy.
Conclusion: The infections reported in our series are much more frequent under anti IL6 treatment and bacteria are the most incriminating pathogenic agents in our patients.
REFERENCES:
[1] Simon, T. A.,and al. Comparative risk of malignancies and infections in patients with rheumatoid arthritis initiating abatacept versus other biologics: a multi-database real-world study. Arthritis Research & Therapy, 21(1). (2019).
[2] Pawar, A.,and al Risk of serious infections in tocilizumab versus other biologic drugs in patients with rheumatoid arthritis: a multidatabase cohort study. Annals of the Rheumatic Diseases, annrheumdis–2018–214367(2019).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3197

AB0233 REASONS AND RISK FACTOR FOR DISCONTINUATION OF BIOLOGIC AGENTS FOR RHEUMATOID ARTHRITIS PATIENTS IN LONG-TERM OBSERVATION

K. Terabe[1], N. Takahashi[1], S. Asai[1], Y. Hirano[2], Y. Kanayama[3], T. Kojima[1]. *[1]Nagoya University School of Medicie, Orthopedic Surgery, Nagoya, Japan; [2]Toyohashi Municipal Hospital, Rheumatology, Toyohashi, Japan; [3]Toyota Kosei Hospital, Orthopedic Surgery, Toyota, Japan*

Background: Rheumatoid arthritis (RA) patients who failed a first biologic agent due to any reasons have the option of switching to a second one along with the strategy of biologic agent treatment. Patients go over switching to the next one at failing their biologic agent. On the other hand, there are some patients who discontinue any biologic agent treatment due to various reasons such as tolerability concern, complications, economic issue, remission and so on[1 2]. The impact of this concern has been less studied.
Objectives: The objective of this study was to investigate the reasons and the risk factors for discontinuation any biologic agent in RA patients.
Methods: To Include patients who are observed long-term, patients who underwent biologic agent treatment between 2003 and 2007 at Nagoya University Hospital and 12 other institutes (Tsurumai Biologics Communication Study Group) were enrolled. 570 patients who were confirmed continuation or discontinuation of biologic agent treatment were enrolled. The last observation was September 2017. We analyzed the retention rate of biologic agent treatment and the reasons for discontinuation. To identify the risks for discontinuation, baseline demographics were compared between the continuing group and the disc continuing group using cox hazard regression analysis.
Results: In total 570 patients, the average duration of treatment with biologics was 6.6±3.3 (years) and total patient-year was 3739 in this study. 458 patients were administered biologics continuously, 112 patients were withdrawn. Table 1 showed the demographic data in total patients. The retention rate was 96.0% (discontinuation n=23) at least 1 year from starting biologics treatment, 92.6% (n=42) at 3 years, 88.2% (n=67) at 5 years, 84.4% (n=89) at 7 years, 81.1% (n=108) at 10 years. In 112 patients who discontinued, the reasons were adverse events in 74 patients, lack of effectiveness in 11 patients, others in 27 patients. Comparison of incidence for discontinuation using cumulative hazard function, the reason of adverse events was significantly higher than others reasons

(Figure 1). To identify the risks of discontinuation, we analyzed by multivariable Cox proportional hazard modeling in patients who discontinued treatment due to adverse events, the risk factors (hazard ratio: HR, confidence interval: CI) were over 3 of Steinblocker class (HR 1.85 [1.02-2.04]), age (HR:1.07 [1.04-1.10]) and Non-concomitant with methotrexate (HR 1.90 [1.08-3.33]) (Figure 2).

Table 1.

Age (years)	56.1 ± 13.4
Gender	
n (% male)	110 (19%)
n (% female)	460 (81%)
Disease duration (years)	11.1 ± 9.8
stage	
1,2	104 (19%)
3,4	455 (81%)
class	
1,2	336 (60%)
3,4	225 (40%)
Methotrexate use, no (%)	400 (70%)
Glucocorticoid use, no (%)	262 (47%)
Rheumatoid Factor, no (%)	287 (65%)
anti CCP antibody, no (%)	137 (87%)

Conclusion: The most common reason for discontinuation was adverse events in long term observation. The risk factors for discontinuation were class, age, and non-concomitant MTX. These results suggested that comorbidity has a significant impact on continuation rates because there are some reasons of non-concomitant MTX in addition to relate with age and the activities of daily living.

REFERENCES:

[1] Marussa B, et al. j.clin thera. 2011; 33(7): 901-913
[2] Alejandro S, et al. Rheumatol. 2016; 55(3): 523-34

Figure 1

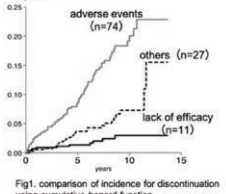


Fig1. comparison of incidence for discontinuation using cumulative hazard function

Figure 2

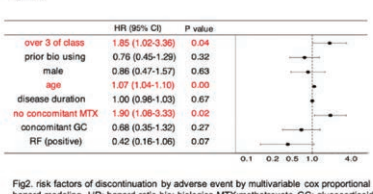


Fig2. risk factors of discontinuation by adverse event by multivariable cox proportional hazard modeling. HR: hazard ratio bio: biologics MTX:methotrexate GC: glucocorticoid RF: rheumatoid factor

Disclosure of Interests: KENYA TERABE: None declared, Nobunori Takahashi Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Janssen, Mitsubishi Tanabe, Ono, Pfizer, Takeda, and UCB Japan, Shuji Asai Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Janssen, Takeda, and UCB Japan, Yuji Hirano Speakers bureau: Tanabe-Mitsubishi, Pfizer, Eisai, Abbie, Chugai, Bristol-Meyers, Jansen, Astellas, UCB, Eli-Lilly, Asahikasei, Daiichi-Sankyo, Amgen, Yasuhide Kanayama: None declared, Toshihisa Kojima Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda, Consultant of: AbbVie, Grant/research support from: Chugai, Eli Lilly, Astellas, Abbvie, and Novartis

DOI: 10.1136/annrheumdis-2021-eular.3387

AB0234 SURVIVAL OF ABATACEPT IN RHEUMATOID ARTHRITIS PATIENTS: A REAL-LIFE STUDY

E. Molteni[1], F. Ceccarelli[1], C. Castellani[1], F. Giardina[1], C. Alessandri[2], M. Di Franco[2], V. Riccieri[2], F. R. Spinelli[2], R. Scrivo[2], R. Priori[3,4], F. Conti[2]. [1]*Sapienza University of Rome, Rheumatology, Roma, Italy*; [2]*Sapienza University of Rome, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Roma, Italy*; [3]*Policlinico Umberto I, Rheumatology, Roma, Italy*; [4]*Policlinico Umberto I, Rheumatology Unit, Roma, Italy*

Background: Abatacept (ABA) is a biological drug approved for the treatment of rheumatoid arthritis (RA) patients that, by working on CTLA4, can inhibit T-cell activation. Randomized controlled trials have demonstrated both the efficacy and a good safety profile, characterized by a lower infectious risk in comparison with other biological DMARDs, in RA patients. In a real-life setting, the drug retention rate could be considered as a surrogate of drug effectiveness. Data from the literature reported a retention rate of ABA ranging from 55 to 76% at 12 months and from 54 to 64% at 24 months (1-3).

Objectives: In the present longitudinal analysis, we evaluated the retention rate of ABA in a large monocentric RA cohort.

Methods: We enrolled consecutive RA patients starting treatment with intravenous (IV) or subcutaneous (SC) ABA according to the standard of care. All the patients fulfilled the 2010 ACR/EULAR classification criteria for RA. For each patient, we collected demographic parameters, serological status, previous and concomitant treatments, and disease activity by DAS28 with C reactive protein (DAS28-CRP). All the patients were assessed at baseline, and after 4 and 12 months (T4 and T12, respectively). The reasons for withdrawal of treatment were registered and classified as primary or secondary inefficacy or adverse events (AEs). Kaplan-Meier statistical analysis has been done to evaluate the survival of the treatment in patients with at least 12 months follow-up.

Results: We evaluated 161 patients [M/F 21/140; median age 67 years (IQR 21.7), median disease duration 180 months (IQR 161)]. RF was positive in 70.3% of patients, ACPA in 66.4%. ABA was the first biological DMARD in 66 patients (41%). At baseline, the median DAS28-CRP was 4.3 (IQR 1.6) and ABA was administered in association with MTX in 96 patients (59.6%). One hundred-eleven patients (68.9%) started SC ABA [M/F 16/95; median age 64.5 years (IQR 21.5), median disease duration 156 months (IQR 132)], the remaining 50 IV ABA [M/F 5/45, median age 71 years (IQR 60.2), median disease duration 187 months (IQR 157)]. Median age and disease duration were significantly higher in patients receiving IV in comparison with SC ABA (p=0.008 and p=0.03, respectively). We found a significant reduction of DAS28-CRP values during the follow-up in comparison with baseline [4 months: median 3.5 (IQR 1.9), p<0.0001; 12 months: median 3.2 (IQR 1.4), p<0.0001]. Seven patients were lost to follow-up, in the remaining 154 patients a median treatment duration of 33 months (IQR 49) was registered. Data on drug survival are reported in Figure 1A: at 12 months, 92% of patients persisted on treatment; this percentage decreased to 78.2% at 24 months and to 67.9% at 36 months. Furthermore, we did not find any differences in drug survival either with respect to SC vs IV administration (12 months: 93.7% versus 88.6%; 24 months 78.9% versus 72.6%; 36 months 63.7% versus 72.6%; Figure 1B) or according to the association with MTX. Concerning the withdrawal reasons, 46 patients (29.9%) stopped ABA due to inefficacy (primary in 28, secondary in 18), 11 patients (7.1%) due to AEs, and 7 for inadequate adherence (4.5%). Finally, 10 patients switched from IV to SC administration, due to patient's preference.

Conclusion: In our monocentric RA cohort, we have observed a high retention rate of ABA at both 12 and 24 months, confirming the good profile of this drug in terms of effectiveness and safety, irrespective of the route of administration and association with MTX.

REFERENCES:

[1] Cagnotto, Arthritis Res Ther 2020; (2) Salmon, J Clin Med 2020; Westhovens, Rheumatol Int 2020.

Acknowledgements: I would like to acknowledge Dr. F. Ceccarelli, for her patience.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3689

AB0235 RITUXIMAB (BIOSIMILAR) IN RHEUMATOID ARTHRITIS: CLINICAL & IMMUNOLOGICAL RESPONSE TO VARYING DOSES- EXPERIENCES FROM A TERTIARY CARE CENTER IN SOUTH INDIA

J. Antony[1], R. Sankaralingam[1], R. Maheshwari[1], B. Chilukuri[1], S. Chinnadurai[1]. [1]*Sriramachandra Medical College, Rheumatology, Chennai, India*

Background: Rituximab (RTX) is a chimeric monoclonal antibody against CD20. There is a paucity of studies done with RTX biosimilars. This is a Retrospective and Observational study from January 2018 to December 2019 done in the Department of Clinical Immunology & Rheumatology, Sri Ramachandra Institute of Higher Education and Research, Chennai, India.

Objectives: 1.To find the effects of varying doses of RTX in attaining clinical remission in RA.

2.To find if CD19, CD20 & IgG help in identifying impending flare & if these levels help in deciding the timing of the next dose of RTX.

Methods: Rheumatoid arthritis (RA) cases who were given Rituximab from January 2018 were selected. Clinical Response at 6 & 12 months & wherever feasible at 18 & 24 months was assessed by Simplified Disease Activity index (SDAI). RTX initial dose was given at 0 and 14 days followed by fixed dose at six months interval.CD19, CD20 B cell count, IgG levels were tested in patients in whom it was feasible at baseline & 6 months (select patients at 12,18 &24 months). Patients were divided in to 5 groups (DMARD naïve, DMARD resistant & Interstitial Lung disease (ILD) [Lung involvement>20% in Computed Tomography (CT)]) and (500mg & 1g). Patients were divided into three clinical groups, (DMARD naïve, DMARD resistant & Interstitial Lung disease (ILD) [Lung involvement>20% in Computed Tomography (CT)]) and two treatment groups (500mg & 1g) based on clinical indication for RTX and dose of RTX,

respectively. In patients with ILD, CT scan & FVC were compared at baseline & 12 months.

Results: 29 patients (seropositive 28 (RF/Anti CCP/BOTH+VE), seronegative 1) were given RTX for RA over a 2-year period of which 12 had CD19, CD20 & IgG tested. Mean SDAI reduction from baseline to 6 months post treatment was 30%, 32% & 14% while complete remission (SDAI<3.3) was attained in 100%, 18% & 20% in DMARD naïve, DMARD resistant & ILD groups, respectively. CD19, CD20 & IgG reduced from 18.6%, 18.4% & 18.53g/L to 3.7%,3.7% & 9.7g/L respectively FVC improved from 62.4% to 67% at 12. The percentage of patients with lung involvement >20% reduced from 53.3% to 46.7%. Flare was observed in one patient who received 500mg RTX. CD19, CD20 & IgG levels increased from 7.9%, 8% & 9.8g/L to 27%, 25% & 13g/L respectively. 3 patients in the 1g group were followed up at 12,18 & 24 months. In these patients there were no flares or worsening symptoms. 1 patient was double negative for RF & Anti CCP and this patient did not attain clinical remission even after 2 doses of 1g RTX.

Conclusion:

[1] Patients with early arthritis (diagnosis made within 1 year) and who were DMARD naïve had an excellent response to Rituximab.
[2] Complete remission was observed in more patients the 1g compared to 500mg group.
[3] Reduction in CD19 & CD20 was associated with significant reduction in the SDAI score.
[4] There was no significant reduction of CD19 & CD20 with 500mg dose of Rituximab where either a partial remission or mild flare was observed.
[5] There was reduction in the lung involvement to less than 20%(CT) in few patients with 1g dose.
[6] Double negative Rheumatoid arthritis poorly responded to Rituximab.
[7] The positive effects of 1g Rituximab could be noted up to 24 months.
[8] Flare of RA was associated with significant increase in CD19 & CD20.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3794

AB0236 DOWN-TITRATION STRATEGY OF TUMOR NECROSIS FACTOR-INHIBITOR AGENTS FOR RHEUMATOID ARTHRITIS IN TUNISIA

K. Saadaoui[1], H. Sahli[1], S. Boussaid[1], J. Samia[1], R. Sonia[1], C. Elhem[1], E. Mohammed[1]. [1]*La Rabta Hospital, Rheumatology, Tunis, Tunisia*

Background: Tumor necrosis factor (TNF) blocking agents are effective in treating rheumatoid arthritis, but they are associated with several adverse effects and high costs. Some studies have assessed the effectiveness of down-titration compared with continuation of standard dose.

Objectives: The aim of our study is to assess dose tapering in Tunisia.

Methods: A retrospective study including 170 rheumatoid arthritis patients treated by TNF blocker agent and with either low disease activity or remission (ACR/EULAR criteria). Two groups were compared, in the first group (G1) the interval of TNFi administration was extended, in the second group (G2) the standard dose and rhythm of administration were maintained.

Results: The TNFi tapering group (G1) included 96 persons whereas the group having the same drug administration rhythm (G2) included 74 case. The baseline age of the down-dosing drug group was 56.6 ± 12.6 years versus 52.9 ± 11.6 years in the other group (p = 0.046) and the average disease duration were respectively 12.3 ± 7.2 years versus 11.2 ± 6 years (p = 0.346). Women represented 88.5% in G1 versus 93% in G2 (p = 0.298). Rheumatoid Factors and ACPA were positive respectively in (85.5% versus 83.8; p = 0.748) and (76.4% versus 67.8%; p= 0.309). Etanercept, adalimumab, certolizumab pegol and infliximab were respectively used in 84.4%, 9.4%, 4.2% and 2.1% cases (G1), whereas they were used in 48.6%, 16.2%, 27% and 8.1% cases in the second group (G2). In the TNFi down dosing group, methotrexate was associated to TNFi in 74% cases while 71.6% of patient received methotrexate in the standard rhythm of administration group (p = 0.734). Corticosteroids were used by 40.6% of patients in G1 vs. 56.8% of patients in G2 (p = 0.037). The average DAS_{28} at baseline was 5.91 ± 0.81 (G1) versus 5.95 ± 0.80 (G2) (p = 0.759). There was no statistically significant difference between the two groups for rates of TNFi withdrawal (p = 0.798). In fact, TNFi was interrupted due to inefficacy for 17 patients (17.7%) in the down-dosing group versus 12 patients (16.2%) in the other group.

Conclusion: Our study add evidence that TNFi drugs tapering could be equivalent to maintenance strategy. This could be beneficial to decrease the risk of adverse effect or reduce costs. Further studies are needed to confirm those results and identify patients who could benefit of TNFi administration rhythm step-down.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3804

AB0237 INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH RITUXIMAB AND ANTI-TNF INHIBITOR

N. Zehraoui[1], R. Benaziez.Boutaleb[1], H. Hafirassou[1], F. Mechid[1], N. Bahaz[1], C. Makhloufi-Dahou[1]. [1]*Mohamed Lamine Debaghine University Hospital, Rheumatology, Algiers, Algeria*

Background: Biological therapies have significantly improved the management of rheumatoid arthritis (RA). These molecules are very effective, but are known for their specific risks, especially infectious. It depends on several factors including the type of molecule used.

Objectives: The objective of our study is to compare the rate of infection in RA patients treated with rituximab and anti-TNFα.

Methods: Prospective, observational, monocentric study. Were included RA patients (ACR / EULAR 2010 criteria) treated with rituximab and anti-TNFα (adalimumab, infliximab and Etanercept) after inadequate response to DMARDs. Demographic characteristics, comorbidities, association with methotrexate and corticosteroids were collected and compared for each group.

The number, type and severity of the infections in both cases were noted.

SPSS (Statistical Package for Social Science) was used for data analysis.

Results: 40 RA patients treated with rituximab and 31 patients who received anti-TNFα were included.

Patient characteristics and Comparison of rate of infection in RA patients between the two groups are summarized in Table 1

Table 1.

Parameters	Rituximab	Anti-TNFα	*p*
Number of patients	**40**	**31**	
Average age (years)	**56,28**	**46,06**	**0,01**
Sexratio	**0,14**	**0,11**	**0,7**
Average duration of evolution (years)	**15,83**	**13,74**	**0,3**
Patients under corticosteroid (%)	**97,5**	**87,1**	**0,08**
Average corticosteroid dose	**6,41**	**5,48**	**0,3**
patients under methotrexate (%)	**37,5**	**45,2**	**0,5**
Diabetes (%)	**20**	**16,1**	**0,7**
Patients with infection (%)	**32,5**	**51,6**	**0,1**
Number of infections	**18**	**24**	**0,4**
Number of serious infections	**5**	**0**	**0,04**

Conclusion: The rate of infections in patients with RA treated with rituximab or anti-TNF was similar. However, the infections observed were more serious in patients with RA treated with rituximab

REFERENCES:

[1] Fabiola Atzeni MD PhD and al. Infections and Biological Therapy in Patients with Rheumatic Diseases. IMAJ . VOL 18. march-APRIL 2016.
[2] Huifeng Yun and al. Comparative Risk of Hospitalized Infection Associated with Biologic Agents in Rheumatoid Arthritis Patients Enrolled in Medicare. ARTHRITIS & RHEUMATOLOGY. Vol. 68, No. 1, January 2016, pp 56–66.
[3] Manjari Lahiri and al. Risk of infection with biologic antirheumatic therapies in patients with rheumatoid arthritis. Best Practice & Research Clinical Rheumatology (2015) 1-16.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3854

AB0238 SECOND BIOLOGICAL DMARD THERAPY IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT ANALYSIS

K. Saadaoui[1], H. Sahli[1], S. Jemmali[1], S. Boussaid[1], S. Rekik[1], E. Cheour[1], M. Elleuch[1]. [1]*La Rabta Hospital, Rheumatology, Tunis, Tunisia*

Background: The development of biologic disease modifying antirheumatic drugs (bDMARD) has dramatically improved the management of rheumatoid arthritis (RA). However, some patients did not respond or partially respond to biologic agents. Management of first bDMARD failure may involve another biotherapy.

Objectives: The aim of our study is to assess the efficacy of second line biologic as well as survival rates of 2nd line biotherapy in RA.

Methods: This is a retrospective study based on Tunisian data including 374 RA patients treated with biologic agent from 2014 and followed until December 2018.

Results: Tumor necrosis factor inhibitor (TNFi) was the most prescribed class as first-line therapy with 86.4% patients (Etanercept: ETA 54%; adalimumab: ADA 13.6%; certolizumab pegol: CZP 12.8% and infliximab: IFX 5.9%), IL-6 inhibitor (Tociluzimab: TCZ) and anti-CD 20 (Rituximab: RTX) were given respectively to 6.4% and 7.2% cases. The first biotherapy was discontinued for 146 patients (39%). Of these, 79 patients (21.1%) received a second bDMARD (mean age 52.6 ± 11.8; sex ratio = 0.12; ETA 17.7%, ADA 7.6%, CZP 41.8%, IFX 1.3%, TCZ 24.1% and RTX 7.6%). Average DAS_{28} at second line biotherapy initiation was 5.93 ±

0.96. Overall survival rates of 2nd line bDMARD at 12, 24 and 36 months was respectively 91%, 76.4% and 72.1%. Among the patients receiving second biologic agent, 30.4% patients (24 cases) achieved either low disease activity (LDA) or remission. On average 38 weeks [14 – 96] were needed to reach that therapeutic target. In fact, 27.8% of the TNFi vs. 40% of the non TNFi patients achieved LDA (p = 0.277). Second biotherapy was withdrawn in 16.7% of the cases of TNFi group vs. 20% of the non TNFi group (p = 0.718). Moreover, no significant difference has emerged between the TNFi and the non-TNFi patients when comparing time to biotherapy discontinuation (15.8 months vs. 20.9; p = 0.11).

Conclusion: In our study, no significant difference was found between TNFi and non-TNFi switcher in RA. But, treatment strategy after first bDMARD failure is still controversial. Further studies have to be done to get the most beneficial strategy in RA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3871

AB0239 PERSISTENCE TO BIOLOGICAL DMARDS TNF INHIBITORS VS BIOLOGICAL DMARDS NO TNF INHIBITORS AFTER FAILURE TO SYNTHETIC CONVENTIONAL DMARDS IN RA PATIENTS TREATED IN STANDARD CLINICAL PRACTICE

B. Hernández-Cruz[1], P. Muñoz Reinoso[2], I. García Hernández[3], G. Jurado Quijano[3], L. Fernández de la Fuente Bursón[3], I. M. Fernández-Maeztu Palacín[3], A. Fernández Reboul Fernández[3], D. Ruiz-Montesinos[3], J. J. Pérez Venegas[3]. [1]*Hospital Universitario Virgen Macarena, Rheumatology, Seville, Spain*; [2]*Hospital Universitario Virgen Macarena, Rheumatologyy, Sevilla, Spain*; [3]*Hospital Universitario Virgen Macarena, Rheumatology, Sevilla, Spain*

Background: There are no RA response predictors for our patients. The decision to initiate a first biological depends on multiple factors such as rheumatologist experience, clinical characteristics of the patient and health system. What is clear is that the best strategy is T2T.

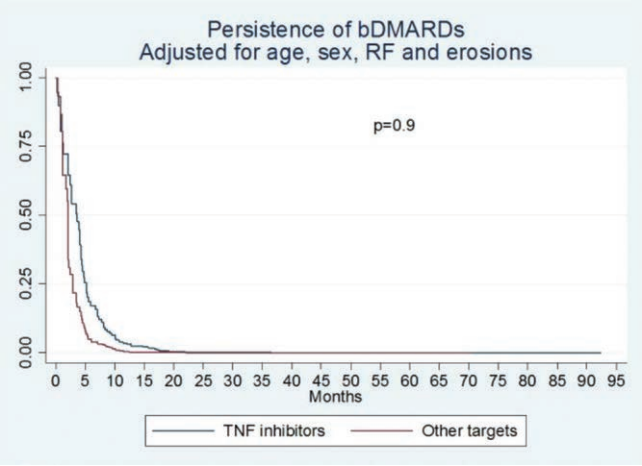
Objectives: To know the clinical characteristics and persistence of the first biological DMARD in patients receiving bDMARDS TNF inhibitors vs DMARDs aimed at other targets.

Methods: A observational cohort of adult RA patients (ACR/EULAR 2010) in a rheumatology department of a third-level university hospital. All patients were treated with a first bDMARD marketed in Spain, from 2010 to December 2020 and prescribed according to product data sheet. Biological drugs were divided into TNF inhibitors drugs (adalimumab, etanercept, infliximab, golimumab, certolizumab) and Other targets (abatacept, rituximab, sarilumab, tocilizumab). Clinical data, duration of treatment and EULAR response were collected from each patient. The data were analyzed with descriptive, bivariate statistics and survival analysis adjusted for age, sex, FR, erosions and duration of the disease.

Results: Data were collected from 332 patients (table 1). Patients treated with other target bDMARDs were mostly female, with higher activity, shorter disease duration, and treated without MTX.b Survival graphs showed that regardless of the target chosen as fist bDMARD, EULAR response rates and persistence to the drug were similar.

Table 1.

Variable	TNF inhibitors n=194	Other targets n = 138	Total n =332	p
	n (%)	n (%)	n (%)	0.02
Female	142 (73)	115 (83)	257 (77)	0.2
FR +	163 (82)	121 (88)	284 (86)	0.6
ACPA +	125 (63)	84 (61)	209 (63)	0.9
Erosions	177 (89)	80 (58)	257 (77)	0.01
Concomitant MTX	153 (77)	62 (47)	215 (65)	0.003
EULAR response				
Good	103 (77)	67 (71)	170 (75)	0.2
Moderate	24 (18)	16 (17)	40 (17)	
No	7 (5)	11 (11)	18 (8)	
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (years)	55.7 ± 13.3	57.6 ± 11.9	56.5 ± 12.7	0.1
Evolution of RA (years)	9.6 ± 10.2	7.5 ± 7.5	8.7 ± 9.2	0.04
Persistence (months)	19.3 ± 20.5	16.07 ± 15.11	17.5 ± 18.5	0.04
DAS28VSG4V basal	5.02 ± 1.5	5.59 ± 1.03	5.25 ± 1.3	0.001
DAS28VSG4V final	2.68 ± 1.1	2.84 ± 1.4	2.7 ± 1.25	0,31



Conclusion: Patients receiving Anti-TNF vs bDMARD with other mechanisms of action have clinical differences. However, the response and persistence to the drug are similar, perhaps due to the implementation of the correct T2T strategy.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3920

AB0240 PREDICTORS OF RESPONSE TO BIOLOGIC AGENTS IN RHEUMATOID ARTHRITIS

K. Saadaoui[1], H. Sahli[1], S. Jemmali[1], S. Boussaid[1], S. Rekik[1], E. Cheour[1], M. Elleuch[1]. [1]*La Rabta Hospital, Rheumatology, Tunis, Tunisia*

Background: In rheumatoid arthritis (RA), the 'treat-to-target' therapeutic approach imposes rigorous control of disease activity. Although biological agents have been shown to be effective, these therapies fail sometimes to achieve therapeutic goals.

Objectives: In this study we tried to determine predictive factors of good therapeutic response to biologic disease-modifying antirheumatic drugs (bDMARD).

Methods: This is a retrospective study including 374 Tunisian patients who received their first biotherapy between 2014 and 2016. Categorical variables were reported in numbers and percentages, while quantitative variables were expressed by mean with standard deviations. The univariate analysis was performed using the student t-test or the Chi2 test. Multivariate analysis was performed by binary logistic regression.

Results: Average age of our cohort was 55 ± 12.5 years with a female predominance of 87.2%. The average duration of RA was 11.7 ± 6.7 years. Rheumatoid factors were positive in 79% and ACPA were positive in 72% of cases. After the introduction of biotherapy, low disease activity (LDA) or remission was achieved in 55% of cases (206 patients).

No statistically significant difference between biotherapy responder and non-responder groups for age (55.7 vs. 54.7 years; p = 0.44), gender (Female: 86.5% vs. 88.7%; p = 0.08) and disease duration (12 years vs. 11.4 years; p = 0.41). A significant difference between the two groups was found for the positivity of rheumatoid factors (76.4% vs. 88.9%; p = 0.004), methotrexate's association (65% vs. 53.4%; p = 0.02) and corticosteroids' use (50% vs. 66.5%; p < 0.001).

Positive predictive factors of remission or LDA by biotherapy were female sex (Odds Ratio = 2.2; p = 0.026), presence of rheumatoid factors (Odds Ratio = 2.64; p = 0.001), association with methotrexate (Odds Ratio = 1.69; p = 0.028). Whereas, corticosteroid use (OR = 0.41; p < 10-3) was a negative predictor of disease control by bDMARDs.

Conclusion: Achieving LDA low level or even remission is currently achievable with biological treatments. Certain factors need to be studied in order to optimize RA treatment and adapt the right bDMARD for each patient.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3928

AB0241 FACTORS THAT DIFFERENTLY ASSOCIATE WITH THE RETENTION ON TARGETED THERAPY OF PATIENTS WITH RHEUMATOID ARTHRITIS

E. Zhilyaev[1,2], G. Lukina[3], E. Koltsova[3,4], K. Lytkina[5], E. Shmidt[6]. [1]*European Medical Center, Medical Derection, Moscow, Russian Federation*; [2]*Russian Medical Academy of Continous Professional Education, Rheumatology, Moscow, Russian Federation*; [3]*A.S.Loginov Moscow Clinical Scientific Center, Rheumatology, Moscow, Russian Federation*; [4]*Research Institute of the Organization of Health and Healthcare Managment, Organizational and Methodological Department of Rheumatology, Moscow, Russian Federation*; [5]*City Clinical Hospital, Rheumatology, Moscow, Russian Federation*; [6]*N.I.Pirogov City Clinical Hospital, Rheumatology, Moscow, Russian Federation*

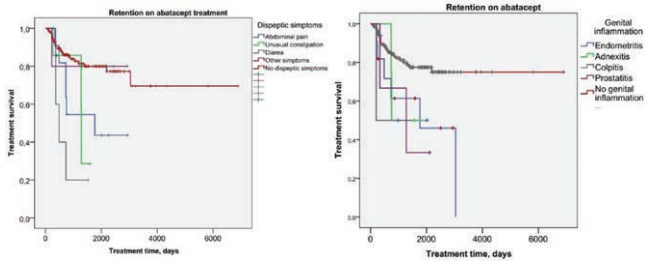
Background: A personalized approach to prescribing targeted drugs implies the availability of data that can be used to suggest that a particular drug is better suited for a given patient than others. Retention on the treatment can be considered as an integral indicator of the acceptability of the drug in real practice. For the purposes of treatment personalization, the indicators that are associated with better retention on some drugs and with worse retention, or that do not have a clear association with retention on others, are of particular interest.
Objectives: to identify predictors those are differently associated with retention on different targeted drugs for the treatment of rheumatoid arthritis.
Methods: Data of the patients with rheumatoid arthritis (RA) from the Moscow Unified Register of Arthritis (MUAR) were used. The analysis includes episodes of treatment with biological or synthetic targeted drugs (tDMARDs) that continue or end during the patient's follow-up in the registry. Within the framework of the Cox proportional risk regression model, significant independent predictors of tDMARDs cancellation were identified. These indicators were later considered as confounders. Further, in the generated linear regression risk model, all available indicators were tested for the presence of a statistically significant interaction with the factor of used tDMARD.
Results: The study included 944 episodes of tDMARDs treatment (Table 1.) in 832 patients. The average age is 55.3 + 12.4 years. There were 131 males (16.1%). The average duration of the disease is 13.1 + 9.4 years. Smoking, family history of RA, and the nature of RA onset (acute or gradual) were identified as reliable mutually independent predictors of retention on tDMARDs treatment. As a result of the search for indicators that reliably interact with used tDMARD, patient's reports of the association of the onset of arthritis 1) with symptoms of intestinal dyspepsia ($p < 0.001$), 2) with genital inflammatory disease ($p = 0.002$) were revealed. Most strongly associated with factor 1) was retention on abatacept (ABA), rituximab (RIT), and tofacitinib (TOFA). The second indicator was most strongly associated with retention on ABA, adalimumab (ADA) and TOFA (Picture 1).

Table 1. Description of treatment episodes included in the analysis

	ABA	ADA	CER	ETAT	GOL	INF	RIT	TOC	TOFA	Total
Number of episodes	175	150	34	186	8	55	130	113	93	944
Completed	39	51	13	55	2	39	31	14	9	253
(%)	(22,3%)	(34,0%)	(38,2%)	(29,6%)	(25,0%)	(70,9%)	(23,8%)	(12,4%)	(9,7%)	(26,8%)
Line of treatment										
1	83	24	113	120	3	50	70	66	35	564
	(47,4%)	(70,6%)	(60,8%)	(80,0%)	(37,5%)	(90,9%)	(61,9%)	(50,8%)	(37,6%)	(59,7%)
2	62	6	52	24	2	4	22	39	30	241
	(35,4%)	(17,6%)	(28,0%)	(16,0%)	(25,0%)	(7,3%)	(19,5%)	(30,0%)	(32,3%)	(25,5%)
3	22	1	13	6	1	1	15	21	14	94
	(12,6%)	(2,9%)	(7,0%)	(4,0%)	(12,5%)	(1,8%)	(13,3%)	(16,2%)	(15,1%)	(10,0%)
> 3	8	3	8	0	2	0	6	4	14	45
	(4,6%)	(8,8%)	(4,3%)	(0,0%)	(25,0%)	(0,0%)	(5,3%)	(3,1%)	(15,1%)	(4,8%)

ABA – abatacept, ADA – adalimumab, CER – certolizumab paegol, ETA- etanercept, GOL – golimumab, INF – infliximab, TOC- tocilizumab, TOFA – tofacitinib.

Conclusion: Anamnestic indications of the association of the onset of rheumatoid arthritis with symptoms of intestinal dyspepsia and with preceding genital inflammation are differently associated with retention on different targeted drugs in patients with RA. These indicators can be used to personalize the treatment.



Picture 1. Retention on the abatacept depending on the features of the onset of rheumatoid arthritis

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3953

AB0242 CERTOLIZUMAB IN MONOTHERAPY AS EFFECTIVE THAN IN COMBINATION IN RHEUMATOID ARTHRITIS PATIENTS

P. Osorio[1], L. Villarreal[1], W. Rivero[2], L. Ibata[3], S. Martinez[3], A. Rojas-Villarraga[4], P. Santos-Moreno[5]. [1]*Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, Administration, Bogota, Colombia*; [2]*Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, Pharmaceutical Chemist, Bogota, Colombia*; [3]*Epithink Health Consulting, Epidemiology, Bogota, Colombia*; [4]*Fundacion Universitaria de Ciencias de la Salud - FUCS, Research Division, Bogota, Colombia*; [5]*Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, Rheumatology, Bogota, Colombia*

Background: Tumour necrosis factor-a (TNFa) inhibitors are one of the most used biological therapy for rheumatoid arthritis (RA) patients without response to conventional disease-modifying antirheumatic drugs (cDMARDs). There is scarce information about biological DMARDs (bDMARDs) effectiveness as monotherapy in real life.
Objectives: To assess the effectiveness of Certolizumab pegol in real-life clinical practice in a cohort of patients with RA and previous failure to cDMARDs who received certolizumab as monotherapy, combined with Methotrexate (MTX), combined with leflunomide (LFN), or both MTX and LFN.
Methods: A retrospective cohort study was conducted at a specialized center for RA management in Colombia. Patients treated with Certolizumab as monotherapy or in combination with MTX, or LFN, or both MTX plus LFN, (2012 – 2020) were included. The indication of certolizumab was a independent decision based on disease activity. Patients could be taking adjuvant medications for pain and/or corticosteroids. Certolizumab was administered 400 mg SC monthly after three induction doses at weeks 0, 2 y 4, as monotherapy or in combination with MTX (until 25 mg/week), LFN (20 mg/day) or both as a first-line treatment after failure with cDMARDs or as a second-line treatment after failure with one or more bDMARDs. Effectiveness was assessed at three, six, and twelve months according to the change in DAS28. Exploratory comparisons of numeric variable data between groups were done (ANOVA). Chi-square test and Fisher's exact test were used for categorical variables. Multivariate analyses (logistic regressions) were performed to analyse factors related to the response at 6 and 12 months.
Results: Of 181 enrolled patients, 24 received certolizumab as monotherapy, 62 combined with MTX, 47 in combination with LFN and 48 in combination with MTX and LFN. 55.2% of patients were first-line treatment, without significant differences between groups. Mean age of subjects included was 57.87 ± 12.33 with a mean age of around 60 years in patients treated with CERTO+MTX and CERTO+LFN (p=0,014). Women predominated in all groups (84% of the total) (p=0,275). The duration of arthritis on average was 8.27 ± 8.73 years, without significant differences between treatment groups (p=0,871). In terms of disease activity, 78.5% of patients were in moderate or high disease activity, according to DAS28, without significant differences between the groups (p=0,787). Differences in the number of biologicals and corticoid use were observed, patients in the combination groups had used in a higher proportion two or more biological (p=0,046) than in the monotherapy group and had used corticosteroids (p=0,042) more frequently. Overall, there were decreased disease activity, at 3 and 6 months with no significant differences between groups (p=0,08). At 12 months of treatment, there was a higher maintenance in mild activity/remission response in monotherapy group compared to the others (p=0,01). In the multivariate analysis, no differences were observed in the response at 6 and 12 months between the treatment groups. The response at three months was the only variable associated with the 6-month response (OR 5.46; CI 95% 2.08 – 14.32). The response at three months (OR 4.04; CI 95% 1.28-12.69) and positive anti-CCP (OR 3.83; CI 95% 1.11-13.21) were associated with 12-month response.
Conclusion: These exploratory results show a clear trend of Certolizumab being effective as monotherapy in patients previously treated with cDMARDs and even after being treated with one bDMARD. Although results are not statistically different, it seems that certolizumab in monotherapy could be as least as effective as combination therapy. Prospective studies with larger sample size and with a structured follow-up are needed to confirm these findings.
Disclosure of Interests: Paola Osorio: None declared, Laura Villarreal: None declared, Wilberto Rivero: None declared, Linda Ibata: None declared, Susan Martinez: None declared, Adriana Rojas-Villarraga: None declared, Pedro Santos-Moreno Speakers bureau: has received fees for conferences from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Consultant of: has received fees for counseling, advisory boards from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Grant/research support from: has received fees for research grants from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi
DOI: 10.1136/annrheumdis-2021-eular.4008

AB0243

CONSIDERING THE COMBINATION OF TWO BIOLOGICS IN CASE OF FAILURE OF THE MONOTHERAPY IN JUVENILE ONSET RHEUMATOID ARTHRITIS

A. Haddouche[1], K. Ait Bellabas[1], W. F. Hamrani[1], S. Sahraoui[1], R. Fatma[1], F. Rahal[2], S. Slimani[3], F. Hanni[1]. *[1]EHS Ben Aknoun, Rheumatology, Algiers, Algeria*; *[2]CHU Beni Messous, Rheumatology, Algiers, Algeria*; *[3]Private Practice Office, Rheumatology, Batna, Algeria*

Background: The management of rheumatoid arthritis refractory to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) is currently well codified and includes different types of biologics and even targeted sDMARDs. A rotation of biologic therapies is recommended in order to better control the disease.

Methods: We report the case of a 20-year-old patient followed in our hospital for the management of a deforming and erosive seropositive rheumatoid arthritis (FR +, ACPA +) with a juvenile onset at the age of 8 years. The diagnosis of an immunopositive polyarticular form of JIA was retained in 2010 (9 years old); the patient was treated with methotrexate (MTX) at a dose of 10 mg per week and methylprednisolone at doses varying between 4 and 10 mg per day. Following the failure of MTX, etanercept was introduced for 6 months without success, followed by tocilizumab in 2012 at a dose of 8mg/kg/month for a year, without good response. In 2014, a course of rituximab (RTX) at a dose of 2 shots of 500mg, 2 weeks apart was prescribed followed 9 months later by etanercept at a dose of 50 mg a week for 3 years then by adalimumab (40mg/ week) because of the multiple treatment failures.

In 2018, the repetition of RTX at a dose of 1g, renewed 15 days later, improved the patient for only 3 months. Then, a combination of two biologics, namely RTX (2 x 1g, 15 days apart) and adalimumab 1 month later (40mg / week) was received by the patient with a good response at 3 months. The latter was maintained for 7 months even after stopping the adalimumab following confinement for COVID-19. In September 2020, flares occurred and the adalimumab (ADA) has been delivered but without success during 3 months, stopped later for a benign form of COVID-19 (15 months after RTX). In January 2021, the association RTX + ADA was given again and we hope that it will be as effective as the first prescription.

Results: The clinical and biological severity of our patient's rheumatoid arthritis led us to give a combination of two biological treatments. Indeed, we do not have other therapeutic classes to deliver to her, that encouraged us to rotate between all the available biological therapies in our country. The combination of a CD20 inhibitor (RTX) with a TNF blocker (ADA) was safe and made possible, for the first time, the achievement of clinical and biological remission during 7 months, even after stopping the TNF blocker. Greenwald *et al*. reported the safety of the combination of RTX + TNF inhibitors in a randomized clinical trial in 51 patients. Its efficacy, a secondary goal of the study, was suggested at 24 weeks by the percentage of ACR 20 and ACR 50 responses that was greater than in the RTX placebo group.

Conclusion: The combination of RTX with a TNF blocker can be a real alternative therapy in rheumatoid arthritis with failure to a biological monotherapy.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4058

AB0244

INFLUENCE OF BIOLOGICAL DRUGS ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Jriri[1], S. Boussaid[1], S. Rekik[1], M. Abbes[1], M. Ben Majdouba[1], S. Jemmali[1], H. Sahli[1], M. Elleuch[1]. *[1]RABTA, Rhuematology, Tunis, Tunisia*

Background: The level of the Health-related quality of life (HRQL) in patients with rheumatoid arthritis (RA) is often negleglected in their medical care. While, theese patients are suffering from a precarious quality of life, resulting from pain, impaired physical function and fatigue. The use of biological agents for treating this disease is then a challenge, leading to the possibility of reducing the consequences of the disease.

Objectives: The main purpose of this study was to compare the level of HRQL in patients with rheumatoid arthritis (RA) during therapy applying disease-modifying antirheumatic drugs (DMARDs) with conventional synthetics (csDMARDs) or with csDMARDs in combination with biological drugs (bDMARDs).

Methods: The study involved 120 patients with RA, divided into two groups: group I –treated using csDMARDs (combination therapy: methotrexate and salazopyrine), group II – using csDMARDs in association with bDMARDs which included TNF inhibitors (etanercept and adalimumab). All the studied patients were surveyed with the use of the following questionnaires: *the short-form health survey (SF-36)* for HRQL that assesses eight domains: functional capacity (ten items), physical aspects (four items), pain (two items), general health (five items), vitality (four items), social aspects (two items), emotional issues (three items) and mental health (five items), in addiction to one item to compare current health status and that of the previous year, *The AIMS2-SF*, and *Health Assessment Questionnaire* (HAQ). The questionnaires were filled out at the consultation after patient's consent.The 28-Joint Disease Activity Score (DAS-28) was calculated.

Results: Group I consisted of 72 persons including 55 women and 17 men with a mean age of 58.4 years. Group II contaned 48 patients where females predominated (sex ratio: 0.3), the mean age was 52.4 years. The majority of patients (53.3%) had been diagnosed with RA for more than five years. Most of the SF-36 domains showed significant improvement in the second group ($p<0.01$), highlighting the social aspects, pain, physical functioning, emotional issues, vitality and physical aspects. The mean score of HAQ II decreased from 1.97 up to 1.23 with biological therapy ($p<0.01$). The highest AIMS scores were comparatively in the two groups (I vs II): in social activity (6.49±1.93 vs 6.23±1.56), pain (4.70±2.04 vs 4.01±2), depression (4.70±2.23 vs 4.66±2.03), and physical activity (4.03±2.10 vs 4.01±2.08). The DAS-28 value, the number of swollen joints, and the duration of morning stiffness were significantly smaller among patients from group II ($P=0.04$). After logistical regression,treatement with biotherapy was isolated as a fundamental independent factor influencing the mentel component of SF-36 scale with an OR of 1.59.

Conclusion: we conclude that the use of biologic therapy in patients with RA proved to be an important pharmacological strategy for improving HRQL and functional capacity as assessed by the HAQ II and SF-36 instruments.The intensity of the activity of RA as well as experiencing pain and the duration of morning stiffness were smaller among patients applying csDMARDs plus bDMARDs compared with patients treated only with csDMARDs.

REFERENCES:

[1] Blair, H. A., & Deeks, E. D. (2016). *Infliximab Biosimilar (CT-P13; Infliximab-dyyb): A Review in Autoimmune Inflammatory Diseases. BioDrugs, 30(5), 469–480.*

[2] Araújo, F., Gonçalves, J., & Fonseca, J. E. (2016). *Biosimilar DMARDs: What Does the Future Hold? Drugs, 76(6), 629–637.*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4223

AB0245

ANALYSIS OF THE CLINICAL AND ANTIDESTRUCTIVE EFFECTS OF RITUXIMAB DEPENDING ON GENDER IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Kudryavtseva[1], G. Lukina[1], E. Aronova[1], G. Gridneva[1], S. Glukhova[1], A. Smirnov[1]. *[1]V.A.Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Therapy, Moscow, Russian Federation*

Background: Rheumatoid arthritis is a chronic autoimmune disease characterized by inflammation of the synovial tissue and destruction of the underlying cartilage and bones. It was found that RA more often affects women than men, with a sex ratio of 3: 1. And the question of the influence of gender on the outcomes and course of RA remains controversial, there is no consensus on whether RA is worse in women or men. Recent reports indicate that women are less likely to achieve remission than men. Women suffer from RA at an earlier age and have higher markers of disease activity such as DAS28 and HAQ. Rituximab is a chimeric monoclonal antibody that targets the CD20 molecule expressed on the surface of B cells, it has been successfully and widely used for the treatment of rheumatoid arthritis, so it is of interest to assess whether gender influences the therapeutic and radiological effects of RTX.

Objectives: The aim of this study was to analyze the impact of gender on the response to rituximab (RTX) in patients with RA.

Methods: Initially, 221 women(w), 27 men(m), were examined to assess the clinical and X-ray effect (88w/6m), who received RTX treatment (1000 mgx2 or 500 mgx2). Both groups were comparable in terms of the main clinical and laboratory characteristics (age, duration of the disease, the number of preceding DMARDs, in both groups most patients were RF + and ACCP +, a high degree of activity according to DAS 8 - men - 5.6 [4.6-6.7], women - 6.04 [5.2-6.63] Initially, the degree of radiological changes in men is slightly higher than in women ($p> 0.05$). Clinical effect was scored by EULAR criteria, radiographic progression was assessed using Sharp/van der Heijde modified scoring method.

Results: When assessing the clinical effect after 48 weeks in men, a significantly better effect of RTX treatment was noted in comparison with women (Δ DAS28, a significantly better effect was noted in men - Δ DAS28 =3.75[2.8-4.14], and Δ DAS28=1.3[0.37-2.72] in women, ($p=0.04$). Analyzing the X-ray effect after 48 weeks of RTM treatment: the absence of progression in terms of the total score in 83.33% of men and 60.98% of women; there was no progression in narrowing of the joint space in 83.33% of men and 65.85% of women, noteworthy that the account of erosion practically reaches statistical significance - inhibition of destruction in 100% of men and 74.31% of women ($p = 0.06$).

Conclusion: Thus, having analyzed the clinical and antidestructive effects of RTM therapy depending on gender, we can conclude that the effect is significantly

higher in the male group. Also, there is a tendency towards more effective inhibition of radiographic progression in men.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4262

AB0246 **COMORBIDITIES APPEARING UNDER BIOLOGIC THERAPY: PREVALENCE AND ASSOCIATED FACTORS**

T. El Joumani[1], T. Latifa[1], I. Hmamouchi[2,3], S. Ahid[4], R. Abouqal[5], L. Achemlal[6], I. El Bouchti[7], A. El Maghraoui[8], I. Ghozlani[9], H. Hassikou[10], T. Harzy[11], I. Linda[12], O. Mkinsi[13], R. Niamane[14], R. Bahiri[15], H. Rkain[1], F. Allali[1]. *[1]El Ayachi Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Department of Rheumatology B, Rabat, Morocco*; *[2]Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco, Laboratory of Biostatistical, Clinical and Epidemiological Research, Rabat, Morocco*; *[3]Provincial Hospital of Temara, Morocco, Department of Rheumatology, Rabat, Morocco*; *[4]Mohammed V University, Rabat, Morocco, Research Team of Pharmacoeconomics & Pharmacoepidemiology, Rabat, Morocco*; *[5]Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Laboratory of Biostatistical, Clinical and Epidemiological Research, Rabat, Morocco*; *[6]Military Hospital Mohammed V, Ibn Sina University Hospital, Rabat, Morocco, Department of Rheumatology, Rabat, Morocco*; *[7]Arrazi University Hospital, Marrakech, Morocco, Department of Rheumatology, Rabat, Morocco*; *[8]Private Medical Office, Rabat, Morocco, Rheumatology, Rabat, Morocco*; *[9]University Hospital of Agadir, Morocco, Department of Rheumatology, Agadir, Morocco*; *[10]Military Hospital Moulay Ismail, Hassan II University Hospital, Meknès, Morocco, Department of Rheumatology, Meknes, Morocco*; *[11]Hassan II University Hospital, Fès, Morocco, Department of Rheumatology, fes, Morocco*; *[12]Mohammed VI University Hospital, Department of Rheumatology, Oujda, Morocco*; *[13]Ibn Rochd University Hospital, Department of Rheumatology, casablanca, Morocco*; *[14]Military Hospital Avicenne, Mohammed VI University Hospital, Department of Rheumatology, marrakech, Morocco*; *[15]El Ayachi Hospital, Ibn Sina University Hospital, Department of Rheumatology A, Salé, Morocco*

Objectives: The aims of our study are to determine the new comorbidities appearing under biologic therapy, their prevalence, and the factors implicated in their appearance.

Methods: It's a multicentric historical-prospective cohort including 10 rheumatology departments of Moroccan University Hospitals. The data were collected from the national register of patients under biologic therapy supervised by the Moroccan Society of Rheumatology. An electronic follow-up questionnaire is completed every 6 months by the investigator.

Results: The study included 418 patients: 224 with Rheumatoid Arthritis (RA) who represented 53.6% and 194 with spondyloarthropathy (SP) who represented 46.4%.

The prevalence rate of comorbidities appearing after one year of treatment with biologic therapy was 15.7% in RA and 8.4% in SP. The rate of cardiovascular diseases was 12.9% (arterial hypertension, myocardial infarction and/or ischemic stroke), 6.4% was the same value of hypercholesterolemia and depression, diabetes 3.3%, ulcer 3.2%, and osteoporosis 9.7%. The sedentary rate was 54.8% and smoking was about 3.3%.

No patient had developed hypertriglyceridemia or chronic obstructive pulmonary disease.

In the group of patients with RA, the average age of the patients who had developed a new comorbidity was 51,8 ± 11,3 years, women represented 87.5%, the average of Body Mass Index (BMI) was 27,6 ± 5,9 and the average duration of the disease was 14,1 ± 9,2 years. The disease activity score (DAS28) had an average of 3,15 ± 1,47.

59.6% of patients used Rituximab, 23.8% Tociluzimab, 8.1% Etanercept, 5.8% Adalimumab, 0.18% Infliximab, and 0.9% Golimumab.

In the group of patients with SP, the average age of the patients who had developed a new comobidity was 40,2 ± 13,7 years, men represented 63.4%, and the average of BMI was 24,3 ± 4,94.

The activity of the desease, had an average Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of 2,62 ± 1,79 and ankylosing Spondylitis Disease Activity **Score** (ASDAS) of 1,93 ± 1,09.

Regarding the type of biologic therapy, 33.2% of patients used Etanercept, 30.1% Adalimumab, 24.9% Infliximab, 9.8% Golimumab, 1.6% Secukinumab, and 0.5% Tociluzimab.

Conclusion: Our study showed a high prevalence of cardiovascular disease in patients under biologic therapy. This can be explained by the sedentary lifestyle secondary to rheumatic disease.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4280

Rheumatoid arthritis - non biologic treatment and small molecules

AB0247 **ANALYSIS OF THE IMPACT OF TOFACITINIB TREATMENT ON WEIGHT IN PATIENTS WITH RHEUMATOID ARTHRITIS**

J. Wollenhaupt[1], J. Morel[2], C. Daien[2], A. Ruyssen-Witrand[3], C. Lukas[2], C. Richez[4], A. Shapiro[5], D. Chapman[6], M. Cros[7], J. L. Rivas[8], G. Citera[9]. *[1]Struenseehaus Centre for Rheumatology and Clinical Immunology, Hamburg, Germany*; *[2]CHU Montpellier and University of Montpellier, Department of Rheumatology, Montpellier, France*; *[3]Hopital Purpan, CHU Toulouse, Department of Rheumatology, Toulouse, France*; *[4]Groupe Hospitalier Pellegrin-CHU de Bordeaux, Department of Rheumatology, Bordeaux, France*; *[5]Pfizer Inc, Inflammation and Immunology, Peapack, NJ, United States of America*; *[6]Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*; *[7]Pfizer Inc, Inflammation and Immunology, Paris, France*; *[8]Pfizer SLU, Inflammation and Immunology, Madrid, Spain*; *[9]Instituto de Rehabilitación Psicofísica, Section of Rheumatology, Buenos Aires, Argentina*

Background: A prior post hoc analysis of tofacitinib clinical trial data reported improvements in rheumatoid arthritis (RA) outcomes with tofacitinib vs placebo (PBO) through Month (M)6, regardless of baseline (BL) body mass index (BMI).[1]

Objectives: To assess change from BL (Δ) in BMI, and disease activity by BL BMI status, in patients (pts) with moderate/severe RA receiving tofacitinib through M12.

Methods: This post hoc analysis included data pooled from Phase 3 and 3b/4 studies of pts who were methotrexate-naïve (NCT01039688) or inadequate responders to conventional synthetic (cs) or biologic DMARDs (NCT00960440; NCT00847613; NCT00814307; NCT00856544; NCT00853385; NCT02187055; NCT02831855). Pts received ≥1 dose of tofacitinib 5 or 10 mg twice daily (BID) or 11 mg once daily (QD), ± csDMARDs, or PBO. Least squares (LS) mean ΔBMI (linear mixed model repeated measures; observed cases) was summarised for all treatment groups at M3/6/12 (M3/6 only for tofacitinib 11 mg QD and PBO). Other assessments at M3/6/12 included ΔBMI ± BL concomitant glucocorticoids (GCs) or antidepressants (descriptive statistics), LS mean ΔDAS28-4(ESR) stratified by BL BMI status (<25, ≥25–<30, ≥30), and correlations between LS mean ΔBMI and ΔDAS28-4(ESR).

Results: In total, 2349, 1611, 694 and 681 pts received tofacitinib 5 mg BID, 10 mg BID, 11 mg QD or PBO, respectively. Demographics/baseline characteristics were generally similar across treatments, except for some numerical differences in the tofacitinib 11 mg QD group, eg fewer female pts, more White pts and fewer pts receiving concomitant GCs, compared with other treatment groups. At M3/6, LS mean BMI significantly increased from BL with all tofacitinib doses vs PBO (all p<0.05); LS mean ΔBMI was greatest with 10 mg BID and lowest with 11 mg QD (Figure 1a). LS mean ΔBMI was greater in pts receiving tofacitinib as monotherapy vs combination therapy at M3/6/12 (Figure 1b). ΔBMI was generally similar in pts receiving treatment ± concomitant GCs or antidepressants (data not shown). Improvements in DAS28-4(ESR) were observed in each BL BMI status group at M3/6/12 and were greatest with all tofacitinib doses vs PBO. LS mean ΔDAS28-4(ESR) was generally numerically highest for pts with BMI <25 and numerically lowest for pts with BMI >30, for all tofacitinib doses. LS mean ΔDAS28-4(ESR) was generally greatest with tofacitinib 10 mg BID and 11 mg QD vs 5 mg BID across BL BMI status groups (Figure 1c). Across treatments, model-adjusted associations between LS mean ΔDAS28-4(ESR) and ΔBMI were weak (correlation coefficients all <0.3; Table 1).

Table 1. Correlations between LS mean ΔDAS28-4(ESR) and ΔBMI through M12

	Tofacitinib 5 mg BID		Tofacitinib 10 mg BID		Tofacitinib 11 mg QD		PBO	
	N	Correlation coefficient	N	Correlation coefficient	N	Correlation coefficient	N	Correlation coefficient
M3	2021	0.1169	1348	0.1240	641	0.0907	554	0.0783
M6	1918	0.1305	1270	0.1397	611	0.0438	150	0.1556
M12	1455	0.1213	874	0.1826	-	-	-	-

Slopes for associations between LS mean ΔBMI and ΔDAS28-4(ESR) were significantly different from 0 at M3/6/12 with tofacitinib 5 and 10 mg BID (all p<0.05). Correlations were analysed by a general linear model method, which included BL age, gender, race and RA duration. For pts receiving tofacitinib 11 mg QD in ORAL Shift (NCT02831855), only data to M6 were included. Pts who advanced from PBO to tofacitinib were not analysed post-advancement-DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; N, number of pts analysed

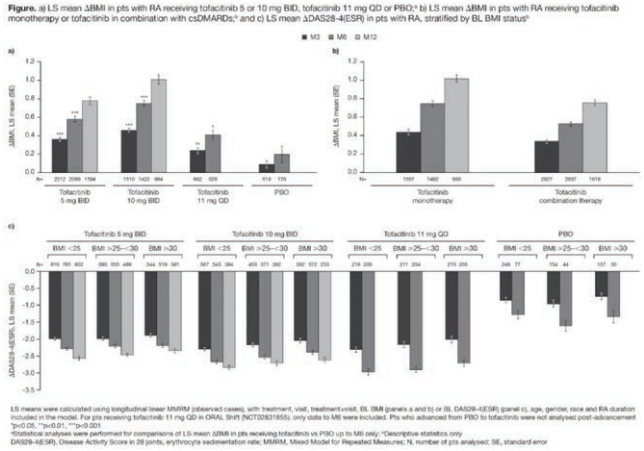


Figure. a) LS mean ΔBMI in pts with RA receiving tofacitinib 5 or 10 mg BID, tofacitinib 11 mg QD or PBO;[a] b) LS mean ΔBMI in pts with RA receiving tofacitinib monotherapy or tofacitinib in combination with csDMARDs;[a] and c) LS mean ΔDAS28-4(ESR) in pts with RA, stratified by BL BMI status[b]

LS means were calculated using longitudinal linear MMRM (observed cases), with treatment, visit, treatment-visit, BL BMI (panels a and b) or BL DAS28–4(ESR) (panel c), age, gender, race and RA duration included in the model. For pts receiving tofacitinib 11 mg QD in ORAL Shift (NCT02831855), only data to M6 were included. Pts who advanced from PBO to tofacitinib were not analysed post-advancement
*p<0.05, **p<0.01, ***p<0.001
[a]Statistical analyses were performed for comparisons of LS mean ΔBMI in pts receiving tofacitinib vs PBO up to M6 only; [b]Descriptive statistics only
DAS28–4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; MMRM, Mixed Model for Repeated Measures; N, number of pts analysed; SE, standard error

Conclusion: LS mean ΔBMI was greater with tofacitinib (all doses) vs PBO at M3/6, and with tofacitinib monotherapy vs combination therapy at M3/6/12. Improvements in DAS28-4(ESR) were seen across all BL BMI status groups. BMI increases with tofacitinib were only weakly associated with DAS28-4(ESR) improvements. The relationship between disease activity and ΔBMI requires further investigation.

REFERENCES:

[1] Dikranian et al. Arthritis Rheumatol 2018; 69 (S10): Abs 2371.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Anthony G McCluskey, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: Jürgen Wollenhaupt Speakers bureau: Pfizer Inc, Consultant of: Pfizer Inc, Jacques Morel Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Novartis, Pfizer Inc, Sanofi Genzyme, Grant/research support from: Bristol-Myers Squibb, Pfizer Inc, Claire Daien Consultant of: Abivax, Grant/research support from: AbbVie, Bristol-Myers Squibb, Chugai, Eli Lilly, MSD, Novartis, Pfizer Inc, Sandoz, Adeline Ruyssen-Witrand Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Mylan, Novartis, Pfizer Inc, Sanofi Genzyme, Grant/research support from: AbbVie, Amgen, Mylan, Pfizer Inc, Cédric Lukas Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer Inc, Sanofi Genzyme, UCB, Grant/research support from: Novartis, Pfizer Inc, Christophe Richez Consultant of: AbbVie, Amgen, AstraZeneca, Biogen, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Mylan, Pfizer Inc, Grant/research support from: Biogen, Eli Lilly, Glenmark, Nordic Pharma, Roche, Andrea Shapiro Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Douglass Chapman Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Magali CROS Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Jose Luis Rivas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Gustavo Citera Consultant of: AbbVie, Amgen, Eli Lilly, Gema, Genzyme, Novartis, Pfizer Inc, Sanofi Genzyme, Grant/research support from: AbbVie, Amgen, Eli Lilly, Gema, Genzyme, Novartis, Pfizer Inc, Sanofi Genzyme

DOI: 10.1136/annrheumdis-2021-eular.360

AB0248 INFLUENZA ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THE TOFACITINIB CLINICAL PROGRAMME

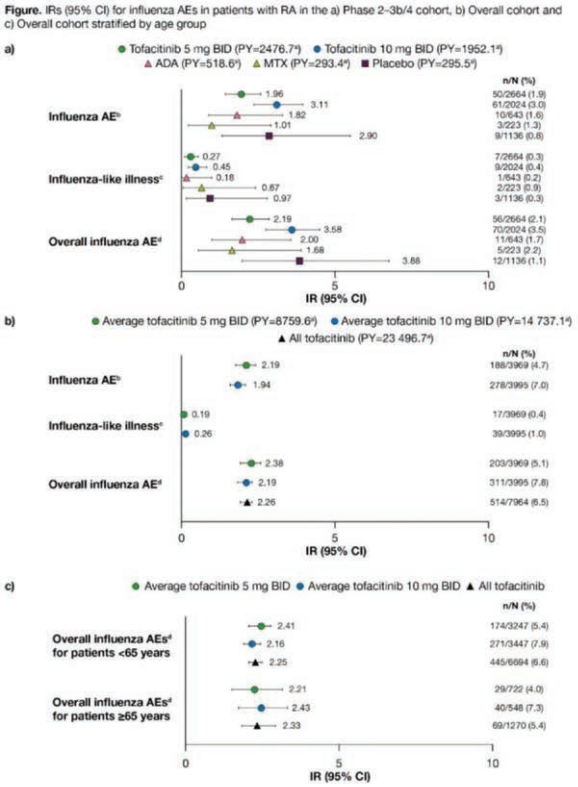
K. Winthrop[1], A. Yndestad[2], D. Henrohn[3], H. Jo[4], S. Marsal[5], M. Galindo-Izquierdo[6], A. Diehl[7], A. Shapiro[8], S. B. Cohen[9]. [1]*Oregon Health & Science University, Portland, OR, United States of America*; [2]*Pfizer Inc, Inflammation and Immunology, Oslo, Norway*; [3]*Pfizer Inc, Inflammation and Immunology, Sollentuna, Sweden*; [4]*Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*; [5]*Vall d'Hebron Hospital, Rheumatology Department, Barcelona, Spain*; [6]*Hospital Universitario 12 de Octubre, Rheumatology Unit, Madrid, Spain*; [7]*Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America*; [8]*Pfizer Inc, Inflammation and Immunology, Peapack, NJ, United States of America*; [9]*Metroplex Clinical Research Center, Dallas, TX, United States of America*

Background: Patients (pts) with rheumatoid arthritis (RA) have an increased susceptibility to seasonal influenza and its complications.[1] In light of the COVID-19 pandemic, there is a need to better understand acute respiratory viral RNA infections, such as influenza, in pts with RA.

Objectives: To present a comprehensive summary of data on influenza adverse events (AEs) occurring in the tofacitinib RA clinical programme.

Methods: Influenza AEs were evaluated in pts with RA from 21 Phase (P)1–3b/4 trials and two open-label, long-term extension (LTE) studies from 2005–2019. These were analysed as two cohorts: P2–3b/4 cohort (pts who received tofacitinib 5 or 10 mg twice daily [BID] as monotherapy or with conventional synthetic [cs]DMARDs, adalimumab, methotrexate or placebo, in P2–3b/4 controlled studies) and Overall cohort (pts who received ≥1 tofacitinib dose, as monotherapy or with csDMARDs, in P1–3b/4 and LTE studies; data were summarised by average tofacitinib dose [average tofacitinib 5 or 10 mg BID based on average total daily dose of <15 or ≥15 mg, respectively]). Incidence rates (IRs; unique pts with events/100 pt-years of exposure; censored at day of first event or up to last dose +28 days) were evaluated for influenza AEs, influenza complication AEs, influenza-like illness (all composites of several MedDRA preferred/verbatim terms) and overall influenza AEs (composite of all preferred/verbatim terms included under influenza AEs, influenza complication AEs and influenza-like illness). In the Overall cohort, the incidence of serious non-influenza AEs within 28 days of the start of an overall influenza AE and time taken to resolution of overall influenza AEs by action taken were summarised descriptively.

Results: In total, 7964 pts were included; 517 (6.5%) pts reported overall influenza AEs, three of which occurred outside the risk period. In the P2–3b/4 cohort (N=6690), IRs for influenza AEs, influenza-like illness and overall influenza AEs generally appeared similar across treatment arms (Figure 1a). In the Overall cohort, IRs for influenza AEs and influenza-like illness were similar between tofacitinib doses (Figure 1b), and IRs for overall influenza AEs were similar between tofacitinib doses and pt age groups (Figure 1c). No influenza complication AEs (eg pneumonia/encephalitis influenzal) were reported in either cohort. Among pts with overall influenza AEs, nine (1.7%) had serious overall influenza AEs (average tofacitinib 5 mg BID, n=6; average tofacitinib 10 mg BID, n=3). Of these pts, eight (1.5%) were hospitalised (average tofacitinib 5 mg BID, n=6; average tofacitinib 10 mg BID, n=2) and two (0.4%) died (average tofacitinib 5 mg BID, n=1; average tofacitinib 10 mg BID, n=1). Both deaths occurred in pts with H1N1 Influenza A. Twelve (2.3%) pts had a serious non-influenza AE within 28 days of the start of the overall influenza AE (average tofacitinib 5 mg BID, n=6; average tofacitinib 10 mg BID, n=6). The most common serious non-influenza AEs (one event each in average tofacitinib 5 and 10 mg BID groups) were acute respiratory distress syndrome and pneumonia. In most pts with overall influenza AEs, no change to tofacitinib treatment was made (70.2%, n=363) or treatment was stopped temporarily (28.2%, n=146) for a mean duration of 11.0 days. The mean number of days to resolution of overall influenza AEs was numerically similar, ranging from 10.4–11.8 days across tofacitinib doses, irrespective of these actions.



IRs were calculated as the number of unique pts with events (per 100 PY) during the time between the first and last dose +28 days, divided by the pt time accrued during the first and last dose +28 days, or up to the first event, whichever occurred earlier. 95% CI are based on the Exact Poisson method adjusted for exposure time
[a]Total PY of study drug exposure for all pts in treatment group
[b]Included all PTs under the high-level term 'influenza viral infections', and a collection of VTs for influenza AEs
[c]Included the PT 'influenza-like illness' and a collection of VTs for influenza-like illness
[d]Included all PTs and VTs included under influenza AEs, influenza complication AEs and influenza-like illness; no events of influenza complication AEs were reported
ADA, adalimumab; CI, confidence interval; MTX, methotrexate; PT, preferred term; PY, pt-years; VT, verbatim term

Conclusion: This post hoc analysis of influenza AEs across the tofacitinib RA clinical programme, over 14–15 influenza seasons, showed generally similar rates between treatment groups, and between tofacitinib doses and pt age groups. Limitations include varying exposure across treatment arms in the P2–3b/4 cohort. Most influenza AEs were non-serious (98.3%), and were not associated with changes to tofacitinib treatment.

REFERENCES:

[1] Blumentals et al. BMC Musculoskelet Disord 2012; 13: 158.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Kirsten Woollcott, CMC Connect, and funded by Pfizer Inc.
Disclosure of Interests: Kevin Winthrop Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead Sciences, Pfizer Inc, Roche, UCB, Arne Yndestad Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Dan Henrohn Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Hyejin Jo Consultant of: Pfizer Inc, Employee of: Syneos Health, Sara Marsal Shareholder of: IMIDomics, Consultant of: AbbVie, Celgene, Galapagos, Gilead Sciences, Pfizer Inc, Sandoz, Sanofi, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Jansen-Cilag, MSD, Novartis, Pfizer Inc, Roche, Sandoz, Sanofi, UCB, María Galindo-Izquierdo Grant/research support from: AbbVie, Eli Lilly, GSK, Janssen-Cilag, Annette Diehl Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Andrea Shapiro Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Stanley B. Cohen Consultant of: AbbVie, Eli Lilly, Genentech, Gilead Sciences, Pfizer Inc, Grant/research support from: AbbVie, Eli Lilly, Genentech, Gilead Sciences, Pfizer Inc
DOI: 10.1136/annrheumdis-2021-eular.361

AB0249 SAFETY OF BARICITINIB IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS (RA): THE 2020 INTERIM REPORT FROM ALL-CASE POST MARKETING SURVEILLANCE IN CLINICAL PRACTICE

T. Fujii[1], T. Atsumi[2], N. Okamoto[3], N. Takahashi[4], N. Tamura[5], A. Nakajima[6], A. Nakajima[7], H. Matsuno[8], N. Tsujimoto[9], A. Nishikawa[9], T. Ishii[9], T. Takeuchi[10], M. Kuwana[11], M. Takagi[12]. [1]*Wakayama Medical University, Department of Rheumatology and Clinical Immunology, Wakayama, Japan*; [2]*Hokkaido University, Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine, Sapporo, Hokkaido, Japan*; [3]*Osaka Medical College, Department of Rheumatology and Allergy of Pediatrics, Takatsuki, Osaka, Japan*; [4]*Nagoya University Graduate School of Medicine, Department of Orthopaedics/Rheumatology, Nagoya, Japan*; [5]*Juntendo University School of Medicine, Department of Internal Medicine and Rheumatology, Tokyo, Japan*; [6]*Ueno Touseki Clinic, Ueno Touseki Clinic, Fukuoka, Japan*; [7]*Mie University Hospital, Center for Rheumatic Diseases, Mie, Japan*; [8]*Matsuno Clinic for Rheumatic Diseases, -, Toyama, Japan*; [9]*Eli Lilly Japan K.K., -, Kobe, Japan*; [10]*Keio University School of Medicine, Division of Rheumatology, Tokyo, Japan*; [11]*Nippon Medical School Graduate School of Medicine, Department of Allergy and Rheumatology, Tokyo, Japan*; [12]*Yamagata University Faculty of Medicine, Department of Orthopaedic Surgery, Yamagata, Japan*

Background: An all-case post marketing surveillance (PMS) of baricitinib (Bari), that started in Sep 2017, collects safety and effectiveness for the first 24 wks of treatment and continues to collect serious adverse events (SAEs) for 3 yrs.
Objectives: To evaluate Bari safety in RA patients (pt) in clinical practice.
Methods: We report pt baseline demographics and adverse events (AEs) up to 24 wks for pts whose case report files for 24-wk data were completed as of Jun 2020.
Results: Data from 3445 pts were analyzed (females=80%, mean age=64yr, mean RA duration 12yr). Bari dose regimen was as follows: 4mg, 60%, 2mg, 27%, 4mg→2mg, 5%, 2mg→4mg, 5%, and others, 2%. Concomitant use of MTX and glucocorticoid was 65% and 48%, respectively. 74% continued treatment for 24 wks. AE and SAE were recognized in 887 (26%) and 122 pts (4%), respectively. 6 pts died of pneumonia, aspiration pneumonia, bacterial pneumonia, cerebral infarction/ILD/aspiration pneumonia, adenocarcinoma, and colorectal cancer. Major AEs were as follows: herpes zoster=3%, liver dysfunction=3%, serious infection=1%, anemia=1%, hyperlipidemia=1%, malignancy=0.3%, interstitial pneumonia=0.2%, MACE=0.1%, and VTE=0.1%.
Conclusion: Data do not show new safety concerns and encourage guideline-compliant use of Bari.
Disclosure of Interests: Takao Fujii Speakers bureau: Chugai Pharmaceutical Co. Ltd.; Eisai Co. Ltd; Eli Lilly Japan K.K.; Janssen Pharmaceutical K.K.; Ono Pharmaceutical Co. Ltd., Consultant of: Asahikasei Pharma Corp, Grant/research support from: Asahikasei Pharma Corp; AbbVie Japan GK; Chugai Pharmaceutical Co. Ltd., Eisai Co. Ltd; Eli Lilly Japan K.K.; Mitsubishi-Tanabe Pharma Co.; Ono Pharmaceutical Co., Ltd., Tatsuya Atsumi Speakers bureau: AbbVie Japan GK; Astellas Pharma Inc.; Bristol-Myers Squibb Co. Ltd; Chugai Pharmaceutical Co. Ltd.; Daiichi Sankyo Co. Ltd.; Eisai Co. Ltd.; Eli Lilly Japan K.K.; Mitsubishi Tanabe Pharma Co.; Pfizer Japan Inc.; Takeda Pharmaceutical Co. Ltd., UCB Japan Co. Ltd., Consultant of: AbbVie Japan GK; AstraZeneca plc.; Boehringer Ingelheim Co. Ltd.; Medical & Biological Laboratories Co. Ltd.; Novartis Pharma K.K.; Ono Pharmaceutical Co. Ltd.; Pfizer Japan Inc., Grant/research support from: Astellas Pharma Inc., Alexion Inc.; Chugai Pharmaceutical Co. Ltd., Daiichi Sankyo Co. Ltd., Mitsubishi Tanabe Pharma Co., Otsuka Pharmaceutical Co., Ltd.
Pfizer Japan Inc.; Takeda Pharmaceutical Co. Ltd., Nami Okamoto Speakers bureau: AbbVie Japan GK; Asahikasei Pharma Co.; AYUMI Pharmaceutical Co. Eisai Co. Ltd; Bristol-Myers Squibb Co. Ltd.; Eli Lilly Japan K.K.; Mitsubishi-Tanabe Pharma Co.; Pfizer Japan Inc.
Sanofi K.K.; Chugai Pharmaceutical Co. Ltd.; Novartis Pharma Co.; Teijin Pharma Ltd.; Torii Pharmaceutical Co., Ltd., Nobunori Takahashi Speakers bureau: AbbVie Japan GK; Eisai Co. Ltd.; Mitsubishi Tanabe Pharma Co.; Pfizer Japan Inc.; Chugai Pharmaceutical Co., Ltd.; Eli Lilly Japan K.K.; Janssen Pharmaceutical K.K.; UCB Japan Co. Ltd.; Astellas Pharma Inc.; Bristol Myers Squibb Co. Ltd., Grant/research support from: Bristol Myers Squibb Co. Ltd., Naoto Tamura Speakers bureau: AbbVie Japan GK; Bristol Myers Squibb Co. Ltd.; Chugai Pharmaceutical Co. Ltd.; Eisai Co. Ltd.; Eli Lilly Japan K.K.; Glaxo Smith Kline K.K.; Janssen Pharmaceutical K.K.; Mitsubishi-Tanabe Pharma Co.; Novartis Pharma Co., Atsuo Nakajima: None declared, Ayako Nakajima Speakers bureau: AbbVie Japan GK; Actelion Pharmaceuticals Japan Ltd., Asahi Kasei Pharma Co., Astellas Pharma Inc., Ayumi Pharmaceutical Co., Bristol Myers Squibb Co., Ltd.,Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., Glaxo Smith Kline K.K., Hisamitsu Pharmaceutical Co. Inc., Kyorin Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Otsuka Pharmaceutical Co. Ltd., Pfizer Japan Inc., Teijin Pharma Ltd., Grant/research support from: Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Hiroaki Matsuno Speakers bureau: Chugai Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Eli Lilly Japan K.K., Consultant of: Mochida Pharmaceutical Co., Ltd., Grant/research support from: Astellas Pharma Inc., Eli Lilly Japan K.K.; Janssen Pharmaceutical K.K, Naoto Tsujimoto Shareholder of: Eli Lilly, Employee of: Eli Lilly Japan K.K., Atsushi Nishikawa Shareholder of: Eli Lilly, Employee of: Eli Lilly Japan K.K., Taeko Ishii Shareholder of: Eli Lilly, Employee of: Eli Lilly Japan K.K., Tsutomu Takeuchi Speakers bureau: AbbVie Japan GK, Ayumi Pharmaceutical Co., Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co, Ltd. Daiichi Sankyo Co., Ltd. Eisai Co., Ltd. Eli Lilly Japan K.K.; Gilead Sciences, Inc. Janssen Pharmaceutical K.K.; Mitsubishi-Tanabe Pharma Co.; Novartis Pharma Co.; Pfizer Japan Inc.; Sanofi K.K.; UCB Japan Co., Ltd., Consultant of: AbbVie Japan GK, Astellas Pharma, Inc.; Chugai Pharmaceutical Co, Ltd.; Eli Lilly Japan K.K.; Eisai Co., Ltd.; Gilead Sciences, Inc.; Janssen Pharmaceutical K.K.; Mitsubishi-Tanabe Pharma Corp., Pfizer Japan Inc., Grant/research support from: AbbVie Japan GK, Asahikasei Pharma Corp., Chugai Pharmaceutical Co, Ltd., DNA Chip Research Inc.; Eisai Co., Ltd., Eli Lilly Japan K.K.; Mitsubishi-Tanabe Pharma Corp., UCB Japan Co., Ltd., Masataka Kuwana Speakers bureau: AbbVie Japan GK, Astellas Pharma Inc., Asahi Kasei Pharma Co., Boehringer-Ingelheim, Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Medical &Biological Laboratories Co., Ltd.; Mitsubishi Tanabe Pharma Co.; Mochida Pharmaceutical Co., Ltd., Nippon Shinyaku Co., Ltd.; Ono Pharmaceutical Co., Ltd.; Pfizer Japan Inc., Consultant of: Boehringer-Ingelheim, Chugai Pharmaceutical Co., Ltd., Corbus Pharmaceuticals Holdings, Inc.; Medical &Biological Laboratories Co., Ltd.; Mochida Pharmaceutical Co., Ltd., Grant/research support from: Boehringer-Ingelheim, Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Medical &Biological Laboratories Co., Ltd; Mitsubishi Tanabe Pharma Co., Ono Pharmaceutical Co., Ltd., Michiaki Takagi Speakers bureau: Yes, but sponsored lectures without COI in the academic meetings, only.
DOI: 10.1136/annrheumdis-2021-eular.433

AB0250 TOFACITINIB SUPPRESSES SEVERAL JAK-STAT PATHWAYS IN RHEUMATOID ARTHRITIS AND BASELINE SIGNALING PROFILE ASSOCIATES WITH TREATMENT RESPONSE

M. Palmroth[1], K. Kuuliala[2], R. Peltomaa[3], A. Virtanen[1], A. Kuuliala[2], A. Kurttila[1], A. Kinnunen[4], M. Leirisalo-Repo[3], O. Silvennoinen[1,5,6], P. Isomäki[1,4]. [1]*Tampere University, Faculty of Medicine and Life Sciences, Tampere, Finland*; [2]*University of Helsinki, Department of Bacteriology and Immunology, Faculty of Medicine, Helsinki, Finland*; [3]*University of Helsinki and Helsinki University Hospital, Faculty of Medicine, Helsinki, Finland*; [4]*Tampere University Hospital, Centre for Rheumatic Diseases, Tampere, Finland*; [5]*Fimlab Laboratories, Pirkanmaa Hospital District, Tampere, Finland*; [6]*University of Helsinki, Institute of Biotechnology, HiLIFE Helsinki Institute of Life Sciences, Helsinki, Finland*

Background: Cytokines are important mediators of inflammation and tissue destruction in rheumatoid arthritis (RA) [1]. Several cytokines involved in RA pathogenesis act through Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway [2]. The effects of JAK-inhibitor tofacitinib on cytokine signaling *in vitro* are well established, while *in vivo* evidence in patients remains scarce.
Objectives: To investigate *in vivo* in rheumatoid arthritis patients i) which JAK-STAT pathways are inhibited by tofacitinib and ii) if baseline signaling profile is associated with the treatment response.
Methods: Sixteen patients with active RA, despite treatment with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), received tofacitinib 5 mg twice daily for three months. Levels of basal and cytokine-induced phosphorylated STATs and total STAT1 and STAT3 in peripheral blood monocytes, T cells and B cells were measured by flow cytometry. mRNA expression of JAKs, STATs and suppressors of cytokine signaling (SOCS) were measured from peripheral blood mononuclear cells (PBMCs) by quantitative PCR. Association of baseline signaling profile with treatment response (the change from baseline in disease activity score (DAS28)) was studied by calculating correlation coefficients.
Results: Treatment with tofacitinib and csDMARDs decreased median DAS28 from 4.4 to 2.6 ($p < 0.001$). Tofacitinib significantly decreased cytokine-induced phosphorylation of all JAK-STAT pathways studied. Basal STAT1, STAT3, STAT4 and STAT5 phosphorylation in monocytes and/or T cells was downregulated by tofacitinib. No changes were observed in STAT1 and STAT3 protein

levels, while gene expression of *STAT3*, *STAT4*, *STAT5A*, *JAK1*, *JAK3* and all studied *SOCS*s was significantly suppressed. Baseline STAT phosphorylation levels in T cells and monocytes and *SOCS3* expression in PBMCs correlated with treatment response.

Conclusion: Tofacitinib suppresses multiple JAK-STAT pathways in RA patients *in vivo*. Baseline JAK-STAT signaling profile may be applicable as a prognostic marker for treatment response to tofacitinib.

REFERENCES:

[1] McInnes, I. B., Buckley, C. D. & Isaacs, J. D. Cytokines in rheumatoid arthritis-shaping the immunological landscape. *Nature Reviews Rheumatology* vol. 12 63–68 (2016).

[2] Schwartz, D. M., Bonelli, M., Gadina, M. & O'Shea, J. J. Type I/II cytokines, JAKs, and new strategies for treating autoimmune diseases. *Nat. Rev. Rheumatol.* **12**, 25–36 (2016).

Acknowledgements: This study was supported by Pfizer Inc.

Disclosure of Interests: Maaria Palmroth Consultant of: Pfizer and from 1/21 a part-time employee of MedEngine and consultant for Pfizer, Krista Kuuliala Grant/research support from: Pfizer, Ritva Peltomaa Speakers bureau: Boehringer Ingelmheim, Pfizer, Sanofi, Paid instructor for: Boehringer Ingelheim, Eli Lilly and Company, Janssen, Abbvie, UCB Pharma, Anniina Virtanen: None declared, Antti Kuuliala: None declared, Antti Kurttila: None declared, Anna Kinnunen: None declared, Marjatta Leirisalo-Repo: None declared, Olli Silvennoinen Speakers bureau: Pfizer, AbbVie, Pia Isomäki Speakers bureau: Abbvie, Eli Lilly and Company, Pfizer, Roche, Paid instructor for: Abbvie, Eli Lilly and Company, Pfizer, Roche, Grant/research support from: Pfizer

DOI: 10.1136/annrheumdis-2021-eular.448

AB0251 INCREASED ACCUMULATION OF ERYTHROCYTE METHOTREXATE POLYGLUTAMATES DURING EARLY PHASE SUBCUTANEOUS VERSUS ORAL METHOTREXATE TREATMENT OF RHEUMATOID ARTHRITIS PATIENTS

R. Hebing[1,2], I. Muller[3], M. Lin[3], S. Mahmoud[1], S. Heil[4], W. Lems[1,2], M. Nurmohamed[1,2], R. De Jonge[3], G. Jansen[3]. *[1]Reade, Rheumatology, Amsterdam, Netherlands*; *[2]Amsterdam UMC, Location VUmc, Rheumatology, Amsterdam, Netherlands*; *[3]Amsterdam UMC, Location VUmc, Clinical Chemistry, Amsterdam, Netherlands*; *[4]Erasmus MC, Clinical Chemistry, Rotterdam, Netherlands*

Background: Optimal dosing of methotrexate (MTX) for individual rheumatoid arthritis (RA) patients to achieve adequate disease control is an ongoing challenge. Assessment of erythrocyte MTX-polyglutamates (PGs) levels has been employed as a tool to monitor clinical response of RA patients in the first 3-12 months of treatment and MTX-PG_{2-4} and total MTX-PGs were associated with a lower DAS28 over 9 months.[1] However, data from earlier time points, MTX-PG_6 and per route of administration are unavailable.

Objectives: To investigate the pharmacokinetics and -dynamics of erythrocyte MTX-PG accumulation in RA patients receiving oral or subcutaneous MTX in the early phase (1, 2, and 3 months) of MTX treatment initiation.

Methods: In a clinical prospective cohort study (MeMo study (NTR7149)), newly diagnosed RA patients were administered oral (n=24) or subcutaneous (n=22) MTX, mostly according to the COBRA-light schedule (start 10 mg MTX, increased to 25 mg MTX in 8 weeks). At 1, 2, and 3 months after start of therapy, blood was collected and individual MTX-PGs (MTX-PG_1 – MTX-PG_6) were analyzed in erythrocytes at a minimal detection limit of 1 nmol/L, using a validated UHPLC-MS/MS method with labeled internal standards.[1] Dosing, concomitant treatments and DAS28-ESR assessments were in conformity with clinical practice. Adverse events were recorded.

Results: 46 consecutive patients were included in this study; 76% female, mean age: 57.8 years, BMI: 25.8, 20% smokers, mean baseline DAS28-ESR: 3.5. Notwithstanding marked interpatient variability, patients starting subcutaneous MTX had accumulated significantly higher (approximately 2-fold) long chain MTX-PGs (MTX-PG_{4-6}) when compared to patients in the oral MTX group at 1 and 2 months (Figure 1A, Table 1). Similarly, MTX-PG_{1-6} and MTX-PG_3 accumulation were higher in subcutaneous MTX-users at month 1 (p=0.022 and p=0.011) compared to the oral group (median 68.6 nmol/L (IQR:40.5) vs 51.9 (55.6) and 17.4 (11.1) vs 11.2 (15.6), respectively (Figure 1B, Table 1).

Table 1. ***Linear regression of MTX-PG levels and administration route, corrected for age, baseline DAS28, smoking, BMI, eGFR and MTX dose.***

month	ß (P-value) 1	ß (P-value) 2	ß (P-value) 3
MTX-PG_{1-6}	1.65 (0.022)	1.51 (0.073)	1.30 (0.233)
MTX-$PG_{1,2}$	1.13 (0.599)	1.19 (0.470)	1.12 (0.623)
MTX-PG_3	1.75 (0.011)	1.51 (0.071)	1.19 (0.439)
MTX-PG_{4-6}	1.97 (0.036)	2.04 (0.033)	1.55 (0.136)

Mean MTX dose at baseline was 10.5mg (SD 1.5) for both groups, 15.4 (4.4) and 16.8 (1.8) at 1 month and 22.8 (3.9) and 22.4 (5.2) at 2 months for oral and subcutaneous use respectively.

DAS28 decreased with 1.6 in the oral group and 1.1 in the subcutaneous group (p=0.382). With and without corrections for age, baseline DAS28, eGFR, MTX dose (1 month before sampling), smoking and BMI, no significant relation between MTX-PG concentrations and DAS28 was observed during the first 3 months of treatment.

43 patients reported any side effect, mostly headache and dizziness, which was similar in both groups and uncorrelated with MTX-PG levels.

No association was found between MTX-PG_1 levels and number of days between timing of blood withdrawal and last administration.

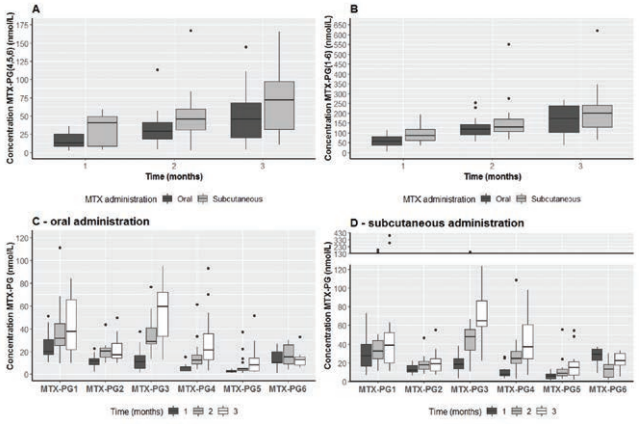


Figure 1. *Erythrocyte long chain MTX-PG (**A**) and total MTX-PG (**B**) accumulation in RA patients of the first 3 months of oral (**C**) or subcutaneous (**D**) MTX administration. At 3 months, 18 patients using oral and 18 patients using subcutaneous MTX were still continuing MTX treatment. Medians and IQR are depicted.*

Conclusion: This study shows the feasibility of measuring erythrocyte MTX-PGs early on in the treatment of RA patients with MTX and demonstrated significantly higher accumulation of MTX-PGs following subcutaneous versus oral MTX administration. Early phase erythrocyte MTX-PG analyses may hold potential for positioning in optimizing individual patient MTX dose scheduling.

REFERENCES:

[1] de Rotte MC, et al. Methotrexate polyglutamates in erythrocytes are associated with lower disease activity in patients with rheumatoid arthritis. *Ann Rheum Dis* 2015(74):408-14.

Acknowledgements: We would like to thank all participating patients and Pfizer (grant 53233663 / WI230458).

Disclosure of Interests: Renske Hebing Grant/research support from: Pfizer, Ittai Muller: None declared, Marry Lin: None declared, Sohaila Mahmoud: None declared, Sandra Heil: None declared, WIllem Lems: None declared, Michael Nurmohamed: None declared, Robert De Jonge: None declared, Gerrit Jansen: None declared

DOI: 10.1136/annrheumdis-2021-eular.525

AB0252 EFFICACY OF A SECOND JANUS KINASE INHIBITOR THAT WAS SWITCHED FOR DIFFICULT-TO-TREAT RA IN CLINICAL PRACTICE

M. Kamiya[1], D. Togawa[2], S. Mori[2], K. Yamazaki[2]. *[1]Nara Hospital, Kindai University, Orthopedic Surgery and Rheumatology, Ikoma-City, Japan*; *[2]Nara Hospital, Kindai University, Orthopaedic Surgery and Rheumatology, Ikoma-City, Japan*

Background: In clinical practice, when refractory rheumatoid arthritis (RA) is present, of which the definition implies previous use of at least two biologic disease-modifying antirheumatic drugs (bDMARDs) (generally tumour necrosis factor inhibitors (TNFis)), the next treatment choice often made is a bDMARD of another class (non-TNFis) [1]. However, patients who are inadequately responding to bDMARDs need new treatment options because subsequent bDMARDs treatment reduces their response [2]. Janus Kinase inhibitors (JAKis) are the first targeted synthetic DMARDs (tsDMARD) licensed for the treatment of RA with comparable efficacy to bDMARDs. Unlike the single cytokine targeting approach of bDMARDs, JAKis are specifically designed to inhibit intracellular signalling molecules common to the receptors of multiple inflammatory cytokines implicated in RA pathogenesis. The choice of therapeutic agents for refractory RA is increasing, and its efficacy is expected. On the other hand, it is also true that some patients discontinued JAKis at a rate that cannot be overlooked because

of insufficient efficacy. Difficult-to-treat (D2T) RA is defined as refractory to two or more b/ts DMARDs with different mechanisms of action, with active and progressive disease, as published by Eular(3)

Objectives: To evaluate real world efficacy of approved JAKis switching in patients with D2T RA who were unable to control their disease activity due to insufficient efficacy despite the sequential use of multiple bDMARDs and JAKis, focusing on the drug retention rate.

Methods: In our hospital, RA was diagnosed according to the 1987 or 2010 classification criteria, and when two or more bDMARDs (including both TNFis and non-TNFis) were inadequately effective, it was defined as D2T RA. We retrospectively investigated patients who switched to JAKis for D2T RA. The drug retention rate was investigated by the Kaplan-Meier method, and the difference was tested by the Logrank test.

Results: The 1-year retention rate of JAKis for D2T RA was 50.8% in TOF 38 cases [28 women, age average 70.2 years, disease duration average 12.4 years, past bDMARDs use average 3.5 drugs, MTX combination 9 cases, DAS28 ESR average 4.11] and 66.3% in BAR 35 cases [26 cases, 73.0 years old, 14.8 years, 4.17 agents, 9 cases, 3.68], and there was no significant difference (P = 0.30). Among them, there were 17 cases [11 cases, 70.6 years old, 13.5 years, 4.18 drugs, 2 cases, 3.65] of switching between JAKis, all of which were switching from TOF to BAR. The 1-year retention rate was 45.8% [reason for discontinuation: insufficient effect in 3 cases, adverse events in 6 cases], which was not significantly different but tended to be lower than 72.7% [reason for discontinuation: insufficient effect in 1 case, adverse event in 2 cases, patient's convenience in 1 case] in 16 patients [13 cases, 76.3 years old, 17.1 years, 3.19 drugs, 7 cases, 3.69] who received BAR as the first JAKi for D2T RA patients (P = 0.089).

Conclusion: Although the number of cases is small in the retrospective survey, it is suggested that the retention rate of BAR switched to D2T RA may be slightly lower in patients with a history of TOF discontinuation due to insufficient efficacy than in JAKi naive patients. It is expected that the number of new JAKi usage cases will increase in the future, and it is necessary to consider switching between other JAKis in addition to switching from BAR to TOF.

REFERENCES:

[1] Smolen JS, Landewe R, Bijlsma J et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 2017;76:960_77.

[2] Rendas-Baum R, Wallenstein GV, Koncz T et al. Evaluating the efficacy of sequential biologic therapies for rheumatoid arthritis patients with an inadequate response to tumor necrosis factor-α inhibitors. Arthritis Res Ther 2011;13:R25.

[3] Nagy G, et al. EULAR definition of difficult-to-treat rheumatoid arthritis. Ann Rheum Dis 2021;80:31–35. doi:10.1136/annrheumdis-2020-217344.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.541

AB0253

COMPARISON OF PHARMACODYNAMICS OF METHOTREXATE AS METHOTREXATE-POLYGLUTAMATES CONCENTRATIONS IN RHEUMATOID ARTHRITIS; INTERIM DATA EVALUATION OF MIRACLE STUDY CONDUCTED IN JAPAN, KOREA AND TAIWAN

H. Tamai[1], Y. Kaneko[1], H. Kameda[2], M. Kuwana[3], Y. Okano[4], T. Ishii[5], K. Ikeda[6], H. Taguchi[7], S. Sato[8], T. Miyamoto[9], S. Hirata[10], H. Yasuoka[11], T. Kojima[12], S. H. Park[13], K. Shin[14], H. J. Baek[15], Y. J. Lee[16], I. A. Choi[17], J. Kim[18], P. N. Hsu[19], C. F. Kuo[20], C. M. Huang[21], M. Y. Weng[22], W. Y. Sung[23], W. C. Tsai[23], T. T. Cheng[24], T. Taninaga[25], M. Mori[25], H. Miyagishi[25], Y. Sato[26], T. Takeuchi[1].

[1]Keio University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan; [2]Toho University Ohashi Medical Center, Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan; [3]Nippon Medical School Graduate School of Medicine, Department of Allergy and Rheumatology, Tokyo, Japan; [4]National Hospital Organization Tokyo Medical Center, Department of Connective Tissue Diseases, Tokyo, Japan; [5]Tohoku University Graduate School of Medicine, Department of Hematology and Rheumatology, Sendai, Japan; [6]Chiba University Hospital, Department of Allergy and Clinical Immunology, Chiba, Japan; [7]Kawasaki Municipal Kawasaki Hospital, Department of Internal Medicine and Center for Arthritis and Rheumatic Disease, Kawasaki, Japan; [8]Tokai University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Isehara, Japan; [9]Seirei Hamamatsu General Hospital, Department of Rheumatology, Hamamatsu, Japan; [10]Hiroshima University Hospital, Department of Clinical Immunology and Rheumatology, Hiroshima, Japan; [11]Fujita Health University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Aichi, Japan; [12]Nagoya University Graduate School of Medicine, Department of Orthopedic Surgery, Nagoya, Japan; [13]Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea); [14]Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea); [15]Gachon University College of Medicine, Gil Medical Center, Division of Rheumatology, Department of Internal Medicine, Incheon, Korea, Rep. of (South Korea); [16]Seoul National University Bundang Hospital, Division of Rheumatology, Department of Internal Medicine, Seongnam, Korea, Rep. of (South Korea); [17]Chungbuk National University, Department of Internal Medicine, Cheongju, Korea, Rep. of (South Korea); [18]Chungnam National University College of Medicine, Department of Internal Medicine, Daejeon, Korea, Rep. of (South Korea); [19]National Taiwan University Hospital, Department of Internal Medicine, Taipei, Taiwan, Republic of China; [20]Chang Gung Medical Foundation, LinKou Chang Gung Memorial Hospital, Division of Rheumatology, Allergy and Immunology, Department of Internal Medicine, Taoyuan, Taiwan, Republic of China; [21]China Medical University Hospital, Division of Rheumatology and Immunology, Department of Internal Medicine, Taichung, Taiwan, Republic of China; [22]National Cheng Kung University Hospital, Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Tainan, Taiwan, Republic of China; [23]Kaohsiung Medical University Chung-Ho Memorial Hospital, Department of Allergy, Immunology, and Rheumatology, Kaohsiung, Taiwan, Republic of China; [24]Chang Gung Medical Foundation, Kaohsiung Chang Gung Memorial Hospital, Division of Rheumatology, Allergy and Immunology, Department of Internal Medicine, Kaohsiung, Taiwan, Republic of China; [25]Eisai Co., Ltd., Tokyo, Japan; [26]Keio University School of Medicine, Department of Preventive Medicine and Public Health, Tokyo, Japan

Background: Methotrexate (MTX) is the first-line therapy for rheumatoid arthritis (RA). The concentrations of MTX-polyglutamates (PG) in erythrocytes, an active form of MTX, are useful markers for the optimal usage of MTX in patients with RA. The concentrations of MTX-PG have been reported to be different between Japanese and Caucasians. However, the difference among Asian ethnicity remains unclear.

Objectives: To examine MTX-PG concentrations in association with MTX dose during the first 24 weeks after the initiation of MTX for newly diagnosed RA patients in Japan, Korea and Taiwan.

Methods: MIRACLE study is a multicenter, open-label, randomized, 48 weeks interventional study conducted in Japan, Korea and Taiwan to evaluate non-inferiority of low dose to high dose of MTX as an add-on therapy to adalimumab in 300 patients with RA who do not achieve remission after 24 weeks MTX monotherapy in stipulated dosage. In the first 24 weeks, MTX was started at 6 to 8 mg/week for newly diagnosed RA patients, and promptly escalated to the maximum tolerable dose in 12 weeks in principle. This interim data evaluation was intended to investigate the differences among countries in the relationship between MTX dose, safety and MTX-PG concentrations in erythrocytes during the first 24 weeks. The efficacy of the treatment is not included at this point.

Results: A total of 166 patients (106 in Japan, 35 in Korea, 25 in Taiwan) were included in this interim data. The age at treatment initiation was 57.2 years old on average and female was 79.5%. The time course changes in total and individual MTX-PG levels differed in the three countries. At 24 weeks, whereas the mean total MTX-PG concentrations were comparable (112.9 nmol/L in Japan, 104.4 nmol/L in Korea, and 115.7 nmol/L in Taiwan) with a dose of MTX of 12.3 mg/week, 14.1 mg/week, and 12.2 mg/week, respectively, the individual MTX-PG concentrations were different. The MTX-PG1 and MTX-PG2 concentrations were lower in Korea than Japan and Taiwan whereas MTX-PG3, MTX-PG4 and MTX-PG5 concentrations were the highest in Korea.

Conclusion: The distribution of short-chain and long-chain MTX-PG concentrations were various among Asian countries despite similar dose of MTX administration: NCT03505008.

Disclosure of Interests: Hiroya Tamai: None declared, Yuko Kaneko Speakers bureau: AbbVie, Astellas, Ayumi, Bristol–Myers Squibb, Chugai, Eisai, Eli Lilly, Hisamitsu, Jansen, Kissei, Kirin, Pfizer, Sanofi, Takeda, Tanabe-Mitsubishi, and UCB., Grant/research support from: Sanofi, Hideto Kameda Speakers bureau: AbbVie, Pfizer, Consultant of: AbbVie, Grant/research support from: AbbVie, Eisai, Masataka Kuwana Speakers bureau: Astellas, Asahi Kasei Pharma, Boehringer- Ingelheim, Chugai, Eisai, Janssen, Mochida, Nippon Shinyaku, Ono Pharmaceuticals, Pfizer, Mitsubishi-Tanabe, Consultant of: Corbus, Grant/research support from: AbbVie, Asahi Kasei Pharma, Boehringer- Ingelheim, Chugai, Eisai, MBL, Nippon Shinyaku, Ono Pharmaceuticals, Mitsubishi-Tanabe, Yutaka Okano: None declared, Tomonori Ishii Speakers bureau: Chugai, Mitsubishi- Tanabe, Glaxo Smith Kline, Pfizer, Eli Lilly, Janssen, AbbVie, Eisai, Astellas, Kei Ikeda Speakers bureau: AbbVie, Eli Lilly, Novartis, Mitsubishi-Tanabe, Eisai, BMS, Grant/research support from: Mitsubishi-Tanabe, Hiroaki Taguchi: None declared, Shinji Sato: None declared, Toshiaki Miyamoto: None declared, Shintaro Hirata Speakers bureau: AbbVie, Asahi Kasei Pharma, Astellas, Ayumi, Bristol Myers Squibb, Chugai, Eisai, Eli Lilly, Janssen, Glaxo Smith Kline, Kissei, Pfizer, Sanofi, Mitsubishi- Tanabe, UCB, Paid instructor for: AbbVie, Mitsubishi- Tanabe, Consultant of: AbbVie, Eisai, Gilead, Grant/research support from: AbbVie, Chugai, Mitsubishi-Tanabe, UCB, Hidekata Yasuoka Speakers bureau: AbbVie, Asahi Kasei Pharma, Astellas, Daiichi- Sankyo, Eisai, Kissei, Takeda, Mitsubishi- Tanabe, Chugai, Novartis, Eli Lilly, Pfizer, Janssen, Sanofi, Teijin, Boehringer- Ingelheim, Bayer, Glaxo Smith Kline, Paid instructor

for: AbbVie, Consultant of: AbbVie, Asahi Kasei, Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Toshihisa Kojima Speakers bureau: AbbVie, Pfizer, Eisai, Grant/research support from: AbbVie, Sung-Hwan Park: None declared, Kichul Shin: None declared, Han Joo Baek: None declared, Yun Jong Lee Grant/research support from: research fund, In Ah Choi Speakers bureau: Abbvie, Eizai, Grant/research support from: Abbvie, Eizai, Jinhyun Kim: None declared, Ping-Ning Hsu: None declared, Chang-Fu Kuo: None declared, Chun-Ming Huang Paid instructor for: AbbVie, Pfizer, Meng-Yu Weng Consultant of: AbbVie, Wan-Yu Sung: None declared, Wen-Chan Tsai: None declared, Tien-Tsai Cheng Paid instructor for: AbbVie, Grant/research support from: AbbVie, Takehiro Taninaga Shareholder of: Eisai Co., Ltd., Employee of: Eisai Co., Ltd., Masahiko Mori Shareholder of: Eisai Co., Ltd., Employee of: Eisai Co., Ltd., Hideaki Miyagishi Employee of: Eisai Co., Ltd., Yasunori Sato: None declared, Tsutomu Takeuchi Speakers bureau: Astellas, Abbvie, Daiichi Sankyo, Ayumi, Eisai, GlaxoSmithKline, Mitsubishi Tanabe, Chugai, Novartis, Eli Lilly, Pfizer, Bristol Myers Squibb, Janssen, UCB, TaishoToyama, Sanofi–Aventis, Nipponkayaku, Taiho, Gilead, Boehringer Ingelheim, Grant/research support from: Asahikasei, Astellas, Abbvie, Daiichi Sankyo, Ayumi, Eisai, Takeda, Mitsubishi Tanabe, Chugai, Eli Lilly, UCB, Sanofi–Aventis, Nipponkayaku, Boehringer Ingelheim

DOI: 10.1136/annrheumdis-2021-eular.762

AB0254 NEUROPSYCHIATRIC ADVERSE DRUG REACTIONS ASSOCIATED WITH LOW DOSE METHOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS

J. Van Lint[1], T. Bakker[1], P. Ten Klooster[2,3], H. Vonkeman[2,4], N. Jessurun[1].
[1]Netherlands Pharmacovigilance Centre Lareb,'s Hertogenbosch, Netherlands; *[2]University of Twente, Psychology, Health & Technology, Enschede, Netherlands*; *[3]Transparency in Healthcare B.V., -, Hengelo, Netherlands*; *[4]Medisch Spectrum Twente, Rheumatology and Clinical Immunology, Enschede, Netherlands*

Background: Neuropsychiatric adverse drug reactions (NPADRs) are well known with high dose methotrexate treatment. However, NPADRs have also been observed with low dose methotrexate (LDMTX) treatment in real world rheumatology data.
Objectives: To evaluate the association between LDMTX and NPADRs, the impact of these NPADRs on further treatment and on health related quality of life (HRQoL) in patients with rheumatoid arthritis (RA) using real world data.
Methods: The nature and frequency of NPADRs associated with LDMTX in the Dutch DREAM-RA registry were described. We assessed the causality of each NPADR with the Naranjo Probability Scale (NPS), the impact of NPADRs on further LDMTX treatment and the impact on patient reported HRQoL. NPADRs were structured using terminology of the Medical Dictionary for Regulatory Activities.
Results: A total of 71 NPADRs (frequency 6.8%) associated with LDMTX were captured in the DREAM-RA registry. NPADRs were registered for 62 (5.9%) out of 1048 patients with 10.9 NPADRs per 1000 patient years (Table 1). The most frequently reported NPADRs were headache, dizziness and depression. The causality was considered probable for 67 NPADRs (94.4%) and definite for 1 NPADR (1.4%). The NPADRs led to LDMTX withdrawal in 34 cases (47.9%) and LDMTX was not restarted in 16 cases (47.1%). Median mental HRQoL was significantly decreased around the occurrence of the NPADR and remained significantly lower after the event. Median physical HRQoL was not significantly affected.

Table 1. Baseline characteristics of DREAM-RA patients using methotrexate with at least one neuropsychiatric adverse drug reaction

Characteristics N=62		N (%)
Female sex		40 (64.5%)
Age in years, mean (± SD), range		59.8 (± 13.1), 25 – 82
Rheumatoid factor	Positive	43 (69.4%)
	Negative	13 (21.0%)
	Unknown	6 (9.7%)
Anti-CCP, n (%)	Positive	34 (54.8%)
	Negative	19 (30.7%)
	Unknown	9 (14.5%)
Methotrexate dosage in mg/week, mean (± SD)		18.7 (± 5.9)
Specific methotrexate dosage	< 15 mg / week	5 (7.0%)
	15 mg/week	28 (39.4%)
	20 mg/week	11 (15.5%)
	25 mg/week	14 (19.7%)
	30 mg/week	5 (7.0%)
	Unknown	8 (11.3%)
Concomitant medication at moment of NPADR	Folic acid	68 (95.8%)
	Prednisolone	20 (28.2%)

Anti-CCP: anti cyclic citrullinated peptides, NPADR: neuropsychiatric adverse drug reaction, SD: Standard Deviation

Conclusion: The association between NPADRs and LDMTX in RA patients was recognised by HCPs and frequently led to LDMTX withdrawal and a decrease in mental HRQoL. Many NPADRs scored 'probable' using the NPS. Knowledge on the nature, frequency and impact of these NPADRs will enhance attention towards potential NPADRs during LDMTX therapy allowing better risk assessment and communication to patients.
Disclosure of Interests: Jette van Lint: None declared, Tom Bakker: None declared, Peter ten Klooster: None declared, Harald Vonkeman Consultant of: BMS, Celgene, Celltrion, Galapagos, Gilead, Janssen-Cilag, Lilly, Novartis, Pfizer, Sanofi-Genzyme, Grant/research support from: Abbvie, Naomi Jessurun: None declared

DOI: 10.1136/annrheumdis-2021-eular.882

AB0255 BASELINE CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH UPADACITINIB IN GERMAN REAL-WORLD PRACTICE: RESULTS FROM THE POST-MARKETING OBSERVATIONAL UPwARDS STUDY

T. Witte[1], U. Kiltz[2,3], F. Haas[4], E. Riechers[1], U. Prothmann[5], D. Adolf[6], C. Holland[7], R. Hecht[7], A. Roessler[7], K. Famulla[7], K. Krueger[8]on behalf of the UPwArds Study Group. *[1]Hannover Medical University, Clinic for Rheumatology and Immunology, Hannover, Germany*; *[2]Rheumazentrum Ruhrgebiet, Rheumatology, Herne, Germany*; *[3]Ruhr-Universität Bochum, Rheumatology, Bochum, Germany*; *[4]Internistisch-Rheumatologische Facharztpraxis, Rheumatology, Tübingen, Germany*; *[5]Knappschaftsklinikum Saar, Rheumatology, Puettlingen, Germany*; *[6]StatConsult GmbH, Statistics, Magdeburg, Germany*; *[7]AbbVie Germany GmbH & Co. KG, Immunology, Wiesbaden, Germany*; *[8]Praxiszentrum St. Bonifatius, Rheumatology, Munich, Germany*

Background: The efficacy and safety of upadacitinib (UPA), a selective Janus kinase inhibitor, has been evaluated in the SELECT rheumatoid arthritis (RA) clinical program,[1–6] but its real-world effectiveness remains to be investigated. The UPwArds study will assess the association of C-reactive protein (CRP) level with remission and other efficacy outcomes in patients with RA treated with UPA in German real-world practice.
Objectives: To describe the baseline characteristics of patients enrolled in the UPwArds study.
Methods: The prospective, open-label, multicenter, non-interventional, post-marketing UPwArds study included adult patients with moderate-to-severe RA (swollen joint count [SJC28] ≥3 and inadequate response or intolerance to ≥1 disease-modifying antirheumatic drug [DMARD]). Patients were treated with UPA 15 mg once daily, as monotherapy or in combination with methotrexate (MTX; 50:50 mono:combo enrollment planned), according to the German label. Variables assessed included medical history (disease duration, previous RA therapy, and vaccination status), CRP level, and disease activity (disease activity score [DAS28(CRP)], tender joint count [TJC28], and SJC28). There was no recruitment restriction regarding CRP level. This descriptive interim analysis reports patient baseline characteristics after enrollment was complete. All data were analyzed as observed, with no imputation of missing data.
Results: 533 patients (UPA monotherapy: 257 [48%]; UPA plus MTX: 276 [52%]) were included. Mean patient age was 58 years; mean disease duration was 9 years (Table 1). Despite having active RA, almost half the population (44%; n=237) did not have elevated CRP at the start of UPA treatment. Mean DAS28(CRP) was 4.6; mean TJC28 and SJC28 were 7.7 and 5.6, respectively. Overall, 39% of patients had not been treated with any biologic (b) DMARD or targeted synthetic (ts) DMARD before enrollment; 25% and 36% had previously been treated with 1 or ≥2 bDMARDs or tsDMARDs, respectively (Figure 1). 8.7% of patients had previously received a herpes zoster vaccination (8.1% Shingrix; 0.6% Zostavax).
Conclusion: In German clinical practice, the population of patients with RA in the UPwArds study was predominantly treatment-refractory. Half of these patients had no elevated CRP despite active disease; future analyses will assess the impact of CRP on efficacy outcomes.

REFERENCES:

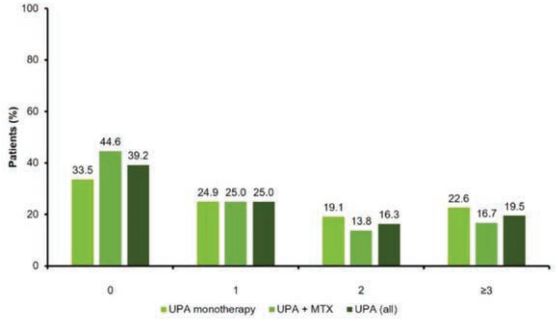
[1] Smolen JS, et al. Lancet 2019;393:2303–11;
[2] Burmester GR, et al. Lancet 2018;391:2503–12;
[3] Genovese MC, et al. Lancet 2018;391:2513–24;
[4] van Vollenhoven R, et al. Arthritis Rheumatol 2020;72:1607–20;
[5] Fleischmann R, et al. Arthritis Rheumatol 2019;71:1788–800;
[6] Rubbert-Roth A, et al. N Engl J Med 2020;383:1511–21.

Table 1. Baseline characteristics

	UPA	UPA + MTX	Total
Age, years	57.7 (13.2) n=257	58.1 (11.4) n=276	57.9 (12.3) n=533
Disease duration, years	9.4 (8.3) n=253	8.5 (7.7) n=272	9.0 (8.0) n=525
CRP, mg/dL	1.3 (1.9) n=257	1.1 (1.7) n=276	1.2 (1.8) n=533
CRP >ULN, n (%)	137 (53.3) n=257	159 (57.6) n=276	296 (55.5) n=533
TJC28	7.4 (6.0) n=257	7.9 (6.4) n=276	7.7 (6.2) n=533
SJC28	5.5 (3.7) n=257	5.6 (4.1) n=276	5.6 (3.9) n=533
Patient's Global Assessment	6.2 (1.9) n=257	6.3 (1.8) n=276	6.3 (1.8) n=533
Physician's Global Assessment	5.8 (1.5) n=257	5.9 (1.6) n=276	5.9 (1.6) n=533
DAS28(CRP)	4.6 (1.0) n=257	4.6 (1.0) n=276	4.6 (1.0) n=533
DAS28(ESR)	4.8 (1.1) n=224	4.9 (1.2) n=239	4.9 (1.1) n=463
CDAI	24.9 (10.2) n=257	25.7 (10.8) n=276	25.4 (10.5) n=533
SDAI	26.2 (10.5) n=257	26.9 (11.3) n=276	26.6 (10.9) n=533
RAID	5.7 (2.0) n=255	5.7 (2.0) n=275	5.7 (2.0) n=530
Pain (RAID-1)	6.2 (2.2) n=255	6.1 (2.3) n=275	6.2 (2.2) n=530
SF-12 Physical Component Summary	32.6 (8.5) n=245	33.9 (8.6) n=262	33.3 (8.6) n=507
SF-12 Mental Component Summary	42.4 (11.6) n=245	42.6 (11.3) n=262	42.5 (11.5) n=507
HAQ-DI	1.3 (0.7) n=250	1.3 (0.6) n=270	1.3 (0.6) n=520
PHQ-9	8.9 (5.3) n=252	8.6 (5.3) n=272	8.7 (5.3) n=524
Erosions, n (%)	87 (33.9) n=257	95 (34.4) n=276	182 (34.1) n=533

Data are mean (SD), n unless otherwise stated

Figure Number of prior bDMARDs or tsDMARDs for rheumatoid arthritis



bDMARD, biologic DMARD; DMARD, disease-modifying antirheumatic drug; tsDMARD, targeted synthetic DMARD

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and in the writing, review, and approval of the abstract. AbbVie and the authors thank all study investigators for their contributions and the patients who participated in this study. No honoraria or payments were made for authorship. Medical writing support was provided by Grant Thomas Kirkpatrick, MSc, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Disclosure of Interests: Torsten Witte Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Chugai, Gilead, Janssen, Lilly, MSD, Mylan, Novartis, Pfizer, Roche, and UCB., Uta Kiltz Consultant of: AbbVie, Biocad, Eli Lilly and Company, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Amgen, Biogen, Fresenius, GSK, Hexal, Novartis, and Pfizer, Florian Haas Consultant of: AbbVie, Celgene, Novartis, and Pfizer, Grant/research support from: AbbVie, BMS, Celgene, Chugai, MSD, Novartis, Pfizer, Roche, and Sanofi Genzyme, Elke Riechers Consultant of: AbbVie, Chugai, Novartis, and UCB, Grant/research support from: AbbVie, Chugai, Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Ulrich Prothmann Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Chugai, Glaxo Smith Kline, Novartis, Pfizer, Roche, Sanofi, SOBI, and UCB, Daniela Adolf Employee of: Employee of StatConsult and may own stock or options, Carsten Holland Employee of: Employee of AbbVie and may own stock or options, Rouven Hecht Employee of: Employee of AbbVie and may own stock or options, Alexander Roessler Employee of: Employee of AbbVie and may own stock or options, Kirsten Famulla Employee of: Employee of AbbVie and may own stock or options, Klaus Krueger Grant/research support from: AbbVie, Biogen, BMS, Celltrion, Gilead, Hexal, Janssen, Lilly, Medac, MSD, Novartis, Pfizer, Roche, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.886

AB0256 BARICITINIB (BARI) VERSUS BIOLOGICS IMPACT ON STEROID TAPERING IN RHEUMATOID ARTHRITIS (RA)

L. Cometi[1], C. Bruni[1], L. Tofani[1], G. Tesei[1,2], F. Nacci[1], G. Fiori[1], F. Bartoli[1], M. Matucci-Cerinic[1]. [1]*Careggi University Hospital, Experimental and Clinical Medicine, Division of Rheumatology, Firenze, Italy*; [2]*Ospedale "Infermi" di Rimini, Medicina e Reumatologia, Rimini, Italy*

Background: Biologic and target synthetic disease modifying anti-rheumatic drugs (bDMARDs and tcDMARDs) are recommended to control RA disease activity, pain and steroid use. Following randomized clinical trials (RCTs) and their post-hoc analyses, the Janus Kinase Inhibitor tsDMARDs BARI was superior to reference bDMARD Adalimumab in reducing disease activity, pain and functional disability. In addition, BARI monotherapy also determined more significant pain reduction and functional improvement when compared to Tocilizumab monotherapy (3).

Objectives: to confirm RCT results in a real-life clinical setting, with focus on disease activity, pain, functional disability and steroid tapering, when comparing BARI to bDMARDs for the treatment of active RA.

Methods: RA patients starting BARI or a bDMARD for active RA were retrospectively evaluated from June 2019 to June 2020. Disease activity (DAS28CRP, SDAI, CDAI), pain visual analogic scale (pain_VAS), functional disability (HAQ) assessments and mean prednisone dosage (pred_dose) were collected at baseline (BL), 3 months (3M) and 6 months (6M) after BARI/bDMARD initiation. The changes of the outcome measures were evaluated between BL-3M, 3M-6M and BL-6M, as well as between BARI and bDMARDs groups. Finally, we assessed the variables associated with prednisone tapering in the whole population.

Results: 90 out of 100 RA patients evaluated (baseline: age 57±12 years, disease duration 131±100 months, DAS28PCR 4.8±1.0, pain_VAS 61±23 mm, prednisone dose 5.5±5.3 mg) were eligible for the study; 49 received BARI and 41 bDMARDs (17 abatacept, 12 TNF inhibitors, 11 tocilizumab, 1 rituximab). At BL, the two groups did not differ statistically in terms of age, sex, disease duration, disease activity, pain_VAS, previous bDMARD failure or ts/bDMARD naive, concomitant conventional synthetic DMARDs treatment, pred_dose. Both BARI and bDMARDs determined a significant reduction in activity scales and HAQ when comparing BL-3M and BL-6M, with only pain_VAS and pred_dose showing a significant decrease in the 3M-6M interval. When comparing the two groups, BARI showed a significantly higher reduction of pred_dose (-3.2±5.1 vs -1.7±3.7 mg at BL-3M, and -4.1±5.3 vs -1.9±4.6 mg at BL-6M), which was not significant after adjusting for BL pred_dose. No other difference was seen when the two groups, including the numerically higher reduction of pain_VAS in the BARI group (-29±28 vs -20±27 mm at BL-3M and -35±25 vs -30±28 mm at BL-6M comparison). The analysis of the predictors for steroid tapering (Δmean_pred) in the two intervals, showed that BL DAS28PCR, DAS28PCR BL-3M change and BL pred_dose were associated with BL-3M Δmean_pred, while 3M pain_VAS and 3M pred_dose were associated with 3M-6M Δmean_pred.

Conclusion: Although limited by the small samples and the retrospective nature, our real-life comparison shows similar efficacy of BARI and bDMARDs in terms of disease activity control, functional disability and pain. In addition, the treatment with BARI or bDMARD did not influence the steroid tapering, which was driven mostly by its initial dose, disease activity and pain. Larger real-life multi-center studies are warranted to confirm our results.

REFERENCES:

[1] Taylor PC et al. Baricitinib versus Placebo or Adalimumab in Rheumatoid Arthritis. N Engl J Med. 2017 Feb 16;376(7):652-662.

[2] Fautrel B et al. Effect of Baricitinib and Adalimumab in Reducing Pain and Improving Function in Patients with Rheumatoid Arthritis in Low Disease Activity: Exploratory Analyses from RA-BEAM. J Clin Med. 2019 Sep 5;8(9):1394.

[3] Fautrel B et al. Comparative effectiveness of improvement in pain and physical function for baricitinib versus adalimumab, tocilizumab and tofacitinib monotherapies in rheumatoid arthritis patients who are naïve to treatment with

Disclosure of Interests: Laura Cometi: None declared, Cosimo Bruni Speakers bureau: Actelion, Consultant of: Eli Lilly, Grant/research support from: Fondazione Italiana Ricerca sull'Artrite (FIRA), Gruppo Italiano lotta alla Sclerodermia (GILS), New Horizon Fellowship, European Scleroderma Trials and Research (EUSTAR) group, Foundation for Research in Rheumatology (FOREUM)., Lorenzo Tofani: None declared, Giulia Tesei: None declared, Francesca Nacci: None declared, Ginevra Fiori: None declared, Francesca Bartoli: None declared, Marco Matucci-Cerinic Speakers bureau: Biogen

Italia, Actelion, Bayer, Boehringer Ingelheim, CSL Behring, Eli-Lilly, Consultant of: Biogen Italia, Actelion, Bayer, Boehringer Ingelheim, CSL Behring, Eli-Lilly, Grant/research support from: Biogen Italia, Actelion, Bayer, Boehringer Ingelheim, CSL Behring, Eli-Lilly,
DOI: 10.1136/annrheumdis-2021-eular.1343

AB0257 IMPACT OF CONVENTIONAL ANTIRHEUMATIC TREATMENT ON CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

D. Gerasimova[1], E. Gerasimova[2], T. Popkova[2], A. Melkumyan[1]. [1]*I.M. Sechenov First Moscow State Medical University (Sechenov University), Department of Organization and Economy of Pharmacy, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases Laboratory, Moscow, Russian Federation*

Background: Cardiovascular diseases (CVD) are the most common and socially significant comorbidities and the main cause of premature mortality in rheumatoid arthritis (RA). Appropriate RA therapy should not only suppress RA activity, but also reduce CVD risk.
Objectives: To evaluate CVD risk and analyze its association with the use of conventional therapy in RA patients (pts).
Methods: The study included 100 pts with RA (92 women and 8 men) aged 30 to 60 without established CVD. The median age was 49.5 [44.5;53] years, duration of RA was 144 [60;240] months, DAS28 was 4.4 [3.3;5.3] points. Eighty six RA pts (86%) treated with disease-modifying antirheumatic drugs (DMARDs) (methotrexate, n=55; leflunomide, n=12; hydroxychloroquine, n=8; sulfasalazine, n=11), including 33 pts (33%) in combination with glucocorticoids (GCs). Fourteen pts (14%) received monotherapy with GCs. Pts were divided into three treatment groups: DMARDs group, n=53; GCs group, n=14; DMARDs+GCs group, n=33. CVD risk was calculated with ASSIGN, QRISK3, and ERS-RA scales.
Results: No differences were found between the groups when calculating CVD risk using ASSIGN (table 1). Estimated CVD risk by QRISK3 was lower in DMARDs group (4.9 [3.0; 7.7]) than in DMARDs+GCs group (7.1 [4.1; 13.6], p<0.05). High CVD risk on the ERS-RA scale was determined less frequently (13%) and median CVD risk was lower in DMARDs group (4.2 [2.2; 5.4]) than in GCs group (57%; 8.9 [4.8; 11.7], p<0.01) and DMARDs+GCs group (39%; 6.6 [3; 9.3], p<0.05, respectively). In DMARDs group, significant differences in CVD risk by ERS-RA were found in pts treated with hydroxychloroquine (2 [1.4; 5.8]) and leflunomid (6.2 [2.8; 12.3], p<0.05).
Conclusion: RA pts treated with DMARDs have a reduced risk for CVD than pts treated with GCs or a combination of DMARDs and GCs. GCs significantly increase CVD risk. To clarify the impact of hydroxychloroquine and leflunomid on CVD risk, a study on a larger number of pts is required.

Table 1. The impact of conventional antirheumatic therapy on CVD risk.

Treatment	ASSIGN		QRISK3		ERS-RA	
	High CVD risk, %	median [25-75 percentiles]	High CVD risk,%	median [25-75 percentiles]	High CVD risk,%	median [25-75 percentiles]
DMARDs, n=53	6	11 [6.5;14]	2	4.9 [3;7.7] ˅	13*˅	4.2 [2.2;5.4] *˅
GCs, n=14	7	9.5 [7;13]	7	6.6 [4.4;15.8]	57*	8.9 [4.8;11.7] *
DMARDs+GCs, n=33	15	10 [5;13.5]	9	7.1 [4.1;13.6] ˅	39˅	6.6 [3;9.3] ˅

Note: * - p<0.01 between pts receiving DMARDs and GCs; ˅ - p<0.05 between pts receiving DMARDs and DMARDs+GCs.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1554

AB0258 DMARD-TREATMENT OF UNDIFFERENTIATED ARTHRITIS INTENSIFIED DURING THE LAST DECENNIA, BUT DID NOT RESULT IN IMPROVED LONG TERM OUTCOMES

M. Verstappen[1], X. Matthijssen[1], A. Van der Helm - van Mil[1,2]. [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [2]*Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands*

Background: EULAR guidelines stress timely initiation of DMARD-treatment in early arthritis patients also when classification criteria are not yet fulfilled. Consequently, undifferentiated arthritis (UA) patients may be increasingly treated with disease modifying antirheumatic drugs (DMARDs), despite inadequate placebo-controlled evidence for its effectivity. Implementation of this guideline also hampers future placebo-controlled trials in UA. However, historical data, with inclusion period as instrumental variable, can provide insight whether long term outcome is improved with increased DMARD-use, and thus serve to investigate if DMARD-treatment is effective in UA.
Objectives: With 25-years of observational data of newly referred UA-patients, we studied whether enhanced treatment strategies resulted in better long term outcomes for UA.
Methods: Between 1993 and 2019, 1132 consecutive UA-patients, not fulfilling the 1987/2010 criteria for RA or any other distinct diagnosis, were included in the Leiden Early Arthritis Cohort; patients were divided in 5 inclusion periods (1993-1998, 1999-2005, 2006-2010, 2011-2014, 2015-2019). Frequency of DMARD-initiation after diagnosis was compared. We studied the following outcomes: the course of disease activity scores (DAS28-CRP) and Health assessment questionnaires (HAQ), progression to RA after 1-year (according to the 1987 and/or 2010 criteria) and the frequency of prolonged DMARD-free status within 10-years of follow-up (this was defined as either spontaneous remission or sustained remission after discontinuation of DMARD-treatment).
Results: The current population of UA-patients, thus not fulfilling 1987 or 2010 criteria, had rather mild disease: the median SJC was 1, the median TJC 2, 95% was autoantibody-negative and the median HAQ was 0.6. These characteristics were similar in the different inclusion periods. Initiation of DMARD-treatment in UA increased over time: 18%, 35%, 38%, 43% up to 55% in respectively 1993-1998, 1999-2005, 2006-2010, 2011-2014 and 2015-2019, in which methotrexate became more common in the last decade. Frequency of progression to RA after 1-year did not decrease and was 14%, 21%, 26%, 19% and 28% in the respective inclusion periods. Long-term DAS28CRP-scores improved from 2011 onwards (range -0.18, -0.24; p<0.05). However HAQ-score over time did not improve compared to the 1993-1998 period (range -0.00, -0.08; p>0.05). Also the percentages of patients in DMARD-free status after 10-years of follow-up did not significantly improve over time: 57%, 58%, 59% (for 1993-1998, 1999-2005, 2006-2010 respectively, p=0.59).
Conclusion: Intensified DMARD-treatment of patients with UA did not result in improved outcomes. These data may indicate overtreatment of UA-patients. Yet, methods to stratify which UA-patients should be treated remains warranted.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1559

AB0259 EVALUATION OF THE EFFECT OF FILGOTINIB ON THE PHARMACOKINETICS OF ROSUVASTATIN, ATORVASTATIN, AND PRAVASTATIN

K. Anderson[1], C. Nelson[1], Q. Gong[1], M. Alani[1], T. Tarnowski[1], A. A. Othman[1]. [1]*Gilead Sciences, Inc., Foster City, United States of America*

Background: Filgotinib is an orally administered small molecule that preferentially inhibits Janus kinase 1 and is approved for use in Europe and Japan in adult patients with rheumatoid arthritis (RA) who have had an inadequate response to conventional therapies. Patients with RA are at a higher risk of cardiovascular morbidity and mortality relative to the general population[1]. Thus, it is important to understand potential drug-drug interactions of filgotinib with lipid-lowering agents such as statins. Based on in vitro studies, filgotinib is not expected to significantly increase exposure of statins via inhibition of the organic anion transporting peptide (OATP) at clinically relevant exposures. Hence, in Phase 2 and Phase 3 clinical studies, statins were allowed for use with filgotinib. A post-hoc analysis showed no increase in statin-induced AEs such as muscle or liver toxicities when statins were coadministered with filgotinib ("Concomitant Use of Statins in Filgotinib-Treated Patients with Rheumatoid Arthritis: A Post Hoc Analysis," submitted to EULAR 2021).
Objectives: The objectives of this study (NCT04608344) were to evaluate the effect of filgotinib on the pharmacokinetics of atorvastatin, pravastatin, and rosuvastatin, which are sensitive substrates for the OATP-1B1/1B3, and the short-term safety of administering filgotinib with or without statins.
Methods: This was an open-label, randomized, two-way, crossover study in healthy adult volunteers (n = 27). Study participants received a single dose of atorvastatin (ATV 40 mg) and a single dose of a cocktail of pravastatin (PRA 40 mg)/rosuvastatin (ROS 10 mg), on two different occasions with washout in between, alone or in combination with filgotinib (200 mg QD for 11 days). Serial pharmacokinetic sampling was performed and pharmacokinetic parameters for each statin were calculated. Safety was assessed throughout the study. An analysis of variance using a mixed-effects model was applied to the natural logarithmic transformation of pharmacokinetic parameters (C_{max} and AUC_{inf}) for ATV, 2-OH-ATV (active metabolite of ATV), PRA, and ROS. Geometric-least squares means (GLSM) ratios and 90% confidence intervals (90% CI) of pharmacokinetic parameters were estimated for each analyte and were compared against pre-specified lack of pharmacokinetic alteration boundaries of 70 to 143%.
Results: Of the 27 enrolled participants, 25 participants completed all study treatments. Most AEs and laboratory abnormalities were Grade 1 or 2 in severity; 1 participant discontinued due to a Grade 3 increase in creatine kinase and 1 participant discontinued due to difficulty in blood draws. Following coadministration of filgotinib with ATV, relative to ATV alone, ATV AUC_{inf} was unaffected

(GLSM ratio (90% CI): 0.91 (0.84, 0.99)), but ATV C_{max} was slightly reduced (GLSM ratio (90% CI): 0.82 (0.69, 0.98)). 2-OH-ATV exposure (C_{max} and AUC_{inf}) were unaffected (GLSM ratio (90% CI): 0.98 (0.81, 1.18) for C_{max} and 1.12 (1.02, 1.22) for AUC_{inf}), and were within the pre-specified lack-of-effect bounds. Following coadministration with filgotinib, PRA AUC_{inf} was unaffected (GLSM ratio (90% CI): 1.22 (1.06, 1.42)), but PRA C_{max} was slightly higher (1.25 (1.01, 1.54)). ROS exposure (C_{max} and AUC_{inf}) were moderately higher upon coadministration with filgotinib (GLSM ratio (90% CI): 1.68 (1.43, 1.97) for C_{max} and 1.42 (1.30, 1.56) for AUC_{inf}), and these changes in rosuvastatin exposure are not considered to be clinically relevant.

Conclusion: All study treatments were generally well tolerated. Co-administration with filgotinib did not have a clinically meaningful impact on the exposure of ATV, PRA, and ROS. These data support concomitant use of filgotinib with OATP substrates such as statins.

REFERENCES:

[1] Piepoli MF, Hoes AW, Agewall S, et al. *Eur Heart J.* 2016;37(29): 2315-2381.

Disclosure of Interests: Kacey Anderson Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Cara Nelson Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Qi Gong Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Muhsen Alani Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Thomas Tarnowski Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Ahmed A. Othman Shareholder of: Gilead Sciences, Employee of: Gilead Sciences

DOI: 10.1136/annrheumdis-2021-eular.1685

AB0260 LONG-TERM EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS FROM CHINA, BRAZIL, AND SOUTH KOREA WITH RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: RESULTS AT 64 WEEKS

X. Zeng[1,2], D. Zhao[3], S. Radominski[4], M. Keiserman[5], C. K. Lee[6], N. Martin[7], S. Meerwein[8], Y. Sui[9], W. Park[10]. *[1]Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences, Beijing, China*; *[2]National Clinical Research Center for Dermatologic and Immunologic Diseases (NCRC-DID), Dermatology and Immunology, Beijing, China*; *[3]Shanghai Changhai Hospital, Rheumatology and Immunology, Shanghai, China*; *[4]Universidade Federal do Paraná, Rheumatology, Curitiba, Brazil*; *[5]Pontifical Catholic University, Rheumatology, Porto Alegre, Brazil*; *[6]Asan Medical Center, Rheumatology, Seoul, Korea, Rep. of (South Korea)*; *[7]AbbVie Inc, Immunology, Quebec, Canada*; *[8]AbbVie Deutschland GmbH & Co. KG, Immunology, Ludwigshafen, Germany*; *[9]AbbVie Inc, Immunology, North Chicago, Illinois, United States of America*; *[10]School of Medicine, Inha University, Rheumatology, Incheon, Korea, Rep. of (South Korea)*

Background: Upadacitinib (UPA), an oral Janus kinase inhibitor, in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), showed significant improvements in clinical and functional measures compared with placebo (PBO) up to 12 weeks (wks), in patients (pts) from China, Brazil, and South Korea with rheumatoid arthritis (RA) and prior inadequate response to csDMARDs (csDMARD-IR).[1]

Objectives: To assess the efficacy and safety of UPA up to 64 wks (long-term extension; LTE) in csDMARD-IR pts with RA from China, Brazil, and South Korea.

Methods: Pts were randomized to 12 wks of blinded treatment with UPA 15 mg once daily (QD) or PBO, in combination with csDMARDs. From Wk 12 onward, pts could continue to receive open-label UPA 15 mg QD. Efficacy endpoints were analyzed by original randomized treatment group sequences over 64 wks and included American College of Rheumatology (ACR) responses, and key remission and low disease activity measures. Non-responder imputation was used to handle missing data for binary endpoints. Treatment-emergent adverse events (TEAEs) per 100 patient-years (PY) were summarized for pts receiving ≥1 dose of UPA from baseline through to Wk 64.

Results: Of 338 randomized pts who received ≥1 dose of study drug, 310 (91.7%) entered the LTE and 275 (81.4%) completed 64 wks of treatment. Among those initially randomized to UPA, the proportion of pts achieving 20%/50%/70% improvement in ACR criteria, and key remission and low disease activity measures increased over 64 wks of treatment (Figure 1). Improvements from baseline in the Health Assessment Questionnaire-Disability Index and pts' assessment of pain were observed over 64 wks of UPA treatment (data not shown). By Wk 64, efficacy results for pts who switched from PBO to UPA at Wk 12 followed a similar trajectory to those originally randomized to UPA.

The observed rate of serious infections was 8.1 events/100 PY. Herpes zoster events were mostly non-serious, involving only 1 or 2 dermatomes. Most cases of hepatic disorders were Grade 1 or 2 hepatic transaminase elevations. There was 1 case of venous thromboembolic event (VTE; concurrent pulmonary embolism and deep vein thrombosis [DVT] in a patient with a history of DVT) and 3 cases of malignancy. Adjudicated major adverse cardiovascular events (Table 1) occurred in 2 pts (1 with non-fatal myocardial infarction and 1 with non-fatal stroke) who had underlying risk factors for cardiovascular disease. There were no deaths, active tuberculosis, or renal dysfunction.

Conclusion: UPA 15 mg was effective in treating the signs and symptoms of RA and in improving physical function over 64 wks with no new safety signals[1] in csDMARD-IR pts with RA from China, Brazil, and South Korea.

REFERENCES:

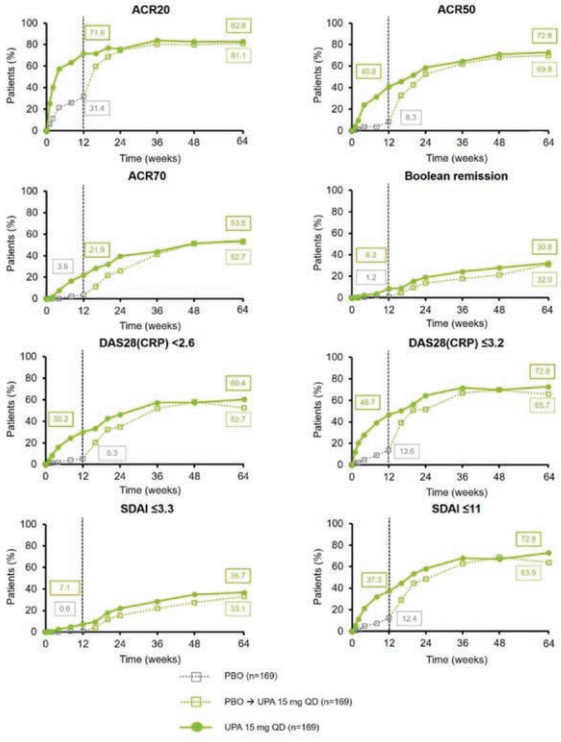
[1] Zeng A, et al. Ann Rheum Dis 2020;79(Suppl 1):1016 [abstract SAT0160]

Table 1. TEAEs at Wk 64

Event (E/100 PY)	UPA 15 mg (n=322; PY=334.5)
Any AE	421.5 (399.8–444.1)
Serious AE	19.1 (14.7–24.4)
AE leading to discontinuation of study drug	9.0 (6.1–12.8)
Deaths[a]	0
AEs of special interest	
Serious infection	8.1 (5.3–11.7)
Opportunistic infection	0.9 (0.2–2.6)
Herpes zoster	9.0 (6.1–12.8)
Hepatic disorder	42.2 (35.5–49.7)
Gastrointestinal perforation (adjudicated)	0.3 (0.0–1.7)
Any malignancy (excluding NMSC)	0.6 (0.1–2.2)
NMSC	0.3 (0.0–1.7)
MACE (adjudicated)[b]	0.6 (0.1–2.2)
VTE (adjudicated)[c]	0.3 (0.0–1.7)
Anemia	11.1 (7.8–15.2)
Neutropenia	11.7 (8.3–15.9)
Lymphopenia	7.8 (5.1–11.4)
CPK elevation	11.1 (7.8–15.2)

[a]Including non-treatment-emergent deaths. [b]Defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke. [c]Including DVT and pulmonary embolism.AE, adverse event; CPK, creatine phosphokinase; E, events; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer

Figure Efficacy over 64 wks (non-responder imputation)



ACR20/50/70, 20%/50%/70% improvement in American College of Rheumatology criteria; DAS28(CRP), Disease Activity Score in 28 joints using C-reactive protein; PBO, placebo; QD, once daily; SDAI, Simple Disease Activity Index; UPA, upadacitinib; wks, weeks

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Yanna Song, PhD, of AbbVie provided statistical support. Medical writing support was provided by Laura Chalmers, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Disclosure of Interests: Xiaofeng Zeng: None declared, Dongbao Zhao: None declared, Sebastiao Radominski: None declared, MAURO KEISERMAN: None declared, Chang-Keun Lee: None declared, Naomi Martin Employee of: AbbVie employee and may own stock or options, Sebastian Meerwein Employee of: AbbVie employee and may own stock or options, Yunxia Sui Employee of: AbbVie employee and may own stock or options, Won Park: None declared
DOI: 10.1136/annrheumdis-2021-eular.1807

AB0261 A MULTINATIONAL, PROSPECTIVE, OBSERVATIONAL STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING BARICITINIB, TARGETED SYNTHETIC OR BIOLOGIC DISEASE-MODIFYING THERAPIES (RA-BE-REAL) – STUDY DESIGN AND BASELINE CHARACTERISTICS

R. Alten[1], G. R. Burmester[2], M. Matucci-Cerinic[3], J. H. Salmon[4], P. López-Romero[5], W. Fakhouri[5], I. De La Torre[5], A. Gentzel-Jorczyk[5], T. Holzkaemper[5], B. Fautrel[6,7]. [1]*University Medicine Berlin, Department of Internal Medicine and Rheumatology, Berlin, Germany*; [2]*Charité Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; [3]*University of Florence, Division of Rheumatology, Florence, Italy*; [4]*CHU de Reims, Traumatologie-Orthopédie, Reims, France*; [5]*Eli Lilly and Company, Lilly Corporate Center, Indianapolis, United States of America*; [6]*Sorbonne University, Department of Rheumatology, Paris, France*; [7]*Pierre Louis Institute of Epidemiology and Public Health, PEPITES Team, Paris, France*

Background: Baricitinib (BARI) is a JAK1-2 inhibitor approved for the treatment of adults with moderately to severely active rheumatoid arthritis (RA). RA-BE-REAL is a 3-year, prospective, observational study of adult RA patients (pts) evaluating adherence to treatment in clinical practice.
Objectives: To describe pt and disease characteristics of pts enrolling into RA-BE-REAL in 5 European countries.
Methods: The primary endpoint of RA-BE-REAL is time until discontinuation of initial treatment for all causes (excluding sustained clinical response) over a 24-month (M) period. Secondary endpoints include clinical and pt reported outcomes, healthcare resource utilization and treatment patterns over a 36M period. Two pt cohorts are assessed: cohort A, started treatment with BARI (2-mg or 4-mg), and cohort B, any other targeted synthetic (ts)DMARDs or biologic (b) DMARD (Fig. 1). Treatment initiation and changes are at the discretion of the pt and physician. Data is collected at baseline and at routine visits (~3M, 6M, 12M, 18M, 24M and 36M). Summaries are presented with t-test and chi-square test of independence.
Results: Between October 2018 and March 2020, 1074 adult RA pts were enrolled from France, Germany, Italy, Spain, and UK. In cohort A, 88.2% of pts are treated with BARI 4-mg. At time of enrolment pts in cohort A are more likely to commence treatment as a monotherapy as compared to pts in cohort B who are more likely to commence treatment in combination with csDMARDs (p<0.001). Cohort A are more likely to be older (59.2 vs 57.0, mean years p=0.009) and have higher Health Assessment Questionnaire-Disability Index (HAQ-DI) scores (1.4 vs 1.3, p=0.03). A greater percentage of cohort A pts have received prior treatment with either 1 b/tsDMARD (15.3 vs 11.0%), 2 b/tsDMARD (20.2 vs 14.7%) or >2 b/tsDMARD (15.9 vs 12.9%), while cohort B are more likely to be treatment naïve (61.4 vs 48.5%). There are no significant differences in other baseline characteristics shown in Table 1.
Conclusion: There are few but potentially clinically important differences between cohorts. Pts in cohort A are more likely to be older, have a longer disease duration, have received prior b/tsDMARD treatment, and are more likely to receive treatment as a monotherapy as compared to pts in cohort B.

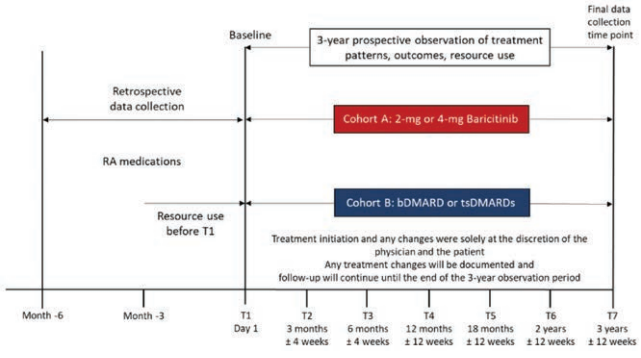


Figure 1. Study Design. Participants entered cohort A or B based on their treatment decision for BARI or another b/tsDMARD, pts in each cohort were with/without concomitant csDMARDs.

Table 1. Patient disposition and baseline characteristics.

	Cohort A Baricitinib (n=509)	Cohort B			Overall (n=1074)
		TNFi (n=338)	non-TNFi (n=161)	tsDMARD (n=66)	
Combination Therapy	238 (46.8)	231 (40.9)	110 (19.5)	38 (6.7)	617 (57.4)
with any csDMARD	271 (53.2)	107 (18.9)	51 (9.0)	28 (5.0)	457 (42.6)
monotherapy	Cohort A	Cohort B	p-value		Overall
Values represent n (%)	(n=509)	(n=565)			(n=1074)
Age in years	59.2 (13.2)	57.0 (13.9)	0.009		58.0 (13.6)
Disease duration in years	10.3 (9.2)	9.1 (9.8)	0.05		9.7 (9.5)
CDAI	24.1 (11.7)	23.9 (12.4)	0.75		24.0 (12.1)
Swollen joint count	5.2 (4.8)	4.7 (4.9)	0.18		4.9 (4.8)
Tender joint count	7.3 (6.1)	7.8 (6.5)	0.19		7.6 (6.3)
PhGA	5.6 (2.0)	5.5 (2.1)	0.39		5.6 (2.0)
PGA	5.9 (2.3)	5.8 (2.4)	0.49		5.9 (2.4)
Pain VAS	59.0 (23.1)	56.4 (24.3)	0.08		57.6 (23.8)
HAQ-DI	1.4 (0.7)	1.3 (0.7)	0.03		1.4 (0.7)
b/tsDMARDs treatment any time before enrolment; n (%)			<0.001*		
Naïve	247 (48.5)	347 (61.4)			594 (55.3)
1 b/tsDMARD	78 (15.3)	62 (11.0)			140 (13.0)
2 b/tsDMARDs	103 (20.2)	83 (14.7)			186 (17.3)
>2 b/tsDMARDs	81 (15.9)	73 (12.9)			154 (14.3)

Values represent mean (SD), unless otherwise stated. b/tsDMARD, biologic/targeted synthetic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; HAQ-DI, Healthy Assessment Questionnaire-Disability Index; P(h)GA, Patient's (Physician's) global assessment of disease activity; VAS, Visual analogue scale. *chi-square test of independence for comparison of b/tsDMARD treatment received before enrolment.

Acknowledgements: The authors would like to acknowledge Luke Healy for medical writing support.
Disclosure of Interests: Rieke Alten Speakers bureau: Janssen Pharmaceuticals, Eli Lilly and Company, Pfizer Inc., and Galapagos, and Gilead Sciences, Consultant of: Eli Lilly and Company, Pfizer Inc., Galapagos NV, and Gilead Sciences, Grant/research support from: Bristol-Myers Squibb, Eli Lilly and Company, Pfizer Inc., Galapagos NV, and Gilead Sciences, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Gilead Sciences, Eli Lilly and Company, and Pfizer Inc., Consultant of: AbbVie, Gilead Sciences, Eli Lilly and Company, and Pfizer Inc., Marco Matucci-Cerinic Speakers bureau: Actelion, Janssen Pharmaceuticals, MSD, Eli Lilly and Company, Biogen Inc., Grant/research support from: MSD, Actelion., Jean-Hugues Salmon: None declared, Pedro López-Romero Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, WALID FAKHOURI Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Inmaculada De La Torre Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Anja Gentzel-Jorczyk Employee of: Eli Lilly and Company, Thorsten Holzkaemper Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Bruno Fautrel Consultant of: AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Janssen Pharmaceuticals, Eli Lilly and Company, Medac, MSD, NORDIC Pharma, Novartis, Pfizer Inc., Roche, Sanofi-Aventis, SOBI, UCB, Grant/research support from: AbbVie, MSD, Pfizer Inc.
DOI: 10.1136/annrheumdis-2021-eular.2035

AB0262 CLINICAL EFFICACY OF SWITCHING FROM ORAL TO SUBCUTANEOUS METHOTREXATE IN MANAGEMENT OF RHEUMATOID ARTHRITIS: EXPERIENCE FROM OUT-PATIENT SETTING OF A DISTRICT GENERAL HOSPITAL IN UK

G. Ansari[1], A. Nandagudi[1], A. Bharadwaj[1]. [1]*Basildon Hospital Mid and South Essex NHS Foundation Trust UK, Rheumatology, Essex, United Kingdom*

Background: Methotrexate (MTX) is an anchor drug in the treatment of Rheumatoid arthritis. The literature review has shown that subcutaneous (SC) methotrexate has shown better efficacy, less adverse side effects and better compliance in inflammatory arthritis. Our department modified Inflammatory arthritis pathway in 2018 where all patient with moderate or severe disease are switched from oral to SC Methotrexate injection for improved management.
Objectives: The aim of our study is to review whether switching of oral methotrexate (PO MTX) to subcutaneous methotrexate (SC MTX) helps to improve disease activity in patients with rheumatoid arthritis and avoids the need to introduce biologic therapy.
Methods: We conducted a retrospective audit of patients with rheumatoid arthritis seen between January 2018 to January 2020 recording their age, gender, diagnosis, date of MTX switch and disease activity score 6 months after switching to SC MTX. Significance of change was calculated with test of proportion/chi square test.

Results: Fifty patients were reviewed, thirty eight (76%) were female and twelve (24%) were male with age ranging between 34 - 86 years (median 61.5 years). Switching to MTX injection was done within 2 yrs of diagnosis in 21 (42%) patients, between 2-5 yrs of diagnosis in 11 (22%) patients and more than 5 yrs after diagnosis in 18 (36%) patients. The main reasons of switching were either maximum MTX dose (25mg) or intolerance to oral MTX at any dose.

After switching methotrexate, review at 6 months showed 26 patients (52%) in remission (compared to 6 at baseline) and 3 (6%) patients avoided the need to go on biologic therapy. Five patient commenced on biologic therapy between 3 and 6 months.

Table 1. Disease activity compared at Baseline and at 6 months

Disease Activity	Baseline	At 6 months
Remission <2.6	6	26 (p<0.0001)
Mild (26-3.19)	11	10
Mod (3.2 - 5.09)	25	9 (p<0.01)
Severe (>5.1)	8	5

Conclusion: Switching to SC Methotrexate even in patients with long duration of disease results in significant number of patients achieving remission or lower disease activity (P<0.001). This may obviate the need of biologics therapy

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2212

AB0263 THE LEVEL OF 7-HYDROXY METHOTREXATE IN BLOOD CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS DIRECTLY CORRELATES WITH THE LEVEL OF POLYGLUTAMATES OF METHOTREXATE

G. Gridneva[1], E. Samarkina[1], S. Glukhova[1], Y. Muraviev[1], A. Kudryavtseva[1], E. Aronova[1], N. Baymeeva[2], V. Sygyrta[1]. [1]*V.A.Nasonova Rheumatology Research Institute, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Drug Therapy, Moscow, Russian Federation*; [2]*Mental Health Center, Pharmacokinetics Laboratory, Moscow, Russian Federation*

Background: 7-hydroxy Methotrexate (7-hydroxy-MTX) is a phase I metabolite of MTX, which is converted by hepatic aldehyde oxidases. It is known that 7-hydroxy MTX can reduce the effectiveness of methotrexate, which is associated with increased excretion of methotrexate due to a decrease in polyglutamation and binding to enzymes [1].

Objectives: To analyze the level of 7-hydroxy-MTX in peripheral blood cells in order to study the correlation of the level of this metabolite with the level of polyglutamates of methotrexate (MTXPGs).

Methods: The prospective study included 65 patients aged 53±11 years, 50 women, 13 men, diagnosed with RA, according to the ACR/EULAR 2020 criteria, methotrexate (MTX) naiive. The duration of the disease was 7,5[4;24] months. All patients were administrated MTX subcutaneously at a dose of 10-15 mg/m2. The visits were carried out at weeks 0, 4, 12, 24 and 36, at all visits samples were taken for the content of MTXPGs with 1,2,3 and 4 glutamate residues and 7-hydroxy MTX separately in red blood cells mass (RBC) and mononuclear cells (MO). The mononuclear fraction was isolated by layering on verografin-ficoll. All patients received folic acid at a standard dose of 5 mg 24 hours after parenteral MTX administration. Samples were collected no earlier than 36 hours after MTX administration. All patients had normal renal function. Disease activity was assessed using the DAS28 index calculated by C-reactive protein.

Results: The average concentration of 7-hydroxy MTX is shown in Table 1.

Table 1. Level of 7-hydroxy MTX in erythrocytes and mononuclear cells, nmol/L, Median [25; 75 quartiles]

7-hydroxy MTX level in:	4 weeks	12 weeks	24 weeks	36 weeks
RBC	18,5[3,1;61,5]	10,2[3,6;50,8]	10,3[1,7;36,8]	7,2[0,1;25,3]
MO	0,8[0,1;15,2]	4,0[0,1;42,2]	3,5[0,1;8,1]	0,4[0,1;8,9]

The level of 7-hydroxy-MTX directly correlated with the level of MTXPGs 1-4, and summary MTXPG in both RBC and MO. Analysis of pairwise correlations according to Pearson showed that: after 4, 12 and 36 weeks, the level of 7-hydroxy-MTX did not correlate with the value of DAS28. After 24 weeks of therapy, the level of 7-hydroxy-MTX in RBC was inversely correlated with DAS28 of the disease (p=0.043).

Conclusion: The preliminary results indicate a positive correlation between the level of 7-hydroxy-MTX and MTXPGs in RBC and MO. In this regard, the concentration of 7-hydroxy-MTX can be used as a prognostic marker for MTX therapy in the absence of opportunities in clinical centers to measure the entire line of MTXPGs in RBC and MO. Since the data obtained are somewhat at odds with the few literary sources, it is necessary to conduct further research on this fact.

REFERENCES:

[1] Baggott JE, Morgan SL (2009) Methotrexate catabolism to 7-hydroxymethotrexate in rheumatoid arthritis alters drug efficacy and retention and is reduced by folic acid supplementation. Arthritis Rheum 60:2257–2261

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2276

AB0264 1-YEAR RESULTS OF A NON-INVASIVE AURICULAR VAGUS NERVE STIMULATION DEVICE IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Marsal[1], H. Corominas[2], J. J. De Agustin[1], C. Perez-Garcia[3], M. Lopez Lasanta[1], H. Borrell Paños[1], D. Reina-Sanz[4], R. Sanmartí[5], J. Narváez[6], C. Franco-Jarava[7], C. Peterfy[8], J. A. Narvaez[9], V. Sharma[10], K. Alataris[11], M. C. Genovese[12], M. Baker[13]. [1]*Hospital Universitari Vall d'Hebron, Rheumatology, Barcelona, Spain*; [2]*Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*; [3]*Hospital Universitari Parc Salut Mar, Rheumatology, Barcelona, Spain*; [4]*Hospital Moisès Broggi, Rheumatology, Barcelona, Spain*; [5]*Hospital Clinic de Barcelona, Rheumatology, Barcelona, Spain*; [6]*Hospital Universitari de Bellvitge, Rheumatology, Barcelona, Spain*; [7]*Hospital Universitari Vall d'Hebron, Immunology, Barcelona, Spain*; [8]*Spire Sciences, NA, Boca Raton, United States of America*; [9]*Clinica Diagonal, Imaging, Barcelona, Spain*; [10]*Nēsos Corp, R&D, Redwood City, United States of America*; [11]*Nēsos Corp, NA, Redwood City, United States of America*; [12]*Gilead Sciences, Clinical Development, Inflammation, Foster City, United States of America*; [13]*Stanford University, Division of Immunology and Rheumatology, Stanford, United States of America*

Background: Despite the clinical benefits of current pharmacological treatments for rheumatoid arthritis (RA), there remains an unmet need for alternative treatment approaches. Initial results of a 12-week proof-of-concept study of non-invasive, vagus nerve stimulation (VNS) of the auricular branch of the vagus nerve from a wearable device to treat RA showed the device to be well-tolerated with significant reductions in the DAS28-CRP and RA disease severity[1].

Objectives: This analysis presents data from the 9-month extension of the original proof-of-concept study.

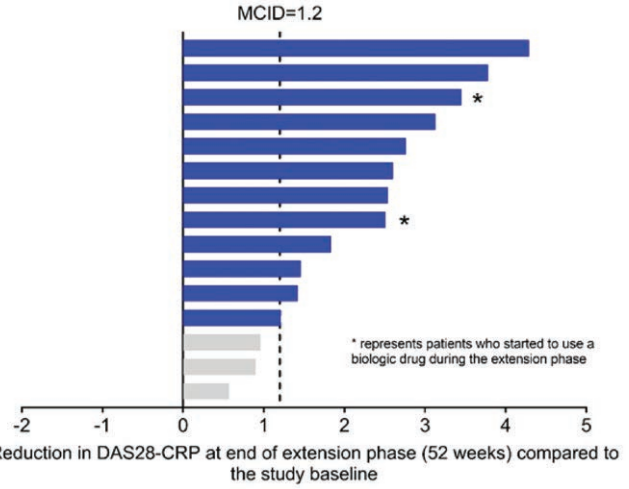
Methods: Following the completion of the 12-week proof-of-concept study, responding patients (defined as achieving a reduction in DAS28-CRP of ≥1.2 from baseline and/or achievement of ACR20) were given the option to enroll in a 9-month extension study. Use of the wearable device continued daily for up to 30 minutes as in the first 12 weeks of the study. Alteration of baseline medication and addition of conventional synthetic disease-modifying antirheumatic drugs (DMARDs) and biologic DMARDs were allowed during the extension phase.

Results: 20/27 patients who completed the initial 12-week study met the enrollment criteria for the extension phase; 19 of those patients consented to participate. 4/19 patients (21%) discontinued the extension study due to lack of efficacy (1 patient after 1 month, 2 patients after 3 months, and 1 patient after 6 months in the extension); 15 patients completed the extension phase. 2/15 patients (13%) added biologic therapy to their treatment regimen. Mean DAS28-CRP reduction from baseline to the end of the extension (12 months total) in all patients completing the extension was 2.23 (95% CI: -1.60, -2.86). For patients who did and did not add biologic therapy, mean DAS28-CRP reduction was 2.98 and 2.11, respectively. Individual DAS28-CRP reductions are shown in the figure 1. Mean HAQ-DI reduction from baseline to the end of the extension in all patients was 0.70. 2 non-device related adverse events were reported in the study extension: one related to cornea transplant and one related to dysesthesia. No serious adverse events were reported during the study extension phase.

Conclusion: Benefits from the use of the wearable device were maintained over longer periods of time from the initial 12-week proof-of-concept study, with few safety concerns as no additional side effects were observed.

REFERENCES:

[1] Marsal S et al. Non-invasive Vagus Nerve Stimulation Improves Signs and Symptoms of Rheumatoid Arthritis: Results of a Pilot Study [in press]. The Lancet Rheumatol, 2021

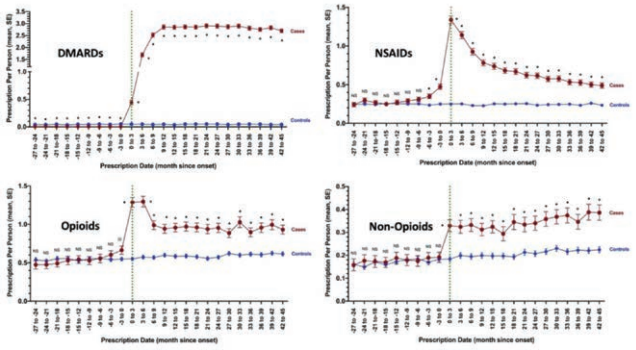


Disclosure of Interests: Sara Marsal Speakers bureau: BMS, Pfizer, UCB, Celgene, Roche, Sanofi, Consultant of: Pfizer, Abbvie, Roche, Celgene, Galapagos, MSD, UCB, BMS, Sanofi, Grant/research support from: Pfizer, Abbvie, Roche, Celgene, MSD, UCB, BMS, Novartis, Janssen, Sanofi, Héctor Corominas: None declared, Juan Jose de Agustin: None declared, Carolina Perez-Garcia: None declared, Maria Lopez Lasanta: None declared, Helena Borrell Paños: None declared, D Reina-Sanz: None declared, Raimón Sanmartí: None declared, J. Narváez: None declared, Clara Franco-Jarava: None declared, Charles Peterfy Speakers bureau: Novartis, Bristol Myers Squibb, Amgen, Consultant of: Multiple companies on behalf of Spire Sciences Inc., Jose Antonio Narvaez: None declared, Vivek Sharma Shareholder of: Nēsos Corp, Employee of: Nēsos Corp, Konstantinos Alataris Shareholder of: Nēsos Corp, Employee of: Nēsos Corp, Mark C. Genovese Shareholder of: Gilead Sciences, Nēsos Corp, Employee of: Gilead Sciences, Matthew Baker Shareholder of: Nēsos Corp, Consultant of: Nēsos Corp
DOI: 10.1136/annrheumdis-2021-eular.2628

AB0265 OPIOIDS AND ANALGESIC USE IN EARLY RHEUMATOID ARTHRITIS: A LONGITUDINAL ANALYSIS OF LINKED REAL-WORLD PRESCRIPTION DATA

M. H. Derakhshan[1], F. Morton[1], G. E. Fragoulis[2], C. Paterson[1], J. Dale[3], N. Basu[1], I. Mcinnes[1], D. Porter[4], S. Siebert[1]on behalf of Scottish Early Rheumatoid Arthritis (SERA) Investigators. *[1]University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; *[2]University of Athens, Laiko General Hospital, Athens, Greece*; *[3]NHS Lanarkshire, University Hospital Hairmyres, Glasgow, United Kingdom*; *[4]NHS Greater Glasgow and Clyde, Gartnavel General Hospital, Glasgow, United Kingdom*

Background: Large numbers of patients with rheumatoid arthritis (RA) receive regular opioids despite significant toxicity and a lack of evidence supporting their use in non-cancer pain. In order to address this situation, we need to understand when opioids are started in early RA where this has not been studied.
Objectives: To examine the temporal trend of opioid prescriptions before and after RA symptom onset and to compare this with DMARD and NSAID prescriptions.
Methods: RA participants (cases) were recruited as part of the Scottish Early Rheumatoid Arthritis (SERA) inception cohort[1]. Controls without RA (five per case), matched for sex, age and post code over the same time period, were obtained through routine data linkage. Prescription data between Jan 2009 to Nov 2019 of cases and matched controls were compared using date of RA symptom onset as reference point. The Prescriptions Per Participant (PPP) for each three-month block was estimated by dividing the number of prescribed drugs in the selected drug classes (assigned using the British National Formulary) in that time block by the number of participants in each group. The differences between mean PPP of the RA cases and controls in each time block were tested by t-test for independent groups and subsequent adjustment for multiple testing.
Results: 1,720,335 prescriptions were available for analysis with 421,961 items for 950 RA cases and 1,299,374 items for 4,558 matched controls. As expected, DMARD prescriptions in the SERA cases increased after the symptom onset period and were then sustained (Figure 1: top left panel). NSAID prescriptions in RA cases peaked during the 3 months after symptom onset and then reduced progressively (top right panel). Opioid analgesic prescriptions for the RA cases increased two-fold during the reference period and then reduced 6-9 months post-symptom onset. However, unlike NSAIDs, after this there was no further significant reduction in opioid prescriptions in the RA cases, which remained stable and significantly higher than in the controls for the remaining study period. The non-opioid analgesic mean PPP increased sharply at the time of symptom onset, with a steady gradual upward trend over time (lower right panel).



Conclusion: Opioid prescriptions increase significantly at the time of RA symptoms onset. Despite rapid introduction of DMARDs and resultant reductions in NSAIDs, analgesic use remains significantly higher than in controls. Further research is required to identify the factors associated with persistent opioid use in early RA with interventions aimed at the first 6 months.
REFERENCES:
[1] Dale et al. BMC Musculoskelet Disord. 2016;17:461.
Acknowledgements: The work was supported by Health Data Research UK which receives its funding from HDR UK Ltd funded by the UKRI MRC, EPSRC, Economic and Social Research Council, Department of Health and Social Care (England), Chief Scientists Office of the Scottish Government Health and Social Care Directorates, Health and Social Care Research and Development Division (Welsh Government), Public Health Agency (Northern Ireland), British Heart Foundation (BHF) and the Wellcome Trust.
The SERA study was jointly funded by the Chief Scientists Office Scotland and Pfizer Ltd.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2672

AB0266 METHOTREXATE AND CARDIOVASCULAR RISK IN RHEUMATIC DISEASES:A COMPREHENSIVE REVIEW

F. Verhoeven[1,2], C. Prati[1,2], M. Chouk[1], C. Demougeot[2], D. Wendling[1,3]. *[1]CHRU Besancon, Rheumatology, Besançon, France*; *[2]Université de Bourgogne - Franche Comté, EA 4267 PEPITE, Besançon, France*; *[3]Université de Bourgogne - Franche Comté, EA 4266 EPILAB, Besançon, France*

Background: The management of inflammatory rheumatic disease has evolved in the last decade with the importance of the management of comorbidities. Methotrexate is the cornerstone of inflammatory rheumatic disease management, but its cardiovascular effects are still poorly understood
Objectives: To assess the cardiovascular impact of methotrexate in inflammatory rheumatic disease.
Methods: A systematic review of the literature, following the prisma recommandations, was performed on the PubMed and Embase databases with the following keywords: ("Methotrexate") AND ("cardiovascular"). We included papers written in English and including patients older than 18 years.
Results: 570 references were identified and, 36 articles were kept for analysis.
The mechanism of action of methotrexate lies mainly on the antagonism of purines. It reduces systemic inflammation, oxidative stress.
In Rheumatoid arthritis, the use of methotrexate was associated with a decreased incidence of high blood pressure, an improvement of the lipid profile and of the insulin resistance. Major adverse cardiovascular events were decreased with methotrexate. The effects of methotrexate on the endothelial

function were more controversial and available data did not argue for a direct vascular effect of MTX in RA.
In psoriatic arthritis, evidences were more scarce. A meta-analysis showed that methotrexate was associated with a reduction of cardiovascular events in patients with psoriatic arthtritis. In psoriatic arthritis, methotrexate did not improve the endothelial function.
In plaque psoriasis, available data were rare. The use of methotrexate in this condition was not associated with a reduction of cardiovascular events. Nevertheless, a decrease in circulating VCAM-1 and in E selectin levels was described with the use of methotrexate.
In HIV infection, a model of pro inflammatory state, the use of methotrexate did not change the endothelial function and thus the cardiovascular events.
Finally, in general population, the use of methotrexate did not decrease the occurrence of cardiovascular events after a myocardial infarction.
Conclusion: The cardiovascular effects of methotrexate are poorly understood at this time. Nevertheless, it seems clear that methotrexate can reduce the occurrence of cardiovascular events in inflammatory disease. The mechanisms explaining this good issue are poorly understood, but it seems possible that the essential effect of methotrexate lies in the reduction of the inflammatory syndrome without a direct vascular impact.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2694

AB0267 HOW EFFECTIVE IS PAIN MANAGEMENT IN THE PATIENTS' OPINION? DATA FROM THE COMPAS STUDY

E. Pogozheva[1], A. Karateev[1], V. Amirdzhanova[1]. [1]*V.A. Nasonova Research Institute, Pain Management, Moscow, Russian Federation*

Objectives: to evaluate the effectiveness and satisfaction of pain management in patients with rheumatic diseases (RD) according to a survey in the COMPAS (Quality of Pain Management according to Patients with Arthritis and Back pain) study.
Methods: the survey involved 1040 patients with RD (rheumatoid arthritis-40.6%, osteoarthritis -32.1%, spondyloarthritis-10.6%, connective tissue diseases-8.6% of patients). 76.8% were women, the mean age was 55.8±14.0 years. 35.7% of patients continued to work in their specialty, 31.6% had various degrees of disability. The effectiveness of pain therapy was evaluated by the patient in the last month preceding the survey on a 5-point scale, where 1 - no effect and 5-excellent effect. Patients ' satisfaction with treatment, possible reasons for the lack of effectiveness of pain therapy and the use of additional treatment tools were also evaluated.
Results: as therapy for the underlying disease, 40% of patients received conventional disease modifying antirheumatic drugs, 33.1% - glucocorticoids, 7.2% - biological agents and 15.2% - symptomatic slow-acting drugs in osteoarthritis. At the same time, 68% of patients needed additional analgesic therapy with nonsteroidal anti-inflammatory drugs (NSAIDs). Slightly less than half of the surveyed patients (46.9%) noted a moderate effect of analgesic therapy, 22.7% - a low effect and 5% - no effect, 23.7% rated the effectiveness of therapy as good and only 1.7% - as excellent. At the same time, only 15.6% of patients were completely satisfied with the result of NSAIDs, 64% were partially satisfied with the treatment and 20.4% were completely dissatisfied. As the reason of insufficient effectiveness of NSAIDs, most often (34.3%) patients named fear of adverse events associated with taking drugs, 19.4% - weak drugs, 15.3% - insufficient attention of doctors to complaints, 6.6% - poor diagnosis of the causes of pain. Others found it difficult to answer or were completely satisfied with the treatment. 40% of patients used additional methods, most often chiropractic (12.3%), acupuncture (4.8%), physiotherapy (12.7%) and folk remedies (7.4%).
Conclusion: A significant proportion of patients with RD don't have adequate pain control. Only 25.4% of patients rate the result of treatment as good and excellent, and even fewer patients (15.6%) are completely satisfied with the results of therapy. Thus, a personalized approach to analgesic therapy is necessary, taking into account the expectations of patients regarding the results of treatment.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2806

AB0268 LOW DOSE TACROLIMUS IS AN EFFECTIVE ADD ON THERAPY FOR PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS – A SINGLE CENTRE EXPERIENCE

N. Prabu[1], V. Petciappan[2], G. Anand[1], T. A[3], A. Nijish[3]. [1]*Sakthi Rheumatology Centre Pvt. Ltd, Rheumatology, Coimbatore, India*; [2]*PSG Institute of Medical Sciences & Research, General Medicine, Coimbatore, India*; [3]*PSG College of Pharmacy, Pharmacy Practice, Coimbatore, India*

Background: Rheumatoid arthritis (RA) a chronic inflammatory arthritis requiring tight control of disease activity. While traditional DMARDS have been used effectively, there always remains a need for add on drugs in good number of patients. Tacrolimus since its first approval in 2004 had been used widely as monotherapy and in combination with conventional and biological DMARDS. The primary concern was safety followed by the efficacy for patients with active disease.
Objectives: The main objective was to ascertain the safety and tolerability of patients who were treated with tacrolimus as an add on therapy over and above the standard care in RA.
Methods: A retrospective analysis of patients who were prescribed Tacrolimus from January 2019 to August 2020 was done. Details of patients along with the change in Blood pressure(BP), Serum creatinine, Blood sugar and Clinical disease activity index(CDAI) before and after tacrolimus were analyzed.
Results: A total of 245 patients with active Rheumatoid arthritis received the drug. The mean age was 48.58(1.49) years and the disease duration was 5.9(0.56) years. Of 245 patients, 24 patients were lost to follow up,103 patients stopped the drug for various reasons and 118 patients are still continuing the drug. The mean tacrolimus dose was 1.24 + 0.46 mg in the patients who are continuing. The commonest reason for stopping the drug was adverse events (57%) followed by lack of efficacy(29%), low disease activity (8%)and others(7%). There was no significant change in the mean blood pressure, Blood sugars and Creatinine levels in both the stopped and continuing group. However the CDAI and the steroid dosages reduced significantly in the patients who are still on tacrolimus.The lost to follow up group had high disease activity at baseline and also were on higher doses of steroids.

PARAMETERS	RA – CONTINUING(118)			RA STOPPED(103)			LOST TO FOLLOWUP (24)
	BEFORE TAC	AFTER TAC	p value	BEFORE TAC	AFTER TAC	P value	BEFORE TAC
SBP mm of hg	100.44(9.54)	101.06(9.80)	0.67	103(9.77)	104(9.92)	0.44	127.35(10.05)
DBP mm of hg	66.30(6.26)	67.22(6.37)	0.30	68.44(6.4)	70.43(6.65)	0.07	82.83(5.05)
SUGAR mg	76.43(13.73)	76.67(11.24)	0.95	71.86(10.79)	76.74(14.1)	0.08	89.12(9.7)
S.CR mg	0.55(0.06)	0.56(0.09)	0.80	0.66(0.16)	0.57(0.06)	0.21	0.74(0.06)
STEROID USE mg	2.82(0.41)	1.65(0.54)	**<0.001**	2.12(0.43)	2.43(0.54)	0.36	2.86(1.42)
CDAI	12.28(1.84)	7.42(1.49)	**<0.001**	12.23(2.03)	10.49(2.69)	0.07	16.62(3.88)

Conclusion: Low dose Tacrolimus is an effective add on therapy for patients with high disease activity and did not lead to change in serum creatinine, blood pressure or change in blood sugars in the study subjects.
REFERENCES:
[1] *Yocum D et al. Safety of tacrolimus in patients with rheumatoid arthritis: long-term experience. Rheumatology 2004; 43:992–999.*
[2] *Shouma Dutta,Yasmeen Ahmad. The efficacy and safety of tacrolimus in rheumatoid arthritis.Therapeutic Advances in Musculoskeletal Disease Ther Adv Musculoskel Dis. 2011; 3(6) 283–291.*
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2822

AB0269 ARE INTERFERON-GAMMA RELEASE ASSAYS RELIABLE TO DETECT TUBERCULOSIS INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH JANUS KINASE INHIBITORS?

C. Castellani[1], E. Molteni[1], A. Altobelli[1], C. Garufi[1], S. Mancuso[1], F. R. Spinelli[1], F. Ceccarelli[1], F. Conti[1], R. Scrivo[1]. [1]*Sapienza University of Rome, UOC Reumatologia - Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Roma, Italy*

Background: The therapeutic armamentarium for patients with rheumatoid arthritis (RA) has recently been enriched with the family of Janus kinase (JAK) inhibitors. Because the risk of reactivation of latent tuberculosis infection (LTBI) following the use of these drugs seems to be similar to that seen with anti-TNF agents, screening for LTBI is recommended in patients with RA before starting

treatment with JAK inhibitors. Interferon(IFN)-gamma release assays (IGRAs) are increasingly used for this purpose. However, JAK inhibitors tend to decrease the levels of IFNs, questioning the reliability of IGRAs during treatment with this novel class of drugs.

Objectives: To compare the performance of the QuantiFERON-TB Gold Plus (QFT-Plus) test with that of QuantiFERON-TB Gold In-tube (QFT-GIT) assay in RA patients before and during treatment with JAK inhibitors.

Methods: A longitudinal, prospective study has been performed in RA patients (ACR/EULAR 2010 criteria) candidates for tofacitinib or baricitinib treatment. All patients underwent QFT-Plus and QFT-GIT at baseline (T0), and after 3 (T3) and 9/12 months (T9/12) of treatment with JAK inhibitors. The agreement of the two tests was calculated at all timepoints. The agreement between IGRAs and tuberculin skin test (TST) or chest radiography at baseline was also determined. Lastly, the variability of QTF-Plus results was assessed during follow-up.

Results: Twenty-nine RA patients (F/M 23/6; median age/IQR 63/15.5 years; median disease duration/IQR 174/216 months) were enrolled: among them, 22 were to start baricitinib (75.9%) and 7 tofacitinib (24.1%). A perfect agreement was found between QFT-Plus and QFT-GIT at all times of observation (κ=1). At baseline, no agreement was recorded between IGRAs and TST (κ=-0.08) and between TST and chest radiography (κ=-0.07), while a low agreement was found between QFT-Plus and chest radiography (κ=0.17). A variation of 33.3% in the results of the QFT-Plus test was recorded at T3 compared to T0, of 29.4% at T9/12 compared to T0, and of 11.8% at T9/12 compared to T3. The median levels of IFN-γ produced by lymphocytes in response to the mitogen of QFT-Plus decreased after 3 months of treatment (1.59/4.72 IU/ml vs 3.08/7.68 IU/ml at baseline), followed by an increase after 9/12 months (2.25/4.61 IU/ml), but these differences were not significant. No significant change in the median number of circulating lymphocytes such as to explain the variation of the QFT-Plus results after 3 months of JAK inhibitor therapy was documented (1815/690/mm^3 vs 2140/750/mm^3 at baseline). At baseline, both QFT-Plus and QFT-GIT showed positive results in 5 patients (17.2%), negative in 19 (65.5%), and indeterminate in 5 (17.2%). Glucocorticoids intake was associated with a higher probability of negative or indeterminate result of IGRAs at baseline (p<0.0001).

Conclusion: Our data show that a response to IGRAs is detectable in the course of treatment with JAK inhibitors. However, similarly to what has been observed during treatment with TNF antagonists, the results of QFT-GIT and QFT-Plus show some variability when longitudinally repeated. These fluctuations occur in the absence of correlation with clinical outcome, thus challenging their interpretation. Since we do not have a sufficiently sensitive test capable of detecting TB infection, an integrated evaluation of risk factors, clinical manifestations and multiple diagnostic tests should be considered for a proper evaluation of the risk of TB infection in immunosuppressed patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2835

AB0270 EFFECTIVENESS OF A SWITCH FROM TOFACITINIB TO BARICITINIB IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE ANALYSIS OF REAL-WORLD DATA IN SWITZERLAND

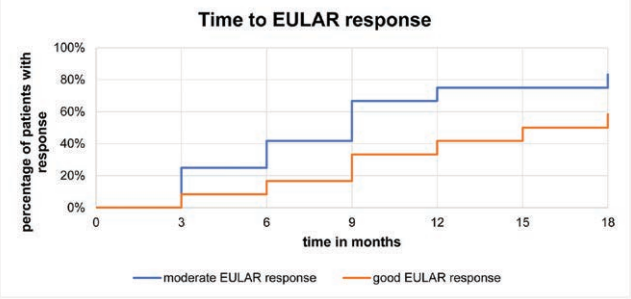
S. Kellerhals[1], J. Amsler[2], H. Schulze-Koops[3], T. Hügle[4], M. J. Nissen[5], H. Paul[6], D. Kyburz[7], R. Muller[6]. [1]*Kantonsspital Aarau, Division of Rheumatology, University Department of Medicine, Medical Faculty of the University of Basel, Aarau, Switzerland*; [2]*Inselspital Bern, Rheumatology, Bern, Switzerland*; [3]*Ludwig-Maximilians-University of Munich, Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, Munich, Switzerland*; [4]*University Lausanne, Division of Rheumatology, University Hospital Lausanne (CHUV), Lausanne, Switzerland*; [5]*Geneva University Hospital, Division of Rheumatology, Geneva, Switzerland*; [6]*Kantonsspital Aarau, Division of Rheumatology, University Department of Medicine, Medical Faculty of the University of Basel, Aarau, Switzerland*; [7]*University of Base, Rheumatology, Basel, Switzerland*

Background: Janus Kinase Inhibitors (JAKi) have recently been approved for the treatment of rheumatoid arthritis (RA) over the last years. JAKi differ in their specificity for the different JAK family members (JAK1, JAK2, JAK3 and TYK2). All three JAKis that are currently approved in Switzerland seem to have comparable efficacy on different disease stages of RA. Whether a JAKi can be effective after discontinuation of another JAKi is one of the open questions of interest according to the EULAR RA guidelines [1].

Objectives: To study the effectiveness of baricitinib in patients with RA after discontinuation of tofacitinib.

Methods: Longitudinal, retrospective chart review conducted between October 2019 and December 2020 of patients with RA at two Swiss centers (Kantonsspital Aarau and Inselspital Bern). Disease activity was assessed by DAS 28.

Results: 12 patients (1 male, 11 female) were treated with 4mg baricitinib/d after tofacitinib was discontinued. Mean age of the patients was 61 years, disease duration 140 months. Patients were previously treated with at least two conventional synthetic DMARDs and 75% with at least one biological DMARD. 58% of patients were positive for ACPA, 42% for rheumatoid factor. 50% of the patients suffered from erosive disease. Tofacitinib was stopped in 92% of the patients because of an insufficient response after a mean of 25.8 months. Moderate EULAR response was achieved in 83.3% of the patients after an average of 8 months treatment with baricitinib, and good EULAR response in 58.3% after an average of 10 months. There were no serious adverse events, neoplasms, opportunistic or serious infections during follow-up.



Conclusion: The first retrospective analysis of real-world data of baricitinib following tofacitinib shows that there is a good clinical response in 70% of cases. Although limited by the number of patients this study therefore supports the notion that baricitinib after discontinuation of tofacitinib in RA patients may be an effective therapeutic option.

REFERENCES:

[1] Smolen JS, Landewé RBM, Bijlsma JWJ, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Annals of the Rheumatic Diseases*. 2020;79(6):685-699. doi:10.1136/annrheumdis-2019-216655, p. 695

Disclosure of Interests: Simon Kellerhals: None declared, Jennifer Amsler: None declared, Hendrik Schulze-Koops: None declared, Thomas Hügle Consultant of: GSK, Abbvie, Pfizer, Jansen, Novartis, Eli Lilly., Michael J. Nissen Consultant of: Abbvie, Celgene, Eli-Lilly, Janssen, Novartis and Pfizer., Hasler paul Consultant of: Abbvie, Lilly, Diego Kyburz Consultant of: Abbvie, Gilead, Lilly, Novartis and Pfizer, outside of the submitted work, Rudiger Muller Consultant of: Abbvie, Novartis, Grant/research support from: Bebro Pharma

DOI: 10.1136/annrheumdis-2021-eular.2872

AB0271

COMPARISON OF DOSE REDUCTION METHODS BETWEEN RAPIDLY AND GRADUALLY DE-ESCALATION IN RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB OVER 15 MONTHS

M. Yamasaki[1]. [1]*Shin-Yokohama Arthritis and Rheumatology Clinic, Rheumatology, Yokohama, Japan*

Background: However tsDMARDs and treatment strategies have improved the outcomes of rheumatoid arthritis (RA), it is unknown who can taper or stop tsDMARDs and strategies for de-escalation.
Objectives: We analyze predictors of de-escalation in RA patients treated with baricitinib over 15 months in each group who start baricitinib with 4mg/day and 2mg/day.
This study will assess and compare (1) characteristic of patients who achieve remission (REM) or low disease activity (LDA) as who can taper baricitinib and (2) two de-escalation methods, rapidly and gradually de-escalation in patients who respond first-line therapy.
Methods: Cases were recruited to SHin-yokohama Arthritis REgister (SHARE) between 2015 and 2020 (n=3,961). Patients were diagnosed according to ACR/EULAR 2010 classification criteria and treated with baricitinib started with 4mg/day(n=42) or 2mg/day(n=108) over 15 months. 45 cases fulfilled EULAR definition for difficult-to-treat RA (D2T-RA). In 150 (Male25, Female125 cases, RA duration 12.5+/-5.9years) cases, Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire-Disability Index (HAQ-DI), anti-CCP2 and clinical parameters were analyzed. Two de-escalation methods were compared in this study. In rapidly de-escalation methods, baricitinib were stopped in patients with stable REM/LDA with no swollen joint over 12 weeks. In gradually de-escalation methods, baricitinib were decreased to 50%, 42%, 28%, 14% in order with stable REM/LDA with no swollen joint over 12 weeks.
Results: (1)" Detect predictors who can achieve REM/LDA with no swollen joint as starting de-escalation baricitinib" In patients started with baricitinib 4mg/day group, 17 patients achieved REM/LDA with no swollen joint(40.5%), there were no differences in duration of RA, onset age of RA, biologics and/or JAK inhibitors naïve, anti-CCP2 titer and CDAI at the start baricitinib between REM/LDA and non-achieved cases. In patients started with baricitinib 2mg/day group, 59 patients achieved REM/LDA with no swollen joint (54.6%). In 2mg/day group, biologics and/or JAK inhibitors naïve was predictor for achieving REM/LDA with no swollen joint. In 2mg/day group, D2T-RA patients was negative predictor.
(2)"Comparison of sustained REM and/or LDA rate between rapidly and gradually de-escalation of baricitinib in rheumatoid arthritis" In whole patients, 15 patients were tapered baricitinib with rapidly de-escalation methods and 61 patients were with gradually de-escalation. Gradually de-escalation methods showed less relapse rate compared with rapidly de-escalation after tapered baricitinib (33.3% vs. 93.8%, p<0.0001). Particularly in 2mg/day group, 12 patients were tapered baricitinib with rapidly de-escalation methods and 47 patients were with gradually de-escalation. Gradually de-escalation methods showed less relapse rate compared with rapidly de-escalation after tapered baricitinib for 32.7 months (33.3% vs. 80.9%, p<0.0001). However 2cases in 4mg/day group and 8cases in 2mg/day showed increase of CDAI, all these cases regain LDA after increasing baricitinib.
Conclusion: Tapering baricitinib using gradually de-escalation methods may help to sucseed deduction of baricitinib in RA patients with sustained clinical REM and/or LDA with no swollen joint in each group who start baricitinib with 4mg/day and 2mg/day.
REFERENCES:
[1] Ann Rheum Dis 2019;78:171-178
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2874

AB0272

CAN NONSTEROIDAL ANTI-INFLAMMATORY DRUGS CONTROL THE SYMPTOMS OF MODERATE RHEUMATOID ARTHRITIS?

E. Pogozheva[1], A. Karateev[1], V. Amirdzhanova[1], E. Filatova[1]. [1]*V.A. Nasonova Research Institute, Pain Management, Moscow, Russian Federation*

Objectives: to evaluate the efficacy of long-term pain therapy with nonsteroidal anti-inflammatory drugs (NSAIDs) in patients with rheumatoid arthritis (RA) with an initially moderate disease activity (DAS 28 <5,1).
Methods: the study included 404 RA patients, disease duration was more than 1 year, mean DAS 28 3.7±1.6, mean age 58.6±10.0 years, 69% women, 76,7% RF "+", 81,5% ACPA "+". 91,2% of the patients received conventional DMARDs (methotrexate), 8,8% - biological agents. All patients received NSAIDs (aceclofenac) to control their symptoms. The follow-up period was 6 months. We evaluated the dynamics of the DAS 28 index, the level of pain and patient global health on a 100- mm visual analog scale (VAS).
Results: the level of pain (VAS) decreased from 63,1 ± 15,4 to 46,3± 8,3 (p=0,001) by 3 months of follow-up and up to 39,5± 11,2 (p= 0,001) by 6 months of follow-up. The patient global health (VAS) also improved from 58,2 ± 13,4 at baseline to 40,3 ± 11,2 (p=0,001) at 3 months and to 35,5 ± 9,7 (p=0,001) at 6 months of follow up. The mean DAS 28 remained within the moderate disease activity and decreased from 3,7±1,5 to 3,4 ±1,1 (p=0,01) after 3 months, and to 3,1± 0,9 (p=0,01) after 6 months.
Conclusion: long-term NSAID therapy allows to control the disease activity in patients with moderate RA. This should be taken into account when planning therapy, including deciding whether to "switch" DMARDs and prescribing biological agents.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2901

AB0273

HYPERSENSIVITY REACTIONS TO NON STEROID ANTI INFLAMMATORY DRUGS: A BOUT 87 CASES

K. Ksouda[1], R. Sahnoun[1], R. Atheymen[1], I. Bouaziz[1], A. Hanène[1], S. Hammami[1], L. Chtourou[2], Z. Khaled[1]. [1]*Medecine School of Sfax, Pharmacovigilance Department, Sfax, Tunisia*; [2]*Hedi Chaker Hopital, Gastroenterology Department, Sfax, Tunisia*

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the leading causes of hypersensitivity reactions to drugs. The pathogenesis may be immunological mechanisms (allergic reactions) or non specific immunological reactions often incriminated in cross reactivity independently of chemical structure of these molecules. Understanding of the underlying mechanism is necessary for prevention and choice of safe alternatives [1, 2].
Objectives: Analyze all cases of non-steroidal anti-inflammatory drugs cutaneous eruption reported to sfax pharmacovigilance service since January 2015 to December 2020 and evaluate the possibility of cross-reactions between different molecules in this class.
Methods: We conducted a retrospective study of all cases reported to sfax pharmacovigilance department. An enquiry of pharmacovigilance was performed in patients who presented side effects to AINS. The imputability study was carried out by the French method of Imputability. Medical history specifies if there is a re-administration to assess tolerance and cross-reactivity.
Results: Our study included 87 patients whose average age was 45, 8 years. The sex ratio (F/M) was 1.18. lysine salicylate acetyl is the most incriminated (31%), then mefenamic acid (19.5%), diclofenac (19.5 %), ketoprofen in (9.2%), piroxicam in (6.9 %), ibuprofen in (5.4%), celocoxib in (3.4%), tiaprofenic acid in (1.1%) and naproxen in 1.1% of cases. The most common skin injury was urticaria in 29 cases (33.3%). Fixed drug eruption was observed in 17 cases. Maculopapular rash was observed in 19 cases, anaphylaxis in 5 cases and 4 cases of photosensitivity were observed. In our study we found cross-reactivity between (NSAIDs) in 8 patients.
Conclusion: The diagnostic approach is often based on the controlled administration of the drug to assess tolerance and to identify safe alternatives. In cases of intolerance to COX 1 inhibitors, cross-reactions to selective cox 2 inhibitors are very rare [3].
REFERENCES:
[1] Inmaculada Dona, Maria Salas, James R Perkins and al. Hypersensitivity Reactions to Non-Steroidal Anti-Inflammatory Drugs. Curr Pharm Des 2016; 22(45):6784-6802.
[2] Flavia Angeletti, Franziska Meier, Nadja Zöller, Markus Meissner, Roland Kaufmann, Eva Maria Valesky. Hypersensitivity reactions to non-steroidal anti-inflammatory drugs (NSAIDs) - a retrospective study. J Dtsch Dermatol Ges 2020 Dec; 18(12):1405-1414.
[3] N Blanca-López, J A Cornejo-García, M C Plaza-Serón, and al. Hypersensitivity to Nonsteroidal Anti-inflammatory Drugs in Children and Adolescents: Cross-Intolerance Reactions. J Investig Allergol Clin Immunol 2015; 25(4):259-69.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2910

AB0274

METHOTREXATE INTOLERANCE IN MOROCCAN RHEUMATOID ARTHRITIS PATIENTS

M. Mahroug[1], H. Azzouzi[1], H. Boutaibi[1], O. Lamkhanat[1], I. Linda[1]. [1]*Mohammed VI University Hospital, Mohammed I University, Faculty of Medicine, Rheumatology, Oujda, Morocco*

Background: Methotrexate intolerance is a principal reason for treatment discontinuation, hence the interest in a more in-depth study.
Objectives: We aimed to study the prevalence of methotrexate gastrointestinal intolerance and determine its associated factors in rheumatoid arthritis (RA) patients.
Methods: We designed a cross-sectional study on our RA patients recruited in January 2021 at our rheumatology department. Methotrexate Intolerance Severity Score (MISS) [1], previously validated in juvenile idiopathic arthritis

patients, was used to determine methotrexate (MTX) intolerance prevalence in RA patients. The MISS consisted of four domains: abdominal pain, nausea, vomiting, and behavioral symptoms, occurring before (anticipatory), after, and when thinking of MTX (associative). MTX intolerance was defined as six or more points on the MISS. Our statistical analysis was based on a descriptive study and logistic regression with SPSS20.

Results: We included 102 RA patients with a mean age of 51.60 ± 14.33 years, Women were predominant (93.1%). The mean disease duration was 14.86 ± 9.78 years, with a mean methotrexate use duration of 7.42 ± 6.44 years. The mean dose of methotrexate was 12.13 ± 9.06 mg per week. The prevalence of methotrexate intolerance was 55.9%, and seventy-six patients (74.5 %) experienced at least one gastrointestinal symptom during MTX treatment. After MTX administration, the most prevalent gastrointestinal symptom was nausea (93% of the intolerant patient), whereas abdominal pain occurred in 73.7% and vomiting in 57.9%. These symptoms were also prevalent before and when thinking of MTX. Anticipatory nausea was reported in 45.6% and associative nausea in 54.5% of the cases, abdominal pain occurred anticipatory in 22.8% and associative in 42.1 %, anticipatory vomiting was the least prevalent, affecting 8.8 %. Behavioral symptoms affected 87.7% of intolerant patients, with restlessness being the most prominent symptom in 71.9% of them. Among the intolerant patients, 45 patients (79%) took parenteral MTX, and 12 (21.1%) took methotrexate orally. In comparison, young patients (49.11 ± 14.95 years) were more intolerant to MTX than old (54.76 ± 13 years, p = 0.048) ones. However, in univariate logistic regression analysis, we did not find any significant association between methotrexate administration route, dose, duration, and digestive intolerance.

Conclusion: Methotrexate intolerance was highly prevalent in our RA population. These results strengthen the idea that early detection of MTX intolerance may avoid effective treatment discontinuation, especially in younger patients.

REFERENCES:

[1] Bulatović M, Heijstek MW, Verkaaik M, van Dijkhuizen EH, Armbrust W, Hoppenreijs EP et al. High prevalence of methotrexate intolerance in juvenile idiopathic arthritis: development and validation of a methotrexate intolerance severity score. Arthritis Rheum. 2011 Jul; 63(7):2007-13.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3315

AB0275 TOFACITINIB EFFECTIVENESS IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER CONVENTIONAL OR BIOLOGICAL THERAPY - IT REAL ROLE IN DIFFERENT LINES OF TREATMENT

W. Rivero[1], L. Ibata[2], S. Martinez[2], A. Rojas-Villarraga[3], P. Santos-Moreno[4].
[1]Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, Pharmaceutical chemist, Bogota, Colombia; *[2]Epithink Health Consulting, Epidemiology, Bogota, Colombia*; *[3]Fundacion Universitaria de Ciencias de la Salud - FUCS, Research Division, Bogota, Colombia*; *[4]Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, Rheumatology, Bogota, Colombia*

Background: rheumatoid arthritis (RA) is a chronic and disabling autoimmune disease, with a high clinical and economic burden. This implies the need to investigate therapies that maximize clinical results. Tofacitinib is recommended as a different alternative to biologic therapy when a patient remains with moderate or high disease activity after conventional DMARDs use, or as an option after failure to biologic therapy.

Objectives: to evaluate the effectiveness of Tofacitinib in RA as first-line (after conventional DMARDs failure) or second-line treatment (after biologic therapy failure) in a real-life cohort of RA patients and its differences.

Methods: this is a descriptive retrospective cohort study conducted at a specialized center for RA in Bogota, Colombia; databases from 2017 to 2019 were used to select and study patients with indication of Tofacitinib, regardless of their previous treatment or disease status. The indication and initiation of Tofacitinib (5 mg BID or 11 mg once daily) was an independent medical decision made as part of the individualized management of every patient. Effectiveness was evaluated in those patients who met the high adherence criteria (at least three visits with a rheumatologist per year), with no change or addition of other conventional DMARDs. Frequencies and proportions in baseline characteristics, differences in disease activity were calculated between the first and second line tofacitinib treatment. Comparisons of continuous variables data between the two patient groups were made using the t-test; the chi-square test and Fisher's exact test were used for statistical analysis of categorical variables. Logistic regressions were performed to analyze related factors with therapeutic response outcomes.

Results: we included 152 RA patients who received tofacitinib: first-line (T1) (n= 85, 55.9%) or second-line (T2) (n= 67, 44.1%). T1 first-line group was younger than the T2 second-line patients (53±12.8 years and 59±11.4 years, p-value 0.01) and they had a shorter disease duration than T2 patients (11.8 vs. 12.8 years, p-value 0.01). Comparative analysis of response to treatment showed a reduction in DAS28 at 3, 6 and 12 months in both study groups. The response in disease activity at 3 months was a major factor related to 6-month response (OR 13.4, 95% CI 4.5-39.4, p value 0.000), while non-response at 3 months were associated with no response at 6 months of follow-up. Baseline DAS28 was significantly associated with response at 12 months (OR 1.9, 95% CI 1.11-3.25, p-value 0.028). At 12 months of treatment, both groups showed disease response and control according to the DAS28 from baseline, but a higher proportion of T1 patients achieved remission (45% vs 23%). A subgroup analysis to evaluate T2 second-line Tofacitinib therapy showed no statistically significant differences in any response criteria according to the number of previously received biologicals.

Table 1. Regression analysis (risk of response of the disease at 6 and 12 months of treatment with Tofacitinib)

Factor	Response at Month 6			Response at Month 12*		
	OR	IC95%	P value	OR	IC95%	P value
Age	1.00	0.97-1.03	0.788	1.02	0.98-1.06	0.211
Male	1.82	0.65-5.08	0.251	0.81	0.27-2.38	0.709
Duration of RA	0.99	0.94-1.04	0.908	1.02	0.96-1.08	0.444
Positive Rheumatoid Factor	0.81	026-2.56	0.730	0.63	0.17-2.26	0.485
Positive Anti-CCP	0.34	0.068-1.6	0.189			
Initial DAS28	1.61	1.04-2.49	0.033	1.9	1.11-3.25	0.018
First line	0.44	0.19-1.01	0.054	1.47	0.56-3.83	0.423
Treatment period	1.12	0.80-1.55	0.492	1.1	0.75-1.61	0.607
Dose: 11 mg.	0.95	0.42-2.13	0.904	0.75	0.258-1.9	0.565
Response at Month 3	13.42	4.57-39.4	0.000	2.32	0.87-6.18	0.091

*Positive Anti-CCP at month 12 was omitted because of collinearity

Conclusion: Tofacitinib is an effective treatment option for patients with RA after conventional DMARDs and in patients after biologic therapy failure, but maybe is better used it as a T1 first-line of treatment. Further studies are required to determine the real role of tofacitinib in different lines of RA treatment.

Disclosure of Interests: Wilberto Rivero: None declared, Linda Ibata: None declared, Susan Martinez: None declared, Adriana Rojas-Villarraga: None declared, Pedro Santos-Moreno Speakers bureau: Pedro Santos-Moreno has received fees for conferences from: Abbvie, Biopas-UCB, Bristol, Janssen, Pfizer, Sanofi., Consultant of: Pedro Santos-Moreno has received fees for counseling and advisory boards from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi., Grant/research support from: Pedro Santos-Moreno has received research grants from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi.

DOI: 10.1136/annrheumdis-2021-eular.3770

AB0276 HOW FAST CAN METHOTREXATE BE ESCALATED IN RHEUMATOID ARTHRITIS? A MULTICENTRE, PARALLEL-GROUP RANDOMIZED CONTROLLED TRIAL (MEIRA)

S. Jain[1], V. Dhir[1], A. Aggarwal[2], S. Maurya[2], R. Gupta[3], B. Leishangthem[1], A. Khullar[1], V. Dhawan[4], G. Naidu[1], S. K. Sharma[1], A. Sharma[1], S. Jain[1].
[1]PGIMER, Division of Clinical Immunology and Rheumatology, Department of Internal Medicine, Chandigarh, India; *[2]SGPGIMS, Department of Clinical Immunology and Rheumatology, Lucknow, India*; *[3]AIIMS, Department of Rheumatology, New Delhi, India*; *[4]PGIMER, Department of Experimental Medicine and Biotechnology, Chandigarh, India*

Background: Literature regarding the optimal dose escalation strategy of methotrexate (MTX) in RA is scant and ambiguous (1). Concerns regarding the safety of rapid escalation may lead to delayed attainment of the optimal dose and treatment target.

Objectives: To compare the efficacy, safety and tolerability of fast versus usual dose escalation of oral MTX in RA.

Methods: This multicenter, open-label (assessor blinded) RCT included patients with active RA (SJC≥2 and TJC≥4) aged 18-55 years, not on DMARDs (except HCQ and/or low-dose prednisolone) and with disease duration <5 years. Patients were randomized 1:1 into two groups with the same starting dose of oral MTX (15 mg/week), but escalated either by 5 mg every 2 weeks (fast escalation group) or 5 mg every 4 weeks (usual escalation group), till a maximum of 25 mg/wk. Primary outcome was proportion of EULAR good responders at 16 weeks. Secondary outcomes were change in DAS28-3 and EULAR responders (good or moderate) at 8 and 16 weeks, change in Indian HAQ at 16 weeks, and symptomatic (questionnaire based) and laboratory adverse effects over 16 weeks. RBC MTX polyglutamate-3 levels were measured using HPLC in both groups. There was an open-label extension phase till 24 weeks (use of other DMARDs was permitted beyond 16 weeks if target was not met), and DAS28-3 at 24 weeks was compared.

Trial Reg: CTRI/2018/12/016549

Results: 178 patients (mean age 39.8 (8.6) years, 84% females) with mean disease duration of 1.9 (1.4) years were randomized (89 in each group). Mean DAS28ESR-3 and DAS28CRP-3 at enrollment were 6.3 (0.9) and 5.4 (1.1). At 16 weeks, there was no significant difference in good EULAR response by DAS28ESR-3 (5.6, 7.9%, p=0.9) or DAS28CRP-3 (28.1, 22.5%, p=0.8) between the two groups (Figure 1).

The change in DAS28-ESR-3 at 8, 16 and 24 weeks (or by DASCRP-3, not shown) and improvement in HAQ at 16 weeks were also not significantly different (Table 1). Notably, there was no significant difference in symptomatic GI or CNS adverse effects, incidence of cytopenia, transaminitis or rates of drug discontinuation. RBC MTX polyglutamate-3 levels at 8 and 16 weeks were also similar (Table 1).

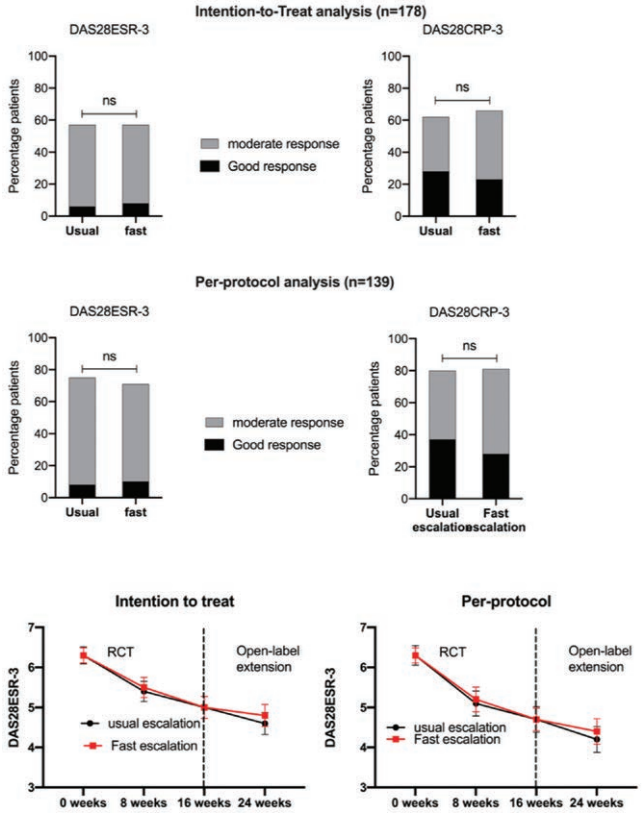


Figure 1. EULAR response and change in DAS28ESR-3 over time

Table 1. Key secondary efficacy and safety outcomes

Parameter	Usual	Fast	p-value
Efficacy			
Delta DAS28-ESR-3 (Mean±SD)			
-8 wk			
-ITT (n=178)	-0.9 ± 1.0	-0.8 ± 0.9	0.5
-PP (n=139)	-1.2 ± 1.0	-1.1 ± 1.0	0.5
-16 wk			
-ITT	-1.3 ± 1.1	-1.3 ± 1.0	0.9
-PP	-1.6 ± 1.1	-1.6 ± 0.9	1
-24 wk			
-ITT	-1.6 ± 1.3	-1.5 ± 1.1	0.3
-PP	-2.1 ± 1.2	-1.8 ± 1.1	0.14
Delta Indian HAQ (16 wk)	-0.7 ± 0.6	-0.8 ± 0.6	0.2
Adverse effects			
Serious AE	0	0	-
Death	0	0	-
Symptomatic AE ever n (%)*			
Vomiting	7 (8)	7 (8)	1
Nausea	22 (26)	26 (30)	0.5
Stomach ache	16 (19)	17 (20)	0.9
Loss of appetite/bad taste	21 (25)	27 (31)	0.3
Lethargy	20 (24)	21 (25)	1
Dizziness	19 (23)	16 (19)	0.5
Irritability/anxiety	14 (16)	14 (16)	1
Laboratory AE ever [n/N times done (%)]*			
Transaminitis episodes (>40IU/L)	52/224 (23)	52/219 (24)	0.9
-Significant (>80 IU/L)	5/224 (2)	8/219 (4)	0.4
Thrombocytopenia episodes (<150000/uL)	10/224 (5)	13/218 (6)	0.5
-Significant (<100000/uL)	2/224 (1)	2/218 (1)	1
Leucopenia episodes (<4000/uL)	2/224 (1)	3/220 (1.5)	0.8
-Significant (<3500/uL)	1/224 (0.5)	2/220 (1)	0.8
Methotrexate levels			
MTX-polyglutamate-3 (nmol/L)			
-8 wk	25.8 ± 10.5	26.9 ± 13.6	0.6
-16 wk	40.7 ± 20.9	40.1 ± 23.4	0.9

*Ever=any time during the studyITT= intention-to-treat, PP=per-protocol, AE=adverse effect

Conclusion: A faster escalation of MTX (5 mg every 2 weeks) reaching 25 mg/week by 4 weeks did not have a significantly higher rate of adverse effects (symptomatic or laboratory) compared to an escalation by 5 mg every 4 weeks. Although not more efficacious, it may shorten the time to recognize MTX failure, and optimize treat-to-target.

REFERENCES:

[1] Visser K, Katchamart W, Loza E, et al. Multinational evidence-based recommendations for the use of methotrexate in rheumatic disorders with a focus on RA: integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3E Initiative. Ann Rheum Dis. 2009;68(7):1086–93

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3864

AB0277

ASSOCIATION BETWEEN INTRA-ERYTHROCYTE METHOTREXATE POLYGLUTAMATE CONCENTRATION AND CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS IN PATIENTS TREATED WITH METHOTREXATE INJECTABLE SUBCUTANEOUSLY

M. Poudret[1], M. Norman[2], S. Hodin[3], A. S. Amouzougan[1], K. Boussoualim[1], A. Coassy[1], T. Neel[1], T. Thomas[1,2], X. Delavenne[3], H. Marotte[1,2]. [1]*CHU Saint-Etienne, Rheumatology, Saint-Etienne, France*; [2]*Université de Lyon, SAINBIOSE LBTO, INSERM 1059, Saint-Etienne, France*; [3]*Université de Lyon, SAINBIOSE DVH, INSERM 1059, Saint-Etienne, France*

Background: Methotrexate (MTX) is the first-line treatment for rheumatoid arthritis (RA). Due to its short half-life, blood MTX dosage is not performed in current practice. Erythrocyte MTX-polyglutamate (MTX-PG), which penetrates into the red blood cells, would be correlated with the area under the MTX curve and would be more accessible for dosing. When treatment is initiated, its concentration correlates with efficacy and therapeutic adherence.

Objectives: To determine the interest of erythrocyte MTX-PG dosage in case of failure of 1st line MTX treatment.

Methods: In this single-centre cross-sectional study, RA patients presenting for consultation at the Saint-Etienne University Hospital, with a stable dose of MTX for more than 3 months at least 15 mg/week subcutaneously with either clinical remission (DAS28<2.6) or active disease (DAS28>3.2) were included between July 2nd 2018 and May 28th 2020. In order to assess therapeutic compliance, the patient completed the compliance questionnaire of Rheumatology (CQR) questionnaire. The determination of erythrocytic MTX-PG was performed on a 5 mL blood sample by liquid chromatography method for the determination of the different PG forms.

Results: Sixty patients were included, 34 in the active RA group and 26 in the RA group in remission. One patient withdrew his consent. Only 16% of patients were observed with a CQR score > 80%. Patients in remission were leaner with a longer duration of disease and MTX treatment. The sex ratio, RA status, creatinine clearance and MTX dose was not different in both groups. The CQR was better in the remission group than in the active RA group. However, total MTX-PG was not different in the two groups. The same results were observed for the different forms of MTX-PG 1, 2, 3 or 4. In contrast, in the remission PR group, total MTX-PG or MTX-PG2, 3, 4 and 5 correlated inversely with BMI while MTX-PG3 correlated positively with BMI in the active PR group. In the active PR group, MTX-PG5 correlated with MTX dose.

Conclusion: MTX-PG dosage is not a biomarker of good response to MTX in our study. However, compliance is a key factor to be considered in RA with active disease in adapting patient management.

REFERENCES:

[1] Pasma A, Boer E den, Spijker A van 't, Timman R, Bemt B van den, Busschbach JJV, et al. Nonadherence to disease modifying antirheumatic drugs in the first year after diagnosis: comparing three adherence measures in early arthritis patients. Rheumatology 2016;55:1812–1819.

[2] Haandel L van, Becker ML, Leeder JS, Williams TD, Stobaugh JF. A novel high-performance liquid chromatography/mass spectrometry method for improved selective and sensitive measurement of methotrexate polyglutamation status in human red blood cells. Rapid Commun Mass Spectrom RCM 2009;23:3693–3702.

[3] Dervieux T. Pharmacogenetic and metabolite measurements are associated with clinical status in patients with rheumatoid arthritis treated with methotrexate: results of a multicentred cross sectional observational study. Ann Rheum Dis 2005;64:1180–1185.

Disclosure of Interests: Marion POUDRET: None declared, Myriam Norman: None declared, Sophie Hodin: None declared, Adamah Stanislas AMOUZOUGAN: None declared, Karima BOUSSOUALIM: None declared, Astrid Coassy: None declared, Tiphany Neel: None declared, THIERRY THOMAS: None declared, Xavier DELAVENNE: None declared, Hubert MAROTTE Speakers bureau: Pfizer, Nordic, Paid instructor for: Amgen, Consultant of: Novartis, Grant/research support from: Nordic

DOI: 10.1136/annrheumdis-2021-eular.4028

SLE, Sjögren's and APS – treatment

AB0278 OFF-LABEL RITUXIMAB FOR SYSTEMIC AUTOIMMUNE DISEASES: A CASE SERIES FROM A THIRD LEVEL HOSPITAL DURING A 5 YEAR- PERIOD

C. Sieiro Santos[1], C. Moriano Morales[1], E. Diez Alvarez[1], I. González Fernández[1], A. López Robles[1], T. Pérez Sandoval[1]. [1]*Complejo Asistencial Universitario de León, Rheumatology, León, Spain*

Background: Rituximab (RTX) is a drug composed of chimeric monoclonal antibodies against the CD20 protein that leads to B cell lymphocyte depletion and is currently licensed for rheumatoid arthritis. There is growing evidence of off-label use of rituximab for severe and refractory systemic autoimmune diseases (SAD).
Objectives: Analysing the clinical effectiveness of RTX for SADs such as vasculitis (VS), systemic lupus erythematosus (SLE), systemic sclerosis (SS), primary sjögren syndrome (pSS), necrotizing myopathy (NM) and dermatomyositis (DM) in a rheumatology outpatient clinic in a third level hospital during a 5 year-period (2015 –2020).
Methods: We conducted a retrospective analysis of patients with SAD treated with RTX in the last 5 years. We evaluated demographic and clinical data, indication for RXT, previous treatments, cumulative dose of rituximab and corticosteroids, clinical response, and the presence of adverse events. We considered follow-up period between the first and the last clinical evaluation. Clinical response was considered complete with symptom and analytical remission; incomplete with partial symptom or analytical response and no response if there was no symptom or analytical response.
Results: 35 patients were included (54% women, mean age 60.16 ±17 years). The diagnosis were: pSS (31.4%), SS (17%), SLE (17%), VS (20%), NM (8.8%) and DM (5.8%). Indications for treatment were pulmonary disease in 37% of cases, renal disease in 17%, articular manifestations in 11.4%, haematological manifestations in 14.3%, skin involvement in 8.8%, neurologic manifestations in 5.7% and myopathy in 5.8%. RTX was used after therapeutic failure with previous treatments in 80% (20% of which had receiving treatment with biological disease-modifying antirheumatic drugs) and as first line treatment in only 20% of the cases. After rituximab, 60% of patients had complete response, 17% partial response, and 20% nonresponding. Mean corticosteroid dose post-rituximab was significantly reduced by 60% in pSS (p 0.02), 65% in VS (p 0.03), 50% in SS (p 0.04) and NM (p 0.046). Five patients (14%) had infectious complications, 2 of which needed hospitalization. 7 patients (17%) discontinued therapy, 5 due to ineffectiveness (2 SLE, 1 NM, 1 DM and 1 SS) and 2 patients (14%) due to infectious complications (1 pSS and 1 VS). Patients underwent a median of 2 treatment cycle. The median follow-up after starting RTX was 48.5 (IQR 25.9-74.4) months.

Table 1. Clinical characteristics

	pSS	VS	SLE	SS	NM	DM
%	31.4%	20%	17%	17%	8.8%	5.8%
Age (years)	63.8 (19-73)	63.5 (43-82)	59.2 (43-78)	65.8 (56-78)	58.5 (54-63)	48.5 (26-52)
Female	100%	71%	50%	66%	50%	50 %
Duration of disease (months)	80.5 (24-108)	39 (12-60)	38.4 (36-90)	56.4 (14-96)	69 (48-90)	60 (25-82)
Cumulative RTM dose (g/m2)	2.5 (0.75-6)	3.2 (0.5-8)	1.4 (0.75-5)	2.8 (0.5 – 7)	1.2 (0.5 – 5)	0.56 (0.38-0.75)
Complete clinical response	63%	86%	33%	71%	33%	0%
Incomplete response	18%	14%	33%	14%	0%	50%
No response	18%	0%	33%	14%	66%	50%
Glucocorticoid dose (mg/day) Before RTMX	12.5 (5-20)	21.3 (5-30)	9 (0-15)	9 (5-15)	15 (7.5 – 25)	15 (7.5 – 25)
Glucocorticoid dose (mg/day) After RTX	5 (2.5-15)	7.5 (5-15)	5 (2.5-15)	4.5 (2.5-10)	10 (7.5-25)	12.5 (8 – 20)
Immunosuppressants Before RTX	81%	71%	90%	50%	33%	50%
Immunosuppressants After RTX	54%	28%	57%	66%	67%	50%
Severe infusion-related side effects including need for admission	0%	14%	16%	0%	0%	0%
Other infusion-related side effects	9%	29%	17%	17%	0%	0%

Conclusion: Treatment with RTX was very effective in SADs, particularly in VS, SS and pSS. Further studies are needed to clarify RTX efficacy and safety in SADs, as well as indications and optimal RTX regimens.
REFERENCES:
[1] Berghen N, Vulsteke JB, Westhovens R, Lenaerts J, De Langhe E. Rituximab in systemic autoimmune rheumatic diseases: indications and practical use. Acta Clin Belg. 2019 Aug;74(4):272-279.
[2] Hofmann K, Clauder AK, Manz RA. Targeting B Cells and Plasma Cells in Autoimmune Diseases. Front Immunol. 2018 Apr 23;9:835.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.174

AB0279 THE IMPACT OF HYDROXYCHLOROQUINE DAILY DOSE IN THE PREVENTION OF FLARES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN REMISSION

S. Fasano[1], V. Messiniti[1], M. A. Coscia[1], E. Gaggiano[1], M. Iudici[2], F. Ciccia[1]. [1]*University of Campania, Department of Precision Medicine, Rheumatology Unit, Naples, Italy*; [2]*Cochin Institute, National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, Department of Internal Medicine, Paris, France*

Background: The EULAR recommendations for the management of systemic lupus erythematosus (SLE) suggest a hydroxychloroquine (HCQ) dose of ≤5.0 mg/kg/day instead of 6.5 mg/kg/day to reduce the risk of HCQ-induced retinopathy (1). This change in HCQ dose may potentially lead to undertreatment with blood levels below the presumed therapeutic range.
Objectives: The aim of this study was to compare flare rates and HCQ blood levels between the two different oral dosages in patients with SLE in remission.
Methods: Eligible patients were SLE patients in clinical remission according to the preliminary Definitions of Remission in SLE (DORIS) criteria for at least one year and treatment with stable dose of HCQ for at least six months and stable dose of glucocorticoids and/or immunosuppressants (2). Flares were defined by SELENA-SLEDAI Flare Index (3). A venous blood sample was collected on two different occasions from all patients, reflecting actual therapeutic adherence. The biosamples were analyzed in a UPLC-MS/MS system composed of a Nexera chromatograph (Shimadzu) coupled with a Q-trap 6500 spectrometer (AB Sciex). A mean [HCQ] value ([HCQm]) for each patient was then calculated. Predictors of flares were analyzed by Cox regression.
Results: We selected 66 patients who were stratified according to HCQ oral dose in two groups (Table 1). We observed 23 (35%) flares that developed in mean 26,0 (±15,1) months: 8/32 (25%) patients taking HCQ 5 mg/kg/day; 15/34 (44%) in the other group. No statistically significant difference was observed between the two group in number of flares (p=0,106), mean time of occurrence (p=0,904) and median [HCQm] (p=0,983). At regression analysis, older age at baseline was protective against flare occurrence (HR 0,93), while concomitant immunosuppressive therapy showed significant positive association (HR 3,66).
Conclusion: Our study suggests that low dosage of HCQ (5 mg/kg/day) may safely be prescribed in SLE patients in remission, without significant differences in terms of blood concentration and impact on the clinical course of SLE.
REFERENCES:
[1] Fanouriakis A, et al. Ann Rheum Dis 2019;78:736-745.
[2] van Vollenhoven R, et al. Ann Rheum Dis 2017;76:554-561.
[3] Petri M, et al. Arthritis Rheum. 2012;64(8):2677-2686.

Table 1. Demographic, clinical and therapeutic features of the cohort and follow up data.

	All patients (n= 66)	HCQ ≤5mg/Kg/die (n=32)	HCQ 6,5mg/Kg/die (n=34)	*P*
Sex, female	65 (99)	31 (97)	34 (100)	*0,3026*
Age, y, mean (SD)	42,00±11,27	41,80±10,25	42,10±12,30	*0,9140*
Disease duration, y, mean (SD)	15,70 (9,02)	17,80 (8,01)	13,67 (9,50)	*0,0624*
SLEDAI, median (range)	2 (0-4)	1 (0-4)	2 (0-4)	*0,6480*
SLICC, median (range)	0 (0-2)	0 (0-2)	0 (0-1)	*0,8556*
[HCQm] ng/mL, median (range)	512,60 (104,41-3105,66)	457,16 (104,41-3105,66)	538,49 (149,24-1239,15)	*0,5989*
[DCQ] ng/mL, median (range)	73,41 (4,16-649,84)	66,84 (4,16-649,84)	66,31 (10,75-258,41)	*0,9380*
Time remission, y, median (range)	2,00 (1-11)	2,96 (1-10)	2,00 (1-11)	*0,6588*
Previous renal involvement	31 (47)	15 (47)	16 (47)	*0,9882*
Time HCQ, y, median (range)	5 (0-32)	8 (0-26)	5 (1-32)	*0,2391*
Glucocorticoids	33 (50)	18 (56)	15 (44)	*0,4700*
Mycophenolate mofetil	6 (9)	2 (6)	4 (12)	*0,4396*
Azathioprine	7 (11)	4 (14)	3 (9)	*0,6305*
Methotrexate	1 (2)	0	1 (3)	*0,3320*
Cyclosporine	2 (3)	1 (3)	1 (3)	*0,9655*
Belimumab	1 (2)	0	1 (3)	*0,3320*
Follow up time, m, median (range)	49 (4-67)	52 (7-67)	43 (4-67)	*0,1115*
Number of flares	23 (35)	8 (25)	15 (44)	*0,1060*
Time to flare, m, mean (SD)	26,0 (±15,1)	26,6 (±16,4)	25,8 (±14,9)	*0,9042*
Ocular alterations	6 (9)	4 (12)	2 (6)	*0,0947*

	HR	95% CI	p
Age, y	0,9336	0,8947 to 0,9742	**0,0016**
Disease duration, y	0,9712	0,9257 to 1,0191	0,2340
SLEDAI	1,1193	0,8084 to 1,5498	0,4971
SLICC	1,5583	0,7785 to 3,1191	0,2102
[HCQm] ng/mL	0,9997	0,9987 to 1,0007	0,5983
[DCQ] ng/mL	0,9973	0,9922 to 1,0024	0,3048
Clinical remission off/on therapy	1,3702	0,6001 to 3,1282	0,4546
Complete remission off/on therapy	0,7298	0,3197 to 1,6663	0,4546
Time remission	0,7984	0,6287 to 1,0138	0,0647
Previous renal involvement	1,1207	0,4942 to 2,5416	0,7850
Time HCQ	0,9735	0,9128 to 1,0383	0,4140
Glucocorticoids	2,1489	0,8966 to 5,1502	0,0863
Immunosuppressive therapy	3,6639	1,5924 to 8,4304	**0,0023**
HCQ dosage	0,4995	0,2113 to 1,1805	0,1137

Figure 1. Predictors of flares analyzed by Cox regression.*Serena Fasano and Valentina Messiniti contributed equally to this abstract

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.192

AB0280

THE INFLUENCE OF TARGET THERAPY AS WELL AS GLUCOCORTICOIDS TAPERING ON DISEASE FLARE IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM A PROSPECTIVE CHINESE COHORT

Y. Hao[1], L. Ji[1], D. Gao[2], Y. Fan[1], B. Wei[1], Y. Geng[1], X. Zhang[1], G. Li[1], Z. Zhang[1]. *[1]Peking University First Hospital, Department of Rheumatology and Clinical Immunology, Beijing, China*; *[2]Peking University First Hospital, Department of Rheumatology and Clinical Immunology, Beijing,*

Background: Treat-to-target in systemic lupus erythematosus (SLE) has been proposed for 7 years and several recommendations were developed [1]. In these recommendations, prevention of flares should be a realistic target. Meanwhile, 'remission' or 'low disease activity' was recommended as the treatment target and minimizing glucocorticoids (GC) dose or withdrawal if possible was suggested in the maintenance treatment. However, would target therapy and GC tapering/withdrawal influence disease flare?
Objectives: To investigate the frequency and determinants of disease flare, especially the influence of target therapy as well as GC tapering on flare in Chinese lupus patients.
Methods: The baseline and follow-up data of all consecutive patients in a prospective longitudinal lupus cohort from January 2017 to June 2020 were collected. The lupus low disease activity state (LLDAS) was defined as in Golder et al., 2019[2]. The criteria for remission were from DORIS definitions [3]. Flare was assessed using the SELENA-SLEDAI flare index [4].
Results: We enrolled 185 patients with disease duration at recruitment of 2.3 (0.8–7.7) years. During the 26.2 (12.5-34.5) months of follow-up, 73 (39.5%) patients experienced 95 flares, including 70 mild/moderate and 25 severe flares. The incidence of flare per patient-year was 0.27. Kaplan-Meier analyses showed that compared with those who never achieved LLDAS or DORIS, the patients who achieved the target at least once had a higher flare free survival rate; meanwhile, the patients with prednisone withdrawn had significantly lower flare free rate compared with those with small dose of GC maintained (≤7.5mg/d) (Figure 1A), but among the patients with different prednisone maintain doses (7.5~5mg, 5~2.5mg, and ≤2.5mg) there was not significant difference (Figure 1B). Cox regression analysis showed that younger age at disease onset and lower Complement 3 (C3) level at recruitment were independent risk factors for flare and achieving LLDAS or DORIS ≥50% of visits was independent protective factor (Table 1).
Conclusion: In this Chinese prospective SLE cohort, age at disease onset, C3 level at recruitment and therapeutic target achieving influenced disease flare independently and significantly. GC tapering in appropriate patients and with appropriate pace did not increase the flare rate, but prednisone withdrawal may induce more disease exacerbation, which needs to be confirmed by large prospective studies.

REFERENCES:

[1] Van Vollenhoven R F, et al. Treat-to-target in systemic lupus erythematosus: recommendations from an international task force. Ann Rheum Dis, 2014. 73(6): 958-967
[2] Golder, V., et al. Lupus low disease activity state as a treatment endpoint for systemic lupus erythematosus: a prospective validation study. The Lancet Rheumatology, 2019. 1(2): p. e95-e102.
[3] van Vollenhoven R, et al. A framework for remission in SLE: consensus findings from a large international task force on definitions of remission in SLE (DORIS). Ann Rheum Dis. 2017. 76(3): 554–561.
[4] Petri M, et al. Classification and definition of major flares in SLE clinical trials. Lupus. 1999. 8(8): 685-691.

Table 1. Determinants of disease flare by multivariate Cox regression analyses

	Model 1 (LLDAS) Δ			Model 2 (RONT) Δ			Model 3 (Complete RONT) Δ		
	HR	95%CI	P value	HR	95%CI	P value	HR	95%CI	P value
Age at disease onset (years)†	0.97	0.95-0.99	0.004	0.97	0.95-0.99	0.003	0.97	0.95-0.99	0.003
Anti-dsDNA positive at recruitment	1.34	0.82-2.18	0.217	1.12	0.68-1.85	0.649	1.19	0.73-1.96	0.486
C3 (mg/L) at recruitment	0.998	0.997-0.999	0.004	0.998	0.997-0.999	0.007	0.998	0.997-1.000	0.010
Minimum prednisone dose during follow-up (mg/d)	0.98	0.90-1.08	0.716	1.01	0.94-1.08	0.747	1.04	0.97-1.11	0.243
Therapeutic target achieved≥50% of observations Δ	0.60	0.39-0.94	0.001	0.54	0.34-0.87	0.011	0.68	0.51-0.92	0.011

Δ In the three hazard models, the different target achievement status were included respectively.RONT: Clinical remission on treatment; Complete RONT: Complete remission on treatment.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.623

AB0281

MORTALITY PREDICTORS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE TERTIARY CENTER REFERRAL EXPERIENCE

C. M. Gamboa-Alonso[1], G. Figueroa-Parra[1], A. L. De-Leon-Ibarra[1], M. Á. Villarreal-Alarcón[1], J. Díaz-Angulo[1], D. Vega-Morales[1], D. Á. Galarza-Delgado[1]. *[1]Universidad Autónoma de Nuevo León, Reumatología e Inmunología Clínica, Monterrey, Mexico*

Background: Systemic Lupus Erythematosus (SLE) is a heterogeneous chronic multisystemic disease that has an increased risk of requiring inpatient management with higher morbidity and mortality rates.
The most frequent causes of mortality are a high disease activity, infections, and cardiovascular diseases.
Objectives: To determine the predictors of mortality in patients diagnosed with SLE.
Methods: A longitudinal, descriptive, observational study was performed from March 2017-March 2020 at the University Hospital of the Autonomous University of Nuevo León, México, including patients with a diagnosis of SLE according to the ACR-EULAR 2012/2019 criteria.
Descriptive statistics were used for demographic variables. Associations between mortality and clinical variables were determined using binary logistic regression analysis; a p <0.05 was considered statistically significant. The SPSS program version 20 was used.
Results: One-hundred and eighty-six patients with SLE diagnosis who fulfilled ACR-EULAR 2012/2019 criteria were included, 161 (86.6%) were women; the mean age was 35.8 (SD 15.41) years. The main chief complaints were dyspnea 31 (16.7%), fever in 28 (15.1%), renal involvement in 21 (11.29%), and arthritis in 19 (10.22%) patients.
Of the 186 patients, 34 (18.3%) had a readmission, 13 (7%) required intensive care unit management, 68 (36.6%) had some type of infection and 22 (11.8%) died. Factors associated with mortality are shown in table 1.
Patients receiving steroids and immunosuppression previous to hospitalization were 73 (39.2%) and 92 (49.5%) respectively.
Conclusion: Infections remain the leading cause of death in SLE patients. Factors that predispose to infections are a chronic use of steroids and immunosuppression as well as high activity of disease.

REFERENCES:
[1] Wu X-Y, Yang M, Xie Y-S, Xiao W-G, Lin J, Zhou B, et al. Causes of death in hospitalized patients with systemic lupus erythematosus: a 10-year multicenter nationwide Chinese cohort. Clin Rheumatol. enero de 2019;38(1):107-15.

Table 1. Association between clinical and therapeutic factors with mortality in SLE patients.

Factors associated with mortality	Univariado	Multivariado
	β (95 % IC)	β (95 % IC)□
Age	0.93 (0.96-1.02)	0.98 (0.96-1.02)
Use of mechanical ventilation	3.83 (1.07-13.4)*	3.07 (0.59-16.04)
Previous use of steroids	3.92 (1.51-10.15)*	2.04 (0.58-7.35)
Previous use of immunosupression	4.04 (1.42-11.45)*	2.85 (0.71-11.48)
Infection	3.57 (1.41-9.01)*	3.25 (1.19-8.86)*

p <0.05 *

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.941

AB0282

SAFETY, TOLERABILITY AND SELECTIVE EXPANSION OF REGULATORY T CELLS BY A SINGLE DOSE OF THE NOVEL IL-2 MUTEIN PT101 IN A PHASE 1 STUDY IN HEALTHY VOLUNTEERS

J. S. Sundy[1], K. L. Otipoby[1], N. Higginson-Scott[1], J. Visweswaraiah[1], E. Sampson[1], K. Kis-Toth[1], A. Monsef[1], P. Petaipimol[1], D. Essayan[2], M. E. Cosenza[3], R. Kakkar[1], J. Viney[1]. *[1]Pandion Therapeutics, Watertown, MA, United States of America*; *[2]Oncord, Inc, West Lake Village, CA, United States of America*; *[3]MEC Regulatory Consulting, LLC, Moorpark, CA, United States of America*

Background: Activation and expansion of regulatory T cells (Tregs) has been proposed as a strategy to treat autoimmunity. When administered in low doses, IL-2 expands and activates Tregs leading to clinical response in several autoimmune diseases. However, the narrow therapeutic window of IL-2 results in loss of selectivity for Tregs and concurrent activation of conventional T cells (Tconv) and NK cells, limiting its clinical utility. This loss of selectivity may negate the clinical benefit of Treg activation and lead to dose-limiting side effects. PT101 is a novel engineered variant of IL-2 fused to an Fc protein backbone which in preclinical studies selectively activates Tregs without expanding Tconv or NK cells. PT101 is in clinical development for the treatment of patients with autoimmune diseases.
Objectives: To assess the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of PT101 after a single dose in healthy human volunteers.
Methods: We conducted a randomized, double-blind, single-ascending dose trial of PT101 or placebo (3:1 allocation). Five dose levels from 1 mg to 10 mg were administered by subcutaneous injection. Adverse events, physical examination findings, and clinical laboratory results were assessed for 29 days. Serum PT101 levels and antidrug antibody were assessed. Changes in mononuclear cell populations were measured in peripheral blood by flow cytometry.
Results: 56 subjects were administered PT101 or placebo. All subjects completed the study. There were no deaths, serious adverse events, dose limiting toxicities, or clinically significant changes in vital sign, ECG, or laboratory results. All adverse events were Grade 1 or 2 and self-limited. Injection site reactions were the most common adverse event. Transient increases in eosinophil counts were observed in some subjects, consistent with the known class effect of IL-2. Peak levels of PT101 occurred 11.0 to 14.6 hours after administration, and declined with a mean half-life of 20.4 to 28.3 hours, demonstrating linear exposure through the dose range. No anti-drug antibodies were induced. PT101 caused dose-related expansion of Tregs that plateaued at doses between 3.5 and 10 mg. Mean maximum expansion above baseline was 3.6-fold for total Tregs and 72.5-fold for the CD25bright subset of Tregs. Maximal expansion was observed by Day 8-10 with a return toward baseline by Day 29. Over 80% of subjects achieved a 2-fold or greater expansion of total Tregs (Table 1). No significant expansion of Tconv or NK cells was observed at any dose level.

Table 1. Percent Total Treg Responders

	Placebo	1 mg	3.5 mg	5 mg	7.5 mg	10 mg
Fold Change Total Tregs	(n=14)	(n=6)	(n=12)	(n=12)	(n=6)	(n=6)
≥ 2X	7%	33%	83%	83%	100%	100%
≥ 3X	0%	0%	58%	75%	33%	50%
≥ 4X	0%	0%	24%	42%	33%	17%

Conclusion: PT101 was safe and well tolerated after a single dose in healthy volunteers. Marked expansion of both total Treg and CD25bright Treg cells was observed. High selectivity for Tregs was observed with no significant expansion of pro-inflammatory Tconv and NK cells even at the highest dose studied. These results support the therapeutic potential of PT101 in planned multiple dose studies in systemic lupus erythematosus, ulcerative colitis, and other autoimmune diseases.

REFERENCES:
[1] Klatzmann, D., Abbas, A. The promise of low-dose interleukin-2 therapy for autoimmune and inflammatory diseases. Nat Rev Immunol 15, 283–294 (2015)

Acknowledgements: Pandion Therapeutics acknowledges the participants and research staff who contributed to this clinical trial

Disclosure of Interests: John S Sundy Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Kevin L. Otipoby Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Nathan Higginson-Scott Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Jyothsna Visweswaraiah Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Erik Sampson Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Katalin Kis-Toth Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Adrianne Monsef Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Parika Petaipimol Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, David Essayan Consultant of: Pandion Therapeutics, Mary Ellen Cosenza Consultant of: Pandion Therapeutics, Rahul Kakkar Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Jo Viney Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics
DOI: 10.1136/annrheumdis-2021-eular.1200

AB0283

CHOREOATHETHOSIS AND LONGITUDINALLY EXTENSIVE TRANSVERSE MYELITIS AS RARE AND SEVERE MANIFESTATIONS OF NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS AND PRIMARY SJÖGREN'S SYNDROME – A TWO-CENTER EXPERIENCE

P. Korsten[1], M. Plüß[1], S. Glaubitz[2], A. Jambus[3], R. Vasko[1], B. M. Göricke[2], S. Piantoni[4]. *[1]Universitätsmedizin Göttingen, Department of Nephrology and Rheumatology, Göttingen, Germany*; *[2]Universitätsmedizin Göttingen, Department of Neurology, Göttingen, Germany*; *[3]Universitätsmedizin Göttingen, Department of Neuroradiology, Göttingen, Germany*; *[4]University of Brescia, Department of Rheumatology and Clinical Immunology, Brescia, Italy*

Background: Systemic lupus erythematosus (SLE) can affect almost any organ system. Nevertheless, Lupus nephritis and neuropsychiatric manifestations (NPSLE) are associated with increased mortality (1). Therapeutic options include glucocorticoids, often pulse methylprednisolone (MP), and other immunosuppressive therapies. In refractory cases, therapeutic plasma exchange, rituximab, or intravenous immunoglobulins are often used (2). However, an optimal therapeutic strategy has not been established because NPSLE is an exclusion criterion in most clinical trials. In addition, NPSLE can present with a broad spectrum of manifestations ranging from cognitive dysfunction to severe and life-threatening disease with choreoathetosis or transverse myelitis (TM). In primary Sjögren's syndrome (pSS), neurological manifestations most often include peripheral neuropathies, but TM has also been reported.
Objectives: To analyze the clinical presentation and outcomes after treatment in severe, life-threatening NPSLE.
Methods: We retrospectively analyzed clinical, laboratory, and imaging features in severe NPSLE manifestations in SLE and pSS patients at two tertiary academic centers (University Medical Center Göttingen, Germany, and ASST Spedali Civili Brescia, Italy) with a high volume of SLE patients. Severe NPSLE was defined as either severe movement disorder or extensive tetra- or paraplegia secondary to (longitudinally extensive) transverse myelitis.
Results: Our retrospective chart review resulted in seven patients fulfilling the inclusion criteria (six with SLE and 1 with pSS). Of these, five were females (71.4%). Median age was 26 (16-55) years. Three were of Asian origin, four were of European descent. Median disease duration was 15 (2-228) months. Three patients presented with severe choreoathetosis, all had positive ANA, anti-dsDNA antibodies (abs), and complement consumption. Of note, all three had at least one positive antiphospholipid antibody (APLA). All patients received IV MP 1g x 3 and mycophenolate mofetil and achieved complete remission. Of the four patients with longitudinally extensive TM, all were ANA positive, only two had anti-dsDNA abs. None of them had APLA, and only one tested positive for anti-aquaporine-4 abs. Of all patients, only one had positive ribosomal P-abs. Patients with TM received IV MP 1g x 5 and either RTX (4 cycles with 375 mg/m^2 or IVIg 0.4 g/kg/d x 5). All four TM patients improved; two improved markedly, two only moderately with residual deficits as assessed by EDMUS-grading scale and functional independence measure.
Conclusion: Severe NPSLE, defined as choreoathetosis or TM require intensive treatment. While the former patients achieved complete remission, two of four patients with TM only achieved partial remission. Our data support the use of early

and aggressive immunosuppressive therapy. Nevertheless, therapy for TM in the context remains insufficient and should be assessed in a controlled clinical trial setting.

REFERENCES:

[1] Monahan RC, et al. Mortality in patients with systemic lupus erythematosus and neuropsychiatric involvement: A retrospective analysis from a tertiary referral center in the Netherlands. Lupus. 2020 Dec;29(14):1892–901.

[2] Papachristos DA, et al. Management of inflammatory neurologic and psychiatric manifestations of systemic lupus erythematosus: A systematic review. Semin Arthritis Rheum. 2020 Dec 17;51(1):49–71.

Disclosure of Interests: PETER KORSTEN Consultant of: PK has received honoraria by Abbvie, Bristol-Myers-Squibb, Chugai, Gilead, Glaxo Smith Kline, Janssen-Cilag, Pfizer, and Sanofi-Aventis, all unrelated to this study., Grant/research support from: PK has received research grants from GSK, unrelated to this study., Marlene Plüß: None declared, Stefanie Glaubitz: None declared, Ala Jambus: None declared, Radovan Vasko: None declared, Bettina Meike Göricke: None declared, Silvia Piantoni: None declared

DOI: 10.1136/annrheumdis-2021-eular.1210

AB0284 COMBINATION THERAPY WITH RITUXIMAB AND BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

A. Mesnyankina[1], E. Aseeva[1], N. Nikishina[1], A. Torgashina[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Federal State Budgetary Scientific Institution, Moscow, Russian Federation*

Objectives: To assess the efficacy of combined therapy with rituximab (RTM) and belimumab (BLM) in patients with active systemic lupus erythematosus (SLE).

Methods: The study included 12 SLE pts (1M/11F) with severe (SLEDAI2K≥10 – 8pts.) and moderate (SLEDAI2K<10- 4pts.) disease activity; out of them 5 patients had lupus nephritis, vasculitis and 7 had predominantly mucocutaneous and articular manifestations of SLE. The dose of oral GC was: 60 mg in one patient with vasculitis, LN, cerebrovasculitis; in 9 patients from 10 to 5 mg; in 2 patients without oral glucocorticoids. All patients with SLE with kidney damage, CNS, and vasculitis received cytostatics. All patients with vasculitis, LN, etc. received mycophenolate mofetil or cyclophosphamide. Rituximab (RTM) was administered at 500-2000 mg, with subsequent adding of Belimumab (BLM) 1-6 months later at a standard dosing regimen 10 mg/kg once a month a total of 7 infusions. The following parameters were evaluated: the effectiveness of therapy, the concentration of autoantibodies, the dose of oral corticosteroids initially at the time of RTM administration and then every 3 months after the initiation of BLM therapy.

Results: 8 pts demonstrated the decrease in clinical and laboratory SLE activity, starting from 3mo of follow-up. After the start of BLM infusions, a decrease in SLE activity was observed in all patients. Among them, 9 had SLEDAI-2K activity of less than 4 points (SLEDAI-2k Me 12 [9,5;17], after treatment of RTM and BLM 4[2;4]). Only one patient (№4) had a relapse of SLE, due to the omission of the BLM infusion. He was receiving standard GC doses. In dynamics, a decrease anti-double DNA titres (Me 101 [39;250]U/ml vs 19 [9;70] U/ml), C3 (0,44 [0,39;0,59]g/l vs 0,81 [0,72;0,87] g/l), C4 (0,06 [0,031;0,1] g/l vs 0,14 [0,13;0,14] g/l) was registered. The GC dose was reduced in most patients (tab. 1), but the previously prescribed immunosuppressive therapy continued. There were no cases of severe infection.

Conclusion: Combination therapy allows to gain control over disease activity in short time, due to the effect of RTM, while added BLM provides further prolongation of the effect achieved, minimizing the risk of flare. The use of such therapy contributes to a rapid and effective reduction in the activity of the disease, normalization of laboratory markers of SLE (at to ds-DNA, C3, C4), the use of lower doses of oral GCs. This combination may be used as a method of choice in pts with severe SLE involving vital organs, and in persistent cutaneous-articular disease and high immunological activity.

Table 1. Dose of oral glucocorticoids (prednisone), mg

№ patient	Before the introduction of RTM, mg	1st 7th injection of of BLM, mg	7th injection of BLM, mg	
1	20	20	15	↓
2	7,5	5	5	↓
3	5	5	5	=
4	10	10	10	↓
5	5	5	5	=
6	60	7,5	2,5	↓↓↓
7	10	2,5	0	↓↓↓
8	10	10	5	↓
9	2,5	2,5	2,5	=
10	10	10	5	↓
11	0	0	0	=
12	0	0	0	=

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1499

AB0285 EFFECTIVENESS OF IMMUNOSUPPRESSIVE THERAPY FOR CONNECTIVE TISSUE DISEASE–ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

R. Kishikawa[1], M. Hatano[1,2], S. Ishii[1], M. Shimbo[1], A. Saito[1], S. Minatsuki[1], Y. Iwasaki[3], K. Fujio[3], I. Komuro[1]. *[1]Graduate School of Medicine, The University of Tokyo, Department of Cardiovascular Medicine, Tokyo, Japan*; *[2]Graduate School of Medicine, The University of Tokyo., Department of Therapeutic Strategy for Heart Failure, Tokyo, Japan*; *[3]Graduate School of Medicine, The University of Tokyo, Department of Allergy and Rheumatology, Tokyo, Japan*

Background: Connective tissue disease (CTD) associated pulmonary arterial hypertension (PAH) is considered to be an indication for immunosuppressive therapy (IT) except scleroderma associated PAH. However, the response rate defined by improvement of WHO functional class and hemodynamic parameters is reported to be around 50% [1]. Since CTDs are systemic diseases, it may be difficult to evaluate the efficacy of IT by subjective symptoms. Although there are previous studies reporting that the combined use of IT and pulmonary vasodilators significantly improved hemodynamics [2], response to IT without titration of pulmonary vasodilators remains to be elucidated.

Objectives: To examine whether IT is effective for CTD-PAH.

Methods: We retrospectively examined the medical records of consecutive 13 patients with CTD-PAH (female 13, mean age 47 ± 15 years) treated with methylprednisolone (1 mg/kg/day, oral) and intravenous bolus cyclophosphamide (IVCY) (500 mg/m^2) every four weeks for six times. Patient characteristics are described in Table 1. Right heart catheterization (RHC) was done at prior to IT, before adding PAH specific agents, and at the fifth or sixth course of IVCY. In treated cases, the previous vasodilators remained unchanged during the first term of IT.

Results: At the first follow up RHC, decrease of mean pulmonary arterial pressure over 5 mmHg was observed in all patients, and decrease of pulmonary vascular resistance (PVR) was observed in twelve out of 13 patients (Figure 1). Over 20% of PVR reduction was observed more in the patients of pulmonary vasodilator naïve and started IT within one year from symptoms than others (6/7 vs 1/6, p=0.03). Although six-minutes walk distance (6MWD) tended to be prolonged between first and second RHC (298 ± 70 m vs 382 ± 81 m; p=0.054; n = 9), 6MWD was shortened in some cases with good hemodynamic improvement (2/5). All patients were prescribed oral PAH specific agents finally, but no one needed parenteral prostanoids. Two patients (15%) died during maintenance therapy for causes other than PAH. Three-year and five-year survival rates were 91.7% and 81.5%, respectively.

Conclusion: IT without titration of pulmonary vasodilators significantly improved hemodynamic parameters despite of less improvement in 6MWD in CTD-PAH patients. Considering that CTDs itself might affect the exercise tolerance regardless of PAH, these hemodynamic changes may contribute to better prognosis and IT might be considered especially for patients early in clinical courses and treatment naïve.

REFERENCES:

[1] Jais X, Launay D, Yaici A, et al. Immunosupressive therapy in lupus-and mixed connective tissue disease-associated pulmonary arterial hypertension. ARTHRITIS RHEUM. 2008; 58(2): 521-531.

[2] Yamamoto M S, Fukumoto Y, Sugimura K, et al. Intensive immunosuppressive therapy improves pulmonary hemodynamics and long-term prognosis in patients with pulmonary arterial hypertension associated with connective tissue diseasae. Circ J. 2011; 75: 2668-2674.

Table 1. Characteristics of patients

Patient	Age, yr	Connective Tissue Disease	Years from symptom to immunosuppressive therapy	Previous vasodilators	vasodilators at final visit
1	47	SS	1.5	PGI2	ERA
2	62	SS, RA	2	none	PDE5
3	32	SS	1	none	ERA
4	57	SS, SSc	0.5	none	PDE5
5	26	SS,MCTD, SLE,SSc	0.5	none	PDE5
6	70	SSc, SS s/o	13	sGC, ERA	sGC, ERA
7	32	SS s/o, SLE	0.1	none	PDE5
8	31	MCTD	3	ERA,PDE5, PGI2	ERA,PDE5, PGI2
9	43	SSc, SLE	0.6	ERA, PDE5	ERA,PDE5, PGI2
10	67	MCTD,PM	0	none	sGC
11	41	SS	0.1	none	ERA, PDE5
12	69	SS	0.3	none	PDE5
13	44	SS, MCTD s/o, SLE s/o	0.1	none	ERA, sGC

N.A, not acquired; s/o, suspect of; SS, Sjögren's syndrome; RA, rheumatoid arthritis; SSc systemic sclerosis; SLE, systemic lupus erythematosus; MCTD, mixed connective tissue disease; PM, Polymyositis; PGI2, prostacyclin derivative; sGC, soluble guanylate cyclase stimulator; ERA, endothelin receptor antagonist; PDE5, phosphodiesterase type 5 inhibitor.

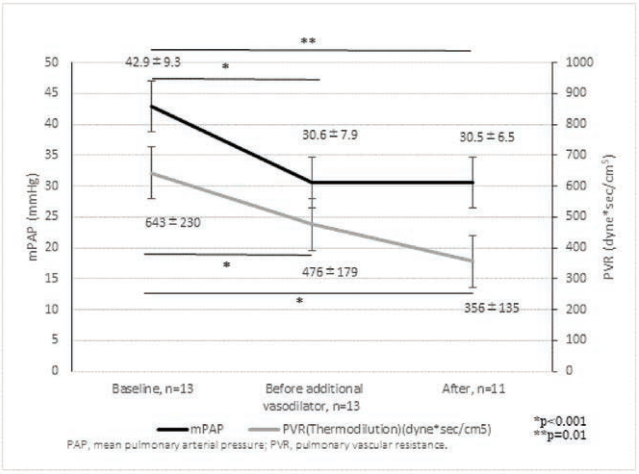


Figure 1. Hemodynamic changes during immunosuppressive therapy

Disclosure of Interests: Risa Kishikawa: None declared, Masaru Hatano Speakers bureau: Janssen Pharmaceutical K.K, Bayer Yakuhin, Ltd., Grant/research support from: Janssen Pharmaceutical K.K, Nippon Shinyaku Co., Ltd., MOCHIDA PHARMACEUTICAL CO., LTD., Satoshi Ishii: None declared, Mai Shimbo: None declared, Akihito Saito: None declared, Shun Minatsuki: None declared, Yukiko Iwasaki: None declared, Keishi Fujio Speakers bureau: Tanabe Mitsubishi, Bristol Myers, Eli Lilly, Chugai, Jansen, Pfizer, Ono, AbbVie, Ayumi, Astellas, Sanofi, Novartis, Daiichi Sankyo, Eisai, Asahi Kasei, Japan Blood Products Organization, and Kowa, Grant/research support from: Tanabe Mitsubishi, Bristol Myers, Eli Lilly, Chugai, AbbVie, Ayumi, Astellas, Sanofi, Eisai, Tsumura & Co., and Asahi Kasei., Issei Komuro Speakers bureau: AstraZeneka, Daiichi Sankyo Company, Limited, Takeda Pharmaceutical Company Limited, Bayer Yakuhin, Ltd, Pfizer Japan Inc., and Ono Pharmaceutical Co., Ltd., Grant/research support from: Daiichi Sankyo Company, Ltd, Sumitomo Dainippon Pharma Co., Ltd., Takeda Pharmaceutical Company Ltd, Mitsubishi Tanabe Pharma Corporation, Teijin Pharma Limited, Idorsia Pharmaceuticals Ltd, Otsuka Pharmaceutical Co., Ltd., Bayer Yakuhin, Ltd. Ono Pharmaceutical Co., Ltd. Toa Eiyo Ltd

DOI: 10.1136/annrheumdis-2021-eular.1573

AB0286 EFFICACY OF MYCOPHENOLATE MOFETIL PLUS RITUXIMAB COMPARED WITH INTRAVENOUS CYCLOPHOSPHAMIDE PLUS RITUXIMAB IN PATIENTS WITH RELAPSING LUPUS NEPHRITIS

L. D. Fajardo Hermosillo[1]. [1]*Centro Médico Nacional de Occidente IMSS, Rheumatology, Guadalajara, Mexico*

Background: Lupus nephritis (LN) remaining as one of the most devastating manifestations of systemic lupus erythematosus (SLE). Only 60% of patients with LN achieve a complete (CR) or partial remission (PR) with mycophenolate mofetil (MMF) or intravenous (iv) cyclophosphamide (CY) plus corticosteroids. Of those nearly one-half will have a relapse following maintenance therapy [1]. Rituximab (RTX) is considered a treatment of relapsing LN [2]. Although potential benefits have been revealed in descriptive studies, efficacy has not been established in randomized trials [3,4].
Objectives: This study compares the efficacy achieving a CR or PR with MMF+RTX versus iv CY+RTX in patients with relapsing LN.
Methods: Mexican SLE patients classified by SLICC 2012 criteria were recruited from 2013 to 2019 with LN diagnosed by renal biopsy who previously having achieved a CR with MMF or iv CY followed by the maintenance therapy with azathioprine (AZA) or MMF and subsequently present relapsing LN consisting of a new active urinary sediment (US), worsening proteinuria and renal function. Demographic, renal clinical and paraclinical variables were examined. All patients received oral prednisone (1 mg/kg/d) accompanying MMF 3 g/d or CY 0.5–1 g/m^2 monthly plus RTX 1 g at 0 and 14 days. The data were evaluated at 0, 6, 12 and 24 month(s) after the start both treatments. CR was defined as normal serum creatinine (SCr), inactive US, plus 24-Hour Urine Protein (24hUP) <500 mg/d and PC was established as 50 percent improvement in renal parameters. Fisher's exact and Student´s-t tests were performed by univariate analysis.
Results: Of nine SLE patients with relapsing LN, seven were women. The mean age [standard deviation (SD)] was 25.1 (6.4) years. The mean time at the onset of SLE (SD) was 3.44 (1.12) years ago. Four and five patients had class IV and IV/V LN respectively. Time of relapsing LN after of CR (SD) was 21.2 (7.17) months. Seven patients used CY followed by AZA and two employed MMF previously of relapsing LN. The mean of basal SLEDAI and SLICC (SD) were 19.11(3.2) and 1.22 (0.44) respectively. The mean of basal 24hUP (SD) was 4.67 (2.6) g/d and sCr (SD) was 2.0 (0.84) mg/dl. Five patients used MMF+RTX and four patients utilized CY+RTX. No statistically significant differences were found for CR, PR, 24hUP, sCr, US, anti-dsDNA and complement between both groups. At 6 months one patient achieved a CR and six reached a PR. At 12 months four patients fulfilled a CR and seven had a PR. Finally, at 24 months seven patients showed a CR and a CP. Only two patients did not achieve a CR or PR at 24 months.
Conclusion: This study suggests that the most of SLE patients with relapsing LN treated with CY or MMF plus RTX achieved CR or PR at 24 months, although were no found differences between both treatments. However, these observations must be confirmed in larger and prospective studies.
REFERENCES:
[1] Ann Rheum Dis 2020;79(6):713;
[2] Nephrol Dial Transplant 2019;34(1):22;
[3] Clin J Am Soc Nephrol 2009;4(3):579;
[4] Arthritis Rheum 2012;64(4):1215
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1612

AB0287 EFFECTS OF HYDROXYCHLOROQUINE ON PERIPHERAL BLOOD CYTOKINE EXPRESSION ASSOCIATED WITH ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

R. Wakiya[1], K. Ueeda[1], H. Shimada[1], S. Nakashima[1], M. Kato[1], M. Mahmoud Fahmy Mansour[1], T. Miyagi[1], K. Sugihara[1], Y. Ushio[1], M. Mizusaki[1], R. Senba[1], T. Kameda[1], H. Dobashi[1]. [1]*Kagawa University, Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Kagawa, Japan*

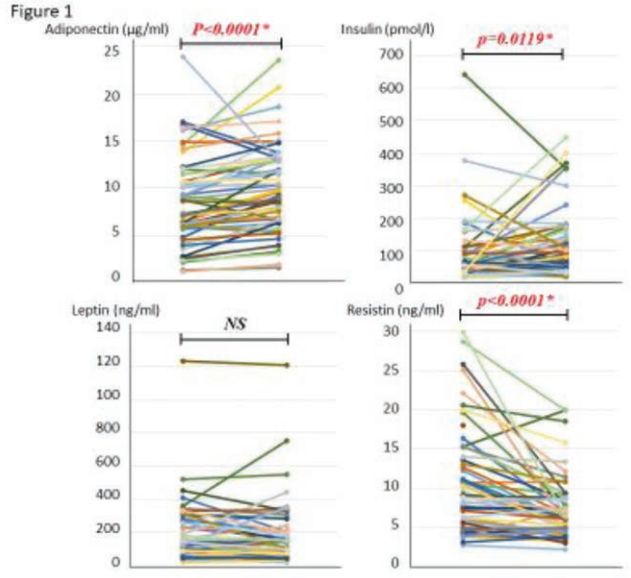
Background: In systemic lupus erythematosus(SLE), a higher frequency of atherosclerotic lesions is associated with a poor life prognosis (1). Hydroxychloroquine (HCQ) has been reported to improve the prognosis of life and dyslipidemia in SLE (2), and the mechanism has been unclear.
Objectives: To determine the effect of HCQ treatment on serum cytokines associated with atherosclerosis in SLE.
Methods: SLE patients who received additional HCQ and maintained low disease activity between January 2016 and September 2020 were included in this study. Disease activity was assessed by SLEDAI, CLASI and LLDAS, and serum complement titers, anti-ds-DNA antibodies, serum insulin and serum cytokines (adiponectin, resistin and leptin) were analyzed before and after HCQ treatment.
Results: Fifty-four patients (3 males, 51 females, mean age 41.9±12.8 years) were included (Table 1). Thirty-two patients achieved LLDAS at baseline. Serum adiponectin and insulin levels were significantly increased after 3 months of HCQ treatment compared to baseline, and serum resistin levels were significantly lower (Figure 1). Patients with a history of renal disease had greater degree of changes in serum adiponectin and resistin levels. Among SLE patients who did not achieve LLDAS at baseline, those who still did not achieve LLDAS after 3 months had significantly lower serum leptin levels before HCQ treatment than those who achieved it after 3 months.
The change of serum resistin levels correlated with those of serum S100A8 levels (r=0.5, p=0.0001).
Conclusion: Additional HCQ treatment in SLE patients improves lipid abnormalities. HCQ may improve prognosis by controlling disease activity in SLE and reducing risk factors for atherosclerosis.
REFERENCES:
[1] Gregory Katz, et al. Systemic Lupus Erythematosus and Increased Prevalence of Atherosclerotic Cardiovascular Disease in Hospitalized Patients. Mayo Clin Proc. 2019; 94:1436-1443.
[2] Laura Durcan, et al. Longitudinal Evaluation of Lipoprotein Parameters in Systemic Lupus Erythematosus Reveals Adverse Changes with Disease Activity and Prednisone and More Favorable Profiles with Hydroxychloroquine Therapy. J Rheumatol. 2016; 43: 745–750.

Table 1. Characteristics of SLE patients enrolled in this study

Characteristics	n=54, no.(%)
Female, no(%)	51(94)
Age, years, mean±SD	41.9±12.8
Disease duration, years, mean±SD	15.1±11.1
Past involvement	
Renal involvement	23 (43)
NPSLE	5 (9)
Complication	
APS	10 (19)
Dyslipidemia	2 (4)
Diabetes	1 (2)
Concomitant immunosuppressive treatments	
Prednisone	
No.(%)	46 (85)
Median Dosage, mg/day (range)	5.0 (1-10)
Disease activity	
SLENA-SLEDAI score	3.9±2.0
Current skin involvement	30 (56)
anti-dsDNA positive, no(%)	21 (39)
low complement, no(%)	29 (54)

Anti-dsDNA positive means anti ds-DNA titer increases over 12 IU/mlLow complement means any of C3, C4 and CH50 decreases to less 68mg/dl, less 12mg/dl, 30U/ml.APS: Anti-phospholipid antibody syndrome, NPSLE: neuropsychiatric SLE,

Figure 1



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2362

AB0288

SAFETY OF BELIMUMAB IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: YEAR 2 FOLLOW-UP OF A LARGE PHASE 4, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

S. Sheikh[1,2], M. Scheinberg[3], J. C. C. Wei[4,5], D. Tegzová[6], W. Stohl[7], T. Mucenic[8], R. Punwaney[9], R. Kurrasch[10], J. Harris[11], S. Muzaffar[12], S. Fernandes[13], N. L. Fox[9], A. Liu[14], H. Quasny[15], D. Roth[16]. *[1]University of North Carolina, Thurston Arthritis Research Center, Chapel Hill, NC, United States of America*; *[2]University of North Carolina at Chapel Hill School of Medicine, Department of Medicine, Division of Rheumatology, Allergy and Immunology, Chapel Hill, NC, United States of America*; *[3]Hospital Abreu Sodré, Centro de Pesquisas Clinicas, Sao Paulo, Brazil*; *[4]Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan, Republic of China*; *[5]Graduate Institute of Integrated Medicine, China Medical University, Taichung, Taiwan, Republic of China*; *[6]Institute of Rheumatology, Department of Rheumatology, Prague, Czech Republic*; *[7]University of Southern California Keck School of Medicine, Division of Rheumatology, Los Angeles, CA, United States of America*; *[8]Moinhos de Vento, Moinhos de Vento, Porto Alegre, Brazil*; *[9]GlaxoSmithKline, Clinical Development, Collegeville, PA, United States of America*; *[10]GlaxoSmithKline, Immunoinflammation, Collegeville, PA, United States of America*; *[11]GlaxoSmithKline, Statistics, Uxbridge, United Kingdom*; *[12]GlaxoSmithKline, Clinical Science, Stevenage, United Kingdom*; *[13]GlaxoSmithKline, Medical Affairs, Stevenage, United Kingdom*; *[14]GlaxoSmithKline, Global Clinical Safety and Pharmacovigilance, Uxbridge, United Kingdom*; *[15]GlaxoSmithKline, Immunology & Specialty Medicine, Chapel Hill, NC, United States of America*; *[16]GlaxoSmithKline, Research and Development, Collegeville, PA, United States of America*

Background: Belimumab (BEL), a recombinant human monoclonal antibody that inhibits B-lymphocyte stimulator (BLyS), is approved for the treatment of systemic lupus erythematosus (SLE). Clinical studies have yielded varying incidence rates of mortality and adverse events of special interest, such as malignancies, thereby necessitating large-scale, long-term assessment following BEL exposure.

Objectives: To assess all-cause mortality and new primary malignancies during post-treatment Year 2 follow-up in adult patients with active, autoantibody-positive SLE who received intravenous (IV) BEL or placebo (PBO), plus standard therapy in the 52-week double-blind treatment period of the ongoing BASE trial.[1]

Methods: This was a post-treatment follow-up of the Phase 4, double-blind study (BASE[1]; GSK Study BEL115467; NCT01705977), which randomised 4019 adults with active SLE and receiving standard therapy to BEL (10 mg/kg IV) or PBO on Days 0, 14, 28, and monthly thereafter until Week 48. All patients (including those who discontinued BEL before the end-of-treatment phase) were contacted by phone annually (+/-30-day time window). Rates of mortality and new primary malignancy are summarised for Year 2 follow-up, presented by the treatment received during the 52-week double-blind treatment period (Year 1).

Results: Baseline patient characteristics and disease activity collected at the start of the study, evaluated in patients with Year 2 follow-up were similar to the overall Year 1 study population. Cumulatively by Year 2 follow-up, 10.7% and 9.5% of patients had been exposed to commercial BEL in the BEL and PBO groups, respectively. Cumulative follow-up adjusted mortality and malignancy rates (per 100 patient years) were lower in the BEL vs PBO Year 1 treatment group (Table 1).

Conclusion: Year 2 follow-up results of BASE, the largest clinical trial of SLE to date,[1] provide continued support for the BEL safety profile. No new BEL safety concerns were identified in patients with active, autoantibody-positive SLE receiving standard therapy.

Funding: GSK

REFERENCES:

[1] Sheikh SZ, et al. *Lancet Rheum*. 2020 (ePub ahead of print) doi.org/10.1016/S2665-9913(20)30355-6

Table 1. Year 2 post-treatment* follow-up mortality and new primary malignancy rates by study treatment during Year 1

	BEL	PBO	Total
Year 1 as-treated population	**N=2002**	**N=2001**	**N=4003**
Year 1 deaths, n (%)	13 (0.65)	22 (1.10)	35 (0.87)
Year 1 new primary malignancies, n (%)	9 (0.45)	10 (0.50)	19 (0.47)
Year 2 (as-treated in Year 1) population	**N=1681**	**N=1666**	**N=3347**
Year 2 deaths by MedDRA SOC, n (%)	9 (0.54)	21 (1.26)	30 (0.90)
Cardiac disorders	2 (0.12)	6 (0.36)	8 (0.24)
Infections and infestations	4 (0.24)	2 (0.12)	6 (0.18)
Uncoded	1 (0.06)	3 (0.18)	4 (0.12)
General disorders/administration site conditions	1 (0.06)	2 (0.12)	3 (0.09)
Gastrointestinal disorders	1 (0.06)	1 (0.06)	2 (0.06)
Neoplasms	0	2 (0.12)	2 (0.06)
Other	0	5 (0.30)†	5 (0.15)
Cumulative deaths by Year 2 follow-up, n (%)	22 (1.10)	43 (2.15)	65 (1.62)
Incidence rate per 100 patient years	0.60	1.18	0.89
Year 2 new primary malignancies by MedDRA SOC, n (%)	3 (0.18)	4 (0.24)	7 (0.21)
Neoplasms	2 (0.12)	4 (0.24)	6 (0.18)
Hepatobiliary disorders	1 (0.06)	0	1 (0.03)
Cumulative malignancies by Year 2 follow-up, n (%)	12 (0.60)	14 (0.70)	26 (0.65)
Patient incidence rate per 100 patient years	0.34	0.40	0.37

*Patients in the post-treatment follow-up period are no longer receiving study treatment; †1 event/patient: blood/lymphatic system, musculoskeletal/connective tissue, nervous system, psychiatric, and renal/urinary disorders.MedDRA, Medical Dictionary for Regulatory Activities; SOC, system organ class.

Acknowledgements: Medical writing assistance was provided by Katalin Bartus, PhD, Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.

Disclosure of Interests: Saira Sheikh Grant/research support from: Pfizer, Morton Scheinberg Consultant of: GSK, Pfizer, Alnylam, AbbVie, PTC Therapeutics, James Cheng-Chung Wei Consultant of: TSH Biopharm, AbbVie, BMS, Celgene, Chugai, Eisai, Janssen, Novartis, Pfizer, Sanofi-Aventis and UCB pharma, Grant/research support from: AbbVie, Amgen, Astellas, BMS, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer Sun and UCB, Dana Tegzová: None declared, William Stohl Consultant of: GSK, Grant/research support from: GSK, Pfizer, Gilead, Tamara Mucenic Speakers bureau: Novartis, Janssen, BMS, AbbVie, Pfizer, Roche, Grant/research support from: GSK, Janssen, Roche, Eli Lilly,

Gilead, UCB, Raj Punwaney Shareholder of: GSK, Employee of: GSK, Regina Kurrasch Shareholder of: GSK, Employee of: GSK, Julia Harris Shareholder of: GSK, Employee of: GSK, Saima Muzaffar Shareholder of: GSK, Employee of: GSK, Sofia Fernandes Shareholder of: GSK, Employee of: GSK, Norma Lynn Fox Shareholder of: GSK, Employee of: GSK, Andrew Liu Shareholder of: GSK, Employee of: GSK, Holly Quasny Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK

DOI: 10.1136/annrheumdis-2021-eular.2552

AB0289 PATIENT REPORTED PHYSICAL HEALTH COMPARED TO CLINICIAN RECORDED BILAG-2004 MUSCULOSKELETAL SYSTEM SCORES – DISCORDANCE BETWEEN PATIENTS AND CLINICIANS

E. Olech[1,2], D. Stull[3], B. Williams[3], S. Bean[3], G. Abreu[4], E. Schwetje[5], R. Tummala[5], S. O'quinn[6]. [1]*IQVIA, Rheumatology Center of Excellence Therapeutic Strategy & Science Unit, San Diego, United States of America*; [2]*IQVIA, Rheumatology Center of Excellence, Las Vegas, United States of America*; [3]*IQVIA, Patient Centered Endpoints, New York, United States of America*; [4]*AstraZeneca, BioPharmaceuticals R&D, Gothenburg, Sweden*; [5]*AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, United States of America*; [6]*AstraZeneca, BioPharmaceuticals Medical: Evidence, Gaithersburg, United States of America*

Background: The musculoskeletal organ system BILAG-2004 (MSK BILAG) assessment is of critical importance in SLE clinical trials. Severe active polyarthritis, MSK BILAG A, by definition includes significant impairment of basic activities of daily living (ADLs), as opposed to MSK BILAG C, D, or E where ability to perform ADLs is expected to be preserved. In clinical trials, BILAG is scored by clinicians without formal review of patient reported outcomes (PROs). The Physical Health domain of the LupusQoL (LQol PH) (range 0 – 100) can be used to assess the patient's physical function and ADLs. LQoL PH score thresholds defining impairment severity have not been established; however, a transformed LQoL PH score ≤50 suggests more impaired function, which would not be expected in MSK BILAG C, D, or E. Conversely, a score >50 implies no major issues with ADLs, which would be contradictory to the definition of MSK BILAG A.

Objectives: To assess correlation of patient reported LQoL PH with MSK BILAG scores recorded by clinicians at various timepoints using data from the phase 3 TULIP studies [1,2] and to investigate the percent of discordance between patients and clinicians.

Methods: Data from TULIP 1 and 2 studies (anifrolumab 300 mg and placebo arms) were pooled to evaluate the relationship between LQoL PH and MSK BILAG scores at baseline, weeks 24 and 52 using Spearman correlations as post-hoc analysis. Mean LQoL PH scores were assessed for each MSK BILAG category at the three timepoints using one-way ANOVA. Percent of patients with MSK BILAG A and LQoL PH scores >50 and patients with MSK BILAG C, D, or E and LQoL PH scores ≤50 was calculated at baseline, week 24 and 52. MSK BILAG B was excluded from the analysis because discordance could not be easily defined for this category compared with the more extreme MSK BILAG categories.

Results: Total of 690 patients were included in the pooled analysis (Table 1). Significant correlations between LQoL PH and MSK BILAG scores were found at each time point (nominal p<0.0001); this relationship became stronger over time. Mean LQoL PH scores were different in each MSK BILAG category, with the highest in MSK BILAG D/E and the lowest in the MSK BILAG A category, thus confirming the discriminatory ability of the LQoL PH (Table 1).

Table 1. Correlation coefficients (CC) between LQoL PH and MSK BILAG scores, and mean LQoL PH scores with standard deviations (SD) per each MSK BILAG category at baseline, weeks 24 and 52.

	Baseline		Week 24		Week 52	
	CC	N	CC	N	CC	N
Total Population	-0.25	690	-0.36	626	-0.41	552
MSK BILAG	Mean LQoL PH Score (SD)		Mean LQoL PH Score (SD)		Mean LQoL PH Score (SD)	
0 (D/E)	69.3 (24.7)	17	74.2 (22.1)	186	74.5 (21.3)	237
1 (C)	62.3 (25.4)	60	64.0 (23.9)	233	60.6 (22.5)	184
8 (B)	56.6 (24.4)	398	55.1 (24.2)	163	51.3 (24.3)	105
12 (A)	44.9 (25.8)	215	43.9 (25.9)	44	44.2 (26.2)	26

At baseline, 40% of patients who were assessed by clinicians as having MSK BILAG A reported minimal impairment in physical function and ADLs (LQoL PH >50) and 24.1% who had MSK BILAG C, D, or E reported difficulties with ADLs (LQoL HP ≤50), suggesting discordance between patients and clinicians. This discordance slightly decreased over time (Figure 1).

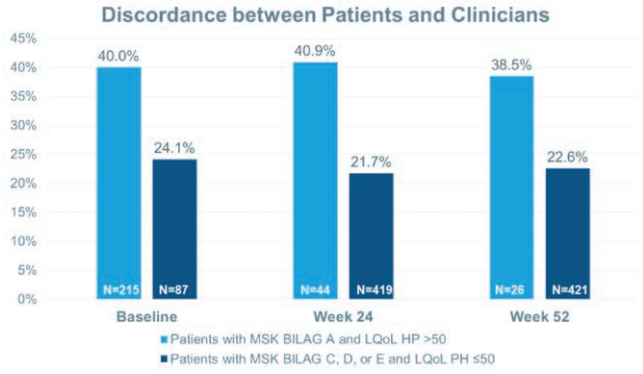


Figure 1. Percent of patients with MSK BILAG A and LQoL PH scores >50 and patients with MSK BILAG C, D, or E and LQoL PH scores ≤50 at baseline, weeks 24 and 52.

Conclusion: Patient reported LQoL PH scores correlated with MSK BILAG scores and showed discriminant validity for MSK BILAG scores. Greater discordance was seen between LQoL PH and MSK BILAG A compared with C, D, or E. These findings suggest a need for further investigation of a role for PROs in MSK BILAG scoring. Formal review of PROs by clinicians during MSK BILAG assessment could be considered in future SLE clinical trials.

REFERENCES:

[1] Furie R et al. Lancet 2019

[2] Morand EF et al. N Engl J Med 2020

Acknowledgements: This study was sponsored by AstraZeneca.

Disclosure of Interests: Ewa Olech Speakers bureau: Abbvie, Amgen, Merck, Pfizer, and UCB, Grant/research support from: BMS, Donald Stull: None declared, Betsy Williams: None declared, Stephanie Bean: None declared, Gabriel Abreu Employee of: AstraZeneca, Erik Schwetje Employee of: AstraZeneca, Raj Tummala Employee of: AstraZeneca, Sean O'Quinn Shareholder of: AstraZeneca, Employee of: AstraZeneca

DOI: 10.1136/annrheumdis-2021-eular.2560

AB0290 TREATMENT OF INTERSTITIAL LUNG INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS: EXPERIENCE IN A THIRD LEVEL HOSPITAL

I. González Fernández[1], C. Moriano[1], E. Diez Álvarez[1], C. Sieiro Santos[1], C. Álvarez Castro[1], M. Martín Martín[1], M. E. Vallejo Pascual[2], M. T. Perez Sandoval[1]. [1]*Complejo Asistencial Universitario de León, Reumatología, León, Spain*; [2]*Universidad de León, Facultad de CC. EE y Empresariales, León, Spain*

Background: There are few studies[1] on the treatment of diffuse interstitial lung disease (ILD) associated with systemic lupus erythematosus (SLE). Corticosteroids are usually used in cases of mild to moderate decrease in diffusion and the association with immunosuppressants (Cyclophosphamide, Rituximab…) is reserved for cases of more severe affectation.

Objectives: Assess the main treatments used in ILD associated with SLE in a third level hospital and analyze the therapeutic response through improvement in imaging tests and in respiratory function studies.

Methods: Descriptive observational study of patients diagnosed with SLE (SLICC criteria) who developed ILD in our hospital between 1973 and 2020. As variables of response to treatment, HRCT pattern at diagnosis and at two years, respiratory function tests at diagnosis and at one year were analyzed. Likewise, the different treatments used before and after diagnosis were studied such as hydroxychloroquine (HCQ), prednisone, methotrexate (MTX), Rituximab (RTX), belimumab (BLM), Cyclophosphamide (CFM), azathioprine (AZA) and mycophenolate mofetil (MMF).

Results: A total of 455 patients diagnosed with SLE were included, of which 20 had ILD (4.4%). 65% of the analyzed sample were women with a mean age at diagnosis of 63 ± 16.23 years. 30% presented ILD as the first clinical data for the diagnosis of SLE. Only 3 patients died (due to causes other than ILD and SLE). At diagnosis, 90% had symptoms such as dyspnea (75%) and cough (60%).

85% had alterations in the X-ray and 100% in the HRCT, where the predominant pattern was NINE (65%). Spirometry showed an obstructive (25%), restrictive (20%) and normal (55%) pattern; 90% had decreased diffusion, the majority being mild (67%). With the treatment administered, HRCT stability was observed

at two years in 30% of cases and progression in 25%; while, at the functional level, 40% remained stable with worsening in 4 patients per year (20%).
50% of the patients with SLE received treatment with HCQ and MTX before the diagnosis of ILD; and 35% corticosteroids (4 + 7.3 mg / day). With ILD diagnosed, HCQ was administered to 95% of patients and the standard of treatment was based on corticosteroids in monotherapy at a mean dose of 13 ± 10.5 mg / day due to stability both at radiological level and in function tests respiratory. 25% and 15% required treatments such as RTX and BLM as they did not have an adequate response with the previous one.
In our study, we did not find any statistical significance between the variables analyzed, due to the small sample size.
Conclusion: 1)ILD in SLE is a rare manifestation, present in 4.4% of our series. Standard treatment with hydroxychloroquine and corticosteroids appears to be a useful therapeutic option, stabilizing radiological progression in one third of cases early. More studies with a larger sample size are needed to analyze the role of immunosuppressive treatment in this type of lung involvement.
REFERENCES:
[1] Aguilera-Pickens G, Abud-Mendoza C. Pulmonary Manifestations in Systemic Lupus Erythematosus: Pleural Involvement, Acute Pneumonitis, Chronic Interstitial Lung Disease and Diffuse Alveolar Hemorrhage. Clinical rheumatology. Vol.14 Issue. 5. Pages 294-300 (September-October 2018).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2700

AB0291 PROGNOSTIC VALUE OF LATE GADOLINIUM ENHANCEMENT ON CARDIAC MAGNETIC RESONANCE IMAGING IN SYSTEMIC LUPUS ERYTHEMATOSUS

A. J. Velvet[1], S. Vohra[1], T. David[2], B. Keavney[3], I. Bruce[2], B. Parker[2], K. Bratis[1]. *[1]Manchester University NHS Foundation Trust, Cardiology, Manchester, United Kingdom*; *[2]Manchester University NHS Foundation Trust,The Kellgren Centre for Rheumatology, Manchester, United Kingdom*; *[3]The University of Manchester, NIHR Manchester Musculoskeletal Biomedical Research Centre, Manchester, United Kingdom*

Background: Cardiac Magnetic Resonance Imaging (CMRI) with Late Gadolinium Enhancement (LGE) has an established value in the diagnostic and prognostic assessment of ischaemic and non-ischaemic cardiomyopathies. Although CMRI is widely used for the detection of myocardial involvement in subclinical Systemic Lupus Erythematosus (SLE), its prognostic value has not been determined.
Objectives: To determine the prognostic value of CMRI with LGE for major adverse cardiovascular events (MACE) in patients with SLE, and investigate its correlation with the severity of systemic inflammation.
Methods: A retrospective tertiary single-centre review of patients with SLE who underwent a CMRI study at Manchester Foundation Trust between 2009-2020 was conducted. Patients were categorized into two groups; those who experienced a MACE (cardiac death, myocardial infarction (MI), stroke/TIA or heart failure) and those who did not. We compared cardiovascular (CV) risk factors, CMRI findings, SLE risk scores and biochemistry between the 2 groups.
Results: We identified 20 female patients who underwent a CMRI, with a mean age of 46 years at the time of the scan. Indications for CMRI were assessment for worsening dyspnoea and new onset left ventricular systolic dysfunction. Table 1 demonstrates the clinical, laboratory and CMRI characteristics of the two groups. There were no significant differences in the clinical background and traditional CV risk factors between the 2 groups. 5/20 (25%) patients experienced a MACE. The SLEDAI-2K score was >12 in 2/5 (40%) of patients who suffered a MACE and they presented with a stroke within a year of CMRI study, suggesting that systemic inflammation contributes to poor vascular outcomes. 3/5 (60%) patients who reported a MACE demonstrated LGE on their CMRI study compared to 3/15 (20%) of those who did not (p-0.045). The LGE was predominantly diffuse, mid myocardial in distribution and not ischaemic in pattern, signifying a complex pathophysiological substrate in the development of myocardial pathology in SLE. Additionally, an increase in left ventricular end-diastolic, end-systolic volumes and left atrial diameter was noted in patients who had a MACE (p<0.05). Patients who had a MACE showed a higher incidence of valvular abnormalities and pericardial disease in their CMRI studies. On looking at the medications around the CMRI, the majority of MACE positive patients 4/5 (80%) were on conventional Disease Modifying Anti-Rheumatic Drugs (DMARDs) such as Mycophenolate, Tacrolimus, Cyclophosphamide, Methotrexate or hydroxychloroquine and none on biologics like Rituximab or Belimumab. While 9/15 of the MACE negative patients were on DMARDs and 4/15 were on biologics.

Table 1. clinical, laboratory and CMRI characteristics of SLE patients with and without MACE. LVEDV-left ventricular end-diastolic volume, LVESV-left ventricular end-systolic volume, LA-left atrial, LVEF-Left ventricular ejection fraction, SLEDAI- SLE Disease Activity Index, +ve-positive.

	MACE+ (n = 5)	MACE- (n = 15)
Mean age of SLE diagnosis (years)	35.6	34.4
Mean duration to CMRI (years)	8.8	11.71
Lupus nephritis	20%	20%
Raynaud's	40%	27%
Previous CV involvement	0	2
SLEDAI-2K > 12	2(40%)	11(73%)
Lupus anticoagulant +ve	20%	27%
Anticardiolipin +ve	2(40%)	2(14%)
anti-dsDNA (iu/ml)+ve	3(60%)	6(40%)
Low C3 (g/L)	2(40%)	6(40%)
Mean prednisolone dose	28.33	8.21
Conventional DMARDs	4/5(80%)	9/15(60%)
Biologics	0/5	4/15
Mean LVEF (%)	47.4	56.7
CMR LGE	3(60%)	3(20%)
Valvular abnormalities	2(40%)	4(27%)
Mean LA area (cm^2)	29.6	20.6
Pericardial effusion	40%	27%

Conclusion: In our small SLE cohort, we add to existing knowledge that CMRI with LGE is an indispensable tool to investigate cardiac involvement in SLE and may indeed add important prognostic information. Larger scaled studies are required to confirm the use of CMRI with LGE as a predictor of MACE in patients with SLE.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2748

AB0292 A RETROSPECTIVE STUDY OF PERIOPERATIVE MANAGEMENT OF PATIENTS WITH SLE IN TOTAL HIP ARTHROPLASTY

I. Kushnareva[1], M. Makarov[1], T. Popkova[2], A. Khramov[1], S. Maglevaniy[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Orthopaedic Department, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Systemic Rheumatic Diseases, Moscow, Russian Federation*

Background: Aseptic necrosis (AN) of bones is one of the most serious complications of systemic lupus erythematosus (SLE), which is characterized by multicomponent joint damage mainly in young people. Long-term observations show that two thirds of patients have multiple aseptic necrosis of bones, with the femoral head being most often affected. Obviously, caused by much strain on the hip joint. In this regard, total hip arthroplasty (THA) is an integral part of the treatment of SLE patients. Despite the fact that THA in these patients allows to achieve good functional outcomes, the amount of complications remains high.
Objectives: To retrospectively analyze the outcomes and structure of complications to determine the tactics of perioperative management of patients with SLE.
Methods: The retrospective group included patients over 18 years of age with a reliable diagnosis of SLE, established according to the classification criteria (SLICC, 2012, ACR, 1997). 123 THA were performed in 77 patients. Outcomes and the structure of complications were analyzed for the period from 1998 to 2016 inclusive.
Results: The period of hospital stay of patients was analyzed. Cementless fixation of the components of the endoprosthesis was used and the friction pair was metal-polyethyleneIn all cases. In 23 patients, additional fixation of the acetabular component with screws was performed, which indirectly indicates a poor quality of bone tissue. A more detailed analysis of these patients revealed a long period of glucocorticoid therapy (from 1.5 to 35 years). In 3 patients, during preparation for implantation of the femoral component, a femoral fracture occurred, which required using the cerclages. One patient also had a fracture of the acetabulum, which required the implantation of a Müller anti-protrusio ring. The above-described technical features led to increasing of the total time of surgery, which significantly increased the volume of blood loss. Thus, this required transfusions of blood components: fresh frozen plasma (FFP), erythrocyte suspension, as well as replenishment the circulating blood volume with colloidal solutions.
Prevention of thromboembolism. All patients in the postoperative period underwent common measures of prevention of venous thromboembolism.

The drugs of choice were calcium nadroparin (Fraxiparin) 0.3 or 0.6 ml subcutaneously - depending on body weight, respectively, or Dabigatran etexilate (Pradaxa) 220 mg per day, or rivaroxaban (Xarelto) 10 mg per day.
Prevention of infectious complications. The first injection of antibiotic is carried out immediately before surgery achieve it's maximum concentration in blood plasma just in the time of first incision. In the postoperative period, antibiotic therapy was carried out for at least 5 days. In 1 patient, the course of antibiotic therapy was prolonged and another broad-spectrum antibiotic was added due to a history of tuberculosis infection. Postoperative rehabilitation in patients with SLE met standard protocols: activation in bed and verticalization was carried out on day 1, standing with crutches and walking on day 2.
Conclusion: During the period of hospital stay in the early postoperative period, not a single one thromboembolic event developed, as well as no cases of infectious complication occurred. There was one case of dislocation of the femoral component of the endoprosthesis, which was immediately repaired in the early postoperative period.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3031

AB0293 IDENTIFYING PREDICTORS OF SHORT-TERM RESPONSE TO RITUXIMAB IN PRIMARY SJOGREN'S SYNDROME

S. Pepple[1], J. Arnold[1], E. Vital[2,3], A. Rawstron[4], C. Pease[1], S. Dass[1], P. Emery[1,3], M. Y. MD Yusof[1,3]. *[1]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[1]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[3]Leeds Teaching Hospitals NHS Trust, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*; *[4]Leeds Teaching Hospitals NHS Trust, Haematological Malignancy Diagnostic Service, Leeds, United Kingdom*

Background: Randomised controlled trials of rituximab (RTX) in primary Sjogren's syndrome (pSS) have aimed to alleviate glandular symptoms and fatigue with only limited data on efficacy/effectiveness of the initial and repeat cycles of RTX on extra-glandular pSS.
Objectives: To assess the effectiveness of RTX on extra-glandular symptoms and identify predictors of short-term response with a view to personalised B-cell depleting therapy in patients with pSS.
Methods: An observational study was conducted in 40 consecutive RTX-treated pSS patients in a single centre for over 15 years. All patients fulfilled the 2002 AEG criteria and were CCP negative. Clinical response at 6 months was defined as ≥3 reduction of ESSDAI from baseline. B-cell subsets were measured using highly sensitive flow cytometry. Predictors of short-term response were analysed using penalised logistic regression.
Results: 38/40 (95%) patients were female, mean (SD) Age 54 (13.7) years, median (IQR) disease duration 5 (2-9) years, 39/40 (98%) had positive ANA, 26/40 (65%) were on concomitant immunosuppressant (IS). Mean (SD) ESSDAI at RTX initiation was 11.5 (6.7); main domains for RTX were articular (73%), skin (23%), PNS (15%) and muscular (15%). 169 RTX cycles were administered with a total follow-up of 165PY. In Cycle 1 (C1) RTX, the proportion of patient achieving ESSDAI response from baseline was 29/40 (73%; 95% CI 58-87). There were significant reductions in ESSDAI, daily prednisolone dose and IgG levels at 6 months (all p<0.05). Of C1 responders, 23/29 received retreatment on clinical relapse; of which 8/23 (35%) lost response [secondary non-depletion non response (2NDNR) associated with anti-RTX antibodies=4 (17%) as we previously observed in SLE[1], side effects=2, ineffective=2]. Of C1 non-responders, 9/11 were retreated but only 2/9 responded in C2. Overall, 13/40 (33%) discontinued RTX within two cycles. In multivariable analysis, concomitant IS and achieving compete B-cell depletion in C1 reduced non-response to RTX (Table 1).
Conclusion: All pSS patients should be prescribed concomitant immunosuppressant with RTX and therapy should aim to achieve complete depletion. About 1 in 6 pSS patients lose response in repeat cycles which is associated with 2NDNR phenomenon. The use of humanised or type 2 anti-CD20mAbs should overcome these issues and improve the clinical response of extra-glandular pSS.
REFERENCES:
[1] Md Yusof et al. ARD 2017 (2520 characters – allowed around 2600 as Table 1 is included too)

Table 1. MVA logistic regression of risk factors for RTX non-response

Predictors	Continued Response (N=27)	Non-response within 2 RTX Cycles (N=13)	Univariable OR (95% CI); p-value	Multivariable OR (95% CI); p-value
Age, mean (SD) per 10 years	55 (14)	52 (12)	0.87 (0.53-1.41); 0.572	Excluded from final model
Disease duration, median (IQR)	5 (2-9)	6 (3-9)	0.97 (0.87-1.08); 0.565	Excluded from final model
Concomitant IS, %	81.5%	30.8%	0.10 (0.02-0.46); 0.003	0.07 (0.01-0.52); **0.010**
IgG, mean (SD), g/L	15.5 (6.3)	18.4 (5.8)	1.08 (0.97-1.20); 0.175	1.13 (0.97-1.32); 0.116
Clinical ESSDAI, median (IQR)	10 (6-16)	8 (6-10)	0.96 (0.85-1.08); 0.487	0.91 (0.79-1.05); 0.185
Baseline Plasmablast (x1000), 10^9 cells/L, median (IQR)	2.6 (1 -5.2)	2.3 (1.6-9.5)	1.00 (0.94-1.07); 0.885	Excluded from final model
Complete B-cell depletion post-RTX, %	55.6%	8.5%	0.07 (0.01-0.64); 0.018	0.04 (0.02-0.82); **0.036**

Disclosure of Interests: Sophanit Pepple: None declared, Jack Arnold: None declared, Edward Vital Grant/research support from: Dr Vital has received honoraria and research grant support from Roche, Andrew Rawstron: None declared, Colin Pease: None declared, Shouvik Dass Grant/research support from: Dr Dass has received honoraria from Roche, Paul Emery Consultant of: Professor Emery has received consultant fees from Roche., Grant/research support from: Professor Emery has received research grants paid to his employer from Roche., Md Yuzaiful Md Yusof: None declared
DOI: 10.1136/annrheumdis-2021-eular.3266

AB0294 PREDICTORS OF CHLOROQUINE AND DERIVATES TREATMENT INVOLVING OCULAR TOXICITY: RESULTS FROM A COHORT

R. Dos-Santos[1], D. Fernández Fernández[1], I. González Fernández[1], M. Sanchez-Wonenburger[1], P. Castro-Santamaria[1], A. Souto Vilas[1], E. Perez-Pampín[1], A. Mera Varela[1]. *[1]Clinical University Hospital in Santiago de Compostela, Rheumatology Department, Santiago de Compostela, Spain*

Background: Chloroquine (CQ) and hydroxychloroquine (HCQ) have been employed in a huge range of indications, from autoimmune diseases (such as rheumatoid arthritis [RA], cutaneous lupus or systemic erythematosus lupus [SLE]) to infectious ones (as malaria or helminthiasis).[1] A newer purpose came upon the new coronavirus disease 2019 (COVID-19), where they seem to be effective modulating immune response. Controversial results have been published from clinical and observational data concerning its effectiveness.[2] Ocular toxicity have been described as a serious adverse event of these antimalarial drugs and screening protocols have been displayed for its prevention.[3]
Objectives: To evaluate CQ/HCQ ocular toxicity and to identify potential predictors of appearance. Also to asses screening protocols compliance.
Methods: Demographic, diagnostic and treatment data were collected from patients under CQ or HCQ treatment in the Clinical University Hospital in Santiago de Compostela (Spain) during the first wave of the COVID-19 pandemic (January to April 2020).
Univariable logistic regression was performed to identify potential predictors of maculopathy. Variables with p<0.20 were selected for multivariable testing.
Stata 15.1 was used to perform statistical analysis.
Results: 503 patients taking CQ/HCQ were identified. 495 were women. Most frequent diagnosis were SLE (48.28%), cutaneous lupus (22.85%) and rheumatoid arthritis (RA, 12.54%). Mean age at diagnosis was 44.99 years (SD 17,88). 93.33% of patients were under treatment with HCQ. Mean age at beginning of CQ/HCQ treatment was 48.10 years (SD 17.79) and mean time between diagnosis and CQ/HCQ onset was 2.03 years (SD 5.50). Mean maximum HCQ dosage per patient was 3.83 mg/kg (SD 1,59; 252.57 mg per day, SD 89.98) and CQ was 3.24 mg/kg (SD 1,91; 219.49 mg per day, SD 103.90). Mean time under CQ/HCQ treatment was 6.39 years (SD 5.63). 20 patients developed maculopathy. Mean time between CQ/HCQ onset and maculopathy appearance was 2.67 years (SD 3.10). Only 25 patients did not complete ophthalmologic exams for maculopathy screening.
After univariable analysis, higher age at diagnosis and age at beginning of CQ/HCQ treatment were identified as potential predictors of maculopathy (p<0.20). After multivariable analysis, both higher age at diagnosis and higher age at CQ/HCQ onset were identified as predictors for suffering maculopathy under treatment with CQ/HCQ (OR 1.06 [CI95% 1.03-1.10] p=0.000 and OR 1.09 [CI95% 1.02-1.16] p=0.008, respectively).

Conclusion: Ocular toxicity remains as one of the most harmful and disabling adverse events in patients under CQ/HCQ treatment. Higher age at diagnosis and higher age at beginning of treatment appear to be risk factors for maculopathy appearance. Screening protocols are well-assumed by patients and seemed to be helpful for preventing and early identifying events. CQ/HCQ usage in COVID-19 patients should be individualized, specially in older patients, and protocols involving ocular toxicity should be implemented in the follow-up of this population.

REFERENCES:

[1] T Dörner. Hydroxychloroquine in SLE: old drug, new perspectives. *Nat Rev Rheumatol* 6, 10-11 (2010).
[2] S Chowdhury, J Rathod, J Gernsheimer. A rapid systematic review of clinical trials utilizing chloroquine and hydroxychloroquine as a treatment for COVID-19. Acad Emerg Med. 2020;27(6):493-504.
[3] J C S Yam, A K H Kwok. Ocular toxicity of hydroxychloroquine. Hong Kong Med J. 2006;12(4):294-304.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3278

AB0295 TREATMENT OF HIGH RISK/REFRACTORY OBSTETRIC ANTIPHOSPHOLIPID SYNDROME. A SINGLE CENTRE EXPERIENCE

A. Hoxha[1], P. Marson[2], M. Favaro[3], M. Tonello[3], M. Zen[3], T. Del Ross[3], A. Calligaro[3], A. Ruffatti[4]. [1]*San Bortolo Hospital, Department of Medicine, Vicenza, Italy*; [2]*University-Hospital of Padua, Padua, Italy, Apheresis Unit, Blood Transfusion Service, Padua, Italy*; [3]*University Hospital of Padua, Padua, Italy, Department of Medicine, Rheumatology Unit, Padua, Italy*; [4]*University Hospital of Padua, Padua, Italy, Department of Medicine, Padua, Italy*

Background: The most efficacious strategy to manage pregnant patients with antiphospholipid syndrome (APS) who are at high risk of adverse pregnancy outcomes ± refractory to conventional heparin/low-dose aspirin treatment is currently unknown (1, 2).

Objectives: The purposes of this study were to investigate the efficacy and safety of a second-line treatment protocol administered in addition to twice daily low molecular weight heparin and low-dose aspirin to pregnant patients affected with high-risk ± refractory primary APS.

Methods: Patients were included in the study if satisfying the following criteria were: 1) the presence of triple antiphospholipid antibody positivity (IgG/IgM anticardiolipin + IgG/IgM anti-β2 Glycoprotein I antibodies + lupus anticoagulant), 2) previous thrombosis and/or a history of one or more early and severe pregnancy complications. The second-line treatment protocol included weekly plasmapheresis or immunoadsorption and fortnightly 1g/kg intravenous immunoglobulins.

Results: Twenty-four pregnancies occurring between 2002 and 2019 in 19 primary APS patients, (mean age 35.1 ± 3.5 SD) were monitored. Triple antiphospholipid positivity was detected in all 19 cases (100%). Seven of these women (36.8%) had a history of thrombosis, five (26.3%) one or more previous failed pregnancies associated to severe pregnancy complications and seven (36.8%) both clinical criteria. Twenty-three pregnancies (95.8%) produced live neonates (13 females and 10 males), all born between the 26th and 38th week of gestation (mean 33.6 ± 3.5 SD); birth weight percentile was 35.8 ± 24.1 SD and mean Apgar score at 5min 8.7 ± 1.1 SD. Due to premature birth (24th week) complicated by fetal sepsis, one pregnancy (4.2%) had a negative outcome. During the treated pregnancy there were no episodes of thrombosis; there were five cases (20.8%) of severe maternal complications during pregnancy or puerperium and four of fetal complications (16.6%), all followed by complete recovery after delivery. No side-effects of the treatment were registered.

Conclusion: Given the high live birth rate and the safety associated to it, the second-line treatment protocol described here could be taken into consideration when the treatment of a high-risk APS pregnancy ± refractory to conventional therapy is being evaluated.

REFERENCES:

[1] Tektonidou MG, et al. Ann Rheum Dis 2019;**0**:1–9. doi:10.1136/annrheumdis-2019-215213
[2] Giacomelli et al. Autoimmun Rev. 2020;102738. doi.org/10.1016/j.autrev.2020.102738

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3449

AB0296 PASSIVE TRANSFER OF ANTI-SSA, ANTI-Ro52, AND ANTI-MITOCHONDRIAL M2 FROM INTRAVENOUS IMMUNOGLOBULIN PRODUCTS TO PATIENTS WITH RHEUMATIC DISEASES

L. J. Yang[1], H. G. Li[1], A. Q. Zeng[1], Z. M. Ouyang[1], X. N. Wei[1], Q. H. Li[1], D. H. Zheng[1], L. Dai[1], Y. Mo[1]. [1]*Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Department of Rheumatology, Guangzhou, China*

Background: Passive transfer of ANA and anti-SSA has been reported in patients with common variable immunodeficiency disorder who received intravenous immunoglobulin (IVIG). IVIG is also recommended to treat some special or life-threatening rheumatic diseases.

Objectives: This study was aimed to explore whether any extractable nuclear antibodies (ENAs) were transferred to these rheumatic patients who received IVIG therapy.

Methods: IVIG products of three batches were tested for ANA by using indirect immunofluorescent assay, and for ENAs by using line immunoassay (LIA) and chemiluminescence immunoassay (CLIA). These IVIG products were administrated to rheumatic patients at a dose of 20g/d×3 days (day1 to day3). Serum samples of these patients before IVIG (day0) and after IVIG (day4, day8, day10, day12, and more than one month) were tested by using LIA and CLIA. Anti-SSA was also detected using ELISA.

Results: In these IVIG products, ANA was positive at a titer of 1:640 (cytoplasmic speckled) and 1:80 (speckled). Among 14 types of ENAs that could be tested using LIA, anti-SSA, anti-Ro52, anti-mitochondrial M2, and anti-centromere B antibodies were clearly detectable in IVIG products (Table 1). Likewise, another assay CLIA also detected the same positive autoantibodies in these products. LIA showed the highest concentration in anti-mitochondrial M2, while CLIA showed the highest concentration in anti-mitochondrial M2 and anti-Ro52. One 31-year-old male patient who was diagnosed as SLE (Figure 1) and one 72-year-old male patients who was diagnosed as necrotizing myositis received these IVIG products. Anti-SSA, anti-Ro52, anti-mitochondrial M2, but not anti-centromere B, were positive in the day4 serum samples, although all of these antibodies were negative at baseline (day0). The concentration of these antibodies decreased gradually as days passed and became undetectable around one month after IVIG.

Table 1. The concentration of autoantibodies in intravenous immunoglobulin products

	anti-SSA	anti-Ro-52	anti-mitochondrial M2	anti-centromere B	Cut-off
LIA(grey value)	20±3	28±3	69±10	19±4	≥11
CLIA (U/ml)	333±107	444±86	434±66	390±89	>20
ELISA (U/ml)	90±13	NA	NA	NA	>20

LIA, line immunoassay; CLIA, chemiluminescence immunoassay; ELISA, enzyme linked immunosorbent assay

Conclusion: This study preliminarily reported transient positivity of anti-SSA, anti-Ro52, and anti-mitochondrial M2 in rheumatic patients maybe because the passive transfer of these antibodies from IVIG products to the patients, although the potential influence of this transfer on the rheumatic diseases remained unknown.

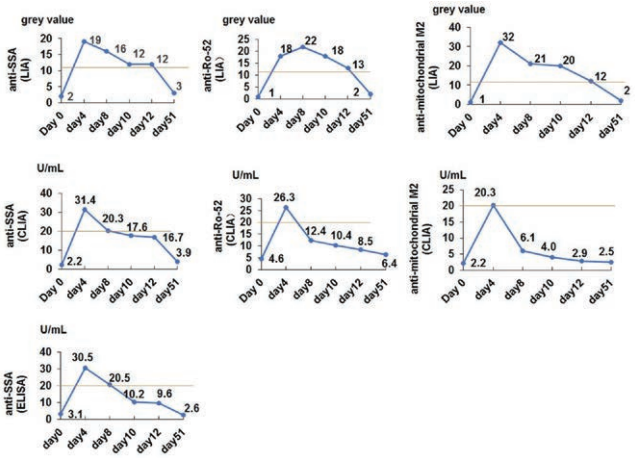


Figure 1. The concentration of autoantibodies in a 31-year-old male SLE patient receiving intravenous immunoglobulin at a dose of 20g/d×3 days (day1 to day3). Serum samples of these patients before IVIG (day0) and after IVIG (day4, day8, day10, day12, and day51) were tested by using line immunoassay (LIA) and chemiluminescence immunoassay (CLIA). Anti-SSA was also detected using ELISA. The horizontal red lines were the corresponding cut-off values of each assay.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3544

SLE, Sjögren's and APS - clinical aspects (other than treatment)

AB0297

MORTALITY AND DISEASE RELATED COMORBIDITIES IN SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM AN EGYPTIAN COHORT WITH SYSTEMIC LUPUS ERYTHEMATOSUS-PHASE I

R. Hamdy Abdellatif Mohammed[1], H. Lotfy Fayed[2], N. Emara[2]. [1]*School of Medicine- Cairo University, Rheumatology and Rehabilitation, Gizah, Egypt*; [2]*School of Medicine- Cairo University, Rheumatology and Rehabilitation, Cairo, Egypt*

Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disorder with considerably high mortality.
Objectives: To investigate the survival rates 5, 10, 15 and 20 years and the impact of disease related morbidity and mortality among Egyptians patients afflicted by SLE.
Methods: This is a single center observational study performed in one of the leading medical school governmental hospital for teaching and training in the north African region and middle east sectors Kasr Alainy School of Medicine-Cairo University. Medical records of adult SLE patients ≥ 16 years (classified according to ACR 1997 SLE classification criteria set forth by Hochberg, 1997) who received longitudinal clinical care during the time period from 1999 to 2019 were included. Data analysis: causes of mortality, damage score and survival were determined from the time of SLE diagnosis to the last contact or date of death.
Results: Records of two hundred and two SLE patients were included, 91.1% were females and 8.9% patients were males (ratio is 10:1). The mean age at diagnosis 26.71 ± 7.93 years with a mean follow up between mean: 6.6 ± 4.58 years, 34.15% had damage in at least one of the organ systems by SLICC/ACR-DI in the first 6 months. Considering an outcome label of dead or alive at the end of follow up period, results showed a total of 52 mortalities, 88.5% were females, the mean age at death onset was 30.9±8.8 years. Results identified the following death causalities in the studied SLE patients in order of frequency: Septic shock and disseminated intravascular coagulation in 11.5 %, acute respiratory distress syndrome ARDS in 11.5 %, congestive heart failure in 9.6%, thrombotic microangiopathy 5.7%, cerebritis, acute renal failure 5.7%, intracranial hemorrhage 5.7%, hypertensive encephalopathy in 5.7%. Alveolar hemorrhage, infection, intraoperative deaths each contributed to deaths in 3.8%. Hypovolemic shock, acute liver failure, brain edema, thrombotic thrombocytopenic purpura, end stage kidney disease, pulmonary renal syndrome, suicide and acute hydrocephalus contributed to fatalities in 1.9%. The cause of death was unclearly identified in 26.9%. Results of the Kaplan Meier survival curve in the studied SLE cohort showed an overall cumulative probability of survival at 5, 10, 15 and 20 years after SLE diagnosis was 82.9%, 68.8%,51.4% and 20.4%, respectively. Multivariate regression analysis revealed psychosis, chronic kidney disease and heart failure were independent predictors of survival (HR= 4.3 times, 3.58 times and 3 times respectively, $p < 0.001$), while the use of hydroxychloroquine and AZA showed a protective effect.

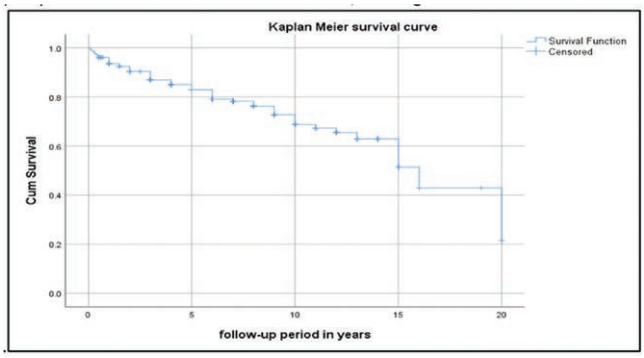


Figure 1. Kaplan-Meier estimated survival function, starting at date of SLE diagnosis.

Conclusion: The cumulative probability of survival at 5, 10, 15 and 20 years after SLE diagnosis was 82.9%, 68.8%,51.4% and 20.4%, respectively. The presence of renal manifestations, neuropsychiatric lupus and heart failure were independent predictors of poor survival in our cohort. The use of hydroxychloroquine and AZA were protective.

Corresponding author: Reem Hamdy Abdellatif Mohammed (Reem H A Mohammed), e-mail: rmhamdy@yahoo.com,. https://orcid.org/0000-0003-4994-7687, Scopus Author ID: 35280107100.

REFERENCES:

[1] Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997 Sep;40(9):1725. doi: 10.1002/art.1780400928. PMID: 9324032.
[2] Kasitanon N, Magder LS, Petri M. Predictors of survival in systemic lupus erythematosus. Medicine (Baltimore) 2006;85:147–56.
[3] Gladman D, Ginzler E, Goldsmith C, et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum 1996;39:363–9.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.149

AB0298

PREGNANCY IN RHEUMATIC DISEASE: A REGION WIDE SURVEY OF CURRENT PRACTICE AMONGST CLINICIANS IN THE WESSEX MULTI-DISCIPLINARY CONNECTIVE TISSUE DISEASE NETWORK

L. Parker[1], A. Mason[2], M. Coleman[3], B. Davidson[2]. [1]*University Hospitals Dorset NHS Foundation Trust, Rheumatology Department, Christchurch, United Kingdom*; [2]*University Hospital Southampton NHS Foundation Trust, Rheumatology Department, Southampton, United Kingdom*; [3]*University Hospital Southampton NHS Foundation Trust, Maternal Medicine Department, Southampton, United Kingdom*

Background: Rheumatic diseases frequently affect females of child-bearing age, with implications for foetal and maternal outcomes.
Two-thirds (66%) of the women who died in the 2016-18 MBRRACE report were known to have pre-existing medical problems[1]. The NHS long-term plan supports creation of Maternal Medicine Networks to facilitate access to specialist care and advice in pregnancy.
Guidelines exist for use of disease modifying anti-rheumatic drugs (DMARDs) during pregnancy but other aspects of pregnancy related care in rheumatic disease remain less well defined. The Wessex wide connective tissue disease (CTD) network provides a multi-disciplinary forum to discuss cases, to obtain approval for high cost drugs, to compare practice in multiple hospitals but does not specifically discuss pregnancy related uncertainties.
Objectives: To survey variations in clinical practice relating to rheumatic disease in pregnancy
Methods: Following careful project planning with the tertiary referral centre obstetric lead consultant for maternal medicine, several areas of care were identified which were prone to local and individual variation. An anonymous online survey relating to these specific areas of pregnancy related care was circulated amongst members of the CTD network, including rheumatology consultants, rheumatology practitioners and specialist trainees.
Results: 16 responses were obtained across 7 hospital sites; 56% were from rheumatology consultants. 12/16 (75%) reported routinely offering contraceptive advice when prescribing DMARDs. Only 4/16 (25%) were aware of a specific pre-natal obstetric clinic available in their hospital. There was major variation in planned frequency of clinical review. 10/16 would increase frequency of review during pregnancy if a patient's disease became active or unstable; 6/16 would aim to review patients approximately 3 monthly; 3/16 would not routinely increase frequency of review during pregnancy. Planned post-natal care was equally varied. 3/16 would routinely prescribe aspirin to all lupus women during pregnancy despite this being recommended for all women with SLE for prevention of pre-eclampsia[2]. Prescription of low molecular weight heparin was variable, and several responses were at odds with the current RCOG guidance on the subject[3]. 8/16 (50%) would prescribe corticosteroids judiciously in case of an acute disease flare.
Conclusion: This survey has revealed significant variation in practice relating to rheumatic disease in pregnancy. Integrated care with colleagues from the regional referral centre for maternal medicine is required, in keeping with the recently published NICE guidance on the subject[4]. Adopting a hub and spoke model, with local centres working closely alongside a tertiary centre, will help optimise peri-partum care and outcome for patients with long-term rheumatic conditions.

REFERENCES:

[1] Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK) Saving Lives, Improving Mothers' Care Maternal Report (December 2020). Available at https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/maternal-report-2020/

MBRRACE-UK_Maternal_Report_Dec_2020_v10.pdf [Accessed 28 January 2021]
[2] National Institute for Health and Care Excellence (2019) Hypertension in pregnancy: diagnosis and management (NICE guideline 133) Available at https://www.nice.org.uk/guidance/ng133 [Accessed 28 January 2021]
[3] Royal College of Obstetricians and Gynaecologists (2015) Reducing the risk of venous thromboembolism during pregnancy and the puerperium (Green-top Guideline Number 37a) Available at https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37a.pdf [Accessed 5 January 2021]
[4] National Institute for Health and Care Excellence (2019) Intrapartum care for women with existing medical conditions or obstetric complications and their babies (NICE guideline 121) Available at https://www.nice.org.uk/guidance/ng121 [Accessed 5 January 2021]

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.203

AB0299 QUANTITATIVE EVALUATION OF PROTEINURIA WITH URINALYSIS TEST AND COMPARING ITS CORRELATION WITH RANDOM SPOT URINE PROTEIN-CREATININE RATIO AND 24 HOUR URINE PROTEIN IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS –A SINGLE CENTRE EXPERIENCE IN MALAYSIA

C. R. Ng[1], Y. L. Loh[1]. [1]*Sultan Ismail Hospital, Rheumatology Unit, Johor Bahru, Malaysia*

Background: Lupus nephritis is an important concern among Systemic Lupus Erythematosus (SLE) patients in Asia and its mortality rate was reported to be 6 times higher compared to the general population [1]. Without prompt treatment it can lead to end stage renal failure and affect quality of life. 24 hour urine protein collection has long been used as the gold standard test to assess proteinuria. However due to its cumbersome process random spot urine protein-creatinine ratio is used as an alternative to replace the former in some centres before subjecting patients to renal biopsy. In a study done by Matar HE et al in 2012, he showed that there was a significant correlation between 24 hour urine protein and urine protein creatinine ratio in his 95 subjects [2].
Urinalysis is a semi-quantitative screening tool for early detection of potential kidney disorders. A survey done by Siedner MJ et al on practice preferences among American Rheumatologists in 2005 reported that 64.6% of them preferred to use urinalysis as the primary tool to screen for proteinuria [3].
Objectives: To assess the correlation of urinalysis test with random spot urine protein-creatinine ratio PCR) compared with 24 hour urine protein.
Methods: This was a retrospective study. The electronic medical records of all SLE patients seen in the rheumatology clinic of Hospital Sultan Ismail from 1/1/2017 to 31/12/2020 were reviewed. Patients who had urinalysis, urine protein creatinine ratio and 24 hour urine protein tests done were identified. Data on demography, urinalysis, random spot urine protein creatinine ratio and 24 hour urine protein were obtained and analysed.
Results: There were a total of 131 patients and 124 were females. The majority were Malays (75/131) followed by the Chinese (45/131),Indians (9/141) and others (2/131). The mean age group for the studied subjects was 34 (13-67). The urinalysis test showed that 34 of them had negative results, 37 of them had urine protein of 1 +, 18 of them had urine protein of 2+ followed by 23 patients with urine protein of 3 + and the rest had urine protein of 4+. The correlation between urinalysis and 24 hour urine protein was strong (r = 0.702), whereas the correlation between urinalysis and urine PCR ratio was stronger (r = 0.797).
Conclusion: We conclude that urinalysis correlates well with both random spot urine protein creatinine ratio and 24 hour urine protein and the correlation is stronger with urine PCR.

REFERENCES:
[1] Yap DY, Tang CS, Ma MK, Lam MF, Chan TM. Survival analysis and causes of mortality in patients with lupus nephritis. Nephrol Dial Transplant. 2012;27:3248–3254. [PubMed]
[2] Matar HE, Peterson P, Sangle S, D'Cruz DP. Correlation of 24-hour urinary protein quantification with spot urine protein: creatinine ratio in lupus nephritis. Lupus 2012 Jul;21(8): 836-9. doi:10.1177/0961203312437438. Epub 2012 Feb 13.
[3] Siedner MJ, Christopher-Stine L, Astor BC, Gelber AC, Fine DM. Screening for proteinuria in patients with lupus: a survey of practice preferences among American rheumatologists. J Rheumatol. 2007;34:973–977. [PubMed].

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.450

AB0300 LUPUS DISEASE ACTIVITY CORRELATES WITH QUALITY OF LIFE BUT NOT WITH HEALTH LITERACY STATUS

E. Eraslan[1], R. Bilici Salman[2], H. Satış[2], A. Avanoglu Guler[2], H. Karadeniz[2], H. Küçük[2], S. Haznedaroglu[2], M. A. Ozturk[2], A. Tufan[2], B. Goker[2]. [1]*Gazi University Faculty of Medicine, Internal Medicine, Ankara, Turkey*; [2]*Gazi University Faculty of Medicine, Rheumatology, Ankara, Turkey*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease of unknown etiology that can affect any organ of the body. SLE is associated with adverse effects on both health and non-health-related quality of life (HRQOL and non-HRQOL). Lupus PRO is a patient reported outcome measure that has been validated in many languages. It has 44 items that cover both HRQOL and non-HRQOL (1). Health literacy is defined as the degree to which individuals have the capacity to obtain, process and understand basic health information and services needed to make appropriate health decisions. Multiple studies indicate that people with limited health literacy have worse health status and higher rates of hospitalization (2).
Objectives: We aimed to evaluate the relationship between the LLDAS (Lupus Low Disease Activity State) criteria and the Lupus PRO test, as well as the health literacy status of lupus patients.
Methods: 83 SLE patients (94% women) were included in the study. We performed Lupus PRO and the European Health Literacy Survey tests during the routine follow-up visits of lupus patients to our rheumatology outpatient clinic and admissions to rheumatology inpatient clinic. Available clinical data on medical records were obtained, physician global assessments (PGA) were recorded by the attending physician.
Results: LLDAS criteria strongly and inversely correlated with the total score, as well as the mood subunit of the Lupus PRO. Similarly, it also significantly inversely correlated with the body appearence and goals subunits. Health literacy status of the patients did not correlate with their LLDAS scores, ie their disease activities.
Conclusion: Our results suggest that lupus disease activity, assessed by LLDAS criteria, significantly correlates with measures of quality of life, spesicifically Lupus PRO test, but not with health literacy status. Further studies are needed to evaluate if health literacy is related with damage, hospitalization or mortality associated with lupus.

REFERENCES:
[1] Jolly M, Pickard AS, Block JA, Kumar RB, Mikolaitis RA, Wilke CT, et al., editors. Disease-specific patient reported outcome tools for systemic lupus erythematosus. Seminars in arthritis and rheumatism; 2012: Elsevier.
[2] Paasche-Orlow MK, Parker RM, Gazmararian JA, Nielsen-Bohlman LT, Rudd RR. The prevalence of limited health literacy. Journal of general internal medicine. 2005;20(2):175-84.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.581

AB0301 CRITERIA FULLFILLMENT OF PRIMARY SJÖGREN'S SYNDROME ACCORDING TO TIME OF EVOLUTION OF SICCA SYMPTOMS

C. M. Gamboa-Alonso[1], D. Vega-Morales[1], J. C. Riegatorres[1], B. R. Vázquez Fuentes[1], L. Á. Ceseñas-Falcón[1], G. Figueroa-Parra[1], D. Á. Galarza-Delgado[1]. [1]*Universidad Autónoma de Nuevo León, Reumatología e Inmunología Clínica, Monterrey, Mexico*

Background: Primary Sjǒgren´s Syndrome (PSS) is an autoimmune disease characterized by sicca symptoms, autoantibodies and lymphocytic infiltrate in exocrine glands.
Classification and diagnosis of PSS is performed by applying 2002 AECG, 2012 ACR or 2016 ACR-EULAR criteria.
Time of evolution of symptoms has been associated with different clinical, serological and pathology findings.
Objectives: Document sicca profiles and compare findings according to time of evolution of symptoms.
Methods: A descriptive retrospective observational study was performed in 116 patients with sicca symptoms in a Rheumatology center in México.
Patients were separated according to time of evolution of sicca symptoms in ≤1 year, ≤2 years, ≤3 years, and ≥3 years. Clinical, serological, and histopathology features were assessed at each established time.
Time from symptom onset to diagnosis was reported in median and interquartil range (IQR); age at symptom onset and age at diagnosis was expressed in mean and standard deviation (SD).
Patients were classified as PSS if they fullfilled the 2002 AECG or 2016 ACR-EULAR criteria. Serology of Rheumatoid factor (RF), ANA, Anti-Ro, and Anti-La were documented.
Description of MSGB was performed reporting presence of foci, lobules, atrophy, adipose tissue infiltration and ductal dilatation.
Results: One hundred and sixteen sicca patients had a complete profile and 97 (83.62%) fulfilled AECG 2002 SSP criteria. Eighty-two (70.6%) patients with an ocular staining score were able to classify as PSS using the 2016 ACR-EULAR criteria.
Of the sicca cohort, 112 (96.6%) were female. The mean age of symptom onset was 48.4 (SD 13.11) years, and the mean age at diagnosis was 53.33 (SD 12.43) years. The median time from symptom onset to diagnosis was 36 (IQR 12-84) months.
Fullfilment the 2002 AECG PSS classification criteria according to duration of sicca symptoms is described in Table 1.

Table 1. Classification PSS criteria according to time of evolution of sicca symptoms

	<12 months	<24 months	<36 months	>37 months	
Oral symptoms	28%	40%	48%	89%	
Ocular symptoms	26%	39%	47%	93%	
Altered Salivary flow rate test	21%	32%	41%	81%	
Altered Schirmer test	19%	28%	38%	75%	
Positive Anti Ro	13%	19%	26%	47%	
Positive Anti La	3%	6%	10%	16%	
≥1 foci score/4mm2	14%	24%	34%	67%	
2002 AECG Criteria*	22%	34%	44%	84%	
*AECG-American European Consensus Group					
	0%	25%	50%	75%	100%

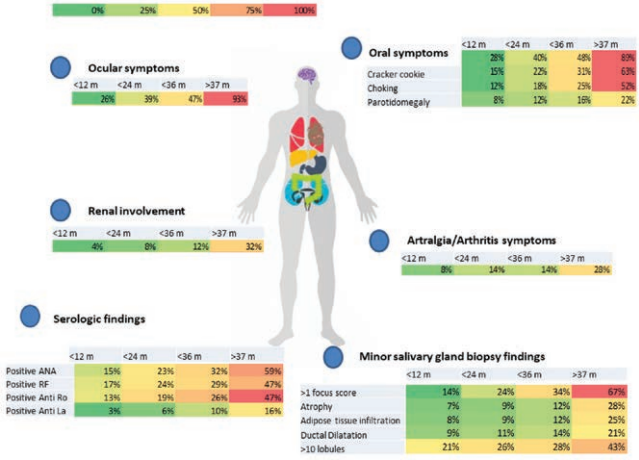


Figure 1. Clinical, serologic and histopathologic findings according to sicca symptom duration

Extra-classification criteria such as severe oral symptoms (choking, cracker cookie) were more common with prolonged symptom duration. Figure 1
Conclusion: The probability and capability of fulfilling PSS criteria is time dependent, this should be taken into consideration when evaluating patients referring sicca symptoms. Longer symptom duration was associated with more severe clinical, serological and histopathology profiles.
REFERENCES:
[1] Shiboski CH, Baer AN, Shiboski SC, et al (2018) Natural History and Predictors of Progression to Sjögren's Syndrome Among Participants of the Sjögren's International Collaborative Clinical Alliance Registry. Arthritis Care Res (Hoboken) 70:284–294. https://doi.org/10.1002/acr.23264
Acknowledgements: We thank Dr. Jazzia Emily Díaz Angulo and Dr. Gabriela Luna Limón for their help in data compilation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.922

AB0302 FACTORS ASSOCIATED WITH GESTATIONAL DIABETES MELLITUS (GDM) IN A MULTI-ETHNIC SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COHORT

S. S. Shaharir[1], R. Mustafar[2], M. S. Mohamed Said[1], R. Abd Rahman[3]. [1]*Universiti Kebangsaan Malaysia Medical Centre, Rheumatology Unit, Department of Medicine, Cheras, Malaysia*; [2]*Universiti Kebangsaan Malaysia Medical Centre, Nephrology Unit, Department of Medicine, Cheras, Malaysia*; [3]*Universiti Kebangsaan Malaysia Medical Centre, Obstetrics and Gynaecology, Cheras, Malaysia*

Background: The risks of insulin resistance and diabetes mellitus are elevated in systemic lupus erythematosus (SLE) patients. The use of glucocorticoid and anti-double stranded DNA antibodies positive are among the factors reported to be associated with the risk of gestational diabetes mellitus (GDM) in SLE patients. However, the relationship between GDM in Asian SLE patients is still obscure.
Objectives: To determine the prevalence of gestational diabetes mellitus (GDM) in a multi-ethnic SLE cohort in Malaysia and the associated risk factors.
Methods: This was a retrospective study of SLE pregnant women who have completed their antenatal care in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) from 2004 until 2019. Screening and diagnosis of gestational diabetes mellitus (GDM) were as recommended in the guidelines by the Ministry of Health Malaysia. Information on SLE disease activity and treatment at 6 months before pregnancy and during pregnancy were determined from the medical records. Univariate and multi-variable logistic regression analyses were performed to determine the factors associated with GDM in the SLE patients.
Results: A total of 89 patients with 202 pregnancies were included in the study. Malay was the predominant ethnic in this cohort (n=82, 67.2%), followed by Chinese (n=33,27.0%) and Indian (n=7, 5.7%). The most common system involvement of SLE was musculoskeletal (n=91, 74.6%), followed by haematological (n=78, 63.9%), lupus nephritis (54.9%, n=67) and mucocutaneous (n=66, 54.1%). The prevalence of GDM was 8.9% (n=18). More patients with GDM had positive anti-cardiolipin IgG antibody (aCL IgG) and lupus anticoagulant (LA) antibody as compared to the patients with no GDM, (55.6% vs 25.8%, p=0.01) and (50.0% vs 25.4%, p=0.05) respectively. On the other hand, the use of hydroxychloroquine (HCQ) in pregnancy was significantly lower in GDM patients (11.1%) as compared to no GDM group (39.1%), p=0.02. There was no significant difference in the ethnicity, SLE system involvement, disease activity status and immunosupressant use including steroid, azathioprine and cyclosporine A at 6 months before and during pregnancy between the GDM and non-GDM group. A forward logistic regression which include aCL IgG, LA and HCQ use in pregnancy, only the HCQ use remained significantly associated with lower risk of GDM in the model with OR= 0.12, 95% C.I = 0.02-0.94, p=0.04.
Conclusion: Our study demonstrates the potential benefit of hydroxychloroquine in reducing the risk of gestational diabetes mellitus in SLE patients. The prevalence of antiphospholipid antibodies particularly aCL IgG and LA was found to be higher among patients with GDM. Further prospective studies are needed to confirm this association.
REFERENCES:
[1] Dong Y, Dai Z, Wang Z, et al. Risk of gestational diabetes mellitus in systemic lupus erythematosus pregnancy: a systematic review and meta-analysis. BMC Pregnancy and Childbirth. 2019 May;19(1):179. DOI: 10.1186/s12884-019-2329-0.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1044

AB0303 VALIDATION OF THE THREE CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) ON A PATIENT COHORT FROM A V.A. NASONOVA SCIENTIFIC RESEARCH INSTITUTE OF RHEUMATOLOGY: A PROSPECTIVE STUDY

T. Reshetnyak[1,2], A. Shumilova[3], S. Glukhova[4], F. Cheldieva[1,2], T. Lisitsyna[1], N. Seredavkina[1], A. Lila[2,3]. [1]*V.A. Nasonova Research Institute of Rheumatology,*

Moscow, Russia;, Vascular Rheumatology, Moscow, Russian Federation; [2]*Russian Medical Academy of Continuing Professional Education, Ministry of Health of Russia, Department of Rheumatology, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia;, Department of Rheumatology, Moscow, Russian Federation*; [4]*V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia;, Laboratory of Medical and Social Problems of Rheumatology, Moscow, Russian Federation*

Background: Classification criteria for SLE need validation and selection of the most advanced ones for clinical practice
Objectives: To validate Systemic Lupus International Collaborating Clinics (SLICC)-12, American College of Rheumatology (ACR)-97 and 2019 European League against Rheumatism/American College of Rheumatology (EULAR/ACR-2019) for Systemic
Lupus Erythematosus classification criteria on a patient cohort from V.A. Nasonova Scientific Research Institute of Rheumatology (Moscow)
Methods: This prospective study included 252 (n=152 with SLE and n=100 non SLE: 74 – with systemic sclerosis (SC) and 26 – with primary antiphospholipid syndrome (pAPS)) patients who were sequentially admitted to the 4th Rheumatology Department from December 2018 to June 2020. All of the patient records were reevaluated by expert rheumatologist in order to determine if they agree with the diagnosis. For every patient, a check-list of SLE-related features was filled out. The association between clinical diagnosis and diagnosis generated on the basis of ACR-97, SLICC-12 and EULAR/ACR-2019classification criteria was assessed. The overall sensitivity and specificity of ACR-97, SLICC-12 and EULAR/ACR-2019 classifications, as well as the sensitivity and specificity according to disease duration was calculated. The predictive value of every criterion in ACR-97, SLICC-12 and 2019 EULAR/ACR classification was assessed using logistic regression analysis and receiver operating characteristic (ROC) curves.
Results: According to ACR-97 criteria, reliable SLE was diagnosed in 131 (86%), according to SLICC-2012 – in 145 (95.3%) and according to EULAR/ACR-2019 – in 144 (94.7%) of 152 patients, respectively. We identified the criteria that were significantly more represented in the SLE-group. The sensitivity and specificity (Table 1) did not change depending on the ANA titers (1/160 and 1/320) and the duration of the disease.

Table 1. The sensitivity and specificity of SLE criteria in 152 SLE patients and 100 non SLE patients

SLE classification criteria	AUC, 95% CI	Cut point	Sensivity	Specifity
ACR-97	0.654 (0.550-0.758)	4	89.7	36
SLICC-12	0.616 (0.505-0.728)	4	93.1	43
2019 EULAR/ACR	0.609 (0.492-0.727)	10*	97.4	48

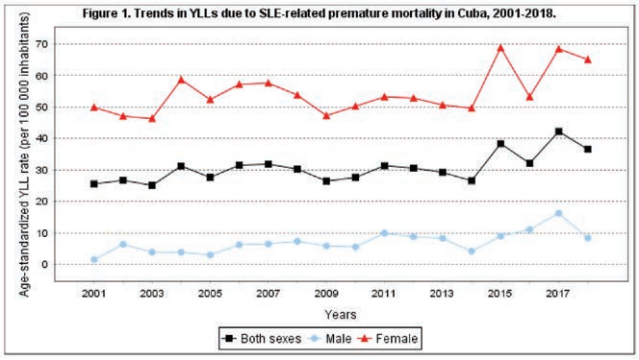
Note. ACR-97 – American College of Rheumatology classification from 1997; SIICC-12 – Systemic lupus International Collaboration Clinics classification from 2012; 2019 European League Against Rheumatism/American College of Rheumatology. ANA – anti-nuclear antibody more than 1/320 n=116; ANA < 320 n= 36. AUC – area under the ROC curve; Cut point - reference point for the number of criteria, * number of points ≥ 10.

When excluding patients with SC in a single-factor logistic model of patients with SLE and pAPS, indicating the number of criteria, the sensitivity was for ACR-97 - 86, for SIICC-12 - 95, for 2019 EULAR/ACR - 95, the specificity was 100, 62 and 62, respectively.
Conclusion: Evaluation of the criteria by level ANA revealed the highest sensitivity for 2019 EULAR/ACR and SLICC-12, the specificity was low for all three criteria. In the analysis of patients with SLE and pAPS, the sensitivity was highest for 2019 EULAR/ACR and SLICC-12, the specificity was 100 for ACR-97.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1051

AB0304 LEVELS AND TRENDS IN PREMATURE MORTALITY BURDEN DUE TO SYSTEMIC LUPUS ERYTHEMATOSUS IN CUBA

H. Hernández-Negrín[1]. [1]*Universidad de Ciencias Médicas de Villa Clara, Internal Medicine, Santa Clara, Cuba*

Background: Analysis of the causes of premature mortality is an essential function of public health surveillance. A variety of methods have been used to accurately assess and report the level and trends of premature mortality; however, many have significant limitations, particularly in capturing actual early deaths. Years of life lost (YLL) has been recognized as a robust and comprehensive measure of premature mortality.[1] Systemic lupus erythematosus (SLE) is among the leading causes of premature mortality burden in young women in the United States and premature mortality from SLE is increasing in Latin America.[2, 3] However, the premature mortality burden from SLE has not been fully characterized in Cuba.
Objectives: To identify levels and trends in premature mortality burden due to SLE in Cuba during 2001-2018.
Methods: Data were obtained from the mortality database of the Ministry of Public Health of Cuba (International Classification of Diseases-10, code 32 as underlying cause of death). YLL were calculated using the standard life expectancy of the WHO's global health estimates. Age- and sex-specific YLL rates were calculated using the Cuban mid-year population estimates and the age-standardized YLL rate (ASYR) was estimated by the direct method using the WHO's standard population. The 2001-2018 temporal trends were analyzed using Joinpoint software.
Results: During 2001-2018, 1 475 patients died from SLE. These deaths contributed 66 605 YLL (women= 59 166; men=7 433), with a mean of 45.1 YLL per death (women= 45.2; men= 44.5). The 40-44 age group was the most affected in both sexes with 9 266 YLL (women=8 177; men=1 086). The ASYR was higher in 2018 than in 2001 for both sexes (Figure 1). A significantly increasing trend in ASYR due to SLE was identified throughout the period (average annual percent change [AAPC] =1.9; 95% confidence interval [CI] = 0.9 to 3.0), more pronounced in men (AAPC = 7.0; 95% CI = 3.5 to 10.6) than in women (AAPC = 1.3; 95% CI = 0.3 to 2.3).
Conclusion: The high levels and growing trends in premature mortality burden from SLE in Cuba, demands its recognition as an important health problem and immediate actions that help mitigate it.
REFERENCES:
[1] Martinez R, Soliz P, Caixeta R, Ordunez P. Reflection on modern methods: years of life lost due to premature mortality-a versatile and comprehensive measure for monitoring non-communicable disease mortality. Int J Epidemiol. 2019; 48(4): 1367-1376.
[2] Yen EY, Singh RR. Lupus - an unrecognized leading cause of death in young women: Population-based study using nationwide death certificates, 2000-2015. Arthritis Rheumatol. 2018;70:1251–5.
[3] Soares CR, Viana K, Moraes-Santos F, Vieira CL, Lamarão F, Iglesias-Rodriguez M. Mortality rate and premature mortality due to systemic erythematosus lupus in Latin America US and England and Wales. Value Health. 2015;18:A805–81.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1147

AB0305 IS THERE HYPERCOAGULATION IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME AND BEHCET'S DISEASE?

N. Seredavkina[1], T. Reshetnyak[1,2], T. Lisitsyna[1], A. Lila[1,2]. [1]*VA Nasonova Research Institute of Rheumatology, Department of Vascular Rheumatology, Moscow, Russian Federation*; [2]*Federal State Budgetary Educational Institution of Further Professional Education "Russian Medical Academy of Continuous Professional Education" of the Ministry of Healthcare of the Russian Federation, Department of Rheumatology, Moscow, Russian Federation*

Background: Whereas antiphospholipid syndrome (APS) is a non-inflammatory vasculopathy and is associated with thrombosis in 98% of cases, Behcet's disease (BD) is a systemic vasculitis of unknown etiology, characterized by vascular damage of any calibre. Both venous and arterial thromboses occur in 45% of BD patients and are associated not with hypercoagulable disease but with inflammatory changes in the vascular wall mediated by hypersecretion of pro-inflammatory cytokines and endothelial cells dysfunction. Thrombodynamics (TD) is a new global test for diagnosing plasma haemostasis disorders, identifying bleeding and thrombosis risks, and can be used to detect a prothrombotic state and assess the influence of disease activity and course on the hypercoagulation process.
Objectives: comparative assessment of TD in patients with APS and BD before anticoagulant therapy (AC).
Methods: The study included 20 patients (9 APS and 11 BD) and 8 age and sex-matched healthy controls (HC). None of the subjects received AC. Thromboses

in past history were registered in 5/9 (55%) APS patients and 2/11 (18%) BD patients and none of HC. Fetal loss occurred only in women with APS (4/4 (100%) who had pregnancy during the disease). All the patients were hospitalized and underwent fool investigation according to the diagnosis including TD, local coagulation tests and antiphospholipid antibodies profile.

Results: the velocity of clot growth in APS was lower, than in BD and in HC: 23.7 [22.6; 24.7] vs 29.0 [28.2; 34.4] and 31.1 [28.9; 33.5] Um/min, respectively (p=0.001). Clot size at 30 minutes in APS also was lower, than in BD and HC: 972.1 [921.3; 1007.4] vs 1152.7 [1098.3; 1225.4] and 1226.6 [1140.5; 1295.1] Um, respectively (p=0.001). Spontaneous clotting was registered only in 2 BD patients in mean time 2 minutes. Clot density and lag time (Tlag, the delay between the test start and the onset of clot formation) were the same in all three groups. Prolonged APTT was found in APS (33.7 [30.6; 47.1] sec) and normal APTT - in BD (30.9 [29.1; 31.1] sec) and HC (29.7 [28.2; 30.8] sec). Increased soluble fibrin-monomer complexes were revealed in all APS patients (100%), 91% BD patients and 25% HC (p=0.01). After interpretation the TD results were distributed as follows: hypocoagulation was noted in 1 APS patient with a positive lupus anticoagulant, while all other APS patients had normocoagulation. Thrombotic readiness status (TRS) was diagnosed only in 2 BD patients. The frequency of normocoagulation and hypercoagulation did not differ between BD and HC. Local coagulation tests (APTT, thrombin time, prothrombin time) were the same depending on hypo- and hypercoagulation by TD results. Fibrinogen level in BD patients with hypercoagulation was higher, than in BD patients with normocoagulation and TRS: 4.2 [3.6; 4.7] vs 2.8 [2.7; 3.0] and 2.8 [2.7;2.8] g/l respectively, p=0.04. BD activity by Behcet's Disease Current Activity Form correlated with stationary velocity of clot growth (R_s = 0.68, p<0.05).

Conclusion: Thrombodynamics results showed: before anticoagulant therapy there were normocoagulation with a tendency to hypocoagulation in APS and hypercoagulation in BD. In BD hypercoagulation associated with disease activity.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1319

AB0306 OBESITY PHENOTYPES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

L. Kondrateva[1], T. Panafidina[1], T. Popkova[1], M. Cherkasova[2], A. Lila[3], E. Nasonov[3]. *[1]V.A.Nasonova Research Institute of Rheumatology, Department of Systemic Rheumatic Diseases, Moscow, Russian Federation*; *[2]V.A.Nasonova Research Institute of Rheumatology, Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*; *[3]V.A.Nasonova Research Institute of Rheumatology, Scientific Department, Moscow, Russian Federation*

Background: The so-called "obesity paradox" when cardiovascular risk is lower in overweight compared to lean patients accompanies some chronic conditions. A possible explanation for this phenomenon comes from variability of obesity phenotypes, i.e., "classical" obesity as exemplary perception of obesity is equal to increased body mass index (BMI) and metabolic disorders; but there are also "metabolically healthy" overweight individuals (increased BMI without metabolic disorders), and "latent" obesity phenomenon (when normal weight is associated with metabolic disorders, especially with insulin resistance (IR) and adipocytokines imbalance). Serum leptin concentrations increase has been established in obese, therefore, this adipocytokine synthesized in adipose tissue, can be used as a marker of body fat mass. Higher cardiovascular risks are known even in young patients with systemic lupus erythematosus (SLE), but obesity phenotypes have not been studied.

Objectives: To find out the rate of various obesity phenotypes and to identify factors contributing to "latent" obesity in SLE pts without diabetes mellitus (DM) or hyperglycemia.

Methods: A total of 49 SLE pts (46 women, 3 men, 40 [33;48] years old) without established DM or hyperglycemia were enrolled in the study. The median disease duration was 3,0[0,7;8,0] years, SLEDAI-2K was 5[2;8]. SLE pts were treated with glucocorticoids (GC) (84%) and hydroxychloroquine (78%), immunosuppressive drugs (20%) and biological agents (10%). Insulin levels were measured using electrochemiluminescence assay Elecsys (Roche Diagnostics), serum leptin concentrations were estimated using ELISA (DBS-Diagnostics Biochem Canada Inc.). IR was defined as Homeostasis Model Assessment of Insulin Resistance index (HOMA-IR) ≥2,77. Leptin levels were considered elevated at values ≥11,1 ng/ml for women, ≥5.6 ng/ml for men. The overweight / obesity status was determined by World Health Organization criteria in patients with body mass index (BMI) ≥25kg/m^2.

Results: Overweight / obesity were established in 45% of pts, normal BMI was in 55% of SLE pts. The combination of IR and high leptin levels was found in 32% of overweight / obese pts and 11% of pts with normal BMI (p=0,2), an isolated increased leptin levels - in 64% and 41%, respectively (p=0,1). Metabolic disturbances were absent in 4% of overweight pts and 48% of pts with a normal BMI (p=0,001). Thus, "classical" obesity was found in 43% of cases, "metabolically healthy" obesity - in 2%, and "latent" obesity - in 29% of SLE pts. Leptin levels correlated with BMI (r=0,5, p=0,02), waist circumference (r=0,5, p=0,02) in the overweight / obesity group, and with disease duration (r=0,5, p=0,02), SLEDAI-2K (r=-0,6, p=0,002), anti-dsDNA (r=-0,7, p<0,001), C3 complement (r=0,5, p=0,01), maximum (r=0,7, p<0,001) and current GCs doses (r=0,4, p=0,03) in patients with normal weight. There was a trend to association between leptin levels and duration of GCs therapy in SLE pts with normal BMI (r=0,4, p=0,06).

Conclusion: Metabolic disorders - most often increased leptin levels - were diagnosed in the majority of overweight / obese patients, as well as in about 50% of SLE patients with normal weight. There were only isolated cases of "metabolically healthy" obesity in SLE patients. Metabolically obese normal weight ("latent" obesity) phenotype was strongly associated with GCs therapy and decreased disease activity.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1356

AB0307 IS THERE ANY INFLUENCE OF THE ANTIRHEUMATIC THERAPY ON ECHOCARDIOGRAPHIC FINDINGS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS?

T. Panafidina[1], T. Popkova[1], L. Kondrateva[1], A. Volkov[2], E. Nasonov[3], A. Lila[3]. *[1]V.A.Nasonova Research Institute of Rheumatology, Department of Systemic Rheumatic Diseases, Moscow, Russian Federation*; *[2]V.A.Nasonova Research Institute of Rheumatology, Department of Instrumental Diagnostics, Moscow, Russian Federation*; *[3]V.A.Nasonova Research Institute of Rheumatology, Scientific Department, Moscow, Russian Federation*

Background: Cardiovascular diseases are becoming the leading cause of death among SLE patients due to increasing life-spans. Transthoracic echocardiography (TTE) is a routine and widely available modality in everyday clinical practice useful to identify specific pathological cardiac changes and predictors of heart failure.

Objectives: The goal was to identify potential abnormalities in the TTE findings in SLE patients, with and without antirheumatic therapy.

Methods: This is a prospective cross-sectional study including 91pts (91% females, aged 32[28-41]years (median [interquartile range 25%-75%]) with SLE (SLICC 2012 criteria). All patients were divided into 2 groups: the 1st group was composed of "untreated" patients and the 2nd – of patients receiving antirheumatic therapy. The 1st group included 43pts (93% females) aged 31[27–40]years who were not receiving steroids, immunosuppressants and biological agents at the time of enrollment, 5(12%) of them were on hydroxychloroquine (HCQ) therapy 200 mg/day. The 2nd group is represented by 48pts (89% females) with median age 34[28-45]years. Out of them 47(98%) patients were on prednisone therapy at 10[8-15]mg/day, 10(21%)- on cyclophosphamide, 6(13%)-azathioprine, 4(8%)-mycophenolate mofetil, 4(8%)-methotrexate, 37(71%)–HCQ, and 9(19%)–on biologic (rituximab, belimumab). Both groups were matched by age and gender. Patients receiving antirheumatic therapy (group 2) had longer disease duration (96 vs 18 months, p<0,00001), lower disease activity (SLEDAI-2K 4 vs 11 scores, p<0,001), higher SLICC/DI (1 vs 0 score, p<0,001); lower percentage of them had skin lesions (11 vs 57%, p<0,0001), arthritis (22 vs 52%, p<0,05) and hematological disorders (24 vs 74%, p<0,0001) than "untreated" patients from the 1st group.

Results: Valve insufficiency with varying degree of clinically insignificant regurgitation and pericarditis were the commonest pathology found in "untreated" and "treated" SLE patients based on TTE data. No differences in rates of valve insufficiency (95% and 83%), pericarditis (43% and 47%) (both exudative and adhesive), endocarditis (26% and 33%), median left ventricular (LV) ejection fraction (64[59-68]% and 64[61-69]%), LV end-systolic dimension (30[27-32]mm and 29[25-31]mm), LV end-diastolic dimension (48[45-50]mm and 45[42-49]mm), pulmonary artery systolic pressure (25[22-31]mm Hg and 23[22-30]mm Hg), LV diastolic disfunction (26% and 21%) and LV systolic dysfunction (9% and 6%), LV myocardial hypertrophy (14% and 21%) and left atrium dilatation (9% and 21%) were found between the "untreated" SLE patients and patients receiving antirheumatic therapy (p>0,05 for all cases). Higher rates of mitral and tricuspid valves prolapse was seen more often in "treatment-naïv" SLE patients: 16(47%) vs 10(21%), p<0,01.

Conclusion: Valvular dysfunction (insufficiency with clinically insignificant regurgitation), pericarditis, endocarditis and LVDD were the most common cardiac TTE abnormalities in SLE patients. Antirheumatic therapy seems not to worsen structural and functional cardiac abnormalities based on TTE findings in SLE patients. Only mitral and tricuspid valves prolapse was seen more often in "treatment-naïv" SLE patients.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1360

AB0308 COGNITIVE IMPAIRMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME PATIENTS

A. Borisova[1], T. Lisitsyna[2], D. Veltishchev[1], T. Reshetnyak[2], O. Seravina[1], O. Kovalevskaya[1], F. Cheldieva[2], E. Nasonov[3]. [1]*Moscow Research Institute of Psychiatry, Serbsky NMRC PN MoH, Department of mental Disorders in Somatic Diseases, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Vascular Rheumatology, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Scientific Director of the Institute, Moscow, Russian Federation*

Background: Cognitive impairment (CI) in systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) patients have been poorly described and recognized.
Objectives: to describe the rates and spectrum of CI in primary (PAPS) and secondary to systemic lupus erythematosus (SLE) (SAPS) APS patients
Methods: 113 patients (70 with APS (37 – PAPS, 33 – SAPS) and 43 - SLE without APS), 89 (78,8%) – women, were consecutively enrolled in the study. The mean (M±SD) age was 37,9±11,9 years. SLE activity was measured by SLEDAI scale. Mental disorders (MD) were diagnosed by psychiatrist in accordance with ICI-10 in semi-structured interview. CI were diagnosed with psychology and neuropsychology methods
Results: CI of varying severity were found in 105 (92,9%) patients: 62,9% - mild, 23,8% - moderate and 13,3% - severe. Severe and moderate CI were more associated with APS (48,6% in PAPS and 39,5% in SAPS vs 18,6% in SLE, p=0,004 and p=0,04, accordingly). CI were predominantly organic origin in all patients, but vascular dementia was detected only among patients with APS (10,8% of PAPS and 3,03% of SAPS patients). There was no association of CI with clinical manifestations and SLE activity. In patients with PAPS CI was associated with stroke, livedo reticularis and lupus anticoagulant positivity. In 84 patients (74,3%) CI were also specifically bounded to MD. Current MD were detected in 100 (88,5%) patients: schizotypal disorder was found in 10 (8,85%) patients and was associated with PAPS (13,5% vs 9,09% in SAPS and 4,65% in SLE); anxiety-depressive spectrum disorders (ADDs) - in 95 (84,1%) (chronic and recurrent depression prevailed 37 (32,7%) and 42 (37,2%) resp.); the structure of MDs in accordance with ICI-10 differed slightly between groups, but no statistically significant differences were obtained.
Conclusion: cognitive impairment, mainly of an organic type, are characteristic of most patients with SLE and APS. The significant associations of cognitive impairment with clinical manifestations and activity of SLE were not identified, but patients with cognitive impairments were more likely to have anxiety and depressive disorders, strokes, livedo reticularis and lupus anticoagulant positivity
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1402

AB0309 SAFETY OF 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

G. Tarasova[1], B. Belov[1], M. Cherkasova[2], E. Aseeva[3], T. Reshetnyak[4], N. Kosheleva[4], T. Popkova[5]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Drug Therapy, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Intensive Therapy Laboratory, Moscow, Russian Federation*; [4]*V.A. Nasonova Research Institute of Rheumatology, Vascular Rheumatology Laboratory, Moscow, Russian Federation*; [5]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases Laboratory, Moscow, Russian Federation*

Background: Vaccination of patients with autoimmune diseases with pneumococcal vaccines is necessary to prevent severe respiratory infections in this group of patients. The main issue of immunization of patients with systemic lupus erythematosus (SLE) remains the issue of safety.
Objectives: The aim of the study was to study the safety of the 23-valent polysaccharide pneumococcal vaccine (PPV-23) in patients with SLE.
Methods: The study included 73 patients with a reliable diagnosis of SLE, of which women - 64, men - 9, aged 19 - 68 years. 69 patients received glucocorticoids (GC) 5-30 mg/day, 55- hydroxychloroquine (GCH), 37-cytostatics (CS), 27 – biologics (14 – rituximab (RTM), 11 – belimumab (BLM), 2-BLM and RTM). 1 dose (0.5 ml) of PPV23 was administered subcutaneously. 60 patients were examined within 1 year, 13 - within 2-3 months.
Results: Vaccination tolerance was assessed in 73 patients: in 33 (45.2%) - vaccine reactions were absent, in 36 (49.3%) - local reactions of mild and moderate severity were noted (pain, swelling, skin hyperemia at the injection site of the vaccine), lasting from 2 to 7 days, in 1 (1.4%) - general weakness within 1 month, in 2 (2.7%) - mild diarrhea within 1 day. Vaccinal reactions were typical and completely reversible, did not require additional appointments. One patient (1.4%) developed a hyperergic reaction of the Artyus phenomenon type, which was arrested within 7 days by the use of antihistamines and topical GCs. None of the 60 patients, whose follow-up period was 1 year, had no exacerbations of the disease directly related to vaccination (i.e., in the next 2-3 months). Vaccination was carried out both at a low degree of activity (n = 33 (55%)) and remission (n = 6 (10%)), and at an average (n = 12 (20%)) and high (n = 9 (15%))) the degree of SLE activity. The dynamics of the SLE activity index SLEDAI-2k (Me) during the year was as follows: initially - 4 (2; 6), after 2-3 months - 2 (2; 4), after 12 months - 2 (2; 4). During the year, 7 out of 60 patients had a moderate exacerbation of the disease, which was not related to the vaccination in terms of timing: after 3.5-5 months (3), 12 months (4). An exacerbation occurred in 4 - with a decrease in the HA dose, in 1 - after psychological stress, in 1 - against the background of persistently high immunological activity and insufficient therapy, in 1 - without an increase in immunological activity. In 4 out of 7, exacerbation was manifested by skin rashes and articular syndrome, in 1 - by the development of panniculitis, in 2 - by leukopenia. All these symptoms were noted earlier in the period of exacerbation. In all, the exacerbation was quickly stopped by a moderate increase in the HA dose. In 60 patients, the dynamics of immunological markers of SLE was analyzed during the year after vaccination. There was no evidence of a significant increase in the immunological activity of SLE after vaccination with PPV-23. After vaccination, no new autoimmune phenomena have been identified. In the first 3 months. after vaccination, in isolated cases, there was a transient increase / decrease in SLE markers (a-DNA, ANF, C3, C4) with a subsequent return to the initial values, without symptoms of exacerbation of the disease.
Conclusion: 1. During the year of observation, no exacerbations were observed that were reliably associated with vaccination. 2. Vaccination with PPV-23 is safe for SLE patients during periods of low and moderate activity. If necessary, vaccination is possible at high activity without the development of adverse events. 3. The multidirectional dynamics of the main markers of SLE observed during the year reflects the instability of immunological parameters characteristic of SLE.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1440

AB0310 TOLERABILITY AND SAFETY OF 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINE IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME, PRELIMINARY RESULTS

G. Tarasova[1], B. Belov[1], M. Cherkasova[2], E. Aseeva[3], T. Reshetnyak[4], N. Kosheleva[4], T. Popkova[5]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Drug Therapy, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Intensive Therapy Laboratory, Moscow, Russian Federation*; [4]*V.A. Nasonova Research Institute of Rheumatology, Vascular Rheumatology Laboratory, Moscow, Russian Federation*; [5]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Diseases Laboratory, Moscow, Russian Federation*

Background: Antiphospholipid syndrome (APS) is an autoimmune disease often associated with severe, life-threatening vascular complications. The majority of patients (and in case of secondary APS, in 100% of cases) receive immunosuppressive therapy. Immunization with pneumococcal vaccines in patients with both primary APS (PAPS) and APS+SLE or secondary (sAPS) is necessary to prevent severe respiratory infections in these patients.
Objectives: Purpose of the study - to study the tolerance and safety of 23-valent polysaccharide pneumococcal vaccine (PPV-23) in patients with PAPS and sAPS.
Methods: At this stage, the study included 28 patients with APS, of which 10 with PAPS, 18 with sAPS proceeding against the background of systemic lupus erythematosus (SLE), of which 23 women (82%), 5 men (18%). The average age (Me) of patients was 43 (35.5; 53.0) g. 20 patients received glucocorticoids (GC) 5-30 mg/day equivalent to prednisone, 17- hydroxychloroquine, 6- cytostatics (3-cyclophosphamide, 2-azathioprine, 1- mycophenolate mofetil), 8- biologics: 5-rituximab (RTM), 3-belimumab (BLM); 20-received anticoagulants (direct-10, indirect-10).
1 dose (0.5 ml) of PPV-23 was administered subcutaneously. The follow-up time was 1 year in 23 patients and 5-5.5 months in 5-5.5 months. During the visits, standard clinical and laboratory tests were performed, immunological blood test and the level of antibodies to S.pneumoniae
Results: Vaccination was well tolerated in all patients. In 29% of cases, vaccine reactions of mild severity were observed: in 7 (25%) - a local reaction (pain in the arm for 1-3 days-at 7, redness up to 2 cm at the injection site-at 1), in 1 (3,6%), the patient experienced general weakness (moderately pronounced) for 1 month. Vaccinal reactions were completely reversible and did not require additional prescriptions. Post-vaccination complications develop, as a rule, in the first 1-2

months after vaccination. During the observation period, none of the patients had an exacerbation of the disease, reliably associated with the vaccination. There was no recurrence of thrombosis, both in patients receiving anticoagulant therapy and without it. No new autoimmune phenomena, both clinical and laboratory, were identified. The dynamics of the production of anti-streptococcal antibodies during the year was followed in 16 patients. One year after vaccination, 31% of patients showed a significant (more than 2-fold compared to the initial) increase in the concentration of antibodies to polysaccharides of the cell wall of S. pneumoniae ("responders"), 69% of patients were "non-responders" to the vaccine. At the same time, all 5 patients with PAPS were "non-responders", and 45.5% "respondents" with sAPS.

Conclusion: Preliminary results show that patients with APS tolerate PPV-23 vaccination well. In the next post-vaccination period, exacerbations of the disease, thrombosis were not recorded. Attention is drawn to the large number of "non-responders" in PAPS, however, to obtain statistically reliable results, it is necessary to continue the study and recruit more patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1447

AB0311 INCREASED LEVELS OF SERUM WISTERIA FLORIBUNDA AGGLUTININPOSITIVE MAC-2 BINDING PROTEIN IN RHEUMATIC DISEASES INCLUDING SLE

T. Yoshikawa[1], K. Azuma[1], T. Furukawa[1], M. Tamura[1], T. Hashimoto[1], M. Morimoto[1], N. Azuma[1], K. Matsui[1]. [1]*Hyogo College of Medicine College Hospital, Division of Allergology and Rheumatology, Department of Internal Medicine, Nishinomiya-City, Japan*

Background: Mac-2 binding protein is a cell-adhesive glycoprotein of the extracellular
matrix secreted as a ligand of galectin-3 (Mac-2). Recently, a Wisteria floribunda agglutinin positive-M2BP (M2BP) assay developed using a lectin-antibody sandwich
immunoassay has shown promise as a new fibrotic marker in liver fibrosis and interstitial
lung disease (ILD) to detect unique fibrosis-related glycoalteration.

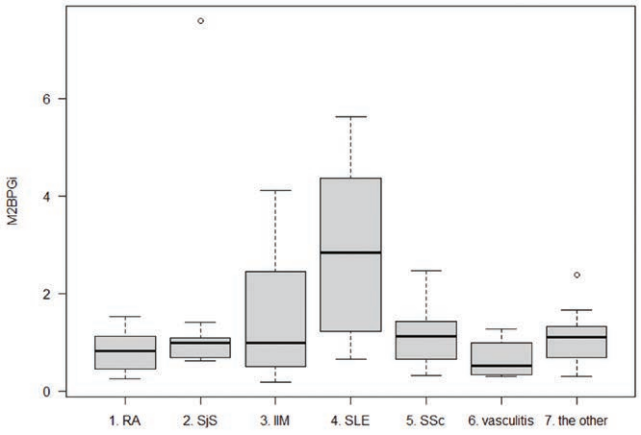
Objectives: The aim of this study is to evaluate the utility of serum Mac-2 binding protein glycosylation isomer (M2BPGi) levels in patients with rheumatic diseases (RD).

Methods: We retrospectively measured serum M2BPGi levels in 68 patients with RD and 16 healthy controls (HC). There were no patients of cirrhosis and active hepatitis. Serum levels of M2BPGi were measured using HISCL M2BP glycosylation isomer Assay Kit. We examined the relationship between serum M2BPGi levels and clinical parameters in patients with RD.

Results: In patients with RD, the median age was 62.0 years and 79.4% of them were female.

Serum M2BPGi levels were significantly higher in patients with RD than in HC (median 0.98 cutoff index [COI], 0.32 COI, respectively; $P < 0.00001$). Patients with SLE tended to have higher serum M2BPGi levels than other rheumatic diseases.

In patients with RD, a significant correlation was not found between serum M2BP levels and inflammation markers such as CRP or ferritin. However, serum M2BPGi levels were significantly correlated with B cell activation markers such as immunoglobulin free light chain and IgG ($r = 0.588$, 0.504) and T cell activation marker such as sIL-2R ($r = 0.408$).



Conclusion: Most of the rheumatic diseases in this study were considered to be type I interferonopathy diseases such as rheumatoid arthritis, Sjogren's syndrome, inflammatory myositis, scleroderma and SLE.

Serum M2BPGi was reported to have a significant correlation with SLE disease activity [SS Ahn et al. Lupus. 2018; 27: 771], and also to have a significant correlation with Gakectin-9, a novel biomarker for IFN signiture [Lucas L van den Hoogen et al. Ann Rheum Dis. 2018; 77: 1810].

So, it was suggested that serum M2BPGi may be a novel biomarker that indirectly indicates how much IFN is activated in rheumatic diseases.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1494

AB0312 INCREASED PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN INDIVIDUALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

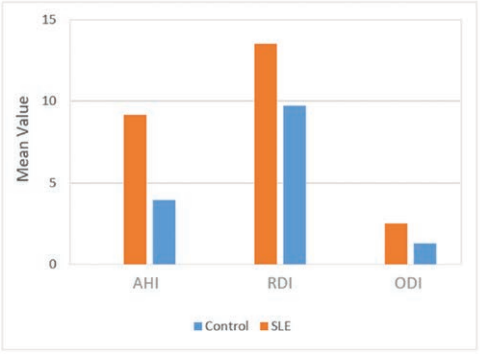
R. Meidan[1,2], D. Paran[2,3], R. Tauman[2,4], V. Furer[2,3], T. Eviatar[2,3], D. Levartovsky[2,3], A. Polachek[2,3], J. Wollman[2,3], H. Padova[2,3], M. Zisapel[2,3], M. Anouk[2,3], E. Seyman[2,5], O. Elkayam[2,3], O. Elalouf[2,3]. [1]*Tel Aviv Sourasky Medical Center, Internal Ward B, Tel Aviv, Israel*; [2]*Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel*; [3]*Tel Aviv Sourasky Medical Center, Rheumatology, Tel Aviv, Israel*; [4]*Tel Aviv Sourasky Medical center, Sleep Medicine Center, Tel Aviv, Israel*; [5]*Tel Aviv Sourasky Medical Center, Neurology, Tel Aviv, Israel*

Background: Sleep disturbances are common in individuals with rheumatological diseases in general and systemic lupus erythematosus (SLE) in particular[1]. Studies suggest that obstructive sleep apnea (OSA) might correlate with SLE disease activity and the presence of additional symptoms such as pain, fatigue, affective symptoms and steroid use[2]. Sleep disturbances symptomatology such as fatigue and increased pain overlap with constitutional inflammatory symptoms of SLE and may mimic or mask disease related relapse[3,4]. Therein lies the importance of diagnosing and treating such disorders in SLE.

Objectives: To determine whether patients with SLE have increased prevalence of OSA as assessed by the apnea hypopnea index (AHI) and to explore possible contributors to OSA including SLE disease activity and accrued damage, medications, secondary fibromyalgia and depression.

Methods: 42 consecutive patients with SLE (38 women, 4 men) and 20 healthy, sex, body mass index (BMI) and age matched controls (15 women, 5 men) were consecutively recruited and underwent an ambulatory sleep study using the WatchPAT device. All participants completed questionnaires including Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Functional Assessment of Chronic Illness Therapy (FACIT), Widespread Pain Index (WPI), Symptoms Severity Scale (SSS) and Beck Depression Inventory. SLE disease activity and damage were assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Systemic Lupus International Collaborating Clinics (SLICC) damage index.

Results: The mean AHI was 9.19 ± 6.79 in the SLE group and 3.95 ± 3.47 in the control group ($p=0.004$). Moderate-severe OSA (AHI≥15) was significantly more common in patients with SLE (23.6% vs. 0%, $p=0.04$). Patients with SLE had lower sleep efficiency (83.38 ± 6.15 vs. 87.22 ± 4.24, $p=0.03$), increased sleep arousals (7.72 ± 5.66 vs. 5.13 ± 2.29, $p=0.01$), higher PSQI and FACIT scores SLE (8.14 ± 3.47 vs. 5.10 ± 2.64, $p=0.001$, 16.89 ± 11.19 vs. 7.29 ± 5.93, $p=0.0008$ respectively) and had more fibromyalgia as assessed by WPI and SSS



SLE, Systemic Lupus Erythematosus; RDI, Respiratory Disturbance Index; AHI, Apnea Hypopnea Index; ODI, Oxygen Desaturation Index

(19.5% vs. 0%, p=0.04). BMI and the SLICC score were independent predictors of OSA (p=0.03 and p=0.02 respectively). A correlation between SLEDAI and moderate-severe OSA was found (p=0.03), although an association to medications, secondary fibromyalgia and depression was not found.

Conclusion: Patients with SLE have increased prevalence of OSA with lower sleep quality compared to healthy controls. Our findings suggest a possible correlation between accrued damage as assessed by the SLE damage index and OSA.

REFERENCES:

[1] Wu, L., Shi, P. L., Tao, S. S., Tao, J. H. & Wu, G. C. Decreased sleep quality in patients with systemic lupus erythematosus: a meta-analysis. *Clin. Rheumatol.* (2020) doi:10.1007/s10067-020-05300-3.

[2] Palagini, L. *et al.* Sleep disorders and systemic lupus erythematosus. *Lupus* vol. 23 115–123 (2014).

[3] Javaheri, S. & Javaheri, S. Update on Persistent Excessive Daytime Sleepiness in OSA. *Chest* vol. 158 776–786 (2020).

[4] Mertz, P. *et al.* Towards a practical management of fatigue in systemic lupus erythematosus. *Lupus Science and Medicine* vol. 7 (2020).

Table 1. WatchPAT sleep parameters analysis

	SLE group n = 42	Control group n = 20	P value
RDI ± SD	13.52 ± 6.54	9.72 ± 3.60	0.04
AHI ± SD	9.19 ± 6.79	3.95 ± 3.47	0.004
ODI ± SD	2.54 ± 2.72	1.27 ± 1.45	0.04
Sleep efficiency (%) ± SD	83.38 ± 6.15	87.22 ± 4.24	0.03
Number of arousals ± SD	7.72 ± 5.66	5.13 ± 2.29	0.01
Saturation (%) ± SD	96.10 ± 1.37	95.75 ± 1.39	0.45
Sleep latency ± SD	21.25 ± 9.33	18.46 ± 6.63	0.27
REM latency ± SD	87.88 ± 49.06	73.60 ± 46.21	0.09
REM ± SD	25.35 ± 14.03	27.32 ± 6.79	0.15
Light sleep ± SD	57.63 ± 12.37	52.70 ± 11.63	0.18
Deep sleep ± SD	17.89 ± 5.59	18.76 ± 6.70	0.54

SLE, Systemic Lupus Erythematosus; RDI, Respiratory Disturbance Index; SD, Standard Deviation; AHI, Apnea Hypopnea Index; ODI, Oxygen Desaturation Index; REM Rapid Eye Movement.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1524

AB0313 THE CLINICAL CHARACTERISTICS OF PATIENTS WITH IMMUNE-ASSOCIATED ADVERSE PREGNANCY

W. Su[1,2], Y. Zhuang[1,2], J. Zhu[1,2]. [1]*Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Department of Rheumatology and Immunology, Chengdu, China*; [2]*Chinese Academy of Sciences Sichuan Translational Medicine Research Hospital, Department of Rheumatology and Immunology, Chengdu, China*

Background: Immune-associated adverse pregnancy is the adverse pregnancy outcomes induced by autoimmune factors or autoimmune diseases, including infertility, recurrent spontaneous abortion, failed assisted reproduction, fetal growing restriction. It is helpful to explore the mechanism and improve the management by analyzing the clinical characteristics of patients with immune-associated adverse pregnancy.

Objectives: To find the risk factors of Immune-associated adverse pregnancy by analyzing the clinical characteristics of patients with immune-associated adverse pregnancy.

Methods: The patients involved in this study were from the multi-department clinic of immune-associated adverse pregnancy, during April 2019 and August 2020. They were diagnosed with autoimmune diseases according to relative classification standards or with autoimmune abnormality. Patients with adverse pregnancy due to anatomic, endocrine, infectious and chromosomal factors were excluded.

Results: A total of 107 patients were included. The average age was 29.3 years old. The number of total adverse pregnancy was 115 and the average was 1.07. For the diagnosis, 22 (22.4%) were autoimmune abnormality (with autoantibody but cannot be classified to any autoimmune disease), 30 (28.0%) were antiphospholipid syndrome (APS), 17 (15.9%) were systemic lupus erythematosus (SLE), 13 (12.1%) were mixed connective tissue disease (MCTD), 8 (7.5%) were undifferentiated connective tissue disease, 5 (4.7%) were Sjogren syndrome (SS), other autoimmune disease account for 10 (9.4%). For the antibodies, the positive rate of ANA was 44.8% (48/107), anti-SSA 36.4% (39/107), anti-RNP 15.0% (16/107), anti-dsDNA8.4% (9/107), anti-Sm 9.3% (10/107), anticardiolipin antibody 17.8% (19/107), anti-B2GP1 24.3% (26/107), LA 8.4% (9/107), non-criteria antiphospholipid antibody 3.7% (4/107).

Conclusion: Our data showed that autoimmune abnormality, SLE, APS, MTCD and SS impacted immune-associated adverse pregnancy the most. The most crucial antibodies were ANA, anti-SSA, anti-RNP, anti-dsDNA and antiphospholipid antibodies.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1806

AB0314 SEMAPHORIN 3A LEVELS IN LUPUS WITH AND WITHOUT SECONDARY ANTIPHOSPHOLIPID ANTIBODY SYNDROME AND RENAL INVOLVEMENT

G. S. Kart-Bayram[1], D. Bayram[1], A. Erden[2], S. C. Güven[2], B. Özdemir[2], H. Apaydın[2], A. Omma[2], Ö. Karakaş[2], B. Armagan[2], K. Gok[2], Y. Maraş[2], O. Ateş[3], C. Topçuoğlu[3], O. Küçükşahin[2], S. Erten[2]. [1]*Ankara Şehir Hastanesi, Internal Medicine, Ankara, Turkey*; [2]*Ankara Şehir Hastanesi, Rheumatology, Ankara, Turkey*; [3]*Ankara Şehir Hastanesi, Biochemical, Ankara, Turkey*

Background: In this study, we aimed to evaluate sema3A levels in SLE patients with and without renal involvementor secondary antiphospholipid antibody syndrome (APS), to further elucidate the contribution ofsema3A in etiopathogenesis these conditions

Objectives: Aim of this study is to evaluate sema3A levels in systemic lupus erythematosus patients (SLE) with and without renal involvement and secondary antiphospholipid antibody syndrome (APS).

Methods: SLE patients were grouped according to presence of secondary APS or renal involvement. The control group consisted of age-matched, non-smoker, healthy volunteers. Sema3A levels were compared among groups. All SLE patients were regrouped according to presence of thrombotic events, miscarriages and proteinuria and sema3A levels were investigated. Finally, sema3A levels of all SLE patients as a single group were compared to controls.

Results: The mean sema3A values were 16.16±2.84 ng/dL in the control group, 11.28±5.23 ng/dL in SLE patients without nephritis and APS, 9.05±5.65 ng/dL in SLE with APS group, and 8.53±5.11 ng/dL in lupus nephritis group. When all three patient groups were examined as a single group, mean sema3A value was significantly lower than that of the control group. Sema3A was reduced in SLE patients with thromboembolism and/or miscarriage.

Conclusion: Sema3A levels were lower in all patient groups compared to the control group. Moreover, the reduced sema3A levels in patients with a history of thromboembolism and/or miscarriage suggests that sema3A may play an important role in the pathogenesis of vasculopathy

Table 1. Comparison of sema3A levels between SLE patient groups and control subjects

	Patient groups				p
	Group A (N=20)	**Group B (N=20)**	**Group C (N=19)**	**Control (N=19)**	
Sema3A, ng/dL, mean ± SD	9.05 ± 5.65	11.28 ± 5.23	8.53 ± 5.11	16.16 ± 2.84	Group A vscontrol<0.001 Group B vscontrol<0.001 Group C vscontrol<0.001 Group A vs B = 0.203 Group A vs C = 0.766 Group B vs C = 0.106
					<0.001
All patients (N=59) 16.16 ± 2.84		**Control (N=19)** 9.64 ± 5.38			
		Patients with thrombotic events and/or miscarriages (N=31)		**Patients without thrombotic events and/or miscarriages (N=48)**	
0.032		9.96 ± 5.11		12.33 ± 5.84	<0.001
Patients with proteinuria and/or thrombotic events and/or miscarriages (N=45) 14.91± 4.50		**Patients without proteinuria and/or thrombotic events and/or miscarriages (N=34)**		9.05 ± 5.09	

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1864

AB0315 DISEASE DAMAGE ACCRUAL AND LOW BONE MINERAL DENSITY IN FEMALE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

M. Correa Rodríguez[1,2], G. Pocovi-Gerardino[2], J. L. Callejas-Rubio[2,3], R. Ríos Fernández[2,3], S. Delolmo-Romero[1], N. Ortego[2,4], B. Rueda-Medina[1,2]. [1]*University of Granada, Nursing, Granada, Spain*; [2]*Biohealth Research Institute*

in Granada (ibs.GRANADA), Biohealth Research Institute in Granada (ibs.GRANADA), Granada, Spain; [3]*Unidad de Enfermedades Autoinmunes Sistémicas, Servicio de Medicina Interna, Hospital Universitario San Cecilio., Unidad de Enfermedades Autoinmunes Sistémicas, Servicio de Medicina Interna, Hospital Universitario San Cecilio., Granada, Spain*; [4]*University of Granada, Department of Medicine. Faculty of Medicine. University of Granada, Granada, Spain*

Background: Osteoporosis is a common comorbidity in patients with systemic lupus erythematosus (SLE). Available evidence showed that autoimmunity and associated inflammation play main effect in the pathogenesis of negative skeletal effects in SLE patients. However, the potential contribution of disease-associated factors to bone status in SLE is not well known since the reported risk factors from different studies differ greatly.
Objectives: The aim of this study was to examine frequency of reduced bone mass in SLE women, and determine their potential associations with disease activity, damage accrual and SLE-related clinical markers.
Methods: A cross-sectional study including a total 121 Caucasian pre-menopausal and postmenopausal women was conducted (mean age 49.29±12.43 years). The SLE Disease Activity Index (SLEDAI-2K) and the SDI Damage Index were used to asses disease activity and disease-related damage, respectively. Bone mineral density (BMD) of the left femoral neck and lumbar spine (L2–L4) were measured by dual-energy X-ray absorptiometry (Hologic QDR 400).
Results: Ten patients (8.3%) had osteoporosis, 63 (52.1%) patients had osteopenia and 6.8% of women had history of previous fracture. Patients with low bone mass had a significantly higher mean SDI (1.36±1.26 versus 0.70±1.09 p=0.003). T-score at lumbar spine was inversely correlated with SDI score (r=-0.222, p=0.014) and complement C3 level (r=-0.206, p=0.024). Results of bivariate correlations showed that T-score at lumbar spine was inversely correlated with SDI score (r=-0.222, p=0.014) and complement C3 level (r=-0.206, p=0.024). SDI scores were significantly different between patients with osteoporosis, osteopenia and normal BMD after adjusting for age, menstrual status, BMI, time since diagnosis and corticoid use (p=0.004).
Conclusion: There is a high prevalence of low BMD in Caucasian women with SLE and this status of osteopenia/osteoporosis was associated with higher damage accrual scores, supporting that disease damage may itself be a major contributor to the low BMD. SLE women with organ damage require regular bone status monitoring to prevent further musculoskeletal damage. Since diminished BMD is a main comorbidity it is therefore essential to study, monitor and prevent osteoporosis in SLE women to avoid fractures leading to reduced quality of life.
REFERENCES:

[1] Wang X, Yan S, Liu C, Xu Y, Wan L, Wang Y, et al. Fracture risk and bone mineral density levels in patients with systemic lupus erythematosus: a systematic review and meta-analysis. Osteoporos Int 2016;27:1413–23.
[2] Mendoza-Pinto C, Rojas-Villarraga A, Molano-Gonzalez N, Jimenez-Herrera EA, De La Luz Leon-Vazquez M, Montiel-Jarquõn A, et al. Bone mineral density and vertebral fractures in patients with systemic lupus erythematosus: A systematic review and meta-regression. PLoS One 2018;13:1–15.
[3] Xia J, Luo R, Guo S, Yang Y, Ge S, Xu G, et al. Prevalence and Risk Factors of Reduced Bone Mineral Density in Systemic Lupus Erythematosus Patients: A Meta-Analysis. Biomed Res Int 2019;2019.
[4] Carli L, Tani C, Spera V, Vagelli R, Vagnani S, Mazzantini M, et al. Risk factors for osteoporosis and fragility fractures in patients with systemic lupus erythematosus. Lupus Sci Med 2016;3:1–5.

Acknowledgements: This research was supported by the grant PI0523-2016 from "Consejería de igualdad, salud y políticas sociales" (Junta de Andalucía) and is part of the research group LyDIMED "Lupus y Dieta Mediterránea".
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2011

AB0316 ADHERENCE TO THE MEDITERRANEAN DIET AND ITS ASSOCIATION WITH DISEASE ACTIVITY AND DAMAGE ACCRUAL IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

M. Correa Rodríguez[1,2], G. Pocovi-Gerardino[2], J. L. Callejas-Rubio[2,3], R. Ríos-Fernández[2,3], M. Martín Amada[4], M. Cruz-Caparrós[5], B. Rueda-Medina[1,2], N. Ortego[2,6]. [1]*University of Granada, Nursing, Granada, Spain*; [2]*Biohealth Research Institute in Granada (ibs.GRANADA), Granada, Spain*; [3]*Unidad de Enfermedades Autoinmunes Sistémicas, Servicio de Medicina Interna, Hospital Universitario San Cecilio., Unidad de Enfermedades Autoinmunes Sistémicas, Granada, Spain*; [4]*Unidad de Enfermedades Autoinmunes Sistémicas. Servicio de Medicina Interna. Complejo Hospitalario de Jaén, Spain., Unidad de Enfermedades Autoinmunes Sistémicas., Jaén, Spain*; [5]*Unidad de Enfermedades Autoinmunes Sistémicas. Servicio de Medicina Interna. Hospital de Poniente, El Ejido, Spain, Unidad de Enfermedades Autoinmunes Sistémicas, Almería, Spain*; [6]*University of Granada, Department of Medicine. Faculty of Medicine. University of Granada. Avenida de la Investigación, 11, 18016 Granada, Spain., Granada, Spain*

Background: There is limited evidence regarding the impact of the Mediterranean Diet (Med Diet) on autoimmune diseases although it has been proposed that adherence to the Med Diet may decrease the risk of certain autoimmune diseases. However, the potential usefulness of the Med Diet as a high-quality dietary pattern for other autoimmune diseases such as SLE has not yet been investigated.
Objectives: The aim of this study was to evaluate the potential association between the adherence to the Med Diet and disease activity, damage accrual and SLE-related clinical markers in a large cohort of women with SLE.
Methods: In this cross-sectional study, we assessed Med Diet adherence through a 14-item questionnaire in 253 women with SLE (mean age 46.74 ± 12.70 years). The SLE Disease Activity Index (SLEDAI-2K) and the SDI Damage Index were used to asses disease activity and disease-related damage, respectively. Levels of C-reactive protein (CRP; mg/dL), homocysteine (Hcy; mol/L), anti-double stranded DNA antibodies (anti-dsDNA) (IU/mL), complement C3 (mg/dL), and complement C4 (mg/dL) were determined.
Results: The Med Diet adherence score was classified as follows: low adherence (≤ 5 points); medium adherence (6–9 points) and good adherence (≥ 10 points). Only 50.2% of the SLE women had good adherence to the Med Diet. The ANCOVA models showed significant differences between patients with good adherence to the Med Diet and those with medium and low adherence in SLEDAI ($p \leq 0.001$) and SDI ($p \leq 0.001$). Age, medical treatment (immunosuppressors, corticoids, or antimalarials), smoking status, and body mass index (BMI) were included as confounding factors. The odds ratio (OR) for having active SLE (SLEDAI ≥ 5) or the presence of damage (SDI ≥ 1) was lower among patients whose Med Diet score was higher ($p \leq 0.001$).
Conclusion: Adherence to the Med Diet influences disease activity and damage accrual in SLE women. Thus, these patients would benefit from nutritional counselling and education on modification, to help adapt their lifestyles towards the Med Diet pattern. This would help slow the progression of SLE and the damage it causes.
REFERENCES:

[1] Sedaghat F, Jessri M, Behrooz M, Mirghotbi M, Rashidkhani B. Mediterranean diet adherence and risk of multiple sclerosis: a case-control study. Asia Pac J Clin Nutr. 2016;25(2):377–84.
[2] orsyth C, Kouvari M, D'Cunha NM, Georgousopoulou EN, Panagiotakos DB, Mellor DD, et al. The effects of the Mediterranean diet on rheumatoid arthritis prevention and treatment: a systematic review of human prospective studies. Rheumatol Int. 2018 May 18;38(5):737–47.
[3] Minihane AM, Vinoy S, Russell WR, Baka A, Roche HM, Tuohy KM, et al. Low-grade inflammation, diet composition and health: current research evidence and its translation. Br J Nutr. 2015 Oct 14;114(7):999–1012.

Acknowledgements: This research was supported by the grant PI0523-2016 from "Consejería de igualdad, salud y políticas sociales" (Junta de Andalucía) and is part of the research group LyDIMED "Lupus y Dieta Mediterránea".
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2054

AB0317 ADHERENCE TO MEDITERRANEAN DIET AND NUTRITIONAL STATE IN ITALIAN WOMEN WITH ISOLATED SJÖGREN'S SYNDROME

R. Izzo[1], S. Colafrancesco[1], A. Pinto[2], A. Gattamelata[1], F. Giardina[1], F. Claudia[2], L. M. Donini[2], R. Priori[1]. [1]*Sapienza Università di Roma, Dipartimento di Medicina interna e Specialità Mediche, Roma, Italy*; [2]*Sapienza Università di Roma, Dipartimento di Medicina Sperimentale, Roma, Italy*

Background: The Mediterranean Diet (MD) has anti-inflammatory and immunomodulatory effects[1,2] suggesting a protective role in rheumatic diseases. There is limited knowledge about the eating habits and the nutritional state in patients with isolated Sjögren Syndrome (SS) living within the Mediterranean area.
Objectives: assessment of adherence to the MD and analysis of the nutritional state in women with SS and their correlations with the clinical, laboratory and histological data of the disease.
Methods: patients classified as isolated SS according to AECG criteria 2002[3] who had undergone to minor salivary gland biopsy during the previous twelve months were consecutively enrolled during follow-up visits. The adherence to the MD was assessed by the Med Diet (MDiet)[4] which includes eleven groups of foods; to each group is assigned a value ranging between 0 and 5 based on the frequency of monthly intake. The total score spans from 0 (poor adherence) to 55 (maximum adherence). The level of physical activity was measured by the 6-minutes walking test (6MWT) and by the International Physical Activity Questionnaire (IPAQ). Systemic disease activity was evaluated with the EULAR SS disease activity index (ESSDAI); EULAR SS patient-reported index (ESSPRI) was calculated as well. A subgroup of patients was asked to fill a daily food

diary processed with FOOD CONS software which allows to study in detail their eating habits. Nutritional state, muscle strength and basal metabolic rate were assessed. Alcoholism or drug abuse, diabetes mellitus, specific dietary models, treatment with drugs and/or food supplements with anti-inflammatory and/or antioxidant activity were considered exclusion criteria. Multivariate linear regression was performed with R project for Statistical Computing.

RESULTS:

N= 40	N= 26
Age, median (range)	53 (25-80) 33 (25-71)
BMI, median (range)	21 (19-29.3) 25.1 (19-33.7)
MedDiet score, median (range)	33 (26-43) 33 (23-40)
ESSDAI, median (range)	2 (0-16) 1 (0-16)
ESSPRI, median (range)	6 (0-8.6) 5.3 (1.6-9)
ESSPRI dryness, median (range)	6 (0-10) 6 (2-10)
Focus score, median (range)	2.5 (0-9.6) 1.7 (0.8-6.24)
ASM kg, median (range)	- 16.8 (13.3-21.7)
IPAQ meters, median (range)	- 1386 (99-11865)
6MWT meters, median (range)	- 595 (536-680)

BMI, body mass index; ASM appendicular skeletal mass; IPAQ International Physical Activity Questionnaire; 6MWT, six minute walking test.

MDiet was administered to 40 female SS outpatients. Even if not reaching significativity, patients with a higher focus score in their MSG have a lower value of MDiet score (p = 0.058, r = -1.00). The MDiet score is not associated with ESSDAI (p = 0.85, r 0.02), but only with lower serum levels of C3 (p = 0.004, r = - 0.08).

In 26 patients, daily food questionnaire shows that their diet consists of 43% of carbohydrates while fats represent 40% of total energy intake, the remaining 17% daily energy comes from proteins. Fat consumption is higher compared to the levels of energy and nutrient intake for the Italian population[5]. Six patients had a reduction in muscle mass; sarcopenia is not associated to ESSDAI (p = 0.610). The MDiet score and the amount eaten of polyunsaturated fatty acids (PUFA) were reduced in patients with high value of subscale dryness of ESSPRI (p = 0.057, r -1.21; p =0.610, r -1.00).

Conclusion: This study highlights a lower degree of glandular lymphocytic infiltration (expressed as focus score) in minor salivary glands in patients following MD, so its anti-inflammatory role of seems to be confirmed. SS patients have an unbalanced diet because of a higher intake of fat foods, likely for their lubricating effect. Despite the absence of correlation with objective parameters, the increased dryness in patients with a reduced intake of PUFA arouses our interest in a future study including omega-3 supplementation.

REFERENCES:

[1] **Schwingshackl L et al., Nutr Metab Cardiovasc Dis 2014**
[2] **Mena MP et al., Am J Clin Nutr. 2009**
[3] **Vitali C et al, ARD 2002**
[4] **Panagiotakos D et al., J Med Food 2007**
[5] **LARN 2014**

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2154

AB0318 RISK FOR CONCOMITANT AUTOIMMUNITY IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME; A SWEDISH COHORT STUDY

N. Karandyszowska[1], J. Oesman[1], H. Alagündüz[1], M. Magnusson[2], E. Svenungsson[1], M. Bruzelius[1], A. Antovic[3]. *[1]Karolinska Institutet, Department of Medicine Solna, Stockholm, Sweden*; *[2]Karolinska Institutet, Clinical Chemistry and Blood Coagulation, MMK, Stockholm, Sweden*; *[3]Karolinska Institutet, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden*

Background: In patients with the antiphospholipid syndrome (APS), concomitant systemic autoimmune rheumatic diseases (SARD) are common and often associated with more disease associated damage.

Less is known about the prevalence of non-rheumatic autoimmune diseases (NRAID) in patients with APS.

Objectives: To evaluate the incidence and prevalence of concomitant autoimmune diseases (AID) in a cohort of APS patients. The risk of AID was also evaluated with respect to the antiphospholipid antibodies (aPL) profiles.

Methods: This retrospective cohort study comprises consecutive patients identified with APS through review of electronic medical records at Karolinska University Hospital, Sweden between 2014 and 2020. Exclusion criteria were misdiagnosis and age <18. Descriptive statistics was used for baseline data and multivariable Cox proportional hazard regression analysis to investigate the risk factors to develop new onset AID. Ethical approval was obtained from the Swedish Ethical Review Authority (2020-02333).

Results: Of 271 included patients, 66% were women and the median age at diagnosis of APS was 43 years (IQR 31–55). At inclusion, 130 (48%) patients presented with other AID; 101 (37%) of them had a concomitant SARD while 54 (19%) had a NRAID. Systemic lupus erythematosus (SLE) was the most frequent in 30% of patients, followed by autoimmune thyroid disease (ATD) in 10% of patients.

In addition, 35 (13%) APS-patients developed AID during the study period, corresponding to an incidence rate of 28.4 (95% CI; 19.3-40.3) per 1.000 person-years with mean time at risk of 4 (±2) years. Twenty-one (8%) patients developed a SARD and further 14 (5%) were diagnosed with a NRAID.

The cumulative incidence for AID was significantly higher in patients with high titers of IgG aPL. Patients that developed SARD had significantly higher median titers of a-β2GPI IgG isotype, p=0.05. In the NRAID group, median a-β2GPI and aCL IgG isotypes were significantly increased, p=0.02 and p=0.04, respectively. *The hazard ratio to develop diagnosis of AID was significantly increased in patients with high titers of the IgG isotype aPL (HR 2.4 95% CI; 1.1-5.3). Obstetric APS manifestations were associated with a significantly increased hazard ratio of 2.8 (95% CI; 1.1-7.7) to develop SARD, and also trendwise for AID, as a compound variable.*

During the study period, 52 patients had at least one new APS manifestation, as defined by the Sydney criteria (1). In comparison to patients without new manifestations, these patients had significantly higher median titers of aPL of the IgG isotype, and concomitant AID at first visit (p=0.01, p=0.02, respectively).

Conclusion: APS patients are at high risk to develop other AID, and APS patients with concomitant AID had an increased risk to develop new clinical APS manifestations. These findings might be helpful when considering risk stratification and alternate treatment options in this patient group.

REFERENCES:

[1] Miyakis S, Lockshin MD, Atsumi T et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006; 4: 295–306.

Acknowledgements: I have no acknowledgements to declare.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2194

AB0319 HEALTH-RELATED QUALITY OF LIFE ASSESSED BY LUPUSQOL IN 1102 LUPUS PATIENTS FROM RUSSIAN FEDERATION (RF), KIRGHIZSTAN AND KAZAKHSTAN (RENAISSANCE COHORT)

E. Aseeva[1], S. Solovyev[1], G. Koilubaeva[2], B. Issayeva[3], M. Saparbayeva[3], N. Nikishina[4], A. Mesnyankina[4], A. Lila[1]. *[1]Rheumatology Federal State Research Institution (FSRI) named after V.A . Nasonova, Intensive Care Department, Moscow, Russian Federation*; *[2]Rheumatology, National Center of Cardiology and Internal Medicine named after Academician M. Mirrahimov (NCCIM), Rheumatology Department, Bishkek, Kyrgyzstan*; *[3]Asfendiyarov National Medical University, City Rheumatology Center, Almaty, Kazakhstan*; *[4]Rheumatology Federal State Research Institution (FSRI) named after V.A. Nasonova, Intensive Care Department, Moscow, Russian Federation*

Background: Health related quality of life (HRQoL) is an aspect that is generally underexplored in the routine clinical practice but it is attracting more and more attention. Lack of concordance between physician derived outcomes of disease activity and patient HRQoL outcomes is commonly found in SLE. This is due to the fact that the former is influenced by the immunologic pathogenic inflammatory mechanisms while the latter may be affected by a variety of psychological, social and co-morbid conditions.

Objectives: The aim of this study was to compare health-related quality of life assessed by LupusQoL in 1102 Lupus patients (pts) from the Russian Federation, Kirghizstan and Kazakhstan (RENAISSANCE cohort).

Methods: 1102 SLE pts who fulfilled SLICC 2012 criteria were enrolled into the study. The SLEDAI 2K index activity, SLICC damage index, and HRQoL using the LupusQoL questionnaire (validated for the Russian-speaking population in 2018) were evaluated. Descriptive statistics, Spearman's correlation coefficients were performed to analyze the data.

Results: 400/600/102 Lupus pts from RF, Kirghizstan and Kazakhstan respectively were studied. The pts were predominantly female (91%/93%/98%) and of indigenous nationality (Russian 83%/ Kirghiz 88%/ Kazakh 76%) with a mean±SD age of 34,2±11,5/35,07±12,2/33,8±10,5 years (p=0,36; p=0,96) respectively. The mean disease duration (Me) in RF/ Kazakhstan was 6 [3;12]/ 5[2;9] years (p=0,15), in Kirgizstan - 2[0,6; 7] years(p≤0,05). Kazakh pts (p=0,00) have higher disease activity (SLEDAI 2K) 17,6±8,8 than Kirghiz pts 15,1±8,3 and Russian pts 9,4±8,1. SLICC damage index 2,39±1,61 in Kazakh pts (p=0,00) was higher than in Russian 1,57±1,54 and Kirghiz 0,79±0,32 pts. 54% pts from RF and 58 % from Kazakhstan had high education. Only 33% pts from Kirgizstan also had high education. 45%/24%/33% pts from RF, Kirgizstan and Kazakhstan respectively had steady employment, 53%/30%/32% pts received disability benefits. HRQoL assessed by LupusQoL was low in all patients with SLE. The mean scores for each of the domains of LupusQoL are shown in Table 1. The statistically significant lowest HRQoL in all 8 domains is obtained among

Kirghiz patients in the comparative analysis of HRQoL in SLE patients of RF and Kazakhstan. The HRQoL was comparable in lupus patients from RF and Kazakhstan. There was a strong correlation between Sum LupusQoL domain and age (r = -0.19), steady employment (r=0,28), high education (r = 0.19), disease duration (r = -0.29), SLEDAI 2K index activity (r = -0.22), SLICC damage index (r = -0.25).

Table 1. HRQoL Assessed by LupusQoL in 1102 Lupus Patients from The Russian Federation, Kirgizstan and Kazakhstan

LupusQoL domains	Russian Federation Mean (SD)	Kazakhstan Mean (SD)	P	Kyrgyztan Mean (SD)	P
Physical health	67,2±23,04	63,1±24,5	0,25	44,6±28,6	0,00
Pain	70,2±24,5	65,2±25,5	0,3	45,9±29,3	0,00
Planning	64,4±28,9	65,9±27,4	0,17	46,5± 31,5	0,00
Intimate	59,3±39,9	58,4±36,7	0,5	57,5±38,5	0,00
relationships					
Burden to others	57,1±27,7	56,6±27,7	0,34	41,1±30,9	0,00
Emotional health	64,9±24,9	65,9±23,4	0,21	48,3±27,9	0,00
Body image	61,4±31,6	62,5±26,5	0,17	57,7±28,6	0,00
Fatigue	63,0±24,8	58,6±26,3	0,16	47,7±28,1	0,00
LupusQoL Sum	63,1±20,4	60,8±20,1	0,25	48,5±23,5	0,00

Conclusion: HRQoL assessed by LupusQoL was low in SLE pts from the RF, Kirgizstan and Kazakhstan. The lowest HRQoL is reported among Kirghiz patients in the comparative analysis of HRQoL with SLE patients in RF and Kazakhstan. The low HRQoL is associated with age, unavailability of work, low education, disease duration, disease activity and damage.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2277

AB0320

CLINICAL FEATURES AND TREATMENT OF 1102 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN THE RUSSIAN FEDERATION (RF), KIRGIZSTAN AND KAZAKHSTAN IN REAL CLINICAL PRACTICE (RENAISSANCE COHORT)

E. Aseeva[1], S. Solovyev[1], G. Koilubaeva[2], B. Issayeva[3], M. Saparbayeva[3], N. Nikishina[1], A. Mesnyankina[1], A. Lila[1]. [1]*Rheumatology Federal State Research Institution (FSRI) named after V.A . Nasonova, Intensive Care Department, Moscow, Russian Federation*; [2]*Rheumatology, National Center of Cardiology and Internal Medicine named after Academician M. Mirrahimov (NCCIM), Rheumatology Department, Bishkek, Kyrgyzstan*; [3]*Asfendiyarov National Medical University, City Rheumatology Center, Almaty, Kazakhstan*

Background: Clinical features of systemic lupus erythematosus may differ significantly in various regions and are frequently associated with the ethnicity of patients.

Objectives: The aim of this study was to compare clinical features and treatment of patients with systemic lupus erythematosus in the Russian Federation (RF), Kirgizstan and Kazakhstan in real clinical practice.

Methods: 1102 SLE pts who fulfilled SLICC 2012 criteria were enrolled into the study. Disease activity was evaluated by the SLEDAI-2K, and chronic damage by the Systemic Lupus International Collaborating Clinics Damage Index score (SDI).

Results: 400/600/102 Lupus pts from RF, Kirgizstan and Kazakhstan respectively were studied. Pts were predominantly female (91%/93%/98%) with a mean±SD age of 34,2±11,5/35,07±12,2/33,8±10,5 years (p=0,36; p=0,96) respectively. The mean disease duration (Me) in RF/ Kazakhstan was 6 [3;12]/ 5[2;9] years (p=0,15), in Kirgizstan- 2[0,6; 7] years(p≤0,05). Kazakh pts (p=0,00) have higher disease activity (SLEDAI 2K) 17,6±8,8 than Kirghiz pts 15,1±8,3 and Russian pts 9,4±8,1. The higher SLICC damage index 2,39±1,61was in Kazakh pts (p=0,00) as compared to the Russian. Clinical features of 1102 patients with systemic lupus erythematosus in the Russian Federation (RF), Kirgizstan and Kazakhstan are shown in Table 1. Among the Kirghiz, most of the patients were with Neuropsychiatric disorders (33%), vasculitis (27%), serositis (49%) and lupus nephritis (41%). Patients in RF and Kazakhstan were more likely to have arthritis (60%/80%) and mucocutaneus lesions (44%/74%) respectively.

Russian/Kirghiz/ Kazakh pts received corticosteroids per os with duration (Me) 48[18; 106] /24[7,2; 84]/ 37[13; 84] months. The mean±SD dosage was 17,8±12,0/23,2± 19,9/12,33±9,8 mg per day. Among cytostatic drugs, patients in Kirgizstan were prescribed more often cyclophosphamide (64%) and methotrexate (27%). They were prescribed mofetila micofenolate much less frequently (4%) than patients from Russia (20%) and Kazakhstan (46%). Prescription of cyclophosphamide, azathioprine and methotrexate in the Russian and Kazakhstan pts was approximately of the same frequency and ranged from 10 to 23%. Hydroxychloroquine was obtained in 67%/26%/51% Russian/Kirghiz/ Kazakh pts respectively. Disability benefits in RF included payment for biological therapy. Lupus patients in Kirgizstan and Kazakhstan bought biological drugs at their own expense. In RF rituximab was administrated in 34% cases and belimumab -in 10%. In Kirgizstan and Kazakhstan rituximab was administrated in 2% and 6% respectively.

Table 1. Clinical Features of 1102 Patients with Systemic Lupus Erythematosus in the Russian Federation (RF), Kirgizstan and Kazakhstan

Clinical features	Russian Federation n (%)	Kyrgyztan n (%)	Kazakhstan n (%)
Pyrexia	52(13%)	276 (46%)	15 (15%)
Neuropsychiatric	68 (17%)	198 (33%)	34(33%)
Mucocutaneus	176 (44%)	396 (66%)	75 (74%)
Vasculitis	40 (10%)	162 (27%)	4 (4%)
Arthritis	240 (60%)	282 (47%)	81(80%)
Myocarditis	16 (4%)	78 (13%)	-
Serositis	52 (13%)	294 (49%)	12 (12 %)
Lupus nephritis	116 (29%)	246 (41%)	24 (24%)
Leukopenia≤3x10^9	36 (9%)	96 (16%)	6 (6%)
Trombocytopenia ≤ 100X 10 ^{9}	12 (3%)	90(15%)	5(5%)
Anti dsDNA ≥20 Ед\мл	276 (69%)	198 (33%)	80 (80%)
Low complement	200 (50%)	324 (54%)	6 (6%)

Conclusion: Significant differences have been revealed in the Kirghiz patients as compared to those of the RF and Kazakhstan. Disease activity in vital organs was more often revealed in the Kirghiz patients: neuropsychiatric disorders, vasculitis, serositis and lupus nephritis. As a result, they received a higher mean corticosteroids dose and cyclophosphamide was administered more often. Prescription of biological therapy was limited by a high cost of such sort of drugs. In spite of this fact, the highest SLICC damage index was demonstrated by the Kazakh cohort (2,38 score, while the lowest of merely 0,79) was in the Kirghiz cohort.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2312

AB0321

SALIVARY GLANDS ULTRASONOGRAPHY AS A DIAGNOSTIC TOOL IN PRIMARY SJÖGREN'S SYNDROME ON THE RUSSIAN COHORT OF PATIENTS

J. Khvan[1], A. Torgashina[1], B. Chalcev[1], E. Sokol[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Intensive Care of Rheumatic Diseases, Moscow, Russian Federation*

Background: In the international scientific community there has been a long discussion about the role of ultrasound and ultrasound scores for assessing the structure of the salivary glands in Sjögren's syndrome. Stomatological examination according to The American College of Rheumatology (ACR) 2012 classification criteria of primary Sjögren's syndrome (pSS) includes only labial salivary gland biopsy (focus score - FS) and the ACR with European League Against Rheumatism (ACR/EULAR) 2016 criteria include FS and unstimulated saliva flow test (SFT).

Objectives: to compare the diagnostic value of ultrasonography salivary glands (SGUS) with other methods (sialography, stimulated SFT, FS).

Methods: From 2016 to 2020, we examined 94 patients (93 women, 1 man) with the mean age 48.6 ± 14.3 years (minimum 18, maximum 78) with newly diagnosed pSS according to Russian criteria 2001, 86% of patients fulfilled ACR 2012 criteria and 87% - the ACR/EULAR 2016 criteria. All patients underwent classical examination (stomatological, ophthalmological, immunological), and SGUS was performed using GE LOGIQ 9 on the two parotid and two submandibular glands. Ultrasound images were evaluated with the OMERACT SS severity scoring system from grades 0 to 3 (1). Statistical analyses (Spearman coefficient p <0.05) were performed using STATISTICA version 12.

Results: All patients in SGUS had inhomogeneity structure from mild to diffuse with hypoechoic areas from single to multiple. 4 patients had no signs of sialectasia on sialography, however, in ultrasound we found SGUS grade 2. In 5 patients with SGUS grade 0 we determined punctate sialectasia. Detailed characteristics of patients are presented in Table 1.

Table 1.

Parameters	N	%
Oral dryness	78	83,0
Enlargement of parotid salivary glands	32	34,0
Recurrent parotitis	19	20,2
Retention pain	31	33,0
RF positive >2UNL (>30 IU/ml)	51	54,2
anti-SSA (anti-Ro) positive (>25 IU/ml)	81	86,1
anti-SSB (anti-La) positive (>25 IU/ml)	48	51,0
ANA ≥ 1:320	94	100,0
SGUS 0	8	8,5
SGUS 1	1	1,0
SGUS 2	20	21,2
SGUS 3	65	69,1
Stimulated SFT < 2,5ml/5 min	59	62,8
Sialectasia on parotid sialography	90	94,7
Punctate sialectasia	12	12,6
Globular sialectasia	63	66,3
Cavitary sialectasia	10	10,5
Distructive sialectasia	6	6,3
FS ≥ 1foci/4 mm2	83	88,2

Correlation was calculated for each SGUS (0-3) with clinical and classical methods of examination of the salivary glands. Pronounced changes in SGUS 3 correlated with recurrent parotitis r = 0.22 (p = 0.03), enlargement of parotid salivary glands r = 0.23 (p = 0.02) and cavitary sialectasia r = 0.23 (p = 0.02). Histological changes FS ≥ 1 correlated with all grades on ultrasound (SGUS 0 r = -0.24 (p = 0.01), SGUS 1 r = 0.41 (p = 0.000027), SGUS 2 r = - 0.21 (p = 0.03), SGUS 3 r = 0.40 (p = 0.00006)). The punctate sialectasia correlated with SGUS 1 r = -0.28 (p = 0.005) and SGUS 0 r = 0.45 (p = 0.000004). Stimulated SFT didn't correlate with ultrasound changes.

Conclusion: : Probably, in everyday clinical practice, SGUS can be used as an additional method for salivary gland assessment, given the availability and safety of the method. The most convenient system for assessing the salivary glands, at present, is the OMERACT SS severity scoring system, however, now we don't have a score for the complete differentiation in pSS and lymphoproliferative complications.

References: :

[1] Jousse-Joulin, Sandrine et al. "Video clipassessment of a salivary gland ultrasound scoring system in Sjögren's syndrome using consensual definitions: an OMERACT ultrasound working group reliability exercise." Annals of therheumatic diseases vol. 78,7 (2019): 967-973. doi:10.1136/annrheumdis-2019-215024

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2455

AB0322 ASSOCIATION OF DEPRESSIVE SYMPTOMS ASSESSED BY BDI II WITH PHYSICAL ACTIVITY IN PATIENTS WITH PRIMARY SJÖGREN´S SYNDROME

S. Beider[1], T. Witte[1], D. Ernst[1]. *[1]Medical School Hanover, Department of Rheumatology and Immunology, Hannover, Germany*

Background: Patients with primary Sjögren´s syndrome (pSS) suffer from pain, oral or ocular dryness and fatigue. Such symptoms can have a detrimental impact on health-related quality of life. The prevalence of mental health disorders in patients with pSS is considerably higher than in the general population [1]. Regular physical activity, such as nordic walking, improves aerobic capacity and may reduce reported fatigue [2]. According to current European League Against Rheumatism (EULAR) recommendations, management of pSS concomitant diseases should be evaluated in patients presenting with fatigue and pain, and severity scored using specific tools [3].

Objectives: This study analyses the frequency and severity of depressive symptoms in patients with pSS and their relationship to fatigue and physical activity.

Methods: In this monocentric, cross-sectional study, patients with pSS attending our Rheumatology clinic between January 2019 and March 2020 completed standardized questionnaires: Beck´s depression inventory second edition (BDI II) and the international physical activity questionnaire short form (IPAQ-SF). Data were analyzed using SPSS 26 (IBM, Armonk, NY, USA). The tests include bivariate and partial correlations and nonparametric Kruskal-Wallis-Test.

Results: In total, 134 patients were included. The majority were female (117/134, 87.3 %), and the patients median age was 57 [21 – 85] years. Median duration of disease-related symptoms at inclusion was 56 months (range 0-388 months). Physical activity was low in 44. 8 % (n = 60), moderate in 32.1 % (n = 43), and high in 23.1 % (n = 31) of patients. Depressive symptoms of varying severity were identified in 76/134 (56.7%) of patients. Severe depression occurred in 10/76 (13.2%) and moderate depression in 14/76 (18.4%) patients. The remaining 52/76 (68.4%) patients had minimal or mild depression. Over two-thirds (67.7%) of patients reporting high physical activity showed no depression and no one with a high level of physical activity had severe depression. There was a clear association between the BDI II depression score and the level of physical activity (p = 0.003) regardless of age and illness duration. However, not all the symptoms assessed by BDI II had the same impact. From 21 items of the BDI II Inventory, symptoms such as loss of energy and fatigue were profoundly relevant, being reported by over 75 % of patients. The main depressive symptoms, which had a strong negative correlation with the level of physical activity were loss of energy (p < 0.001), sadness (p=0.018), inability to make decisions (p=0.007) and loss of pleasure (p=0.004). Somatic symptoms of decreased activation such as fatigue (p=0.026) and concentration difficulty (p=0.013) were also significant. The cognitive, self-negative symptoms were not associated with the level of physical activity.

Conclusion: A negative correlation of physical activity with fatigue and depression in patients with pSS has been demonstrated. The somatic symptoms of decreased activation played a profound role in this association, while the cognitive self-negotiation symptoms were not influenced by physical activity in our patients. Such symptoms as fatigue and loss of energy could potentially be reduced by exercises and functional training and consequently decrease the level of depression. An intervention study in this regard would be recommended.

REFERENCES:

[1] Cui, Y., et al., Anxiety and depression in primary Sjögren's syndrome: a cross-sectional study. BMC psychiatry, 2018. 18(1): p. 1-8.

[2] Strömbeck, B., E. Theander, and L. Jacobsson, Effects of exercise on aerobic capacity and fatigue in women with primary Sjögren's syndrome. Rheumatology, 2007. 46(5): p. 868-871.

[3] Ramos-Casals, M., et al., EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. Annals of the rheumatic diseases, 2020. 79(1): p. 3-18.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2647

AB0323 INTIMA-MEDIA THICKNESS IS INDEPENDENTLY ASSOCIATED WITH STROKE IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

L. D. Azoulay[1], A. Mathian[1], F. Cohen[1], J. Haroche[1], M. Pha[1], P. Cherin[1], P. Cluzel[2], Z. Amoura[1]. *[1]Pitié-Salpetrière, Internal Medicine 2, Paris, France*; *[2]Pitié-Salpêtrière, Cardiovascular Imaging and Interventionnal Radiology, Paris, France*

Background: Compared to secondary antiphospholipid syndrome (APS), little is known on intima-media thickness (IMT) in primary APS. Previous reports suggest that intima-media thickness may be associated with anti-cardiolipin antibodies, anti-β2-glycoprotein-1 antibodies, and with stroke in APS[1].

Objectives: To assess clinical significance of intima-media thickness in primary APS.

Methods: We have included 29 patients with primary APS (defined according to international consensus criteria) seen, at least once, in our tertiary center for a cardiovascular risk assessment from April 2014 to November 2018.

Results: 29 patients were included (females 83%). Mean (SD) age at evaluation was 48 years (16.1). Mean APS duration before assessment was 9.1 years (6.2). 27 patients had thrombotic APS (93%), among which 13 (45%) had a history of arterial thrombosis (12 strokes and 1 myocardial infarction) and 16 (55%) of venous thrombosis. Obstetrical APS was present in 7 patients (24%). Positive APL antibodies were: anti-cardiolipin antibodies (aCL) n = 15 (54%), anti-β2-glycoprotein I (anti-β2GP1) n = 10 (36%), lupus-anticoagulant (LAC) n = 11 (39%) and anti-phospholipid antibodies (aPL) n = 19 (68%). Mean IgG levels (GPL) were 52.4 (80.3) UGPL, 52.2 (124) UI, 39.2 (40.5) UGPL for aCL anti-βG2P1, and aPL, respectively. 6 patients (21%) were simple positive, 3 (11%) were double positive, and 10 (36%) were triple positive.

Cardiovascular risk factors were: smoking n = 6 patients (21%), overweight n = 11 (39%), hypercholesterolemia n = 12 (43%), arterial hypertension n = 11 (38%), chronic kidney disease (defined by estimated glomerular filtration rate < 60 mL/mn) n = 5 (17%). No patient had diabetes mellitus. Median risk SCORE was 0.65 (0-2.4). Male sex, obesity, chronic kidney disease and risk SCORE were significantly more frequent in patients with arterial APS compared to patients with venous and/or obstetrical APS (38% vs 0%, P=0.01; 33% vs 0%, P=0.02; 38% vs 0%, P=0.01; 2.3 vs 0.7, P=0.03).

22 patients (76%) underwent an IMT measurement. Mean IMT was 0.57 (0.14) millimeters (mm). Median IMT was significantly higher in APS patient with stroke

than in those without (0.63 IQR (0.55-0.77) mm versus 0.51 (0.44-0.55) mm, P=0.02) (Figure 1A). IMT was neither correlated with duration of APS nor with antibody titers.

Variables associated with IMT were studied on uni- and multivariate analysis (Table 1). On univariate analysis, age, aCL positivity and stroke were significantly associated with IMT and were included in the multivariate analysis. On multivariate analysis, there was a positive, independent and significant association between IMT and stroke (P=0.047) and between IMT and age (P=0.024). aCL positivity was not associated with IMT on multivariate analysis (Figure 1B).

Conclusion: Intima-media thickness is independently associated with stroke in primary antiphospholipid antibody syndrome.

REFERENCES:

[1] Medina G. Increased carotid artery intima-media thickness may be associated with stroke in primary antiphospholipid syndrome. *Ann Rheum Dis*. 2003;62(7):607-610. doi:10.1136/ard.62.7.607

Characters from table content including title and footnotes.

Table 1. Predictors of intima-media thickness on uni- and multivariate analysis.

	Univariate analysis		Multivariate analysis*	
	β	*P*-value	β	*P*-value
Age (years)	0.006	<0.001	0.004	0.024
Female sex	-0.102	0.18		
APS duration (years)	0.0004	0.31		
Smoker	-0.05	0.61		
Overweight	0.066	0.39		
Arterial hypertension	0.047	0.48		
Hypercholesterolemia	0.05429	0.412		
Anti-cardiolipin antibodies	0.12	0.05	0.084	0.076
Anti-phospholipid antibodies	0.054	0.44		
Anti-β2GP1	0.094	0.15		
Lupus-anticoagulant	0.044	0.49		
Anticoagulation	-0.07	0.31		
Stroke	0.139	0.02	0.099	0.047

β Linear regression coefficients**APS** Antiphospholipid antibody syndrome* Variables with a *P*-value <0.1 on univariate analysis were included

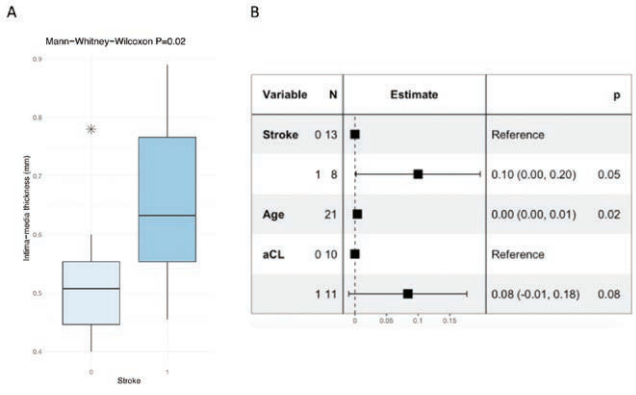


Figure 1. A. Intima-media thickness according to stroke status**B.**Multivariate analysis forest-plot of intima-media thickness predictors**OR** Odds-ratio**aCL** anti-cardiolipin antibodies

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2661

AB0324 ALLERGIC DISORDERS AND DRUG ALLERGIES IN PRIMARY SJÖGREN'S SYNDROME AND RHEUMATOID ARTHRITIS

M. Higashida-Konishi[1], K. Izumi[1,2], S. Hama[1], H. Takei[1], H. Oshima[1], Y. Okano[1]. [1]*National Hospital Organization Tokyo Medical Center, Department of Connective Tissue Diseases, Tokyo, Japan*; [2]*Keio University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan*

Background: Allergic disorders have been reported in a variety of rheumatic diseases. A high prevalence of allergic disorders was found in patients with Sjoegren's syndrome [1]. Nevertheless, it was not clear what is a risk factor for allergic disorders and drug allergies in patients with primary Sjögren's syndrome (pSS). Drug allergies may lead to delayed treatment and unnecessary clinical tests.

Objectives: The primary aim of this study was to compare the prevalence of allergic disorders and drug allergies in patients with pSS and rheumatoid arthritis (RA). The secondary aim was to compare the clinical features with and without drug allergies in patients with pSS.

Methods: We retrospectively examined consecutive patients diagnosed with pSS or RA in our hospital from 2010 to 2020. The patients with SS met the criteria of the 1999 revised Japanese Ministry of Health criteria[2]. We included patients with pSS without RA or other rheumatic diseases. The patients with RA met the EULAR/ACR 2010 criteria. We included patients with RA without other rheumatic diseases.

The first analysis was performed on six types of allergic reactions: (1) food allergy (exanthema, angioedema and anaphylaxis after foods exposure), (2) drug allergy (exanthema, angioedema and anaphylaxis after drug exposure), (3) allergic contact dermatitis such as metals, alcohol swab, and other cosmetics, (4) seasonal allergic rhinitis and/or allergic conjunctivitis, and allergic rhinitis and/or allergic conjunctivitis associated with house dust, (5) asthma, and (6) atopic dermatitis.

The secondary analysis was performed on patient baseline laboratory data at diagnosis of pSS and RA patients with or without drug allergies.

Results: In the first analysis, 292 patients with pSS and 413 patients with RA were enrolled (Table 1). The mean ages (pSS, RA) were 57.3±15.8, 66.0±14.6 years old. Females were 94.2%, 78.2%. The mean observation period was 82.7±70.8, 65.6±37.0 months. 54.8% of pSS patients and 34.9% of RA patients presented at least one type of allergic disorders or drug allergies. These included food allergy, drug allergy, allergic rhinitis/conjunctivitis, asthma, and atopic dermatitis. Allergic disorders and drug allergies were more frequent in patients with pSS.

In the second analysis, 77 patients with drug allergies and 215 patients without drug allergies were enrolled. The mean ages with drug allergies and without drug allergies were 56.0±15.8 and 57.8±15.8 years old, respectively; females were 96.1% and 93.5%; the mean observation period was 90.9±72.4 and 79.8±70.2 months. The pSS patients with drug allergies had higher levels of Immunoglobulin G (IgG) (2028±1409 mg/dL, 1726±587 mg/dL: p = 0.01), higher levels of eosinophils (220±247/μL, 126±112/μL: p<0.019), and higher positivity rate of anti–Sjögren's-syndrome-related antigen A autoantibody (anti-SSA antibody) than those without drug allergies (89.6%, 79.7%: p = 0.06).

Conclusion: Patients with pSS had a higher prevalence of allergic disorders and drug allergies than patients with RA. Among patients with pSS, patients with drug allergies had higher levels of IgG, higher levels of eosinophils, and higher positivity rate of anti-SSA antibody than those without drug allergies.

Table 1. Allergic Disorders and Drug Allergies in pSS and RA

	pSS (n = 292)	RA (n = 413)	P
at least one type of allergy, n (%)	160 (54.8)	144 (34.9)	<0.01
food allergy, n (%)	35 (12.0)	27 (6.7)	0.02
drug allergy, n (%)	76 (26.1)	69 (16.7)	<0.01
allergic contact dermatitis, n (%)	10 (3.4)	19 (4.6)	0.6
allergic rhinitis and/or conjunctivitis, n (%)	99 (33.9)	35 (8.5)	<0.01
asthma, n (%)	29 (9.9)	25 (6.1)	0.06
atopic dermatitis, n (%)	15 (5.1)	0 (0)	<0.01

REFERENCES:

[1] Hama et al. Clinical features of patients with Sjoegren syndrome associated with adult onset Still's disease. Japan College of Rheumatology Annual Congress 2020.

[2] Fujibayashi et al. Revised Japanese criteria for Sjögren's syndrome (1999): availability and validity. Mod Rheumatol. 2004; 14: 425-34.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2704

AB0325 FREQUENCY OF ATHEROMATOUS PLAQUES IN CAROTID ARTERIES BY DOPPLER IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, SANTO DOMINGO, DOMINICAN REPUBLIC

J. Santana Peralta[1], T. Polanco Mora[2], A. Cornelio[1], Y. Cruz[1], E. Rodriguez Bautista[1], T. Valdez[1], R. Muñoz[1], A. Feriz[1]. [1]*Hospital Docente Padre Billini, Rheumatology, Santo Domingo, Dominican Republic*; [2]*Hospital Docente Padre Billini, Rheumatology, Santo DOMINGO, Dominican Republic*

Background: Systemic lupus erythematosus (SLE) is a multisystemic autoimmune disease. [1] Atherosclerosis is considered an alteration of the arteries by the abnormal deposit of lipids and fibrous tissue. [2] Cardiovascular disease is one of the leading causes of morbidity and mortality, especially due to its precocity, which occurs in women during childbearing age, is associated with a higher prevalence of cardiovascular disease (CVD), due to accelerated atherosclerosis[3,4,5]. Patients with rheumatic diseases have an increased cardiovascular risk due to

systemic inflammation and endothelial dysfunction, which promotes accelerated atherosclerosis[2].

Objectives: Evaluate the frequency of atheromatous plaques in patients with systemic lupus erythematosus.

Methods: Observational, prospective, cross-sectional study. Carotid Doppler was performed on patients with SLE from the external consultation of the rheumatology service from November 2019 to 2020. Inclusion criteria: > 18 years old, diagnosis SLE with the classification criteria ACR 2007, realization of Doppler. Controls: no disease, equated by age and sex. The data was analyzed with SPSS V23.

Results: 116 patients met inclusion criteria, including 116 female controls. Mean sick time was 6.23 years. 14.65% (17) had atheromaus plates, 29.4% calcified plates (5). 34.7% Dyslipidemia (63.1%) (73), obesity 34.7% (33), high blood pressure 23.1% (22), diabetes 3.44% (4), smokers 0% (0). The activity rate using SLEDAI showed 68.96% (80) without activity, 13.79% (16) low, 11.20% (13) moderate, 6.03% (7) high activity. About control group (116), 19.82% (23) showed atheromatous plates, 39.13% (9) calcified plates.

Conclusion: Our study shows that less than a quarter of patients have atheromatous plaques in the carotid Doppler. In relation to LES activity, the vast majority are in low activity. We suggest the realization of Carotid Doppler in patients with low activity SLE for evaluation and monitoring of cardiovascular risk. Our study showed that there is no increased risk of atheroma plaque formation in SLE patients, compared to the general population.

REFERENCES:

[1] Hernández Muñiz, Y., Guibert Toledano, Z. and Reyes Llerena, G., 2015. Correlation of C Reactive Protein Figures and Atherosclerosis In Patients with Systemic Lupus Erythematosus.

[2] Saldarriaga Rivera, L., Ventura Ríos, L., Hernández Díaz, C. and Pineda Villaseñor, C., 2016. Measurement of the thickness of the intimate-half carotid: utility and ultrasound diagnosis of subcline atherosclerosis in rheumatic diseases. Literature review. Rev Col Reum, 23(2), pp.92-101.

[3] Telles, R., Lanna, C., Ferreira, G., Souza, A., Navarro, T. and Ribeiro, A., 2008. Carotid atherosclerotic alterations in systemic lupus erythematosus patients treated at a Brazilian university setting. Lupus, 17(2), pp.105-113.

[4] Nienhuis, H., by Leeuw, K., Bijzet, J., van Doormaal, J., van Roon, A., Smit, A., Graaff, R., Kallenberg, C. and Bijl, M., 2010. Small artery elasticity is decreased in patients with systemic lupus erythematosus without increased intima media thickness. *Arthritis Research & Therapy*, 12(5), p.R181.

[5] Frerix et al. Arthritis Research & Therapy 2014, 16: R54.

[6] Marta, M., Joan T., Stefano B., Chapt 2 - Assessment of Disease Activity in Systemic Lupus Erythematosus, Systemic Lupus Erythematosus, Mosby, 2007.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2745

AB0326 USEFULNESS OF THE INTIMA-MEDIA THICKNESS INDEX BY CAROTID DOPPLER IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS OF HOSPITAL DOCENTE PADRE BILLINI, DOMINICAN REPUBLIC

J. Santana Peralta[1], T. Polanco Mora[1], A. Cornelio[1], Y. Cruz[1], E. Rodriguez Bautista[1], T. Valdez[1], R. Muñoz[1], A. Feriz[1]. [1]*Hospital Docente Padre Billini, Rheumatology, Santo Domingo, Dominican Republic*

Background: Systemic lupus erythematosus (SLE) is a multisistemic autoimmune disease. [1]There are studies where the increase in the thickness of the intimate/media average in carotid (IMT) is valued, most have shown increase[2]. Cardiovascular disease is one of the leading causes of morbidity, especially due to its precocity, which occurs in women during the fertile potential, is associated with a higher prevalence of cardiovascular disease (CVD), due to accelerated atherosclerosis[3,4,5]. Patients with rheumatic diseases have an increased cardiovascular risk due to systemic inflammation and endothelial dysfunction, which promotes accelerated atherosclerosis[2]. Values below 0.9mm of IMT are considered normal.

Objectives: Evaluate the thickness of the intimate/media average in carotid in patients with systemic lupus erythematosus.

Methods: Prospective, Observational, cross-sectional study. Carotid Doppler was performed on patients in the outpatient clinic with a diagnosis of SLE from November 2019 to 2020 of the rheumatology service of the Hospital Docente Padre Billini and healthy controls. Inclusion criteria: > 18 years old, SLE diagnosis with ACR 2007 classification criteria, carotid Doppler, measurement of IMT. Controls without disease, matched by sex and age. The data was analyzed with SPSS V23.

Results: 116 patients with SLE. 95 patients met inclusion criteria;95 healthy controls were included. 97.8% female. Average disease of 6.23 years. 71. 57% (68) use glucocorticoids, antimalarials 70.52% (67), 38.94% (37) mofetil mycophenolate, 20% (19) methotrexate, 11. 57% (11) rituximab, 5.26% (5) azathioprine, 1.05% (1) cyclosporine, 1.05% (1) cyclophosphamide and 0.86% (1) tacrolimus. Dyslipidemia (63.1%) (73), obesity 34.7% (33), high blood pressure 23.1% (22), diabetes 3.44% (4), smokers 0% (0). The carotid doppler with SLE showed 17.89% (17) atheromatous plates, 29.4% (5) calcified plates, Carotid Doppler in healthy controls showed 20% (19) atheromatous plates, 36.84% (7) calcified plates. The activity rate using SLEDAI showed 68.96% (80) without activity, 13.79% (16) low, 11.20% (13) moderate, 6.03% (7) high activity. 78% (75) patients with SLE had increased IMT mean (SD) 2.15mm (0.99). About control 71.57% (68) had an increase of IMT, mean (SD) 1.27mm (1.07) (p-0.046).

Conclusion: Our study found that most patients with SLE had IMT increase. The activity ratio of SLE showed that the vast majority of our patients are in low activity. Alterations in IMT were associated with low SLEDAI and glucocorticoid use. There was no significant difference in the intima-media carotid thickness index with respect to the control group. We suggest the realization of Doppler in patients with SLE despite being in low activity for evaluation and monitoring of cardiovascular risk.

REFERENCES:

[1] Hernández Muñiz, Y, Guibert Toledano, Z. and Reyes Llerena, G., 2015. Correlation of C Reactive Protein Figures and Atherosclerosis in Patients with Systemic Lupus Erythematosus.

[2] Saldarriaga Rivera, L., Ventura Ríos, L., Hernández Díaz, C. and Pineda Villaseñor, C., 2016. Measurement of the thickness of the intimate-half carotid: utility and ultrasound diagnosis of subcline atherosclerosis in rheumatic diseases. Literature review. Rev Col Reum, 23(2), pp.92-101.

[3] Telles, R., Lanna, C., Ferreira, G., Souza, A., Navarro, T. and Ribeiro, A., 2008. Carotid atherosclerotic alterations in systemic lupus erythematosus patients treated at a Brazilian university setting. Lupus, 17(2), pp. 105-113.

[4] Nienhuis, H., by Leeuw, K., Bijzet, J., van Doormaal, J., van Roon, A., Smit, A., Graaff, R., Kallenberg, C. and Bijl, M., 2010. Small artery elasticity is decreased in patients with systemic lupus erythematosus without increased intima media thickness. *Arthritis Research & Therapy*, 12(5), p.R181.

[5] Frerix et al. Arthritis Research & Therapy 2014, 16: R54

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2750

AB0327 DRUG-INDUCED LUPUS ERYTHEMATOSUS SECONDARY TO ANTI-TNF-A AGENTS IN PATIENTS WITH SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS

A. Martins[1], D. Santos Oliveira[1,2], F. R. Martins[3], M. Rato[1], F. Oliveira Pinheiro[1], D. Fonseca[4], S. Garcia[1], B. M. Fernandes[1], S. Pimenta[1,5], M. Bernardes[1,5], L. Costa[1]. [1]*Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*; [2]*Faculdade de Medicina da Universidade do Porto - FMUP, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; [3]*University Hospital Center of Algarve, Rheumatology, Faro, Portugal*; [4]*Centro Hospitalar Vila Nova de Gaia / Espinho - Unit 1, Rheumatology, Vila Nova de Gaia, Portugal*; [5]*Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal*

Background: Induction of autoantibodies is frequently observed in patients treated with TNF-α antagonist and the possible development of drug-induced lupus erythematosus (DILE) remains a matter of concern. The prevalence of DILE secondary to anti-TNF-α therapy is estimated around 0.5-1% and clinical features include arthritis/arthralgia, rash, serositis, fever, myalgias, cytopenias, among others. According to the literature, DILE secondary to anti-TNF-α agents differs in several ways from the clinical and laboratory findings typically associated with classic DILE.

Objectives: To estimate the incidence of induction of antinuclear antibodies (ANA) and DILE in a monocentric cohort of patients with spondyloarthritis and psoriatic arthritis treated with anti-TNF-α agents. To describe the clinical and laboratorial features and outcomes of patients with DILE.

Methods: We performed a retrospective analysis of patients with spondyloarthritis and psoriatic arthritis treated with anti-TNF-α agents, from our University Hospital, who have been registered on the Portuguese Rheumatic Diseases Register (Reuma.pt) between July 2001 and December 2020. Patients with

positive ANA (titer > 1/100) before the anti-TNF-α therapy were excluded. Because specific criteria for the diagnosis of DILE have not been established, we considered the diagnosis in case of a temporal relationship between clinical manifestations and anti-TNF-α treatment and fulfillment of ACR/EULAR 2019 classification criteria for SLE. In patients with DILE, clinical features, laboratory findings, systemic therapies and outcome after discontinuation of medication were collected from reuma.pt and medical records. For the clinical and demographic predictors, continuous variables were analyzed using a two-sided t-test and categorical variables using a Fisher's exact test. P-value <0.05 was considered statistically significant.

Results: In the spondyloarthritis group, 290 patients were included (44.8% females, mean age at diagnosis of 33.3 ± 11.5 years and mean disease duration of 15.1 ± 10.4 years) and in the psoriatic arthritis group, 116 patients were included (50.0% females, mean age at diagnosis of 40.1 ± 11.0 years and mean disease duration of 13.1 ± 6.8 years). In our study, we observed high serology conversion rates (positive ANA in 67.9% and 58.6% of patients with Spondyloarthritis and Psoriatic Arthritis, respectively), with similar conversion rates between different anti-TNF drugs. Three patients with spondyloarthritis (1.0%) and 1 patient with psoriatic arthritis (0.9%) developed DILE. Etanercept was the causative agent in 2 cases, infliximab and adalimumab in 1 case, each. Peripheral arthritis (new onset or abrupt worsening) occurred in 2 patients, serositis in 1 patient, constitutional symptoms in 2 patients, subnephrotic proteinuria in 1 patient, lymphopenia in 2 patients and hypocomplementemia in 1 patient. Specific treatment was prescribed to the 4 patients (oral corticosteroids) and they achieved complete recovery. After anti–TNF-α treatment interruption, no patient had recurrent disease. We observed that patients with DILE had a significantly longer disease duration (> 8.4 years; p=0.04) and a significantly longer duration of therapy with anti-TNF (> 4.0 years; p=0.04) when compared to patients without DILE.

Conclusion: Despite the frequent induction of autoantibodies, the development of DILE secondary to anti–TNF-α agents is rare. Our study demonstrates an incidence rate similar to other studies reported before. The clinical and laboratorial characteristics of our patients with DILE attributable to anti–TNF-α agents differ significantly from DILE due to more traditional agents, as is described in literature. Overall, patients in this study had mild disease that improved after therapy discontinuation, without recurrence of the disease. It seems that a longer disease duration and a longer period under anti-TNF-α therapy may increase the risk of DILE development.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2953

AB0328 CLINICAL AND SEROLOGICAL DIFFERENCES BETWEEN PRIMARY SJOGREN'S SYNDROME PHENOTYPES

X. E. Larco Rojas[1], E. Diez Alvarez[1], C. Moriano[1], A. López Robles[1], T. Pérez Sandoval[1]. [1]*Complejo Asistencial Universitario de León, Rheumatology, León, Spain*

Background: Primary Sjogren's Syndrome (PSS) is an autoimmune and lymphoproliferative disease with a heterogeneous presentation. It has been postulated that there may be different phenotypes, in some cases presenting a more aggressive disease with systemic manifestations and a higher risk of developing complications. This phenotype has been associated with a higher autoimmune load and an earlier age of presentation. Furthermore, the presence of anti La + has been related to an increased risk of developing Lymphoma.

Objectives: To describe the phenotypic characteristics of seronegative PSS in a sample of patients from our practice. To compare the clinical and laboratory characteristics between patients with Ro + / La + and Ro + / La- antibodies. To Analyze if there are differences in patients diagnosed at an early age, compared to a later age.

Methods: Clinical and serological characteristics of patients with the diagnosis of PSS were collected from the Rheumatology database of León`s Hospital between 2014-2020. All patients who met the ACR / EULAR 2016 criteria were classified as seronegative Sjogren.

In the group of patients with positive autoimmunity, anti-Ro + / La + were compared with the anti-Ro + / La- patients and by age, stratifying them into the following groups: 0-49; 50-69 and> 70 years. The clinical variables analyzed were: glandular inflammation, Raynaud's phenomenon (RP), pulmonary and neurological involvement, presence of Lymphoma and other tumours. The serological variables were: positivity of ANA, Rheumatoid Factor (RF), hypocomplementemia, hypergammaglobulinemia and B2 microglobulin.

Results: 72 patients were analysed, 9 were excluded because didn't meet the criteria. Of the remaining: 90,4% were women, with a mean age of 58,7+/-15,8 years, 12,6% (8) were seronegative. In the seronegative group 25% presented lung involvement (Lymphoid Interstitial Pneumonia), 50% presented with glandular inflammation and only one patient had RP. As complications 1 patient presented Lymphoma and 1 Breast Carcinoma.

58,7% (37) Ro + / La + and 28,5% (18) Ro + / La- patients were identified, no statistically significant differences were found between the two groups when comparing: glandular inflammation (8/37 vs 2/18, p = >0.05) RP (9/37 vs 4/18, p = >0.05), pulmonary involvement (5/37 vs. 6/18, p = >0.05), neurological involvement (2/37 vs. 1/18, p = >0.05), presence of Lymphoma (2/37 vs. 0 / 18, p = >0,05), other tumours (2/37 vs 3/18, p = >0.05), ANA positivity (36/37 vs 16/18, p =>0,05), Hypocomplementemia (4/37 vs 3/18, p =>0.05) and Hypergammaglobulinemia (20/37 vs 10/18, p =>0.05). But a higher frequency of positive RF linked to anti La positivity (29/37 vs 6 / 18p = 0.002) was found.

When comparing by age groups, the association between RF + and La + remained in the group of 50-69 years (15/18 vs 3/18, p = 0.002) while in the other age groups there were no statistically significant differences. We also observed an increasing trend of the levels of B2microglobulin in La+ patients and later age (p=0,04)

Conclusion: The presence of anti La + seems to be associated with other components of autoimmunity such as RF in patients with PSS, although this study did not show a relation with a higher frequency of complications or systemic disease. Also, the presence of La+ at older ages was associated with higher levels of B2 microglobulin. We didn't find differences with the other described markers of B cell reactivation. Findings differ from those found in the literature, which may be largely due to sample size.

REFERENCES:

[1] Quartuccio L., Baldini C., Bartoloni E., et al. Anti-SSA/SSB-negative Sjogren's syndrome shows a lower prevalence of lymphoproliferative manifestations, and a lower risk of lymphoma evolution. Autoimmunity Reviews 14 (2015) 1019–1022.

[2] Quartuccio L, Isola M, Baldini C, Priori R, Bartoloni Bocci E, Carubbi F, et al. Biomarkers of lymphoma in Sjögren's syndrome and evaluation of the lymphoma risk in prelymphomatous conditions: results of a multicenter study. J Autoimmun 2014; 51:75–80.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2959

AB0329 HIGHER PREVALENCE OF ECHOCARDIOGRAPHIC ABNORMALITIES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

N. Guajardo-Jauregui[1], J. R. Azpiri-López[2], D. Á. Galarza-Delgado[1], I. J. Colunga-Pedraza[1], R. A. Reyna-de la Garza[3], S. Lugo-Perez[2], A. B. Rodriguez-Romero[1], A. Cárdenas[1], H. Azpiri-Diaz[2], O. A. Cepeda-Ayala[2]. [1]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*; [2]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico*; [3]*Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Internal Medicine, Monterrey, Mexico*

Background: Systemic lupus erythematosus (SLE) is a chronic, inflammatory, and autoimmune disease that damages vital organs such as the heart. Patients with SLE have a higher risk of developing a cardiovascular (CV) disease than the general population (1).

Objectives: The aim of this study was to compare the echocardiographic findings in patients with SLE and controls.

Methods: This was a cross-sectional, observational, and comparative study. A total of 38 patients with SLE according to the 2019 EULAR/ACR classification criteria, ≥18 years old and 38 matched controls by age (±5 years) and gender, were recruited for this study. Exclusion criteria were a poor echocardiographic window, patients with a previous CV event, such as myocardial infarction, cerebrovascular event or peripheral arterial disease, and pregnant women. A transthoracic echocardiogram, including speckle tracking technique,

was performed, by two certified echocardiographers, in all study subjects. Distribution was evaluated with Kolmogorov-Smirnov test. Comparisons were done with χ^2 and Fisher´s Exact test for qualitative variables, and Student's t test and Mann-Whitney´s U test for quantitative variables. A p-value <0.05 was considered statistically significant.

Results: When comparing demographic characteristics there were no significant differences in age, gender, and comorbidities between SLE patients and controls. In the echocardiographic findings a significant difference was found in the left ventricular ejection fraction (LVEF), lower in SLE patients compared to controls (57.02% vs 61.89%, p=0.001), in the global longitudinal strain (GLS), reduced in SLE patients (-19.55% vs -22.00%, p=0.001), in the tricuspid annular plane systolic excursion (TAPSE), lower in SLE patients (22.00mm vs 24.00mm, p=0.011), in the left atrial volume index, higher in SLE patients (28.44ml/m^2 vs 22.29ml/m^2, p=0.014) and in the presence of mitral regurgitation, more prevalent in SLE patients (31.6% vs 10.5%, p=0.024) (Table 1).

Conclusion: Patients with SLE have a worse left ventricular function, evaluated by LVEF and GLS, a worse right ventricular systolic function, evaluated by TAPSE, an increased left atrial volume index and a higher prevalence of mitral regurgitation, which are associated with a higher risk of CV death. It is important to consider including a transthoracic echocardiogram as part of the CV evaluation in patients with SLE, which may result in an early detection of CV abnormalities and an opportune treatment.

REFERENCES:

[1] Avina-Zubieta JA, To F, Vostretsova K, et al. Risk of Myocardial Infarction and Stroke in Newly Diagnosed Systemic Lupus Erythematosus: A General Population-Based Study. Arthritis Care Res (Hoboken) 2017;69(6):849-56. doi: 10.1002/acr.23018

Table 1. Demographic characteristics and echocardiographic findings.

	SLE patients (n=38)	Controls (n=38)	p
Age years, median (p25-p75)	37.5 (24.5-43.2)	45.0 (24.0-50.0)	NS
Women, n (%)	34 (89.5)	37 (97.4)	NS
T2DM, n (%)	1 (2.6)	3 (7.9)	NS
HTN, n (%)	9 (23.7)	3 (7.9)	NS
Dyslipidemia, n (%)	3 (7.9)	3 (7.9)	NS
Obesity, n (%)	1 (2.6)	5 (13.2)	NS
Active smoking, n (%)	7 (18.4)	3 (7.9)	NS
Echocardiographic findings			
Left ventricle indexed mass g/m^2, median (p25-p75)	64.00 (50.66-87.09)	60.30 (52.97-76.74)	**0.009**
RWT, median (p25-p75)	0.37 (0.30-0.46)	0.38 (0.33-0.45)	NS
Left ventricular ejection fraction %, mean ± SD	57.02 ± 7.37	61.89 ± 5.23	**0.001**
Global longitudinal strain %, median (p25-p75)	-19.55 (-21.02 – -15.95)	-22.00 (-21.00 – -20.00)	**0.001**
Left atrium indexed volume ml/m^2, median (p25-p75)	28.44 (20.34-33.56)	22.29 (17.97-27.13)	**0.014**
TAPSE mm, median (p25-p75)	22.00 (20.00-24.00)	24.00 (21.00-25.00)	**0.011**
Valvular abnormalities			
Aortic regurgitation, n (%)	2 (5.3)	1 (2.6)	NS
Mitral regurgitation, n (%)	12 (31.6)	4 (10.5)	**0.024**
Tricuspid regurgitation, n (%)	16 (42.1)	17 (44.7)	NS

SLE, systemic lupus erythematosus; NS, not significant; T2DM, type 2 diabetes mellitus; HTN, hypertension; RWT, relative wall thickness; TAPSE, tricuspid annular plane systolic excursion.

Acknowledgements: We have no acknowledgements to declare.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3041

AB0330

ANTIPHOSPHOLIPID ANTIBODIES AND ANTICOAGULANT TREATMENT: CAPILLAROSCOPIC FINDINGS

G. Ferrari[1], E. Gotelli[1], G. Pesce[2], L. Nanni[3], B. Colombo[4], S. Paolino[1], C. Pizzorni[1], A. Sulli[1], V. Smith[5], M. Cutolo[1]. [1]*Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic Hospital, Genova, Italy*; [2]*Autoimmunity Laboratory, Department of Internal Medicine, University of Genova, IRCCS San Martino Polyclinic Hospital, Genova, Italy*; [3]*Medicine Laboratory, IRCCS San Martino Polyclinic Hospital, Genova, Italy*; [4]*Italian Cardiovascular Network, IRCCS San Martino Polyclinic Hospital, Genova, Italy*; [5]*Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Department of Rheumatology, Ghent University Hospital – Department of Internal Medicine, Ghent University, Belgium, Ghent, Belgium*

Background: Antiphospholipid syndrome (APS) is an autoimmune condition characterized by arterial and/or venous thrombosis and/or obstetric morbidity, associated with the presence in the serum of antiphospholipid antibodies (aPL) [1]. Subjects with confirmed positivity of aPL in absence of thrombotic/obstetric manifestations are identified as aPL carriers [2] The microangiopathy detected by nailfold videocapillaroscopy (NVC) in APS and in aPL-carrier patients is poorly investigated, as well as the possible interference of anticoagulant drugs [3].

Objectives: To compare microvascular damage in APS, aPL carriers and a group of patients (CTR) without aPL positivity and on regular warfarin therapy for cardiovascular indications

Methods: NVC investigations were performed as part of standard procedures in APS patients (18, mean age 50.0±12.8 years), aPL carriers (24, mean age 46.4±16.4 years) and CTR without aPL (18, mean age 74±12.5 years) in therapy with oral anticoagulant (warfarin) for non-immunological vascular complications (atrial fibrillation, mechanical heart valve, deep venous thrombosis). Only patients affected by primary APS form were selected from data files (2006 Sapporo classification criteria). The following NVC parameters were availble: dilated capillaries, giant capillaries, microhemorrhages (with particular attention to linear and thin hemosiderin deposits, arranged perpendicularly and parallel to the nailfold bed, "comb-like"), abnormal shape (i.e. brunched "bushy" capillaries) and capillary number reduction. Those parameters were scored according to a semi-quantitative scale [4,5]. Statistical analysis was performed by non-parametric tests. Any p values equal or lower than 0.05 was considered statistically significant.

Results: APS patients showed a higher score for dilated capillaries (p=0.001), more frequent microhemorrhages (p=0.03), in particular "comb-like" microhemorrhages (p=0.007) than simply aPL carriers. Of note, there wasn't a statistically significant difference in the number of microhemorrhages between APS and CTR group (p=0.23), but again the number of "comb-like" hemorrhages, was almost absent in the CTR group (p=0.03). No significant correlation was found between the different aPL subtypes and the NVC parameters.

Conclusion: APS patients showed significantly higher number of non-specific NVC abnormalities than aPL carriers. Anticoagulant treatment could represent a further risk factor for the appearance of microhemorrhages in all the patients, being the NVC "comb-like" pattern mainly associated with the APS. Further investigations with larger cohorts of patients are needed for the definition of a possible APS specific NVC-pattern.

REFERENCES:

[1] Ruiz-Irastorza G et al. Lancet. 2010;376(9751):1498-509. 2. Pengo V et al. Semin Thromb Hemost. 2012;38:322-7. 3. Sulli A et al. J Rheumatol. 2000;27:1574-6. 4. Smith V et al. 2020. Autoimmun Rev. 19:102458. 5. Sulli A et al. Ann Rheum Dis. 2008;67:885-7.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3072

AB0331

PULMONARY INVOLVEMENT IN A SINGLE CENTER COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

N. Senkal[1], E. Kiyan[2], E. Kocasoy-Orhan[3], A. Demir[4], M. Aydogan[5], Y. Yalçınkaya[6], A. Gul[6], M. Inanc[6], M. L. Ocal[6], B. Artim-Esen[6]. [1]*Istanbul University Istanbul Faculty of Medicine, Internal Medicine, Istanbul, Turkey*; [2]*Istanbul University Istanbul Faculty of Medicine, Chest Diseases, Istanbul, Turkey*; [3]*Istanbul University Istanbul Faculty of Medicine, Neurology, Istanbul, Turkey*; [4]*Fulya Radiologic Imaging Center, Radiology, Istanbul, Turkey*; [5]*Istanbul University Istanbul Faculty of Medicine, Cardiology, Istanbul, Turkey*; [6]*Istanbul University Istanbul Faculty of Medicine, Rheumatology, Istanbul, Turkey*

Background: The prevalence of SLE pulmonary involvement varies depending on several factors, including diagnostic methods [1].
Objectives: We aimed to determine the frequency of involvement with different diagnostic methods in a single center cohort.
Methods: 300 SLE patients were included. Chest x-ray (CXR), lung spirometry, carbonmonoxide diffusion test (DLCOc) and echocardiography were performed. High resolution thorax computed tomography (HRCT) was done for a definite diagnosis of interstitial lung disease (ILD) whilst diagram electromyography (EMG), ultrasonography (USG) and magnetic resonance imaging (MR) were utilized to diagnose shrinking lung syndrome (SLS).
Results: The mean age and follow-up time were 43 and 11,5 years respectively. Of 300 patients, 16% had ILD, 6,7% had pulmonary hypertension (PHT), 3% had SLS, 0,3% had pulmonary infarction. At the start of the study, patients' records showed that 4% had ILD, 5% PHT, 0,3% SLS and 0,3% pulmonary infarction. The median age, mean duration of disease and follow-up time were significantly higher and longer in patients with ILD compared to patients without (p<0.05). Forced expiratory volume (FEV1), forced vital capacity (FVC), DLCOc and total lung capacity (TLC) were significantly lower in patients with ILD and with SLS (p<0,001). Patients with ILD had significantly higher frequency of arthritis, serositis, Raynaud myositis and anti-Scl70 positivity. Avascular necrosis, diabetes and malignancy were significantly more frequent in those patients. All patients with suspected SLS undergone diagram EMG, USG and MR. Out of 10 suspected cases, in 6 EMG, in 5 USG and in 9 MR was compatible with SLS diagnosis. 5 patients had 3 of the diagnostic methods positive to diagnose SLS. Muscle atrophy and weakness, avascular necrosis were more frequent in this group of patients (p<0.05). There were more patients treated with mycophenolate mofetil (MMF) and cyclophosphamide in the SLS group whilst more with MMF in the ILD group. Significantly higher frequency of patients had stopped using hydroxychloroquine (HCQ) in the ILD group (p=0,04).
Conclusion: Interstitial lung disease is common in patients with SLE and considerable number of patients have SLS [2]. Spirometry, DLCOc and CXR are simple but valuable to diagnose pulmonary involvement in SLE patients. Diaphragm MR, USG and EMG are complementary methods for definite diagnosis in SLS [2]. Considering the significant difference of prevalence between the start and the end of the study, one of the possibbilities is the underrecognition of SLE pulmonary disease due to its being part of a multisystemic presentation. Higher usage of immunosuppressives in these patients may support a multisystemic active disease. Although drug effect is another concern, it is hard to establish a causal relationship due to the study's cross-sectional design. HCQ may have a role in ILD prevention.
REFERENCES:

[1] Keane MP, Lynch JP. Pleuropulmonary manifestations of systemic lupus erythematosus. Thorax 2000;55:159-166.
[2] Singh R, Huang W, Menon Y, Espinoza LR. Shrinking lung syndrome in systemic lupus erythematosus and Sjogren's syndrome. J Clin Rheumatol. 2002 Dec;8(6):340-5.

Table 1. Spirometry; DLCO; diaphragm EMG, USG and MRI results of patients with SLS.

Patient/	1/	2/	3/	4/	5/	6/	7/	8/	9/	10/
Age/	44/	57/	39/	38/	23/	60/	58/	37/	66/	28/
Sex	F	F	F	M	F	F	F	F	F	F
FEV1 (%)	47	65	59	63	67	62	71	53	70	39
FVC (%)	56	73	59	62	79	70	72	55	62	37
DLCO (%)	45	50	44	65	53	55	47	65	62	45
TLC (%)	61	71	65	66	78	64	54	63	62	45
USG deep inspiration (L)	4,70	4,74	2,59	3,01	3,06	3,06	5,73	4,17	2,12	1,59
USG deep inspiration (R)	3,72	1,98	2,26	2,24	2,77	2,17	4,67	2,83	4,62	2,49
USG diaphragm thickness (L)	4,82	3,00	2,48	2,84	2,55	1,59	2,09	3,18	1,62	1,44
USG diaphragm thickness R(R)	1,23	1,04	1,84	1,80	2,19	1,31	1,79	1,97	2,08	1,63
MR high side	R	R	R	R	R		R	R	L	L
MR height difference	4,92	6,19	2,87	2,64	1,67		2,45	1,73	0,95	0,78
EMG resting AMP (R)	0,2	0,3	0,6	0,5	0,6	0,4	0,1	0,8	0,9	0,7
EMG resting LAT (R)	7	6,4	7,1	6	6,7	8	6,15	4,75	6	5,8
EMG resting AMP (L)	0,4	0,5	0,8	0,7	1,2	0,6	0,3	1,2	0,5	0,5
EMG resting LAT (L)	6,35	5,75	6,85	5,6	6,05	6	6	4,35	5,2	6,15

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3152

AB0332

IS MINOR SALIVARY GLAND HISTOLOGY A GOOD BIOMARKER SCORE TO PREDICT THE EXTRAGLANDULAR INVOLVEMENT IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME?

A. Martins[1], R. Ferreira[1], S. Pimenta[1,2], L. Costa[1]. [1]*Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*; [2]*Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal*

Background: The minor salivary gland biopsy (MSGB) is considered the "*gold standard*" for the diagnosis of primary Sjögren's syndrome (pSS). The histological hallmark is focal lymphocytic infiltration with the presence of 50 or more lymphocytes per 4 mm^2 (focus score ≥ 1). Several studies have documented the association between focus score (FS) and extraglandular involvement, suggesting that FS could be used as a histological index of disease severity and a prognostic tool.
Objectives: To investigate the association between the FS and clinical, haematological and serological findings in a cohort of patients with pSS.
Methods: We performed a retrospective analysis of patients with pSS who fulfilled the ACR/EULAR 2016 classification criteria that were submitted to a minor salivary gland biopsy (MSGB). Demographic data, disease duration, extraglandular involvement and histopathologic data were collected and analyzed. The severity of histologic changes was graded according to the Chisholm and Mason scoring system and the FS was determined. Fisher's exact test/Chi-square test and Mann-Whitney U test were used to compare the patients with and without positive biopsy (FS <1 versus FS ≥ 1). Futhermore, to investigate the association between the quantitative value of focus score in groups with and without each extraglandular manifestations the authors used the Mann-Whitney U test. P-value < 0.05 was considered statistically significant.
Results: A total of 59 pSS patients were included. Regarding the histopathologic pattern, 40 of 59 patients had a FS ≥ 1, while 19 patients had a FS <1. Although described as having FS ≥ 1, the pathologists failed to report the absolute value in 11 of 40 (27,5%) patients. Germinal center-like structures were found in 1 (1,7%) patient. The demographic and clinical features in pSS patients with FS <1 and with FS ≥ 1 are presented in table 1. Anti-SSA was strongly associated with FS <1 (p <0,001). No significant difference in demographic and clinical features were found between the two groups.

Table 1. Demographic and clinical features in pSS patients with FS <1 and with FS ≥ 1 (* Fisher's exact/Chi-square test; † T-test; ‡ Mann-Whitney U test).

	FS <1 (n=19)	FS ≥ 1 (n=48)	p-value
Gender (female), n (%)	17 (89,5)	34 (85,0)	0,639 *
Current age (years) (mean ± SD)	60,11+-13,39	54,78 (+-13,48)	0.16 †
Disease duration (years) (median, P25-P75)	3 (2-7)	4 (3-5)	0,507 ‡
Extraglandular involvement			
Arthralgias/Arthritis, n (%)	6 (31,7)	22 (55,0)	0,092 *
Myositis, n (%)	0 (0)	1 (2,5)	-
Pulmonary involvement, n (%)	3 (15,8)	5 (12,5)	0,704 *
PNS involvement, n (%)	0 (0)	1 (2,5)	-
CNS involvement, n (%)	0 (0)	1 (2,5)	-
Cutaneous involvement, n (%)	1 (5,3)	1 (2,5)	0,544 *
Lymphoma, n (%)	0 (0)	2 (5,6)	-
Haematological and serological characteristics			
Leukocytopenia, n (%)			
Hypergammaglobulinaemia, n (%)	10 (52,6)	16 (40,0)	0,361 *
RF positivity, n (%)	5 (26,3)	10 (25,6)	1 *
ANA positivity, n (%)	18 (94,7)	34 (85,0)	0,411*
Anti-SSA positivity, n (%)	19 (100)	21 (52,5)	< 0,001 *
Anti-SSB positivity, n (%)	7 (36,8)	12 (32,5)	0,742 *
ESSDAI score (median, P25-P75)	2 (0-8)	2 (0-7,25)	0,816 ‡

When comparing the quantitative value of FS in groups with and without each extraglandular manifestation, the authors found that patients with articular involvement had a significant higher FS value than patients without articular manifestations (p=0.037). No other significant association was found.
Conclusion: Regarding the clinical manifestations, we didn't find a significant difference between patients with a FS < 1 and those with a FS ≥ 1. Anti-SSA was strongly associated with a FS <1, which corroborates the importance of anti-SSA for the pSS diagnosis in patients with a negative biopsy. We found that a higher FS value was associated with articular involvement. However, this study has limitations such as a small sample and a low incidence of extraglandular manifestations. In conclusion, more studies are needed to clarify the associations found in the literature.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3220

AB0333

USEFULNESS OF MULTI-PARAMETRIC EVALUATION INCLUDING MINOR SALIVARY GLAND BIOPSY FOR THE DIFFERENTIAL DIAGNOSIS OF SICCA SYNDROME IN A SPANISH SINGLE-CENTER EXPERIENCE

J. Álvarez Troncoso[1], C. M. Oñoro López[1], C. Soto Abánades[1], E. Ruiz Bravo[2], L. Blasco Santana[2], A. Noblejas Mozo[1], E. Martínez Robles[1], Á. Robles Marhuenda[1], L. Ramos Ruperto[1], J. J. Rios[1], F. Arnalich Fernández[1]. [1]*Hospital Universitario La Paz, Internal Medicine, Madrid, Spain*; [2]*Hospital Universitario La Paz, Pathology, Madrid, Spain*

Background: Sjögren's syndrome (SS) is a systemic autoimmune disease characterized by mononuclear cell infiltration of the exocrine glands, which leads to sicca syndrome and systemic manifestations. The minor salivary gland biopsy (MSGB) is undoubtedly important for the classification, diagnosis and prognosis of SS. However, differentiating SS and non-Sjögren's sicca syndrome (NSS) can be challenging.
Objectives: The aim was to evaluate the histological characteristics of MSGB besides focus score (FS) in patients with sicca syndrome and the usefulness of the different clinical, serological and histological parameters to diagnose, classify and describe the prognosis of patients with Sjögren's syndrome.
Methods: Prospective observational single-center study of patients referred for study of sicca syndrome with multi-parametric evaluation from January 2019 to December 2020. A diagnostic protocol based on Schirmer's test, unstimulated whole salivary flow (UWSF) and minimally invasive MSGB was applied. Patients fulfilling 2016 ACR-EULAR classification criteria were classified as SS.
Results: In a cohort of 115 patients with sicca syndrome, 55 (47.8%) were diagnosed with SS. The mean age was 56.9±14.5 years and most of the patients were women (81,7%) with no significant differences between SS and NSS. SS were more likely to present positive Schirmer's test, positive UWSF, anti-Ro+, FS≥1, antinuclear antibodies (ANA+), rheumatoid factor (RF+) and anti-La+ among others.
MSGB was a safe procedure and very effective (only 7% insufficient biopsies) in our cohort. The mean gland size of the MSGB was 5.7±0.37 mm^2. Furthermore, it was the individual parameter that most correlated with SS, even more than anti-Ro+, Schirmer's and UWSF. Seronegative SS (Anti-Ro-) was 47.3%. These patients could not have been diagnosed except by MSGB. Scintigraphy did not help to differentiate SS from NSS, neither patient-referred xerostomia nor xerophthalmia. The most frequent histological diagnosis was focal lymphocytic sialadenitis (FLS) (81.8%) followed by nonspecific chronic sialadenitis (9.1%). However, only FLS had a correlation with SS. There were no MSGBs labeled normal among the SS patients. Mean FS was 2.22±0.2 (16.7% had FS≥3).
The rest of the histological parameters that showed a positive correlation with SS were glandular atrophy (GA), germinal centers (GC), lymphoepithelial lesions (LEL) and lymphoid follicles (LF). FS≥1 is the current histological classification criteria for ACR/EULAR. However, the presence of lymphocytic infiltrates (LI) (although not FS≥1) and FLS were suggestive markers of SS with greater sensitivity (SE) and specificity (SP). FS≥3, GC, LEL and LF were only found in SS and were associated in previous studies with higher risk of lymphoma and systemic disease.

		Prevalence			Test	
		SS	NSS	p value	Sensitivity	Specificity
Classification criteria	Schirmer's test	78.6%	57.6%	p=0.019	0.78	0.42
	UWSF	65.5%	38.3%	p=0.004	0.65	0.62
	Anti-Ro+	52.7%	6.7%	p<0.001	0.53	0.93
	FS≥1	66.7%	25%	p=0,027	0.67	0.75
Non classification criteria	Anti-La+	18.5%	1.8%	p=0.003	0.43	0.87
	ANA+	74.5%	28.3%	p<0.001	0.75	0.72
	RF+	38.2%	10.0%	p=0.001	0.43	0.87
	Scintigraphy	49.1%	38.3%	p=0.245	0.49	0.62
	Xerostomia	76.1%	77.9%	p=0.663	0.76	0.2
	Xerophthalmia	74.5%	83.8%	p=0.302	0.74	0.16
Histological characteristics	LI	92.2%	27.5%	p<0.001	0.9	0.78
	FLS	81.8%	6.7%	p<0.001	0.82	0.93
	GA	75.5%	50.9%	p=0.010	0.76	0.49
	GC	2.0%	-	p=0.310	0.02	1.00
	LEL	12.2%	-	p=0.011	0.11	1.00
	LF	4.1%	-	p=0.153	0.04	1.00

Conclusion: SS is a heterogeneous disease that requires a comprehensive clinical, serological, functional and histological evaluation. MSGB is a simple, safe, repeatable procedure that provides enormous information. It was the single parameter that best correlated with SS and allowed the diagnosis of seronegative SS. In summary, the use of MSGB is essential not only for the differential diagnosis of sicca syndrome but also as a prognostic marker for SS.
REFERENCES: :
[1] Bautista-Vargas et al. Autoimmun Rev. 2020 Dec;19(12):102690.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3251

AB0334

THE FIRST 1000 DAYS OF LIFE AND REPRODUCTIVE DISORDERS IN WOMAN WITH RHEUMATIC DISEASE (RDS)

M. Orlandi[1], S. Vannuccini[2], K. El Aoufy[1], M. R. Melis[1], G. Lepri[1], S. Bellando-Randone[1], S. Guiducci[1], M. Matucci-Cerinic[1], F. Petraglia[2]. [1]*University of Florence, Department of Experimental and Clinical Medicine, Florence, Italy*; [2]*Obstetrics and Gynecology, AOU Careggi, Department of Maternity and Infancy, Florence, Italy*

Background: Gynaecological problems are often ignored by rheumatologist and have a negative impact on quality of life of RDs patients.
Objectives: The aim of this study was to describe gynaecological, reproductive and sexual problems in premenopausal woman with RDs.
Methods: A monocentric, cross-sectional observational study was conducted in the Rheumatology Department of Careggi Hospital in Florence. Inclusion criteria: female gender, premenopausal age (and≥18 years old), diagnosis of rheumatic diseases. All patients have been investigated about gynaecological anamnesis and symptoms and subjected to a self-administered validated questionnaire.
Results: From May 4 th to November 30th, 2020, 200 patients were enrolled (mean age 39.1± 8.7 years (M±SD)): 58% arthritis, 40% connective tissue disease and 1.5% systemic vasculitis. In the history, spontaneous, full-term birth in 91% and 93% of patients, respectively, was observed and pre-term birth was reported in 8.1%. 63% of patients were breastfed. In family history, menorrhagia, dysmenorrhea, or chronic pelvic pain were reported in 59%, 55 and 7% of patients, respectively. The first menstruation was at 12.3±2.0 years (M±DS) and mostly woman reported menstrual disorders during adolescence (56% experienced dysmenorrhea and 52% menorrhagia). Menstrual disorders and abnormal bleeding were frequently reported also in adulthood: 71% had dysmenorrhea, 38% heavy menstrual cycles and 9% metrorrhagia. Moreover, 26% of patients referred non- menstrual pelvic pain, 19% urinary pain and 18% pain during defecation. Vaginal symptoms were frequently reported: 36% of patients referred vaginal dryness, 29% burning, 19% recurrent vaginal infections and dyspareunia in 39% of patients. Uterine fibroma was present in 23% and endometriosis in 10% of patients. Fertility problems were reported by 10% of patients in a time frame of 7.5±6.4 years and 30% of patients experienced at least one miscarriage; otherwise, 56% of patients have had at least one full-term pregnancy.
Conclusion: RDs patients show a high prevalence of various gynaecological problems affecting their quality of life. The management of female RDs patients is a challenge for the clinician and should include an accurate evaluation of the gynaecological aspects (menstruation, fertility, maternity, sexuality) as well as a multidisciplinary teamwork (rheumatologist and gynaecologists).
REFERENCES:
[1] Critchley H., Babayev E., Bulun E., et al. Menstruation: Science and society | Elsevier Enhanced Reader. (s.d.). https://doi.org/10.1016/j. American Journal of Obstetrics & Gynecology 2020.06.004
[2] Østensen M, Andreoli L, Brucato A,et al. State of the art: Reproduction and pregnancy in rheumatic diseases. Autoimmun Rev. 2015 May;14(5):376-86. doi: 10.1016/j.autrev.2014.12.011. Epub 2014 Dec 30. PMID: 25555818.
[3] Marder W, Johnson TRB. Rheumatic diseases and maternal-fetal medicine. Best Pract Res Clin Obstet Gynaecol. 2020 Apr;64:1-2. doi: 10.1016/j.bpobgyn.2019.11.007. Epub 2019 Dec 17. PMID: 31983554.
[4] Sammaritano LR, Bermas BL, Chakravarty EE,et al. 2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases. Arthritis Rheumatol. 2020 Apr;72(4):529-556. doi: 10.1002/art.41191. Epub 2020 Feb 23. PMID: 32090480.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3282

AB0335

SURVIVAL ASSESSMENT IN PATIENTS WITH SLE AND PULMONARY MANIFESTATIONS IN A COLOMBIAN COHORT WITH 2-YEAR FOLLOW-UP

S. Herrera[1], J. C. Diaz-Coronado[1,2], S. Monsalve[2], S. Guerra-Zarama[2], M. F. Saavedra Chacón[2], J. Barbosa[2], J. D. Serna Giraldo[2], J. D. Lopez[2], J. M. Gutiérrez[2], T. Vega[2], D. Orozco[2], D. Ocampo[2], N. Zuluaga[2], D. Hernandez-Parra[1], D. Rojas-Gualdrón[3], R. Pineda.Tamayo[1]. [1]*Artmedica, Clinical Information Group, Medellín, Colombia*; [2]*CES University, Department of Internal Medicine, Medellín, Colombia*; [3]*CES University, Facultad de medicina, Medellín, Colombia*

Background: Systemic lupus erythematosus (SLE) is a multisystemic autoimmune disease with heterogenous and variable behavior. The frequency of pulmonary involvement ranges from 10-90%, with this variability in occurrence attributed to differences in populations and heterogeneity in detection methods and study designs.
Objectives: To analyze survival in patients with SLE and the presence of pulmonary manifestations according to clinical and demographic characteristics in a cohort of patients in Colombia
Methods: Observational-analytical, retrospective, follow-up study of a cohort of adult patients with SLE. We included 559 adult patients who fulfilled the 2012 SLICC SLE classification criteria and with at least 6 months of disease evolution, treated in a medical center specialized in rheumatology with locations in 6 cities in Colombia between 2015 and 2018. Pregnant patients and those who had incomplete data or visits were excluded. Immunoserological profile was characterized and pulmonary involvement was followed for 1 year. The diagnosis of pulmonary involvement was obtained from the rheumatology report in the clinical chart. The prevalence of pulmonary manifestations and the immunoserological profile were determined and subsequently a logistic regression adjusted for age, sex and level of education was performed to establish the association between pulmonary manifestations and a positive autoantibody profile
Results: Median age was 44.5 ± 14 years, 96.6% were women. In patients with pulmonary compromise 9.7% were smokers, 12.4% had an active alcohol intake, 58.4% had a low socioeconomic status, 38.1% medium and 4.7% high. Pulmonary involvement was present in 20% of patients, the most common manifestations were pleuritis (14.3%), lupus pneumonitis (3.6%), pulmonary hypertension (3.2%), interstitial lung disease (2.3%), pulmonary embolism (2.3%), pulmonary fibrosis (2.14%), alveolar hemorrhage (1.4%), shrinking lung (0.2%). there was no significant difference in the follow up at one year. Immunoserological characteristics shows ANA positivity in 92%, anti-DNA in 53%, ENAS in 97%, with anti-RNP being the most common (41.7%), and low complement levels in 53%. Mortality for pulmonary compromise was 1.4%, and survival at 2 years did not have a statistically significant difference (p=0.155)
Conclusion: Survival was not found to be lower in patients with SLE and pulmonary involvement (p=0.155) when compared to SLE patients without pulmonary involvement after 2-year follow-up. This finding was independent of age, gender, and educational level. Previous large cohorts like GLADEL and RELESSER describe an association between pulmonary involvement and lower survival HR 2,79 (95% CI: 1,80-4,31), p <0,001 and HR 3.13, (95% IC: 1.56– 6.28, P = 0.00 respectively. In the RELESSER cohort pleural involvement and pulmonary embolism was found to have low to minimal impact on survival.
In our cohort pleuritis was the most common finding whereas the other pulmonary manifestations were reported in less than 4% of patients. This difference could explain our differences with other cohorts. Other causes for this difference are a smaller sample size and a short follow-up.
The results of our study do not suggest that there is an association between pulmonary involvement and mortality in Colombian patients with SLE during a 2-year follow-up. We will continue to monitor and report in this regard
REFERENCES:
[1] Narváez J, Borrell H, Sánchez-Alonso F, Rúa-Figueroa I, López-Longo FJ, Galindo-Izquierdo M, et al. Primary respiratory disease in patients with systemic lupus erythematosus. (RELESSER) cohort. Arthritis Res Ther. 2018;20(1):1–10.
[2] Keane MP, Lynch JP. Pleuropulmonary manifestations of systemic lupus erythematosus. Vol. 55, Thorax. Thorax; 2000. p. 159–66.
[3] Haye Salinas MJ, Caeiro F, Saurit V, Alvarellos A, Wojdyla D, Scherbarth HR, et al. Pleuropulmonary involvement in patients with systemic lupus erythematosus from a Latin American inception cohort (GLADEL). Lupus. 2017;26(13):1368–77
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3428

AB0336 PULMONARY MANIFESTATIONS IN A COLOMBIAN COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

S. Herrera[1], J. C. Diaz-Coronado[1,2], S. Monsalve[2], S. Guerra-Zarama[2], M. F. Saavedra Chacón[2], J. Barbosa[1], J. D. Serna Giraldo[2], J. D. Lopez[2], J. M. Gutiérrez[2], T. Vega[2], D. Orozco[2], D. Ocampo[2], N. Zuluaga[2], D. Hernandez-Parra[1], D. Rojas-Gualdrón[3], R. Pineda.Tamayo[1]. [1]*Artmedica IPS, Clinical Information Group, Medellín, Colombia*; [2]*CES University, Department of Internal Medicine, Medellín, Colombia*; [3]*CES University, Facultad de medicina, Medellín, Colombia*

Background: Pulmonary manifestations are frequent in systemic lupus erythematosus (SLE) with a frequency of 30-90% that depends on the cohort and the methods used for their identification. The association of this compromise with mortality highlights its importance and the need for biomarkers to adequately predict this complication. We describe the prevalence of pulmonary manifestations, and the clinic and immunoserological characteristics of 551 Colombian patients with SLE
Objectives: We performed an observational and analytic study of a retrospective cohort with adult SLE patients who fulfilled the 2012 SLICC classification criteria and that had a history of at least 6 months of the disease. These patients were treated in a specialized center of rheumatology with presence in six cities of Colombia between 2015 and 2018. We excluded pregnant patients and those with incomplete data for our survey. The first clinic consult occurred between 2015 and 2018, being defined as moment one. The follow up one year later was defined as moment two. We obtained 710 registries that were potentially eligible and analyzed 465 patients at moment two after applying the exclusion criteria
Methods: In 465 eligible patients, 20,5% had pulmonary compromise (93.8% female) with a median age of 42,4 years. The average SLICC Damage Index of 551 patients with SLE was 0,9 in women and 1.05 in men, while the average SDI of patients with pulmonary compromise was 1. The most frequent manifestation was pleural (14.3%), followed by Lupus pneumonitis (3.6%) and pulmonary hypertension (3.2%). Other manifestations and serological characteristics are recorded in Table 1. Of note, ANA homogeneous pattern was the most common (34.5%), anti-RNP positivity was 41.7%, anti-dsDNA positivity was 53.1% and 53.1% had hypocomplementemia.
Results: The prevalence of pulmonary manifestations in our cohort was 20,5%, which is lower that in the previous described GLADEL cohort (28,4%). This could be explained by the regional differences of ethnicities in Latin America and in immune-serological profiles. Anti-RNP positivity was frequent (41.7%) and new pulmonary compromise for one year follow-up was rare. Of not, the mean damage index for our patients with pulmonary manifestations was 1, this could highlight the importance of this organ as a causa of higher damage accrual and mortality, which we will explore in the future
Conclusion: The prevalence of pulmonary manifestations in our cohort was 20,5%, which is lower that in the previous described GLADEL cohort (28,4%). This could be explained by the regional differences of ethnicities in Latin America and in immune-serological profiles. Anti-RNP positivity was frequent (41.7%) and new pulmonary compromise for one year follow-up was rare. Of not, the mean damage index for our patients with pulmonary manifestations was 1, this could highlight the importance of this organ as a causa of higher damage accrual and mortality, which we will explore in the future
REFERENCES:
[1] G. Aguilera-Pickens, C. Abud-Mendoza. Pulmonary Manifestations in Systemic Lupus Erythematosus: Pleural Involvement, Acute Pneumonitis, Chronic Interstitial Lung Disease and Diffuse Alveolar Hemorrhage. Reumatol Clin. 2018;14(5):294–300.
[2] Haye Salinas MJ, Caeiro F, Saurit V. Pleuropulmonary involvement in patients with systemic lupus erythematosus from a Latin American inception cohort (GLADEL). Lupus (2017) 0, 1–10.
[3] Santamaria-Alza Y, Sanchez-Bautista J, Fajardo-Rivero J. Acute respiratory involvement in Colombian patients with systemic lupus erythematosus undergoing chest computed tomography. Int J Rheum Dis. 2019;00:1–7.

Table 1. clinical and immunoserological characteristics

		n	%
Women		106	93,8
Global mortality		46	8,3
Pulmonary compromise mortality		8	7,1
ANA		104	92
Anti-DNA		60	53,1
ENAS			97,2
Ro		35/87	40,2
La		14/85	16,5
SM		32/88	36,4
RNP		35/84	41,7
	Follow up 1 %	Follow up 2 %	P Value *
Pulmonary hypertension	3,2	2,8	0,28
Pulmonary fibrosis	2,14	2,6	1
Shrunken lung	0,2	0,2	1
Pleuritis	14,3	15,05	0,42
Lupus pneumonitis	3,6	3,01	0,85
Alveolar hemorrhage	1,4	1,3	0,76
Pulmonary embolism	2,3	1,93	0,72

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3452

AB0337 ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE IN SYSTEMIC LUPUS ERYTHEMATOSUS USING THE SLEQoL (SYSTEMIC LUPUS ERYTHEMATOSUS-SPECIFICQUALITY OF LIFE QUESTIONNAIRE)

M. Brahem[1], M. Ardhaoui[1], S. Arfa[2], H. Hachfi[1], B. Ben Rejeb[2], R. Sarraj[1], M. Hassayoun[1], S. Abdellatif[1], A. Ben Salem[1], R. Ben Tekaya[1], O. Berriche[2], Y. Mohamed[1]. [1]*Taher Sfar Hospital, Rheumatology, Mahdia, Tunisia*; [2]*Taher Sfar Hospital, Internal Medicine, Mahdia, Tunisia*

Background: Patients withsystemic lupus erythematosus (SLE) have a better survival than decades ago. Nevertheless, they still experience a low health-related quality of life (HRQoL). The Systemic Lupus Erythematosus-Specific Quality of Life Questionnaire (SLEQoL) is one of the most widely used specific tools for measuring HRQoL in SLE.
Objectives: The aim of our study is to assess the impact of the SLE in the HRQoL using the SLEQoL tool.
Methods: This is a cross-sectional study during a period of the year 2020, including patients followed in the departments of Internal Medicine and Rheumatology in Mahdia, Tunisia. All patients were diagnosed with SLE based in ACR 1997/ SLICC2012. The SLEQoL is composed of 40 items scored from 1 to 7, it includes six HRQoL domains: physical functioning (Items 1 to 6), activities (items 7 to 15), symptoms (items 16 to 23), treatment (items 24 to 27), mood (items 28 to 31) and self-image (items 32 to 40) with higher values corresponding to worse HRQoL.
Results: Forty patients were enrolled. The age of the SLE patients (36 females/4 males) ranged from 11 to 87 years. The mean age was 47.75±17.59 years. The mean disease duration was 2.3 ±2.9 years. The mean SLEDAI score was 5.78±4.94. The main target organs involved were cutaneous, musculoskeletal, neurological, pulmonary, cardiovascular and renal in 85%, 82.5%, 32.5%, 17.5%, 15% and 7.5% of cases respectively. The biologic analysis showed the positivity of anti-nuclear antibodies in 97.5% of cases, low serum complement C3 and C4 in 20% and 32.5% of cases respectively. A biological inflammatory syndrome was found in 37.5% of cases and Anemia in 42.5%. 85% of SLE patients were treated by anti-malarial, 62.5% were treated by Glucocorticoids and 5% by Methotrexate. The mean SLEQoL global score was 77.92 ± 34.02 [40-153]. The means of different domains (physical functioning, activities, symptoms, treatment, mood and self-image) were respectively 12.1±6.49 [6-30]; 19.6±10.9 [9-49]; 16.4±8.1 [8-34]; 5.5±2.36 [4-14]; 9.6±5.4 [4-20]; 14.9±7.5 [9-36]. The most severely impacted domains were activities and symptoms. The less affected domains were treatment and mood. The SLEQoL global score was correlated with increased age (p=0.03), longer disease duration (p=0.05), SLEDAI score (p=0.02), visual analog scale of pain (p=0.04), musculoskeletal manifestations (p=0.04), cutaneous manifestations (p=0.05) and pulmonary manifestations (p=0.05). By analyzing biological tests of our patients, we found a correlation between the SLEQoL global score and Erythrocyte sedimentation rate [ESR] (p=0.05), Anemia (p=0.04), low serum complement C3 (p=0.02) and C4 (p=0.003). SLEQoL global score and its six domains were not correlated with gender, educational level nor marital status.
Conclusion: Our study showed that HRQoL is impaired in patients with SLE. The most important predictors of low HRQoL were older age, longer disease duration, some clinical manifestations, biological activity disease indicators (ESR, anemia and low complement level) and the SLEDAI score.
REFERENCES:
[1] Leong, K. P., Kong, K. O., Thong, B. Y. H., Koh, E. T., Lian, T. Y., Teh, C. L., et al (2005). *Development and preliminary validation of a systemic lupus erythematosus-specific quality-of-life instrument (SLEQOL). Rheumatology, 44(10), 1267–1276.*
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3651

AB0338 PREGNANCY OUTCOMES IN ADOLESCENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

P. Alba[1], Y. Tissera[1], N. Cucchiaro[2], V. Savio[1], R. Serrano Morales[3], M. I. Quaglia[1], J. A. Albiero[1], V. Juarez4, C. A. Gobbi[5], M. Yorio[1], M. E. Crespo Espindola[2]. *[1]Universidad Nacional de Cordoba, Catedra de Semiologia. Servicio de Reumatologia Hospital Cordoba, Cordoba, Argentina*; *[2]Hospital Señor del Milagro, Servicio de Reumatologia, Salta, Argentina*; *[3]Centro de Enfermedades autoinmunes y Reumaticas, Maternidad Oroño, Rosario, Argentina*; *[2]Hospital Señor del Milagro, Servicio de Reumatologia, Salta, Argentina*; *[5]Universidad Nacional de Cordoba, Catedra de Medicina I. Servicio de Reumatologia Hospital Cordoba, Cordoba, Argentina*

Background: Systemic lupus erythematosus (SLE) is a autoimmune disease that affects adolescents and young women of childbearing age. In spite of the improvement in fetal and maternal SLE pregnancy outcome in the last decades, they have increased risk of adverse outcomes including disease flare, abortions, preeclampsia (PE) and premature birth (PB). However, pregnancy outcomes among adolescents with SLE have not been well explored.
Objectives: To evaluate maternal and fetal outcomes in pregnant adolescents with SLE.
Methods: We retrospectively studied all pregnant SLE adolescent patients, who attended to 3 Maternity Hospitals in Argentina in the last 5 years. Demographic, clinical, and laboratory data were collected. The presence of Antiphospholipid Syndrome (APS) and the Antiphospholipid antibodies (AA), and maternal and fetal outcome were evaluated. Adolescent pregnancy was defined it is happened between 10 and 19 years old. Lupus activity was evaluated by SELENA SLEDAI at the conception and each trimester of pregnancy and puerperium.
Results: 32 pregnancies in 21 patients were included. Mean age was 18 years old, 66% was mestizo ethnicity and mean disease duration of 2 years. Renal involvement was found in 19, Mucocutaneous in 21, and hematological in 14 patients. 4 patients had positive Anti-SSA/Ro antibodies, 1 Anti-SSB/La, 2 Lupus anticoagulant, 6 Ig G ACL, 3 Ig M ACL, and 8 patients fulfilled APS criteria. Activity disease was 0 SELENA SLEDAI in 1 ° trimester, 4 in 2°,3° trimester and puerperium. Maternal and fetal outcomes are shown in Table 1. Cesarean section was performed in 58%(n=18) of the patients, 6 had abortions and 1 fetal death.

Table 1.

Maternal outcomes	
Disease Flares	13(41%) 7 renal
(PE)/Hellp	6 (19%)
Gestational Diabetes	1 (3%)
Maternal outcomes Spontaneous Membrane Rupture	1 (3%)
Mortality	0
Fetal outcome	
Live birth	24 (75%)
Gestational age (weeks)	32 (32-38)
Weight (grs)	2805 (2100-3340)
IUGR	5 (16%)
PB	8 (25%)

Conclusion: Maternal and fetal complications were high in adolescent pregnancy with SLE, including disease activity, PE and PB. A tight control of patients should be performed before and after conception. These patients should be managed by a multidisciplinary team, thus allowing an improvement of maternal and fetal prognosis.
REFERENCES:
[1] Ling N, Lawson E, von Scheven E. Adverse Pregnancy outcome in adolescents and young women with systemic lupus erythematosus: a national estimate. Pediatric Rheumatology 2018, 16:26.
[2] FraserA, Brockert J, Ward R: Association of young maternal age with adverse reproductive outcomes. N Engl J Med 1995, 223:1113-1117. 26.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3658

AB0339 PREVALENCE AND ASSOCIATED FACTORS OF LOW BONE MINERAL DENSITY IN ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

M. Ardhaoui[1], M. Brahem[1], S. Arfa[2], H. Hachfi[1], B. Ben Rejeb[2], M. Hassayoun[1], R. Sarraj[1], S. Abdellatif[1], A. Ben Salem[1], R. Ben Tekaya[1], O. Berriche[2], Y. Mohamed[1]. *[1]Taher Sfar Hospital, Rheumatology, Mahdia, Tunisia*; *[2]Taher Sfar Hospital, Internal Medicine, Mahdia, Tunisia*

Background: Patients with Systemic Lupus Erythematosus (SLE) are at risk of osteoporosis (OP) and fragility fractures (FFx) because of the disease or its treatments. We assessed the prevalence and risk factors for OP in patients with SLE.
Objectives: Our objective is to determine the prevalence of bone mineral density (BMD) loss and fracture risk factors in SLE patients undergoing dual-energy X-ray absorptiometry (DXA).
Methods: This is a cross sectional study conducted during the year 2020 in the Rheumatology and internal medicine departements in Taher Sfar hospital of Mahdia, Tunisia. We included patients aged ≥18 years with a diagnosis of SLE according to the 1997 ACR or 2012 SLICC criteria. Patients with renal or hepatic osteodystrophy, or receiving bisphosphonates were excluded from the study. The BMD values were measured by DXA. The T-score, Z-scores and BMD of the lumbar spine (LS) and femoral neck (FN) were determined. OP was defined as a value of the T-score less or equal to -2.5 SD for postmenopausal women and men aged more than 50 years old, and Z-scores less or equal to -2 for premenopausal women and men aged less than 50 years old.
Results: Forty-six SLE patients were included. The mean age was 47.19±16.45 years [18-85], with a mean disease duration of 2.52±3.46 years [15days-15years]. The mean SLEDAI score was 5.34±4.82. As regards menstrual history of female patients: 56.5% were premenopausal, 43.5% were post-menopausal and 6% had premature menopause. 13% of our patients gave history of smoking. The mean BMI was 27.6 ± 6 kg/m2 [15-39.8]. FFx were diagnosed in 4 patients (9%) and the mean age of the first fracture was 45years. GCs were used in 65.2% of cases (30 patients). The mean daily dose of GCs was 10 mg/day and the mean cumulative dose was 20g. Calcium and Vitamin D intake was mentioned in 65.2% of cases (30 patients). The association of SLE with other rheumatic diseases was found in 14 of patients. The mean T-score at FN and LS were respectively 0.02±1.17 and -1.32±1.36. The mean Z-score at FN and LS were respectively 0.53±1.14 and -0.6±1.26. It was found that 17 patients (37% of cases) had OP, 12 had osteopenia (26%) and 17 patients (37%) had normal BMD. 37% of patients had OP at LS, 23.9% osteopenia at LS, 6.5% OP at FN and 21.7% osteopenia at

FN. Low BMD was significantly correlated with increased age (p=0.01) and disease duration(p=0.05),post-menopausal status(p=0.04), higher BMI (p=0.004), musculoskeletal involvement (p=0.01), association to other rheumatic diseases (p=0.01), higher disease activity by SLEDAI score (p=0.05), higher Erythrocyte sedimentation Rate (p=0.01) and C-Reactive Protein (p=0.007), low serum complement C3 (p=0.009) and C4 (p=0.04) and cumulative doses of GCs (p=0.01). We found also that BMD at LS was mostly affected by GCs intake, BMI and CRP while BMD at FN was mostly affected by SLEDAI score, C3 and C4 (p<0.001 in all cases). Gender, history of smoking and cardiovascular comorbidities had no significant impact on BMD.

Conclusion: OP is a common but unrecognised complication of SLE with increased frequency of both peripheral and vertebral FFx. Our study suggests a high risk profile for OP and FFx in SLE which seems to be associated with age, disease duration, post-menopausal status, BMI and GCs.

REFERENCES:

[1] Dey, M., & Bukhari, M. (2018). *Predictors of fracture risk in patients with systemic lupus erythematosus. Lupus, 27(9), 1547–1551.*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3717

AB0340 PATIENTS WITH LABORATORY CRITERIA OF ANTIPHOSPHOLIPID SYNDROME AND "NON-CRITERIA" MANIFESTATIONS: A MULTICENTER STUDY

G. Pires Da Rosa[1,2], E. Ferreira[2,3], B. Sousa-Pinto[4,5], P. Bettencourt[2,6], R. Cervera[1], G. Espinosa[1]. *[1]Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS), University of Barcelona, Department of Autoimmune Diseases, Barcelona, Catalonia, Spain*; *[2]University of Porto, Faculty of Medicine, Porto, Portugal*; *[3]Centro Hospitalar Universitário de São João, Department of Internal Medicine, Porto, Portugal*; *[4]CINTESIS – Center for Health Technology and Services Research, Porto, Portugal*; *[5]Faculty of Medicine, University of Porto, MEDCIDS – Department of Community Medicine, Information and Health Decision Sciences, Porto, Portugal*; *[6]Hospital CUF, Department of Internal Medicine, Porto, Portugal*

Background: Patients with laboratory criteria for antiphospholipid syndrome (APS) and presenting only "non-criteria" clinical manifestations are scarcely described in the literature [1-3].

Objectives: To describe a cohort of these patients, portraying potential associations between "non-criteria" manifestations, antiphospholipid antibodies (aPL) and treatments.

Methods: Retrospective analysis of patients with aPL positivity fulfilling APS criteria assessed in two tertiary European hospitals between 2005 and 2020. Those without criteria clinical manifestations but with the presence of "non-criteria" manifestations were included.

Results: A total of 75 patients were analyzed. The predominant non-obstetric involvements were hematologic (thrombocytopenia, hemolytic anemia) and "mild" neurological (white matter lesions, migraine), with an absence or near absence of cutaneous, cardiac, pulmonary and more severe neurologic manifestations (Table 1). In obstetric morbidity, two spontaneous abortions before 10 weeks and infertility were the more frequent manifestations. LA positivity was positively associated with non-obstetric manifestations (OR=4.2, 95% CI 1.5-11.9; p=0.007) while an aCL profile was associated with obstetric manifestations (OR 7.0, 95% CI 2.3-21.3; p=0.001). A suspicion of progression towards SLE was considered plausible in 13 (19%) of non-SLE individuals. Twelve (40.0%) of patients with thrombocytopenia as their only hematological involvement required corticosteroids. History of infertility (OR 6.1, 95% CI 1.3-28; p=0.02) and IVF recurrent failure (OR 6.5, 95% CI 1.2-36.3; p=0.032) were associated with pregnancy treatment with LMWH/LDA combination. Among patients under anticoagulation, clinical manifestations included brain white matter lesions, APS nephropathy, superficial vein thrombosis, amaurosis fugax, and livedoid vasculopathy. A higher value of GAPSS was observed in patients with non-obstetric (median 9, IQR 5-13) in comparison to those with obstetric manifestations (median 5, IQR 4-5.5).

Conclusion: The present article stresses the clinical relevance of these patients, with an impression that at least some manifestations will contribute in the future to the classification of individuals as definite APS.

REFERENCES:

[1] J. Alijotas-Reig *et al.*, Comparative study of obstetric antiphospholipid syndrome (OAPS) and non-criteria obstetric APS (NC-OAPS): report of 1640 cases from the EUROAPS registry. *Rheumatology (Oxford)*, (2019).

[2] M. Fredi *et al.*, Risk Factors for Adverse Maternal and Fetal Outcomes in Women With Confirmed aPL Positivity: Results From a Multicenter Study of 283 Pregnancies. *Front Immunol* **9**, 864 (2018).

[3] E. Sevim *et al.*, Characteristics of Antiphospholipid Antibody Positive Patients in AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking. *Arthritis Care & Research* **n/a**.

Table 1. "Non-criteria" clinical manifestations present in the analyzed population.

Clinical manifestation	n (%)
Non-obstetric	**n = 49**
Thrombocytopenia	34 (69.4)
Coombs´ positivity	11 (22.4)
Migraine	11 (22.4)
Hemolytic anemia	5 (10.2)
Brain MRI white matter lesions	5 (10.4)
Raynaud´s phenomenon	5 (10.2)
Superficial vein thrombosis	4 (8.1)
Evans syndrome	4 (8.1)
Amaurosis fugax	3 (6.1)
APS nephropathy	2 (4.1)
Livedo reticularis	1 (2.0)
Livedoid vasculopathy	1 (2.0)
Memory lapses	1 (2.0)
Pseudo-multiple sclerosis	1 (2.0)
Sensorineural hearing loss	1 (2.0)
Splinter hemorrhages	1 (2.0)
Obstetric	**n = 38**
Two spontaneous abortions <10 weeks	16 (42.1)
Infertility	14 (36.8)
≥ 2 or more IVF failures	11 (28.9)
Late IUGR (>34 weeks)	7 (18.4)
Premature birth between 34 and 37 weeks	7 (18.4)
Placental ischemia	5 (13.1)
Late preeclampsia (>34 weeks)	3 (8.0)
Placental abruption	2 (5.3)
Placental hematoma	2 (5.3)

Abbreviations –aCL: anticardiolipin antibodies; AI: Autoimmune; AID: Autoimmune disease; aPL: Antiphospholipid antibodies; IUGR: Intrauterine growth restriction; IVF: *in vitro* fertilization; LA: Lupus anticoagulant.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3757

AB0341 SLE PREGNANCIES AT HIGH RISK FOR PRE-ECLAMPSIA BENEFIT MOST FROM COMBINATION OF LOW DOSE ASPIRIN AND HYDROXYCHLOROQUINE

I. Haase[1], G. Chehab[1], O. Sander[1], M. Schneider[1], R. Fischer-Betz[1]. *[1]Heinrich-Heine-University Duesseldorf, Policlinic for Rheumatology & Hiller Research Unit for Rheumatology, Duesseldorf, Germany*

Background: Women with SLE face a high risk of preeclampsia (PE). Low dose Aspirin (LDA) is known to protect against PE in non-autoimmune patients and is recommended for SLE patients[1]. Besides, a beneficial effect of hydroxychloroquine (HCQ) on the occurrence of PE has recently been discussed[2].

Objectives: To investigate the influence of LDA and HCQ on the occurrence of PE in SLE patients.

Methods: Pregnancies of women with SLE from an outpatient pregnancy clinic were prospectively evaluated. Clinical characteristics, medication use and pregnancy outcomes were analysed. Association of LDA use (latest from gestational week 16 on) and HCQ use (from 1st trimester on) with PE were analysed using a multiple logistic regression model (adjustment for age, BMI, hypertension, disease activity in 1st trimester, lupus nephritis, nulliparity, history of PE and high-risk aPL profile[3]).

Results: We enrolled 190 lupus pregnancies (148 women, 1995-2019). Additional risk factors for PE were present in 83.7%: 55.8% showed a high-risk profile (HRP) for PE according to ACOG[4] (history of PE, hypertension, lupus nephritis or aPL), another 27.9% had at least one moderate risk factor (nulliparous, BMI>30 or age>35) (see table 1).

Each 20.5% of pregnancies received HCQ only or LDA only, while 22.6% were prescribed both drugs. 36.3% took neither HCQ nor LDA. Women with HRP were more likely to take LDA alone or in combination with HCQ (28.3% and 35.8%, respectively).

PE occurred in 13.2% of pregnancies (7.7% in HCQ only, 15.4% in LDA only, 14.0% in HCQ and LDA, 14.5% in no HCQ or LDA). Most pregnancies affected by PE carried a HRP (88.0%).

Use of LDA was significantly associated with a lower risk for PE [aOR 0.21 (95%-CI 0.05-0.99), p<0.05]. HCQ use also had a moderating effect on the incidence of PE, but this effect did not reach significance [aOR 0.47 (95%-CI 0.15-1.52), p=0.21]. If only pregnancies with HRP were considered, the effect size increased for HCQ (LDA [aOR 0.18 (95%-CI 0.04-0.96), p<0.05], HCQ [aOR 0.28 (95%-CI 0.07-1.14), p=0.075]).

Conclusion: In this prospective real-life cohort, timely LDA medication was associated with a lower risk of PE in SLE pregnancies. In a multiple regression model taking LDA and HCQ into account, the favourable effect on the occurrence of PE was partially explained by HCQ. In particular, SLE patients at high risk

for PE seem to benefit from HCQ during pregnancy. Future research may reveal mechanisms by which HCQ might lower the incidence of PE.

REFERENCES:
[1] doi: 10.1136/annrheumdis-2016-209770
[2] doi: 10.1111/bcp.14131
[3] doi: 10.1136/annrheumdis-2019-215213
[4] doi: 10.1097/AOG.0000000000002708

Table 1. Patient characteristics and risk profile

		HCQ only (n=39)	LDA only (n=39)	HCQ + LDA (n=43)	no HCQ or LDA (n=69)
Patient characteritics	Age (years), median (IQR)	29 (25-33)	32 (30-33)	30 (28.5-33.5)	31 (28-35)
	BMI, median (IQR)	23.5 (22-25)	23 (22-24)	22 (22-24)	23 (22-24)
	Chronic Hypertension, n (%)	7 (17.9%)	9 (23.1%)	6 (14.0%)	9 (13.0%)
	Preconception counselling, n (%)	23 (59.0%)	28 (71.8%)	35 (81.4%)	41 (59.4 %)
Obstetrical history	Nulliparous, n (%)	20 (51.3%)	26 (66.7%)	33 (76.7%)	36 (52.2%)
	Previous fetal loss, n (%)	1 (2.6%)	10 (25.6%)	14 (32.6%)	10 (14.5%)
	Previous PE, n (%)	2 (5.1%)	4 (10.3%)	4 (9.3%)	5 (7.2%)
SLE characteristics and therapy	Disease duration (years), median (IQR)	7.0 (2.0-11.0)	7.5 (3.0-11.5)	6.7 (3.4-10.0)	6.0 (3.0-9.2)
	SLEDAI, median (IQR)	2.0 (1.0-4.3)	2.0 (0-2.5)	4.0 (2.0-4.0)	2.0 (0-4.0)
	Lupus nephritis, n (%)	9 (23.1%)	13 (33.3%)	18 (41.9%)	14 (20.3%)
	Anti-dsDNA antibodies, n (%)	22 (56.4%)	15 (38.5%)	36 (83.7%)	33 (47.8%)
	Prednisolone therapy, n (%)	26 (66.7%)	15 (38.5%)	25 (58.1%)	29 (42.0%)
	Prednisolone (mg/d), median (IQR)	5.0 (5.0-8.0)	5.0 (5.0-7.5)	5.0 (4.0-5.0)	5.0 (5.0-8.0)
aPL status	APS, n (%)	-	12 (30.8%)	14 (32.6%)	2 (2.9%)
	Any positive aPL, n (%)	-	20 (51.3%)	19 (44.2%)	5 (7.2%)
	LAC, n (%)	-	15 (38.5%)	13 (30.2%)	3 (4.3%)
	ACL, n (%)	-	14 (35.9%)	13 (30.2%)	4 (5.8%)
	β2-GP1, n (%)	-	12 (30.8%)	12 (27.9%)	2 (2.9%)

LAC = Lupus anticoagulant, ACL = Anticardiolipin antibody, β2-GP1 = β2-Glycoprotein I antibody

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3839

AB0342 OBSTETRIC AND THROMBOTIC ANTIPHOSPHOLIPID SYNDROME: ARE THEY DIFFERENT ENTITIES?

R. Serrano Morales[1], R. Nieto[1], S. Porta[1], K. Roberts[1], L. Lema[1], C. Maldini[1], Y. Tissera[1], J. A. Albiero[1], V. Savio[1], C. Goizueta[1], V. Lobo[1], A. Broll[1], N. Cucchiaro[1], S. ¨perez[1], P. Izaguirre[1], A. Estevez[1], A. I. Abalo[1], M. Etcheverry[1], V. I. Bellomio[1], M. L. Leguizamón[1], N. Antoniol[1], C. Perandones[1], C. Pisoni[1], M. L. De la Torre[1], M. García[1], M. S. Velloso[1], M. Sacnun[1], C. Gobbi[1], D. Guaglione[1], F. Vivero[1], V. Saurit[1], N. Benzaquen[1], V. Nemman[1], G. Remondino[1], M. Machado Escobar[1], M. Scolnik[1], C. Danielsen[1], G. Gomez[1], A. M. Babini[1], A. Brigante[1], A. Luissi[1], V. V. Castro Coello[1], L. Sorrentino[1], H. Berman[1], P. Alba[1], G. Pons-Estel[1]on behalf of Antiphospholipid Syndrome Study GroupArgentine Society of Rheumatology..
[1]*Argentine Society of Rheumatology,APS Study Group, Buenos Aires, Argentina*

Background: Several studies showed two main clinical phenotypes of antiphospholipid syndrome (APS): thrombotic (TAPS) and obstetric APS (OAPS). Although they have the same autoantibody profile, one of them developed thrombosis and other one obstetric morbidity.
Objectives: To study clinical, demographic and antibody profile in patients with TAPS and OAPS.
Methods: we retrospectively evaluated TAPS and OAPS patients who were included in Argentine Antiphospholipid antibodies registry. We studied clinical, demographic and antibody profile in both groups.
Results: 238 patients were included in the registry. 201 (84.81%) of them were female. 122 (60.69 %) of them fullfilled APS Sydney classification criteria, 47 (38.52%) TAPS and 52 (42.62%) OAPS. 23 (18.85%) patients had both thrombotic and obstetric events so they were excluded in this analysis.
Arterial Hypertension (HBP) and Hyperlipidemia were more frequent in TAPS versus OAPS. Older age was found in TAPS as well as in association with Systemic lupus erythematosus (SLE). There was no difference in antibody profile between the 2 groups, and the Global Antiphospholipid Syndrome Score (aGAPSS) was higher in TAPS than OAPS.
18 (38.3%) of TAPS patients had at least 1 pregnancy. Mean number of pregnancies of TAPS was 2.5 (1.10) and 3.84 (1.86) in OAPS. Thrombotic events were not found in TAPS during pregnancy and puerperium. HBP and gestational diabetes (GD) and other pregnancy related comorbidities were found in TAPS.

	OAPS (n=52)	TAPS (n=47)	P		OAPS (n=52)		TAPS (n=18)	
SLE, *n (%)*	11 (21.2)	28 (59.6)	0.0002		N	% (DE)	N	% (DE)
aGAPSS, *mean (RIQ)*	4 (5)	8 (5)	<0.0001	Abortions (<10 weeks)	33	38.4 (36.2)	8	26.5 (35.3)
Age, mean *(DE)*	39.3 (6.24)	43.1 (13.5)	<0.0001	Live Birth	36	33.5 (28.1)	16	72.2 (34.7)
HBP, *n (%)*	5 (9.6)	15 (31.9)	0.0121	>37 weeks	21	16.4 (2.38)	16	61.1 (31.7)
Hyperlipidemia, *n (%)*	4 (7.7)	12(25.5)	0.0267	Prematurity <37 >34 weeks	11	8.76 (1.97)	0	-
GD, *n (%)*	3(5.8)	2(4.3)	0.9999	Prematurity <34 weeks	9	6.37 (1.49)	1	1.39 (5.89)
Obesity, *n (%)*	8 (15.4)	4 (8.5)	0.2912	Pre eclampsia >34-<37 weeks	1	0.490 (0.0350)	2	4.63 (0.138)
Smoking, *n (%)*	11 (21.1)	13 (27.6)	0.4019	Placental Hematoma	3	1.86 (8.18)	1	2.78 (11.8)
Sedentary lifestyle, *n (%)*	16 (30.8)	17 (36.2)	0.8486	Abruptio Placentae	2	1.96 (9.80)	2	4.17 (12.9)
Triple Positivity	5	4	0.8323	Normal delivery	20	17.8 (27.9)	14	47.7 (33.9)
	9.6	8.5						
Double Positivity	1	3		Cesarean section	22	17.2 (21.6)	2	11.1 (32.3)
	1.9	6.4						
Simple Positivity	29	19		Urgent Cesarean section	13	9.80 (20.3)	4	12.5 (24.6)
	38.5	40.4						
				GD	2	1.37 (7.49)	1	2.78 (11.8)
				HBP	6	3.46 (10.3)	3	10.2 (26.3)

Conclusion: Antibody profile was similar in TAPS and OAPS. However, clinical manifestations and cardiovascular risk were different. These results should be evaluated in prospective studies.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3842

AB0343 THE CHARACTERISTICS OF T CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH ANXIETY BASED ON MACHINE LEARNING

X. Gu[1], Y. Jin[1], R. Li[1], D. Zhang[1], C. Dong[1], Q. Zhang[2], Z. Xue[2], Z. Gu[1].
[1]*Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*; [2]*Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China*

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease, the immune system of patients to be disordered, especially in T cell subsets[1]. They were prone to mental diseases, anxiety particularly, which lead to suicide[2]. The recent study had reported that $CD4^+$ T cells in the peripheral blood played the key role in like anxiety behavior of mice[3]. Although there showed that the level of serum TNF-α in SLE patients with anxiety was higher than without anxiety[4], finding the important special mediators especially in T cell subsets was still necessary for the prevention of anxiety in SLE patients.
Objectives: In total, 108 SLE patients, which met the diagnostic criteria of the American Society of rheumatology (v1997), were enrolled in this study from Affiliated Hospital of Nantong University, China. Exclusion criteria included other autoimmune diseases and active infection (including hepatitis B or C virus, Epstein-Barr virus, human immunodeficiency virus or Mycobacterium tuberculosis infection).
Methods: We surveyed the abundance of 74 immune cell subpopulations from 108 SLE patients using flow cytometry, and investigated their differences between patients with and without anxiety (24 versus 84). Moreover, machine learning including Lasso regression, Random forest (RF) and Sparsity partial least squares discriminant analysis (sPLS-DA) was employed to build models and futher selected important features for the classification of SLE patients with anxiety.
Results: SLE patients with anxiety showed higher body mass index (BMI) and lower quality of life. In their peripheral blood, the proportion of internal cell subsets composition of Th cell and Treg cells changed. By machine learning, we

finally found that BMI and PD1$^-$CD28$^-$ Treg played important rules to developing lupus anxiety.

Conclusion: In this study, machine learning was applied to build models to select the most important T cell subset in SLE patients with anxiety. These findings suggested that BMI and imbalance of PD1$^-$CD28$^-$ Treg containing effector memory Treg cells and effector Treg cells mostly played important roles in the development of SLE anxiety.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3857

AB0344 PREVALENCE AND RISK FACTORS FOR SEROSITIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE CONTROL STUDY

L. Gimeno-Torres[1], I. Carrión Barberà[1], X. Duran[2], T. C. Salman Monte[1]. *[1]Hospital del Mar, Rheumatology, Barcelona, Spain; [2]IMIM, Statistics, Barcelona, Spain*

Background: Systemic lupus erythematosus (SLE) is an autoimmune multisystemic disease with a wide variety of clinical manifestations, being one of them serositis, which includes pericarditis, pleuritis and peritonitis [1]. Incidence of serositis ranges between 11-54% [2].

Objectives: To determine the prevalence of serositis in patients (pt) with SLE attended at the outpatient Lupus Unit and identify factors that could be used as predictors of this manifestation.

Methods: Retrospective case-control study. 297 medical records of SLE pt were reviewed: 28 pt were diagnosed with serositis (cases) and were age- and sex-matched with 2 controls with SLE without serositis. Differences between cases and controls were analyzed as well as factors associated with serositis.

Results: Patient's characteristics are described in Table 1. The prevalence of serositis in our cohort was 9.42%. The difference between the prevalence of serositis in men and women was statistically higher in men, 30% vs 7.9% (p=0.001, CI 95%: 1.7%-42.4%). Serositis was diagnosed at an age of 41 ±14 years (y) and in 40.7% it was the first symptom. Time from SLE diagnosis to serositis was 4±5.3 y. 10 pt had recurrences: 6 had 2, and 4 had 3. Incidence of pericarditis and pleuritis was 78.6% and 82.1% respectively. 2 pt suffered from pericardial tamponade. Mean prednisone dose received during the serositis was 44.6±26.6mg. At the moment of serositis 100% were ANA+, 85.7% antidsDNA+, 80% CrithidiaDNA+, 57.9% antiRo60+, 52.6% antiRo52+, 15.9% antiLa+, 47.4% antiRNP+, 21.1% antiSm+, and 77.8% had low C3.

When looking for serositis-associated factors we only found association with antidsDNA measured by Crithidia (p=0.016) and different measures of glucocorticosteroids (GC), having cases needed higher doses than controls (Table 1). Those with serositis had significantly received more mycophenolic acid (p=0.021) and marginally, more belimumab (p=0.056).

Table 1. Characteristics of cases and controls. *indicates mean±SD, Bold=statistically significant difference.

VARIABLES	CASES (28)	CONTROLS (54)	p-value
Female	22 (33.3%)	44 (66.7%)	0.775
Male	6 (37.5%)	10 (62.5%)	
Caucasian	20 (32.8%)	41 (67.2%)	0.693
Hispanic American	7 (38.9%)	11 (61.1%)	
Others	1(33.3%)	2 (66.6%)	
Arthritis	22 (38.6%)	35 (61.4%)	0.219
Leukopenia	17 (34.0%)	33 (66.0%)	1.000
Lymphopenia	25 (33.8%)	49 (66.2%)	1.000
Thrombocytopenia	5 (20.8%)	19 (79.2%)	0.128
Nephritis	8 (50.0%)	8 (50.0%)	0.152
Raynaud's phenomenon	6 (42.9%)	8 (57.1%)	0.263
Haemolytic anaemia	3 (42.9%)	4 (57.1%)	0.686
Antinuclear antibodies	28 (34.6%)	53 (65.4%)	1.000
AntidsDNA	23 (37.7%)	38 (62.3%)	0.295
AntiSm	9 (42.9%)	12 (57.1%)	0.425
AntiRo52	10 (41.7%)	14 (58.3%)	0.444
AntiRo60	13 (37.1%)	22 (62.9%)	0.645
AntiRNP	14 (43.8%)	18 (56.3%)	0.159
CrithidiaDNA	19 (47.5%)	21 (52.5%)	**0.016**
Low C3	21 (39.6%)	32 (60.4%)	0.224
Low C4	13 (38.2%)	21 (61.8%)	0.637
Low CH50	13 (39.4%)	20 (60.6%)	0.480
SLICC*	0.54 (±0.9)	0.49 (±1.1)	0.717
SLEDAI*	3.1 (±3.1)	2.98 (±3.2)	0.844
Corticosteroids			
Ever	27 (38.6%)	43 (61.4%)	**0,051**
Pulses ever	9 (60.0%)	6 (40.0%)	**0.033**
Maximum prednisone dose ever:			
<10mg	18 (85.7%)	3 (14.3%)	**0.003**
10-29mg	14 (87.5%)	2 (12.5%)	
30-60mg	11 (45.8%)	13 (54.2%)	
>60mg	8 (47.1%)	9 (52.9%)	

Conclusion: The prevalence of serositis was 9.42%. Serositis is significantly more frequent in SLE men than in women: almost ⅓ will develop serositis, so we need greater awareness of serositis in SLE men.

CrithidiaDNA+ was identified as an associated factor of serositis. Furthermore, pt with serositis significantly received more pulses of GC and a higher maximum dose throughout the disease, which could imply a more aggressive form of SLE than in those without serositis. No correlation was found between serositis and any other characteristic.

REFERENCES:

[1] Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1725

[2] Ryu S, Fu W, Petri MA: Associates and predictors of pleurisy or pericarditis in SLE. Lupus. Science. 2017, 4(1):e000221.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3932

AB0345 TH9 CELLS AND THEIR ASSOCIATED CYTOKINES: THE PROBABLE PLAYERS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND TYPE 1 DIABETES MELLITUS (T1DM)

N. Mohannad[1], M. Moaaz[2], R. Mohamed Shehata[3]. *[1]Alexandria University Hospitals, Faculty of Medicine, Alexandria University, Internal Medicine Department, Alexandria, Egypt; [2]Medical Research Institute, Alexandria University, Immunology & Allergy, Alexandria, Egypt; [3]Molecular Biology Department, Faculty of Science, Alexandria University*

Background: SLE is an autoimmune disease (AID) of unknown origin. Several factors can contribute to immune dysfunction in SLE.

Interleukin 9 (IL9) is a newly emerging T cell-derived factor preferentially expressed by CD4+T cells: T helper 9 (Th9)

IL9 targets different cell lineages, and can contribute to the development of allergic & AIDs

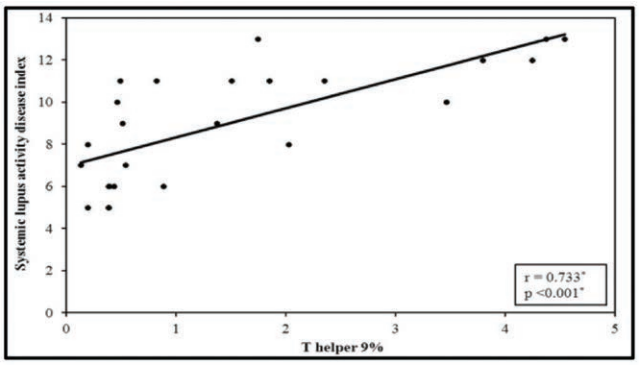
Whether abnormal expression and secretion of IL9 are present in SLE patients (pts) still unidentified. It is also unclear whether IL9 exerts main proinflammatory or anti-inflammatory activities in SLE. T1DM is characterized by inflammation of the pancreatic islets of Langerhans. Insulitis progresses over time and β cells become destroyed then clinical DM is established. T1DM is regarded as a T cell-driven AID

Objectives: Evaluation of the expression of CD4+ IL9+ T cells & the level of IL9 in SLE pts compared to both healthy subjects & pts with another AID: T1DM.Also, to evaluate the correlation of these expressions with clinical features, laboratory parameters and SLE activity

Methods: The study included: **Group I** 25 SLE pts fulfilling SLICC classification criteria divided into 2 subgroups (gps) according to SLE disease activity index (SLEDAI) IA: 20 pts with mild to moderate activity (<12) IB:5 pts with severe activity (>12) recruited from rheumatology clinic or internal medicine ward (Rheumatology unit), Main University Hospital, Alexandria. **Group II** 15 healthy individuals as a first control gp. **Group III** 15 pts with T1DM fulfilling the American Diabetes Association criteria as a second control gp. All pts were subjected to history taking, clinical examination,laboratory investigations: CBC,LFT,KFT,ESR,CRP,ANA,Anti-dsDNA,Th9 cell expression detection by flowcytometry and serum IL9 by ELISA

Results: There was no statistical difference between all gps as regards age & sex but a significant increased ESR in SLE compared to controls & T1DM p< 0.001 p=0.001

Th9 expression was highly increased in SLE pts, range 0.13-4.54% & mean ±SD=1.50 ± 1.47% than both control gps. In healthy controls Th9 ranged between 0.0-1.29% with mean 0.37 ±0.52%, while in T1DM pts ranged between 0.03



to 2.13% with mean of 0.67 ± 0.59%. A high significant difference was found between SLE pts and controls p=0.001, an insignificant rise was seen in SLE pts compared to T1DM pts p=0.157. A high significant increase in Th9 was found in severe SLE: mean of 3.74 ±1.15% than in pts with mild to moderate SLE: mean 0.94±0.88% p=<0.001

IL9 level was highly increased in SLE pts: mean of 42.83± 23.98 pg/ml than both control gps. In healthy controls the mean was 8.54±13.27, while in T1DM with mean of 29.17±16.09 pg/ml. A high significant difference was found between SLE pts and normal controls p<0.001 but an insignificant rise with T1DM p=0.294. A high significant increase in IL9 in pts with severe ds compared to mild to moderate pts p<0.001.A significant direct correlation between Th9 & IL9 and SLEDAI/105 A significant direct correlation between damage index and Th9 p=0.040 but not IL9 p=0.053

In SLE no significant relation between Th9 or IL9 & clinical manifestations or disease duration. A direct correlations between Th9 & ESR p=0.046 and CRP p=0.025,a significant correlation between IL9 and CRP p=0.033, no correlations between Th9&IL9 level and anti-dsDNA p=0.593& 0.4 Significant direct correlation between Th9 and IL9 in T1DM pts, still no correlation with glycemic profile. IL9 levels were significantly increased in SLE with elevated CRP p=0.033 & the % of Th9 cells were increased with elevated ESR and CRP p=0.025, 0.046

Conclusion: In SLE pts; IL9 level and Th9 cells expression were significantly elevated compared to healthy controls. IL9 levels and the percentages of Th9 directly correlated with the SLE disease activity. IL9 levels also were significantly increased in T1DM pts compared to controls,but they were less expressed than in SLE. This suggests an important role of IL9 in the pathogenesis AIDs as SLE

REFERENCES:

[1] Tahernia L et al. Cytokines in SLE: their role in pathogenesis of disease and possible therapeutic opportunities. Rheum Res 2017

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3946

AB0346 RHUPUS SYNDROME: CLINICAL ANALYSIS OF 21 PATIENTS

M. Ben Brahim[1], S. Daada[1], M. Elghali[2], J. Mahbouba[3], N. Bergaoui[3], S. Hammami[1]. [1]*Fattouma Bourguiba University Hospital, Internal Medicine, Monastir,Tunisia*; [2]*Fattouma Bourguiba University Hospital, Immunology, Monastir,Tunisia*; [3]*Fattouma Bourguiba University Hospital, Rhumatology, Monastir,Tunisia*

Background: Rhupus syndrome is a clinical condition characterized by a combination of the clinical and immunologic features of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) (1). However, this definition did not establish whether Rhupus syndrome is a distinct clinical entity or is an overlap between RA and SLE. To date, fewer than 200 cases of Rhupus have been reported (1).

Objectives: Our purpose was to analyze the clinical and serological characteristics of patients with Rhupus and compare them with patients with SLE.

Methods: We undertook a retrospective study covering 10 years (2009 to 2019) of experience in our University Hospital: Department of Internal Medicine and department of Rheumatology. 238 patients hospitalized were evaluated during this period. The clinical and laboratory parameters of 21 patients with Rhupus syndrome were compared with those of 217 SLE without RA patients

Results: Twenty one patients were included (all fulfilled ACR criteria for SLE as well as for RA).They were 19 female and 2 male. The mean age of patients at the disease onset was 43.5 years. Among these, 9 patients (42.8%) were diagnosed with RA at the onset of disease and then developed SLE over an average period of 6.2 years. Six patients (28.5%) had a diagnosis of SLE prior to the RA diagnosis with an interval of 8.6 years between diagnoses. Six patients (28.5%) were diagnosed with RA and SLE concomitantly. Patients with Rhupus experienced more often arthritis, joint swelling, morning stiffness and joint erosions then patients with SLE alone (p<0.001). Comparison of extra-articular manifestations showed that, renal involvement was less often in patients with Rhupus when compared to patients with SLE-alone. There were no significant differences in the prevalence of malar rash, serositis, neurological and hematological features between the Rhupus and SLE-alone groups. Rheumatoid factor and anticyclic citrullinated peptide (CCP) antibody were significantly more prevalent in the Rhupus group than in the control group. The incidences of increased erythrocyte sediment rate (ESR) and C-reactive protein (CRP) were also significantly higher in Rhupus patients. (Table 1)

Table 1. Comparison of clinical and biological features between Rhupus Syndrome (Rhupus Group) and SLE-alone patients (Control Group).

	Rhupus Group N=21 (%)	Control Group N=217 (%)	p
Malar rash	12 (57.1)	120 (55.3)	0.87
serositis	6 (28.5)	47 (21.7)	0.46
Lupus nephritis	4 (19)	56 (25.8)	0.49
Hemolytic anemia	1 (4.7)	8 (3.6)	1
Leucopenia	8 (38)	90 (41.4)	0.15
Thrombopenia	4 (19)	27 (12.4)	1
Polyarthritis	21 (100)	54 (24.8)	<0.001
Erosion of joint	21 (100)	0	<0.001
Increased ESR	20 (95.2)	155 (71.4)	0.019
Increased CRP	18 (85.7)	88 (40.5)	<0.001
Anti-DNA antibodies	16 (76.1)	134 (61.7)	0.61
Anti-Sm antibodies	6 (28.5)	63 (29)	0.57
Rhumatoide Factor	12 (57.1)	52 (23.9)	0.04
Anti-CCP antibody	6 (28.5)	14 (6.5)	0.027

CRP: C-reactive protein, ESR: erythrocyte sediment rate, Anti-CCP: anticyclic citrullinated peptide antibody.

Conclusion: Patients sharing features of both RA and SLE have been observed infrequently. In fact, the incidence of Rhupus syndrome in SLE patients is estimated at 1.3% **(2)**. In our study, this incidence was 8.8%. The findings of our study are consistent with those of most studies with respect to the frequencies arthritis, lupus related features, and serological disorders **(2,3)**.

REFERENCES:

[1] Rubini E, Foddai SG, Radin M, Cecchi I, Rossi D, Sciascia S, et al. Ab1177 How to Define Rhupus Syndrome: Systematic Review of the Current Literature. Ann Rheum Dis. 2019 Jun 1;78(Suppl 2):2049–50.

[2] Li J, Wu H, Huang X, Xu D, Zheng W, Zhao Y, et al. Clinical Analysis of 56 Patients with Rhupus Syndrome: Manifestations and Comparisons with Systemic Lupus Erythematosus. Medicine(Baltimore). 2014; 93(10): 958-63.

[3] Liu T, Li G, Mu R, Ye H, Li W, Li Z. Clinical and laboratory profiles of rhupus syndrome in a Chinese population: a single-centre study of 51 patients. Lupus. 2014;23(9):958–63.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3969

AB0347 RENAL BIOPSY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: IS IT ONLY LUPUS NEPHRITIS?

E. Duran[1], T. Yıldırım[2], U. Kalyoncu[1], A. Taghiyeva[3], E. Bilgin[1], E. Arzu Sağlam[4], M. Üner[4], J. Jabrayilov[2], E. C. Bolek[1], C. Önal[2], B. Farisoğulları[1], N. S. Koç[2], G. K. Yardımcı[1], S. Girgin[2], G. Ayan[1], Z. Özsoy[1], G. Sandal Uzun[1], L. Kılıç[1], Ş. R. Yılmaz[2], A. Akdoğan[1], Ş. A. Bilgen[1], O. Karadag[1], S. Kiraz[1], B. Altun[2], Y. Erdem[2], M. Arıcı[2], A. İ. Ertenli[1]. [1]*Hacettepe University School of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; [2]*Hacettepe University School of Medicine, Department of Internal Medicine, Division of Nephrology, Ankara, Turkey*; [3]*Hacettepe University School of Medicine, Department of Internal Medicine, Ankara, Turkey*; [4]*Hacettepe University School of Medicine, Department of Department of Pathology, Ankara, Turkey*

Background: Renal biopsy is a cornerstone in the diagnosis and management of renal involvement in patients with systemic lupus erythematosus (SLE). However, non-lupus nephritis has been also observed in SLE patients with renal disease (1).

Objectives: The aim of this study was to draw attention to the causes of non-lupus nephritis in SLE patients with kidney biopsy.

Methods: This retrospective, descriptive study included 139 SLE patients who had at least one kidney biopsy between 2001 and 2020. All patients had fulfilled the SLICC or EULAR/ACR criteria for SLE. According to the pathology report results, 116 of the patients were diagnosed with lupus nephritis (LN), 18 patients had non-lupus nephritis, 2 biopsies were normal, and 3 biopsies were insufficient. Demographics, SLE disease duration, and renal biopsy diagnosis were derived from our hospital medical records.

Results: Of the 23 patients (female:18/male:5), the mean age at the SLE diagnosis was 30.5 years and the median SLE disease duration was 8.5 (11.6) years. Pathologic report findings were compatible with focal segmental glomerulosclerosis in 6 patients, membranous nephropathy with no cellular proliferation and inflammation in 4 patients, thrombotic microangiopathy in 3 patients, IgM nephropathy in 2 patients, tubulointerstitial nephritis in 2 patients, and proliferative glomerulonephritis with monoclonal IgG deposits in one patient. There were no different for SLE manifestation in both gropus. LN vs other renal pathologies

laboratory comparing as follow: ANA (+) ≥ 1:320 89 (76.7%) vs 14 (60.9%), APS antibodies 31 (33.7%) vs 8 (57.1), anti-Sm (+) 8 (11.8%) vs 1 (4.3%) were similar for LN and other renal pathologies, but anti-ds-DNA positivity 94 (84.7%) vs 10 (50%), median ds-DNA level 421 (591) vs 150 (340) and low level of C3 and C4 were more frequent in LN (p<0.001; p=0.005; p<0.001, respectively).In addition, the rate of active urinary sediment and renal SLEDAI score were significantly high in LN patients.

Conclusion: Various renal lesions unrelated to lupus nephritis can be observed in SLE patients. Renal biopsy plays a critical role in identifying these lesions, which may have prognostic and therapeutic implications distinctive from those of lupus nephritis. Also, anti ds-DNA positivity/level, low C3 and C4, active urinary sediment and renal SLEDAI scores may give us some clues in terms of renal pathology for SLE patients. Moreover, almost half of the patients without LN in renal biopsy have anti ds-DNA positivity.

REFERENCES:

[1] Howell DN. Renal biopsy in patients with systemic lupus erythematosus: Not just lupus glomerulonephritis! Ultrastruct Pathol. 2017 Mar-Apr;41(2):135-146.

Table 1. Demographic, clinical characteristics and results of patients with and without lupus nephritis

Variables*	Lupus nephritis (N=116)	Other pathologies (N=23)	P
Age at the SLE diagnosis, years	22.5±13.1	30.5±14.5	**0.006**
Sex, female	93 (80.2)	18 (78.3)	0.83
SLE disease duration	8 (8.7)	8.5 (11.6)	0.27
Manifestation of SLE			
-Musculoscletal	75 (66.4)	14 (63.6)	0.8
-Mucocutaneous	60 (52.6)	9 (40.9)	0.31
-Hematologic	47 (40.9)	10 (43.5)	0.49
-Serosal	26 (23.2)	4 (17.4)	0.54
-Neurological	6 (5.3)	1 (4.3)	0.85
Laboratory values for kidney biopsy			
-Creatinine level (mg/dL)	0.7 (0.5)	0.9 (0.6)	0.17
-GFR (ml/min)	110 (67)	77 (65)	0.06
-24-hour urine protein			
≥ 1 gr/day	72 (71.3)	17 (77.3)	0.63
≥ 3 gr/day	36 (35.6)	11 (50)	0.23
-Active urinary sediment	91 (83.5)	6 (27.3)	**<0.001**
Renal SLEDAI at the biopsy	12 (8)	4 (4)	**<0.001**
End-stage renal disease	13 (11.2)	2 (8.7)	0.72
Renal transplantation	5 (4.3)	1 (4.3)	0.99
Exitus	8 (7)	1 (4.3)	0.99

** n (%), if otherwise specified. Med (IQR) for numerical data excluding age; mean ± SD for age.GFR: Glomerular filtration rate, LN: Lupus nephritis, SLEDAI: Systemic lupus erythematosus disease activity index*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4003

AB0348

ALBUMIN-TO-GLOBULIN RATIO AS A POTENTIAL PREDICTOR OF RENAL REMISSION IN LUPUS NEPHRITIS

T. Knežević[1], I. Padjen[2], S. Bulimbašić[3], M. Ćorić[3], V. Ivković[1], M. Laganović[4], B. Anić[2]. [1]*University Hospital Centre Zagreb, Division of Nephrology, Hypertension, Dialysis and Transplantation, Department of Internal Medicine, ZAGREB, Croatia*; [2]*University Hospital Centre Zagreb and University of Zagreb, School of Medicine, Zagreb, Croatia, Division of Clinical Immunology and Rheumatology, Department of Internal Medicine, ZAGREB, Croatia*; [3]*University Hospital Centre Zagreb and University of Zagreb, School of Medicine, Zagreb, Croatia, Department of Pathology and Cytology, University Hospital Centre Zagreb, Croatia, ZAGREB, Croatia*; [4]*University Hospital Centre Zagreb and University of Zagreb, School of Medicine, Zagreb, Croatia, Division of Nephrology, Hypertension, Dialysis and Transplantation, National Referral Centre for Glomerular and Tubulointerstitial Diseases, Zagreb, Croatia, ZAGREB, Croatia*

Background: Optimal prognostic predictors in lupus nephritis (LN) are still not clearly defined. Studies have recently shown that albumin-to-globulin ratio (A/G) is not only a good predictor of outcomes in malignancy, infection and renal disease, but is also a potential marker of increased immunoglobulin synthesis and LN activity and might be useful as a predictor of the development of LN in SLE patients. Studies on the role of A/G in predicting outcomes in LN are, however, lacking.

Objectives: To assess a potential prognostic value of A/G at renal biopsy in predicting outcomes in LN.

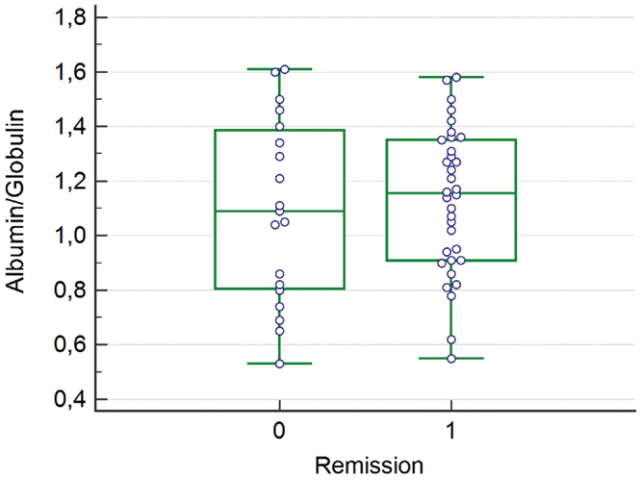
Methods: In this retrospective study we analyzed the demographic, histologic, laboratory and clinical characteristics of patients with biopsy-proven LN diagnosed between 2011 and 2020. All patients met the 1997 revised American College of Rheumatology classification criteria for SLE. Complete remission was defined as proteinuria <0.5 g/day and serum creatinine within 10% from baseline, and partial remission as more than 50% reduction in proteinuria to sub-nephrotic levels and serum creatinine within 10% from baseline.

Results: We have included 55 patients (80% women) with biopsy-proven LN (age at biopsy 38±13 years). On renal histology, one patient was class I LN, two patients were class II, 7 were class III, 5 were class III+V, 23 were class IV, two were class IV+V, 11 class VI and 4 had other features. Median eGFR and proteinuria at biopsy were 69 (IQR: 44, 100) mL/min/1.73 m^2 and 3.5 (2.3, 5.6) g/day, respectively. Baseline mean A/G was 1.12±0.29 and did not differ between LN classes (p=0.91). At one-year follow-up eGFR increased non-significantly (69 vs. 82 mL/min/1.73 m^2, p=0.13) and proteinuria decreased (3.5 vs. 0.6 g/day, p<0.001). Eighteen patients achieved complete remission (CR), 16 partial remission and 21 did not achieve remission. None progressed to ESRD and two patients died, both from sepsis. A/G at the time of biopsy did not differ between group which achieved CR/PR vs. no remission (p>0.05; Figure 1) and was not a significant predictor of remission in a multivariate regression model (OR 5.9, 95% CI 0.6, 63.2).

Conclusion: While being a potential marker for transition of SLE to LN, A/G was not showed to be a predictor of renal remission in LN.

REFERENCES:

[1] Liu XR, et al. Lupus. 2021 Jan 6:961203320981139.
[2] Kwon OC, et al. Semin Arthritis Rheum. 2018 Dec;48(3):462-466ck



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4111

AB0349

NEUTROPHIL-TO-LYMPHOCYTE RATIO, PLATELET-TO-LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME IN LUPUS NEPHRITIS

T. Knežević[1], I. Padjen[2], S. Bulimbašić[3], M. Ćorić[3], V. Ivković[4], M. Laganović[1], B. Anić[2]. [1]*University Hospital Centre Zagreb and University of Zagreb, School of Medicine, Zagreb, Croatia, Division of Nephrology, Hypertension, Dialysis and Transplantation, Department of Internal Medicine, ZAGREB, Croatia*; [2]*University Hospital Centre Zagreb and University of Zagreb, School of Medicine, Zagreb, Croatia, Division of Clinical Immunology and Rheumatology, Department of Internal Medicine, ZAGREB, Croatia*; [3]*University Hospital Centre Zagreb and University of Zagreb, School of Medicine, Zagreb, Croatia, Department of Pathology and Cytology, University Hospital Centre Zagreb, Croatia, ZAGREB, Croatia*; [4]*University Hospital Centre Zagreb and University of Rijeka, Faculty of Health Studies, Rijeka, Croatia, Division of Nephrology, Hypertension, Dialysis and Transplantation, Department of Internal Medicine, ZAGREB, Croatia*

Background: A number of blood count parameters are associated with inflammatory and autoimmune diseases. There is discordant evidence whether neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and mean platelet volume (MPV) might reflect inflammatory response and have prognostic value in SLE patients. However, the studies examining the potential role of these markers in LN are missing.

Objectives: To examine NLR, PLR and MPV at the time of biopsy in patients with LN and evaluate their association with prognosis.

Methods: In this retrospective study we analyzed the demographic, histologic, laboratory and clinical characteristics of patients with biopsy-proven LN diagnosed between 2011 and 2020. All patients met the 1997 revised American College of Rheumatology classification criteria for SLE. Complete remission was defined as proteinuria <0.5 g/day and serum creatinine within 10% from baseline,

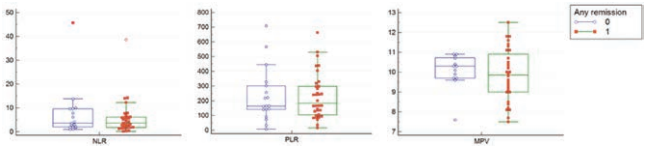
and partial remission as more than 50% reduction in proteinuria to sub-nephrotic levels and serum creatinine within 10% from baseline.

Results: We have included 55 patients (80% women) with biopsy-proven LN (age at biopsy 38±13 years). On renal histology, one patient was class I LN, two patients were class II, 7 were class III, 5 were class III+V, 23 were class IV, two were class IV+V, 11 class VI and 4 had other features. Median baseline NLR was 3.64 (IQR: 1.85, 6.93), PLR was 167 (IQR: 116, 300) and MPV was 10.0 (IQR: 9.2, 10.8). There were no differences in any of the three parameters between different classess of LN (all p>0.05). Eighteen patients achieved complete remission (CR), 16 partial remission and 21 did not achieve remission. None progressed to ESRD and two patients died, both from sepsis. There no differences in NLR, PLR and MPV at the time of biopsy between group which achieved CR/PR vs. no remission (all p>0.05; Figure 1). We constructed a thorough multivariate regression model which showed that neither NLR, PLR or MPV are predictors of renal remission in LN.

Conclusion: NLR, PLR and MPV are not useful prognostic markers in predicting renal remission in LN.

REFERENCES:

[1] Hartmann LT, et al. Open Rheumatol J. 2018 Aug 31;12:129-138.
[2] Chen SY, et al. J Res Med Sci. 2018 May 30;23:48.
[3] Zhao CN, et al. Rheumatol Int. 2018 Sep;38(9):1635-1641.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4164

AB0350 MATERNAL AND FETAL OUTCOME IN MEXICAN WOMEN WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME, SECONDARY ANTIPHOSPHOLIPID SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS WITH ANTIPHOSPHOLIPID ANTIBODIES

A. A. Sánchez[1], D. Miranda[1], M. A. Saavedra[1], A. Sanchez Gonzalez[1], Z. Castro[1]. [1]*Hospital de Especialidades La Raza, Rheumatology, Ciudad de México, Mexico*

Background: Primary antiphospholipid syndrome (APS) is associated with a higher frequency of maternal-fetal adverse outcomes, with increased risk when APS is associated with systemic lupus erythematosus (SLE).

Objectives: We compared maternal-fetal complications in patients with primary APS, APS associated with SLE and SLE with anti-phospholipid antibodies (aPLs).

Methods: Observational, analytical, retrospective, cross-sectional, comparative study, between 2009-2019. Three groups were compared: primary APS, APS associated with SLE and SLE with anti-phospholipid antibodies (aPLs).

Results: We include 179 pregnant women, 31.8% with primary APS, 35.8% with APS associated with SLE, and 32.4% with SLE and aPLs A history of a higher frequency of abortions was found in APS associated with SLE (62.5%, p <0.001) and thrombosis (61.9%, p <0.001) and aCL IgG + in primary APS (80.7%, p = 0.011). More frequent use during pregnancy of antimalarials is applied in associated APS (81.30%, p <0.001) and aspirin / heparin in primary APS (96.5% / 94.7%, p <0.001). Abortions were observed more frequently in APS associated with SLE (23.80%, p = 0.021) and preeclampsia / HELLP in primary APS (31.6% and 15.8%, p = 0.047) who were also less frequently the use of antimalarial (24% vs. 81.3% vs. 72.4%, p <0.001) compared to the other groups. Table 1

Conclusion: Patients with APS and SLE have an increased risk of miscarriage whereas those with primary APS have an increased risk for preeclampsia / HELLP. The use of antimalarials could reduce the risk of hypertensive disorders of pregnancy.

REFERENCES:

[1] Schreiber K, Sciascia S, de Groot PG, et al. Antiphospholipid syndrome. Nat Rev Dis Primers 2018;4:17103.
[2] De Carolis S, Tabacco S, Rizzo F, et al. Antiphospholipid syndrome: An update on risk factors for pregnancy outcome. Autoimmun Rev. 2018;17: 956-66.

Table 1. Comparison between groups of adverse maternal-fetal outcome.

	Secondary antiphospho-lipid syndrome (n=64)	Primary antiphospho-lipid syndrome (n=57)	Systemic lupus erythematosus with antiphospholipid antibodies (n=58)	P
Fetal complications	48 (76.20%)	43 (75.40%)	31 (56.40%)	0.034
Growth restriction	9 (14.30%)	8 (14%)	7 (12.50%)	0.955
Oligohydramnios	6 (9.50%)	5 (8.80%)	5 (8.90%)	0.989
Prematurity	23 (52.30%)	25 (56.80%)	19 (42.20%)	0.37
Abortion	15 (23.80%)	3 (5.40%)	9 (16.10%)	0.021
Stillbirth	7 (11.10%)	10 (17.90%)	5 (9.10%)	0.343
Low birth weight	20 (52.60%)	21 (48.80%)	15 (37.50%)	0.373
Malformations	5 (8.10%)	0 (0%)	0 (0%)	0.01
Maternal complications	40 (63.50%)	25 (43.90%)	21 (36.80%)	0.01
Pre-eclampsia.	15 (23.80%)	18 (31.60%)	7 (12.30%)	0.046
HELLP	4 (6.30%)	9 (15.8%)	2 (3.50%)	0.047
Premature rupture of membranas	7 (11.10%)	5 (8.8%)	4 (7.10%)	0.75
Maternal death	1 (1.60%)	0 (0%)	1 (1.80%)	0.616

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4187

AB0351 PROGRESSION TO SEVERE LUPUS NEPHRITIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOUS: UPDATE FROM A COLOMBIAN COHORT

S. Herrera[1], J. Marenco Maldonado[1], J. C. Diaz-Coronado[1,2], D. Rojas-Gualdrón[3], D. Hernandez-Parra[1], R. Pineda.Tamayo[1]. [1]*Artmedica IPS, Clinical Information Group, Medellín, Colombia*; [2]*CES University, Department of Internal Medicine, Medellín, Colombia*; [3]*CES University, Facultad de medicina, Medellín, Colombia*

Background: Continuous monitoring of patients with Systemic lupus erythematosus (SLE) provides relevant information

Objectives: To update the analysis of clinical and immunological characteristics associated with time to severe renal involvement in patients with Systemic Lupus Erythematous in a Colombian cohort followed from January 2015 to October 2020

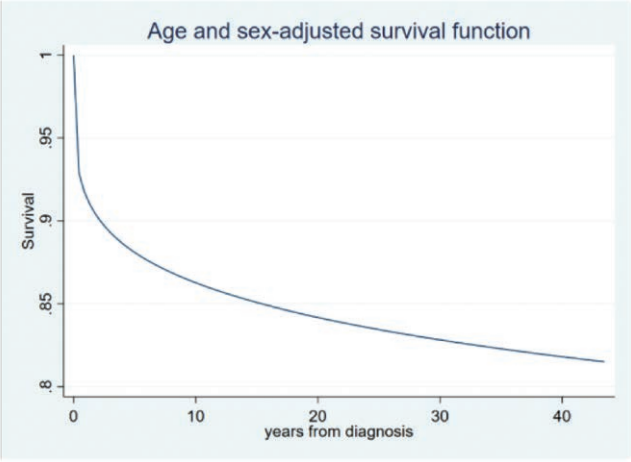
Methods: A retrospective follow-up study based on clinical records. Patients with SLE diagnosis fulfilled either 1987 American College of Rheumatology Classification Criteria for SLE or 2011 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE. We included patients with the diagnosis of lupus nephritis according to Wallace and Dubois criteria. Patients who did not have at least two follow-up measurements or had a cause of nephritis other than lupus were excluded. The primary outcome was defined as the time from diagnosis to severe renal involvement defined as creatinine clearance ≤50ml/min, 24-hour proteinuria ≥3.5 grams o end-stage renal disease. Updated age and sex-adjusted survival functions and Hazard ratios (HR) with 95% confidence intervals and p-values were estimated using parametric Weibull models for interval-censored data. P values <0.05 were considered statistically significant. Descriptive statistics were previously reported in EULAR 2020 (1)

Results: 548 patients were analyzed: 67 were left-censored as they presented renal involvement at entry, 25 were interval censored as outcome occurred between study visits (19 new events), and 456 were right-censored as involvement was not registered during follow-up. In this cohort update Age and sex-adjusted Hazard Ratios for high blood pressure were HR = 3.1 (95%CI 1.5-6.3; p-value = 0.003) and Anti-RO (per unit increase) HR = 1.003 (95%CI 1.001-1.005; p-value = 0.029). Figure 1 shows the updated age and sex-adjusted survival function

Conclusion: In this cohort update, we found similar clinical and immunological characteristics associated with time to severe renal involvement in SLE patients to those reported in (1). However, continuous follow-up allows us to deepen our understanding of the progression to severe renal involvement in SLE patients

REFERENCES:

[1] Herrera S, Diaz-Coronado JC, Rojas-Gualdrón D, Betancur-Vasquez L, Gonzalez-Hurtado D, Gonzalez-Arango J, et al. SAT0210 factors associated with time to severe lupus nephritis in a cohort of colombian patients. Ann Rheum Dis. junio de 2020;79(Suppl 1):1048.2-1048



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4284

Vasculitis – large vessel vasculitis

AB0352 **ANTICARDIOLIPIN ANTIBODIES AND ACTIVITY OF GIANT CELL ARTERITIS**

A. Hočevar[1,2], R. Jese[1], J. Kramarič[1], S. Cucnik[1], M. Tomsic[1,2], Z. Rotar[1,2]. *[1]University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia*; *[2]Medical Faculty, University of Ljubljana, Internal Medicine, Ljubljana, Slovenia*

Background: Anticardiolipin antibodies (aCL) can be detected in newly diagnosed GCA as reactive antibodies to endothelial lesions. Their prognostic role, as a marker of disease activity, has not been extensively studied in GCA.
Objectives: Our aim was to determine whether aCL IgG might represent laboratory marker of active GCA.
Methods: We included patients with new clinical diagnosis of GCA supported by histology or imaging between September 2011 and July 2019, who completed at least a 48-week follow-up at our secondary/tertiary rheumatology center. Follow up visits with predetermined clinical and laboratory tests, including aCL IgG, were performed 12, 24, 48, and 96 weeks after diagnosis. GCA relapse was defined as worsening or new disease activity after initial remission. Other reasons for the disease-related symptoms, elevated inflammatory markers (C reactive protein or erythrocyte sedimentation rate) had to be excluded. aCL IgG were determined in the patients' sera samples at baseline and at follow up visits, using an in-house solid phase enzyme-linked immunosorbent assay[1]. A value above the 99th percentile of the healthy control population was taken as significant.
Results: During the observation period we identified 288 newly diagnosed GCA patients. Two hundred and twelve GCA patients (66.5% females, median (IQR) age 73.9 (67.0–78.7) years) fulfilled the study inclusion criterion, among them 145 patients completed the 96-week follow up visit. At baseline, 129/212 (60.8%) GCA patients had positive aCL IgG. During in total 781 follow up visits, we recorded 77 (9.9%) episodes of active/relapsing GCA (clinical, laboratory or combined in 4 (5.2%), 48 (62.3%), 25 (32.5%) episodes, respectively). aCL IgG were present at 155/781 (19.8%) measurements (at 24/77 episodes of relapsing/active and 131/573 episodes of quiescent GCA). The correlation between active/relapsing GCA and aCL IgG positivity was only weekly positive (r coefficient=0.094; p= 0.015).
Conclusion: The role of aCL IgG as a biomarker for GCA activity seems to be rather limited.
REFERENCES:
[1] Božič B, et al. Int Arch Allerg Immunol. 1997; 112:19-26. doi.org/10.1159/000237426
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.322

AB0353 **ADRENAL INSUFFICIENCY AFTER GLUCOCORTICOID TREATMENT OF GIANT CELL ARTERITIS**

A. Hočevar[1,2], R. Jese[1], J. Kramarič[1], M. Tomsic[1,2], Z. Rotar[1,2]. *[1]University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia*; *[2]Medical Faculty, University of Ljubljana, Internal Medicine, Ljubljana, Slovenia*

Background: Adrenal insufficiency is frequently neglected and underappreciated, potentially severe complication of systemic glucocorticoid therapy.
Objectives: We aimed to evaluate the prevalence of glucocorticoid induced adrenal insufficiency in giant cell arteritis (GCA).
Methods: We analysed adrenal function data in a cohort of GCA patients diagnosed between July 2014 and July 2019, in whom discontinuation of methylprednisolone therapy was planned. Adrenal function was tested by Corticotropin stimulation test (CST). To perform the CST, methylprednisolone was substituted with hydrocortisone (20mg qd in three divided doses) for one to four weeks before the test. Adrenal insufficiency was defined as cortisol level <450 nmol/l measured 30 minutes after the corticotropin injection; additionally, the result of the CST was defined as borderline when the cortisol level 30 minutes after corticotropin injection was between 450 nmol/l and 500 nmol/l.
Results: Adrenal function was tested in 74/215 GCA patients before definite methylprednisolone withdrawal (after a median 13.5 (12.9 – 22.4) months of glucocorticoid therapy). The mean (SD) methylprednisolone dose, prior to substitution with hydrocortisone and subsequent CST, was 3.1 (1.6) mg. Adrenal insufficiency was detected in 36/74 patients (48.6%); additionally, 10/74 patients (13.5%) had a borderline CST result. Seventeen patients with either adrenal insufficiency or borderline CST result, had a repeated CST after median (IQR) 11.6 (8.9; 12.6) months. Adrenal insufficiency persisted in 11/17 (64.7%) patients, and 1/17 patients had a borderline CST. A third CST was performed in 4/12 patients with abnormal second CST after median (IQR) 8.3 (6.9; 10.6) months. Adrenal function recovered in one patient, while the adrenal insufficiency persisted in the remaining 3 patients.
Conclusion: Adrenal insufficiency is a common and potentially long-lasting glucocorticoid induced adverse event in GCA patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.323

AB0354 **FDG-PET-DETECTED LARGE VESSEL VASCULITIS DOES NOT PREDICT DISEASE OUTCOME IN PATIENTS WITH GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA**

E. Hysa[1], D. Camellino[2], C. Bernini[3], E. Gotelli[4], S. Paolino[1], C. Schenone[4], G. Ferrari[4], A. Sulli[1], M. Cutolo[1], M. A. Cimmino[4]. *[1]Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa, Italy*; *[2]Division of Rheumatology, Local Health Trust 3, Musculoskeletal System Department, Genoa, Italy*; *[3]Operational Unit of Internal Medicine 2, Department of Internal Medicine, University of Genoa, Genoa, Italy*; *[4]Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa, Italy*

Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are tightly associated inflammatory conditions of the elderly [1]. Both disorders can exhibit an increased articular and vascular uptake of 18-fluorodeoxyglucose (18-FDG) at positron emission tomography (PET)/computed tomography (CT) scan [2].
Objectives: This study evaluated if large-vessel vasculitis (LVV) detected by PET/CT in patients with PMR and/or cranial GCA had a negative prognostic value.
Methods: 108 patients (35 men and 73 women) with a median age of 74 years (range 50-92 years) were prospectively enrolled in our centre over 4 years. PMR was diagnosed by Bird et al. criteria and GCA by the ACR criteria. Six patients died shortly after the first visit (V_0) and six were lost at follow-up. Of the remaining 96 patients, 77 were classified as PMR, 6 as GCA and 13 were affected by both diseases.
At V_0, patients underwent a clinical, laboratory and PET/CT evaluation, and were stratified according to the presence or not of LVV. Follow-up visits

were performed every 6 months for a median of 40 months. Disease outcomes were: prednisone (PDN) use and its cumulative dosage, need of methotrexate (MTX), number of relapses, patients' death, and PMR disease activity score (PMR-DAS). The independent variables were age, sex, disease duration, fever, C-reactive protein (CRP) concentration, platelet count (PLT), presence of cranial GCA, degree of joint and vascular uptake of FDG, and presence of LVV. The predictive role of LVV was tested by multiple regression.

Results: LVV was seen in 47 patients (49 %), 31 with PMR, 6 with GCA and 10 with both diseases. Patients with or without LVV did not significantly differ in terms of demographic and laboratory parameters except for a non-significant higher number of PLT in patients with LVV. Clinical and laboratory parameters at V_0, stratified per disease and considered together, did not significantly change between PET+ and PET- patients (table 1). Lastly, none of the independent variables, including LVV, could predict disease outcomes.

Conclusion: The presence of a PET-detected LVV at diagnosis does not seem a negative prognostic factor in PMR and GCA. As a consequence, routine investigation by PET/CT of patients with PMR and GCA is not indicated to predict disease outcome.

REFERENCES:

[1] Dejaco C, Duftner C, Buttgereit F, Matteson EL, Dasgupta B. The spectrum of giant cell arteritis and polymyalgia rheumatica: revisiting the concept of the disease. Rheumatology (Oxford). 2017 Apr 1;56(4):506-515. doi: 10.1093/rheumatology/kew273. PMID: 27481272.

[2] Blockmans D, Coudyzer W, Vanderschueren S, Stroobants S, Loeckx D, Heye S et al. Relationship between fluorodeoxyglucose uptake in the large vessels and late aortic diameter in giant cell arteritis. Rheumatology (Oxford). 2008 Aug;47(8):1179-84. doi: 10.1093/rheumatology/ken119. Epub 2008 May 31. PMID: 18515868.

Table 1. Clinical, laboratory and imaging features between PET+ and PET- patients at V_0

Features at V_0	PET+ patients	PET- patients	p
Morning stiffness (min)	30 (0-480)	60 (0-360)	0.20
Haemoglobin (g/dL)	12.3±1.5	12.6±1.5	0.28
Platelets (x 10^3/mm^3)	349 (108-643)	297(159-571)	0.08
C-reactive protein (mg/dL)	35.5 (3.4-149)	36.2 (2-149)	0.54
Erythrocyte sedimentation rate (mm/h)	62.5 (10-120)	57.5 (10-120)	0.29
Total Vascular Score at PET	20 (4-41)	6 (0-12)	0
Total Joint Score at PET	18 (5-30)	18 (5-32)	0.77

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.570

AB0355 THE VALUE OF PLATELET-TO-LYMPHOCYTE AND NEUTROPHIL-TO-LYMPHOCYTE RATIOS AS INFLAMMATORY MARKERS IN BIOPSY-PROVEN GIANT CELL ARTERITIS

U. Møller Døhn[1], M. Stormly Hansen[2], Y. Subhi[2], V. Fana[1], M. Radmer Jensen[3], J. Maestri Brittain[4], C. Faber[2], S. Heegaard[2,5], O. N. Klefter[2], A. K. Wiencke[2], S. E. Hamann[2], L. Terslev[1]. [1]*Rigshospitalet, Glostrup; University of Copenhagen, Center for Rheumatology and Spine Diseases, Glostrup, Denmark*; [2]*Rigshospitalet, University of Copenhagen, Department of Ophthalmology, Glostrup, Denmark*; [3]*Bispebjerg & Frederiksberg Hospital, Department of Clinical Physiology and Nuclear Medicine, Copenhagen, Denmark*; [4]*Rigshospitalet, University of Copenhagen, Department of Clinical Physiology, Nuclear Medicine and PET, Copenhagen, Denmark*; [5]*Rigshospitalet, University of Copenhagen, Eye Pathology Section, Department of Pathology, Copenhagen, Denmark*

Background: Platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) have been shown to correlate with disease activity in various rheumatic diseases. High PLR and elevated platelet count are potentially useful in diagnosing some systemic vasculitides, eg. giant cell arteritis (GCA)[1] and has been suggested predictive for diagnosing GCA, even in the absence of characteristic temporal artery involvement[2].

Objectives: To evaluate the role of PLR and NLR as inflammatory markers in the diagnosis of GCA in patients referred to temporal artery biopsy (TAB).

Methods: During 10 months, all patients referred to TAB at the Department of Ophthalmology (Rigshospitalet, Copenhagen, Denmark) in suspected GCA were included. Immediately prior to TAB, ultrasound of bilateral temporal arteries was performed at the Center for Rheumatology and Spine Disease (Rigshospitalet, Copenhagen, Denmark) by rheumatologists experienced in vascular ultrasound. Ultrasound signs of GCA were a positive Halo sign or compression sign. Patients had C-reactive protein (CRP), erythrocyte sedimentation ratio (ESR), platelets, white blood cells with differential counts, hemoglobin and platelets measured. Final clinical diagnosis, based on rheumatological expert opinion, and fulfilment of ACR1990 classification criteria for temporal arteritis at six months was noted, with clinical diagnosis being the reference standard.

Results: 106 patients were included and had a TAB evaluated. Forty-five (42%) had a clinical diagnosis of GCA at 6 months of which 28 (62%) also were TAB positive. US was performed in 74 (70%), of these 20 (67%) of the GCA patients had a positive ultrasound for GCA (termed US GCA patients). There was no significant difference in mean age or gender distribution between GCA and non-GCA patients. ESR, CRP and platelets were significantly higher in GCA than non-GCA patients ($p<0.001$). PLR was significantly higher in GCA than non-GCA patients ($p<0.007$), while NLR was not ($p=0.076$). For US GCA patients vs. US non-GCA patients, platelets were significantly higher in the US GCA group ($p=0.025$). Both PLR and NLR were significantly higher in the US GCA group compared to the US non-GCA group ($p= 0.003$ and $p=0.007$, respectively).

Conclusion: In this cohort of patients, suspected of GCA and referred to TAB, PLR but not NLR was significantly higher in GCA patients than in non-GCA patients. In patients with US findings of GCA, both PLR and NLR were significantly higher in GCA compared to non-GCA. An elevated PLR could be considered an additional feature in diagnosing GCA.

REFERENCES:

[1] El-Dairi MA et al.: J Neuroophthalmol 2015;35:246-53

[2] Bornstein G et al.: Clin Rheumatol 2018;37:2819-2

	GCA (n=45)	Non-GCA (n=61)	*P*-value
Age (years)	73.6 (7.5)	72.6 (10.4)	0.575
Females, n (%)	34 (76)	38 (62)	0.148
Fulfilling ACR1990 criteria, n (%)	36 (80)	16 (26)	**<0.001**
TAB positive for GCA, n (%)	28 (62)	0 (0)	**<0.001**
Ultrasound positive for GCA*, n (%)	20 (67)	9 (20)	**<0.001**
Sedimentation rate (mm/hr)	58 (30)	33 (31)	**<0.001**
Haemoglobin (mmol/L)	7.68 (0.92)	7.96 (1.05)	0.154
CRP (mg/L), median (IQR)	38 (15-92)	8 (2-40)	**<0.001**
White blood cells (10^9/L)	9.54 (3.18)	8.99 (3.63)	0.407
Lymphocytes (10^9/L)	1.72 (0.78)	1.87 (0.93)	0.367
Monocytes (10^9/L)	0.71 (0.37)	0.77 (0.41)	0.441
Neutrophils (10^9/L)	6.85 (2.94)	6.01 (3.02)	0.157
Basophils (10^9/L)	0.05 (0.04)	0.05 (0.05)	0.464
Eosinophils (10^9/L)	0.15 (0.14)	0.18 (0.21)	0.410
Platelets (10^9/L)	400 (154)	289 (111)	**<0.001**
Neutrophil-to-lymphocyte ratio	4.91 (3.22)	3.87 (2.52)	0.076
Platelet-to-lymphocyte ratio	287 (189)	193 (147)	**0.007**

*Values are mean and standard deviation unless notedComparison between groups by independent samples t-test (continuous variables), χ^2-test (categorical variables) and Mann-Whitney for CRP (not normal distributed continuous variable)ACR=American College of Rheumatology; CRP=C-reactive protein; GCA=giant cell arteritis; IQR=interquartile range; n=number; SD=standard deviation; TAB=temporal artery biopsy*Ultrasound not done in 32 patients (15 with GCA and 17 without)*

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.826

AB0356 VENOUS INVOLVEMENT IN BEHÇET'S DISEASE

Ö. Özdemir Işık[1], S. Şan[1], A. Yazici[1], A. Cefle[1]. [1]*Kocaeli University School of Medicine, Rheumatology, Kocaeli, Turkey*

Background: Behçet's disease (BD) is a vasculitic multisystem inflammatory disorder. It may also involve the skin, mucosa, eyes, blood vessels, joints, gastrointestinal system, and central nervous system.

Objectives: In this study, we aimed to present venous involvement data in patients followed up with a diagnosis of BD.

Methods: The clinical, demographic, laboratory and medication data of 394 patients who were followed up with a diagnosis of BD in our

rheumatology outpatient clinic between 2000 and 2020 were retrospectively evaluated.

Results: Venous involvement was detected in 17.6% (n:76) patients who were followed up with a diagnosis of BD. 75% of the patients were male, and their mean diagnosis age was 27.1±9.9, disease duration was 14.2±6.3 years. While the thrombosis of lower extremity veins, cervical veins, and vena cava were observed in 85.5% of BD patients, superficial thrombophlebitis was found in 31.6%. Cerebral venous involvement (CVI) was evaluated in cranial involvement. Oral aphthous ulcer was found in 97.4 % of the patients, genital ulcer in 65.8%, pathergy positivity in 44.7%, papulopustular lesion in 34.2%, erythema nodosum in 40.8%. 27.6% of the patients were evaluated for hereditary thrombophilia and 5.3% (n:7) had hereditary thrombophilia. Deep venous thrombosis was found in 85.7% (6/7) of these patients, renal artery occlusion in 14.3%, pulmonary artery thrombosis in 14.3%, and cerebral venous thrombosis in 28.6%. Patients with and without venous involvement were compared in terms of clinical findings. A significant difference was observed in terms of retinal vasculitis, artery occlusion, arterial aneurysm, family history for BD and gender. In logistic regression analysis, a significant relationship was observed between venous involvement and gender, family history, retinal vasculitis, artery occlusion, arterial aneurysm (Table1).

Table 1. Comparison of data of patients with and without venous involvement

	Venous Involvement (+) n:76	Venous Involvement (-) n:318	P	OR* (%95CI)
Gender			***0.000***	2.78
Female	19(25)	153(48.1)		(1.58-4.88)
Male	57(75)	165(51.9)		
Family History	4(5.3)	44(13.8)	***0.049***	0.035 (0.12-0.99)
Oral Aphthous Ulcer	74(97.4)	305(95.9)	0,745	
Genital Ulcer	50(65.8)	206(64.8)	0,894	
Papulopustular lesion	26(34.2)	103(32.4)	0,786	
Erythema Nodosum	31(40.8)	119(37.4)	0,601	
Pathergy	34(44.7)	151(47.5)	0,772	
Uveitis	20(26.3)	118(37.1)	0,083	
Retinal Vasculitis	5(6.6)	6(1.9)	***0.036***	3.66 (1.08-12.33)
Arthritis	13(17.1)	85(26.7)	0,104	
Artery Occlusion	6(7.9)	3(0.9)	***0.002***	8.97 (2.19-36.74)
Arterial Aneurysm	7(9.2)	8(2.5)	***0.013***	3.93 (1.37-11.20)
Gastrointestinal involvement	6(7.9)	11(3.5)	0,111	
Cardiac involvement	3(3.9)	3(0.9)	0,089	
Cranial involvement	7(9.2)	17(5.3)	0,282	

* Significant data in logistic regression analysis were presented

Conclusion: Superficial venous thrombosis and deep vein thrombosis are the most frequent vascular involvements in BD patients. Significant correlations exist between CVI and pulmonary artery involvement (PAI), intracardiac thrombosis and PAI. It should be recalled that lower extremity venous thrombosis is often present in these associations, and even precede them (1).

REFERENCES:

[1] Seyahi E. Behçet's disease: How to diagnose and treat vascular involvement. Best Practice & Research Clinical Rheumatology. 30 (2016) 279-295

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1144

AB0357 LANDSCAPE REVIEW OF PATIENT-REPORTED OUTCOME MEASURES IN GIANT CELL ARTERITIS

H. H. Colwell[1], S. Mathias2, K. Kato[3], C. E. Najem[4], A. M. Archer[5]. *[1]Health Outcomes Solutions, Outcomes Research, Winter Park, United States of America*; *[1]Health Outcomes Solutions, Outcomes Research, Winter Park, United States of America*; *[3]Janssen Pharmaceutical Companies of Johnson & Johnson, Patient Reported Outcomes, Raritan, United States of America*; *[4]Janssen Pharmaceutical Companies of Johnson & Johnson, Rheumatology Clinical Research, Spring House, United States of America*; *[5]Janssen Pharmaceutical Companies of Johnson & Johnson, Translational Medicine, Spring House, United States of America*

Background: Giant cell arteritis (GCA) is a systemic large vessel vasculitis that results in symptoms (e.g., headaches, jaw claudication, fatigue, pain, etc.) that can have multiple negative impacts on an individual's health-related quality of life.

Objectives: To identify important symptoms and impacts experienced by individuals with GCA, develop a conceptual model, and evaluate available patient reported outcome (PRO) measures for appropriateness for inclusion in GCA clinical studies.

Methods: Published literature on disease experience from databases, conference abstracts, and Guidance/OMERACT documents were reviewed. A GCA conceptual model was developed based on the symptoms and impacts identified from this literature and supplemented with clinical input. A detailed review of selected PROs was then conducted to assess concept coverage and gaps to evaluate appropriateness for a GCA population.

Results: Of 245 identified citations, 24 abstracts and 18 articles were reviewed. Key symptoms affecting GCA patients (e.g., ischemic and constitutional symptoms) and impacts to the lives of GCA patients (e.g., reduced physical, social and emotional functioning) formed the basis for a GCA conceptual model (see Figure 1).

No GCA-specific PROs were identified. Therefore, the PROs that were used most frequently in GCA clinical studies were reviewed and evaluated. These included the SF-36, FACIT-Fatigue, Patient Global Assessment (PtGA), Multidimensional Fatigue Inventory (MFI), EQ-5D, Health Assessment Questionnaire (HAQ), Brief Illness Perception Questionnaire (BIPQ), and Visual Functioning Questionnaire-25 (VFQ-25). These PROs included some key impacts but did not assess most GCA-specific symptoms (e.g., headaches, fever, etc.). No measures were developed with input from GCA patients and there has been limited evaluation of the measurement properties of these PROs in GCA patients.

The FACIT-Fatigue, SF-36, and the PtGA, which were frequently administered in published GCA studies, measure key GCA concepts such as fatigue, functioning, impact on daily activities and disease status. The measurement properties (reliability, validity, sensitivity to change) have been documented in several other rheumatologic diseases (Table 1).

Conclusion: In the absence of a GCA-specific PRO, the SF-36, FACIT-Fatigue, and PtGA are recommended for use in GCA clinical studies for the assessment of key concepts identified in the literature. Qualitative and quantitative research should be conducted with GCA patients to assess the content validity and measurement properties of these PROs in a GCA population.

Figure 1: Conceptual Model

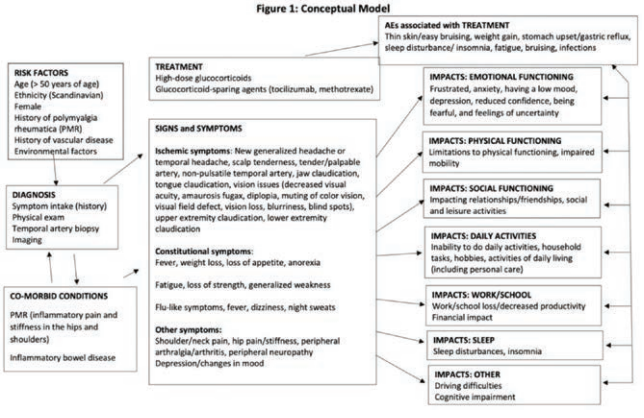


Table 1. Summary of Recommended Measures

Description	SF-36	FACIT-Fatigue	PtGA
Type	Generic, health status measure	Fatigue and impact on function/daily activities	Measure of disease activity
Method of Administration	Self/Interviewer	Self/Interviewer	Self
# of Items	36	13	1
Recall period	Past 4 weeks/past week	Past 7 days	Varies
Scoring	8 domain scores; 2 component summary scores	Total score	Total score
Measurement properties	Measurement properties demonstrated in other rheumatologic diseases (SLE, RA, SpA, and chronic knee pain); construct validity demonstrated in a single study with GCA patients	Measurement properties demonstrated in rheumatologic populations including SLE, PsA, and RA	Select measurement properties have been demonstrated in GCA and other populations (RA, TAK, RP)
Concept coverage	GCA impacts (emotional, physical, and social functioning, and daily activities), bodily pain, fatigue	Fatigue	Overall assessment of disease activity
Administered in recent GCA studies	YES	YES	YES

SLE= systemic lupus erythematosus, SpA = spondyloarthritis, PsA=psoriatic arthritis, RA=rheumatoid arthritis, GCA= giant cell arteritis, TAK=Takayasu's arteritis, RP=relapsing polychondritis

Disclosure of Interests: Hilary H Colwell Consultant of: Janssen Pharmaceutical Companies of Johnson & Johnson, Susan Mathias Consultant of: Janssen Pharmaceutical Companies of Johnson & Johnson, Kelly Kato Employee of: Janssen Pharmaceutical Companies of Johnson & Johnson, Catherine E Najem Shareholder of: Johnson & Johnson, Employee of: Janssen Pharmaceutical Companies of Johnson & Johnson, Amy M Archer Employee of: Janssen Pharmaceutical C ompanies of Johnson & Johnson

DOI: 10.1136/annrheumdis-2021-eular.1199

AB0358 ABATACEPT AS A bDMARD IN STEROID-REFRACTORY POLYMYALGIA RHEUMATICA

E. Toussirot[1], M. Michaud[2], D. Wendling[3], V. Devauchelle-Pensec[4]. [1]*CHU de Besançon, INSERM CIC-1431, Besancon, France*; [2]*Hôpital Joseph Ducuing, Centre de Compétence Maladies Lysosomales, Toulouse, France*; [3]*CHU de Besançon, Rhumatologie, Besancon, France*; [4]*CHU de Brest, Rhumatologie, Brest, France*

Background: polymyalgia rheumatica (PMR) is a chronic inflammatory disorder affecting elderly people. Glucocorticoids (GC) are the mainstay of therapy for PMR. Despite this treatment, the disease may relapse or GC dosage cannot be tapered. Methotrexate (MTX) may be helpful in these cases. Blockade of IL-6 has an effective steroid-sparing effect in patients with giant cell arteritis (GCA) and may improve the clinical symptoms of patients with PMR. The pathophysiology of PMR still remains uncertain but there are evidences for a participation of Th1 and Th17 lymphocytes. Recently, blockade of the costimulatory pathway by abatacept (ABA) gave favorable results in GCA.

Objectives: to report our experience (efficacy and safety) of ABA in the treatment of patients with isolated PMR who required longstanding GC and who failed to respond to MTX and/or IL-6 receptor blocking agents.

Methods: a call for observations of all cases of patient with PMR who received at least one dose (SC or IV) of ABA was sent to the members of the French specialist network "Club Rhumatismes & Inflammation" (CRI: www.cri-net.com)(rheumatologist and internal medicine). Patients must satisfy the EULAR/ACR criteria for PMR and have isolated PMR without associated GCA.

Results: 4 cases were declared during a 12 months period: 2 men and 2 women; age (median [range]): 60.7 [50-68] years; disease duration 30 [7-48] months; duration of GC treatment before starting ABA: 60 [10-72] months. They all required prednisolone with a daily dosage of 14.5 mg [10-20]. Before ABA administration, they all received MTX while 2 patients were treated by IL-6R inhibitor (tocilizumab 6 months and sarilumab 3 months, respectively) without improvement. ABA was given as a monthly infusion (10 mg/kg) in one case and subcutaneously (every week) in 3 cases. ABA treatment duration ranged from 3 to 18 months. Two patients responded to the treatment with a progressive decline of DAS-PMR and GC dosage tapering during a 12 month follow-up, while there was no improvement for the 2 others (Table 1). CRP levels also decreased for one responder. The safety was excellent for all. ABA was still maintained in one responder. Among the non-responders, one patient was switched to tocilizumab and the second still received high GC dosage.

Conclusion: ABA may be effective in certain PMR patients who were unable to taper GC, with a good safety profile. A randomized controlled trial is required in order to determine its place in the treatment of PMR and to select the appropriate patients who could potentially benefit from this biological agent.

REFERENCES:

[1] Langford CA *et al.* Vasculitis Clinical Research Consortium. A Randomized, Double-Blind Trial of Abatacept (CTLA-4Ig) for the Treatment of Giant Cell Arteritis. Arthritis Rheumatol. 2017; 69: 837-845

Table 1. changes in DAS-PMR and CRP levels in 4 patients with PMR while receiving abatacept (M: months; CRP in mg/L).

Cases	DAS- PMR M0	DAS- PMR M3	DAS-PMR M6	DAS -PMR M12	CRP M0	CRP M3	CRP M6	CRP M12
1	20	21	21	NA	5	8.6	8.4	NA
2	31.1	30.5	NA	NA	21	25	NA	NA
3	10.7	8.35	5	13	37.2	22.7	22	22
4	18	22	17.2	12	1.2	3.3	3.5	3

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1246

AB0359 CRANIAL INVOLVEMENT IN BEHÇET'S DISEASE

Ö. Özdemir Işık[1], S. Şan[1], A. Yazici[1], A. Cefle[1]. [1]*Kocaeli University School of Medicine, Rheumatology, Kocaeli, Turkey*

Background: Behçet's disease (BD) is a vasculitic multisystem inflammatory disorder. It may also involve the skin, mucosa, eyes, blood vessels, joints, gastrointestinal system, and central nervous system (CNS).

Objectives: In this study, we aimed to present CNS involvement data in patients followed up with a diagnosis of BD.

Methods: The clinical, demographic, laboratory and medication data of 394 patients who were followed up with a diagnosis of BD in our rheumatology outpatient clinic between 2000 and 2020 were retrospectively evaluated.

Results: CNS involvement was detected in %5.6(24) patients who were followed up with a diagnosis of BD. 66.7% of the patients were male, and their mean diagnosis age was 25.1±8.2 years, mean CNS involvement age was 28.39±9.6 years. Neurological symptoms occurred in an average of 3.3 years after the diagnosis of BD. Parenchymal involvement was present in 54.2% of the patients with CNS involvement, 45.8 % had cerebral venous thrombosis. Oral apthous ulcer was found in 91.7 % of the patients, genital ulcer in 70.8%, pathergy positivity in %45.8 papulopustular lesion in %37.5, erythema nodosum in %45.8. Patients with CNS involvement had headache, vision loss, diplopia, hemiparesis, epilepsy, proptosis, and ataxic gait and walking difficulty in 66.6%, 12.5%, 25%, 12.5%, 8.3%, 8.3% and 12.5%, respectively. Patients with and without CNS involvement were compared in terms of clinical findings and medications. A significant difference was observed in terms of cardiac involvement (Table 1). While one of the 2 patients with cardiac involvement had a thrombus in the right ventricle, the other had pericardial effusion. The patient with cardiac thrombus also had cerebral venous thrombus. Steroid, azathioprine, cyclophosphamide treatments have been used at a higher in patients with CNS involvement. In addition, the patients with parenchymal and cerebral venous involvement were compared in terms of clinical, demographics findings and medications. The presence of papulopustular lesions (9.1% vs 57.1%) and pathergy positivity (18.2% vs 71.4%) were higher in patients with parenchymal involvement (p:0.033, p: 0.020, respectively).

Table 1. Comparison of data of patients with and without CNS involvement

n (%)	CNS Involvement (+) n:24	CNS Involvement (-) n:370	P
Gender			0.396
Female	8(33.3)	164(44.3)	
Male	16(66.7)	206(55.7)	
Oral Aphthous Ulcer	22(91.7)	357(96.5)	0.230
Genital Ulcer	17(70.8)	239(64.6)	0.661
Papulopustular lesion	9(37.5)	120(32.4)	0.655
Erythema Nodosum	11(45.8)	139(37.6)	0.516
Pathergy	11(45.8)	174(47)	0.988
Uveitis	9(37.5)	129(34.9)	0.827
Retinal Vasculitis	1(4.2)	10(2.7)	0.504
Arthritis	3(12.5)	95(25.7)	0.221
Deep Venous Involvement	6(25)	59(15.9)	0.256
Artery Occlusion	1(4.2)	8(2.2)	0.436
Arterial Aneurysm	1(4.2)	14(3.8)	1
GIS involvement	2(8.3)	15(4.1)	0.277
Cardiac involvement	2(8.3)	4(1.1)	***0.046***

Conclusion: It has been reported that neurological symptoms occur in an average of 2.5 to 6.5 years after the diagnosis of BD. On the other hand, it has been stated that neurological complications may be the first involvement in 3-33% of the cases and this situation will cause diagnostic difficulties[1]. These data are consistent with our study.

REFERENCES:

[1] Noel N, Drier A, Wechsler B, ve ark. Neurological manifestations of Behcet's disease. Rev Med Interne 2014;35(2):112–120.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1365

AB0360

A DECADE OF SUSPECTED GIANT CELL ARTERITIS: CLINICAL FEATURES OF A HIGHLY HETEROGENEOUS DISEASE

A. Castro[1], J. Mathew[2], O. Azzouqah[3], J. Diaz[4], A. Reimold[1,2], K. Shwin[1,2]. *[1]UT Southwestern Medical Center, Rheumatology, Dallas, United States of America*; *[2]Dallas VA Medical Center, Rheumatology, Dallas, United States of America*; *[3]Presbyterian Rust Medical Center, Rheumatology, Rio Rancho, United States of America*; *[4]Universidad de los Andes, Epidemiology, Bogotá, Colombia*

Background: Giant cell arteritis is the most common chronic systemic vasculitis in older adults. Permanent visual loss is the most concerning complication can occur in up to 20% of patients (1). Diagnosis is based on a combination of clinical findings, laboratory evidence of inflammatory markers, and temporal artery biopsy (TAB) confirming histologic evidence of inflammation. There are no definitive markers of the disease when TAB is negative.

Objectives: The objective of this study was to illustrate the clinical features of subjects suspected with GCA evaluated at the Dallas Veterans Affairs Medical Center (VAMC) and identify those features that would differentiate between TAB positive GCA, TAB negative GCA and non-GCA patients.

Methods: This retrospective study searched the Dallas VAMC database for subjects between January of 2010 until December 2019 with ICD-9 and ICD-10 entry code for GCA. Based on the 1990 ACR clinical classification criteria for GCA, suspected patients were classified as TAB positive GCA, TAB negative GCA and non-GCA. Subjects with incomplete data needed for classification were excluded. Group comparisons were performed with Fisher's exact test for categorical variables and the Mann-Whitney test for continuous variables.

Results: One-hundred and sixty-nine subjects had ICD-9/10 entry code for GCA. Ophthalmology was the specialty who did the initial evaluation in 46% of the suspected cases. Seventy-one patients were excluded due to incomplete data. Of the remaining 98 patients, 42 (42.9%) were diagnosed with GCA out of which 10 patients had a positive TAB. Seventy-six percent of patients diagnosed with GCA had negative temporal artery biopsies. In 56 (57.1%) patients GCA was ruled out (Figure 1). New-onset headache was the predominant symptom suggestive of GCA affecting 88.9% TAB positive and 100% of TAB negative cases compared to 56.6% of non-GCA patients (p< 0.001), followed by scalp tenderness in 33.3%, 58.1% and 10.9%, respectively (p< 0.001), jaw claudication in 57.1%, 34.5% and 14.9% (p=0.021), and elevated sedimentation rate in 33%, 65.6% and 33% (p=0.013) (Table 1). Polymyalgia rheumatica was present in 28.6% and 21.7% of patients diagnosed with GCA compared to zero percent in non-GCA cases (p=0.017). More than 30% of patients with GCA had normal acute phase reactants in this cohort.

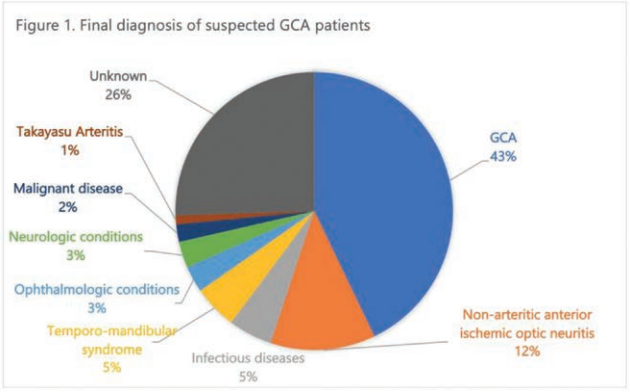


Table 1. Comparison of demographics and clinical features of patients with suspected GCA

	GCA TAB Positive (n=10)		GCA - TAB Negative (n=32)		non-GCA (n=56)		
	n	%	n	%	n	%	p
Age (mean/sd)	71.3 (7.8)		67.3 (8.1)		67.3 (8.9)		0.367
Male	9	90	30/32	93.8	51/56	91.1	0.885
Clinical findings							
New onset headache	8/9	88.9	32/32	100	30/53	56.6	<0.001
Visual symptoms	9/10	90	22/32	68.8	42/54	77.8	0.351
Jaw claudication	4/7	57.1	10/29	34.5	7/47	14.9	0.021
PMR	2/7	28.6	5/23	21.7	0/30	0	0.017
Scalp tenderness	2/6	33.3	18/31	58.1	5/46	10.9	<0.001
Fever	0/5	0	5/23	21.7	2/35	5.7	0.117
ESR > 50	1/3	33.3	21/32	65.6	18/54	33.3	0.013
CRP > 10	1/3	33.3	5/30	16.7	6/54	11.1	0.473
Anemia (hemoglobin < 12 g/ dl)	2/7	28.6	15/32	46.9	21/52	40.4	0.642
Thrombocytosis (platelets >400)	2/7	28.6	3/32	9.4	4/51	7.8	0.228

Conclusion: There is clinical heterogeneity within the patients diagnosed with GCA regardless of TAB. A high index of clinical suspicion needs to be the cornerstone of diagnosis. There is need for new classification criteria to include patients with negative TAB.

REFERENCES:

[1] Soriano A, et al. Nat Rev Rheumatol. 2017 Aug;13(8):476-484.

Disclosure of Interests: Adela Castro: None declared, Jiby Mathew: None declared, Ola Azzouqah: None declared, Jesus Diaz: None declared, Andreas Reimold Consultant of: Lilly, Grant/research support from: Abbvie
Pfizer
Gilead, Kyawt Shwin: None declared

DOI: 10.1136/annrheumdis-2021-eular.1461

AB0361 EFFECTIVENESS AND SAFETY OF INFLIXIMAB DOSE ESCALATION IN PATIENTS WITH REFRACTORY TAKAYASU ARTERITIS: A REAL-LIFE EXPERIENCE FROM A MONOCENTRIC COHORT

A. Tomelleri[1], C. Campochiaro[1], S. Sartorelli[1], F. Baldassi[2], F. Fallanca[2], M. Picchio[2], E. Baldissera[1], L. Dagna[1]. [1]*IRCCS San Raffaele Hospital, Unit of Immunology, Rheumatology, Allergy and Rare diseases, Milan, Italy*; [2]*IRCCS San Raffaele Hospital, Unit of Nuclear Medicine, Milan, Italy*

Background: Most published evidence on infliximab (IFX) in Takayasu arteritis (TAK) refers to its use at the standard dose of 5 mg/kg every 6-8 weeks[1]. However, in other diseases such as rheumatoid arthritis or Crohn's disease[2,3], it has been already demonstrated that IFX often requires a dose escalation to maintain its response.
Objectives: To evaluate effectiveness and safety of IFX dose escalation in TAK patients. To identify predictors of refractoriness to standard-dose IFX.
Methods: Medical records of IFX-treated TAK patients from a large single-centre observational cohort were reviewed. Decisions on IFX start, interruption, and dose modification were always made by the same experienced physician (EB). IFX therapy duration and reasons for dose escalation and therapy suspension were evaluated. Occurrence of adverse events was recorded. A comparison between patients who maintained IFX standard-dose and those who needed dose-escalation was performed. Factors predicting standard-dose refractoriness were analyzed.
Results: Forty-one patients were included (38 women; median age at IFX start, 36 [IQR, 28-45] years; median disease duration, 22 [13-60] months). Starting IFX dose was 5 mg/kg 6-weekly; 39 patients (95%) were on concomitant csDMARD and 38 patients (93%) on systemic glucocorticoids (GC). IFX dose escalation was performed in the majority of patients (n=28, 68%) (Figure 1). Persistence/recurrence of clinical symptoms was the most frequent reason for dose escalation (62%). Median IFX therapy duration was 39 (26-61) months in the standard-dose and 68 (38-87) months in the intensified-dose group. Patients in the intensified-dose group had a higher number of relapses (3.4 vs 0.8 events/patient), expression of a more aggressive disease phenotype. Nevertheless, in only 8 patients (29%) from this group IFX was suspended, after a median of 38 (31-71) months. Causes of suspension were loss of response (n=7) or patient's request (n=1). GC were successfully suspended in 4 patients from the standard-dose (36%) and 3 patients from intensified-dose (11%) group. Median daily prednisone dose was reduced from 10 (6-10) to 3 (0-5) mg in the standard-dose group, and from 13 (9-18) to 5 (4-5) mg in the intensified-dose group. Three patients from the intensified-dose group had a serious infection; one patient from the standard-dose group developed paradoxical psoriasis. At univariate analysis, younger age at diagnosis and at IFX start were associated with IFX escalation (Table 1).

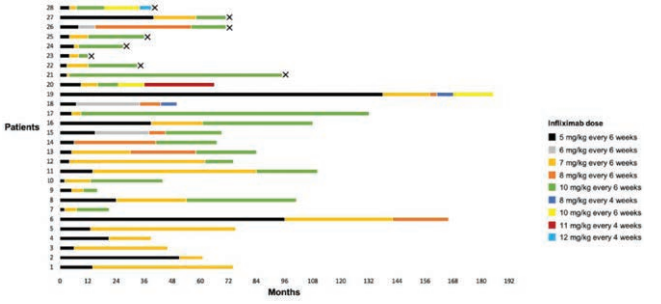


Figure 1. Infliximab dose escalation regimens (the cross (x) indicates treatment suspension)

Table 1. Factors influencing IFX dose escalation in patients with TAK (Cox proportional hazards model)

	Standard-dose IFX	Intensified-dose IFX	*P*-value
Age at diagnosis, years	40 (34-46)	30 (23-40)	**0.031**
Diagnostic delay, months	12 (7-77)	27 (15-50)	0.73
Age at IFX start, years	42 (38-61)	34 (27-44)	**0.040**
Delay before IFX start, months	33 (14-90)	24 (11-53)	0.48
Daily PDN at IFX start, mg	8.75 (5-10)	11.25 (8.5-16.25)	0.051
CRP at IFX start, mg/L	6.5 (2.1-9.3)	10.7 (5.2-20.9)	0.07
Class V Numano, n (%)	3 (30)	16 (57)	0.133
PETVAS score	8 (6-12)	12 (9-16)	0.056

Conclusion: In TAK, dose escalation can be a safe strategy to optimize IFX durability in refractory patients. Younger patients seem to be more refractory to standard dosages.

REFERENCES:

[1] Mekinian A, Néel A, Sibilia J, et al. Efficacy and tolerance of infliximab in refractory Takayasu arteritis: French multicentre study. Rheumatology. 2012; 51:882–6
[2] Ollendorf DA, Massarotti E, Birbara C, et al. Frequency, predictors, and economic impact of upward dose adjustment of infliximab in managed care patients with rheumatoid arthritis. J Manag Care Pharm. 2005;11(5):383-93
[3] Taxonera C, Olivares D, Mendoza JL, et al. Need for infliximab dose intensification in Crohn's disease and ulcerative colitis. World J Gastroenterol. 2014;20(27):9170-7

Disclosure of Interests: Alessandro Tomelleri: None declared, Corrado Campochiaro: None declared, Silvia Sartorelli: None declared, Francesco Baldassi: None declared, Federico Fallanca: None declared, Maria Picchio: None declared, Elena Baldissera Speakers bureau: Pfizer, Roche, Sanofi-Genzyme, Consultant of: Novartis, Lorenzo Dagna Consultant of: Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Galapagos, GlaxoSmithKline, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI., Grant/research support from: The Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR) received unresctricted research/educational grants from Abbvie, Bristol-Myers Squibb, Celgene, GlaxoSmithKline,Janssen, Merk Sharp & Dohme, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi Genzyme, and SOBI
DOI: 10.1136/annrheumdis-2021-eular.1537

AB0362 DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF BEHCET'S DİSEASE PATIENTS

S. Şan[1], Ö. Özdemir Işık[1], A. Yazici[1], A. Cefle[1]. [1]*Kocaeli Üniversitesi Tıp Fakültesi, Rheumatology, Kocaeli, Turkey*

Background: Behcet's Disease (BD) is a systemic variable vessel vasculitis that involves the skin, mucosa, joints, eyes, arteries, veins, nervous system and the gastrointestinal system.
Objectives: In this study we aimed to present variety of involvements in patients who were followed up in our outpatient clinic with a diagnosis of BD.
Methods: Data of 394 patients diagnosed with BD between 2000-2020 were retrospectively reviewed clinical, demographic characteristics and systemic involvements.
Results: In our study 43.7% of BD patients were female, 56.3% were male and the mean age was 40±11years, disease average age of onset 36.5±10.6, disease duration was 12.8±6.8years. It was observed mucocutaneus involvement 98% of the patients, uveitis in 35%, retinal vasculitis in 2.8%, arthritis in 24.9%, arterial occlusion in 2.3%, arterial aneurysm in 3.8%, venous involvement in 19.8%, gastrointestinal (GIS) involvement in 4.3%, cardiac involvement in 1.5%, and cranial involvement 7.1 (Table 1).

Table 1. The Data of Behçet Disease

n (%)	n= 394
Gender	
Female	*172 (43.7)*
Male	*222 (56.3)*
Family History	48 (12.2)
Fever & Weight Loss	21 (5.3)
Mucocutaneus involvement	386 (98)
Oral Aphthous Ulcer	*379 (96.2)*
Genital Ulcer	*256 (65)*
Papulopustular lesions	*129 (32.7)*
Erythema Nodosum-like lesions	*150 (38.1)*
Skin Pathergy Reaction	185 (47)
Uveitis	138 (35)
Retinal Vasculitis	11 (2.8)
Venous involvement	76 (17.6)
Thrombophlebitis	*30 (7.6)*
	67 (17)
Deep venous thrombosis	
Arthritis	98 (24.9)
Monoarthritis	*74 (75.5)*
Oligoarthritis	*21 (21.4)*
Sacroiliitis	*3 (3.0)*
Artery Occlusion	9 (2.3)
Arterial Aneurysm	15 (3.8)
GIS involvement	17 (4.3)
İleum	*9 (2.3)*
Colon	*2 (0.5)*
Rectum	*1 (0.3)*
İleocolonic	*4 (1)*
Cardiac involvement	6 (1.5)
Pericarditis	*2 (0.5)*
Ventricular thrombosis	*3 (0.7)*
Atrial thrombosis	*1 (0.2)*
Cranial involvement	24 (5.6)
Parenchymal involvement	*13 (4.6)*
Cerebral Venous Thrombosis	*11 (2.8)*
Pulse steroid	15 (3.8)
1mg/kg steroid	48 (12.2)
Infliximab	13 (3.3)
Azathioprine	184 (46.7)
Cyclophosphamide	31 (7.9)

When all patients evaluated in terms of renal findings, proteinuria was observed in 5 patients and hematuria was observed in 2 patients. 3 patients had proteinuria over than 500mg/day. Their renal biopsy findings; 2 of them were nonspecific involvements and one of them was minimal mesangioproliferative changes.

Conclusion: As a multi-system disease, general data have been presented, as clinical symptoms involve almost all systems of the body (1).

REFERENCES:

[1] Behcet's disease Fereydoun Davatchi 1Int J Rheum Dis.2014 May;17(4):355-7. doi: 10.1111/1756-185X.12378.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1543

AB0363 PERIOPERATIVE MANAGEMENT WITH BIOLOGICS ON SEVERE AORTIC VALVE REGURGITATION CAUSED BY BEHÇET'S SYNDROME: THE EXPERIENCE FROM A SINGLE CENTER

L. Sun[1], J. Liu[1], W. Zheng[1]. [1]*Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Rheumatology and Clinical Immunology, Beijing, China*

Background: Cardiovascular involvement in Behçet's syndrome (BS) is associated with poor prognosis and accounts for the leading cause of mortality and morbidity in BS[1, 2]. Perioperative management of severe aortic valve regurgitation (AR) caused by BS is critical while challenging. AR caused by BS is associated with a high incidence of severe postoperative complications, especially paravalvular leakage (PVL) due to the fragilities of aortic lesions and tissue inflammation, leading to a significantly increased risk of re-operation and life-threatening conditions[3-5]. For the perioperative management of patients with AR caused by BS, many patients respond inadequately to the combination therapies of glucocorticoids (GCs) and immunosuppressants. Meanwhile, rapid and efficient control of inflammation is critical in preserving cardiac function and surgical management. However, the application of biologics in the perioperative treatment of AR attributable to BS has not yet been evaluated.

Objectives: To investigate the efficacy and safety of biologics in the perioperative management of severe AR caused by BS.

Methods: We retrospectively analyzed twenty patients with severe AR caused by BS and were treated with biologics during the perioperative cardiac surgeries in our center between February 2016 and October 2020.

Results: Twenty patients with severe AR were enrolled, including 19 males and 1 female, with a mean age of 39.1±8.8 years and median course 8 (IQR, 5.25-10) years. Before biologics administration, 92.9% of the patients who underwent aortic valve replacement surgeries had failed conventional therapy and developed postoperative paravalvular leakage (PVL) at a median interval of 4 months. Biologics was administered during the perioperative period of 22 aortic valve surgeries, including preoperatively with a median interval of 3.5 (IQR, 2.75-4.25) months in 13 cases, or within three-month postoperatively in 9 cases, with background glucocorticoids (GCs) and immunosuppressants. After a median follow-up of 21 (IQR, 15-32) months, 11 out of 13 cases (84.6%) preoperatively and 8 out of 9 cases (88.9%) postoperatively treated with biologics were event-free. The BDCAF score improved significantly (7 vs. 0, median, p<0.0001). Significant decrease of ESR (25.0 (IQR, 11-36.25) mm/h vs. 6.5 (IQR, 4-8.8) mm/h, p<0.001), and CRP (20.77 (IQR, 7.19-29.58) mg/L vs. 1.53 (IQR, 0.94-2.92) mg/L, p=0.001) were achieved rapidly and effectively. The dosage of GCs tapered from 40 (IQR, 30-60) mg/d to 10 (IQR, 5-11.25) mg/d, p<0.0001. Immunosuppressants were tapered in number and dosage in 6 (30%) and 20 patients (100%), respectively. No serious adverse event was observed.

Conclusion: Our study suggests that biologics was effective and well-tolerated for the perioperative management of severe and refractory AR caused by BS, which significantly reduced the occurrence of postoperative PVL and had a favorable GCs- and immunosuppressants- sparing effect.

REFERENCES:

[1] Saadoun D, Wechsler B, Desseaux K, *et al*. Mortality in Behcet's disease. *Arthritis Rheum* 2010; 62: 2806-2812.

[2] Thomas T, Chandan JS, Subramanian A, *et al*. Epidemiology, morbidity and mortality in Behcet's disease: a cohort study using The Health Improvement Network (THIN). *Rheumatology (Oxford)* 2020; 59: 2785-2795.

[3] Ando M, Kosakai Y, Okita Y, *et al.* Surgical treatment of Behcet's disease involving aortic regurgitation. *Ann Thorac Surg* 1999; 68: 2136-2140.

[4] Han JK, Kim HK, Kim YJ, *et al.* Behcet's disease as a frequently unrecognized cause of aortic regurgitation: suggestive and misleading echocardiography findings. *J Am Soc Echocardiogr* 2009; 22: 1269-1274.

[5] Guo X, Tian Z, Liu Y, *et al*. Preoperative immunosuppressive therapy reduces paravalvular leakage after aortic valve surgery in patients with aortic regurgitation attributable to Behcet's disease. *Clin Exp Rheumatol* 2016; 34: S26-S33.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1568

AB0364 DO PATIENTS PARTICIPATING IN MEETINGS REPRESENT THE ACTUAL PATIENT POPULATION IN BEHÇET SYNDROME?

S. S. Taflan[1,2], S. N. Esatoglu[1,2], Y. Ozguler[1,2], B. Yurttas[1,2], M. Melikoglu[1,2], G. Hatemi[1,2]. [1]*Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*; [2]*Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Behcet Disease Center, Istanbul, Turkey*

Background: The importance of patient involvement in healthcare research is increasingly emphasized. Patients participate as research partners in designing studies and development of management recommendations, measurement tools and outcome measures. However, ensuring representation of the general patient population by specific patient groups may be challenging for multisystem diseases with heterogenous phenotype.

Objectives: We aimed to evaluate whether patients with Behcet syndrome (BS) participating in a patient convention represent the actual patient population attending the clinic.

Methods: A questionnaire was applied to 104 BS patients (Meeting group) attending the patient convention which was held during the Cerrahpasa Behcet Disease Symposium in Istanbul in February 2020. Patients had been invited to the convention through posters, advertisement on our website and social media. The questionnaire was conducted with a keypad given to the patients and it consisted of 21 items including age, gender, education level, working status, disease duration, BS manifestations, and treatment. The same questionnaire was filled by 97 consecutive patients (Clinic group) who attended our rheumatology outpatient clinic for their routine controls. Chi-square test was used to compare the groups.

Results: Table 1 shows demographic and disease characteristics of the patient groups. The groups were similar in terms of sex and education level. There were more men in both groups, probably reflecting the more severe disease course among men in BS. There were significantly more patients who were >40 years of age and had a disease duration more than 20 years in the Meeting group. Although there were more patients who had a job in Clinic group, the difference was not significant. Central nervous system involvement, vascular involvement, genital ulcers, erythema nodosum, and arthritis were significantly more common in patients in the Meeting group compared with those in the Clinic group. The frequency of eye involvement, gastrointestinal involvement and papulopustular lesions were similar in the two groups. Cyclophosphamide use was significantly more common in Meeting group compared to the Clinic group.

Table 1. Demographics, clinical characteristics, and treatments

	Meeting Group (n=104) (n/N, %)	Clinic Group (n=97) (n, %)	*P*
Oral aphthous ulcers	88/97(91)	94(97)	0.13
Genital ulcers	86/104(83)	68(70)	***0.045***
Erythema nodosum	77/103(75)	47(48)	***0.0003***
Papulopustular skin lesions	69/103(67)	75(77)	0.09
Arthritis	78/102(77)	46(47)	***<0.0001***
Eye involvement	51/103(50)	53(55)	0.48
Vascular involvement	42/98(43)	25(26)	***0.036***
CNS involvement	14/103(14)	2(2)	***0.016***
GI involvement	14/97(14)	6(6)	0.10
Prednisolone - still using	30/104(29)	34(35)	0.37
Prednisolone - ever used	88/104 (85)	72(74)	0.08
Colchicine - still using	43/100 (43)	46(47)	0.57
Colchicine - ever used	86/100(86)	74(76)	0.10
AZA - still using	45/100 (45)	41(42)	0.77
AZA - ever used	81/100 (81)	74(76)	0.49
CYC - still using	1/96(1)	0(0)	NS
CYC - ever used	16/96(17)	7(7)	***0.048***
bDMARDs - still using	20/101(20)	26(27)	0.31
bDMARDs - ever used	28/101(28)	32(33)	0.44

* Adjusted *P*-values by Bonferroni correction were <0.001.BS: Behcet Syndrome, CNS: Central nervous system, GI: Gastrointestinal, AZA: Azathioprine, CYC: Cyclophosphamide; bDMARDs: Biologic disease-modifying anti-rheumatic drugs; NS: non-significant

Conclusion: Patients in the Meeting group had more severe disease compared to the Clinic group. Patients with all types of involvement were adequately represented in the Meeting group.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1643

AB0365

CLINICAL, LABORATORY AND IMAGING OUTCOMES IN TOCILIZUMAB-TREATED PATIENTS WITH LARGE VESSEL-GIANT CELL ARTERITIS ACCORDING TO EARLY ONSET THERAPY

D. Prieto-Peña[1], I. Martínez-Rodríguez[2], B. Atienza-Mateo[1], O. Cuenca-Vera[2], F. J. Gomez de la Fuente[2], A. Sanchez-Salmón[2], M. A. González-Gay[1], R. Blanco[1]. *[1]Hospital Universitario Marques de Valdecilla, IDIVAL, Rheumatology, Santander, Spain*; *[2]Hospital Universitario Marques de Valdecilla, IDIVAL, Nuclear Medicine, Santander, Spain*

Background: Tocilizumab (TCZ) has shown efficacy in large vessel vasculitis (LVV)-Giant Cell Arteritis (LVV-GCA) **(1-2)**. ^{18}F-fluodeoxyglucose positron emission tomography (^{18}F-FDG PET/CT) is useful to assess LVV disease activity **(3-5)**. It is unknown if early treatment with TCZ may have an influence on clinical, laboratory and imaging outcomes.
Objectives: To assess clinical, laboratory and PET/CT activity improvement in LVV-GCA patients treated with TCZ according to the time from disease diagnosis to TCZ onset.
Methods: Comparative single-center study of 30 LVV-GCA patients treated with TCZ who were divided into 2 groups depending on the time of onset of TCZ: **a)** early onset (≤ 6 months; n=15) and **b)** late onset (> 6 months; n=15). All patients had a baseline and a follow-up PET/CT scan. Complete clinical improvement and normalization of laboratory markers (CRP ≤0.5mg/dL and/or ESR ≤ 20 mm/1st hour) was assessed. For imaging evaluation, normalization of total visual score (TVS) was considered when TVS = 0 and normalization of semiquantitative activity if the target to background ratio (TBR) at the thoracic aorta was <1.34.
Results: 30 patients were included (24 women/6 men); mean age 65.7± 9.8 years. Patients in the TCZ early-onset group were receiving higher doses of prednisone (10.0[5.9-15.0] vs 5.0 [5.0-7.5] mg/day; p< 0.01) and had higher TVS scores (7.0 [4.0-9.0] vs 3.0 [2.0-5.0]; p< 0.01) at baseline (Table 1). Following TCZ initiation, after a mean of 10.8±3.7 months, most patients achieved complete clinical improvement and normalization of ESR and CRP in both groups. Uncoupling with imaging outcomes was observed in both groups. Although non-significant statistical differences were observed, complete TBR normalization (TBR <1.34) and complete TVS normalization (TVS=0) tended to be more frequent in the group of patients who received early-onset TCZ therapy (Figure 1).

Table 1.

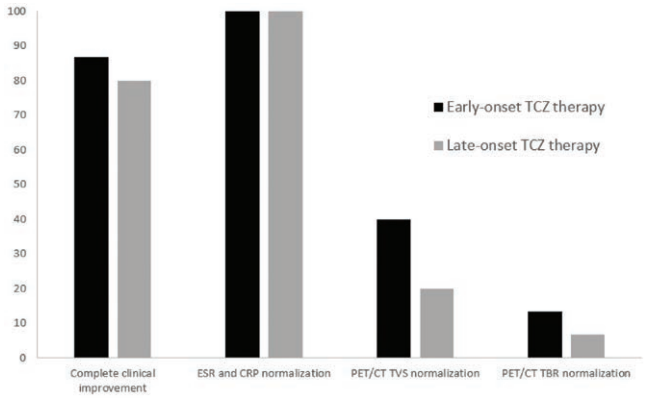
	Early-onset TCZ therapy (n= 15)	Late-onset TCZ therapy (n=15)	p
General features			
Age (years), mean ± SD	65.8 ± 9.9	65.5 ± 10.1	0.94
Sex (female), n (%)	11 (73.3)	13 (86.7)	0.65
GCA evolution before TCZ onset, median [IQR]	2.0 [1.0-5.0]	18.0 [9.0-34.0]	**< 0.01**
Laboratory			
ESR (mm/1st hour), mean ± SD	34.7 ± 26.3	30.8 ± 28.7	0.70
CRP (mg/dL), median [IQR]	1.1 [0.6-2.3]	0.8 [1.8 -2.5]	0.28
Prednisone dose (mg/day), mean ± SD	10.0 [5.9-15.0]	5.0 [5.0-7.5]	**0.01**
TCZ therapy			
Intravenous, n (%)	10 (66.7)	11(73.3)	0.99
Combined with MTX, n(%)	6 (40)	8 (53.3)	0.46
PET /CT activity			
TBR at thoracic aorta	1.86 ± 0.69	1.54 ± 0.18	0.09
TVS	7.0 [4.0-9.0]	3.0 [2.0-5.0]	**< 0.01**
Complete clinical improvement, n (%)	13 (86.7)	12 (80)	0.99
Normalization of ESR and CRP, n (%)	15 (100)	15 (100)	0.99
PET/CT improvement			
Complete TBR normalization	6 (40)	3 (20)	0.23
Complete TVS normalization	2 (13.3)	1 (6.7)	0.54

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; TBR: target-to-background ratio. * Normalization of TBR was considered when TBR < 1.34. ** Normalization of TVS was considered when TVS=0.

Conclusion: TCZ was effective in patients with LVV-GCA regardless the time from disease diagnosis to TCZ onset. However, complete normalization of vascular activity in PET/CT scans tended to occur more likely in patients who receive early-onset TCZ therapy within the first 6 months of the disease.

REFERENCES:

[1] Calderón-Goercke M et al. Semin Arthritis Rheum. 2019; 49:126-135. PMID: 30655091
[2] Prieto Peña D et al. Clin Exp Rheumatol. 2020. PMID: 33253103
[3] González-Gay MA et al. Expert Rev Clin Immunol. 2018; 14:593-605. PMID: 29877748
[4] Martínez-Rodríguez et al. Semin Arthritis Rheum.2018; 47(4): 530-537. PMID: 28967430
[5] Prieto-Peña D et al. Semin Arthritis Rheum. 2019; 48:720-727. PMID: 28967430



Disclosure of Interests: Diana Prieto-Peña Grant/research support from: UCB Pharma, Roche, Sanofi, Pfizer, AbbVie and Lilly, Isabel Martínez-Rodríguez: None declared, Belén Atienza-Mateo: None declared, Oriana Cuenca-Vera: None declared, Francisco Javier Gomez de la Fuente: None declared, Aida Sanchez-Salmón: None declared, Miguel A González-Gay Grant/research support from: Abbvie, MSD, Jansen and Roche and had consultation fees/participation in company sponsored speaker´s bureau from Abbvie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Ricardo Blanco Grant/research support from: Abbvie, MSD and Roche, and had consultation fees/participation in company sponsored speaker´s bureau from Abbvie, Lilly, Pfizer, Roche, Bristol-Myers, Janssen, UCB Pharma and MSD
DOI: 10.1136/annrheumdis-2021-eular.1733

AB0366

TOCILIZUMAB FOR TAKAYASU ARTERITIS: MULTICENTER STUDY OF 54 WHITE PATIENTS

D. Prieto-Peña[1], P. Bernabéu[2], P. Vela-Casasempere[2], J. Narváez[3], C. Fernández-López[4], M. Freire González[4], B. González-Alvarez[5], R. Solans-Laqué[6], J. L. Callejas-Rubio[7], N. Ortego[7], C. Fernández-Díaz[8], E. Rubio Romero[9], S. García Morillo[9], M. Minguez[10], C. Fernández-Carballido[10], E. De Miguel[11], S. Melchor[12], E. Salgado-Pérez[13], B. Bravo[14], S. Romero-Yuste[15], J. Salvatierra[7], C. Hidalgo[16], S. Manrique Arija[17], C. Romero-Gómez[17], P. Moya[18], N. Alvarez-Rivas[19], J. Mendizabal[20], F. M. Ortiz Sanjuan[21], I. Pérez de Pedro[22], J. L. Alonso Valdivieso[23], P. S. Laura[24], R. M. Rosa[24], N. Fernández-Llanio[25], R. Gómez de la Torre[26], S. Suarez[26], M. J. Montesa[5], M. Delgado Sanchez[5], J. Loricera[1], B. Atienza-Mateo[1], S. Castañeda[8], M. A. González-Gay[1], R. Blanco[1]. *[1]Hospital Universitario Marques de Valdecilla, IDIVAL, Rheumatology, Santander, Spain*; *[2]H. General de Alicante, -, Alicante, Spain*; *[3]H. Bellvitge,., Barcelona, Spain*; *[4]CHU A Coruña,., A Coruña, Spain*; *[5]H Nuestra Sa Candelaria,., Tenerife, Spain*; *[6]H. Vall d'Hebron,., Barcelona, Spain*; *[7]H. San Cecilio,., Granada, Spain*; *[8]H. La Princesa,., Madrid, Spain*; *[9]H. Virgen Rocío,., Sevilla, Spain*; *[10]H. San Juan Alicante,., Alicante, Spain*; *[11]H. La Paz,., Madrid, Spain*; *[12]H. 12 Octubre,., Madrid, Spain*; *[13]CHU Ourense,., Ourense, Spain*; *[14]H. Virgen Nieves,., Granada, Spain*; *[15]CHU Pontevedra,., Pontevedra, Spain*; *[16]CHU Salamanca,., Salamanca, Spain*; *[17]H. Regional Malaga,., Malaga, Spain*; *[18]H. San Pau,., Barcelona, Spain*; *[19]H. San Agustin,., Aviles, Spain*; *[20]CH Navarra,., Pamplona, Spain*; *[21]H. La Fe,., Valencia, Spain*; *[22]H. Carlos Haya,., Malaga, Spain*; *[23]H. Burgos,., Burgos, Spain*; *[24]H. Reina Sofía,., Cordoba, Spain*; *[25]H. Arnau Vilanova,., Valencia, Spain*; *[26]H. Central Asturias,., Oviedo, Spain*

Background: Tocilizumab (TCZ) has shown to be effective for large vessel vasculitis including Takayasu arteritis (TAK) **(1-3).** Most evidence in TAK comes from Asian patients. However, white patients seem to have different clinical and prognostic features.
Objectives: Our aims were to: **a)** assess the efficacy and safety of TCZ in white patients with refractory TAK, **b)** determine if clinical improvement correlates with imaging outcomes, **c)** compare TCZ in monotherapy (TCZ_{MONO}) vs combined with conventional immunosuppressive drugs (TCZ_{COMBO})
Methods: Multicenter study of white patients with refractory TAK who received TCZ.Outcomes variables were remission, glucocorticoid-sparing effect, improvement in imaging techniques, and adverse events. A comparative study between patients who received TCZ_{MONO} and TCZ_{COMBO} was performed.
Results: 54 patients (46 women/8 men; median age 42.0 [32.5-50.5] years). TCZ was started after 12.0 [3.0-31.5] months since TAK diagnosis. Remission was achieved in 12/54 (22.2%), 19/49 (38.8%), 23/44 (52.3%) and 27/36 (75%)

at 1, 3, 6 and 12 months, respectively. Prednisone dose was reduced from 30.0 [12.5-50.0] to 5.0 [0.0-5.6] mg/day at 12 months (Table 1). 10 (26.3%) of the 38 patients in whom an imaging follow-up test was performed showed no radiographic improvement after a median of 9.0 [6.0-14.0] months. 4 of them were in clinical remission.23 (42.6%) patients were on TCZ_{MONO} and 31 (57.4%) on TCZ_{COMBO}: MTX (n=28), cyclosporine A (n=2), azathioprine (n=1). Patients on TCZ_{COMBO} were younger (38.0 [27.0-46.0] vs 45 [38.0-57.0] years; p= 0.048), with a trend to longer TAK duration (21.0 [6.0-38.0] vs 6.0 [1.0-23.0] months; p= 0.08) and higher C-reactive protein (2.4 [0.7-5.6] vs 1.3 [0.3-3.3] mg/dL; p=0.16). Despite these differences, similar outcomes were observed in both groups (log rank p=0.862) (Figure 1). Relevant adverse events were reported in 6 (11.1%) patients, but only 3 developed severe events that required TCZ withdrawal.

Table 1.

	Baseline n=54	**Month 1** N=54	**Month 3** N=49	**Month 6** N=44	**Month 12** N=36
Clinical remission, n (%)		12 (22.2)	19 (38.8)	23 (52.3)	27 (75.0)
Laboratory improvement					
CRP (*mg/dL*), median [IQR]	1.5 [0.5-3.5]	0.2 [0.1-0.7]*	0.2 [0.5-0.5]*	0.2 [0.1-0.5]*	0.1 [0.0-0.4]*
ESR (*mm/1st hour*), median [IQR]	30.5 [8.7-52.7]	7.0 [3.0-14.0]*	4.5 [2.0-8.0]*	5.0 [2.0-6.0]*	4.0 [2.0-9.5]*
Hemoglobin (*g/dL*), mean ± SD	12.4 ±1.5	13.0 ±1.2*	13.0 ±1.4*	13.2 ±1.5*	12.9 ±1.6*
Prednisone dose, median [IQR]	30.0 [12.5-50.0]	20.0 [10.0-30.0]*	10.0 [5.0-20.0]*	5.0 [5.0-10.5]*	5.0 [0.0-5.6]*

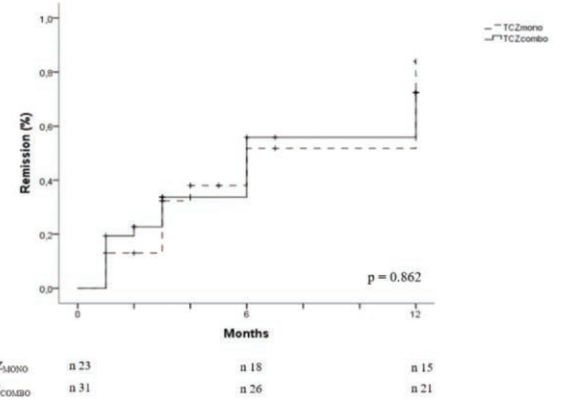
CRP: C-Reactive Protein; **ESR**: Erythrocyte Sedimentation Rate; **IQR:** interquartile range; n: number. *p<0.01 vs baseline (Wilcoxon test).

Conclusion: TCZ is effective and safe in white patients with refractory TAK. A discordance between clinical and imaging activity assessment may exist.

REFERENCES:

[1] Prieto Peña D et al. Clin Exp Rheumatol 2020 Nov 27. PMID: 33253103.
[2] Loricera J, et al. Clin Exp Rheumatol 2016; 34:S44-53. PMID: 27050507.
[3] Calderón-Goercke M, et al. Semin Arthritis Rheum 2019; 49:126-35. PMID: 30655091

FIGURE 1



Disclosure of Interests: Diana Prieto-Peña Grant/research support from: DP-P has received research support from UCB Pharma, Roche, Sanofi, Pfizer, AbbVie and Lilly., Pilar Bernabéu: None declared, Paloma Vela-Casasempere: None declared, J. Narváez: None declared, Carlos Fernández-López: None declared, Mercedes Freire González: None declared, Beatriz González-Alvarez: None declared, Roser Solans-Laqué: None declared, Jose Luis Callejas-Rubio: None declared, Norberto Ortego: None declared, Carlos Fernández-Díaz: None declared, Esteban Rubio Romero: None declared, SALVADOR GARCÍA MORILLO: None declared, Mauricio Minguez: None declared, Cristina Fernández-Carballido: None declared, Eugenio de Miguel: None declared, Sheila Melchor: None declared, Eva Salgado-Pérez: None declared, Beatriz Bravo: None declared, Susana Romero-Yuste: None declared, Juan Salvatierra: None declared, Cristina Hidalgo: None declared, Sara Manrique Arija: None declared, C. Romero-Gómez: None declared, Patricia Moya: None declared, Noelia Alvarez-Rivas: None declared, Javier Mendizabal: None declared, Francisco Miguel Ortiz Sanjuan: None declared, I. Pérez de Pedro: None declared, JOSE LUIS ALONSO VALDIVIESO: None declared, Pérez Sánchez Laura: None declared, Roldán Molina Rosa: None declared, Nagore Fernández-Llanio: None declared, Ricardo Gómez de la Torre: None declared, Silvia Suarez: None declared, María Jesús Montesa: None declared, Monica Delgado Sanchez: None declared, J. Loricera: None declared, Belén Atienza-Mateo: None declared, Santos Castañeda: None declared, Miguel A González-Gay Grant/research support from: MAG-G received grants/research supports from Abbvie, MSD, Jansen and Roche and had consultation fees/participation in company sponsored speaker´s bureau from Abbvie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Ricardo Blanco Grant/research support from: RB received grants/research supports from Abbvie, MSD and Roche, and had consultation fees/participation in company sponsored speaker´s bureau from Abbvie, Lilly, Pfizer, Roche, Bristol-Myers, Janssen, UCB Pharma and MSD.

DOI: 10.1136/annrheumdis-2021-eular.1747

AB0367 DIAGNOSTIC DELAY IN PATIENTS WITH GIANT CELL ARTERITIS

M. Van Nieuwland[1], E. Colin[1], D. Boumans[1], M. Vermeer[2], E. Brouwer[3], C. Alves[1]. *[1]Hospital Group Twente, Rheumatology and Clinical Immunology, Almelo, Netherlands*; *[2]Hospital Group Twente, ZGT Academy, Almelo, Netherlands*; *[3]University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*

Background: Giant cell arteritis (GCA) is the most common systemic vasculitis in the elderly which can lead to severe complications when treatment is delayed. Therefore, timely diagnosis and start of treatment is essential. Several forms of delay (consultation, referral and diagnostic delay) can contribute to the total delay towards GCA diagnosis. In the Dutch healthcare system, treatment is not started by a general practitioner (GP). When GCA is suspected, GPs refer to specialists. In our hospital, a fast track clinic (FTC) is used to expedite diagnosis. However, information on factors contributing to delay is scarce.

Objectives: The aim of this study was to describe the different components of delay towards diagnosis in GCA suspected patients in a general hospital, Ziekenhuisgroep Twente (the Netherlands).

Methods: For this descriptive study, a retrospective cohort consisting of patients with suspected GCA between January 1st 2017 and October 1st 2019 was used to analyse components of delay in diagnosis, as suggested by Prior et al. Consultation delay was defined as the time between start of symptoms and a patient's first consultation with a GP. Referral delay was defined as the time between a patient's first consultation with a GP and first visit to the FTC. Diagnostic delay was defined as the time between the first visit to the FTC and treatment initiation. Total delay was defined as the time from symptom onset until start of treatment. Delays were described using the median and interquartile ranges (IQR).

Results: In our cohort, 206 patients were included for analysis of whom 62 had GCA. Controls (n=144) were suspected of but did not have GCA. Comparing GCA patients with controls, 66.1% and 50.7% were female and the mean (SD) age was 74.2 (9.4) and 70.2 (11.0) years, respectively. In our cohort, the majority of patients (n=42, 67.7%) had cranial GCA (C-GCA). Furthermore, 8 (12.9%) had large vessel GCA (LV-GCA) and 12 (19.4%) had a combination of C-GCA and LV-GCA. For GCA patients, median consultation delay was 2.1 (IQR 0.8-5.8) weeks, referral delay 1.4 (IQR 0.4-4.6) weeks and diagnostic delay 0 (IQR 0-0.1) weeks (Figure 1). For delay regarding consultation and referral, results of controls were comparable to GCA patients. The median total delay was 4.4 weeks (IQR 1.57-10.14) for GCA patients.

Conclusion: With a median total delay of 4.4 weeks, delay in our cohort is almost half the delay described in a review by Prior et al. This difference might be due to FTC implementation and subsequent awareness in our hospital and by local GPs. Patients generally received treatment within one day after FTC visit. Nevertheless, contribution of consultation and referral delay is not resolved by introduction of the FTC, as shown in our data. Timely diagnosis is essential as severe complications can develop instantly, which emphasizes the need to tackle consultation and referral delay.

REFERENCES:

[1] Prior JA, Ranjbar H, Belcher J, et al. Diagnostic delay for giant cell arteritis – a systematic review and meta-analysis. BMC Med. 2017;15(1):120.

Table 1. Baseline characteristics of GCA patients and controls in our retrospective cohort. *CDUS=Colour Doppler Ultrasound; **Temporal Artery Biopsy;*18-FDG-Positron Emission Tomography/Computed Tomography.**

	GCA patients (n=62)		Controls (n=144)	
		Range		Range
Gender, % female (n)	66.1 (41)		50.7 (73)	
Age (years), mean (SD)	74.2 (9.4)	51 – 91	70.2 (11.0)	50 – 97
ESR, mean (SD)	78.4 (30.3)	22 – 120	39.9 (32.4)	2 – 124
Missing	*3*		*9*	
CRP, mean (SD)	74.7 (60.0)	2 - 283	35.8 (52.9)	0.4 -280
Missing	*1*		*6*	
Polymyalgia Rheumatica, % yes (n)	21 (13)		11.8 (17)	
Cranial symptoms, % yes (n)	80.6 (50)		75.0 (108)	
Vision loss, %yes (n)	27.4 (17)		15.3 (22)	
Compliant with GCA (i.e. AION, central retinal artery occlusion diplopia)				
Diagnostics				
CDUS* %yes (n)	96.8 (60)		96.5 (139)	
TAB** %yes (n)	58.1 (36)		18.8 (27)	
PET/CT***%yes (n)	40.3 (25)		16.0 (23)	

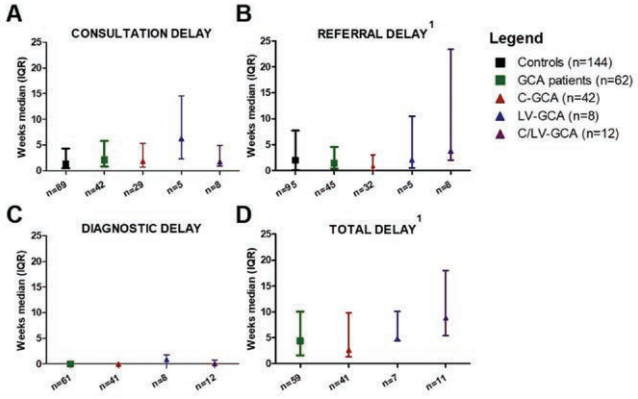


Figure 1. Description of consultation (A); referral (B); diagnostic (C) and total (D) delay in weeks for controls (black) and GCA patients (green), stratified for C-GCA (red), LV-GCA (blue) and C/LV-GCA (purple). [1]Not possible for controls as no GCA-indicated treatment was started.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1830

AB0368 CLINICAL CHARACTERISTICS AND RADIOGRAPHIC OUTCOME OF VASCULAR BEHCET'S DISEASE INVOLVING AORTA AND ITS MAJOR BRANCHES

S. Lee[1], S. Y. Kang[1], Y. H. Eun[1], H. Kim[1], J. Lee[1], E. M. Koh[1], H. S. Cha[1]. [1]*Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Medicine, Seoul, Korea, Rep. of (South Korea)*

Background: Behcet's disease (BD) is an immune-mediated systemic vasculitis affecting any size of blood vessels. Previous studies showed that BD may involve large arterial vessels [1] but the radiographic outcome has not been well known due to its low prevalence.
Objectives: To evaluate the radiographic outcome of vascular BD involving aorta and its major branches and the clinical characteristics of each prognosis group.
Methods: We retrospectively analyzed the medical records of patients who visited a single-center tertiary hospital in Seoul, Korea, across a 19-year period (Jan 2002 to Dec 2020). All patients fulfilled the International Criteria for Behcet's Disease. The patients included in this study had undergone CT angiography (CTA) of the aorta and its major branches at least twice in a 2–5 year interval and showed characteristic vascular involvements (aneurysm, stenosis, occlusion, vessel wall thickening, and thrombosis). Due to lack of the validated definition of radiographic progression of large vessel vasculitis in BD, we defined 20% changes of existing lesions or occurrence of new lesions as a radiographic progression.
Results: 22 patients with BD met the inclusion criteria. 5 patients (22.7%) progressed radiographically between the initial and follow-up CTA despite low acute phase reactant levels (AUC of ESR and CRP were 13.94 mm/h and 0.32 mg/dl, respectively). Aneurysm was the most frequent form of vascular involvement followed by thrombosis (21 [95.5%] and 11 [50.0%] patients, respectively, Table 1). Patients with radiographically progressive disease had longer disease duration (1.63 vs. 6.61 years, p=0.010) at initial CTA evaluation. Other clinical characteristics, including ESR, CRP, medication use, and follow up duration, were not different between two groups (Table 2).

Table 1. Radiographic characteristics of the cohort.

	Overall	Not progressed	Progressed	
n	22	17	5	p
Aneurysm (%)	21 (95.5)	16 (94.1)	5 (100.0)	>0.999
Stenosis (%)	5 (22.7)	4 (23.5)	1 (20.0)	>0.999
Occlusion (%)	5 (22.7)	5 (29.4)	0 (0.0)	0.440
Wall thickening (%)	4 (18.2)	4 (23.5)	0 (0.0)	0.589
Thrombosis (%)	11 (50.0)	9 (52.9)	2 (40.0)	>0.999

Conclusion: A considerable number of vascular BD patients involving aorta and its major branches progressed radiographically despite low disease activity. Radiographically progressed patients had longer disease duration, but other clinical characteristics were not significantly different whether progressed or not.
REFERENCES:
[1] Kural-Seyahi, Emire MD et al. The Long-Term Mortality and Morbidity of Behçet Syndrome. Medicine. 2003 Jan;82(1):60-76.

Table 2. Clinical characteristics of the cohort.

	Overall	Not progressed	Progressed	
n	22	17	5	p
Sex (Male) (%)	22 (100.0)	17 (100.0)	5 (100.0)	NA
Age (yr)	46.43 (7.71)	45.06 (8.06)	51.10 (4.03)	0.126
Disease duration (yr)	2.77 (3.99)	1.63 (2.66)	6.61 (5.61)	0.01
HTN (%)	5 (22.7)	4 (23.5)	1 (20.0)	>0.999
DM (%)	1 (4.5)	1 (5.9)	0 (0.0)	>0.999
Dyslipidemia (%)	6 (27.3)	5 (29.4)	1 (20.0)	>0.999
CKD (%)	7 (31.8)	4 (23.5)	3 (60.0)	0.321
BMI (kg/m^2)	42.91 (91.28)	48.23 (103.94)	24.82 (1.69)	0.626
AUC of CRP (mg/dl)	0.32 (0.37)	0.31 (0.41)	0.37 (0.12)	0.758
AUC of ESR (mm/h)	13.94 (11.40)	13.30 (12.77)	16.12 (4.66)	0.638
Immunosuppressive agent use (%)	18 (81.8)	14 (82.4)	4 (80.0)	>0.999
Steroid use (%)	22 (100.0)	17 (100.0)	5 (100.0)	NA
f/u duration (yr)	3.54 (0.80)	3.56 (0.79)	3.50 (0.92)	0.885

Data are presented as mean (SD) unless otherwise specified

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1939

AB0369 EVALUATION OF BASELINE POSITRON EMISSION TOMOGRAPHY IN THE DIAGNOSIS AND ASSESSMENT OF GIANT CELL ARTERITIS

B. Ince[1], E. G. Işık[2], Z. G. Özkan[2], Y. Yalçınkaya[1], B. Artim-Esen[1], A. Gül[1], M. L. Ocal[1], M. Inanc[1]. [1]*Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*; [2]*Istanbul University, Istanbul Faculty of Medicine, Department of Nuclear Medicine, Istanbul, Turkey*

Background: Positron emission tomography (PET/CT) has gained importance in the diagnosis and assessment of large vessel vasculitis (LVV) recently.
Objectives: We aimed to investigate the diagnostic importance and clinical significance of PET/CT findings in giant cell arteritis (GCA).
Methods: Data of the patients who underwent PET/CT to investigate large vessel involvement and who had at least 6 months of follow-up with a clinical diagnosis of GCA were retrospectively evaluated. PET/CT images were assessed by an experienced nuclear medicine specialist, regions of interest were drawn for major vascular territories and standardized maximum uptake values (SUVmax) of these areas were recorded.
Results: Twenty-nine consecutive patients (median age 68 (50-83), mean follow-up time 37.1 ± 48.8 (6-242)) were included into the study. All patients were over 50 years old and had erythrocyte sedimentation rate (ESR) over 50 mm/h at the time of imaging. Twenty patients (68.9%) met the ACR 1990 Classification criteria (ACR (+) group). The number of patients who had hypermetabolism in the aorta and its major branches in favour of LVV in PET/CT was 23 (79.3%) (PET-CT (+) group). Thoracic and abdominal aorta involvement were detected in 22 (75.8%) and 16 (55.2%) patients, respectively. There was positive correlation

between SUVmax in thoracic and abdominal aorta on PET/CT and ESR at diagnosis (r = 0.63 p = 0.002 and r = 0.77 p <0.001, respectively) and SUVmax in thoracic aorta and CRP (r=0.50 p=0.026). PET/CT (-) patients had more frequent disease flares during the follow-up (4/6 vs. 5/23 p = 0.035 OR = 7.2 (1.01- 51)). Three distinct subgroups were defined by implementing both ACR criteria and PET/CT positivity. Among ACR (+) patients (n=20); comparison of PET/CT (+) (n=14) and PET/CT (-) (n=6) patients did not show any difference in age of diagnosis, presence of polymyalgia rheumatica (PMR), flare rate and damage scores. Among PET/CT (+) patients (n=23), the mean age at diagnosis was higher, PMR and bilateral axillary artery involvement was more frequent in ACR (+) group (n=14) (Table 1).

Conclusion: PET/CT is increasingly used in the diagnosis and assessment of GCA in our center. The level of FDG uptake of the vessel wall in PET/CT correlates with the acute phase response. Flare was rarely observed in PET/CT (+) patients at diagnosis. Axillary artery involvement detected on PET/CT may be associated with the classical GCA clinic in ACR(+) patients (1). PET/CT (+) patients who does not met ACR criteria seems to have a diverse clinic features like young age and rare presence of PMR. PET/CT findings may be helpful in recognizing subgroups and predicting prognosis of GCA although prospective studies with follow-up scans are warranted.

REFERENCES:

[1] Grayson PC, Maksimowicz-McKinnon K, Clark TM, Tomasson G, Cuthbertson D, Carette S, et al. Distribution of arterial lesions in Takayasu's arteritis and giant cell arteritis. Annals of the rheumatic diseases. 2012;71(8):1329-34.

Table 1. Comparison of patients who fulfilled and not fulfilled ACR 1990 classification criteria among PET/CT (+) patients.

	ACR (+) PET/CT (+) (n=14)	ACR (-) PET/CT (+) (n=9)	p	OR (%95 CI)
Age at diagnosis	**68,8±4,5**	**63.3±9,2**	**0.004**	
PMR	**10**	**2**	**0.021**	**2.5 (1 – 6.1)**
History of flare	4	1	NS	
CRP at diagnosis	**75,1±30,6**	**130,8±93,4**	**0.024**	
ESR at diagnosis	93,9±28,1	112,5±21,2	NS	
Brachiocephalic artery	9	6	NS	
Right subclavian	8	5	NS	
Lef subclavian	9	5	NS	
Right carotid	8	5	NS	
Left carotid	9	6	NS	
Right axillary	**7**	**0**	**0.011**	**2 (1.18 – 3.3)**
Bilateral axillary	**6**	**0**	**0.022**	**1.75 (1.1-2.7)**
Thoracic aorta SUVmax (mean)	3,9±1,1	4,6±1,3	NS	
Abdominal aorta SUVmax (mean)	4,5±1,2	5,3±1,8	NS	

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2036

AB0370

UTILITY OF CRP AND ESR IN THE DIAGNOSIS OF GIANT CELL ARTERITIS RELAPSE IN A PHASE 2 TRIAL OF MAVRILIMUMAB

S. Unizony[1], M. C. Cid[2], E. Brouwer[3], L. Dagna[4,5], B. Dasgupta[6], B. Hellmich[7], E. Molloy[8], C. Salvarani[9], B. C. Trapnell[10], K. J. Warrington[11], I. Wicks[12], M. Samant[13], T. Zhou[13], L. Pupim[13], J. F. Paolini[13]. *[1]Massachusetts General Hospital, Vasculitis and Glomerulonephritis Center, Department of Rheumatology, Allergy and Immunology, Boston, United States of America*; *[2]Hospital Clínic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Vasculitis Research Unit, Department of Autoimmune Diseases, Barcelona, Spain*; *[3]University of Groningen, University Medical Center, University of Groningen, University Medical Center, Groningen, Netherlands*; *[4]IRCCS San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), Milan, Italy*; *[5]Vita-Salute San Raffaele University, Vita-Salute San Raffaele University, Milan, Italy*; *[6]Southend University Hospital NHS Foundation Trust, Southend University Hospital NHS Foundation Trust, Westcliff-on-sea, United Kingdom*; *[7]Medius Kliniken, Department of Internal Medicine, Rheumatology, and Immunology, Kirchhelm unter Teck, Germany*; *[8]St Vincent's University Hospital, St Vincent's University Hospital, Dublin, Ireland*; *[9]Arcispedale Santa Maria Nuova, Arcispedale Santa Maria Nuova, Reggio Emilia, Italy*; *[10]Cincinnati Children's Hospital, Translational Pulmonary Science Center, Cincinnati, United States of America*; *[11]Mayo Clinic, Mayo Clinic, Rochester, United States of America*; *[12]Walter & Eliza Hall Institute & Melbourne Health, Walter & Eliza Hall Institute & Melbourne Health, Melbourne, Australia*; *[13]Kiniksa Pharmaceuticals Corp., Clinical Development, Lexington, United States of America*

Background: No universally accepted definition of flare currently exists in giant cell arteritis (GCA). Although relapses are defined mostly on clinical grounds (recurrence of GCA-related signs/symptoms), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) help clinicians assess disease activity. In fact, >70% of patients on glucocorticoids (GCs) alone have increased CRP or ESR when the disease is active. In contrast, tocilizumab, given its IL-6-blockade effect in the liver, rapidly reduces CRP and ESR levels, rendering them unreliable for disease activity monitoring. Mavrilimumab – a GM-CSF receptor α inhibitor with demonstrated efficacy in a Phase 2 GCA trial[1] – downregulates inflammation upstream of IL-6. We hypothesized that mavrilimumab would not interfere with the utility of CRP and ESR in monitoring disease activity and in identifying GCA relapse.

Objectives: To analyze the relationship between CRP/ESR and clinical disease activity in GCA patients treated with mavrilimumab.

Methods: New-onset and relapsing GCA patients with active disease were recruited. GC-induced remission (no GCA symptoms and CRP <1 mg/dL or ESR <20 mm/hr) was required by baseline. Patients were randomized 3:2 to mavrilimumab 150 mg or placebo subcutaneously every 2 weeks plus a protocol-defined 26-week prednisone taper. The primary efficacy endpoint was time to relapse by Week 26. Relapse (adjudicated) was defined as recurrent GCA-related signs/symptoms, including new/worsening vasculitis on imaging, concurrent with CRP ≥1 mg/dL and/or ESR ≥30 mm/hr. CRP and ESR were also measured periodically during the trial.

This post hoc analysis assessed the association of recurrent GCA-related signs/symptoms with concurrent CRP or ESR elevation post-randomization by treatment arm. We also assessed the proportion of patients with CRP or ESR elevation without GCA-related signs/symptoms up to Week 26.

Results: Seventy patients were enrolled (mavrilimumab, N=42; placebo, N=28). The association of CRP or ESR elevation with unequivocal GCA-related signs/symptoms post-randomization was consistent regardless of treatment arm: 8/8 in the mavrilimumab group and 13/13 in the placebo group (Table 1). During relapse, median (range) CRP was 1.8 (1.4 – 8.4) mg/dL (mavrilimumab group) and 1.8 (1.1 – 9.0) mg/dL (placebo group). Corresponding ESR values were 39.5 (30 – 102) mm/hr (mavrilimumab group) and 49 (31 – 101) mm/hr (placebo group). Four mavrilimumab recipients had self-limited, equivocal GCA-related signs/symptoms without concurrent CRP or ESR elevation; all 4 completed the prespecified GC taper by Week 26 without need for rescue GCs, so relapse was not confirmed. At least 1 elevated CRP or ESR value in the absence of GCA-related signs/symptoms was observed in 58.8% of mavrilimumab recipients and 93.3% of placebo recipients by Week 26.

Conclusion: The observed association of CRP or ESR elevation with GCA-related signs/symptoms is consistent with the upstream mechanism and supports the utility of the stringent protocol definition of relapse. The frequency and magnitude of CRP and ESR elevations at relapse were similar in both treatment groups, suggesting that CRP and ESR remain useful in assessments of disease activity in mavrilimumab-treated patients. CRP and ESR elevations without GCA-related signs/symptoms occurred more often in placebo recipients.

REFERENCES:

[1] Cid, Unizony et al. Arthritis Rheumatol. 2020; 72 (suppl 10)

Table 1. CRP and ESR levels in patients with or without GCA relapse

Assessment[§]	Mavrilimumab	Placebo	Mavrilimumab	Placebo
	N=42	N=28	N=42	N=28
	With Relapse		Without Relapse	
# of patients	8 (19.1)	13 (46.4)	34 (81.0)	15 (53.6)
Elevated CRP* or ESR†	**8 (100.0)**	**13 (100.0)**	**20 (58.8)**	**14 (93.3)**
Elevated CRP*	7 (87.5)	10 (76.9)	10 (29.4)	11 (73.3)
Median (range) mg/dL	1.8 (1.4 - 8.4)	1.8 (1.1 - 9.0)	2.6 (1.3 – 7.0)	2.0 (1.0 – 6.6)
Elevated ESR†	6 (75.0)	9 (69.2)	16 (47.1)	10 (66.7)
Median (range) mm/hr	39.5 (30 - 102)	49.0 (31 - 101)	41.5 (30 - 110)	53.5 (30 - 82)

[§]# (%), except where indicated otherwise.*CRP ≥ 1 mg/dL†ESR ≥ 30 mm/hr

Disclosure of Interests: Sebastian Unizony Consultant of: Janssen and Kiniksa, Grant/research support from: Genentech, Maria C. Cid Speakers bureau: Roche and Kiniksa, Paid instructor for: GSK and Vifor, Consultant of: Janssen, GSK, and Abbvie, Grant/research support from: Kiniksa, Elisabeth Brouwer Speakers bureau: Dr. E.Brouwer as an employee of the UMCG received speaker fees and consulting fees from Roche in 2017 2018 which were paid to the UMCG., Consultant of: Dr. E.Brouwer as an employee of the UMCG received speaker fees and consulting fees from Roche in 2017 2018 which were paid to the UMCG., Lorenzo Dagna Speakers bureau: Abbvie, Amgen, Biogen, BMS, Celltrion, Galapagos, Glaxo SmithKline, Novartis, Pfizer, Roche, Sanofi-Genzyme,

SOBI, Consultant of: Abbvie, Amgen, Biogen, BMS, Celltrion, Galapagos, Glaxo SmithKline, Novartis, Pfizer, Roche, Sanofi-Genzyme, SOBI; clinical trial for Kiniksa, Grant/research support from: Abbvie, Amgen, BMS, Celltrion, Galapagos, Novartis, Pfizer, Roche, Sanofi-Genzyme, SOBI, Merk Sharp &Dohme, Janssen, Kiniksa, Bhaskar Dasgupta Paid instructor for: Educational grant symposium/workshop for Roche-chugai, Sanofi, and Abbvie, Consultant of: CI UK for the Kiniksa trial, Grant/research support from: Educational grant symposium/workshop for Roche-chugai, Sanofi, and Abbvie, Bernhard Hellmich Consultant of: Honoraria paid to the institution for participation in the clinical trial, Eamonn Molloy: None declared, Carlo Salvarani: None declared, Bruce C. Trapnell Consultant of: Consultant member of DSMB for Kiniksa., Kenneth J Warrington Consultant of: Clinical trial support from Eli Lilly and Kiniksa, Ian Wicks: None declared, Manoj Samant Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals, Teresa Zhou Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals, Lara Pupim Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals, John F. Paolini Shareholder of: Kiniksa Pharmaceuticals, Employee of: Kiniksa Pharmaceuticals

DOI: 10.1136/annrheumdis-2021-eular.2221

AB0371 PATIENTS WITH PROLONGED SYMPTOMS BEFORE GCA DIAGNOSIS DO NOT INCUR HIGHER RATES OF VISUAL LOSS

V. Yang[1], C. Mcmaster[1,2], C. Owen[1,2], J. Leung[1,2], R. Buchanan[1,2], D. Liew[1,2]. [1]*Austin Health, Rheumatology, Heidelberg, Australia*; [2]*The University of Melbourne, Medicine, Parkville, Australia*

Background: Giant cell arteritis (GCA), if left untreated, confers the threat of serious cranial ischaemic complications including permanent visual loss. Although achieving a prompt and accurate diagnosis remains challenging, early diagnosis is viewed as being paramount in preventing significant morbidity.[1] This raises the question of whether GCA patients are at greater risk of developing visual sequelae if there is a longer window between symptom onset and presentation.

Objectives: To compare the frequency of lasting visual loss in patients diagnosed with GCA undergoing temporal artery biopsy (TAB) within three months and after three months of symptom onset.

Methods: Patients who underwent TAB from January 2011 to November 2020 were identified from the pathology database of an Australian rheumatology referral centre. The diagnosis of GCA was established for each patient based on either positive TAB or, in the setting of negative TAB, clinical diagnosis by a rheumatologist. Baseline demographics, symptoms and major confounders – including age, sex, history of polymyalgia rheumatica or inflammatory arthritis, headache, jaw pain, fatigue, temporal artery tenderness or diminished pulse, and number of 1990 American College of Rheumatology (ACR) classification criteria for GCA[2] fulfilled – were manually extracted from electronic medical records, as was the duration between onset of GCA symptoms and TAB, and the presence of visual loss before and after TAB. Logistic regression log-likelihood tests were used to examine the two cohorts presenting before and after three months.

Results: There were 167 patients who underwent TAB during the study period with accessible clinical information. Of these, 31 (19%) had a delayed presentation of greater than three months from symptom onset. There were no statistical differences in patient demographics between the two groups (Table 1). No patients with delayed presentation experienced lasting, objective visual loss. In contrast, there were three cases in the cohort of patients who presented more promptly; these included two patients who developed permanent unilateral blindness, and one who experienced unilateral vision loss with some improvement at three months of follow-up.

Table 1. ***Patient characteristics by time from symptom onset to TAB.***

	Presentation <3 months	Presentation ≥3 months	p-value
Age (years)	73.45±10.06	69.84±10.75	0.080
Female	92 (67.65%)	20 (64.52%)	0.738
History of polymyalgia rheumatica	23 (16.91%)	4 (12.90%)	0.586
History of inflammatory arthritis	6 (4.41%)	2 (6.45%)	0.633
Headache	110 (80.88%)	23 (74.19%)	0.406
Jaw pain	37 (27.21%)	5 (16.13%)	0.206
Fatigue	28 (20.59%)	6 (19.35%)	0.878
Temporal artery tenderness or diminished pulse	46 (33.82%)	11 (35.48%)	0.860
ACR classification criteria	2.83±0.99	2.58±0.89	0.199

Conclusion: GCA patients with a lengthier course of symptoms before diagnosis did not experience any enduring visual loss. This may reflect a pattern of more aggressive disease leading to earlier presentation, but further study should explore whether longer symptom duration before diagnosis necessitates a higher degree of clinical concern.

REFERENCES:

[1] Font C, Cid MC, Coll-Vinent B, López-Soto A, Grau JM. Clinical features in patients with permanent visual loss due to biopsy-proven giant cell arteritis. Br J Rheumatol. 1997 Feb;36(2):251-4. doi: 10.1093/rheumatology/36.2.251. PMID: 9133940.

[2] Hunder GG, Bloch DA, Michel BA, Stevens MB, Arend WP, Calabrese LH, Edworthy SM, Fauci AS, Leavitt RY, Lie JT, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. Arthritis Rheum. 1990 Aug;33(8):1122-8. doi: 10.1002/art.1780330810. PMID: 2202311.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2234

AB0372 TOCILIZUMAB WAS EFFECTIVE IN REFRACTORY ARTERIAL INVOLVEMENT OF BEHCET'S DISEASE: A REAL-LIFE SINGLE- CENTER EXPERIENCE IN CHINA

H. Zhong[1], T. Liu[1], Y. Liu[1], X. Zhang[1], Y. Zhou[1], Y. Su[1]. [1]*Peking University People's Hospital, Department of Rheumatology and Immunology, Beijing, China*

Background: Behcet's disease (BD) is a chronic and relapsing vasculitis, in which major vessel involvement is a main cause of mortality and morbidity. The therapeutic arsenal is mainly composed of classical immunosuppressants. However, when faced with resistance to these drugs, no alternative therapeutic strategy is currently recommended.

Objectives: To assess the efficacy and safety of interleukin 6 receptor inhibitor tocilizumab (TCZ) in refractory arterial involvement of BD in a real-life observational setting.

Methods: 10 patients were enrolled in our center between 2014 and 2019. All patients met the international criteria for BD and had severe arterial involvement evaluated by echocardiography, angio-Computerized Tomography scan and vascular Doppler. The diagnosis of refractory arterio-BD was based on objective vascular symptoms not explained by any other known disease and non-response to conventional immunosuppressants combined with glucocorticoids therapy. All patients underwent TCZ infusions at 8mg/kg every 4 weeks. Concomitant therapy with immunosuppressants and glucocorticoids was continued. Clinical and imaging findings were assessed before and after TCZ therapy. All adverse events were recorded during follow-up.

Results: All the patients were males, with a mean age of 44.3±10.5 years in this study. The mean age at presentation of arterial involvement was 40.8±9.2 years old. The patterns of arterial involvement were aneurysm (n=9), stenosis (n=3) and aortic valve lesion (n=2). After a mean follow-up of 26.8±7.2 months, TCZ yielded rapid and maintained clinical improvement in 9 patients, with complete remission in 6 of them and partial response in 3 of them. Discontinuation of TCZ treatment due to relapse occurred in one case as the enlargement of abdominal aortic aneurysm. The mean glucocorticoid dosage was tapered from 54.5±20.6mg/d to 8.3±3.6mg/d ($p<0.001$). And the use of immunosuppressants was tapered in 4 (40.0%) patients. As for serological improvement, the median ESR and CRP levels decreased from 50 (2-82) mm/h and 32.9 (2.1-62.3) mg/dL to 4 (1-10) mm/h ($p<0.001$) and 2.9 (0.2-12.1) mg/dL ($p<0.001$), respectively. Radiologic improvement of artery lesion was demonstrated in 4(40%) patients. None of the patients had serious adverse events during follow-up.

Conclusion: TCZ was a safe and effective therapeutic option for refractory arterial involvement of BD, with a favorable steroid-sparing effect.

REFERENCES:

[1] G Hatemi, R Christensen, D Bang, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis. 2018;77(6):808-818.

[2] Y Ozguler, P Leccese, R Christensen, et al. Management of major organ involvement of Behcet's syndrome: a systematic review for update of the EULAR recommendations. Rheumatology (Oxford). 2018;57(12):2200-2212.

[3] M Akiyama, Y Kaneko, T Takeuchi. Effectiveness of tocilizumab in Behcet's disease: A systematic literature review. Semin Arthritis Rheum. 2020;50(4):797-804.

Table 1. Tocilizumab therapy in ten cases of refractory arterio-BD

Patient	Age, year	Disease duration, months	Clinical features*	Arterial lesions	Previous therapy	Response at week 24
1	34	228	O, G, P, S, I	Stenosis of CA/ SMA/RA/ SCA, aortic valve prolapse	Pred/CYC/ MMF	CR
2	20	24	O, S	Dissecting aneurysm of AA (Debakey I)	Pred/MMF	PR
3	67	276	O, G, P, S, A	thoracoabdominal aortic aneurysm	Pred/CYC/ TAC	CR
4	67	75	O, S, U	Stenosis of LAD/LCX/RCA	Pred /CYC	CR
5	50	80	O, G, A	Abdominal and coronary aortic aneurysms	Pred /CYC	Relapse
6	48	26	O, G	Aortic insufficiency	Pred /CYC	PR
7	26	147	O, P, S, V	Iliac artery aneurysm	Pred /MMF	CR
8	49	466	O, S, V	Thoracoabdominal and coronary aortic aneurysms	Pred /CYC/ AZA	CR
9	27	181	O, P, S	Pseudoaneurysm of CCA	Pred /CYC	PR
10	Male/55	354	O, P, S	Abdominal aneurysm, stenosis of LAD/LCX/RCA	Pred /CYC/ AZA	CR

*O: oral ulcer; G: genital ulcer; P: pathergy test; S: skin lesions; I: intestinal ulcer; A: arthritis; U: uveitis; V: venous thrombosis

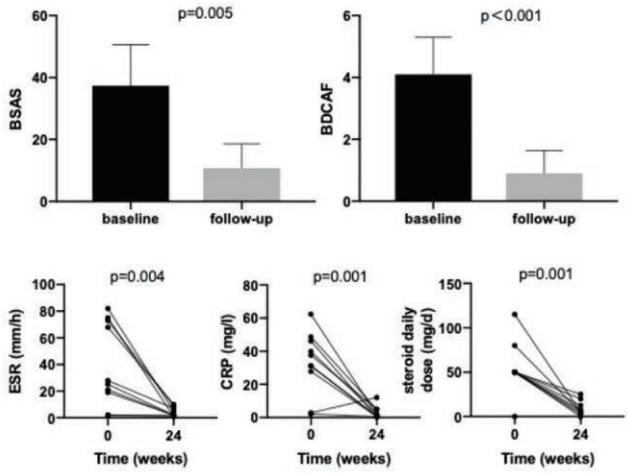


Figure 1. Changes from baseline in BSAS, BDCAF, ESR, CRP and steroid daily dose at 24 weeks

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2302

AB0373 PSYCHOMETRIC PROPERTIES OF OUTCOME MEASUREMENT INSTRUMENTS FOR LARGE VESSEL VASCULITIS: A SYSTEMATIC LITERATURE REVIEW

G. Boleto[1], A. Berti[2], P. A. Merkel[3], S. Aydin[4], H. Direskeneli[5], C. Dejaco[6], L. Carmona[7], S. Ramiro[8,9]. *[1]Université de Paris, Hôpital Cochin, Rheumatology, Paris, France*; *[2]Santa Chiara Regional Hospital and Department of Cellular, Computational and Integrative Biology (CIBIO), University of Trento, Rheumatology, Trento, Italy*; *[3]Vasculitis Clinical Research Consortium; Hospital of the University of Pennsylvania, Rheumatology Division, Philadelphia, United States of America*; *[4]University of Ottawa Faculty of Medicine, Rheumatology, Ottawa, Canada*; *[5]Marmara University, Internal medicine, division of Rheumatology, Istanbul, Turkey*; *[6]Medical University of Graz, Rheumatology, Graz, Austria*; *[7]Instituto de Salud Musculoesquelética (InMusc), Rheumatology, Madrid, Spain*; *[8]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[9]Zuyderland Medical Center, Rheumatology, Heerlen, Netherlands*

Background: Giant cell arteritis (GCA) and Takayasu arteritis (TAK) are two forms of chronic progressive large-vessel vasculitis (LVV) of unknown etiology. In 2016, the OMERACT Vasculitis Working Group proposed the development of a Core Domain Set of outcome measures for LVV including organ and arterial function, fatigue, pain, biomarkers, and death (1). Understanding the psychometric properties of outcome measurement instruments is essential when selecting among instruments to use in research; a summary of such properties for measures of LVV has not been developed.

Objectives: To systematically review and summarize the psychometric properties of outcome measurement instruments used to measure the domains of the OMERACT core domain set for LVV.

Methods: A comprehensive search of several databases (Medline, EMBASE, Cochrane, among others) from inception to July 14, 2020 was conducted. Articles were included if they covered psychometric properties of instruments used in LVV. Following the COSMIN and OMERACT frameworks, different psychometric properties (validity, inter- and intra-observer reliability, sensitivity to change, and feasibility) of outcome measurement instruments used in LVV (GCA and TAK) were assessed. Risk of bias was assessed according to the COSMIN checklist.

Results: Among the 3534 articles identified, 15 studies focusing on the development or validation of psychometric properties on LVV met the predefined criteria. Two were development studies and 13 were validation studies. These studies provided information on 13 instruments: 5 instruments specific to TAK, 2 specific to systemic vasculitides, and 6 general, non-disease-specific instruments. No instruments specific to GCA were identified.

Of the main psychometric properties assessed in the included studies, 40% had a low, 47% had moderate, and 13% had high risk of bias. Construct validity was the property most frequently assessed (in 93% of the tools) (Figure 1).

In TAK, the Indian Takayasu Clinical Activity Score 2010 (ITAS2010) showed good consistency (r=0.97), reliability (intra-observer, ICC=0.60; inter-observer, ICC=0.92) and validity (correlation with Physician Global Assessment (PGA) (r=0.73)) for disease activity. Regarding disease damage, the Disease Extent Index-Takayasu (DEI-Tak) showed good validity (correlation with NIH score 94%, k=0.85). Non-specific vasculitis instruments such as the Vasculitis Damage Index (VDI) and the Birmingham Vasculitis Activity Score (BVAS) showed moderate validity in the assessment of disease damage in GCA (cumulative glucocorticoid dose and disease duration, r=0.30 and r=0.29) and TAK (cumulative glucocorticoid dose and disease duration, r=0.29 and r=0.25) in the former and disease activity in GCA in the later (PGA, r=0.50).

Six non-vasculitis-specific patient-reported outcomes (PROs) instruments were identified, all showing low to moderate validity in GCA/TAK.

Psychometric properties among 13 outcomes instruments developed and/or validated for largel-vessel vasculitis

DOMAIN	INSTRUMENTS	VALIDITY				RELIABILITY			FEASIBILITY	RESPONSIVENESS
		FACE	CONTENT	CONSTRUCT	CRITERION	INTERNAL CONSISTENCY	INTRA-OBSERVER	INTER-OBSERVER		
Disease activity	ITAS2010	✓		✓		✓	✓	✓	✓	✓
	ITAS A	✓					✓	✓	✓	✓
	BVAS	✓		✓					✓	
Disease activity and damage	DEI Tak	✓		✓						
	Kerr et al NIH	✓							✓	
Disease damage	VDI	✓		✓						
	TADS	✓		✓						
Patient-reported outcomes	BIPQ			✓						
	ADVS			✓						
	SF-36			✓	✓	✓				
	VCM1			✓						
	PtGA			✓					✓	
	MFI			✓						

Abbreviations: ITAS2010=Indian Takayasu Activity Score 2010; ITAS A=Indian Takayasu Activity Score A;, DEI Tak=Disease Extent Index Takayasu;, VDI=Vasculitis Damage Index; BVAS=Birmingham Vasculitis Activity Score; TADS=Takayasu Arteritis Damage Score; BIPQ=Brief Illness Perception Questionnaire; ADVS=Activities of Daily Vision Scale; SF-36=Medical Outcomes Study Short-Form 36; VCM1=Vision Core Measurement 1; PtGA: Patient Global assessment; MFI=Multidimensional Fatigue Inventory.

Conclusion: The psychometric properties of 13 outcome measures to study LVV covering the OMERACT domains of disease activity, damage, and patient-reported outcomes were assessed. ITAS2010, DEI-Tak, VDI, and BVAS were the instruments with better psychometric properties for disease activity and/or damage. Disease activity and/or damage instruments specific for GCA, and validated PROs for both GCA and TAK are needed.

REFERENCES:

[1] Sreih GA, Alibaz-Oner F, Kermani TA, Aydin SZ, Cronholm PF, Davis T, et al. Development of a Core Set of Outcome Measures for Large-vessel Vasculitis: Report from OMERACT 2016 | The Journal of Rheumatology [Internet]. [cité 26 avr 2020]. Disponible sur: http://www.jrheum.org/content/44/12/1933.long

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2304

AB0374 CHARACTERISTICS OF A GIANT CELL ARTERITIS COHORT IN LATINOAMERICA

T. Urrego Callejas[1,2], D. Álvarez[3], D. Jaramillo Arroyave[4,5], A. L. Vanegas-García[2,6], C. Muñoz[2,3,5]on behalf of Grupo de Reumatología de la Universidad de Antioquia. *[1]Universidad de Antioquia, Facultad de Medicina, Medellín, Colombia*; *[2]Universidad de Antioquia, Grupo de Reumatología Universidad de Antioquia, Medellín, Colombia*; *[3]Hospital San Vicente Fundación, Internal Medicine, Rionegro, Colombia*; *[4]Grupo de Epidemiología, Universidad CES,*

Epidemiología, Medellín, Colombia; [5]*IPS Universitaria Servicios de Salud Universidad de Antioquia, Rheumatology, Medellín, Colombia*; [6]*Hospital San Vicente Fundación, Rheumatology, Medellín, Colombia*

Background: Giant cell arteritis (GCA) is a large vessel vasculitis (LVV) that affects mostly the elderly (1). Temporal artery biopsy (TAB) has been defined as the gold standard, although this has come to question (3). EULAR guidelines recommended non-invasive imaging techniques such as the temporal artery Doppler ultrasound to aid in LVV diagnosis (2). The characterization of GCA in Latin American countries, and specifically in Colombia, is scarce.

Objectives: To perform a clinical, demographical, histopathological, and radiological characterization of
Colombian GCA patients.

Methods: Retrospective data from GCA patients at two teaching hospitals in Medellín, Colombia, was collected. A bioethics committee previously approved the research protocol. Inclusion criteria: diagnosis of GCA, based on clinical characteristics or imaging/biopsy findings. Exclusion criteria: HIV diagnosis, paraneoplastic large vessel vasculitis. Clinical, radiological, and histopathological variables were selected based on the clinicians' expertise and the 2018 EULAR recommendations for a core data set to support observational research and clinical care in giant cell arteritis (3). The data were analyzed in SPSS v22.0 (IBM, USA).

Results: Twenty-two patients were collected. Demographical and clinical characteristics are summarized in Table 1. Most patients were women (68.1%), with a mean age of 71.8 years, mean duration of symptoms of 5.3 months. In the cranial form of the disease, the most common symptoms were headache and jaw claudication (95% and 68%). Six patients experienced visual loss: complete unilateral visual loss in two, partial unilateral in two, complete bilateral in one, and partial bilateral in one patient.

Sixteen patients (72.7%) underwent TAB; the most common finding was mononuclear infiltrate and internal elastic fragmentation in 43.7% of the biopsies. Giant cells were observed in 6 biopsies (37.5%). Doppler ultrasound was performed in 19 patients (86.35%), finding intima-media thickening and the halo sign t in 7 patients (36.8%).

Table 1. Demographical and clinical characteristics

Characteristic	n = 22
Mean age (years SD)	71.8 (10.6)
Female sex n (%)	15 (68.1%)
Mean symptoms duration (months ± SD)	5.3 ± 6.8
Mestizo n (%)	20 (90%)
Headache n (%)	21 (95.4%)
Jaw claudication n (%)	15 (68.1%)
Weight loss n (%)	13 (59%)
Scalp sensitivity n (%)	11 (50%)
Fever n (%)	8 (36.3%)
Presence of polymyalgia rheumatica n (%)	7 (31.8%)
Visual loss n (%)	6 (27.2%)
Amaurosis fugax n (%)	1 (4.5%)
Glucocorticoids n (%)	22 (100%)
Pulse n (%)	8 (36.3%)
Mean dose (mg ± SD)	47.1 ± 16.7
Methotrexate n (%)	17 (77.7%)
Azathioprine n (%)	2 (9%)
Tocilizumab n (%)	1 (4.5%)

Conclusion: In this GCA cohort, the main phenotype was cranial GCA, with 95% of the patients presenting with headache. The most common imaging study performed was Doppler ultrasound of temporal arteries, with intima-media thickening and halo sign being the most common findings. The mainstay of treatment was glucocorticoids with methotrexate as a sparing agent. To our knowledge, this study is the first to perform a specific characterization of GCA patients in the Colombian population, and it can represent the foundation of further research for these patients.

REFERENCES:

[1] Lazarewicz K, Watson P. Giant cell arteritis. BMJ. 2019 May 30;365:l1964.
[2] Dejaco C, Ramiro S, Duftner C, Besson FL, Bley TA, Blockmans D, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheum Dis. 2018 May;77(5):636–43.
[3] Ehlers L, Askling J, Bijlsma HWJ, Cid MC, Cutolo M, Dasgupta B, et al. 2018 EULAR recommendations for a core data set to support observational research and clinical care in giant cell arteritis. Ann Rheum Dis. 2019;78(9):1160–6.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2436

AB0375

EXTERNAL VALIDATION OF THE GIANT CELL ARTERITIS PROBABILITY SCORE IN THE NETHERLANDS

L. M. Neuman[1], M. Van Nieuwland[1], M. Vermeer[2], D. Boumans[1], E. Colin[1], C. Alves[1]. [1]*Hospital Group Twente, Rheumatology and Clinical Immunology, Almelo, Netherlands*; [2]*Hospital Group Twente, ZGT Academy, Almelo, Netherlands*

Background: Severe complications of giant cell arteritis (GCA), such as blindness and ischemic stroke, can be prevented by timely treatment. This requires early and accurate diagnosis. In 2019, Laskou et al. developed a clinical GCA probability score (GCAPS) that allows physicians to assess the probability of GCA at initial assessment. The GCAPS is suitable for easy implementation in daily practice. It has a high sensitivity (95.7%) and specificity (86.7%) at a cut-off value of 9.5 as proposed by Laskou et al.

Objectives: The aim of this study was to externally validate the GCAPS in a general hospital.

Methods: A retrospective cohort of patients with suspected GCA between January 1st 2017 and October 1st 2019 at Ziekenhuisgroep Twente (the Netherlands) was used. As the parameter extra-cranial artery abnormality was not available in our cohort, a modified version of the GCAPS was used (m-GCAPS). The m-GCAPS was compared to clinical diagnosis of a rheumatologist after six months in accordance with Laskou et al. The validity of the m-GCAPS was assessed by plotting a receiver operating characteristic (ROC) curve and assessing sensitivity and specificity for multiple cut-off values. For practical purposes, risk stratifications as proposed by Sebastian et al. (2020) were applied to our data (low-risk <9; intermediate-risk 9-12; high-risk >12).

Results: In our cohort, 40 GCA patients and 95 controls (suspected of GCA) had complete records and were therefore used for analysis. In the patient group, 29 (72.5%) were female and mean (SD) age was 73.3 (1.6). The area under the ROC curve (AUC) was 0.83 (95% CI 0.75 – 0.91). At our optimal cut-off value of 10.5, sensitivity was 80.0% and specificity was 75.8%. In total, 5 patients and 45 controls were stratified as low, 7 patients and 35 controls as intermediate and 28 patients and 15 controls as high-risk.

Conclusion: The m-GCAPS showed good discrimination in our cohort. Risk stratification of patients looks promising, although cut-off values by Sebastian et al. might need optimization based on population and modification to the GCAPS. Colour Doppler ultrasound is recommended by EULAR as the first-choice diagnostic test to confirm GCA in case of high pre-test probability and exclude GCA for low pre-test probability. The (m-)GCAPS may aid in quantification of this pre-test probability.

REFERENCES:

[1] Laskou F, Coath F, Mackie SL et al. A probability score to aid the diagnosis of suspected giant cell arteritis. Clin Exp Rheumatol. 2019;37 Suppl 1(2):104–8.
[2] Sebastian A, Tomelleri A, Kayani A et al. Probability-based algorithm using ultrasound and additional tests for suspected GCA in a fast-track clinic. RMD Open. 2020 Sep 1;6(3):e001297.
[3] Dejaco C, Ramiro S, Duftner C et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheum Dis. 2018 May 1;77(5):636 LP – 643.

Table 1. Cut-off values of the m-GCAPS stratified into risk categories as proposed by Sebastian et al. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) and the number of patients scoring above or below the cut-off values are described (optimal cut-off value in blue). The total number of patients with a score within low- (red), intermediate- (orange) and high- (green) risk categories are depicted.

	GCA+ (N) N=40	GCA- (N) N=95	Score m-GCAPS		GCA+ (N)	GCA- (N)	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)
Low-risk <9	**5 (12.5%)**	**45 (47.4%)**	5.5	<5.5	0	14	100	14.7	33.1	100
				>5.5	40	81				
			8.5	<8.5	5	45	87.5	47.4	41.2	90
				>8.5	35	50				
Intermediate-risk	**7 (17.5%)**	**35 (36.8%)**	9.5	<9.5	8	56	80	58.9	45.1	87.5
				>9.5	32	39				
9-12			*10.5*	*<10.5*	*8*	*72*	*80*	*75.8*	*58.2*	*90*
				>10.5	*32*	*23*				
			11.5	<11.5	10	74	75	77.9	58.8	88.1
				>11.5	30	21				
High-risk >9	**28 (70.0%)**	**15 (15.8%)**	12.5	<12.5	12	80	70	84.2	65.1	87
				>12.5	28	15				
			14.5	<14.5	18	89	55	93.7	78.6	83.2
				>14.5	22	6				
			19.5	<19.5	37	95	7.5	100	100	72
				>19.5	3	0				

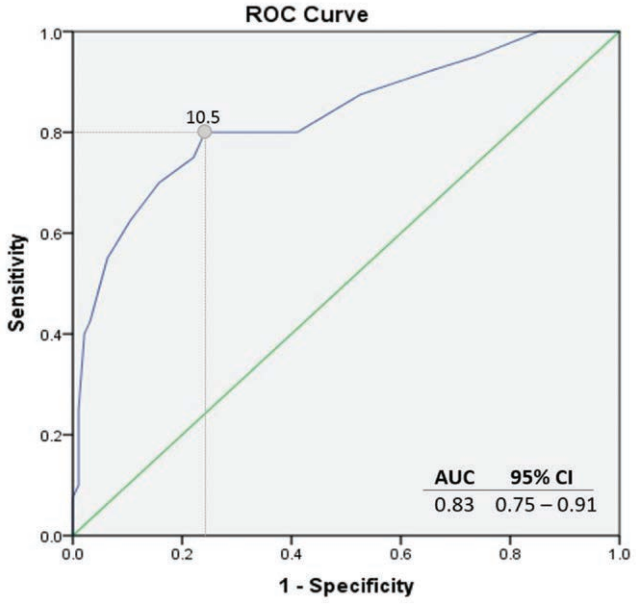


Figure 1. ROC curve depicting sensitivity and (1-) specificity. The AUC was 0.83 (95.0% CI 0.75-0.91) with an optimal cut-off value of 10.5 (sensitivity 80.0%, specificity 75.8%).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2466

AB0376

LEVEL OF DIAGNOSTIC AND THERAPEUTIC KNOWLEDGE, SKILLS AND COMPETENCIES IN GIANT CELL ARTERITIS AMONG EMERGENCY MEDICAL STAFF

C. Guillén-Astete[1], I. Perea-Fuentes[2], L. Ayala-Terrados[2], N. García-Montes[3]. *[1]Hospital Ramón y Cajal, Rheumatology, MADRID, Spain*; *[2]CEU San Pablo, Medicine, Madrid, Spain*; *[3]Hospital Ramón y Cajal, Emergency, Madrid, Spain*

Background: Giant cell arteritis (GCA) is the most frequently diagnosed vasculitis in Spain. The highest incidence recorded in the country is 17 new cases per 100,000 inhabitants/year. Its delayed diagnosis exposes the patient to an increased risk of multiple ischaemic complications. Among them, vision loss has been reported in up to 1 in 6 cases. Most of these patients, according to unpublished local observations, presented with headache, visual disturbances or polymyalgic symptoms to an emergency department facility and were not correctly or prompted diagnosed.
Objectives: To determine the level of knowledge, skills and diagnostic and therapeutic competencies of the medical staff of multiple emergency departments in our city in regard to giant cell arteritis.
Methods: We designed an observational study based on a single survey carried out between February and March 2020 to medical staff from 12 emergency departments in the city of Madrid. Four private and eight public emergency departments were deliberately included. The selection of the surveyed staff was randomly selected to reach 50% of the total number of physicians in each department. A total of 229 surveys were distributed by e-mail. A total of 125 physicians responded (final response rate 54.5%). Twenty-two physicians (9.2%) did not respond to the request and the rest declined to participate, although they responded to the demographic section (35.8%).
The survey included the following sections: respondent profile, knowledge of epidemiological aspects, identification of clinical manifestations, diagnostic and therapeutic skills, and educational interest.
Results: Forty respondents (33.6%) worked in a privately managed emergency department and 79 (66.4%) in a public centre.The mean age of respondents was 37.3 SD 5.9 years, and the proportion of women was 62.4%. Mean length of service was 3.4 SD 1.2 years among physicians in private emergency departments and 5.7 SD 2.3 in a public management unit. Sixty-four respondents (53.7%) were specialists in Family and Community Medicine, and 46 (38.6%) in internal medicine. No significant differences in demographic characteristics were identified between respondents who agreed to participate and those who declined.
In regard to epidemiological knowledge, 50.6% of respondents were unable to identify the age group at highest risk of GCA, 32.7% did not recognise its predominance in the female sex, and 26% did not know the approximate incidence of the disease.
In terms of diagnostic suspicion, 46.2% of respondents were able to identify at least five clinical manifestations of the disease. Elevated ESR, CRP and the presence of anaemia were recognised as positive analytical data by 98.3%, 85.7% and 57.7% of respondents, respectively. Ultrasonography of temporal arteries was identified by 97.5% of respondents as a useful diagnostic technique.
One hundred and two respondents (81.6%) indicated that they had not suspected GCA in the last month. In the last year, 34 respondents (27.2%) reported having diagnosed the disease on at least one occasion. Regarding treatment, in cases of absence of ischaemic lesion 85.7% indicated suboptimal corticosteroid therapy guidelines, however, 63.0% of the respondents self-rated their therapeutic skills as very good or excellent.
Finally, 88.2% of respondents expressed interest in participating in training programmes in diagnosis and treatment of GCA.
Conclusion: There are important areas for improvement in knowledge, diagnostic skills and therapeutic competencies among emergency physicians in relation to the suspicion and management of GCA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2815

AB0377

CLINICAL REVIEW OF 19 CASES WITH IDIOPATHIC AORTITIS – A SINGLE CENTRE STUDY

M. J. Villar[1], S. Sangle[2], D. D'cruz[2]. *[1]Clinica Alemana, Reumatología, Vitacura, Chile*; *[2] Guys and St Thomas' Hospital NHS Foundation Trust, Louise Coote Lupus Unit, London, United Kingdom*

Background: Aortitis is a group of disorders leading to inflammation in the aorta. When aortitis has no clinical evidence of systemic vasculitis, it is called idiopathic aortitis or clinically isolated aortitis (CIA).
There is no consensus on the management of CIA.
Objectives: Our purpose is to describe our cohort of patients with CIA and their response to treatment.
Methods: This is a retrospective analysis of 19 patients with CIA. All records of patients with CIA were analyzed and demographic variables, comorbidities, symptoms, images, histology, treatment
received, outcome and mortality were recorded. The description of quantitative variables was made using the median and the interquartile range (IQR).
Results: Nineteen patients were analyzed. Diagnosis was made by imaging in 18 (94.7%), one patient was diagnosed by histology after aortic root surgery. Patient characteristics are detailed in Table 1.
The median duration of follow- up was 38 months (IQR 43). Seven patients (36.8%) had constitutional symptoms including fever, weight loss, sweats and fatigue. 4 (21.05%) presented with back or abdominal pain for a mean duration of 3 months (SD 0.81) before the diagnosis. In 8 (42.1%) patients the diagnosis was made incidentally.
All patients had negative treponema, hepatitis B, hepatitis C and Human Immunodeficiency Virus (HIV) serology.
All patients had negative autoimmune serology included ANCA. Interestingly 4 (21.05%) had positive lupus anticoagulant without other manifestation of antiphospholipid syndrome.
The type of aortic involvement was aortitis in 10 patients (52.6%), inflammatory aneurysm in 8 (42.1%) and dissection in 1 (5.2%).
Seven (36.8%) patients had thoracic and abdominal aorta involvement, 6 (31.5%) only thoracic aorta and 6 (31.5%) only abdominal aorta.
Aortic histology was obtained in 5 patients, 2 had necrotizing arteritis with giant cell pattern and 2 had lymphoplasmacytic pattern. Temporal artery biopsy was done in one patient and the result was negative for GCA.
All patients received corticosteroids as a remission inducing agent, 12 (63.1%) received methotrexate and 2 (10.5%) mycophenolate. 2 patients died (10.5%).
The median prednisone dose at the beginning was 20 mg (IQR 20) and at remission was 5 mg (IQR 20). 41.6% (5/12) of patients treated with steroids plus methotrexate were able to stop steroids without reactivation over a median follow-up time of 23.5 months (IQR 31). (Table 2.)
Details of treatment, ESR and CRP pre and post treatment is shown in Figure 1.
Seven patients (36.8%) had follow-up imaging, none of them showed active inflammation, new aneurysm, dissection or disease progression.
Conclusion: Treatment of isolated aortitis with steroids and methotrexate was effective resulting in clinical and laboratory improvement and allowed cessation or decrease in steroids to 5 mg or less in 83% of patients. This therapeutic approach may be useful in patients with CIA.

Table 1. Characteristic of the patients.

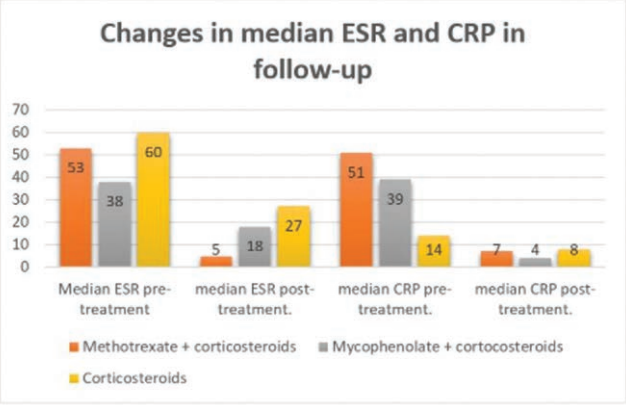
Nº Patients		19
Female		6 (31.5%)
Male		13 (68.4%)
Age median		64 (IQR18)
Ethnicity	Black	4 (21.05%)
	Caucasian	15 (78.9%)
Comorbidities		
Diabetes mellitus type 2		2 (10.5%)
Hypertension		12 (63.1%)
Obesity		5 (26.3%)
Hypercholesterolemia		9 (47.3%)
Smoker		6 (31.5%)
Nº (%) patients with prednisone ≤ 5 mg at end of follow-up according to treatment received		
Only steroids (5)		1(20%)
Steroids + methotrexate (12)		10 (83.3%)
Steroids + mycophenolate (2)		1 (50%)

REFERENCES:

[1] Cinar, I., Wang, H., & Stone, J. R. (2017). *Clinically isolated aortitis: pitfalls, progress, and possibilities. Cardiovascular Pathology, 29, 23–32.*

Disclosure of Interests: None declared

Figure 1.



DOI: 10.1136/annrheumdis-2021-eular.3373

AB0378 UTILITY AND ACCURACY OF SOUTHEND PRETEST PROBABILITY SCORE IN GCA FAST-TRACK CLINIC: ANALYSIS IN 261 CONSECUTIVE PATIENTS

J. Ortega[1], I. Monjo[2], E. Fernández-Fernández[2], E. De Miguel[1,2]. *[1]Universidad Autónoma Madrid, Rheumatology, Madrid, Spain*; *[2]Universitary Hospital La Paz, Rheumatology, Madrid, Spain*

Background: Strategies for early diagnosis of Giant Cell Arteritis (GCA) have been implemented in the last decade in order to reduce the occurrence of blindness, ischemic events and other manifestations of the disease. The Southend pretest probability score (SPTPS) [1] seem to be useful in stratifying and select the referral patients sent to the GCA fast-track clinics.

Objectives: The aim of this study was to test the validity and utility of this score in our patients.

Methods: Retrospective available data records of all the patients referred to our GCA fast-track clinic in the last three years were collected. The clinical and laboratory features at referral were evaluated, and the SPTPS was generated. All patients had ultrasound of cranial and large vessel examination (axillary, subclavian and carotid arteries). GCA diagnosis was confirmed by the doctor after at least six months of follow-up. Quartile frequencies, ROC curves and accuracy of the SPTPS was calculated.

Results: 261 patients (180 females) with suspicions of GCA were evaluated in our fast-track clinic. Mean age (±SD) was 76±9.2 years, and C-reactive protein 75.7±68.6 mg/l. The time since the first symptoms was less of 6, 6-12, 12-24 or >24 weeks in 37.5%, 19.9, 12.3 and 15.7 respectively. Mean SPTPS was 11.4±4.4, with values of 9.1±3.2 and 12.9±4.4. The area under the ROC curve was 0.761 (95% confidence interval: 0.703-0.819). PTPS overall showed a 50th percentile score of 11 and a 75th percentile score of 14. We, therefore, classified "Low Risk" (LR) as SPTPS <11, "Intermediate Risk" (IR) 11–14 and "High Risk" (HR) >14. Of 261 referrals, 156 had GCA with cases categorised as LR (119), IR (91) and HR (51). HR score showed a specificity of 96.2% and in IR the specificity ranged between 86.7 and 94.3% (Table 1). Score below 7 appears in 29 cases with only 8 cases of GCA with a probability of GCA < 5%, more of these cases was associated a large vessel vasculitis: 3 cranial arteritis (CA), 4 large vessel vasculitis (LVV) and 1 mixed pattern (MP). LR score included 72 of the 105 (68.6%) non-GCA cases but 47 of 156 (30.1%) GCA patients (20 CA, 11 LVV and 16 MP). IR risk score included 26 (24.8%) of the non-GCA cases and 65 (41.7%) of GCA patients (31 CA, 13 LVV and 21 MP). Finally HR score had only 7 non-GCA cases and 44 (28.2%) patients with GCA (20 CA, 11 LVV and 13 MP). Mean score in cranial forms was 13.1±4.5 and in large vessel vasculitis 12.8±5.0 (p=0.807).

Table 1. Sensitivity and Specificity of SPTPS at different cut-off points

Cut-off point	Sensitivity	1-Specificity
2	1.000	1.000
3.5	0.994	0.971
4.5	0.987	0.943
5.5	0.987	0.876
6.5	0.949	0.790
7.5	0.897	0.676
8.5	0.846	0.476
9.5	0.750	0.362
10.5	0.679	0.248
11.5	0.538	0.133
12.5	0.449	0.086
13.5	0.353	0.057
14.5	0.218	0.038
15.5	0.147	0.019
16.5	0.128	0.019
17.5	0.077	0.010
19	0.038	0,000
20.5	0.032	0,000
21.5	0.019	0,000
22.5	0.013	0,000
24	0.000	0,000

Conclusion: The SPTPS is helpful to stratified patients sent to the fast-track clinic. Scores below of 7 points has a very low probability to have GCA. The diagnostic probability increases directly with the score. There were minor differences without statistical significance between cranial or large vessel vasculitis patterns in the score.

REFERENCES:

[1] Sebastian A, Tomelleri A, Kayani A, Prieto-Pena D, Ranasinghe C, Dasgupta B. Probability-based algorithm using ultrasound and additional tests for suspected GCA in a fast-track clinic. RMD Open. 2020 Sep;6(3):e001297. doi: 10.1136/rmdopen-2020-001297. PMID: 32994361; PMCID: PMC7547539.

Disclosure of Interests: Javier Ortega: None declared, Irene Monjo Speakers bureau: Roche, Novartis, UCB, Gedeon Richter, Consultant of: Roche, Elisa Fernández-Fernández: None declared, Eugenio de Miguel Speakers bureau: AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi., Paid instructor for: Janssen, Novartis, Roche, Consultant of: AbbVie, Novartis, Pfizer, Galapagos, Grant/research support from: Abbvie, Novartis, Pfizer

DOI: 10.1136/annrheumdis-2021-eular.3385

AB0379 BARICITINIB IN POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS: REPORT OF SIX CASES

D. Camellino[1], C. Dejaco[2,3], A. Giusti[1], F. Martini[4], R. Cosso[5], G. Girasole[1], G. Bianchi[1]. *[1]Local Health Trust 3, Genoa, Division of Rheumatology, Department of Medical Specialties, Genoa, Italy*; *[2]Medical University Graz, Department of Rheumatology, Graz, Austria*; *[3]Hospital of Bruneck (ASAA-SABES), Department of Rheumatology, Bruneck, Italy*; *[4]Local Health Trust 1, Medical Department, Sanremo, Italy*; *[5]Local Health Trust, 3, Medical Department, Genoa, Italy*

Background: Glucocorticoids (GC) are the cornerstone of the treatment of polymyalgia rheumatica (PMR) and giant cell arteritis (GCA), but they are associated with several adverse events (AEs). Moreover, a considerable proportion of patients relapse during GC tapering.

Objectives: To describe the efficacy and safety of the JAK-inhibitor baricitinib (BARI) in a group of patients with PMR and/or GCA.

Methods: Case series of patients with PMR and/or GCA with a refractory disease course, despite several lines of therapy, including methotrexate (MTX) and tocilizumab (TCZ), started treatment with BARI. All patients underwent periodic, standardised clinical and laboratory examinations, and also FDG-PET/CT. PMR-activity score (AS) was calculated at each visit except in patients with isolated large vessel vasculitis (LVV) or GCA.

Results: A total of six patients (five females and one male, median age 64 years, range 50-83) were treated with BARI. Two of them had isolated PMR (patients #1 and #6), two had PMR with associated LVV (patients #2 and #5), and one (patient #3) had cranial-GCA. Demographic and clinical characteristics are provided in Table 1. At the time of starting BARI, patients were taking a median prednisone dose of 8.75 mg/day (range 0-25), and the 4 patients with PMR±LVV had a median PMR-activity score (PMR-AS) of 23.3 (indicating high disease activity), which decreased to 1.58 after 6 months of treatment with BARI. Two of them could stop GC and continued BARI monotherapy (in one case, BARI was tapered down to 2 mg/day after 12 months).

After starting BARI, patient #3 (GCA) could gradually taper prednisone from 25 mg/day to 10 mg/day in six months, without reporting fever or headache. After one year of treatment, she feels well while taking prednisone 7.5 mg/day.

Patient #4 (LVV) remained clinically stable during the treatment with BARI, but a follow-up FDG-PET/CT showed LVV, and we decided to stop BARI and restart TCZ. After 4 months of treatment with BARI, patient #5 suffered from pneumonia, while she was also taking prednisone 15 mg/day. BARI was therefore stopped. No other AEs attributable to BARI were detected.

Conclusion: BARI appears as an appealing option for treating patients with PMR and/or GCA. Although these preliminary results should be confirmed by a RCT, BARI lowered rapidly disease activity and exerted a significant steroid-sparing effect, allowing GC withdrawal in 2 out of 6 patients.

Table 1. Demographic and clinical characteristics of patients.

Patient #	Sex	Age	Diagnosis	Previous treatment	Disease duration (months)	PMR-AS
1	F	66	PMR	MTX, HCQ, SSZ	25.5	40.5
2	F	78	PMR+LVV	TCZ, MTX	41.8	28.8
3	F	61	GCA	CYC, MMF, TCZ	119.8	N/A
4	F	60	LVV	TCZ	16.4	N/A
5	F	83	PMR+LVV	MTX, TCZ	24.4	15.2
6	M	50	PMR	MTX	24.6	17.8

CYC: cyclophosphamide, GCA: giant cell arteritis, HCQ: hydroxychloroquine, LVV: large vessel vasculitis, MMF: mycophenolate mofetil, MTX: methotrexate, N/A: not applicable, PMR: polymyalgia rheumatica, PMR-AS: PMR-activity score, SSZ: sulfasalazine, TCZ: tocilizumab.

Disclosure of Interests: Dario Camellino Speakers bureau: Medac, Eli Lilly, Paid instructor for: Mylan, Consultant of: Accord, Celgene, Novartis, Sanofi, Christian Dejaco Speakers bureau: Eli Lilly (<10.000€), Andrea Giusti Speakers bureau: UCB, Amgen, Kyowa Kirin, Abiogen Pharma, and Eli Lilly, Consultant of: EffRx, Abiogen Pharma, FRANCO MARTINI: None declared, Renzo Cosso: None declared, Giuseppe Girasole: None declared, Gerolamo Bianchi Speakers bureau: Amgen, MSD, Novartis, Pfizer, Roche, Sanofi, Genzyme, and Servier, Consultant of: Abbvie, Abiogen Pharma, BMS, Celgene, Eli Lilly, GSK, Janssen-Cilag, Medac

DOI: 10.1136/annrheumdis-2021-eular.3435

AB0380

MACHINE LEARNING CAN PREDICT GIANT CELL ARTERITIS RELAPSE AFTER GLUCOCORTICOID TAPERING

V. Venerito[1], G. Emmi[2], L. Cantarini[3], N. Lascaro[4], M. Fornaro[1], O. Angelini[5], L. Coladonato[1], F. Cacciapaglia[1], P. Leccese[4], G. Lopalco[1], F. Iannone[1].
[1]University of Bari Aldo Moro, Department of Emergency and Organ Transplantations - Rheumatology Unit, Bari, Italy; *[2] University of Firenze, Department of Experimental and Clinical Medicine, Firenze, Italy*; *[3]University of Siena, Research Center of Systemic Autoinflammatory Diseases and Behçet's Disease Clinic, Siena, Italy*; *[4] San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, Rheumatology Institute of Lucania (IRel) and the Rheumatology Department of Lucania, Potenza, Italy*; *[5]Amazon Research Center, Amazon Research Center, Cambridge, United Kingdom*

Background: To date reliable biomarkers and risk factors for relapsing giant cell arteris (GCA) after glucocorticoid (GC) tapering are still lacking.

In an increasing number of social and clinical scenarios, machine learning (ML) is emerging as a promising tool for the implementation of complex multi-parametric decision algorithms. A ML approach allows to handle complex non-linear relationships between patient attributes that are hard to model with traditional statistical methods, merging them to output a forecast or a probability for a given outcome.

Objectives: To assess whether ML algorithms can predict GCA relapse after glucocorticoid tapering.

Methods: GC-naïve GCA patients who presented to 4 tertiary care centers between January 2015 and January 2019, who underwent GC therapy and regular follow up visits for at least 12 months were retrospectively analyzed and used for training and validation (through 10-fold cross-validation) of n.2 ML algorithms, namely Decision Trees (DT) and Random Forest (RF).

Test of the algorithms was carried out GCA patients referred to the same centers from March 2019 to September 2020 whose data was longitudinally recorded during the 12 months after presentation.

Demographic, clinical an laboratory characteristics (Erythrocyte Sedimentation Rate (ESR) and C Reactive Protein (CRP) levels) were gathered.

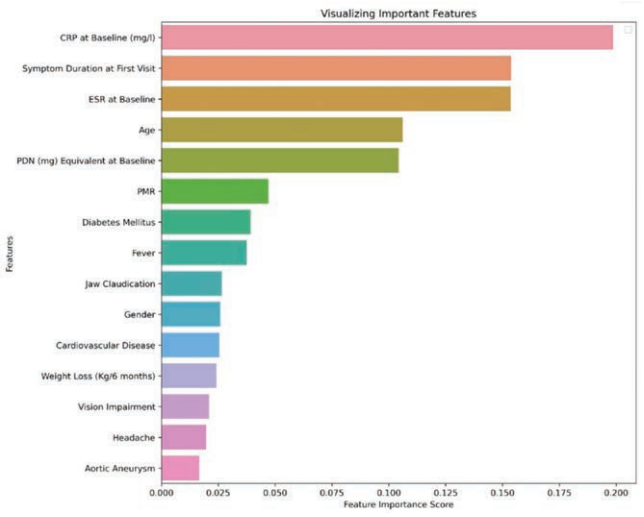
The outcome of interest was the GCA relapse within 12 months after induction of remission, during GC tapering.

The accuracy of the algorithms in both validation and test phases was assessed.

Results: The training and validation dataset consisted of n.85 GCA patients (59 female, 69.4%) with mean age 73.8 (±8.7) years at presentation. They were treated with 27.1 (±17.4) mg prednisone (PDN) equivalent at first visit. During GC tapering 34 of them (40%) experienced a disease relapse within 12 months. The test dataset consisted of n.22 patients (14 female, 63.4%) with mean age 75.5 (±8.7) years at presentation, who underwent GC induction therapy with a mean dose of 30.3 (±17.3) mg PDN equivalent. Nine of them (40.9%) had a GCA flare during GC tapering, within 12 months. Accuracy of DT and RF in predicting the outcome of interest on the training dataset was 68.3% and 73.4% respectively. On testing datasets DT and RF accuracy was 57.1 and 72.4%, respectively.

As shown in Figure 1, the most important patient attributes for RF forecast were found to be CRP and ESR baseline levels as well as age and symptom duration (months) at first visit.

Conclusion: RF algorithm can predict GCA relapse after glucocorticoid tapering with fairly good accuracy. To date this is one of the most accurate predictive modeling for such outcome. This ML method represents a reproducible tool executable on computers as well as mobile devices and capable of supporting clinicians in GCA patient management.



REFERENCES:

[1] Hellmich B., Agueda A., Monti S., *et al.* 2018 Update of the EULAR recommendations for the management of large vessel vasculitis *Annals of the Rheumatic Diseases* 2020;79:19-30.

[2] Venerito, V., Angelini, O., Cazzato, G. *et al.* A convolutional neural network with transfer learning for automatic discrimination between low and high-grade synovitis: a pilot study. *Internal and Emergency Medicine* 2021.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3923

AB0381 **VALIDATING DRAFT DCVAS CRITERIA IN A SINGLE CENTER GCA COHORT IN SOUTHERN NORWAY**

P. Andel[1,2,3], S. Brådland[3], A. Diamandopoulos[4,5], G. Myklebust[3], G. Haugeberg[3,6]. *[1]Østfold Hospital Trust, Department of Cardiology, Kalnes, Norway*; *[2]University of Oslo, Department of Clinical Medicine, Oslo, Norway*; *[3]Hospital of Southern Norway, Department of Rheumatology, Kristiansand, Norway*; *[4]Akershus University Hospital, Department of Rheumatology, Oslo, Norway*; *[5]Martina Hansens Hospital, Department of Rheumatology, Kristiansand, Norway*; *[6]Norwegian University of Science and Technology, Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, Trondheim, Norway*

Background: Giant cell arteritis (GCA) is the most common medium- and large vessel vasculitis in the elderly population. The diagnostic algorithm has changed in recent years in many institutions from temporal artery biopsy (TAB) to imaging based diagnosis (1). However, classification criteria that relied on TAB remained unchanged since 1990 (2). Reflecting the recent change in practice the Diagnostic and Classification Criteria for Vasculitis Study (DCVAS) group presented a draft classification criteria set for GCA. Endorsement by major scientific societies is currently pending (3).

Objectives: To test the accordance of the GCA cohort of a single center in southern Norway between 2006 and 2018 to the draft DCVAS classification criteria in GCA.

Methods: All patients diagnosed with GCA between 2006 and 2018 in our clinic were identified by international classification of disease (ICD) code for GCA (m31.5/m31.6) in the local electronic database. The draft DCVAS classification criteria were applied to all patients at the time of diagnosis, irrespective of the algorithm used to diagnose GCA. In the draft DCVAS classification criteria a score of 6 would be necessary to classify a patient as having GCA.

Results: A total of 77 patients (55 female) diagnosed with GCA in the defined timespan were identified. Mean age was 69.2 years (57 – 83 years). As all patients were diagnosed with vasculitis and were older than 40 years of age, all patients met the compulsory criteria. The table 1 below shows the absolute number of patients that fulfilled the single criteria.

The number of patients fulfilling the draft DCVAS classification criteria was 75 (97.4%). In the female cohort 96.4% patients finally diagnosed with GCA would be classified as having GCA as would 100% in the male cohort.

Mean score was 12.4 (range 3-25). In 33.3 % of patients imaging was critical for classification. Laboratory findings were critical for classification in 9.3 %, head ache and scalp tenderness in 5.3%, temporal artery biopsy, morning stiffness and jaw claudication in 2.7%. The differentiation in possible and definite vasculitis in TAB did not change the result in any patient. Neither did sight-loss contribute to classify any patient. Five patients (6.5%) were diagnosed on clinical features and laboratory findings alone. Thirteen patients diagnosed with GCA and fulfilling DCVAS criteria had negative biopsies, three patients had an inconclusive TAB. Mean arterial biopsy length was 9 mm.

Table 1.

Draft DCVAS classification criteria		Aboslute number
Age>40 years and vasculitis diagnosis (compulsatory)		77
New temporal headache	+2	48
Scalp tenderness	+2	21
Sudden visual loss	+2	2
Morning stiffness shoulder/neck	+2	34
Jaw claudication	+2	22
ESR > 50 mm/h or CRP > 10 mg/l	+3	72
TAB showing possible vasculitis	+3	8
TAB showing definite vasculitis	+5	16
Halo sign	+5	61
Bilateral axillary involvement	+3	25
PET showing aortitis	+3	4

Conclusion: A high percentage (97.4 %) of the patients diagnosed with GCA in our cohort fulfilled the draft DCVAS classification criteria. The high mean score (12.4) showed that DCVAS criteria did not depend heavily on single criteria. As diagnosis in our cohort was mainly based on ultrasound, imaging was the most critical item. This might be desirable as clinical features and laboratory markers should in general be confirmed by either imaging or TAB to ascertain diagnosis. However, five patients were solely diagnosed on clinical features and laboratory markers. Sight-loss did not contribute to classification in our cohort as most patients were seen in a fast-track clinic (FTC), but might be valuable in cohorts without FTC.

REFERENCES:

[1] Dejaco C et al, Ann Rheum Dis. 2018;77(5):636-643
[2] Hunder GG et al, Arthritis Rheum. 1990 Aug;33(8):1122-8
[3] Merkel PA: oral presentation, *American College of Rheumatology Annual Meeting 2018: October 19-24; 2018*

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4128

AB0382 **DOES THE ULTRASOUND IMAGE OF THE LARGE VESSEL WALLS DIFFER IN THE SUBTYPES OF GCA AND PMR OR THERE IS A SYSTEMIC SUBCLINICAL COMMON INFLAMMATION?**

E. Fernández-Fernández[1], I. González-Mazón[2], I. Monjo[1], J. M. Mostaza[3], C. Lahoz[3], E. De Miguel[1]. *[1]La Paz University Hospital, Rheumatology, Madrid, Spain*; *[2]Marqués de Valdecilla University Hospital, Rheumatology, Santander, Spain*; *[3]Carlos III Hospital, Internal Medicine, Madrid, Spain*

Background: Several clinical patterns of giant cell arteritis (GCA) have been described including cranial GCA (c-GCA), large vessel GCA (LV-GCA), mixed forms of c-GCA and LV-GCA (mixed-GCA), and even polymyalgia rheumatica (PMR) that has been associated with GCA and some degree of subclinical vascular inflammation could be present in the patients. However, many questions about this disease and its subtypes remain unanswered.

Objectives: To investigate the affectation of the arterial wall of GCA and its subtypes and PMR and to know if there really are different ultrasound patterns that can be determined or if otherwise they present a common subclinical systemic inflammation with only different degrees of involvement of the vascular wall.

Methods: All available ultrasound examinations of patients referred to our fast-track GCA clinic for suspected GCA in the last three years were reviewed and retrospectively collected data. Patients who had undergone ultrasound examination of both cranial and large vessels (axillary, subclavian and carotid arteries) were included. The videos and images of the large vessels of each patient were reviewed and intima-media thickness (IMT) and hypoechoic halo measurements were taken. The data of the following groups, established according to the final diagnosis confirmed by the doctor after a follow-up between six months and three years, were compared: GCA group (within it 3 other groups were included: c-GCA, LV-GCA and mixed-GCA), PMR group and the group without ACG or PMR (non-GCA).

Results: We analyzed the examinations of 300 patients and 161 baseline examinations were included: 76 with GCA (32 c-GCA, 14 LV-GCA and 30 mixed-GCA), 29 with PMR and 56 non-GCA. The mean IMT for each large vessel explored and the statistical significance between the different groups

Table 1. Ultrasound IMT and halo measures in the different subtypes of GCA, PMR and controls

Arteries	Non-GCA n=56	GCA n=76	c-GCA n=32	LV-GCA n=14	Mixed-GCA n=30	PMR n=29	p < 0.05
Right axillary (mean ± SD)	0.67±0.19	0.95±0.30	0.75±0.20	1.03±0.33	1.11±0.27	0.65±0.13	2*, 3*, 4*, 5*, 6, 7*, 8*
Left axillary (mean ± SD)	0.61±0.12	0.92±0.29	0.77±0.19	0.99±0.25	1.03±0.33	0.66±0.13	1*, 2*, 3*, 4, 5*, 6, 7*, 8*
Right subclavian (mean ± SD)	0.70±0.15	1.00±0.31	0.79±0.16	1.09±0.36	1.10±0.29	0.70±0.20	2*,3*, 4*, 5*, 7*, 8*
Left Subclavian (mean ± SD)	0.62±0.14	0.95±0.27	0.76±0.16	1.05±0.25	1.06±0.26	0.64±0.18	1*, 2*, 3*, 4*, 5*, 7*, 8*
Right CCD (mean ± SD)	0.79±0.22	0.97±0.26	0.99±0.22	0.91±0.29	1.05±0.28	0.81±0.10	1*, 3*, 6*, 8*
Left CCD (mean ± SD)	0.81±0.16	0.99±0.22	0.95±0.20	0.97±0.17	1.03±0.27	0.82±0.20	1, 2, 3*, 8

SD: Standard deviation; CCD: common distal carotid artery.1=c-GCA vs non-GCA; 2=LV-GCA vs non-GCA; 3=mixed-GCA vs non-GCA; 4=c-GCA vs LV-GCA; 5=c-GCA vs mixed-GCA; 6=PMR vs c-GCA; 7=PMR vs LV-GCA; 8=PMR vs mixed-GCA; *p < 0.01.

are shown in Table 1. All arteries except the carotid arteries had a significantly higher IMT in the LV-GCA and mixed-GCA groups when compared with both c-GCA and non-GCA groups. There were no differences in IMT between mixed-GCA and LV-GCA. There were also no differences in any explored artery between PMR and non-GCA. There were statistically significant differences in the IMT of the bilateral axillary and subclavian arteries between the PMR group and all the GCA subtypes, being greater in the latter. IMT tended to be higher in the c-GCA group when compared to non-GCA, reaching statistical significance in the left arteries (axillary, subclavian, and distal carotid). Although there was also a tendency for IMT to be higher in mixed-GCA patients than in LV-GCA patients, the differences did not reach statistical significance.

Conclusion: Large vessel ultrasound does not differ between healthy patients and those with PMR without confirmed GCA. Our data suggest that mixed-GCA subtype is not an intermediate form between the cranial and LV-GCA suptypes but could have a higher inflammatory burden.

Disclosure of Interests: Elisa Fernández-Fernández: None declared, Iñigo González-Mazón: None declared, Irene Monjo Speakers bureau: Roche, Novartis, UCB, Gedeon Richter, Consultant of: Roche, José María Mostaza: None declared, Carlos Lahoz: None declared, Eugenio de Miguel Speakers bureau: AbbVie, Novartis, Pfizer, MSD, BMS, UCB, Roche, Grunental, Janssen, Sanofi, Paid instructor for: Janssen, Novartis, Roche, Consultant of: AbbVie, Novartis, Pfizer, Galapagos, Grant/research support from: Abbvie, Novartis, Pfizer

DOI: 10.1136/annrheumdis-2021-eular.4134

AB0383 OCULAR MANIFESTATIONS DURING GIANT CELL ARTERITIS

A. Mzabi[1], N. Adaily[1], L. Ines[1], I. Ben Hassine[1], J. Anoun[1], M. Karmani[1], F. Ben Fredj[1], C. Laouani[1]. [1]*University Hospital Center of Sahloul, Internal Medicine, Sousse, Tunisia*

Background: Horton's disease (HD) or giant cell arteritis (GCA) is a segmental and plurifocal giant cell inflammatory panarteritis, predominant in large and medium sized vessels. Ocular damage during giant cell arteritis is frequent and is considered the most serious damage, possibly causing blindness in 15% of cases in recent series (1).
Objectives: Describe the different ophthalmological manifestations during GCA.
Methods: This is a retrospective monocentric descriptive study of 19 files of subjects diagnosed with HD, hospitalized in the internal medicine department of de Sousse between January 2000 and December 2020.
Results: The average age of patients at diagnosis was 70 years, with extremes of 53 and 92 years. There were 14 females (71.4%) and 5 males (28.6%). Ophthalmologic manifestations were present in 13 patients (71%), 6 of whom were female.
Decreased visual acuity was reported in 8 cases (58.33%) with biolateral blindness in one case, visual blur in 9 cases (75%), eye pain in two cases.
Ophthalmological examination was normal in 8 cases (42%). A decrease in visual acuity was objective in 4 cases (21%). One case of nodular episcleritis was noted. The fundus showed anterior ischemic optic neuropathy in 2 cases (10.5%) and left optic atrophy in another case. A visual field was performed in 2 cases showing associated retrobulbar optic neuritis. Therapeutically, Methylprednisolone boli were prescribed in patients with anterior ischemic optic neuropathy, followed by oral corticosteroid therapy at a dose of 1mg/kg/day. A dose of 0.7 mg/kg/day of prednisone was prescribed in the other cases. Blindness was irreversible.
Conclusion: The most common eye diseases in HD are acute anterior ischemic optic neuritis, retinal artery occlusion and posterior ischemic optic neuropathy. Episcleritis is a rare ophthalmologic manifestation of this vasculitis (2). More exceptionally, Horton's disease may cause NORB by affecting the vessels that supply the optic nerve (< 5% of cases)(3,4). In our series of studies, acute anterior ischemic optic neuritis was less observed than in the literature. This is probably due to the reduced number of patients.
REFERENCES:

[1] M.Khedher. I.Rachdi. Z.Aydi. F.Daoud. B.Ben Dhaou. F.Boussema. Eye damage during Horton's disease: about 42 cases. La Revue de Médecine Interne 2017; 38:115.
[2] Rim Klii. Wafa Chebbi. Nodular episcleritis: an unusual inaugural manifestation of Horton's disease. Pan Afr Med J 2015; 21: 20.
[3] M.EssouriI.RachdiF.DaoudZ.AydiH.ZoubeidiB.Ben Dhaou et al. Retrobulbar Optic Neuropathy in Internal Medicine. La Revue de Médecine Interne 2018; 39: 132.
[4] M A González-Gay, C García-Porrúa, J Llorca, A H Hajeer, F Brañas, A Dababneh et al. Visual manifestations of giant cell arteritis. Trends and clinical spectrum in 161 patients. Medicine (Baltimore) 2000;79(5): 283-92.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4143

AB0384 IMPACT OF TEMPORAL ARTERY ULTRASOUND ON SURVIVAL OF PATIENTS WITH GIANT CELL ARTERITIS

P. Estrada[1], D. Reina[1], V. Navarro[1], O. Camacho[1], D. Cerda[1], D. Roig Vilaseca[1], S. Heredia[1], H. Corominas[2]. [1]*Hospital de Sant Joan Despí Moisès Broggi, Rheumatology, Sant Joan Despí, Spain*; [2]*Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*

Background: Giant cell arteritis (GCA) is the most common primary systemic vasculitis in adults over 50 years of age. Its incidence increases with age, with a peak between 70-80 years and predominates in women, 3:1. It is a medical emergency that, if not diagnosed, can lead to irreversible complications. The delay in time from diagnosis to start of treatment is crucial to avoid possible serious outcomes on short, medium and long term. Survival in GCA is estimated between 60-90% at 5 years and 48-81% at 10 years. Efforts have been made to implement rapid diagnostic circuits to assess patients and initiate treatment without delay with good results both in reducing permanent vision loss and in reducing the costs of these patients due to emergency visits and admissions. The morbidity and mortality of this disease is high, but the use of efficient diagnostic strategies, such as ultrasound of superficial temporal arteries, has proven to be a useful, practical, cost-effective and, above all, quick tool to make the diagnostic approach.
Objectives: Analyze the impact of early temporal artery ultrasound on survival for patients with GCA.
Methods: Survival study of 48 patients with GCA, in two different "stages" in terms of diagnostic approach: Group A (n = 27), patients diagnosed between 2002 - 2011 using only ACR 1990 criteria and Group E (n = 21) diagnosed between 2010-2015 using ACR criteria and TAUS. TAUS was performed by Rheumatologists with extensive experience in ultrasound and within a period of no more than 7 days for these patients. The definitive diagnosis of GCA was based on the clinical criteria of the Rheumatologist within the clinical and analytical context and with the specific complementary examinations for each case (Ultrasound, PET-CT, biopsy). Demographic data, comorbidities, signs and symptoms at debut, analytical data, complementary examinations, treatment and evolution were obtained retrospectively through the electronic medical record of the patient, based on the database of our GCA cohort. A survival analysis was performed considering death as the main outcome. The statistic used was the Kaplan-Meier test. In addition, other complications related to treatment or pathology are collected.
Results: The mean age at diagnosis of our patients was 79 + - 6 years, with a female: male ratio of 3: 1. The follow-up was between 2 and 16 years with a mean of 5.8 + - 3 years, until the last visit collected or until the outcome of death. Group A had a survival at 5 and 10 years of 53.4% and 36.7% respectively, while group E of 79.5% at both cut-off points. (Figure 1).
There is a significant difference between the survival of both groups, p <0.01, this being better in the group in which TAUS was implemented for rapid diagnosis (group E). The main causes of death were cardiovascular

events, 30%, predominantly in group E (75%), and infection, 30%, predominantly in group A. The median from diagnosis to death was 3 years (range 1 - 13).

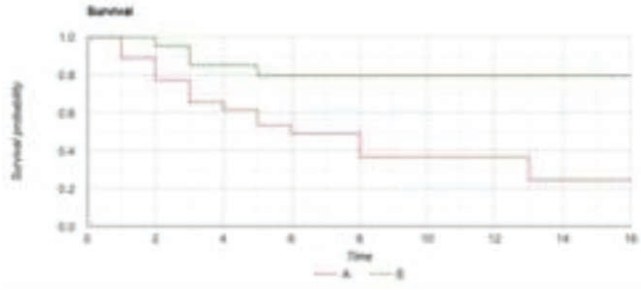


Figure 1. Group A (red line) according to ACG 1990 criteria and Group B (green line) according to ACG criteria and implementing TAUS for rapid diagnosis

Conclusion: The implementation of temporal artery ultrasound (TAUS) is associated with a significant improvement in the survival rate of patients with GCA and a reduction in treatment-related complications in patients who were diagnosed with ultrasound in less than 7 days compared to those diagnosed by the conventional healthcare attention routes.

REFERENCES:

[1] Gonzalez-Gay MA, et al. Giant cell arteritis: epidemiology, diagnosis, and management. DOI: 10.1007/s11926-010-0135-9
[2] Patil P, et al. Fast track pathway reduces sight loss in giant cell arteritis: results of a longitudinal observational cohort study. PMID: 26016758
[3] Breuer GS, et al. Survival of patients with giant cell arteritis: a controversial issue. PMID: 31969222
[4] Diamantopoulos AP, et al. The fast-track ultrasound clinic for early diagnosis of giant cell arteritis significantly reduces permanent visual impairment: towards a more effective strategy to improve clinical outcome in giant cell arteritis? 10.1093/rheumatology/kev289

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4158

Vasculitis – small vessel vasculitis

AB0385

THE EFFECTIVENESS OF THE ANTI-TUMOR NECROSIS FACTOR THERAPY INFLIXIMAB IN NEURO-BEHCET'S DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

R. Hamdy Abdellatif Mohammed[1], Y. Woldeamanuel[2]. [1]*Kasr Alainy School of Medicine- Cairo University., Rheumatology and Rehabitation, Cairo, Egypt*; [2]*Stanford University, Stanford Headache Center, Department of Neurology- Center for Innovation in Global Health- Stanford University School of Medicine: Stanford, CA, US., Stanford-CA, United States of America*

Background: The use and benefit of biologic targeted therapy in the treatment of refractory manifestations of behcet's syndrome remain unclearly defined due to the relative paucity of published research. Neuro-behcet's disease represents a challenging clinical presentation. The lack of identified effective strategies in the management of refractory neuro-behcet's adds to the disease burden and contributes to lack of tight control. [1-3]

Objectives: The aim of this systematic review and meta-analysis is to examine the effect of anti-TNF therapy on refractory NBD by performing a systematic review and meta-analysis of the previously published studies assessing the effectiveness of anti-TNF therapy in patients with BD having refractory or recurrent neurological manifestations.

Methods: Authors used the PICO Model (P= population, I= intervention, C= comparator, O= outcome) used for designing the research question. The PRISMA statement was used for developing the study protocol search methodology. Literature searches were done for articles in published in English language only from January 2000 till January 2020 (considering the first till the last available publication that addresses the research question and satisfied eligibility criteria). The study was registered on the Prospero PROSPERO website for systematic reviews and meta-analysis. Random-effects meta-analysis was performed. Inter-study heterogeneity was explored using I2 statistics. Cumulative meta-analysis was conducted to assess temporal trend for accumulating evidence from accruing published studies. Meta-regression was used to analyze possible confounders.

Authors of the current systematic review and meta-analysis worked on a simple score "Hamdy and Woldeamanuel simple response score, 2020", the aim behind the score was to incorporate standard evaluation parameters for assessment of responses driven by the measures used in each study. The authors used numerical values to grade the pattern of response in each parameter considered attempting to standardize the quantification of the responses and minimize tendency towards overestimation. The score included clinical and radiographic points rated on a scale of 5.

Results: Twenty-one studies involving 64 patients were included, 52 male patient and 12 females at a ratio of 4.3:1, with a mean age of 38 .21 years, mean disease duration of 84.76 5 months. Effect size analysis showed that 59 out of 64 patients i.e. 93.7% of the treated patients with neuro-behcet's disease in the analysis were responders to infliximab therapy (CI 88% - 99.3%). There was no significant inter-study heterogeneity (I2 = 0%, p = 0.744). Cumulative analysis showed accumulating evidence favoring increasing effectiveness over the last 20 years. There was no statistically significant confounding of infliximab effect size by age (p = 0.89), sex ratio (p = 0.29), and disease duration (p = 0.67).

Conclusion: In this systematic review and meta-analysis Infliximab showed a strong therapeutic effectiveness in the treatment of refractory neuro-behcet's disease. There is an increasing trend of effectiveness observed in the last two decades which may be due to improved neuro-behcet's diagnostic accuracy.

REFERENCES:

[1] Uygunoğlu U, Siva A. Behçet's Syndrome and Nervous System Involvement. *Curr Neurol Neurosci Rep*. 2018;18(7):35. Published 2018 May 23. doi:10.1007/s11910-018-0843-5.
[2] Ohno S, Ohguchi M, Hirose S, Matsuda H, Wakisaka A, Aizawa M. Close Association of HLA-Bw51 With Behçet's Disease. *Arch Ophthalmol.* 1982; 100(9):1455–1458. doi:10.1001/archopht.1982.01030040433013.
[3] Kalra, S., Silman, A., Akman-Demir, G., et al. Diagnosis and management of Neuro-Behçet's disease: international consensus recommendations. Journal of neurology, 2014; 261(9): 1662–1676. https://doi.org/10.1007/s00415-013-7209-3.

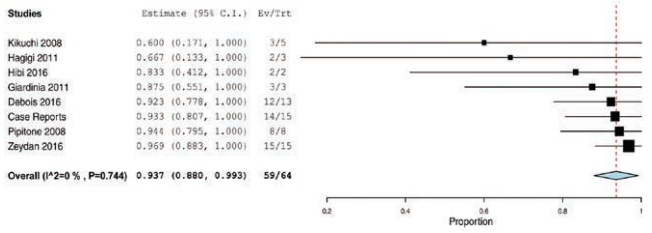


Figure 1 a. Forest plot summarizing the meta-analysis results on the effectiveness of infliximab to treat Neurobehcet disease. Overall, 94% of patients responded to infliximab.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.52

AB0386

CORONAVIRUS INFECTION AND VASCULITIS: IDENTIFYING ASSOCIATIONS MINING THE BIOMEDICAL LITERATURE

A. Rodriguez-Pla[1], R. Cartin-Ceba[2]. [1]*Mayo Clinic Scottsdale Campus, Rheumatology, Scottsdale, United States of America*; [2]*Mayo Clinic Hospital, Pulmonary, Phoenix, United States of America*

Background: Based on recent publications suggesting an association between COVID-19 and vascular
Inflammation.

Objectives: Our aim was to explore new associations between coronavirus infections and vasculitis utilizing semantic mining of PubMed results.

Methods: The following literature search string: "(vasculitis OR vascular inflammation OR vascular damage) AND (coronavirus OR SARS virus OR

MERS-CoV OR Covid-19)" was used to retrieve abstracts from the whole PubMed database, using Semantic MEDLINE 2. on 6/7/2020. This application represents a network of semantic predications (triples of the form subject-predicate-object, e.g. COVID-19 causes Disease) on a knowledge graph. The system allows for choosing the maximum number of nodes represented, the central topic, and the length of the network. For our network we chose to display all relations, COVID-19 (31 edges) as the central term, 3 lengths, and selecting the most informative nodes. Automatic summarization eliminated the less informative predications.

Results: The search string retrieved 152 citations from PubMed and identified 1,028 predications. The

network (Figure 1), displayed using COVID-19 as the central term, consisted of 72 nodes and 140 edges. The 5 most connected nodes were 'Patients: 19 nodes', COVID-19: 13', 'Inflammation: 13', 'Lung: 11', and 'Disease: 11'. Multiple links have been found between coronavirus and vasculitis. Animal coronaviruses, including the one causing feline infectious peritonitis (FIP), the murine coronavirus mouse hepatitis virus (MHV), the SARS-CoV in transgenic mice and coronavirus in ferrets, are known to cause vasculitis in animals. It is known that coronaviruses that infect animals can evolve and become new human coronaviruses. SARS produces inflammation in blood vessels. In 2005, a link between the coronavirus HCoV-NL63 or New Haven Coronavirus (HCoV-NH) and KD was reported,

although later studies concluded that HCoV-NH did not play a dominant role in the etiology or

pathogenesis of KD. In 2014, serological testing suggested the possible involvement of CoV-229E in the development of KD. There has also been a report of KD patients being infected by coronavirus OC43/HKU1.COVID-19 may infect the vessels and trigger inflammatory reactions like those of vasculitis, including vasculitis-like cutaneous lesions. COVID-19 patients develop thrombosis, and increased risk of thrombosis is also present in primary vasculitic syndromes. Children, many of whom tested positive for COVID-19 antibodies, developed Multisystem Inflammatory Syndrome in Children (MIS-C), an inflammatory condition similar to Kawasaki Disease (KD).

Conclusion: Knowledge integration and discovery methods are an efficient and powerful way of retrieving and analyzing relevan information from multiple papers. Their main advantages are finding relations among biomedical concepts, generating new hypotheses, and opening them to literature-based discovery.

SARS-CoV-2 may cause vasculitis or vasculitis-like syndromes. The KD-like syndrome reported mainly in children with COVID-19 revives the previous suspicion of coronavirus as a possible triggering agent of KD and the decades-old hypothesis of infection involvement in the pathogenesis of vasculitis.

REFERENCES:

[1] Rindflesch TC,et al. Semantic MEDLINE: An advanced information management application for biomedicine. Information Services & Use 2011;31:15-21.

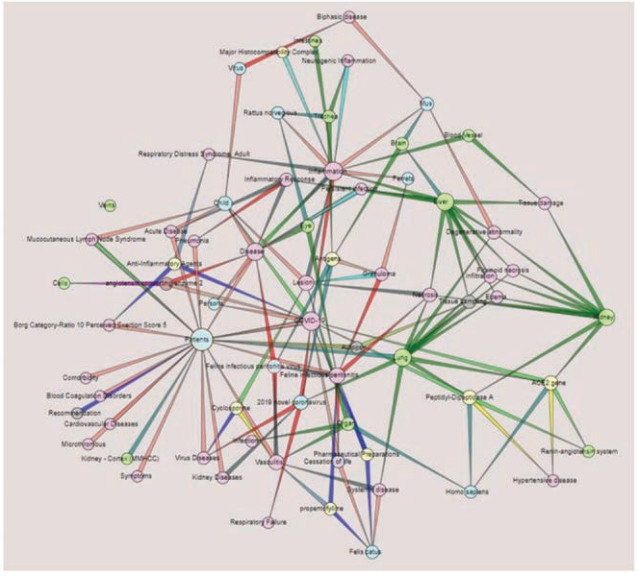


Figure 1. Semantic Networks Resulting from Pubmed. All relations COVID-19 (edges:140) 3 lengths Max nodes: F (all nodes considered relevant).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.329

AB0387

SYSTEMIC AND LOCAL THERAPIES FOR EAR, NOSE AND THROAT MANIFESTATIONS IN ANCA-ASSOCIATED VASCULITIS: A SYSTEMATIC REVIEW

R. Krol[1], R. Klaasen[2], H. H. F. Remmelts[3], M. W. Heijstek[1], J. Spierings[1]. [1]*UMC Utrecht, Rheumatology and Clinical Immunology, Utrecht, Netherlands*; [2]*Meander Medical Center, Rheumatology, Amersfoort, Netherlands*; [3]*Meander Medical Center, Nephrology, Amersfoort, Netherlands*

Background: Ear, nose and throat (ENT)-involvement is common in antineutrophil cytoplasmic autoantibody- (ANCA-)associated vasculitis (AAV), can lead to permanent damage and is correlated with reduced quality of life. Yet, guidelines on management of ENT-manifestations are lacking.

Objectives: The aim of this study was to evaluate the efficacy of systemic and local therapies for ENT- involvement in AAV.

Methods: A systematic review was conducted. Clinical studies between January 2005 – April 2020, in adults with AAV and ENT-involvement using outcomes reflecting disease activity, relapse and damage were included. Case reports, congress abstracts and non-English articles were excluded.

Results: The search yielded 4,586 results. For full-text assessment, 109 articles were selected. Finally, 25 articles were included (Figure 1). Two placebo-controlled trials were available. The other observational studies had a limited level of evidence (LoE) of 2b-4 according to the Oxford Centre for Evidence-based Medicine.

Ten studies (n=127) with subglottic stenosis evaluated dilatation (n=94), intralesional steroids (n=63), surgery (n=51) or rituximab (n=8), which mostly resulted in temporary response (12-34 months) (Table 1). Otologic manifestations were treated with various disease modifying anti-rheumatic drugs (DMARDs) in 251 patients in six studies. All studies demonstrated improvement in hearing thresholds, but relapse rates were high (47%). Five studies assessed DMARDs or surgery for sinonasal symptoms showing remission in 21-82%. Six studies, which did not specify ENT-symptoms of the included patients, reported remission in 86-96%. Due to heterogeneity across studies no meta-analysis could be performed.

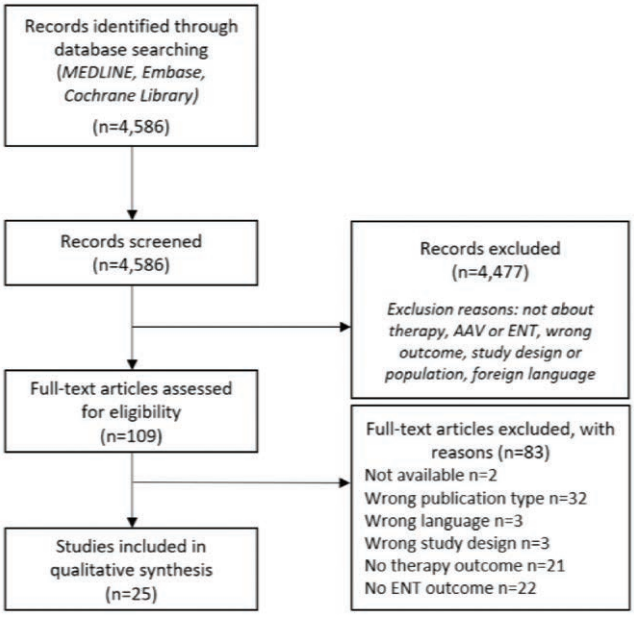


Figure 1. Flowchart of article selection

Table 1. Overview of studies on treatment for ENT-involvement.

ENT-involvement	AAV type per study	Therapy	Results	LoE
Otitis Media / Hearing loss	OMAAV (n=6)	RTX	Remission 100% Mean hearing gain AC 22 dB BC 11 dB	2b
	OMAAV (n=104)	Steroids	Response (hearing) 56% Relapse 47%	4
	OMAAV (n=122)	Steroids + csDMARD	Relapse 36%	4
	OMAAV (n=8) GPA (n=11)		Response (hearing) 68% Relapse 0% Response (hearing) 81% Response (hearing) 100%	4
Vestibular symptoms	OMAAV (n=3)	Steroids + CYC	Remission (patient-reported) 100%	4
Subglottic stenosis	GPA (n=9)	Dilatation	Relapse 78%	4
	GPA (n=15)		Mean number of procedures 4	
	GPA (n=34)	Intralesional steroids + dilatation	Median response 34 months	2b
	GPA (n=8)		Response 88% Median response 12 months Mean number of procedures 3	4
	GPA (n=18)	Intralesional steroids + dilatation + resection	Mean intervention-free interval 26 months	2b
	GPA (n=5)	Dilatation + resection	Response 80%	4
	GPA (n=13)	Surgery	Response (dyspnea) 100% Relapse 39%	4
	GPA (n=11)		Higher QoL 77% Response (airway) 91%	4
	GPA (n=6)	Surgery or dilatation + intralesional steroids or csDMARDs	Relapse 83.3%	4
	GPA (n=8)	RTX	Remission 38% Response 50%	2b
Sinonasal symptoms	GPA (n=3)	RTX	Response: 67%	2b
	EGPA (n=29)	Steroids + csDMARDs	Remission 82%	2b
	EGPA (n=44)		Remission 21% Response 32%	2b
	GPA (n=19)	Surgery	Response 76%	4
	EGPA (n=65)	Mepolizumab	Remission 28%	1b
ENT symptoms NOS	AAV (n=7)	RTX	Relapse 22%	2b
	GPA (n=11)		Drop in daily steroid dosage	
	EGPA (n=61)		Drop in daily steroid dosage Response 93% Relapse 17%	4 2b
	GPA (n=28) EGPA (n=15)	Steroids + csDMARDs	Remission 96% Relapse 42%	4
	GPA (n=51)	RTX (n=51) MTX	Remission 86% 92% of observational period in remission 54%	4 2b

AC: air-conduction, BC: bone-conduction, csDMARD: conventional synthetic disease modifying antirheumatic drug, CYC: cyclophosphamide, dB: decibel, EGPA: eosinophilic GPA, GPA: granulomatosis with polyangiitis, MTX: methotrexate, NOS: not otherwise specified, OMAAV: otitis media associated ANCA-vasculitis, QoL: quality of life, RTX: rituximab.

Conclusion: On the treatment of ENT manifestations in AAV 25 studies were available, mainly with small patient numbers and low LoE (1b-4). Heterogeneity in treatments and outcome measures impaired comparison between studies. More placebo-controlled studies are needed to guide treatment.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.678

AB0388 USE OF MESNA PROPHYLAXIS IN CYCLOPHOSPHAMIDE-TREATED PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: RESULTS OF AN ELECTRONIC SURVEY

L. Joos[1], S. Gonzalez Chiappe[1], T. Neumann[1], A. Mahr[1]. [1]*Kantonsspital St.Gallen, Division of Rheumatology, St. Gallen, Switzerland*

Background: Co-prescribing 2-mercaptoethane sodium sulfonate (mesna) with cyclophosphamide (CYC) for ANCA-associated vasculitis (AAV) aims to prevent the potential urotoxic effects of CYC. The evidence for this practice is often considered weak, and there may be some diversity in what practitioners do in clinical practice.
Objectives: To investigate current clinical practice related to prescribing mesna prophylaxis or not and the underlying rationale for CYC-treated patients with AAV.
Methods: We searched MEDLINE for publications with the MeSH term "ANCA-associated vasculitis" over a 10-year period up to October 2020. Email addresses of authors of these publications were extracted from the online information available in MEDLINE. These authors were invited by email to participate in an anonymous online SurveyMonkey survey of 21 to 24 questions asking about the characteristics of the respondent, their experience with AAV, and their practice in using CYC to treat AAV and using mesna in CYC-treated patients with AAV and the underlying rationale. Respondents were eligible to take the full survey if they were involved in deciding and/or monitoring therapy with CYC for patients with AAV. We compared 15 response variables to identify factors associated with the use or not of mesna. Response variables with multiple categories were first analyzed across all categories; if the omnibus test result was significant, additional analyses were used to identify the categories, which were the sources of group separation. We analyzed by-country variations for only countries with ≥ 10 respondents. Statistical analyses involved Pearson's chi-square test or Fisher's exact test, as appropriate. For multiple-response variables, the Rao-Scott correction was applied.
Results: The invitation for the electronic survey was emailed twice in October 2020 to 1,374 unique email addresses; 156 individuals responded; 139 were eligible and completed the survey. The 139 participants were from 34 countries and were essentially MDs (98%) who mainly worked in rheumatology (50%), nephrology (25%) or internal medicine/clinical immunology (18%). Mesna was given in conjunction with CYC systematically, never, or on a case-by-case basis by 68%, 19% and 13% of respondents, respectively. As compared with systematic mesna-prescribers, never/occasional mesna-prescribers reported a longer time since receiving their degree as a health professional (≥ 15 years: 80% vs 50%, P<0.001), were more frequently based in England/United States (than in France/Germany/Italy) (78% vs 21%, P<0.001), had longer involvement in care of patients with AAV (≥ 15 years: 62% vs 37%, P=0.006), had less practice in using intermittent pulse therapy as the exclusive/predominant CYC administration scheme (62% vs 89%, P<0.001), and, as a rationale underpinning their mesna practice, had less adherence to local operational procedures (47% vs 73%, P=0.002) or (inter)national management guidelines for AAV (16% vs 49%, P<0.001). Never/occasional versus systematic use of mesna did not differ across medical specialties (5 categories, P=0.192) or healthcare settings (3 categories, P=0.437), and was not associated with prior experience of CYC-related urotoxic events (3 categories, P=0.495) or severe mesna toxicity issues (3 categories, P=0.957). The confidence that their practice reflected the best possible patient care did not differ between never/occasional and systematic mesna-prescribers (7-point Likert scale, P=0.794).
Conclusion: Practice with regard to prescribing mesna in conjunction with CYC to treat AAV is heterogeneous, although systematic mesna use prevailed over never or occasional use. The decision to prescribe or not mesna may be based more on circumstantial than structural reasons.
Disclosure of Interests: Lukas Joos: None declared, Solange Gonzalez Chiappe: None declared, Thomas Neumann Speakers bureau: GSK, Grant/research support from: Xifor, Alfred Mahr Speakers bureau: Amgen, Celgene, Roche, Chugai, Consultant of: Amgen, Celgene, Roche, Chugai
DOI: 10.1136/annrheumdis-2021-eular.1034

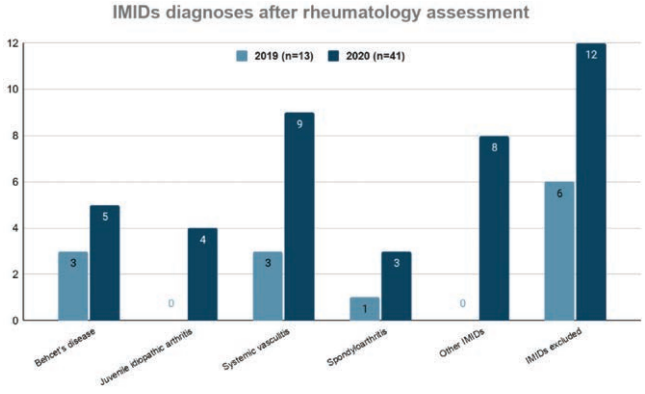
AB0389 A COMBINED RHEUMATOLOGY-OPHTHALMOLOGY CLINIC IMPROVED DIAGNOSIS AND TREATMENT OF IMMUNE-MEDIATED AND INFLAMMATORY DISEASES AMONG PATIENTS PRESENTING WITH INFLAMMATORY EYE DISEASES

A. Giollo[1], F. Bosello[2], A. Bonora[2], M. Rossini[1]. [1]*University of Verona, Rheumatology Section, Department of Medicine, Verona, Italy*; [2]*University of Verona, Ophthalmology Clinic, Department of Neurosciences, Biomedicine and Movement Sciences, Verona, Italy*

Background: Patients presenting with an inflammatory eye disease may have underlying immune-mediated and inflammatory diseases (IMIDs). However, IMIDs are challenging to diagnose. A combined rheumatology-ophthalmology evaluation could enhance detection of IMIDs in this group.
Objectives: To investigate whether the implementation of a combined rheumatology-ophthalmology clinic could increase the sensibility of IMIDs diagnosis.
Methods: A combined rheumatology-ophthalmology clinic started in January 2020. A rheumatologist with expertise in IMIDs assessed outpatients of a tertiary care ophthalmologic clinic specialised in inflammatory eye disease consecutively referred between 01/01/20 and 31/12/20. Two separate visits confirmed

both ophthalmology and rheumatology diagnoses. The same period of the year 2019 was used as a comparator.

Results: We noticed a three-fold increase in the number of ophthalmology patients who underwent an evaluation with a rheumatologist in 2020 compared to 2019 (41 vs 13, +315%; Table). There were no differences in sex distribution or age between the two years. However, the median time before rheumatology assessment was shorter in 2020 than 2019 (median days 0 [range 0-6] vs 12 [range 0-91]). IMIDs diagnoses increased by 27% in 2020 compared to 2019 (29/41 vs 7/13, 71% vs 54%), mainly driven by new diagnoses of systemic vasculitis and Behcet's disease (Figure 1). There was also an increase in diagnoses of non-IMIDs systemic conditions (3 cancers and one infection in 2020 vs none in 2019). After rheumatology evaluation, immune-modulating therapy was initiated in 18/41 (44%) vs 3/13 (23%).



Ophthalmology assessment and referrals to rheumatology	Referrals 2019 (n=13)	Referrals 2020 (n=41)
Inflammatory eye disease, n (%)	6 (46)	36 (88)
Uveitis, n	6	21
Vasculitis, n	2	4
AION, n	3	5
Conjunctivitis, n	1	0
Scleritis, episcleritis, n	0	1
Other, n	1	5

Conclusion: An integrated approach with rheumatologist appeared to remarkably increase the likelihood to detect IMIDs among patients presenting with inflammatory eye diseases.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1046

AB0390

CHARACTERISTICS AND PROGNOSIS OF AGE-DEPENDED ANCA-ASSOCIATED VASCULITIS IN JAPAN

M. Kato[1], T. Kameda[1], H. Shimada[1], S. Nakashima[1], M. Mahmoud Fahmy Mansour[1], R. Wakiya[1], T. Miyagi[1], K. Sugihara[1], Y. Ushio[1], R. Senba[1], M. Mizusaki[1], H. Dobashi[1]. [1]*Kagawa University, Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Kagawa, Japan*

Background: It is known that most of ANCA-associated vasculitis (AAV) patients are elderly. A cohort study showed that the mean age of onset was 71.1 years, especially in patients with microscopic polyangiitis (MPA)[1)]. However, the characteristics and prognosis of age-depended AAV patients are still unclear.

Objectives: To clarify the differences in age-related characteristics and prognosis between Japanese patients with AAV.

Methods: We enrolled 44 patients with AAV who underwent remission induction therapy at our hospital from January 2016 to December 2020. They were divided with under 70 years old group (<70 yo group, n=12) and over 70 years old group (≥70 yo group, n=32). We investigated between two groups as follows; clinical characteristics and laboratory data at diagnosis, rates of complete remission (CR) at 6 months, defined as Birmingham Vasculitis Activity Score (BVAS)=0 and prednisone ≤7.5 mg/day, adverse events, and relapse free survival.

Results: Mean age were 61.9 ± 9.74 years old in <70 yo group and 77.5 ± 4.61 years old in ≥70 yo group (p<0.01). There were significantly fewer newly diagnosed cases in the <70 yo group, and half of the patients with relapsing disease. There was no difference in the type of ANCA, organ involvement, or BVAS. Remission induction therapy was performed with CY or RTX, and no difference was observed between these two groups. In addition, there was also no difference in maintenance therapy (Table 1). CR rate in <70 yo group and in ≥70 yo group were 55% and 46 % respectively (p=0.73). Severe infections occurred with no patient (0%) in <70 yo group and with 5 patients (16%) in ≥70 yo group (p=0.30). 5 patients of relapse were observed in the <70 yo group and 1 patient in the ≥70 yo group, and relapse free survival was significantly lower in the <70 yo group (p=0.001) (Figure 1).

Table 1. Clinical characteristics at baseline and treatment drugs between <70 yo group and ≥70 yo group.

	<70 yo 群 (n=12)	≥70 yo 群 (n=32)	p value
Age (year)	61.9 ± 9.74	77.5 ± 4.61	< 0.01*
Female, n (%)	10 (83)	28 (87)	0.66
AAV type	6 (50) / 6 (50)	26 (81) / 6 (19)	0.06
MPA, n (%) / GPA, n (%)			
Newly diagnosed, n (%)	6 (50)	27 (84)	0.045*
ANCA positivity			
MPO, n (%) / PR3, n (%)	11 (92) / 0 (0)	30 (94) / 3 (9)	1 / 0.55
negative, n (%)	1 (8)	1 (3)	0.48
CRP (mg/dl)	3.34 ± 4.01	8.15 ± 6.86	0.03*
eGFR (mL/min)	55.8 ± 25.3	57.7 ± 24.7	0.93
BVAS	12.0 ± 8.0	14.8 ± 6.8	0.23
Remission induction therapy	5 (42) / 7 (58)	16 (50) / 16 (50)	0.74
CY, n (%) / RTX, n (%)			
Maintenance therapy			
AZA, n (%)	7 (58)	14 (44)	0.50
RTX, n (%)	1 (8)	6 (19)	0.65
others, n (%)	2 (17)	3 (9)	0.60
without IS, n (%)	2 (17)	9 (28)	0.70

The p-value was estimated using Fisher's exact or Wilcoxson rank sum test. yo, years old; AAV, ANCA-associated vasculitis; MPA, microscopic polyangiitis; GPA, granulomatosis with polyangiitis; CY, cyclophosphamide; RTX, rituximab; AZA, azathioprine; IS, immunosuppressants. *p<0.05

Conclusion: There was no difference in remission rate between two groups. Severe infections were observed only in the ≥70 yo group. We suggest that younger AAV patients need attention to relapse after the remission because of lower relapse free survival in <70 yo group.

REFERENCES:

[1] Sada KE, et al. Arthritis Res Ther 2014; 16: R101.

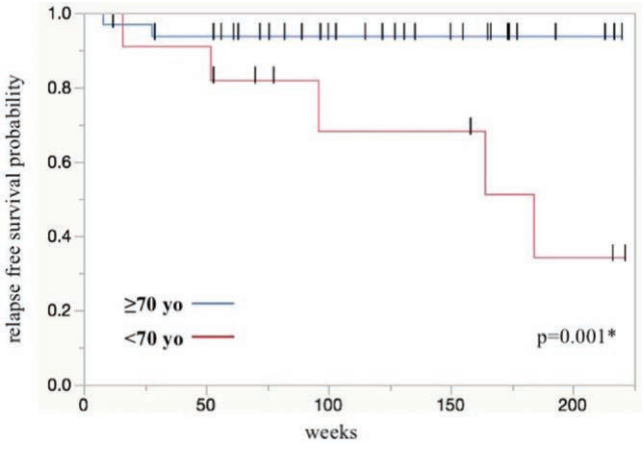


Figure 1. Relapse free survivalRelapse free survival was calculated by Kaplan-Meier method and compared by log-rank test. *p<0.05

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1367

AB0391

LOW SERUM COMPLEMENT C3 LEVEL AS A RISK FACTOR FOR RELAPSE OF ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS: A RETROSPECTIVE COHORT STUDY

H. Sakai[1], H. Yamashita[1], S. Nakajima[1], Y. Takahashi[1], H. Kaneko[1]. [1]*National Center for Global Health and Medicine, Division of Rheumatic Diseases, Tokyo, Japan*

Background: The alternative pathway of complement activation has recently been recognized as a key pathogenic event in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Some previous studies have reported that low serum complement C3 level in AAV patients is associated with more severe renal disease, worse renal prognosis, or higher mortality. However, the correlation between low serum C3 level and AAV relapse remains unclear.
Objectives: To analyze the clinical characteristics and outcomes of AAV patients with low serum C3 levels at the time of diagnosis.
Methods: We conducted a retrospective observational cohort study including 83 consecutive patients diagnosed with AAV in our hospital from January 1999 to December 2020. Serum C3 levels were measured at diagnosis. AAV included microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA); patients with ANCA-negative AAV were excluded. Patients were divided into low- and high-C3 groups (C3 < 100 and ≥ 100 mg/dL, respectively). We compared the clinical characteristics, and relapse-free and overall survival rates, of the two groups, and identified predictors of AAV relapse.
Results: Of the 83 patients (MPA, n = 61; GPA, n = 18; EGPA, n = 4), 20 (24%) were in the low-C3 group. We found no significant group difference in sex, body mass index, disease type, ANCA subtype, Birmingham Vasculitis Activity Score (BVAS), or treatment. The low-C3 group patients were older (p=0.01), and had a higher Five Factor Score (FFS) (p=0.01) and a lower remission rate (p=0.02), than the high-C3 group. The generalized Wilcoxon test revealed that the relapse-free survival time was significantly shorter in the low-C3 group (29 months; 95% confidence interval [CI]: 15–49) than in the high-C3 group (82 months; 95% CI: 61–NA; p=0.01) (Figure 1A). The overall survival was also shorter in the low-C3 group (83 months; 95% CI: 8-121) than in the high-C3 group (112 months; 95% CI: 77-NA; p=0.03) (Figure 1B). In the Cox proportional hazards model, a low C3 level (< 100 mg/dL) (hazard ratio [HR], 3.01; 95% CI: 1.29–7.04], p=0.01) and GPA (HR, 3.04; 95% CI: 1.32–7.01; p=0.01) were independent predictors of AAV relapse.

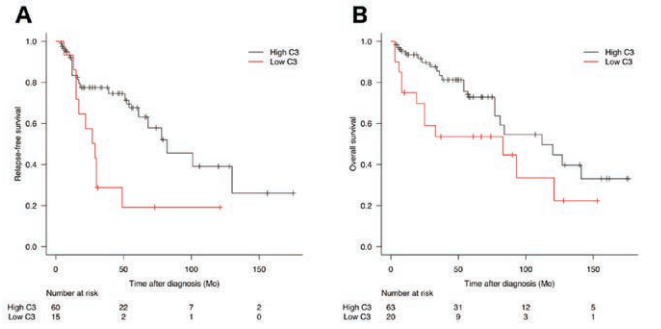


Figure 1. Kaplan-Meier estimates of the relapse-free (A) and overall (B) survival rates of AAV patients by baseline serum C3 levels. Eight patients who did not show remission were excluded in the relapse-free survival analysis. Black line: high-C3 group (≥ 100 mg/dL); red line: low-C3 group (< 100 mg/dL).

Conclusion: AAV patients with low C3 levels at diagnosis were at higher risk of relapse. Larger prospective studies are required to confirm these findings.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1517

AB0392

PRELIMINARY VALIDATION OF THE ITALIAN VERSION OF ANCA-ASSOCIATED VASCULITIS PATIENT-REPORTED OUTCOME (AAV-PRO_ITA) QUESTIONNAIRE: FATIGUE AND CHRONIC PAIN AS UNMET NEEDS BY CURRENT TREATMENTS

E. Treppo[1], A. Palese[2], S. De Vita[1], L. Quartuccio[1]. [1]*University of Udine, Rheumatology Clinic, Udine, Italy*; [2]*School of Nursing, University of Udine, Department of Medicine, Udine, Italy*

Background: The ANCA-associated vasculitis patient-reported outcome (AAV-PRO) questionnaire is a 29-item disease-specific PRO measure for AAV (1), proving to be valid, reliable, feasible, and able to discriminate among disease states.
Objectives: The purpose of this study is to validate the Italian version of AAV-PRO questionnaire (AAV-PRO_ita).
Methods: AAV-PRO has been translated in collaboration with Oxford and Bristol University (UK). Then, consecutive Italian-speaking AAV-patients were collected in order to validate the questionnaire. Inclusion criteria are AAV diagnosis (ANCA positivity at least one time and/or biopsy-proven AAV), and age ≥18 years old. Participants completed the AAV-PRO_ita three different times: at baseline, after 5-7 days, and at month 3. Friedman test was applied to verify internal consistency of the questionnaire over time.
Results: 27 AAV-patients (16 females, 11 males) were recruited and completed the questionnaire at baseline, after 5-7 days, and at month 3. The main diagnosis was granulomatosis with polyangioitis (GPA) (19/27, 70.4%), following by eosinophilic granulomatosis with polyangioitis (EGPA) (8/27, 29.6%). Mean (SD) BVASv3 was 1 (2) at baseline, and it was unchanged at month 3 in 25/27 (92.6%). The mean age at onset of disease was 54.7±17.3 years and the median disease duration was 51 months (1-3 interquartile range 34-76). Their history was characterized by at least one relapse in 10/27 (37%) patients, at least one hospitalization due to AAV in 19/27 (70.4%), and ESRD in 1/27 (3.7%). At the last follow up, 24/27 (88.9%) of patients were taking an immunosuppressive drug [rituximab (8/24), azathioprine (8/24), methotrexate (7/24) or mycophenolate mofetil (1/24)] and more than two-thirds were also taking glucocorticoids (19/27, 70.3%). Fatigue (item 9) and arthralgia (item 6) were the most important symptoms, and half of the patients (14/27, 51.9%) classified them as "moderate" or "severe". Nearly one-third of patients (8/27, 29.6%) admitted to being "usually" or "always" concerned about their future (item 19) and long-term therapy (item 29) (Figure 1). Friedman test was not significant (p>0.05), indicating internal consistency of the questionnaire. A large multicentre Italian study has been organized based on this preliminary data coming from the coordinating centre, and it is now recruiting. The results will be soon available by the Italian Vasculitis Study Group.
Conclusion: The AAV-PRO_ita is a new disease-specific PRO measure for AAV. It is a self-administered questionnaire and could become an important tool to evaluate health-related quality of life in AAV (2). As in other systemic autoimmune diseases, fatigue and chronic pain represent an unmet need to be addressed by future treatment strategies.
REFERENCES:
[1] J. C. Robson *et al.*, «Validation of the ANCA-associated vasculitis patient-reported outcomes (AAV-PRO) questionnaire», *Ann. Rheum. Dis.*, 2018, vol. 77, n. 8, p. 1157–1164, doi: 10.1136/annrheumdis-2017-212713.
[2] L. Quartuccio, *et al.,* «Healthcare and economic burden of ANCA-associated vasculitis in Italy: an integrated analysis from clinical and administrative databases», *Intern Emerg Med*, July 2020, doi: 10.1007/s11739-020-02431-y.

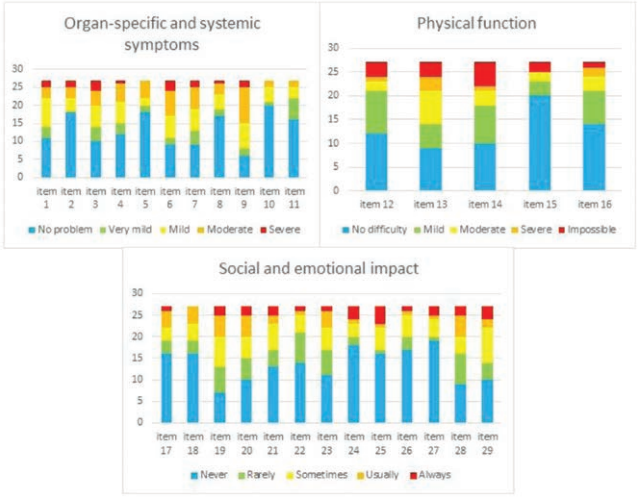


Figure 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2123

AB0393

PRE-EXISTING MORBIDITY AS A RISK FACTORS FOR MORTALITY IN IgA VASCULITIS

J. Nossent[1,2], D. Preen[3], W. Raymond[1], H. Keen[3,4], C. Inderjeeth[1,2]. [1]*The University of Western Australia, Medical School, Rheumatology Section, Perth, Australia*; [2]*Sir Charles Gairdner Hospital, Rheumatology, Nedlands, Australia*; [3]*The University of Western Australia, School for Population and Global health, Perth, Australia*; [4]*Fiona Stanley Hospital, Rheumatology, Murdoch, Australia*

Background: IgA vasculitis is generally considered to be a self-limiting condition, but this is at odds with the increased mortality observed in adult patients with IgA vasculitis (1).

Objectives: With sparse data on prognostic factors in IgAV, we investigated whether pre-existing conditions are risk factors for mortality in adult IgAV patients.
Methods: Observational population-based cohort study using state-wide linked longitudinal health data for adults with IgAV (n=267) and matched controls (n=1080) between 1980-2015. Charlson comorbidity index (CCI) and serious infections (SI) were recorded over an extensive lookback period prior to diagnosis. Date and causes of death were extracted from the WA Death Registry. Mortality rate (deaths/1000 person-years) ratios (MRR) and time dependent survival analysis assessed the risk of death. Age and gender specific mortality rate data were obtained from the Australian Bureau of Statistics.
Results: During 9.9 (±9.8) years lookback IgAV patients accrued higher CCI scores (2.60 vs1.50 p<0.001) and had higher risk of SI (OR 8.4, p<0.001), not fully explained by CCI scores. During 19 years follow-up, the risk of death in IgAV patients (n=137) was higher than in controls (n=397) (MRR 2.06, CI 1.70-2.50, p<0.01) and the general population (SMRR 5.64, CI 4.25, 7.53, p<0.001). Survival in IgAV was reduced at five (72.7 vs. 89.7 %) and twenty years (45.2% vs. 65.6 %) (both p<0.05). CCI (HR1.88, CI:1.25 - 2.73, p=0.001), renal failure (HR 1.48, CI: 1.04 - 2.22, p=0.03) and prior SI (HR 1.48, CI:1.01 – 2.16, p=0.04) were independent risk factors. Death from infections (5.8 vs 1.8%, p=0.02) was significantly more frequent in IgAV patients.
Conclusion: Premorbid accrual of comorbidity is increased and predicts premature death in IgAV patients. However, comorbidity does not fully explain the increased risk of serious infections prior to diagnosis or the increased mortality due to infections in IgAV.
REFERENCES:
[1] Villatoro-Villar M, Crowson CS, Warrington KJ, Makol A, Ytterberg SR, Koster MJ. Clinical Characteristics of Biopsy-Proven IgA Vasculitis in Children and Adults: A Retrospective Cohort Study. Mayo Clin Proc. 2019;94(9):1769-80.
Acknowledgements: The authors would like to acknowledge the support of the Arthritis Foundation of WA and acknowledge the Western Australian Data Linkage Branch, the Western Australian Department of Health, and the data custodians of, the Hospital and Morbidity Data Collection, the Emergency Department Data Collection the WA Cancer Register and the WA Death Register for their assistance with the study.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2307

AB0394 CLINICAL CHARACTERISTICS OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: A SINGLE-CENTER RETROSPECTIVE ANALYSIS ON 52 CASES OF CHINESE PATIENTS

L. F. Chen[1], Y. Mo[1], Q. H. Li[1], D. H. Zheng[1], L. Dai[1]. [1]*Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Rheumatology, Guangzhou, China*

Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare and heterogeneous systemic vasculitis. Different patients or the same patient in different stages show different manifestations, which may lead to misdiagnosis and delay treatment.
Objectives: To analyze the clinical characteristics in Chinese patients with EGPA.
Methods: EGPA patients who fulfilled the 1990 ACR classification criteria were included between December 2003 and April 2020. The demographic and clinical characteristics were collected and analyzed retrospectively.
Results: There were 52 EGPA patients recruited, 34 (65.4%) patients were males and the median age at onset was 47(38~55) years. The median duration from disease onset to diagnosis was 30(4~96) months. For initial symptoms, respiratory manifestations (61.5%) were the most common, including 42.3% patients beginning with asthma, followed by 21.2% with nose/paranasal sinuses manifestations. Respiratory medicine (53.8%) were the most common department at first visit, followed by rheumatology medicine (11.5%, Figure 1A). There were 44.2% EGPA patients definitely diagnosed at the department of rheumatology or after consultation by rheumatologists.
During the whole disease process, the most common clinical manifestations were asthma (88.5%), then nose/ paranasal sinuses (84.6%), pulmonary (76.9%) and nervous system (61.5%) manifestations, followed by constitutional symptom (44.2%), heart (36.5%) and skin (23.1%) involvement. Only 9.6% patients had gastrointestinal tract involvement and 3.8% had renal involvement (Figure 1B).
There were 46 (88.5%) patients showing the ratio of peripheral blood eosinophils >10% at diagnosis. Among the rest 6 patients, 3 had higher eosinophil ratio before diagnosis, while the other 3 patients had been treated with glucocorticoid before diagnosis, of whom 2 patients showed pathological eosinophil infiltration in lung or paranasal sinuses mucosa, respectively. There were 8(15.4%) patients with positive ANCA. Compared with EGPA patients with negative ANCA, they had lower incidence of asthma (62.5% vs. 93.2%), but higher incidence of constitutional symptoms (87.5% vs. 36.4%), arthralgia (50.0% vs. 6.8%) and renal involvement (25.0% vs. 0.0%), higher peripheral eosinophil count [2.06(0.80~4.51) $\times10^9$/L vs. 1.81(0.93~3.32) $\times10^9$/L], ESR [20(7~77) mm/h vs. 18(9~42) mm/h] and CRP [18.5(3.2~65.9) mg/L vs. 3.3(3.2~13.0) mg/L], higher Birmingham vasculitis activity score [17(10~22) vs. 13(9~15)] and vasculitis damage index [3(1~3) vs. 2(1~2), all P<0.05]. There were 21.2% EGPA patients showing poor prognostic factors according to five-factor score (FFS) and 34.6% patients according to the revised FFS.
Conclusion: EGPA patients may have no asthma especially those with positive ANCA. Multi-disciplinary collaboration especially based on rheumatologists and pulmonologists should be emphasized for early identification and prompt treatment.

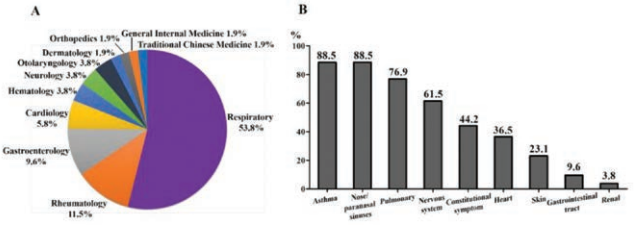


Figure 1. Department at first visit (A) and clinical manifestations during the whole disease process of 52 Chinese EGPA patients(B).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2359

AB0395 RENAL INVOLVEMENT IN HENOCH-SCHÖNLEIN PURPURA

N. Ben Chekaya[1], S. Daada[1], M. Brahim[1], I. Chaabene[1], R. Klii[1], M. Kechida[1], S. Hammami[1]. [1]*Fattouma Bourguiba Hospital, Internal Medicine and Endocrinology Departement, Monastir, Tunisia*

Background: Henoch-Schönlein purpura (HSP), also known as rheumatic purpura, is an immune complex vasculitis affecting small vessels with dominant IgA deposits. Clinical manifestations mainly involve cutaneous purpura, arthralgias and/or arthritis, acute enteritis and glomerulonephritis. HSP is more common among children than adults. Kidney damage is the principal prognostic determinant in HSP. The aim of this study is to evaluate the renal manifestations of HSP.
Objectives: The aim of this study is to evaluate the renal manifestations of HSP.
Methods: This was a retrospective study of 35 patients with diagnosed HSA, who were admitted between the time period may 2008 and november 2018. All of these patients met the American College of Rheumatology classification criteria for a diagnosis of HSP. Renal involvement was defined as the presence of proteinuria or hematuria.
Results: The study group consisted of 35 patients, 20 women (57%) and 15 men (43%). The mean age was 48.8± 18.7 years. The incidence rates of skin, joint, gastrointestinal and central nervous system involvement were 91.4, 77.1, 54.2 and 2.8%, respectively. Elevated serum IgA levels occurred in 5.7 %. Six patients (17.1%) were given corticosteroids during the first 3 months of their HSP, which were indicated for severe gastrointestinal (n=5) or renal involvement (n=1). Eighteen of the thirty five patients (51.42%) had renal involvement. There were 12 women and six men. All patients had proteinuria (100%). Hematuria has been identified in 11 patients (61.1%) and renal insufficiency in 4 patients (22.2%). The renal involvement was mainly detected in the first month. Renal biopsy was affected in four patients (22.2%). An endocapillary glomerulonephritis was found in 3 patients and an extra capillary necrotizing glomerulonephritis in one patient. The immunofluorescence showed the presence of IgA deposits in 4 patients.
Conclusion: Renal involvement dominates the prognosis for the disease. The most common clinical expression is the association of microscopic hematuria with proteinuria.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2670

AB0396 RAPID IMPROVEMENT IN CYSTOID MACULAR EDEMA WITH HIGH DOSE INTRAVENOUS METHYLPREDNISOLONE IN NON-INFECTIOUS UVEITIS OF DIFFERENT IMMUNE MEDIATED INFLAMMATORY DISEASES

N. Vegas-Revenga[1], J. L. Martín-Varillas[2], V. Calvo-Río[3], I. González-Mazón[3], L. Sanchez-Bilbao[3], E. Beltrán[4], A. Fonollosa[5], O. Maiz-Alonso[6], A. Blanco[7], M. Cordero-Coma[8], N. Ortego[9], I. Torre-Salaberri[10], F. Francisco[11], S. Muñoz Fernandez[12], M. D. M. Esteban-Ortega[13], M. Díaz-Llopis[14], J. Cañal[15], J. A. Ventosa[15], R. Demetrio-Pablo[15], L. Domínguez[16], M. Agudo-Bilbao[3],

S. Castañeda[17], I. Ferraz-Amaro[18], M. A. González-Gay[3], R. Blanco[3]. *[1]Hospital Galdakao-Usansolo, Rheumatology, Galdakao, Spain*; *[2]Hospital de Sierrallana, Rheumatology, Sierrallana, Spain*; *[3]Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*; *[4]Hospital Universitario Doctor Peset, Rheumatology, Valencia, Spain*; *[5]Hospital Universitario de Cruces, Ophthalmology, Barakaldo, Spain*; *[6]Hospital Universitario Donostia, Rheumatology, San Sebastian, Spain*; *[7]Hospital Universitario Donostia, Ophthalmology, San Sebastian, Spain*; *[8]Hospital de León, Ophthalmology, León, Spain*; *[9]Hospital Universitario San Cecilio, Ophthalmology, Granada, Spain*; *[10]Hospital Universitario de Basurto, Rheumatology, Bilbao, Spain*; *[11]Hospital Universitario de Gran Canaria Doctor Negrín, Rheumatology, Gran Canaria, Spain*; *[12]Hospital Universitario Infanta Sofía, Rheumatology, Madrid, Spain*; *[13]Hospital Universitario Infanta Sofía, Ophthalmology, Madrid, Spain*; *[14]Hospital Universitario La Fe, Ophthalmology, Valencia, Spain*; *[15]Hospital Universitario Marqués de Valdecilla, Ophthalmology, Santander, Spain*; *[16]Hospital Universitario San Agustín, Rheumatology, Avilés, Spain*; *[17]Hospital Universitario de La Princesa, Rheumatology, Madrid, Spain*; *[18]Hospital Universitario de Canarias, Rheumatology, Canarias, Spain*

Background: Cystoid Macular Edema (CME) is the most important cause of blindness in non-infectious uveitis (NIU) **(1).** Corticosteroids and conventional and/or biological immunosuppressant may be required **(1-6).** High-dose intravenous methylprednisolone (IVMP) pulse therapy may induce a rapid improvement.
Objectives: To evaluate the efficacy and safety of IVMP pulse therapy in CME of different immune mediated inflammatory diseases (IMID).
Methods: Multicentre study of 66 patients with severe ocular inflammation who received IVMP. The underlying diseases were: Vogt Koyanagy Harada disease (VKHD)(n=24), Behçet's disease (BD) (19) and idiopathic NIU (23). The main outcome variable was macular thickness and macular edema (Optical coherence tomography [OCT] >300 µm); that was assessed at 0 (basal), 2-5, 7, 15 and 30 days after IVMP.
The results are expressed as mean ±SD for normally distributed variables, or as median [IQR] when are not. Comparison of continuous variables was performed using the Wilcoxon test.
Results: We studied 43♀/ 23♂ patients. The main features are shown in TABLE 1. IVMP dose ranged from 250 to 1000 mg/day administered for 3-5 consecutive days, the dose was established according to the presence or not of other systemic manifestations apart from uveitis. All of them had active intraocular inflammation at the moment of the study.

Table 1. Main features of 66 patients with cystoid macular edema.

	VKHD (n=24)	Idiophatic (n=23)	Behcet's disease (n=19)	Overall (n=66)
Men/Women, n	**5/19**	9/14	9/10	66
Mean age (years)	**42 ± 11**	47 ± 15	33 ± 10	-
Unilateral/Bilateral, n (%)	**2 (8.3) /22 (91.7)**	10 (43.5) / 13 (56.5)	4 (21) / 15 (79)	16/50
Inflammatory ocular patterns, n (%)				
Posterior uveitis	6 (25)	9 (39.1)	3 (15.8)	18
Panuveitis	18 (75)	14 (60.9)	16 (84.2)	48
Laboratory data, n (%)				
ANA	2 (8.34)	2 (8.7)	0 (0)	4
HLA B27	0 (0)	4 (17.4)	0 (0)	4
HLA B29	0 (0)	1 (4.3)	0 (0)	1
HLA B51	0 (0)	5 (21.7)	8 (42)	13

A rapid and maintained statistically improvement was observed in OCT values in all underlying diseases (FIGURE 1**).** No major side effects were observed.
Conclusion: High-dose IVMP pulse therapy is useful and safe in the prompt control of CME, regardless of the underlying IMID.
REFERENCES:

[1] Vegas-Revenga N, et al. Am J Ophthalmol. 2019; 200:85-94. doi: 10.1016/j.ajo.2018.12.019.
[2] Calvo-Río V, et al. Clin Exp Rheumatol. 2014;32(4 Suppl 84): S54-7. PMID: 25005576.
[3] Santos-Gómez M, et al. Clin Exp Rheumatol. 2016;34(6 Suppl 102): S34-S40. PMID:27054359.
[4] Atienza-Mateo B, et al. Rheumatology (Oxford) 2018;57(5):856-864. doi: 10.1093/rheumatology/kex480.
[5] Atienza-Mateo B, et al. Arthritis Rheumatol. 2019; 71(12):2081-2089. doi: 10.1002/art.41026.
[6] Martín-Varillas JL, et al. Ophthalmology. 2018;125(9):1444-1451. doi: 10.1016/j.ophtha.2018.02.020.

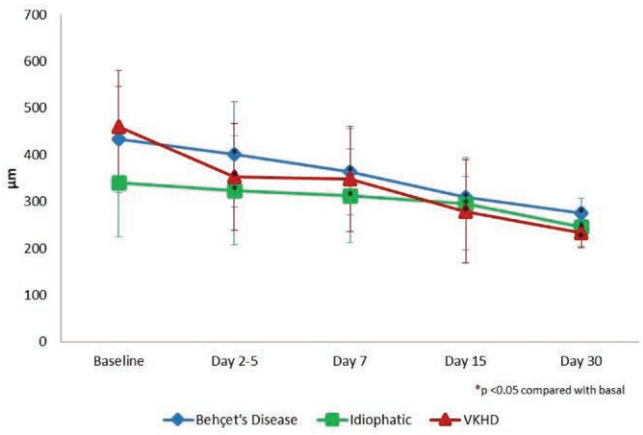


Figure 1. Improvement of OCT in 66 patients with cystoid macular edema.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3247

AB0397

EPIDEMIOLOGY AND CLINICAL FEATURES OF OPHTHALMOLOGICAL MANIFESTATIONS IN BEHÇET'S DISEASE. STUDY OF 50 PATIENTS OF A SERIES OF 120 PATIENTS IN A REGION IN NORTHERN SPAIN

A. Herrero-Morant[1], G. Suárez-Amorín[1], R. Demetrio-Pablo[1], L. Sanchez-Bilbao[1], C. Álvarez-Reguera[1], D. Martínez-López[1], R. Fernández Ramón[1], J. L. Martín-Varillas[2], M. C. Mata-Arnaiz[3], M. Á. González-Gay[1], R. Blanco[1]. *[1]Hospital Universitario Marqués de Valdecilla, Rheumatology and Ophtalmology, Santander, Spain*; *[2]Hospital de Sierrallana, Rheumatology, Sierrallana, Spain*; *[3]Hospital de Laredo, Rheumatology, Laredo, Spain*

Background: Ophthalmological involvement is one of the most feared manifestations of Behçet's disease [1-6].
Objectives: Our aim was to define the main demographic and clinical features of ophthalmological involvement in a well-defined cohort of patients with Behçet's disease.
Methods: Descriptive study of a cohort of 120 patients diagnosed with Behçet's disease from January 1, 1980 to December 31, 2019. Finally, following the 2014 International Criteria for Behçet's Disease (ICBD) (*J Eur Acad Dermatol Venereol 2014; 28:338-47*) 94 patients were chosen for this study.
Results: 50 patients (28 men/22 women; male to female ratio of 1:0.8) had ocular involvement. Mean age at diagnosis was 37.6±11.8 years. Mean ICBD score was 5.8±1.3 points. Neurological involvement was the most frequent manifestation in this group. Genital ulcers were more frequent in the non-ophthalmological involvement group. Systemic clinical domains are shown in Figure 1.
The most frequent ocular manifestations were uveitis (n=44, 88.0%), retinal vasculitis (n=5, 10%) and dry eye (n=5, 10%). Likewise, the most frequent type of uveitis was anterior (n=17, 38.6%), followed by posterior uveitis (n=14, 31.8%). 26 (59.1%) of all uveitis were unilateral. Panuveitis was more frequent among patients under 60 years. Similarly, anterior uveitis was predominant in patients older than 70 years. There were no remarkable differences between genders. Main clinical features are shown in Table 1.

Table 1. Clinical characteristics of ocular Behçet's disease.

	n (%)	Unilateral, n (%)	Bilateral, n (%)
Uveitis	44 (88.0)	26 (59.1)	18 (40.9)
Anterior	17 (38.6)	13 (76.5)	4 (23.5)
Intermediate	2 (4.5)	-	2 (100)
Posterior	14 (31.8)	9 (64.3)	5 (35.7)
Panuveitis	11 (25.0)	4 (36.4)	7 (73.6)
Retinal vasculitis	5 (10.0)	-	-
Dry eye	5 (10.0)	-	-
Cystoid macular edema	4 (8.0)	-	-
Episcleritis	3 (6.0)	3 (100)	-
Optic neuritis	2 (4.0)	-	-

Conclusion: Ophthalmological involvement in Behçet's disease was more frequent in men. Uveitis and retinal vasculitis were the most frequent ocular manifestation. No remarkable differences in clinical features were observed between genders.

REFERENCES:
[1] Atienza-Mateo B, et al. *Arthritis Rheumatol.* 2019; 71(12):2081-2089. doi: 10.1002/art.41026
[2] Martín-Varillas JL, et al. Ophthalmology. 2018; 125(9):1444-1451. doi: 10.1016/j.ophtha.2018.02.020
[3] Atienza-Mateo B, et al. *Rheumatology (Oxford).* 2018;57(5):856-864. doi: 10.1093/rheumatology/kex480
[4] Vegas-Revenga N, et al. *Am J Ophthalmol.*2019;200:85-94. doi: 10.1016/j.ajo.2018.12.019
[5] Calvo-Río V, et al. Clin Exp Rheumatol. 2014;32(4 Suppl 84): S54-7. PMID: 25005576
[6] Santos-Gómez M, et al. Clin Exp Rheumatol. 2016;34(6 Suppl 102): S34-S40. PMID:27054359

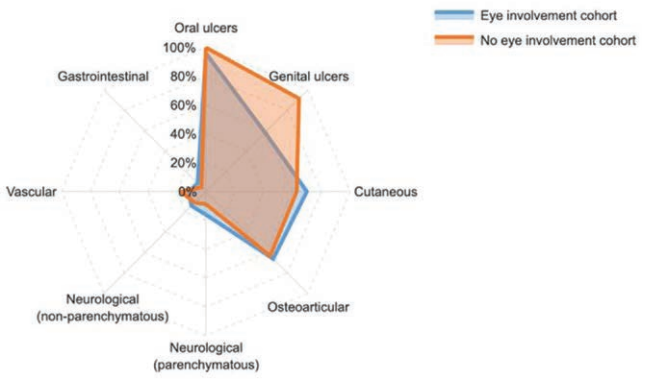


Figure 1. Comparison between clinical domains in patients with and without ophthalmological involvement.

Disclosure of Interests: Alba Herrero-Morant: None declared, Guillermo Suárez-Amorín: None declared, Rosalía Demetrio-Pablo: None declared, Lara Sanchez-Bilbao: None declared, Carmen Álvarez-Reguera: None declared, David Martínez-López: None declared, Raúl Fernández Ramón: None declared, José Luis Martín-Varillas Grant/research support from: AbbVie, Pfizer, Lilly, Janssen, and Celgene, M. Cristina Mata-Arnaiz: None declared, Miguel Á. González-Gay Speakers bureau: AbbVie, Pfizer, Roche, Sanofi, Lilly, Celgene and MSD, Grant/research support from: AbbVie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, Sanofi, Lilly and MSD, Grant/research support from: AbbVie, MSD, and Roche
DOI: 10.1136/annrheumdis-2021-eular.3478

AB0398 CASE SERIES OF PATIENTS WITH CHOLESTEROL CRYSTAL EMBOLISM SYNDROME THAT MIMICS SYSTEMIC VASCULITIS

Z. M. Ouyang[1], W. C. Zeng[1], X. N. Wei[1], D. H. Zheng[1], J. Lin[1], Q. H. Li[1], L. Dai[1], Y. Mo[1]. [1]*Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Department of Rheumatology, Guangzhou, China*

Background: Cholesterol crystal embolism (CCE) syndrome is a multisystemic disorder caused by small arteries cholesterol crystal emboli subsequent to small pieces of atheromatous plaques from the aorta or other major arteries break off. CCE is often overlooked because it mimics symptoms of systemic vasculitis due to its clinical characteristics such as ulceration and gangrene of toes, livedo reticularis, renal insufficiency. Acute inflammatory reactants such as ESR, CRP may elevate in CCE patients since the cholesterol crystals trigger a foreign-body inflammatory reaction around the arterioles.
Objectives: This study aimed to explore the clinical characteristics of CCE patients, to make rheumatologists learn more about this disease.
Methods: Peer-reviewed articles in the electronic databases Medline, PubMed, Science Citation Index, China Biomedical Literature Database (CBM), China Journal Full Text Database (CNKI), and WANFANG Data were searched using the terms "cholesterol crystal embolism syndrome", "cholesterol embolism", "atherosclerotic embolism", "atherosclerotic nephropathy", or "CCE". Only articles or case reports containing detailed medical records of CCE patients were included. We also included CCE patients in our department.
Results: A 66-year-old male CCE patient presented with multiple ulceration and gangrene of toes and heels (Figure 1), subacute renal insufficiency, and elevated CRP and ESR. This patient had been considered as "suspected systemic vasculitis" and was referred to our rheumatology department. Another 39 Chinese CCE patients from the above databases were qualified for analysis. Among these 40 patients, 87.5% (35/40) were male and the mean age was 68±6 years. The most common involved was kidney and 90% (36/40) of patients presenting with renal insufficiency including the progressive increase of serum creatinine, hematuria, proteinuria, or sudden (or sharp) aggravation of hypertension. Next common involved was skin that occurred in 87.5% (35/40) of patients, especially in the toes and heels. For skin manifestations, blue toe syndrome occurred in 82.5% (33/40) of patients, ulceration or gangrene in 25% (10/40), and livedo reticularis in 15% (6/40). Additionally, 12.5% (5/40) showed ocular involvement such as visual impairment and visual field defect. In 2 patients, embolized cholesterol crystal in retinal arteries that is called Hollenhorst plaques was detected by fundoscopy. There were 62.5% (25/40) of patients having elevated CRP or ESR. The positive rate for skin or subcutaneous biopsies was 58% (11/19) and for kidney biopsies was 100% (6/6). The precipitating factors preceding the occurrence of classical symptoms such as blue toe syndrome, livedo reticularis and/or subacute renal insufficiency is important for CCE diagnosis especially for patients who had contraindications or were intolerant to biopsy. The precipitating factors include endovascular intervention (80%), vascular surgery (5%), and anticoagulant or thrombolytic therapy (2.5%). Only 12.5% (5/40) of patients were spontaneous and didn't have any predisposing factors. General interventions of CCE included statins (82.5%), antiplatelets (32.5%), and dialysis (32.5%). Twelve patients (30%) received glucocorticoids and 75% (9/12) of them renal function improved and ulceration healed (Figure 1). Among 36 patients who presented with renal insufficiency, the renal function returned to normal after treatment in 2 patients (5.6%), but 27 patients (75%) still showed abnormal renal function even though somewhat improved, and 7 patients (19.4%) needed renal replacement therapy or dialysis for maintenance.
Conclusion: This study reported CCE patients had high prevalence of renal insufficiency, blue toe syndrome, and ulceration or gangrene of toes, as well as elevated CRP or ESR, thus rheumatologists should be alert to this disease as one of the differential diagnosis of systemic vasculitis, especially for elderly patients with evidence of atherosclerosis who undergo a recent cardiovascular procedure.

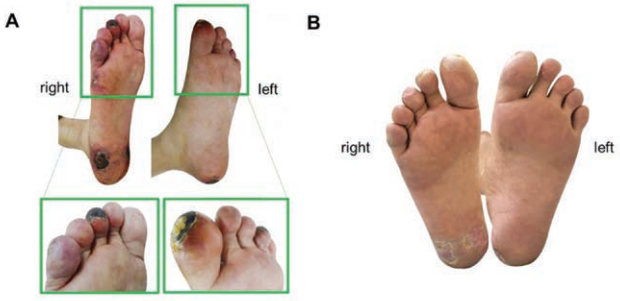


Figure 1: A 66-year-old male CCE patient presenting with multiple ulceration and gangrene of toes and heels (A). Skin gangrene with or without ulceration scab was seen in bilateral heels, the third right toe, and the first and fourth left toes. The fifth right toe showed blue color (named as blue toe syndrome). After 6-month glucocorticoids treatment, the skin ulceration completely healed (B).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3500

AB0399 EPIDEMIOLOGY OF BEHÇET DISEASE IN A NORTHERN SPANISH HEALTH REGION

L. Sanchez-Bilbao[1], G. Suárez-Amorín[2], C. Álvarez-Reguera[1], A. Herrero-Morant[1], D. Martínez-López[1], J. L. Martín-Varillas[3], M. C. Mata Arnaiz[4], R. Demetrio-Pablo[2], M. A. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*; [2]*Hospital Universitario Marqués de Valdecilla, Ophthalmology, Santander, Spain*; [3]*Hospital Sierrallana, Rheumatology,Torrelavega, Spain*; [4]*Hospital de Laredo, Rheumatology, Laredo, Spain*

Background: Behçet disease (BD) is a systemic and potentially severe disease. Its incidence varies widely worldwide. In Spain, published BD's epidemiological studies are scarce.

TABLE 1.

	Diagnostic criteria and study period	n cases / population size	Mean age at onset and sex (%female)	Prevalence (over 100000) / incidence	Oral / genital ulcers (%)	Skin lessions/ pathergy test (%)	Ocular involvement (%)	Joint involvement (%)	Neurobehcet/ Vascular/ Gastrointestinal involvement (%)
Sánchez. L et al. Southern Europe (Cantabria, Spain)	Expert opinion, ISG, ICBD / 1980- 2020	120 (expert opinion) / 96 (ICBD) / 59 (ISG) / 581641	37.6 ±13.8/ 48.3	20.6 (expert opinion), 16.5 (ICBD), 10.1 (ISG) / 0.022 (expert opinion), 0.018 (ICBD), 0.011 (ISG)	94.2 / 59.2	63.3 / 25. 2	41.6	65	10.8 / 11.6 / 6.6
Calamia, K. T. et al. North America (Minnesota, USA)	ISG / 1960-2005	13 / NR	31 / 30	5.2 / 0.38	100 / 62	85 / NR	62	46	23 / 23 / NR
Altenburg, A. et al. Northern Europe (Berlin, Germany)	ISG and ABD classification tree / 1961-2005	590 / 3391344	26 / 58	4.9 / 1 (estimated)	98.5 / 63.7	62.5 / 33.7	58.1	53	10.9 / 22.7 / 11.6
Mohammad, A. et al. Northern Europe (Skane County, Sweden)	ISG / 1997-2010	40 / 809317	30.5 / 33	4.9 / 0.2	100 / 80	88 / NR	53	40	0 / 20 / NR
Mahr, A. et al. Southern Europe (SeineSaint-Denis County, France)	ISG / 2003	79 / 1094412	27.6 / 43	7.1 / NR	100 / 80	90 / 20	51	59	10 / NR / 10
Salvarani, C. et al. SouthernEurope (Reggio Emilia, Italy)	ISG, 1988-2005	18 / 486961	33 / 50	3.7 / 0.24	100 / 78	100 / NR	56	50	11 / 6 / NR
Azizlerli, G. et al. Middle East (Istambul, Turkey)	ISG / prevalence study	101 / 23986	NR / 48.5	42 / NR	100 / 70.2	Not globally reported / 69.3	27.7	Not globally reported	NR / Not globally reported / NR
Davatchi, F. et al. Middle East (Iran nationwide)	Expert opinion / 1975-2018	7641 / NR	25.6 / 44.2	80 / NR	97.5 / 64.4	62.2 / 50.4	55.6	38.1	3.9 / 8.9 / 6.8
Krause, I. et al. Middle East (Galilee, Israel)	ISG / 15 years (not specific years have been reported)	112 / 737000	30.6 / 47	15.2 / NR	NR / 68	41 / 44.4	58	70	11.6 / Not globally reported / NR
Nishiyama, M. et al. Asia (Japan nationwide)	1987 JCBD / 1991	3316 / NR	35.7 / 50.6	NR / NR	98.2 / 73.2	87.1 / 43.8	69.1	56.9	11 / 8.9 / 15.5

JCBD: Japanese diagnostic Criteria of Behçet's Disease; *n*: number of cases; NR: Not Reported

Objectives: In a well-defined Northern Spanish population-based cohort, the aim of this study was **a)** to estimate epidemiological variations, **b)** clinical domains and **c)** to compare our results with other regions.

Methods: Study of unselected all consecutive patients diagnosed with definitive or possible BD by expert rheumatologists between 1980 and 2020 in our health region. Two classification criteria were applied: **a**) International Study Group (ISG) for BD **[1]**, and **b**) International Criteria for BD (ICBD) **[2]**. In addition, a literature review of Medline publications was carried out.

Results: In this study, from a total of 120 patients diagnosed with BD by expert opinion (58 women/62 men), 96 met ICBD and 59 ISG criteria. Mean age of the cohort at diagnosis was 37.6±13.8 years similar to other countries, as well as sex distribution.

Prevalence was higher than in most European populations regardless the diagnostic criteria applied: expert opinion (20.6), ICBD (16.5) or ISG (10.1) (TABLE 1). Incidence was lower (expert opinion: 0.022, ICBD: 0.018, ISG: 0.011). Clinical domains' frequency was in line with other regions except vascular and gastrointestinal involvement, which were lower.

Conclusion: BD's prevalence in Northern Spain is higher than in most European populations. These differences likely reflect a combination of true geographic variation, methodological artifacts as well as the easy access to Public Health System and its efficiency. In contrast, clinical phenotypes are similar to other regions.

REFERENCES:

[1] *Lancet. 1990; 335:1078-80*

[2] *J Eur Acad Dermatol Venereol. 2014; 28:338-47*

Disclosure of Interests: Lara Sanchez-Bilbao: None declared, Guillermo Suárez-Amorín: None declared, Carmen Álvarez-Reguera: None declared, Alba Herrero-Morant: None declared, David Martínez-López: None declared, José Luis Martín-Varillas: None declared, M. Cristina Mata Arnaiz: None declared, Rosalía Demetrio-Pablo: None declared, Miguel A González-Gay Speakers bureau: AbbVie, Pfizer, Roche, Sanofi, Celgene and MSD., Grant/research support from: AbbVie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD., Grant/research support from: AbbVie, MSD and Roche.

DOI: 10.1136/annrheumdis-2021-eular.3577

AB0400

URINARY ALBUMIN-TO-CREATININE RATIO INDICATES NECROTIZING AND CRESCENTIC GLOMERULONEPHRITISIN ANCA-ASSOCIATED VASCULITIS

S. Hakroush[1], B. Tampe[2]. [1]*University Medical Center Göttingen, Institute of Pathology, Göttingen, Germany*; [2]*University Medical Center Göttingen, Department of Nephrology and Rheumatology, Göttingen, Germany*

Background: Renal involvement is a common and severe complication of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) as it can cause acute kidney injury (AKI), end-stage renal disease (ESRD) or death.

Objectives: We have previously reported that elevated urinary albumin-to-creatinine ratio (uACR) correlates with rapid deterioration of kidney function in ANCA GN. Therefore, we here aimed to describe the association between proteinuric findings and histopathological diagnosis of necrotizing and crescentic ANCA GN in 50 urinary samples at admission and corresponding renal biopsies of patients with AAV.

Methods: A total number of 50 urinary samples at admission and corresponding renal biopsies with confirmed renal involvement of AAV were retrospectively included between 2015 till 2020 in a single-center observational study.

Results: Renal involvement of AAV revealed variable proteinuria ranging from low-range to nephrotic syndromes, however most patients presented with subnephrotic proteinuria. Severe deterioration of kidney function requiring RRT within 30 days after admission was associated with elevated levels of nonselective proteinuria, mostly attributed to albuminuria (uACR). Because we have previously shown that histologically confirmed ANCA GN with glomerular crescents and necrosis is associated with AKI and requirement of RRT during short-term disease course and elevated uACR levels were equally associated with AKI and requirement of RRT during the short-term course after disease onset, we next analyzed the association between uACR measurements at admission and histopathological findings within renal biopsies performed thereafter. Severely increased uACR levels >300 mg/g correlated with reduction of normal glomeruli, attributed to increased glomerular crescents and necrosis. By contrast, no such association was observed for global sclerotic glomeruli, revealing that uACR reflects crescentic ANCA GN rather than adaptive glomerular hyperfilitration in chronic sclerosing stage. Since uACR levels could reflect both, either a specific renal involvement with necrotizing and crescentic ANCA GN or severity of systemic AAV disease, we next correlated uACR levels assessed at admission with extrarenal disease manifestation. We observed no association between uACR levels and extrarenal manifestation of AAV disease including pulmonary hemorrhage, skin involvement and BVAS assessment, suggesting that uACR levels reflected specific renal involvement in AAV. These observations were further confirmed by survival analysis for cumulative incidence of RRT during the short-term course of disease.

Conclusion: Early identification of patients who mostly benefit from aggressive immunosuppressive therapy is of clinical importance. Our observation that uACR levels at disease onset predict necrotizing and crescentic ANCA GN requires further investigation for therapeutic decision especially in patients with severe deterioration of kidney function.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4298

Scleroderma, myositis and related syndromes

AB0401 **CAN DUAL-ENERGY CT LUNG PERFUSION DETECT ABNORMALITIES AT THE LEVEL OF LUNG CIRCULATION IN SYSTEMIC SCLEROSIS (SSC)? PRELIMINARY EXPERIENCE IN 101 PATIENTS**

V. Koether[1,2], A. Dupont[3], J. Labreuche[4], P. Felloni[3], T. Perez[3], P. Degroote[5], E. Hachulla[1,2,6], J. Remy[3], M. Remy-Jardin[3], D. Launay[1,2,6]. [1]*Lille, CHU Lille, Service de Médecine Interne et Immunologie Clinique, Centre de référence des maladies autoimmunes systémiques rares du Nord et Nord-Ouest de France (CeRAINO), Lille, France*; [2]*Lille, Université de Lille, U1286 - INFINITE - Institute for Translational Research in Inflammation, Lille, France*; [3]*Lille, From the Department of Thoracic Imaging, Hôpital Calmette, Lille, France*; [4]*Lille, Université de Lille, CHU Lille, ULR 2694-METRICS: Évaluation des technologies de santé et des pratiques médicales, France (J.L.)., Lille, France*; [5]*Lille, Université de Lille, CHU Lille, Département de Cardiologie, Institut National de la Santé et de la Recherche Médicale, Lille, France*; [6]*Lille, Inserm-U1286, Lille, France*

Background: Systemic sclerosis (SSc) is an autoimmune disorder that is characterized by a interplay of vascular abnormalities, immune system activation and an uncontrolled fibrotic response associated with interstitial lung disease affecting about 40% of patients. Identification of ILD relies on high-resolution CT that identify features suggestive of the histologic patterns of SSc(1). CT is used to determine pattern and extent of ILD and participates in the prediction of ILD progression(2).

All group of pulmonary hypertension (PH) may occur with an overall prevalence reported in up to one fifth of patient. Whereas extensive SSc-ILD can be responsible for PH, PH can also be seen as a consequence of myocardial abnormalities or as primarily affecting small pulmonary arteries and classified as pulmonary arterial hypertension.

Dual-energy CT introduction offers perspectives in the evaluation of SSc-related pulmonary manifestations. While these are not strictly perfusion images, they have been reported as adequate surrogate markers of lung perfusion (3). In the field of PH, detection of perfusion defects highly concordant with V/Q scintigraphic findings has been reported in the diagnostic approach of CTEPH but also in the differential diagnosis between PAH and peripheral forms of CTEPH (4).

Objectives: To investigate lung perfusion abnormalities in patients with SSc.

Methods: The study population included 101 patients who underwent dual-energy CT (DECT) angiography in the follow-up of SSc. CT examinations were obtained on a 3rd-generation dual-source CT system with reconstruction of morphologic and perfusion images. All patients underwent pulmonary function tests within two months of the follow-up CT scan. Fifteen patients had right heart catheterization-proven PH.

Results: Our population included patients without SSc lung involvement (Group 1; n=37), patients with SSc-related ILD (Group 2; n=56) of variable extent (Group 2a: ≤10%: n=17; Group 2b: between 11-50%: n=31; Group 2c: >50%: n=8) and patients with PVOD/PCH (Group 3; n=8). Lung perfusion was abnormal in 8 patients in G 1 (21.6%), 14 patients in G 2 (25%) and 7 patients in G 3 (87.5%). Perfusion changes were mainly composed of bilateral perfusion defects, including patchy, PE-type perfusion defects and areas of hypoperfusion of variable size. In G 1 and G 2a (n=54): (a) patients with abnormal lung perfusion (n=14) had a significantly higher proportion of NYHA III/IV scores of dyspnea (p=0.031), a shorter mean walking distance at the 6MWT (p=0.042) and a trend towards lower mean DLCO% (p=0.055) when compared to patients with normal lung perfusion (n=40); (b) a negative albeit weak correlation was found between the iodine concentration in both lungs and the DLCO% (r=-0.27; p=0.059) whereas no correlation was found with PAPs (r=0.16; p=0.29) and walking distance during the 6MWT (r=-0.029; p=0.84).

Conclusion: DECT lung perfusion provides complementary information to HRCT scans, depicting perfusion changes in SSc patients with normal or minimally infiltrated lung parenchyma.

REFERENCES:

[1] Kim EA, Lee KS, Johkoh T, Kim TS, Suh GY, Kwon OJ, et al. Interstitial lung diseases associated with collagen vascular diseases: radiologic and histopathologic findings. Radiogr Rev Publ Radiol Soc N Am Inc. 2002 Oct;22 Spec No:S151-165.

[2] Goh NSL, Desai SR, Veeraraghavan S, Hansell DM, Copley SJ, Maher TM, et al. Interstitial lung disease in systemic sclerosis: a simple staging system. Am J Respir Crit Care Med. 2008 Jun 1;177(11):1248–54.

[3] Fuld MK, Halaweish AF, Haynes SE, Divekar AA, Guo J, Hoffman EA. Pulmonary perfused blood volume with dual-energy CT as surrogate for pulmonary perfusion assessed with dynamic multidetector CT. Radiology. 2013 Jun;267(3):747–56.

[4] Giordano J, Khung S, Duhamel A, Hossein-Foucher C, Bellèvre D, Lamblin N, et al. Lung perfusion characteristics in pulmonary arterial hypertension and peripheral forms of chronic thromboembolic pulmonary hypertension: Dual-energy CT experience in 31 patients. Eur Radiol. 2017 Apr;27(4):1631–9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.69

AB0402 **SELF-ASSESSMENT OF SCLERODERMA SKIN THICKNESS: DEVELOPMENT AND VALIDATION OF THE PASTUL QUESTIONNAIRE**

J. Spierings[1,2], V. Ong[1], C. Denton[1]. [1]*Royal Free and University College Medical School, University College London, Division of Medicine, Department of Inflammation, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom*; [2]*University Medical Centre Utrecht, Rheumatology and Clinical Immunology, Utrecht, Netherlands*

Background: Evaluation of skin is central to both clinical practice and trials in systemic sclerosis (SSc). This is generally done with the modified Rodnan Skin Score (mRSS). Remote consultations are now widely implemented in response to the COVID-19 pandemic, which has inevitably limited evaluation of skin. To monitor skin during this pandemic and to further explore ways to assess skin, we developed the PASTUL (Patient self-Assessment of Skin Thickness in Upper Limb) questionnaire.

Objectives: This study evaluated feasibility and validity of PASTUL in SSc.

Methods: The PASTUL questionnaire uses a simple self-assessed grading of skin as normal, mild, moderate, or severely thickened at eight sites of upper limb corresponding to mRSS. Assessed grades were converted to an integer scale [0, 1, 2, 3]. Detailed instructions for patients were provided. Scleroderma Skin PRO (SSPRO) and Scleroderma Health Assessment Disability Index (SHAQ-DI) were also completed. For comparison, physician assessed mRSS was performed in a subgroup of patients. Construct validity was evaluated by examining the correlation between PASTUL, mRSS, SSPRO and SHAQ-DI using Pearson's correlation coefficient. Content validity was evaluated by scoring relevance, clarity and practical difficulty. Test-retest reliability was estimated using intraclass correlation coefficient (ICC).

Results: 130 patients were invited of which 104 (80%) completed the questionnaires. The mRSS was undertaken in 78 patients (n=42, 54% limited cutaneous SSc (lcSSc)). The PASTUL was completed by patients (86%) or by a partner/friend (14%). Mean PASTUL score was 11 (SD 7), mean HAQ-DI 1.41 (SD 0.77) and mean SSPRO 48.3 (SD 27.0). PASTUL strongly correlated with total SSPRO and SSPRO subdomain physical limitations (r=0.60 and 0.62, respectively) (Figure 1A). Correlations between PASTUL and mRSS and mRSS upper limbs were moderate (r=0.56 and 0.58, respectively) (Figure 1B). An overview of all correlations is provided in Table 1. Correlation between PASTUL and mRSS was stronger in lcSSc compared to diffuse cutaneous SSc patients (r=0.53 vs 0.43) and when assessed by a partner/friend compared to patients themselves (r=0.90 vs 0.54). The PASTUL demonstrated excellent test-retest reliability (ICC of 0.93, p<0.001) and good content validity.

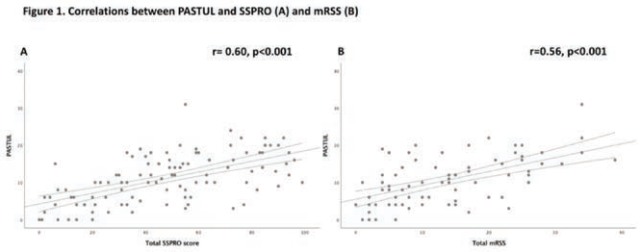
Table 1. Correlations between PASTUL, mRSS, SHAQ-DI and SSPRO.

Outcome measure	Pearson's correlation coefficient	P-value
mRSS	0.56	<0.001
mRSS upper limbs	0.58	<0.001
SHAQ-DI	0.38	<0.001
SHAQ VAS scores		
- VAS pain	0.28	0.004
- VAS GI	0.01	0.333
- VAS breathing	0.17	0.168
- VAS RP	0.16	0.114
- VAS DU	0.26	0.008
- VAS Limitations	0.32	0.001
SSPRO	0.60	<0.001
SSPRO subdomains		
- Physical effects	0.59	<0.001
- Physical limitations	0.62	<0.001
- Emotional effects	0.48	<0.001
- Social effects	0.42	<0.001

DU, digital ulcers; GI, gastrointestinal; mRSS, modified Rodnan Skin Score; PASTUL, Patient self-Assessment of Skin Thickness in Upper Limb; RP, Raynaud's Phenomenon; SD, standard deviation; SHAQ-DI, Scleroderma Health Assessment Questionnaire Disability Index; SSPRO, Scleroderma Skin Patient-Reported Outcome; VAS, visual analogue score

Conclusion: The significant correlation of PASTUL scores with total SSPRO and physical limitation scores and moderate correlation with mRSS support the potential of PASTUL for remote evaluation of skin thickness in virtual clinical settings. Future studies may explore sensitivity to change and utility in clinical trials.

Disclosure of Interests: None declared



DOI: 10.1136/annrheumdis-2021-eular.75

AB0403 ORBITAL MYOSITIS: AN UNCOMMON OPHTHALMIC PRESENTATION IN RHEUMATIC DISEASES - CASE SERIES AND SYSTEMIC REVIEW OF CASE REPORTS

P. S. Wong[1], B. G. T. Coumbe[1], P. Mangat[1], H. Beynon[1], R. Stratton[1]. [1]*Royal Free Hospital and University College Medical School, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom*

Background: Ophthalmic conditions are common manifestations in patients with rheumatic diseases (RDs), orbital myositis (OM) remain rare. Only 1 case each for scleroderma and undifferentiated connective tissue disease (UCTD) reported.
Objectives: Report frequency of Rheumatic Diseases with OM (RDs-OM), diagnosis and treatments.
Methods: Patients database were obtained from trust electronic record and literature review of case reports were performed.
Results: 4 out of 7 patients in our clinic with RDs-OM. Both Scleroderma-myositis (SCM) patients were positive for anti-PM/SCL antibody. All received glucocorticosteroid (GCS) and Mycophenolate as steroid-sparing or rescue therapy with good tolerance and outcome. One idiopathic OM has residual muscle paresis.

Table 1. Case series of patients with Orbital Myositis

	Idiopathic OM (n=3)	Rheumatology Diseases (n=4)	p-value
Age (years)	48 (27-72)	42.75 (21-60)	P= 0.8571
Gender – Female (Male)	2 (1)	4(0)	
Median Period Of Follow Up (months)	24.60 (7-37)	47.25(1-120)	
Underlying RD			
I.UCTD	-	1	
II.Overlap Scleromyositis	-	2	
III.Behcet's Disease	-	1	
Biopsy			
I.Pathological significant	1	1	
II.Normal	1	1	
III.Not done	1	2	

Total 93 cases with RDs-OM reviewed and the characteristic of patients represented in Figure 1.

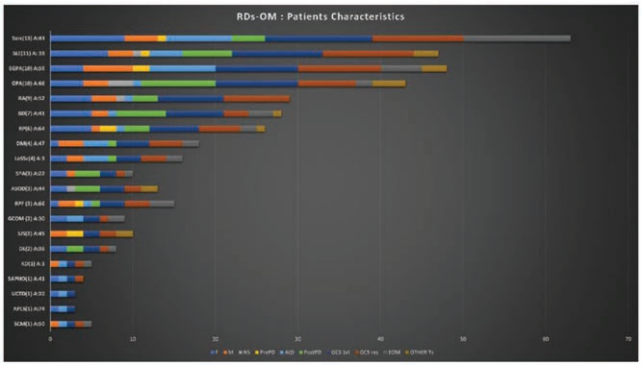


Figure 1. Characteristics of orbital myositis in patients with rheumatic diseases. F: female, M:male, NS: not-specified, PrePD: onset before RD, AtD: onset with RD,PostPD: onset after RD, GCS 1st: Glucocorticoid as first line treatment, GCS res: Glucocorticoid responder, BxEOM: biopsy of extra-ocular muscle, OtherTs: Other Biopsy A: Median age at diagnosis, Sarc: sarcoidosis, SLE: Lupus, EGPA: Eosinophilic Granulomatous Polyangitis, GPA: Granulomatous Polyangitis, RA: rheumaoid Arthritis, BD: Behcet;s Disease, RP: Relapsing Polychondritis, DM: Dermatomyositis, LoSSC: Localized Sclerderma, SPA: Spondyloarthropathy, ASOD: Adult Onset Still's Disease, RPF: Retroperitoneal Fibrosis, GCOM: Giant Cell OM, SJS: Sjogren Syndrome, DL: Discoid Lupus, KD: Kawasaki Disease, SAPHO: Synovitis, acne, pustulosis, hyperostosis, and osteitis, APLS: Antiphospholipid Syndrome.

OM although is rare but can present in most RDs. Our review showed OM commonest in patients with RA, GPA, EGPA and sarcoidosis. Only 1 each for SCM, APLS, UCTD, SAPHO and Kawasaki Disease.
Most RDs-OM patients are female. 89.2% OM diagnosed concurrently with primary RD diagnosis. Majority RA, BD and GPA developed OM along the course of RDs (83%-90%).
Except for routine RDs screening, thyroid eye disease, infections, malignancy (eg. lymphoma) and myasthenia gravis, atypical infective screenings include mycobacterium, fungal, *Borrelia* and spirochetes were excluded. Histopathological diagnosis is important diagnostic tool for IgG4 disease, neoplasm, sarcoidosis and vasculitis. 59% patients underwent tissue biopsy, 71% of these were sampled from EOM, some from involved organs. Orbital MRI or CT were the commonest diagnostic imaging, 5 reported had Ocular ultrasound as single or complementary imaging and 1 had PET-CT for exclusion of other diagnosis.
Only 40% GPA and 20% of EGPA patients were positive for ANCA either c-ANCA, p-ANCA and MPO which is similar in other literatures.
97.8% (n=91) patients received GCS with 79% of these patients reported improvement or resolution of ocular symptom with or without steroid-sparing agents. Immunosuppressants used are those not foreign among rheumatologists while biologics prescribed for refractory cases were Rituximab(2), Infliximab(4), Adalimumab(2) and Tocilizumab(1). Orbital decompression and orbital radiation were other measures. 13 patients had residual EOM paresis.
Conclusion: 1.RDs-OM is increasing recognized.
2.Most OM in RA, BD and GPA occurs along its primary RDs.
3.40% GPA and 20% of EGPA patients were ANCA positive.
4.GCS remain the primary treatment, three quarter patients responded.

REFERENCES:

[1] Murray PI. The eye and inflammatory rheumatic diseases. Best Practice & Research Clinical Rheumatology. 2016.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.122

AB0404 EXTENDED MYOSITIS PANEL AND THE CLINICAL ASSOCIATION IN PATIENT WITH SUSPECTED INFLAMMATORY DISEASE, A RETROSPECTIVE STUDY

S. Al Nokhatha[1], E. Alfares[2], N. Conlon[2], R. Conway[1]. [1]*St James's Hospital, Rheumatology, Dublin, Ireland*; [2]*St James's Hospital, Immunology, Dublin, Ireland*

Background: The idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of conditions characterized by proximal muscle weakness. Autoantibodies are identified in more than 80% of patients with polymyositis (PM) or dermatomyositis (DM). Some are also found in other connective tissue diseases (CTD), while others are more specific to IIM. Thus, they are classified into two categories named myositis associated antibodies (MAA) and myositis specific antibodies (MSA). MSA have been reported as being 90% specific for IIM while MAA are found in up to 50% of myositis patients. [1]
Objectives: The aim of the study was to evaluate the myositis antibody prevalence and to assess the associations of these antibodies with clinical manifestations, final diagnosis, medication received and outcomes.
Methods: A retrospective chart review study was conducted at St. James's Hospital from 2015-2020. All positive myositis panels were obtained. The MAA evaluated were PMScl (100/75), U1snRNP, Ku and Ro52, while MSA were Mi2a, Mi2b, TIF1, MDA5, NXP2, SAE1, Jo-1, SRP, PL-7, PL-12, EJ and OJ.
Results: We identified 52 patients who were positive for one or more MSA/MAAs. The mean age was 58.9 years, the majority were female (65.3%). The most prevalent MAA was anti-Ro52 (29/52) followed by anti-PMScl 100/75 (7/52), anti-Ku and anti-U1RNP were seen in (3/52) each. The prevalence of MSA were (4/52) for anti-PL12 and (3/52) for anti-SAE1 followed by (2/52) for each of anti-Mi2b, anti-NXP2, anti-Jo, anti-SRP, anti-PL7, anti-EJ and anti-OJ while only (1/52) for anti-MDA5. The most common observed clinical phenotypes in our cohort were arthralgia (20/52), ILD (18/52) and cutaneous manifestations (15/52). Less than a quarter of the studied population had arthritis (8/52), myositis (7/52), raynauds (7/52) and malignancy (4/52). Various diagnosis were allocated for these patients, while only eight cases were diagnosed with dermatomyositis. Medication received and the final outcome for those with strong positive MSA were summarized in table1.
Conclusion: IIM was the final diagnosis in only 15% of positive myositis panels and the presence of antisynthetase antibodies didn't necessarily indicate the presence of antisynthetase syndrome thus signifying low specificity in our cohort.

REFERENCES:

[1] Ghirardello A, Borella E, Beggio M, Franceschini F, Fredi M, Doria A. Myositis autoantibodies and clinical phenotypes. *Auto Immun Highlights*. 2014;5(3):69-75. Published 2014 Aug 23.

IIM MAA	MSA	ILD	Arthritis	Arthralgia	Myositis	Raynauds	Cutanous	Malignancy	Final diagnosis	Treatment Outcome
	NXP2				+		+		Dermatomyositis Myasthenia gravis	Prednisolone + IVIG Remission/stable +Azathioprine + pyridostigmine
	MDA5			+			+		Amyopathic dermatomyositis	Prednisolone + MTX Remission/stable
	SAE1				+		+		Dermatomyositis	Prednisolone + MTX Remission/stable
ILD	PL12	+							IPF	No medication Remission/stable
Ro52	PL12	+							IPF	Prednisolone Died
	SAE1/ OJ	+							IPF	No medication Lost follow-up
	EJ	+							IPF	No medication Remission/stable
	PL12	+							Interstitial pneumonia with autoimmune feature (IPAF)	Under evaluation Remission/stable
Ro52	PL7	+	+	+		+	+		Anti-synthetase syndrome	Prednisolone + cyclophosphamide Remission/stable then azathioprine
	PL7	+			+				Anti-synthetase syndrome	Prednisolone + Remission/stable Rituximab
	JO-1	+				+			Anti-synthetase syndrome	No medication Remission/stable
Ro52	JO-1	+							Anti-synthetase syndrome	Prednisolone + MMF Remission/stable then rituximab
CTD	SAE1/ SRP	+						+	Progressive pulmonary fibrosis (post COVID, ARDS and recurrent aspiration) Esophageal Ca T1N2M0 s/p esophagectomy	Antibiotics + supportive care Remission/stable
	SRP					+	+		Limited cutaneous scleroderma	Nifedipine Remission/stable
Ro52	EJ			+					Sjogren	HCQ Remission/stable
Others	OJ		+	+	+		+		MCTD	Prednisolone+ Remission/stable
U1snRNP/ Ro52									Autoimmune hepatitis	Azathioprine+HCQ
	NXP2			+					Polymyalgia rheumatica	Prednisolone Remission/stable
ku	Mi2b			+					large vessel vasculitis	Prednisolone+ Remission/stable Tocilizumab
	PL12		+	+			+		PsA	MTX Remission/stable
	Mi2b								PBC	Ursodeoxycholic acid Remission/ stable

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.184

AB0405 FIBROBLAST GROWTH FACTOR-23 IS ASSOCIATED WITH HIGH-DENSITY LIPOPROTEIN IN SYSTEMIC SCLEROSIS PATIENTS

A. Alvarez de Cienfuegos[1], L. Cantero-Nieto[2], J. A. García-Gómez[3], R. Ríos Fernández[4], J. Martin Ibanez[5], M. A. González-Gay[6], N. Ortego[4]. *[1]Hospital Vega-Baja, Department of Rheumatology, Alicante, Spain*; *[2]Hospital Santa Ana, Department of Emergency, Granada, Spain*; *[3]Hospital General de Elche, Infectious Diseases Unit, Alicante, Spain*; *[4]Hospital Universitario San Cecilio, Systemic Autoimmune Diseases Unit, Granada, Spain*; *[5]IPBLN-CSIC, Institute of Parasitology and Biomedicine López-Neyra, Granada, Spain*; *[6]University of Cantabria, School of Medicine, Santander, Spain*

Background: Systemic sclerosis (SSc) is characterized by calcification, vasculopathy, and endothelial wall damage, all of which can increase the risk for atherosclerosis and cardiovascular disease. Mechanisms by which atherosclerosis is promoted in connective tissue diseases remain unknown, but is believed to be secondary to chronic inflammation, altered lipid profiles and function, autoantibodies, and endothelial dysfunction. Fibroblast growth factor-23 (FGF23) is a circulating regulator of phosphate and vitamin D metabolism and has been implicated as a putative pathogenic factor in cardiovascular disease. FGF23 could exert hormonal control on fat mass and glucose metabolism, since it shares structural similarities with the other FGF subfamily members (FGF15/19 and FGF21) that are involved in carbohydrate and lipid metabolism.

Objectives: The objectives of this study were: to compare serum FGF23 levels between SSc patients and healthy controls and to investigate possible associations between FGF23 and serum lipid profile in SSc patients.

Methods: This cross-sectional study was performed in San Cecilio Hospital, Granada (Spain) from November 2017 to May 2019. Sixty-two women with SSc and 62 age and sex matched healthy controls were enrolled in this study. All patients included in this study had normal serum creatinine (Cr) levels and met the 2013 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for SSc. Total cholesterol and triglyceride levels were determined by fully enzymatic techniques. High-density lipoprotein (HDL) was determined after precipitation of apolipoprotein B (apoB)–containing lipoproteins with magnesium sulfate and dextran sulfate. Low-density lipoprotein (LDL) was calculated using the Friedewald formula. Serum FGF23 was analyzed using ELISA.

Results: A total of 62 female patients were included in our study, with a mean (SD) age of 53 ± 10 years. The majority were Caucasian (90.5%). The mean disease duration was 8.8 ± 6.9 years. Forty-four (70.9%) patients had a limited form of the disease and 18 (29.1%) had a diffuse form.

There was no significant differences in FGF23 levels between the patients and controls (78.2 ± 60.5 vs. 80.3 ± 56.3 pg/mL, p= 0.662), but we found a statistically significant inverse relationship between FGF23 and HDL-c measurements (r= -0.27; p= 0.03) in women with SSc. In addition, in the linear regression model, higher FGF23 concentrations were associated with lower HDL-c [β = -1.45 95% CI (-2.81, -0.08); $p < 0.05$].

Conclusion: We report an association between circulating FGF23 and HDL-c in SSc female patients, representing a novel pathway linking high FGF23 to an increased cardiovascular risk.

REFERENCES:

[1] Ho M, Veale D, Eastmond C, et al. Macrovascular disease and systemic sclerosis. Ann Rheum Dis. 2000; 59(1):39–43.

[2] McMahon M, Grossman J, FitzGerald J, et al. Proinflammatory high-density lipoprotein as a biomarker for atherosclerosis in patients with systemic lupus erythematosus and rheumatoid arthritis. Arthritis Rheum. 2006; 54(8):2541–9.

[3] O'Neill SG, Giles I, Lambrianides A, et al. Antibodies to apolipoprotein A-I, high-density lipoprotein, and C-reactive protein are associated with disease activity in patients with systemic lupus erythematosus. Arthritis Rheum. 2010; 62(3):845–54.

[4] Mirza MA, Alsio J, Hammarstedt A, et al. Circulating fibroblast growth factor-23 is associated with fat mass and dyslipidemia in two independent cohorts of elderly individuals. Arterioscler Thromb Vasc Biol. 2011; 31:219–227.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.302

AB0406 ASSOCIATION OF ENDOTHELIN-1 WITH PULSE WAVE VELOCITY IN SYSTEMIC SCLEROSIS PATIENTS

A. Alvarez de Cienfuegos[1], L. Cantero-Nieto[2], J. A. García-Gómez[3], J. L. Callejas-Rubio[4], J. Martin Ibanez[5], N. Ortego[4]. *[1]Hospital Vega-Baja, Department of Rheumatology, Alicante, Spain*; *[2]Hospital Santa Ana, Department of Emergency, Granada, Spain*; *[3]Hospital General de Elche, Infectious Diseases Unit, Alicante, Spain*; *[4]Hospital Universitario San Cecilio, Systemic Autoimmune Diseases Unit, Granada, Spain*; *[5]IPBLN-CSIC, Institute of Parasitology and Biomedicine López-Neyra, Granada, Spain*

Background: Systemic sclerosis (SSc) is a multisystemic disease featured by vascular and immunological disorders along with an excessive accumulation of the components of the connective tissue that cause cutaneous sclerosis and

fibrosis of different organs. The occurrence of endothelial dysfunction together with fibrosis indicates that endothelial cell-derived factors, such as endothelin-1 (ET-1), may have an important role in the pathogenesis of SSc. The upregulation of ET-1 activates inflammatory cells and leads to nitric oxide synthase inhibition associated with arterial stiffness.

Objectives: The purpose of this study was to evaluate ET-1 serum levels in women with systemic sclerosis (SSc) compared with healthy controls and to examine possible associations between ET-1 and markers of arterial stiffness.

Methods: This cross-sectional study was performed in San Cecilio Hospital, Granada (Spain) from November 2017 to May 2019. Sixty-two women with SSc and 62 age and sex matched healthy controls were enrolled in this study. Pulse Wave Velocity (PWV) was measured non-invasively along the carotid–femoral arterial segment. Serum ET-1 was analysed using indirect enzyme-linked immunosorbent assay (ELISA).

Results: A total of 62 female patients were included in our study, with a mean (SD) age of 53 ± 10 years. The majority were Caucasian (90.5%). The mean disease duration was 8.8 ± 6.9 years. Forty-four (70.9%) patients had a limited form of the disease and 18 (29.1%) had a diffuse form.

There was a significant difference in ET-1 serum levels between SSc female patients and healthy controls (28.4 ± 10.6 vs. 21.1 ± 11.7 pg/ml, $p = 0.001$). Serum levels of ET-1 were positively associated with PWV ($r = 0.26$, $p < 0.05$), within the study group. In addition, in the linear regression model, higher ET-1 concentrations were associated with higher PWV [$\beta = 0.03$ 95% CI (0.001, 0.060); $p < 0.05$].

Conclusion: This study shows that ET-1 serum levels are associated with PWV in women with SSc. Therefore, drugs that block ET-1 may be effective in reducing large artery stiffness in women with SSc, and thus cardiovascular risk.

REFERENCES:

[1] LeRoy EC, Black C, Fleischmajer R, Jablonska S, Krieg T, Medsger TA Jr, et al. Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. J Rheumatol 1988; 15(2):202-205.

[2] Shi-Wen X, Denton CP, Dashwood MR, Holmes AM, Bou-Gharios G, Pearson JD, et al. Fibroblast matrix gene expression and connective tissue remodeling: role of endothelin-1. J Invest Dermatol 2001; 116(3):417–425.

[3] Heintz B, Dörr R, Gillessen T, Walkenhorst F, Krebs W, Hanrath P, et al. Do arterial endothelin 1 levels affect local arterial stiffness?. Am Heart J 1993; 126 (4): 987–989.

[4] McEniery CM, Qasem A, Schmitt M, Avolio AP, Cockcroft JR, Wilkinson IB. Endothelin-1 regulates arterial pulse wave velocity in vivo. J Am Coll Cardiol 2003; 42 (11): 1975–1981.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.304

AB0407 CARDIOVASCULAR BURDEN IN SYSTEMIC SCLEROSIS: QRISK3 VERSUS FRAMINGHAM FOR RISK ESTIMATION

M. Di Battista[1], S. Barsotti[1], A. Della Rossa[1], M. Mosca[1]. [1]*University of Pisa, Rheumatology Unit, Pisa, Italy*

Background: Cardiovascular (CV) diseases, namely myocardial infarction and stroke, are not among the most known and frequent complications of systemic sclerosis (SSc), but there is growing evidence that SSc patients have a higher prevalence of CV diseases than the general population [1].

Objectives: To compare two algorithms for CV risk estimation in a cohort of patients with SSc, finding any correlation with clinical characteristics of the disease.

Methods: SSc patients without previous myocardial infarction or stroke were enrolled. Traditional CV risk factors, SSc-specific characteristics and ongoing therapies were assessed. Framingham and QRISK3 algorithms were then used to estimate the risk of develop a CV disease over the next 10 years.

Results: Fifty-six SSc patients were enrolled. Framingham reported a median risk score of 9.6% (IQR 8.5), classifying 24 (42.9%) subjects at high risk, with a two-fold increase of the mean relative risk in comparison to general population. QRISK3 showed a median risk score of 15.8% (IQR 19.4), with 36 (64.3%) patients considered at high-risk. Both algorithms revealed a significant role of some traditional risk factors and a noteworthy potential protective role of endothelin receptor antagonists ($p=0.003$). QRISK3 was also significantly influenced by some SSc-specific characteristics, as limited cutaneous subset ($p=0.01$), interstitial lung disease ($p=0.04$) and non-ischemic heart involvement ($p=0.03$), with the first two that maintain statistically significance in the multivariate analysis ($p=0.02$ for both).

Conclusion: QRISK3 classifies more SSc patients at high-risk to develop CV diseases than Framingham, and it seems to be influenced by some SSc-specific characteristics. If its predictive accuracy were prospectively verified, the use of QRISK3 as a tool in the early detection of SSc patients at high CV risk should be recommended.

REFERENCES:

[1] Ngian GS, Sahhar J, Proudman SM, Stevens W, Wicks IP, Van Doornum S. Prevalence of coronary heart disease and cardiovascular risk factors in a national cross-sectional cohort study of systemic sclerosis. Ann Rheum Dis. 2012;71:1980-3.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.327

AB0408 SYSTEMIC SCLERODERMA AND ENVIRONMENTAL RISK FACTORS: IDENTIFYING ASSOCIATIONS MINING THE BIOMEDICAL LITERATURE

A. Rodriguez-Pla[1]. [1]*Mayo Clinic Scottsdale Campus, Rheumatology, Scottsdale, United States of America*

Background: A debate still exists concerning the role of occupational and environmental factors in the pathogenesis of systemic scleroderma (SSc).

Objectives: Our aim was to explore associations between SSc and environmental factors utilizing an automatic semantic interpretation of PubMed results.

Methods: The literature search string: ("systemic sclerosis" OR "scleroderma") AND ("occupational exposure" OR "environmental" OR "risk factor") was used to retrieve abstracts from the entire PubMed database, using Semantic MEDLINE 2, on 6/14/2020. This application represents a network of semantic predications (triples of the form subject-predicate (or relation) -object, e.g. Occupational Exposure *causes* Systemic Scleroderma) on a knowledge graph. Subject and object arguments of each predication are concepts from the Unified Medical Language System (UMLS) Metathesaurus and the relation is taken from the UMLS Semantic Network. The system allows for choosing the central topic ("Systemic Scleroderma"), the length of the network (3 nodes), and automatic summarization, eliminating the less informative predications.

Results: The search string retrieved 864 citations and identified 6,397 predications by using 34 types of relations. Initially, we focused our attention on the 'CAUSES' type of relation (Figure 1), displaying a network with 59 nodes and 57 edges.

The central concepts of this network, identified as having causal relationship with SSc are autoimmune diseases/autoimmunity, chemicals such as bleomycin, occupational and environmental exposure, especially silica, vinyl chloride and trichloroethylene, genes, including HLA and non-HLA genes, genetic polymorphisms, transcription factors (TFs) such as Fli1 and KLF5, and fibrosis. Eosinophilia-myalgia syndrome, toxic oil syndrome and infection were all causally linked to autoimmune diseases. Minerals were associated with occupational exposure and with autoimmune diseases. Concepts causally linked to fibrosis were rare diseases, HLA genes, other non-HLA genes, such as STAT4, IR4, IR5, TLR4, TLR7 and Rho-associated Kinase, and vinyl chloride monomer. Pathogenic factors associated with SSc were endothelial dysfunction and extracellular matrix proteins. Many of the papers in the network also suggested that hormonal factors are involved.

Conclusion: Inspection on the knowledge graphs reveals concepts central to research on the etiopathogenesis of SSc. The relations in which these concepts participate, provide more specific information. The Semantic MEDLINE graph supports the kind of patterns that underpin literature-based discovery.

Although the pathogenesis of SSc remains elusive, it is accepted that initial vascular damage driven by autoimmunity and environmental factors causes abnormalities in the vasculature resulting in the activation of fibroblasts in various organs. Silica and solvents such as trichloroethylene seem to be the most consistently suspected environmental agents in SSc.

REFERENCES:

[1] Rindflesch TC,et al. Semantic MEDLINE: An advanced information management application for biomedicine. Information Services & Use 2011;31:15-21.

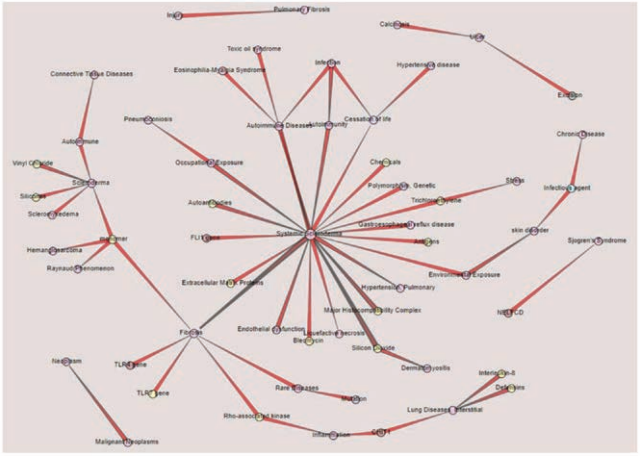


Figure 1. Semantic Network of Casual Relationships of Systemic Scleroderma.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.330

AB0409 INTRAVENOUS ILOPROST: A REGION WIDE SURVEY OF CURRENT PRESCRIBING AMONGST HOSPITALS IN THE WESSEX MULTI-DISCIPLINARY CONNECTIVE TISSUE DISEASE NETWORK

L. Parker[1], A. Mason[2], B. Davidson[2]. [1]*University Hospitals Dorset NHS Foundation Trust, Rheumatology Department, Christchurch, United Kingdom*; [2]*University Hospital Southampton NHS Foundation Trust, Rheumatology Department, Southampton, United Kingdom*

Background: Digital ulceration in systemic sclerosis is a severe and disabling aspect of this complex, multi-system disease. Traditionally, intravenous (IV) iloprost has been prescribed to treat the problem. Alternative oral medications including sildenafil and bosentan are now readily available, although NHS clinical commissioning policy is yet to be updated to reflect changes in drug costs. Use of IV iloprost across Wessex was audited to review current practice across the region.
Objectives: To compare use of IV iloprost across 7 different hospital rheumatology departments
Methods: Data was collected across 7 different NHS hospital sites using rheumatology specific pharmacy records for high cost drug prescribing and a single uniform data collection proforma, which was then analysed by 1 person to ensure uniformity of results. Case notes were reviewed retrospectively to determine diagnosis, frequency and duration of iloprost treatment, if patients had been considered for sildenafil treatment (including if sildenafil was prescribed, any cautions or contra-indications to treatment, dose and any reason for discontinuation of treatment) and if patients had been considered for bosentan treatment and if it was prescribed.
Results: 45 patients were identified currently receiving IV iloprost. 32/45 (71%) had a diagnosis of systemic sclerosis, mixed connective tissue disease (CTD) or undifferentiated CTD (to be called scleroderma group). 13/45 had other miscellaneous diagnoses which had resulted in digital ulceration. These 13 patients were excluded from further analysis relating to sildenafil or bosentan prescribing as these medications were not indicated for other causes of digital ulceration. In the scleroderma group, 27/32 (84%) had been considered for sildenafil treatment. Of these, 8/27 started and discontinued due to intolerance and 17/27 remained on sildenafil. In the scleroderma group, 9/32 had been considered for bosentan treatment, and of these 7/9 remained on bosentan.
Conclusion: The authors have identified that IV iloprost is still widely used for management of digital ulceration in rheumatology departments across seven different hospitals in Wessex. Most of this group of patients would likely be eligible for treatment with sildenafil or bosentan. Sildenafil intolerance is a challenge to management. Consideration of bosentan as a treatment option was limited in this group, and may be a cost-effective alternative to IV iloprost which would also eliminate the risk of infection associated with IV access in a potentially immunosuppressed group of patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.331

AB0410 S100A4 PLASMA LEVELS CORRELATE WITH DISEASE ACTIVITY, SKIN FIBROSIS AND INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS PATIENTS

H. Štorkánová[1,2], L. Andres Cerezo[1], S. Oreska[1,2], M. Špiritović[1,3], B. Heřmánková[1,3], M. Komarc[4], K. Pavelka[1,2], J. Vencovský[1,2], J. H. W. Distler[5], L. Šenolt[1,2], R. Bečvář[1,2], M. Tomcik[1,2]. [1]*Institute of Rheumatology, -, Prague, Czech Republic*; [2]*1st Faculty of Medicine, Charles University, Prague, Czech Republic, Department of Rheumatology, Prague, Czech Republic*; [3]*Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Department of Physiotherapy, Prague, Czech Republic*; [4]*Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Department of Methodology, Prague, Czech Republic*; [5]*University of Erlangen-Nuremberg, Erlangen, Germany, Department of Internal Medicine III and Institute for Clinical Immunology, Erlangen, Germany*

Background: In our previous study we demonstrated that S100A4 is overexpressed in scleroderma (SSc) skin, SSc fibroblasts and preclinical models of SSc in a TGF-β dependent manner. We showed that S100A4 is a new regulator of TGF-β signalling and its inhibition prevents the pro-fibrotic effects of TGF-β. Inactivation of S100A4 prevented dermal fibrosis induced by bleomycin and in Tsk-1 mice
Objectives: The aim of this study was to evaluate S100A4 in the peripheral blood of SSc patients and characterize its potential association with SSc-related features.
Methods: A total of 33 patients (29 females; mean age 52.8; disease duration 4.2 years; dcSSc/lcSSc = 8/25) who met the 2013 EULAR/ACR classification criteria for SSc and 20 healthy age- and sex-matched individuals were included in this study. Plasma levels of S100A4 were measured using ELISA (CUSABIO, Houston, USA). Data are presented as median (IQR).
Results: S100A4 plasma levels were significantly increased in SSc patients compared to healthy controls (78.6(32.3-146.5) vs. 43.4(32.3-53.4)ng/mL,p=0.011). Patients with diffuse cutaneous (dc)SSc had significantly higher levels of S100A4 than patients with limited cutaneous (lc)SSc or healthy controls (168.5(81.5-347.5) vs. 63.4(30.9-130.6),p=0.017,p=0.001, respectively). Plasma levels of S100A4 positively correlated with mRSS (r=0.556,p=0.001). Furthermore, S100A4 negatively correlated with forced vital capacity (FVC) and peripheral oxygen saturation (SpO2) (r=- 0.362,p=0.038;r=-0.414,p=0.029, respectively). S100A4 levels positively correlated with ESSG activity score (r=0.750,p<0.001). However, only correlations between S100A4 and mRSS, and ESSG activity score were approved at corrected level of statistical significance after Bonferroni's correction (p<0.01). In a prospective analysis of patients (n=40) with progressive SSc-ILD treated with 6 (n=24) or 12 (n=16) monthly i.v. pulses of cyclophosphamide (CPA, 500 mg/m^2), we observed a significant decrease in plasma S100A4 levels between the baseline samples (month 0) and blood drawn after 6 months of CPA treatment (76.3(52.9–98.6) vs. 73.2(44.4–98.6)ng/mL,p=0.013). Furthermore, baseline S100A4 levels predicted the change (m0-m6) in CRP and ESR levels after 6 months of CPA therapy (r=0.472,p=0.004;r=0.528,p=0.003, respectively).
Conclusion: We demonstrate that plasma S100A4 levels are significantly increased in SSc patients compared with healthy controls. Increased S100A4 is associated with the dcSSc subset, skin involvement, deteriorated parameters of interstitial lung disease and higher disease activity. In patients with progressive SSc-ILD, S100A4 declines after 6 months of cyclophosphamide therapy and predicts the systemic inflammatory response. These data further support our previous findings on the role of S100A4 as a regulator of TGF-β induced fibrosis in SSc.
Acknowledgements: Supported by MHCR023728, SVV–260373.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.462

AB0411 CHALLENGES IN THE MANAGEMENT OF MIXED CONNECTIVE TISSUE DISEASE: A RETROSPECTIVE ANALYSIS OF THE MCTD COHORT IN A TERTIARY REFERRAL CENTRE

A. Wanzenried[1], A. Garaiman[1], S. Jordan[1], O. Distler[1], B. Maurer[1]. [1]*University Hospital Zurich, Department of Rheumatology, Zürich, Switzerland*

Background: As a rare, complex, and heterogeneous disease, mixed connective tissue disease (MCTD) represents a challenge for clinical practice.
Objectives: We aimed to unravel potential pitfalls including correct referral diagnosis, fulfilment of diagnostic criteria, distinction from other CTDs, disease course and activity, and treatment modalities.
Methods: We analysed the prospectively collected MCTD cohort at our tertiary referral centre. The patients' medical histories were investigated for fulfilment of Sharp's (1), Kasukawa's (2), and Alarcón-Segovia's (3) diagnostic MCTD criteria. We defined overlap syndromes as simultaneous fulfilment of clinical as well as immunological criteria of two defined rheumatic diseases. Disease conversion was defined as emergence of new symptoms and autoantibodies consistent with another rheumatic disease. Remission was defined by simultaneous systemic lupus erythematosus disease activity index 2000 (SLEDAI-2 K) of 0 and European League Against Rheumatism scleroderma trial and research (EUSTAR) activity index <2.5. Disease phenotype and disease activity were monitored over time and all patients were evaluated for fulfilment of classification criteria of various connective tissue diseases.
Results: Out of 85 patients initially referred as MCTD, only one third fulfilled the diagnostic MCTD criteria. Most of the remaining patients had undifferentiated CTD (29%) or overlap syndromes (20%). In our final cohort of 33 MCTD patients, 6 (48%) also met the classification criteria of systemic sclerosis, 13 (39%) those of systemic lupus erythematosus (SLE), 6 (18%) those of rheumatoid arthritis, and 3 (9%) those of primary myositis. Over the median observation period of 4.6 (1.6, 9.9) years, only two patients (6%) underwent disease conversion from MCTD to SLE and no patient converted towards other diseases. The number of patients in remission increased from 6 (18%) to 15 (45%) due to introduction of immune modulatory treatment. Combination therapy was favoured in most cases (17 patients, 52%), whereas monotherapy was less frequent (12 patients, 36%), and only 4 (12%) patients remained without immune modulators until the end of the follow-up period. Hydroxychloroquine, prednisone, and methotrexate were the most frequently used medications in our cohort.

Conclusion: Our study showed a high risk for misdiagnosis for patients with MCTD. Phenotype conversion was a very rare event. As a multi-organ disease, MCTD required prolonged (combined) immunosuppressive therapy to achieve remission. The establishment of an international registry with longitudinal data from observational multi-centre cohorts might represent a first step to address the many unmet needs of MCTD.

REFERENCES:

[1] Sharp GC. Diagnostic criteria for classification of MCTD. In: Kasukawa R, Sharp GC, editors. Mixed connective tissue disease and anti-nuclear antibodies: proceedings of the International Symposium on Mixed Connective Tissue Disease and Anti-nuclear Antibodies, Tokyo, 29-30 August 1986. no. 719. Amsterdam: Elsevier Science Publishers B.V. (Biomedical Division); 1987. p. 23-30.

[2] Kasukawa R, Tojo T, Miyawaki S, Yoshida H, Tanimoto K, Nobunaga M, et al. Preliminary diagnostic criteria for classification of mixed connective tissue disease. In: Kasukawa R, Sharp GC, editors. Mixed connective tissue disease and anti-nuclear antibodies: proceedings of the International Symposium on Mixed Connective Tissue Disease and Anti-nuclear Antibodies, Tokyo, 29-30 August 1986. no. 719. Amsterdam: Elsevier Science Publishers B.V. (Biomedical Division); 1987. p. 41-7.

[3] Alarcón-Segovia D, Villarreal M. Classification and diagnostic criteria for mixed connective tissue disease. In: Kasukawa R, Sharp GC, editors. Mixed connective tissue disease and anti-nuclear antibodies: proceedings of the International Symposium on Mixed Connective Tissue Disease and Anti-nuclear Antibodies, Tokyo, 29-30 August 1986. no. 719. Amsterdam: Elsevier Science Publishers B.V. (Biomedical Division); 1987. p. 33-40.

Disclosure of Interests: Adrian Wanzenried: None declared, Alexandru Garaiman: None declared, Suzana Jordan: None declared, Oliver Distler Consultant of: O.D. had consultancy relationship and/or has received research funding from Abbvie, Actelion, Acceleron Pharma, Amgen, AnaMar, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, Catenion, Competitive Drug Development International Ltd, CSL Behring, ChemomAb, Curzion Pharmaceuticals, Ergonex, Ga-lapagos NV, Glenmark Pharmaceuticals, GSK, Inventiva, Italfarmaco, iQone, iQvia, Lilly, medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Target Bio Science and UCB in the area of potential treatments of scleroderma and its complications., Britta Maurer Consultant of: Boehringer-Ingelheim, Grant/research support from: AbbVie, Protagen, and Novartis Biomedical Research as well as congress support from Pfizer, Roche, Actelion, mepha, and MSD.

DOI: 10.1136/annrheumdis-2021-eular.545

AB0412 LIPID PROFILE IN IIM PATIENTS AND ITS ASSOCIATION WITH DISEASE ACTIVITY, DURATION, AND GLUCOCORTICOID TREATMENT

S. Oreska[1,2], H. Štorkánová[1,2], M. Špiritović[1,3], B. Heřmánková[3], M. Vrablik[4], K. Pavelka[1,2], L. Šenolt[1,2], H. Mann[1,2], J. Vencovský[1,2], M. Tomčík[1,2]. *[1]Institute of Rheumatology, Department of Rheumatology, Prague, Czech Republic*; *[2]1st Faculty of Medicine, Charles University, Department of Rheumatology, Prague, Czech Republic*; *[3]Faculty of Physical Education and Sport, Charles University, Department of Physiotherapy, Prague, Czech Republic*; *[4]General University Hospital and 1st Faculty of Medicine, Charles University, 3rd Department of Internal Medicine, Prague, Czech Republic*

Background: Systemic inflammation, limited mobility, and glucocorticoid treatment in idiopathic inflammatory myopathies (IIM) can have a negative impact on intermediate metabolic pathways, especially on lipid metabolism.

Objectives: The aim of this study was to assess the differences in the lipid profile of IIM patients and healthy controls (HC) and the association with disease-specific features.

Methods: 133 patients with IIM (106 females; mean age 60.3; disease duration 2.2 years; DM 47 / PM 41 / IMNM 45) and 133 age-/sex-matched HC (106 females, mean age 60.2) were included. Patients with DM and PM fulfilled the Bohan/Peter criteria for PM/DM; patients with IMNM fulfilled the ENMC criteria. Levels of selected parameters of lipid metabolism were measured in sera. In IIM patients, disease activity, damage, and muscle involvement were evaluated (MITAX, MDI, MMT-8); comorbidities and current treatment were recorded. Data are presented as median.

Results: Several differences in disease activity, the dose of glucocorticoids, prevalence of comorbidities, and serum lipid levels were observed in IIM compared to HC, and among the three subtypes of IIM; the most significant changes were observed in IMNM. All the differences in lipid profile between IIM and HC, as well as the correlations of lipid profile parameters with disease-specific features in IIM patients, are demonstrated in the table 1.

Conclusion: We have observed significant alterations in serum lipid parameters in our IIM patients compared to healthy age-/sex-matched individuals. Differences were also found among the three subtypes of IIM. These alterations were associated with laboratory parameters of disease activity and the current dose of corticosteroids.

Table 1. Lipidogram in IIM patients compared to healthy controls

Parameter of lipidogram, median	IIM (n = 133)	DM (n = 47)	PM (n = 41)	IMNM (n = 45)	HC (n = 133)	p-value IM-HC; DM-HC; PM-HC; IMNM-HC
TC (mmol/L);	**5.79**	**5.36**	**5.65**	**6.3**	**5.14**	**<0.001;** 0.135; **0.040; <0.001**
TG (mmol/L);	**2.02**	**1.91**	**1.88**	**2.27**	**1.28**	**<0.001; <0.001; 0.002; <0.001**
LDL-C (mmol/L);	**3.13**	**2.95**	**3.12**	**3.58**	**2.82**	**0.005**; 0.436; 0.131; **<0.001**
Apo-B (g/L);	**1.06**	**1.02**	**0.98**	**1.26**	**0.91**	**<0.001**; 0.160; **0.017**; **<0.001**
Non-HDL-C (mmol/L);	**4.4**	**4.25**	**4.15**	**5.1**	**3.9**	**<0.001**; 0.262; **0.040; <0.001**
Lp(a) (g/L);	**0.1**	**0.1**	**0.1**	**0.12**	**0.15**	0.098; 0.733; 0.242; **0.032**
HDL-C (mmol/L);	**1.122**	**1.13**	**1.18**	**1.36**	**1.2**	0.913; 0.917; 0.503; 0.928
Apo-A (g/L);	**1.7**	**1.76**	**1.75**	**1.68**	**1.8**	0.073; 0.782; 0.267; **0.025**
AI (log(TG/ HDL-C);	**3.85**	**3.9**	**3.85**	**3.7**	**3.15**	**0.003**; 0.425; 0.071; **0.002**

Significant correlations of lipid profile parameters and disease-specific features in all IIM patients (n=133)

Correlated parameters	Spearman's r	p-value	Correlated parameters	Spearman's r	p-value
TC: Disease duration; LD; PED; Age; CK; Myoglobin	-0.322; 0.343; 0.292; 0.193; 0.198; 0.249	<0.001; <0.001; <0.001; 0.027; 0.025; 0.007	**non-HDL-C**: Disease duration; LD; BMI; CK; Myoglobin; PED	-0.303; 0.322; 0.202; 0.214; 0.270; 0.275	<0.001; <0.001; 0.027; 0.015; 0.003; 0.002
TG: Disease duration; PED; BMI	-0.326; 0.316; 0.271	<0.001; <0.001; 0.003	**HDL-C**: CRP	-0.230	0.010
LDL-: Disease duration; LD; Age; CK; Myoglobin;	-0.310; 0.359; 0.212; 0.257; 0.289	<0.001; <0.001; 0.015; 0.003; 0.002	**Apo-A**: CRP; CK; Myoglobin	-0.293; -0.214; -0,258	<0.001; 0.016; 0.005
Apo-B: Disease duration; LD; PED; Age; BMI; MMT-8; CK; Myoglobin; Glycemia	-0.311; 0.348; 0.307; 0.220; 0.239; -0.214; 0.256; 0.307; 0.201	<0.001; <0.001; <0.001; 0.012; 0.009; 0.017; 0.004; <0.001; 0.031	**AI**: BMI	0.209	0.021

Acronyms: TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein; Apo-B, apolipoprotein B; non-HDL-C, non-high-density lipoprotein (TC minus measured HDL-C); Lp(a), lipoprotein A; HDL-C, high-density lipoprotein; Apo-A, apolipoprotein A; AI, atherogenic index of plasma = *log(TG/ HDL-C);* LD, lactate dehydrogenase; PED, current prednisolone equivalent dose; CK, creatine kinase; BMI, body mass index; MMT-8, manual muscle testing-8; CRP, C-reactive protein

Acknowledgements: AZV NV18-01-00161A, MHCR-00023728, GAUK-312218

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.816

AB0413 HIGH-RESOLUTION COMPUTED TOMOGRAPHY FOR THE SCREENING, RE-SCREENING AND FOLLOW-UP OF SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE: RESULTS OF A EUSTAR-SCTC SURVEY

C. Bruni[1,2], L. Chung[3], A. M. Hoffmann-Vold[4], S. Assassi[5], A. Gabrielli[6], D. Khanna[7], E. Bernstein[8], O. Distler[2]on behalf of European Scleroderma Trials and Reserach (EUSTAR) group and Sclerodermia Clinical Trial Consortium (SCTC).. *[1]Careggi University Hospital, Experimental and Clinical Medicine, Division of Rheumatology, Firenze, Italy*; *[2]University Hospital of Zürich, University of Zurich - Department of Rheumatology, Zürich, Switzerland*; *[3]Stanford University School of Medicine and Palo Alto VA Health Care System, Department of Medicine and Dermatology, Division of Immunology and Rheumatology, Palo Alto (CA), United States of America*; *[4]Oslo University hospital, Rheumatology, Oslo, Norway*; *[5]The University of Texas Health Science Center at Houston, Division of Rheumatology, Houston, United States of America*; *[6]Marche Polytechnic University Faculty of Medicine, Clinical and Molecular sciences, Ancona, Italy*; *[7]University of Michigan, Scleroderma Program, Ann Arbor, United States of America*; *[8]Columbia University Irving Medical Center, Division of Rheumatology, Department of Medicine, New York, United States of America*

Background: High-resolution computed tomography (HRCT) is the gold standard diagnostic test for Interstitial lung disease (ILD), a significant cause of morbidity and mortality in systemic sclerosis (SSc). Different algorithms have been proposed for the screening of SSc-ILD, including the use of pulmonary function tests (Forced Vital Capacity - FVC, Lung Diffusion of Carbone Monoxyde - DLCO). A prior survey reported that 50-66% of general rheumatologists and SSc experts ordered HRCT for ILD screening in newly diagnosed SSc patients (1).
Objectives: Given the recent availability of on-label treatment for SSc-ILD (2), the publication of consensus recommendations for the identification of SSc-ILD (3) and recent awareness programs for the use of HRCT to detect SSc-ILD, we aimed to re-evaluate the use of HRCT for screening, re-screening and follow-up of SSc-ILD.
Methods: An invitation was sent to the European Scleroderma Trials and Research (EUSTAR) and Scleroderma Clinical Trials Consortium (SCTC) members, also advertised through social media. Answers were recorded between Nov 25th and Dec 31st 2020. Questions were asked on the use of chest HRCT at baseline, the re-screening of patients with a negative baseline HRCT and the follow-up of HRCT positive SSc-ILD patients. When HRCT was not routinely requested, additional details were collected about the parameters guiding its use. The results of the survey were tested for association with geographical origin, medical specialty, working environment, SSc referral institute and scientific group membership of the responders, using Chi-squared test.
Results: 205/630 (32.5%) physicians replied to the survey. Participants were widely distributed in terms of geographical origin (130 Europe, 23 Asia, 23 North America, 31 other continents), medical specialty (156 rheumatology, 21 internal medicine, 14 clinical immunology, 14 other), working environment (176 University Hospital, 12 community hospital, 17 other), SSc dedicated clinic (179 referral and 26 non-referral) and scientific group membership (98 EUSTAR, 42 SCTC, 42 EUSTAR and SCTC, 23 not declared).
At SSc diagnosis, 95.7% of responders would perform HRCT: 66.7% as routine screening for ILD (67,4% of SSc referral and 62% for non-referral physicians) and 29% for diagnostic purposes (among the latter, if crackles on auscultation – 92.5%, FVC<80% predicted - 86.6%, FVC±DLCO relative decline reaching the current definition of ILD progression, 86.6% or dyspnea at rest/exercise - 85.1/83.3%).
During follow-up, 78.8% of responders would repeat an HRCT in baseline negative cases: 20.3% as a yearly routine screening and 64.5% for diagnostic aims (decision on the latter group was more frequently driven by FVC±DLCO relative decline indicative of ILD progression– 90.6%, new onset or worsening of dyspnoea at rest/exercise – 80.5/86.6%, new onset or worsening of lung crackles on auscultation – 82.6%).
Finally, 94.5% of responders would repeat a chest HRCT after SSc-ILD diagnosis: 36.8% as a yearly routine and 56.7% according to clinical evaluation (driven by new FVC±DLCO relative decline based ILD progression – 90.8%, new onset or worsening of dyspnoea at rest/exercise – 83.2/81.7%; 5.2% to evaluate treatment effects). We found no difference in the distribution of answers among groups.
Conclusion: The use of baseline HRCT for the screening of SSc-ILD has slightly increased in non-referral and remained stable in referral centers compared to previous surveys, indicating that the implementation of guidelines might be successful and awareness programs should be continued. In addition, we provide new data on use of HRCT in re-screening and follow-up. The development of validated algorithms to further support the appropriate application of HRCT at follow-up is highly needed.
REFERENCES:
[1] Bernstein EJ et al. Arthritis Rheumatol. 2018 Jun;70(6):971-972.
[2] Distler O et al. N Engl J Med. 2019 Jun 27;380(26):2518-2528.
[3] Hoffmann-Vold AM et al. The Lancet Rheumatology, Volume 2, Issue 2, e71 - e83.
Disclosure of Interests: Cosimo Bruni Speakers bureau: Actelion, Consultant of: Eli Lilly, Grant/research support from: Foundation for Research in Rheumatology (FOREUM), Gruppo Italiano Lotta alla Sclerodermia (GILS), Fondazione Italiana per la Ricerca sull'Artrite (FIRA), New Horizon Fellowship, European Sclerodermia Trial and Reserach (EUSTAR) Group., Lorinda Chung Consultant of: Boehringer Ingelheim, Eicos, Mitsubishi Tanabe, Reata., Anna-Maria Hoffmann-Vold Consultant of: Actelion, ARXX therapeutics, Bayer, Boehringer-Ingelheim, Medscape, MSD, Lilly, Roche, Shervin Assassi Speakers bureau: Integrity Continuing Education, Consultant of: Boehringer Ingelheim, Novartis, and Corbus, Armando Gabrielli: None declared, Dinesh Khanna Consultant of: Acceleron, Actelion, Abbvie, Amgen, Bayer, Boehringer Ingelheim, CSL Behring, Corbus, Gilead, Galapagos, Genentech/Roche, GSK, Horizon, Merck, Mitsubishi Tanabe Pharma, Sanofi-Aventis, and United Therapeutics Leadership, Grant/research support from: NIH, Immune Tolerance Network, Bayer, BMS, Horizon, Pfizer, Employee of: Equity position – Chief Medical Officer, Eicos Sciences, Inc., Elana Bernstein Consultant of: Boehringer Ingelheim, Oliver Distler Consultant of: Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB., Grant/research support from: Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143).
DOI: 10.1136/annrheumdis-2021-eular.849

AB0414 CROSS-CULTURAL ADAPTATION, CONVERGENT VALIDITY, AND RELIABILITY OF THE TURKISH VERSION OF THE COCHIN 17-ITEM SCLERODERMA FUNCTIONAL SCALE

N. G. Tore[1], D. Oskay[1], A. Avanoglu Guler[2], A. Tufan[2]. [1]*Gazi University, Physiotherapy and Rehabilitation, Ankara, Turkey*; [2]*Gazi University, Internal Medicine, Ankara, Turkey*

Background: The Cochin 17-item Scleroderma Functional (CSF-17) Scale is a patient-reported outcome measure evaluating activities and participation in patients with systemic sclerosis (SSc).
Objectives: The aim of the present study was to translate and cross-culturally adapt the CSF-17 into the Turkish language and investigate its convergent validity and reliability in Turkish-speaking patients with SSc.
Methods: The CSF-17 was cross-culturally adapted according to Beaton's guideline. Participants completed CSF-17 Scale, Scleroderma Health Assessment Questionnaire (SHAQ), Short Form-12 (SF-12) Health Survey and Hospital Anxiety and Depression Scale (HADS). Internal consistency and test-retest reliability were determined interpreting Cronbach's alpha and Intraclass Correlation Coefficient (ICC) values, respectively. Convergent validity was tested using Pearson's correlation coefficient.
Results: Fifty-six patients with SSc were enrolled in the study. Cronbach's alpha and ICC values of the CSF-17 total score were found to be as 0.963 and 0.958, respectively, indicating excellent reliability. As for the convergent validity, it was determined that CSF-17 total score has a good correlation with SHAQ. Correlations of subscales of CSF-17 with subscales of SF-12 and HADS ranged from poor to moderate (Table 1).
Conclusion: Tukish version of CSF-17 met the set criteria of reliability and convergent validity. According to the results of the analysis, it was concluded that the Turkish version of the CSF-17 is a reliable and valid tool for Turkish-speaking SSc patients.
REFERENCES:
[1] Daste C, Abdoul H, Foissac F et al. Development of a new patient-reported outcome measure to assess activities and participation in people with systemic sclerosis: the Cochin 17-item Scleroderma Functional scale. British Journal of Dermatology 2020; 183:710-718.
[2] Beaton DE, Bombardier C, Guillemin F et al. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine 2000; 25(24):3186-3191.
[3] Karadag DT, Karakas F, Tekeoglu S et al. Validation of Turkish version of the Scleroderma Health Assessment Questionnaire. Clin Rheumatol, 2019,38(7):1917-1923.
[4] Ware Jr J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med. Care, 1996,34:220-233.
[5] Zigmond A, Snaith R. The hospital anxiety and depression scale. Acta Psychiatr Scand, 1983,67:361-370.
[6] Terwee CB, Bot SD, de Boer MR et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol, 2007,60:34–42.

Table 1. Convergent validity of the CSF-17

Scales	CSF-17		
	Section A	Section B	Total
SHAQ	0.680**	0.640**	0.702**
HADS-A	0.405*	0.472**	
HADS-D	0.460**	0.605**	
SF-12 MCS	-0.482**	-0.491**	
SF-12 PCS	-0.745**	-0.700**	

CSF-17: Cochin 17-item Scleroderma Functional scale, SHAQ: Scleroderma Health Assessment Questionnaire, HADS-A: Hospital Anxiety and Depression Scale-Anxiety, HADS-D: Hospital Anxiety and Depression Scale-Depression, SF 12 MCS: Short Form-12 Mental Component Score, SF-12 PSC: Short Form-12 Physical Component Score.*p<0.05, **p<0.001

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.865

AB0415

ANXIETY AND DEPRESSION IN SSc – ASSESSING FUNCTION, QUALITY OF LIFE AND GASTROINTESTINAL INVOLVEMENT

B. Samões[1], D. Fonseca[1], T. Beirão[1], M. Guerra[2], R. Vieira[1], F. Campos Costa[1], T. Videira[1], A. Aleixo[1], P. Pinto[1]. [1]*Centro Hospitalar Vila Nova de Gaia/Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; [2]*Centro Hospitalar Universitário Cova da Beira, Rheumatology, Covilhã, Portugal*

Background: Systemic Sclerosis (SSc) is a chronic disease with multi-organ manifestations that may contribute to disability and low quality of life.[1] Therefore, anxiety and depression are more frequent in SSc patients than in general population.[2]
Objectives: To assess the prevalence of anxiety and depression in a SSc cohort and to evaluate its correlation with function, quality of life and assessment of gastrointestinal (GI) involvement scores.
Methods: A cross-sectional study was conducted evaluating a cohort of SSc patients. All patients answered to the Hospital Anxiety and Depression Scale (HADS) questionnaire. A cut-off score < 8 was considered normal. Health Assessment Questionnaire (HAQ), Scleroderma HAQ (SHAQ), 36-Item Short Form Health Survey (SF-36), EuroQol-5D (EQ-5D) and University Of California, Los Angeles, Scleroderma Clinical Trials Consortium Gastrointestinal Scale (UCLA SCTC GIT) 2.0 questionnaires were also obtained. Clinical data was obtained and analyzed.
Results: We included 20 patients, 17 females [n = 17 (85%)], median (min, max) age was 52.5 (28, 75) years-old. Regarding disease classification, 13 (65%) had limited SSc, 4 (20%) had diffuse SSc and 3 (15%) had early SSc. A score ≥ 8 was found in 14 (70%) patients on HADS-A [median (min, max) = 9 (2, 19)] and in 12 (60%) patients on HADS-D [median (min, max) = 8 (1, 15)]. Depressive patients had significantly worst scores on the measures of function, such as HAQ and lung and gastrointestinal involvements and patient global assessment of SHAQ, of quality of life, such as EQ-5D and physical functioning, role physical, bodily pain, vitality, social functioning and mental health domains of SF-36, and on the UCLA SCTC GIT 2.0 scale. Anxious patients had significantly worst scores on social functioning and mental health domains of SF-36 and on the UCLA SCTC GIT 2.0 scale (Table 1).
Conclusion: The prevalence of depression and anxiety on SSc patients is high and should not be neglected. Overall disability and multiorgan manifestations, particularly GI involvement, may contribute to a low quality of life and consequently to depression and anxiety.
REFERENCES:
[1] Firestein & Kelley's Textbook of Rheumatology 2-Volume Set, 11th Edition
[2] Brett D. Thombs et al. Depression in Patients With Systemic Sclerosis: A Systematic Review of the Evidence. Arthritis & Rheumatism (Arthritis Care & Research) Vol. 57, 2007, pp 1089–1097

Table 1. Function, quality of life and gastrointestinal (GI) involvement assessment according to HADS score.

Results, median [min, max]	HADS-D ≥ 8 (n = 12)	HADS-D < 8 (n = 8)	P-value	HADS-A ≥ 8 (n = 14)	HADS-A < 8 (n = 6)	P-value
SHAQ						
- GI involvement	26.5 [0, 90]	2 [0, 40]	**0.009**	18.5 [0, 90]	2.5 [0, 40]	0.091
- Lung involvement	48.5 [5, 90]	2.5 [0, 30]	**0.001**	18 [0, 90]	3 [0, 65]	0.126
- Patient global assessment	67.5 [30, 100]	4 [0, 85]	**0.011**	53.5 [2, 100]	41.5 [0, 85]	0.509
HAQ	1.375 [0.5, 2]	0.1875 [0, 1]	**0.001**	1.25 [0, 2]	0.875 [0, 1.125]	0.147
EQ5D	0.3667 [-0.0573, 0.6937]	0.6752 [0.2870, 1]	**0.006**	0.4640 [-0.0573, 0.7667]	0.6752 [0.287, 1]	0.075
SF36						
- Physical functioning	25 [15, 75]	75 [50, 100]	**0.001**	40 [15, 100]	72.5 [25, 85]	0.106
- Role physical	31.25 [0, 75]	72.875 [31.25, 100]	**0.025**	37.5 [0, 100]	65.625 [31.25, 100]	0.214
- Bodily pain	41 [0, 74]	68 [20, 88]	**0.011**	41 [0, 88]	61.5 [20, 74]	0.428
- Vitality	25 [0, 43.75]	65.625 [25, 75]	**0.001**	37.5 [0, 75]	65.625 [12.5, 75]	0.135
- Social functioning	37.5 [12.5, 87.5]	87.5 [50, 100]	**0.002**	50 [12.5, 100]	87.5 [87.5, 100]	**0.003**
- Mental health	45 [25, 80]	65.7 [51.4, 85]	**0.012**	45 [25, 75]	77.5 [51.4, 85]	**0.005**
UCLA SCTC GIT 2.0						
- Reflux	0.38 [0, 1.25]	0 [0, 1.25]	**0.024**	0.25 [0, 1.25]	0 [0, 1]	0.139
- Distension	1 [0.5, 2]	0.25 [0, 1.5]	**0.017**	1 [0.25, 2]	0.125 [0, 1]	**0.024**
- Total	0.44 [0.1, 0.99]	0.04 [0, 0.97]	**0.010**	0.34 [0.04, 0.99]	0.02 [0, 0.44]	**0.018**

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1166

AB0416

THE IMPACT OF FATIGUE ON SYSTEMIC SCLEROSIS PATIENTS

B. Samões[1], D. Fonseca[1], T. Beirão[1], M. Guerra[2], R. Vieira[1], F. Campos Costa[1], T. Videira[1], A. Aleixo[1], P. Pinto[1]. [1]*Centro Hospitalar Vila Nova de Gaia/Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; [2]*Centro Hospitalar Universitário Cova da Beira, Rheumatology, Covilhã, Portugal*

Background: Fatigue is a frequent and commonly undervalued symptom among rheumatic disease, including Systemic Sclerosis (SSc).[1,2]
Objectives: To determine the prevalence of severe fatigue in a SSc cohort and to evaluate how it correlates with disability, quality of life and mental illness.
Methods: A cross-sectional study was conducted evaluating a cohort of SSc patients. Fatigue was evaluated using Functional Assessment Chronic Illness Therapy (Fatigue) (FACIT-F) questionnaire. A value < 30 was defined as severe fatigue. Health Assessment Questionnaire (HAQ), Scleroderma HAQ (SHAQ), 36-Item Short Form Health Survey (SF-36), EuroQol-5D (EQ-5D) and Hospital Anxiety and Depression Scale (HADS) questionnaires were also filled. Clinical data was obtained and analysed.
Results: We included 20 patients, 17 females [n = 17 (85%)], median (min, max) age was 52.5 (28, 75) years-old. Regarding disease classification, 13 (65%) had limited SSc, 4 (20%) had diffuse SSc and 3 (15%) had early SSc. The median FACIT-F score was 34 (3, 48). The prevalence of severe fatigue was 40% (n = 8). Fatigue had a moderate negative correlation with HAQ (τ = -0.641; p < 0.001) and a weak negative correlation with lung (τ = -0.345; p = 0.039) and gastrointestinal (τ = -0.419; p = 0.011) involvements and with patient global assessment (τ = -0.325; p = 0.047) subtopics of SHAQ. A moderate positive correlation was found between FACIT-F and EQ-5D (τ =0.625; p < 0.001) and physical functioning (τ = 0.560; p = 0.001) and vitality (τ = 0.777; p < 0.001) domains of SF-36. The remaining SF-36 domains had a weak positive correlation with FACIT-F (Table 1). Regarding mental illness, there was a moderate negative correlation between FACIT-F and HADS-D (τ = -0.638; p < 0.001) and HADS-A (τ =-0.535; p = 0.001).
Conclusion: Severe fatigue is frequent among SSc patients. The greater the fatigue, the greater the disability, the lower the quality of life and the worse the score on the scale of depression and anxiety.
REFERENCES:
[1] F. Basta, A. Afeltra, D.P.E. Margiotta. Fatigue in systemic sclerosis: a systematic review. Clin Exp Rheumatol 2018; 36 (Suppl. 113): S150-S160
[2] Sarah Hewlett, Emma Dures, And Celia Almeida. Measures of Fatigue. Arthritis Care & Research Vol. 63, No. S11, November 2011, pp S263–S286

Table 1. Correlation of FACIT-F with measures of disability, quality of life and mental illness

Variables	Kendall's τ coefficient	p-value
HAQ	-0.641	**0.000**
SHAQ		
- GI involvement	-0.345	**0.039**
- Lung involvement	-0.419	**0.011**
- Vascular involvement	-0.215	0.192
- Digital ulcers	0.102	0.549
- Patient global assessment	-0.325	**0.047**
EQ-5D	0.625	**0.000**
SF-36		
- Physical functioning	0.560	**0.001**
- Role physical	0.491	**0.003**
- Bodily pain	0.463	**0.006**
- General health	0.341	**0.045**
- Vitality	0.777	**0.000**
- Social functioning	0.443	**0.009**
- Role emotional	0.350	**0.041**
- Mental health	0.376	**0.024**
HADS-D	-0.638	**0.000**
HADS-A	-0.535	**0.001**

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1176

AB0417

COMPARATIVE ANALYSIS OF THE FREQUENCY OF GASTRO-INTESTINAL SYMPTOMS IN THE CLINICAL EVALUATION VERSUS WITH UCLA SCTC GIT 2.0

B. Samões[1], D. Fonseca[1], R. Vieira[1], T. Videira[1], A. Aleixo[1], P. Pinto[1], M. Guerra[2]. [1]*Centro Hospitalar Vila Nova de Gaia/Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; [2]*Centro Hospitalar Universitário Cova da Beira, Rheumatology, Covilhã, Portugal*

Background: It is estimated that the gastrointestinal (GI) tract is involved in about 90% of patients with Systemic Sclerosis (SSc).[1] The UCLA Scleroderma Clinical Trials Consortium Gastrointestinal Tract 2.0 (UCLA SCTC GIT 2.0) questionnaire has been validated in several countries as a useful tool in the assessment of GI symptoms in this pathology.[2]
Objectives: To assess whether the application of the questionnaire has an added value in clinical practice by comparing the frequency of GI symptoms found during the clinical evaluation in the consultation vs. application of the questionnaire.
Methods: A cross-sectional study was carried out in a cohort of patients with SSc. During the consultation, patients were asked about the presence of GI symptoms and the UCLA SCTC GIT 2.0 questionnaire was handed in for completion. Subgroups that analyse reflux, bloating, dirt, diarrhea and constipation were evaluated and their responses were transformed into dichotomous variables (present/absent). Clinical data was obtained and analysed.
Results: 27 patients were included, most of them female [n = 23 (85.2%)], with an average age of 53.3 ± 13.5 years. All patients met the classification criteria of Leroy/Medsger of 2001 or ACR/EULAR of 2013: 14 (51.9%) had limited ES, 6 (22.2%) had Overlap Syndrome, 4 (14.8%) had diffuse ES and 3 (11.1%) had early SS. The prevalence of symptoms in all evaluated subgroups was higher in the questionnaire than in the clinical evaluation, with a statistically significant difference in the reflux subgroup [n = 16 (59.3%) vs. n = 13 (48.1%), p = 0.018]. In the remaining subgroups, this difference, although not statistically significant, was also found [abdominal distension n = 20 (74.2%) vs. n = 1 (3.7%), p = 1.0; dirt n = 2 (7.4%) vs. n = 0 (0%); diarrhea n = 22 (91.7%) vs. n = 3 (11.1%), p = 1.0; constipation n = 11 (40.7%) vs. n = 4 (14.8%), p = 0.273]. In the clinical evaluation, 12 patients said they were asymptomatic from the GI point of view, but all of them reported some GI symptoms when filling out the questionnaire. The subgroups in which the disagreement between the answers during the clinical evaluation and the filling out of the questionnaire were more frequent were distension [n = 19 (70.4%) and diarrhea [n = 19 (79.2%)].
Conclusion: The results of the present study reinforce the usefulness of the UCLA SCTC GIT 2.0 questionnaire, usually more applied in clinical trials, in clinical practice, concluding that it allows to find more GI symptoms in patients with SSc than the clinical evaluation in a consultation, this difference being statistically significant in the subgroup that evaluates reflux. The considerable difference found in the subgroups that assess symptoms of the low GI tract, such as diarrhea and constipation, although non statistical significant, may be due to the fact that the patient does not feel comfortable talking about it, a struggle that can be overcome with application of the questionnaire. On the other hand, this tool can also be a means of quantifying the severity of symptoms, monitoring their progress and making the consultation time more profitable. More studies with larger samples are needed to continue studying its role in clinical practice.
REFERENCES:
[1] Kirby DF and Chatterjee. Evaluation and management of gastrointestinal manifestations in scleroderma. Curr Opin Rheumatol 2014, 26:621–629
[2] Pope J. Measures of Systemic Sclerosis (Scleroderma). Arthritis Care & Research Vol. 63, No. S11, November 2011, pp S98–S111
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1177

AB0418 SHEAR WAVE ELASTOGRAPHY FOR THE ASSESSMENT OF LIVER FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS AND SYSTEMIC SCLEROSIS/ PRIMARY BILIARY CHOLANGITIS OVERLAP COMPARED TO PRIMARY BILIARY CHOLANGITIS

V. Korendovych[1], J. G. Rademacher[1], G. Petzold[2], P. Korsten[1].
[1]Universitätsmedizin Göttingen, Department of Nephrology and Rheumatology, Göttingen, Germany; *[2]Universitätsmedizin Göttingen, Department of Gastroenterology, Gastrointestinal Oncology and Endocrinology, Göttingen, Germany*

Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by vasculopathy and skin as well as organ fibrosis. The lungs, skin, and gastrointestinal care frequently affected. Primary biliary cholangitis (PBC) is an autoimmune disease of the liver associated with potential progression to liver fibrosis. More recently, these two disorders have been described as an overlapping entity, especially in patients with limited, anti-centromere (CENP-B) positive SSc (1). Here, we report the first results of a pilot study of shear wave elastography (SWE) in patients with SSc and SSc/PBC compared to PBC patients.
Objectives: To assess liver stiffness in patients with SSc, SSC/PBC overlap, and PBC with shear wave elastography.
Methods: We analyzed a sample of 10 SSc to 11 PBC patients. In all patients, a baseline US examination of the liver and liver stiffness measurement by 2D SWE were performed using a GE logiq E10 ultrasound machine. Normal values for SWE in healthy people have recently been published (2). Liver stiffness measurement was performed according to the recommendations of the manufacturer and the recommendations of the current "EFSUMB Guideline and Recommendation on the Clinical Use of Liver Elastography" (3). In addition, age, body mass index (BMI), and antibody profiles were assessed.
Results: Of 8 SSc patients without PBC, 6 were anti-CENPB pos., 1 had Scl70, and 1 Pm/Scl antibody. Median age was 59.5 (47-71). Median BMI was 23.1 (19.6-25). 1 patient had SSc/PBC overlap, 1 had hepatic steatosis. 1 was positive for CENP-B/AMA-M2 antibodies, the other patient was Scl70 positive. Median age of these 2 patients was 55.5 (55-56), BMI was 23.86 (20.9-26.8). 11 patients with PBC were positive for AMA-M2 antibodies, median age was 58 (41-78) years, BMI was 27.8 (15.8-50.3). The differences were not statistically different. Liver stiffness is expressed in kPa. Measurements had an interquartile range/median ratio <30%, indicating sufficient quality of the measurement. Liver stiffness was higher in patients with SSc/PBC overlap/hepatic steatosis (9.4±0.18, **p=0.0133) and PBC alone (7.359±2.51, **p=0.0163) compared to SSc alone (4.526±0.89 kPa). The results indicate that PBC is the main driver of liver stiffness in patients with SSc, and SSc alone may not necessarily lead to an increased liver stiffness (figure 1).

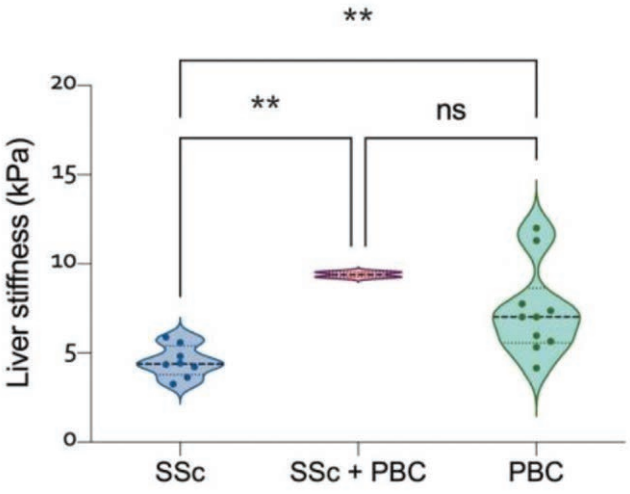


Figure 1.

Conclusion: Our results indicate that SWE is a useful tool in for the non-invasive assessment of liver stiffness in SSc and SSc/PBC overlap. We will further increase the sample size, especially of patients with SSc/PBC overlap. Of note, other liver diseases, such as hepatic steatosis, have to be kept in mind when SWE is performed as they may contribute to liver stiffness.
REFERENCES:
[1] Lepri G, Randone SB, Cerinic MM, Allanore Y. Systemic sclerosis and primary biliary cholangitis: An overlapping entity?: Journal of Scleroderma and Related Disorders [Internet]. 2018 Oct 25 [cited 2020 Jun 17]; Available from: https://journals.sagepub.com/doi/10.1177/2397198318802763
[2] Petzold G, Hofer J, Ellenrieder V, Neesse A, Kunsch S. Liver Stiffness Measured by 2-Dimensional Shear Wave Elastography: Prospective Evaluation of Healthy Volunteers and Patients With Liver Cirrhosis. J Ultrasound Med. 2019 Jul;38(7):1769–77.
[3] Dietrich CF, Bamber J, Berzigotti A, Bota S, Cantisani V, Castera L, et al. EFSUMB Guidelines and Recommendations on the Clinical Use of Liver Ultrasound Elastography, Update 2017 (Long Version). Ultraschall Med. 2017 Aug;38(4):e48.
Disclosure of Interests: Viktor Korendovych: None declared, Jan-Gerd Rademacher: None declared, Golo Petzold: None declared, PETER KORSTEN Speakers bureau: Abbvie, Pfizer, Boehringer-Ingelheim, Novartis, Chuigai, Sanofi, GSK, all unrelated., Consultant of: Abbvie, Pfizer, Boehringer-Ingelheim, Novartis, Chuigai, Sanofi, GSK, Gilead, Lilly, all unrelated., Grant/research support from: GSK, unrelated to this study.
DOI: 10.1136/annrheumdis-2021-eular.1212

AB0419 ACCESS TO TREATMENT FOR RAYNAUD'S PHENOMENON AND DIGITAL ULCERS FOR PATIENTS WITH SYSTEMIC SCLEROSIS DOESN'T FOLLOW EULAR/EUSTAR GUIDELINES

L. Martin Calderon[1], M. Baron[2], J. Pope[3]on behalf of Canadian Scleroderma Research Group (CSRG). *[1]Western University, Medicine, London, Canada*;

[2]McGill University, Rheumatology, Montreal, Canada; [3]Western University, Rheumatology, London, Canada

Background: Patients with Raynaud's Phenomenon (RP) from systemic sclerosis (SSc) may experience severe complications. Digital ulcers (DUs), occur in approximately half the patients with SSc, and cause hand dysfunction, severe pain, and decreased quality of life. DUs lead to increased healthcare utilization and systemic economic burden through hospitalizations, ED visits, and ambulatory services (1). However, access to medications such as PDE5 inhibitors and prostacyclins that are within the EULAR/EUSTAR SSc guidelines (2) in a country with global health care but patchy pharmacare such as Canada has not been studied.

Objectives: The purpose of this study was to elucidate the access to treatment of medications for RP and DU in patients with SSc in Canadian provinces through identifying the provincial and private insurance coverage of PDE5 inhibitors (PDE5i) and prostanoids, the timelines and procedures of requesting these medications, and the process of administering IV prostanoids if required for patient care.

Methods: We designed an online survey and collected data through the Survey Monkey platform. The survey was administered to rheumatologists affiliated with the Canadian Scleroderma Research Group (CSRG) from December 2020 to January 2021. Responders were asked to report if the province or private insurance automatically provided PDE5i for patients with RP and DU or if a dedicated process was required to attain these medications. Additionally, responders were asked to describe the process of administering Iloprost, Epoprostenol and Alprostadil and the barriers inherent to their administration. Of note, there is no DIN number for Iloprost in Canada so every time it is used there must be an application to Health Canada.

Results: The survey was completed by 100% of CSRG researchers (17/17), representing 8 provinces in Canada. None of the provincial governments provided coverage for PDE5i without special requests that were adjudicated on a case by case basis with approximately half the provinces paying for PDE5i upon special request if a patient was eligible for provincial drug insurance (ex elderly, youths, low income families). Two provinces, Quebec and Saskatchewan, provided PDE5i "all the time". Whereas NS, MB, ON, BC, and AB provided them "sometimes"; NFLD provided them "never". Provincial governments and private insurance fulfilled requests "within 1 month" 62% of the time and the other requests took longer to be answered. Private insurance approved coverage with special request in AB, MB, QC, ON, and NS. Respondents described administration of IV prostanoids as "inconsistent", requiring "a lot of work", and that patients in most jurisdictions be admitted as in-patients for provinces to cover these medications.

Conclusion: Most jurisdiction within Canada do not provide coverage for PDE5i and the process to obtain access for patients is delayed, non-uniform, and often not approved. Intravenous prostanoid infusions are difficult to obtain and have system barriers. Advocacy and cost effectiveness data should be used to advocate for access to medications that are recommended within SSc recommendations.

REFERENCES:

[1] Morrisroe K, et al. Digital ulcers in systemic sclerosis: their epidemiology, clinical characteristics, and associated clinical and economic burden. Arthritis research & therapy. 2019 Dec;21(1):1-2.

[2] Kowal-Bielecka O, et al. Update of EULAR recommendations for the treatment of systemic sclerosis. Annals of the rheumatic diseases. 2017 Aug 1;76(8):1327-39.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1265

AB0420

CIRCULATING MONOCYTES HAVE DISTINCT PHYSICAL PROPERTIES THAT CORRELATE WITH DISEASE ACTIVITY AND SEVERITY AND PREDICT PROGRESSION IN SYSTEMIC SCLEROSIS

A. E. Matei[1], K. Markéta[2], A. H. Györfi[1], E. Boxberger[1], D. Soteriou[2], M. Papava[1], J. Muth[1], M. Kräter[2,3], G. Schett[1], J. Guck[2,3], J. H. W. Distler[1]. [1]Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology; 2Deutsches Zentrum für Immuntherapie (DZI), Erlangen, Germany; [2]Max Planck Institute for the Science of Light & Max-Planck-Zentrum für Physik und Medizin, Guck Division, Erlangen, Germany; [3]Center for Molecular and Cellular Bioengineering,Technische Universität Dresden, Biotechnology Center, Dresden, Germany

Background: Systemic sclerosis (SSc) is associated with high morbidity and is one of the autoimmune rheumatic diseases with the highest mortality. However, tools to evaluate disease activity, response to treatment or to predict disease progression are scarce. Dysregulated immune responses are major pathogenic players at the onset and in the progression of SSc. Recent evidence demonstrates that mechanical properties of circulating leukocytes reflect their states and functions, and during activation ensure their adaptation to the changing physical requirements (e.g. softening to extravasate and migrate in the tissues) (1). Real-time fluorescence and deformability cytometry (RT-FDC) is a novel technique that allows the identification of cells from a heterogenous population by marker expression, with their subsequent mechanical phenotyping in a high-throughput manner (2, 3).

Objectives: Here we characterized the physical properties of circulating immune cells in SSc patients, aiming to identify disease-related changes in their phenotypes, clinical correlates of these changes and their potential to predict disease progression.

Methods: 51 patients fulfilling the 2013 ACR/EULAR classification criteria for SSc and 17 age- and sex-matched healthy controls were included in the study. Blood was collected from the donors between 05.2019 and 10.2020. Peripheral blood mononuclear cells (PBMCs) were isolated and stained with antibodies against major circulating lymphoid ($CD8^+$, $CD4^+$ T cells, B cells, NK cells, NKT-like cells) and myeloid subpopulations (classical, intermediate and inflammatory monocytes, conventional dendritic cells and plasmacytoid dendritic cells). Each subpopulation was identified in RT-FDC by standard gating based on its marker expression and its area, deformation and apparent Young's modulus (a measure of cell stiffness) were determined. The analysis was conducted using a custom Python script. For the patients included, demographic and clinical data were collected at every visit. Correlations with clinical parameters were analyzed in R.

Results: All three subpopulations of monocytes identified by expression of HLA-DR, CD14 and/or CD16 had higher deformation and cross-sectional area in SSc patients as compared to healthy controls. From the SSc patients, monocytes had higher deformation and area in those with diffuse cutaneous SSc, extensive lung fibrosis and active disease as compared to those with limited cutaneous SSc, limited lung fibrosis and stable disease, respectively. Moreover, monocyte deformation and area significantly correlated with the EUSTAR activity index, with mRSS, with the extent of lung involvement on HR-CT (positive correlation), with DLCO and FVC (negative correlation). Follow-up data collected one year after the measurements showed that a higher monocyte deformation and cross-sectional area at baseline predicts future progression of lung disease, defined according to the INBUILD study, as well as future progression of skin fibrosis.

Conclusion: We demonstrated that circulating subsets of monocytes in SSc patients show an increase in deformation and cross-sectional area, that these changes correlate with current disease activity and can identify patients with high risk of future progression of skin or lung fibrosis. These changes might reflect an activated state of circulating monocytes in SSc that facilitate their tissue migration. Mechanical phenotyping of monocytes by RT-FDC might thus serve as a useful tool for clinical evaluation of SSc patients.

REFERENCES:

[1] Bashant KR, Toepfner N, Day CJ, Mehta NN, Kaplan MJ, Summers C, et al. The mechanics of myeloid cells. Biol Cell. 2020;112(4):103-12.

[2] Otto O, Rosendahl P, Mietke A, Golfier S, Herold C, Klaue D, et al. Real-time deformability cytometry: on-the-fly cell mechanical phenotyping. Nat Methods. 2015;12(3):199-202, 4 p following.

[3] Rosendahl P, Plak K, Jacobi A, Kraeter M, Toepfner N, Otto O, et al. Real-time fluorescence and deformability cytometry. Nat Methods. 2018;15(5):355-8.

Disclosure of Interests: Alexandru-Emil Matei: None declared, Kubánková Markéta: None declared, Andrea-Hermina Györfi: None declared, Evgenia Boxberger: None declared, Despina Soteriou: None declared, Maria Papava: None declared, Julia Muth: None declared, Martin Kräter: None declared, Georg Schett: None declared, Jochen Guck: None declared, Jörg H.W. Distler Consultant of: Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, Grant/research support from: Anamar, Active Biotech, Array Biopharma, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB, Employee of: Stock owner of 4D Science and Scientific head of FibroCure

DOI: 10.1136/annrheumdis-2021-eular.1274

AB0421

MANAGEMENT OF ULCERATION IN SYSTEMIC SCLEROSIS BY A SPECIALIST PODIATRY SERVICE; A CASE SERIES

L. Parker[1], R. Field2, J. Marks[1]. *[1]University Hospitals Dorset NHS Foundation Trust, Rheumatology Department, Christchurch, United Kingdom*; *[1]University Hospitals Dorset NHS Foundation Trust, Rheumatology Department, Christchurch, United Kingdom*

Background: Systemic sclerosis is a chronic disorder characterised by diffuse fibrosis and vascular abnormalities in the skin and major organs. Digital ulceration is a common complication, often resulting in patient disability. These ulcers can form through a variety of processes and management should be tailored according to aetiology. In Dorset, the specialist podiatry service has created a unique facility for optimal wound care in the setting of digital ulceration.
Objectives: In this case series, we outline podiatric management of 4 common causes of digital ulceration in systemic sclerosis.
Methods: Tissue ischaemia, infection, micro-trauma and calcinosis were identified as four major contributory factors resulting in ulceration or delayed wound healing. Four cases exemplifying management of each different contributory factor were identified and their case notes reviewed in order to extract clinically relevant data and images.
Results: Case 1 illustrates treatment of ischaemic tissue injury to promote earlier healing, using careful wound care, debridement under local anaesthetic and low-level laser therapy.
Case 2 illustrates the importance of identifying repeated micro-trauma as a contributing factor to non-healing ulceration.
Case 3 demonstrates how surgical debridement or removal of the subcutaneous calcinosis in an outpatient setting can be a useful adjunct in encouraging ulcer healing.
Case 4 illustrates the complexity of correctly identifying infection in the setting of ulceration, with prompt management promoting wound healing.
Conclusion: The pathophysiology of ischaemic tissue damage in scleroderma is complex and can reflect a broad range of vascular pathologies, often occurring concurrently[1] including vasospasm, macrovascular disease and microvascular vasculopathy, leading to digital ulceration. Rapid identification of which processes are driving the ischaemia is critical in targeting therapy to the affected individual. A local podiatry service with expertise in management of tissue -related complications of systemic sclerosis is invaluable in promoting wound healing and preventing further complications.
REFERENCES:
[1] Hughes M, Herrick A L. Digital ulcers in systemic sclerosis. *Rheumatology* 2017; 56(1):14-25.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1276

AB0422

DIAGNOSTIC PERFORMANCE OF THE ACR/EULAR 2013 CLASSIFICATION CRITERIA FOR SYSTEMIC SCLEROSIS IN A ROUTINE CARE SETTING

M. T. Schiaffino[1], B. Serrano-Benavente[2], M. DI Natale[1], K. Carpio[2], J. Martínez-Barrio[2], P. Sanchez-Mateos[1], J. M. Alvaro-Gracia[2], I. Castrejón Fernández[2]. *[1]Hospital Gregorio Marañón, Immunology, Madrid, Spain*; *[2]Hospital Gregorio Marañón, Rheumatology, Madrid, Spain*

Background: An ACR/EULAR task force released new criteria in 2013 to classify patients with systemic sclerosis (SSc).
Objectives: This study evaluates the diagnostic performance of these criteria in a multidisciplinary care setting.
Methods: Patients with an active follow-up in a Systemic Autoimmune Diseases Unit with a clinical diagnosis of SSc were matched by age and gender with consecutive patients referred to a capillaroscopy clinic. The classification criteria were tested on discrimination and diagnostic accuracy between both groups of patients defined as cases-SSc and controls. Receiver operating characteristic (ROC) curve and the area under the curve (AUC) was calculated for the global score to define the best cut off to classify the patients as having SSc.
Results: A total of 130 patients with SSc and 130 matched-controls were included in this analysis, 90% women, with a mean age of 61.5. Main diagnosis for the control groups were primary Raynaud´s phenomenon (34.6%), undiferentiated connective tissue disease (13.1%), and mixed connective tissue disease (9.2%). The 92% and 8% of patients in the SSc-cases and control groups met the 2013 ACR/ EULAR SSc classification criteria respectively. Sensitivity and specificity of the criteria were 81.5% and 93.7%, respectively. The best cut offs for the total score were 8 and 9, and the AUC (95%CI) was 0.962 (0.939-0.985). The individual items with a better discriminatory capacity were abnormal capillaroscopy, telangiectasia and anticentromere antibody positivity.

Table 1. Demographic data and ACR/ EULAR SSc classificacion criteria of SSC patients and controls.

	Cases-SSc, n= 130	Controls, n= 130	p
Age, mean (SD)	62.4 (16.0)	61.3 (14.8)	0.58
Female, %	90.5	90.8	0.92
Disease duration from onset of symptoms, mean (SD)	7.5 (6.4)	7.8 (6.7)	0.73
% Patients with individual ACR/EULAR 2013 Criteria Items			
Skin thickening	15.8	0.7	<0.001
Sclerodactily	45.5	6.1	<0.001
Puffy fingers	27.7	1.5	<0.001
Digital tip ulcers	30.2	5.3	<0.001
Fingertip pitting scars	18.8	4.6	0.001
Telangiectasia	51.5	6.1	<0.001
Abnormal nailfold capillaries	79.4	0.8	<0.001
Pulmonary Arterial Hypertension	16.3	3.8	0.001
Pulmonary fibrosis	18.8	6.2	0.002
Raynaud´s phenomenon	90.7	66.9	<0.001
Anticentromere antibody	60.7	18.9	<0.001
Scl70	12.0	0	<0.001
Total Score	**12.5 (4.8)**	**3.4 (2.9)**	**<0.0001**

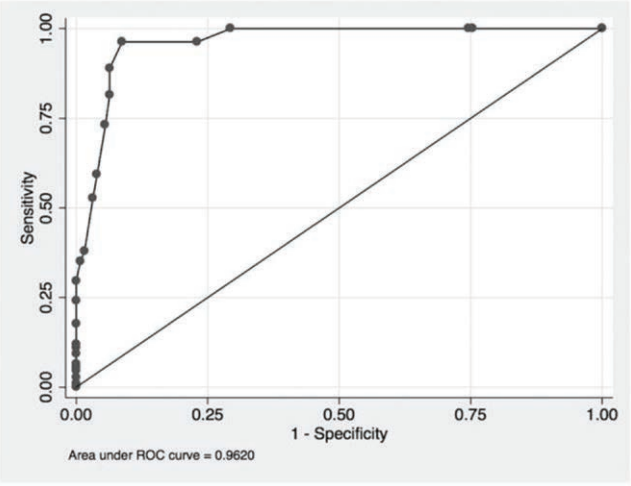


Figure 1. ROC curve for global score of the ACR/EULAR2013 SSc classification criteria.

Conclusion: The ACR/EULAR 2013 criteria showed good diagnostic properties in this cohort reflecting daily practice. Individual items showing the highest discriminatory capacity were abnormal capillaroscopy, telangiectasia and anticentromere antibody positivity.
REFERENCES:
[1] van den Hoogen F, Khanna D, Fransen J, et al. 2013 classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative. Annals of the Rheumatic Diseases 2013;72:1747-1755.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1318

AB0423

SAFETY AND TOLERABILITY OF RITUXIMAB IN THE TREATMENT OF SYSTEMIC SCLEROSIS: LONG-TERM FOLLOW-UP

L. Garzanova[1], L. P. Ananyeva[1], O. Koneva[1], O. Desinova[1], O. Ovsyannikova[1], M. Starovoytova[1], R. Shayakhmetova[1], S. Glukhova[2]. *[1]VA Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*; *[2]VA Nasonova Research Institute of Rheumatology, Educational and Methodical Department, Moscow, Russian Federation*

Background: Rituximab (RTX) has been used for the treatment of systemic sclerosis (SSc) for a long time, but data on tolerance and long-term adverse events (AE) are insufficient.
Objectives: To assess the tolerability and safety of RTX in the patients (pts) with SSc in long-term prospective follow-up.
Methods: Data on the safety and tolerability of RTX were evaluated in 149 SSc pts who received at least one RTX infusion in a long-term open-label prospective observational study. The mean age was 48±13,5 years (17-74), women - 122 (82%), diffuse cutaneous subset of the disease had 52%, limited-37% and overlap-11%.

The mean disease duration was 6,4±5,8 years (0,5-30). The observation period was 12 years. All pts received prednisolone at a dose of 11,7±4,8mg/day, and 73 patients (49%) received immunosuppressants at inclusion. The indications for the appointment of RTX were ineffectiveness or impossibility of standard therapy and a severe course of the disease with high activity and unfavorable prognosis factors. AE were assessed and recorded by a physician at a hospital immediately after the infusion of RTX, then by patient reported outcome during the observation period. Severe AE were defined as those that required hospitalization for more than 24 hours, exacerbation of the disease requiring therapy, malignancies, life-threatening situations. All causes of death were considered, regardless of treatment.

Results: The mean follow-up period after the first infusion of RTX was 5,6±2,6 years [834,4 patient-years (PY)]. Pts received a mean of 3,4 courses of RTX (1–10). The cumulative mean dose of RTX was 3,2±2,4 gr (0,5-11). AE were reported in 77 patients (52%), the overall frequency of AE was 9,3/100 PY (95% Confidence Interval (CI) 8-11). The highest frequency of all AE was observed in the first 2-6 months after the first infusion of RTX, however these were mainly mild AE (71%). There was a decrease of AE in the follow-up period (3,4/100 PY, 95% CI 2,4-4,9 – at the period from 3 to 10 course of RTX). The overall incidence of serious AE was 2,22/100 PY (95% CI 1,4–3,5). The specter of serious AE included: pneumonia in 7 pts, infusion reactions in 5, as well as in one case: cerebral ischemia, acute pancreatitis, allergic pneumonitis, lymphoma of pharynx, purulent arthritis, lower limb vein thrombosis, pulmonary embolism of small arteries. The most frequent AE were infections (n=53), with no serious opportunistic infections reported. The overall incidence of all infections was 6,4/100 PY (95% CI 4,9-8,3), serious infections – 1,32/100 PY (95% CI 0,7-2,4). The level of immunoglobulin G during follow-up period decreased from 12,9±4,9 to 10,1±3,4g/l (p=0,0001), but remained within normal limits. Infusion reactions occurred in 15 pts (1,8/100 PY, 95% CI 1-3). Other AE were observed in 9 pts (6%) (1,1/100 PY, 95% CI 0,53-2,12). Sixteen deaths were recorded – 10,7% or 1,91/100 PY, 95% CI 1,2-3,1. In most cases, pts died from the progression of the major organ failure. The causes of death were: progression of the interstitial lung disease (ILD) in 4 pts, heart failure associated with SSc cardiomyopathy (2), renal crisis (4), pulmonary arterial hypertension and ILD (2), pneumonia (2), sepsis after tooth extraction (1), acute pulmonary embolism (1).

Conclusion: In our study, we considered the overall safety profile of RTX in SSc as favorable. It was similar to the AE profile in other autoimmune diseases treated with RTX. With an increase of the cumulative dose of RTX, there was no increase in AE. RTX could be considered as a relatively safe drug for the complex therapy of SSc when standard therapy is ineffective or impossible.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1325

AB0424 **NUTRIENT DEFICIENCIES IN SYSTEMIC SCLEROSIS: A SYSTEMATIC REVIEW**

A. Nguyen[1], Z. Mcmahan[2], E. Volkmann[3]. [1]*David Geffen School of Medicine at UCLA, Medicine, Los Angeles, United States of America*; [2]*Johns Hopkins University School of Medicine, Medicine - Rheumatology, Baltimore, United States of America*; [3]*David Geffen School of Medicine at UCLA, Medicine - Rheumatology, Los Angeles, United States of America*

Background: Malnutrition is a critical concern in patients with systemic sclerosis (SSc).[1,2] However, the extent and types of nutrient deficiencies in SSc remain unclear.

Objectives: 1) To identify the nutrient deficiencies commonly reported in SSc; 2) To evaluate associations between specific nutrient deficiencies and SSc subtype and clinical manifestations.

Methods: We conducted a systematic review of all published reports on SSc and nutrition in PubMed from its inception to August 2020. Clinical trials, observational studies, and case series (with ≥20 cases) containing data on nutritional deficiency and SSc were included. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for reporting our findings. Two reviewers (ADN and ERV) studied the titles and abstracts of all search results with pre-specified inclusion and exclusion criteria (Figure 1).

Results: Among 790 retrieved publications, 35 full-length articles and 3 abstracts met the inclusion criteria. Included studies took place across multiple geographic locations and included patients with both diffuse and limited cutaneous SSc. Vitamin D deficiency was the most commonly reported deficiency described in SSc, followed by vitamin B12, folate, selenium, zinc, and iron (Table 1). In addition, some small studies found deficiencies in thiamine, pyridoxine, alpha-tocopherol, and carotene. Interstitial lung disease was associated with vitamin D deficiency and elevated homocysteine (Hcy), while pulmonary hypertension was associated with elevated Hcy. Vitamin D deficiency was also associated with increased modified Rodnan skin score (mRSS) and increased risk of SSc-related organ involvement.

Conclusion: Nutrient deficiencies are common in SSc and are associated with specific SSc features. Routine screening for nutrient deficiencies may lead to early detection of malnutrition. Future studies are needed to understand how nutritional interventions affect patient outcomes in SSc.

REFERENCES:

[1] Harrison E, Herrick AL, McLaughlin JT, Lal S. Malnutrition in systemic sclerosis. *Rheumatology*. 2012;51(10):1747-1756. doi:10.1093/rheumatology/kes160

[2] Baron M, Hudson M, Steele R, et al. Malnutrition is common in systemic sclerosis: Results from the Canadian Scleroderma Research Group database. *J Rheumatol*. 2009;36(12):2737-2743. doi:10.3899/jrheum.090694

Figure 1. Article selection for systematic review.

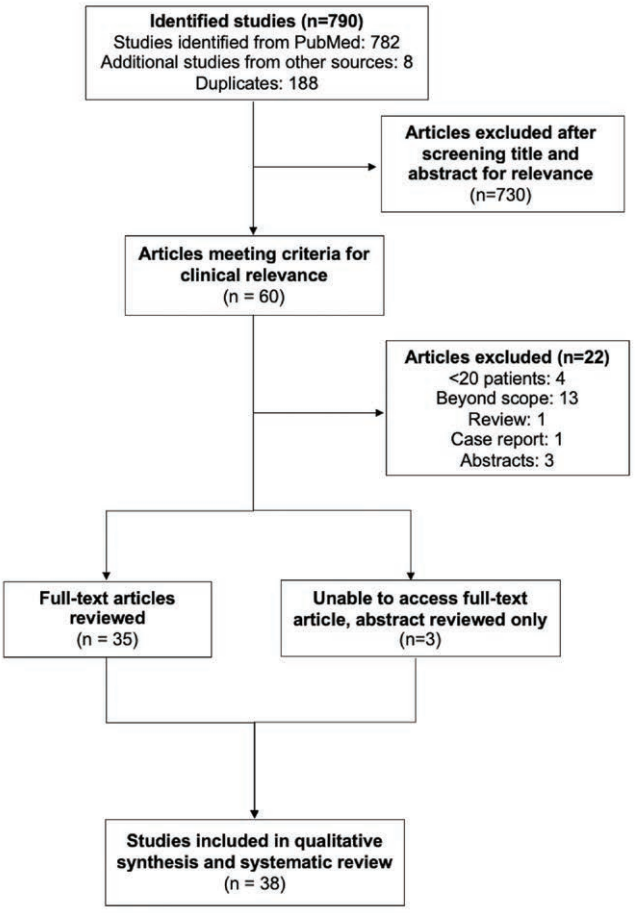


Table 1. Nutrient deficiencies and their clinical correlates in SSc.

	Number of studies that found deficiency[a]	Number of studies that did not find deficiency	Clinical correlates of nutrient deficiency
Vitamin D	23	0	▪Increased risk of SSc-related organ involvement ▪ILD[c] ▪Higher mRSS[c]
Homocysteine[b]	5	4	▪ILD[c] ▪PH
Vitamin B12	3	4	▪None identified
Folate	3	2	▪None identified
Vitamin C	2	0	▪▪None identified
Selenium	5	0	▪Increased risk of SSc-related organ involvement
Zinc	3	1	▪None identified
Iron	1	1	▪None identified
Copper	0	2	▪None identified
Other nutrients			▪None identified for all nutrients
Thiamine	1	0	
Pyridoxine	1	0	
Alpha-tocopherol	1	0	
Carotene	1	0	

[a] Deficiency defined as below normal levels based on study reference ranges[b] Studies looked for elevation versus no elevation of homocysteine in SSc[c] Some studies found significant correlation while others did not

Acknowledgements: I have no acknowledgements to declare.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1420

AB0425 CLINICAL AND PATHOLOGICAL FEATURES OF BREAST CANCER IN PATIENTS WITH SYSTEMIC SCLEROSIS: PRELIMINARY DATA FROM THE SCLERO-BREAST STUDY

A. Spinella[1], A. Toss[2], C. Isca[2], C. Vacchi[1], A. Iannone[3], L. Magnani[4], P. Castrignanò[1], M. De Pinto[1], C. Laura[2], A. Maiorana[5], C. Salvarani[1,4], M. Dominici[2], D. Giuggioli[1]. *[1]University of Modena and Reggio Emilia, Scleroderma Unit, Rheumatology Unit, Modena, Italy*; *[2]University of Modena and Reggio Emilia, Department of Oncology and Hematology, Modena, Italy*; *[3]University of Modena and Reggio Emilia, Department of Surgery, Medicine, Dentistry and Morphological Sciences with Transplant Surgery, Oncology and Regenerative Medicine Relevance, Modena, Italy*; *[4]AUSL-IRCCS of Reggio Emilia, Italy, Rheumatolgy, Reggio Emilia, Italy*; *[5]University of Modena and Reggio Emilia, Pathology Unit, Modena, Italy*

Background: Systemic Sclerosis (SSc) is a rare and life-threatening connective tissue disease characterized by vascular dysfunction, specific autoimmune abnormalities and fibrosis of the skin and internal organs. Previous studies have shown a 1.5-fold increase in cancer risk in SSc patients compared with the general population, including breast cancer (BC). The relationship between BC and SSc has long been discussed but past research has been contradictory and inconclusive on this topic.
Objectives: The aim of our project was to analyze clinical and pathological characteristics of BC developed by SSc subjects and possible correlations with scleroderma features. Here we present the preliminary data from the Sclero-Breast study.
Methods: Our observational retrospective multicenter study enrolled 33 SSc women with a personal history of BC identified at two Rheumatology/SSc Units in the north of Italy between January 2017 and December 2019 (lc/dcSSc 23/9, 1 unknown; mean age at SSc onset 57 years, range 32-73). All patients underwent general and instrumental assessment: smoking habits; presence of skin ulcers, calcinosis, teleangectasia; presence of gastro-intestinal and kidney involvement; interstitial lung disease (at HR-CT); pulmonary function tests; ECG abnormalities; echocardiographic assessment of pulmonary arterial hypertension (PAH); videocapillaroscopic pattern; autoantibody profile; exposure to immunosuppressive and vasoactive therapies; status at last follow-up evaluation and cause of death. Clinical and pathological characteristics of BC were also evaluated: age at diagnosis; menopausal status; histotype; hormone receptor status; MIB1, HER2 expression; clinical and pathological stage at diagnosis; metastatic sites; type of loco-regional treatment (surgery and radiotherapy); type of systemic treatment (neoadjuvant/adjuvant chemotherapy and endocrine treatment); other cancers and time from diagnosis of the first disorder to the second one.
Results: A total of 54.5% of subjects developed BC before SSc (median interval of 5 years), whereas 45.5% of patients developed BC after SSc (median delay of 8 years). 54.5% of patients showed interstitial lung disease and the cause of death of the 6 deceased subjects was PAH. A significant association ($p<0.05$) was observed between the use of immunosuppressive therapy and diffuse skin extension, negative ACA, positive Anti-Scl-70 and interstitial lung disease, but not with BC status. 93.1% of patients were diagnosed with an early-stage tumor, 70.8% of invasive carcinomas with a low MIB-1, 8.3% with a tubular histotype, while 42.8% presented with a Luminal A-like tumor. 66.6% underwent breast conserving surgery and 55.5% RT after surgery. 40% of patients developed interstitial lung disease after RT and 20% dcSSc.
Conclusion: According to our preliminary data, SSc patients developed BC at good prognosis, suggesting a de-escalation strategy of cancer therapies. On these grounds, a proper screening is mandatory in order to allow for early cancer detection in SSc patients. Further investigations on larger numbers of patients are needed. First of all, they would further clarify the intriguing relationship between BC and SSc. Secondly, they would help to explore the common biological and molecular pathways at the basis of these two disorders, with the aim to improve BC diagnosis and prognosis and to personalize oncological targeted treatments in this subset of fragile patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1450

AB0426 CANCER SCREENING IN IDIOPATHIC INFLAMMATORY MYOPATHIES: TEN YEARS EXPERIENCE FROM A SINGLE CENTER

E. Trallero-Araguás[1], A. Gil-Vila[2], X. Martínez-Gómez[3], M. Alvarado-Cardenas[2], M. Simo-Perdigó[4], J. Ros[5], I. Pinal-Fernandez[6], A. Selva-O'callaghan7. *[1]Vall d'Hebron Hospital, Rheumatology, BARCELONA, Spain*; *[2]Vall d'Hebron Hospital, Medicine, Barcelona, Spain*; *[3]Vall d'Hebron Hospital, Preventive Medicine and Epidemiology, Barcelona, Spain*; *[4]Vall d'Hebron Hospital, Nuclear Medicine, Barcelona, Spain*; *[5]Vall d'Hebron Hospital, Medical Oncology, Barcelona, Spain*; *[6]National Institutes of Health, Rheumatology, Bethesda, Spain*; *[2]Vall d'Hebron Hospital, Medicine, Barcelona, Spain*

Background: There is a well-recognized association between cancer and myositis, so cancer screening at diagnosis is recommended.
Objectives: We aim to report the results of our cancer screening strategy and to ascertain the reliability of using PET/CT to identify cancer-associated myositis (CAM) in a large cohort of patients with myositis from a single center over 10 years.
Methods: This retrospective observational study included all patients diagnosed with any type of myositis except for inclusion body myositis. Cancer screening strategy was individualized according to clinical and serological data, including PET/CT as the main test to detect occult cancer (OC). Procedures derived from a positive PET/CT were registered. Qualitative data expressed as percentages, and quantitative data as the median with the interquartile range were analyzed. A ROC curve was used to estimate the reliability of PET/CT for CAM diagnosis.
Results: Seventy-seven out of 131 patients underwent a PET/CT for OC screening. The performance of the PET/CT in patients with myositis at disease onset yielded an area under the curve ROC of 0.87 (0.73-0.97) for CAM diagnosis. Invasive procedures in 7 (9%) patients without a final diagnosis of cancer did not cause derived complications. Patients not evaluated for OC did not develop cancer after a median follow-up of 3.3 years (1.7-6.7).
Conclusion: Cancer screening strategy should be individualized. PET/CT at myositis onset seems to be an efficient approach to rule out CAM. This practice does not seem to significantly increase harm to patients related to the additional tests needed to clarify inconclusive results.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1457

AB0427 ANTI-NOR90 AUTOANTIBODIES: FAVORABLE OR UNFAVORABLE PROGNOSIS?

C. Valero[1], J. P. Baldivieso[1], I. Llorente[1], E. F. Vicente-Rabaneda[1], L. Esparcia Pinedo.[2], R. Garcia de Vicuna[1], M. A. Alfranca[2], S. Castañeda[1]. *[1]Hospital Universitario de la Princesa, Rheumatology, Madrid, Spain*; *[2]Hospital Universitario de la Princesa, Immunology, Madrid, Spain*

Background: Anti-NOR 90 autoantibodies (anti-NOR90 Ab) are autoantibodies that target nucleolar transcription factor 1 or hUBF, involved in transcription of RNA polymerase I. These autoantibodies have been detected in 6.1% of patients with Systemic Sclerosis (SSc), but their clinical or prognostic significance has not been clearly defined. Anti-NOR90 Ab have been mostly associated with limited scleroderma with mild organ involvement and can also be found in other rheumatic diseases such as rheumatoid arthritis, systemic lupus erythematosus or Sjogren's syndrome.
Objectives: The aim of this study was to identify the main clinical characteristics of patients with positive anti-NOR90 in our Centre.
Methods: This is a retrospective, descriptive, cross-sectional study of all patients with positive anti-NOR90 Ab between January 2013 and December 2020 in a single center. Autoantibodies testing was performed using Euroimmun EUROLINE SSc profile IgG autoAb assay kit. Patient demographics, clinical characteristics, associated diagnoses, laboratory and immunological findings were collected.
Results: We identified a total of 26 patients with at least a positive value for anti-NOR90 Ab (Table 1). In most cases anti-NOR90 patients were ANA positive, predominantly with nucleolar pattern and coexisted with other SSc autoantibodies. 12 patients had rheumatic diseases and two had SSc, both with limited cutaneous SSc and absence of organ involvement. 14 patients had no definite diagnosis. Clinical features of anti-NOR90 patients are represented in Figure 1. Five patients presented Raynaud's phenomenon, two cases with pathological nailfold capillaroscopy and one patient had SSc. There was no patient with skin ulcers, calcinosis, interstitial lung disease or pulmonary hypertension. Four patients had gastroesophageal reflux disease and one patient presented antral vascular ectasia. Six patients developed some neoplasm.

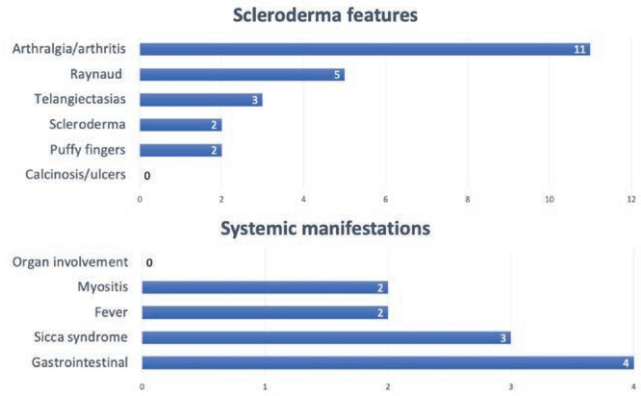


Figure 1. Clinical characteristics of anti-NOR90 Ab patients.

Conclusion: In our case series anti-NOR90 Ab were associated with multiple rheumatic diseases with heterogeneity of clinical manifestations. We did not observe a further progression to SSc or presence of organ involvement or severe scleroderma, so these autoantibodies could be related with a favorable prognosis. In contrast with previous reports, a striking association with cancer has been detected in our population.

Table 1. Demographic characteristics and main diagnoses of anti-NOR90 positive patients.

Characteristics	Total Anti-NOR90: 26 patients
Sex, n	19 women/ 7 men
Age, mean (years)	58,9 IQR [46,3-72,2]
Race, n	Asian: 1; Hispanic: 7; Caucasian: 18
Smoker, n	3
Positive ANA (>1/160), n	24
Pattern, n	7 Homogeneous, 4 Nucleolar, 4 Speckled, 1 Centromere, 5 Speckled -nucleolar, 3 Homogeneous-nucleolar.
Positive ENA, n	3 2 Anti-SSA-Ro52 and Ro60, 1 anti-RNP and anti-Sm
Systemic sclerosis autoantibodies, n	• Anti-Ku: 7 • Anti-U3RNP (Fibrilarin): 6 • Anti-RNA polymerase III: 5 • Anti Th/To: 4 • Anti-centromere: 4 (CENP B +/- CENPA) • Anti-topoisomerase I: 2 • Anti-Ro52: 3 • Anti-PM-Scl: 3
Main diagnosis, n	12 Rheumatic diseases: 2 systemic Sclerosis (2 limited/0 diffuse) 1 rheumatoid arthritis 1 LES 1 Sjögren's syndrome, 3 undifferentiated conective tissue disease 2 overlap (1 Sjögren + LES, 1 Sjögren + MCTD 1) s: 1 morphea, 1 cutaneous graft versus host disease
Neoplasm, n	6: 2 solid organ cancer (bladder, kidney), 1 lung adenocarcinoma, 1 multiple myeloma, 1 acute myeloid leukemia: 1 basal cell carcinoma.

Abbreviations: LES: systemic lupus erythematosus; MCTD: mixed connective tissue disease

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1477

AB0428

ULTRASOUND ASSESSED NAIL BED THICKNESS AS AN EARLY SCREENING MARKER FOR INTERSTITIAL LUNG DISEASE IN SCLERODERMA

P. Dekate[1], S. Vodnala[2], R. Dudam3. [1]*Hyderabad Rheumatology Center, Rheumatology, Hyderabad, India*; [2]*Hyderabad Rheumatology Center, Radiology, Hyderabad, India*; [1]*Hyderabad Rheumatology Center, Rheumatology, Hyderabad, India*

Background: Interstitial lung disease (ILD) is the most frequent pulmonary manifestation of scleroderma and is seen in 80% of the patients with diffuse and in 20% of the limited forms of scleroderma.[1] Even seen in early stages of the disease with varying degrees of severity, it does not correlate with the clinical manifestations.[2] Hence, it is difficult to select patients for ILD screening based on symptoms. Digital clubbing is a common feature of ILD and has been associated with poor prognosis.[3]
Objectives: To assess the ultrasound measured nail bed thickness (NBT) in cases of scleroderma as a screening marker to detect ILD and its inter-digital variation.

Methods: A prospective observational study involving 15 patients each of scleroderma with ILD, without ILD and controls visiting our clinic from August 2020 to December 2020 were included. The presence of ILD was confirmed by HRCT thorax. Patients with a history of smoking, alcohol intake or pre-existing cardio-respiratory illnesses were excluded. Ultrasound assessed NBT was calculated using Philips affiniti 70 eL18-4 probe. A total of 436 nail beds were recorded (142 of scleroderma with ILD, 144 of scleroderma without ILD and 150 of control group). 14 nails were excluded due to trauma. Statistical analysis was done using ANOVA test. Results were considered significant at p value < 0.05.
Results: On comparing nail bed thickness among scleroderma with ILD, scleroderma without ILD and control groups, the difference in NBT was statistically significant in all the three groups, except for left 1st finger (Table 1). NBT's among scleroderma patients without ILD and control group did not show significant difference between the two groups. Whereas, when scleroderma patients with ILD were compared with control group, statistical significance were found (p<0.001) in all the fingers of both the hands, except 1st and 2nd finger of left and right hand respectively. On comparing NBT's among individual fingers of right hand in patients of scleroderma with ILD and without ILD, a statistically significant difference among the two groups in 2nd (p =0.002), 4th (p=0.009) and 5th finger (p=<0.001) was noted. In left hand, same fingers had statistically significant difference (p<0.001).
Conclusion: Patients of scleroderma with ILD are predisposed for an increase in the NBT, which can be detected using ultrasound. Thus, an increased NBT may have a role in early screening for the detection of ILD in scleroderma patients. Further studies with large patient data should be done to look at ultrasound assessed NBT as it may be utilized as a marker for ILD in scleroderma, as a widely available and an inexpensive tool.

REFERENCES:

[1] Boin F, Wigley FM. Clinical Features and Treatment of Scleroderma. In:- Firestein G, Budd R, Sherine E, et al, eds. Kelley's Textbook of Rheumatology. Philadelphia, PA: Elsevier; 2013:1366–1403.
[2] Hassan RI, et al. Lung ultrasound as a screening method for interstitial lung disease in patients with systemic sclerosis. JCR: Journal of Clinical Rheumatology. 2019;25(7):304-7.
[3] T.E. King Jr., J.A. Tooze, M.I. Schwarz, K.R. Brown, R.M. CherniackPredicting survival in idiopathic pulmonary fibrosis: scoring system and survival model Am. J. Respir. Crit. Care Med., 164 (7) (2001), 1171-81.

Table 1. Nail bed thickness in patients of scleroderma with ILD, without ILD and control groups.

		Scleroderma with ILD n=15		Scleroderma without ILD n=15		Control n=15		
	Finger	Mean	SD	Mean	SD	Mean	SD	p-value
Right	1st	1.86	0.239	1.71	0.081	1.69	0.107	**0.021**
	2nd	1.73	0.303	1.50	0.079	1.61	0.108	**0.003**
	3rd	1.89	0.200	1.75	0.091	1.50	0.131	**<0.001**
	4th	1.80	0.263	1.39	0.147	1.35	0.078	**<0.001**
	5th	1.80	0.119	1.24	0.095	1.29	0.069	**<0.001**
Left	1st	1.98	0.442	1.72	0.084	1.68	0.050	**0.078**
	2nd	1.82	0.123	1.57	0.125	1.57	0.092	**<0.001**
	3rd	2.05	0.309	1.76	0.078	1.42	0.109	**<0.001**
	4th	1.92	0.246	1.36	0.130	1.35	0.107	**<0.001**
	5th	1.81	0.158	1.15	0.368	1.23	0.103	**<0.001**

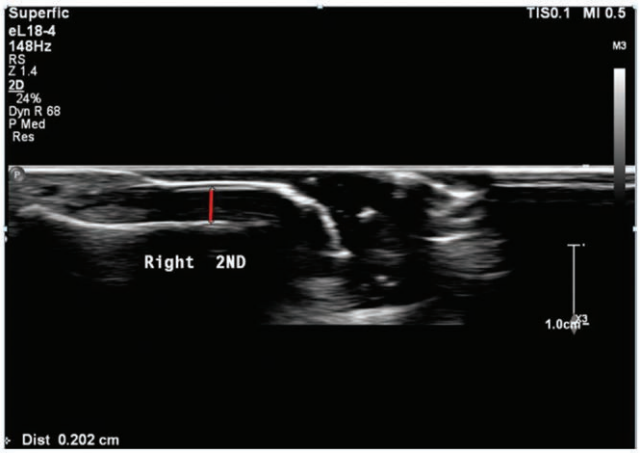


Figure 1. NBT measurement of right 2nd finger in scleroderma patient with ILD on ultrasound

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1585

AB0429 BELFAST TRUST EXPERIENCE OF IDIOPATHIC INFLAMMATORY MYOPATHIES

S. Loughrey[1], A. Herron[1], M. Mchenry[1], E. Ball[1]. [1]*Musgrave Park Hospital, Rheumatology, Belfast, United Kingdom*

Background: The Idiopathic Inflammatory Myopathies (IIM) are a heterogeneous group of diseases where there is a growing field of knowledge and experience. Presentation is usually of onset of muscle weakness in combination with typical muscle biopsy findings and specific serum autoantibodies. There is a significant morbidity and mortality associated with IIM, due to its potential systemic nature, associated malignancy risk and side effects of immunosuppressive therapy1. There is no published guideline on management of IIM, with treatment limited to best practice experience.
Objectives: Review Belfast Trust experience of Adult IIM from 2009-2020
Methods: Review of Electronic Records of 18 patients diagnosed with IIM between 2009-2020
Results: 18 patients diagnosed with IIM. Mean age at diagnosis is 64, with age range of 46-83. Mean duration of treatment is 4 years. 14 patients are in remission, 2 have active disease and 2 are deceased with cause of death unrelated to IIM.
Muscle Biopsy was performed in 17 patients. 11 patients biopsies were diagnostic and 6 were supportive. Of the patients with DM who did not have diagnostic muscle biopsies, all 3 had diagnostic skin biopsies. Of 6 patients with a negative ANA, 5 had a muscle biopsy performed (diagnostic in 4 patients and supportive in 1 patient.)
Conclusion: Extended myositis panels have only readily become available in the Belfast Trust in recent years. This has enhanced patients phenotypes and vigilance for extra-muscular complications. There is a recognised elevated risk of cancer in patients with IIM2. In our patients, with a mean disease duration of 4 years, none have developed malignancy. All of our patients had a tissue sample obtained, either muscle or skin. In the Belfast Trust, Rheumatologists perform muscle biopsies and all of the samples contributed to diagnosis. A limitation of diagnostic tests is restricted access to EMGs. We introduced a variety of DMARDs to limit exposure to steroids. 50% of our patients are in remission and off steroids. The only biologic we used was Rituximab. In contrast to other rheumatological conditions, there is no published protocol for administration of Rituximab in IIM. For patients with refractory disease, IVIG was used in the short term to allow for introduction of alternative immunosuppressants to maintain remission. This review highlights the complex nature of this group of diseases, and our experience with a variety of treatment options. We have diagnosed and treated 18 patients, and although we have experience with the medications used to treat IMM further work is needed to establish evidence based treatment.

Table 1. Overview of diagnosis and treatment of patients with IIM. PM - Polymyositis DM - Dermatomyositis IBM - Inclusion Body Myositis IMNM Immune Mediated Necrotising Myositis EP - Extended Panel ILD - Interstitial Lung Disease RA - Rheumatoid Arthritis RTx - Rituximab IVIG - Intravenous Immunoglobulin MTx - Methotrexate AZA - Azathioprine MMF - Mycophenolate Mofetil SLZ - Sulphasalazine HLQ - Hydroxychloroquine

Diagnosis	ANA/Extra muscular	Failed/ Intolerance	RTx	IVIG	Mtx	AZA	MMF	Ciclos-porin	SLZ/ HLQ	Prednisolone duration (months)
PM	Jo-1 Ro	AZA					X			18
PM	Jo-1 Myocarditis	AZA	x	x				x		12
PM	Negative. No EP	AZA/MMF/ RTx			x					Maint. 3mg
PM	Negative. No EP				x					22
PM	Jo-1 ILD, Mechanic Hands	Mtx/MMF	x						x	Maint. 7mg
PM	Negative. No EP					x				36
PM	Negative. No EP			x						18, reducing dose
PM	Negative. No EP			x		x				Maint. 5mg
PM	Ro ILD, Dysphagia				x					6, reducing dose
DM	MDA5, Ro Rash, ILD	AZA	x	x			X			18
DM	Mi2 Rash	Mtx	x				X			20
DM	PM-SCL Rash									Deceased
DM	Ro52 Sicca			x						6, reducing dose
DM	MDA5, NXP2 Rash			x			x			Maint, 12.5mg
DM-Amyopathic	SAE Rash	MTx	x	x			X			Deceased
IBM	Ro/La			x	x				x	Unknown duration. Now stopped
IMNM	HMGCR				x					12
IMNM	HMGCR			x	x	x				18, reducing dose

REFERENCES:

[1] Barsotti, Lundberg et al 'Current Treatment for Myositis' Curr Treatm Opt Rheumatol vol 4 (4) 2018 p299-315 2. Kang et al 'Temporal relationship between cancer and myositis identifies two distinctive subgroups of cancers: impact on cancer risk and survival in patients with myositis' Rheum vol 55 (9) 2016 p1631-1641

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1602

AB0430 CONTRIBUTION OF SCLERODERMA/MYOSITIS-RELATED ANTIBODIES DETECTED BY IMMUNOBLOT TO THE DIAGNOSIS OF SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES IN 134 PATIENTS FROM A SINGLE REFERRAL CENTER

D. Prieto-Peña[1], B. Atienza-Mateo[1], M. A. González-Gay[1], R. Blanco[1], M. Lopez-Hoyos[2]. [1]*Hospital Universitario Marques de Valdecilla, IDIVAL, Rheumatology, Santander, Spain*; [2]*Hospital Universitario Marques de Valdecilla, IDIVAL, Immunology, Santander, Spain*

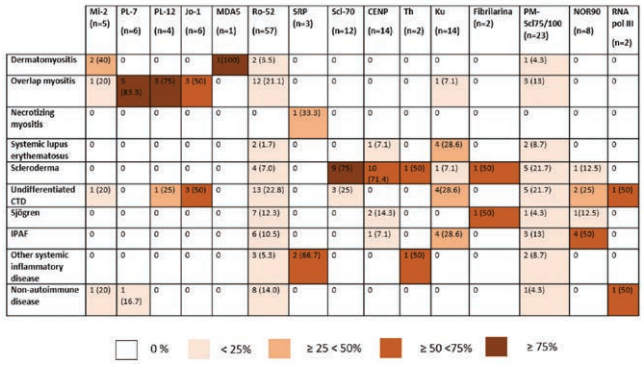
Background: Immunoblot assays are increasingly used in clinical practice as part of the diagnostic armamentarium of systemic autoimmune rheumatic diseases (SARDs).
Objectives: To assess the contribution of an extended scleroderma/myositis-related antibodies (Ab) determination by immunoblot to the diagnosis of patients with SARDs.
Methods: We reviewed all medical records of patients with positive scleroderma/myositis-related Ab line blot determinations (Euroimmune AG, Lübeck, Germany) in our center from November 2017 to September 2020. These assays were requested due to high suspicion of SARDs in patients presenting with non-specific symptoms.
Results: 134 patients (37men/97women; mean age 59.6 ± 14.8 years) were positive for at least 1 Ab, 25 of them were positive for 2 Abs. Main clinical features at the time of immunoblot requests were: arthralgia/arthritis (n=88), Raynaud's phenomenon (n=59), rash (n=27), sicca syndrome (n=14.9%), myopathy (n=18). During follow-up, 28 patients were diagnosed with undifferentiated connective tissue disease (UCTD), 26 scleroderma, 23 overlap myositis, 18 interstitial pneumonia with autoimmune features (IPAF), 8 other inflammatory diseases, 8 Sjögren's syndrome, 7 systemic lupus erythematosus, 5 dermatomyositis, 1 necrotizing myositis. In 10 patients the diagnosis of SARD was finally ruled out (Figure 1). Interstitial lung disease (ILD) was present in 50 patients, being particularly frequent in those with anti-PL12, anti-PL7 and anti-MDA5 Abs. Cancer was detected in 9 (6.7%) patients, 6 of them were anti-Ro52 + (Table 1).
Conclusion: Immunoblot assays are of great help in the diagnosis of patients with high clinical suspicion of SARDs. While some Abs, such as anti-Ro52, anti-Ku and anti-PMScl75/100, remain to be nonspecific, other Abs including anti-PL12, anti-PL7 or anti-MDA5 are particularly helpful in detecting SARDs patients with associated ILD.

REFERENCES:

Table 1.

	Mi-2 (n=5)	PL-7 (n=6)	PL-12 (n=4)	Jo-1 (n=6)	MDA5 (n=1)	antiRo52 (n=57)	SRP (n=3)	Scl-70 (n=12)	CENP (n=14)	Th(n=2)	Ku (n=14)	Fibrilarina (n=2)	PM-Scl75/100 (n=23)	NOR90 (n=8)	RNA pol (n=2)
ILD	0	4 (66.7)	4 (100)	3 (50)	1 (100)	19 (33.3)	0	7 (58.3)	1 (7.1)	0	7 (50)	1 (50)	9 (39.1)	5 (62.5)	0
Cancer	1 (20)	0	0	0	0	6 (10.5)	1 (33.3)	0	0	0	1 (7.1)	0	0	0	0

FIGURE 1



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1724

AB0431

EXPLORING THE UTILITY OF THE AMERICAN COLLEGE OF RHEUMATOLOGY (ACR) CRISS IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

F. Del Galdo[1], O. Distler[2], C. Denton[3], Y. Allanore[4], D. Wachtlin[5], M. Alves[6], D. Khanna[7]. *[1]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine and NIHR Biomedical Research Centre, Leeds, United Kingdom*; *[2]University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland*; *[3]University College London Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom*; *[4]Descartes University, APHP, Cochin Hospital, Department of Rheumatology A, Paris, France*; *[5]Boehringer Ingelheim Pharma GmbH & Co. KG, Biostatistics + Data Sciences, Ingelheim, Germany*; *[6]Boehringer Ingelheim International GmbH, TA Inflammation Med, Ingelheim, Germany*; *[7]University of Michigan, Department of Medicine, Ann Arbor, United States of America*

Background: The ACR Composite Response Index in diffuse cutaneous Systemic Sclerosis (CRISS) was developed to measure the probability of improvement in response to treatment in patients with early diffuse cutaneous SSc (dcSSc), accounting for new/worsening cardiopulmonary involvement and/or renal crisis, and changes in modified Rodnan skin score, forced vital capacity, health assessment questionnaire disability index, and patient's and physician's global impressions. In patients with SSc-ILD, treatment response may be reflected as slower progression, stabilisation or improvement.

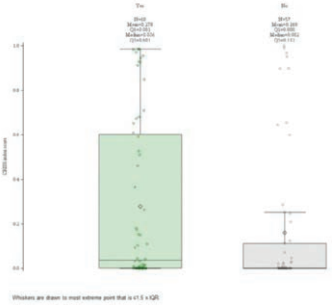
Objectives: Using data from patients with dcSSc and ILD in the placebo group of the SENSCIS trial, we analysed the probability of improvement using the ACR CRISS score at week 52. We also evaluated whether the CRISS numerator could provide information on the spectrum of responses in this patient population.

Methods: The SENSCIS trial enrolled subjects with SSc-ILD with onset of first non-Raynaud symptom ≤7 years before screening, FVC ≥40% predicted, and fibrotic ILD ≥10% extent on an HRCT scan. Subjects on prednisone ≤10 mg/day (or equivalent) and/or stable therapy with mycophenolate or methotrexate were allowed to participate. Subjects were randomised to receive nintedanib or placebo. Subjects were not randomised by use of mycophenolate. In patients randomised to receive placebo who had dcSSc and/or mRSS >15 at baseline, we analysed the ACR CRISS and its numerator at week 52 in subgroups by use of mycophenolate at baseline. Analyses were exploratory and descriptive.

Results: Of 117 analysed subjects in the placebo group who had dcSSc and/or mRSS >15 at baseline, 60 (51.3%) were taking mycophenolate at baseline. Compared with patients not taking mycophenolate at baseline, those taking mycophenolate had a lower mean age (48.4 [SD 11.8] vs 53.1 [13.4] years), lower mean FVC % predicted (68.8 [17.0] vs 73.0 [14.6]), and a greater proportion were female (76.7% vs 71.9%); median time since first onset of non-Raynaud symptom was similar (3.9 vs 4.5 years, respectively) as was mean (SD) mRSS (16.5 [7.7] vs 15.9 [8.0], respectively). One patient (taking mycophenolate at baseline) had limited cutaneous SSc. At week 52, median (Q1, Q3) ACR CRISS score was 0.036 (0.001, 0.601) in subjects taking mycophenolate and 0.002 (0.000, 0.112) in subjects not taking mycophenolate at baseline, and mean (SD) ACR CRISS score was 0.28 (0.37) in subjects taking mycophenolate and 0.16 (0.31) in subjects not taking mycophenolate at baseline (Figure 1). In these groups, respectively, 25.0% and 14.0% of subjects had CRISS score >0.6 (considered improved) at week 52. The CRISS numerator provided a broader distribution of response values, but was not informative in this patient population.

Conclusion: In exploratory analyses, among subjects with dcSSc and ILD who received placebo in the SENSCIS trial, the proportion considered improved at week 52 based on ACR CRISS score was numerically greater in patients taking than not taking mycophenolate at baseline. There remains a need for composite scores that provide better interpretation of the magnitude of response in patients with SSc.

Figure. Box-and-whisker plot of CRISS score at week 52 in subjects with SSc-ILD with dcSSc and/or mRSS >15 at baseline in the placebo group of the SENSCIS trial by use of mycophenolate at baseline



Acknowledgements: The SENSCIS trial was funded by Boehringer Ingelheim. Medical writing support was provided by FleishmanHillard Fishburn, London, UK. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE).

Disclosure of Interests: Francesco Del Galdo Speakers bureau: Actelion and AstraZeneca, Consultant of: Actelion, AstraZeneca, Boehringer Ingelheim, Capella BioScience, ChemomAb and Mitsubishi Tanabe Pharma, Grant/research support from: Capella BioScience, Kymab and Mitsubishi Tanabe Pharma, Oliver Distler Consultant of: AbbVie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Bayer, Blade Therapeutics, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos NV, GlaxoSmithKline, Glenmark Pharmaceuticals, Horizon (Curzion) Pharmaceuticals, Inventiva, IQVIA, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Merck Sharp & Dohme, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Target Bioscience, Topadur Pharma and UCB, Grant/research support from: Kymera Therapeutics and Mitsubishi Tanabe Pharma, Christopher Denton Speakers bureau: Boehringer Ingelheim, Corbus, Janssen, and Mallinckrodt Pharmaceuticals, Consultant of: Acceleron Pharma, Arxx Therapeutics, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos NV, GlaxoSmithKline, Horizon Therapeutics, Janssen, Mallinckrodt Pharmaceuticals, Roche, Sanofi and UCB, Grant/research support from: Arxx Therapeutics, GlaxoSmithKline and Servier, Yannick Allanore Consultant of: Boehringer Ingelheim, Medsenic, Menarini and Sanofi, Grant/research support from: Alpine Pharmaceuticals, Daniel Wachtlin Employee of: Currently an employee of Boehringer Ingelheim, Margarida Alves Employee of: Currently an employee of Boehringer Ingelheim, Dinesh Khanna Shareholder of: Eicos Sciences, Inc. (less than 5%), Consultant of: Acceleron Pharma, Actelion, AbbVie, Amgen, Bayer, Boehringer Ingelheim, CSL Behring, Corbus, Gilead Sciences, Galapagos NV, Genentech/Roche, GlaxoSmithKline, Horizon Therapeutics, Merck, Mitsubishi Tanabe Pharma, Sanofi-Aventis and United Therapeutics, Grant/research support from: Bayer, Bristol-Myers Squibb, Horizon Therapeutics, Immune Tolerance Network, National Institutes of Health and Pfizer, Employee of: Chief Medical Officer-CiviBioPharma/Eicos Sciences, Inc.

DOI: 10.1136/annrheumdis-2021-eular.1760

AB0432

SURVIVAL AND PROGNOSIS IN SYSTEMIC SCLEROSIS: RESULTS FROM A SINGLE-CENTER COHORT

M. Rojas-Giménez[1], R. Ortega Castro[1], C. López-Medina[1], J. Calvo Gutierrez[1], M. Á. Aguirre-Zamorano[1], A. Escudero Contreras[1]. *[1]Reina Sofía University Hospital, Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC), Córdoba University (UCO), Córdoba, Spain., Cordoba, Spain*

Objectives: To analyze survival, causes of death, and risk factors associated with mortality in a cohort of patients with Systemic Sclerosis (SSc) at a single center

Methods: We performed a retrospective observational study of a cohort of patients with SSc undergoing follow-up during 2012 and until August 2020. We used the Kaplan-Meier method to estimate survival from onset of symptoms and multivariate Cox regression analysis to obtain independent risk factors associated with mortality

Results: The study population included 85 patients (women, 85.8%; mean age at diagnosis, 64.4 ± 12.7 years). A total of 19 patients (22.6%) died (table 1). Of these 11 (57.9%) died of a cause related to the disease itself (interstitial lung disease [ILD], 5 (26.3%); pulmonary hypertension, 2 (10.5%); or a combination of both, 3 (15.8%). The main cause of non–SSc-related death was cancer (21.1%). Survival rates at 5, 10, and 20 years were 98%, 92%, and 75%, respectively. Survival was statistically significantly poorer for the absence of ACA, the presence of antitopoisomerase I antibodies, proximal skin thickening, pulmonary hypertension, ILD, cancer and the diffuse subtype. The multivariate analysis performed to determine which factors were independently associated with mortality confirmed that older age at diagnosis of the disease, lower FVC in spirometry at diagnosis of ILD, and proximal skin thickening were associated with greater mortality

Table 1. Clinical and immunological characteristics of patients who died and patients who lived

	Dead (n=19)	Alive (n=66)	*p*-value
Female sex, n (%)	17 (89.5)	55 (83.3)	0.594
Age at diagnosis (years), mean (SD)	56.9 (13.7)	50.4 (13.6)	0.076
Time since diagnosis (years), mean (SD)	11.6 (7.3)	14.2 (9.2)	0.215
lcSSc, n (%)	6 (33.3)	50 (75.7)	**< 0.001**
dcSSc, n (%)	12 (66.7)	10 (15.1)	**< 0.001**
Digital ulcers, n (%)	9 (47.4)	33 (50)	0.748
Calcinosis, n (%)	1 (5.3)	16 (24.2)	0.061
Telangiectasias, n (%)	15 (78.9)	56 (84.8)	0.184
ILD, n (%)	15 (78.9)	32 (48.5)	**0.021**
FEV_1 at diagnosis of ILD, mean (SD)	78.3 (19.3)	78.7 (17.7)	0.955
FVC at diagnosis of ILD, mean (SD)	65.2 (13.1)	78.1 (20.7)	**0.043**
DLCO at diagnosis of ILD, mean (SD)	56.9 (17.5)	63.9 (16.7)	0.301
Pulmonary hypertension, n (%)	11 (57.9)	14 (21.9)	**0.002**
sPAP (mmHg), mean (SD)	49.2 (24.7)	30.2 (8.2)	**0.009**
Gastrointestinal involvement, n (%)	13 (68.4)	30 (45.4)	0.125
Cardiac involvement, n (%)	3 (15.8)	11 (16.7)	0.907
Muscle involvement, n (%)	1 (5.3)	2 (3.03)	0.851
Arthritis or arthralgia, n (%)	5 (26.3)	23 (34.8)	0.436
Renal crisis, n (%)	0	2 (3.03)	**<0.001**
Cancer, n (%)	5 (26.3)	2 (3.03)	**0.001**
Positive ACA, n (%)	5 (26.3)	35 (53.03)	**0.034**
Positive ATA, n (%)	10 (52.6)	9 (13.6)	**< 0.001**

Abbreviations: ILD: diffuse interstitial lung disease, SSc: systemic sclerosis, FEV_1: forced expiratory volume in the first second, FVC: forced vital capacity, DLCO: diffusing capacity for carbon monoxide, sPAP: systolic pulmonary artery pressure, ACA: anticentromere antibody, ATA: antitopoisomerase I antibody.

Conclusion: Survival at 10 years was greater than 90% in the study cohort. The main causes of death were ILD, pulmonary hypertension and cancer. The main factors associated with mortality were proximal skin thickening, older age at diagnosis, and lower forced vital capacity

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1777

AB0433

STUDY DESIGN FOR THE RANDOMISED CONTROLLED PHASE II RESSCUE TRIAL: SAFETY AND EFFICACY OF FAECAL MICROBIOTA TRANSPLANTATION BY ANAEROBIC CULTIVATED HUMAN INTESTINAL MICROBIOME (ACHIM) IN PATIENTS WITH SYSTEMIC SCLEROSIS

H. Fretheim[1], I. Barua[1], V. Sarna[2], M. N. Carstens[1], O. Distler[3], D. Khanna[4], E. Volkmann[5], Ø. Midtvedt[1], H. Didriksen[1], A. Dhainaut[6], A. K. H. Halse[7,8], G. Bakland[9], I. C. Olsen[10], M. E. Pesonen[10], Ø. Molberg[1], A. M. Hoffmann-Vold[1]. *[1]Oslo University Hospital, Department of Rheumatology, Oslo, Norway*; *[2]Oslo University Hospital, Department of Gastroenterology, Oslo, Norway*; *[3]University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland*; *[4]University of Michigan, Division of Rheumatology, Ann Arbor, United States of America*; *[5]University of California, Division of Rheumatology, Los Angeles, United States of America*; *[6]St. Olavs hospital, Department of Rheumatology, Trondheim, Norway*; *[7]University of Bergen, Department of Clinical Science, Bergen, Norway*; *[8]Haukeland University Hospital, Department of Rheumatology, Bergen, Norway*; *[9]University Hospital of Northern Norway, Department of Rheumatology, Tromsø, Norway*; *[10]Oslo University Hospital Research Support Services, Oslo Centre for Biostatistics and Epidemiology (OCBE), Oslo, Norway*

Background: Gastro-intestinal tract (GIT) symptoms is highly prevalent in patients with systemic sclerosis (SSc). The GIT-symptoms impact on the quality of life is significant, and available treatment alternatives are limited. Recently published articles show associations between gut microbiota changes and GIT-symptoms in SSc. We, therefore, performed a successful feasibility trial on faecal microbiota transplantation (FMT) in SSc patients using the single-donor bacterial culture "Anaerobic Cultivated Human Intestinal Microbiome (ACHIM)". Based on the promising results from the feasibility trial, we aim to evaluate the safety and efficacy of FMT by ACHIM in SSc patients. (NCT04300426)

Objectives: To design a clinical trial that explores the safety and efficacy of FMT in SSc patients.

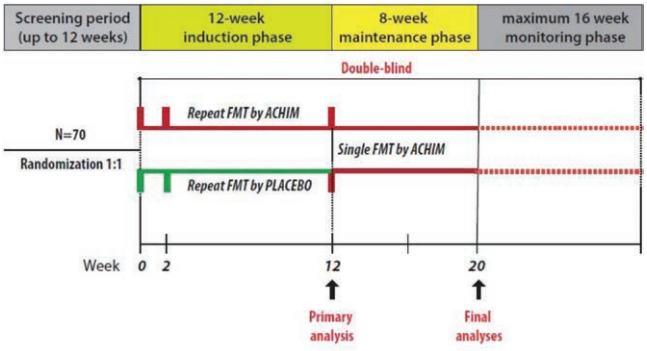
Methods: The ReSScue trial is a phase II, placebo-controlled, randomised 20-week, multicentre trial. The trial comprises three parts. In the induction phase (A1) lasting from week 0 to week 12, participants are randomised 1:1 to repeat infusions of 30 ml ACHIM or placebo at week 0 and 2 by gastro-duodenoscopy. In the maintenance phase (A2), all study participants will receive 30 ml ACHIM at week 12 and are followed continued blinded until week 20.

For longer-term data on intervention effects and safety, the participant will be followed for a maximum extended monitoring period of 16 weeks (part B).

The primary endpoint is change from baseline to week 12 in UCLA GIT scores on bloating or diarrhoea, depending on the worst symptom at baseline evaluated separately for each patient. Secondary endpoints are changes in UCLA GIT scores (bloating, diarrhoea and total) and safety measures.

Results: We aim to enrol 70 SSc patients based on the power calculations for the primary endpoint "change in worst symptom from baseline to week 12", with a considered drop out rate of 10%. This number of patients is expected to give a power of 80% of detecting a change in mean (p=0.05, two-sided) of -5.0 (or higher) if the relating standard deviation is 0.70 or lower. The patient screening started in September 2020, and we expect the study to be completed in May 2022.

Conclusion: The ReSScue-study is to our knowledge the first FMT-study in SSc. This trial will assess the safety and efficacy of FMT in SSc patients with lower GI-symptoms, possibly leading to a novel treatment approach in SSc patients.



Disclosure of Interests: Håvard Fretheim Grant/research support from: Received travel bursaries from Actelion, and remuneration from Bayer., Imon Barua: None declared, Vikas Sarna: None declared, Maylen N Carstens: None declared, Oliver Distler Speakers bureau: Below, Consultant of: Below, Grant/research support from: OD has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx, Baecon Discovery, Blade, Bayer, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos NV, Glenmark, GSK, Horizon (Curzion), Inventiva, iQvia, Italfarmaco, iQone, Kymera, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Dinesh Khanna Consultant of: Abbvie, Actelion/Janssen, Acceleron Pharma, Amgen, Bayer, Boehringer Ingelheim, CSL Behring, GSK, Horizon Pharmaceuticals, Mitsubishi Tanabe Pharma, Pfizer, Roche, Sanofi, United Therapeutics. DK is chief medical officer of Eicos Sciences, Inc., Grant/research support from: Abbvie, Actelion/Janssen, Acceleron Pharma, Amgen, Bayer, Boehringer Ingelheim, CSL Behring, GSK, Horizon Pharmaceuticals, Mitsubishi Tanabe Pharma, Pfizer, Roche, Sanofi,

United Therapeutics. DK is chief medical officer of Eicos Sciences, Inc., Elizabeth Volkmann Consultant of: Boehringer Ingelheim, Grant/research support from: Corbus, Forbius, Boehringer Ingelheim, Øyvind Midtvedt Shareholder of: Son of owner of ACHIM., Henriette Didriksen Speakers bureau: Travel bursary - GSK, Alvilde Dhainaut: None declared, Anna-Kristine H Halse: None declared, Gunnstein Bakland: None declared, Inge Christoffer Olsen: None declared, Maiju E Pesonen: None declared, Øyvind Molberg: None declared, Anna-Maria Hoffmann-Vold Consultant of: Actelion, ARXX, Bayer, Boehringer Ingelheim, Medscape, Merck Sharp & Dohme, Lilly and Roche., Grant/research support from: Actelion, ARXX, Bayer, Boehringer Ingelheim, Medscape, Merck Sharp & Dohme, Lilly and Roche.

DOI: 10.1136/annrheumdis-2021-eular.2184

AB0434 VITAMIN D IN SYSTEMIC SCLEROSIS PATIENTS

M. M. Sirufo[1], F. De Pietro[1], M. Raggiunti[1], M. De Martinis[1], L. Ginaldi[1]. *[1]Department of Life, Health & Environmental Sciences, University of L'Aquila, Italy; Allergology and Clinical Immunology Unit, AUSL 04, Teramo, Italy., Department of Life, Health & Environmental Sciences, University of L'Aquila, Italy; Allergology and Clinical Immunology Unit, AUSL 04, Teramo, Italy., Teramo, Italy*

Background: Systemic Sclerosis (SSc) is a generalized and systemic autoimmune disease that affects the connective tissue of the skin and internal organs, especially kidneys, heart and lungs [1].
Objectives: Numerous data from recent literature confirm the regulatory action of vitamin D on the immune system and, therefore, how a deficit of this micronutrient can lead to alterations in the immune response, as is known to happen in many allergic and autoimmune diseases [2]. We studied the association between vitamin D levels and SSc, evaluating their correlation with the characteristic manifestations of the pathology.
Methods: We dosed the serum levels of 25 hydroxy-vitamin D in 42 patients with SSc (average age 64.63 +/-7.33) and 40 healthy controls comparable for sex and age. The diagnosis of SSc was formulated in accordance to 2013 ACR/EULAR criteria. None of the subjects involved in the study took vitamin D products.
Results: Patients' vitamin D levels (26.22+/-9.82 ng/ml), although they tended to be lower than controls (27.80 +/- 16.53 ng/ml), showed no significant decrease. In patients with pulmonary fibrosis, vitamin D levels were 23.28 +/- 12.30 lower than in patients with trophic ulcers and compared to patients without complications 26.07 +/- 9.92, although with not statistically significant values. No statistically significant difference was found between vitamin D levels in patients with trophic ulcers compared to controls without complications.
Conclusion: According to the studies in the literature, in our sample, vitamin D deficiency was therefore greater in patients with SSc, especially with pulmonary fibrosis, than in controls [3,4]. Vitamin D levels in diffused-type SSc patients were significantly lower than those in limited-type SSc patients. Further studies are needed to clarify the role that vitamin D deficiency plays in SSc, but lower vitamin D levels in these patients may suggest the need to monitor blood levels of vitamin D and supplement it appropriately.
REFERENCES:

[1] De Martinis M, Ciccarelli F, Sirufo MM, Ginaldi L. An overview of environmental risk factors in systemic sclerosis. Expert Rev Clin Immunol. 2016;12(4):465-78. doi: 10.1586/1744666X.2016.1125782. Epub 2015 Dec 19. PMID: 26610037.
[2] Yang, CY., Leung, P.S.C., Adamopoulos, I.E. *et al.* The Implication of Vitamin D and Autoimmunity: a Comprehensive Review. *Clinic Rev Allerg Immunol* **45,** 217–226 (2013). https://doi.org/10.1007/s12016-013-8361-3.
[3] Trombetta AC, SmithV, Gotelli E, Ghio M, Paolino S, Pizzorni C, et al. (2017) Vitamin D deficiency and clinical correlationsin systemic sclerosis patients: A retrospective analysis for possible future developments. PLoS ONE 12(6): e0179062.https://doi.org/10.1371/journal. pone.0179062.
[4] Sarita Gupta, Vikram K. Mahajan, Rajinder S. Yadav1, Karaninder S. Mehta, Satya Bhushan1, et al. Evaluation of Serum Vitamin D Levels in Patients with Systemic Sclerosis and Healthy Controls: Results of a Pilot Study Article July 2018 DOI: 10.4103/idoj.IDOJ_328_17.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2268

AB0435 CAPILAROSCOPY DOES NOT PREDICT CARDIOVASCULAR EVENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS: A RETROSPECTIVE STUDY

I. Coman[1], L. Groseanu[1,2], V. Bojinca[1,2], D. Mazilu[1,2], S. Daia[1,2], I. Saulescu[1,2], C. L. Constantinescu[1,2], M. Abobului[1,2], A. Borangiu[1,2], M. M. Negru[1,2], C. Cobilinschi[1,2], M. Duna[1], D. Predeteanu[1,2], F. Berghea[1,2], A. Balanescu[1,2], R. Ionescu[1,2]. *[1]Saint Mary Hospital, Rheumatology, Bucureşti, Romania*; *[2]Carol Davila University of Medicine and Pharmacy, Medicine, Bucureşti, Romania*

Background: Systemic sclerosis is associated with increased risk of cardiovascular disease (CVD) (1) and studies using MRI suggest that microvascular disease has an important role (2). Capillaroscopy is a non invasive and safe technique that assesses peripheral microvascular damage (3).
Objectives: The objective of this study was to evaluate the predictive value of the capillaroscopy in relation to major adverse cardiovascular events (MACE).
Methods: Retrospective study with three timepoints (at baseline, at 5 and 10 years) including patients with scleroderma from EUSTAR center 096. Data were collected from the registry and observation papers. We performed capillaroscopy to all patients at the time of inclusion in the EUSTAR registry (2004) and at baseline (2009). Also, CV risk scores were calculated at baseline and were reassessed at 5 and at 10 years using the SCORE calculator. Risk score was considered low if was between 0 and 2, moderate 3-9 and high >10. The relation between capillaroscopy and MACE was tested in using bivariate regression.
Results: Of 22 patients, mean (standard deviation (SD)) age was 43.1 (11.5), all patients were females, mean (SD) disease duration was 5.4 (4.5). During the 10 years of follow up, 5 (22.7) patients had been lost of follow up and 8 (36.4) patients had died. Only 9 (40.9) patients completed the 10 year follow up.
At the time of inclusion in the EUSTAR, one patient showed early scleroderma pattern at capilaroscopy, 15 had active pattern and 6 patients had late pattern. Capillaroscopic scoring showed 2 (9.1) patients with disarranged (<50%) aspect, 5 (22.7) patietns with disarranged (>50%) aspect, 4 (18.2) patients with local paucity, 10 (45.5) patients with enlarged loop bordering local paucity and 1 patient (4.5) with complete paucity.
Capilaroscopy at baseline showed active pattern in 4 patients and late pattern in 18 patients. Thus, 13 (59.1) of patients had a progression of the disease at capilaroscopy before follow up.
At baseline, 14 (63.6) patients had traditional CV risk factors. Cardiovascular risk scores found 21 (95.5) patients with a low risk score and 1 (4.5) patient with a moderate risk score. At 5 years 11 (0.5) patients had a low risk score and 1 (4.5) patient had moderate risk score and at 10 years, 5 (22.7) and 2 (9) patients had low and moderate risk scores, respectively. We found 6.2 MACE/100 patient-year and 5.5 deaths/100 patient-year.
Capillaroscopy (p=0.684), disease progression on capillaroscopy (p=0.781), capillaroscopic scoring (p=0.92) and CV risk score (p=0.98) were not predictive factors of MACE.
Conclusion: Patients with systemic sclerosis are at high risk of MACE and traditional CV risk scores underestimate this risk. Changes/progression on capilaroscopy is not predictive for MACE. However, this hypothesis needs to be tested on a bigger cohort.
REFERENCES:

[1] Xintao Cen, SIning Feng, Shanshan Wei, Lu Wan, Ledong Sun, Systemic sclerosis and risk of cardiovascular disease: A PRISMA – compliant systemic review and meta-analysis of cohort studies, Medicine (Baltimore), 2020, 99(47)
[2] N Galea, E Rosato, A Gigante, C Borrazzo, A Fiorelli et al, Early myocardial damage and microvascular dysfunction in asymptomativ patients with systemic sclerosis: A cardiovascular magnetic resonance study with cold pressor test, PLoS One 2020, 15 (12)
[3] F Ingegnoli, R Gualtierotti, A systematic overview on the use and relevance of capillaroscopy in systemic sclerosis, Expert Rev CLin Ummunol, 2013, 9(11):1091-7

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2430

AB0436 OUTCOMES OF DOSE-REDUCTION OR DISCONTINUATION OF TOCILIZUMAB IN PATIENTS WITH EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

Y. Isomura[1], Y. Yamasaki[1], Y. Shirai[1], M. Kuwana[1]. *[1]Nippon Medical School, Graduate School of Medicine, Department of Allergy and Rheumatology, Tokyo, Japan*

Background: Potential efficacy and favorable safety profiles of tocilizumab (TCZ) have been demonstrated in patients with diffuse cutaneous systemic sclerosis (dcSSc) [1, 2]. However, clinical outcomes after dose-reduction or discontinuation of TCZ due to an improvement of skin thickness remain unclear.
Objectives: To investigate the clinical outcomes after dose-reduction or discontinuation of TCZ in patients with dcSSc in a real-world setting.
Methods: This is a single-center, retrospective, observational study using a database of consecutive SSc patients who visited our center between April 2014 and October 2020. For this study, we selected eligible patients from the database based on the following criteria: patients who (i) fulfilled the ACR/EULAR classification criteria, (ii) were classified as having dcSSc, (iii) had been treated with TCZ for at least 6 months, and (iv) were follow-up >6 months after TCZ introduction. Clinical information including demographic and clinical characteristics at TCZ introduction; dosing, administration route, and adherence of TCZ; and serial clinical parameters

(modified Rondan total skin thickness score [mRSS], and percent predicted forced vital capacity [%FVC]), safety profiles, and outcomes after TCZ introduction regardless of TCZ continuation were extracted from the database.

Results: Of 404 patients enrolled in the database, 13 dcSSc patients were eligible for this study. Baseline characteristics included a mean age of 51 ± 9 years, 85% female, disease duration of 27 ± 24 months, and mRSS of 19.5 ± 10.6. Seven patients (54%) had HRCT-confirmed ILD at baseline, and 9 (69%) were positive for anti-topoisomerase I antibody. Two (14%) and 11 (85%) were on mycophenolate mofetil and low-dose prednisolone (7.2 ± 6.0 mg/day), respectively. Seven patients (54%) each had active skin disease and elevated inflammatory markers defined in the phase III clinical trial [2], while only 4 (31%) fulfilled the inclusion criteria. TCZ was initially administered intravenously (8 mg/kg every 4 weeks) in 8 patients and subcutaneously in 5 (162 mg every 2 weeks in 4 and every week in one). At one year, mRSS was improved from 20.9 ± 11.4 to 10.7 ± 8.9 in 11 patients (p = 0.007), and %FVC was stable in 7 patients with ILD (76.8 ± 15.0 to 78.6 ± 16.1). During the observation period of 60.4 ± 26.7 months, 4 patients were treated with a stable dose of TCZ, while TCZ dose was reduced and/or discontinued in 9. Four of them discontinued TCZ due to adverse events (n = 2; acute lung injury and phlegmon) or prominent improvement of skin thickening (n = 2). Of 9 patients with dose reduction/discontinuation of TCZ, 4 patients who discontinued TCZ (n = 3) or received dose reduction of TCZ (n = 1) experienced a recurrence of progressive skin thickening together with inflammatory complications, including edematous induration of the skin, progression of ILD, polyarthritis, and/or pericarditis with increased inflammatory markers. The interval between dose-reduction/discontinuation of TCZ and clinical worsening ranged from 2 to 11 months. These manifestations were promptly improved by dose-escalation or resumption of TCZ in all patients except one who experienced progressive ILD and died of respiratory failure 27 months later.

Conclusion: In dcSSc patients who experienced improvement of skin thickness during treatment with TCZ, dose-reduction or discontinuation of TCZ may result in a recurrence of the disease. Randomized comparative studies are necessary to examine optimal timing for dose-reduction or discontinuation of TCZ in dcSSc patients after improvement of skin thickness.

REFERENCES:

[1] Khanna, D., et al., *Safety and efficacy of subcutaneous tocilizumab in systemic sclerosis: results from the open-label period of a phase II randomised controlled trial (faSScinate).* Ann Rheum Dis, 2018. **77**(2):212-220.

[2] Khanna, D., et al., *Tocilizumab in systemic sclerosis: a randomised, double-blind, placebo-controlled, phase 3 trial.* Lancet Respir Med, 2020; 8(10): 963-974.

Disclosure of Interests: Yohei Isomura: None declared, Yoshioki Yamasaki Speakers bureau: Boehringer-Ingelheim, Nippon Shinyaku, Bristol Myers, Yuichiro Shirai Speakers bureau: Janssen, Grant/research support from: Janssen, Masataka Kuwana Speakers bureau: Abbie, Astellas, Asahi Kasei Parma, Boehringer-Ingelheim, Chugai, Eisai, Janssen, MBL, Mochida, Nippon Shinyaku, Ono Pharmaceuticals, Pfizer, Tanabe-Mitsubishi, Consultant of: Boehringer-Ingelheim, Chugai, Corbus, MBL, Mochida, Grant/research support from: Boehringer-Ingelheim, Chugai, Eisai, MBL, Ono Pharmaceuticals, Tanabe-Mitsubishi

DOI: 10.1136/annrheumdis-2021-eular.2471

AB0437 OESOPHAGEAL DILATATION ON HIGH-RESOLUTION CT CHEST IN SYSTEMIC SCLEROSIS: SIGNIFICANT INDEX?

Y. Erez[1], A. Karakas[1], S. Gulle[1], E. Yılmaz[2], G. Can[1], İ. Sari[1], F. Onen[1], M. Birlik[1]. [1]*Dokuz Eylul University School of Medicine, Division of Rheumatology, İzmir, Turkey*; [2]*Dokuz Eylul University School of Medicine, Division of Radiology, İzmir, Turkey*

Background: Systemic sclerosis (SSc) is chronic, autoimmun multisystem disorder presented by thickening and fibrosis of the skin and internal organs. Esophageal involvement is one of the most common manifestation. Esophageal enlargement on HRCT is a common finding in scleroderma patients and may also be associated with other scleroderma-related clinical findings (1).

Objectives: The aim of this study to evaluate the association between esophageal dilatation on chest HRCT at diagnosis with the other SSc features.

Methods: The study was planned for SSc patients registered between October 2007 and September 2020 in Dokuz Eylul University Rheumatology Department database. Demographics, clinical features and medical history were recorded. The baseline HRCT reports were screened in terms of esophageal dilatation. Then, the initial HRCT images were assessed for esophageal dilatation by an experienced chest radiologist according to recommendation of *Pitrez et al.*

Results: In our study, there were 233 SSc patients (f:206 M:27, mean age 59.9±12.7 years) 71 (31.4%) of them diagnosed with diffuse disease. Median follow-up of study was 73 (1-272) months. Esophageal dilatation on HRCT was detected in 60 (25.8%) of SSc patients. 67 out of 155 patients (43.2%) had proof of esophageal involvement in esophageal transit scintigraphy. There is no statistical correlation was found between esophageal dilatation on HRCT with gender, smoking, arthritis, pulmonary hypertension and autoantibody subtypes. Development of digital ulcer and telangiectasia is statistically higher in SSc patients with oesophageal dilatation on baseline chest HRCT (p=0.001 and p=0.039, respectively). There was a positive correlation between Modified Rodnan Skin Score (mRss) and esophageal dilatation (r=0.213, p: 0.004).

Conclusion: HRCT can be a reproducible and non-invasive method for evaluating esophageal dilatation. Presence of esophageal dilatation at baseline HRCT might be indicative for pulmonary involvement and SSc related gastrointestinal complications. Consecutive chest HCRT should be evaluated to obtain more reliable data about the relationship between esophageal dilatation and SSc related clinical features.

REFERENCES:

[1]Pitrez EH, Bredemeier M, Xavier RM *et al*.Ooesophageal dysmotility in systemic sclerosis:comparison of HRCT and scintigraphy. *Br J Radiol* 2006; 79: 719–24.

Table 1. Clinical and demographic characteristics of the presence of esophageal dilatation on HRCT

			Esophageal dilatation on HRCT				
	Total (n=233)		Yes (n=60, 25.8%)		No (n=173, 74.2%)		p
	Mean±SD.		Mean±SD.		Mean±SD.		
Age, years	59.9±12.7		59.7±12.2		60.1 ±12.6		>0.05
	n	**%**	**n**	**%**	**n**	**%**	
Female	206	88,4%	53	88,3%	149	86,1%	>0.05
Smoking	79	33,9%	19	31,7%	60	34,7%	>0.05
Diffuse SSc	71	30,5%	23	38,3%	44	25,4%	>0.05
Overlap syndrome	33	14,2%	8	13,3%	25	14,5%	>0.05
Pulmonary fibrosis	118	50,6%	42	70,0%	76	43,9%	>0.05
Arthritis	80	34,3%	23	38,3%	56	32,4%	>0.05
Telengiectasia	156	67,0%	48	80,0%	105	60,7%	**0,039**
Digital ulcer	87	37,3%	34	56,7%	51	29,5%	**0,001**
Anti-Scl 70 (+)	89	38,2%	28	46,7%	59	34,1%	>0.05
Anti-centromer (+)	75	32,2%	15	25,0%	59	34,1%	>0.05

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2512

AB0438 SERUM HOMOCYSTEINE AND BONE STATUS IN SYSTEMIC SCLEROSIS PATIENTS

S. Paolino[1], A. Cere2, A. Casabella2, C. Pizzorni2, A. Sulli2, E. Alessandri2, A. Lercara2, E. Hysa2, C. Schenone2, G. Pacini2, E. Gotelli2, M. Cutolo2. [1]*Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS Polyclinic San Martino, Genova, Italy, Genova, Italy*; [1]*Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS Polyclinic San Martino, Genova, Italy, Genova, Italy*

Background: Systemic sclerosis (SSc) is a complex autoimmune connective tissue disease characterized by self-amplifying microvascular damage sustained by autoimmune response and progressive skin and visceral fibrosis. Besides, SSc patients show higher incidence of bone micro/macroarchitectural damages and bone fractures. Emerging data demonstrate that high serum levels of homocysteine (Hcy) could modulate osteoclastogenesis and are recognized as risk factors for osteoporosis (2). Furthermore, serum levels of Hcy were found to be higher in SSc patients than in healthy controls (3).

Objectives: to evaluate the bone status according to HCy serum levels in a cohort of SSc patients.

Methods: 20 female patients fulfilling ACR 2013 criteria for SSc underwent a dual-energy X-ray absorptiometry scan (DXA) (Lunar Prodigy) to evaluate bone status. We analysed bone quantity and quality respectively by bone mineral density (BMD) and trabecular bone score (TBS). According to the WHO criteria, osteoporosis was defined as a bone density of 2.5 standard deviations below that of a young adult (T-Score). Fasting blood samples were obtained from all patients in order to test serum Hcy level and bone turnover markers after obtaining the informed consent. All subjects underwent morphometric spine X-Ray to evaluate vertebral fractures. Statistical analysis was performed using non-parametric tests.

Results: The mean age of patients was 64.15 ± 10.8 years with a mean disease duration of 9.1 ± 2.3 years. The mean modified Rodnan Skin Score (mRSS) was 10.7 ± 8.5. All patients showed a "scleroderma pattern" at nailfold Videocapillaroscopy (NVC): in particular, 7 patients showed the "Late*"* pattern, 9 patients the "Active" pattern and 4 patients the "Early" NVC pattern. Hyperomocisteinemia (HHcy) was found in 25% of patients. Interestingly, SSc patients with the "Late" NVC pattern showed a significantly higher serum level of Hcy compared to the "Early/Active" group (11.15 ± 4.4 *vs* 17.17 ± 6.4, p=0.03). No significant differences were observed in relation to the autoantibody profiles. Of note, 60% of patients with HHcy were found osteoporotic and 40% had bone fractures.

Considering the bone status, patients with Hcy showed a significantly lower TBS (p=0.03); the average values of BMD on the lumbar spine (p=0.79) and femoral neck (p=0.13) were found lower compared to, but without any statistical significance. Furthermore, no significant differences were observed in bone turnover markers according to Hcy levels.

Conclusion: The study demonstrates a relationship between higher levels of Hcy and lower TBS values within SSc patients, particularly in those with most severe microvascular damage al NVC ("Late" SSc pattern). Therefore it is concluded that higher serum levels of Hcy associate to both bone microarchitectural and microvascular damage in SSc.

REFERENCES:

[1] Cutolo M et al Expert Rev Clin Immunol 2019; 15: 753-64
[2] Behera J et al. J Cell Physiol 2017;232(10):2704-2709
[3] Yan-lie Zhang et al. Rheumatol 2018; 28(4):681-689

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2520

AB0439 CAPILLAROSCOPIC PATTERNS IN PATIENTS WITH SYSTEMIC SCLEROSIS-POLYMYOSITIS/ DERMATOMYOSITIS (SSc-PM/DM) OVERLAP SYNDROME

O. Desinova[1], M. Starovoytova[1], L. P. Ananyeva[1]. [1]*VA Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*

Background: Impaired microcirculation is one of the leading factors in local and general pathogenesis of SSc. Widefield nail-fold video-capillaroscopy (NFVC) stands as the most informative and at the same time simple method used for evaluation of capillary circulation.

Objectives: To identify characteristic and specific for SSc– PM/DM capillaroscopic features.

Methods: Both hand II – V fingers of 68 pts with SSc-PM/DM were subjected to widefield NFC, evaluated using a binocular 20x magnification Olympus microscope and analyzed in view of specific skin lesions discriminating diffuse and limited SSc forms.

Results: SSc-specific dilatations of capillary loops were the most common for SSc-PM/DM and were found in all pts; 50% of them had signs of active scleroderma pattern, such as capillary loss or "avascular areas" (50%) and hemorrhages (51.5%), associated with generalized microvascular spasm in early disease and capillary sclerosis in advanced disease. The morphological capillary abnormalities such as varying degrees of capillary loops tortuosity/vascular inhomogeneity were present in 63% of examined nailfolds, branching bushy behavior of capillary loops and mega-capillaries predominated; architectural disorientation/disarrangement of capillary loops with formation of subcutaneous plexus was seen in more than 50% of them. Capillaroscopic changes consistent with active scleroderma pattern were present in 54 % and were associated with lab signs of inflammatory muscle syndrome and immunological disorders: giant capillaries (p<0.02), disorientation of capillary loops (p<0.02) and ramified/ bushy capillaries (p<0.04) were significantly more frequent in patients with severe muscle syndrome, increased CPK, ANF -positivity and hemorrhages (p<0.03).

Conclusion: Thus, widefield NFVC revealed a "mixed" nature of capillaroscopic changes, combining features specific for SSc (capillary dilation, avascular areas, hemorrhages) and for PM/DM (bushy and giant capillaries, disorientation of capillary loops of the nailfold with formation of subcutaneous plexuses.)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2540

AB0440 CLINICAL AND IMMUNOLOGICAL FEATURES OF THE SYSTEMIC SCLEROSIS-OVERLAP SYNDROMES

O. Desinova[1], M. Starovoytova[1], L. P. Ananyeva[1], O. Koneva[1], L. Garzanova[1], R. Shayakhmetova[1], O. Ovsyannikova[1]. [1]*VA Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*

Background: Systemic Sclerosis (SSc) overlap syndromes (SSc with polymyositis / dermatomyositis (PM/DM), rheumatoid arthritis (RA), etc.) still remain a group of very heterogenous and not very well studied clinical variants of SSc that are characterized by certain clinical and immunological features.

Objectives: Identify clinical and immunological features of the SSc-overlap syndromes

Methods: 80 pts with SSc-PM/DM and 35 pts with SSc-RA undergoing standard clinical examination and laboratory immunological evaluation.

Results: ANA Hep2 was positive in 98% of SSc-PM/DM pts; a-Scl-70 was in 34%, a - PM-Scl and RF were in 20%. ACA (6%), a-RNP (9%), and a - Jo-1 (5%) were significantly less common. Correlation analysis showed significant prevalence of conduction abnormalities in pts with a-Scl-70- (p<0.03); PM-Scl was rarely associated with cardiac arrhythmia (p<0.02) and pericarditis (p<0.03), but there was an association between ACA and presence of digital ischemia (p<0.04). Three pts with limited skin had Scl-70 and PM-Scl antibodies, two of them manifested clinical features of DM. A-Jo-1 was found in 3 pts with a longstanding disease (14,10 and 7 years), and one of these pts was also positive for a-Scl-70. All pts had limited skin and two had interstitial lung disease with FVC values of 79% and 74.8%.

ANA Hep2 was positive in 96% of SSc-RA pts; a-Scl-70 – in 28%, and a-RNP - in 30%. RF-positivity was in 72% of pts, and Anti-CCP - in 27%. Simultaneous Anti-CCP and a-Scl-70 was found in one case, and Anti-CCP - anti-RNP – in another, both were associated with low RF titers. All pts had early joint involvement which became prevailing in subsequent years, and onset of the disease between 30 and 36 years. There was a correlation between laboratory signs of inflammatory activity and immunological disorders: ESR and a-Scl-70 (p<0.03). Anti-CCP and a-Scl-70 co-positivity was a significantly less frequent phenomenon (p<0.04). There was a remarkable 28% proportion of a-Scl-70 cases in SSc-RA with limited cutaneous which is usually characterized by ACA-positivity.

Conclusion: SSc-PM/DM and SSc-RA appear to be an active disease from the immunological point of view, confirming therefore an important role of immune alterations in disease progression. Laboratory findings display specific pathogenetic features of SSc-overlap syndromes; laboratory abnormalities can be used to measure the activity and specify characteristics of the pathological process.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2550

AB0441 NAILFOLDCAPILLAROSCOPY AND CANDIDATE BIOMARKER LEVELS IN SYSTEMIC SCLEROSIS-ASSOCIATED PULMONARY HYPERTENSION; PROFILING OF NON-INVASIVE MARKERS, A COHORT STUDY

J. Lemmers[1], C. H. M. Van den Ende[1], R. Smeets[2], B. Kersten[1], A. Van Caam[3], S. Van Leuven[1], J. Van Haren-Willems[4], A. Van Dijk[5], M. Vonk[1]. [1]*Radboud University Medical Center, Rheumatology, Nijmegen, Netherlands*; [2]*Radboud University Medical Center, Laboratory for Clinical Chemisty, Nijmegen, Netherlands*; [3]*Radboud University Medical Center, Laboratory of Experimental Rheumatology, Nijmegen, Netherlands*; [4]*Radboud University Medical Center, Pulmonology, Nijmegen, Netherlands*; [5]*Radboud University Medical Center, Cardiology, Nijmegen, Netherlands*

Background: Systemic sclerosis (SSc) is characterized by inflammation, vasculopathy and progressive fibrosis. Pulmonary Hypertension (PH) is one of the leading causes of death in SSc (1). Currently, most patients with SSc are screened for the presence of PH, and focus lies on early detection and early treatment. Recent literature describes potential for both nailfoldcapillaroscopy (NCM) and several biomarkers to serve as non-invasive tools to identify SSc patients at risk for developing PH (2). Ideally this could attribute to further improvement of risk stratification in SSc and PH screenings algorithms.

Objectives: To explore NCM characteristics and plasma levels of selected candidate biomarkers in a cross-sectional cohort of SSc patients with and without different forms of PH.

Methods: From 02-2018 until 02-2019 we included 40 consecutive SSc patients with associated PH (30 (75%) were female, 32 (80%) LcSSc, median age 72 years (IQR 69-77), median SSc duration 10.7 years (IQR 4.3-17.8), median PH duration 3.9 years (IQR 1.5-7.06)) and 40 without PH (28 (70%) were female, 26 (65%) had a LcSSc, median age 59 years (IQR 51-71), median SSc duration 6 years (IQR 3.1-8.6). In each group NCM characteristics (both quantitative and qualitative) and plasma levels of IL4, IL6, IL8, IL13, PDGFAA, PDGFAB-BB, 6Ckine, sTRAIL, MMP1, MMP7, sICAM1, sVCAM, CCL19/MIP3b, Endostatin, sVEGFR1, sVEGFR2, sVEGFR3, CXCL4, Endothelin1, FGF1, FGF2, VEGF-A, VEGF-C, and VEGF-D using Luminex kits, and vascular auto-antibodies AT1R and ETAR using ELISA (Celltrend GmbH, Luckenwalde, Germany) were determined. NCM characteristics were compared using t-tests, biomarker levels were compared by using Mann-Whitney U tests.

Results: We observed no differences in mean capillary density, number of abnormally shaped capillaries, number of fingers with density <3 capillaries/mm and in overall NCM pattern between patients with and without PH. Plasma levels showing significant differences between the two groups are presented in table 1.

Conclusion: We found significant differences in several of the selected biomarkers in SSc patients with and without PH, but not in NCM characteristics between the groups. However, we did observe a tendency toward more morphologic abnormalities and an overall late pattern in the SSc-PH group. Future longitudinal research should explore the added value of these NCM parameters and biomarkers in personalized risk stratification for the development of PH.

REFERENCES:

[1] Elhai M, Meune C, Boubaya M, Avouac J, Hachulla E, Balbir-Gurman A, et al. Mapping and predicting mortality from systemic sclerosis. Ann Rheum Dis. 2017;76(11):1897-905.
[2] Guillén-Del-Castillo A, Simeón-Aznar CP, Callejas-Moraga EL, Tolosa-Vilella C, Alonso-Vila S, Fonollosa-Pla V, et al. Quantitative videocapillaroscopy correlates with functional respiratory parameters: a clue for vasculopathy as a pathogenic mechanism for lung injury in systemic sclerosis. Arthritis Res Ther. 2018;20(1):281.

Table 1.

NCM	SSc PH (n=40)	SSc noPH (n=38, 2 missing)	P value
Mean capillary density/mm (±SD)	5.0 (±1.4)	5.4 (±1.6)	0.39
Mean number of fingers with density <3 (±SD)	2.3 (±1.9)	1.7 (±2.1)	0.20
Mean abnormally shaped capillaries/ mm (±SD)	1.2 (±0.46)	0.99 (±0.53)	0.07
NCM pattern (n)			0.103
Normal/aspecific	1	3	
early	0	3	
active	4	7	
late	34	25	
Not interpretable	1	2	
Biomarkers*	SSc PH (n=33, 7 missing) (median, IQR)	SSc noPH (n=40) (median, IQR)	P value
IL6 pg/ml	4.8 (1.7-8.2)	2.5 (1.3-5.6)	0.047
PDGF-AB-BB pg/ml	29535 (24777-33458)	32221 (29409-37549)	0.0034
sTRAIL pg/ml	36.6 (20,4 -50,6)	60.8 (40.7 -82.4)	<0.0001
sVCAM1 ng/ml	311 (254-374,)	265 (228 - 323)	0.0236
Endostatin ng/ml	53.8 (41.9- 72.6)	39 (28.6 - 46)	<0.0001
sVEGFR2 pg/ml	10388 (7276- 13323)	13736 (10282 -16554)	0.0006
CXCL4 ng/ml	3347 (2546-4708)	5309 (4089-6322)	<0.0001
VEGF-A pg/ml	672 (248 - 955)	346 (175-703)	0.0424
VEGF-D pg/ml	671 (421-1012)	515 (262-734)	0.0296

* only significant values with a p<0.05 are shown

Disclosure of Interests: Jacqueline Lemmers: None declared, C.H.M. van den Ende: None declared, R. Smeets: None declared, Brigit Kersten: None declared, Arjan van Caam: None declared, Sander van Leuven: None declared, Jolanda van Haren-Willems: None declared, Arie van Dijk Speakers bureau: Actelion(-Janssen), Consultant of: Actelion(Janssen), Grant/research support from: Unrestricted educational Grant for PhD student from Actelion (Janssen), Madelon Vonk Speakers bureau: Actelion(Janssen), Boehringer Ingelheim, Roche, Consultant of: Advisory Board from Actelion(Janssen) and Boehringer Ingelheim, Grant/research support from: Unrestricted Educational Grant and research support from Actelion(Janssen), research support from Ferrer

DOI: 10.1136/annrheumdis-2021-eular.2722

AB0442 CLINICAL FEATURES OF POLYMYOSITIS AND DERMATOMYOSITIS PATIENTS WITH SEVERE DYSPHAGIA

Y. Hayashi[1], K. Izumi[1], S. Hama[1], M. Higashida-Konishi[1], M. Ushikubo[1], H. Oshima[1], Y. Okano[1]. [1]*National Hospital Organization Tokyo Medical Center, Rheumatology, Tokyo, Japan*

Background: Polymyositis (PM) and dermatomyositis (DM) are autoimmune inflammatory diseases characterized by proximal myositis. Dysphagia has been reported to develop in 35 to 62% of PM/DM patients and known as poor prognosis factor.

Objectives: The purpose of this study is to determine the clinical characteristics of PM/DM patients who present with deglutition disorder.

Methods: Consecutive patients with PM/DM who visited National Hospital Organization Tokyo Medical Center between April 2010 and January 2021 are included in this study. We compared clinical features between the patients with and without dysphagia. The diagnosis of dysphagia was based on videofluorography swallow study, and dysphagia requiring gastrostomy was defined as severe dysphagia. The clinical characteristics compared in this study were following: age of onset, levels of serum creatine kinase (CK) and lactate dehydrogenase(LDH), sense of dysphagia, manual muscle test (MMT) score, and complication of malignancy or interstitial pneumonia.

Results: A total of 73 patients with PM/DM were identified. Among them, 12 patients were diagnosed with dysphagia, and 5 patients developed severe dysphagia. Patients with dysphagia had the following characteristics compared to patients without dysphagia: higher levels of serum LDH (833.7 ± 500.1 U/L vs 471.9 ± 321.0 U/L, p = 0.0088), higher levels of serum CK at initial examination (6070.3 ± 7184.8 IU/L vs 1534.7 ± 2978.8 IU/L, p = 0.0086) and more frequent sense of dysphagia (90.9% vs 10.6%, p< 0.0001), lower MMT score(3.18 ± 1.07 vs 4.31 ± 0.75, p = 0.0017). In addition to those, patients with severe dysphagia presented older age of onset (mean age 69.4 ± 12.0 vs 51.7 ± 14.8, p = 0.014), more frequent complication of malignancy (80.0% vs 14.8%, p= 0.0048) and less frequent complication of interstitial pneumonia (0.0% vs 55.5%, p= 0.023).

Conclusion: These results indicate that dysphagia develops frequently in PM/DM patients with higher levels of serum LDH or CK, sense of dysphagia and low MMT score. Among them, patients with elderly onset or malignancy are at risk for sever dysphagia, and should be treated carefully.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2757

AB0443 BIOMARKER SUCH AS IL-17, IL-21 AND TIMP-1, IS USEFUL FOR PREDICTING THE PATHOPHYSIOLOGY OF CONNECTIVE TISSUE DISEASE-ASSOCIATED PULMONARY HYPERTENSION

S. Nakashima[1], T. Kameda[1], H. Shimada[1], M. Mahmoud Fahmy Mansour[1], R. Wakiya[1], M. Kato[1], Y. Ushio[1], K. Sugihara[1], H. Dobashi[1]. [1]*Kagawa University, Division of hematology, Rheumatology and Respiratory Medicine, Department of Internal medicine, Kagawa, Japan*

Background: Connective tissue disease-associated pulmonary hypertension (CTD-PH) is constructed by a variety of pathologies, including cardiac, pulmonary, and vascular involvement, as well as immune abnormalities. Because of its various constructs, it is difficult for many respiratory physicians, cardiologists, and rheumatologists to determine a treatment strategy for CTD-PH. In addition, CTD-PH has different pathologies from iPAH, and there are cases in which immunosuppressive therapy is effective. These suggests that the two PAHs may have different pathogenesis, including inflammation in the pulmonary artery. However, there are not enough biomarkers to distinguish pathologies. On the other hand, it has been reported that various cytokines such as TIMP-1, Interleukin (IL)-6, IL-17, and IL-21 are involved in the pathogenesis of CTD-PH or vasculitis. (1,2) However, the relationship between these cytokine expression and the pathogenesis or treatment of CTD-PH has not been fully clarified.

Objectives: To clarify the relationship between cytokine profile and clinical features, change in cytokines and hemodynamics by treatment, association with the effectiveness of immunosuppressive therapy.

Methods: Patients suspected PH was included. At the time of cardiac catheterization(RHC), sera in pulmonary pre and post-capillary were collected and TIMP-1, MCP-1, IL-17 and IL-21, IL-12p70 and IL-6 were analyzed by ELISA(ABCAM UK, Ella simple plex USA). The following clinical data were collected: age, gender, underlying disease, complication of interstitial lung disease, treatment (immunosuppressant and pulmonary vasodilator), hemodynamics. Furthermore, we investigated the relationship between cytokines and clinical data.

Results: 15 cases of CTD-PH, 13 cases of non-CTD-PH, and 6 cases of non-PH were analyzed. (SSc 12 cases, MCTD 7cases, SLE 2 cases, and others 13 cases) 28 cases were diagnosed with PH by RHC. There was a positive correlation between IL-6 and mean pulmonary arterial pressure in all PH case. In addition, MCP-1, IL-6, and TIMP-1 tend to be high in SSc-PH cases. On the other hand, in Non-SSc-PH, IL-12p70 and IL-17 were high. In cases who pulmonary vascular hemodynamics improved by treatment, IL-17, IL-21, and TIMP-1 decreased.

Conclusion: Biomarker profiles in pulmonary capillaries may differ depending on the disease. Furthermore, it suggested that IL-17, IL-21 and TIMP-1 may be biomarkers of therapeutic effect.

REFERENCES:

[1] Hashimoto-Kataoka T. et al. Proc Natl Acad Sci U S A. 2015 May 19;112(20):E2677-86.

[2] Jun Ishizaki et al. Arthritis Res Ther. 2017 Sep 29;19(1):218.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2765

AB0444 CLINICAL-IMMUNOLOGICAL CHARACTERISTICS OF PATIENTS WITH INFLAMMATORY MYOPATHIES

A. Khelkovskaia-Sergeeva[1], O. Desinova[1], M. Starovoytova[1], L. P. Ananyeva[1], M. Cherkasova[2], R. Shayakhmetova[1]. [1]*VA Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*; [2]*VA Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology, Moscow, Russian Federation*

Background: Inflammatory disorders of the skeletal muscle include polymyositis (PM), dermatomyositis (DM), amyopathic dermatomyositis ADM, (immune mediated) necrotizing myopathy (NM), overlap syndrome with myositis (overlap myositis, OM) and including anti-synthetase syndrome (ASS).

The detection of myositis-specific antibodies, the clinical effect of which remains to be determined, may be of great importance for diagnosis.

Objectives: To study clinical-immunological characteristics of patients with inflammatory myopathies.

Methods: 57 pts were enrolled in this study: 28 (47%) pts were diagnosed with DM, 14 (23%) pts – OM, 5(8%) pts – PM, 5 (8%) pts-NM, 4 (7%) pts-ADM, 1 (2%)- ACC. Duration of disease in average 11,29 (2-48) month. Standard clinical examination and laboratory immunological evaluation including myositis-specific autoantibodies were performed.

Results: There were 3 age groups: 18-39 years old – 16 (28%) pts, 40-49 yo – 28 (49%) pts and > 60 yo – 13 (33%) pts. Symptoms of myositis were muscle weakness 57 (100%) pts, dysphagia 29 (51%) pts, arthritis -12 (21%) pts, Raynaud's phenomenon 21 (37%) pts, skin lesions- 37 (65%) pts (Gottron signs- 7 (12%) pts, digital ulcers -11 (19) pts, panniculitis – 6(11%) pts, hand of mechanic 16(28%) pts). MMT 8 was 55,57 (SD 18,49) (20-80) score. Clinical features of myositis were myocarditis 8 (14%) pts and arrhythmia 9 (16%) pts, interstitial lung

disease 20 (35%) pts, esophageal involvement 29 (51%) pts of them 5 (9%) pts needed enteral feeding. 2 (4%) pts had oncopathology. CK was increased in 49 (86%) pts: < 10 N -15 (26%) pts, >10 N – 28 (49%) pts, > 50 N – 6 (11%). ANA positive - in 39 (70%) pts. Antibodies identified in 25(44%) pts: Pm-Scl 7 (12%) pts, PL-7 1 (2%), Mi-2 10 (17,5%), Ku 2 (3,5%) pts, AMA-M2 2 (2%)pts, a-SRP 4 (7%) and SS-A/Ro-52 13 (23%), SS-A/Ro-60 2 (3%) pts.

Conclusion: The group of inflammatory myopathies is characterized by clinical and immunological heterogeneity. Finding antibodies specific for myositis can help diagnose the disease.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3101

AB0445 FIRST CLINICAL ANALYSIS OF MYOSITIS PATIENTS REGISTERED AT REUMA.PT/MYOSITIS PROTOCOL: DATA FROM A SINGLE-CENTER

A. T. Melo[1,2], E. Dourado[1,2], P. Martins[1,2], N. Khmelinskii[1,2], J. E. Fonseca[1,2], I. Cordeiro[1,2], R. Campanilho-Marques[1,2]. [1]*Lisbon, Serviço de Reumatologia e Doenças Ósseas Metabólicas, Hospital de Santa Maria, CHULN, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal*; [2]*Lisbon, Unidade de Investigação em Reumatologia, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Lisbon, Portugal*

Background: Idiopathic inflammatory myopathies are a group of rare heterogeneous diseases that require a multidisciplinary and standardized approach.

Table 1. Clinical characteristics and immunological profile of the patients.

Diagnosis (n)	Clinical features					Myositis antibodies (n)
	Skin disease, median [IQR]/ (n)	**MMT-8, median [IQR]**	**Lung disease (n)**	**Others (n)**	**Malignancy (n)**	
Definite DM (28)	DAS Skin 2 [0-2] Calcinosis (3) Mechanic hands (2)	80 [75-80]	NSIP (2); COP (1)	Arthritis (6)	Breast cancer (1)	anti-Ro52 (6); anti-Mi2b (5); anti-PmScl100 (4); anti-MI2a (3); anti-NXP2 (3); anti-SAE (2); anti-MDA5 (2); anti-Ku (2); anti-Tif1g (1)
Antisynthetase syndrome (21)	DAS Skin 0 [0-0] Calcinosis (1) Mechanic hands (4)	80 [80-80]	NSIP (11); UIP (3); LIP (1)	Arthritis (15); RP (10)	–	anti-Jo1 (14); anti-Ro52 (12); anti-Mi2b (1); anti-PL7 (3); anti-PL12 (1)
Probable DM (19)	DAS Skin 0 [0-0]	80 [78-80]	COP (1)	Arthritis (5); RP (6)	–	anti-Mi2a (4); anti-Mi2b (2); anti-Tif1g (2); anti-Ku (2); anti-PmScl75 (2)
CADM (16)	DAS Skin 1 [0-2] Calcinosis (1) Mechanic hands (1)	80 [77-80]	NSIP (1); COP (1)	Arthritis (5); RP (4)	–	anti-Mi2b (5); anti-Ro52 (2); anti-Mi2a (1); anti-MDA5 (1); anti-EJ (1); anti-SAE (1); anti-SRP (1); anti-Ku (1); anti-Tif1g (1)
MCTD (12)	DAS Skin 0 [0-1]	80 [79-80]	NSIP (1)	Arthritis (8); RP (10)	–	anti-U1 RNP (12); anti-Ro52 (7)
PM (7)	DAS Skin 0 [0-0] Calcinosis (1)	80 [72-80]	NSIP (1)	Arthritis (1)	Ovarian cancer (1); non-Hodgkin lymphoma (1)	anti-Ro52 (2); anti-SRP (1)
UCTD (5)	DAS Skin 0 [0-2] Calcinosis (1) Mechanic hands (1)	80 [79-80]	NSIP (2)	Arthritis (1); RP (5)	–	anti-ThTo (2); anti-SRP (1); anti-PL12 (1)
Overlap syndromes (12)	DAS Skin 0 [0-2] Mechanic hands (2)	80 [77-80]	NSIP (3); UIP (1)	Arthritis (4); RP (8)	–	anti-PmScl75 (4); anti-PmScl100 (1); anti-Ro52 (1); anti-Ro60 (1); anti-RNAPIII (1); anti-NOR90 (1); anti-MDA5 (1); anti-Ku (1)
Necrotizing myopathy (1)	DAS Skin 0	80	–	–	–	–

DM – dermatomyositis; CADM – clinically amyopathic dermatomyositis; MCTD – mixed connective tissue disease; PM – polymyositis; UCTD – undifferentiated connective tissue disease; ILD – interstitial lung disease; NSIP – nonspecific interstitial pneumonia; LIP – lymphocytic interstitial pneumonitis; UIP – usual interstitial pneumonia; COP – cryptogenic organizing pneumonia; RP – Raynaud phenomenon

Objectives: To clinically characterize patients with inflammatory myopathies followed at an hospital's Rheumatology Department, using the Rheumatic Diseases Portuguese Register (Reuma.pt).

Methods: An observational transversal study was performed. Data on demographic variables, clinical features, antibodies and treatment were collected.

Results: Of the 121 included patients, 78% were female, with a median age of 56 [44-68] years and a median disease duration of 2 [0-4] years. The most frequent diagnosis was dermatomyositis (DM; n=28, 23%) followed by antisynthetase syndrome (ASyS; n=21, 17.4%). At the time of the analysis, the median Manual Muscle Test (MMT-8) was 80 [78-80], the median modified skin Disease Activity Score was 0 [0-2] and global disease activity was 0.5 [0-0.75]. Calcinosis was found in 6% of the patients (n=7), mostly DM cases. Interstitial lung disease (ILD) was present in 29 patients (24%), of those, 52% (n=15) had antisynthetase syndrome (ASyS). Three patients presented as a paraneoplastic syndrome. Ninety-nine patients (82%) had a myositis autoantibody identified: antisynthetase autoantibodies were the most commonly identified (n=20, 16%). 62% of the patients were treated with steroids and 35% with ≥2 disease-modifying anti-rheumatic drugs.

Table 1 depicts the main clinical characteristics and the immunologic profile for each diagnosis

Conclusion: In our cohort the most frequent myositis subtype was DM. Almost a quarter of patients had associated ILD, which is an important cause of morbidity and mortality. ILD was more frequent in ASyS patients and was most commonly related to anti-Jo1 antibodies, which is consistent with the literature.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3150

AB0446 DEMOGRAPHIC AND CLINICAL FEATURES OF IDIOPATHIC INFLAMMATORY MYOSITIS AND PREVALENCE OF MYOSITIS-RELATED ANTIBODIES

G. K. Yardımcı[1], E. Erul[2], B. Farisoğulları[1], G. Ayan[1], L. Kılıç[1], O. Karadag[1], Ş. A. Bilgen[1]. [1]*Faculty of Medicine; Hacettepe University, Rheumatology, Ankara, Turkey*; [2]*Faculty of Medicine; Hacettepe University, Internal Medicine, Ankara, Turkey*

Background: Idiopathic inflammatory myopathies (IIM) are heterogeneous groups of connective tissue diseases. Diagnosis of IIM is sometimes challenging, but newly defined myositis specific autoantibodies (MSAs) are helpful in diagnosing of IIM and revealing the clinical signs [1].

Objectives: To describe demographic and clinical features of IIMs and to evaluate the frequency and clinical associations of myositis-specific and myositis associated antibodies (MAAs) in IIM.

Methods: Samples obtained from patients tested for MSA/MAA as of 2017 to 2020 were retrospectively evaluated. Patients were diagnosed with IIM according to clinician diagnosis. The prevalence and clinical associations of myositis-related antibodies were assessed with univariate and multivariate analysis.

Results: 152 patients (70.4% female) were tested for myositis-related antibodies during the study period. 81 patients were diagnosed with IIM (38 DM, 43PM). DM patients were diagnosed at an earlier age and its association with malignancy was more relevant, although the relationship with malignancy was not statistically significant. Differences of clinical characteristics between DM and PM patients were skin features which were more frequent in DM, and interstitial lung disease which was more common in PM patients.

MSAs/MAAS were found in 65.4% and 43.2% in IIM patients, more frequently than patients without IIM (p=0.000 and 0.0225, respectively). MSAs were equally frequent in both IIM groups, whereas MAAs were more common in the PM group (although no significant difference in overlap with other connective tissue diseases within these two diseases). The most common MSAs in DM were anti-TIF1-γ (23%), anti-MDA5 (16%), anti-NXP2 (13%) and in PM were anti-Jo-1 (28%), anti-MDA5 (12%), anti-ku (12%), anti-PL7 (12%) respectively. Predictors of ILD in IIM were Anti-Jo-1 positivity and age (RR:10 [CI:2-41] p=0.003 and RR:1.07 [CI:1.02-1.12] p=0.04 respectively)

Conclusion: The general characteristics of DM and PM patients and the frequencies of myositis-specific autoantibodies were similar to the literature, except that anti-TIF1-γ antibodies (14%) were more common in our Turkish cohort [2].

REFERENCES:

[1] Cruellas, M.G., et al., *Myositis-specific and myositis-associated autoantibody profiles and their clinical associations in a large series of patients with polymyositis and dermatomyositis.* Clinics (Sao Paulo), 2013. **68**(7): p. 909-14.

[2] Gonzalez-Bello, Y., et al., *Myositis-Specific Antibodies and Myositis-Associated Antibodies in Patients With Idiopathic Inflammatory Myopathies From the PANLAR Myositis Study Group.* J Clin Rheumatol, 2020.

Table 1. Baseline characteristics of the patients with DM and PM

	DM (n=38)	PM (n=43)	*P*
Female, n (%)	27 (71.1)	29 (67.4)	0.457
Age at onset, years	33 (15-48)	47 (38-58)	0.002
Skeletal muscle features			
Muscle weakness, n (%)	34 (89.5)	37 (86.0)	0.451
Myalgia, n (%)	23 (60.5)	30 (69.8)	0.261
Artritis, n (%)	8 (21.1)	9 (20.9)	0.601
Skin features, n (%)			
Heliotrope rash, n (%)	18 (47.4)	0 (0)	<0.001
Gottron papules, n (%)	25 (65.8)	0 (0)	<0.001
Gottron sign, n (%)	18 (47.4)	0 (0)	<0.001
Generalize erythema, n (%)	10 (26.3)	0 (0)	<0.001
Calcinosis, n (%)	4 (10.5)	1 (2.3)	0.143
Dysphagia, n(%)	10 (26.3)	12 (27.9)	0.537
Interstitial lung disease (ILD), n (%)	8 (21.1)	20 (47.6)	0.012
Other connective tissue diseases overlap, n (%)	6 (15.8)	13 (30.2)	0.102
Malignancies, n (%)	5 (13.5)	3 (7)	0.275
Laboratory data			
Creatine kinase (IU/L)	505 (110-3616)	801 (402-1868)	0.655
C-reactive protein (mg/dl)	0.3 (0.1-0.8)	1.2 (0.5-2.8)	<0.001
ESR (mm/h)	19 (8-27)	25 (17-48)	0.005
MAAs (Ro-52, pm-scl 100, pm-scl75), n (%)	11 (28.9)	24 (55.8)	0.013
MSAs, n (%)	28 (73.7)	25 (58.1)	0.108
Anti- TIF1- γ, n (%)	9 (23.7)	2 (4.7)	0.014
Anti-Jo-1, n (%)	2 (5.3)	12 (27.9)	0.007
Anti-PL-7, n (%)	0	5 (11.6)	0.038

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3349

AB0447 PREVALENCE OF PRIMARY BILIARY CIRRHOSIS IN SYSTEMIC SCLEROSIS AND SJÖGREN'S SYNDROME OVER TIME: A SYSTEMATIC REVIEW

S. Upadhyaya[1], D. Starcevic[2], M. Turk[3], J. Pope[1]. [1]*Western University, Rheumatology, London, Canada*; [2]*Western University, Schulich School of Medicine & Dentistry, London, Canada*; [3]*Western University, Medicine, London, Canada*

Background: Primary biliary cirrhosis (PBC) is a rare slowly progressive autoimmune disease characterized by inflammatory destruction and fibrosis of intrahepatic bile ducts. It is known to coexist together with rheumatological conditions such as Sjögren's syndrome (SS) and systemic sclerosis (SSc). There is a wide range in reported prevalence of disease overlap with these entities; however, the exact prevalence rates remain unclear.
Objectives: The objectives were to determine the prevalence of: 1) PBC in patients with SS and SSc (and the subsets of limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc)), 2) SSc and SS in patients with PBC, and 3) to analyze changes in frequency over time. SSc occurs in 3/10,000 and PBC in 4-40/10,000 but these rare autoimmune diseases are known to coexist together. We speculated that there could be more cases diagnosed due to increasing availability of standardized antibody tests such as ANA, centromere antibodies, ENA and mitochondrial antibodies.
Methods: A systematic review of the literature was performed using Medline, EMBASE, CINAHL, and the Cochrane Library databases up till June 16, 2020. Only full text articles in the English language with at least 40 patients were included. Cohorts, case series, cross-sectional studies, correspondences and registries with reported prevalence rates of both PBC in patients with SS and SSc as well as SSc and SS in patients with PBC were included. Data on frequency of co-existent diseases was studied by year of publication to determine if prevalence changed over time using linear regression. We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist to assess the quality of the studies.
Results: Of 2876 citations identified, 67 were included in the analysis (n=33 for PBC, 15 for SSc, 18 for SS and 1 for SSc/SS). STROBE checklist scores ranged from 7-21. The prevalence of PBC was 5% in patients with SSc. Within the subsets, the prevalence of PBC in lcSSc was 8% and in dcSSc was 1%. In patients with SS, the prevalence of PBC was 4%. The prevalence of SSc overall in those with PBC was 5% and, within the subsets was 6% in lcSSc and 0% in dcSSc. The prevalence of SS in PBC was 18%. There was also no significant association between year of publication and prevalence. There was a lack of standardized definitions so misclassification may have occurred.
Conclusion: PBC is increased in SSc but mostly in the lcSSc subset. SS in PBC is common at nearly 1 in 5. Over the years, there was no change in the prevalence of PBC in SSc indicating stability over time.
Acknowledgements: Meagan Stanley, Western University Librarian.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3433

AB0448 SYSTEMIC SCLEROSIS ASSOCIATED PULMONARY ARTERIAL HYPERTENSION: PREDOMINANCE OF PULMONARY FIBROSIS AS A RISK FACTOR FOR MORTALITY IN A SINGLE CENTER COHORT

S. Amikishiyev[1], Y. Yalçınkaya[1], N. Aliyeva[1], K. Mammadova[2], B. Artim-Esen[1], A. Gül[1], A. K. Bilge[3], G. Okumuş[2], M. Inanc[1]. [1]*Istanbul Faculty of Medicine, Istanbul University, Division of Rheumatology, İstanbul, Turkey*; [2]*Istanbul Faculty of Medicine, Istanbul University, Department of Chest Diseases, İstanbul, Turkey*; [3]*Istanbul Faculty of Medicine, Istanbul University, Department of Cardiology, İstanbul, Turkey*

Background: Pulmonary arterial hypertension (PAH) is a severe vasculopathic complication for systemic sclerosis (SSc) patients. The availability of oral-specific vasodilator therapies has provided better outcomes.
Objectives: We aimed to analyze the characteristics of SSc-PAH patients and factors associated with mortality.
Methods: Medical records of 291 SSc patients fulfilling ACR/EULAR criteria (2013) and followed–up during 2008-2020 years were screened and the patients who diagnosed PAH evaluated by right heart catheterization (mean PAB≥20 mmHg) (n=26, 8,9%) were included into this retrospective cross-sectional study.
Results: The characteristics of 26 SSc-PAH(24 females) patients were summarised in Table 1.

Table 1. Characteristics of SSc patients with PAH

	SSc-PAH (n=26)
Demographics	
Age(yrs)	53.6±8.9
Duration of Raynaud's(yrs)	16.1±11.8
Duration of Non-Raynaud's(yrs)	9.2±6.6
Raynaud's to ***Diagnosis of PAH***(yrs)	10.8±6.7
Clinical Characteristics (%)	
LcSSc	9 (34.6)
DcSSc	18 (65.4)
Digital ulcer	14 (53.8)
Gastrointestinal	20 (69.0)
Synovitis	5(19.2)
Flex contractures	7 (26.9)
Tendon friction rubs	3(11.5)
Renal crisis	1 (3.8)
Pulmonary fibrosis	19 (73.1)
Auto-antibodies (%)	
ANA	23 (88.5)
Anti-centromere	6(23.1)
Anti-Scl70	13(50)
Treatment (%)	
Specific vasodilator	
ERA (bosentan/macicentan/ambricentan)	15 (51.7)
PDE5-i (sildenafil/tadalafil)	17 (58.6)
Prostacyclin-analog (İloprost/treprostenil/selexipag)	15 (51.7)
Riociguat	5 (17.2)
Immunosuppressives	21(80.8)
Steroids	16(61.5)

Twenty-four (92,3%) of the SSc-PAH patients had PAH-related symptoms at the time of diagnosis, 2 (7,7%) were asymptomatic and diagnosed by screening. RHC and treatment details were stated in Table 2.

Table 2. Right Heart Catheterization (RHC) ve treatment details of SSc-PAH patients

	n=26
Initial RHC	
-mean PAB	30,4±7,9 (median 28, 20-53mmHg)
-PVR	5,1±2,4 (median 4, 3-9 woods)
-PCWP	10,8±5,5 (median 10, 0-15 mmHg)
Initial treatment	
-monotherapy	5 (19,2%)
-combination	10 (38,5%)
-add-on combination	12 (46,2%)

Eleven out of 26 patients (42,3 %) were deceased after a mean follow up of 43,7±24,6 (median 48,1-84) from PAH diagnosis and 15,1±9,9 (median 13, 0,6-34) years after SSc diagnosis. Deceased patients were younger and had younger age at disease onset (49,1± 8,8 vs 56,9±7,7, p=0.032 and 30,8±13,0 vs 42.0 ±10,9, 0.027). All deceased patients had associated pulmonary fibrosis (100 vs 53.3%, p=0.01). No significant difference was observed for initial RHC parameters between deceased and survived SSc-PAH patients. Specific monotherapy was found to be more frequent in deceased patients (45,5 vs 0%, p=0,007).

Conclusion: The prevalence of SSc-PAH was found to be 8.9% with increased mortality in our cohort. SSc-PAH patients predominantly had diffuse cutaneous involvement with digital vasculopathy, pulmonary fibrosis, and anti-Scl70 positivity. PAH was diagnosed after a median of 10 years of the Raynaud's, mainly in symptomatic patients. Mortality in PAH-SSc patients was associated with early onset of disease, pulmonary fibrosis, and monotherapy. Initial RHC parameters were not found to be related to mortality.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3460

AB0449 CLINICAL CHARACTERISTICS AND RISK FACTORS OF SYSTEMIC SCLEROSIS WITH HEMATOLOGIC SYSTEM DAMAGES

J. Zheng[1], Z. R. Dong[1], Y. P. Tang[1], Y. Q. Huang[2], Q. B. Zhang[2], F. Dai[1], Y. F. Qing[1]. [1]*Institute of Rheumatology and Immunology, Department of Rheumatology and Immunology, Nanchong, China*; [2]*Institute of Rheumatology and Immunology, Department of Geriatrics, affiliated Hospital of North Sichuan Medical College, Nanchong, China*

Background: SSc characterized by varying degrees of fibrosis of the skin and internal organs, clinicians pay more attention to skin and viscera conditions, tend to ignore hematologic system damage. Studies have shown that rheumatic disease such as SLE, RA, pSS often accompanied with hematologic system damages, and hematologic system damages is multiple organ involvement and risk factor of poor prognosis[1-2].

Objectives: To investigate the the clinical features, laboratory characteristics and risk factors of Systemic Sclerosis (SSc) patient with hematologic system damages.

Methods: The clinical data of 180 patients were collected from January 2010 to April 2020, at the Affiliated Hospital of North Sichuan Medical College. The demographic information, laboratory tests, and clinical symptoms were analyzed retrospectively.

Results: Among 180 SSc patients, 70(38.9%) cases were complicated with hematologic system damages. 51(72.9%) cases had anemia, 24 cases (34.3%) had leukopenia, 24 cases (34.3%) had thrombocytopenia, and 22 cases had hematologic system damages associated with more than two cell line involvement. Clinical symptoms: arthritis was significantly higher in the hematologic system damages group than patient without (P<0.05), however, there was no significantly difference in gender, age, disease course, respiratory symptoms, gastrointestinal symptoms, Raynaud's phenomenon, interstitial lung disease and pulmonary hypertension (all P>0.05). Laboratory tests: ESR and hsCRP were increased in the hematologic system damages group, while the albumin decreased (all P<0.05). The positive rates of resistance to anti-dsDNA antibody and anti-ribosomal P protein antibody was higher in the hematologic system damages group (all P<0.05). Prognosis: During follow-up, leukopenia was more likely to recover, while the thrombocytopenia was more difficult to recover. Logistics regression analysis showed that positive of anti-ribosomal P protein antibody maght be a risk factor for SSc complicated with hematologic system damages [OR = 3.930(P<0.05)] (Table 1).

Conclusion: SSc complicated with hematologic system damages is common, and patients with hematologic system damages have more serious clinical symptoms, some of whom have difficulty in recovey. Anti-ribosomal P protein antibody may be a risk factor of SSc hematologic system damages.

Table 1. Bivariate logistics regression analysis on risk factors associated with hematologic damages in SSc.

Factor	*B*	*SE*	*Wald*	*OR(95%CI)*	*P* value
arthritis	0.654	0.347	3.543	1.922(0.973-3.797)	0.060
ESR	-0.081	0.487	0.028	0.922(0.355-2.393)	0.868
hsCRP	-0.007	0.492	0.000	0.993(0.379-2.607)	0.989
anti-dsDNA	0.868	0.673	1.664	2.393(0.637-8.916)	0.197
anti-Rib-P	1.369	0.636	4.633	3.930(1.130-13.666)	0.031

REFERENCES:

[1] González-Naranjo L A, Betancur O M, Alarcón G S, et al. Features associated with hematologic abnormalities and their impact in patients with systemic lupus erythematosus: Data from a multiethnic Latin American cohort[J]. Seminars in Arthritis and Rheumatism, 2016,45(6):675-683.DOI:10.1016/j.semarthrit.2015.11.003.

[2] Skare T, Damin R, Hofius R. Prevalence of the American College of Rheumatology hematological classification criteria and associations with serological and clinical variables in 460 systemic lupus erythematosus patients[J]. Revista Brasileira de Hematologia e Hemoterapia, 2015,37(2):115-119. DOI:10.1016/j.bjhh.2015.01.006

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3465

AB0450 PERIPHERAL MACROVASCULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS AS COMPARED WITH HEALTHY CONTROLS: A SMALL COHORT STUDY BY COLOR AND SPECTRAL DOPPLER ULTRASONOGRAPHY

R. D'alessandro[1], E. Garcia Gonzales[1], P. Falsetti[1], C. Baldi[1], F. Bellisai[1], E. Selvi[1], B. Frediani[1]. [1]*Rheumatology Unit, Policlinico Le Scotte, Department of Medical Sciences, Surgery and Neuroscience, Siena, Italy*

Background: Together with autoimmune-inflammation and fibrosis, microvasculopathy is a hallmark of SSc. However, also macrovascular changes may occur including peripheral proliferative vasculopathy. Whether this changes may represent a specific SSc marker with a predictive value remains a matter of debate. [1,2,3]

Objectives: To study peripheral macrovascular involvement by color doppler ultrasound (CDUS) with spectral wave analysis (SWA) in a cohort of 40 SSc patients as compared to healthy controls. To further analyze any differences among the SSc population.

Methods: Forty SSc patients and 36 healthy controls were examined by CDUS with SWA of both hands. Macrovascular involvement was assessed by measuring the resistivity index (RI) of distal ulnar and radial arteries. Examinations were performed with an Esaote MyLab Twice machine equipped with a linear 10-22 MHz probe. Ultrasound examination was carried out by two independent rheumatologists blinded to clinical conditions of the patients. Statistical analysis was performed by using MaxStat software.

Results: The RI index resulted increased in the SSc cohort as compared with healthy controls (left ulnar RI 0.977 vs 0.715; right ulnar RI 0.996 vs 0.699; left radial RI 0.988 vs 0.706; right radial RI 0.999 vs 0.688; p<0.001). SSc patients with an increased RI in one artery were more probable to have an increased RI in the other vessels too ($r^2 = 0.35$; p<0.01). In addition, 8 out of 40 SSc patients presented left ulnar artery occlusion (UAO) and 7 out of 40 SSc patients presented right UAO, of which 6 presented bilateral UAO. Awaiting to enlarge the cohort for further analysis, descriptive data regarding increased RI at CDUS/SWA and clinical features, including years from onset of the disease, subtype of SSc, mRSS, history of digital ulcers, interstitial lung disease and PAH are described in Table 1.

Conclusion: Peripheral macrovascular involvement was observed in SSc patients as compared with healthy controls. Further studies will determine whether this feature may have specificity for diagnosis/prognosis in SSc.

REFERENCES:

[1] Lescoat A, Yelnik CM, Coiffier G et al. Ulnar Artery Occlusion and Severity Markers of Vasculopathy in Systemic Sclerosis: A Multicenter Cross-Sectional Study. Arthritis Rheumatol. 2019;71:983-990.

[2] Lescoat A, Coiffier G, Rouil A et al. Vascular Evaluation of the Hand by Power Doppler Ultrasonography and New Predictive Markers of Ischemic Digital Ulcers in Systemic Sclerosis: Results of a Prospective Pilot Study. Arthritis Care Res (Hoboken). 2017;69:543-551.

[3] Schioppo T, Orenti A, Boracchi P, De Lucia O, Murgo A, Ingegnoli F. Evidence of macro- and micro-angiopathy in scleroderma: An integrated approach combining 22-MHz power Doppler ultrasonography and video-capillaroscopy. Microvasc Res. 2019;122:125-130.

Table 1. Main clinical features of the SSc cohort (n=40) studied by CDUS for macrovascular involvement.

SSc cohort (n = 40)	
Years from onset	range (35 y – 0 y) mean = 10.5 y
Autoantibodies	ACA 13/40 Anti-TopoI 14/40 Other 13/40
mRSS	range (0 -30) mean = 3
ILD	17/40
PAH	7/40
Capillaroscopy pattern	Early 10/40 Active 11/40 Late 6/40
History of digital ulcers	16/40
Left ulnar IR	0.977
Left radial IR	0.988
Right ulnar IR	0.996
Right radial IR	0.999

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3481

AB0451

TO EVALUATE THE PREVALENCE OF INTERSTITIAL LUNG DISEASE (ILD) AND/OR PULMONARY ARTERIAL HYPERTENSION (PAH) IN PATIENTS AFFECTED BY SYSTEMIC SCLEROSIS (SSC) AND TO DETERMINE THE FACTORS ASSOCIATED WITH ILD

R. Ortega Castro[1], R. Mariscal-Ocaña[2], M. Rojas-Giménez[1], J. Calvo Gutierrez[1], A. Escudero Contreras[1], C. López-Medina[1]. *[1]Reina Sofia Universitary Hospital/Maimonides Institute of Biomedical Research of Córdoba (IMIBIC), University of Cordoba, Clinical Management Unit of Rheumatology, Córdoba, Spain*; *[2]Reina Sofia Universitary Hospital/University of Cordoba, Clinical Management Unit of Rheumatology, Córdoba, Spain*

Background: Systemic sclerosis (SSc) is a chronic autoimmune disease that carries significant mortality. Despite diagnostic and therapeutic advances in recent years, there is still a significant percentage of patients who do not present a complete clinical response, with the associated increase in morbidity and mortality. Specifically, pulmonary disease is frequent and entails a poor prognosis, with interstitial lung disease (ILD) and pulmonary hypertension (PAH) being the two most important complications, the first and second cause of mortality, respectively.

Objectives: To evaluate the prevalence of ILD and/or PAH in patients affected by SSc and to determine the factors associated with ILD.

Methods: Cross-sectional observational study of 102 patients diagnosed with SSc (Limited, Diffuse, SSc without scleroderma or Pre-scleroderma), treated between 1975 and 2020 at the Reina Sofia University Hospital in Cordoba. A descriptive study of the cohort was carried out and factors independently associated with ILD were evaluated using a multiple logistic regression model.

Results: 102 patients were included, 87.3% of these were female with an average age of 50.8 (14) years. There were 20 deaths (19.8%), from which 55% died because of SSc and the main reason was ILD and/or PAH. Respiratory complications (as ILD or as PAH) were present in 59 patients (57.8%), of whom 52 were diagnosed with ILD (90.4% with a pattern of non-specific interstitial pneumonia) and 25 PAH, whose mean pulmonary artery systolic pressure was 47.16 (18.54) mmHg. Anti-topoisomerase I antibodies were positive in 34.6% of patients who developed ILD, while anticentromere antibodies were more frequent in SSc without interstitial lung disease (80%). Independent factors associated with ILD were type of SSc, proximal skin involvement, anticentromere antibodies, current treatment with corticoids and the death.

Conclusion: Just over half of the patients with SSc have lung disease (as ILD or as PAH). The main risk factors associated with ILD are proximal skin involvement and treatment with glucocorticoids, probably in the context of more severe forms that require more treatment. Anticentromere antibodies are more prevalent in patients with Limited SSc and their expression decreases the risk of developing ILD in these patients.

REFERENCES:

[1] Orlandi M, Barsotti S, Lepri G, et al. Clin Exp Rheumatol 2018 Jul-Aug; 36 Suppl 113: 3-23
[2] Hao Y, Hudson M, Baron M, et al. Arthritis Rheumatol. 2017;69(5):1067-1077.
[3] Furue M, Mitoma C, Mitoma H, et al. Immunol Res. 2017 Aug; 65: 790-7.
[4] Nihtyanova SI, Schreiber BE, Ong VH, et al. Arthritis Rheumatol. 2014 Jun; 66: 1625-35.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3524

AB0452

GENDER FEATURES IN PSYCHOLOGICAL STATUS IN PATIENTS WITH LUNG ULTRASOUND SYNDROME

N. Shamsutdinova[1], D. Abdulganieva[2], E. Kirillova[2], D. Gaisina[1], A. Fatikhova[1]. *[1]Kazan State Medical UniversIty, Hospital Therapy, Казань, Russian Federation*; *[2]Kazan State Medical UniversIty, Hospital Therapy, Kazan, Russian Federation*

Background: The use of lung ultrasound (LUS) in the management of patients with ILD has the advantage of lower cost and the absence of x-ray radiation.

Objectives: to establish the relationship between ultrasound manifestations of interstitial syndrome and indicators of psychological status in patients with secondary ILD in patients with rheumatic diseases.

Methods: 25 patients with secondary ILD in patients with rheumatic diseases (15 patients with systemic scleroderma, 8 patients with ANCA associated systemic vasculitis, 2 patients with dermatomyositis) were investigated. All patients underwent a standard clinical examination, high-resolution RCT of lungs. To assess depression and anxiety were used the following scales: State-Trait Anxiety Inventory, symptomatic questionnaire SCL-90-R, Beck Depression Inventory. LUS was carried out for the evaluation of the location and number of B-lines on both right and left hemithoraces using commercially available echographic equipment with a 5-12 MHz linear transducer (Accuvix A30, Samsung Medison).

Results: Most patients had an average number of B-lines 24,5[11,5;34,0]. In woman the total number of B-lines correlated with the situational anxiety (r=-0,71, p<0,05), with the personal anxiety (r=-0,6, p<0,05) and with somatization (r=-0,67, p<0,05). Also there was a trend between somatic (r=-0,49, p=0,08) and affective (r=-0,51, p=0,07) subscales, general depression (r=-0,48, p=0,1), but did not achieve statistical significance, probably due to the small number of patients. Among patients, including men and women, no statistically significant correlation was found.

Conclusion: The relationship between situational, personal anxiety, somatization and the total number of B-linesamong women with secondary ILDwas found. More research is needed to clarify details.

REFERENCES:

[1] Dietrich CF, Mathis G, Blaivas M, Volpicelli G, Seibel A, Wastl D, Atkinson NS, Cui XW, Fan M, Yi D. Lung B-line artefacts and their use. J Thorac Dis 2016;8(6):1356-1365. doi: 10.21037/jtd.2016.04.55
[2] Tatiana Barskova, Luna Gargani, Serena Guiducci, et al. Lung ultrasound for the screening of interstitial lung disease in very early systemic sclerosis Ann Rheum Dis 2013;72:390–395. doi:10.1136/annrheumdis-2011-201072

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3546

AB0453

THE CHARACTERISTICS OF SSc-ILD PATIENTS WITH ACTIVE THERAPY IN DIFFERENT PROGNOSIS INTERVALS BASED ON DISCRIMINANT ANALYSIS

O. Ovsyannikova[1], L. Garzanova[1], L. P. Ananyeva[1], O. Koneva[1], S. Glukhova[2], O. Desinova[1], M. Starovoytova[1], R. Shayakhmetova[1]. *[1]VA Nasonova Research Institute of Rheumatology, Laboratory of microcirculation and inflammation, Moscow, Russian Federation*; *[2]VA Nasonova Research Institute of Rheumatology, Educational and methodical department, Moscow, Russian Federation*

Background: Interstitial lung disease (ILD) frequently complicates SSc and can be a debilitating disorder with a poor prognosis. Several risk factors for progressive SSc-ILD have been identified and prognostic scoring systems have identified predictors of mortality. It's important to develop treatment recommendation.

Objectives: To use the discrimination function for pts with SSc-ILD and highlight pts with different prognosis.

Methods: It was a longitudinal study involving 140pts with SSc-ILD. The mean age was 46.7±13.9ys, females 82%, SSc duration 6.2±5.8ys, diff subset-54%. The mean duration of follow up was 73,2±27,8months. All pts received low- and moderate-dose glucocorticoids (Gc), RTM (the mean dose 3,14±2,38g) and 77 pts had received parenteral CyP(mean dose 15,9±15,6g).

We have got the discrimination function that included: ground glass opacities (GGO)(1–the absents of GGO; 2–the presents of GGO); index EScSG(the digital value); FVC(FVC≥75=0, FVC<75=1); the maximum daily dose of Gc (the digital value,mg); Gamma globulins (the digital value,%); cyclophosphamide (CYC) (the absence of CyP=0, the treatment of CYC =1);DLco(DLco<52% =0, DLco≥52=1). We assessed all parameters at the entry in the study except DLco evaluated after one year of follow up. Based on this analysis the equation was developed.

The equation of prognosis is 3.14GGO+0,70index EScSG–1,326 FVC-0,1 the maximum daily dose of glucocorticoids+0,136 Gamma globulins+1.066 CYP–1.075DLCO≤5,8.

Value of equation of prognosis to 5.8 corresponds to stabilization or good prognosis and value after 5.8 corresponds to poor prognosis.

Results: On results of discrimination function pts were distributed in the following order: 22 pts(16%) were into zone of stabilization(Group 1) and 118(84%) - in zone of poor prognosis, among which 13pts died during the study. That`s why pts in zone of poor prognosis were divided into group 2 - survived pts (n=105(75%)) and group 3– died pts(n=13 (9%)).So we have got 3groups; the age, SSc duration, gender proportion and SSc forms, were similar in the all groups(p>0,05).

Table 1. Baseline characteristics of the groups

Parameters	Group 1 (n=22) M±SD	Group 2 (n=105) M±SD	Group 3 (n=13) M±SD
CRP mg/ml	9,4±10,4	11,5±23,4	21,5±27,1
ME [25‰/75‰]	7,5 [1,9;11,2]	5 [1,6;10,4]	9,9 [5;32,8]
ESR mm/h	17±16,35	23,6±17	22,9±14,3
a-Scl-70 u/ml	62,5±85*	118,6±93,09*	102,1±96
Skin score	9,63±7,7	11,5±9,9	9±9,23
Index EScSG	1,9±1,7**	3,4±1,9**	2,9±1,1
Mean PAP mm hg	31,9 ±7β ββ	35±11,9 β	47,5±23,3ββ
Cumulative dose of CyP g	1,5±3γ γγ	11,4±14,4γ	18,9±23,3γγ
ME [25‰/75‰]	0 [0;2]	4,9 [0;17]	4 [0;46,5]
Cumulative dose of RTM, g	3,15±1,6	2,63±1,36	2,2±1,5

* - p=0,01; **p=0,0008; β - p=0,006; ββ - p=0,03; γ- p=0,002; γγ - p=0,0018Mean level a-Scl-70, Index EScSG were significantly lower in group 1 vs group 2. Mean value of PAP and dose of CyP were significantly increased in group 3. It should be noted that pts with good prognosis have had low level of all parameters and high dose of RTM.

Conclusion: The discrimination function is a proposed screening algorithm for pts with SSc-ILD who could develop progression disease. Usage of discrimination function revealed that 84% pts with ILD-SSc have got poor prognosis and 9% of them have got fatal outcome. Usage the equation of prognosis is very useful to choice of treatment and observation pts SSc-ILD.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3589

AB0454 SPECIFICITY OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS POSITIVE FOR A-TOPO-1 AND A-RNP

R. Shayakhmetova[1], L. P. Ananyeva[1], O. Koneva[1], M. Starovoytova[1], O. Desinova[1], O. Ovsyannikova[1], L. Garzanova[1], A. Khelkovskaia-Sergeeva[1], S. Glukhova[1]. [1]*V.A. Nasonova Research Institute of Rheumatology;, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: The classification criteria of SSC (EULAR/ACR 2013) compared to the criteria of 1980 showed high sensitivity and allow to detect the full spectrum of systemic sclerosis (SSc). The use of the new criteria led to the fact that some of the patients who were diagnosed with MCTD began to meet the criteria of SSc. Since these patients have hyperproduction of antibodies to RNP, but no other SSc-specific autoantibodies, we believe that they represent a special clinical and immunological phenotype of SSc. Lung involvement in SSc impaires the quality of life and the prognosis, so the study of interstitial lung disease(ILD) in different phenotypes is relevant.
Objectives: To compare the main manifestations of ILD in two groups of patients who meet the classification criteria of SSc 2013 - positive for a-Topo-1 and for a-RNP.
Methods: The study included 100 patients. The first group - 50 patients positive for a-Topo-1 (45 women and 5 men, mean age 55±10 years, duration of the disease 10.2±8 years, subset of the disease: diffuse 52%, limited 48%) and the second group - 50 patients positive for a-RNP (43 women and 7 men, mean age 44.5±14 years, duration of the disease 11.7±8 years; form of the disease: diffuse 14%, limited 86). The diagnosis of ILD was established by HRCT.
Results: In patients of group I ILD was detected in 94% of cases, in group II - 68% (p<0.05). In both groups a decrease in functional lung tests was noted with a high frequency, but a severe decrease in the lung diffusion capacity was significantly more often observed in group I.

Table 1. Data of laboratory and instrumental parameters

Parameters	a-Topo-1- positive n (%)	a-RNP-positive n (%)	p
Decrease of DLCO < 80%	49 (98)	43 (86)	p<0,05
DLCO <55%,	33 (66)	16 (32)	p<0,05
Decrease of FVC< 80 %	19 (38)	10 (20)	p<0,05
FVC<70%	13 (26)	7 (14)	NS
Ground glass opacity	25 (50)	26 (52)	NS
Honeycombing	17 (34)	8 (16)	p<0,05
SPAP >40mm.Hg,	6 (12)	10 (20)	NS
including PAH**	2 (4)	3 (4,6)	NS
ANA> 1:640	37 (74)	45 (90)	p<0,05

** ANA – antinuclear antibodies, PAH – pulmonary arterial hypertension, SPAP - systolic pulmonary artery pressure ** confirmed by the data of catheterization of the right heart*

Typical changes according to HRCT were detected in both groups, but fibrotic changes dominates in group I. There were no significant differences in the frequency of occurrence of PAH. Patients of group II had high level of ANA more often.
Conclusion: In both groups, a high frequency and similar manifestations of ILD were noted. In patients with SSc positive for anti-U1RNP, despite the predominance of limited skin lesions (in 86% of patients), a high incidence of ILD was detected, while the frequency of PAH was comparable to SSc in general. Compared with a-Topo-1 positive patients, ILD was significantly less frequent in anti-U1RNP positive patients and was accompanied with a smaller reduction of DLCO and/or FVC and a lower frequency of severe lung fibrosis. These data confirm the similarity of lung involvement in compared phenotypes of SSc and indicate the importance for screening for ILD in patients with hyperproduction of a-RNP, especially at an early stage of the disease.
REFERENCES:
[1] Van den Hoogen F, Khanna D, Fransen J, et al. 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2013;72:1747-55.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3591

AB0455 MODIFICATION OF PROGNOSIS INTERVALS WAS DERIVED BY THE DISCRIMINATION FUNCTION FOR SSc-ILD PATIENTS

O. Ovsyannikova[1], L. P. Ananyeva[1], L. Garzanova[1], O. Koneva[2], S. Glukhova[2], M. Starovoytova[1], O. Desinova[1], R. Shayakhmetova[1]. [1]*VA Nasonova Research Institute of Rheumatology, Laboratory of Microcirculation and Inflammation, Moscow, Russian Federation*; [2]*VA Nasonova Research Institute of Rheumatology, Educational and Methodical Department, Moscow, Russian Federation*

Background: Systemic sclerosis (SSc) is a multisystem autoimmune disease. Pulmonary alterations are the major cause of mortality in SSc. SSc-ILD has heterogeneous disease progression: many patients will have a chronic, indolent course while others may develop progressive, life-threatening disease.
Objectives: To assess prognosis intervals for pts with SSc-ILD.
Methods: It was a longitudinal study involving 140 pts with SSc-ILD. The mean age was 46.7±13.9years, females 82%, SSc duration 6.2±5.8 years, diffuse subset - 54%. The mean duration of follow up was 73,2±27,8 months. Clinical, laboratory, and immunologic data were collected on all patients.
Based on analysis of discrimination function the equation of prognosis was developed. The equation is 3.14GGO (ground glass opacities) + 0,7 index EScSG – 1,326 FVC - 0,1 the maximum daily dose of glucocorticoids + 0,136 Gamma globulins + 1.066 CYP – 1.075 DLCO ≤ 5,8. Value of equation of prognosis to 5.8 corresponds to stabilization or good prognosis and value after 5.8 corresponds to poor prognosis. The equation of prognosis had 86% sensitivity and 56% specificity. The cut-off point 4.7 was represented 65% sensitivity and 67% specificity. The prognosis intervals were following: value of equation to 4.7 corresponds to good prognosis; value from 4.8 to 5.8 corresponds to stabilization and value after 5.8 corresponds to poor prognosis.

Results: Pts were distributed into groups depending on results of discrimination function: 14 pts (10%) - zone of good prognosis; 8 pts (6%) - zone of stabilization and 118 (84%) - zone of poor prognosis. We have decided to join pts from zone good prognosis and zone stabilization into united group (U-group) - 22 pts (16 %).

Table 1. Comparative characteristics of the groups

Parameters	Group 1 (n=14)	Group 2 (n=8)	U-Group (n=22)	Group 3 (n=118)
Age years	45,4±16,4	50,2±15,8	47,2±16	47,5±13
P>0,05				
Gender				
Male	3(21%)	1(12,5%)	4(18%)	21(18%)
Female	11(79%)	7(87,5%)	18(82%)	97(82%)
P>0,05				
Limited form	8(57%)	2(35%)	10(46%)	54(46%)
Diffuse form	6(43%)	6(75%)	12(54%)	64(54%)
P>0,05				
Duration of disease years	6,8±7,6	5±4,2 p>0,05	6,2±6,4	6,5±5,7
CRP mg/ml	10±10	8,5±10,6	9,4±10,4	12,6±23,9
p>0,05				
ESR mm/h	16,7±13,1	17,4±21,9	17±16,3	23,5±16,7
p>0,05				
ANA-hep-2	525±322*	420±190	487±281*	774±430*
p: Gr1 vs Gr3 =0,038; Gr2 vs Gr3=0,02; Gr1,2 vs Gr3 =0,032				
a-Scl-70 u/ml	59,9±82,7*	67±94,5	116±93**	62,5±85* **
p: Gr1 vs Gr3 =0,03; Gr1,2 vs Gr3 =0,013				
Ejection fraction(EF)(%)	67,3±5,3*	65,5±6,1	66,7±5,5**	63±6,8* **
	p: Gr1 vs Gr3 =0,02; Gr1,2 vs Gr3 =0,017			
PAP mm hg	31,6±5,8	32,4±9,3	31,9±7	36,4±14
p>0,05				
6MWT m	490±110	477±104	485±104	430±100
(6 Minute walk test)				

p>0,05

The age, SSc duration, gender proportion and SSc forms, were similar in the all groups (p>0,05). In the study mean dates of ANF-hep-2, a-Scl-70 were significantly lower and EF was significantly higher in groups 1 and U-group than in group 3. In groups 1,2 and U-group the mean levels of ESR, CRP, PAP were lower and value of 6MWT were higher than mean levels in group 3 accordingly. So separately group 2 didn't have significant differences with group 1 and 3.
Conclusion: In the study we didn't find any correlation between meanings of group 2 and groups 1,3 but the meanings of group 1 and U-group have had the

same correlation. It would be rational to highlight only one zone of prognosis before and after 5,8.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3627

AB0456 HYDROXYCHLOROQUINE MIGHT REDUCE MORTALITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

M. Ozmen[1], E. Otman Akat[1], S. Gucenmez[1], G. Kabadayi[1], E. Durak Ediboglu[1], G. Alp[1], H. Cinakli[1], E. Erpek[1], İ. Kurut Aysin[1], O. Bayindir[1], D. Solmaz[1], S. Akar[1]. [1]*Izmir Katip Celebi University Faculty of Medicine, Rheumatology, Izmir, Turkey*

Background: Systemic sclerosis (SSc) is a devastating disease that has a profound impact on life expectancy, reflected by a standardised mortality ratio of 3,5. There is still limited data regarding the predictive factors for mortality in patients with SSc. Determining those factors could guide in disease management and follow up.[1]

Objectives: We aimed to identify the predictive factors for death in SSc.

Methods: Patients followed in a tertiary rheumatology clinic in the last 5 years were included in this retrospective study. All of the patients met the ACR / EULAR SSc 2013 criteria. Medical records of the patients were reviewed. Follow up time was defined as the time period from the first admission of the patient to our rheumatology clinic until the date of death or the date on which the study was performed. Candidate predictive factors for mortality were tested by Kaplan-Meier (with Log rank) and Cox-regression analyses.

Results: In total 146 patients (mean age 55.6±12.3 years, female 89.7%, diffuse cutaneous type SSc 45.2%) were included in the study (Table 1). The mean age at diagnosis of study group was 48±13.7 years. The median duration of follow up was 71 (6-228) months. Fourteen (10%) patients died during follow-up. The causes of death were: pulmonary (7), renal (2) and cardiac diseases (1), infection (3) and cancer (1).

Univariate analysis revealed that age at diagnosis (p=0.028), SSc subtype (p=0.035), the presence of interstitial lung disease (p=0.002), oesophageal involvement (on computed tomography) (p=0.030), pulmonary artery systolic pressure of ≥35 mmHg (measured by transthoracic echocardiography) (p=0.004), glucocorticoid (p=0.029), hydroxychloroquine (p=0.002) and cyclophosphamide (p=0.006) usage at any time were associated with mortality (Figure 1). Multivariate analyses model formed with age at diagnosis (B: 0.055, 95% CI, 1.005-1.112; **p=0.033**), SSc subtype (B: 0.963, 95% CI 0.541-12.684; p=0.231), glucocorticoid (B: 1.396, 95% CI, 0.487-33.507; p=0.196) and hydroxychloroquine usage (B: -1.50, 95% CI, 0.061-0.816; **p=0.023**) showed that age at diagnosis and hydroxychloroquine usage were independent predictive factors for mortality in patients with SSc.

Conclusion: The results of the study revealed for the first time that apart from the age at diagnosis hydroxychloroquine might reduce mortality in patients with SSc. Further studies are needed to prove of this information.

REFERENCES:

[1] Elhai M, et al. Ann Rheum Dis 2017;0:1–9. doi:10.1136/annrheumdis-2017-211448

Table 1. The demographic and clinical features in patients with systemic sclerosis.

Characteristic	Baseline
Age at diagnosis*	48±13.7
Female sex, n (%)	131 (89.7)
Duration of follow-up, months**	71 (6-228)
Disease subtype, n (%)	
Diffuse / Limited	66 (45.2) / 80 (54.8)
Autoantibodies, n (%)	
Anti-Scl70 antibody	50/143 (35.0)
Anti-Centromere antibody	62/143 (43.4)
Immunsuppresive medication, ever, n (%)	
Hydroxychloroquine	91/143 (63.6)
Mycophenolate mofetil	18/145 (12.4)
Azathioprine	47/145 (32.4)
Cyclophosphamide	24/145 (16.6)
Glucocorticoid	80/140 (57.1)
Others, n (%)	
ILD	68/130 (52.3)
Pericardial effusion, ever	26/133 (19.5)
Esophageal dilation (detected by CT)	51/128 (39.8)
sPAP ≥35mmHg, ever (measured by ECHO)	46/142 (32.4)

*Parameter presented as mean±SD**Parameter presented as median (min-max)CT, computed tomography; ECHO, echocardiogram; ILD, interstitial lung disease; sPAP, systolic pulmonary artery pressure

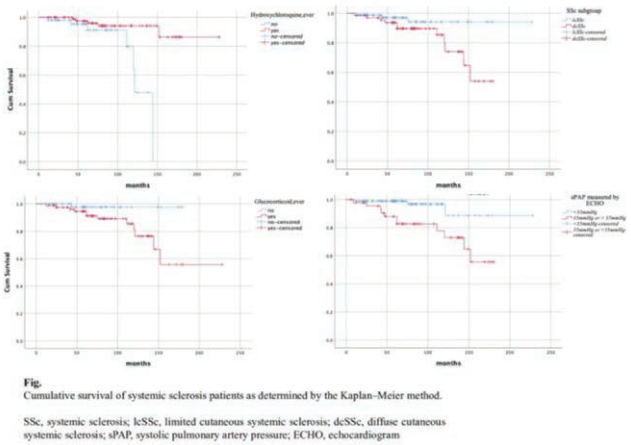


Fig.
Cumulative survival of systemic sclerosis patients as determined by the Kaplan–Meier method.

SSc, systemic sclerosis; lcSSc, limited cutaneous systemic sclerosis; dcSSc, diffuse cutaneous systemic sclerosis; sPAP, systolic pulmonary artery pressure; ECHO, echocardiogram

Figure 1.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3685

AB0457 HIPPOCAMPAL SUBFIELDS VOLUMES REDUCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS: A LONGITUDINAL MAGNETIC RESONANCE IMAGING (MRI) VOLUMETRIC STUDY

D. Pereira[1], M. Freschi[1], R. Frittoli[1], A. C. Londe[1], T. Amaral[2], S. Dertkigil[3], A. P. Del Rio[4], F. Cendes[5], L. Rittner[6], S. Appenzeller[4]. [1]*UNICAMP, Pathophysiology Graduate Program, Campinas, Brazil*; [2]*UNICAMP, Medicine, Campinas, Brazil*; [3]*UNICAMP, Radiology, Campinas, Brazil*; [4]*UNICAMP, Orthopedics, Rheumatology and Traumatology, Campinas, Brazil*; [5]*UNICAMP, Neurology, Campinas, Brazil*; [6]*UNICAMP, Electrical Engeneering, Campinas, Brazil*

Background: Systemic sclerosis (SSc) is a multisystem disease characterized by functional and structural abnormalities of small blood vessels, fibrosis of the skin and internal organs. In addition, volume reduction and shape abnormality of the hippocampus have been demonstrated in rheumatic and neurodegenerative diseases. However, the neuroanatomy of the hippocampus is complex and is not a uniform structure, consisting of subfields with distinct morphology: cornu ammonis (CA) subfields CA1–4, dentate gyrus (DG), fimbria, and adjacent subiculum and presubiculum [1].

Objectives: To investigate the hippocampal subfields volumes reduction in SSc patients using MRI.

Methods: In this study we included 37 SSc patients (33 women, mean age of 53.46, SD ± 12.29; range 30 - 78) and 37 healthy controls (HC) (31 women, mean age of 48.41, SD±12.20; range 29 - 80). Cognitive evaluation was performed using the Montreal Cognitive Assessment (MoCA), mood disorders were determined through Beck's Depression (BDI) and Beck's Anxiety Inventories (BAI). SSc patients were further assessed for clinical and laboratory SSc manifestations, disease activity (Valentini Activity Index), severity activity (Medsger Severity Index). MRI protocol consisted of: Sagittal T1-weighted images performed with a Philips 3.0T MRI scanner. MRI brain structure volumetric was done through volBrain [2]. After 48 months MRI acquisition were repeated in 26 SSc patients and 12 healthy volunteers. Statistics was performed according nature of the variable.

Results: We observed a significant reduction in hippocampal subfields volumes in SSc patients when compared to controls: Total hippocampi (SSc: mean volume = 4.78 cm^3; SD = 0.38; HC: mean volume = 5.01 cm^3; SD = 0.38; p = 0.033). Reduction in volume of the total hippocampi was associated with Raynaud's phenomenon (p = 0.006). A longitudinal study showed a reduction in volume of the hippocampus subfields volumes when compared to patient's baseline: Total hippocampi (mean initial volume = 4.78 cm^3; mean follow-up volume = 4.50 cm^3, p = 0.027); Total CA1 (mean initial volume = 1.59 cm^3; mean follow-up volume = 1.58 cm^3, p < 0.0001); Reduction in volume of the total hippocampi was associated with presence of current use of prednisone (p = 0.008). Reduction in left CA1 left associated with current use of prednisone (p = 0.014). Reduction in total subiculum was associated with presence of calcinosis (p = 0.023). No significant changes were observed in hippocampal subfields volumes in controls over the follow-up period.

Conclusion: This study provides evidence of hippocampus subfields volumes reductions in SSc patients when compared to controls and was associated with

Raynaud's phenomenon, current use of losartan and correlated with BAI scores. Also, a longitudinal study showed a reduction in volume of the hippocampus subfields volumes when compared to patient's baseline associated with calcinosis and current use of prednisone.

REFERENCES:

[1] Eichenbaum, Howard. "A cortical–hippocampal system for declarative memory." Nature Reviews Neuroscience 1.1 (2000): 41-50.
[2] Manjon JV, Coupe P (2016) volBrain: an online MRI brain volumetry system. Front Neuroinform 10:30.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3815

AB0458 SURVIVAL OF SCLERODERMA PATIENTS WITH INTERSTITIAL LUNG DISEASE: OBSERVATION DATA FROM A MALAYSIAN TERTIARY CENTRE

J. Raja[1], S. Muthusamy[1], C. M. Ng[2]. [1]*University of Malaya, Division of Rheumatology, Department and Faculty of Medicine, Kuala Lumpur, Malaysia*; [2]*University of Malaya, Institute of Mathematical Sciences, Faculty of Science, Kuala Lumpur, Malaysia*

Background: Interstitial lung disease (ILD) is the leading cause of death in scleroderma (SSc) with decline in FVC as a predictor of mortality in patients with SSc-ILD, especially in the early course of the disease.

Objectives: The aim of this study is to determine the survival rate of SSc-ILD in a Malaysian cohort of patients from University Malaya Medical Centre (UMMC).

Methods: 61 patients clinically diagnosed with SSc-ILD were identified and prospectively recruited. Baseline demographic data were collected. Kaplan-Meier analysis was used to estimate the survival.

Results: Females were predominant (56, 91.8%). 39 (64%) had limited cutaneous SSc. Majority were ethnicity Chinese 30 (49.2%), followed by Malays 20 (32.8%), Indians 7 (11.4%) and others 4 (6.6%). Mean age was 56.25 (SD ± 12.5) years while mean duration of disease (non-Raynaud's disease onset) was 10.5 years (SD ± 9.2) (range of 1 year to 44 years) years. 29 (47.5%) patients were positive for anti-ScL-70, whereas 6 (9.8%) patients were anti-centromere positive. There were 16 (26.2%) deaths. Median survival was 24 years. Patients had a sharper drop in survival probability for the first 10 years compared to the next 20 years (Figure 1). Median survival in limited subset was 24 years whereas in diffuse subset was 11 years. Patients from the limited subset appeared to have higher chance of surviving for 10 years and above, compared to those in the diffuse subset (Figure 2).

Conclusion: The results demonstrate the poor survival in SSc-ILD patients. The survival rate tends to be worse in the first 10 years of SSc disease duration. Survival rate was poorer in patients with diffuse cutaneous subset.

REFERENCES:

[1] Parelas A et al. Lancet Resp Med 2020
[2] Goh NS *et al. Am J Respir Crit Care Med* 2008

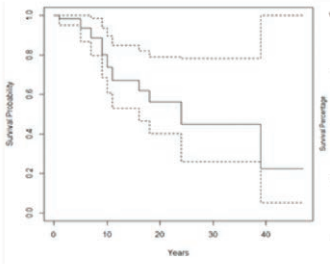


Figure 1

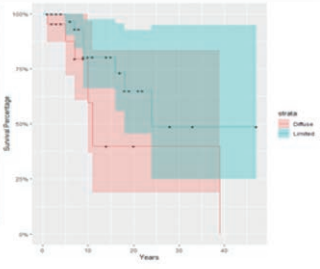


Figure 2

Disclosure of Interests: JASMIN RAJA Speakers bureau: For Boehringer Ingelheim for topic on Scleroderma-ILD, Grant/research support from: From Boehringer Ingelheim for scleroderma research, Shantini Muthusamy: None declared., CHOUNG MIN NG: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3830

AB0459 ARTICULAR INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

A. Karakas[1], Y. Erez[1], S. Gulle[1], G. Can[1], İ. Sari[1], F. Onen[1], M. Birlik[1]. [1]*Dokuz Eylul University Faculty of Medicine, Rheumatology, Izmir, Turkey*

Background: SSc (systemic sclerosis) is a connective tissue disease characterized by small vessel vasculopathy, production of autoantibodies, and fibroblast dysfunction leading to increased deposition of extracellular matrix in the skin and internal organs mainly. Therewithal, many SSc patients develop musculoskeletal symptoms during the course of their illness. Different rheumatic complaints such as arthralgia, arthritis, contractures, tendon friction rubs, calcinosis, and acroosteolysis can be seen as musculoskeletal symptoms in SSc patients [1].

Objectives: To provide an overview of the spectrum of articular involvement in SSc and determine the relationship between these involvements and Rheumatoid factor (RF) and Anti-cyclic citrullinated peptide (Anti-CCP) positivity and organ involvements.

Methods: We performed a retrospective cohort study involving 232 SSc patients who were followed up in our department of rheumatology between 2000 and 2020 years. The patients were divided into two groups as limited and diffuse SSc. Age, gender, weight, height, smoking habits, duration of illness, follow-up duration, other systemic organ involvement, and radiographic findings were recorded. Diagnostic tests such as RF, Anti-CCP, ANA, ENA panel tests, direct radiographs were examined.

Results: The mean age of the patients was 59.9 ± 12.8 and 88.4% of them were women. 69.3% of patients were limited SSc. At any stage of the disease, 39.1% of all patients had arthralgia and 34.1% had arthritis. The arthritis rate was similar between the SSc groups (p = 0.396). RF and anti-CCP positivity rates were similar between the SSc groups. Although RF and anti-CCP positivity rates were higher in the patient group with arthritis, it was not statistically significant (respectively p=0.563, p=0.072). Interestingly, the lung involvement rate was higher in patients with arthritis (63.3% versus 46.4%) (p=0.015). Other clinical, demographic characteristics, laboratory, and radiographic findings of the patients are shown in Table 1.

Conclusion: Articular involvement in SSc is a common clinical feature seen in one-third of patients regardless of the type of disease. Although RF and Anti-CCP positivity are more common in patients with arthritis, it was not statistically significant. Interestingly, arthritis is a more common manifestation in patients with lung involvement.

REFERENCES:

[1] R. D. Sandler, M. Matucci-Cerinic, and M. Hughes, "Musculoskeletal hand involvement in systemic sclerosis," *Seminars in Arthritis and Rheumatism*, vol. 50, no. 2. 2020, doi: 10.1016/j.semarthrit.2019.11.003.

Table 1. Demographic and clinical characteristics of b/tsDMARDs patients

Table-1	Limited SSc (n=161)	Diffuse SSc (n=71)	All patients (n=232)	P
Age (years) (Mean±SD)	60.5 ± 12.7	58.6 ± 12.9	59.9 ± 12,8	0.295
Disease duration (years) (Mean±SD)	11.5 ± 6.6	12.4 ± 8.1	11.8 ± 7,1	0.384
Weight (kg) (Mean±SD)	68.2 ± 13.3	66.2 ± 15.6	67.6 ± 14.1	0.331
BMI (kg/m^2) (Mean±SD)	27.6 ± 5.5	26.2 ± 6.1	27.1 ± 5.7	0.102
Female, n (%)	146 (90.7)	59 (83.1	205 (88.4)	0.097
Current and ex smoker, n (%)	60 (37.2)	18 (25.4)	78 (33.6)	0.077
Digital ulcer, n (%)	53 (32.9)	34 (47.9)	87 (37.5)	**0.03***
Contracture on hand	28 (17.4)	28 (39.4)	56 (24.1)	**<0,001***
Arthralgia, n (%)	63 (39.1)	29 (31.5)	92 (39.7)	0.806
Arthritis, n (%)	52 (32.3)	27 (38)	79 (34.1)	0.396
Joint space narrowing on X-ray, n (%)	44 (51.2)	30 (63.8)	74 (55.6)	0.160
Joint erosion on X-ray, n (%)	17 (19.8)	14 (29.8)	31 (23.3)	0.205
Acroosteolysis on X-ray, n (%)	9 (10.5)	16 (34)	25 (18.8)	**0.001***
ANA positivity, n (%)	155 (96.3)	69 (97.2)	224 (96.6)	0.728
Anti-Scl positivity, n (%)	41 (28.7)	48 (71.6)	89 (42.4)	**<0.001***
Anti-centromere positivity, n (%)	65 (45.5)	10 (14.9)	75 (35.7)	**<0.001***
RF positivity, n (%)	27 (17.5)	14 (20.6)	41 (18.5)	0.589
Anti-CCP positivity, n (%)	16 (12.7)	7 (11.3)	23 (12.2)	0.782

P*Independent Samples t Test, Pearson Chi-Square Test, **BMI;** Body mass index, **ANA**; Anti nuclear antibody,**RF**; Rheumatoid factor**, Anti-CCP**;Anti- Cyclic citrullinated peptide

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4103

AB0460 THE UTILITY OF USB CAPILLAROSCOPE FOR ASSESSMENT OF RAYNAUD'S PHENOMENON PATIENTS

S. Lambova[1]. [1]*Medical University - Plovdiv, Department of propaedeutics of Internal Diseases, Plovdiv, Bulgaria*

Background: Videocapillaroscopy is the gold standard for evaluation of nailfold capillaries and the major tool used for differentiation of primary and secondary Raynaud's phenomenon (RP) in rheumatology practice. However, nowadays, there are also accessible alternatives such as USB capillaroscopes, which offer the opportunity to apply capillaroscopic examination at a significantly lower price.

Objectives: The aim of the current study was to study the utility of USB capillaroscope (Dinolite) *via* assessment of capillaroscopic images obtained by patients with primary and secondary RP in rheumatic diseases.

Methods: The study represents analysis of capillaroscopic images of 32 patients with RP – primary and secondary in the context of SSc or other rheumatic diseases i.e., undifferentiated connective tissue disease (UCTD) and systemic lupus erythematosus (SLE). All the patients had signed an informed consent for participation in a study of their capillaroscopic, laboratory and clinical associations. The study represents retrospective analysis of the capillaroscopic images obtained from 8 fingers (II-V bilaterally) using USB capillaroscope (Dinolite) at magnification 200x. Capillary diameters were measured (arterial, venous and apical loop) as well as the number of capillaries per millimeter. The capillaroscopic images were categorized into the following groups i.e., I. Absence of microangiopathy: i) normal pattern, ii) nonspecific changes (dilated capillaries with arterial diameter > 0.015mm, venous > 0.020mm; haemorhhages and/or other nonspecific changes), II. Presence of microangiopathy i.e., "scleroderma"/"scleroderma-like" pattern. Presence of giant capillaries with capillary diameter >0.050mm was considered as a sufficient criterion for classifying the image as "scleroderma"/"scleroderma-like" pattern. For "scleroderma" type images in SSc patients staging of Cutolo et al (2000) was used i.e., "early", "active", "late" phase (1).
Results: Images suitable for analysis with good visibility that permits analysis of the major capillaroscopic parameters were available in all patients. Among 32 included patients, 9 patients were with SSc, 12 cases with primary RP, and 10 patients with secondary RP in other CTD (7 patients with UCTD and 3 patients with SLE). „Scleroderma" pattern was detected in 6 patients with SSc and in all these cases the capillaroscopic images were classifiable into one of the three distinct phases i.e., "early", "active" and "late" phase. Presence of microvascular changes ("scleroderma-like" pattern) was detected also in 5 among the 10 patients with other CTD i.e., UCTD and SLE. In primary RP patients capillaroscopy revealed either normal pattern or nonspecific findings but without features of microangiopathy.
Conclusion: Good capillaroscopic images, which could be analyzed and interpreted, are usually obtained using USB capillaroscope. This permits evaluation of the major capillaroscopic parameters. The available software although less sophisticated *vs* those of videocapillaroscopes, gives the opportunity for measurement of capillary diameters, mean capillary density, etc. The images received from USB capillaroscope are easily classified into "scleroderma", "scleroderma-like", non-specific changes and normal pattern. The most important conclusion from capillaroscopy is about presence or absence of microangiopathy. This was easily detected *via* USB capillaroscope that could be suggested as an ideal alternative for videocapillaroscopes in every day rheumatology practice especially at low budget cases. Measurements of capillary diameters and capillary density provide quantitative data that make these devises also appropriate for scientific research.
REFERENCES:
[1] Cutolo M, Sulli A, Pizzorni C AS. Nailfold videocapillaroscopy assessment of microvascular damage in systemic sclerosis. J Rheumatol. 2000;27(1):155–60.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4159

AB0461 "SCLERODERMA-LIKE" PATTERN AS A PRESENTING FEATURE OF CONNECTIVE TISSUE DISEASES

S. Lambova[1]. [1]*Medical University - Plovdiv, Department of Propaedeutics of Internal Diseases, Plovdiv, Bulgaria*

Background: The role of capillaroscopy for early diagnosis of systemic sclerosis (SSc) is well-known and pathological capillaroscopic pattern is a component of the new set of criteria for SSc (EULAR/ACR 2013). While it is also known that similar microvascular changes i.e., "scleroderma-like" could be observed in other rheumatic diseases i.e., undifferentiated connective tissue disease (UCTD), overlap syndromes, systemic lupus erythematosus (SLE), etc., the data about the time of their appearance in other rheumatic diseases different from SSc are scarce.
Objectives: The aim of the study was to evaluate the prevalence of capillaroscopic features of microangiopathy in Raynaud's phenomenon (RP) patients at the time of their first referral to rheumatology setting.
Methods: 22 in- and outpatients were included in the study that were referred for consultation in our rheumatology unit in the last 6 months. Inclusion criteria were presence of RP at their first consultation or still unclear diagnosis. Presence of known rheumatic disease diagnosed at previous consultation with rheumatologist as well as signs of definite diagnosis SSc were exclusion criteria. All the patients underwent capillaroscopic examination with USB capillaroscope Dinolite (magnification 200x). Routine laboratory tests were ordered i.e., complete blood count, ESR, CRP, biochemistry as well as immunological tests. ANA test was performed in all patients while antibodies against extractable nuclear antigens, antiphospholipid antibodies or other tests were ordered depending on the clinical presentation and overall context. The patients signed an informed consent for participation of the study.
Results: 12 of the examined patients were diagnosed with primary RP and their capillaroscopic examination revealed absence of microangiopathy i.e., normal pattern or non-specific changes (mainly dilated capillaries). In 7 patients the final diagnosis was UCTD and 4 of them exhibited microvascular pathology i.e. "scleroderma-like" pattern, while in 3 cases the capillaroscopic findings were non-specific. Among other patients 1 case was diagnosed with prescleroderma with "early" phase "scleroderma" pattern (according to definition of Cutolo et al., 2000 (1)), 1 case was with onset of SLE ("scleroderma-like" pattern, active phase) and in one case the microvascular pathology that included single giant capillary loop no other signs of connective tissue disease were found and the final conclusion was "suspected secondary" RP with necessity for a regular follow-up.
Conclusion: In conclusion, definite features of microvascular pathology, known as "scleroderma-like" capillaroscopic pattern, could be observed as an initial pathological feature in CTD different from SSc such as UCTD and SLE and the overall diagnosis should be made in the overall context. Capillaroscopy inherits its high significance in patients with UCTD, in whom clinical presentation could be obscure in the beginning and identification of microvascular capillaroscopic pathology is among the crucial signs to support the diagnosis. Future studies are necessary to delineate the role of microvascular pathology for prediction of future evolution of UCTD.
REFERENCES:
[1] Cutolo M, Sulli A, Pizzorni C AS. Nailfold videocapillaroscopy assessment of microvascular damage in systemic sclerosis. J Rheumatol. 2000;27(1):155–60.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4172

Spondyloarthritis – treatment

AB0462 BMI IS ASSOCIATED WITH BOTH DISEASE ACTIVITY AND TNF-α INHIBITOR SERUM TROUGH LEVELS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS ON LONG-TERM TREATMENT WITH TNF-α INHIBITORS

L. De Wolff[1], S. Arends[1], E. Brouwer[1], H. Bootsma[1], A. Spoorenberg[1]. [1]*University Medical Centre Groningen and University of Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*

Background: TNF-α inhibitors (TNFi) are widely used in axial spondyloarthritis (axSpA) patients with active disease. Approximately half of patients stop TNFi treatment, often due to loss of treatment efficacy.[1] TNFi serum trough levels have been associated with initial therapeutic response in axSpA patients.[2] Additionally, a relation was found between serum trough TNFi levels and BMI.[3]
Objectives: To explore in axSpA patients on long-term TNFi therapy associations between randomly measured TNFi serum trough levels, disease activity and BMI.
Methods: Patients from the UMCG on adalimumab or etanercept and a regular visit in the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort were approached for a random TNFi serum trough level measurement. Based on reference values of Sanquin[3], serum trough levels were stratified in therapeutic and below therapeutic levels. The Ankylosing Spondylitis Disease Activity Score (ASDAS) from a regular outpatient GLAS visit was used for analyses, if assessed <2 months of the serum trough level measurement. Active disease according to ASDAS was defined as ≥2.1. Correlations and univariable logistic regression were performed. Multivariable logistic regression was performed to correct the relation between therapeutic drug levels and ASDAS for potential confounders.
Results: 94 axSpA patients on adalimumab or etanercept were approached for a random TNFi serum trough level measurement, of which 55 (59%) had a measurement taken. See Table 1 for patient characteristics. No significant correlations were found for adalimumab or etanercept serum trough levels (as continuous variable) with ASDAS (adalimumab: r=-0.16, p=0.39; etanercept: r=-0.29, p=0.20). According to Sanquin definitions of therapeutic TNFi levels, 26 patients (47%) had therapeutic serum trough levels: 19/34 (56%) for adalimumab and 7/21 (33%) for etanercept. Univariable logistic regression showed no significant associations between therapeutic levels (yes/no) and ASDAS. In multivariable analyses, BMI was identified as the only confounder for the relationship between therapeutic drug levels and ASDAS. Median BMI was higher, although not statistically significant, in patients with below-therapeutic serum trough levels compared to therapeutic levels (27.1, IQR 24.6-31.7 vs. 24.3, IQR 22.7-31.4, p=0.08). Furthermore, BMI had a significant, negative correlation with adalimumab and etanercept serum levels (adalimumab: r=-0.48, p=0.01, etanercept: r=-0.46, p=0.04) (Figure 1). Patients with active disease according to ASDAS had higher BMI than patients with inactive disease (median 29.7 vs. 24.5, p=0.01).
Conclusion: In this cross-sectional, observational study of axSpA patients on long-term TNFi treatment, BMI was significantly correlated with adalimumab and etanercept serum trough levels. Furthermore, BMI was significantly higher

in patients with active disease. Therefore, overweight /obese patients on TNFi treatment and active disease, might benefit from an increase in TNFi dose.

REFERENCES:
[1] Arends et al, Clin Exp Rheumatol 2017;35:61-68
[2] Kneepkens et al, Ann Rheum Dis 2015;74:396-401
[3] Rosas et al, Clin Exp Rheum 2017;35:145-148
[4] Sanquin Amsterdam. Diagnostic tests. Available via: www.sanquin.org/nl/producten-en-diensten/diagnostiek/diagnostische-testen/index

Table 1. Characteristics of 55 axSpA patients with random adalimumab or etanercept serum trough level measurements

	Adalimumab (n=34)	*Etanercept (n=21)*
Age (years)	45 ± 13	46 ± 12
Gender (male)	14 (41)	12 (57)
BMI (kg/m^2)	26.6 (24.5-32.7)	24.3 (21.9-29.5)*
Symptom duration (years)	21 ± 14	20 ± 8
HLA-B27 positive	26 (79)	16 (84)
ASDAS	2.3 (1.7-3.1)	1.6 (1.3-2.0)**
Treatment duration current TNFi (months)	27 (7-57)	58 (12-76)
Serum trough level (µg/ml)	5.2 (3.7-8.0)	1.6 (1.1-2.4)

Values are mean ± SD, median (IQR) or n (%)*Significant difference (p<0.05) and **(p<0.01) compared to patients on adalimumab

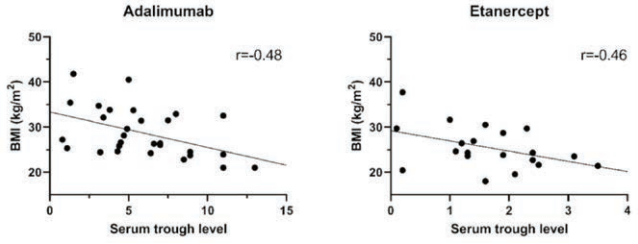


Figure 1. Scatterplot of BMI and serum trough level of adalimumab (A) and of etanercept (B)

Disclosure of Interests: Liseth de Wolff: None declared., Suzanne Arends Grant/research support from: Pfizer, Elisabeth Brouwer Grant/research support from: Pfizer, Hendrika Bootsma: None declared., Anneke Spoorenberg Consultant of: Abbvie, Pfizer, MSD, Novartis and UCB, Grant/research support from: Abbvie, Pfizer and Novartis.

DOI: 10.1136/annrheumdis-2021-eular.521

AB0463

IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES IN ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH GOLIMUMAB: SUB-ANALYSIS OF ASIAN PATIENTS ENROLLED IN PHASE-3 CLINICAL TRIALS

W. C. Tsai[1], C. Bao[2], D. Furtner[3], K. H. Lo[4], Y. Zhou[4], E. C. Hsia[4,5]. [1]*Kaohsiung Medical University, Department of Internal Medicine, Kaohsiung, Taiwan, Republic of China*; [2]*Renji Hospital, Department of Rheumatology, School of Medicine, Shanghai Jiao Tong University, Shanghai, China*; [3]*Janssen, a Division of Jonson & Johnson Pte Ltd., Singapore, Singapore*; [4]*Janssen Research & Development, LLC, Spring House, United States of America*; [5]*University of Pennsylvania Medical Center, Rheumatology, Philadelphia, United States of America*

Background: Clinical efficacy and safety of golimumab (GLM) for patients with ankylosing spondylitis (AS) who have not received prior biologic therapy were studied in two phase-3 clinical trials (NCT00265083 - GO RAISE and NCT01248793). In both studies, a greater proportion of patients treated with GLM 50 mg every 4 weeks achieved improvement in clinical signs and symptoms measured by ASAS20 and in patient-reported outcomes, such as Health Related Quality of Life (HRQoL) and sleep disturbance when compared with placebo (PBO) at Weeks 14 and 24.
Objectives: To assess the effect of GLM on HRQoL, back pain, and sleep disturbances in phase-3 studies in Asian patients with AS.
Methods: Post-hoc sub-analysis to examine HRQoL, measured with the Short Form 36 (SF-36) Physical and Mental Component Summary (PCS and MCS), total back pain (VAS) and sleep disturbance, assessed with the Jenkins Sleep Evaluation Questionnaire (JSEQ) in active AS patients enrolled from Asian countries (China, including Taiwan region and South Korea). Improvement from baseline to Week 24 was expressed as mean and standard deviation (SD) for SF-36 PCS and MCS and total back pain. Reduction of sleep disturbance was expressed as the proportion of patients with improvement from baseline ≥2 points in the JSEQ, defined as baseline value minus post-baseline value with lower scores indicating the better sleep evaluation.
Results: At Week 24, active AS patients treated with GLM 50 mg had greater mean improvements in SF-36 and total back pain than PBO. The pooled results were comparable with patients enrolled from other regions (Table 1). A higher proportion of Asian patients who received GLM had reduced sleep disturbance (JSEQ ≥2) after 24 weeks than PBO (59.7% [83/139] vs 38.5% [47/122]; Δ21.2) and the results were similar with AS patients on GLM (67.4% [64/95] vs 45.6% [26/57]; Δ21.8) pooled from other regions.
Conclusion: Asian patients with AS treated with GLM demonstrated improved HRQoL, total back pain, and reduced sleep disturbance. The pooled results were comparable with other regions.

Table 1. Mean Improvement from Baseline in HRQoL and total back pain at Week 24: Randomized Patients in AS Studies Pooled for Asia and all other regions

	Pooled AS in APAC				Pooled AS in All Other Regions			
Parameter	Placebo		GLM 50 mg		Placebo		GLM 50 mg	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
SF-36 PCS	122	2.51 (6.372)	139	7.10 (8.434)	58	1.91 (8.268)	99	10.12 (11.096)
SF-36 MCS	122	0.22 (9.609)	139	3.32 (9.280)	58	1.20 (9.705)	99	1.98 (8.032)
Total Back Pain	120	1.86 (2.469)	135	2.73 (2.607)	58	0.79 (2.688)	99	3.39 (3.210)

APAC, Asia-Pacific; AS, ankylosing spondylitis; GLM, golimumab; HRQoL, Health Related Quality of Life; MCS, mental component summary; PCS, physical component summary; SD, standard deviation; SF-36, Short Form 36

Disclosure of Interests: Wen-Chan Tsai Consultant of: Pfizer, AbbVie, Roche, and Eli Lilly, Chunde Bao: None declared., Daniel Furtner Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson Pte. Ltd., Singapore, Kim Hung Lo Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Yiying Zhou Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC.

DOI: 10.1136/annrheumdis-2021-eular.951

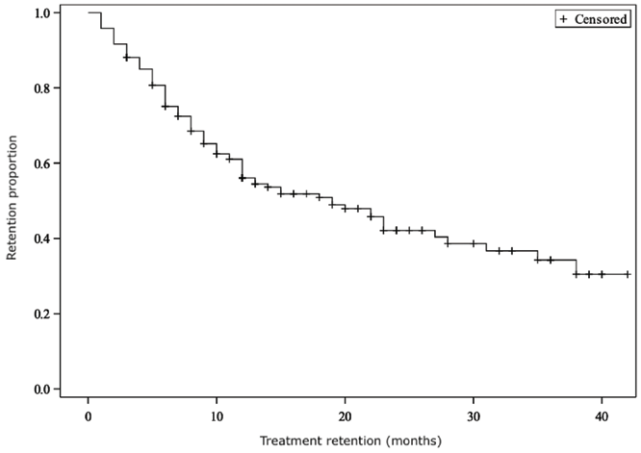
AB0464

DRUG SURVIVAL OF TNFI AND SECUKINUMAB IN AXIAL SPONDYLARTHRITIS: A REAL-WORLD MULTICENTRIC COHORT OF 370 PATIENTS

T. Delepine[1], P. Philippe[1], E. Cailliau[2], E. Houvenagel[3], X. Deprez[4], R. M. Flipo[1], J. G. Letarouilly[1]. [1]*Lille University Hospital, Department of Rheumatology, Lille, France*; [2]*Lille University Hospital, Biostatistics, Lille, France*; [3]*Saint-Philibert Hospital, Rheumatology, Lomme, France*; [4]*Valenciennes Hospital, Department of Rheumatology, Valenciennes, France*

Background: IL17 inhibitors (IL17i) are an alternative for patients with axial spondyloarthritis (axSpA) who did not respond to TNF inhibitors (TNFi). Secukinumab (SEC) is the first human monoclonal antibody that binds to the protein interleukin-17A.
Objectives: The objectives of this study were to describe the characteristics of axSpA patients treated with IL17i and TNFi and to assess the persistence with IL17i and TNFi in a real world cohort.
Methods: A retrospective multicenter observational study was conducted. axSpA patients (pts) according to ASAS criteria initiating a IL17i or TNFi between June 2016 and December 2019 were included. Demographic features, current and previous use of biologic Disease-modifying antirheumatic drugs (bDMARDs) were collected. Date and reasons of discontinuation – i.e., lack of efficacy, safety issue, sustained remission or others – were collected. Kaplan-Meyer analysis were performed.
Results: 370 pts were included. Among the 202 patients who received TNFi, 90 (44.6%) were female, mean age was 43.2 +/- 13.2 years, mean body mass index was 26.1 kg/m^2 +/- 5.4, 49 pts (46.7%) were smokers. The most common SpA phenotype was axial radiographic (n = 89, 54,9%) and 114 (68.3%) pts were HLA B27 positive, mean BASDAI was 57.5 +/- 14.6, median disease duration was 8.6 years [3.0-10.5]. Among the 168 patients who received SEC, 78 (46.4%) were female, mean age was 47.7 +/- 11.8 years, mean body mass index was 27.2 kg/m^2 +/- 5.8, 45 pts (44.1%) were smokers. The most common SpA phenotype was axial radiographic (n = 106, 76,3%) and 114 (78.1%) pts were HLA B27 positive, mean BASDAI was 62.8 +/- 14.8, median disease duration was 9 years [5.0-19.0]. TNFi was the first line bDMARD in 116/202 pts (57.4%) and SEC was the first line bDMARD in 15/168 pts (8.9%). SEC was prescribed at 150mg every month in 121/168 (73.3%) pts. The median persistence with TNFi and SEC were 18.0 months [11.0-27.0] and 12.0 months [6.0-22.0],

respectively. During the 3-year follow-up, 130 pts (42 with TNFi and 88 with SEC) discontinued treatment: 80 (22 with TNFi and 58 with SEC) for lack of effectiveness, 41 (16 with TNFi and 25 with SEC) for adverse events. No patient



treated with SEC presented a new-onset inflammatory bowel disease.

Figure 1. Persistence with SEC after 3 years of follow-up

Conclusion: In this real world cohort of AxSpA pts, SEC was mostly prescribed at second and third-line, contrary to axSpA pts treated with TNFi. Most reason of discontinuation were related to lack of effectiveness with both therapeutic classes.

Disclosure of Interests: Thibaut DELEPINE: None declared., Peggy Philippe Speakers bureau: Abbvie, MSD, Fresenius, Pfizer, UCB Pharma, Novartis, Consultant of: Abbvie, MSD, Fresenius, Pfizer, UCB Pharma, Novartis, Emeline Cailliau: None declared., Eric Houvenagel: None declared., Xavier Deprez Speakers bureau: Pfizer, UCB, Abbvie, Novartis, MSD, Consultant of: Pfizer, UCB, René-Marc Flipo Speakers bureau: Novartis, Lilly, Abbvie, Pfizer, MSD, Consultant of: Novartis, Lilly, Abbvie, Pfizer, MSD, Jean-Guillaume Letarouilly Grant/research support from: Pfizer (research grant).

DOI: 10.1136/annrheumdis-2021-eular.1012

AB0465

INDIVIDUAL COMPONENTS CONTRIBUTING TO THE ACHIEVEMENT OF ASAS40 RESPONSE IN BIOLOGIC NAÏVE PATIENTS WITH RADIOGRAPHIC AXSPA: RESULTS FROM THE COAST-V TRIAL

D. Poddubnyy[1], S. Attar[2], M. J. Nissen[3], E. Filippi[4], H. Russ[5], A. Erdogan[6], Y. Schymura[7], S. Liu Leage[8], E. Collantes Estevez[9], F. Ciccia[10]. [1]*Charité University Medicine, Department of Rheumatology, Berlin, Germany*; [2]*King Abdulaziz University, Department of Internal Medicine, Jeddah, Saudi Arabia*; [3]*Geneva University Hospital (HUG), Department of Rheumatology, Geneva, Switzerland*; [4]*Eli Lilly and Company Ltd., Immunology & Oncology Medical Affairs, Indianapolis, United States of America*; [5]*Eli Lilly and Company Ltd., Bio-Medicines CRP, Indianapolis, United States of America*; [6]*Eli Lilly and Company Ltd., Medical Director, Indianapolis, United States of America*; [7]*Eli Lilly and Company Ltd., Statistics, Indianapolis, United States of America*; [8]*Eli Lilly and Company Ltd., International Medical-Derma, Indianapolis, United States of America*; [9]*Reina Sofia University Hospital/Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Department of Rheumatology, Cordoba, Spain*; [10]*University of Campania "Luigi Vanvitelli", Rheumatology Unit, Naples, Italy*

Background: Ixekizumab (IXE), an IL-17A antagonist, is effective in patients with radiographic axial spondyloarthritis (rad-axSpA). Assessment in SpondyloArthritis International Society (ASAS) 40 response – the primary study endpoint – was achieved at week (wk) 16 by 48% of those treated with 80mg subcutaneous IXE every 4 wks (Q4W) in the phase 3 COAST V trial (NCT 02696785) [1]. Until now, no information has been available on the efficacy of IXE on the components of ASAS40 composite endpoint.

Objectives: To describe which individual components of ASAS40 drive achievement of efficacy response.

Methods: This exploratory post-hoc analysis was based on COAST V data. Patients enrolled in COAST V met ASAS criteria for rad-axSpA and were biological disease-modifying antirheumatic drug (bDMARD)-naïve. Patients were assigned 1:1:1:1 to subcutaneous placebo (PBO), IXE Q4W, IXE Q2W or 40 mg adalimumab (ADA). Only data for approved doses are shown.

To reach ASAS40 response, patients must have an improvement of at least 40% and at least 2 units for at least 3 of 4 individual components which define response (patient global assessment of disease activity, spinal pain, inflammation (defined as the mean of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6), and function (Bath Ankylosing Spondylitis Functional Index - BASFI)), without worsening in the remaining component. We describe the percentage of patients who achieved this change, had an insufficient response, or deteriorated in each component out to wk 16 for IXE Q4W, ADA and PBO. The time course of the change from baseline in individual components of the ASAS response is depicted descriptively per treatment arm by use of the mean and standard deviation. Observed data have been utilised.

Results: IXE Q4W response at 16 wks was driven by all 4 individual components of the ASAS40 with the largest improvements for patients treated with IXE Q4W seen in inflammation and spinal pain (Figure 1).

At wk 16, at least 50% of all patients treated with IXE Q4W achieved response on spinal pain (60.3%), inflammation (60.3%) and patient global assessment (50%), with 43.6% of patients meeting the response criteria for function (Table 1). The corresponding results for ADA were 43.2%, 47.7% 39.8%, and 35.2%.

Conclusion: Our findings show that meeting ASAS40 response criterion for an individual component at 16 wks by patients treated with IXE Q4W was broadly similar between individual components. However, a clinically relevant improvement was more frequently observed for the spinal pain and inflammation components.

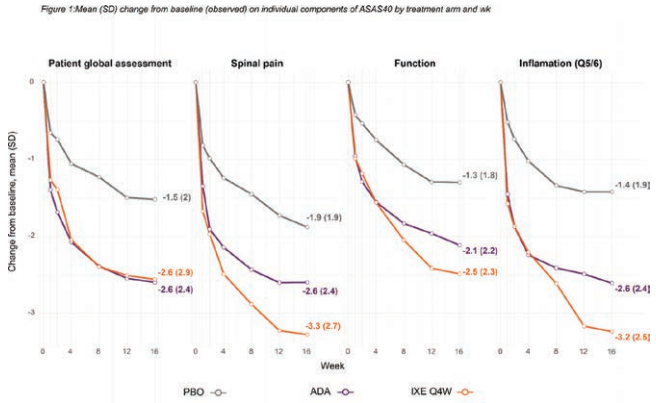
REFERENCES:

[1] Dougados, M., et al. (2020). Ann Rheum Dis **79**(2): 176-185.

Table 1. ***Observed changes from baseline (CFB), percentage improvements and response status of patients enrolled in COAST V trial at wk 16***

Measure	*Observed CFB (SD)*	*Observed % improvement (SD)*	*Improvement >=40% and >=2 units n (%)*	*Insufficient response n (%)*	*Deterioratedn (%)*
IXE Q4W (N=78)					
Patient global assessment	-2.6 (2.9)	32.3 (51.1)	39 (50.0)	30 (38.5)	9 (11.5)
Spinal pain	-3.3 (2.7)	43.4 (34.4)	47 (60.3)	27 (34.6)	4 (5.1)
Inflammation*	-3.2 (2.5)	46.8 (32.8)	47 (60.3)	25 (32.0)	6 (7.7)
Function	-2.5 (2.3)	39.6 (31.0)	34 (43.6)	37 (47.4)	7 (9.0)
ADA (N=88)					
Patient global assessment	-2.6 (2.4)	35.2 (33.4)	35 (39.8)	48 (54.5)	5 (5.7)
Spinal pain	-2.6 (2.4)	36.8 (34.7)	38 (43.2)	44 (50.0)	6 (6.8)
Inflammation*	-2.6 (2.4)	38.4 (36.9)	42 (47.7)	37 (42.0)	9 (10.2)
Function	-2.1 (2.2)	35.2 (34.3)	31 (35.2)	48 (54.6)	9 (10.2)
PBO (N=86)					
Patient global assessment	-1.5 (2.0)	18.0 (37.9)	21 (24.4)	54(62.8)	11(12.8)
Spinal pain	-1.9 (1.9)	25.8 (26.7)	23 (26.8)	55(64.0)	8(9.3)
Inflammation*	-1.4 (1.9)	20.9 (33.9)	19 (22.1)	53 (61.6)	14 (16.3)
Function	-1.3 (1.8)	19.1 (31.6)	16 (18.6)	51 (59.3)	19 (22.1)

*Inflammation is the mean of BASDAI 5 (Morning stiffness severity) and BASDAI 6 (Morning stiffness duration)



Mean baseline values for PBO, ADA and IXE Q4W respectively: Patient global assessment (7.1, 7.1, 6.9), spinal pain (7.4, 7.0, 7.2), inflammation (Q5/6) (6.7, 6.6, 6.5), function (6.3, 6.1, 6.1)

Acknowledgements: Alan Ó Céilleachair, an employee of Eli Lilly and Company, provided editorial and writing support.

Disclosure of Interests: Denis Poddubnyy Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly and Company, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Biocad, Gilead, GlaxoSmithKline, Eli Lilly and Company, MSD, Novartis, Pfizer, Samsung Bioepis, and UCB, Grant/research support from: AbbVie, Eli Lilly and Company, MSD, Novartis, and Pfizer, Suzan Attar:

None declared., Michael J. Nissen Speakers bureau: AbbVie, Celgene, Eli Lilly and Company, Janssen, Novartis and Pfizer., Consultant of: AbbVie, Celgene, Eli Lilly and Company, Janssen, Novartis and Pfizer., Grant/research support from: AbbVie, Erica Filippi Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Hagen Russ Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Alper Erdogan Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Yves Schymura Employee of: Eli Lilly and Company, Soyi Liu Leage Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Eduardo Collantes Estevez Speakers bureau: Novartis, Janssen, Eli Lilly and Company, AbbVie, Paid instructor for: Novartis, Grant/research support from: Eli Lilly and Company, francesco ciccia Speakers bureau: AbbVie, Celgene, UCB, Pfizer, MSD, Amgen, Eli Lilly and Company, Novartis, Sobi, Roche, BMS, Paid instructor for: Novartis, UCB, Pfizer, Consultant of: Novartis, UCB, Pfizer, Grant/research support from: Pfizer, Roche, UCB.

DOI: 10.1136/annrheumdis-2021-eular.1361

AB0466 RETENTION RATE AND EFFECTIVENESS OF SECUKINUMAB VERSUS TNF INHIBITOR SWITCHING IN ANKYLOSING SPONDYLITIS PATIENTS WITH A HISTORY OF TNF INHIBITOR TREATMENT: DATA FROM A KOREAN NATIONWIDE REGISTRY

H. K. Min[1], K. Y. Kang[2]. [1]*Konkuk University Medical Center, Internal Medicine, Seoul, Korea, Republic of (South Korea)*; [2]*The Catholic University of Korea Incheon St. Mary's Hospital, Internal Medicine, Incheon, Korea, Republic of (South Korea)*

Background: The choice of second-line biologics for ankylosing spondylitis (AS) patients previously treated with a tumour necrosis factor inhibitor (TNFi) remains unclear

Objectives: Here, we compared drug retention and clinical efficacy between AS patients who switched biologics to secukinumab and those who switched to a different TNFi.

Methods: AS patients enrolled in the Korean College of Rheumatology BIOlogics registry were included. Patients with previous TNFi exposure were divided into the secukinumab group and the TNFi switching group. Drug retention and clinical efficacy (BASDAI50, ASAS20, ASAS40, ASDAS <2.1, ASDAS clinically important improvement, and ASDAS major improvement) were assessed at the 1 year follow-up. Propensity score (PS)-matched and covariate-adjusted logistic regression analyses were performed.

Results: 246 had available 1 year follow-up data. Secukinumab as third- or later-line biologics was more frequent than alternative TNFi (54% vs. 14%). PS-matched and multiple covariate-adjusted analyses showed that the odds ratio (OR) for drug discontinuation was comparable between the secukinumab and TNFi switching groups (OR=1.136; 95% CI, 0.843–1.531 and OR=1.000; 95% CI, 0.433–2.308, respectively). The proportion of patients who achieved BASDAI50 was also comparable between the two groups (OR=0.833; 95% CI, 0.481–1.441 in PS-matched analysis). Other clinical efficacy parameters were also comparable. In the subgroup analysis of AS patients with previous TNFi discontinuation due to ineffectiveness, all clinical efficacy parameters were comparable between the two groups.

Conclusion: In AS patients with previous exposure to a TNFi, switching biologics to secukinumab and switching to an alternative TNFi resulted in comparable drug retention and clinical efficacy.

REFERENCES:

[1] Micheroli R, Tellenbach C, Scherer A, et al. Effectiveness of secukinumab versus an alternative TNF inhibitor in patients with axial spondyloarthritis previously exposed to TNF inhibitors in the Swiss Clinical Quality Management cohort. Ann Rheum Dis 2020;79:1203-9.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1489

AB0467 EFFECTIVENESS OF GOLIMUMAB AFTER T NF-INHIBITOR FAILURE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, OR AXIAL SPONDYLOARTHRITIS: RESULTS AT 3 MONTHS FROM THE GO-BEYOND ITALY STUDY

S. D'angelo[1], E. Tirri[2], A. M. Giardino[3], M. Matucci-Cerinic[4], L. Dagna[5], L. Santo[6], F. Ciccia[7], B. Frediani[8], M. Govoni[9], F. Bobbio Pallavicini[10], R. D. Grembiale[11], A. Delle Sedie[12], S. Cercone[13], R. Mule'[14], F. P. Cantatore[15], R. Foti[16], E. Gremese[17], R. Perricone[18], F. Salaffi[19], O. Viapiana[20], A. Cauli[21], R. Giacomelli[22], L. Arcarese[23], G. Guggino[24], R. Russo[25], D. Capocotta[26], F. Nacci[27], M. G. Anelli[28], V. Picerno[29], F. Iannone[30]on behalf of GO-BEYOND Italy. [1]*Istituto Reumatologico Lucano (I.Re.L) e Dipartimento Regionale di Reumatologia, AOR San Carlo di Potenza, Potenza, Italy*; [2]*Ospedale "San Giovanni Bosco" Napoli, UOSD di Reumatologia, Napoli, Italy*; [3]*MSD Italia, Medical Affairs, Rome, Italy*; [4]*AOC Careggi, Dipartimento medicina Sperimentale e Clinica, SOD Reumatologia, Firenze, Italy*; [5]*IRCCS San Raffaele, San Raffaele University, Scientific Institute & Vita-Salute, Milan, Italy*; [6]*ASL BT - DSS 4 Barletta, U.O.S. Reumatologia, Barletta, Italy*; [7]*Università della Campania L. Vanvitelli, Dipartimento di Medicina di precisione, Napoli, Italy*; [8]*Policlinico "Le Scotte", U.O.C. Reumatologia, Siena, Italy*; [9]*AOU S. Anna di Ferrara - University of Ferrara, UOC Reumatologia, Ferrara, Italy*; [10]*Fondazione IRCCS Policlinico San Matteo, S.C. di Reumatologia, Pavia, Italy*; [11]*University "Magna Græcia, Rheumatology Research Unit, Department of Health Sciences, Catanzaro, Italy*; [12]*A.O. Universitaria Pisana, U.O. Reumatologia, Pisa, Italy*; [13]*MSD Italia, Medical Affairs, Roma, Italy*; [14]*policlinico Sant'Orsola, Programma dipartimentale di malattie reumatiche, del connettivo e malattie metaboliche dell'osso, Bologna, Italy*; [15]*University of Foggia Medical School, Rheumatology Clinic, Department of Medical and Surgical Sciences, Foggia, Italy*; [16]*A.O.U. Policlinico S. Marco, U.O di Reumatologia, Catania, Italy*; [17]*Fondazione Policlinico Universitario A. Gemelli-IRCCS, Università Cattolica del Sacro Cuore, U.O.C. di Reumatologia, Roma, Italy*; [18]*Policlinico Tor Vergata, Dipartimento di Medicina dei Sistemi - UOC Reumatologia, Roma, Italy*; [19]*Universita' Politecnica delle Marche, Dipartimento di Scienze Cliniche e Molecolari, Ancona, Italy*; [20]*Ospedale Borgo Roma Policlinico G.B. Rossi, U.O.C. Reumatologia, Verona, Italy*; [21]*AOU and University of Cagliari, Rheumatology Unit, Cagliari, Italy*; [22]*Campus biomedico di Roma, Immunoreumatologia, Roma, Italy*; [23]*Campus Biomedico di Roma, Immunoreumatologia, Roma, Italy*; [24]*Università degli Studi di Palermo, Dipartimento PROMISE, Palermo, Italy*; [25]*Azienda Ospedaliera RN, A.Cardarelli, U.O.S. Reumatologia, Napoli, Italy*; [26]*Ospedale "San Giovanni di Napoli, U.O.S. Dipartimentale di Reumatologia, Napoli, Italy*; [27]*AOU Careggi, Dipartimento medicina Sperimentale e Clinica, SOD Reumatologia, Firenze, Italy*; [28]*Policlinico, U.O. di Reumatologia Universitaria, Bari, Italy*; [29]*Istituto Reumatologico Lucano (I.Re.L), e Dipartimento Regionale di Reumatologia, AOR San Carlo di Potenza, Potenza, Italy*; [30]*Policlinico, U.O. di Reumatologia Universitaria, Bari, Italy*

Background: Golimumab showed trial efficacy in subjects with active rheumatoid arthritis (RA) previously treated with TNF-inhibitors (TNFi); no trial data are available for psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA).

Objectives: To assess the effectiveness of golimumab after TNFi failure in patients with RA, PsA, or axSpA in a real-world setting.

Methods: GO-BEYOND-Italy is an ongoing, multicenter, prospective, observational study of RA, PsA, or axSpA patients starting golimumab after TNFi failure. Patients were enrolled between July 2017 and December 2019, and followed for 1 year, with evaluations at 3, 6, and 12 months. This interim analysis estimates the effectiveness after 3 months of golimumab therapy. Differences from baseline were tested by paired t-tests.

Results: 193 patients were enrolled: 38 (19.7%) with RA (median age 54 years; median disease duration 9.5 years), 91 (47.2%) with PsA (median age 53 years; median disease duration 9.0 years) and 64 (33.2%) with axSpA (median age 54 years; median disease duration 7.2 years). Majority of the RA (73.7%), PsA (51.6%) and axSpA (53.1%) were females. Previous TNFi treatment included etanercept (44.6% of patients), adalimumab (42.0%), infliximab (8.8%) and certolizumab (4.7%). The main reason for switching to golimumab was loss of efficacy of TNFi (78.9% in RA, 83.5% in PsA, 75% in axSpA). Comorbidities were highly prevalent (RA 65.8%, PsA 65.9%, axSpA 75%); hypertension (31.1%), dyslipidaemia (13.5%), fibromyalgia (10.4%) were the most common ones. DAS28-CRP significantly reduced in RA and PsA ($p<0.01$) after 3 months of treatment. In RA, rates of DAS28-CRP remission and low disease activity (LDA) were 29.6% and 22.2%, respectively, and 65.2% of patients achieved good/moderate EULAR response. As for PsA, good/moderate EULAR response was observed in 78.8% of patients and 28% of patients achieved minimal disease activity. In axSpA, ASDAS-CRP ($p<0.01$), BASDAI ($p<0.01$) and ASAS-HI ($p=0.032$) significantly reduced; rates of ASDAS-CRP inactive disease and LDA were 15.2% and 26.1%, respectively; 14% of patients had a ≥50% improvement in baseline BASDAI. After 3 months of golimumab treatment, there was a decrease in the prevalence of enthesitis (32.9% to 16.5%), nail (17.6% to 12.9%) and skin psoriasis (42.4% to 34.1%) in PsA patients; the frequency of extra articular manifestations tended to decrease also in axSpA patients.

Conclusion: Preliminary results of the GO-BEYOND-Italy study showed a good short-term effectiveness of golimumab in RA, PsA and axSpA after TNFi failure.

Table 1. Effectiveness of golimumab at 3 months in the GO-BEYOND-Italy study

Rheumatoid arthritis (n=38)		Psoriatic arthritis (n=91)		Axial spondyloarthritis (n=64)	
DAS28-CRP, mean (SD)	n=27	DAS28-CRP, mean (SD)	n=47	ASDAS-CRP, mean (SD)	n=44
V0 / V1	4.05 (0.8) / 3.10* (1.0)	V0 / V1	3.66 (1.0) / 2.79* (1.2)	V0 / V1	2.86 (1.0) / 2.33* (1.0)
V1: DAS28-CRP disease activity, n (%)	n=27	V1: EULAR response, n (%)	n=33	V1: ASDAS-CRP disease activity, n (%)	n=46
Remission	8 (29.6)	Good	16 (48.5)	Inactive disease	7 (15.2)
Low disease activity	6 (22.2)	Moderate	10 (30.3)	Low disease activity	12 (26.1)
Moderate disease activity	13 (48.1)	No response	7 (21.2)	High disease activity	22 (47.8)
				Very high disease activity	5 (10.9)
V1: EULAR response, n (%)	n=23	V1: MDA, n (%)	n=75		
Good	7 (30.4)	Yes	21 (28.0)	BASDAI, mean (SD)	n=50
Moderate	8 (34.8)			V0 / V1	5.99 (2.1) / 4.92 (2.3)*
No response	8 (34.8)			V1: BASDAI50, n (%)	7 (14.0)
				ASAS-HI, mean (SD)	n=48
				V0 / V1	10.67 (3.8) / 9.68 (4.6)^

*p value for the difference from V0 <0.01. ^ p for the difference from V0=0.032Abbreviations: ASDAS: Ankylosing Spondylitis Disease Activity Score; ASAS-HI: Assessment of SpondyloArthritis international society Health Index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; DAS: disease activity score; EULAR: European League Against Rheumatism; MDA: Minimal Disease Activity; SD: standard deviation; V0: baseline; V1: 3 months evaluation.

Disclosure of Interests: Salvatore D'Angelo Speakers bureau: AbbVie, BMS, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, UCB, Consultant of: AbbVie, BMS, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, UCB, Enrico Tirri Speakers bureau: AbbVie, Eli Lilly, Novartis, Pfizer, Angela Maria Giardino Employee of: MSD Italia, Marco Matucci-Cerinic Speakers bureau: BMS, Pfizer, Actelion, Consultant of: Eli-Lilly, Celgene, Chemomab, CSL Behring, Grant/research support from: BMS, Pfizer, Celgene, CSL Behring, Lorenzo Dagna Consultant of: Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI, Leonardo Santo: None declared., francesco ciccia: None declared., Bruno Frediani: None declared., Marcello Govoni: None declared., Francesca Bobbio Pallavicini: None declared., Rosa Daniela Grembiale: None declared., Andrea Delle Sedie: None declared., Stefania Cercone Employee of: MSD Italia, RITA MULE': None declared., Francesco Paolo Cantatore Speakers bureau: Pfizer, Sanofi Genzyme and Roche, Consultant of: Pfizer, Sanofi Genzyme and Roche outside this work., Rosario Foti: None declared., Elisa Gremese: None declared., Roberto Perricone: None declared., Fausto Salaffi: None declared., Ombretta Viapiana Speakers bureau: Novartis, UCB, Abbvie, MSD, Fresenius kabi, Gilead, Biogen, Consultant of: Novartis, Abbvie, Fresenius kabi, Gilead, Biogen, Alberto Cauli Speakers bureau: Abbvie, Alfa-Sigma, BMS, Celgene, Galapagos, Glaxo, MSD, Novartis, Janssen, Pfizer, Sanofi, UCB, Consultant of: Abbvie, Alfa-Sigma, BMS, Celgene, Galapagos, Glaxo, MSD, Novartis, Janssen, Pfizer, Sanofi, UCB, Rorberto Giacomelli: None declared., Luisa Arcarese: None declared., Giuliana Guggino Speakers bureau: Novartis, Celgene, Abbvie, Sandoz, Eli Lilly, Pfizer, Jansen, ROMUALDO RUSSO: None declared., Domenico Capocotta: None declared., Francesca Nacci: None declared., Maria Grazia Anelli: None declared., valentina picerno: None declared., Florenzo Iannone Speakers bureau: Pfizer, AbbVie, Janssen, Celgene, Novartis, MSD, BMS, UCB, Roche, Consultant of: Pfizer, AbbVie, Janssen, Celgene, Novartis, MSD, BMS, UCB, Roche outside this work.
DOI: 10.1136/annrheumdis-2021-eular.1518

AB0468

IS THE USE OF INTERLEUKIN 17 INHIBITORS IN SPONDYLOARTHRITIS RELATED TO THE CLINICAL MANIFESTATIONS? 12-MONTH EXPERIENCE OF ONE RHEUMATOLOGY CENTER

M. Khapsirokova[1], Z. Kolkhidova[1], S. Erdes[2]. *[1]V.A. Nasonova Research Institute of Rheumatology, Moscow, Clinic, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia., Clinic, Moscow, Russian Federation*

Background: Therapy with interleukin 17 (iIL17) inhibitors in Russia is indicated for patients with ankylosing spondylitis (AS) or psoriatic arthritis (PSA). If standard therapy is ineffective in these diseases, both tumor necrosis factor inhibitors (iTNF) and iIL17 can be prescribed as the first biologics.

Objectives: To study the clinical features of patients with spondyloarthritis (SPA) who were first prescribed iIL17 in a rheumatology center for 12 months.

Methods: During the period from January to December 2019, iIL17 was initiated to 43 SPA patients. To compare the clinical picture, the study additionally included 40 SPA patients who were prescribed iTNF during the same period. The diagnosis of AS was based on the mNY criteria, and psoriatic arthritis was based on the CASPAR criteria. In the combined group of 83 patients, AS was in 52 (62.7%), and PSA – in 31; the age of patients was 39.3±10.8 years, and the duration of the disease was 15.1±8.2 years; men were 47 (56.6%).

Results: In the iIL17 group, AS had 23 (53.5%) patients, and PSA – 20 (46.5%), while in the iTNF group, respectively, 29 (72.5%) and 11 (27.5%; $\chi 2$=3.2, p=0.76). Among the patients who were prescribed iIL17, men were 29 (67%), and in the iTNF group – 18 (45%; $\chi 2$=4.2, p=0.04). In terms of activity indicators (ESR, CRP, BASDAI ASDAS-CRP), patients who were prescribed iIL17 or iTNF did not differ significantly from each other. Peripheral arthritis, dactylitis, and entesitis were observed with almost the same frequency in both groups. In the iIL17 group, there were almost 2 times more patients with psoriasis (53.5% and 25.0%; p<0.05) than in group iTNF and among them, significantly more frequent the patients had previous experience of iTNF treatment (41,9% and 17.5%; p<0.05). Disease-modifying antirheumatic drugs often received patients in iTNF group (80.0% and 48.8%; p<0.05).

Conclusion: Thus, in clinical practice iIL17 often prescribed for SPA male patients with psoriasis and previous treatment experience by iTNF. The activity of the disease and the presence of non-axial manifestations practically do not affect the choice of biological therapy.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1548

AB0469

PROTON PUMP INHIBITORS MAY IMPAIR RESPONSE TO TNF-INHIBITORS IN SPONDYLOARTHRITIS PATIENTS

M. Masson[1], M. Kostine[1], T. Barnetche[1], A. Saraux[2], A. Ruyssen-Witrand[3], T. Thomas[4], D. Wendling[5], M. E. Truchetet[1], C. Richez[1], T. Schaeverbeke[1]. *[1]Bordeaux University Hospital, Rheumatology, Bordeaux, France*; *[2]Brest University Hospital, Rheumatology, Brest, France*; *[3]Toulouse University Hospital, Rheumatology, Toulouse, France*; *[4]Saint-Etienne University Hospital, Rheumatology, Saint-Etienne, France*; *[5]Besançon University Hospital, Rheumatology, Besaonçon, France*

Background: Considering the potential role of the gut microbiota in the pathophysiology of spondyloarthritis (SpA) as in the therapeutic response to biologics (1), we evaluated the hypothesis that co-medications known to interfere with the gut microbiota could impair the therapeutic response to TNF-inhibitors (TNF-i) in SpA patients. This was first suggested by the results of a retrospective cohort showing that a co-medication with proton pump inhibitors (PPIs), non-steroidal anti-inflammatory drugs (NSAIDs) or antibiotics was significantly associated with a decreased chance to respond to a first TNF-I, independently of each other (2).

Objectives: To validate in a replication cohort the potential negative association between therapeutic response to TNF-i and co-medication with commonly used drugs.

Methods: Demographic information and disease characteristics were retrospectively collected. Patients were classified as responder (R) or non-responder (NR) according to the BASDAI (< 40/100) value at month 6 or to the clinician judgment (when BASDAI was not available). We collected all drugs known to interfere with the gut microbiota that were administered 1 month before and during the first 3 months of the TNF-i treatment. We only considered drugs given to more than 5% of patients. Univariate and multivariate analyses were performed to evaluate the relationship between co-medications, predictors of response known from literature and TNF-i response. All analyses were computed on STATA 13.1 with a statistically significant threshold of 0.05.

Results: We included from 4 different centres 185 patients having axial SpA with radiographic or magnetic sacroiliitis in 75% and 73% of cases, respectively. One third of them had peripheral involvement. 73% were B27 positive. TNF-i administrated were infliximab (8%), etanercept (22%), adalimumab (44%) golimumab (19%), certolizumab (7%). 127 patients (69%) were considered as R. 59.4% of patients who received NSAIDs were R, compared to 81% not treated with NSAIDs (p< 0.0001). 43,3% of patients receiving PPIs were R compared to 83% of patients PPI free (p< 0.0001). Differences were not significant for antibiotics, methotrexate (MTX), psychotic drugs and corticosteroids. Considering known predictors of response, a magnetic sacroiliitis and the age at TNF-i initiation were significantly associated with a higher proportion of R patients (p=0.048 and 0.018 respectively). In multivariate analysis, PPIs intake remained associated with a poorer response to a first TNF-i (p<0.001), even though 88% of patients exposed to PPIs received also NSAIDs.

	Univariate analysis	Multivariate analysis
	Odd Ratio (95% Confidence Interval)	
Gender	1.43 (0.76; 2.72)	
Disease duration	1.02 (0.99; 1.06)	
Age at TNF-I initiation	0.97 (0.95; 0.995)	0.97 (0.94; 0.999)
Magnetic sacroiliitis	0.46 (0.21; 0.99)	0.63 (0.26; 1.52)
Baseline BASDAI	1.02 (0.99;1.04)	
Baseline CRP	0.99 (0.98; 1.02)	
Positive B27	0.81 (0.4;1.68)	
Peripheral involvement	0.79 (0.4; 1.56)	
NSAIDs	2.91 (1.47; 5.77)	1.08 (0.41; 2.79)
PPIs	6.4 (3.25; 12.7)	6.9 (2.8;17)
Antibiotics	1.87 (0.84; 4.16)	
Psychotics	1.94 (0.75; 4.97)	
Corticosteroids	1.11 (0.39; 3.11)	
Methotrexate	2.29 (0.97; 5.38)	

Conclusion: Co-medication with PPIs was considered as an independent factor associated with TNF-i failure. The hypothesis that this effect is due to their interference with the gut microbiota is only speculative but, regardless of the reason for this interaction, clinicians should be aware of the potential negative effect on TNF-i response.

REFERENCES:

[1] Bazin, T., Hooks, K.B., Barnetche, T. *et al.* Microbiota Composition May Predict Anti-Tnf Alpha Response in Spondyloarthritis Patients: an Exploratory Study. *Sci Rep* **8,** 5446 (2018). https://doi.org/10.1038/s41598-018-23571-4

[2] Masson M, Kostine M, Barnetche T, Truchetet ME, Richez C, Schaeverbeke T. Ab0661 Co-Medications May Alter the Response to Tnf-Inhibitors in Spondyloarthritis Patients: A Pharmacomicrobiomic Effect? Annals of the Rheumatic Diseases. 1 juin 2020;79(Suppl 1):1625-6.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1716

AB0470 EXPERIENCE WITH THE USE OF INTERLEUKIN 6 INHIBITOR IN SEVERE ANKYLOSING SPONDYLITIS

D. Rumiantceva[1], E. Agafonova[1], M. Urumova[1], S. Erdes[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*

Background: Inhibitors of interleukin 6 (IL6) have been found to be ineffective in ankylosing spondylitis (AS) based on the results of randomized clinical trials (RCTs) on tocilizumab (TCZ) and sarilimumab [1, 2]. However, there is evidence that IL6 is actively involved in the pathogenesis of the disease [3]. In addition, the efficacy of IL6 inhibitors has been shown in patients with secondary AA amyloidosis [4].

Objectives: to analyze the effectiveness of IL6 inhibitor - TCZ in patients with AS with high disease activity and secondary AA-amyloidosis.

Methods: The analysis included 10 patients with AS receiving TCZ therapy, of which 8 (80%) men, 2 (20%) women, and 100% HLA B27 positive. The average age of the patients was 40 ± 8.6 years, the average age of disease onset was 13.4 ± 7.5 years, the average duration of AS was 25.6 ± 6.5 years. 9 patients had histologically confirmed secondary AA-amyloidosis: 100% had kidney amyloidosis, 6 (66.6%) patients also had gastrointestinal amyloidosis and 3 (33.4%) patients had heart amyloidosis. All patients had arthritis and coxitis.

Results: As the first biological drug, TCZ was prescribed to 2 patients due to the presence of manifestations of secondary AA-amyloidosis, and 8 patients had previous experience of treatment with one or more inhibitors of tumor necrosis factor-α (TNF-α). The average duration of TCZ treatment was 22.0 months [1.0; 36.0]. 8 (80%) patients continue to take TCZ therapy to date, and 2 (20%) - are transferred to TNF-α inhibitors. Table 1 shows the main clinical and laboratory characteristics of patients at the initiation of TCZ therapy and during the last hospitalization at the V.A. Nasonova Research Institute of Rheumatology. As you can see, against the background of TCZ therapy, both the level of CRP, proteinuria and the indices of AS activity (BASDAI, ASDAS CRP) significantly decreased. The number of patients with inflammatory back pain (IBP), arthritis and coxitis also decreased significantly.

Table 1. The main clinical and laboratory characteristics of patients at the initiation and after of TCZ therapy.

	Before TCZ	After TCZ	p
CRP, Me [25‰; 75‰], mg/l	95.2 [52.2; 189.0]	10,8 [0.8; 8.0]	**p<0,05**
Proteinuria, Me [25‰; 75‰], g/day.	1,6 [1,0; 2,1]	0,08 [0; 0,3]	**p<0,05**
BASDAI, Mean (SD)	6,1 (1,6)	3,3 (0,9)	**p<0,05**
ASDAS CRP, Mean (SD)	4,3 (1,1)	2,2 (0,7)	**p<0,05**
IBP, N (%)	10 (100%)	2 (20%)	**p<0,05**
Arthritis, N (%)	10 (100%)	2 (20%)	**p<0,05**
Cocxitis, N (%)	10 (100%)	5 (50%)	**p<0,05**
Enthesitis, N (%)	7 (70%)	6 (60%)	p>0,05

Conclusion: The above data showed that the method of treating AS with IL6 inhibitors, in certain clinical situations, primarily such as ineffectiveness of TNF-α inhibitors, high CRP level and the development of secondary AA-amyloidosis, can be highly effective. Therefore, it is advisable to continue the set of clinical observations on the treatment of especially severe patients with AS treated with non-standard methods.

REFERENCES:

[1] Sieper J, Porter-Brown B, Thompson L, et al. Assessment of short-term symptomatic efficacy of tocilizumab in ankylosing spondylitis: results of randomised, placebo-controlled trialsAnn Rheum Dis 2014; 73: 95–100. doi:10.1136/annrheumdis-2013-203559.

[2] Sieper J, Braun J, Kay J, et al. Sarilumab for the treatment of ankylosing spondylitis: results of a Phase II, randomised, double-blind, placebo-controlled study (ALIGN). Ann Rheum Dis. 2015; 74: 1051–1057. doi:10.1136/annrheumdis-2013-204963.

[3] Londono J, Romero-Sanchez MC, Torres VG, et al. The association between serum levels of potential biomarkers with the presence of factors related to the clinical activity and poor prognosis in spondyloarthritis. Rev Bras Reumatol 2012; 52: 536-44.

[4] Yılmaz S, Tekgöz E, Çınar M. Recurrence of proteinuria after cessation of tocilizumab in patients with AA amyloidosis secondary to FMF. Eur J Rheumatol. 2018; 5: 278-80. DOI: 10.5152/eurjrheum.2018.17183.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1740

AB0471 PATIENTS WITH RADIOGRAPHIC AXSPA WHO PROGRESSED FROM ASAS20 AT WEEK 16 TO ASAS40 AT WEEK 52: RESULTS FROM COAST-W

X. Baraliakos[1], A. Deodhar[2], S. Liu Leage[3], Y. Schymura[4], R. Bolce[5], D. Sandoval[5], J. A. Walsh[6], J. Sieper[7]. [1]*Ruhr-University Bochum, Rheumatology, Bochum, Germany*; [2]*Oregon Health & Science University, Division of Arthritis & Rheumatic Diseases, Portland, United States of America*; [3]*Eli Lilly and Company Corporate Center, Rheumatology, Indianapolis, United States of America*; [4]*Eli Lilly and Company Corporate Center, Statistics, Indianapolis, United States of America*; [5]*Eli Lilly and Company Corporate Center, Medical Affairs, Indianapolis, United States of America*; [6]*University of Utah, Rheumatology, Salt Lake City, United States of America*; [7]*Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Rheumatology, Berlin, Germany*

Background: The timeframe for maximum treatment response varies across patients with radiographic axial spondyloarthritis (r-axSpA). Understanding which patients may benefit from additional time on treatment could influence treatment decisions.

Objectives: This post-hoc analysis aims to determine the percentage of patients, previously exposed to TNFi, who progressed from ASAS20 at week 16 to ASAS40 response at week 52 with ixekizumab (IXE) treatment and to explore factors that may associate with additional improvement after 16 weeks.

Methods: Patients who achieved Assessment of SpondyloArthritis International Society (ASAS)20 at week 16 from COAST-W (NCT02696798), a Phase 3, randomized, double-blind, placebo-controlled trial, in tumour necrosis factor inhibitor (TNFi)-experienced patients who fulfilled the ASAS criteria for r-axSpA, were analysed. Patients treated with IXE 80 mg Q4W were categorized according to their ASAS response at week 52: sustaining ASAS20 but not reaching an ASAS40 response or achieving ASAS40. Patient demographics and disease characteristics at baseline were analysed by descriptive statistics, and the individual components determining ASAS response at baseline and at week 52 are provided.

Results: At week 16, 22.8% (n=26/114) of patients achieved ASAS20 but not ASAS40; of these, 2 patients discontinued the study before week 52. Amongst the patients who continued through week 52, 50% (12/24) of patients achieved ASAS40; the other 50% sustained their ASAS20 response. Patients who achieved ASAS40 at week 52 were older, had longer disease duration, were less likely to be HLA-B27 positive, and had worse BASDAI and BASFI scores at baseline (Table 1, part a). Achieving ASAS40 appeared to depend most on the Patient Global Assessment of Disease Activity and spinal pain score over time (Table 1, part b).

Table 1. a) Demographics and Characteristics at Baseline (week 0) and b) Descriptive observed data for the individual components of the ASAS response criteria at week 52, mean (SD)

a)	IXEQ4W	
	Patients sustaining an ASAS20 but not reaching an ASAS40 response at week 52 (n=12)	Patients achieving an ASAS40 response at week 52 (n=12)
Age, years	47.3 (13.3)	49.6 (12.3)
Duration of symptoms since axSpA onset, years	16.4 (9.2)	18.6 (12.6)
HLA B27 positive, n (%)	12 (100)	9 (75)
Current tobacco use, n (%)	4 (33.3)	1 (8.3)
ASDAS Score	4.0 (1.0)	4.2 (1.1)
BASDAI Score	7.4 (1.2)	7.8 (1.7)
Serum CRP concentration (mg/L)	23.0 (47.1)	28.0 (66.0)
Spinal Pain due to Ankylosing Spondylitis (NRS)	8.2 (0.8)	8.5 (1.6)
Patient Global Assessment of Disease Activity (NRS)	7.8 (1.3)	8.6 (1.2)
BASFI	7.1 (1.4)	7.4 (2.3)
BASDAI stiffness score	7.1 (1.5)	7.6 (2.2)
b)	IXEQ4W	
Patient Global Assessment of Disease Activity (NRS)	5.5 (1)	3.2 (1.3)
Spinal Pain due to Ankylosing Spondylitis (NRS)	5.6 (1)	3 (1.9)
BASFI	5.0 (1.5)	3.7 (2.1)
BASDAI stiffness score	4.1 (1.4)	3.4 (2.3)

Values are mean (SD) unless stated otherwiseASAS= Assessment of SpondyloArthritis International Society; ASDAS= Ankylosing Spondylitis Disease Activity Score; axSpa = axial spondyloarthritis; BASDAI= Bath Ankylosing Spondylitis Disease Activity Index; BASFI= Bath Ankylosing Spondylitis Functional Index; CRP= C-reactive protein; HLA= human leucocyte antigen; NRS = numeric rating scale; SD= standard deviation

Conclusion: For patients with r-axSpA previously exposed to TNFis and showing modest response to IXE over 16 weeks, longer exposure to IXE may be required to achieve ASAS40.

Acknowledgements: The authors would like to acknowledge Philana Fernandes, an employee of Eli Lilly, for her editorial and writing support.

Disclosure of Interests: Xenofon Baraliakos Speakers bureau: Abbvie, BMS, Chugai, Celgene, Eli Lilly, Pfizer, Galapagos, UCB, MSD, Consultant of: Abbvie, BMS, Chugai, Celgene, Eli Lilly, Pfizer, Galapagos, UCB, MSD, Grant/research support from: Abbvie, Celgene, MSD, Atul Deodhar Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Giliad, GlaxoSmith & Kline, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Boehringer Ingelheim, Eli Lilly, GlaxoSmith & Kline, Novartis, Pfizer, UCB, Soyi Liu Leage Employee of: Eli Lilly, Yves Schymura Employee of: Eli Lilly, Rebecca Bolce Shareholder of: Eli Lilly, Employee of: Eli Lilly, David Sandoval Shareholder of: Eli Lilly, Employee of: Eli Lilly, Jessica A. Walsh Consultant of: AbbVie, Novartis, Eli Lilly, UCB, Amgen & Pfizer, Grant/research support from: AbbVie, Pfizer, Merck, Joachim Sieper Speakers bureau: Abbvie, Janssen, Eli Lilly and Novartis, Consultant of: Abbvie, Janssen, Eli Lilly and Novartis.

DOI: 10.1136/annrheumdis-2021-eular.1823

AB0472

DISEASE ACTIVITY AND OUTCOME IN PREGNANCIES OF PATIENTS WITH SPA - DATA FROM THE GERMAN PREGNANCY REGISTER RHEKISS

A. Weiß[1], C. Bungartz[1], J. Richter[2], S. Spaethling-Mestekemper[3], X. Baraliakos[4], P. M. Aries[5], R. Fischer-Betz[2], A. Strangfeld[1]. *[1]German Rheumatism Research Centre, Epidemiology Unit, Berlin, Germany*; *[2]University Hospital Düsseldorf, Department of Rheumatology & Hiller Research Unit, Düsseldorf, Germany*; *[3]Rheumapraxis München-Pasing, Rheumatology, München, Germany*; *[4]Rheumazentrum Ruhrgebiet, Rheumatology, Herne, Germany*; *[5]Rheumatologie, Rheumatology, Hamburg, Germany*

Background: Spondyloarthritis (SpA) is a severe chronic inflammatory disease, which affects quality of life and functional status. It frequently occurs in women of childbearing age. Active disease and TNFi discontinuation at early pregnancy were found to be risk factors for flares during pregnancy (1).

Objectives: To compare disease activity during pregnancy in patients with or without bDMARD exposure at conception and during pregnancy and to assess pregnancy outcomes.

Methods: RHEKISS is a prospective longitudinal cohort study including patients with confirmed diagnose of inflammatory rheumatic disease. Pregnant patients are eligible to be enrolled until the 20th week of gestation regardless of drug treatment. During observation, information on treatment, disease and pregnancy course, and outcome is collected from rheumatologists and patients. For this analysis, pregnancies of patients with SpA were selected and stratified into three groups according to their exposure to bDMARDs.

Results: Of 140 SpA pregnancies included, 74 (53%) were not exposed to bDMARDs at conception (group 1), 38 (27%) were exposed to bDMARDs at conception, but not during pregnancy (group 2) and 28 (20%) were continuously exposed to bDMARDs at conception and during pregnancy (group 3). Certolizumab (50%), Adalimumab (20%), Etanercept (8%) and Infliximab (8%) were the most frequently prescribed bDMARDs at beginning of pregnancy. Baseline characteristics according to treatment exposure are shown in Table 1. Frequency of flares was highest in group 2: 21%, 38%, and 39% of patients flared during the 1st, 2nd, and 3rd trimester. These rates were 20%, 25%, and 21% in group 1 and 8%, 20%, and zero in group 3. The difference in flare rates was also mirrored in the course of physician assessed global disease activity (Figure 1). Whereas patients in group 1 seemed to have a quite stable disease activity during pregnancy, those who were in group 2 had an increasing activity of disease during pregnancy with an even higher increase of disease activity after giving birth. Patients in group 3 had the lowest disease activity.

Of 137 singleton pregnancies, 130 (95%) ended in live birth. Of 6 spontaneous abortions 2 were in every of the three groups. One pregnancy in group 1 was terminated in gestational week 22 due to suspect malformation. One baby of the triple pregnancy was born and two aborted. All babies of the twin pregnancies were born healthy.

Conclusion: SpA patients treated with bDMARDs at conception are not at higher risk for adverse pregnancy outcomes. Our results in a larger patient population confirmed that discontinuation of bDMARDs after conception is associated with increased disease activity during pregnancy and after birth and a higher risk of flares.

REFERENCES:

[1] van den Brandt S et al., Arthritis Res Ther. 2017; 19(1):64.

Table 1. Baseline characteristics; numbers are n (%) if not otherwise specified; * value at beginning of pregnancy: first 22 weeks after conception

Parameter	no bDMARD at conception (group 1) n=74	bDMARD at conception and discontinued during pregnancy (group 2) n=38	bDMARD at conception and continued during pregnancy (group 3) n=28	Total n=140
Singleton	72 (97)	37 (97.4)	28 (100)	137 (97.9)
Twin	1 (1.4)	1 (2.6)	0	2 (1.4)
Triple	1 (1.4)	0	0	1 (0.7)
New-York criteria fulfilled	21 (33)	17 (49)	10 (48)	48 (40)
disease duration in years, mean (SD)	6.4 (5.9)	7 (4.1)	5.8 (4)	6.4 (5.1)
age*, mean (SD)	33.4 (4.9)	32.3 (4)	31.6 (3.4)	32.7 (4.4)
severity of illness*: asymptomatic	4 (6)	0 (0)	3 (14)	7 (6)
mild	31 (48)	6 (17)	4 (19)	41 (34)
moderate	24 (38)	21 (60)	14 (67)	59 (49)
severe	5 (8)	8 (23)	0	13 (11)
HLA-B27 positive	41 (62)	24 (80)	15 (75)	80 (69)
CRP in mg/l *, mean (SD)	6.6 (8.2)	5.4 (8.2)	5.2 (4.9)	6 (7.6)
CRP >5mg/l *	25 (41)	9 (30)	8 (35)	42 (37)
physician global* (NRS 0-10), mean (SD)	2.6 (2)	2.3 (2.5)	1.7 (1.4)	2.4 (2.1)
BASDAI* (0-10), mean (SD)	3.2 (2)	2.9 (2.3)	2.8 (1.5)	3.1 (2)
patient global* (NRS 0-10), mean (SD)	3.3 (2.7)	3 (2.8)	3 (2.3)	3.1 (2.6)

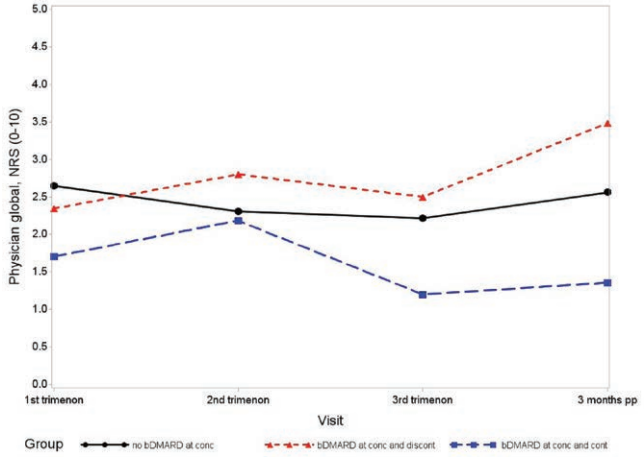


Figure 1 Course of physician assessed global disease activity

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2087

AB0473 TREATMENT OF ANKYLOSING SPONDYLITIS (AS) DURING PREGNANCY

O. Krichevskaya[1], T. Dubinina[1], E. Ilinykh[1], S. Glukhova[1], A. Demina[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Medical and Social Problems of Rheumatology, Moscow, Russian Federation*

Background: The use of medications during pregnancy remains a challenge for both rheumatologists and patients. The lack of compelling evidence of the safety of a line of different drugs, as well as the traditional idea of the incompatibility of therapy and gestation that is common view in Russia, lead to unjustified withdrawal of drugs by both pregnant women and rheumatologists.
Objectives: to describe the frequency of drug usage in pregnant women with AS, to determine the relationship of AS activity and pregnancy complications.
Methods: 49 pregnant women with confirmed AS (modified New York criteria, 1984) were included for prospective observation. 50 pregnancies in total were traced. The average age of the patients was 31.6±4.9 years, the duration of the disease was 134.4±85.8 months. The visits were conducted at 10-11, 20-21, and 31-32 weeks of pregnancy. The BASDAI in the month of conception and in the trimesters of pregnancy was: 1,4[0,6; 3,3]; 2,3[1,2; 4,4]; 2,8[1,4; 4,2] and 2,2[1,6; 4,0], respectively. 48 pregnancies ended with the birth of alive children at an average of 39±1.1 weeks, the height of newborns-51.6±2.1 cm, weight-3397.3±433.1 g. 8 (16.3%) newborns had malformations, 7 of them - minor heart development anomalies, 1 - hydronephrosis. Pregnancy complications: early toxicosis - 18% of pregnant women, threatening of early abortion - 10%, threatening of late abortion-4.1%, threatening of early preterm birth - 6.3%; premature birth – 3 (6.3%) at 36.8±0.1 weeks.
Results: NSAIDs. After inclusion in the study, the drug of choice was ibuprofen, which was canceled for all women no later than the 32-nd week of pregnancy. At the time of conception and in the first, second and third trimesters of pregnancy, NSAIDs were taken by 23 (46%), 20 (40%), 30 (60%) and 21 (43.8%) women, respectively. No effect of NSAIDs on the activity of AS was revealed.
Sulfasalazine (SS) was taken for 3 months before pregnancy by 11(22%) women, during pregnancy – 6 (12%) at a dose of 1.25±0.25 g because of arthritis. The withdrawal of SS was not associated with the recurrence of arthritis.
Glucocorticoids (GC) at a dose of 7.5±2.5 mg 3 months before pregnancy and in the trimesters of pregnancy were taken: 1 (2%), 4 (8%), 8 (16%) and 10 (20.8%) women, of whom 1 patient had arthritis and 1 had inflammatory bowel disease. The remaining patients received GC due to the high activity of AS due to axial manifestations and the unavailability of bDMARDs) intake. Against the background of taking GC, the AS activity did not decrease: BASDAI in the 2nd and 3rd trimesters was 5.5±0.6 and 5.8±1.3 (p>0.05).
bDMARDs. TNF inhibitors for 3 months before pregnancy and on trimesters were received by 11 (22%), 7 (14%), 6 (12%) and 2 (4.2%) patients, of which 1 woman in the second trimester obtained firstly initiated therapy with certolizumab pegol due to the recurrence of uveitis. In those who canceled bDMARDs therapy (both independently and due to the recommendation of a rheumatologist), an increase in AS activity was noted on the eve of pregnancy; BASDAI in the month of conception and in the I, II, and III trimesters was: 2,7 [0,8; 3,5]; 5,1[3,1; 5,9]; 5,5 [5;6] and 6,7 [5,3; 7;3], p<0,05 compared to the month of conception. Undoing the bDMARDs in the month of conception is a risk factor for high activity as (BASDAI>4) in the second trimester (OR OF 30.4; 95% CI 1,5-612,3; p=0.03) and in the third trimester (OR A 32.7; 95% CI 1,6-662,2; p=0.02).
The relationship between pregnancy complications, malformations of the newborns and the used medications was not revealed.
Conclusion: NSAIDs and GC in low doses do not reduce the activity of AS. Withdrawal of TNF inhibitors on the eve of pregnancy is a predictor of high AS activity. It is necessary to increase the knowledge of rheumatologists and patients about the therapeutic possibilities during pregnancy to avoid unjustified drug withdrawal.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2427

AB0474 THE USE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) IN WOMEN WITH ANKYLOSING SPONDYLITIS (AS) DURING PREGNANCY

O. Krichevskaya[1], T. Dubinina[1], E. Ilinykh[1], S. Glukhova[1], A. Demina[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Medical and Social Problems of Rheumatology, Moscow, Russian Federation*

Background: NSAIDs remain the first-line drugs in treatment of AS. During pregnancy, COX-2 non-selective NSAIDs are allowed for intake up to 32 weeks, but the question of the dose-dependent effect of NSAIDs on fetal organogenesis in the 1st trimester and on fetal kidney function and the increased risk of bleeding in childbirth when taken in the second half of pregnancy continues to be discussed. At the same time, data on the effectiveness of NSAIDs, including their low and medium doses, during pregnancy are extremely small.
Objectives: to describe the frequency of using NSAIDs during pregnancy, to determine relationship between the dose of NSAIDs, adherence to therapy with the activity of AS.
Methods: 50 pregnancies were followed in 49 pregnant women with confirmed AS (modified New York criteria, 1984). The average age of the pts was 31.6 ± 4.9 years, the duration of the disease was 134.4 ± 85.8 months. The visits were conducted at 10-11, 20-21, and 31-32 weeks of pregnancy. The BASDAI in the month of conception and in the trimesters (trim.) of pregnancy was: 1,4[0,6; 3,3]; 2,3[1,2; 4,4]; 2,8[1,4; 4,2] and 2,2[1,6; 4,0], respectively. The level of nocturnal back pain according to the NRS in the first, second and third trim. was: 3.2±2.0; 5.4±2.5 and 5.2±2.6, respectively. The drug of choice was ibuprofen at a maximum daily dose of 1200 mg, its withdrawal - no later than 32 weeks of pregnancy.
Adherence to NSAID therapy was defined as the ratio of the actual dose taken to the prescribed dose; an indicator of less than 80% was regarded as non-adherence to therapy. The total dose of NSAIDs was determined by the NSAID intake index (M. Dougados, 2001). The" actual daily dose" of ibuprofen was the sum of the doses of ibuprofen taken, divided by the number of actual days of taking the drug. The "average daily dose" was defined as the sum of the ibuprofen doses taken, divided by the number of days in the trimester.
Results: At the time of conception and in the first, second and third trim. of pregnancy, NSAIDs were taken 23 (46%), 20 (40%), 30 (60%) and 21 (43.8%) women, respectively. The NSAID intake index, the actual and average daily dose of ibuprofen are shown in the Table 1.

	month of conception	trim. 1	trim. 2	trim. 3
the actual daily dose, mg	-	700 [425; 800]	800 [400; 1000]	750 [400; 1200]
the average daily dose, mg	-	158 [87,9; 307,7]	355,1 [138,5; 685,7]	580 [320; 1200]
NSAIDs intake index	28,6 [16,7; 50]	5,8 [2,9; 11,8]	15,5 [4,7; 30,9]	24,4 [9,5; 50]

The index of NSAID intake in the first trim. was lower than before pregnancy and in the second half of gestation (p<0.05 compared to the month of conception, II and III trim.). The average daily dose of ibuprofen was also lower in the first trim. than in the second and third trim. (p<0.05), while the actual daily dose in the second trim. was higher than in the first and third trim. (p<0.05 in all cases).
There was no correlation between BASDAI AS activity, the level of nocturnal pain and the ibuprofen intake index, likewise the fact of NSAID withdrawal throughout pregnancy. In addition, there were no differences in BASDAI levels and back pain in women with a subjective need for NSAIDs, who did and did't take ibuprofen.
50% of women were committed to NSAID therapy in the first trim., 43.5% in the second trim., and 67.4% in the third trim. In pts with non-adherence to NSAID therapy, the BASDAI level was higher than in those who followed the recommendations of the rheumatologist throughout pregnancy: in the first trim. – 3.8[3.4; 4.7] and 1.7[0.8; 2.2]; in the second trim. - 3[2.3; 4.6] and 1.4[0.8; 2.7]; in the

third trim. - 3.1[2.1; 4.0] and 1.7[1.1; 4.0], p<0.05 in all cases. However, women with adherence > 80% were initially less active and NSAIDs were prescribed "on demand", which increased their compliance.
Conclusion: intake of ibuprofen in low doses does not affect the activity of AS. Due to the ongoing discussion about the effect of NSAIDs on neonatal outcomes, further international studies are required for development an optimal treatment regimen during pregnancy with a possible extension of the indications for the appointment of TNF inhibitors (BASDAI<4).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2463

AB0475 COMPARATIVE EFFECTIVENESS OF BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN REAL CLINICAL PRACTICE ACCORDING TO THE MOSCOW UNIFIED ARTHRITIS REGISTER (MUAR)

E. Rozochkina[1], E. Koltsova[2], G. Lukina[1,3], E. Shmidt[4], K. Lytkina[5], A. Zagrebneva[6], E. Zhilyaev[7,8]. *[1]A.S.Loginov Moscow Clinical Scientific Center, Rheumatology, Moscow, Russian Federation*; *[2]Research Institute of the Organization of health and healthcare management, Rheumatology, Moscow, Russian Federation*; *[3]V.A. Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*; *[4]N.I.Pirogov City Clinical Hospital 1, Rheumatology, Moscow, Russian Federation*; *[5]City Clinical Hospital 4, Rheumatology, Moscow, Russian Federation*; *[6]City Clinical Hospital 52, Rheumatology, Moscow, Russian Federation*; *[7]Russian Medical Academy of Continuous Professional Education of the Ministry of Healthcare of the Russian Federation, Rheumatology, Moscow, Russian Federation*; *[8]European Medical Center, Rheumatology, Moscow, Russian Federation*

Background: This study is the first analysis of biological disease-modifying anti-rheumatic drugs (bDMARDs) for ankylosing spondylitis (AS) within the Moscow Unified Arthritis Register (MUAR).
Objectives: to compare the effectiveness of bDMARDs in patients with AS using data from the MUAR.
Methods: The analysis included the data of patients with AS who were included in the MUAR and received biological therapy for at least 6 months. The effectiveness of the drugs was assessed by the achieved values of the indices of diseases activity and its manifestations: ASDAS(C-RP), BASDAI, LEI, MASES, indicators of the functional ability of patients (BASFI, HAQ) at the last completed visit. Comparison of indicators between drugs was in a general linear model, adjusted for the identified confounders. The search for confounders was in 2 stages: first, by univariate analysis, were identified indicators significantly related to the achieved ASDAS. Then, within the multivariate general linear model, by backward stepwise selection were determinate variables significantly and independently associated with ASDAS.
Results: The current study included 363 episodes of treatment with bDMARDs in 361 patients. There were 240 men (66.5%). The average age of the included patients was 46.3 ± 11.2, the age at the onset of the disease was 27.3 ± 11.4. The average duration of a treatment episode until the patient was assessed 1135 ± 900 days. Significant differences of the values of ASDAS(p = 0.033) and ESR (p = 0.007) between bDMARDs were revealed. In pairwise comparisons of the achieved ASDAS using the Shidak adjustment, demonstrated that the values on infliximab and adalimumab were significantly lower than on certolizumab pegol (p = 0.009 and p = 0.041, respectively). Also significantly higher ESR values on certolizumab compared to all other drugs (p < 0.001 for all) were found. There were no statistically significant differences between the drugs for other studied parameters.
Conclusion: The studied bDMARDs (infliximab, adalimumab, etanercept, certolizumab pegol, golimumab, secukinumab) demonstrate generally similar clinical efficacy in real clinical practice. The effect of golimumab and sekukinumab which have been recently introduced into clinical practice doesn't differ significantly from the effect of TNF inhibitors which has been used for a long time.

Table 1. Achieved values of the indices of activity and functional ability against the background of treatment with bDMARDs.

	ASDAS(C-RP)		BASDAI		HAQ		BASFI	
	unadjusted	adjusted	unadjusted	adjusted	unadjusted	adjusted	unadjusted	adjusted
ADA	1,89 ± 0,89	1,54 ± 0,29	3,07 ± 1,61	2,89 ± 0,25	0,63 ± 0,42	0,60 ± 0,07	3,25 ± 2,02	3,09 ± 0,32
GOL	2,08 ± 0,99	2,22 ± 0,31	3,09 ± 1,96	3,44 ± 0,49	0,66 ± 0,61	0,78 ± 0,14	3,74 ± 2,93	4,00 ± 0,63
INF	1,57 ± 0,82	1,29 ± 0 ,32	2,64 ± 1,55	2,19 ± 0,38	0,56 ± 0,52	0,57 ± 0,11	2,81 ± 2,29	2,93 ± 0,49
ETA	1,96 ± 0,85	1,94 ± 0,24	3,19 ± 1,69	3,44 ± 0,19	0,65 ± 0,53	0,72 ± 0,06	3,39 ± 2, 26	3,88 ± 0,24
CER	2,69 ± 1,03	2,95 ± 0,46	4,07 ± 2,28	3,65 ± 0,52	1,12 ± 0,82	0,84 ± 0,15	5,07 ± 2,95	4,19 ± 0,67
SEK	2,69 ± 1,31	1,66 ± 0,51	3,72 ± 2,22	3,71 ± 0,49	0,85 ± 0,47	0,85 ± 0,14	3,46 ± 2,13	3,46 ± 0,63

ADA – Adalimumab, GOL – Golimumab, INF – Infliximab, ETA – Etanercept, CER – Certolizumab pegol, SEK – Sekukinumab, ASDAS - Ankylosing Spondylitis Disease Activity Score, BASDAI Bath Ankylosing Spondylitis Disease Activity Index, BASFI - Bath Ankylosing Spondylitis Functional Index, HAQ - Health Assessment Questioner, C-RP – C-reactive protein.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2819

AB0476 VITAMIN D SERUM CONCENTRATION VARIES ACCORDING TO DISEASE ACTIVITY IN SPONDYLOARTHRITIS

M. Rato[1], F. Oliveira Pinheiro[1], S. Garcia[1], B. M. Fernandes[1], D. Fonseca[2], D. Santos Oliveira[1,3], A. Martins[1], F. R. Martins[4], A. Bernardo[1], M. Bernardes[1,5], L. Costa[1]. *[1]Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*; *[2]Centro Hospitalar de Vila Nova de Gaia/Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; *[3]Faculdade de Medicina da Universidade do Porto - FMUP, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; *[4]Centro Hospitalar Universitário do Algarve - Faro, Rheumatology, Faro, Portugal*; *[5]Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal*

Background: Several studies have shown dissimilar results for the relationship between serum 25-hydroxyvitamin D concentration (25-OH-D) and disease activity in spondyloarthritis (SpA).
Objectives: This study aims to assess whether vitamin D levels vary according to disease activity in patients with SpA before and after starting treatment with biologic disease-modifying anti-rheumatic drugs (bDMARDs).
Methods: An observational retrospective study was performed in SpA patients followed in the Rheumatology department of a tertiary university hospital. Demographic and clinical data were collected from the Rheumatic Diseases Portuguese Register (Reuma.pt). Patients were assessed for 25-OH-D levels before and after 6 months of treatment with the first bDMARD. Correlation between 25-OH-D levels and disease activity measured by Ankylosing Spondylitis Disease Activity Score (ASDAS) at baseline and after 6 months were assessed using student's t-test for two samples and one-way ANOVA and with post hoc tests for multiple comparisons.
Results: A total of 189 patients were included. Ninety-seven patients were females (51.3%). The mean age at diagnosis was 34.8±11.2 years and the median disease duration at the start of the first bDMARD was 4.9 years (min: 0.1; max: 46.0). All patients fulfilled the ASAS criteria for SpA. Nonsteroidal anti-inflammatory drugs were used by 102 patients (54.0%) and conventional synthetic DMARDs by 69 patients (36.5%). At 6 months, 188 patients were treated with tumor necrosis factor inhibitors and one with interleukin-17 inhibitor. According to ASDAS criteria, at baseline 36.8% of patients had high disease activity and 59.5% had very high disease activity. After 6 months of treatment with bDMARD 14.7% of patients have inactive disease, 21.6% low disease activity, 36.3% high activity and 12.6% very high disease activity. The mean value of 25-OH-D at baseline was significantly lower in the group of patients with very high disease activity compared to the patients with high disease activity (21.9±11.1 ng/ml vs 26.1±11.6 ng/ml, p= 0.02). At 6 months of treatment the mean value of 25-OH-D in inactive, low, high and very high disease activity was 31.0±17.1ng/ml, 28.5±11.2ng/ml, 25.8±10.8ng/ml and 19.3 ±9.5ng/ml, respectively. There was a statistically significant difference between the groups, as determined by one-way ANOVA (p = 0.001). A post hoc Dunnett T3 test revealed that patients with very high disease activity have significantly lower mean 25-OH-D levels (19.29 ± 9.5) than patients with inactive disease (31.0 ± 17.1, p = 0.025) and low activity (28.5 ± 11.2, p = 0.009). Among the groups with high and very high disease activity, the significance is only marginal (p = 0.068).
Conclusion: Vitamin D serum concentration varies according to disease activity in SpA. In fact, SpA patients with lower levels of 25-OH-D are associated with higher rates of disease activity, even in patients treated with biologics agents. It is important to be aware of vitamin D level as it can play a role in the management and treatment of the disease, mainly in the most severe patients.
REFERENCES:
[1] Zhao SZ, Thong D, Duffield S, Goodson N. Vitamin D Deficiency in Axial Spondyloarthritis is Associated With Higher Disease Activity. Arch Rheumatol. 2017 Mar 24;32(3):209-215. doi: 10.5606/ArchRheumatol.2017.6212. PMID: 30375524; PMCID: PMC6190948.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2921

AB0477

EFFECT OF ANTI-TNF THERAPY ON BONE MINERAL DENSITY IN ANKYLOSING SPONDYLORTHITIS

A. Ajerouassi[1], K. Nassar[1], S. Janani[1]. [1]*faculté de médecine et de pharmacie de cabalanca, centre hospitalier universitaire ibn rochd, rhumatologie, Casablanca, Morocco*

Background: Osteoporosis is common in spondyloarthritis, due to reduced spinal mobility, and inflammation. Anti-inflammatory treatments have a beneficial effect on the bone, and there is a significant increase in bone density during treatment with anti-TNF alpha.
Objectives: to study bone mineral density in patients with ankylosing spondyloarthritis (AS) treated with anti-TNF alpha.
Methods: This is a retrospective descriptive study of patients with AS meeting the modified New York criteria. Bone mineral density, assessed by dual energy x-ray absorptiometry (DXA), of AS patients treated with anti-TNF alpha was compared to that of a control group of AS patients not treated with anti-TNF alpha.
Inclusion criteria:
- Male patients
- Patients who do not have an abnormality disrupting phosphocalcic and bone metabolism
- For Patients on anti-TNF alpha: the treatment must be received for more than 6 months
Results: A total of 22 patients were included, including 11 patients on anti-TNF alpha and 11 patients not on anti-TNF. The mean age (standard deviation) was 28 (± 7.2) years and 41 (± 14.8) in the cases and controls respectively. The mean body mass index in the AS group on anti-TNF was 22.16 kg / m2 and in the control group was 19.64 kg / m2. In the AS group on anti-TNF alpha, the mean bone mineral density of the spine was 1.092 g / cm2 (mean T score = -0.63) and that of the femoral neck, the mean bone mineral density was 0.888g / cm2 (mean T score = -1.04). In the control group, the mean bone mineral density of the spine was 0.959 g / cm2 (mean T score = -1.91) and the mean bone mineral density of the femoral neck was 0.774 g / cm2 (mean T score = -1.99). Bone mineral density in the spine and cervix was higher in the group receiving anti-TNF alpha (p = 0.09, p = 0.173 respectively)
Conclusion: Our study shows the increase, although not statistically significant, in bone mineral density in AS patients receiving anti-TNF alpha agents compared to controls. Our results agree with those of the literature which support the bone protective effect of anti-TNF alpha. The non-significant difference can be explained by the delay in the introduction of biotherapy at the advanced stage of the structural evolution of AS. The best solution is to start TNF inhibitors at the early inflammatory stage of AS.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2940

AB0478

IN PREVIOUSLY BIOLOGIC-NAÏVE RHEUMATIC PATIENTS WITH DRUG INDUCED LUPUS SECONDARY TO A FIRST ANTI-TNF THERAPY, IS IT SAFE TO SWITCH TO A SECOND ANTI-TNF-α AGENT?

A. Martins[1], D. Santos Oliveira[1,2], F. R. Martins[3], F. Oliveira Pinheiro[1], M. Rato[1], D. Fonseca[4], S. Garcia[1], B. M. Fernandes[1], S. Pimenta[1,5], M. Bernardes[1,5], L. Costa[1]. [1]*Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*; [2]*Faculdade de Medicina da Universidade do Porto - FMUP, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; [3]*University Hospital Center of Algarve, Rheumatology, Faro, Portugal*; [4]*Centro Hospitalar Vila Nova de Gaia / Espinho - Unit 1, Rheumatology, Porto, Portugal*; [5]*Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal*

Background: Drug-induced lupus erythematosus (DILE) secondary to anti-TNF-α agents results from an immunogenicity phenomena not yet fully understood and is a rare condition. Withdrawal of anti-TNF- α therapy usually leads to total resolution of symptoms, however sometimes immunosuppression is needed. It is not clear if this condition is drug specific or class related. Therefore, there are doubts about the safety of switching to a second TNF inhibitor: will a further anti-TNF-α agent increase the risk of DILE recurrence?
Objectives: To analyze the outcomes in patients with DILE secondary to an anti-TNF-α agent that switch to a second anti-TNF-α agent.
Methods: We performed a retrospective analysis of patients with spondyloarthritis, psoriatic arthritis and rheumatoid arthritis from our University Hospital, who developed DILE secondary to an anti-TNF-α agent as a first biologic and switch to a second anti-TNF-α agent. Because specific criteria for the diagnosis of DILE have not been established, DILE diagnosis was considered when a temporal relationship between clinical manifestations and anti-TNF alpha treatment was found and ACR/EULAR 2019 classification criteria for SLE were fulfilled. Clinical and laboratorial features and outcomes were collected from the Portuguese Rheumatic Diseases Register (Reuma.pt) and medical records.
Results: Six of 617 patients developed DILE secondary to anti-TNF-α agents (2 secondary to etanercept, 2 to adalimumab and 2 to infliximab). These patients had total resolution of symptoms and autoantibodies (ANA and anti-DNAds), induced by the therapy, disappeared after withdrawal of the anti-TNF-α agent implied.
Afterwards, 4 of these 6 patients switched to a second anti-TNF-α agent: 1 to etanercept, 1 to certolizumab, 1 to adalimumab and another to golimumab. The time interval between the two therapies was 2,0 ± 0,8 months. Regarding the outcomes, in all four patients, no DILE recurrence or autoantibodies induction recurrence was observed. These patients have a good response to the new biotherapy, without side effects reported, and a significant clinical improvement was observed.
Conclusion: Our study results are in agreement with the literature described before. It seems that exist a low rate of DILE recurrence with an alternative anti-TNF-α agent. Thus, this condition seems to be drug specific rather than class related. Therefore, it seems secure to use a second anti-TNF-α agent, even in a short period of time after DILE development. There is no evidence about the best or securest second TNF inhibitor, so any anti-TNF-α agent can be prescribed. A carefully monitoring of symptoms of relapse should be ensured. In conclusion, DILE secondary to a TNF inhibitor should not be an absolute contraindication to the use of a subsequent anti-TNF-α agent.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2992

AB0479

LONGTERM RETENTION RATE OF CERTOLIZUMAB PEGOL IN AXIAL SPONDYLOARTHRITIS IS HIGHER: DATA FROM TURKBIO

S. S. Koca[1], Y. Pehlivan[2], S. Akar[3], S. Şenel[4], A. Avanoglu Guler[5], O. Sosyal[6], A. Yazici[7], S. Yılmaz[8], R. Piskin Sagir[1], N. Inanc[9], A. Karatas[1], G. Yildirim Cetin[10], P. Atagündüz[9], F. Onen[11]on behalf of TURKBIO Study Group. [1]*Firat University School of Medicine, Department of Rheumatology, Elazig, Turkey*; [2]*Uludağ University, School of Medicine, Department of Rheumatology, Bursa, Turkey*; [3]*Katip Çelebi University, School of Medicine, Department of Rheumatology, Izmir, Turkey*; [4]*Erciyes University School of Medicine, Department of Rheumatology, Kayseri, Turkey*; [5]*Gazi University School of Medicine, Department of Rheumatology, Ankara, Turkey*; [6]*Celal Bayar University School of Medicine, Department of Rheumatology, Manisa, Turkey*; [7]*Kocaeli University School of MEdicine, Department of Rheumatology, Kocaeli, Turkey*; [8]*Selcuk University School of Medicine, Department of Rheumatology, Konya, Turkey*; [9]*Marmara University School of Medicine, Department of Rheumatology, Istanbul, Turkey*; [10]*Kahramanmaraş Sutçu Imam University School of Medicine, Department of Rheumatology, Kahramanmaraş, Turkey*; [11]*9 Eylul University School of Medicine, Department of Rheumatology, Izmir, Turkey*

Background: Choosing the best treatment strategy for a patient is one of the most difficult issues in modern rheumatology, as there are various factors affecting drug therapy in chronic diseases, such as efficacy, safety, and compliance. Physicians take care of long-term retention rate and responses for discontinuation of candidate drug.
Objectives: The purpose of this study to assess the drug survival of certolizumab pegol (CZP) in patients with axial spondyloarthritis (ax-SpA) and to identify the predictors and reasons for discontinuation.
Methods: Data on patient characteristics, demographics, diagnosis, duration of disease, treatment and outcomes have been collected since 2011 in Turkish Biologic (TURKBIO) Registry. By the end of December 2020, 410 ax-SpA patients received CZP and were included. Kaplan Meier plot was used for drug survival analysis. Cox regression analysis was performed to evaluate the predictor associated with drug survival.
Results: During the median 54 months follow-up, 92 (22.4%) patients discontinued the CZP treatment. The reasons for discontinuation: ineffectivity was 58.7% (n=54), adverse events was 6.5%, pregnancy was 3.3% and surgery was 4.3%. The baseline characteristics of patients continue with CZP and discontinuation due to ineffectiveness were shown in the Table 1. Patients who discontinued CZP had higher HAQ, BASFI and BASDAI values. Moreover, they were more co-treated with NSAIDs and csDMARDs. At the month 36, retention rate of CZP was 71.5% in patients with ax-SpA (Figure 1).

Conclusion: Real life experience from this nationwide TURKBIO registry show higher long-term retention rate of CZP in ax-SpA. Higher baseline disease activity and functional limitation predict discontinuation of CZP. Adding NSAIDs and csDMARDs to the treatment of the patient with poor prognosis cannot increase retention rates.

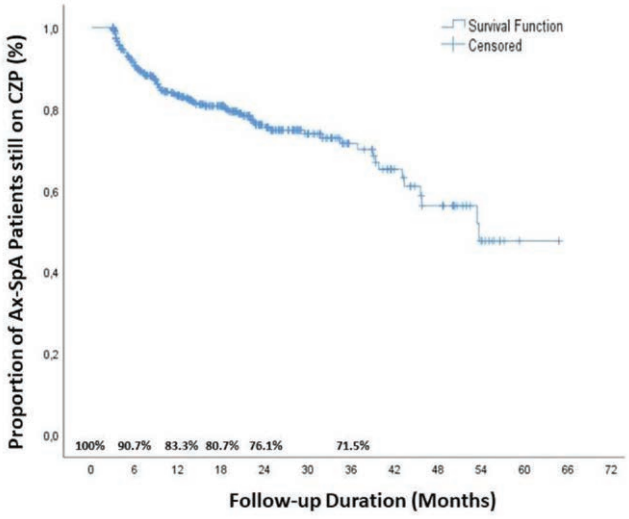


Figure 1 Drug survival of CZP in patients with Ax-SpA

Table 1. Baseline characteristics of ax-SpA patients who continue and discontinue CZP

		All patients (n=410)	Continue to CZP (n=318)	Discontinue to CZP* (n=54)	p
Females, n (%)		185 (49,7)	157 (49,4)	28 (51,9)	0,736
Age, years		42 (34-49)	41 (34-49)	45 (34-54)	0,064
Symptom duration, years		11 (7-17)	11 (6-16)	12 (8,5-20)	0,054
HLA-B27, n (%)		150 (63,8)	129 (64,5)	21 (60)	0,609
Previous bDMARDs, n (%)	**Adalimumab**	54 (14,5)	42 (13,2)	12 (22,2)	0,082
	Etanercept	**53 (14,2)**	**40 (12,6)**	**13 (24,1)**	**0,025**
	Golimumab	11 (3)	7 (2,2)	4 (7,4)	0,060
	Infliximab	39 (10,5)	35 (11)	4 (7,4)	0,425
Co-treated drugs, n (%)	**NSAID**	**206 (55,4)**	**169 (53,1)**	**37 (68,5)**	**0,036**
	Methotrexate	**35 (9,4)**	**22 (6,9)**	**13 (24,1)**	**<0,001**
	Sulphasalazine	**61 (16,4)**	**40 (12,6)**	**21 (38,9)**	**<0,001**
	Leflunomide	**5 (1,3)**	**2 (0,6)**	**3 (5,6)**	**0,023**
ESH, mm/h		21,5 (10-37)	21 (10-37)	23 (10-34)	0,999
CRP, mg/dl		7 (3-20)	7 (3-20)	7 (3-22)	0,727
HAQ		**0,63 (0,25-0,94)**	**0,5 (0,25-0,88)**	**0,75 (0,38-1,25)**	**0,009**
BASFI		**21 (7-45)**	**20,5 (6-41)**	**31 (13-58)**	**0,011**
BASDAI		**30,5 (13-52)**	**30 (12-50)**	**43 (23-61,5)**	**0,002**
ASDAS		2,7 (1,8-3,7)	2,7 (1,8-3,6)	2,9 (2,3-4)	0,062

*Discontinue due to ineffectivity.

REFERENCES:

[1] Iannone F, et al. Effectiveness of Certolizumab-Pegol in Rheumatoid Arthritis, Spondyloarthritis, and Psoriatic Arthritis Based on the BIOPURE Registry: Can Early Response Predict Late Outcomes? Clin Drug Investig. 2019;39(6):565-575.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3140

AB0480

INFLUENCE OF ANTI TNF THERAPIES AND HYPERHOMOCYSTEINEMIA ON BONE MINERAL DENSITY IN ANKILOSING SPONDYLITIS PATIENTS

D. Anghel[1], E. M. Hoinoiu[1], M. M. Negru[2], O. G. Petrache[1], N. O. Costache[1], V. Iachim[1], R. A. Bursuc[3], A. Ghiatau[4], A. Manolache[4], V. V. Smedescu[4], C. F. Plesa[5]. *[1]Central Military Emergency University Hospital Carol Davila, Rheumatology, Bucharest, Romania*; *[2],Sfânta Maria" Clinical Hospital, Rheumatology, Bucharest, Romania*; *[3]Central Military Emergency University Hospital Carol Davila, Nefrology, Bucharest, Romania*; *[4]Central Military Emergency University Hospital Carol Davila, Internal Medicine, Bucharest, Romania*; *[5]Central Military Emergency University Hospital Carol Davila, Neurology, Bucharest, Romania*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease associated with an important risk factor of osteoporosis. A high serum level of Homocysteine (Hcy) has been recently recognized as a risk factor for osteoporosis and osteoporotic fractures. Treatment with TNF-α blockers might influence bone metabolism and prevent structural bone damage in AS.
Objectives: The aim of the study was to evaluate the influence of anti-TNF therapies and hyperhomocysteinemia on bone mineral density in AS patients.
Methods: In our retrospective study were enrolled 73 AS patients with anti TNF-α therapies (29 Adalimumab 40mg/2weeks, 24 Etanerceptum50mg/week, 20 Infliximabum5 mg/kg/8 weeks) and 45 AS patients non anti TNF-α therapies. All patients included in this study met the modified New York criteria. The current medications used by the non anti TNF-α therapies patients were nonsteroidal anti-inflammatory drugs.
We used Dual energy *x* ray absorptiometry (DXA) method for measuring bone mineral density (BMD). Osteoporosis is defined as a T score of ≤ −2.5 SD, according to the WHO criteria. BMD of the hip and lumbar spine (L1-L4) was determined at baseline and after 6 months. Hcy concentrations were measured by using a chemiluminescence immunoassay method. The normal serum Hcy level is considered to be below 15mmol/L. In both group we followed the activities disease (C reactive protein-CRP, eritrocytes sedimentation rate-ESR, Bath ankylosing spondylitis disease activity index-BASDAI score) and determined vitamin D3 level.
All parameters were determined at baseline and after 6 months.
Results: The mean age of study group1 was 47.4±11.1 years and 42±9,8year in group2. The mean disease duration was 11.9 ± 6.1 years. 83,5% of patients were HLA-B27 positive in group1 and 71,1% in group2.
BMD measurements revealed more severe osteoporosis in patients with positive HLA-B27 in both groups at baseline. After 6 months in group1 BMD increased by 0.4% at lumbar spine and 0.1% in the hip and in group2 decreased by 0.9% and 0.6% in the same sites. No significant differences between type of anti-TNF therapies and BMD. In group 1, HLA-B27 positive status was positive correlated with decrease BMD(p=0.001) after 6 months. Hcy levels were found significantly increased (14.8 ± 3.8 mg/mL vs. 12.4 ± 4.2 mg/mL; P < 0.001) at baseline in both groups. Serum levels of Hcy were inversely correlated to lumbar spine BMD ($p<$ 0.005) and femur neck BMD(p=0,001) after 6 months in group1. At baseline the mean level of 25-hydroxyvitamin D_3 was 22.8 ± 14.1 ng/mL in group1 *and* 26.6 ± 12.5 ng/mL in group2. In anti TNF patients group, we found a positive correlation between decrease BMD, low level of 25-hydroxyvitamin D_3 and high level of Hcy(p=0,001) after six months. No correlation was found between BMD and BASDAI score and inflammatory parameters (ESR, CRP).
Conclusion: Bone mineral density measurements revealed more severe osteoporosis in positive HLA-B27 AS patients and hyperhomocysteinemia. Association of low level of 25-hydroxyvitamin D3 and hiperhomocysteinemia is correlated with high-risk fracture in positive HLA-B27 patients. Anti TNF therapies reduce this risk.

REFERENCES:

[1] Kim JI, Moon JH, Chung HW, Kong MH, Kim HJ. Association between homocysteine and bone mineral density according to age and sex in healthy adults. J Bone Metab 2016; 23:129-34.

[2] Fratoni V, Brandi ML. B Vitamins, homocysteine and bone health. Nutrients 2015; 7:2176-92.

[3] Jahn O, Wex T, Klose S, Kropf S, Adolf D, Piatek S, *et al.* Cathepsin K in treatment monitoring following intravenous zoledronic acid. Biomed Rep 2014; 2:915-7.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3523

AB0481 PATIENT'S PERSPECTIVE ON PATIENT EDUCATION IN AXIAL SPONDYLOARTHRITIS: A QUALITATIVE STUDY

Y. M. van der Kraan[1], D. Paap[1,2], N. Lennips[1], E. C. A. Veenstra[1], S. Kieskamp[1], A. Spoorenberg[1]. [1]*University Medical Center Groningen, Department of Rheumatology and Clinical Immunology, Groningen, Netherlands*; [2]*University Medical Center Groningen, Department of Rehabilitation, Groningen, Netherlands*

Background: Within the EULAR recommendations patient education (PE) is stated as the basis of axial spondyloarthritis (axSpA) management, since PE contributes to reaching treatment goals.[1] However, educational needs are scarcely qualitatively studied in patients with axSpA and the EULAR recommendations of PE are primarily based on research in patients with rheumatoid arthritis. The World Health Organization advocates the incorporation of qualitative research into the development of guidelines and recommendations,[2] since it generates rich and detailed data providing explanations and understanding of the complexity of human behaviour and decision-making.[3]
Objectives: To explore perceptions, experiences and needs of PE in patients with axSpA.
Methods: An interpretive phenomenological approach was applied and data was collected through semi-structured in-depth interviews with axSpA patients with a broad variation in characteristics. The data collection and analysis was conducted in an iterative manner. Thematic analysis was applied to translate experiences and perceptions from the interviews into themes.[4] Multiple strategies were used to enhance credibility: data saturation, research triangulation, bracketing, member checking, theoretical notes, and peer debriefing.
Results: Twelve patients participated, for characteristics see Table 1. From the participants' perspective three interrelated themes regarding PE are important for healthcare professionals (HCP) to pay attention to: *illness perception, content* and *availability*. 1) *Illness perception*, defined as patients' personal understanding and belief about their disease, affects how patients experience and process PE which consequently influences coping strategies with their disease. 2) The following topics concerning *content* are reported as most important in PE for patients with axSpA: prognosis, treatment, and the influence of lifestyle aspects. 3) *Availability* of PE: face-to-face contact with a HCP is the preferred method for exploring patients' personal needs in PE. Additionally, active self-education is preferred to learn more about the different subjects which patients can apply when preferred. Furthermore, participants reported a relationship of trust between patient and HCP and sufficient amount of time in combination with a comprehensible amount of information to support their understanding (health literacy) as prerequisites for effective PE.

Table 1. Characteristics of the patients with axSpA in this study

Participants	Sex	Age	Symptom years	Diagnosis years	ASDAS	Disease activity	PASS	Level of education	Marital status
1	M	39	18	15	0.47	ID	Yes	ISCED 7	Single
2	M	56	30	30	2.90	HDA	No	ISCED 3	Divorced
3	M	24	10	9	0.88	ID	Yes	ISCED 7	In a relationship
4	M	32	20	13	1.04	ID	Yes	ISCED 6	In a relationship
5	M	66	24	23	1.33	LDA	Yes	ISCED 3	Married
6	M	33	7	5	1.20	ID	Yes	ISCED 7	Married
7	M	56	9	6	2.72	HDA	-	ISCED 2	Married
8	F	30	15	9	2.11	HDA	No	ISCED 3	Single
9	F	36	14	12	1.22	ID	Yes	ISCED 7	Married
10	F	56	18	17	3.23	HDA	-	ISCED 2	Married
11	F	33	10	5	1.66	LDA	Yes	ISCED 3	Divorced
12	F	27	3	2	1.90	LDA	No	ISCED 7	In a relationship

M = Male; F = Female; ASDAS = Ankylosing Spondylitis Disease Activity Score; ID = inactive disease, LDA = low disease activity, HDA = high disease activity; PASS = Patient Acceptable Symptom State Questionnaire; ISCED 2011 = International Standard Classification of Education 2011

Conclusion: This first bottom-up qualitative study exploring perceptions, experiences and needs of PE in patients with axSpA, shows that HCP should pay attention to patients illness perception to promote effective delivery of PE. Additionally, diagnosis, treatment and lifestyle aspects are important subjects and a combination of face to face contact and self-education is preferred by the patients. These results will provide disease specific content for future guidelines regarding PE in axSpA.

REFERENCES:

[1] Zangi HA, et al. Ann Rheum Dis. 2015;74:954-962
[2] Downe S, et al. Heal Res Policy Syst. 2019;17,1-12
[3] Kelly A, et al. J Rheumatol. 2021;48,6-15
[4] Braun V, et al. Qual Res Psychol. 2006;3:77–101

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3553

AB0482 PHARMACOLOGICAL TREATMENT OF ENTHESITIS - A SYSTEMATIC REVIEW ON THE EFFICACY OF THE AVAILABLE OPTIONS

R. Pinheiro Torres[1,2], S. Rodrigues-Manica[1,2], F. Pimentel Dos Santos[1,2,3]. [1]*Hospital Egas Moniz, Rheumatology, Lisboa, Portugal*; [2]*CEDOC, Rheumatology, Lisboa, Portugal*; [3]*Nova Medical School, Rheumatology, Lisboa, Portugal*

Background: Enthesitis is a recognized as a hallmark of spondyloarthrtis (SpA), including psoriatic arthritis (PsA). However, it is an underestimated disease domain in both in clinical trials and clinical practice (1).
Objectives: This systematic literature review (SLR) assessed the efficacy of the available pharmacological options for enthesitis.
Methods: A SLR was conducted following the PRISMA reporting guidelines. Studies were sourced from PubMed and Embase databases, using the MeSH terms: enthesitis, entheses, treatment, spondylarthritis, ankylosing spondylitis and psoriatic arthritis. The search was limited to articles in English published between January 2000 and July 2020. Two independent reviewers screened the titles and abstracts.
Results: A total of 65 articles matched the research criteria. The included populations, the time to assessment of the primary endpoint and the chosen outcome for assessment of enthesitis was heterogeneous across studies. There were no studies assessing the effect of non-steroidal anti-inflammatory drugs, glucocorticoids, or csDMARDs. In PsA, all TNFis showed superiority in monotherapy against placebo (PBO). However, when combined with methotrexate (MTX), only some TNFi showed superiority against MTX monotherapy. In SpA, there was conflicting evidence regarding the efficacy of TNFi in enthesitis. Regarding IL23i in PsA, Ustekinumab was superior to PBO, and to TNFis. Guselkumab was superior to PBO when given every 4 weeks. Regarding IL7i, Secukinumab (SEC) was superior to PBO, only for some dosing schemes. Ixekizumab (IXE) was superior to PBO for the treatment of enthesitis only in TNF-naïve patients. Studies comparing SEC and IXE to ADA, showed no difference. There was no reported data on IL17i for enthesitis in SpA. In PsA, Tofacitinib was superior to PBO in naïve patients, and Tofacitinib 10mg was superior to PBO in bioexperienced patients. Apresmilast 30mg showed superiority to PBO for enthesitis. All finding are summarized on Table 1.

Table 1. Findings of the systematic literature review on treatment options for enthesitis

Disease	Tested drug vs Reference	Superiority of the treatment arm against reference arm (p<0.05)	Reference
PsA	TNFi vs PBO	YES	NCT00051623 (IFX)
			NCT00265096 (GOL)
			NCT01087788 (CZP)
	TNFi+MTX vs PBO+MTX (PBO+ETN one study) vs PBO+MTX	NO	NCT00367237 (IFX)
			NCT02065713 (GOL)
			NCT02376790 (ETN)
	UST vs PBO	YES	NCT01009086
	UST vs TNFi	YES	NCT01077362 EudraCT 2017-003799-29 β
	GUS q4w vs PBO	YES	NCT03162796
	GUS q8w vs PBO	NO	NCT03158285
	SEC (pooled dose) vs PBO	YES	NCT01392326
			NCT01752634
	SEC 300mg vs PBO	YES	NCT01989468
	SEC 150mg vs PBO	NO	
	SEC 300mg with loading vs PBO	YES	NCT02404350
	SEC 150mg with loading vs PBO	YES	
	SEC 150mg no loading vs PBO	NO	
	IXE vs PBO	YES	NCT01695239
	ADA vs PBO	NO	
	IXE vs PBO	PsA Bionaive NO	NCT02349295
	IL17i (SEC/ ADA) vs TNFi	PsA Bioexperienced NO	NCT02745080 (SEC)
			NCT03151551 (ADA) β
	APR 20mg vs PBO	NO	NCT01172938
	APR 30mg vs PBO	YES	
	TOF 5mg vs PBO	NO	NCT01877668
	TOF 10mg vs PBO	YES	(TNFi-naive)
	ADA 40mg vs PBO	NO	
	TOF vs PBO	NO	NCT01882439 (TNFi-failure)
SpA	ETN vs SSZ	YES (imaging)/ NO (clinical) axSpA	NCT00844142
	ETN vs PBO	YES for nr-axSpA	NCT01258738
	ADA vs PBO	YES for r-axSpA	NCT00195819
		NO for nr-axSpA	NCT00939003
		YES for perSpA	NCT01064856
	GOL IV vs PBO	YES for r-axSpA	NCT02186873
	GOL 100mg vs PBO	YES	NCT00265083
	GOL 50mg vs PBO	NO	
	GOL vs PBO	For r-axSpA YES nr-axSpA	NCT01453725

β-Open-label; PsA: Psoriatic arthritis; r-axSpA: Radiologic axial spondylarthritis; nr-axialSpA: non radiological axial spondylarthritis; PBO: Placebo; TNFi: Tumor necrosis factor inhibitors; ETN: Etanercept; IFX: Infliximab; ADA: Adalimumab; GOL: Golimumab; UST: Ustekinumab; CZP: Certolizmab; GUS: Guselkumab; SEC: Secukinumab; IXE: Ixekizumab; APR: Apremilast; TOF: Tofacitinib; MTX - Methotrexate

Conclusion: This SLR emphasizes the current heterogeneity in the assessment and report of enthesitis. There is still an unmet need for further studies to improve our understanding about enthesopathy.

REFERENCES:

[1] Schett G. et al. Enthesitis: from pathophysiology to treatment. Nat Rev Rheumatol. 2017;13(12):731-41.

Disclosure of Interests: Rita Pinheiro Torres: None declared., Santiago Rodrigues-Manica Speakers bureau: Novartis, Janssen and MSD, Fernando Pimentel dos Santos: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3681

AB0483 CAN WE PREDICT WHICH PATIENTS WITH SPONDYLOARTHRITIS WILL NEED DOSE ESCALATION OF SECUKINUMAB TO 300 MG MONTHLY?

D. Fonseca[1], F. Oliveira Pinheiro[2], M. Rato[2], B. M. Fernandes[2], S. Garcia[2], A. Martins[2], D. Santos Oliveira[2,3], F. R. Martins[4], M. Bernardes[2,5], L. Costa[2]. *[1]Centro Hospitalar de Vila Nova de Gaia / Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; *[2]Centro Hospitalar Universitário de São João, Rheumatology, Porto, Portugal*; *[3]Center for Health Technology and Services Research (CINTESIS), University of Porto, Faculty of Medicine, Porto, Portugal*; *[4]Centro Hospitalar Universitário do Algarve, Rheumatology, Faro, Portugal*; *[5]Faculdade de Medicina da Universidade do Porto (FMUP), Rheumatology, Porto, Portugal*

Background: Secukinumab is a fully human monoclonal antibody against interleukin-17A, approved in several countries for the treatment of ankylosing spondylitis (AS) and psoriatic arthritis. It is known that some patients benefit from increasing the monthly dose of secukinumab from 150mg, the most commonly used dose, to 300mg. However, the baseline clinical characteristics that differentiate these patients are not yet fully understood.

Objectives: This study aimed to investigate whether there are any variables at the beginning of biologic therapy that might predict a greater probability of having to increase the dose of secukinumab to 300mg in order to obtain a response to treatment.

Methods: This is a retrospective cohort study, including all the spondyloarthritis and psoriatic arthritis patients under secukinumab at our Rheumatology Department and registered in the national database (Reuma.pt).

Demographic, clinical and laboratorial characteristics and disease activity measures were collected from the first visit before the patient began secukinumab. For comparison between the 2 groups, continuous variables were analyzed using Mann-Whitney U and T-tests and categorical variables were analyzed using a Chi-square test. Multivariate regression analyses assessed the impact of selected variables on the need to increase the dose of secukinumab to 300mg.

Results: Thirty-two patients with a mean age of 53±11.96 years were included, 19 (58%) were females and 16 (48.5%) had psoriasis. Twenty-seven (81.8%) patients were under a nonsteroidal anti-inflammatory drug (NSAID), 11(33.3%) were under corticosteroid and 11(33.3%) were under conventional synthetic disease-modifying antirheumatic drug (csDMARD); 25 (75,8%) had previously been treated with a biological disease-modifying antirheumatic drug (bDMARD). The mean patient baseline VAS and physician baseline VAS were 74,39±19,77 and 47,55±23,38, respectively; the mean erythrocyte sedimentation rate (ESR) and C-Reactive Protein (CRP) were 26,33±22,62 mm/hr and 10,81±16,88 mg/dL, respectively; the mean swollen joint count (SJC) and tender joint count (TJC) were 1,30±1,63 and 3,67±3,14, respectively; the mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS) were 6,18±2,06 and 3,41±0,84, respectively; the mean Bath Ankylosing Spondylitis Metrological Index (BASMI) and Bath Ankylosing Spondylitis Functional Index (BASFI) were 4,22±1,58 and 6,28±2,53, respectively; the mean Maastrich Ankylosing Spondylitis Enthesitis Score (MASES) was 2,85±3,23.

Nineteen patients (57.6%) had the dose of secukinumab increased to 300mg. At the baseline visit, the group of patients which had their secukinumab monthly dose increased to 300mg were more frequently men (12 vs 2, p=0.005) and had psoriasis (12 vs 4, p=0.049). On the other hand, these patients also exhibited lower MASES values (2±1.089 VS 4±0.501, p=0.022).

A regression analysis was conducted, estimating the relationships between the outcome binary variable of the monthly dose of secukinumab and the following predictors: gender, psoriasis, MASES value and use of corticosteroid. Female gender (OR 0.070, CI95% 0.005-0.890; p=0.040) and absence of psoriasis (OR 0.104, CI95% 0.011-0.952; p=0.045) were predictors for maintaining secukinumab at a dose of 150mg monthly.

Conclusion: Our data suggest that the most common characteristics of patients in need of increasing the monthly dose of secukinumab from 150 to 300 mg to achieve a better treatment response are: male gender, coexistence of psoriasis and lower MASES value at baseline. The first two variables remained statistically significant in a multivariate model of regression analysis. Nonetheless, we insist it is of paramount importance to conduct larger studies to confirm these findings.

REFERENCES:

[1] Deodhar A, et all. Long-term safety of secukinumab in patients with moderate-to-severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis. Arthritis Res Ther. 2019 May 2;21(1):111.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4001

AB0484 TROUGH LEVELS OF TNF-A INHIBITORS AND THEIR IMMUNOGENICITY IN THE TREATMENT OF RHEUMATIC DISEASES AND INFLAMMATORY BOWEL DISEASES

T. Nuriakhmetova[1], I. K. Valeeva[2], J. Shevnina[3], D. Abdulganieva4. *[1]Kazan State Medical University, Hospital therapy, Kazan, Russian Federation*; *[2]Kazan State Medical University, Central Scientific Research Laboratory, Kazan, Russian Federation*; *[3]Republican clinical hospital n.a. N.A. Semashko, consultative polyclinic, Simferopol, Russian Federation*; *[1]Kazan State Medical University, Hospital therapy, Kazan, Russian Federation*

Background: The features of the underlying immune-mediated disease can affect the efficacy, pharmacokinetics and immunogenicity of the biologic agents, which are among the important predictors of loss of response to TNF-α inhibitors (TNFi).

Objectives: To compare the frequency of TNFi low trough levels and their immunogenicity in the treatment of rheumatic diseases (RD) (ankylosing spondylitis (AS) and rheumatoid arthritis (RA)) and inflammatory bowel diseases (IBD) (Crohn's disease (CD) and ulcerative colitis (UC)).

Methods: Among 120 patients (40 with AS (33.3%), 19 with RA (15.8%), 42 with CD (35%), and 19 with UC (15.8%)), trough level of infliximab (INX) (n=36, 30%), adalimumab (ADM) (n=45, 37.5%) and certolizumab pegol (CZP) (n=39, 32.5%) and the level of anti-drug antibodies (ADAb) were measured in the serum samples drawn directly before the planned drug administration.

Results: Low drug level (below 0.5 μg/mL for INX[1], 4.9 μg/ml for ADM[2], and 20 μg/l for CZP[3]) was found in 54 (45%) patients: in 33 (55.9%) patients with RD and 21 (34.4%) patients with IBD. In the RD group, low drug trough level was observed more often than in IBD (55.9% vs 34.4%, OR 2.418, 95% CI 1.157 to 5.052, p=0.018). Only in UC was there a relationship between the received low dose of the drug (up to 200 mg of INX, 40 mg of ADM, and 200 mg of CZP) and its low level in the serum (p=0.026). Among the additional factors associated with a low TNFi level, lower dose of concomitant therapy at the time of a biologic initiation (66.7% vs 20.8%, OR 7.6, 95% CI 1.388 to 41.617, p=0.033) and the absence of pseudopolyps (78.9% vs 21.1%, p=0.045) were found in IBD, and in case of RD these factors included the age of 30 to 45 years (72.7% vs 41.9%, OR 3.692, 95 % CI 1.136 to 12.0, p=0.026), the absence of comorbidities (58.6% vs 41.4%, OR 3.44, 1.09 to 10.858, p=0.032) and male gender (78.8% vs 50% in women, OR 3.714, 95% CI 1.194 to 11.552, p=0.02).

ADAb were detected in 29 (24.2%) patients (7 to INX (19.4%), 8 (17.8%) to ADM, 14 (35.9%) to CZP), 23 (79.3%) of which had also a concomitant low trough level of the drug. There were no significant differences in the frequency of ADAb formation between the pathologies. In the AS group, antibodies to CZP were detected in all patients with a low level of the biologic, while only in 25% of patients receiving ADM, a low level was associated with the formation of ADAb (p=0.019). In addition, among patients with AS, ADAb were detected only in those patients who did not take prednisone at the time of blood serum sampling (100% vs 37.9%, p=0.037).

Conclusion: Low level of TNFi is more common in RD than in IBD. For each group, the factors associated with a low trough level of TNFi were identified. There were no significant differences in the frequency of ADAb formation between nosologies.

REFERENCES:

[1] Steenholdt C, Bendtzen K, Brynskov J, et al. Cut-off levels and diagnostic accuracy of infliximab trough levels and anti-infliximab antibodies in Crohn's disease. Scand J Gastroenterol 2011; 46: 310–318.

[2] Bartelds GM, Krieckaert CL, Nurmohamed MT, van Schouwenburg PA, Lems WF, Twisk JW, Dijkmans BA, Aarden L, Wolbink GJ. Development of antidrug antibodies against adalimumab and association with disease activity and treatment failure during long-term follow-up. JAMA. 2011;305:1460–1468. doi: 10.1001/jama.2011.406.

[3] Gehin, J.E., Goll, G.L., Warren, D.J. et al. Associations between certolizumab pegol serum levels, anti-drug antibodies and treatment response in patients with inflammatory joint diseases: data from the NOR-DMARD study. Arthritis Res Ther 21, 256 (2019). https://doi.org/10.1186/s13075-019-2009-5

Disclosure of Interests: Tatiana Nuriakhmetova Grant/research support from: A grant to purchase reagents for scientific research from Novartis Pharmaceuticals,

Ildariya Khairullovna Valeeva: None declared., Jana Shevnina: None declared., Diana Abdulganieva: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4006

AB0485 DOES THE REASON OF DISCONTINUATION OF THE FIRST TNF INHIBITOR INFLUENCE THE RESPONSE TO THE SECOND TNF INHIBITOR IN SPONDYLOARTHRITIS? PILOT STUDY FROM THE MOROCCAN RBSMR REGISTRY

T. Fatima Zahrae[1], T. Latifa[2], H. Rkain[2], I. Hmamouchi[2], L. Achemlal[2], I. El Bouchti[3], A. Elmaghraoui[2], I. Ghozlani[4], H. Hassikou[5], T. Harzy[6], L. Ichchou[7], O. Mkinsi[8], R. Niamane[9], R. Bahiri[2], F. Allali[2]. [1]*Faculty of Medicine and Pharmacy of Tangier, Adelmalek Essaadi University, Rheumatology, Tangier, Morocco*; [2]*Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rheumatology, Rabat, Morocco*; [3]*Arrazi University Hospital, Rheumatology, Marrakech, Morocco*; [4]*University Hospital of Agadir, Rheumatology, Agadir, Morocco*; [5]*Military Hospital Moulay Ismail, Hassan II University Hospital, Rheumatology, Meknes, Morocco*; [6]*Hassan II University Hospital, Rheumatology, Fez, Morocco*; [7]*Mohammed VI University Hospital, Rheumatology, Oujda, Morocco*; [8]*Ibn Rochd University Hospital, Rheumatology, Casablanca, Morocco*; [9] *Military Hospital Avicenne, Mohammed VI University Hospital, Rheumatology, Marrakech, Morocco*

Background: In rheumatoid arthritis, studies have shown that the response to a second TNF inhibitor is better if the first TNF inhibitor was stopped for a secondary failure or adverse event compared to a primary failure [1,2]. However, few studies have provided evidence regarding the response to a second TNF inhibitor based on the reason for discontinuation of the first TNF inhibitor in patients with a diagnostic of spondyloarthritis (SpA).
Objectives: To evaluate the efficacy of the 2nd TNF inhibitor in real life from a cohort of patients with SpA from the Moroccan registry of biological therapies in rheumatic diseases (RBSMR Registry), according to the reason for discontinuation of the 1st TNF inhibitor.
Methods: We have included from the RBSMR Registry any patient with a diagnosis of SpA starting a 2nd TNF inhibitor on inclusion in the registry or during the 1st year of follow-up. A descriptive study was conducted by measuring the therapeutic maintenance of the 2nd TNF inhibitor as well as the disease activity in different groups of patients according to the reason for stopping the first TNF inhibitor: stopping for ineffectiveness, side effect or non-availability of the drug.
Results: Of the total 194 patients with SpA included in the RBSMR registry, 40 patients were on their 2nd TNF inhibitor at one year follow-up. The mean age of the patients was 43.6 ± 15.1 with a male predominance (57.5%) and a mean of disease duration of 13.75±6.95 years. At 1 year, treatment was maintained in 72.5% of all patients: 100% after ineffectiveness, 82% after discontinuation for side effects and 52.9% for unavailability of the first TNF inhibitor. Moderate disease activity as defined by an Ankylosing Spondylitis Disease Activity Score using ASDAS-CRP <2.1 was achieved at 1 year in 75%, 64.7% and 52.9% respectively in patients who stopped their first TNF inhibitor for side effects, ineffectiveness or unavailability of treatment.
Conclusion: This pilot study gives us a small insight into the fate and efficacy of the 2nd TNF inhibitor based on the reason for discontinuation of the first. The follow-up data at 2 and 3 years will allow us to include more patients and thus be able to do a real statistical study with a comparison between the different groups.
REFERENCES:

[1] Remy A, Avouac J, Gossec L, Combe B. Clinical relevance of switching to a second tumour necrosis factor-α inhibitor after discontinuation of a first tumour necrosis factor-α inhibitor in rheumatoid arthritis: a systematic literature review and meta-analysis. Clin Exp Rheumatol. 2011;29:96–103.
[2] Chatzidionysiou K, Askling J, Eriksson J, Kristensen LE, van Vollenhoven R, ARTIS group. Effectiveness of TNF inhibitor switch in RA: results from the national Swedish register. Ann Rheum Dis. 2015;74:890–6.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4104

AB0486 ONE-YEAR DIRECT COSTS OF BIOLOGICAL THERAPY IN ANKYLOSING SPONDYLITIS AND ITS PREDICTIVE FACTORS: DATA FROM THE MOROCCAN RBSMR REGISTRY

S. Bahloul[1], H. Rkain[2], S. Fellous[2], S. Ahid[3], R. Abouqal[4], T. Latifa[2], I. Hmamouchi[5], L. Achemlal[6], I. El Bouchti[7], A. EL Maghraoui[6], I. Ghozlani[8], H. Hassikou[9], T. Harzy[10], I. Linda[11], O. Mkinsi[12], R. Niamane[13], R. Bahiri[2], F. Allali[2]. [1]*El Ayachi Hospital, Rheumatology, Salé, Morocco*; [2]*El Ayachi Hospital, Rheumatology, salé, Morocco*; [3]*Mohamed 5 university, Pharmaco economic - pharmaco epidemology Laboratory, RABAT, Morocco*; [4]*Mohamed 5 university, laboratory of biostatiscal clinical and epidemiological research, RABAT, Morocco*; [5]*Provincial hospital of temara, Rheumatology, Temara, Morocco*; [6]*military hospital Mohamed 5, Rheumatology, RABAT, Morocco*; [7]*Razi unvesity Hospital, Rheumatology, Marrakech, Morocco*; [8]*university hospital, Rheumatology, agadir, Morocco*; [9]*military hospital moulay ismail, Rheumatology, Meknes, Morocco*; [10]*Hassan II university hospital, Rheumatology, Fes, Morocco*; [11]*Mohamed 5 university, Rheumatology, OUJDA, Morocco*; [12]*Ibn Rochd university Hospital, Rheumatology, Casablanca, Morocco*; [13]*military hospital avicenne, Rheumatology, Marrakech, Morocco*

Background: NA
Objectives: To estimate the annual direct costs of biological therapies in Spondyloarthropathies (SpA) and to establish possible factors associated with those costs.
Methods: The main data source was the Moroccan registry of biological therapies in rheumatic diseases (RBSMR). We included SpA patients with available 1-year data. Variables related to socioeconomic status, disease and biological therapy were collected. Differences in costs across groups were tested by Mann–Whitney and Kruskal–Wallis tests. Correlations analysis was performed in search of factors associated with high costs.
Results: We included 89 SpA patients. The mean age was 40.6± 13.6 years, with male predominance 68.9 %. Patients received one of the following therapies: TNF-blockers (n =79), Biosimilar of TNF-blockers (n =8) and Il17-blockers (n =2). Median one-year biologic costs per patient were 9 569, 39 €. The total annual of biotherapies in AS patients was 851 675, 98 €.

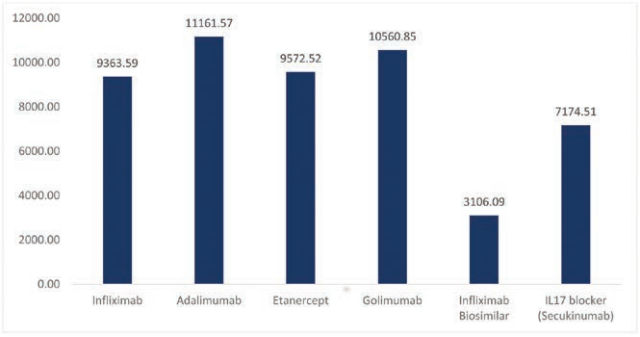


Figure 1 Annual mean drug costs per treated patient (€: Euro)

The costs are presented in Euro using an exchange rate of (1 Moroccan Dirham = 0.091Euro).
TNF-blockers constituted 95 % of the total annual budget. Biosimilar of TNF-blockers and Il17-blockers represented 3 % and 2 % of this overall budget, respectively. Although the costs were not significantly different in terms of gender or level of study, the insurance type significantly affected the cost estimation.
No correlation was found between the annual direct costs of biotherapies and body mass index nor with BASFI or BASDAI.
Conclusion: In Morocco, a developing country, the annual direct costs of biological therapies are high in AS patients. Our results may contribute to the development of strategies for better governance of these costs.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4117

Spondyloarthritis - clinical aspects (other than treatment)

AB0487 HEPSIDINE LEVEL IN PATIENTS WITH ANKYLOSING SPONDYLITIS, RELATIONSHIP WITH HEMOPOESIS AND FERROKINETICS

O. Zviahina[1], S. Shevchuk[1]. [1]*National Pirogov Memorial Medical University, Vinnytsya, Internal Medicine Chair # 2, Vinnytsya, Ukraine*

Background: Hypoferimia, as a manifestation of systemic inflammation, is quite common in patients with ankylosing spondylitis (AS). Anemic syndrome can be represented by anemia of chronic disease (ACD), iron deficiency anemia (IDA) and their combination. Its frequency of occurrences ranges from 18.5 to 45.8 %. The discovery of the hormone hepcidin in 2001 changed the perception of iron metabolism disorders and demonstrated its association with the inflammatory component. Over the last decade, scientific databases have accumulated a lot

of information about hepcidin and its role in the development of anemia and the response to inflammation. However, in the context of the AS, such data are contradictory and therefore need further study.

Objectives: To determine the level of hepcidin in patients with ankylosing spondylitis and to assess its relationship with hematopoiesis and ferrokinetics.

Methods: The hepcidin levels of 76 patients with ankylosing spondylitis (13 women and 63 men with a mean age of 43.67±0.97 years). The diagnosis of AS was made according to the New York modified criteria of 1984. All patients were divided into three groups: without anemia (n=47), with anemia (n=29) and the control group, representative by age and sex (n=26). According to the percentile analysis, all patients were divided into a group with an optimal <25 ng/ml, extremely high - 25-35 ng/ml and a high level of hepcidin > 35 ng/ml. In addition to hepcidin, hematopoiesis and ferrokinetic parameters were measured in each patient: hemoglobin (Hb), erythrocyte, MCV, serum iron, total serum iron-binding capacity (TIBC), serum ferritin, transferrin saturation (TS). Statistical processing of the obtained results was performed with the use of statistical software package "Microsoft Office Excel 2007".

Results: When conducting a percentile comparison in 95 % of people in the control group, the level of hepcidin was in the range of 17.97-38.8 ng/ml (P_5 - P_{95}), and in patients with AS in 95 % - 14.62-87.38 ng/ml. At P_{95}, the level of hepcidin in patients with AS was 2.3 times higher than in P_{95} control group. Comparing the mean values of hepcidin, a significant difference was found between the group of patients without anemia, where it was 36.08±2.57 ng/ml and the group of patients with anemia, where the level of hepcidin was 51.77±4.62 ng/ml. The lowest level of hepcidin was in patients with IDA (35.8 ±7.50 ng/ml), and the highest (62.78±5.94 ng/ml) - among patients with ACD. The group of patients with ACD and iron deficiency, according to the levels of hepcidin (48.53±9.50 ng/ml) took an intermediate place.

In terms of hematopoiesis and ferrokinetics, the level of hemoglobin and erythrocytes did not differ significantly between the groups of optimal, extremely high and high levels of hepcidin. According to the levels of serum iron, TS and ferritin in the group of patients with anemia, a significant association with hepcidin was established (with increasing levels of hepcidin, the values of serum iron, TS and ferritin also increased). In contrast,sTfR levels were the highest in the group with optimal hepcidin levels (6.02±0.71 mg/l) and decreased to 4.88±0.64 mg/l in the group with high hepcidin levels. Such changes in hematopoiesis and ferrokinetics were explained by the accumulation of mostly people with symptoms of ACD in the group with high levels of hepcidin, and the group with optimal levels of hepcidin consisted mainly of patients with IDA.

Conclusion: Patients with AS have elevated serum hepcidin levels, it is higher in individuals with anemic syndrome than in patients without anemia and is associated with serum iron, TS and ferritin levels.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.382

AB0488 SPONDYLOARTHRITIS DISEASE BURDEN AS PERCEIVED BY PATIENTS: BASELINE PATIENT-REPORTED OUTCOME DATA FROM THE ITALIAN PROSPECTIVE SIRENA STUDY

R. Foti[1], G. Cardinale[2], L. Costa[3], F. Franceschini[4], F. Ciccia[5], A. Marchesoni[6], G. Guggino[7], M. Rossini[8], E. Lubrano DI Scorpaniello[9], B. Frediani[10], M. S. Chimenti[11], G. Bianchi[12], G. Galfo[13], S. Marelli[14], E. Favalli[15]on behalf of SIRENA Study Group. *[1]Azienda Ospedaliero Universitaria Policlinico Vittorio Emanuele, U.O. Reumatologia, Catania, Italy*; *[2]Distretto nr. 1 ULSS6 Euganea, U.O.S. Reumatologia, Padova, Italy*; *[3]Università degli Studi di Napoli Federico II, U.O.C. Reumatologia, Dipartimento di Medicina Clinica e Chirurgia, Naples, Italy*; *[4]ASST Spedali Civili, Università di Brescia, U.O.C. Reumatologia and Immunologia Clinica, Dept of Clinical and Experimental Sciences, Brescia, Italy*; *[5]Università della Campania L Vanvitelli, U.O.C. Reumatologia, Dipartimento di Medicina di Precisione, Naples, Italy*; *[6]ASST Centro Specialistico Ortopedico Traumatologico Gaetano Pini – CTO, S.C. Day Hospital di Reumatologia, Milan, Italy*; *[7]AOU Policlinico Paolo Giaccone e Università degli Studi di Palermo, U.O. Reumatologia, Palermo, Italy*; *[8]Azienda Ospedaliera Universitaria Integrata, U.O.C. Reumatologia, Verona, Italy*; *[9]Università degli Studi del Molise, U.O.S.V.D. Reumatologia, Dipartimento di Medicina e Scienze della Salute, Campobasso, Italy*; *[10]Azienda Ospedaliera Universitaria Senese, U.O.C. Reumatologia, Siena, Italy*; *[11]Università di Roma Tor Vergata, Reumatologia, Allergologia e Immunologia Clinica, Dipartimento di Medicina dei Sistemi, Rome, Italy*; *[12]ASL3 Genova, S.C. Reumatologia, Genova, Italy*; *[13]Azienda Provinciale Sanitaria di Ragusa, U.O. Reumatologia e Medicina Generale, Lungodegenza Ospedale Busacca, Scicli (RG), Italy*; *[14]Janssen, Medical Affairs Department, Immunology, Cologno Monzese (MI), Italy*; *[15]ASST Centro Specialistico Ortopedico Traumatologico Gaetano Pini – CTO, S.C. Reumatologia, Milan, Italy*

Background: Previous studies have compared Patient-Reported Outcomes (PROs) in Spondyloarthritis (SpA); a recent one has found similarity in Psoriatic Arthritis (PsA) and axial patients[1].

Objectives: To describe PROs at SpA diagnosis (new or confirmed), by type of SpA and by gender.

Methods: SIRENA is an Italian, prospective Registry of SpA patients diagnosed according to ASAS criteria and naïve to any DMARDs. At inclusion, patients were classified as predominant axial (AxSpA) or mainly peripheral (pSpA). PROs showed in the Table 1 were collected and analysed descriptively.

Table 1. PhGA and PROs at diagnosis*

	AxSpA*			pSpA		
	All	**Women**	**Men**	**All**	**Women**	**Men**
	(n=123)	**(n=64)**	**(n=58)**	**(n=227)**	**(n=109)**	**(n=118)**
PhGA, n	115	60	54	222	105	117
mean (SD)	50.2 (28.6)	54.8 (26.7)	45.0 (30.1)	45.4 (25.9)	49.9 (25.6)	41.3 (25.6)
median (min, max)	52.0 (0-100)	62.0 (0-100)	43.5 (0-100)	48.5 (0-100)	50.0 (1.0-100)	40.0 (0-95.0)
PtGA, n	112	59	52	209	102	107
mean (SD)	56.4 (27.8)	61.5 (25.8)	50.3 (29.2)	50.3 (26.2)	56.4 (23.1)	44.5 (27.7)
median (min, max)	63.0 (0-100)	70.0 (2.0-100)	50.0 (0-100)	50.0 (0-100)	58.5 (7.0-100)	47.0 (0-100)
Pain VAS score, n	113	60	52	207	101	106
mean (SD)	56.7 (28.3)	61.1 (26.6)	50.6 (29.1)	51.9 (26.8)	57.4 (25.3)	46.8 (27.3)
median (min, max)	60.0 (0-100)	69.5 (2.0-100)	50.0 (0-100)	53.0 (0-100)	61.0 (0-100)	48.5 (0-100)
Sleep VAS score, n	113	60	52	211	103	108
mean (SD)	55.3 (29.3)	57.4 (29.5)	52.3 (29.2)	44.0 (30.1)	50.4 (29.8)	37.9 (29.2)
median (min, max)	59.0 (0-100)	61.5 (0-100)	53.0 (0-100)	44.0 (0-100)	53.0 (0-100)	34.0 (0-100)
BASFI, n	110	58	51	133	65	68
mean (SD)	4.6 (2.8)	5.2 (2.6)	3.9 (2.8)	3.5 (2.6)	4.0 (2.6)	3.1 (2.4)
median (min, max)	5.1 (0-9.7)	5.8 (0-9.4)	3.6 (0-9.6)	2.9 (0-10.0)	3.9 (0-10.0)	2.45 (0-8.9)
BASDAI, n	112	59	52	139	70	69
mean (SD)	5.2 (2.4)	5.8 (2.3)	4.5 (2.3)	5.2 (2.3)	5.8 (2.1)	4.6 (2.3)
median (min, max)	5.5 (0-9.3)	6.2 (0-9.3)	4.5 (0.3-9.2)	5.5 (0.2-10.0)	6.1 (1.0-10.0)	4.8 (0.2-9.2)
HAQ-DI score, n	109	58	50	203	99	104
mean (SD)	0.9 (0.7)	1.1 (0.7)	0.6 (0.6)	0.7 (0.7)	0.9 (0.7)	0.6 (0.6)
median (min, max)	0.8 (0.0-2.5)	1.1 (0-2.5)	0.5 (0-2.3)	0.6 (0.0-2.8)	0.8 (0-2.8)	0.4 (0-2.6)
WPAI						
% work time missed, n	49	19	30	107	45	62
mean (SD)	7.3 (21.4)	4.2 (9.5)	9.2 (26.3)	8.8 (24.7)	8.6 (25.6)	8.9 (24.3)
median (min, max)	0 (0-100)	0 (0-35.1)	0 (0-100)	0 (0-100)	0 (0-100)	0 (0-100)
% impairment at work, n	67	33	34	134	61	73
mean (SD)	48.2 (31.9)	58.5 (26.6)	38.2 (33.7)	39.7 (31.4)	45.4 (30.9)	34.9 (31.2)
median (min, max)	50.0 (0-100)	60.0 (0-100)	25.0 (0-100)	40.0 (0-100)	50.0 (0-100)	30.0 (0-100)
% overall work impairment, n	48	19	29	106	45	61
mean (SD)	44.1 (33.0)	52.4 (27.9)	38.7 (35.3)	40.1 (33.0)	45.1 (33.1)	36.4 (32.7)
median (min, max)	45.0 (0-100)	60.0 (0-100)	20.0 (0-100)	40.0 (0-100)	50.0 (0-100)	30.0 (0-100)
% activity impairment, n	100	53	46	183	93	90
mean (SD)	56.7 (28.6)	63.4 (23.9)	48.0 (31.0)	48.5 (30.3)	55.3 (28.7)	41.4 (30.4)
median (min, max)	60.0 (0-100)	70.0 (0-100)	50.0 (0-100)	50.0 (0-100)	60.0 (0-100)	40.0 (0-100)

* The sum does not add up to the total because of some missing values.

Results: From 23 sites, 123 AxSpA and 227 pSpA patients were analysed. Diagnosis was new in 58% of AxSpA and 77% of pSpA. 85.5% of the pSpA had PsA, while in AxSpA the most frequent type was Ankylosing Spondylitis (48.8%). Time from symptom onset to diagnosis was higher in AxSpA than in pSpA (median 36 vs 24 months, respectively). At inclusion, composite disease activity measures showed high disease activity for AxSpA (mean ASDAS-CRP 3.1) and moderate disease activity for pSpA (mean DAS28 3.6; mean DAPSA 22.5). AxSpA patients had numerically worse values than pSpA in all the PROs collected, except for BASDAI score that was similar (mean 5.2). For both AxSpA and pSpA, all PROs were worse in women than men, except

for the % of work time missed. PtGA scores were higher than PhGA, in each group and gender.
Conclusion: At diagnosis, SpA patients perceive a slightly higher disease burden than assessed by Physicians. For PROs other than BASDAI, AxSpA reported a worse impact than pSpA. Overall, women showed a higher disease impact than men.
References: [1]Michelsen B. et al. PLoS ONE 2015; 10(4): e0123582.
Disclosure of Interests: Rosario Foti Speakers bureau: Speaker bureau honoraria from Eli Lilly, Sanofi, MSD, Janssen, AbbVie, Bristol-Myers Squibb, Celgene, Roche, Consultant of: Consultancy fees from Eli Lilly, Sanofi, MSD, Janssen, AbbVie, BMS, Celgene, Roche, Gabriella Cardinale: None declared., Luisa Costa: None declared., Franco Franceschini: None declared., Francesco Ciccia Speakers bureau: Speaker bureau honoraria from AbbVie, Abiogen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer, Novartis, Roche, Consultant of: Consultancy fees from Novartis, Pfizer, Janssen, Eli Lilly, Roche, Celgene, Grant/research support from: Grant/research support from Pfizer, Novartis, Celgene, Janssen, Roche, Antonio Marchesoni: None declared., Giuliana Guggino Speakers bureau: Speaker bureau honoraria from Celgene, Sandoz, Pfizer, Grant/research support from: Grant/research support from Pfizer, Celgene, Maurizio Rossini: None declared., Ennio Lubrano Di Scorpaniello: None declared., Bruno Frediani: None declared., Maria Sole Chimenti: None declared., Gerolamo Bianchi: None declared., Giuseppe Galfo: None declared., Silvia Marelli Employee of: Employee of Janssen-Cilag SpA Italy, Ennio Favalli Speakers bureau: Consulting fees and/or speaking engagements from AbbVie, Bristol-Myers Squibb, Lilly, Merck Sharp & Dohme, Pfizer, Galapagos, Sanofi-Genzyme, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.624

AB0489 CORRELATION BETWEEN DISEASE ACTIVITY AND SERUM TNF-ALPHA LEVELS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

K. Kraev[1,2], M. Geneva-Popova[1,3], S. Popova[1,3]. [1]*Medical University Plovdiv, Propedeutics of Internal Diseases, Plovdiv, Bulgaria*; [2]*Multiprofile Hospital for Active Treatment "Kaspela", Rheumatology, Plovdiv, Bulgaria*; [3]*Multiprofile Hospital for Active Treatment "St.George", Rheumatology, Plovdiv, Bulgaria*

Background: Ankylosing spondylitis (AS) is an immune-mediated rheumatic disease, it belongs to the spectrum of the axial spondyloarthritis. Several elements are important for the pathogenesis of AS - they include interactions in the context of a specific genetic origin between the intestinal microbiome, innate immunity, lymphoid cells and anatomical structures, which are the entheses of the axial skeleton and peripheral joints. The main mediators of the inflammatory process are TNF - α, IL-17 and IL-17A.
Objectives: To study the level of TNF-alpha in the serum of patients with ankylosing spondylitis and to assess its relationship with the indices of disease activity before starting therapy with TNF-alpha blockers and in the dynamics after initiation of treatment.
Methods: The present study included 50 patients with ankylosing spondylitis and 31 healthy controls similar in age, sex, and BMI. Clinical and non-clinical methods of examination and evaluation were used for proper assessment and follow-up of patients. The disease activity indices that were used were BASDAI and ASDAS. Statistical analysis was performed with the IBM SPSS program, v.24., To prove the relationship between the level of TNF-alpha in the serum of patients and disease activity, a correlation analysis of Spearman Rho was used.
Results: The level of TNF-α in patients with AS was highest before treatment initiation with biologics, 89.77 ± 36.89 pg / ml, and was significantly higher than that of healthy controls. At the next visit, the TNF-α level decreased to 27.59 ± 23.88 pg / ml, the difference being significant from baseline. 24 months after initiation of treatment with biological therapy average level of TNF-α in patients with AS did not differ reliably from its levels in 6 and 12 month after initiation of treatment, respectively, 22.36 ± 22.38 pg/ml, 19,29 ± 21.07 pg/ml. The level of this cytokine significantly correlates with the activity of the disease, measured by the activity indices BASDAI, ASDAS.
Conclusion: The level of the pro-inflammatory cytokine TNF-alpha is significantly higher in patients with ankylosing spondylitis and significantly correlates with the disease activity in them, measured by the respective indices (BASDAI, ASDAS).
REFERENCES:
[1] Arends S., N. Lebbink, A. Spoorenberg et al., "The formation of autoantibodies and antibodies to TNF-α blocking agents in relation to clinical response in patients with ankylosing spondylitis", Clin Exp Rheumatol, 2010, 28: 661- 668.
[2] Bal A., E. Unlu, G. Bahar et al., "Comparison of serum IL-1 beta, sIL-2R, IL-6, and TNF-alpha levels with disease activity parameters in ankylosing spondylitis." Clin Rheumatol, 2007, 26: 211–215.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.931

AB0490 IMPACT OF SPONDYLOARTHRITIS ON WORK PRODUCTIVITY: A REAL LIFE STUDY

M. Ben Majdouba[1], S. Boussaid[1], S. Rekik[1], S. Jemmali[1], H. Ajlani[1], H. Sahli[1], M. Elleuch[1]. [1]*La Rabta hospital, Rheumatology, Tunis, Tunisia*

Background: Work productivity of patients with spondyloarthritis is frequently affected by their disease.
Objectives: We aim to identify disease-related factors associated with poor work productivity in patients with spondyloarthritis.
Methods: A cross-sectional study was performed in patients with spondyloarthritis. Data on disease characteristics were collected as well as specific indices: Visual analogue scale (VAS) for fatigue and pain, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score with CRP (ASDAS-CRP), Bath Ankylosing Spondylitis Functionnel Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI). EuroQol-5D (EQ5D) was used to assess health-related quality of life. Work productivity was assessed by the Work Productivity and Activity Impairment scale (WPAI:SpA). Factors associated with presenteeism, absenteeism and work productivity loss were evaluated.
Results: One hundred patients were enrolled (73 men and 27 women); mean age was 43.68 ± 10.3 years. Fifty nine percent of patients were employed, 26% were off work and 15% were retired of which 8% were in early retirement. Sixty seven percent of patients had ankylosing spondylitis, 17% had rheumatism associated with inflammatory bowel disease and 16% had psoriatic rheumatism. The average disease duration was 12.24 ± 8.73 years. Mean age at onset was 33.2 ± 10 years [18-59]. The average diagnostic delay was 2.41 ± 3 years; it was more than five years in 17% of cases. Sacroiliac pain has been noted in 69 patients, lumbar or cervical stiffness in 78 patients and peripheral joint involvement in 18 cases. Thirty one percent of patients had hip joint involvement and 49% had extra-articular manifestation. Fifty percent had inflammatory biological syndrome, 63% were treated with anti-TNFα and 58% needed symptomatic treatment regularly. The mean fatigue and pain VAS was respectively 5.58 ± 2.5 and 5.56 ± 2.9. The mean BASDAI was 4.4 ± 2.4, the average BASFI was 4.6 ± 2.7 and the average ASDAS-CRP was 2.77 ± 1.18. The mean BASMI was 4.4 ± 2.8. The mean EQ5D score was 0.485 ± 0.378. Among employed patients, mean absenteeism, presenteeism and work productivity loss was 21.8 ± 33.13%, 42 ± 32% and 46.5 ± 35.31%, respectively. These work outcomes were correlated to diagnostic delay ≥ 2 years ($p<0.03$), peripheral joint involvement ($p=0.006$), psoriasis ($p=0.02$), inflammatory biological syndrome ($p<0.001$), need of symptomatic treatment ($p=0.001$), fatigue and pain VAS ≥ 4 ($p<0.001$), BASDAI ≥ 4 ($p<0.001$), ASDAS-CRP ≥ 2.1 ($p<0.001$), BASFI ≥ 4 ($p<0.001$), BASMI ≥ 4 ($p=0.002$) and low EQ5D score ($p<0.001$). Work productivity loss was in addition correlated to age at onset < 25 years ($p=0.03$).
Conclusion: Active disease, reduced physical function and poorer quality of life are associated with reduced work productivity. Early diagnosis and good disease management especially fatigue and pain can potentially improve work outcomes in patients with spondyloarthritis.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1079

AB0491 THE IMPORTANCE OF MUSCULOSKELETAL SYMPTOM QUESTIONING IN INFLAMMATORY BOWEL DISEASES

B. Farisoğulları[1], O. Keskin[2], B. Usta[3], G. K. Yardımcı[1], E. Parlak[2], T. Kav[2], U. Kalyoncu[1], O. Karadag[1]. [1]*Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; [2]*Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Gastroenterology, Ankara, Turkey*; [3]*Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Ankara, Turkey*

Background: Spondyloarthritis (SpA) occurs in up to 13% of patients with inflammatory bowel disease (IBD) (1). Early diagnosis and treatment of SpA in IBD patients prevents irreversible musculoskeletal diseases.
Objectives: The aim of this study is to emphasize the importance of questioning musculoskeletal symptoms in patients with IBD.
Methods: In the Hacettepe University Gastroenterology Clinic, patients with IBD were questioned for musculoskeletal symptoms between March 2019 and September 2020. For this purpose, a validated DETAIL questionnaire (2) consisting of six questions was asked (1. Have you ever had a finger or a toe and/or another joint swollen and painful for no apparent reason? 2. Occasionally, has an entire finger or toe becomes swollen, making it look like a 'sausage'? 3. Have you had pain in your heels? 4. Have you ever had back pain lasting at least 3 months that was not injury related? 5. Do you have low back pain in the morning and/or after resting that improves with exercise? 6. Do you wake up at night because of low back pain?). Patients with at least 1 positive out of 6 questions were consulted in the rheumatology clinic, and patients were evaluated for SpA by physical examination, laboratory, and imaging. Demographic and clinical characteristics of IBD patients with and without SpA were compared.

Results: 217 IBD patients were included in the study. Twenty patients with previously known rheumatologic diseases were excluded from the study. 49 (24%) of the remaining 197 patients had a positive answer to at least one question in the DETAIL query. 39 (20%) of these patients were evaluated in the rheumatology clinic, and 16 (8.1%) of them were diagnosed with SpA (spondylitis: 9, peripheral arthritis: 7) (Figure 1). There were no significant differences in terms of age, gender, IBD type, duration of IBD, current treatment, fibromyalgia syndrome (FMS) and depression according to Beck depression inventory between patients with IBD with and without SpA (Table 1).

Table 1. Clinical, demographic characteristics of the IBD patients according to SpA.

	IBD with SpA n= 16	IBD without SpA n= 23	p
Age, years, median (IQR)	47.03 (27.4)	35.9 (14.1)	0.052
Female, n (%)	8 (50)	17 (74)	0.12
IBD disease duration, months, median (IQR)	66.7 (70.7)	44.8 (70)	0.26
IBD type, n (%)			
CD	6 (37)	11 (48)	0.19
UC	9 (56)	12 (52)	
IC	1 (7)		
Smoking (ever), n (%)	10 (62.5)	11 (48)	0.37
HLA-B27 positivity, n (%)	2 (12.5)	1 (4.3)	0.57
Current medication, n (%)			
- Steroid (oral and/or topical)	6 (37.5)	5 (21.7)	0.31
- 5-ASA	11 (68.8)	14 (61)	0.61
- Immunosuppressants (AZA, MTX)	6 (37.5)	8 (34.8)	0.86
- bDMARD	2 (12.5)	4 (17.4)	1
FMS, n (%)	1 (6.7)	3 (13)	1
Beck depression Inventory, level of depression, n (%)			
-minimal	1 (9)	5 (22)	0.13
-mild	8 (73)	7 (30)	
-moderate	2 (18)	9 (39)	
-severe	0	2 (9)	

Harvey-Bradshaw Index for CD disease activity and Mayo score for UC disease activity were used.**SD:** standard deviation, **IQR:** inter-quartile range**IBD:** inflammatory bowel disease; **SpA:** Spondyloarthritis**, bDMARD:** biological disease modifying anti-rheumatic drug**, CD:** Crohn's disease, **UC:** Ulcerative colitis, **IC:** indeterminate colitis; **HBI:** Harvey-Bradshaw Index **ASA:** 5-aminosalicylic acid; **AZA:** azathioprine; **MTX:** methotrexate; **FMS:** Fibromyalgia syndrome

Conclusion: By questioning the musculoskeletal system in IBD patients, 20% of the patients were evaluated in the rheumatology department, and nearly half of these patients (8%) were diagnosed with SpA. The findings point to the importance of musculoskeletal symptom questioning in routine outpatient clinic control in IBD patients.

REFERENCES:

[1] Karreman MC et al. The prevalence and incidence of axial and peripheral spondyloarthritis in inflammatory bowel disease: a systematic review and meta-analysis. Journal of Crohn's and Colitis, 2017, 11.5: 631-642.

[2] Di Carlo M et al. The DETection of Arthritis in Inflammatory boweL diseases (DETAIL) questionnaire: development and preliminary testing of a new tool to screen patients with inflammatory bowel disease for the presence of spondyloarthritis. Clinical rheumatology, 2018, 37.4: 1037-1044.

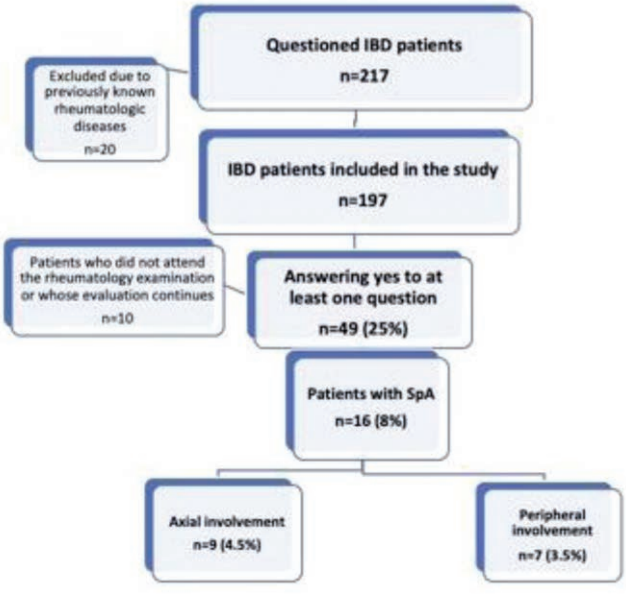


Figure 1 Flow chart of IBD patients in the study

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1232

AB0492 DETERMINING FACTORS RELATED TO POOR QUALITY OF LIFE IN PATIENTS WITH SPONDYLOARTHRITIS: A REAL LIFE STUDY

M. Ben Majdouba[1], S. Boussaid[1], S. Rekik[1], S. Jemmali[1], H. Ajlani[1], H. Sahli[1], M. Elleuch[1]. [1]*La Rabta hospital, Rheumatology, Tunis, Tunisia*

Background: When treating people with spondyloarthritis (SA), rheumatologists are focused on reducing disease activity based on activity measurement scores; but there may be other factors not directly captured by these tools, which impact on quality of life.

Objectives: We aim to identify factors associated with poor quality of life in patients with spondyloarthritis.

Methods: A cross-sectional study was performed in 100 patients with spondyloarthritis. Data on sociodemographic and disease characteristics were collected as well as specific scores: Visual analogue scale (VAS) for fatigue and pain, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score with CRP (ASDAS-CRP), Bath Ankylosing Spondylitis Functionnel Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI). EuroQol-5D (EQ5D) was used to assess health-related quality of life.

Results: A total of 100 Patients were enrolled (73 men and 27 women); the mean age was 43.68 ± 10.3 years. Thirteen percent of patients had high level of education (> 12 years), 47% had BMI ≥ 25 and 47% were smoking. Sixty seven percent of patients had ankylosing spondylitis, 17% had rheumatism associated with inflammatory bowel disease and 16% had psoriatic rheumatism. The average disease duration was 12.24 ± 8.73 years. Mean age at onset was 33.2 ± 10 years. The average diagnostic delay was 2.41 ± 3 years. Sacroiliac pain has been noted in 69 patients, lumbar or cervical stiffness in 78 patients and peripheral joint involvement in 18 cases. Thirty one percent of patients had hip joint involvement and 49% had extra-articular manifestation. Fifty percent had inflammatory biological syndrome, 63% were treated with anti-TNFα and 58% needed symptomatic treatment regularly. The mean fatigue and pain VAS was respectively 5.58 ± 2.5 and 5.56 ± 2.9. The mean BASDAI was 4.4 ± 2.4, the average BASFI was 4.6 ± 2.7 and the average ASDAS-CRP was 2.77 ± 1.18. The mean BASMI was 4.4 ± 2.8. EQ5D questionnaire showed that: 37 patients had no problems with mobility, 61 had some problems and two had extreme problems; 39 patients had no problems with self-care, 55 had some problems and six had extreme problems; 35 patients had no problems with performing usual activities, 60 had some problems and five had extreme problems; 13 patients had no pain or discomfort, 61 had moderate pain or discomfort and 26 had important pain or discomfort; 42 patients had no anxiety or depression, 46 had moderate anxiety or depression and 12 had extreme anxiety or depression. The mean EQ5D score was 0.485 ± 0.378 [-0,448-1] and the mean general health EQ5D VAS was 59 ± 25% [7-100]. Poor quality of life was associated with smoking (p=0.03), physical inactivity (p<0.001), cervical and lumbar stiffness (p=0.001), peripheral joint involvement (p=0.006), inflammatory biological syndrome (p<0.001), need of symptomatic treatment (p<0.001), BASDAI > 4 (p<0.001), ASDAS > 2.1 (p<0.001), BASFI > 4 (p<0.001) and BASMI > 4 (p<0.001).

Conclusion: Active disease and reduced physical function are the main causes of poor quality of life in patients with spondyloarthritis. Good disease management, smoking cessation and encouragement of physical activity can potentially improve patients' quality of life.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1269

AB0493 WHAT IS THE DIAGNOSTIC VALUE OF IMPAIRED SPINAL MOBILITY MEASUREMENTS IN INFLAMMATORY BACK PAIN PATIENTS? DATA FROM THE DESIR COHORT

C. Lukas[1,2], G. Khoury[3], M. A. D'agostino[4,5], B. Combe[1,2], J. Morel[2,6]. [1]*University Montpellier, IDESP, Montpellier, France*; [2]*University hospital Montpellier, Rheumatology, Montpellier, France*; [3]*University hospital Montpellier, rheumatology, Montpellier, France*; [4]*University Paris Ouest-Versailles-Saint-Quentin-en-Yvelines, Rheumatology, Boulogne Billancourt, France*; [5]*Ambroise Pare Hospital, Rheumatology, Boulogne Billancourt, France*; [6]*University Montpellier, IGMM, Montpellier, France*

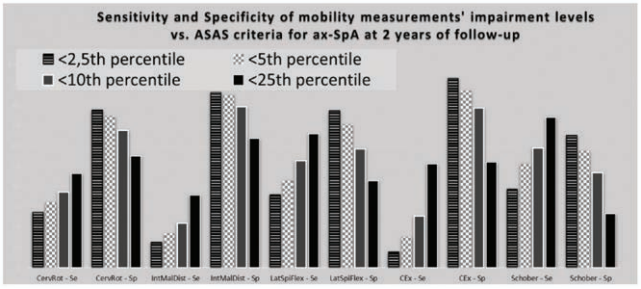
Background: The diagnostic process in a patient with early inflammatory back pain suggestive of axial spondyloarthritis (ax-SpA) requires assessment and integration of multiple aspects, including clinical examination, biological measurements and radiologic assessments. Among the physical examination features, alteration of spinal mobility is often observed in ax-SpA. However,

whether mobility impairment might really increase diagnostic likelihood, and which of the measurements made have relevant diagnostic value remains unknown.

Objectives: To describe the frequency and severity of mobility impairment in multiple traditional measurements in patients suspect of early ax-SpA at initial assessment time, and to analyze their individual diagnostic performances in reference to usual classification criteria applied after 2 years of follow-up.

Methods: Data from the DESIR cohort, which included patients aged 18-50 with inflammatory back pain lasting for 3 months to 3 years and a clinical suspicion of ax-SpA diagnosis were used. Baseline measurements of Schober's test (Schober), chest expansion (CEx), lateral spinal flexion (LatSpiFlex), cervical rotation (CervRot) and intermalleolar distance (IntMalDist) collected at baseline were classified according to reference data from the general population adjusted for age and -when appropriate- for height. Cutoffs were defined as above 2.5th, 5th, 10th and 25th percentiles. With ASAS classification for ax-SpA applied at 2 years follow-up visit as external reference, diagnostic performances (Sensitivity [Se], Specificity [Sp], Positive [PPV] and Negative [NPV] Predictive Values) were calculated.

Results: Complete data were available for 575 patients (of whom 377 (66%) fulfilled the ASAS criteria at 2 years). Schober, CEx, LatSpiFlex, CervRot and IntMalDist were above 5th percentile in respectively 278 (48%), 82 (14%), 220 (38%) and 93 (16%) patients. None of the measurements showed a clinically relevant compromise between both Se and Sp, but Sp was highest for CEx-most impaired cutoffs (Figure 1). The highest PPV (73.6%) and NPV (39.4%) were observed for LatSpiFlex.



Conclusion: Measures of mobility and their levels of impairment do not show sufficient individual diagnostic value for ax-SpA among patients with early inflammatory back pain. However, highest degrees of impairment when compared to general population are more specifically observed in patients finally classified with ax-SpA for CEx, which was –consistently- 1 of the 2 mobility measures that was retained in the modified New York criteria for ankylosing spondylitis.

Disclosure of Interests: Cédric Lukas Speakers bureau: AbbVie; Lilly; Merck; Novartis; Pfizer; Roche-Chugai;, Consultant of: AbbVie; Bristol-Myers Squibb; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; UCB; Sanofi;, Grant/research support from: Pfizer: Novartis, Gisèle Khoury Grant/research support from: Pfizer, Maria-Antonietta d'Agostino: None declared., Bernard Combe Speakers bureau: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Consultant of: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Novartis, Pfizer, and Roche-Chugai, Jacques Morel Speakers bureau: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Consultant of: AbbVie; Bristol-Myers Squibb; Gilead; Janssen; Lilly; Merck; Novartis; Pfizer; Roche-Chugai; and Sanofi, Grant/research support from: Novartis, Pfizer, and Roche-Chugai.

DOI: 10.1136/annrheumdis-2021-eular.1336

AB0494

COGNITIVE IMPAIRMENT IN AXIAL SPONDYLOARTHRITIS?

S. Kleinert[1,2], P. Rapp[1], F. Schuch[1], M. Ronneberger[1], J. Wendler[1], P. Sternad[3], F. Popp[3], P. Bartz-Bazzanella[4], C. B. Von der Decken[5], K. Karberg[6], G. Gauler[7], P. Wurth[7], S. Spaethling-Mestekemper[8], C. Kuhn[9], M. Englbrecht[10], W. Vorbrüggen[11], G. Adler[12], M. Welcker[3]. *[1]Praxisgemeinschaft Rheumatologie – Nephrologie (PGRN.de), Rheumatology, Erlangen, Germany*; *[2]University Hospital of Würzburg, Department of Internal Medicine II, Rheumatology/ Clinical Immunology, Würzburg, Germany*; *[3]Medizinisches Versorgungszentrum für Rheumatologie Dr. M. Welcker GmbH, Rheumatology, Planegg, Germany*; *[4]Rhein-Maas-Klinikum, Klinik für Internistische Rheumatologie, Würselen, Germany*; *[5]Medizinisches Versorgungszentrum für Rheumatologie, Rheumatology, Stolberg, Germany*; *[6]Praxis für Rheumatologie und Innere Medizin, Rheumatology, Berlin, Germany*; *[7]Rheumatology Practice, Rheumatology, Osnabrück, Germany*; *[8]Rheumatologische Gemeinschaftspraxis München, Rheumatology, München, Germany*; *[9]Praxis für Rheumatologie Karlsruhe, Rheumatology, Karlsruhe, Germany*; *[10]Freelance Healthcare Data Scientist, Statistics, Eckental, Germany*; *[11]Verein zur Förderung der Rheumatologie e.V., Rheumatology, Würselen, Germany*; *[12]Institut für Studien zur Psychischen Gesundheit (ISPG), Mannheim, Psychology, Mannheim, Germany*

Background: There is some evidence that neuropsychiatric changes occur in systemic lupus(1) and rheumatoid arthritis(2). However, little is known regarding a possible disease-related impairment of cognitive abilities in axial spondyloarthritis (axSpA).

Objectives: To evaluate patients with axSpA regarding cognitive impairments.

Methods: Patients with axSpA attending two rheumatology practices were routinely evaluated by rheumatologists and underwent a computer-based memory and attention test (MAT) (3, 4) with subscale scores ranging from 0 (worst) to 15 (best). The results of short-term memory and working memory were compared to an age-, sex- and education-matched control group of healthy subjects. Descriptive results are presented as median (IQR) for interval data and n (%) for nominal data if not stated otherwise. Two-tailed Wilcoxon signed-rank tests including Bonferroni-Holm adjustment for multiple tests were conducted to investigate the magnitude of potential differences in cognitive abilities.

Results: 101 consecutive patients were tested (Table 1). After multiple testing adjustment for two subscales, Wilcoxon signed-rank tests returned significant findings for working memory ($V = 539.5$, $p = 0.006$, $|r| = 0.204$) but not for short-term memory ($V = 1075$, $p = 0.351$, $|r| = 0.078$). Regarding the scales' anchors, descriptive results on pairwise differences suggested axSpA patients to have working memory scores that are on average 10.7% lower compared to control participants (mean $\Delta = -1.64$, SD $\Delta = 5.95$).

Table 1. Patients and disease characteristics

	n	%	Mean	SD	Median	25% Quantile	75% Quantile
Age	101	100	51.1	11.6	52	42	60
Age (female)	48	47.5	52.6	11.7	54	44.5	61
Age (male)	53	52.5	49.8	11.5	51	41	57
< 13 years formal education	47	46.5					
≥ 13 years formal education	54	53.5					
HLA B27 positive n/N	64/92	63.4					
Disease duration (years)	101	100	13.7	11.7	12	4	21
Disease duration (female, years)	48	47.5	11.6	9.9	9	4	17.2
Disease duration (male, years)	53	52.5	15.5	12.9	15	5	23
BASDAI	92	91.1	3.7	1.7	3.8	2.4	5
BASFI	91	90.1	3	2.4	2.3	1.2	4.5
BASMI	75	74.3	1.9	2.3	1	0	3
ASDAS	98	97	2.3	0.8	2.3	1.8	2.8

Conclusion: The MAT computerized testing is a feasible test and was well accepted by patients. Results regarding working memory suggest that cognitive abilities needed to accomplish everyday tasks may be impaired in axSpA patients. Further work is needed to characterise possible causes of or associations with this cognitive impairment.

REFERENCES:

[1] Zabala A, Salgueiro M, Saez-Atxukarro O, Ballesteros J, Ruiz-Irastorza G, Segarra R. Cognitive Impairment in Patients With Neuropsychiatric and Non-neuropsychiatric Systemic Lupus Erythematosus: A Systematic Review and Meta-analysis. J Int Neuropsychol Soc. 2018:1-11.

[2] Vitturi BK, Nascimento BAC, Alves BR, de Campos FSC, Torigoe DY. Cognitive impairment in patients with rheumatoid arthritis. J Clin Neurosci. 2019;69:81-7.

[3] Adler G, Bektas M, Feger M, Lembach Y. [Computer-based assessment of memory and attention: evaluation of the memory and attention test (MAT)]. Psychiatr Prax. 2012;39(2):79-83.

[4] Adler G, Lembach Y. Memory and selective attention in multiple sclerosis: cross-sectional computer-based assessment in a large outpatient sample. Eur Arch Psychiatry Clin Neurosci. 2015;265(5):439-43.

Acknowledgements: This study was funded by the RHADAR GbR (A Network of Rheumatologists), Bahnhofstr. 32, 82152 Planegg, Germany. RHADAR GbR has received a grant for this study from Novartis Pharma GmbH.

Disclosure of Interests: Stefan Kleinert Consultant of: Novartis, Abbvie, Grant/research support from: Novartis, Praxedis Rapp: None declared., Florian Schuch Speakers bureau: Novartis, Abbvie, Gilead, Consultant of: Novartis, Abbvie, Gilead, Monika Ronneberger: None declared., Joerg Wendler Speakers bureau:

Roche, Pharma, JanssenCilag, Novartis, Abbvie, Consultant of: JanssenCilag, Patrizia Sternad: None declared., Florian Popp: None declared., Peter Bartz-Bazzanella: None declared., Cay-Benedict von der Decken: None declared., Kirsten Karberg Speakers bureau: Roche, Sanofi, Abbvie, Lilly, Georg Gauler Speakers bureau: Abbvie, Gilead, Novartis, Lilly, Consultant of: Lilly, Gilead, Abbvie, Patrick Wurth Speakers bureau: Abbvie, Lilly, UCB, Medac, Susanna Spaethling-Mestekemper Speakers bureau: Abbvie, BMS, Celgene, Gilead, GSK, Hexal, Lilly, MSD, Novartis, Pfizer, Sanofi, UCB, Christoph Kuhn: None declared., Matthias Englbrecht Speakers bureau: AbbVie, Chugai, Eli Lilly, Novartis, Roche, Sanofi, Mundipharma, Paid instructor for: AbbVie, Chugai, Roche, Consultant of: AbbVie, Novartis, Roche, Sanofi, Grant/research support from: Roche, Chugai, Wolfgang Vorbrüggen: None declared., Georg Adler: None declared., Martin Welcker Speakers bureau: Abbvie, Actelion, Amgen, Biogen,BMS, Berlin Chemie, Celgene, Galapagos, Gilead, GSK, Hexal, Janssen, Medac, MSD, Mundipharma, Mylan, Novartis, Pfizer, Roche, Sanofi, SOBI, UCB, Grant/research support from: Novartis, Abbvie.

DOI: 10.1136/annrheumdis-2021-eular.1353

AB0495 BIOMECHANICAL STRESS IN THE CONTEXT OF COMPETITIVE SPORTS TRAINING TRIGGERS ENTHESITIS

D. Simon[1], A. Kleyer[1], S. Bayat[1], J. Knitza[1], L. Valor[1], M. Schweiger[1], G. Schett[1], K. Tascilar[1], A. Hueber[2]. [1]*Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany*; [2]*Sozialstiftung Bamberg, Section Rheumatology, Erlangen, Germany*

Background: Preclinical models have indicated that biomechanical stress can trigger entheseal inflammation (1). Furthermore, enthesitis is a hallmark of psoriatic arthritis (PsA) and spondyloarthritis (SpA), suggesting that mechanoinflammation is an important step in their pathogenesis (2). However, the relation between mechanical stress and enthesitis in humans is poorly investigated. Competitive badminton is a demanding stop-and-go sport that strains entheseal sites in particular and provides an opportunity to assess the impact of physical activity on the development of an instant inflammatory response in the entheses.

Objectives: To evaluate the influence of mechanical stress on the development of immediate enthesitis.

Methods: BEAT (Badminton Enthesitis Arthrosonography Study) is an interventional study that assessed entheses in competitive badminton players before and immediately after a 60-minute intensive training session by ultrasound. Power Doppler (PD) signal and Gray-Scale (GS) changes were evaluated at the insertions sites of both Achilles tendon, patellar tendons and lateral humeral epicondyles and quantified using a validated scoring system (3). Pre- and post-training scores were compared using linear mixed-effects models. We used interaction terms to assess possible differential effects on patellar, elbow and Achilles entheses.

Results: Thirty-two badminton players (22 men, 10 women) with an average age of 31.1±13.0 years were included (Table 1). On average, they had been playing badminton for 16.2±10.1 years. 192 entheseal sites were examined twice. The respective empirical total scores for PD examination were 0.1 (0.3) before and 0.5 (0.9) after training (Figure 1). Mean total GS scores were 2.9 (2.5) and 3.1 (2.5) before and after training, respectively. The mean total PD score difference of 0.4 between pre- and post -training was significant with a p value of 0.0014, whereas the p value for the mean total GS score difference of 0.2 was 0.63. Overall, seven participants (22%) showed an increased empirical total PD score. A mixed-effects model showed a significant increase of PD scores after training, with a mean increase per site of 0.06 (95%CI 0.01 to 0.12, p=0.017).

Table 1. Baseline characteristics

Demographic characteristics	
N, total	32
Females, N (%)	10 (31.3)
Age, years (mean ± SD)	36.1 ± 13.0
Height, cm (mean value ± SD)	178.6 ± 9.9
Body weight, kg (mean value ± SD)	74.7 ± 13.5
Smoking, N (%)	11 (34.4)
Alcohol, N (%)	24 (75.0)
Concomitant Diseases	
Inflammatory bowel disease, N (%)	0
Psoriasis, N (%)	0
Uveitis, N (%)	0
Diabetes mellitus, N (%)	0
Hypertension, N (%)	2 (6.3)
Sports history	
Years Badminton (mean ± SD)	16.2 ± 10.1

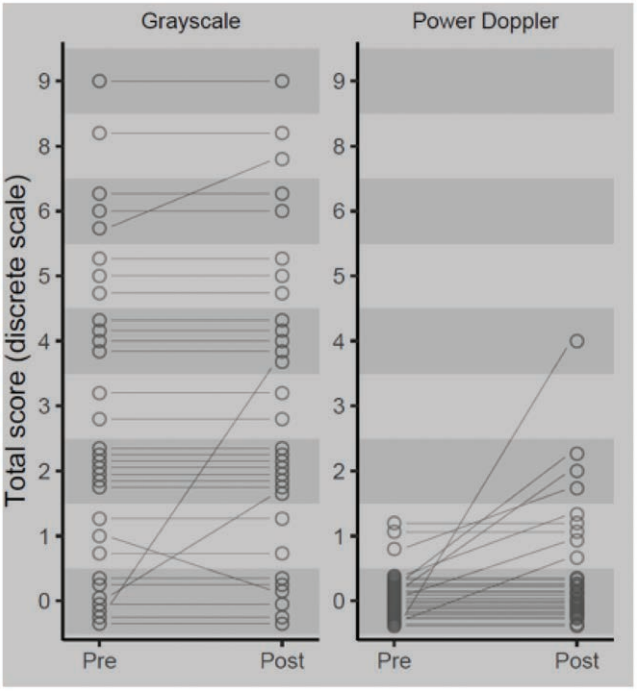


Figure 1. Ultrasound scores before and after trainingFigure 1. A Spaghetti plots depicting inividual Gray-Scale and Power Doppler ultrasound scores before and after training

Conclusion: Mechanical stress leads to rapid inflammatory responses in the entheseal structures of humans. These data support the concept of mechanoinflammation in diseases associated with enthesitis. However, while such responses may be self-contained in healthy subjects, they may be prolonged and more pronounced in certain risk groups, such as patients with PsA or SpA.

REFERENCES:

[1] Cambré I, et al. Mechanical strain determines the site-specific localization of inflammation and tissue damage in arthritis. Nature Communications. 2018; 9:4613.

[2] Schett G, et al. Enthesitis: from pathophysiology to treatment. Nat Rev Rheumatol. 2017; 13:731-741.

[3] Balint PV, et al. Reliability of a consensus-based ultrasound definition and scoring for enthesitis in spondyloarthritis and psoriatic arthritis: an OMERACT US initiative. Annals of the Rheumatic Diseases. 2018; 77:1730.

Disclosure of Interests: David Simon: None declared., Arnd Kleyer: None declared., Sara Bayat: None declared., Johannes Knitza: None declared., Larissa Valor: None declared., Marina Schweiger: None declared., Georg Schett: None declared., Koray Tascilar: None declared., Axel Hueber Grant/research support from: Novartis Research Grant.

DOI: 10.1136/annrheumdis-2021-eular.1793

AB0496 COMPARISON OF THE DISTRIBUTION BY DEPARTMENT OF THE PREVALENCE OF SPONDYLOARTHRITIS AND INFLAMMATORY BOWEL DISEASES IN METROPOLITAN FRANCE AND THEIR EVOLUTION BETWEEN 2008 AND 2018

O. Fakih[1], C. Prati[1,2], D. Wendling[1,3], F. Verhoeven[1,2]. [1]*Centre hospitalier régional universitaire de Besançon, Rhumatologie, Besançon, France*; [2]*UFR Santé, Université de Franche-Comté, EA 4267 'PEPITE', Besançon, France*; [3]*UFR Santé, Université de Franche-Comté, EA 4266 'EPILAB', Besançon, France*

Background: Epidemiology of spondyloarthritis (SpA) has been rarely described in France. One study based on a phone survey found a prevalence of 0.30% in 2001 [1], and another study based on a national cohort showed an estimated prevalence of 0.43% in 2010 [2]. To our knowledge, there is no data regarding the geographical distribution of SpA in France. Furthermore, it is known that SpA occurs in up to 13% of patients with inflammatory bowel disease (IBD), and that there is a significant north-south gradient in IBD cases in France.

Objectives: To determine the prevalence of SpA and IBD in metropolitan France and compare the geographical distribution of SpA and IBD in 2008 and 2018.

Methods: Age-and sex-standardized prevalences were collected from data freely available on the French national health insurance website concerning patients with long-term disability (LTD) #27 (SpA) and #24 (IBD). Data for December 31, 2008 and December 31, 2018 were collected. National data are available by diagnosis coded according to the ICD-10 classification, and data by department only concern all patients benefiting from a given LTD.
Results: National prevalence of SpA is estimated at 0.11% in 2008 (43.8% of women, average age 50 years) and 0.27% in 2018 (54% of women, average age 53 years). National prevalence of IBD is estimated at 0.19% in 2008 (55.6% of women, average age 46 years) and 0.27% in 2018 (55% of women, average age 49 years). Standardized prevalences by pathology are detailed in Table 1. Standardized prevalences by department are shown in Figure 1.

Table 1. Standardized SpA and IBD prevalence (per 100000) by disease in 2008 and 2018.

	Ankylosing Spondylitis	Psoriatic Arthritis	Crohn's Disease	Ulcerative colitis
2008	95	31	103	84
2018	181	57	153	126

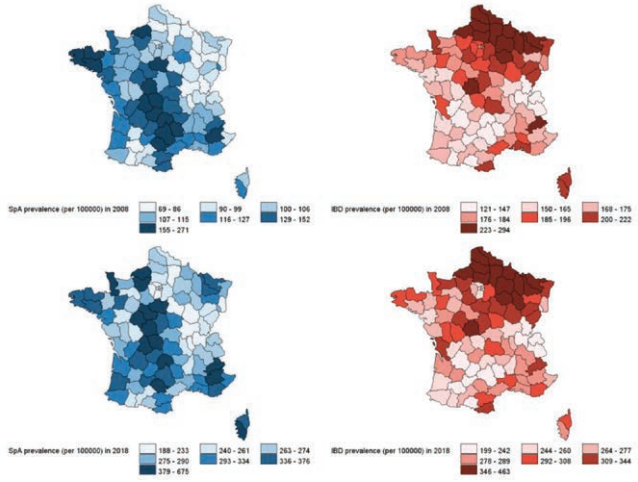


Figure 1. Standardized SpA and IBD prevalence by department in 2008 and 2018.

SpA prevalences found in this study are lower than those indicated in the literature: 0.27% versus 0.43% [2]. This may be explained by the fact that not all patients suffering from SpA or IBD benefit from LTD. Moreover, there is a 2.42-fold increase over ten years, which may correspond to the increase in prescription of biotherapies, which requires the benefit of LTD. North-south gradient in the prevalence of IBDs has been found, which is not the case for SpA, which seems to be less prevalent in the north-eastern quarter of the country. These differences in geographical distribution appear to be stable between 2008 and 2018. While IBD and SpA share many physiopathological similarities, their different geographical distributions suggest the importance of different environmental factors in the development of each condition.
Conclusion: The north-south gradient in the distribution of IBD in metropolitan France is not found in SpA. Despite an increasing prevalence, these distributions appear to be stable over time suggesting an important impact of environmental factor in the expression of these close diseases.
REFERENCES:
[1] Saraux A, Guillemin F, Guggenbuhl P, *et al.* Prevalence of spondyloarthropathies in France: 2001. *Ann Rheum Dis* 2005;**64**:1431–5. doi:10.1136/ard.2004.029207
[2] Costantino F, Talpin A, Said-Nahal R, *et al.* Prevalence of spondyloarthritis in reference to HLA-B27 in the French population: results of the GAZEL cohort. *Ann Rheum Dis* 2015;**74**:689–93. doi:10.1136/annrheumdis-2013-204436
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1805

AB0497 IMPACT OF COXITIS ON THE BONE MINERAL DENSITY OF THE HIP IN ANKYLOSING SPONDYLITIS

A. Feki[1], I. Sellami[2], R. Akrout[1], S. Ben Jemaa[1], Z. Gassara[1], M. Ezzeddine[1], M. H. Kallel[1], H. Fourati[1], S. Baklouti[1]. [1]*Hedi Chaker Hospital, Rheumatology, Sfax, Tunisia*; [2]*Hedi Chaker Hospital, Occupational medicine, Sfax, Tunisia*

Background: Ankylosing spondylitis (AS) is an inflammatory disease, with new bone formation and ossification of the ligamentous apparatus as the primary pathological changes. The osteoporosis is coexisting with new bone formation. It is well known a common complication of this chronic disease. Hip involvement is common in AS [1].
Objectives: The objective of this work is to assess the impact of chronic inflammation of the hip (coxitis) on the bone density at this site.
Methods: This is a cross-sectional study of patients who fulfil the modified New York criteria for AS. These patients had not medical history of osteoporosis or other condition that may affect bone metabolism. Hip involvement was appreciated by physical examination and pelvic x-ray. The functional hip gene was assessed by Lequesne Algofunctional Index (LFI). Bone mineral density at the femoral site was measured using Lunar Prodigy dual-energy X-ray absorptiometry. Osteoporosis is defined when T score is ≤ -2.5 DS (standards deviations). Osteopenia is defined when T score is ≤ -1 DS but more than -2.5 DS. A p value <0.05 was considered significant.
Results: Forty-seven AS patients were collected, 12 women and 35 men with a mean age of 43.8 ± 13.4 years. Smoking was noted in 25% of cases. AS clinical form was axial in 33 cases (70.2%) and mixed (axial and peripheral) in 14 cases (29.8%). The mean duration of AS was 15 ± 10.9 years. Nineteen patients (40.4%) were on DMARD at the time of the study. Coxitis was present in 31 patients (66%). It was bilateral in 13 cases (42.5%). The mean of the LFI was 7.1 ± 6.5 with extremes of 0 to 18. Coxitis form was early in 18 cases (40.9%), synostosis in 15 cases (34.1%) and destructive in 11 cases (25%). Twenty-nine patients (61.7%) had normal femoral bone densitometry, 13 patients (27.7%) had osteopenia and 4 patients (8.5%) had osteoporosis. The mean T-score value at femoral neck site was -0.5 SD ± 1.303 [-3– -2]. Patients with coxitis had a significantly lower T score at the femoral site compared to those without coxitis (-0.77 ± 1.31 DS versus 0.07 ± 1.11 DS respectively with p = 0.036).
Conclusion: Our study confirms the role of chronic inflammation in the genesis of bone loss in AS. Given the risks of developing secondary complications as a result of low bone density, early management of AS should be recommended in order to control the inflammatory process and prevent the onset of osteoporosis.
REFERENCES:
[1] Toussirot E, Wendling D. Bone mass in ankylosing spondylitis. Clin Exp Rheumatol 2000:16–20.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1911

AB0498 INFLUENCE OF SYNOVITIS OF THE HIP JOINTS ON X-RAY PROGRESSION OF COXITIS IN AXIAL SPONDYLOARTHRITIS. RESULTS OF TWO YEARS FOLLOW-UP

E. Agafonova[1], S. Erdes[1], T. Dubinina[1], A. Demina[1], D. Rumiantceva[1], A. Smirnov[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of spondyloarthritis and psoriatic arthritis, Moscow, Russian Federation*

Background: Almost half of patients with axial spondyloarthritis (axSpA) in Russia have hip joint lesions (HJ), but only in 7% of cases it becomes so severe and requires arthroplasty. The causes and rates of progression of coxitis have not been studied.
Objectives: To assess the relationship between disease activity and the sonographic synovitis of the hip joint with the progression of X-ray coxitis in patients with axSpA with a 2-year follow-up.
Methods: The study included 77 patients (mean age 28 ± 5.92 years) with axSpA (ASAS criteria 2009), who were followed up for at least 2 years. Among them, AS (mNY criteria, 1984) had 66 (86%) patients, and nonradiographic axSpA - 11 (14%). The median duration of the disease was 30 [3–60] months, BASDAI - 4.5 [3.2; 5.9], BASFI - 2.4 [0.9; 4.8]. All patients underwent clinical examination, X-ray and ultrasound investigation of the hip joint during the monitoring period. For ultrasound, coxitis was considered an increase in the cervical-capsular distance (CCD) of more than 7 mm. An increase in BASRI hip by 1 stage in 2 years was considered as progression of radiographic coxitis (PRC).
Results: At the time of enrollment, 66 (86%) patients out of 77 patients had pain in the hip joint, and after 24 months - 48 (62%) (p> 0.05). At the time of inclusion, the median pain in the hip joint was 4 [2; 5]; severe pain (≥4.0) had 38% of patients. The median CCD at the time of inclusion was 7.3 [6.4; 8.2] mm, and two years later 6.6 [5.9; 8.2] mm (p> 0.05). At the sonographic examination at the beginning of follow-up 63 (82.0%) patients had coxitis, and after 2 years - 45 (58%) (p <0.05). X-ray coxitis at the time of inclusion was present in 19 (25%) patients, and after 2 years - in 48 (62%) (p <0.05). Depending on the presence or absence of PRC after 2 years, the patients were divided into 2 groups (Table 1). All patients with PRC at the start of the study had sonographically diagnosed synovitis, while among those without progression, only half of them; relative risk of X-ray progression in the presence of ultrasound of synovitis (RR) = 10.5 (p

<0.05). The groups did not differ in terms of activity indicators and the presence of extra-axial manifestations.

Table 1. Characteristics of patients with axSpA at the time of inclusion in the study who had PRC after 24 months of observation.

Parametrs	ΔBASRI hip=0 n=33	ΔBASRI hip >0 n = 44	p
Sex (m/w), n	22/11	32/12	>0,05
The duration of the disease, m., Me [25;75‰]	36 [19;132]	48 [24;84]	>0,05
Age, years, Me [25;75 ‰]	30 [26;34]	28 [24;34]	>0,05
BASDAI, Me [25;75 ‰]	4,3 [3,1;5,8]	4,7 [3,8;6,3]	>0,05
BASFI, Me [25;75 ‰]	3,4 [0,6;5,6]	2,1 [1,1;4,2]	>0,05
ASDAS (SRP), Me [25;75 ‰]	2,6 [1,6;3,9]	3,2 [2,3;4,2]	>0,05
ESR, mm/h, Me [25;75 ‰]	15 [7;30]	23,0 [12;35]	>0,05
SRP, mg/l, Me [25;75 ‰]	12,8 [1,8;31,0]	17,8 [5,6; 50,3]	>0,05
Peripheral arthritis, n %	26 (79%)	32 (73%)	>0,05
US synovitis n%	19 (58%)	44 (100%)	<0,05*
Pain in HJ n%	28 (85%)	38 (86%)	>0,05

Conclusion: X-ray progression of coxitis is associated with ultrasound synovitis and does not depend on the activity of the disease.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2002

AB0499 PHYSICAL ACTIVITY ASSESSMENT IN TUNISIAN PATIENTS WITH SPONDYLOARTHRITIS: THE IPAQ EVALUATION

F. Majdoub[1], M. Sellami[1], S. Miladi[1], A. Fazaa[1], L. Souabni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, La Marsa, Tunis, Tunisia*

Background: The occurrence of Spondyloarthritis (SpA) often conditions patients' quality of life and hinders their well-being. Physical activity (PA) is associated with various health-related benefits among adults with chronic inflammatory rheumatism but may be insufficiently performed.

Objectives: This study aimed to assess PA in patients with SpA and explore its associated factors.

Methods: This is a single-center cross-sectional study, involving patients with SpA, visiting our outpatient hospital over eight weeks. Patients responded to the International Physical Activity Questionnaire-Short form (IPAQ-S).

Results: Sixty patients were included (39 M/21 F) with an average age of 45.8 years [25-78]. The mean duration of SpA was 13.2 years [1-25]. About 80% of patients were from an urban setting. Sixty-three percent of patients had a professional activity, while 13.3% were retired. Twenty-nine patients (48.3%) had axial and peripheral form, 18 patients (30%) had SpA with enteropathic arthritis, 8 (13.3%) with psoriatic arthritis, 3 patients (5%) had axial spondyloarthritis, and only 2 patients (3.3%) with SAPHO-Syndrom. About 23% of patients had hip arthritis and only 5% had uveitis. Fifty-eight patients were on TNF-inhibitor (21/58 Adalimumab, 15/58 Infliximab, 14/58 Etanercept, 8/58 Golimumab). The average BASDAI was 2.7/10. The average $ASDAS_{CRP}$ was 2.1/10. The average BASFI was 3.3/10. IPAQ results were distributed as follows: 78.3% of patients were in the « low physical activity » category, 21.7% were in the « moderate physical activity » while none of the patients were in the « high physical activity ». Patients without employment had lower levels of physical activity (29.7%) but no association was observed between those two items (p=0.082). Disease activity objectified with BASDAI was related to low physical activity (p=0.045) whereas no association was observed with $ASDAS_{CRP}$ (p=0.870) or BASFI (p=0.056). Otherwise, TNF-inhibitor treatment was not related to different levels of PA (p=0.09).

Conclusion: Tunisian patients with SpA don't perform enough physical activity. Except for high disease activity, the different levels of PA did not appear to be explained by other disease-related variables. Thereby, physical activity should be encouraged in SpA.

REFERENCES:

[1] Fabre, S., Molto, A., Dadoun, S. et al. Physical activity in patients with axial spondyloarthritis: a cross-sectional study of 203 patients. Rheumatol Int 36, 1711–1718 (2016).

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2053

AB0500 IMPACT OF COVID-19 PANDEMIC IN OVERALL HEALTH AND FUNCTIONING IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE REUMAVID STUDY (PHASE 1)

D. Benavent[1], M. Garrido-Cumbrera[2,3], C. Plasencia[1], L. Christen[4], H. Marzo-Ortega[5], J. Correa-Fernández[2], P. Plazuelo-Ramos[3], D. Webb[6], V. Navarro-Compán[1]. [1]*Hospital La Paz, IdiPAZ, Rheumatology Department, Madrid, Spain*; [2]*Universidad de Sevilla, Health & Territory Research, Sevilla, Spain*; [3]*Axial Spondyloarthritis International Federation (ASIF), London, United Kingdom*; [4]*Novartis Pharma, AG, Basel, Switzerland*; [5]*University of Leeds, NIHR Leeds Biomedical Research Centre, LTHT and LIRMM, Leeds, United Kingdom*; [6]*NASS, London, United Kingdom*

Background: Evidence on the impact of the COVID-19 pandemic on the overall health and functioning in patients with axial spondyloarthritis (axSpA) is scarce.

Objectives: To analyse the impact of the COVID-19 pandemic on the overall health and functioning in patients with axSpA.

Methods: Data from axSpA patients participating in the first phase of the REUMAVID study were analysed. REUMAVID is a cross-sectional, observational study collecting data through an online questionnaire of unselected patients with rheumatic and musculoskeletal diseases (RMDs), recruited by patient organizations. The survey was disseminated during the beginning of the COVID-19 pandemic (April-July 2020) in seven European countries (Cyprus, France, Greece, Italy, Portugal, Spain, and the United Kingdom). Patients with axSpA who completed the ASAS health index (ASAS-HI) questionnaire were included in this analysis. Descriptive analyses were used to present socio-demographic and clinical characteristics, as well as daily habits. Overall health and functioning were defined according to the ASAS-HI (0-17), as follows: good health (ASAS-HI ≤5), acceptable health (ASAS-HI 6-11), and poor health (ASAS-HI ≥12). As secondary outcomes, well-being (WHO-5), self-perceived health status, and HADS for anxiety and depression were assessed.

Results: Out of 670 axSpA patients, 587 (87.6%) completed ASAS-HI. Of these, 70.4% were female, 72.6% were married or in a relationship, 46.7% had university studies and 37.6% were currently employed. Mean age was 49.9±12.8 years and mean BMI was 26.7±5.5. Regarding extraarticular manifestations, 13.6% had psoriasis, 12.1% inflammatory bowel disease and 18.7% uveitis. Before the COVID-19 pandemic, 50.9% were receiving biological drugs, 46.3% NSAIDs, 26.4% painkillers, 24.7% conventional DMARDs, and 11.9% oral corticosteroids. According to the ASAS-HI, 19.6 % of patients were classified as having poor health, with the most affected aspects being pain (92.0%), movement (86.5%), maintenance of body position (80.6%), energy (79.0%) and sleep (75.3%). Regarding self-perceived health status, 14% reported their health status as "bad" or "very bad", and 46.8% reported worsening health during the pandemic (Table 1). A distribution of the results of the total ASAS-HI scores can be seen in Figure 1.

Table 1. Overall health and well-being, disease activity, and mental health.

Primary Outcome (ASAS-HI)	**Mean ± SD or n (%)**
ASAS-HI (0-17), n=587	8.0 (±3.9)
ASAS-HI	
<5 (good health)	159 (27.1)
5-12 (acceptable health)	313 (53.3)
≥12 (poor health)	115 (19.6)
Secondary Outcomes	
WHO-5	
WHO-5, (0-100), n=584	46.3 (±23.1)
WHO- 5 Poor wellbeing WHO- ≤50	330 (56.5)
Self-perceived health status, n=585	
Very good	33 (5.6)
Good	214 (36.6)
Fair	256 (43.8)
Bad	69 (11.8)
Very bad	13 (2.2)
Change in health status during lockdown, n=587	
Much worse than before	54 (9.2)
Moderately worse	220 (37.6)
Same as before	270 (46.0)
Moderately better	35 (6.0)
Much better than before	6 (1.0)
HADS	
HADS Anxiety (0-21), n=587	8.4 (±4.1)
HADS Anxiety	
No case (0-7)	248 (42.7)
Borderline case (8-10)	151 (26.0)
Case (11-21)	182 (31.3)
HADS Depression (0-21), n=587	7.0 (±4.3)
HADS Depression	
No case (0-7)	329 (56.6)
Borderline case (8-10)	134 (23.1)
Case (11-21)	118 (20.3)

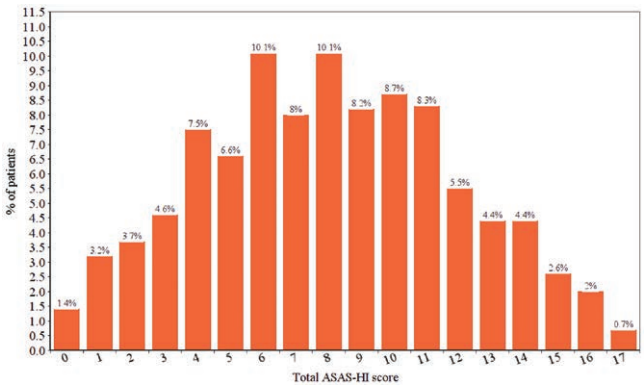


Figure 1. Distribution of the result of ASAS-HI scores (N= 587)

Conclusion: One out of five patients with axSpA reported poor health and functioning according to the ASAS-HI, and almost half of patients reported worsening self-perceived health status during the first wave of the COVID-19 pandemic.

Keywords: COVID-19, axial spondyloarthritis, ASAS-HI, health

Disclosure of Interests: Diego Benavent Grant/research support from: Abbvie, Novartis and Roche, Marco Garrido-Cumbrera: None declared., Chamaida Plasencia Grant/research support from: Pfizer, Sanofi, Novartis, Roche and Lilly, Laura Christen Employee of: Novartis Pharma AG, Helena Marzo-Ortega Grant/research support from: Abbvie, Celgene, Janssen, Elli-Lilly, Novartis, Pfizer, UCB and Takeda Pharmaceutical Company, José Correa-Fernández: None declared., Pedro Plazuelo-Ramos: None declared., Dale Webb: None declared., Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, UCB.

DOI: 10.1136/annrheumdis-2021-eular.2153

AB0501 CORRELATION BETWEEN AXIAL AND PERIPHERAL ENTHESIS IN SPONDYLARTHRITIS

H. Ferjani[1], M. Yasmine[1], K. Maatallah[1], E. Labbene[2], H. Riahi[2], D. Kaffel[1], M. Bouaziz[2], W. Hamdi[1]. [1]*Kassab Institute of Orthopedics, Rheumatology,Tunis, Tunisia*; [2]*Kassab Institute of orthopedics, Radiology,Tunis,Tunisia*

Background: Enthesitis is the clinical hallmark of spondylarthritis. It refers to the inflammation of joint attach in the bone. Several sites enthesitis may be affected, and a wide variety of scoring systems were available.

Objectives: We aimed to determine the prevalence of axial enthesitis in the anterior chest wall (ACW), and its correlation with peripheral sites especially, the Achilles tendon (AT).

Methods: We conducted a prospective study including patients with SpA according to the ASAS criteria. Sociodemographic data, as well as disease characteristics, were recorded. The Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) was used to assess clinical entheses (first and seventh costochondral joints, posterior superior iliac spine, anterior superior iliac spine, iliac crest, and Achilles tendon insertion). The presence of enthesitis on the US was then assessed in the right and left sternoclavicular (SCJ), manubriosternal (MSJ) joints, as well as in the AT, using Esaote My Lab 50.

Results: The study included 47 patients with SpA: axial (n=26), axial and peripheral (n=21). There was a female predominance (sex ratio: 0.2). The mean age was 42.2 years ± 12.6 [11-70]. The age of onset of the disease was <40 years in 59.6% of cases. Tenderness in entheseal sites was found in 63.8% of patients, especially in the plantar fascia and AT (32.7%, 6%, respectively). The mean MASES score was 2.9 [0-13]. Clinical ACW involvement (29.1%) was at follows: 1st right chondro-sternal joint (CSJ) (19.1%), 1st left CSJ (25.5%), 7th right CSJ (27.7%) and 7th left CSJ (31.9%).US involvement of the ACW was 14.3%. Enthesitis of the AT was found in 70% of cases on US examination. ACW US involvement was correlated neither to the BMI nor to MASES score (p=0.16, p=0.6 respectively). Similarly, there was no correlation between the presence of US ACW enthesitis and clinical nor the US AT enthesitis (p=0.09, p=0.209, respectively).

Conclusion: Our study showed that ACW enthesitis is frequent in SpA, especially by US screening. This axial enthesitis, don't necessarily reflect a simultaneous clinical or US involvement of the peripheral entheses. Further studies are needed to characterize this subtype of SpA.

REFERENCES:

[1] Verhoeven F, Guillot X, Godfrin-Valnet M, Prati C, Wendling D. Ultrasonographic evaluation of the anterior chest wall in spondyloarthritis: a prospective and controlled study. J Rheumatol. 2015;42(1):87-92

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2229

AB0502 HEALTH-RELATED QUALITY OF LIFE MEASURES IN SPONDYLOARTHROPATY PATIENTS UNDER BIOLOGICAL THERAPIES IN REAL LIFE

E. Grau García[1], M. De la Rubia Navarro[1], C. Pávez Perales[1], S. Leal Rodriguez[1], C. Riesco Barcena[1], A. V. Huaylla Quispe[1], E. Vicens Bernabeu[1], R. Negueroles Albuixech[1], J. Ivorra Cortés[1], F. M. Ortiz Sanjuan[1], I. Martínez Cordellat[1], I. Chalmeta Verdejo[1], J. J. Fragío Gil[1], L. Gonzalez Puig[1], J. E. Oller Rodríguez[1], C. Alcañiz Escandell[1], I. Cánovas Olmos[1], C. Nájera Herranz[1], A. J. Cañada Martinez[2], J. A. Román Ivorra[1]. [1]*HUP La Fe, Rheumatology Department, Valencia, Spain*; [2]*IIS La Fe, Biostatistics Unit, Valencia, Spain*

Background: Spondyloarthropathy patients have reduced health-related quality of life (HRQL) compared to general population. Biological treatment strategies in real life aim to reduce patients' symptoms and different HRQL parameters would share the same behavior as patients' symptoms and disease activity.

Objectives: We aim to assess the differences in HRQL reported by spondyloarthropathy patients during the first six months of biological therapy according to the treatment effectiveness.

Methods: We performed a prospective observational study of six months of follow-up in spondyloarthropathy patients who are newly on biological therapy. A basal visit and 1, 3 and 6 months follow-up visits were conducted. We analyzed changes during follow-up in the HRQL parameters reported by patients through AsqoL and ASAS-health-index questionnaires. Moreover we measured functional disability through HAQ and BASFI index, disease activity by BASDAI, ASDAS-CRP and ASDAS-ESR index.

Statistical analyses were achieved using R software, through multivariate linear regression models for continuous data and Bayesian mixed ordinal regression models with monotonic effect for ordinal data. The corresponding odd ratios (OR) were calculated with their confidence intervals (CI 95%).

Results: We included 53 patients (71.77% male), the 73.58% diagnosed with ankylosing spondylitis (AS) and the 26.42% with axial spondyloarthritis. Mean age at the beginning of treatment was 48.74 (11.21) years, mean age at diagnosis was 41.57 (11.97) and mean disease evolution was 7.19 (9.24) years. 60.42% of them exhibited HLAb27 positivity.

34 patients started biological therapy with TNF-α inhibitors and 19 with IL-17 inhibitors. The 81.13% of patients were under monotherapy, and the other 18.87% was treated with DMARDs. The 77.36% of the total number of patients was on the biological therapy at 6 months of follow-up, while the 22.64% discontinued at 6 months of follow-up (9 due to inefficacy and 3 due to adverse effects).

42 patients completed the follow-up at 6 months, and 3 patients achieved until visit 3 due to treatment failure. In 1 case visit 1 and in 7 cases visit 3 could not be performed due to COVID19 pandemic situation.

We observed a significant correlation among AsqoL and ASAS-hi values with disease activity indexes (BASDAI, ASDAS-CRP, ASDAS-ESR) and functional disability (HAQ, BASFI). The statistical analyses showed a significant association where AsqoL and ASAS-hi values are significantly decreased in treatment failures compared to the successful treatment (, and in patients with previous biological therapy compared to naïve patients. No effect of years of disease evolution and the type of biological treatment in the AsqoL and ASAS-hi values was observed. (See Table 1) These results were consistent with the significant association found among the disease activity and functional disability with the biological therapy efficacy and the previous biological treatment.

Table 1.

Comparison with effectiveness of biological therapy	Odds Ratio (OR)	95% CI	Comparison with previous biological therapy	Odds Ratio (OR)	95% CI
AsqoL	1.502	1.123–2.033	AsqoL	10.704	1.232–108.504
ASAS-HI	1.56	1.184–2.078	ASAS-HI	11.553	1.299–108.974
BASDAI	1.5	1.199–2.04	BASDAI	11.96	1.823–86.901
BASFI	1.348	1.036–1.76	BASFI	18.37	2.15–176.988
ASDAS-CRP	1.538	1.176–2.036	ASDAS-CRP	8.869	2.001–42.272
ASDAS-ESR	1.944	1.166–3.384	ASDAS-ESR	44.621	2.886–1077.816
HAQ	1.524	1.154–2.027	HAQ	24.111	1.779–371.742

Conclusion: The AsqoL and ASAS-hi questionnaire results are correlated with disease activity and functional disability and showed the same behaviour as these parameters, being also associated to the biological therapy efficacy as

well as to previous biological therapies. The HRQL variables would be additional clinical results that make it possible to achieve a better management of biological therapies in spondyloarthropathy patients.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2282

AB0503 DISEASE CONTROL IN ANKYLOSING SPONDYLITIS PATIENTS WITH PERIPHERAL ARTHRITIS IN REAL CLINICAL PRACTICE IN SPAIN: MiDAS STUDY RESULTS

X. Juanola[1], C. Fernández-Carballido[2], A. Muñoz Jimenez.[3], J. Sanz[4], A. Urruticoechea-Arana[5], P. Moya[6], J. M. Belzunegui Otano[7], C. Sanabra[8], C. Sastré[8]on behalf of MIDAS group. [1]*Hospital Universitari Bellvitge, IDIBELL, rheumatology service, L'Hospitalet de Llobregat, Barcelona, Spain*; [2]*Hospital Universitario San Juan de Alicante, rheumatology service, Alicante, Spain*; [3]*Hospital Universitario Virgen Rocío, rheumatology service, Sevilla, Spain*; [4]*Hospital Universitario Puerta de Hierro, rheumatology service, Madrid, Spain*; [5]*Hospital Can Misses, rheumatology service, Ibiza, Spain*; [6]*Hospital de la Santa Creu i Sant Pau, rheumatology service, Barcelona, Spain*; [7]*Hospital Universitario de Donostia, rheumatology service, San Sebastián, Spain*; [8]*Novartis Farmacéutica, rheumatology, Barcelona, Spain*

Background: MIDAS study assessed disease activity in patients (pts) with ankylosing spondylitis (AS) treated in clinical practice in Spain.
Objectives: This subanalysis compared disease activity status between AS pts with and without peripheral arthritis (PA).
Methods: Observational, non-interventional, cross-sectional, multicenter study. Pts ≥18 years with ≥6 months diagnosis, fulfilling ASAS and modified New York criteria; undergoing treatment ≥3 months. Disease activity was measured by BASDAI and ASDAS-CRP. The number of painful and swollen joints was recorded in AS pts according to the OMERACT recommendations.[1]
Results: 313 AS pts included: 251 (80.2%) without PA and 62 (19.8%) with PA (Table 1). The most frequently involved painful joints in pts with PA were knees (29.0%) and hips (25.8%), while the swollen ones were proximal interphalangeal joints of the hands (17.7%), knees (9.7%) and wrists (8.1%). According to BASDAI (Figure 1A), pts with PA showed a higher score 4.2 (2.4) and a lower percentage 58.1% had disease activity controlled (BASDAI<4) than total AS pts (3.1 [2.2] and 64.5%, respectively) and pts without PA (2.8 [2.1] and 70.1%, respectively). According to ASDAS-CRP (Figure 1B), mean (SD) score was 1.9 (1.1) for AS pts, 2.4 (1.1) for pts with PA and 1.8 (1.1) for pts without PA, while 29.4% AS pts, 14.5% pts with PA and 33.1% pts without PA had inactive disease (ASDAS-PCR<1.3). By combining both indices (ASDAS-CRP and BASDAI), 51.8% AS pts showed adequate control (inactive disease/remission) of disease activity, 29.0% of pts with PA and 57.4% of pts without PA.

Table 1. Baseline demographic and clinical characteristics of the AS pts

	AS (n=313)	AS without PA (n=251)	AS with PA (n=62)
Age (years), mean (SD)	50.4 (12.0)	50.1 (11.9)	51.5 (12.5)
Sex (male), n (%)	237 (75.7%)	193 (76.9%)	44 (71.0%)
Time since diagnosis (years), mean (SD)	15.5 (11.6)	15.4 (11.4)	16.0 (12.6)
Time from onset of symptoms to diagnosis (years), mean (SD)	5.0 (7.2)	4.9 (7.1)	5.6 (7.6)
Presence of HLA-B*27+, n (%)	245 (78.5%)	197 (78.8%)	48 (77.4%)
Family history of AS, n (%)	66 (21.1%)	55 (21.9%)	11 (17.7%)
Family history of psoriasis, n (%)	43 (13.7%)	34 (13.5%)	9 (14.5%)
Pts previously treated with bDMARD, n (%)	99 (31.6%)	79 (31.5%)	20 (32.3%)
Swollen joint count (0-66), mean (SD)	0.1 (0.9)	0.0 (0.0)	0.7 (1.9)
Painful joint count (0-68), mean (SD)	0.6 (2.4)	0.0 (0.0)	3.0 (4.7)
CRP levels (mg/l), mean (SD)	5.1 (8.2)	4.7 (7.6)	6.7 (10.3)
Active disease, n (%)*			
BASDAI ≥4	111 (35.5%)	26 (41.9%)	75 (29.9%)
ASDAS-CRP ≥2.1	133 (42.4%)	93 (37.1%)	40 (64.5%)
BASFI, mean (SD)	3.4 (2.7)	3.1 (2.6)	4.5 (2.8)
MASES index, mean (SD)	0.2 (0.8)	0.2 (0.7)	0.4 (1.2)
SPARCC index, mean (SD)	0.4 (1.1)	0.3 (1.0)	0.6 (1.4)
Pts perceived disease control (PASS), n (%)	270 (86.3%)	221 (88.0%)	49 (79.0%)
ASAS-HI, mean (SD)	5.8 (4.4)	5.4 (4.2)	7.6 (4.6)

*Refers to the percentage of pts with active disease according to BASDAI≥4 and ASDAS-CRP ≥2.1.

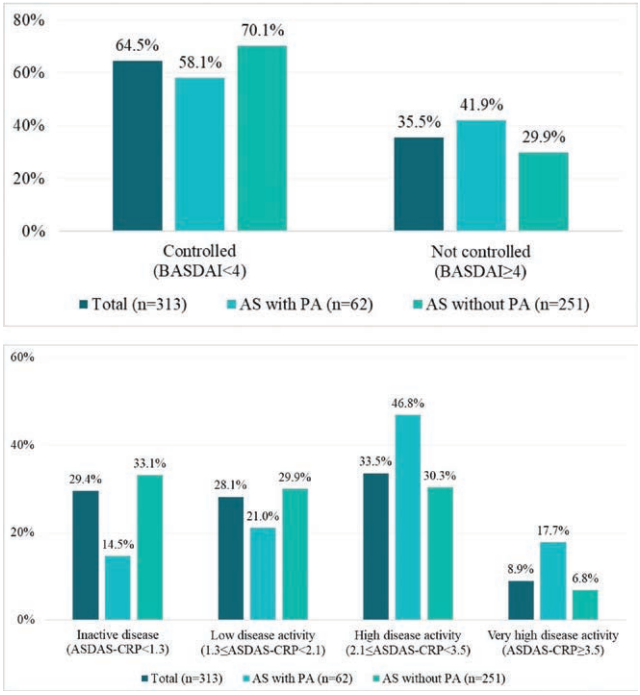


Figure 1. Disease status according to peripheral joints involvement**A)**Disease control according to BASDAI**B)**Disease activity according to ASDAS-CRP

Conclusion: Patients of the MiDAS study with peripheral disease showed higher disease activity and worse physical function, suggesting a severe and complex phenotype more than the one of the AS pts without PA.
REFERENCES:
[1] J Rheumatol 1993;20:526-91.
AS, ankylosing spondylitis; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score- C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; PA, peripheral arthritis.
Acknowledgements: We thank to MIDAS group investigators and patients included in the study.
Disclosure of Interests: Xavier Juanola Speakers bureau: Novartis, Abbvie, Pfizer, Lilly, Consultant of: Novartis, Lilly, Abbvie, Cristina Fernández-Carballido Speakers bureau: I have received lectures fees from Abbvie, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB., Consultant of: I have worked as a paid consultant for Abbvie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB., Alejandro Muñoz Jimenez.: None declared., Jesus Sanz Speakers bureau: Abbvie, Janssen-Cilag, Novartis, Lilly, Consultant of: Abbvie, Janssen-Cilag, Novartis, Lilly, Amgen, Grant/research support from: Abbvie, ANA URRUTICOECHEA-ARANA Speakers bureau: Abbvie, Bristol, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer and UCB, Consultant of: Abbvie, Bristol, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer and UCB, Patricia Moya Speakers bureau: Abbvie, Novartis and UCB, Consultant of: Roche, Joaquin Maria Belzunegui Otano Speakers bureau: Lilly, Amgen, Novartis, Abbvie, Janssen., Cristina Sanabra Employee of: Novartis employee, Carlos Sastré Employee of: Novartis employee.
DOI: 10.1136/annrheumdis-2021-eular.2357

AB0504 TOPOGRAPHY OF 18F-FDG PET/CT INFLAMMATORY SITES IN SPONDYLOARTHRITIS IN COMPARISON TO POLYMYALGIA RHEUMATICA AND TO PATIENTS WITHOUT INFLAMMATORY RHEUMATIC DISEASE

N. Giraud[1], M. Sondag[1], M. Chouk[1], F. Verhoeven[1], D. Wendling[1], C. Prati[1]. [1]*University Hospital Besancon, Rheumatology, BESANCON, France*

Background: Spondyloarthritis (SpA) is a common inflammatory rheumatism, characterized by axial and/or peripheral enthesitis. The positron emission tomography (PET/CT) allows the detection of inflammation.
Objectives: Our objective was to study the rhizomelic fixation with 18F-FDG (18-Fluorine deoxyglucose) PET/CT in SpA, compared to a Polymyalgia Rheumatica (PMR) group and to a control without rheumatological manifestations
Methods: Monocentric and retrospective study, including patients who have benefited from PET/CT. 2 groups of patients, with SpA on the one hand, and PMR on the other hand, fulfilling standard diagnostic criteria. A third group of controls (CN) benefiting from PET/CT in the context of assessment of a neoplasia. The rhizomelic fixations were evaluated according to the average of semi-quantitative scores. This in different rhizomelic sites, articular (gleno-humeral, coxo-femoral) and extra-articular (sub acromial (BSAD), trochanteric bursitis).
Results: 147 patients were included: 44 SpA, 50 PMR, and 53 CN. The rhizomelic fixations were significantly lower in SpA compared to PMR: on the pelvic girdle [0.31(0.7)

vs 1.15(1.04), p=1.2*10-10], the scapular girdle [0.15(0.44) vs. 1.35(1.2), p=7.09*10-15], the hip joints [0.27(0.62) vs 1.16(1.16), p=1.6*10-5], glenohumeral joints [0.18(0.49) vs. 1.71(1.04), p=4.75*10-12], the trochanteric bursae [0.36(0.77) vs 1.14(0.91), p=3.54*10-6], BSADs [0.11(0.38) vs. 0.98(1.24),p=4.63*10-5], or overall rhizomelic fixation. [0.23(0.59) vs. 1.26(1.14), p= 4.47*10-24]. The fixation was also significantly lower for SpA compared to CN, in trochanters [0.36(0.77) vs 0.58(0.68),p=3.54*10-6], at the glenohumeral joints [0.18(0.49) vs 0.58(0.66),p=3.27*10-5], pelvic girdle [0.31(0.7) vs. 0.49(0.67),p=0.0028] and scapular girdle [0.15(0.44) vs. 0.41(0.66), p=7.09*10-15] and on the global overall rhizomelic fixation [0.23(0.59) vs. 0.49(0.67), p=1.22*10-6].

Conclusion: Our study is the first to study the rhizomelic fixations with 18f-FDG in SpA, compared to another rheumatism inflammatory and controls. We found a lower fixation in SpA compared to PMR, confirming the major and specific rhizomelic fixation of PMR. We found a lower fixing of SpA compared to CN, without anatomical, articular or extra-articular systematization. SpA seems to be a condition with low uptake on 18f-FDG PET/CT, particularly at the rhizomelic level, compared to PMR and controls.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2444

AB0505 DISEASE FEATURES ASSOCIATED WITH A HIGH DISEASE IMPACT IN AXIAL SPONDYLOARTHRITIS: POST HOC ANALYSIS OF A SINGLE-CENTER CROSS-SECTIONAL STUDY

R. Queiró Silva[1], S. Alonso Castro[1], L. C. Charca Benavente[1], M. Pino Martínez[1], S. Burger[1], M. Alperi-López[1]. [1]*Hospital Universitario Central de Asturias, Rheumatology, OVIEDO, Spain*

Background: Currently available information on disease factors associated with a high life impact on axial spondyloarthritis (axSpA) is still very limited. Therefore, information on disease factors associated with a high life impact is crucial for the optimal management of this condition.

Objectives: To define disease factors associated with a high disease impact (HDI) in axSpA.

Methods: *Post hoc* analysis of a cross-sectional observational study conducted in 111 consecutive patients diagnosed with axSpA[1]. We defined the Assessment of SpondyloArthritis international Society-Health Index (ASAS HI) functioning and health status groups thresholds using the Ankylosing Spondylitis Disease Activity Score (ASDAS) as external anchor. To establish the ASAS HI cut-off, receiver operating characteristic (ROC) curves of the different activity categories of the ASDAS were constructed. A multivariate analysis was carried out to evaluate the disease factors associated with HDI.

Results: Median ASDAS was 2.1 (IQR: 1.5-2.7). Average score for ASAS-HI was 5.4 ± 3.8 (IQR: 3-8). ASAS HI values > 6, area under the ROC curve 0.86 (95%CI: 0.78-0.92), identified the patients belonging to the groups of high-very high disease activity. Among the study population, 69 patients had an ASAS HI ≤ 6 while 42 showed an ASAS HI > 6 (Table 1). In the multivariate regression model, HLA-B27 [OR 0.15 (95%CI: 0.05-0.48), p=0.001], NSAID intake [OR 5.4 (95%CI: 1.2-23.3), p=0.023, and a family history of SpA [OR 3.1 (95%CI: 1.01-10.6), p=0.043] were independently related to HDI.

Table 1. Disease features among patients with and without high disease impact

Feature	ASAS HI ≤ 6 (n: 69)	ASAS HI > 6 (n: 42)	P-values
Age, yrs (SD)	42.7 (11.2)	44.3 (9.8)	NS
Disease duration, yrs (SD)	7.6 (7.5)	7.8 (5.2)	NS
Men, n (%)	49 (71)	25 (59.5)	NS
Women, n (%)	20 (29)	17 (40.5)	NS
AS, n (%)	47 (68.1)	27 (64.3)	NS
Family history, n (%)	6 (8.7)	10 (23.8)	0.040
HLA-B27, n (%)	62 (89.9)	26 (61.9)	0.001
Education level:			
-Primary, n (%)	25 (36.2)	18 (42.9)	NS
-Secondary, n (%)	20 (29)	14 (33.3)	
-University, n (%)	24 (34.8)	10 (23.8)	
CVRF:			
-Smoking, n (%)	25 (36.2)	19 (45.2)	NS
-Obesity, n (%)	8 (11.6)	10 (23.8)	
-Diabetes, n (%)	3 (4.3)	3 (7.1)	
-HBP, n (%)	9 (13)	5 (11.9)	
-Dyslipidemia, n (%)	17 (24.6)	9 (21.4)	
Radiographic features:			
-Bilateral SI, n (%)	57 (82.6)	30 (71.4)	NS
-Squaring, n (%)	13 (18.8)	9 (21.4)	
-Syndesmophytes, n (%)	12 (17.4)	9 (21.4)	
SpA-associated features:			
-Enthesitis, n (%)	7 (10.1)	1 (2.4)	NS
-Anterior uveitis, n (%)	12 (17.4)	2 (2.8)	0.045
-IBD, n (%)	2 (2.9)	4 (9.5)	NS
Fibromyalgia, n (%)	0 (0)	3 (7.1)	0.052
Depression, n (%)	2 (2.9)	6 (14.3)	0.032
Treatments:			
-NSAID, n (%)	50 (72.5%)	39 (92.9)	0.013
-DMARDs, n (%)	4 (5.8%)	2 (4.8)	NS
-Biologic therapy, n (%)	40 (58)	27 (64.3)	NS

ASAS HI: Assessment of SpondyloArthritis international **Society**-Health Index, yrs: years, SD: standard deviation, AS: ankylosing spondylitis, HLA: human leukocyte antigen, CVRF: cardiovascular risk factors, HBP: high blood pressure, SI: sacroiliitis, SpA: spondyloarthritis, IBD: inflammatory bowel disease, NSAID: non-steroidal anti-inflammatory drugs, DMARDs: disease modifying antirheumatic drugs.

Conclusion: In this study, patients with regular NSAID intake and those with a positive family history of SpA were more likely to be in a high-impact category according to the ASAS HI. On the other hand, HLA-B27 carriers reduced that possibility by 85%. Our data may contribute to providing more personalized attention focused on patients` needs.

REFERENCES:

[1] Alonso S, Pardo E, Charca L, et al. Performance of the ASAS health index for the evaluation of spondyloarthritis in daily practice. J Rheumatol 2020; 47: 1483-1489.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2559

AB0506 PREVALENCE AND CLINICAL CHARACTERISTICS OF SPONDYLOARTHRITIS IN CENTRAL AMERICA AND CARIBBEAN (PRECAES)

A. Garcia Kutzbach[1,2,3], P. Camilo Estrella[4], V. Khoury[4], H. Alonzo[5], C. S. Pastelín[5], G. Guerra Batista[6], A. Ogdie[7]on behalf of AGAR team. [1]*Guatemalan Association Against Rheumatic Diseases (AGAR), Rheumatology, Guatemala City, Guatemala*; [2]*UFM School of Medicine, Internal Medicine - Rheumatology Section, Guatemala City, Guatemala*; [3]*Private Practice, Rheumatology, Guatemala City, Guatemala*; [4]*Private Practice, Rheumatology, Santiago de los Caballeros, Dominican Republic*; [5]*Private Practice, Rheumatology,Tegucigalpa, Honduras*; [6]*Private Practice, Rheumatology, Panama, Panama*; [7]*Perelman School of Medicine, University of Pennsylvania, Rheumatology, Philadelphia, United States of America*

Background: Spondyloarthritis (SpA) is a group of interrelated disorders: axial spondyloarthritis (Ankylosing Spondylitis [AS] /Non Radiographic Axial Spondyloarthritis [Nr-AxSpA]), psoriatic arthritis (PsA), reactive arthritis (ReA), inflammatory bowel disease-associated arthritis (IBD), and undifferentiated SpA (USpA).[1]

Objectives: The objectives of this study were: a) to examine the epidemiology, disease subsets, and clinical characteristics of patients with SpA in Central America and the Caribbean region; and b) to describe the natural history of these conditions in their acute and chronic forms, to determine clinical sub-types and severity.

Methods: PRECAES is a cross-sectional observational study, including patients from private rheumatology clinics in three Central American countries (Guatemala, Honduras and Panama) and one in the Caribbean (Dominican Republic). Patients were enrolled between April 25th, 2018 and July 31st, 2019. Inclusion criteria: SpA diagnosis fulfilling ASAS classification criteria, age 18 - 45 years, sign informed consent and willing to perform protocol procedures during a single visit. Exclusions: any other rheumatic diseases, malignancy or HIV.

Results: Each center identified 50 consecutive patients with SpA. The main reason for exclusion from this analysis was not meeting the age requirement (N=94). Therefore, we analyzed 25 from Dominican Republic (DR), 25 from Guatemala, 32 from Honduras and 24 from Panama.

When applying ASAS axial and peripheral SpA definitions, all countries had high number of AS Patients. Subclinical classification by country showed the most frequent diagnosis was AS (64.1%), followed by PsA (16%), ReA (9.4%), Undifferentiated SpA (7.5%), IBD associated arthritis (1.9%) and Nr-AxSpA (0.9%) (p<0.001); characteristics of patient population and sub-clinical classification by country, Table 1. When clinical manifestations were classified as axial or peripheral SpA, 70.7% were axial in the four countries.

Table 1. Patient population characteristics and Sub-clinical classification by Country

		Dominican Republic	Guatemala	Honduras	Panama	Total
Age Years	Number patients	25	25	32	24	106
	Mean Age	32.48	32.28	33.66	32.71	
	SD	8.45	7.63	8.91	6.34	
Gender	Female	6	9	13	8	36
	Male	19	16	19	16	70
Place of living	City	1	14	26	20	61
	Rural/outside city	24	11	6	4	45
Scholarity	Elementary	0	3	2	1	6
	High School	7	5	17	4	33
	Middle School	1	1	2	2	6
	University	17	16	11	17	61
Smoking Habit	Yes	2	2	5	1	10
Sub-clinical classification by country	USpA	1	5	1	1	**08 (7.5%)**
	ReA	2	6	1	1	**10 (9.4%)**
	Nr-AxSpA	0	1	0	0	**01 (0.9%)**
	AS	19	7	26	16	**68 (64.1%)**
	IBD associated arthritis	1	1	0	0	**02 (1.9%)**
	PsA	2	5	4	6	**17 (16%)**
	p < 0.001					

SD or ± = Standard DeviationUndifferentiated SpA (USpA), Reactive Arthritis (ReA), Nonradiographic Axial SpA (Nr-AxSpa), (AS), Inflammatory Bowel Disease-Associated Arthritis (IBD), Psoriatic Arthritis (PsA)

Time from onset symptoms to diagnosis ranged in years, from 3.15 (Guatemala) to 8.2 (Honduras), among the four countries. BASMI scores were higher in Honduras (mean 5.15) and lowest in Panama (mean 1.61). Of note, the time from symptom onset to diagnosis was also longest in Honduras.

NSAIDs and DMARDs were used in most countries. Glucocorticoids were rarely used in this population. Biologics are mainly used in Panama (16%), and Honduras (11%); only 8% of the enrolled patients in Dominican Republic and 2% in Guatemala.

Conclusion: The most prevalent SpA diagnosis in the region is Ankylosing Spondylitis. Patient diagnosis is delayed up to 8.2 years and only 2 to 16% of the patients receive a proper treatment with a biologic therapy.

This data invites to further investigation and brings opportunity to improve patients care.

REFERENCES:

[1] Rudwaleit, M. et al. The assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann. Rheum. Dis. 2011. 70, 25-31

Acknowledgements: Dr. Helga Garcia Ferrer for her thorough review of the abstract throughout the study.

Disclosure of Interests: Abraham Garcia Kutzbach Grant/research support from: Novartis Pharmaceutical Inc. for this PRECAES IIT study (CAIN457FGT01T)., Pablo Camilo Estrella Grant/research support from: Novartis Pharmaceutical Inc. for this PRECAES IIT study (CAIN457FGT01T)., Vianna Khoury Grant/research support from: Novartis Pharmaceutical Inc. for this PRECAES IIT study (CAIN457FGT01T)., Hugo Alonzo Grant/research support from: Novartis Pharmaceutical Inc. for this PRECAES IIT study (CAIN457FGT01T)., Carlos Santiago Pastelín Grant/research support from: Novartis Pharmaceutical Inc. for this PRECAES IIT study (CAIN457FGT01T)., Generoso Guerra Batista Grant/research support from: Novartis Pharmaceutical Inc. for this PRECAES IIT study (CAIN457FGT01T)., Alexis Ogdie Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Janssen, Novartis, Pfizer, Takeda Pharmaceutical Company and UCB, Grant/research support from: AbbVie, BMS, Celgene, Eli Lilly, Gilead, Galapagos, Janssen, Novartis, Pfizer ans USB.

DOI: 10.1136/annrheumdis-2021-eular.2775

AB0507 ASSESSMENT OF FIBRINOGEN TO ALBUMIN RATIO IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: CORRELATION WITH DISEASE ACTIVITY

M. Slouma[1,2], S. Bouzid[1,3], K. Lahmar[1,3], R. Dhahri[1,3], I. Gharsallah[1,3], L. Metoui[1,3], B. Louzir3. [1]*The Military Hospital of Tunis, Rheumatology, Tunis, Tunisia*; [2]*The Military Hospital of Tunis, Internal Medicine, Tunis, Tunisia*; [2]*The Military Hospital of Tunis, Internal Medicine, Tunis, Tunisia*

Background: Radiographic axial spondyloarthritis is a chronic inflammatory disease that involves the spine and the sacroiliac joints. No specific biomarker that reflects disease activity is yet available.

Objectives: This study aimed to assess the relationship between fibrinogen (Fib) to albumin (ALB) ratio (FAR) and disease activity in radiographic axial spondyloarthritis.

Methods: We performed a cross-sectional study including 51 patients with radiographic axial spondyloarthritis. Disease activity was assessed using Ankylosing Spondylitis Disease Activity Score (ASDAS). C-reactive protein (CRP), fibrinogen (Normal value: 2 -4g/L), erythrocyte sedimentation rate (ESR) and albumin levels (Normal value: 35 -50 g/L) were measured. The fibrinogen to albumin ratio (FAR) was calculated. We excluded patients with infectious disease, hematological disease, and those with malabsorption syndrome

Statistical analysis was performed using SPSS 26.

Results: The study included 43 males and 8 females with a mean age of 41.25 ± 10.97 years. The mean disease duration was 117.92 (85.4 months). The mean fibrinogen and albumin levels were 3.94 ± 1.24 g/L and 36.94 ± 5.89 g/L, respectively. Fibrinogen level was elevated in 45% patients and albumin levels was decreased in 51% cases. Mean FAR was 0.11 ± 0.44.

ESR levels were elevated in 67% with a mean of 40.22 ± 34.64 mm. CRP levels were high in 61% with a mean of 28.57 ± 33.25 mg/L. Mean ASDAS was 3.32 ± 1. 27 patients had very high disease activity (ASDAS>3.5).

Significant correlation was found between FAR and following parameters: ESR (r = 0.836, p< 0.001), CRP (r = 0.785, p < 0.001), and ASDAS (r = 0.463, P < 0.001).

The ability of FAR to distinguish patients with very high disease activity from those without very high disease activity was excellent, with Aire under the curve of 0.819. The optimal FAR cutoff value with the highest accuracy was 0,1065 with a sensitivity of 0,792 and specificity of 0,852.

Conclusion: Our study showed that fibrinogen to albumin ratio correlate with ESR, CRP and ASDAS. This finding suggests that this ratio may be a used to assess disease activity in radiographic axial spondyloarthritis (1).

REFERENCES:

[1] Liu M, Huang Y, Huang Z, Zhong Z, Deng W, Huang Z, et al. The role of fibrinogen to albumin ratio in ankylosing spondylitis: Correlation with disease activity. Clin Chim Acta. juin 2020;505:136-40.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2880

AB0508 PHYSICAL ACTIVITY IN TUNISIAN ADULTS WITH ANKYLOSING SPONDYLITIS

A. Feki[1], I. Sellami[2], R. Akrout[1], S. Ben Jemaa[1], Z. Gassara[1], M. Ezzeddine[1], M. H. Kallel[1], H. Fourati[1], S. Baklouti[1]. [1]*Hedi Chaker Hospital, Rheumatology, Sfax, Tunisia*; [2]*Hedi Chaker Hospital, Occupational medicine, Sfax, Tunisia*

Background: Physical activity (PA) is associated with multiple health-related benefits among the general population and adults with chronic diseases like Ankylosing spondylitis (AS) [1]. As known, AS affects primarily enthesis and can lead to loss of function and decreased mobility.

Objectives: The aim of this study was to explore the PA levels of adults with AS and to examine associations between PA, sociodemographic characteristics, immunological features, disease activity and treatment type.

Methods: Cross-sectional clinical and laboratory data were collected on 68 AS patients. BASDAI (Bath ankylosing spondylarthritis disease activity index) and BASFI (Bath ankylosing spondylarthritis functional index) were calculated. Physical activity was measured using IPAQ-SF (International Physical Activity Questionnaire-Short Form). Its items record the time spent on physical activity of three intensity levels (vigorous, moderate and walking) as well as the time spent on sitting (referred to as sedentary in this study) in the past week. Both continuous (expressed as metabolic equivalent of task (MET)-min /week) and categorical (3 levels proposed: low, moderate and high level of PA) scores of IPAQ-SF were determined. Sedentary time (median) was reported in minutes/week. A p value < 0.05 was considered significant.

Results: Cross-sectional clinical and laboratory data were collected on 68 AS patients. BASDAI (Bath ankylosing spondylarthritis disease activity index) and BASFI (Bath ankylosing spondylarthritis functional index) were calculated. Physical activity was measured using IPAQ-SF (International Physical Activity Questionnaire-Short Form). Its items record the time spent on physical activity of three intensity levels (vigorous, moderate and walking) as well as the time spent on sitting (referred to as sedentary in this study) in the past week. Both continuous (expressed as metabolic equivalent of task (MET)-min /week) and categorical (3 levels proposed: low, moderate and high level of PA) scores of IPAQ-SF were determined. Sedentary time (median) was reported in minutes/week. A p value < 0.05 was considered significant.

Conclusion: Our study proved that physical activity in people with AS decreased with age and activity disease with a concomitant increase in sedentary activity. Given the risks of developing secondary chronic disease as a result of low levels of physical activity, physical exercise should be recommended as part of comprehensive AS care.

REFERENCES:

[1] Conigliaro P, Triggianese P, Ippolito F, Lucchetti R, Chimenti MS, Perricone R. Insights on the Role of Physical Activity in Patients with Rheumatoid Arthritis. Drug Dev Res. 2014;75:S54–6.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3187

AB0509 FREQUENCY AND RISK FACTORS OF HIP INVOLVEMENT DURING SPONDYLOARTHRITIS IN MILITARY PATIENTS

L. Kharrat[1], M. Slouma[1], S. Rahmouni[1], R. Dhahri[1], I. Gharsallah[1], L. Metoui[1], B. Louzir[1]. [1]*The Military Hospital of Tunis, Rheumatology, Tunis, Tunisia*

Background: Hip involvement can reveal a spondyloarthritis (SA) or appear later. It hampers patient's life quality and can be responsible of significant handicap (1). Military patients are a special population. They are more exposed to physical stress which makes their SA characteristics quite different to other patients.

Objectives: We aimed to determine the frequency of hip involvement in SA and to study its characteristics and associated factors in military patients.

Methods: We conducted a cross-sectional study carried out in Rheumatology department of Military Hospital of Instruction of Tunis over a 10-year period (2010-2020) including SA patients meeting The Assessment of SpondyloArthritis international Society (ASAS). For each patient we collected the following informations: age, characteristics of hip involvement, ASDAS (Ankylosing Spondylitis Disease Activity Score), BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), BASMI (Bath Ankylosing Spondylitis Metrology Index) and BASRI (Bath Ankylosing Spondylitis Radiology Index). We also measured Erythrocyte Sedimentation rate (ESR) and C-reactive protein (CRP).

Results: One hundred forty-one patients were included. They were 103 men and 38 women. The mean age was 43.01± 12.9 years. The mean age at the onset was 34.28±12.05 years. The mean delay of the disease was 9.16±8.98 years.

The mean BASDAI and l'ASDAS-CRP were 3.89±2.29 and 3.07±1.83, respectively.

Hip involvement was noted in 35.5% of the cases (n=50). It was bilateral in 41 of the cases. The number of affected hips was thus 91. The mean delay between the onset of SA and the discovery of hip involvement was 32.24±53.58 months [0-264 months].

A significant difference was noted in the axial mobility between patients who have hip involvement and those who don't (BASMI was 3,8±2.45 *versus* 1,45±1.8, p<0.0001).

Moreover, functional impact was higher in patients with hip involvement (BASFI was 5.7±2.24 versus 3.45±2.86, p<0.0001).

Patients with hip involvement had significantly higher BASRI compared to patients with no hip involvement (5.79±3.17 *versus* 3.14±2.42, p<0.0001).

However, no difference was found between patients who have hip involvement and those who don't with these following parameters: ESR, CRP, BASDAI and ASDAS-CRP.

Conclusion: Our study showed that hip involvement is quite common in military SA patients. It is responsible of an important functional impact and it seems to be associated to a major limitation of axial mobility. Nevertheless, hip involvement was not associated neither to inflammation parameters levels nor to the disease activity, this suggest that hip involvement may progress independently of the disease activity in military patients due to physical stress and micro traumas.

REFERENCES:

[1] López-Medina C, Castro-Villegas MC, Collantes-Estévez E. Hip and Shoulder
Involvement and Their Management in Axial Spondyloarthritis: a Current Review. Curr
Rheumatol Rep. sept 2020;22(9):53.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3308

AB0510 THE ROLE OF BONE SCINTIGRAPHY FOR THE FOLLOW-UP EVALUATION OF INFLAMMATORY ACTIVITY IN PATIENTS WITH SERONEGATIVE SPONDYLOARTHRITIS

I. Borges[1], T. Barroso[2], F. Nunes[2], J. Caetano[2], B. Grima[2], J. Antonio Pereira Delgado Alves[2]. *[1]Hospital do Divino Espírito Santo de Ponta Delgada, E.P.E:R, Internal Medicine, Ponta Delgada, Portugal*; *[2]Hospital Professor Doutor Fernando da Fonseca E.P.E, Amadora, Internal Medicine, Lisboa, Portugal*

Background: The use of bone scintigraphy (Sc) in spondyloarthritis (SpA) as a technique for diagnosis, assessment of activity and treatment decision has been questioned by the scientific community. Due to its low cost compared to Magnetic Resonance Imaging - MRI (the gold standard)[1], some studies proposed to evaluate Sc's diagnostic accuracy. These studies have shown that Sc has a low diagnostic sensitivity of 50-55%[2]. Also, there is a poor correlation between symptoms and scintigraphic uptake[3]. We aimed to evaluate the use of Sc for management and follow-up of patients with SpA.

Objectives: To determine if Sc activity correlates with patients' complaints (peripheral and axial), inflammatory markers, disease activity scores and whether it influenced physicians' treatment decisions during the follow-up of the disease.

Methods: We performed a retrospective review of all patients at our department with SpA with at least one Sc from 2018 to 2020. The following variables were analyzed: demographic data, spondyloarthropathy subtype (ankylosing, enteropathic, psoriatic and undifferentiated SpA), axial or peripheral pain, Sc findings (inflammatory vs no-inflammatory activity), inflammatory markers (sedimentation rate - ESR and C-Reactive Protein - CRP), disease activity scores within one year since the Sc (Ankylosing Spondylitis Disease Activity Score with Erythrocyte Sedimentation Rate - ASDAS-ESR and Bath Ankylosing Spondylitis Disease Activity Index - BASDAI) and treatment at the time of the Sc (non-steroidal anti-inflammatory drugs, conventional synthetic disease-modifying antirheumatic drugs (DMARDs), target synthetic DMARDs and biologic DMARD. Treatment decisions (escalation, de-escalation or maintenance) in accordance to Sc results were also reviewed.

We used the non-parametric Mann-Whitney's U test for comparisons between ordinal or numerical variables. For correlations between categorical variables we used the Fisher's exact test and the $\chi 2$-independence test. Tests with $p < 0.05$ were statistically significant.

Results: Fifty-five patients were reviewed, 75% women; median age of 48 years. Seventy-one percent had ankylosing SpA, 15% enteropathic SpA, 5% psoriatic SpA, 5% undifferentiated and 4% reactive SpA. Sixty-two percent of the patients had both axial and peripheral pain and 24% only axial complaints. Sixty-two percent of the patients had a Sc with no inflammatory changes, 27% had peripheral and 25% had axial inflammatory changes; 15% had evidence of both peripheral and axial inflammation. For ankylosing SpA, the median ASDAS-ESR was 2.89 and according to the BASDAI, 66% had active disease. The median CRP and ESR in patients with inflammatory vs a normal Sc was not different (p=0.02 vs p=0.36, respectively). Similarly, Sc findings were not correlated with patients' axial (p=0.10) or peripheral pain (p=1.0), neither with the ASDAS-ESR (p=0.29) or the BASDAI (p=0.29). There was no correlation between inflammatory activity in Sc and the decision to maintain, escalate or de-escalate treatment (p=0.65), including the decision to start a biological DMARD (p=1.0) or to switch between biological DMARDs (p=0.19).

Conclusion: There was no correlation between Sc findings and ESR, patients' complaints, disease activity or treatment decisions. Considering previous research showing a low diagnostic sensitivity, our findings seem to support a limited role of bone Sc for the follow-up and management of patients with seronegative SpA.

REFERENCES:

[1] Khmelinskii N, Regel A, Baraliakos X. The Role of Imaging in Diagnosing Axial Spondyloarthritis. *Front Med*. 2018;5. doi:10.3389/fmed.2018.00106
[2] Poddubnyy D. Classification vs diagnostic criteria: the challenge of diagnosing axial spondyloarthritis. *Rheumatology*. 2020;59(Supplement_4):iv6-iv17. doi:10.1093/rheumatology/keaa250
[3] Shim JS, Kim C, Ryu JJ, Choi SJ. Correlation between TM joint disease and rheumatic diseases detected on bone scintigraphy and clinical factors. *Sci Rep*. 2020;10(1):4547. doi:10.1038/s41598-020-60804-x

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3340

AB0511

EFFECT OF SECUKINUMAB ON THE REDUCTION OF MYOCARDIAL DYSFUNCTION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

S. Lapshina[1], L. Feiskhanova[1]. [1]*Kazan State Medical University, Department of Hospital Therapy, Kazan, Russian Federation*

Background: In ankylosing spondylitis (AS), early subclinical changes in the myocardium mostly remain undiagnosed. The impact of genetic engineering biological therapy on these changes is also unclear.
Objectives: Aim: to establish the relationship between taking of secukinumab and changes in systolic and diastolic myocardial function in patients with AS.
Methods: 69 patients with AS were examined, of which the first group included 33 people (average age 38.8±4.74, 63.6% of men) who received the interleukin 17 inhibitor (IL17) - secukinumab, the second group - 36 people who did not receive biological therapy, average age 42.5±11 years, 66.7% of men. The control group included 40 healthy individuals, comparable in gender and age. Patients underwent tissue dopplerography of the heart and transthoracic echocardiography. The research materials were subjected to statistical processing using the program STATISTICA 10.0.
Results: The patients with AS had significantly higher left ventricular mass index and ejection fraction (p<0.01) compared to the control group. Moreover, among patients who do not take biological therapy, the indicators were the highest (tabl.1).

Table 1. Comparison of transthoracic echocardiography parameters in the study groups according to the Craskell-Wallis test.

Показатель	group 1	group 2	control group	p
LVMI	85 [81; 100]	93 [81,3; 114,2]	79,5 [72; 86,5]	p=0,002
EF	63 [62; 64]	64,5 [63; 66]	60 [59,5; 64,5]	p=0,003

LVMI – ventricular myocardial mass index, *EF – ejection fraction.*

A comparison of tissue dopplerography of the heart between the groups established statistically higher values of peak velocity of the ring of the mitral valve in early diastole (e'L) in the 1st group (14 [9,5; 14]) and control (13 [11; 15,5]) compared with the indicator of the second group (10,5 [8,3; 13]), p<0,01; the peak speed of movement of the septum in early diastole, (e'S) in patients with secukinumab is higher (11 [9; 11]) compared to 2th (8.1 [7; 12]) and control groups 10 [8.5; 11]), p<0.05, and in the 2nd group lower than in the control (p=0.03). Significant differences in the parameters were supported by a comparison of the frequency of detection of diastolic dysfunction in the study groups. Diastolic dysfunction was diagnosed only in this group - in 38.9%. Against the background of the use of secukinumab, an increase in the systolic function of the myocardium was revealed.
Conclusion: The patients with AS are characterized by a high frequency of subclinical heart dysfunction. Inhibition of IL17 can reduce diastolic dysfunction, which is confirmed by an improvement in myocardial contractility during secukinumab therapy.
REFERENCES:
[1] ankylosing spondylitis, spondylarthritis, diastolic myocardial dysfunction, secukinumab
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3474

AB0512

CLINICAL AND RADIOLOGICAL FEATURES OF SHOULDER INVOLVEMENT IN SPONDYLARTHRITIS

C. Ines[1], H. Ferjani[1], K. Maatallah[1], S. Miri[1], H. Hajji[1], M. Yasmine[1], D. Kaffel[1], W. Hamdi[1]on behalf of Rheumatology department of Med kassab institute of orthopaedics.. [1]*Manouba, Rheumatology, Mannouba, Tunisia*

Background: Peripheral joint involvement is frequent among patients with peripheral spondylarthritis (SA). However, the root joint involvement, such as hip involvement, has been described as being associated with axial spondylarthritis, while data for shoulder involvement are scarce. Cuff tendonitis and enthesitis are common features in the shoulder in patients with SA.
Objectives: This study aimed to identify the prevalence of shoulder involvement in SA patients and describe its clinical and radiological features.
Methods: We conducted a retrospective study including SA patients, all fulfilling the assessment of Spondyloarthritis International Society (ASAS) criteria.
For all patients, we collected the following data: Age, the clinical presentation of SA, the inflammatory biomarkers C-reactive protein (CRP), and the disease activity assessed by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).
Regarding shoulder involvement, we assessed the following items: tenderness, mobility, rotator cuff tests, as well as the results of X-ray and Ultrasound examination (US).
Results: We included one hundred and thirty-one SA patients (mean age 39,77 years). Among them, sixty-two percent were male. Ten percent of patients were smokers, 46,6% had the peripheral beginning of the disease. Fourteen patients complained of shoulder pain. The majority of them were male.
X-rays showed no abnormalities (n=2), while a destructive form was noted in (n=7).
Rotator cuff rupture or enthesopathy was also revealed by the reduction of subacromial space (n=5), condensation of the greater tuberosity (n=3), crooked aspect of the acromion (n=2), and Moloney's line disruption(n=1).
US showed no abnormalities (n=1), supraspinatus tendinopathy (n=5), supraspinatus transfixing tear (n=1), infraspinatus tendinopathy (n=2), supraspinatus enthesopathy (n=2), infraspinatus enthesopathy (n=1), moderate synovitis (n=1), subacromiodeltoid bursitis (n=1).
Shoulder involvement was correlated significantly with the peripheral beginning of SA (P < 0.05). There were no significant differences in gender, tobacco use, CRP value, and the disease activity between the two groups (P > 0.05).
Conclusion: The shoulder involvement was rare in our study. It is characterized by cuff tendonitis and enthesitis, especially in supraspinatus insertion. However, the glenohumeral synovitis was uncommon in our series, even in the peripheral form of the disease.
REFERENCES:
[1] Hip and Shoulder Involvement and Their Management in Axial Spondyloarthritis: a Current Review Clementina López-Medina1,2,3,4 & M. Carmen Castro-Villegas1,2,3 & Eduardo Collantes-Estévez1,2,3, 23 July 2020.
Acknowledgements: I would like to thank all the authors listed above, for they helped me make writing my first abstract less harder.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3503

AB0513

THE RELATIONSHIP OF PERIARTICULAR TISSUES LESIONS AND JOINTS DEGENERATIVE CHANGES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

G. Gainullina[1], E. Kirillova[1], D. Abdulganieva[1], E. Belousova[1], A. Odincova[2]. [1]*Kazan State Medical University, Therapy, Kazan, Russian Federation*; [2]*Republican Clinical Hospital, Gastroenterology, Kazan, Russian Federation*

Background: Inflammatory bowel diseases (IBD) are associated with a variety of extra-intestinal manifestations. The most frequent of these is joint involvement, which affects 16–33 % of IBD patients, whereas 5–10 % are affected by enthesitis [1, 2]. Recent studies have shown the superiority of ultrasound over clinical findings in the evaluation of joints and periarticular tissues [3].
Objectives: To assess of joint and entheseal involvement in patients with Crohn's disease (CD) and ulcerative colitis (UC) using ultrasound with Power Doppler.
Methods: We prospectively included 70 IBD patients into the study. Peripheral joints and entheses were imaged by ultrasound, using Samsung Accuvix A30 5-13 MHz linear array transducer. Ultrasound examination of 14 peripheral joints (hip, knee, ankle, shoulder, acromioclavicular, elbow, wrist) and 35 entheses was performed. Vascularization was assessed with Power Doppler (PD). Statistical analysis was done by Mann-Whitney test by "Statistica" software.
Results: In 70 patients UC was in 40 (57%), CD - in 30 (43%). The mean age of patients was 32 (27; 36) years. The mean duration of the disease was 48 (12; 84) months. The majority of patients had highly active disease: moderate and severe activity was observed in 47 (67%).
Osteophytes were found in 32 (46%) IBD pts, in 10 pts (14%) - osteophytes were found in three or more joints. We divided pts into two groups. In first group we included pts without degenerative changes in the joints, in the second - with identified osteophytes.
Osteophytes were found more often in the acromioclavicular joints - 13 pts (41%) and in the hip joints - 10 pts (31%). With the same frequency (9 pts), osteophytes were detected in the wrist, knee and ankle joints. The mean age of pts and mean duration of IBD were significantly higher in the second group patients (p = 0.00002 and p = 0.019).
Enthesitis (echogenicity reduction and thickening) without vascularization were detected in 26 patients of the first group (68%) and 29 patients of the second group (91%) (p = 0.009). The rate of vascularized enthesitis in the two groups was the same: enthesitis with vascularization were observed in 14 pts of the first group (37%) and 14 of the second group (44%) (p = 0.822). Structure damage (erosions and enthesophytis) was more frequent in the second group (p = 0.025 and p = 0.001). There were no significant differences in the incidence of tendinitis and tenosynovitis between two groups.
Conclusion: Joint and periarticular tissues damage in IBD patients increases with age and duration of the disease. The presence of degenerative changes in the joints is associated with more frequent detection of enthesitis and enthesopathies.
REFERENCES:
[1] The First European Evidence-based Consensus on Extra-Intestinal Manifestations in IBD. JCC. 2016; 10 (3): 239-254.

[2] Rovisco J, Duarte C, Batticcioto A et al. Hidden musculoskeletal involvement in inflammatory bowel disease: a multicenter ultrasound study. BMC Musculoskelet Disord. 2016; 17: 84.
[3] Yu-Fen Hsiao, Shu-Chen Wei, Cheng-Hsun Lu et al. Patients with Inflammatory Bowel Disease have Higher Sonographic Enthesitis Scores than Normal Individuals: Pilot Study in Taiwan. Journal of Medical Ultrasound. 2014 Dec; 22(4): 194-199.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3520

AB0514 PRELIMINARY DATA ON THE STUDY OF THE POSSIBILITY OF USING ULTRASOUND TO OBJECTIFY THE MOBILITY OF THE SPINE IN ANKYLOSING SPONDYLITIS

M. Kurbanmagomedov[1], K. Sakharova[1], A. Demina[1], S. Erdes[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Moscow, Clinic, Moscow, Russian Federation*

Background: Spinal damage with limited mobility requires the search for diagnostic methods that allow us to accurately and quantitatively assess the developing decline in function and track this change in dynamics. One of these possible methods is ultrasound examination of the spine, which was recently described in the article Yurdakul O. V. [1].
Objectives: to study the possibility of using ultrasound for dynamic monitoring of sagittal mobility of the spine in ankylosing spondylitis (AS).
Methods: Ultrasound of the spine was performed in 15 patients with AS according to the method described in the article Yurdakul O. V. - determination of the sonographic distance between the spinous processes C5-C6, Th11-Th12 and L4-L5 of the vertebra (initial - vertical position, and when tilted - maximum sagittal flexion). All patients underwent a double examination: at inclusion in the study and after 2 weeks. The average age of the patients was 40.8±11.4 years, and the average duration of the disease was 5.5±3.5 years. 93.3% of patients were positive for HLA-B27. All patients were treated with nonsteroidal anti-inflammatory drugs, and 9 (60%) had biological therapy. The differences (Δ) between the indicators obtained on the first day and after 2 weeks - were calculated and further compared.
Results: During 2 weeks of follow-up, ESR practically did not change (it was 16 [6;48], after 2 weeks 14 [6;27], p=0.45), CRP decreased by 3.5 times (22.3 [2.5;40.5] and 5.9 [3.0;23.7], p=0.4), BASDAI (7.2-3.1,p=0.003), ASDAS-CRP (3.7-2.2,p=0.001) and BASFI (5.5-2.5, p=0.001), but not BASMI 10 (24-22, p=0.18). There were also no significant changes in mobility indicators according to sonographic measurements for 2 weeks. However, the correlation analysis of the dynamics of indicators for the study period showed the following results (see the Table 1):

Table 1. Correlation (r) between spinal ultrasound parameters and AS activity indices and metrological indices at the beginning of the study and after 2 weeks.

Δ of the indicators	$\Delta_i C_5$-C_6	$\Delta_s C_5$-C_6	$\Delta_i Th_{11}$-Th_{12}	$\Delta_s Th_{11}$-Th_{12}	$\Delta_i L_4$-L_5	$\Delta_s L_4$-L_5
ΔESR	-0.5*	-0.4*	-0.3	-0.2	-0.5*	-0.4*
ΔCRP	-0.3	-0.1	-0.4	-0.5	-0.4*	-0.7*
ΔASDAS	-0/4	-0.5	0.1	-0.3	0.1	0.2
ΔBASDAI	-0.2	-0.1	-0.2	-0.3	-0.3*	-0.5*
ΔBASFI	-0.6*	-0.5*	-0.5	0.2	0.3	-0.3
ΔBASMI 10	-0.2	-0.1	-0.2	-0.3	-0.3*	-0.5*

Note: *-p<0.05, Δi - C5-6, Th11-12, L4-5, mm – the difference between the indicators obtained by ultrasound in the vertical position at admission and after 2 weeks, Δs – the difference between the indicators at maximum sagittal flexion.

A correlation was found between an increase in the interspinous distance in the cervical and lumbar spine and a decrease in the level of ESR, and in the lumbar spine - with CRP. There is also a significant relationship between the activity of AS according to the BASDAI index and the mobility of the spine at the level of L4-5, which was manifested by an increase in the interspinous distance with a decrease in the activity of the disease. Sonographic measurements of all three levels of the spine show a negative correlation with the combined metrological index BASMI 10, most significantly with the L4-5 level of the spine.
Conclusion: The method of ultrasound examination of spinal mobility in AS allows not only to objectify the indicators, but can also be used to monitor the function of the axial skeleton during follow-up.
REFERENCES:
[1] Yurdakul APA, e.a. Medicine: September 2018; doi: 10.1097/MD.0000000000012609.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3541

AB0515 MICRONUTRIENT DEFICIENCIES IN PATIENTS WITH SPONDYLOARTHRITIS: AGE AND GENDER IMPLICATIONS

P. Triggianese[1], F. Caso[2], A. D'antonio[1], P. Conigliaro[1], S. Ferrigno[1], L. Costa[2], M. Tasso[2], M. S. Chimenti[1], R. Perricone[1]. *[1]Rheumatology, Allergology and Clinical Immunology, Department of "Medicina dei Sistemi", University of Rome Tor Vergata, Roma, Italy*; *[2]Rheumatology Unit, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy*

Background: Micronutrient deficiencies (MNDs) are common among patients with chronic inflammatory diseases. These are associated with a pro-inflammatory status and co-morbidities, and influenced by several factors, such as age and gender.
Objectives: No any study has investigated MNDs and their correlation with gender in Spondyloarthritis (SpA). With this purpose, this study analyzed the occurrence of anemia and the status of ferritin (Fe), vitamin D [25(OH)D], vitamin B12 (B12), and folic acid (FA) in a cohort of patients with SpA.
Methods: Levels of Hb, Fe, 25(OH)D, B12, FA, were evaluated in 220 SpA outpatients (137 females and 83 age-matched males) with Psoriatic arthritis (PsA, n=110) and SpA (n=110). Disease activity was assessed by DAPSA or ASDAS-CRP as appropriate and functional status was evaluated with HAQ score. Body Mass Index (BMI) was selected as a metabolic clinic parameter.
Results: Male and female patients were similar for disease duration and severity as well as the distribution of diagnosis and treatments (Table 1). In males, BMI was higher than in females (P=0.03) and positively correlated with the age (P=0.01). In female patients, BMI directly correlated with HAQ (P=0.03). The prevalence of anemia (Hb<12) was 13.6% of the study cohort; half of anemic patients had PsA, the others had enteropathic SpA (ESpA). Anemia resulted almost wholly in female patients (99%). In the male group, Hb resulted inversely related to age (P=0.01) and CRP levels (P=0.008). Ferritin was lower in females than in males (P=0.0003). 25(OH)D deficiency (≤20 ng/ml) was present in 23.2% of the cohort: males had lower 25(OH)D than females (P=0.02). Among male patients, disease duration correlated positively with ferritin (P<0.001) and inversely with 25(OH)D (P=0.02). Low levels of serum B12 (≤200 pmol/l) were rare (13.2%), while deficiency in FA (≤4 ng/ml) was frequent (22%) and associated with B12 defect in 31% of cases, with almost similar occurrence in males and females. A diagnosis of ESpA occurred in 55% of cases with B12 deficiency and 62.5% of FA defect, without gender difference. Mean levels of ferritin, 25(OH)D, B12, and FA did not differ significantly between PsA and SpA patients.

Table 1. Data from the study population.

	Females (n=137)	Males (n=83)	*P*
Age (yrs; §)	**51.65 ± 13**	**52.9 ± 12.8**	***NS***
BMI (*)	**24 [17.2 - 50.2]**	**25.8 [19.6 - 43.6]**	**< 0.05**
CRP (mg/l; *)	**2.9 [0 - 53]**	**2 [0 - 61]**	***NS***
Hb (g/dl; §)	**13 ± 1.2**	**14.4 ± 1.4**	***NS***
Fe (mg/l; *)	**37 [2 - 148]**	**64 [4 - 452]**	**< 0.05**
25(OH)D (ng/ml; *)	**28.2 [5 - 67]**	**25 [5 - 50]**	**< 0.05**
Vitamin B12 (pmol/l; *)	**350 [60 - 990]**	**313 [47 - 797]**	***NS***
Folic Acid (ng/ml; *)	**7 [1.7 - 40]**	**6.9 [1.8 - 39]**	***NS***
PsA (N/%)	**73/68.23**	**34/31.77**	***NS***
SpA (N/%)	**64/41**	**49/59**	***NS***
Concomitant IBD (n/%)	**56/65.9**	**29/34.1**	***NS***
Disease duration (months; *)	**69 [6 - 540]**	**76.5 [3 - 768]**	***NS***
Low D.A. (N/%)	**62/45.25**	**47/56.6**	***NS***
Moderate-high D.A. (N/%)	**75/54.75**	**36/43.4**	***NS***
COXIB-inhibitors (N/%)	**21/15.4**	**8/9.6**	***NS***
cDMARDs monotherapy (N/%)	**35/25.5**	**10/12**	***NS***
bDMARDs (N/%)	**81/59.12**	**65/78.4**	***NS***

BMI, body mass index; CRP, C-reactive protein; Hb, haemoglobin; Fe, ferritin; 25(OH)D, vitamin D; PsA, psoriatic arthritis; SpA, spondyloarthritis; IBD, inflammatory bowel disease; D.A., disease activity; cDMARDs, conventional Disease Modifying Antirheumatic Drugs; bDMARDs, biological DMARDs; § mean ± SD; * median [min-max].

Conclusion: Our study describes for the first time the possibility of a relevant prevalence of MNDs in SpA patients. Furthermore, we show that MNDs could be also influenced by gender difference and age. Of note, our findings highlight the importance of a screening focused on MNDs in SpA patients. This could be key in optimizing management of SpA patients, in which inflammatory-dependent dysmetabolism is frequent.
REFERENCES:
[1] Yamamoto EA, Jørgensen TN. Relationships Between Vitamin D, Gut Microbiome, and Systemic Autoimmunity. Front Immunol. 2020;10:3141.
[2] Charoenngam N, Holick MF. Immunologic Effects of Vitamin D on Human Health and Disease. Nutrients. 2020;12:2097.
[3] Bañuls-Mirete M, Ogdie A, Guma M. Micronutrients: Essential Treatment for Inflammatory Arthritis? Curr Rheumatol Rep. 2020;22:87.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3687

AB0516

THE INCONSISTENCY IN THE ASSESSMENT OF SACROILIAC JOINTS MRI PERFORMED BY A BLINDED AND UNBLINDED RHEUMATOLOGISTS AND A RADIOLOGISTS AFTER AND WITHOUT SPECIAL MRI TRAINING

E. Vasilenko[1,2], I. Gaydukova[1], V. Mazurov[1], R. Samigullina[1], A. Dadalova[1], I. Crylov[3], A. Krylova[3]. [1]*North-Western State Medical University named after I. I. Mechnikov, St. Petersburg, Russia, Department of Therapy, Rheumatology, Examination of Temporary Disability and Quality of Medical Care named after E.E. Eichwald, St. Petersburg, Russian Federation*; [2]*Clinical Rheumatology Hospital №25, outpatient department, St. Petersburg, Russian Federation*; [3]*Clinical Rheumatology Hospital №25, radiology department, St. Petersburg, Russian Federation*

Background: Despite of the development the criteria for the diagnosis of axial spondyloarthritis (axSpA) the problem of late axSpA diagnostics is not resolved. The difficulties in the assessment of MRI sacroiliitis (SI) could be of the reasons of axSpA diagnostic delay.

Objectives: to evaluate the inconsistency in the assessment of sacroiliac joints MRI that was performed by a blinded and unblinded rheumatologists and a radiologists.

Methods: The assessment of 80 magnetic-resonance tomograms of sacroiliac joints (SIJ) was performed by 4 independent readers, one which was blinded to clinical data radiologist (BR), another radiologist was informed that the study was performed for axSpA (unblinded radiologist - UR), another 2 readers were blinded to diagnosis rheumatologists. One of the rheumatologists was trained in SIJ MRI (BTRh), another rheumatologist was not trained specially in MRI of SIJ (BURh). The study was carried out on the magnetic resonance tomography (GE Discovery MR750W 3.0T) in T1 and STIR regimens. 65 MRI were performed in pts that fulfilled the ASAS criteria for the axSpA and history of active SII (bone marrow edema) on previous SIJ MRI. According CT of SIJ 25 (38.5%) of these pts had nr-axSpA, 22 (33.8%) had SI grade II / III, in 18 (27.7%) of the pts SI grade IV was detected. 15 MRI scans were performed in healthy volunteers who did not meet the ASAS 2009 criteria at the time of the study and had no CT changes in SIJ.

The number of detected by each reader cases of active SII as defined by ASAS were analyzed with the calculation of the inter-reader reliability.

Results: There was found that there was inter-reader reliability between results of blinded and unblinded radiologists (73.8%) with statistical differences in the number of detected and undetected signs of SII ($p < 0.05$).

The inter-reader reliability scores between the unblinded rheumatologist and the radiologist were 97.5% and did not have statistically significant statistical differences ($p \geq 0.05$).

And for a trained rheumatologist and a blinded untrained rheumatologist it was 53.5% and had significant statistical differences ($p<0.05$).

The results of 4 readers SIJ MRI assessments are presented at Table 1.

Table 1. The results of MRI sacroiliitis assessments performed by blinded and unblinded radiologists and rheumatologists

	BR	UbR	BtRh	BURh
Revealed SII in axSpA (n = 65), n(%)	44 (67.7)*	64 (98.5)#	62(95.4)	26 (40)*
Undetected SII in axSpA (n = 65), n(15)	21(32.3)*	1(1,5)	3(4.6)	39(60)*
Revealed SII in controls (n = 15), n(%)	2 (13.3)*	3 (20) #	3(20)	1(6.7)*
Undetected SII in controls (n=15), n(%)	13(86.7)*	12(80) #	12(80)	14(93.3)*

*inter-reader reliability with the results of all another reader with $p<0.05$. # inter-reader reliability between unblinded radiologist (UR) and blinded treated rheumatologist (BtRh) with $p<0.05$. BURh – blinded untreated rheumatologist. BR – blinded radiologist.

Conclusion: The better agreement in inter-reader reliability in MRI of SIJ assessment was detected between unblinded radiologist and trained blinded rheumatologist. Blinded radiologist had shown lower inter-reader agreement with another specialists. The lowest of all inter-reader agreement had shown untrained blinded rheumatologist. Special MRI of SII assessment trainings for rheumatologists and radiologists are unmet need for the improvement of in-time axSpA diagnostics.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3861

AB0517

THE HIDDEN FACE OF SMOKING IN AXIAL SPONDYLOARTHRITIS

S. Bouden[1], L. Kharrat[1], A. Ben Tekaya[1], O. Saidane[1], R. Tekaya[1], I. Mahmoud[1], L. Abdelmoula[1]. [1]*Hospital Charles Nicolle, Rheumatology, Tunis, Tunisia*

Background: The deleterious effect of smoking on spondyloarthritis has been studied for several decades. Indeed, smoking increases inflammation and disease activity, hence, promotes bone damage.

Objectives: The aim of our study was to evaluate the clinical, biological and radiological impact of smoking on axial spondyloarthritis (axSpA).

Methods: We conducted a retrospective study including patients meeting the Assessment of SpondyloArthritis international Society (ASAS) criteria between 2000 and 2020.

The following parameters were collected: age, smoking, ASDAS, BASDAI, and BASFI. We also measured inflammatory biomarkers (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)).

Results: We included 138 patients. Sixty-eight per cent of them were males. The mean age was 45.73 ± 12.66 years. The mean age at the disease onset was 28.89 ± 12.54 years. The mean CRP was 33.38 ± 39.65 mg/dL. The mean BASDAI and ASDAS-CRP were 4.21 ±2.23 and 3.06 ± 1.26, respectively. The mean BASFI was 4.77 ± 2.58.

Fifty-one of our patients were smokers (37%). They were 48 men and 3 women. The mean pack-year was 45 ± 17.15.

Smokers had a significantly younger age of the disease onset (25.21 ± 11.37 *versus* 31.96 ± 12.67, p=0.009).

Moreover, patients who smoke Tabaco had developed significantly more ankylosis compared to patients who don't (p=0.026).

Osteoporosis was also more frequent in smoking patients (p=0.032).

However, no association was found between smoking and ESR, CRP, ASDAS-CRP, BASDAI and BASFI.

Conclusion: Our results reveal that smoking can be responsible of a younger axSpA onset, and can lead to more severe structural damages regardless the disease activity. This highlights the importance of smoking cessation in preventing early bone damage in axSpA.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3924

AB0518

ATHEROSCLEROTIC RISK IN PATIENTS WITH ANKYLOSING SPONDYLITIS: BIOMARKERS VERSUS SCORE

R. Dhahri[1], S. Miri[1], M. Slouma[1], B. Louzir[1], L. Metoui[1], I. Gharsallah[1]. [1]*The Military Hospital of Tunis, Rhumatology, Tunis, Tunisia*

Background: Chronic inflammatory rheumatic diseases are associated with a high cardiovascular risk. However, data in ankylosing spondylitis (AS) are still limited.

Objectives: The aim of our study was to assess the atherosclerotic risk in patients with AS, by comparing the Systematic coronary risk evaluation: SCORE, with biomarkers of atherosclerosis: High sensitivity C-reactive protein (Hs-CRP), LDL/HDL ratio and apoliprotein A1 (Apo A) /apolipoprotein B (Apo B) ratio.

Methods: We conducted a cross-sectional observational study of 40 patients with AS, over a period of 3 months. Socio-demographic data, clinical characteristics of the disease, as well as biological, radiological and therapeutic data were collected for each patient. Coagulated blood samples were collected following a 12-hour fast. Cardiovascular risk was considered high for Hs-CRP>3.0 mg/L [1], LDL/HDL> 3.5 in men and 3.0 in women [2], and ApoB/ApoA level>0.9 [3,4]. SCORE was calculated for all patients.

Results: The mean age of our population was 44±10 years. Male predominance was noted with a sex ratio =11.1. The mean ASDAS-CRP and BASDAI levels were 2.1±0.95 and 2.25±1.33. Thirty-two percent of the patients had a high risk of cardiovascular diseases according to Hs-CRP level, with an average of 10.7 mg/L. The mean LDL/HDL ratio was high in twenty-two percent of the patients. The mean value of ApoA1 and ApoB was respectively 1.3 g/l. and 0.9 g/l. Low values of Apo A1 were determined in 12.5% of the subjects, and high values of ApoB were found in 15% of subjects. The mean value of ApoA/ApoB ratio was 0.7. Ten percent of the studied subjects had an unfavourable ApoB/ApoA1. The predicted 10-year risk of CV mortality according to SCORE was high in 5% of the patients, very high in 2.5% and moderate in 35% of them. Over 17 patients with moderate, high and very high risk according to SCORE: Four patients (23.5%) had high LDL/HDL ratio, 8 (47%) had high waist/hip ratio, 5 (29.4%) had high Hs-CRP level, and 2 (11.7%) had high ApoB/ApoA ratio.

We found ApoB/ApoA to be positively correlated with Hs-CRP (r=0.31, p=0.05). The SCORE was correlated to the age at the onset of the disease (r=0.78, $p<10^{-3}$).

Conclusion: The atherosclerotic risk in our population ranged from 10 to 43%. SCORE presented with the highest percentage, making it more suitable for mass screening. Biomarkers on the other hand are more precise. Hs-CRP is biomarker to be included in daily practice, even when AS is in remission. Accuracy of the apoB/apoA ratio is significantly great and appears to be associated with inflammation.

REFERENCES:

[1] Myers GL, Rifai N, Tracy RP, Roberts WL, Alexander RW, Biasucci LM, et al. CDC/AHA Workshop on Markers of Inflammation and Cardiovascular Disease: Application to Clinical and Public Health Practice: Report From the

Laboratory Science Discussion Group. Circulation [Internet]. 2004 Dec 21 [cited 2020 Oct 20];110(25).
[2] Munoz. Lipoprotein ratios: Physiological significance and clinical usefulness in cardiovascular prevention. VHRM. 2009 Sep;757.
[3] Walldius G, Jungner I, Holme I, Aastveit AH, Kolar W, Steiner E. High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): a prospective study. The Lancet. 2001 Dec;358(9298):2026–33.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3938

AB0519 PHYSICAL ACTIVITY AND OBESITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

R. Dhahri[1], S. Miri[1], M. Slouma[1], B. Louzir[1], L. Metoui[1], I. Gharsallah[1]. [1]*The Military Hospital of Tunis, Rhumatology, Tunis, Tunisia*

Background: Ankylosing Spondylitis (AS) is associated with an increased cardiovascular risk. Obesity and limited activity in patients with AS may contribute to this cardiovascular risk.
Objectives: We aimed to evaluate physical Activity and obesity in patients with AS.
Methods: We conducted a cross-sectional observational study of 40 patients with AS, over a period of 3 months. We evaluated the level of physical activity using the IPAQ (International Physical Activity Questionnaire). We also measured body mass index (BMI), body fat percentage, waist circumference, hip circumference and their ratio in all patients.
Results: The mean age of our population was 44±10 years. A male predominance was noted with a sex ratio =11.1. The mean ASDAS-CRP and BASDAI levels were 2.1±0.95 and 2.25±1.33. The mean of IPAQ was 3900 MET minutes per week, with a median of 3069 and extremes of 339 and 11000. 45.5% of patients had moderate physical activity and 20% had low activity.The mean BMI was 26.5 + 4.7 kg/m^2. Twenty percent of patients were obese. The mean body fat percentage was 25% with a median of 23.7% and extremes of 8-46%. Forty-five percent of the patients had a high fat mass. The mean waist circumference was 95±13 cm, hip circumference 104±9.5 cm. The mean waist to hip ratio was 0.9±0.07. Thirty-seven percent of patients had a high waist to hip ratio. BMI and body fat percentage were negatively correlated with HDL level; (r=-0.365,p=0.024)and(r=-0.393,p=0.015) respectively.
Conclusion: The majority of our patients have moderate or low levels of physical activity. The increase in BMI and fat mass appear to be associated with disturbance of the lipid balance, with low HDL values.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4023

AB0520 PUBIC SYMPHYSIS INVOLVEMENT IN NON-RADIOGRAPHIC SPONDYLARTHRITIS

H. Ferjani[1], M. Moalla[1], K. Maatallah[1], D. Ben Nessib[1], W. Triki[1], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab institute of Orthopedics, Rheumatology, Manouba, Tunisia*

Background: Structural change within pubic symphysis (PS) occurs in 20–25% of patients with spondylarthritis (SpA). It occurs in all developmental stages, even in the early stages of the disease. Changes in the symphysis can sometimes precede spine and sacroiliac involvement. Radiological findings in PS were poorly described in the SpA, especially on its non-radiographic form (nr-axSpA).
Objectives: We aimed in this study to evaluate pubic symphyseal features in patients with a confirmed diagnosis of nr-axSpA and to assess the correlation of these changes with clinical and imaging features of nr-axSpA in these patients. We also focused on the relationship between parity and radiographic changes in pubic symphysis (PS).
Methods: We retrospectively reviewed the data of 40 patients diagnosed with nr-axSpA according to the ASAS criteria. Radiological-morphological changes of PS were assessed in pelvic radiography by two distinct rheumatologists. Grading symphysial involvement was made as follow: scores ranged from 0-4 per reading: grade 0 = normal; grade 1 = subtle irregularity and/or subchondral sclerosis, grade 2 = clear erosions, 3 = marked sclerosis, grade 4 = ankylosis.
For all patients, we calculated the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the BASRI (Bath Ankylosing Spondylitis Radiology Index).
For all patients, we recorded the sacroiliac changes showed by the previous pelvic radiography and/or the pelvic scanner and/or by magnetic resonance imaging (MRI).
Results: We enrolled forty patients with a sex-ratio H/F=1/3. Mean age of patients at diagnosis was 39,9 +/- 10,8 [17-59]. Forty percent of patients had peripheral enthesitis, and 45% had peripheral arthritis. BASDAI mean score was 4,63 +/- 0,9 [0-8,6]. HLA B-27 was present in 32,3% of cases. We noted radiographic changes in PS in 37,5% (15 patients): grade 1 (n=1), grade 2 (n=10), grade 3 (n=3) and grade 4 (n=1). There was not a significant difference between the sex group (p=0,85). A comparison of 2 groups (women with 3 children or more and women with less than 3 children) concluded that childbirth did not modify PS changes (p=0,9). Also, PS changes did not differ with age (p=0,5). There was no correlation between the BASRI value with the presence of PS changes nor with its grades (p=0,5 and p=0,89, respectively). Also, disease activity did not influence the PS involvement (p=0,4). Radiological findings in PS was not correlated with the sacroiliac features found on MRI or pelvic CT scan (p=0,59 and p=0,1).
Conclusion: In SpA criteria, PS changes were not considered. It can be an additional help in making the diagnosis. Interestingly, pubic symphysis may exist without sacroiliitis.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4147

Psoriatic arthritis – treatment

AB0521 EARLY REAL-WORLD EXPERIENCE OF TOFACITINIB FOR PSORIATIC ARTHRITIS: DATA FROM A UNITED STATES HEALTHCARE CLAIMS DATABASE

P. J. Mease[1,2], P. Young[3], D. C. Gruben[4], L. Fallon[5], R. Germino[6], A. Kavanaugh[7]. [1]*Swedish Medical Center/Providence St Joseph Health, Rheumatology Clinical Research Division, Seattle, WA, United States of America*; [2]*University of Washington School of Medicine, Rheumatology Clinical Research Division, Seattle, WA, United States of America*; [3]*Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America*; [4]*Pfizer Inc, Inflammation and Immunology, Groton, CT, United States of America*; [5]*Pfizer Inc, Inflammation and Immunology, Kirkland, QC, Canada*; [6]*Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America*; [7]*University of California, San Diego School of Medicine, Division of Rheumatology, Allergy, and Immunology, San Diego, CA, United States of America*

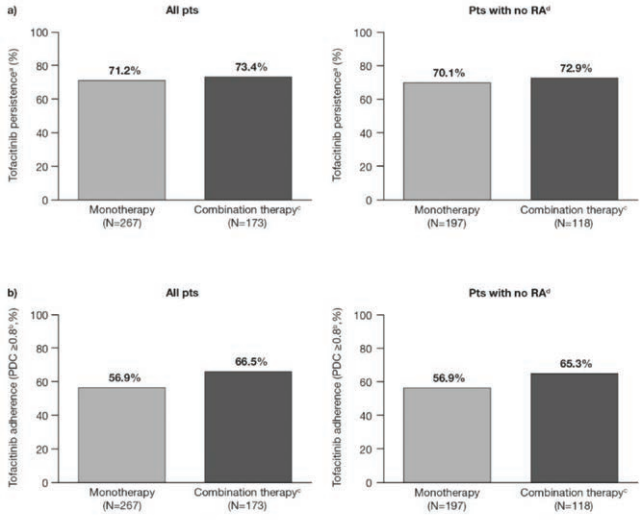
Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of psoriatic arthritis (PsA). It was approved in the United States (US) in December 2017 for use in combination with non-biologic disease-modifying antirheumatic drugs (DMARDs).
Objectives: This analysis of real-world data assessed demographic and baseline clinical characteristics, as well as treatment persistence/adherence, in patients (pts) with PsA who had newly initiated tofacitinib treatment.
Methods: This retrospective cohort study included pts aged ≥18 years in the Truven MarketScan™ US Commercial and Medicare Supplemental Claims and Encounters database with ≥1 tofacitinib claim (first = index) between 14 December 2017–30 April 2019, and PsA diagnoses (≥1 inpatient or ≥2 outpatient [30–365 days apart]) on or within 12 months pre-index. Pts were continuously enrolled for 12 months pre-index and 6 months post-index, with no pre-index claims for tofacitinib. Pt demographic and clinical characteristics on the day of index, history of advanced therapy treatment (≥1 claim for biologic DMARDs or apremilast within 12 months pre-index) and tofacitinib treatment regimen (monotherapy or combination therapy [≥1 claim for conventional synthetic DMARDs or apremilast on or within 90 days post-index]) were recorded. Outcomes at 6 months post-index included tofacitinib persistence (<60-day gap without tofacitinib treatment) and adherence (proportion of days covered ≥80% and medication possession ratio [data not shown]). A sensitivity check was performed by analysing a sub-cohort that excluded pts with a diagnosis of rheumatoid arthritis (RA) on or within 12 months pre-index and within 6 months post-index.
Results: Of 17 321 pts receiving tofacitinib, 440 pts met the inclusion criteria for the overall cohort, with 315 pts included in the sub-cohort. In the overall cohort, pts were mostly female, with a mean age of 52.3 years and a mean PsA duration of 738 days (data not shown). Most pts were exposed to ≥1 advanced therapy within 12 months pre-index (mean = 1.1; range = 0–4); most commonly secukinumab (Table 1). Overall, 60.7% of pts received monotherapy and 39.3% of pts received tofacitinib combination therapy post-index; most commonly methotrexate (data not shown). At 6 months post-index, persistence was similar in pts receiving tofacitinib monotherapy vs combination therapy; adherence was slightly lower in pts receiving tofacitinib monotherapy vs combination therapy (Figure 1). Results were similar in the sub-cohort (Table 1, Figure 1).

Table 1. History of advanced therapy on or within 12 months pre-index in pts with PsA

	All pts (N=440)	Pts with no RA[a] (N=315)
Pts exposed to advanced therapy, n (%)[b]		
Any advanced therapy[c]	336 (76.4)	241 (76.5)
Secukinumab	113 (25.7)	91 (28.9)
Adalimumab	93 (21.1)	58 (18.4)
Apremilast	81 (18.4)	59 (18.7)
Etanercept	70 (15.9)	47 (14.9)
Unique advanced therapy prescriptions		
Mean (SD)	1.1 (0.8)	1.1 (0.8)
Median (IQR)	1 (1–2)	1 (1–2)
Range	0–4	0–4
Number of unique advanced therapies, n (%)		
0	104 (23.6)	74 (23.5)
1	214 (48.6)	153 (48.6)
2	100 (22.7)	73 (23.2)
≥3	22 (5.0)	15 (4.8)

[a]Excludes pts with a diagnosis of RA on or within 12 months pre-index and within 6 months post-index; [b]Pts with ≥1 claim for biologic DMARDs or apremilast within 12 months pre-index; [c]Other advanced therapies reported in <10% of all pts were abatacept, certolizumab, golimumab, infliximab, ixekizumab and ustekinumabIQR, interquartile range; N, number of pts per cohort; n, number of pts per category; SD, standard deviation

Figure. Tofacitinib treatment a) persistence[a] and b) adherence (PDC ≥0.8)[b] in pts with PsA at 6 months post-index



[a]Pts with <60-day gap without tofacitinib treatment; [b]Pts achieving ≥80% of days covered; [c]Pts with ≥1 claim for a conventional synthetic DMARD or apremilast on or within 90 days post-index; [d]Excludes pts with a diagnosis of RA on or within 12 months pre-index and within 6 months post-index
N, number of pts in each cohort; PDC, proportion of days covered; SD, standard deviation

Figure 1

Conclusion: This analysis of US-based claims data indicated that pts newly initiated tofacitinib treatment an average of 2 years after PsA diagnosis, with the majority (>60%) of pts receiving tofacitinib as monotherapy. High levels of persistence and adherence to tofacitinib were observed 6 months after treatment initiation. Findings were similar when pts with PsA who also had a diagnosis of RA were excluded. Data were limited in that claims data cannot confirm that pts took the medication for which they filed a claim.

Acknowledgements: Study sponsored by Pfizer Inc. Medical writing support was provided by Gemma Turner, CMC Connect, and funded by Pfizer Inc.

Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Genentech, Janssen, Novartis, Pfizer Inc, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer Inc, Sun, UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer Inc, Sun, UCB, Pamela Young Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, David C Gruben Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lara Fallon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Rebecca Germino Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Arthur Kavanaugh Grant/research support from: Pfizer Inc.

DOI: 10.1136/annrheumdis-2021-eular.390

AB0522

SAFETY PROFILE OF UPADACITINIB UP TO 3 YEARS IN PATIENTS WITH PSORIATIC ARTHRITIS: AN INTEGRATED ANALYSIS FROM THE PHASE 3 PROGRAM

G. R. Burmester[1], K. Winthrop[2], R. Blanco[3], P. Nash[4], P. Goupille[5], V. F. Azevedo[6], C. Salvarani[7], A. Rubbert-Roth[8], E. Lesser[9], R. Mccaskill[9], J. Liu[9], B. Pierre-Louis[9], S. Walko[9], R. Lippe[10], A. Lertratanakul[9], E. Ruderman[11].
[1]Charité University Medicine, Rheumatology and Clinical Immunology, Berlin, Germany; *[2]Oregon Health and Science University, School of Medicine, Oregon, United States of America*; *[3]Hospital University Marques de Valdecilla, Division of Rheumatology, Santander, Spain*; *[4]Griffith University, School of Medicine, Brisbane, Australia*; *[5]University Hospital and CIC1415, Department of Rheumatology, Tours, France*; *[6]Federal University of Paraná, Department of Internal Medicine, Curitiba, Brazil*; *[7]Azienda USL-IRCCS di Reggio Emilia and Università di Modena e Reggio Emilia, Rheumatology Unit, Reggio Emilia, Italy*; *[8]Cantonal Clinic St Gallen, Division of Rheumatology, St Gallen, Switzerland*; *[9]AbbVie, Immunology, North Chicago, United States of America*; *[10]AbbVie Deutschland GmbH & Co. KG, Immunology, Wiesbaden, Germany*; *[11]Northwestern University, Feinberg School of Medicine, Chicago, United States of America*

Background: The efficacy and safety of upadacitinib (UPA), an oral Janus kinase inhibitor, in patients (pts) with active psoriatic arthritis (PsA) were demonstrated through 24 weeks in the phase 3 SELECT-PsA 1 and SELECT-PsA 2 placebo-controlled clinical trials.[1,2]

Objectives: To describe the long-term integrated safety profile of UPA relative to adalimumab (ADA) in pts with PsA treated in the SELECT program.

Methods: The SELECT-PsA program enrolled pts with prior inadequate response or intolerance to ≥1 non-biologic DMARD (SELECT-PsA 1) or ≥1 biologic DMARD (SELECT-PsA 2). Both trials include UPA 15 mg and 30 mg, and only SELECT-PsA 1 includes long-term comparison with ADA 40 mg every other week. Treatment-emergent adverse events (TEAEs: AE onset ≥first dose and ≤30 days after last dose for UPA and ≤70 days for ADA) were summarized for the following: pooled UPA 15; pooled UPA 30; and ADA. TEAEs are reported as exposure-adjusted event rates (EAERs; events/100 pts years [E/100 PY]) up to a cut-off date of 20 June 2020.

Results: 2257 pts received ≥1 dose of UPA 15 (N=907; 1247.2 PYs), UPA 30 (N=921; 1257.4 PYs), or ADA (N=429; 549.7 PYs), with median (max) exposures of 69 (155), 69 (154), and 68 (152) weeks, respectively. EAERs of TEAEs and serious AEs were generally similar between UPA 15 and ADA and higher with UPA 30; rates of AEs leading to study drug discontinuation were generally similar across all groups (Table 1). Similarly, rates of serious infection were comparable between UPA 15 and ADA and higher with UPA 30 (Figure 1 next page). The most common serious infection was pneumonia. Rates of herpes zoster were lower with UPA 15 than UPA 30 but higher than ADA. Most herpes zoster events involved a single dermatome; no events involved the central nervous system or other internal organs. Lower rates of opportunistic infections (OI) excluding tuberculosis were observed with UPA 15 vs UPA 30; the most common OI was mucosal candida infection. Malignancies were reported at similar rates across all treatment groups; no events of lymphoma were reported. Age-gender-adjusted standardized incidence ratios for malignancies excluding NMSC indicated no increased risk with UPA compared to the general population. Rates of adjudicated major adverse cardiovascular events and venous thromboembolic events were ≤0.3 E/100 PY for both UPA arms; all pts had ≥1 risk factor. One adjudicated gastrointestinal perforation was reported with UPA 15.

Table 1. Overall Treatment-emergent AEs for Upadacitinib and Adalimumab (E/100 PY [95% CI])

	UPA 15 mg QD N=907 (1247.2 PY)	UPA 30 mg QD N=921 (1257.4 PY)	ADA 40 mg EOW N=429 (549.7 PY)
AEs	263.9 (254.9, 272.9)	321.5 (311.6, 331.5)	286.5 (272.4, 300.7)
Serious AEs	10.3 (8.6, 12.1)	13.2 (11.2, 15.2)	9.6 (7.0, 12.2)
AE leading to discontinuation	6.7 (5.2, 8.1)	7.8 (6.2, 9.3)	7.8 (5.5, 10.2)
Deaths[a]	0.2 (-0.1, 0.4)	0.2 (-0.0, 0.5)	0.2 (-0.2, 0.5)

[a]Deaths included non-treatment emergent deaths: UPA 15, 1; UPA 30, 1.ADA, adalimumab; AE, adverse event; CI, confidence interval; E, event; EOW, every other week; PY, patient years; QD, once daily; UPA, upadacitinib.

Hepatic disorders were mostly transient, non-serious transaminase increases. Creatine phosphokinase elevations were reported more frequently with UPA 30 vs UPA 15; most were asymptomatic with no rhabdomyolysis reported. AEs of anemia, neutropenia, and lymphopenia were generally mild or moderate, non-serious. Except for rates of lymphopenia (higher with UPA 15), hepatic disorders, and neutropenia (both higher with ADA), lab-related TEAEs occurred at generally consistent rates between UPA 15 and ADA. Study drug discontinuation due to lab-related TEAEs was uncommon.

Conclusion: The safety profiles of UPA 15 and ADA were generally similar; the rates of most AEs were higher with UPA 30 compared with ADA. Through the cut-off date, the safety profile of UPA 15 and UPA 30 in PsA pts demonstrated consistent results compared to what has been observed with UPA in rheumatoid arthritis.[3]

REFERENCES:

[1] McInnes IB et al. *Ann Rheum Dis*, 2020; 79:12.
[2] Mease PJ et al. *Ann Rheum Dis*, 2020.
[3] Cohen SB et al. *Ann Rheum Dis*, 2020.

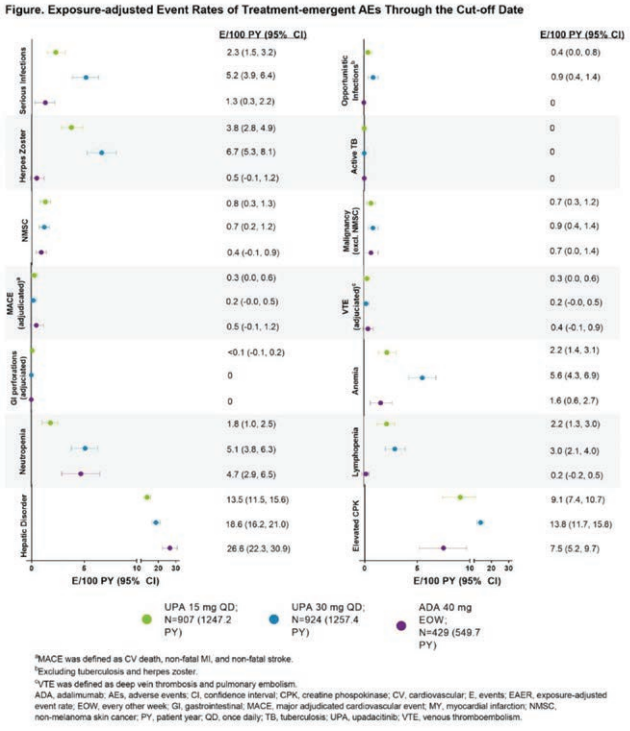


Figure 1

Acknowledgements: AbbVie and the authors thank the patients, study sites, and investigators who participated in this clinical trial. AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. No honoraria or payments were made for authorship. Medical writing support was provided by Ramona Vladea, PhD of AbbVie Inc.

Disclosure of Interests: Gerd Rüdiger Burmester Speakers bureau: AbbVie, Gilead, Lilly, Pfizer, Consultant of: AbbVie, Gilead, Lilly, Pfizer, Kevin Winthrop Consultant of: UCB Pharma, Pfizer, Bristol-Myers Squibb, Eli Lilly, AbbVie, Gilead, Galapagos, and Roche, Grant/research support from: UCB Pharma, Pfizer, Bristol-Myers Squibb, Eli Lilly, AbbVie, Gilead, Galapagos, and Roche, Ricardo Blanco Consultant of: Abbvie, Lilly, Novartis, Pfizer, Roche, Bristol-Myers, Janssen, and MSD, Grant/research support from: Abbvie, MSD and Roche, Peter Nash Consultant of: AbbVie, BMS, Roche, Pfizer, Janssen, Amgen, Sanofi-Aventis, UCB, Eli Lilly, Novartis, and Celgene, Grant/research support from: AbbVie, BMS, Roche, Pfizer, Janssen, Amgen, Sanofi-Aventis, UCB, Eli Lilly, Novartis, and Celgene, Philippe Goupille Consultant of: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Grant/research support from: AbbVie, Amgen, Biogen, BMS, Celgene, Chugai, Janssen, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Valderilio F Azevedo Consultant of: AbbVie, BMS, Pfizer, Janssen, Amgen, Novartis, Eli Lilly, UCB, Celltrion and GSK, Grant/research support from: AbbVie, BMS, Pfizer, Janssen, Amgen, Novartis, Eli Lilly, UCB, Celltrion and GSK, Carlo Salvarani Consultant of: Roche, Sanofi-Genzyme, AbbVie, Pfizer, Lilly, Novartis, Amgen, Grant/research support from: Roche, Sanofi-Genzyme, AbbVie, Pfizer, Lilly, Novartis, Amgen, Andrea Rubbert-Roth Consultant of: AbbVie, BMS, Chugai, Roche, Gilead, Janssen, Lilly, Sanofi, Amgen, Novartis, Grant/research support from: AbbVie, BMS, Chugai, Roche, Gilead, Janssen, Lilly, Sanofi, Amgen, Novartis, Elizabeth Lesser Shareholder of: AbbVie, Employee of: AbbVie, Reva McCaskill Shareholder of: AbbVie, Employee of: AbbVie, Jianzhong Liu Shareholder of: AbbVie, Employee of: AbbVie, Bosny Pierre-Louis Shareholder of: AbbVie, Employee of: AbbVie, Sandra Walko Shareholder of: AbbVie, Employee of: AbbVie, Ralph Lippe Shareholder of: AbbVie, Employee of: AbbVie, Apinya Lertratanakul Shareholder of: AbbVie, Employee of: AbbVie, Eric Ruderman Consultant of: AbbVie, Amgen, Gilead, Janssen, Lilly, Novartis, and Pfizer.

DOI: 10.1136/annrheumdis-2021-eular.395

AB0523

LONG-TERM SAFETY AND EFFECTIVENESS OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS AT 56 WEEKS FROM THE SELECT-PsA 1 STUDY

I. McInnes[1], K. Kato[2], M. Magrey[3], J. F. Merola[4,5], M. Kishimoto[6], C. F. Pacheco Tena[7], D. Haaland[8,9], L. Chen[2], Y. Duan[2], P. Zueger[2], J. Liu[2], R. Lippe[10], A. Pangan[2], F. Behrens[11]. [1]*University of Glasgow, College of Medical Veterinary and Life Sciences, Glasgow, United Kingdom*; [2]*AbbVie, Immunology, North Chicago, United States of America*; [3]*MetroHealth Medical Center, Case Western Reserve University School of Medicine, Cleveland, United States of America*; [4]*Harvard Medical School, Division of Rheumatology, Boston, United States of America*; [5]*Brigham and Women's Hospital, Division of Rheumatology, Immunology and Allergy, Boston, United States of America*; [6]*Kyorin University School of Medicine, Department of Nephrology and Rheumatology, Tokyo, Japan*; [7]*Universidad Autonoma de Chihuahua, Facultad de Medicina, Chihuahua, Mexico*; [8]*McMaster University, Hamilton, Canada*; [9]*The Waterside Clinic, Barrie, Canada*; [10]*AbbVie Deutschland GmbH & Co. KG, Immunology, Wiesbaden, Germany*; [11]*Goethe University & Fraunhofer IME-TMP and CIMD, Frankfurt, Germany*

Background: In the SELECT-PsA 1 study, through 24 weeks (wks), once daily upadacitinib 15 mg (UPA15) and 30 mg (UPA30) showed improvements in musculoskeletal symptoms, psoriasis, physical function, pain, fatigue, and quality of life, as well as inhibition of radiographic progression in patients (pts) with psoriatic arthritis (PsA) and inadequate response or intolerance to ≥1 non-biologic disease-modifying antirheumatic drug (DMARD).[1]

Objectives: To report the efficacy and safety of UPA vs adalimumab (ADA) up to 56 wks from the ongoing long-term extension of SELECT-PsA 1.

Methods: Pts received UPA15 or UPA30, ADA 40mg every other wk for 56 wks, or PBO through wk 24 switched thereafter to either UPA15 or UPA30 until wk 56. Efficacy endpoints as listed and defined in the Table 1 were analyzed at wk 56. Results for binary endpoints are based on non-responder imputation analysis; treatments were compared using the Cochran-Mantel-Haenszel test. Results for non-radiographic continuous endpoints are based on mixed model repeated measures model based on as observed data. Radiographic endpoints were analyzed based on linear extrapolation. Treatment-emergent adverse events (TEAEs) per 100 pt years (PY) were summarized for pts who received ≥1 dose of study drug.

Table 1. Efficacy Endpoints at Week 56

Endpoint	PBO → UPA15	PBO → UPA30	UPA15	UPA30	ADA
ACR20, %	73.0	74.1	74.4	74.7#	68.5
ACR50, %	54.5	60.4	59.7*	60.5#	51.3
ACR70, %	29.9	35.8	40.6*	43.7#	31.2
Minimal Disease Activity, %	29.4	35.8	44.8	47.3#	39.6
PASI75[a], %	58.3	60.2	65.4	63.3	61.1
PASI90[a], %	41.7	53.7	49.1	49.5	46.9
PASI100[a], %	22.3	38.9	34.6	39.5	31.3
Resolution of enthesitis by Leeds Enthesitis Index[b], %	38.1	45.5	59.3	58.1	54.0
Resolution of dactylitis by Leeds Dactylitis Index[c], %	47.7	59.0	75.0	74.8	74.0
Δ from BL in Bath Ankylosing Spondylitis Disease Activity Index[d]	-3.1	-3.1	-3.3	-3.2	-2.8
Δ from BL in modified total Sharp/van der Heijde Score (mTSS)	0.44[e]		-0.05†	0.02‡	-0.06

* and †, p≤0.05; for UPA15 vs ADA and PBO, respectively; # and ‡, p≤0.05; for UPA30 vs ADA and PBO, respectively.[a] for pts with psoriasis affecting ≥3% of body surface area at BL. [b] for pts with LEI >0 at BL. [c] for pts with LDI >0 at BL. [d] for pts with psoriatic spondylitis at BL. [e]pooled PBO.ACR20/50/70, ≥20%/50%/70% improvement in American College of Rheumatology criteria; ADA, adalimumab; BL, baseline; PASI75/90/100, ≥75%/90%/100% improvement in Psoriasis Area and Severity Index; PBO, placebo; pts, patients; UPA, upadacitinib.

Results: Of 1704 pts who received ≥1 dose of study drug, 1419 (83.2%) completed 56 wks of treatment on study drug. Across all treatment groups, the proportions of pts who had achieved ACR20/50/70, MDA, PASI75/90/100, resolution

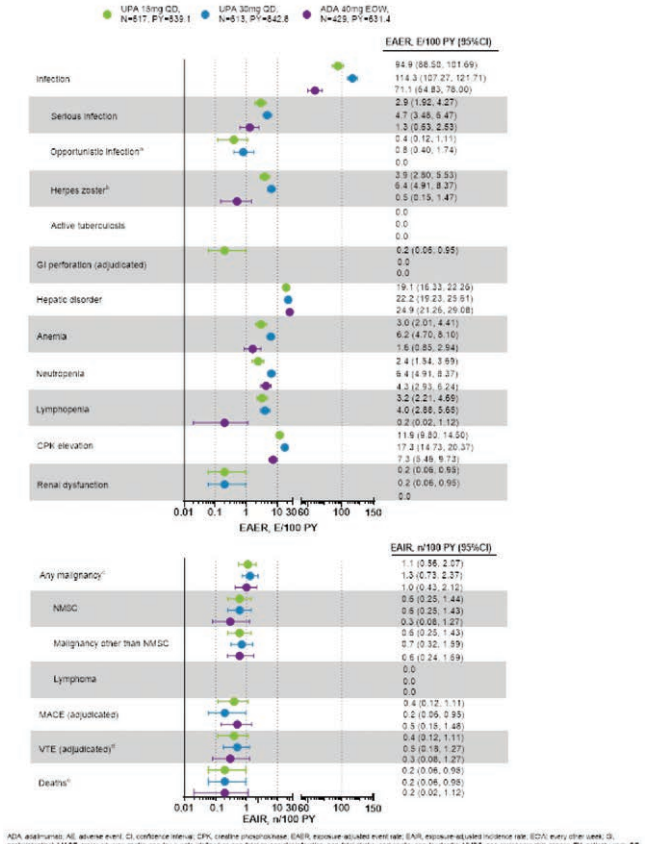
of enthesitis, and resolution of dactylitis were maintained or further improved from wk 24[1] through wk 56; these proportions were generally greater for pts originally randomized to UPA vs ADA (Table 1). At wk 56, mean change from BL in mTSS was similar with UPA15, UPA30, and ADA. Improvements in pts who switched from PBO to UPA were generally similar to those originally randomized to UPA at wk 56. Through wk 56, the rates of TEAEs and serious AEs, including serious infections, were similar in the UPA15 and ADA arms and higher with UPA30 (Figure 1). The rate of herpes zoster was higher with UPA vs ADA in a dose-dependent manner. Malignancies were reported at similar rates among all treatment groups. Adjudicated venous thromboembolic events and major adverse cardiovascular events were reported in all groups with comparable rates. Two deaths were reported with UPA15, 2 with UPA30, and 1 with ADA; 1 death was reported with PBO during the 24-wk PBO-controlled period.

Conclusion: Efficacy responses were maintained or further improved with UPA15 and UPA30 over 56 wks and were numerically higher vs ADA. The inhibition of radiographic progression was maintained at wk 56 and was similar with UPA and ADA. At wk 56, improvements in efficacy were observed in pts who switched from PBO to UPA. No new safety findings were observed with longer exposure to UPA.

REFERENCES:

[1] McInnes IB et al. *Ann Rheum Dis*, 2020; 79:12

Figure. Exposure-adjusted Event and Incidence Rates of Treatment-emergent AEs Through Week 56



ADA, adalimumab; AE, adverse event; CI, confidence interval; CPK, creatine phosphokinase; EAER, exposure-adjusted event rate; EAIR, exposure-adjusted incidence rate; EOW, every other week; GI, gastrointestinal; MACE, major adverse cardiovascular events, defined as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death; NMSC, non-melanoma skin cancer; PY, patient years; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolism (defined as deep vein thrombosis [DVT] and pulmonary embolism [PE])

*Opportunistic infections excluding tuberculosis and herpes zoster; UPA15: one event each of candida urethritis, bronchopulmonary aspergillosis, and oral fungal infection; UPA30: one event each of cytomegalovirus infection, oropharyngeal candidiasis, and pneumocystis jirovecii pneumonia, and four events of oral fungal infection.

†Herpes zoster: most events were mild or moderate in severity, limited to 1 dermatome, and did not lead to study drug discontinuation.

‡UPA15: 4 basal cell carcinomas, 2 squamous cell carcinoma of skin, and 1 event each of endometrial adenocarcinoma, lung adenocarcinoma, lung cancer metastatic, malignant melanoma, and neuroendocrine carcinoma; UPA30: 2 basal cell carcinomas, 2 squamous cell carcinoma of skin, and 1 event each of adenocarcinoma of colon, Bowen's disease, breast cancer, clear cell renal cell carcinoma, invasive breast carcinoma, lung adenocarcinoma, and plasma cell myelomas; ADA: 2 basal cell carcinomas, and 1 event each of colon cancer metastatic, ovarian cancer, pancreatic carcinoma metastatic, and uterine cancer.

§10 VTEs were reported in 9 patients. UPA15: 1 DVT, 1 PE. 1 pt had had concurrent DVT and PE; UPA30: 1 DVT, 3 PEs; ADA: 2 DVTs

¶Deaths: UPA15: 1 due to metastatic lung cancer and 1 due to lower respiratory tract infection; UPA30: 1 due to corona virus infection and 1 due to interstitial lung disease; ADA: traffic accident. One death was reported in the placebo group during the 24-week placebo-controlled period in a patient who was driving and experienced an unspecified emergency.

Figure 1

Acknowledgements: AbbVie and the authors thank the patients, study sites, and investigators who participated in this clinical trial. AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. No honoraria or payments were made for authorship. Medical writing support was provided by Ramona Vladea, PhD of AbbVie Inc.

Disclosure of Interests: Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sanofi Regeneron, UCB Pharma, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sanofi Regeneron, UCB Pharma, Koji Kato Shareholder of: AbbVie, Employee of: AbbVie, Marina Magrey Consultant of: UCB, Novartis, Eli Lilly, Pfizer and Janssen, Grant/research support from: Amgen, AbbVie, and UCB Pharma, Joseph F. Merola Consultant of: Merck, Bristol-Myers Squibb, AbbVie, Dermavant, Eli Lilly, Novartis, Janssen, UCB, Celgene, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Sorono, Avotres and Leo Pharma, Mitsumasa Kishimoto Consultant of: AbbVie, Amgen-Astellas BioPharma, Asahi-Kasei Pharma, Astellas, Ayumi Pharma, BMS, Celgene, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Kyowa Kirin, Novartis, Ono Pharma, Pfizer, Tanabe-Mitsubishi, Teijin Pharma, and UCB Pharma, Cesar Francisco Pacheco Tena Consultant of: Eli Lilly, AbbVie, Roche, Pfizer, Janssen, Astra-Zeneca, UCB, Gilead, R-Pharm, Sanofi Regeneron, Grant/research support from: Eli Lilly, AbbVie, Roche, Pfizer, Janssen, Astra-Zeneca, UCB, Gilead, R-Pharm, Sanofi Regeneron, Derek Haaland Speakers bureau: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Novartis, Pfizer, Roche, Sanofi Genzyme, Takeda, Consultant of: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi Genzyme, Takeda, UCB, Grant/research support from: AbbVie, Adiga Life-Sciences, Amgen, Bristol-Myers Squibb, CanFite Biopharma, Celgene, Eli Lilly, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, UCB, Liang Chen Shareholder of: AbbVie, Employee of: AbbVie, Yuanyuan Duan Shareholder of: AbbVie, Employee of: AbbVie, Patrick Zueger Shareholder of: AbbVie, Employee of: AbbVie, Jianzhong Liu Shareholder of: AbbVie, Employee of: AbbVie, Ralph Lippe Shareholder of: AbbVie, Employee of: AbbVie, Aileen Pangan Shareholder of: AbbVie, Employee of: AbbVie, Frank Behrens Consultant of: Pfizer, AbbVie, Sanofi, Lilly, Novartis, Genzyme, Boehringer, Janssen, MSD, Celgene, Roche, Chugai, BMS, UCB Pharma, Grant/research support from: Pfizer, Janssen, Chugai, Celgene and Roche.

DOI: 10.1136/annrheumdis-2021-eular.397

AB0524

EFFICACY OF GUSELKUMAB ACROSS BASDAI COMPONENTS IN TREATING AXIAL-RELATED SYMPTOMS OF PSORIATIC ARTHRITIS: RESULTS FROM TWO PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED STUDIES

F. Behrens[1], P. J. Mease[2], P. Helliwell[3], M. Shawi[4], W. Noel[5], S. D. Chakravarty[6,7], A. Kollmeier[8], X. L. Xu[8], S. Xu[9], Y. Wang[9], X. Baraliakos[10].

[1]Goeth University, Rheumatology and Fraunhofer ITMP - Translational Medicine and Pharmacology, Frankfurt, United States of America; *[2]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America*; *[3]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[4]Janssen Global Services, LLC, Immunology, Horsham, United States of America*; *[5]Janssen Scientific Affairs, LLC, Immunology, Brussels, Belgium*; *[6]Janssen Scientific Affairs, LLC, Immunology, Horsham, United States of America*; *[7]Drexel University College of Medicine, Medicine, Philadelphia, United States of America*; *[8]Janssen Research & Development, LLC, Immunology, San Diego, United States of America*; *[9]Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; *[10]Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany*

Background: The monoclonal antibody guselkumab (GUS; anti- IL-23p19-subunit) is approved to treat psoriatic arthritis (PsA). Post hoc analyses of DISCOVER-1&2 suggested that GUS may be effective in improving symptoms of axial manifestation of PsA.

Objectives: Evaluate the efficacy of GUS across components of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in improving symptoms of axial manifestations of active PsA patients (pts) using data from Phase 3, randomized, placebo (PBO)-controlled studies.

Methods: DISCOVER-1&2 enrolled pts with active PsA; pts were randomized to subcutaneous injections of guselkumab 100 mg every 4 weeks (Q4W) or at Wk0, 4, and Q8W, or PBO. These post hoc analyses included pts who were identified by the investigator as having axial symptoms and sacroiliitis (prior X-ray or MRI or screening X-ray). BASDAI scores were assessed at Wks 0, 8, 16, 24, and 52. Mean BASDAI component scores through Wk52 are reported by treatment group. Pooled data from the two studies are reported. Mean BASDAI component scores are reported using observed data; total BASDAI scores with missing components were set to missing. The proportion of pts achieving ≥50% improvement in BASDAI (BASDAI 50) was also determined; pts with missing data or who met the treatment failure criteria (discontinued study agent or used prohibited medications) were considered nonresponders at all subsequent timepoints.

Results: These analyses included 312 pts from DISCOVER-1&2 (103 GUS Q4W, 91 GUS Q8W, 118 PBO); mean total BASDAI scores at Wk0 were 6.4, 6.5, and 6.6, respectively. Demographics and mean baseline BASDAI component scores (ie, fatigue, spinal pain, joint pain, enthesitis, qualitative morning stiffness, and quantitative morning stiffness) were similar across treatment groups (Table 1). In comparison with the total study population, this subgroup of pts had a higher mean C-reactive protein level at baseline and a higher proportion of pts with enthesitis and included a slightly higher proportion of males. Mean scores for all six BASDAI components, including spinal pain, decreased through

Wk24 in GUS-treated pts, with separation from PBO observed as early as Wk8; improvements were maintained at Wk52. At Wk24, BASDAI 50 response rates were higher in the Q4W and Q8W groups vs PBO (38% and 40% vs 19%).[1] At WK52, mean BASDAI component scores for PBO pts who crossed over to GUS Q4W at Wk24 were similar to those for pts who were randomized to GUS.[2] A similar trend was observed for BASDAI50 response.

Conclusion: Among PsA pts with axial symptoms and sacroiliitis (via investigator-confirmed imaging) in the DISCOVER-1&2 trials, GUS treatment resulted in lower mean scores for all six BASDAI components compared with PBO as early as Wk 8 and through Wk24, with mean scores maintained at Wk52.

REFERENCES:

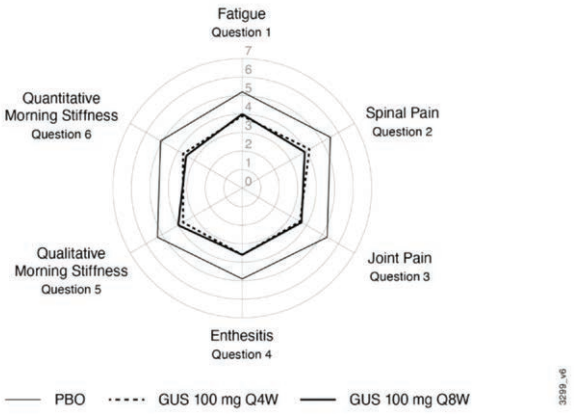
[1] Helliwell P, et al. Ann Rheum Dis. 2020; 79; Suppl 1.
[2] Mease PJ, et al. Arthritis Rheumatol. 2020; 72 (suppl 10).

Table 1. Baseline demographic and disease characteristics for patients who were identified by physicians as having symptoms consistent with spondylitis and had sacroiliitis confirmed via prior radiograph/MRI or screening radiograph

	GUS Q4W	GUS Q8W	Placebo
Patients, n	103	91	118
Male, n (%)	68 (66)	54 (59)	69 (59)
Age, years	44.9 ± 11.8	45.0 ± 10.7	45.3 ± 11.0
BASDAI			
Patients, n	95	84	110
Score	6.4 ± 1.7	6.5 ± 1.8	6.6 ± 1.5
BASDAI Components			
Fatigue	6.4 ± 2.0	6.7 ± 1.9	6.5 ± 1.9
Spinal pain	6.6 ± 2.1	6.5 ± 2.3	6.7 ± 2.0
Joint pain	6.3 ± 1.9	6.5 ± 2.2	6.8 ± 1.7
Enthesitis	6.3 ± 2.1	6.4 ± 2.2	6.3 ± 2.2
Qualitative morning stiffness	6.8 ± 2.1	6.7 ± 2.5	7.0 ± 2.0
Quantitative morning stiffness	6.2 ± 2.9	5.7 ± 2.9	6.1 ± 2.8

Data are mean ± standard deviation unless otherwise noted.BASDAI, Bath ankylosing spondylitis disease activity index

Figure. Mean scores of BASDAI components at week 24, DISCOVER-1 and DISCOVER-2



Disclosure of Interests: Frank Behrens Speakers bureau: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Chugai, Eli Lilly, Galapagos, Genzyme, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Chugai, Eli Lilly, Galapagos, Genzyme, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Grant/research support from: Celgene, Chugai, Janssen, Pfizer, and Roche, Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB, Philip Helliwell Consultant of: Galapagos, Janssen, Novartis, Grant/research support from: AbbVie, Janssen, Pfizer, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, Wim Noel Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, Soumya D Chakravarty Shareholder of: Johnson & Johnson, Employee of: Janssen Scientific Affairs, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, Stephen Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, Yanli Wang Employee of: IQVIA providing statistical support (funded by Janssen), Xenofon Baraliakos Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.398

AB0525

GUSELKUMAB TREATMENT SHOWS RAPID ONSET OF EFFECT ON COMPONENTS OF AMERICAN COLLEGE OF RHEUMATOLOGY RESPONSE CRITERIA: RESULTS OF 2 RANDOMIZED PHASE 3 TRIALS

P. Nash[1], I. McInnes[2], C. T. Ritchlin[3], W. C. Tsai[4], Y. Y. Leung[5], L. S. Tam[6], D. Furtner[7], M. Shawi[8], S. Xu[9], S. Sheng[9], A. Kollmeier[10], A. Deodhar[11].
[1]Griffiths University and University of Queensland, Rheumatology Research Unit, Maroochydore, Australia; *[2]University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; *[3]University of Rochester Medical Center, Department of Medicine, Allergy/Immunology and Rheumatology, Rochester, United States of America*; *[4]Kaohsiung Medical University, Division of Allergy, Immunology and Rheumatology, Kaohsiung City, Taiwan, Republic of China*; *[5]Singapore General Hospital, Duke -NUS Medical School, Rheumatology & Immunology, Singapore, Singapore*; *[6]The Chinese University of Hong Kong, Department of Medicine & Therapeutics, Shatin, Hong Kong (SAR)*; *[7]Janssen, a division of Johnson & Johnson Pte. Ltd, Immunology, Singapore, Singapore*; *[8]Janssen Scientific Affairs, LLC, Immunology, Spring House, United States of America*; *[9]Janssen Research & Development, LLC, Biostatistics, Spring House, PA, United States of America*; *[10]Janssen Research & Development, LLC, Immunology, San Diego, CA, United States of America*; *[11]Oregon Health & Science University, Division of Arthritis & Rheumatic Diseases, Oregon, United States of America*

Background: Guselkumab (GUS), an anti-interleukin-23p19-subunit monoclonal antibody, demonstrated efficacy vs placebo (PBO) in achieving American College of Rheumatology 20% improvement (ACR20) response in patients (pts) with active psoriatic arthritis (PsA) in two phase 3 trials, DISCOVER-1 & 2.[1,2]

Objectives: To assess the differential treatment effects of GUS across individual components of ACR response in PsA pts participating in the DISCOVER-1 & 2 trials.

Methods: In DISCOVER-1 & 2, 1120 pts were randomized & treated with GUS 100 mg every 4 weeks (Q4W; N=373); GUS 100 mg at Week (W)0 and W4, then Q8W (N=375); or matching PBO (N=372). Pts were evaluated by independent joint assessors at study visits. ACR20 response is defined as ≥20% improvement from baseline in both tender joint count (0-68 [TJC68]) and swollen joint count (0-66 [SJC66]) and ≥20% improvement from baseline in ≥3 of 5 assessments: Patient Assessment of Pain [Pt Pain], Patient Assessment of Global Disease Activity (arthritis) [PtGA], Physician Assessment of Global Disease Activity [PGA], Patient assessment of physical function as measured by Disability Index of the Health Assessment Questionnaire (HAQ-DI), and C-reactive protein (CRP). For each ACR component, achievement of ≥20% improvement from baseline was assessed over time through W24 for the combined (Q4W+Q8W) GUS groups, and median time to onset of treatment effect was determined with Kaplan-Meier curves by randomized group.

Results: Median time to response for all components except SJC66 occurred earlier with GUS than PBO. Time to onset of ACR20 treatment effect is shown in Figure 1. CRP data show 56% of GUS-treated pts had diminution of systemic inflammation by W4 (Table 1). Reduction in systemic inflammation was accompanied or rapidly followed by GUS-related improvement in both PtGA and PGA (median W4-8). Although SJC66/TJC68 data showed similar patterns, there was also a high PBO response (data not shown). Consistent with early reductions in systemic inflammation, 48-61% of GUS-treated pts had ≥20% improvement in TJC68/SJC66/PGA at W4 (Table 1), and 45-48% had ≥20% improvement in HAQ-DI, PtGA, and Pt Pain by W8. By W24, >80% of GUS-treated pts had ≥20% improvement in SJC66/TJC68/PGA, followed by 63-64% with this degree of improvement in PtGA, CRP, and Pt Pain, and 57% for HAQ-DI.

Conclusion: GUS demonstrated ACR20 improvements with separation from PBO in ACR components as early as W4, which is consistent with reduced inflammation by GUS and prior serological studies.[3] At early study time points, both pts and physicians were able to discern improvements in signs and symptoms of arthritis that rapidly followed reductions in systemic inflammation (CRP). The predominant drivers of ACR20 response rates at W24 in GUS pts were SJC66/TJC68/PGA.

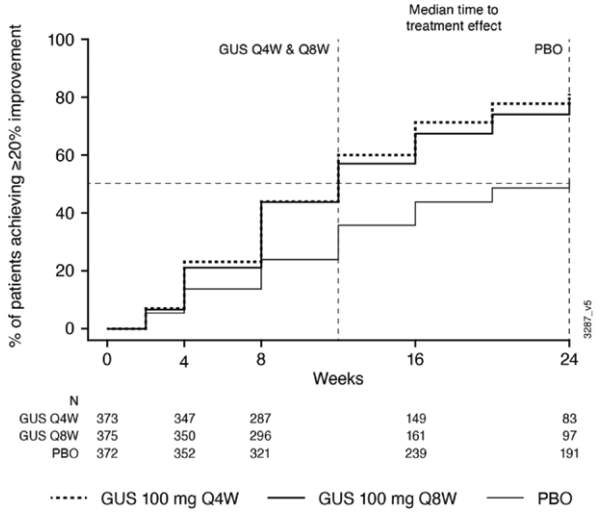
REFERENCES:

[1] Deodhar A et al. Lancet. 2020;395:1115-25
[2] Mease P et al. Lancet. 2020;395:1126-36
[3] Siebert S et al. EULAR 2020. Presentation OP0229

Table 1.

	W4	W8	W12	W16	W20	W24
ACR20	20	39	50	56	*60*	*61*
HAQ-DI score	36	45	52	54	56	57
SJC66	*61*	*74*	**84**	**86**	**87**	**88**
TJC68	48	*65*	*75*	*79*	**80**	**81**
PGA	50	*67*	*74*	*78*	**81**	**81**
PtGA	35	48	58	59	*62*	*64*
Pt Pain	32	48	55	58	*61*	*63*
CRP	56	*60*	*62*	*63*	*64*	*64*

Figure. Median time to ACR20 response.



Data shown at W2 were derived solely from DISCOVER-2, as DISCOVER-1 did not include assessments at W2. The intersection of horizontal and vertical dashed lines denotes the time at which 50% of patients in a treatment group achieved ACR20 response.

Figure 1

Disclosure of Interests: Peter Nash Consultant of: AbbVie, Bristol Myers Squibb, Boehringer, Celgene, Gilead, Eli Lilly, Janssen, Novartis, Pfizer, Roche, Sandoz, Sun, Grant/research support from: AbbVie, Bristol Myers Squibb, Boehringer, Celgene, Gilead, Eli Lilly, Janssen, Novartis, Pfizer, Roche, Sandoz, Sun, Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Janssen, Eli Lilly, Gilead, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, and UCB, Wen-Chan Tsai Consultant of: AbbVie, Eli Lilly, Janssen, Pfizer, and Novartis, Ying Ying Leung Consultant of: Abbvie, Eli Lilly, Janssen, and Novartis, Lai-Shan Tam Consultant of: AbbVie, Boehringer Ingelheim, Janssen, Lilly, Pfizer, and Sanofi, Grant/research support from: Amgen, Boehringer Ingelheim, Janssen, GSK, Novartis, and Pfizer, Daniel Furtner Employee of: Janssen, a division of Johnson & Johnson Pte. Ltd., May Shawi Employee of: Janssen Research and Development, LLC, Stephen Xu Employee of: Janssen Research and Development LLC, Shihong Sheng Employee of: Janssen Research and Development, LLC, Alexa Kollmeier Employee of: Janssen Research and Development, LLC, Atul Deodhar Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer, and UCB.
DOI: 10.1136/annrheumdis-2021-eular.434

AB0526

SUSTAINED GUSELKUMAB RESPONSE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS REGARDLESS OF BASELINE DEMOGRAPHIC AND DISEASE CHARACTERISTICS: POOLED RESULTS THROUGH WEEK 52 OF TWO PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED STUDIES

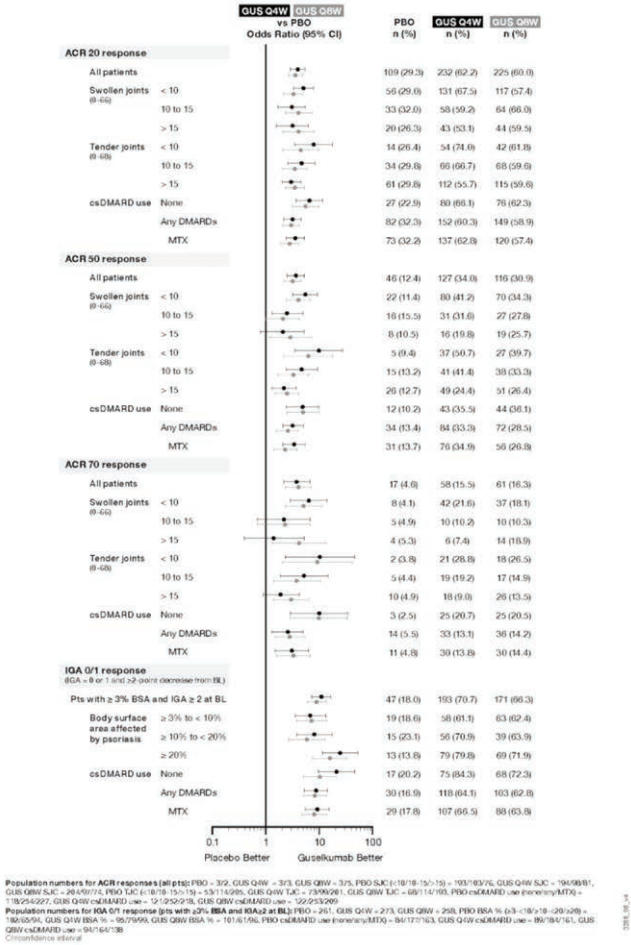
C. T. Ritchlin[1], P. J. Mease[2], W. H. Boehncke[3], J. Tesser[4], E. Schiopu[5], S. D. Chakravarty[6,7], A. Kollmeier[8], E. C. Hsia[8,9], X. L. Xu[8], M. Shawi[10], Y. Jiang[11], S. Sheng[11], J. F. Merola[12], I. McInnes[13], A. Deodhar[14].
[1]University of Rochester Medical Center, Rochester, Department of Medicine - Allergy/Immunology and Rheumatology, Rochester, United States of America; *[2]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America*; *[3]Geneva University Hospitals, Dermatology, Geneva, Switzerland*; *[4]Arizona Arthritis and Rheumatology Associates, Rheumatology, Phoenix, United States of America*; *[5]Michigan Medicine Rheumatology Clinic, Rheumatology & Internal Medicine, Ann Arbor, United States of America*; *[6]Janssen Scientific Affairs, LLC, Immunology, Horsham, United States of America*; *[7]Drexel University College of Medicine, Rheumatology, Philadelphia, United States of America*; *[8]Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; *[9]University of Pennsylvania Medical Center, Rheumatology, Philadelphia, United States of America*; *[10]Janssen Global Services, LLC, Immunology, Horsham, United States of America*; *[11]Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; *[12]Brigham and Women's Hospital, Harvard Medical School, Department of Dermatology, and Department of Medicine, Division of Rheumatology and Immunology, Boston, United States of America*; *[13]University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; *[14]Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America*

Background: In the Phase 3 DISCOVER-1[1] & DISCOVER-2[2] trials, guselkumab (GUS), a human monoclonal antibody targeting the IL-23p19-subunit, was effective in psoriatic arthritis (PsA) across joint & skin endpoints. At Week 24 (W24), GUS benefit was consistent regardless of baseline (BL) demographic & disease characteristics.[3]
Objectives: We assessed whether GUS efficacy was sustained through W52 in pooled DISCOVER-1 & -2 patients (pts) across select BL subgroups.
Methods: Adults with active PsA despite standard therapies were enrolled in DISCOVER-1 (swollen [SJC] ≥3 & tender joint count [TJC] ≥3, C-reactive protein [CRP] ≥0.3 mg/dL) & DISCOVER-2 (SJC ≥5 & TJC ≥5, CRP ≥0.6 mg/dL). 31% of DISCOVER-1 pts had received 1-2 prior tumor necrosis factor inhibitors; DISCOVER-2 pts were biologic naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO). Pts randomized to PBO received GUS 100 mg Q4W starting at W24 & were excluded from these analyses assessing maintenance of effect from W24 to W52. GUS effects on joint (American College of Rheumatology [ACR]20/50/70) & skin (Investigator's Global Assessment [IGA=0/1 + ≥2-grade reduction from W0] in pts with ≥3% body surface area [BSA] with psoriasis & IGA ≥2 at W0) endpoints were evaluated by pt BL SJC, TJC, conventional synthetic disease-modifying antirheumatic drug (csDMARD) use, body mass index (BMI), PsA duration, & % BSA with psoriasis. Missing data were imputed as nonresponse through W52.
Results: BL pt characteristics in DISCOVER-1 (N=381) & DISCOVER-2 (N=739) were well balanced across randomized groups.[1,2] Among 1120 pooled pts, mean SJC was 11, mean TJC was 21, & 68% used csDMARDs (primarily methotrexate [MTX]). At W24, 62% (232/373) & 60% (225/375), respectively, of GUS Q4W- & Q8W-treated pts achieved ACR20 vs 29% (109/372) of PBO, with GUS effect consistently observed across pt BL subgroups (Figure 1). ACR20 response rates were sustained or increased at W52 in the GUS Q4W (72%) & Q8W (70%) groups & across SJC (61-79%), TJC (68-76%), & csDMARD use (68-80%) subgroups (Table 1) & pt subgroups defined by BL BMI, PsA duration, & % BSA with psoriasis (data not shown). ACR50 & 70 response patterns were similar to ACR20 (Table 1). In pts with ≥3% BSA psoriasis & IGA ≥2 at BL, 71% (193/273) & 66% (171/258) of GUS Q4W- & Q8W-treated pts, respectively, vs 18% (47/261) of PBO, achieved IGA 0/1 at W24, with GUS effect consistently observed across pt BL subgroups (Figure 1). IGA 0/1 response rates were also sustained or increased at W52 in the GUS Q4W (80%) & Q8W (71%) groups & across % BSA with psoriasis (67-87%) & csDMARD use (68-87%) subgroups (Table 1) & pt subgroups defined by BL BMI and PsA duration (data not shown).
Conclusion: Treatment with GUS 100 mg Q4W & Q8W resulted in sustained improvement in signs & symptoms of active PsA through W52 regardless of pt BL characteristics.

REFERENCES:

[1] Deodhar A, et al. Lancet 2020;395:1115-25;
[2] Mease P, et al. Lancet 2020;395:1126-36;
[3] Deodhar A, et al. American College of Rheumatology 2020; Poster P0908.

Figure. ACR & IGA Responses at W24 by Select BL Characteristics



Population numbers for ACR responses (all pts): PBO = 3/2, GUS Q4W = 3/3, GUS Q8W = 3/5, PBO SJC (<10/10-15/>15) = 193/183/76, GUS Q4W SJC = 194/98/81, GUS Q8W SJC = 264/97/74, PBO TJC (<10/10-15/>15) = 53/114/985, GUS Q4W TJC = 73/99/281, GUS Q8W TJC = 68/114/193, PBO csDMARD use (none/any/MTX) = 118/254/227, GUS Q4W csDMARD use = 121/252/218, GUS Q8W csDMARD use = 122/253/269
Population numbers for IGA 0/1 response (pts with ≥3% BSA and IGA≥2 at BL): PBO = 267, GUS Q4W = 273, GUS Q8W = 258, PBO BSA % (≥3-<10/≥10-<20/≥20) = 182/65/94, GUS Q4W BSA % = 95/79/99, GUS Q8W BSA % = 101/61/96, PBO csDMARD use (none/any/MTX) = 84/177/163, GUS Q4W csDMARD use = 89/184/161, GUS Q8W csDMARD use = 94/164/138
CI=confidence interval

Figure 1

Table 1. ACR & IGA Responses at Weeks 24 & 52 & by Select BL Characteristics

	Guselkumab Q4W		Guselkumab Q8W	
	N=373		N=375	
	Week 24	Week 52	Week 24	Week 52
ACR20, %	**62**	**72**	**60**	**70**
SJC (<10/10-15/>15)	68/59/53	79/61/67	57/66/60	68/68/76
TJC (<10/10-15/>15)	74/67/56	73/76/69	62/60/60	75/68/68
csDMARD use (none/any/MTX)	66/60/63	80/68/68	62/59/57	73/68/68
ACR50, %	**34**	**49**	**31**	**45**
SJC (<10/10-15/>15)	41/32/20	58/39/38	34/28/26	46/40/49
TJC (<10/10-15/>15)	51/41/24	58/53/43	40/33/26	52/46/43
csDMARD use (none/any/MTX)	36/33/35	53/46/48	36/29/27	51/42/40
ACR70, %	**16**	**27**	**16**	**27**
SJC (<10/10-15/>15)	22/10/7	32/20/24	18/10/19	30/23/26
TJC (<10/10-15/>15)	29/19/9	34/32/22	27/15/14	35/28/24
csDMARD use (none/any/MTX)	21/13/14	30/26/27	21/14/14	34/24/23
	N=273		N=258	
IGA 0/1, %	**71**	**80**	**66**	**71**
BSA % with psoriasis (≥3-<10/≥10-<20/≥20)	61/71/80	76/87/79	62/64/72	67/72/74
csDMARD use (none/any/MTX)	84/64/67	87/77/78	72/63/64	77/68/68

Disclosure of Interests: Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Gilead, Janssen, Eli Lilly, Novartis, Pfizer, and UCB Pharma, Grant/research support from: AbbVie, Amgen, and UCB Pharma, Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN, and UCB Pharma, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB Pharma, Wolf-Henning Boehncke Speakers bureau: AbbVie, Almirall, Celgene, Janssen, Leo, Eli Lilly, Novartis, UCB Pharma, Consultant of: AbbVie, Almirall, Celgene, Janssen, Leo, Eli Lilly, Novartis, UCB Pharma, Grant/research support from: Pfizer, John Tesser Speakers bureau: AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Crescendo Biosciences/Myriad, GlaxoSmithKline, Genentech, Janssen, Eli Lilly, and Pfizer, Consultant of: AbbVie, AstraZeneca, Bristol Myers Squibb, Gilead, Janssen, Eli Lilly, Novartis, and Pfizer, Grant/research support from: AbbVie, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Horizon, Janssen, Eli Lilly, Merck KG, Novartis, Pfizer, Sandoz, Sun Pharma, Setpoint, and UCB Pharma, Elena Schiopu Consultant of: Janssen, Grant/research support from: Janssen, Soumya D Chakravarty Shareholder of: Johnson & Johnson, of which Janssen Research & Development is a wholly owned subsidiary, Employee of: Janssen Scientific Affairs, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, of which Janssen Research & Development is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, of which Janssen Research & Development is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, of which Janssen Research & Development is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC, May Shawi Shareholder of: Johnson & Johnson, of which Janssen Research & Development is a wholly owned subsidiary, Employee of: Janssen Global Services, LLC, Yusang Jiang Employee of: Cytel, Inc., providing statistical support (funded by Janssen), Shihong Sheng Shareholder of: Johnson & Johnson, of which Janssen Research & Development is a wholly owned subsidiary, Employee of: Janssen Research & Development, LLC, Joseph F. Merola Consultant of: AbbVie, Arena, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma, Iain McInnes Consultant of: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB Pharma, Grant/research support from: Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, and UCB Pharma, Atul Deodhar Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Eli Lilly, GlaxoSmithKline, Novartis, Pfizer, UCB Pharma.
DOI: 10.1136/annrheumdis-2021-eular.437

AB0527

CORRELATIONS BETWEEN REDUCTIONS IN FATIGUE SEVERITY AND IMPROVEMENTS IN PHYSICAL FUNCTION AND CLINICAL RESPONSE IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM THE PHASE 3 DISCOVER PROGRAM

A. Kavanaugh[1], Y. Liu[2], A. Deodhar[3], P. J. Mease[4], P. Helliwell[5], L. Gossec[6], A. Kollmeier[2], E. C. Hsia[2,7], M. Shawi[8], C. Han[2], P. Rahman[9]. *[1]University of California San Diego, Center for Innovative Therapy, San Diego, United States of America*; *[2]Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; *[3]Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America*; *[4]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Rheumatology Research, Seattle, United States of America*; *[5]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[6]Sorbonne Université, Hôpital Pitié-Salpétrière, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Prof of Rheumatology, Paris, France*; *[7]University of Pennsylvania School of Medicine, Rheumatology, Philadelphia, United States of America*; *[8]Janssen Global Services, LLC, Immunology, Horsham, United States of America*; *[9]Memorial University of Newfoundland, Craig L Dobbin Genetics Research Centre, St. John's, Canada*

Background: In patients (pts) with psoriatic arthritis (PsA), fatigue is a major driver of perceived impact of disease and has been identified as an important domain to be assessed in clinical trials.[1,2] The association between fatigue and other PsA domains (eg, physical function) or clinical response is not well understood.

Objectives: Fatigue was measured with the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue questionnaire in the pivotal DISCOVER-1 and DISCOVER-2 Phase 3 studies of guselkumab (GUS) vs placebo (PBO). This post hoc analysis explores the correlation between FACIT-Fatigue and physical function and clinical response in the DISCOVER program.

Methods: This analysis used pooled data from pts (N=1120) treated with GUS or PBO. In DISCOVER-1 and DISCOVER-2, 381 pts with active PsA (swollen joint count [SJC] ≥3, tender joint count [TJC] ≥3, C-reactive protein [CRP] ≥0.3 mg/dL) and 739 pts with active PsA (SJC ≥5, TJC ≥5, CRP ≥0.6 mg/dL) and inadequate response to standard therapies, respectively, were randomized 1:1:1 to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or PBO. PBO pts switched to GUS 100 mg Q4W at W24. The FACIT-Fatigue questionnaire has 13 items that assess self-reported fatigue/tiredness over the last 7 days. Items are scored from 0 (very much fatigued) to 4 (not at all fatigued). FACIT-Fatigue response was defined as an increase of ≥4 points from baseline. Physical function was evaluated with the Health Assessment Questionnaire-Disability Index (HAQ-DI). HAQ-DI response was defined as a decrease of ≥0.35 points from baseline. Clinical response was defined as achievement of ≥20%

improvement in the American College of Rheumatology (ACR 20) criteria. Relationships between FACIT-Fatigue and HAQ-DI at W8/16/24 were assessed by Pearson correlation coefficients. Mean changes in HAQ-DI scores at W8/16/24 were summarized in FACIT-Fatigue responders and nonresponders. A logistic regression model was applied to estimate odds ratios (ORs) for achievement of HAQ-DI and ACR 20 response by FACIT-Fatigue response status at each visit. A multiple linear regression model was used to evaluate the association between FACIT-Fatigue and HAQ-DI at W24 after adjusting for SJC, TJC, CRP, and pt assessment of pain.

Results: FACIT-Fatigue and HAQ-DI scores and changes from baseline were negatively correlated at W8, W16, and W24 (Table 1). Mean changes in HAQ-DI were −0.31, −0.43, and −0.48 at W8, W16, and W24, respectively, in FACIT-Fatigue responders and −0.06, −0.07, and −0.09, respectively, in FACIT-Fatigue nonresponders. FACIT-Fatigue responders were significantly more likely than nonresponders to achieve HAQ-DI and ACR 20 response (OR [95% CI] at W8, 2.8 [2.2-3.7] and 2.4 [1.9-3.1]; at W16, 3.6 [2.8-4.7] and 2.9 [2.3-3.7]; and at W24, 4.4 [3.4-5.7] and 3.2 [2.5-4.2], respectively; Figure 1). Correlations between FACIT-Fatigue and HAQ-DI remained significant after adjusting for SJC, TJC, CRP, and pt assessment of pain.

Conclusion: In pts with PsA, fatigue response is a clinically meaningful predictor of improvements in physical function and achievement of ACR 20 response, reinforcing the importance of assessing fatigue in PsA disease management.

REFERENCES:

[1] Leung YY et al. J Rheumatol. 2020;96:46-9.
[2] Gudu T et al. Joint Bone Spine. 2016;83:439-43.

Table 1. Correlation* of FACIT-Fatigue and HAQ-DI

Visit	HAQ-DI and FACIT Fatigue Scores	Changes From Baseline in HAQ-DI and FACIT-Fatigue Scores
W8	−0.61 (p<0.0001)	−0.42 (p<0.0001)
W16	−0.60 (p<0.0001)	−0.47 (p<0.0001)
W24	−0.62 (p<0.0001)	−0.50 (p<0.0001)

*Determined by Pearson correlation coefficient; p-values derived from hypothesis tests of correlation ρ=0 (ie, no correlation).

Figure. HAQ-DI and ACR 20 Responders by FACIT-Fatigue Responder Status (Y/N)

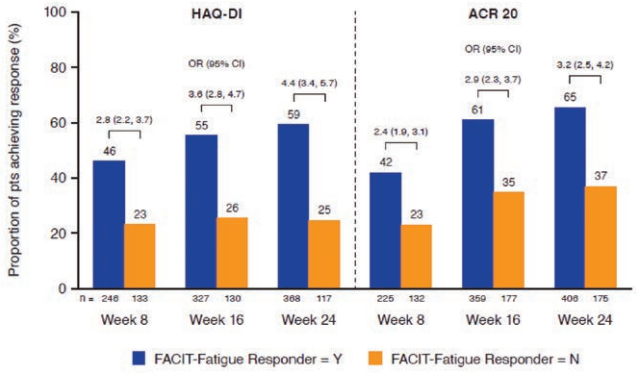


Figure 1

Disclosure of Interests: Arthur Kavanaugh Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Genentech, Janssen, Eli Lilly, Merck, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Genentech, Janssen, Eli Lilly, Merck, Novartis, Pfizer and UCB, Yan Liu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Atul Deodhar Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, GSK, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, UCB, Philip J Mease Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB; and personal fees from Boehringer Ingelheim and GlaxoSmith-Kline, Philip Helliwell Consultant of: Galapagos, Janssen, Novartis, Grant/research support from: Abbvie, Janssen, Pfizer, Laure Gossec Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Biogen, Celgene, Gilead, Janssen, Eli Lilly, Novartis, Pfizer, Samsung Bioepis, Sanofi-Aventis, UCB, Grant/research support from: Amgen, Galapagos, Janssen, Eli Lilly, Pfizer, Sandoz, Sanofi, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Chenglong Han Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Proton Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis.

DOI: 10.1136/annrheumdis-2021-eular.475

AB0528

COMPARABLE SAFETY PROFILE OF GUSELKUMAB IN PSORIATIC ARTHRITIS AND PSORIASIS: RESULTS FROM PHASE 3 TRIALS THROUGH 1 YEAR

A. B. Gottlieb[1], J. F. Merola[2], A. Armstrong[3], R. Langley[4], M. Lebwohl[1], C. E. M. Griffiths[5], M. Shawi[6], Y. W. Yang[6], E. C. Hsia[7,8], A. Kollmeier[9], X. L. Xu[9], M. Izutsu[9], P. Ramachandran[10], S. Sheng[11], Y. You[11], M. Miller[10], C. T. Ritchlin[12], I. McInnes[13], P. Rahman[14]. *[1]Icahn Medical School/Mount Sinai, Department of Dermatology, New York, United States of America*; *[2]Brigham and Women's Hospital, Harvard Medical School, Dermatology, Rheumatology, Immunology and Allergy, Boston, United States of America*; *[3]Keck School of Medicine, University of Southern California, Clinical Research, Los Angeles, United States of America*; *[4]Dalhousie University, Division of Clinical Dermatology & Cutaneous Science, Halifax, Canada*; *[5]The University of Manchester, Manchester Centre for Dermatology Research, Manchester, United Kingdom*; *[6]Janssen Global Services, LLC, Immunology, Horsham, United States of America*; *[7]University of Pennsylvania School of Medicine, Rheumatology, Philadelphia, United States of America*; *[8]Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; *[9]Janssen Research & Development, LLC, Immunology, San Diego, United States of America*; *[10]Janssen Research & Development, LLC, Immunology, Spring House, United States of America*; *[11]Janssen Research & Development, LLC, Biostatistics, Spring House, United States of America*; *[12]University of Rochester, Department of Medicine, Allergy/Immunology and Rheumatology, Rochester, United States of America*; *[13]University of Glasgow, Institute of Infection Immunity and Inflammation, Glasgow, United Kingdom*; *[14]Memorial University of Newfoundland, Craig L Dobbin Genetics Research Centre, St. John's, Canada*

Background: DISCOVER 1&2 (PsA) and VOYAGE 1&2 (PsO) are Phase 3 trials of guselkumab (GUS).

Objectives: Compare safety results through up to 1yr of GUS in PsA and PsO pts.

Methods: In DISCOVER, 1120 pts with active PsA despite standard therapy were treated. Most pts were biologic-naïve; ~30% in DISCOVER 1 had previous exposure to 1-2 TNFi. Concomitant MTX (57%), oral corticosteroids (17%), and NSAIDs (64%) were permitted. Pts were randomized to SC GUS 100mg at W0, W4, then Q8W; GUS 100mg Q4W; or PBO. At W24, PBO patients were switched to GUS 100mg Q4W. In VOYAGE, in which concomitant MTX use was prohibited, 1245 pts with moderate to severe PsO were treated and randomized to SC GUS 100 mg at W0, W4, W12, then Q8W; or PBO at W0, W4, W12, with crossover to GUS at W16, W20, then Q8W. AEs and laboratory parameters, analyzed by National Cancer Institute-Common Terminology Criteria for AEs [NCI-CTCAE] toxicity grades, were summarized through the PBO-controlled periods and 1yr.

Results: Safety profiles were generally consistent across the GUS PsO and PsA clinical programs (Table 1). Time-adjusted incidence rates for numbers of AEs, serious AEs, serious infections, malignancy, MACE and AEs leading to d/c were generally similar between PsO and PsA. No cases of anaphylaxis or opportunistic infections were reported. Proportions of pts with decreased neutrophil counts and elevations in hepatic transaminases were slightly higher in PsA vs PsO. These abnormalities were mostly of NCI-CTCAE Grade 1 or 2 (<LLN-1000/mm^3 for neutrophils; <5.0 x ULN for AST/ ALT), generally transient, required no medical interventions, resolved spontaneously, and did not lead to interruption or d/c of treatment. Through 1yr, proportions of pts with ALT/AST elevations in PsA trials were slightly higher for GUS Q4W than Q8W and in pts with vs without baseline MTX use.

Conclusion: The GUS safety profile was generally consistent in PsA and PsO GUS-treated pts through 1yr of the DISCOVER and VOYAGE trials.

Table 1. Treatment-Emergent AEs During PBO-controlled Period and Through 1Yr: VOYAGE & DISCOVER Trials

	Pooled VOYAGE 1&2			Pooled DISCOVER 1&2					
Time Period	W0-16		Through 1Yr	W0-24[b]		Through 1Yr			
(N=)	PBO (422)	GUS Q8W (823)	Combined GUS[a] (1221)	PBO[c] (372)	GUS Q8W (375)	GUS Q4W (373)	GUS Q8W (375)	GUS Q4W (373)	Combined GUS† (1100)
Total pt-yrs of follow-up	128	255	974	173	173	172	384	385	973
Incidence/100 pt-yrs (95% CI)[d]									
AEs	317 (287,349)	330 (308,353)	259 (249, 270)	219 (198,243)	256 (232,281)	221 (200, 245)	218 (203,233)	177 (164,191)	191 (182, 199)
SAEs	5 (2, 10)	6 (4, 10)	6 (5, 8)	9 (5, 15)	4 (2, 8)	5 (2, 10)	6 (4, 9)	4 (2, 7)	6 (4, 7)
AEs leading to study agent d/c	3 (0.9, 8)	4 (2, 8)	2 (2, 4)	4 (2, 8)	3 (1, 7)	7 (4, 12)	2 (1, 4)	4 (2, 6)	3 (2, 5)
Infections	86 (71, 104)	98 (86, 111)	98 (92, 104)	58 (48, 71)	58 (47, 71)	63 (51, 76)	58 (50, 66)	53 (46, 61)	55 (50, 60)
Serious Infections	0. 8 (0, 4)	0.4 (0, 2)	1 (0.5, 2)	4 (2, 8)	0.6 (0, 3)	2 (0.4, 5)	2 (0.6, 3)	1 (0, 2)	2 (0.9, 3)
All Malignancy	0 (0, 2)	0.4 (0, 2)	1 (0.4, 2)	0.6 (0, 3)	1 (0, 4)	0 (0, 2)	0.5 (0, 2)	0 (0, 0. 8)	0 (0, 1)
MACE	0 (0, 2)	0.4 (0, 2)	0.4 (0, 1)	0.6 (0, 3)	0 (0, 2)	0.6 (0, 3)	0 (0, 0.8)	0.3 (0, 1.4)	0.1 (0, 0.6)
% pts with ≥1 injection site rxn	3.1	4.5	5.0	0.3	1.3	1.1	1.6	2.4	1.7

[a]Placebo crossover pts were included in the combined GUS column after crossover to GUS[b]For all pts who d/c study treatment early with the last dose of PBO/GUS prior to W24 and who did not receive any PBO/GUS at or after Wk24, all data including the final safety follow-up visit collected through 1yr were included[c]For pts in PBO group who switched to GUS due to cross-over or inadvertently, only data prior to first administration of GUS were included.[d]CI based on an exact method assuming observed number of events follows a Poisson distribution

Disclosure of Interests: Alice B Gottlieb Consultant of: Anaptyps Bio, Avotres Therapeutics, Beiersdorf, Boehringer Ingelheim, Bristol-Myers-Squibb, Eli Lilly, Janssen, LEO Pharma, Novartis, Sun Pharmaceuticals, UCB, and Xbiotech, Grant/research support from: Boehringer Ingelheim, Janssen, Novartis, Sun Pharmaceuticals, UCB, and Xbiotech, Joseph F. Merola Consultant of: AbbVie, Arena, Biogen, BMS, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, UCB, April Armstrong Consultant of: AbbVie, Janssen, Lilly, Leo, Novartis, UCB, Ortho Dermatologics, Dermira, KHK, Sanofi, Regeneron, Sun Pharma, BMS, Dermavant, and Modernizing Medicine, Richard Langley Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, LEO Pharma, Merck, Novartis, Pizer, Sun Pharmaceutical, and UCB Pharma, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, LEO Pharma, Merck, Novartis, Pizer, Sun Pharmaceutical, and UCB Pharma, Mark Lebwohl Consultant of: Aditum Bio, Allergan, Almirall, Arcutis, Inc., Avotres Therapeutics, BirchBioMed Inc., BMD skincare, Boehringer-Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Evelo, Evommune, Facilitate International Dermatologic Education, Foundation for Research and Education in Dermatology, Inozyme Pharma, Kyowa Kirin, LEO Pharma, Meiji Seika Pharma, Menlo, Mitsubishi, Neuroderm, Pfizer, Promius/Dr. Reddy's Laboratories, Serono, Theravance, and Verrica., Grant/research support from: Abbvie, Amgen, Arcutis, Boehringer Ingelheim, Dermavant, Eli Lilly, Evommune, Incyte, Janssen, Leo Pharmaceutucals, Ortho Dermatologics, Pfizer, and UCB, Christopher E.M. Griffiths Speakers bureau: AbbVie, Amgen, Almirall, BMS, Boehringer Ingelheim Celgene, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Sun Pharma, UCB Pharma., Consultant of: AbbVie, Amgen, Almirall, BMS, Boehringer Ingelheim Celgene, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Sun Pharma, UCB Pharma., Grant/research support from: AbbVie, Amgen, Almirall, BMS, Boehringer Ingelheim Celgene, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Sun Pharma, UCB Pharma., May Shawi Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Ya-Wen Yang Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Elizabeth C Hsia Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Alexa Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Xie L Xu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Miwa Izutsu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Paraneedharan Ramachandran Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Yin You Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Megan Miller Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB Pharma, Grant/research support from: AbbVie, Amgen, and UCB Pharma, Iain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, and Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Proton Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis.

DOI: 10.1136/annrheumdis-2021-eular.556

AB0529

CHARACTERIZATION OF REMISSION IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH UPADACITINIB: POST-HOC ANALYSIS FROM TWO PHASE 3 TRIALS

P. J. Mease[1], A. Kavanaugh[2], D. D. Gladman[3], O. Fitzgerald[4], E. Soriano[5], P. Nash[6], D. Feng[7], A. Lertratanakul[7], K. Douglas[7], R. Lippe[8], L. Gossec[9].
[1]Department of Rheumatology, Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, United States of America; *[2]University of California San Diego, Rheumatology, San Diego, United States of America*; *[3]Krembil Research Institute, Toronto Western Hospital, University Health Network, Division of Rheumatology, Department of Medicine, and Institute of Medical Science, University of Toronto, Toronto, Canada*; *[4]Conway Institute for Biomolecular Research, University College, Dublin, Ireland*; *[5]Internal Medicine Services, Hospital Italiano de Buenos Aires and Instituto Universitario Italiano, Buenos Aires, Argentina*; *[6]School of Medicine, Griffith University, Brisbane, Australia*; *[7]AbbVie Inc, Rheumatology, North Chicago, United States of America*; *[8]AbbVie, Deutschland GmbH & Co. KG, Wiesbaden, Germany*; *[9]Sorbonne Université and Rheumatology Department, Hôpital Pitié Salpêtrière, Paris, France*

Background: For patients (pts) with PsA, several disease activity measures are available including very low/minimal disease activity (VLDA/MDA), cutoffs based on the Disease Activity in PsA (DAPSA) score, and on the Psoriatic Arthritis Disease Activity Score (PASDAS) score.
Objectives: To assess the rates of pts achieving these remission or low disease activity (LDA) criteria at Wk 24 using data from the SELECT-PsA 1 and SELECT-PsA 2 phase 3 studies;[1,2] Additionally, we assessed the distribution of individual MDA components among pts who did or did not achieve MDA criteria at Wk 24.
Methods: In SELECT-PsA 1 and SELECT-PsA 2, pts with PsA and prior inadequate response (IR) or intolerance to ≥1 non-biologic DMARD (N=1705) or ≥1 biologic DMARD (N=642), respectively, were randomized to once daily upadacitinib (UPA) 15mg, UPA 30mg, adalimumab (ADA) 40mg every other week (SELECT-PsA 1 only), or placebo (PBO). Remission and LDA were assessed using VLDA/MDA, DAPSA scores of ≤4/≤14, and PASDAS scores of ≤1.9/≤3.2, at Wk 24 (Table 1). Non-responder imputation (NRI) was used for handling missing data; pts rescued at Wk 16 were considered non-responders. Pairwise comparisons between UPA doses and PBO or ADA were conducted using the Cochran-Mantel-Haenszel test.
Results: Overall, 2345 pts were analyzed; mean age 51 years, 53% female. In both studies, higher rates of remission and LDA were observed with both UPA doses vs PBO at Wk 24 (nominal P-values <0.05 for both time points; Table 1). Generally, higher rates of remission and LDA were also observed with UPA30 vs ADA in non-biologic DMARD-IR pts (nominal P-values <0.05). Greater rates of MDA/VLDA were observed at Wk 24 with UPA15 and UPA30 vs PBO in both studies and with UPA30 vs ADA in non-biologic DMARD-IR pts (nominal P-values <0.05 for all comparisons). The proportion of responder or non-responder pts receiving UPA15 or UPA30 was similar for each of the MDA components in both studies. At Wk 24, more responder and non-responder pts in both studies achieved Swollen Joint Count (SJC) 66 ≤1, Psoriasis Area and Severity Index (PASI) ≤1 or Body Surface Area-Psoriasis (BSA-Ps) ≤3%, and Leeds Enthesitis Index (LEI) ≤1 (Figure 1). Conversely, the proportion of pts Achieving Tender Joint Count (TJC) 68 ≤1 and Pt's Global Assessment of Pain ≤1.5 tended to be lower.

Conclusion: Regardless of previous biologic DMARD failure, pts treated with UPA15 or UPA30 achieved a higher rate of remission or LDA measured by various disease activity measures vs PBO at Wk 24; higher rates of response were observed in most of the remission and LDA measures with UPA30 vs ADA in non-biologic DMARD-IR pts. Among pts who did or did not achieve MDA criteria at Wk 24, a greater proportion of UPA-treated pts achieved physician derived measures such as SJC ≤1, PASI ≤1 or BSA-Ps ≤3%, and LEI ≤1.

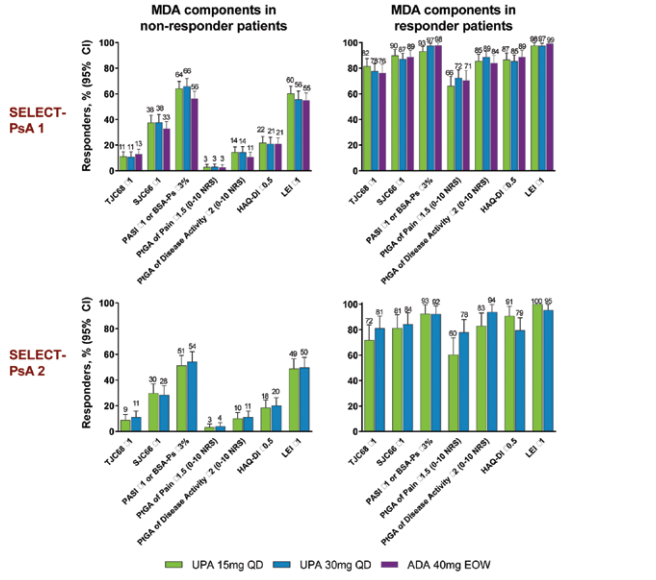
REFERENCES:

[1] McInnes IB, et al. Ann Rheum Dis, 2020; 79:12.
[2] Genovese MC, et al. Ann Rheum Dis, 2020; 79:139.

Table 1. Proportion of Patients Achieving Remission and LDA Measures at Week 24

	SELECT-PsA 1				SELECT-PsA 2		
Endpoint, n (%)	PBO N=423	ADA 40mg EOW N=429	UPA 15mg QD N=429	UPA 30mg QD N=423	PBO N=212	UPA 15mg QD N=211	UPA 30mg QD N=218
MDA	52 (12.3)	143 (33.3)	157 (36.6) *,#	192 (45.4) *,†,#	6 (2.8)	53 (25.1) *,#	63 (28.9) *,#
≥6 VLDA components	25 (5.9)	90 (21.0)	105 (24.5) *	134 (31.7) *,†	3 (1.4)	26 (12.3) *	44 (20.2) *
VLDA	11 (2.6)	62 (14.5)	55 (12.8) *	72 (17.0) *	3 (1.4)	16 (7.6) *	21 (9.6) *
DAPSA REM	9 (2.1)	43 (10.0)	47 (11.0) *	79 (18.7) *,†	1 (0.5)	15 (7.1) *	28 (12.8) *
DAPSA LDA	70 (16.5)	198 (46.2)	204 (47.6) *	235 (55.6) *,†	14 (6.6)	73 (34.6) *	91 (41.7) *
PASDAS REM	12 (2.8)	51 (11.9)	60 (14.0) *	91 (21.5) *,†	4 (1.9)	20 (9.5) *	31 (14.2) *
PASDAS LDA	63 (14.9)	168 (39.2)	195 (45.5) *	211 (49.9) *,†	9 (4.2)	69 (32.7) *	82 (37.6) *

*P ≤ 0.05 for UPA15 and UPA30 vs PBO; †P ≤ 0.05 for UPA30 vs ADA; #Statistically significant in the multiplicity-controlled analysis.**MDA (5/7) and VLDA (7/7):** TJC ≤ 1; SJC ≤ 1; PASI ≤ 1 or BSA-Psoriasis ≤ 3%; Patient's Assessment of Pain NRS ≤ 1.5; PtGA-Disease Activity NRS ≤ 2.0; HAQ-DI score ≤ 0.5; and tender entheseal points ≤ 1.DAPSA REM ≤ 4; DAPSA LDA ≤ 14.PASDAS REM ≤ 1.9; PASDAS LDA ≤ 3.2.



ADA, adalimumab; BSA, body surface area; CI, confidence interval; EOW, every other week; HAQ-DI, Health Assessment Questionnaire – Disability Index; LEI, Leeds Enthesitis Indices; MDA, minimal disease activity; NRS, numerical rating scale; PASI, Psoriasis Area Severity Index; Ps, psoriasis; PtGA, Patient's Global Assessment of Disease Activity; QD, once daily; SJC, Swollen Joint Count; TJC, Tender Joint Count; UPA, upadacitinib.

Figure 1

Acknowledgements: AbbVie and the authors thank the patients, study sites, and investigators who participated in this clinical trial. AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. No honoraria or payments were made for authorship. Medical writing support was provided by Ramona Vladea, PhD of AbbVie Inc.

Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB., Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB., Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB., Arthur Kavanaugh Consultant of: AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Grant/research support from: AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Dafna D Gladman Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene Corporation, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer Inc, and UCB, Oliver FitzGerald Speakers bureau: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Consultant of: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Enrique Soriano Speakers bureau: AbbVie, Amgen, Bristol Myers, Celgene, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi, and UCB, Consultant of: AbbVie, Amgen, Bristol Myers, Celgene, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers, Celgene, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi, and UCB, Peter Nash Speakers bureau: AbbVie, BMS, Roche, Pfizer, Janssen, Amgen, Sanofi-Aventis, UCB, Eli Lilly, Novartis, and Celgene, Consultant of: AbbVie, BMS, Roche, Pfizer, Janssen, Amgen, Sanofi-Aventis, UCB, Eli Lilly, Novartis, and Celgene, Grant/research support from: AbbVie, BMS, Roche, Pfizer, Janssen, Amgen, Sanofi-Aventis, UCB, Eli Lilly, Novartis, and Celgene, Dai Feng Shareholder of: AbbVie, Employee of: AbbVie, Apinya Lertratanakul Shareholder of: AbbVie, Employee of: AbbVie, Kevin Douglas Shareholder of: AbbVie, Employee of: AbbVie, Ralph Lippe Shareholder of: AbbVie, Employee of: AbbVie, Laure Gossec Consultant of: AbbVie,Amgen, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Samsung, Sanofi, UCB, Grant/research support from: Lilly, Pfizer, and Sandoz.

DOI: 10.1136/annrheumdis-2021-eular.574

AB0530

EFFECT OF SKIN SYMPTOMS ON DISEASE IMPACT IN PATIENTS WITH PSORIATIC ARTHRITIS RECEIVING THE IL-12/23 INHIBITOR USTEKINUMAB OR TNF INHIBITORS IN THE REAL-WORLD PSABIO STUDY

J. S. Smolen[1], T. Korotaeva[2], M. Nurmohamed[3], S. Siebert[4], P. Bergmans[5], K. De Vlam[6], E. Gremese[7], B. Joven-Ibáñez[8], W. Noel[9], P. Sfikakis[10], E. Theander[11], L. Gossec[12,13]. [1]*Medical University of Vienna, Division of Rheumatology, Department of Medicine III, Vienna, Austria*; [2]*VA Nasonova Research Institute of Rheumatology, Department of Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*; [3]*Reade and VU University Medical Center, Department of Rheumatology, Amsterdam, Netherlands*; [4]*University of Glasgow, Institute of Infection Immunity and Inflammation, Glasgow, United Kingdom*; [5]*Janssen-Cilag BV, Biostatistics, Breda, Netherlands*; [6]*University Hospitals Leuven, Division of Rheumatology, Leuven, Belgium*; [7]*Catholic University of the Sacred Heart, Fondazione Policlinico A Gemelli IRCCS, Rome, Italy*; [8]*University Hospital 12 de Octubre, Department of Rheumatology, Madrid, Spain*; [9]*Janssen Pharmaceutica NV, Medical Affairs, Beerse, Belgium*; [10]*National and Kapodistrian University of Athens Medical School, First Department of Propaedeutic and Internal Medicine, Athens, Greece*; [11]*Janssen-Cilag AB, Medical Affairs, Solna, Sweden*; [12]*Sorbonne University, INSERM, Pierre Louis Institute of Epidemiology and Public Health, Paris, France*; [13]*Pitié-Salpêtrière Hospital, AP-HP, Department of Rheumatology, Paris, France*

Background: Psoriatic arthritis (PsA) is characterised by musculoskeletal symptoms, and patients (pts) with PsA usually experience psoriasis concurrently. Real-world data reflecting impact of skin symptoms on PsA disease burden are limited.

Objectives: Analyse effectiveness of ustekinumab (UST) and tumour necrosis factor inhibitor (TNFi) therapy on extent of skin involvement, and the impact this has on PsA disease burden and drug persistence.

Methods: PsABio (NCT02627768) is a prospective, observational study of 1st/2nd/3rd-line UST or TNFi treatment in PsA in 8 European countries. Extent of skin involvement was categorised as body surface area (BSA): clear/almost clear; <3% but not clear/almost clear; 3–10%; or >10%. Pt-reported disease impact was evaluated by PsAID-12, including assessment of two skin-related domains (D): D3 (skin problems, including itching) and D10 (embarrassment and/or shame because of appearance). Estimated persistence at 1 year was assessed across baseline (BL) BSA categories.

Results: At BL, significantly more pts receiving UST than TNFi had BSA >10% (Figure 1). BL disease impact (PsAID-12) was worse in pts with BSA >10% than <3% in D3, D10 and total (non-overlapping 95% CIs suggest significance) (Table 1). BSA improved from BL to 1 year with both treatments. At 1 year, 64% of pts in both groups had clear/almost clear skin and only 3% had BSA >10% (Figure 1). At 1 year, both treatments significantly reduced disease impact (PsAID-12 total), and D3 and D10 scores, irrespective of BL BSA category, but most markedly in pts with higher BL BSA (Table 1). Worse BL psoriasis was generally associated with longer persistence for both treatments; however, at 1 year, pts

with BSA >10% had significantly shorter persistence with TNFi (mean [95% CI]: 361 [336; 387] days) than with UST (410 [394; 426] days).

Conclusion: In PsA, interleukin-12/23 inhibition (UST) and TNFi therapy in routine care rapidly and substantially reduced extent of skin involvement and related disease impact. Pts with highest BL skin involvement had significantly longer drug persistence with UST than with TNFi. Together, PsABio data suggest that successful treatment of skin involvement in PsA with biologics reduces disease burden and may improve persistence, especially in pts with worse BL psoriasis.

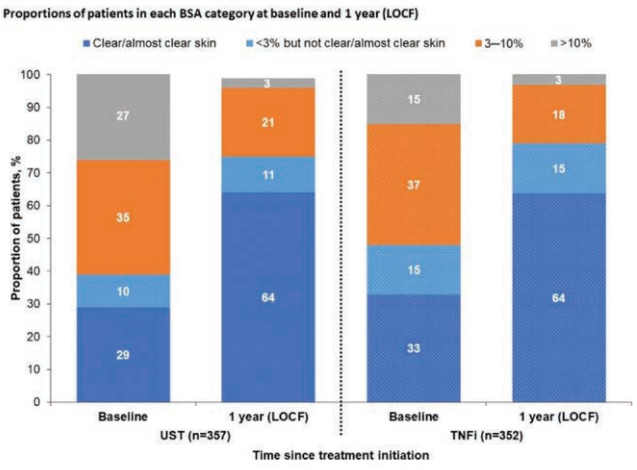


Figure 1

Table 1. PsAID-12 scores at BL and change from BL scores at 6 months and 1 year, by BL BSA category

Mean (95% CI)	Domain 3 (skin problems, including itching)		Domain 10 (embarrassment and/or shame because of appearance)		Total PsAID-12	
	UST	TNFi	UST	TNFi	UST	TNFi
PsAID-12 score at BL by BL BSA						
<3%	4.2 (3.7; 4.8)	3.1 (2.7; 3.6)	3.9 (3.3; 4.4)	3.1 (2.6; 3.6)	5.7 (5.3; 6.0)	5.0 (4.6; 5.3)
3–10%	6.4 (5.9; 6.8)	5.8 (5.3; 6.3)	4.1 (3.5; 4.7)	4.5 (3.9; 5.1)	5.4 (5.1; 5.8)	5.8 (5.4; 6.1)
>10%	7.9 (7.5; 8.3)	6.7 (6.0; 7.5)	6.1 (5.4; 6.8)	5.8 (4.8; 6.8)	6.2 (5.7; 6.6)	6.1 (5.6; 6.7)
Change from BL in PsAID-12 score at 6 months by BL BSA						
<3%	-1.5 (-2.1; -0.9)	-0.8 (-1.3; -0.3)	-1.5 (-2.0; -0.9)	-1.2 (-1.6; -0.7)	-1.6 (-2.0; -1.2)	-1.9 (-2.2; -1.5)
3–10%	-3.2 (-3.8; -2.7)	-2.4 (-3.0; -1.9)	-1.9 (-2.5; -1.3)	-2.0 (-2.5; -1.5)	-2.0 (-2.4; -1.6)	-2.4 (-2.8; -2.0)
>10%	-4.2 (-4.9; -3.6)	-2.5 (-3.2; -1.9)	-2.9 (-3.5; -2.2)	-1.6 (-2.4; -0.8)	-2.4 (-2.8; -2.0)	-2.2 (-2.7; -1.7)
Change from BL in PsAID-12 score at 1 year (LOCF) by BL BSA						
<3%	-1.5 (-2.1; -0.9)	-0.8 (-1.3; -0.3)	-1.6 (-2.2; -1.1)	-1.2 (-1.7; -0.7)	-1.6 (-2.0; -1.2)	-1.9 (-2.3; -1.5)
3–10%	-3.5 (-4.0; -2.9)	-3.2 (-3.7; -2.7)	-2.0 (-2.6; -1.4)	-2.5 (-3.0; -2.0)	-2.2 (-2.6; -1.7)	-3.0 (-3.4; -2.6)
>10%	-4.9 (-5.5; -4.3)	-3.1 (-4.0; -2.3)	-3.5 (-4.2; -2.8)	-2.7 (-3.7; -1.8)	-2.9 (-3.4; -2.4)	-2.9 (-3.5; -2.2)

PsAID-12 total score ≤4 is considered a patient-acceptable symptom state.BL, baseline; BSA, body surface area; CI, confidence interval; LOCF, last observation carried forward; PsAID-12, 12-item Psoriatic Arthritis Impact of Disease questionnaire; TNFi, tumour necrosis factor inhibitor; UST, ustekinumab

Acknowledgements: This study was funded by Janssen.

Disclosure of Interests: Josef S. Smolen Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO, Janssen, Lilly, MSD, Novartis- Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Grant/research support from: AbbVie, AstraZeneca, Lilly, Novartis, Roche, Tatiana Korotaeva Speakers bureau: AbbVie, Amgen, Biocad, Janssen, Lilly, MSD, Novartis, Novartis-Sandoz, Pfizer, UCB, Consultant of: AbbVie, Amgen, Biocad, Janssen, Lilly, MSD, Novartis, Novartis-Sandoz, Pfizer, UCB, Grant/research support from: Pfizer, Michael Nurmohamed Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi, UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi, UCB, Stefan Siebert Speakers bureau: AbbVie, Amgen (previously Celgene), Biogen, Janssen, Novartis, UCB, Consultant of: AbbVie, Janssen, UCB, Grant/research support from: Amgen (previously Celgene), Boehringer Ingelheim, Bristol-Myers Squibb, GSK, Janssen, Novartis, Pfizer, UCB, Paul Bergmans Shareholder of: Johnson & Johnson, Employee of: Janssen, Kurt de Vlam Speakers bureau: AbbVie, Amgen, Eli Lilly, Novartis, UCB, Paid instructor for: Amgen, Galapagos, UCB, Consultant of: Eli Lilly, Galapagos, Johnson & Johnson, Novartis, UCB, Grant/research support from: Celgene, Elisa Gremese: None declared., Beatriz Joven-Ibáñez Speakers bureau: AbbVie, Celgene, Janssen, Novartis, MSD, Pfizer, Wim Noel Employee of: Janssen, Petros Sfikakis Consultant of: AbbVie, Actelion, Boehringer Ingelheim, Enorasis, Farmaserv-Lilly, Genesis, Gilead, MSD, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Faran, Janssen, Pfizer, Roche, Elke Theander Employee of: Janssen, Laure Gossec Consultant of: AbbVie, Amgen, Bioepis, Biogen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Samsung Sanofi-Aventis, UCB, Grant/research support from: Amgen, Galapagos, Janssen, Lilly, Pfizer, Sandoz, Sanofi.

DOI: 10.1136/annrheumdis-2021-eular.767

AB0531

THERAPIES FOR PERIPHERAL JOINT INVOLVEMENT IN PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

Y.Y. Leung[1], T. Korotaeva[2], L. Candia[3], S. Juhl Pedersen[4], W. Bautista-Molano[5], E. Ruderman[6], R. Bisoendial[7], R. Perez Alamino[8], W. Olsder[9], B. Moeller[10], S. Grazio[11], T. Gudu[12], G. Mody[13], C. Pineda[14], H. Raffayova[15], S. Rohekar[16], O. Fitzgerald[17]on behalf of GRAPPA treatment recommendations peripheral arthritis working group. [1]*Singapore General Hospital, Rheumatology & Immunology, Singapore, Singapore*; [2]*Russia, V.A. Nasonova Institute of Rheumatology, Moscow, Russian Federation*; [3]*Universidad Juárez del Estado de Durango, Faculty of Medicine, Durango, Mexico*; [4]*Rigshospitalet, Center for Rheumatology and Spine Diseases, Copenhagen, Denmark*; [5]*Universidad el Bosque, University Hospital Fundación Santa Fe de Bogota, Bogotá, Colombia*; [6]*Northwestern University Feinberg School of Medicine, Rheumatology, Chicago, United States of America*; [7]*Maasstad hospital, Department of Rheumatology and Clinical immunology, Rotterdam, Netherlands*; [8]*Hospital Avellaneda, Rheumatology Section, Tucumán, Argentina*; [9]*Patient Research Partner,., Eindhoven, Netherlands*; [10]*Inselspital University Hospital Bern, Switzerland, Rheumatology & Immunology, Bern, Switzerland*; [11]*University Clinical Centre Sestre milosrdnice, Department for Rheumatology, Physical and Rehabilitation Medicine, Zagreb, Croatia*; [12]*Cambridge University Hospitals NHS FT, Rheumatology, Cambridge, United Kingdom*; [13]*University of KwaZulu-Natal, Department of Rheuamtology, Durban, South Africa*; [14]*Instituto Nacional de Rehabilitación Luis Guillermo Ibarra, Medicine and rehabilitation, Mexico City, Mexico*; [15]*National Institute of Rheumatic Diseases,., Piešťany, Slovakia (Slovak Republic)*; [16]*Western University, London, Ontario, Rheumatology, London, Canada*; [17]*Conway Institute for Biomolecular Research, University College Dublin,., Dublin, Ireland*

Background: Much new information has been reported since the last evidence-based GRAPPA recommendations for the treatment of psoriasis and psoriatic arthritis (PsA).

Objectives: We aimed to compile the evidence for the efficacy and safety of established and newly developed drugs targeting the peripheral arthritis domain in PsA so as to provide information for the revised GRAPPA treatment recommendations.

Methods: A working group consisting of clinicians and patient research partners (PRPs) was convened. We performed an updated systematic literature review (SLR) of randomized controlled trials (RCTs) for the treatment of PsA, including peripheral arthritis, from the date of the last GRAPPA SLR, from February 19, 2013 to August 28, 2020. The working group reviewed the evidence supporting the efficacy on peripheral arthritis for each class of drug, according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach, for three patients groups: 1) naïve to treatment; 2) refractory to conventional (-c) DMARDs; and 3) with prior biological (-b)DMARD experience. We also evaluated the evidence for non-pharmacological treatments. A set of important outcomes for the peripheral arthritis domain was assessed for each class of medication. The certainty of evidence supporting each class of drugs for each patient group was evaluated. Recommendations were derived through consensus meetings.

Results: 87 articles from 52 RCTs were included. For patients with mild disease who are naïve to treatment, the working group strongly recommends csDMARDs (methotrexate, sulfasalazine, leflunomide) and PDE4i, and weakly recommends them for severe disease, where TNFi are preferred over csDMARDs. Other bDMARDs (IL-17i, IL-12/23i, IL-23i) and JAKi are strongly recommended to treat peripheral arthritis for treatment naïve patients. For patients with inadequate response to csDMARDs, we strongly recommend TNFi, IL-17i, IL-12/23i, IL-23i and JAKi. For those who had prior experience with bDMARDs,

we strongly recommend a second TNFi, IL-17i, IL-23i and JAKi. Certainty of evidence (GRADE) and recommendations for peripheral arthritis domain of PsA for different population groups are shown in Table 1. While the evidence supporting non-pharmacological treatments was low, we derived the recommendations from clinician/PRP expert opinion, included advocating an increase in physical activity, smoking cessation and a healthy diet to control weight gain.

Conclusion: Evidence supporting drug treatment for the peripheral arthritis domain of PsA was compiled, providing required information for the revised GRAPPA treatment recommendations. Further work seeking agreement from a broader group of stakeholders is in progress.

Table 1. Certainty of evidence (GRADE) and Recommendation for peripheral arthritis of PsA

	Treatment naive		csDMARD inadequate response		bDMARD inadequate response	
Drug class	**evidence (GRADE)**	**Recommendation**	**evidence (GRADE)**	**Recommendation**	**evidence (GRADE)**	**Recommendation**
PDE-4i	Mod to high	**Strong for** (mild/ mod disease) **Conditional for** (severe disease)	Mod to High	**Strong for**	bDMARD exp: Mod bDMARD IR: Mod (NS)	**Conditional for** (bDMARD exp) **Conditional against** (bDMARD IR)
TNFi	High	**Strong for**	High	**Strong for**	Mod	**Strong for a 2nd TNFi**
TNFi Vs. MTX	High	**Strong for TNFi as 1st line for severe disease**	-	**-**	-	**-**
IL-17i	High	**Strong for**	High	**Strong for**	Mod to high	**Strong for**
IL-12/23i	Mod to high	**Strong for**	Mod to High	**Strong for**	Low	**Conditional for**
IL-23i	High	**Strong for**	High	**Strong for**	Mod	**Strong for**
JAKi	Mod*	**Strong for**	High	**Strong for**	Mod to High	**Strong for**
CTLA4i	Very Low	**Conditional for†**	Low	**Conditional for†**	Mod (NS)	**Conditional for†**
Dual TNFi/ IL17i	Moderate	**NA¥**	Mod	**NA¥**	NA	**NA¥**
IL-6i	Very Low	**Conditional against**	Very low to low	**Conditional against**	NA	**Conditional against**

NS: not statistically significant; *included data from abstract; ¥ not making recommendation due to not approved and not available in market; †reserve for no alternatives. Mod: Moderate; exp: experienced; IR: inadequate response.

Acknowledgements: We are grateful to the contribution of our patient research partner, Rodrigo Firmino.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.900

AB0532

MAINTENANCE OF RESPONSE THROUGH 5 YEARS OF CONTINUOUS GUSELKUMAB TREATMENT: RESULTS FROM THE PHASE-3 VOYAGE 1 TRIAL

C. E. M. Griffiths[1,2], K. Papp[3,4], M. Song[5], M. Miller[5], Y. You[6], Y. K. Shen[6], A. Blauvelt[7]. *[1]NIHR Manchester Biomedical Research Centre, University of Manchester, Dermatology Centre, Manchester, United Kingdom*; *[2]Salford Royal NHS Foundation Trust, Dermatology Department, Salford, United Kingdom*; *[3]K. Papp Clinical Research, Department of Dermatology, Waterloo, Ontario, Canada*; *[4]Probity Research Inc., Clinical Research, Waterloo, Ontario, Canada*; *[5]Janssen Research & Development, LLC, Department of Immunology, Spring House, Pennsylvania, United States of America*; *[6]Janssen Research & Development, LLC, Clinical Biostats, Spring House, Pennsylvania, United States of America*; *[7]Oregon Medical Research Center, Department of Dermatology, Portland, Oregon, United States of America*

Background: VOYAGE 1, a phase-3, double-blinded, placebo- and active comparator-controlled study evaluated the efficacy and safety of guselkumab (GUS; a fully human anti-interleukin-23 monoclonal antibody) in patients with moderate-to-severe plaque psoriasis.[1,2,3]

Objectives: To assess the efficacy and safety through 5 years of continuous GUS treatment.

Methods: In VOYAGE 1, patients were randomized to GUS 100 mg at Weeks 0, 4, 12, then every 8 weeks (q8w); placebo at Weeks 0, 4, 12 followed by GUS 100 mg at Weeks 16, 20 then q8w; or adalimumab 80 mg at Week 0, 40 mg at Week 1, then 40 mg every 2 weeks (q2w) through Week 47. At Week 52, all patients continued open-label GUS through Week 252. Efficacy assessments included proportions of patients achieving ≥90% or 100% improvement in Psoriasis Area and Severity Index (PASI 90, PASI 100), and Investigator's Global Assessment scores of cleared/minimal or cleared (IGA 0/1, IGA 0). Three statistical methods were used to analyze efficacy: prespecified Treatment Failure Rules (TFR), Nonresponder Imputation (NRI), and As Observed (OBS). For TFR analyses, patients who discontinued study agent due to lack of efficacy, worsening of psoriasis, or use of a protocol-prohibited psoriasis treatment were considered nonresponders. For NRI analyses, patients with missing efficacy data (regardless of the reason) after application of TFR were counted as nonresponders. For OBS analyses, missing data were not imputed. Safety was assessed through Week 264.

Results: Among a total of 494 patients randomized to GUS at Week 0 (N=329) and placebo patients who crossed over to GUS at Week 16 (N=165), 76.9% (380/494) continued study agent through Week 252. PASI 90 responses were well-maintained with up to 5 years of continuous GUS use. At Week 52, PASI 90 response rates were 79.7%, 75.5%, and 80.6% based on TFR, NRI, and OBS analyses, respectively; corresponding rates at Week 252 were 84.1%, 66.6%, and 86.6%. Likewise, PASI 100, IGA 0/1, and IGA 0 responses were maintained from Week 52 through Week 252 (Table 1). Efficacy was also maintained through Week 252 in patients randomized to GUS at Week 0 (N=329). Through the end of the study for all patients (GUS group and adalimumab→GUS crossover group; N=774), the proportion of patients reporting at least one adverse event (AE), serious AE, or discontinuation due to AEs were 87.7%, 16.4%, and 6.1%, respectively. Rates of AEs of interest through Week 264 were as follows: serious infections (2.8%), malignancies (nonmelanoma skin cancer [1.7%]; cancer other than nonmelanoma skin cancer [2.3%]), major adverse cardiovascular events (1.0%), and suicidal ideation and behavior (0.6%).

Conclusion: High efficacy response rates were maintained (regardless of the method used to analyze data) and no new safety concerns were identified through 5 years of continuous GUS treatment in VOYAGE 1.

REFERENCES:

[1] Blauvelt A et al. *J Am Acad Derm* 2017;76:405-417

[2] Griffiths CEM et al. *J Drugs Dermatol* 2018;17:826-832

[3] Griffiths CEM et al. *J Dermatol Treat* 2020;13:1-9

Table 1. Proportion of Patients in the GUS Group[a] Achieving Clinical Responses by Analysis Type at Week 52 and Week 252

	Week 52			Week 252		
	TFR (N=468) (%)	NRI (N=494) (%)	OBS (N=463) (%)	TFR (N=391) (%)	NRI (N=494) (%)	OBS (N=380) (%)
PASI 90	77.9	75.5	80.6	84.1	66.6	86.6
PASI 100	49.7	46.6	49.7	52.7	41.7	54.2
IGA 0	84.6	80.2	85.5	82.4	65.2	84.7
IGA 0	53.3	50.8	54.2	54.7	43.3	56.3

GUS, guselkumab; IGA, Investigator's Global Assessment; NRI, nonresponder imputation method; OBS, As Observed method; PASI, Psoriasis Area and Severity Index; TFR, treatment failure rules method[a]Includes patients randomized to GUS and placebo patients who crossed over to GUS at Week 16

Disclosure of Interests: Christopher E.M. Griffiths Speakers bureau: AbbVie, Eli Lilly, Janssen, Leo, Novartis, Pfizer, Sandoz, and Sun Pharma, Consultant of: AbbVie, Eli Lilly, Janssen, Leo, Novartis, Pfizer, Sandoz, and Sun Pharma, Grant/research support from: AbbVie, Eli Lilly, Janssen, Leo, Novartis, Pfizer, Sandoz, and Sun Pharma, Kim Papp Speakers bureau: AbbVie, Amgen, Astellas, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Dermira, Eli Lilly, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa-Hakko Kirin, Leo Pharma, MedImmune, Merck-Serono, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, Sanofi-Genzyme, Stiefel, Sun Pharma, Takeda, UCB, and Valeant, Consultant of: AbbVie, Amgen, Astellas, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Dermira, Eli Lilly, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa-Hakko Kirin, Leo Pharma, MedImmune, Merck-Serono, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, Sanofi-Genzyme, Stiefel, Sun Pharma, Takeda, UCB, and Valeant, Grant/research support from: AbbVie, Amgen, Astellas, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Dermira, Eli Lilly, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa-Hakko Kirin, Leo Pharma, MedImmune, Merck-Serono, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, Sanofi-Genzyme, Stiefel, Takeda, UCB, and Valeant, Michael Song Shareholder of: Johnson and Johnson, Employee of: Janssen Research & Development, LLC, Megan Miller Shareholder of: Johnson and Johnson, Employee of: Janssen Research & Development, LLC,

Yin You Shareholder of: Johnson and Johnson, Employee of: Janssen Research & Development, LLC, Yaung-Kaung Shen Shareholder of: Johnson and Johnson, Employee of: Janssen Research & Development, LLC, Andrew Blauvelt Speakers bureau: AbbVie, Consultant of: AbbVie, Aclaris, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Dermira, Eli Lilly, FLX Bio, Forte, Galderma, Janssen, Leo, Novartis, Ortho, Pfizer, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma.

DOI: 10.1136/annrheumdis-2021-eular.960

AB0533 COMBINATION OF METHOTREXATE AND LEFLUNOMIDE IS SAFE AND HAS GOOD DRUG RETENTION AMONG PATIENTS WITH PSORIATIC ARTHRITIS

M. Haroon[1], S. Batool[2], S. Asif[2], F. Hashmi[2], S. Ullah[2]. *[1]Fatima Memorial Hospital & FMH College of Medicine and Dentistry, Department of Rheumatology, Lahore, Pakistan*; *[2]Fatima Memorial Hospital & FMH College of Medicine and Dentistry, Department of Rheumatology, Lahore, Pakistan*

Background: Among patients with psoriatic arthritis (PsA), there remains a considerable confusion regarding the effectiveness of conventional synthetic DMARDs (csDMARDs), especially methotrexate (MTX). The availability of biologic DMARDs and targeted synthetic DMARDs have revolutionised the management of psoriatic disease; however, it comes with a significant cost burden. We believe that combination of DMARDs, especially combining MTX and Leflunomide (LEF) provides a valuable low-cost treatment option for patients with PsA after failure of MTX monotherapy. Hence, in our practice, we are inclined to use combination of potent DMARDs after MTX failure, prior to considering biologic therapies. Little is known about the combination use of LEF and MTX in PsA, especially in the context of drug retention time and tolerability.

Objectives: We aimed to review our PsA cohort data especially examining the drug retention of first-line csDMARD monotherapy and combination csDMARDs.

Methods: In our centre, MTX is a preferred first line csDMARD, unless contraindicated, and patients are followed up with a protocol on 4-6 weekly basis unless complete remission is achieved. MTX if needed is escalated to the maximum tolerated dose (up to 25mg/week), and if PsA is still active then preferably LEF is added (usual starting dose for add-on therapy is 10mg a day and if needed escalated to 20mg a day, without any loading dose). Other csDMARDs, such as sulphasalazine are used, if needed. For this study, after written-informed consent, only those adult patients were included who had a follow up of at least 6 months with our rheumatology services, and were fulfilling CASPAR criteria. Moreover, only patients who were DMARD-naïve (no prior DMARD therapy for any cause, including psoriasis), and initiated DMARD as monotherapy after 1 April 2018 were included. If any patient had already been on any DMARDs prior to attending our rheumatology services was excluded.

Results: A total of 81 PsA patients [mean age 45.6±6 years; 52% male; mean PsA disease duration=9±4 years; 35% with dactylitis, 42% with enthesitis, 17% with sacroiliitis, median current PASI=2.6, median number of swollen joints=8.0, median number of tender joints= 11.0] fulfilled the inclusion and exclusion criteria. As regards first-line csDMARD monotherapy, 88% (n=71) of patients were commenced on MTX. In total, 79% (n=56 out of 71) of patients who were started on MTX as their first-line csDMARD therapy failed this monotherapy during follow-up (51=ineffective, 5=intolerance). After a median follow-up of 22 months, MTX median drug retention among all MTX monotherapy users (n=71) was only 7 months (IQR 5-7); and among MTX failures (n=56), MTX monotherapy median drug retention was 6.0 months (IQR 4-8). Eighty percent (n=45 out of 56) of the MTX monotherapy failure cohort was started on combination therapy of MTX and LEF (combo MTX+LEF); among them, only 7 patients needed escalation of therapy to bDMARDs, and the rest are still using combo MTX+LEF. It was noted that to date median drug retention time of combo MTX+LEF has been 8 months (IQR 7-11), and 84% (n=38 out of 45) of these patients are still using this combo therapy. Significantly more patients managed to continue the combo MTX+LEF therapy compared to MTX monotherapy (84% vs. 21%, p<0.001)

Conclusion: Among csDMARD naïve PsA patients, 79% of patients failed MTX monotherapy with median drug retention time of only 6 months. Combination of MTX and LEF was well tolerated and had good drug retention time, with 84% of patients having ongoing treatment to date. Our data provides initial evidence that MTX and LEF combination therapy could be an effective treatment option for PsA

Disclosure of Interests: Muhammad Haroon Speakers bureau: Roche, Novartis, Grant/research support from: Abbvie, Pfizer, Shabnam Batool: None declared., Sadia Asif: None declared., Farzana Hashmi: None declared., Saadat Ullah: None declared.

DOI: 10.1136/annrheumdis-2021-eular.978

AB0534 THE IMPACT OF AXIAL INVOLVEMENT ON ACR RESPONSE IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS OF SUBANALYSIS OF THE PATERA STUDY

T. Korotaeva[1], I. Gaydukova[2], V. Mazurov[2], A. Samtsov[3], V. Khayrutdinov[3], A. Bakulev[4], A. Kundzer[5], N. Soroka[6], A. Eremeeva[7]. *[1]Nasonova Research Institute of Rheumatology, Laboratory of Spondyloarthritides and Psoriatic Arthritis, Moscow, Russian Federation*; *[2]Mechnikov North-Western State Medical University, Department of Therapy and Rheumatology of Temporary Disability and Medical Care Quality Expertise, St-Petersburg, Russian Federation*; *[3]Kirov Military Medical Academy, Department of Skin and Veneral Diseases, St-Petersburg, Russian Federation*; *[4]Razumovsky Saratov State Medical University, Department of Dermatovenereology and Cosmetology, Saratov, Russian Federation*; *[5]Belarusian Medical Academy of Postgraduate Education, Department of Cardiology and Rheumatology, Minsk, Belarus*; *[6]Belarusian State Medical University, Department of Internal Diseases №2, Minsk, Belarus*; *[7]JSC BIOCAD, Clinical Development Department, St-Petersburg, Russian Federation*

Background: Inflammatory back pain (IBP) is a common symptom of axial disease in patients with psoriatic arthritis (PsA). The reported prevalence of axial disease in patients with PsA is quite variable and must be taken into account while choosing treatment strategy. Netakimab (NTK) is an anti-interleukin-17A monoclonal antibody approved for psoriasis, ankylosing spondylitis, PsA in Russia and Belarus.

Objectives: A subanalysis was aimed to investigate the ACR (American College of Rheumatology) 20/50/70 response rate in PsA patients with/without the axial disease, defined by the presence of IBP according to self-reported ASAS IBP criteria, 2009 at baseline.

Methods: PATERA is an ongoing phase 3 international double-blind, placebo-controlled clinical study (NCT03598751). 194 adult patients with PsA (CASPAR criteria, 2006) with inadequate response to csDMARD or one TNFi, were randomly assigned to receive NTK 120mg or placebo at weeks 0,1,2,4,6,8,10,14,18,22. The ACR response was calculated in NTK-treated patients with IBP (IBP(+)) and NTK-treated patients without IBP (IBP(-)) according to self-reported ASAS IBP criteria, 2009. Patients with missing values for categorical variables were considered as non-responders in the analysis.

Results: 97 PsA patients (N=54 IBP(+), N=43 IBP(-)) received NTK. Both subpopulations were comparable in gender, age, and PsA activity at baseline. There were no significant differences in ACR20 achievement between the groups (Figure 1). The percentage of patients with ACR50 was significantly (p<0.05) higher in the IBP(-) subpopulation at weeks 4-20 (data not shown), but not at week 24 with 63% IBP(+) and 79% IBP(-) responders (p≥0.05). Similarly, IBP(+) patients had a lower frequency of ACR70 response (Figure 1).

Conclusion: NTK is effective in PsA treatment irrespectively of the presence of axial disease. Both IBP(-) and IBP(+) subpopulations achieved ACR20/50/70 as well, however, the benefit in IBP(-) patients was more pronounced.

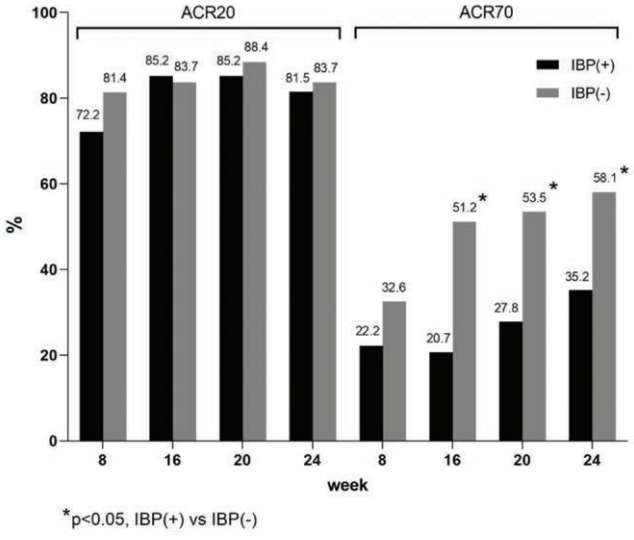


Figure 1 ACR response rates

Acknowledgements: This study was sponsored by JSC BIOCAD.

Disclosure of Interests: Tatiana Korotaeva Speakers bureau: Abbvie, Biocad, Eli Lilly, Johnson & Johnson, Janssen, Novartis, Pfizer, UCB, Inna Gaydukova

Speakers bureau: Abbvie, Biocad, Eli Lilly, MSD, Novartis, Pfizer, Sandoz, V Mazurov: None declared., Aleksey Samtsov: None declared., Vladislav Khayrutdinov: None declared., Andrey Bakulev: None declared., Alena Kundzer: None declared., Nikolaj Soroka: None declared., Anna Eremeeva Employee of: Biocad.
DOI: 10.1136/annrheumdis-2021-eular.992

AB0535 PRESCRIPTION PATTERNS OF THE SECOND BIOLOGIC DMARD IN PSORIATIC ARTHRITIS THROUGH THE LAST DECADE: HURBIO-PsA REAL LIFE EXPERIENCE

U. Kalyoncu[1], O. Karadag[1], L. Kılıç[1], A. Akdoğan[1], I. Dogan[1], Ş. A. Bilgen[1], E. Bilgin[1], E. C. Bolek[1], A. Erden[2], B. Armagan[2], A. Sarı[3], E. Duran[1], B. Farisoğulları[1], G. K. Yardımcı[1], Z. Özsoy[1], G. Ayan[1], A. İ. Ertenli[1], M. Çalgüneri[1], S. Kiraz[1]. *[1]Hacettepe University, Internal Medicine, Rheumatology, Ankara, Turkey*; *[2]Ankara City Hospital, Internal Medicine, Rheumatology, Ankara, Turkey*; *[3]Yenimahalle Research and Education Hospital, Internal Medicine, Rheumatology, Ankara, Turkey*

Background: Psoriatic arthritis (PsA) is a multi-dimensional chronic disease, which can affect joints, skin and enthesis. Extrapolation of the positive treatment results of anti-tumor necrosis factor (TNF) alpha agents on spondyloarthritis and rheumatoid arthritis to the treatment practice of PsA lead to a new era for the management of PsA. However, unmet needs in the management of PsA lead to development of several drugs targeting different molecules and cytokines. The impact of these developments on PsA patients who are intolerant/unresponsive to the first biological disease-modifying anti-rheumatic drugs (bDMARD) still needs to be defined.
Objectives: To explore the second biologic agent trends on PsA patients of our 10-years of single-center experience.
Methods: HURBIO-PsA (Hacettepe University Rheumatology Biologic Registry) is a single center biological disease modifying anti-rheumatic drug (DMARD) registry since 2005 on PsA patients. Until the end of the 2020, 19 different rheumatologists contributed to the development of HURBIO-PsA. Anti-TNF drugs were approved as first line bDMARD for PsA patients. Distribution of the second-line biological agents (switch from first-line biological agent because of either adverse events or unresponsiveness) was calculated according to 5-year periods starting from the 2011. Also, demographic and serologic data of RA patients were reported.
Results: A total of 225 PsA (225/443, 50.8%) patients, who was prescribed a second biological agent, was registered in HURBIO-PsA by the end of 2020. Of these patients, 74.7% was female. Mean age at the starting of bDMARD was 47.1 ± 11.6 years. 90 (40.0%) and 135 (60.0%) patients were prescribed with their second bDMARD in 2011-2015 and 2016-2020, respectively. There was a trend towards the increasing prescription of non-Anti-TNF bDMARDs as second-line over time, especially for secukinumab.

Table 1. Distribution of second biologic DMARDs in PsA patients according to 5-years periods

	2011-2015	2016-2020	Total
Adalimumab	30 (33.3)	33 (24.4)	66 (29.3)
Etanercept	33 (36.7)	8 (5.9)	41 (18.2)
Infliximab	9 (10)	15 (11.1)	24 (10.6)
Golimumab	9 (10)	5 (3.7)	14 (6.2)
Certolizumab	5 (5.6)	34 (25.2)	39 (17.3)
Anti-TNF	86 (95.6)	95 (70.4)	181 (80.5)
Secukinumab	0	26 (19.3)	26 (11.5)
Ustekinumab	0	10 (7.4)	10 (4.4)
Abatacept	4 (4.4)	2 (1.5)	6 (2.6)
Tofacitinib	0	2 (1.5)	2 (0.9)
Non-Anti-TNF	4 (4.4)	40 (29.6)	44 (19.5)
Total	90 (100)	135 (100)	225 (100)

***Approval years of drugs in Turkey**; Infliximab: 2003, etanercept:2004, adalimumab: 2005, golimumab: 2013, certolizumab: 2014, secukinumab: 2018, ustekinumab: 2018; abatacept and tofacitinib were given with the permission from the Ministry of Health of Turkey for off-label use authorization*

Conclusion: Almost half of the PsA patients switched their anti-TNF drugs to others. Non-Anti-TNF bDMARDs, especially secukinumab, becoming more frequently used as a second-line biologic agent in PsA in recent years. These bDMARD prescription trend is appropriate to EULAR PsA recommendations.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1222

AB0536 EFFICACY OF TNF INHIBITORS IN MONOTHERAPY VERSUS COMBINATION THERAPY WITH csDMARDs IN PORTUGUESE PATIENTS WITH PSORIATIC ARTHRITIS: A REAL-WORLD STUDY

F. Oliveira Pinheiro[1], B. M. Fernandes[1], S. Garcia[1], M. Rato[1], D. Fonseca[2], D. Santos Oliveira[1,3], A. Martins[1], F. R. Martins[4], P. Madureira[1], M. Bernardes[1,5], L. Costa[1]. *[1]Centro Hospitalar Universitário de São João, Rheumatology Department, Porto, Portugal*; *[2]Centro Hospitalar Vila Nova de Gaia/Espinho, Rheumatology Department, Vila Nova de Gaia, Portugal*; *[3]Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; *[4]Centro Hospitalar Universitário do Algarve, Rheumatology Department, Faro, Portugal*; *[5]Faculty of Medicine, University of Porto, Medicine Department, Porto, Portugal*

Background: Tumor necrosis factor inhibitors (TNFi) are a key therapeutic weapon in psoriatic arthritis (PsA), and can be used as monotherapy or in combination with other csDMARDs, which are usually used as first line therapy in these patients, although its efficacy is not as well documented as in other rheumatic diseases. The optimal use of iTNF in PsA, as monotherapy or in combination therapy with csDMARDs, is still under debate.
Objectives: We aimed to compare the response to treatment with TNFi in monotherapy and combined with csDMARDs, as first biologic, in patients with PsA.
Methods: Retrospective study that included PsA patients followed at our Rheumatology department under TNFi as first biologic, fulfilling CASPAR classification criteria and registered in Reuma.pt. Clinical and laboratory data were collected at the start of the first iTNF and in the last visit of 2019. Disease activity was assessed using CDAI, SDAI, DAS28(4V), BASDAI, ASDAS, and the response measured using the BASDAI50, ASDAS, ASAS, ACR and PsARC responses. Comparison between groups was performed using the chi-square test, Mann-Whitney U/t-test (categorical and continuous variables, respectively). Logistic regression analyses were performed to determine predictors of bDMARD failure, and survival analysis to measure persistence under the first bDMARD regarding csDMARD status at baseline.
Results: We included 99 patients, 47 (47.5% females) with a mean age of 47.9 ± 11.7 years at the start of the first iTNF. Fifty-one patients (51.5%) had symmetric polyarthritis, 26 (26.3%) spondyloarthritis, 16 (16.2%) asymmetric oligoarthritis, 3 (3.0%) distal arthritis and 1 (1.0%) arthritis mutilans. Sixty-three percent were under corticosteroid therapy and 77.8% under csDMARD therapy at the start of the first iTNF (mostly methotrexate, in 55.6% of patients under csDMARD). Etanercept (41, 41.4%), golimumab (25, 25.3%), adalimumab (22, 22.2%), infliximab (9, 9.1%) and certolizumab (2, 2.0%) were the iTNF started in these patients.
Patients who started iTNF as monotherapy had more frequent involvement of axial skeleton compared with combined therapy (54.5% vs 19.5%, p=0.001), were less exposed to corticosteroids (26.3% vs 72.6%, p<0.001) and had higher mean BASMI (3.7±1.8 vs 3.0±0.8, p=0.021) and BASFI (6.7±1.3 vs 4.7±2.5, p=0.036). Patients who were on iTNF monotherapy at the last consultation (43.4%) had lower mean tender (1.0±1.5 vs 3.6±4.3, p=0.002) and swollen (0.2±0.7 vs 0.8±1.0, p=0.012) joint counts, median patient VAS (30±46 vs 50±44, p=0.023), mean CDAI (5.6±4.4 vs 8.7±4.9, p=0.019), SDAI (6.2±4.6 vs 9.1±5.1, p=0.032), and DAS28(4V) (2.2±0.8 vs 2.7±0.9, p=0.047). iTNF failure was not significantly different in both groups. In the regression models, we found that basal DAS28(4V) (OR 1.874, 1.147-3.062 95%CI; p=0,012) was a predictor of first iTNF failure; there were no differences regarding csDMARD status.
When evaluating only patients without spondyloarthritis, we found that, at the last visit, iTNF monotherapy patients still had less exposure to corticosteroids (26.9% vs 54.3%, p=0.002), fewer mean tender (0.7±1.0 vs 2.6±4.4, p=0.006) and swollen (0.2±0.7 vs 1.1±2.5, p=0.025) joint counts, with no other differences observed. In the regression models, we found no differences regarding csDMARD status in these patients, while adalimumab (OR 0.009, 0.001-0.139 95% CI; p=0.009) was a negative predictor of bDMARD failure. Survival analysis revealed no differences between mono- and combined therapy.
Conclusion: We can conclude that the differences observed regarding csDMARD status in patients with PsA are mainly due to different patterns of arthritis, namely, predominance of axial involvement. In patients without spondyloarthritis, iTNF monotherapy did not differ significantly in terms of response to treatment and disease activity measures, nor does monotherapy predict bDMARD failure and treatment response. These results suggest that iTNF monotherapy is possible in PsA without compromising treatment response.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1295

AB0537 PSORIATIC ARTHRITIS BURDEN, QUALITY OF LIFE AND FUNCTIONAL ABILITY IMPAIRMENTS IN PATIENTS INITIATED ON APREMILAST IN THE ROUTINE CARE IN GREECE: INTERIM RESULTS FROM THE MULTICENTER PROSPECTIVE STUDY "APROACH"

P. Katsimpri[1], D. Vassilopoulos[2], G. Katsifis[3], G. Vosvotekas[4], D. Bogdanos[5], P. Sidiropoulos[6], P. Vounotrypidis[7], A. Georgountzos[8], A. Bounas[9], A. Garyfallos[10], S. Gazi[11], P. Georgiou[12], E. Kataxaki[13], C. Papagoras[14], A. Elezoglou[15], S. N. Liossis[16], A. Tzioufas[17], P. Voulgari[18], F. Satra Tzoufra[19], Z. Anagnostopoulos[19], N. Antonakopoulos[19], P. Sfikakis[20]. *[1]"Attikon" University Hospital, Rheumatology and Clinical Immunology Unit,4th University Pathology*

Clinic, Athens, Greece; [2]*General Hospital of Athens "Hippokratio", Department of Medicine, National and Kapodistrian University of Athens, Athens, Greece*; [3]*Athens Naval hospital, Rheumatology, Athens, Greece*; [4]*Euromedica General Clinic of Thessaloniki, Rheumatology, Thessaloniki, Greece*; [5]*University General Hospital of Larissa, Department of Rheumatology and Clinical Immunology, Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece*; [6]*General University Hospital of Heraklion, Rheumatology, Heraklion, Greece*; [7]*424 General Military Hospital, Rheumatology, Thessaloniki, Greece*; [8]*General Hospital of Athens "G. Gennimatas", Rheumatology, Athens, Greece*; [9]*General Clinic of Patras "Olympion", Rheumatology, Patras, Greece*; [10]*General Hospital of Thessaloniki "Ippokratio", Rheumatology, Thessaloniki, Greece*; [11]*General Hospital of Attica "KAT", Rheumatology, Athens, Greece*; [12]*General Hospital of Patras "Ag. Andreas", Rheumatology, Patras, Greece*; [13]*General Hospital of Elefsina "Thriasio", Rheumatology, Athens, Greece*; [14]*University Hospital of Alexandroupolis, Rheumatology, Alexandroupolis, Greece*; [15]*"Asklipieion" General Hospital of Voula, Rheumatology, Athens, Greece*; [16]*Patras University Hospital, Rheumatology, Patras, Greece*; [17]*General Hospital of Athens "Laiko", Department of Pathophysiology, School of Medicine, University of Athens, Athens, Greece, Athens, Greece*; [18]*Medical School, University of Ioannina, Rheumatology Clinic, Department of Internal Medicine, Ioannina, Greece*; [19]*Genesis Pharma S.A., Medical, Athens, Greece*; [20]*General Hospital of Athens "Laiko", First Department of Propeudeutic and Internal Medicine, Athens University Medical, Athens, Greece*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease associated with substantial psychosocial burden and health-related quality of life (HRQoL) and functional ability impairments.
Objectives: To characterize the profile of patients with PsA initiating therapy with apremilast in routine care settings, in terms of the physician-assessed clinical disease burden and the patient-reported generic and disease-related HRQoL and functional disability.
Methods: This is an ongoing 52-week multicenter, prospective study conducted in the Greek healthcare environment. Eligible patients are bio-naïve adults with active peripheral PsA, inadequate (within the first 12 months of treatment) response/intolerance to a prior conventional synthetic disease-modifying antirheumatic drug (csDMARD), and no prior use of tofacitinib, initiating apremilast as per the approved label. Data are being collected by physician assessments, as performed in routine clinical practice, and by patient-reported outcomes. 170 patients enrolled in the study; data at apremilast initiation (baseline) from the first 100 eligible consenting patients are presented in this interim analysis as per protocol.
Results: 99 evaluable patients were consecutively enrolled in 19 rheumatology departments between 15-Apr-2019 and 13-Jan-2020. At baseline (Table 1) [mean (SD) age: 53.8 (11.7) years], 43.4% of the patients had at least one (30.3% had ≥2) ongoing comorbidity other than PsA/PSO. The median [interquartile range (IQR)] PsA and psoriasis duration were 1.9 (1.0-3.5) and 7.5 (3.9-16.8) years, respectively. All subjects were on csDMARD while 24.2% received combination therapy, oral non-steroid anti-inflammatory drugs (32.3%), topical treatments (20.2%) and systemic steroids (11.1%). Based on the Clinical Disease Activity in PsA (cDAPSA) score, 58.6% of the patients had moderate, and 29.3% high disease activity. In the EuroQol (EQ) 5-Dimensions (5D) 5-Levels questionnaire, 93.9, 82.8, 82.8, 73.7, and 51.5% of the patients reported problems in 'pain/discomfort', 'anxiety/depression', 'usual activities', 'mobility', and 'self-care', respectively. The median (IQR) baseline UK-weighted EQ-5D index and EQ-Visual Analogue Scale scores were 0.55 (0.44-0.70) and 50.0 (40.0-70.0), respectively. The median (IQR) Health Assessment Questionnaire-Disability Index (HAQ-DI) and mean (SD) PsA Impact of Disease 12-item (PsAID12) scores were 1.0 (0.5-1.4) and 4.6 (2.0), respectively.
Conclusion: More than 8 out of 10 bio-naïve patients initiated on apremilast in the routine clinical care in Greece have at least moderate disease activity, active psoriasis, and problems with pain/discomfort, anxiety/depression, and performance of usual activities at a median of 2 years post-diagnosis. HAQ-DI and PsAID12 scores indicate moderate impairment of physical functionality and PsA-related HRQoL. The findings underscore considerable disease burden early in the disease course.

Table 1. Baseline characteristics

	N	%/Mean/ Median
Women, %	57/99	57.6
Peripheral joint involvement only, %	92/99	92.9
Polyarthritis (≥5 joints), %	69/99	69.7
cDAPSA (range: 0-154), median (IQR)	99	22.0 (16.0-29.0)
Number of SJC (0-66) / TJC (0-68), median (IQR)	99	4 (2-8) / 6 (2-10)
Active psoriasis (BSA>0%), %	83/99	83.8
BSA score, median (IQR)	77/83	5.0 (2.0-12.0)
Nail involvement, %	38/96	39.6
Enthesitis and/or dactylitis, %	30/95	31.6
Dactylitis, %	11/95	11.6
Finger and toe Dactylitis Severity Score (DSS) (range: 0-60), median (IQR)	10/11	2.0 (1.0-6.0)
Enthesitis, %	22/95	23.2
LEI score (range: 0-14), median (IQR)	22	2.0 (1.0-2.0)
Extra-articular manifestations (mainly fatigue), %	10/99	10.1
Comorbidities in ≥15% of the patients		
Hypertension, Essential hypertension, %	23/99	23.2
Dyslipidemia, hypercholesterolemia, (type V) hyperlipidemia, %	15/99	15.2
Total PsAID12 score (range: 0-10), mean (SD)	98	4.6 (2.0)
Total HAQ-DI score (range: 0-3), median (IQR)	99	1.0 (0.5-1.4)

Disclosure of Interests: PELAGIA KATSIMPRI Speakers bureau: Janssen, Genesis pharma, Novartis, Abbvie, UCB, Hospital Line, Actelion Pharmaceuticals, Pfizer, Consultant of: Janssen, Genesis pharma, Novartis, Abbvie, UCB, Hospital Line, Actelion Pharmaceuticals, Pfizer, Dimitrios Vassilopoulos Speakers bureau: AbbVie, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Grant/research support from: AbbVie, GenesisPharma, Novartis, Pfizer, Roche, UCB, Janssen, MSD, Gkikas Katsifis Speakers bureau: Abbvie, Aenorasis, Amgen, Genesis Pharma, Bausch Health, BMS, Celgene, Janssen, MSD, Novartis, Roche, Pfizer, UCB, Grant/research support from: Abbvie, Aenorasis, Amgen, Genesis Pharma, Bausch Health, BMS, Celgene, Janssen, MSD, Novartis, Roche, Pfizer, UCB, GEORGIOS VOSVOTEKAS Speakers bureau: MSD, Consultant of: AbbVie, Novartis, Dimitrios Bogdanos Speakers bureau: Menarini, Novartis, Consultant of: Fresenius Kabi Hellas, Novartis, Grant/research support from: Aenorasis, Elpen, Genesis Pharma, GlaxoSmithKline, Boehringer Ingelheim, Lilly, Prodromos Sidiropoulos Grant/research support from: University of Crete Special Account for Research and pharma, Periklis Vounotrypidis Speakers bureau: Genesis Pharma, MSD, Novartis, Grant/research support from: Genesis Pharma, MSD, Novartis, Athanasios Georgountzos Grant/research support from: AbbVie, Genesis Pharma, Janssen, Mylan SAS, Pfizer, Roche, UCB, Andreas Bounas: None declared., Alexandros Garyfallos Speakers bureau: AbbVie, BGP, Roche, Consultant of: Genesis Pharma, UCB, Pfizer, Sousana Gazi: None declared., Panagiotis Georgiou Grant/research support from: Janssen-Cilag, Novartis, UCB, Evaggelia Kataxaki Speakers bureau: Novartis, Charalampos Papagoras Speakers bureau: Abbvie, Novartis, Genesis, Lilly, Biogen, Aenorasis, GSK, Pfizer, ANTONIA ELEZOGLOU: None declared., Stamatis-Nick Liossis: None declared., Athanasios Tzioufas Grant/research support from: AbbVie, Genesis Pharma, GSK, Horizon, Lilly, Novartis, Pfizer, Paraskevi Voulgari Speakers bureau: GlaxoSmithKline, Novartis, UCB, Consultant of: GlaxoSmithKline, Novartis, UCB, FOTEINI SATRA TZOUFRA Employee of: GENESIS PHARMA S.A., ZAFEIRIOS ANAGNOSTOPOULOS Employee of: GENESIS PHARMA S.A., NIKOLAOS ANTONAKOPOULOS Employee of: GENESIS PHARMA S.A., Petros Sfikakis Speakers bureau: AbbVie, Boehringer Ingelheim, GenesisPharma, Novartis, Pfizer, UCB, Consultant of: AbbVie, Boehringer Ingelheim, GenesisPharma, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Boehringer Ingelheim, GenesisPharma, Novartis, Pfizer, UCB.
DOI: 10.1136/annrheumdis-2021-eular.1326

AB0538

POOLED SAFETY RESULTS FROM TWO PHASE-3 TRIALS OF GUSELKUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS THROUGH 1 YEAR

C. T. Ritchlin[1], P. Rahman[2], P. Helliwell[3], W. H. Boehncke[4], I. Mcinnes[5], A. B. Gottlieb[6], S. Kafka[7], A. Kollmeier[8], E. C. Hsia[8,9], X. L. Xu[8], M. Shawi[10], S. Sheng[11], P. Agarwal[11], B. Zhou[11], P. Ramachandran[12], P. J. Mease[13]. [1]*University of Rochester, School of Medicine and Dentistry, Rochester, United States of America*; [2]*Memorial University of Newfoundland, Disicpline of Medicine, Faculty of Medicine, St. Johns, Canada*; [3]*University of Leeds, Clinical Rheumatology, Leeds, United Kingdom*; [4]*Geneva University Hospitals, Department of Dermatology, Geneva, Switzerland*; [5]*University of Glasgow, Director of Dermatology, Glasgow, United Kingdom*; [6] *Icahn School of Medicine/Mt Sinai, Department of Dermatology, New York, United States of America*; [7]*Janssen Scientific Affairs, MED GROUP RHEUM TA, Horsham, United States of America*; [8]*Janssen Research & Development, LJ IMMUNOLOGY CLINIC, Spring House, United States of America*; [9]*University of Pennsylvania Medical Center, Division of Rheumatology, Philadelphia, United States of America*; [10]*Janssen Scientific Affairs, GMA COMMERCIAL OPS, Horsham, United States of America*; [11]*Janssen Research & Development, CLINICAL BIOSTATS PA, Spring House, United States of America*; [12]*Janssen Research & Development, MSA US PA, Spring House, United States of America*; [13]*Swedish Medical Center/Providence St Joseph Health and University of Washington School of Medicine, Department of Internal Medicine, Seatle, United States of America*

Background: DISCOVER 1 & 2, two double-blind, phase-3, psoriatic arthritis (PsA) trials of guselkumab (GUS, an IL-23 inhibitor), demonstrated significant improvement with GUS vs placebo (PBO) in signs and symptoms of PsA, with good tolerability, at week (w) 24 during the PBO-controlled period.[1,2] Beyond w24, all patients (pts) switched to GUS. Continued treatment maintained efficacy through w52.[3,4]
Objectives: To describe pooled safety results from the DISCOVER 1 & 2 trials through 1-year of GUS treatment.

Table 1. Number of Patients with AEs per 100 PY and Incidence of AEs of Interest

Time Period	24 Weeks				1 Year*			
Treatment Group	PBO	GUS SC 100 mg			PBO to GUS‡	GUS SC 100 mg		
Dosing Schedule	Matching	q8w	q4w	GUS Combined†	q4w	q8w	q4w	GUS Combined‡
N	372	375	373	748	352	375	373	1100
Total PY Follow-Up	173	173	172	346	204	384	385	589
Patients with AEs per 100 PY, n (95% CI)								
≥1 AE	143 (123, 166)	148 (127, 171)	154 (132, 178)	151 (136, 167)	92 (77, 108)	114 (100, 130)	115 (101, 131)	109 (100, 117)
≥1 Serious AE	7.1 (3.7, 12)	4.1 (1.6, 8.4)	4.7 (2.0, 9.3)	4.4 (2.5, 7.3)	7.0 (3.8, 11.8)	4.8 (2.9, 7.6)	4.0 (2.2, 6.6)	4.9 (3.6, 6.6)
≥1 Infection	50 (39, 62)	47 (37, 59)	52 (42, 65)	49 (42, 58)	39 (31, 49)	41 (34, 48)	38 (31, 45)	39 (35, 44)
≥1 Serious Infection	1.7 (0.4, 5.1)	0.6 (0.0, 3.2)	1.8 (0.4, 5.1)	1.2 (0.3, 3.0)	2.5 (0.8, 5.8)	1.3 (0.4, 3.1)	0.8 (0.2, 2.3)	1.3 (0.7, 2.3)
Discontinued due to AE	4.1 (1.6, 8.4)	2.9 (1.0, 6.8)	4.7 (2.0, 9.3)	3.8 (2.0, 6.5)	3.5 (1.4, 7.1)	2.1 (0.9, 4.1)	2.6 (1.3, 4.8)	2.6 (1.7, 3.8)
AEs of Interest§, n (%)								
Death	2 (0.5)	0	0	0	0	0	0	0
Malignancy	1 (0.3)	2 (0.5)	0	2 (0.3)	1 (0.3)	2 (0.5)	0	3 (0.3)
Major Adverse Cardiac Events	1 (0.3)	0	1 (0.3)	1 (0.1)	0	0	1 (0.3)	1 (0.1)
Opportunistic Infections	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
Inflammatory Bowel Disease	1 (0.3)	0	0	0	0	0	0	0
Injection-Site Reaction	1 (0.3)	5 (1.3)	4 (1.1)	9 (1.2)	4 (1.1)	6 (1.6)	9 (2.4)	19 (1.7)
Anti-GUS Antibody+	-	6/373 (1.6)	9/371 (2.4)	15/744 (2.0)	14/350 (4.0)	18/373 (4.8)	17/371 (4.6)	49/1094 (4.5)

*Through w60 for DISCOVER 1 and w52 for DISCOVER 2; †Combined GUS q8w and q4w; ‡For patients who switched from PBO to GUS, only data on and after first GUS administration were included in this group; §PBO N=370.AE, adverse event; CI, confidence interval; GUS, guselkumab; PBO, placebo; PY, patient year; q4w, every 4 weeks; q8w, every 8 weeks; SC, subcutaneous; w, week

Methods: Adults with active PsA (DISCOVER 1: ≥3 tender/swollen joints and C-Reactive protein [CRP] ≥0.3 mg/dL; DISCOVER 2: ≥5 tender/swollen joints and CRP ≥0.6 mg/dL) were randomized to subcutaneous GUS 100 mg at w0, w4, then every 8 w (q8w); GUS 100 mg q4w; or PBO. At w24, PBO pts switched to GUS 100 mg q4w. Pts were biologic naive except ~30% pts in DISCOVER 1. Safety was reported through w60 in DISCOVER 1 and through w52 in DISCOVER 2.

Results: Baseline characteristics were similar between treatment groups in the pooled studies. Through w24 and 1 year, numbers of pts per 100 patient years with ≥1 event were similar among treatment groups for adverse events (AEs), serious AEs, infections, serious infections, and discontinuations due to AE (Table 1). At 1 year, there were no cases of active tuberculosis, opportunistic infections (including candida), or inflammatory bowel disease in GUS-treated pts; 2 deaths in PBO pts; and low incidences that were similar across treatment groups for malignancy, major adverse cardiac events, and injection-site reactions. Incidence of anti-GUS antibodies was 4.5%, and most were not neutralizing. Mild elevations in serum hepatic transaminases and decreases in neutrophil counts were consistent at 1 year with the results at w24 (Table 1).

Conclusion: GUS regimens of q8w and q4w were well tolerated in PsA pts through 1 year of treatment in the phase-3 DISCOVER trials, consistent with the w24 results. No meaningful differences between incidences of AEs were reported in the q8w and q4w groups. The safety profile of GUS in PsA pts is generally comparable with the previously established safety profile of GUS.

REFERENCES:

[1] Deodhar A et al. *Lancet.* 2020;395:1115
[2] Mease P et al. *Lancet.* 2020;395:1126
[3] Ritchlin C et al. *EULAR 2020* # SAT0397
[4] McInnes I et al. *EULAR 2020* # SAT0402

Disclosure of Interests: Christopher T. Ritchlin Grant/research support from: Received grant/research support from UCB Pharma, AbbVie, Amgen, consultation fees from UCB Pharma, Amgen, AbbVie, Lilly, Pfizer, Novartis, Gilead, Janssen, Proton Rahman Speakers bureau: Received speakers fees from Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, and Pfizer., Philip Helliwell Consultant of: Consultation fees paid to charity (AbbVie, Amgen, Pfizer, UCB) or himself (Celgene, Galapagos), Grant/research support from: Received grants/research support paid to charity (AbbVie, Janssen, Novartis), Wolf-Henning Boehncke Consultant of: Received consultation fees from Janssen, Grant/research support from: Received grant/research support from Janssen Research & Development, LLC, Iain McInnes Consultant of: Received consultation fees from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Received grant/research support from Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Alice B Gottlieb Speakers bureau: Received speakers fees from Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB, Consultant of: Received consultation fees from Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB, Grant/research support from: Received grant/research support from Pfizer, AbbVie, BMS, Lilly, MSD, Novartis, Roche, Sanofi, Sandoz, Nordic, Celltrion and UCB, Shelly Kafka Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Alexa Kollmeier Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Elizabeth C Hsia Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Xie L Xu Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, May Shawi Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Shihong Sheng Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Prasheen Agarwal Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Bei Zhou Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Paraneedharan Ramachandran Shareholder of: Shareholder of Johnson & Johnson, Employee of: Employee of Janssen Research & Development, LLC, Philip J Mease Speakers bureau: Received speakers fees from Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau, Consultant of: Received consultation fees from Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB, Grant/research support from: Received grant/research support from Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB.

DOI: 10.1136/annrheumdis-2021-eular.1334

AB0539

IXEKIZUMAB TREATMENT RESPONSE: CONSISTENCY OVER TIME AND AT EACH VISIT IN PSORIATIC ARTHRITIS

L. C. Coates[1], D. Sandoval[2], R. Bolce[2], C. Y. Lin[2], K. Stenger[2], A. T. Sprabery[2], A. Kavanaugh[3]. *[1]Oxford University, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, London, United Kingdom*; *[2]Eli Lilly and Company, Lilly Corporate Center, Indianapolis, United States of America*; *[3]UC San Diego, School of Medicine, San Diego, United States of America*

Background: Ixekizumab (IXE), a high-affinity monoclonal antibody targeting IL-17A, has demonstrated superiority in achieving the combined endpoint of ACR50 and PASI100 at week (Wk) 24 compared to adalimumab (ADA) in the SPIRIT-H2H trial [1]. In this analysis, we looked at the efficacy responses at the individual patient (pt) level to assess consistency over time and at each visit.

Objectives: To determine the American College of Rheumatology 50% (ACR50) response and Disease Activity in psoriatic arthritis (PsA) (DAPSA) response in pts treated with IXE and describe response consistency over time and at each visit from Wk 24 through Wk 52.

Methods: This post-hoc analysis used data from SPIRIT-H2H (NCT03151551), a phase3b/4 randomised, open-label parallel-group study between IXE and ADA. Pts were randomised to receive either IXE 80 mg, every 4 Wks (IXE Q4W)) or ADA 40 mg, every 2 Wks (ADA Q2W)). The proportion (%) of pts in the intent-to-treat population who achieved each endpoint, either ACR50 or DAPSA≤14, at Wk 24 and at each post-baseline visit out to Wk 52 was assessed. Nine pts with active psoriasis and body surface area (BSA) ≥3% were assessed as PASI=0 at baseline, a medical inconsistency that was resolved using medical judgement. These pts were considered PASI100 responders if PASI=0 and BSA=0 at post baseline visits.

Results: A total of 566 patients enrolled in the trial received either IXE (N=283) or ADA (N=283). Of the 143 pts treated with IXE who achieved ACR50 at Wk 24, 65% (N=93) maintained ACR50 at every visit. In total, 83% (N=118) of the ACR50 achievers at Wk 24 maintained ACR50 with some (18% (N=25)) fluctuations, between ACR50 and

ACR20 (Figure 1). Of the 132 pts treated with ADA who achieved ACR50 at Wk 24, 55% (N=72) maintained ACR50 at every visit. In total, 80% (N=105) of ACR50 achievers maintained ACR50 with some (25% (N=33)) fluctuations between ACR50 and ACR20 (Table 1). Furthermore, of the174 pts treated with IXE who achieved low DA (DAPSA≤14) at Wk 24, 68% (N=119) maintained low DA at every visit. Of the low DA achievers at Wk 24, 82% (N=142) of pts maintained low DA with some (13% (N=23)) fluctuations between moderate and low DA (Figure 1B). Of the 171 pts treated with ADA who achieved low DA at Wk 24; 57% (N=97) maintained low DA at every visit. In total, 77% (N=131) of low DA achievers at Wk 24 maintained low DA with some (20% (N=34)) fluctuations between moderate and low DA (Table 1).

Conclusion: This analysis demonstrates that a numerically higher proportion of pts treated with IXE versus ADA show consistency of response, as measured by ACR50 and DAPSA responses, over time and for each visit at the pt level.

REFERENCES:

[1] Mease et al. Ann Rheum Dis. 2020;79(1):123-131

Table 1. Consistency over time of the effect of ADA in pts with PsA.

	IXE Q4W (N=283)		ADA Q2W (N=283)	
	ACR50 Response, % (n)	DAPSA≤14 low DA, % (n)	ACR50 Response, % (n)	DAPSA≤14 low DA, % (n)
Patients who achieved the response at Wk 24	51% (143)	61% (174)	47% (132)	60% (171)
Achieved endpoint at Wk 24 and maintained out to Wk 52 with some fluctuations*	83% (N=118)	82% (N=142)	80% (105)	77% (131)
Maintained endpoint at every visit	65% (N=93)	68% (N=119)	55% (72)	57% (97)
Had some fluctuations*	18% (N=25)	13% (N=23)	25% (33)	20% (34)

* fluctuations between ACR50 and ACR20, or between low and moderate disease activity.

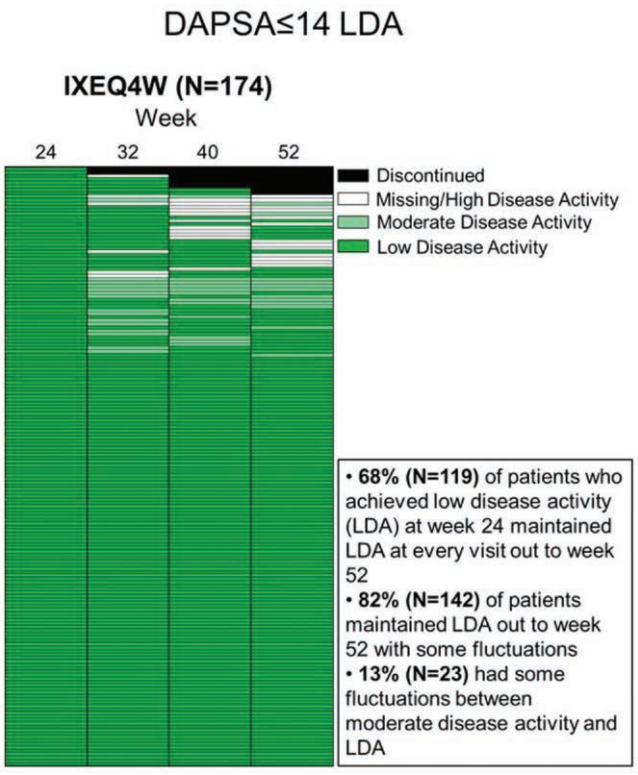


Figure 1. Heatmap diagram describing consistency over time of the effect of IXE in pts with PsA who achieved DAPSA≤14 (low disease activity) at Wk 24.

Acknowledgements : Edel Hughes, an employee of Eli Lilly and Company, provided editorial and writing support.

Disclosure of Interests: Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Gilead, Eli Lilly, Janssen, Medac, Novartis, Pfizer, and UCB., Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Pfizer, and Novartis, David Sandoval Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, Rebecca Bolce Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, Chen-Yen Lin Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, Keri Stenger Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, Aubrey Trevelin Sprabery Shareholder of: Eli Lilly and Company; Johnson and Johnson, Employee of: Eli Lilly and Company, Arthur Kavanaugh Consultant of: AbbVie, Amgen, Eli Lilly, BMS, Pfizer, Novartis, Janssen.

DOI: 10.1136/annrheumdis-2021-eular.1514

AB0540

COMPARISON OF EQ-5D HEALTH STATUS IN PSORIATIC ARTHRITIS PATIENTS WITH OR WITHOUT AXIAL DISEASE: RESULTS OF SUBANALYSIS OF THE PATERA STUDY

I. Gaydukova[1], T. Korotaeva[2], V. Mazurov[1], A. Samtsov[3], V. Khayrutdinov[3], A. Bakulev[4], A. Kundzer[5], N. Soroka[6], A. Eremeeva[7]. *[1]Mechnikov North-Western State Medical University, Department of Therapy and Rheumatology of Temporary Disability and Medical Care Quality Expertise, St-Petersburg, Russian Federation*; *[2]Nasonova Research Institute of Rheumatology, Laboratory of Spondyloarthritides and Psoriatic Arthritis, Moscow, Russian Federation*; *[3]Kirov Military Medical Academy, Department of Skin and Veneral Diseases, St-Petersburg, Russian Federation*; *[4]Razumovsky Saratov State Medical University, Department of Dermatovenereology and Cosmetology, Saratov, Russian Federation*; *[5]Belarusian Medical Academy of Postgraduate Education, Department of Cardiology and Rheumatology, Minsk, Belarus*; *[6]Belarusian State Medical University, Department of Internal Diseases №2, Minsk, Belarus*; *[7]JSC BIOCAD, Clinical Development Department, St-Petersburg, Russian Federation*

Background: Netakimab (NTK) is an anti-interleukin-17A monoclonal antibody approved for psoriasis, ankylosing spondylitis, psoriatic arthritis (PsA) in Russia and Belarus. PATERA is an ongoing phase 3 international double-blind, placebo-controlled clinical study of NTK in PsA (NCT03598751).

Objectives: A subanalysis was performed to assess the effect of NTK on domains of the 5-level EuroQol 5 Dimensions questionnaire (EQ-5D-5L) in patients with inflammatory back pain (IBP) (IBP(+)) and without (IBP(-)) at baseline according to self-reported ASAS IBP criteria, 2009.

Methods: 194 adult patients with PsA (CASPAR criteria, 2006) with inadequate response to csDMARD or one TNFi, were randomly assigned to receive NTK 120mg or placebo at weeks 0,1,2,4,6,8,10,14,18,22. The proportion of patients reported >1 problem in each domain was evaluated. Patients with missing values were considered as non-responders in the analysis.

Results: 97 PsA patients (N=54 IBP(+), N=43 IBP(-)) received NTK. The subpopulations didn't differ significantly in gender, age, and PsA activity at baseline. Comparable percentage of patients reported any problems for each domain at baseline (p≥0.05) (data not shown). IBP(-) subpopulation had a greater improvement for all domains except of anxiety/depression. The absolute declines for IBP(+) vs IBP(-) patients were as followed: 24.1% vs 41.9% (mobility), 18.5 vs 41.9% (self-care), 24.0% vs 51.1% (usual activities), 24.1% vs 37.2% (pain/discomfort), 33.3% vs 9.3% (anxiety/depression). However, the only significant difference between IBP(+) and IBP(-) was observed in usual activity (Figure 1).

Conclusion: NTK resulted in the growing improvement of each EQ-5D-5L domain through 24 weeks irrespectively of the presence of IBP. IBP(-) subjects showed trend to greater benefit compared to IBP(+).

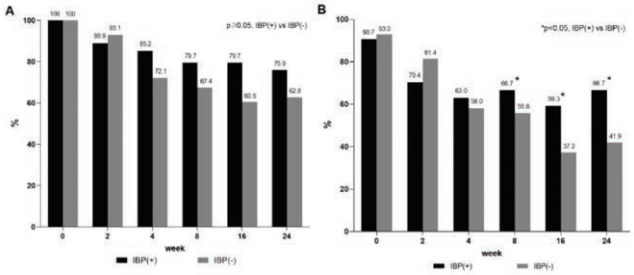


Figure 1 Percentage of patients reported any problems in (A) pain/discomfort, (B) in usual activity at each visit

Acknowledgements: This study was sponsored by JSC BIOCAD.

Disclosure of Interests: Inna Gaydukova Speakers bureau: Abbvie, Biocad, Eli Lilly, MSD, Novartis, Pfizer, Sandoz, Tatiana Korotaeva Speakers bureau: Abbvie, Biocad, Eli Lilly, Johnson & Johnson, Janssen, Novartis, Pfizer, UCB, V Mazurov: None declared., Aleksey Samtsov: None declared., Vladislav Khayrutdinov: None declared., Andrey Bakulev: None declared., Alena Kundzer: None declared., Nikolaj Soroka: None declared., Anna Eremeeva Employee of: Biocad.

DOI: 10.1136/annrheumdis-2021-eular.1535

AB0541

PREDICTING THE INITIATION OF BIOLOGIC DMARDS IN EARLY PSORIATIC ARTHRITIS WITHIN 1-YEAR OF TREAT-TO-TARGET STRATEGY

E. Loginova[1], T. Korotaeva[1], E. Gubar[1], Y. Korsakova[1], S. Glukhova[2]. *[1]V.A. Nasonova Research Institute of Rheumatology, Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Medical and Social Problems in Rheumatology, Moscow, Russian Federation*

Background: According to the EULAR recommendations and treat-to-target (T2T) strategy synthetic (s) DMARDs are the first-line of PsA therapy and biologic (b) DMARDs are the second one [1]. The value of early intervention by bDMARDs in PsA has been demonstrated recently [2]. But factors which can predict bDMARDs initiation have not been evaluated yet.

Objectives: To identify prognostic factors for initiation of bDMARDs within 1-year of T2T strategy in early PsA.

Methods: 70 patients (pts) (M/F=35/35) with active early PsA fulfilling the CASPAR criteria treated by T2T strategy were included. Mean age 36.9±10.2 years (yrs), PsA duration 11.3±10.6 months (mos.), psoriasis duration 80.6±89.9 mos. Median DAPSA= 29.4 [23.1;36.0]. At baseline (BL) all pts were given therapy with Methotrexate (MTX) s/c with escalating dose from 5 to 25 mg/wk, then over a period of 12 mos pts with ineffectiveness of MTX were added bDMARDs. At BL and every 3 month of therapy all pts underwent standard clinical examinations of PsA activity. DAPSA, ESR (mm/h), CRP (mg/l), the number of pts with dactylitis, enthesitis by LEI and plantar fascia, BSA (%), HAQ and fatigue by FACIT (Functional Assessment of Chronic Illness Therapy) Fatigue Scale (Version 4), BMI (kg/m^2) were evaluated. DAPSA > 28 indicate high activity, a score FACIT < 30 - severe fatigue, BMI >25 overweight and obese. At 12 mos. pts were divided into two groups. Group 1 included 42 pts who were treated with MTX only and group 2 - 28 pts those with added bDMARDs during 12 mos. Multi-dimensional step-by-step discriminant analysis was used to identify a group of signs associated with the need to initiate bDMARDs within 12 mos.

Results: Comparative analysis of two groups showed the following features proved to be the most informative at BL and at 3 mos. of sDMARDs therapy with MTX: high PsA activity by DAPSA ≥ 30 (p = 0.009), BMI (kg/m^2) ≥ 27 (p = 0.019), entesitis ≥ 1 (p= 0.005), ESR ≥ 20 mm/h (p= 0.007), FACIT < 30 (p= 0.074), male sex (p = 0.098). Early PsA pts with combination of these features at the first visit and at 3 mos. of MTX monotherapy have more chance to initiate bDMARDs in comparison to pts without them. Area Under ROC Curve (AUC) 0.892; 95% CI (0.818-0.966). Sensitivity/ Specificity of model 82% / 76% accordingly. (Figure 1).

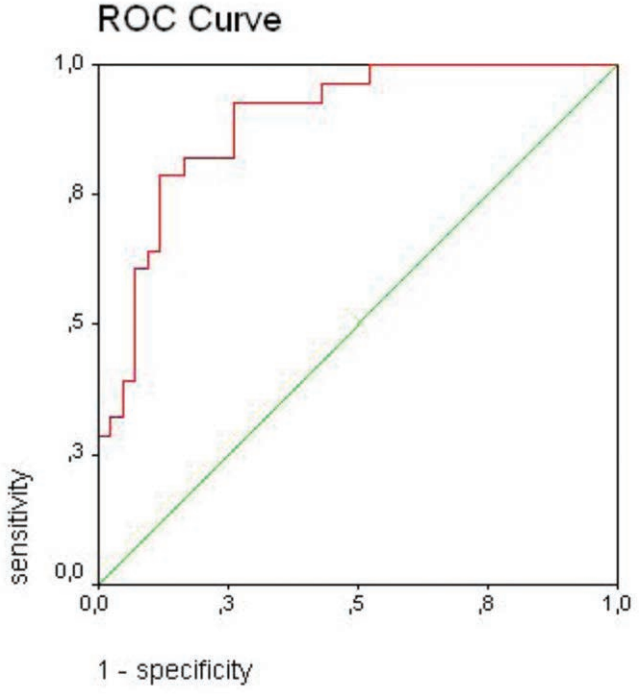


Figure 1.

Conclusion: It is a combination of features from first visit to clinic and at 3 mos. of MTX monotherapy – high PsA activity by DAPSA, male gender, persistent entesitis, obesity, ESR increase and severe fatigue by FACIT - that constitutes a prognostic factor for the initiation of bDMARDs at an early-stage of PsA. These factors should be considered in clinical practice to avoid losing time for the early initiation of bDMARDs and improved outcomes of PsA.

REFERENCES:

[1] Gossec L, et al. Ann Rheum Dis. 2020;79:700–712. doi:10.1136/annrheumdis-2020-217159. **2.** van Mens LJJ, et al. Ann Rheum Dis 2019;78:610–616. doi:10.1136/annrheumdis-2018-214746

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1541

AB0542

EVALUATION OF APREMILAST USE IN THE ROUTINE CLINICAL PRACTICE IN PATIENTS WITH PSORIATIC ARTHRITIS NAÏVE TO BIOLOGICAL TREATMENTS

J. Gratacos-Masmitja[1], J. L. Álvarez Vega[2], E. Beltrán[3], A. Urruticoechea-Arana[4], C. Fito-Manteca[5], F. Maceiras[6], J. M. Belzunegui Otano[7], J. Fernández-Melón[8], E. Chamizo Carmona[9], A. Hernández[10], I. Ros[11], E. Pascual[12], J. C. Torre[13]. *[1]Hospital Parc Tauli, Barcelona, Rheumatology, Barcelona, Spain*; *[2]Hospital Infanta Cristina, Badajoz, Rheumatology, Badajoz, Spain*; *[3]Hospital del Mar, Rheumatology, Barcelona, Spain*; *[4]Hospital Can Misses, Rheumatology, Eivissa, Illes Balears, Spain*; *[5]Complejo Hospitalario de Navarra, Rheumatology, Pamplona, Navarra, Spain*; *[6]Complejo Universitario de Vigo, Rheumatology, Pontevedra, Spain*; *[7]Hospital Universitario Donostia, Rheumatology, Donostia, Gipuzkoa, Spain*; *[8]Hospital Universitari Son Espases, Rheumatology, Palma, Illes Balears, Spain*; *[9]Hospital de Merida, Rheumatology, Mérida, Badajoz, Spain*; *[10]Hospital Virgen del Puerto, Rheumatology, Plasencia, Cáceres, Spain*; *[11]Hospital Universitario Son Llàtzer, Rheumatology, Palma, Illes Balears, Spain*; *[12]Amgen S.L., Medical, Barcelona, Spain*; *[13]Hospital Monte Naranco, Rheumatology, Oviedo, Asturias, Spain*

Background: Apremilast is a non-biologic systemic agent approved for the treatment of plaque psoriasis, oral ulcers of Behcet's disease and PsA with proven efficacy in clinical trials [1,2]. However, more real-world evidence of apremilast use and effectiveness is needed to identify the patient profile most likely to benefit from this treatment [3].

Objectives: To evaluate the persistence of apremilast treatment in patients with PsA naïve to biological treatments in routine clinical practice and assess its effectiveness. Baseline clinical characteristics on patients who started apremilast were also evaluated.

Methods: Observational, prospective, multicenter (20 centers) study including consecutive adult patients with PsA naïve to biological therapies who had started treatment with apremilast during the previous 5 to 7 months and were followed-up during 12 months. Variables recorded were persistence of treatment with apremilast at 6 months (6mo) and number of swelling joints, presence of enthesitis and dactylitis, and disease activity, measured by the Disease Activity in Psoriatic Arthritis (DAPSA) score and Physician Global Assessment (PGA) of psoriasis, collected at baseline (BL) (i.e., apremilast treatment start) and 6mo; comorbidities were retrospectively collected at BL. Categorical and quantitative variables were compared using McNemar's and Wilcoxon test, respectively. Data sets analyzed included all assessable patients.

Results: Of the 60 patients recruited at the time of this interim analysis, 54 (90.0%) [mean (SD) age 53.4 (13.9) years] were assessable; 41 (75.9%) of these continued treatment with apremilast at 6mo. At BL, 34 (63.0%) patients had at least one comorbidity, the most frequent being cardiovascular disease (n=15, 27.8%), including hypertension (n=8, 14.8%), metabolic/endocrine disease (n=18, 33.3%), including obesity (n=8, 14.8%) and dyslipidemia (n=10, 18.5%). Psychiatric disease (i.e., depression) (n=5, 9.3%) and neoplasia (n=8, 14.8%) were also observed. The number of swelling joints decreased from median (Q1, Q3) 4.0 (2.0, 7.0) at BL to 1.5 (0.0, 4.0) at 6mo (p=0.0012). Patients with dactylitis and enthesitis decreased from 19 (35.2%) and 16 (29.6%) at BL to 10 (18.5%) and 9 (16.7%) at 6mo (p=0.0225 and p=0.0391), respectively. The distribution of patients in the different disease activity categories according to DAPSA scale changed between BL and 6mo, indicating a favorable disease evolution (Figure 1 next page). According to PGA, at BL (n=53), disease activity was categorized as mild in 18.0%, as moderate in 72.0%, and as severe in 10% of patients and, at 6mo (n=54), as mild in 70.6%, as moderate in 25.5%, and as severe in 3.9% of patients. Fifteen (27.8%) patients interrupted treatment permanently (n=13, 24.1%) or temporarily (n=2, 3.7%), due to no/partial response (n=8, 14.8%), tolerability issues leading to adverse events (n=3, 5.6%), patient decision (n=2, 3.7%), and other reasons (n=2, 3.7%) after a mean (SD) treatment of 3.05 (2.20) months.

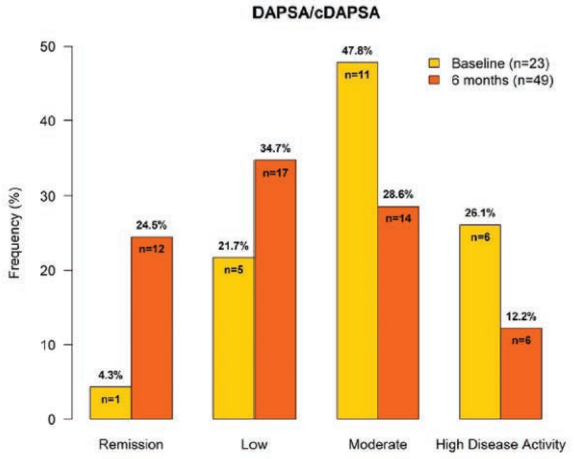


Figure 1. Classification of disease activity according to DAPSA at the indicated timepoints. Percentages in each category were calculated based on the number of patients with available data at each timepoint. DAPSA, Disease Activity in Psoriatic Arthritis.

Conclusion: Forty-one (75.9%) patients with PsA naïve to biological therapies were treated with apremilast during ≥6 months. After treatment, the number of swelling joints, and dactylitis and enthesitis decreased and changes in disease activity according to DAPSA and PGA pointed to a favorable disease evolution. Apremilast treatment provides a clinical benefit to patients with PsA treated in clinical practice.

REFERENCES:

[1] Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis. 2016 Feb 10;75(3):499 LP-510

[2] Torres T and Puig L. Apremilast: A novel oral treatment for psoriasis and psoriatic arthritis. Am J clin Dermatol. 2018 Feb;19(1):23-32

[3] Coates LC, Kavanaugh A, Mease PJ et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015. Treatment Recommendations for Psoriatic Arthritis. Arthritis Rheumatol. 2016;68(5):1060– 71.

Disclosure of Interests: Jordi Gratacos-Masmitja Speakers bureau: MSD, Pfizer, AbbVie, Janssen Cilag, Novartis, Celgene y Lilly., Consultant of: MSD, Pfizer, AbbVie, Janssen Cilag, Novartis, Celgene y Lilly., José Luis Álvarez Vega Speakers bureau: Abbvie, Amgen, MSD, Lilly, Roche, Esteve, UCB, Menarini, Pfizer, GSK, BMS, Janssen, Novartis, Gebro., Consultant of: Abbvie, Amgen, MSD, Lilly, Roche, Esteve, UCB, Menarini, Pfizer, GSK, BMS, Janssen, Novartis, Gebro., Grant/research support from: Abbvie, Amgen, MSD, Lilly, Roche, Esteve, UCB, Menarini, Pfizer, GSK, BMS, Janssen, Novartis, Gebro., Emma Beltrán Speakers bureau: Abbvie, Bristol, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Consultant of: Abbvie, Bristol, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB, ANA URRUTICOECHEA-ARANA: None declared., C. Fito-Manteca: None declared., Francisco Maceiras: None declared., Joaquin Maria Belzunegui Otano Speakers bureau: Lilly, Amgen, Novartis, Abbvie, Janssen., J. Fernández-Melón Speakers bureau: Amgen SL, Eugenio Chamizo Carmona: None declared., Abad Hernández Speakers bureau: MSD, Abbvie, Pfizer, Kern, Novartis, Biogen, Sandoz, Amgen, Sanofi, Lilly, Roche and Janssen-Cilag, Consultant of: MSD, Abbvie, Pfizer, Kern, Novartis, Biogen, Sandoz, Amgen, Sanofi, Lilly, Roche and Janssen-Cilag, Grant/research support from: MSD, Abbvie, Pfizer, Kern, Novartis, Biogen, Sandoz, Amgen, Sanofi, Lilly, Roche and Janssen-Cilag, Inmaculada Ros Consultant of: Amgen, Grant/research support from: MSD, Roche, Novartis, lilly, Pfizer, Amgen, Eva Pascual Shareholder of: Amgen, Employee of: Amgen, Juan Carlos Torre Speakers bureau: Amgen, Lilly, Novartis, Janssen, Pfizer, Consultant of: Amgen, Lilly, Novartis, Janssen, Pfizer, Grant/research support from: Amgen, Lilly, Novartis, Janssen, Pfizer.

DOI: 10.1136/annrheumdis-2021-eular.1621

AB0543 CHARACTERISTICS AND TREATMENT CHANGES IN PATIENTS WITH PSORIATIC ARTHRITIS SEEN IN A COMBINED DERMATOLOGY-RHEUMATOLOGY CLINIC

K. Klavdianou[1], M. Stavropoulou[2], P. Panagakis[3], M. Papoutsaki[4], A. Panagiotopoulos[1], C. Koutsianas[1], A. Stratigos[4], D. Rigopoulos[4], D. Vassilopoulos[1]. [1] *Hippokration General Hospital, 2nd Department of Medicine and Laboratory, Clinical Immunology - Rheumatology Unit, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece*; [2]*National and Kapodistrian University of Athens, MSc Program "Rheumatology – Musculoskeletal Health", Athens, Greece*; [3]*A. Syggros Hospital, Department of Dermatology-Venereology, Athens, Greece*; [4]*A. Syggros Hospital, 1st Department of Dermatology and Venereology, National and Kapodistrian University of Athens, Athens, Greece*

Background: Data on patients with Psoriasis (PSO) referred to a combined Dermatology-Rheumatology outpatient Clinic (Derm-Rheum) with suspected psoriatic arthritis (PsA) are limited.

Objectives: To assess patient characteristics and treatment changes in PsA patients referred to a Derm-Rheum Clinic.

Methods: Prospective study of PSO patients referred to a combined Derm - Rheum Clinic from February 2018 to June 2020 in a Tertiary University Hospital.

Results: Among 151 patients with PSO referred to the Clinic, 129 (85%) with a final diagnosis of PsA were included. In 73% of patients (n=94) PsA was diagnosed there for the 1st time. 56% were females with a mean age of 55 years and a median disease duration of 14.2 years. At initial evaluation, 95% had peripheral arthritis, 45% nail involvement, 23% axial involvement, 12% enthesitis and 6% dactylitis with a median DAPSA score of 20.5 and PASI score of 1.6, respectively. 31% of the patients were not receiving any systemic treatment, 45% were on biologics (30% as monotherapy, 15% in combination with non-biologics), 29% were on non-biologics (14% as monotherapy, 15% in combination with biologics or targeted synthetic agents] and 10% were on targeted synthetic (ts) agents. At last visit (median follow-up: 15 months) only 8% did not receive any systemic therapy ($p<0.001$ compared to 1st visit), 62% were on biologics (39% monotherapy – 23% in combination with non-biologics, $p=0.009$), 46% were on non-biologics (20% as monotherapy – 26% in combination with biologics or ts agents, $p=0.01$) and 10% of the patients were on apremilast. The median DAPSA and PASI scores at last visit were 5.3 and 0, respectively.

Conclusion: About 2/3 of patients with PSO referred to a combined Derm - Rheum Clinic with suspicious musculoskeletal complaints were diagnosed for the 1st time as PsA. During follow-up the percentage of PsA patients who started or continued systemic therapy significantly increased with significant improvement of disease activity indices. These data emphasize the value of combined Derm - Rheum Clinics for earlier diagnosis and more efficacious treatment of PsA patients.

Acknowledgements: This work was supported by research grants from the Special Account for Research Grants (S.A.R.G.), National and Kapodistrian University of Athens, Athens, Greece.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1640

AB0544 EFFICACY AND SAFETY OF TILDRAKIZUMAB IN PATIENTS WITH AND WITHOUT METABOLIC SYNDROME: 5-YEAR POOLED DATA FROM reSURFACE 1 AND reSURFACE 2

A. B. Gottlieb[1], N. Mehta[2], A. Menter[3,4], A. M. Mendelsohn[5], S. Rozzo[5], M. Lebwohl[1]. [1]*Icahn School of Medicine at Mount Sinai, Department of Dermatology, New York, United States of America*; [2]*National Institutes of Health, National Heart, Lung and Blood Institute, Bethesda, United States of America*; [3]*Baylor Scott & White, Division of Dermatology, Dallas, United States of America*; [4]*Texas A&M College of Medicine, Division of Dermatology, Dallas, United States of America*; [5]*Sun Pharmaceutical Industries, Inc., Medical Affairs, Princeton, United States of America*

Background: Patients with psoriasis and metabolic syndrome (MetS) may have reduced absolute Psoriasis Area and Severity Index (PASI) response and long-term drug survival. Tildrakizumab is approved for the treatment of moderate to severe plaque psoriasis in the US, EU, Australia, and Japan. Efficacy and safety of tildrakizumab were previously shown to be comparable in patients with vs without MetS after 1 and 3 years of treatment.[1]

Objectives: This post hoc analysis of pooled data from reSURFACE 1 and reSURFACE 2 (NCT01722331/NCT01729754) assessed tildrakizumab efficacy and safety through up to 5 years of treatment in patients with psoriasis with and without MetS.

Methods: reSURFACE 1 and 2 were 3-part, double-blind, randomized controlled phase 3 trials with long-term extensions evaluating tildrakizumab 100 or 200 mg monotherapy at Weeks 0, 4, and every 12 weeks thereafter in adults with moderate to severe plaque psoriasis.[2] Patients who achieved ≥50% improvement from baseline PASI score (PASI 50 response) at both week 28 and at the end of the phase 3 studies could enter the long-term extension studies continuing the same dose of tildrakizumab.[1] This post hoc analysis reports results from a pooled data analysis through up to 5 years of tildrakizumab exposure from patients with and without MetS by National Cholesterol Education Program-Adult Treatment Panel III criteria who continuously received the same dose of tildrakizumab throughout the base studies and entered the long-term extensions. Efficacy was assessed as change from baseline PASI score; missing data were handled using multiple

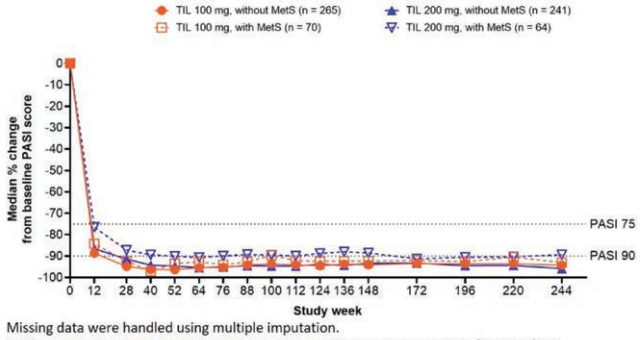
imputation. Safety was assessed from exposure adjusted incidence rates of serious adverse events (SAEs) and treatment-emergent AEs of special interest.
Results: Analyses included 70/265 patients with/without MetS receiving tildrakizumab 100 mg and 64/241 patients with/without MetS receiving tildrakizumab 200 mg. Median percentage change from baseline PASI score is shown in Figure 1. Among patients with/without MetS receiving tildrakizumab 100 mg, 78.6%/87.9% achieved PASI 75, 57.1%/63.8% achieved PASI 90, and 25.7%/32.5% achieved PASI 100 response at week 244; the PASI 75, PASI 90, and PASI 100 response rates at week 244 in patients with/without MetS receiving tildrakizumab 200 mg were 76.6%/85.1%, 46.9%/61.4%, and 26.6%/36.5%, respectively. Safety outcomes over the 5-year extension period were consistent with the known safety profile of tildrakizumab. Rates of SAEs were <8.5 per 100 patient-years among all patients, and there were no new safety signals in patients with vs without MetS (Table 1).

Table 1. SAEs and TEAEs of special interest by MetS status through up to 5 years of tildrakizumab exposure

	TIL 100 mg		TIL 200 mg	
	Without MetS	With MetS	Without MetS	With MetS
	n = 265	n = 70	n = 241	n = 64
n (EAIR per 100 PY)	**1149.1 PY**	**304.1 PY**	**1057.1 PY**	**287.6 PY**
SAEs	53 (4.61)	22 (7.23)	52 (4.92)	24 (8.35)
TEAEs of special interest	24 (2.09)	6 (1.97)	27 (2.55)	15 (5.22)
Infections and infestations	10 (0.87)	2 (0.66)	13 (1.23)	6 (2.09)
Malignancies[a]	5 (0.44)	1 (0.33)	4 (0.38)	3 (1.04)
Nonmelanoma skin cancer	3 (0.26)	1 (0.33)	6 (0.57)	1 (0.35)
Confirmed extended MACE	3 (0.26)	1 (0.33)	3 (0.28)	3 (1.04)
Drug hypersensitivity	2 (0.17)	1 (0.33)	1 (0.09)	2 (0.70)
Melanoma skin cancer	2 (0.17)	0	0	0
Injection site reactions[b]	1 (0.09)	0	0	0

Incidence rates reported as events per 100 PY.[a]Excluding nonmelanoma and melanoma skin cancer.[b]Not considered of special interest in the extension study.AE, adverse event; EAIR, exposure adjusted incidence rate; MACE, major adverse cardiovascular events; MetS, metabolic syndrome; PY, patient-years; SAE, serious AE; TEAE, treatment-emergent AE; TIL, tildrakizumab.

Figure 1. Median percent change from baseline PASI score through week 244 in patients with and without MetS



Missing data were handled using multiple imputation.
MetS, metabolic syndrome; PASI, Psoriasis Area and Severity Index; PASI 75/90, 75%/90% improvement from baseline PASI score; TIL, tildrakizumab.

Conclusion: The efficacy and safety of tildrakizumab were maintained in patients with and without MetS following 5 years of treatment.
REFERENCES:
[1] Lebwohl, M et al. *JAAD*. 2020;S0190-9622(20)32637-2.
[2] Reich K, et al. *Lancet.* 2017;390:276–88.
Disclosure of Interests: Alice B Gottlieb Shareholder of: Xbiotech (only stock options, which she has not used)., Consultant of: Anaptyps Bio, Avotres Therapeutics; Beiersdorf; Boehringer Ingelheim; Bristol-Myers Squibb Co.; Eli Lilly; Janssen; LEO Pharma; Novartis; Sun Pharmaceutical Industries, Inc.; UCB; and Xbiotech, Grant/research support from: Boehringer Ingelheim; Janssen; Novartis; Sun Pharmaceutical Industries, Inc.; UCB; and Xbiotech., Nehal Mehta Grant/research support from: Grants to the NIH from AbbVie, Celgene, Janssen, and Novartis., Employee of: Full-time employee of the US government., Alan Menter Speakers bureau: AbbVie, Abbott Labs, Amgen, Anacor, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen Biotech, LEO Pharma, Merck & Co., Novartis, Sienna, and UCB., Consultant of: AbbVie, Abbott Labs, Amgen, Anacor, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen Biotech, LEO Pharma, Merck & Co., Novartis, Sienna, and UCB., Grant/research support from: AbbVie, Abbott Labs, Amgen, Anacor, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen Biotech, LEO Pharma, Merck & Co., Novartis, Sienna, and UCB., Alan M Mendelsohn Shareholder of: Has individual shares in Johnson and Johnson, and as part of retirement account/mutual funds, Employee of: Sun Pharmaceutical Industries, Inc., Stephen Rozzo Employee of: Sun Pharmaceutical Industries, Inc., Mark Lebwohl Consultant of: Aditum Bio; Allergan; Almirall; Arcutis; Avotres Therapeutics; BirchBioMed, Inc.; BMD Skincare; Boehringer Ingelheim; Bristol-Myers Squibb; Cara Therapeutics; Castle Biosciences; Corrona; Dermavant Sciences; Evelo; Facilitate International Dermatologic Education; Foundation for Research and Education in Dermatology; Inozyme Pharma; Kyowa Kirin; LEO Pharma; Meiji Seika Pharma; Menlo; Mitsubishi; Neuroderm; Pfizer; Promius/Dr. Reddy's Laboratories; Serono; Theravance; and Verrica., Grant/research support from: AbbVie; Amgen; Arcutis; Boehringer Ingelheim; Dermavant; Eli Lilly; Incyte; Janssen Research & Development, LLC; LEO Pharma; Ortho Dermatologics; Pfizer; and UCB.
DOI: 10.1136/annrheumdis-2021-eular.1827

AB0545

COMPARISON BETWEEN METHOTREXATE AND APREMILAST IN PSORIATIC ARTHRITIS-A SINGLE BLINDED RANDOMIZED CONTROLLED TRIAL (APREMEPsA STUDY)

J. Samanta[1], G. Naidu[1], A. Chattopadhyay[2], A. Basnet[1], T. Narang[3], S. Dogra[3], A. Sharma[1]. [1]*Post Graduate Institute of Medical Education and Research, Clinical Immunology and Rheumatology Division, Internal Medicine, Chandigarh, India*; [2]*Institute of Post Graduate Medical education and Research, Rheumatology, Kolkata, India*; [3]*Post Graduate Institute of Medical Education and Research, Dermatology, Chandigarh, India*

Background: Both methotrexate and apremilast were found to be effective in controlling joint disease in psoriatic arthritis (PsA) patients [1-4]. However, there are no head-to-head trials comparing the efficacy of these two drugs in PsA.
Objectives: Primary outcome measure was rate of major cDAPSA response (>85% change in cDAPSA score from baseline) at week 24 and secondary outcome measures were ACR 20 response, change in Psoriasis Area and Severity Index (PASI), Maastricht enthesitis score, Leeds dactylitis index, and health assessment questionnaire-disability index (HAQ-DI) and number of adverse events at week 24 between methotrexate and apremilast groups.
Methods: Single blinded (physician), parallel group, randomized controlled trial was conducted at a single centre in India between October 2019 and December 2020. Adult PsA patients (age>18 years), fulfilling CASPAR criteria, not receiving methotrexate/apremilast in last 3 months and never receiving bDMARDs or, JAK inhibitors, having active articular disease (one or more swollen joint or, having one or more tender entheseal point) were recruited in this study.
Results: A total of 31 patients were recruited (15 in apremilast arm and 16 in methotrexate arm) amongst whom 26 patients completed 24 weeks follow up (13 patients in apremilast arm and 13 patients in methotrexate arm). At baseline, median (IQR) swollen joints were 2 (1) in apremilast group and 2.5 (4) in methotrexate group. Median cDAPSA score at baseline was 23 (9) in apremilast group and 20 (21) in methotrexate group. Major cDAPSA response at week 24 was achieved in three (20%) subjects in apremilast arm and six (37.5%) subjects in methotrexate arm (p=0.433). Seven (46.67%) subjects in apremilast group and nine (56.25%) subjects in methotrexate group achieved ACR 20 response at 24-weeks (p=0.724). The change of PASI score from baseline was significant in apremilast group (2.0, p=0.003) and methotrexate group (0.35, p=0.003), but when compared between the two groups, there was no significant difference(p=0.378). Change in enthesitis score was not significant in both the groups (0.0 in apremilast group, p=0.285; 0.0 in methotrexate group, p=1.0). The median change in dactylitis score [0.0 (9.1), p=0.028] and HAQ-DI score (0.33, p=0.01) were significant in methotrexate group only. However, when compared to the change in apremilast group, the difference was not significant for both the parameters. A total of 9 minor adverse events, 3 with apremilast and 6 with methotrexate, were observed with transaminitis (number of events) being the commonest event noted with methotrexate. There were no serious adverse events noted in either of the groups.
Conclusion: There was no significant difference between methotrexate and apremilast in terms of efficacy as measured by cDAPSA and ACR20 responses. Both the drugs were well tolerated by the study population. A larger study with head-to-head comparison between methotrexate and apremilast is needed to conform these findings.
REFERENCES:
[1] Baranauskaite A, Raffayová H, Kungurov NV, et al; RESPOND investigators. Infliximab plus methotrexate is superior to methotrexate alone in the treatment of psoriatic arthritis in methotrexate-naive patients: the RESPOND study *Ann Rheum Dis*. 2012;71:541-8.
[2] Mease PJ, Gladman DD, Collier DH, et al. Etanercept and Methotrexate as Monotherapy or in Combination for Psoriatic Arthritis: Primary Results From a Randomized, Controlled Phase III Trial. *Arthritis Rheumatol* 2019;71:1112-24.

[3] Gladman DD, Kavanaugh A, Gómez-Reino JJ, et al. Therapeutic benefit of apremilast on enthesitis and dactylitis in patients with psoriatic arthritis: a pooled analysis of the PALACE 1-3 studies. *RMD Open*. 2018;4(1):e000669.
[4] Wells AF, Edwards CJ, Kivitz AJ, et al. Apremilast monotherapy in DMARD-naive psoriatic arthritis patients: results of the randomized, placebo-controlled PALACE 4 trial. *Rheumatology (Oxford)* 2018;57:1253-63.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1850

AB0546 5 YEARS FOLLOW-UP OF PSORIATIC ARTHRITIS PATIENTS TREATED ACCORDING TREAT-TO-TARGET STRATEGY. PRELIMINARY RESULTS

P. Tremaskina[1], E. Loginova[1], T. Korotaeva[1], S. Glukhova[2], A. Lila[1,3]. [1]*V.A. Nasonova Research Institute of Rheumatology, Spondyloarthritis and psoriatic arthritis, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, medical and social problems in rheumatology, Moscow, Russian Federation*; [3]*Medical Academy of Continuing Professional Education, Rheumatology, Moscow, Russian Federation*

Background: The concept of treat to target (T2T) in psoriatic arthritis (PsA) has been established recently and already shown its benefits [1]. But the long-term outcomes of the T2T have not been studied yet.
Objectives: To study 5 years (yrs) follow-up of PsA patients (pts) treated according to T2T strategy at the early stage.
Methods: 35 (M/F–17/18) PsA pts fulfilling CASPAR criteria, who were treated according to T2T strategy at the early stage (PsA duration≤2 yrs) within 24 months (mos) were analyzed. At the time of evaluation mean age is 42.7±11.2 yrs, median (Me) PsA duration 72 [60;95] mos, psoriasis duration 120 [88;180] mos. All pts underwent standard clinical examinations of PsA before started T2T therapy and at follow-up. Within 24 mos of T2T strategy all pts were taking Methotrexate (MTX) monotherapy in increasing dose up to 25 mg/wk and 18 out of 35 (51%) pts received MTX in combination with iTNF. When T2T study was stopped all pts were treated according to standard care with NSAIDs, bDMARDs, MTX, tsDMARDs based on PsA activity and physician decision. The number of pts achieved minimal disease activity (MDA, 5 of 7) and remission by DAPSA (≤4)/ low disease activity (LDA)≤14) at the 24 mos of T2T strategy and at 5 yrs follow-up were calculated. The results are presented in the form of mean values, median, upper and lower quartiles.
Results: Me duration of follow-up is 68 [53.5;81.5] mos. At 24 mos Me DAPSA 3.48 [0.45;21.76], remission by DAPSA (REM-DAPSA) were seen in 20 out of 35 (57%) pts, LDA-DAPSA in 4 (12%) pts, moderate activity (MoA) by DAPSA in 6 (17%) pts and high disease activity by DAPSA (HDA-DAPSA) in 5 (14%) pts. MDA was noted in 21 out of 35 (60%) pts. At 5 yrs Me DAPSA 7.4 [2.22;13.87], REM-DAPSA was noted in 12 (34%) pts, LDA-DAPSA in 14 (40%), MoA-DAPSA in 5 (14%), HDA-DAPSA in 4 (12%) pts. MDA was observed in 17 of 35 pts (49%). Among 20 pts who had REM-DAPSA at 24 mos only 6 pts (30%) remained in remission at 5 yrs follow-up and 12 out of 21 pts (57.14%) remained in MDA status.
Conclusion: In early PsA pts remission and MDA are achievable goal of T2T strategy. But most pts lost remission/MDA after this strategy was changed to a standard care, despite being in remission/MDA status before change of therapy. Further investigations of the long-term outcomes of T2T strategy in PsA, including radiographic outcomes are needed.
REFERENCES:
[1] Coates LC, Moverley AR, McParland L, et al. Lancet 2015; 386: 2489–98.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1985

AB0547 ASSOCIATION BETWEEN ACHIEVEMENT OF LOW DISEASE ACTIVITY OR REMISSION WITH IMPROVEMENT IN QUALITY OF LIFE IN UPADACITINIB-TREATED PATIENTS IN THE PHASE 3 SELECT-PsA 1 AND 2 STUDIES

A. Kavanaugh[1], P. J. Mease[2], K. Douglas[3], F. Behrens[4], D. Haaland[5], P. Palominos[6], A. Lertratanakul[3], M. Lane[3], R. Lippe[7], D. Aletaha[8], P. Nash[9]. [1]*University of California San Diego, Division of Rheumatology, Allergy and Immunology, San Diego, California, United States of America*; [2]*Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology, Seattle, Washington, United States of America*; [3]*AbbVie Inc., Immunology, North Chicago, United States of America*; [4]*Rheumatology and Fraunhofer ITMP - Translational Medicine and Pharmacology, Goethe University, Rheumatology, Frankfurt, Germany*; [5]*McMaster University, Hamilton, Ontario and The Waterside Clinic, Rheumatology, Barrie, Ontario, Canada*; [6]*Hospital de Clínicas de Porto Alegre, Rheumatology Service, Porto Alegre, Brazil*; [7]*AbbVie Deutschland GmbH & Co. KG, Immunology, Wiesbaden, Germany*; [8]*Medical University of Vienna, Währinger Gürtel, Department of Medicine III, Division of Rheumatology, Vienna, Austria*; [9]*Griffith University, Rheumatology Research Unit, Sunshine Coast, Brisbane, Queensland, Australia*

Background: The efficacy and safety of upadacitinib (UPA) in patients (pts) with active psoriatic arthritis (PsA) was demonstrated in the phase 3 SELECT-PsA 1 and SELECT-PsA 2 clinical trials.[1,2]
Objectives: To explore the relationship between achievement of low disease activity (LDA) or remission (REM) and pt-reported outcomes (PROs) in SELECT-PsA 1 and 2.
Methods: The SELECT-PsA program enrolled pts with prior inadequate response or intolerance to ≥1 non-biologic disease-modifying antirheumatic drug (DMARD; SELECT-PsA 1) or ≥1 biologic DMARD (SELECT-PsA 2). Pts were randomized to 56 weeks (wks) of blinded treatment with UPA 15 or 30 mg once daily (QD), placebo switched to UPA 15 or 30 mg QD at Wk 24, or adalimumab (SELECT-PsA 1 only) 40 mg every other wk. LDA and REM were evaluated using the minimal disease activity (MDA; fulfillment of 5 out of 7) criteria and the Disease Activity index for Psoriatic Arthritis (DAPSA; cutoff ≤4), respectively. PROs assessed included Health Assessment Questionnaire-Disability Index (HAQ-DI), 36-Item Short-Form Survey physical component summary (SF-36 PCS), 5-Level EuroQol 5-Dimension (EQ-5D-5L) Index, and EQ-5D-5L Visual Analog Scale (VAS). Integrated data through Wk 56 from SELECT-PsA 1 and 2 from the full analysis set with both continuous UPA 15 mg and 30 mg groups were analyzed by responder status at Wks 24 and 56. Changes from baseline (BL) in PROs were analyzed using mixed effects repeated measures models (fixed effects for study, current use of non-biologic DMARDs, treatment group, visit, responder status, and continuous BL PROs). As-observed data were used in the models.
Results: A total of 1281 pts were included in the analysis (UPA 15 mg, n=640; UPA 30 mg, n=641). MDA was achieved by 33% (UPA 15 mg) and 40% (UPA 30 mg) of patients at
Wk 24, and 40% (UPA 15 mg) and 43% (UPA 30 mg) at Wk 56; and DAPSA-REM by 10% (UPA 15 mg) and 17% (UPA 30 mg) at Wk 24, and 16% (UPA 15 mg) and 18% (UPA 30 mg) at Wk 56. Pts who achieved MDA or DAPSA-REM (responders) at Wk 56 achieved larger reductions in HAQ-DI and larger increases in SF-36 PCS, EQ-5D-5L Index and EQ-5D-5L VAS compared with non-responders (Table 1) (all p<0.0001; statistical significance was exploratory in nature). MDA or DAPSA-REM response at Wk 24 was also associated with greater PRO improvements at Wk 56 (Figure 1). Consistent with the results presented for MDA and DAPSA-REM, patients who achieved Very Low Disease Activity or DAPSA-LDA also experienced greater improvements in PROs than those who did not.

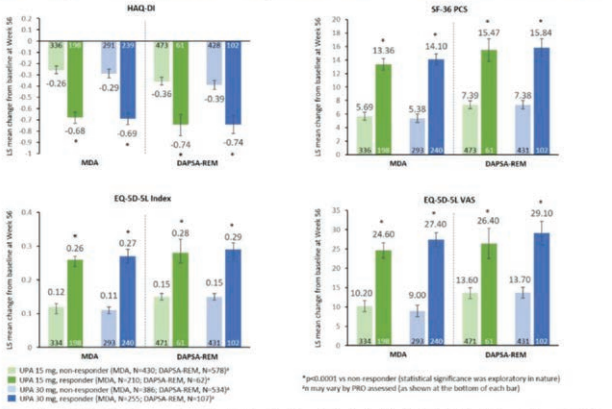
Table 1. Change from BL in PROs at Wk 56 by MDA and DAPSA-REM responder status at Wk 56

	UPA 15 mg QD (n=640)		UPA 30 mg QD (n=641)	
Least squares mean change from BL (95% CI), unless stated otherwise	Non-responder	Responder	Non-responder	Responder
MDA, n[a]	386	254	368	273
HAQ-DI	−0.26 (−0.30, −0.22)	−0.61* (−0.66, −0.56)	−0.27 (−0.31, −0.23)	−0.69* (−0.74, −0.64)
SF-36 PCS	5.25 (4.60, 5.90)	12.63* (11.84, 13.41)	5.09 (4.42, 5.75)	13.84* (13.08,14.59)
EQ-5D-5L Index	0.11 (0.09, 0.12)	0.25* (0.23, 0.26)	0.10 (0.09, 0.12)	0.27* (0.25, 0.28)
EQ-5D-5L VAS	9.3 (7.8, 10.9)	23.3* (21.4, 25.1)	9.0 (7.4, 10.5)	26.1* (24.4, 27.9)
DAPSA-REM, n[a]	539	101	526	115
HAQ-DI	−0.36 (−0.39, −0.32)	−0.63* (−0.71, −0.55)	−0.39 (−0.43, −0.35)	−0.71* (−0.78, −0.63)
SF-36 PCS	6.99 (6.39, 7.59)	14.54* (13.22, 15.86)	7.43 (6.82, 8.03)	15.16* (13.91, 16.40)
EQ-5D-5L Index	0.14 (0.13, 0.15)	0.27* (0.24, 0.30)	0.15 (0.14, 0.16)	0.29* (0.26, 0.31)
EQ-5D-5L VAS	12.7 (11.3, 14.0)	26.7* (23.7, 29.8)	13.3 (11.9, 14.7)	30.0* (27.1, 32.8)

*p<0.0001 vs non-responder (statistical significance was exploratory in nature)[a]n may vary by PRO assessed

Conclusion: Among UPA-treated pts with PsA, improvements in quality of life and physical function were greater in pts who achieved MDA or DAPSA-REM than in those who did not. Despite DAPSA-REM being a more stringent measure (achieved by a smaller proportion of patients), these improvements were similar between MDA and DAPSA-REM responders.
REFERENCES:
[1] McInnes I, et al. Ann Rheum Dis 2020;79(Suppl 1):16–7; 2. Mease PJ, et al. Ann Rheum Dis 2020

Figure Change from BL in PROs at Wk 56 by MDA and DAPSA-REM responder status at Wk 24



BL, baseline; DAPSA, Disease Activity Index for Psoriatic Arthritis; EQ-5D-5L, 5-Level EuroQol 5-Dimension Index; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; MDA, minimal disease activity; PRO, patient-reported outcome; REM, remission; SF-36 PCS, 36-Item Short-Form Survey physical component summary; VAS, Visual Analog Scale; Wk, week

Figure 1.

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Laura Chalmers, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Disclosure of Interests: Arthur Kavanaugh Grant/research support from: Research grants and/or personal fees from AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, and Pfizer, Philip J Mease Grant/research support from: Research grants and personal fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, and Janssen; and personal fees from Boehringer Ingelheim, Galapagos, Genentech, and Gilead, Kevin Douglas Employee of: Employee of AbbVie and may own stock or options, Frank Behrens Grant/research support from: Research grants from Celgene, Chugai, Janssen, Pfizer, and Roche; personal fees from AbbVie, Boehringer Ingelheim, Celgene, Chugai, Eli Lilly, Genzyme, Janssen, MSD, Novartis, Pfizer, Roche, and Sanofi; and investigator fees from Eli Lilly, Derek Haaland Speakers bureau: Advisory board/speaker bureau membership for AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, GSK, Janssen, Novartis, Pfizer, Roche, Sanofi, and Takeda, Consultant of: Honoraria or other fees from AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GSK, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, Takeda, and UCB, Grant/research support from: Research grants from AbbVie, Adiga Life Sciences, Amgen, Bristol-Myers Squibb, Can-Fite Biopharma, Celgene, Eli Lilly, Gilead, GSK, Janssen, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and UCB, Penelope Palominos Speakers bureau: Advisory board/speaker bureau membership for Janssen and Novartis, Consultant of: Personal fees from AbbVie, Grant/research support from: Research support from Novartis, Pfizer, and Roche, Apinya Lertratanakul Employee of: Employee of AbbVie and may own stock or options, Michael Lane Employee of: Employee of AbbVie and may own stock or options, Ralph Lippe Employee of: Employee of AbbVie and may own stock or options, Daniel Aletaha Consultant of: AbbVie, Grünenthal, Janssen, Medac, Mitsubishi Tanabe, MSD, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Grünenthal, Janssen, Medac, Mitsubishi Tanabe, MSD, Pfizer, Roche, and UCB, Peter Nash Grant/research support from: Received honoraria and research support from AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Eli Lilly, Gilead/Galapagos, Janssen, MSD, Novartis, Pfizer, Roche, Samsung, Sanofi, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2000

AB0548

EFFECTIVENESS OF IXEKIZUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM A REAL-WORLD EUROPEAN SURVEY

W. Tillett[1,2], V. Navarro-Compán[3], N. Booth[4], T. Holzkaemper[5], J. Hill[5], E. Lubrano[6], T. Truer[5]. [1]*Royal National Hospital for Rheumatic Diseases, Department of Rheumatology, Bath, United Kingdom*; [2]*University of Bath, Department of Pharmacy and Pharmacology, Bath, United Kingdom*; [3]*University Hospital La Paz, IdiPaz, Madrid, Spain*; [4]*Adelphi Real World, Adelphi Real World, Bollington, United Kingdom*; [5]*Eli Lilly & Company, Eli Lilly & Company, Indianapolis, United States of America*; [6]*Università degli Studi del Molise, Academic Rheumatology Unit, Dipartimento di Medicina e Scienze della Salute "Vincenzo Tiberio", Campobasso, Italy*

Background: Limited real world (RW) data are available for IL-17A blocker ixekizumab (Ixe), approved for psoriatic arthritis (PsA) in EU Feb 2018.
Objectives: Describe RW outcomes for PsA patients (pts) receiving Ixe.
Methods: Cross-sectional, observational study of PsA pts treated with Ixe in the 2020 Adelphi PsA Plus Program (FR, DE, ES & UK). Rheumatologists recruited the first 6 consecutive consulting Ixe pts and provided demographics, PsA manifestations, clinical measures (66 swollen joint count (SJC), 68 tender joint count (TJC), psoriasis area and severity index [PASI], body surface area [BSA] affected by psoriasis [PsO]), rheumatologist-recorded pt measures (skin/joint pain & fatigue [0-10 numeric rating scales (NRS)], health assessment questionnaire [HAQ-DI]) & prescribed dose. All outcomes recorded for pts with scores available at Ixe initiation (II) & at last assessment (LA).
Results: 124 rheumatologists provided data for 698 Ixe pts, mean age 49 years (19-79), 48% female, mean BMI 27 (18-44), 56% dermatologist co-managed and mean time diagnosed 6 years (0-35). At Ixe initiation, 78% of pts with known BSA had concomitant mod-sev-PsO defined as BSA≥10% (mean 19.8, n=428) and mean PASI 26.3 (n=164). The predominant PsA phenotype was polyarthritic in 49% (n=345), mono/oligoarthritic in 30% (n=208), axial in 12% (n=81) and enthesitic in 8% (n=55). Previous treatment before Ixe included ≥1 conventional synthetic DMARD (csDMARD) for 71% of pts. Of bio-experienced pts (57%), 40% had received ≥2 biologics. Mean Ixe treatment duration (n=698) 39.4 weeks (wks, 0-170), of which 575 (82%) had received >12 wks of Ixe. 71% of pts received label recommended dose (80mg every 4wks). 52% pts received csDMARD in combination with Ixe. In the RW, Ixe improved TJC, SJC, joint pain, BSA, fatigue and HAQ-DI, Table 1.

Table 1. Outcomes for pts receiving Ixe >12weeks (n=575)

	Overall	BSA ≥10% at Ixe initiation	Mod-sev-PsO physician judgement	Predominant mono/oligo arthritis	Predominant polyarthritis	With csDMARD	Without csDMARD
BSA, n mean [SD]	356	270	254	98	184	188	168
Ixe initiation (II)	19.8 [14.8]	24.7 [13.5]	23.1 [13.6]	17.4 [15.0]	20.9 [15.0]	21.8 [15.0]	17.4 [14.2]
Last Assessment (LA)	6.6 [7.5]	9.3 [8.7]	7.9 [7.9]	5.0 [6.0]	7.6 [8.4]	7.3 [7.9]	5.9 [7.1]
Mean weeks on Ixe	43	41	41	50	41	41	46
TJC*, n mean [SD, %<5]	125	72	86	39	72	56	69
II	12.2 [10.6, 29]	14.4 [11.3, 18]	12.9 [11.1, 21]	6.4 [8.2, 59]	15.4 [10.8, 12]	13.0 [9.9, 25]	11.5 [11.1, 32]
LA	4.1 [6.4, 77]	5.2 [7.7, 71]	3.6 [6.3, 80]	1.1 [1.4, 97]	6.2 [7.7, 64]	3.4 [3.9, 73]	4.6 [7.8, 80]
SJC*, n mean [SD, %<5]	145	82	102	44	84	60	85
II	14.8 [13.5, 33]	18.8 [14.4, 22]	16.3 [13.8, 26]	7.2 [8.5, 68]	18.2 [13.6, 12]	14.5 [12.0, 37]	15.1 [14.8, 31]
LA	4.8 [8.7, 79]	7.0 [10.7, 66]	5.1 [9.3, 75]	0.9 [1.9, 95]	6.6 [9.0, 68]	3.1 [7.8, 90]	5.9 [9.1, 71]
Joint pain (NRS 0-10), n mean [SD]	575	270	349	166	291	294	281
II	6.6 [1.7]	6.7 [1.7]	6.7 [1.7]	6.2 [1.8]	7.0 [1.5]	6.6 [1.7]	6.6 [1.6]
LA	2.7 [1.9]	3.0 [2.1]	2.8 [2.0]	2.1 [1.6]	3.0 [2.1]	2.8 [1.9]	2.5 [1.9]
Fatigue (NRS 0-10), n mean [SD]	575	270	349	166	291	294	281
II	5.4 [2.5]	5.8 [2.4]	5.7 [2.5]	4.7 [2.5]	5.7 [2.4]	5.7 [2.4]	5.1 [2.5]
LA	2.6 [2.1]	2.7 [2.1]	2.7 [2.2]	2.0 [1.9]	2.9 [2.2]	2.7 [2.1]	2.6 [2.1]
HAQ DI, n mean [SD, %<0.5]	59	41	42	10	28	31	28
II	1.8 [0.7, 5]	1.9 [0.6, 0]	1.8 [0.7, 2]	1.9 [0.7, 10]	1.8 [0.8, 7]	1.9 [0.6, 3]	1.7 [0.8, 7]
LA	0.8 [0.6, 41]	0.8 [0.6, 32]	0.8 [0.7, 45]	0.7 [0.7, 60]	0.7 [0.6, 36]	0.7 [0.5, 32]	0.7 [0.8, 50]

*Additional analysis for pts whose fatigue/joint pain rating improved (from ≥4 at Ixe initiation to ≤3 at LA), their mean TJC was 2.7 & SJC 4.3 at LA for fatigue, TJC 1.7 & SJC 2.7 at LA for joint pain.When BSA was not recorded, physician judgement of PsO severity was used. No imputation of missing data.

Conclusion: We report RW outcome data amongst pts treated with Ixe including mono/oligo arthritis and a limited sample of enthesitis and dactylitis pts. Our results are consistent with clinical trial populations across disease domains, including an improvement in joint pain.

Disclosure of Interests: William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, Pfizer Inc. and UCB, Consultant of: AbbVie, Amgen, Celgene, Lilly, Janssen, Novartis, MSD, Pfizer Inc. and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly & company, Janssen and UCB, Victoria Navarro-Compán Speakers bureau: AbbVie, BMS, Janssen, Eli Lilly & Co, MSD, Novartis, Pfizer, Roche and UCB, Consultant of: AbbVie, BMS, Janssen, Eli Lilly & Co, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: AbbVie, BMS, Janssen, Eli Lilly & Co, MSD, Novartis, Pfizer, Roche and UCB, Nicola Booth: None declared., Thorsten Holzkaemper Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, Julie Hill Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, Ennio Lubrano Speakers bureau: Alfa-Sigma, Abbvie, Galapagos, Janssen Cilag, Lilly., Consultant of: Alfa-Sigma, Abbvie, Galapagos, Janssen Cilag, Lilly., Tamas Truer Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company.

DOI: 10.1136/annrheumdis-2021-eular.2001

AB0549 PREDICTIVE FACTORS FOR SWITCHING IN PATIENTS WITH PSORIATIC ARTHRITIS UNDERGOING ANTI-TNFA, ANTI-IL12/23 OR ANTI-IL17 DRUGS: A FIFTEEN-YEAR MONOCENTRIC REAL-LIFE STUDY

M. Lorenzin[1], A. Ortolan[1], G. Cozzi[1], A. Calligaro[1], M. Favaro[1], T. Del Ross[1], A. Doria[1], R. Ramonda[1]. [1]*University of Padova, Rheumatology Unit, Department of Medicine DIMED, Padova, Italy*

Background: Biological Disease-Modifying Anti-Rheumatic Drugs (bDMARDs) targeting Tumor Necrosis Factor (TNF) alpha, Interleukin (IL) 12/23 and IL17, have been approved for Psoriatic Arthritis (PsA) treatment, in this chronological order.

Objectives: The aims of our study were to evaluate 1) predictors of first bDMARD failure, including mechanism of action 2) factors associated to failure of multiple (>=2) therapies.

Methods: Consecutive patients attending our Rheumatology Unit, classified as PsA according to CASPAR criteria and beginning treatment with bDMARDs in the period 2004-2020, were enrolled. Disease characteristics, previous/ongoing treatments, comorbidities and follow-up duration were recorded. Demographic, clinical and laboratory data, disease-activity and functional indexes [including Disease Activity in PSoriatic Arthritis (DAPSA), PASI (Psoriasis Area and Severity Index) and Health Assessment Questionnaire (HAQ)], were recorded at baseline and yearly and were compared between switchers (>=1 switch/swap) and non-switchers. Date and reason for switching were collected. Effectiveness was evaluated over-time with descriptive statistics. A multivariable Cox-Proportional-Hazard (PH) model was built to evaluate the influence of mechanism of action (anti-TNFalpha/anti-IL12/23/anti-IL17) and of negative prognostic factors for drug response on time to first bDMARD discontinuation. Furthermore, a multivariable logistic regression model was built to assess the association between negative prognostic factors for drug response (independent variables) and failure of>=2 bDMARDs ("multifailure", outcome). Kaplan-Meier curves were used to assess differences in time-to-first bDMARD discontinuation according to the targeted cytokine. P values <=0.05 were considered significant. Infections and adverse events were recorded.

Results: Our study included 264 patients, 117 (44.32%) females, mean age 56±12 years, mean PsA duration 15±3 years;117 (44.32%) switched bDMARDs at least once. Switchers were mostly females, with higher PASI and worse HAQ at baseline (Figure 1). Mean time-to-first bDMARD discontinuation was 72 months; 2-year and 5-year retention rate was 75% and 60%, respectively. Survival curves for anti-TNFalpha/anti-IL12/23/anti-IL17 were similar (log-rak test=0.83;p=0.66). Main reasons for switching were inefficacy (79) and adverse events (38). The Cox PH model showed that female sex was independently associated to a higher risk of first bDMARD discontinuation (HR=2.39; 95%CI:1.50-3.81), while initiating therapy before 2015 was protective (HR=0.40; 95%CI:0.22-0.73). Other independent variables, including mechanism of action (HR=0.76; 95%CI:0.30-1.74 for anti-IL17; HR=0.53; 95%CI 0.15-1.86 for anti-IL12/23; reference: anti-TNFalpha), age (HR=1.00; 95%CI:0.99-1.03), baseline DAPSA (HR=0.98; 95%CI:0.96-1.00), PASI (HR=0.95; 95%CI:0.86-1.04), HAQ (HR=1.29; 95%CI:0.91-1.83), Body Mass Index BMI (HR=1.02; 95%CI:0.98-1.07) and comorbidities (HR=1.10; 95%CI:0.92-1.31) were not associated to the outcome. In the logistic regression model, only female sex was significantly associated to failure of>=2 therapies (OR=1.99, 95%CI:1.07-3.69); bDMARD mechanism of action, age, and initiating therapy before 2015 were instead not independently associated.

Conclusion: Survival rate was good for anti-TNFalpha and other bDMARDs. Female sex was a predictor of first bDMARD discontinuation, unlike mechanism of action, comorbidities and BMI.

Baseline characteristics of the monocentric cohort at the beginning of bDMARDs, comparison between switchers and non-switchers.

Characteristics	Non-switchers N=147	Switchers N=117	p-value
Female sex	**48 (32.65%)**	**69 (58.97%)**	**<0.0001**
Age (years)	56.0 (46.0-65.0)	57.0 (49.0-65.0)	0.06
Psoriatic arthritis duration (years)	15.0 (10.0-22.0)	15 (10.0-21.0)	0.94
Psoriasis duration (years)	25.0 (17.0-36.0)	24.0 (15.0-34.0)	0.67
Family history	9 (6.12%)	14 (11.96%)	0.07
Psoriasis	127 (86.39%)	102 (87.18%)	0.73
Inflammatory bowel disease	1 (0.68%)	3 (2.56%)	0.22
Uveitis	4 (2.72%)	0 (0%)	0.11
Tender joints (66/68 joint count)	5.0 (2.0-8.0)	4.0 (2.0-8.0)	0.44
Swollen joints (66/68 joint count)	2.0 (0.0 -4.0)	2.5 (0.0 -6.0)	0.60
VAS pain 0-10	7.0 (5.3 -8.0)	7.0 (5.0 -7.6)	0.90
VAS global health 0-10	6.0 (4.5 -7.0)	6.5 (5.0 -8.0)	0.35
CRP mg/L	6.0 (3.0 -15.5)	5.5 (2.9 -12.0)	0.37
ESR mm/h	17.0 (8.0 -34.0)	19.0 (9.0 -36.0)	0.42
DAPSA	20.2 (15.1 -27.9)	18.9 (15.3 -25.7)	0.67
Leeds Enthesitis Index (0-6)	0.0 (0.0 -1.0)	0.0 (0.0 -1.0)	0.69
Dactylitis (presence/absence)	18 (12.24%)	15 (12.85%)	0.23
HAQ	**0.5 (0.25 -1.0)**	**0.62 (0.25 -1.5)**	**0.046**
PASI 0-72	**1.0 (0.3 -3.0)**	**1 (0.0 -2.7)**	**0.047**
Smoking			
Non-smokers	91 (61.90%)	83 (70.94%)	0.46
Ever smokers	56 (38.10%)	34 (29.06%)	
BMI	25.3 (22.9 -27.7)	25.4 (23.4 -27.6)	0.86
Updated Charlson Comorbidity Index	1 (0 -3)	1 (0 -7)	0.79
Association therapy with a csDMARDs	56 (38.10%)	39 (33.33%)	0.61
First line biological drug			
Anti-TNFalpha	120 (81.63%)	106 (90.59%)	-
Anti-IL12/23	15 (10.20%)	8 (6.84%)	-
Anti-IL17	12 (8.16%)	3 (2.56%)	-

Legend. VAS=Visual Analogue Scale; CRP=C-reactive Protein; ESR=Erythrocyte Sedimentation Rate; DAPSA=Disease Activity in PSoriatic Arthritis; HAQ=Health Assessment Questionnaire; PASI=Psoriasis Area and Severity Index; BMI=Body Mass Index; csDMARD=conventional synthetic Disease-Modifying Anti-Rheumatic Drugs. Significant results are highlighted in bold. Continuous variables are shown as medians and interquartile range. p≤0.05

Figure 1.

Disclosure of Interests: Mariagrazia Lorenzin: None declared., Augusta Ortolan: None declared., Giacomo Cozzi: None declared., Antonia Calligaro: None declared., Maria Favaro: None declared., Teresa Del Ross: None declared., Andrea Doria Grant/research support from: AD has received honoraria and speaker fees from Novartis, Abbvie, Pfizer, MSD, Janssen., Roberta Ramonda Grant/research support from: RR has received honoraria and speaker fees from Novartis, Abbvie, Pfizer, MSD, Janssen.

DOI: 10.1136/annrheumdis-2021-eular.2019

AB0550 EFFICACY OF UPADACITINIB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND A LOW OR HIGH SWOLLEN JOINT COUNT: A SUBGROUP ANALYSIS OF 2 PHASE 3 STUDIES (SELECT-PSA 1 AND SELECT-PSA 2)

L. Gossec[1,2], D. D. Gladman[3], E. Mcdearmon-Blondell[4], P. Sewerin[5], C. T. Ritchlin[6], D. Feng[4], A. Lertratanakul[4], R. Ranza[7], L. S. Tam[8], A. Marchesoni[9], L. C. Coates[10], P. Nash[11]. [1]*Sorbonne Université, Rheumatology, Paris, France*; [2]*APHP, Pitie Salpetriere Hospital, Rheumatology Department, Paris, France*; [3]*Toronto Western, University of Toronto, Rheumatology, Toronto, Canada*; [4]*AbbVie Inc., Immunology, North Chicago, Illinois, United States of America*; [5]*Heinrich Heine University Düsseldorf, Department and Hiller Research Unit of Rheumatology, Düsseldorf, Germany*; [6]*University of Rochester Medical Center, Rheumatology, Rochester, New York, United States of America*; [7]*Hospital de Clinicas, Universidade Federal de Uberlândia, Rheumatology, Uberlândia, Minas Gerais, Brazil*; [8]*The Prince of Wales Hospital, The Chinese University of Hong Kong, Department of Medicine & Therapeutics, Hong Kong, China*; [9]*ASST, Gaetano Pini-CTO, Rheumatology, Milan, Italy*; [10]*University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; [11]*Griffith University, School of Medicine, Brisbane, Australia*

Background: Although most patients with psoriatic arthritis (PsA) enrolled in clinical trials have polyarticular arthritis, patients in clinical practice may present with oligoarthritis. Data on the efficacy of Janus kinase inhibitors in patients with PsA with low joint counts are limited.

Objectives: To evaluate the efficacy of upadacitinib (UPA) in subgroups of patients with PsA with a low (baseline swollen joint count [SJC] <5) or high (SJC ≥5) SJC (LSJ or HSJ).

Methods: Data were pooled across the SELECT-PsA 1[1] (non-biologic disease-modifying antirheumatic drug [non-bDMARD] inadequate response [IR] or intolerance) and SELECT-PsA 2[2] (bDMARD IR or intolerance) trials, which both enrolled patients with ≥3 involved joints (SJC ≥3 and tender joint count [TJC] ≥3). Subgroup analysis was performed for patients with LSJ or HSJ treated with UPA 15 mg once daily (QD) or placebo (PBO). Efficacy endpoints included minimal disease activity (MDA), very low disease activity (VLDA), Psoriatic Arthritis Disease Activity Score (PASDAS) low disease activity (LDA; ≤3.2), PASDAS remission (≤1.9), and 20/50/70% improvement in American College of Rheumatology (ACR) criteria (ACR20/50/70), all at Week 24, and Psoriasis Area Severity Index (PASI) 75 and static Investigator Global Assessment of Psoriasis (sIGA) 0/1 at Week 16.

Results: At baseline, patients with HSJ (n=1060) had similar demographic characteristics but tended to have higher overall disease activity than patients with LSJ across multiple disease domains (n=215; Table 1). UPA efficacy appeared comparable in patients with LSJ and HSJ, with similar proportions of patients achieving composite (MDA, VLDA, PASDAS LDA, and PASDAS remission) measures at Week 24, and skin endpoints (PASI 75 and sIGA 0/1) at Week 16 (Figure 1). At Week 24, 60.0/36.8/22.1% of patients with LSJ receiving UPA 15 mg achieved ACR20/50/70 vs 40.0/17.5/5.8% in the PBO group; rates were 70.3/49.7/26.2% (UPA 15 mg) and 36.1/15.3/3.3% (PBO) in those with HSJ.

Table 1. Baseline characteristics

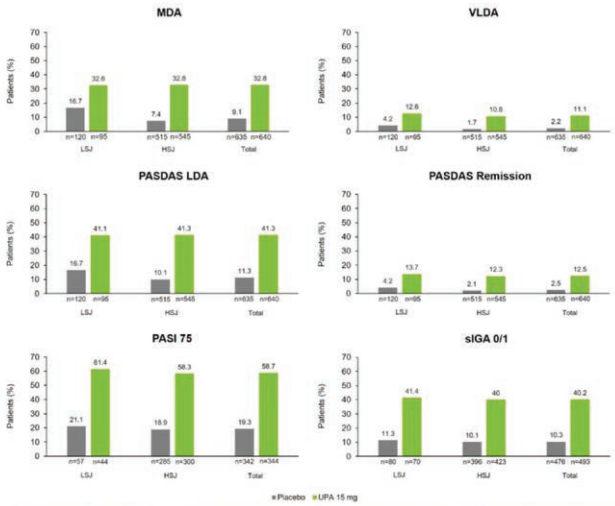
	PBO		UPA 15 mg QD		Total	
	LSJ n=120	HSJ n=515	LSJ n=95	HSJ n=545	LSJ n=215	HSJ n=1060
Female, n (%)	65 (54.2)	266 (51.7)	49 (51.6)	302 (55.4)	114 (53.0)	568 (53.6)
Age (years), mean (SD)	52.2 (12.7)	51.5 (12.0)	52.0 (10.6)	52.0 (12.4)	52.1 (11.8)	51.8 (12.2)
Duration since PsA symptoms (years), mean (SD)	10.5 (9.2)	11.1 (10.2)	9.8 (8.2)	10.3 (8.9)	10.2 (8.7)	10.7 (9.6)
BMI, mean (SD)	29.7 (6.3)	31.1 (7.2)	29.8 (6.2)	30.7 (6.9)	29.7 (6.2)	30.9 (7.0)
Prior failed bDMARDs, n (%)						
0	3 (2.5)	15 (2.9)	1 (1.1)	15 (2.8)	4 (1.9)	30 (2.8)
1	22 (18.3)	113 (21.9)	22 (23.2)	104 (19.1)	44 (20.5)	217 (20.5)
2	4 (3.3)	31 (6.0)	7 (7.4)	28 (5.1)	11 (5.1)	59 (5.6)
≥3	4 (3.3)	20 (3.9)	7 (7.4)	27 (5.0)	11 (5.1)	47 (4.4)
Use of ≥1 non-bDMARD at baseline, n (%)	87 (72.5)	360 (69.9)	63 (66.3)	388 (71.2)	150 (69.8)	748 (70.6)
Dactylitis (LDI >0), n (%)	21 (17.5)	169 (32.8)	15 (15.8)	176 (32.3)	36 (16.7)	345 (32.5)
Enthesitis (LEI >0), n (%)	60 (50.0)	325 (63.1)	60 (63.2)	343 (62.9)	120 (55.8)	668 (63.0)
TJC68, mean (SD)	12.5 (11.3)	23.9 (15.8)	14.6 (13.5)	23.1 (15.8)	13.4 (12.3)	23.5 (15.8)
SJC66, mean (SD)	3.5 (0.5)	13.2 (8.3)	3.6 (0.5)	12.9 (9.0)	3.6 (0.5)	13.0 (8.7)
HAQ-DI, mean (SD)	1.0 (0.6)	1.2 (0.7)	0.9 (0.6)	1.2 (0.6)	0.9 (0.6)	1.2 (0.7)
hs-CRP > ULN (mg/L), n (%)	82 (68.3)	363 (70.5)	62 (65.3)	388 (71.2)	144 (67.0)	751 (70.8)
BSA-Ps, median (range)	3.0 (0.1–70.0)	4.0 (0.1–95.0)	2.0 (0.1–80.0)	3.0 (0.1–97.0)	3.0 (0.1–80.0)	3.0 (0.1–97.0)
BSA-Ps ≥ 3%, n (%)	57 (47.5)	285 (55.3)	44 (46.3)	300 (55.0)	101 (47.0)	585 (55.2)
PASI (baseline BSA-Ps ≥ 3%), mean (SD)	7.7 (7.5)	12.1 (11.9)	8.2 (7.0)	10.2 (10.0)	7.9 (7.2)	11.1 (11.0)
PASI (baseline BSA-Ps ≥ 3%), median (range)	5.3 (0.1–39.4)	7.9 (0.3–64.8)	6.5 (0.2–35.4)	6.8 (0.1–70.8)	6.0 (0.1–39.4)	7.3 (0.1–70.8)

Conclusion: UPA efficacy was generally similar in patients with PsA with LSJ or HSJ, with both patient groups showing improvements in composite clinical endpoints and skin responses vs PBO.

REFERENCES:

[1] McInnes I, et al. Ann Rheum Dis 2020;79(Suppl. 1):16–17;
[2] Mease PJ, et al. Ann Rheum Dis 2020; Epub ahead of print.

Figure Proportion of patients (%) achieving MDA, VLDA, PASDAS LDA, and PASDAS remission at Week 24, and PASI 75 and sIGA 0/1 at Week 16 for UPA vs PBO, by arthritis subtype



HSJ, high swollen joint count; LDA, low disease activity; LSJ, low swollen joint count; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area Severity Index; PBO, placebo; sIGA, static Investigator Global Assessment of Psoriasis; UPA, upadacitinib; VLDA, very low disease activity

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Grant Kirkpatrick, MSc of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Disclosure of Interests: Laure Gossec Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Dafna D Gladman Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Novartis, Pfizer, and UCB, Erin McDearmon-Blondell Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Philipp Sewerin Consultant of: AbbVie, Amgen, Axiom Health, Biogen, Bristol-Myers Squibb, Celgene, Chugai, Deutscher Psoriasis Bund, Eli Lilly, Fresenius Kabi, Gilead, Hexal, Janssen, Johnson & Johnson, Medi-login, Mediri, Novartis, Onkowissen, Pfizer, Roche, Rheumazentrum Rhein-Ruhr, Sanofi, Swedish Orphan Biovitrum, and UCB, Grant/research support from: AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Bundesministerium fuer Bildung und Forschung, Deutsche Forschungsgesellschaft, Deutscher Psoriasis Bund, Eli Lilly, Fresenius Kabi, Gilead, Hexal, Janssen, Novartis, Pfizer, Rheumazentrum Rhein-Ruhr, Roche, Sanofi, and UCB, Christopher T. Ritchlin Consultant of: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Sun, and UCB, Grant/research support from: AbbVie, Amgen, and UCB, Dai Feng Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Apinya Lertratanakul Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, R Ranza Consultant of: AbbVie, Eli Lilly, Janssen, Novartis, and Pfizer, Grant/research support from: AbbVie, Janssen, Novartis, and Pfizer, Lai-Shan Tam Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly, Janssen, Pfizer, and Sanofi, Grant/research support from: Amgen, Boehringer Ingelheim, GSK, Janssen, Novartis, and Pfizer, Antonio Marchesoni Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, and UCB, Laura C Coates: None declared., Peter Nash Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB.

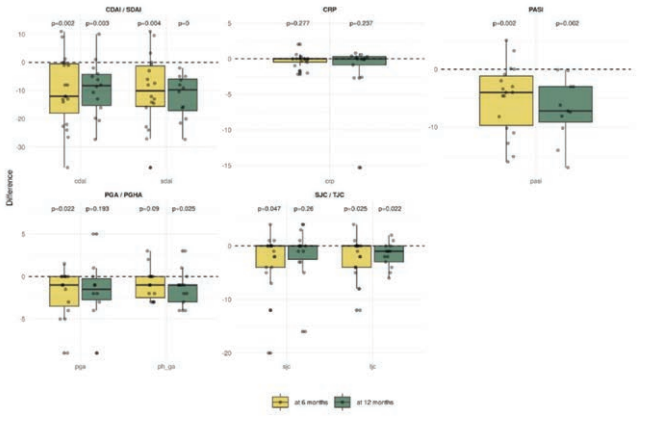
DOI: 10.1136/annrheumdis-2021-eular.2127

AB0551

TREATMENT WITH IXEKIZUMAB FOLLOWING SECUKINUMAB FAILURE IN PATIENTS WITH PSORIATIC ARTHRITIS: REAL-LIFE EXPERIENCE FROM A RESISTANT POPULATION

J. Berman[1], V. Furer[2], M. Berman[2], O. Isakov[1], D. Zisman[3], A. Haddad[3], H. Matz[4], O. Elkayam[2]. [1]*Sourasky Medical Center, Department of Medicine 'T', Tel Aviv, Israel*; [2]*Sourasky Medical Center, Department of Rheumatology, Tel Aviv, Israel*; [3]*Carmel Medical Center, Department of Rheumatology, Haifa, Israel*; [4]*Sourasky Medical Center, Department of Dermatology, Tel Aviv, Israel*

Background: Anti-IL17 agents, such as Secukinumab (SEC) and Ixekizumab (IXE) have been shown to be efficacious for the treatment of psoriasis and PsA[12]. In the field of psoriasis, there is growing evidence of a successful switching between the two anti-IL-17 agents in case of an insufficient response to one of the treatments[3] There is no information on the efficacy of switching between anti IL17 agents in PsA.
Objectives: To assess the clinical response to IXE in patients with PsA following SEC failure.
Methods: A retrospective observational study was conducted in two rheumatology centers in Israel, including PsA patients with a history of treatment with SEC, further treated with IXE for a minimum of 3 months. Lack of efficacy, loss of efficacy, and side effects over time were reported as a reason for switching to another anti-IL17 agent. The mean difference between the beginning of the follow up period and the different follow up points (6 and 12 months) was tested using a one-sample t-test. Time until treatment failure was estimated using Kaplan–Meier curves, and compared using the log-rank test. Hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) were calculated using the Cox proportional-hazards model to test the association between each variable and the time to treatment failure.
Results: The study included 23 PsA patients (11♀/12♂), mean age 58.7 years±13.4 SD. Most patients (n=20, 86%) received 2+ TNFi and 10 patients (43%) received both TNFi and ustekinumab. Median number of biologics prior to SEC was 3 (IQR 2-4). There was a significant improvement in TJC at 6 and 12 months (-2.16 [-4.0, -0.3]; p=0.025 and-1.69 [-3.09, -0.28]; p=0.022, respectively). SJC was significantly improved at 6 months but not at 12 months (-2.68 [-5.3, -0.04]; p= 0.046 and -1.50 [-4.25,1.25]; p=0.26, respectively). CDAI score was significantly improved at 6 months (-10.19, [-16.26, -4.1], p=0.002) and at 12 months (-9.29 [-14.8, -3.71], p=0.003) as was SDAI score (-10.13 [-16.4, -3.8], p=0.003 and -12.2 [-17.1, -7.2], p=0.0002). At six months, PASI50 was achieved by 81% (13 patients), PASI75 was achieved by 63% (10 patients), PASI90 was achieved by 50% (8 patients) and PASI100 by 31% (10 patients). At 12 months, PASI50 and PASI75 was achieved by 57% (8 patients), PASI90 was achieved by 43% (6 patients) and PASI100 by 21% (3 patients).
Over time, of the 23 patients treated with IXE, 15 patients (65%) had experienced treatment failure, with a median treatment period of 8 months (IQR 6.5-13.5), of which 4 (17%) had primary treatment failure and 11 patients (48%) secondary treatment failure. Reasons for treatment cessation were: worsening psoriasis (4 patients (27%)), worsening peripheral arthritis (4 patients (27%)), both (7 patients (47%)), worsening of axial disease (2 patients (13%)) and adverse events (1 patient, 6%).
Conclusion: patients after failure of multiple biologic treatments experienced significant response of peripheral arthritis and dermatologic disease on IXE after they had previously failed SEC. . However, in this refractory cohort of PsA, the effect was limited on time with 65% failure after a median time of 8 months.Within class switch from SEC to IXE is a plausible therapeutic option in PsA patients following secukinumab failure.
REFERENCES:
[1] Mease PJ, McInnes IB, Kirkham B, et al. *N Engl J Med*. 2015;373(14):1329-1339.
[2] Nash P, Kirkham B, Okada M, et al. *Lancet Lond Engl*. 2017;389(10086):2317-2327.
[3] Bokor-Billmann T, Schäkel K. *J Dermatol Treat*. 2019;30(3):216-220



Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2186

AB0552

PROBABILITY OF ACHIEVING TREATMENT TARGETS WITH APREMILAST MONOTHERAPY IN BIOLOGIC-NAIVE PSORIATIC ARTHRITIS PATIENTS IN ACTIVE WITH MODERATE AND HIGH BASELINE DISEASE ACTIVITY

P. Nash[1], S. Richter[2], S. Jardon[2], L. Teng[3], J. A. Walsh[4]. [1]*Griffith University, Medicine, Brisbane, Australia*; [2]*Amgen Inc., Global Medical Affairs, Thousand Oaks, United States of America*; [3]*Amgen Inc., Statistics, Thousand Oaks, United States of America*; [4]*University of Utah, Rheumatology, Salt Lake City, United States of America*

Background: Patients with psoriatic arthritis (PsA) in moderate disease activity (ModDA) who are naive to disease-modifying antirheumatic drugs (DMARDs) have a higher probability of achieving the Clinical Disease Activity Index for PsA (cDAPSA) treatment targets after receiving apremilast 30 mg BID (APR) than those in high disease activity (HDA). In Europe, APR is indicated for the treatment of active PsA in adult patients who had an inadequate response or were intolerant to a prior DMARD therapy. Achievement of cDAPSA treatment targets with APR monotherapy in biologic-naive patients with PsA who had previously taken a maximum of 1 conventional synthetic DMARD (csDMARD) has not been evaluated.
Objectives: To assess the predictive value of baseline clinical disease status on achieving long-term cDAPSA treatment targets at Week 52 among biologic-naive patients with PsA in the phase 3b, randomized, placebo-controlled Assessing Apremilast Monotherapy in a Clinical Trial of Biologic-Naive Patients With PsA (ACTIVE).
Methods: ACTIVE enrolled adults with PsA who had ≥3 swollen and ≥3 tender joints and were biologic naive with prior failure of a maximum of 1 csDMARD. In this post hoc analysis, we assessed the probabilities of achieving cDAPSA treatment targets of remission (REM; ≤4) or low disease activity (LDA; >4 to ≤13) at Week 52 in patients randomized to APR and stratified by cDAPSA ModDA (>13 to ≤27) or HDA (>27) at baseline. Patients with enthesitis at baseline in each stratum were analyzed separately.
Results: Of the 109 patients randomized to APR, 35 were in ModDA (32.1%) and 71 were in HDA (65.1%) at baseline (Table 1). For patients with ModDA vs HDA at baseline, swollen (4.6 vs 10.8) and tender (6.7 vs 21.7) joint counts were lower, and the prevalence of enthesitis was lower (42.9% vs 57.7%) (Table 1). Patients in ModDA at baseline were estimated to be more than twice as likely to achieve treatment targets at Week 52 vs patients in HDA at baseline (Figure 1). Consistent with these results, a higher proportion of patients with ModDA + enthesitis at baseline achieved treatment targets at Week 52 than patients with HDA + enthesitis at baseline (58.9% vs 32.8%).

Table 1. Baseline Demographics and Disease Characteristics

Baseline cDAPSA Category	ModDA (n = 35)	HDA (n = 71)
Age, mean (SD), years	48.5 (12.9)	51.6 (11.8)
Women, n (%)	20 (57.1)	36 (50.7)
White, n (%)	34 (97.1)	71 (100.0)
PsA duration, mean (SD), years	4.5 (4.6)	3.8 (4.5)
Enthesitis, n (%)	15 (42.9)	41 (57.7)
SJC (0-66), mean (SD)	4.6 (1.6)	10.8 (4.3)
TJC (0-68), mean (SD)	6.7 (2.2)	21.7 (11.5)
PtGA (0-10 NRS), mean (SD)	4.9 (1.4)	6.5 (2.0)
PhGA (0-10 NRS), mean (SD)	5.4 (1.2)	6.6 (1.5)

The n represents the total sample. The number of patients with data available may vary. Not included are 3 patients in LDA at baseline. NRS = Numeric Rating Scale; PhGA = Physician's Global Assessment of Disease Activity; PtGA = Patient's Global Assessment of Disease Activity; SJC = swollen joint count; TJC = tender joint count.

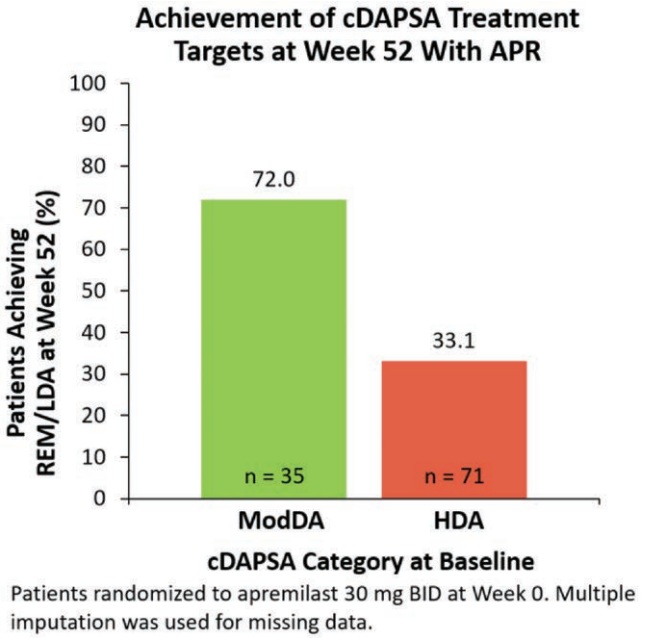


Figure 1.

Conclusion: Similar to observations in DMARD-naive patients with PsA, patients who were biologic naive but may have had experience with a maximum of 1 csDMARD, including those with enthesitis, and who were in ModDA at baseline had a higher probability of achieving treatment targets (cDAPSA REM or LDA) at Week 52 with continued APR treatment compared with those with HDA.

Acknowledgements: This study was funded by Celgene. Additional analyses were funded by Amgen Inc. Writing support was funded by Amgen Inc. and provided by Kristin Carlin, RPh, MBA, of Peloton Advantage, LLC, an OPEN Health company.

Disclosure of Interests: Peter Nash Consultant of: AbbVie, BMS, Celgene, Gilead/Galapagos, GSK, Janssen, Lilly, MSD, Novartis, Pfizer, and Samsung, Grant/research support from: AbbVie, BMS, Celgene, Gilead/Galapagos, GSK, Janssen, Lilly, MSD, Novartis, Pfizer, and Samsung, Sven Richter Employee of: Amgen Inc., Shauna Jardon Employee of: Amgen Inc., Lichen Teng Employee of: Amgen Inc., Jessica A. Walsh Consultant of: AbbVie, Amgen Inc., Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen Inc., Janssen, Lilly, Merck, Novartis, Pfizer, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2198

AB0553

BASELINE DISEASE ACTIVITY AS A PREDICTOR FOR ACHIEVING cDAPSA TREATMENT TARGETS WITH APREMILAST IN DMARD-NAIVE PATIENTS WITH MANIFESTATIONS OF ACTIVE PSORIATIC ARTHRITIS

P. J. Mease[1], A. Kavanaugh[2], A. Ogdie[3], A. F. Wells[4], M. Bergman[5], D. D. Gladman[6], F. Behrens[7], Y. Klyachkin[8], S. Richter[8], L. Teng[8], J. S. Smolen[9].
[1]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Department of Rheumatology, Seattle, United States of America; *[2]University of California, San Diego, School of Medicine, Division of Rheumatology, Allergy, and Immunology, La Jolla, United States of America*; *[3]University of Pennsylvania, Department of Rheumatology, Philadelphia, United States of America*; *[4]Aurora Rheumatology and Immunotherapy Center, Department of Rheumatology, Franklin, United States of America*; *[5]Drexel University College of Medicine, Division of Rheumatology, Philadelphia, United States of America*; *[6]Schroeder Arthritis Institute, Rheumatology, Toronto, Canada*; *[7]Rheumatology and Fraunhofer ITMP – Translational Medicine and Pharmacology, Goethe University, Department of Rheumatology, Frankfurt, Germany*; *[8]Amgen Inc., Global Medical Affairs, Thousand Oaks, United States of America*; *[9]Medical University of Vienna, Department of Rheumatology, Vienna, Austria*

Background: In PALACE 4, DMARD-naive patients (pts) with moderately active (ModDA) psoriatic arthritis (PsA) at baseline (BL) were more likely to achieve Clinical Disease Activity Index for PsA (cDAPSA) treatment targets (cDAPSA remission [REM] or low disease activity [LDA]) at Week 52 with continued apremilast 30 mg BID (APR) treatment than pts with high disease activity (HDA) at BL. Pts who achieved cDAPSA treatment targets also had no or mild articular and extra-articular disease activity by Week 52. Whether specific PsA manifestations other than arthritis impact the achievement of cDAPSA treatment targets in this population is unknown.

Objectives: To assess the predictive value of BL clinical disease status on achieving cDAPSA treatment targets in DMARD-naive pts in PALACE 4 with PsA in ModDA or HDA who exhibited manifestations of skin involvement, enthesitis, and/or dactylitis at BL.

Methods: This post hoc analysis included APR-treated pts in ModDA or HDA with available cDAPSA data at BL and Week 52 who exhibited any of the PsA manifestations at BL, including skin-involved body surface area (BSA) ≥3%, Maastricht Ankylosing Spondylitis Entheses Score (MASES) >0, or dactylitis count >0. Pts were divided into 4 subgroups based on number of manifestations: ≥1, only 1, any 2, or all 3. The proportions of pts who shifted across ModDA (>13 to ≤27) and HDA (>27) cDAPSA categories at BL to REM (≤4) and LDA (>4 to ≤13) treatment targets at Week 52 were calculated (data as observed).

Results: In 176 PALACE 4 pts with PsA receiving APR, 165 had involvement in ≥1 PsA manifestation in addition to peripheral arthritis (ie, skin/enthesitis/dactylitis) at BL. This population had a mean age of 48.8 years, PsA duration of 3.6 years, Psoriasis Area and Severity Index (PASI) score of 6.6, MASES of 3.8, and dactylitis count of 3.5 (Table 1). Within this subgroup, 32.7% had only 1 of these non-arthritic PsA manifestations, 50.9% had any 2, and 16.4% had all 3. In pts with ≥1 manifestation, a greater proportion in ModDA achieved REM/LDA at Week 52 than those in HDA (66.7% vs 32.2%; risk difference: 0.34) (Figure 1). Similarly, greater rates of treatment target achievement were observed in subgroups of pts in ModDA vs HDA and only 1 (72.2% vs 39.1%; risk difference: 0.33), any 2 (57.1% vs 28.6%; risk difference: 0.29), or all 3 (75.0% vs 33.3%; risk difference: 0.42) PsA manifestations (Figure 1).

Conclusion: In DMARD-naive pts exhibiting various non-arthritic manifestations of active PsA (ie, skin/enthesitis/dactylitis), those in ModDA at BL were more likely to achieve cDAPSA REM or LDA at Week 52 of APR treatment than pts in HDA. This observation was consistent whether pts had only 1 or multiple manifestations. These findings are consistent with the probability of achieving treatment targets demonstrated in the overall population in PALACE 4 (61.7% ModDA vs 28.2% HDA).

Table 1. BL Demographics and Disease Characteristics in Pts With ≥1 Manifestations of PsA (Skin Involvement, Enthesitis, and/or Dactylitis) Treated With APR (N = 165)

Age*, years	48.8 (12.5)
Women, n (%)	87 (52.7)
BMI*, kg/m^2	29.9 (6.5)
Duration of PsA*, years	3.6 (5.0)
Duration of psoriasis*, years	15.5 (13.3)
cDAPSA (0-154)*	39.4 (19.7)
Swollen joint count (0-66)*	10.3 (7.7)
Tender joint count (0-68)*	18.5 (12.9)
Pt's Assessment of Pain (VAS 0-100 mm)*	52.8 (21.5)
Pt's Global Assessment (VAS 0-100 mm)*	53.8 (20.1)
Physician's Global Assessment (VAS 0-100 mm)*	52.2 (17.6)
PASI score (0-72)*,†	6.6 (5.1)
MASES (0-13)*,‡	3.8 (3.0)
Dactylitis count (0-20)*,§	3.5 (3.3)
Corticosteroid use, n (%)	13 (7.9)
NSAID use, n (%)	126 (76.4)

*Mean (SD). †In pts with BSA ≥3% at BL. ‡In pts with enthesitis at BL. §In pts with dactylitis at BL.

Acknowledgements: This study was funded by Celgene. Additional analyses were funded by Amgen Inc. Writing support was funded by Amgen Inc. and provided by Kristin Carlin, RPh, MBA, of Peloton Advantage, LLC, an OPEN Health company.

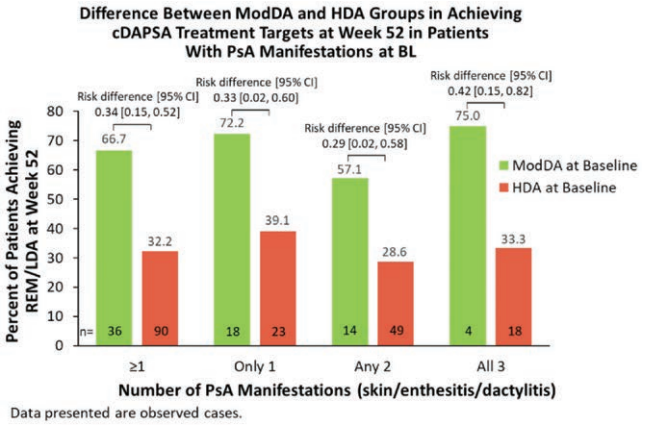


Figure 1.

Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen Inc., Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen Inc., Boehringer Ingelheim, BMS, Celgene, Eli Lilly, Galapagos, GSK, Novartis, Pfizer, Sun, and UCB, Grant/research support from: AbbVie, Amgen Inc., Boehringer Ingelheim, BMS, Celgene, Eli Lilly, Galapagos, GSK, Novartis, Pfizer, Sun, and UCB, Arthur Kavanaugh Grant/research support from: AbbVie, Amgen Inc., AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Alexis Ogdie Consultant of: AbbVie, Amgen Inc., BMS, Celgene, Corrona, Eli Lilly, Gilead, Novartis, Pfizer, and UCB, Grant/research support from: Novartis and Pfizer, Alvin F. Wells Speakers bureau: AbbVie, Alexion, Amgen Inc., BMS, Celgene, Horizon, Lilly, Novartis, and UCB, Consultant of: AbbVie, Alexion, Amgen Inc., BMS, Celgene, Horizon, Lilly, Novartis, and UCB, Grant/research support from: AbbVie, Celgene, and Lilly, Martin Bergman Shareholder of: Johnson & Johnson, Speakers bureau: AbbVie, Amgen Inc., Novartis, Pfizer, and Sanofi, Consultant of: AbbVie, BMS, Celgene, Genentech, Janssen, Merck, Novartis, Pfizer, and Sanofi, Dafna D Gladman Consultant of: AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB, Frank Behrens Speakers bureau: AbbVie, Biotest, Boehringer Ingelheim, Celgene, Chugai, Eli Lilly, Genzyme, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Chugai, Janssen, Roche, and Pfizer, Yuri Klyachkin Employee of: Amgen Inc., Sven Richter Employee of: Amgen Inc., Lichen Teng Employee of: Amgen Inc., Josef S. Smolen Speakers bureau: AbbVie, Amgen Inc., AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, Medimmune, MSD, Novartis, Pfizer, Roche, Samsung, Sanofi, and UCB, Consultant of: AbbVie, Amgen Inc., AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, Medimmune, MSD, Novartis, Pfizer, Roche, Samsung, Sanofi, and UCB, Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Medimmune, Pfizer, and Roche.

DOI: 10.1136/annrheumdis-2021-eular.2224

AB0554

SLEEP QUALITY IN PATIENTS WITH PSORIATIC ARTHRITIS

P. Benzin[1], Z. R. Stisen[1], M. Skougaard[1], T. Schjødt Jørgensen[1], R. L. Hansen[1], L. M. Perez-Chada[2], M. Mogensen[3], J. F. Merola[2], L. E. Kristensen[1]. [1]*Parker Institute, Clinical Research Unit, Frederiksberg, Denmark*; [2]*Brigham And Women's Hospital, Department of Dermatology and Department of Medicine, Division of Rheumatology, Boston, United States of America*; [3]*Bispebjerg and Frederiksberg Hospital, Department of Dermatology, København, Denmark*

Background: Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease. It has a heterogeneous clinical presentation with main features being joint swelling and pain, skin and nail psoriasis, enthesitis, and dactylitis. Self-reported outcomes such as quality of sleep and fatigue are often neglected topics although having great impact on patients' everyday lives.

Objectives: The primary objective was to analyze the prevalence of PsA patients suffering from poor quality of sleep, defined by Pittsburgh Sleep Quality Index (PSQI) score ≥ 5, and to study the association between being a good or poor sleeper and clinical- and patient-reported outcomes.

Secondary, the effects on outcomes after initiation of treatment.

Methods: Patient characteristics, disease activity and self-reported outcomes were obtained from the PIPA cohort. To evaluate the primary objective, a cross-sectional analysis was conducted including PSQI score at baseline and corresponding data. Patients were divided into two groups, defined as good or poor sleepers (Table 1).

Data from initiation of treatment (baseline) and 4 months follow-up were included when assessing the effect of treatment. Transition of good and poor sleepers from baseline to 4 months follow-up was depicted by a chi-squared test.

A crosstab analysis was performed with baseline PSQI and whether they had widespread pain to investigate a possible link, additionally a Mann-Whitney U test.

Results: From January 2018-November 2020 a total of 109 patients were included. The prevalence of PsA patients suffering from poor quality of sleep at baseline were 66.1% whereas the remaining 33.9% were deemed good sleepers. There was no statistically significant difference in patient demographics when comparing good and poor sleepers at baseline. There was a statistically significant difference in patient-reported outcomes such as Visual Analogue Scale (VAS) pain, VAS global, Health Assessment Questionnaire (HAQ) score and Disease Activity Score (DAS28-CRP), with poor sleepers scoring higher.

57 patients had complete data at 4 months follow-up. At baseline 71.9% of them were classified as poor sleepers (Figure 1). A chi-squared test presented the transition at 4 months follow-up. 47.4% of the patients were now classified as poor sleepers.

While 27 poor sleepers became good sleepers, 13 good sleepers became poor sleepers, with data being statistically significant (p 0.001).

The crosstab analysis exposed 75 patients without widespread pain (mean 7.13±3.79) and 31 patients with widespread pain (mean 9.52±4.93).

Baseline PSQI and whether the patients had widespread pain was statistically significant (p 0.018).

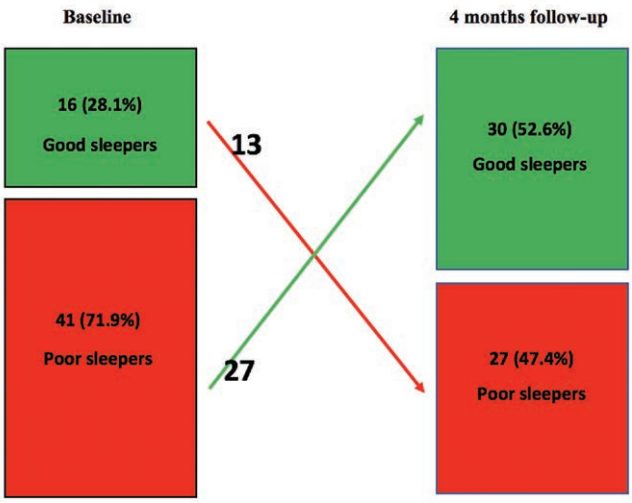
Conclusion: Overall, PsA patients with poor quality of sleep have higher levels in terms of self-reported pain and disease activity.

The amount of good sleepers after 4 months increased, but there was a negative transition of patients going from good to poor sleepers. This could indicate that more factors are important for quality of sleep, e.g. sociopsychological aspects like anxiety, depression, ability to work.

Table 1. Patient characteristics

	Total n = 109	Good sleepers PSQI ≤ 5 n = 37		Poor sleepers PSQI > 5 n = 72		
			n		n	p
Female, n (%)	65 (59.4%)	19 (51.4%)	37	46 (63.9%)	72	0.206
Age, yrs	53.9 (45.4-62.25)	60.4 (45.5-65.2)	37	51.5 (44.7-59.95)	72	0.144
Disease duration, yrs	3.86 (1.0-11.0)	4.5 (1.04-11.06)	34	2.91 (1.0-10.75)	68	0.352
csDMARD, n (%)	71 (65.1%)	26 (70.2%)	37	45 (62.5%)	72	0.420
bDMARD, n (%)	70 (64.2%)	24 (64.8%)	37	46 (63.9%)	72	0.920
Patient pain assessment 0-100 mm VAS	50.0 (21.0-74.5)	27.0 (9.0-60.5)	37	63.5 (32.25-78.0)	72	<0.001
Patient global assessment 0-100 mm VAS	61.0 (27.5-78.5)	35.0 (17.5-59.0)	37	69.5 (50.0-85.75)	72	<0.001
PsAID fatigue	6.0 (3.0-8.0)	4.0 (2.5-7.0)	37	6.5 (4.0-8.0)	72	0.488
HAQ score, 0-3	0.75 (0.38-1.25)	0.38 (0.25-0.81)	37	0.88 (0.63-1.38)	72	<0.001
PASI	1.7 (0.0-9.75)	2.0 (0.0-7.3)	35	1.2 (0.0-11.5)	65	0.940
DAS28-CRP	3.77 (3.02-4.58)	3.44 (2.65-3.94)	37	4.07 (3.28-4.93)	72	0.001

Figure 1. Quality of sleep



Disclosure of Interests: Peter Benzin: None declared., Zara Rebecca Stisen: None declared., Marie Skougaard: None declared., Tanja Schjødt Jørgensen Speakers bureau: Received consulting fees and/or speaking fees from AbbVie, Pfizer, Roche, Novartis, UCB, Biogen and Eli Lilly, Consultant of: Received consulting fees and/or speaking fees from AbbVie, Pfizer, Roche, Novartis, UCB, Biogen and Eli Lilly, Rebekka L. Hansen: None declared., Lourdes M. Perez-Chada: None declared., Mette Mogensen: None declared., Joseph F. Merola Consultant of: Consultant and/or investigator for Merck, Bristol-Myers Squibb, AbbVie, Dermavant, Eli Lilly, Novartis, Janssen, UCB, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Sorono, Avotres and Leo Pharma., Lars Erik Kristensen Speakers bureau: Received fees for speaking and consultancy from Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals., Consultant of: Received fees for speaking and consultancy from Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals.

DOI: 10.1136/annrheumdis-2021-eular.2294

AB0555

IMPACT OF ADALIMUMAB VERSUS NON-BIOLOGIC THERAPY ON CLINICAL AND PATIENT-REPORTED OUTCOMES IN PSORIATIC ARTHRITIS OVER 24 MONTHS – RESULTS OF THE COMPLETE-PsA CANADIAN OBSERVATIONAL STUDY

M. Khraishi[1], S. Silverberg[2], Y. Setty[3], M. C. Laliberté[4], L. Bessette[5]. [1]*Memorial University of Newfoundland, Memorial University of Newfoundland, St. John's, Canada*; [2]*Etobicoke General Hospital, Etobicoke General Hospital, Toronto, Canada*; [3]*Grey Bruce Health Services, Grey Bruce Health Services, Owen Sound, Canada*; [4]*AbbVie Corporation, Montreal, AbbVie Corporation, Montreal, Montreal, Canada*; [5]*Laval University, Centre Hospitalier de l'Université Laval, Laval University, Centre Hospitalier de l'Université Laval, Quebec City, Canada*

Background: COMPLETE-PsA was a Canadian observational study of biologic-naïve adults with active psoriatic arthritis (PsA) treated with adalimumab (ADA) or conventional systemic disease-modifying anti-rheumatic drugs (csDMARDs) after switch from a previous conventional therapy.

Objectives: To compare the impact of ADA vs csDMARDs on clinical and patient-reported outcomes due to PsA over 24 months.

Methods: Eligible patients were biologic naïve adults with active PsA who required change in their treatment due to inadequate response or non-tolerance, as per treating physician judgement. Patients were enrolled between July/2011 and December/2017 and followed for a maximum 24 months. Treatment was as per routine care. Outcome measures included tender/swollen joint count (TJC/SJC), morning stiffness (min/day), patient's global assessment of disease activity (PtGA) and pain (both 100 mm VAS), quality of life (DLQI), and functional disability (HAQ-DI). Outcome changes over time were evaluated using multivariable models adjusting for baseline measures. Achievement of modified minimal disease activity [mMDA, 5/7 of: TJC and SJC ≤1 each, psoriasis BSA ≤3%, pain ≤15 (VAS, mm), PtGA ≤20, HAQ-DI ≤0.5, and no enthesitis], and presence of enthesitis and dactylitis, were assessed descriptively. Analyses were conducted in the intent-to-treat population.

Results: A total of 277 ADA and 148 csDMARD-treated patients were included in the analysis. At baseline, 61.7% of ADA and 81.1% of csDMARD patients reported concomitant methotrexate. Compared to the csDMARD group, ADA-treated

patients demonstrated significantly (p<0.05) greater baseline disease severity with respect to mean (SD) joint count [TJC: 8.9 (6.2) vs. 7.4 (6.6); SJC: 7.4 (5.0) vs. 5.9 (4.6)], morning stiffness [83.5 (98.2) vs. 61.8 (77.4) min/day], PtGA [56.1 (24.1) vs. 45.1 (24.7) mm], pain [58.5 (24.3) vs. 50.1 (24.0) mm], DLQI scores [6.1 (6.9) vs. 4.3 (5.3)] and HAQ-DI [1.1 (0.6) vs. 0.8 (0.6)]. The rate of baseline mMDA was slightly lower for ADA patients (4.3% vs. 7.4%; p=0.178). Baseline prevalence of enthesitis was comparable (ADA: 28.4% vs. csDMARD: 23.4%; p=0.276), while dactylitis was significantly more prevalent for csDMARD patients (26.2% vs. 36.3%; p=0.031).

Overall effect of treatment group, over 24 months, significantly (p<0.05) favored the ADA vs. csDMARD-treated patients for TJC [estimate (95%CI): -2.4 (-3.4, -1.4)] SJC [-1.8 (-2.5, -1.2)], PtGA [-3.7 (-9.3, 1.9)], DLQI [-1.5 (-2.5, -0.5)], and HAQ-DI [-0.1 (-0.2, 0.0)] (Figure 1). There was no significant difference for morning stiffness and pain.

At month 24, statistically comparable (p>0.05) baseline-adjusted values (the least square means: LSM) were observed for ADA- vs. csDMARD-treated patients for TJC [LSM (95%CI): 1.8 (1.2, 2.4) vs. 3.0 (2.1, 3.8)], SJC [1.2 (0.8, 1.7) vs. 2.1 (1.5, 2.7)], morning stiffness [32.4 (19.1, 45.6) vs. 29.9 (11.1, 48.6) min/day], PtGA [31.6 (28.1, 35.2) vs. 36.9 (31.8, 41.9) mm], pain [35.3 (31.5, 39.0) vs. 38.4 (33.1, 43.7) mm], DLQI [2.9 (2.2, 3.6) vs. 2.9 (2.0, 3.8)], and HAQ-DI [0.7 (0.6, 0.8) vs. 0.9 (0.8, 1.0)].

Achievement of mMDA at month 24 was reported by 34.1% and 34.9% of ADA- and csDMARD-treated patients, respectively (p=0.892). Rates of dactylitis (10.6% vs. 10.0%) and enthesitis (9.6% vs. 14.4%) were comparable in the ADA vs. csDMARDs groups respectively.

Conclusion: The results of this real-world Canadian study indicate a physician selection bias for treatment with ADA for PsA patients with more severe disease burden, indicated by greater baseline disease activity and PROs. ADA-treated patients experienced a greater treatment effect over 24 months compared to csDMARD-treated patients. However, despite the greater treatment effect of ADA, residual disease burden in the two groups was comparable at 24 months.

Acknowledgements: The authors wish to acknowledge JSS Medical Research for their contribution to the statistical analysis, medical writing, and editorial support during the preparation of this abstract. AbbVie provided funding to JSS Medical Research for this work.

Disclosure of Interests: Majed Khraishi Speakers bureau: Speaker for AbbVie, Consultant of: Consultant for AbbVie, Grant/research support from: Principal Investigator for AbbVie, Samuel Silverberg Consultant of: Consultant for AbbVie, Janssen, and Pfizer, Yatish Setty Consultant of: Advisory Board meetings with AbbVie and Janssen, Marie-Claude Laliberté Employee of: Employee of AbbVie, Louis Bessette Speakers bureau: Speaker for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Gilead, Sandoz, Fresenius Kabi, Consultant of: Consultant for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, Gilead, Sandoz, Samsung Bioepis, Fresenius Kabi, Grant/research support from: Investigator for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Gilead.

DOI: 10.1136/annrheumdis-2021-eular.2589

AB0556 COMPARING EFFICACY OF GUSELKUMAB VERSUS USTEKINUMAB IN PATIENTS WITH PSORIASIS ARTHRITIS: AN ADJUSTED COMPARISON USING INDIVIDUAL PATIENT DATA FROM DISCOVER 1&2 AND PSUMMIT TRIALS

J. Diels[1], P. Thilakarathne[2], A. Schubert[3], F. Hassan[4], S. Peterson[5], W. Noel[1]. [1]*Janssen Pharmaceutica, HEMAR Department, Beerse, Belgium*; [2]*JanssenCilag Ltd, HEMAR Department, Beerse, Belgium*; [3]*Janssen-Cilag Poland, HEMAR Department, Warsaw, Poland*; [4]*Janssen-Cilag Ltd, HEMAR Department, High Wycombe, United Kingdom*; [5]*Janssen Global Services, LLC, Janssen Immunology Global Commercial Strategy Organization, Raritan, NJ, United States of America*

Background: Guselkumab is an anti-interleukin (IL)-23 monoclonal antibody recently approved for a treatment of Psoriasis arthritis (PsA). In two large Phase III trials of patients with PsA (DISCOVER -1 & -2) guselkumab has shown to be superior versus placebo. In this indication no direct comparison is available between guselkumab and ustekinumab, a monoclonal antibody targeting IL-12 and IL-23. Indirect comparisons based on relative treatment effects versus a common comparator (placebo) only allow for analyses up to week 24 due to cross-over to active arms in available PsA trials.

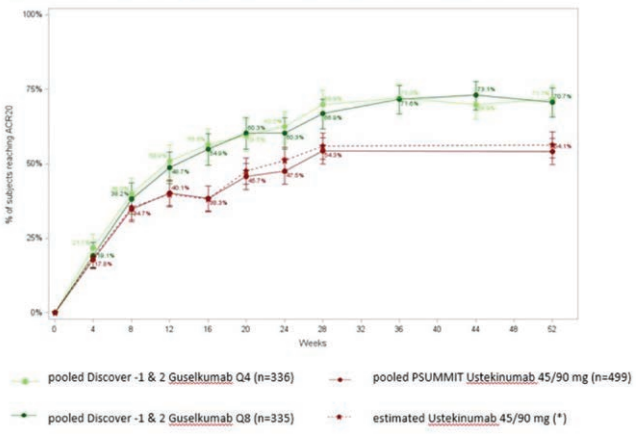
Objectives: To compare indirectly joint and skin efficacy of guselkumab versus ustekinumab up to week 52, using pooled patient-level trial data from DISCOVER 1&2 and PSUMMIT 1&2, adjusting for cross-trial population differences.

Methods: Patient level data, including baseline characteristics and outcome data on American College of Rheumatology (ACR) response, Psoriasis Area Severity Index (PASI) response from the guselkumab arms of DISCOVER -1 & -2 were pooled with the data from the ustekinumab trials PSUMMIT -1&-2. Analyses were performed for bio-naïve and bio-experienced populations separately. Differences in patient characteristics across trial populations were adjusted for using multivariate logistic regression, including: gender, age, body mass index, previous TNF use, disease duration, PASI level, number of swollen and tender joints. This method of indirect comparisons allows for analysis of comparative efficacy beyond controlled induction period and odds ratios' resulting from this model were translated into predicted response rates for ustekinumab, assuming same patient population, as enrolled in the guselkumab trial arms.

Results: Majority of baseline characteristics for patients on guselkumab (100mg q8w; 100mg q4w) were comparable to patients on ustekinumab 45/90mg, in both in bio-naïve and bio-experienced group of patients. The probability of reaching a ACR 20 in both the bio-naïve & bio-experienced population was significantly higher for guselkumab vs ustekinumab at weeks 52 for both dosing regimens of guselkumab (bio-naïve ACR 20: q8w OR= 1.88 [1.28;2.76]), q4w (OR= 1.92 [1.29;2.86]; bio experienced ACR20 q8w OR= 2.72[1.17;6.31], q4w OR=4.77 [1.95;11.63]). Similarly guselkumab was superior over ustekinumab on PASI 90 outcome at week 52 in both bio-naïve & bio-experienced patients with BSA ≥3 % at baseline (bio-naïve: q8w OR= 2.59 [1.68;3.99]), q4w OR= 3.19 [2.03;5.00], and bio-experienced q8w OR= 3.96[1.39,11.27], q4w OR=13.10[4.18,41.04]). Figure 1 represents unadjusted pooled DISCOVER 1&2 trial results and estimated proportions of ustekinumab treated patient group achieving ACR 20 in bio-naïve patient group up to week 52 using the method described above.

Conclusion: An adjusted comparison using patient level data from pivotal Phase III studies demonstrates both dosages of guselkumab to be significantly more effective versus ustekinumab in both skin and joint outcomes in both bio-naïve & bio experienced patients up to week 52.

Figure 1 ACR 20 response for guselkumab vs ustekinumab in bio-naïve patients



Disclosure of Interests: Joris Diels Shareholder of: Janssen, Employee of: Janssen, Pushpike Thilakarathne Employee of: Janssen, Agata Schubert Shareholder of: Janssen, Employee of: Janssen, Fareen Hassan Shareholder of: Janssen, Employee of: Janssen, Steve Peterson Shareholder of: Janssen, Employee of: Janssen, Wim Noel Shareholder of: Janssen, Employee of: Janssen.

DOI: 10.1136/annrheumdis-2021-eular.2595

AB0557 ACHIEVING TREATMENT TARGETS IN PSORIATIC ARTHRITIS WITH APREMILAST IN CANADIAN PRACTICE: REAL WORLD RESULTS FROM APPRAISE

V. Chandran[1], L. Bessette[2], C. Thorne[3], M. Sheriff[4], P. Rahman[5], D. D. Gladman[1], S. Anwar[6], J. Jelley[7], A. J. Gaudreau[7], M. Chohan[7], J. S. Sampalis[8]. [1]*Schroeder Arthritis Institute, Rheumatology, Toronto, Canada*; [2]*Laval University, Rheumatology, Quebec City, Canada*; [3]*Southlake Regional Health Centre, Rheumatology, Newmarket, Canada*; [4]*Nanaimo Regional General Hospital, Rheumatology, Nanaimo, Canada*; [5]*Memorial University of Newfoundland, Rheumatology, New Foundland, Canada*; [6]*Windsor Regional Hospital, Rheumatology, Windsor, Canada*; [7]*Amgen Canada Inc., Global Medical Affairs, Mississauga, Canada*; [8]*McGill University and JSS Medical Research, Epidemiology, Montreal, Canada*

Background: Real-world evidence on achieving treatment targets with apremilast (APR) in patients (pts) with PsA is limited. In the phase 3 PALACE trials, pts reached remission (REM)/low disease activity (LDA) targets at 52 wks most frequently when early APR treatment was initiated and pts were in moderate disease activity, as measured by Clinical Disease Activity Index for PsA (cDAPSA) score. In APPRAISE, we assessed APR effectiveness/tolerability in pts with PsA in routine clinical practice in Canada.

Objectives: This interim efficacy analysis focused on the available data on APR effectiveness measuring rate of achieving cDAPSA REM or LDA at 12 mos and Pt Acceptable Symptom Status (PASS) results.

Methods: The prospective, multicenter, observational APPRAISE study assessed APR effectiveness/tolerability in adults with active PsA in routine clinical care enrolled from July 2018-March 2020. Pts were followed from treatment initiation to 12 mos, with visits suggested every 4 mos. The primary effectiveness endpoint was the rate of achieving at least LDA (cDAPSA <14) at 12 mos. Pt-reported outcome measures were assessed. Data reported are as observed in pts continuing APR treatment.

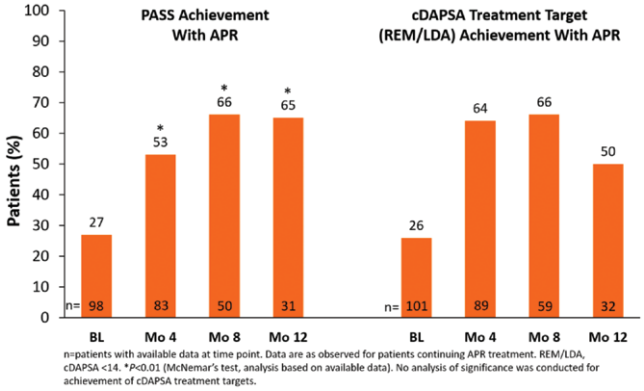
Results: In total, 101 pts were enrolled in APPRAISE. Mean age was 52 yrs; 56% were women. Mean (SD) PsA duration at baseline (BL) was 6 (8) yrs. Oligoarticular disease (≤4 joint involvement) was most common (41%), followed by polyarticular (35%). Most pts (92%) received prior conventional DMARDs and 17% received prior biologic therapy; concomitant MTX was reported in 41% at BL. By 12 mos, 41/101 enrolled pts discontinued, 35 reached 12 mos follow-up (4 mos: n=92; 8 mos: n=61), and 25 have yet to reach 12 mos. The majority (92%) of discontinuations due to lack/loss of effectiveness or AEs occurred within 4-8 mos. AEs were primarily GI related early in treatment. The proportion of pts with continued APR achieving cDAPSA REM/LDA treatment targets increased significantly over time (Figure 1). Significant reductions were seen over 12 mos in swollen/tender joint counts and plaque psoriasis, with reduced mean (SD) body surface area of –4% (9%) (Table 1). Prevalence of dactylitis/enthesitis at BL, 4, 8, and 12 mos was 17%/33%, 9%/24%, 5%/19%, and 0%/21%, respectively. Pain assessment (VAS) significantly improved over time. The proportion of pts achieving PASS with continued APR increased significantly over 12 mos (BL: 27%; 12 mos: 65%) (Figure 1). COVID restrictions impacted in-office assessment visits, necessitating reliance on virtual visits.

Conclusion: Pts with PsA receiving APR were assessed at regular intervals in routine clinical care in Canada. This interim analysis revealed a greater number of pts receiving APR (66%) who completed the 12-mo follow-up achieved REM or LDA, as measured by cDAPSA over 12 mos. A majority of pts (65%) reported satisfaction with their disease state, as measured by PASS. No new safety signals were observed.

Table 1. Change in Clinical Parameters and Pt-Reported Outcomes From BL to 4, 8, and 12 Mos

Outcome Measure*, Mean (SD)	BL (n = 101)	4 Mos (n = 92)	8 Mos (n = 61)	12 Mos (n = 35)
Disease/Clinical Parameters				
Tender joint count (0-68)	7.5 (6.7)	–2.5 (6.3)*	–3.9 (5.2)*	–2.2 (6.4)
Swollen joint count (0-66)	5.4 (5.4)	–3.0 (4.5)*	–3.1 (4.3)*	–3.1 (4.4)*
PhGA	42.9 (18.8)	–19.0 (24.6)*	–24.2 (24.2)*	–21.2 (26.3)*
Body surface area, %	3.1 (6.1)	–2.2 (6.0)*	–2.7 (7.5)*	–4.2 (9.1)*
cDAPSA	22.2 (13.3)	–7.9 (12.1)*	–10.1 (13.5)*	–6.9 (12.0)*
Pt-Reported Outcomes				
PtGA, mm	50.0 (24.6)	–10.2 (27.5)*	–9.1 (31.9)*	–3.6 (39.7)
Pain, mm	48.3 (25.3)	–9.5 (26.2)*	–12.2 (28.7)*	–7.3 (26.0)
HAQ-DI	0.9 (0.7)	–0.13 (0.5)*	–0.15 (0.6)	–0.1 (0.7)

*Denotes significant change from BL ($P<0.05$) from paired-sample *t*-tests; note that mean change from BL may be greater than the mean BL value when improvements of large magnitude, for pts with relatively elevated BL values, are observed in samples with lower n's. HAQ-DI = Health Assessment Questionnaire-Disability Index; PhGA = Physician's Global Assessment; PtGA = Patient's Global Assessment.



n=patients with available data at time point. Data are as observed for patients continuing APR treatment. REM/LDA, cDAPSA <14. *$P<0.01$ (McNemar's test, analysis based on available data). No analysis of significance was conducted for achievement of cDAPSA treatment targets.

Acknowledgements: This study was funded by Celgene and Amgen Inc. Writing support was funded by Amgen Inc. and provided by Kristin Carlin, RPh, MBA, of Peloton Advantage, LLC, an OPEN Health company.

Disclosure of Interests: Vinod Chandran Consultant of: AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Louis Bessette Consultant of: AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Janssen, Merck, Pfizer, Sanofi, Novartis, UCB, Grant/research support from: AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Janssen, Merck, Pfizer, Sanofi, Novartis, UCB, Carter Thorne Speakers bureau: AbbVie, Amgen, Celgene Corporation, Eli Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sandoz, Sanofi, Consultant of: Centocor, Medexus/Medac, Merck, Grant/research support from: Novartis, Pfizer, Maqbool Sheriff Speakers bureau: AbbVie, Celgene Corporation, Eli Lilly, Janssen, Merck, Pfizer, Sandoz, Proton Rahman Speakers bureau: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, UCB, Dafna D Gladman Consultant of: AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, UCB, Sabeen Anwar Consultant of: AbbVie, Amgen Inc., BMS, Novartis, and Pfizer, Grant/research support from: AbbVie, Amgen Inc., Eli Lilly, Janssen, and Pfizer, Jennifer Jelley Employee of: Amgen Canada Inc., Anne-Julie Gaudreau Employee of: Amgen Canada Inc., Manprit Chohan Employee of: Amgen Canada Inc., John S. Sampalis Employee of: JSS Medical Research.

DOI: 10.1136/annrheumdis-2021-eular.2599

AB0558

CLINICAL EFFECTIVENESS AND SAFETY OF ADALIMUMAB VERSUS NON-BIOLOGIC THERAPY IN PSORIATIC ARTHRITIS PATIENTS OVER 24 MONTHS – RESULTS OF THE COMPLETE-PsA CANADIAN OBSERVATIONAL STUDY

M. Khraishi[1], J. Stewart[2], Y. Setty[3], M. C. Laliberté[4], L. Bessette[5]. [1]*Memorial University of Newfoundland, Memorial University of Newfoundland, St. John's, Canada*; [2]*University of British Columbia, University of British Columbia, Penticton, Canada*; [3]*Grey Bruce Health Services, Grey Bruce Health Services, Owen Sound, Canada*; [4]*AbbVie Corporation, AbbVie Corporation, Montreal, Canada*; [5]*Laval University, Centre Hospitalier de l'Université Laval, Laval University, Centre Hospitalier de l'Université Laval, Quebec City, Canada*

Background: COMPLETE-PsA was an observational study of biologic-naïve Canadian adults with active psoriatic arthritis (PsA) treated with adalimumab or non-biologic disease-modifying anti-rheumatic drugs (nbDMARD) after switch from initial therapy.

Objectives: The aim of this analysis was to assess the 24-month clinical effectiveness and safety of adalimumab vs. nbDMARD in the treatment of PsA in a real-life setting.

Methods: Eligible patients were biologic naïve adults, with active PsA who required change in their treatment regimen due to inadequate response or intolerance, per the judgment of the treating physician. Patients were enrolled between July/2011 and December/2017 and followed for up to 24 months. Patients were treated as per routine care. The primary endpoint, change in DAS-28 to month 24, was assessed with baseline-adjusted multivariable models and the least square mean (LSM) estimates were generated; Physician's Global Assessment of disease activity (PGA, 100mm VAS) was assessed using similar methodology. Probability of achieving the following therapeutic response thresholds was ascertained and odds ratios (ORs) were generated: 50%/70% improvement in the American College of Rheumatology criteria (ACR50/ACR70), DAS-28<3.2 (low disease activity or remission; LDA/remission), DAS-28<2.6 (remission), modified minimal disease activity (mMDA: achievement of 5/7 of: TJC and SJC ≤1 each, BSA ≤3%, pain ≤15 (VAS, mm), Patient Global Assessment [PtGA] ≤20, HAQ-DI ≤0.5, and no enthesitis), and psoriasis (PsO) BSA <3%.

Results: A total of 277 adalimumab and 148 nbDMARD- treated patients were included as part of the intent-to-treat population. Baseline methotrexate was reported by 61.7% and 81.1% of adalimumab and nbDMARD-treated patients, respectively. PsO BSA at baseline was predominantly <3% for both adalimumab (60.2%) and nbDMARD (64.6%) patients. Adalimumab-treated patients reported significantly ($p<0.05$) higher mean (SD) disease activity for both DAS-28 [4.8 (1.2) vs. 4.3 (1.1)] and PGA [59.4 (19.5) vs. 51.0 (21.8) mm] at baseline.

For the primary endpoint, baseline-adjusted month 24 DAS-28 levels were significantly lower for adalimumab vs. nbDMARD patients [LSM (95%CI): 2.4 (2.2-2.6) vs. 3.0 (2.7-3.3); p=0.037]. In addition, rapid and sustained reductions in DAS-28 were observed for adalimumab-treatment patients, with overall treatment effect significant ($p<0.001$) in favor of adalimumab [estimate (95%CI): -1.1 (-1.4, -0.7)]; similar results were observed for PGA [-12.9 (-1.7, -8.0)]. Adalimumab-treated

patients were at significantly higher (p<0.001) odds of attaining therapeutic response thresholds compared to DMARD-treated patients, specifically: DAS-28 LDA/remission [OR (95%CI): 4.5 (2.8, 7.3)] or remission [OR (95% CI): 4.1 (2.7-6.3)], ACR50 [OR (95% CI): 3.0 (2.0-4.6)], ACR70 [OR (95% CI): 3.1 (2.0-4.9)], mMDA [OR (95% CI): 2.4 (1.6-3.6)], and PsO BSA <3% [OR (95% CI): 2.2 (1.2-3.7)].

Overall, 32 (10.7%) of adalimumab-treated patients reported 86 AEs, the most common related to infections [16 events in 10 (3.3%) patients].

Conclusion: Real-world treatment with adalimumab was more effective in improving disease activity and psoriasis severity, over 24 months when compared to nbDMARDs and was associated with significantly greater likelihood of achieving minimal disease activity. Observed AEs were consistent with the established safety profile of adalimumab.

Disclosure of Interests: Majed Khraishi Speakers bureau: Speaker for AbbVie, Consultant of: Consultant for AbbVie, Grant/research support from: Principal Investigator for AbbVie, Jacqueline Stewart Speakers bureau: Speaker for Abbvie, Janssen, and Johnson & Johnson, Consultant of: Advisory Board Consultant for AbbVie, Amgen, Celgene, Merck, Novartis, Pfizer, and Sanofi-Genzyme;, Grant/research support from: Participated in research with AbbVie, Bristol Myers Squibb, Janssen, and Roche, Yatish Setty Consultant of: Advisory Board meetings with AbbVie and Janssen, Marie-Claude Laliberté Employee of: Employee of AbbVie, Louis Bessette Speakers bureau: Speaker for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Gilead, Sandoz, and Fresenius Kabi, Consultant of: Consultant for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, Gilead, Sandoz, Samsung Bioepis, and Fresenius Kabi, Grant/research support from: Investigator for Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, and Gilead.

DOI: 10.1136/annrheumdis-2021-eular.2644

AB0559

EFFICACY AND SAFETY OF RISANKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AFTER INADEQUATE RESPONSE OR INTOLERANCE TO DMARDs: 24-WEEK RESULTS FROM THE PHASE 3, RANDOMIZED, DOUBLE-BLIND KEEPsAKE 1 TRIAL

L. E. Kristensen[1], M. Keiserman[2], K. Papp[3], L. Mccasland[4], D. White[5], L. Barcomb[6], W. Lu[6], Z. Wang[6], A. M. Soliman[6], A. Eldred[6], F. Behrens[7].
[1]Copenhagen University, The Parker Institute, Copenhagen, Denmark; *[2]Pontifical Catholic University, Rheumatology Section, Porto Alegre, Peru*; *[3]Probity Medical Research, K Papp Clinical Research, Waterloo, Canada*; *[4]Loyola University Medical Center, Department of Rheumatology, Maywood, United States of America*; *[5]Waikato Hospital, Rheumatology Department, Hamilton, New Zealand*; *[6]AbbVie, Inc, Not Applicable, North Chicago, United States of America*; *[7]Goethe University Frankfurt, CIRI/Rheumatology & Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Frankfurt, Germany*

Background: Risankizumab (RZB) is a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits interleukin 23 by binding to its p19 subunit. RZB is being investigated as a treatment for adults with psoriatic arthritis (PsA).

Objectives: To compare the efficacy and safety of RZB vs placebo (PBO) for the treatment of active PsA in patients who have had inadequate response or intolerance to ≥ 1 conventional synthetic disease modifying antirheumatic drug (csDMARD-IR).

Methods: In KEEPsAKE 1 (NCT03675308), eligible adults (csDMARD-IR with ≥ 5 swollen joints [SJC] and ≥ 5 tender joints [TJC]) were randomized (1:1) to receive blinded subcutaneous RZB 150 mg or PBO at weeks 0, 4, and 16. The primary endpoint was the proportion of patients achieving 20% improvement in American College of Rheumatology score (ACR20) at week 24. Ranked secondary and other secondary endpoints are shown in the Table 1. Safety was assessed throughout the study. Results reported here are from the 24-week double-blind period; the open-label period with all patients receiving RZB is ongoing.

Results: 964 patients (RZB, N = 483; PBO, N = 481) were evaluated at week 24. Demographics and baseline characteristics were generally balanced between treatment groups (mean duration of PsA: 7.12 years; mean SJC: 12.2; mean TJC: 20.6; mean body surface area involved with psoriasis [BSA] in patients with BSA ≥ 3%: 16.7%). A significantly greater proportion of RZB- vs PBO-treated patients (57.3% and 33.5%, respectively) achieved the primary endpoint of ACR20 at week 24 (P < .001; Table 1). Significant differences were also observed for RZB vs PBO for the first 8 ranked secondary endpoints (P < .001 for all; Table 1). Serious adverse events were reported for 2.5% and 3.7% of RZB- and PBO-treated patients, respectively; serious infections were reported for 1.0% and 1.2%. There was 1 death in the RZB group.

Conclusion: RZB resulted in significantly greater improvements in signs and symptoms of PsA compared with PBO and was well tolerated in patients who were csDMARD-IR.

Table. Efficacy Results

	RZB 150 mg N = 483	PBO N = 481	Difference (95% CI)	*P* value
Primary endpoint				
ACR20, %	57.3	33.5	24.0 (18.0, 30.0)	< .001***
Ranked secondary endpoints				
HAQ-DI, change	−0.3	−0.1	−0.2 (−0.3, −0.1)	< .001***
PASI 90,[a] %	52.3	9.9	42.5 (35.6, 49.3)	< .001***
ACR20 at week 16, %	56.3	33.4	23.1 (16.8, 29.4)	< .001***
MDA, %	25.0	10.2	14.8 (10.2, 19.4)	< .001***
mNAPSI,[a] change	−9.8	−5.6	−4.2 (−5.7, −2.7)	< .001***
PGA-F,[a] change	−0.8	−0.4	−0.4 (−0.6, −0.3)	< .001***
Resolution of enthesitis,[a,b] %	48.4	34.8	13.9 (7.6, 20.2)	< .001***
Resolution of dactylitis,[a,b] %	68.1	51.0	16.9 (7.5, 26.4)	< .001***
PsA-mTSS, change	0.2	0.3	−0.1 (−0.4, 0.2)	.50
SF-36 PCS, change	6.5	3.2	3.3 (2.4, 4.2)	< .001†
FACIT-Fatigue, change	6.5	3.9	2.6 (1.5, 3.7)	< .001†
Other Secondary Endpoints				
ACR50, %	33.4	11.3	22.2 (17.3, 27.2)	< .001†
ACR70, %	15.3	4.7	10.5 (6.9, 14.2)	< .001†

ACR20/ACR50/ACR70, ≥ 20/50/70% improvement in American College of Rheumatology score; HAQ-DI, Health Assessment Questionnaire-Disability Index; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-

Disclosure of Interests: Lars Erik Kristensen Speakers bureau: LK has received honoraria or fees for serving as a speaker or consultant from AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Gilead, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB., Consultant of: LK has received honoraria or fees for serving as a speaker or consultant from AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Gilead, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB., MAURO KEISERMAN Speakers bureau: MK has received honoraria or fees for serving on advisory boards, as a speaker or as a consultant, and grants as a principal investigator from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Novartis, Pfizer, Roche, and UCB., Consultant of: MK has received honoraria or fees for serving on advisory boards, as a speaker or as a consultant, and grants as a principal investigator from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Novartis, Pfizer, Roche, and UCB., Grant/research support from: MK has received honoraria or fees for serving on advisory boards, as a speaker or as a consultant, and grants as a principal investigator from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Novartis, Pfizer, Roche, and UCB., Kim Papp Speakers bureau: KP has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant, as well as grants as principal investigator from AbbVie, Amgen, Astellas, Bausch Health (Valeant), Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO Pharma, Lilly, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB., Consultant of: KP has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant, as well as grants as principal investigator from AbbVie, Amgen, Astellas, Bausch Health (Valeant), Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO Pharma, Lilly, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB., Grant/research support from: KP has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant, as well as grants as principal investigator from AbbVie, Amgen, Astellas, Bausch Health (Valeant), Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO

Pharma, Lilly, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda, and UCB., Leslie McCasland Speakers bureau: LM has received fees for serving on an advisory board from Lilly., Douglas White Speakers bureau: DW has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant from AbbVie, Merck, Novartis, and Roche., Consultant of: DW has received honoraria or fees for serving on advisory boards, as a speaker, and as a consultant from AbbVie, Merck, Novartis, and Roche., Lisa Barcomb Shareholder of: LB is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Employee of: LB is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Wenjing Lu Shareholder of: WL is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Employee of: WL is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Zailong Wang Shareholder of: ZE is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Employee of: ZE is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Ahmed M. Soliman Shareholder of: AMS is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Employee of: AMS is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Ann Eldred Shareholder of: AE is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Employee of: AE is a full-time employee of AbbVie, and may hold AbbVie stock or stock options., Frank Behrens Speakers bureau: FB has received research grants, honoraria, or fees for serving as a consultant or speaker from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Chugai, Galapagos, Genzyme, Gilead, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, and Sanofi., Consultant of: FB has received research grants, honoraria, or fees for serving as a consultant or speaker from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Chugai, Galapagos, Genzyme, Gilead, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, and Sanofi., Grant/research support from: FB has received research grants, honoraria, or fees for serving as a consultant or speaker from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Chugai, Galapagos, Genzyme, Gilead, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, and Sanofi.

DOI: 10.1136/annrheumdis-2021-eular.2678

AB0560

EFFECT OF DEUCRAVACITINIB ON THE PSORIATIC ARTHRITIS IMPACT OF DISEASE (PsAID) QUESTIONNAIRES 12 AND 9: ANALYSIS OF A PHASE 2 STUDY OF ACTIVE PSORIATIC ARTHRITIS

L. Gossec[1], L. C. Coates[2], A. Ogdie[3], P. J. Mease[4], T. Lehman[5], M. Nowak[6], L. Wei[7], J. Ye[8], J. Choi[9], J. Zhuo[9], B. Becker[9]. [1]*Sorbonne Université, Pitié Salpêtrière Hospital, Department of Rheumatology, Paris, France*; [2]*University of Oxford, Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; [3]*Perelman School of Medicine, University of Pennsylvania, Division of Rheumatology and Center for Clinical Epidemiology and Biostatistics, Philadelphia, United States of America*; [4]*Swedish Medical Center/Providence St. Joseph Health and University of Washington, Rheumatology Research, Seattle, United States of America*; [5]*Bristol Myers Squibb, Rheumatology, Princeton, United States of America*; [6]*Bristol Myers Squibb, Clinical R&D, Princeton, United States of America*; [7]*Bristol Myers Squibb, Medical Immunology, Princeton, United States of America*; [8]*Bristol Myers Squibb, Medical Affairs, Princeton, United States of America*; [9]*Bristol Myers Squibb, HEOR, Princeton, United States of America*

Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates IL-23, IL-12, and IFNα/β signaling. Deucravacitinib is a novel, oral selective inhibitor of TYK2 via the TYK2 regulatory domain. Phase 2 results showed deucravacitinib was efficacious and well tolerated versus placebo (PBO) in patients (pts) with active psoriatic arthritis (PsA). The Psoriatic Arthritis Impact of Disease (PsAID) questionnaire is a EULAR-developed, validated instrument designed to specifically assess the impact of PsA on health-related quality of life (HRQoL) from the pt's perspective and is available as separate versions for clinical practice (PsAID-12) and clinical trials (PsAID-9).[1]

Objectives: To compare the effect of deucravacitinib vs PBO on PsAID-12 and PsAID-9 responses and to assess relationships between PsAID scores and clinical and pt-reported outcome (PRO) measures.

Methods: This is an ongoing, 1-year, double-blind, Phase 2 trial (NCT03881059). Pts with active PsA were randomized 1:1:1 to deucravacitinib 6 mg or 12 mg once daily, or PBO for 16 weeks (wk). PsAID-12 and PsAID-9, other PROs, and clinical response outcomes were assessed at baseline (BL) and Wk 16. Mean changes from BL in PsAID-12 and PsAID-9 total scores at Wk 16 were determined for each treatment group as well as by response outcomes (ie, achievement of response at Wk 16 for PROs and select clinical response outcomes; Table 1). Spearman correlations between PsAID-12 and PsAID-9 scores and clinical and PRO measures were also assessed.

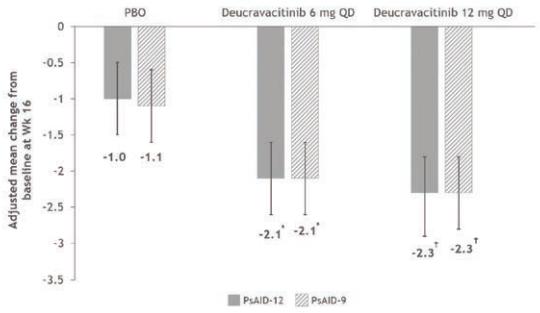
Results: 203 pts were randomized and BL characteristics were similar across groups. Adjusted mean changes from BL in PsAID-12 and PsAID-9 scores at Wk 16 were significantly greater in the deucravacitinib groups vs PBO (Figure 1). Adjusted mean changes from BL in PsAID-12 and PsAID-9 scores at Wk 16 were significantly improved with deucravacitinib vs PBO in pts who achieved response for PROs, as well as PASDAS low disease activity and PASI 75 response (Table 1). Adjusted mean changes from BL were generally similar with deucravacitinib vs PBO in nonresponders. Spearman correlation analysis revealed significant correlations at BL and Wk 16 between PsAID-12 and PsAID-9 scores and clinical and PRO measures (P<0.0001).

Conclusion: With deucravacitinib vs PBO, PsAID-12 and PsAID-9 scores were significantly improved vs BL at Wk 16. PsAID detected additional improvements among pts achieving response for multiple other PROs and select clinical outcome measures.

REFERENCES:

[1] Gossec L et al. *Ann Rheum Dis.* 2014;73:1012-9.

Figure. Adjusted mean change from baseline in PsAID-12 and PsAID-9 total scores at Wk 16



*P≤0.002 vs PBO; †P≤0.0005 vs PBO.
PBO, placebo; PsAID-9, 9-item Psoriatic Arthritis Impact of Disease questionnaire; PsAID-12, 12-item Psoriatic Arthritis Impact of Disease questionnaire; QD, once daily.

Table 1. Adjusted mean change from BL in PsAID-12 total scores at Wk 16 in patients who achieved PRO or clinical response

	Mean change from BL in PsAID-12 total score				
Response Definition	**PBO n=66**	**Deucravacitinib 6 mg QD n=70**	***P* value vs PBO**	**Deucravacitinib 12 mg QD n=67**	***P* value vs PBO**
PROs					
Patient global VAS (≤ -10.0)	-1.6 (n=40)	-2.8 (n=54)	0.0008	-2.9 (n=48)	0.0003
Patient pain VAS (≤ -10.0)	-2.3 (n=32)	-3.4 (n=44)	0.004	-3.3 (n=45)	0.004
HAQ-DI (≤ -0.35)	-2.8 (n=10)	-3.8 (n=27)	0.09	-3.8 (n=27)	0.11
FACIT-Fatigue (≥ 4.0)	-2.4 (n=27)	-3.3 (n=36)	0.02	-3.6 (n=41)	0.002
SF-36 PCS (≥ 2.5)	-1.7 (n=35)	-2.7 (n=44)	0.02	-3.1 (n=43)	0.001
SF-36 MCS (≥ 2.5)	-2.1 (n=21)	-3.5 (n=33)	0.005	-3.8 (n=31)	0.0009
Clinician assessments					
PASDAS (≤ 3.2)	-3.1 (n=6)	-4.2 (n=14)	0.004	-4.5 (n=15)	0.0006
PASI 75 (≥75% improvement from BL)	-2.4 (n=11)	-3.7 (n=25)	0.05	-3.9 (n=31)	0.02

PsAID-9 results were generally consistent with PsAID-12 (data not shown).Response definitions based on published literature.Higher FACIT-Fatigue scores indicate less fatigue.Higher SF-36 PCS and SF-36 MCS scores indicate less disability.BL, baseline: FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCS, Mental Component Summary; NA, not applicable; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area and Severity Index; PCS, Physical Component Summary; PRO, patient-reported outcome; QD, once daily; SF-36, 36-item Short Form Health Survey; VAS, visual analog scale.

Acknowledgements: This study was sponsored by Bristol Myers Squibb. Professional medical writing assistance was provided by Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

Disclosure of Interests: Laure Gossec Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Amgen, Galapagos, Janssen, Lilly, Pfizer, Sandoz, Sanofi, Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Gilead, Eli Lilly, Janssen, Medac, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Pfizer, and Novartis, Alexis Ogdie Consultant of: Abbvie, Amgen, BMS, Celgene, Corrona, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB; Grants: Pfizer to Penn, Novartis to Penn, Amgen to Forward/NDB; Royalties: Novartis to husband, Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB, Thomas Lehman Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Miroslawa Nowak Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Lan Wei Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, June Ye Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Jiyoon Choi Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Joe Zhuo Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Brandon Becker Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb.

DOI: 10.1136/annrheumdis-2021-eular.2709

AB0561 DISEASE DURATION AND HLA-B27 POSITIVITY ALTER LONGTERM RETENTION RATE OF CERTOLIZUMAB PEGOL IN PATIENTS WITH PSORIATIC ARTHRITIS

S. S. Koca[1], Y. Pehlivan[2], S. Akar[3], S. Şenel[4], H. Karadeniz[5], O. Sosyal[6], A. Yazici[7], S. Yılmaz[8], R. Piskin Sagir[1], N. Inanc[9], A. Karatas[1], G. Yildirim Cetin[10], F. Onen[11]on behalf of TURKBIO Study Group. *[1]Firat University School of Medicine, Department of Rheumatology, Elazig, Turkey*; *[2]Uludağ University, School of Medicine, Department of Rheumatology, Bursa, Turkey*; *[3]Katip Çelebi University, School of Medicine, Department of Rheumatology, Izmir, Turkey*; *[4]Erciyes University School of Medicine, Department of Rheumatology, Kayseri, Turkey*; *[5]Gazi University School of Medicine, Department of Rheumatology, Ankara, Turkey*; *[6]Celal Bayar University School of Medicine, Department of Rheumatology, Manisa, Turkey*; *[7]Kocaeli University School of MEdicine, Department of Rheumatology, Kocaeli, Turkey*; *[8]Selcuk University School of Medicine, Department of Rheumatology, Konya, Turkey*; *[9]Marmara University School of Medicine, Department of Rheumatology, Istanbul, Turkey*; *[10]Kahramanmaraş Sutçu Imam University School of Medicine, Department of Rheumatology, Kahramanmaraş, Turkey*; *[11]9 Eylul University School of Medicine, Department of Rheumatology, Izmir, Turkey*

Background: Several factors such as effectiveness, safety and compliance affect the drug survival in chronic disorders. Physicians take care of long-term retention rate and responses for discontinuation of candidate drug. Identification of predictors of clinical response to certolizumab-pegol (CZP) may aid the decision-making process for treating patients psoriatic arthritis (PsA).

Objectives: The purpose of this study to assess the drug survival of certolizumab pegol (CZP) in patients with PsA and to identify the predictors and reasons for discontinuation.

Methods: Data on patient characteristics, demographics, diagnosis, disease duration, treatment and outcomes have been collected since 2011 in Turkish Biologic (TURKBIO) Registry. By the end of December 2020, 68 PsA patients received CZP and were included. Kaplan Meier plot was used for drug survival analysis. Cox regression analysis was performed to evaluate the predictors associated with drug survival.

Results: During the median 47 months follow-up, 17 patients discontinued the CZP treatment. The reasons for discontinuation were ineffectivity (35.3%), adverse event (17.6%) and pregnancy (5.9%). The baseline characteristics of the patients who continued and discontinued CZP were shown in the Table 1. Patients who discontinued CZP had higher mean age and disease duration. HLA-B27 positive patients had lower retention rate while bDMARD naive patients had higher retention rate. At the month 36, retention rate of CZP was 61.6% on patients with PsA (Figure 1).

Conclusion: Real life experience from this nationwide TURKBIO registry show that the retention rate of CZP in PsA are lower in older patients and with longer disease duration. Moreover, bDMARD naive patients have higher retention rate.

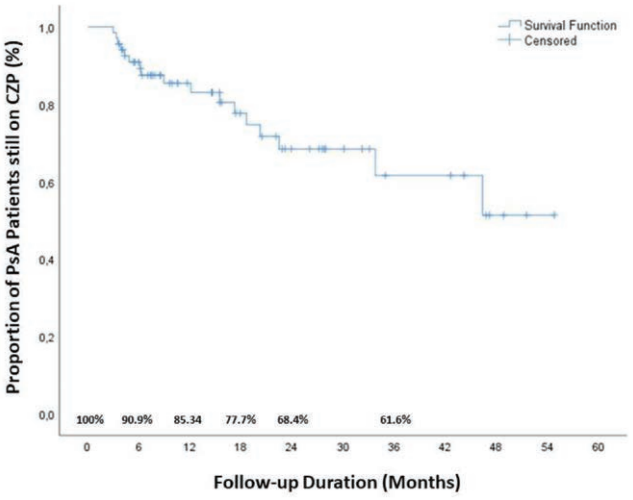


Figure 1. Drug survival of CZP in patients with PsA

Table 1. Baseline characteristics of PsA patients who continue and discontinue CZP

	All Patients (n=68)	Continue to CZP (n=51)	Discontinue to CZP (n=17)	p
Females, n (%)	52 (76,5)	37 (72,5)	15 (88,2)	0,322
Age, years	**44 (36-57)**	**40 (35-53)**	**51 (42-60)**	**0,012**
Disease Duration, years	**9 (5-13)**	**8 (5-12)**	**14 (10,5-17)**	**0,002**
Symptom duration, years	**11 (7-16)**	**10 (7-15)**	**15,5 (11,5-20)**	**0,014**
Order of CZP in bDMARDs	1 (1-2)	1 (1-2)	2 (1-2)	0,062
HLA-B27, n (%)	**9 (28,1)**	**3 (14,3)**	**6 (54,5)**	**0,035**
ESR, mm/h	23,5 (11-37)	23 (9-35)	24 (17-52)	0,246
Swollen Joint Counts, n	0 (0-2)	0 (0-2)	1 (0-2)	0,480
Tender Joint Counts, n	2 (0-4)	1 (0-4)	2 (1-5)	0,143
CRP, mg/dl	4 (3-13,65)	3,14 (3-13)	5 (3-19)	0,107
HAQ	0,63 (0,25-1)	0,63 (0,25-1)	0,75 (0,63-0,94)	0,097
VAS-Physicians	20 (12-31,5)	20 (12-26)	30 (15-50)	0,074
VAS-Patient Global	50 (27-70)	50 (20-70)	61,5 (46,5-70)	0,342
VAS-Patient Pain	53 (28-75)	50 (20-75)	69 (49,5-75)	0,122
DAS-28-CRP	3,35 (2,2-3,9)	2,85 (2-3,8)	3,6 (2,9-4,4)	0,086
BASFI	15 (8-27)	14 (5-26)	23,5 (12-30,5)	0,133
BASDAI	28 (16-40)	27,5 (14-36)	39 (22,5-41,5)	0,060
ASDAS	2,7 (1,9-3,2)	2,6 (1,9-3,1)	3 (2,35-3,4)	0,122
DAPSA-28	15,35 (7,2-21,9)	14,9 (6,1-21,17)	18,9 (14,15-29,3)	0,108

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2832

AB0562 POTENTIAL BIOMARKERS OF PERSONALIZED TREATMENT BASED ON CARDIOVASCULAR-RELATED COMORBIDITIES IN PSORIATIC ARTHRITIS

I. Arias de la Rosa[1], M. D. López Montilla[2], C. Román-Rodriguez[2], I. Gómez García[2], M. J. Pérez Galán[3], I. Añón Oñate[3], M. D. C. Abalos-Aguilera[2], C. Perez-Sanchez[2], D. Ruiz[2], A. M. Patiño-Trives[2], M. Luque-Tévar[2], M. L. Ladehesa Pineda[2], C. López-Medina[2], C. Lopez-Pedrera[2], A. Escudero Contreras[2], E. Collantes Estevez[2], N. Barbarroja Puerto[1]. *[1]Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/Reina Sofia Hospital/University of Cordoba, Medicine Department, Cordoba, Spain*; *[2]Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/Reina Sofia Hospital/University of Cordoba, Rheumatology Department, Cordoba, Spain*; *[3]University Hospital of Jaen, Rheumatology Department, Jaen, Spain*

Background: Psoriatic Arthritis (PsA) displays increased traditional cardiovascular (CV) risk factors, such as insulin resistance (IR), metabolic syndrome or obesity. Thus, it is an urgent need to treat and manage these

cardiometabolic comorbidities associated. Some evidence points out that methotrexate could improve CV risk due to its anti-inflammatory properties, however the effect of PDE4 inhibitor treatment on CV risk have not been elucidated yet.

Objectives: 1) To evaluate the effect of conventional therapy and PDE4 inhibitor in PsA patients with high prevalence of cardiometabolic comorbidities. 2) To identify a molecular patient profile susceptible of being benefit from each therapy regarding disease activity and CV risk.

Methods: Thirty biological-naïve patients with PsA were treated with the PDE4 inhibitor (Apremilast), Methotrexate or combined therapy (Apremilast and Methotrexate) following the clinical routine practice for 6 months. A cohort of 30 age and sex-matched healthy donors (HDs) was included. Plasma and peripheral blood mononuclear cells (PBMCs) were isolated from peripheral blood of patients and HDs. Different parameters related to the cardiometabolic risk were analyzed, including: atherogenic index, ratio apolipoprotein B (apo B)/apolipoprotein A (apo A), insulin resistance (IR), metabolic syndrome, obesity, arterial hypertension, and the SCORE. Clinical and analytical parameters were collected: lipid profile (total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, apo A and apo B), glucose and insulin, body surface area (BSA) affected by psoriasis, number of tender and swollen joints, DAPSA, C-reactive protein and erythrocyte sedimentation rate. A panel of 92 proteins involved in cardiovascular disease (cardiovascular panel II, Olink) and an adipocytokine profile was measured in plasma and PBMCs. Hard cluster analysis was carried out in order to identify two distinctive molecular phenotypes depending on the treatment response related to the reduction of CV risk.

Results: Among the 92 CV-related proteins, the higher levels of two molecules, CD163 and FABP4 observed in PsA patients compared to HDs, were strongly associated with elevated rates of CV risk factors such as apolipoprotein B/A and atherogenic risks, metabolic syndrome, obesity, IR, arterial hypertension and smoking. Thus, we could identify two clinical profiles of patients according to the plasma levels of these molecules: cluster 1 defined by 20 patients with low levels of CD163 and FABP4 and low prevalence of CV comorbidities and cluster 2 defined by 10 patients with high levels of CD163 and FABP4 and high prevalence of CVD comorbidities. Regarding cluster 2, those patients that were treated with Apremilast or combined therapy had a significant reduction of CD163 and FABP4 associated with a drop in total cholesterol, apo B, IR state and body mass index. In addition, both PDE4 inhibitor and combined treatment reduced activity disease. However, Methotrexate in monotherapy did not show a beneficial effect in PsA patients displaying higher levels of CD163, FABP4, total cholesterol and no changes in disease activity after treatment. In regard to cluster 1, the three therapy strategies reduced disease activity after 6 months. Even with low rates of comorbidities, those patients treated with Apremilast had reduced levels of total cholesterol and apolipoprotein B and body mass index after 6 months of therapy. However, no changes were observed in the treatment with Methotrexate or Methotrexate combined with Apremilast.

Conclusion: 1- CD163 and FABP4 could be considered as potential biomarkers of treatment efficacy regarding cardiometabolic comorbidities. 2- Apremilast might target metabolic alterations in PsA modulating lipid profile, insulin resistance and body mass index, decreasing the levels of surrogate CV-related molecules. 3- Apremilast treatment should be considered in PsA patients with higher rates of cardiometabolic comorbidities.

Funded by ISCIII (PI17/01316 and RIER RD16/0012/0015) co-funded with FEDER.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2956

AB0563 DISCONTINUATION OF ANTI-TNFA IN PATIENTS WITH PSORIATIC ARTHRITIS: A SINGLE-CENTER EXPERIENCE

D. Graceffa[1], V. Lora[1], A. Cristaudo[1], F. Elia[1], A. Morrone[1], C. Bonifati[1]. [1]*San Gallicano Dermatological Institute, IRCCS, Clinical Dermatology, Rome, Italy*

Background: TNF inhibitors have been largely demonstrated to be effective and reasonably safe for the treatment of psoriatic arthritis (PsA). Current EULAR guidelines recommend the use of an anti-TNF as first choice treatment in patients with PsA for whom a synthetic DMARD (usually methotrexate or leflunomide) is not efficacious or not well tolerated [1]. In a scenario where biologic treatments are easily available, and the treat to target strategy is widely accepted, a complete disease remission or at least a minimal disease activity are considered realistic goals to be achieved in a growing proportion of patients [2]. However, there remains very little research regarding anti-TNF discontinuation in patients who achieved a complete remission [3-5].

Objectives: The primary aim of this study was to measure the disease-free interval after anti-TNF discontinuation, secondary it was investigated whether the use of Power Doppler Ultrasound (PDUS) and Contrast Enhanced Ultrasound (CEUS) could improve the diagnostic accuracy in the recognition of the relapse. Finally, we wanted to characterize the clinical features of the disease recurrence.

Methods: From June 2018, 35 patients with PsA (27 males and 8 female) treated with anti-TNF, in stable remission were prospectively monitored for 1 year after treatment discontinuation. Remission was defined as documented absence of clinical and ultrasonographic signs of arthritis or enthesitis. Complete rheumatological and dermatological examinations were performed in all participants, at baseline and every 8-12 weeks: American College of Rheumatology (ACR) 66-68 joint count; Psoriasis Area Severity Index (PASI); patient pain visual analog score (VAS); patient global disease activity VAS; Health Assessment Questionnaire (HAQ); Leeds Enthesitis Index (LEI); Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Bath Ankylosing Spondylitis Functional Index (BASFI); Power Doppler Ultrasound (PDUS) of the involved joints and entheses, Contrast Enhanced Ultrasound (CEUS) of a selected joint or enthesis and laboratory inflammation tests.

Results: 31 out of the 35 enrolled patients, experienced a disease recurrence with an average disease-free interval of 27.9±21.1 weeks (Figure 1). In 3 patients the treatment was restored for a relapse of the skin psoriasis, 8 patients reported only axial symptoms of disease relapse and 20 patients had both axial and peripheral joints involvement (average DAPSA score of 23.6±11.1; average BASDAI score of 4.7±2.6; average BASFI score 4.5±2.9). In all cases the disease flare was moderate and all patients promptly regained remission after restarting the treatment. Both PDUS and CEUS were safe and reliable showing a good percentage of accordance (95,4%) in detecting synovitis and enthesitis.

Conclusion: The rate of disease relapse of PsA after anti-TNF discontinuation is relevant. However the disease-free interval was not short. Retreatment with the same anti-TNF was effective and safe.

REFERENCES:

[1] Gossec L, Baraliakos X, Kerschbaumer A, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis. 2020 Jun;79(6):700-712.
[2] Dures E, Shepperd S, Mukherjee S, et al. Treat-to-target in PsA: methods and necessity. RMD Open. 2020 Feb;6(1):e001083.
[3] Stober C, Ye W, Guruparan T, et al. Prevalence and predictors of tumour necrosis factor inhibitor persistence in psoriatic arthritis. Rheumatology (Oxford). 2018 Jan 1;57(1):158-163.
[4] Huynh DH, Boyd TA, Etzel CJ, et al. Persistence of low disease activity after tumour necrosis factor inhibitor (TNFi) discontinuation in patients with psoriatic arthritis. RMD Open. 2017 Jan 16;3(1):e000395.
[5] Ye W, Tucker LJ, Coates LC. Tapering and Discontinuation of Biologics in Patients with Psoriatic Arthritis with Low Disease Activity. Drugs. 2018 Nov;78(16):1705-1715.

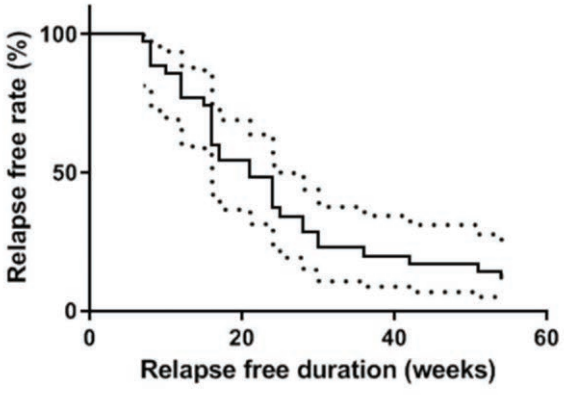


Fig.1 Relapse-free rates after discontinuing anti-TNF. Kaplan–Meier curve demonstrated the disease free interval after biologic cessation.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3002

AB0564 RHEUMATOLOGISTS' VIEWS AND EXPERIENCES IN MANAGING PSA PATIENTS BASED ON TREATING TO TARGET STRATEGY: A CROSS-SECTIONAL STUDY IN CHINA

L. Xu[1], Z. Wang[1], J. Xue[1], M. Bai[1], H. Zhong[1], Y. Su[1]. [1]*Peking University People's Hospital, Department of Rheumatology and Immunology, Beijing, China*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis with progressive, erosive destruction associated with functional impairment. Principles of treat-to-target (T2T) have been widely used in rheumatoid arthritis, which has powerfully improved patient outcomes. In 2017, the concept of T2T has proposed to apply in PsA patients. However, the awareness and implementation of evidence-based T2T treatment guidelines varies across different geographical regions of China, hospital grades, professional status and specialities.
Objectives: The study aimed to investigate Rheumatologists' views and experiences in managing PsA patients with T2T strategy in china.
Methods: A cross-sectional questionnaire survey of Rheumatologists in China from 5 August to 15 August 2020 was conducted for this study. Rheumatologists were contacted by WeChat (a Chinese cell/web app) and asked to complete a web-based questionnaire anonymously. The electronic questionnaire was sent out by the internet platform of WenJuanXing via WeChat (https://www.wjx.cn/). The questionnaire was designed to collect: (a) demographic information; (b) patient management in clinical practice for Rheumatologists; (c) familiarity and application of T2T strategy in Rheumatologists. *P* values ≤0.05 were considered significant.
Results: (1) A total of 823 rheumatologists (69.87% female, 30.13% male) provided valid answers to the questionnaire. 71.09% of the participants major in Modern Western Medicine, 28.91% major in traditional chinese medicine. A total of 75.94% worked in Grade-A Tertiary Hospital. A total of 52.73% had more than 10 years of work experience and 63.55% had High-level title. **(2)** More than half of the patients were followed up by 69% Rheumatologists in their daily practice. The proportion of follow-up patients increased powerfully in the group of Rheumatologists who major in Modern Western Medicine (P=0.014), work in Grade-A Tertiary Hospital (P<0.001), have more than 10 years of work experience (P<0.001) and High-level title (P<0.001). **(3)** 36.45% Rheumatologist thought the frequency for patient disease activity assessment was every 1 month and 53.1% was every 3 months. And 41.7% Rheumatologist prefer to use PASDAS for disease activity criteria, and only 3.6% choose MDA. **(4)** A total of 62.43% thought they were familiar with T2T strategy, and 83.6% Rheumatologists applied T2T strategy in clinical practice. Among 135 Rheumatologists who did not apply T2T strategy, 62.2% of Rheumatologists thought that the main barrier to T2T application was that they did not fully understand the strategy. The frequency of application of T2T strategy in clinical practice was significantly different between Rheumatologists who major in Modern Western Medicine (60.75%) and traditional chinese medicine (22.84%) (P=0.023).
Conclusion: In china, the management of PsA patients need to be standardized to improve patient outcomes. And the promotion of T2T strategy in PsA need to be further strengthened.
REFERENCES:
[1] Smolen JS, Schöls M, Braun J,et al. Treating axial spondyloarthritis and peripheral spondyloarthritis, especially psoriatic arthritis, to target: 2017 update of recommendations by an international task force. Ann Rheum Dis. 2018 Jan;77(1):3-17.
[2] Tucker LJ, Ye W, Coates LC. Novel Concepts in Psoriatic Arthritis Management: Can We Treat to Target? Curr Rheumatol Rep. 2018 Sep 18;20(11):71.
[3] Coates LC, Helliwell PS. Treating to target in psoriatic arthritis: how to implement in clinical practice. Ann Rheum Dis. 2016;75(4):640-643.

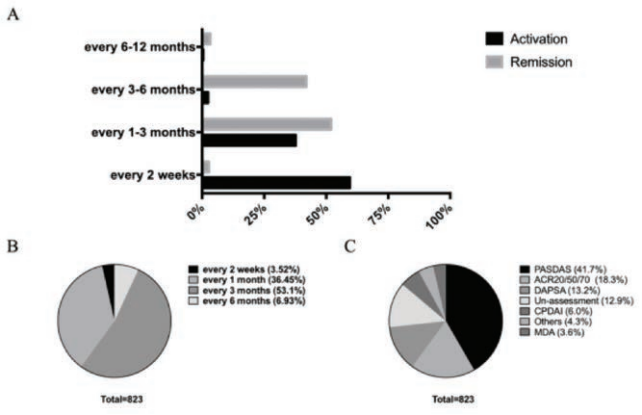


Figure 1 A. Rheumatologist priority of frequency for patient follow-up in different disease status. B. Rheumatologist priority of frequency for patient disease activity assessment in clinical practice. C. Rheumatologist priority of disease activity criteria for PsA patients.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3438

AB0565 **JAK INHIBITORS AND PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

F. Campanaro[1], A. Zaffaroni[2], A. Batticciotto[1], A. Cappelli[1], M. P. Donadini[3], A. Squizzato[3]. *[1]ASST Sette laghi, Ospedale Di Circolo - Fondazione Macchi, Rheumatology Unit, Internal Medicine Department, Varese, Italy*; *[2]University of Varese Insubria, Department of Medicine and Surgery, Varese, Italy*; *[3]University of Varese Insubria, Department of Medicine and Surgery, Research Center on Thromboembolic Diseases and Antithrombotic Therapies, Varese, Italy*

Background: Despite the therapeutic armamentarium for the treatment of psoriatic arthritis (PsA) has considerably expanded over the last thirty years, there is a huge necessity of finding effective drugs for this disease. JAK inhibitors (JAKi) are small molecules able to interfere with the JAK/STAT pathway, involved in the pathogenesis of PsA (1). Up to now Tofacitinib is the only JAKi approved by the European Medicines Agency (EMA) for the treatment of PsA but in the next few years the number of approved JAKi is expected to rise significantly.
Objectives: To assess the efficacy and safety of different JAKi for the treatment of PsA.
Methods: A systematic review of the literature was performed to identify randomized controlled trials (RCTs), by electronic search of MEDLINE and EMBASE database until October 2020. Studies were considered eligible if they met the following criteria: I) study was a RCT; II) only patients with PsA were included; III) JAKi was compared to placebo in addition to the standard of care. Two reviewers (FC and AZ) performed study selection, with disagreements solved by the opinion of an expert reviewer (AS). The outcomes were expressed as odds ratio (OR) and 95% confidence intervals (95% CI). Statistical heterogeneity was assessed with the I^2 statistic.
Results: We identified 557 potentially relevant studies. A total of 554 studies were excluded based on title and/or abstract screening. Three RCTs for a total of 947 PsA patients treated with JAKi were included (2,3,4). Two were phase III studies on the efficacy and safety of Tofacitinib (OPAL Beyond and OPAL Broaden) and one was a phase II study on Filgotinib (Equator). All three studies were judged at low risk of bias according to Cochrane criteria (5). The primary efficacy outcome in all the studies was the number of patients who achieved the response rate of the American College of Rheumatology 20 score (ACR20). The outcomes evaluation was performed at 12 week for the Filgotinib trial and at 16 week for the Tofacitinib trials. We used for the main analyses the group of patients randomized to Tofacitinib 5 mg because this is the only dosage approved by the EMA for the treatment of PsA. JAKi showed a significantly higher ACR20 response rate compared to placebo (OR 3.54, 95% CI 1.76 - 7.09, I^2 = 74%). JAKi also showed a significantly higher ACR50 response rate (OR 3.36, 95% CI 2.22 - 5.09, I^2 = 0%), ACR70 response rate (OR 2.82, 95% CI 1.67 - 4.76, I^2 = 20%), PsARC response rate (OR 2.67, 95% CI 1.26 - 5.65, I^2 = 79%), PASI75 response rate (OR 3.15, 95% CI 1.61 - 6.15, I^2 = 45%) compared to placebo. JAKi were also associated with significantly better HAQ-DI (mean difference -0.23 95% CI -0.31 - -0.14) and fatigue, measured with FACIT-F (mean difference 3.54 95% CI 2.13 - 4.94). JAKi compared to placebo were associated with a non-statistically significant different risk of serious adverse events (OR 0.56, 95% CI 0.11 - 2.91, I^2 = 38%).
Conclusion: This is the first published systematic review that performed a comprehensive and simultaneous evaluation of the efficacy and safety of JAKi for PsA in RCTs. Our analysis suggests a statistically significant benefit of JAKi, that appears to be effective and safe over placebo. The impact of these data on international clinical guidelines needs further investigation.
REFERENCES:
[1] George E Fragoulis, et al. JAK-inhibitors. New players in the field of immune-mediated diseases, beyond rheumatoid arthritis, Rheumatology, Volume 58, Issue Supplement_1, February 2019, Pages i43–i54
[2] Mease P, et al. Tofacitinib or adalimumab versus placebo for psoriatic arthritis. N Engl J Med 2017; 377: 1537-50.
[3] Gladman D, et al. Tofacitinib for psoriatic arthritis in patients with an inadequate response to TNF inhibitors. N Engl J Med 2017; 377: 1525-36.
[4] Mease P, et al. Efficacy and safety of filgotinib, a selective Janus kinase 1 inhibitor, in patients with active psoriatic arthritis (EQUATOR): results from a randomised, placebo-controlled, phase 2 trial. Lancet 2018;392:2367–77.
[5] Higgins JP, et Al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557-560

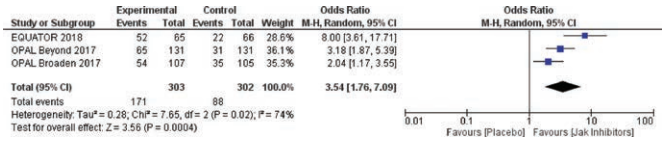


Figure 1. ACR20 response rate of Jaki over Placebo

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3671

Psoriatic arthritis - clinical aspects (other than treatment)

AB0566 CONSENSUS-BASED RECOMMENDATIONS FOR THE MANAGEMENT OF PSORIATIC ARTHRITIS IN THE KINGDOM OF SAUDI ARABIA

H. Alrayes[1], M. Alazmi[2], K. Alderaan[3], M. Alghamdi[4], N. Alghanim[5], A. Alhazmi[6], N. Alkhadhrawi[7], M. Almohideb[8], S. Attar[9], Z. A. Alzahrani[10], M. Bedaiwi[11], N. Zakaria[12], H. Halabi[13]. *[1]Prince Sultan Military Medical City, Department of Rheumatology, Riyadh, Saudi Arabia*; *[2]Prince Mohammed Medical City, Department of Rheumatology, Al Jouf, Saudi Arabia*; *[3]King Fahad Specialist Hospital, Department of Rheumatology, Dammam, Saudi Arabia*; *[4]University of Bisha, Department of Rheumatology, Bisha, Saudi Arabia*; *[5]King Saud Medical City, Department of Rheumatology, Riyadh, Saudi Arabia*; *[6]King Fahad Armed Force Hospital, Department of Rheumatology, Jeddah, Saudi Arabia*; *[7]Prince Sultan Military Medical City, Department of Family Medicine, Riyadh, Saudi Arabia*; *[8]King Saud bin Abdulaziz University for Health Sciences and King Abdulaziz Medical City, Department of Dermatology, Riyadh, Saudi Arabia*; *[9]King Abdulaziz University, Department of Rheumatology, Jeddah, Saudi Arabia*; *[10]King Abdulaziz Medical City, Department of Rheumatology, Jeddah, Saudi Arabia*; *[11]King Saud University Medical City, Department of Rheumatology, Riyadh, Saudi Arabia*; *[12]Novartis Saudi Limited, Medical - I&D, Riyadh, Saudi Arabia*; *[13]King Faisal Specialist Hospital and Research Center, Department of Rheumatology, Jeddah, Saudi Arabia*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory condition associated with psoriasis. The common clinical features of PsA include peripheral arthritis, dactylitis, enthesitis, spondylitis, skin and nail disease[1]. Considering the heterogeneous course of disease and the different patient characteristics, there is a need to standardize management of PsA patients. At present, no established guidelines are available on PsA care pathway in Saudi Arabia.
Objectives: To provide consensus-based guidance to all Saudi health care providers (HCPs) on the management of PsA patients including referral pathway, definition of remission and treat-to-target approach.
Methods: A Delphi technique was used to understand PsA patient care pathway. In first step, a targeted literature review was conducted and a survey questionnaire including 16 questions was developed to explore PsA patient journey. In second step, this questionnaire was submitted to 127 HCPs and 33 of them provided their response. In third step, a panel of 12 experts including 10 rheumatologists, 1 dermatologist and 1 general physician reviewed the available evidence along with survey results to align on final recommendations.
Results: The most common management guidelines recommended for PsA were European League against Rheumatism (EULAR, 100% agreed) and American College of Rheumatology (ACR, 100% agreed). Psoriasis Epidemiology Screening Tool (PEST) was recommended by 67% of experts as validated screening tool for PsA in dermatology clinic. The laboratory investigations included were C-reactive protein (CRP, 100%), erythrocyte sedimentation rate (ESR, 100%), complete blood count (92%), urea and creatinine (92%), liver function (92%), rheumatoid factor (56%) and X-ray of affected joints (75%). For patients with additional symptoms of back pain, X-ray of sacroiliac joints and human leukocyte antigen B27 (HLA-B27) test to be included. Only rheumatologists should recommend a magnetic resonance imaging based on the individual clinical picture. The agreement criteria for HCPs for referring patient to a rheumatologist were presence of psoriasis (100%) and one of the following features: dactylitis [100%], joint pain [100%], arthritis [100%], nail dystrophy [91%]. Patient with active arthritis should be referred to rheumatologist within 4 weeks. The referral pathway agreed by the experts for PsA patients is presented in Figure 1. Majority of experts (57%) defined clinical remission as absence of disease activity in all facets of disease assessed using the disease activity in psoriatic arthritis (DAPSA) or minimal disease activity (MDA) index. For treat-to-target, 71% of experts agreed on EULAR recommendations[2]. For remission and treat-to-target, experts identified a need for more clear definition.
Conclusion: This expert consensus aimed to provide guidance to Saudi HCPs on standardizing diagnosis and care of PsA patients. Most experts recommended PEST as validated screening tool for PsA along with laboratory investigations such as CRP, ESR, X-ray, etc. Referral to a rheumatologist should be considered for patient with presence of psoriasis and one of the other defining features for PsA. There is a need for more clear definition of remission and treat-to-target.

REFERENCES:

[1] Ogdie A, et al. Rheum Dis Clin North Am. 2015;41(4):545–568.
[2] Gossec L, et al. Ann Rheum Dis. 2020;79:700–712.

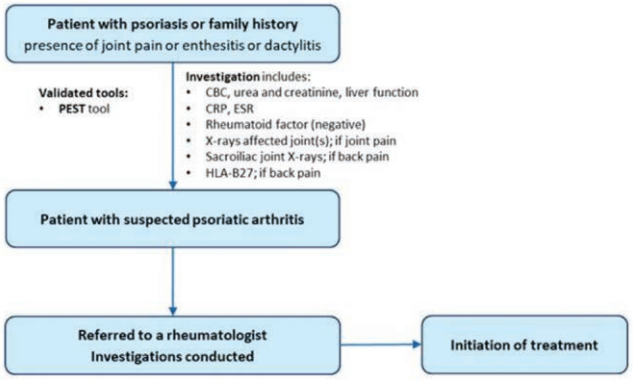


Figure 1. Referral pathway for psoriatic arthritis patientsCRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; CBC: Complete blood count; HLA-B27: Human leukocyte antigen B27; PEST: Psoriasis Epidemiology Screening Tool

Acknowledgements: This project was supported by Novartis Saudi Ltd., Saudi Arabia and the Saudi Society for Rheumatology. We would also like to thank Dr. Xenofon Baraliakos for his support.
Disclosure of Interests: Hanan Alrayes: None declared., Mansour Alazmi Speakers bureau: Pfizer, Abbvie, Khaled Alderaan: None declared., Mushabab Alghamdi: None declared., Nayef Alghanim: None declared., Ahmed Alhazmi: None declared., Nadeer Alkhadhrawi: None declared., Mohammad Almohideb Speakers bureau: Novartis, Abbvie, Celgene, Lilly, Jansen and Sanofi, Grant/research support from: Sanofi and Abbvie, Suzan Attar Speakers bureau: Lectures in symposium about different diseases in rheumatology and management, Grant/research support from: Research in recruiting patient, Zyad ahmed Alzahrani Speakers bureau: Pfizer, Novartis, MSD, Janssen, Abbvie, Lilly, Consultant of: Pfizer, Novartis, MSD, Janssen, Abbvie, Lilly, Mohamed Bedaiwi: None declared., Nancy Zakaria Employee of: Novartis, Hussein Halabi: None declared.
DOI: 10.1136/annrheumdis-2021-eular.298

AB0567 USING Q-RISK SCALE FOR CHECKING CARDIOVASCULAR RISK IN PATIENTS WITH PSORIATIC ARTHRITIS

S. Smiyan[1], A. Bilukha[1]. *[1]Ternopil State Medical University, Internal Medicine №2, Ternopil, Ukraine*

Background: Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis. In addition to skin and joint involvement, there is a growing evidence suggesting that patients with PsA also have increased risk of clinical and subclinical cardiovascular disease (CVD), mostly due to endothelial dysfunction and accelerated atherosclerosis, which are the main causes of elevated mortality rate among patients with PsA. For prevention and monitoring progression of CVD in clinical practice scale SCORE usually used, but it isn't adapted for checking in patients with autoimmune diseases and can be used only for patients after forty years old.
Objectives: To check a cardiovascular risk in patient with PsA using Q-risk scale.

Methods: In total, ninety-four patients with PsA, who fulfilled the disease criteria (CASPAR) were examined using standard diagnostic methods (including C-reactive protein, lipid profile). The QRISK-3 and SCORE scales were used to assess the 10-year risk of CVD.
Results: Intermediate (12.4 ± 0,75 %) risk of adverse cardiovascular events within the next 10 years was estimated for PsA patients and it was 7 to 8 – fold higher than the Q - score of a healthy age, sex, and ethnicity – matched subjects. Using classical SCORE, the risk was estimated as low (1,9±0.24 %). Healthy Heart Age was about 25 % higher than predicted as assessed by QRISK.
Conclusion: The Q-risk Scale considers not only classical of such risk factors as age, sex, smoking, systolic blood pressure, total cholesterol (which used SCORE) but also index of atherogenity, BMI, family history of coronary artery disease, treatment with antihypertensive drugs and glucocorticosteroids, comorbidity, systemic inflammatory disease and can be used for different age groups and ethnicity.
Q-risk scale appears to be adaptive and informative in patients with chronic inflammatory and autoimmune diseases as compared with SCORE, because it uses mostly all important etiological and trigger factors of CVD especially presence autoimmune inflammatory process in our case.

REFERENCES:

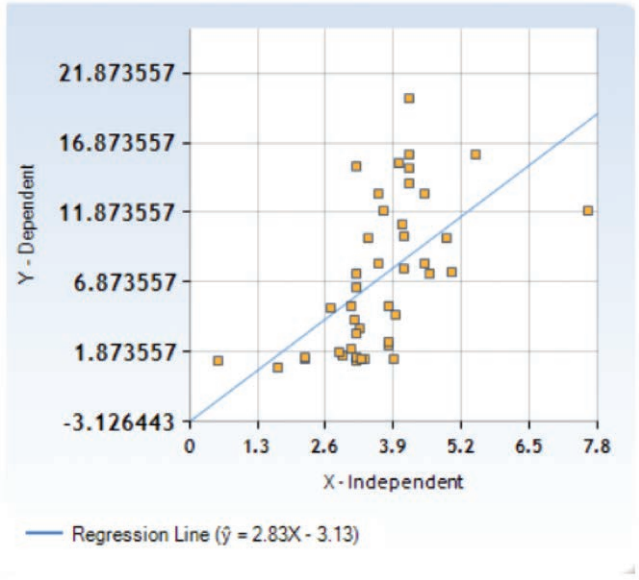
[1] Abrar Ahmed Wagan. Cardiovascular risk score in Rheumatoid Arthritis. Pak J Med Sci, Vol. 32, Issue 3, 2016, P.534-538;
[2] Frank Verhoeven, Clément Prati. Cardiovascular risk in psoriatic arthritis, a narrative review. Joint Bone Spine, Vol. 87, Issue 5, 2020, P.413-418;
[3] Julia Hippisley-Cox, Carol Coupland. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. BMJ, Vol. 23, 2017, P.357;
[4] Naveen Garg, Subrat K. Muduli. Comparison of different cardiovascular risk score calculators for cardiovascular risk prediction and guideline recommended statin uses. Indian Heart J, Vol. 69, Issue 4, 2017, P.458-463;

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.905

AB0568 CORRELATION BETWEEN SKIN AND JOINT INVOLVEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS: EXPERIENCE FROM A THIRD LEVEL HOSPITAL

C. Sieiro Santos[1], C. Moriano[1], C. Álvarez Castro[1], X. E. Larco Rojas[1], E. Diez Alvarez[1], T. Pérez Sandoval[1]. [1]*Complejo Asistencial Universitario de León, Rheumatology, León, Spain*

Background: Determining the relationship between severity of skin and joint disease is essential for better phenotyping of patients and determine whether clinical features of arthritis can associate with psoriasis.
Objectives: To characterize the relationship between skin and joint activity in patients with psoriatic arthritis (PsA) and psoriasis (PsO) at enrolment.
Methods: We performed a retrospective and descriptive study including patients diagnosed with PsA with a history of PsO. Age, sex, disease onset and duration, pattern of PsA and PsO, sites of skin and joint involvement were collected. PsA patients were evaluated at enrolment for skin activity by Psoriasis Area and Severity Index (PASI), joint activity by Disease Activity Score 28 (DAS28) for peripheral arthritis and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for axial involvement. A PASI>10% was used to define moderate-severe psoriasis (MS-P). We compared clinical characteristics of patients with PsA based on PASI score and evaluated the relationship of skin and joint activity with linear regression.
Results: A total of 50 patients were collected, 64% were women with a mean age of 57.4 ±11.9 years. Patients with MS-P had a long-standing history of PsO (16.6±7.9 vs 14.15±8.2 years, p 0.03) and arthritis (12.2±7.6 vs 10.6±7.6 years, p 0.05). PsO was diagnosed more frequently before arthritis in the group of MS-P (73% vs 42%, p 0.03). Nail (73% vs 34%, OR 4.27 (1.38-20.14), p 0.015) and hairline psoriasis (67% vs 29%, OR 5 (1.36-18.35), p 0.03) were more frequent in the group of MS-P. Polyarthritis was the most common clinical pattern (60% vs 26%, p 0.02) and peripheral arthritis, in shoulder, elbows and wrists was more associated to patients with MS-P. No significant difference regarding sex, age, arthritis onset, dactylitis, enthesitis or HLA-B27 was found. Patients with MS-P had a higher joint activity for peripheral arthritis (4.1 vs 2.44, p 0.02). The correlation between the skin and joint activity was positive and statistically significant r=0.568 (p 0.02), (graph 1).
Conclusion: Patients with PsA with MS-P associate nail and hairline psoriasis, polyarthritis, and peripheral joint involvement more often. Cutaneous disease activity is correlated with joint activity. Collaboration between dermatologists and rheumatologists is recommended for a proper assessment of psoriatic arthritis with skin involvement.



Graph 1. Correlation between skin and joint activity

Table 1. Demographic and clinical characteristics of 50 patients

	PASI <10% N = 35	PASI> 10% N=15	OR 95%IC	P value
Age	54.4 ±10.4	53.9 ±12.9	-	0.86
Female	63%	73%	0.62 (0.16-2.34)	0.53
Duration of psoriasis	14.15 ±8.2	16.6±7.9	-	0.03
Duration of arthritis	10.6 ±7.4	12.2 ±7.6	-	0.05
Psoriasis onset	42%	73%	3.67 (1.97-13.8)	0.03
Arthritis onset	17%	20%	1.21 (0.26-5.64)	1
Nail psoriasis	34%	73%	4.27 (1.38-20.14)	0.015
Hair line	29%	67%	5 (1.36-18.35)	0.03
Enthesitis	14%	13%	1.08 (0.19-6.32)	0.96
Dactylitis	20%	33%	0.5 (0.13-0.96)	0.47
HLA B27	34%	13%	3.39 (0.66-17.56)	0.18
Type of arthritis				
Axial	26%	13%	0.44 (0.08-2.36)	0.47
Peripheral	42.8%	73%	6.88 (1.77-26.76)	0.05
Both	31%	13%	0.34 (0.06-1.75)	0.29
Joint involvement				
Back	14%	20%	0.67 (0.14-3.24)	0.68
Shoulders	17%	53%	5.52 (1.44-21.14)	0.02
Elbows	5.7%	33%	8.25 (1.38-49.21)	0.02
Wrists	31%	73%	6 (1.56-23.11)	0.01
Fingers	54%	60%	1.26 (0.37-4.32)	0.77
Knees	29%	47%	2.19 (0.63-7.65)	0.33
Ankles	40%	60%	2.25 (0.65-7.73)	0.22
Toes	46%	53%	1.36 (0.4-4.56)	0.76
Articular pattern				
Polyarthritis	26%	60%	4.33 (1.2-15.61)	0.02
Asymmetric oligoarthritis	29%	27%	0.91 (0.23-3.54)	1
DIP involvement	14.3%	13.3%	0.92 (0.16-5.39)	1
Spondyloarthritis	11.4%	13.3%	1.19 (0.19-7.33)	1
Arthritis mutilans	-	-	-	-
DAS28	2.44 ±0.95	4.1±1.2	-	0.02

REFERENCES:

[1] Mease PJ, Etzel CJ, Huster WJ. Understanding the association between skin involvement and joint activity in patients with psoriatic arthritis: experience from the Corrona Registry. RMD Open. 2019 May 24;5(1):e000867. doi: 10.1136/rmdopen-2018-000867. PMID: 31245045; PMCID: PMC6560

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1226

AB0569 PSORIATIC ARTHRITIS, ALLIED DISEASES AND MORTALITY - A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 12 PATIENTS

Á. Apáthy[1], M. Bély[2]. [1]*St. Margaret Clinic, Department of Rheumatology, Budapest, Hungary*; [2]*Hospital of the Order of the Brothers of Saint John of God, Department of Pathology, Budapest, Hungary*

Background: Psoriasis (**P**) may be complicated by psoriatic arthritis (psoriatic arthropathy (**PsA**), in 15 % of psoriatic patients [1]. The risk of mortality is increased in **PsA** outpatients compared to the general population [2].
Objectives: The **aim** of this study was to determine the mortality of **PsA** or associated diseases in an in-patient autopsy population.
Methods: At the National Institute of Rheumatology **11860** patients died between 1968 and 1998; among them **12** patients with **PsA** (**females** 6. mean age of 68.17 years, range 86 – 52, onset of **PsA** 53.60, average duration of **PsA** 15.40 years; **males** 6, mean age of 62.83 years, range 82 – 33, onset of **PsA** 46.67, average duration of **PsA** 3.67 years). All patients were autopsied.
The basic disease, complication(s), and cause of death were determined by a detailed review of extensive histological material, all the available clinical and pathological reports retrospectively. From each patient a total of 50-100 tissue blocks of 16 organs were studied microscopically.
PsA was confirmed clinically according to the criteria of the **ACR** updated by Sukfa (2019) [1].
Results: The cause of death was related to **PsA** only in **one** (8.33 %) of 12 patients; a 33 year old man who died of pulmonary embolism after synovectomy. In **11** (91.66 %) of 12 **PsA** patients the cause of death was related to allied diseases namely **atherosclerosis** (**Ath**) in **9** (75 %), **tuberculosis** complicated by miliary dissemination (**TB- mTB**) in **1**(8.33 %), and **alcoholic cirrhosis** (**AC**) in **1** (8.33 %). **Ath** was complicated by hypertension (**HT**) and adult type diabetes mellitus (**DM**) in 4, was associated with **TB** in 1 and with **AC** in 1 of 9 patients; **HT** and **DM** were present in one **PsA** patient without **Ath** (Table 1).
AA amyloidosis (**AAa**) complicated **PsA** in **2** (16.66 %) of 12 **PsA** patients; in one case due to the long standing and severe inflammation of **PsA**, and in the other case the **AAa** was associated with **TB** and **mTB**.

Table 1.

	P-PsA	Basic disease (leading to death)	Complication(s)	Cause of death
1	P-PsA	Ath, TB	Adhesive pericarditis and pleuritis	Circulatory failure
2	P-PsA	Ath-HT-DM Hyperplasic prostate	Postoperative complication	Pulmonary embolism
3	P-PsA	Ath-HT-DM	Brain necrosis, Pulmonary embolism	Circulatory failure
4	P-PsA	Ath	Purulent bronchitis-Bronchopneumonia	Circulatory failure
5	P-PsA	TB-mTB	AAa, Arosion bronchial artery	Massive bronchial bleeding
6	P-PsA	Ath	AAa, Coronary artery thrombosis	Myocardial infarction
7	P-PsA		Synovectomy	Pulmonary embolism
8	P-PsA	Ath-HT-DM	Coronary artery thrombosis	Myocardial infarction
9	P-PsA	Ath	Myocardial fibrosis	Circulatory failure
10	P-PsA	Ath, Alcoholic cirrhosis	Ascites, Purulent bronchitis	Circulatory failure
11	P-PsA	Alcoholic cirrhosis, HT-DM	Ascites	Hepatorenal syndrome
12	P-PsA	Ath-HT-DM	Myocardial fibrosis	Circulatory failure

Conclusion: In our autopsy population **Ath** (with or without **HT** and **DM**) was the most important basic disease leading to circulatory failure and death of **PsA** patients. Diseases of the circulatory system were also the most common cause of death in Wong's outpatient **PsA** population as well [2].
PsA is not a mild disease, but is not a life-threatening complication of **P**, however in association with **Ath**, **HT**, **DM** or **TB** it may increase mortality, as was also found by Arumugam and McHugh (2012): 'the mortality of **PsA** may be increased in a more severe disease' [3].
REFERENCES:
[1] **Sukfa P** (2019) https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Psoriatic-Arthritis#sthash.kN0iC8N7.dpu
[2] Wong K, et al: *Arth Rheum* 1997; 40(10):1868-1872 PMID: 9336423
[3] Arumugam R, McHugh NJ: *J Rheumatol Suppl*, 2012; 89:32-5. doi: 10.3899/jrheum.120239
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1230

AB0570 BONE MINERAL DENSITY, TRABECULAR BONE SCORE AND PROXIMAL FEMUR 3D-DXA ANALYSIS IN PSORIATIC DISEASES

E. Toussirot[1], R. Winzenrieth[2], M. Desmarets[1], D. Wendling[3], F. Aubin[4], G. Dumoulin[5]. *[1]CHU de Besançon, INSERM CIC-1431, BESANCON, France*; *[2]GALGO MEDICAL, Imaging software, Barcelona, Spain*; *[3]CHU de Besançon, Rhumatologie, Besancon, France*; *[4]CHU de Besançon, Dermatologie, Besancon, France*; *[5]CHU de Besançon, Biochimie, Besancon, France*

Background: current data regarding areal bone mineral density (aBMD) in patients with psoriasis (PsO) or psoriatic arthritis (PsA) are conflicting. Results on Trabecular Bone Score (TBS) in these patients are lacking. 3D-analysis of cortical and trabecular bone from hip DXA is a new method for non-invasive bone structure assessment, providing separate assessment of the cortical layer and trabecular macrostructure.
Objectives: Case-control study (NCT02849795)
Methods: 52 PsO and 52 PsA cases (CASPAR criteria) were each paired to a control subject matched for age, sex and body mass index (BMI). aBMD measurements at (L2-4) lumbar spine (LS), femoral neck (FN) and total hip (TH) were performed using DXA, Lunar GE. TBS was calculated from antero-posterior L2-L4 BMD image using TBS iNsight V1.8 (Med-Imaps, Pessac, France). 3D-SHAPER software (version 2.10, Galgo Medical S.L, Barcelona, Spain) was used to derive a 3D analysis from the hip DXA scans.
Results: LS and TH aBMD measurements did not differ between patients with PsO or PsA and their respective controls (Table 1). Left FN BMD was higher in patients with PsO compared to controls (p = 0.028), a difference not observed on the right FN. TBS was similar in PsA patients and their controls while decreased values were observed in PsO patients (p = 0.04). In 3D analysis, none of the parameters differed between patients with PsA and their controls. For patients with PsO, no difference was found with the controls for 3D-DXA parameters from the right FN, while total hip cortical surface BMD (sBMD) of the left FN was higher in PsO compared to their controls (p = 0.037). Similarly, cortical thickness (Cth) of the intertrochanteric and shaft regions of the left FN was also higher in PsO (p = 0.032 and p = 0.033). Finally, analysis by region (neck, intertrochanteric and shaft) showed higher values for cortical sBMD from each region of the left FN in the patients with PsO (all p <0.05).
Conclusion: Our results showed comparable aBMD, TBS and 3D proximal femur parameters in patients with PsA and controls. This supports that PsA population is not at increased risk of osteoporosis. In patients with PsO, while LS bone microarchitecture seems impaired, FN displayed better cortical parameters than the controls. Although these results seem marginal, they support the fact that patients with PsO are not at high risk for osteoporosis and hip fracture.

Table 1. PsA: psoriatic arthritis; PsO: psoriasis; M: male; F: female; BMI: body mass index; PASI: psoriasis area severity index; CPDAI: composite psoriatic disease activity index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; aBMD: areal bone mineral density; LS: lumbar spine; FN: femoral neck; TH: total hip; TBS: trabecular bone score; sBMD: surface bone mineral density; Cth: cortical thickness; quantitative data are mean ± standard deviation; * and *: paired *t* test comparing patients with psoriatic arthritis or psoriasis alone to their respective controls; * p < 0.05; *** p < 0.001).**

	PsA	PsA controls	PsO	PsO controls
N	52	52	52	52
Age (years)	52.5 ± 11.7	52.8 ±11.1	50.5 ± 12.8	50.7 ± 12.8
Sex (M/F)	25/27	25/27	38/14	36/16
Menopausal women	18 (67%)	16 (59%)	5 (36%)	8 (50%)
BMI (Kg/m^2)	27.4 ± 5.9	27.7 ± 6.4	28.4 ± 5.8	28.2 ± 6.1
PASI	2.4 ± 4.1		8.4 ± 4.9	
CPDAI	7.4 ± 3.3			
ESR (mm/h)	19.8 ± 16.6 ***	6.9 ± 5.8	10.7 ± 8.8 ***	6.4 ± 6.4
CRP (mg/L)	10.5 ± 11.7 ***	3.9 ± 4.8	6.0 ± 9.0	4.7 ± 5.5
LS (L2-4) aBMD (g/cm^2)	1.27 ± 0.49	1.20 ± 0.20	1.25 ± 0.21	1.20 ± 0.18
FN aBMD (g/cm^2)				
right	0.96 ± 0.12	0.94 ± 0.14	0.98 ± 0.15	0.98 ± 0.15
left	0.96 ± 0.16		1.0 ± 0.14 *	
		0.93 ± 0.12		0.97 ± 0.13
TH aBMD (g/cm^2)	1.01 ± 0.16	1.00 ± 0.15	1.11 ± 0.22	1.06 ± 0.21
L2-L4 TBS	1.32 ± 0.11	1.32 ± 0.15	1.23 ± 0.15 *	1.30 ± 0.16
Cortical sBMD (left FN) (mg/cm^2)	169.7 ± 32.8	163.1 ± 29.7	182.0 ± 31.0 *	173.5 ± 30.3
Cth intertrochanteric (left FN) (mm)	1.91 ± 0.20	1.94 ± 0.18	2.03 ± 0.23 *	1.97 ± 0.19
Cth shaft (left FN) (mm)	2.98 ± 0.31	3.01 ± 0.28	3.19 ± 0.36 *	3.09 ± 0.29
Cortical sBMD (left FN) (mg/cm^2)				
neck	135.27 ± 26.9	129.67 ± 21.9	140.29 ± 24.2 *	134.6 ± 22.5
intertrochanteric	162.32 ± 31.1	155.34 ± 29.3	171.39 ± 29.1 *	163.1 ± 28.9
shaft cort	269.20 ± 49.0	257.12 ± 47.3	286.2 ± 47.5 *	272.7 ± 45.2

Disclosure of Interests: ERIC TOUSSIROT: None declared., Renaud Winzenrieth Employee of: GALGO MEDICAL, maxime DESMARETS: None declared., Daniel Wendling: None declared., Francois AUBIN: None declared., Gilles DUMOULIN: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1242

AB0571

RELATIONSHIP BETWEEN SERUM CALPROTECTIN LEVEL AND PRESENCE OF SUBCLINICAL ATHEROSCLEROSIS AND ARTERIAL STIFFNESS IN PATIENT WITH PSORIATIC ARTHRITIS

I. T. Cheng[1], M. LI[1], E. K. LI[1], A. P. W. Lee[1], L. S. Tam[1]. [1]*The Chinese University of Hong Kong, Medicine and Therapeutics, Hong Kong, Hong Kong (SAR)*

Background: Calprotectin is a member of S100 leukocyte. Serum calprotectin is a sensitive biomarker of disease activity in patients with psoriatic arthritis (PsA). While various CV risk score only shown modest correlation with augmented CV risk in patient with PsA, whether calprotectin could play an addition role remains uncertain.

Objectives: To elucidate the association between serum calprotectin and subclinical atherosclerosis and arterial stiffness in patient with PsA

Methods: Seventy-eight PsA patient (age: 53±11 years, 47(54%) male) without CV event was recruited into this cross-sectional study. High resolution carotid ultrasound was performed to assess the presence of carotid plaque and intima-media thickness (IMT). Arterial stiffness was measured by branchial-ankle pulse wave velocity (PWV) and augmentation index (AIx). Serum calprotectin level was measured by QUANTA Lite Calprotectin Extended Range ELISA kit from (INOVA Diagnostics, San Diego, CA, USA).

Results: 29/78 (38%) of patient had carotid plaque (CP+). Subject in CP+ group were of older age and higher inflammatory burden in terms of higher number of swollen joint and longer disease duration. The use of statins were also higher in CP+ group. Serum calprotectin level were significantly higher in CP+ group (639.2ng/ml ±378.2 in CP- group vs 911.8ng/ml ±429.4 in CP+ group, p=0.005) (Figure 1). Using multivariate logistic regression analysis, higher level of ln calprotectin were significantly associated with presence of carotid plaque (OR: 3.25, 95%CI: 1.22 to 8.69, p=0.019) after adjusting for baseline covariates. There was also significant correlation between calprotectin level and C-Reactive Protein (CRP) (r=0.237, p=0.037), mean IMT (r=0.301, p=0.021) and maximum IMT (r=0.265, p=0.043). However, no significant association were observed between calprotectin level and PWV or AIx.

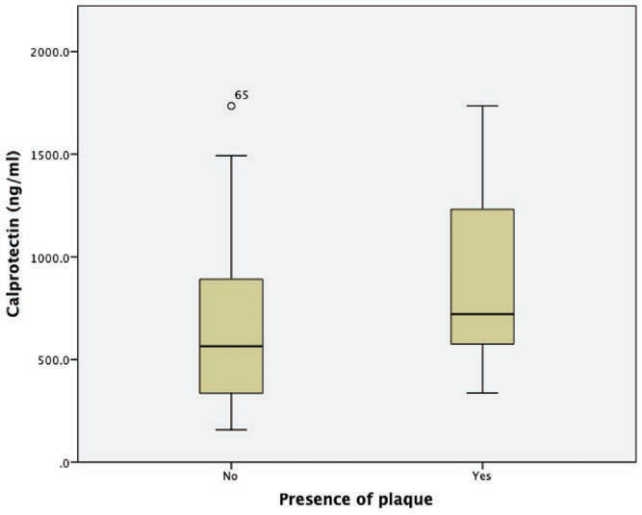


Figure 1.

Conclusion: Increased calprotectin level were associated with presence of plaque and increased IMT. Serum calprotectin may be a novel biomarker for assessing CV risk in patient with PsA.

Table 1. Multivariate analysis for factors associated with presence of carotid plaque.

	OR	95% CI	*p*
Disease duration (years)	1.10	1.02 to 1.19	0.018
Ln Calprotectin	3.25	1.22 to 8.69	0.019

*Factors included in the multivariate analysis: age, gender, disease duration, swollen joint count, hyperlipidemia, Framingham 10-year CVD risk >10%, current use of statins, and calprotectin level

Disclosure of Interests: Isaac T. Cheng: None declared., Martin Li: None declared., Edmund K. Li: None declared., Alex Pui Wai Lee: None declared., Lai-Shan Tam Grant/research support from: Grants from Norvatis, Pfizer.

DOI: 10.1136/annrheumdis-2021-eular.1249

AB0572

CARPAL TUNNEL SYNDROME IN PATIENTS WITH PSORIATIC ARTHRITIS; ULTRASONOGRAPHY AND MAGNETIC RESONANCE IMAGING FINDINGS

E. Akyildiz Tezcan[1], F. Levendoglu[2], M. S. Durmaz[3], H. Kara[4], E. Balevi Batur[2], I. Albayrak Gezer[2], M. K. Korez[5]. [1]*Cumra State Hospital, Department of Physical Medicine and Rehabilitation, KONYA, Turkey*; [2]*Selcuk University Medical Faculty, Department of Physical Medicine and Rehabilitation, KONYA, Turkey*; [3]*Selcuk University Medical Faculty, Department of Radiology, KONYA, Turkey*; [4]*Erzurum Horosan State Hospital, Department of Physical Medicine and Rehabilitation, ERZURUM, Turkey*; [5]*Selcuk University Medical Faculty, Department of Statistics, KONYA, Turkey*

Background: Carpal tunnel syndrome(CTS) is the most common form of entrapment neuropathies,caused by compression of the median nerve in the carpal tunnel at the wrist. But there is no gold standard technique for diagnosing CTS. Electrodiagnostic studies (EDS) are generally used but have some limitations. Recent years, magnetic resonance imaging(MRI) and ultrasonography(US) have facilitated the diagnosis of CTS. The median nerve cross section area(CSA) measured by US or MRI has been found to be associated with CTS[1]][2].CTS is usually idiopatic but it can be seen more in some disease. Psoriatic arthritis(PsA) occurs in up to 30% of people with psoriasis and can have serious debilitating effects on the peripheral joints, spine, tendon insertions, and fingers[3]. Because of arthritis, steroid use and flexor tenosynovitis play an important role in the pathogenesis of CTS, we think that CTS can be seen more in PsA patients.

Objectives: We aimed to investigate the CTS in PsA patients with EDS, US and MRI than compare them with healthy controls.

Methods: 68 people, including 39 PsA (according to CASPAR criteria) and 28 healthy volunteers were included in study within 1 year. EDS, US and MRI were performed within maximum 2 weeks, and measurements were made by different doctors who were blind to other measurments. EDS was started with median and ulnar nerve motor conduction study than continued with sensory conduction studies. CTS diagnose was made according to the routine laboratory standards. The CSA measurement was made from the inner border of the hyperechoic ring around median nerve by using continuous tracing method at psiform bone level. US examinations were performed with a high frequency linear transducer (4-14 MHz), MRI examinations were performed on a 3-T imaging system. The statistical analyses were performed with Statistical Package for the Social Science Program Version 22. Descriptive statistics, T tests, chi-square test, Pearson correlation test were used.

Results: No statifically significant difference was found between the groups for demographic characteristics. 12 (30.76%) of 39 PsA patients had CTS, whereas CTS was not detected in the control group(p= 0.001). US and MRI show larger CSA in PsA patients compared to the healthy control group(9,49 ± 3,00 mm^2 vs 8,30 ±1,73mm^2 p=0,005, 11,24 ± 3,41mm^2 vs 9,35 ± 1,81mm^2 p<0,001); in patients with CTS compared to others(11,63 mm^2 ± 3,25 vs 8,60 ± 2,26mm^2 p=0,002, 13,37 ± 3,37 mm^2 vs 9,90 ± 1,58mm^2 p<0,001) and in PsA patients which have CTS compared to PsA patients with normal EDS(11,63 ± 3,25 mm^2 vs 8,87 ± 2,64 mm^2 p=0,001, 13,37 ± 3,37 mm^2 vs 10,52 ±3,15 mm^2 p=0,003). When the CSA compared PsA patients which have normal EDS and healthy volunteers; US (8,87 ± 2,64 vs 8,30 ±1,73 p=0,180) and MRI (10,52 ±3,15 vs 9,35 ± 1,81 p=0,026) show larger CSA in PsA patients. But differance isn't statistically significant for US measurments. The Pearson correlation coefficient between MRI and US measurements of the CSA was 0.85 (P<0,001).

Conclusion: CTS is more common in patients with PsA. The relationship between CTS diagnosed by EDS and CSA measured by US or MRI was observed in both PsA patients and all participants. Diagnosis can be supported by US or MRI in patients who can not undergo EDS or who do not accept EDS. For PsA patients, cut off values obtained from normal people should not be used. The limitations of our study were that our CTS population was small and most of them was mild. We think that this study will be the precursor of CTS studies in PsA patients.

REFERENCES:

[1] M. S. Cartwright *et al.*, "Evidence-based guideline: Neuromuscular ultrasound for the diagnosis of carpal tunnel syndrome," *Muscle and Nerve*, vol. 46, no. 2, pp. 287–293, Aug. 2012.

[2] M. Ikeda, M. Okada, M. Toyama, T. Uemura, K. Takamatsu, and H. Nakamura, "Comparison of median nerve cross-sectional area on 3-T MRI in patients with carpal tunnel syndrome," *Orthopedics*, vol. 40, no. 1, pp. e77–e81, Jan. 2017.

[3] C. T. Ritchlin, R. A. Colbert, and D. D. Gladman, "Psoriatic Arthritis," *N. Engl. J. Med.*, vol. 376, no. 10, pp. 957–970, Mar. 2017.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1261

AB0573

DUPILUMAB-INDUCED ENTHESITIS/ARTHRITIS IN PATIENTS WITH ATOPIC DERMATITIS: A RETROSPECTIVE OBSERVATIONAL STUDY

J. Nathan[1], C. Hughes[1], S. Patel[1], L. Mathew[2], C. Smith[2], A. Pink[2], R. Woolf[2], B. Menon[1], L. B. Kirkham[1]. [1]*Guys and St Thomas' NHS Foundation Trust,*

Rheumatology, London, United Kingdom; [2]*Guy's and St Thomas' NHS Foundation Trust, St John's Institute of Dermatology, London, United Kingdom*

Background: Atopic dermatitis (AD) is a common skin condition with a prevalence of 2–10% in adults[1]. IL-4 and IL-13 play a key role in the pathogenesis. Dupilumab, a human IgG_4 monoclonal antibody binding the alpha subunit of the IL-4 receptor, blocking IL-4 and IL-13 signaling, has important efficacy in this difficult to treat disease. We first reported a musculoskeletal (MSK) adverse effect of enthesis/arthritis developing in 3 patients in 2019[2].

Objectives: To report the ongoing experience at our centre of this new clinical paradigm, incidence and patient progress including clinical presentation, imaging and management.

Methods: Clinical and radiological data was collected from electronic case records of all cases presenting with features of enthesitis/arthritis between October 2018 and January 2021.

Results: Since initiation of dupilumab at GSTT, approximately 400 adults with moderate-to-severe AD have received at least one dose. Of these, 23 patients (14 men, 9 women) had the clinical syndrome of inflammatory enthesitis/tenosynovitis/arthritis. Nine patients had both enthesitis and arthritis, 10 enthesitis, 3 enthesitis and tenosynovitis and 1 arthritis only. Four of these also reported new onset inflammatory back pain symptoms. None had a preceding history of arthritis or enthesitis. Median onset of symptoms following initiation of dupilumab was 4 months. However, onset of symptoms ranged between 2 weeks and 48 months. Imaging (US/MRI) was performed in 18 patients, 11 with Doppler US positive enthesitis confirming clinical findings. Most common sites were lateral epicondyles, achilles and patella tendons. Two patients with more disabling symptoms had MRI confirmed gluteus medius and hamstring enthesitis and arthritis. Spine and SI joint MRI in 4 patients was negative. Most patients had normal inflammatory markers except 2; CRP 117, ESR 96 and CRP 13, ESR 10. All patients had very good AD response to dupilumab, average EASI score before and after Dupilumab was 21 and 4.2 respectively. One patient developed skin manifestations of guttate psoriasis, with subsequent disabling arthritis/enthesitis. Due to the life-changing beneficial effect of dupilumab therapy most patients did not want to stop therapy. We used NSAID therapy, etoricoxib/celecoxib/naproxen for symptom relief which was usually partly effective allowing continuation of dupilumab treatment in most. Five patients with severe MSK symptoms stopped Dupilumab completely. Some patients temporarily paused therapy but re-started as their AD became worse, often changing from the usual 2 weekly to 4 weekly dosing. Most patients continuing dupilumab had persistent MSK symptoms. Four patients who stopped dupilumab were treated with baricitinib, which has potential efficacy for both MSK symptoms and AD. Two did not tolerate it and remained on NSAID therapy.

Conclusion: These data further characterize a new syndrome of enthesitis and/or arthritis induced by Dupilumab. In those with mild MSK symptoms use of NSAIDs allows continuation of full-dose dupilumab, in moderate cases reducing dupilumab dose frequency plus NSAID therapy maintains function. Most patients had on-going MSK symptoms. In more severe cases JAKi therapy may be an effective strategy. Our initial hypothesis that inhibition of IL-4/13 by dupilumab triggers an IL-17/23/TNF-mediated inflammatory MSK syndrome in some patients is supported by a recent in vitro study[3].

REFERENCES:

[1] Beck L et al. Dupilumab Treatment in Adults with Moderate-to-Severe Atopic Dermatitis. July 10, 2014. N Engl J Med 2014; 371:130-139

[2]Willsmore ZN *et al.* Development of inflammatory arthritis and enthesitis in patients on dupilumab: a case series. Br J Dermatol 2019; **0**. doi:10.1111/bjd.18031.

[3] Bridegwood C et al. Regulation of entheseal IL-23 expression by IL-4 and IL-13 as an explanation for arthropathy development under dupilumab therapy. Rheumatology (Oxford). 2020 Nov 30:keaa568. doi: 10.1093/rheumatology/keaa568

Disclosure of Interests: Joseph Nathan: None declared., Catherine Hughes Speakers bureau: Presented for Abbvie, Samir Patel: None declared., Libin Mathew: None declared., Catherine Smith Grant/research support from: Grants/research support; Professor Smith is a PI/CoPI on a number of commercially supported studie (Abbvie, Janssen, Leo, Sanofi)., Andrew Pink Paid instructor for: Speaker or advisor to Lilly, Abbvie, Sanofi, Leo, Almirall, Novartis, Janssen, UCB, Galderma, BMS, La-Roche Posay, Richard Woolf: None declared., Bina Menon Speakers bureau: Presented for Abbvie, L Bruce Kirkham Grant/research support from: Professor Kirkham has received honoraria and/or research funding from AbbVie, Eli Lilly, Gilead, Janssen, Novartis, Pfizer and UCB.

DOI: 10.1136/annrheumdis-2021-eular.1363

AB0574 UVEITIS IN 406 PATIENTS WITH PSORIATIC ARTHRITIS. STUDY FROM A SINGLE UNIVERSITARY CENTER

A. De Vicente-Delmás[1], L. Sanchez-Bilbao[2], D. Martínez-López[2], I. González-Mazón[2], V. Calvo-Río[2], N. Barroso García[1], N. Palmou-Fontana[2], M. A. González-Gay[2], R. Blanco[2]. [1]*Hospital Universitario Puerta del Mar, Rheumatology, Cádiz, Spain*; [2]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*

Background: Uveitis is an extraarticular manifestation of psoriatic arthritis (PsA) and it has been described as the most frequent ocular manifestation in PsA. Uveitis in PsA has been described to be more likely insidious in onset, continuous, posterior, and active bilaterally compared with uveitis in patients with Spondyloarthritis *(Paiva ES, et al. Ann Rheum Dis. 2000;59: 67-7)*. Anti-TNF agents, especially monoclonal antibodies have been effective in prevention and treatment of refractory non-infectious uveitis.

Objectives: Our aim was to assess **a)** epidemiology and clinical features of uveitis associated to PsA, **b)** to compare patients who developed uveitis and those who did not and **c)** its relationship with biological treatment used in PsA.

Methods: We conducted a cross-sectional study of 406 patients with PsA from a single reference University Hospital with: **a)** PsA classified by CASPAR criteria and, **b)** diagnosis of uveitis by expert ophthalmologists. Demographic features, clinical findings, complementary tests, occurrence of other extraarticular manifestations and treatment were recorded.

Results: We studied 406 (202 women/204 men) patients with PsA, mean age of 46.3±12.3 years.

Uveitis was observed in 20 (12 women/8 men) of 406 patients (prevalence 4.9%); mean age of 43.1±14.5 years. Uveitis was most frequently anterior (80%), unilateral (80%), of acute onset (100%), and recurrent (50%).

In the comparative study between patients who developed uveitis and who did not (Table 1), in patients with uveitis was more frequent the presence of HLA-B27 positive (45%), sacroiliitis in MRI (25%), ocular surface pathology (10%), and higher mean PsAID score (4.8±2.5).

Ten (50%) patients with PsA related uveitis received biological therapy, 12 (60%) of the treatments were anti-TNF monoclonal antibodies and 1 (5%) was etanercept. The 2 (10%) remaining therapies were other biological therapy non anti-TNF (Figure 1).

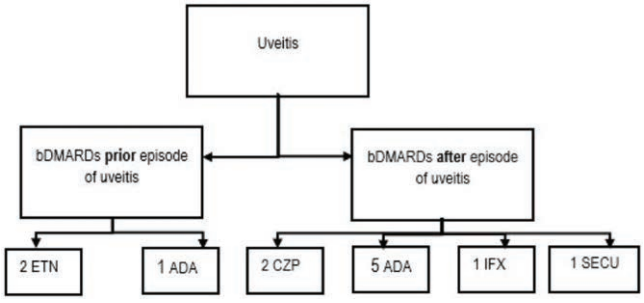


Figure 1. Biologic immunosuppressive drugs in PsA patients related uveitis.

Conclusion: Uveitis was observed in 4.9% of patients with PsA.Most of the PsA related uveitis had an acute onset with anterior and unilateral pattern. HLA-B27 positive, presence of sacroiliitis on MRI and ocular surface pathology were more frequent in patients who developed uveitis. PsAID score is higher in patients with uveitis.

Table 1. General features of 406 patients with PsA. Comparison between with and without uveitis.

	Overall (n= 406)	Uveitis (n= 20)	Non uveitis (n= 386)	p
Main general features				
Age, years, mean±SD	46.3±12.3	43.1±14.5	46.5±12.2	0.225
Sex, women/men, N (% of women)	202/204(49.8)	12/8 (60)	218/168 (56.5)	0.757
HLAB-27 positive, N (%)	38(9.4)	9 (45)	29 (7.5)	**0.000***
PsA pattern				
Axial pattern, N (%)	48 (11.8)	4 (20)	44 (11.4)	0.277
Peripheral pattern, N (%)	236 (58.1)	12 (60)	224 (58)	0.862
Mixed pattern, N (%)	122 (30.1)	4 (20)	118 (30.6)	0.315
PsA Scores				
PsAID, mean±SD	3±2.4	4.8±2.5	2±2.6	**0.003***
Radiological features				
Sacroiliitis on MRI, N (%)	37 (9.1)	5 (25)	32 (8.3)	**0.027***
Other extraarticular manifestations				
Inflammatory bowel disease, N (%)	21 (5.2)	2 (10)	19 (4.9)	0.277
Ocular surface pathology, N (%)	5 (1.2)	2 (10)	3 (0.8)	**0.021***
Biologic treatments				
bDMARDs, N (%)	280 (68.9)	15 (75)	265 (68.7)	0.550
Etanercept	31 (7.6)	1 (5)	30 (7.8)	0.999
TNFi monoclonal antibodies	160 (39.4)	12 (60)	148 (38.3)	0.053

Disclosure of Interests: A. De Vicente-Delmás: None declared., Lara Sanchez-Bilbao: None declared., David Martínez-López: None declared., Iñigo González-Mazón: None declared., Vanesa Calvo-Río Speakers bureau: AbbVie, Lilly, Celgene, Grünenthal and UCB Pharma, Grant/research support from: MSD and Roche, Nuria Barroso García: None declared., Natalia Palmou-Fontana Speakers bureau: Celgene, AbbVie, Lilly, Miguel A González-Gay Speakers bureau: Pfizer, Abbvie, MSD, Grant/research support from: Pfizer, Abbvie, MSD, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD, Grant/research support from: AbbVie, MSD, and Roche.

DOI: 10.1136/annrheumdis-2021-eular.1873

AB0575 FACTORS ASSOCIATED WITH PSORIATIC ARTHRITIS ACTIVITY IN CLINICAL PRACTICE

Y. Korsakova[1], E. Loginova[1], T. Korotaeva[1], E. Gubar[1], S. Glukhova[2], E. Vasilenko[3], A. Vasilenko[4], N. Kuznetsova[5], I. Patrikeeva[6], E. Nasonov[1,7]on behalf of RU-PsART study group. *[1]V.A. Nasonova Research Institute of Rheumatology, Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*; *[2]V.A. Nasonova Research Institute of Rheumatology, Medical and Social Problems in Rheumatology, Moscow, Russian Federation*; *[3]North-Western State Medical University named after I. I. Mechnikov, Therapy, Rheumatology, Examination of Temporary Disability and Quality of Medical Care named after E.E.Eichwald, Saint Petersburg, Russian Federation*; *[4]Novgorod Regional Clinical Hospital, rheumatology, Veliky Novgorod, Russian Federation*; *[5]Municipal Autonomous Institution, "City Clinical Hospital No. 40", Yekaterinburg, Russian Federation*; *[6]Tyumen Regional Clinical Hospital No.1, Tyumen Regional Clinical Hospital No.1, Tyumen, Russian Federation*; *[7]I.M. Sechenov First Moscow State Medical University, Ministry of Health of Russia, I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Background: Psoriatic Arthritis (PsA) is a multifaceted disease with various clinical domains. A number of composite indices has been developed recently [1, 2]. DAPSA (**D**isease **A**ctivity in **PS**oriatic **A**rthritis) is the valid instrument for assessment of PsA activity focused on peripheral arthritis. But other factors can influence on PsA activity and haven't studied yet.

Objectives: to identify factors that are associated with PsA activity based on the data from RU-PsART cohort.

Methods: 117 (M/F=63(54%)/54(46%)) patients (pts) with active PsA fulfilling the CASPAR criteria mean age 44.3 ± 10.9 yrs, mean DAPSA 37.8±21.4, mean PsA duration 73.4±78.4 mo, mean PsO duration 213.4±152.5 mo, were included. Data was collected from 43 rheumatology centers of the Russian Federation. All pts underwent standard clinical examination of PsA activity at enrollment. DAPSA, ESR (mm/h), CRP (mg/L), dactylitis, enthesitis by LEI plus Plantar Fascia, BSA (%), HAQ-DI and fatigue by Fatigue Scale (V.4) FACIT (Functional Assessment of Chronic Illness Therapy), BMI (kg/m^2) were evaluated. DAPSA > 28 indicate high activity. Multi-dimensional step-by-step discriminant analysis was used to identify a group of features that are associated with high PsA activity by DAPSA. M±SD, %, OR 95% (CI) were performed.

Results: The following features proved to be the most informative: LEI (p=0.739), tenderness of the Plantar Fascia (p=0.003), age (p=0.0004), FACIT (p=0.092), PsA duration >2 yrs (p=0.013), BSA>3% (p=0.021), Nail PsO (p=0.092), BMI (kg/m^2) (p=0.22). The area under the ROC-curve (AUC) 0.768, 95% CI (0.624-0.913). Sensitivity/ Specificity of model 77.0%/ 69% accordingly (Figure 1).

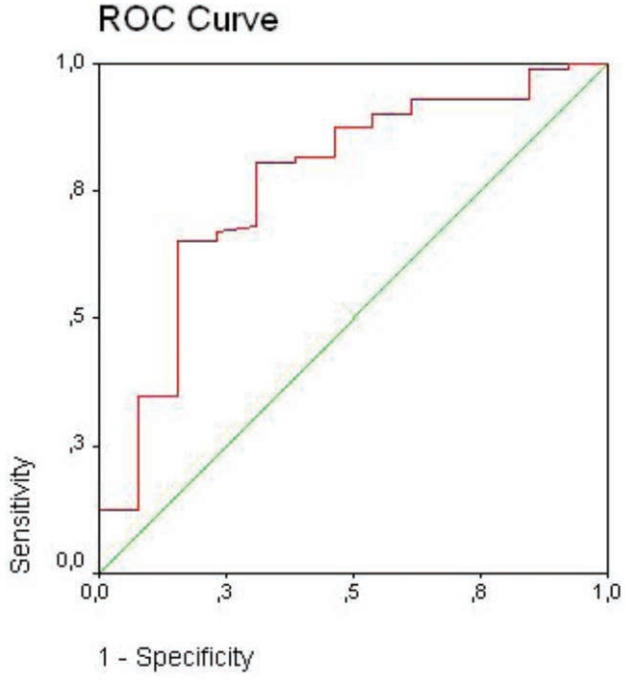


Figure 1 ROC analysis of the Sensitivity and Specificity of the model.

Conclusion: Weight, enthesitis, skin and nail PsO severity, fatigue and PsA duration >2 yrs are associated with high PsA activity as well as articular symptoms. New combination indices based on these features should be developed and validated in clinical practice.

REFERENCES:

[1] Helliwell P, et al. The development of candidate composite disease activity and responder indices for psoriatic arthritis (GRACE project). Ann Rheum Dis. 2013; 72: 986-91. doi: 10.1136/annrheumdis-2012-201341.

[2] Salaffi F, et al. Disease Activity in Psoriatic Arthritis: Comparison of the Discriminative Capacity and Construct Validity of Six Composite Indices in a Real World. BoiMed Res Int 2014; 2014:52805 http://dx.doi.org/10.1155/2014/528105

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2151

AB0576 BONE EROSION IN PSORIATIC ARTHRITIS ASSOCIATED WITH PSORIASIS DURATION, SKIN, NAIL AND JOINT DISEASE SEVERITY

M. Chamurlieva[1], E. Loginova[1], T. Korotaeva[1], Y. Korsakova[1], E. Gubar[1], S. Glukhova[1], E. Nasonov[1,2], N. Kuznetsova[3], I. Umnova[4], V. Sorotskaya[5], I. Patrikeeva[6], I. Shchendrigin[7]. *[1]V.A.Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*; *[2]I.M.Sechenov First Moscow State Medical University (Sechenov University), Ministry of Health of Russia, Rheumatology, Moscow, Russian Federation*; *[3]Municipal Autonomous Institution "City Clinical Hospital No. 40", Rheumatology, Yekaterinburg, Russian Federation*; *[4]Omsk region "Regional clinical hospital", Rheumatology, Omsk, Russian Federation*; *[5]Medical Institute of the Tula State University, Rheumatology, Moscow, Russian Federation*; *[6]Tyumen Regional Clinical Hospital №1, Rheumatology, Tyumen, Russian Federation*; *[7]Center of responsible rheumatology "Induktsia", Rheumatology, Stavropol, Russian Federation*

Background: Psoriatic arthritis (PsA) is heterogeneous in its clinical presentation and disease course, but many patients (pts) develop a destructive form of arthritis. Psoriasis (PsO) precedes arthritis by an average of 7 years. [1]. Theory of transition from PsO to PsA has been proposed recently [2]. But association between skin disease severity and joint disease are still unclear.

Objectives: to evaluate association between bone erosion, PsO duration, skin and nail disease severity in PsA pts based on data from clinical practice (RU-PsART cohort).

Methods: 737 (M/F=350/387) PsA pts fulfilling the CASPAR criteria were included. Mean age 47.4±12.7 years (yrs), PsA duration 55[17;120] mos., PsO duration 165[74.5;292] mos., mean DAPSA 23.3[14;36.9] mos., HAQ-DI - 0.98 [0.5;1.38], CRP - 7.4 [2.1;18] mg/l. All pts underwent standard clinical examination (tender joins count (TJC)/68, swelling joints count (SJC)/66, CRP (mg/l), DAPSA, dactylitis, enthesitis by LEI + Plantar Facia (PF), HAQ-DI. Mild disease was defined as body surface area (BSA)≤10%, moderate to severe as BSA>10%. The presence/absent of nail PsO was evaluated. X-ray of feet and hand were done in 622 out of 737 pts. The one-factor model of logistic regression was used to identify a group of features that are associated with achievement MDA. M±SD, Me [Q25; Q75], Min-Max, %, t-test, Pierson-χ2, Manna-Whitney tests, ORs with 95% CI were performed. All p<0.05 were considered to indicate statistical significance.

Results: PsO precedes of PsA by an average of 9.2 years. BSA≤10% was found in 615 out of 672 pts (91.5%), BSA>10% - in 57 out of 672 pts (8.5%). Nail PsO were seen in 230 out of 737 (31.2%). Bone erosion was found in 237 out of 622 of pts (38.1%). Among these pts nail PsO were seen in 67 out of 237 pts (28.3%). Enthesitis found in 236 out of 737 pts (42.1%), dactylitis – in 197 out 731 pts (27%), axial PsA – in 315 out of 731 pts (43.1%). Bone erosion significantly associated with PsO duration more than 5 yrs., skin and nail PsO severity, high PsA activity by DAPSA, axial manifestation and duration of PsA > 36 mos. (Figure 1).

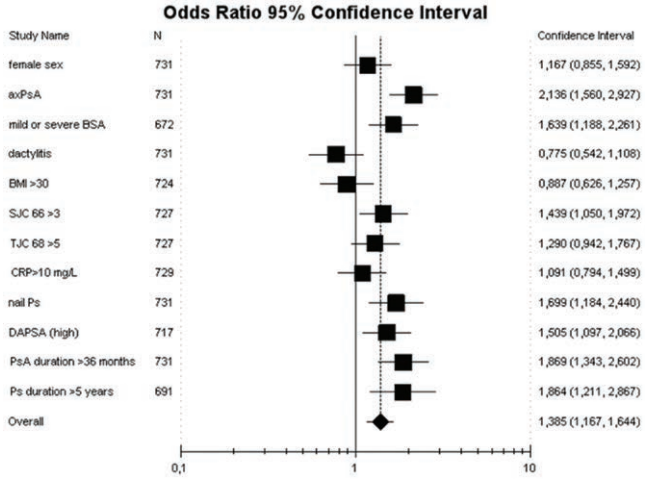


Figure 1 Forest plot of factors associated with bone erosion in PsA pts.

Conclusion: In our cohort the majority of PsA pts had mild PsO preceded PsA on average of 9.2 yrs. Bone erosion was found in 30% of PsA pts which associated with PsO duration, skin and nail disease severity as well as with PsA activity. Early diagnosis and therapeutic intervention within a "window of opportunity" are very important for improving outcomes and prevent structural damage in PsA.

REFERENCES:

[1] Tillett W, et al. Interval between onset of psoriasis and psoriatic arthritis comparing the UK Clinical Practice Research Datalink with a hospital-based cohort. Rheumatol. 2017; 56, 2109–2113

[2] Scher JU, et al. Preventing psoriatic arthritis: focusing on patients with psoriasis at increased risk of transition. Nat Rev Rheumatol. 2019;15(3):153-166. doi: 10.1038/s41584-019-0175-0. PMID: 30742092.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2796

AB0577 METABOLIC SYNDROME IN PSORIATIC ARTHRITIS SEEMS ASSOCIATED TO INFLAMMATORY STATUS OF THE DISEASE

C. L. Iñíguez[1], J. A. Mosquera Martínez[2], L. Fernández-Dominguez[3], F. Maceiras-Pan[4], C. García-Porrúa[1], J. L. Guerra-Vázquez[5], V. Quevedo Vila[6], M. Caeiro-Aguado[7], J. Lorenzo-Alvarez[8], J. A. Pinto Tasende[7,9]on behalf of GIGAPs. *[1]Hospital Lucus Augusti, Rheumatology, Lugo, Spain*; *[2]Hospital Montecelo (Pontevedra), Rheumatology, Pontevedra, Spain*; *[3]Complexo Hospitalario Universitario de Ourense, Rheumatology, Ourense, Spain*; *[4]Hospital do Meixoeiro, Rheumatology, Vigo, Spain*; *[5]Hospital Arquitecto Marcide, Rheumatology, Ferrol, Spain*; *[6]Hospital Comarcal de Monforte de Lemos, Rheumatology, Monforte de Lemos, Spain*; *[7]Hospital Universitario da Coruña, Rheumatology, La Coruña, Spain*; *[8]Hospital Universitario da Coruña, Internal Medicine, La Coruña, Spain*; *[9]INIBIC, Rheumatology, A Coruña, Spain*

Background: Evidence suggests that inflammation plays a causal role in the development of Metabolic Syndrome (MetS) and elevated peripheral levels of proinflammatory mediators, such as C-reactive protein (CRP) confering cardiovascular and metabolic risk.

Objectives: The objective of this study was to evaluate Metabolic Syndrome among patients with PsA naïve to biologics and to evaluate its association with inflammatory activity status previous start them.

Methods: We performed a retrospective cross-sectional study of a cohort of patients ≥18 years of age, all patients with a diagnosis of PsA (CASPAR criteria), included in the Sueiro Cohort. Patients were managed according to a standard protocol adopted at the Rheumatology outpatient clinic of six hospitals and they were patients on follow-up for at least 6 months. Collected variables included age and gender, blood biochemistry, blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), HLA-B27 and rheumatoid factor, glucocorticoid, NSAID and conventional or biologic DMARD, smoking habit, hyperuricemia, type 2 diabetes mellitus, obesity (BMI kg/m2). MetS was defined by a combination of abdominal obesity, impaired fasting glucose, atherogenic dyslipidemia, and elevated blood pressure. Status of disease activity was supported by tender and swollen joint counts (TJC68 and SJC66) from patients who were going to start treatment with biologics and Patient-reported outcome measure were collected with Patient Global Assessment (0-10 cm) and Patient Pain Assessment (0-10 cm). Remission and low disease activity status was obtained by DAPSA score and its defined cut-off. Tests were two-tailed with a significance level of 5%. Data were analyzed using SPSS V21.0 statistical software (IBM Corp. NY, USA).

Results: A total of 416 were included in the study: 222 PsA patients treated with csDMARD kept in remission or low disease activity and 194 patients needed to be treated with bDMARD. The mean age of the patients was 53.0 years (SD: 11.8). Two hundred and twenty-eight were males (56.2%).

Fifty-six patients had MetS (13.8%) and it was more frequent in patients who were in clinical activity and they needed biologics (17.9% vs 10.4%, p 0.028) with mean (SD) of DAPSA of 16.7 (11.1). Patients starting treatment with biologics and with MetS had more proportion of patients older than 50 years (24.2 % vs 8.3%, p 0.006) and CRP >5 mgr/L (71.4% vs 52.6%, p 0.042) and DAPSA had higher values than in patients without MetS (18.6 vs 16.2) but there were not significant statistical differences. Binary regression analysis showed increased risk of MetS for age > 50 years old (OR 3.287 [95%CI: 1.258-8.591], p 0.015) and CRP > 5 mgr/L (OR 2.684 [95%CI: 1.141-6.313], p 0.024) but not for gender (OR 2.136 [95%CI: 0.932-4.893], p 0.073) neither for DAPSA>14 (OR 1.539 [95%CI: 0.695-3.409], p 0.288).

Conclusion: Patients with PsA active despite csDMARD had more prevalence of MetS and this was associated with those patients over 50 years old and CRP higher than normal values. DAPSA was higher in patients with MetS but without reaching significant statistical difference.

REFERENCES:

[1] Lee YH, Pratley RE. The evolving role of inflammation in obesity and the metabolic syndrome. Current Diabetes Reports. 2005;5:70–75

Acknowledgements: I have acknowledgements to SOGARE.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2947

AB0578 SUBCLINICAL ENTHESITIS IN PSORIASIS PATIENTS AS PREDICTOR OF ARTHRITIS (EPESCA STUDY): PRELIMINARY RESULTS

E. Di Donato[1], A. Becciolini[1], S. DI Nuzzo[2], N. Chernyschova[3], C. Commisso[4], S. Lamorte[4], M. Brusasco[2], E. Pierobon[2], D. Santilli[1], G. Lucchini[1], M. Riva[1], N. Sverzellati[4], F. Mozzani[1], A. Ariani[1]. *[1]Azienda Ospedaliero-Universitaria di Parma, Internal Medicine and Rheumatology Unit, Parma, Italy*; *[2]University of Parma, Department of Medicine and Surgery, Parma, Italy*; *[3]Azienda Ospedaliero-Universitaria, Section of Radiology, Parma, Italy*; *[4]University of Parma, Department of Radiological Sciences, Parma, Italy*

Background: Enthesitis is one of the typical pathological signs of spondyloarthritis such as psoriatic arthritis (PsA) and it seems to be the *Primum movens* of the disease. Clinical assessment of enthesitis showed to be less sensitive, compared to ultrasound (US) evaluation, in identifying enthesitis in patients with PsA [1].

OMERACT defined US enthesitis as: "hypoechoic and/or thickened insertion of the tendon close to the bone (within 2 mm from the bony cortex), which exhibits Doppler signal if active and that may show erosions, enthesophytes/calcifications as a sign of structural damage" [3]

The reported prevalence of subclinical enthesitis in psoriasis (PsO) patients in different countries ranges between 7% and 20% [2].

Objectives: The main objective of this study was to estimate, by US evaluation, the prevalence of subclinical enthesitis in PsO patients without any clinical signs of enthesitis. Secondary objectives were to analyze differences, in terms of age, sex, BMI, PsO onset and diagnosis, among patients with enthesitis (active or not active), enthesopathy and without any alteration of enthesis.

According to the OMERACT definition of ultrasound enthesitis, patients were divided into 4 groups: patients with active enthesitis (AE) defined as the presence of power-Doppler signal in a hypoechoic and/or thickened insertion of the tendon close to the bone; patient with enthesitis (En) defined as hypoechoic and/or thickened insertion of the tendon close to the bone without PD signal; patients with enthesopathy (Ep) defined as the presence of structural damage (erosions, enthesophytes/calcifications); patients without any alteration of enthesis (WE).

Methods: Patients with at least 18 years and a diagnosis of PsO made by a Dermatologist were included. Exclusion criteria were the presence of clinical symptoms or signs of articular or entheseal involvement, diagnosis of arthritis and therapy with bDMARDs or tsDMARDs.

All patients underwent US examination on grey scale and Power Doppler (PD) ultrasonography of 6 sites (Achilles, quadriceps, distal and proximal patellar, plantar fascia and triceps enthesis) bilaterally. Ultrasound was performed by an experienced sonographer, using a Logiq P9 equipped with 6-12 MHz broad band linear transducer. Data were reported as frequencies and median with interquartile range. To check differences among these four groups, we used chi-square test or Kruskall-Wallis test. P-value ≤ 0.05 is considered statistically significant.

Results: We enrolled 124 consecutive psoriasis patients (47 [37.9%] female) with median age 57.7 (45.3-66.5) years, median disease duration 20.4 (10.1-30.8) years, median BMI 27 [24-29]. Patients with AE, En, Ep were 20.2% (25/124), 49.2% (61/124) and 18.5% (23/124), respectively.

Patients WE (12.1%, 15/124) showed significantly lower BMI, younger age and shorter diagnostic delay compared to the other patients.

All signs of enthesopathy/enthesitis were more frequently observed at Achilles (33.1%, 41/124), triceps (23.4%, 29/124), quadriceps (20.2%, 25/124), distal patellar (18.5%, 23/124) and proximal patellar (4.8%, 6/124) enthesis.

Conclusion: Subclinical enthesitis is quite common in PsO patients, and about 20% showed active enthesitis. The enthesopathy seems to be more frequent in patients with increased delay in PsO diagnosis, older age and higher BMI.

REFERENCES:

[1] Bandinelli F. et al. Ultrasound detects occult entheseal involvement in early psoriatic arthritis independently of clinical features and psoriasis severity. Clin Exp Rheumatology. Mar-Apr 2013;31(2):219-24.

[2] Zuliani F. et al. Ultrasonographic detection of subclinical enthesitis and synovitis: a possible stratification of psoriatic patients without clinical musculoskeletal involvement. Clin Exp Rheumatol Jul-Aug 2019;37(4):593-599.

[3] Balint P. V. et al. Reliability of a consensus-based ultrasound definition and scoring for enthesitis in spondyloarthritis and psoriatic arthritis: an OMERACT US initiative. Ann Rheum Dis 2018 Dec;77(12):1730-1735.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3149

AB0579

INSTRUMENTS FOR SCREENING PSORIATIC ARTHRITIS AMONG PATIENTS WITH PSORIASIS: A SYSTEMATIC LITERATURE REVIEW

G. Can[1], G. Ayan[2], A. Ozdede[3], M. Bektaş[4], N. Akdogan[5], B. Yalici-Armagan[5], E. Oksum Solak[6], S. Yazici[7], U. Kalyoncu[2], E. Ozsoy Adisen[8], N. Atakan[5], E. Bulbul Baskan[7], M. Borlu[6], B. Engin[9], V. Hamuryudan[3], M. Inanc[4], S. Kiraz[2], F. Onen[1], S. Ugurlu[3], S. Yayli[10], G. Hatemi[3]. [1]*Dokuz Eylul University, Medical Faculty, Department of Internal Medicine Division of Rheumatology, Izmir, Turkey*; [2]*Hacettepe University Medical Faculty, Department of Internal Medicine Division of Rheumatology, Ankara, Turkey*; [3]*Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine Division of Rheumatology, ISTANBUL, Turkey*; [4]*Istanbul University Istanbul Medical Faculty, Department of Internal Medicine Division of Rheumatology, ISTANBUL, Turkey*; [5]*Hacettepe University Medical Faculty, Department of Dermatology, ANKARA, Turkey*; [6]*Erciyes University Medical Faculty, Department of Dermatology, Kayseri, Turkey*; [7]*Uludag University Medical Faculty, Department of Dermatology, Bursa, Turkey*; [8]*Gazi University Gazi Medical Faculty, Department of Dermatology, ANKARA, Turkey*; [9]*Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Dermatology, ISTANBUL, Turkey*; [10]*Karadeniz Technical University, Medical Faculty, Department of Dermatology, Trabzon, Turkey*

Background: Timely diagnosis is essential for the optimal management of psoriatic arthritis (PsA). Several instruments have been developed for screening PsA among patients with psoriasis. However, a delay in diagnosis is still frequently reported, possibly due to the lack of a wide use of these instruments.

Objectives: We aimed to identify and compare the reported performance of these instruments with special emphasis on the PsA phenotypes.

Methods: We conducted a systematic literature search on PubMed until 15 August 2020 using the keyword 'psoriatic arthritis'. Two independent reviewers identified all studies published in English, that report on the validation, psychometric evaluation or use of an instrument for screening PsA. Any disagreements were resolved by the third investigator. Data on sensitivity, specificity, positive (PPV) and negative (NPV) predictive values were extracted or calculated for each instrument. Additionally, instruments were assessed for their performance in patients with different disease phenotypes.

Results: A total of 10754 references were screened, and 42 were identified that reported on 15 different screening instruments. Psoriatic Arthritis Screening and Evaluation (PASE), Psoriasis Epidemiology Screening Tool (PEST), Early Arthritis for Psoriatic Patients questionnaire (EARP) were the most commonly used instruments. There was important variability across studies regarding the sensitivity, specificity, PPV and NPV of these instruments based on the cut-offs for positivity, setting, patient population and disease phenotypes (Table 1). Specificity was higher when patients with a previous diagnosis of other rheumatic diseases were excluded. Lower sensitivity was reported among patients with shorter disease duration and when patients with a prior diagnosis of PsA were excluded from the study, whereas higher sensitivity was reported among patients with prior NSAID use. Screening tools showed differences in sensitivity in different domains (Figure 1).

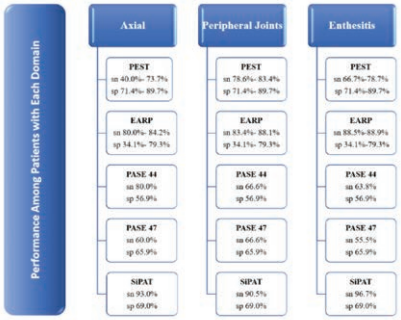


Figure: Range of sensitivity (sn) and specificity (sp) among patients with PEST and EARP, sensitivity and specificity value among patient with PASE 44, PASE 47, SiPAS. ***PEST**:Psoriasis Epidemiology Screening Tool, **EARP**: Early Arthritis for Psoriatic Patients, **PASE 44**:* Psoriatic Arthritis Screening and Evaluation 44, ***PASE 47**:* Psoriatic Arthritis Screening and Evaluation-47, ***SiPAT**: Siriraj Psoriatic Arthritis Screening Tool*

Figure 1. Performance Among Patients with Each Domain

Conclusion: This systematic literature review revealed wide variability in the diagnostic estimates of currently available questionnaire-based screening instruments for identifying PsA among psoriasis patients, depending on study populations and disease phenotypes. There is an unmet need for a screening instrument with a better performance in all disease domains.

Table 1. Diagnostic estimates of screening tools in different studies

Instrument	Number of studies	Sensitivity %	Specificity %	PPV %	NPV %
PASE	18	24-91	38-95	18-88	13-96
PEST	11	40 – 85	37.2-98.6	23-96	47.1-99.3
EARP	9	41-97.2	34-97.2	14-93.3	57.5-100
TOPAS	6	41-89.1	29.7-90	25.7-91.8	68-81.6
TOPAS-II	4	44-95.8	80.5-98	63.4-95.8	91-98
PsA-Disk questionnaire	1	87.2	46.4	58.6	78.5
CONTEST	2	70-76.5	56.5-91	16-89	68-95
STRIPP	1	91.5	93.3	79.6	97.5
SiPAS	1	79	87	73	90
PASQ	2	67-92.7	64-81.8	43	83
GEPARD	2	77	70	66	80
Swedish- Psoriasis Assessment Questionnaire	1	63	72	45	85
PAQ	1	60	62	26	87.5
SiPAT	1	69	69	91	69
A novel, short, and simple screening questionnaire	1	86.9	71.3	53	93.6

PASE: Psoriatic Arthritis Screening and Evaluation, PEST: Psoriasis Epidemiology Screening Tool, EARP: Early Arthritis for Psoriatic Patients questionnaire, TOPAS: Toronto Psoriatic Arthritis Screening Questionnaire, STRIPP: Screening Tool for Rheumatologic Investigation,SIPAS: Simple Psoriatic Arthritis Screening questionnaire, PASQ: Psoriasis and Arthritis Screening Questionnaire, GEPARD: German Psoriatic Arthritis Diagnostic Questionnaire, PAQ: Psoriatic and Arthritic Questionnaire, SiPAT: Siriraj Psoriatic Arthritis Screening Tool

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3275

AB0580

EFFECT OF FATIGUE ON DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES (PROS) IN PATIENTS (PTS) WITH PSORIATIC ARTHRITIS (PSA)

L. Vorobyova[1], T. Korotaeva[1], E. Loginova[1], Y. Korsakova[1], E. Gubar[1], P. Tremaskina[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Department of Spondyloarthritis and Psoriatic Arthritis, Moscow, Russian Federation*

Background: Fatigue is an important symptom in patients (pts) with psoriatic arthritis (PsA) and was recently added to the core domain set for PsA randomized controlled trials (RCTs) due to the impact that it has on a PROs.

Objectives: to study the influence of fatigue on disease activity and PROs in pts with PsA.

Methods: 187 (M/F=97 (50.2%)/90(48.8%) PsA pts fulfilling the CASPAR criteria were included. Mean age 45.6 + 11.7 years (yrs), median (Me) PsA duration 88 [16;421] mo. 67,8% of pts 67,8% were treat biological DMARDs, 32,1% of pts was monotherapy conventional synthetic disease-modifying antirheumatic drugs (csDMARDs, mostly Methotrexate). On visit PsA activity was evaluated by Tender Joint Count (TJC68), Swollen Joint Count (SJC66), DAPSA. PROs were measured by PtGA VAS, PtPain VAS, BASDAI, HAQ, EQ-5D, PsAID12, WPAI. Fatigue symptoms were assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale. Higher PsAID12 scores are considered to be worse and correspond to poorer PsA-specific health-related quality of life. M±SD, Me [Q25; Q75], %, t-test, Manna-Whitney tests were performed. All p<0.05 were considered to indicate statistical significance.

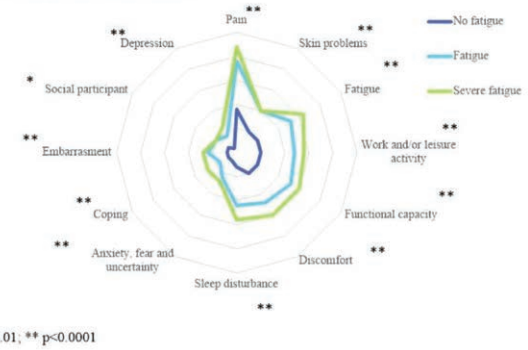
Table 1. The effect fatigue on disease activity and PROs

Parameters, M±SD	No fatigue n=99	Fatigue n=68	Severe fatigue n=20
TJC68	9.51±7.86	14.5±9.89*	19.05±8.15**
SJC66	7.66±5.5	11.5±8.2*	13.4±6.9**
BASDAI	2.6±1.85	5.8±2.47*	7.2±2.0**
DAPSA	21.05±21.03	39.9±21.13*	47.9±15.6**
CRP (mg/l)	12.6±9.4	30.0±25.4*	20.9±11.6**
PtPain, VAS, mm	33±24.7	59±25.2*	66.8±18.1**
PtGA, VAS, mm	30.7±23.8	54.0±22.2*	64.7±16.2**
ESR (mm/h)	15.19±11.7	30.1±23.7*	30.1±20.8**
Total PsAID12 score (over past week, 0- 10)	1.87±1.76	5.41±2.17*	6.5±1.93**
HAQ	0.72±0.59	1.37±0.84*	2.04±0.86**
EQ-5D TTO	0.75±0.17	0.46±0.16*	0.51±0.15**
Work time missed (absenteeism)	0.08±0.26	0.11±0.25	0.31±0.15**
Impairment while working (presenteeism)	0.085±0.15	0.258±0.256*	0.23±0.13**
Overall work productivity impairment (absenteeism + presenteeism)	0.15±0.26	0.35±0.34*	0.37±0.26**
Daily activity impairment	0.22±0.23	0.59±0.25*	0.73±0.22**

*p<0.001 – differences from "No fatigue" to "Fatigue"; ** p<0.0001 – differences from "No fatigue" to "Severe Fatigue";

Results: According to the results of the FACIT-F, the patients were identified: no fatigue (52-34 points) – 99 (53.1%), the presence of fatigue (21-33and less points) – 68 (36.3%) and severe fatigue (20 and less points) -20 (10.6%). By patient with fatigue and severe fatigue significant worse in all activity indexes and PROs than in patients not experiencing fatigue (p<0,001 and p<0,0001), (Table 1). Similar results were demonstrated across all PsAID12 domains (Figure 1), especially the domains "Pain", "Skin problems", "Work and/or leisure activity", "Sleep disturbance", "Function capacity" and "Discomfort" (p<0.0001).
Conclusion: In patients with PsA fatigue affected significant and clinically considerable impairment of PsA activity and PROs.

Figure 1. The effects fatigue on PsAID12 domains



Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3698

AB0581

NAIL PSORIASIS AMONG PATIENTS WITH PSORIATIC ARTHRITIS IS MORE ASSOCIATED WITH THE SEVERITY OF SKIN PSORIASIS THAN WITH FEATURES OF SEVERE ARTHRITIS

M. Haroon[1], S. Farrukh[2], S. Batool[1], S. Asif[1], O. Fitzgerald[3]. *[1]Fatima Memorial Hospital & FMH College of Medicine and Dentistry, Department of Rheumatology, Lahore, Pakistan*; *[2]University Hospital Kerry, Department of Rheumatology, Tralee, Ireland*; *[3]University College Dublin, Conway Institute for Biomolecular Research, Dublin, Ireland*

Background: Nail disease is an important feature of psoriasis arthritis (PsA), and has been recognised as one of the 6 important clinical domains by GRAPPA. Little is known about how patients with PsA and nail disease compare to patients without nail disease. Nail disease has been found to associate with severe PsA.
Objectives: The objective of this study was to examine the association of nail disease with patient demographics and features of active psoriasis and PsA.
Methods: For this cross-sectional study, data from 3 PsA cohorts was studied (St Vincent's University Hospital Dublin, Ireland; University Hospital Kerry, Ireland; and Fatima Memorial Hospital Lahore, Pakistan). Following informed consent, patients underwent detailed skin and rheumatologic assessments including disease activity measures. Since a large number of patients were in clinical remission at the time of assessment, we made 2 documentations of reversible clinical variables (e.g., current skin scores (PASI), current nail disease, current tender and swollen joint counts, current enthesitis, current dactylitis) at the time of study entry and, through extensive medical record review, we identified patient's maximum skin and joints disease activity scores ever documented, e.g., maximum skin scores (PASI max), TJC max, SJC max, nail disease ever, dactylitis ever, enthesitis ever. Nail disease was stratified by the presence or absence of nail psoriasis.
Results: Data on 476 PsA patients was assessed (age 53.8±10.8, PsA duration 13.9±10 years, BMI 29±5; current PASI 2.5±3.2, current TJC 1.8±2.6 years, current SJC 1.4±2.2 years; 37% of the cohort had enthesitis ever, 46% had dactylitis ever, 30.7% had current dactylitis, and 28% with current enthesitis). 63.4% (n=302) of the cohort ever had nail disease, and 45.4% (n=216) had current nail disease at the time of assessment. On univariate analysis, significant or marginally significant statistical association of current nail disease was noted with current PASI (p<0.001), enthesitis ever (p=0.004), current enthesitis (p=0.11), dactylitis ever (p=0.027), current dactylitis (p=0.07), MDA not achieved (p<0.001), current SJC (p=0.08), and current TJC (p=0.32); however, no statistical association was noted with age, gender, disease duration, smoking status, low education status.The following variables were included in multiple stepwise regression analysis: current PASI, current enthesitis, current dactylitis, current TJC, current SJC, MDA not achieved, and low education status; a significant association of current nail disease was noted with current PASI (OR 2.2, CI 1.83-2.54, p<0.001) with a borderline association of current dactylitis (OR 1.6, CI 0.94-2.58, p=0.083). When we used nail disease ever as a dependent variable in the multiple regression model using covariates of PASI max, TJC max, SJC max, dactylitis ever, enthesitis ever, MDA not achieved and low education status, a significant association of nail disease ever was noted with PASI max (OR 1.09, CI 1.01-1.17, p=0.01), TJC max (OR 1.08, CI 1.02-1.14, p=0.005) and borderline association with dactylitis ever (OR 1.74, CI 0.96-3.15, p=0.067)
Conclusion: The presence of nail disease among patients with PsA is significantly associated with severity of skin psoriasis with only borderline associations with measures of active musculoskeletal involvement.
Disclosure of Interests: Muhammad Haroon Speakers bureau: Roche, Novartis, Grant/research support from: Abbvie, Pfizer, shehla farrukh: None declared., Shabnam Batool: None declared., Sadia Asif: None declared., Oliver FitzGerald Speakers bureau: Abbvie, Janssen, Pfizer, Consultant of: BMS, Celgene, Eli Lilly, Janssen, Pfizer, Grant/research support from: Abbvie, BMS, Eli Lilly, Novartis, Pfizer.
DOI: 10.1136/annrheumdis-2021-eular.3848

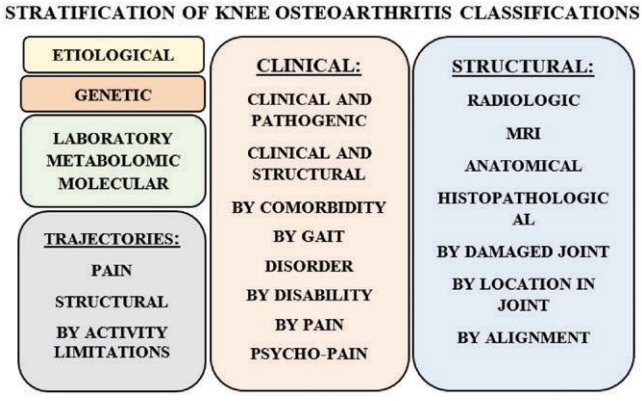
Osteoarthritis

AB0582

KNEE OSTEOARTHRITIS PHENOTYPES STRATIFICATION

K. Korochina[1], T. Chernysheva[1], I. Korochina[2], V. Klementeva[1], G. Kuznetsov[1]. *[1]Orenburg State Medical University, The Department of Internal Diseases, Orenburg, Russian Federation*; *[2]Orenburg State Medical University, The Department of Polyclinic Therapy, Orenburg, Russian Federation*

Background: Osteoarthritis (OA) relevance is determined by its record prevalence with progredient growth throughout the world [1]. Clinical and pathogenic heterogeneity of disease actualizes problem of its stratification [2]. Lack of unified understanding of OA and its phenotype determination results in incredible number of attempts to group OA, using of different classification criteria in last decade.
Objectives: To analyze and systematize available OA classifications, proposals and phenotypes, to highlight the most promising of them.
Methods: We studied publications from MEDLINE / PubMed and Google Scholar databases found by the keywords "osteoarthritis", "phenotypes", "subphenotypes", "classification", "subtypes", "subsets", "subgroups", "subpopulations", "profiles" and "endotypes" in various combinations in English and Russian. We did not set a time frame, but aimed to include as many different methods as possible in order to reflect evolution of scientists' views on structuring of this disease.
Results: A total of 55 OA grouping methods were covered so that OA was structured by different determinants into 6 big boxes.



First OA classifications were characterized by complex etiopathogenetic approach, while subsequent studies differed in joint-mediated approach, and the knee joint was undisputed "champion" in this "race". One of the first attempts to group OA was division into primary, or idiopathic, and secondary, due to known causes. It is now obvious that it is becoming obsolete, and criteria for OA primacy are difficult to determining. Genomic highly specialized studies based on isolation of "favorable" and "unfavorable" genes develops prerequisites to genetic OA classifying. Clinical variants occupy central place as they are the most fully consistent with modern phenotype conception [3], considerating as subtypes of disease shared by underlying pathobiological and pain mechanisms and their structural and functional consequences. Trajectories of OA progression are distinguished by longitudinal design, that is, the determinants for grouping here are disease characteristics in dynamics. The ancestor of structural OA trajectories can be considered Kellgren-Lawrence grades;

subsequent studies identified complex of clinical, laboratory and morphological factors contributing to development of trajectories. Structural OA variants are diverse depending on visualization methods, and many of them can be naturally considered phenotypes, since they drive certain clinical OA manifestations. Morphological changes were described at macro- and microscopic levels; it is interesting to note the absence of histopathological norm in patients without OA. Laboratory profiles of patients are determined by content of systemic (serum, urinary) or local, "proximal" (in synovial fluid) biomarkers, which seem to be more precise. Metabolomic analysis is perspective new direction of laboratory studies based on joint metabolic products identification in the synovial fluid. New trend in OA research is molecular phenotyping. The specific molecular pathway explaining observed phenotype properties is called "endotype". Endotype is related to certain pathobiological scenario, and laboratory markers are potentially effective for its diagnosis.

Conclusion: Thus, a large amount of accumulated information and its diversity soon will probably lead to qualitatively new knowledge level with deep understanding of phenotype-associated strategy for managing OA patients.

REFERENCES:

[1] Wallace IJ, Worthington S, Felson DT, et al. Knee osteoarthritis has doubled in prevalence since the mid-20th century. Proc Natl Acad Sci USA. 2017 Aug 29;114(35): 9332-9336. doi: 10.1073/pnas.1703856114 Epub 2017 Aug 14.

[2] Deveza LA, Nelson AE, Loeser RF. Phenotypes of osteoarthritis: current state and future implications. Clin Exp Rheumatol 37 Suppl 2019;120(5):64-72.

[3] Van Spil WE, Bierma-Zeinstra SMA, Deveza LA, et al. A consensus-based framework for conducting and reporting osteoarthritis phenotype research. Arthritis Res Ther. 2020;22(1):54. doi:10.1186/s13075-020-2143-0

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.36

AB0583 FRAILTY IN THE PATIENTS WITH OSTEOARTHRITIS OF THE KNEE WAS NOT CAUSED BY SARCOPENIA

K. Inui[1,2], K. Mandai[1], T. Ikawa[1], Y. Minami[1], K. Ueno[1], H. Ohashi[1]. [1]*Osaka Saiseikai Nakatsu Hospital, Orthopaedic Surgery, Osaka, Japan*; [2]*Osaka City University Graduate School of Medicine, Orthopaedic Surgery, Osaka, Japan*

Background: Osteoarthritis of the knee (knee OA) decreases mobility of the elderly, which function could be significantly improved with artificial joint replacement in many cases. Successful results of the surgery depend on several factors including preoperative muscle strength of lower limbs.

Objectives: We assessed morbidity and skeletal muscle mass and strength in patients with knee OA immediately before undergoing arthroplasty and investigated the relationship between impairment of mobility and skeletal muscle function.

Methods: All patients scheduled to undergo knee arthroplasty at our hospital after July 2020 were assessed for basic attributes, clinical assessment, blood tests, radiography, whole-body mode DXA, knee muscle strength by dynamometer with written consent (UMIN ID: 000040940). And Japanese Cardiovascular Health Study criteria for frailty, and sarcopenia by Asian Working Group for Sarcopenia 2019 criteria were evaluated.

Results: Among 46 patients (40 women, mean age 75.4 years) the overall distribution in frailty is no: 15.9%, pre-frailty: 56.8%, and frailty: 27.3%. That in sarcopenia is no: 91.3%, yes: 2.2%, and severe: 4.3%. Ninety-one % of the patients with frailty did not suffer from sarcopenia. Between the patients with frailty and those without frailty there was a significant difference in walking speed (0.71±0.29m/sec, 1.12±0.29m/sec; p=0.004 adjusted by age and sex). Meanwhile, between those 2 groups of patients no significant differences were observed in skeletal muscle mass (6.40±0.87 kg/m^2, 6.59±1.09 kg/m^2; p=0.35) and knee extension power (120.4±37.4 N, 143.7±67.9 N; p=0.88) adjusted by age and sex. Together with these results, decrease in lower limb motor functions of the patients with knee OA was not caused by sarcopenia. In other words, improvement of mobility in the patients with knee OA could be expected by surgical intervention because of pain relief and ROM improvement.

Conclusion: In the patients with knee OA immediately before arthroplasty, frailty was not caused by sarcopenia.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.416

AB0584 THE QUALITY OF REPORTING IN RANDOMIZED CONTROLLED TRIALS OF HOME BASED REHABILITATION FOR KNEE OSTEOARTHRITIS: UTILIZING PEDRO SCORE AND CONSORT CRITERIA

M. Meran[1,2], B. Unver[1], E. Çağlar[3]. [1]*Dokuz Eylul University, School of Physical Therapy and Rehabilitation, Izmir, Turkey*; [2]*Istanbul Beykoz University, School of Physical Therapy and Rehabilitation, Istanbul, Turkey*; [3]*Istanbul Gelisim University, Faculty of Health Science/ Physical Therapy and Rehabilitation, Istanbul, Turkey*

Background: Osteoarthritis of the knee (KOA) is a very common rheumatic disease, and its global burden is gradually increasing (1). The benefits of exercise in patients with KOA are supported by high-level evidence and take their place in primary care therapy (2). Today, coronavirus disease 2019 has developed as a pandemic all over the world, creating difficulties in healthcare and highlighting home-based rehabilitation (HBR) (3). Randomized controlled trials (RCTs) are considered the gold standard for evaluating the effects of clinical interventions, but poorly reported results can have negative consequences. The Physiotherapy Evidence Database (PEDro) evaluates the methodological quality of RCTs (4). The CONSORT (Consolidated Standards of Reporting Trials) statement has been developed to improve the reporting quality of RCTs (5).There are no studies examining the quality of RCTs related to HBR in patients with KOA.

Objectives: The aim of this study was to assess the reporting quality of HBR trials for KOA, and explore the factors associated with the reporting.

Methods: Two independent researchers investigated HBR RCTs in patients with KOA published between 1999 and 2020 were sourced from PubMed, the Cochrane Reviews and Web of Science. Each researcher evaluated the methodological quality of the included studies using the PEDro scoring and reporting aspects using 9 items from CONSORT. The relationship between adherence to the CONSORT criteria and the PEDro score were evaluated.

Results: Twenty-five RCTs met our eligibility criteria. The mean PEDro score of studies is 5.76 ± 1.48. Only one study found high quality (PEDro score: ≥ 9). The PEDro scores were: randomization type (96%, 24/25) and baseline comparability (92%, 23/25); all studies described group comparisons and variablity measures. In contrast, concealed allocation (18%, 7/25), blinding of participants (16%, 4/25) and therapists (0%) were not included in most studies. The CONSORT criteria were: flow diagram (92%, 23/25), sample size, subgroup analysis and sources of funding (56%, 11/25 for all three), while the majority of studies the trial registration number (16%, 4/25) was not available. A high level of correlation was found between meeting the CONSORT criteria and PEDro scores ($r=0.820$, $p<0.001$).

Conclusion: The majority of RCTs based on HBR for KOA are low-to-modarate quality studies based on the PEDro score. Adherence to the CONSORT criteria is linked to high quality scores. If the studies are planned and written in accordance with the CONSORT criteria, we think that better quality studies will emerge.

REFERENCES:

[1] Safiri S, Kolahi AA, Smith E, Hill C, Bettampadi D, Mansournia MA, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. Ann Rheum Dis. 2020;79(6):819-28.

[2] Skou ST, Pedersen BK, Abbott JH, Patterson B, Barton C. Physical Activity and Exercise Therapy Benefit More Than Just Symptoms and Impairments in People With Hip and Knee Osteoarthritis. J Orthop Sport Phys. 2018;48(6):439-47.

[3] Karasavvidis T, Hirschmann MT, Kort NP, Terzidis I, Totlis T. Home-based management of knee osteoarthritis during COVID-19 pandemic: literature review and evidence-based recommendations. J Exp Orthop. 2020;7(1):52.

[4] Sherrington C, Herbert RD, Maher CG, Moseley AM. PEDro. A database of randomized trials and systematic reviews in physiotherapy. Man Ther. 2000;5(4):223-6.

[5] Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. Int J Surg. 2012;10(1):28-55.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.476

AB0585 COMPARISON OF THE EFFECTIVENESS OF HYALURONIC ACID PREPARATIONS WITH DIFFERENT MOLECULAR WEIGHTS AND IN COMBINATION WITH CHONDROITIN SULFATE DEPENDING ON THE STAGE OF OSTEOARTHRITIS OF THE KNEE JOINT

V. Bialik[1], M. Makarov[1], E. Bialik[1], S. Makarov[1], V. Nesterenko[1], M. Nurmukhametov[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Rheumoorthopedic and Rehabilitation, Moscow, Russian Federation*

Background: intra-articular (IA) injections of hyaluronic acid (HA) preparations are one of conservative treatment of the knee osteoarthritis (OA). However, the results of this treatment are inconsistent.

Objectives: to evaluate the effectiveness of HA preparations with different molecular weights and in combination with chondroitin sulfate (HS) for IA injections in the treatment of patients with stage I-III knee OA.

Methods: IA HA injections were performed 160 patients with primary and post-traumatic knee OA of the I-III stages at the department of rheumoorthopaedic and rehabilitation, V. A. Nasonova Research Institute of Rheumatology for the period from September 2017 to June 2019. Patients were divided into 4 groups. Group 1 consisted of 80 patients treated with low molecular weight (LMW) HA, group 2 - 20 patients treated with medium molecular weight (MMW) HA, group 3 - 30 patients treated with high molecular weight (HMW) HA, and group 4 - 30

patients who were intraarticular introduced HA with HS. The course of IA injections was 2 for LMW, HMW, and HA with HS, and 3 for MMW HA. Injections were performed with an interval of 1 week. To evaluate the results of treatment, we studied the intensity of pain according to VAS and the total score of KOOS before treatment and on follow-up examinations 1, 3 and 6 months after the course of IA HA injections.

Results: the maximum reduction in pain with IA HA injections at stage I of knee OA occurred by 3 months after the course of treatment. Moreover, improvement was detected by 1 month in 84.3% of cases, and remained until the end of the study in 71.1% of patients. All HA preparations used in stage I of knee OA were effective. At stage II of the knee OA after 3 months after the course of IA HA, different efficiencies of HA preparations were revealed. So, in the groups of LMW, MMW and HA with HS, the improvement persisted up to 3 months, and in the group of HMW HA - up to 1 month. After 3 months, the best results were shown by HA with HS, by 6 months the results were comparable. IA HA injections at the II stage of knee OA led to good and excellent results 1 month after the course of treatment in 53.9% of cases, but by the end of the study, improvement remained in only 30.8% of patients. In the case of the use of HA in stage III of the knee OA, the effectiveness of the studied drugs was comparable, and the maximum improvement was achieved by 1 month. The positive effect of IA HA injections in patients with stage III of the knee OA one month after the course of treatment was obtained in 40.6% of cases, by 3 months it decreased to 18.8%, and by 6 months - to 15.7% of patients.

Conclusion: IA injections of HA at stage I of the knee OA is a highly effective method of conservative treatment, which allows to relieve pain and improve the condition of the knee joint for a period of 6 months or more. The use of HA preparations at stage II of the knee OA allows reducing pain up to 3 months with IA injections of LMW and MMW HA, as well as HA with HS. HMW HA helps reduce pain intensity for a period of 1 month. The use of HA preparations in stage III of the knee OA leads to a short-term relief of symptoms of OA.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.485

AB0586 PREVALENCE OF EARLY SYMPTOMATIC KNEE OSTEOARTHRITIS ACCORDING TO THREE CLINICAL CLASSIFICATION CRITERIA

M. Törnblom[1,2], A. Bremander[2,3,4,5], K. Aili[2,6,7], M. Andersson[2,4], A. Nilsdotter[8,9], E. Haglund[2,4,10]on behalf of The Halland Osteoarthritis study group.
[1]Helsingborg Hospital, Department of Rehabilitation, Helsingborg, Sweden; *[2]Spenshult, Research and Development Centre, Halmstad, Sweden*; *[3]Department of Regional Health Research, University of Southern Denmark, Odense, Denmark*; *[4]Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund, Sweden*; *[5]Danish Hospital for Rheumatic Diseases, University Hospital of Southern Denmark, Sønderborg, Denmark*; *[6]Halmstad University, School of Health and Welfare, Halmstad, Sweden*; *[7]Karolinska Institutet, Institute of Environmental Medicine, Stockholm, Sweden*; *[8]Department of Orthopaedics, Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Göteborg, Sweden*; *[9]Sahlgrenska University Hospital, Department of Orthopaedics, Göteborg, Sweden*; *[10]Rydberg Laboratory of Applied Sciences, Halmstad University, Halmstad, Sweden*

Background: Knee osteoarthritis (KOA) is a heterogeneous disease. Different classification criteria for symptomatic KOA (SKOA) have been proposed. Determining the prevalence and comparing the different criteria of SKOA in patients with knee pain will serve as a base when studying the predictive ability of these criteria in a longer perspective.

Objectives: To study the prevalence of SKOA in individuals with knee pain according to three different classification criteria: the American College of Rheumatology (ACR), (1), the European League Against Rheumatism (EULAR)(2), and the National Institute for Health and Care Excellence (NICE) (3).

Methods: Baseline data from an ongoing longitudinal study (HALLOA) including 296 individuals with knee pain, recruited by advertisement, were analysed. The individuals were categorized according to the classification criteria of SKOA (ACR, EULAR and NICE) based on age, clinical examination (crepitation), and self-reported data from KOOS (pain, symptoms, ADL, and sport/recreation), and dichotomized as fulfilling the criteria (SKOA) or not (no SKOA). BMI was measured (kg/m^2). Radiographic KOA (RKOA) was assessed according to Ahlbäck criteria (1-5), defined as RKOA with grade 1 or more in at least one knee. Prevalence was calculated (frequencies, %) for each criterion, and Chi-Square test or the Independent-Samples t-test were used for comparisons between individuals fulfilling SKOA or not.

Results: The mean age was 52 (min-max 24-73) years, 70% were women and 22% were classified with RKOA. The prevalence of SKOA according to each criterion was 57% (ACR), 51% (EULAR) and 73% (NICE) respectively. In total, 48% had SKOA according to all three criteria and whereof 32% had RKOA, compared to 10% RKOA among individuals with no SKOA. Regardless of the criterion, significantly more individuals classified with SKOA also had RKOA compared to individuals with no SKOA, p<0.001. Those classified as SKOA were significantly older and had higher BMI compared with no SKOA (Table 1).

Conclusion: Approximately 50-70% of the individuals with knee pain were classified as having SKOA, where EULAR criteria had the lowest prevalence. A better understanding of early knee pain classification according to different clinical criteria is essential for the ability to capture and follow the long-term prognosis of early SKOA. Further longitudinal studies are needed.

REFERENCES:

[1] Altman R et al. Arthritis Rheum. 1986;29(8):1039-49.
[2] Zhang W et al. Ann Rheum Dis. 2010;69(3):483-9.
[3] Health NIf, Excellence C. UK: National Institute for Clinical Excellence. 2014.

Table 1. Comparisons between the ACR, EULAR and NICE criteria of symptomatic knee osteoarthritis, stratified for symptomatic knee osteoarthritis or not

		ACR			EULAR			NICE		
	Total	**OA**	**No OA**	P-value	**OA**	**No OA**	P-value	**OA**	**No OA**	P-value
N *(%)*	296 (100)	170 (57.4)	98 (33.1)		152 (51.4)	114 (38.5)		215 (72.6)	58 (19.6)	
Age *(Y), Mean (SD)*	51.6 (8.7)	53.3 (7.0)	49.0 (10.3)	**<0.001**	54.5 (5.1)	48.1 (10.8)	**<0.001**	54.7 (4.9)	40.5 (9.8)	**<0.001**
Gender, *female (%)*	208 (70.3)	121 (71.2)	66 (67.3)	0.511	108 (58.4)	77 (67.5)	0.538	154 (71.6)	36 (62.1)	0.160
BMI *(kg/m^2), Mean (SD)*	26.4 (4.6)	26.5 (4.5)	25.8 (4.3)	0.179	26.9 (4.5)	25.4 (4.2)	**0.005**	26.7 (4.5)	24.8 (3.8)	**0.004**
RKOA, *n (%)*	64 (21.6)	45 (26.5)	12 (12.2)	**0.003**	47 (30.9)	10 (8.7)	**<0.001**	58 (27.0)	1 (1.7)	**<0.001**

Independent-samples t-test and Chi-2-test. **Bold**=Significant correlation (p≤0.05). **OA** = Osteoarthritis. **ACR** = American College of Rheumatology. **EULAR** = the European League Against Rheumatism. **NICE** = the National Institute of Care and Excellence. **BMI** = Body Mass Index. **RKOA** = Radiographic Knee Osteoarthritis (Ahlbäck, with grade ≥1 in ≥1 knee).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.520

AB0587 ASSESSING THE CHARACTERISTICS AND MANAGEMENT OF KNEE OSTEOARTHRITIS PATIENTS WITH HYPERTENSION BY CLINICIAN SPECIALITY

D. Baldock[1], E. Baynton2, C. F. Ng[3]. *[1]Ipsos MORI, Healthcare Service Line, london, United Kingdom*; *[1]Ipsos MORI, Healthcare Service Line, london, United Kingdom*; *[3]Ipsos Sdn Bhd, Healthcare Service Line, Kuala Lumpur, Malaysia*

Background: Though the pathogenesis of knee osteoarthritis (OA) is complex, patients with OA frequently have other comorbidities, including hypertension, which eludes to other considerations needed when deciding appropriate treatment management.

Objectives: This study aims to examine the profiles of knee OA patients with hypertension vs. those without any comorbidities, and to elucidate key differences between these patient groups as potential areas of consideration.

Methods: A multi-center, online medical chart review study of patients with OA was conducted between May – July 2020 among US rheumatologists (rheums), orthopedic surgeons (orthos), primary care physicians with a focus in sports medicine (SM PCPs), and pain specialists. Physicians recruited were screened for duration of practice in their specialty (3-50 years) and caseload (>=35 knee OA patients personally managed, at least 10 being moderate-severe). Patient charts were recorded for the next 5 eligible patients seen during the screening period. Respondents abstracted patient demographics and treatments used. Descriptive statistics were used to analyse the data.

Results: 260 physicians were recruited and collectively reported 796 knee OA patients; 559 were reported to experience hypertension whilst 237 were reported as not experiencing any comorbidities.

Reported hypertension patients were significantly older (mean 67 vs 59 years old, respectively; p≤0.01) and weighed more (mean 82kg vs 77kg, respectively; p≤0.01) than patients without comorbidities; they were also significantly more likely to be previous smokers compared to those without comorbidities (23% vs 8%, respectively; p≤0.01). With regards to current knee OA severity, both orthos and SM PCPs reported a significantly higher proportion of hypertension patients that were deemed 'severe' (physician opinion) vs patients without comorbidities (orthos: 50% vs 32%, respectively; SM PCPs: 42% vs 23%, respectively; p≤0.01). Rheums and pain specialists reported greater mild opioid usage amongst hypertension patients compared to those without comorbidities (rheums: 28% vs 10%, respectively (p≤0.05); pain specialists: 40% vs 9%, respectively; (p≤0.01)); orthos and SM PCPs stated significantly greater use of corticosteroid injections amongst their reported hypertension patients vs those without comorbidities (orthos: 60% vs 41%, respectively; SM PCPs: 40% vs 19%, respectively; p≤0.01). Hypertension patients reported by orthos and SM PCPs are more likely to be

considered for total knee replacement (TKR) surgery compared to those without comorbidities (orthos: 59% vs 32%, respectively; SM PCPs: 37% vs 19%, respectively; p≤0.01). Conversely, hypertension patients reported by rheums are less likely to be considered for TKR vs those without comorbidities (41% vs 18%, respectively; p≤0.05).

Reported hypertension patients had a significantly higher mean Visual Analogue Scale for Pain (VAS) score than patients without comorbidities (6.6 vs 5.9, respectively; p≤0.01). A significantly higher proportion of patients with hypertension demonstrate radiographic evidence of bone erosion compared to those without comorbidities (69% vs 56%, respectively; p≤0.01).

Conclusion: From the sample surveyed, knee OA patients with hypertension may require a more specific and holistic treatment approach that takes into account their CV status and managing physician specialty. Further investigation using comparator cohort is warranted.

REFERENCES:

[1] Ipsos Osteoarthritis Therapy Monitor (May – July 2020, 260 specialists reporting on 769 knee OA patients seen in consultation, data collected online. Participating physicians were primary treaters and saw a minimum number of 35 knee OA patients). Data © Ipsos 2021, all rights reserved.

[2] Ipsos Osteoarthritis Therapy Monitor (May – July 2020, 260 specialists reporting on 769 knee OA patients seen in consultation, data collected online. Participating physicians were primary treaters and saw a minimum number of 35 knee OA patients). Data © Ipsos 2021, all rights reserved.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.549

AB0588 "ESORT" ITALIAN SOCIETY OF RHEUMATOLOGY (SIR) REGISTER ON OSTEOARTHRITIS (OA): PRELIMINARY DATA

G. Gigliucci[1], O. De Lucia[2], A. Fioravanti[3], F. Galluccio[4], S. Guiducci[5], A. Moretti[6], M. Matucci-Cerinic[5], A. Murgo[2], S. Parisi[7], R. Ramonda[8], S. Tenti[3], E. Tirri[9], A. Migliore[1]on behalf of Study group on osteoarthritis - Italian Society of Rheumatology (SIR). [1]*San Pietro Hospital, Rheumatology Unit, Roma, Italy*; [2] *ASST Gaetano Pini-CTO Institute, Division of Clinical Rheumatology, Milan, Italy*; [3]*Azienda Ospedaliera Universitaria Senese - Policlinico Le Scotte, Department of Medicine, Surgery and Neuroscience - Rheumatology Unit, Siena, Italy*; [4]*Careggi University Hospital - University of Florence, Department of Clinical and Experimental Medicine - Division of Rheumatology, Firenze, Italy*; [5]*Careggi University Hospital - University of Florence, Department of Clinical and Experimental Medicine - Department of Geriatric Medicine - Division of Rheumatology and Scleroderma Unit, Firenze, Italy*; [6]*University of Campania Luigi Vanvitelli, Multidisciplinary Department of Medical and Surgical Specialties and Dentistry, Naples, Italy*; [7]*Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Department of General and Specialty Medicine - Unit of Rheumatology, Turin, Italy*; [8]*University of Padova, Department of Medicine-DIMED - Rheumatology Unit, Padova, Italy*; [9]*Hospital San Giovanni Bosco, UOSD Reumatologia, Naples, Italy*

Background: In Italy Osteoarthritis (OA) is a widespread and disabling disease that affects an increasingly large number of patients in the population, representing one of the main causes of morbidity and disability with high socio-economic costs. The etiology of OA is multifactorial, even if the significant association with some modifiable risk factors like mechanical overload and obesity is now well demonstrated. Early diagnosis and treatment strategies in OA could reduce both patient morbidity and associated costs.

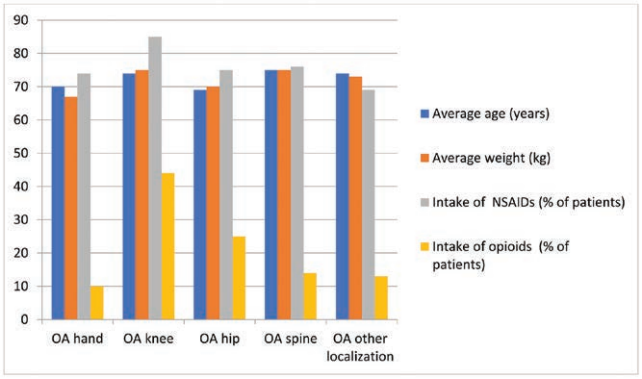
Objectives: Promoted by the Italian Society of Rheumatology (SIR), The Early Symptomatic OsteoaRThritis (ESORT) registry has the aim to study the natural history of OA from the earliest stages (pre- radiographic) considering risk factors in the progression of the disease, and the influence of therapeutic factors on long-term disease outcomes. The ESORT register aims to describe the socio-demographic and clinical characteristics of patients affected by OA in Italy; evaluates the extent of symptoms, functional damage, comorbidities, the frequency of use of drugs currently indicated in our country, and differences related to clinical subsets according with comorbidities and geographical localization of the patient.

Methods: Actually 8 Italian Rheumatology centers are involved in the online data entry data of the SIR registry (developed and validated by SIR Study Center), considering patients affected by OA. In particular, the electronic database collects information about main demographic variables, significant anamnestic elements (risk factors and comorbidities), localization of OA, laboratory data, clinimetric indices with WOMAC / FIHOA / VAS scales, radiographic instrumental data and therapy in act. These data are reported in specific forms in the register with annual reassessment.

Results: Currently, 318 patients with OA are included in the "ESORT" registry with an extension of observation up to 48 months, 214 women and 104 men with an average age of 71 years and an average weight of 72 kg. About 14% of patients affected by knee OA show Kellgren and Lawrence radiological stage 0 in presence of painful symptoms at the knees. The most frequent localization of OA is the knee (63%), followed by the hip (41%), hand (36%), spine (34%), and other sites (16%). The Table 1 shows details of some parameters (average age, average weight, intake of NSAIDs, intake of opioids and intake of chondroprotectors) according to the localization of the disease. From the registry data, patients with OA results treated mainly with NSAIDs and chondroprotectors, and patients with knee OA are the most frequently treated with opioid analgesics (44%), less used in other OA locations.

Conclusion: The "ESORT" register is a useful tool for epidemiological and clinical information relating to patients with OA and for monitoring the evolution of the disease and the response to therapy.

	Average age (years)	Average weight (kg)	Intake of NSAIDs (% of patients)	Intake of opioids (% of patients)	Intake of chondroprotectors (% of patients)
OA hand	70	67	74%	10%	25-31%
OA knee	74	75	85%	44%	53-59%
OA hip	69	70	75%	25%	24-28%
OA spine	75	75	76%	14%	19-28%
OA other localization	74	73	69%	13%	15-35%



Disclosure of Interests: Gianfranco Gigliucci: None declared., Orazio De Lucia: None declared., Antonella Fioravanti: None declared., Felice Galluccio: None declared., Serena Guiducci: None declared., Antimo Moretti: None declared., Marco Matucci-Cerinic Speakers bureau: Consulting fees or honorarium from Actelion, Janssen, Inventiva, Bayer, Biogen, Boehringer, CSL Behring, Corbus, Galapagos, Mitsubishi, Samsung, Regeneron, Acceleron, MSD, Chemomab, Lilly, Pfizer, Roche, Grant/research support from: Consulting fees or honorarium from Actelion, Janssen, Inventiva, Bayer, Biogen, Boehringer, CSL Behring, Corbus, Galapagos, Mitsubishi, Samsung, Regeneron, Acceleron, MSD, Chemomab, Lilly, Pfizer, Roche, Antonella Murgo: None declared., Simone Parisi Speakers bureau: Personal fees (as speaker and/or consultant) from NOVARTIS, BMS, LILLY, UCB, MSD, PFIZER, ABBVIE, BIOGEN, AMGEN, JANSENN CILAG, CHIESI and GRUNENTHAL outside the submitted work;, Consultant of: Personal fees (as speaker and/or consultant) from NOVARTIS, BMS, LILLY, UCB, MSD, PFIZER, ABBVIE, BIOGEN, AMGEN, JANSENN CILAG, CHIESI and GRUNENTHAL outside the submitted work;, Roberta Ramonda: None declared., Sara Tenti: None declared., Enrico Tirri: None declared., Alberto Migliore Speakers bureau: Grants from Abiogen,Lilly,Fidia,Jansen (outside the submitted work), Consultant of: Grants from Abiogen,Lilly,Fidia,Jansen (outside the submitted work), Grant/research support from: Grants from Abiogen,Lilly,Fidia,Jansen (outside the submitted work).

DOI: 10.1136/annrheumdis-2021-eular.1001

AB0589 STUDY OF THE EFFECTIVENESS OF PELOID THERAPY IN THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE JOINTS IN THE CONDITIONS OF THE SANATORIUM " CHUVASHIYAKURORT»

N. Zhuravleva[1], L. Karzakova[1], S. Kudryashov[1], A. Arkhipova[2]. [1]*Federal State Budgetary Educational Institution of Higher Education "The Chuvash State University named after I.N. Ulyanov", Department of Internal Medicine, Cheboksary, Russian Federation*; [2]*Budget Institution "Republican Clinical Hospital" of Public Health Ministry of the Chuvash Republic, rheumatology department, Cheboksary, Russian Federation*

Background: Peloids are successfully used in the treatment of various diseases. The sapropel mud-silt deposits of freshwater reservoirs are the most widely used for joint diseases. The sapropel mud from the freshwater lake «Kogoyar»

(Russia, Cheboksary) has unique properties. The right to extract and use sapropel belongs to the sanatorium "Chuvashiyakurort" (Russia) [1]. The organic biostimulants of the sapropel mud (bitumen, fatty and humic acids, amino acids, hormones, lipids) have a pronounced anti-inflammatory effect on cartilage. High humidity (87%) provides sapropel high thermal qualities.

Objectives: The aim of the research was to study the effectiveness of peloid therapy in patients with osteoarthritis of the knee joints at the II X-ray stage using the sapropel mud of Lake «Kogoyar».

Methods: The object of the study was 150 patients of the sanatorium "Chuvashiyakurort" aged from 55 to 62 years (89 women and 61 men). The patients were randomly divided into 2 groups. The first group (75 people) received basic therapy - chondroprotectors (Teraflex) and nonsteroidal anti-inflammatory drugs (NSAIDs) on demand. The second group (75 people) received basic therapy with the addition of peloid application. The peloid was used in the natural, minimally modified, undiluted form. The peloid therapy protocol: the peloid was heated to 50 °C before use and applied to the affected joint with a layer of 4-5 cm thick and wrapped with a warm cloth on top. The procedure took 30 minutes. Five three-day cycles of applications with one-day breaks were performed. At the end of the procedure, a patient was unraveled, the mud was removed from him and he took a warm shower. Then he had a rest for 30 to 40 minutes in the recreation room. Before the start of treatment and after its completion, a survey of patients was conducted with the fixation of pain on the VAS scale, the duration of morning stiffness, fatigue and decreased performance, general discomfort, dependence on taking NSAIDs.

Results: The analysis of the survey results revealed a decrease in VAS pain and morning stiffness in both groups. However, patients in the second group had a more pronounced reduction in the average VAS pain score (26% lower compared to the first group) and the duration of morning stiffness (20% lower compared to the first group). In addition, the number of patients who indicated a decrease in dependence on taking NSAIDs was 28% higher than in the group that received only standard therapy.

Conclusion: Peloid therapy enabled to reduce the pain on the back, reduce the frequency of the need for NSAIDs, improve the condition of patients, which is the reflection of the positive clinical dynamics in patients with osteoarthritis of the knee joints, and contributed to the effectiveness of treatment.

REFERENCES:

[1] Sakharova A.S. Modern methods of medical rehabilitation in the practice of doctors of various specialties. Cheboksary: Publishing House of Chuvash State University, 2019: 110-115.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1256

AB0590 ARTHRITIS OF THE KNEE AND BALANCE DISORDER

W. Belhaj[1], S. Miladi[2], A. Fazaa[2], M. Sellami[2], K. Ouenniche[1], L. Souebni[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. *[1]University of tunis el manar, Faculty of Medicine of Tunis, Mongi slim Hospital, Rheumatology Department, Tunis, Tunisia*; *[2]University of Tunis el manar, Faculty of Medicine of Tunis, Mongi slim Hospital, Rheumatology Department, TUNIS, Tunisia*

Background: Knee osteoarthritis has been identified as a risk factor for falls and balance disorders. Several clinical scales have been put in place to assess this risk.

Objectives: The aim of this work was to assess the risk of falls in patients followed for osteoarthritis of the knee.

Methods: A prospective study was conducted over a period of 4 weeks. Sixty-six patients followed for knee osteoarthritis at different stages of the disease were included into this work. Epidemiological data, physical examination data and x-ray data were collected. The impact of knee osteoarthritis was evaluated by the Lequesne and WOMAC indices. The patients were asked about the history of a fall since the onset of knee osteoarthritis and they had the Tinetti test where a score less than 20 reflects a very high risk of falling, from 20 to 23 significant risk, from 24 to 27 moderate risk and 28 means a normal test.

Results: In the studied population, the majority of patients were women (87%) with an average age of 55 years and an average body mass index of 29kg / m2. The most common comorbidities were high blood pressure (61%), diabetes (38%) and osteoporosis (36%). Sixty-nine percent of patients took more than two oral treatments. The average duration of development of osteoarthritis of the knee was 9 years. The most common radiological stage was stage 1 (58%) followed by stage 2 (31%). The site was femorotibial in 88% of cases, patellofemoral in 4% of cases and bi or tri compartmental in 8% of cases. The arthritis most often affected both knees: 86% of cases. The average of the Lequesne index was 11. The mean WOMAC index was 12 in pain, 1.5 in stiffness and 48 in dysfunction. Patients who had a normal Tinetti score represented 39% of the studied population, those who had a score from 24 to 27 were 35% of the studied population, those who had a score between 20 and 23 were 14% of the studied population, and those who had a score below 20 were 12% of the studied population.

Patients reporting a history of one or multiple falls were 19%. Among these patients 93% were women and 88% were hypertensive under antihypertensive treatment. The average age of these patients was 61 years. The Tinetti test revealed in this group of patients that 40% had a very high risk of falling, 48% had a high risk of falling, 10% had a moderate risk and 2% had a normal Tinetti test. These patients had been followed for knee osteoarthritis for an average of 10 years. The average Lequesne index was 12.5. The average WOMAC index was 12 for pain, 2 for stiffness and 55 for dysfunction.

In the following Table 1 we summarized the different stages of risk of falling according to the Tinetti score according to the epidemiological data and the characteristics of knee osteoarthritis:

Tinetti score	Less than 20	From 20 to 23	From 24 to 27	Equal to 28
Average age (years)	66	65	56	47
Women (%)	78	81	88	89
Men (%)	22	19	12	11
Average BMI (kg/m^2)	31,7	30,4	29,3	28,6
High blood pressure (%)	77	60	67	57
Average Lesquene	12,5	11	11	10,5
WOMAC pain	14	12	12	10
WOMAC stiffness	2	1,5	1	1
WOMAC dysfunction	58	49	46	44

Conclusion: The epidemiological characteristics as well as the knee osteoarthritis characteristics are statistically close in the different groups of stages of risk of fall according to Tinetti test. Indeed, according to this study, knee osteoarthritis does not represent a significant risk factor for falls.

REFERENCES:

[1] Mat S, Tan MP, Kamaruzzaman SB, Ng CT. Physical therapies for improving balance and reducing falls risk in osteoarthritis of the knee: a systematic review. Age Ageing. 2015 Jan;44(1):16-24. doi: 10.1093/ageing/afu112. Epub 2014 Aug 22. PMID: 25149678.

[2] Köpke S, Meyer G. The Tinetti test: Babylon in geriatric assessment. Z Gerontol Geriatr. 2006 Aug;39(4):288-91. doi: 10.1007/s00391-006-0398-y. PMID: 16900448.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1540

AB0591 ASSESSMENT OF KNEE-RELATED SYMPTOMS, ACTIVITIES, AND QUALITY OF LIFE IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

P. Kabakchieva[1,2], T. Georgiev[3,4], A. Gateva[1,2], Z. Kamenov[1,2]. *[1]Medical University - Sofia, Department of Internal Medicine, Sofia, Bulgaria*; *[2]Aleksandrovska University Hospital, Clinic of Endocrinology, Sofia, Bulgaria*; *[3]Medical University - Varna, First Department of Internal Medicine, Varna, Bulgaria*; *[4]St. Marina's Hospital, Rheumatology Clinic, Varna, Bulgaria*

Background: Osteoarthritis (OA) is a slowly progressive disease that probably begins in young adulthood when a timely treatment would present the possibility to reverse or slow down the disease process. Obesity and sex hormones play an essential role in the pathogenesis of OA in women and their influence on joint function persists throughout the whole life [1]. Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women of reproductive age characterized by sex-hormonal disbalance, metabolic abnormalities, and most commonly obesity. It seems that PCOS presents the best opportunity to study the complex interactions among hormonal disbalance, obesity, and (pre) osteoarthritis.

Objectives: Our study aims to assess the knee-related symptoms, activities, and quality of life in young women with PCOS and to compare them with healthy volunteers using Knee Injury and Osteoarthritis Outcome Score (KOOS) developed for younger and more active individuals [2].

Methods: Fifty-four patients with PCOS who met the Rotterdam criteria were compared with 26 healthy women. Both groups were matched by age and body mass index (BMI). The exclusion criteria of the study were: the presence of inflammatory/autoimmune rheumatic disease and/or another endocrine disorder. Pregnant women and participants, who used systemic corticosteroids, antiandrogens, or insulin-sensitive drugs in the last 3 months were also excluded from the study. After written informed consent all participants filled in the questionnaire. KOOS was scored in each of its 5 domains: pain, symptoms, activities of daily living (ADL), sport and recreation function, and knee-related quality of life (QoL). Additionally, detailed anthropometric data, clinical examination, and hormonal assessment (testosterone, dehydroepiandrosterone sulfate [DHEAS], androstenedione, 17-OH-progesterone, luteinizing hormone [LH], follicle stimulating hormone [FSH], and estradiol) were carried out in all overnight-fasted participants during a follicular phase of a menstrual cycle.

Results: Patients and healthy volunteers had similar anthropometric and demographic characteristics but PCOS women were expectedly more hyperandrogenic and hirsute than controls. Patients and controls did not differ significantly in their knee pain, knee-related QoL, and sport and recreation function. Knee-related symptoms were more prominent in the PCOS group compared to controls ($p = 0.035$). ADL associated with the knee joint were also more impaired in patients ($p = 0.001$). Obese PCOS women had a significantly lower score in the ADL domain than normal and overweight patients ($p = 0.035$). In the PCOS group, both knee-related ADL and sport and recreation function correlated significantly with weight ($p = 0.025$ and $p = 0.034$, respectively) and waist circumference ($p = 0.011$ and $p = 0.016$, respectively), among all studied anthropometric parameters. Sex hormones did not correlate with any of the evaluated KOOS subscales.

Conclusion: PCOS patients may experience impaired physical function related to daily life due to knee problems. Obesity may further contribute to knee-related ADL dysfunction. Hormonal disturbances did not show any association with knee complaints in our study.

REFERENCES:

[1] Georgiev T, Angelov AK. Modifiable risk factors in knee osteoarthritis: treatment implications. Rheumatol Int. 2019 Jul;39(7):1145-1157

[2] Roos EM, Toksvig-Larsen S. Knee injury and Osteoarthritis Outcome Score (KOOS) - validation and comparison to the WOMAC in total knee replacement. Health Qual Life Outcomes 2003;1:17.

Acknowledgements: The study was performed with the financial support of Medical University-Sofia, Bulgaria, Young Investigator 2020, Project No 8378/20.11.2019, Contract D-85/24.06.2020.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2072

AB0592 ASSESSMENT OF KNOWLEDGE OF THE APPLICATION OF TOPICAL ANALGESICS

S. Miladi[1], W. Belhaj[1], A. Fazaa[1], M. Sellami[1], K. Ouenniche[1], L. Souebni[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*University of Tunis el Manar, Faculty of Medicine of Tunis, Mongi slim Hospital, Rheumatology Department, Tunis, Tunisia*

Background: In chronic osteoarticular pain, especially knee osteoarthritis, topical analgesics and topical non-steroidal anti-inflammatory drugs represent an interesting therapeutic alternative for patients with several comorbidities in order to avoid side effects and medical interactions.

Objectives: The aim of this work was to assess how patients apply a topical analgesic.

Methods: A prospective study has been conducted over a period of 4 weeks. Sixty-six patients followed for knee osteoarthritis at different stages of the disease and under topical analgesic treatment were integrated into this study. Epidemiological data, physical examination and x-ray data were collected. The impact of knee osteoarthritis was evaluated by the Lequesne and WOMAC indices. Patients were asked about how long they apply the treatment, how often they use the treatment per week and whether they are massaging the aching area while applying the treatment.

Results: In the studied population, the majority of patients were women (87%) with an average age of 55 years. Forty percent of the patients were illiterate as long as 21% received a college education. Patients' occupations were distributed as follows: 59% housewives, 21% retirees, 12% manual occupations and 8% non-manual occupations.

The most common comorbidities were high blood pressure (61%), diabetes (38%) and osteoporosis (36%).

The average duration of development of osteoarthritis of the knee was 9 years. The most common radiological stage was stage 1 (58%). The site was femorotibial in 88% of cases, patellofemoral in 4% of cases and bi or tri-compartmental in 8% of cases. The osteoarthritis most often affected both knees: 86% of cases

The average of the Lequesne index was 11. The average WOMAC index was 12 for pain, 1.5 for stiffness and 48 for dysfunction.

All the interviewed patients were on topical analgesics for an average of 5 years. The average frequency of application of topical analgesics was 9 times per week. Housewives and retirees used the treatment on average 14 times per week while working patients use the treatment on average 5 times per week. Seventy-two percent of patients reported that they performed an average massage lasting 11 minutes with each application.

Among patients with secondary and university education, 64% of patients reported that they performed a massage on the painful knee while applying the medication.

Patients followed for knee osteoarthritis for more than 10 years tend to apply the local analgesic for a shorter period of time (an average of 5 minutes).

Conclusion: Patients followed for osteoarthritis of the knee who are taking topical analgesics tend to make misuse, including massaging for a long time and applying treatment less frequently than recommended. The level of education does not seem to play a role in knowing the right way to apply. However, patients who have been followed for a longer period for knee osteoarthritis use the treatment more correctly.

REFERENCES:

[1] Flores MP, Castro AP, Nascimento Jdos S. Topical analgesics. Rev Bras Anestesiol. 2012 Mar-Apr;62(2):244-52. doi: 10.1016/S0034-7094(12)70122-8. PMID: 22440379.

[2] Barkin RL. The pharmacology of topical analgesics. Postgrad Med. 2013 Jul;125(4 Suppl 1):7-18. doi: 10.1080/00325481.2013.1110566911. PMID: 24547599.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2148

AB0593 PERCEPTION OF THE EFFECTIVENESS OF TOPICAL ANALGESICS IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE

W. Belhaj[1], S. Miladi[1], A. Fazaa[1], M. Sellami[1], K. Ouenniche[1], L. Souebni[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*University of Tunis el Manar, Faculty of Medicine of Tunis, Mongi slim Hospital, Rheumatology Department, Tunis, Tunisia*

Background: Osteoarthritis of the knee is one of the most common joint diseases. It mainly manifests as pain and can become disabling over time. Several symptomatic therapeutic methods are used to relieve patients with knee osteoarthritis and give them more autonomy. Topical analgesics are considered as an interesting alternative for old and poly-medicated patients.

Objectives: The aim of this work was to assess the perception of the effectiveness of topical analgesics by patients followed for knee osteoarthritis.

Methods: A prospective study has been conducted collecting 66 patients followed for knee osteoarthritis at different stages of the disease and under topical analgesic treatment. Epidemiological data, physical examination and x-ray data were collected. The impact of knee osteoarthritis was evaluated by the Lequesne and WOMAC indices. Patients were asked to evaluate their perception about: the time that makes the medication to act, the duration of action and overall satisfaction with the topical analgesic by rating it from 0 to 5. Zero represents complete dissatisfaction while 5 represents complete satisfaction. Patients were also asked about the side effects observed after the use of the topical treatment and whether they recommended this treatment to a friend or a parent.

Results: In the studied population, the majority of patients were women (87%) with an average age of 55 years. The most common comorbidities were high blood pressure (61%), diabetes (38%) and osteoporosis (36%). Sixty-nine percent of patients were taking more than two oral treatments. The average duration of development of osteoarthritis of the knee was 9 years. The most common radiological stage was stage 1 (58%). The site was femorotibial in 88% of cases, patellofemoral in 4% of cases and bi or tri compartmental in 8% of cases. The osteoarthritis most often affected both knees in 86% of cases.

The average of the Lequesne index was 11. The average WOMAC index was 12 for pain, 1.5 for stiffness and 48 for dysfunction.

All the patients surveyed were on topical non-steroidal anti-inflammatory drugs (NSAIDs), 37.7% combined local herbal medicine with local NSAIDs, 53% were taking oral analgesics, and 19% were using oral non-steroidal anti-inflammatory drugs in the past month.

The average rating for time that takes the topical treatment to act was 2.9, for duration of action was 1.2, and for overall satisfaction was 2.8. No adverse effects of topical treatment have been reported.

For patients over 60 years old, better satisfaction was noted (the average score for overall satisfaction was 3.2).

Patients with a WOMAC Pain Index greater than 10 were less satisfied (the average overall satisfaction score was 1.1). Patients who took both topical NSAIDs and topical herbal medicine reported that topical NSAIDs were more effective in 66% of cases. Forty percent of patients recommended topical treatment to a friend or a family member.

Conclusion: In patients with chronic pain associated to osteoarthritis of the knee, topical analgesics are considered a good long-term therapeutic alternative. Patients are generally satisfied with the effectiveness of the local treatment, in particular the immediate effect felt after application, but less satisfied with the duration of action. Perception of effectiveness appears to be affected by age and degree of pain.

REFERENCES:

[1] D. Y. Wall, "Topical Nonsteroidal Anti-Inflammatory Drugs for Chronic Musculoskeletal Pain in Adults," p. 3, 2017.

[2] R. L. Barkin, "The Pharmacology of Topical Analgesics," *null*, vol. 125, no. sup1, pp. 7–18, Jul. 2013, doi: 10.1080/00325481.2013.1110566911.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2164

AB0594 IMPROVING OSTEOARTHRITIS CARE BY AUTOMATIC MEASUREMENT OF HIP EFFUSION USING AI

J. L. Jaremko[1], B. Felfeliyan[2], A. Rakkunedeth[1], B. Thejeel[1], V. Quinn-Laurin[1], M. Østergaard[3], P. G. Conaghan[4], R. Lambert[5], J. Ronsky[6], W. P. Maksymowych[5]. [1]*University of Alberta, Radiology and Diagnostic Imaging, Edmonton, Canada*; [2]*University of Calgary, Biomedical Engineering, Calgary, Canada*; [3]*Copenhagen University, Department of Clinical Medicine, København, Denmark*; [4]*University of Leeds, School of Medicine, Leeds, United Kingdom*; [5]*University of Alberta, Department of Medicine, Edmonton, Canada*; [6]*University of Calgary, Department of Mechanical and Manufacturing Engineering, Calgary, Canada*

Background: Osteoarthritis (OA) is the commonest disease affecting hip joints and has high prevalence across various age groups [1,2]. Effusion is a hallmark of OA and could represent a potential target for therapy [3–5]. Positive correlations of effusion to clinical outcomes are not well established, partly due to variability in manual assessment. Voxel-based volume quantification could reduce this variability [6].
Objectives: We examine the inter-observer agreement of manual assessment of voxel-based effusion volume from coronal STIR MRI sequences at two time points and examine the feasibility of using Artificial Intelligence (AI) for standalone volume assessment.
Methods: Our algorithm is based on Mask R-CNN [7] and was trained on labeled effusion regions in MRI slices from 68 patients with hip osteoarthritis. For validation, 2 human readers measured effusion from MRI STIR sequences of 25 patients at baseline and at 8 weeks follow-up. AI was used to measure effusion volume as an independent reader. Agreement between human readers and AI was assessed using absolute difference in volume (DV), Coefficients of Variation (CoV) and intraclass correlation coefficient (ICC).
Results: Effusion regions detected by AI closely correlated with manual segmentation (Figure 1) for all samples. Differences in volumes measured by each pair of readers are summarized in Table 1. Agreement was excellent between human readers (ICC=0.99) and for each reader vs AI (ICC = 0.85-0.87).

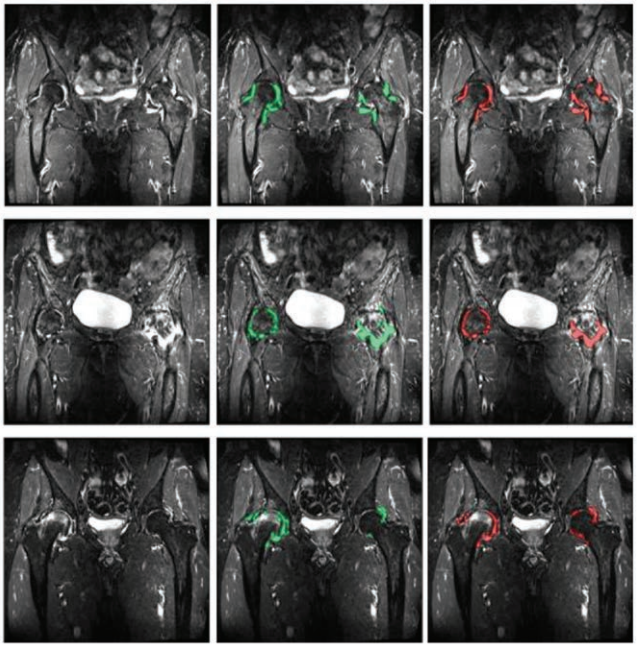


Figure 1. Mask overlays of regions of joint fluid detected by human readers (green, column 2) and AI (red, column 3) from 3 different patients. Raw MRI images are shown in column 1.

Table 1. Comparison of volumes measured in cubic millimeters and agreement between each pair of readers (with AI as the 3rd reader)

Volumes measured by readers		Agreement between reader pairs			
Reader	Overall Volume Mean ± Standard Deviation	Reader Pair	Difference in Volume Mean ± Standard Deviation	CoV	ICC
Reader 1	6943 ± 5845	Reader 1-2	1127 ± 900	0.21	0.99 [0.98, 1.0]
Reader 2	7638 ± 5619	Reader 1-AI	3311 ±1643	0.35	0.87 [0.7, 0.94]
AI	11014 ± 4454	Reader 2-AI	4151 ± 4986	0.27	0.85 [0.66,0.94]

Conclusion: Initial results of automatic effusion measurement using AI show high agreement with human experts. This has potential to reduce variability and save expert time in OA MRI assessment, and to lead to improved OA care.

REFERENCES:
[1] Sharif B, Garner R, Hennessy D, Sanmartin C, Flanagan WM, Marshall DA. Productivity costs of work loss associated with osteoarthritis in Canada from 2010 to 2031. Osteoarthritis Cartilage. 2017 Feb;25(2):249–58.
[2] Sharif B, Kopec J, Bansback N, Rahman MM, Flanagan WM, Wong H, et al. Projecting the direct cost burden of osteoarthritis in Canada using a microsimulation model. Osteoarthritis Cartilage. 2015 Oct;23(10):1654–63.
[3] Loeuille D, Chary-Valckenaere I, Champigneulle J, Rat A-C, Toussaint F, Pinzano-Watrin A, et al. Macroscopic and microscopic features of synovial membrane inflammation in the osteoarthritic knee: correlating magnetic resonance imaging findings with disease severity. Arthritis Rheum. 2005 Nov;52(11):3492–501.
[4] Fernandez-Madrid F, Karvonen RL, Teitge RA, Miller PR, An T, Negendank WG. Synovial thickening detected by MR imaging in osteoarthritis of the knee confirmed by biopsy as synovitis. Magn Reson Imaging. 1995;13(2):177–83.
[5] Atukorala I, Kwoh CK, Guermazi A, Roemer FW, Boudreau RM, Hannon MJ, et al. Synovitis in knee osteoarthritis: a precursor of disease? Ann Rheum Dis. 2016 Feb;75(2):390–5.
[6] Quinn-Laurin V, Thejeel B, Chauvin NA, Brandon TG, Weiss PF, Jaremko JL. Normal hip joint fluid volumes in healthy children of different ages, based on MRI volumetric quantitative measurement. Pediatr Radiol. 2020 Oct;50(11):1587–93.
[7] He K, Gkioxari G, Dollár P, Girshick R. Mask r-cnn. In: Proceedings of the IEEE international conference on computer vision. openaccess.thecvf.com; 2017. p. 2961–9.

Acknowledgements: Jacob Jaremko is supported by the AHS Chair in Diagnostic Imaging at the University of Alberta. Medical Imaging Consultants (MIC) funds musculoskeletal radiology fellowships for Vanessa Quinn-Laurin at the University of Alberta, and provides Jacob Jaremko and Robert Lambert with protected academic time. Banafshe Felfeliyan is supported by an Alberta Innovates Graduate Student Scholarship for Data-Enabled Innovation.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2196

AB0595 CURCUMA LONGA AND BOSWELLIA SERRATA FOR OSTEOARTHRITIS PAIN MANAGEMENT: A LITERATURE REVIEW OF SPECIFIC FORMULATED EXTRACTS FOR COMBINATION

V. Sethi[1], K. Siddiqui[1], M. Garg[2]. [1]*GSK Consumer Healthcare Pte Ltd, Pain Relief Medical Affairs, Singapore, Singapore*; [2]*University of Newcastle Callaghan, Nutraceuticals Research Program, Newcastle, Australia*

Background: The need for safe, effective pain management for osteoarthritis (OA) is important as the number of australian people with OA is expected to grow by 30% from year 2015 to year 2030. Extracts from *Boswellia serrata* and *Curcuma longa* are described to have anti-inflammatory and analgesic properties. Clinical studies have also reported efficacy for improving joint pain and stiffness and tolerability. A combination of *Boswellia serrata* and *Curcuma longa* formulated extracts might provide benefits in OA pain management.
Objectives: To review the literature describing the efficacy, safety and bioavailability of a formulated *Boswellia serrata* extract enriched with boswellic acids and a *Curcuma longa* extract formulated with piperine for OA pain management.
Methods: PubMed searches for studies reporting efficacy, safety, and/or bioavailability data for Boswellia and Curcumin formulations were conducted on 4 December 2020 with no publication date limitations.
Results: For the enriched Boswellia formulation, two clinical studies in OA assessing efficacy and one preclinical bioavailability study were identified[1,2,3]. For the curcumin formulation, 2 clinical studies were identified[4,5]. Two double-blind, randomized, parallel, placebo-controlled studies (each N=60) demonstrated significant improvement in Western Ontario and McMaster Universities OA index (WOMAC) pain and stiffness subscale scores in patients with knee OA receiving the enriched Boswellia formulation (100mg/d): In the first study[1], a 30-day treatment with enriched Boswellia, compared with placebo, significantly reduced WOMAC pain (–23.6; placebo, –5.6; P<0.0001) and stiffness (–18.8; placebo, –3.4; P=0.0014) scores. Improvement in pain visual analog scale (VAS) score was significant versus placebo at day 5 (P<0.05). In the second study[2], A 90-day treatment with enriched Boswellia also significantly improved WOMAC pain (–31.1; placebo, –8.4; P<0.0001) and stiffness (–27.7; placebo, –9.9; P<0.0001) scores versus placebo; Of note, a significant reduction in pain score and functional ability was observed as early as day 7. For the curcumin/piperine formulation, piperine was added to increase the bioavailability of curcumin in humans as established in a comparative bioavailability and pharmacokinetic study[4]. The results obtained in his study demonstrates that piperine enhances the oral bioavailability of curcumin without side effects. Curcumin/piperine monotherapy (350-400mg curcumin TID) was also shown to significantly reduce WOMAC, VAS and Lequesne's pain functional index (LPFI) compared to placebo in a randomized double-blind placebo-controlled parallel-group study (N=40)[5]. In a sub-study that measured inflammatory biomarkers (N=40), there is no significant difference in the magnitude of changes

in the inflammatory biomarkers (IL-4, IL-6, hs-CRP, TNF-α, TGF-β and mean ESR between the curcuminoid treatment group and the placebo group ($p>0.05$)[6].

Conclusion: Enriched boswellic acid and curcumin/piperine formulations demonstrate efficacy and safety for suitable treatment option: both ingredients, often cited as natural alternatives to address OA pain and stiffness could be evaluated to explore the potential benefit as a formulated combination.

REFERENCES:

[1] *Vishal et al. Int. J. Med. Sci. 2011, 8*
[2] *Sengupta et al. Int. J. Med. Sci. 2010, 7*
[3] *Sengupta et al. Mol Cell Biochem. 2011, 354:189-197.*
[4] *Shoba et al. Planta Med. 1998 May;64(4):353-6*
[5] *Panahi et al. Phytother. Res. 28: 1625–1631 (2014).*
[6] *Rahimnia A-R et al. Drug Res 2015; 65: 521–525.*

Disclosure of Interests: Vidhu Sethi Employee of: Employee of GSK Consumer Healthcare, Kamran Siddiqui Employee of: Employee of GSK Consumer Healthcare, Manohar Garg: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2247

AB0596 THE POSSIBLE CONTRIBUTION OF DEHYDROEPIANDROSTERONE SULFATE FOR OSTEOARTHRITIS OF THE KNEE

I. Bashkova[1,2], I. Madyanov[1,3], K. Misko[1], E. Preobrazhenskaia[4]. [1]*Chuvash State University named after I.N. Ulyanov, Department of Hospital Therapy, Cheboksary, Russian Federation*; [2]*Federal Center of Traumatology, Orthopedics and Endoprosthesis, Consultative polyclinic, Cheboksary, Russian Federation*; [3]*Republican Clinical Hospital, Department of Endocrinology, Cheboksary, Russian Federation*; [4]*Federal Center of Traumatology, Orthopedics and endoprosthesis, Scientific and Educational Department, Cheboksary, Russian Federation*

Background: Genetic, biochemical, metabolic, hormonal (primarily imbalance of sex hormones) factors are involved in the progression of osteoarthritis (OA). Dehydroepiandrosterone and its metabolite, dehydroepiandrosterone sulfate (DHEA-S), have a stress-limiting, anti-atherogenic, anti-diabetic, antihypertensive, anti-infective, immunomodulatory effects. Heroprotective effect is not excluded. Experimental studies have identified a relationship between an age-related decrease in DHEA-S levels and various adverse effects of aging.

Objectives: To identify the contribution of DHEA-S to the pathogenesis of OA, it`s advisable to conduct a comparative analysis of connection of the adrenal hormones with clinical, laboratory, radiological signs of the course of OA.

Methods: Patients with primary OA with a lesion of the knee joints (n=90, including 22 men) were examined. The age of the patients - 29-69 years, the duration of the disease – 1.5-20 years. The control group (n=114, including 26 men) was formed by random sampling of the population from healthy people, it`s representative by gender and age. We investigated the serum levels of cortisol, DHEA-S, estradiol (in women), testosterone (in men) and carried out radiography of the knee joints. OA was diagnosed using R.D. Althman, the x-ray stage-according to the classification of Kellgren and Lawrence. Statistically determined the mean value, standard deviation. Differences between the samples were considered statistically significant at $p<0.05$. To create a model of OA pathogenesis, the method of principal components of factor analysis was used.

Results: The DHEA-S level in the blood of patients with OA was lower than that of the control group (2.40±1.20 vs 3.66±1.45 μg/ml, $p=0.001$),in women-was lower, than in men (2.25±1.17 vs 2.89±1.23 μg/ml, $p=0.045$). In the control group, gender differences were not statistically significant ($p>0.05$). All patients with OA showed an inverse correlation between age and DHEA-S ($r=-0.511$, $p=0.0001$, and $r=-0.549$, $p=0.0001$ respectively). For factor analysis the most important signs for the course of OA are ESR levels, C-reactive protein (CRP) in the blood (as markers of inflammatory component of OA, or factor 2) were selected, and the radiological stage of OA (degenerative component, or factor 1). In women, we regarded factor 1 as «degenerative», the maximum contribution to total dispersion was made by the «x-ray stage» (+0.72). This symptom was opposed by the «DHEA-S level» (-0.79) and «estradiol blood level» (-0.68), which suggests a link between degenerative and dystrophic processes in the knee joint in women with OA and a decrease in blood levels of DHEA-S and estradiol. Factor 2 we interpreted as «inflammatory». This was indicated by the values of «CRP» (+0.66) and «ESR» (+0.64). The «inflammatory» factor in women from hormonal indicators was opposed by the «blood cortisol content» (-0.31) and «DHEA-S level» (-0.26). Factor 1 in men accounted for 46% of the total variance. Since factor 1 in men included the most significant «CRP» (+0.85), «X-ray stage» (+0.77) and «ESR» (+0.72), we called it «antidegenerative anti-inflammatory factor». The maximum value (modulo) in factor 1 is for DHEA-S (-0.76) and the lower is for testosterone (-0.53). So, in men, a sufficient level of DHEA-S is closely related to the «antidegenerative-anti-inflammatory» factor of OA pathogenesis and DHEA-S counteracts 2 key pathogenetic processes simultaneously-degenerative and inflammatory.

Conclusion: In women, a decrease in DHEA-S is a risk factor for the predominantly degenerative component of OA, in men it`s a universal risk factor, predisposing both to the development of inflammation and degenerative changes in the joints

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2308

AB0597 COMPLIANCE WITH CLINICAL PRACTICE GUIDELINES IN KNEE OSTEOARTHRITIS

M. Yasmine[1], L. Souebni[1], S. Miladi[1], A. Fazaa[1], S. Mariem[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: Knee osteoarthritis (OA) is a leading cause of disability among older adults. Recently, evidence-based guidelines for the comprehensive management of osteoarthritis (OA) were developed by the American College of Rheumatology (ACR).

Objectives: The aim of this study was to assess compliance of doctors with ACR 2019 clinical practice guidelines for the management of knee OA.

Methods: We conducted a prospective study including rheumatologists and general practitioners. The doctors were invited to answer a structured questionnaire via Google Form. The outcomes of interest concerned the medical management of knee OA as well as alternative medicine.

Results: The study included 100 doctors: 75 rheumatologists and 25 general practitioners. Almost half of them (49%) have been practicing medicine for more than 10 years. Forty four percent of doctors see between 10 to 20 patients with knee OA per month and 47% of them declared seeing more than 20 patients. Regarding the pharmacological treatment of knee OA flares, oral Non-steroidal Anti-inflammatory drug (NSAIDs) was the initial molecule of choice (91%) followed by grade I analgesics (86 %) and topical NSAIDs (68%). Tramadol and non-Tramadol opioids as well as intraarticular glucocorticoid injections were prescribed respectively in 41% and 46 % of cases. Glucosamine and chondroitin sulfate were prescribed in 49% and 54% of cases respectively and as a combination in 20% of cases. The reasons for non-prescribing these molecules were non-affordable prices (n=19), a lack of efficacy (n=6) and potential sides effects (n=1). Seventy three percent of doctors prescribe hyaluronic acid injections, with a frequency of three weekly injections in 38.7 % of cases and according to the response to the first injection in 61.3% of cases. The combination of both corticosteroids and hyaluronic acid injection was preferred in 38% of cases. The majority of doctors (84%) referred their patients to physical therapy as a first-line prescription (82.1%) or after medical treatment failure (17.9%). The use of alternative medicine was at follows: acupuncture (42.7%), prolotherapy (28.1%) and platelet-rich plasma injections (16.7%). Thirty eight doctors recommended against alternative medicine.

Conclusion: Our study showed a poor compliance to guidelines regarding the use of intra-articular injections and alternative medicine. Even though, these guidelines provide direction for clinicians, doctors and patients should engage in shared decision-making that accounts for patients' values, preferences, and susceptibilities.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2896

AB0598 EFFICACY OF ULTRASOUND GUIDED INJECTIONS OF A CROSS-LINKED SODIUM HYALURONATE COMBINED WITH TRIAMCINOLONE HEXACETONIDE FOR OSTEOARTHRITIS OF THE KNEE

F. Porta[1], G. Filippou[2], G. Sakellariou[3]. [1]*Florence, Istituto di Neuroscienze, Florence, Italy*; [2]*Luigi Sacco University Hospital, Rheumatology Department, Milano, Italy*; [3]*University of Pavia, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy*

Background: According to guidelines, the use of steroid and/or hyaluronate (HA) intra-articular injections for knee osteoarthritis (KOA) is controversial. Heterogeneity of studies and difference in HAs characteristics does not allow to draw safe conclusions. One of the major concerns is the accuracy of the procedure as up to 1/3 of injections could miss joint space when performed blindly (1), negatively affecting the efficacy of HA that needs to be placed correctly in the joint space

Objectives: The aim of our study was to evaluate the longterm efficacy of a novel association of a Cross-Linked Sodium Hyaluronate Combined With Triamcinolone Hexacetonide (SHCTH) in patients with KOA in a real life setting.

Methods: We retrospectively evaluated the clinical and ultrasonographic (US) data of patients (pts) affected by symptomatic KOA with intra-articular injections of SHCTH (1 injection every 6 months). Pts with concomitant inflammatory arthropaties were excluded. US guidance was carried out with the "in plane" technique choosing either the lateral suprapatellar or midpatellar approach. All pts were evaluated for pain with a VAS 0-10 for pain at baseline and after 2 weeks, 1, 3, 6, 9 and 12 months, with the WOMAC questionnaire and with US, scoring joint effusion, synovial hypertrophy (SH) and power Doppler (PD) synovial signal. Due to the retrospective design, the WOMAC data were available as VAS or Likert scales; to allow comparability these values were standardized. Clinical and US variables at different time points were compared using the Wilcoxon rank sing test, the McNemar test or the paired samples t-test, depending on the variable.

Results: 49 knees (43 pts, median age 70.6 years, 24 women) were included in the study. Kellgren Lawrence grade was 1 for 5 knees, 2 for 10, 3 for 17 and 4 for 9. SHCTH was delivered correctly in the joint space in all patients as assessed by US check during the injection and no side effects occurred. Of the 49 knees, 28 had an available 6 months follow-up, while 21 completed the 12 months follow-up, with an attrition mostly related to the COVID 19 pandemic. A rapid and sustained statistically significant decrease of both VAS pain and the WOMAC subscales was observed. The reduction of pain was already significant at 2 weeks, probably thanks to the corticosteroid component. At US evaluation, effusion significantly decreased at all time points. Although SH scores also significantly decreased, the effect on the proportion of affected joints was not as relevant. The reduction of PD was significant until month 9. Detailed results are presented in Table 1.
Conclusion: Our data show that US guided SHCTH injections provide a rapid and sustained clinical response in patients with symptomatic OA. Besides the effect on pain, the US data confirm the effect of the drug on the inflammation. US guidance guaranteed the correct placement of the product in all patients and eliminated the bias of wrong placement that may occur with blind injections, thus allowing to draw safe conclusions on the efficacy of SHCTH for the treatment of KOA.
REFERENCES:
[1] Jones A, Regan M, Ledingham J, *et al.* Importance of placement of intra-articular steroid injections. *BMJ* 1993;**307**:1329–30.

Table 1. Clinical and US measures. p values refer to the comparison with baseline. WOMAC subscales were compared by paired samples t test. *hypothesis test not applicable

	baseline	2 weeks	1 month	3 months	6 months	9 months	12 months
VAS (median,IQR)	6 (5-8)	3 (1-4.25) p<0.0001	2 (0.5-3-5) p<0.0001	1.5 (0-3) p<0.0001	1.5 (0-4) p<0.0001	1 (0-2.75) p<0.0001	1 (0-3.25) p<0.0001
WOMAC pain	-	-	p 0.028	p 0.0004	p 0.0036	p 0.0096	p 0.0064
WOMAC stiffness	-	-	p 0.048	p 0.040	p 0.0388	p<0.0001	p 0.0083
WOMAC function	-	-	p 0.043	p 0.0005	p 0.0014	p 0.01	p 0.007
Effusion 0-3 (median,IQR)	2 (1-2)	-	1 (0-1) p<0.0001	1 (0-1) p<0.0001	1 (0-1) p 0.0001	0 (0-1) p<0.0001	1 (0-1) p<0.0001
Synovial Hypertrophy 0-3 (median,IQR)	1 (1-2)	-	1 (1-1) p 0.002	1 (1-1) p 0.0001	1 (1-1) p 0.0001	1 (0-1) p 0.0001	1 (0.5-1) p 0.0001
PD 0-3 (median,IQR)	0 (0-0)	-	0 (0-0) p 0.03	0 (0-0) p 0.03	0 (0-0) P 0.06	1 (0-1) p 0.01	0 (0-0) p 0.31

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3035

AB0599 EFFICACY AND SAFETY OF COMBINATION THERAPY WITH NSAIDS AND ANTICONVULSANT, COMPARED WITH NSAID MONOTHERAPY FOR CHRONIC PAIN IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE JOINTS

E. Filatova[1], L. Alekseeva2, E. Taskina[1], N. Kashevarova[1], A. Lila[1], E. Sharapova3. *[1]VA Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*; *[1]VA Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*; *[1]VA Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*

Background: In 20-44% of patients with osteoarthritis of the knee joints neuroplastic changes occur due to central sensitization (1,2), which is the rationale for complex therapy, including centrally acting drugs, for more effective pain control.
Objectives: To evaluate the efficacy and safety of combination therapy with NSAID and anticonvulsant in comparison with NSAID monotherapy in patients with osteoarthritis of the knee joints and signs of central sensitization or nocyplastic pain
Methods: The study included 60 women with osteoarthritis of the knee joints (OAK) with signs of nocyplastic pain. Nocyplastic pain were revealed by neuropathic scales (DN4 questionnaire > 4 points), subject to the absence of patients lesions of the somatosensory nervous system. All patients were randomized into two age- and sex-matched groups: group I (n=30) received combination therapy with aceclofenac and pregabalin, group II (n=30) - monotherapy with aceclofenac. The observation period was 42 days and included three visits. All patients underwent a clinical and neurological examination, we assessed the overall WOMAC index, pain intensity at rest with the visual analogue scale (VAS), nocyplastic pain (DN4 and Pain DETECT questionnaires), anxiety and depression (HADS questionnaire) and the quality of life (EQ-5D questionnaire).
Results: The intensity of pain at rest according to VAS in patients of group I significantly decreased after 14 days (visit 2) and even further after 42 days (visit 3) (64.0 [50.0; 72.0] vs 49.0 [33.0; 55.0] vs 33.5 [22.0; 49.0] p = 0.006). In group II the intensity of pain at rest also decreased after 14 days (visit 2) (63.0 [41.0; 72.0] vs 48.0 [35.0; 58.0] p <0.001), however, did not change significantly from visit 2 to 3 (48.0 [35.0; 58.0] vs 44.0 [35.0; 60.0]) (p = 0.57).
The dynamics of neuropathic pain indicators according to the DN4 and Pain DETECT questionnaires was as follows: group I (visit 1-3) DN4 (6.0 [5.0; 7.0] vs 3.0[1.0; 4.0], p=0.001) and Pain DETECT (17.0 [16.0;20.0] vs 8.0 [5.0; 14.0], p=0.001). Group II DN4 (6.0[5.0;6.0] vs 5,0 [3,0; 6,0],p=0,05), Pain DETECT (17,0 [15,0; 19,0] vs 16.0 [14,0; 19,0],p=0,53).
The overall WOMAC index decreased significantly in both groups.
Significant positive dynamics in terms of the level of anxiety (9.0 [7.0;14.0] vs 7.0 [4.0;10.0], p=0.001), depression (8.0 [5.0;10.0] vs 6.5 [4.0;9.0], p= 0.03) and quality of life (0.52 [-0.02;0.52] vs 0.52 [0.52;0.59], p=0.01) was observed compared to baseline in group I but not in group II. Before the start of therapy, the groups were comparable in the studied parameters, however, after 42 days, anxiety (7.0 [4.0;10.0] vs 9.0 [7.0;12.0], p=0.02) and depression levels (6.5 [4.0;9.0] vs 8.0 [6.0;9.0], p=0.05) were statistically different. Moreover, the median anxiety and depression levels still exceeded 7 points in group II, indicating the presence of anxiety and depression.
Conclusion: Combination therapy of chronic pain with signs of nocyplastic pain with pregabalin and aceclofenac in patients with knee osteoarthritis has been shown to be effective in terms of pain intensity, the presence of neuropathic descriptors and the severity of anxiety compared with aceclofenac alone.
REFERENCES:
[1] Hochman JR, French MR, Bermingham SL, Hawker GA. The nerve of osteoarthritis pain. Arthritis Care Res (Hoboken). 2010;62:1019–23.
[2] Hochman JR, Gagliese L, Davis AM, Hawker GA. Neuropathic pain symptoms in a community knee OA cohort. Osteoarthr Cartil. 2011;19:647–54.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3062

AB0600 VISCOSUPPLEMENTATION VERSUS PHYSICAL REHABILITATION IN KNEE OSTEOARTHRITIS COMPARATIVE STUDY ABOUT 117 CASES

S. Lahrichi[1], K. Nassar[1], S. Janani[1]. *[1]University Hospital of IBN ROCHD, Rheumatology, Casablanca, Morocco*

Background: Viscosupplementation with hyaluronic acid, and physical rehabilitation are part of the adjunct treatments for osteoarthritis, and particularly knee osteoarthritis.They can be used alone or combined.
Objectives: To compare the efficacy of rehabilitation and viscosupplementation in patients followed for stage II and III osteoarthritis.
Methods: This is a cross-sectional study, conducted in the department of rheumatology of the University Hospital ofIbn Rochd, Casablanca, between August 2020 and December 2020. Inclusion criteria: patients with stage II and III knee osteoarthritis fulfilling the ACR criteria. The diagnosis was made on standard x-rays including antero-posterior and lateral views. The functionalassessmentwas made with functional algo indices, WOMAC and Lequesnne. Pain was assessed with a visual analogue scale (VAS) on Day 0 and after 3 months. The patients were divided into 3 groups of 39 patients, the first (G1) received an infiltration of hyaluronic acid according to different protocols (multiple injections or single injection), the second (G2) benefited from a rehabilitation program twiceor three timesa week for three months, and the third group (G3) benefited from viscosupplementation associated with rehabilitation. Patients who received an intra-articular corticosteroid injection in the last 3 months were excluded.
Results: There were 117 patients. The mean age was 59.6 ± 8.6, with a female predominance of 96.8%. Knee osteoarthritis was clinically patent for 5.8 years, with an average of 7.4 painful flares. Gonarthrosis was bicompartmental in 52 patients and tri-compartmental in 18 patients. 45% had a family history of osteoarthritis. 28% were hypertensive, 18 patients were diabetic and 51.87% were obese according to the body mass index, with an average of 30.5 ± 5.2 kg/m^2. 65% had already received oral anti-arthritis drugs for an average of 1 year. Functional improvement was approximately 38% in G1, 26% in G2, and 42% in G3. A significant algo-functional improvement was noted in G1 (p = 0.04) and G3 (p = 0.03). LEQUESNE's index went from an average of 8 in the 3 groups to an average of 4 inG1 and G3 versus 6 in G2, which corresponds to an average handicap (p = 0.2). The final value of the WOMAC index in G1 was 26.57 versus 32.21 in G2 (p = 0.01) and versus 22.36 in G3 (p = 0.02).
Conclusion: In our study, the final evaluation showed a decrease in pain and an improvement in functional capacity ranging from 36 to 58%. This improvement in algo-functional indices was significantly more marked in G3[1]. Our study shows that the combination of visco-supplementation with physical rehabilitation gives better results by improving the algo-functional indices than by visco-supplementation alone. Our findings are consistent with the results of the literature[2].
REFERENCES:
[1] Lebib S, Ben SalahFZ, Ksibi I, Dziri C. The´rapeutiques non me´dicamen-teuses de l'arthrose des membres infe´rieurs: e´tats de lieux et perspectives. RevFr Geriat Gerontol 2006;126(XIII):296–30
[2] Bruyere O, Cooper C, Pelletier JP, Branco J, Luisa BrandiM, GuilleminF, etal. AnalgorithmrecommendationforthemanagementofkneeosteoarthritisinEuropeandinternationally:areportfromataskforceoftheEuropeanSocietyforClinicalandEconomicAspectsofOsteoporosisandOsteoarthritis(ESCEO). Semin Arthritis Rheum. 2014;44(3):253–26
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3109

AB0601

COMPARISON OF THE EFFECT OF DIFFERENT PHYSICAL THERAPY PROGRAM IN THE REHABILITATION OF KNEE OSTEOARTHRITIS PATIENTS

A. Vizdoaga[1], V. Salaru[2], M. Cebanu[3], V. Sadovici-Bobeica[4], N. Loghin-Oprea[4], L. Mazur-Nicorici[4], T. Rotaru[4], M. Garabajiu[2], M. Mazur[4]. *[1]Nicolae Testemitanu State University of Medicine and Pharmacy, University Medical Rehabilitation Center, Chisinau, Moldova, Republic of*; *[2]Nicolae Testemitanu State University of Medicine and Pharmacy, Family Medicine, Chisinau, Moldova, Republic of*; *[3]Nicolae Testemitanu State University of Medicine and Pharmacy, Emergency medicine, Chisinau, Moldova, Republic of*; *[4]Nicolae Testemitanu State University of Medicine and Pharmacy, Internal Medicine, Chisinau, Moldova, Republic of*

Background: Knee osteoarthritis (OA) is an increasingly common and disabling problem in worldwide. Exercises are considered the cornerstone of non-surgical management of knee OA and is recommended in all current clinical guidelines. The diversity of exercise programs determines the need to compare their efficiency, in order to recommend the best option for the patient.
Objectives: The aim of the present study was to compare the effect on knee functionality of conventional exercises program and combinate with manual therapy in patients with knee osteoarthritis.
Methods: 164 patients that fulfilled the ACR classification criteria for knee osteoarthritis (127 females and 37 males) ranging in age from 42 to 84 years (mean 62,2 SD 8,76), participated in a 10 days two-arm randomized trial. One group (Gr.1) received an exercises program, the other group additionally manual therapy methods (Gr.2). Pain and function were measured with a Visual Analogue Scale (VAS, mm) and Knee Injury and Osteoarthritis Outcomes Score (KOOS) with 5 domains (Pain, Symptoms, Activity in Daily Living (ADL), Sport and recreation (Sport/rec.) and Quality of life (QoL)).
Results: In the Gr.1 were 82 patients mean age 61,8±9,2 years and in Gr.2 – 82 patients 62,7±8,3 years (p>0.05). The initial level of pain (63,4±14,2 vs 60,2±18,8mm) and knee functionality according to KOOS (Tab1.) were similar in both groups, p>0.05. After 10 days rehabilitation program, VAS in Gr.1 was 39,6±14,8 mm, in Gr.2- 28,5±11,6 mm, (p<0.01). The KOOS results at the end of the rehabilitation program were with improvement, statistically significative in the Gr.2 (p<0,05).

Table 1. The KOOS results at baseline and after 10 days of rehabilitation program.

KOOS scales	Group 1		Group 2	
(M±SD), %	Baseline	After 10 days	Baseline	After 10 days
Pain	55,5 ±13,8	63,4±13,6	53,0±22,3	64,3±19,1
Symptoms	59,0±18,7	65,6±18,1	56,6±19,0	69,0±15,9
ADL	46,3±15,5	54,5±16,0	43,0±19,9	55,1±18,2
Sport/rec	15,6±17,3	23,1±19,6	16,0±24,3	30,5±23,6
QoL	29,3±22,2	36,5± 22,9	34,8±23,9	50,6±18,9

Conclusion: The reduction of pain and recovery of function were found in both groups, with better results in patients who received manual therapy and exercises program. This study supports the routine manual therapy in rehabilitation program in patients with knee osteoarthritis.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3570

AB0602

IMPACT OF SOCIOECONOMIC FACTORS ON PAIN AND FUNCTION IN KNEE OSTEOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

T. W. Swinnen[1], M. Willems[2], I. Jonkers[2], F. P. Luyten[3], J. Vanrenterghem[1], S. Verschueren[1]. *[1]KU Leuven, Research Group for Musculoskeletal Rehabilitation, Department of Rehabilitation Sciences, Leuven, Belgium*; *[2]KU Leuven, Human Movement Biomechanics Research Group, Department of Movement Sciences, Leuven, Belgium*; *[3]KU Leuven, Skeletal Biology and Engineering Research Center, Leuven, Belgium*

Background: The personal and societal burden of knee osteoarthritis (KOA) urges the research community to identify factors that predict its onset and progression. A mechanistic understanding of disease is currently lacking but needed to develop targeted interventions. Traditionally, risk factors for KOA are termed 'local' to the joint or 'systemic' referring to whole-body systems. There are however clear indications in the scientific literature that contextual factors such as socioeconomic position merit further scientific scrutiny, in order to justify a more biopsychosocial view on risk factors in KOA.
Objectives: The aims of this systematic literature review were to assess the inclusion of socioeconomic factors in KOA research and to identify the impact of socioeconomic factors on pain and function in KOA.
Methods: Major bibliographic databases, namely Medline, Embase, CINAHL, Web of Science and Cochrane, were independently screened by two reviewers (plus one to resolve conflicts) to identify research articles dealing with socioeconomic factors in the KOA population without arthroplasty. Included studies had to quantify the relationship between socioeconomic factors and pain or function. Main exclusion criteria were: a qualitative design, subject age below 16 years and articles not written in English or Dutch. Methodological quality was assessed via the Cochrane risk of bias tools for randomized (ROB-II) and non-randomized intervention studies (ROBIN-I) and the Newcastle-Ottawa Scale for assessing the quality of non-randomised studies. Due to heterogeneity of studies with respect to outcomes assessed and analyses performed, no meta-analysis was performed.
Results: Following de-duplication, 7639 articles were available for screening (120 conflicts resolved without a third reader). In 4112 articles, the KOA population was confirmed. 1906 (25%) were excluded because of knee arthroplasty and 1621 (21%) because of other issues related to the population definition. Socioeconomic factors could not be identified in 4058 (53%) papers and were adjusted for in 211 (3%) articles. In the remaining papers covering pain (n=110) and/or function (n=81), education (62%) and race (37%) were most frequently assessed as socioeconomic factors. A huge variety of mainly dichotomous or ordinal socioeconomic outcomes was found without further methodological justification nor sensitivity analysis to unravel the impact of selected categories. Although the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was the most popular instrument to assess pain and function, data pooling was not possible as socioeconomic factors estimates were part of multilevel models in most studies. Overall results showed that lower education and African American race were consistent predictors of pain and poor function, but those effects diminished or disappeared when psychological aspects (e.g. discrimination) or poverty estimates were taken into account. When function was assessed using self-reported outcomes, the impact of socioeconomic factors was more clear versus performance-based instruments. Quality of research was low to moderate and the moderating or mediating impact of socioeconomic factors on intervention effects in KOA is understudied.
Conclusion: Research on contextual socioeconomic factors in KOA is insufficiently addressed and their assessment is highly variable methodologically. Following this systematic literature review, we can highlight the importance of implementing a standardised and feasible set of socioeconomic outcomes in KOA trials[1], as well as the importance of public availability of research databases including these factors. Future research should prioritise the underlying mechanisms in the effect of especially education and race on pain and function and assess its impact on intervention effects to fuel novel (non-)pharmacological approaches in KOA.
REFERENCES:
[1] Smith TO et al. The OMERACT-OARSI Core Domain Set for Measurement in Clinical Trials of Hip and/or Knee Osteoarthritis J Rheumatol 2019. 46:981–9.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3634

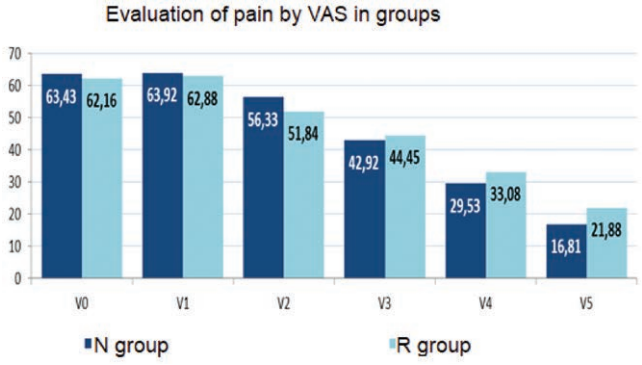
AB0603

THE NEW POSSIBILITIES OF USING CHONDROITIN SULFATE IN PATIENTS WITH KNEE OSTEOARTHRITIS

E. Sharapova[1], N. Kashevarova[1], E. Taskina[1], D. Kusevich[1], L. Alekseeva[1,2], A. Lila[2,3]. *[1]V.A. Nasonova Research Institute of Rheumatology, Laboratory of Osteoarthritis, Moscow, Russian Federation*; *[2]Russian Medical Academy of Continuous Professional Education, Rheumatology, Moscow, Russian Federation*; *[3]V.A. Nasonova Research Institute of Rheumatology, director, Moscow, Russian Federation*

Background: Administration of Chondroitin Sulfate for treatment of osteoarthritis included treatment types include systemic and parenteral therapies. The benefits of local therapies between difference route is ambivalent.
Objectives: To evaluate effectiveness and safety of Chondroitin Sulfate (CS) by intramuscular and concomitant (intramuscular and intraarticular) route of administration in patients with knee osteoarthritis (OA).
Methods: In total 150 patients with knee OA according by ACR criteria and with radiological stages 2 and 3 according to Kellgren-Lawrence were enrolled. Patients were divided by 2 groups: 75 patients (R) received course of 25 intramuscular injection every other day: at the first 3 injection's in dose 100 mg, and in continue in dose 200 mg, 75 patients in 2nd group (N) received 5 intra-articular injections in target knee in dose 200 mg once per 3 days, in continue 16 intramuscular injections every other day in dose 200 mg. All patients received NSAID - meloxicam in stable dose 15 mg per day. All patients were checked by WOMAC, pain by visual analog scale (VAS), McGill Pain Questionnaire (MPQ).

At the baseline, standard clinical examination for all patients were blood tests, urine test, coagulation panel and ECG.
Results: After comparing of two groups by the end of course the intensity of pain by VAS was significantly greater in R group (21,88±13,24 vs 16,81±13,49; p<0,0001). There were no significant differences between groups in improvement of WOMAC, WOMAC subscales and MPQ from baseline. Serious adverse events (AE) were absent. 11 AE's were detected 3,3% (5/150), but in 100% of cases AE's were resolved by the end of course.
Conclusion: CS is effective decreased intensity of pain and stiffness, improved functional ability of joints both intramuscular and concomitant route of administration. However, significantly greater results at pain intensity by VAS shows combination: pain intensity by the end of course was significantly lower in group with concomitant intramuscular and intra-articular injections. Probably, it was associated with faster resolution of synovitis by intraarticular route of administration, that leads to choose this route for patients with comorbidity.

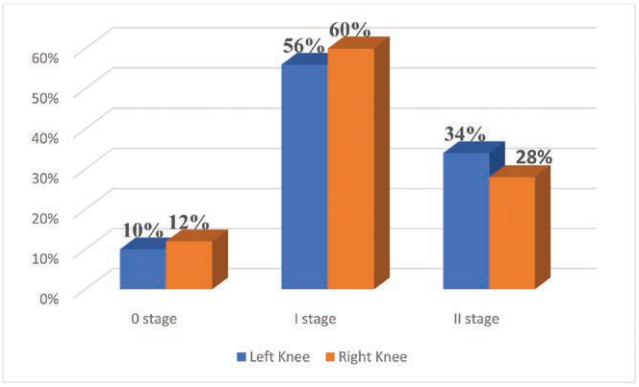


Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3778

AB0604 FACTORS ASSOCIATED WITH PAIN IN EARLY KNEE OSTEOARTHRITIS (PRELIMINARY DATA)

L. Alekseeva[1,2], E. Taskina[1], N. Kashevarova[1], K. Telyshev[1], E. Strebkova[1], S. Anikin[1], E. Sharapova[1], A. Lila[1,2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory of Osteoarthritis, Moscow, Russian Federation*; [2]*Russian Medical Academy of Postgraduate Education, Rheumatology, Moscow, Russian Federation*

Background:
Objectives: To identify factors associated with pain in patients with early knee osteoarthritis fulfilling ESKOA criteria [1].
Methods: 50 patients (46 women (92%); 4 men (8%)) fulfilling ESKOA criteria were enrolled in the trial, every participant signed up the consent form. Median age of patients was 47 ± 8 yrs (36 – 63 yrs), body mass index (BMI) was 28.5 ± 4.9 kg/m^2 (40% of patients had obesity). Every patient, after signing the standard informed consent form, was addressed to a physician, who would fill in an individual case report form (CRF), including anthropometric parameters, history of OA, comorbidities and physical examination data. Knee pain was also assessed with the use of visual analog scale (VAS). All participants underwent knee X-ray according to the standardized fixed flexion protocol with the use of positioning frame [2].
Results: Most of the patients (70%) were between the ages of 35 and 50 and only 15 of them (30%) were older than 50 years. Median knee pain duration was found to be 16 (12-20) weeks, intensity of VAS – knee pain was 46 mm (42-50). Median number of episodes of knee pain (in the last 6 months) was 3 (2-6); 30 participants (60%) had episodes of knee pain lasting less than a week, 8 of them (6%) had pain lasting for around a week, 12 of them (24%) had episodes of pain lasting more than one week. In most patients (74%) pain relieved with time, without any additional therapy. Most of the patients had episodes of knee pain linked to increased overload (48 (96%)), when squatting (41 (82%)), most of the patients also reported pain when climbing up and down the stairs (80%) and short joint stiffness when starting movement (76%). Knee pain after sitting was reported in 54% of cases and 20 participants (40%) also reported some walking limitations due to knee discomfort.
Knee X-ray revealed that most of the patients had I Kellgren&Lawrence (K&L) stage knee OA (picture 1). All the included participants had ESR (7 (5-10 mm/hr)) and CRP (1.24 (0.8-2.2 mg/l)) within normal range.
Picture 1 – Radiological knee OA stage (K&L) distribution in the study group



In the Spearman correlation analysis, we have estimated the factors, which may be associated with more severe pain in patients with early knee OA fulfilling the ESKOA criteria. We found out that higher BMI (r=0.38, p=0.02), presence of metabolic syndrome (r=0.37, p=0.008) and hypertension (r=0.29, p=0.04), as well as walking limitations (r=0.33, p=0.008) are associated with knee pain.
Conclusion: The use of ESKOA criteria in patients with short duration of knee pain can facilitate diagnosis of osteoarthritis on an early stage. In addition, the acquired data show that timely diagnosis and correction of certain components of metabolic syndrome may be beneficial for the course of knee pain intensity in patients with early knee OA, further continuation of this trial is necessary.
REFERENCES:
[1] Migliore A et al. Rheumatol Int. 2017 Aug;37(8):1227-1236.
[2] Mazzuca SA et al. Osteoarthritis Cartilage. 2008 Dec;16(12):1555-9.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3829

AB0605 ACTIGRAPHY-BASED PHYSICAL ACTIVITY MONITORING IN PATIENTS WITH KNEE OSTEOARTHRITIS AND COMORBID FIBROMYALGIA

O. Dzekan[1]. [1]*Vinnytsya Regional Clinical Hospital, Rheumatology, Vinnytsya, Ukraine*

Background: Low physical activity (PA) levels are common in patients with diseases associated with pain syndrome, such as osteoarthritis (OA) of the knee joints. Recent studies show that OA may be accompanied by concomitant fibromyalgia (FM) – a chronic pain syndrome associated with sedentary behavior [1]. As far as low PA levels are associated with poor quality of life and higher all-cause mortality, PA measurement in patients with knee OA and concomitant FM is of considerable interest [2,3].
Objectives: The aim of this study was to investigate and compare physical activity measured by an actigraph in knee OA patients with and without comorbid FM.
Methods: A total of 70 patients with painful knee osteoarthritis (OA) – 35 subjects - (30 females and 5 males) with concomitant fibromyalgia (FM) aged 59.8±14.9 (M±SD) years and 35 patients (30 females and 5 males) without concomitant FM aged 58.5±15.7 (M±SD) years were enrolled in the study. 35 healthy controls of the same age and gender underwent the same investigation. OA diagnosis was established according to ACR 1986 Osteoarthritis Knee Criteria. FM was diagnosed if both modified 2010 ACR diagnostic criteria and 2016 Fibromyalgia Diagnostic Criteria were met. All participants wore an actigraph (GT3X model accelerometer) on the wrist for the period of 5 working days. Average daily minutes in light, moderate and vigorous PA were calculated.
Results: All OA patients with and without FM spent significantly less time in vigorous PA compared to controls. Obtained results did not indicate significant difference between time in vigorous activity in OA patients with and without FM. Patients with OA alone showed insignificant decrease in time in moderate activity in comparison with healthy subjects. OA patients with comorbid FM showed significantly less time in moderate activity compared to OA patients without FM and healthy individuals.
Conclusion: Our study results revealed that patients with painful knee OA and comorbid FM have greater activity limitations than patients with painful knee OA alone and healthy individuals.
REFERENCES:
[1] Mahgoub MY, Elnady BM, Abdelkader HS, Abdelhalem RA, HassanWA. Comorbidity of Fibromyalgia in Primary Knee Osteoarthritis: Potential Impact on Functional Status and Quality of Life. Open Access Rheumatol. 2020;12: 55—63.

[2] Ali K. Q. Al-Rubaye, Klara Johansson, Laith Alrubaiy. The association of health behavioral risk factors with quality of life in northern Sweden—A cross-sectional survey. J Gen Fam Med. 2020 Sep; 21(5): 167–177.
[3] GBD 2017 Mortality Collaborators. Global, regional, and national age-sex-specific mortality and life expectancy, 1950–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1684–735. pmid:30496102

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4189

Osteoporosis

AB0606 IMPACT OF ABDOMINAL AORTIC CALCIFICATION AND SERUM CREATININE-TO-CYSTATIN C RATIO TO BONE FRAGILITY FRACTURE

I. Yoshii[1]. [1]*Yoshii Hospital, Rheumatology and Musculoskeletal Medicine, Shimanto City, Japan*

Background: Relationship between bone fragility fracture (BFF) and abdominal aortic calcification (AAC) has been discussed in recent decade.
Objectives: Now we investigated the relationship between the two and a new factor of BFF: serum creatinine-to cystatin C ratio (Cr/CysC).
Methods: A total of nine-hundred and thirty one osteoporotic patients were recruited. Diagnosis of osteoporosis was indexed by the criteria of Japanese Primary Osteoporosis Diagnostic Criteria. Patient's lumbar spine X-ray pictures were taken and dual-energy X-ray absorptiometry (DXA) of lumbar spine and hip joint were tested at the same time, and all of them were followed us for more than one year up to nine years with at least an administration of vitamin D. Anti-osteoporotic drugs were administrated for 660 patients.
Vertebral compression fracture (VF) and AAC were evaluated with lateral view of X-ray picture. VF was classified in accordance with Semi-quantified method (SQ), and AAC was classified as follows: Grade0; No calcification, Grade1; Partial calcification not continued over one vertebral height, Grade2; Calcification continuous over one vertebral height. BFF history of the patients except of VF was harvested from the medical record and with interview. Patients' background at first measurement were measured and Cr/CysC was calculated as well. Prevalence of BFF at the baseline for each grade with SQ was compared according to the grade of AAC. Background factors including bone mineral densities (BMD) of the lumbar spine and hip joint measured using DXA were compared for each AAC grade.
Occurrence of BFF was picked up during following up (BFF_F/U) of the patients. Prevalence of BFF_F/U for each ACC grade was statistically compared, and relationship between BFF_F/U and factors at the baseline was statistically evaluated.
Results: A total of 219 of Grade0, 428 of Grade1, and 278 of Grade2 were recruited. Prevalence of BFF at baseline for each VF group was 182, 16, 9, and 12 for Grade0, 138, 98, 122, and 70 for Grade1, and 53, 45, 82, and 144 for Grade2, with Grade-0, Grade-1, Grade-2, and Grade-3 by SQ, respectively (p<0.01). Factors that demonstrated significant correlation with occurrence of BFF were sex, age, BMD of the lumbar spine and the hip joint, and Cr/CysC with univariate mode binary logistic regression anaysis. However, Cr/CysC did not demonstrate significant correlation using multivariate model.
Occurrence of BFF_F/U for each AAC group was 26, 90, and 82 for Grade0, Grade1, and Grade2, respectively (p<0.01). The only factor that demonstrated significantly correlated with occurrence of BFF_F/U was Cr/CysC in the Grade1 and the Grade2 of the AAC classification.
Conclusion: ACC grade significantly correlates with occurrence of BFF. Cr/CysC also significantly correlates with occurrence of BFF after follow up under presence of AAC.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.269

AB0607 DO HIP STRUCTURAL ANALYSIS MEASUREMENTS PREDICT FRACTURE RISK IN PATIENTS WITH POLYMYALGIA RHEUMATICA?

R. Ark[1,2], M. Bukhari[1,2]. [1]*Lancaster University, Lancaster Medical School, Lancaster, United Kingdom*; [2]*University Hospitals of Morecambe Bay NHS Foundation Trust, Royal Lancaster Infirmary, Lancaster, United Kingdom*

Background: Polymyalgia Rheumatica (PMR) is an inflammatory condition which commonly affects the elderly. Risk of fracture is higher in this group of patients compared to the general population and can lead to increased morbidity and mortality (1). Hip structural analysis (HSA) is a technique that uses dual-energy X-ray absorptiometry (DEXA) images to assess hip bone structure (2).
Objectives: To identify whether HSA measurements help predict fracture in patients with PMR.
Methods: Data were collected from June 2004 to October 2010 from PMR patients who had a DEXA scan at a District General Hospital. This included hip axis length (HAL), cross-sectional area (CSA), cross-sectional moment of inertia (CSMI), distance from centre of femoral head to centre of femoral neck (D1) and to inter-trochanteric line (D2), mean femoral neck diameter (D3), shaft angle (A) neck/shaft angle (Θ) and proximal femur strength index (SI) and distance from centre of mass of femoral neck to superior neck margin (Y). Fracture was predicted by a series of binomial logistic regression models, adjusted for age and sex. Odds ratios with 95% confidence intervals and area under the receiver operating characteristic curve (AUC) were calculated.
Results: 714 patients with PMR were identified, 182 were male and the mean age was 70.5. HAL, CSMI, D1, D2, D3, A, Θ, SI and Y were not significant predictors of fracture in regression models; odds ratios are included in Table 1. CSA predicted fracture risk; odds ratio was 0.988 with a 95% confidence interval of 0.980-0.997. The AUC for the CSA regression model was 0.6739.

Table 1. Odds ratios of fracture for different HSA parameters

HSA Parameter	Odds Ratio (95% confidence interval)
HAL	1.008 (0.982 - 1.035)
CSMI	1.000 (0.999 - 1.000)
CSA	0.988 (0.980 - 0.997)
D1	1.029 (0.972 - 1.089)
D2	1.010 (0.981 - 1.040)
D3	1.033 (0.962 - 1.109)
Y	1.087 (0.966 - 1.223)
A	0.983 (0.940 - 1.029)
Θ	1.007 (0.975 - 1.039)
SI	0.683 (0.406 - 1.150)

Conclusion: These data suggest that CSA helps predict the risk of fracture in patients with PMR. HAL, CSMI, D1, D2, D3, A, Θ, SI and Y do not predict fracture risk. Limitations of the study are that it was retrospective and only studied patients who underwent DEXA scans. The study may have been underpowered to detect the impact of some HSA measurements on fracture risk.
REFERENCES:
[1] Chatzigeorgiou C, Mackie SL. Comorbidity in polymyalgia rheumatica. Reumatismo. 2018; 70 1:35-43. Available from: http://eprints.whiterose.ac.uk/132109/\\.
[2] Kaptoge S, Beck TJ, Reeve J, Stone KL, Hillier TA, Cauley JA, et al. Prediction of Incident Hip Fracture Risk by Femur Geometry Variables Measured by Hip Structural Analysis in the Study of Osteoporotic Fractures. Journal of Bone and Mineral Research. 2008; 23 (12): 1892-1904. Available from: doi: https://doi.org/10.1359/jbmr.080802
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.337

AB0608 BONE MINERAL DENSITY, VITAMIN D STATUS AND BONE METABOLISM IN A COHORT OF ADULT PATIENTS WITH INFLAMMATORY BOWEL DISEASE

B. M. Fernandes[1], M. Bernardes[1], D. R. Gonçalves[2], F. Magro[3], L. Costa[1]. [1]*Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*; [2]*Centro Hospitalar Entre Douro e Vouga, Rheumatology, Santa Maria da Feira, Portugal*; [3]*Centro Hospitalar Universitário São João, Gastroenterology, Porto, Portugal*

Background: Patients with inflammatory bowel disease (IBD) have an increased risk of low bone mineral density (BMD) and bone fractures due to several mechanisms. However, the best management of osteoporosis in this population is yet to determine.
Objectives: To evaluate bone mineral density and other clinical, analytical and demographic features related with the risk of bone fractures in an IBD cohort.
Methods: Retrospective monocentric study including all the patients with IBD consecutively reffered from Gastroenterology to the Rheumatology Department in a tertiary university hospital between January of 2013 and October 2020. Demographic, clinical and analytical data and BMD by dual-energy X-ray absorptiometry (DXA) (total hip, femoral neck and lumbar spine) were collected at the time of the first visit in the Rheumatology outpatient center. Correlations between variables were evaluated by Spearman rank test and Mann-Whitney U test was used in the comparison analysis between groups (significance level at p<0.05), using SPSS 25.0 software.
Results: A total of 222 patients were included: 128 (57.7%) females, mean age of 43.4 (±13.6) years, mean IBD duration of 11.6 (±9.7) years. Regarding IBD: 163 (73.4%) had Crohn's disease (CD) and 59 (26.6%) had ulcerative colitis

(UC); azathioprine (41.9%) and infliximab (29.8%) were the most frequently used drugs; 10 patients (4.5%) were taking glucocorticoids, 104 (46.8%) had been previously treated with glucocorticoids and 65 (29.3%) had already been exposed to high doses of glucocorticoids (prednisolone equivalent dose ≥ 7.5 mg/day).
Ten patients (4.5%) had previous fragility fractures and 32 (14.4%) fulfilled diagnostic criteria of osteoporosis by DXA (T score ≤ -2.5). One hundred eighty-one (81.5%) patients exhibited low levels of 25-hydroxy vitamin D (<30ng/mL), 24 (10.8%) had high levels of parathormone and 150 (67.6%) showed elevated serum concentrations of beta-carboxy-terminal type-1 collagen crosslinks (beta-CTX). Three patients (1.4%) were under treatment with bisphosphonates and 18 (8.1%) were taking calcium and/or vitamin D supplements.
Of interest, serum levels of albumin correlated negatively with beta-CTX (r=-0.401; p<0.001) and positively with osteocalcin (r=0.259; p<0.001). Correlations between clinical/analytical variables and BMD are presented in Table 1.
Patients under glucocorticoids had lower mean total hip BMD (0.874±0.159 vs 1.008±0.176; p=0.022) and femoral neck BMD values (0.797±0.174 vs 0.933±0.179; p=0.014) in comparison with the group of patients that were not taking glucocorticoids.
No statistically significant differences in BMD values were found between the following subgroups: DC vs UC; normal vs low levels of 25-hydroxy vitamin D; patients exposed vs not exposed to high doses of glucocorticoids.

Table 1. Correlations between clinical/analytical variables and the BMD in an IBD population (BMD: Bone Mineral Density; IBD: Inflammatory Bowel Disease; n.s. not significant).

	Total hip BMD	Femoral neck BMD	Lumbar Spine BMD
Age	r=-0.356;p<0.001	r=-0.469;p<0.001	r=-0.259;p<0.001
Age at IBD diagnosis	r=-0.254;p<0.001	r=-0.327;p<0.001	r=-0.226;p=0.001
IBD duration	r=-0.147;p=0.031	r=-0.218;p=0.001	n.s.
Hemoglobin	r=0.249;p<0.001	r=0.209;p=0.002	n.s.
Albumin	r=0.189;p=0.005	r=0.208;p=0.002	n.s.
Erythrocyte sedimentation rate	r=-0.231;p=0.001	r=-0.206;p=0.003	n.s.

Conclusion: Our results show an important prevalence of undiagnosed and untreated osteoporosis in patients with IBD. Stronger correlations were found between clinical/analytical variables and femoral neck BMD. Of note are the weak correlations of BMD with acute-phase markers (negative correlation with erythrocyte sedimentation rate and positive correlations with hemoglobin and albumin) and of nutritional status (evaluated by albumin) with bone markers (negative correlation with the bone reabsorption marker beta-CTX and positive correlation with the bone formation marker osteocalcin).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.494

AB0609 RADIOFREQUENCY ECHOGRAPHIC MULTI-SPECTROMETRY FOR THE ASSESSMENT OF BOTH FEMORA IN PREGNANT WOMEN

E. Kirilova[1], N. Kirilov[2], S. Vladeva[3]. [1]*UMBAL Dr. Georgi Stranski, Rheumatology, Pleven, Bulgaria*; [2]*UMBAL Dr. Georgi Stranski, Orthopedics and Traumatology, Pleven, Bulgaria*; [3]*Trakia University, Rheumatology, Stara Zagora, Bulgaria*

Background: Radiofrequency Echographic Multi-Spectrometry (REMS) is a non-ionizing innovative approach for the assessment of REMS-$_{based}$ bone mineral density (BMD) of the axial skeleton. The principle of the REMS technology is based on the analysis of native raw unfiltered ultrasound signals during an echographic scan of the lumbar spine or the femoral neck [1]. Several studies demonstrated the high concordance with dual energy X-ray absorptiometry (DXA) in terms of measured BMD with this novel technology [2,3]. In previous published literature it was envisaged to apply this technology for the examination of the axial bone density in pregnant women. Pregnancy-associated bone loss has been demonstrated as decreased bone mineral density (BMD) in previous studies [4].
Objectives: The aim of the current study is to compare the BMD values of both femora between pregnant and non-pregnant women matched for age and BMI using the novel REMS technology.
Methods: Of total fifty women twenty pregnant women (40%) and thirty non-pregnant women (60%) were included in the study. The mean age of the pregnant women was 32 years ± 5 standard deviations (SD), (range 25-41 years) and the mean age of the non-pregnant women was 30 years ± 6 standard deviations (SD), (range 24-39 years). REMS approach was used to assess REMS-$_{based}$ BMD and REMS-$_{based}$ Z-score values of the femoral neck. Furthermore, body mass index (BMI) and gestational age in weeks were evaluated.
Results: The mean BMI of the pregnant women was 26 kg/m^2 ± 7 kg/m^2 (range 14 kg/m^2-42 kg/m^2) and those of the non-pregnant women was 25 kg/m^2 ± 5 kg/m^2 (range 16 kg/m^2-35 kg/m^2). The mean gestational age was 20 weeks' gestation ± 5 weeks' gestation (range 13-27 weeks' gestation). REMS-$_{based}$ mean BMD of the left femoral neck of the pregnant women was 0.793 g/cm^2 ± 0.167 g/cm^2 (range 0.563 g/cm^2-1.154 g/cm^2). REMS-$_{based}$ mean BMD of the right femoral neck of the pregnant women was 0.828 g/cm^2 ± 0.153 g/cm^2 (range 0.570 g/cm^2-1.161 g/cm^2). After comparing left femoral neck BMD with the right femoral neck BMD of the pregnant women, we found a linear correlation (R=0.764). Left femoral neck BMD value (0.793 g/cm^2) of the pregnant women was significantly lower than those of the non-pregnant women (0.854 g/cm^2), p=0.002. The mean left femoral Z-score of the pregnant women (-0.1 SD with range -2.5 SD-2.9 SD) was also significantly lower compared to those of the non-pregnant women (1.2 SD with range -1.5 SD-3.1 SD), p=0.003.
Conclusion: This is the first study which provides data about BMD and Z-score values of both femora in pregnant women assessed with the radiation-free REMS technology. Pregnant women demonstrated significantly lower femoral neck BMD values and Z-scores compared to those of the non-pregnant women. Innovative REMS method could be very helpful for making decision about the treatment of pregnant women who are at risk of lower BMD due to concomitant diseases and/or treatment associated with osteoporosis.
REFERENCES:
[1] Casciaro S, Conversano F, Pisani P, Muratore M. New perspectives in echographic diagnosis of osteoporosis on hip and spine. Clin Cases Miner Bone Metab. 2015; 12(2):142-150.
[2] Nikolov M, Nikolov N. AB0908 Assessment of the impact of the lean mass with body composition by dual-energy x-ray absorptiometry on the bone mineral density. Annals of the Rheumatic Diseases 2020; 79:1756.
[3] Chakova M., Chernev D., Kashukeeva P., Krustev P., Abedinov F. Lumbar Sympathectomy - Literature Review. International Journal of Science and Research (IJSR) Volume 7 Issue 8, August 2018 ISSN (Online): 2319-7064.
[4] Degennaro, V. A.; Cagninelli, G.; Lombardi, F. A. "VP34.12: First assessment of maternal status during pregnancy by means of radiofrequency echographic multi-spectrometry technology". Ultrasound in Obstetrics & Gynecology. 2020, 56 (S1): 199.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1061

AB0610 NORMOCALCAEMIC HYPERPARATHYROIDISM AND BONE HEALTH – WORSE THAN ANTICIPATED?

D. Masieh[1], S. Deshpande[1], M. K. Nisar[1]. [1]*Luton and Dunstable University Hospital, Rheumatology, Luton, United Kingdom*

Background: Since the formal recognition of normocalcaemic hyperparathyroidism (nHPT) as a distinct entity in 2008, several studies have been published describing the characteristics of these individuals. Controversy exists regarding diagnostics and the role of parathyroidectomy in such cases. A chief reason for lack of consensus is the disagreement among experts regarding the potential complications and a bias towards perhaps benign nature of this condition.
Objectives: In order to understand the challenges posed by this cohort, we aim to characterise these patients at presentation to our metabolic bone diseases unit with a focus on bone health.
Methods: We interrogated our departmental database and undertook retrospective analysis of all patients presenting to metabolic bone service at our large university teaching hospital with a catchment population of 350,000. Individuals were included in the survey based on criteria of Vit D >70 nmol/L, normal calcium (2.20-2.60 mmol/L), eGFR>60ml/min and PTH >6.9 pmol/L measured twice at least three months apart.
Results: Over six months review period, of 134 referrals, 42 (31%) were identified with nHPT. Follow up duration was two years. Mean age was 60 years (25-86). 38 (90%) were women with 31 (81%) post menopause. 34 (80%) were of Caucasian descent. All had comorbidities with median of five (1-14). Polypharmacy (>4 prescribed medicines) was common (36/42, 85%) with mean of seven prescribed medications (0-22). Mean Vit D was 88 (70.4-133.6), calcium 2.43 (2.26-2.58), creatinine 69.8 (48-115) and PTH 8.8 (7.2-14.2). Ten (24%) had already had fragility fractures with mean of two (0-4). 21 had DXA scan with mean T score of -3.78 (-2.1 - -6.0). 13/21(31%) had osteoporosis. Oral and IV bisphosphonates, denosumab and teriparatide were prescribed to 12 (28.5%), 14 (33%), 4 (10%) and one patient respectively.
Conclusion: Our study suggests high prevalence of nHPT among patients referred to metabolic bone service with confirmed bone health issues. Nearly a third of patients have nHPT in this secondary care setting and a quarter have already suffered fragility fractures. These patients carry high comorbidity, polypharmacy and osteoporosis burden. Management of such patients is challenging owing to complex interplay of various ailments. Bone active agents are required for nearly two-thirds of this group. Though the natural course of nHPT is an area of active research, our data adds to the growing body of evidence that this is not a benign condition with particularly high fracture burden and poor bone quality.

nHPT is perhaps responsible for the onset and progression of the similar osseous complications as described in classical PHPT. Further longitudinal studies are required to help devise best management plan to mitigate against the skeletal encumbrance of nHPT.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1095

AB0611 OSTEOPOROSIS IN RHEUMATOID ARTHRITIS: A NECESSARY EVIL?

S. Athimni[1], S. Bouden[1], A. Ben Tekaya[1], A. Dghais[1], O. Saidane[1], R. Tekaya[1], I. Mahmoud[1], L. Abdelmoula[1]. [1]*Charles Nicolle Hospital, Rheumatology,Tunis, Tunisia*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that is characterized by local and general bone loss. Osteoporosis (OP) is one of the most frequent comorbidities associated with RA. Many factors are incriminated in bone loss in RA such as inflammation, glucocorticoid (GC) use, and immobility.

Objectives: -To determine the prevalence of OP in a population of actual RA patients.

-To determine the risk factors of bone mineral density (BMD) reduction

Methods: One hundred-fifty-two RA followed in the rheumatology department between 2015-2020 were enrolled in the study. The diagnosis of RA was established according to the American College of rheumatology/European League Against Rheumatism (ACR/EULAR) criteria 2010. BMD in lumbar spine and total hip was systematically measured in the recruited patients. Measures were taken with dual-energy x-ray absorptiometry (DEXA), and age-specific values were compared with pooled values from a local population of healthy subjects free from earlier fractures.

Results: The mean age was 42.7±13 years. The sex ratio M/F was 0.24. The mean onset disease was 6±1.8 years. Fifty-sex patients (36.3%) were receiving conventional treatment DMARDs and 96 (63.6%) were under biological treatment. 35.5% were taken steroids with mean doses at 7.7±3.3mg/day. RF and ACPA were positive respectively in 87.3% and 82.4% of the patients. The mean disease activity score DAS28CRP was 4.8 ±2.7.

Sixty-eight point eight 68.8% of the RA population had bone loss: 37.5% had osteopenia and 31.3% had OP. Regarding the OP group, sex ratio M/F was 0.45. The mean age was 42±5.3 years. Among the 31 women, 77.4% had postmenopausal OP. The BMI average was 31.18 ± 6.19 kg/m^2. Fifteen patients (33.33%) had OP in the hip site and 20 patients had OP in the lumbar site (48.8%). Ten patients had both trabecular and cortical OP.

Advanced age, glucocorticoid use and high DAS28CRP were independent risk factors for OP (respectively p=0.04, p=0.02 and p=0.01). Body mass index, smoking, disease duration high Health Assessment Questionnaire (HAQ) score (p=0.545) and smoking (p=0.326) were not associated with high risk of OP. The biological treatment was not a protective factor in OP (p=0.972). All the population subjects were free from earlier fractures, the fractural risk estimated by dint of the mean FRAX™ score was at 1.4 ± 2.3.

Conclusion: Previous studies estimated that, approximately, osteoporosis affected one-third of RA patients which is in concordance with our study. Advanced age, glucorticoid treatment and severe disease were the most common risk factor in our study.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1235

AB0612 THE FRACTURE PREVENTION UNIT OF THE VIRGEN MACARENA HOSPITAL REDUCES THE GAP IN THE MANAGEMENT OF OP, PARTICULARLY IN MALES AND MEETS IOF/ESCEO QUALITY STANDARDS

B. Hernández-Cruz[1], F. J. Olmo Montes[2], M. J. Miranda García[2], M. D. Jimenez Moreno[2], M. A. Vázquez Gómez[3], M. Giner García[3], M. A. Colmenero Camacho[2], J. J. Pérez Venegas[1], M. J. Montoya García[3]. [1]*Hospital Universitario Virgen Macarena, Rheumtology, Sevilla, Spain*; [2]*Hospital Universitario Virgen Macarena, Internal Medicine, Sevilla, Spain*; [3]*University Medical School, Internal Medicine, Sevilla, Spain*

Background: The Virgen Macarena University Hospital belongs to the Public Health System of Andalusia and serves 481,296 inhabitants in Seville, Spain. In 2018 the Fracture Liaison Service switched to a multidisciplinary unit.

Objectives: To describe FLS, to know the characteristics of patients with emphasis on gender differences and to know the completion of International Osteoporosis Foundation quality standards.

Methods: Prospective, observational, analytical, research of usual clinical practice. All the consecutive patients attended from May 2018 to October 2019, ≥50 years, with a fragility fracture (occurred in the previous 24 months) were included. The study was approved by the Ethics Committee, Code 1084-N-16.

Results: Our FLS is a type A multidisciplinary Unit, with a high level of intervention in the evaluation, estimation of fracture risk and fall risk, treatment prescription and follow-up of the patients. We included 408 patients, 80% females, one third with ≥80 years. Fragility fractures recorded in 328 women were hip (132, 40%), clinical vertebral (81, 25%) and no hip no vertebral (115, 35%). Those recorded in 82 males were hip (53, 66%), clinical vertebral (20, 24%) and no hip no vertebral (9, 10%), p=0.0001. Males had a higher rate of secondary causes of OP, drinker, and smoking. The most relevant gender difference was the low percentage of patients receiving pre-FF OP treatment. Forty-nine (16%) women versus 9 (7%) males had received it at some point in their life, p=0.04. Two hundred and seventy-one (86%) women vs 48 males (63%) had received it at after their FF in their reference unit, and all them were treated after the FLS evaluation. The probability of a male not receiving prior treatment was 2.5 (95% CI 1.01- 6.51); p=0,04. This probability was 0.64 (0.38-1.09) after the FF. After twelve months of follow-up in FLs, 96% continued treatment, with no differences between men and women. The completion of IOF quality standards was bad (red light) for patient identification items and FLS reference time. It was poor (amber traffic light) for initial OP screening standard and was good (green light) for the remaining 10 indicators. The completion of IOF quality standards was bad (red light) for patient identification items and FLS reference time. It was poor (amber traffic light) for initial OP screening standard and was good (green light) for the remaining 10 indicators (Figure 1).

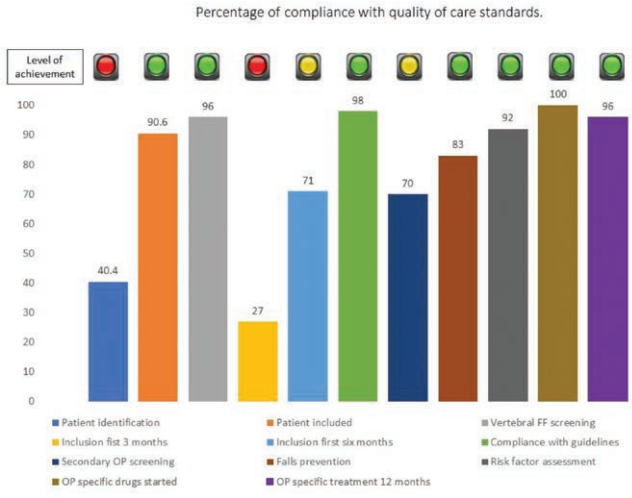


Figure 1.

Conclusion: The FLS is a multidisciplinary type A. Its operation has narrowed the gap in diagnosis, treatment, and follow-up of FF patients, especially males. It is essential to improve patient recruitment, reduce referral times and increase the overall assessment of the patients.

REFERENCES:

[1] Ganda K. et al. Models of care for the secondary prevention of osteoporotic fractures: a systematic review and meta-analysis, Osteoporos Int 2013;24:293-406.

[2] Javaid MK et al. A patient-level key performance indicator set to measure the effectiveness of fracture liaison services and guide quality improvement: a position paper of the IOF Capture the Fracture Working Group, National Osteoporosis Foundation and Fragility Fracture Network. Osteoporos Int. 2020 Jul;31(7):1193-1204.

Acknowledgements: Spanish Society of Research in Mineral and Bone Metabolism for its support through the competitive project FLS Excellence 2018 to obtain a training grant from the case management nurse.

Disclosure of Interests: Blanca Hernández-Cruz Speakers bureau: Sociedad Española de Reumatología, Abbvie, Roche, Bristol, MSD, Lilly, Pfizer, Amgen, Sanofi, Consultant of: Abbvie, Lilly, Sanofi, STADA, UCB, Amgen, Galapagos., Grant/research support from: Fundación para la Investigación Sevilla, Junta de Andalucía

Fundación Andaluza de Reumatología, Sociuedad Española de Reumatología., Francisco Jesús Olmo Montes: None declared., Maria José Miranda García: None declared., María Dolores Jimenez Moreno: None declared., María Angeles Vázquez Gómez: None declared., Mercedes Giner García: None declared., Miguel Angel Colmenero Camacho: None declared., José Javier Pérez Venegas: None declared., María José Montoya García: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1448

AB0613 FREQUENCY AND RISK OF FRAGILITY FRACTURES IN PATIENTS WITH SYSTEMIC SCLEROSIS

A. Efremova[1], O. Nikitinskaya[1], N. Toroptsova[1], O. Dobrovolskaya[1], N. Demin[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Department of Osteoporosis, Moscow, Russian Federation*

Background:
Objectives: To assess the frequency of fragility fractures and the 10-year risk of major osteoporotic fractures using the fracture risk assessment tool (FRAX) tool in patients with systemic sclerosis (SSc).
Methods: The study included 136 patients with SSc who met the ACR/EULAR 2013 criteria: 110 (80.9%) postmenopausal women and 26 (19.1%) men over 50 years of age, mean age 59,3+7.5 years. The duration of the disease was 10,0 [6.0; 15.0] years in women and 6,0 [3.5; 9.0] years in men. A questionnaire was conducted and the risk of major osteoporotic fractures was calculated according to FRAX tool, as a result of which patients were divided into groups of low, moderate or high risk. Individuals at moderate risk underwent dual-energy X-ray absorptiometry (DXA) of the proximal femur, followed by a 10-year probability of major osteoporotic fractures recalculation with the inclusion of the femoral neck T-score. According to the obtained fracture risk assessment tool value, patients were assigned as having a low, high or very high risk.
Results: Fragility fractures of various localization were found in 50 (36,7%) people: 41 (37,3%) women and 9 (34.6%) men. Vertebral and peripheral bone fractures occurred with the same frequency (19,8%) without significant differences depending on the patient's gender. Only 1 (3,8%) male had a history of proximal femoral fracture. Fractures of both the vertebra and the peripheral bone occurred in 4 (2,9%) people: 3 (2,7%) women and 1 (3,8%) man.
9 (8,2%) women and 16 (61,5%) men had a low risk of major osteoporotic fractures according to FRAX, 60 (54,5%) and 10 (38,5%) - a moderate risk, respectively, while 41 (37,3%) women were at high risk. Among 86 patients without a history of low-energy fractures (69 women and 17 men), 8 (11,6%) women and 16 (94,1%) men were at low risk of major osteoporotic fractures, and 57 (82,6%) and 1 (5,9%), respectively, were at moderate risk. Only 4 (5,8%) women were assigned to the high-risk group. After recalculation of the fracture risk assessment tool with inclusion of the femoral neck T-score in persons with moderate risk without a history of fragility fractures, 9 (13,0%) women and 1 (5,9%) man were found to be at high risk, 14 (20,3%) women - at very high risk and 34 (49,3%) women - at low risk.
Among moderate-risk patients with prior fractures after FRAX recalculation 3 (7,3%) women and 7 (77,8%) men became at low risk, 1 (11,1%) male - at high and 1(11,1%) male – at very high risk. Thus, 55 (50,0%) women and 1 (3,8%) man were at very high, 12 (10,9%) and 2 (7,7%), respectively, - at high, and 43 (39,1%) and 23 (88,5%), respectively, - at low risk of major osteoporotic fractures.
Conclusion: In the examined cohort of patients with SSc, the frequency of fragility fractures was 37,3% in women and 34,6% in men. A high and very high risk of major osteoporotic fractures was found in 60,9% of women and 11,5% of men. 3 (2,7%) women and 6 (23,1%) men with a history of previous fractures were in the low-risk group by FRAX, but they need to consider the appointment of anti-osteoporotic therapy as for patients at high and very high risk.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1502

AB0614 DENSITOMETRIC VERTEBRAL FRACTURE ASSESSMENT: FACTORS LIMITING GOOD VISIBILITY OF THE VERTEBRA

S. Mariem[1], M. Yasmine[1], S. Miladi[1], A. Fazaa[1], E. Frigui[1], L. Souebni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: The radiograph of the spine is the gold standard for identifying vertebral fractures (VF). Vertebral Fracture Assessment (VFA) is a new feature available on modern densitometers that could assess VF. This technique offers the advantage of low irradiation over standard radiography but at the cost of lower image quality.
Objectives: The aim of this study was to assess factors associated with good vertebra visibility when using VFA.
Methods: This is a cross-sectional study including patients referred by their physicians for bone mineral density (BMD) measurement. Anthropometric data were recorded. BMD was measured using standard methods over the lumbar spine L1-L4, the total proximal femur. Results were expressed as T-scores using Dual-energy X-ray absorptiometry (DEXA). The screening for VF was performed by VFA. A professional operator analyses VFA scans and assessed the good visibility of the vertebra.
Results: The study included 100 patients. The mean age was 61.7 ±12.6 years [18-83].The average body mass index (BMI) was 28.9 ± 24.2 kg/m2 [14.2-45.3]. The mean T-score at the vertebral site was -1.5 DS [-4.9-1.5] with a mean mass of 0.95g/cm^2 [0.58-1.371]. Osteoporosis was found in 27.7 % of patients. A vertebral fracture was diagnosed in 25% of cases. The visualization of the vertebra was impaired in the upper thoracic region in 60% of cases. Poor visibility was observed in 19% of cases in the mid-thoracic spine and only in 2% of cases in the lumbar spine. No statistically significant correlation was found between good vertebral visibility and age (p=0.2), weight (p=0.5), or BMI (p=0.7). However, good visibility of the vertebra was associated with a lower height (1.7 m vs 1.5 m, p=0.03). A better vertebrae visualization was correlated neither to the BMD of the right hip (0.84 vs 0.87, p=0.4) nor to the left hip (0.85 vs 0.89, p= 0.3). Similarly, the absence of vertebral osteoporosis was not correlated with a better vertebral visualization (p=0.6).
Conclusion: Visibility of the vertebra on VFA does not appear to be altered by the BMD and vertebral osteoporosis, suggesting safe use in the elderly. However, precautions may be taken when interpreting VFA in patients with high heights.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2092

AB0615 ASSESSMENT OF THE IMPACT OF OBESITY ON BONE LOSS

M. Yasmine[1], S. Mariem[1], S. Miladi[1], A. Fazaa[1], E. Frigui[1], L. Souebni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: Most of the available evidence supports a lower risk of vertebral fracture in obese adults. This belief was partially suggested by the positive correlation between bone mineral density (BMD) and body mass index (BMI).
Objectives: We aimed to assess the association of BMI with BMD and to explore their relation with age and gender.
Methods: This is a cross-sectional study including Tunisian patients referred for an assessment of BMD through dual-energy X-ray absorptiometry (DXA). BMD was measured using standard methods over the lumbar spine L1-L4, the total proximal femur. The results were expressed as T-scores according to the World Health Organization definition. Patients were sub-grouped according to age (≤50 and >50 years). Association between BMD and age as well as BMI was also assessed (G1: obese patients and G2: non-obese patients). The level of significance was fixed for p<0.05
Results: The study included 100 patients with a female predominance (sex ratio =10.1). The mean age for women was 61.9 ±13 [18-83] years and the mean age for men was 59.7± 7.5 [47-72] years. The mean body mass index was 29.1± 5 kg/m^2 [15-45] for women and 27.6 ±3.6 Kg/m^2 [22.8-32.9] for men. Forty percent of all patients were obese with a mean BMI of 32.9 kg/m^2 ± 4.3. Osteopenia was diagnosed in half of the men (55.5%) and most of the women (70%). Twenty-nine percent of patients suffered from osteoporosis. BMD of the spine was similar between men and women (p=0.53). Men had higher BMD of the hip than women (p=0,038). The mainstream of the subjects >50 years had more vertebral fractures, suffered more from osteoporosis and had a higher BMI than those < 50 years (95% % vs 5%; p=0.04), (92.3% vs 77 %; p=0.03) and (82.5% vs 17.5%; p=0.05) respectively. There was no correlation between BMD of the spine and higher BMI (0.94 in G1 vs 0.98 in G2, p=0.3). Similarly, there was no correlation between BMD of the hip and higher BMI (0.9 in G1 vs 0.84 in G2, p=0.2). Moreover, Obese patients had less a vertebral fracture but with no statistically significant correlation (21% in G1 vs 25% in G2; p=0.2).
Conclusion: Our study showed that obesity was frequent among Tunisian patients but was not associated with a higher BMD. Older age was directly associated with a lower BMD and higher risk for vertebral fracture.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2106

AB0616 RISK FACTORS FOR PREVALENT VERTEBRAL FRAGILITY FRACTURES - STUDY IN A LONDON URBAN BOROUGH

N. Mothojakan[1], M. Zaman[2], A. Perren[1], S. Mahendrakar[1], R. Rajak[1]. [1]*Croydon University Hospital, Rheumatology, Croydon, United Kingdom*; [2]*St George's Hospital, Rheumatology, London, United Kingdom*

Background: Vertebral fragility fractures (VFFs) are commonly underdiagnosed, often resulting in chronic pain and reduced quality of life. It is particularly important to identify and manage VFFs, as they are important predictors of future VFFs and non-VFFs. Patients with VFFs often have multiple risk factors, which are important to identify to formulate a tailored and appropriate management plan. There is a paucity of studies that have investigated risk factors specifically for VFFs.
Objectives: To identify the prevalence of osteoporosis risk factors in patients with VFFs.

Methods: Retrospective review of patients seen between July 2018 and July 2019 at Purley Memorial Hospital, covering a large urban borough. Patients included in the study had prevalent moderate and severe VFFs (defined by Ghent criteria).
Results: 84 patients were included, of which there were 71 females and 13 males. Median age was 76 (IQR 67 – 82) and BMI was 25 (IQR 21 – 27), with 6% of patients noted to be underweight (BMI <18.5). 38% of patients had a family history of osteoporosis and 21% of patients reported a history of parental hip fracture. 21% of patients had experienced recurrent falls. Over half (56%) of patients were noted to have had 2-or-more previous fragility fractures. Of the female cohort, 24% had early menopause, 13% were nulliparous and 1% had late menarche. Of the modifiable risk factors, alcohol (24%), sedentary lifestyle (21%) and smoking (13%) were the most common. Thyroid-disease (18%) was the most common medical condition associated, followed by coeliac/malabsorption (7%), endocrinopathy (6%) and COPD (6%). Proton Pump Inhibitors (PPIs) and steroids were the most common medications associated with 16% and 14% of cases respectively. 73% of patients had good calcium intake and 62% had calcium supplements. Overall, 27 patients had 3-or-fewer risk factors, 35 patients had 4-to-6 risk factors, 19 had 7-to-9 risk factors, and 3 had greater than 10 risk factors.
Conclusion: Our study identified several risk factors and their prevalence. The majority of patients were female, of which 24% had early menopause. Several modifiable risk factors such as low BMI, alcohol, smoking and sedentary lifestyle were commonly seen, emphasising the need to identify these risk factors in the initial consultation. Over half of patients (56%) had had 2-or-more previous non-VFFs, suggesting the need to screen for VFFs in patients with multiple fragility fractures at baseline assessment. A number of co-existing medical conditions were also observed with thyroid disease being the most prevalent. PPIs and steroids were found to be important risk factors, which may lead to the consideration of alternative medications. Overall, it was found that patients had multiple risk factors, thus it is important to have a holistic assessment of VFF patients and a multi-system management approach to prevent future fractures.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2201

AB0617 BISPHOSPHONATES DANS L'OSTÉOPOROSE ET LE RISQUE D'OSTÉONÉCROSE DE LA MÂCHOIRE, ENVIRON 896 CAS

A. R. Halidou[1], K. Nassar[1], S. Janani[1]. [1]*Université Hassan II, médecine, Casablanca, Morocco*

Background: Bisphosphonates (BF) are used in the treatment of osteoporosis, Paget's disease of bone, hypercalcemia and in patients with cancer. When used to treat osteoporosis, the optimal duration of treatment is 3 to 5 years; however, their long-term use has been rarely associated with osteonecrosis of the jaw.
Objectives: To assess the risk of developing osteonecrosis of the jaw in patients followed for osteoporosis and on bisphosphonates (BP).
Methods: Type of study: retrospective study conducted at the rheumatology department of the IBN ROCHD CHU in Casablanca.
Duration: from October 2013 to October 2020 (7 years).
Inclusion criteria: all patients followed for osteoporosis in the weakening osteopathies unit of the bone and treated with oral or intravenous bisphosphonates.
Exclusion criteria: patients followed for other than osteoporosis.
Results: 896 patients were treated during this period. The average age was 62.74 years (28 to 90 years), of which 85.16% were women and 14.84% were men, for a sex ratio (F / M) of 5.74. As a history, 18.75% of patients are diabetic, 26.56% followed for breast neoplasm, 14.06% of patients had received long-term corticosteroid therapy for various pathologies such as chronic inflammatory rheumatism. Osteoporosis was postmenopausal in 687 patients, ie 76.67% of cases, 14.06% after long-term corticosteroid therapy, 8.15% following hormone therapy (anti-aromatases) and 6.92% following chemotherapy; note that 18.16% of these patients were found in at least two of the situations. The mean bone mineral density (BMD), T-score pair considered in all [T-score (BMD)] is -3 (0.736) in the lumbar spine (L1-L4), -2.9 (0.658) at the femoral neck, -2.6 (0.804) at the total hip before the start of treatment. 69.97% of the patients were put on Alendronic acid, 12.50% on Residronic acid, 10.93% on Zolidronic acid, 3.46% on Pamidronic acid and 3.14% received Strontium Ranelate, note that before the start of the treatment all the patients benefited from a dental consultation followed by care of any lesions, the bisphosphonates were only introduced after having ruled out all their dental contraindications, the average duration of treatment for all the molecules was 4.71 years (2 to 5 years) and no patient developed osteonecrosis of the jaw. The change in control BMD on average after 2 years of treatment was -2.7 (0.782) at the lumbar spine, -2.6 (0.749) at the femoral neck and -2.4 (0.713) at the hip total, after 5 years -2.4 (0.874) at the spine, -2.1 (0.809) at the femoral neck and -1.93 (861) at the total hip.
Conclusion: The occurrence of ONJ in the treatment of osteoporosis with the use of BFs is rare, and appears to be unpredictable; but maintaining therapeutic caution, consisting in diagnosing and treating any dental lesions before starting treatment, can considerably reduce or even cancel the risk of occurrence; especially in patients treated with long-term intravenous pamidronate.
REFERENCES:
[1] Dr Halidou Idrissa Abdoul-Rahamane, Pr Kawtar Nassar, PR Saadia Janani.
[2] Rheumatology department of the IBN ROCHD CHU in CASABLANCA. Casablanca Faculty of Medicine and Pharmacy. Hassan II University. Morocco
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2399

AB0618 GLUCOCORTICOID INDUCED OSTEOPOROSIS PREVENTION IN THE OUTPATIENT RHEUMATOLOGY CLINIC

Z. Vaghaiwalla[1], G. Kaeley[1]. [1]*University of Florida College of Medicine-Jacksonville, Rheumatology, Jacksonville, United States of America*

Background: Patients with rheumatic disease are at risk of developing glucocorticoid induced osteoporosis (GIOP) as many are prescribed systemic oral glucocorticoids as an adjunct to their maintenance therapy. Based on the 2017 ACR Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis, a good practice recommendation exists that "initial clinical fracture risk assessment should be performed as soon as possible, but at least within six months of the initiation of long term glucocorticoid treatment.[1]" Long-term glucocorticoid use is defined by duration of 3 months or greater. Fracture risk assessment should include dual energy-ray absorptiometry (DEXA) scan. Patients on greater than or equal to 2.5 mg of prednisone should be treated with an optimal dose of calcium and vitamin D and may benefit from oral bisphosphonate as primary prevention against GIOP if their fracture risk is moderate to high.[1]
Objectives: The aim of this Quality Improvement Project is to assess the current status of provider implementation of GIOP recommendations in the rheumatology clinic. Ultimate goal is to improve osteoporosis prevention in the rheumatology clinic.
Methods: We conducted a retrospective chart review of 60 patients in two outpatient rheumatology clinics. Clinic 1 follows patients with lower socioeconomic status and Clinic 2 follows patients with higher socioeconomics. Inclusion criteria were patients on long-term glucocorticoid use, defined as at least 3 months of corticosteroid use of at least 2.5 mg prednisone daily, as well as age less than 65. Females aged 65 or older were omitted to prevent overlap of the United States Preventative Taskforce recommendation for all women ≥ 65 years to be screened for osteoporosis with DEXA scans.[2] DEXA scan orders, calcium and vitamin D prescriptions, and osteoporosis medication prescriptions were abstracted. After baseline data obtained, intervention of education of the rheumatology fellows and faculty, and internal medicine residents in the guidelines for GIOP prevention was implemented. In addition, a smartphrase in the electronic medical record was created for provider use when treating patients on chronic corticosteroids. Subsequently, two audit cycles were completed for retrospective chart review.
Results: Upon completion of second audit cycle, there was no change in percentage of DEXA scan orders at Clinic 1, however there was a 10% overall improvement in DEXA scan orders in the Clinic 2.
In terms of Calcium and Vitamin D prescriptions, there was an overall improvement in both clinics of 19.7% and 13.3% in Clinics 1 and 2 respectfully after the second audit cycle.
Additionally, there was a 3.4% increase in osteoporosis medication prescriptions overall subsequent to the second audit cycle in Clinic 1. However in Clinic 2 there was an overall decrease in osteoporosis medication prescriptions of 6.6%.

Clinic 1	Prior to Audit	Audit cycle 1	Audit cycle 2
Patient percentage without DEXA scan orders	30%	33.30%	30%
Patient percentage without Vitamin D/Calcium orders	26.40%	8.30%	6.70%
Patient percentage with osteoporosis medication orders	23.30%	8.30%	26.70%
Clinic 2			
Patient percentage without DEXA scan orders	50%	37.00%	40%
Patient percentage without Vitamin D/Calcium orders	30%	26.00%	16.70%
Patient percentage with osteoporosis medication orders	23.30%	11.10%	16.70%

Conclusion: Overall, the results of the intervention were strongest for improvements in Vitamin D and Calcium orders in both clinics. Improvements in DEXA scan orders and osteoporosis medications were present in Clinic 2 and not present in Clinic 1. This reveals continued efforts and education of providers need to be made for improvement in bone health monitoring.
REFERENCES:
[1] Buckley, Lenore, et al. "2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced

Osteoporosis." *Arthritis & Rheumatology*, vol. 69, no. 8, June 2017, pp. 1521–1537., doi:10.1002/art.40137.
[2] *Final Recommendation Statement: Osteoporosis to Prevent Fractures: Screening*. U.S. Preventive Services Task Force. July 2019.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2583

AB0619 CLINICAL RISK FACTORS, BONE DENSITY AND FALL'S HISTORY AND FRACTURES RELATION: STUDY BY HOSPITAL SURVEY ABOUT 448 CASES

K. Nassar[1], S. Janani[2]. [1]*Ibn Rochd University Hospital, Hassan II University of Medicine and Pharmacy, Rheumatology Department, CASABLANCA, Morocco*; [2]*Ibn Rochd University Hospital,. Hassan II University of Medicine and Pharmacy, Rheumatology Department, CASABLANCA, Morocco*

Background: Osteoporosis is a disease that affects bone mineral density (BMD) and bone microarchitecture at the origin of an increased risk of fracture. The reduction in bone density assessed by dual-energy X ray absorptiometry (DXA) and fall history represent the first two risk factors of non-vertebral fracture after menopause. Given the high prevalence of osteoporosis among fallers subjects with common risk factors, causing a surisk of fracture. Several publications including the osteoporosis recommendations indicate DXA in women experienced falls in search of bone fragility may justify a treatment for osteoporosis, especially as the FRAX tool does not include at present the fall of history, an important parameter in the assessment of fracture risk.
Objectives: Because of the low attention given to the evaluation of falls'risk, the main objective of the study was to determine the prevalence and the relationship between the past history of fall, reduction of bone mineral density and prevalent fracture.
Methods: Transversal and descriptive epidemiological cohort study conducted for 24 months in 448 patients referred by physicians regularly use prescription of BMD. The realization of this exploration by the same DXA-Hologic in the rheumatology department at Ibn Rochd University Hospital was the criterion for entry into the study. All patients were interviewed on the same day on the risk factors for osteoporosis and fractures justifying the prescription of a BMD.
Results: Data included 413 women and 35 men. Most women were postmenopausal (89.6%). The average age was 59 years (σ = 13.40), 33.7% were ≥ 65 years. The mean BMI was at 27.50 (σ = 5,2). 18.5% of patients had at least a history of falls in the previous 12 months and 22.5% a history of fracture after a low-energy trauma. 42.9% were osteoporotic and 57.1% had osteopenia in at least one of these sites: lumbar spine, femoral neck, total hip. We did not find significant association between BMD osteoporosis and fall history (p = 0.916). Thus, cases of osteoporosis fractures were not statistically associated with a fall (p = 0.170). Also, the falls were occurring than 18.4% of osteopenic patients (p = 0.220). However, in our study, the fall was an independent risk factor for fracture (p = 0.003) and osteopenic fractures were significantly higher among fallers (p = 0.009 and 0.006 respectively, a drop of history and at least one past fall history).
Conclusion: The fall history is a independent risk factor for fracture. This risk is particularly important in case of fragility bone densitometry. The clinical history and fall risk factors should be taken into consideration in the assessment of fracture risk and in the anti-ostoporotique treatment strategy. Thus, the fall seems to be a legitimate indication for DXA and as a parameter to be integrated into the assessment of fracture risk by the FRAX score.
REFERENCES:
[1] MH. Edwards, K. Jameson, H. Denison, NC.Harvey, Sayer A. Aihie, EM Dennison, and C Cooper. Clinical risk factors, bone density and fall history in the predection of incident fracture among men and women. Bone. 2013; 52(2): 541–547.

Table 1. Multivariate Logistic Regression Results: Adjustment for predictors factors of falls

Variables	OR (95% IC)	p-value
Age ≥ 65 ans	0,986 (0,412-2,357)	0,974
Past history of fracture	4,271 (1,719-10,611)	0,02
Walking aid	11,214 (2,815-44,670)	0,01
Vision disturbances	8,587 (3,540-20,829)	<0,001
Rhumatoid arthritis	8,047 (2,218-29,192)	0,02
Diabete	3,194 (1,217-8,382)	0,018
Corticosteroid ≥ 3 mois	0,603 (0,156-2,331)	0,463
Smoking	0,241 (0,013-4,518)	0,341
Ostéopenia (-1 ≤ T-score < -2,5)	2,204 (0,875-5,552)	0,094

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2705

AB0620 MODIFICATION OF THE DECISION OF THE ANTI-OSTEOPOROSIS TREATMENT AFTER PERFORMING THE VFA

H. Tantaoui[1], K. Nassar[1], S. Janani[1]. [1]*Faculty of Medicine and Pharmacy, Hassan II University, Ibn Rochd University Hospital Center, Rheumatology, Casablanca, Morocco*

Background: Spinal fractures are the most common of all osteoporotic fractures. Its diagnosis is essential, because the discovery of a vertebral fracture testifies the gravity of osteoporosis and modifies the therapeutic intervention threshold by justifying a specific anti-osteoporosis treatment. The evolution of densitometers now makes it possible to take a true X-ray image using software called "Vertebral Fracture Assessment" or VFA.
Objectives: To assess the impact of VFA results on therapeutic decision-making after measuring bone mineral density.
Methods: We conducted a retrospective and descriptive study in the rheumatology department.
We included all patient followed at the consultation for bone pathologies, in whom a measurement of bone mineral density and a supplementation of VFA were performed. Clinical data, BMD, VFA and the therapeutic decision by anti-osteoporosis treatment before and after VFA were collected.
Results: Sixty-one patients were included. The mean age was 62.8 years [38 - 85 years]. Sex ratio (female / male) was 19.3. At BMD level, patients with osteoporosis and osteopenia were 49% and 51% respectively. VFA objectified at least one spinal fracture in 64% of patients. Prior to VFA, anti-osteoporosis therapy was indicated to 49% of patients, based on clinical data and BMD. After performing VFA, the prescription of anti-osteoporosis therapy was indicated to 80% of patients.
Conclusion: Patients who had no indication for osteoporosis treatment based on BMD data, VFA was able to modify their therapeutic treatment by detecting vertebral fractures in patients who had back pain.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3318

AB0621 THE MAIN CAUSES OF MORTALITY IN PATIENTS WITH OSTEOPOROTIC HIP FRACTURES

J. Averkieva[1], M. Letaeva[1], O. Malyshenko[1], M. Koroleva[1], T. Raskina[1]. [1]*Kemerovo State Medical University, Department of Propedeutics of Internal Medicine, Kemerovo, Russian Federation*

Background: Increasing life expectancy is one of the main achievements of modern medicine. However, longevity is inevitably associated with the growth of so-called "age-associated diseases," among which osteoporosis occupies an important place.
Objectives: To study the causes of mortality in patients with hip osteoporotic fractures during 12 months after injury.
Methods: Traced the causes of mortality 432 patients with osteoporotic hip fractures were under observation: 328 women and 104 men. The mean age of women was 75.4 ± 9.27 years, the mean age of men was 71.5 ± 10.39 years.
Results: This study traced the causes of deaths by the main classes of ICD-10. It was found that 6 months after a hip fracture in 63 (66.3%) patients, death occurred from diseases of the circulatory system: in men - 13 (59.0%) cases and in women - 50 (68.4%) (p = 0.9). Respiratory diseases, as a cause of death, were identified in 18 (18.9%) patients (in men - 5 (22.9%) cases and in women - 13 (17.8%) (p = 0.1)), neoplasms - in 10 (10.5%) men and women: 2 (9.1%) and 8 (10.9%) cases, respectively (p = 0.5). Diseases of the digestive system accounted for a small percentage of the total number of deaths (3.2%), without statistically significant differences by gender (in men - 1 (4.5%) case and in women - 2 (2.9%) cases (p = 0.75)). Among the dead men, 1 (1.1%) death from an infectious disease was registered. 12 months after the fracture, most of the deaths in both men and women were due to diseases of the circulatory system. The total number of deaths was 93 (67.8%): in men - 22 (66.0%) cases, in women - 71 (68.3%) (p = 0.65). Respiratory diseases caused death in 23 (16.8%) patients: in men - 5 (15.1%) cases and in women - 18 (17.3%) (p = 0.31). There is an increase in the number of deaths from neoplasms to 15 (10.9%) cases without statistically significant differences by gender: in men - 3 (9.09%) cases and in women - 12 (11.5%) (p = 0, 45). Diseases of the digestive system, as a cause of death, were identified in 5 (3.6%) men and women (2 (6.06%) and 3 (2.9%) cases, respectively (p = 0.1)). No new cases of deaths from infectious diseases were registered.

Conclusion: Most of the deceased men and women had cardiovascular and respiratory diseases. There were no statistically significant differences registered in the structure of mortality by gender for all classes of diseases.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3436

AB0622 WHEN OSTEOPOROSIS, COELIAC DISEASE AND MULTIPLE MYELOMA CO-EXIST

S. Khalid[1], R. Smith[1]. [1]*Salisbury District Hospital, Rheumatology, Salisbury, United Kingdom*

Background: Secondary causes of bone loss are sometimes overlooked in patients who are diagnosed as having osteoporosis. This is especially true if more than one risk factor for secondary osteoporosis is present, with clinicians focusing on the more common cause. Here we present a case of secondary osteoporosis caused by coeliac disease *and* multiple myeloma.
Objectives: Secondary osteoporosis should be suspected in patients with very low bone mineral density and those with no obvious risk factors. Comprehensive examination and investigations must be done to look for all secondary causes because sometimes, as seen in our patient, you may find more than one.
Methods: A 74 year old gentleman presented to the rheumatology clinic for assessment of osteoporosis. He had been recently diagnosed with coeliac disease. DXA scan showed a T score of -3.5 at the lumbar spine, -2.5 at the left hip and a low Z score of -2.9. He had not sustained any fractures in the past. There was no history of corticosteroid exposure and no parental history of hip fracture or osteoporosis. He drank up to 21 units of alcohol a week and was an ex-smoker. He was managing a gluten-free diet. His testosterone and vitamin D levels were normal. Serum electrophoresis, done as part of the osteoporosis workup, revealed a diagnosis of multiple myeloma. He then developed back pain and given his new diagnosis of myeloma, prompt investigations were carried out. A skeletal survey showed T7 fracture and a subsequent MRI scan showed impending cord compression, which were treated successfully with radiotherapy. He underwent chemotherapy and autologous stem cell transplantation for his myeloma.
He recently had an OGD following one week post gluten rechallenge after an established gluten free diet. His biopsy shows no evidence of coeliac disease. Interestingly, the stem cell transplantation did not only treat our patient's myeloma, but also his coeliac disease.
Results: Z-score is a useful indicator of possible secondary osteoporosis. A score of –2.0 or less is below the expected range for age and should prompt careful scrutiny for an underlying cause.
Coeliac disease is a gluten-sensitive enteropathy and a known cause for secondary osteoporosis. It likely causes bone loss by secondary hyperparathyroidism from vitamin D deficiency. Multiple myeloma is a disease of aging adults resulting in osteolytic and/or osteoporotic bone disease through increased bone resorption and decreased bone formation from pro-inflammatory cytokines. While coeliac disease patients are at increased risk of all malignancies, association with multiple myeloma is rare, but has been described.
Conclusion: This case highlights the importance of evaluating for secondary causes for low bone mineral density and often, one may find more than one contributory factor. It also shows that a Z-score of –2.0 could help identify patients with a secondary cause for osteoporosis and those who would especially benefit from a thorough history and examination.
REFERENCES:
[1] Sahin, Idris & Demir, Cengiz & Alay, Murat & Eminbeyli, Lokman. (2011). The Patient Presenting with Renal Failure Due to Multiple Myeloma Associated with Celiac Disease: Case Report. UHOD - Uluslararasi Hematoloji-Onkoloji Dergisi. 21. 10.4999/uhod.09087.
[2] İpek, Belkız & Aksungar, Fehime & Tiftikci, Arzu & Coskun, Abdurrahman & Serteser, Mustafa & Unsal, Ibrahim. (2016). A rare association: celiac disease and multiple myeloma in an asymptomatic young patient. Turkish Journal of Biochemistry. 41. 10.1515/tjb-2016-0053.
[3] Swaminathan K, Flynn R, Garton M, Paterson C, Leese G. Search for secondary osteoporosis: are Z scores useful predictors? Postgrad Med J. 2009 Jan;85(999):38-9. doi: 10.1136/pgmj.2007.065748. PMID: 19240287.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3594

AB0623 OSTEOPOROSIS: SCREENING, DIAGNOSIS AND TREATMENT IN TUNISIA: INVENTORY

S. Jriri[1], N. El Amri[1], K. Baccouche[1], S. Lataoui[1], H. Zeglaoui[1], E. Bouajina[1]. [1]*Farhat Hached, rhuematology, sousse, Tunisia*

Background: Osteoporosis has become a public health issue due to the increasing number of complications in osteoporotic women in terms of morbidity and mortality.His screening has improved since the refund of the bone densitometry, but prevention, diagnosis and treatment of this pathology remain suboptimal.
Objectives: a qualitative study to understand barriers towards care initiation and levers to improve awareness and management of osteoporosis among general and specialist practitioners.
Methods: The survey was conducted among a random sample of general practitioners and specialists.An anonymous questionnaire was used for this study carried out by mail.It contained 22 questions concerning the socio-demographic characteristics of each practitioner and his patient group, general questions on osteoporosis and questions on the practice in terms of management.The survey lasted about six weeks.
Results: 102 doctors have answered.55,3% were experienced doctors and 44.7% were young doctors in training.They were 43 general practitioners,21 rheumatologists,15 orthopedists,13 gynecologists and 10 endocrinologists.The sector of activity in urban and periurban areas was noted in 90% of casesand 5% in rural.43% exercised a liberal activity and57% had a hospital-university activity.60% of participants believed that osteoporosis is a condition associated with morbi-mortality and 85% confirmed that it is an underestimated disease. In 72% of physicians,women over 50 accounted for 25 to 75% of their female patient base.86% of doctors looked for recent information on osteoporosis from medical journals andrecommendations and 11% from representatives of pharmaceutical companies.In a recently menopausal patient,68% of physicians often looked for risk factors for osteoporosis which were: Age in 90% of cases, early menopause in 84%,presence of a family or personal history of fracture in 65 %,a history of prolonged systemic corticosteroid therapy in 46% ofcases;endocrine pathologies in 29%;Chronic inflammatory rheumatism was investigated in 19% of cases,Smoking and alcoholism were investigated in 11% of cases.The diagnosis of osteoporosis was mentioned in case of bone transparency on standard X-rays in 76% of cases,a low-energy trauma fracture in 43.5% and the presence of a risk factor in 35% of cases.98% of responding physicians rely on bone densitometry to make the diagnosis of osteoporosis.41.2% of doctors said they were looking for a secondary cause of osteoporosis or a differential diagnosis by requesting a biology.This assessment included:blood phosphocalcic assessment in 88%,vitamin D in 90%,thyroid assessment in 35%,protein electrophoresis in 38%, inflammatory biologic markers in 20% and immunological factors were requested in 6% of cases.The choice of anti-osteoporosis treatment depended on the bone densitometry result in 88% of casesand the presence of a personal history of fractures in 36.5% of cases.Bisphosphonates were at the top of the therapeutic arsenal of general practitioners and specialists (99.8%).100% of the participants knew the reimbursement criteria for anti-osteoporosis treatment by the national health insurance fund and take them into account when prescribing in 91% of cases.The duration of a therapeutic sequence varied from one practitioner to another: 13% of the doctors did not specify it, 45% treated their patients for five years and 42% kept the treatment for 3 years.When a fracture occurred during treatment, 64% of general practitioners had recourse to a rheumatologist, the rest carried out a densitometric reassessment.
Conclusion: The deficits found in the knowledge of both the general practitioners and among others specialists, should be addressed by providing updated information and better awareness of health professionals in order to improve osteoporosis prevention and treatment.
REFERENCES:
[1] Taylor, J. C., Sterkel, B., Utley, M., Shipley, M., Newman, S., Horton, M., & Fitz-Clarence, H.2001. Opinions and Experiences in General Practice on Osteoporosis Prevention, Diagnosis and Management. Osteoporosis International, 12(10), 844–848
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4049

AB0624 COMPARISON OF DIFFERENT FRAX SCORES WITHOUT BONE MINERAL DENSITY FOR THE EVALUATION OF RISK FRACTURE IN MEXICAN PATIENTS WITH RHEUMATIC DISEASES

G. Figueroa-Parra[1], A. Y. Lujano Negrete[1], R. Moyeda Martinez[1], C. M. Gamboa-Alonso[1], D. Á. Galarza-Delgado[1], C. M. Skinner Taylor[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Servicio de Reumatología, Monterrey, Mexico*

Background: Osteoporosis (OP) is characterized by compromised bone strength and deterioration of quality, often leading to fragility fractures(1). Dual-energy x-ray absorptiometry (DXA) is the recommended test for OP screening(1). However, there are limitations to perform DXA on all patients, and the clinicians use screening tools to identify those patients with higher risk, like the FRAX score(2).

Nevertheless, these scores have showed low to moderate correlation with DXA in RD patients(3).

Objectives: To evaluate the fracture risk in RD patients, using different versions of FRAX scores without a bone mineral density (BMD) measure.

Methods: An observational prospective study was performed at the Rheumatology Clinic in the University Hospital "Dr. Jose Eleuterio Gonzalez" in Monterrey, Mexico, between August and October 2020. Consecutive patients with a RD were evaluated as part of a "Bone Health Program"(3). Demographics and the risk factors included in FRAX tool was collected from ≥40 years-old patients; FRAX score was calculated online at https://www.sheffield.ac.uk/FRAX/ (algorithm for Mexicans). Four versions were calculated: 1) FRAX score without (w/o) BMD; 2) FRAX score with a T-score of -1.0 (w/Op); 3) FRAX score with a T-score of -2.5 (w/OP) and a FRAX score with positive previous fracture (Fx+). Then were classified as low (<10% for OP or <1% for hip), intermediate (10%-19% for OP or 1%-<3% for hip) and high risk (≥20% for OP or ≥3% for hip). Results are shown in means (SD) or frequency (%). A chi-square test was used to compare groups. Spearman's correlation test (rho) was done between OP risk and Hip risk in each version of FRAX. P<0.05 was considered statistically significant.

Results: One hundred and three patients were included, 93.2% were woman. The most frequent diagnosis was RA in 51.5% of patients, followed by osteoarthritis in 7.8%. 62.1% of patients had a previous BMD measured by DXA. 21.4% had history of previous fracture. 61.2% of patients were taking glucocorticoids. (Table 1). According to FRAX risk w/o BMD, 82 (79.6%) had low risk, 13 (12.6%) had intermediate risk, and 8 (7.8%) had high risk for OP. According to FRAX risk w/o BMD, 59 (57.3%) had low risk, 24 (23.3%) had intermediate risk, and 20 (19.4%) had high risk for hip fracture (Table 2). The correlations between OP risk and Hip risk in each version were as follow: FRAX w/o BMD (rho= .734, P= <.001) FRAX w/Op (rho= .308, P= .002); FRAX w/OP (rho= .476, P= <.001); FRAX with Fx+ (rho= .634, P= <.001).

Conclusion: There is a wide variability among the different FRAX risk scores evaluated, and moderate to high correlation between the OP and Hip risk in patients with RD.

REFERENCES:

[1] Ann Intern Med. 2017;166(11):818-839. doi:10.7326/M15-1361
[2] Arthritis Rheumatol. 2019;71(suppl 10):3924-3925
[3] Ann Rheum Dis. 2020;79:1190-1191

Table 1. FRAX score risk factors

	N= 103	95% C.I.
Age, years, mean (SD)	57.0 (9.56)	55.1 – 58.9
Female, n (%)	96 (93.2)	86.4 – 96.9
Weight, kg, mean (SD)	68.2 (14.88)	65.3 – 71.2
Height, cm, mean (SD)	154.6 (6.73)	153.3 – 155.9
Previous Fracture, n (%)	22 (21.4)	14.5 – 30.3
Parent Fractured Hip, n (%)	12 (11.7)	6.7 – 19.4
Current Smoking, n (%)	12 (11.7)	6.7 – 19.4
Glucocorticoids, n (%),	63 (61.2)	51.5 – 70.0
Rheumatoid arthritis, n (%)	53 (51.5)	41.9 – 60.9
Secondary osteoporosis, n (%)	1 (1.0)	0.0 – 5.8
Alcohol use, n (%)	1 (1.0)	0.0 – 5.8
Previous DXA, n (%)	64 (62.1)	52.5 – 70.9

Table 2. Fracture risk according different FRAX score versions

	Low risk (<10% for OP or <1% for hip)	Intermediate (10%-19% for OP or 1%-<3% for hip)	High risk (≥20% for OP or ≥3% for hip)	*P*
FRAX risk w/o BMD, n (%)				
Osteoporosis	82 (79.6)	13 (12.6)	8 (7.8)	<.001
Hip	59 (57.3)	24 (23.3)	20 (19.4)	
FRAX risk w/Op, n(%)				
Osteoporosis	101 (98.1)	2 (1.9)	-	<.001
Hip	98 (95.1)	4 (3.9)	1 (1.0)	
FRAX risk w/OP, n(%)				
Osteoporosis	96 (93.2)	4 (3.9)	3 (2.9)	<.001
Hip	10 (9.7)	80 (77.7)	13 (12.9)	
FRAX risk with Fx+, n(%)				
Osteoporosis	86 (83.5)	13 (12.6)	4 (3.9)	<.001
Hip	49 (47.6)	38 (36.9)	16 (15.5)	

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4144

AB0625 ARE TUNISIAN WOMEN PRONE TO VERTEBRAL FRACTURES AT A YOUNGER AGE?

C. Daldoul[1], N. El Amri[1], S. Laataoui[1], K. Baccouche[1], H. Zegaloui[1], E. Bouajina[1]. [1]*Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*

Background: There is an evident increased risk of vertebral fractures (VF) related to ageing. This is due to alterations in trabecular microarchitecture and a decrease in cortical thickness. The International Society of Clinical Densitometry (ISCD) recommend an age threshold of 70 years for VF screening in women. However, a large proportion of VF occurs below this threshold. In Tunisia, there was no previous study evaluating the association between age and VF.

Objectives: The aim of this study was to evaluate the relationship between age and prevalent VF in Tunisian women.

Methods: We conducted a cross-sectional study over a period of 5 months at the rheumatology department. The study included post-menopausal women without a previous diagnosis of VF referred for BMD measurement. Each participant had an extensive medical history investigation, a BMD assessment and a VFA scan to detect prevalent VF using dual energy X absorptiometry DeXa. VF were identified according the Genant semi-quantitative method and grade 1 VF were ruled out. We used the WHO criteria for the diagnosis of osteoporosis and osteopenia. For age, the results were expressed as means with standard deviations (SD) and extreme values and then analyzed with two-tailed Student t test. The receiver operating characteristics curve (ROC) determined cut-offs for age. Statistical significance was set at 5%.

Results: Two hundred and ten women were included in this study. The mean age of our patients was 61.51±8.49 with extremes ranging from 40 to 81 years. The distribution of our patients in 10 years age groups showed that: 9% were aged between 40 and 50 years, 34.3% were aged between 50 and 60 years, 38.6% were aged between 60 and 70 years, 17.1% were aged between 70 and 80 years and 1% were aged above 80 years. The mean BMI was 31.04±5.52 kg/m2. Thirty-seven percent of our participants had at least one fragility fracture and a severe fragility fracture was recorded in 10.5%. An early menopause was found in 19.5% of our women. Twenty percent of our population were receiving corticosteroids. The mean vertebral and total hip BMD was 0.955±0.165 g/cm2 and 0.850±0.135 g/cm2 respectively. Osteoporosis and low BMD were found in respectively 50% and 34.28%. The mean age in the VF group was significantly higher compared to the non-VF group (64.37 years vs. 60.50 years, p=0.003). The ROC curve identified an age cut-off of 60 years for VF. Age above 60 years was significantly associated with VF (65.5% vs. 43.9%, p=0.006) with an unadjusted risk of 5.42 (95%CI [1.278-4.597]). Among women with VF, 74.5% (41 women) were aged under 70 years which is the threshold proposed by the ISCD for VF screening. Among women aged under 70 years and having at least one VF (41 women), 6 women (14.63%) had an indication for VF screening as they reported a historical height loss of 4 cm and 8 women (19.51%) had an indication for VF screening as they were receiving corticosteroids. Hence, 27women (65.85%) had at least one VF and no indication for VF screening according to the ISCD.

Conclusion: Tunisian women over 60 years were at higher risk of VF. Applying the ISCD criteria for VF screening would miss 65.85% of women with VF. Those findings highlight the particularity of this population experiencing osteoporotic VF at an early age.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4201

AB0626 THE CHARACTERISTICS AND TREATMENT OF PATIENTS ADMITTED WITH FRAGILITY FRACTURE OF THE HIP

H. Baharuddin[1,2], R. Nasadurai[2], S. S. Ch'ng[2], Y. Z. Cheng[2], D. R. Ramakrishna Rao[2], P. A. Megat Mohamad Zainuddin[2], S. Sabir Husin Athar[3], M. Mohd Zain[2]. [1]*Universiti Teknologi MARA, Department of Internal Medicine, Sungai Buloh, Malaysia*; [2]*Selayang Hospital, Department of Medicine, Batu Caves, Malaysia*; [3]*Selayang Hospital, Department of Orthopaedics, Batu Caves, Malaysia*

Background: Hip fractures are associated with significant morbidity, mortality, loss of independence and financial burden.[1] There is a positive influence of calcium and vitamin D supplementation on the fracture-healing outcome.[2]

Recent evidence supports starting bisphosphonate in the acute post-fracture period.[3]

Objectives: To investigate the characteristics and treatment of patients admitted with fragility fracture of the hip.

Methods: This is a retrospective study on all patients admitted with fragility fracture of the hip throughout 2018, included in the hospital registry. Data collected included patients' characteristics, place of falls, types of fracture, in-patient surgical treatment and medical treatment prescribed up until one year follow-up. Outcome of hospitalisation were reported as alive, death and at-own-risk discharge. Continuous and categorical data were described using mean (±SD) and no of patients (%). Comparison of continuous data was performed using student t-test.

Results: One-hundred and sixty-seven patients were admitted with fragility fracture of the hip. There were 44 (26.3%) male and 123 (73.7%) female patients, with a mean age of 77.1(±9.8) years. Male patients were significantly younger compared to female patients [73.1(±10.5) years vs 78.5(±9.1) years, p=0.002]. Eighty-six (51.5%) patients were Chinese, followed 57 (34.1%) Malay and 24 (14.4%) Indian patients. Chinese patients were significantly older than Malay patients [80.4(±8.2) years vs 74.6(±9.8) years, p<0.001] and Indian patients [80.4(±8.2) years vs 71.0(±10.5), p<0.001].

Most patients, 96 (57.5%) fell within the vicinity of their homes while the other 26 (12.7%) patients fell outside of their home. The place of fall was not documented for 45 (26.9%) patients. The types of fractures were neck of femur in 70 (41.9%), inter-trochanteric fracture in 93 (55.7%) and subtrochanteric in 4 (2.4%) patients.

Of 167 patients, 100 (59.9%) patients underwent surgical treatment and 67 (40.1%) patients were treated conservatively. The prescription of calcium and vitamin D was significantly higher in female patients (Table 1). Of 167 patients, 148 (88.6%) were discharged home, 12 (7.2%) patients died during hospital admission and 7 (4.2%) patients opted for at-own-risk discharge.

Table 1. Treatment prescribed to patients admitted with fragility fracture of the hip.

Treatment		Male, no of patients (%)	Female, no of patients (%)	p-value
Surgery	Yes (n=100)	30 (30)	70 (70)	0.209
	No (n=67)	14 (20.1)	53 (79.1)	
Calcium	Yes (n=91)	18 (19.8)	73 (80.2)	0.035
	No (n=76)	26 (34.2)	50 (65.8)	
Vitamin D	Yes (n=88)	16 (18.2)	72 (81.8)	0.011
	No (n=79)	28 (35.4)	51 (64.6)	
Bisphosphonate	Yes (n=13)	0	13 (100)	NA
	No (n=154)	44 (28.6)	110 (71.4)	

Conclusion: There was a high proportion of female patients admitted with fragility fracture of the hip. Majority of patients were Chinese, who were significantly older compared to Malay and Indian patients. We found a low prescription of osteoporosis medications for patients following fragility fracture of the hip. The care of osteoporosis can be improved through multidisciplinary approach.

REFERENCES:

[1] Schnell S, et al. The 1-Year Mortality of Patients Treated in a Hip Frature Program for Elders. Geriatr Orthop Surg Rehabil, 2010; 1: 6-14.

[2] Fischer V, et al. Calcium and Vitamin D in Bone Fracture Healing and Post Traumatic Bone Turnover. European Cells and Materails, 2018; 35: 365-385.

[3] Barton DW, et al. Timing of Bisphosphonate Initiation After Fracture: What Does the Data Really Say? Geriatr Orthop Surg Rehabil, 2020; 11; 1-5.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4240

AB0627 THE EFFECT OF BIOLOGICALLY ACTIVE FOOD SUPPLEMENT WITH CALCIUM AND VITAMIN D3 ADMINISTRATION ON CALCIUM HOMEOSTASIS AND FALLS INCIDENCE IN PATIENTS WITH HIGH FRACTURE RISK UNDERGOING MEDICAL REHABILITATION

L. Marchenkova[1], V. Vasileva[1]. [1]*National Medical Research Center for Rehabilitation and Balneology of Ministry of Health of Russian Federation, Rehabilitation department for somatic patients, Москва, Russian Federation*

Background: Vitamin D and calcium deficiencies is of particular importance in older patients undergoing medical rehabilitation and having a high risk of fractures. Preventing falls and fractures, including during the course of rehabilitation, is an important challenge that can be addressed in these patients, in particular through improved nutrition and vitamin D and calcium supplementation.

Objectives: to evaluate the effect of long-term calcium and vitamin D3 intake on calcium homeostasis and fall's rate in patients with high fracture risk starting rehabilitation course.

Methods: The study enrolled 119 men and women aged 50-80 y.o. with high absolute fracture probability by FRAX who started medical rehabilitation. 41 patients have been receiving antiresorptive therapy already comprised group 1, other patients were randomized into groups 2 (n=39) and 3 (control, n=39). In groups 1 and 2, a food supplement containing calcium citrate 1000 mg and vitamin D3 600 IU was prescribed for 12 months. All patients undergo laboratory examination, food calcium intake and fall assessment at baseline, in 6 and 12 months.

Results: Daily calcium intake in the study sample (n=119) was 782.9±243.4 mg. Vitamin D deficiency was detected in 38.4% of the examined. An increase in 25(OH)D level was noted in groups 1 and 2 after 6 and 12 months (p<0.01). Patients in group 1 showed an increase in serum osteocalcin and calcium levels after 6 and 12 months (p<0.05). In group 3, there was an increase of immunoreactive parathyroid hormone levels after 6 (p<0.05) and 12 months (p<0.01), C-terminal telopeptide of type I collagen level and alkaline phosphatase activity after 12 months (p<0.05). In group 1, there was also a decrease in proportion of patients who fell after 6 months ($\chi 2$=4.97, p=0.026) and a decrease in the total number of falls after 12 months ($\chi 2$=4.89, p=0.027). Group 2 showed a decrease in the number of patients who fell after 6 and 12 months ($\chi 2$=48.58, p=0.0034 at both stages of the study) and the number of falls in general after 6 months ($\chi 2$=6.02, p=0.0142).

Conclusion: The obtained data allow us to recommend prescription of dietary supplements containing calcium and vitamin D3 as a part of complex rehabilitation of patients with high fracture risk.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4254

Crystal diseases, metabolic bone diseases other than osteoporosis

AB0628 PRE-INFUSION GLUCOCORTICOID ELIMINATION IN PATIENTS WITH UNCONTROLLED GOUT TREATED WITH PEGLOTICASE: A CASE SERIES

V. Newsome[1], A. Amatucci[2], T. Stainbrook[1], B. Lamoreaux[2]. [1]*Penn Highlands Healthcare, Rheumatology, DuBois, United States of America*; [2]*Horizon Therapeutics plc, Medical Affairs, Deerfield, United States of America*

Background: Pegloticase is indicated for treating uncontrolled gout, but some patients develop anti-drug antibodies that have been associated with a loss of efficacy and infusion reactions (IRs).[1] Per the pegloticase prescribing information, pre-infusion medications, including glucocorticoids (GCs), should be given to minimize IR risk.[2] Given that GCs have a significant side effect profile and patients with uncontrolled gout generally have multiple comorbidities,[3,4] minimizing steroid exposure is desirable.

Objectives: The current case series examines a community rheumatology practices' experience with pre-infusion GC elimination in uncontrolled gout patients treated with pegloticase.

Methods: This retrospective chart review was conducted at a rheumatology practice that discontinues pre-infusion GC use in patients treated with pegloticase. Patients treated from 2016-2020 who had pre-infusion GCs discontinued during therapy were included. Pre-infusion prophylaxis at this practice includes methylprednisolone (125 mg IV), diphenhydramine (50 mg oral + 12.5 mg IVP), famotidine (40 mg oral), and acetaminophen (1000 mg) administered immediately before infusions. All other IR prophylaxis continued when GCs were stopped without tapering. Demographics, number of pegloticase infusions, and safety (adverse events [AEs], clinical lab values) were examined. Patients self-managed gout flares with oral methylprednisolone (24 mg then 5-day taper).

Results: Nine patients (8 male) with tophaceous gout met inclusion criteria. Mean age was 72.3 ± 6.9 years (65-84 years), mean BMI was 28.7 ± 5.6 kg/m^2, and mean pre-therapy serum uric acid (sUA) was 7.3 ± 2.7 mg/dL (3.9-12.7 mg/dL). Two patients were co-treated with oral methotrexate (15 and 20 mg/week) and one patient was on hemodialysis. Most common comorbidities included osteoarthritis (9 patients), hypertension (8 patients), chronic kidney disease (5 patients), kidney stones (5 patients), and diabetes (5 patients). A median of 27 pegloticase infusions (range: 9-84) were administered, with 8 of 9 patients receiving ≥12 infusions. Median number of infusions before and after initial GC

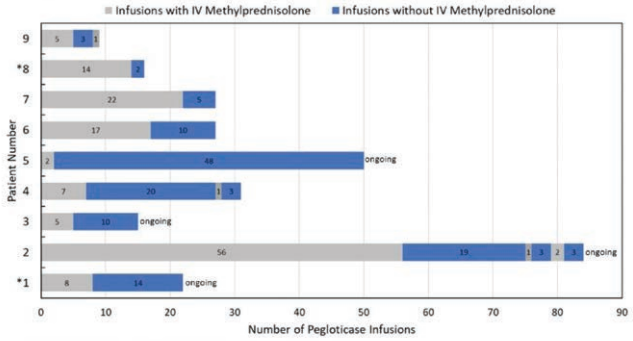
discontinuation was 7 (range: 2-56) and 10 (range: 2-48), respectively. Pre-infusion steroids were re-started in 3 patients after a rise in sUA, with 1 regaining sUA response (patient 2) and 2 discontinuing therapy (patients 4 and 9). An additional patient had a loss of sUA response (patient 7) and discontinued, 1 patient discontinued due to hospitalization (patient 6), and 1 patient chose to discontinue therapy (patient 8). At the time of data collection, 4 patients remained on therapy (patients 1-3, 5). Eight patients had at least one AE (all deemed unrelated to treatment), including influenza, hypertensive crisis, and toe amputation. No IRs occurred.

Conclusion: In this case series, 8 of 9 patients received 6 months or more (≥12 infusion) of pegloticase. These cases suggest that pre-infusion GC discontinuation may be possible in some patients treated with pegloticase (particularly those over 70 years). Further investigation exploring this concept is warranted, including evaluating the optimal time and conditions to discontinue pre-infusion GCs with pegloticase.

REFERENCES:

[1] Sundy JS, et al. *JAMA.* 2011;306(7):711-720.
[2] KRYSTEXXA (pegloticase) [prescribing information] Horizon.
[3] Saag KG. *Bull NYU Hosp Jt Dis* 2012;70(Suppl 1):S21-S25.
[4] Pillinger MH, et al. *Bull NYU Hosp Jt Dis* 2010;68:199-203.

Figure. Pegloticase infusions administered with and without pre-infusion IV methyprednisolone at time of data collection



*patient administered oral methotrexate before and during pegloticase therapy.
Patients 4, 7, and 9 (ages 65-67) discontinued due to loss of sUA response.

Disclosure of Interests: Veronica Newsome Speakers bureau: Abbvie, Anthony Amatucci Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Tim Stainbrook: None declared., Brian LaMoreaux Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc.

DOI: 10.1136/annrheumdis-2021-eular.70

AB0629 ACCURACY OF SYNOVIAL FLUID ANALYSIS FOR THE IDENTIFICATION OF CALCIUM PYROPHOSPHATE CRYSTALS: AN ANCILLARY STUDY OF OMERACT CRITERION VALIDITY STUDY FOR ULTRASOUND IN CPPD

A. Adinolfi[1], S. Sirotti[2], M. Gutierrez[3], C. Pineda[3], D. Clavijo Cornejo[3], T. Serban[4], A. Dumitru[5], A. Scanu[6], M. A. D'agostino[7], H. Keen[8], L. Terslev[9], P. Sarzi-Puttini[2], C. A. Scirè[10], A. Iagnocco[11], G. Filippou[2]on behalf of Omeract Ultrasound working group, subgroup CPPD.
[1]ASST Grande Ospedale Metropolitano Niguarda, Rheumatology Unit, Milan, Italy; *[2]Luigi Sacco University Hospital, Rheumatology Department, Milan, Italy*; *[3]Instituto Nacional de Rehabilitacion, Division of Musculoskeletal and Rheumatic Diseases, Mexico City, Mexico*; *[4]Ospedale La Colletta, ASL3 Genovese, Rheumatology Department, Genoa, Italy*; *[5]Carol Davila University of Medicine and Pharmacy, Department of Pathology, Bucharest r, Romania*; *[6]University of Padova, Department of Medicine-DIMED, Rheumatology Unit, Padova, Italy*; *[7]Università Cattolica del Sacro Cuore, Policlinico Universitario Agostino Gemelli IRCSS, Rheumatology Department, Rome, Italy*; *[8] The University of Western Australia, Medicine and Pharmacology Department, Murdoch, Perth, Australia*; *[9]Copenhagen University, Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark*; *[10]Società Italiana di Reumatologia, Epidemiology Research Unit, Milan, Italy*; *[11]Università degli Studi di Torino, Rheumatology Unit, Department of Clinical and Biological Sciences, Torino, Italy*

Background: Synovial fluid analysis (SFA) via compensated polarized light microscopy is still considered the gold standard for the identification and diagnosis of Calcium Pyrophosphate Deposition disease (CPPD)-related arthropathies[1], but very few studies have been published about its diagnostic accuracy.

Objectives: The aim of this study was to evaluate the accuracy of SFA in the identification of calcium pyrophosphate dihydrate (CPP) crystals compared to microscopic analysis of joint tissues as the reference standard.

Methods: This is an ancillary study of an international, multicentre cross-sectional study performed by the CPPD subgroup of the OMERACT Ultrasound working group[2]. Consecutive patients with knee osteoarthritis (OA) waiting for total knee replacement surgery were enrolled in the study from 2 participating centres, Mexico and Romania. During surgical procedures synovial fluid (SF), menisci and hyaline cartilage were collected and analysed within 48 hours after surgery under transmitted light microscopy and compensated polarised light microscopy for the presence/absence of CPP crystals. All slides were analysed by expert examiners on site, blinded to other findings. A dichotomic score (absence/presence) was used for scoring both SF and tissues. Microscopic analysis of knee tissues was considered the gold standard. Sensitivity, specificity, accuracy, positive and negative predictive values (PPV and NPV) of SFA in the identification of CPP crystals were calculated.

Results: 15 patients (53% female, mean age 68yo ± 8.4) with OA of grade 3 or 4 according to Kellgren-Lawrence scoring were enrolled. 12 patients (80%) were positive for CPP crystals at SFA and 14 (93%) at tissues microscopic analysis. Among 12 SFA positive patients, all were positive for CPP crystals in either medial or lateral meniscus, and 11 were positive in both; 10 patients were positive at the hyaline cartilage, and all 10 were also positive for at least one meniscus. Regarding the 3 SFA negative patients, only one had no crystals in the examined tissues, while the other 2 patients had CPP crystals in both menisci and hyaline cartilage. The overall diagnostic accuracy of SFA compared to histology analysis for CPPD was 87%, with a sensitivity of 86% and a specificity of 100%, the PPV was 100% and the NPV was 33% (Table 1).

Table 1. sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of synovial fluid analysis compared to the reference standard. CI: Confidential Interval. SF: synovial fluid, in parentheses: numerators and denominators for all percentages provided.

	Sensitivity	Specificity	PPV	NPV	Accuracy
SF analysis	86% (12/14) (0.65-0.99) CI 95%	100% (1/1) (0.0-0.25) CI 95%	100% (12/12) (0.65-0.99) CI 95%	33% (1/3) (0.0-0.25) CI 95%	87% (13/15)

Conclusion: SFA demonstrated to be an accurate test for the identification of CPP crystals in patients with advanced OA. However, is not always feasible and carries some risks for the patient. Considering the availability of validated imaging techniques for the detection of CPPD, such as US, SFA could be used in those patients where imaging and clinical data are not definitely confirmatory of the disease.

REFERENCES:

[1] W. Zhang *et al.*, 'European League Against Rheumatism recommendations for calcium pyrophosphate deposition. Part I: terminology and diagnosis', *Ann Rheum Dis*, vol. 70, no. 4, pp. 563–570, Apr. 2011, doi: 10.1136/ard.2010.139105.
[2] G. Filippou *et al.*, 'Criterion validity of ultrasound in the identification of calcium pyrophosphate crystal deposits at the knee: an OMERACT ultrasound study', *Ann Rheum Dis*, p. annrheumdis-2020-217998, Sep. 2020, doi: 10.1136/annrheumdis-2020-217998.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.601

AB0630 PEGLOTICASE/METHOTREXATE CO-THERAPY IMPROVED JOINT AND PATIENT-REPORTED HEALTH ASSESSMENTS IN PATIENTS WITH UNCONTROLLED GOUT: 12-MONTH EXPLORATORY OUTCOMES OF THE MIRROR OPEN-LABEL TRIAL

J. Botson[1], P. M. Peloso[2], K. Obermeyer[2], B. Lamoreaux[3], L. Zhao[2], M. E. Weinblatt[4], J. Peterson[5]. *[1]Orthopedic Physicians Alaska, Medical,*

Anchorage, United States of America; [2]*Horizon Therapeutics plc, Research and Development, Deerfield, United States of America*; [3]*Horizon Therapeutics plc, Medical Affairs, Deerfield, United States of America*; [4]*Brigham and Women's Hospital, Division of Rheumatology, Immunology and Allergy, Boston, United States of America*; [5]*Western Washington Medical Group, Arthritis Clinic, Bothell, United States of America*

Background: Gout development follows persistent serum uric acid (sUA) elevation. Patients who are refractory to or cannot tolerate oral urate lowering therapies (ULTs) have limited treatment options. Pegloticase is effective in treating refractory gout, but many patients develop anti-drug antibodies (ADAs), which are associated with loss of urate-lowering efficacy[1-3] and infusion reactions (IRs).[1,2] In phase 3 trials, the pooled pegloticase responder rate during Months 3 and 6 combined was 42% (8 mg infusion every 2 weeks), with high-titer ADA positive patients losing efficacy prior to 6 months.[1] The 6-month results from the MIRROR open-label trial (79% response rate [11/14], 95%CI 49-95%)[4] suggest that methotrexate (MTX) administered in conjunction with pegloticase increases treatment responder rate.

Objectives: To examine longer-term (12-month) exploratory endpoints from the MIRROR open-label trial, including joint, overall health, and gout global assessments. Serial dual-energy computed tomography (DECT) images were also examined when available.

Methods: Adult patients with uncontrolled gout (sUA ≥6 mg/dL with ≥1 of the following: sUA ≥6 mg/dL despite ULT use, intolerance to ULT, or functionally limiting tophaceous deposits) were included. Patients with immunocompromised status, G6PD deficiency, severe renal impairment, or MTX contraindication were excluded. Patients were administered oral MTX (15 mg/week) and folic acid (1 mg/day) 4 weeks prior to and throughout pegloticase therapy (8 mg biweekly infusion for up to 52 weeks). Exploratory outcomes included mean change from baseline (CFB) in number of affected joints (tophi, swollen, tender), Health Assessment Questionnaire (HAQ) scores (Disability Index [DI; score 0–3], Pain [score 0–100], Health [score 0–100]), and Gout Global Assessments (Patient, Physician; score 0–10). A decrease in these measures reflects clinical/patient-reported health improvement. Change in urate deposition volume, as measured on DECT imaging, was also examined as available. Analyses were performed on the modified intent-to-treat (mITT) population (≥1 pegloticase infusion received).

Results: 14 patients (all male, mean±SD age: 49.3±8.7 years) made up the mITT population. Mean±SD sUA prior to pegloticase treatment was 9.2±2.5 mg/dL and 13 patients had visible tophi. 3 patients discontinued due to 2 consecutive sUA levels >6 mg/dL and 1 patient completed the study at week 24 (pre-protocol amendment extending treatment from 24 to 52 weeks). 10 patients completed the 52-week study. Of these, 8 patients received 26 infusions and 2 patients received 12 infusions, discontinued pegloticase after meeting their treatment goal at 24 weeks, and started allopurinol while remaining in study under observation. At week 52 (n=10, sUA=1.1±2.5 mg/dL), the number of affected joints improved, along with HAQ measures (Figure 1). Global Assessments of Gout also improved (Physician: CFB=-5.7±2.6, Patient CFB=-4.6±2.1) and majority of subjects had a score of 0 or 1 (0="excellent health") at week 52 (Physician: 0.3±0.5, Patient: 1.1±1.3). Two patients had available DECT imaging. One received pegloticase/methotrexate co-therapy thru week 52 and had a marked reduction in total urate volume (baseline: 128.76 cm^3, week 52: 1.33 cm^3). The other received only 5 pegloticase infusions, but also showed total urate volume reduction (baseline: 59.20 cm^3, week 10: 25.07 cm^3). Both patients displayed improvement in bone erosion healing.

Conclusion: These 12-month exploratory endpoints of the MIRROR open-label trial suggest that MTX/pegloticase co-therapy results in meaningful changes in clinical evaluations (tophaceous, tender, and swollen joint counts), and patient-reported outcomes (pain, disability) in patients with uncontrolled gout.

REFERENCES:

[1] Sundy JS et al. *JAMA* 2011;306:711-20
[2] Baraf HS et al. *J Clin Rheumatol* 2014;20:427-32
[3] Lipsky PE et al. *Arthritis Res Ther* 2014, 16:R60
[4] Botson JK et al. *J Rheum* 2020 [Epub ahead of print]

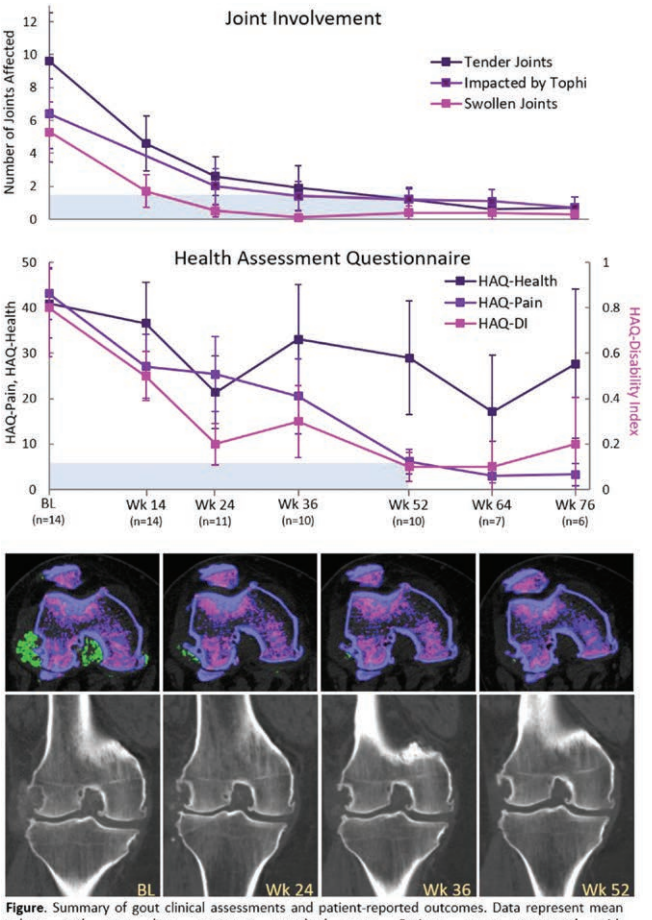


Figure. Summary of gout clinical assessments and patient-reported outcomes. Data represent mean values and error bars represent standard error. Patients were co-treated with pegloticase/methotrexate for up to 52-weeks (light blue bar; 52 weeks in 8 patients, 24 weeks in 2 patients). Week 64 and 76 represent the 3 and 6 month follow-up visits, respectively. DECT imaging shows progressive urate volume decrease in this knee (BL: 22.6 cm^3, Week 52: 0.1 cm^3) and bone erosion healing concomitant with clinical improvement. BL, baseline; HAQ, health assessment questionnaire; DI, disability index.

Disclosure of Interests: John Botson Speakers bureau: Horizon Therapeutics, Celgene, Novartis, and AbbVie, Consultant of: Horizon Therapeutics, Celgene, Novartis, and AbbVie, Grant/research support from: Horizon Therapeutics and Radius Health, Paul M. Peloso Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Katie Obermeyer Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Brian LaMoreaux Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Lin Zhao Shareholder of: Horizon Therapeutics plc, Employee of: Horizon Therapeutics plc, Michael E. Weinblatt Shareholder of: Lycera, Can-Fite BioPharma, Scipher Medicine, Inmedix, and Vorso, Consultant of: Bristol Myers Squibb, Corona, Lilly, AbbVie, Amgen, Arena, GlaxoSmithKline, Gilead Sciences, Horizon Therapeutics, Lycera, Novartis, Pfizer, Roche, Samsung, Scipher Medicine, and Set Point, Grant/research support from: Amgen, Bristol-Myers Squibb, Crescendo Bioscience, Lilly and Sanofi, Jeff Peterson Speakers bureau: Horizon Therapeutics plc, Grant/research support from: Horizon Therapeutics plc.
DOI: 10.1136/annrheumdis-2021-eular.996

AB0631

THE PREVALENCE AND FACTORS ASSOCIATED WITH CORONARY HEART DISEASE IN PATIENTS WITH GOUT

E. Markelova[1], M. Eliseev[2], E. Ilinykh[3], S. Glukhova[4], T. Popkova5. [1]*V.A. NASONOVA RESEARCH INSTITUTE OF RHEUMATOLOGY, Laboratory of Systemic Rheumatic Diseases, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, Moscow, Laboratory of Crystal Diseases, Moscow, Russian Federation*; [3]*V.A. NASONOVA RESEARCH INSTITUTE OF RHEUMATOLOGY, Laboratory of Crystal Diseases, Moscow, Russian Federation*; [4]*Moscow, Laboratory of Systemic Rheumatic Diseases, Moscow, Russian Federation*; [1]*V.A. NASONOVA RESEARCH INSTITUTE OF RHEUMATOLOGY, Laboratory of Systemic Rheumatic Diseases, Moscow, Russian Federation*

Background: Gout is associated with increased risk of cardiovascular disease (CVD) morbidity and mortality. Therefore, an association between coronary heart disease (CHD) and gout deserves careful examination.
Objectives: The aim of this study was to determine the prevalence of CHD and factors associated with CHD in patients (pts) with gout.
Methods: 286 male patients fulfilling Wallace proposed criteria for gout were included: age 51.2 [42.8;59.4] years (ys), disease duration – 6.2 [3.8;12.1] ys. All patients underwent standard clinical examination, screening traditional risk factors (TRF) of CVD, blood chemistry test with estimation of serum uric acid, serum creatinine, C-reactive protein (CRP), as well as lipid profile. Carotid intima-media thickness (cIMT) was measured using a high-resolution B-mode ultrasound machine. CHD included history of angina pectoris and/or myocardial infarction. We estimated the adjusted odds ratio (OR) and 95% confidence interval (95% CI).
Results: CHD was found in 111 out of the 286 pts (38.8 %). Compared to individuals with CHD, participants without CHD were older (56.7[52.1; 61.1] vs 46.2[40.6; 53.4] ys), had longer duration of gout (9.3[4.7; 15.1] vs 5.6[3.3; 9.7] ys), higher number of joints involved during disease course (8[6; 15] vs 6[4; 10]), duration of smoking (24[10; 40] vs 20[10; 28]), higher serum creatinine level accordingly, (for all $p<0.05$). The frequency of family history of CHD (63% vs 46.8%), intraosseous tophi (61.3% vs 33.1%), was higher in pts with CHD compared pts without CHD accordingly, (for all $p<0.01$). Prevalence of arterial hypertension, diabetes mellitus, nephrolithiasis, heart failure and renal failure was greater in pts with CHD than pts without CHD ($p<0.001$). Gout pts with CHD had a significantly higher cIMT compare to those without CHD - 0.95[0.8;1.08]/0.8[0.7;0.9] accordingly, $p<0.001$. We didn't find differences of lipid profile, serum uric acid, and CRP level in gout pts with/without CHD.
Abdominal obesity (OR, 5.5; 95% CI, 2.2-13.6), body mass index >30 kg/m^2 (OR, 5.8; 95% CI, 1.8-18.5), family history of CHD (OR, 2.7; 95% CI, 1.3-5.4), disease duration of gout more 10 ys (OR, 2.6; 95% CI, 1.3-5.1), age of gout onset < 35 ys (OR, 3.0; 95% CI, 1.5-6.1), intraosseous tophi (OR, 3.1; 95% CI, 1.4-7.0), C-RP (OR, 2.2; 95% CI, 1.1-4.7), renal failure (OR, 18,8; 95% CI, 1.1-312.9), increased the risk for CHD in patients with a gout.
Conclusion: The prevalence of CHD was 38.8% among individuals with gout. Our study showed that both TRFs of CVD and the severity of gout and a history of renal failure contribute to the development of CHD in patients with gout.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1241

AB0632

COMORBIDITIES AND DRUG-INDUCED LIVER INJURY DUE TO NSAIDS INTAKE IN PATIENTS WITH GOUT

E. Mikhnevich[1], P. Tatsiana[1], R. Tatsiana[1], H. Diana[1]. [1]*Belarusian State Medical University, Internal Disease, Minsk, Belarus*

Background: One of the side effects of NSAIDs is hepatotoxicity or Drug-Induced Liver Injury (DILI). Despite the short course of NSAIDs, the patients with gout may develop DILI. At the same time, besides NSAIDs, there are additional factors that affect the functional state of the liver: demography, comorbidities or concomitant medication (1).
Objectives: To determine comorbidities associated with the risk of DILI when taking NSAIDs during the attack of gouty arthritis.
Methods: Our retrospective study included 200 patients with GA. Inclusion criteria for the study: presence of gout (ACR, 1977), initially normal serum ALT level, NSAIDs as anti-inflammatory drugs in gout. Exclusion criteria: presence of a known liver disease. All patients were divided into 2 groups: those who developed DILI (n = 86) and the control group without cytolysis during NSAID treatment (n = 114). The severity of the cytolytic syndrome was revealed as follows: mild form (2-3-fold excess of the ALT norm) in 81,4 % (n = 70); moderate (3-5 times higher ALT) in 15.1% (n = 13); severe (5-10 fold excess of ALT) in 3.4% (n = 3). The mean age of 55 (49-60) years and 54 (44-59.5) years as well as the sex distribution (men made 90.1% and 93.3%, respectively) were compatible in both groups ($p>0,05$). When studying the age distribution, statistical differences were revealed in the groups under 52 years ($p<0,05$), so, this parameter was included into logistic regression model. During the follow-up period, all patients took NSAIDs above average doses. Patients in both groups were comparable in duration of gout. The following parameters were compared: AH, IHD, diabetes mellitus, obesity, dyslipidemia, metabolic syndrome according to ATPIII, CKD, alcohol abuse, age under 52.
Results: After conducting logistic regression analysis, the next comorbidities have been revealed to be statistically significant: obesity (OR – 2,15; 95%CI 1,16-3,98), dyslipidemia (OR – 3,41; 95% CI 1,56-7,44) and alcohol abuse (OR – 2,45; 95%CI 1,22-4,91). Worth to note that age under 52 was also a risk factor for DILI (OR – 2,14; 95%CI 1,13-4,04). Thus, among our patients, the younger ones with an unhealthy lifestyle and no serious comorbidities, including cardiovascular, were at a greater risk for developing DILI while taking NSAIDs during the gout attack.
Conclusion: In the study group of patients with gout, the hepatotoxicity (cytolysis syndrome) risk due to NSAIDs intake increased in younger patients in the presence of signs of metabolic syndrome (obesity, dyslipidemia) and alcohol abuse.
REFERENCES:
[1] European Association for the Study of the Liver. EASL Clinical Practice Guidelines Drug-induced liver injury. J. of Hepatology. 2019; 30: 1-40.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1381

AB0633

HEALTH RELATED QUALITY OF LIFE IN GOUT, PSORIATIC ARTHRITIS, RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS: RESULTS FROM A QUESTIONNAIRE STUDY

A. Landgren[1], M. Dehlin[1], L. T. H. Jacobsson[1], U. Bergsten[2], E. Klingberg[1]. [1]*Institute of Medicine, Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*; [2]*County of Halland, R&D Department at Region Halland, Halmstad, Halmstad, Sweden*

Background: Gout, psoriatic arthritis (PsA), rheumatoid arthritis (RA), ankylosing spondylitis (AS), are common inflammatory joint diseases (IJD) that substantially affect HRQoL (Health Related Quality of Life). To our knowledge, this is the first study comparing HRQoL in gout, PsA, RA and AS in the same setting.
Objectives: To compare HRQoL assessed with the Short Form health survey (SF-36) between gout, PsA, RA and AS.
Methods: We performed a cross-sectional questionnaire study in Sweden. Individuals ≥18 years and with at least one ICD-10 diagnosis for gout, PsA, RA, or AS, recorded at a health care visit to a physician at a rheumatology clinic (for all diagnoses) or at a primary care center (for gout patients) from 2015 through 2017 were identified. Patients with gout (n=1589), PsA (n=1200), RA (n=1246) and AS (n=1095) were sent a questionnaire including questions regarding Visual Analogue Scales (VAS) for General Health, Pain, Fatigue, Health Asssessment Questionnaire (HAQ), as well as the SF-36. The eight domains (a higher score indicating a better health status) as well as the overall physical (PCS) and mental (MCS) component scores (a value of 50 corresponds to unaffected HRQoL) of the SF-36 are presented. Respondents were matched on age, sex. ANOVA was used for between group comparisons of mean values. For non-normally distributed data, Kruskal Wallis test was used. For comparing distributions, the Chi-Square test was used.
Results: In total, 2896 (56.5%) individuals responded. After matching for age, sex, 249 individuals per diagnosis group remained. Gout patients reported significantly higher scores on SF-36 subscales as well as PCS (consistent with results seen before matching for age and sex). Lower values of HRQoL were noted in physical domains as compared to mental domains in all IJDs. Disability measured by HAQ was significantly lower in gout and VAS scores were more favourable compared to other IJDs.
Conclusion: Patients with gout report higher HRQOL compared to PsA, RA, AS.

Table 1. Age-matched comparisons across diagnoses

	Gout	PsA	RA	AS	p-value	p-value Gout vs PsA	p-value Gout vs RA	p-value Gout vs AS	p-value PsA vs RA	p-value PsA vs AS	p-value RA v AS
Total (n)	249	249	249	249	N/A						
Age, mean (SD)	62.5 (11.2)	64.2 (10.2)	63.1 (11.6)	62.8 (10.5)	NS						
Education ≤12 years, n (%)	132 (53.0)	148 (59.4)	160 (64.3)	139 (55.8)	NS						
HAQ, mean (SD)	0.19 (0.40)	0.48 (0.55)	0.60 (0.63)	0.58 (0.58)	***	***	***	***	NS	NS	NS
VAS General Health, mean (SD)	2.6 (2.3)	3.7 (2.4)	3.8 (2.6)	4.0 (2.3)	***	***	***	***	NS	NS	NS
VAS Pain, mean (SD)	2.6 (2.4)	4.0 (2.6)	3.8 (2.6)	4.2 (2.4)	***	***	***	***	NS	NS	NS
VAS Fatigue, mean (SD)	3.6 (2.6)	4.5 (2.7)	4.3 (2.6)	4.9 (2.5)	***	***	*	***	NS	NS	*
SF-36 domains, median (IQR)											
Physical function	90.0 (75.0-95.0)	70.0 (51.3-95.0)	70.0 (45.0-90.0)	75.0 (50.0-90.0)	***	***	***	***	NS	NS	NS
Role physical	100.0 (33.3-100.0)	50.0 (0.0-100.0)	50.0 (0.0-100.0)	50.0 (0.0-100.0)	***	***	***	***	NS	NS	NS
Bodily pain	72.0 (42.0-100.0)	52.0 (41.0-74.0)	52.0 (41.0-74.0)	52.0 (41.0-64.0)	***	***	***	***	NS	NS	NS
General Health	67.0 (47.8-80.8)	56.0 (35.0-72.0)	55.0 (37.0-72.0)	50.0 (35.0-71.0)	***	***	***	***	NS	NS	NS
Vitality	65.0 (50.0-77.5)	57.5 (37.5-75.0)	57.5 (42.5-72.5)	50.0 (32.5-70.0)	***	*	*	***	NS	NS	NS
Social function	100.0 (68.8-100.0)	81.3 (57.8-100.0)	81.3 (67.2-100.0)	81.3 (50.0-100.0)	***	**	**	***	NS	NS	NS
Role emotional	100.0 (66.7-100.0)	100.0 (33.3-100.0)	100.0 (33.3-100.0)	100.0 (33.3-100.0)	**	NS	**	**	NS	NS	NS
Mental health	82.0 (66.0-92.0)	78.0 (60.0-92.0)	78.0 (60.0-92.0)	73.0 (60.0-88.0)	**	NS	*	**	NS	NS	NS
SF-36 summary scores, median (IQR)											
Physical component score	48.4 (38.8-54.7)	40.2 (28.5-50.2)	40.2 (28.2-49.0)	38.7 (30.1-48.2)	***	***	***	***	NS	NS	NS
Mental component score	51.7 (43.7-56.5)	51.0 (39.2-56.4)	50.7 (39.6-56.3)	47.7 (37.1-55.3)	*	NS	NS	*	NS	NS	NS

HAQ=Health Assessment questionnaireIRQ=Interquartile rangeSD=Standard deviation-VAS=Visual Analogue ScaleNS=non-significant*=significant at p<0.05**=significant at p<0.01***=significant at p<0.001

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1582

AB0634

BELIEFS ABOUT URATE LOWERING THERAPY DIFFER BETWEEN GENERAL PRACTITIONERS AND RHEUMATOLOGISTS

F. Veenstra[1], J. Vriezekolk[1], H. J. Schers[2], N. Van Herwaarden[1,3], B. Van den Bemt[4,5], M. Flendrie[1]. [1]*Sint Maartenskliniek, Rheumatology, Ubbergen, Netherlands*; [2]*Radboud University Medical Center, Primary and Community Care, Nijmegen, Netherlands*; [3]*Radboud University Medical Center, Rheumatology, Nijmegen, Netherlands*; [4]*Sint Maartenskliniek, Rheumatology & Pharmacy, Ubbergen, Netherlands*; [5]*Radboud University Medical Center, Pharmacy, Nijmegen, Netherlands*

Background: Uric acid lowering therapy (ULT) can be effective in gout if taken correctly (1), but non-adherence is a known problem (2). Although patients' adherence barriers regarding ULT, such as lack of knowledge on disease and therapy, and beliefs, have been widely studied (3), less is known physicians' beliefs.
Objectives: To investigate the physicians' beliefs on ULT treatment in both primary and secondary care in the Netherlands.
Methods: Cross-sectional study among all rheumatologists of the Sint Maartenskliniek and to all General Practitioners (GPs) of 17 practices, participating in the practice-based research network Family Medicine Network Nijmegen, Netherlands. All participants filled out the beliefs about medication questionnaire (BMQ), adjusted for physicians; in addition data were collected on physician characteristics including working experience in total and gout consultations. The BMQ consists of two parts, a specific part with 10 questions about beliefs on necessity (N=5) and concerns (N=5) regarding ULT and a general part with 8 questions about beliefs on harms (N=4) and overuse (N=4) regarding medication in general. Each question is scored on a Likert-scale from 1-5, a higher score corresponds to higher beliefs on that category. Sum scores for all four categories were calculated. With the total scores on the specific BMQ including necessity and concerns beliefs, physicians were classified in four different categories (Table 1)(4).
Results: In total 112 physicians received the questionnaire, 28 of 37 rheumatologists (76%) and 45 of 75 GPs (60%) responded. Rheumatologists had less years of experience than GPs (median 8.5 years (IQR 3 – 14) versus (vs) 13 years (IQR 8-20)) and less hours of patient contact per week (15 hours (IQR 8.5 – 20) vs 24 hours (IQR 20 – 30)). Rheumatologists reported more consultations for gout per week than GPs: median 4 (IQR 1 – 6.6) vs 1 (IQR 0.2– 1).
Rheumatologists scored higher on the BMQ necessity scale, 17.5 (95% CI 16.6 – 18.5) compared to GPs 16.1 (95% CI 15.1 – 17.1). GPs scored higher on BMQ concern scale, 12.1 (95% CI 11.4 – 12.7) compared to rheumatologists, 10.4 (95% CI 9.7 – 11.2). On medication in general, GPs scored higher on both overuse and harms scales compared to rheumatologists, 11.3 (95% CI 10.7 – 12) versus 9.9 (95% CI 9 – 10.7)and 8.3 (95% CI 7.9 – 8.7) vs 7.1 (95% CI 6.5 – 7.7), respectively. Table 1 shows classification according to the BMQ specific for both groups.

Table 1. Classification based on the adapted BMQ

	Rheumatologists (N=28)	GPs (N=45)
Acceptant (%)	19 (67.9)	16 (35.6)
Ambivalent (%)	0	8 (17.8)
Sceptic (%)	1 (3.6)	5 (11.1)
Indifferent (%)	8 (28.6)	16 (35.6)

Conclusion: For the majority of rheumatologist the necessity beliefs outweighs concern beliefs towards the use of ULT outweighs concern beliefs. GPs show a more heterogenic profile, including acceptant, indifferent and ambivalent beliefs towards ULT use. GPs also show higher harm and overuse concerns regarding medication in general. Next step is to investigate possible associations with actual ULT use and disease outcome.
REFERENCES:
[1] Doherty M, et al. Lancet (London, England). 2018;392(10156):1403-12.
[2] Reach G. Joint, bone, spine: revue du rhumatisme. 2011;78(5):456-9.
[3] Harrold LR et al. Chronic illness. 2010;6(4):263-71.
[4] Toelichting BMQ. [updated 2011-12-10; cited 2021-01-28] Available trough: https://meetinstrumentenzorg.nl/instrumenten/beliefs-about-medicine-questionnaire-bmq-bmq-specific-bmq-general/
Acknowledgements: This study is sponsored by Grünenthal
Disclosure of Interests: Frouwke Veenstra: None declared., Johanna Vriezekolk: None declared., Henk J Schers: None declared., Noortje van Herwaarden: None declared., Bart van den Bemt Speakers bureau: Pfizer, AbbVie, UCB, Biogen and Sandoz, Consultant of: Delivered consultancy work for UCB, Novartis and Pfizer, Grant/research support from: UCB, Pfizer and Abbvie, Marcel Flendrie Consultant of: M. Flendrie has received consultancy fees from Menarini and Grunenthal., Grant/research support from: M. Flendrie has received grants from Menarini and Grunenthal.
DOI: 10.1136/annrheumdis-2021-eular.1834

AB0635

EVALUATION OF THE INTIMA-MEDIA THICKNESS INDEX BY CAROTID DOPPLER IN PATIENTS WITH MONOSODIUM URATE DEPOSITION ARTHRITIS OF THE HOSPITAL DOCENTE PADRE BILLINI, DOMINICAN REPUBLIC

A. Cornelio[1,2], J. Santana Peralta[2], T. Polanco Mora[2], Y. Cruz[2], E. Rodriguez Bautista[2], T. Valdez[2], R. Muñoz[2], A. Feriz[2]. [1]*Hospital Docente Padre Billini, Reumatologia, Santo Domingo, Dominican Republic*; [1]*Hospital Docente Padre Billini, Reumatologia, Santo Domingo, Dominican Republic*

Background: Hyperuricemia and gout are risk factors for atherosclerosis subclinical and cardiovascular complications. (1) However, it is still debated whether uric acid is an independent predictor of cardiovascular risk. (2) Vascular Doppler and in particular the measurement of the intima-media thickness and the detection of plaques are useful in the evaluation of cerebrovascular disease and cardiovascular risk. (3) An intima-media thickness greater than 0.9mm and / or the presence of atheromatous plaques in the carotid are predictive of high cardiovascular risk and silent heart disease. (4) Gouty arthritis has been associated with alteration of the carotid intima media thickness (cIMT) and subclinical atherosclerosis. Cukurova et al studied patients with gout, finding an increase in cIMT compared to patients with asymptomatic hyperuricemia. (5)
Objectives: Assess the carotid intima-media thickness in patients with monosodium urate deposits arthritis

Methods: Prospective, observational, cross-sectional study. Carotid Doppler was performed on patients in the outpatient clinic with a diagnosis of gout from November 2019 to 2020 of the rheumatology service of the Hospital Docente Padre Billini and healthy controls. Inclusion criteria, patients> 18 years, diagnosis of monosodium urate deposits arthritis according to the ACR / EULAR 2015 classification criteria, carotid Doppler, measurement of the cIMT. Controls without disease, matched by sex and age. The data was analyzed with SPSS V23 for Windows 10.
Results: Of 37 patients with a diagnosis of arthritis due to deposition of monosodium urate crystals, (34) met inclusion criteria, 100% male, 34 healthy controls. Average of 61.5 years. Average of the disease 8.2 years. Distribution 61% (21) intercritical gout, 32% (11) chronic tophaceous gout, 0.5% (2) acute gouty arthritis. Comorbidities 67% (23) dyslipidemia, 35% (12) hyperglycemia. 26% (9) presented arterial hypertension. 20% (7) have diabetes mellitus. 58% (20) are alcohol drinkers, 11% (4) smokers. Mean uric acid 8.6 mg / dl at Doppler, 52% (18) elevated serum creatinine. Carotid Doppler in patients with gout showed a 55% (19) increase in the cIMT > 0.9mm, with a mean of 2.03mm (1.95 SD). Carotid Doppler in healthy controls 17% (6) increased cIMT, mean of 1.8mm (2.2 SD) (P = 0.040). Patients with gout had 29% (10) atheromatous plaques, 17% (6) calcified plaques versus 14% (5) atheromatous plaques, 8% (3) calcified in healthy controls.
Conclusion: Our study showed that half of the patients with gout had increased cIMT compared to a third of the healthy controls. The presence of atheromatous and calcified plaques was mainly associated with dyslipidemia, so we can conclude that the evaluation of the intima-media thickness by carotid Doppler allows it to be a predictor of cardiovascular disease in patients with gout.
REFERENCES:
[1] Choi HK, Curhan G (2007) Independent impact of gout on mortality and risk for coronary heart disease. Circulation 116:894–900
[2] Feig DI, Kang DH, Johnson RJ (2008) Uric acid and cardiovascular risk. N Engl J Med 359:1811–1821
[3] Choi, HK. Rho, Y-H., Zhu, Y., Cea-Soriano, L., Aviña-Zubieta, JA. Zhang, Y. The risk of pulmonary embolism and deep vein thrombosis in rheumatoid arthritis: A UK population-based outpatient cohort study. Ann Rheum Dis. 2013; 72 (7): 1182-7
[4] Gkaliagkousi, E., Gavriilaki, E., Doumas, M., Petidis, K., Aslanidis, S., Stella, D. Cardiovascular risk in rheumatoid arthritis: Pathogenesis, diagnosis, and management. J ClinRheumatolPract Rep Rheum Musculoskelet Dis. 2012; 18 (8): 422-30
[5] Cukurova S, Pamuk ÖN, Ünlü E, Pamuk GE, C¸ akir N. Subclinical atherosclerosis in gouty arthritis patients: a comparative study. Rheumatol Int. 2012; 32(6):1769–73.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2747

AB0636 ASYMPTOMATIC HYPERURICEMIA IN INFLAMMATORY RHEUMATIC DISEASES

A. Fonturenko[1], R. Bashkinov[1,2], V. Mazurov[1,2], M. Petrova[2,3], O. Inamova[2,3], I. Gaydukova[1,2]. [1]*Clinical Rheumatological Hospital No25, Center for diagnosis and treatment of autoimmune diseases, Saint-Petersburg, Russian Federation*; [2]*North-Western State Medical University named after II Mechnikov, Department of Therapy, Rheumatology, Examination of Temporary Disability and Quality of Medical Care named after E. E. Eichwald, Saint-Petersburg, Russian Federation*; [3]*Clinical Rheumatological Hospital No25, City Clinical Center of Gout, Saint-Petersburg, Russian Federation*

Background: Uric acid (UA) is well-known biomarker of cardiovascular risk and inflammation. However, the data about interrelations between asymptomatic hyperuricemia (AHU) and rheumatic diseases (RD) are limited and contradictory [1].
Objectives: to identify the occurrence of AHU in pts with different RD and to evaluate the interrelations between the AHU and clinical features of the RD.
Methods: The study included data from 822 pts with AHU and RD involved in the Saint-Petersburg Register of Pts with AHU in period from the 01jan2000 to the 01apr2020. The AHU was defined as the serum level of uric acid (UA) that exceeded 360 µmol/l without signs of gouty arthritis. Pts with the secondary reasons of AHU (an oncologic diseases, late stages of chronic kidney disease, ets), and inflammatory diseases another than RD were excluded from the study.
Patient's demographical characteristics, duration of AHU, level of UA, activity of RD, ESR, CRP, urate-lowering therapy (ULT) were analyzed. The study was approved by local ethic committee. Statistics was performed with SPSS17.
Results: Characteristics of the Patients with the RD and AHU are present in Table 1. The duration of AHU in pts with the RD was 3.4±3.4 [0.08-18] years, mean duration of follow-up 2.7±4.0 years, mean number of visits during the period of follow-up was 3,2 [min 1; max 7], ESR 26.0±14.1 mm / h, CRP 19.6±21.0 mg/l.

Table 1. Characteristics of the Patients with the Rheumatic diseases and asymptomatic hyperuricemia.

	Age, years (Mean±SD)	Male, %**	Serum UA, µmol/l (Mean±SD)	Normalization of UA during the follow-up, n (%)
RD, n=822	56.7±14.5	40.27	493.3±98.5	242 (29.44)[##]
RA, n=329	64.2±12.1	3.74	504.8±107.5[#]	99 (30.09)[##]
PsA, n= 149	56.6±12.9	53.69	531.5±94.9[#]	32 (21.48)[##]
SpA, n= 107	45.6±15.1*	33.43	520.8±86.5[#]	18 (16.82)[##]
SLE, n=137	50.3±14.1*	20.44	451.6±91.4	57 (41.61)
SSc, n= 57	61.0±12.4	22.81	456.2±99.5	20 (35.09)
SD, n= 43	62.0±10.7	16.28	442.4±107.5	16 (37.21)

RD – rheumatic disease; RA — rheumatoid arthritis; PsA — psoriatic arthritis; SpA — spondyloarthritis; SLE — systemic lupus erythematosus; SSc — systemic sclerosis; SD — Sjogren's disease; * — p<0.001 for the differences with RD, RA, PsA, SSc, SD; ** — p < 0.01 for all intergroup differences; [#] — p < 0.01 for the differences with RD, RA, SSc, SD; [##]— p < 0.01 for the differences with RA, SSc, SD.

Were revealed the interrelations between the level of UA and ESR (Spearmen's R=0.1, p=0.01), and UA and CRP (Spearmen's R =0.12, p=0.001).
The level of UA in male pts was 507.0 [361-940], in female pts 450.0 [361-1010] µmol /l (p<0.0001), in SLE pts with elevated anti-nuclear factor (ANF) UA was 429 [361-940] and with normal 494 [361-973] (p<0.0001). In pts with high and low RD activity UA was 490 [361-940] and 454 [363-1010]) µmol /l respectively, (p<0.0001). The higher UA level was found in any RD as compared with UA in low activity of the same RD (p<0.0001 for all the differences).
Normalization of UA was found in 243 (29.6 %) pts, lack of normalization of UA in 434 (52.8 %) of cases, n = 677, Table 1. ULT received 219 (26.6 %) pts. Normalization of UA without ULT was registered in 16 (1.9 %) of the pts.
Conclusion: UA level is higher and normalize less often in patients with SpA and PsA as compered with RA, SLA, SSc and SD pts. In any of analyzed rheumatic diseases the level of UA is higher in male pts and in pts with high disease activity.
REFERENCES:
[1] K.Bosmansky, M. Ondrasik. Ter Arkh.1987;59(4):22-5.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2980

AB0637 THE STATE OF GOUT MANAGEMENT IN WALES RHEUMATOLOGY UNITS

M. Saleh[1]. [1]*University Hospital of Wales, Rheumatology, Cardiff, United Kingdom*

Background: Gout is the most common inflammatory arthritis with both the prevalence and incidence showed significant rise in the UK in recent years[1].
The most frequent reasons for referral from primary care were diagnostic uncertainty 54%, failure to respond to primary care management 28%, and complex comorbidity 25%[2].
From primary care perspective, increased urate level (p=0.0001), young age (p=0.009), fewer comorbidities (p=0.039) constituted the most common risk for gout General Practice consultations and in addition to poor compliance to urate lowering treatment ULT (p=0.004) and lower CVS risk scores (p=0.038) these all factors comprised the independent risk factors for Gout flares[3].
Objectives: To compare the management of gout in the rheumatology services in Wales against the 2017 British Society for Rheumatology (BSR) Guidelines.
Methods: •A descriptive study over an 8-week period from January to February 2019, used Simple Analysis in calculating the frequency (%).
•Data were collected from notes of 79 patients referred to rheumatology departments across Wales using the British Society for Rheumatology (BSR) 2017 Gout Guidelines Audit Tool.
•The audit cohort comprised 62% of chronic gout patients and 38% of acute admissions.

Results:

Gout Audit	All Wales 2019 (BSR Guidelines 2017)	UK National Audit (BSR Guidelines 2007)*
Education material	54%	No available data
Newly start ULT	59%	42%
ULT was prescribed	87%	33%
ULT was continued	78%	76%
Prophylaxis	94%	94%
Febuxostat	21%	10%
ULT main indication	>2 attacks (71%)	Tophi (81%)
eGFR <60 ml/min	40%	30%
Urate level checked	83%	72%
Urate <300 umol/L	36%	25%
Urate <360 umol/L	58%	45%

Conclusion: •Gout management by rheumatologists across Wales concords well with the recent BSR guidelines for most audit standards and showed an improvement in percentage of patients who achieved a target serum uric acid level <300 and <360 umol/L according to the BSR and EULAR guidelines, respectively.
•Areas for improvement include documentation of Patient Education, improvement of audit tool (Age, Alcohol, current ULT).
•To spread the message to primary care setting, where gout is predominantly managed, to ensure that ULT is optimized to achieve target serum uric acid level to benefit patients.

REFERENCES:

[1] Kuo C, Grainge MJ, Mallen C*, et al* Rising burden of gout in the UK but continuing suboptimal management: a nationwide population study, *Annals of the Rheumatic Diseases* 2015;**74:**661-667.
[2] *Management of gout by UK rheumatologists: a British Society for Rheumatology national audit.*Roddy E, Packham J, Obrenovic K, Rivett A, Ledingham JM.Rheumatology (Oxford). 2018 May 1; 57(5):826-830.*
[3] Callear J, Blakey G, Callear A*, et al* Gout in primary care: Can we improve patient outcomes? *BMJ Open Quality* 2017;6:u210130.w4918. doi: 10.1136/bmjquality.u210130.w4918

Acknowledgements: Dr Martin Bevan for supervising the work and Rheumatology Units across Wales for collecting data and the British Society for Rheumatology in formulating the audit tool.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2985

AB0638 CYTOKINE STATUS IN METABOLIC SYNDROME IN PATIENTS WITH GOUTY ARTHRITIS

K. Zhigulina[1], S. Spitsina[1,2]. *[1]Federal State Budgetary Educational Institution of Higher Education "Volgograd State Medical University" of the Ministry of Healthcare of the Russian Federation, Department of hospital therapy, Volgograd, Russian Federation*; *[2]Federal State Budgetary Institution "Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky", Clinical Biochemical Laboratory, Volgograd, Russian Federation*

Background: Gout is an inflammatory and metabolic disease. Hyperuricemia can contribute to inflammation, hypertension and cardiovascular disease, adipogenesis and lipogenesis, impaired insulin and glucose metabolism, and the development of liver disease. In turn, non-alcoholic fatty liver disease is the most common chronic liver disease worldwide; is closely related to obesity, type 2 diabetes mellitus, dyslipidemia and other metabolic risk factors included in metabolic syndrome (MS). Interest in the problem of MS has not faded for many years, which is associated with its extremely rapid spread in the world.
Objectives: To assess the cytokine status in patients with gouty arthritis (GA) in combination with metabolic syndrome (MS).
Methods: There were 60 patients with reliable GA under observation. Among the surveyed men and women accounted for 60% and 40%, respectively, with an average age of 54 years, an average duration of the disease of 8 years. A family history of gout was present in 42% of patients. The onset of gouty arthritis was observed at 35.6 ± 10 years. Hypouricemic therapy was prescribed in 70% of patients. Thirty-six patients were diagnosed with the tofus form, 24 had no tofus. Patients were included in the study during arthritis remission. Blood samples were taken for general clinical and biochemical analyzes (ESR according to Westergren and uric acid levels were estimated), as well as for determination of serum concentrations of TNF-alpha and IL-6 by enzyme immunoassay.
Results: The patients were divided into two groups: group 1 - 40 people with GA without signs of MS, group 2 - 20 patients with GA and MS. Patient groups were matched by sex, age, form and severity of the disease. In the 1st group, the body mass index ranged from 28.00 to 34.25 kg / m2, in the 2nd group - from 29.05 to 49.39 kg / m2. In patients with isolated gout, the waist in men averaged 96 cm, in women - 86.5 cm; in the 2nd group: in men - 98 cm, in women - 88 cm. Among the criteria for MS, in addition to abdominal obesity, in the 2nd group, arterial hypertension (in 64%), dyslipidemia (mainly types IIa and IIb) were significantly more frequent, violation of carbohydrate metabolism (fasting glycemic level 8.0 + 2.0 mmol / l), a higher level of uricemia (from 397.8 to 660.5 mmol / l) compared with the 1st group. The average level of IL-6 in the serum of patients in group 1 was 1.46 pg / ml, in group 2 - 14.03 pg / ml, the average level of TNF-alpha in group 1 was 0.51 pg / ml, in group 2 - 1.28 pg / ml.
Conclusion: In GA patients with signs of MS, there is a significant increase in the production of key proinflammatory cytokines, namely IL-6, TNF-alpha. It was found that with a combination of MS and GA, the concentrations of IL-6, on average, 9.6 times, and TNF-alpha - 2.5 times, exceed the parameters of patients without signs of MS. A direct relationship was established between the expression of IL-6 and TNF-alpha with body mass index, as well as with insulin resistance and fluctuations in blood pressure. Thus, the cytokine imbalance is associated with increased risks of both cardiometabolic complications and the progressive course of GA.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3016

AB0639 EXOSOMES DERIVED FROM ENDOTHELIAL CELLS PREVENT OSTEOBLAST APOPTOSIS IN STEROID-INDUCED OSTEONECROSIS OF THE FEMORAL HEAD RAT MODEL VIA THE PI3K/AKT/Bcl-2 SIGNAL PATHWAY

J. Sun[1], W. Zheng[2], Y. Zhang[1], Z. Gu[3]. *[1]Affiliated Hospital of Nantong University, Department of Orthopaedics, Nantong, China*; *[2]Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China*; *[3]Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China*

Background: Osteonecrosis of the femoral head (ONFH) is a common disease caused by many trauma factors and un-trauma factors. Among those un-trauma factors, steroid-induced osteonecrosis of the femoral head (SNFH) accounted for a large proportion and mainly concentrated in young people. SNFH has been reported as an irreversible disease and associated with the damage of blood vessels and the loss balance of bone homeostasis. Circulating endothelial progenitor cells (CEPCs), one part of circulating endothelial cells (CECs), are immature precursor cells with proliferative potential. The damage of vascular endothelial cells in SNFH has been confirmed by many studies, but the changes of CECs and CEPCs in the peripheral blood of patients with SNFH have not been studied yet.
Objectives: The objective of the study is to explore the number of CECs and CEPCs in SNFH patients and normal people and then investigate whether EC-secreted exosomes (EC-exos) could prevent the progression of SNFH in rat model and its mechanism of action.
Methods: We collect peripheral blood of 3 SNFH patients and 3 heathy people and detected the levels of CECs and CEPCs by Flow cytometer. TEM, NTA and western blot was used to characterize the isolated EC-exos. Annexin V-FITC/PI double staining with flow cytometric analysis and western blot were used to evaluate MC3T3-E1 cells apoptosis. CCK-8, scratching experiment and transwell were used to evaluate MC3T3-E1 cells viability and migration ability. Micro-CT and morphological staining were used to evaluate the progress of SNFH in rat model.
Results: Firstly, we found that the number of CECs and CEPCs in the peripheral blood was decreased in SNFH patients than normal people. Then our results indicated that EC-exos could improve the migration, viability and prevent apoptosis of osteoblasts under dexamethasone by activating the PI3K/AKT/Bcl-2 signal pathway in vitro. Finally, our Micro-CT and morphological staining results in SNFH rat model revealed that EC-exos prevented the progression of SNFH.
Conclusion: EC-exos could enhance the cell viability and migration ability of osteoblasts under dexamethasone and play an anti-apoptosis role against steroids-induced osteoblast apoptosis by activating the PI3K/AKT/Bcl-2 signal pathway. EC-exos prevented the progression of SNFH in rat model.

REFERENCES:

[1] Zalavras CG, Lieberman JR. Osteonecrosis of the femoral head: evaluation and treatment. J Am Acad Orthop Surg. 2014;22(7):455-64.
[2] Microsurgery Department of the Orthopedics Branch of the Chinese Medical Doctor A, Group from the O, Bone Defect Branch of the Chinese Association of R, Reconstructive S, Microsurgery, Reconstructive Surgery Group of the Orthopedics Branch of the Chinese Medical A. Chinese Guideline for the Diagnosis and Treatment of Osteonecrosis of the Femoral Head in Adults. Orthop Surg. 2017;9(1):3-12.
[3] Mont MA, Jones LC, Hungerford DS. Nontraumatic osteonecrosis of the femoral head: ten years later. J Bone Joint Surg Am. 2006;88(5):1117-32.
[4] Yuan HF, Zhang J, Guo CA, Yan ZQ. Clinical outcomes of osteonecrosis of the femoral head after autologous bone marrow stem cell implantation: a meta-analysis of seven case-control studies. Clinics (Sao Paulo). 2016;71(2):110-3.
[5] Houdek MT, Wyles CC, Packard BD, Terzic A, Behfar A, Sierra RJ. Decreased Osteogenic Activity of Mesenchymal Stem Cells in Patients With Corticosteroid-Induced Osteonecrosis of the Femoral Head. J Arthroplasty. 2016;31(4):893-8.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3088

AB0640 MORTALITY IN CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION DISEASE: PRELIMINARY DATA

M. Eliseev[1], A. Novikova[1], O. Sheliabina[1], M. Chikina[1]. *[1]VA Nasonova Research Institute of Rheumatology, Laboratory of Microcrystalline Arthritis, Moscow, Russian Federation*

Background: Calcium pyrophosphate crystal deposition disease (CPPD) is associated with a high frequency of comorbidities and vascular calcification [1], but it is unknown whether these factors affect cardiovascular mortality.
Objectives: To study the structure of mortality in patients with CPPD and compare with the structure of mortality in the Russian Federation.
Methods: 217 patients with crystal-verified diagnosis of CPPD (McCarty criteria) were included in the prospective study, aged ≥18 years, mean age 59.2 ± 12.6 years, 82 (38%) men and 134 (62%) women. The median follow-up was 3.9 [1.9; 7.2] years, patients were followed up for at least a year. The exclusion criteria are the presence of other rheumatic diseases with arthritis symptoms. The examination of patients included the history taking, assessment of anthropometric parameters, the presence of comorbidity and the following laboratory tests: determination of serum creatinine level (with calculation of glomerular filtration rate (eGFR) using the MDRD formula), total cholesterol (TC), C-reactive protein (CRP). Statistica 12.0 package was used for statistical data processing.
Results: A total of 217 patients were included. Arterial hypertension was detected in 115 (53%) patients, coronary heart disease in 51 (24%) patients, diabetes mellitus in 26 (12%) patients, chronic renal failure in 17 (8%) patients, hyperparathyroidism in 18 (8%) patients, chronic heart failure in 22 (10%) patients. 65 (30%) patients had a family history for CVD, 31 (14%) patients were smokers. 122 (56%) patients had an increased level of total cholesterol> 5.0 mmol/L and 54 (25%) patients – the level of CRP>5 mg/L.
23 (11%) patients, 12 (52%) men and 11 (48%) women, died, the average age of the deceased being 62.7±9.2 years. In 15 (65%) cases out of 23, death occurred due to cardiovascular complications, which is higher than the cardiovascular mortality rate in the Russian Federation (53%). Among CVD, the distribution was as follows: acute myocardial infarction - 6 (40%) patients,apoplectic attack - 5 (33) patients, thrombosis - 2 (13%) patients, rhythm disturbances – 1 (7%) patient and decompensation of chronic heart failure - 1 (7%) patient.
Conclusion: CVD is the main cause of death in patients with CPPD and the total frequency of mortality from CVD exceeds the population one. Further research is needed, including studies of the risk factors for overall and cardiovascular mortality in patients with CPPD.
REFERENCES:
[1] Abhishek A, Doherty S, Maciewicz R, et al. Association between low cortical bone mineral density, soft-tissue calcification, vascular calcification and chondrocalcinosis: a case-control study. Ann Rheum Dis. 2013;73(11):1997-2002. doi: 10.1136/annrheumdis2013-203400
Disclosure of Interests: Maxim Eliseev Speakers bureau: Berlin Chemie Menarini Group, Novartis International AG, EGIS, Aleksandra Novikova: None declared., Olga Sheliabina: None declared., Maria Chikina: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3142

AB0641 EFFECT OF AGE ON PARATHYROID HORMONE RESPONSE TO VITAMIN D INSUFFICIENCY IN PRIMARY HYPERPARATHYROIDISM

V. Deshani[1], M. Khalid[1], K. Jadoon[1]. [1]*The Royal Wolverhampton NHS Trust, Diabetes and Endocrinology, Wolverhampton, United Kingdom*

Background: Primary hyperparathyroidism (PHPT) is a common endocrine condition, commonly seen with increasing age. In vast majority, it is diagnosed incidentally and causes no particular symptoms. Symptoms are usually related to acute hypercalcaemia or the complications of chronically elevated serum calcium level. Vitamin D deficiency is common among general population and in patients with PHPT. Studies in secondary hyperparathyroidism (SHPT) have shown that parathyroid hormone (PTH) response is affected by age, with those over 80 showing greater rise in PTH levels. We wanted to see if age has a similar impact on PTH response to vitamin D in those with PHPT.
Objectives: To evaluate the impact of age on PTH response to vitamin D insufficiency in those with PHPT.
Methods: Patients with primary hyperparathyroidism (PHPT), attending general endocrine clinic of a district general hospital, were divided into two groups based on age; less than 70 (n=73) and 70 and above (n=61).Each group was subdivided into vitamin D insufficient (VDI) and vitamin D sufficient (VDS) subgroups. We compared calcium and parathyroid hormone levels and forearm BMD (presented as T score) in VDI and VDS subgroups in the two age groups, at the time of diagnosis. Data were analyzed using unpaired t-test and presented as mean ± SEM, using Graphpad Prism 9.0.1.
Results: There was significant difference in Vitamin D levels in VDI and VDS subgroups, in both age groups (<70; mean vitamin D 27.98 vs. 68.44, p<0.0001; ≥70; mean vitamin D 34.44 vs. 75.74, p<0.0001). The two groups were significantly different in terms of age (mean age 58 vs. 76, p<0.0001). Although there was no difference in calcium and forearm BMD in VDI and VDS, in both age groups, those under 70 showed a greater PTH response to vitamin D insufficiency (mean PTH 19.29 vs. 12.91 respectively, p<0.001).
Conclusion: While in SHPT, those with increasing age show greater rise in PTH levels, our data show that in PHPT, younger patients show a greater PTH rise in response to vitamin D insufficiency. Further work is needed to elucidate the underlying mechanisms.
REFERENCES:
[1] Wyskida et al., Parathyroid hormone response to different vitamin D levels in population-based old and very-old Polish cohorts, Experimental Gerontology, Volume 127, 2019, 110735, ISSN 0531-5565, https://doi.org/10.1016/j.exger.2019.110735.
[2] Malik M Z, Latiwesh O B, Nouh F, et al. (August 15, 2020) Response of Parathyroid Hormone to Vitamin D Deficiency in Otherwise Healthy Individuals. Cureus 12(8): e9764. doi:10.7759/cureus.9764
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3288

AB0642 CLINICAL CHARACTERISTICS AND FACTORS ASSOCIATED WITH BONE EROSION IN GOUT PATIENTS WITH TOPHI

W. Deng[1], Y. Huang[1], Y. Liu[1], Z. Huang[1], S. Chen[1], Q. Huang[1], T. W. LI[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*

Background: Bone erosion is a frequent complication of gout patients with tophi and can lead to joint damage, deformity and musculoskeletal disability. Few studies have focused on clinical characteristics and factors associated with bone erosion in gout patients with tophi.
Objectives: The aim of this study was to describe clinical characteristics of bone erosion in gout patients with tophi.
Methods: Bone erosion was detected by X-ray. Gout patients with tophi were divided into bone erosion group and non bone erosion group. The clinical characteristics were recorded. Comparison of clinical characteristics and risk factors for bone erosion were analyzed between two groups. Multivariate logistic regression analysis was conducted.
Results: A total of 171 gout patients with tophi were enrolled, 121 patients with bone erosion and 50 patients without bone erosion. Bone erosion group were older, with prolonged duration with gout and tophi, higher levels of serum creatinine, lower levels of glomerular filtration rate (GFR), C-reactive protein and BMI. In univariate regression analysis, age, gout duration, tophi duration, GFR were associated with bone erosion. In multivariable logistic regression analysis, tophi duration was independently associated with bone erosion.
Conclusion: Gout patients with bone erosion present different clinical characteristics compared with those without bone erosion. Tophi duration was strongly associated with bone erosion in patients with gout.

Table 1. Comparison of clinical characteristics between bone erosion patients and non bone erosion patients.

	Non Bone erosion	Bone erosion	*P* Value
N(male)	50(47)	121(118)	0.255
Age(year)	45.82±14.15	53.74±14.88	0.002
BMI (kg/m2)	26.01±4.58	24.18±4.72	0.027
WBC(10^9/mL)	9.73±3.40	11.37±13.26	0.404
PLT(10^9/mL)	329.86±96.22	328.31±124.02	0.938
HGB(g/L)	86.58±63.78	102.75±51.16	0.201
ALT(U/L)	37.74 ±26.56	34.26±35.26	0.561
sUA(umol/L)	540.16±121.79	539.00±121.46	0.962
sCr(umol/L)	111.47±25.26	135.77±52.43	<0.001
GFR	74.01±27.94	56.68±22.84	0.003
(ml/min/1.73m^2)			
ESR(mm/h)	61.78±37.32	53.08±36.70	0.181
CRP(mg/L)	60.00±58.26	36.45±42.62	0.014
Gout duration (year)	9.22±5.46	12.63±7.59	0.001
Tophi duration(year)	3.77±3.22	6.64±4.81	0.001
Hypertension, n	17	52	0.277
Diabetes, n	9	12	0.143
Smoking history, n	20	55	0.513
Drinking history, n	14	37	0.737
Ulceration, n	10	35	0.228

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3389

AB0643 IL-1 BLOCKAGE WITH ANAKINRA IN GOUT PATIENTS. SCOPING REVIEW OF THE PUBLISHED LITERATUR.

S. Jeria Navarro[1], H. Park[1], M. A. Pou[2], E. Calvo-Aranda[3], C. Diaz-Torne[1]. [1]*Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*; [2]*EAP Encants, ICS Atenció Primària, Barcelona, Spain*; [3]*Hospital Universitario Infanta Leonor, Rheumatology, Madrid, Spain*

Background: Gout is the most common inflammatory arthritis in adults. It is caused by the chronic deposition of monosodium urate crystals in joints. Hypertension, diabetes mellitus, chronic kidney disease (CKD) and cardiovascular disease are highly prevalent in gout patients.
Nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids or colchicine are the first line therapeutic agents for flares. These drugs can be contraindicated in a large group of gout patients. Off label prescription of IL-1 receptor blockage with anakinra can be an alternative for this complex patients.
Objectives: The main objective of this study is to perform a scoping review about patient characteristics, comorbidity, effectivity and safety profile of patients with gout treated with anakinra.
Methods: A total of 1119 citations were screened. The reviewers performed a two-stage screening by title/abstract and full-text screening. Thirty six articles that finally met selection criteria, were included for data extraction and synthesis. Treatment duration of ≥12 weeks was considered chronic.
Results: Four hundred forty three patients were included in the study. 20 patients (4,5%) received chronic treatment and 423 (95,5%) flare treatment. Outcomes from 496 flares were finally analyzed.
The mean age of the patients was 63.6 years and 84% were men. The clinical presentation was polyarticular in 47.9% and tophaceous gout in 66.5%. Some of these patients presented atypical forms of the disease such as spinal gout, autoinflammatory syndromes or sternoclavicular joint arthritis.
Most of the patients presented comorbidities, the most prevalent being arterial hypertension in 127 (70.5%) and chronic kidney disease (≥ 3 stage) in 220 (51.8%). History of transplant in 37 (14.6%) with stem cell, kidney, heart, and liver transplant. More than half of patients had more than one associated comorbidity. Demographic and clinical characteristics of gouty arthritis patients are presented in Table 1. Flare was present in admitted patients in 260 (57.5%). Anakinra was administered in 52 patients with an active infection.
Different treatment regimens were described. Daily administration was used in 98% of the patients. 92.8% of the flares were treated seven days or less, being the three days regimen the most prevalent. In the chronic group the longest treatment reported was 5 years.
Efficacy of treatment with anakinra was evidenced, in flare 426 patients (93%) and chronic 19 patients (91%). Overall, anakinra was well tolerated. In the case of flares, thirty-three (7.9%) adverse effects related to anakinra administration were registered: seven (1.6%) site injection reactions, five (1.1%) reversible hematological alterations and five acute infections (H1N1, herpes zoster, severe cold, pulmonary abscess and nosocomial pyelonephritis). In chronic treated patients, adverse infectious events were more prevalent, seven (32%) infections (*Staphylococcus aureus* tophus (2), *Staphylococcus aureus* lung abscess, erysipela of the leg, *Streptococcus B* urinary tract infection, *Staphylococcus aureus* knee arthritis and tuberculous cervical lymphadenitis).
Conclusion: Anakinra has been shown to be effective and safe in treatment for flares in gout complex or resistant patients. It has been shown in multiples scenarios like active infections, dialysis, transplants, chronic kidney disease, tophi and polyarticular disease refractory to standard treatment. It has also shown its effectiveness as chronic treatment, but there are more concerns about its safety. These findings need to be confirmed with controlled clinical trials for anakinra inclusion in treatment recommendations in special situations of flares in complex or resistant gout patients.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3455

AB0644 EVALUATION OF MONOCYTE TO HIGH-DENSITY LIPOPROTEIN RATIO AND CAROTID INTIMA MEDIA THICKNESS IN GOUT PATIENTS

C. Kadıyoran[1], A. Kucuk[2], H. Aydemir[2], A. U. Uslu[3]. [1]*Necmettin Erbakan University, Radiology department, Konya, Turkey*; [2]*Necmettin Erbakan University, Rhomatology Department, Konya, Turkey*; [3]*Eskisehir Yunus Emre State Hospital, İnternal Medicine Department, Eskisehir, Turkey*

Background: The aim of this study is to investigate, evaluation of monocyte to high density liporotein ratio and carotid intima media thickness in gout patients.
Objectives: Gout disease is an autoinflammatory disease caused by the accumulation of monosodium urate crystals (MSU) in tissues and organs due to hyperuricemia (1). It is a common cause of arthritis due to the changes in lifestyle and eating habits. The effects of the inflammatory process and hyperuricemia in gout are not limited to the joints, but are associated with increased atherosclerosis and cardiovascular disease (1,2) Monocyte to high-density lipoprotein cholesterol ratio (MHR) is a systemic inflammatory marker and has recently been used quite widely for the evaluation of inflammation in cardiovascular disorders (3,4).
Methods: Fourty eight patients who were evaluated in the rheumatology clinic with an arthritis attack and diagnosed with Gout, and 48 healthy individuals whose age, gender and body mass index were matched were included in our study. Basic laboratory and biochemical parameters of the period when gout patients were asymptomatic were examined. Carotid intima-media thickness (CIMT), which is a non-invasive procedure due to its widespread use, was used as a marker.
Results: MHR and CIMT values were 18.22 ± 9.01 and 0.76 ± 0.11 mm in patients with gout. In the control group, it was 13.62 ± 4.48 and 0.65 ± 0.13 ($p = 0.002$, $p < 0.0001$, respectively). When evaluated within the study group, it was found that there was a positive correlation between MHR and CIMT ($r = 0.253$, $p = 0.013$), and according to linear regression analysis, there was an independent relationship between MHR and CIMT (beta [β] = 0.293, $p = 0.049$). When assessing Gout patients in the study population, a cutoff value of 13.85 with sensitivity of 66 %, specificity of 53 %, and $p = 0.011$ (area under curve: 0.650, 95% confidence interval 0.540-0.760), was observed according to receiver-operating characteristic curve analysis (Figure 1).

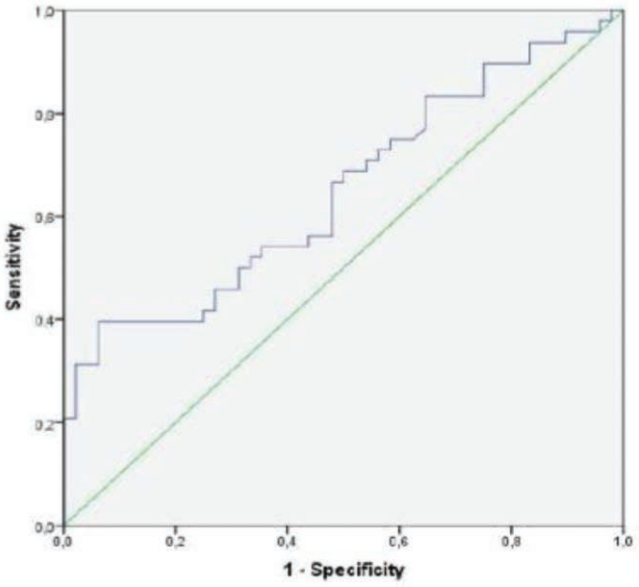


Figure 1. Receiver-operating characteristic curve analysis.

Conclusion: This study showed us that MHR can be an inexpensive and easily accessible marker that can be used in the evaluation of atherosclerotic lesions. We think that studies with larger number of patients are needed on this subject.
REFERENCES:
[1] Çukurova S, Pamuk ON, Unlu Ercument, Pamuk GE, Cakır NE. Subclinical atherosclerosis in gouty arthritis patients: a comparative study. Rheumatol Int. 2012 Jun; 3 2(6): 1769-73.
[2] Choi HK, Curhan G. Independent impact of gout on mortality and risk for coronary heart disease. Circulation 2007 Aug 21; 116 (8): 894-900.
[3] McAdams-DeMarco MA, Maynard JW, Coresh J, Baer AN.Anemia and the onset of gout in a population-based cohort of adults: Atherosclerosis Risk in Communities study. Arthritis Res Ther. 2012 Aug 20; 14(4): R193.
[4] Enhos A, Cosansu K, Huyut MA, Turna F, Karacop E, Bakshaliyev N, Nadir A, Ozdemir R, Uluganyan M. Assessment of the Relationship between Monocyte to High-Density Lipoprotein Ratio and Myocardial Bridge. Arq Bras Cardiol. 2019 Jan;112(1):12-17.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3579

AB0645 CLINCAL CHARACTERISTICS OF GOUT PATIENTS WITH RENAL CYSTS

F. Feng[1], Y. Huang[1], Y. Liu[1], Z. Zhong[1], W. Deng[1], T. W. Li[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou Shi, China*

Background: Gout is a crystal-related arthropathy caused by monosodium urate deposition, which is a common and treatable form of inflammatory arthritis and becoming more prevalent[1]. A few studies have found that gout patients have an increased prevalence of simple renal cysts[2, 3]. The relationship between gout and renal cysts is still insufficient.
Objectives: Compare the difference between gout with renal cyst and without renal cyst.
Methods: We retrospectively collected data on 200 gout patients. The data includes age, gender, uric acid, creatinine, glomerular filtration rate, 24-hour urine collection, and whether they have kidney stones, renal cysts, coronary heart disease, hypertension, and diabetes. Chi-square and exact Fisher's tests were utilized, while continuous variables were assessed by Student's t-test. A P value of less than 0.05 was considered statistically significant.
Results: Of the 200 gout patients, 56 have kidney cysts(28%). In gout patients who had a renal cyst, were significantly older than patients without renal cysts

(59.14 vs. 46.87, P = 0.000), more number of people suffering from coronary heart disease (7 vs. 5, P = 0.016). The glomerular filtration rate was lower (58.5 vs. 71.6, P = 0.000), with lower urinary creatinine, uric acid, and urinary potassium.
Conclusion: Gout patients with and without simple renal cysts have significant differences in age, hypertension, cardiovascular disease, GFR, serum creatinine, urine creatinine, and urine potassium.
REFERENCES:
[1]N. Dalbeth, T.R. Merriman, L.K. Stamp, Gout, Lancet 388(10055) (2016) 2039-2052.
[2] E.M. Hasegawa, R. Fuller, M.C. Chammas, F.M. de Mello, C. Goldenstein-Schainberg, Increased prevalence of simple renal cysts in patients with gout, Rheumatol Int 33(2) (2013) 413-6.
[3] Y. Han, M. Zhang, J. Lu, L. Zhang, J. Han, F. Zhao, H. Chen, Y. Bao, W. Jia, Hyperuricemia and overexcretion of uric acid increase the risk of simple renal cysts in type 2 diabetes, Sci Rep 7(1) (2017) 3802.

Table 1. Clinical characteristics of gout patients

	Renal cyst(n=56)	Without Renal cyst(n=144)	P
Disease duration, (month)	98.7(±64.1)	91.2(±67.0)	0.468
Age, (year)	59.14(±14.3)	46.78(±15.9)	0.000
Gender, n(F/M)	7/49	11/133	0.281
Smoking history, n(%)	18(32.1%)	47(32.6%)	0.946
Drinking history, n(%)	10(17.9%)	32(22.2%)	0.496
Hypertension, n(%)	31(55.3%)	49(34.0%)	0.006
Diabetes, n(%)	9(16.1%)	15(10.4%)	0.269
CVDs, n(%)	7(12.5%)	5(3.4%)	0.016
Nephrolithiasis, n(%)	14(25%)	43(29.9%)	0.494
UA, (μmol/L)	494.8(±158.0)	544.3(±121.0)	0.037
Serum creatinine, (μmol/L)	139.4(±57.2)	116.5(±35.45)	0.007
GFR, (ml/L)	58.5(±22.5)	71.6(±22.3)	0.000
FEUA, (%)	7.0(±3.2)	6.0(±3.2)	0.052
Urine creatinine, (μmol/L)	4687.09(±1832.9)	5565.2(±2599.8)	0.008
Urine Uric acid, (μmol/L)	1204.9(±772.0)	1542.1(±1048.5)	0.030
Urine sodium, (mmol)	132.1(±68.7)	131.2(±76.6)	0.939
Urine potassium, (mmol)	25.6(±12.5)	31.8(±14.2)	0.005

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.3702

AB0646 COMPARATIVE ANALYSIS OF ASYMPTOMATIC HYPERURICEMIA AND GOUT - AN IMPACT ON KIDNEY STRUCTURE AND FUNCTION

M. Hristova[1], A. Kundurdzhiev[1], T. Kundurzhiev[2], R. Gancheva[3]. [1]*University Hospital St Ivan Rilski, Medical University Sofia, Internal Medicine, Sofia, Bulgaria*; [2]*Faculty of Public Health, Medical University Sofia, Department of Occupational Medicine, Sofia, Bulgaria*; [3]*University Hospital St Ivan Rilski, Medical University Sofia, Rheumatology, Sofia, Bulgaria*

Background: The significance of asymptomatic hyperuricemia (AH) continues to be debated. At the population level, asymptomatic hyperuricemia is associated with multiple comorbidities, including hypertension, coronary artery disease, diabetes and chronic kidney disease.[1]
Objectives: To investigate the impact of asymptomatic hyperuricemia on renal functional and structural parameters in comparison with symptomatic gout.
Methods: The subjects included in the study were divided into two groups - 46 patients with asymptomatic hyperuricemia and 18 diagnosed with gout according to ACR/EULAR 2015 criteria.[2] For renal function assessment urine analysis, albuminuria, estimated glomerular filtration rate (eGFR) based on Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation were used. Diagnostic ultrasound as well as renal biopsy were performed to evaluate structural and histological kidney changes. Statistical analysis was performed using SPSS 22.0 software (SPSS Inc, Chicago, USA).
Results: There were no significant differences between the two groups on serum uric acid levels, albuminuria, and eGFR. However, erythrocyturia (p=0.047) and nephrolithiasis (p<0.001) prevailed significantly in patients with gout, 66.7% and 61.1% respectively. We did not find any histological differences between the two groups regarding the number of affected glomeruli, tubular atrophy and percentage of interstitial fibrosis based on light microscopy scans.
Conclusion: Our results indicate that patients with AH need renal screening since both AH and gout show similar kidney changes. Further research is needed to elucidate the role of early treatment with xanthine oxidase inhibitor for asymptomatic hyperuricemia as prevention of complications such as erythrocyturia and nephrolithiasis.
REFERENCES:
[1] Yip K, Cohen RE, Pillinger MH. Asymptomatic hyperuricemia: is it really asymptomatic? CurrOpin Rheumatology 2020; 32(1):71-79 doi: 10.1097/BOR.0000000000000679.
[2] Neogi T, Jansen TL, Dalbeth N et al. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheumatogy 2015;67(10):2557-68. doi: 10.1002/art.39254.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.4306

Infection-related rheumatic diseases

AB0647 CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME TRIGGERED BY CONCURRENT VZV AND HSV INFECTION. A CASE REPORT

L. Kakoullis[1], K. Parperis[2,3], S. Psarelis[4], E. Papachristodoulou[1], G. Panos[5,6]. [1]*University of Cyprus Medical School, Department of Medicine, Nicosia, Cyprus*; [2]*University of Cyprus Medical School, Department of Medicine, Division of Rheumatology, Nicosia, Cyprus*; [3]*University of Arizona College of Medicine, Department of Medicine, Division of Rheumatology, Phoenix, Arizona, United States of America*; [4]*Nicosia General Hospital, Department of Rheumatology, Nicosia, Cyprus*; [5]*University General Hospital of Patras, Department of Internal Medicine, Section of Infectious Diseases, Patras, Greece*; [6]*University of Cyprus Medical School, Department of Internal Medicine, Nicosia, Cyprus*

Background: Catastrophic antiphospholipid syndrome (CAPS) is a severe autoimmune condition, characterized by multiorgan failure due to thromboses and/or hemorrhage. Concurrent HSV/VZV infection is an exceedingly rare event, occurring mostly in immunocompromised patients. Herein, we report the first case of CAPS triggered by concurrent HSV/VZV infection, manifesting with zosteriform rash and haemorrhages at multiple sites.
Objectives: To describe a case of CAPS provoked by concurrent HSV/VZV infection, manifesting with zosteriform rash and haemorrhages at multiple sites.
Methods: A 36-year-old male, with a history of antiphospholipid syndrome (APS) presented with a 5-day history of epigastric pain, associated with fever, hematuria, rash and swelling in bilateral ears. Past medical history was remarkable for APS, based on 4 episodes of DVT/PE and triple positive antiphospholipid antibodies, on chronic well-maintained warfarin anticoagulation. On examination, a purpuric rash was evident on the right side of the neck as well as on both ears, consistent with a C3 dermatomal distribution (Figure 1). Laboratory studies revealed anemia, thrombocytopenia and acute kidney injury.

Figure 1.

Results: A full-body CT scan demonstrated the presence of multifocal lymphadenopathy, alveolar infiltrates suggestive of diffuse alveolar haemorrhage, and haemorrhage in both kidneys and the left adrenal gland; anticoagulation was held, despite the INR being within the patient's baseline therapeutic levels. He was admitted with a working diagnosis of CAPS and possible zoster infection. Appropriate immunologic workup was requested. He was prescribed intravenous acyclovir, antibiotics, pulse dose of glucocorticoids, and IVIG. Bronchoscopy with bronchoalveolar lavage revealed the presence of haemosiderin-laden macrophages. The rash regressed, and the patients' condition improved. He was discharged with glucocorticoid tapering regimen, hydroxychloroquine, aspirin and warfarin.

Antibody titers were taken prior to IVIG administration at presentation, and at 4 weeks. High VZV IgG titers found at presentation regressed over four times on follow-up. Furthermore, at 4 weeks the patient had developed IgM antibodies against both VZV and HSV. These findings confirmed a concurrent infection.

Conclusion: This is the first report of coexisting HSV/VZV infection associated with CAPS. A literature review identified a total of 28 patients with coexisting HSV/VZV infection, whereas only one case of CAPS triggered by HSV was identified[1]. This case illustrates that concurrent infection can occur in the absence of immunosuppressive therapy in patients with APS, serving as a trigger for hemorrhagic CAPS. Simultaneous treatment with antiviral against herpesviruses, glucocorticoids and IVIG may mitigate the inflammatory cascade associated with CAPS.

REFERENCES:

[1] Catoggio C, Alvarez-Uría A, Fernandez PL, Cervera R, Espinosa G. Catastrophic antiphospholipid syndrome triggered by fulminant disseminated herpes simplex infection in a patient with systemic lupus erythematosus. Lupus. 2012 Oct;21(12):1359-61.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.470

AB0648 REACTIVE ARTHRITIS IN SYPHILIS MIMICKING RHEUMATOID ARTHRITIS: A CASE REPORT

S. M. Lao[1], J. Patel[2]. [1]*Mount Sinai West, Internal Medicine, New York, United States of America*; [2]*Mount Sinai West, Rheumatology, New York, United States of America*

Background: Reactive arthritis is a form of spondyloarthritis with aseptic joint involvement occurring after a gastrointestinal or urogenital infection. Most commonly associated with *Chlamydia trachomatis*, *Salmonella, Shigella, Campylobacter*, and *Yersinia.* Syphilis is an infection caused by the spirochete *Treponema pallidum* and is not usually associated with reactive arthritis. Syphilis is a great imitator of other diseases due to its broad presentation including painless chancre, constitutional symptoms, adenopathy, rash, synovitis, neurological and ocular findings.

Objectives: To discuss a patient who presented with symptoms of rheumatoid arthritis (RA) but was later diagnosed with syphilis.

Methods: 31 year old male, former tobacco smoker, referred to Rheumatology for sudden onset joint pains, elevated anti-cyclic citrullinated peptide (anti-CCP), and elevated inflammatory markers. He reported pain in bilateral wrists, fingers, and right elbow for 6 weeks. Associated with 45 minutes of morning stiffness and new onset lower back pain without stiffness. He denied trauma, fever, chills, skin rash, dysuria, or diarrhea. Initiated trial naproxen 500mg twice a day only to have minimal relief. Patient is sexually active with men and was recently diagnosed with oropharyngeal gonorrhea treated with azithromycin 4 months prior. All other STI screening including syphilis, gonorrhea, HIV were negative at that time. Patient is on emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis. He denied family history of immune mediated conditions. Exam was significant for mild synovitis of both wrists and bilateral 2nd metacarpophalangeal joints. Initial labs revealed weakly positive anti-CCP 21 (normal <20), sedimentation rate 64 (normal ESR 0-15 mm/hr), C-reactive protein 24 (normal CRP 0-10 mg/L), and negative RF, ANA, HLA B27. During a short trial of prednisone taper, there was temporary improvement in symptoms, however synovitis recurred upon completion. Hydroxychloroquine (HCQ) 200mg twice a day was started for possible RA and he was referred to Ophthalmology for baseline retinopathy screening. Incidentally, he developed right sided blurry vision 2 weeks after initiation of HCQ. He was diagnosed with panuveitis of the right eye with inflammation of the optic nerve head and prednisone 40mg daily was initiated for presumed ocular manifestation of RA. However, further workup of panuveitis revealed reactive *Treponema pallidum* antibody and RPR quantity 1:32. Prednisone was immediately discontinued and he was referred to the emergency department for possible neurosyphilis.

Results: Lumbar puncture showed cerebral spinal fluid with 260 red blood cells, 1 white blood cell, 27mg/dL protein, 60mg/dL glucose, non reactive VDRL, reactive pallidum IgG antibody, and negative cultures. Meningitis and encephalitis panels were negative. Patient completed a 14 day course of IV penicillin G with complete remission of joint pain, visual symptoms, and normalization of anti-CCP, ESR, and CRP.

Conclusion: This case highlights how syphilis may mimic signs and symptoms of RA including symmetrical small joint pain, morning stiffness, elevated inflammatory markers, and positive anti-CCP. Anti-CCP is >96% specific for RA but was a false positive in this patient. There have only been few reported cases noting positive anti-CCP with reactive arthritis. This is a rare case of reactive arthritis secondary to syphilis with resolution of symptoms upon treating the syphilis.

REFERENCES:

[1] Carter JD. Treating reactive arthritis: insights for the clinician. Ther Adv Musculoskelet Dis. 2010 Feb;2(1):45-54.

[2] Cohen SE, Klausner JD, Engelman J, Philip S. Syphilis in the modern era: an update for physicians. Infect Dis Clin North Am. 2013 Dec;27(4):705-22.

[3] Singh Sangha M, Wright ML, Ciurtin C. Strongly positive anti-CCP antibodies in patients with sacroiliitis or reactive arthritis post-E. coli infection: A mini case-series based review. Int J Rheum Dis. 2018 Jan;21(1):315-321.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1687

AB0649 INFECTION PROFILE OF IMMUNE-MODULATORY DRUGS USED IN AUTOIMMUNE DISEASES: ANALYSIS OF SUMMARY OF PRODUCT CHARACTERISTIC DATA

M. Dey[1,2], K. Bechman[3], C. Smith[4], A. Cope[3], E. Nikiphorou[3], J. Galloway[3]. [1]*University of Liverpool, Institute of Life Course and Medical Sciences, Liverpool, United Kingdom*; [2]*Aintree University Hospital, Liverpool University Hospitals NHS Foundation Trust, Department of Rheumatology, Liverpool, United Kingdom*; [3]*King's College London, Centre for Rheumatic Disease, Weston Education Centre, London, United Kingdom*; [4]*King's College London, St John's Institute of Dermatology, London, United Kingdom*

Background: The number of immune-modulatory drugs used to treat immune-mediated inflammatory diseases (IMIDs) has exponentially increased in recent decades. While effective in controlling disease, serious infection remains a concern.

Accurate information on immune-modulatory drugs, including infections, is required to guide prescribing decisions. The "summary of product characteristics" (SmPC) by the European Medicines Agency (EMA) provides a useful repository of information on adverse events e.g. infections, from clinical trials and post-marketing pharmacovigilance (1).

To date, no comparison has been undertaken on reported infection frequencies across SmPCs for immune-modulators.

Objectives: To compare infection frequency, site and type across the most commonly-prescribed immune-modulatory drugs used to treat IMIDs, using information provided by SmPCs.

Methods: A drug was included if licensed in Europe for treatment of one of the following: rheumatoid arthritis, axial spondyloarthritis, connective tissue disease, autoimmune vasculitis, autoinflammatory syndromes, inflammatory bowel disease (Crohn's and ulcerative colitis), psoriasis, multiple sclerosis and other rarer conditions.

The Electronic Medicines Compendium (EMC) was searched for commonly prescribed immune-modulatory drugs used for the above indications. SmPC documents were manually searched for information on infection frequency, extracted from sections 4.4 and 4.8. Infection frequency was recorded as per convention in the SmPC: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000) (1), for each drug. Information was further extracted on infection site (e.g. respiratory, skin etc), type (e.g. bacterial, viral etc) and individual pathogenic organisms.

25% of included SmPCs were screened and extracted by a second reviewer. Disagreements were resolved with input from a third reviewer.

Results: In total, 39 drugs were included, used across 20 indications: nine conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), six targeted synthetic DMARDs (tsDMARDs; four Janus kinase [JAK] inhibitors, two sphingosine 1-phosphate receptor modulators) and 24 biologic DMARDs (17 cytokine-targeted; seven cell-targeted).

Twelve sites of infection were recorded. Minimal or no site information was available for most csDMARDs and siponimod, certolizumab pegol and rituximab. The most common sites of infection are listed by drug group in Figure 1. Upper respiratory tract was the most common site, especially with bDMARDs. Lower respiratory, ear/nose/throat (including sinusitis) and urinary tract infections were moderately common, with clustering within drug groups. No drugs reported risk of cardiac infections; the eye, musculoskeletal, neurological, oral and reproductive sites were the least commonly-reported sites of infection.

Infection data for 27 distinct pathogens were recorded, the majority viruses, especially with bDMARD use. Herpes simplex and zoster were the most frequently

listed (mainly with bDMARDs and tsDMARDs), followed by influenza. Common non-viral causes of infection were candida and tinea species.
Variable or absent reporting was noted for opportunistic infections (e.g. tuberculosis and fungi) and certain high-prevalence viruses e.g. Epstein-Barr.
Conclusion: The SmPC literature reports differences in infection risk, by site and pathogen, between immune-modulatory drugs. The findings can be used to visualise differences and aid treatment decisions. However, some of the patterns we have shown lack face-validity to clinicians familiar with real-world safety data. The data fail to capture risk of rare infections, are likely skewed by trial selection criteria, varying number of trials per drug and quirks of individual study-reporting methodologies.
The findings highlight the need for robust post-marketing pharmacovigilance studies.
REFERENCES:
[1] A Guideline on Summary of Product Characteristics Module 1.3. 2008.

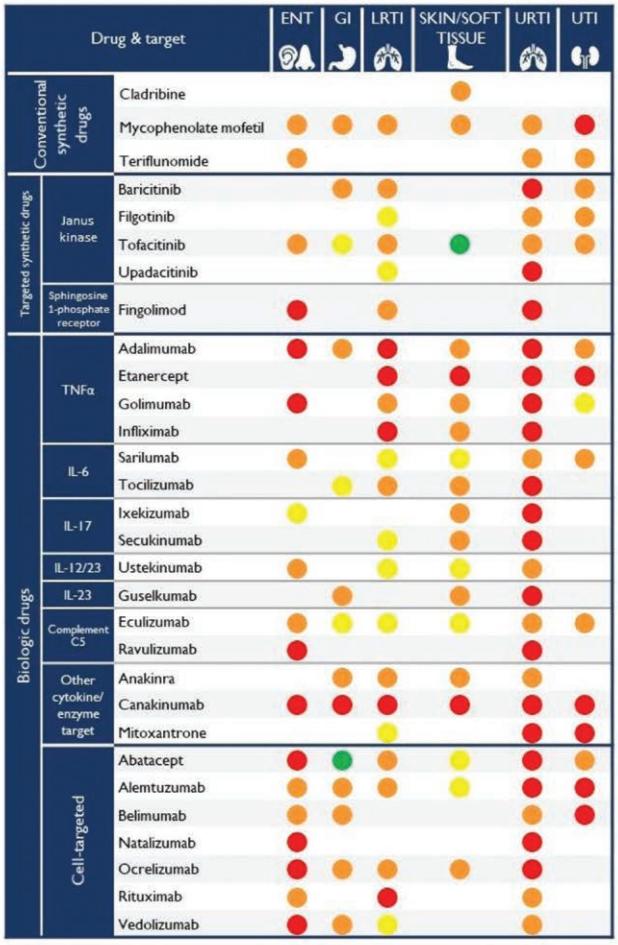


Figure 1: Summary of common sites of infection for immune-modulatory drugs.
Key: Very common ●; Common ●; Uncommon ●; Rare ●;
Blank- no information available

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2207

AB0650 SCREENING TESTS FOR LATENT TUBERCULOSIS OF CANDIDATES TO BIOLOGIC THERAPY: DATA FROM THE TUNISIAN BINAR REGISTRY

R. Ben Aissa[1], S. Boussaid[2], S. Kochbati[1], M. El Euch[2], A. Laatar[3], L. Abdelmoula[4], W. Hamdi[5], E. Bouagina[6], I. Gharsallah[7], M. Younes[8], N. Bergaoui[9], S. Baklouti[10]. [1]*Habib Thameur Hospital, Department of Internal Medicine, Tunis, Tunisia*; [2]*Rabta Hospital, Department of Rheumatology, Tunis, Tunisia*; [3]*Mongi Slim Hospital, Department of Rheumatology, Marsa, Tunisia*; [4]*Charles Nicolle Hospital, Department of Rheumatology, Tunis, Tunisia*; [5]*Med Taieb Kassab Institute, Department of Rheumatology, Mannouba, Tunisia*; [6]*Farhat Hachad Hospital, Department of Rheumatology, Sousse, Tunisia*; [7]*Military Hospital, Department of Internal Medicine, Tunis, Tunisia*; [8]*Tahar Sfar Hospital, Department of Rheumatology, Mahdia, Tunisia*; [9]*Fattouma Bourguiba Hospital, Department of Rheumatology, Monastir, Tunisia*; [10]*Hedi Chaker Hospital, Department of Rheumatology, Sfax, Tunisia*

Background: The screening and treatment of latent tuberculosis infection (LTBI) is required before starting biologic therapy. Tuberculin skin test (TST) and interferon γ gamma release assay (IGRA) are the two commonly used tests.
Objectives: The aim of our study was to analyze data from the Biological National Registry BINAR between 2016 and 2020 in order to compare the diagnostic value of TST and IGRA tests.
Methods: We collected data of patients diagnosed with LTBI (having had a TST and/or IGRA before receiving any biotherapy) from the BINAR registry (a National Tunisian registry of patients with inflammatory rheumatic diseases under biologic therapy since less than two years from the inclusion date).
Results: From a total of 298 patients included in our study, 199 patients (66.8%) were screened by TST and 159 patients were screened (53.4%) by IGRA.
Thirty-four patients (11.4%) had a positive TST and 27 patients (9.1%) had a positive IGRA test.
Three patients having negative TST and two having negative IGRA developed tuberculosis.
There was no significant difference in our study between these two tests for LTBI diagnosis. The reactivation of tuberculosis can occur even when LTBI screening is negative using TST and IGRA tests.
Conclusion: Our results show that the predictive diagnostic value for these two tests is the same. It would be more interesting to practice one of those tests prior to biotherapy.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.2938

COVID-19

AB0651 CASE-REPORT: ORGANIZING PNEUMONIA IN A PREGNANT WOMAN WITH RHEUMATOID ARTHRITIS DURING COVID-19 PANDEMIC

A. Cornillie[1], C. Grivegnee[2]. [1]*Erasme-ULB, Pneumology, Bruxelles, Belgium*; [2]*Erasme-ULB, Pneumology, Bruxelles, Belgium*

Conclusion: Case-report: Organizing pneumonia in a pregnant woman with rheumatoid arthritis during Covid-19 pandemic
CORNILLIE Alexia, GRIVEGNEE Camille, CHU Charleroi Marie-Curie
Introduction
Rheumatoid arthritis (RA) is a systemic inflammatory disease characterized by destructive polyarthritis and extra-articular organ involvement. Lungs are one of the most commonly affected organ in RA, and the lung involvement in RA results in a various clinical features including interstitial lung disease (ILD) and organizing pneumonia (OP).
OP is a histologic term characterized by the presence of buds of granulation tissue in bronchioles and alveoli. OP can be either idiopathic (cryptogenic organizing pneumonia) or secondary to underlying disease such as infection, drugs or connective tissue disease including RA.
Lung biopsy is usually recommended for the diagnosis, but the following criteria fulfilled by patients can lead to the diagnosis: (1) specific radiological manifestations (nonsegmental randomized consolidation with/without ground grass opacities in chest CT), (2) no causative infectious agent, (3) no response to antibiotics and (4) good response to corticosteroid therapy.
We describe here the case of organized pneumonia discovered in a pregnant woman with known rheumatoid arthritis during COVID-19 pandemic.
Case description
A 39-year old moroccan woman, gravida 4, para 1, was admitted during COVID-19 pandemic at 30 weeks' gestation to maternity hospital with a 1-week history of cough, dyspnea and fever. Her medical history included rheumatoid arthritis and gestational diabetes. She was treated with 5mg of prednisolone daily for her RA. Blood sample showed white blood cell count and C reactive protein at a level of 6860/mm3 and 42mg/L respectively. Chest CT performed at her admission revealed diffuse irregular nodular condensations associated with ground glass infiltrates and a right lower lobe parenchymal condensation with airbronchogram in favor of superinfection. Given circumstances, she was tested twice for SARS-Cov-2 48 hours apart by PCR on nasopharyngeal sample and results came back negative. She was treated empirically with ceftriaxone and azithromycin during the first week and described an improvement in her clinical condition but symptoms reappeared 4 days after stopping treatment. During the 2 following months, until the delivery, the patient remained subpyretic with a nonproductive cough and moderate dyspnea. 5 days after the delivery, due

to persistant dyspnea and fever, a new chest CT was performed and revealed similar image findings but some of the irregular nodular condensations showed a reversed halo sign and had a migrating character. Considering this typical image findings, the absence of causative infectious agents (excluded by bronchoalveaolar lavage performed after delivery) and the absence of response to antibiotics, we concluded with a diagnosis of OP secondary to RA without performing lung biopsy samples. A treatment with 48mg of methylprednisolone (and 100mg of azathioprine a few weeks later) was initiated. One month later, she showed a spectacular improvement in her clinical condition. A new chest CT highlighted disappearance of the majority of the ground glass areas and of all the condensations previously described. Methylprednisolone was then progressively tapered.

Conclusion

OP is a common pulmonary complication that can develop in RA. However, despite ou research, we have not found any other clinical case describing this disorder during pregnancy with RA. Since OP is a non-specific inflammatory response to an aggression of the organism, could we consider that the pregnancy is a state of aggression capable of causing such a response?

In addition, this clinical case illustrates the diagnostic challenge of this pathology during the Covid-19 pandemic.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.49

AB0652 FERRITIN IS ASSOCIATED WITH THE SEVERITY OF LUNG INVOLVEMENT BUT NOT WITH WORSE PROGNOSIS IN PATIENTS WITH COVID-19: DATA FROM TWO ITALIAN COVID-19 UNITS

F. Carubbi[1], A. Alunno[2], L. Salvati[3], C. Ferri[1], D. Grassi[1]. [1]*Internal Medicine and Nephrology Unit, University of L'Aquila, Department of Life, Health and Environmental Sciences, L'Aquila, Italy*; [2]*Rheumatology Unit, University of Perugia, Department of Medicine, Perugia, Italy*; [3]*Infectious Diseases Unit, Ospedale SS Filippo e Nicola ASL 1 Avezzano-Sulmona-L'Aquila, Department of Medicine, Avezzano, Italy*

Background: The coronavirus 2019 disease (COVID-19) is characterised by a heterogeneous clinical presentation and a wide range of imaging findings, depending on disease severity and time course. The pathophysiology is complex, involving immune and hematologic systems, epithelial cells and vascular system and to date reliable biomarkers aimed at stratifying patients and predicting worse outcomes have not been identified

Objectives: The aim of this study was to describe clinical, serological and CT imaging features of a cohort of patients with COVID-19 pneumonia and identify possible relationships between the variables and disease outcomes (admission to intensive care unit (ICU) and/or death).

Methods: We evaluated hospitalized patients with proven SARS-CoV-2 infection, clinical signs of COVID-19 and computed tomography (CT) scan-proven pulmonary involvement. Clinical and serological records of patients admitted to two COVID-19 Units in Italy with proven SARS-CoV-2 pulmonary involvement investigated with CT scan, assessed at the time of admission to the hospital, were retrospectively collected.

Results: Sixty-one patients (22 females and 39 males) of median age 65 years were enrolled. Fifty-six patients were discharged while death occurred in 5 patients. None of the lung abnormalities detected by CT was different between discharged and deceased patients. No differences were observed in the features and extent of pulmonary involvement according to age and gender. Logistic regression analysis with age and gender as covariates demonstrated that ferritin levels over the 25th percentile were associated with the involvement of all 5 pulmonary lobes (OR=14.5, 95% CI=2.3-90.9, p=0.004), the presence of septal thickening (OR=8.2, 95% CI=1.6-40.9, p=0.011) and the presence of mediastinal lymph node enlargement (OR=12.0, 95% CI=1.1-127.5, p=0.039) independently of age and gender.

Conclusion: We demonstrated that ferritin levels over the 25th percentile are associated with a more severe pulmonary involvement, independently of age and gender, but not with disease outcomes (admission to ICU/death). The identification of reliable biomarkers in patients with COVID-19 may help guiding clinical decision, tailoring therapeutic approaches and ultimately improving the care and prognosis of patients with this disease.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.61

AB0653 COURSE OF COVID-19 INFECTION IN A SERIES OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C. Cetin[1], N. Aliyeva[1], Y. Yalçınkaya[1], A. Gül[1], M. Inanc[1], B. Artim-Esen[1]. [1]*Istanbul Faculty of Medicine, Rheumatology, İstanbul, Turkey*

Background: Infection is a remarkable cause of morbidity and mortality in patients with SLE.

Objectives: We aimed to determine the clinical course of COVID-19 infection in our patients with SLE and the factors affecting this course

Methods: SLE patients (2012 SLICC criteria) diagnosed with COVID-19 infection by a positive PCR test and/or typical findings of lung involvement in CT (computed tomography) imaging were included. Data regarding cumulative clinical and laboratory characteristics, histopathology results, autoantibody profiles, immunsuppressives and damage (SLICC damage index/**SDI**)) were retrieved from the existing database and revised. SLE Disease Activity Index (**SLEDAI-2K**) was determined at the time of infection.

Results: Sixteen SLE patients with COVID-19 infection were identified. Most (87.5%) of these patients were female. Seventy % (n=11) had lupus nephritis. Twenty-five % had thrombotic antiphospholipid syndrome.

PCR was positive in 70% (n=11) of the patients. Pulmonary parenchymal findings compatible with COVID-19 were observed in 56% (n=9) of those patients. Regarding complaints upon admission, 50% (n=8) had fever, 44% (n=7) cough, 44% (n=7) dyspnea, 19% (n=3) myalgia, 12.5% (n=2) headache, 12.5% (n=2) nausea /vomiting, 6% (n=1) diarrhea, and 6 % (n=1) had anosmia. Eight patients were hospitalized. Six of these patients needed oxygen therapy via nasal cannula. None needed a follow-up in the intensive care unit. The mean hospitalization duration was 14 ± 5 (8-25) days.

Regarding disease activity at the time of infection, 9 had inactive disease with a SLEDAI-2K score of 0 whilst in 5 patients SLEDA-2K score was ≥4. The mean SLEDAI-2K score at the time of infection was 1.7 ± 2.3 (0-6). System/organwise, 1 patient with chronic thrombocytopenia presented with a worsening platelet count accompanied by serologic activity. This patient was a non-adherent to treatment who had stopped taking mycophenolic acid months before COVID19. Three patients 2 of whom had proliferative nephritis experienced nephritic flares.1 patient who had a history of cutaneous lupus and was in remission presented with oral ulcer, leukopenia and hypocomplementemia during infection. Of 16 patients, 7 had system damage at the time of infection. The mean SDI score of the patients was 1.4±1.8. Comparison of patients with and without damage revealed no significant differences in disease activity, symptoms associated with COVID, in the need for hospitalization, hospitalization duration, and the requirement for oxygen therapy. However,CT findings compatible with COVID19, were more common in patients with damage (87% vs.33%,p=0.04) and their mean CRP levels were higher at diagnosis (65 ± 47 vs.22 ± 48 mg/l;p=0.032).

All patients received similar treatment for COVID-19 except active patients who required high dose steroids (2 with active renal, 1 with thrombocytopenia and 1 with oral ulcer, leukopenia and hypocomplementemia).The patient with thrombocytopenia also received intravenous immunoglobulin and 1 with cutaneous active disease received tocilizumab as she developed macrophage activation syndrome. Six patients (37.5%) had received rituximab (RTX) in the last 6 months before COVID. No significant difference, in terms of hospitalization and need for oxygen therapy due to COVID19 was found between patients who had received RTX vs who had not. No hypogammaglobulinemia was detected in patients who received RTX despite lower levels of IgG (998 ± 184 vs 1481± 51 mg/dl, p=0.02)

Conclusion: Although half of the patients in our series of COVID19 infected SLE patients required hospitalization, there were no mortalities. More patients with damage (none pulmonary) displayed CT findings compatible with COVID19 and further follow up will reveal whether they will suffer from fibrotic lung disease. Patients can experience disease flares during COVID. But it is also important to consider that some manifestations such as thrombocytopenia may also be a sign of severe infection. Immunosupressive agents may not have a negative impact on the course of infection.

*the first two authors contributed equally

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.368

AB0654 TOCILIZUMAB IS PROTECTIVE AGAINST SARS-COV2 INFECTION OR NOT?

F. Fayed[1], E. Abdelkarim[1]. [1]*Alexandria University Students` Hospital, Rheumatology and Immunology Department, Alexandria, Egypt*

Background: SARS-COV2 (Covid19) pandemic has a scaring burden on hospitals and health care providers all over the world. Unfortunately, after one year of pandemic, millions of persons are infected either mild symptoms or critical ones and unexplained deaths. Till now, No effective treatment or vaccination. Researches showed that Covid 19 associated with elevated interleukin-6. Subsequently, Studies reported that tocilizumab (IL-6 antagonist) may be effective in critical patients even though other were shown that it is not associated with reduction in the mortality.[1,2] Therefore the question is that patients with rheumatic diseases who are already receiving tocilizumab having a primary

protection against infection of Covid 19 in comparing to other receiving the other biologicals or conventional Therapy or not.
Objectives: Our objective was to determine if tocolizumab had a primary protection against SARS-COV2 in comparing to patients were on other biologics.
Methods: A Retrospective study was done among 100 patients with rheumatic diseases (Group 1: 10 on tocilizumab, Group2: 40 (30 on antiTNF and 10 on IL17 antagonist), Group3: on cDMARDs) from March to Dec 2020. Detailed history, clinical presentation, laboratory, computed tomography of chest and PCR for covid 19 if presented among infected patients.
Results: Among 100 patients of median age 21, 19 patient (19%) had infected with Covid 19 (2 on tocilizumab, 6 on antiTNF, 1 on IL17 antagonist, 10 on cDMARDs). Symptoms were reported fever (89.4%), Fatigue (78.9%), myalgia (78.9%), Headache (73.7%), Dyspnea (52.6%), Cough (47.3%), chest pain (26.3%) and hypoxia (5%). CT findings were positive in 10 patients (52.63%) while PCR was done and positive in 15 out of 19 (78.94%). Nevertheless, there was no significant statistically difference between groups according to infection with SARS-COV2. (p=0.704)
Conclusion: Tocilizumab is not shown to be protective against SARS-COV2 (COVID 19) infection compared to other biological or cDMARDs in patients with rheumatic diseases.
REFERENCES:
[1] Tleyjeh IM, Kashour Z, Damlaj M, et al. Efficacy and safety of tocilizumab in COVID-19 patients: A living systematic review and meta-analysis. Clinical Microbiology and Infection. 2020 Nov 5.
[2] Tsai, A., Diawara, O., Nahass, R.G. *et al.* Impact of tocilizumab administration on mortality in severe COVID-19. 2020;*Sci Rep* **10:**19131
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.461

AB0655 RHEUMATOID ARTHRITIS ACTIVITY BEFORE AND AFTER COVID-19 LOCKDOWN PERIOD

M. Jordhani[1], D. Ruci2, F. Skana2, E. Memlika2. [1]*UHC Mother Teresa,Tirana, Albania, Internal Medicine,Tirana, Albania*; [1]*UHC Mother Teresa,Tirana, Albania, Internal Medicine,Tirana, Albania*

Background: The COVID-19 global pandemic has had a great impact on world population due to morbidity, mortality and restriction measures in order to stop the progression of COVID-19.
Patients with rheumatic and musculoskeletic diseases, and especially rheumatoid arthritis (RA) patients, being one of the vulnerable classes of chronic patients, were recommended to follow the government's rules[1].
Objectives: The aim of this study was to evaluate DAS-28-ESR in patients with rheumatoid arthritis before and after lockdown period.
Methods: This is a multi-center observational study including 85 patients which were evaluated before and after lockdown for their disease activity score according to DAS-28-ESR score. They had been diagnosed with rheumatoid arthritis more than 5 years ago. A thorough physical examination was performed before and after the lockdown period. It included examination of tender and swollen joints and patient's global health. They were completed with all required laboratory data, including erythrosedimentation rate. For a more accurate calculation, DAS-28-ESR was used in an electronic version. Patients with other inflammatory or infective diseases were excluded from the study. All data were statistically evaluated using statistical tests such as t-student test.
Results: The first group (the one before lockdown) had an average DAS-28-ESR of 4.7 while after the lockdown period, the average DAS-28-ESR was 5.16.
After statistically evaluating all data, it was found that there exists a significant difference between DAS-28-ESR score before and after COVID-19 lockdown (p=0.0011).
Conclusion: Our study showed that lockdown period due to COVID-19 pandemic, has aggravated disease activity in patients with Rheumatoid Arthritis. This may be consequence of various causes such as physical inactivity and difficulty to follow-up or to take the medication properly.
REFERENCES:
[1] Landewé RB, Machado PM, Kroon F, *et al*, EULAR provisional recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2, *Annals of the Rheumatic Diseases* 2020;**79:**851-858.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.576

AB0656 SARS-COV-2 INFECTION IN PATIENTS WITH RHEUMATIC DISEASE: A TERTIARY SINGLE-CENTER EXPERIENCE

A. Halbac[1], B. Balan[1], C. Tamas[1], M. M. Tamas[1,2], I. Felea[1], I. Filipescu[1,2], L. Damian[1], L. Muntean[1,2], S. P. Simon[1,2], S. Rednic[1,2]. [1]*County Emergency Hospital, Rheumatology, Cluj Napoca, Romania*; [2]*University of Medicine and Pharmacy "Iuliu Hatieganu", Rheumatology, Cluj-Napoca, Romania*

Background: In the context of the coronavirus (SARS-CoV-2) pandemic, several studies looked at the relation between rheumatic disease and SARS-CoV-2. It remains unclear whether these patients are at increased risk of developing more severe cases of coronavirus disease (COVID-19) or not.
Objectives: The objective of this descriptive study is to report the characteristics and outcomes of rheumatic patients that had a history of confirmed SARS-CoV-2 infection. Findings have also been compared to some of the existing publications on COVID-19 in these patients.
Methods: Between November 17, 2020 and January 18, 2021, a single-centre observational study was conducted in the rheumatology department of the Emergency Clinical County Hospital and the University of Medicine and Pharmacy "Iuliu Hatieganu" in Cluj-Napoca, Romania. The sample consisted of 62 rheumatic patients with a positive polymerase chain reaction test from nasopharyngeal/oral swab. Data on both systemic autoimmune disease and COVID-19 was collected using a survey, by means of telephone or in the outpatient clinic setting. Data on the patient rheumatologic condition was also collected from the electronic health records available within our department
Results: 62 patients were included, with 85.48% females and 14.51% males, and a median age of 52 years (SD +/- 14).
The most frequent comorbidities were high blood pressure (HBP) 46.77%, dyslipidaemia 19.35%, liver disease 17.74%, and interstitial lung disease (ILD) 12.90%. Recurrent COVID-19 symptoms included: cough (62%), fever (46,77%), anosmia (46.77%), ageusia (30.64%), headache (29.03%), gastrointestinal symptoms (27.41%) and myalgia (25.80%).
Out of the entire 62 sample, 41 patients had an inflammatory arthritis (IA) diagnosis, with the most frequent being rheumatoid arthritis (RA) - 68.29%, followed by ankylosing spondylitis - 21.95%, psoriatic arthritis - 7.31% and 2.43% with Still disease. Only 10 patients suffered from connective tissue disease (CTD): 3 systemic lupus erythematosus, 2 poli/dermatomyositis, 2 Sjogren syndrome (SjS), 2 mixed connective tissue disease, 1 systemic sclerosis (SSc). Another 10 patients had overlapping syndromes with the most frequent (40%) overlap between RA and SSc. One patient had osteoarthritis.
49 patients followed a treatment with conventional synthetic disease-modifying anti-rheumatic drugs with 51.2% of them being treated with Methotrexate.
14 of our patients received glucocorticoids (GC), but no relation between the GC dose and COVID-19 severity could be observed. Only 3 patients with doses greater than 10mg/day were present in the cohort and 2 developed mild while 1 developed an asymptomatic COVID-19 course.
22 patients had received biological treatment. Anti TNF alpha medication was administered to 13 of these, and mostly consisted of Adalimumab, Etanercept and Golimumab. The anti TNF alpha patients were asymptomatic or had mild forms of COVID-19 (93.30%).
8 cases had ILD: 3 RA patients, 3 overlapping syndromes, 1 SSc and 1 SjS. The median age was 59,5 years (SD +/- 10). 25% exhibited severe, 37,5% moderate, 25% mild and 12.5% asymptomatic COVID-19.
The COVID-19 severity in our sample was as follows: 12.90% of the patients were asymptomatic, 59.67% exhibited a mild form, 19.35% a moderate one, and out of the 8.06% with a severe case of COVID-19, 1 patient died. The median age in the severe cases of COVID-19 was 66 years (SD +/- 12) and HBP was the most common comorbidity.
Conclusion: Most patients in this sample were either asymptomatic or had a mild COVID-19 evolution. Although the research design has multiple limitations, rheumatic pathology does not seem to be a higher risk factor for severe COVID-19 than other associated comorbidities. With that in mind, ILD patients should be closely monitored as even in on our limited sample size a worse evolution of COVID-19 has been observed. Biological treatments, especially anti TNF alpha might help in reducing the severity of COVID-19, but this outcome could have been associated in our sample with other factors like lower median age and less comorbidities.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.740

AB0657 PERCEIVED STRESS AND FOOD INSECURITY IN PREGNANT AND POSTPARTUM WOMEN WITH RHEUMATIC DISEASES DURING THE COVID-19 PANDEMIC

L. G. Espinosa Banuelos[1], P. R. Ancer Rodríguez[2], M. G. Herrera López[2], C. M. Skinner Taylor[1], L. Pérez Barbosa[1], R. Moyeda Martinez[1], R. A. Rodriguez Chavez[1], A. Y. Lujano Negrete[1], A. Cárdenas[1], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Servicio de Reumatología, Monterrey, Mexico*; [2]*Hospital Universitario Dr. José Eleuterio González, Clínica de Nutrición, Departamento de Medicina Interna, Monterrey, Mexico*

Background: The SARS-CoV-2 pandemic has directly impacted the psychological and physical health of individuals worldwide, as well as the global economy. Food insecurity rates have risen especially in vulnerable countries like Mexico. Furthermore, social isolation and economic uncertainty have multiplied depression and anxiety disorders. Pregnant and postpartum women are particularly vulnerable to food insecurity, increased stress, depression, and anxiety.
Objectives: The aim of this study is to determine the perception of food insecurity (FI) and perceived stress in pregnant and postpartum women with rheumatic disease during the SARS-CoV-2 pandemic.
Methods: An observational, cross-sectional and descriptive study was conducted. Patients from to the pregnancy and rheumatic diseases clinic of the University Hospital "Dr. José E. González" in Northeast Mexico evaluated between August to October 2020 were included. The Spanish validated versions of the Household Food Security Access Scale (HFIAS) and the Perceived Stress Scale (PSS-10) were applied by telephonic interview. The WHO recommendations were employed to determine the appropriate intake for each food group in a week. The Kolmogorov-Smirnov test was used to determine normality of the data. The Spearman correlation coefficient and the Kruskal-Wallis test were used for statistical analysis.
Results: A total of 29 women were included. Six (20.6%) women were found to have moderate or severe degrees of food insecurity. In addition, 12 (40.30%) perceived moderate and severe levels of stress in the PSS-10. No relationship was found between food insecurity and perceived stress (p= 0.059). The food groups that exceeded the recommended weekly frequency were oils and sugars exceeded 3.9 and 2.9 frequencies, respectively.
Conclusion: We found that 20.6% women suffered household food insecurity and 40.3% suffered moderate and severe levels of stress. No relationship was found between food insecurity with the HIFAS scale and perceived stress measures with the PSS-10. We found that oils and sugars exceeded more by the double of the recommended frequency per week.
REFERENCES:
[1] Pérez-Escamilla R, Cunningham K, Moran VH. COVID-19 and maternal and child food and nutrition insecurity: a complex syndemic. Matern Child Nutr. 2020;16(3):e13036. doi:10.1111/mcn.13036
[2] Adams EL, Caccavale LJ, Smith D, Bean MK. Food Insecurity, the Home Food Environment, and Parent Feeding Practices in the Era of COVID-19. Obesity (Silver Spring). 2020;28(11):2056-2063. doi:10.1002/oby.22996

Table 1. Socio-demographic characteristics and scale results.

Age, years, mean (SD)	27.5 (7.03)
Diagnosis, n (%)	
RA	16 (55.1)
SLE	7 (24.4)
Others	6 (20.6)
Results per scales	
HFIAS, n (%)	
No risk	13 (44.8)
Mild	10 (34.4)
Moderated	3 (10.3)
Severe	3 (10.3)
EPP-10, n (%)	
Mild	17 (58.6)
Moderated	9 (31.0)
Severe	3 (10.3)

SD: standard deviation, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, HFIAS: Household food security access component scale, EPP-10: Perceived stress scale 10 items.

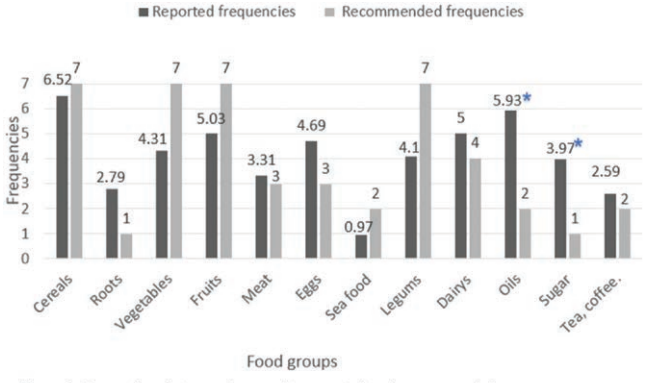


Figure 1. Comparison between frequencies reported and recommended.
*Intake significantly higher.

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.807

AB0658 **FEAR OF COVID-19 IN POSTPARTUM WOMEN WITH RHEUMATIC DISEASE**

L. G. Espinosa Banuelos[1], M. E. Corral Trujillo[1], C. M. Skinner Taylor[1], L. Pérez Barbosa[1], R. A. Rodriguez Chavez[1], A. Y. Lujano Negrete[1], R. Moyeda Martinez[1], A. Cárdenas[1], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Servicio de Reumatología, Monterrey, Mexico*

Background: In Mexico, the SARS-CoV-2 pandemic has totaled almost two million cases and exceeded 150,000 deaths (29/01/2021). Currently, COVID-19 has become the leading cause of death in pregnant women in Mexico. COVID-19 has additionally impacted the psychological health of individuals including women with rheumatic diseases.
Objectives: The aim of this study is to compare the Fear of COVID-19 Scale (FCV-19S) in postpartum women with and without autoimmune rheumatic diseases.
Methods: A cross-sectional, descriptive, and comparative study was conducted. The Spanish FCV-19S version was applied by telephone or e-mail. The instrument consists of seven items, each with a five-point Likert scale of options. The participant must choose the options that best represent their perception about the statements presented. The maximum possible total is 35 points. Sociodemographic information was collected from the clinical charts. The Kolmogorov-Smirnov test was used to determine normality of the data. Statistical analysis was done using the Mann-Whitney U test.
Results: Forty-four postpartum women were included (22 from the Pregnancy and Rheumatic Diseases Clinic and 22 from the Obstetrics Department, both groups from the University Hospital "Dr. José E. González in Monterrey, México). The mean level of fear found in women with rheumatic disease was 16 (6.6) points versus 14 (4.6) points in the non-rheumatic patients group. No significant difference was found between groups (p=0.65). Regarding the rheumatic diseases group, women in the category of other diagnoses (that included Sjögren's Syndrome, antiphospholipid syndrome, and dermatomyositis) had a greater mean FCV-19S score (20.2), than patients with systemic lupus erythematosus (17.3) and rheumatoid arthritis (15.4).
Conclusion: Women with postpartum rheumatic disease had a higher FCV-19S score than postpartum women without rheumatic diseases, although this difference was not statistically significant.
REFERENCES:
[1] Lumbreras-Marquez MI, Campos-Zamora M, Seifert SM, et al. Excess Maternal Deaths Associated With Coronavirus Disease 2019 (COVID-19) in Mexico. Obstet Gynecol. 2020;136(6):1114-1116. doi:10.1097/AOG.0000000000004140
[2] Yan H, Ding Y, Guo W. Mental Health of Pregnant and Postpartum Women During the Coronavirus Disease 2019 Pandemic: A Systematic Review and Meta-Analysis. Front Psychol. 2020;11:617001. Published 2020 Nov 25. doi:10.3389/fpsyg.2020.617001

Table 1. Sociodemographic data

	Women with rheumatic diseases N= 22	Women without rheumatic diseases N= 22	*p*=
Age, years, mean, (SD)	28 (6.8)	23 (5.0)	0.65
Occupation, n (%)			
Housewive	14 (63.6)	18 (81.8)	
Employee	5 (22.7)	3 (13.6)	
Other	3 (13.6)	1 (4.5)	
Education level, n (%)			0.28
Middle school	10 (45.45)	16 (72.72)	
High School	8 (36.36)	5 (22.72)	
College	4 (18.18)	1 (4.54)	
Rheumatic diagnosis, n(%)			
Rheumatoid arthritis	9 (40.9)		
Systemic lupus erythematosus	8 (36.6)		
Others (SS, APS, DM)	5 (22.7)		

SS: Sjögren's syndrome, APS: antiphospholipid syndrome, DM: dermatomyositis

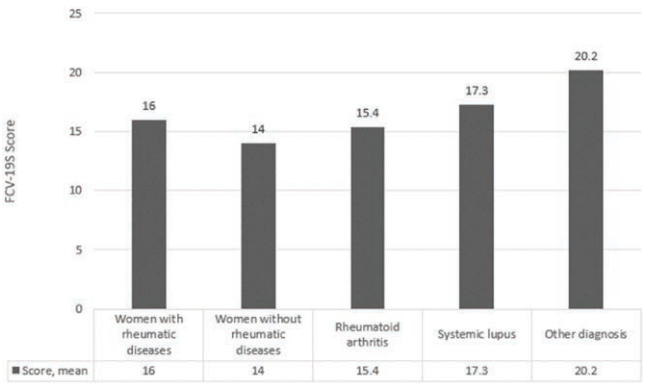


Figure 1. FCV-19S total scores per groups

Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.854

AB0659 THE LOCKDOWN REPERCUSSION ON THE RHEUMATOLOGIST'S LIFE

P. Lemesle[1], L. Poulain[2], X. Grapton[3], N. Bouhedja[2]on behalf of CREER. [1]*Hospital of Courbevoie, Clinic Rives de Seine, Courbevoie, France*; [2]*La Garenne-Colombes, Private practice, La Garenne-Colombes, France*; [3]*Neuilly-sur-Seine, Private practice, Neuilly-sur-Seine, France*

Background: We have just experienced an exceptional period of time and it seemed interesting to know what this particular time of isolation in a population of rheumatologists has brought about
Objectives: To analyze what the doctor felt in his personal and professional life as a result of the crisis. To determine the reactions, feelings and attitudes that may have emerged during these weeks of confinement.
Methods: 38 private practice rheumatologists from the Ile-de-France region, average age 63 yo, 58% male (M). 13 questions, 9 appendices, ranking of the most frequently cited reactions
Results: 3 feelings stand out: anger 71-84%, fear of being contaminated and of transmitting M 91/F 69%, concern about an unknown pandemic M 86/F69%.
Anger at the indifference to the exposure of doctors in the city 84%, the unpreparedness of the authorities M 95/F 62%, the mortality in EHPAD (Nursing homes) 81%, the media cacophony 79%, the hidden reality 71%.
On a personal level, according to 61%, the Rh is not anxious about the world after, has no psychological repercussions (sleep, melancholy, etc.) 58% and his degree of commitment was guilt-free 55%.
Professionally: perplexity in the face of the contradictions of experts and scientific journals 79%, wide acceptance of constraints in the practice (10h/d mask wearing, 92%, spaced reception of patients 95%, education of barrier gestures 97%), adaptation of the exercise (teleconsultation, telephone consultation) 78%, fear of abandoning treatment or diagnostic delay M82/F62%, financial arrangements necessary M86/F53%.
For M: worries about the pandemic, anger and uncertainty about what will happen next predominate in this order. For F, anger (untruths and lack of means) is the main feeling. Anger, fear and uncertainty are the most frequently cited feelings
Conclusion: The Rh at the end of this period of confinement is worried M>F and anger especially in front of the sanitary unpreparedness M>F. On a personal level the private life has been little affected F>M and he has been able to adapt professionally. Nevertheless, the de-confinement has not been a banal return to normal 63% M= F.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.862

AB0660 COVID-19 SHARES CLINICAL FEATURES WITH ANTI-MELANOMA DIFFERENTIATION ASSOCIATED PROTEIN 5 POSITIVE DERMATOMYOSITIS AND ADULT STILL'S DISEASE

Y. Kondo[1], Y. Kaneko[1], H. Takei[1], H. Tamai[1], T. Takeuchi[1]. [1]*Keio University, Division of Rheumatology, Shinjuku City, Japan*

Background: The coronavirus disease 2019 (COVID-19), caused by a novel corona virus named SARS-CoV-2, has emerged as a global pandemic. Severe inflammatory process is one of main pathogenesis of COVID-19 and this involves cytokine storm along with overactivation of macrophage. On another front, cytokine storm with macrophage activation is frequently observed in various connective tissue diseases including dermatomyositis with positive antimelanoma differentiation-associated protein 5 (anti-MDA5) autoantibodies and adult Still's disease. Macrophage activation during inflammatory states is partially characterized by an increased serum ferritin levels and hyperferritinaemia and characteristics shared by the three diseases are a topic of interest to rheumatologists, however, no study has evaluated anti-MDA5-positive dermatomyositis and adult Still's disease in comparison to COVID-19.
Objectives: The aim of this study was to highlight the homology and heterogeneity of COVID-19, anti-MDA5 dermatomyositis, and adult Still's disease by comparing clinical pictures of each disease in order to discuss their respective pathogeneses.
Methods: We reviewed consecutive, newly diagnosed, untreated patients with COVID-19, anti-MDA5 dermatomyositis, or adult Still's disease. We compared their clinical, laboratory, and radiological characteristics, including the prevalence of macrophage activation syndrome and lung involvement in each disease.
Results: The numbers of patients with COVID-19, anti-MDA5 dermatomyositis, and adult-onset Still's disease with hyperferritinaemia (serum ferritin ≥ 500ng/dL) who were included for main analysis were 22, 14, and 59, respectively. COVID-19 and adult Still's disease both featured hyperinflammatory status, such as high fever and elevated serum C-reactive protein, whereas COVID-19 and anti-MDA5 dermatomyositis both presented with severe interstitial lung disease and hypoxaemia. While two-thirds of the patients in each group met the criteria for macrophage-activated syndrome that is used in systemic juvenile idiopathic arthritis, the HScore, an indicator of haemophagocytic lymphohistiocytosis, was low in anti-MDA5 dermatomyositis and COVID-19 even in severe or critical cases. The findings of chest computed tomography were similar between COVID-19 and anti-MDA5 dermatomyositis (Figure 1).
Conclusion: COVID-19 shared clinical features with rheumatic diseases characterised by hyperferritinaemia, including anti-MDA5 dermatomyositis and adult Still's disease. These findings should be investigated further in order to shed light on the pathogenesis of not only COVID-19 but also the aforementioned rheumatic diseases.
REFERENCES:
[1] Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. (2020) 395: 1033-4.
[2] Gono T, Sato S, Kawaguchi Y, et al. Anti-MDA5 antibody, ferritin and IL-18 are useful for the evaluation of response to treatment in interstitial lung disease with anti-MDA5 antibody-positive dermatomyositis. Rheumatology (Oxford). 2012; 51(9):1563-70.

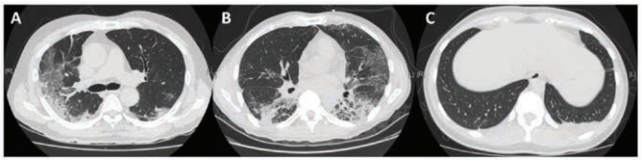


Figure 1. Imaging characteristics of chest CT scans in patients with COVID-19, anti-MDA5 dermatomyositis, and adult Still's diseaseA)Bilateral ground-glass and consolidative opacities with peripheral distribution in COVID-19.B)Bilateral ground-glass opacities with peripheral consolidations in anti-MDA5 dermatomyositis.C)Pleural effusion with pleural thickening on the left side in adult Still's disease.

Disclosure of Interests: Yasushi Kondo: None declared., Yuko Kaneko: None declared., Hisoshi Takei: None declared., Hiroya Tamai: None declared., Tsutomu Takeuchi Grant/research support from: received research grants outside the submitted work from Abbvie, Astra Zeneca, Bristol Myers Squibb, Chugai Pharmaceutical, Eisai Pharmaceutical, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Novartis, Takeda Pharmaceutical, Abbott Japan Co., Ltd., Astellas Pharma, Ltd., Daiichi Sankyo, Pfizer, Sanofi–Aventis, Santen Pharmaceutical, Teijin Pharma Ltd., Asahikasei Pharma Corp., SymBio Pharmaceuticals Ltd., Celtrion, Nipponkayaku Co. Ltd., Eli Lilly Japan, and Taisho Toyama Pharmaceutical.
DOI: 10.1136/annrheumdis-2021-eular.1031

AB0661

EFFECT OF COVID-19 PANDEMIC ON SLEEP DISORDERS IN PATIENTS WITH INFLAMMATORY ARTHRITIS

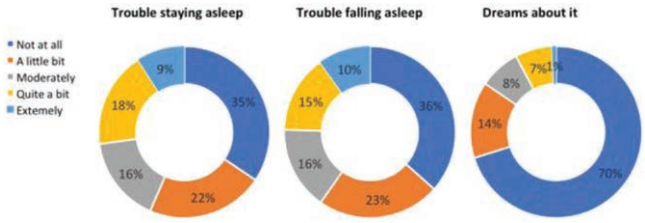
F. Ingegnoli[1], M. Buoli[2], C. Posio[3], R. DI Taranto[1], R. Caporali[1]. [1]*Università degli Studi di Milano, Division of Clinical Rheumatology, ASST Pini, Dept. of Clinical Sciences & Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Milano, Italy*; [2]*Università degli Studi di Milano, Dept. of Pathophysiology and Transplantation, Dept. of Neurosciences and Mental Health, Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Milano, Italy*; [3]*Università degli Studi di Milano, Dept. of Pathophysiology and Transplantation, Milano, Italy*

Background: A decrease in physical activity, exposure to daylight and a decline in psychological wellbeing due to COVID19 pandemic have led to increased incidence of sleep disorders such as difficulties falling asleep, sleep disruption, insomnia, nightmares and daytime sleepiness (1). Patients with inflammatory arthritis are more vulnerable to pain, depression, anxiety and sleep disorders. These complaints are linked in a cyclical pattern that may negatively affect daily-life activities (2-4). To our knowledge, the impact of pandemic on sleep disturbances in patients with inflammatory arthritis has not been evaluated yet.

Objectives: The aim of this study is to establish the COVID-19 related impact on sleep disturbances among patients with inflammatory arthritis who experienced the COVID-19 quarantine in Italy.

Methods: Data about chronic inflammatory arthritis (rheumatoid arthritis [RA], psoriatic arthritis [PsA] and ankylosing spondylitis [AS]) were retrieved from a large nationwide online survey involving patients affected by different rheumatic diseases. From May to September 2020, eleven patients' associations sent a call to rheumatic patients asking them to complete an anonymous online survey with specific questions also about sleep disturbances and pre- and post-lockdown self-reported use of psychopharmacotherapy. Data were analysed by a binary logistic regression model having the presence of sleep disturbances during COVID 19 pandemic as dependent variable.

Results: 375 of 507 (74%) of patients had inflammatory arthritis: 249 RA, 77 PsA and 49 AS. 291 (77.6%) were females with a median (IQR) age of 54 (44-63) years. There was an increase in the use of psychiatric compounds after quarantine period (59 [15,7%] vs 65 [17,3%]), especially for sleep medications (23 [6,1%] vs 28 [7,5%]) and anxiolytics (15 [4%] vs 18 [4,8%]). 246 (65.6%) of patients had trouble staying asleep, 238 (63.5%) had trouble falling asleep, and 112 (29.9%) had dreams about pandemic (Figure 1 below).



The binary logistic regression suggests that older age (OR= 1.038, p = .040), assumption of medication for psychiatric symptoms before COVID-19 (OR = 25.819, CI 11.465-58.143) and presence of COVID infection (OR = 2.783, CI 1.215-6.372) were predictive of insomnia during pandemic.

Conclusion: These results confirm that sleep disturbances have been a relevant concern in patients with inflammatory arthritis after COVID-19 national lockdown. Changes in daily life related to confinement have influenced psychological distress leading to a significant impact on sleep difficulties such as inability to fall early asleep or to maintain adequate sleep. Furthermore, older patients who had coronavirus infection and were previously treated for psychiatric disorders were at higher risk developing sleep disorders.

REFERENCES:

[1] Voulgaris A, et al. Sleep Med. 2020;73:170-176.
[2] Wolfe F, et al. J Rheumatol. 2006;33:1942-51
[3] Irwin MR, et al. Sleep. 2012;35:537-4
[4] Zielinski MR, et al. Front Immunol. 2019;10:1827.

Acknowledgements: We wish to thank the Lombard Association of Rheumatic Diseases (ALOMAR) for its invaluable contribution to the planning and dissemination the survey, all the Italian associations among which the National Association of People with Rheumatic and Rare Diseases (APMARR) and National Association of People with Rheumatic Diseases (ANMAR) that disseminated the survey through social media. The authors are grateful to all patients for contributing to this project.

Disclosure of Interests: Francesca Ingegnoli: None declared., Massimiliano Buoli: None declared., Cristina Posio: None declared., Raffaele Di Taranto: None declared., Roberto Caporali Speakers bureau: Abbvie, Amgen, BMS, Celltrion, Galapagos, Gilead, Lilly, Pfizer, Roche, UCB, Sanofi, Fresenius Kabi, Samsung bioepis, MSD, Consultant of: Galapagos, Gilead, Lilly,Janssen, MSD.

DOI: 10.1136/annrheumdis-2021-eular.1185

AB0662

IMPACT OF THE SARS-CoV-2 PANDEMIC IN A POPULATION OF PATIENTS FOLLOWED IN A RHEUMATOLOGY DEPARTMENT

S. Lahrichi[1], K. Nassar[2], S. Janani[3]. [1]*University Hospital of IBN ROCHD, rheumatology,Ccasablanca, Morocco*; [2]*University Hospital of IBN ROCHD, Rheumatology, Casablanca, Morocco*; [3]*University Hospital of IBN ROCHD, Rheumatology, Casablanca, Morocco*

Background: The COVID-19 pandemic had various impacts onpatients' realities. It had many physical but also psychological repercussions. It led to the onset of general stress, anxiety and depression affecting different age groups. In this study, we report the frequency of anxiety in patients followed in the department of rheumatology during the COVID-19 outbreak.

Objectives: To assess the impact of the COVID-19 pandemic in patients followed for inflammatory rheumatic disorders (IRD) or degenerative diseases in the Department of Rheumatology during the period of breakdown and health restrictions.

Methods: This is a cross-sectional study conducted in the department of rheumatology over a 5-month period from August 2020 to December 2020. Included patients were followed for IRD or degenerative pathology in the department. A pre-established questionnaire collected the symptoms and results of COVID-19 tests, the possible deterioration of the general condition since breakdown, as well as the increase of the disease activity of the rheumatism, pain, fatigue, anxiety, and the onset of signs of depression or sleep disturbances.The impact of the decrease in physical activity and the cessation of basic treatments of rheumatism with the different causes was also collected.

Results: 159 patients were included: 27 with Rheumatoid arthritis, 58 with Spondyloarthropathies, 32 with chondrocalcinosis, 9 with gouty arthropathies, and 33 with osteoarthritis. Of these, 15% had symptoms consistent with COVID-19. 25 patients performed the PCR test, of which 17 were positive and only 3 required hospitalization.None were put on oxygen. 32% reported a worsening of their rheumatism since the beginning of the epidemic, of which 35.9% reported increased pain and 21 noted a decrease in physical activity. 27.1% felt more stressed and irritated, and 14% felt more depressed. 54% had more sleepdisturbance, 22.2% had more fatigue compared to their state before the epidemic. 41.2% were afraid to come for consultation or hospitalization. 11.8% had stopped the basic treatment of their rheumatism, either for a shortage of the product in the pharmacy, or for the inability to obtain a travel authorization from the authorities

Conclusion: The physical and mental impact of the COVID-19pandemic affected approximately one-third of our population. Patients described worsening rheumatism and pain, as well as impaired sleep, fatigue and anxiety[1].Decreased physical activity was associated with increased rheumatism activity and pain. More than 50% of the patients presented a deterioration in their physical and mental health linked to the health situation[2]. Our results are consistent with the literature. It is classically admitted that rheumatic pathologiesare disabling and therefore lead to a withdrawal into oneself, generating an anxious state. It is essential to assess the psychological status of patients followed for rheumatism in order to develop preventive treatments and prevent its worsening linked to the impact of the pandemic[3].

REFERENCES:

[1] ChenN,ZhouM,DongX,etal.Epidemiologicalandclinicalcharacteristicsof-99casesof2019novelcoronaviruspneumoniainWuhan,China:adescriptives-tudy.Lancet2020;395:50713
[2] GuanWJ,NiZY,HuY,etal.Clinicalcharacteristicsofcoronavirusdisea-se2019inChina.NEnglJMed2020,http://dx.doi.org/10.1056/NEJMoa2002032
[3] HuangC,WangY,LiX,etal.Clinicalfeaturesofpatientsinfectedwith2019novel-coronavirusinWuhan,China.Lancet2020;395:497–5064

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1283

AB0663

COMPARING METHODS FOR DETERMINING ANTIBODIES TO SARS-COV-2 USING A RAPID TEST AND ENZYME-LINKED IMMUNOSORBENT ASSAY

G. Gridneva[1], E. Aronova[1], S. Glukhova[1], M. Cherkasova[1], B. Belov[1], K. Nurbaeva[1], E. Salyanova[1]. [1]*V.A.Nasonova Rheumatology Research Institute, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Drug Therapy, Moscow, Russian Federation*

Background: An accessible and sensitive and sensitive method for determining antibodies to a new coronavirus infection is often the key to timely provision of the necessary medical care to patients with rheumatic diseases
Objectives: Compare methods for determining antibodies to SARS-CoV-2 using a rapid test and enzyme-linked immunosorbent assay (ELISA)
Methods: Methods for determining antibodies to SARS-CoV-2 using an express test (Chromatographic express test SARS-CoV-2 IgG / IgM (Xiamen Biotime Biotechnology, China)) and by ELISA (Reagent kit for enzyme immunoassay of class G immunoglobulins and class M to SARS-CoV-2 (Vector-Best, Russia)) were compared.
80 patients were included with a diagnosis of rheumatoid arthritis 26 (33%), psoriatic arthritis - 9 (11%), osteoarthritis - 15 (19%), rheumatic heart disease 1 (1%), SLE 2 (3%), deramtomyositis 3 (4%), systemic sclerosis 5 (6%), systemic connective tissue diseases 4 (5%), including Sjogren's syndrome, spondyloarthritis 15 (19%).
17 (21%) denied a history of COVID-19 symptoms. 63 (79%) noted any signs of COVID-19 3.095 ± 1.45 months before the test (Median 3 [2; 4] months). 63 (79%) noted any signs of COVID-19 109 ± 43 days before the test (Median 111 [78; 135] months). The ELISA method was considered the standard.
Results: When comparing the results of the express test and the determination of IgG antibodies to SARS-CoV-2 in serum, the following was obtained: the sensitivity of the express test is 99%. When comparing the results of the express test and the determination of IgM antibodies to SARS-CoV-2 in serum, it was obtained: among 66 samples with a negative result by the express test method, IgM was detected in 6 cases by ELISA/ So, 7.5% of 80 samples were false negative. In 3 of 14 samples with a positive result by the express test, IgM by ELISA was not detected. So, 3.75% of 80 samples were false-positive. (Table 1). When comparing the results of the IgM express test and ELISA, the following was obtained: the sensitivity of the express test was 33%, the specificity was 85%.

Table 1.

	Antibodies, express-test	Antibodies (ELISA), absent	Antibodies (ELISA), present	Row Totals
IgG	absent	0	1	1
	Row %	0.00%	100.00%	
	present	3	76	79
	Row %	3.80%	96.20%	
	Totals	3	77	80
IgM	absent	60	6	66
	Row %	90.91%	9.09%	
	present	11	3	14
	Row %	78.57%	21.43%	
	Totals	71	9	80

Conclusion: When comparing the results of the express test and the determination of IgG antibodies to SARS-CoV-2 in serum, the sensitivity of the express test is 99%. Determination of IgM antibodies to SARS-CoV-2 using a rapid test is less reliable than determination using ELISA.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1311

AB0664 THE PSYCHOLOGICAL STATE OF THE PATIENTS WITH RHEUMATIC DISEASES AND HOSPITAL WORKERS DURING THE CORONAVIRUS DISEASE (COVID-19) OUTBREAK

T. Lisitsyna[1], D. Veltishchev[2], A. Borisova[2], E. Nasonov[3], A. Lila[4]. [1]*V.A. Nasonova Research Institute of Rheumatology, Vascular rheumatology, Moscow, Russian Federation*; [2]*Moscow Research Institute of Psychiatry, Serbsky NMRC PN MoH, Department of mental disorders in somatic diseases, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, scientific director of the Institute, Moscow, Russian Federation*; [4]*V.A. Nasonova Research Institute of Rheumatology, director of the Institute, Moscow, Russian Federation*

Background: Patients with rheumatic diseases are more likely to suffer from anxiety-depressive disorders and, in the context of the current coronavirus pandemic, are most likely to be more susceptible to stress response, depression, and anxiety.
Objectives: to evaluate the frequency of anxiety-depressive symptoms and stress levels in patients with various rheumatic diseases (RD) and hospital workers of the Moscow Institute of Rheumatology in Russia
Methods: 148 RD inpatients, mostly with rheumatoid arthritis (44 (30%)), spondyloarthritis (31 (21%)), systemic lupus erythematosus (28 (19%)), systemic sclerosis (10 (7%)), primary Sjögren syndrome (7 (5%)), polymyositis (6 (4%)), and 32 hospital workers of the Nasonova Research Institute of Rheumatology were screened using the DASS-21 (The Depression, Anxiety, Stress scales-21, *Lovibond* S.H. & *Lovibond* P.F. (1995)) in the period from July to November 2020. The majority of RD-patients and hospital workers were women (73 and 93% resp). The mean age (M±SD) of RD-patients and hospital workers was 43,2±16,2 and 40,7±14,6 years resp.
Results: The frequency of depression (34,5% vs 34,4%), anxiety (41,9% vs 34,4%) and post-traumatic stress (27,7% vs 25,0%) in RD-patients were found to be comparable to that found among the hospital workers, and the level of anxiety was statistically significantly higher in patients (2,0 [1,0; 6,0] vs 1,0 [0; 4,5], p=0,038). There was no association of depression, anxiety and stress with RD activity. There was a weak positive correlation between the level of depression (R=0,30), anxiety (R=0,26) and stress (R=0,33) with a higher dose of glucocorticoids taken by patients, as well as a negative correlation between the severity of depression (R=-0,7) and stress (R=-0,17) with the age of patients and hospital workers.
19 (12,8%) of RD-patients and 7 (21,9%) of hospital workers had contracted COVID-19 in previous months. Survivors of the COVID-19, both among RD-patients and hospital workers, were more likely to experience symptoms of depression, anxiety and stress: accordingly, depression had 31,6% vs 27,9%, anxiety – 47,4% vs 41,9% and stress – 26,3% vs 28,7% RD-patients who had been ill or not, and among hospital workers: depression – 28,6% vs 36,0%, anxiety – 42,8% vs 28,0%, stress – 42,8% vs 20,0%. 66,4% of RD-patients and 71,9% of hospital workers reported that the pandemic had a psychological impact on them.
Conclusion: The COVID-19 pandemic has had and continues to have a significant negative psychological impact on both RD-patients and hospital workers. About 25-47% of patients and hospital workers experienced significant level of depression, anxiety and stress, and their frequency was higher in those who had contracted COVID-19.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2021-eular.1335

AB0665 SWITCHING INTRAVENOUS ABATACEPT AND TOCILIZUMAB TO SUBCUTANEOUS INJECTIONS DURING THE COVID-19 PANDEMIC: A FRENCH EXPERIENCE

A. Combier[1], S. Wanono[1], L. Poiroux[1], C. Frantz[1], E. Descamps[1], O. Fogel[1], M. Boisson[1], X. Ayral[1], C. Bottois[2], Y. Allanore[1], J. Avouac[1]. [1]*Cochin Hospital, Rheumatology, Paris, France*; [2]*Cochin Hospital, Pharmacy Department, Paris, France*

Background: The COVID-19 pandemic requires measures to reduce patient exposure to the risk of contamination, in particular by limiting hospital admissions and promoting lockdown. In order to respond to these healthcare measures, patients were offered to replace intravenous infusions (IV) of abatacept (ABT) and tocilizumab (TCZ) to subcutaneous injections (SC).
Objectives: To assess the outcome of patients who switched from IV ABT or TCZ to SC during the COVID-19 pandemic.
Methods: A survey was conducted in December 2020 in partnership with the national AFP-RIC patient association to assess the outcome and satisfaction of patients who switched from ABT or TCZ IV to SC during the first wave of COVID-19 pandemic.
We also analysed the outcome of patients who switched from IV ABT or TCZ to SC in the rheumatology department of Cochin Hospital during the lockdown in April/may 2020. Articular activity parameters (swollen joint count, pain joint count, visual analogic pain scale, CRP, DAS-28 activity score) were assessed at medical visits before and 6 months after switching from IV to SC.
The data collected from the AFP-RIC patient association and the rheumatology department of Cochin Hospital were then aggregated and analyzed by Chi-square and Wilcoxon tests.
Results: 81 patients responded to the survey carried out by AFP-RIC patient association, including 29 treated with IV ABT (n=15, 52%) or TCZ (n=14, 48%). 17/29 (59%) were offered to switch from IV to SC, 14/17 patients (82%) accepted and 7 patients were still receiving ABT or TCZ SC injections in December 2020. In the rheumatology department of Cochin hospital, 71 patients were scheduled in April/May 2020 to receive IV ABT or TCZ, and 27 (38%) switched to SC. After 6 months, 19 patients (70%) had maintained SC injections, were satisfied with this injection route of administration and their articular activity parameters were unchanged (Table 1).

Table 1. Course of Disease parameters evaluated in the 19 patients who maintained abatacept or tocilizumab SC injections in the Rheumatology department of Cochin Hospital

Parameter, mean(SD)	Inclusion visit Switch to SC (n=19)	6 month visit (n=19)	*P-value*
DAS28	2.3 (1.2)	2.3 (0.7)	0.62
Tender joint count	2.5 (3.5)	1.3 (1.7)	0.49
Swollen joint count	1.3 (2.5)	0.9 (0.6)	0.35
Patient Global Health (cm)	3.2 (1.9)	2.6 (1.8)	0.60
CRP (mg/L)	3.2 (4.1)	5.2 (4.9)	0.56

CRP: C-Reactive Protein, SD: Standard Deviation

The combined analysis of these two populations included 41 patients (33 rheumatoid arthritis, RA, 7 juvenile idiopathic arthritis, JIA and 1 polymyalgia rheumatica) who switched to SC ABT or TCZ. 26/41 (63.5%) patients maintained SC injections and IV was re-established in 15/41 (36.5%). Reasons for returning to IV were poor tolerance of SC injections (n=6, 40%), worsening symptoms (n=11, 73%), patient preference to see a rheumatologist in hospital (n=10, 67%) and the high number of SC injections (n=2, 13%). The proportion of patients returning to IV was higher in RA patients compared to patients with JIA (42% vs. 14%, p = 0.08). Age and disease duration were not significantly different between patients who maintained SC injections and those who returned to IV (respectively p=0.97 and p=0.63).

Conclusion: Our study suggests that switching from IV ABT or TCZ to SC is an acceptable procedure during the COVID-19 pandemic, especially for patients with JIA.

Acknowledgements: Association AFP-RIC (Angélique Hochedé, Cyrielle Beller, Sandrine Rollot) and the members of the association for their help in the conduction of the survey

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1355

AB0666 PROGNOSTIC VALUE OF SERUM KREBS VON DEN LUNGEN-6 GLYCOPROTEIN CIRCULATING LEVELS IN COVID-19 PNEUMONIA: A PROSPECTIVE COHORT STUDY

D. Lobo Prat[1], I. Castellví[1], D. Castillo[2], S. Orozco[2], A. Mariscal[3], L. Martínez-Martínez[3], A. M. Millán Arciniegas[1], P. Moya[1], A. Laiz[1], C. Díaz-Torné[1], B. Magallares[1], S. P. Fernandez-Sanchez[1], S. Jeria Navarro[1], L. Sainz Comas[1], H. Codes[1], J. Casademont[4], P. Domingo[5], H. Corominas[1]. *[1]Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*; *[2]Hospital de la Santa Creu i Sant Pau, Pneumology, Barcelona, Spain*; *[3]Hospital de la Santa Creu i Sant Pau, Immunology, Barcelona, Spain*; *[4]Hospital de la Santa Creu i Sant Pau, Internal Medicine, Barcelona, Spain*; *[5]Hospital de la Santa Creu i Sant Pau, Infectious Diseases, Barcelona, Spain*

Background: Currently, there are no biomarkers to predict respiratory worsening in patients with Coronavirus infectious disease, 2019 (COVID- 19) pneumonia.

Objectives: We aimed to determine the prognostic value of Krebs von de Lungen-6 circulating serum levels (sKL-6) predicting COVID- 19 evolving trends.

Methods: We prospectively analyzed the clinical and laboratory characteristics of 375 COVID- 19 patients with mild lung disease on admission. sKL-6 was obtained in all patients at baseline and compared among patients with respiratory worsening.

Results: 45.1% of patients developed respiratory worsening during hospitalization. Baseline sKL-6 levels were higher in patients who had respiratory worsening (median [IQR] 303 [209-449] vs. 285.5 [15.8-5724], P=0.068). The best sKL-6 cut-off point was 408 U/mL (area under the curve 0.55; 33% sensitivity, 79% specificity). Independent predictors of respiratory worsening were sKL-6 serum levels, age >51 years, time hospitalized, and dyspnea on admission. Patients with baseline sKL-6 ≥ 408 U/mL had a 39% higher risk of developing respiratory aggravation seven days after admission. In patients with serial determinations, sKL-6 was also higher in those who subsequently worsened (median [IQR] 330 [219-460] vs 290.5 [193-396]; p<0.02).

Conclusion: sKL-6 has a low sensibility to predict respiratory worsening in patients with mild COVID-19 pneumonia. Baseline sKL-6 ≥ 408 U/mL is associated to a higher risk of respiratory worsening. sKL-6 levels are not useful as a screening tool to stratify patients on admission but further research is needed to investigate if serial determinations of sKL-6 may be of prognostic use.

REFERENCES:

[1] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-62. 5.

[2] Tian W, Jiang W, Yao J, Nicholson CJ, Li RH, Sigurslid HH, et al. Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis. J Med Virol. 2020.

[3] Wang D, Li R, Wang J, Jiang Q, Gao C, Yang J, et al. Correlation analysis between disease severity and clinical and biochemical characteristics of 143 cases of COVID-19 in Wuhan, China: a descriptive study. BMC Infect Dis. 2020;20(1):519.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1359

AB0667 A PROSPECTIVE STUDY INTO COVID-19 LIKE SYMPTOMS IN PATIENTS WITH AND WITHOUT IMMUNE MEDIATED INFLAMMATORY DISEASES OR IMMUNOMODULATING DRUGS

L. van Ouwerkerk[1], A. Van der Meulen[2], M. Ninaber[3], Y. K. O. Teng[4], T. Huizinga[1], C. Allaart[1]. *[1]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[2]Leiden University Medical Center (LUMC), Gastorenterology, Leiden, Netherlands*; *[3]Leiden University Medical Center (LUMC), Pulmonology, Leiden, Netherlands*; *[4]Leiden University Medical Center (LUMC), Nephrology, Leiden, Netherlands*

Background: Patients with an immune mediated inflammatory disorder or post solid organ transplantation (IMIDT), are at risk for infectious complications especially if they are treated with immunosuppressive drugs (imeds). There is still great uncertainty whether these IMIDT patients are more susceptible to COVID-19 than controls, and/or should be advised to avoid taking their immunosuppressive treatment.

Objectives: To evaluate whether patients with IMIDT are more at risk for CLS than controls.

Methods: The IENIMINI study is a prospective cohort study in patients with IMIDT and controls (healthy or no IMIDT) who were identified based on the registration database of the Leiden University Medical Center. Over time, participants registered COVID-like symptoms (CLS) as they occurred, and filled in additional questionnaires. Univariate and multivariate regression analyses were done to identify variables associated with having CLS.

Results: Of the 8670 individuals approached, 2110 with IMIDT and 1067 controls agreed to participate. In March and April, 454 (22%) of IMIDT patients and 242 (23%) of controls recorded to have CLS, mostly mild with a median (IQR) duration of seven (3-14) days in the IMIDT group and six days (4-11) in the control group. Eleven (5%) of the IMIDT patients with immunosuppressive medication (imed), 6 (3%) of IMIDTs without imed and 2 (1%) of controls were hospitalized with CLS (p=0.04). In May and June, fewer episodes overall were recorded. Being female (OR 1.45 95%CI 1.15;1.82), having a lung disease (OR 1.50 95%CI 1.20;1.88) and wearing a face mask (OR 1.42 95%CI 1.13-1.77) were independently associated with a higher risk, while higher age (OR 0.96 95%CI 0.96;0.97) and having an IMIDT with immunosuppressive medication use (OR 0.68 95%CI 0.51;0.91) were independently associated with a lower risk (see Table 1). Similar results were found after data imputation.

Table 1. Univariate & multivariate analysis of variables associated with having CLS or not (OR with 95% CI)

	n⁰	Univariate	Multivariate*
Sex, female	2546	1.89 (1.58;2.25)	1.45 (1.15;1.82)
BMI	2391	0.99 (0.97;1.01)	1.00 (0.98;1.03)
Age	2546	0.97 (0.96;0.97)	0.96 (0.96;0.97)
IMIDT without imed†	2546	1.00 (0.82;1.23)	0.94 (0.72;1.24)
IMIDT with imed †	2546	0.79 (0.65;0.97)	0.68 (0.51;0.91)
Smoking (current)	2463	1.35 (1.02;1.78)	1.05 (0.74;1.50)
Physical contact with family**	2220	1.47 (1.22;1.78)	1.22 (0.98;1.53)
Visiting other people (not family)	2205	1.26 (1.05;1.51)	0.96 (0.77;1.20)
Wearing a face mask	2196	1.46 (1.20;1.76)	1.42 (1.13;1.77)
Close contact (at work)	2180	1.65 (1.34;2.03)	1.27 (0.97;1.66)
Self-reported Diabetes Mellitus	2381	0.69 (0.50;0.96)	0.89 (0.58;1.36)
Self-reported lung disease	2396	1.30 (1.09;1.54)	1.50 (1.20;1.88)
Self-reported heart disease	2399	0.85 (0.69;1.04)	1.09 (0.83;1.43)
Daily alcohol use	2416	0.84 (0.71;1.00)	1.20 (0.96;1.50)
Influenza vaccination***	2415	0.71 (0.60;0.84)	0.96 (0.76;1.21)
Solid organ transplantation	2546	0.74 (0.54;1.03)	0.79 (0.47;1.35)
Good adherence to lockdown rules	2245	1.17 (0.41;3.29)	2.46 (0.65;9.38)
Use of oral corticosteroids	2546	0.84 (0.66;1.06)	1.44 (0.95;2.20)
Working outside the house	2435	1.39 (1.16;1.68)	0.92 (0.71;1.20)

Abbreviations: BMI=body mass index; CI= confidence intervals; CLS=Covid like symptoms; IMIDT= with immune mediated inflammatory disorders or transplant organ; n0=number of observations; OR=odds ratio.

** number of observations: 1835*

*** physical contact specified as 'holding/shaking hands, hugging etcetera'*

**** in autumn 2019† control group = reference group*

Conclusion: Between March and July 2020, IMIDT patients, whether or not taking imeds, did not show an increased risk of reported COVID-like symptoms compared to controls. Continuing immunosuppressant drugs as long as not ill, while following the Dutch COVID rules, appears to be safe.

Disclosure of Interests: Lotte van Ouwerkerk: None declared., Andrea van der Meulen Speakers bureau: Dr. van der Meulen reports personal fees from Janssen, grants and personal fees from Takeda, personal fees from Galapogos, grants from Nestle, grants from Norgine, outside the submitted work., Grant/ research support from: Dr. van der Meulen reports personal fees from Janssen, grants and personal fees from Takeda, personal fees from Galapogos, grants from Nestle, grants from Norgine, outside the submitted work., Maarten Ninaber: None declared., Y.K. Onno Teng: None declared., Thomas Huizinga: None declared., Cornelia Allaart: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1387

AB0668 THE ONSET OF RHEUMATOID ARTHRITIS AFTER COVID-19 – COINCIDENCE OR CONNECTED?

V. Derksen[1], T. Kissel[1], F. Lamers-Karnebeek[2], A. Van der Bijl[3], A. C. Venhuizen[4], T. Huizinga[1], R. Toes[1], A. H. E. Roukens[5], D. Van der Woude[1]. *[1]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[2]Bernhoven hospital, Rheumatology, Uden, Netherlands*; *[3]Isala hospital, Rheumatology, Zwolle, Netherlands*; *[4]Rivierenland Hospital, Rheumatology, Tiel, Netherlands*; *[5]Leiden University Medical Center (LUMC), Infectious Diseases, Leiden, Netherlands*

Background: COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been suggested to induce autoimmune phenomena. Multiple studies have reported the presence of autoantibodies in patients with COVID-19. Also the presence of anti-citrullinated protein antibodies (ACPA) and flaring of rheumatoid arthritis (RA) after COVID-19 has been described.[1, 2] Furthermore, in rheumatology clinics patients may present with polyarthritis compatible with RA shortly after SARS-CoV-2 infection. However, it is unclear how often ACPA occur after COVID-19 and whether preceding COVID-19 impacts on disease presentation of RA and phenotype of the ACPA response.

Objectives: This study aims to determine the seroprevalence of ACPA after COVID-19 and to investigate the association between preceding COVID-19 infection and disease presentation of new-onset RA, including clinical phenotype and autoantibody response.

Methods: To estimate the prevalence of ACPA after COVID-19 we measured ACPA IgG in samples from 61 patients visiting the specialized post-COVID outpatient clinic of the LUMC 5 weeks after hospitalization, using routine tests or in-house ELISA. Furthermore, we identified 5 patients presenting with polyarthritis compatible with RA after SARS-CoV-2 infection. To study the impact of COVID-19 on disease presentation, we examined clinical phenotype, autoantibody isotype positivity and ACPA IgG variable domain (V-domain) glycosylation of these patients and compared these features to regular RA patients. Autoantibody isotypes, including rheumatoid factor (RF) IgM/IgA, anti-CCP2 IgG/ IgM/ IgA and anti-carbamylated protein antibodies (anti-CarP) IgG were measured using in-house ELISA's. The percentage of V-domain glycosylation of purified ACPA IgG was measured with UHPLC.

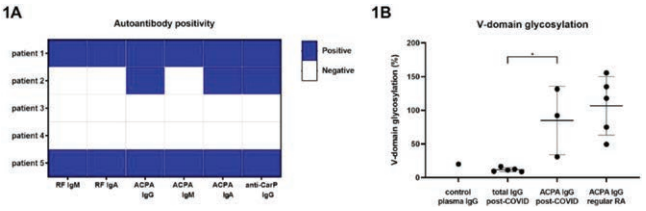
Results: None of the 61 post-COVID patients tested positive for ACPA 5 weeks after hospitalization, except two patients previously diagnosed with ACPA-positive RA. Thus, we could not observe an increase in ACPA-positivity shortly after COVID-19. Of the 5 patients who developed polyarthritis compatible with RA after SARS-CoV-2 infection, the average age was 63.6 years and 2/5 were female. 4/5 patients had been hospitalized due to severe COVID-19. On average, joint complaints started 6.6 weeks after infection, although two patients reported symptoms before infection. 4/5 patients fulfilled the ACR 2010 criteria for RA. Three patients (patient 1, 4, 5) were phenotypically very similar to regular new-onset RA patients. Patient 3 had a history of seronegative RA and had been in DMARD-free remission for 5 years. She flared 6 weeks after SARS-CoV-2 infection. Patient 2 had a remarkably different presentation. He was admitted with a suspected septic polyarthritis or pneumonia with reactive polyarthritis 6 weeks after COVID-19. ACPA level was low positive. The patient died unexpectedly after two days and autopsy revealed dilating myocarditis of unclear underlying cause. No causative pathogen could be identified.

Previous studies have shown that RA-patients are most often either seronegative or triple-positive for RF, ACPA and anti-CarP antibodies. Autoantibody measurements on sera of the post-COVID polyarthritis patients revealed a similar pattern (Figure 1A) with two patients being completely seronegative, and three patients positive for a range of autoantibodies. In all post-COVID samples, the percentage of ACPA IgG V-domain glycosylation was significantly increased compared to total IgG (Figure 1B), similar as in regular RA.

Conclusion: In conclusion, we found that the seroprevalence of ACPA is not increased post-COVID and that most patients presenting with polyarthritis after COVID-19 resemble regular RA patients, both regarding clinical phenotype and autoantibody characteristics. Although sample size and follow-up was limited, it appears that RA post-COVID may be coincidence rather than connected.

REFERENCES:

[1] Vlachoyiannopoulos et al. Ann Rheum Dis, 2020.
[2] Perrot et al. The Lancet Rheumatology, 2020.



Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1398

AB0669 DEPRESSION AND ANXIETY MIGHT NOT BE INCREASED DURING COVID-19 PANDEMIC IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

E. Erpek[1], D. Solmaz[1], D. Bayraktar[2], G. Duran[3], G. Kabadayi[1], E. Durak Ediboglu[1], E. Otman Akat[1], G. Alp[1], H. Cinakli[1], İ. Kurut Aysin[1], S. Gucenmez[1], O. Bayindir[1], M. Ozmen[1], S. Akar[1]. *[1]Izmir Katip Celebi University Faculty of Medicine, Rheumatology, Izmir, Turkey*; *[2]Izmir Katip Celebi University Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Izmir, Turkey*; *[3]Dokuz Eylul University, Institute of Health Sciences, Department of Physiotherapy and Rehabilitation, Izmir, Turkey*

Background: Anxiety and depression are most common psychiatric disorders in chronic inflammatory rheumatic condition as well as axial spondyloarthritis (axSpA) (1). The prevalence of depression has been reported as 11-64% depending on the criteria used. Also self-reported depression and anxiety were found to be associated with disease activity and function in axSpA (1,2). It is observed that mental health is affected among healthy subjects during the COVID-19 pandemic, but this condition has not been systematically reviewed in axSpA patients.

Objectives: We aimed to compare frequency of self-reported depression and anxiety before and during the Covid-19 pandemic in patients with axSpA.

Methods: Seventy-six axSpA patients who were evaluated for the presence of depression and anxiety by using Hospital Anxiety and Depression scale (HADs) before pandemic were included in this study. All participants were classified according to the ASAS axSpA classification criteria. Patients were contacted by phone to participate and complete the HADS questionnaire. Demographic and disease related characteristics including BASDAI, BASFI and Patient Acceptable Symptom State (PASS) were recorded during interview. The HADs cut off value was taken as >7 in both groups to define the presence of anxiety or depression. Before and during pandemic period anxiety and depression scores were statistically compared.

Results: The demographic and disease related characteristics of axSpA patients with and without anxiety/depression were summarized in Table 1. The frequency of anxiety (43.4% vs %43.4; p>0.05) and depression (46.1% vs 44.7%; p>0.05) were found to be similar before and during pandemic period. Patients with anxiety (HADs>7) and depression (HADs>7) had higher BASDAI and BASFI scores and much less PASS positivity (Table 1). Although the frequency of depression was similar between before and during the pandemic period, symptom severity in depression was slightly increased during the pandemic (Figure 1).

Table 1. Patients' demographics and characteristics according to the presence of anxiety and depression

Variables	Presence of depression n:35	Absence of depression n:41	P	Presence of anxiety n:33	Absence of anxiety n:43	P
Age (years) mean ± SD	41.8±11.2	44.1±9.3	>0.05	42.0±10.9	43.6±10.0	>0.05
Male n(%)	21(60.0)	26(63.4)	>0.05	18(54.5)	29(67.4)	>0.05
Education time (years) mean ± SD	9.6±4.8	11.0±4.2	>0.05	9.7±5.0	10.6±4.1	>0.05
Current smoker n(%)	18(51.4)	15(36.6)	>0.05	15(45.5)	18(41.9)	>0.05
Alcohol consumption n(%)	12(34.3)	12(29.3)	>0.05	10(30.3)	14(32.6)	>0.05
Current BMI kg/m^2 mean ± SD	26.0±4.8	26.8±4.5	>0.05	26.4±5.0	26.5±4.3	>0.05
Sleep time (hours) mean ± SD	7.6±1.7	7.6±1.3	>0.05	7.5±1.6	7.7±1.4	>0.05
Current BASDAI mean ± SD	2.5±1.6	1.4±1.6	**<0.05**	2.7±1.8	1.3±1.3	**<0.001**
Current BASFI mean ± SD	2.4±2.1	1.1±1.3	**<0.05**	2.4±2.0	1.2±1.4	**<0.05**
PASS positivity n(%)	16(45.7)	29(70.7)	**<0.05**	14(42.4)	31(72.1)	**<0.05**

Current depression and anxiety scores were correlated with disease activity (HADs Depression vs BASDAI r:0.530, p<0.001; HADs Anxiety vs BASDAI r:0.500, p<0.001) and function (HADs-Depression vs BASFI r:0.519, p<0.001; HADs-Anxiety vs BASFI r:0.391, p<0.001). These relationships were also observed in the pre-pandemic period (HADs-Depression vs BASFI r:0.326, p<0.05; HADs-Anxiety vs BASDAI r:0.342, p<0.05).

Conclusion: Depression and anxiety symptoms seems to be comparable before and after the COVID-19 pandemic. Regardless of this period, the presence of both depression and anxiety are associated with disease activity, function and less patient acceptable symptom state.

REFERENCES:

[1] Zhao S, Thong D, Miller N, et al. The prevalence of depression in axial spondyloarthritis and its association with disease activity: a systematic review and meta-analysis. Arthritis Res Ther. 2018;20:140.

[2] Barışan E, Bayır D, Solmaz D. Aksiyel spondiloartrit hastalarında anksiyete düzeyinin çeşitli ölçeklerle değerlendirilmesi ve anksiyete ile ilişkili faktörler. Dokuz Eylül Üniversitesi Tıp Fakültesi Dergisi. 2019; 129-137.

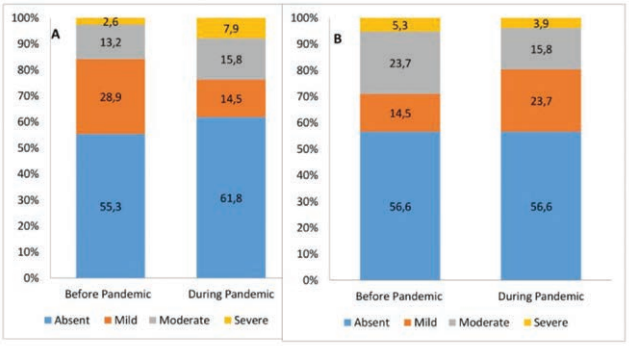


Figure: Severity of depression and anxiety in AxSpA before and during COVID-19 pandemic

Figure 1.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1422

AB0670 THE COURSE AND OUTCOMES OF COVID-19 IN PATIENTS WITH ANCA-ASSOCIATED SYSTEMIC VASCULITIS, RECEIVING ANTI-B CELL THERAPY WITH RITUXIMAB

T. Beketova[1], V. Babak[1], M. Suprun[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Currently, the issues of the effect of anti-B cell therapy on the risk of severe course of COVID-19 in patients (pts) with ANCA-associated vasculitis (AAV) has not been completely studied.

Objectives: We present an analysis of the COVID-19 incidence and outcomes in 126 AAV pts treated with rituximab (RTX) from one rheumatology center registry.

Methods: Data were collected with telephone/online surveying between 11-15th November 2020 from all 126 AAV pts (58- granulomatosis with polyangiitis, GPA; 38- microscopic polyangiitis, MPA; 22- eosinophilic granulomatosis with polyangiitis, EGPA (54% ANCA-negative); and 8- uncertain AAV). Pts age was 51 (20-81) yr, 62% women. Due to AAV activity or risk of relapse, during the pandemic RTX was prescribed in 48% pts.

Results: The incidence of COVID-19 in AAV pts was 3.5% during the first 3 months of the pandemic, the course was uneventful, and all pts recovered. Since September 2020 a 4-fold increase in the incidence alongside with more severe course of COVID-19 were reported. After 8 months of the pandemic, COVID-19 was diagnosed in 21 (16.6%) pts with median age 55 yr, 57% women. COVID-19 incidence was lower in GPA (15.5%) vs MPA (21.1%) or EGPA (27.7%). The mortality rate was 14.3% (2- MPA, 1- GPA). When analyzing the 5-year survival rate of AAV pts treated with RTX, prognosis worsening was noted; in 2020 there were 3 deaths due to COVID-19, in the previous 5 years- only 2 deaths.

Conclusion: Taking into account the fact the mechanisms of AAV and severe COVID-19 are largely synergistic (Table 1), primarily in the context of obstructive thromboinflammation as manifestation of acute inflammatory syndrome in COVID-19 [1], AAV can potentially contribute to the severe course of COVID-19. Anti-CD20 therapy seems to have a protective effect against severe COVID-19 [2], which, however, can be insufficient in AAV pts with active disease and multiple organ damage. Further analysis of COVID-19 cases in pts with AAV and other rheumatic diseases is exceptionally important.

Table 1. Comparison of AAV and severe COVID-19

Parameter	AAV	Severe COVID-19
Lung damage	High frequency of lung damage	Possibly destructive lung damage
Damage to other organs	Typically affects the upper and lower airways and kidneys; Other organs can be involved	Possible extrapulmonary localization
Vascular involvement	Systemic necrotizing vasculitis of small vessels; In the active phase, hypercoagulation	Obstructive thromboinflammation of the microcirculation of lungs and extrapulmonary vessels; Increased incidence of Kawasaki syndrome during the pandemic
Inflammation	High or very high	Very high
Autoantibodies	ANCA pathogenetic role	Dominant extrafollicular B cell responses; Correlation between SARS-CoV-2 antibody titer and severity of COVID-19; High titers of IFN-α2/ω autoantibodies
Neutrophil	Neutrophils are the most important effector cells in the pathogenesis	Changes in the morphology of neutrophils were noted; Netosis, the release of proteases from neutrophils promote the complement system activation, hypercoagulation, endotheliitis, production of pro-inflammatory cytokines; An increase of neutrophils in the blood and bronchoalveolar lavage fluid were noted
Complement	Complement is crucial in the pathogenesis; C5a receptor antagonist Avacopan efficacy	Activation of alternative/lectin complement pathways; C5 antagonist Eculizumab has been reported to be effective
Treatment	Immunosuppressants; In the active phase, anticoagulants	Anticoagulants; Glucocorticoids, pro-inflammatory cytokine antagonists, JAK inhibitors, cyclosporine
Prognosis	Serious	High mortality rate

REFERENCES:

[1] Ciceri F, et al. Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS): an atypical acute respiratory distress syndrome working hypothesis. Crit Care Resusc. 2020;22(2):95-7

[2] Montero-Escribano P, et al. Anti-CD20 and COVID-19 in multiple sclerosis and related disorders: A case series of 60 patients from Madrid, Spain. Mult Scler Relat Disord. 2020;42:102185

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1953

AB0671 NO EVIDENCE OF SARS-COV-2 IN THE KNEE JOINT: A CADAVER STUDY

M. Grassi[1], V. Giorgi[2], M. Nebuloni[3], P. Zerbi[3], M. R. Gismondo[4], F. Salaffi[5], P. Sarzi-Puttini[2], S. G. Rimoldi[4], A. Manzotti[1]. [1]*ASST-Fatebenefratelli L. Sacco University Hospital, Orthopaedic and Traumatology Unit, Milan, Italy*; [2]*ASST Fatebenefratelli L.Sacco University Hospital, Rheumatology Unit, Milan, Italy*; [3]*ASST-FBF Sacco, University of Milan, Pathology Unit, Department of Biomedical and Clinical Sciences, Milan, Italy*; [4]*ASST-Fatebenefratelli L. Sacco University Hospital, Microbiology Unit, Milan, Italy*; [5]*Università Politecnica delle Marche, Rheumatology Department, Jesi, Italy*

Background: Despite the considerable research efforts being made to learn more about COVID-19, little is known about the presence of SARS-CoV-2 genetic material in biological fluids other than respiratory droplets, blood, and feces [1,2]. In particular, little is known about the presence of SARS-CoV-2 in the joints either *post mortem* [3] or *in vivo* [4]. To the best of our knowledge, only Lopéz-Gonzalez *et al.*[5] have published a description of acute arthritides occurring during hospitalisation due to COVID-19, and they did not find any SARS-CoV-2 genetic material in the patients' synovial fluid samples.

Objectives: The aim of this *post mortem* study was to assess the presence of SARS-CoV-2 RNA in the knee synovial fluid, synovial tissue, and bone tissue of COVID-19 patients in order to discover whether the joint is a possible route of transmission during orthopaedic surgical procedures, and clarify the possible role of SARS-CoV-2 as a directly arthritogenic virus.

Methods: *Post mortem* synovial fluid, synovial tissue and bone tissue samples were collected from the knees of five patients who died of COVID-19 in our hospital between September and October 2020, and analysed for the presence of SARS-CoV-2 using a commercial real-time polymerase chain reaction (RT-PCR) panel. Quantitative RT-PCR was used to test *post mortem* nasopharyngeal swabs of all of the patients.

Results: No SARS-CoV-2 RNA was detected in any of the knee samples, despite the positivity of the throat swab.

Conclusion: Our findings indicate that SARS-CoV-2 was not detected in knee synovial fluid, synovial membrane or bone. Therefore, our results suggest that all

healthcare professionals performing surgical procedures on the joints of COVID-19 patients are exposed to a risk of contagion due to exposure to respiratory droplets, blood and body fluids, but not to direct exposure to joint- or bone-related tissues. Furthermore, given that some case reports of arthritis in COVID-19 patients [5-8] show that it is possible that COVID-19 patients display viral-mediated arthralgias and arthritis, the absence of the virus in the knee highlighted by our study suggests that it is unlikely that SARS-CoV-2 has a direct inflammatory action on the joint, but it could induce an inflammation-related reaction, manifesting as a reactive arthritis [9].

REFERENCES:

[1] Cheng ZJ, Shan J. 2019 Novel coronavirus: where we are and what we know. *Infection*. 2020;(0123456789):1-9. doi:10.1007/s15010-020-01401-y
[2] Chen Y, Chen L, Deng Q, et al. The Presence of SARS-CoV-2 RNA in Feces of COVID-19 Patients. *J Med Virol*. April 2020. doi:10.1002/jmv.25825
[3] Maiese A, Manetti AC, La Russa R, et al. Autopsy findings in COVID-19-related deaths: a literature review. *Forensic Sci Med Pathol*. 2020. doi:10.1007/s12024-020-00310-8
[4] Baldanti F, Novazzi F, Cassaniti I, Piralla A, Di A, Bruno R. Detection of the SARS-CoV-2 in different biologic specimens from positive patients with COVID-19, in Northern Italy. *Authorea*. 2020. doi:10.22541/au.159724509.93056098
[5] López-González M-C, Peral-Garrido ML, Calabuig I, et al. Case series of acute arthritis during COVID-19 admission. *Ann Rheum Dis*. 2020;0(0):annrheumdis-2020-217914. doi:10.1136/annrheumdis-2020-217914
[6] Parisi S, Borrelli R, Bianchi S, Fusaro E. Viral arthritis and COVID-19. *Lancet Rheumatol*. 2020;2(11):e655-e657. doi:10.1016/S2665-9913(20)30348-9
[7] Alivernini S, Cingolani A, Gessi M, et al. Comparative analysis of synovial inflammation after SARS-CoV-2 infection. *Ann Rheum Dis*. 2020;0(0):2-3. doi:10.1136/annrheumdis-2020-218315
[8] Talarico R, Stagnaro C, Ferro F, Carli L, Mosca M. Symmetric peripheral polyarthritis developed during SARS-CoV-2 infection. *Lancet Rheumatol*. 2020;2(9):e518-e519. doi:10.1016/S2665-9913(20)30216-2
[9] Di Carlo M, Tardella M, Salaffi F. Can SARS-CoV-2 induce reactive arthritis? *Clin Exp Rheumatol*. 2020;In press.

Acknowledgements: We would like to thank the clinical staff of the Pathology Unit for their collaboration in performing the autopsies.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2033

AB0672 PSYCHOLOGIC STATE OF PATIENTS WITH RHEUMATIC DISEASES AFTER THE OUTBREAK OF SARS-COV2

M. Yasmine[1], S. Mariem[1], S. Miladi[1], A. Fazaa[1], L. Souebni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: The ongoing Coronavirus-19 disease epidemic is a public health emergency of international concern which could pose a challenge to psychological resilience. This is mainly the case of patients with rheumatic diseases (RD).
Objectives: The aim of this study was to establish the prevalence of psychiatric symptoms in patients with RD and to identify factors associated with psychological stress.
Methods: A cross-sectional study was conducted among patients with RD. They were invited to respond to a survey designed to assess their psychological response after the outbreak of the SARS-COV2 pandemic. Mental health status after the Covid-19 was evaluated using the Depression and Anxiety Scale (DASS-21). The total depression subscale score was divided into normal (0–9), mild depression (10–12), moderate depression (13–20), severe depression (21–27), and extremely severe depression (28–42). The total anxiety subscale score was divided into normal (0–6), mild anxiety (7–9), moderate anxiety (10–14), severe anxiety (15–19), and extremely severe anxiety (20–42).The Impact of Event Scale-Revised (IES-R) is a 22-item self-administered questionnaire that assesses the post-traumatic state (PTS). A cut-off point of 33 provided the best diagnostic accuracy for PTS. The level of significance was fixed at 0.05.
Results: Sixty patients were included (42 with rheumatoid arthritis and 18 with spondylarthritis) with a mean age of 51.3 ± 13.1 years [18-75]. The majority of patients were women (63.3%), married (81.7%), with a household size of 3–5 people (67.9%). The mean disease duration was 11.9 ±5.6 [1-23] years.
According to DASS depression score almost half of the patients (47%) suffered from depression, which was classified as severe in 10% of cases. The mean DASS anxiety subscale was 12.6 ± 8.2 [1-35]. The level of anxiety was mild in 23% of cases, moderate in 25% of cases, and severe in 23.3% of cases. The mean ILES-R score was 20.4 ± 10.2 [20-38]. Women experienced more PTS than men (26.3% vs 22.7%) without reaching a statistically significant correlation (p=0.9). Patients with higher education had lower IES-R, depression, and anxiety subscale scores as compared to those who were illiterate without a statistically significant correlation (p=0.5, p=0.2, p=0.4 respectively). A positive correlation was found between anxiety score and IES-R (p=0.00). Other sociodemographic variables including disease duration, parental status, marital status, and household size were not associated with IES-R and DASS subscale scores (p>0.05).
Conclusion: Our study showed that many of our patients with RD experienced anxiety, depression, and PTS after the outbreak of Covid-19. Professional status as well as other sociodemographic data was not associated with psychological stress.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2116

AB0673 THE ROUTINE HEALTH CARE OF PATIENTS WITH RHEUMATIC DISEASES DURING THE PANDEMIC OF COVID-19

S. Mariem[1], M. Yasmine[1], S. Miladi[1], A. Fazaa[1], L. Souebni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: The coronavirus pandemic poses a great threat to patients with rheumatic diseases (RD). Because of the state of immunodepression, they are perceived as vulnerable and at high risk of contracting the virus. This may lead to a delay in the health care routine.
Objectives: The aim of our study was to assess the routine of patients with rheumatic diseases in the era of covid-19.
Methods: We conducted a prospective study after the outbreak of Covid-19 including patients with RD: rheumatoid arthritis (RA) and Spondylarthritis (SpA). All of them were invited to answer a questionnaire about adherence to protective measures, health services, hospital visits, treatment modalities, as well as the level of satisfaction with the medical support or information received for COVID-19. We also evaluated the post-traumatic state (PTS) with the Impact of Event Scale-Revised (IES-R). A cut-off point fixed at 33 provided the best diagnostic accuracy for PTS. The level of significance was fixed at 0.05.
Results: The study included 60 patients with a female predominance (sex ratio=1.7). The mean age was 51.3 ± 13.1 years [18-75] and the mean disease duration was 11.9 ±5.6 [1-23] years. Forty-two patients had RA and 18 patients had SpA. The majority of respondents were women (63.3%), married (81.7%), with a household size of 3–5 people (67.9%). The mean DASS depression and anxiety subscale was 9.5 ±7.6 [2-32] and 12.6 ± 8.2 [1-35] respectively. PTS was found in 25% of cases. Twenty-two patients stopped working in the second outbreak. The adherence to protective measures was as follows: compliance with lock-down (92.5%), adherence to stay home warnings (82%), wearing masks (96.3%), social distancing (68%), and washing hands immediately after sneezing (59.3%). Information was mainly sourced from both social media and the Internet in 78.2% of cases. Most of the patients were satisfied with the information provided and only 5 demanded more information about vaccination protocol. Of the patients having direct contact with a person affected with Covid-19 (20%), seven patients experienced symptoms. Three patients were diagnosed with SARS-COV2 and three other patients were hospitalized because of flares. The majority of the respondents (98.2%) had confidence in their own doctors' ability to recognize Covid-19. The majority of patients (91%) were afraid of getting sick and 83.1% feared stigma and discrimination after the infection. Fifty patients did attend their consultation appointment and 13.3% had a phone consultation. About a third of patients (26.7%) of patients experienced a delay in treatment. A positive correlation was found between marital status and the fear of other family members getting Covid-19 (p=0.029). Patients who did not consult experienced more PTS and severe anxiety than those who did not delay hospital visits (p=0.07, p=0.04 respectively).
Conclusion: Our study showed that during the outbreak of Covid-19, patients with RD exhibited a high level of protection towards the virus. Despite these precautionary measures, a delay in hospital routine was observed.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2125

AB0674 RAPID ADOPTION OF TELEMEDICINE IN RHEUMATOLOGY TRAINING: RESULTS FROM THE COVID-19 GLOBAL RHEUMATOLOGY ALLIANCE TRAINEE SURVEY

S. A. Yeoh[1], K. Young[2], M. Putman[3], E. Graef[4], F. Berenbaum[5,6,7], R. Conway[8], R. Grainger[9], A. Kilian[10], M. Konig[11], J. Liew[12], P. M. Machado[1], S. E. Sattui[13], J. Sparks[14,15], P. Sufka[16], M. Ugarte-Gil[17], L. Upton[18], Z. Wallace[15,19], J. Yazdany[20], A. Jayatilleke[21]on behalf of the COVID-19 Global Rheumatology Alliance. [1]*University College London, Rheumatology, London, United Kingdom*; [2]*University of Texas Southwest Medical Center, Rheumatology, Dallas, United States of America*; [3]*Medical College of Wisconsin, Rheumatology, Milwaukee, United States of America*; [4]*Emerson Hospital, Department of Medicine,*

Concord, United States of America; [5]*Sorbonne University, Rheumatology, Paris, France*; [6]*AP-HP Saint-Antoine Hospital, Rheumatology, Paris, France*; [7]*Inserm, Rheumatology, Paris, France*; [8]*St James's Hospital, Rheumatology, Dublin, Ireland*; [9]*University of Otago Wellington, Department of Medicine, Wellington, New Zealand*; [10]*George Washington University, School of Medicine and Health Sciences, Washington DC, United States of America*; [11]*Johns Hopkins University, Rheumatology, Baltimore, United States of America*; [12]*Boston University, Rheumatology, Boston, United States of America*; [13]*Hospital for Special Surgery, Department of Medicine, New York, United States of America*; [14]*Brigham and Women's Hospital, Rheumatology, Boston, United States of America*; [15]*Harvard Medical School, Rheumatology, Boston, United States of America*; [16]*HealthPartners & Regions Hospital, Rheumatology, St. Paul, United States of America*; [17]*Universidad Científica del Sur, Rheumatology, Lima, Peru*; [18]*Georgetown University, School of Medicine, Washington DC, United States of America*; [19]*Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America*; [20]*University of California San Francisco, Division of Rheumatology, San Francisco, United States of America*; [21]*Temple University Lewis Katz School of Medicine, Rheumatology, Philadelphia, United States of America*

Background: The COVID-19 pandemic led to a rapid increase in remote consultations in rheumatology care. Due to the potential impact of this change on rheumatology clinical training, we investigated trainees' experiences with telemedicine.
Objectives: To assess the impact of telemedicine use during the COVID-19 pandemic on rheumatology training, including supervision.
Methods: A voluntary, anonymous web-based survey was administered in English, Spanish, or French from 19/08/2020 to 05/10/2020. Adult and paediatric rheumatology trainees worldwide in training in 2020 were invited to participate via social media and email. Using multiple choice questions, Likert scales, and free text answers, we collected data regarding prior and current telemedicine use, training, and supervision.
Results: 302 respondents from 33 countries completed the survey, with most (83%, 252/302) in adult rheumatology training. Reported use of telemedicine increased from 13% (39/302) pre-pandemic to 82% (247/302) (Table 1). European trainees predominantly utilised audio-only compared to trainees from the rest of the world (ROW) who predominantly utilised audio-video telemedicine.
Most trainees continued to evaluate new patients using telemedicine (65%, 161/247). A larger proportion of trainees were comfortable using telemedicine to evaluate follow-up (69% 170/247) versus new patients (25%, 41/161) (Figure 1). Only 32% (97/302) were trained in telemedicine, with the highest proportion among United States (US) trainees (59%, 69/116); subjects included software, clinical skills, and billing. The majority of trainees found this helpful (92%, 89/97). Supervision was most frequently in the form of verbal discussion after the consultation (Table 1); 24% (59/247) had no telemedicine supervision during the pandemic. In general, trainees found telemedicine negatively impacted their supervision (51%, 123/242) and clinical teaching quality (70%, 171/244); only 9% reported a positive impact on these areas.
Conclusion: Adoption of telemedicine during the COVID-19 pandemic has led to areas of concern for rheumatology trainees including inadequate supervision and clinical teaching. Our results suggest a need for education on evaluation of new patients using telemedicine, increasing telemedicine training, and ensuring adequate supervisory arrangements.

Table 1. Telemedicine use, supervision, and training by region. Data is presented as n (%). Rest of the world (ROW) data includes Asia (50), Central and South America (23), Canada (12), Australia (8), and Africa (4).

		Europe n = 89	US n = 116	ROW n = 97	Combined n = 302
Telemedicine use	Pre-pandemic	15 (17)	9 (8)	15 (15)	39 (13)
	During pandemic	64 (72)	112 (97)	71 (73)	247 (82)
Telemedicine modality	Audio-only	14 (93)	3 (33)	8 (53)	25 (64)
	Audio-video	1 (7)	7 (78)	7 (47)	15 (38)
pre-pandemic					
Telemedicine modality during pandemic	Audio-only	56 (88)	47 (42)	51 (72)	154 (62)
	Audio-video	7 (11)	100 (89)	29 (41)	136 (55)
Supervision	Real-time observation (part of visit)	0 (0)	4 (44)	3 (20)	7 (18)
pre-pandemic	Real-time observation (full visit)	0 (0)	2 (22)	2 (13)	4 (10)
	Verbal discussion after	8 (53)	3 (33)	7 (47)	18 (46)
	Written communication after	0 (0)	0 (0)	1 (7)	1 (3)
	None	7 (47)	2 (22)	5 (33)	14 (36)
Supervision during pandemic	Real-time observation (part of visit)	2 (3)	54 (48)	15 (21)	71 (29)
	Real-time observation (full visit)	3 (5)	32 (29)	8 (11)	43 (17)
	Verbal discussion after	32 (50)	65 (58)	28 (39)	125 (51)
	Written communication after	7 (11)	15 (13)	9 (13)	31 (13)
	None	28 (44)	9 (8)	22 (31)	59 (24)

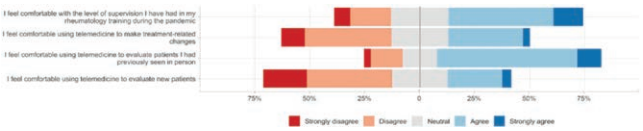


Figure 1. Rheumatology trainee comfort levels in using telemedicine during the pandemic.

Disclosure of Interests: Su-Ann Yeoh: None declared, Kristen Young: None declared, Michael Putman: None declared, Elizabeth Graef: None declared, Francis Berenbaum: None declared, Richard Conway: None declared, Rebecca Grainger Speakers bureau: Speaker fees from Abbvie, Janssen, Novartis, Pfizer, Cornerstones, all not related to this work, Consultant of: Consultancy fees from Abbvie, Janssen, Novartis, Pfizer, Cornerstones, all not related to this work, Grant/research support from: Travel assistance from Pfizer, not related to this work, Adam Kilian: None declared, Maximilian Konig: None declared, Jean Liew Grant/research support from: Research grant from Pfizer unrelated to this manuscript, Pedro M Machado Speakers bureau: Speaker fees from Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript, Consultant of: Consulting fees from Abbvie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript, Sebastian E. Sattui: None declared, Jeffrey Sparks Consultant of: Consultancy for Bristol-Myers Squibb, Gilead, Inova Diagnostics, Optum, and Pfizer unrelated to this manuscript, Grant/research support from: Research support from Bristol-Myers Squibb unrelated to this manuscript, Paul Sufka: None declared, Manuel Ugarte-Gil Grant/research support from: Research grants from Janssen and Pfizer unrelated to this manuscript, Laura Upton: None declared, Zachary Wallace: None declared, Jinoos Yazdany Consultant of: Consultancy for Astra Zeneca, Eli Lilly, and Pfizer, not related to this work, Grant/research support from: Research grants from Gilead and Pfizer, not related to this work, Arundathi Jayatilleke: None declared
DOI: 10.1136/annrheumdis-2021-eular.2205

AB0675

COUNTRY COMPARISON ON THE IMPACT OF THE COVID-19 PANDEMIC ON PATIENTS WITH RHEUMATIC DISEASES. RESULTS FROM THE REUMAVID STUDY (PHASE 1)

M. Garrido-Cumbrera[1], H. Marzo-Ortega[2,3], L. Christen[4], L. Carmona[5], J. Correa-Fernández[1], S. Sanz-Gómez[1], E. Mateus[6,7], S. Makri[8], P. Plazuelo-Ramos[9], L. Grange[10,11], S. Mingolla[12], K. Antonopoulou[13], D. Webb[14], C. Jacklin[15], S. Irwin[16], V. Navarro-Compán[17]on behalf of REUMAVID working group. [1]*Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; [2]*University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; [3]*Leeds Teaching Hospitals Trust, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*; [4]*Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; [5]*Institute for Musculoskeletal Health, InMusc, Madrid, Spain*; [6]*Liga Portuguesa Contra as Doenças Reumáticas (LPCDR), Management, Lisbon, United Kingdom*; [7]*NOVA Medical School, Comprehensive Health Research Centre (CHRC), Lisbon, Portugal*; [8]*Cyprus League Against Rheumatism (CYPLAR), Management, Nicosia, Cyprus*; [9]*Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; [10]*French League Against Rheumatism (AFLAR), Management, Grenoble, France*; [11]*Centre Hospitalier Universitaire de Grenoble, Rheumatology, Grenoble, France*; [12]*Italian National Association of People with Rheumatic and Rare Diseases (APMARR), Communication, Bari, Italy*; [13]*Hellenic League Againts Rheumatism (ELEANA), Management, Athens, Greece*; [14]*National Axial Spondyloarthritis Society (NASS), Management Department, London, United Kingdom*; [15]*National Rheumatoid Arthritis Society (NRAS), Management Department, London, United Kingdom*; [16]*Arthritis Action, Management, London, United Kingdom*; [17]*Hospital Universitario La Paz, IdiPaz, Madrid, Spain*

Background: The COVID-19 pandemic has impacted every aspect of life of European patients with rheumatic and musculoskeletal diseases (RMDs).
Objectives: The aim is to evaluate country differences on the impact of the first wave of the COVID-19 pandemic on life habits, healthcare access, health status, mental health and wellbeing in European patients with RMDs.
Methods: REUMAVID is an international collaboration led by the Health & Territory Research group at the University of Seville, together with a multidisciplinary team including patient organisations and rheumatologists. This cross-sectional study consisting of an online survey gathering data from patients with a diagnosis of 15 RMDs in Cyprus, France, Greece, Italy, Portugal, Spain, and the United Kingdom. Participants were recruited by patient organisations (April-July 2020). The Kruskal-Wallis and χ^2 tests were used to analyse differences between countries and independent variables.
Results: 1,800 patients participated in the first wave of the COVID-19 pandemic (REUMAVID). 37.8% of Spanish patients increased their smoking consumption

during the pandemic followed by Cyprus (32.1%) and Portugal (31.0%), while alcohol consumption was higher in the UK (36.3%) and France (27.0%). 82.3% of patients in Spain unable to attend their appointment with their rheumatologist, either due to cancellations or other personal reasons. Access to primary care was most limited in Portugal and Italy, where only 45.0% and 51.6% got access. 61.9% in Italy and 53.3% in Spain experienced a worsening of their health during the pandemic. 68.5% in Spain and 67.8% in Portugal were at risk of anxiety. The highest proportion at risk of depression was found in Greece (55.4%), Cyprus (55.1%), and Italy (54.8%). 66.9% of patients in Spain reported poor wellbeing, compared to 23.8% in Italy and 30.1% in Portugal (Table 1).

Conclusion: The first wave of the pandemic and the related containment measures heterogeneously affected patients with RMDs across European countries, who overall increased harmful habits, experienced more difficulties in accessing healthcare and, reported poor mental health and well-being.

Table 1. Bivariate analysis between European countries (N=1,800, unless specified)

	Mean ± SD or n (%)						
	UK n: 558	**Spain n: 464**	**France n: 229**	**Greece n: 57**	**Cyprus n: 101**	**Italy n: 127**	**Portugal n: 264**
- Inflammatory arthritis[1]	509 (91.2)	402 (86.6)	147 (64.2)	33 (57.9)	57 (56.4)	89 (70.1)	120 (45.5)
- Fibromyalgia	53 (9.5)	14 (3.0)	26 (11.4)	14 (24.6)	28 (27.7)	53 (41.7)	124 (47.0)
- Connective tissue disease[2]	36 (6.5)	15 (3.2)	13 (5.7)	25 (43.9)	33 (32.7)	30 (23.6)	61 (23.1)
- Osteoarthritis	140 (25.1)	29 (6.3)	102 (44.5)	0 (0.0)	8 (7.9)	15 (11.8)	13 (4.9)
- Osteoporosis	50 (9.0)	3 (0.6)	20 (8.7)	2 (3.5)	9 (8.9)	18 (14.2)	12 (4.5)
- Vasculitis[3]	9 (1.6)	1 (0.2)	6 (2.6)	3 (5.3)	3 (3.0)	5 (3.9)	9 (3.4)
- Sapho (only France)			15 (6.6)				
Smoking, More than before. N= 556	16 (10.3)	48 (37.8)	22 (24.7)	8 (23.5)	9 (32.1)	8 (20.5)	26 (31.0)
Alcohol consumption, More than before. N= 1,085	99 (36.3)	48 (10.3)	27 (27.0)	4 (7.0)	4 (4.0)	4 (13.3)	11 (18.3)
Unable to meet rheumatologist. N= 722	83 (48.8)	186 (82.3)	27 (30.3)	18 (64.3)	22 (51.2)	9 (31.0)	77 (56.2)
Access to primary care. N= 689	87 (76.3)	65 (67.7)	32 (76.2)	14 (60.9)	17 (60.7)	65 (51.6)	117 (45.0)
Change in health status, Much worse or worse. N=1,786	214 (38.4)	245 (53.3)	98 (43.0)	24 (42.9)	38 (38.4)	78 (61.9)	135 (51.9)
WHO-5. Poor well-being (≤50). N= 1,777	292 (52.5)	303 (66.9)	100 (43.9)	21 (37.5)	46 (46.5)	30 (23.8)	78 (30.1)
Risk of anxiety. N= 1,769	241 (43.6)	309 (68.5)	118 (52.0)	31 (55.4)	61 (62.2)	78 (61.9)	175 (67.8)
Risk of depression. N= 1,769	186 (33.6)	232 (51.4)	101 (44.5)	31 (55.4)	54 (55.1)	69 (54.8)	138 (53.8)

Note: all relations were significant at the 0.001 level. [1]Including: Axial Spondyloarthritis, Rheumatoid Arthritis, Psoriatic Arthritis, Juvenile Idiopathic Arthritis, Gout and Peripheral Spondyloarthritis; [2]Including: Systemic Lupus Erythematosus, Sjögren's Syndrome, Systemic Sclerosis and Myositis; [3]Including: Polymyalgia Rheumatic and Vasculitis or Arteritis.

Acknowledgements: This study was supported by Novartis Pharma AG. We would like to thank all patients that completed the survey as well as all of the patient organisations that participated in the REUMAVID study including: the Cyprus League Against Rheumatism (CYPLAR) from Cyprus, the Association Française de Lutte Anti-Rhumatismale (AFLAR) from France, the Hellenic League Against Rheumatism (ELEANA) from Greece, the Associazione Nazionale Persone con Malattie Reumatologiche e Rare (APMARR) from Italy, the Portuguese League Against Rheumatic Diseases (LPCDR), from Portugal, the Spanish Federation of Spondyloarthritis Associations (CEADE), the Spanish Patients' Forum (FEP), UNiMiD, Spanish Rheumatology League (LIRE), Andalusian Rheumatology League (LIRA), Catalonia Rheumatology League and Galician Rheumatology League from Spain, and the National Axial Spondyloarthritis Society (NASS), National Rheumatoid Arthritis (NRAS) and Arthritis Action from the United Kingdom.

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Helena Marzo-Ortega Speakers bureau: AbbVie, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Takeda and UCB, Consultant of: AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Grant/research support from: Janssen and Novartis, Laura Christen Employee of: Novartis Pharma AG, Loreto Carmona: None declared, José Correa-Fernández: None declared, Sergio Sanz-Gómez: None declared, Elsa Mateus Grant/research support from: Lilly Portugal, Sanofi, AbbVie, Novartis, Grünenthal S.A., MSD, Celgene, Medac, Janssen-Cilag, Pharmakern, GAfPA., Souzi Makri Grant/research support from: Novartis, GSK and Bayer., Pedro Plazuelo-Ramos: None declared, LAURENT GRANGE: None declared, Serena Mingolla: None declared, KATY ANTONOPOULOU: None declared, Dale Webb Grant/research support from: AbbVie, Biogen, Janssen, Lilly, Novartis and UCB, Clare Jacklin Grant/research support from: Abbvie, Amgen, Biogen, Eli Lilly, Gilead, Janssen, Pfizer, Roche, Sanofi & UCB, Shantel Irwin: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB

DOI: 10.1136/annrheumdis-2021-eular.2372

AB0676

FEARS AND HOPES DURING THE COVID-19 PANDEMIC IN PATIENTS WITH RHEUMATIC DISEASES. RESULTS FROM THE REUMAVID STUDY (PHASE 1)

M. Garrido-Cumbrera[1], H. Marzo-Ortega[2,3], L. Christen[4], L. Carmona[5], J. Correa-Fernández[1], S. Sanz-Gómez[1], P. Plazuelo-Ramos[6], D. Webb[7], C. Jacklin[8], S. Irwin[9], L. Grange[10,11], S. Makri[12], E. Mateus[13,14], S. Mingolla[15], K. Antonopoulou[16], V. Navarro-Compán[17]on behalf of REUMAVID working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Sevilla, Spain*; *[2]University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[3]Leeds Teaching Hospitals Trust, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*; *[4]Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; *[5]Institute for Musculoskeletal Health, InMusc, Madrid, Spain*; *[6]Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; *[7]National Axial Spondyloarthritis Society (NASS), Management, London, United Kingdom*; *[8]National Rheumatoid Arthritis Society (NRAS), Management, London, United Kingdom*; *[9]Arthritis Action, Management, London, United Kingdom*; *[10]French League Against Rheumatism (AFLAR), Management, Grenoble, France*; *[11]Centre Hospitalier Universitaire de Grenoble, Management, Grenoble, France*; *[12]Cyprus League Against Rheumatism (CYPLAR), Management, Nicosia, Cyprus*; *[13]Liga Portuguesa Contra as Doenças Reumáticas (LPCDR), Management, Lisbon, Portugal*; *[14]NOVA Medical School, Comprehensive Health Research Centre (CHRC), Lisbon, Portugal*; *[15]Italian National Association of People with Rheumatic and Rare Diseases (APMARR), Communication, Bari, Italy*; *[16]Hellenic League Againts Rheumatism (ELEANA), Management, Athens, Greece*; *[17]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*

Background: The first wave of the COVID-19 pandemic led to a rapidly evolving global crisis characterized by major uncertainty.

Objectives: The objective is to assess COVID-19-related fears and hopes in patients with rheumatic and musculoskeletal diseases (RMDs) during the first wave of the pandemic.

Methods: REUMAVID is an international collaboration led by the Health & Territory Research group at the University of Seville, together with a multidisciplinary team including patient organisations and rheumatologists. This cross-sectional study consisting of an online survey gathering data from 1,800 patients with a diagnosis of 15 RMDs recruited by patient organisations in Cyprus, France, Greece, Italy, Portugal, Spain and, the United Kingdom. Data are collected in two phases, the first phase between April and July 2020, the second in 2021. Participants rated a series of fears (infection, medication consequences, lack of medication, impact on healthcare, job loss, civil disorder) on a Likert scale from zero ("no concern at all") to five ("extremely concerned") and their hopes (treatment/vaccine availability, going outside, travel, economic situation, treatment continuation, health status) on a Likert scale from zero ("not hopeful at all") to five ("extremely hopeful"). The Mann-Whitney and Kruskal-Wallis tests were used to analyse the different fears and hopes according to socio-demographics characteristics, disease and health status.

Results: 1,800 patients participated in the first phase of REUMAVID. The most frequent RMDs group was inflammatory arthritis (75.4%), the mean age was 52.6 years and 80.1% were female. The most important fear for patients was the impact of the COVID-19 pandemic on healthcare (3.1 out of 5), particularly for those younger in age (3.0 vs 3.2, p=0.004), female gender (3.2 vs 2. 9 of men, p=0.003), experiencing greater pain (3.1 vs 2.8, p=0.007), with higher risk of anxiety (3.3 vs 2.9 of without anxiety, p<0.001) and depression (3.3 vs 2.9 without depression, p<0.001). The possible impact of anti-rheumatic medication and the development of severe disease if they became infected with COVID-19,was mostly feared (2.8 out of 5), by those receiving biological therapy (3.1 vs 2.5 not biological therapy, p<0.001) or those with underlying anxiety (2.9 vs 2.6 without anxiety, p=0.007). The risk of contracting COVID-19 due to their condition (2.8 out of 5), was especially feared by those with vasculitis (3.2 out of 5), who were female (2.9 vs 2.5, p<0.001), using biologics (2. 9 vs 2.7 of no use, p=0.003), in greater pain (2.8 vs 2.4, p<0.001), with a risk of anxiety (3.0 vs 2.6 without anxiety, p=0.004), and risk of depression (3.0 vs 2.6 without depression, p<0.001). The major hopes were to be able to continue with their treatment as usual (3.7 out of 5), particularly for those taking biologics (3.8 vs 3.6 not taking, p=0.026), those with a better well-being (3.8 vs 3.6 with worse well-being, p=0.021), without anxiety (3.8 vs 3.6 at risk, p=0.004) and without depression (3.8 vs 3.6 at risk,

p=0.007). Hoping not to become infected with COVID-19 and to maintain the same health status, were especially those who were older (3.6 vs 3.4 p=0.018) without anxiety (3.4 vs 3.6 at risk, p=0.005), and without depression (3.6 vs 3.4 at risk, p=0.006). Another important hope was the availability of a treatment or vaccine for COVID-19, which was important for patients experiencing better well-being (3.3 vs 3.0 with worse well-being, p<0.001; Figure 1).

Conclusion: The outstanding COVID-19-related fear expressed by European patients with RMDs was its impact on healthcare, while the greatest hope was to be able to continue treatment. Younger patients reported more fears while older patients were more hopeful. Those receiving biologics had greater fears and hopes associated with their treatment. In addition, patients at risk of mental disorders presented greater fears and less hopes.

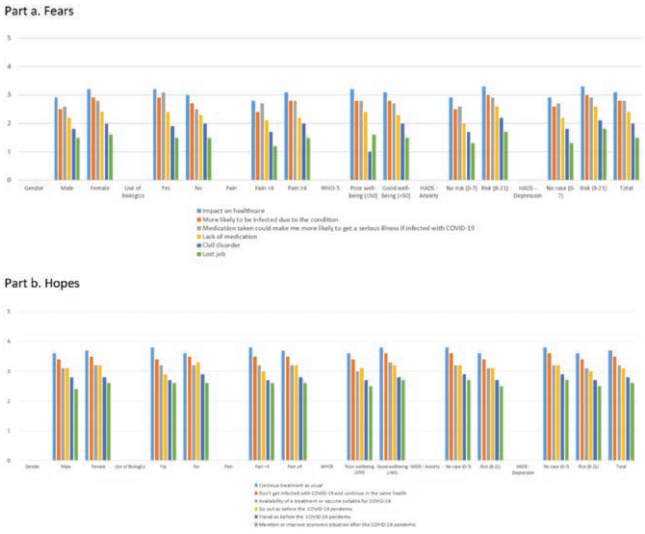


Figure 1. Fears and Hopes of REUMAVID participants

Acknowledgements: This study was supported by Novartis Pharma AG. We would like to thank all patients that completed the survey as well as all of the patient organisations that participated in the REUMAVID study including: the Cyprus League Against Rheumatism (CYPLAR) from Cyprus, the Association Française de Lutte Anti-Rhumatismale (AFLAR) from France, the Hellenic League Against Rheumatism (ELEANA) from Greece, the Associazione Nazionale Persone con Malattie Reumatologiche e Rare (APMARR) from Italy, the Portuguese League Against Rheumatic Diseases (LPCDR), from Portugal, the Spanish Federation of Spondyloarthritis Associations (CEADE), the Spanish Patients' Forum (FEP), UNiMiD, Spanish Rheumatology League (LIRE), Andalusian Rheumatology League (LIRA), Catalonia Rheumatology League and Galician Rheumatology League from Spain, and the National Axial Spondyloarthritis Society (NASS), National Rheumatoid Arthritis (NRAS) and Arthritis Action from the United Kingdom.

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Helena Marzo-Ortega Speakers bureau: AbbVie, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Takeda and UCB, Consultant of: AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Grant/research support from: Janssen and Novartis, Laura Christen Employee of: Novartis Pharma AG, Loreto Carmona: None declared, José Correa-Fernández: None declared, Sergio Sanz-Gómez: None declared, Pedro Plazuelo-Ramos: None declared, Dale Webb Grant/research support from: AbbVie, Biogen, Janssen, Lilly, Novartis and UCB., Clare Jacklin Grant/research support from: Abbvie, Amgen, Biogen, Eli Lilly, Gilead, Janssen, Pfizer, Roche, Sanofi & UCB, Shantel Irwin: None declared, LAURENT GRANGE: None declared, Souzi Makri Grant/research support from: Novartis, GSK and Bayer., Elsa Mateus Grant/research support from: Lilly Portugal, Sanofi, AbbVie, Novartis, Grünenthal S.A., MSD, Celgene, Medac, Janssen-Cilag, Pharmakern, GAfPA., Serena Mingolla: None declared, KATY ANTONOPOULOU: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB

DOI: 10.1136/annrheumdis-2021-eular.2405

AB0677

GENDER DIFFERENCES ON THE IMPACT OF THE COVID-19 PANDEMIC AND LOCKDOWN IN PATIENTS WITH RHEUMATIC DISEASES. RESULTS FROM THE REUMAVID STUDY (PHASE 1)

M. Garrido-Cumbrera[1], H. Marzo-Ortega[2,3], L. Christen[4], L. Carmona[5], J. Correa-Fernández[1], S. Sanz-Gómez[1], P. Plazuelo-Ramos[6], S. Makri[7], E. Mateus[8,9], S. Mingolla[10], K. Antonopoulou[11], L. Grange[12,13], C. Jacklin[14], D. Webb[15], S. Irwin[16], V. Navarro-Compán[17]on behalf of REUMAVID working group. *[1]Universidad de Sevilla, Health & Territory Research (HTR), Seville, Spain*; *[2]University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[3]Leeds Teaching Hospitals Trust, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*; *[4]Novartis Pharma AG, Patient Engagement, Basel, Switzerland*; *[5]Institute for Musculoskeletal Health, InMusc, Madrid, Spain*; *[6]Spanish Federation of Spondyloarthritis Associations (CEADE), Presidency, Madrid, Spain*; *[7]Cyprus League Against Rheumatism (CYPLAR), Management, Nicosia, Cyprus*; *[8]Liga Portuguesa Contra as Doenças Reumáticas (LPCDR), Management, Lisbon, Portugal*; *[9]NOVA Medical School, Comprehensive Health Research Centre (CHRC), Lisbon, Portugal*; *[10]Italian National Association of People with Rheumatic and Rare Diseases (APMARR), Communication, Bari, Italy*; *[11]Hellenic League Againts Rheumatism (ELEANA), Management, Athens, Greece*; *[12]French League Against Rheumatism (AFLAR), Management, Grenoble, France*; *[13]Centre Hospitalier Universitaire de Grenoble, Rheumatology, Grenoble, France*; *[14]National Rheumatoid Arthritis Society (NRAS), Management, London, United Kingdom*; *[15]National Axial Spondyloarthritis Society (NASS), Management, London, United Kingdom*; *[16]Arthritis Action, Management, London, United Kingdom*; *[17]Hospital Universitario La Paz, IdiPaz, Madrid, Spain*

Background: The COVID-19 pandemic has impacted health, lifestyle, treatment and healthcare of European patients with rheumatic and musculoskeletal diseases (RMDs).

Objectives: The aim is to evaluate gender differences on the impact of the first wave of the COVID-19 pandemic in the wellbeing, life habits, treatment, and healthcare access of European patients with RMDs.

Methods: REUMAVID is an international collaboration led by the Health & Territory Research at the University of Seville, together with a multidisciplinary team including patient organisations and rheumatologists. This cross-sectional study consisting of an online survey gathering data from 1,800 patients with a diagnosis of 15 RMDs, recruited by patient organisations in Cyprus, France, Greece, Italy, Portugal, Spain, and the United Kingdom during the first phase of the pandemic (April-July 2020). Mann-Whitney and χ^2 tests were used to analyse differences between gender regarding sociodemographic characteristics, life style, treatment, healthcare, and patient-reported outcomes.

Results: 1,797 patients were included in this analysis. 80.2% were female and a mean age of 52.6 years. The most common diagnosis was inflammatory

Table 1. Bivariate analysis by gender (N= 1,797 unless specify)

		Mean ± SD or n (%)		P- value
		Male (N= 355)	**Female** (N= 1,442)	
Sociodemographic characteristics				
Disease	Inflammatory arthritis[1]	290 (81.7)	1,064 (73.8)	
	Fibromyalgia	25 (7.0)	287 (19.9)	
	Connective tissue disease[2]	18 (5.1)	195 (13.5)	
	Osteoarthritis	52 (14.6)	255 (17.7)	
	Osteoporosis	10 (2.8)	104 (7.2)	
	Vasculitis[3]	7 (2.0)	29 (2.0)	
	SAPHO	1 (0.3)	14 (1.0)	
Age, years		52.8 ± 14.2	52.5 ± 12.9	0.896
Educational level	University	162 (45.6)	711 (49.3)	0.215
Marital status	Married or in relationship	269 (75.8)	983 (68.2)	**0.002***
Member of a Patient organisation, N=1,795	Yes	188 (53.0)	559 (38.8)	**<0.001***
Patient-reported outcomes				
HADS Anxiety, N=1,766	Risk	168 (48.1)	843 (59.5)	**<0.001***
HADS Depression, N=1,766	Risk	130 (37.2)	680 (48.0)	**<0.001***
Wellbeing, N=1,774	WHO-5 ≤ 50	188 (53.4)	681 (47.9)	0.064
Self-perceived health, N=1,783	Fair or bad	182 (51.4)	958 (67.0)	**<0.001***
Change in health status during COVID-19 pandemic, N=1,783	Worse	333 (94.1)	1,339 (93.7)	0.799
Life style during COVID-19 pandemic				
Smoking, N=555	More than before	20 (17.5)	117 (26.5)	**0.001***
Alcohol consumption, N=1,083	Quit drinking	71 (25.4)	277 (34.5)	**0.013**
Physical activity, N=1,126	Yes	144 (60.3)	470 (53.0)	**0.045***
Treatment and healthcare				
Able to meet rheumatologist, N= 721	No	89 (65.9)	332 (56.7)	**0.049***
Access to GP, N=688	No	43 (39.4)	248 (42.8)	0.512

[1]Including: Axial Spondyloarthritis, Rheumatoid Arthritis, Psoriatic Arthritis, Juvenile Idiopathic Arthritis, Gout and Peripheral Spondyloarthritis; [2]Including: Systemic Lupus Erythematosus, Sjögren's Syndrome, Systemic Sclerosis and Myositis; [3]Including: Polymyalgia Rheumatic and Vasculitis or Arteritis.

arthritis (81.7% male vs 73.8% female). There was a higher prevalence of fibromyalgia among females (20% vs 7.0% male). Overall, females reported worse self-perceived health (67.0% vs 51.4%, p<0.001), higher risk of anxiety (59.5% vs 48.1%, p<0.001), and depression (48.0% vs 37.2%, p<0.001). Females reported a greater increase in smoking (26.5% vs 17.5%, p=0.001), although they were less likely to drink alcohol (34.5% vs 25.4%, p=0.013), and also engaged less in physical activity (53.0% vs 60.3%, p=0.045). Overall, females were more likely to keep their scheduled rheumatology appointment (43.3% vs 34.1% of males (p=0.049; Table 1) with a higher proportion of females having their rheumatic treatment changed (17.0% vs 10.7%, p=0.005).

Conclusion: The first wave of the COVID-19 pandemic and the containment measures have worsened self-perceived health status of patients with RMDs, affecting genders differently. Females reported worse psychological health and life habits such as increased smoking and reduced physical activity, while males increased their alcohol consumption and were less likely to attend their rheumatology appointments.

Acknowledgements: This study was supported by Novartis Pharma AG. We would like to thank all patients that completed the survey as well as all of the patient organisations that participated in the REUMAVID study including: the Cyprus League Against Rheumatism (CYPLAR) from Cyprus, the Association Française de Lutte Anti-Rhumatismale (AFLAR) from France, the Hellenic League Against Rheumatism (ELEANA) from Greece, the Associazione Nazionale Persone con Malattie Reumatologiche e Rare (APMARR) from Italy, the Portuguese League Against Rheumatic Diseases (LPCDR), from Portugal, the Spanish Federation of Spondyloarthritis Associations (CEADE), the Spanish Patients' Forum (FEP), UNiMiD, Spanish Rheumatology League (LIRE), Andalusian Rheumatology League (LIRA), Catalonia Rheumatology League and Galician Rheumatology League from Spain, and the National Axial Spondyloarthritis Society (NASS), National Rheumatoid Arthritis (NRAS) and Arthritis Action from the United Kingdom.

Disclosure of Interests: Marco Garrido-Cumbrera: None declared, Helena Marzo-Ortega Speakers bureau: AbbVie, Biogen, Celgene, Janssen, Lilly, Novartis, Pfizer, Takeda and UCB, Consultant of: AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Grant/research support from: Janssen and Novartis, Laura Christen Employee of: Novartis Pharma AG, Loreto Carmona: None declared, José Correa-Fernández: None declared, Sergio Sanz-Gómez: None declared, Pedro Plazuelo-Ramos: None declared, Souzi Makri Grant/research support from: Novartis, GSK and Bayer, Elsa Mateus Grant/research support from: Pfizer, grants from Lilly Portugal, Sanofi, AbbVie, Novartis, Grünenthal S.A., MSD, Celgene, Medac, Janssen-Cilag, Pharmakern, GAfPA., Serena Mingolla: None declared, KATY ANTONOPOULOU: None declared, LAURENT GRANGE: None declared, Clare Jacklin Grant/research support from: Abbvie, Amgen, Biogen, Eli Lilly, Gilead, Janssen, Pfizer, Roche, Sanofi & UCB., Dale Webb Grant/research support from: AbbVie, Biogen, Janssen, Lilly, Novartis and UCB., Shantel Irwin: None declared, Victoria Navarro-Compán Grant/research support from: Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB

DOI: 10.1136/annrheumdis-2021-eular.2417

AB0678 RATES OF SURGICAL PROCEDURES OF THE KNEE AND HIP DURING THE "FIRST WAVE" OF COVID 19 IN SWEDEN

A. Dell'isola[1], A. Kiadaliri[1], A. Turkiewicz[1], V. Hughes[1], K. Magnusson[1,2], J. Runhaar[3], S. M. A. Bierma-Zeinstra[3], M. Englund[1]. [1]*Lund University, Clinical Epidemiology Unit, Orthopedics, Department of Clinical Sciences Lund, Lund, Sweden*; [2]*Norwegian Institute of Public Health, Cluster for Health Services Research, Oslo, Norway*; [3]*Erasmus MC, University Medical Center, Department of General Practice, Rotterdam, Netherlands*

Background: Many countries imposed lockdowns in March 2020, in anticipation of the "first wave" of COVID-19 and the massive healthcare resources required to meet its acute medical needs. Sweden adopted a different strategy to contain the epidemic, opting for non-binding recommendations. Nonetheless, elective and acute surgical procedures in health care may have been affected.

Objectives: To investigate the effect of the "first-wave" of COVID-19 and the government's response in Sweden on the rates of total joint replacements (TJR), arthroscopies, and fracture surgeries of the knee and hip.

Methods: We used register data for the entire population of Skåne, the southernmost region in Sweden with 1.3 million inhabitants (13% of the total Swedish population). We identified all residents aged ≥18 years who between 1st January 2015 and 31st November 2020 underwent any of the following surgical procedures of the knee or hip: TJR (TJR due to fracture excluded), arthroscopy, and surgery due to fracture (including TJR). To demarcate pre-event and post-event periods, we established a differentiation point corresponding to mid-March 2020, the timepoint at which the the Swedish Public Health Agency began recommending social distancing, working from home, distance learning for secondary schools and universities,. At the aggregate level, we modelled the number of surgeries per 10,000 adults from January 2015 up to September 2020. We did an interrupted time-series (ITSA) analysis using segmented ordinary least-squares regression to estimate changes in the levels and trends of surgical procedures compared to pre-COVID-19 levels, adjusting for seasonal variations. The month of March was treated as a "phase-in" period to give time for the new recommendations to be implemented. In addition, we estimated the absolute and relative difference (with its 95% confidence interval [CI]) between the predicted and the counterfactual scenario in the monthly number of surgeries from April 2020, where the counterfactual is the rate of surgery that would have been expected if COVID-19 had not happened. To account for the possibility that other co-occurring events may be responsible for the observed changes, we assessed changes in the number of surgeries due to fractures, which are normally treated as emergencies that cannot be cancelled or rescheduled, and thus should be less affected, at least by policies at the hospital level.

Results: We identified a total of 20,831 TJRs, 12,156 arthroscopies and 15,041 fracture surgeries of the knee or hip over the study period. The monthly rate of surgeries and ITSAs are presented in Figure 1, with the pre-COVID period starting from February 2019 for readability (Figure 1). The results suggest that in April 2020, there was a decrease of 2.08 (95%CI 1.81; 2.35) TJRs per 10,000 adults which corresponds to a decrease of 74% (95%CI 65%; 85%) when compared to the counterfactual scenario. This was followed by a positive trend signifying a monthly increase of 0.36 (95%CI 0.31; 0.40) TJRs per 10,000 adults. The rate of arthroscopies followed a similar pattern with a decrease of 0.55 (95%CI 0.39; 0.71) arthroscopies per 10,000 adults in April, which corresponds to a 49% decrease (95%CI 28%; 63%) followed by a positive trend signifying a monthly increase of 0.11 (95%CI 0.07; 0.15) arthroscopies per 10,000 adults. The rate of surgery due to knee or hip fractures showed no decrease in April and was followed by a negative trend signifying a monthly decrease of 0.03 (95%CI 0.002; 0.04) surgeries per 10,000 adults.

Conclusion: In Sweden, we observed a marked decrease in the number of typical elective knee and hip surgeries such as TJRs and arthroscopies, following the government's response to Covid-19. We then observed a slow but steady recovery that brought the rates of procedures towards expected levels by Fall 2020, before the "second wave" hit the country. The number of acute fracture surgeries showed no sharp drop, instead showing a steady and slow decline potentially due to reduction in commuting and in physical activities linked to recommendations of social

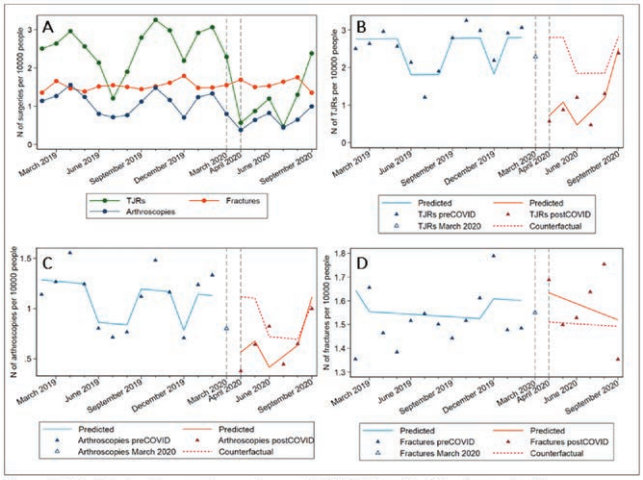


Figure 1: Monthly incidence of surgeries per 10,000 Skåne inhabitants aged > 18
A: Monthly incidence for TJR, arthroscopies and fracture-related surgeries. Interrupted time series for **B:** TJR, **C:** arthroscopies, and **D:** fracture-related surgeries. Pre-COVID data is presented from February 2019 onwards for readability.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2494

AB0679 NAILFOLD VIDEOCAPILLAROSCOPY RESULTS IN COVID-19 PATIENTS RECOVERED FROM DIFFERENT DISEASE SEVERITY

E. Gotelli[1], P. F. Bica[1], T. Aloe'[2], A. Sulli[1], M. Grosso[2], C. Pizzorni[1], F. Cattelan[1], S. Paolino[1], E. Barisione[2], V. Smith[3], M. Cutolo[1]. [1]*Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine and Specialties, University of Genova, IRCCS San Martino Polyclinic, Genova, Italy*; [2]*Interventional Pneumology Unit, IRCCS San Martino Polyclinic, Genoa, Italy*; [3]*Department of Rheumatology – Department of Internal Medicine – Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent University Hospital, Ghent, Belgium*

Background: COVID-19 is a multifaceted condition with a wide range of clinical manifestations, including microvascular/endothelial dysfunction, that starts in the early phase of the disease and may become dramatically harmful in the late stage, causing a massive pro-thrombotic state. Nailfold videocapillaroscopy (NVC) is the most used tool to identify microvascular status in a large spectrum

of diseases [1]. Recently, non-specific NVC abnormalities have been described in a cohort of COVID-19 patients (no controls used) [2].
Objectives: To assess microvascular damage in recovered COVID-19 patients (range of 40-270 days from recovery) by considering the previous severity of the disease, and, as mandatory, the comparison with matched individuals suffering from primary Raynaud's phenomenon (PRP) and healthy volunteers (HV).
Methods: NVC investigations were performed during standard clinical assessments in forty-four recovered COVID-19 patients (mean age 58±14 years, mean days from disease onset 129±54, mean days from disease recovery 106±52), twenty-two patients with PRP (mean age 60±15 years, mean years from disease onset 11±10) and twenty-two HV (mean age 60±14 years). COVID-19 patients were divided into two subgroups, according to the need of oxygen supplementation: twenty-two patients with severe lung involvement (need of Continuous Positive Airways Pressure and/or mechanical ventilation, mean age 57±12 years) vs twenty-two patients with mild-moderate lung involvement (need of Venturi mask or no need of oxygen supplementation, mean age 59±15 years). Clinical and demographic data of all the enrolled subjects were collected, during NVC examination. The following capillaroscopic parameters were evaluated: capillary number, dilated capillaries, giant capillaries, microhemorrhages, angiogenesis, disorganization of the microvascular array. A validated semiquantitative scoring (0-3) was adopted for NVC abnormalities [3-5]. Statistical analysis was carried out by non-parametric tests.
Results: After COVID-19 recovery, no statistically significant difference was observed between COVID-19 patients and control groups of subjects concerning the score for the following NVC parameters: dilated capillaries, giant capillaries, disorganization of the microvascular array, angiogenesis. However, the capillary number per linear millimeter was significantly lower in COVID-19 patients (8.3±0.9) than in PRP (8.8±0.7, p=0.05) and HV (9.3±0.6, p<0.0001). Surprisingly, recovered COVID-19 patients showed significantly less microhemorrhages (score 0.4±0.3) than subjects of the other groups (PRP 0.6±0.5, p=0.01; HV 0.6±0.6, p=0.05). In particular, recovered patients who had more severe COVID-19 showed less microhemorrhages than patients with mild/moderate disease (score 0.18±0.4 vs 0.36±0.5), but this didn't reach the statistical significance (p=0.18). On the other hand, patients recovered from severe SARS-CoV-2 infection also showed higher rate of angiogenesis (0.18±0.4) than patients with mild/moderate disease (no case, p=0.04).
Conclusion: COVID-19 doesn't seem to significantly induce, in short-term, specific alterations in peripheral microvascular array as evaluated by NVC, despite the severity of the disease, except for a significant reduction of the absolute number of nailfold capillaries. The topic needs longer time of evaluation and larger number of COVID-19 recovered cases to also assess the role of concomitant therapies.
REFERENCES:
[1] Ingegnoli F et al. Curr Rheumatol Rev. 2018;14:5-11.
[2] Natalello G et al. Microvasc Res. 2021;133:104071.
[3] Smith V et al. Autoimmun Rev 2020;19:102458.
[4] Cutolo M et al. Clin Rheumatol. 2019;38:2293-2297.
[5] Sulli A et al. Ann Rheum Dis. 2008;67:885-7.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2526

AB0680 SARCOPENIA RATE IN COVID-19 SURVIVORS

D. Levy[1], M. Giannini[1,2], W. Oulehri[3], M. Riou[1], C. Marcot[4], A. Meyer[1,2,5], B. Geny[1,2]. *[1]Hôpitaux Universitaires de Strasbourg, Physiology, Strasbourg, France*; *[2]Université de Strasbourg, Fédération de Médecine Translationnelle de Strasbourg (FMTS), Faculté de Médecine, EA 3072 « Mitochondrie, Stress oxydant et Protection Musculaire », Strasbourg, France*; *[3]Hôpitaux Universitaires de Strasbourg, Service de Réanimation Chirurgicale, Strasbourg, France*; *[4]Hôpitaux Universitaires de Strasbourg, Service de Pneumologie, Strasbourg, France*; *[5]Hôpitaux Universitaires de Strasbourg, Service de Rhumatologie, Strasbourg, France*

Background: COVID-19 survivors may have high risks of developing sarcopenia, which is associated to handicap, poor quality of life, higher healthcare costs, increased risk of falls, increased mortality (1).
Objectives: To assess sarcopenia rate (which has not been described yet) following COVID-19 hospitalization and to highlights features associated with sarcopenic vs. non-sarcopenic patients.
Methods: Major confirmed COVID-19 patients undergoing intensive care unit (ICU) or Pneumology Department admission in Strasbourg University Hospital between March and June 2020 were prospectively included. Muscle and cardio-respiratory evaluations were performed 3 months after discharge. Sarcopenic patients were compared to non-sarcopenic ones. A second muscle assessment 6 months after discharge was performed in patients with pathologic muscle tests.
Results: 127 patients were included, 39 (30.7%) not requiring ICU care, 88 (69.3%) requiring ICU care. The cohort consisted of 71% male patients, with a median age of 63 years [28-82]. Forty-one-percent were obese (BMI>30 kg/m^2). Most individuals had preexisting comorbidities (82 patients, 70%), mainly hypertension and diabetes mellitus. The median total hospital stay duration was 22 days and up to 89 days. At the 3 months assessment, 17/127 (13%) patients were diagnosed with sarcopenia which comprised 6/17 (35%) severe sarcopenia (4.7% of the total cohort). At the 6 months assessment, only 4/15 (27%) of the initial sarcopenic patients remained sarcopenic (3% of the total cohort) and 3 of these 4 patients had severe sarcopenia. BMI (26,3 vs. 29,3, p=0.03), COPD (20% vs. 3%, p=0.03), comorbidities (93% vs. 67%, p=0.04), total hospital stay duration (33 vs. 20 days, p=0.03) and ICU stay duration (33 vs. 13 days, p=0.01) were significantly associated with sarcopenic vs. no sarcopenic patients. However, there was no significant difference concerning cardio-pulmonary evaluations between these two groups.
Conclusion: We here highlighted a sarcopenia prevalence at 3 and 6 months following a hospitalization for COVID-19 of 13% and 3% respectively, occurring mainly in patients with comorbidities. Sarcopenia was not associated to worse cardio-pulmonary results in comparison with non-sarcopenic patients.
REFERENCES:
[1] Di Filippo L, De Lorenzo R, D'Amico M, Sofia V, Roveri L, Mele R, et al. COVID-19 is associated with clinically significant weight loss and risk of malnutrition, independent of hospitalisation: A post-hoc analysis of a prospective cohort study. Clinical Nutrition [Internet]. oct 2020. https://linkinghub.elsevier.com/retrieve/pii/S0261561420305896
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2531

AB0681 HOW COMMON IS COVID-19 IN CHILDREN, YOUNG PEOPLE AND ADULTS WITH RHEUMATIC DISEASES? RESULTS FROM THE INTERNATIONAL COVID-19 EUROPEAN PATIENT REGISTRY

S. Shoop-Worrall[1,2], S. Verstappen[2,3], W. Costello[4,5], S. Angevare[4,6], Y. Uziel[7,8], C. Wouters[9,10], N. Wulffraat[11], R. Beesley[4,12]. *[1]The University of Manchester, Centre for Health Infomatics, Manchester, United Kingdom*; *[2]The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom*; *[3]Manchester University NHS FT, Manchester Academic Health Science Centre, NIHR Manchester BRC, Manchester, United Kingdom*; *[4]ENCA, European Network for Children with Arthritis, Geneva, Switzerland*; *[5]iCAN Ireland, iCAN Ireland, Bansha, Ireland*; *[6]KAISZ, KAISZ, Amsterdam, Netherlands*; *[7]Meir Medical Center, Pediatric Rheumatology Unit, Kefar Sava, Israel*; *[8]Sackler School of Medicine, Department of Pediatrics, TelAviv, Israel*; *[9]University Hospitals Leuven, Pediatric Rheumatology Division, Leuven, Belgium*; *[10]KU Leuven University, Department of Microbiology and Immunology, Leuven, Belgium*; *[11]Wilhelmina Children's Hospital (WKZ), Department of Pediatric Rheumatology, Utrecht, Netherlands*; *[12]Juvenile Arthritis Research, Juvenile Arthritis Research, Tonbridge, United Kingdom*

Background: People with rheumatic diseases may be at increased risk of contracting COVID-19 due to their rheumatic disease or immunosuppressive treatments. It is currently unclear what the COVID-19 disease burden is for these people and whether any of their personal or disease characteristics are associated with contracting COVID-19.
Objectives: To explore the proportion of, and characteristics associated with, contracting COVID-19 in children and young people (CYP) with rheumatic diseases and adults with rheumatic diseases from March 2020 to December 2020 during the COVID-19 pandemic.
Methods: CYP and adults recruited to the international COVID-19 European Patient Registry, a parent-led, online, self-referred prospective cohort recruiting participants from around the globe, were included in current study if enrolled between 20th March 2020 and 30th December 2020. Demographic information was collected at enrolment and rheumatic disease, diagnoses of COVID-19 and lifestyle factors were collected at weekly intervals.
The proportion of CYP and adults diagnosed with COVID-19 were assessed separately. Associations between contraction of COVID-19 at any point over follow-up and participant demographics, rheumatic disease and lifestyle factors at enrolment were assessed descriptively and via Mann-Whitney U-tests, Chi-squared tests and Fisher's exact tests.
Results: Within 642 CYP and 3646 adults, the majority were female (67%, 89%) and most commonly from the UK (43%, 82%), respectively. The most frequent diagnoses were polyarticular JIA (37%) in the CYP cohort and RA in the adults (63%). Comorbidities were common (45%, 61%) and the majority were taking one or more immunosuppressive therapies (88%, 92%), respectively. At the time of enrolment, 51% and 54% were practising social distancing, respectively.
In both cohorts ~3% contracted COVID-19 at some point during follow-up (n=18 (2.8%) in CYP and n=103 (2.8%) in the adult cohort).
In CYP, those who contracted COVID-19 were older (no COVID, median: 10, IQR: 7, 13, vs COVID, median: 14, IQR: 12, 16, p<0.001) and less often had oligoarticular JIA (no COVID: 31%, COVID: 22%) or polyarticular JIA (No COVID: 38%, COVID: 11%). Systemic JIA (no COVID: 7%, COVID: 11%) and enthesitis-related JIA (no COVID: 5%, COVID: 22%) were more common in those who contracted COVID. No other differences between those with and without COVID-19 were observed with respect to country of residence (p=0.335), gender (p=0.624), control of rheumatic disease (p=0.459), comorbidities (p=0.752), immunosuppressive medication (p=0.713) or social distancing (p=0.729).

In the adult cohort, those contracting COVID-19 were more commonly from Russia (no COVID: 2%, COVID: 14%) and less commonly from the UK (no COVID: 82%, COVID: 71%, p<0.001). There was greater female representation in those that contracted COVID-19 (no COVID: 88%, COVID: 93%, p=0.022). Although there were no differences in overall presence of comorbidity (p=0.923), kidney disease was overrepresented in those that had contracted COVID-19 (no COVID: 2%, COVID: 8%, p<0.001). Finally, there were lower levels of social distancing in those who contracted COVID (no COVID: 54%, COVID: 44%, p=0.047). There were no significant differences in age (p=0.203), BMI (p=0.617), smoking status (p=0.120), rheumatic disease (p=0.181) and its control (p=0.218) or immunosuppressive use (p=0.208) between those who did and did not contract COVID-19 in the adult cohort.

Conclusion: A low proportion of CYP and adults with rheumatic diseases contracted COVID-19 in the 9 months since March 2020. However, given the self-reported nature of the survey and limited testing available across many countries, this study may underestimate the true burden of COVID-19 in the rheumatic disease community. Factors associated with COVID-19 differ between CYP and adults, with age and type of rheumatic disease associated in CYP and gender, kidney comorbidity and social distancing associated in adults.

Acknowledgements: The authors thank all of the participants and families involved in the international COVID-19 European Patient Registry, as well as administrators. We also thank the team of volunteers who helped translate the surveys. We also thank ENCA, PRES and representatives from the international rheumatology community for their expertise and support.

Disclosure of Interests: Stephanie Shoop-Worrall: None declared, Suzanne Verstappen: None declared, Wendy Costello: None declared, Saskya Angevare: None declared, Yosef Uziel: None declared, Carine Wouters: None declared, Nico Wulffraat Speakers bureau: Sobi, Grant/research support from: AbbVie, Richard Beesley: None declared

DOI: 10.1136/annrheumdis-2021-eular.2535

AB0682 RHEUMATOLOGY TEACHING IN TIMES OF COVID-19

Y. Chang[1], J. Nicholls[1]on behalf of Medical Education team of George Eliot Hospital NHS Trust. [1]*George Eliot Hospital NHS Trust, Medical Education, Nuneaton, United Kingdom*

Background: The COVID-19 pandemic has affected the delivery of face-to-face teaching especially bedside teaching for medical students in the hospitals. Rheumatology outpatient clinics have mostly become virtual or telephone consultation clinics which prevent medical students from seeing patients in person. Students are deprived of the opportunities to take rheumatology history, examining patients and seeing signs of rheumatologic diseases. New adaptations have to be made to ensure equitability and that students still receive the relevant teaching in line with their learning curriculum and to help them prepare for their examinations.

Objectives: Our aims are:

1)To adapt bedside teaching in the wards to simulated teaching in the classroom using trained simulated 'patients'; and

2)To create simulation teaching of patient journeys in Objective Structured Clinical Examination (OSCE) format known as Clinically Observed Medical Education Tutorials (COMET) (Nair et al., 2001).

Methods: 1)For simulated teaching in the classroom, we have trained our teaching colleagues as simulated or standardized patients (SPs). We write up fictitious patient histories which simulate common presentations at rheumatology clinics. We train the SPs to give as accurate a history as possible and to simulate pains in different joints (e.g. pain at the metacarpophalangeal joints and proximal interphalangeal joints in rheumatoid arthritis) on clinical examinations. For clinical presentations that are not easily simulated, we use photographs of the relevant signs. This method is used not only as formative assessments but also as end-of-placement summative assessments.

2)COMET comprises 3 OSCE-style stations with a tutor each where the students perform different tasks based on a patient's clinical problem (e.g. acute hot swollen joint). The first station is initial A-to-E assessment of the patient (using a simulator), followed by investigations and interpretations of lab results and imaging (station 2) and lastly, management (including prescribing medications) and communication skills (e.g. explain arthrocentesis to the patient).

Results: The overall feedback from students is very positive. We use Likert scale to assess confidence level before and after the teaching session, and pre-session and post-session multiple choice questions to assess learning and knowledge gained.

Conclusion: While simulated teaching cannot replace encounters with real patients, students do enjoy these sessions as they get to 'experience' a large variety of rheumatologic cases and practice their clinical skills which at times are limited with real patients due to reluctance and pain of the patients.

REFERENCES:

[1] Nair, R., Morrissey, J., Carasco, D., Desilva, S. & Patel, V. (2001) COMET: Clinically Observed Medical Education Tutorial - a novel educational method in clinical skills. *International Journal of Clinical Skills*

[2] Van der Vleuten, C.P.M. & Swanson, D.B. (1990) Assessment of clinical skills with standardized patients: state of the art. *Teach Learn Med,* 2: 58-76.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2635

AB0683 OSTEOARTHRITIS PAIN AND COVID-19 PANDEMIC: THE LOCKDOWN IMPACT

F. Orsini[1], O. De Lucia[1], F. Ingegnoli[1], G. Cincinelli[1], G. Armentaro[1], R. DI Taranto[1], R. Caporali[1]. [1]*Istituto Ortopedico Gaetano Pini, Rheumatology, Milano, Italy*

Background: Both peripheral and central nervous system processes are involved in osteoarthritis (OA) pain. Several aspects such as environmental, psychological and constitutional factors contribute to OA pain and they were enhanced during and after lockdown, for COVID-19 pandemic.

Objectives: The purpose of this study is to assess the impact of the modified lifestyle forced by lockdown on joint pain using Visual Analogic Scale (VAS) scale. the variation of VAS pain, the reduction of physical activity, the variation of body weight, the stress values defined by Perceived Stress Scale (PSS) and the use of anxiolytics and antidepressant drugs were measured in OA patiens during the lockdown period.

Methods: 74 adult patients affected by primary or secondary OA were included. The median age was 69.8 years old and 55/74 (74%) of the patients were female. Sex, age, comorbidities, pharmacological therapy, variation rate of VAS pain referred to OA symptoms (0-100) during lockdown, weight variation, degree of physical activity (defined as: absent 0 h, low 1-5 h, moderate 6-10 h, high > 10 h) were recorded. Perceived stress using PSS was recorded and patients were divided into two classes: low (0-13) or moderate-high (14-40) stress scale. This observational retrospective real-life study was conducted in May 2020. A linear regression model was used to analyze the different patients groups separately. Overall variables were expressed on analogic scales. To assess the impact on VAS pain, regression models were estimated with VAS pain as dependent variable, and weight increase, physical activity and perceived stress as independent variable.

Results: Patients enrolled with a pre lockdown VAS pain < 40 were 30, whereas 44 patients referred a pre lockdown VAS pain > 40. Patients taking anxiolytics, antidepressant, anxiolytics or antidepressant drugs were 14/74 (19%), 7/74 (9%), 19/74 (26%) respectively. PSS score Low (score 0-13), Med (score 14-26), High (score 27-40) was recorded in 34/74 (46%), 36/74 (49%), 4/74 (5%) patients respectively. Patients were divided in two different groups on the basis of baseline pre lockdown VAS pain: low VAS pain (< 40) (n=30) and moderate-high (≥ 40) (n=44). In the low-VAS group there was an average increase of pain by 1,36 points, an average increase of weight by 0.63 kg, and an average decrease of weekly physical activity by 6.4 hours that was statistically relevant (p< 0.0001). In moderate-high VAS group an average increase of pain and weight, by 2.62 points and 0.35 kg respectively, and a significant decrease of physical activity by 3.15 h weekly (p< 0.0001) has been recorded

	MODERATE PAIN (VAS<40) (n=30)		HIGH PAIN (VAS≥40) (n=44)	
	Before LD	During LD	Before LD	During LD
Gender, Female: n (%)	17 (56.7%)		38 (86.4%)	
Age (years) : median (Q1, Q3)	63 (57,73)		73 (66, 79)	
Weight (Kg) : median (Q1, Q3)	66.5 (57.0,76.5)	67.5 (58.0, 77.7)	64.0 (57.7, 74.2)	67.0 (57.7, 75.0)
Physical activity (h/week) : n (%)				
0	0 (0.0%)	11 (36.7%)	10 (22.7%)	26 (59.0%)
1-5	4 (13.3%)	10 (33.3%)	10 (22.7%)	12 (27.3%)
6-10	14 (46.7%)	6 (20.0%)	18 (41.0%)	5 (11.4%)
>10	12 (40.0%)	3 (10.0%)	6 (13.6%)	1 (2.3%)
Perceived Stress:n (%)				
LOW		13 (43.3%)		21 (47.7%)
MED		15 (50.0%)		21 (47.7%)
HIGH		2 (6.7%)		2 (4.5%)
VAS PAIN (score) : mean (sd)	18.7 (10.4)	28.7 (22.1)	54.1 (10.0)	56.2 (16.3)

In low VAS group, 43% of the patients perceived low stress values vs 57% moderate-high. In VAS > 40 group 47% of the patients perceived low stress value vs 53% high-moderate. 80% of low- VAS <group did not take anxiolytics and antidepressant drugs and for this cluster of patients was not recorded a VAS increase regardless of PSS. 16.7% of patients (5/30) with VAS < 40, taking anxiolytics / antidepressant medications and with a moderate-high PSS displayed an average increase of VAS pain by 20 mm. In the VAS > 40 group a VAS variation was not recorded, regardless of taking anxiolytics / antidepressant medications and PSS.
Conclusion: Lockdown impact on OA pain has been higher in the cluster of patients who were taking anxiolytics / antidepressant drugs with a moderate-high PSS. VAS pain increase in this cluster of patients exceeds minimal clinically relevant difference reported in literature [1]. A relevant physical activity decrease which might negatively impact on OA course has also been recorded.

REFERENCES:

[1] Hawker G. et al. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res (Hoboken), 2011.*

Disclosure of Interests: Francesco Orsini: None declared, Orazio De Lucia: None declared, Francesca Ingegnoli: None declared, Gilberto Cincinelli: None declared, GIUSEPPE ARMENTARO: None declared, Raffaele Di Taranto: None declared, Roberto Caporali Speakers bureau: Abbvie, Amgen, BMS, Celltrion, Galapagos, Gilead, Lilly, Pfizer, Roche, UCB, Sanofi, Fresenius Kabi, Samsung bioepis, MSD, Consultant of: Galapagos, Gilead, Lilly, Janssen, MSD
DOI: 10.1136/annrheumdis-2021-eular.2688

AB0684 LESS THAN 20% OF PATIENTS WITH A CHRONIC INFLAMMATORY RHEUMATIC DISEASE CHANGED THEIR IMMUNOSUPPRESSIVE MEDICATION BECAUSE OF THE COVID 19 PANDEMIC

I. Andreica[1], R. Jast[1], G. Rezniczek[2], U. Kiltz[1], D. Kiefer[1], B. Buehring[1], X. Baraliakos[1], J. Braun[1]. [1]*Rheumazentrum Ruhrgebiet, Ruhr-Universität Bochum, Rheumatology, Herne, Germany*; [2]*Marien Hospital Herne, Hospital of the Ruhr-University Bochum, Department of Obstretics and Gynecology, Research Lab, Herne, Germany*

Background: The best treatment options of patients with chronic inflammatory rheumatic diseases (CIRD) in the pandemic have not been completely clear, especially in the beginning of the lockdown. Whether and to which degree pandemic-related therapy changes have occurred, has not been studied in detail.
Objectives: To study the behaviour of patients with CIRD initially facing the COVID 19 pandemic related to their disease status and medication.
Methods: Patients with CIRD were contacted by telephone to assess their health status and ask for changes in medication. Standardized assessment tools were used to assess disease activity, depression and anxiety. High disease activity was assumed if RADAI-5 ≥ 3.2 and BASDAI ≥ 4. Anxiety (HADS-A) and depression (HADS-D) of patients were assessed using HADS. A score < 8 was taken as indication of no major problem in this regard.
Results: A total of 886 patients was interviewed between April 15 and June 15 of 2020. Here we report on 550 patients with complete information on standard assessments (62%). About 60% were female, mean age 54.4±13.7, mean disease duration 12.2±10.5 years. Most had spondyloarthritis (SpA, n=287) including axial SpA (axSpA, n=172) and psoriatic arthritis (PsA, n=116), in total 52.2%, while 40.2% had rheumatoid arthritis (RA, n=221), and 7.6% connective tissue diseases (CTD, n=42). Most RA patients were on methotrexate (48.8%), while 43.8% took glucocorticoids. In addition, 61.0% of patients were on bDMARDs, mostly on TNF inhibitors (59.6%). More SpA than RA patients were on bDMARDs: 71.0% vs 49.7% respectively. A recent change in medication was reported by 182 patients (33.1%): 89 with RA (40.2%), 88 with SpA (30.6%) and 5 with CTD (11.9%). Half of those who changed (n=92; 50.5%) admitted that the change was mainly made due to fear of the pandemic (16.7% of all patients). Altogether, significantly more patients changed bDMARDs (68.5%) than csDMARDs (57.3%). The data of patients who changed vs patients who didn't change is shown in the Table 1, including subgroup analyses. The median HADS scores were < 8.
Conclusion: Two thirds of patients did not change medication but one third changed. A relatively high number of patients did so due to fear of the pandemic, mostly those on biologics. There were no major differences between RA and SpA. Anxiety and depression do not seem to play an important role for the decision to change medication (Table 1 below).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2693

AB0685 IMPACT OF COVID-19 ON PATIENTS WITH RHEUMATIC DISEASES: EXPERIENCE OF THE DEPARTMENT OF RHEUMATOLOGY OF THE UNIVERSITY HOSPITAL OF IBN ROCHD OF CASABLANCA

H. El Moutaouakil[1], Z. El Ouali[1], K. Nassar[1], S. Janani[1]. [1]*University Hospital of Ibn Rochd, Department of Rheumatology, Casablanca, Morocco*

Background: The COVID-19 outbreak has been a source of major concern for the management of rheumatic patients, particularly those under immunosuppressants. It is generally admitted that patients followed for autoimmune diseases have an increased risk of infectious complications compared to the general population (1). However, to date, there is no established relationship between autoimmune diseases and an increased risk of infection with SARS-CoV-2 (2).
Objectives: The primary objective was to assess the severity of COVID-19 in patients followed in our department. The secondary objective was to assess the subgroup of patients on immunosuppressants.
Methods: We conducted a descriptive retrospective study of patients followed in the Department of Rheumatology of the University Hospital of Ibn Rochd, Casablanca. The patients who presented with COVID-19 between 08/2020 and 12/2020 were included. Epidemiological, clinical, therapeutic, and evolutionary data were collected and analyzed.
Results: Our series included 30 patients, with a sex ratio M/F of 0.3. The mean age of the patients was 46.4 years (±16.3), with a mean follow-up time of 8.1 years. 7 patients had a metabolic syndrome. Patients were followed for rheumatoid arthritis (n = 4), spondyloarthritis (n = 10), systemic lupus erythematosus (n = 5), scleroderma (n = 2), polymyalgia rheumatica (n = 1), adult onset Still's

Table 1. RA and SpA patients who changed and who did not change their medication

Group (N) / Reason	N	Active disease (%)	HADS-D ≥ 8 (%)	HADS-A ≥ 8 (%)	bDMARD therapy (%)
Rheumatoid arthritis	221	134 (60.6)	76 (35.0) [4]	94 (43.3) [4]	110 (50.9) [5]
Spondyloarthritis	287	130 (45.4)	83 (29.5) [6]	109 (38.8) [6]	204 (72.6) [6]
P [a] (RA vs SpA)		**<0.001**	0.228	0.354	**<0.001**
Patients did not change their medication					
Rheumatoid arthritis (%)	132 (59.7)	84 (63.6)	46 (35.9) [4]	58 (45.3) [4]	62 (48.4) [4]
Spondyloarthritis (%)	199 (69.3)	88 (44.2)	58 (30.1) [6]	69 (35.8) [6]	137 (71.0) [6]
P (RA vs SpA)	**0.031**	**<0.001**	0.358	0.101	**<0.001**
Patients changed their medication					
Rheumatoid arthritis	89 (40.3)	50 (56.2)	30 (33.7)	36 (40.4)	48 (54.5) [1]
P (vs no change)		0.331	0.846	0.567	0.457
Reason	[9]				
Pandemic	41 (51.3)	15 (36.6)	11 (26.8)	14 (34.1)	24 (60.0) [1]
Inactive disease	23 (28.8)	12 (52.2)	6 (26.1)	10 (43.5)	12 (52.2)
Active disease [b]	16 (20.0)	14 (87.5)	6 (37.5)	7 (43.8)	7 (43.8)
P (reasons)		**0.003**	0.687	0.687	0.526
Spondyloarthritis	88 (30.7)	42 (47.7)	25 (28.4)	40 (45.5)	67 (76.1)
P (vs no change)		0.673	0.889	0.157	0.451
Reason	[6]				
Pandemic	50 (61.0)	22 (44.0)	13 (26.0)	22 (44.0)	42 (84.0)
Inactive disease	15 (18.3)	7 (46.7)	4 (26.7)	7 (46.7)	10 (66.7)
Active disease [b]	17 (20.7)	11 (64.7)	6 (35.3)	6 (35.3)	11 (64.7)
P (reasons)		0.331	0.756	0.774	0.156
P (RA vs SpA)	0.031	0.294	0.950	0.603	0.004

Data are presented as numbers (percentage proportions; across rows except for column N) or medians (interquartile ranges). Missing values are in square brackets.[a] P values calculated using χ^2 test or Mann-Whitney rank sum test.[b] Self-reported claim of disease activity.

disease (n = 1), polyosteoarthritis (n = 6), benign osteopathy (n = 1). 17 patients were in low disease activity when they presented the COVID-19. 8 patients presented moderate to high activity, of which 2 (25%) developed a form requiring hospitalization. 7 patients were under NSAIDs, 13 under corticosteroids, 19 under csDMARD, 7 under bDMARD. The COVID-19 disease was symptomatic in 83% of cases, with fatigue (68%), cough (52%), back pain (48%), anosmia (48%), ageusia (44%), arthritis (44%), fever (36%). The diagnosis was made with polymerase chain reaction (83%), serology (10%), CT scan (23%). The CT lung lesions reached 25-50% in 2 lupus patients with a moderate disease activity, under corticosteroids and hydroxychloroquine. The involvement was > 75% in 2 patients, who admitted to intensive care: one was followed for polyarthrosis and was hypertensive and poorly balanced diabetic, and the other was followed for Horton's disease. The treatment was administered on an outpatient basis in 77.4% of cases, in an intensive care unit in 16% of cases. 30 patients fully recovered from infection, one patient died secondary to pulmonary embolism. The subgroup of patients on immunosuppressants consisted of 23 patients (76%), of whom 5 (22%) developed a moderate to severe form of COVID-19 requiring hospitalization. Among these hospitalized patients, 2 (40%) had moderate to high disease activity of their rheumatism.

Conclusion: Most of the patients in our series presented a mild form of COVID-19, including those under immunosuppressants. Patients who were under hydroxychloroquine were not spared from COVID-19, but developed a mild form. The disease activity of the chronic rheumatism did not appear to influence the severity of the COVID-19.

REFERENCES:

[1] Grange L, Guilpain P, Truchetet M-E, Cracowski J-L. Challenges of autoimmune rheumatic disease treatment during the COVID-19 pandemic: A review. Therapies. 2020;75(4):335-42.

[2] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. Jama. 2020;323(13):1239-42.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2744

AB0686 IMPACT OF COVID19 IN SPONDYLOARTHRITIS (SPA) PATIENTS IN A TERTIARY HOSPITAL

C. L. Garcia Gomez[1], D. Montero[1], L. Vega[1], O. Ibarguengoitia[2], I. Calvo[2], C. E. Perez[1], J. M. Blanco[1], E. Galindez[1], A. R. Inchaurbe[1], M. E. Ruiz[1], I. Torre[1], E. Cuande[1], I. Gorostiza[3], M. R. Exposito-Molinero[1], M. L. García Vivar[1].
[1]Universitary Hospital of Basurto, Rheumatology, Bilbao, Spain; *[2]Hospital of Galdakao, Rheumatology, Galdakao, Spain*; *[3]Universitary Hospital of Basurto, Investigation, Bilbao, Spain*

Background: This tertiary hospital is the referall centre of 360.000 inhabitants, population with a Covid seroprevalence of 8,4% at final 2020.

Since march, we have had a special concern for rheumatologic patients with systemic diseases and under inmunosupressive agents, including disease modifying antirheumatic drugs (DMARDs) and biological therapy (BT). This is why a special protocol for this population was set. It included performance of serology (CLIA test) for patients under BT and PCR and CLIA testing prior to new treatments. PCR testing was also generally performed: if symptomatology consistent with Covid; before hospitalisation; to tight contacts of infected people; and before procedures.

Objectives: To evaluate the impact of COVID-19 in our SpA patients in terms of severity of viral infection and its effect on SpA.

Methods: Data of 665 SpA patients and confirmed Covid infection seen in our center from March 15th to December 15th was crossed. 3 miscoded patients with rheumatoid arthritis and 2 with non definite CLIA positivity were excluded. Finally 49 patients' clinical records were reviewed. Data regarding epidemiologic features, SpA characteristics, comorbidities, therapy received, clinical activity before and after Covid, and severity of the infection was collected. IBM SPSS v23 was used for statistical analysis.

Results: Among 49 SpA patients, 59% were male, mean aged 56,63 years (range 23-79). 62,2% presented at least 1 comorbidity. 65% were psoriatic arthritis. They mostly had longstanding disease (median 10,5 years -range- 1-35). Previously 63% had received DMARDs, mainly methotrexate, and 32 % BT.

When Covid was diagnosed 37,2% were under DMARDs and 53% under BT (69,2% TNF inhibitors, 26,9% anti-Il 17, 3,9% ustekinumab). At this point, disease activity was controlled in 82% of patients (39% in remission, and 43% in low disease activity state). Only 18% showed moderate activity.

Within the 49 patients, 34 were diagnosed by PCR and 15 by CLIA tests. 9 required hospitalisation, of whom 4 developed more severe disease (3 received glucocorticoid pulses and 2 tocilizumab). A woman with PsA under secukinumab presented pneumonia and PE. None required mechanical ventilation. There were no exitus.

Due to Covid infection 9 patients (50%) stopped DMARDs treatment, (5 of them hospitalised). 9 patients withdrew BT after Covid diagnosis; 60% of the BT-hospitalised, and 28.5% of the BT- non-hospitalised. 1 suffered a flow with severe disease activity after withdrawal of Il-17 inhibitor.

Conclusion: Prevalence of SARS cov 2 infection in SpA patients was not greater than in general population. Most were asymptomatic or suffered mild disease. Only 9 were hospitalised. Factors related to hospitalisation seem similar to those of general population, even if statistical significance was not found due to the small sample. BT does not seem to relate to hospitalisation in SpA and we had no deaths to date in them.

More studies should be made to throw out conclusions.

Baseline characteristics of SpA patients with confirmed Covid19	Hospitalised (N 9)	Non-hospitalised (N 40)	Total (N 49)
Mean age (range) – yr	62,56 (43-74)	55,3 (23-79)	56,63 (23-79)
Male sex - no. (%)	6 (66,6)	23 (57,5)	29 (59,1)
Smoking habit (active, ex-smokers) - no. (%)	2 (22,2)	23 (57,5)	25 (51)
Non comorbidities - no. (%)	2 (22,2)	17 (42,5)	19 (38,8)
Hypertension - no. (%)	3 (33)	14 (35)	17 (35)
Diabetes - no. (%)	1 (11)	6 (15)	7 (14,2)
Dyslipidemia - no. (%)	4 (44)	9 (22,5)	13 (26,5)
Obesity (BMI >30) - no. (%)	4 (44)	12 (30)	16 (32,7)
Chronic obstructive pulmonary disease - no. (%)	2 (22,2)	4 (10)	6 (12,2)
Asthma - no. (%)	0 (0)	4 (10)	4 (8,2)
Cardiopathy - no. (%)	1 (11,1)	8 (20)	9 (18,4)
Median disease time since diagnosis (range) – yr	14, 5 (7-20)	10 (1-35)	10,5 (1-35)
SpA type			
Psoriatic arthritis - no. (%)	8 (88,8)	24 (60)	32 (65,3)
Ankylosing spondylitis - no. (%)	1 (11,1)	15 (37,5)	16 (32,7)
Non-Rx ankylosing spondylitis - no. (%)	0 (0)	1 (2,5)	1 (2)
Current treatment when diagnosed (N 48)			
DMARDs - no. (%)	6 (66,6)	12 (30)	18 (37,5)
BT - no. (%)	5 (55,5)*	21 (52,5) **	26 (54,1)

* 5 anti-TNF (1 etanercept), 2 anti Il-17, 1 anti Il-12-23.
** 12 anti-TNF (4 etanercept), 5 anti Il-17.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2960

AB0687 EFFECT OF COVID-19 ON PATIENTS ATTENDING AMBULATORY DEEP VENOUS THROMBOSIS OUT-PATIENT CLINIC: A RETROSPECTIVE, COHORT ANALYSIS[KI1] [KI1]101 CHARACTERS

T. Hill[1], K. P. Iyengar[1], A. Nune[2]. *[1]Southport & Ormskirk Hospital NHS Trust, Trauma and Orthopaedics, Southport, United Kingdom*; *[2]Southport & Ormskirk Hospital NHS Trust, Rheumatology, Southport, United Kingdom*

Background: COVID-19 has been acknowledged as an procoagulant disorder with increased risk of venous thromboembolism (VTE) [1]. High rates of VTE in patients admitted to intensive care unit have been reported [2]. However effect of COVID-19 on ambulatory patients attending out-patient clinics has not been described.

Objectives: This retrospective, observational cohort study analyses the impact of COVID-19 on incidence of Deep Venous Thrombosis (DVT) in patients referred to Ambulatory Deep Venous Thrombosis Out-patient Clinic (ADOC). A comparative analysis of patients attending ADOC during a similar period in 2019 is undertaken.

Methods: Patients who attended the ADOC with suspected DVT during the 'first wave' of the COVID-19 pandemic between 01 February and 30 June 2020 at Southport and Ormskirk NHS Trust were studied and compared to a similar period in 2019. Patients characteristics, comorbidities, risk factors, incidence of DVT and relationship with COVID-19 with the evaluation of haematological parameters including D-dimer and two- tier Wells score. Additionally we examined patients outcomes including morbidity, mortality and hospital admissions.

Results: Overall, there was a decrease in the number of patients attending the ADOC from 290 in 2019 to 233 in 2020. However, a total of 38 patients tested positive for DVT, a rate of 16.3%, which is compared to an incidence of 7.9% in 2019. Due to evolving protocols, the COVID-19 status of all patients attending the ADOC could not be ascertained. However, 5/233 of the 2020 cohort patients either had a positive test result (n=4) or were symptomatic of COVID-19 (n=1).

Conclusion: There has been a 129% increase in the incidence of DVT in patients presenting to ADOC at our trust during the 'first wave' of the COVID-19

pandemic. Furthermore, despite fewer patients presenting with DVT symptoms to the ADOC, there appears to be a higher incidence of confirmed DVTs in ambulatory patients during COVID-19.

Although there is a strong association inferred between COVID-19 and VTE [3], lack of access to SARS-CoV-2 nasal swab testing of patients attending ADOC for VTE assessment was a limiting factor to establish an association in this study. Because of this, we cannot extrapolate a definite association in patients with mild to moderate COVID-19 illness in the community and DVT.

What we postulate is perhaps the higher incidence in the 2020 cohort could be a marker for a mild case of asymptomatic COVID-19 in these patients. Currently there is no guidance as to whether point of care testing should be available in ADOC. We wonder whether a point of care COVID-19 testing of these patients would have positive impact on the rate at which COVID-19 is identified in the community. Furthermore patients have been avoiding hospitals during the pandemic, greater testing should help to reassure and encourage them to seek help earlier during their illness, minimising potential complications such as PE, hospital admission and death.

REFERENCES:

[1] Malas MB, Naazie IN, Elsayed N et al. Thromboembolism risk of COVID-19 is high and associated with a higher risk of mortality: A systematic review and meta-analysis. ***EClinicalMedicine.*** 2020 Dec;29:100639. doi: 10.1016/j.eclinm.2020.100639.]#

[2] Helms J, Tacquard C, Severac F et al. CRICS TRIGGERSEP Group (Clinical Research in Intensive Care and Sepsis Trial Group for Global Evaluation and Research in Sepsis). High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. ***Intensive Care Med.*** 2020 Jun;46(6):1089-1098. doi: 10.1007/s00134-020-06062-x.

[3] Di Minno A, Ambrosino P, Calcaterra I, Di Minno MND. COVID-19 and Venous Thromboembolism: A Meta-analysis of Literature Studies. ***Semin Thromb Hemost.*** 2020 Sep 3. doi: 10.1055/s-0040-1715456.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2987

AB0688 SEVERITY OF COVID-19 INFECTION IN RHEUMATIC IMMUNE-MEDIATEDINFLAMMATORY DISEASES. STUDY IN A SINGLE UNIVERSITY HOSPITAL

D. Martínez-López[1], D. Prieto-Peña[1], L. Sanchez-Bilbao[1], A. Herrero-Morant[1], C. Álvarez-Reguera[1], M. Trigueros-Vazquez[1], M. A. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*

Background: Immune-mediated inflammatory diseases (IMID) may have a global increased risk of infections due to the disease itself, and/or immunosuppressive therapy. The severity and characteristics of COVID-19 in patients with rheumatic IMID (R-IMID) remain unknown.

Objectives: To analyze the severity of COVID-19 infection in R-IMID.

Methods: Cross-sectional study in a single University Hospital. We included all consecutive patients with a diagnosis of a R-IMID and a positive test for COVID-19 up to November 6th, 2020. Confirmed infection was defined if the patient had a positive nasopharyngeal swab for SARS-CoV-2.

Medical records of 11,199 patients with COVID-19 in our region, and 6891 with R-IMID from our hospital were reviewed.

COVID-19 case severity was divided into mild, moderate, severe and critical according to the United States National Institute of Health (NIH) COVID-19 guidelines **(1)**. Mild/moderate COVID19 was compared with critical.

Results: We included 147 patients (96 women/51 men), mean age 60±18 years. Most cases were mild to moderate (n=123, 83.7%), 30 of them (20.4%) were asymptomatic. The remaining patients presented severe (n=5, 3.4%) or critical (n=19, 12.9%) disease (Table 1). Fatal outcome occurred in 12 patients (8.2%).

More frequent underlying R-IMID were Rheumatoid Arthritis (n=36; 24.5%), Psoriatic Arthritis (n=30; 20.4%), axial spondyloarthritis (n=24; 16.3%), conectivopathies (n=19; 12.9%), polymyalgia rheumatica (n=16; 10.9%) and vasculitis (n=9; 6.1%) (Figure 1).

Main comorbidities were hypertension (n=65, 44.2%), dyslipidemia (n=64, 43.5%), age higher than 65 years old (n=55, 37.4%), obesity (n=35, 23.8%), coronary vascular disease (CVD) (n=27, 18.4%) and diabetes mellitus (n=22, 15%).

Comorbidities and R-IMID associated with critical disease (p<0.05) were hypertension, age higher than 65 years,CVD and Polymyalgia Rheumatica. Critical compared with mild/moderate disease showed significantly higher levels of creatinine and D-dimer, and lower level of lymphocytes and platelets (Table 1) and received more frequently systemic glucocorticoids. Tocilizumab and Anakinra were used only in critical patients, 2 cases each.

Conclusion: Although most cases are mild, COVID-19 can be a severe life threatening disease in patients with R-IMID. Hypertension, older age, CVD and polymyalgia rheumatica were associated with critical disease.

REFERENCES:

[1] COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/.

Table 1. Clinical severity of 147 with R-IMID diagnosed with COVID-19, (analytical findings and Immunosuppressants are at COVID diagnosis)

	Overall N= 147	Mild/Moderate N= 123	Severe N= 5	Critical N= 19	Mild/moderate vs critical; p
Analytical findings (mean±SD)					
Creatinine (mg/dl)	1.04±1.14	1.27±0.65	1.18±0.47	1.35±0.61	**0.001***
Platelets (x10^3 /µL)	206 ±93	226 ± 95	154 ±87	159 ±62	**0.01***
Lymphocytes (x10^3 /µL)	1.11±0.65	1.27±0.65	0.8±0.29	0.71±0.5	**0.001***
D-Dimer (ng/mL)	1162±1356	915±986	782±483	1947±2024	**0.026***
Immunosuppressants, n(%)					
Oral GC	38 (25.9)	32 (26)	0	5 (26.3)	0.8
HCQ	25 (17)	23 (18.7)	0	2 (10.5)	0.58
MTX/ Other cDMARDs	27 (18.4)/19 (13)	26 (21.1)/18 (14.6)	0/ 0)	1 (5.3/1 (5.3)	0.18/0.45
TNF inhibitors	13 (8.8)	12 (9.8)	1 (20)	0	0.33
RTX	5 (3.4)	2 (1.6)	1 (20)	2 (10.5)	0.15
Other bDMARDs	13 (8.8)	10 (8.1)	1 (20)	2 (10.5)	0.28
JAKINIB	3 (2)	3 (2.4)	0	0	0.87
COVID-19 therapy, n (%)					
No treatment	94 (64)	88 (71.5)	1 (20)	5 (26.3)	**0.0003***
HCQ	37 (25.2)	25 (20.3)	4 (80)	8 (42.1)	0.07
Systemic GC	17 (11.6)	8 (6.5)	1 (20)	8 (42.1)	**0.00001***
Antivirals	20 (13.6)	13 (10.6)	0	7 (36.8)	0.07
Anti IL1/IL6 agents	4 (2.7)	0	0	4 (21.1)	**0.00001***

GC: Glucocorticoids, HCQ: Hydroxychloroquine, MTX: Methotrexate, RTX: Rituximab
* P < 0.05

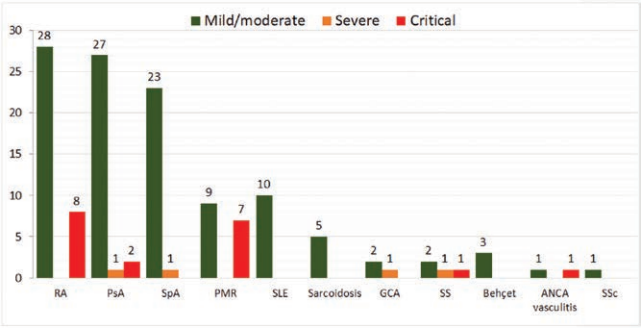


Figure 1. Severity of COVID-19 according to underlying R-IMID. Data are number of cases

GCA: Giant cell arteritis, PsA: Psoriatic arthritis, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, SpA: Axial spondyloarthritis, SSc: Systemic scleroderma.

Disclosure of Interests: David Martínez-López: None declared, Diana Prieto-Peña Grant/research support from: UCB Pharma, Roche, Sanofi, Pfizer, Abbvie and Lilly, Lara Sanchez-Bilbao: None declared, Alba Herrero-Morant: None declared, Carmen Álvarez-Reguera: None declared, Martin Trigueros-Vazquez: None declared, Miguel A González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi, MSD, Consultant of: Abbvie, Pfizer, Roche, Sanofi, MSD, Grant/research support from: Abbvie, MSD, Janssen and Roche., Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD, Grant/research support from: Abvie, MSD and Roche

DOI: 10.1136/annrheumdis-2021-eular.3012

AB0689 INCIDENCE AND SEVERITY OF COVID-19 IN PATIENTS WITH SPONDYLOARTHRITIS IN ARGENTINA: EXPERIENCE IN A COUNTRY WITH STRICT ISOLATION

V. Martire[1], C. Airoldi[2], M. S. Gálvez Elkin[3], M. Machado Escobar[4], N. Callahuara[5], V. Duarte[6], J. Alcivar Navarrete[7], E. Buschiazzo[8], E. Saturansky[9], M. J. Gamba[10], P. Girard Bosch[1], D. Zelaya[11], R. Garcia Salinas[12], M. A. Medina[13], M. Cosatti[14], S. Scarafia[15],

M. L. Acosta Felquer[16], V. Cosentino[11], F. Sommerfleck[17], R. Luis[11], G. P. Pendon[18], R. Águila Maldonado[19], S. Nasi[20], R. Nieto[2], L. Abbas[21], D. Vila[22], E. Kerzberg[11], M. Benegas[17]on behalf of Grupo de estudios de la Sociedad Argentina de Reumatología de Espondiloartritis axial y Artritis reactiva (GESAR EspAax-ARe). *[1]Instituto Médico Platense, Rheumatology, La Plata, Argentina*; *[2]Hospital Provincial, Rheumatology, Rosario, Argentina*; *[3] Instituto Cardiológico, Rheumatology, Santiago del Estero, Argentina*; *[4]Hospital Eva Perón, Rheumatology, Tucumán, Argentina*; *[5]Hospital Rivadavia, Rheumatology, La Plata, Argentina*; *[6]Clínica Monte Grande, Rheumatology, La Plata, Argentina*; *[7]Hospital Tornú, Rheumatology, Buenos Aires, Argentina*; *[8]Hospital del Milagro, Rheumatology, Buenos Aires, Argentina*; *[9]Sanatorio Mendez, Rheumatology, Buenos Aires, Argentina*; *[10]Hospital Posadas, Rheumatology, Buenos Aires, Argentina*; *[11]Hospital Ramos Mejía, Rheumatology, Buenos Aires, Argentina*; *[12]Hospital Italiano de La Plata, Rheumatology, La Plata, Argentina*; *[13]Hospital Tornú, Rheumatology, Buenos Aires, Argentina*; *[14]CEMIC, Rheumatology, Buenos Aires, Argentina*; *[15]Hospital Municipal San Cayetano, Rheumatology, Buenos Aires, Argentina*; *[16]Hospital Italiano de Buenos Aires, Rheumatology, La Plata, Argentina*; *[17]Sanatorio Mendez, Rheumatology, Buenos Aires, Argentina*; *[18]Hospital Gutierrez, Rheumatology, Buenos Aires, Argentina*; *[19]Hospital San Martín, Rheumatology, La Plata, Argentina*; *[20]Hospital El Carmen, Rheumatology, Buenos Aires, Argentina*; *[21]PSORIAHUE, Rheumatology, Buenos Aires, Argentina*; *[22]Hospital Virgen del Carmen de Zárate, Rheumatology, Zárate, Argentina*

Background: There are limited data worldwide on the behavior of SARSCOV2 in patients with Spondyloarthritis (SpA).
Objectives: To describe the incidence and severity of COVID-19 disease in patients with SpA in Argentina.
Methods: Patients with axial spondyloarthritis (AxSpA) radiological (EA) and non-radiological (AxSpA-nr) and peripheral spondyloarthritis (according to ASAS criteria) and psoriatic arthritis (PsA) (according to CASPAR criteria) were included. Sociodemographic data, comorbidities, disease activity and treatments were collected at baseline. The patients were followed up by phone or in person monthly. Data were collected from 1/4/2020 to 9/20/2020. Descriptive statistics were performed with mean and standard deviation (SD) and median and quartile 25-75 according to distribution, and the cumulative incidence (AI) of the disease was calculated.
Results: 320 patients were included, of which 55% were male, with a mean age of 50 SD 13, 21.6% had a diagnosis of AS, 6.9% SpAax-nr, 6.9% SpAp, and 64.7% PsA, BASDAI 3.65 (3), BASFI 3 (1.5-9), PASI 0.3 (0-7), BSA 0.2 (0-6). Fourteen patients with a diagnosis of COVID-19 (4.4%) were reported, of which 10 diagnoses were by positive PCR and 4 by positive symptoms and close contact. 93% (13) of the cases were patients from the Province of Buenos and CABA and 1 patient from Santiago del Estero. The total IA for the country was 0.04. Of the 14 patients with COVID-19, 7 (50%) were men, 4 had a diagnosis of AS, 1 of SpAax-nr, 9 (64.3%) PsA. 100% live in urban areas, 2 (14%) have hypertension, 1 (7%) DBT, 1 (7%) COPD, 2 (14%) depression or anxiety, 11(97%) had received influenza vaccine 2020, 13 (93%), Antineumoccic 23, 14 (100%) Antineumoccic 13. Regarding the treatments: 4 (28.6%) were in treatment with anti TNF (3 with Adalimumab, 1 with certolizumab pegol), 4 (28.6%) with Anti IL17 (3 with Secukinumab, 1 with Ixekizumab), 8 (57%) with methotrexate and 2 (14%) with Leflunomide. Place of follow-up of the disease: 10 (71.4%) at home, 3 (21.4%) in the common room and 1 (7) in the intensive care unit. Treatments received for COVID-19: 1 (7%) antiretroviral, 1 (7%) antibiotic and 1 (7%) steroids. None of the patients died from COVID-19.
Conclusion: An incidence of 4.4% of COVID-19 was found in this population with SpA and most of the patiend had mild symptoms and no deaths were reported.
Disclosure of Interests: Victoria Martire: None declared, Carla Airoldi: None declared, María Soledad Gálvez Elkin: None declared, MAXIMILIANO MACHADO ESCOBAR: None declared, Noel Callahuara: None declared, Vanesa Duarte Employee of: Novartis, José Alcivar Navarrete: None declared, Emilio Buschiazzo: None declared, Etel Saturansky: None declared, María Julieta Gamba: None declared, Paula Girard Bosch: None declared, David Zelaya: None declared, Rodrigo Garcia Salinas: None declared, María Alejandra Medina: None declared, Micaela Cosatti Employee of: Jannsen, SANTIAGO SCARAFIA: None declared, Maria Laura Acosta Felquer: None declared, Vanesa Cosentino: None declared, Fernando Sommerfleck: None declared, Ramiro Luis: None declared, Gisela Paola Pendon: None declared, Rodrigo Águila Maldonado: None declared, Silvina Nasi: None declared, Romina Nieto: None declared, Leila Abbas: None declared, Diego Vila: None declared, Eduardo Kerzberg: None declared, Mariana Benegas: None declared
DOI: 10.1136/annrheumdis-2021-eular.3066

AB0690 HOW DID COVID-19 AFFECT PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES TREATED WITH DMARDS – EXPERIENCE FROM A ROMANIAN RHEUMATOLOGY HOSPITAL

A. Trandafir[1], I. Saulescu[1,2], A. Balanescu[1,2], D. Opris-Belinski[1,2], V. Bojinca[1,2], F. Berghea[1,2], D. Mazilu[1,2], S. Daia-Iliescu[1,2], D. Predeteanu[1,2], A. Borangiu[1,2], L. Groseanu[1,2], M. M. Negru[1,2], C. L. Constantinescu[1,2], M. Abobului[1,2], V. Violeta[1,2], R. Ionescu[1,2]. *[1]Saint Mary Hospital, Internal Medicine and Rheumatology, București, Romania*; *[2]Carol Davila University of Medicine and Pharmacy, Internal Medicine and Rheumatology, București, Romania*

Background: Certainly, the year 2020 changed the healthcare system due to SARS-CoV2 pandemic that affected globally, more than 100 million people, causing more than 2 million of deaths worldwide. The evidence of how this infection impact patients with rheumatic and musculoskeletal diseases treated with disease modifying anti-rheumatic drugs is still an unmet need.
Objectives: The main focus of this study is to evaluate the influence of DMARDs therapy on the evolution of COVID-19 disease in patients with RMDs. The second objective is to study and find correlations between the severity of infection in patients with rheumatic diseases.
Methods: A retrospective observational study was conducted between June 2020 and January 2021, enrolling 81 patients with rheumatic diseases that went through SARS-CoV2 infection. The data was collected using patients' clinical documents and through telemedicine, in accordance with EULAR COVID-19 Rheumatological Database.
Results: Among the 81 patients, 53 (65,43%) were females and 28 (34,56%) were males. The mean age was 47,9 years old (49,49 years old for females and 45,25 years old for males). The majority lives in urban areas – 62 patients (76,54%).
The temporal trends of COVID-19 observed in this cohort was in consonance with the evolution of the pandemic in Romania: one third of cases were recorded between June and October 2020 and two-thirds between November 2020 and January 2021, when the number of COVID-19 cases tripled in the general population.
Surprisingly, more than 27% of patients in this study were asymptomatic at the time of COVID-19 diagnosis. They were tested according to the protocol before admission to the hospital. 9,8% of patients also asymptomatic, were tested positive as a screening before leaving the country. The majority (45,6%) were symptomatic or contact with someone infected with SARS-CoV2-and tested positive with RT-PCR.
We divided the cohort in 3 groups: patients with mild infection that required no hospitalization (22 patients counting for 27,16%), moderate infection – hospitalization but not in the Intensive Care Unit (52 patients – 64,19%) and severe infection – admission to the ICU/deaths (7 patients in the ICU, 4 deaths – 4,9%).
Mild and moderate COVID 19 disease was identified in patients with axial spondyloarthtis (56,7%), with remission or with low disease activity, with a few or no comorbidities, with a mean age of 47,56 years old and also in patients in treatment with MTX (14,86%) or TNF alfa inhibitors (35,13%). 51% of patients stopped the therapy during COVID19 diseases.
Factors correlated with severe infection and death were age (the mean age was 62,14), high and moderate disease activity RA, overlap syndromes (RA with SLE or Sjogren Syndrome) and important cardiovascular comorbidities. Two of the deceased patients were in treatment with MTX and RTX (the last infusion was more than 6 months).
Conclusion: The data in our study suggests that the use of cs DMARDs (MTX) and TNF alfa inhibitors is associated with better outcomes for patients with RMDs and COVID-19. These results are in accordance with the data found in literature [1,2,3]. The limitation of this study is the little number of patients and the fact that the real number of COVID-19 cases might be higher in reality due to asymptomatic or pauci-symptomatic patients.
REFERENCES:
[1] Filière des Maladies Autoimmunes et Autoinflammatoires Rares (FAI2R); Hôpital Huriez, CHU Lille, Univ. Lille, Lille, France, Severity of COVID-19 and survival in patients with rheumatic and inflammatory diseases: data from the French RMD COVID-19 cohort of 694 patients, Annals of the Rheumatic Diseases Published Online First: 02 December 2020
[2] Sanchez-Piedra C et al., On behalf of the BIOBADASER study group, et al, Clinical features and outcomes of COVID-19 in patients with rheumatic diseases treated with biological and synthetic targeted therapies,Annals of the Rheumatic Diseases 2020;79:988-990.
[3] Hyrich, K.L et al. Rheumatic disease and COVID-19: epidemiology and outcomes. Nat Rev Rheumatol 17, 71–72 (2021)
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3092

AB0691

ANALYSIS OF SARS-COV-2 ANTIBODIES IN NON-COVID-19 PATIENTS: COMPARISON BETWEEN SYSTEMIC SCLEROSIS PATIENTS AND HEALTHY CONTROLS

L. Giardullo[1], C. Rotondo[1], A. Corrado[1], N. Maruotti[1], R. Colia[1], A. Altomare[1], E. Sanpaolo[1], D. Cici[1], F. P. Cantatore[1]. [1]*University of Foggia "Policlinico Riuniti", Medical and Surgical Sciences, Rheumatology Clinic "Mario Carrozzo", Foggia, Italy*

Background: Previous study evidenced a cross-reactivity between Sars-Cov-2 antibodies and autoimmune tissue antigen involved in connective tissue diseases, as nuclear antigen (NA), extractable nuclear antigen (ENA), histone and collagen (1). No study has been published about the titer of Sars-Cov-2 antibodies in non-infected patients with autoimmune disease.

Objectives: To evaluate the titer of SARS-CoV-2 antibodies in non-COVID-19 patients and compare it between systemic sclerosis (SSc) patients and healthy controls (HC).

Methods: A total of 58 patients with SSc (who fulfilled ACR/EULAR 2013 SSc classification criteria) and 18 HC were enrolled. Sera of all participants were collected, and SARS-CoV-2 antibodies (IgG and IgM) were evaluated by means ELISA. In all participants swabs for SARS-CoV-2 by real-time reverse-transcriptase-polymerase-chain-reaction assay were reported negative. Demographic, clinical, and autoimmune serological characteristics of SSc patients were recorded. The normal distribution was assessed using the Shapiro–Wilk's test. Exclusion criteria was previous or actual Sars-Cov-2 infection. Comparisons between study groups of patients were evaluated by the Student's t-test or Mann – Whitney U-test as appropriate. The differences between categorial variables were assessed by Pearson chi-square or Fisher's exact test, as opportune. Statistical significance was set at $p \leq 0.05$.

Results: We observed significant differences between SSc patients and HC in serum levels of Sars-Cov-2 antibodies (IgG: 1,4±2,1 AU/ml vs 0,36±0,19 AU/ml respectively (p=0,001); and IgM: 2,5±3,1 AU/ml vs 0,8±0,7 AU/ml (p=0,022)). In 5 SSc patients was found titer of Sars-Cov-2 antibodies (IgG) exceeding the cut-off, but the control of swabs for SARS-CoV-2 by real-time reverse-transcriptase-polymerase-chain-reaction assay were negative. No significative differences in Sars-Cov-2 autoantibodies titer were found in subgroup of SSc patients with or without ILD or PAH, limited or diffuse skin subset, and different autoantibodies profile. Furthermore, antibodies titer was not associated with different drugs (steroid, methotrexate, mofetil-mycophenolate and bosentan) in use.

Conclusion: A cross mimicking between Sars-Cov-2 antibodies and antinuclear antibodies or anti ENA could be hypothesized. Further studies are necessary to unravel the reliability of Sars-Cov-2 antibodies detection in autoimmune disease.

REFERENCES:

[1] Vojdani, A., Vojdani, E., & Kharrazian, D. (2021). Reaction of human monoclonal antibodies to SARS-CoV-2 proteins with tissue antigens: Implications for autoimmune diseases. Frontiers in Immunology, 11, 3679

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3143

AB0692

REACTIVE ARTHRITIS ASSOCIATED WITH COVID-19 INFECTION: A REVIEW

F. Alkindi[1], K. Alseiari[2], K. Al Naqbi[3]. [1]*Tawam Hospital, Internal Medicine, Al Ain, United Arab Emirates*; [2]*Tawam Hospital, Internal Medicine, AlAin, United Arab Emirates*; [3]*Tawam Hospital, Rheumatology Department, AlAin, United Arab Emirates*

Background: The incidence of COVID-19 infection is increasing globally with high mortality rate. Cytokine release syndrome might contribute to extra-pulmonary manifestations such as acute kidney injury, venous thrombosis, neurological complications, hepatic and myocardial injury. Reactive arthritis is an emerging musculoskeletal (MSK) manifestation post COVID-19 infection. Reactive arthritis manifests as asymmetrical, oligoarthritis mainly involving peripheral or axial joints of lower extremities and associated with extra-articular manifestations.

Objectives: review the clinical presentation and management outcomes of COVID-19 associated reactive arthritis.

Methods: A literature research was conducted using PubMed and Google scholar for published abstracts, case reports, and studies from January 2020 to January 2021. We used search keywords" reactive arthritis", "COVID-19 pneumonia", " SARS CoV2 infection", and "Musculoskeletal". Descriptive analysis was used due to small sample size.

Results: COVID-19 associated reactive arthritis is rarely reported. In review of literature, 10 cases were identified and we included our case of hip arthritis and avascular necrosis post COVID-19 infection. The mean age of cases (n=11) was of 42.8 years and 54.5 % of patients were males. (Table 1) The median duration of reactive arthritis diagnosis from COVID-19 infection ranged from 1 to 8 weeks. The severity of COVID-19 infection varied from mild (n= 6) to severe disease (n=2) per description in each reported case. Majority of the patients had oligoarticular involvement (2 to 4 joints) 45.5%, followed by monoarticular 36.4%, and polyarticular (> 4 joints) in 18%. Extra-articular manifestations were identified in 54.5% of patients including skin rash (erythematous itchy rash), urticarial rash, wrist tendinitis, Achilles enthesitis /tendonitis and balanitis. HLA-B27 testing was done in five patients and only one patient had a positive result. Plain radiographs were normal. Therapy provided of such cases were NSAIDS (n=4), steroids (oral, intra-articular) (n=1) or combination of steroids and NSAIDS (n=3) with favorable outcomes. The median reported follow up period ranged from 1.5 to 8 weeks.

Table 1. Characteristics of the reported reactive arthritis cases post COVID-19 infection

Clinical data of patients (n=11)	**Results (n=11)**
Age (mean)	42.8 Years old
Sex %	Female (n= 5 [45.5%])
	Male (n= 6 [54.5%])
Severity of COVID-19 infection	Mild (n=6 [54.5%])
	Moderate (n=3 [27.3%])
	Severe (n= 2 [18%])
Prior history of rheumatologic disease	(n=0)
Time to onset of reactive arthritis (median)	1 to 8 weeks
Number of joints involved at time of diagnosis	Monoarticular (n= 4[36.4%])
	Oligoarticular (n= 5[45.5%])
	Polyarticular (n= 2[18%])
Location of involved joints (upper vs. lower limbs)	Upper joints (18%)
	Lower joints (54.5%)
	Both (27.3%)
Enthesitis	(n= 1[9%]) Achilles
Tendonitis	(n= 2[18%]) (wrist / Achilles tendonitis)
Extra-articular involvement (eyes, skin, GI, GU, others)	- Skin rash (n=2 [18%]) (erythematous itchy rash, urticarial rash)
	- GU: balanitis (n=1 [9%])
Inflammatory back pain	(n=0)
Avascular necrosis of bone	(n= 1[9%])
HLA-B27	(n= 1[9%]), (n = 5 tested)
Autoimmune workup	Negative
Treatment of reactive arthritis:	DMARDs (n=0)
	NSAIDs (n=4 [36.4%])
	Steroids (n=1 [9%])
	NSAIDs and steroids (n= 3[27.3%])
	Not provided (n=2), others (n=1)
Outcomes of MSK symptoms	Improvement (n=11 [100%])
Follow up period (Median, weeks)	1.5 to 8 weeks

Gastrointestinal (GI), genitourinary (GU), NSAIDs: non-steroidal anti-inflammatory drug

Conclusion: Reactive arthritis is a rare MSK manifestations post COVID-19 infection. HLA-B27 positive testing might indicate severe and delayed form of arthritis with risk of recurrence. Larger studies are required to delineate the potential risk factors and long-term management outcomes for reactive arthritis associated with COVID-19 infection.

REFERENCES:

[1] Ono K, Kishimoto M, Shimasaki T, et al. Reactive arthritis after COVID-19 infection, RMD Open 2020;6:e001350. doi: 10.1136/rmdopen-2020-001350

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3174

AB0693

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS DURING CORONAVIRUS 19 PANDEMIC: WHAT DO TUNISIAN RHEUMATOLOGISTS THINK?

H. Ferjani[1], H. Boussaa[1], K. Maatallah[1], H. Khalfalli[1], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab Institute of Orthopedics, Rheumatology, La Manouba, Tunisia*

Background: Concerns over the safety of non-steroidal anti-inflammatory drugs (NSAIDs) use during severe acute respiratory syndrome associated with coronavirus 19 disease (covid-19) have raised. NSAIDs are one of the most commonly prescribed and used pain medications for acute and chronic rheumatic diseases such as spondyloarthritis (SpA) and osteoarthritis.

Objectives: This study aimed to assess the impact of covid-19 pandemic on NSAIDs prescription.

Methods: A cross-sectional web survey was disseminated to all Tunisian rheumatologists through a mailing system and social media. The French version was accessible on Google form. It included close-ended questions about the prescription of NSAIDs during covid-19 pandemic. Participation was anonymous. Data collection and analysis was performed between January the first and January 30, 2021.

Results: Among one hundred and thirty Tunisian rheumatologists, thirty responded to the online questionnaire. Ninety percent of participants were women. The mean age of rheumatologists was 34 years [25-57]. The duration of

practice was inferior to 5 years in 59.3%, between 5 and 10 years in 18.5%, and superior to 10 years in 22.2% of cases. Sixty-three percent of rheumatologists reported that their activity decreased during covid-19 pandemic. NSAIDs prescription was avoided as much as possible in 40.7% of cases.
The participants indicated NSAIDs less frequently in 33.3% of cases, and as much as before the pandemic in one-quarter of cases.
Rheumatologists believed that NSAIDs worsen the respiratory symptoms (67%), delay recovery (55%), and increase mortality (48%), hospitalization in intensive care (44%), and infectious complications (33%).
The participants suggested that the most incriminated NSAIDs were: Ibuprofen (7.4%), indomethacin (7.4%), celecoxib (7.4%), and diclofenac (3.4%). The majority of rheumatologists (74%) believed that all NSAIDs had a similar risk.
For patients with osteoarthritis, rheumatologists replaced NSAIDs with paracetamol and corticoids in 78% and 11% of cases, respectively. If mandatory, reducing NSAIDs doses or duration was an option in 22% and 74% of cases.
For patients with SpA, half of rheumatologists did not change the treatment. However, the participants limited the use of NSAIDs or discontinued the treatment in patients with comorbidities. More than 60% of rheumatologists didn't know the effect of NSAIDs in the post-covid-19 syndrome.
Conclusion: Covid-19 pandemic has affected rheumatologists' practice. Rheumatic disease management during this pandemic may be challenging. More evidence is mandatory to standardize treatment prescription, especially with NSAIDs.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3221

AB0694 COVID-19 İNFECTION IN PATIENTS WITH RHEUMATIC DISEASES: TWO CENTERS EXPERIENCE

A. Şahin[1], M. A. Gedikli[2], M. E. Derin[3], B. Karakaş[1], B. Karataş[1], N. Çabuk Çelik[1], İ. Yalçın[1]. [1]*Sivas Cumhuriyet University, Internal Medicine – Rheumatology, Sivas, Turkey*; [2]*Sivas Cumhuriyet University, Internal Medicine, Sivas, Turkey*; [3]*Sivas Numune Hospital, Internal Medicine – Rheumatology, Sivas, Turkey*

Background: Coronavirus disease 2019 (COVID-19) is a new viral infection characterized by dry cough, fever, shortness of breath, fatigue and lymphopenia. It may be complicated by interstitial pneumonia leading to severe acute respiratory distress syndrome(1). The COVID-19 outbreak has increased concerns in those with rheumatological diseases(2).
Objectives: To present the clinical course of COVID-19 infection in patients with rheumatological disease and comorbid conditions of patients and drug use.
Methods: 70 COVID-19 patients with autoimmune and autoinflammatory rheumatic diseases over the age of 18 who were followed up in the internal diseases-rheumatology department of Sivas Cumhuriyet University Hospital and Sivas Numune Hospital between April 2020 and January 2021 were included in this study. An application was made to the ethics committee of Sivas Cumhuriyet University Hospital and approval was obtained. Demographic data, comorbidities, smoking, treatments for their diseases, symptoms and hospitalization status of the patients were evaluated.
Results: The median age of the women patients was 48 years (min: 20-max: 73), 41 years in men (min: 21-max: 78). 15 patients (21.4%) were male, 55 patients (78.6%) were female. The most common rheumatic disease was rheumatoid arthritis (RA, 21, 30%) followed by ankylosing spondylitis (19, 27.1%), familial Mediterranean fever (13, 18.6%), Behçet's disease (12, 17.1%). 22 (31.4%) patients hydroxychloroquine sulfate, 14 (20%) leflunomide, 7 (10%) patients methotrexate, 6 (8.6%) patients sulfasalazine, 10 (14.3%) patients azathioprine/mycophenolate mofetil, 22 (31.4%) patients were using colchicine. As a biological medicine; 20 (28.6%) patients were using infliximab, 5 (7.1%) patients were using adalimumab, 6 (8.6%) patients were using rituximab, and 4 (5.7%) patients were using tocilizumab. Other are summarized in Table 1. The most common comorbidities were hypertension (25.7%) and diabetes mellitus (DM 17.1%). While 56 patients (80%) had symptoms of COVID-19, 14 patients (20%) were asymptomatic. The most common symptoms was fever (32, 45.7%) followed by cough (29, 41.4%), dyspnea (28, 40%), myalgia (25, 35.7%), loss of taste and smell (18, 25.7%). 21 pneumonia cases were diagnosed. 22 (31.4%) patients were hospitalized. Mortality rate was 2/70, 2.9%. Two RA patients who just treated with rituximab and tocilizumab were died. 10 cases were using >10 mg/day prednisolone, 2 died, 8 cases were hospitalized and had severe disease. They had hypertension and DM. Characteristics of the patients are summarized in Table 2.
Conclusion: The course of COVID-19 in rheumatic diseases is not clearly. Meta-analysis has shown that the frequency of COVID-19 is increased in autoimmune diseases. However, this increase was mostly associated with the use of> 10mg/day prednisolone. It has been stated that the use of biological drugs and Dmard causes the SARS-CoV 2 process with a milder course and therefore their use is safe (3). Similar results have been obtained in global registry registers (4). In our data, there was no increase in the mortality rate compared to the normal population. However, especially the use of rituximab may increase the rate of severe disease and mortality, so its use should be careful. There is a need for more comprehensive studies.
REFERENCES:
[1] Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020.
[2] N. Chen, M. Zhou, X. Dong,et al., Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, Lancet 395 (10223) (2020) 507*513
[3] Akiyama S,Hamdeh S, Micic D, et al, Prevalence and clinical outcomes of COVID-19 in patients with autoimmune diseases: a systematic review and meta-analysis,Ann Rheum Dis 2020 Oct 13;annrheumdis-2020-218946.
[4] Gianfrancesco M, Hyrich KL, Al-Adely S,et al, Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis. 2020 Jul;79(7):859-866.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3289

AB0695 PATTERN OF COVID-19 IN PATIENTS WITH RHEUMATIC DISEASES UNDERGOING BIOLOGICAL THERAPY: A COHORT EXPERIENCE

C. Ancuta[1,2], C. Pomirleanu[1,2], G. Strugariu[2], L. Petrariu[2], E. Ancuta[3], C. Bran[4,5], R. Chirieac[6], C. Mihailov[7,8]. [1]*University of Medicine and Pharmacy "GRIGORE T. POPA" IASI, Rheumatology, IASI, Romania*; [2]*Clinical Rehabilitation Hospital, Rheumatology, IASI, Romania*; [3]*"Elena Doamna" Clinical Hospital, Research, IASI, Romania*; [4]*Emergency Hospital "Sf Ioan", Rheumatology, IASI, Romania*; [5]*University Stefan Cel Mare Suceava, Semiology and Immunology, Suceava, Romania*; [6]*Sanocare Medical and Research Center, Rheumatology, IASI, Romania*; [7]*Clinical CF Hospital of Constanta, Rheumatology, Constanta, Romania*; [8]*Faculty of Medicine, "Ovidius" University Constanta, Internal Medicine and Rheumatology, Constanta, Romania*

Background: Despite emerging vaccines, the world is in the midst of a coronavirus disease 2019 (COVID-19) pandemic. Outcomes of SARS-CoV2 infection remain a major concern in patients with rheumatic and musculoskeletal diseases, especially for those with uncontrolled disease.
Objectives: We aimed to investigate trends and outcomes of COVID-19 occurring in patients with chronic inflammatory rheumatic conditions treated with biologics and targeted synthetic disease modifying antirheumatic drugs (bDMARDs, tsDMARDs).
Methods: We included all confirmed cases of COVID-19 regardless of severity in patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) undergoing bDMARDs or tsDMARDs treatment registered in our local COVID-19 reporting database. We collected relevant information about comorbidities, rheumatologic-related clinical activity (RAPID5, SDAI, BASDAI, DAPSA), type of DMARD and glucocorticoid use, as well as COVID-19 related data as severity (ranging from asymptomatic to life-threatening forms), medication, hospitalization, intensive care unit admission, invasive mechanical ventilation and death.
We did a subgroup analysis among patients with a specific rheumatologic diagnosis, among different class of medication, patients who were or not hospitalized with COVID-19 looking how age, comorbidities, type of rheumatic condition and treatments impact COVID outcomes.
Results: 40 COVID-19 cases (positive PCR for SARS-CoV2) (4.67%) were identified during the 6-month study period among 855 patients registered in our database of patients under biologic treatment, including 20 RA, 18 SpA, 2 PsA patients. The majority were in either low disease activity or remission, only two patients had active uncontrolled disease at the onset of coronavirus infection.
16 cases (40%) were asymptomatic and were tested RT-PCR-positive during routine follow-ups for their disease, 13 cases (32.5%) had mild and 8 cases (20%) moderate illness; severe pneumonia and critical disease with acute respiratory distress syndrome were reported in only 3 cases, 2 recovered after; the only patients who died was 69 years old, had cardiac disease, hypertension and diabetes, had undertaken regular rituximab perfusion one month before coronavirus infection and developed pulmonary embolism followed by septic shock.
Extreme fatigue was the dominant COVID-19 associated symptom apart from the classical ones including fever, cough, shortness of breath, sore throat, nasal congestion, headache, anosmia and ageusia myalgias and anorexia.
No specific pattern for patients requiring intensive care unit admission.
Conclusion: The COVID-16 infection rate in patients with inflammatory rheumatic disorders receiving biologics and tsDMARDs is pretty low; although immunosuppressed, these patients seem not to be at risk for severe COVID-19 illness and outcomes. These findings might reflect a potential protective role of certain biologics and/or JAK inhibitors for development and severity of COVID-19 in patients.

REFERENCES:

[1] WHO, COVID-19 clinical management, Living Guidance, 25 Jan 2021

Disclosure of Interests: CODRINA ANCUTA Speakers bureau: Abbvie, Pfizer, Lilly, Novartis, Sandoz, Consultant of: Abbvie, Pfizer, Lilly, Novartis, Sandoz, Cristina Pomirleanu Speakers bureau: Abbvie, Pfizer, Lilly, Novartis, Sandoz, Georgiana Strugariu Speakers bureau: Abbvie, Pfizer, Lilly, Novartis, Sandoz, Luiza Petrariu Speakers bureau: Abbvie, Pfizer, Lilly, Novartis, Sandoz, Eugen Ancuta: None declared, Codruta Bran Speakers bureau: Abbvie, Pfizer, Lilly, Novartis, Sandoz, Rodica Chirieac Speakers bureau: Abbvie, Pfizer, Lilly, Novartis, Sandoz, Claudia Mihailov Speakers bureau: Abbvie, Pfizer, Lilly, Novartis, Sandoz, Consultant of: Abbvie, Pfizer, Lilly, Novartis, Sandoz

DOI: 10.1136/annrheumdis-2021-eular.3467

AB0696 ANTI-PHOSPHOLIPID AUTOANTIBODIES IN COVID-19 PATIENTS

M. Jordhani[1], D. Ruci[1], V. Ruci[2]. [1]*UHC Mother Teresa, Tirana, Albania, Internal Medicine, Tirana, Albania*; [2]*University Trauma Hospital Tirana, Orthopaedics, Tirana, Albania*

Background: Because of the inflammation boosting cytokines, Coronavirus disease 2019 (COVID-19) has demonstrated thrombotic consequences that have increased its morbidity and mortality. There is evidence that mechanisms that contribute in thrombosis in COVID-19 patients are similar to those in anti-phospholipid syndrome (aPS). In fact, there is a possibility that anti-phospholipid autoantibodies (aPLs) might impulse thrombosis in patients with COVID-19, as literature suggests[2].

Objectives: The aim of our study was to evaluate the anti-phospholipid autoantibody titre in patients with COVID-19 during and after the infection.

Methods: This is an observational study which included 71 patients with a recent COVID-19 up to 4 weeks after. Every patient was completed with aPL titre about IgG and IgM anti-cardiolipine (ACA) and lupus anticoagulant (LAC) autoantibodies. According to titre results, the patients were divided into groups in order to better show the immunologic results.

Results: After gathering and analysing the data, it was estimated that 21 patients (29.6%) were positive for at least one type of aPL antibody: 12 patients were found positive for lupus anticoagulant autoantibodies (57.1%), 6 patients were double positive for LAC and ACA (28.6%), and 3 patients were positive for anti-cardiolipin antibodies (14.3%). Seven patients were IgM positive for any aPL (33.3%), 6 patients were found to have positive IgM and IgG (28.6%) and 8 patients had only IgG antibodies (38.1%).

Conclusion: From this study it was observed that a significant proportion of patients with recent COVID-19 infection had positive anti-phospholipid antibodies, compared to the general population prevalence. This suggests that the impact of aPLs in COVID-19 might be of great importance. It should be carefully evaluated in order to better understand the mechanisms of thrombotic complications.

REFERENCES:

[1] Wise Jacqui. Covid-19 and thrombosis: what do we know about the risks and treatment? BMJ 2020; 369:m2058

[2] Zuo, Yu, et al. "Prothrombotic autoantibodies in serum from patients hospitalized with COVID-19." *Science translational medicine* 12.570 (2020).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3521

AB0697 ANTI-SARS-COV-2 ANTIBODIES AND AUTOANTIBODIES IN COVID-19 PATIENTS SURVIVED AFTER ICU ADMISSION, 6 MONTHS LATER

K. Bitzogli[1], E. Magira[2], L. Chatzis[1], E. Jahaj[2], H. Alexopoulos[1], M. Dalakas[1], A. Kotanidou[2], A. Tzioufas[1], P. Vlachoyiannopoulos[1]. [1]*School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece*; [2]*School of Medicine, National and Kapodistrian University of Athens, 1st Department of Intensive Care Medicine, Athens, Greece*

Background: We[1] and others[2] have previously shown that ICU admitted patients with COVID-19 developed high titers of anti-SARS-CoV-2 antibodies, but also autoantibodies, some of which are pathogenic. We re-evaluated 8 patients of those survived after admission to the ICU of Evangelismos Hospital of Athens -1st Department of Internal Medicine, Medical School, NKUA[3] 6 months later. We did not know whether these autoantibodies still exist, are associated with COVID-19 or with ARDS as described after septic shock[4].

Objectives: To investigate the presence and titers of anti-SARS-CoV-2 antibodies and autoantibodies in patients survived after COVID-19 ICU stay, in the ICU and 6 months later.

Methods: Case series to evaluate titers of anti-SARS-CoV-2 antibodies, specificities of autoantibodies as well as clinical features in ICU admitted COVID-19 patients, initially and 6 months after their discharge. Evaluation of current clinical status included evaluation of lung, heart, kidney, central and peripheral nervous system and mental status using standardized methods. Methods for detection of anti-SARS-CoV-2 antibodies and autoantibodies were described in our previous report[1].

Results: We had initially evaluated[1] 29 ICU admitted COVID-19 patients' files and sera, of which 4 had been already died during serum evaluation. Six more patients died thereafter. Out of 19 having been discharged, 8 were willing to be re-evaluated. On second evaluation 6 months later, serum anti-SARS-CoV-2 antibodies were highly positive, although at lower titers compared to the titers at disease onset (median [range]) 8.705 (range: 7.95-9.56) vs 6.640 (range: 6.29-6.76), p=0.0002, Mann-Whitney test. Initially 3 out of 8 patients expressed antinuclear antibodies (ANA) at titers 1/160, 1/320 and 1/320 with a fine speckled pattern with the second patient also expressing at a titer of 1/160, antimitochondrial (AMA) antibodies. Six months later the same patients and not anyone else expressed ANA of the same pattern at titers 1/640, 1/160 and 1/160 respectively. Two patients with 1/20 p-ANCA and 1/640 c-ANCA initially, lost their respective autoantibodies after 6 months. One patient initially negative for IgM anti-β2GPI became positive at low titer and an initially positive became negative. One patient initially positive for anti-Ro60 antibody continued to be positive 6 months later. One patient initially negative developed anti-Tg antibodies and 3 patients initially positive for anti-TPO antibodies remained positive 6 months later.

Conclusion: Patients with COVID-19 survived after ICU admission still retain high titers of anti-SARS-CoV-2 antibodies but significantly lower that at disease onset, but they tend to lose autoantibodies with pathogenic potential.

REFERENCES:

[1] Vlachoyiannopoulos P et al, Ann Rheum Dis 2020,

[2] 2. Wang EY et al, medRxiv preprint doi: https://doi.org/10.1101/2020.12.10.20247205

[3] National and Kapodistrian University of Athens, Athens, Greece

[4] Burbelo et al. Journal of Translational Medicine 2010

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3554

AB0698 CORONAVIRUS 19 DISEASE VACCINE: PERCEPTIONS AND INTENTIONS OF TUNISIAN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Ben Abdelghani[1], H. Boussaa[1], S. Miladi[1], M. Sellami[1], L. Souabni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], A. Fazaa[1], A. Laatar[1]. [1]*Mongi Slim University Hospital, Rheumatology, La Marsa, Tunisia*

Background: Coronavirus disease 2019 (covid-19) has now spread to millions of persons worldwide to become a global pandemic. Covid-19 is asymptomatic for some individuals and for others it can cause symptoms ranging from flu-like to acute respiratory distress syndrome, pneumonia and death. Several vaccine candidates are now available, and patients with chronic inflammatory disease such as rheumatoid arthritis (RA) are encouraged to get vaccinated.

Objectives: The aim of this study was to determine perceptions of RA patients about the covid-19 vaccine.

Methods: We conducted a cross-sectional study including Tunisian patients with RA (ACR/EULAR 2010). Demographic and disease parameters were collected: age, gender, educational status, disease duration, erythrocyte sedimentation rate (ESR), disease activity score (DAS28), and treatments being used. All patients responded to a questionnaire on their perceptions and concerns about the covid-19 vaccine, and whether they intended to get vaccinated or not. A *p* value inferior to 0.05 was considered significant.

Results: We included 54 patients (45 women and nine men) with a mean age of 55±11 years old [23-69]. Thirty-one percent of patients were illiterate. The mean disease duration was 9.9±5.9 years [0-20]. The mean DAS28 ESR was 4.68±1.35 [1.50-7.16].

NSAIDs were used in 13% of patients, corticosteroids in 63% of patients at a mean daily dose of 8mg [2.5-20] of prednisone equivalent, methotrexate in 63% of patients, sulphasalazine in 13% of patients, leflunomide in 3.7%, and biologics in 22.2% of patients.

None of these patients had contracted the covid-19. Seventeen percent of patients had been in close contact with someone positive for the disease. All the patients reported that they respected the preventive measures. Fifteen percent of patients had stopped their treatment because they were afraid of the covid-19: Methotrexate (n=4), sulphasalazine (n=1), tocilizumab (n=2), and rituximab (n=1).

More than half of patients (67.7%) reported that they didn't want to get vaccinated against covid-19. The reasons given by these patients were: presumed adverse events (100%), religious beliefs (86.7%). presumed inefficiency (83.3%), no recommendation from their doctor (80%), fear that the vaccine would interact with their treatment (76.7%), lack of trust in the pharmaceutical laboratories (76.7%), fear from vaccines in general (53.3%), fear that the vaccine would make RA worse (50%), and presumed overprice of the vaccine (30%).

A significant association was noted between educational status and, religious beliefs (p=0.001), lack of trust in the pharmaceutical laboratories (p=0.007), fear that the vaccine would make RA worse (p=0.008) or interact with other treatments (p=0.022), and presumed overprice of vaccine (p<0.001).
Conclusion: Most of RA patients expressed their unwillingness to get vaccinated against covid-19. Doubts about the vaccine's efficiency and security and religious beliefs were the main reasons for this choice.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3667

AB0699 RETROSPECTIVE ANALYSIS OF 52 SARS-COV2 POSITIVE PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASE: A SINGLE CENTER EXPERIENCE

Y. Karabulut[1]. [1]*Private Yıldırım Doruk Hospital, Division of Rheumatology, Bursa, Turkey*

Background: It is a generally accepted opinion that autoimmune and inflammatory rheumatic diseases or drugs used in the treatment of these conditions increase the risk of infection. During the pandemic period, the follow-up and treatment of patients who were diagnosed with rheumatic disease and used corticosteroid, immunosuppressive, biological or synthetic DMARDs and disease management during sars-cov2 infection still remain a problem.
Objectives: In this study, it was aimed to share the demographic data of 52 patients with inflammatory rheumatic disease diagnosed with SARS-COV2 who were followed up and treated in the Rheumatology Department of Private Doruk Hospital during the SARS-COV2 pandemic. Additionally, it is aimed to examine the primary rheumatological diseases of the patients, their biological and conventional DMARD treatments, their comorbidities and the course of SARS-COV2.
Methods: Fifty-two patients who were diagnosed with SARS-COV2 by PCR method while being followed up and treated in the rheumatology center between May 2020 and November 2020 and get COVID treatment in the same center were included in the study. All patients diagnosed with SARS-COV2 and required hospitalization were hospitalized in the same center and followed up and treated. The files and electronic records of the patients were retrospectively recorded by the rheumatologist who followed the patients.
Results: In this retrospective study conducted from a single center, 52 patients whose diagnosis of SARS-COV2 was confirmed by PCR were included. Distribution of primary rheumatic diseases of the patients; 19 rheumatoid arthritis (RA), 14 Ankylosing spondylitis (AS), 4 Psoriatic Arthritis (PsA), 4 Systemic lupus erythematosus (SLE), 5 Behcet's Disease (BD), 4 Familial Mediterranean Fever (FMF), 2 Sjögren's syndrome. 76.8% of the patients were female, 22.2% male, their mean age was 47 ± 18. Biological drug use rate of 37 patients in RA, AS and PsA groups was 83.7% (monotherapy or combination 31/37).
Moreover, 16.2% (6/37) of the patients were using synthetic DMARD combination (MTX+SLZ +HCQ) and 40.5% (15/37) of the patients were using a combination of biological and synthetic DMARDs. While 73% (38/52) of 52 patients had a mild course, 27% (14/52) had severe SARS-COV2 requiring hospitalization. 14 patients who had severe SARS-COV2 infection and required hospitalization, 10 were followed up with the diagnosis of RA, 2 with AS and 2 with SLE. Hospitalization of patients using monotherapy biological drugs (TNF inhibitor, Tocilizumab, IL 17-A) due to severe SARS-COV2 was found to be lower than the group using combined synthetic DMARDs with steroids (MTX+SSZ+HCQ) (p <0.05). The corticosteroid dose of the RA patients was in the range of 5-10 mg/day. The rate of having severe SARS-COV2 was found to be higher in the combination group using biological or synthetic DMARD and low dose corticosteroids compared to group using monotherapy biologicals (p <0.05). The rate of having severe SARS-COV2 was found to be significantly higher in the group using 10/mg or more at the time of diagnosis (p <0.05). Two patients with SLE multiple organ involvement had severe SARS-COV2 while using rituximab, and hospitalization was required. In terms of comorbidities, hypertension was the most common comorbidity with 64.2% (9/14) in the group with severe SARS-COV2, followed by obesity with 21.4% (3/14).
Conclusion: In patients with inflammatory rheumatic disease, SARS-COV-2 infection and the drugs used for the treatment of primary disease are still considered to be a difficult situation in terms of prognosis. In our study with limited cases, data suggesting that there is no increased risk of SARS-COV2 requiring hospitalization in patients using TNF inhibitors, tocilizumab and IL17-A blockers. It was thought that there might be a drug-induced increased risk due to the severe SARS-COV2 infection that developed in our two patients who used rituximab, but the disease-related risk increase was not ignored because the patients were SLE patients with active multi-organ involvement.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3672

AB0700 TOCILIZUMAB DID NOT REDUCE MORTALITY IN SEVERE COVID-19 PATIENTS BUT CAUSED THROMBOCYTOSIS

Z. Öztürk[1], S. M. Türk[1], D. Karataş[1], Ü. Erkorkmaz[2], K. Özmen Süner[3], H. Dheir[4], E. Güçlü[5], E. Gönüllü[1], O. Karabay[5]. [1]*Sakarya University Training and Research Hospital, Rheumatoloji, Adapazarı, Turkey*; [2]*Sakarya University Training and Research Hospital, Biostatistics, Adapazarı, Turkey*; [3]*Sakarya University Training and Research Hospital, Anesthesia, Adapazarı, Turkey*; [4]*Sakarya University Training and Research Hospital, Nephrology, Adapazarı, Turkey*; [5]*Sakarya University Training and Research Hospital, Infectious Diseases and Microbiology, Adapazarı, Turkey*

Background: TCZ is a monoclonal antibody against Interleukin-6 receptor (IL-6R) which is used for relieving inflammation and reducing mortality in COVID-19 patients. Safety and efficacy of Tocilizumab (TCZ) in Covid-19 pneumonia is uncertain yet. In this study, we aimed to determine clinical outcomes in patients treated with TCZ.
Objectives: In this study we aimed to share our retrospective results which we had obtained from patients with COVID-19 diagnosis received TCZ.
Methods: We performed a retrospective case control study between May and August 2020 in Turkey. We compared outcomes in patients who received TCZ with those who did not. Death in hospital and intensive care unit (ICU) requirements were evaluated as endpoints. Demographic data, comorbidities, additional treatment, treatment side effects, laboratory and clinical results were retrospectively assessed. There are no significant differences between groups according to age, gender and Charlson Comorbidity Index (CCI).
Results: 12 (27.3%) patients died in standard group and eight (18.6%) patients died in TCZ group (p=0.150).Days of staying in the hospital were eight days in standard treatment group and 12 days in TCZ group (p=0.03). 10 of 43 patients in TCZ group were admitted to ICU. MV support was needed in 8 of these patients. 18 of 44 patients (40.9%) within the standard group were admitted to ICU and 12 patients (27.3%) were intubated (p=0.125,p=0.480). Significant IL-6 decrease was not observed post treatment in TCZ group according to pre-treatment period (p=0.60). Significant decreases were examined in CRP and ferritin values through TCZ treatment. However, D-dimer and thrombocyte values increased.
Conclusion: TCZ may not be an effective treatment for reducing ICU requirement, to prevent intubation or death, for shortening period for staying in hospital. The patients should be followed up closely for possible thrombosis because of increased D-dimer and thrombocytes with TCZ treatment.
REFERENCES:
[1] Sharma A, Tiwari S, Deb MK, Marty JL. Severe acute respiratory syndrome coronavirus-2 (SARS-Cov-2): A global pandemic and treatment strategies. IntJ Antimicrob Agents. 2020 Aug; 56(2):106054.
[2] Singhal T. A rewiev of coronavirus Disease-2019(COVID-19). Indian J Pediatr. 2020 Apr;87(4):281-286.
[3] Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall R.S, Manson J.J. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020;395(10229):1033-
[4] Teijaro J.R. Cytokine storms in infectious diseases. SeminImmunopathol. 2017;39:501–503.
[5] Zhang Y, Li J, Zhan Y, Wu L, Yu X, Zhang W et al. Analysis of Serum Cytokines in Patients with Severe Acute Respiratory Syndrome. Infect Immun 2004 Aug;72(8):4410-4415.
[6] Zhang C, Wu Z, Li JW, Zhao H, Wang GQ. Cytokine release syndrome in severe COVID-19: interleukin-6 receptor antagonist tocilizumab may be the key to reduce mortality. Int J Antimicrob Agents. 2020 May; 55(5):105954.
[7] Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8(4):420–2
[8] Fu B, Xu X, Wei H. Why tocilizumab could be an effective treatment for severe COVID-19? J Transl Med 18,164 (2020).
[9] Guaraldi G, Meschiari M, Cozzi-Lepri A, Milic J, Tonelli R, Menozzi M et al. Tocilizumab in patients with severe COVID-19: a retrospective cohort study. Lancet Rheumatol. 2020 Aug;2(8):e474-e484.
[10] Gupta S, Wang W, Hayek S.S, Chan L, MathewsK.S, Melamed M.L et al. Association Between Early Treatment With Tocilizumab and Mortality Among Critically Ill Patients With COVID-19. JAMA Intern Med. 2021 Jan1;181(1):41-51.
[11] Campochiaro C, Della-Torre E, Cavalli G, De Luca G, Ripa M, Boffini N et al Efficacy and safety of tocilizumab in severe COVID- 19 patients: a single-centre retrospective cohort study. Eur J Intern Med. 2020 Jun;76:43-49.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3697

AB0701

ANTIBODY RAPID TEST POSITIVE HEALTH CARE WORKERS AT A GERMAN UNIVERSITY HOSPITAL: FIRST WAVE CHARACTERISTICS

M. Beck[1,2], A. Nieters[2], M. Rizzi[1], U. Salzer[1], J. Thiel[1], N. Venhoff[1], N. Peter[1], H. Eibel[1], R. Voll[1], S. Finzel[1]. [1]*Faculty of Medicine, University of Freiburg, Department of Rheumatology and Clinical Immunology, University Medical Centre, Freiburg im Breisgau, Germany*; [2]*Institute of Immunodeficiency, Centre for Chronic Immunodeficiency, Freiburg im Breisgau, Germany*

Background: Freiburg was among the most heavily affected German cities during the first wave of Sars-Cov-2 infections in spring 2020. Consequently, the University Medical Center Freiburg was one of the first hospitals in Germany to treat Covid19 patients.
Objectives: To assess the proportion and characteristics of health care workers (HCW) that have been infected during that first wave SARS-CoV-2 serum IgG and IgM antibodies were measured.
Methods: HCW (n=902, mean age: 40.7 years) participated in this study, and filled out an epidemiological questionnaire. Serum samples were analysed for SARS-Cov-2 IgG/IgM antibodies via rapid diagnostic test (RT) and via ELISA. Statistical analyses were performed using STATA 14.2. An exposure prevention score was developed to quantify the adherence to preventive measures in everyday life.
Results: 902 HCW were tested by RT, and 499 by ELISA. In total, 11.5% of recruited HCW were antibody-positive in the RT, 12.2% in the ELISA. 87.5% of RT positives, 98% of ELISA-positives reported symptoms, compared to 74.6% and 78% of negatives, respectively. Symptoms such as cough (57%/46%), loss of smell and taste (34%/5.2%), fatigue (68%/45%), fever (48%/24%), body aches (45%/22%), and headaches (58%/46%) were reported by significantly more RT positives compared to negatives. The respective differences were even more pronounced ($p<0.001$) among ELISA-positives compared to negatives with >50% of those positive reported impaired smell or taste compared to less than 7% among the group of ELISA-negatives ($p<0.00001$).
In logistic regression models, shift work and belonging to the lowest quartile of the exposure prevention score were significantly associated with seropositivity in both tests. Exposure towards children was inversely associated with seropositivity, however, in the finally adjusted model only significant for those that were RT-positive, but not ELISA-positive, reflecting the lower specificity of the former.
Conclusion: The endemic infection rate in HCW was high. HCW adhering to preventive measures in everyday life had lower infection rates.
Disclosure of Interests: Manuel Beck: None declared, Alexandra Nieters: None declared, Marta Rizzi: None declared, Ulrich Salzer: None declared, Jens Thiel Speakers bureau: BMS, Nils Venhoff Speakers bureau: Novartis, Nicole Peter: None declared, Hermann Eibel: None declared, Reinhard Voll Speakers bureau: Novartis, Grant/research support from: BMS, Pfizer, Novartis, Stephanie Finzel Speakers bureau: Novartis
DOI: 10.1136/annrheumdis-2021-eular.3780

AB0702

PITFALLS IN THE DIAGNOSIS OF COVID-19 – EXPERIENCES FROM A RHEUMATOLOGY OUTPATIENT CLINIC

S. G. Werner[1], H. E. Langer[1], P. Höhenrieder[2], R. Chatelain[2,3]. [1]*RHIO (Rheumatology, Immunology, Osteology) Düsseldorf, RHIO Research Institute Düsseldorf, Düsseldorf, Germany*; [2] *University of Witten-Herdecke, Faculty of Health, Witten, Germany*; [3]*Evangelical Hospital Düsseldorf, Departement of Dermatology, Düsseldorf, Germany*

Background: PCR (Polymerase Chain Reaction) is generally considered the gold standard for confirming the diagnosis in the early stages of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection. However, in our rheumatology outpatient clinic we observed a significant discrepancy between clinical evidence of COVID-19 and PCR results.
Objectives: Aim of this retrospective study was to analyze the significance of PCR and serologic tests in the diagnosis of COVID-19 (Corona Virus Disease 2019) in a cohort of patients with rheumatic diseases.
Methods: Between March 2020 and January 2021, 35 patients with a history of established COVID-19 or typical signs and symptoms were identified on the occasion of a routine rheumatology follow-up examination in our institution. Previous diagnostic work-up in external facilities (results of PCR or antibody testing, imaging) was documented. Antibody ELISA-tests (IgG, IgA, IgM, Euroimmun) were performed in patients reporting typical signs and symptoms of COVID-19 in the past.
Results: PCR diagnostics had been performed in 15/35 patients (43%), in 13/35 (39%) at the onset of the first symptoms, in 2 subjects only 2 months later. PCR was positive in 7/13 (54%) of those tested early, but negative in the two patients tested later. In 29/35 patients (83%) SARS-CoV-2-ELISA tests were performed on the occasion of the routine rheumatologic examination (interval between first symptoms and testing on average 98 days, median86, range 4-283 days). In two of the initially negative individuals the second PCR was positive. ELISA tests were positive in all patients. SARS-CoV-2 IgM antibodies were positive in only two patients (however 55 and 71 days after disease onset), n=8/29 (28%) IgG only, n=9/29 (31%) IgG and IgA, n=12/29 (41%) IgA only. In these subjects, IgG antibodies did not develop even in the further course. Antibody titers were in part very high, but in part also very low (only just above the normal value), so even low titers were diagnostic obviously. In all patients with negative PCR, ELISA was positive and retrospectively led to confirmation of the diagnosis. Only in 13/35 patients (37%) diagnosis had been made with the onset of the first symptoms or in the course of clinically manifest disease and had led to appropriate quarantine measures and contact tracing by the health authorities. In contrast, in the majority of patients (63%), the diagnosis of COVID-19 infection was only made retrospectively on the occasion of a routine rheumatologic follow-up. However, 5 of these 22 patients (23%) had quarantined themselves during the symptomatic phase. Titer histories were available from 12 patients. The titer became negative in 7 patients, after a mean of 188 days (median 202, min 51, max 296 days), and remained positive in 5 individuals (mean 190 days, median 191, min 122, max 260 days). The change of the titer was independent of disease severity or antirheumatic therapy.
Conclusion: The results suggest that the importance of PCR in the diagnosis of COVID-19 may be overestimated. Therefore, antibody testing for SARS-CoV-2 should be performed in cases of clinical suspicion and negative PCR. In antibody diagnostics, special features were observed compared to other viruses, in particular, in some patients only low antibody titers or the absence of seroconversion with lack of development of IgG antibodies. Normalization of antibody titers in some patients supports the recommendation to vaccinate even after expired COVID-19 disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3798

AB0703

THE COURSE OF COVID-19 INFECTION IN PATIENTS WITH ARTHRITIS RECEIVING TARGETED DMARDS

E. Koltsova[1,2], G. Lukina[2], E. Shmidt[3], K. Lytkina[4], E. Rozochkina[2], E. Zhilyaev[5,6]on behalf of MUAR. [1]*Research Institute of the Organization of Health and Healthcare Management, Rheumatology, Moscow, Russian Federation*; [2]*Moscow Clinical Scientific Center, Rheumatology, Moscow, Russian Federation*; [3]*City Clinical Hospital 1 named after N.I. Pirogov, Rheumatology, Moscow, Russian Federation*; [4]*City Clinical Hospital#4, Rheumatology, Moscow, Russian Federation*; [5]*Russian Medical Academy of Continuing Professional Education, Rheumatology, Moscow, Russian Federation*; [6]*CJSC European Medical Center, Rheumatology, Moscow, Russian Federation*

Background: WHO declared the COVID-19 outbreak as a pandemic on March 12th, 2020. Assessing the risk of severe course in patients with rheumatic diseases, especially those who receive targeted immunosuppressive treatment, is an urgent problem for rheumatologists.
Objectives: determine the relationship between used targeted biologic and synthetic DMARDs (tDMARDs) and the severity of course of COVID-19 infection.
Methods: The analysis included the data of patients with chronic arthritis and COVID-19, used tDMARDs. COVID-19 infection was confirm by serology tests or immune system molecules (immunoglobulins/antibodies). The presence of symptoms, the need for hospitalization, and the need for oxygen therapy were considered as indicators of the severity of the infection. We also analyzed the spread of the lung involvement according to CT data, symptoms during the disease (fever, cough, anosmia, diarrhea).
Results: Analyses included 78 patients, among them 32 patients has ankylosing spondylitis, 31 patients - rheumatoid arthritis, 12 patients has psoriatic arthritis, 3 patients - juvenile arthritis. The average age of the included patients was 51,8 ± 11,69. Most of patients used TNF inhibitors - 43 (Adalimumab -10, Golimumab -4, Infliximab – 4, Certolizumab pegol -3, Etanercept – 22), JAK inhibitor tofacitinib used 13 patients, 5 patients each was treated with Abatacept and Tocilizumab, 3 patients used Rituximab and 2 patients each used Netakimab and Ustekinumab (Table 1). None of the patients included in the analysis required treatment in the ICU and/or mechanical ventilation. The course of the disease in patients treated with tDMARDs did not seem to be more severe than in 5 patients with arthritis who stopped treatment with tDMARDs before the onset of the pandemic. There was a direct correlation between the severity of the infection and the age of the patients ($p=0.007$). There were no significant differences in the severity of the infection depending on the drug, including when adjusting for age.

Conclusion: COVID-19 does not look extremely dangerous in patients with rheumatic diseases, used target DMARDs. Used of tsDMARDs doesn't reliably increase the risk of COVID-19 severity. There is reliable correlation between age and COVID-19 severity.

Table 1. Cohort characteristics

Drugs	Mean age	Number of patients	Patients with symptoms	Hospitalized patients	Asymptomatic course
Adalimumab	41,0±11,4	10	9	2	1
Golimumab	51,0±11,03	4	4	0	0
Infliximab	42,7±11,8	4	0	0	4
Certolizumab	41,6±11,7	3	3	0	0
Etanercept	50,7±11,4	22	20	6	2
Tofacitinib	56,8±10,4	13	12	2	1
Abatacept	57,4±10,9	5	4	1	1
Tocilizumab	48,8±10.9	5	3	1	2
Rituximab	55,6±10,7	3	3	1	0
Netakimab	44,0±15,8	2	2	1	0
Ustekinumab	48,0±10,5	2	1	0	1

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3867

AB0704 TELEMEDICINE AT THE TIME OF COVID-19: THE EXPERIENCE WITH RA PATIENTS TREATED WITH JAK-INHIBITORS

C. Garufi[1], F. R. Spinelli[1], S. Mancuso[1], F. Ceccarelli[1], F. Conti[1]. [1]*Sapienza University of Rome, Reumatologia, Dipartimento di Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Roma, Italy*

Background: The spread of COVID-19, the lockdown, the limited access to care reevaluated the role of tele-consultation and self-assessment.
Objectives: Our aim was to evaluate in a cohort of Rheumatoid Arthritis (RA) patients treated with JAK-inhibitors (JAKi): the self-assessed disease activity during lockdown, the lockdown impact on fatigue, anxiety, depression and the prevalence of Covid-19.
Methods: We enrolled RA patients treated with baricitinib or tofacitinib. At baseline (BL) and follow-up we collected: patients' demographic data, composite disease activity indices (CDAI, $DAS28_{CRP}$), global assessment (PGA), pain visual analogue scale (VAS), FACIT (functional assessment of chronic illness therapy) and a self-rating scale for disease impact on anxiety and depression (Zung-A/D). Patients were instructed on how to perform self-assessment through video-material and fulfilled the online form of "Rheumatoid Arthritis Impact of Disease" (RAID)[1] and "RA Disease Activity Index" (RADAI). To capture the pandemic effect, we compared patients in different status (remission, low, moderate and high-disease activity) at the last in-person visit (preCoV) through the $DAS28_{CRP}$ and CDAI, to the tele-health visit (THV), measured by the RAID. BL and pre-CoV ZUNG-A, ZUNG-D, FACIT questionnaires were compared with the online results during the pandemic. Exposure, tests and symptoms of Covid-19 were recorded. Data were expressed as mean±standard deviation or median(IQR) according to distribution.
Results: Twenty patients (median age 58.2±11.9 and mean disease duration 153.5 ± 112.7 months) were treated with tofacitinib and 27 with baricitinib. The median time-lapse between the pre-CoV visit and the THV was 12 (IQR 4) weeks. DAS28CRP and CDAI significantly decreased from BL to pre-CoV visit. During the last in-person visit, 21 patients (48.83%) were in remission, 9 (20.93%) in low disease activity; according to the RAID, 15 (31.91%) and 7 (14.89%) patients were respectively in remission and low disease activity during the THV (Table A). PGA and pain significantly decreased from BL to pre-Cov visit but worsened during the lockdown (Table A). FACIT remaining stable during THV. At THV, we detected a significant improvement of anxiety from BL (Zung-A) and a tendency to lower depression scores compared to BL (Table A). JAKi showed a good safety profile considering Covid-19 symptoms, none of the patients was diagnosed with SarsCoV2 infection.
Conclusion: This is the first study on virtual assessment in RA patients treated with JAKi. The unique social experiment of the pandemic impaired the clinical response already achieved before the lockdown, without a collateral worseling of FACIT, anxiety and depression.
REFERENCES:
[1] Gossec L, et al. *Ann Rheum Dis*. 2009
[2] Stucki G, et al. *Arthritis Rheum*. 1995

Table A. DAS28, CDAI, RAID scores and patient-reported outcomes assessment at baseline and during the follow-up

		BL	pre-CoV	THV
DISEASE ACTIVITY		**N (%)**	**N (%)**	**N (%)**
REMISSION	**DAS28**	0 (0%)	21 (48.8%)	
	CDAI	0 (0%)	10 (22.7%)	
	RAID			15 (31.9%)
LOW DISEASE	**DAS28**	1(2.1%)	9 (20.9%)	
	CDAI	7(14.8%)	23 (52.2%)	
	RAID			7 (14.9%)
MODERATE	**DAS28**	33 (70.2%)	12 (27.9%)	
	CDAI	17 (37.1%)	8 (18.1%)	
	RAID			13 (27.6%)
HIGH	**DAS28**	13 (27.6%)	1 (2.3%)	
	CDAI	23 (48.9%)	3 (6.8%)	
	RAID			12 (25.5%)
GH		70 (30)	20 (49.5)*	45 (45)*#
Pain		70 (28)	25 (45.5)*	40 (48.5)*#
Zung A		37 (9)	37 (10.2)	35 (14)*
Zung-D		39 (17)	39 (13)*	38 (12)
FACIT		11.5 (17.2)	8 (19.5)	7(15)

* p≤0.001 vs BL# p ≤0.04vs preCoVData expressed as median (IQR)

Disclosure of Interests: Cristina Garufi: None declared, Francesca Romana Spinelli Speakers bureau: Abbvie, Eli Lilly, Consultant of: Gilead/Galapagos, Eli Lilly, Grant/research support from: Pfizer, Silvia Mancuso: None declared, Fulvia Ceccarelli: None declared, Fabrizio Conti Speakers bureau: Abbvie, Eli Lilly, Sanofi, Pfizer, Consultant of: Gilead/Galapagos
DOI: 10.1136/annrheumdis-2021-eular.3892

AB0705 SHORT-TERM OUTCOMES OF COVID-19 IN PATIENTS WITH RHEUMATIC DISEASES WHO ARE TREATED BY BIOLOGICAL AND TARGETED SYNTHETIC DMARDS: OBSERVATIONAL SINGLE-CENTER STUDY

E. Luchikhina[1], D. Karateev[1], O. Semenova[1], O. Matveychuk[1], T. Kuznetsova[1]. [1]*Moscow Regional Research and Clinical Institute n.a. M.F. Vladimirsky (MONIKI), Moscow Regional Rheumatology Center and Department of Rheumatology, Moscow, Russian Federation*

Background: The course of new coronavirus infection in patients with rheumatic diseases (RD) undergoing treatment with biological and targeted drugs is still poorly understood.
Objectives: To study outcomes of COVID-19 in patients with RD receiving treatment biological and targeted synthetic DMARDs.
Methods: We studied cases of COVID-19 in patients with RD, included in "Moscow regional registry of patients with rheumatic diseases receiving treatment with biological and targeted synthetic drugs" – observational cohort, started in 2018. A total number of patients, included in the registry, is 1048 at December 2020.
Results: By January 2021, 44 known cases of COVID-19 were registered among patients included in the registry (4,2%). This group included 29 (65,9%) females, 15 (34,1%) males, with mean age 45,09±12,7 (median 47,0 [34,0; 57,0]) y.o. The vast majority of patients had rheumatoid arthritis (19, 43,2%) and ankylosing spondylitis (19, 43,2%), there were 3 (6,8%) patients with psoriatic arthritis, and one patient each (2,3%) with systemic lupus erythematosus, systemic sclerosis, and ANCA-vasculitis. Before COVID-19, 20 (45,5%) patients received TNF inhibitors (adalimumab, infliximab, etanercept, certolizumab, golimumab), 7 (15,9%) – IL-6 receptor inhibitors (tocilizumab, sarilumab), 7 (15,9%) – rituximab (period between last infusion and COVID-19 was 1-4 months), 5 (11,4%) – sekukinumab, 2 (4,5%) – tofacitinib, and one patient each (2,3%) received abatacept and ustekinumab. Also, 22 (50%) received methotrexate, 4 (9,1%) – leflunomide, 3 (6,8%) - mycophenolate mofetil, 1 (2,3%) – sulfasalazine; 12 (27,3%) took oral steroids. COVID-19 presented as mild disease in 23 (52,3%) patients, and 21 (47,7%) had viral interstitial pneumonia verified by computed tomography. 16 (36,4%) patients were hospitalized, only one patient underwent artificial lung ventilation. We found no significant associations between particular diagnosis and treatment on the one hand, and hospitalization for COVID-19 on the other hand. For treatment of COVID-19, two (4,5%) patients did not receive any medications, and the rest of patients received antiviral and antibacterial therapy according to standardized protocol. In addition, corticosteroids were administered for COVID-19 in 15 (34,1%) patients, mainly (12 cases) in hospital, and two (4,5%) patients in hospital were treated by tocilizumab. The outcome in all cases was favorable, all patients successfully recovered from the new coronavirus infection.

Conclusion: In this observational study, we found no association between biologic and targeted therapy for rheumatic diseases and severe course of new coronavirus infection, as well as with the need for hospitalization for COVID-19. The outcome of COVID-19 was favorable in all patients receiving treatment with biological and targeted synthetic drugs for rheumatic diseases.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3997

AB0706 ASSOCIATED RISK FACTORS AND OUTCOMES IN HOSPITALISED COVID-19 PATIENTS WITH BIOLOGICS AND JAK-INHIBITORS: A REPORT FROM A CENTER SPECIALISED IN IMMUNE-MEDIATED DISEASES

A. M. Anzola Alfaro[1,2,3], L. R. Caballero Motta[1,2,3], J. C. Nieto González[1,2,3], L. Menchen Viso[4,5], O. Baniandrés[4,6], C. Lobo Rodríguez[5], I. Monteagudo[1,2,3], J. M. Alvaro Gracia[1,2,3], C. Gonzalez[3,7,8]. [1]*Gregorio Marañón Hospital, Rheumatology, Madrid, Spain*; [2]*Centro de Enfermedades Inflamatorias Mediadas por la Inmunidad (CEIMI), Rheumatology, Madrid, Spain*; [3]*Fundación Investigación Biomedica Hospital Gregorio Marañón, Rheumatology, Madrid, Spain*; [4]*Gregorio Marañón Hospital, Gastroenterology, Madrid, Spain*; [5]*Centro de Enfermedades Inflamatorias Mediadas por la Inmunidad (CEIMI), Nurse Supervisor, Madrid, Spain*; [6]*Centro de Enfermedades Inflamatorias Mediadas por la Inmunidad (CEIMI), Gastroenterology, Madrid, Spain*; [7]*Centro de Enfermedades Inflamatorias Mediadas por la Inmunidad (CEIMI), Dermatology, Madrid, Spain*; [8]*Gregorio Marañón Hospital, Dermatology, Madrid, Spain*

Background: There's little data of patients with immune diseases (ID) treated with biologic and JAK-inhibitors and COVID19. Current consensus is to keep treatment, however more studies are needed to ascertain the risk in these patients.
Objectives: To describe the associated risk factors and outcomes in hospitalized patients with ID treated with biologics and JAK-inhibitors of a tertiary center.
Methods: Observational retrospective study of patients with COVID19 from March 1st 2020 to January 31st 2021. Out of all the patients receiving subcutaneous (SC) or intravenous (IV) biologics and oral (PO) JAK-inhibitors, we selected those requiring hospitalization due to pneumonia for analysis. We collected demographic data, comorbidities, seasonal flu vaccination, smoking history and the outcome (discharge/admission in an intensive care unit (ICU)/death). We used a composite index (Charlston's index) for comorbidities.
Results: Of 153 patients, 29 (18.9%) were hospitalized. 18 (62%) were women with a median age of 61 (IQ 52-69). 14 (48.2%) had rheumatoid arthritis, 5 (17%) had axial spondylarthritis and 4 (13.7%) had Chron's disease. The main IV was Rituximab in 3 (50%), and abatacept, infliximab and vedolizumab had one each. Of the SC, tocilizumab and adalimumab had 5 (22.7%) each, etanecept and golimumab had 3 (13.6%) each and secukinumab, ustekinumab and abatacept had 2 (9%) each. The PO was tofacitinib. There were no outcome differences for each treatment.
24 (82.7%) patients had at least 1 comorbidity with significative difference between patients (Table 1). There were 6 (20.6%) deaths, 3 (50%) in the ICU, 2 (33%) did not meet the ICU criteria, and 1 (16%) before ICU admission. None them had the same ID.

Table 1. Baseline data.

Variables, (%)	Total 29 (100)	Deaths 6 (20.6)	Discharged 23 (79.3)	P
Women (%)	18 (62)	4 (66.6)	14 (61)	0.79
Age, Median (IQ range)	61 (52-69)	69.5 (62-78.5)	59.9 (51-65.5)	0.09
Flu vaccine (%)	15 (51.7)	5 (83.3)	10 (43.7)	0.08
ICU (%)	8 (27.5)	3 (50)	5 (22)	0.16
Treatment				
IV (%)	6 (20.1)	**4 (66.7)**	2 (8.7)	0.001
SC (%)	22 (75.8)	**2 (33.3)**	20 (87)	<0.0001
PO (%)	1 (3.4)	0 (0)	1 (4.3)	0.6
Comorbidities				
Charlston, Mean (standard deviation)	2.72 (+/-1.6)	**5.16 (+/- 1.8)**	2.08 (+/-1.5)	<0.0001
Hypertension/HTA (%)	16 (55)	5 (83.3)	11 (48)	0.11
Dyslipidemia/DL (%)	12 (41.3)	4 (66.7)	8 (34.8)	0.15
Obesity (%)	10 (34.5)	1 (16.7)	9 (39.1)	0.30
Chronic obstructive pulmonary disease/COPD (%)	3 (10.3)	**3(50)**	0 (0)	<0.0001
Heart disease (%)	8 (27.5)	**4 (66.6)**	4 (17.4)	0.01
Chronic kidney disease/CKD (%)	7 (24.1)	**4 (66.6)**	3 (13)	0.006
Diabetes mellitus /DM (%)	7 (24.1)	**3 (50)**	4 (17.4)	0.001
Previous or current smokers (%)	9 (31)	3 (50)	6 (26)	0.26

Conclusion: The rate of COVID19 hospitalization in our patients was comparable to the general population's (between 19-24% from 60 years plus) and the risk of in-patient death is also similar, around 24%[1]. Our study suggests that neither their ID nor their treatment influences their risk of a worse outcome.
COPD, DM and previous heart disease were associated with worse outcome; however it seems that the main prognostic factor was the overall impact of comorbidities associated; as measured by the Charlston's index, being significantly higher in the patients with a fatal outcome.
A fatal outcome was more likely in IV biologics, however it could be explained by indication bias probably due to higher comorbidity and disability in these patients rather than an independent prognostic variable.
REFERENCES:
[1] Mesas AE et al. Predictors of in-hospital COVID-19 mortality: A comprehensive systematic review and meta-analysis exploring differences by age, sex and health conditions. PLoS One. 2020 Nov 3;15(11)
[2] Jovani, V et al.Incidence of severe COVID-19 in a Spanish cohort of 1037 patients with rheumatic diseases treated with biologics and JAK-inhibitors. ARD 2020–218152.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4000

AB0707 RHEUMATOLOGY PATIENT CARE IN THE COVID-19 PANDEMIC: TELEMEDICINE, DELEGATION, PATIENT SATISFACTION AND VACCINATION BEHAVIOUR

T. Thiele[1], S. Beider[1], H. Kühl[1], G. Miehlke[1], A. Cossmann[1], A. Holz[2], C. Happle[3], K. Hoeper[1], T. Witte[1], A. Jabonka[1], D. Ernst[1]. [1]*Medizinische Hochschule Hannover, Clinic for Rheumatology and Immunology, Hannover, Germany*; [2]*Rheumatologische Facharztpraxis, Rheumatologie, Hildesheim, Germany*; [3]*medizinische Hochschule Hannover, Clinic for Pediatric Pneumology, Allergology and Neonatology, Hannover, Germany*

Background: Use of telemedicine in Germany has increased due to the COVID-19 lockdown. Between March and May 2020, government restrictions led to cancellation of routine outpatient appointments to limit viral spread and optimize resources.
Objectives: This study assesses patient satisfaction of follow-up telemedicine appointments among patients known to be in disease remission, attending either secondary or tertiary care Rheumatology clinics. Appointments were conducted either by a rheumatologist or a qualified medical assistant for rheumatology (RFA). Additional data regarding perceived concerns arising from the COVID-19 pandemic as well as attitudes to vaccination were collected.
Methods: Methods: Patients not requiring adjustment of their DMARDs at the two previous attendances were considered stable. At cancellation of the planned attendance, patients were offered participation in the study and provided verbal informed consent. Participants were randomized to a telemedicine appointment by either a physician or RFA. Telemedicine appointments consisted of a standardized patient interview, including assessment of disease activity (modified CDAI score), attitudes to vaccination as well as current vaccine status and concerns about COVID-19. Following participation, all patients received a pseudonymized postal questionnaire to evaluate appointment satisfaction (FAPI-Score).
Results: In total 112/116 (96%) patients that were offered appointments, participated in the study (RA 50%, axSpA 30%, PsA 20%). Of these 88/112 (79%) returned their postal questionnaires. Overall patient satisfaction was excellent (mean 4.3/5 modified FAPI score) and did not differ between care setting or clinical status of the interviewer. RFAs conducted 19/112 (17%) of appointments, 6 (32%) of which required additional physician intervention. Change of DMARDs occurred in 19/112 (17%) appointments. Patients reporting a pain score ≥7 (VAS 1-10) were most dissatisfied with the telemedicine appointment (p=0.036). Concerns about COVID-19 correlated with disease activity: high disease activity (p = 0.031), presence of tender joints (p=0.001), high pain levels (p=0.009) correlated with concern of contracting COVID-19 or experiencing severe disease course. Only 38% of the patients had been vaccinated against pneumococci in the past 5 years and 54% had been vaccinated against influenza in 2019/2020.
Conclusion: Telemedicine can contribute to patient care in stable patients. RFAs can also contribute to patient care especially for follow-up appointment when patients are in remission. Vaccination rates and motivation needs to be improved as influenza and pneumococcal vaccination is recommended to all patients with rheumatic diseases without contraindications.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4005

AB0708

HIGH DRUG RETENTION RATES DESPITE B/TSDMARD INTERRUPTIONS IN COVID-19 PANDEMIC CHAOS

S. Gulle[1], Y. Erez[1], A. Karakas[1], T. Yüce İnel[1], S. B. Kocaer[2], T. Demirci Yıldırım[1], G. Can[1], İ. Sari[1], M. Birlik[1], F. Onen[1]. *[1]Dokuz Eylul University Faculty of Medicine, Rheumatology, Izmir, Turkey*; *[2]Kastamonu Research and Training Hospital, Rheumatology, Kastamonu, Turkey*

Background: A significant increased risk of COVID-19 related adverse outcomes of the biological or target-directed synthetic DMARDs (b/tsDMARDs) has not yet been reported. For this reason, it is recommended to continue b/tsDMARD treatments with maximum compliance with pandemic measures.
Objectives: The aim of this study was to evaluate the effects of patients using b/tsDMARDs on drug survival and rheumatic disease control during pandemic.
Methods: In this study, patients diagnosed with rheumatic disease using b/tsDMARDs and who were followed up during the 12-month period (January 2020-2021) including the onset of the Covid-19 pandemic at Dokuz Eylul University Faculty of Medicine Rheumatology Clinic were evaluated. In the first 3 months of the pandemic (March-June 2020), the patients skipped at least 2 cycles of treatment with the fear of Covid-19 infection except for infection / surgical reasons was considered as a disruption of the drug. The drug retention rates of the patients on b/tsDMARDs treatments during the pandemic process and the factors affecting this situation were evaluated.
Results: The rate of disrupting their b/tsDMARDs was higher in patients> 65 years of age, with a diagnosis of RA and who needed to come to the hospital for bDMARD treatment (p=0.007, p=0.015 and p=0.004, respectively).
The overall 1-year b/tsDMARD retention rates was found 91%. It was determined that a history of interruption in b/tsDMARD treatments in the first 3 months of the pandemic [OR: 1.28 (CI: 1.042-8.71), p=0.014] and the need to come to the hospital to receive bDMARD [OR: 0.59 (CI: 0.64-13.11), p=0.041] caused unresponsiveness to return to the same bDMARD treatment and a significant increase in the risk of discontinuation of the biologic treatment.
Conclusion: We conclude that it is important for patients to continue taking b/tsDMARD treatments without interruption in the days past abnormal periods such as pandemic conditions and to make sufficient effort for minimum dose of CS and low disease activity by determining patient-based risk.

Table 1. Demographic and clinical characteristics of b/tsDMARDs patients

	Total (n=521)	b/tsDMARD Continue (n=424) (82.4%)	b/tsDMARD Interruption (+) (n=97) (17.6%)	P
	Median (Min./Max.)	Median (Min./Max.)	Median (Min./Max.)	
Age, years	48 (18/86)	47 (18/82)	52 (21/81)	**0.008[t]**
Disease Duration, years	11,2 (2/43.3)	130 (22/490)	142 (22/519)	0.41[t]
b/ts DMARD Duration, months	40 (12/192)	40 (12/192)	40 (12/156)	0.176[t]
	n (%)	n (%)	n (%)	
Female	278 (53.4)	225 (53.1)	53 (54.6)	0.826
Most common rheumatic diseases				
AxSpa or other SpA	283 (54.3)	232 (54.7)	51 (52.6)	0.737
RA	134 (25.7)	100 (23.6)	34 (35.1)	**0.015[l]**
PsA	44 (8.4)	40 (9.4)	4 (4.1)	0.109
Vasculitis	32 (6.1)	27 (6.4)	5 (5.2)	0.817
Others	28 (5.4)	25 (5.9)	3 (3.1)	0.338
b/tsDMARD at Hospital/ Health center	140 (26.9)	102 (24.1)	38 (39.2)	**0.004[l] (OR: 0.59)**
b/tsDMARD administration route (IV)	137 (26.3)	100 (23.6)	37 (38.1)	**0.005[l]**
Active/Progressive Disease	92 (17.7)	14 (3.3)	78 (80.4)	**<0.001[l] (OR: 4.8)**
Start/continue with the same b/tsDMARD	55 (10.6)	3 (0.7)	52 (53.6)	**<0.001[p]**
Unresponsiveness, b/tsDMARD switch	16 (3.1)	9 (2.1)	7 (7.2)	**0.017[p]**
b/tsDMARD stopped permanently/deceased	29 (5.6)	9 (2.1)	20 (20.6)	**<0.001[ff]**
b/tsDMARD retention (Total)	474 (91)	406 (95.8)	68 (70.1)	**<0.001**

[t]Independent Samples t Test (Bootstrap), [p]Pearson Chi-Square Test (Monte Carlo), [ff]Fisher freeman Halton Test (Monte Carlo), [l]Linear-by-Linear Association Test(Monte Carlo, Exact), SD.: Standard deviation; * OR, Odds Ratio,

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4068

AB0709

CHARACTERIZATION OF NAILFOLD CAPILLAROSCOPY IN COVID-19: A CASE CONTROL STUDY

P. E. Bermudez Bermejo[1], R. Jimenez-Soto[2], A. Sanchez Rodríguez[1], A. Turrent[1], D. Mercado Velasco[2], I. Bravo-Lee[2], M. B. Colli-Cortés[3], E. Alvarez Hernandez[4], M. D. C. Amigo Castañeda[1]. *[1]ABC Medical Center, Rheumatology, Mexico City, Mexico*; *[2]ABC Medical Center, Internal Medicine, Mexico City, Mexico*; *[3]Regional Hospital "General Ignacio Zaragoza" ISSSTE, Rheumatology, Mexico City, Mexico*; *[4]Hospital General de Mexico, Rheumatology, Mexico City, Mexico*

Background: Nailfold capillaroscopy is a relatively easy-to-access, low-cost clinical tool that could help identify early coagulopathy in subjects with SARS-CoV-2, but specific findings vs. controls and its possible prognostic role has not been studied.
Objectives: To describe capillaroscopic findings and their usefulness in patients with COVID-19 compared to healthy controls.
Methods: We designed a cross-sectional study, carried out in a single care center for critical patients with SARS-CoV-2 pneumonia at the ABC Medical Center, Mexico City, which included patients from an intensive care unit (ICU) and internal medicine ward from March to April 2020. Demographic, biochemical and clinical features were collected. All patients signed the informed consent and the study was approved by the hospital ethics committee. All patients underwent nail capillary imaging of the 3 central fingers of each hand with a portable microscope with 60-100x magnification coupled to a smartphone with 7 megapixel images in an immersion medium. Capillaroscopy was performed in patients who did not have fever or hypothermia, or need vasopressors at the time of evaluation. Control subjects are healthy subjects matched on age and sex from a database of healthy controls without rheumatic diseases. Image evaluation of COVID-19 patients was performed in a blinded way for their characteristics. Prior to the analysis of the images, a pilot test was obtained with 4 rheumatologists in random cases, obtaining an acceptable global agreement in the visualization of capillaries and specific alterations of the nail bed. (Kappa = 0.58, p = 0.0019). Obtained data from capillaroscopies were used to be compared between severe and moderate cases of SARS-CoV-2 pneumonia. Additionally, we compared the findings against a healthy population in order to establish a reference.
Results: We included data from 27 patients and 32 controls with similar demographic features. Patients with COVID-19 patients had a mean age of 43 +/- 13.8 years, 63% female. Comorbidities were present in 44.4% with: type II Diabetes Mellitus 18.5%, systemic arterial hypertension 18.5%, and rheumatoid arthritis 3.7%. The mean length of stay time was 13 +/- 7.1 days, 48.1% were admitted to the ICU, and 40.7% required invasive mechanical ventilation. In the capillaroscopic review remarkable findings of patients vs. controls were hemosiderin deposits (33 vs 12.5%, p=0.05), less frequently observable capillaries (77 vs 100%, p=0.005), any abnormality in capillaries (25.9 vs. 6.3%, p=0.03). Of notice, specific findings in COVID-19 patients were capillary tortuosities in 19%, dilatation in 9.5%, serpentine pattern in 4.8%, bush pattern in 9.5% and decreased density in only 4.8% of the cases. No avascular areas or capillaries of neoformation were observed. Finally, the presence of hemosiderin was associated with worse presentation and risk factors for severe COVID-19: Male sex 66.7 vs. 27.8%, (p = 0.024); Admission to ICU 77% vs 33% (p = 0.029); BMI > 30 kg/m2 66.7 vs. 27.8% (p = 0.053). And risk for ICU admission OR = 7.0 (95% CI 1.098 - 44.6). No significant associations were found for abnormalities in capillary morphology.
Conclusion: We present one of the first reports of nailfold capillaroscopic findings in patients with COVID-19 and the first to compare to healthy controls. Previous data on this regard suggests the presence of endothelial dysfunction and microvascular complications such as micro hemorrhage or micro thrombosis. Further studies may confirm these findings and prognostic value for worse outcomes in COVID-19 patients.

REFERENCES:

[1] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507–13.
[2] Cutolo M, Cortes S. capillaroscopic patterns in rheumatic diseases. Acta Reumatol Port. 2007 Jan-Mar;32(1):29-36.

[3] Natalello G, De Luca G, Gigante L, et al. Nailfold capillaroscopy findings in patients with coronavirus disease 2019: Broadening the spectrum of COVID-19 microvascular involvement. Microvasc Res. 2021;133:104071.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4210

AB0710 ANISOCYTOSIS INDEX AS AN EARLY PREDICATOR OF HOSPITAL MORTALITY IN PATIENTS WITH COVID-19 PNEUMONIA FROM A LEVEL III HOSPITAL. LIMA PERU

J. Ravelo[1]. [1]*San Juan Bautista Clinic, Lima, San Juan de Lurigancho, Peru*

Background: RDW has been analyzed in recent decades as a poor prognostic factor, associated with an increased risk of mortality from all causes: heart disease, lung disease, sepsis, influenza, cancer, complications associated with heart failure, coronary disease, viral hepatitis, COPD, development of DM2, stroke and anemia, which makes it a nonspecific marker of disease with the potential to provide a stratified quantification of risk in a new disease.
Objectives: To determine if laboratory tests predict mortality in patients with COVID-19 pneumonia upon admission to hospital. Secondary outcome: evaluate if any laboratory parameter predicts longer hospitalization in patients with COVID-19 pneumonia.
Methods: Case control retrospective study of COVID-19 pneumonia patients, admitted to the Peruvian Air Force Hospital from April 6th to June 27th, 2020. Patients were divided in two groups: recovered and deceased and their laboratory parameters entered the statistical analysis. Cox regression was performed (95% CI, p value <0.05, as statistically significant). Bivariate analysis to compare the RDW means of recovered vs. deceased and multivariate analysis with binary logistic regression to evaluate the predictive value of RDW in relation to hospital mortality in our cohort. The statistical package Stata version 14.2 was used.
Results: 186 patients were included. The mean age of the recovered patients was 53.6 ± 16.4 years vs 75.9 ± 13.9 years in the deceased group (p <0.0001). The mean value of RDW was 13.14% in recovered vs. 13.96% of deaths (p< 0.0005), associated with an Odds Ratio (OR) of 1.66 (CI: 1.58-1.74) adjusted for the model.
Conclusion: The finding of a RDW ≥ 13% in patients with COVID-19 pneumonia was associated with higher mortality.
REFERENCES:

[1] Imam Z, Odish F, Gill I, O'Connor D, Armstrong J, Vanood A, et al. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. J Intern Med. 2020 Jun 22. DOI: 10.1111/joim.13119
[2] Foy BH,…….

Table 1. Characteristics and comorbidities in patients with COVID-19 Pneumonia

		Total (N:188)	Recovered (n:147)	Death (n:41)	P
Age(years)	Media (DS)	59.79 (17.48)	55.32 (15.64)	75.80 (14.15)	< 0.000 *
Sex	Femenino	81 (43.09 %)	64 (79.01 %)	17 (20.99 %)	0.813
	Masculino	107 (56.91 %)	83 (77.57 %)	24 (22.43 %)	
Hypertension	No	145 (77.13 %)	119 (82.07 %)	26 (17.93 %)	0.018
	Si	43 (22.87%)	28 (65.12 %)	15 (34.88 %)	
Diabetes mellitus	No	158 (84.04 %)	124 (78.48 %)	34 (21.52 %)	0.825
	Si	30 (15.96 %)	23 (76.67 %)	7 (23.33)	
ESRD	No	179 (95.21 %)	143 (79.89 %)	36 (20.11 %)	0.012
	Si	9 (4.79 %)	4 (44.44 %)	5 (55.56 %)	
Asthma	No	183 (97.34 %)	145 (79.23 %)	38 (20.77 %)	0.036
	Si	5 (2.66 %)	2 (40 %)	3 (60 %)	
Obesity	No	181 (96.28 %)	142 (78.45 %)	39 (21.55 %)	0.659
	Si	7 (3.72 %)	5 (71.43 %)	2 (28.57 %)	
Other comorbidities	No	133 (71.12 %)	114 (85.71 %)	19 (14.29 %)	< 0.000
	Si	54 (28.88 %)	32 (59.26 %)	22 (40.74 %)	
Leukocytes	Media (DS)	9.68 (4.44)	9.49 (4.52)	10.35 (4.13)	0.281*
Lymphocytes	Media (DS)	1.44 (0.88)	1.59 (0.90)	0.90 (0.53)	< 0.000*
CRP	Media (DS)	94.04 (95.61)	82.34 (88.95)	136.48 (107.50)	0.001*
pO2	Media (DS)	83.73 (24.39)	83.94 (22.28)	82.98 (31.18)	0.827*
pCO2	Media (DS)	33.40 (5.06)	33.32 (4.96)	33.67 (5.47)	0.699*
Sat O2	Media (DS)	95.73 (8.74)	95.23 (5.10)	97.55 (16.09)	0.138*
Admission days	Media (DS)	11.75 (9.04)	10.88 (7.08)	14.82 (13.59)	0.013*
TSS Score	Media (DS)	7.33 (3.50)	6.59 (3.03)	10.05 (3.80)	< 0.000**
RDW	Media (DS)	13.323 (1.284)	12.971 (1.081)	13.411(1.715)	<0.003**

Table 2. Multivariate Analysis Using Binary Logistic Regression to Predict Mortality

	Adjusted OR	p	CI 95%
RDW	1.67	0.004	1.18 –2.35
Lymphocytes	0.27	0.012	0.09 – 0.74
Age	1.08	< 0.001	1.04 – 1.13

Disclosure of Interests: Jorge Ravelo Speakers bureau: Less than 10 speech for Grunenthal and Novartis, Paid instructor for: 1 time for Riverpharma, Grant/research support from: I am working as PI doing sponsored clinical trials since 2008
DOI: 10.1136/annrheumdis-2021-eular.4212

AB0711 FOLLOW-UP OF PATIENTS UNDER BIOLOGICS IN THE ERA OF LOCKDOWN

V. F. Boussougou[1], K. Nassar[1], S. Janani[1]. [1]*University Hospital of Ibn Rochd, Department of Rheumatology, Casablanca, Morocco*

Background: The management of patients with inflammatory rheumatic diseases under biologics has raised many questions about the global management of patients in the time of COVID-19 pandemic. This period could have been particularly painful for the patients due to the virus itself, and to the difficulty to access to healthcare facilities due to the lockdown.
Objectives: To assess the impact of the lockdown in patients under biologics.
Methods: This is a descriptive study, conducted between 03/01/2021 and 07/31/2021 in the Department of Rheumatology of the University Hospital of Ibn Rochd in Casablanca. Inclusion criteria were all patients on biologics during the lockdown period. The number of painful, swollen joints, pain visual analogue scale, and disease activity were collected before and during the lockdown.
Results: Thirty-one patients under biologics were included. The average age was 43.4 years. There were 17 males and 14 females (sex ratio M/F 1,21). Cormibidities were hypertension and type 2 diabetes (9.7%), hypertension and dyslipidemia (6.5%), arrhythmia (6.5%), smoking (9.7%), hypertension and dysthyroidism (3.2%). All the patients were under biologics with an average duration of 2 years distributed as follows: 3 patients on etanercept (9.67%), 8 patients on tocilizumab (28.8%), 10 patients on infliximab (32.25%), 5 patients on adalimumab (16.12%)), 4 patients under golimumab (12.90%), 1 under secukinumab (3.22%). Biologics were associated with conventional synthetic disease-modifying antirheumatic drugs in 38.7% (methotrexate 12.9%, salosopyrine25, 8%), corticosteroids in 25.7%, non-steroidal anti-inflammatory drugs in 16.1%. The disease activity before COVID-19 of the patients was: 48.39% weak activity, 35.4% remission, 16.13% moderate activity. No patient reported a flare of the disease. During lockdown, 5 patients reported a flare of their disease (16.12%) They were followed for: 2 spondyloarthritis, 1 rheumatoid arthritis, 1 psoriatic arthritis, 1 adult onset Still's disease. All the patients have temporarily stopped their drugs because they couldn't come to their appointments because of the lockdown.
Conclusion: Our study notes that the patients who kept their follow-up during lockdown have maintained a control of their disease activity. Our results are consistent with the observations of a French study on the impact of lockdown on the activity of rheumatoid arthritis. However, those who couldn't come to their control appointment due to the lockdown had a flare of their disease. This study remains limited due to the monocentric nature and the small size of our sample.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4271

AB0712 THE INCIDENCE OF SARS-COV-2 INFECTION IN PATIENTS WITH RHEUMATIC DISEASES ON THERAPY BIOLOGICAL DISEASE MODIFYING ANTIRHEUMATIC DRUGS

A. Dadalova[1], E. Vasilenko[1], R. Samigullina[1], V. Mazurov[1]. [1]*North-Western State Medical University named after I.I. Mechnikov, Department of Therapy,*

Rheumatology, Examination of Temporary Disability and Quality of Medical Care named after E.E.Eichwald, St. Petersburg, Russian Federation

Background: At the moment, a highly relevant issue is the course of SARS-CoV-2 infection in patients with rheumatic pathology, especially, those receiving therapy with biological disease modifying antirheumatic drugs.
Objectives: of the current study to assess the prevalence and course of SARS-CoV-2 infection in patients receiving various biological disease modifying antirheumatic drugs.
Methods: to assess the severity of the course of SARS-CoV-2, discharged epicrisis from hospitals or the conclusion of computed tomography were used. The average age of the patients ranged from 41.4 + 11.6 years. In the evaluated sample, 47 patients (49.47%) were males. Among the infected of SARS-CoV-2 were patients with rheumatoid arthritis - 45 (47.4%), spondyloarthritis - 39 (41.1%), systemic connective tissue diseases - 11 (11.5%).
Results: Since March 2020, among the 1319 patients with rheumatic diseases observed at the St. Petersburg Center of therapy biological disease modifying antirheumatic drugs, 95 patients (7,2%) had SARS-CoV-2 infection. In 57,9% (55 patients) there was a mild course of infection, in 35,8% of cases (34 patients) - a moderate course, in 6,3% (6 patients) - a severe course. Inpatient treatment was received by 29,5% (28 patients). A favorable outcome was noted in 95.8%, and a lethal outcome in 4,2%. The use of interleukin-6 inhibitors was required in 2,1% of patients (2) due to the development of a cytokine storm. The structure of the received biological therapy in the severity of the course is shown in Table 1.

Table 1. The structure of the received biological therapy in the severity of the course SARS-CoV-2 infection

	Mild course	CT-1 (<25%)	CT-2 (25-50%)	CT-3 (50-75%)	CT-4 (>75%)
TNF-α inhibitors, n (%)	30 (31,6)	11 (11,6)	7 (7,3)	3 (3,2)	0 (0,0)
anti B-cell therapy (rituximab), n (%)	2 (2,1)	1 (1,1)	2 (2,1)	1 (1,1)	2 (2,1)
Abatacept, n (%)	3 (3.2)	0 (0,0)	2 (2,1)	0 (0,0)	0 (0,0)
Janus kinase inhibitors, n (%)	5 (5,3)	1 (1,1)	1 (1,1)	0 (0,0)	0 (0,0)
Interleukin-6 inhibitors, n (%)	6 (6,3)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Interleukin-17 inhibitors, n (%)	8 (8,4)	2 (2,1)	2 (2,1)	0 (0,0)	0 (0,0)
Other, n (%)	1 (1,1)	4 (4,2)	1 (1,1)	0 (0,0)	0 (0,0)

Among 95 infected patients, who were observed in the center, 51 received therapy with TNF-α inhibitors (8.5% of the total number of patients receiving therapy), 8 - rituximab therapy (2.7%), 5 - abatacept (6.3%), 7 - Janus kinase inhibitors (0.9%), 6 – interleukin-6 inhibitors (9.2), 12 - interleukin -17 inhibitors (14.1%), 6 patients treated with other drugs (10%).

Conclusion: Taking into account the SARS-CoV-2 pandemic, further study of the course of infection in patients with rheumatic diseases, including those receiving biological therapy, is required. More information is also needed on the safety and efficacy of vaccination in this patient population.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4323

Pain in rheumatic diseases, including fibromyalgia

AB0713 EVALUATION OF THE EFFECTIVENESS OF LASER THERAPY IN THE TREATMENT OF RHEUMATOID ARTHRITIS

N. Zhuravleva[1], L. Karzakova2, S. Kudryashov3, E. Petrova[4]. [1]*Federal State Budgetary Educational Institution of Higher Education "The Chuvash State University named after I.N. Ulyanov", Department of Internal Medicine, Cheboksary, Russian Federation*; [1]*Federal State Budgetary Educational Institution of Higher Education "The Chuvash State University named after I.N. Ulyanov", Department of Internal Medicine, Cheboksary, Russian Federation*; [1]*Federal State Budgetary Educational Institution of Higher Education "The Chuvash State University named after I.N. Ulyanov", Department of Internal Medicine, Cheboksary, Russian Federation*; [4]*Federal State Budgetary Educational Institution of Higher Education "The Chuvash State University named after I.N. Ulyanov", Department of Instrumental Diagnostics, Cheboksary, Russian Federation*

Background: Despite the fact that the introduction of biological disease-modifying antirheumatic medicines (bDMARDs) and the early start of treatment for rheumatoid arthritis (RA) can effectively stop the inflammatory process in RA, a fairly large number of patients continue to experience joint pain [1]. It is assumed that in some cases, joint pain in patients with RA is not associated with the inflammation, so it requires consideration of the possibility of using alternative strategies for the treatment of RA.
Objectives: The aim of the research is to study the effectiveness of laser therapy in the treatment of RA.
Methods: 114 patients with RA aged from 32 to 53 years have been monitored for 6 months. There were 82 women (71.9 %) and 32 men (28.1%) among them. The patients were randomly divided into 2 groups. The first group of patients (57 people) received basic medical therapy with methotrexate 15 mg intramuscularly once a week and nonsteroidal anti-inflammatory medicines (NSAIDs) on demand. The dose of methotrexate was selected taking into account the disease activity index DAS 28. The second group of patients (57 people) received basic medical therapy with methotrexate 15 mg intramuscularly once a week and NSAIDs on demand. In addition, the cutaneous low-intensity laser irradiation of the joints was added along the projection of the joint gap in a pulse mode with a wavelength of 0.89 microns. The pulse frequency is 80-1500 Hz, the pulse power is 5 W, the exposure time in the field is 1-2 minutes and the total radiation time per session is no more than 10 minutes [2]. The course of treatment consisted of 10 procedures (the device "Milta F-8 RD", Russia, Moscow). The course of laser therapy was repeated after 4 weeks. To assess clinical indicators, patients were examined using the SF-36 questionnaire before treatment and 6 months after the start of treatment.
Results: The survey after 6 months revealed the significant decrease in the severity of pain on the VAS from the initial average indicator 4.5±0.2 to 3.69±0.2 points ($p<0.01$) and morning stiffness from 60±5 to 40.8±4 minutes ($p<0.01$). In the first group, the dynamics of clinical indicators were not statistically significant: the intensity of pain decreased from 4.6±0.2 to 4.2±0.3 points ($p>0.05$) and the duration of morning stiffness reduced from 62±7 to 58.6±6 minutes ($p>0.05$). In the second group the decrease in the need for NSAIDs was observed in 21 patients, while in the first group the same was observed only in 10 patients ($p_{x2} = 0.020$).
Conclusion: Laser therapy in the treatment of patients with RA enabled to decrease the frequency of the need for NSAIDs and reduce morning stiffness. We recommend using laser therapy in patients with RA at the second radiological stage as an addition to basic therapy.
REFERENCES:
[1] Altawil R et al. *Arthritis Care Res (Hoboken).* 2016; 68(8): 1061-1068.
[2] Burger M et al. *Physiother Theory Pract.* 2017; 33(3): 184-197.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.238

AB0714 COMPARISON OF THE EFFECT OF SUBACROMIAL ADMINISTRATION OF HYALURONIC ACID AND PLATELET RICH PLASMA IN CASES OF DAMAGE TO THE TENDONS OF THE ROTATORS OF THE SHOULDER IN INDIVIDUALS OF DIFFERENT AGE GROUPS

V. Nesterenko[1,1], A. Karateev[1], E. Bialik[1], M. Makarov[1], S. Makarov[1], V. Bialik[1], M. Nurmukhametov[1], A. Chernikova[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Rheumatology, Moscow, Russian Federation*

Background: Everyone has had shoulder pain at least once in their life. From 70 to 80% of chronic pain in the shoulder joint is associated with subacromial impingement syndrome. The use of non-steroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids does not always meet the needs of patients and have a number of adverse reactions. Local administration of PRP and HA preparations is widely used for chronic shoulder pain. However, the question of the effectiveness of these drugs in patients of different ages has been insufficiently studied.
Objectives: To compare the efficacy of GLA and PRP in patients with chronic shoulder pain by age.
Methods: The study group included 100 patients, 46% women and 54% men, aged 51.5 ± 15.1, with chronic shoulder pain (≥3 months) caused by damage to the tendons of the muscles of the shoulder rotators. Patients <45 years old accounted for 34%, patients ≥45 years old - 66%. All patients were randomly divided into 2 groups. Patients in group 1 received 2 consecutive subacromial injections of GLK, groups 2 - 3 consecutive subacromial injections of PRP. Pain dynamics were assessed using a 100-mm visual analogue scale (VAS),

functional impairments according to ASS (American Shoulder and Elbow Surgeons Assessment) and CS (Constant Score), and a decrease in the need for NSAID use after 6 months. after the course of treatment.

Results: The dynamics of pain and functional disorders in the treatment of GLC and PRP did not differ. The pain decreased from 57.6 ± 17.8 to 30.2 ± 26.3 and 56.0 ± 14.6 to 31.8 ± 26.3 (p = 0.768), ASS from 54.7 ± 15.1 to 77.3 ± 22.5 and 54.8 ± 13.8 to 74.6 ± 22.4 (p = 0.552), CS from 47.8 ± 16.9 to 65.6 ± 19.3 and 59.2 ± 14.4 to 66.9 ± 17.4 (p = 0.245). In general, with the treatment of GLA and PRP, the dynamics of pain and functional disorders was significantly better in patients <45 years old than in patients ≥45 years old. So, pain according to VAS after 6 months. was 22.4 ± 26.3 and 35.5 ± 26.2 (p = 0.022), ASS 83.3 ± 20.9 and 72.1 ± 22.6 (p = 0.017), CS 76.2 ± 16, 1 and 63.2 ± 18.2 (p = 0.001). There was no need to take NSAIDs in 82.4% and 65.2% of patients (p = 0.103). No serious adverse reactions have been reported with the treatment of GLC and PRP.

Conclusion: The efficacy of GLA and PRP in chronic shoulder pain caused by damage to the tendons of the muscles of the rotator of the shoulder does not differ. The clinical response to both drugs was significantly higher in those under 45 years of age.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.517

AB0715 THE PREVALENCE OF FIBROMIYALGIA IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER AND THE RELATIONSHIP BETWEEN FATIGUE AND QUALITY OF LIFE

S. Ugurlu[1], T. Civi Karaaslan[2], Z. Toker Dincer[1], E. Tarakci[2]. *[1]Cerrahpasa Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*; *[2]Faculty of Health Sciences, Physiotherapy and Rehabilitation, Istanbul, Turkey*

Background: Familial Mediterranean Fever (FMF) can cause various muscle diseases. Because it is a chronic auto inflammatory disease, painful trigger points may be encountered in the examination due to a decrease in the pain threshold (1-3).

Objectives: The aim of this study was to determine the prevalence of Fibromiyalgia in patients with FMF, at the same time to identify the relationship between fatigue and quality of life.

Methods: Sixtyseven patients (38 female, 29 male) with FMF were enrolled in the study. They were diagnosed with FMF based on the Livneh diagnostic criteria (4). Fibromyalgia involvement of the patients was evaluated according to the Fibromyalgia Impact Questionnaire (FIQ). Patients with diagnose with other chronic disease were excluded. Fatigue Severity Scale (FSS) was used to evaluate fatigue. Quality of life was evaluated with Short Form-36 (SF-36).

Results: Respectively, the mean age, disease duration and body mass index were 34.46±12.69 years, 12.66±7.86 years and 24.96±5.42 kg/m^2. In addition, 65% of the patients had no rheumatic disease in their family history. The mean of scores of FIQ was 38.66±25.14, the mean of FSS was 38.07±17.56, the mean of SF-36-PCS was 45.55±10.54 and SF36-MCS was 30.93±17.39. Patients were categorized as mild (n=28), moderate (n=24) and severe (n=15) affected according to their FİQ score. The relationships of scores of FIQ, FSS and SF-36 were demonstrated Table 1.

Table 1. The correlations of FIQ, FSS and SF-36 scores.

		FSS	SF-36 PCS	SF-36 MCS
FIQ-mild	mean±sd	23.78±14.88	53.34±7.01	40.98±13.73
	r	0.595**	-0.014	-0.551**
	p	0.001	0.944	0.002
FIQ-moderate	mean±sd	45.75±10.83	41.09±8.89	38.13±9.19
	r	0.053	-0.379	-0.145
	p	0.806	0.068	0.498
FIQ-severe	mean±sd	52.46±10.11	38.13±9.19	20.32±15.68
	r	0.622*	-0.548*	-0.268
	p	0.013	0.035	0.333

-Pearson Correlation

Conclusion: Fibromyalgia symptoms can be seen in FMF. According to our results, it has been shown that patients with moderate and severe symptoms have increased fatigue levels and decreased quality of life. In the light of these results, we can say that also the fibromyalgia symptom of patients with FMF should be considered in the treatment.

REFERENCES:

[1] Sari, Ismail; Birlik, Merih; Kasifoglu, Timucin. Familial Mediterranean fever: an updated review. European journal of rheumatology, 2014, 1.1: 21.

[2] Alayli G, Durmus D, Ozkaya O, Sen HE, Genc G, Kuru O. Frequency of juvenile fibromyalgia syndrome in children with familial Mediterranean fever: effects on depression and quality of life. Clin Exp Rheumatol 2011; 29: S127-32.

[3] Langevitz P, Buskila D, Finkelstein R, Zaks N, Neuman L, Sukenik S, et al. Fibromyalgia in familial Mediterranean fever. J Rheumatol 1994; 21: 1335-7.

[4] Bashardoust, Bahman. Familial Mediterranean fever; diagnosis, treatment, and complications. Journal of nephropharmacology, 2015, 4.1: 5.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1288

AB0716 FIBROMYALGIA SYNDROME SEVERITY ACCORDING TO AGE CATEGORIES: RESULTS FROM A NATIONAL REGISTER

M. Di Carlo[1], S. Farah2, L. Bazzichi[3], F. Atzeni[4], M. Govoni[5], G. Biasi[6], M. DI Franco[7], F. Mozzani[8], E. Gremese[9], L. Dagna[10], A. Batticciotto[11], F. Fischetti[12], R. Giacomelli[13], S. Guiducci[14], G. Guggino[15], M. Bentivegna[16], R. Gerli[17], C. Salvarani[18], G. Bajocchi[19], M. Ghini[20], F. Iannone[21], V. Giorgi[22], M. Cirillo[4], S. Bonazza[5], S. Barbagli[6], C. Gioia[7], N. G. Marino[8], A. Capacci[9], G. Cavalli[10], A. Cappelli[11], F. Carubbi[23], F. Nacci[14], R. Ilenia[17], M. Cutolo[24], L. Sinigaglia[25], P. Sarzi-Puttini[22], F. Salaffi[1]on behalf of Italian Fibromyalgia Registry. *[1]Università Politecnica delle Marche, Dipartimento di Scienze Cliniche e Molecolari - Rheumatology Clinic, Jesi, Italy*; *[1]Università Politecnica delle Marche, Dipartimento di Scienze Cliniche e Molecolari - Rheumatology Clinic, Jesi, Italy*; *[3]AOU Pisana, Rheumatology Unit, Pisa, Italy*; *[4]Università di Messina, Department of Internal Medicine, Rheumatology Unit, Messina, Italy*; *[5]University of Ferrara and Azienda Ospedaliera-Universitaria di Ferrara, Rheumatology, Department of Medical Sciences, Ferrara, Italy*; *[6]University of Siena, Rheumatology Unit, Department of Medical Sciences, Surgery and Neurosciences, Siena, Italy*; *[7]Sapienza University of Rome, Department of Internal Medicine and Medical Specialities, Rheumatology Unit, Roma, Italy*; *[8]Azienda Ospedaliero-Universitaria di Parma, Department of Medicine, Internal Medicine and Rheumatology Unit, Parma, Italy*; *[9]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Reumatologia, Roma, Italy*; *[10]IRCCS San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), Milano, Italy*; *[11]ASST Settelaghi, Ospedale Di Circolo - Fondazione Macchi, Rheumatology Unit, Internal Medicine Department, Varese, Italy*; *[12]University of Trieste, Department of Medical Sciences, UCO Medicina Clinica (SSD Reumatologia), Trieste, Italy*; *[13]University of Rome "Campus Biomedico" - School of Medicine, Division of Rheumatology and Clinical Immunology, Roma, Italy*; *[14]University of Florence, Department of Experimental and Clinical Medicine, Divisions of Internal Medicine and Rheumatology AOUC, Firenze, Italy*; *[15]University of Palermo, Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties, Palermo, Italy*; *[16]ASP 7, Scicli Hospital, Integrated Reference Center of Rheumatology, Ragusa, Italy*; *[17]University of Perugia, Rheumatology Unit, Department of Medicine, Perugia, Italy*; *[18]University of Modena and Reggio Emilia, Azienda USL-IRCCS di Reggio Emilia, Rheumatology Unit, Reggio Emilia, Italy*; *[19]S. Maria Hospital - USL, IRCCS Institute, Rheumatology Unit, Reggio Emilia, Italy*; *[20]Azienda USL di Modena, Rheumatology Unit, Modena, Italy*; *[21]University of Bari, Rheumatology Unit, Department of Emergency and Organ Transpantations, Bari, Italy*; *[22]ASST Fatebenefratelli-Sacco, Milan State University School of Medicine, Rheumatology Unit, Internal Medicine Department, Milano, Italy*; *[23]University of L'Aquila, Clinical Unit of Rheumatology, School of Medicine, L'Aquila, Italy*; *[24]University of Genoa, IRCCS San Martino, Department of Internal Medicine, Research Laboratory and Division of Clinical Rheumatology, Genova, Italy*; *[25]ASST Gaetano Pini-CTO, Division of Rheumatology, Milano, Italy*

Background: Fibromyalgia syndrome (FM) is characterised by a complex symptom spectrum, dominated by the presence of chronic widespread pain, fatigue and unrefreshing sleep. FM affects between 2 and 3% of the general population. It is a condition that mainly involves middle-aged women, although it is increasingly being diagnosed in younger people. The severity of symptoms can vary greatly between individual patients, and is influenced by many factors (e.g. sex,

body mass index) [1]. To date, there is little information about changes in severity in accordance with patient age.

Objectives: The aim of this study was to investigate variations in symptom severity in FM patients according to age categories.

Methods: A cross-sectional study of adult FM patients diagnosed according to the American College of Rheumatology 2010/2011 criteria was performed. The case series was included from an Italian national registry [2]. Patients were grouped according to five age categories: 18-40 years, 41-50 years, 51-60 years, 61-70 years, over 71 years. Symptom severity was assessed through the revised Fibromyalgia Impact Questionnaire (FIQR) and domains, including FIQR physical function (items 1-9), FIQR health status (items 10-11), and FIQR symptoms (items 12-21). Between-group characteristics were analysed using one-way analysis of variance (ANOVA).

Results: This study included a total of 2889 patients, 403 aged 18-40 years, 756 aged 40-50 years, 1035 aged 50-60 years, 528 aged 60-70 years, and 167 over 70 years, respectively. The mean (standard deviation [SD]) score of the total FIQR was 52.68 (11.82). Total FIQR and individual domains all showed a normal distribution. Analysing the data by age category, there were statistically significant differences between the categories for the total FIQR (p = 0.030). The age categories with the highest disease severity were those above 71 years (FIQR 62.14, SD 22.45), and between 51-60 years (FIQR 60.31, SD 22.89) (Table 1). Significant differences between age categories were also found for the domains physical function (p = 0.006) and health status (p = 0.012), but not for the domain symptoms (p = 0.164).

Table 1. Mean values of FIQR total score and domains according to age categories.

FIQR and domains	18-40 years	41-50 years	51-60 years	61-70 years	≥71 years	p*
FIQR total, mean (SD)	57.90 (21.76)	59.25 (23.30)	60.31 (22.89)	57.13 (23.59)	62.14 (22.45)	0.030
FIQR physical function, mean (SD)	15.51 (7.56)	16.44 (7.77)	16.77 (7.51)	15.96 (7.82)	17.68 (7.26)	0.006
FIQR health status, mean (SD)	11.19 (5.85)	11.24 (5.99)	11.49 (5.93)	10.57 (6.11)	12.21 (5.97)	0.012
FIQR symptoms, mean (SD)	31.32 (10.48)	31.56 (11.32)	32.10 (11.01)	30.68 (11.47)	32.24 (11.34)	0.164

Abbreviations and legend. FIQR = revised Fibromyalgia Impact Questionnaire; SD = standard deviation; * = one-way analysis of variance (ANOVA).

Conclusion: Distinguishing the disease severity in FM patients according to age categories, a bimodal distribution emerges, with the disease severity being greatest in patients over 71 years and in the 51-60 years decade. The main differences in severity, according to what can be detected through the FIQR, are attributable to the domains physical function and health status, which show higher scores in the two classes with higher severity.

REFERENCES:

[1] Sarzi-Puttini P et al., Fibromyalgia: an update on clinical characteristics, aetiopathogenesis and treatment. *Nat Rev Rheumatol* 2020; 16: 645–660.

[2] Salaffi F et al., The Italian Fibromyalgia Registry: a new way of using routine real-world data concerning patient-reported disease status in healthcare research and clinical practice. *Clin Exp Rheumatol* 2020; Suppl 123: 65-71.

Acknowledgements: Società Italiana di Reumatologia (SIR) and Italian Ministry of Health

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1507

AB0717 PREVALENCE OF MIGRAINE AND NEUROPATHIC PAIN AMONG PATIENTS WITH RHEUMATIC DISEASES

S. Miladi[1], M. Yasmine[1], A. Fazaa[1], S. Mariem[1], K. Ouenniche[1], L. Souebni[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: Pain in rheumatic diseases (RD) is primarily due to mechanical or inflammatory mechanism, but neuropathic pain (NP) component is yet to be fully evaluated and described, with a particular attention to the distinction with nociceptive pain [1].

Objectives: The aim of our study was to assess the prevalence of migraine and neuropathic pain in patients with RD and to explore factors associated with NP.

Methods: Prospective study including patients with rheumatoid arthritis (RA) and spondylarthritis (SpA) were invited to complete a validated self-assessment questionnaires. Sociodemographic data as well as disease related characteristics were recorded. Migraine was diagnosed according to the IHS migraine diagnostic criteria. NP was evaluated using DN4 (Douleur Neuropathique 4 Questions) and Pain DETECT questionnaire (PDQ). Neuropathic pain was retained in case of a total score of 4 or more at DN4-interview questionnaire or a score ≥19 with the PDQ.

Results: A total of 60 patients with RD were included (42 RA/18 SpA). Females outnumbered males (sex-ratio=1.7). The mean age was 51.3 ± 13.1 years [18-75] and the mean disease duration was 11.9 ±5.6 [1-23] years. The prevalence of migraine was 15%. This latter was higher among women than men and among RA patients than SpA (18% vs 9%, 16.6% vs 11.2%) with no statistically significant correlation (p=0,329, 0,581 respectively). Parameters associated with a higher prevalence of migraine were an older age (p=0,042). However, there was no correlation between the presence of migraine and the type of the RD, disease duration or the level of anxiety (p=0,059, p=0,459 respectively). Chronic pain with neuropathic characteristics was found in 21.7% with the DECT score and 16.7% with DN4 questionnaire. NP was most prevalent among patients with comorbidities (28.5% vs 6%, p=0.021) and with higher body mass index (p=0.01). Prevalence was significantly higher in the RA group (19%) than in the SpA group (11%) without a statistically significant correlation (p=0.45). Similarly, NP was not associated with Salazopyrine intake (p=0.9).

Conclusion: We found a high prevalence of migraine and NP in our sample of patients with RD. It seems therefore important to check the presence of migraine or NP especially in patients with comorbidities and older ones.

REFERENCES:

[1] Bailly F, Cantagrel A, Bertin P, et al. Part of pain labelled neuropathic in rheumatic disease might be rather nociplastic. RMD Open. 2020;6:e001326.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2132

AB0718 ASSESSMENT OF SEXUAL DYSFUNCTION IN WOMEN AND MEN WITH FIBROMYALGIA SYNDROME

G. Mouna[1], J. Mahbouba[1], S. Zrour[1], I. Bejia[1], M. Touzi[1], N. Bergaoui[1]. [1]*Rhumatology Departement of CHU Fattouma Bourguiba, Rhumatology Departement of CHU Fattouma Bourguiba, Monastir, Tunisia*

Background: Fibromyalgia syndrome is a chronic musculoskeletal disease, which compromises physical, mental, and sexual health. Although concerns related to sexuality are commonly reported, the literature on sexual functioning in patient with fibromyalgia is limited to female patients.

Objectives: The aim of our study is to identify sexual dysfunction in women and men with fibromyalgia syndrome compared with patients with rheumatoid arthritis.

Methods: This is a cross-sectional comparative study: '34 patients with fibromyalgia syndrome compared to 100 patients with rheumatoid arthritis' conducted in the rheumatology department of CHU Fattouma Bourguiba de Monastir over a period from February to November 2017. We used the Female Sexual Function Index (FSFI) and the Sexual Health Inventory for Men (SHIM).

Results: Our sample comprised 34 patients with fibromyalgia (31 females and 3 males) and 100 patients with rheumatoid arthritis (58 females and 15 males). Sexual dysfunction was present in 100% of female patients with fibromyalgia syndrome compared to 60% of female patients with rheumatoid arthritis. Female patients with fibromyalgia syndrome had a decreased FSFI score: 10,3±8,74 versus 16,86±8,87 in the rheumatoid arthitis group with p=0.001. While among the male patients, we found no significant difference between the two groups.

Conclusion: Fibromyalgia syndrome had negative side effect on the sexual life of female patients. Recognition of this dysfunction and its inclusion in the multidisciplinary management of fibromyalgia must be part of the treatment.

REFERENCES:

[1] P. Romero-Alcalá *et al.*, « Sexuality in male partners of womenwithfibromyalgiasyndrome: A qualitative study », *PLoS One*, vol. 14, n° 11, nov. 2019, doi: 10.1371/journal.pone.0224990.

[2] M. D. H. Besiroglu et M. D. M. Dursun, « The association betweenfibromyalgia and femalesexualdysfunction:asystematicreview and meta-analysis of observationalstudies », *Int J ImpotRes*, vol. 31, n° 4, p. 288-297, juill. 2019, doi: 10.1038/s41443-018-0098-3.

[3] T. M. Matarín Jiménez, C. Fernández-Sola, J. M. Hernández-Padilla, M. Correa Casado, L. H. Antequera Raynal, et J. Granero-Molina, « Perceptions about the sexuality of womenwithfibromyalgiasyndrome:aphenomenologicalstudy », *J Adv Nurs*, vol. 73, n° 7, p. 1646-1656, juill. 2017, doi: 10.1111/jan.13262.

[4] L. Bazzichi*et al.*, « Fibromyalgia and sexualproblems », *Reumatismo*, vol. 64, n° 4, p. 261-267, sept. 2012, doi: 10.4081/reumatismo.2012.261.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3721

AB0719

ASSOCIATION BETWEEN FIBROMYALGIA AND CHRONIC AUTOIMMUNE THYROIDITIS. RETROSPECTIVE OBSERVATIONAL DATA FROM A MONOCENTRIC ENDOCRINOLOGIST-RHEUMATOLOGIST COLLABORATIVE ANALYSIS

F. Fischetti[1], S. Bernardi2, S. Lovriha2, F. Bozzao2, P. Tomietto[3], B. Fabris2. *[1]University of Trieste, Department of Medical, Surgery and Health Sciences, Trieste, Italy*; *[1]University of Trieste, Department of Medical, Surgery and Health Sciences,Trieste, Italy*; *[3]Azienda Sanitaria Universitaria Giuliano Isontina; Cattinara Hospital, Department of Medicine,Trieste, Italy*

Background: Endocrine and metabolic imbalance conditions can affect the development of subjective abnormal perceptions within fibromyalgia (FMR). In the case of autoimmune thyroid disease (ATD), prolonged, clinically active states of impaired glandular function may be associated with an FMR-type condition. Less clear is the association between subclinical or rapidly well-controlled states of thyroid disease and the presence of FMR, since this assessment, although analysed in some previous studies, was usually performed on cohorts of subjects where the absence of any other confusing factors was not well defined.
Objectives: To evaluate the prevalence of subclinical autoimmune thyroid disease, or functionally controlled autoimmune thyroid disease, in a retrospective cohort of consecutively diagnosed patients suffering from fibromyalgia condition.
Methods: Over a 2 years period of time (2018-2019) a monocentric joint evaluation was activated with the endocrinology section of our healthcare area in order to consecutively monitor the subjects belonging to both specialist clinics. Patients with ATD were not unfrequently firstly evaluated in the rheumatology ambulatory. Diagnosis of FMR was defined according to the American College of Rheumatology 2010/2011 criteria. At the same time, at the rheumatology clinics, all cases addressed with diagnosis of fatigue or chronic pain of no defined origin were analysed in order to carefully identify any associated, comorbidity problems. The diagnosis of ATD was confirmed according to recognized international criteria. The following results will focus on subjects with chronic Hashimoto type Thyroiditis (HT).
Results: Among the HT patients, 98% were women, aged between 28 and 64. Over the 2 years considered period of time, 65 subjects suffering from HT, showing no active disease or unstable endocrine function were addressed to the rheumatology clinics owing to FMR related symptoms. Among them, 55 (84.6%) had a confirmed diagnosis of FMR. Within this time, we recognized 239 consecutive diagnoses of FMR in subjects aging 22-76 years, with a number of 114 found to be devoid of factors (other than ATD) able to be responsible for chronic pain, except for a modest component of situational anxiety, or mild mood depression, not requiring any specific drug intervention. Among the 114, so called "primary" FMR, 35.6% showed to suffer from TCH, under confirmed clinical/hormonal remission, or in a preclinical, early stage of onset. Within the 125 subjects, carrying a FMR condition related to previous or associated fostering pathology, 26.8% were positive for current or previous thyroid problems. The prevalence of TCH, in the "secondary" FMR conditions differed significantly ($p<0.01$) from that of other FMR promoting diseases (eg connective tissue diseases, such as Sjogren Syndrome), except for moderate-severe mood disorders and/or anxiety, and the most severe chronic osteoarthritis conditions, showing a confirmed secondary neuropathy.
Conclusion: Although limited in number, the here reported data confirm the hypothesis of a significant association between ATD and FMR, even in subjects who were considered to be in a subclinical condition or in full clinical remission by the endocrinology colleagues. The physiopathology of this association needs further appropriate insights.
Acknowledgements: We thank Dr Alberto Petterle for his previous helpful contribution
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3985

Paediatric rheumatology

AB0720

HIP INVOLVEMENT IN A COHORT OF EGYPTIAN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

A. Radwan[1], H. Alzahrani[2], Y. Alzahrani[2], A. Elsaman[3]. *[1]Sohag University Hospital, Rheumatology and Rehabilitation, Sohag,*; *[2]Armed Forces Specialized Center for Health Rehabilitation, Altaif, Kingdom of Saudi Arabia, Rehabilitation Depatment,Taif, Saudi Arabia*; *[3]Sohag University Hospital, Rheumatology and Rehabilitation, Sohag, Egypt*

Background: The hip joint is frequently involved in Juvenile Idiopathic Arthritis (JIA). It is more common with polyarticular, systemic and enthesitis-related forms and with severe uncontrolled disease. Chronic hip arthritis leads to irreversible joint damage with marked impairment of quality of life and functional limitation [1]. Unilateral or bilateral hip arthritis occurs in 30- 50% of children with JIA [2].
Objectives: The aim of this study is to assess the pattern of hip involvement in a cohort of Egyptian JIA patients in terms of epidemiological aspects, JIA pattern, bilateralism, associated extra-articular manifestations, radiological features, treatment and prognosis.
Methods: We included 179 patients who fulfilled the International league against rheumatism criteria for JIA. Epidemiological, clinical, radiological, and therapeutic parameters were assembled and analyzed. Hip involvement was assessed using a semi-quantitative score of pain and tenderness for the hip, CARSH radiographic score of the hip, and Harris functional hip score. JADAS-27 was used for assessment of disease activity.
Results: We included 113 girls and 66 boys; with a female: male ratio of nearly 2:1. The age at onset mean was 8.8±3 years (8.9±2.9 for females and 8.6±3.1 for males). The mean age at the study time was 13.3±4.1 years. The disease duration mean was 4.5±2.9 years.
Clinically; 20.1% of the cases had hip involvement (12.8% unilateral and 7.3% bilateral), while by imaging, around 30.7% of the cases have hip involvement (19.6% unilateral and 11.2% bilateral). The mean age for cases with hip involvement was 14.1±4.3, compared to 12.9±4 among those with no hip involvement. The mean disease duration for those with hip arthritis (either clinical or by imaging) was 5.5±2.9 years, compared to 4.1±2.9 among those with no hip involvement (Figure 1).

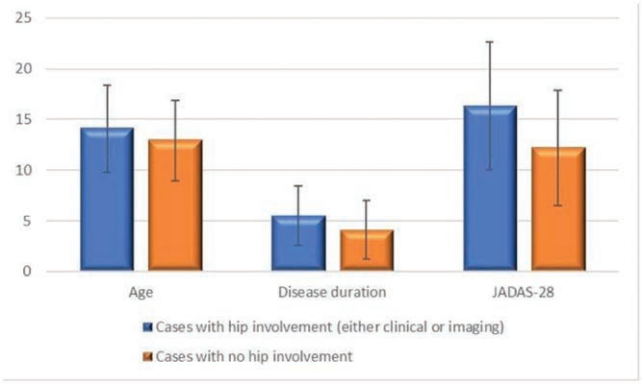


Figure 1. Difference between JIA cases with and without hip involvement.

The Mean JADAS-27 was 13.5±6.2 and for those with hip involvement was 16.3±6.3. The commonest pattern of JIA with hip arthritis was polyarticular followed by enthesitis-related arthritis. There was a strong significant correlation between JADAS-27 and hip involvement at one hand and Harris score, semi-quantitative score for pain and tenderness at the other hand. Further, disease duration was significantly correlated with hip involvement as well. Among cases with hip involvement, 25% demonstrated destructive changes and 30% showed growth abnormalities.
Conclusion: Hip arthritis in JIA is related to polyarticular and enthesitis-related pattern. Longer disease duration, seropositive polyarticular pattern were related to poor prognosis for hip arthritis.
REFERENCES:
[1] Singh JA, Cleveland JD. Juvenile idiopathic arthritis is associated with higher healthcare utilization after total knee or hip replacement. Scandinavian journal of rheumatology 2021; **50:** 34-9.
[2] Rostom S, Amine B, Bensabbah R, Abouqal R, Hajjaj-Hassouni N. Hip involvement in juvenile idiopathic arthritis. Clinical rheumatology 2008; **27:** 791-4.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.712

AB0721

CLINICAL AND LABORATORY CHARACTERISTICS, GENETIC FEATURES OF MACROPHAGE ACTIVATION SYNDROME IN CHILDREN WITH SYSTEMIC-ONSET JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE CENTER EXPERIENCE

I. Kriulin[1,2], E. Alexeeva[1,2], T. Dvoryakovskaya[1,2], K. Savostyanov[3], A. Pushkov[3], K. Isaeva[1], R. Denisova[1], O. Lomakina[1], A. Mamutova[1], A. Chomakhidze[1], A. Fetisova[1], M. Gautier[1], E. Krekhova[1,2], I. Tsulukiya[1], A. Gromov[2]. [1]*National Medical Research Center of Children's Health, Rheumatology, Moscow, Russian Federation*; [2]*Sechenov First Moscow State Medical University, Pediatric, Moscow, Russian Federation*; [3]*National Medical Research Center of Children's Health, Genetic, Moscow, Russian Federation*

Background: Macrophage activation syndrome (MAS) is a life-threatening complication of systemic-onset juvenile idiopathic arthritis (sJIA) characterized by fever, hepatosplenomegaly, lymphadenopathy, coagulopathy, and rapid development of multiple organ failure. MAS is triggered by viral and bacterial infections, most often Epstein-Barr viruses, cytomegalovirus, influenza and parainfluenza viruses, parvavirus B19, yersiniosis, salmonellosis, sepsis.

Despite modern diagnostic and treatment technologies, MAS still remains a formidable complication of sJIA, it is characterized by an aggressive course, a heterogeneous clinical presentation, especially in conditions of treatment with genetically engineered biological drugs, an ambiguous response to pathogenetic therapy and is accompanied by mortality in 5-10% of patients.

Objectives: To analyze the clinical and laboratory features of MAS in children with sJIA and to study the genetic predisposition of this syndrome.

Methods: The study included 24 patients with MAS who are being followed up in the rheumatology department of the National Medical Research Center of Children's Health, Moscow. The clinical presentation and laboratory manifestations were assessed in 24, and genetic features were described in 7 patients using a new generation sequencing with further biostatistical processing of the obtained genetic data.

Results: Of 24 patients, 23 (98%) had fever, 16 (68%) patients had rash, 17 (72%) - organomegaly, 4 (16%) - polyserositis, 2 (7%) - myalgia and myopathy. All 24 (100%) patients had an increase in ferritin level of more than 684 ng/ml, 98% of them had a high level of lactate dehydrogenase (LDH) and 97% - a high level of triglycerides. In CBC, cytopenia was found in 80% of children: in 54% - erythrocytopenia, in 74% - leukopenia, in 88% - thrombocytopenia, in 15% - sharp decrease in erythrocyte sedimentation rate. In a coagulogram of 24 patients, 90% had an increase in D-dimer, 85% had a decrease in fibrinogen. Hyponatremia presented in 95% of patients. Thus, 85% of patients met the diagnostic criteria of the HLH-2004 protocol, adapted for children with sJIA. Genetic characteristics were analyzed in 7 children out of 94 patients with MAS. They are presented in Table 1. These patients have rare and frequent variants, as well as genes polymorphisms that are associated with macrophage activation syndrome.

Table 1. The number of genetic variants in children with MAS (n=7).

Gene	Patient № 1	Patient №2	Patient № 3	Patient № 4	Patient №5	Patient №6	Patient №7
LYST	0	24	7	3	4	6	4
NLRC4	4	4	4	4	4	6	3
NLRP12	5	10	6	4	4	12	4
NLRP3	1	8	5	5	5	7	5
TNFAIP3	2	2	2	0	2	2	2
UNC13D	18	2	5	10	18	26	18
XIAP	1	1	0	0	1	3	1

Conclusion: The macrophage activation syndrome has a typical clinical presentation, there are clinical and laboratory manifestations: fever, hyperferritinemia, cytopenia, hyponatremia, increased levels of LDH and triglycerides, based on which, a diagnosis can be made. Patients with MAS at our center also had genetic characteristics that predisposed to the development of this condition.

REFERENCES:

[1] Crayne CB, Albeituni S, Nichols KE, Cron RQ. The Immunology of Macrophage Activation Syndrome. Front Immunol. 2019 Feb 1;10:119. doi: 10.3389/fimmu.2019.00119. PMID: 30774631; PMCID: PMC6367262.

[2] Henderson LA, Cron RQ. Macrophage Activation Syndrome and Secondary Hemophagocytic Lymphohistiocytosis in Childhood Inflammatory Disorders: Diagnosis and Management. Paediatr Drugs. 2020 Feb;22(1):29-44. doi: 10.1007/s40272-019-00367-1. PMID: 31732958; PMCID: PMC7334831.

[3] Ravelli A, Davì S, Minoia F, Martini A, Cron RQ. Macrophage Activation Syndrome. Hematol Oncol Clin North Am. 2015 Oct;29(5):927-41. doi: 10.1016/j.hoc.2015.06.010. Epub 2015 Aug 25. PMID: 26461152.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1491

AB0722

TREATMENT RESPONSE TO METHOTREXATE MONOTHERAPY IN ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS: DATA FROM THE NOR-DMARD STUDY

I. Bardan[1], K. M. Fagerli[2], J. Sexton[2], G. Bakland[3], P. Mielnik[4], L. M. Paucar Loli[5], T. K. Kvien[1,2], E. Kristianslund[2], A. B. Aga[2,6]. [1]*University of Oslo, Faculty of Medicine, Oslo, Norway*; [2]*Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway*; [3]*University Hospital Northern Norway, Department of Rheumatology, Tromsø, Norway*; [4]*Helse Førde, Section for Rheumatology, Department for Neurology, Rheumatology and Physical Medicine, Førde, Norway*; [5]*Lillehammer Hospital for Rheumatic Diseases, Department of Rheumatology, Oslo, Norway*; [6]*Oslo University Hospital, Department of Rheumatology, Oslo, Norway*

Background: Juvenile idiopathic arthritis (JIA) can cause considerable pain and disability in childhood and adulthood. The number of studies exploring the efficacy of medications in adult JIA patients is limited. Methotrexate (MTX) is a commonly used medication for this patient group.

Objectives: To explore the effects of MTX monotherapy (mono) on disease activity in adult patients diagnosed with JIA, compared to a weighted rheumatoid arthritis (RA) cohort.

Methods: Data from NOR-DMARD, a longitudinal observational study enrolling patients > 18 years starting or switching DMARD treatment for inflammatory joint disease, was used [1]. Patients starting MTX mono treatment, and with a clinical diagnosis of JIA or other inflammatory arthropathies diagnosed before the age of 16 years, were identified from the study population. RA patients starting the same treatment regimen were included for comparative purposes.

Disease activity measurements and remission rates were collected at baseline, 3 and 6 months. Changes in disease activity and absolute remission rates after 3 and 6 months were calculated. Remission rates and change in disease activity from baseline were compared between JIA patients and a weighted RA cohort with weights based on age and gender, using linear and logistic regression for continuous and categorical variables, respectively.

Results: 2201 patients were included in the analyses, 101 JIA patients (80.2% female, mean (SD) age 35.6 (13.0) years, mean (SD) diagnosis duration 24.8 (12.9) years), and 2100 RA patients (69.4% female, mean (SD) age 56.6 (13.6) years, mean (SD) diagnosis duration 4.1 (8.1) years) were included in the analyses. Age, gender distribution and disease duration differed significantly between cohorts.

Both the JIA and RA group improved significantly across all disease activity measures from baseline to 3 and 6 months (Table 1). Both groups had a progressive increase in remission rates from baseline to 6 months (Table 1, Figure 1). The RA group had a significantly greater improvement in ESR after 3 months, SJC28 after 6 months and TJC28, DAS28, SDAI and MHAQ after 3 and 6 months. There were no significant group differences in remission rates.

Table 1.

	Baseline			Change to 3 months			Change to 6 months		
	JIA*	RA*	Diff.§	JIA*	RA*	Diff.§	JIA*	RA*	Diff.§
ESR, mm/h	20.4 (18.2)	28.7 (22.2)	3.7 (-0.6 to 8.1)	-3.1 (15.8)	-9.6 (18.7)	-5.7 (-10.1 to -1.4)	-3.0 (17.5)	-11.3 (19.8)	-5.4 (-10.8 to 0.03)
SJC28	3.9 (4.8)	6.9 (5.7)	2.0 (0.9 to 3.2)	-1.8 (3.3)	-3.5 (5.5)	-0.9 (-1.9 to 0.02)	-1.8 (3.3)	-4.2 (5.6)	-1.5 (-2.6 to -0.5)
TJC 28	4.5 (4.9)	8.0 (7.1)	3.1 (1.9 to 4.2)	-0.8 (4.2)	-3.5 (7.4)	-1.9 (-3.1 to -0.7)	-1.4 (3.8)	-4.0 (6.8)	-2.3 (-3.4 to -1.1)
DAS28	4.0 (1.3)	4.9 (1.3)	0.6 (0.2 to 0.9)	-0.6 (1.2)	-1.2 (1.5)	-0.5 (-0.9 to -0.2)	-0.7 (1.2)	-1.4 (1.5)	-0.6 (-1.0 to -0.2)
SDAI	18.3 (11.3)	26.0 (13.6)	5.6 (2.7 to 8.4)	-6.0 (9.7)	-11.0 (14.0)	-3.1 (-5.9 to -0.2)	-6.3 (8.2)	-12.8 (14.2)	-5.1 (-7.8 to -2.2)
PGA	51.0 (24.6)	48.3 (24.3)	-4.5 (-10.0 to 1.1)	-13.2 (25.3)	-14.7 (26.5)	-1.0 (-7.4 to 5.3)	-11.3 (23.8)	-14.3 (26.7)	-4.6 (-11.9 to 2.7)
MHAQ	0.5 (0.5)	0.7 (0.5)	0.1 (-0.05 to 0.2)	-0.2 (0.3)	-0.2 (0.5)	-0.1 (-0.2 to -0.0)	-0.1 (0.3)	-0.2 (0.5)	-0.16 (-0.3 to -0.1)

*Mean (SD) § Weighted group difference, RA coefficient (95 % confidence interval)

Conclusion: Adult JIA patients had significant improvement across all the presented disease activity measures 3 and 6 months after treatment initiation with MTX mono. The magnitude of improvement was smaller than in the RA group, but JIA patients obtained remission at similar rates as RA patients.

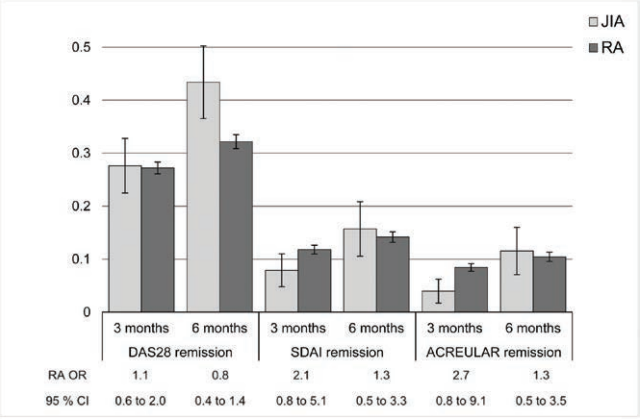


Figure 1. Mean 3- and 6-month remission rates with error bars (SE)

REFERENCES:

[1] Kvien, T.K., et al., A Norwegian DMARD register: prescriptions of DMARDs and biological agents to patients with inflammatory rheumatic diseases. Clin Exp Rheumatol, 2005. **23**(5 Suppl 39): p. S188-94.

Disclosure of Interests: Imane Bardan: None declared, Karen Minde Fagerli: None declared, Joe Sexton: None declared, Gunnstein Bakland Speakers bureau: Abbvie, Consultant of: UCB, Pfizer, Novartis, Pawel Mielnik: None declared, Liz Marina Paucar Loli: None declared, Tore K. Kvien Speakers bureau: Amgen, Celltrion, Egis, Evapharma, Ewopharma, Hikma, Oktal, Sandoz and Sanofi, Consultant of: AbbVie, Amgen, Biogen, Celltrion, Eli Lilly, Gilead, Mylan, Novartis, Pfizer, Sandoz and Sanofi, Grant/research support from: AbbVie, Amgen, BMS, MSD, Pfizer and UCB, Eirik kristianslund: None declared, Anna-Birgitte Aga Grant/research support from: Dr. Aga reports personal fees from Abbvie, Eli Lilly, Novartis and Pfizer, outside the submitted work

DOI: 10.1136/annrheumdis-2021-eular.1606

AB0723 JUVENILE BEHCET'S DISEASE: WHICH PARTICULARITIES?

O. Jomaa[1], O. Berriche[1], S. Arfa[1], A. Fraj[1], W. Romdhane[1], R. Makhloufi[1], M. Hermassi[1], M. Belkhiri[1]. *[1]University Hospital Tahar Sfar Mahdia, Tunisia, Internal Medicine Department, Mahdia, Tunisia*

Background: Behcet's disease (BD) is a systemic vasculitis that affects young adults aged between 20 and 30 years old. It is rare in childhood.

Objectives: This work aims to analyze the clinical features of this form by comparing it with adult BD.

Methods: Through a retrospective study including 192 cases with BD seen in The Internal Medicine Department at Tahar Sfar Hospital Mahdia TUNISA, we report 8 cases of juvenile BD (4.2%) that occurred under the age of 16 years.

Results: There were 8 male. The average age of BD onset was 14 years [11, 16 years]. Genital aphthosis was noted in 5 patients. Ophthalmologic damage was observed in 4 patients, dominated by uveitis (75% of cases). No cases of blindness were observed. Joint damage was seen in 5 patients and vascular and neurological damage in 2 patients respectively. All patients received colchicine in addition to a platelet aggregation inhibitors at the moment of BD diagnosis. When comparing juvenile BD group with that of adults, we have noticied, the frequency of cutaneo-mucous and articular manifestations, the rarity of neurological damage and the absence of cardiac and digestive damage in the juvenile BD group.

Conclusion: Juvenile BD is a rare form, with a male predominance. The younger age is not a poor prognostic factor. Early diagnosis and treatment can reduce the disease's complications.

REFERENCES:

[1] doi: 10.1007/s00296-018-4208-9

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1669

AB0724 CANDIDATE PREDICTIVE BIOMARKERS OF POOR TREATMENT RESPONSE IN OLIGOARTICULAR ONSET JUVENILE ARTHRITIS TO EARLY STEROID INJECTIONS

A. Kozhevnikov[1,2], N. Pozdeeva[1], O. Maricheva[3], M. Nikitin[1], S. Bogdanova[4], G. Novik[2]. *[1]H.Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery, Trauma Sequelae and Rheumatoid Arthritis Clinic, Saint-Petersburg, Russian Federation*; *[2]St.Petersburg State Pediatric Medical University, Department of Children's Diseases named after Professor I. M. Vorontsov, Saint-Petersburg, Russian Federation*; *[3]H.Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery, Diagnostic Radiology, Saint-Petersburg, Russian Federation*; *[4]H.Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery, Laboratory Diagnostics, Saint-Petersburg, Russian Federation*

Background: Intra-articular corticosteroid injections are the first-line antirheumatic drugs of oligoarticular onset juvenile arthritis. Despite significant advances in treatment (anti-TNF, block IL6) this choice of pediatric chronic joint disease still remains relevant. Pediatric rheumatologists and to this day there are no consensus on the best modality for treatment.

Objectives: The aim of this study was to search of biomarkers ineffective of early intra-articular steroid injections of oligoarticular onset juvenile arthritis.

Methods: Clinical, imaging, laboratory data (blood and synovial fluid), and effect of early isolated intra-articular injections (is-IAI) of triamcinolone acetonide 92 children (89% girls) aged median (IQR) 4,2 (1,6 – 7,6) years with oligoarticular onset juvenile arthritis without extra-articular manifestations (oligo-JA) were collected retrospectively and analyzed. All children were met ILAR criteria. Triamcinolone acetonide (TA) was administered intra-articular at a dose of 20-40 mg with an injection interval of 3-6-12 months which was depended on the activity of the disease. All children were divided into two groups: active / inactive arthritis based on the effectiveness of local corticosteroid treatment. The average follow-up was 48 [38; 62] months.

Results: 32 children (35%; all girls) were achieved remission oligo-JA after is-IAI of TA with mean of 2 [1,75; 2] injection per joint (inactive arthritis > 24 months). The mean interval between two consecutive is-IAI was 7 [5,25; 10] months. Other children did not achieve inactive oligo-JA after is-IAI of TA with mean of 3 [2; 4] injection per joint. The mean interval between first two consecutive injection was 5,5 [4,25; 7] months and other injections - 2 [2; 3] months. All children who did not achieve remission oligo-JA for is-IAI were treated by DMARDs. Statistical analyses were performed to determine the relationships between clinical, instrumental, laboratory signs and efficacy is-IAI of TA. Measures included the number of swollen or tender joints [active joint counts]; biological inflammatory markers [erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum and synovial fluid level of interleukin 6 (IL6) and tumor necrosis factor alfa (TNF-α)]; autoimmunity [titer of antinuclear factor (ANF)] and physicians' assessment of JIA disease activity [clinical Juvenile Arthritis Disease Activity Score including maximal 10 joints (cJADAS10)]. Efficacy is-IAI of TA was no associated significantly with number of active joint of onset oligo-JA, cJADAS10, serum level of CRP mg/ml, ESR mm/h, IL6 pg/ml and TNF-α pg/ml, titer of ANF. The mean inflamed synovial fluid of IL6 levels 2208 [710; 4564] / 3234 [1265; 16902] pg/ml and TNF-α levels 3,3 [2,5; 3,8] / 1,1 [0,6; 3,7] pg/ml at onset of inactive and active oligo-JA were not significantly differ. The analysis revealed a correlation between a short phase of beneficial effect after is-IAI of TA and risk of activity disease (with an inactive phase of arthritis less than 3 months, the risk activity was OR = 2.09, p <0.001; with an inactive phase less than 2 months - OR = 8.9, p <0.001).

Conclusion: TA is an effective and safe treatment in children with oligo-JA. Research was revealed that about a third of children with oligo-JA achieved inactive arthritis of average after two intra-articular injections of TA (all girls). There are no biomarkers for prediction of poor treatment response in oligo-JA to early steroid injections. But a short phase of beneficial effect after is-IAI of TA may be sign of risk activity disease. In addition boys with oligoarticular onset juvenile arthritis may be considered like potentially ineffective for local steroid therapy.

REFERENCES:

[1] Kozhevnikov A.N., Pozdeeva N.A., Konev M.A., Maricheva O.N., Afonichev K.A., Novik G.A. X-ray diagnosis of juvenile chronic oligoarthritis. *Bulletin of Siberian Medicine*. 2017; 16 (3): 224–234 DOI:10.20538/1682-0363-2017-3-224–234.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1819

AB0725 MACROPHAGE ACTIVATION SYNDROME IN CHILDREN WITH RHEUMATIC DISEASES: ANALYSIS OF CASE SERIES

M. Kaleda[1], I. Nikishina[1], V. Matkava[1], A. Shapovalenko[1], E. Fedorov[1], S. Salugina[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Pediatric Department, Moscow, Russian Federation*

Background: Macrophage activation syndrome (MAS) is a rare, but severe life-threatening complication of chronic rheumatic disease (RD) in children, which associated with high risks of the multiple organ failure and mortality.

Objectives: To analyze demographic, clinical and laboratory parameters, timing of MAS and disease outcome in patients (pts) with MAS and RD.

Methods: The study included all pts of single center with RD, who developed the MAS. The diagnosis was recognized according to Classification criteria for MAS in sJIA [1].

Results: We observed 52 pts with RD and MAS: 31 (59.6%) with sJIA, 19 (36.5%) – SLE, 1(1.9%) – juvenile dermatomyositis (JDM), 1 (1.9%) – overlap syndrome (JIA+JDM). Pts with MAS accounted of 26% of all pts with sJIA, 7.6% of all pts with SLE. The mean age of pts at onset of sJIA was 2.6 y [1.5; 5.75], at onset of SLE – 11.8 y [8.6; 13.95]. The patient with JDM was 6.5 years old, pts with overlap syndrome – 3.5 years old. Male to female ratio was 1:1,7. A total of 63 episodes of MAS was recorded (41 – in sJIA, 20 – SLE, 1 – JDM, 1 - overlap syndrome). 23 pts (44.2%) had MAS at onset, 26 pts (50%) – "classic" MAS (during the course of disease), 3 pts (5.8%) – recurrent MAS. The clinical manifestations of MAS included fever (90.4%), hepatomegaly (50%), pericarditis (46.2%), hemorrhagic rash (32.7%), neurologic involvement (42.3%), lung involvement (34.6%). We found hyperferritinemia in 98%, thrombocytopenia in 78.8%, increased transaminases in 88.5%, hypofibrinogenemia in 40.4%, hypertriglyceridemia in 42.3 % of pts. Most severe course of MAS was established in pts with ferritin levels >1500 ng/ml and with hypertriglyceridemia more than 6.0 mmol/l at an early stage. Bone marrow investigation was performed in 21 pts, and the evidence of haemophagocytosis was confirmed in 8 pts (38%). First features of MAS were fever, sleepiness, lower platelet counts, high TA. Lesions of the skin and mucous were mainly represented by point hemorrhages at an early stage in pts with SLE and MAS, the development of a bright rash with itching was typical for pts with sJIA and MAS. There are no principal differences between course of MAS in sJIA and other RD in children, but mild "subclinical" cases of MAS were observed only in pts with sJIA on biologics. For treatment of MAS all pts were administered high dose of glucocorticoids (per os+iv). Pts with SLE received: cyclophosphamide iv - 5 (26.3%), cyclosporine per os 1 (5.2%), IVIGs - 6 (31.6%), rituximab - 2 pts (10.5%). Pts with sJIA received: cyclosporine per os - 20 (64.5%), IVIGs - 25 (80.6%), 1 etoposide - (3.2%). Patient with overlap syndrome received cyclosporine per os. 8 pts (15.4%) died from MAS (3 with sJIA, 5 – with SLE).

Conclusion: MAS can develop in various children's RD, but more often in pts with sJIA. In our observation more pts had MAS during the course of disease, not at onset. Rapid recognition of MAS can improve treatment outcomes and prognosis.

REFERENCES:

[1] Ravelli A, Minoia F, Davì S, et al. 2016.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2098

AB0726 BIOLOGICS IN CHILDREN WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: AN EXPERIENCE OF SINGLE CENTER

M. Kaleda[1], I. Nikishina[1], V. Matkava[1], Z. Kolkhidova[1], S. Arsenyeva[1], A. Shapovalenko[1]. *[1]V.A. Nasonova Research Institute of Rheumatology, Pediatric Department, Moscow, Russian Federation*

Background: Juvenile dermatomyositis (JDM) is the most common idiopathic inflammatory myopathy (IIM) of childhood, but the involvement of muscle also can be complication of systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD) and different overlap syndromes. The presence of myopathy can significantly affect the prognosis of the disease and the quality of life. Despite of the absence of official indication for biological therapy fo IIM, it`s may be needed in severe course of disease.

Objectives: To analyze in retrospective study the efficacy and safety of Biologics (B) in patients (pts) with IIM in our pediatric rheumatology center.

Methods: The study included all pts with rheumatic diseases (RD), who had IIM and received B during past 10 years.

Results: A total of 17 pts (10 females) were identified: 23.5% with JDM, 11.8% - SLE, 35.3% - MCTD, 29.4% - overlap syndromes. The median age at the onset of RD was 9.75 years [interquartile range (IQR) 6.9; 13.5]. The median disease duration at the onset of myopathy was 7.0 months [3.0; 10.0], in all pts with JDM – at onset. All pts had myopathic syndrome. The rash tipical for JDM was in 8 pts (47%). The lung involvement observed in 6 pts (35.3%). Levels of serum muscle enzymes (CK, ALT, AST and lactate dehydrogenase [LDH]) were elevated in 88.2% of pts: CK in 52.9% (mean ± std 624.35±1007.2 U/L), ALT – 82.4% (mean ± std 142.18±148.16U/L), AST – 82.4% (mean ± std 159.6±201.1 U/L), LDH – 88.2% (mean ± std 492.5±229.2 U/L). Abnormal EMG findings were in 10 pts (59.4%). Nailfold capillaroscopic changes tipical for IIM had 10 pts (59.4%). Before B 94.1% of pts received corticosteroids (CS), 58.8% - methotrexate, 29.4% - hydroxychloroquine, 17.6% - cyclophosphamide, 11.8% - cyclosporine, 5.9% - mycophenolate mofetil, 5.9% - azathioprine, 47% - IVIG. B therapy was started due to insufficient efficacy of previous therapy. The median age at start of B was 12.3 years [IQR 9.5; 15.0]. The median disease duration prior to treatment with B was 2.25 years [IQR 0,8; 3.6]. 58.8% of pts received rituximab (RTX), 41.2% - abatacept (ABA). The median time between each course of RTX was 182 days [IQR 156–315]. 80% of pts underwent more than one course of RTM therapy, with a maximum of 5 courses. The median duration of ABA therapy was 2.8 years [IQR 1.6; 5.0]. Discontinuation of B due to serious AE was observed in 1 patient with overlap syndrome (5.9%) – macrophage activation syndrome (MAS) 8 day after RTX infusion (5th course, 1st infusion). One patient (female, 12.3 yo) died from MAS (at onset of SLE, developed before B), the others achieved remission. B therapy allowed to reduce the dose of CS to maintenance in all pts, decrease of calcinosis in 2 pts and improve the quality of life.

Conclusion: Our study demonstrated that B is highly effective in children with IIM and have the acceptable safety. Early diagnosis and initiation of intensive therapy are important in reducing symptoms of myopathy in RD. It seems that the development of IIM in other RDs, not JDM, indicates the need for B and its good efficacy. The further extended studies are needed.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2133

AB0727 STUDY OF MEFV GENE MUTATIONS IN A COHORT OF CHILDREN: A SINGLE CENTER

T. Kriulina[1,2], E. Alexeeva[1,2], T. Dvoryakovskaya[1,2], I. Kriulin[1,2], K. Isaeva[1], R. Denisova[1], O. Lomakina[1], A. Mamutova[1], A. Chomakhidze[1], A. Fetisova[1], M. Gautier[1], E. Krekhova[1,2], I. Tsulukiya[1], A. Gromov[2]. *[1]National Medical Research Center of Children's Health, Rheumatology, Moscow, Russian Federation*; *[2]Sechenov First Moscow State Medical University, Pediatric, Moscow, Russian Federation*

Background: Familial Mediterranean fever (FMF) is a monogenic autoinflammatory hereditary disease characterized by recurrent episodes of fever with sterile peritonitis, pleural inflammation, arthritis, and/or erysipelas-like rash. Among all variants of the MEFV gene, according to the literature, five pathogenic ones have been identified, which in 75% of cases lead to the development of a typical clinical presentation: V726A, M694V, M694I, M680I, and E148Q. Among them, the M694V variant is the most common and occurs in patients with FMF in 20-65% of cases. At the same time, approximately 10 to 20% of patients meeting the diagnostic criteria for FMF do not have pathogenic variants in the MEFV gene. Despite the fact that the molecular genetic, pathogenetic and clinical features of the disease have been studied detailed, the diagnosis remains difficult due to the lack of a clear correlation between the patient's clinical and genetic data.

Objectives: To analyze the obtained genetic data of patients with pathogenic variants in the MEFV gene.

Methods: The study included 103 patients who are mainly observed at the rheumatology department of the National Medical Research Center of Children's Health of Ministry of Health of the Russian Federation in Moscow. All patients underwent analysis of the MEFV gene using Sanger sequencing with further statistical processing of the data obtained.

Results: Of 103 patients, the pathogenic variant of the MEFV gene was found in 93 patients (90.3%), in 10 patients (9.7%) - the pathogenicity of the revealed variant was contradictory. Of 93 patients with the pathogenic variant of MEFV, the clinical presentation of the disease fits to FMF in 37 patients (39.6%). 11 (29.7%) of them had a mutation in M694V. Out of 37 children who met the criteria for FMF diagnosis, 15 (40.5%) children had a homozygous pathogenic variant of MEVF, and 22 (59.5%) children had two mutations in a heterozygous state. 57 patients who do not have a typical clinical presentation, which is specifical for FMF are observed at the departments of rheumatology, cardiology and nephrology, 13 patients are on an outpatient observation, and 6 patients at the time of the study are over 18 years old. 8 (14%) of them had a mutation in M694V. Among 57 patients with pathogenic heterozygous variants in a, 22 patients (38.6%) are observed in the rheumatology department, among them:

- Enthesitis-related arthritis - 2 patients (9%);
- Systemic juvenile arthritis - 13 patients (59%);
- Oligoarthritis - 5 patients (23%);
- Polyarthritis- 2 patients (9%).

Conclusion: Analysis of the obtained data showed that FMF is characterized by a combination of the clinical presentation and the pathogenic variant in the MEFV gene. However, the disease manifests itself not only in the homozygous pathogenic variant, but also in the combination of two mutations in heterozygous. The presence of one heterozygous mutation, generally, does not lead to the development of FMF.

REFERENCES:

[1] Konstantopoulos, A. Kanta, C. Deltas, V. Atamian, D. Mavrogianni, A.G. Tzioufas, I. Kollainis, K. Ritis, H.M. Moutsopoulos, Familial Mediterranean fever associated pyrin mutations in Greece Ann. Rheum. Dis., 62 (2003), pp. 479-481, 10.1136/ard.62.5.479.

[2] Gershoni-Baruch R, Brik R, Zacks N, Shinawi M, Lidar M, Livneh A: The contribution of genotypes at the MEFV and SAA1 loci to amyloidosis and disease severity in patients with Mediterranean Fever,Seminars in Arthritis and Rheumatism,Volume 43, Issue 3, 2013, Pages 387-391familial Mediterranean fever. *Arthritis Rheum* 2003; 48: 1149–1155.

[3] Booty MG, Chae JJ, Masters SL, et al. Familial Mediterranean fever with a single MEFV mutation: where is the second hit? Arthritis Rheum 2009; 60:185.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2259

AB0728 OSTEOGENESIS IMPERFECTA: ABOUT 12 CASES

O. Jomaa[1], J. Mahbouba[1], S. Zrour[1], I. Bejia[1], M. Touzi[1], N. Bergaoui[1]. *[1]University Hospital Fattouma Bourguiba Monastir,Tunisia, Rheumatology Department, Monastir,Tunisia*

Background: Osteogenesis imperfecta (OI), is a rare hereditary disease characterized by bone fragility and low bone mass. The clinical presenatation is various with varying severity skeletal signs and inconstant extra-skeletal signs. Type 1 is the most common form (60% of cases).
Objectives: Our objective is to describe the various clinical features observed over a period of 15 years.
Methods: This is a retrospective descriptive study including 12 patients followed for OI, hospitalized in the Rheumatology Department at Fattouma Bourguiba Hospital Monastir TUNISIA between 2006 and 2019. Files were collected and analyzed.
Results: They are 9 boys and 3 girls with an average age of 14.9 ± 8.6 years. Consanguinity was reported in 25% of cases. The reason leading to consultation was, recurrent fractures (75%), blue sclera (16.7), and bone deformity (8.3%). The number of previous fractures was on average of 5, all of which were caused by a low energy trauma. Similar family cases were noted in 41.6%. The mean age of the first fracture was 4.41 ± 3.2 years. The most frequent fracture sites were respectively: femur (7/12), leg (6/12), tibia (3/12), humerus (4/12), ankle (2/12), and forearm (2/12). A deformity was noted in 58.3% of the cases: lumbar kyphosis (2), exaggerated dorsal kyphosis (2), femurs in parenthesis (2), and an anarchic deformity of 2 lower limbs (1). Imperfect dentinogenesis was found in 8.3% of cases, while ENT examination revealed conductive and sensorineural hearing loss in 2 patients each. The main radiological abnormalities were diffuse bone demineralization (9 patients), cortical thinning (5 patients), vertebral compression (3 patients), and fracture (2 patients). The bone densitometry showed a mean Z score of 3.49±1.4 in the lumbar spine. The average serum calcium level was 2.38±1.15, alkaline phosphatases were elevated in all cases with an average of 756±624.9. The vitamin D level was deficient in all cases with an average of 22.75±5.3. All patients received in addition to the vitamin-calcium supplementation, pamidronate intravenously at a dose of 9mg/kg/year with a mean number of 6 cures. The main side effects observed during the infusion were abdominal pain, polyarthralgia and asthenia (1 patient), chest pain (1 patient) and fever and chills (1 patient). The control bone densitometry showed a mean Z score of 1.81±1.2 in the lumbar spine.
Conclusion: Despite advances in the OI diagnosis and treatment, more research is needed. Bisphosphonate treatment decreases long-bone fracture rates, but such fractures are still frequent. New antiresorptive and anabolic agents are being investigated but efficacy and safety of these drugs, especially in children, need to be better established before they can be used in clinical practice.
REFERENCES:
[1] https://doi.org/10.1097/med.0000000000000367
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2364

AB0729 CLINICO-EPIDEMIOLOGICAL PROFILE OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) PATIENTS IN KENYA; DATA FROM THE KENYA PEDIATRIC RHEUMATOLOGY (KAPRI) REGISTRY

A. Migowa[1], R. Odhiambo[2], J. Orwa[3], J. Shah[4]. *[1]Aga Khan University Hospital-Westlands, Pediatrics and Child Healh, Nairobi, Kenya*; *[2]Aga Khan University Hospital-Westlands, Institute of Human Development, Nairobi, Kenya*; *[3]Aga Khan University Hospital-Westlands, Population Health, Nairobi, Kenya*; *[4]Aga Khan University Hospital-Westlands, Internal Medicine, Nairobi, Kenya*

Background: Pediatric rheumatic diseases are chronic illnesses that impart a significant disease burden upon societies (1-3). Determination of the burden and clinical characteristics of these diseases is a critical first step to improving access to care and optimizing use of existing health systems for the well-being of these patients (4-6). A pediatric rheumatology registry is critical in defining the spectrum, clinical characteristics, outcomes and responses of various interventions for pediatric rheumatic diseases. Given that none exists in Kenya, the Kenya Pediatric Rheumatology Registry (KAPRI) registry offers a platform to generate this much needed data in sub-Sahara Africa.
Objectives: Our objective was to determine the baseline patient characteristics, clinical features and outcomes of the Juvenile Idiopathic Arthritis (JIA) patients assessed at the Aga Khan University Medical College East Africa who were enrolled into the KAPRI registry from inception in March 2019 to December 2020.
Methods: All patients with an ICD 10 M code diagnosis of Juvenile Arthritis were selected from the KAPRI registry database. Age, gender, laboratory and clinical features at diagnosis and treatment options offered were extracted from the database. A further detailed chart review was undertaken to determine the proportion of patients who achieved remission or minimally active diseases.
Results: Among the 207 patients enrolled thus far, 16 (7.7%) were diagnosed to have JIA. Majority of the patients were females (75%; n=12) with a mean age of 7 years and 3 months (Range:1 year – 13 years 7 months).
All patients had joint pain and swelling as the initial presenting complaints. Majority of the patients had polyarticular JIA (75%, n=12). The other 4 patients were oligoarticular (n=2) and systemic JIA (n=2). Among the polyarticular JIA patients (n=12), only 3 (25%) were rheumatoid factor (RF) positive and 1 was antinuclear antibody (ANA) positive. The oligoarticular and systemic JIA patients were all negative for antinuclear antibody, rheumatoid factor and cyclic citrullinated peptide antibodies (anti-ccp). Seven patients (43.8%) required biological therapies; tocilizumab (n=2: systemic JIA), adalimumab (n=2: polyarticular JIA), etanercept (n=2: polyarticular JIA) and tofacitnib (n=1: polyarticular JIA). One patient with systemic JIA on tocilizumab developed herpes simplex which was successfully managed with oral acyclovir. All the other patients did not develop any infections, allergic reactions or any other untoward events as adverse outcomes following the use of biological therapies. Five patients have attained remission as illustrated in the Table 1 below. Two patients have been lost to follow up.
Conclusion: Seronegative polyarticular JIA was the predominant form of JIA observed with a predilection to affect more girls and boys. Over a period of 2 years, remission has been attained among 31.25% of the patients (5 of 16) with use of synthetic disease modifying anti-rheumatic drugs and biological therapies.
REFERENCES:
[1] Moorthy LN, Peterson MG, Hassett AL, Lehman TJ. Burden of childhood onset arthritis. Pediatr Rheumatol Online J. 2010;8:20.
[2] Minden K, Niewerth M, Listing J, et al. The economic burden of juvenile idiopathic arthritis-results from the German paediatric rheumatologic database. Clin Exp Rheumatol. 2009;27(5):863–9.
[3] Bernatsky S, Duffy C, Malleson P, Feldman DE, St Pierre Y, Clarke AE. Economic impact of juvenile idiopathic arthritis. Arthritis Rheum. 2007;57(1):44–8.
[4] Migowa A, Colmegna I, Hitchon C, Were E, Ng'ang'a E, Ngwiri T, et al. The spectrum of rheumatic in-patient diagnoses at a pediatric hospital in Kenya. Pediatric Rheumatology (2017)
[5] Woolf AD. The bone and joint decade 2000–2010. Ann Rheum Dis. 2000; 59(2):81–2.
[6] Scott C, Webb K. Pediatric rheumatology in sub-Saharan Africa. Rheumatology (Oxford). 2014;53(8):1357–8.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2565

AB0730 HIP INVOLVEMENT IN JUVENILE IDIOPATHIC ARTHRITIS

S. Bouden[1], N. Ben Chekaya[1], A. Ben Tekaya[1], O. Saidane[1], R. Tekaya[1], I. Mahmoud[1], L. Abdelmoula[1]. *[1]Charles Nicolle Hospital, Rheumatology,Tunis, Tunisia*

Background: Juvenile idiopathic arthritis (JIA) is a heterogeneous group of diseases that have in common an onset before the age of 16 years, more than 6-month duration, and the presence of arthritis for at least 6 weeks with no identifiable cause. Hips are the commonly affected joints in severe destructive JIA. Hip disease develops in 20% to 50% of children with JIA.
Objectives: We aimed to analyze the epidemiological, clinical, and radiological aspects of hip involvement in Tunisian JIA.
Methods: A retrospective study including 35 patients was conducted between 2010 and 2019. The patients enrolled met the ILAR criteria for the diagnosis of JIA. Clinical, biological and radiological parameters relating to the hip involvement were collected.
Results: Thirty-five patients were enrolled. The mean age of the disease onset was 9 years [3-15]. The mean age of the patients at the time of the study was 37.8 years [17-69]. The mean duration of the disease was 27 years [2- 56]. These patients were assigned to discrete JIA categories: rheumatoid factor positive polyarthritis (43.5%), rheumatoid factor negative polyarthritis (21.7%), enthesitis-related arthritis (17.4%), oligoarthritis (13%) and psoriatic arthritis (4.4%). A biological inflammatory syndrome was noted in 52% of patients. Hip involvement was noted in 43.5% of patients. Coxitis occurred on average 15 years after the JIA onset [[4-37]. Thirty four percent of the patients had bilateral hip involvement. The mean Lequesne index was 14. Joint space narrowing and erosions were noted in respectively 68% and 34% of cases. The majority of patients (82.6%) received medical treatment combining nonsteroidal anti-inflammatory drugs (NSAID) and rehabilitation. In the other cases, a total hip replacement was necessary. Coxitis was significantly correlated with rheumatoid factor positive polyarthritis subtype (p=0.02) and with the presence of biological inflammatory syndrome (p=0.03).

Conclusion: Hip involvement is a major and highly prevalent issue in our JIA patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2619

AB0731 CERVICAL SPINE INVOLVEMENT IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

S. Bouden[1], N. Ben Chekaya[1], A. Ben Tekaya[1], O. Saidane[1], R. Tekaya[1], I. Mahmoud[1,1], L. Abdelmoula[1]. [1]*Charles Nicolle Hospital, Rheumatology, Tunis, Tunisia*

Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. In contrast to adult rheumatoid arthritis, where numerous studies have shown a high prevalence of involvement of the cervical spine, few studies have been published examining this entity in JIA.
Objectives: We aimed to analyze clinical and radiological findings of cervical spine involvement in patients with JIA.
Methods: A retrospective study including 35 patients was conducted between 2010 and 2019. The patients enrolled met the ILAR criteria for the diagnosis of JIA. Clinical, biological, and radiological data were collected. Patients had a radiological evaluation that included cervical spine x-rays in antero-posterior, lateral and lateral views with flexion.
Results: Thirty-five patients were enrolled. The mean age of the disease onset was 9 years [3-15]. The mean age of the patients at the time of the study was 37.8 years [17-69]. The mean duration of the disease was 27 years [2-56]. These patients were assigned to discrete JIA categories: rheumatoid factor positive polyarthritis (43.5%), rheumatoid factor negative polyarthritis (21.7%), enthesitis-related arthritis (17.4%), oligoarthritis (13%) and psoriatic arthritis (4.4%). Sixteen patients (45%) reported neck pain. Cervical spine involvement occurred on average 7 years [0-13] after the JIA onset. Cervical spine radiographs showed anterior atlantoaxial subluxation (> 5mm) in 8 patients. Magnetic-resonance imagining was performed in 9 patients that had abnormal neurological examination showing a pannus formation of C1-C2 junction (3 cases), a basilar invagination (4 cases) and erosions of the odontoid process (2 cases). A cervical collar has been used for immobilization in patients with significant cervical spine damage. A C1-C2 arthrodesis was proposed to 4 patients.
Conclusion: These findings suggest that the presence of cervical involvement in JIA patients is frequent. Radiologic assessment of cervical spine should be systematically performed for early detection and to prevent its complications.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2648

AB0732 JUVENILE IDIOPATHIC ARTHRITIS IN ADULTHOOD

N. Ben Chekaya[1], S. Bouden[1], A. Ben Tekaya[1], O. Ben Saidane[1], R. Tekaya[1], I. Mahmoud[1], L. Abdelmoula[1]. [1]*Charles Nicolle Hospital, Rheumatology, Tunis, Tunisia*

Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of unknown aetiology in childhood. Approximately 40- 60% of patients with juvenile idiopathic arthritis (JIA) have continuous or recurrent disease activity extending into adulthood.
Objectives: The aim of this study was to evaluate the clinical, biological and radiological course of JIA in adulthood.
Methods: A retrospective study including 35 patients was conducted between 2010 and 2019. The patients enrolled met the ILAR criteria for the diagnosis of JIA. Patients with JIA older than 20 years were included. Data regarding sociodemographic features, Physical growth, disease activity, biological and radiological parameters were analysed.
Results: Thirty one patients were recruited. The sex ratio was 0.53. The mean age at the time of the study was 38.9 years [20-69]. The mean age of the disease onset was 9 years [3-16]. These patients were assigned to discrete JIA categories: rheumatoid factor positive polyarthritis (47.7%), rheumatoid factor negative polyarthritis (23.9%), oligoarthritis (14.2%), enthesitis-related arthritis (9.5%), and psoriatic arthritis (4.7%).A failure to thrive was seen in 33.3% of patients. Overweight and obesity were found in 38% and 19% of patients, respectively. Biological inflammatory syndrome was noted in 52% of patients, and 65.2% had active disease. Hip involvement was noted in 43.5% of patients and 17.4% of them had a total hip replacement. Sixteen patients had neck pain and the imagining showed an atloid-axoid dislocation in 50% of them. Radiographs showed a joint destruction in 60.9% of patients and a wrist arthritis was the most frequent involvement.
Conclusion: Most of our included patients maintain active disease and have functional impairment in adulthood.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2658

AB0733 DADA2 VASCULITIS PRESENTING AS POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES): AN ATYPICAL PRESENTATION

M. Mamadapur[1], S. Mahadevan[1], A. Singh[1], R. Chakravarthy C H2, R. S2, T. T N2. [1]*Madras Medical College, Clinical Immunology and Rheumatology, Chennai, India*; [1]*Madras Medical College, Clinical Immunology and Rheumatology, Chennai, India*

Background: Deficiency of Adenosine Aminase deficiency 2 is monogenic disease presenting with multisystem involvement of vasculitis,Stroke[1],hematological manifestations. We hereby present a young child who presented with PRES initially and later diagnosed as DADA2.Only one case of DADA2 presenting as PRES is reported so far[2].This case highlights the atypical presentation of DADA2.
Objectives: A case report to highlight the rare presentation of DADA2 vasculits.
Methods: 8 year old developmentally normal male child,born out of consanguineous marriage presented with with fever,abdominal pain, seizures 1 year back. Ultrasound of abdomen revelaed mesenteric lymphadenitis and MRI Brain was suggestive of Meningoencephalitis.He was managed with antivirals and antibiotics then.
6 months later,he had fever,skin rash,pain abdomen,status epilepticus,hypertension followed by gangrene of fingers and toes.APLA,ANA,ANCA workup was negative. Complete Hemogram was normal. CRP was 130mg/dl. CT Abdomen was normal and no evidence of aneurysms. Renal Doppler Ultrasound was normal.CT upper limb showed left radial and ulnar artery significant narrowing with patchy occlusion. MRI Brain showed bilateral fronto parietal,occipital,putamen,left insula and subcortical and cortical T2W FLAIR hyperintensity without diffusion restriction suggestive of PRES. He was diagnosed as Childhood Polyarteritis Nodosa and treated with cyclophosphamide. Genetic Analysis of ADA2(CECR1) gene mutation by Sanger Sequencing of exons 2 to 10 showed a known variant (rs202134424) in ADA2 gene.

Figure 1. Gangrene of left 1-5th digits and right 4th and 5th digit resorption

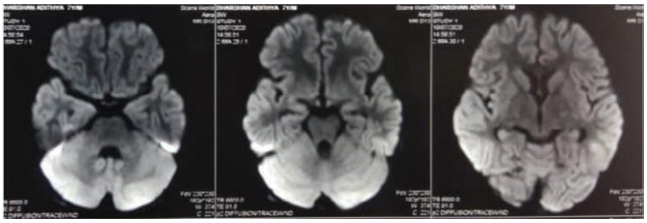


Figure 2. T2W FLAIR image showing bilateral fronto parietal,occipital,putamen,left insula and subcortical and cortical hyperintensity without diffusion restriction suggestive of PRES.

Results: He was started on Infliximab and is on follow up. No further events noted so far.Rehabilitation of left upper hand was done.
Conclusion: DADA2 can present with varied CNS manifestations like infarct,hemorrhage,aneurysms and PRES.High index of suspicion and early recognition can help in maintaining vascular integrity.
REFERENCES:
[1] Ganhão S, Loureiro G, Oliveira D, dos-Reis-Maia R, Aguiar F, Quental R et al. Two cases of ADA2 deficiency presenting as childhood polyarteritis

nodosa: novel ADA2 variant, atypical CNS manifestations, and literature review. Clinical Rheumatology. 2020;39(12):3853-3860.
[2] Sharma A, Naidu G, Sharma V, Jha S, Dhooria A, Dhir V et al. Deficiency of Adenosine Deaminase 2 in Adults and Children: Experience From India. Arthritis & Rheumatology. 2020;73(2):276-285.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2660

AB0734 REMISSION IN JUVENILE IDIOPATHIC ARTHRITIS AFTER WITHDRAWAL OF SYSTEMIC TREATMENT

L. C. Charca Benavente[1], L. Trives Folguera[2], L. R. Caballero Motta[2], A. M. Anzola Alfaro[2], K. López Gloria[2], J. M. Alvaro Gracia[2], I. Monteagudo[2], J. C. Nieto González[2]. [1]*Hospital Universitario Central de Asturias, Rheumatology, Oviedo, Spain*; [2]*Gregorio Marañón Hospital, Pediatric Rheumatology, Madrid, Spain*

Background: Juvenile idiopathic arthritis (JIA) requires frequent systemic treatments, the ideal goal being to achieve remission. Questions remain as to when treatment can be stopped and how to balance the risks and benefits of continuing medications against the possibility of a flare after discontinuation. There is currently little conclusive evidence on the management of JIA in remission.
Objectives: To determine the time to remission and frequency of flares in patients with JIA after withdrawal of systemic treatment in a single-centre cohort.
Methods: Patients with JIA visited in the last 15 years were included. A retrospective cross-sectional study was performed. Demographic data such as sex, age at diagnosis, current age, subcategories of JIA were collected. Systemic treatment was also collected (date of discontinuation, date of flare after discontinuation, time in remission, time of treatment until discontinuation, discontinuation of biologic therapy while maintaining methotrexate). For the analysis of qualitative variables, absolute and relative frequencies were used; for quantitative variables, median and IR; for comparative analysis, Chi-square and Mann-Whitney U test.
Results: We included 146 patients with JIA. Demographic data are shown in Table 1. 134 (90.4%) patients required systemic treatment (synthetic and/or biological DMARDs), of which 61 (45.5%) discontinued treatment completely at some point. Of the total number of patients who discontinued all systemic treatment, 19 (31.1%) had a flare with a median time in remission of 4.1 years (IR 1.3-9.1). 17 of the 134 patients (12.7%) with systemic treatment discontinued biologic therapy while maintaining methotrexate, of which 12 (70.6%) patients had a flare with a median time in remission of 0.9 years (IR 0.6-1.2). The differences between the frequency of flares and median time in remission between both treatment discontinuation groups (all systemic treatment versus discontinuation of biologic while maintaining methotrexate) were statistically significant (p<0.001). The median time from systemic treatment to complete withdrawal was 3.2 years (IR 1.9-4.8).

Table 1. Demographic characteristics of patients with JIA

Variables	N 146
Sex: Women n (%)	89 (60.3)
Age at onset (years, median (IR))	4.6 (2.5-9.2)
Current age (years, median (IR))	16.7 (11.1-20.9)
Types of JIA:	
Persistent oligoarticular n (%)	66 (45.2)
Extended oligoarticular n (%)	11 (7.5)
Polyarticular RF - n (%)	29 (19.9)
Polyarticular RF + n (%)	3 (2.1)
Enthesitis-related n (%)	12 (8.2)
Psoriatic n (%)	9 (6.2)
Systemic n (%)	16 (11.0)

Conclusion: One third of the patients in whom all systemic treatment was withdrawn had a flare (70% remain in remission without medication) with a median time in remission of 4 years. On the other hand, two-thirds of patients in whom biologic therapy was withdrawn while maintaining methotrexate had a flare, with a shorter time in remission. The differences between both groups with withdrawal of systemic treatment are statistically significant (p<0.001).
REFERENCES:

[1] Halyabar O, Mehta J, Ringold S, Rumsey DG, Horton DB. Treatment Withdrawal Following Remission in Juvenile Idiopathic Arthritis: A Systematic Review of the Literature. Paediatr Drugs. 2019 Dec;21(6):469-492. doi: 10.1007/s40272-019-00362-6.
[2] Simonini G, Ferrara G, Pontikaki I, Scoccimarro E, Giani T, Taddio A, Meroni PL, Cimaz R. Flares After Withdrawal of Biologic Therapies in Juvenile Idiopathic Arthritis: Clinical and Laboratory Correlates of Remission Duration. Arthritis Care Res (Hoboken). 2018 Jul;70(7):1046-1051. doi: 10.1002/acr.23435.
[3] Chhabra A, Robinson C, Houghton K, Cabral DA, Morishita K, Tucker LB, Petty RE, Larché M, Batthish M, Guzman J. Long-term outcomes and disease course of children with juvenile idiopathic arthritis in the ReACCh-Out cohort: a two-centre experience. Rheumatology (Oxford). 2020 Dec 1;59(12):3727-3730. doi: 10.1093/rheumatology/keaa118.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2718

AB0735 POLYMORPHISMS OF GENES CD14, C-REACTIVE PROTEIN, FIBRINOGEN BETA CHAIN, ASSOCIATED WITH THE DEVELOPMENT OF KAWASAKI DISEASE AND CORONARY ARTERY ANEURYSMS IN CHILDREN FROM CENTRAL RUSSIA

M. Kantemirova[1], S. Kurbanova[1], Y. Novikova[1], A. Glazyrina[1], M. Azova[2], E. Zheludova[2], E. Tarasenko[2], D. Ovsyannikov[1]. [1]*RUDN University, Department of Pediatrics, Moscow, Russian Federation*; [2]*RUDN University, Department of Biology and General Genetics, Moscow, Russian Federation*

Background: Kawasaki disease (KD) is a multifactorial disease with a genetic predisposition, systemic vasculitis complicated by the formation of coronary artery aneurysms (CAA). Its pathogenesis is based on immune inflammation with an increase in the concentration of pro-inflammatory cytokines, the level of C-reactive protein (CRP), and coagulation disorder.
Objectives: to search for polymorphisms of genes cluster of differentiation CD14, CRP, fibrinogen beta chain (FGB), associated with the KD development and a predisposition to the CAA formation among patients with KD living in Moscow and the Moscow region.
Methods: genotyping for gene polymorphisms CD14 –159 C>T (rs2569190), CRP 3872 C>T (rs1205), FGB – 455 G>A (rs1800790) by PCR in 31 children 1 month – 10 years old (median age 19 months [9,0; 38,5]) with KD, among them, in 10 patients the disease was complicated by CAA formation according to echocardiography, and 30 children of the control group.
Results: Three out of six investigated SNPs showed statistically significant difference in genotype and allele distribution: CRP C3872T, CD14 C159T and FGB G455A. CRP gene polymorphism: in patients with KD significantly less frequent is homozygous type TT (RR 0,22, 95% CI: 0,05–0,91, p=0,0168).
CD14 gene polymorphism: in control group heterozygous genotype CT is predominant, (RR 0,58, 95% CI: 0,4–0,83, p=0,0017) among patients with KD homozygous genotypes CC and TT are predominant. (RR 3,61, 95% CI: 1,14–11,49, p=0,0057).
FGB gene polymorphism: genotype GA is predominant in control group (RR 0,48, 95% CI: 0,26–0,9, p=0,0149). In patients with KD significantly less frequent is homozygous type GG (RR 1,69, 95% CI: 1,03–2,8, p=0,0297).
We didn't find any significant difference in genotype and allele distribution in KD patients with and without CA lesions.
Conclusion: statistically significant differences (p<0,05) were revealed in the distribution of genotypes for polymorphisms of the CD14 –159 C>T, CRP 3872 C>T and FGB –455 G>A genes among patients with KD and children of the control group; when comparing the results of KD patients with CAA and the control group, statistically significant differences (p<0,05) were revealed only in the polymorphism CD14 –159 C>T. It can be assumed that these polymorphisms are associated with the development of KD and CAA in these patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2807

AB0736 JUVENILE IDIOPATHIC ARTHRITIS IN ADULTHOOD: TRENDS OF THE DISEASE AND SOCIO-PROFESSIONAL FUTURE

S. Miladi[1], M. Yasmine[1], S. Mariem[1], A. Fazaa[1], K. Ouenniche[1], L. Souebni[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: Juvenile idiopathic arthritis (JIA) is the most common arthropathy of childhood that may lead to physical disability and reduced quality of life, thus hindering the ability of the patients to achieve a meaningful adult life.
Objectives: The aim of this study was to assess the trends of the disease and socio-professional future.
Methods: We conducted a retrospective study including adult patients aged > 18 years with a history of JIA according to the International League of Associations for Rheumatology (ILAR). Collected data included age, sex, the

characteristics of the disease (subtype of JIA, disease duration). The level of education, marital status as well as the profession were recorded.
Results: The study included 32 patients with a female perdominance: sex ratio was 1,5. The mean age was 29,5 years old [18-64]. The mean age of onset of the disease was 6 years and 2 months [2-17]. The frequency of each JIA subset was at follows: polyarticular with rheumatoid factor (n= 14), polyarticular without rheumatoid factor (n=9), systemic (n= 2), enthesitis-related arthritis (n=7), oligoarthritis (n= 5). Four patients suffered from bilateral cataract due to corticosteroid intake. Polyarticular RF+ and RF- progressed into an authentic seropositive and seronegative RA in 71.4% and 66.7% respectively. Among oligoarticular subtype, an extension of the disease to a polyarticular FR+ form (n=1) and to a seronegative rheumatoid arthritis (n=1) was noted. Systemic JIA forms remained in remission with an articular involvement. All the patients with ERA developed spondylarthritis. Although forty–two percent of the patients were married, only half of them had children. Ten percent of patients stopped attending school because of disease flares and deformation. A university level was found in 16% of cases. Only Thirty patients had a profession. Of the patients, 74.4% had received disease-modifying anti-rheumatic drugs (DMARDs) and 36.3% of them were still taking a DMARD. Ten patients were on biologics. Severe disability was found in 20% of patients and concerned mainly the hip (57,2%), the wrist (28,5%) and the elbows (14,3%). Prosthetic joint replacement was found in 2% of cases with a revision of the latter in one patient.
Conclusion: Adults with JIA often have significant levels of disability, usually related to severe joint complications. There is a clear requirement for a better transition to adulthood and a socio-professional rehabilitation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2924

AB0737 THE NAIL FOLD CAPILLAROSCOPIC FINDINGS OF ADOLESCENTS WITH ANOREXIA NERVOSA AND BULIMIA NERVOSA

M. Kasap-Cuceoglu[1], M. Pehlivanturk-Kizilkan[2], E. Sag[1], S. Sener[1], Z. Balik[1], S. Akgul[2], O. Derman[2], Y. Bilginer[1], N. Kanbur[2], S. Özen[1]. [1]*Hacettepe University Faculty of Medicine, Pediatric Rheumatology, Ankara, Turkey*; [2]*Hacettepe University, Department of Pediatrics Division of Adolescent Medicine, Ankara, Turkey*

Background: The nail fold video capillaroscopy (NVC) is usually performed on patients with microcirculation problems, such as Raynaud's phenomenon. It is also used to distinguish between primary and secondary Raynaud's Phenomenon and identify the scleroderma pattern.
Objectives: To describe the acute phase nail fold capillaroscopic findings of adolescents with anorexia nervosa (AN) and bulimia nervosa (BN) and to compare these findings with adolescents diagnosed with primary Reynaud's phenomenon (RP).
Methods: We included 17 AN, 2 BN patients and 6 adolescents with primary RP as a control group. The nail fold video capillaroscopy (NVC) data of three study groups were compared. AN and BN patients were classified according to DSM-5. The participants in these two groups were assessed for the presence of Reynaud's phenomenon/acrocyanosis and the weight loss history (amount and duration), daily calorie intake, vital signs, hydration status, amenorrhea presence and time, the presence and frequency of compensatory behaviors, and drug usage were recorded. Adolescents with primary RP were diagnosed according to 'International consensus criteria for the diagnosis of RP. The initial NVC was performed at the acute phase of AN and BN. For AN acute phase is defined as the period where the nutritional rehabilitation has not yet taken place. The NVC analysis was be performed with a digital USB microscopy by an expert blinded to the participant's clinical status and diagnosis. Eight fingers were evaluated for each patient and average of all fingers' scores were used as quantitative measures.
Results: Among adolescents with AN, 14 of them had enlarged capillaries (capillary diameter 20-50 µm) and 6 of them had mild tortuosity (<50%) which were considered as minor capillaroscopic changes. 5 patients had at least one giant capillary (>50µm), 3 of them had microhemorrhages, 4 of them had capillary ramifications, and 1 of them had capillary disorganization which were considered as major capillaroscopic changes. Two adolescents had capillary loss (6 capillaries/mm). None of them had active or late phase scleroderma findings. In the primary RP group, there were minor findings as five adolescents had mild capillary dilation (capillary diameter 20-50 µm), and 5 had mild tortuosity (<50%). However, none had scleroderma (early-active-late phase) findings. Microangiopathy assessment scores revealed no difference between the AN patients with and without RP and primary RP patients.(Table 1) A positive correlation was found between capillary ramification scores and initial daily calorie intake (r: -0.47; p=0.04).

Table 1. Measurements of capileroscopy findings according to patient groups

	AN+RP+ n=4	AN+RP- n=13	BN n=2	Primer RP kontrol n=6	p
Microangiopathy score	0.84 (IQR 0.98)	0.92 (IQR 0.96)	0.71	0.65 (IQR0.23)	0.62
• **Capillary loss score**	0.22 (IQR 0.62)	0.06 (IQR 0.41)	0.15	0.0 (IQR 0.26)	0.58
• **Capillary ramification score**	0.18 (IQR 0.25)	0.13 (IQR 0.25)	0.09	0.09 (IQR 0.18)	0.88
• **Disorganized capillaries score**	0.38 (IQR 0.48)	0.56 (IQR 0.68)	0.46	0.43 (0.32)	0.98
Enlarged capillaries score (20-50 µm)	0.56 (IQR 0.78)	0.31 (IQR 0.72)	0.73	0.58 (IQR 0.42)	0.60
Giant capillaries score (>50 µm)	0.06 (IQR 0.22)	0.00 (IQR 0.03)	0.18	0.03 (0.14)	0.14
Microhaemorrhage score	0.00	0.00	0.00	0.01	0.67

Conclusion: Preliminary results of our study suggest that adolescents with AN are at risk for vasculopathy especially during the acute phase of the disease.
REFERENCES:
[1] Smith V, et al Autoimmun Rev. 2020 Mar;19(3):102458.
[2] American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders (DSM-5). American Psychiatric Pub, Arlington
Acknowledgements: Muserref Kasap-Cuceoglu and Melis Pehlivanturk-Kizilkan contributed equally.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3075

AB0738 JUVENILE IDIOPATHIC ARTHRITIS AND SCHOOLING

H. Tantaoui[1], K. Nassar[1], S. Janani[1]. [1]*Faculty of Medicine and Pharmacy, Hassan II University, Ibn Rochd University Hospital Center, Rheumatology, Casablanca, Morocco*

Background: Juvenile idiopathic arthritis (JIA) refers to all chronic inflammatory rheumatism in children without a recognized cause, onset before the age of 16. JIA is associated with significant short- and long-term disability, which influences the education and socio-professional integration of patients who suffers from it.
Objectives: Evaluate the impact of JIA on the education and professional integration of affected patients.
Methods: This is a retrospective, descriptive and cross-sectional study carried out in the rheumatology department.
We included all patient followed in our JIA training.
The following information was collected from a questionnaire survey: Educational attainment, main problems experienced during studies, cause of dropping school, and professional data.
Results: Forty-two patients were included. The average age was 27.15 years old [18 - 61 years old]. Sex-Ratio (M / F) was 0.9. The forms of JIA were dominated by spondyloarthropathy (48.64%) and the seropositive polyarticular form (18.91%). The mean age of onset of JIA was 10.8 years [6 months - 16 years]. The mean duration of JIA progression was 14.4 years [4 - 27 years].
Regarding education, 2.94% were illiterate, 23.52% had a primary level, 55.87% a secondary level and 17.64% a higher level. The majority of patients (85%) experienced several problems during their studies: joint pain and stiffness (73.52%), absenteeism (50%), limitation in activities (26.47%), problem with adaptation and social integration (11.76%) and fatigue (5.88%). Only 2.94% of patients benefited from an individualized reception protocol apart from a sports exemption which represents 38.23%. 73.52% of patients received encouragement to continue their studies by those around them (parents, teachers and attending physicians).
Discontinuation of schooling was observed in 70.58% of patients with 8.82% of patients dropping school before the onset of JIA and 61.76% of patients related to JIA. School studies were still ongoing in 23.52% of patients.
Regarding the professional side, unemployment affects 52.94% of these patients and workers represent 23.52%.
Conclusion: In our series, the level of education of JIA patients does not exceed secondary level in 80% of cases. The implementation of an individualized reception protocol is strongly recommended to facilitate the education of these patients and to fight against the main problems experienced. The professional integration of patients with JIA should also be adopted.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3276

AB0739

MULTISYSTEM INFLAMMATORY SYNDROME ASSOCIATED WITH SARS-COV-2 INFECTION AND E.COLI SEPSIS: THE POTENTIAL ROLE OF PROCALCITONINE AS A RAPID DIAGNOSTIC BIOMARKER TO DISTINGUISH TWO DIFFERENT PHASES OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME

M. Gilio[1], S. B. Morella[1], F. Picaro[1], C. Acierno[1], D. Palazzo[1], A. Erezanu[1], M. Frontuto[1], G. Mastroberti[1], G. De Stefano[1]. [1]*San Carlo Hospital, Infectious Diseases, Potenza, Italy*

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is typically very mild and often asymptomatic in children. A complication is the rare multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19, presenting 4-6 weeks after infection as high fever, organ dysfunction, and strongly elevated markers of inflammation. The pathogenesis is unclear but has overlapping features with Kawasaki disease suggestive of vasculitis and a likely autoimmune etiology.
Objectives: We report a case of multisystem inflammatory syndrome in children (MIS-C) in patient with SARS-CoV-2 infection and Enteropathogenic Escherichia coli (EPEC) sepsis due to acute enteritis, observed at end of December 2020 to a tertiary-care center (San Carlo Hospital), in Basilicata region (Italy).
Methods: This healthy 12-year- old male patient was tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Clinical presentations was characterized by fever, abdominal pain, gastrointestinal complaints and evanescent rash. Laboratory values were remarkable for high levels of procalcitonin, C-reactive protein (CRP), D-dimers, B-type natriuretic peptide (BNP), and troponin. He also had low albumin levels. Autoantibodies tests were negative. Chest tomography showed ground-glass opacities in less than 25% of the lungs, small bilateral pleural effusion and increased cardiac area; abdominal tomography showed enlargement of the lymphnodes and ascites. Evaluation for other infectious etiologies showed molecular test positivity on fecal samples for EPEC E. coli. He received broad spectrum intravenous antibiotics (macrolids and quinolones and then carbapenems). On the seventh day the enteritis resolved and procalcitonin normalized, however he continued to have lymphopenia, thrombocytopenia, hypoalbuminemia, elevated levels of CRP, D-dimers, ferritin, troponin, and increased BNP. On the ninth day he was feverish again and developed severe cardiac and respiratory failure requiring advanced respiratory support and admission to the intensive care unit. He received IVIG (intravenous immunoglobulin at 2 g/Kg, glucocorticoids (Methylprednisolone 1mg/kg) and enoxaparin.
Results: The patient was discharged asymptomatic at home after 28 days of hospital stay.
Conclusion: We observed multisystem inflammatory syndrome in children (MIS-C) in a previously healthy patient with SARS-CoV-2 infection and E.coli sepsis, who became critically ill with multisystem involvement. In this case viral and bacterial infections could be considered as a double hit for the etiopathogenesis of MIS-C. The trend of procalcitonin was better than C-reactive protein for differentiating bacterial from non-bacterial phase of systemic inflammatory response syndrome (SIRS) in this critically ill child. Although the accuracy of both tests is moderate. Diagnostic accuracy could be enhanced by combining these tests with bedside clinical judgment.
REFERENCES:

[1] Consiglio CR, Cotugno N, Sardh et al. The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19. Cell. 2020 Nov 12;183(4):968-981.e7. doi: 10.1016/j.cell.2020.09.016. Epub 2020 Sep 6. PMID: 32966765; PMCID: PMC7474869.
[2] Nakra NA, Blumberg DA, Herrera-Guerra A, Lakshminrusimha S. Multi-System Inflammatory Syndrome in Children (MIS-C) Following SARS-CoV-2 Infection: Review of Clinical Presentation, Hypothetical Pathogenesis, and Proposed Management. Children (Basel). 2020 Jul 1;7(7):69. doi: 10.3390/children7070069. PMID: 32630212; PMCID: PMC7401880.
[3] Simon L, Saint-Louis P, Amre DK, Lacroix J, Gauvin F. Procalcitonin and C-reactive protein as markers of bacterial infection in critically ill children at onset of systemic inflammatory response syndrome. Pediatr Crit Care Med. 2008 Jul;9(4):407-13. PMID: 18496408.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3300

AB0740

IMPACT OF DIAGNOSIS DELAY ON DISEASE PARAMETERS DURING JUVENILE IDIOPATHIC ARTHRITIS

H. Bettaieb[1], H. Ferjani[1], K. Maatallah[1], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab Institute of Orthopedics, Rheumatology, Tunis, Tunisia*

Background: Juvenile idiopathic arthritis (JIA) is the most common type of arthritis in childhood (1). Prompt diagnosis is mandatory to avoid joint destruction and growth abnormalities. However, it's often misdiagnosed by pediatricians and general practitioners leading to longer diagnosis delay (2).
Objectives: The aim of this study was to evaluate the lag time between JIA symptoms onset and diagnosis and its impact on disease activity and bone loss.
Methods: A retrospective monocentric study was carried out on JIA patients (ILAR criteria). Diagnosis delay was collected from the patient's medical files. Disease activity at JIA diagnosis was evaluated by JADAS10 (Juvenile Arthritis Disease Activity Score) in poly and oligoarticular subtypes and by BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) in arthritis related enthesitis form. The data were analyzed using the SPSS statistical package. A p value < 0.05 was considered significant.
Results: We enrolled 48 JIA (31 male and 17 female) with a mean age at disease onset of 11.2 ± 3.8 years. The median disease duration was 84 months [2-408]. The median JIA diagnosis delay was 8 months [1-108]. The JIA subgroups were in decreasing order of frequency: Enthesitis-related Arthritis (n=32), Polyarticular RF- (n=4), Polyarticular RF+ (n=2), Oligoarticular (n=6), Systemic (n=2), Psoriatic Arthritis (n=1) and Undifferentiated (n=1).
At diagnosis, median ESR and CRP were 44 mm/hour [2-100] and 24 mg/l [2-86] respectively. Median JADAS10 score was 4 [0-21]. Median BASDAI score was 6.2 [2-9.4].
At follow-up, five patients (10.4%) had atlantoaxial subluxation and 17 had coxitis (43.8%).
At bone densitometry, 45% of patients had osteroposis and 27.5% had osteopenia.
An agreement was assessed between a long diagnosis delay and the following parameters: male gender (p=0.04) and osteoporosis (p=0.018). A Significant positive correlation was found between delay in JIA diagnosis and BASDAI score (p=0.047, r=0.63). No association was found between JIA diagnosis delay and JADAS score (p=0.56). Neither ESR (p=0.19) nor CRP (p=0.42) was associated with JIA diagnosis delay.
Finally, no link was observed with the occurrence of hip arthritis (p=0.281) or atlantoaxial subluxation (p=0.137).
Conclusion: In this study, delay in diagnosis was associated with higher disease activity scores and bone loss. Our results suggest that early identification and treatment of JIA leads to improved outcomes as well as bone mass.
REFERENCES:

[1] Petty R.E., Southwood T.R., Manners P. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31(2):390.
[2] Foster HE, Scott C, Tiderius CJ,et al. Improving musculoskeletal health for children and young people - A 'call to action'. Best Pract Res Clin Rheumatol. 2020 Oct;34(5):101566.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3472

AB0741

PREVALENCE AND ASSOCIATED FACTORS OF ATLANTO-AXIAL INSTABILITY IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

H. Bettaieb[1], H. Ferjani[1], K. Maatallah[1], H. Boussaa[1], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab Institute of Orthopedics, Rheumatology, Tunis, Tunisia*

Background: Atlanto-axial instability (AAI) is a serious complication during Juvenile Idiopathic Arthritis (JIA). It can lead to severe neurological morbidity or mortality if left untreated (1).
Objectives: To determine the prevalence of AAI in patients with JIA and to identify factors associated with an increased risk of its occurrence.
Methods: A retrospective monocentric study was carried out on JIA patients (ILAR criteria). Data, including age at disease onset, JIA type, disease activity at AAI diagnosis and treatment were collected. Disease activity at JIA diagnosis was evaluated by JADAS10 (Juvenile Arthritis Disease Activity Score) in poly and oligoarticular subtypes and by BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) in arthritis related enthesitis form. Standard radiographs of the cervical spine were analyzed. The data were analyzed using the SPSS statistical package. A p value < 0.05 was considered significant.
Results: We enrolled 48 JIA (31 male and 17 female) with a mean age at disease onset of 11.2 ± 3.8 years. The median disease duration was 84 months [2-408]. The median JIA diagnosis delay was 8 months [1-108]. The JIA subgroups were in decreasing order of frequency: Enthesitis-related Arthritis (n=32), Polyarticular RF- (n=4), Polyarticular RF+ (n=2), Oligoarticular (n=6), Systemic (n=2), Psoriatic Arthritis (n=1) and Undifferentiated (n=1).

At diagnosis, median ESR and CRP were 44 mm/hour [2-100] and 24 mg/l [2-86] respectively. Median JADAS10 score was 4 [0-21]. Median BASDAI score was 6.2 [2-9.4].
At follow-up, five patients (10.4%) had atlantoaxial subluxation and 17 had coxitis (43.8%).
At bone densitometry, 45% of patients had osteroposis and 27.5% had osteopenia.
An agreement was assessed between a long diagnosis delay and the following parameters: male gender (p=0.04) and osteoporosis (p=0.018). A Significant positive correlation was found between delay in JIA diagnosis and BASDAI score (p=0.047, r=0.63). No association was found between JIA diagnosis delay and JADAS score (p=0.56). Neither ESR (p=0.19) nor CRP (p=0.42) was associated with JIA diagnosis delay.
Finally, no link was observed with the occurrence of hip arthritis (p=0.281) or atlantoaxial subluxation (p=0.137).
Conclusion: In our study, the prevalence of AAI was 10.4%. Prolonged corticosteroid use and elevated inflammatory markers were the major factors associated with an increased risk of upper cervical spine involvement. Hence, targeted treatments are required to prevent cervical spine instability.
REFERENCES:
[1] Hospach T, Maier J, Müller-Abt P, Patel A, Horneff G, von Kalle T. Cervical spine involvement in patients with juvenile idiopathic arthritis - MRI follow-up study. *Pediatr Rheumatol Online J*. 2014;12:9.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3501

AB0742 PREVALENCE AND RISK FACTORS OF OSTEOPOROSIS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

H. Bettaieb[1], H. Ferjani[1], K. Maatallah[1], H. Boussaa[1], D. Kaffel[1], W. Hamdi[1]. [1]*Mohamed Kassab Institute of Orthopedics, Rheumatology, Tunis, Tunisia*

Background: Childhood rheumatic diseases are associated with reduced Bone mass and increased risk of fractures (1). Several factors may interact to determine osteoporosis other than direct bone detrimental effects of the disease or its treatment.
Objectives: In this work, we aimed to investigate the prevalence of bone loss in patients with JIA and to determine the relative factors associated with osteoporosis during this chronic disease.
Methods: A retrospective monocentric study was carried out on JIA patients (ILAR criteria).Dual-energy x-ray absorptiometry (DEXA) was used to determine bone status. Disease activity was evaluated by JADAS10 (Juvenile Arthritis Disease Activity Score) in poly and oligoarticular subtypes and by BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) in arthritis related enthesitis form. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were noted. The data were analyzed using the SPSS statistical package. A p value < 0.05 was considered significant.
Results: The sample included 40 JIA (25 male and 15 female) with a mean age at disease onset of 11.3 ± 3.6 years. The median disease duration was 90 months [7-408].The median JIA diagnosis delay was 8 months [1-108]. The JIA subgroups were in decreasing order of frequency: Enthesitis-related Arthritis (n=27), Polyarticular RF- (n=4), Polyarticular RF+ (n=1), Oligoarticular (n=4), Systemic (n=2), Psoriatic Arthritis (n=1) and Undifferentiated (n=1). Median ESR and CRP were 29 mm/hour [2-98] and 14.5 mg/l [0-70] respectively. Median BASDAI score was 4.3 [1-9.7]. Median JADAS10 score was 1[1-21].
Overall, 45% of patients had osteoporosis, 27.5% had osteopenia, and 27.5 % had normal bone densitometry. None of the patients had a history of vertebral or peripheral fractures.
Thirty per cent of patients (n=12) were on long term corticosteroid therapy with a mean dose of 6.6 ± 2.8 mg/day. Only 12.5% (n=5) of them had a regular physical activity.
Osteoporosis was associated with age at JIA onset (p=0.005), disease duration (p=0.001), ESR (p=0.08), CRP (p=0.04), BASDAI score (p=0.017) and sedentarily (p=0.026). Osteopenia was only associated with corticosteroid therapy (p=0.01). Neither osteoporosis (p=0.37) nor Osteopenia (p=0.25) was associated with disease activity score.
Conclusion: In our study, osteoporosis was a common feature during JIA. A long term corticosteroid therapy and sedentarily seem to be correlated with more impaired bone abnormalities. Hence, targeted interventions are urgently required to preserve bone health during JIA.
REFERENCES:
[1] McDonagh JE. Osteoporosis in juvenile idiopathic arthritis. Curr Opin Rheumatol. 2001;13(5):399-404.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3522

AB0743 SINGLE CENTER EXPERIENCE OF BIOLOGICAL THERAPY IN PATIENTS WITH JUVENILE SYSTEMIC SCLERODERMA

D. Alexseev[1], I. Nikishina[1], L. Ananieva[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Pediatric, Moscow, Russian Federation*

Background: Juvenile systemic scleroderma (jSSC) is a rare multisystem disease with a poor prognosis. The current therapy is imperfect. Biologics, as a modern efficient option for treatment of rheumatic diseases don`t have official indication for jSSC, but it seems to be useful in severe cases, especially lung and heart damage.
Objectives: To analyze the existing experience of Biologics therapy in children with jSSC in single center in order to improve the understanding of the indications for use and the results of using these drugs.
Methods: The retrospective study include 9 patients with jSSC with severe course of disease, 7 of them were girls.
Results: Among this group of patients the age at disease onset was 9.1 years (min-max 1.1-15.1). Clinical manifestations: Raynaud's syndrome (n = 9), ulcers (n = 3), skin changes (n = 9), joints (n = 8), muscles (n = 4), interstitial lungs disease (n = 6), heart (n = 3), esophagus (n = 5), calcification (n = 3). The main therapy prior to the use of biological agents: glucocorticoids (GC) (n = 9), cyclophosphamide (CF) (n = 2), hydroxychloroquine (HC) (n = 5), therapy for the microcirculation improvement. Biologics were prescribed in the case of insufficient effectiveness of previously conducted therapy, primarily in relation to lung damage (interstitial disease) and heart (with reduced contractility, arrhythmia), as well as changes in the skin and musculoskeletal system. In addition, the possibility to reduce the dose of GC (n=6), withdrawal of CF (n=2) was taken into account. Our experience consist of follows: rituximab (RTM) (n=7) at a dose of 375 mg/m2 interval 3-6 months, abatacept i.v.(ABT) (n=2) 10 mg/kg every 4 weeks, tocilizumab i.v.(TCZ) (n=2) 8 mg/kg. In all cases Biologics was prescribed not earlier than 1.5 year after disease onset (4.6 years in average). By present most patients continued to use biological therapy; of them - RTM was used for 2.2 (0.5-6.0) years, in 1 patient – was canceled after 6 years due to the loss of efficasy; ABT is used in 2 children for 0.5 and 3.6 years, TCZ - in 2 children for 0.3 (withdrawal) and 2.0 years (continues to use)., TCZ was prescribed in 1 patient after 6 years of RTM use. In 1 patient TCZ was withdrawal due to an infusion reaction, and ABT was prescribed. As a result of the therapy, it has been found to improve habitus, quality of life and well-being, reduce skin tightening, improve joint function; no progression of changes in the lungs according to CT and functional tests (FVC, DLCO), improvement in cardiac lesions. It seems that disease improvement became notable at least 3-6 months after the Biologics start. In most patients there were no serious adverse events (AE). No significant infections have been reported. But we met an unexpected case of substantial increasing of neutrophil's count just after each TCZ infusions up to 21,000 and reversed by following infusions for a one year of treatment from 2 years of total duration of using.
Conclusion: Our data shown that Biologics could be efficient and well-tolerated option for severe and resistant to «traditional» therapy course of jSSC. Because this kind of condition is extremely rare further multicenter study is needed.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3558

AB0744 HOW JUVENILE IDIOPATHIC ARTHRITIS PATIENTS PERCEIVE THEIR ILLNESS?

K. Maatallah[1], M. Yasmine[1], H. Ferjani[1], W. Triki[1], D. Ben Ncib[1], D. Kaffel[1], W. Hamdi[1]. [1]*Kassab Institute of Orthopedics, Rheumatology, Tunis, Tunisia*

Background: Juvenile idiopathic arthritis (JIA) represents the most common inflammatory rheumatism of childhood. Because of a prolonged course of active disease, many patients experience physical and psychosocial limitations. Illness perceptions involve the personal beliefs that patients have about their illness and may influence health behaviors considerably.
Objectives: The present study aimed to investigate the illness perception of patients with JIA.
Methods: We conducted a cross-sectional study including children with JIA (according to the International League of Associations for Rheumatology (ILAR)). We recorded sociodemographic data and the subtype of the JIA. To assess a child's perception of how arthritis affects their life, the Brief Illness Perception Questionnaire (IPQ) was completed by the parent (child age ≤10 years) or by

the child (age ≥11 years). The Brief IPQ is a nine-item questionnaire rated using a 0-to10 response scale that assesses cognitive illness representations: consequences (Item 1), timeline (Item 2), personal control (Item 3), treatment control (Item 4), and identity (Item 5). Two of the items assess emotional representations: concern (Item 6) and emotions (Item 8). One item assesses illness comprehensibility (Item 7).

Results: The study included 22 patients. The mean age was 15 ± 7 years [4-35], and the mean age at diagnosis was 9 ±3 years [3-14]. There was a female predominance (sex ratio= 2.1). The frequency of each JIA subset was at follows: polyarticular with rheumatoid factor (n= 1), polyarticular without rheumatoid factor (n=3), systemic (n= 2), enthesitis-related arthritis (n=9), oligoarthritis (n= 7), undifferentiated (n=1). Non-steroidal anti-inflammatory drugs were prescribed in 72% of cases, and Cs-DMARDs in 59% of patients. The most-reported causal factor in their illness was a history of traumatism (22%). Perceiving symptoms (identity) were significantly related to being affected by the disease (emotional response) *(p= 0.01)*. Conversely, patients who had personal and treatment control expressed less emotional response (r = –0.7, r=-0.2 respectively). Moreover, those who were concerned about the disease perceived more the consequences of their illness (*p=0.09*) and understood it more (p=0.029). We also noted significant correlations between personal control and treatment control (p = 0.033). A positive correlation was found between identity as well as consequences and timeline (p=0.011, p=0.024), showing that the perception of chronicity was associated with pain and the burden of the disease.

Conclusion: Our study highlighted the importance of assessing illness perception in JIA patients. Patient education programs should be implemented since diagnosis for better disease management.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3616

AB0745 BONE STATUS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) ON T2T THERAPY

N. Shevchenko[1,2], Y. Khadzhynova[1,2], L. Bohmat[1,2]. [1]*V.N. Karazin Kharkiv National University, Department of Pediatrics No 2, Kharkiv, Ukraine*; [2]*SI Institute for Children and Adolescents Health Care of NAMS of Ukraine, Department of Cardiorheumatology, Kharkiv, Ukraine*

Background: In recent years approaches to both the diagnosis and treatment of JIA have changed. Among it key positions for bone health are reducing the time to make a diagnosis and initiation of basic therapy, as well as reducing the timing and doses of corticosteroids. The interdependence of osteopenia in children with JIA with established impairment of vitamin D status, the prevalence of which remains very high in this cohort of patients, has also not been definitively elucidated.

Objectives: To study the condition of bone tissue in children with JIA in modern disease management and to identify adverse factors for the development of osteopenia among the clinical manifestations signs.

Methods: The study included 35 children with JIA aged 7 to 17 years, mostly female (77.1%), with oligo - (25.7)%, poly - (60.0%) and undifferentiated (14.3 %) arthritis, 53.4% have not yet received basic therapy. No corticosteroid therapy was available. The study of bone tissue was performed by two-energy X-ray absorptiometry (Explorer QD W-Hologic). All patients were tested for serum parathyroid hormone (PTH), the level of 25-hydroxyvitamin D [25(OH) D], the total and ionized calcium and blood phosphorus. The control group consisted of 12 healthy children of the same age with a normal level of 25 (OH) D.

Results: The average level of 25(OH)D was 20.41±1.35 ng/ml, which is considered insufficient and was lower than in the control group (30.03±2.53 ng/ml, $p<0.05$). Studies of calcium and phosphorus in the blood showed that children with JIA have no deviations from the normative values. The majority of examined patients (98.37%) had normal values of PTH, in average was 30.43±0.90 pg/ml. The PTH was significantly different in children with different variants of JIA, the highest content was recorded in non-differential arthritis (34.33±1.80 pg/ml), the lowest - in the oligoarticular variant (28.36±1.43, p<0,05). PTH had a negative correlation with 25(OH)D status (r = -0.41; p <0.05) and did not depend on the sex and disease activity.

The incidence of osteopenia was 28.57%, its prevalence was almost the same in different variants of arthritis and did not depend on the sex and age of patients, positivity for RF. Osteopenia was more common in ANA-positive than in ANA-negative variant (46.15% vs. 18.18%; $p_{\varphi}<0.05$). In 30.0% patients with osteopenia decreased BMD reached the values of osteoporosis (more than 2.5σ). This group consisted of girls with predominantly polyarticular and undifferentiated JIA, with RF-negative and ANA-positive variant.

Deviations from the age normative values of BMD (Z-score) were associated with BMI (r=0.33; p <0.05), JADAS scale results (r=0.35; p<0.04), the number of active joints (r=0.34; p<0.05), ANA (r=-0.34; p<0.05). In children with osteopenia it was correlated with the duration of the disease (r=-0.67; p<0.05), the number of active joints (r=-0.62; p<0.05), blood phosphorus level (r=0.74; p<0.05) and JADAS scale results (r=0.59; p<0.05). In children with preserved BMD correlations was supplemented by 25(OH)D status (r=-0.33; p<0.05) and BMI (r=-0.40; p<0.05). Analysis of the interdependence of the formation of osteopenia and clinical manifestations signs established the total significance of the main parameters of the disease with the highest coefficient of determination in the polyarticular variant: -112.65 + 0.09(patient's age, mo)+4.33 (patient's sex)-3.74 (ANA, units)-1.80 (RF, units)+0.01 (age of onset, months)-0.34 (number of affected joints)-0.18 (number of active joints)-0.18 (ESR, mm/h)+71.58 (ionized calcium, mmol/l)+5.19 (phosphorus, mmol/l)-0.01 (PTH, ng/ml)+0.18 (25(OH)D, ng/ml)(R^2=99.99%; p<0.001).

Conclusion: With modern JIA management a quarter of children have osteopenia. The state of the bone tissue is more associated with the prevalence, immunological and inflammatory activity of the disease against the background of preserved calcium-phosphorus homeostasis and vitamin D deficiency, and is not associated with the present therapy.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3632

AB0746 THE ASSOCIATION BETWEEN PRESARCOPENIA AND BONE MINERAL DENSITY IN ADULT PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

M. Dzhus[1], M. Kulyk[1]. [1]*Bogomolets National Medical University, Internal Medicine Department №2, Kyiv, Ukraine*

Background: The importance of presarcopenia (low lean mass) in clinical practice is accompanied by a high risk of adverse effects such as early disability, reduced quality of life, and increased mortality.

Objectives: The aim of the study was to assess the link between bone mineral density (BMD) and the state of the muscular system in adult patients with juvenile idiopathic arthritis (JIA).

Methods: The study was performed in Oleksandrivska Clinical Hospital of Kyiv, Ukraine, where adult patients were transferred from pediatric rheumatologists. Inclusion criteria: patients aged 18-44 years at the time of signing the informed consent; diagnosis of JIA in childhood, verified according to ILAR criteria, duration of JIA >3 years. According to the European Working Group on Sarcopenia in the Elderly (EWGSOP) 2019, patients with a decrease in muscle mass alone were diagnosed with presarcopenia. The BMD and muscle tissue were determined in standard localizations using dual X-ray absorptiometry (DXA).

Results: The study included 26 adult patients with JIA, including 10 male patients and 16 female patients. The mean age at the time of examination was 22.3 ± 8.15 years; the mean age at the onset of the disease was 9.04 ± 4.9 years. According to the ILAR classification, patients had the following variants of JIA: 3 patients with RF-negative polyarticular variant, 8 patients with persistent oligoarthritis, 4 patients with extended oligoarthritis, 6 patients with RF-positive polyarthritis variant, and 5 patients with systemic JIA. According to the EWGSOP, 2019 reduced muscle mass was calculated by skeletal muscle index (SMI); the cut-off points were considered by SMI <7 kg/m2 for male, <6 kg/m2 for female. Patients were divided into two groups depending on the presence or absence of presarcopenia. The first group (1-st group) included 16 patients with reduced muscle mass (SMI – 5,22± 0,72 kg/m2), and the second group (2-nd group) included 10 patients without reduced muscle mass (SMI – 8,05± 0,94 kg/m2). It was found that the height and weight of patients in the group of presarcopenia was lower than in the group without a low lean mass (height 1,6±0,07 m vs 1,7±0,09 m, t=-2,53; p=0,01; weight 55,06±8,3 kg, 70,0±10,8 kg, t=-3,9; p=0,0007, respectively). The age of patients (25,3±10,1 and 21,3±5,9 years for 1-st and 2-nd groups respectively) and the duration of the disease (17,1±9,5 and 10,3±6,1 for 1-st and 2-nd groups respectively) did not differ statistically between the groups. The age of the onset of JIA in both groups also did not differ (7,8±4,5 and 11,5±4,1 for the 1-st and 2-nd group respectively). The following data were obtained by DXA. The patients of 1-st group had statistically reduced BMD in the region of femoral neck - 0,927±0,15 g/cm2 vs 1,179±0,13 g/cm2, t=-3,18; p=0,006; total hip - 0,977±0,16 g/cm2 vs 1,184±0,05 g/cm2, t=-3,05, p=0,0080; total body - 1,080±0,1 g/cm2 vs 1,193±0,15 g/cm2, t=-2,19; p=0,03; and ultra-distal radius - 0,286±0,06 g/cm2 vs 0,482±0,11 g/cm2, t=-3,60; p=0,007. The BMD in the region of lumbar spine did not differ in two groups - 1,152±0,16 g/cm2 vs 1,137±0,17 g/cm2, t=0,21; p=0,8. In the group of presarcopenia there was a visible decrease in the level of the metabolite of vitamin 25(OH)D3, but not statistically significant: 15,5±7,3 nmol/l vs 19,7±8,6 nmol/l, t =1,0; p=0,3. The study has strengths such as first described presarcopenia in young adults with JIA and potential limitations such as mono-center study and a small number of patients.

Conclusion: The BMD in the region of total hip, femoral neck, ultra-distal radius, and total body in patients with decreased muscle mass was significantly lower than in patients without low lean mass.

REFERENCES:

[1] Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis [published correction appears in Age Ageing. 2019 Jul 1;48(4):601]. Age Ageing. 2019;48(1):16-31

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3641

AB0747 MATERNAL AND FETAL OUTCOMES IN PREGNANT WOMEN WITH JUVENILE IDIOPATHIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

R. Pinheiro Torres[1,2], M. H. Fernandes Lourenco[1,2], A. Neto[1,2,3], F. Pimentel Dos Santos[1,2,4], I. Silva[1,4], A. F. Mourão[1,2,4], H. Donato[5], M. Costa[1], J. Branco[1,2,4]. *[1]Hospital Egas Moniz, Rheumatology, Lisboa, Portugal*; *[2]CEDOC, Rheumatology, Lisboa, Portugal*; *[3]Hospital Central Funchal, Rheumatology, Funchal, Portugal*; *[4]Nova Medical School, Rheumatology, Lisboa, Portugal*; *[5]Centro Hospitalar e Universitário de Coimbra, 5. Serviço de Documentação e Informação Científica, Coimbra, Portugal*

Background: Juvenile idiopathic arthritis (JIA), one of the most common chronic diseases in children, can be classified in seven different categories according to its onset presentation. Concerns about pregnancy outcomes play a secondary role in disease approach. However, recent data showed an increased risk of pre-term birth in women with JIA instead the small patient samples analysed.

Objectives: In this review, our aim is to describe the current available knowledge on JIA adverse, maternal and fetal, outcomes.

Methods: A systematic literature review was conducted since January of 2000 until December 2020, by searching the PubMed and Embase bibliographic databases. The search was limited to articles in English language, presenting a comparator group (healthy individuals or patients without known auto-immune rheumatic diseases) and at least one clinical outcome of interest. Two independent reviewers screened the titles and abstracts followed by a full-text review to assess papers regarding their eligibility.

Results: Ten observational studies out of 1560 references, fulfilled the inclusion criteria, of which, 9 were retrospective and 1 prospective. A total of 6.214 women with JIA (with 6.811 pregnancies) and 18.659.513 healthy controls (with 21.339.194 pregnancies) were included in this review.

Concerning maternal outcomes, delivery by caesarian section (CS) was more frequent among JIA women (in 4 out of 6 studies). Pre-eclampsia was referred in 3 out of 6 studies and a higher risk of vaginal bleeding and placenta previa in one additional study. No study found an increased risk for gestational diabetes or hypertension in pregnant women with JIA.

Regarding fetal outcomes, 8 studies revealed significantly increased of pre-term birth (only in first births in one study) but one study didn't show any increased risk. Two studies showed a higher risk of small gestational age (SGA) and in another 2, increased risk for low birth weight (LBW). No evidence of increased risk of major congenital malformations.

Conclusion: This systematic review suggests an increased risk for pre-eclampsia, preterm birth, delivery by CS, SGA and LBW, among pregnant women with JIA. Conclusions should be carefully interpreted, giving the heterogeneity of studied populations regarding demography, disease type, disease activity, and prescribed medication.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3647

AB0748 ARE ANY DIFFERENCES BETWEEN JIA - ASSOCIATED UVEITIS, DEVELOPED BEFORE AND AFTER JOINT MANIFESTATION

M. Chakhalian[1], E. Gaidar[2], T. Nikitina[3], E. Isupova[4], I. Chikova[2], M. Dubko[2], V. Masalova[2], T. Likhacheva[2], L. Snegireva[2], M. Kaneva[2], O. Kalashnikova[2], V. Chasnyk[2], M. Kostik[2]. *[1]Saint-Petersburg State Pediatric Medical University, Department of Hospital Pediatrics, Pediatric Rheumatology (Department of Pediatrics #3); Hospital Pediatry, Saint-Petersburg, Russian Federation*; *[2]Saint-Petersburg State Pediatric Medical University, Saint-Petersburg State Pediatric Medical University; Pediatric Rheumatology, Saint-Petersburg, Russian Federation*; *[3]Saint-Petersburg State Pediatric Medical University, Saint-Petersburg State Pediatric Medical University; Ophthalmologist, Hospital Pediatry, Saint-Petersburg, Russian Federation*; *[4]Saint-Petersburg State Pediatric Medical University, Department of Hospital Pediatrics, Pediatric Rheumatology, Saint-Petersburg, Russian Federation*

Background: Uveitis is the most common extra-articular manifestation of juvenile idiopathic arthritis (JIA). Usually uveitis developed during first two years after arthritis occurred [1]. In the previous studies was shown the shorter time interval between arthritis and uveitis the severe uveitis course was observed [2]. Information about course of uveitis developed before arthritis is scarce.

Objectives: We aimed to evaluate the clinical features and therapy of JIA-associated uveitis, which developed before and after joint manifestation.

Methods: In the retrospective study 191 pediatric autoimmune uveitis included. The onset age ranged from 1 to 17 years. We evaluated differences in clinical, laboratorial and treatment differences between groups, i) where uveitis developed before (n=58) and ii) after (n=133) arthritis. Chronic autoimmune uveitis without joint manifestations was excluded.

Results: Uveitits before arthritis developed in 58 (30.4%) cases. Patients whom uveitis developed before arthritis had were elder and characterized equal gender involvement, rare ANA positivity, and rare use of immunosupression, e.g. corticosteroids, biologics and methotrexate, due to treatment by ophthalmologist predominantly. Patients developed uveitis before arthritis received biologics earlier due to severity of uveitis (LogRank test, p=0.016, HR=1.97 (95%CI: 1.3; 3.1, p=0.004). Data are in the Table 1 and Figure 1.

Conclusion: Patients with JIA associated uveitis with initial ocular presentation demonstrated more severe course and delayed diagnostics and treatment due to lack of contacts with pediatric rheumatologist. Cooperation between ophthalmologist and pediatric rheumatologist is strictly required in all cases with chronic anterior uveitis.

Table 1.

Parameter	Uveitis before arthritis (n=58)	Uveitis after arthritis (n=133)	p
Sex, female	32 (55,2)	97 (72,9)	0.016
Onset age, years	6.7 (4.6; 10.2)	3.2 (2; 6.1)	0.000001
JIA category			
Oligoarthritis	41 (70.7)	84 (63.6)	0.174
Polyarthritis	9 (15.5)	36 (27.3)	
Enthesytis-related arthritis	8 (13.8)	12 (9.1)	
Type of uveitis			
Anterior	44 (75.9)	111 (84.1)	0.315
Peripheral	3 (5.2)	2 (1.5)	
Posterior	3 (5.2)	3 (2.3)	
Panuveitis	8 (13.8)	16 (12.1)	
Unilateral uveitis, n (%)	19 (32.8)	48 (36.1)	0.632
ANA posititivity, n (%)	25/54 (46.3)	72/110 (65.5)	0.019
HLA B27 positivity, n (%)	8/35 (22.9)	13/62 (21.0)	0.828
Methotrexate, n (%)	3 (5.2)	57/132 (43.2)	0.0000001
Systemic corticosteroids, n (%)	3 (5.2)	44/131 (33.6)	0.00003
Biologic, n (%)	26 (44.8)	88 (66.2)	0.006
ESR, mm/h	19.0 (4.0; 25.0)	23 (15.0; 32.0)	0.095
CRP, mg/l	97.0 (0.1; 107.5)	8.1 (0.9; 57.4)	0.493
Time between arthritis and uveitis, years	2.7 (0.9; 4.3)	4.0 (2.0; 7.1)	0.016
Time before biologic, years	2.5 (0.9; 3.5)	1.3 (0.5; 5.0)	0.462

This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001).

REFERENCES:

[1] Verazza S, et al. Pediatr Rheumatol Online J 2008;6(Suppl 1):77.
[2] Zannin ME, et al. Acta Ophthalmol 2012;90:91-5.

Disclosure of Interests: None declared

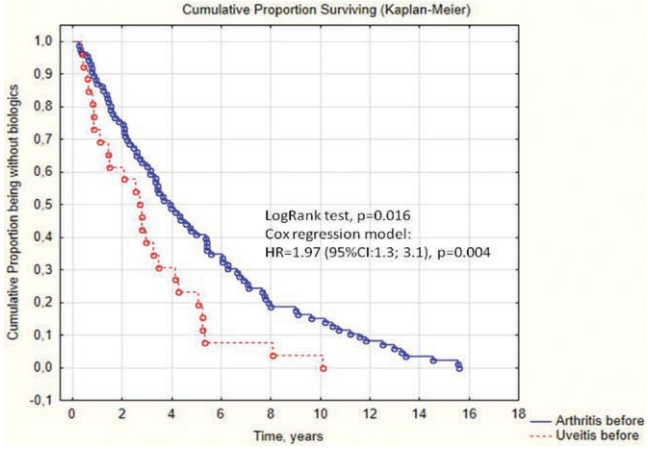


Figure 1.

DOI: 10.1136/annrheumdis-2021-eular.3704

AB0749

LABORATORY MARKERS OF INFLAMMATORY ACTIVITY IN PATIENTS WITH MONOGENIC AND POLYGENIC AUTOINFLAMMATORY DISEASES

E. Fedorov[1], S. Salugina[1], M. Cherkasova[2], A. Gerasimenko[1], M. Kaleda[1]. *[1]V.A.Nassonova Research Institute of Rheumatology, Pediatrics, Moscow, Russian Federation*; *[2]V.A.Nassonova Research Institute of Rheumatology, Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation*

Background: Auto-inflammatory diseases (AIDs) – a group of diseases of monogenic and polygenic nature, manifested by recurrent attacks of systemic inflammation in the form of fever, accompanied by multi-system symptoms, which are based on the pathology of natural immunity in the absence of autoantibodies and markers of infection.
Objectives: to evaluate the serum levels of markers of systemic inflammation in patients(pts) with monogenic AIDs (FMF, CAPS, TRAPS) and polygenic AID-systemic Juvenile Arthritis (sJA).
Methods: In 85 pts (68 children and 17 adults) with monogenic AIDs and sJA, the concentrations of C-reactive protein (CRP), serum amyloid A(SAA) and ferritin in the blood serum were detected. SRP and SAA were determined by the nephelometric method using Siemens reagents on a BN Prospect Siemens analyzer. Normal CRP values are 0-5 mg/L, normal SAA values are 0-5 mg/L. Ferritin was determined by ELISA using kits manufactured by Orgentec Diagnostica GmbH(normal values of 7-142 μg/l). During statistical processing of the material, the median(Me), lower and upper quartiles(LQ and UQ), minimum and maximum values were evaluated, and the reliability of differences between the groups was evaluated using the Mann-Whitney U criterion. The correlation between the values of CRP and SAA, CRP and ferritin was estimated by the Pearson criterion.
Results: The study included 30 with systemic JIA, FMF-17 pts, CAPS 25- pts and TRAPS- 17 pts. The results of the detection of CRP, SAA, and ferritin are presented in Table 1.

Table 1. CRP, SAA, and ferritin values in patients with sJA, FMF, CAPS and TRAPS.

Value	sJA	FMF	CAPS	TRAPS
	CRP (N=0-5 mg/L)			
Me (LQ - UQ)	6,95(0,5- 51,7)	30,8(9,41-47,4)	4,61(0,36-20,4)	5,41(2,77-14,7)
Min	0,15	0,48	0,15	0,15
Max	229,0	109,0	80,3	90,1
SAA(N=0-5 mg/L)				
Me (LQ - UQ)	19,05(3,05-257,0)	85,2(38,4-276,0)	7,83(2,25-122,0)	10,6(5,7-72,7)
Min	0,88	1,58	0,88	0,88
Max	962,0	923,0	346,0	516,0
Ferritin (N=7-142 μg/l)				
Me (LQ - UQ)	61,09(22,03-385,76)	57,22(21,36-133,51)	20,49(8,13-28,88)	16,52(5,42-67,27)
Min	0,73	3,36	0,98	2,42
Max	1500,0	174,22	183,57	930,1

Serum concentrations of CRP that exceeded the reference values were observed in 15(50%) pts with sJA, 11(65%) pts with FMF, 17(65%) pts with CAPS, and 5 (29%) pts with TRAPS. An increase in SAA was observed in 23(77%) pts with sJA, 12(71%) pts with FMF, 17(68%) pts with CAPS, and 8 (47%) pts with TRAPS. An increase in ferritin was observed in 9(30%) pts with sJA, 1(6%) pts with FMF, 1(4%) pts with CAPS, and 1 (6%) pts with TRAPS.

A statistically significant difference in the Mann-Whitney U test for SAA concentration was found only between the CAPS and FMF groups (P=0.03), and in the CRP concentration also only between the CAPS and FMF groups(P=0.009). The strongest statistically significant correlation according to the Pearson criterion in the whole study group was noted for CRP and SAA: r= 0.74(p=0.0000), which corresponds to the average correlation strength, a slightly weaker correlation was noted for the pair of CRP/ferritin values: r=0.53 (p=0.0000), which also corresponds to the average correlation strength. For the SAA/ferritin pair as a whole, the lowest correlation was observed in the studied group: r=0.36(p=0.0008). The maximum correlation of studied parameters was observed in the group of patients with TRAPS: for the CRP/SAA pair, it was r= 0.9(p=0.00003), for the SAA/ferritin pair it was r= 0.7(p=0.0072), and for the CRP/ferritin pair, r= 0.59(p=0.0345). For FMF, there was a strong correlation in the SRP/SAA pair r=0.89(p=0.0000).

Conclusion: In the study group, all AIDs, both monogenic(FMF, TRAPS, CAPS) and sJA, were characterized by an increase in the levels of CRP and SAA, but to the greatest extent these indicators were increased in sJA and FMF, and to the least in CAPS. CRP and SAA correlate well with each other, especially with TRAPS and FMF. The maximum values of ferritin and the highest frequency of its increase were noted in the sJA group. Ferritin in the majority of pts with monogenic AIDs were normal.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3711

AB0750

FUNCTIONAL CONDITION OF KIDNEYS IN THE LONG-TERM COURSE OF SLE IN ADOLESCENTS

L. Bohmat[1,2], N. Shevchenko[1,2], I. Bessonova[1,3]. *[1]SI Institute for Children and Adolescents Health Care of NAMS of Ukraine, Department of Cardiorheumatology, Kharkiv, Ukraine*; *[2]V.N. Karazin Kharkiv National University, Department of Pediatrics No 2, Kharkiv, Ukraine*; *[3]V.N. Karazin Kharkiv National University, Department of Pediatrics, Kharkiv, Ukraine*

Background: Lupus nephritis is the most severe and adverse systemic lupus erythematosus (SLE) syndrome. According to modern recommendations, the clinical manifestations of active nephritis should be taken under medical control in 6 months after the start of the disease's treatment[1].
Objectives: The aim of this study was to examine the functional status of the kidneys in children with SLE in the course of the disease for more than one year.
Methods: The analysis included case histories of 43 patients with SLE, mostly females (41), aged 7 to 18 years (mean age 14.4 years) with disease duration of 4.75 ± 0.58 years of whom 22 were less than three years, 21 - more than three years. All children received corticosteroid therapy, at the time of the examination the average dose was 13.85 ± 1.86 mg per day in terms of prednisolone. The second component of therapy was azathioprine (average dose 97.61 ± 2.11 mg). All children received hydroxychloroquine (5 mg/kg per day).
To determine the functional state of the kidneys a clinical analysis of urine, a study of the scope of specific gravity of urine during the day (Zymnytsky test), the content of creatinine and urea in serum to determine the glomerular filtration rate (GFR), the level of microalbuminuria per day were evaluated.
Results: Renal involvement in the developed SLE occurred in 73.08% of patients. Among them, therapy during the first 6 months was considered quite effective in 58.06% of patients. It was found that in children with disease duration from one to three years proteinuria was registered in 68.18%, a decrease in GFR in 4.45% and hyperfiltration in 9.09%. In the group of children with duration of SLE more than three years revealed deeper changes in renal function; there was proteinuria in 90.47%, the frequency of GFR decreased was in 19.04%, a decrease of renal concentration function was in 14.28% of cases.
Indicators of renal function in children with SLE depending on the duration of the disease (M ± m)

Indicator	Duration of the disease	
	from 1 year to 3 years n = 22	over 3 years n = 21
Creatinine, mmol/l	0,080 ± 0,014	0,090 ± 0,018
Мочевина, mmol/l	5,66 ± 1,42	5,63 ± 1,61
GFR, ml/min	117,05 ± 19,68	100,20 ± 18,98 *
Microalbuminuria, mg/day	24,41 ± 13,13	34,73 ± 24,76
Density min	1,007 ± 0,005	1,006 ± 0,005
Density max	1,024 ± 0,005	1,019 ± 0,005 **

*p<0,03;**p<0,01 the probability of differences when comparing between groups

Conclusion: Long-term follow-up of children with SLE over one year reveals a prolongation of renal dysfunction, which worsens after three years, and is the basis for the development of irreversible renal impairment.
REFERENCES:
[1] European evidence-based recommendations for the diagnosis and treatment of childhood-onset lupus nephritis: the SHARE initiative /Noortje Groot, Nienke de Graeff, Stephen D Marks et all. //Ann Rheum Dis. 2017 Dec;76(12):1965-1973.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3930

AB0751 JUVENILE UVEİTİS: THE 3RD LEVEL EXPERIENCE

S. N. Tigrak[1], Ş. Çekiç[1], O. Yalcinbayir[2], S. S. Kilic[3]. [1]*Uludağ Üniversitesi Tıp Fakültesi Hastanesi, Pediatrics, Bursa, Turkey*; [2]*Uludağ Üniversitesi Tıp Fakültesi Hastanesi, Ophtalmology, Bursa, Turkey*; [3]*Uludağ Üniversitesi Tıp Fakültesi Hastanesi, Pediatric Immunology -Rheumatology, Bursa, Turkey*

Background: Uveitis is the inflammation of the uveal components of the eye (iris, choroid and retina) and is the third leading cause of blindness in the world. It is less common in children than adults. Young children are usually diagnosed late, as they cannot express their complaints.
Objectives: With this work; We aimed to contribute to the literature by determining the underlying primary diagnosis and evaluating the treatment response in patients who were followed up in our clinic with a diagnosis of non-infectious uveitis, mostly juvenile idiopathic arthritis.
Methods: 93 patients under 18 years of age who were followed up with a diagnosis of non-infectious uveitis were included in the study. The data of the patients were scanned retrospectively. According to the last biomicroscopic examinations, the patients were classified as remission, inactive period and active disease. Clinical characteristics, laboratory findings, family history, drugs used during the disease and duration of treatment were examined.
Results: The male to female ratio was 1,06 (48/45). The mean age at diagnosis of childhood uveitis was found to be 10±4.02. 49 Patients (52.6%) were diagnosed with idiopathic uveitis, 33 (33.5%)with juvenile idiopathic arthritis, 11 (11.7%) with Behçet's, 2 (2.2%) with FMF. Juvenile idiopathic arthritis was the most common systemic disease in the patient group. The mean age of patients with uveitis to be diagnosed with rheumatological disease was 10.1±5.32. ANA test was positive in 30 (32.2%) patients. 23 (69.7%) of juvenile idiopathic arthritis patients were oligoartricular type. Anterior uveitis was present in 37 (39.8%) of the patients. Anterior uveitis was most common in the juvenile idiopathic arthritis cases. Of the patients with uveitis, 24 (25.8%) were intermediate, 11 (11.8%) were posterior, 21 (22.6%) were panuveitis. Anti-TNFα agents were administered to patients with unresponsiveness to immunosuppressive therapy and high risk of vision loss. Most used anti-TNFα agents were infliximab and adalimumab. Glaucoma, cataract, and posterior synechiae were common complications in the patients during follow-up.
Conclusion: The most common systemic disease that cause noninfectious uveitis in children is juvenile idiopathic arthritis. In juvenile idiopathic arthritis, the most common involvement of the eye was the anterior segment, and it was thought that the location of the eye involvement could be useful in determining the underlying systemic disease. It is important to ensure regular eye examination in patients with rheumatologic symptoms.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3933

AB0752 CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS: A SINGLE-CENTER CASE SERIES

G. Dallagiacoma[1], T. Buzzegoli[2], M. Karner[2], P. Matzneller[3], B. Raffeiner[4], C. Dejaco[1]. [1]*Hospital of Bruneck, Rheumatology, Bruneck, Italy*; [2]*Hospital of Bruneck, Radiology, Bruneck, Italy*; [3]*Hospital of Schlanders, Rheumatology, Schlanders, Italy*; [4]*Hospital of Bolzano, Rheumatology, Bolzano, Italy*

Background: Chronic recurrent multifocal osteomyelitis (CRMO) is a chronic autoinflammatory disease that primarily affects the skeleton of children and adolescents in the absence of an infectious etiology[1]. CRMO lesions presentation varies widely ranging from episodic bone pain to growth disturbance; lytic and sclerotic bone lesions can be found on X-ray, however magnetic resonance imaging is very useful for evaluating the extent of disease and follow-up [2].
Objectives: To report demographic, clinical and laboratory characteristics and response to therapy in a single center Italian cohort of CRMO patients.
Methods: We reviewed retrospectively the clinical records of seven patients affected by CRMO diagnosed between 2008 and 2019 at rheumatologic service of South Tyrol region in Italy.
Results: We identified 7 patients with CRMO, 4 were female patients, median age of onset of symptoms was seven years. Median delay in diagnosis was seven months; all patients had bone pain as initial symptom and 6 patients presented joint swelling. Median number of lesions was two; all patients had a recurrent pattern, 4 patient had multifocal distribution and 5 had appendicular skeleton involvement. None of our patients had antinuclear antibodies or HLA-B27 positivity. Mean erythrocyte sedimentation rate was 52 mm/h and C-reactive protein 1,96 mg/dL. Regarding other organs involvement one patient presented palmoplantar pustulosis, one psoriatic arthritis and one psoriasis guttata; three patient referred familiarity for psoriasis. Histopathological diagnosis was confirmed in 3 patients. NSAIDs were used in six patients, methotrexate in two patients and bisphosphonates in 6 patients. Among biological DMARDs Adalimumab was used in two patients, one patient was treated subsequently with Secukinumab and Ustekinumab. 3 patients achieved remission (Table 1).

Table 1. Demographic, clinical and laboratory characteristics of patients with chronic recurrent multifocal osteomyelitis.

	Total (n=7)
Demographics	
Female (%)	4 (57)
Age at disease onset, years, median (range)	7 (6-24)
Delay in diagnosis, months, median (range)	7 (2-14)
Follow-up, months, median (range)	69 (11-151)
Initial symptoms	
Bone pain, n (%)	7 (100)
Swelling, n (%)	5 (71)
Limp, n (%)	3 (43)
Fever, n (%)	1 (14)
Clinical features	
Number of lesions, median (range)	2 (1-10)
Axial skeleton involvement, n (%)	2 (29)
Appendicular skeleton involvement, n (%)	5 (71)
Distribution of involvement	
Femur, n (%)	3 (43)
Radius/ulna, n (%)	2 (29)
Humerus, n (%)	1 (14)
Tibia/fibula, n (%)	5 (5)
Tarsal bones, n (%)	1 (14)
Others, n (%)	3 (43)
Laboratory tests	
Hemoglobin, g/dL, mean ± SD	13.1±0.6
Leukocytes $\times 10^3/mm^3$, mean ± SD	8.48 ±1.7
Platelets $\times 10^3/mm^3$, mean ± SD	384±130
Erythrocyte sedimentation rate mm/h, mean ± SD	52±37
C-reactive protein, mg/dL, mean ± SD	1.96±2.35
Positive antinuclear antibodies, n (%)	0 (100)
HLA-B27 positive, n (%)	0 (100)
Comorbidities	
Any type of autoimmunity, n (%)	2 (29)
Others, n (%)	3 (43)
Histological confirmation, n (%)	3 (43)
Treatment	
NSAIDs, n (%)	6 (86)
Glucocorticoids, n (%)	0 (0)
Bisphosphonates, n (%)	6 (86)
TNF blocking agents, n (%)	2 (29)
Biological DMARDs, n (%)	1 (4)
Methotrexate, n (%)	2 (29)
Antibiotics, n (%)	3 (43)
Reached remission, n (%)	3 (43)

Conclusion: CRMO remains a rare diagnosis. From our experience most of the patients had delay in diagnosis, laboratory tests showed mild elevation of inflammatory parameters, was found association with psoriatic arthritis and psoriasis, remission was achieved with combination of bisphosphonate and immunosuppressive therapy in less than half of the cohort
REFERENCES:
[1] A. Taddio, F. Zennaro, S. Pastore, e R. Cimaz, «An Update on the Pathogenesis and Treatment of Chronic Recurrent Multifocal Osteomyelitis in Children», *Pediatr. Drugs*, vol. 19, n. 3, pagg. 165–172, giu. 2017.
[2] S. J. Menashe *et al.*, «The Many Faces of Pediatric Chronic Recurrent Multifocal Osteomyelitis (CRMO): A Practical Location- and Case-Based Approach to Differentiate CRMO From Its Mimics», *J. Magn. Reson. Imaging JMRI*, pag. e27299, ago.2020
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4048

AB0753 ASSESSMENT OF SLEEP PROBLEMS IN PATIENTS WITH KAWASAKI DISEASE: A SURVEY-BASED STUDY

S. Tharwat[1]. [1]*Mansoura University, Internal Medicine, Rheumatology & Immunology, Mansoura, Egypt*

Background: Kawasaki disease (KD) is a type of vasculitis that affects mainly medium and small arteries,especially the coronary arteries (1).It mainly affects children under the age of five (2).Sleep disturbances are more prevalent among medically ill children and adults and may have a negative impact on their health related quality of life (3, 4).To the best of our knowledge,sleep problems have not previously studied in KD patients.
Objectives: This study aimed to investigate sleep problems, sleep disturbances and the relation between sleep problems and clinical manifestations among patients with KD.
Methods: A cross-sectional study was performed using a written survey. Participants were invited through social media groups including patients and parents of children with KD. The survey included questions about demographic data, KD manifestations, disease duration and treatment received for management of the disease. Children's Sleep Habits Questionnaire (33-item version) was also included in the survey (5).

Results: There was a total of 262 survey participants (130 KD and 132 age- and sex matched healthy controls). There was no significant difference in the frequency of clinically significant sleep disturbance between patients with KD and healthy controls. However, the total sleep score was significantly higher in KD patients than health controls (p<.001).Total sleep duration was significantly higher in patients with KD (4.94±1.88 vs 3.74 ±1.14 hr, p<.001).Additionally KD patients had significantly higher scores regarding sleep onset delay (p=.001),night wakings (p<.001),parasomnias (p<.001) and sleep disordered breathing (p<.001) when compared to healthy controls.KD Patients who manifested with chronic heart disease or lethargy had significantly higher sleep score than patients without (p=.015,.039 respectively).

Conclusion: This study showed that patients with KD had more sleep disturbance than their healthy peers. The presence of either chronic heart disease or lethargy is associated with poor sleep quality.This study highlights the need for assessment of sleep disorders in KD patients.

REFERENCES:

[1] Hedrich CM, Schnabel A, Hospach T. Kawasaki Disease. Front Pediatr. 2018;6:198-.
[2] Singh S, Gupta MK, Bansal A, Kumar RM, Mittal BR. A comparison of the clinical profile of Kawasaki disease in children from Northern India above and below 5 years of age. Clinical and experimental rheumatology. 2007;25(4):654-7.
[3] van Golde EG, Gutter T, de Weerd AW. Sleep disturbances in people with epilepsy; prevalence, impact and treatment. Sleep medicine reviews. 2011;15(6):357-68.
[4] Roehrs T, Diederichs C, Gillis M, Burger AJ, Stout RA, Lumley MA, et al. Nocturnal sleep, daytime sleepiness and fatigue in fibromyalgia patients compared to rheumatoid arthritis patients and healthy controls: a preliminary study. Sleep medicine. 2013;14(1):109-15.
[5] Silva FG, Silva CR, Braga LB, Serrão Neto A. Portuguese Children's Sleep Habits Questionnaire-validation and cross-cultural comparison. Jornal de pediatria. 2014;90(1):78-84.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4081

AB0754 THE INFLUENCE OF PHYSICAL ACTIVITY ON BODY COMPOSITION AND SELF-ESTEEM IN ADULTS WITH JUVENIL IDIOPATHIC ARTHRITIS

R. De Oliveira[1], P. Julio[1], P. Fernandes[2], R. Marini[3], S. Appenzeller[4]. *[1]UNICAMP, Child and Adolescent Graduate Program, Campinas, Brazil*; *[2]UNICAMP, Sport Sciences, Campinas, Brazil*; *[3]UNICAMP, Pediatrics, Campinas, Brazil*; *[4]UNICAMP, Orthopedics, Rheumatology and Traumatology, Campinas, Brazil*

Background: With improvement of treatment, long-term factors influencing quality of life have to be addressed in the care of juvenile idiopathic arthritis (JIA) patients.

Objectives: To compare body composition, level of physical activity and self-esteem of adult patients with JIA with control group (CG).

Methods: The levels of physical activity were analyzed using the International Physical Activity Questionnaire (IPAQ) short version. The body composition data were collected using the Omrom HBF 514 C vertical electric bioimpedance device. The Rosenberg Self-Esteem Scale was used to assess positive and negative attitude and feelings about themselves, where the lower the score, the higher the individual's self-esteem. For the statistical analysis of the data, the IBM SPSS software was used with a significance index of p <0.05.

Results: We included 81 individuals >18 years, 38 with JIA and 43 healthy people. The female sex was the largest participant in this research, being. There was no significant difference regarding sex [female =28 (73.7%) in JIA and 26 (60.5%) in CG] and age of the groups (29.39 ± 7.6 vs. 31.1 ± 3.1, p = 0.18). The CG showed greater height and body weight (163.5 ± 9.8 vs. 169.6 ± 8.0, p<0.001; 63.07 ± 16.65 vs. 69.33 ± 6.88, p = 0.003, respectively), but no difference in Body Mass Index (BMI) was observed (24.32 ± 4.9 vs. 24.12 ± 2.09, p = 0.8). JIA had a higher percentage of total fat mass (31.65 ± 10.20 vs. 28.47 ± 4.9, p = 0.07), while the CG had a higher percentage of total muscle mass (29.7 ± 6.5 vs. 35.86 ± 6.05, p<0.001). The self-esteem of JIA patients was lower than in the CG (21 ± 3.9 vs. 16.26 ± 4.3, p<0.001). In the IPAQ classifications, JIA patients were classified as less physically active than the CG (2.63% vs. 20.93%, p = 0.022), less irregularly active (5.26% vs. 23.25, p = 0.023) and a higher level of sedentary lifestyle (65.78% vs. 25.58%, p<0.001). A higher percentage of muscle mass was associated with greater self-esteem (r=-0.3; p=0.01).

Conclusion: The low practice of physical activities by patients with JIA seems to directly influence both, their body composition and their self-esteem. These patients should be encouraged to increase physical activity from an early age by a multiprofessional healthcare team to seek improvement their quality of life.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4085

AB0755 THE FIRST CASE OF AN AUTOLOGOUS STEM CELL TRANSPLANTATION FOR AN EXTREMELY REFRACTORY PROGRESSIVE SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PATIENT IN BRASÍLIA, BRAZIL

M. Rodrigues Pereira Almeida[1], S. Veloso[1], A. Siqueira Afonso[1]. *[1]Hospital da Criança de Brasília José Alencar, Pediatric Rheumatology, Brasilia, Brazil*

Background: Systemic juvenile idiopathic arthritis (sJIA) is one of the most perplexing diseases of childhood, with a wide range of presentation features and severity. Advances in treatment have improved the outcome, such as the use of modulators of proinflammatory cytokines and their receptors, but in a considerable number of children, especially in polyarticular or sJIA, refractoriness tends to be progressive. As of late, extreme cases have required Autologous Stem Cell Transplantation (ASCT) as a last resort.

Objectives: To describe an extremely refractory clinical evolution in a sAIJ patient, the first one to be submitted to an ASCT for an autoinflammatory condition in Brasília, Brazil's capital.

Methods: Case Report

The patient was classified according to the Pediatric International League of Associations for Rheumatology for sJIA.

I.T.S.M, female, 15-years-old, was diagnosed with sJIA at 6 with the onset of polyarthritis, daily fever for 6 weeks, rash and enlargement of liver and spleen. In the initial investigation infectious and neoplastic causes were ruled out.

The use of prednisone and methotrexate lead to a preliminary effective clinical control, however after an year, there was clinical deterioration and etanercept was associated, leading to a short term improvement. At that time, in addition to anti-tumour necrosis factor medications, no other biological drugs were available in Brazil.

Despite some brief periods of clinical improvement, after different regimes, the patient manifested recurrent flares. Since the diagnosis she has already been treated with:

[1] Methotrexate (2011 to 2014*, 2016 to 2020). *In 2015, it was replaced by Leflunomide (up to May 2016, discontinued due to intolerance);
[2] Etanercept (2012);
[3] Cyclosporine (August to December 2012);
[4] Adalimumab (2013);
[5] Tocilizumab (May 2014 to January 2015);
[6] Canaquinumab (March 2015 to April 2016);
[7] Mycophenolate Mofetil (February 2016, discontinued in May 2017 due to start of Cyclophosphamide);
[8] Rituximab (May 2016 to April 2017);
[9] Cyclophosphamide at a dose of 2 grams /m2 as well as Filgrastim for mobilization and collection of stem cells (May 2017, in a attempt of ASCT), but the parents were unable to reach a mutual agreement to consent to the continuation of this therapy;
[10] Cyclophosphamide (500mg /m^2) in a mensal scheme application for nine consecutive months since June 2017, once was observed a clinical improvement after the intensive immunosuppression previous to ASCT attempt;
[11] Several courses of methylprednisolone and human immunoglobulin since the initial diagnosis;
[12] Abatacept (November 2019 to October 2020);
[13] ASCT was suggested again in 2020, this time with the consent of all family members.

Results: An intensive immunosuppression [Cyclophosphamide and anti-thymocyte globulin (ATG)] followed by ASCT (October 2020) resulted in apparent sustained remission. The patient's evolution since the transplant has been optimistic. She is currently on a low dose prednisone prescription. To ensure a less profound depletion of T cells, a better control of systemic disease and antimicrobial and antiviral prophylaxis after transplantation, slow tapering of corticosteroids were performed.

Conclusion: The goal of hematopoietic stem cell transplantation in patients with autoimmune disease is to reprogram the immune system with the eradication of autoreactive cells, renew the population of regulatory T cells and restore the diversity of T cell receptor function.

ASCT has been used in some refractory children with sJIA as well as hematologic malignancy and some progressive autoimmune diseases. However it is associated with significant morbidity and mortality, due to prolonged and severe depression of T cell immunity.

REFERENCES:

[1] D.M.C. Brinkman et al. Arthritis Care & Research (2007)
[2] Voltarelli Júlio C. et al. Rev. Bras. Hematol. Hemoter. (2010)
[3] Angelo De Cata et al. Clin Exp Med. (2016)
[4] Joost F. Swart et al. Nature Reviews Rheumatology (2017)

Acknowledgements: We kindly thank the Hematology service of Hospital da Criança de Brasília, where the patient was subjected to the autologous stem-cell transplantation.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4132

Other orphan diseases

AB0756 IMMUNE-MEDIATED BASIS FOR A PHASE 2A CLINICAL STUDY COMPARING RILZABRUTINIB VS GLUCOCORTICOIDS IN RITUXIMAB-REFRACTORY PATIENTS WITH IGG4-RELATED DISEASE

L. Long[1], M. Baker[2], M. Carruthers[3], A. Meysami[4], R. Spiera[5], M. Reddy[1], M. Kavanagh[1], M. Francesco[1], C. Langrish[1], A. Neale[1], P. Arora[1], J. H. Stone[6]. [1]*Principia Biopharma Inc, a Sanofi Company, Clinical Development, South San Francisco, United States of America*; [2]*Stanford University, Department of Medicine, Division of Immunology and Rheumatology, Stanford, United States of America*; [3]*Division of Rheumatology, University of British Columbia, Rheumatology, Vancouver, Canada*; [4]*Division of Rheumatology, Henry Ford Health System, Rheumatology, Detroit, United States of America*; [5]*Hospital for Special Surgery, Rheumatology, New York, United States of America*; [6]*Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Rheumatology, Boston, United States of America*

Background: IgG4-related disease (IgG4-RD) is an immune-mediated disorder causing fibro-inflammatory lesions. Although the cause remains unknown, it may be driven by interactions between B lymphocytes and CD4+ cytotoxic and regulatory T cells and is characterized by an increase in short-lived plasmablasts, circulating antibodies, and macrophages. Standard therapy mainly includes glucocorticoids (GC), limited by toxicity with long-term use (> 6 mo), and to a lesser extent, immunosuppressives (eg, rituximab). Bruton tyrosine kinase (BTK) plays an important role in the activation of multiple immune effector cells such as B cells, mast cells, eosinophils, basophils, monocytes/macrophages, and neutrophils. Dysregulation of the activation of these immune cells results in autoimmune inflammation, tissue damage, and development of fibrosis. Rilzabrutinib is a highly selective oral BTK inhibitor that targets multiple pathways of innate and adaptive immunity (with direct effects on B-cell and FcR pathways) and has the potential to inhibit antigen presentation to autoreactive T cells.
Objectives: To provide the biological rationale for rilzabrutinib in IgG4-RD.
Methods: Rilzabrutinib has been evaluated in biochemical, *in vitro* studies, and *in vivo* models of inflammatory diseases. Additional support is provided by the phase 2 trial for oral rilzabrutinib in patients with pemphigus vulgaris and the phase 2 trial for oral rilzabrutinib in patients with immune thrombocytopenia (ITP).
Results: Rilzabrutinib inhibited the activity of BTK and B-cell receptor in B cells (IC_{50} 5-123 nM) and Fc gamma receptor in IgG/Fc gamma receptor-stimulated monocytes (IC_{50} 56 nM) and blocked IgG- and IgM-mediated antibody production in enriched B cells when stimulated in T-cell dependent (anti-CD40+IL-21) and T-cell independent (TLR-9/CpG and TNP-LPS) pathways. The impact of rilzabrutinib on innate cell pathways was further confirmed by significant dose-dependent inhibition of macrophage and neutrophil-driven passive rat Arthus reaction ($P < 0.01$ vs vehicle) and antibody-induced murine ITP ($P < 0.05$ vs vehicle). In a 12-week phase 2 pemphigus vulgaris trial, 54% of patients achieved the primary endpoint, control of disease activity (CDA) on low-dose corticosteroids by week 4, and 73% achieved it by week 12. In the phase 2 trial of ITP patients (median 6 prior therapies), rilzabrutinib 400 mg bid showed rapid and sustained improvement in platelet counts and only grade 1/2-related adverse events[1]. In responders, platelet counts increased as early as day 8, potentially due to innate immune mechanisms. Collectively, results in both B and innate immune cells provide an initial basis for evaluating rilzabrutinib in IgG4-RD. The ongoing phase 2a study (NCT04520451) is investigating rilzabrutinib 400 mg bid (+tapered GC) vs GC control (3:1) for 12 weeks in IgG4-RD patients refractory to rituximab. The primary objective is to evaluate the safety and ability of rilzabrutinib to induce GC-free remission at week 12. Coupled with known preclinical/clinical findings, mechanistic analyses in this ongoing IgG4-RD study will profile B and other immune cell effects pre-/post-rilzabrutinib dosing to enhance the clinical understanding of rilzabrutinib in IgG4-RD.
Conclusion: Studies of rilzabrutinib that show beneficial effects on both B-cell and innate cell pathways provide support for its therapeutic role in immune-mediated diseases and for targeting the underlying pathophysiological effects of IgG4-RD. Effective and safe therapies that rapidly induce and maintain clinical responses, while minimizing the need for continuous GC treatment, remain an unmet need for patients with IgG4-RD.
REFERENCES:
[1] Kuter et al. *Res Pract Thromb Haemost*. 2020;4(suppl 1): PB1318.
Disclosure of Interests: Li Long Employee of: Principia Biopharma, a Sanofi Company, Matthew Baker: None declared, Mollie Carruthers: None declared, Alireza Meysami: None declared, Robert Spiera Consultant of: research funding and personal fees for consulting from Chemocentryx, Formation Biologics, Roche-Genentech, and Sanofi, Grant/research support from: research funding fees from BMS, Boehringer Ingelheim, Corbus, GSK, and Inflarx; personal fees from AbbVie, CSL Behring, GSK, and Janssen, Mamatha Reddy Employee of: Principia Biopharma, a Sanofi Company, Marianne Kavanagh Employee of: Principia Biopharma, a Sanofi Company, Michelle Francesco Employee of: Principia Biopharma, a Sanofi Company, Claire Langrish Employee of: Principia Biopharma, a Sanofi Company, Ann Neale Employee of: Principia Biopharma, a Sanofi Company, Puneet Arora Employee of: Principia Biopharma, a Sanofi Company, John H. Stone Consultant of: research funding and personal fees for consulting from Principia and Sanofi
DOI: 10.1136/annrheumdis-2021-eular.407

AB0757 ON THE ISSUE OF DIFFERENTIAL DIAGNOSIS OF PANNICULITIS

O. Egorova[1], V. Gorodetskiy[1], B. Belov[1], A. Potapova[2], S. Radenska-Lopovok[3], N. Probatova[4]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Drug Therapy, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*; [3]*FSBEI HE "I.M. Sechenov First Moscow State Medical University", Department of Pathological Anatomy, Moscow, Russian Federation*; [4]*Federal State Budgetary Scientific Institution "N.N. Blokhin Russian Cancer Research Center", Department of Morphological and Molecular Genetic Diagnostics of Tumors, Moscow, Russian Federation*

Background: Diagnosis of panniculitis (Pn) is associated with significant difficulties due to the variety of etiological factors, which include panniculitis-like T-cell lymphoma (PLTCL) – a rare variant of non-Hodgkin lymphoma.
Objectives: to study clinical and laboratory features of PLTCL in rheumatology.
Methods: Over 8 years PLTCL was diagnosed in 10 patients (9 women and 1 man, average age 37.2 ± 7.4) who were referred to V.A. Nasonova Research Institute of Rheumatology with a diagnosis of erythema nodosum or panniculitis. In addition to general clinical study, serum concentrations of α-1 antitrypsin, amylase, lipase, ferritin, creatine phosphokinase, immunological parameters (ANF-Hep2, dsDNA, C3 and C4 complements, CRP, ANCA, Scl-70, antibodies to cardiolipins G and M) were determined, and positron emission tomography combined with computed tomography (PET-CT), histological and immunohistochemical examination (IHC) of the biopsy sample of skin with subcutaneous fat from the affected areas were performed.
Results: The clinical picture of PLTCL was characterized by generalized red-crimson moderately painful (VAS pain intensity 45mm) subcutaneous nodes on the upper limbs and trunk (100%), face (60%) and lower extremities (75%), without ulceration and oily fluid leakage. A "trembling saucer" symptom was evident in 75% of the observed cases. All patients had febrile fever. No enlargement of the lymph nodes of the liver and spleen was observed. The blood test revealed leukopenia (up to 2.0·x 10^9 /l) in 50% of cases, an increase in ESR and CRP by three or more times in 100% of cases. The biochemical blood test demonstrated an increase in LDH activity by two or more times in all patients. PET-CT in 100% of cases revealed an intense accumulation of 18F-FDG in the nodes which correlated with a high proliferative activity index. The morphological picture resembled lobular panniculitis without vasculitis. Tumor lymphocytes had an immunophenotype of cytotoxic T-lymphocytes: CD3+, CD8+, granzyme B+. To confirm the tumor nature of the infiltrate the rearrangements of the T-cell receptor genes were studied. Glucocorticoid therapy (23.5±9.6 mg/day) was ineffective which required polychemotherapy in most patients.
Conclusion: PLTCL presents a complex diagnostic task that requires a multidisciplinary approach to verify the diagnosis and treatment tactics.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.602

AB0758 CLINICAL PROFILES DIFFER IN IGG4-RELATED DISEASE WITH AND WITHOUT ATOPY: A LARGE CASE-CONTROL STUDY IN CHINA

Z. Zhao[1], Y. Liu[1], Y. Su[1]. [1]*Peking University People's Hospital, Rheumatology and Immunology, Beijing, China*

Background: IgG4-related ophthalmic disease (IgG4-ROD) is one of the phenotypes of IgG4-related disease (IgG4-RD), and its lesions are mainly located in the ocular. Currently, there are few studies on IgG4-ROD and no study has compared the phenotypic differences between IgG4-ROD and non IgG4-ROD (nIgG4-ROD). Thus, it is difficult to establish the optimal treatment strategy for IgG4-ROD.
Objectives: The aim of this study was to identify the disparities between the two groups and to clarify the risk factors for IgG4-ROD relapse.
Methods: The IgG4-RD patients diagnosed at Peking University People's Hospital between January 2009 and January 2020 were recruited in this study. Patients were divided into IgG4-ROD and nIgG4-ROD group according to the ophthalmic involvement. Demographic, clinical and laboratory data of two groups were collected and compared. Cox regression analysis was used to identify the independent risk factors for IgG4-ROD relapse.

Results: Two hundred and fifty-five cases of IgG4-ROD were identified in 434 IgG4-RD patients in this study. IgG4-ROD group had almost equal sex ratio (male to female 0.96:1 vs 2.14:1, *P*<0.001), younger age of disease onset (51.1±13.2 vs 55.5±13.5, *P*<0.001) and diagnosis (54.4±12.6 vs 56.9±13.4, *P*=0.054) comparing with nIgG4-ROD patients. As compared to nIgG4-ROD group, higher percentage of IgG4-ROD patients met the 2019 American College of Rheumatology/European League Against Rheumatism classification criteria (AECC) for IgG4-RD (89.4% vs 64.8%, *P*<0.001), moreover, IgG4-ROD patients had higher AECC scores (37.0±12.9 vs 27.2±14.0, *P*<0.001) and IgG4-RD responder index (11.4±6.0 vs 10.2±6.3, *P*=0.045). Allergic diseases (65.5% vs 26.3%, *P*<0.001) and multiorgan involvement [6(4-7) vs 3(2-5), *P*<0.001] were more common in IgG4-ROD group. IgG4-ROD was frequently associated with salivary gland (92.5% vs 45.3%, *P*<0.01), paranasal sinuses (38.8% vs 12.8%, *P*<0.01), lung (47.8% vs 32.4%, *P*<0.01) and lymph node (64.3% vs 46.4%, *P*<0.01) involvement, while retroperitoneal fibrosis (7.1% vs 21.2%, *P*<0.01) and biliary system lesions (25.1% vs 35.2%, *P*<0.05) were more common in nIgG4-ROD. IgG4-ROD patients had higher serum IgG4 levels [983(409-1838) vs 523(225-1370), *P*<0.001], IgG4/IgG ratio [0.529(0.272-0.879) vs 0.294(0.143-0.629), *P*<0.001], IgE levels [339.7(160.8-847.6) vs 259.4(83.1-653.3), *P*=0.022] and lower CRP levels [2.24(1.00-4.70) vs 3.05(1.26-12.45), *P*=0.004]. The initial glucocorticoid plus immunosuppressant was a protective factor for IgG4-ROD relapse (HR 0.279, 95%CI 0.165-0.470, P<0.001), and IgG4-ROD patients treated with initial glucocorticoid plus immunosuppressant had longer relapse-free survival time than patients treated with initial glucocorticoid monotherapy (43 vs 17, P<0.001).
Conclusion: IgG4-ROD patients had distinctive clinical features compared with nIgG4-ROD patients. The initial glucocorticoid plus immunosuppressant was a protective factor for IgG4-ROD relapse, which could prolong the relapse-free survival time of IgG4-ROD patients. These findings may have important implications for understanding and management of IgG4-ROD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.652

AB0759 INDEX OF COMORBIDITY IN PATIENTS WITH LOBULAR PANNICULITIS-LIPODERMATOSCLEROSIS

O. Egorova[1], B. Belov[1], A. Potapova[2]. [1]*V.A. Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Drug Therapy, Moscow, Russian Federation*; [2]*V.A. Nasonova Research Institute of Rheumatology, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Early diagnosis of comorbid burden and treatment of rheumatological patients, especially panniculitis (Pn), is a complex problem, the solution of which lies in an interdisciplinary approach and the development of a general algorithm for managing patients.
Objectives: To study the structure and frequency of comorbid conditions in patients with Pn-lipodermatosclerosis (LDS).
Methods: We examined 53 patients (3 men and 50 women aged 18 to 80) with verified LDS, who were observed at the V.A. Nasonova Research Institute of Rheumatology for ten years on average. The duration of the disease varied from 2 weeks to 20 years. Clinical, laboratory and instrumental examination of patients was carried out twice a year. Clinical examination was carried out to determine localization, prevalence, color and number of the affected areas of skin and subcutaneous fat (SCF), as well as pain intensity according to the Visual Analogue Scale (VAS). Laboratory and instrumental research included standard blood and urine tests, as well as computed tomography of the chest and Doppler ultrasound of the lower extremities. To assess the relationship between the presence of comorbid pathology and the course of LDS the patients were analyzed with the CIRS and Charlson indices.
Results: Most patients were overweigh women (60.3%) with average weight of 91.5±21.8 kg. Based on the duration of the disease we identified the main variants of the course of the disease: acute (up to 3 months), subacute (from 3 to 6 months), and chronic (more than 6 months). Skin lesions were associated with polyarthralgias (n=18) and/or myalgias (n=12), mainly in the area of the affected limb. In 16 patients an increase in the erythrocyte sedimentation rate was recorded on average up to 23.8 ±7.8 mm/h. The level of C-reactive protein (CRP) was more than 3 times higher than normal in 7 patients, 4 of them had an acute course of LDS. In the study group 17 patients did not have comorbid diseases, 64.7% of them were under 50 years old with an acute course of LDS (p=0.02). Concomitant pathology was detected in 68% of patients mainly with chronic LDS. In 67.9% of cases it was presented by chronic venous insufficiency (CVI), in 60.3% – by exogenous constitutional obesity, in 45.2% – by rheumatic diseases (75% of these patients had osteoarthritis, 17% – rheumatoid arthritis, 8% – antiphospholipid syndrome) and in 39.6% – arterial hypertension. Most patients had one concomitant disease, almost a fifth of patients had two concomitant diseases. The proportion of patients with three comorbid diseases was 11.1%, four comorbid diseases – 8.3% and five comorbid diseases – 5.5%. When assessing the Charlson index, 10-year survival rates over 90% (index values from 0 to 2 points) were registered in 66% of patients, from 53 to 77% (index values of 3-4) – in 26.4% and less than 21% (≥5 points) – in 7.5%. The comorbidity index correlated with the age of patients (r = 0.8; p<0.05). There was no correlation between the Charlson index and the duration of LDS (r=0.3; p=0.2). In patients older than 61 one or more comorbid conditions were recorded. The CIRS index for this group averaged 4.2 ± 0.3 points (range 0-10), in most patients (45.2%) the CIRS index did not exceed 5 points. An analysis of the relationship between the Charlson and the CIRS scales confirmed their significant correlation at the level of r=0.5, p=0.0000001.
Conclusion: In patients with LDS a high incidence of comorbid pathology was detected. The treatment of this variant of panniculitis requires an interdisciplinary approach and interaction between doctors of different specialties.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.861

AB0760 HIGH SERUM IGA LEVELS HAVE LIMITED CLINICAL SIGNIFICANCE IN PATIENTS WITH IGG4-RELATED DISEASE DIAGNOSED BY EXPERTS

S. Tsuge[1], I. Mizushima[1], S. Shin[1], T. Yoshinobu[1], R. Hoshiba[1], R. Nishioka[1], T. Zoshima[1], S. Hara[1], Y. Suzuki[1], K. Ito[1], M. Kawano[1]. [1]*Kanazawa University Hospital, Department of Rheumatology, Kanazawa, Japan*

Background: While the diagnostic and classification criteria for IgG4-related disease (IgG4-RD) have been recently developed [1-3], it is known that, without appropriate exclusions, some non-IgG4-RDs may meet these criteria. In particular, hyper IL-6 syndromes, including Castleman disease, can be misdiagnosed as IgG4-RD. Some clinical findings, including elevated serum levels of C-reactive protein (CRP) or IgA, have been suggested to be useful for differentiating hyper IL-6 syndromes from IgG4-RD [4]. However, since few clinical studies have focused on IgG4-RD with high serum IgA levels, its clinical significance has not been well known.
Objectives: This study aimed to clarify the clinical significance of high serum IgA levels in patients with IgG4-RD.
Methods: We retrospectively investigated the clinical features of 170 patients with IgG4-RD on the basis of the presence or absence of elevated serum IgA levels (>410 mg/dL) at the time of diagnosis. The diagnosis of IgG4-RD was made by experts on the basis of the fulfillment of the comprehensive diagnostic criteria and/or each organ-specific diagnostic criteria.
Results: Elevated serum IgA levels were observed in 18 patients (10.6%). In the patients with elevated serum IgA levels, serum CRP levels were higher (1.14 ± 1.18 vs. 0.31 ± 0.63 mg/dL, p=0.003) and the prevalence of relapse during the clinical course was lower (5.6% vs. 27.6%, p=0.046) than in those without elevated serum IgA levels. However, there were no significant differences in the other clinical features including the number of involved organs (2.4 ± 1.3 vs. 2.8 ± 1.6, p=0.443) and inclusion scores of the ACR/EULAR classification criteria (32 ± 14 vs. 36 ± 17, p=0.374). To evaluate the influence of serum IgA elevation on relapse, we performed Cox regression analysis, which showed that the elevated serum IgA levels had no significant association with lower incidence of relapse but a tendency of it (hazard ratio 0.997, 95% confidence interval 0.994-1.000, p=0.055) during the clinical course. In addition, a prompt improvement in the IgG4-RD responder index [5] during the clinical course was seen in the patients with serum IgA elevation, suggesting a similar good response to glucocorticoids as in those without it.
Conclusion: The findings of the present study suggest that IgG4-RD patients with high serum IgA levels can be diagnosed and treated in the same way as those without it, although they may be characterized by mild serum CRP elevation.
REFERENCES:
[1] Wallace ZS et al. The 2019 American College of Rheumatology/European League Against Rheumatism classification criteria for IgG4-related disease. Ann Rheum Dis. 2020;79:77-87.
[2] Umehara H et al. The 2020 Revised Comprehensive Diagnostic (RCD) Criteria for IgG4-RD. Mod Rheumatol. 2020 Dec 4:1-14. doi: 10.1080/14397595.2020.1859710. Online ahead of print.
[3] Umehara H et al. Current approach to the diagnosis of IgG4-related disease - Combination of comprehensive diagnostic and organ - specific criteria. Mod Rheumatol. 2017;27:381-91.
[4] Sato Y et al. Systemic IgG4-related lymphadenopathy: A clinical and pathologic comparison to multicentric Castleman's disease. Mod Pathol.2009;22:589-99.
[5] Carruthers MN et al. Development of an IgG4-RD Responder Index. Int J Rheumatol. 2012;2012:259408.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.944

AB0761

HISTOPATHOLOGY OF CHECKPOINT INHIBITORS INDUCED ARTHRITIS: RETROSPECTIVE ANALYSIS OF 3 CASES

M. D. B. Laurent[1,2], A. Sandrone[3], D. R. Silvana[2], C. Frank[4], P. Renaud[5], C. Galant[6], B. Lauwerys[7], P. Durez[7]. [1]*Cliniques Universitaires Saint-Luc, Rheumatology, Brussels, Belgium*; [2]*CHU Saint-Pierre, Rheumatology, Brussels, Belgium*; [3]*UZ Brussel, Oncology, Brussels, Belgium*; [4]*Cliniques Universitaires Saint-Luc, Oncology, Brussels, Belgium*; [5]*Clinique Saint-Pierre, Oncology, Ottignies, Belgium*; [6]*Cliniques Universitaires Saint-Luc, Pathology, Brussels, Belgium*; [7]*Cliniques Universitaires Saint-Luc, Rhumatologie & Institut de Recherche Expérimentale et Clinique, Brussels, Belgium*

Background: Induced arthritis (IA) is a rare immune related adverse event occurring in 0.5 to 2% of patients exposed to Immune (irAEs) Checkpoint Inhibitors (CPI). In some patients, this condition may be severe and long lasting even after CPI cessation. Cross-reactivity between tumor- and self-antigens was considered in the etiology of several cases of irAEs but disease mechanisms in IA remain elusive.

We systematically collect synovial tissue of patients with IA (Ethical Committee B403201942386).

Objectives: Here, we report the histopathological findings from ultrasound guided (USG) synovial biopsies from the 3 first patients of our cohort. The immune cell infiltration in CPI IA patients is compared to the histopathological findings in rheumatoid arthritis.

Methods: Patients were referred through their oncologist after the onset of an arthritis in the context of a CPI therapy. The diagnostic of arthritis was confirmed by a rheumatologist and by ultrasound assessment. USG biopsies were performed before initiation of specific therapies.

Pathological and immunohistochemical analyses include semi quantitative scoring of the following: synovial hyperplasia, fibrinoid necrosis, chorion cellular infiltrate, vascular hyperplasia, CD3-, CD20-, CD68- and CD138-positive cells.

All patients gave written informed consent.

Results: Three patients went through the USG biopsy procedure: 2 males and 1 female. No adverse events were recorded.

All patients had metastatic neoplasms and time-to-arthritis was on average 6.7 months after CPI initiation. The USG biopsies were performed from 1 week after the onset of the IA to 16 months. The target joints displayed strong synovial thickening on ultrasound. Histological and immunohistochemistry studies showed light to moderate synovial hyperplasia and inflammatory cell infiltration of the sublining by macrophages and T cells, but no or little B cells (Table 1).

Table 1. Clinical Characteristics and histopathological analyses on synovial biopsies.

	Patient 1	Patient 2	Patient 3
Cancer	uterus	bladder	lungs
Biopsied joint	first metatarsophalangial joint	wrist	knee
Time-to-synovial biopsy	1 week	2 months	16 months
Grey scale on ultrasound	3/3	3/3	3/3
Hematoxylin-eosin staining:			
synovial hyperplasia	+	+	++
fibrinoid necrosis	0	+	++
chorion cellular infiltrate	+	++	+
vascular hyperplasia	0	0/+	++
Immunochemistry staining:			
CD3	+	++	+
CD20	0	0	0/+
CD68	++	0/+	++
CD138	0	0	0/+

Conclusion: USG synovial biopsies have been safely performed and the histopathological analysis have confirmed the synovitis with mainly a macrophage infiltrate (myeloid pattern). IA synovitis is characterized by synovial hyperplasia and macrophage and T cell infiltration of the sublining. Increased collaboration between oncologists and rheumatologists is needed to create opportunities for referral of patients between the two specialties and optimize treatment. Further analyses (such as global or single-cell RNA sequencing) are needed to learn more about IA physiopathology.

REFERENCES:

[1] Humby F, Lewis M, Ramamoorthi N & al. Synovial cellular and molecular signatures stratify clinical response to csDMARD therapy and predict radiographic progression in early rheumatoid arthritis patients. Ann Rheum Dis. 2019 Jun;78(6):761-772. doi: 10.1136/annrheumdis-2018-214539.

[2] Postow MA, Sidlow R, Hellmann MD. Immune-Related Adverse Events Associated with Immune Checkpoint Blockade. N Engl J Med. 2018 Jan 11;378(2):158-168. doi: 10.1056/NEJMra1703481. PMID: 29320654.

Disclosure of Interests: Meric de Bellefon Laurent: None declared, Aspeslagh Sandrone: None declared, Di Romana Silvana: None declared, Cornelis Frank: None declared, Poncin Renaud: None declared, Christine Galant: None declared, Bernard Lauwerys Employee of: Bernard Lauwerys is currently employed at UCB Biopharma, Patrick Durez: None declared

DOI: 10.1136/annrheumdis-2021-eular.1112

AB0762

THE CHARACTERISTICS OF PERIPHERAL LYMPHOCYTE SUBSETS IN PATIENTS WITH IGG4-RELATED DISEASE

Y. Y. Wang[1], X. Yu[1], R. Su[1], X. LI[1], C. Wang[1]. [1]*The Second Hospital of Shanxi Medical University, Department of Rheumatic Immunology, Taiyuan, China*

Background: Immunoglobulin G4-related disease (IgG4-RD) is an autoimmune disease with chronic systemic inflammation and fibrosis. The main feature of the disease was diffuse swell of the affected organs, and the serum IgG4 level was increased. Histopathology of the lesions showed infiltration of IgG4+ plasma cells. However, the pathogenesis of IgG4-RD is still unclear[1].

Objectives: To explore the clinical characteristic of lymphocyte subsets of IgG4-related disease patients, and make comparisons with healthy controls.

Methods: A total of 31 patients with IgG4-RD who were admitted to the Rheumatic Immunology Department of the Second Hospital of Shanxi Medical University from January 2016 to June 2020 were included. We collected their Clinical and laboratory data, and selected 30 age and sex matched healthy people as the control group. Flow cytometry was used to detect the percentage and absolute number of lymphocyte subsets (T, B, NK, CD4+T, CD8+T) and CD4+T subsets (Th1, Th2, Th17, CD4+CD25+Foxp3+Treg) in peripheral blood of IgG4-RD patients and healthy controls.

Results: (1)The percentage of CD4+T cells in peripheral blood of IgG4-RD patients was higher than that of healthy controls [45.00(33.97-51.48) vs. 39.36(33.78-43.30), P<0.05]. (2)The percentage and absolute number of Th17 cells was increased in IgG4-RD patients [1.13(0.70-1.55) vs. 0.77(0.43-1.07), P<0.05; 7.90(5.20-12.23) vs. 5.60(3.12-8.47), P<0.05], while the percentage of Treg cells was decreased [3.37(2.82-5.65) vs. 4.96(4.18-6.34), P<0.01]. But Treg cells number showed no difference between the two groups. (3) Th17/Treg ratio was significantly increased in IgG4-RD patients [0.29(0.16-0.46) vs. 0.15(0.08-0.23), P<0.01], and it was positively correlated with IgG4-RD response index score(r=0.491, P<0.01). (Table 1).

Table 1. Comparation of absolute number and percentage of peripheral blood lymphocyte subsets between IgG4-RD patients(n=31) and healthy controls (n=30).

cell subsets	IgG4-RD (n=31)	HC(n=30)	*P* value
B	150.59(120.14-212.38)	203.27(152.90-244.27)	0.089
B%	8.74(6.46-11.45)	10.03(8.26-13.21)	0.059
NK	261.98(178.82-303.08)	290.83(179.93-451.45)	0.175
NK%	13.14(9.92-18.10)	16.50(11.24-21.75)	0.105
CD3+T	1357.44(992.00-1844.82)	1305.81(978.24-1597.94)	0.708
CD3+T%	72.62(69.32-76.96)	71.62(64.97-75.25)	0.135
CD8+T	436.40(342.71-596.86)	513.50(359.73-620.53)	0.665
CD8+T%	24.26(19.48-31.27)	26.50(20.67-32.90)	0.535
CD4+T	741.00(562.78-1095.52)	664.50(585.52-789.97)	0.428
CD4+T%	45.00(33.97-51.48)	39.36(33.78-43.30)	**0.032**
Th1	162.32(108.11-216.61)	144.27(81.52-161.66)	0.094
Th1%	19.00(15.24-25.54)	18.46(14.86-24.27)	0.644
Th2	7.82(5.35-11.78)	8.25(5.32-10.87)	0.817
Th2%	1.00(0.76-1.27)	1.24(0.89-1.64)	0.399
Th17	7.90(5.20-12.23)	5.60(3.12-8.47)	**0.010**
Th17%	1.13(0.70-1.55)	0.77(0.43-1.07)	**0.026**
Treg	24.45(19.76-44.79)	34.55(27.29-46.57)	0.076
Treg%	3.37(2.82-5.65)	4.96(4.18-6.34)	**0.003**
Th1/Th2	20.00(13.78-36.36)	14.97(10.31-21.58)	0.135
Th1/Treg	5.72(2.92-8.86)	3.68(2.53-4.77)	**0.021**
Th2/Treg	0.27(0.16-0.52)	0.22(0.15-0.32)	0.199
Th17/Treg	0.29(0.16-0.46)	0.15(0.08-0.23)	**0.002**

Conclusion: Th17/Treg immune disorder exists in IgG4-RD patients, and it is related to the disease activity, indicating that Th17/Treg imbalance may be an important pathogenesis of IgG4-RD.

REFERENCES:

[1] Kamisawa T, Zen Y, Pillai S, et al. IgG4-related disease[J]. Lancet, 2015, 385(9976): 1460-1471.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1239

AB0763

IGG4-RELATED CORONARY PERIARTERITIS: SYSTEMATIC LITERATURE REVIEW WITH OUR CASE SERIES

T. Ito[1,2], S. Fukui[1], T. Kanie[3], T. Nakai[1], G. Kidoguchi[1], H. Ozawa[1], S. Kawaai[1], Y. Ikeda[1], A. Koido[1], Y. Haji[2], A. Nomura[1], H. Tamaki[1], K. Yamaguchi[1],

M. Okada[1]. [1]*St. Luke's International Hospital, Immuno-Rheumatology Center, Tokyo, Japan*; [2]*Daido Hospital, Rheumatology Department, Nagoya, Japan*; [3]*St. Luke's International Hospital, Cardiology Department, Tokyo, Japan*

Background: Coronary periarteritis is one of the clinical manifestations of IgG4-related disease. It can cause serious conditions such as angina and ruptured aneurysms. Therefore, it is important to recognize the clinical and radiological characteristics, which was little known.
Objectives: We report four patients with IgG4-related coronary periarteritis with a systematic literature review.
Methods: We identified four patients with IgG4-related coronary periarteritis at the St. Luke's International Hospital in Tokyo, Japan from 2014 to 2020. A systematic literature review was conducted for English articles on IgG4-related coronary periarteritis cases with a full text or abstract available. We summarized patient demographics, IgG and IgG4 titers, the site and morphological type of coronary lesion, and other organ involvements.
Results: Our 4 cases and 38 cases identified by the literature review were assessed. Coronary artery lesions were detected by a coronary CT in all but two cases. Wall thickening was the most common type of the lesion. Moreover, there were 32 (76.1%) patients with other organ involvements. The commonest other lesion was peri-aortitis in 21 (50.0%) patients. In cases with peri-aortitis, IgG and IgG4 titers were significantly higher than those without peri-aortitis (IgG4; 1540 [705.0, 2570.0] vs 246.0 [160.0, 536.3]; p = 0.001, IgG; 3596.5 [2838.3, 4260.0] vs 1779.0 [1288.3, 1992.8]; p =0.040). In addition, 15 (71.4%) patients of them had three or more IgG4 related organ involvements.
Conclusion: Coronary CT was a useful imaging modality for the diagnosis of IgG4-related coronary periarteritis, and wall thickening was the most common lesion. Moreover, about half cases coexisted with peri-aortitis. Peri-aortitis and other organ involvements should be screened in those with higher IgG and IgG4.

Table 1. Characteristics of our cases and the literature review cases.

Table 1. Characteristics of our cases and the literature review cases.

	All cases (n=42)				Total number of coronary lesions (n=126)
Age (years)	64.0 [58.0, 69.8]	The number of organ involvements		Lesion distribution	
Male (%)	35 (83.3)	≥ three (%)	20 (47.6)	RCA (%)	45 (35.7)
IgG4 (mg/dL)	625.0 [214.0, 2090.0]	two (%)	12 (28.6)	LAD (%)	48 (38.1)
IgG (mg/dL)	2841.5 [1672.3, 4138.8]	one (%)	10 (23.8)	LCx (%)	33 (26.2)
Diagnosis criteria		With other organ involvements		Lesion type	
possible (%)	10 (23.8)	all cases (%)	32 (76.1)	stenosis (%)	28 (22.2)
probable (%)	9 (21.4)	peri-aortitis (%)	21 (50.0)	wall thickening (%)	70 (55.6)
definite (%)	23 (54.8)	gland (%)	12 (28.6)	aneurysm (%)	28 (22.2)
		pancreas (%)	9 (21.4)		
		lymph (%)	6 (14.3)		
		kidney (%)	4 (9.5)		
		retroperitoneal (%)	4 (9.5)		
		pulmonary (%)	2 (4.8)		
		colon (%)	1 (2.4)		
		Coronary branch lesion counts			
		mono (%)	14 (33.3)		
		double (%)	11 (23.8)		
		triple (%)	16 (38.1)		

RCA: right coronary artery, LAD: left anterior descending artery, LCx: left circumflex artery

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1293

AB0764 MANIFESTATIONS OF BEHCET'S DISEASE

R. Goloeva[1], Z. Alekberova2. [1]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Disease, Москва, Russian Federation*; [1]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Disease, Москва, Russian Federation*

Background: Behcet's disease (BD) is a systemic vasculitis of unknown etiology, characterized by recurrent oral and genital erosions and ulcerations, as well as involvement of joints, ocular, vascular, gastrointestinal (GI), and central nervous system (CNS).
Objectives: To study the influence of such factors as patient's gender, age at the disease onset and initial manifestations of the disease on the severity of BD.
Methods: 95 patients with confirmed BB were examined. The majority of patients were males (70 men, 25 women) with the 2.8:1 M:W ratio. Patients' mean age (median [interquartile range]) was 29 years [22; 34], from 16 to 51 years, the average age at disease onset was 20 years [14; 24]; and mean disease duration was 8 years [4; 15].
Results: The following clinical manifestations of BD were documented at disease onset (%): recurrent aphthous stomatitis – 63.1; skin lesions – 12.6; genital ulcers – 4.2; ocular lesions – 6.3; joint syndrome -7.4; CNS lesions -2.1; gastrointestinal tract involvement -2.1; thrombosis -1; epididymitis -1. 11.6% of all patients had signs of organ system involvement by the time of establishing BD diagnosis. Recurrent aphthous stomatitis was more common in female patients at BD onset– 76% vs. 58.6%, p=0.01, while organ system involvement was more common in males-14% vs. 4% in females, p=0.02.
Progression from initial symptoms to the mature BD phenotype allowing to verify the diagnosis occurred within 4.3 years on average [1; 6], although 30.5% of patients progressed to a full-blown disease within 1 year.
Analysis of potential predisposing or precipitating factors prior to BD onset identified such in only 12 patients, including frequent episodes of tonsilitis in 3 patients, cold exposure with hypothermia in 2, dental procedures in 2, stressful events - in 2, and one case of each - herpes labialis, frontal sinus puncture and appendectomy. Other patients could not recall any potential precipitator of BD.
Mean age at BD onset was 20 years [14; 24], including 30.5% of patients with disease onset before 16 years, 22.1% aged from 16 to 21 years, 36.8% aged from 21 to 30 years at disease onset, and in remaining 10.5% the disease manifested after 30 years of age. BD onset in men and women was documented at approximately the same time. There were no signs or correlations indicating that patient's age at disease onset could be associated with specific clinical symptoms in males or females. However, analysis of gender-associated differences in disease severity based on Krause's Clinical Severity Scoring yielded the following results: mild BD was found in 15.7% men and 44% women (p=0.009), moderate disease - in 7.1% men and 16% women, (p>0.05), and severe BD - in 77% men and 40% women, respectively, (p=0.001). The risk of developing severe BD was 5-fold higher in men vs women [OR = 5.06, 95% CI 1.7-15.1].
Conclusion: First BD symptoms manifested in the majority of patients before the age of 30 years, with only 10% of patients with BD onset at the age of > 30 years. In more than 50% of all patients aphthous stomatitis was the first manifestation of the disease, and was more common in women. Prognostically unfavorable BD signs were found in 11.6% of patients already at the initial stages of the disease in men. No correlation was found between the age at BD onset and clinical symptoms of the disease in both males and females.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1364

AB0765 PHENOTYPES OF BEHCET'S DISEASE IN DIFFERENT ETHNIC GROUPS

R. Goloeva[1], Z. Alekberova2. [1]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Disease, Москва, Russian Federation*; [1]*V.A. Nasonova Research Institute of Rheumatology, Systemic Rheumatic Disease, Москва, Russian Federation*

Background: Early diagnosis and identification of predominant organ system involvement in Behcet's disease (BD) is crucial for identifying most optimal treatment. The study evaluates 6 described phenotypes of BD - cutaneous-mucous, articular, ophthalmic, vascular, neurological and intestinal in different ethnic groups.
Objectives: To assess the occurrence of Behcet's disease (BD) phenotypes in different ethnic groups.
Methods: The study included 202 patients with BD from the 5 most common ethnic groups.
The male-female ratio was 2.4:1. Patients' mean age was 31 years [24;37], mean age at the disease onset was 21 years [15;28]; and mean disease duration was 7 years [3;14]. The severity of BD (mild, moderate and severe) was assessed based on the I. Krause's Clinical Severity Scoring for BD.
Results: Severe BD was more often diagnosed in Azerbaijanis and indigenous residents of Dagestan compared to Russians (75 and 70.4% vs. 36.2%), in Armenians - 50% and Chechens - 54.5% out of all BD cases.
Russians were significantly more likely to have a neurological phenotype (15.5% vs. 0-9.4% in all other ethnic groups) and intestinal phenotype (36.2% vs. 13.8-22.7 in all other ethnic groups). Azerbaijanis demonstrated higher prevalence of ocular involvement (68.7% versus 36.2% in Russians, 50% - in Chechens and Armenians, and 57% - in Dagestanis). Dagestanis were more likely to have a vascular phenotype (40.7% versus 15.6% in Azerbaijanis and 18.9% in Russians). The male/female ratio among Russian patients was 1:1, among Dagestanis 4.4:1, Azerbaijanis 3.5:1, Chechens and Armenians 2.6: 1.
Conclusion: BD phenotypes vary and demonstrate significant association with the patient's ethnic affiliation therefore, ethnicity should be viewed as the prognostic marker of specific organ-system involvement in case of a disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1373

AB0766 SUCCESSFUL TEATMENT OF ANKYLOSING SPONDILITIS ASSOCIATED AA AMYLOIDOSIS WITH SECUKINUMAB: A CASE SERIES WITH THREE PATIENTS

M. Bektaş[1], N. Koca[1], E. Oguz[1], C. Cetin[1], B. Ince[1], Y. Yalçınkaya[1], B. Artim-Esen[1], M. L. Ocal[1], M. Inanc[1], A. Gül[1]. [1]*Istanbul Faculty of Medicine, Internal Medicine, Rheumatology Division, Istanbul, Turkey*

Background: Systemic AA amyloidosis is a serious and life-threatening complication of chronic inflammatory diseases such as rheumatoid arthritis, spondyloarthritis (SpA), and periodic fever syndromes. While most common cause of AA amyloidosis is Familial Mediterranean Fever; Ankylosing Spondylitis (AS) is another frequent cause of AA amyloidosis in Turkey.
Objectives: We aimed to evaluate the response of secukinumab (SEC) treatment in three patients with AS and AA amyloidosis (AS-AA) in our tertiary referral centre.
Methods: We retrospectively evaluated three AA amyloidosis patients who fulfilled Modified New York Criteria for diagnosis of AS in our AA amyloidosis cohort with 163 patients. Diagnosis of AA amyloidosis was confirmed by Congo red stain and by monoclonal AA-specific antibodies.
Results: *Patient 1:* 61-year-old male patient with inflammatory back pain (IBP) and peripheral arthritis for 14 years was evaluated in our clinic. After methotrexate (MTX) failure, he used adalimumab (ADA), etanercept (ETA) and certolizumab (CZP). Nephrotic range proteinuria was detected when he was on CZP, and rectum biopsy documented AA amyloidosis 3 years ago. After the diagnosis, CZP treatment was switched to infliximab (IFX). IFX was ineffective in controlling inflammatory findings. SEC was started 15 months ago and he responded partially. The dose of SEC was increased to 300 mg monthly, which resulted in a sustained improvement in clinical and laboratory findings.
Patient 2: 69-year-old woman was admitted to our clinic with peripheral arthritis in addition to the history of IBP for 19 years in 2005. MTX, NSAID and prednisolone were started. Because of inefficacy to conventional treatments and development of nephrotic range proteinuria, ETA was added to treatment. The patient responded to ETA and was followed-up for 13 years without symptoms of AS and proteinuria. ETA was switched to IFX due to secondary inefficacy two years ago. On the third month of IFX treatment, she developed demyelinating polyneuropathy. IFX treatment was switched to SEC and she is still being followed-up on SEC without any findings of AS and proteinuria.
Patient 3: 49-year-old woman who was on sulphasalasine for 24 years for treatment of ulcerative colitis (UC) was evaluated for recent onset IBP and peripheral arthritis in 2007. After failure of MTX, she started to receive IFX. She did not respond to first IFX and then ADA and CZP, and she developed nephrotic range proteinuria when she was on anti-TNF. Her serum creatinine increased progressively, and haemodialysis (H/D) was started six months later. Due to ongoing IBP and elevated acute phase response with CZP treatment, SEC was started. Significant improvement was observed in both clinical and laboratory findings with no worsening of UC.

Table 1. Clinical characteristics, laboratory findings and treatment responses of patients

	Patient 1	Patient 2	Patient 3
Age (year)	61	69	49
Sex	Male	Female	Female
Age of AS onset (year)	47	35	25
Age of amyloidosis diagnosis (year)	57	50	46
Amyloidosis duration (months)	42	168	30
Family history	No	AS and amyloidosis in siblings	No
HLA-B 27 status	Positive	Positive	Not available
MEFV status	Negative	Negative	M694V heterozygous
Organ involvement of amyloidosis	GIS and kidney	Kidney, liver, heart, bone marrow	GIS, kidney
Secukinumab duration (months)	15	18	24
CRP (mg/L)			
Before	27	15	23
After	2.4	4.5	2.8
Creatinine (mg/dl)			
Before	0.5	1.6	H/D
After	0.5	1.3	H/D
Proteinuria (g/day)			
Before	4.2	5.5	H/D
After	2.4	0.9	H/D
Albumin (g/dL)			
Before	2.7	2.5	3.1
After	3.1	4.3	4.2
ASDAS			
Before	4.1	1.6	4.6
After	1.8	1.1	1.7

GIS: Gastrointestinal System, ASDAS: Ankylosing Spondylitis Disease Activity Score

Conclusion: AA amyloidosis is a rare complication of SpA, and SEC treatment was found to be safe and effective in our three patients with AS-AA. Although anti-TNF agents have previously used successfully in treatment of AS-AA, SEC may be a new option especially in patients who are resistant or intolerant to anti-TNFs.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1469

AB0767 SEVERE BREAST ULCERATION IN BEHÇET'S DISEASE TREATED WITH CYCLOPHOSPHAMIDE: A CASE REPORT

E. Ball[1], D. Okane[2], C. Mccourt[2], M. Mccarron[1], C. Riddell[1]. [1]*Belfast City Hospital, Rheumatology, Belfast, United Kingdom*; [2]*Belfast City Hospital, Dermatology, Belfast, United Kingdom*

Background: Behcet's disease is a systemic autoimmune vasculitis that typically involves mucocutaneous surfaces, the eyes and the skin with varying manifestations. Skin ulceration often secondary to pathergy is a common feature.
Objectives: To raise awareness of breast ulceration as a clinical manifestation in Behcet's disease.
Methods: We report a case of complex Bechet's disease associated with severe refractory breast ulceration successfully treated with cyclophosphamide.
Results: A 27 year old female patient presented to the rheumatology department with a non-healing lesion on her face secondary to a cat scratch. She reported previous episodes of ulceration usually as a result of minor trauma such as IV cannulation, as well as a two year history of severe oral and genital ulceration. She had also been diagnosed with 'colitis' requiring iliocaecal resection two years prior to presentation. Previous treatments for her bowel included azathioprine, infliximab, adalimumab and vedolizumab. Over the next three years she developed recurrent eye involvement in the form of scleritis with ongoing oral and genital ulceration. Further treatment under our care included ustekinumab, entanercept, benepali, certolizumab and tacrolimus with background prednisolone. She then developed a small area of broken skin on her left breast which continued to extend and ulcerate despite treatment with IV steroids. Tissue biopsy showed deep focal vasculitis with intravascular thrombi. Anticoagulation was commenced and she was treated with tocilizumab IV for 3 months with no clinical improvement. Involvement extended to include 80 percent of the breast surface and the nipple self-amputated. Due to the severity and extent of the ulceration which was extremely painful and distressing, she was given 3 months of IV cyclophosphamide at a dose of 15mg/kg every 2-3 weeks. The ulceration showed rapid clinical improvement (see Figure 1).

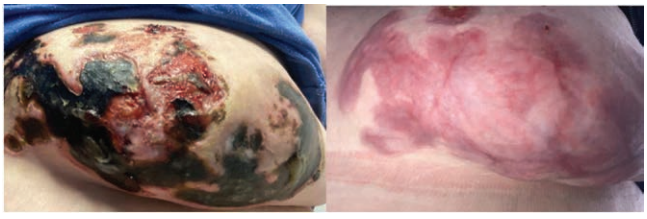


Figure 1. Breast ulceration before and after 3 months of cyclophosphamide treatment

Conclusion: Involvement of the breast in systemic vasculitides (such as GPA or PAN) has been reported, although usually manifesting as a palpable mass with diagnosis on biopsy [1]. Similar presentations in Behcet's disease have been recognised [2], although much less commonly. Our case demonstrates that severe breast ulceration can be a clinical manifestation of this condition and can be refractory to usual therapies.

REFERENCES:

[1] Ren J, Liu J, Su J, Zhang J, Zhao J. Systemic vasculitis involving the breast: a case report and literature review. Rheumatol Int. 2019 Aug;39(8):1447-1455
[2] Soleto MJ, Marcos L. Behçet's disease involving the breast. Eur Radiol. 2002 Dec;12 Suppl 3:S98-S100. doi: 10.1007/s00330-002-1420-4.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1639

AB0768 NEUROLOGICAL MANIFESTATIONS IN GRANULOMATOSIS WITH POLYANGIITIS: ABOUT 11 CASES

O. Jomaa[1], O. Berriche[1], S. Arfa[1], A. Fraj[1], M. Belkhiri[1], R. Makhloufi[1], W. Romdhane[1], M. Hermassi[1]. [1]*University Hospital Tahar Sfar Mahdia, Tunisia, Internal Medicine Department, Mahdia, Tunisia*

Background: Granulomatosis with polyangiitis (GPA) is a rare systemic vasculitis, affecting mainly the superior airways, lungs and kidneys. Neurological impairment is frequent, described in 22 to 54% of cases, and rarely inaugurates the disease.

Objectives: The objective of our work was to evaluate its prevalence and its different aspects.
Methods: A retrospective study including 11 files of GPA patients followed over a period of 10 years in The Internal Medecine Department at Tahar Sfar Hospital Mahdia TUNISIA.
Results: Neurological manifestations were reported in 5 patients: a pyramidal syndrome was noted in 3 patients with a normal cerebral MRI, a disabled headache was described in one patient with a normal cerebral MRI. Peripheral neuropathy in 2 cases, and the Electroneuromyogram objectified a mononeuropathy affecting the ulnar nerve, peroneal nerve, and musculocutaneous nerve in one patient and a distal sensitivomotor poly neuropathy in one patient. Cranial nerves damage was noted in two cases, one VII (1 case) and one V (1 case).
Conclusion: Our study results, show the importance of timely diagnosis of these neurological manifestations, as their evolution will depend on the early GPA treatment.
REFERENCES:
[1] doi: 10.1016/j.autrev.2017.07.007
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1660

AB0769 EROSIVE SYNOVITIS, DACTYLITIS, HYPERCALCAEMIA, LYMPHADENOPATHY, ELEVATED SERUM ACE & HYPOTHYROIDISM – AN UNUSUAL PRESENTATION OF IGG4-RELATED DISEASE

E. Tranah[1], A. Khan2, N. Bhadauria[1], D. Mukerjee[1]. *[1]North Middlesex University Hospital, Rheumatology, London, United Kingdom*; *[1]North Middlesex University Hospital, Rheumatology, London, United Kingdom*

Background: IgG4-related disease (IgG4-RD) is a fibroinflammatory disorder which can affect almost any tissue in the body. We describe a challenging case of IgG4-RD which reflects the great heterogeneity of this disease.
Objectives: A 49-year-old Mauritanian gentleman was referred to Rheumatology with chronic progressive symmetrical synovitis affecting the upper and lower limbs. He had no features suggestive of a spondyloarthropathy or connective tissue disease. Blood tests revealed a raised C-reactive peptide (CRP) of 194 mg/L and erythrocyte sedimentation rate (ESR) of 46 mm/hr. His rheumatoid factor and anti-cyclic citrullinated peptide antibodies were negative. Anti-nuclear antibody was weakly positive at 1:80 with a speckled pattern, but extractable nuclear antigen antibodies, anti-double-strand DNA-antibodies and anti-neutrophil cytoplasm antibodies were negative. Complement proteins and creatine kinase were normal. Radiographs of the hands and feet demonstrated widespread erosive changes worst at the metacarpophalangeal, metatarsophalangeal and first tarsometatarsal joints, as well as swan-neck deformities of the fifth phalanges in both hands. Chest radiograph and serological virology screen were both unremarkable. He was subsequently diagnosed with a seronegative inflammatory arthritis and treated with intramuscular methylprednisolone. He was awaiting subcutaneous methotrexate.
Methods: He was hospitalised shortly after with worsening polyarthritis and hypercalcaemia (3.34 mmol/L). Examination demonstrated synovitis, new lymphadenopathy and dactylitis. Other investigations revealed a normocytic anaemia (Hb 80 g/dL, MCV 80 fL), neutrophilia (20 x 10^9/L), eosinophilia (4 x 10^9/L), thrombocythaemia (500 x 10^9/L), hypoalbuminaemia (25 g/L), CRP 200 mg/L and ESR 60 mm/hr. All immunoglobulins were raised with IgG 30.5 g/L. IgG4 subset was 3.0 g/L. Parathyroid hormone was low (< 0.7 pmol/L) and vitamin D was 125 nmol/L. Thyroid function, myeloma screen and blood tumour markers were unremarkable. Blood film revealed no blasts. Serum angiotensin-converting enzyme (ACE) was elevated at 171.9 U/L. A CT-chest-abdomen-pelvis revealed an enlarged thyroid with retrosternal extension and widespread lymphadenopathy above the diaphragm.
Results: Biopsies of the thyroid gland and submandibular lymph node demonstrated lymphoplasmacytic fibroinflammatory changes and > 40% of IgG4 cells. Neither biopsy showed evidence of sarcoidosis, tuberculosis or malignancy. He was treated with a weaning regimen of high-dose oral corticosteroids resulting in normalisation of haematological, inflammatory and biochemical parameters. His musculoskeletal pain, swelling and early morning stiffness significantly improved too. Subcutaneous methotrexate was commenced and titrated upwards to 20 mg. Two months later, his arthritis relapsed upon reduction of corticosteroids. Again, there was a marked inflammatory response with raised CRP and ESR. He had also developed a new hypothyroidism (TSH > 100 mU/L, T4 0.5 µg/dL, positive TPO-antibody). Repeat hand and feet radiographs revealed severe erosive progressive disease (Figure 1). He awaits commencement of rituximab.

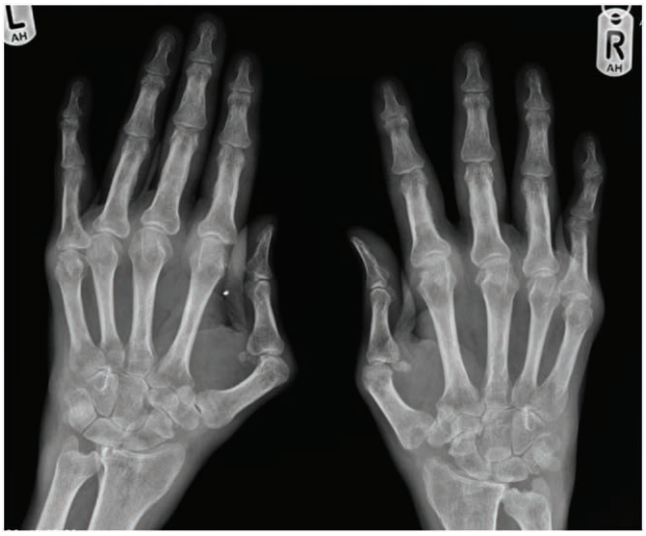


Figure 1. Plain hand radiograph demonstrating extensive erosive arthritis.

Conclusion: This is a unique presentation for a rare disease. There are few case reports of IgG4-RD causing erosive synovitis with rheumatoid-like swan-neck deformities or hypercalcaemia. Furthermore, this is the first case report as far as we know, of the disease associated with dactylitis or a raised serum ACE. Prior to biopsy, our main working diagnoses were sarcoidosis or a lymphoproliferative malignancy. The peculiar presentation necessitated a second opinion via the national IgG4-RD MDT who confirmed the histological diagnosis of IgG4-RD. We hope that this interesting case highlights the importance of histology in diagnosis of complex cases. In addition, the case presentation adds to the multitude of clinical manifestations of IgG4-RD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1921

AB0770 A RARE CASE OF SYNOVIAL METASTASIS REVEALED BY KNEE PAIN

M. Yasmine[1], S. Miladi[1], A. Fazaa[1], S. Mariem[1], K. Ouenniche[1], L. Souebni[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. *[1]Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: Intra-articular masses are not frequently encountered in clinical practice. However, the differential diagnosis can be broad. Synovial metastasis is a rare presentation that carries a poor prognosis with a poor survival rate.
Objectives: Here by a case of synovial metastasis of the knee joint in a patient diagnosed with an adenocarcinoma of the lung.
Methods: A 60-year-old man with no remarkable past medical history presented to our department of rheumatology with right knee pain. He described a dull ache and swelling in his right knee with a dragging sensation, waking him up at night on a regular basis. The symptoms lasted from 6 months and were partially improved by analgesics and anti-inflammatory drugs. On examination, temperature was normal. The knee was edematous, erythematous, and warm with a range of motion of <90°. Laboratory investigations showed high acute phase reactants, the erythrocyte sedimentation rate was 75 mm. A plain radiograph of the left knee demonstrated a lytic lesion of the upper tibia. A magnetic resonance imaging of the right knee showed diffuse enlargement of the joint space due to a tissue infiltration within the synovium. These structures demonstrated heterogeneously increased T2 signal and intermediate T1 intensity characteristics. Most of the joint space was replaced by hyper enhancing synovium. At that time, differential considerations included severe inflammatory arthritis and synovial chondromatosis rather than unusual metastasis.
Results: Biopsy concluded to synovial metastasis from primary adenocarcinoma. Further investigations were necessary. Chest tomography showed a tumor process of left lower lobe associated with mediastinal lymphadenopathy. The patient was treated with palliative external radiotherapy to the right knee. The evolution was marked by the appearance of *multiple tracheobronchial fistulas*. The patient died 3 months later due to the progression of the disease.

Conclusion: We report a rare case of synovial metastasis concomitant to a lung adenocarcinoma. It is important to make a rapid diagnosis as early recognition of malignant infiltration into joints ensure appropriate multidisciplinary management decisions.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2143

AB0771 HIGH DOSE INTRAVENOUS METHYLPREDNISOLONE INDUCES RAPID IMPROVEMENT OF VISUAL ACUITY IN NON-INFECTIOUS UVEITIS OF DIFFERENT IMMUNE MEDIATED INFLAMMATORY DISEASES

N. Vegas-Revenga[1], J. L. Martín-Varillas[2], V. Calvo-Río[3], I. González-Mazón[3], L. Sanchez-Bilbao[3], E. Beltrán[4], A. Fonollosa[5], O. Maiz-Alonso[6], A. Blanco[7], M. Cordero-Coma[8], N. Ortego[9], I. Torre-Salaberri[10], F. Francisco[11], S. Muñoz Fernandez[12], M. D. M. Esteban-Ortega[13], M. Díaz-Llopis[14], J. Cañal[15], J. A. Ventosa[15], R. Demetrio-Pablo[15], L. Domínguez[16], M. Agudo-Bilbao[3], S. Castañeda[17], I. Ferraz-Amaro[18], M. A. González-Gay[3], R. Blanco[3].
[1]Hospital Galdakao-Usansolo, Rheumatology, Galdakao, Spain; *[2]Hospital de Sierrallana, Rheumatology, Torrelavega, Spain*; *[3]Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*; *[4]Hospital Universitario Doctor Peset, Rheumatology, Valencia, Spain*; *[5]Hospital Universitario de Cruces, Ophthalmology, Barakaldo, Spain*; *[6]Hospital Universitario Donostia, Rheumatology, San Sebastian, Spain*; *[7]Hospital Universitario Donostia, Ophthalmology, San Sebastian, Spain*; *[8]Hospital de León, Ophthalmology, León, Spain*; *[9]Hospital Universitario San Cecilio, Ophthalmology, Granada, Spain*; *[10]Hospital Universitario de Basurto, Rheumatology, Bilbao, Spain*; *[11]Hospital Universitario de Gran Canaria Doctor Negrín, Rheumatology, Gran Canaria, Spain*; *[12]Hospital Universitario Infanta Sofía, Rheumatology, Madrid, Spain*; *[13]Hospital Universitario Infanta Sofía, Ophthalmology, Madrid, Spain*; *[14]Hospital Universitario La Fe, Ophthalmology, Valencia, Spain*; *[15]Hospital Universitario Marqués de Valdecilla, Ophthalmology, Santander, Spain*; *[16]Hospital Universitario San Agustín, Rheumatology, Avilés, Spain*; *[17]Hospital Universitario de la Princesa, Rheumatology, Madrid, Spain*; *[18]Hospital Universitario de Canarias, Rheumatology, Canarias, Spain*

Background: Rapid and effective remission-inducing therapy is mandatory in uveitis to avoid irreversible structural and functional damage. In some severe cases biological agents might be required **(1-6).**
High-dose intravenous methylprednisolone (IVMP) may achieve prompt control of inflammation in most immune mediated inflammatory diseases (IMID), including non-infectious uveitis (NIU).
Objectives: To evaluate the efficacy and safety of IVMP pulse therapy in NIU of different IMID.
Methods: Multicentre study of 71 patients with severe uveitis who received IVMP. The underlying diseases were: Vogt Koyanagy Harada disease (VKHD) (n=24), Behçet disease (BD) (19), Sarcoidosis (5) and idiopathic NIU (23). The main outcome variable was Best-Corrected Visual Acuity (BCVA) estimated using the Snellen chart. BCVA that was assessed at 0 (basal), 2-5, 7, 15 and 30 days after IVMP.
The results are expressed as mean ±SD in normally distributed variables, or as median [IQR] when are not. Comparison of continuous variables was performed using the Wilcoxon test.
Results: We studied 46♀/ 25♂ patients. The main features are shown in Table 1. IVMP dose ranged from 250 to 1000 mg/day administered for 3-5 consecutive days, the dose was established according to the presence or not of other systemic manifestations apart from uveitis. All of them had active intraocular inflammation at the moment of the study. BCVA values improved considerably after 1 month (Figure 1**).** No major side effects were observed.

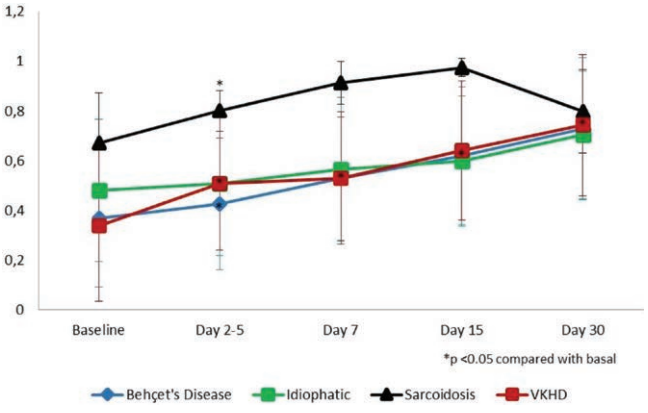


Figure 1. Improvement of best corrected visual acuity (BCVA).

Conclusion: High-dose IVMP pulse therapy is useful and safe for a prompt control of BCVA regardless of the underlying IMID.
REFERENCES:
[1] Vegas-Revenga N, et al. Am J Ophthalmol. 2019; 200:85-94. doi: 10.1016/j.ajo.2018.12.019
[2] Calvo-Río V, et al. Clin Exp Rheumatol. 2014;32(4 Suppl 84): S54-7. PMID: 25005576
[3] Santos-Gómez M, et al. Clin Exp Rheumatol. 2016;34(6 Suppl 102): S34-S40. PMID:27054359
[4] Atienza-Mateo B, et al. Rheumatology (Oxford) 2018;57(5):856-864. doi: 10.1093/rheumatology/kex480.
[5] Atienza-Mateo B, et al. Arthritis Rheumatol. 2019; 71(12):2081-2089. doi: 10.1002/art.41026.
[6] Martín-Varillas JL, et al. Ophthalmology. 2018;125(9):1444-1451. doi: 10.1016/j.ophtha.2018.02.020

Table 1. Main features of 71 patients with NIU. Data are of affected eyes.

	VKHD (n=24)	Idiophatic (n=23)	Behcet's disease (n=19)	Sarcoidosis (n=5)	Overall (n=71)
Men/Women, n	5/19	9/14	9/10	2/3	71
Mean age (years) ±SD	42 ±11	47 ± 15	33±10	42 ± 22	-
Unilateral/Bilateral NIU, n (%)	2 (8.3)/22(91.7)	10 (43.5)/13(56.5)	4 (21)/15 (79)	3(60)/2(40)	19/52
NIU patterns, n (%)					
Posterior uveitis	6 (25)	9 (39.1)	3 (15.8)	1 (20)	19
Panuveitis	18 (75)	14 (60.9)	16 (84.2)	4 (80)	52
Laboratory data, n (%)					
ANA	2 (8.34)	2 (8.7)	0 (0)	1 (20)	5
HLA B27	0 (0)	4 (17.4)	0 (0)	0 (0)	4
HLA B29	0 (0)	1 (4.3)	0 (0)	0 (0)	1
HLA B51	0 (0)	5 (21.7)	8 (42)	3 (60)	16
Angiotensin Converting Enzyme (ACE)	1 (4.17)	2 (8.7)	0 (0)	1 (20)	4

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2159

AB0772 JAK INHIBITORS IN REFRACTORY ADULT AND CHILDHOOD ONSET STILL'S DISEASE

L. Gillard[1], S. Mitrovic[1,2], H. Reumaux[3], M. Michaud[4], F. Cohen[1,2], J. Pouchot[5], B. Fautrel[1,2,6]. *[1]Pitié-Salpêtrière, AP-HP, Rheumatology Department, Paris, France*; *[2]Sorbonne Université, Rheumatology Department, Paris, France*; *[3]Jeanne de Flandre Hospital, Rheumatology, Lille, France*; *[4]Hospital Joseph Ducuing, Medecine Interne, Toulouse, France*; *[5]European Hospital Georges Pompidou, Medecine Interne, Paris, France*; *[6]Pierre Louis Institute of Epidemiology and Public Health, INSERM UMR 1136, Paris, France*

Background: Excessive and inappropriate production of pro-inflammatory cytokines such as interleukin (IL)-1, IL-6 or IL-18, is a pathogenic cornerstone in adult and childhood onset Still's disease. Beyond therapies targeting IL-1 or IL-6, Janus kinases (JAK) inhibitors have been proposed for adult-onset Still's disease (AOSD) patients refractory to or intolerant of treatment with biologicals. Recently, it has been suggested that JAK inhibitors might be efficient in refractory AOSD patients[1].
Objectives: To assess the efficacy and safety of JAK inhibitors in the treatment of refractory systemic juvenile idiopathic arthritis (sJIA) or AOSD.
Methods: This retrospective study was based on a national survey of the departments of rheumatology, paediatric rheumatology and internal medicine in all French hospitals from an online call of the "Club Rhumatismes et Inflammation" (www.cri-net.com). The data were collected using a standardized questionnaire, and analyzed at different time points (treatment initiation, M1, M3, M6 and end of the follow-up). The response to JAK inhibitors was categorized as: complete remission (resolution of all clinical and biologic signs), partial remission (clinical improvement with persistence of a few symptoms) or failure (lack of clinical or biological improvement).
Results: 6 patients (5 adults and 1 child) were recruited (Table 1). Mean age at treatment start was 39.6 years for the AOSD patient and 6 years for the sJIA patient, and mean disease duration was 5.3 years. The clinical expression was predominantly systemic in 5 five patients and chronic articular in one. Response to corticosteroids, conventional synthetic or biological Disease Modifying Anti-Rheumatic Drugs had been considered inadequate in all patients. Baricitinib was used in 3 patients, ruxolitinib in 2, and tofacitinib in 1. Steroids were concurrently used in all patients, anakinra in one, methotrexate and anakinra in one. At a mean (SD) follow-up of 9.5 months, partial response was observed in 4 (66.7%) cases (patients with ruxolitinib, tofacitinib

Table 1. Characteristics of the AOSD patient

No.	Sex	Age (year)	Main symptoms	Treatments before JAKi onset	JAK inhibitors	Steroids at onset (mg/day)	Concomitant treatment	Response at last F-U	Steroids at the end of F-U (mg/day)	F-U (months)
1	F	6	Fever, polyarthritis, rash	AINS, ANAKI, TOCI, CANAKI, ADA, THALI, INFLIX	RUXOLITINIB 5mgx2/day	3	0	P	1	23
2	M	28	Fever, polyarthritis, rash	ANAKI	BARICITINIB 4mg/day	80	0	**N**	10	1
3	M	32	Fever, polyarthritis, rash	TOCI+MTX, ANAKI+MTX, CANAKI+MTX, ADA, CICLO, IgIV	BARICITINIB 4mg/day	16	MTX 20 mg/week ANAKINRA 100mg/day	P	12	19
4	F	40	Fever, polyarthritis, rash	MTX, IMUREL, CICLO, ETANERCEPT, ANAKI+MTX, TOCI+MTX, IgIV	RUXOLITINIB 15mgx2/day	60	ANAKI 200mg/day	P	30	4
5	F	48	Fever, polyarthritis, rash	TOCI, ANAKI, CICLO, CANAKI, IMUREL	TOFACITINIB 5mgx2/day	50	0	P	7.5	9
6	F	50	Fever, polyarthralgia, rash	ANAKI	BARICITINIB 4mg/day	60	0	**N**	40	1

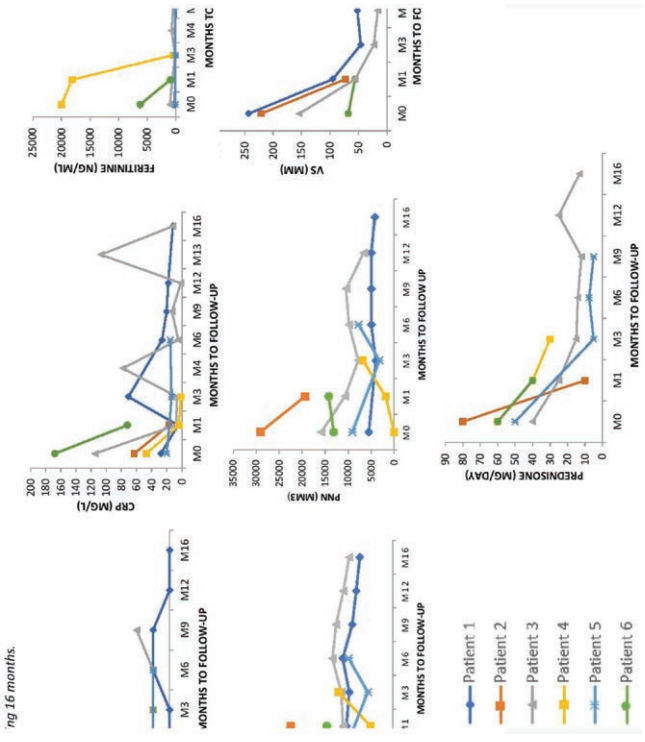
***F-U**: Follow-up**N**: No response**P**: Partial response*

or baricitinib) and failure in 2 (33.3%) (patients with baricitinib). No patient achieved complete remission. At the last visit, steroids could be decreased but not stopped in all patients. Patients with partial response had an average decrease of 72,8% (90% for tofacitinib, 70% for baricitinib, 58.5% for ruxolitinib between the start and the follow-up end date) and non-responder patients were yet able to reduce steroids by 60,5% (Table 1). Tolerance of JAK inhibitors was excellent, however patient 4 experienced an episode of infectious pulmonary disease.

Conclusion: JAK inhibitors therapy may be helpful for some patients with refractory Still's disease. However, no complete response was observed in this short series of cases. There might be a difference of response between the molecules, although the number of patients is too low to draw conclusions. Additional information is thus needed to evaluate more precisely the risk-benefit ratio of this treatment, and a possible difference in efficacy among the different groups of JAK inhibitors.

REFERENCES:

[1] Hu Q, Wang M, Jia J, et al. Ann Rheum Dis 2020;0:1–3. doi:10.1136/annrheumdis-2019-216



Acknowledgements: I thank all the coauthors, particularly Stéphane Mitrovic and Bruno Fautrel. Also, a special thank to the CRI.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2210

AB0773 PATTERN OF MACROPHAGE ACTIVATION SYNDROME IN RHEUMATIC DISEASES

R. Maheshwari[1], R. Sankaralingam2, R. R2, S. Chinnadurai2, B. Chilukuri2, M. Mani2, J. Antony2. *[1]Sri Ramachandra Institute of Higher Education and Research, Clinical Immunology and Rheumatology, Chennai, India*; *[1]Sri Ramachandra Institute of Higher Education and Research, Clinical Immunology and Rheumatology, Chennai, India*

Background: Macrophage activation syndrome (MAS) is a rare, potentially fatal condition complicating autoimmune diseases, as their initial manifestation or during its course.

Objectives: To describe the pattern of MAS and its salient features in patients with rheumatic diseases.

Methods: A retrospective observational study was conducted in 16 patients diagnosed with MAS, due to rheumatic diseases in Department of Rheumatology, SRIHER, Chennai from January 2018-December 2020.

Results: The primary diseases were Systemic Lupus Erythematosus(SLE) in 75%(n=12),Adult Onset Still Disease(AOSD) in18.7%(n=3) and Kikuchi Disease in 6.25%(n=1). 50%(n=8) presented with MAS as the initial manifestation.Others had a known rheumatic disease with an average duration of 6.5 years.Occult MAS was seen in 25%(n=4). The most frequent clinical features were unremitting fever(n=15) and splenomegaly(n=15).All had hyperferritinemia-mean of 2971.10 ng/mL(531-12536).Sub group analysis showed significant hypofibrinogenemia(129.8 vs 200.62 mg/dl) in patients presenting with MAS as their initial manifestation.Transaminitis(666/252.5 vs 243/217.62 U/L), hypertriglyceridemia(316 vs 275.8 mg/dl), high LDH(2490 vs 938.75) were more severe in this group, but not significant.All with SLE had increased disease activity, with 50%(n=8) having SLEDAI 2K of ≥15. Bone marrow aspiration showed haemophagocytes in 81.25%(n=13).H score of >169 was seen in 93.75%(n=15). Infection was the commonest trigger for MAS(n=9)-bacterial(n=5), viral(n=4), fungal(n=1) and mycobacterial(n=2),-followed by parturition(n=1).All patients were managed with pulse steroids followed by intravenous cyclophosphamide(n=8), rituximab(n=2), mycophenolate mofetil(n=2) in SLE, tocilizumab(n=2) and etoposide(n=1) in AOSD. Mortality rate was 18.75%(n=3).

Conclusion: Spectrum of MAS in rheumatic diseases could be occult, associated with infection,high disease activity,or lead to mortality. High index of clinical suspicion is required, due to overlap of features like fever, cytopenias and organomegaly in MAS & SLE.Hyperferritinemia, high LDH, & transaminitis could aid in differentiating & early diagnosis. New criteria for rheumatic diseases,including these parameters are needed, especially in resource-limited settings where sIL-2Rα & NK cell activity tests are not feasible.

REFERENCES:

[1] Stuart J.Carter et al. Macrophage activation syndrome in adults:Recent advances in pathophysiology, diagnosis and treatment. Rheumatology 2019;58;5-17

[2] Ai-Chun Liu et al.Macrophage activation syndrome in systemic lupus erythematosus:a multicentre,case-control study in China.Clin Rheumatol 2017.

Table 1. MAS-SALIENT FEATURES

FEATURES	INITIAL MANIFESTATIONS [n=8]	KNOWN RHEUMATIC DISEASES[n=8]	P VALUE (<0.05)
Primary rheumatic diseases			
SLE	5(62.5%)	7(87.5%)	-
AOSD	2(25%)	1(12.5%)	
Kikuchi disease	1(12.5%)	0	
Fever	8(100%)	7(87.5%)	0.30
Respiratory	2(25%)	5(62.5%)	0.13
Neurological	1(12.5%)	4(50%)	0.10
Bleeding	2(25%)	1(12.5%)	0.52
Splenomegaly	8(100%)	7(87.5%)	0.30
Hepatomegaly	6(75%)	3(37.5%)	0.13
Haemoglobin(g/dl)	8.58(5.4-11.7)	8.2(5.2-11.5)	0.70
WBC count(/µL)	5550(1000-11800)	3477.5(1200-6200)	0.19
Platelet count(x 10^9/l)	1.41(0.30-2.4)	1.35(0.32-1.8)	0.90
ESR(mm/hr)	76.75(42-137)	68(20-127)	0.65
AST(U/L)	666(36-3481)	257.75(45-642)	0.36
ALT(U/L)	252.5(18-790)	217.62(28-1044)	0.82
LDH(U/L)	2490.12(164-16,000)	938.75(357-1569)	0.44
Ferritin(ng/ml)	2187.46(532-7500)	3754.75(531-12536)	0.37
Triglycerides(mg/dl)	316(53-551)	275.8(160-317)	0.52
Fibrinogen(mg/dl)	129.8(76-178)	200.62(140-292)	0.009
Complement 3(mg/dl)	39.14(13-60)[n=5]	57.72(32-95)[n=7]	0.16
Complement 4(mg/dl)	4.24(1.2-6)[n=5]	14.22(2.8-34)[n=7]	0.07
Anti dsDNA antibodies[ELISA] IU/ml	596.2(90-1151)[n=5]	316.82(10-800)[n=7]	0.26

MAS-Macrophage activation syndrome,WBC-white blood cell,ESR-erythrocyte sedimentation rate,AST-aspartate aminotransferase, ALT-alanine aminotransferase, LDH-lactate dehydrogenase, dsDNA-double standed deoxyribonucleic acid

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2965

AB0774 TREATMENT WITH IL-1 INHIBITORS IN PATIENTS WITH SCHNITZLER'S SYNDROME: A 5-YEAR CLINICAL EXPERIENCE

S. Salugina[1], V. Gorodetskiy[2], E. Fedorov[1], V. Rameev[3], E. Borzova[4,5], N. Lopatina[6]. [1]*V.A.Nasonova Research Institute of Rheumatology, Pediatric Department, Moscow, Russian Federation*; [2]*V.A.Nasonova Research Institute of Rheumatology, Laboratory of Intensive Therapy Methods, Moscow, Russian Federation*; [3]*Sechenov's First Moscow State Medical University, E. M.Tareev Clinic of Rheumatology, Neurology and Occupational Pathology, Moscow, Russian Federation*; [4]*Sechenov's First Moscow State Medical University, Department of Dermatology and Venereology, Moscow, Russian Federation*; [5]*Research and Clinical Institute of Pediatrics n.a.Yuri Veltischev, Department of Clinical Genetics, Moscow, Russian Federation*; [6]*V.A.Nasonova Research Institute of Rheumatology, 5th Rheumatology Department with Hematology Beds, Moscow, Russian Federation*

Background: Schnitzler's syndrome (SchS) is a rare non-monogenic auto-inflammatory disease (AID) which manifests in adults and is characterized by recurrent urticarial lesions, monoclonal gammopathy, and other manifestations of a systemic inflammatory response (fever, muscle / joint / bone pains, leukocytosis, increased ESR, CRP). Off-label treatment with IL-1 inhibitors (anakinra, canakinumab) was shown to be highly effective and well tolerated in pts with SchS based on a few multicenter studies and practical experience.
Objectives: To analyze a real-life experience of the treatment with IL-1 inhibitors in pts with SchS in the rheumatology tertiary care settings.
Methods: The study included 7 pts (3 women, 4 men) with treated with IL-1 inhibitors (anakinra, canakinumab). A median age at the diagnosis was 44 years old (25 – 68). Age at the disease onset ranged from 22 to 66. All pts met the Strasbourg diagnostic criteria. 7 pts received canakinumab, while 3 pts were first treated with anakinra followed by a switch to canakinumab. Anakinra was administered subcutaneously 100 mg per day. Canakinumab was given subcutaneously at a dosage of 150 mg every 8 weeks. The treatment duration with anakinra ranged from 1 week to 2.5 months with further switching to canakinumab. The duration of canakinumab treatment by the time of analysis ranged from 2 months to 5.5 years.
Results: All pts at the inclusion into the study suffered from urticarial rash, pains in bones and joints, fatigue, fever (6), increased acute phase marker levels (ESR, CRP), monoclonal gammopathy, mainly IgMk (4.7 – 9 g/l). An average period between the disease onset and the treatment initiation was 3 years (2 to 4). In all pts lymphoproliferative diseases and monogenic AIDs (CAPS, TRAPS) were excluded. Before the treatment with IL-1 inhibitors, all pts had received NSAIDs and/or GCs, methotrexate - 2, plaquenil-2. During the treatment with IL-1 inhibitors, 6 out of 7 pts had a complete response as demonstrated by a symptom resolution within several days and a rapid decrease in ESR and CRP levels. In 3 pts, who responded anakinra, the treatment was switched to canakinumab. In one patient with a partial response to anakinra, there was a loss of the effect upon switching to canakinumab, In one patient, the interval between canakinumab injections was increased up to 5 months without a symptom relapse. This patient fathered a healthy child whilst on treatment with canakinumab. The therapy was well tolerated in all pts, no SAE were noted.

Table 1. Clinical and demographic characteristics of patients with SchS

Patients	1	2	3	4	5	6	7
Sex	M	F	M	F	F	M	M
Age (y)	44	32	56	68	25	51	49
Age of disease onset (y)	40	29	53	66	22	39	47
Urticarial rash	+	+	+	+	+	+	+
Fever	+	-	+	+	+	+	+
Fatigue	+	+	+	+	+	+	+
Bone pain	+	+	+	+	+	+	+
Arthralgia/arthritis	+	+	+	+	+	+	+
ESR(normal <15mm/h)	31	140	100	49	81	53	56
CRP (normal <5mg/n)	107	44	192	96	369	76	41,82
IgM kappa (g/l)	7,1-5,2	4,7-7,8	7,6	-	-	5,2	9
IgM lambda(g/l)	-	-	1,36	-	-	-	-
IgG kappa (g/l)	-	-	-	5,1	-	-	-
IgG lambda (g/l)	-	-	-	-	10,7	-	-

Conclusion: SchS is a rare disease that occurs in the practice of a rheumatologist. Short and long acting IL-1 inhibitors are highly efficient and safe treatment options for pts with SchS. A switching from short to long acting IL-1 inhibitors can be effective in SchS pts.
REFERENCES:
[1] Krause K, Tsianakas A, Wagner N, Fischer J, Weller K, Metz M, et al. Efficacy and safety of canakinumab in Schnitzler syndrome: a multicenter randomized placebo-controlled study. J Allergy Clin Immunol 2017;139:1311-20.
[2] Betrains A., Staelsa F, Vanderschueren S. Efficacy and safety of canakinumab treatment in schnitzler syndrome: A systematic literature review Seminars in Arthritis and Rheumatism 50 (2020) 636-642.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3176

AB0775 MANY RARE AND SERIOUS LOCALIZATIONS IN ONE CASE WITH HEREDITARY EXOSTOSES

R. Sarraj[1], M. Ghali[1], R. Ben Chehida[1], G. Mouna[1], I. Bejia[1], J. Mahbouba[1], S. Zrour[1], M. Touzi[1], N. Bergaoui[1]. [1]*Fattouma Bourguiba Hospital, Rheumatology, Monastir,Tunisia*

Background: Multiple hereditary exostoses (MHE) is an inherited disorder of bone growth. People who have MHE grow exostoses or boney bumps on their bones that vary in size, location and number. Some localizations are rare but potentially serious such as ribs, spine or pelvis due to proximity to important structures.
Objectives: The aim of this case report was to illustrate the clinical and radiographic features of some rare localizations of MHE.
Methods: We are reporting a rare case of a thirty one-year-old male with severe localizations of MHE.
Results: A thirty one-year-old male affected by hereditary multiple exostoses., not followed up, came to our consultation complaining about chest pain. On examination, he walks with a limp because of the unequalness of his limbs.The osteoarticular examination revealed numerous palpable osseous masses at the distal and proximal end of the 2 arms, 2 forearms, 2 thighs and 2 legs and at the right iliac wing. Neurological examination revealed vivid deep tendon reflexes, bilateral positive Hoffmann'sign and Babinski reflex associated with right hemiparesis. The pulmonary exam was normal. Medullary MRI showed medullary compression with spinal cord atrophy and sign of myelopathy of c1 c2 segment. The ct –scan revealed multiple exostosis, the two largest lesions were located in the second rib measuring 45mm * 35mm axially and 52mm in height compromising blood vessels, and in the right iliac bone with a retroperitoneal growing mass measuring 126 * 94 mm axially and 100 mm in height leading to a serious entrapment of the axial skeleton and the abdominal organs. It also confirmed thickening of the cartilage cap of the right iliac bone suggestive of malignant chondrosarcomatous transformation.
Conclusion: Exostoses are the most common benign bone tumors. Its complications are rare but can cause a functional disability or even a vital risk.
REFERENCES:
[1] Eke GK, Omunakwe HE, Echem RC. Hereditary multiple exostoses in a 15-year-old boy: A case report and review of literature. Niger J Paediatr. 2016;43(4):295.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3296

AB0776 MULTIPLE AUTOIMMUNE SYNDROME

A. Fraj[1], S. Arfa[1], O. Jomaa[1], F. Boubaker[1], I. Bannour[2], O. Berriche[1], H. Sfar[1]. *[1]University Hospital Tahar Sfar Mahdia,Tunisia, Internal Medicine and Endocrinology Department, Mahdia,Tunisia*; *[2]University Hospital Fattouma Bourguiba Monastir,TUNISIA, 2-Immunology Department, Monastir,Tunisia*

Background: Multiple autoimmune syndrome (MAS) is a rare entity, defined by the association of three autoimmune diseases in the same patient. MAS can be classified into three groups.
Objectives: The objective of this work was to describe the autoimmune diseases profile in MAS in An Internal Medicine Department.
Methods: We report a retrospective analysis including 14 cases of MAS seen in The Internal Medicine Department at Taher Sfar Hospital, Mahdia, TUNISIA over a period of 10 years.
Results: We followed 14 patients with MAS. They were 14 women. The mean age of patients was 52 years. SAM was type 3 in 12 patients (85%), type 2 in one patient (7.1%) and one patient satisfied both type 2 and type 3 MAS criteria (7.1%). No cases of MAS type 1 had been reported. We found 13 patients with 3 associated autoimmune diseases and one patient with 4 associated autoimmune diseases. The autoimmune diseases were: Sjögren's syndrome in 14 patients (100%), Hashimoto's thyroiditis in 11 cases (78%), systemic lupus erythematosus in 7 cases (50%), Addison's disease in 4 cases (28, 5%), scleroderma, thymoma, vitiligo, Biermer and primary biliary cholangitis each in one case (7.1%).
Conclusion: Multiple autoimmune syndrome remains a rare but probably under-diagnosed entity. Thus, in patients with autoimmune disease, initial investigation and follow-up of clinical signs and biological stigmas of other autoimmune diseases should be cautious.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3297

AB0777 A RARE CASE OF A SOLITARY PLASMOCYTOMA OF A LUMBAR VERTEBRA

D. Khalifa[1], H. Hachfi[1], N. Ben Chekaya[1], M. Brahem[1], M. Younes[1]. *[1]Taher Sfar Hospital, Rheumatology, Mahdia,Tunisia*

Background: Solitary plasmocytoma is a rare tumour that represents around 2 to 5% of all plasma cell dyscrasias. It normally affects soft tissu but rarely the bone. Diagnosis is based on histology, the absence of bone marrow involvement.
Objectives: To drag attention to think of solitary plasmocytoma of bone when dealing with a vertebral fracture in the absence of the CRAB criteria of multiple myeloma.
Methods: We report a rare case of a vertebral fracture of the 4th lumbar vertebra (L4) revealing a solitary plasmocytoma of bone.
Results: A 67-year-old female patient presented to our rheumatology department with back and left radicular pain of brutal onset, 15 days prior to her visit. Pain was severe and awakened her at nights. On examination, mobilities of the spine were unchanged but on palpation she had exquisite pain of L4. Laboratory tests showed a normal sedimentation rate of 15mm the first hour, a negative c-reactive protein, normal calcemia and kidney tests. X-rays of lumbar spine showed a vertebral fracture with a destruction over 50% of the vertebral size and cortical rupture. MRI of the spine showed the absence of other lytic lesions or other fractures or spinal cord compression and showed the total destruction oft he anterior vertebral body of L4 (Figure 1). Protein electrophoresis was in normal range and 24h urinary proteinuria was negative. Other tests rules out gynecological, thyroid, and renal neoplasms. Sternal puncture showed a rich bone marrow of normal cells without further infiltration. Bone biopsy of the detected lesion showed tumour cells made of mature plasmocytes confirming the diagnosis of solitary plasmocytoma of the bone. The patient was treated with radiation therapy. The evolution after 24 months showed a stabalised lesion and the absence of progression to multiple myeloma.

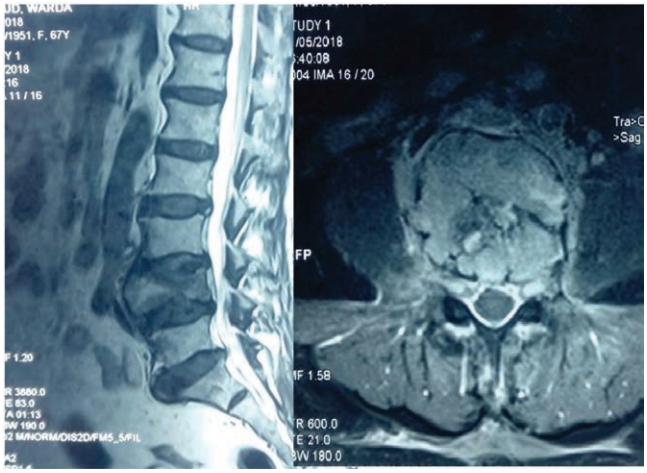


Figure 1. T2 weighted MRI showing the vertebral fracture of L4

Conclusion: It is important to keep in mind the diagnosis of solitary plasmocytoma of bone when facing a solitary lesion or vertebral fracture despite relatively non agressive radiological signs. It is also important to note the possible evolution to multiple myeloma and keep a hawk-eyed guard.
REFERENCES:
[1] Masmoudi K, Elleuch E, Akrout R, et al. Le plasmocytome solitaire osseux: à propos de 3 cas et revue de la littérature. *Pan Afr Med J*; 25. Epub ahead of print 6 December 2016. DOI: 10.11604/pamj.2016.25.219.10933.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3313

AB0778 VENOUS THROMBOSIS IN UNUSUAL SITES

A. Fraj[1], O. Berriche[1], S. Arfa[1], O. Jomaa[1], W. Romdhane[1], H. Sfar[1]. *[1]University Hospital Tahar Sfar Mahdia,Tunisia, Internal Medicine and Endocrinology Department, Mahdia,Tunisia*

Background: Unusual site venous thrombosis (USVT), which includes venous thromboses of the upper limbs, digestive tract, cellar and brain, are rarely observed compared to those of the lower limbs and require both an etiological approach and a rigorous management.
Objectives: Our objective is to identify the epidemiological, clinical, therapeutic and evolutionary characteristics of USVT.
Methods: Retrospective study including 33 patients files with USVT followed in The Internal Medicine Departments at Tahar Sfar University Hospital Mahdia TUNISIA over a period of 10 years.
Results: They were 21 females (63.6 %) and 12 males (36.4%) with an average age of 45.2 ± 18 years. Cerebral venous thrombosis was the most frequent localization identified in 10 patients (30.3%), followed by gastrointestinal thrombosis in 9 cases (27.3%), vena cava thrombosis in 9 cases (27.3%) and upper limb thrombosis in 5 cases (15.2%). The risk factors were respectively: age (42.4%), obesity (42.4%), smoking (30%), prolonged downtime (24.2%), surgical interventions (6.1%) and pregnancy (3%). An etiology was identified in 21 patients (66.6%), dominated by constitutional thrombophilia (27.3%), followed by BVL (15.1%) and Behçet's disease (16.4%). Rare causes were neoplasia in one case (3%), scleroderma in one case (3%) and inflammatory bowel disease in one case (3%). The etiological investigation was negative in 36.3% of cases. Treatment was based on heparin therapy followed by vitamin K therapy. Progression was favourable without accident or recurrence in 25 patients (75.5%). Complications were dominated by recurrence in 12.1% of cases, post-thrombotic disease in 6% of cases and pulmonary embolism in 3% of cases. We reported one death related to a hemorrhagic event.
Conclusion: USVT is a multifactorial pathology that involves both acquired and constitutional risk factors. Heparin therapy with an early relay by antivitamin K remains the treatment of choice today. The duration of treatment depend on the etiology, the recurrence of venous thrombosis and the risk of hemorrhagic complications.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3332

AB0779 CAN INFLAMMATION COEXIST IN PATIENTS WITH PROGRESSIVE PSEUDORHEUMATOID DYSPLASIA?

S. Mahadevan[1], B. Navaneethan[1], N. Gopalakrishnapillai Syamala[1], M. Mamadapur[1], R. S[1], T. Tn[1]. *[1]Madras Medical College, Rheumatology, Chennai, India*

Background: Progressive pseudorheumatoid dysplasia(PPRD) is considered as a degenerative genetic bone disorder. It is caused by loss of function mutation in WNT-1 inducible signaling pathway protein-3(WISP-3)[1]. WISP-3 gene function is required for the normal function of cartilage and skeletal development. The patients are normal at birth and start developing symptoms around 3-6 years of age[2]. The disease is characterised by stiffness, pain, deformity due to enlargement of the ends of short and long bones. Often, such patients are misdiagnosed as Juvenile idiopathic arthritis(JIA). In general, PPRD being considered as non-inflammatory disease, immunosuppressants or disease modifying anti rheumatic drugs(DMARDS) like methotrexate treatment are not used for treatment.
Objectives: We report a patient with characteristic findings of PPRD but with coexisting clinical and imaging evidence of inflammation.
Methods: 16 year old male boy born of third degree consanguineous asymptomatic parents presented with progressive swelling, deformity of bilateral small and large joints of upper and lower limbs. He also had pain in both hip and knee for past two years. Pain is associated with difficulty in walking and squatting. On examination he had bony enlargement around bilateral elbow, wrist, proximal and distal interphalangeal joints(Figure 1A). He also had restriction of bilateral hip movements and swelling of bilateral knee with effusion. He had exaggerated lumbar lordosis and flexion deformity of bilateral hip, knee. His blood counts, ESR, CRP were normal. Analysis of Knee joint synovial fluid showed cell count of 200/mm3 with no crystals and sterile culture. USG knee showed evidence of synovial thickening with increased power Doppler signals. Skeletal survey showed typical findings of PPRD with enlargement of epiphysis and osteoarthritis

changes(Figure 1B). MRI hip showed minimal effusion, synovial thickening, edema with STIR hyperintensity and enlargement of bilateral femoral epiphysis. MRI knee showed minimal effusion, marrow edema in patella(Figure 1C, arrow head), femoral condyle, diffuse synovial thickening with contrast enhancement(-Figure 1D, arrow) and deformed patellar contour. Immunological tests showed negative RF, ACPA and positive ANA(Hep2) speckled 4+. Immunoblot for ENA was negative. His ophthalmological evaluation showed no evidence of uveitis.

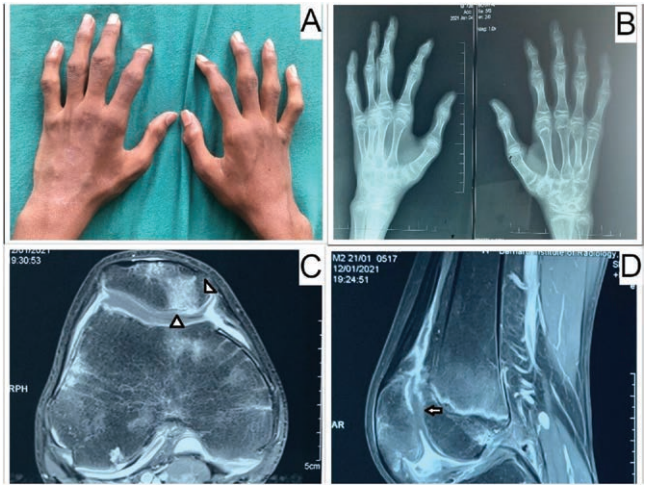


Figure 1. Clinical picture showing typical hand deformity and swelling at bone ends(A), hand radiograph showing epiphyseal enlargement(B), MRI knee T2 STIR showing bone marrow edema(arrow head) in patella(C) and synovial thickening(arrow) with contrast enhancement in fat saturated T1 MRI with contrast.

Results: Patient tested positive for homozygous mutation in WISP-3 gene. He was treated with ibuprofen and supportive measures. Orthopedic consultation obtained and planned for hip, knee replacement during follow up. Follow up imaging and acute phase response was advised after three months.
Conclusion: Although PPRD was classically described as a degenerative disease, the findings presented in our case show coexisting inflammation. Bone marrow edema in weight bearing areas, synovial effusion may be explained as part of cartilage degeneration like in osteoarthritis but synovial hypertrophy with contrast enhancement, power Doppler signals in ultrasound, ANA positivity may be signs of coexisting inflammatory or autoimmune phenomenon.
REFERENCES:
[1] Hurvitz JR, Suwairi WM et al. Mutations in the CCN gene family member WISP3 cause progressive pseudorheumatoid dysplasia. Nat Genet. 1999 Sep;23(1):94-8. doi: 10.1038/12699. PMID: 10471507.
[2] Garcia Segarra N, Mittaz L et al. The diagnostic challenge of progressive pseudorheumatoid dysplasia (PPRD): a review of clinical features, radiographic features, and WISP3 mutations in 63 affected individuals. Am J Med Genet C Semin Med Genet. 2012 Aug 15;160C(3):217-29. doi: 10.1002/ajmg.c.31333. Epub 2012 Jul 12. PMID: 22791401.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3480

AB0780 GENDER FEATURES OF VERIFICATION OF DIAGNOSIS UNDIFFERENTIATED ARTHRITIS

O. Malyshenko[1], M. Koroleva[1], M. Letaeva[1], J. Averkieva[1], T. Raskina[1].
[1]*Kemerovo State Medical University, Department of Propedeutics of Internal Medicine, Kemerovo, Russian Federation*

Background: Undifferentiated arthritis (UDA) is an inflammatory arthritis that does not meet the criteria for any rheumatologic disease. Early verification of UDA is currently one of the main goals of modern rheumatology, since a diagnosis established at an early date allows determining a therapeutic strategy. The high social significance of arthritis lies in the predominant lesion of people of working age, the steady progression of the disease, early disability and a reduction in life expectancy.
Objectives: To study the gender characteristics of verification of the diagnosis of undifferentiated arthritis.
Methods: A retrospective analysis of 74 case histories of patients diagnosed with UDA was carried out. The study group consisted of 26 men and 48 women, mean age 50.6 ± 4.3 years. All patients underwent a comprehensive laboratory and instrumental examination according to the standard of an articular syndrome of unclear genesis.
Results: According to the data obtained, the duration of the articular syndrome averaged 2.53 ± 1.2 years. In 29 patients (21.6% of women and 17.6% of men), on average, after 1.72 ± 0.9 years, the diagnosis of NDA was clarified. Taking into account modern diagnostic criteria, the following diseases were verified: rheumatoid arthritis in 13.5% (12.2% in women and 1.3% in men), ankylosing spondylitis in 10.8% (2.7% in women and 8.1% in men). Osteoarthritis, psoriatic arthritis and APS were diagnosed in 5.4%, 1.4% and 1.4% of women, and gouty arthritis, bone tuberculosis and HIV in 4.1%, 1.4% and 1.4% of men respectively. In 60.8% (43.2% in women and 17.6% in men), the etiology of arthritis was not verified.
Conclusion: In a third of patients with UDA, diagnosis verification takes about 2 years on average. In more than half of patients, the diagnosis remains the same. According to the data obtained, rheumatoid arthritis was more often verified in women, while ankylosing spondylitis in men, which is consistent with statistical data.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3507

AB0781 ONE, NONE, MANY: REFLECTIONS ON A RARE CASE

G. Sandri[1], L. Belletti[1], M. Cavedoni[2], C. Galluzzo[1], S. Bruni[3], M. T. Mascia[1].
[1]*Rheumatology Institute, Department of Clinic and Medical Specialties, Modena, Italy*; [2]*General Practitioner, Department of General Medicine, Modena, Italy*; [3]*Genzyme, Orchard Therapeutics, Modena, Italy*

Background: Rare diseases are all those diseases that present, in the European Union, a prevalence of less than 5 cases per 10,000 people. The number of rare diseases is estimated at roughly 7,000 but there are also longstanding medical conditions that elude diagnosis and could be identified as rare.
Objectives: Demonstrate the importance of international research in orphan diseases.
Methods: We report a case of 44 y/o female patient who arrived to our observation in 2006. Short stature, early puberty, ligament laxity, BMI <17. From the age of 29: recurrent diarrhea, pain in the spine, osteolytic lesions in spine and endosteal thickening in long bones, muscle contractures, strength deficit, muscular hypotrophy and hypotonia, cardiac conduction and blood pressure disorders, demyelinating MS-lesions, hyperprolactinaemia, slow wound healing, sicca syndrome, osteoporosis. No familiarity for bone lesions. In 2007 her first son (21y/o) began to complain pain at limbs. The young man presented the same bone lesions as the mother and shortening of the PR, prolactinoma, recurrent diarrhea, short stature, early puberty. Over the years numerous pathologies have been first hypothesized and then excluded: multiple sclerosis, bone metastases, Paget's disease, celiac disease, McCune Albright, Camurati-Engelmann syndrome, mitochondrial disease. No conclusive diagnosis despite the thousands of kilometers traveled, the numerous experts heard and the countless examinations carried out by the patients.
Results: In September 2009, the patients had been investigated at the NIH (Washington D.C.) during the "Undiagnosed Diseases Program" but without results until 2013 when the patients were informed of the detection of an ATP6V1H gene mutation never described before in humans. The gene encodes a vacuolar ATPase, a multimeric enzyme that plays several roles: is involved in endocytosis, intracellular trafficking, and protein degradation and energy production, appears to be a risk factor in the development of dyslipidemias and type II diabetes, has a bone resorption function. Also in the patient's father were founded the same mutation and asymptomatic bone lesions. In 2016 and 2017 studies have reported mouse models of osteoporosis that were generated by knocking out the ATP6V1H gene.
Conclusion: from this case it is possible to understand the difficulty of diagnosing a rare disease, the need of an international collaboration in research. From these studies it can be deduced moreover that the ATP6V1H gene could be an important target for therapeutic interventions aimed at preventing bone resorption and treating osteoporosis; evidence to support exploration of MMP9 and MMP13 as therapeutic targets for patients with ATP6V1H deficiency.This mutation seems to affect only one family, but it is possible that the penetrance of the disease-causing mutation is variable. In literature is reported an enhanced expression of MMP-9 in a variety of autoimmune diseases and neurological pathologies (2) therefore the mutation can be at the basis of other much more common pathologies.
REFERENCES:
[1] Zhang Y, Huang H, Zhao G, Yokoyama T, Vega H, Huang Y, Sood R, Bishop K, Maduro V, Accardi J, Toro C, Boerkoel CF, Lyons K, Gahl WA, Duan X, Malicdan MC, Lin S. ATP6V1H Deficiency Impairs Bone Development through Activation of MMP9 and MMP13. PLoS Genet. 2017 Feb 3;13(2):e1006481. doi: 10.1371/journal.pgen.1006481.
[2] Ram M, Sherer Y, Shoenfeld Y. Matrix metalloproteinase-9 and autoimmune diseases. J Clin Immunol. 2006 Jul;26(4):299-307. doi: 10.1007/s10875-006-9022-6.
Disclosure of Interests: Gilda Sandri: None declared, Lorenza Belletti: None declared, Michele Cavedoni: None declared, Claudio Galluzzo: None declared, stefano bruni Consultant of: Genzyme, Employee of: Genzyme, Maria Teresa Mascia: None declared
DOI: 10.1136/annrheumdis-2021-eular.3573

AB0782 MONOARTHRITIS: PROBABLE OUTCOMES

M. Osipyan[1], M. Efraimidou[1], V. Vardanyan[2], K. Ginosyan[1]. [1]*1st University Hospital Complex after M. Heratsi, Rheumatology, Yerevan, Armenia*; [2]*Mikaelyan Institute of Surgery, Rheumatology, Yerevan, Armenia*

Background: Numerous joint disorders initially produce swelling in a single joint and new onset monoartritis will probably further lead to the involvement of other joint groups and development of extraarticular manifestations. It is essential to take a proper diagnostic approach for organizing appropriate treatment and lowering possibility of disease progression.
Objectives: The aim of this study was to investigate joint distribution, determine rheumatological diseases of patients with acute monoarthritis and reveal the development of further systemic manifestations.
Methods: 100 patients (age 18-75 years) with clinically apparent monoarthritis of less than 6 weeks duration were included in the study. Criteria of exclusion were infection, trauma and crystal induced arthritis. Joint distribution, presence of systemic manifestations and development of chronic inflammatory rheumatic disease were evaluated. Presence of arthritis was proved with help of ultrasound examination. Complete blood count, ESR, CRP, RF, anti-CCP; HLAB27; MEFV mutations and X-ray of swollen joint were performed for all patients. Temperature was also measured.
Results: Mean age of patients with acute monoarthritis was 46±13 years. Female predominance was noted (61%). 71% of patients had elevated ESR, 69%- CRP. In 24% of cases homozygous or heterozygous mutations of MEFV gene were revealed. 21% of patients had positive RF and 18% - anti-CCP. 11% patients carried HLA-B27 antigen. 28% of examined patients had subfebril fever. Hepatosplenomegaly was determined in 16%, uveitis in 5%, psoriatic plaque in 4%, interstitial pneumonia in 2% of cases
At the baseline 82 patients were diagnosed with rheumatologically disease. Baseline data is shown in the Table 1 bellow.

Table 1. Baseline data

Diagnosis	Number of patients
FMF	23
Osteoarthritis (reactive synovitis)	16
Rheumatoid arthritis	15
Reactive arthritis	10
Ankylosing spondylitis	6
Psoriatic arthritis	4
SLE	3
Schonleyn-Henoch purpura	2
Sarcoidosis	2
Behcet diseases	1

Conclusion: In this study monoarhtritis in majority of cases underlies FMF. Though FMF is not considered as a frequent cause of acute monoarthritis, more attention should be paid on this pathology in focus of monoarthritis, especially in specific for FMF region. Further follow up of acute monoarthritis progression is needed.
REFERENCES:
[1] A. Becker, J. Daily, K. Pohlgeers. Acute Monoarthritis: Diagnosis in Adults. *Am Fam Physician* 2016; 94(10): 810-816
[2] S. Camacho-Lovillo, A. García-Martínez. Arthritis as presentation of familial Mediterranean fever. An Pediatr (Barc). 2015; 83(2):130. DOI: 10.1016/j.anpede.2015.07.007
[3] J. Ellis. Acute monoarthritis. JAAPA. 2019, 32(3):25-31. doi: 0.1097/01.JAA.0000553379.52389.eb
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3630

AB0783 "RICE AND SARDINES": AN UNUSUAL CAUSE OF RASH AND JOINT SWELLING

V. Thanopoulou[1], S. A. O. Jafery[2], B. Ramabhadran[1]. [1]*Luton and Dunstable University Hospital, Rheumatology, Luton, United Kingdom*; [2]*Leicester General Hospital, Endocrinology, Leicester, United Kingdom*

Background: Systemic vasculitis presents with numerous widespread manifestations. Various diseases can masquerade as systemic vasculitis (1). It is crucial to carefully evaluate patients with unusual presentations to look for vasculitis mimics. Scurvy, a disease caused by severe and prolonged vitamin C deficiency, still occurs in industrialized countries (2). Ascorbic acid is involved in various biologic processes including the synthesis of mature collagen. Lack of ascorbic acid especially affects blood vessel integrity leading to haemorrhagic manifestations characteristic of scurvy (3).
Objectives: Case report highlighting that scurvy is still prevalent in the west and may present with features resembling vasculitis.
Methods: Information was obtained from the patient's medical records.
Results: A 61 year old Caucasian female presented with a 3 weeks' history of bilateral lower limb pain, rash and swelling. She was referred to acute medicine to exclude deep vein thrombosis suspected by her general practitioner. She was previously fit and well apart from diagnosis of coeliac disease and various food intolerances. She believed her symptoms started following a recent course of Metronidazole for suspected dental infection which manifested with gum bleeding.She was found to have purpuric spots and ecchymosis bilaterally in her legs, from the toes to the groin. The left knee was swollen with evidence of hematoma around the joint.She denied fever, weight loss, night sweats, arthralgia, myalgia, rash, Raynaud's, alopecia, mouth or genital ulcers, ear-nose-throat manifestations. She denied chest pain, difficulty in breathing or symptoms of peripheral neuropathy. There was no history of asthma, inflammatory bowel disease or uveitis. She reported occasional alcohol intake, she did not smoke cigarettes nor use recreational drugs. Examination otherwise revealed no other major abnormalities with normal vital signs.Initial differential diagnosis included platelet or coagulation disorders or vasculitis. Initial blood tests revealed normal full blood count, coagulation screen, ESR, CRP, liver and renal biochemistry.Urine dip was positive for blood but not for protein. Knee aspiration was attempted but no fluid could be aspirated. Knee x-ray was unremarkable. ANA, ANCA and anti-GBM antibody tests were negative.On further review and enquiry into her symptoms and lifestyle she admitted having a diet exclusively of "rice and sardines" for nearly 2 years. This information along with clinical features led to the suspicion of Vitamin C deficiency that was subsequently confirmed. Ascorbic acid levels were <2.8micromol/l (normal range 26.1-84.6.micromol/l).Replenishment of vitamin C was followed by a rapid and sustained recovery. Detailed investigation for additional macro and micronutrient deficiencies were undertaken with referral to a dietician and to gastroenterology.
Conclusion: This case illustrates scurvy can present in previously "well" individuals and should be considered as a possible differential diagnosis of vasculitic lesions in the appropriate clinical context. Detailed dietary history is invaluable.
REFERENCES:
[1] A Review of Primary Vasculitis Mimickers Based on the Chapel Hill Consensus Classification. Zarka et al, Int J Rheumatol, 2020 Feb
[2] Global Vitamin C Status and Prevalence of Deficiency: A Cause for Concern? Sam Rowe1,Anitra C. Carr, Nutrients 2020 July
[3] Adult scurvy. Hirschmann et al, J Am Acad Dermatol 1999 Dec
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3705

AB0784 SPINAL HYDATID CYST DISEASE: WHAT FEATURES IN SURGICAL DEPARTMENTS?

A. Dghaies[1], R. Dhahri[1], M. Slouma[1], L. Metoui[1], I. Gharsallah[1], R. Ayari[2], Y. Mallat[2], K. Amri[2], M. Aloui[3], Y. Arous[3]. [1]*The Military Hospital of Tunis, Rheumatology, Tunis, Tunisia*; [2]*The Military Hospital of Tunis, Traumatology-Orthopedic Department, Tunis, Tunisia*; [3]*The Military Hospital of Tunis, Radiology, Tunis, Tunisia*

Background: Cystic echinococcosis (CE) is a zoonosis caused by the larve of Echinococcus granulosus. Cysts can develop in any part of the body, although the liver and lungs are most frequently involved. Bone echinococcosis is one of the rarest forms of the disease, accounting for 0.5 to 4.0% of all echinococcosis. Spinal cysts are disabling causing destruction similar to malignant bone lesions, with high risk of neurological deficit.
Objectives: To increase awareness of this disease, the clinical data of eight patients with spinal CE were analyzed retrospectively.
Methods: Clinical data of eight patients with spinal CE were analyzed retrospectively, collected over ten years on the department of orthopedics in the Military hospital of Tunis.
Results: The mean age of the patients was 49 years. The median disease duration was five years. All patients presented with back pain and paresthesia without neurological deficit. Radicular pain was reported by two patients. The diagnosis of spinal CE was made after the diagnosis of visceral CE in two patients. Former X rays showed nonspecific abnormalities and patients were treated initially by symptomatic treatments based on paracetamol and non-steroidal antiinflammatory drugs without any improvement. All of the patients needed Magnetic resonance imaging (MRI) to explore chronic back pain with paresthesia, revealing spinal CE. The typical MRI appearance is a multilocular cyst. Six patients had cervical and thoracic spinal cysts, one patient had a lumbar spinal cyst and one patient had cervical, thoracic and lumbar cysts. Further examinations with Computed tomography scans (CTscans) were needed before surgery for better examination bone destruction. All patients underwent surgery.

Cysts were removed with spinal fixation. All the patients showed relapses and needed at least three surgical interventions.
Conclusion: Bone echinococcosis is rare and often misdiagnosed. Radiographic and CT images lack disease-specific characteristics whereas MRI images offers a greater chance of direct diagnosis. Treatment of spinal hydatid disease is entirely surgical with high risk of relapses.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3986

AB0785 TREATING IDIOPATHIC RECURRENT PERICARDITIS WITH INTERLEUKIN-1 INHIBITORS - A SINGLE CENTER EXPERIENCE

P. Andel[1,2,3], S. Brådland[3], G. Haugeberg[3,4]. [1]*Østfold Hospital Trust, Department of Cardiology, Sarpsborg, Norway*; [2]*University of Oslo, Department of Clinical Medicine, Oslo, Norway*; [3]*Hospital of Southern Norway, Department of Rheumatology, Kristiansand, Norway*; [4]*Norwegian University of Science and Technology, Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, Trondheim, Norway*

Background: Pericarditis is a common disease with significant morbidity (1). Idiopathic pericarditis, where an underlying cause cannot be identified, makes up for 80% of cases in the Western World (1). Up to 30% of these patients experience recurrence despite optimal treatment (2). Idiopathic recurrent pericarditis (IRP) is thought to represent an auto-inflammatory process rather than a reinfection (3). 2015 European Society of Cardiology (ESC) guidelines have outlined treatment of acute episodes and first recurrence with nonsteroidal anti-inflammatory drugs (NSAID), acetyl salicylic acid (ASS) and Colchicine as first line and Glucocorticoids (GC) as second line treatment (3). However GC treatment increases the risk of relapse, dependence and toxicity (2). Interleukin-1 (IL-1) inhibitors have been proposed as possible treatments in IRP (3, 4).
Objectives: The aim of this case study is to outline our first experiences treating IRP with the IL-1 inhibitor anakinra in our Rheumatologic clinic.
Methods: All patients referred to our department in 2018/2019 with pericarditis were physically seen in our outpatient clinic. All patients were screened for malignancy, infection or rheumatologic disease as possible cause by clinical measures. Following ESC guideline, patients who suffered either the third recurrence under optimal treatment or significant side effects or dependency from GC were considered for anakinra treatment. Daily injection of anakinra (100mg) were given continuously over at least three months with gradual tapering over at least three months afterwards. Physical emergency department contacts, days hospitalized, colchicine- and GC use, the year prior to Anakinra treatment was recorded retrospectively. During follow up the same data was prospectively recorded.
Results: Over the course of two years 20 patients were referred to our clinic. All fulfilled ESC diagnostic criteria for pericarditis at index episode. In none of the patients could a rheumatologic, infectious or malignant cause be identified. 16 patients could be treated according to 2015 ESC guidelines with first or second line agents. Four patients were aligned to anakinra-treatment. Prior to referral, duration of symptoms was 5 - 120 months (mean 61 months). Further relevant patient- characteristics are outlined in Table 1.
After initiation of anakinra patients were afterwards regularly followed up in scheduled visits every 3 months.

Table 1. Characteristics of the four patients aligned to anakinra prior to anakinra-initiation.

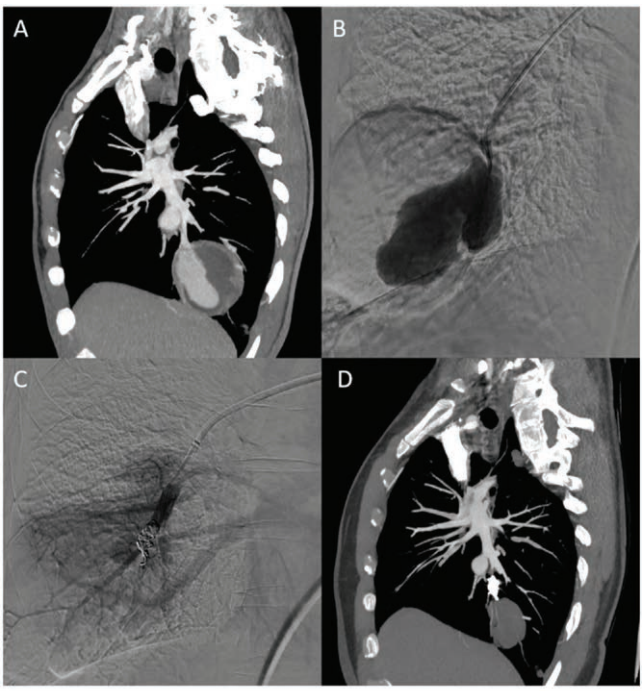
Patient	Number of recurrences	Number emergency hospital contacts related to IRP the year prior to nakinra	Days hospitalized related to IRP the year prior to anakinra	GC dose prior to anakinra	other
I	2	2	3	7.5 mg	steroidglaucoma
II	7	2	4	10 mg	
III	4	7	22	20 mg	
IV	7	3	12	20 mg	

Follow-up after start of anakinra was 6-15 months (mean 11.5 months). No patient was admitted to hospital or emergency department in that period. All four patients could taper and stop GC without recurrence. One patient experienced a mild relapse after discontinuing anakinra and was restarted on a low dose with complete remission. No patient had elevated CRP values at the end of follow-up and no patient experienced tamponade or clinical signs of constriction. No significant side effects were noted, no patient had to stop anakinra-treatment during follow up.
Conclusion: Implementation of anakinra treatment in cases of complicated IRP was both secure and successful in our rheumatologic outpatient department. In our small sample we could confirm findings from bigger trials regarding effect- and side effect rates of anakinra treating IRP.
REFERENCES:
[1] **Klein A et al. Cardiol Rev. 2020 Epub ahead of print. PMID: 32956167.**
[2] **Cremer P et al. J Am Coll Cardiol. 2016;68(21):2311-2328**
[3] **Adler Y et al** *European Heart Journal*, **2015;36(42):2873–2885**
[4] **Imazio M et al Eur J Prev Cardiol. 2020;27(9):956-964**
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4037

AB0786 HUGHES–STOVIN SYNDROME: A PECULIAR AUTOIMMUNE ORIGIN OF PULMONARY ANEURYSMS

P. Triggianese[1], A. D'antonio[1], B. Kroegler[1], A. Ascoli Marchetti[2], L. Belvivere[2], D. Morosetti[3], F. Sabuzi[3], A. Ippoliti[2], R. Argiro[3], R. Perricone[1]. [1]*Rheumatology, Allergology and Clinical Immunology, Department of "Medicina dei Sistemi", University of Rome Tor Vergata, Rome, Italy*; [2]*Vascular Surgery Unit, Biomedicine and Prevention Department, University of Rome Tor Vergata, Rome, Italy*; [3]*Diagnostic Imaging and Interventional Radiology, University Hospital of Rome Tor Vergata, Rome, Italy*

Background: Hughes-Stovin Syndrome (HSS) is a rare potentially fatal vasculitis supposedly belonging to the spectrum of Behçet disease without ocular involvement. HSS tends to play by a temporal pattern, starting with thrombosis and followed by formation of pulmonary aneurysms. Since its mortality can reach 25% of cases, the early recognition and the appropriate therapy represent the major challenges.
Objectives: In this report, we aimed at describing a rare case of HSS successfully treated in accordance with a prompt combined management with endovascular approach and immunosuppressive treatments.
Methods: We described a Caucasian 33-year-old man presented to the Emergency Room of our Hospital with hemoptysis associated with dyspnea and chest pain, without fever and hypotension, with a 2-year history of painful genital and oral ulcers. Blood test revealed anemia, elevated white cell count with increased C-reactive protein (77 mg/L) and D-dimer (2740 ng/mL). Doppler ultrasonography of legs showed thrombosis of the left femoral vein, while CT-angiography reported multiple aneurysms of the pulmonary arteries. An early and extensive work-up for infections and autoimmunity did not document relevant abnormalities. An appropriate genetic assessment revealed the HLA-B51 positivity. The patient immediately underwent endovascular embolization with coils and plugs of the largest pulmonary aneurysm, and inferior vena cava filter placement. Then, he started methylprednisolone (1 mg/kg/day) IV for three days in association with LMWH (6000 IU/day). Prednisone (1 mg/kg/day) in combination with cyclophosphamide (100 mg daily) were started orally, with tapering of steroids within a month. At the tight follow up (1 month and 3 months later), no genital and oral ulcers nor vascular thrombosis occurred, and acute phase reactants were in normal range. The 3-month-CT angiography showed a complete resolution of the aneurysms and no new changes.
Results: The peculiar diagnosis of HLAB51 positive HSS with multiple pulmonary aneurysms was made. The appropriate imaging followed by a prompt endovascular embolization of aneurysms with LMWH treatment were successfully performed. Interestingly, the oral combination therapy with corticosteroid and cyclophosphamide showed a rapid efficacy with a relevant safety profile. At the tight follow up, the young man improved significantly with clinical signs and pulmonary changes (Figure 1 next page).
Conclusion: This case is of interest because of the early recognition of such a rare disease that allowed an adequate combined radiological, vascular, and rheumatologic approach. In our case, LMWH resulted useful in preventing the pulmonary embolism, despite the use of anticoagulants is still debated in HSS. Moreover, the endovascular embolization let a less invasive approach to surgery without the need for multiple surgical procedures. For the first time, we documented that oral cyclophosphamide showed an early efficacy as a first line therapy of a HLA-B51 HSS.
REFERENCES:
[1] Keskin M, Polat G, Ayrancı A, et al. Insidious Hughes Stovin Syndrome: Journey From Pulmonary Embolism to Pulmonary Arterial Aneurysm. Turk Thorac J. 2020;21:350-353.
[2] Valdés-Corona LF, Kimura-Hayama E, Méndez-Cano VH, et al. Hughes-Stovin syndrome: an uncommon cause of pulmonary aneurysms. Rheumatology (Oxford). 2020;59:2183-2184.



A. A large, partly-thrombosed aneurysm of the right pulmonary artery is shown, as well as a smaller aneurysm. B-C. Right pulmonary artery aneurysm in the lower lobe, before and after endovascukar embolization with coils and plug. D. Three-months CT scan after embolization.

Figure 1.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4097

Diagnostics and imaging procedures

AB0787

RECEIVER OPERATING CHARACTERISTIC ANALYSIS OF JOINT INFLAMMATION IN RELATION TO DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS ASSESSED USING A NOVEL COMBINED THERMAL AND ULTRASOUND IMAGING

Y. K. Tan[1], C. Hong[1], H. LI[2], J. C. Allen Jr[3], J. Thumboo[1]. [1]*Singapore General Hospital, Department of Rheumatology and Immunology, Singapore, Singapore*; [2]*Singapore General Hospital, Health Services Research Unit, Singapore, Singapore*; [3]*Duke-NUS Medical School, Centre for Quantitative Medicine, Singapore, Singapore*

Background: A novel combined thermal and ultrasound (CTUS) imaging approach in rheumatoid arthritis (RA) was recently shown to be superior to either imaging modality alone in terms of correlation with the 28-joint disease activity score (DAS28).
Objectives: To determine the performance of CTUS imaging in identifying RA patients with at least moderate disease activity (DAS28 > 3.2).
Methods: Bilateral hand (22 joints) thermal and ultrasound (US) imaging was performed. Thermal imaging provides the surface temperature readings at the joints with MAX, AVG and MIN derived per patient by summing the temperature differences with a control temperature, for the respective maximum (Tmax), average (Tavg) and minimum (Tmin) temperatures at each joint. US imaging assesses joint inflammation by summing up the power Doppler (PD) and grey-scale (GS) joint inflammation scores (graded 0-3 at each joint recess) at each joint to obtain the respective total PD and total GS scores per patient. CTUS imaging utilizes data from both thermal and US imaging to derive the MAX (PD), AVG (PD) and MIN (PD) by multiplying MAX, AVG and MIN by a factor of 2 when a patient's Total PD > median score, which otherwise remained the same as the MAX, AVG and MIN. The results of the imaging parameters were compared between patients with DAS28 ≤ 3.2 and those with DAS28 > 3.2. Sensitivity (Sn), specificity (Sp) and receiver operating characteristic (ROC) curve analysis was performed to determine if the use of CTUS imaging can help identify patients with DAS28 > 3.2.
Results: In this cross-sectional study, 814 joints from 37 RA patients (75.7% female; 75.7% Chinese; baseline mean disease duration, 30.9 months; baseline mean DAS28, 4.43) were imaged. The mean (SD) values for the CTUS—but not single modality—imaging parameters (Table 1) were all significantly greater among patients with DAS28 > 3.2 versus those with DAS28 ≤ 3.2 (P-values were all <0.01). Based on cut-off levels of (a) MAX (PD) ≥ 94.5, (b) MIN (PD) ≥ 42.3 and (c) AVG (PD) ≥ 64.6 in identifying patients with DAS28 > 3.2, the respective area under the ROC curves (AUCs) (95%CIs) were (a) 0.731 (0.541, 0.921) with Sn = 58.1%; Sp = 100.0%; negative predictive value (NPV) = 31.6%; positive predictive value (PPV) = 100.0%; accuracy = 64.9%, (b) 0.758 (0.591, 0.925) with Sn = 61.3%; Sp = 100.0%; NPV = 33.3%; PPV = 100.0%; accuracy = 67.6% and (c) 0.763 (0.596, 0.931) with Sn = 61.3%; Sp = 100.0%; NPV = 33.3%; PPV = 100.0%; accuracy = 67.6%.
Conclusion: The severity of joint inflammation as detected by CTUS—but not single modality—imaging parameters were significantly greater among patients with DAS28 > 3.2 versus those with DAS28 ≤ 3.2. For the first time ever, by applying ROC analysis, this has helped to determine cut-off MAX (PD), MIN (PD) and AVG (PD) levels for identifying patients with DAS28 > 3.2; the usefulness of these cut-off levels will require further validation in independent RA cohorts.

Table 1. Comparison of imaging parameters between patient groups.

Imaging Parameter	DAS28			
	Mean (95% CI)		Difference (95% CI)	P-value
	DAS28 ≤ 3.2	DAS28 > 3.2		
MAX (PD)	75.25 (58.8, 91.7)	119.5 (101.12, 137.87)	-44.25 (-70.49, -18.01)	**0.0022****
MIN (PD)	33.72 (25.82, 41.61)	57.51 (47.63, 67.39)	-23.79 (-37.13, -10.45)	**0.0012****
AVG (PD)	50.72 (39.45, 61.98)	85.39 (71.89, 98.88)	-34.67 (-53.27, -16.07)	**0.0008*****
MAX	67.38 (50.75, 84.02)	82.23 (74.71, 89.75)	-14.85 (-34.11, 4.42)	0.1268
MIN	30.27 (22.06, 38.47)	40.02 (35.02, 45.03)	-9.75 (-22.18, 2.66)	0.1198
AVG	45.45 (33.94, 56.96)	59.11 (52.99, 65.23)	-13.66 (-29.04, 1.72)	0.0801
Total PD	2.83 (-0.23, 5.9)	3.65 (2.71, 4.58)	-0.82 (-3.39, 1.77)	0.5269
Total GS	6.67 (1.31, 12.02)	6.58 (4.12, 9.04)	0.09 (-6.21, 6.38)	0.9780

Statistically significant: **P<0.01, ***P<0.001.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.514

AB0788

MARKER OF CARTILAGE TISSUE LESION IMMUNOPATHOGENESIS OF RHEUMATOID ARTHRITIS

O. Rusanova[1], A. Trofimenko[2], N. Emelyanov[2], O. Emelyanova[1]. [1]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», 1, Волгоград, Russian Federation*; [2]*Federal State Budgetary Educational Institution of Higher Education «Volgoorad State Medical University» of the Ministry of Healthcare of the Russian Federation, 2, Волгоград, Russian Federation*

Background: Collagen type 2 is the basic protein of cartilaginous tissue composing over 80% of its mass. Finding excessive antibodies to collagen type 2 and immune complexes is a diagnostic and prognostic criterion of immune lesion of articular cartilage.
Objectives: To study production of antibodies to collagen type 2 in patients with rheumatoid arthritis using immobilized magnetically controlled forms.
Methods: The antigen was represented by commercial formulation of collagen type 2 produced by Serva (Sweden). Antibodies to collagen type 2 were determined in the patients' blood serum by way of a technique of immunoenzyme assay (ELISA test) using immobilized magnetic sorbents. Magnetic sorbents were polyacrylamide granules from 10 to 100 micron in size containing magnetic material and collagen type 2. We studied 30 apparently healthy donor individuals and 92 patients with a confirmed diagnosis of rheumatoid arthritis.
Results: A study of sera from rheumatoid arthritis patients revealed antibodies to collagen type 2 in 63 patients (68.48%). The correlation coefficient between anti-collagen type 2 antibodies, and IgA / IgM amounted to 0.28 and 0.36, correspondingly. At stage 1 and 2 of disease activity the level of antibodies was higher than in donors (p<0.001). The highest level of antibodies to collagen type 2 was seen in patients with stage 3 of disease activity (0.55±0.02). The amount of antibodies to collagen type 2 in patients with visceral manifestations of rheumatoid arthritis was no different from that in patients without any additional organ involvement, which is hardly surprising since collagen type 2 is mostly localized in articular cartilage and is practically absent from the connective tissue of other organs and systems.
Conclusion: Thus the presence of antibodies to collagen type 2 correlates with the disease activity and is an important marker of articular cartilage lesion in patients with rheumatoid arthritis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.828

AB0789

APPLICATIONS OF LOW-FIELD MAGNETIC RESONANCE IMAGING IN A RHEUMATOLOGY DEPARTMENT

I. M. Fernández-Maeztu Palacín[1], D. Ruiz-Montesinos[1], P. Muñoz Reinoso[1], G. Jurado Quijano[1], J. J. Pérez Venegas[1], L. Fernández de la Fuente Bursón[1]. [1]*Hospital Universitario Virgen Macarena, Rheumatology, Sevilla, Spain*

Background: Low-field MRI (LF-MRI) is a useful Imaging technique for the diagnosis and in the follow-up of high-impact rheumatologic pathology[1]. However, the use of the Low-field MRI is not widespread due to the high cost and the use of other techniques such as Musculoskeletal sonography[2]. The Rheumatology Unit of the HUVM owns a Musculoskeletal Imaging Unit (ECO /MRI) and a standardized protocol for LF-MRI[3], which is performed by a rheumatologist applied in a routine clinical practice. We describe the patterns of use of LF-MRI by general rheumatologists in their routine clinical practice.

Objectives: Perform an analysis of the use of LF-MRI in a Rheumatology department to the assessment of joint inflammatory activity. Correlate the results of the analyses in patients without diagnosis or patients with unclear diagnosis.

Methods: Retrospective analysis using the medical records of the patients referred to the Musculoskeletal Imaging Unit from January to June 2018. The main variables collected were reason for referral as well as previous and final diagnosis after LR-MRI. An evaluation on the usefulness of MRI is made twelve months later to establish the diagnosis.

Results: The global population studied of 114 patients were referred to for LF-MRI. 81 females (71%). The 80% of the patients with previous diagnostic 40% Rheumatoid Arthritis (RA), 24% Psoriatic Arthritis (PAs), 16% other rheumatic diseases, and the remaining 20% with an unclear diagnosis. The most frequent reasons for referral were: 1) A total of patients (female and male) was referred to assessment of inflammatory activity prior to the change of treatment and 2) assessment of subclinical activity in patients with optimized treatment. A total of 23 patients (16 female; 7 male), were referred for diagnostic evaluation or differential diagnosis: 7 arthralgias, 6 suspected psoriatic arthritis, 6 with undiagnosed joint inflammation, 2 for differential diagnosis, 1 suspected of juvenile idiopathic arthritis (JIA), and 1 tendinitis. (Table 1)

Table 1. Undiagnosed patients. Post-imaging diagnosis.

	TENO SYNO-VITIS	NO DIAG	AR	MONO ART-HRITIS	OA	CARPAL TUNNEL	RULE OUT PAs	GOUT	SpA	PLAN-TAR FASCII-TIS	JIA	PAs	OS TRI-GO-NUM
ARTHRALGIAS	1	1	1	0	0	1	0	2	0	1	0	0	0
SWOLLEN JOINT WITHOUT DIAGNOSIS	0	1	1	1	2	0	0	0	0	0	0	0	1
DIFFERENTIAL DIAGNOSIS	0	0	1	0	1	0	0	0	0	0	0	0	0
SUSPECTED PAs	0	2	1	0	0	0	1	0	1	0	0	1	0
SUSPECTED JIA	0	0	0	0	0	0	0	0	0	0	1	0	0
TENDINITIS WITHOUT DIAGNOSIS	1	0	0	0	0	0	0	0	0	0	0	0	0
Total	**2**	**4**	**4**	**1**	**3**	**1**	**1**	**2**	**1**	**1**	**1**	**1**	**1**

Conclusion: The results of our study shown that the addition of the LF-MRI into clinical practice and performed by a rheumatologist is a useful tool in the diagnosis and evaluation of the degree of disease activity in patients with joint inflammatory pathology. The main test-indication of these techniques is to assess the degree of activity of the disease. In a 20% of the cases, the LF-MRI was requested for diagnostic evaluation in patients without a clear diagnosis. The long-term follow-up studies that correlate symptoms with structural damage are necessary to define remission more accurately and evaluate the efficiency of different treatment options.

REFERENCES:

[1] Hunt L, Eugénio G, Grainger AJ. Magnetic resonance imaging in individuals at risk of rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2017 Feb;31(1):80-9.

[2] Mandl P, Ciechomska A, Terslev L, Baraliakos X, Conaghan PG, D'Agostino MA, et al. Implementation and role of modern musculoskeletal imaging in rheumatological practice in member countries of EULAR. RMD Open. 2019 Jun 25;5(2):e000950.

[3] Gorbachova T, Melenevsky Y, Cohen M, Cerniglia BW. Osteochondral Lesions of the Knee: Differentiating the Most Common Entities at MRI. Radiographics. 2018 Sep-Oct;38(5):1478-95.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1444

AB0790

ULTRASOUND-GUIDED VERSUS ANATOMICAL LANDMARK INJECTION OF THE SHOULDER JOINT; A RETROSPECTIVE STUDY

A. Radwan[1], A. Elsaman[1]. [1]*Sohag University Hospital, Rheumatology and Rehabilitation, Sohag, Egypt*

Background: Ultrasound is a widely used tool for diagnostic and interventional purposes for a myriad of musculoskeletal conditions. The question about the value of ultrasound-guided injection over blind injection is debatable [1, 2].

Objectives: To test the value of ultrasound-guided injection versus blind subacromial-subdeltoid bursitis, subcoracoid bursitis, long head of biceps synovial sheath, and intra-articular shoulder injection.

Methods: We included 168 participants (66 subacromial-subdeltoid bursitis, 52 subcoracoid, 10 with long head of biceps tenosynovitis 38 had adhesive capsulitis and performed intra-articular shoulder injection) half of them were injected by blind technique and the other half were injected under ultrasound guidance. All of them were diagnosed by ultrasound. All were injected with methylprednisolone acetate 40 mg (Solumedrol, Pfizer) + lidocaine hydrochloride 1% (Xylocaine Astra Zeneca), 2 ml. SPADI score and range of motion were performed before injection and immediately after the injection, after 2 weeks, and after 4 weeks. Further, complications were recorded immediately after the injection, after 2 weeks, and after 4 weeks.

Results: The mean age of the study group was around 35.5 years, with no significant difference between the two groups, with slightly male predominance (60.7%). The mean SPADI score was similar between the groups before injection, but the improvement was higher among ultrasound-guided group compared to anatomical landmark-guided group, as showed by the significant difference between the two groups regarding SPADI scores at 2 and 4 weeks post-injection. Regarding the improvement of the range of motion, the ultrasound-guided group showed significantly better improvement compared to the anatomical landmark-guided one all over the 4-week course of follow up. The complication rate was slightly higher among the landmark-guided group, but with non-significant difference (Table 1). The difference between the two groups was highest among adhesive capsulitis cases with intra-articular injection.

Conclusion: Ultrasound-guided injections showed better outcomes for all the 4 injections, especially for intra-articular injection, in addition, it showed a significantly less complications than blind injection.

REFERENCES:

[1] Elsaman A, Hamed A, Radwan A. Ultrasound-guided epidural block in axial spondyloarthritis patients with limited spine mobility: a randomized controlled trial. The Korean Journal of Pain 2021; **34:** 114.

[2] Elsaman AM, Mostafa ES, Radwan AR. Ankle Evaluation in Active Rheumatoid Arthritis by Ultrasound: A Cross-Sectional Study. Ultrasound in medicine & biology 2017; **43:** 2806-13.

Table 1. Comparison between the two groups

		Ultrasound – guided (n=84)	Anatomic landmark – guided (n=84)	P value
Age		35.4±9.5	36.0±9.5	0.643
Sex	Male	49(58.3%)	53(63.1%)	0.527
	Female	35(41.7%)	31(36.9%)	
Site	Subacromial-subdeltoid bursitis	33(39.3%)	33(39.3%)	0.998
	Subcoracoid	26(31%)	27(32.1%)	
	Long head of biceps tenosynovitis	5(6%)	5(6%)	
	Adhesive capsulitis	20(23.8%)	19(22.6%)	
SPADI score	Pre-injection	55.8±9.4	54.7±10.1	0.466
	Immediately post-injection	48.6±8.2	51.2±8.9	0.051
	2 weeks post-injection	44.9±10.1	49.6±9.3	0.002
	4 weeks post-injection	42.4±9.7	47.6±7.8	0.001
Range of motion improvement (percent)	Immediately post-injection	33.6±9.7%	29.4±11.2%	0.010
	2 weeks post-injection	37.2±8.5%	32.7±9.9%	0.002
	4 weeks post-injection	40.1±7.3%	33.6±8.3%	<0.001
Complications	Pain	12(14.3%)	19(22.6%)	0.164
	Bleeding	3(3.6%)	8(9.5%)	0.119
	Vasovagal attack	4(4.8%)	3(3.6%)	0.699

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1908

AB0791 THE DIAGNOSIS VALUE OF SYNOVIAL FLUID LYMPHOCYTE IN GOUT PATIENTS

Q. Huang[1], Y. Huang[1], Y. Liu[1], Z. Zhong[1], W. Deng[1], T. W. LI[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*

Background: Synovial fluid cell counts have long been recognised to have utility in the diagnosis and management of arthritis. Few studies have explained the diagnosis value of synovial fluid cell counts in gout patients.
Objectives: The study aims to investigate the diagnosis value of synovial fluid cell counts in gout patients.
Methods: A total of 185 gout, 64 rheumatoid arthritis(RA), 26 axial spondyloarthritis(axSpA) and 24 osteoarthritis(OA) patients were included into the study. According to serum uric acid(sUA) level on attack, gout patients were divided into normal sUA gout patients and high sUA gout patients. The laboratory data was recorded and ROC curve was performed.
Results: The synovial fluid WBC, PBMC, monocyte, PMN and neutrophil in gout patients were higher than OA patients (P<0.05). The synovial fluid PBMC and lymphocyte in gout patients were lower than RA and axSpA patients (P<0.05). Compared with RA, axSpA and OA patients, ROC curve showed that the AUC value of lymphocyte and sUA for gout were 0.728 and 0.881, which were higher than other variables. The optimal cut off value of lymphocyte for gout was 1.362, with sensitivity of 83.3% and specificity of 60.6%. The AUC value of lymphocyte and sUA for normal sUA gout patients were 0.694 and 0.643, which were higher than other variables. The optimal cut off value of lymphocyte for normal sUA gout patients was 1.362, with sensitivity of 81.6% and specificity of 60.6%.
Conclusion: Synovial fluid cell counts of gout patients were different from RA, axSpA, and OA patients. Synovial fluid lymphocyte had a higher diagnosis value for gout.
REFERENCES:

[1] Scanu A, Oliviero F, Ramonda R, et al. Cytokine levels in human synovial fluid during the different stages of acute gout: role of transforming growth factor β1 in the resolution phase. Ann Rheum Dis. 2012, 71(4): 621-4.

Table 1. Basic characteristics of the participants

	Gout(n=185)	RA(n=64)	axSpA (n=26)	OA(n=24)	*P* value
Age (years)	48.58±15.58	56.19±12.39*	32.96±15.19*#	69.63±12.43*#&	**<0.001**
Gender (male/female)	176/9	11/53	21/5	8/16	**<0.001**
WBC(×10^9/L)	18.58±22.94	22.24±20.87	15.52±15.03	3.03±5.59*#&	**0.002**
PBMC(×10^9/L)	1.85±1.99	3.68±2.43*	3.85±3.34*	0.74±1.01*#&	**<0.001**
Monocyte(×10^9/L)	1.02±1.59	1.24±1.11	1.34±1.52	0.29±0.37*#&	**0.030**
PMN(×10^9/L)	16.77±21.51	18.57±19.32	15.75±24.17	2.30±5.00*#&	**0.008**
Lymphocyte (×10^9/L)	0.80±0.83	2.43±1.76*	2.50±2.04*	0.45±0.80#&	**<0.001**
Eosinophil (×10^9/L)	1.32±3.75	0.56±0.93	0.11±0.17	0.49±1.85	**0.098**
Neutrophil (×10^9/L)	16.42±21.16	18.82±20.89	11.13±14.23	2.23±4.87*#	**0.003**
UA(μM)	497.92±132.24	299.31±97.91*	351.81±118.93*	333.38±75.19*	**<0.001**
ESR(mm/h)	61.02±37.68	82.42±32.87*	68.12±36.25	42.34±35.91*#&	**<0.001**
CRP(mg/L)	56.52±45.64	44.01±35.27*	65.49±39.85#	22.11±40.65*#&	**<0.001**

*P<0.05 vs gout group, #P<0.05 vs RA group, &P<0.05 vs axSpA group

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1992

AB0792 IMAGING METHODS IN PREDICTING A RADIOLOGIC PROGRESSION IN RA

O. Alekseeva[1], D. Kudinsky2, A. Smirnov2, A. Volkov2, E. Nasonov[3]. [1]*V.A. Nasonova Research Institute of Rheumatology, Diagnostic Department, Moscow, Russian Federation*; [1]*V.A. Nasonova Research Institute of Rheumatology, Diagnostic Department, Moscow, Russian Federation*; [3]*V.A. Nasonova Research Institute of Rheumatology, Chief Researcher, Moscow, Russian Federation*

Background: Rheumatoid arthritis (RA) is the chronic inflammatory joint disease, and it is responsible for structural damage. Several studies have shown that ACPA + patients were more likely than ACPA– patients to develop erosive changes on radiography. Ultrasound (US) is a well-established method of diagnosis and follow-up in RA, which at the moment may have a prognostic value in assessing the outcomes of the disease.
Objectives: to identify the prognostic role of US in radiologic progression in RA patients.
Methods: 85 RA pts, mean age 53,0 [44,0; 61,0] yrs, mean disease duration 8 [4; 24] months were treated with MTX and biologics according to Treat-To-Target concept. Among them 56 patients with early RA, mean age 53,5 [45,5; 61,0], disease duration 5 [3; 7,5] months. Hands and feet ultrasound (US) with gray scale (GS), power Doppler (PD) and destructive changes (erosion), according to the criteria of OMERACT, were analyzed before initiation of treatment and in 3, 6, 9 and 12 months after. A binary scoring system (presence/absence of erosions) of the joints examined was used. Radiographs were obtained at baseline and 4 years, radiographic changes were assessed using Sharp/van der Heijde modified scoring method. Radiographic progression was documented based on Sharp/Van der Heijde modified score changes during the follow up.
Results: 71 ACPA+ (84%) and 14 ACPA– (16%) patients presented among the 85 patients with RA, among them 49 ACPA+ (87%) and 7 ACPA– (13%) with early RA. RA progression by 4 years the follow-up period was identified in 39% of pts.
During the follow-up period 33 of 85 patients had radiographic progression: the count of erosion increased from 0 [0; 3] to 2 [0; 6]. At the same time, on the background of therapy, a decrease in ultrasound signs of inflammation was determined according to the GS and PD: from 6 [4; 9] to 1 [0; 2] p = 0.000 and from 2 [1; 6] to 0 [0; 1] p = 0.000, respectively, and increase in the number of joints with erosions (from 1 [0; 2] to 2 [0; 4], p = 0.000).
In the group with early RA, the changes were similar.
In ACPA+ general group the count of erosion at 4 years was significantly higher than in ACPA– general group (3 [0; 7] and 0 [0; 1], respectively, p=0.0026).
In ACPA+ early RA group the number of joints with erosions by US at baseline was significantly higher than in ACPA– early RA group (1 [0; 1] and 0 [0; 0], respectively, p=0.017). In ACPA+ early RA group the count of erosion at 4 years was significantly higher than in ACPA– early RA group (2 [0; 4] and 0 [0; 0], respectively, p=0.009) (Table 1)

Table 1. Characteristic of the groups (general group)

at baseline	**ACPA+(71 pts)**	**ACPA- (14 pts)**	**p**
The number of joints with erosions by US	1 [0; 2]	0 [0; 1]	0,36
The number of erosions by X-ray	1 [0; 4]	0 [0; 1]	0,06
after 4 years follow up			
The number of joints with erosions by US	2 [0; 4]	1 [0; 2]	0,16
The number of erosions by X-ray	3 [0; 7]	0 [0; 1]	**0,0026**
Characteristic of the groups (early RA group)			
at baseline	**ACPA+(49 pts)**	**ACPA- (7 pts)**	**p**
The number of joints with erosions by US	1 [0; 1]	0 [0; 0]	**0,017**
The number of erosions by X-ray	0 [0; 2]	0 [0; 0]	0,11
after 4 years follow up			
The number of joints with erosions by US	2 [0; 3]	1 [0; 1]	0,22
The number of erosions by X-ray	2 [0; 4]	0 [0; 0]	**0,009**

Conclusion: Thus, in early RA is advisable to perform an US of the hands and feet to select a group of patients with potentially rapid radiological progression. US evaluation of patients with non-early stage RA is not very important for assessing the prognosis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2431

AB0793 CONTRIBUTION OF INVESTIGATIONS FOR THE QUEST OF PRIMITIVE CANCER IN FRONT OF BONE METASTASIS

S. Boussaid[1], S. Rekik[1], S. Mechergui[1], S. Jemmali[1], E. Cheour[1], H. Sahli[1], M. Elleuch[1]. [1]*Rabta Hospital, Rheumatology Department, Tunis, Tunisia*

Background: Bone metastases (OM) or secondary cancers bones are bony locations of tumor cells, away from a primary malignant tumor. The Bone metastases are the most common metastases. They can be revealing in 20 to 30% cases or complicate the course of a known cancer. The bone metastases are a pejorative prognostic factor.
Objectives: The aim of this study was to identify the Contribution of diagnostic methods for the quest of primitive cancer in presence of bone metastasis.
Methods: We conduct a retrospective study of 35 files of patients who were hospitalized in the rheumatology department. All patients underwent a questionnaire and a clinical examination. Additional radiological assessment, bone biopsies, biopsies of other sites, bone scintigraphy and tumor markers were carried out on a case-by-case basis.
Results: Thirty-five cases (25 men and 10 women) were analysed. The average age was 61 years [45-85]. Seven patients had a known history of neoplasia. One or more bone biopsies were performed in 8 cases. The vertebrae were the most biopsied bone site (6 cases). The bone biopsies were in favour of carcinoma (3 cases), adenocarcinoma (2 cases), squamous cell carcinoma (1 case) and inconclusive (2 cases). Non bony biopsies (2 pulmonary, 2 prostatic, 1 mammary) concluded to an adenocarcinoma (3 cases) and a carcinoma (2 cases). Bone scintigraphy was carried out in 7 cases and showed in all cases diffuse or localized hyperfixation. The localized value of tumor markers appeared relatively low except for Prostate Specific Antigen (PSA). Other metastatic localisations were identified: hepatic (6 cases) and pulmonary (1 case). The primary cancer identified was pulmonary for 11 patients, prostatic for 7, gynaecological for 4 and digestive for 3. One patient had Otorhinolaryngological cancer and another had bone cancer. Bone biopsy allowed the diagnosis in 6 cases (17%). The primary cancer was discovered by a biopsy of other non-bone sites in 5 cases (14%). Neoplastic antecedents and clinical context were considered sufficient in 16 cases (45%). Primary cancer remained undetermined in 8 cases (22%).
Conclusion: Bone biopsy, as well as non-bone biopsy, remains an essential tool in the etiological diagnosis of bone metastases. They are very contributive in the same proportions. PSA is a major diagnostic asset in the search for primary cancer.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2620

AB0794 CONTRIBUTION OF LABIAL SALIVARY GLAND BIOPSY: EXPERIENCE OF THE DEPARTMENT OF RHEUMATOLOGY OF THE UNIVERSITY HOSPITAL OF IBN ROCHD (ABOUT 57 CASES)

Z. El Ouali[1], A. Elkebir[2], K. Nassar[1], M. Karkouri[2], S. Janani[1]. [1]*University Hospital of Ibn Rochd, Department of Rheumatology, Casablanca, Morocco*; [2]*University Hospital of Ibn Rochd, Department of Anatomical Pathology, Casablanca, Morocco*

Background: Labial salivary gland biopsy (LSGB) is a histological examination indicated for the diagnostic workup of systemic diseases such as Sjogren's syndrome, amyloidosis, or sarcoidosis.
Objectives: To study the contribution of LSGB to the diagnosis of Sjogren's syndrome, amyloidosis, and sarcoidosis.
Methods: We conducted a retrospective study of LSGB histopathological reports and clinical data of patient medical records collected in the Department of Rheumatology of the University Hospital of Ibn Rochd, Casablanca, between January 2019 and June 2020. Histology assessed Chisholm and Masson's sialadenitis score, looked for amyloidosis, and sarcoidotic granulomas.
Results: A total of 57 LSGBs were performed, of which 2 were excluded from our study because of lack of clinical data. The sex-ratio M/F was 0.1, and the median age was 53 (22 – 85). The indications were subjective eyes and mouth dryness in 40% of cases, the search for sarcoidosis and amyloidosis in 23.6% of cases, the assessment of a dryness syndrome in the context of chronic inflammatory rheumatism in 18.2% of cases, isolated dryness of the mouth in 14.5% of cases, and the search for amyloidosis in the context of a known primary Sjögren syndrome in 3.6% of cases. The stages of Chisholm and Masson for sialadenitis found were: stage I at 56.6%, stage II at 24.5%, stage III at 11.3%, and stage IV at 7.5%. Among the LSGBs performed for dryness syndrome, stages III and IV were found in 18.2% of cases among subjective eyes and mouth dryness, in 12.5% of cases among isolated mouth dryness, and in 20% of cases among chronic inflammatory rheumatisms. Three cases of AA amyloidosis (5.5%) were diagnosed. No sarcoidosis granulomas were found.
Conclusion: LSGB is a simple and frequent investigation. The Chisholm stage most often found in our series was stage I, followed by stages II, III, and IV respectively. This is consistent with the results of the study of Baeteman et al (1). In addition, amyloidosis was only found in our series in 5.5% of cases, also matching with the results of Baeteman et al. (4.2%). Their study showed that LSGB has a great diagnostic interest in these two pathologies, with a sensitivity of 52-75% and a specificity of 90-100% for Sjogren's syndrome, and a sensitivity of 48-80% and a specificity of 93-100% for amyloidosis (2). LSGB remains a simple investigation test, contributing to the diagnosis of Sjogren's syndrome, amyloidosis, and sarcoidosis.
REFERENCES:

[1] Baeteman C, Guyot L, Bouvenot J, Chossegros C, Cheynet F, Loudot C, et al. Faut-il encore effectuer des biopsies des glandes salivaires accessoires ? Revue de Stomatologie et de Chirurgie Maxillo-faciale. 2008 Jun;109(3):143–7.
[2] Scardina GA, Spanó G, Carini F, Spicola M, Valenza V, Messina P, et al. Diagnostic evaluation of serial sections of labial salivary gland biopsies in Sjögren's syndrome. Med Oral Patol Oral Cir Bucal. 1 déc 2007;12(8):E565-568.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2755

AB0795 DYNAMIC CHANGES IN QUANTITATIVE INDICES OF BODY COMPOSITION BY DUAL-ENERGY X-RAY ABSORPTIOMETRY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS ON DIFFERENT THERAPEUTIC REGIMENS

Y. Gorbunova[1], T. Popkova[1], T. Panafidina[1], N. Demin[2], E. Nasonov[3], A. Lila[3]. [1]*VA Nasonova Research Institute of Rheumatology, Department of Systemic Rheumatic Diseases, Moskva, Russian Federation*; [2]*VA Nasonova Research Institute of Rheumatology, Department of Osteoporosis, Moskva, Russian Federation*; [3]*VA Nasonova Research Institute of Rheumatology, Scientific Department, Moskva, Russian Federation*

Background: A redistribution of body fat (abdominal obesity) is quite common in RA patients. Such parameters as body mass index (BMI) and waist circumference do not distinguish or quantify fat and lean (muscle) mass. For that purpose, dual-energy X-ray absorptiometry (DXA) is usually used.
Objectives: to compare quantitative body composition in patients with early RA at baseline and after 24 weeks of therapy with different regimens.
Methods: The study included 37pts (31 women /6 men) with early RA (ACR/EULAR criteria, 2010), 57 [46.5, 62,0] years old, naïve to treatment with glucocorticoids and disease-modifying anti-rheumatics (DMARDs). Pts were seropositive for IgM RF (76%) and anti-CCP (92%), with highly active RA (DAS28 5,5 [5,1; 6,0]; SDAI 32,4 [22,4; 42], CDAI 29,0 [19,7; 39,5]) scores, and median disease duration of 6.0 [5,5;15.5] months. Methotrexate (MTX) 10 [10-15] mg/week subcutaneously was initiated in all included patients as first line therapy for 12 weeks. By this time point therapy was reviewed in 19 patients (51%) due to MTX inefficacy and adalimumab (ADA) at 40mg once every 2 weeks was added on top of MTX. DXA scan (HOLOGIC, USA) was used to measure body composition at baseline and after 6mths of treatment with the protocol assessing total body, body fat and lean muscle mass.
Results: Based on therapeutic regimens at week 24 all study subjects were divided into 2 groups: Group I (n=18) receiving MTX monotherapy, Group II (n=19) – the combination of MTX and ADA (Table 1). Group I patients had lower body weight, lean and fat mass vs patients from Group II (62 kg vs. 73.7 kg; 40.6 kg vs. 49.7 kg; 21.0 kg vs. 25.8 kg, respectively (p<0.05 in all cases) at baseline. 24 weeks of combination therapy eventuated in body weight gain (73.7 kg vs. 75.8 kg), accumulation of fat (25.8 kg vs. 28.1 kg) and unchanged lean tissue mass. In contrast, patients on MTX monotherapy managed to increase their lean mass (40.6 kg vs. 41.6 kg) without gaining in total fat mass.

Table 1.

Indices	I group (*n*=18), monotherapy MT			II group (*n*=19), combination therapy (MTX, ADA)		
	baseline	24 weeks	Δ,%	baseline	24 weeks	Δ,%
Body fat mass, kg	21,0 [17,2;26,2]**	23,4 [17,5;29,7]	+11	25,8 [18,4;35,0]	28,1 [21,4;37,9]*	+9
Lean mass, kg	40,6 [37,3;44,7]**	41,6 [38,2;46,4]***/*	+2,5	49,7 [39,0;56,1]	49,9 [41,0;57,6]	0,4
Total mass, kg	62,0 [57,7;77,6]**	64,1 [59,5;81,6]***	+3,4	73,7 [64,5;97,9]	75,8 [66,8;102,1]*	+2,8

*p<0,05 reliability of differences in parameters before treatment and after 6mth (Wilcoxon); **p<0.05 differences in baseline values in groups I and II (Mann-Whitney test);***p<0.05 difference in the indices between the groups by the 6mth of therapy; Δ,% difference in indices between the groups by the 6mth of therapy.

Conclusion: In general, RA patients on treatment tend to gain weight by week 24. Patients who failed on MTX monotherapy by week 24 and were switched to combination therapy had higher fat mass at baseline. Mediations used for RA treatment produce multidirectional effects on quantitative parameters of body composition: MTX monotherapy triggers some increase of lean mass, while combination of MTX and bDMARD results in weight gain and increase of total and fat mass. These data need to be confirmed in large-scale studies with longer follow-up period.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3115

AB0796 THE EVALUATION OF LUNG DIAGNOSTIC PROCEDURE AT THE ONSET OF INFLAMMATORY RHEUMATIC DISEASES WITH INTERSTITIAL LUNG DISEASE

T. Hoffmann[1], P. Oelzner[1], F. Marcus[2], M. Förster[2], J. Böttcher[3], G. Wolf[1], A. Pfeil[1]. [1]*Jena University Hospital – Friedrich Schiller University Jena, Department of Internal Medicine III, Jena, Germany*; [2]*Jena University Hospital – Friedrich Schiller University Jena, Department of Internal Medicine I, Jena, Germany*; [3]*Jena University Hospital – Friedrich Schiller University Jena, Institute of Diagnostic and Interventional Radiology, Jena, Germany*

Background: Interstitial lung disease (ILD) in inflammatory rheumatic diseases (IRD) is associated with increased mortality. Moreover, the lung is one of the most effected organs on IRD. Consequently, screening methods were required to the detect ILD in IRD.
Objectives: The objective of the following study is to evaluate the diagnostic value of lung function test, chest x-ray and HR-CT of the lung in the detection of ILD at the onset of IRD.
Methods: The study is designed as a case-control study and includes 126 patients with a newly diagnosed IRD. It was matched by gender, age and the performance of lung function test and chest x-ray. The sensitivity and specificity were verified by crosstabs and receiver operating characteristic (ROC) curve analysis. The study cohort was divided in two groups (ILD group: n = 63 and control group: n = 63). If possible, all patients received a lung function test and optional a chest x-ray. Patients with pathological findings in the screening tests (chest x-ray or reduced diffusing capacity for carbon monoxide (DLCO) < 80 %) maintained a high-resolution computer tomography (HR-CT) of the lung. Additionally, an immunological bronchioalveolar lavage was performed in the ILD group as gold standard for the detection of ILD.
Results: The DLCO (< 80 %) revealed a sensitivity of 83.6 % and specificity of 45.8 % for the detection of ILD. Other examined parameter of lung function test showed no sufficient sensitivity as screening test (FVC = Forced Vital Capacity, FEV1 = Forced Expiratory Volume in 1 second, TLC = Total Lung Capacity, TLCO = Transfer factor of the Lung for carbon monoxide). Also, a combination of different parameter did not increase the sensitivity. The sensitivity and specificity of chest x-ray for the verification of ILD was 64.2 % versus 73.6 %. The combination of DLCO (< 80 %) and chest x-ray showed a sensitivity with 95.2 % and specificity with 38.7 %. The highest sensitivity (95.2 %) and specificity (77.4 %) was observed for the combination of DLCO (< 80 %) and HR-CT of the lung.

Conclusion: The study highlighted that a reduced DLCO in lung function test is associated with a lung involvement in IRD. DLCO represented a potential screening parameter for lung manifestation in IRD. Especially patients with suspected vasculitis should receive an additional chest x-ray. Based on the high sensitivity of DLCO in combination with chest x-ray or HR-CT for the detection of ILD in IRD, all patients with a reduced DLCO (< 80%) should obtained an imaging of the lung.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3119

AB0797 THE ROLE OF ULTRASOUND CRITERIA IN ASSESSING PAIN SYNDROME IN THE KNEE JOINT IN PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

N. Aleksandrova[1], A. Aleksandrov[1,2]. [1]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», Department of Functional Research Method, Volgograd, Russian Federation*; [2]*Volgograd State Medical University, Department of Hospital Therapy, Volgograd, Russian Federation*

Background: Pain syndrome and pathological changes in the synovium detected by ultrasound can be early signs of various diseases of the joints [1].
Objectives: the use of ultrasound criteria for changes in the synovial membrane of the joint cavity to assess the severity of pain in patients with rheumatoid arthritis (RA) and osteoarthritis (OA).
Methods: The study included 36 patients with RA (32 women and 4 men aged 22 to 55 years old) and 38 patients with OA (30 women and 8 men aged 30 to 50 years old) with lesions of the knee joints. A visual analogue scale (VAS) was used to determine the severity of pain. The severity of pain in the knee when walking was at least 40 mm according to the VAS in all examined patients. Joint ultrasound examination was carried out according to the standard technique using a linear transducer with a frequency of 5–12 MHz on an Accuvix V10 ultrasound diagnostic system (Samsung Medison, South Korea). The evaluation of ultrasound changes in the upper inversion of a knee joint was carried out according to the following criteria: the severity of intra-articular effusion (1), synovial proliferation (2), local vascularization of the synovial membrane using power Doppler (3) (Table 1).

Table 1. Parameters of ultrasound criteria for assessing changes in the synovial membrane of the joint cavity

Normal indicators	1 - width of the suprapatellar turn is 6 mm
	2 - thickness of the synovial membrane is 3 mm (from the anterior approach)
	3 - lack of vascularization loci
Minimum changes	1 - delamination of the suprapatellar curl leaves from 7 to 9 mm
	2 - thickness of the synovial membrane 3.1–4.5 mm
	3 - appearance of single loci of vascularization (1-2 in the Doppler field)
Moderate changes	1 - delamination of the leaves of the suprapatellar twist 10-14 mm
	2 - thickness of the synovial membrane is 4.6–6.4 mm
	3 - appearance of moderate (> 5) vascularization loci
Severe changes	1 - delamination of suprapatellar folds of more than 15 mm
	2 - thickness of the synovial membrane is more than 6.5 mm
	3 - multiple foci of vascularization (> 5, merging in places)

Results: Correlations of various severity were found between pain indices according to VAS and the thickness of the synovial membrane of the knee joint ($r = 0.33$, $p = 0.019$) and the number of vascularization foci ($r_S = 0.29$, $p = 0.04$) in RA patients, as well as between pain according to VAS and the severity of intra-articular effusion ($r = 0.28$, $p < 0.002$) in patients with OA.
The patients were divided into three groups according to the severity of pain in the knee joint: group I - 41-59 mm (12 patients with OA and 9 patients with RA), group II - 60-79 mm (16 patients with OA and 12 patients with RA), group III - 80–100 mm on the VAS scale (10 patients with OA and 15 patients with RA). Group I was dominated by OA patients with minimal changes in intra-articular effusion and local vascularization of the synovial membrane, with moderate synovial proliferation (28.6% of the total number of patients in the group). In group II patients with OA with moderate severity of intra-articular effusion and local vascularization (21.4%) and patients with RA with moderate changes in the thickness of the synovium and local vascularization (25%) were equally common. Group III was dominated by RA patients with severe synovial proliferation and moderate local vascularization (28%), as well as patients with OA with moderate intra-articular effusion (20%).
Significant differences in the thickness of the synovium in patients with RA in the first and third groups were noted (H-test = 5.9, $p = 0.025$).
Conclusion: The additional use of ultrasound criteria for changes observed in the synovial membrane of the joint cavity in patients with RA and OA can help predict pain in the knee joint. The manifestation of pain syndrome in patients with OA is most associated with the severity of synovitis in the joint, and in patients with RA - with the severity of synovial proliferation.
REFERENCES:
[1] Sarmanova A et al. *Arthritis Res Ther*. 2017;19(1):281.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3224

AB0798 IS THERE A REPRODUCIBILITY OF THE HISTOGRAM AND GRAY SCALE IN ECOEXTRUCTURAL DAMAGES IN RHEUMATOTOLOGICAL DISEASES?

J. A. Mendonça[1], I. Siste de Almeida Aoki[1], C. C. Cavuto[2], V. A. Leandro-Merhi[3], J. L. B. D. Aquino[3]on behalf of Postgraduate Program in Health Sciences, Pontifical Catholic University of Campinas.. [1]*Pontifical Catholic University of Campinas, Rheumatology/Postgraduate Program in Health Sciences, Campinas, Brazil*; [2]*Pontifical Catholic University of Campinas, Rheumatology/ Scientific Initiation Program, Campinas, Brazil*; [3]*Pontifical Catholic University of Campinas, Postgraduate Program in Health Sciences, Campinas, Brazil*

Background: The gray scale (GS) in high resolution ultrasound is already well validated for use in rheumatological diseases, but the color map or the histogram, can be considered a new proposal, to better define and complement the echotextural damages detection[1].
Objectives: To calculate the lesions area measures reproducibility index in arthropathies, between 3 blind evaluators and correlate these measures using the GS and the histogram.
Methods: Observational and retrospective study approved by the ethics committee of the Pontifical Catholic University of Campinas, with the opinion number: 1.526.307. A total of 29 patients have been assessed (31% males and 69% females) on period 2014 to 2019 in Rheumatology service. A MyLab 50 -Esaote equipment was used with frequency transducer that ranged between 6.0 and 18.0 MHz, 10 different area measures were performed from each recorded images previously, by the GS and the histogram. Statistical analysis: Spearman's correlation coefficients, Lin's concordance coefficient (CCC) and the intraclass correlation coefficient (ICC) and their respective 95% confidence intervals, with the SPSS software package for Windows v. 17.0 (SPSS Inc., Chicago, IL, USA).
Results: Average age 43.5 ± 21.5 years of age; with disease duration that varied between ≤ 1 month (48.3%) and ≥36 months (24.1%); with the following diseases: juvenile idiopathic arthritis (17.24%); osteoarthritis (13.79%); psoriatic arthritis (13.79%); undifferentiated spondyloarthritis (3.44%); gout (20.68%); rheumatoid arthritis (27.58%) and reactive arthritis (3.44%). A total of 840 measures of exudative (27.58%), proliferative (27.58%) and snowstorm appearance (6.89%) synovitis were performed; femoral-condyle cartilage (3.44%); synovial cyst (3.44%); paratendinitis (6.89%); calcification (3.44%); nail enthesitis (3.44%); tenosynovitis (6.89%) and tophi (10.34%) (Figure 1). The concordance correlation coefficient showed values closer to 1; $p < 0.001$, the intraclass correlation coefficients with excellent reproducibility (ICC ≥ 0.75); $p < 0.001$, always in relation to the three evaluators (Table 1) and the Spearman correlation between the GS and the histogram ranged from rs = 0.665 to rs = 1,000; $p < 0.001$.
Conclusion: The histogram can be considered an image method to better identify echotextural damages.
REFERENCES:
[1] Mendonça J, Provenza J, Guissa V, et al AB1059 2D Histogram Ultrasound and 3D Ultrasound Correlation in Rheumatic Diseases Annals of the Rheumatic Diseases 2015; 74:1253-1254.

Table 1. Concordance Correlation Coefficient (CCC) and Intraclass Correlation Coefficient (ICC):

Evaluators	GS - CCC (IC 95%)	p-valor	Histogram (IC 95%)	p-valor
1 e 2	0,998 (0,994-0,999)	<0,001	0,999 (0,995-1,000)	<0,001
1 e 3	0,998 (0,995-0,999)	<0,001	0,999 (0,995-1,000)	<0,001
2 e 3	0,992 (0,980-0,997)	<0,01	0,996 (0,979-0,999)	<0,01
Standard by US 2D	**ICC**		**p-valor**	
GS	0,997(0,992-0,999)		<0,001	
Histogram	0,998(0,992-0,999)		<0,001	

Legends: Gray Scale (GS).

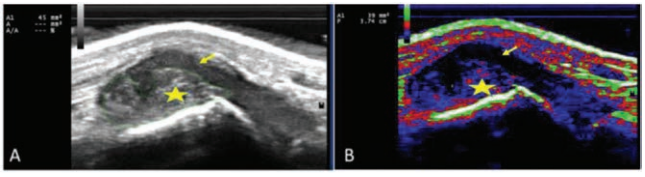


Figure 1. Patient with gout: A and B: Tophi area measures (star) in right metatarsos and efusion (arrow) by GS (45 mm^2) and histogram (39 mm2), respectively.

Disclosure of Interests: José Alexandre Mendonça Speakers bureau: Novartis, Janssen, Bristol, UCB, Isabella Siste de Almeida Aoki: None declared, Caique Chagas Cavuto: None declared, Vânia Aparecida Leandro-Merhi: None declared, José Luis Braga de Aquino: None declared
DOI: 10.1136/annrheumdis-2021-eular.3269

AB0799 DO WE OVERDIAGNOSE SERONEGATIVE RHEUMATOID ARTHRITIS? – THE ROLE OF MUSCULOSKELETAL ULTRASOUND IN CLARIFYING SERONEGATIVE INFLAMMATORY ARTHRITIS

D. Esperança Almeida[1], E. Costa[1], F. Guimarães[2], A. S. Pinto[3], H. Parente[2], S. Azevedo[2], J. Rodrigues[2], J. Tavares-Costa[2], C. Afonso[2], D. Faria[2], M. Cerqueira[1], F. Teixeira[2]. *[1]Hospital de Braga, Serviço de Reumatologia, Braga, Portugal*; *[2]Unidade Local de Saúde do Alto Minho, Serviço de Reumatologia, Ponte de Lima, Portugal*; *[3]Unidade Local de Saúde da Guarda, Serviço de Reumatologia, Guarda, Portugal*

Background: Several data indicate that seronegative rheumatoid arthritis (RA-) and seropositive RA (RA+) may have different mechanisms and prognosis, being well established that rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) have diagnostic and prognostic value. Several conditions, like peripheral spondyloarthritis (SpA), psoriatic arthritis or crystal-related arthropathies may mimic the presentation of RA. Mechanisms and treatment of each of these conditions differ significantly. The authors speculate that RA- may be overdiagnosed in the setting of seronegative chronic inflammatory arthritis and that musculoskeletal ultrasound (US) may help us to better classify these patients through the identification of characteristic lesions of the mentioned diseases.
Objectives: To compare the frequency of US lesions found in joints and entheses between RA- and RA+ patients.
Methods: Cross-sectional study: systematic US evaluation of ten joints, twelve entheses and both flexor and extensor tendons of four fingers (Table 1) in consecutive RA- patients. RA+ patients matched for sex and age were recruited. RA- patients included met every of the following criteria: history of chronic polyarthritis, RF and ACPA negativity, no extra-articular features of SpA or RA nor family history of SpA, no suspected crystal-related arthritis.
Results: Twenty-one RA- patients were included and twenty RA+ patients were recruited as controls. No differences between groups were found in sex, age, body mass index, time of disease evolution or use of biological therapy.
RA- patients had a significantly higher number of entheseal structural and/or inflammatory lesions than RA+ patients (median 2.0 vs. 0.5, U 111.5, p=.008**), with triceps enthesitis being significantly more frequent in RA- patients (p=.036*). In total, 18.7% of RA- entheses had enthesitis lesions vs. only 8.3% of RA+ entheses. One RA- patient had ultrasonographic features of dactylitis which was not clinically evident.
As expected, considering the role of RF and ACPA in erosive RA, RA- patients had a significantly lower number of joints with erosions compared to RA+ patients (median 0.0 vs. 3.0, U 64.5, p<.001***), with significant differences in every considered joint. Erosions were found in 6.7% of RA- joints vs. 32.0% RA+ joints.
Additionally, two RA- patients had hyperechogenic foci in knee cartilage or carpal fibrocartilage suggestive of calcium pyrophosphate deposition.

Table 1. Comparative frequency of ultrasound lesions found in joints and entheses of RA- and RA+ patients.

	RA- (n=21)	RA+ (n=20)	*p*-value
Mdn number of ENTHESES with any lesion per patient ± IQR	2.0 ± 3.0	0.5 ± 2.0	.008**
Triceps – n (%)	8 (38.1%)	2 (10.0%)	.036*
Quadriceps – n (%)	9 (42.9%)	6 (30.0%)	.393
Superior patellar – n (%)	4 (19.0%)	1 (5.0%)	.169
Inferior patellar – n (%)	-	-	-
Achilles – n (%)	9 (42.8%)	4 (20.0%)	.116
Plantar fascia – n (%)	5 (23.8%)	1 (5.0%)	.089
DACTYLITIS – 2^{nd} + 5^{th} finger – n (%)	1 (4.8%)	-	-
Mdn number of joints with EROSIONS per patient ± IQR	0.0 ± 1.0	3.0 ± 3.0	<.001***
Ulnar styloid process – n (%)	5 (23.8%)	11 (55.0%)	.041*
Metacarpophalangeal 2 – n (%)	3 (14.3%)	11 (55.0%)	.006**
Metacarpophalangeal 5 – n (%)	1 (4.8%)	10 (50.0%)	.001**
Metatarsophalangeal 1 – n (%)	-	3 (15.0%)	-
Metatarsophalangeal 5 – n (%)	3 (14.3%)	11 (55.0%)	.006**
CHONDROCALCINOSIS – triangular fibrocartilage + knee – n (%)	2 (9.5%)	-	-
DOUBLE CONTOUR – any joint – n (%)	-	-	-

RA- – seronegative rheumatoid arthritis; RA+ – seropositive rheumatoid arthritis Mdn – median; IQR – interquartile range; n (%) – absolute number (percentage) of patients with the indicated lesion.

Conclusion: We found that some patients diagnosed with RA- had, in fact, ultrasonographic features of different diseases, namely enthesitis/dactylitis and crystal deposition. These data suggest that RA- may be overdiagnosed in clinical practice. Systematic US evaluation of joints and entheses may provide valuable diagnostic information in patients with chronic inflammatory seronegative arthritis and improve patient care.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3588

AB0800 HEMATOLOGICAL MARKERS OF SYSTEMIC INFLAMMATION IN PATIENTS RHEUMATOID ARTHRITIS (RA) AND SPONDYLOARTHRITIS (SPA)

B. Targonska-Stepniak[1], K. Grzechnik[2], M. Majdan[1]. *[1]Medical University of Lublin, Rheumatology and Connective Tissue Diseases, Lublin, Poland*; *[2]Samodzielny Publiczny Szpital Kliniczny nr 4, Rheumatology and Connective Tissue Diseases, Lublin, Poland*

Background: An appropriate assessment of disease activity is essential in the management of patients with chronic inflammatory joint diseases, rheumatoid arthritis (RA) and spondyloarthritis (SpA). Hematological parameters [Neutrophil-To-Lymphocyte (NLR), Platelet-To-Lymphocyte (PLR) and Monocyte-To-Lymphocyte (MLR) ratios] have been demonstrated to be good, promising indicators of systemic inflammation status in different diseases, additionally to conventional inflammatory markers [erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)]. However results remain conflicting in rheumatic patients.
Objectives: The goal of the study was to determine the role of NLR, PLR, MLR in assessing inflammatory disease activity and to compare the biomarkers in RA and SpA patients.
Methods: An observational study was conducted in patients with RA and SpA (ankylosing spondylitis and psoriatic arthritis) treated in the Department of Rheumatology and Connective Tissue Diseases, Medical University of Lublin, Poland. Demographic and clinical information was obtained through structured interview, review of medical records and laboratory tests. The following disease activity and functional scores were registered: CRP and ESR levels, swollen and tender joints counts (SJC, TJC), DAS28 (ESR), HAQ, BASDAI, BASFI, patient global assessment (PtGA) and physician global assessment (PGA) rated on a visual analogue scale (VAS).
The study group consisted of 95 patients (58 women, 37 men), with the mean (SD) age 45.4 (9.9), disease duration 10.0 (8.4) years. There were 58 (61.1%) patients with RA (44 women, 14 men) and 37 (38.9%) patients with SpA. The mean age and disease duration were statistically not different in both patients' groups. The mean (SD) DAS28 was 4.21 (1.8) in RA patients; in SpA patients BASDAI 4.9 (2.6) and BASFI 5.0 (2.8).
Results: In the whole group (95 patients) and in the SpA group, we found positive correlations between the PLR value and the following parameters CRP, ESR; between NLR and CRP, ESR; between MLR and CRP. In the RA group positive correlations were observed between PLR and CRP, ESR; NLR and CRP; MLR did not correlate with CRP and ESR.
In RA patients, there were statistically significant correlations between values of PLR and DAS28 (r=0.356, p=0.006), TJC (r=0.308, p=0.02), SJC (r=0.318, p=0.016), PtGA (r=0.372, p=0.008). No significant correlation was found between NLR, MLR and other disease activity scores.
In SpA patients, we found a significant correlation between NLR and PtGA (r=0.488, p=0.04). No significant correlations were found between NLR, PLR, MLR and BASDAI, BASFI.
The group of RA patients as compared with SpA, was characterized by significantly higher value of PLR [respectively 207.8 (94.0) vs 169.9 (77.7), p=0.04]. In turn, SpA patients compared with RA, were characterized by unfavorable metabolic parameters: higher atherogenic index [respectively 4.03 (0.8) vs 3.57 (1.1), p=0.03], lower HDL-cholesterol [47.4 (10.7) vs 56.1 (16.4) mg/dl (p=0.006); higher serum uric acid [5.6 (1.2) vs 4.5 (1.4) mg/dl (p=0.0001)], higher waist measurement [96.1 (14.2) vs 85.9 (11.5) cm (p=0.0003).
Conclusion: In our study we found, that in patients with RA, PLR was associated with both clinical and inflammatory markers of disease activity; in SpA patients NLR, PLR and MLR were associated with conventional inflammatory markers (CRP, ESR). Hematological inflammatory biomarkers may reflect disease activity and could represent potential parameters to evaluate disease activity not only in RA, but also in SpA.
Disclosure of Interests: Bozena Targonska-Stepniak Speakers bureau: Berlin-Chemie/Menarini, KRKA, Medac, Santen, Krzysztof Grzechnik: None declared, Maria Majdan Speakers bureau: Roche, Medac
DOI: 10.1136/annrheumdis-2021-eular.3942

AB0801

TIME FOR REFERRAL AND DEFINITIVE DIAGNOSIS IN PATIENTS WITH HAND ARTHRALGIA

P. Herrera-Sandate[1], G. Figueroa-Parra[1], D. Vega-Morales[1], J. A. Esquivel Valerio[1], B. R. Vázquez Fuentes[1], M. A. Garza Elizondo[1], Y. G. Ordoñez Azuara[2], R. F. Gutierrez-Herrera[2], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Rheumatology Service, Monterrey, Mexico*; [2]*Hospital Universitario Dr. José Eleuterio González, Family Medicine Department, Monterrey, Mexico*

Background: Early referral of patients with suspicion of progression to rheumatoid arthritis (RA) is of paramount importance in disease prognosis. We had previously described a time delay of 28 months between symptom onset and evaluation by a rheumatologist, and a mean wait time of 9.5 weeks for referral to a secondary-level public hospital (1). The availability of specialized interdisciplinary evaluation of patients in a third-level of care raises the possibility of shortening this time gap, as well as describing patient and physician decisions amidst the referral to a Rheumatology center.

Objectives: Describe the diagnosis profile of patients with hand arthralgia and time of referral to Rheumatology in a Family Medicine clinic.

Methods: A cohort study was conducted in 110 patients from October 2018 to December 2020 in a Family Medicine clinic within the tertiary-care University Hospital "Dr. Jose Eleuterio Gonzalez" in Monterrey, Mexico. Patients with hand arthralgia as their chief complaint were recruited. An observational, descriptive compilation of patient history was retrieved prospectively through medical records. Variables included time of inclusion, number of medical visits until referral and definitive diagnosis. Descriptive statistics, Kaplan-Meier curves and log-rank tests were used to test the association between time of diagnosis and clinical variables of interest.

Results: Assessed variables are shown in Table 1. Out of 110 patients with hand arthralgia, a quarter received a final diagnosis within 3 medical visits. Less than half of patients were referred, and only a third attended the referral indication. It takes 39.3 days from the first medical visit to be referred, and 69 days and 2.89 consultations to receive a definitive diagnosis. Around half of patients will have a definitive diagnosis, osteoarthritis being the most common. The log-rank test for categoric variables including a positive squeeze test or ≥4 criteria of clinically suspect arthralgia did not show a significant association for time of referral and definitive diagnosis (data not shown).

Table 1. Diagnostic and referral characteristics of patients with hand arthralgia attending a Family medicine clinic

Patients recruited in a Family Medicine clinic	n = 110
Female, n (%)	90 (81.8)
Age in years, mean ± SD	49.69 ± 14.90
RF, ACPA, or hand radiography request, n (%)	100 (90.9)
Diagnosis in Family Medicine	
Diagnosed patients after 1 medical visit, cumulative n (%)	5 (4.6)
Diagnosed patients after 2 medical visits, cumulative n (%)	22 (20.0)
Diagnosed patients after 3 medical visits, cumulative n (%)	26 (23.6)
Referral to Rheumatology for diagnostic doubt or clinical follow-up	
Patients referred to a Rheumatology clinic, n (%)	49 (44.5)
Patients attending Rheumatology referral, n (%)	34 (30.9)
Time for referral, days ± SD	39.37 ± 38.64
Global definitive diagnosis	
Patients with a definitive diagnosis, n (%)	51 (46.4)
Osteoarthritis diagnosis, n (%)	23 (20.9)
Rheumatoid arthritis diagnosis, n (%)	13 (11.8)
Overlap syndrome diagnosis, n (%)	5 (4.5)
Time for definitive diagnosis, days ± SD	68.96 ± 106.57
Number of consultations for definitive diagnosis, mean ± SD	2.86 ± 1.05

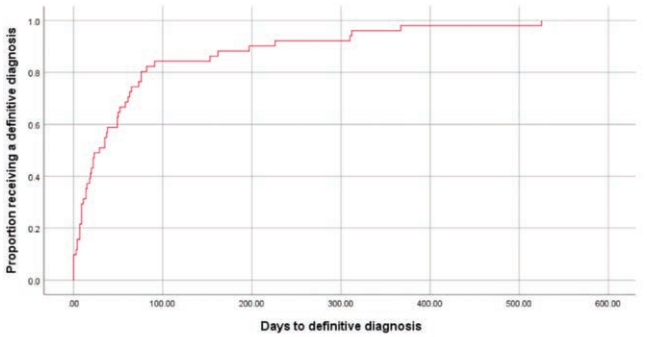
RF, rheumatoid factor; ACPA, anticitrullinated protein antibodies; SD, standard deviation.

Conclusion: Patients with hand arthralgia evaluated in a tertiary-care Rheumatology center receive a timely referral in one month and a definitive diagnosis after 3 medical visits in around two months.

REFERENCES:

[1] Vega-Morales, D., Covarrubias-Castañeda, Y., Arana-Guajardo, A. C., & Esquivel-Valerio, J. A. (2016). Time Delay to Rheumatology Consultation: Rheumatoid Arthritis Diagnostic Concordance Between Primary Care Physician and Rheumatologist. American journal of medical quality: the official journal of the American College of Medical Quality, 31(6), 603.

Graphs:



Graph 1. Kaplan-Meier curve of time to definitive diagnosis in patients with hand arthralgia as their chief complaint in a Family Medicine clinic.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4095

AB0802

THE CORRELATION BETWEEN N-MID OSTEOCALCIN SERUM VALUES AND BONE MINERAL DENSITY VALUES IN FEMALE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WHO RECEIVED ORAL METHYLPREDNISOLONE THERAPY BASED ON CUMULATIVE DOSES

S. Hidayatulloh[1], Z. A. Adnan[2,3], A. Nurudhin[2,3], Y. Werdiningsih[2,3], N. A. Prabowo[2,4]. [1]*Faculty of Medicine, Sebelas Maret University, Internal Medicine, Surakarta, Indonesia*; [2]*Faculty of Medicine, Sebelas Maret University, Internal Medicine, Rheumatology Division, Surakarta, Indonesia*; [3]*Dr. Moewardi General Hospital, Internal Medicine, Rheumatology Division, Surakarta, Indonesia*; [4]*Universitas Sebelas Maret Hospital, Internal Medicine, Sukoharjo, Indonesia*

Background: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease and involves many organ systems in the body. Glucocorticoids are potent anti-inflammatory and immunosuppressive agents used in patients with SLE. The cumulative dose of steroids is a major risk factor for bone loss. A sensitive indicator that reflects bone remodeling activity is a bone turnover marker (BTM), one of which is N-MID Osteocalcin. Bone Mineral Density (BMD) with DXA can be used to assess osteoporosis. DXA is thus not feasible for screening because of its high cost and lack of machine availability. N-MID Osteocalcin is cheaper and more accessible than DXA. The majority of SLE patients at Moewardi Hospital, Surakarta, received the main therapy for methylprednisolone.

Objectives: This study aims to prove the correlation between serum N-MID Osteocalcin values and BMD values in female SLE patients who received oral methylprednisolone therapy based on cumulative doses.

Methods: This is a cross-sectional study with random sampling techniques at Rheumatology Clinic Moewardi Hospital, Surakarta. The 38 samples that met the inclusion criteria were measured BMD by DXA and examined for N-MID Osteocalcin by using the Elecsys N-Mid Osteocalcin Kit with the ECLIA method. The cumulative dose of methylprednisolone is calculated in grams. Data analysis used the Shapiro Wilk test, 2 mean difference test (t-test and Mann Whitney test), Chi-Square test, bivariate correlation analysis and, Moderated Regression Analysis.

Results: There were 38 samples, 34 (89.47%) normal BMD and, 4 (10.53%) Osteoporosis. The N-MID Osteocalcin has a positive and significant correlation both with the BMD Total L1-L4 as well as the BMD NLF ($p < 0.05$). The cumulative dose of MP has a negative and significant correlation both with the BMD Total L1-L4 also with the BMD NLF ($p < 0.05$). MP cumulative dose can significantly function as a moderation of the effect of N-MID Osteocalcin both on the BMD Total L1-L4 or the BMD NLF. The effect of the N-MID Osteocalcin on the total BMD of L1-L4 or the BMD NLF at the Cumulative Dose MP ≥ 8 g was weaker than that of the MP Cumulative Dose <8 g, and the moderating effect of the correlation between N-MID Osteocalcin and BMD was larger on the total BMD of L1-L4.

Conclusion: There is a positive correlation between serum N-MID Osteocalcin values and BMD values in SLE female patients receiving oral methylprednisolone therapy and the cumulative dose of Methylprednisolone affects the correlation between N-MID Osteocalcin values and BMD values in SLE female patients receiving oral methylprednisolone therapy.

REFERENCES:

[1] Suarjana I N. 2014. Imunopatogenesis Lupus Eritematosus Sistemik, Dalam: Setiati, S, Alwi, I, Sudoyo, AW, Simadibrata, M, Setiyohadi, B & Syam, AF (editor). Buku Ajar Ilmu Penyakit Dalam vol 6. BP FKUI. Jakarta.

[2] Ruiz-Irastorza G, Danza A & Khamashta M. 2012. Glucocorticoid use and abuse in SLE. Rheumatology, 51, 1145-1153.

[3] Arslan S, Çeliker R & Karabudak R. 2010. Cumulative Corticosteroid Doses and Osteoporosis in Patients with Muliple Sclerosis. Turk J Rheumatol, 25,191-5.

[4] PEROSI. 2010. Panduan diagnosis dan penatalaksanaan osteoporosis. Pengurus Besar Perhimpunan Osteoporosis Indonesia.

[5] Kalaiselvi VS, Prabhu K, Ramesh M, Venkatesan VS. 2013. The Association of Serum Osteocalcin with the Bone Mineral Density in Post Menopausal Women. Journal of Clinical and Diagnostic Research, Vol-7(5), 814-816.
[6] Ghazi M, Mounach A, Nouijai A, Ghozlani I, Bennani L, Achemlal L, Bezza A, El Maghraoui A. 2007. Performance of the osteoporosis risk assessment tool in Moroccan men. Clin Rheumatol, 26(12), 2037-41
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4285

Public health, health services research, and health economics

AB0803 EXPERIENCES OF SCREENING AND DIAGNOSIS FROM THE PERSPECTIVE OF PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS (PSA)

C. Silverthorne[1,2], J. Lord[2], C. Bowen[3], W. Tillett[3,4], N. Mchugh[3,4], E. Dures[1,2]. [1]*University of the West of England, Faculty of Health and Applied Sciences, Bristol, United Kingdom*; [2]*University Hospitals Bristol and Weston NHS Foundation Trust, Academic Rheumatology, Bristol, United Kingdom*; [3]*Royal United Hospitals Bath NHS Foundation Trust, Rheumatology, Bath, United Kingdom*; [4]*University of Bath, Pharmacy and Pharmacology, Bath, United Kingdom*

Background: Psoriatic arthritis (PsA) is an inflammatory arthritis characterised by pain, swelling and stiffness in the joints and affects approximately 0.3 to 1.02% of the UK population [1]. PsA may result in limited physical function and reduced quality of life [2] and is associated with work disability and unemployment [3]. Patients who have the inflammatory skin condition, psoriasis, are at greater risk of developing PsA than those without.
Objectives: There is no definitive test for PsA. It is usually diagnosed by rheumatologists in secondary care, after referral from primary care. Evidence suggests a delay in diagnosis results in worse outcomes for patients. This study is nested within a randomised controlled trial (RCT) of a new clinical care pathway. The RCT is testing whether screening primary care patients with psoriasis for symptoms of PsA leads to earlier diagnosis and improved outcomes, compared to usual care. This qualitative study explored the acceptability and impact of screening.
Methods: Telephone interviews were conducted with patients with psoriasis from two secondary UK care centres taking part in the RCT. The semi-structured interviews explored patients' thoughts and feelings around screening, the impact of the screening outcome and any changes they made as a result. The semi-structured format allowed flexibility to ask questions that probed more deeply and develop new lines of enquiry based on patients' responses. Patients who did and did not receive a diagnosis of PsA were interviewed.
Results: Twenty-four patients participated in the study (15 women / 9 men) ranging in age from 35 to 73 years old. The length of time patients had psoriasis ranged from 6 to 60 years. Eleven patients were diagnosed with PsA. A Framework Analysis Approach was used to analyse the data. This allowed for an exploration of the predefined areas (the screening process) as well as remaining open to capturing other related experiences and views of patients. Four main themes represent the data (Table 1).

Table 1.

Main theme	Sub-themes
1. Living with psoriasis and psoriatic arthritis:	1. Understanding of psoriasis – causes, symptoms, treatments
'It's [psoriasis] socially debilitating…makes you look a real mess'	2. Effects of psoriasis on self, personal and working life
'It's almost as if the world's on your shoulders'	3. Awareness of PsA
2. Experience of screening:	1. Thoughts and feelings prior to screening
'I was able to talk and be listened to'	2. Valuing 'high quality' care
'It's a lightbulb moment…explained why things were a bit stiff and achy'	3. Impact of screening outcome
3. Gaining control:	1. Increased awareness and knowledge of psoriasis and PsA
'element of surprise that this arthritis should be connected to it [psoriasis]'	2. Improved self-management
'You've got to learn to listen to your body'	3. Early diagnosis of PsA
4. Future screening programs:	1. Changes to questionnaires
'there weren't really any questions about were you in pain'	2. Use of case studies, sign-posting
'support groups…peer support is crucial with long-term conditions'	3. Removing barriers to screening

Conclusion: This study indicates screening was viewed as a positive and reassuring experience. Patients valued the fact that screening appointments were not rushed and felt they were being listened to. Patients valued learning about psoriasis and PsA and referred to making changes beneficial to their health. Screening enabled patients to get the help they needed if diagnosed, provided relief if not diagnosed, and sometimes led to the diagnosis of a different condition.

REFERENCES:
[1]Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis 2005;64(Suppl 2):ii14–7
[2] Tillett W, de-Vries C, McHugh NJ. Work disability in psoriatic arthritis: a systematic review. Rheumatology 2012;51:275–83.
[3] Alinaghi F, Calov M, Kristensen LE et al. Prevalence of psoriatic arthritis in patients with psoriasis: a systematic review and meta-analysis of observational and clinical studies. J Am Acad Dermatol 2019;80:251–65.e19
Acknowledgements: On behalf of the PROMPT study team.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1024

AB0804 ONE YEAR FOLLOW-UP SAFETY AND EFFICACY RESULTS OF VACCINATION PROTOCOL FROM A RHEUMATOLOGY CLINIC

S. Jeria Navarro[1], S. P. Fernandez-Sanchez[1], V. Pomar[2], D. Lobo Prat[1], L. Sainz Comas[1], H. Park[1], A. García-Guillén[1], A. M. Millán Arciniegas[1], C. Díaz-Torné[1], P. Moya[1], B. Magallares[1], I. Castellví[1], A. Laiz[1], H. Corominas[1]. [1]*Hospital Universitari de la Santa Creu i Sant Pau & Dos de Maig, Rheumatology Unit, Barcelona, Spain*; [2]*Hospital Universitari de la Santa Creu i Sant Pau, Internal Medicine, Barcelona, Spain*

Background: Patients with autoimmune inflammatory rheumatic diseases (AIIRD) have a higher burden of infectious diseases compared to the general population. This could be explained by the disturbances in their immune system response, comorbidities and immunosuppressive treatment. Vaccination is the most effective measure to prevent infections.
Objectives: To describe a cohort of patients with AIIRD referred to the infectious disease´s unit according to the vaccination protocol.
Methods: Restrospective and descriptive study of a cohort of 286 patients with AIIRD who were evaluated in the rheumatology service of a tertiary hospital in Barcelona and referred to the infectious disease´s unit according to the vaccination protocol among 1 year,between January 1rst December 31st, 2019. The vaccination protocol included serologies of human immunodeficiency virus,hepatitis A,B and C, varicella zoster,tuberculosis,measles,mumps and rubella virus.The recommended vaccines were *H.influenzae b,S.pneumonia,*influenza,hepatitis A and B(immunity absence),*meningococcus c*,tetanus – diphtheria (low antigenic load),poliomyelitis and human papillomavirus (not vaccinated).The patients included were diagnosed with a rheumatologic condition under immunosuppressive therapy. Demographic variables,diagnosis,treatment,vaccines administered,infections and adverse effects were collected.
Results: Of 286 patients reviewed the mean age was 61, 4 (±14.4) years. The characteristics of the cohort are shown in Table 1. Most of the patients used csDMARDs 149 (52.1%), 77(26.9%) patients used combined treatment. Measles and rubella are part of the triple virus vaccines included in the systematic Spanish vaccination schedule, in our cohort 20 (7%) patients had negative serologies for measles and 26 (9%) for rubella. 57 (20%) patients had latent TB with positive Quantiferon.Forty-one (14.3%) were vaccinated before receiving immunosuppressive treatment. The less administered vaccine was influenza with 44.9% (vaccination rate in Spain in healthy population, in 2019-2020 was 51.2%).No serious adverse effects were reported in relation to the vaccination. The infectious complications during the follow-up period were bronchopneumonia in a patient with RA treated with certolizumab (1), herpes zoster infection in RA on adalimumab(1), recurrent otitis in RA on adalimumab(1), mycobacterium *avium* infection in RA on etanercept(1), TB reactivation in RA with GCs and csDMARDs(1) and Papilloma virus infection in SpA on ustekinumab (1).

Table 1. CHARACTERISTICS OF COHORT OF PATIENTS

Sex n % (women/men)	193/93 (67,5/32,5)
Age, years ± DE	61.4 ± 14.4
Diagnoses AIIRD, n (%)	
Rheumatoid arthritis n (%)	164 (57.3)
Systemic lupus erythematosus n (%)	6 (2.1)
Sjögren´s syndrome n (%)	9 (3.1)
Systemic sclerosis n (%)	1 (0.35)
Inflammatory myopathie n (%)	5 (1.7)
Vasculitis n (%)	36 (12.6)
Polymyalgia rheumatica n (%)	4 (1.4)
Spondyloarthropathy n (%)	46 (16.1)
Others n (%)	15 (5.2)
Treatment AIIRD	
GCs n (%)	116 (40.7)
csDMARDs n (%)	149 (52.1)
bDMARDs n (%)	80 (27.8)
tsDMARDs n (%)	7 (2.4)
Others[1] n (%)	12 (4.2)
GCs + csDMARDs n (%)	59 (21)
GCs + bDMARDs n (%)	14 (4.9)
GCs + csDMARDs + bDMARDs n (%)	4 (1.4)
Vaccines	
PCV 13 n (%)	283 (99)
PPSV23 n (%)	265 (93)
HiB n (%)	265 (93)
NM n (%)	247 (86.7)
Influenza n (%)	128 (44.9)
HBV n (%)	121 (42.3)
Vaccination before IS n (%)	41 (14.3)
Vaccination with IS n (%)	244 (85.3)

Other: Behcet,Adult Stills,Relapsing polychondritis,IGg4 related disease,SarcoidosisOthers[1]: Mycophenolic acid,cyclosporine and tacrolimus

Conclusion: In our cohort, the vaccination protocol proved to be a good tool to improve the vaccination rate of rheumatological patients, despite this, the vaccination of Hepatitis B and specially of influenza, continues to have a lower prevalence to general population.The vaccines were effective since none of the preventable infections occurred during follow up, despite the use of an immunosuppressant. Vaccination showed a good safety profile, without reported serious adverse effects or worsening of the underlying disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1801

AB0805 A SURVEY OF RHEUMATOLOGY PATIENTS' SATISFACTION TO SWITCHING FROM ORIGINATOR TO BIOSIMILAR AGENTS

C. R. Ng[1], S. Samec[1], P. Kavanagh[1], G. Mccarthy[1], S. Donnelly[1], A. G. Wilson[1]. [1]*The Mater Misericordiae University Hospital, Department of Rheumatology, Dublin, Ireland*

Background: The recent widespread switching of patients with inflammatory rheumatic conditions from originators to biosimilars has largely been driven by costs. The views of patients on switching are also important in the successful long term switching to biosimilars. We conducted a survey of patients views on patients satisfaction with the switch to biosimilar therapy.
Objectives: To assess satisfaction and response after switching from originator (Humira or Enbrel) to biosimilar (Amgevita or Benepali respectively), and to describe efficacy, side effects and reactions to biosimilar.
Methods: All patients diagnosed with an inflammatory arthritis and switched to biosimilar were identified using the Irish national HighTech electronic prescriptions system. Participants had been administered the biosimilar for > 3 months and were invited to take part via a telephone survey. This consisted of 4 questions (Question 1: satisfaction with the response to the new medication [Using 5 point Likert scale = 0: very dissatisfied; 1: dissatisfied; 2: neutral; 3 satisfied;4: very satisfied]; Question 2: overall satisfaction with biosimilar compared to originator if originator was 10 [satisfaction rating from 1 – 10 scale: 1,2: very dissatisfied; 3,4: dissatisfied; 5: neutral; 6,7,8: satisfied; 9,10: very satisfied]]; Question 3: adverse effects with biosimilars; Question 4: opinion on usage of new device [0: very difficult; 1: difficult; 2: same as previous device; 3: improvement compare to previous device).
Results: Baseline characteristics of biosimilar switch patients with disease category were:

Category	(n)
Gender	Male (39), Female (56)
Mean age (years)	56
Rheumatoid arthritis	58
Psoriatic arthritis	18
Ankylosing spondylitis	16
Reactive arthritis	1
Enteropathic arthritis	1
Juvenile idiopathic arthritis	1

48 switched from Humira to Amgevita.

The majority of the patients had positive view towards the effectiveness of the biosimilar: 36% very satisfied; 28% satisfied; 13% neutral; 10% dissatisfied; 13% very dissatisfied.
45% of the patients gave score of 9 and 10 in the survey of overall satisfaction to biosimilar if originator was given a score of 10, followed by 32% of them gave a score from 6 to 8, 4% of the patients gave a score of 5 and 7% of them gave a score of 3 and 4. The rest of them gave a score of 1 and 2.
12 participants switched back to originator (Humira, n=5; Enbrel, n=7) for the reasons of unable to use the device, anxiety, hemoptysis, nose bleeding, tongue swelling, neck pain, lethargy and generalized itchiness.
The most common complaints were (12 patients) systemic side effects (tiredness, headache, nausea, skin rashes, hair loss, muscle ache, tongue swelling, mood swing, dizzy, nose bleed, erectile dysfunction, hypertension, hemoptysis and red sclera).
17% of the patients find the biosimilars device easier to use compare to originator and 55% of the patients find both device are similar. 24% and 4% of them find the new device is difficult to very difficult to use respectively.
Conclusion: 69% of patients from Amgevita group and 60% of patients from Benepali group were satisfied with the change. Only 28% of the patients found the new device difficult to use. Overall conclusion from the study showed less than one quarter of the participants showed dissatifaction towards biosimilar and less than 12 % experienced systemic side effects and whether biosimilar could be a next cost effective biologic therapy to replace originator in future requires a longer duration of study.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2981

AB0806 THE JOURNEY OF AXIAL SPONDYLOARTHRITIS IN SPAIN: FROM THE GENERAL PRACTITIONER TO THE RHEUMATOLOGIST

E. Flores-Fernández[1], C. Valera-Ribera[1], I. Vázquez-Gómez[1], A. V. Orenes Vera[1], E. Valls-Pascual[1], À. Martínez-Ferrer[1], D. Ybáñez-García[1], A. Sendra-García[2], J. J. Alegre-Sancho[1]. [1]*Doctor Peset University Hospital, Rheumatology, València, Spain*; [2]*Doctor Peset University Hospital, Hospital Pharmacy, València, Spain*

Background: The delay in the diagnosis of axial spondyloarthropathies (AxSp), with the morbidity and economic burden that this entails, is well known[1,2]. According to the 2017 Atlas of axial spondyloarthritis in Spain[3], the mean diagnostic delay was 8,5 years, with an average total cost per patient of 659,8€ including medical consultations and complementary tests until diagnosis. However, nowadays there are still many patients who are incorrectly referred from the general practitioner (GP) despite showing typical features of AxSp.
Objectives: To describe the AxSp journey until diagnosis and treatment. To analyze additional costs of either a wrong or a delayed referral of the patients with AxSp to rheumatologists.
Methods: Type of study: observational, retrospective, descriptive. We included all the patients who were referred to our Department of Rheumatology from Jan-2019 to Dec-2020 and whose final diagnosis was AxSp. All the data since the first contact to the GP until the final diagnosis and initiation of treatment in Rheumatology were collected, including consultations to our emergency department (EmD) and other specialists. The number of consultations, complementary tests (analytical and imaging), as well as the direct costs of all of them were also collected4. A descriptive and associative analysis of these data was carried out using the SPSS software. We used median and interquartile range (IQR) for descriptive analysis and a significant p value < 0,05.
Results: From Jan-2019 to Dec-2020, 15 patients with AxSp and a median age of 43 (Interquartile range (IQR) 34-51) years were diagnosed, 10 women and 5 men. The main reason for referral was inflammatory low back pain (66.7%). The 60% of the patients were referred from the GP, followed by the EmD (20%). Despite typical symptoms, 4 patients (26,7%) were initially referred to Traumatology, and 3 out of them returned to the GP without the right diagnosis.
The median delay for referral from the GP to the rheumatologist was 47 (IQR 20-173) days. A wrong referral of the patient was associated with a delayed diagnosis (p 0,018) and higher direct costs of management (p 0,034). The average cost (including medical consultation and complementary tests) of the patient referred directly to Rheumatology was 267,71 (IQR 193,7-462,3) €, while the average cost of patients referred to other specialists was 578,83 (IQR 368,32-898,7) €. The extra cost of a wrong referral of a patient with AxSp was 311€ on average per patient in our sample (Table 1).

Table 1.

Women/men	10/5
Median age (years; IQR)	43; 34-51
Median diagnostic delay (days; IQR)	45; 20-173
Median cost of patient referred initially to Rheumatology (€; IQR)	267,71; 193,7-462,3
Median cost of patient referred initially to another specialist (€; IQR)	578,83; 368,32-898,7
Extra cost of wrong referral per patient(€)	311

Conclusion: AxSp is still a disease with a not negligible diagnostic delay, but it seems to be lower than previously reported. A wrong referral of the patient to other specialists, mainly Traumatology, is associated with this delay and can double the cost of managing these patients. This demonstrates the still unmet need of improving the management and referral of the patients with AxSp from the GP to the rheumatologist, ensuring an early diagnosis and treatment at the lowest cost for the system. Our study has limitations due to its small sample size, but preliminary results indicate that a larger-scale study would be necessary to correctly assess the magnitude of this problem.
REFERENCES:
[1] Fernández Carballido C. Diagnosing early spondyloarthritis in Spain: the ESPeranza program. *Reumatol Clin*. 2010;6(SUPPL. 1):6-10
[2] Muñoz-Fernández S et al. A model for the development and implementation of a national plan for the optimal management of early spondyloarthritis: The Esperanza Program. *Ann Rheum Dis*. 2011;70(5):827-830
[3] Garrido Cumbrera M et al. *Atlas de Espondilartritis Axial En España 2017*. Vol 45.; 2017.
[4] Generalitat Valenciana. LEY 20/2017, de 28 de diciembre, de la Generalitat, de tasas. [2017/12159]:96-222.
Acknowledgements: We would like to thank Novartis for its support.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3205

AB0807 TOAST-STUDY: TREATMENT AND OSTEOARTHRITIS, WHAT ARE PEOPLE SAYING ON TWITTER?

A. Mouamnia[1], A. Desvages[2]. [1]*Valenciennes Hospital, Rheumatology, Valenciennes, France*; [2]*Lille University Hospital, Rheumatology, Lille, France*

Background: Osteoarthritis is a very common chronic disease. The information needs of patients vary depending on the health issue. Social media sites represent a novel source of health information and advice for patients with chronic diseases, such as osteoarthritis. Almost half of them use the internet to look for health related information **[1]**. No study has assessed the impact of social media on osteoarthritis and its treatment.
Objectives: The purpose of this study was to evaluate frequently discussed osteoarthritis treatments on the social media Twitter.
Methods: We retrospectively analyzed tweets, published between 1st and 31st January 2020, containing the keywords "osteoarthritis". Only English language tweets were included. Tweets referred to veterinary medicine were excluded.
Results: 3587 tweets were analyzed. We identified 1737 tweets related to osteoarthritis treatment between 1st and 31st January 2020 (49.8%) (Figure 1). Dietary interventions were the most discussed treatment (18.3%, n=318/1737), including fruits, vegetables and plants (n=101), dietary supplements and vitamins (n=80), and spices (n=19). Physical medicine and rehabilitation (17.6%, n=305/1737) including sport (n=151), physiotherapy (n=70) and rehabilitation (n=57), were commonly discussed. Local therapies for osteoarthritis were also discussed by Twitter users (15.8%, n=274/1737). These included topical treatments such as anti-inflammatory gels and creams (n=23), and more invasive local treatments including intra-articular joint injections with corticosteroid (n=56), hyaluronans (n=29), stem cells (n=97), and Platelet-Rich Plasma (n=52). The frequently used systemic drugs were analgesia and non-steroidal anti-inflammatory drugs (n=113). Surgery and interventional radiology (genicular artery embolization) were also discussed (11.5%, n=199/1737). 5.6% tweets (n=97/1737) were related to alternative therapies. Predominant themes were related to marijuana (n=23), acupuncture treatment (n=17), homeopathy (n=10). Last but not least, 356 tweets (20.5%) referred to other websites including health programs.
Conclusion: Our results demonstrate that osteoarthritis treatment is frequently discussed in published tweets. Thereby, social media could have an impact on behaviors and adherence on medication, and it seems interesting that learned societies, involved in osteoarthritis treatment, communicate more using social media.

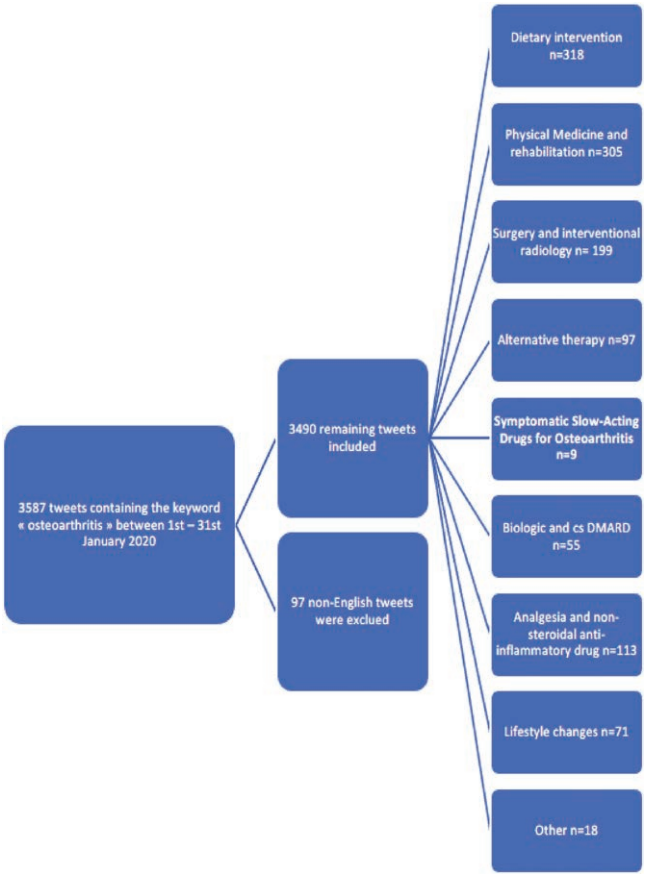


Figure 1. Osteoarthritis treatment discussed in published tweets

REFERENCES:

[1] Wagner TH, Baker LC, Bundorf MK, Singer S. Use of the Internet for health information by the chronically ill. Prev Chronic Dis 2004;1(4):A13.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3299

AB0808

A SYSTEMATIC REVIEW ON SYNDEMICS IN RHEUMATIC AND MUSCULOESKELETAL DISEASES (RMDS)

M. F. Ramirez-Flores[1], C. Cadena-Trejo[2], D. Alpizar-Rodriguez[3], V. Fernandez-Garcia[4], A. Gastelum-Strozzi[5], A. Hernandez-Garduno[6], I. Peláez-Ballestas[7]on behalf of Mexican Syndemic Study Group.
[1]Universidad Nacional Autónoma de México, Plan of Combined Studies in Medicine (PECEM-MD/PhD), Mexico City, Mexico; *[2] Universidad Nacional Autónoma de México, Escuela Nacional de Enfermetía y Obstetricia, Mexico City, Mexico*; *[3]Colegio Mexicano de Reumatología, Research Unit, Mexico City, Mexico*; *[4]Escuela Nacional de Enfermería y Obstetricia, Universidad Nacional Autónoma De México, Research Unit, Mexico City, Mexico*; *[5]Instituto de Ciencias Aplicadas y Tecnología, Universidad Nacional Autónoma de México, Scientific and Industrial Instrumentation, Mexico City, Mexico*; *[6]Private Practice, Private Researcher, Mexico City, Mexico*; *[7]Hospital General de México "Dr. Eduardo Liceaga", Rheumatology, Mexico City, Mexico*

Background: Syndemics comprises the interaction of two or more biological diseases in different socio-cultural situations and in the context of varying healthcare standards that exacerbates their deleterious effects on the health of individuals, communities, and societies (1). There is increasing interest in using syndemics in the study of RMDs.
Objectives: To identify quantitative and qualitative RMDs studies focused on syndemics through a systematic review and synthesize the available evidence.
Methods: Inclusion criteria were using a syndemic framework in methods in RMDs studies. A systematic search of studies published from 2003 up to January 2021 was conducted in two electronic databases (SCOPUS and Web of Science). The systematic search was implemented (Figure 1): 1) the word syndemic(s) was searched using the advanced query string search, in the title, abstract, keywords, and text, to identify the relevant studies; 2) the publications were screened by three peer review groups; 3) the group evaluated each title and abstract and reviewed full-text articles to identify those relevant for review; 4) synthesis focused on identifying the variables of each study and integrating findings.
Results: The initial search yielded 658 unique articles, from which ten studies were identified as syndemics in RMDs. After full-text review, six studies were excluded due to not inclusion of a syndemic framework. Four studies were included (Figure 1). The first quantitative study was on eight Latin-American (LatAm) indigenous communities (n=6,155). RMD´s were highly prevalent in the indigenous people (34.5%), RA prevalence was 2.4% in the Qom group of Argentina, and low back pain (LBP) being the most prevalent RMD (13.3%). RMDs were strongly associated with other comorbidities, unhealthy habits, low education levels, rural areas, socioeconomic conditions, and health inequality. The network analysis was the analytical approach using the Syndemic and Syndemogenesis Elements Modeler (SSEM). The second quantitative study focused on six urban/rural LatAm countries (n=55,724). LBP was significantly associated with comorbidities, unhealthy habits, low educational level, rural areas, and indigenous status. SSEM and cluster analysis showed a significant association between LBP prevalence and social variables. One qualitative study in fisher rural families (n=7) with three fisher rural generations from the Netherlands. A case study using life course theory. The first two generation reported syndemic vulnerability (psychological distress, cardiometabolic conditions, or musculoskeletal pain), and the third generation report less syndemic vulnerability, including musculoskeletal pain. A mixed study was identified focused on osteoarthritis with multimorbidities (cardiovascular, hypertension, diabetes mellitus) in an African American population (n=110) in the USA. The methodology was a descriptive secondary analysis and qualitative interviews. The study found that patients with hypertension (80.9%) reported greater chronic pain than those without. The lack of education added to the incorrect use of nonsteroidal anti-inflammatory drugs might contribute to the worst outcomes in this population, a significant burden of cardiovascular disease.
Conclusion: There is growing interest and urge for integrating syndemics in the study of RMDs. This review has demonstrated that there are only a few publications to date. The statistical power and the analytical approach (SSEM-Syndemic and Syndemogenesis Elements Modeler) in the two quantitative studies are relevant. The qualitative study demonstrated less syndemic vulnerability with better health conditions linked to better socioeconomic advantages. The mixed qualitative study did not show a syndemic framework. It is necessary to carry out studies in RMDs from the syndemic perspective to document the complexity of the clinical and social determinants related to these diseases.

REFERENCES:

[1] Singer M, Bulled N, Ostrach B, et al. Syndemics and the biosocial conception of health. The Lancet 2017;389:941–50.

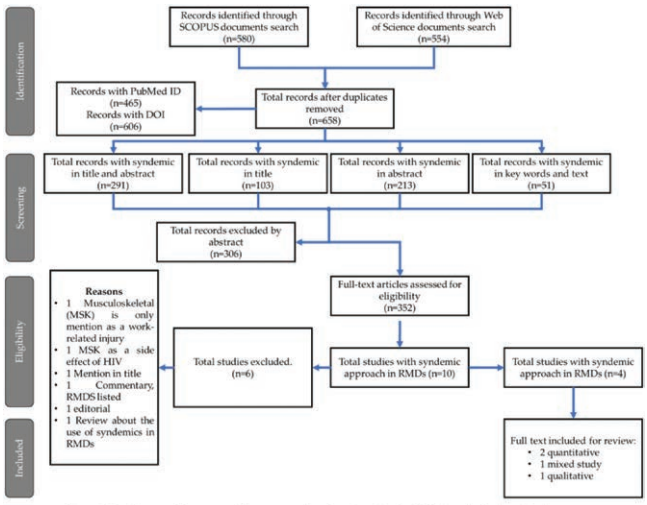


Figure 1. Flow diagram of the systematic literature search and review, using the PRISMA method, of records of syndemic with application in RMDs.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3324

AB0809

PADUA PREDICTION SCORE COMBINED WITH SERUM ALBUMIN FOR THE IDENTIFICATION OF VENOUS THROMBOEMBOLISM OF HOSPITALIZED PATIENTS IN THE DEPARTMENT OF RHEUMATOLOGY

Q. Peng[1], L. Long[1], J. Liu[1]. [1]*Sichuan Provincial People's Hospital, Zunyi Medical University, Department of Rheumatology, Chengdu, China*

Background: Venous thromboembolism (VTE) includes thrombotic disease of venous system, but primarily includes lower extremity deep vein thrombosis (DVT) and pulmonary embolism (PE). Population-based epidemiological studies have shown an association between systemic autoimmune diseases and VTE[1]. The Padua prediction score(PPS) is a new 20-point risk assessment model proposed by Professor Barbar et al[2] in 2010. A large number of researches have shown that low serum albumin concentration is associated with an increased risk of VTE [3],but there is a lack of studies on serum albumin in VTE, and there are no reports on PPS in rheumatology inpatients.
Objectives: To investigate the status of VTE in patients in the department of rheumatology, and to explore the value of PPS combined with serum albumin in the identification of VTE in this patient population.
Methods: Baseline data of inpatients in rheumatology department were collected at Sichuan Provincial People's Hospital from September 2018 to September 2020. Occurrence of VTE was compared between high and low risk groups. PPSs were analyzed in VTE and non-VTE patients. Multivariate logistic regression was used to analyze the independent risk factors of VTE. The receiver operating characteristic curve was used to evaluate the probablity of value of rheumatic inpatients with VTE assessed by PPS,serum albumin and PPS with serum albumin. P<0.05 indicates that the difference was statistically significant.
Results: A total of 2282 patients were included in this study, and 50(2.2%) had symptomatic VTE. Among the symptomatic VTE cases,38(1.6%) had DVT only,8(0.4%) had PE only, and 4(0.2%) were diagnosed with DVT and PE. PPSs in VTE and non-VTE groups were 3.00(2.00~6.00) and2.00(1.00~2.00) respectively (P< 0.05). One hundred and eighty-eight cases was divided into high-risk group of VTE (PPS≥4), while 2094 cases (PPS<4) were in the low-risk group. Logistic regression analysis showed that known thrombophilic condition, history of VTE, reduced mobility, and D-dimer were independent risk factors of VTE in rheumatology patients, the odd ration(OR) values were 161.90, 26.08, 8.73,and1.04. Serum albumin was the independent protection factor [OR= 0.92(95%CI:0.87~0.98)]. The AUC of PPS model, serum albumin model and the combined predictive model were 0.77, 0.75, 0.84, respectively. The difference between the combined prediction model and PPS model was statistically significant (Z=3.813, P<0.05). The optimal sensitivity of PPS and serum albumin models is 60%, 82%, respectively, and the optimal specificity of is 82.5%,58.6%, respectively. The combination model corresponds to a sensitivity of 62% and a specificity of 90.4%.
Conclusion: The incidence of symptomatic VTE was relatively higher in hospitalized patients in rheumatology department. Serum albumin was the protective factor. The combination of albumin and PPS can improve the accuracy of screening for VTE in rheumatology in-patients.

REFERENCES:

[1] Tamaki H,Khasnis A.Venous thromboembolism in systemic autoimmune diseases: A narrative review with emphasis on primary systemic vasculitides. [J].Vasc Med, 2015, 20: 369-76.
[2] Barbar S, Noventa F, Rossetto V,et al. A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score[J]. J Thromb Haemost,2010,8(11):2450–2457.
[3] Kunutsor SK,Seidu S,Katechia DT et al. Inverse association between serum albumin and future risk of venous thromboembolism: interrelationship with high sensitivity C-reactive protein.[J].Ann Med, 2018, 50: 240-248.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3729

AB0810

COST-EFFECTIVENESS ANALYSIS OF THE CLINICAL APPROACH FOR RA PATIENTS IN THE EARLY PHASE VERSUS THOSE IN THE ESTABLISHED PHASE FROM A FOURTH-LEVEL HEALTH SERVICE PROVIDER INSTITUTION IN COLOMBIA

C. Sarmiento Peña[1], G. Quintana Lopez[2,3,4], J. A. Díaz[1]. [1]*Universidad Nacional de Colombia, Farmacia, Bogotá, Colombia*; [2]*School of Medicine - National University of Colombia, Reumavance Research Group. Internal Medicine Department, Bogotá, Colombia*; [3]*Fundacion Santa Fe de Bogota University Hospital, Reumavance Research Group, Internal Medicine Department, Bogotá, Colombia*; [4] *School of Medicine - Universidad de Los Andes, Reumavance Research Group, Internal Medicine Department, Bogota, Colombia*

Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease that without treatment causes disability, pain, quality of life impairment, and premature mortality. It causes significant economic repercussions on patients, their families, and the health system. The costs of RA for Sanitary Systems are described in terms of medications and hospitalization. Also, the cost of treatment for patients whose disease was not adequately controlled from an early stage may involve joint replacement surgery and prolonged hospitalizations.
Objectives: To determine and analyze the cost-effectiveness of the clinical approach to rheumatoid arthritis in a cohort of patients in the early phase *versus* a cohort of patients in the established phase from a fourth-level Health Service Provider Institution in Colombia, from the perspective of the third-party payer with a time horizon of six-months.
Methods: An economic evaluation of the cost-effectiveness of the clinical approach was carried out in the early phase *versus* the established phase in a cohort of patients from May 2013 until December 2018, with rheumatoid arthritis from a fourth-level Health Service Provider Institution in Colombia, from the perspective of the third-party payer with a time horizon of six-months. The costs and effectiveness of each of the phases were estimated. A decision tree model was created, and the incremental cost-effectiveness ratio was calculated. The deterministic and probabilistic sensitivity analysis was performed.
Results: The early phase clinical approach for patients with rheumatoid arthritis represents savings of approximately 600 USD per patient in remission or low disease activity level in the first 6 months of follow-up from the perspective of the third-party payer.
Conclusion: The clinical approach to rheumatoid arthritis in the early phase is a less costly and more effective alternative *versus* established phase and generates savings for the third-party payer with a time horizon of six-months.

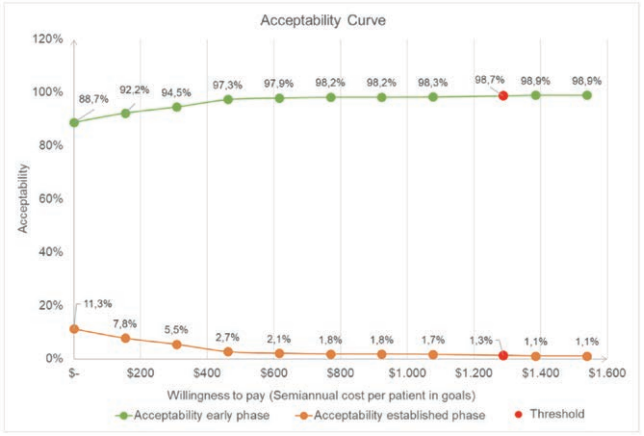


Figure 1. Acceptability curve

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3877

AB0811

DIRECT COST OF BIOLOGICS IN RHEUMATOID ARTHRITIS PATIENTS IN A DEVELOPING COUNTRY: RESULTS FOR THE MOROCCAN RBSMR REGISTRY

S. Farih[1], H. Rkain[1,2], S. Fellous[1], S. Ahid[3], R. Abouqal[4], T. Latifa[1], I. Hmamouchi[5,6], L. Achemlal[7], I. El Bouchti[8], A. EL Maghraoui[9], I. Ghozlani[10], H. Hassikou[11], T. Harzy[12], I. Linda[13], O. Mkinsi[14], R. Niamane[15], R. Bahiri[16], F. Allali[1]. [1] *El Ayachi Hospital, Ibn Sina University Hospital, Department of Rheumatology B, Salé, Morocco*; [2]*Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Physiology Laboratory, Rabat, Morocco*; [3] *Mohammed V University, Research Team of Pharmacoeconomics & Pharmacoepidemiology, Rabat, Morocco*; [4]*Faculty of Medicine and Pharmacy, Mohammed V University, Laboratory of Biostatistical, Clinical and Epidemiological Research, Faculty of Medicine and Pharmacy, Rabat, Morocco*; [5]*Faculty of Medicine and Pharmacy, Mohammed V University, Laboratory of Biostatistical, Clinical and Epidemiological Research, Rabat, Morocco*; [6]*Provincial Hospital of Temara, Department of Rheumatology, Temara, Morocco*; [7]*.Military Hospital Mohammed V, Ibn Sina University Hospital, Department of Rheumatology, Rabat, Morocco*; [8] *Arrazi University Hospital, Department of Rheumatology, Marrakech, Morocco*; [9]*Private Medical Office, Private Medical Office, Rabat, Morocco*; [10] *University Hospital of Agadir, Department of Rheumatology, Agadir, Morocco*; [11] *Military Hospital Moulay Ismail, Hassan II University Hospital, Department of Rheumatology, Meknès, Morocco*; [12]*Hassan II University Hospital, Department of Rheumatology, fes, Morocco*; [13] *Mohammed VI University Hospital, Department of Rheumatology, Oujda, Morocco*; [14]*Ibn Rochd University Hospital, Department of Rheumatology, Casablanca, Morocco*; [15]*Military Hospital Avicenne, Mohammed VI University Hospital, Department of Rheumatology, Marrakech, Morocco*; [16] *El Ayachi Hospital, Ibn Sina University Hospital, Department of Rheumatology A, Salé, Morocco*

Objectives: The aim of this study was to calculate direct costs amount in rheumatoid arthritis (R.A) patients in the Moroccan register of biologicals RBSMR registry.
Methods: Patients in the Moroccan register of biologicals RBSMR registry with available 1-year data were included. Variables related to socio-economic status, disease and biological therapy were collected. Direct costs included prices of biologics, costs of infusions, and subcutaneous injections. Biologic use and costs were compared.
Results: 197 patients data (female sex (86,8%), mean age (52,3± 11 years), illiteraty (45,7%)) were analyzed. The median annual direct costs per patient were €1,665 [€1,472 - €9,879]. For all patients, the mean annual direct costs per treated patient for each biological agent is presented in Figure 1.
The total annual direct costs of biological agents in the RBSMR registry were 978 494 €. Rituximab was given to 67% of patients and constituted 25.7% of the total annual budget. TNF-blockers and Tocilizumab were prescribed in 14.2% and 18.8% of cases and represented respectively 27.3% and 47% of this overall budget.

Conclusion: This study presents a global overview of the direct costs of biological therapy associated with RA patients, taking as a source the Moroccan registry of biological therapies in rheumatic diseases. Those results show that overall cost of biological agents according to the Moroccan register is very high. There is a real need for development of strategies for better governance of those costs.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4071

Epidemiology, risk factors for disease or disease progression

AB0812

BIOMARKERS FOR CONNECTIVE TISSUE DISEASE-ASSOCIATED INTERSTITIAL LUNG DISEASE: A PILOT STUDY

Y. H. Chiu[1,2], M. Voortman[3], E. M. Delemarre[4], S. Nierkens[4], P. De Jong[5], F. Mohamed Hoesein[5], J. M. Van Laar[1], J. Spierings[1]. [1]*University Medical Centre Utrecht, Department of Rheumatology and Clinical Immunology, Utrecht, Netherlands*; [2]*National Defense Medical Center, Division of Rheumatology/Immunology/Allergy, Taipei, Taiwan, Republic of China*; [3]*University Medical Centre Utrecht, Department of Heart and Lung, Utrecht, Netherlands*; [4]*University Medical Centre Utrecht, Center for Translational Immunology, Utrecht, Netherlands*; [5]*University Medical Centre Utrecht, Department of Radiology, Utrecht, Netherlands*

Background: Connective tissue disease (CTD)-associated interstitial lung disease (ILD) has high morbidity and increased mortality risk. Biomarkers that can predict prognosis and response to therapy have been studied in recent years, including cytokines, chemokines, adhesion molecules, growth factors, extracellular remodelling molecules and pneumocyte associated proteins. However, there is still a knowledge gap for interpreting biomarkers in the context of imaging and response.
Objectives: The aim of our study was to identify biomarkers that are associated with inflammatory and fibrotic changes over time on high-resolution computed tomography (HRCT) and response to treatment in CTD-ILD.
Methods: An exploratory set of 38 biomarkers were measured in serum of patients with CTD-ILD using a multiplex immunoassay, chemiluminescence enzyme immunoassay and enzyme-linked immunosorbent assay. Samples were taken at baseline and one year of follow-up. Clinical data was extracted from electronic medical patients records. Two experienced chest radiologists independently and blindly reviewed the HRCTs. A third expert reviewed the scan in case of discrepancies. They classified ILD patterns according to the classification for idiopathic interstitial pneumonia and categorised into fibrotic or inflammatory. Association between biomarkers at baseline and pulmonary function test (PFT) and HRCT changes in response to treatment were analysed by logistic regression. Responsiveness of biomarkers to treatment was determined using the paired Wilcoxon sign rank test. Correlations between the variation of biomarkers and PFT after one year of treatment were examined using Spearman's rank correlation coefficient.
Results: Sixteen patients were included (12 females (75.0%), median age 51 years (IQR 45–62). Underlying CTDs were systemic sclerosis (n=5), Sjogren's syndrome (n=1), inflammatory myopathies (n=6), rheumatoid arthritis (n=1), systemic lupus erythematosus (n=1), mixed connective tissue disease (n=1), and undifferentiated connective tissue disease (n=1). There were three patients with a fibrotic HRCT pattern and 13 patients with an inflammatory HRCT pattern.
Biomarkers attenuation in CXCL11, CTGF, and KL-6 were associated with inflammatory HRCT patterns as well as less HRCT progression and fewer FVC decline. Furthermore, a decrease in CTGF was observed in patients treated with MMF and corticoids, while a reduction in CXCL11 and SPD were seen in patients treated with hydroxychloroquine. (Table 1) Additionally, an increase in levels of galectin-3 at one-year follow-up was associated with improved predicted FVC (Rho 0.5, p=0.048). (Figure 1)

Table 1. Biomarker responses to clinical treatment

Treatment	Biomarkers	Baseline, Median (IQR)	Follow up, Median (IQR)	Variation percentage	p
MMF	CTGF (pg/ml)	110.69 (63.21–158.06)	4.73 (4.73–45.3)	-95.73	0.036
(n=7)	sVCAM (pg/ml)	2061300 (1939200–3042250)	1767600 (1707100–1986350)	-14.25	0.031
HCQ	CXCL11 (pg/ml)	699.30 (392.50–764.50)	333.39 (223.1–487.92)	-52.33	0.031
(n=6)	SPD (ng/ml)	18.70 (13.40–28.73)	16.80 (11.70–22.80)	-10.16	0.031
Steroid	CTGF (pg/ml)	81.93 (20.80–158.06)	12.76 (4.73–56.74)	-84.43	0.044
(n=11)	MMP-7 (pg/ml)	3146.3 (1779.7–3997.0)	4563.3 (2951.9–7625.8)	45.04	0.005

IQR, interquartile range; MMF, mycophenolate mofetil; HCQ, hydroxychloroquine; CTGF, connective tissue growth factor; sVCAM, soluble vascular cell adhesion molecule-1; SPD, surfactant protein D; MMP-7, matrix metalloproteinase 7.

Conclusion: In this pilot study, CXCL11, CTGF, and KL-6 reduction were associated with inflammatory HRCT patterns and better pulmonary outcome. In contrast to previous research in severe ILD, there was a positive correlation between changes of Galectin-3 and FVC in our study. Further research in a larger group and focusing on combining biomarkers to predict outcome and prognosis are needed.

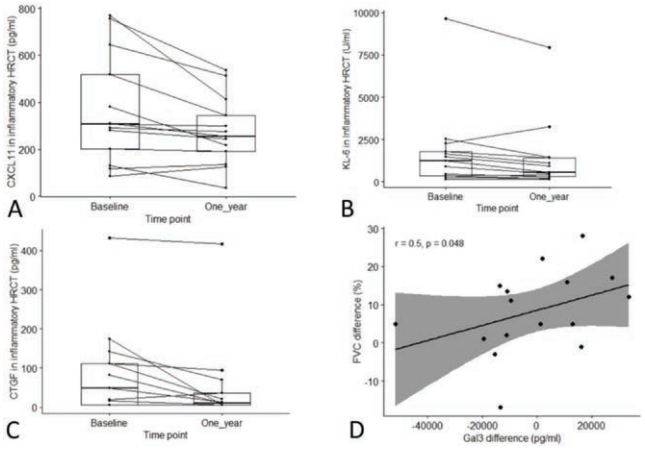


Figure 1.

Acknowledgements: We want to thank the Utrecht Immunity and Infection cohort for providing the serum samples, Marieke Vianen for the support in data management and Annemieke Sloeserwij for her help in collecting the samples. We want to thank Henk Ruven from St. Antonius Hospital Utrecht for measuring Krebs von den Lungen 6, and surfactant protein D. We acknowledge Boehringer Ingelheim B.V. the Netherlands for providing financial support for this study.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.157

AB0813 DEVELOPING SARCOPENIA IS A RISK FACTOR FOR FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS: 4-YEAR DATA FROM THE CHIKARA STUDY

Y. Yamada[1], M. Tada[2], K. Mandai[3], N. Hidaka[2], H. Nakamura[1]. *[1]Osaka City University Graduate School of Medicine, Department of Orthopedic Surgery, Osaka City, Japan*; *[2]Osaka City General Hospital, Department of Orthopedic Surgery, Osaka City, Japan*; *[3] Saiseikai Nakatsu Hospital, Department of Orthopedic Surgery, Osaka City, Japan*

Background: Patients with rheumatoid arthritis (RA) tend to have sarcopenia due to decreased muscle mass and function. We previously reported that 13.2% of RA patients without sarcopenia at baseline developed sarcopenia over a year using data from the prospective, observational CHIKARA study1.

Table 1. Characteristics of 77 RA patients by sarcopenia status at baseline and at 4-year follow-up.

	no development (n=48)	development (n=6)	cured (n=10)	persisted (n=13)	p value
Baseline					
age, years	64.5 (57.8, 72)	70.0 (65.5, 72.3)	61.0 (54.5, 68.3)	72 (68, 81)	0.062
disease duration, years	4.6 (1.1, 9.9)	11.7 (2.8, 18.9)	8.1 (4.2, 14.3)	4.0 (2.2, 7.7)	0.427
biologics use, %	37.5	16.7	30.0	23.1	0.617
GC use, %	27.1	16.7	10.0	23.1	0.678
MMP-3, ng/ml	66.8 (51.8, 103)	52.5 (40.0, 56.7)	82.8 (57.8, 186)	157.5 (90.8, 250)	0.001
DAS28ESR	3.43 ± 0.87	3.48 ± 1.32	3.36 ± 1.08	3.80 ± 1.27	0.661
mHAQ	0.31 (0, 0.50)	0.19 (0.03, 0.44)	0.38 (0, 0.84)	0.50 (0.25, 0.88)	0.383
BMI, kg/m^2	23.4 ± 3.6	21.6 ± 2.4	19.2 ± 1.6	19.5 ± 2.6	<0.001
SMI, kg/m^2	6.8 ± 0.8	6.2 ± 0.6	5.8 ± 0.5	5.7 ± 0.6	<0.001
fat percentage, %	30.4 ± 8.4	29.1 ± 9.1	23.9 ± 4.0	25.1 ± 8.3	0.046
estimated bone mass, kg	2.2 (2.0, 2.4)	1.9 (1.8, 2.1)	2.0 (1.7, 2.1)	1.7 (1.7, 1.9)	0.012
BMR, kcal	1100 (1031, 1197)	1029 (918, 1070)	1012 (917, 1057)	934 (894, 1006)	0.005
Change during 4 years					
ΔDAS28ESR	-0.34 ± 0.97	-0.52 ± 0.98	-0.60 ± 1.46	-0.56 ± 1.14	0.834
ΔmHAQ	0 (-0.25, 0.16)	0.19 (0, 0.56)	-0.06 (-0.44, 0.94)	0 (-0.38, 0.38)	0.357
ΔSMI, kg/m^2	0.0 ± 0.3	-0.6 ± 0.3	0.3 ± 0.4	-0.0 ± 0.3	<0.001
fall, %	43.8	83.3	30.0	23.1	0.079
fracture, %	14.6	83.3	20.0	23.1	0.002

Data are shown as mean ± standard deviation (SD) or median (25th, 75th percentile).GC: glucocorticoids, BMI: body mass index, SMI: skeletal muscle mass index, BMR: body metabolization rate.

Objectives: The aim was to investigate sarcopenia status and the characteristics of RA patients longitudinally.
Methods: Body composition, laboratory data, disease activity, physical function, treatment, and history of falls and fractures were investigated in 100 RA patients who participated in the CHIKARA study at baseline and at 4 years. The patients were divided into 4 groups depending on their sarcopenia status: no sarcopenia development (N group), sarcopenia development (S group), cured (C group), and persisted (P group).
Results: Of the 77 RA patients who completed the survey, 48 were in the N group; their body mass index, skeletal muscle mass index, fat percentage, estimated bone mass, and body metabolization rate at baseline were significantly elevated. On the other hand, 6 patients were in the S group; 83.3% of them experienced fractures during the 4 years, significantly more than in the other groups. Ten patients were in the P group, and their baseline MMP-3 was significantly higher than in the other groups. Thirteen patients were in the C group. There were no differences among the 4 groups in disease activity and physical function (Table 1).

Conclusion: Overall, 7.8% of RA patients developed sarcopenia during the 4-year follow-up period, and they developed fractures more frequently. Evaluation of sarcopenia is important for risk assessment of fractures.

REFERENCES:

[1] Y Yamada, M Tada, K Mandai et al. Glucocorticoid use is an independent risk factor for developing sarcopenia in patients with rheumatoid arthritis: from the CHIKARA study. Clin Rheumatol 2020 Jun;39(6):1757-1764.

Disclosure of Interests: Yutaro Yamada: None declared, Masahiro Tada: None declared, Koji Mandai: None declared, Noriaki Hidaka: None declared, Hiroaki Nakamura Grant/research support from: Astellas and Asahi Kasei
DOI: 10.1136/annrheumdis-2021-eular.277

AB0814 PREGNANCY COURSE ASSESSMENT IN PATIENTS WITH RHEUMATIC DISEASES COMPARED TO CONTROLS

O. Hamdi[1], M. Sellami[1], M. Yasmine[1], A. Fazaa[1], S. Miladi[1], L. Souabni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. *[1]Mongi Slim Hospital, Rheumatology, Tunisia, Tunisia*

Background: Rheumatic diseases such as rheumatoid arthritis (RA) and spondyloarthritis (SA) may occur among women of childbearing age. Adverse events during pregnancy including disease flare, preterm delivery, and neonatal or fetal death have been reported.
Objectives: Our aim was to assess the impact of rheumatic diseases on the course of pregnancy.
Methods: We conducted a cross-sectional study involving patients with RA (2010 ACR/EULAR criteria) and SA (2009 ASAS criteria) (study group) as well as healthy controls (control group) matched by age and gender. All women included had at least one pregnancy. Data were collected through telephonic interviews. We used the Student t test to compare the study group and the control group.
Results: We enrolled 57 patients (30 RA and 27 SA) and 57 controls. The mean age in the study and the control groups were respectively 43.2 ± 8.2 years [26-48] and 37.5 ± 6 years. The mean chronic inflammatory rheumatisms duration was 13.81 ± 6.2 years. A history of primary sterility was found in 3 patients (1 RA and 2 SA) and none in the control group. The mean age during the first pregnancy was significantly higher in the study group (28 ± 6.2 years versus 24 ± 7 years in the control group) (p=0.01). Eight patients (5 RA and 3 SA) had a history of spontaneous miscarriage. A terminated pregnancy was noted in 3 patients (1 RA and 2 SA). Complications during pregnancy in the study group were gestational diabetes (0.3%), premature delivery (0.3), premature rupture of membranes (0.3%), abortion threat (0.3%) and pre-eclampsia (6%). Pregnancy was more associated with complications in the study group (p=0.05). Cesarean section was more used in the study group (28 patients versus 9 in the control group; p= 0.00). The main indications of cesarean section in the study group were macrosomia (11 patients), scar uterus (6 patients), sacroiliitis (4 SA patients), twin pregnancy (2 patients), and undetermined reasons (6 patients). Fetal presentation in the study group was the seat presentation (3%), top presentation (4%), face (2%), and forehead presentation (0.3%) with no significant difference with the control group. Complications of childbirth in the study group were hemorrhage of delivery (10.3%), cord widening (6.6%), perinatal asphyxia (4.9%), and dystocia (1.9%). However, no statistically significant differences were found between the two groups in the prevalence of complications of childbirth. During pregnancy, 5 patients were on salazopyrine, 2 on corticosteroids and, 1 on non-steroidal anti-inflammatories.
Conclusion: Our study showed that pregnancies with rheumatic diseases were at increased risk of having maternal complications and adverse neonatal outcomes.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.413

AB0815 FIRST DEGREE RELATIVES OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS - CLINICAL, SEROLOGICAL AND IMMUNOLOGICAL CORRELATIONS

B. Penev[1], G. Vasilev[2], D. Kyurkchiev[3], S. Monov[4]. [1]*St Anna University Hospital, Internal Medicine, Sofia, Bulgaria*; [2]*St. Ivan Rilski University Hospital, Laboratory of Clinical Immunology, Sofia, Bulgaria*; [3]*St. Ivan Rilski University Hospital, Laboratory of Clinical Immunology, Sofia, Bulgaria*; [4]*St. Ivan Rilski University Hospital, Rheumatology Clinic, Sofia, Bulgaria*

Background: Antinuclear antibodies (ANA) have been unequivocally recognized as essential for diagnosis and play both pathogenic and diagnostic roles in systemic lupus erythematosus (SLE). SLE and ANA have also been found to be more often among relatives of SLE patients. ANA and other immunological changes are known to appear prior to the clinical onset of the disease and thus can be used as predictors. Studies have reported that relatives of SLE patients who later transitioned to SLE displayed more lupus-associated autoantibody specificities and had early clinical signs. They also displayed elevated baseline plasma levels of inflammatory mediators, including B-lymphocyte stimulator (BLyS) and interferon-associated chemokines, with concurrent decreases in levels of regulatory mediators, e.g. tumor growth factor (TGF)-β. Commonly recognized risk factors for SLE are signs of past Epstein-Barr (EBV) infection, use of estrogen drugs and current smoking. It seems that ANA, immunologic changes and risk factors have not been investigated together in relatives of SLE patients.
Objectives: The aim of the study was to determine the relative prevalence of clinical signs of SLE or connective tissue disease (CTD), smoking, use of estrogen drugs and levels of circulating ANA, BLyS, IFN-α, TGF-β, anti-EBV viral capsid antigen (VCA) IgM and IgG antibodies among sera of FDR, non-FDR healthy individuals and SLE patients.
Methods: Forty three FDRs of SLE patients were studied along with 15 SLE patients and 15 clinically healthy subjects as control groups. The FDRs and the healthy answered a questionnaire about early clinical signs of CTD, smoking and estrogen use history. The questionnaire was developed based on the existing Screening Questionnaire for Connective Tissue Diseases and current knowledge of most early signs of CTD. Blood samples were obtained and tested for ANA, both by indirect immunofluorescence and immunoblot, anti-dsDNA by ELISA. ELISA was also performed to measure levels of BLys, IFN-α, TGF-β, anti-EBV IgM and IgG.
Results: More than half of the FDRs displayed ANA in titer 1:160 or more, with predominately AC-4 type of fluorescence according to International Classification on ANA Patterns (ICAP) compared to only AC-1 and AC-0 among patients and controls respectively. A correlation between the ANA titer and the number of complaints was found. This was particularly valid or reported skin complaints and oral ulcers which appeared more frequently when ANA was 1:320 or above (p=0,018 and 0,038 respectively). Furthermore, oral ulcerations showed positive correlation with the presence of anti-Ro60. No associations were found in the healthy group between reported complaints and ANA titers. Smoking and estrogen use did not differ across the three groups. Patients showed significant differences in levels of BLys (p=0,027), TGF-β (p=0,019) and anti-EBV IgG (p=0.041) compared to both FDRs and controls. Without reaching statistical significance, levels of TGF-β tend to split the FDR group into "healthy-like" and "SLE-like".
Conclusion: Our results show that FDR ANA levels are between those of SLE patients and healthy subject groups. This is consistent with previous studies. The data also suggest that ANA positivity correlates with reported complaints, some of which could be interpreted as very early clinical signs of SLE. Of note, anti-Ro60 is known to be among the earliest ANA that appear in "future" SLE patients and in this study they are related to oral complaints that could be caused by early sicca phenomena. Immunologically, our data support previous findings [1] that the FDRs are a heterogenic group with different "lupus-developing" potential.
REFERENCES:
[1] Munroe ME. et al, Soluble Mediators and Clinical Features Discern Risk of Transitioning to Classified Disease in Relatives of Systemic Lupus Erythematosus Patients, Arthritis Rheumatol. 2017 March; 69(3): 630–642.
Disclosure of Interests: Bogdan Penev: None declared, Georgi Vasilev: None declared, Dobroslav Kyurkchiev: None declared, Simeon Monov Speakers bureau: I have been paid for giving lectures on statistical data on efficacy of many pharmaceutical products on various companies
DOI: 10.1136/annrheumdis-2021-eular.511

AB0816 PREDICTORS OF RESPONSE TO THE FIRST BDMARD IN BIOLOGIC-NAÏVE PATIENTS WITH SPONDYLOARTHRITIS: A COHORT STUDY

B. M. Fernandes[1], S. Garcia[1], F. Oliveira Pinheiro[1], M. Rato[1], D. Fonseca[2], D. Santos Oliveira[1,3], A. Martins[1], F. R. Martins[4], M. Bernardes[1,5], L. Costa[1]. [1]*Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*; [2]*Centro Hospitalar Vila Nova de Gaia/Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; [3]*Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; [4]*Centro Hospitalar Universitário do Algarve, Rheumatology, Faro, Portugal*; [5]*Faculty of Medicine, University of Porto, Departamento de Medicina, Porto, Portugal*

Background: Several markers of response to biologic disease-modifying antirheumatic drugs (bDMARDs) have been identified in Rheumatoid Arthritis. However, data on predictors of response in Spondyloarthritis (SpA) are more limited.
Objectives: To identify predictors of response to bDMARDs in a SpA population.
Methods: Monocentric retrospective study including all the SpA patients (ASAS classification criteria) followed at our Rheumatology Department, registered in the national database and treated with bDMARD between July 2001 and August 2020. Demographic, clinical and laboratorial data at baseline and disease activity measures at 6 and 12 months of bDMARD were collected. Mann-Whitney U test and chi-square tests were used to the comparison analysis between groups (continuous and categorical variables, respectively) and univariate logistic regression was used in the prediction analysis.
Results: A total of 325 patients were included, 178 (54.8%) males, 76 (23.4%) smokers and 164 (50.5%) HLA-B27 positive. Concerning SpA subtypes: 236 (72.6%) had Ankylosing Spondylitis, 31 (9.5%) had Inflammatory Bowel Disease Associated SpA and 58 (17.9%) had Undifferentiated SpA. The mean age at the start of the first bDMARD was 41.7 years (±12.2) and the median disease duration was 12.1 years (0.5-52.7). The mean ASDAS-CPR (Ankylosing Spondylitis Disease Activity Score with C-reactive protein) was 4.0 (±0.8) and most patients (57.2%) exhibited very high disease activity at baseline as evaluated by ASDAS-CRP. Ninety-five (29.2%) patients were taking NSAIDs (nonsteroidal anti-inflammatory drugs) and 131 (40.3%) were under csDMARDs (conventional synthetic disease-modifying antirheumatic drugs), being sulfasalazine the most frequent (28.3%). All patients started iTNF (tumor necrosis factor inhibitors): adalimumab (30.2%) and golimumab (24.6%) were the most frequently started bDMARDs.
At 6 and 12 months of bDMARD, 63.5% and 65.7% of the patients had ASDAS response (clinically important improvement or major improvement). Variables that showed statistically significant differences at baseline between those different groups are presented at Table 1.

Table 1. Baseline characteristics that showed statistically significant differences at baseline between groups of patients with vs without ASDAS responses at 6 and 12 months of bDMARD. (bDMARD: biologic disease-modifying antirheumatic drug; BMI: body mass index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate).

	ASDAS response at 6 months			ASDAS response at 12 months		
	yes	no	p-value	yes	no	p-value
Age at start of bDMARD (mean±SD)	39.6±12.2 years	44.2±10.7 years	p=0.012	40.7±12.8 years	44.2±10.9 years	p=0.035
Age at SpA diagnosis (mean±SD)	32.2±11.1 years	35.8±11.9 years	p=0.023	31.3±10.7 years	35.4±11.2 years	p=0.010
BMI (mean±SD)	25.7±4.3 kg/m^2	28.7±6.0 kg/m^2	p=0.045	25.6±4.3 kg/m^2	28.5±5.7 kg/m^2	p=0.005
CRP (mean±SD)	3.2±3.5 mg/dL	1.1±1.2 mg/dL	p<0.001	3.4±3.5 mg/dL	1.4±1.6 mg/dL	p<0.001
ESR (mean±SD)	36±22	25±20	p<0.001	38±24	27±17	p=0.001
ASDAS-CRP (mean±SD)	4.1±0.8	3.5±0.4	p<0.001	4.2±0.8	3.6±0.8	p<0.001
HLA-B27+	61.5%	26%	p=0.006	60.1%	44.4%	p=0.033
Males	62.3%	35.7%	p=0.004	62.3%	37.5%	p=0.001

Body mass index (BMI) (OR 0.89 [0.80-0.99], 95% CI) and ASDAS-CRP at baseline (OR 2.8 [1.2-6.6], 95% CI) predicted ASDAS response at 6 months; moreover, only BMI (OR 0.91 [0.83-0.99], 95% CI) predicted ASDAS response at 12 months of bDMARD.

Conclusion: Our results demonstrate that a higher baseline disease activity predicts the response to bDMARDs in SpA. Interestingly, BMI at baseline also predicts ASAS response at 6 and 12 monthes of treatment with bDMARD, in line with some data that suggest an association between BMI and disease activity in SpA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.921

AB0817 CAN RHEUMATIC CONDITIONS ASSOCIATED INTERSTITIAL LUNG DISEASES BE MANAGED IN A DISTRICT GENERAL HOSPITAL – RESULTS FROM A LONGITUDINAL OUTCOMES SURVEY

A. Francioni[1], J. Gnanapragasam[1], N. Ramsundar[1], V. Joshi[1], M. K. Nisar[1]. [1]*Luton and Dunstable University Hospital, Rheumatology, Luton, United Kingdom*

Background: Interstitial lung disease is a well described extra-articular manifestation in a range of rheumatic diseases. It carries significant morbidity and mortality. Management of rheumatic diseases associated ILD (r-ILD) requires expertise as the needs of such patients are complex and treatment options limited. Historically, such complex ILD has been managed in tertiary referral centres. We set up a combined service incorporating both rheumatology and respiratory domains in a district general hospital (DGH) to help patients avoid long journeys and improve their experience whilst focusing on an integrated care pathway.
Objectives: We evaluated the outcomes of all patients managed over three years in this pilot service model.
Methods: Referrals were accepted from any hospital specialist involved in the management r-ILD. They were triaged by lead ILD pulmonologist to monthly ILD MDT comprising a rheumatologist, respiratory physician, a radiologist and ILD specialist nurse. Appropriate patients were booked into combined clinic, run by the respective rheumatology and chest specialists with ILD interest, attracting a multi-speciality tariff. All the data was recorded electronically with full access to demographics, disease parameters, investigations and drug management.
Results: 111 consecutive patients were included in this evaluation. Mean age was 66.4 yrs (19-92 yrs) and 36% (n=40) were male. 34 (30%) had RA, 31 (28%) had CTD, 20 (18%) had IPAF and 26 others. Most predominant HRCT pattern was NSIP (n=40,36%) followed by UIP (n=31, 28%). Mean FVC was 2.59 L/min (1.93-4.13) with DLCOc of 52.7% (28.9-90.1%) predicted. Only two patients had all antibodies negative whilst 109 had at least one antibody positive with ANA being the most common (n=38).
Most (83%) patients were treated with immunomodulators including 11 with rituximab. 49 (44.1%) patients had significant improvement in clinical, imaging and pulmonary parameters with DLCOc improving to 56.57% and FVC to 2.70 L/min. There were similar improvements in six minute walk test. 21 patients died and 23 patients required long term oxygen therapy.
Conclusion: This pilot real world study confirms the utility of a combined specialist service in a district general hospital. Nearly half of this complex and resource intensive patient cohort had good clinical outcomes and derived benefit from the expertise in one room. Feedback from both patients and referrers was unanimously positive. No patient required tertiary centre referral and all could be managed adequately in the clinical setting.
Our report confirms that r-ILD can be managed in a DGH setting with a stream-lined service offering clear benefits to patients. We would argue that r-ILD service, congruent to satellite pulmonary hypertension clinics in secondary care with hub-and-spoke model liaison with tertiary centre, can be established on similar principles and could help over-stretched tertiary care with repatriation of services whilst helping develop local expertise in the management of chronic ILD.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1102

AB0818 ADVERSE EVENTS UNDER B-CELL DIRECTED THERAPIES IN A LARGE SINGLE-CENTER COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS, SYSTEMIC LUPUS ERYTHEMATOSUS, ANCA-ASSOCIATED VASCULITIS AND RENAL DISEASES

J. G. Rademacher[1], V. Korendovych[1], P. Korsten[1]. [1]*Universitätsmedizin Göttingen, Department of Nephrology and Rheumatology, Göttingen, Germany*

Background: The anti-CD20 antibody rituximab (RTX) is approved for the treatment of rheumatoid arthritis (RA) and ANCA-associated vasculitis (AAV). In addition, RTX is used in a wide range of autoimmune diseases. Belimumab (BEL) is an anti-BAFF antibody approved for the treatment of non-renal systemic lupus erythematosus (SLE) in Europe. These agents are generally well-tolerated but severe adverse events (AEs) can occur. The frequency of and factors associated with AEs are currently unknown.
Objectives: To identify adverse events with the use of B-cell directed therapies in a large population of RA, AAV, and SLE.
Methods: This is a single-center retrospective cohort study using routine clinical data over a ten-year period (2010-2020). We recorded epidemiological and clinical data of patients receiving either BEL or RTX. Data included age, gender, type of disease, number and efficacy of infusions, patient-years and concomitant treatment. Patient records were screened for AEs, such as infections, anaphylaxis, occurrence of malignant disease, laboratory abnormalities and immunoglobulin (Ig) deficiency. Between group comparisons were performed.
Results: Database screening yielded 445 patients treated with RTX and 23 with BEL. After exclusion of patients with incomplete data, 425 RTX and 23 BEL patients were analyzed.
Our preliminary analysis of a sample of 60 of these 448 patients (184 patient-years) resulted in 43 patients (72%) with RA, 8 patients with AAV (13%), 5 patients with a renal disease, and 4 patients with mixed connective tissue disease, as well 23 SLE patients. 46 (77%) were female. In RA, a median of 13 treatments of 1000 mg were administered, corresponding to 3.37 patient-years per patient. Primary non-response occurred in 2 patients, secondary non-response in 13 patients. For AAV, a median of 8.4 treatments were given (3.3 patient-years), no treatment failure was detected. SLE patients received a median of 15 treatments.
15 patients had infectious complications during treatment, 11 needed treatment. Herpes zoster infection occurred in 3 patients with RA. Three of the 8 patients with AAV had an infection requiring treatment. In SLE patients, only 2 developed infectious complications, and no Ig-deficiency occurred.
Lymphopenia was the most common laboratory abnormality detected in 25 patients with RTX, 19 of whom had RA. Ig deficiency was common in RA, affecting 30% of patients. Deficiency of IgM and IgG was recognized in 5 patients each; 1 patient had low levels IgA.
Neither the maintenance prednisolone dosage nor Ig deficiency were associated with risk for infection. However, lymphopenia appeared to be associated with risk for infection.
Conclusion: Our preliminary data observe a 184 patient-year period. RTX and BEL were generally associated with few AEs. RA patients frequently had laboratory abnormalities (lymphopenia, Ig-deficiency) which did not necessarily translate to clinical events. Infections were more common in AAV, BEL was the best tolerated B-cell directed agent. Overall, our data are reassuring, but we suggest a more careful vigilance in AAV patients.
Disclosure of Interests: Jan-Gerd Rademacher: None declared, Viktor Korendovych: None declared, PETER KORSTEN Speakers bureau: Abbvie, Sanofi Aventis, GSK, Chugai, Boehringer-Ingelheim, Novartis, Consultant of: Lilly, Gilead, Boehringer-Ingelheim, Novartis, GSK, Grant/research support from: GSK
DOI: 10.1136/annrheumdis-2021-eular.1214

AB0819 PROFILE OF RHEUMATOLOGIC EMERGENCIES IN THE DEPARTMENT OF RHEUMATOLOGY OF THE UNIVERSITY HOSPITAL OF IBN ROCHD IN 2019

Z. El Ouali[1], S. Lahrichi[1], R. Assadi[1], K. Nassar[1], S. Janani[1]. [1]*University Hospital of Ibn Rochd, Department of Rheumatology, Casablanca, Morocco*

Background: Rheumatology is a medical field often referred to as "cool" because of the low frequency of life-threatening pathologies in common practice (1). However, rheumatologists may be solicited to manage situations that are often depicted as urgent from the point of view of the patient.
Objectives: To profile the consultations received in the emergency unit of the Department of Rheumatology of the University Hospital of Ibn Rochd in Casablanca.
Methods: We conducted a retrospective study on the 2019 emergency consultations register of the Department of Rheumatology of the University Hospital of Ibn Rochd, Casablanca. We collected epidemiological, clinical, and therapeutic data.
Results: 407 emergency consultations were carried out in 2019. The average age of the patients was 50.7 (range 14 - 88). 20% of the consultants were 65 years old or older. The sex ratio M/F was 0.4. 95.6% of the patients were from the Casablanca-Settat region. 86.4% of the patients came from the emergency department of the hospital, 10.6% came from other intra-hospital services, and 3% were referred directly to our department. The most represented socio-professional categories were respectively people without professional activity other than retirees (67.6%), followed by intermediate professions (9.7%), executives and higher intellectual professions (5.8%), and retirees (5.3%). Regarding social insurance, 49.4% of the consultants benefited from a public health assistance scheme, 30% had a public health insurance, 14.4% had no health insurance, and 9.9% had a private health insurance. The most frequent reasons for consultation were polyarthralgia (26.8%), oligoarthralgia (18.9%), low back pain (22.6%), lumbar radiculalgia (16.7%), monoarthralgia (11,8%), neck pain (8.1%), cervicobrachial neuralgia (6.4%), monoarthritis (5.4%), polyarthritis (3.4%), and oligoarthritis (2,7%). The general condition of the patients was good in 83% of cases, 5.2% had asthenia, 4.4% had a fever above 38°C, and 3.7% had anorexia. Extra-articular signs were present in 24.7% of cases. At the end of the consultation, a diagnosis could be made in 57.2% of cases. The diagnoses comprised degenerative (51%), inflammatory rheumatic (8.6%), infectious (7.3%), metabolic (6.7%), and tumor (2.1%) pathologies. The main treatments prescribed were level 1 analgesics in 65.6% of cases, non-steroidal anti-inflammatory drugs in 45% of cases, local treatment in 28.9% of cases, symptomatic slow-acting drugs in 21.9% of cases, muscle relaxants in 17% of cases, rest in 12.5% of cases, and supportive orthotics in 11.6% of cases. Regarding the outcomes of the consultants, 75.4% were referred to a conventional hospital

consultation for rheumatology follow-up, 13.6% of patients were referred to other specialized departments, 9.1% of patients were lost to follow-up, and 3.9% were hospitalized in our department.

Conclusion: The polyarthralgia and the low back pain were the most frequent reasons for consultation in our rheumatology emergency unit. Degenerative pathology is in the lead of the etiologies. Level I analgesics and non-steroidal anti-inflammatory drugs play an important role in symptomatic emergency treatments.

REFERENCES:

[1] Gutiérrez-González LA. Rheumatologic emergencies. Clin Rheumatol. 2015 Dec;34(12):2011–9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1234

AB0820 INFLUENCE OF ANCA ANTIBODIES ON DEMOGRAPHIC AND CLINICAL CHARACTERISTIC OF AAV

K. Wójcik[1], A. Masiak[2], Z. Zdrojewski[2], R. Jeleniewicz[3], M. Majdan[3], I. Brzosko[4], M. Brzosko[4], M. Madej[5], K. Jakuszko[6], J. Kur-Zalewska[7], W. Tłustochowicz[7], H. Storoniak[8], B. Bułło-Piontecka[8], A. Dębska-Ślizień[8], A. Hawrot-Kawecka[9], P. Głuszko[10], M. Stasiek[10], M. Wisłowska[11], E. Kucharz[12], J. Musiał[1]on behalf of POLVAS. *[1]Jagiellonian University Medical College, 2nd Chair of Internal Medicine, Kraków, Poland*; *[2]Medical University of Gdańsk, Department of Internal Medicine, Connective Tissue Diseases and Geriatrics, Gdańsk, Poland*; *[3]Medical University of Lublin, Department of Rheumatology and Connective Tissue Diseases, Lublin, Poland*; *[4]Pomeranian Medical University, Department of Rheumatology and Internal Diseases, Szczecin, Poland*; *[5]Wrocław Medical University, Department of Rheumatology and Internal Medicine, Wrocław, Poland*; *[6]Wrocław Medical University, Department of Nephrology and Transplantation Medicine, Wrocław, Poland*; *[7]Military Medicine Institute, Department of Internal Medicine and Rheumatology, Warszawa, Poland*; *[8] Medical University of Gdańsk, Department of Nephrology, Transplantology and Internal Diseases, Gdańsk, Poland*; *[9] Medical University of Silesia, Department of Internal Medicine and Metabolic Diseases, Katowice, Poland*; *[10] National Institute of Geriatrics, Rheumatology and Rehabilitation, Department of Rheumatology, Warszawa, Poland*; *[11]Central Clinical Hospital of the Ministry of the Interior and Administration, Department of Internal Diseases and Rheumatology, Warszawa, Poland*; *[12]Medical University of Silesia, Department of Internal Medicine and Rheumatology, Katowice, Poland*

Background: ANCA associated vasculitides (AAV) are a heterogeneous group of rare diseases with unknown etiology and the broad clinical spectrum ranging from life-threatening systemic disease, through single organ involvement to minor isolated skin changes. Unfortunately the clinical classification, ANCA specificity or genetic characteristics alone is not able to categorize AAV patients in a satisfactory manner. As a consequence advanced statistical techniques were used to identify and stratify AAV subphenotypes [1, 2]. Here we have analyzed influence of the ANCA type on clinical manifestations and demographic characteristics in various types of AAV, based on data from the POLVAS registry

Objectives: We decided to retrospectively analyze a large cohort of Polish AAV patients deriving from several referral centers – members of the Scientific Consortium of the Polish Vasculitis Registry (POLVAS) – and concentrate on demographic and clinical characteristics of anti-PR3 and anti-MPO positive patients regardless of their clinical diagnosis.

Methods: We conducted a systematic multicenter retrospective study of adult patients diagnosed with AAV between Jan 1990 and Dec 2016. Patients were enrolled by 9 referral centers. We analyzed dichotomous variables: gender; ANCA status – anti-PR3+ or anti-MPO+, ANCA negative; organ involvement - skin, eye, ENT, respiratory, heart, GI, renal, urinary, CNS, peripheral nerves and polytomous variable (number of relapses), supported by quantitative covariates (e.g., age at diagnosis, CRP at diagnosis, maximal serum creatinine concentration ever)[3].

Results: MPO-positive patients (both GPA and EGPA phenotype) were older at the time of diagnosis with a substantial percentage diagnosed > 65 years of age, and with high rate of renal involvement. Interestingly, while in the whole group of patients diagnosed with EGPA male to female ratio was 1:2, the MPO+ EGPA patients showed M:F ratio of 1:1.

The analysis of ANCA negative AAV reveled significant differences in GPA, ANCA negative group is characterized with significantly lower frequency of renal involvement compared to rest GPA (11,5% vs 63,7%) p<0,05 what should be emphasized ANCA negative AAV never lead to ESRD (end stage renal disease) or even transient dialysis.

Conclusion: ANCA specificity is indispensable as a separate variable in any clinically relevant analysis of AAV subcategories. MPO+ group is characterized by older age at time of diagnosis, male to female ration 1:1, kidney involvement, and shows more homogenous clinical phenotype than PR3+ AAV patients. In our group ANCA negative AAV never lead to ESRD (end stage renal disease) or even transient dialysis.

REFERENCES:

[1] Mahr A, Specks U, Jayne D. Subclassifying ANCA-associated vasculitis: a unifying view of disease spectrum. Rheumatol Oxf Engl 2019;58:1707–9. https://doi.org/10.1093/rheumatology/kez148.

[2] Wójcik K, Biedroń G, Wawrzycka-Adamczyk K, Bazan-Socha S, Ćmiel A, Zdrojewski Z et al. Subphenotypes of ANCA-associated vasculitis identified by latent class analysis. Clin Exp Rheumatol. 2020 Sep 1. Epub PMID: 32896241.

[3] Wójcik K, Wawrzycka-Adamczyk K, Włudarczyk A, Sznajd J, Zdrojewski Z, Masiak A, et al. Clinical characteristics of Polish patients with ANCA-associated vasculitides—retrospective analysis of POLVAS registry. Clinical Rheumatology. 1 wrzesień 2019;38(9):2553–63.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1560

AB0821 PSYCHOMETRIC PROFILE OF PATIENTS WITH CHRONIC INFLAMMATORY ARTHRITIS

G. L. Fonti[1], M. S. Chimenti[1], P. Conigliaro[1], P. Triggianese[1], E. Bianciardi[2], G. Tarantino[2], M. Coviello[2], G. Lombardozzi[2], C. Niolu[2], A. Siracusano[2], R. Perricone[1]. *[1]University of Rome Tor Vergata, Rheumatology, Allergology and Clinical Immunology, Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, Rome, Italy*; *[2]University of Rome Tor Vergata, Psychiatric Chair, Department of Systems Medicine, Rome, Italy*

Background: Psoriatic Arthritis (PsA) is a chronic inflammatory disease characterized by a condition of inflammation of joint and periarticular tissues with progressive destruction of bone and cartilage tissues and consequent disability. Numerous studies suggest that the systemic inflammation that characterizes this disease is the basis of the onset of numerous comorbidities, including anxiety and depression.

Objectives: This prospective study aims to examine the psychometric profile of patients with chronic inflammatory arthritis to investigate possible correlations with psychiatric comorbidities and disease status.

Methods: from October 2018 to March 2019, consecutive out-patients with PsA (according to CASPAR criteria) referred to the Rheumatology Unit of the University of Rome Tor Vergata, were evaluated by a dedicated psychiatrist for attachment style (Relationship Questionnaire - RQ), alexithymia (Toronto Alexithymia Scale - TAS20), perceived stress (Perceived Stress Scale - PSS) and depressive symptoms (Beck Depression Inventory - BDI). These indices were then correlated with clinimetric indices, indices of inflammation and therapy taken by the patient. Statistical analysis was performed using Fisher's exact test and Pearson's correlation coefficient.

Results: 33 patients affected by PsA and 40 healthy individuals as control group were enrolled. The RQ test showed that in patients an insecure "avoidant" attachment style prevails (51.5%) compared to the control group (10%) (p<0.0008) [Figure 1]. This result correlates with the presence of alexithymia and with the duration of illness, showing that patients with an "insecure" profile at the RQ test are those who have higher scores on the TAS-20 scale (p=0.035) and a longer duration of illness (p<0.0001). Regarding the perception of stress, at the PSS test women have mean values (18.12±7.31) statistically superior to the values of the male population (11.69±7.79)(p=0.0015). PSS values of the overall study population were directly proportional to RQ values (p<0.0068) and TAS-20 values (p<0.0001). The correlation between PSS and TAS-20 was further confirmed in the analysis of the individual subgroups "patients" (p<0.0001) and control group (p<0.0001)[Figure 2]. No correlation was shown with phlogosis and clinimetric indices.

Conclusion: This study suggests how PsA patients are a more vulnerable subtype of patient from the psychological point of view, with an avoidant attachment style, characterized by the difficulty to express emotions and to rely on others in times of need. These characteristics can influence the adherence to pharmacological therapies and the doctor-patient relationship. This profile is manifested more frequently in female patients, with long duration of illness, high perception of stress. The state of disease activity does not influence these elements, suggesting that the insecure attachment style is not related to the single inflammatory flare, but is the result of years of illness and long-standing disease. Our results support the relevance of early diagnosis in PsA.

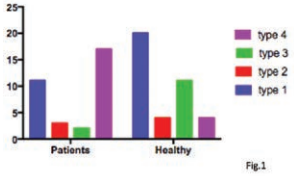


Fig.1

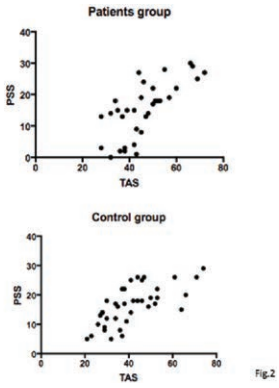


Fig.2

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1725

AB0822

BREASTFEEDING AMONG WOMEN WITH RHEUMATIC DISEASES: ANALYSIS OF DATA FROM THE P-RHEUM. IT STUDY

S. Panaro[1], M. C. Gerardi[1], M. Filippini[1], F. Crisafulli[1], M. Fredi[1], R. Gorla[1], M. G. Lazzaroni[1], D. Lini[1], C. Nalli[1], L. Moschetti[1], F. Regola[1], M. Taglietti[1], A. Bortoluzzi[2], A. Zanetti[3], A. Lojacono[4], S. Zatti[4], C. A. Scirè[2], G. Carrara[3], F. Ramazzotto[4], L. Andreoli[1], F. Franceschini[1], A. Tincani[1]on behalf of SIR. [1]*University of Brescia, Spedali Civili of Brescia, Rheumatology Unit, Brescia, Italy*; [2]*UIniversity of Ferrara, Rheumatology Unit, Ferrara, Italy*; [3]*Italian Society for Rheumatology, Epidemiology Unit, MIlan, Italy*; [4]*Spedali Civili of Brescia, Obsterics and Gynceology Unit, Brescia, Italy*

Background: The World Health Organization recommends that infants should be exclusively breastfed until the age of 6 months. The aim of this study was to assess the ratio of breastfeeding patients with Rheumatic Diseases (RD) and to identify possible causes of its discontinuation.
Objectives: The aim of this study was to assess the ratio of breastfeeding patients with Rheumatic Diseases (RD) and to identify possible causes of its discontinuation.
Methods: This study was embedded in the P-RHEUM.it register, as a nationwide prospective cohort study collecting data of pregnancies in inflammatory RD. Pregnancies, enrolled until the 20th week of pregnancy, are followed from pregnancy until 6 months postpartum. At baseline, sociodemographic parameters, obstetric history, comorbidities are reported. During pregnancy, the course of maternal disease, development of foetus and complications are reported. After delivery, the pregnancy outcome, data on lactation and child development are collected.
Results: From May 2018 to May 2020 data of 349 patients were available. Data on lactation were available in 44 pregnancies. Two months after delivery 37 were continuing breastfeeding (n=26) or mixed feeding (n=11), while 7 were using formula feeding. Among patients using formula feeding 2 had a diagnosis of rheumatoid arthritis (RA), 1 of juvenile idiopathic arthritis, 1 of undifferentiated arthritis (UA), 1 of anti-phospholipid syndrome (APS), 1 of vasculitis and 1 of systemic lupus erythematosus. The reasons of formula feeding were the following: 2 for agalactia, 2 for personal preferences, 3 for drug-related concerns (1 for physician's decision in a patient with APS; 2 for maternal concerns about drugs in patients with RA and UA treated respectively with Adalimumab and Tocilizumab). At 6 months 30 continued breastfeeding (n=23) or mixed feeding (n=7) and 14 formula feeding. The reasons of formula feeding were available in 9 patients: 3 for agalactia, 2 for personal preferences, 2 for physician's decision in a patient with APS and in a patient positive for anti-phospholipid antibodies; 2 for maternal concerns about drugs.
Conclusion: Preliminary data of this prospective study demonstrate a high percentage of breastfeeding/mixed feeding after delivery and after 6 months among women with RD. Drug related concerns are the main reason of discontinuation of breastfeeding, although medication results compatible with lactation. Using our results, strategies supporting patients with RD whishing to breastfeed may be developed.

REFERENCES:

[1] Carina Gotestam Sporken et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis 2016.
[2] Sammaritano et al. 2020 American College of Rheumatology Guideline for the management of reproductive health in rheumatic and muscoloskeletal diseases, Arthritis Rheumatol. 2020.

Acknowledgements: Authors would like to thank SIR study center and all patients who accepted to partecipate to our study

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1814

AB0823

TREATMENT WITH ADALIMUMAB IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: A STUDY OF TREATMENT TRAJECTORIES ON A PATIENT LEVEL IN CLINICAL PRACTICE

I. Redeker[1], S. Moustakis[2], S. Tsiami[2], X. Baraliakos[2], I. Andreica[2], B. Buehring[2], J. Braun[2], U. Kiltz[2]. [1]*Deutsches Rheuma-Forschungszentrum Berlin (DRFZ), Epidemiology, Berlin, Germany*; [2]*Rheumazentrum Ruhrgebiet at Ruhr-University Bochum, Rheumatology, Herne, Germany*

Background: There is evidence that drug retention rates to adalimumab (ADA) in patients (pts.) with chronic inflammatory rheumatic diseases (CIRD) are impaired by loss of efficacy and adverse events, and that about 50% of users had discontinued ADA within 5 years (1). With the introduction of ADA biosimilars in October 2018, non-medical switching from originator to ADA biosimilars is now increasingly part of daily practice in rheumatologic care.
Objectives: The aim was to study treatment trajectories over two years in pts. with CIRD receiving originator ADA.
Methods: Pts. with CIRD on originator ADA who switched to ADA biosimilar from October 2018 onwards were identified and followed until 2020. Disease activity (ASDAS), physical function (HAQ, BASFI), and changes in treatment were documented every 3 months. The four predefined treatment trajectories "continued ADA biosimilar therapy", "back-switch to originator ADA therapy", "switch to other biological (b) disease modifying anti-rheumatic drug (DMARD) therapy", and "stopped bDMARD therapy /death /drop out" were used to compare characteristics of pts. with different trajectories.
Results: A total of 111 CIRD pts. on treatment with originator ADA were switched to ADA biosimilar (Table 1). The majority of pts. 75 continued therapy with ADA biosimilar (Figure 1 next page) while 16% switched back to originator ADA, 7% switched to a different bDMARD, and 9% either stopped treatment (n=9) or died (n=1). Pts. who continued ADA biosimilar were more frequently male, older or with a longer disease duration than those who switched therapy back to originator ADA and those who switched to a different bDMARD (Table 1). The previous duration on originator ADA treatment was increased in patients who continued ADA biosimilar compared to those who switched therapy back to originator ADA and those who switched to a different bDMARD. There was more functional impairment (HAQ, BASFI) and higher disease activity (ASDAS) in pts. who switched compared to those who continued ADA biosimilar therapy (Table 1). Treatment with csDMARDs and glucocorticoids was increased in pts. who continued ADA biosimilar therapy, while pts. who switched therapy had more previous bDMARD therapies (Table 1).

Table 1. Characteristics of patients at baseline for the entire group and stratified by treatment trajectory

		Treatment trajectory			
	Total group N=111 (100%)	continued ADA biosimilar therapy N=75 (67.6%)	back-switch to originator ADA therapy N=18 (16.2%)	switch to different bDMARD therapy N=8 (7.2%)	no bDMARD therapy / death / drop out N=10 (9.0%)
Age, y	51.2 (14.5)	51.5 (13.6)	50.6 (16.8)	43.5 (9.5)	56.4 (19.0)
Women, No. (%)	46 (41.4)	27 (36.0)	9 (50.0)	6 (75.0)	4 (40.0)
RA	23 (20.7)	17 (22.7)	2 (11.1)	1 (12.5)	3 (30.0)
axSpA	68 (61.3)	47 (62.7)	11 (61.1)	6 (75.0)	4 (40.0)
PsA	15 (13.5)	7 (9.3)	4 (22.2)	1 (12.5)	3 (30.0)
Other diagnoses	5 (4.5)	4 (5.3)	1 (5.6)	0 (0.0)	0 (0.0)
Disease duration, median (IQR), y	5.0 (2.0-8.0)	5.0 (2.0-9.0)	3.5 (2.0-6.0)	2.0 (1.0-5.5)	4.5 (2.0-8.0)
Duration previous originator ADA therapy	40.7 (27.7)	45.3 (27.8)	35.0 (25.2)	20.3 (24.7)	32.3 (25.1)
DAS28	3.0 (1.0)	2.9 (1.0)	3.4 (1.0)	-	3.3 (1.2)
CRP, median (IQR), mg/L	0.2 (0.1-0.3)	0.1 (0.1-0.2)	0.2 (0.0-0.5)	0.2 (0.2-1.3)	0.3 (0.2-0.4)
HAQ score	1.3 (0.8)	1.1 (0.7)	1.7 (0.8)	-	1.8 (1.0)
ASDAS	2.2 (1.1)	2.0 (1.0)	3.0 (1.2)	2.7 (0.9)	2.3 (0.2)
BASFI	3.5 (2.6)	3.0 (2.5)	5.4 (2.4)	3.4 (1.6)	5.4 (1.6)

+values are given as mean (SD)

Conclusion: Two thirds of pts. who switched to ADA biosimilar remained on this therapy for 2 years. As many as 16% of pts. switched back to ADA originator. Whether or to what degree this was influenced by nocebo effects needs further

study. The same is true for the effect of functional impairment – it would be interesting to know whether this was due to inflammation or structural damage.

REFERENCES:

[1] Neovius M et al. Ann Rheum Dis 2015; 74:354-360
[2] The study was funded by Hexal Germany.

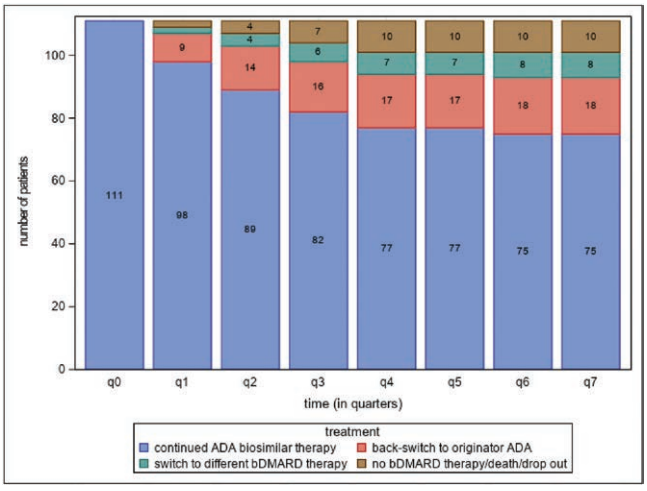


Figure 1. Treatment trajectories of ADA therapy in patients with CIRD during two yearsADA: adalimumab; bDMARD: biological disease modifying anti-rheumatic drug.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1838

AB0824 ANALYSIS OF GUT MICROBIOTA IN RHEUMATOID ARTHRITIS PATIENTS

Q. Wang[1,2], S. X. Zhang[3,4,5], J. Qiao[3,4,5], G. Shi[1], R. Zhao[3,4,5], S. Song[3,4,5], Y. Zhang[3,4,5], Q. Yu[2,6], X. Li[3,4,5], P. F. He[2]. [1]*Shanxi Medical University, Basic Medical College, Taiyuan, China*; [2]*Shanxi Medical University, Medical Data Sciences, Taiyuan, China*; [3]*The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China*; [4]*Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China*; [5]*Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China*; [6]*Shanxi Medical University, School of Management, Taiyuan, China*

Background: Gastrointestinal microbiota, particularly gut microbiota is an indispensable environmental factor in the progression of Rheumatoid Arthritis (RA). Understanding the diversity and function of the intestinal flora in patients with RA is part and parcel to understand the relationship between microbiota and human health.

Objectives: This study aimed to identify the diversity and function of the intestinal flora in patients with RA.

Methods: A total of 166 participants were recruited in this study, comprising 93 RA patients and 73 age and sex-matched healthy controls (HCs). Microbial genome was extracted from approximately 250mg fresh fecal samples from all participants using QIAamp PowerFecal DNA Kit (Qiagen). The V3-V4 variable regions of bacterial 16S rRNA genes were sequenced with the Illumina Miseq PE300 system. Sequence data were compiled and processed using Qiime2. Sequences were grouped into operational taxonomic units (ASVs)[1]. Microbial diversity was estimated by the Simpson index. PICRUSt2 was used to predict KEGG functional pathway differences between RA and HC intestinal flora functions based on ASV Tables[2]. Linear Discriminant Analysis (LDA) Effect Size (LEfSe) analysis was performed using LEfSe software to discovery the different intestinal flora and functions between RA and healthy.

Results: The alpha-diversity index of Simpson the microbiome in RA patients was lower than that of HCs (Figure 1a, P <0.05). Compared with HCs, bacterial Bacilli and Lactobacillales were more abundant in patients with RA (Figure 1b, P <0.05). In contrast, Marinifilaceae, Peptococcaceae, Peptococcales and Phascolarcto bacterium were less abundant in the RA group (Figure 1b, P <0.05). As shown in Figure 1c, propanoate metabolism, taurine and hypotaurine metabolism, ascorbate and aldarate metabolism, biosynthesis of siderophore group nonribosomal peptides and glutathione metabolism were the most significantly altered pathways in RA (P <0.05). Epithelial cell signaling in Helicobacter pylori infection, RNA transport, RNA degradation and plant-pathogen interaction were the most significantly altered pathways in HC (P <0.05). The different KEGG metabolic pathways were mainly concentrated in carbohydrate and amino acid metabolism.

Conclusion: Gut dysbiosis in RA patients mainly characterized by reduced the diversity and impaired abundance of the intestinal flora, which severely influence the metabolism of gastrointestinal microbiota. The discovery of the associated intestinal microbiota of RA may provide a new idea for RA treatment.

REFERENCES:

[1] Han L, Zhao K, Li Y, et al. A gut microbiota score predicting acute graft-versus-host disease following myeloablative allogeneic hematopoietic stem cell transplantation. Am J Transplant 2020;20(4):1014-27. doi: 10.1111/ajt.15654 [published Online First: 2019/10/13]
[2] Liss MA, White JR, Goros M, et al. Metabolic Biosynthesis Pathways Identified from Fecal Microbiome Associated with Prostate Cancer. Eur Urol 2018;74(5):575-82. doi: 10.1016/j.eururo.2018.06.033 [published Online First: 2018/07/17]

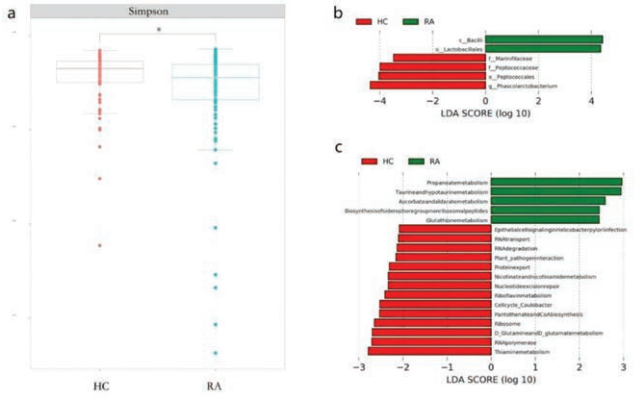


Figure 1 **(a)** Comparison of Simpson index between HC and RA groups was shown using boxplot. **(b)** LEfSe was used to detect difference in Flora according to RA and HC. **(c)** LEfSe was used to detect difference in Flora functions according to RA and HC. Pathway differences plot as LDA score (log 10). Bars to the right of zero represent bacterial functions enriched in the RA, and bars to the left of zero represent bacterial functions in HC. *P <0.05.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1944

AB0825 JAK2 (V617F) MUTATION AND ASSOCIATION TO IMMUNE MEDIATED DISEASES. STUDY OF 130 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL

C. Álvarez-Reguera[1], L. Sanchez-Bilbao[1], A. Batlle-López[2], S. Fernández López[2], M. Á. González-Gay[1], R. Blanco[1]. [1]*Hospital Universitario Marqués de Valdecilla, Rheumatology, Santander, Spain*; [2]*Hospital Universitario Marqués de Valdecilla, Hematology, Santander, Spain*

Background: Janus Kinases (JAK) are tirosin-kinases that can promote cytokine production in immune and hematopoietic cells. The JAK-2 (V617F) mutation is the most frequently detected mutation in myeloproliferative neoplasms (MPN) which include essential thrombocythemia (ET), polycythemia vera (PV), primary myelofibrosis (PMF) and undifferenciated MPN. JAK-2 (V617F) mutation displays a pro-inflammatory phenotype that may be associated to a higher risk of immune mediated diseases (IMID), thromboembolic complications or other cancers **(1-3).**

Objectives: To evaluate the presence of **a)** IMID (rheumatic and non-rheumatic), **b)** cancer and, **c)** Deep vein thrombosis/ Venous thromboembolism (DVT/VTE) events in a cohort of patients with a positive JAK-2 (V617F) mutation.

Methods: We studied all the patients diagnosed with a positive JAK-2 (V16F) mutation in a single University Hospital between January, 2004 and December, 2019.

Results: The study included 130 patients (73 men/57 women; mean age, 70.1±14.5 years). They were diagnosed of ET (n=64, 49.2%), PV 46 (35.4%), undifferentiated MPN (n=12, 9.2%) and PMF (n=8, 6.1%). Of these patients, 54 (41.5 %) (44 non rheumatic and 10 rheumatic) were diagnosed with at least one IMID, 46 (35.4%) with other cancer different of MPN and 36 (27.7%) with DVT/VTE events. (Table 1**/**Figure 1**).**

Conclusion: Due to its prevalence and potential complications, IMID should be taken into consideration when a patient is diagnosed with a positive JAK-2 (V617F) mutation.

REFERENCES:

[1] Perner F, et al. Cells. 2019;8:854.
[2] Xu Q, et al. Clin Rheumatol. 2020 Jul 16.

[3] Hasselbalch HC, et al. 2020; 23;17(1):248.

Table 1. Associated diseases in 130 patients with JAK2 (V617F) mutation. Data are n (%)

Myeloproliferative neoplasms (MPN)	**130 (100)**
Essential thrombocythemia (ET)	64 (49.2)
Polycythemia vera (PV)	46 (35.4)
Undifferentiated MPN	12 (9.2)
Primary myelofibrosis (PMF)	8 (6.5)
Non-rheumatic IMID	**44 (33.8)**
Diabetes mellitus	22 (50)
Asthma	10 (22.7)
Psoriasis	6 (13.6)
Crohn disease	2 (4.5)
Autoimmune thyroiditis	2 (4.5)
Rheumatic IMID	**10 (7.7)**
Rheumatoid arthritis	4 (40)
Polymyalgia rheumatica	3 (30)
Sjögren disease	1 (10)
Antiphospholipid syndrome	1 (10)
Adult-onset Still's disease	1 (10)
Malignancies different of MPN	**44 (33.8)**
Solid tumours // Hematologic malignancies // Skin cancer	22 (50) // 13 (29.5) // 9 (20.4)
Deep vein thrombosis/Venous thromboembolism (DVT/VTE) events	35 (26.9)

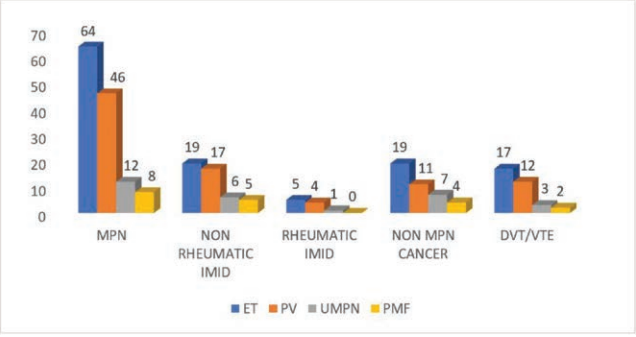


Figure 1. Associated diseases accordingly to the subtype of Myeloproliferative neoplasm. Data are n.

ABBREVIATIONS: DVT/VTE: Deep vein thrombosis/ Venous thromboembolism. ET: Essential Thrombocythemia, IMID: Immune Mediated Diseases, PV: Polycythemia Vera; MPN: Myeloproliferative Neoplasms; PMF: Primary myelofibrosis; UMPN: Undifferenciated myeloproliferative neoplasms.

Disclosure of Interests: Carmen Álvarez-Reguera: None declared, Lara Sanchez-Bilbao: None declared, Ana Batlle-López: None declared, Sara Fernández López: None declared, Miguel Á. González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi and MSD., Grant/research support from: Abbvie, MSD, Janssen and Roche, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Lilly and MSD., Grant/research support from: Abbvie, MSD and Roche

DOI: 10.1136/annrheumdis-2021-eular.2161

AB0826 IMPORTANCE OF PRECONCEPTION CARE AND PLANNING FOR PREGNANCY IN WOMEN OF CHILDBEARING AGE COMPLICATED WITH CONNECTIVE TISSUE DISEASES

H. Shimada[1], R. Wakiya[1], M. Mahmoud Fahmy Mansour[1], S. Nakashima[1], M. Kato[1], T. Miyagi[1], K. Sugihara[1], Y. Ushio[1], T. Kameda[1], H. Dobashi[1].
[1]Kagawa University, Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa, Japan

Background: Previous reports showed that connective tissue disease (CTD) have a high risk for adverse pregnancy outcomes (APOs) such as preterm birth, light-for-date, or preeclampsia[1)]. It was revealed that these APOs were associated with high disease activity or treatment agents, particularly in glucocorticoid[2)]. Some patients, who have no or insufficient preconception care and became unplanned pregnant, exacerbate the underlying disease, and lead to disappointing pregnancy outcomes. Therefore, preconception care and planning for pregnancy is very important to control disease activities and manage the appropriate treatment agents, including glucocorticoid, immunosuppressants, biologics, hydroxychloroquine, and anticoagulants[3)].

Objectives: We investigate whether the presence or absence of preconception care before pregnancy affects clinical disease course and pregnancy outcomes.
Methods: We examined 200 CTD women who delivered their newborns in our institution from March 2006 to January 2021. We analyzed the association between preconception care and the clinical course of underlying diseases during pregnancy or pregnancy outcomes.
Results: Of all 200 cases, 133 (55.9%) cases had preconception care in our institution, while the others had no or insufficient preconception care. We showed the comparison of treatment agents and pregnancy outcomes between the cases with and without preconception care in Table 1. There was no significant difference in the rate of glucocorticoid use and the mean prednisolone dose during pregnancy between these two groups. However, the rate of increased dose of glucocorticoid or pulse therapy was significantly higher in the cases without preconception care. As for pregnancy outcomes, there was no significant difference in the live birth rate. On the other hand, the gestational weeks at delivery were significantly shorter, and the rate of preterm birth was higher in the cases without preconception care. In addition, the rate of the hospitalization of neonatal intensive care unit (NICU) was also significantly higher in the cases without preconception care.
Conclusion: We revealed that preconception care before pregnancy reduced the need for intensified treatment such as increasing dose of glucocorticoid or pulse therapy. The rate of preterm birth and NICU hospitalization was also shown to decrease. Therefore, it is important for our rheumatologists to provide an appropriate preconception care for CTD women of childbearing age and to make a plan for pregnancy.

REFERENCES:

[1] Tsuda S, Sameshima A, Sekine M, Kawaguchi H, Fujita D, Makino, et al. Mod Rheumatol 2019:24;1-10.
[2] Clowse ME, Magder LS, Petri M. J Rheumaotol 2011;38:1012-1016.
[3] Sammaritano LR, Bermas BL, Chakravarty EE, Chambers C, Clowse MEB, Lockshin MD, et al. Arthritis Care Res 2020;72:461-488.

Table 1. Comparison of treatment agents and pregnancy outcomes between the cases with and without preconception care

	Preconception care (+) (n=113)	Preconception care (-) (n=89)	P value
Treatment agents during pregnancy			
Glucocorticoid use (n (%))	64 (56.6)	50 (56.2)	1.00
Mean glucocorticoid dose (mg/day)	6.3±3.9	8.4±6.1	0.09
Dose-up of glucocorticoid (n (%))	11 (9.7)	26 (29.2)	<0.01*
Glucocorticoid pulse therapy (n (%))	0 (0)	8 (9.0)	0.01*
Immunosuppressant (n (%))	14 (12.5)	4 (4.5)	0.08
Hydroxychloroquine (n %))	7 (6.2)	6 (6.7)	1.00
Anticoagulant therapy (n (%))	21 (18.8)	16 (17.8)	1.00
Pregnancy outcome			
Spontaneous abortion (n (%))	8 (7.1)	6 (6.7)	1.00
Live birth (n (%))	100 (88.5)	78 (87.6)	1.00
Gestational weeks at delivery (week)	38.7±1.4	37.3±3.5	0.01*
Birth weight of newborn (gram)	2888.8±453.7	2678.4±732.6	0.25
Adverse pregnancy outcomes (n (%))	26 (26.0)	28 (35.0)	0.20
Preterm birth (n (%))	5 (5.0)	19 (23.8)	<0.01*
Light-for-date (n (%))	10 (10.0)	9 (11.3)	0.81
Hypertensive disorder (n (%))	5 (5.0)	8 (10.0)	0.25
NICU management (n (%))	13 (13.0)	24 (30.0)	<0.01*

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2479

AB0827 SERUM NESPHATIN-1 IN PATHOGENESIS RHEUMATOID ARTHRITIS

T. Kvlividze[1], V. Polyakov[1], B. Zavodovsky[1,2], Y. Polyakova[2], L. Seewordova[2], E. Papichev[2], Y. Akhverdyan[2]. *[1]Volgograd State Medical University, Laboratory Diagnostics, Volgograd, Russian Federation*; *[2]Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», Treatment and Prevention of Joint Disease Laboratory, Volgograd, Russian Federation*

Background: Interest in highly specialized tissue cytokines contributed to the discovery of new biologically active molecules. Nesfatin-1 (NF) - discovered in 2006 as an anorexigenic factor. NF-1 is believed to be involved in the regulation of energy homeostasis by regulating appetite and water intake. The role of NF-1 in the pathogenesis of inflammatory diseases is poorly understood. Recently, studies have found a relationship between an increased level of NF-1 and inflammatory markers in various pathologies.
Objectives: Study of the level of nesfatin-1 in the blood serum of healthy people, determination of the correlation between the level of NF-1 with the severity of clinical symptoms and classic markers of inflammation in patients with RA.

Methods: 120 persons were examined: 90 patients with RA and 30 healthy people. All patients underwent a complete clinical and laboratory examination. Plasma NF-1 levels were determined using commercial test systems (RaiBiotech, cat # EIA-NESF) according to the manufacturer's instructions. Patients with various forms of RA were comparable in age to the group of healthy individuals. Statistical processing of clinical examination data was carried out using the "STATISTICA 10.0 for Windows" software package. Quantitative data were processed statistically using the parametric Student's t-test, qualitative data using the non-parametric chi-square test. The significance of differences between groups was determined using analysis of variance. The results were considered statistically significant at $p < 0.05$.

Results: The average level of NF-1 in blood serum in healthy individuals was 31.79 ± 3.21 ng / ml ($M \pm \sigma$). The level of normal NF-1 values in healthy individuals, defined as $M \pm 2\sigma$, ranged from 25.3 to 37.83 ng / ml. There was no significant difference in the levels of circulating NF-1 and BMI in healthy individuals and patients with RA ($p > 0.05$). The inverse relationship of a lower level of NF-1 with an increase in BMI was not significant.

Group 1 (66 patients with RA) with increased serum NF-1 levels (> 37.83 ng / ml), and group 2 (44 patients) with normal values (<37.83 ng / ml). A high level of NF-1 was characteristic for patients with high activity according to DAS28, RF seropositive, ACCP-positive, with extra-articular manifestations, who had been ill for 10 years or more. A reliable relationship between the level of NF-1 in the blood serum and laboratory parameters of RA activity - ESR, CRP, was shown, and secondary synovitis was more common. Our data show a direct correlation between the NF-1 level of the pro-inflammatory markers of RA.

Conclusion: The positive correlation between the level of NF-1 and classical markers of inflammation, such as CRP and ESR, confirms the involvement of NF-1 in the pathophysiology of inflammation in RA. This is also evidenced by the correlation of a high level of NF-1 in the blood serum with a more severe clinical picture of RA. It is known that NF-1 can promote the release of pro-inflammatory cytokines such as interleukin-8 (IL-8), interleukin-6 (IL-6), and macrophage inflammatory protein-1a (MIP-1a) in the chondrocytes of RA patients.

It is necessary to further study the role of NF-1 in the pathogenesis of systemic inflammatory reactions and the possibility of targeting pro-inflammatory cytokines, the possibility of regulating the level of NF-1 by drugs.

REFERENCES:

[1] Kvlividze T.Z., Zavodovsky B.V., Akhverdyan Yu.R. Kvlividze T.Z., Zavodovsky B.V., Akhverdyan Yu.R., Polyakova Yu.V., Sivordova L.E., Yakovlev A.T., Zborovskaya I.A. Serum nesfatin -1 as a marker of systemic inflammation in rheumatoid arthritis. Klinicheskaya Laboratornaya Diagnostika (Russian Clinical Laboratory Diagnostics). 2019; 64 (1): 53-56 (in Russ.).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2503

AB0828 INFLUENCE OF SEASONAL VARIATIONS ON EMERGENCY RHEUMATOLOGY CONSULTATIONS

Z. El Ouali[1], R. Assadi[1], S. Lahrichi[1], K. Nassar[1], S. Janani[1]. [1]*University Hospital of Ibn Rochd, Department of Rheumatology, Casablanca, Morocco*

Background: The influence of the seasons on the onset of diseases has been demonstrated in epidemiological studies, particularly in infectious pathologies. In rheumatology, recent studies have suggested the role of seasons in the disease activity of rheumatoid arthritis (1,2). However, no epidemiologic data exist on the influence of seasons in urgent rheumatology consultations, all causes combined.

Objectives: To study the influence of seasonal variations on urgent rheumatology consultations received in the Department of Rheumatology of the University Hospital of Ibn Rochd in Casablanca.

Methods: We conducted a retrospective study on the 2019 emergency consultations register of the Department of Rheumatology of the University Hospital of Ibn Rochd, Casablanca. The seasons were divided as follows: winter from December to February, spring from March to May, summer from June to August, and fall from September to November. The studied parameters were age, sex, reasons for consultation, affected joints, and diagnoses.

Results: 407 emergency consultations were carried out, with an average patient age of 50.7 years (range 14 - 88), and a sex ratio M/F of 0.4. The characteristics of the patients throughout the seasons is summed up in Table 1. The distribution of consultations by season was as follows: 29.5% in winter, 26.3% in spring, 25.4% in summer, and 18.8% in fall. The average age of the consultants depending on the season was homogeneous. The most frequent reasons for emergency consultation were respectively back pain (48.6%), polyarthralgia (23.1%), followed by arthritis (12.0%). Back pain slightly predominant in the cold seasons (fall, winter). Polyarthralgias had a winter peak. Arthritis presented a bimodal distribution in seasons of transition (spring, fall). The knees and lumbar spine were the most frequently involved joints throughout the year, with no major differences between the seasons. The most frequent diagnoses over the year were degenerative (51%), inflammatory (8.6%), infectious (7.3%), metabolic (6.7%), and tumor (2.1%) pathologies, respectively. %). Osteoarthritis flares were less frequent in spring and summer. Inflammatory pathologies have not experienced a seasonal peak. Gout flares and infectious pathologies peaked in the spring. Finally, tumor pathologies peaked in the fall.

Conclusion: Seasonal variations seem to have an impact on the distribution of the reasons for consultation as well as the diagnoses made in the context of the rheumatologic emergencies. The cold seasons seemed to favor the onset of back pain and polyarthralgia, while the seasons of transition were conducive to the development of arthritis.

REFERENCES:

[1] Mori H, Sawada T, Nishiyama S, Shimada K, Tahara K, Hayashi H, et al. Influence of seasonal changes on disease activity and distribution of affected joints in rheumatoid arthritis. BMC Musculoskelet Disord. 2019 Dec;20(1):30.

[2] Azzouzi H, Ichchou L. Seasonal and Weather Effects on Rheumatoid Arthritis: Myth or Reality? Pain Research and Management. 2020 Sep 7;2020:1–5.

Table 1. Characteristics of the patients throughout the seasons

	Winter n = 120 (29.5%)	Spring n = 107 (26.3%)	Summer n = 104 (25.4%)	Fall n = 76 (18.8%)	Total n = 407 (100%)
Age	51,2 (16 – 86)	51,6 (14 – 84)	51,3 (16 – 88)	48 (16 – 79)	50,7 (14 – 88)
Sex-ratio M/F	0,25	0,44	0,6	0,36	0,4
Reasons for consultation					
Arthritis (%)	8,3	15	11,5	14	12,0
Polyarthritis (%)	30	21,5	20,2	18,5	23,1
Back pain (%)	51.7	44.9	45.2	54.0	48.6
Joint involvement					
Shoulder (%)	33,3	21,5	22,1	22,4	27,2
Hand (%)	16,7	20,0	15,4	13,2	16,5
Knee (%)	49,2	41,0	48,1	46,1	46,2
Ankle (%)	13,3	14,0	13,5	14,5	13,8
Cervical spine (%)	6,0	10,3	9,6	7,9	8,4
Lumbar spine (%)	44,2	39,3	38,0	47,0	41,8
Diagnoses					
Osteoarthritis (%)	53,4	43,9	47,5	56,8	50,2
Knee osteoarthritis (%)	31,5	22,8	28,8	38,6	30,0
Lumbar osteoarthritis (%)	28,8	22,8	30,5	31,8	28,3
Septic (%)	2.7	7.0	1.7	2.3	3.4
Gout (%)	5.5	10.5	5.1	6.8	6.7
Inflammatory (%)	9.6	8.8	6.7	6.8	9.9
Tumor (%)	1.3	1.8	1.7	4.5	2.1

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2714

AB0829 WHAT ARE THE DIFFERENCES BETWEEN YOUNG AND ELDERLY SUBJECTS IN URGENT RHEUMATOLOGY CONSULTATIONS?

R. Assadi[1], Z. El Ouali[1], S. Lahrichi[1], K. Nassar[1], S. Janani[1]. [1]*University Hospital of Ibn Rochd, Department of Rheumatology, Casablanca, Morocco*

Background: The pattern of rheumatological diseases shows significant differences depending on age. It is commonly admitted that inflammatory rheumatic diseases is the prerogative of young people (1), while degenerative pathology is more important in older ages (2). In the context of the emergency, little epidemiological data exist about the differences between young and old populations.

Objectives: To study the influence of age on emergency rheumatology consultations received in the Department of Rheumatology of the University Hospital of Ibn Rochd.

Methods: We conducted a retrospective study on the 2019 emergency consultations register of the Department of Rheumatology of the University Hospital of Ibn Rochd, Casablanca. Patients were divided in 2 groups: young subjects included patients aged less than 65 years, and the elderly subjects included people aged 65 and above. The studied parameters were gender, medical coverage, socio-professional category, reasons for consultation, joint involvement, duration of symptoms, diagnoses, and treatments.

Results: 407 emergency consultations were carried out, including 81 in the elderly (19.9%) and 326 in young subjects (80.1%). The characteristics are summed up in Table 1. Although we noted a female predominance in both groups, men were more represented in the elderly group. Radiculalgia was a

more frequent reason for consultation in the elderly population, while arthralgia was more frequent in the young population. Young subjects more frequently had peripheral joints complaints. Degenerative and tumor pathologies were more common in the elderly population, while inflammatory, septic, and tendon pathologies were more prominent in the young population. Regarding treatments, non-steroidal anti-inflammatory drugs were more prescribed in young subjects, while the other treatments had a homogeneous distribution in the two groups.

Conclusion: In our emergency unit, the epidemiological distribution of our patients according to age matches the general epidemiological characteristics of rheumatological pathologies: inflammatory causes are more frequent in young ages, while degenerative pathologies are found at a later age.

REFERENCES:

[1] Kobak S, Bes C. An autumn tale: geriatric rheumatoid arthritis. Therapeutic Advances in Musculoskeletal. 2018 Jan;10(1):3–11.

[2] Loeser RF. The Role of Aging in the Development of Osteoarthritis. Trans Am Clin Climatol Assoc. 2017;128:44–54.

Table 1. Patients' characteristics depending on age

	≥ 65 years (81 cases) 19,9%	< 65 years (326 cases) 80,1%
Sex-ratio M/F	0,50	0,38
Social coverage		
Public health assistance scheme	32 (39,5%)	122 (37,42%)
Public/Private insurance	21 (25,92%)	91 (27,91%)
Without	28 (34,57%)	113 (34,66%)
Profession	Précisé = 45	Précisé = 162
Without	36 (80%)	104 (64,2%)
Retirees	7 (15,55%)	4 (2,47%)
Farmer	1 (2,22%)	1 (0,62%)
Intermediate professions	1 (2,22%)	18 (11,11%)
Higher intellectual professions	0	12 (7,41%)
Employees	0	9 (5,55%)
Traders and craftsmen	0	9 (5,55%)
Workers	0	5 (3,09%)
Reason for consultation		
Back pain	35 (43,2%)	137 (48,15%)
Radiculalgia	22 (27,16%)	55 (16,87%)
Arthralgias	34 (41,97%)	165 (50,61%)
Arthritis	10 (12,34%)	37 (11,35%)
Joint involvement		
Axial	41 (50,61%)	170 (52,15%)
Peripheral	53 (65,43%)	248 (76,07%)
Duration of symptoms		
Acute (< 3 weeks)	21 (25,92%)	73 (22,39%)
Chronic (≥ 3 weeks)	60 (74,08%)	253 (77,61%)
Diagnoses		
Osteoarthritis	30 (58,82%)	89 (48,9%)
Knee osteoarthritis	21 (41,17%)	50 (27,47%)
Lumbar osteoarthritis	16 (31,37%)	44 (24,17%)
Septic	2 (3,92%)	11 (6,04%)
Metabolic	6 (13,35%)	9 (4,94%)
Inflammatory	1 (1,96%)	22 (12,08%)
Tumor	3 (5,88%)	2 (1,09%)
Tendinopathies	3 (9,68%)	29 (15,93%)
Treatments		
Analgesics	47 (71,21%)	155 (63,52%)
NSAIDs	19 (28,78%)	118 (48,36%)
Corticosteroids	1 (1,51%)	2 (0,82%)
Local treatments	18 (27,27%)	72 (29,5%)
Symptomatic slow-acting drugs	19 (28,78)	49 (20,08%)
DMARDs	0 (0%)	2 (0,82%)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2734

AB0830

ADVERSE PERINATAL OUTCOMES AND CONGENITAL DEFECTS IN MEXICAN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES

R. A. Rodriguez Chavez[1], C. M. Skinner Taylor[1], L. Pérez Barbosa[1], G. A. López-Uriarte[2], E. Barriga-Maldonado[1], G. Figueroa-Parra[1], I. Perez-Onofre[1], A. Elizondo-Plazas[2], L. G. Espinosa Banuelos[1], R. Moyeda Martinez[1], A. Y. Lujano Negrete[1], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Rheumatology Service, Monterrey, Mexico*; [2]*Hospital Universitario Dr. José Eleuterio González, Genetics Department, Monterrey, Mexico*

Background: Pregnancy in women with autoimmune rheumatic diseases (ARD) is associated with an increase in the risk of adverse perinatal outcomes and birth defects. Many factors have been attributed to these including medication employed and maternal autoantibodies. The national prevalence of congenital anomalies in newborns in Mexico is estimated to be 73.9 per 10,000 births but the rate of these in Mexican women with ARD is unknown.

Objectives: This study aims to describe the frequency of adverse perinatal outcomes and congenital defects in Mexican women with ARD.

Methods: We performed a descriptive and prospective study that included all pregnant patients with ARDs from the clinic of pregnancy and rheumatic diseases in the University Hospital "Dr. José Eleuterio González" who gave birth between February 2019 to November 2020. Demographic information, pregnancy outcome, and congenital defects were prospectively evaluated. Congenital defects were clinically confirmed by a clinical geneticist.

Results: A total of 40 women were taken in the final analyses. The ARD diagnosis is shown in graphic 1. Rheumatoid arthritis was the most frequent diagnosis that had an adverse perinatal outcome with 4 (40%) and congenital defects in 2 (40%). No complications or birth defects were reported in 25 (62.5%). The adverse perinatal outcome was reported in 10 (25%) women and congenital defects in 5 (12.5%). The most frequent adverse perinatal outcomes were preterm birth 6 (15%) and the second most frequent miscarriage 3 (7.5%) (Table 1 below).

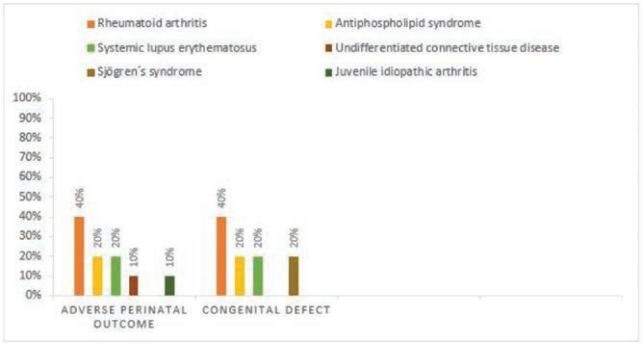
Conclusion: We found a high frequency (12.5%) of adverse perinatal outcomes and congenital defects in Mexican women with ARD. Multidisciplinary groups and clinics are needed to adequately serve this complex population and reduce morbidity and mortality. A multidisciplinary approach before, during, and after pregnancy in patients with ARD may improve morbidity and mortality.

REFERENCES:

[1] Vinet, E., Bernatsky, S. (2017). Outcomes in Children Born to Women with Rheumatic Diseases. Rheum Dis Clin N Am. http://dx.doi.org/10.1016/j.rdc.2016.12.006.

[2] Krishnan AN, Sable CA, Donofrio MT.(2008). Spectrum of fetal echocardiographic findings in fetuses of women with clinical or serologic evidence of systemic lupus erythematosus. J Matern Fetal Neonatal Med. 21(11):776–82.

[3] NAVARRETE HERNANDEZ, Eduardo et al. Prevalencia de malformaciones congénitas registradas en el certificado de nacimiento y de muerte fetal: México, 2009-2010. *Bol. Med. Hosp. Infant. Mex.* [online]. 2013, vol.70, n.6, pp.499-505.



Graphic 1. Percentage of adverse perinatal outcomes and congenital defects due to rheumatic disease.

Table 1. Frequency and percentages of adverse perinatal outcomes and congenital defects.

	Adverse perinatal outcome (n=10) 25%	Congenital defects (n=5) 12.5%
Preterm birth	6 (15%)	-
Miscarriage	3 (7.5%)	-
Stillbirth	1 (2.5%)	-
Congenital heart disease*	-	1 (2.5%)
Congenital cardiac block with pacemaker placement	-	1 (2.5%)
Krabbe´s disease	-	1 (2.5%)
Preauricular appendix	-	1 (2.5%)
Diabetic fetopathy	-	1 (2.5%)

*Tetralogy of Fallot

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3270

AB0831

FREQUENCY OF RENAL CRISIS IN PATIENTS WITH SYSTEMIC SCLEROSIS: NEW DATA FROM A CHINESE COHORT AND A SYSTEMIC REVIEW WITH META-ANALYSIS

D. Xu[1], J. He[2], T. LI[1], R. Mu[1,1,1]. [1]*Peking University Thrid Hospital, Department of Rheumatology and Immunology, Beijing, China*; [2]*The Third People's Hospital of Datong, Department of Rheumatology and Immunology, Datong, China*

Background: Scleroderma renal crisis (SRC) is a rare but life-threatening complication in SSc, which defined as malignant hypertension and progressive renal failure [1]. Previous reports of the prevalence for scleroderma renal crisis (SRC) show variable outcomes.
Objectives: We aim to find out the prevalence for SRC in Chinese, and conduct a meta-analysis to assess the prevalence of SRC in worldwide and investigate possible factors of variability.
Methods: We evaluated the prevalence for SRC and compared the clinical characteristics in SSc patients with or without SRC. A systematic review on the prevalence of SRC was carried out in PubMed, Embase and Cochrane. Meta-analysis was performed using available data on the prevalence for SRC.
Results: 302 patients were enrolled in PKUPH-SSc cohort and the prevalence of SRC was 4.97%. In our cohort, SRC was found in 3.60% limited cutaneous SSc (lcSSc) and 7.75% diffused cutaneous SSc (dcSSc) patients. Twenty-nine studies including a total population of 22686 SSc patients were analyzed in the meta-analysis. The overall pooled prevalence of SRC was 4.0%, but heterogeneity among the studies was substantial (I^2=86.1%, P <0.00001). Meta-regression revealed that subtype of SSc and geographic factors partially explained this heterogeneity. Sub-group analyses demonstrated that the prevalence of SRC in dcSSc and lcSSc were 9.0% and 2.0%. The SRC prevalence in SSc was 3.0% in Asia, 5.0% in Europe, and 3.0% in North America, respectively.
Conclusion: Data on our new cohort showed the prevalence of SRC was around 5% in China, and meta-analysis confirmed that the prevalence of SRC varies among centers. The marked heterogeneity of SRC prevalence was partially explained by subtype of SSc and geographic origin of patients.
REFERENCES:
[1] Woodworth TG, Suliman YA, Li W, Furst DE, Clements P (2016) Scleroderma renal crisis and renal involvement in systemic sclerosis. Nat Rev Nephrol 12 (11):678-91.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3456

AB0832

PREVALENCE OF OCULAR DISEASES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE OBSERVATIONAL STUDY IN A TERTIARY HOSPITAL IN TAIWAN

J. H. Kao[1], T. Y. Lan[1], C. H. Lu[1], C. Y. Shen[1], K. J. LI[1], S. C. Hsieh[1]. [1]*National Taiwan University Hospital, Department of Internal Medicine, Division of Allergy, Immunology and Rheumatology, Taipei, Taiwan, Republic of China*

Background: Systemic lupus erythematosus (SLE) could affect multiple parts of the eye. (1,2) Also, there is risk of ocular toxicity associated with treatment, such as hydroxychloroquine.(3) Early diagnosis is essential to avoid major ocular complications. However, complaints of eye discomfort may be vague, and various presentations may pose challenges on rheumatologists. Knowing the real-world prevalence of ocular problems in patients with SLE is important and helpful, yet this has been less common to be reported.
Objectives: To describe the prevalence of various ophthalmologic diagnoses in patients with SLE.
Methods: This is a retrospective observational study conducted in a tertiary hospital in Taipei, Taiwan. Patients diagnosed with SLE in the period between 1st Jan, 2002 and 31th Dec, 2015 and evaluated by ophthalmologists in 2 years before 29th Jan, 2021 were included. Demographic and clinical data, and ophthalmologic diagnoses were recorded by chart review.
Results: A total of 121 patients were included, and 118 (97.5%) were female. Average age was 46.2 years [standard deviation (SD) 11.4 years] upon ophthalmologic evaluation, and average duration suffering from lupus was 11.6 years (SD 3.3 years). Keratoconjunctivitis sicca (n = 48, 39.7%), myopia (n = 39, 32.2%), and cataract (n = 21, 17.4%) were the most common findings. It was also noted that suspicious finding of hydroxychloroquine retinal toxicity was found in 12 patients (9.9% of total patients). Also, two patients had lupus retinopathy, and another two were diagnosed with cytomegalovirus retinitis. In addition, glaucoma was diagnosed in 9 patients (7.4%), which seemed to be higher than the general population.
Conclusion: Higher prevalence of different ocular problems is noted in this cohort of SLE patients. Keratoconjunctivitis sicca was the most common ocular diagnosis, which is consistent with literature. However, high rates of myopia, cataract, glaucoma, and suspicious hydroxychloroquine retinal toxicity were also found. Above result warrants more aggressive ophthalmologic evaluation in SLE patients. More research on the association of lupus and different ocular diseases is needed in the future.
REFERENCES:
[1] Silpa-archa S, Lee JJ, Foster CS. Ocular manifestations in systemic lupus erythematosus. Br J Ophthalmol. 2016 Jan;100(1):135–41.
[2] Sivaraj RR, Durrani OM, Denniston AK, Murray PI, Gordon C. Ocular manifestations of systemic lupus erythematosus. Rheumatology (Oxford). 2007 Dec;46(12):1757–62.
[3] Jorge A, Ung C, Young LH, Melles RB, Choi HK. Hydroxychloroquine retinopathy - implications of research advances for rheumatology care. Nat Rev Rheumatol. 2018;14(12):693–703.

Table 1. Demographic data and ophthalmologic diagnosis of patients with systemic lupus erythematosus (N = 121)

Variable	n (% of N)
Age (years) average (SD)	46.2 (11.4)
Disease duration average (SD)	11.6 (3.3)
Female sex	118 (97.5)
Chronic medical disease	
Hypertension	28 (23.1)
Diabetes mellitus	4 (3.3)
Dyslipidemia	7 (5.8)
Cancer	3 (2.5)
End-stage renal disease	1 (0.8)
Ophthalmologic diagnosis	
Keratoconjunctivitis sicca	48 (39.7)
Myopia	39 (32.2)
Cataract	21 (17.4)
Glaucoma	9 (7.4)
Suspicious retinopathy related to HCQ	12 (9.9)
Unspecified retinopathy	5 (4.1)
Lupus retinopathy	2 (1.7)
CMV retinitis	2 (1.7)
Central retinal vein thrombosis	1 (0.8)
Retinal break	1 (0.8)
Optic neuritis	1 (0.8)
Vitreal hemorrhage	1 (0.8)
Myodesopia	4 (3.3)
Scleritis	1 (0.8)

SD, standard deviation; HCQ, hydroxychloroquine; CMV, cytomegalovirus.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3746

AB0833

HOSPITAL ADMISSIONS FOR RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY POLYARTHROPATHIES IN THE BRAZILIAN PUBLIC HEALTH SYSTEM

A. Dal Pra Wendt[1], F. Milene Cardozo[1]. [1]*Feevale University, Institute of Health Sciences, Novo Hamburgo, Brazil*

Background: Rheumatoid arthritis is an idiopathic autoimmune disease that is characterized by symmetrical peripheral polyarthritis. The disease leads to the destruction of joints due to erosion of both bone and cartilage. The other inflammatory polyarthropathies are a group composed of 61 diseases, according to the International Classification of Diseases (ICD-10). Drug treatment is carried out through outpatient follow-up, with no need for hospitalization in mild and / or controlled cases. When surgical treatment is recommended or there are complications from rheumatoid arthritis or other inflammatory polyarthropathies, hospitalization is indicated. In addition, Brazil has a broad public health system, called the Unified Health System (UHS), responsible for most health procedures carried out at the national level, especially with regard to the socioeconomically vulnerable population.
Objectives: To investigate the number of hospital admissions for rheumatoid arthritis and other inflammatory polyarthropathies in UHS during the past three years.
Methods: This is a quantitative and retrospective survey based on the data available on the website of the Department of Informatics of the Brazilian Unified Health System. The data are freely accessible and public domain. Information was collected about the period between December 2017 and November 2020, referring to the number of hospitalizations for rheumatoid arthritis and other inflammatory polyarthropathies in all five regions that make up Brazil.
Results: The number of hospitalizations for rheumatoid arthritis and other inflammatory polyarthropathies fluctuated, between December 2017 and November 2020, from 1083 to 1311 per month, with an average of 1184 and a total of 38228 hospitalizations over the three years analyzed. Throughout the national territory, the region with the least monthly admissions was the central-west (which comprises the states of Mato Grosso, Mato Grosso do Sul, Distrito Federal and Goiás), with 2562 total admissions and an average of 71.1 monthly admissions.

In contrast, the region with the highest number of cases was the southeastern region (where the states of Espírito Santo, Minas Gerais, São Paulo and Rio de Janeiro are located), with a total of 13173 hospitalizations and a monthly average of 365.9, representing 34,4% of hospitalizations in the country. Such data is in line with the Brazilian demography, since the central-west region is the second least inhabited (with 16.09 million inhabitants) and the southeastern region is the most densely inhabited (with 80.35 million inhabitants). The number of monthly hospitalizations, which remained above 1000 from the first month analyzed (December 2017) until February 2020, dropped to 990 in March of the same year and 651 in April, maintaining an average of 678.2 in next seven months.

Conclusion: It is concluded that the number of hospitalizations for rheumatoid arthritis and other inflammatory polyarthropathies in Brazil dropped significantly between March and April 2020, a period that coincides with the beginning of the COVID-19 pandemic in the country, possibly as a result both of the changes in the Brazilian medical care model (in relation to the requirements for hospitalization) and as a result of the lower demand by individuals for hospitals due to fear of contamination by the new coronavirus.

REFERENCES:

[1] BATES, B. **Propedêutica Médica**. 12ª ed. Rio de Janeiro: Guanabara Koogan, 2018.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4053

Validation of outcome measures and biomarkers

AB0834

DEVELOPMENT OF A CONCEPTUAL FRAMEWORK FOR A PATIENT REPORTED OUTCOME MEASURE TO CAPTURE PATIENTS' PERCEPTIONS OF GLUCOCORTICOID THERAPY DURING TREATMENT FOR RHEUMATIC DISEASES

S. Bridgewater[1,2], J. Dawson[3], M. Ndosi[1,2], R. J. Black[4,5], J. T. L. Cheah[6], E. Dures[1,2], N. Ghosh[7], E. A. Hoon[8], I. Navarro-Millan[7], D. Pearce-Fisher[7], P. Richards[2], C. Ruediger[8], C. Silverthorne[1,2], J. Tieu[8], S. Mackie[9,10], S. Goodman[7], C. Hill[8], J. Robson[1,11]on behalf of Outcome Measures in Rheumatology (OMERACT) Glucocorticoid Working Group. *[1]University of the West of England - UWE Bristol, Faculty of Health and Applied Sciences, Bristol, United Kingdom*; *[2]University Hospitals Bristol and Weston NHS Foundation Trust, Academic Rheumatology, Bristol, United Kingdom*; *[3]University of Oxford, Nuffield Department of Population Health, Oxford, United Kingdom*; *[4]The University of Adelaide, Discipline of Medicine, Adelaide, Australia*; *[5]Royal Adelaide Hospital, Rheumatology Unit, Adelaide, Australia*; *[6]University of Massachusetts Medical School, Department of Medicine, Division of Rheumatology, Worcester, United States of America*; *[7]Hospital for Special Surgery, Division of Rheumatology, New York, United States of America*; *[8]The Queen Elizabeth Hospital, Department of Rheumatology, Adelaide, Australia*; *[9]Leeds Teaching Hospitals NHS Trust, Leeds Biomedical Research Centre, Leeds, United Kingdom*; *[10]University of Leeds, Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[11]University Hospitals Bristol and Weston NHS Foundation Trust, Academic Rheumatology, Bristol, United Kingdom*

Background: Glucocorticoids (GCs) are a key treatment for the autoimmune rheumatic diseases; however, they produce numerous physical and psychological side effects.[1] The Outcome Measures in Rheumatology (OMERACT) Glucocorticoid Working Group have identified that there are no Patient Reported Outcome Measures (PROMs) for assessing the impact of systemic GC therapy across multiple rheumatic diseases from the patient's perspective.[2,3]

Objectives: The aim is to explore the impact of GCs on the symptoms and health-related quality of life of adults with rheumatic inflammatory diseases, to inform items for inclusion in a PROM. Key considerations will include patient perceptions of GC therapy at diagnosis and over the course of treatment, for use in future randomised controlled trials or in clinical practice.

Methods: An international steering committee comprising researchers, rheumatology clinicians, methodologists and patient partners in the UK, Australia and USA developed an initial conceptual framework informed by a review of the literature. Semi-structured interviews were conducted in each country with patients who had an autoimmune rheumatic disease and had received GC therapy. The interviews explored salient aspects of health-related quality of life associated with being treated with GCs.

Results: Interviews have been completed in three continents with patients who had a range of demographic features, rheumatological conditions and duration and dosage of GC therapy. Figure 1 shows the initial conceptual framework for developing the GC PROM (Steroid PRO).

Conclusion: This conceptual framework will act as an evolving guide in the development of a PROM for assessing patients' perspectives of systemic glucocorticoid therapy. Future work will include inductive analysis of qualitative transcripts to inform candidate questionnaire items, cognitive interviewing, linguistic translatability assessment, and an international validation survey to define the final PROM questionnaire and its measurement properties.

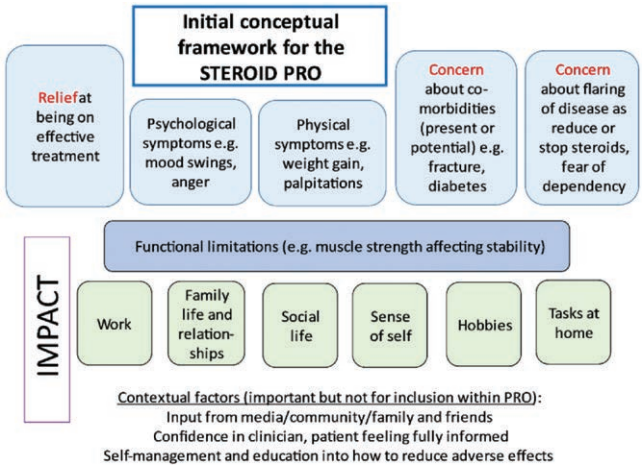


Figure 1.

REFERENCES:

[1] Cheah JTL, Robson JC, Black RJ, *et al*. The patient's perspective of the adverse effects of glucocorticoid use: A systematic review of quantitative and qualitative studies. From an OMERACT working group. *Semin Arthritis Rheum.* 2020 Oct; **50**(5):996-1005.

[2] Black RJ, Robson JC, Goodman SM, *et al.* A Patient-reported Outcome Measure for Effect of Glucocorticoid Therapy in Adults with Inflammatory Diseases Is Needed: Report from the OMERACT 2016 Special Interest Group. *J Rheumatol.* 2017; **44**(11):1754-8.

[3] Cheah JTL, Black RJ, Robson JC, *et al*. Toward a Core Domain Set for Glucocorticoid Impact in Inflammatory Rheumatic Diseases: The OMERACT 2018 Glucocorticoid Impact Working Group. *J Rheumatol.* 2019; **46**(9):1179-1182.

Disclosure of Interests: Susan Bridgewater Grant/research support from: Grant from Vifor Pharma for an independent investigator-led study to develop a PRO for steroids, Jill Dawson: None declared, Mwidimi Ndosi: None declared, Rachel J Black: None declared, Jonathan T.L. Cheah: None declared, Emma Dures: None declared, Nilasha Ghosh: None declared, Elizabeth A Hoon: None declared, Iris Navarro-Millan Consultant of: Received consultant fees from SOBI, Diyu Pearce-Fisher: None declared, Pamela Richards: None declared, Carlee Ruediger: None declared, Christine Silverthorne: None declared, Joanna Tieu Grant/research support from: Vifor Pharma, Sarah Mackie Consultant of: Consultancy on behalf of institution for Roche/Chugai, Sanofi, AbbVie and AstraZeneca, Grant/research support from: Educational grant from Roche to attend EULAR2019, Susan Goodman: None declared, Catherine Hill: None declared, Joanna Robson Speakers bureau: Vifor Pharma for educational webinar, Grant/research support from: Grant from Vifor Pharma for an independent investigator-led study to develop a PRO for steroids

DOI: 10.1136/annrheumdis-2021-eular.164

AB0835

IS BASELINE VITAMIN D STATUS RELATED WITH THE RESPONSE TO BDMARDS IN SPONDYLOARTHRITIS PATIENTS?

B. M. Fernandes[1], S. Garcia[1], F. Oliveira Pinheiro[1], M. Rato[1], D. Fonseca[2], D. Santos Oliveira[1,3], A. Martins[1], F. R. Martins[4], M. Bernardes[1,5], L. Costa[1]. *[1]Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*; *[2]Centro Hospitalar Vila Nova de Gaia/Espinho, Rheumatology, Vila Nova de Gaia, Portugal*; *[3]Faculty of Medicine, University of Porto, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal*; *[4]Centro Hospitalar Universitário do Algarve, Rheumatology, Faro, Portugal*; *[5]Faculty of Medicine, University of Porto, Departamento de Medicina, Porto, Portugal*

Background: Vitamin D is thought to have an important role in immune regulation and is being subject of research in several autoimmune diseases. Some data suggest that vitamin D deficiency is common in Spondyloarthritis (SpA) and may be associated with disease activity and structural damage.

Objectives: To evaluate if there is a relation between baseline vitamin D status and the response to biologic disease-modifying antirheumatic drugs (bDMARDs) in a SpA monocentric cohort.

Methods: Retrospective study including all the SpA patients (ASAS classification criteria) followed at our Rheumatology Department, registered in the

national database and treated with bDMARD between June 2008 and July 2020. Demographic, clinical and laboratorial data (including 25-hydroxyvitamin D [25-OHvitD]) at baseline and disease activity measures at 6 and 12 months of treatment with the first bDMARD were collected. Correlations between variables were evaluated by Spearman rank test, Mann-Whitney U test was used to the comparison analysis between groups and univariate logistic regression was used in the prediction analysis.

Results: A total of 195 SpA patients were included: 103 (52.8%) females, 47 (24.1%) smokers and 91 (46.7%) HLA-B27 positive; 139 (71.3%) had Ankylosing Spondylitis, 18 (9.2%) had Inflammatory Bowel Disease Associated SpA and 38 (19.5%) had Undifferentiated SpA. At the time of the first bDMARD, the mean age was 43.5 years (±9.6) and the median disease duration was 12.4 years (0.7-52.7). The mean ASDAS-CPR (Ankylosing Spondylitis Disease Activity Score with C-reactive protein) was 3.9 (±0.8) and, in addition, 61 (31.3%) patients had 25-OHvitD levels below 30 ng/mL and 12 (6.2%) had 25-OHvitD levels below 20 ng/mL. Fifty-three patients (27.2%) were taking NSAIDs (nonsteroidal anti-inflammatory drugs), 77 (39.5%) were under csDMARDs (conventional synthetic disease-modifying antirheumatic drugs). Adalimumab (56%) and golimumab (33.3%) were the most frequently initiated bDMARDs in the first line.

There were no statistically significant correlations between baseline 25-OHvitD levels and ASDAS-CRP at 6 (r=0.031; p=0.714) and 12 months (r=0.035; p=0.672) of bDMARD.

In the subgroup analysis: there were no statistically significant differences in the response to bDMARD at 6 and 12 months evaluated by ASDAS response and ASAS 20, 40 and 70 responses according to the baseline 25-OHvitD levels (25-OHvitD <20ng/mL vs ≥20ng/mL; 25-OHvitD <30ng/mL vs ≥30ng/mL); and there were no statistically significant differences in the baseline 25-OHvitD levels at baseline according to the response to bDMARD at 6 and 12 months of bDMARD (ASDAS: no response vs clinically important improvement or major improvement; ASAS 20: no response vs response).

In the line of these previous results, baseline 25-OHvitD levels did not predict the ASDAS response at 6 (OR 0.97 [0.95-1.00], 95% CI) or 12 (OR 0.98 [0.95-1.01], 95% CI) months of bDMARD.

Conclusion: Despite some data that suggest that lower levels of 25-OHvitD may be associated with higher disease activity in SpA, our results failed to demonstrate that the baseline 25-OHvitD levels can be related or predict treatment response after 6 and/or 12 months of therapy with the first bDMARD in real-life SpA patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.997

AB0836 DIAGNOSIS VALUE OF INTERLEUKIN 17 IN SPONDYLOARTHRITIS

L. Kharrat[1], M. Slouma[1], A. Tezeghdenti[2], W. Dkhili[2], R. Dhahri[1], E. Ghazouani[2], I. Gharsallah[1], L. Metoui[1], B. Louzir[1]. [1]*Military Hospital of Instruction of Tunis, Rheumatology, Tunis, Tunisia*; [2]*Military Hospital of Instruction of Tunis, Immunology, Tunis, Tunisia*

Background: Interleukin 17 (IL-17) is pro-inflammatory cytokine that plays a crucial role in spondyloarthritis via the Th17/IL-17 axis. (1)

Objectives: We aimed to study the diagnosis value of IL-17 serum in spondyloarthritis.

Methods: We conducted a case-control study, including 104 subjects divided into 2 groups:

-G1: 52 patients meeting the Assessment of SpondyloArthritis International Society (ASAS) criteria for spondyloarthritis (SA)

-G2: 52 healthy controls matched for age and sex.

The IL-17 level was measured using Enzyme-linked immunosorbent assay (ELISA).

We performed a ROC analysis and computed the air under the curve (AUC) at IL-17 to assess the ability of IL-17 to diagnose SA.

Statistical analysis was performed using "IBM SPSS Statistics" software version 25.

Results: Eighty per cent of the patients were men (n=41). The mean age was 44.96 ± 13.09 years. The mean age at the onset of the disease was 35.07 ± 12.66 years. The disease duration was 9.25 ± 8.09 years. Axial radiographic spondyloarthritis and peripheral involvement were found in 53.8% (n=28) and 44.2% (n=23) of cases, respectively. Psoriasis was noted in 46% of cases (n=24). The mean ASDAS-CRP was 3.21 ± 1.64.

IL-17 level was significantly higher in patients compared to healthy controls (92.76 ± 71.85 pg/mL and 2.67 ± 9.01 pg/mL, respectively, p<0.0001).

As shown in Figure 1, the AUC value to distinguish between spondyloarthritis and healthy control was 0.987 (p<0.0001). IL-17 cut-off was 13.79 pg/mL (Sensibility= 94.2%, specificity=98.1%).

Conclusion: According to previous studies, our study showed that serum IL-17 level is significantly higher in SA patients compared to healthy controls (2).

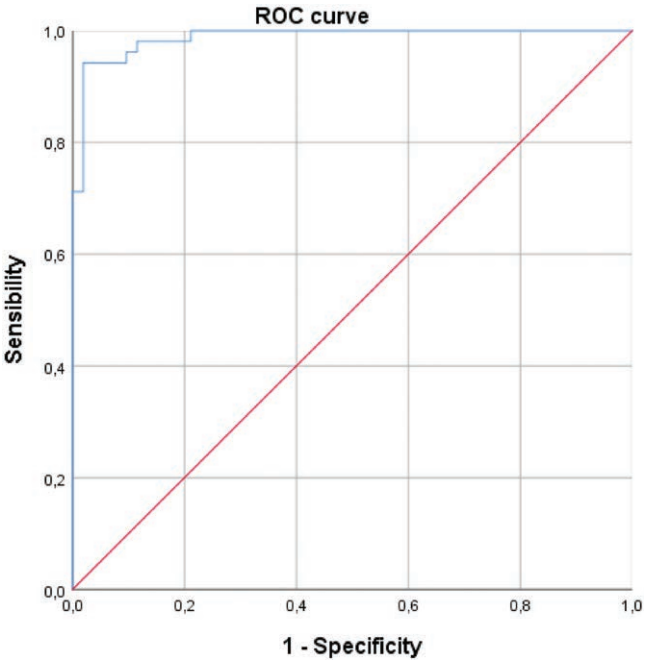


Figure 1. AUC at IL-17 between SA patients and healthy controls 0.987 (p<0.0001)

Interestingly, IL-17 was able to distinguish between SA patients and healthy controls with a cut-off of 13.79 pg/mL. This finding suggests that IL-17 may be useful for the diagnosis of SA.

REFERENCES:

[1] Ruiz de Morales JMG, Puig L, Daudén E, Cañete JD, Pablos JL, Martín AO, et al. Critical role of interleukin (IL)-17 in inflammatory and immune disorders: An updated review of the evidence focusing in controversies. Autoimmun Rev. janv 2020;19(1):102429.

[2] Chen W-S, Chang Y-S, Lin K-C, Lai C-C, Wang S-H, Hsiao K-H, et al. Association of serum interleukin-17 and interleukin-23 levels with disease activity in Chinese patients with ankylosing spondylitis. J Chin Med Assoc. juill 2012;75(7):303-8.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1020

AB0837 SERUM YKL-40 LEVELS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: RELATION TO DISEASE ACTIVITY AND JOINT DESTRUCTION

E. Aleksandrova[1], A. Novikov[1], E. Luchikhina[2], D. Karateev[2], G. Lukina[3]. [1]*Moscow Clinical Scientific Center n.a. A.S. Loginov, Clinical Immunology, Moscow, Russian Federation*; [2]*Regional Research and Clinical Institute (MONIKI), Department of Rheumatology, Moscow, Russian Federation*; [3]*Moscow Clinical Scientific Center n.a. A.S. Loginov, Department of Rheumatology, Moscow, Russian Federation*

Background: YKL-40 (chitinase-3-like 1 protein, human cartilage glycoprotein 39) is one of the major proteins secreted locally in the arthritic joint by activated macrophages, chondrocytes, synoviocytes and neutrophils, YKL-40 an important marker for inflammation, cartilage remodelling and synovial hyperplasia is recognized as a possible auto-antigen in rheumatoid arthritis (RA).

Objectives: The aims of the study were to determine the serum level of YKL-40 in early RA and investigate his relationship with biomarkers of disease activity and joint destruction.

Methods: We studied 22 patients with early RA (ACR/EULAR 2010 classification criteria); 4 males, 18 females; median and interquartile range (25th—75th percentile) of age 55,0 (43,0-64,0) years, disease duration 7,0 (5,0-11,0) months, DAS28 4,9 (4,3-5,8); 86% IgM rheumatoid factor (IgM RF) +; 91% anti-cyclic citrullinated peptide antibody (anti-CCP) +. All patients were treated with methotrexate (MTX). Three (14 %) patients received low oral doses of steroids and intra-articular injections. The control group included 22 healthy donors (HC). Radiographs were scored according to the van der Heijde-modified Sharp score. YKL-40, matrix metalloproteinase-3 (MMP-3), anti-CCP were detected using commercially available enzyme-linked immunosorbent assays (ELISA). The serum levels of IgM RF, C-reactive protein (CRP), serum amyloid A (SAA) were measured by immunonephelometry.

Results: RA patients had significantly higher serum level of YKL-40 than HC (92,1; 68,5-153,1 pg/ml vs 54,0; 41,7-83,2 pg/ml, p<0.01). Serum YKL-40 concentration was positively correlated with DAS 28 (r=0,5; p<0,05), erythrocyte sedimentation rate (ESR) (r=0,5; p<0,05), CRP (r=0,8; p<0,05), SAA (r=0,6; p<0,05) and MMP-3 (r = 0,6; p<0,05). We found no relationship between the level of YKL-40 and articular radiographic changes.
Conclusion: Elevated serum concentration of YKL-40 in early RA is associated with clinical and laboratory indicators of disease inflammatory activity and increased level of MMP-3 - an immunological marker of joint destruction.
Disclosure of Interests: Elena Aleksandrova: None declared, Alexander Novikov: None declared, Elena Luchikhina Speakers bureau: Abbvie, Roche, Pfizer, Biocad, MSD, Sanofi, Johnson & Johnson, Glaxo, UCB, Celgene, Novartis, Consultant of: Abbvie, Biocad, Sanofi, Celgene, Dmitriy Karateev Speakers bureau: Abbvie, Roche, Pfizer, Biocad, MSD, Sanofi, Johnson & Johnson, Glaxo, UCB, Celgene, Novartis, Lilly, Bayer, Paid instructor for: Abbvie, Pfizer, Biocad, Sanofi, Novartis, Lilly, Galina Lukina Speakers bureau: Abbvie, Roche, Pfizer, Biocad, MSD, Sanofi, Johnson & Johnson, Glaxo, UCB, Celgene, Novartis, Paid instructor for: Abbvie, Biocad, Sanofi, Celgene
DOI: 10.1136/annrheumdis-2021-eular.2069

AB0838 ADHERENCE TO TREATMENT IN PATIENTS WITH RHEUMATIC PROFILE DEPENDING ON THE OPTION OF BASIC THERAPY

O. Malyshenko[1], M. Koroleva[1], M. Letaeva[1], J. Averkieva[1], T. Raskina[1]. *[1]Kemerovo State Medical University, Department of Propedeutics of Internal Medicine, Kemerovo, Russian Federation*

Background: Treatment adherence is an important issue in actual clinical practice. As defined by the WHO, adherence to treatment is seen as the degree to which a patient's actions - taking medications, adhering to diet and other lifestyle interventions - correlate with following the doctor's recommendations. Treatment of patients with rheumatic diseases continues for many years, and often for life. The identification of factors associated with adherence to therapy will justify the implementation of a number of measures in order to increase the effectiveness of treatment of patients. Biological disease modifying antirheumatic drugs (bDMARDs) therapy involves more frequent visits of patients to a doctor with close monitoring of their condition, which may have an impact on adherence to treatment in this group of patients.
Objectives: to assess adherence to treatment of patients with rheumatological profile, depending on the basic therapy option.
Methods: A survey of 84 patients was conducted: 48 (57.1%) women and 36 (42.9%) men, mean age 51 years (36.8; 60.3). Most patients are observed with a diagnosis of rheumatoid arthritis - 48 (57.1%) people, with psoriatic arthritis - 26 (30.9%) and with ankylosing spondyloarthritis - 10 (12.0%) people.
The patients were divided into 2 groups depending on the type of basic therapy: Group 1 (40 people) - patients receiving combined therapy with bDMARDs and methotrexate; Group 2 (44 people) - patients with methotrexate monotherapy.
Patients in group 1 received the following bDMARDs: 18 patients received sarilumab (200 mg sc once every 2 weeks), 22 people received secukinumab (150 mg sc once a month). All patients took methotrexate at an average dose of 17.5 (15.0; 20.0) mg / week and NSAIDs.
Adherence to treatment was assessed using the Morisky-Green scale. Each of the 4 points is evaluated according to the principle of answers to the question "yes-no", while the answer "yes" is estimated at 0 points, and the answer "no" - at 1 point. Patients who score 4 points are considered compliant (adherent); insufficiently committed and those at risk for the development of non-commitment - 3 points; not committed - 2 points or less.
Results: The majority of patients are seen by a doctor monthly - 45.2% (38) and once a quarter - 33.3% (28). Only 7.1% (6) people are observed once every 6 months and 4.8% (4) once a year, and 9.6% (8) are not observed at all.
The frequency of medical observations in the 1st group of patients was higher than in the 2nd: monthly - 60.0% (24) and 40.9% (18), every 3 months - 40.0% (16) and 45.5% (20), respectively (p = 0.072 and p = 0.089), and only patients of the 2nd group were observed once every 6 months (4.5% - 2 people) and once a year (9.1% - 4 people). There were no statistically significant differences in adherence indicators.
When assessing adherence to treatment according to the Morisky-Green scale: only 37.5% (15) of patients in group 1 and 29.6% (13) in group 2 (p = 0.12) adhere to therapy, 30.0% are not adherent enough (12) and 22.7% (10) patients (p = 0.31), not adhering to treatment - 32.5% (13) and 47.7% (21) people, respectively (p = 0.39).
Conclusion: Thus, basic therapy bDMARDs with more frequent medical supervision does not affect adherence to treatment. Only about a third of patients are adherent to bDMARDs therapy.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3127

AB0839 A STUDY OF SERUM COMPLEMENT AND SERUM CALPROTECTIN LEVEL IN SYSTEMIC LUPUS ERYTHEMATOSUS

H. Goswami[1], S. Kakati[1]. *[1]Assam Medical College & Hospital, Dibrugarh, General Medicine, Dibrugarh, India*

Background: Serum calprotectin, also known as MRP8/14 or S100A8/A9, has gained attention in recent years as a candidate biomarker in inflammatory diseases like SLE.[1] Proteins of the complement pathway (serum C3 and C4) are linked to the pathogenesis of SLE and their levels have been measured as a means to assess the disease activity.[2]
Objectives:
[1] To study the relation of serum complement and serum calprotectin levels to disease activity in SLE
[2] To study the relation between serum complement and serum calprotectin level in SLE
Methods: Our study was a hospital based observational study conducted in a tertiary care centre in North-East India during the period of June 2019 to May 2020. A total of 102 patients of SLE were taken up for the study. Disease activity was assessed using SLEDAI-2K scores and serum calprotectin level was measured by ELISA. Serum C3 level was assessed by Nephelometric and C4 level by Turbidimetric immunoassay. The statistical significance was fixed at 5% level of significance (p<0.05) for all analysis.
Results: Our study found a predominantly female population (Female: Male ratio 24.5: 1) with majority of the patients (49.02%) in the 30-39 years age group. Higher calprotectin levels were seen in patients with higher disease activity (SLEDAI) and this relation was statistically significant (r=0.84, p<0.001). There was significant negative correlation between disease activity (SLEDAI) and serum C3 (r=-0.35, p<0.001) and serum C4 (r=-0.4, p<0.001) level. There was a significant negative correlation between complement levels and serum calprotectin levels (r=-0.53, p<0.001).
Conclusion: We found a significant positive correlation between serum calprotectin level and disease activity with a significant negative correlation between complement level and disease activity in SLE patients. There was a significant negative correlation between serum complement and serum calprotectin levels. These findings suggest serum calprotectin levels could be a substantial addition in the existing diagnostic array of tools in assessing lupus disease activity.
REFERENCES:
[1] García-Arias M, Pascual-Salcedo D, Ramiro S, Ueberschlag ME, Jermann TM, Cara C, et al. Calprotectin in rheumatoid arthritis: Association with disease activity in a cross-sectional and a longitudinal cohort. Mol Diagnosis Ther. 2013;17(1):49–56.
[2] Walport MJ. Complement and systemic lupus erythematosus. Arthritis Res. 2002;4(Suppl 3):S279-293.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3531

AB0840 DIAGNOSIS VALUE OF INTERLEUKIN 23 IN SPONDYLOARTHRITIS

L. Kharrat[1], M. Slouma[1], A. Tezeghdenti[2], W. Dkhili[2], R. Dhahri[1], E. Ghazouani[2], I. Gharsallah[1], L. Metoui[1], B. Louzir[1]. *[1]The Military Hospital of Tunis, Rheumatology, Tunis, Tunisia*; *[2]The Military Hospital of Tunis, Immunology, Tunis, Tunisia*

Background: Interleukin 23 (IL-23) is a pivotal pro-inflammatory cytokine in the Th17/IL-23 axis which became the center of attention in researches during these last decades, especially during spondyloarthritis (1).
Objectives: We aimed to study the diagnosis value of IL-23 serum in spondyloarthritis.
Methods: We conducted a case-control study, including 144 subjects divided into 2 groups:
-G1: 72 patients meeting the Assessment of SpondyloArthritis International Society (ASAS) criteria for spondyloarthritis (SA)
-G2: 72 healthy controls matched for age and sex.
For each SA patient we collected the following parameters: BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), ASDAS (Ankylosing Spondylitis Disease Activity Score), BASFI (Bath Ankylosing Spondylitis Functional Index), and BASRI (Bath Ankylosing Spondylitis Radiology Index).
The IL-23 level was measured using Enzyme-linked immunosorbent assay (ELISA).
Erythrocyte Sedimentation rate (ESR) and C-reactive protein (CRP) were also measured.
We performed a ROC analysis and computed the air under the curve (AUC) at IL-23 to diagnose SA patients.
Statistical analysis was performed using "IBM SPSS Statistics" software version 25.

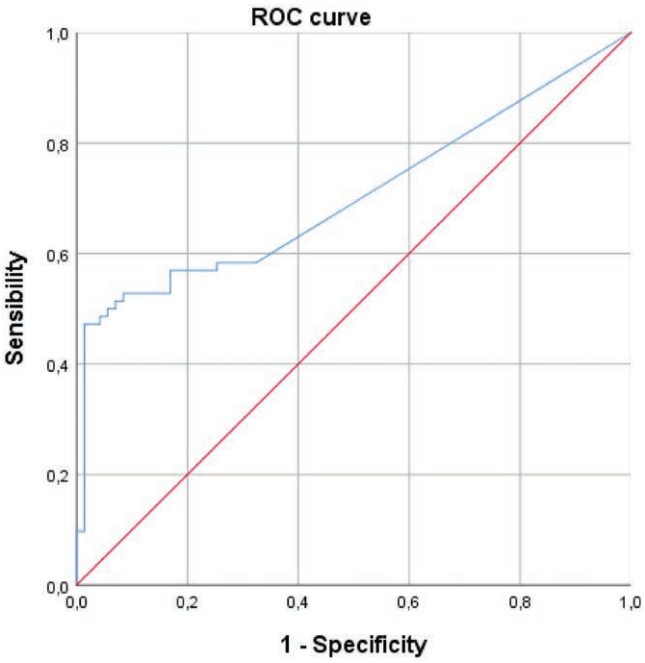


Figure 1. AUC at IL-23 between SA patients 0.705 (p<0.0001)

Nevertheless, no correlation was found between serum IL-23 levels and the following parameters: ESR, CRP, BASDAI, ASDAS-CRP, BASFI and BASRI.

Results: The study included 57 men and 15 women. The mean age was 44.84 ± 13.42 years. The mean age at the onset of the disease was 35.97 ± 12.88 years. The disease duration was 8.54 ± 7.7 years.

Seventy-nine per cent of our patients had axial radiographic spondyloarthritis (n=57). Peripheral involvement was found in 45.8% (n=33). Eighteen patients had both axial and peripheral involvement concomitantly. Psoriasis was found in 36.1% of the cases (n=26).

The mean BASDAI and ASDAS-CRP were 3.21 ± 1.64 and 3.05 ± 1.51, respectively.

The mean was BASFI 3.88 ± 2.69. The mean was BASRI 5.26 ± 4.14.

The mean ESR and CRP were 36.74 ± 29.38 mm/hr and 20.45 ± 25.19 mg/dL, respectively.

IL-23 level was significantly higher in patients compared to healthy controls (23.1 ± 2.72 pg/mL and 5.02 ± 0.59 pg/mL, respectively, p<0.0001).

As shown in Figure 1, the AUC value to distinguish between spondyloarthritis and healthy control was 0.705 (p<0.0001). IL-23 cut-off was 7.96 pg/mL (Sensibility= 69.4%, specificity=98.6%).

Conclusion: As reported to previous studies, our study showed that IL-23 is significantly higher in SA patients (2).

Interestingly, IL-23 was able to distinguish between SA patients and healthy controls with a cut-off of 7.96 pg/mL. This finding suggests that IL-23 may be practical for the diagnosis of SA.

REFERENCES:

[1] K V, D E. IL-23 Responsive Innate-Like T Cells in Spondyloarthritis: The Less Frequent They Are, the More Vital They Appear [Internet]. Vol. 17, Current rheumatology reports. Curr Rheumatol Rep; 2015 [cité 13 avr 2020]. Disponible sur: https://pubmed.ncbi.nlm.nih.gov/25874346/

[2] Wang X, Lin Z, Wei Q, Jiang Y, Gu J. Expression of IL-23 and IL-17 and effect of IL-23 on IL-17 production in ankylosing spondylitis. Rheumatol Int. sept 2009;29(11):1343-7.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3637

AB0841 ALTERED XANTHINE OXIDASE AND XANTHINE DEHYDROGENASE ACTIVITIES IN RED BLOOD CELLS AS A CONTRIBUTION TO AUTOIMMUNE ANEMIA APPEARANCE IN RHEUMATOID ARTHRITIS

E. Mozgovaya[1], A. Trofimenko[1], S. Bedina[1], S. Spitsina[1], M. Mamus[1], I. Zborovskaya[1]. [1]*Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky, Clinical Biochemistry Lab, Volgograd, Russian Federation*

Background: Rheumatoid arthritis (RA) is severe autoimmune joint disease, accompanied by a wide variety of extra-articular manifestations. Anemia is one of the most common organ involvements in RA, being diagnosed in 36-65% patients. Iron metabolism alterations, shortened RBC lifespan, and impaired erythropoiesis in bone marrow are believed to play a leading role in RA-related anemia development. These processes in RA can be mediated by increased effect of proinflammatory cytokines, including IFNγ and TNFα, and similar mechanisms could contribute to high xanthine oxidoreductase (XOR) expression. This enzyme makes multiple pathophysiological effects, some of which can be related to the development of anemia in RA. Reactive oxygen species generated by XOR are capable, in particular, of damaging cell membranes, exerting influence on iron mobilization from ferritin in liver, and inducing changes in intestinal iron absorption.

Objectives: Evaluation of changes in XOR interconvertible forms (xanthine oxidase and xanthine dehydrogenase) activities in RBC of RA patients.

Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles. 75 RA patients with verified RA were enrolled in the study. The diagnosis was verified using the ACR/EULAR criteria (2010). The reference group consisted of 35 healthy individuals. Xanthine oxidase (XO, EC 1.17.3.2) and xanthine dehydrogenase (XDG, EC 1.17.1.4) activities were measured in lysed red blood cells by spectrophotometric method as previously described [1]. The enzymatic activities were expressed as nmol/min/ml and normalized to 1×10^9 cells/ml. Statistical comparison tests were selected in according to common guidelines. Central tendencies were expressed as means±SEM. Differences were considered significant when p<0.05.

Results: Mean age of RA patients was 43.9±0.97 years, and mean RA duration was 8.5±0.3 years. Extra-articular manifestations were diagnosed in 32 (42.7%) RA patients and 17 (53.1%) of them had anemia. We revealed substantial changes in XO and XDG activities in lysed RBC of RA patients with anemia. Increased XO activity and decreased XDG activity were observed in comparison with healthy controls (p<0.001 for both enzymes). In parallel with the increase in DAS28 index, significant growth of XOD/XDG coefficient was observed, which was caused by both XOD activity elevation and XDG activity reduction in lysed RBC (p<0.001 for both enzymes). Enzymatic activities depended also on the extra-articular RA manifestations. Mean XO activity was higher and mean XDG activity were lower in patients with extra-articular manifestations (p<0.05 for both enzymes), but the extent of changes was substantially less comparing to anemia.

Conclusion: Autoimmune inflammation in RA is accompanied by changes in enzymatic activities of XOR interconvertible forms and their ratio. Transformation of XDG into KO ultimately leads to significant increase in the generation of reactive oxygen species that have a damaging effect on lipids, proteins and other cellular components, and specifically in RBC. This fact may be one of the reasons for their premature damage and development of anemia in RA.

REFERENCES:

[1] Zborovskaya I.A., et al. Influence of analgetics on plasma and lymphocytic activity of the purine metabolism enzymes in rheumatoid arthritis patients. Russian Journal of Pain 2018;3:47

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3639

AB0842 CESAREAN SECTION IN MEXICAN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES

A. Y. Lujano Negrete[1], C. M. Skinner Taylor[1], L. Pérez Barbosa[1], F. Hernández[2], R. A. Rodriguez Chavez[1], L. G. Espinosa Banuelos[1], R. Moyeda Martinez[1], A. Cárdenas[1], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Reumatología, Monterrey, Mexico*; [2]*Hospital Universitario Dr. José Eleuterio González, Ginecología y Obstetricia, Monterrey, Mexico*

Background: Rheumatic diseases occur among women of childbearing age, adverse events during pregnancy in rheumatic diseases have been frequently reported. Mexico has one of the largest prevalence of cesarean section in women which negatively impacts the product.

Objectives: The objective of this study is to describe the frequency of cesarean section in women with autoimmune rheumatic diseases compared to a control group.

Methods: We conducted a cross-sectional and retrospective study in patients from the pregnancy and rheumatic diseases clinic, and the Obstetrics department form the University Hospital “Dr. José E. González” in Northeast Mexico. Women with autoimmune rheumatic diseases that gave birth between August 2017 to December 2020 were included. All the data, including the way of birth was retrieved from the clinical files.

Results: One hundred and twelve patients were included (56 in the rheumatic disease group and 56 women without rheumatic diseases), two of them suffered miscarriage (one from the rheumatic disease group and 1 from the control group) giving a total of 110 products. The mean age was 29.6 years for the rheumatic patients and 24.6 for the control group. The most frequent rheumatic disease was RA in 22 patients (39.2%), followed by SLE in 13 patients (23.21%).

From the 56 pregnancies on the rheumatic disease group more than half ended by cesarean section (n=33, 58.92%) and there were 22 simple vaginal delivery. Table 1. On the control group there were 24 cesarean section procedures and

31 simple vaginal delivery. The indications for cesarean sections are presented in Figure 1. No statistically significant difference was found on cesarean section prevalence between both groups (p=0.389).

The most common indication for cesarean section in all patients was previous cesarean procedure. (n=12, 36.36%). There were more pathological fetal cardiotocographic changes (PFCC) as an indication for cesarean section on the rheumatic diseases group (n=11, p 0.002) compared with the control group (n=1).

Conclusion: A higher prevalence of cesarean sections was found in women with rheumatic diseases versus women without rheumatic diseases, although this difference was not statistically significant. Studies with a higher sample size are necessary to elucidate the complications and differences between both groups.

REFERENCES:

[1] Jara LJ, Cruz-Dominguez MDP, Saavedra MA. Impact of infections in autoimmune rheumatic diseases and pregnancy. Curr Opin Rheumatol. 2019;31(5):546-52.

[2] Saavedra MA, Sánchez A, Bustamante R, Miranda-Hernández D, Soliz-Antezana J, Cruz-Domínguez P, et al. [Maternal and fetal outcome in Mexican women with rheumatoid arthritis]. Rev Med Inst Mex Seguro Soc. 2015;53 Suppl 1:S24-9.

[3] Smeele HTW, Dolhain R. Current perspectives on fertility, pregnancy and childbirth in patients with Rheumatoid Arthritis. Semin Arthritis Rheum. 2019;49(3s):S32-s5.

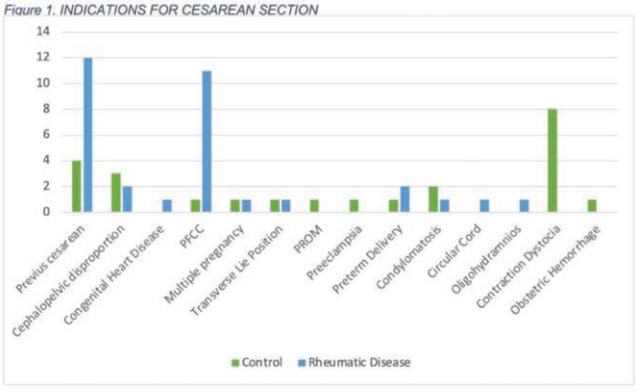
[4] Sugawara E, Kato M, Fujieda Y, Oku K, Bohgaki T, Yasuda S, et al. Pregnancy outcomes in women with rheumatic diseases: a real-world observational study in Japan. Lupus. 2019;28(12):1407-16.

[5] Vinet É, Bernatsky S. Outcomes in Children Born to Women with Rheumatic Diseases. Rheum Dis Clin North Am. 2017;43(2):263-73.

Table 1. Demographic charecteristics

DISEASE	N (%)	AGE, YEARS MEAN	DURATION OF DISEASE, YEARS MEAN	CESAREAN SECTION	SIMPLE VAGINAL DELIVERY	OTHERS
RA	22 (39.2%)	29.95	6.77	11	10	1 Miscarriage
APS	9 (16.98)	28.22	2.77	8	1	
DM	3	20	3.5	2	1	
	(5.35%)					
IA	3	21.5	3	2	1	
	(5.35%)					
SS	4 (7.14%)	30.25	4.75	3	1	
JIA	2 (3.57%)	36	15	1	1	
SLE	13 (23.21)	31.83	5.33	7	5	
TOTAL	56	29.64150943		33	22	

RA: Rheumatoid Arthritis, APS: Anti-phospholipid syndrome, DM: Dermatomyositis, IA: Idiopathic arthritis, SS: Sjogren syndrome, JIA: Juvenile idiopathic arthritis, SLE: Systemic Lupus Erythematosus



Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3679

AB0843

OBSTETRIC AND PERINATAL OUTCOMES IN MEXICAN WOMEN WITH RHEUMATIC DISEASES

F. Hernández[1], A. Y. Lujano Negrete[2], C. M. Skinner Taylor[2], L. Pérez Barbosa[2], E. Barriga-Maldonado[2], R. A. Rodriguez Chavez[2], L. G. Espinosa Banuelos[2], R. Moyeda Martinez[2], G. Figueroa-Parra[2], D. Á. Galarza-Delgado[2]. [1]*Hospital Universitario Dr. José Eleuterio González, Obstetricia, Monterrey, Mexico*; [2]*Hospital Universitario Dr. José Eleuterio González, Reumatología, Monterrey, Mexico*

Background: Rheumatic diseases (RD) are more frequent among women of childbearing age. Adverse events during pregnancy in RDs have been frequently reported, leading some women to avoid pregnancy. “CEER” is an outpatient clinic in Monterrey, Nuevo Leon, Mexico, that was created for pregnant women with RD.

Objectives: The objective is to describe pregnancy outcomes in patients with RD surveilled at a rheumatology outpatient clinic.

Methods: A single-center retrospective study of women with RD at CEER between 2017 and 2020 was conducted. Clinical features and maternal, fetal and neonatal outcomes were retrospectively collected. The rate of adverse perinatal outcomes (APO) was compared with the tertiary referral center´s general obstetric population (GOP). All data was retrieved from clinical files.

Results: Overall, 62 pregnancies in women with RD were recorded. The median maternal age at conception was significantly higher in pregnancies with RD than GOP (29 [24-35] years old vs 23 [19-28] years old, p<0.001).The odds of preterm delivery were increased among pregnancies with RD (OR 1.85, 95% CI 1.03-3.30, p=0.038). Other APO are summarized in Table 1. Rheumatoid arthritis (RA) was the leading diagnosis followed by systemic erythematosus lupus (SLE) and antiphospholipid syndrome (APS).

Cesarean sections were recorded in 41 pregnancies in RD group, more frequent than in GOP (66.1% vs 50.8%, p=0.016). Figure 1 shows the distribution of indications for cesarean sections, the two leading indications were previous cesarean section (43.9%) and Nonreassuring fetal heart rate pattern (19.5%) Pregnancies with RD appeared to have frequent, emergency cesarean sections and preterm deliveries compared with GOP (12.9% vs 15.9%, p=0.02 and 23.7% vs 12.2%, p=0.006, respectively).

Conclusion: Pregnancies with RD were at increased risk for APO. Women of this population should be made aware of these risks and be closely monitored by a multidisciplinary team as a high-risk pregnancy.

REFERENCES:

[1] Aljary H, Czuzoj-Shulman N, Spence AR, Abenhaim HA. Pregnancy outcomes in women with rheumatoid arthritis: a retrospective population-based cohort study. J Matern Fetal Neonatal Med. 2020;33(4):618-24.

[2] Alvarez-Nemegyei J, Cervantes-Díaz MT, Avila-Zapata F, Marín-Ordóñez J. [Pregnancy outcomes before and after the onset of rheumatoid arthritis]. Rev Med Inst Mex Seguro Soc. 2011;49(6):599-604.

[3] Davutoğlu EA, Ozel A, Yılmaz N, Madazli R. Pregnancy outcome in 162 women with rheumatic diseases: experience of a university hospital in Turkey. Arch Gynecol Obstet. 2017;296(6):1079-84.

[4] Harris N, Eudy A, Clowse M. Patient-Reported Disease Activity and Adverse Pregnancy Outcomes in Systemic Lupus Erythematosus and Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2019;71(3):390-7.

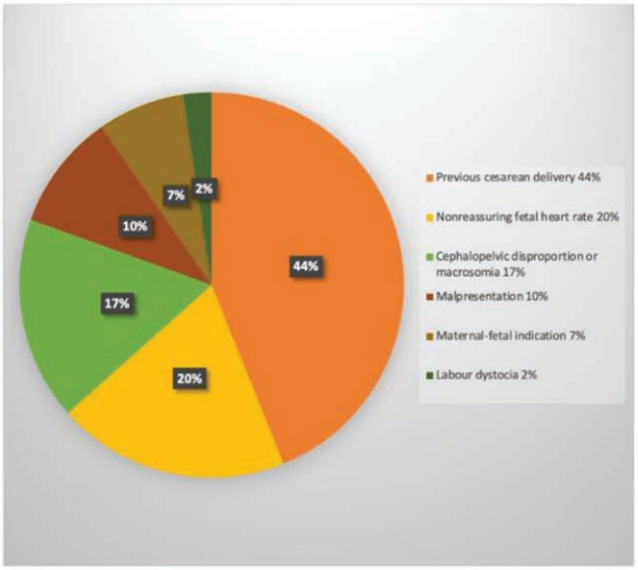
[5] Ideguchi H, Ohno S, Uehara T, Ishigatsubo Y. Pregnancy outcomes in Japanese patients with SLE: retrospective review of 55 pregnancies at a university hospital. Clin Rev Allergy Immunol. 2013;44(1):57-64.

Table 1. Pregnant outcome, maternal, fetal and neonatal adverse events

	RD (n=62)	GOP (n=31254)	OR (CI 95%)	p
Pregnancy outcome				
Pregnancy loss[a]	6 (9.68)	1560 (4.99)	1.94 (0.84-4.49)	0.122
Live births[a]	60 (90.9)	29694 (95)	0.96 (0.67-1.35)	0.8
Gestational age,	37.6 (37-39)	39 (38-40.2)	-	<0.001
median (IQR) (weeks)[b]				
Birth weight,	2831.6 (2677.4-2985.8)	3022.2 (2986.8-3057.6)	-	0.007
mean (CI) (Kg)[c]				
Maternal adverse events				
Preterm deliveries	14 (23.7)	3821 (12.2)	1.85 (1.03-3.3)	0.038
(<37 weeks)[a]				
<34 weeks[a]	3 (5.1)	1065 (3.4)	1.42 (0.45-4.53)	0.553
Gestational diabetes[a]	4 (6.5)	1406 (4.5)	1.43 (0.52-3.95)	0.485
Preeclampsia[a]	5 (8.1)	2471 (7.89)	1.02 (0.41-2.54)	0.97
Postpartum hemorrhage[a]	0	930 (2.97)	0.27 (0.017-4.35)	0.355
Emergency cesarean section[a]	8 (12.9)	1844 (5.9)	2.19 (1.05-4.57)	0.037
Fetal adverse events				
Miscarriages[a]	3 (4.8)	663 (2.12)	2.28 (0.71-7.29)	0.164
Stillbirths[a]	3 (4.8)	897 (2.87)	1.69 (0.53-5.38)	0.377
Congenital abnormalities[a]	4 (6.5)	1094 (3.5)	1.84 (0.67-5.08)	0.237

[a]n,%[b]IQR, interquartile range (25th–75th percentile)[c]CI, confidence interval (95%)

Figure 1. Distribution of indications for cesarean section



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3718

AB0844 HAND GRIP STRENGTH EVALUATION IN RHEUMATOLOGIC DISEASES

A. Caturano[1], P. C. Pafundi[1], R. Galiero[1], M. Tardugno[2], F. C. Sasso[1], G. Cuomo[2]. [1]*University of Campania "Luigi Vanvitelli", Department of Advanced Medical and Surgical Sciences, Naples, Italy*; [2]*University of Campania "Luigi Vanvitelli", Department of Precision Medicine, Naples, Italy*

Background: Handgrip muscle strength test describes the strength of the hand muscles used to grasp or grip. Currently, hand grip evaluation is often used in clinical practice, as a marker of function and disability. In fact, it has already been applied as an outcome measure in arthritis rheumatoid clinical trials, to demonstrate the benefits of several treatments [1]. However, hand disability should also be considered in all other rheumatological diseases.
Objectives: The main aim of this study is to assess the handgrip muscle strength test in a rheumatological cohort of patients as compared to a control group.
Methods: This is a cross-sectional pilot study. We considered eligible 35 rheumatological consecutive female patients followed at our outpatients' clinic of Internal Medicine (I Policlinico of Naples) and 35 healthy control females (HC). Both groups included only right-handed individuals. Rheumatological patients were distributed as follows: 5 rheumatoid arthritis (14,3%), 9 psoriatic arthritis (25,7%), 4 systemic lupus erythematosus (11,4%), 10 systemic sclerosis (28,6%), 4 fibromyalgia (11,4%), 3 juvenile idiopathic arthritis (8,6%). The course of disease was under optimal treatment in all patients.
The type of hand grip used is the power grip, in which an object is held firmly by wrapping the fingers around it, pressing the object against the palm, and using the thumb to apply counter-pressure. We considered as either right or left hand valid measure the mean of three consecutive tests per arm. Between-groups differences were tested both by a uni- and multivariable analysis.
Results: The two subgroups were homogeneously distributed for age (median age 42 yrs. [IQR 33-48] vs. 36 yrs. [IQR 30-52] in HC; p=0.902). At univariate analysis, hand grip strength was significantly lower in the rheumatological patients, both at right hand (right 19.5 kg [IQR 13.6-24.8] vs. 24.5 kg [IQR 20.8-29] in HC; p=0.004) and left hand (18.5 kg [IQR 13.9-22.5] vs. 23.7 kg [IQR 19-27.3] in HC; p=0.002), as compared to HC. This finding was further confirmed at multivariable analysis only as for the left hand (OR 0.919, 95%CI: 0.858-0.984; p=0.016).
Conclusion: Rheumatological diseases are burdened by hand disability, mostly affecting daily activities performance [2,3]. Beyond an optimal disease control, our pilot study shows a decrease in left hand strength as compared to healthy controls. This might be due to a reduced use of the non-dominant hand, which may lead over time to a higher deficit of strength. As such, these patients should be prescribed to a left hand exercise to improve both mobility and strength and, consequently, hand function.
REFERENCES:
[1] Eberhardt K, Sandqvist G, Geborek P (2008) Hand function tests are important and sensitive tools for assessment of treatment response in patients with rheumatoid arthritis. Scand J Rheumatol 37(2):109–112.
[2] Feced Olmos CM, Alvarez-Calderon O, Hervás Marín D, et al. Relationship between structural damage with loss of strength and functional disability in psoriatic arthritis patients. Clin Biomech (Bristol, Avon). 2019 Aug;68:169-174. doi: 10.1016/j.clinbiomech.2019.06.009.
[3] Maddali-Bongi S, Del Rosso A, Mikhaylova S, et al. Impact of hand and face disabilities on global disability and quality of life in systemic sclerosis patients. Clin Exp Rheumatol. 2014 Nov-Dec;32(6 Suppl 86):S-15-20.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3860

AB0845 THE COMBINATION OF PLASMA FIBRINOGEN CONCENTRATION AND NEUTROPHIL-LYMPHOCYTE RATIO (F-NLR) AS A NOVEL INFLAMMATORY MARKER OF RHEUMATOID ARTHRITIS

M. Liu[1], Z. Huang[1], Y. Huang[1], Z. Huang[1], Q. Huang[1], T. W. LI[1]. [1]*Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China*

Background: The combined index of fibrinogen and neutrophil-lymphocyte ratio (F-NLR) has recently been reported as a new predictive factor in patients with cancer. However, the fibrinogen and NLR have not been simultaneously evaluated in rheumatoid arthritis (RA).
Objectives: This study aimed to explore the clinical value of F-NLR in RA and its relationship with disease activity.
Methods: This retrospective study collected 143 RA patients and 82 age- and gender-matched healthy controls. Neutrophil, lymphocyte, monocyte, platelet, fibrinogen, NLR, monocyte to lymphocyte ratio (MLR), platelet to lymphocyte ratio (PLR), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Disease Activity Score of 28 joints-ESR (DAS28-ESR) and other laboratory parameters were recorded. Receiver operating characteristic (ROC) curves were used to defined the optimization cut-off values of fibrinogen and NLR, which were 3.9g/L and 2.42. The F-NLR score was 2 for patients with high fibrinogen (> 3.9g/L) and elevated NLR (> 2.42), while those with one or neither were indexed as 1 or 0. The correlations between F-NLR as well as other inflammatory indexes and DAS28-ESR were measured.
Results: The F-NLR score was higher in RA patients than that in healthy individuals ($P < 0.05$). The proportion of higher F-NLR score increased significantly along with the disease activity ($P < 0.05$). According to the ROC curve which was conducted to discriminate RA patients from healthy subjects, the area under curve (AUC) of F-NLR (0.803, 95% CI: 0.744 - 0.861) was higher than that of fibrinogen (0.735, 95% CI: 0.670 - 0.801), NLR (0.724, 95% CI: 0.655 - 0.794), MLR (0.687, 95% CI: 0.615 - 0.759) and PLR (0.732, 95% CI: 0.664 - 0.800). Furthermore, F-NLR was more strongly associated with DAS28-ESR ($r = 0.572$, $P < 0.001$) when compared with fibrinogen ($r = 0.518$, $P < 0.001$), NLR ($r = 0.365$, $P < 0.001$), MLR ($r = 0.140$, $P = 0.096$), PLR ($r = 0.239$, $P = 0.004$), CRP ($r = 0.539$, $P < 0.001$) and ESR ($r = 0.487$, $P < 0.001$).
Conclusion: The results demonstrated that the F-NLR score was elevated in RA patients. The F-NLR score may be a potential marker to monitor the disease activity of RA patients.
REFERENCES:
[1] Wang H, Zhao J, Zhang M, Han L, Wang M, Xingde L. The combination of plasma fibrinogen and neutrophil lymphocyte ratio (F-NLR) is a predictive factor in patients with resectable non small cell lung cancer. J Cell Physiol. 2018 May; 233(5):4216-4224.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3929

Education

AB0846 CONCEPTION AND FEASIBILITY OF A DIGITAL TELE-GUIDED ABDOMEN, THORAX AND THYROID GLAND ULTRASOUND COURSE FOR MEDICAL STUDENTS

E. Höhne[1], F. Recker[2], E. Schmok[3], P. Brossart[1], T. Raupach[4], V. Schäfer[1]. [1]*University Hospital Bonn, Clinic of Internal Medicine III, Oncology, Hematology, Rheumatology and Clinical Immunology, Bonn, Germany*; [2]*University Hospital Bonn, Department for Obstetrics and Gynecology, Bonn, Germany*; [3]*Amboss GmbH, Institutional Partnerships, Berlin, Germany*; [4]*University Hospital Bonn, Institute for Medical Education, Bonn, Germany*

Background: Over the past few decades, technological advances in both ultrasound (US) and the application of telemedicine have been made [1]. Medical education has shifted to online classes during the COVID-19 pandemic, creating challenges in adequate training of US.

Objectives: In the context of the current COVID-19 pandemic and the discontinuation of traditional classroom teaching, a tele-didactic US course for undergraduate medical students was developed. This study is examining the educational outcome of a new digital US course of the abdomen, thorax and the thyroid gland with the implementation of a modern portable US system.
Methods: A tele-guided US course was established between April 1st and June 20th, 2020, at the University Hospital in Bonn, Germany. Students completed pre- and post-course surveys and underwent six US organ modules. Each module took place in a flipped-classroom concept including a digital learning platform. An objective structured assessment of US skills (OSAUS) [2] was implemented as final exam. Further, US images of the course and exam were rated by the Brightness Mode Quality Ultrasound Imaging Examination Technique (B-QUIET) [3]. Achieved points in image rating were compared to the OSAUS exam and survey results.
Results: A total of 15 medical students were enrolled. There was a significant increase in self-assessed theoretical and practical ability ($p < 0.001$). Students achieved an average score of 154.5 (SD ± 11.72) out of 175 points (88.29%) in OSAUS, which corresponded to the image rating using B-QUIET and self-assessment data obtained in surveys. Interrater analysis of US images showed a favorable agreement with an ICC (2,1) of 0.895 (95% confidence interval $0.858 < ICC < 0.924$).
Conclusion: US training via teleguidance should be considered in medical education. Our pilot study demonstrates the feasibility of this concept that can be used in the future to improve US training of medical students even during a pandemic. The digital implementation with an affordable, portable point-of-care-US device could be an incredible opportunity to expedite US training worldwide.
REFERENCES:

[1] Law J, Macbeth PB. Ultrasound: from Earth to space. Mcgill J Med 2011; 13(2): 59 [PMID: 22399873]
[2] Tolsgaard MG, Todsen T, Sorensen JL, *et al.* International multispecialty consensus on how to evaluate ultrasound competence: a Delphi consensus survey. PLoS One 2013; 8(2): e57687
[https://doi.org/10.1371/journal.pone.0057687][PMID: 23469051]
[3] Bahner DP, Adkins EJ, Nagel R, Way D, Werman HA, Royall NA. Brightness mode quality ultrasound imaging examination technique (B-QUIET): quantifying quality in ultrasound imaging. J Ultrasound Med 2011; 30(12): 1649–55
[4] [https://doi.org/10.7863/jum.2011.30.12.1649][PMID: 22124000]

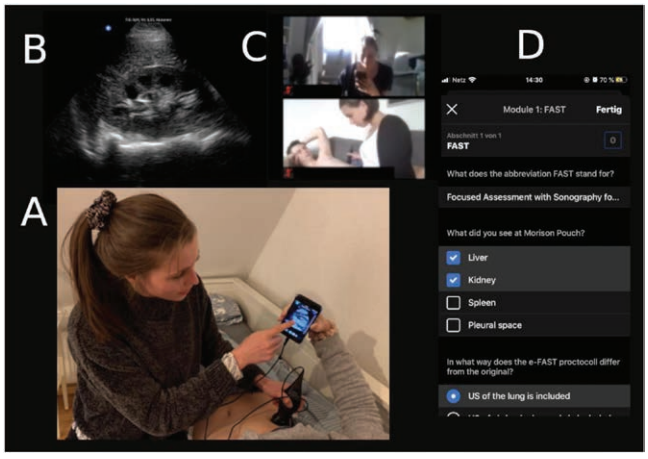


Figure 1. Implementation of the digital ultrasound course concept

Classroom setting is displayed, demonstrating simultaneous screen transmission of ultrasound (US) and camera images. A: The peer tutor's camera image is shared with the students while demonstrating the US examination, B: At the same time the tutor's mobile phone screen is shared with the students in order to visualize the US image acquisition, C: Students performing the US examination on their own, D: Example of a worksheet, which had to be completed within the app and was stored along with the US images in the cloud
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.465

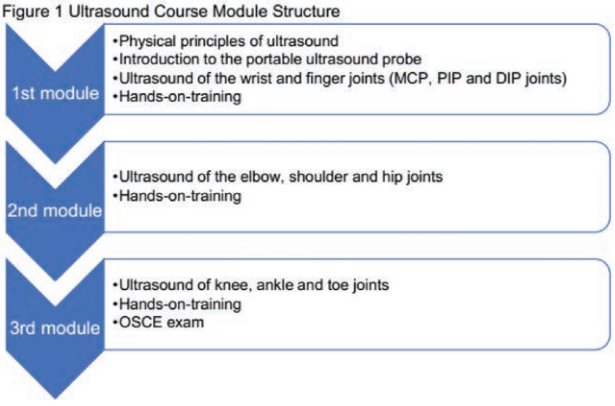
AB0847

ESTABLISHMENT AND VALIDATION OF A DIDACTIC MUSCULOSKELETAL ULTRASOUND COURSE FOR DERMATOLOGISTS USING AN INNOVATIVE HANDHELD ULTRASOUND SYSTEM – THE MUDE STUDY (MUSCULOSKELETAL ULTRASOUND IN DERMATOLOGY)

J. Grobelski[1], F. Recker[2], D. Wilsmann-Theis[3], W. Hartung[4], P. Karakostas[1], P. Brossart[1], V. Schäfer[1]. [1]*University Hospital Bonn, Clinic of Internal Medicine III, Oncology, Haematology, Rheumatology and Clinical Immunology, Bonn, Germany*; [2]*University Hospital Bonn, Centre for Obstetrics and Gynecology, Bonn, Germany*; [3]*University Hospital Bonn, Clinic and Polyclinic for Dermatology and Allergology, Bonn, Germany*; [4]*Bad Abbach, Rheumatology and Clinical Immunology, Bad Abbach, Germany*

Background: In the early detection of arthritis, such as psoriatic arthritis (PsA), ultrasound (US) of painful joints plays an important role in diagnosis. Pathological findings can be missed during clinical examination, especially if conducted by physicians who are not trained. Furthermore, several publications undermine the importance of early PsA detection in psoriasis patients and the key role of the dermatologists in this process.
Objectives: The objective of this study was to examine a pilot musculoskeletal ultrasound (MSUS) course designed specifically for dermatologists.
Methods: To assess the degree of US expertise of the participants, a questionnaire was conducted before the course. The course concept, based on The German Society for Ultrasound in Medicine (Deutsche Gesellschaft fur Ultraschall in der Medizin, DEGUM) covering only the most important US sections of all joints and focused on the detection of joint effusion and hyperperfusion. The course consisted of three modules and was carried out over 6 months. Figure 1 shows the modular course concept. A portable US device in combination with a tablet was provided to enable practice between the courses. The final teaching evaluation was carried out as an objective structured clinical examination (OSCE) consisting of three stations, each representing the three course modules. According to the following grade scoring system, the performance rating was checked: < 60 % failed, ≥ 60 - < 70 % sufficient, ≥ 70% - < 80 % satisfying, ≥ 80% - < 90 % good, ≥ 90 % very good.

Figure 1 Ultrasound Course Module Structure



MCP: Metacarpophalangeal joint, PIP: Proximal interphalangeal joint, DIP: Distal interphalangeal joint, OSCE: objective structured clinical examination

Results: Twelve dermatologists participated. The mean age of our cohort was 39 years (SD ± 9.99 years) with nine females (75 %). Eight were specialists in dermatology in mean for 11.4 years (SD ± 11 years). Four were assistant physicians practicing dermatology in mean for 3.06 years (SD ± 0.97 years).
The survey revealed no prior knowledge of MSUS. The overall mean score of all participants in the OSCE was 21.86 (SD ± 2.12) (87.44%) out of a total of 25 points resulting in a good grade. There was no statistically significant difference between the assistant physicians and the specialists in dermatology regarding the OSCE results. Table 1 shows the OSCE results.

Table 1. Objective structured clinical examination (OSCE) mean results for all three stations

OSCE stations	Mean absolute	Mean absolute	Standard Deviation	Mean percentage	Standard Deviation	Confidence Interval	Grade
1	18.92	18.92	+/- 3.07	75.67%	+/-12.27%	67.87-83.46%	Sufficient
2	23.83	23.83	+/-0.99	95.33%	+/-3.94%	92.83-97.84%	Very good
3	22.83	22.83	+/-0.37	91.33%	+/-1.49%	90.39-92.28%	Very good
OSCE station 1-3	21.86	21.86	+/-2.12	87.44%	+/-8.49%	66.36-108.53%	Good

Conclusion: The innovative US teaching concept was able to demonstrate, that it is appropriate for the training of dermatologists in MSUS, independently of their age, experience in dermatology and US.

Disclosure of Interests: Jakub Grobelski: None declared, Florian Recker: None declared, Dagmar Wilsmann-Theis: None declared, Wolfgang Hartung: None declared, Pantelis Karakostas: None declared, Peter Brossart: None declared, Valentin Schäfer Speakers bureau: AbbVie, Novartis, BMS, Chugai, Celgene, Medac, Sanofi, Lilly, Hexal, Pfizer, Janssen, Roche, Schire, Onkowissen, Royal College London, Consultant of: Novartis, Chugai, AbbVie, Celgene, Sanofi, Lilly, Hexal, Pfizer, Amgen, BMS, Roche, Gilead, Medac, Grant/research support from: Novartis, Hexal, Lilly, Roche, Celgene, Universität Bonn

DOI: 10.1136/annrheumdis-2021-eular.533

AB0848 PARTICIPATION OF UNDERGRADUATE MEDICAL STUDENTS AS INVESTIGATORS IN A RHEUMATOLOGIC COHORT: IMPACT ON DEPRESSION, ANXIETY & STRESS SCALE

S. Basualto[1], J. V. Ziroldo Lopes[2], A. Rizzo Borges[3], M. Abreu[4], C. Albuquerque[5], N. Araújo[6], A. B. Bacchiega[7], B. Bica[4], D. Brito[8], A. Duarte[9], P. Realle[10], G. Ferreira[11], K. Wagner Poti Gomes[12], A. K. Melo13, B. Stadler[14], A. Maria Kakehasi[11], E. Klumb[15], H. Mariz[9], C. Marques[9], L. Mota[5], G. Munhoz[16], E. Paiva[17], H. Pereira[1], G. Salviato Pileggi[7], M. Pinheiro[18], J. R. Provenza[19], A. P. Gomides[5], E. Reis Neto[18], S. Ribeiro[1], E. Sato[18], T. Laroca Skare[14], V. De Souza[10], M. L. M. Teodoro[20], L. D. D. A. Valadares[9], V. Valim[21], D. Calderaro[11]. [1]*Universidade Federal do Amazonas, Medical School, Manaus, Brazil*; [2]*Faculdade de Medicina da Universidade de São Paulo, Medical School, São Paulo, Brazil*; [3]*Centro Universitário de Brasília, Medical School, Brasília, Brazil*; [4]*Universidade Federal do Rio de Janeiro, Medical School, Rio de Janeiro, Brazil*; [5]*Universidade de Brasília, Medical School, Brasília, Brazil*; [6]*Hospital do Servidor Público Estadual de São Paulo, Rheumatology Department, São Paulo, Brazil*; [7]*Faculdade de Medicina de Barretos, Medical School, Barretos, Brazil*; [8]*Universidade Federal da Paraíba, Medical School, João Pessoa, Brazil*; [9]*Universidade Federal de Pernambuco, Medical School, Recife, Brazil*; [10]*Universidade Federal de Juiz de Fora, Medical School, Juiz de Fora, Brazil*; [11]*Universidade Federal de Minas Gerais, Medical School, Belo Horizonte, Brazil*; [12]*Hospital Geral de Fortaleza, Rheumatology Department, Fortaleza, Brazil*; [8]*Universidade Federal da Paraíba, Medical School, João Pessoa, Brazil*; [14]*Hospital Universitário Evangélico Mackenzie, Rheumatology Department, Curitiba, Brazil*; [15]*Universidade do Estado do Rio de Janeiro, Medical School, Rio de Janeiro, Brazil*; [16]*Irmandade da Santa Casa de Misericórdia de São Paulo, Rheumatology Department, São Paulo, Brazil*; [17]*Universidade Federal do Paraná, Medical School, Curitiba, Brazil*; [18]*Universidade Federal de São Paulo, Medical School, São Paulo, Brazil*; [19]*Pontifícia Universidade Católica de Campinas, Medical School, Campinas, Brazil*; [20]*Universidade Federal de Minas Gerais, Psychology School, Belo Horizonte, Brazil*; [21]*Universidade Federal do Espírito Santo, Medical School, Vitória, Brazil*

Background: Mental health was widely affected during the new coronavirus pandemic. In addition, some measures adopted by most countries in order to contain the virus spread, such as isolation and social distancing, leading to the interruption of routine activities, including partial or complete interruption of face-to-face classes may be associated with increased stress, depression and anxiety among undergraduate medical students (1). From March to September, 2020, the Brazilian Society of Rheumatology carried out the Mario Pinotti II Project (MPII), a prospective, multicenter, observational cohort study designed to monitor the COVID-19 in patients with rheumatic disease on hydroxychloroquine, using periodic telephone calls performed by undergraduate medical students (2).

Objectives: To compare the mental health status of medical students who were participating from the MPII with theirs colleagues not involved in this project.

Methods: A web-based survey via google forms platform was developed by a panel composed of undergraduate medical students, rheumatologists, medical school professors, and a psychology professor. It included details on demographic and life habits data and domains regarding depression, anxiety and stress, using the DASS-21 (Depression, Anxiety & Stress Scale), Brazilian version. Data collection occurred from July 20th to August 31st, 2020. Statistical analysis was performed using the SPSS version 20.0. Univariate and multivariate linear regression analysis were performed to verify associations with the DASS-21, defined as dependent variable. A p-value < 0.05 was deemed as significant. This study was approved by the Institutional Research Ethics Committee.

Results: A total of 684 undergraduate medical students were included in this study, of whom 228 as MPII volunteers (VG) and 456 as control group (CG). Median age was 23 years (IQ 21-24) and the CG was older than the VG (p<0.03). Most of them were white (68.8%) and women (63%). There were no significant differences regarding comorbidities, ethnicity, smoking status, alcohol intake and physical activity. Older age, male gender, participation of MPII study, absence of a worsening in sleep pattern during the pandemic and a lower number of prior comorbidities were associated with lower DASS21 scores, suggesting a better mental health (Table 1).

Conclusion: Several aspects may be involved with mental health, including increased emotional maturity, gender and sleep pattern. Although with marginal independent association, medical students with participation in the MPII study had better mental health than their student colleagues not engaged with this research. Our data pointed out that voluntary participation in a research project which foresees interaction by telephone contact with rheumatic patients, professors, rheumatologists, and colleagues is associated with better mental health.

REFERENCES:

[1] Meo SA, Abukhalaf AA, Alomar AA, Sattar K, Klonoff DC. Covid-19 pandemic: Impact of quarantine on medical students' mental wellbeing and learning behaviors. Pakistan J Med Sci 2020;36(COVID19-S4):S43–8.

[2] Gomides A, Ferreira G, Kakehas A, Lacerda M, Marques C, Paiva E et al. Impact of chronic use of antimalarials on SARS-COV-2 infection in patients with immune-mediated rheumatic diseases: protocol design for a multicentric observational cohort in Brazil. JMIR Research Protocols, 2020.Preprint

Table 1. Univariate and multivariate analysis of predictors associated to the DASS-21 in undergraduate medical students during the COVID-19 pandemic

	Univariate analysis			Multivariate analysis		
Variable	B	95%CI	p-Value	B	95%CI	p-Value
Age	-0.32	-0.61 to -0.03	0.03	-0.47	-0.81 to -0.13	0.008
Female gender	4.88	3.021 to 6.76	<0.001	-	-	-
Stable love relationship	-2.49	-4.35 to -0.64	0.008	-2.5	-4.4 to -0.59	0.01
Number of previous comorbidities reported	4.69	3.71 to 5.68	<0.001	4.82	3.73 to 5.92	<0.001
MP-II volunteering	-2.81	-4.74 to -0.86	0.005	-	-	-
Worsening in sleep pattern	6.41	4.62 to 8.20	<0.001	5.01	3.07 to 6.96	<0.001

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1218

AB0849 ONLINE EDUCATION YIELDS SIGNIFICANT GAINS IN RHEUMATOLOGISTS' KNOWLEDGE OF PSORIATIC DISEASE

A. Stan[1], M. Calle[1], P. Schoonheim[1], A. B. Gottlieb[2]. [1]*Medscape, LLC, Education, New York, United States of America*; [2]*Icahn School of Medicine, Mount Sinai, New York, United States of America*

Background: Physicians face challenges staying up-to-date with the latest research and accessing the ever-growing field of knowledge is time-consuming. Online education can make these clinician's tasks more efficient and less time-consuming.

Objectives: As part of a larger curriculum, we developed an online CME activity titled: "Optimizing Treatment in Patients With Moderate to Severe Psoriasis". The goal of this study was to assess whether this online CME accredited video discussion improves physicians' understanding of the prevalence and impact of the various manifestations of psoriatic disease, and how these might impact the choice of treatment in patients with psoriasis and/or psoriatic arthritis.

Methods: Rheumatologists participated in an online CME activity (https://www.medscape.org/viewarticle/931595) consisting of a 30-minute video discussion between 2 experts with synchronized slides. Educational effect was assessed using a 4-question repeated pairs, pre-/post-assessment. A chi-square test determined if a statistically significant improvement (P <.05 significance level) existed in the number of correct responses from the pretest and posttest scores. Cramer's V was used to estimate the level of impact of the education (Modest

[.0]; Extensive [>.26]). The CME activity launched on Jul 6, 2020, and the data were collected through Aug 31, 2020.

Results: A total of 54 rheumatologists completed the pre- and post activity assessments during the study period. Overall the activity had a signficiant impact (*P* =.0002) on rheumatologists' knowledge and competence related to optimisation of treatment in psoriatic disease, with a Cramer's V value of 0.210 indicating a considerable educational impact. The average percentage of correct responses rose from 67% pre-activity to 85% post-activity. A repeated pairs analysis showed that 21% of rheumatologists improved their knowledge and 64% reinforced their knowledge, respectively. The changes in percentage of correct responses from pre- to post-assessment for all questions are shown in Table 1. More than 60% of rheumatologists had a measurable improvement in confidence in their ability to identify patients with psoriatic disease who are candidates for first-line therapy with biologics.

Table 1. Impact of education on rheumatologists' knowledge of psoriatic disease

Question #	Question topic	Aggregated data		Linked Learner Results[a]	
		Average % of correct responses Pre- vs. Post-education	P-value	% Improved[b] learners Pre- vs. Post-education	% Reinforced[c] learners Pre- vs. Post-education
1.	Prevalence of the various manifestations of psoriatic disease	46% vs 80%	.0002	35%	44%
2.	Clinical data with biologic therapies in psoriatic disease	69% vs 78%	NS	17%	61%
3.	Competence related to identification of patients who may benefit from biologic therapy	87% vs 98%	.027	11%	87%

[a]Each individual learner tracked pre and post-education[b]Incorrect answer pre-education, Correct answer post-education[c]Correct answer pre-education, Correct answer post-education

Conclusion: This online CME activity significantly improved rheumatologists' knowledge and competence related to the optimization of treatment in psoriatic disease. However, there is room for further improving physicians' knowledge of clinical trial outcomes with biologics in patients with PsA, since 22% of rheumatologists provided incorrect answers to question 3 post-education. This topic can be addressed in future educational programs.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1569

AB0850 DUTCH RHEUMATOLOGISTS' PERSPECTIVE ON MRI EDUCATION: DO WE NEED TO CHANGE?

M. Cabri[1], C. J. Van der Laken[2], M. Maas[3]. [1]*Amsterdam UMC, Rheumatology, Amsterdam, Netherlands*; [2]*Amsterdam UMC, Rheumatology, 1081HV, Netherlands*; [3]*Amsterdam UMC, Radiology, Amsterdam, Netherlands*

Background: Studies have shown the value of magnetic resonance imaging (MRI) as an objective tool for diagnosis, follow up and detection of complications for a broad spectrum of rheumatology associated diseases [1]. With increasing (potential) clinical applications of MRI, rheumatologists need basic knowledge about the technique and interpretation of the images to get most out of MRI use in clinical practice. Although radiologists will remain the experts of MRI protocols and readings, lack of sufficient rheumatologists training will not yield in optimal interaction between the specialists and will negatively influence the benefit of the MRI contribution to patient care. Despite offered MRI courses within EULAR, in the Netherlands there is currently no structural MRI education for rheumatologists (in training). This while rheumatologists are intrinsically motivated to improve their MRI skills [2,3].

Objectives: By use of a developed questionnaire:

[1] To create an overview of the current communication methods between rheumatologists and radiologists regarding MRI and rheumatologists' perspectives on the efficiency and effectiveness of the imaging requests and radiologists reports.

[2] To make an inventory of current knowledge and interpretation skills of rheumatologists concerning MRI.

[3] To assess the needs of rheumatologists for education to work with MRI requests, reading and reports in routine clinical care by development of a questionnaire to determine the current clinical situation.

Methods: A questionnaire was created.

Results: A total of 109 respondents (28% respons) have filled in the form with a 100% completion rate.

1. Communication:

Communication regarding MRI in rheumatology is done largely per request of the rheumatologist with a high level of satisfaction concerning the quality of the discussion. Most medical centers have no multidisciplinary team meeting with the radiology department, discussions are mostly performed on demand.

2. Interpretation:

Rheumatologist predominantly rely on the conclusion of the radiology report with little understanding of the technical and anatomical characteristics of the images. Only a small percentage (6%) of rheumatologists is able to interpret the images. Half of the responders do not feel competent to teach fellow colleagues about imaging.

3. Educational wishes:

When asked to prioritize the subject of imaging education, most people prefer interpretation skills, followed by instructions on how to provide most optimal clinical information and question(s) on the request form as well as knowledge on anatomy. Least preferred is education concerning the MRI technique itself.

The preferred method of advanced imaging education is a combination of classroom teaching and e-learning.

Conclusion: Dutch rheumatologists express a satisfactory communication with their radiologists, which is mostly not performed structurally. Rheumatologists indicated that education, in particular in MRI imaging reading,will provide a better understanding in the MRI technique and applicability as well as confidence in self-interpretation of the images.

The preferred method of MRI imaging education is blended (e.g., a combination of classroom teaching and e-learning).

The results therefore show that MRI education of rheumatologists is still a need in clinical practice in the Netherlands. MRI education of rheumatologists can contribute to more efficient application of MRI in rheumatology patient care, including a more optimal interaction between radiologists and rheumatologists.

REFERENCES:

[1] Sudol-Szopinska I *et al*: Recommendations of the ESSR Arthritis Subcommittee for the Use of Magnetic Resonance Imaging in Musculoskeletal Rheumatic Diseases. *Seminars in musculoskeletal radiology* 2015

[2] Bandinelli F *et al*: Rheumatology education in Europe: results of a survey of young rheumatologists. *Clinical and experimental rheumatology* 2011

[3] Maksymowych WP *et al*: Diagnosis of Axial Spondyloarthritis: A Primary Unmet Educational Need for Rheumatologists Is Interpretation of MRI [abstract]. Arthritis Rheumatol. 2020

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2553

AB0851 CONDUCTING PATIENT SCHOOLS AS A WAY OF MANAGING RHEUMATOLOGIC DISEASES

A. Sarapulova[1], O. Teplyakova[1]. [1]*MA "New Hospital", Center of Clinical Rheumatology, Yekaterinburg, Russian Federation*

Background: 2020 year has become a landmark for the medical care system around the world. A huge number of patients and doctors were involved in the fight against an unknown and rapidly spreading infection, while many patients with chronic diseases or those who were just planning to see a doctor were left without this opportunity. The consequence was the active development of the online format of patient-doctor communication.

Objectives: To determine the value of conducting schools for patients with rheumatologic diseases or related complaints in a pandemic.

Methods: On the basis of the Clinical Rheumatology Center of the Medical Association "New Hospital", online schools were organized for patients with rheumatological diseases and complaints. In just 3 months, 6 schools were held, in which 299 people took part. At the end of each session, patients were asked to answer questions about the level of satisfaction and the value of the information received. The survey was conducted in Google form.

Results: about 80% of the responders lived in the region where the schools were held, 20% were from other regions of Russia or other countries. One third of patients (33.9%) were 31-40 years old, a quarter (25%) were 51-60

years old, and every fifth (19.6) was from 61 to 70 years old. The overwhelming majority (61.1%) learned about the training from employees' announcements or on the website of a medical organization. Interestingly, almost a third of the participants (31.9%) listened to the lecture to "prevent problems in the future" or "for general development," the rest either get sick themselves or have relatives with these problems. The significance and usefulness of the school on a scale from 0 to 10 points was assessed by 75% participants at 10 points, another 21% from 7 to 9 points, and for 1 participant - by 3 and 4 points. When answering the question: "Will something change in the understanding of your disease or further managing after today's lesson?" most of the listeners answered that "they are planning to change their lifestyle" (55.4%), a little less - "understands that you need to come to an in-person appointment" (27.4%), "listened due to problems with relatives" (30.4%) and "understands that it is necessary to adjust the treatment" (23.2%). 87.5% of the responders rated the degree of interest with which the teacher led the school at 10 points; all 100% of participants expressed a desire to attend the following events. When comparing the school with television programs or other similar events, 83.9% of people noted a higher level of information importance and 87.5% of accessibility of its presentation. All responders with a high probability were ready to recommend schools to another people (85.7% for 10 points), trust the doctor conducting such schools (94.6% for 10 points) and would turn to this doctor if possible (87.5% for 10 points). Also, all participants actively answered the question about the desired topic of future schools.

Conclusion: the conducted evaluation of the online format of schools for patients with rheumatic diseases or complaints has confirmed the high satisfaction of patients with this form of communication, the presence of a certain "request" for such format, clarity and accessibility of the transmitted information. The most important result of the training can be considered the readiness of patients to change their lifestyle and the understanding that it is necessary to observe or consult a doctor.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3046

AB0852 BREAKING THE GLASS CEILING IN MEXICAN RHEUMATOLOGY

I. J. Colunga-Pedraza[1], G. Serna-Peña[1], D. Alpizar-Rodriguez[2], N. Guajardo-Jauregui[1], R. Galarza-Molina[3], D. Á. Galarza-Delgado[1], C. F. Pacheco Tena[2], M. A. Reyes Soto[1]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*; *[2]Colegio Mexicano de Reumatología, Rheumatology, Ciudad de México, Mexico*; *[3]Universidad Auntónoma de Nuevo León, Political Science, Monterrey, Mexico*

Background: The term "glass ceiling" has been used since the late eighties, to designate an invisible barrier that prevents highly qualified women from reaching positions of responsibility in the organizations they work. (1) At first, this concept was used to analyze the career of women who, having a professional career and a high level of competition in their workplaces, encountered an interference when trying to advance in their careers. (2). The so-called "glass ceiling" refers to a last barrier based on prejudice towards women that prevents them from advancing to high-level positions.

Currently, there is almost the same number of men and women affiliated to the Mexican College of Rheumatology (CMR). The position of president is the highest directorial position, we undertook the task of evaluating the percentage of women who have historically held that leadership position.

Objectives: To assess the percentage of woman who have occupied the position of president of the Mexican College of Rheumatology.

Methods: Observational, cross-sectional study. We evaluated the number of man and women who have historically held the position of president of the CMR.

Results: Currently, the CMR has 630 active members, 308 women (48.9%) and 322 men (51.1%). Among rheumatologists younger than 40 years of age, women represent 58% (n=128). We found that historically the CMR has had 48 presidents, of which only 4 (8.3%) are women.

Conclusion: There is a big gender gap between presidents of the CMR. It is important to talk about the gender perspective and recognize the causes that have originated this gap. Incorporating the gender perspective in senior management is a pending issue for our CMR.

REFERENCES:

[1] Barberá E, Ramos A, Sarrió M, et al. Laberinto de cristal en el liderazgo de las mujeres. *Psicothema* 2011;23(2):173-179.

[2] Bustos O. Mujeres rompiendo el techo de cristal: el caso de las universidades. *OMNIA - Revista de la Coordinación de Estudios de Posgrado* 2002(41);1-7.

Acknowledgements: We have no acknowledgements to declare.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3417

Educational cases

AB0853 IGG4-RELATED DISEASE CAUSING OCULAR NERVE PALSIES AND ORBITAL APEX SYNDROME: CASE REPORT AND LITERATURE REVIEW

F. Javed[1], C. Chung[2], H. Fayyaz[1], R. Jeffery[1]. *[1]Northampton General Hospital, Department of Rheumatology, Northampton, United Kingdom*; *[2]Northampton, Department of Ophthalmology, Northampton, United Kingdom*

Background: IgG4-Related Disease (IgG4-RD) is a systemic immune-mediated fibroinflammatory condition. The epidemiology is not well defined: it usually affects adults from middle-age onwards, predominantly male. Both B and T-cells are central in IgG4-RD pathogenesis, as demonstrated by the efficacy of B-cell depletion therapy.IgG4-RD can affect multiple organs including the central and peripheral nervous system, producing a constellation of clinical symptoms and signs, depending on the organ structures involved.

IgG4-related orbital disease is relatively rare can implicate all extra-ocular muscles, structures emerging from the Orbital apex, optic canal, or superior and inferior orbital fissure. Depending on the structures involved, it can produce different or sometimes subtle clinical presentations, posing diagnostic challenge. There were case reports of IgG4-related ophthalmic disease misdiagnosed as intraocular tumour.

Objectives: IgG4-RD is increasingly recognised as an entity affecting the head and neck region. However, it rarely involves skull base and presents with orbital apex syndrome. In this current case report, we describe an interesting case of IgG-related orbital disease presenting with ocular nerve palsies and orbital apex syndrome.

Methods: Case report.

Results: A 36-year-old gentleman with cocaine and alcohol misuse presented with a 2-month history of left sided headache, diplopia, recurrent ear infections, otalgia and hearing loss. Initial imaging suggested left otomastoiditis and intravenous antibiotics were commenced. Contralateral partial third nerve palsy with pupil sparing was elicited. 2 months later, there was worsening right eye ptosis, proptosis, right relative afferent pupillary defect, reduced visual acuity and colour vision as well as a near-complete ophthalmoplegia. Subsequent imaging showed worsening soft tissue swelling centred on the upper left parapharyngeal and masticator space, with multiple perineural enhancement and lateral extension to right orbital apex and orbital fissures. Blood tests only revealed raised IgG4 subclass. Infectious aetiology was excluded. Left nasal mass biopsy performed showed no fungal organism or malignancy. There were lymphoplasmacytic proliferation but no storiform fibrosis or obliterative phlebitis. IgG4 immunostaining on two assessable fields revealed 22 and 17 positive plasma cells respectively, and an IgG4: IgG ratio of <10%, and 50% in the other. Significant improvement was seen clinically and radiologically with antibiotics and a tapering regime of oral Prednisolone. Patient was commenced on Azathioprine as long term immunosuppression.

Conclusion: A high degree of clinical suspicion is necessary to diagnose IgG4-RD when presenting with orbital apex syndrome and ocular nerve palsies,IgG4-RD can mimic mastoiditis of infectious aetiology. Other differentials may include cocaine-induced midline destructive lesions and granulomatosis with polyangiitis. The diagnosis can be supported by elevated serum IgG, elevated IgG index and pathognomonic histopathological findings. . The diagnosis of IgG4-related orbital disease should be deliberated on by a multidisciplinary group, with every effort being made to exclude an infectious aetiology, before embarking on immunosuppressive therapy.Primary treatment is with steroids. However, immunotherapy using azathioprine can be utilised in recurrent disease or patients with steroid intolerance.

REFERENCES:

[1] Goto H, Ueda S. Immunoglobulin G4-related ophthalmic disease involving the sclera misdiagnosed as intraocular tumor: report of one case. OculOncolPathol. 2016;2(4):285–8.

[2] Ohyama K, Koike H, Iijima M, et al. IgG4-related neuropathy: a case report. JAMA Neurol. 2013;70(4):502–5.

[3] AbdelRazek MA, Venna N, Stone JH. IgG4-related disease of the central and peripheral nervous systems. Lancet Neurol. 2018;17(2):183–92.

[4] Kamekura R, Takahashi H, Ichimiya S. New insights into IgG4-related disease: emerging new CD4+ T-cell subsets. Curr Opin Rheumatol. 2019;31(1):9–15.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.939

AB0854 A CASE REPORT OF BROWN SYNDROME COMPLICATING THE MANAGEMENT OF SCLEROMYOSITIS

P. Arora[1], L. Croot[1]. [1]*Barnsley Hospital NHS Foundation Trust, Rheumatology, Barnsley, United Kingdom*

Background: Brown syndrome is a rare ocular motility disorder which has been reported in JRA, RA and SLE but never in a patient with scleromyositis.
Objectives: To report the first case of Brown syndrome in a patient with scleromyositis and increase awareness of this condition.
Methods: A case report and discussion.
Results: The patient was diagnosed with scleromyositis, at the age of 34, after presenting with arthralgia, sclerodactyly, skin pigmentation, Raynaud's phenomenon, mild muscle weakness and dyspnoea. His labs were CRP 47 mg/L, CK 868 IU/L, ANA strongly positive; anticentromere Ab negative and Anti-PM/Scl-75 and Anti- PM/Scl-100 Ab positive. HRCT chest showed extensive pulmonary fibrosis with lower lobe honeycombing. TLCO was 3.98 (33% of predicted).
He was initially managed with high dose steroids and pulsed IV cyclophosphamide with azathioprine for maintenance therapy. His lung disease stabilised and myositis resolved but he continued to develop calcinosis cutis so was switched to 6 monthly IV rituximab.
6 years later, he developed morning headaches with intermittent diplopia, described as double vision in vertical gaze with one image being above the other. Episodes lasting 10 minutes to 2 hours. Examination showed normal visual acuity and fundoscopy, no peripheral or eye muscle weakness.
Investigations to exclude myasthenia gravis, cerebral vasculitis and atypical infection were organised (MRI, AChR antibody, lumbar puncture, MRA) and were normal.
Because of intermittent nature of his episodes, his eye examination was always normal but he captured images in disconjugate gaze with right eye looking upwards and outwards when trying to look straight (Figure 1). Occasionally this was associated with orbital pain and an audible click. These features are suggestive of Brown syndrome.
He continues to have recurrent episodes despite immunosuppression but prednisolone 20mg daily for 1-2 days at onset of each attack causes rapid resolution of symptoms.

Figure 1. Right eye looking upwards and outwards when trying to look straight

Conclusion: Scleromyositis is an overlap syndrome of scleroderma and dermatomyositis. Muscle involvement is mild and clinical presentation can be variable. The PM/Scl antibodies are highly characteristic of the syndrome. (1)
Brown syndrome is an ocular motility disorder, first described in 1950, characterized by the inability to fully elevate the affected eye in adduction due to pathology of the superior oblique tendon sheath. (2)
It can be congenital or acquired, viz, trauma, surgery or sinusitis and also been described in RA, JIA and SLE. (3)
If superior oblique tendon cannot relax or slide freely through the trochlea then the affected eye cannot depress completely, leading to diplopia on upward gaze. (4) In inflammatory disease it is thought that swelling of the posterior part of the superior oblique tendon or tenosynovitis are likely causes of the tendon sheath abnormality. (4) This is likely to be the case in this patient because his symptoms are recurrent, respond to steroids and tend to occur more towards the end of rituximab cycles.
Recognition of this syndrome is important because invasive investigations can be avoided. Also, intermittent diplopia in a patient with autoimmune disease is suggestive of myasthenia gravis which maybe incorrectly diagnosed.
Finally, this case demonstrates the syndrome can be easily managed with short courses of oral steroids, although patients who are already on immunosuppressant treatment may need this in addition.

REFERENCES:

[1] Török L, Dankó K, Cserni G, Szûcs G. PM-SCL autoantibody positive scleroderma with polymyositis (mechanic's hand: clinical aid in the diagnosis). JEADV 2004; 18: 356–359
[2] Brown H W. Congenital structural muscle anomalies. In:Alien J H, ed. Strabismus ophthalmic symposium I. St Louis:CV Mosby, 1950: 205-6.
[3] Cooper C, Kirwan JR, McGill NW, Dieppe PA. Brown's syndrome: an unusual ocular complication of rheumatoid arthritis. Ann Rheum Dis 1990; 49:188-9.
[4] Sandford-Smith JH. Superior oblique tendon syndrome and its relationship to stenosing tenosynovitis. Br JOphthalmol 1973; 57:859-65.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2454

AB0855 FIBROUS ARTHROPATHY AS THE KEY FEATURE OF JUVENILE SCLERODERMA - CASE REPORT

D. Dibrov[1], M. Starovoytova[1], O. Desinova[1]. [1]*V.A. Nasonova Research Institute of Rheumatology, Department of Microcirculation and Inflammation, Moscow, Russian Federation*

Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by endothelial dysfunction, immunological disorders, and excessive synthesis of collagen and its deposition in various tissues and organs. The juvenile onset SSc before the age of 16 is very rare, with annual incidence of 0.27-0.5 cases per million children according to English and Finnish authors [1,2].
Objectives: To present a clinical case of juvenile onset SSc, manifesting from the childhood predominantly with fibrous contractures.
Methods: Patient K., 30 yo. Clinical presentation on admission to the Institute of Rheumatology in September 2020: thickening of the trunk and limbs skin (mRSS 10 scores), pronounced induration of subcutaneous tissues and muscles; contractures of the elbow, shoulder, hip and knee joints, short stature (height 142 cm) with proportional shortening of the limbs. ANA (HEp-2) 1/320, a-Scl-70, a-RNP-70 and ACA tests were negative. Ultrasonography revealed left-sided coxitis, esophagogastroduodenoscopy - Barrett's esophagus. Chest CT, echocardiography, electrocardiography and capillaroscopy yielded no specific findings.
The patient has been ill since the age of 3, when SSc manifested with skin thickening, "dry" arthritis and rapid development of contractures of the large joints. Thorough diagnostic elaboration ruled out such potential causes as phenylketonuria, glycogenosis, mucopolysaccharidoses, primary amyloidosis, and porphyria. Histological findings (2007) of a biopsied skin specimen containing subcutaneous fat and muscle tissue included focal vacuolization of keratinocytes, poor perivascular lymphocytic and histiocytic infiltration, fibrosis and hyalinosis of collagen fibers of varying intensity in the in mid- and deep dermis, infiltration of collagen fibers by fibroblasts, skin appendages atrophy – all of them representing a pattern of morphological changes characteristic of SSc. Therapeutic regimens including prednisone at 5-15 mg/day and D-penicillamine were ineffective.
Results: In this case, in view of fibrotic arthropathy, a differential diagnosis was made with deep morphea and stiff skin syndrome. Visceral involvement, immunological disorders and biopsy findings substantiated a diagnosis of juvenile onset SSc. Oral MTX was initiated at 15 mg to target skin lesion and osteoarticular symptoms.
Conclusion: Predominance of fibrotic arthropathy in presented case caused difficulties in establishing SSc diagnosis, as this patient did not have such inherent features as the Raynaud's phenomenon, interstitial lung disease or pulmonary hypertension. Juvenile onset SSc manifesting before the age of 16 has its own clinical features, usually persisting through the adulthood, and therefore, such one-of-a-kind appearances of juvenile onset SSc should not be missed or misinterpreted.

REFERENCES:

[1] Herrick AL, Ennis H, Bhushan M et al. Incidence of childhood linear scleroderma and systemic sclerosis in the UK and Ireland. Arthritis Care Res. 2010 Feb;62(2):213-8. doi: 10.1002/acr.20070.
[2] Pelkonen PM, Jalanko HJ, Lantto RK et al. Incidence of systemic connective tissue diseases in children: a nationwide prospective study in Finland. J Rheumatol. 1994 Nov;21(11):2143-6

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2840

AB0856 CHRONIC INTESTINAL PSEUDO-OBSTRUCTION WITH HYDRONEPHROSIS: A CASE REPORT ON SUCH DISABLING AND RARE COMPLICATION OF LUPUS

C. S. Ng[1], S. L. Kan[1], A. L. Lim[1]. [1]*Hospital Pulau Pinang, Rheumatology Unit, Medical Department, Georgetown, Malaysia*

Background: Chronic intestinal pseudo-obstruction can be a rare complication of systemic lupus erythematosus. It is often late to be identified in contrast to other commoner organs involvement in systemic lupus erythematosus such as nervous system, joint and kidney.
Objectives: To report a case of uncommon gastrointestinal complication of lupus, with associated hydronephrosis at the ureter, with treatment delay.
Methods: We report a case of chronic intestinal pseudo-obstruction.
Results: A 34 year old, with ten-year history of lupus nephritis, presented with recurrent abdominal pain and diarrhoea past nine months. The patient had just been diagnosed as end-stage renal failure a year ago, on regular haemodialysis. For the past ten years, the patient was not able to tolerate immunosuppressant due to the multiple episodes of infections, including shin carbuncle, herpes zoster, breast abscess and catheter-related candida/bacterial infections. However, the patient did not have any other major organs manifestations of lupus for the past ten years. The patient was apyretic. Multiple stool cultures were negative including Clostridium difficile. The abdominal radiography showed dilated small bowel with diffuse thickening of large and small bowels on computed tomography. Bilateral uretero-hydronephrosis was also noted without any evidence of obstructive uropathy on imaging. Ileocolic resection was done for presumed intestinal obstruction and the ileocolic biopsy did not reveal any granuloma, malignancy or vasculitis except for non-specific inflammation of cecum. Cytomegalovirus inclusion body was absent as well. Tuberculosis culture was negative. Oesophagoduodenoscopy and colonoscopy were offered in view of persistent unexplained loose stool and abdominal pain. But unremarkable findings were noted from multiple biopsy specimens of the small and large bowels. Second relook of the initial hemicolectomy specimen with special actin immunostain on the smooth muscle revealed degenerative changes of the muscularis propria. These were evidenced by cytoplasmic vacuolation, atrophy and pyknotic nucleus of the smooth muscle cells with surrounding oedema. Smooth muscle dysmotility could be the underlying pathology of this patient presentation. The patient responded well to intravenous immunoglobulin followed by azathioprine in addition to prednisolone and prokinetic agent.
Conclusion: Prompt recognition is pivotal in this case could have prevented the unnecessary surgical intervention earlier. It is potentially reversible. Long term prognosis of this rare entity is, however, varying.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2854

AB0857 CERTOLIZUMAB PEGOL RELOADING SUCCESSFULLY CONTROLS INFLAMMATORY ARTHRITIS FLARES DURING PREGNANCY – A CASE REPORT

V. Pavlova[1]. [1]*McMaster University, Department of Medicine, Hamilton, Canada*

Background: Approximately 50% of patients with inflammatory arthritis (IA) experience worsening of disease activity during pregnancy.[1,2] Given the evidence that increased disease activity immediately before or during pregnancy is associated with adverse pregnancy outcomes, it is imperative to maintain tighter disease control during this period.[3] Treatment options are limited to steroids or disease-modifying anti-rheumatic drugs (DMARDs) compatible with pregnancy. Certolizumab pegol (CZP) is a humanized TNF-alpha inhibitor with no to minimal transplacental transfer, making it a suitable option during pregnancy.[4] In patients who relapse while on treatment with a biologic, consideration can be given to optimizing the dose of the biologic. Studies in Crohn's disease demonstrated that increasing the CZP dose from 400 mg Q4W to Q2W is a viable strategy for recapturing efficacy.[5] Similar data is not available for the rheumatology population or for pregnancy.
Objectives: To describe the successful control of juvenile inflammatory arthritis (JIA) flares using a reloading strategy with CZP in a pregnant patient with prior failure of multiple conventional systemic (cs)DMARDs and biologics.
Methods: This is a case report of a 31-year old female with JIA who presented with a disease flare in the 1st trimester of her 2ndpregnancy. The patient was treated with multiple csDMARDs and biologics since age 6. She experienced significant gastrointestinal side effects to subcutaneous methotrexate and leflunomide and inadequate response to hydroxychloroquine and sulfasalazine. Subsequently, she initiated and maintained treatment with etanercept for 14 years until she developed secondary loss of efficacy. She had primary non-response to golimumab and abatacept and experienced a severe allergic reaction to infliximab. Since 2017, she has been treated with CZP 200 mg Q2W with good control of disease activity.
Prior to conception, the patient had low disease activity (Table 1). At 11 weeks gestation, the patient noted worsening of disease activity, with pain at 4/10, fatigue at 7/10, morning stiffness for 60 minutes, swollen joint count (SJC) 4/28, and tender joint count (TJC) 19/28. The patient global assessment of disease activity (PtGA) remained at 4/10 while physician global assessment of disease activity (PhGA) and health assessment questionnaire disability index (HAQ-DI) increased to 6/10 and 1.625, respectively (Table 1). She reported that symptoms worsen one week after CZP injection with more joint pain and swelling in hands, wrists, and feet. The patient declined the addition of hydroxychloroquine, sulfasalazine, and steroids due to previous tolerability, lack of efficacy, and concerns about safety during pregnancy. The patient received 3 loading doses of CZP 400 mg Q2W. She then continued treatment with CZP 200 mg Q2W.

Table 1. Disease activity prior to conception and during pregnancy before and after reloading CZP.

Characteristic	Prior to conception	11 weeks gestation	19 weeks gestation after reloading CZP
SJC (28 joints)	2	4	2
TJC (28 joints)	NA	19	NA
PhGA*	4	6	2
PtGA*	4	4	4
HAQ-DI	1.5	1.625	1.5
Pain*	4	4	2
Fatigue*	7	7	5
Morning stiffness (min)	60	60	20-30

*Assessed on a 10-point scale.

Results: On follow-up at 19 weeks gestation the patient reported 80% improvement in joint pain and swelling and reduction in morning stiffness (Table 1). Pain and fatigue were rated as 2/10 and 5/10, respectively. PtGA score was 4/10, PhGA score was 2/10 and HAQ-DI score was 1.5 (Table 1).
Conclusion: Reloading CZP to control increased IA disease activity during pregnancy may be a viable treatment option. To our knowledge, this is the first report of dose optimization in IA and in pregnancy in a patient treated with CZP.
REFERENCES:
[1] van den Brandt S, *et al*. *Arthritis Res Ther* 2017;19(1):64.
[2] Jethwa, H *et al*, *Arthritis Rheumatol.* 2016;68 (suppl 10).
[3] de Man Y, *et al*. *Curr Opin Rheumatol.* 2014;26:329–333.
[4] Mariette X, *et al. Ann Rheum Dis.* 2018 Feb;77(2):228-233.
[5] Sandborn WJ, *et al*. *American College of Gastroenterology Annual Scientific Meeting.* 2009; Abstract 699
Disclosure of Interests: Viktoria Pavlova Speakers bureau: Amgen, Abbvie, BMS, Jenssen, Lilly, Merk, Novartis, Roche, UCB, Pfizer, Consultant of: Amgen, Abbvie, BMS, Jenssen, Lilly, Merk, Novartis, Roche, UCB, Pfizer, Grant/research support from: UCB
DOI: 10.1136/annrheumdis-2021-eular.3410

AB0858 SUCCESSFUL TERM PREGNANCY IN A PATIENT WITH GRANULOMATOSIS WITH POLYANGIITIS AFTER UNDERGOING RITUXIMAB THERAPY - CASE REPORT

O. Sirenko[1], O. Kuryata[1], T. Lysunets[2], A. Legkobyt[2], H. Mostova[3]. [1]*Dnipropetrovsk Medical Academy, Internal Medicine 2, Dnipro, Ukraine*; [2]*Dnipropetrovsk Regional Clinical Hospital After Mechnicov, Rheumatology, Dnipro, Ukraine*; [3]*Dnipropetrovsk Regional Clinical Hospital After Mechnicov, Obstetrics and Gynecology, Dnipro, Ukraine*

Background: Granulomatosis with polyangiitis (GWP) is a relatively rare disease with the lack of experience in the management of pregnancy currently. Potentially negative factors of pregnancy prognosis are both disease-related and teratogenic effects of specific vasculitis therapy [1].
Objectives: To describe a clinical case of Successful term pregnancy in a patient with Granulomatosis with polyangiitis after undergoing rituximab therapy.
Methods: 19 years-old woman was admitted to the rheumatology department of Clinical Regional Hospital After Mechnicov in 2013 with the debut of Granulomatosis with polyangiitis. Her disease course included recurrent rhinitis and sinusitis, Granulomatosis of the eye orbits. Positive ANCA titers were present in the disease onset. In the preceding 7 years she had been treated with corticosteroids, cyclophospan (discontinuated in 2017 because of lack of efficiency), than azathioprine. Aseptic necrosis of the both femoral head was estimated on fifth disease year. In 2018 azathioprine therapy had been discontinued owing to the disease progression and biological agents were prescribed – rituximab with positive effect. The disease remission was achived by rituximab therapy, the patient was warned about the need for contraception. The last dose of rituximab was introduced in February 2020. However, in March 2020, the patient reported pregnancy and therapy was discontinued. At the onset of pregnancy she was

treated with 6 mg oral methylprednisolone. Daily and this dose was stable till all pregnancy period. Fetal growth assessment, congenital abnormalities screening test, and laboratory tests for gestational diabetes and preeclampsia were unremarkable during all gestational trimesters. The ANCA titers remained negative and renal function was normal and there was no flare during all pregnancy period.

Results: At 38 weeks' gestation a spontataneous labor started without induction. A 3270-g healthy boy delivered with APGAR score of 9 at 1 minute and 5 minutes. Postpartum the disease remained in remission, and the patient was maintained on corticosteroids. The infant was healthy, with normal development.

Conclusion: Thus, the use of biological agents therapy in patients with GWP shows possible ways to safe reproductive potential with disease remission achievement.

REFERENCES:

[1] Daher A, Sauvetre G, Girszyn N, Verspyck E, Levesque H, Le Besnerais M. Granulomatosis with polyangiitis and pregnancy: A case report and review of the literature. *Obstetric Medicine*. 2020;13(2):76-82. doi:10.1177/1753495X18822581

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4016

HPR Measuring health (development and measurement properties of PROs, tests, devices)

AB0859-HPR NETWORK OF SUPPORT AND DEPRESSION IN RHEUMATIC DISEASES

L. Cano Garcia[1], S. Manrique Arija[1], F. Godoy-Navarrete[1], F. G. Jiménez-Núñez[1], R. Redondo[1], N. Mena-Vázquez[1]. [1]*Hospital Regional Universitario de Málaga, Rheumatology, Málaga, Spain*

Objectives: To describe the impact that depression has on the personal support network of patients with rheumatic diseases.

Methods: Design. Cross-sectional observational study of a series of patients with spondyloarthritis (SpA), rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) selected by consecutive sampling of the Rheumatology consultations. Selection criteria: age ≥18 years with AD (ASAS criteria), RA (EULAR / ACR 2010 criteria) and SLE (ACR-EULAR criteria) capable of understanding and willing to take the questionnaires. Protocol: The reference rheumatologist offered to participate in the study to all the patients who attended the consultation between October and December 2019 and met the selection criteria. After their approval and signing the informed consent, they went to the nursing consultation to carry out a battery of questionnaires from the PROMIS platform and collect clinical data. The infirmary was in charge of explaining the questionnaires to the patients. Variables: the main endpoint variable was depression evaluated by PROMIS and the secondary endpoint variables were questionnaires that evaluate the support network in various settings: company, emotional support, instrumental support, support through information. Likewise, data on their disease, comorbidities were collected using Charlson and socio-occupational profile. Statistical analysis: Descriptive analysis, R-Pearson correlation and multivariate linear regression analysis (VD: PROMIS depression).

Results: 151 patients participated: 50 with RA (90% women, mean age 55.12 ± 13.64 years), 51 with AD (51% women, 52.59 ± 12.15 years) and 50 patients with SLE (96 % women, mean age 47.14 ± 11.3 years). The baseline characteristics and comorbidities of the included. The mean (SD) of PROMIS depression in all patients was 16.4 (8.3) and a total of 65 patients (43%) had depression according to the Charlson index. Patients with Charlson depression had a higher mean (SD) of PROMIS depression than those without Charlson depression (24.5 [6.2] vs 10.3 [2.5], p <0.001). An inverse correlation was observed between PROMIS depression with the rest of PROMIS questionnaires: company (r = -0.369, p = <0.001), emotional support (r = -0.533, p = <0.001), information support (r = -0.577, p = <0.001) and instrumental support (r = -0.362, p = <0.001). Likewise, it was observed that patients without depression by Charlson compared with patients with depression had higher mean values (SD) in all questionnaires of the support network compared to those without depression by Charlson: company (17, 8 (2.9) vs 14.7 (4.7), p <0.001), emotional support (37.2 (5.2) vs 29.0 (9.5), p <0.001) and instrumental support (35.7 (7.2) vs 29.4 (8.8), p <0.001).Finally, in the multivariate analysis, the variables that were independently associated with depression by PROMIS were information support (B = -0.390; p <0.001) and emotional support (B = -0.239; p = 0.027). (R2 = 0.340).

Conclusion: Depression in rheumatic diseases negatively influences the support network and the perception of company of these patients. Treating depression is important for social functioning and social relationships in these patients and for any group of chronic patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1167

AB0860-HPR IS THERE A RELATIONSHIP BETWEEN PHYSICAL ACTIVITY, SLEEP QUALITY, ANXIETY AND DEPRESSION IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER?

T. Civi Karaaslan[1], S. Ugurlu[2], E. Tarakci[1]. [1]*Faculty of Health Sciences, Physiotherapy and Rehabilitation, Istanbul, Turkey*; [2]*Cerrahpasa Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*

Background: Maintenance of regular physical activity is associated with better physical and mental health (1). In addition, sleep disturbances and mood disorders are common in chronic inflammatory diseases (2).

Objectives: The aim of this study was to determine the relationship between physical activity, sleep quality, anxiety and depression in patients with FMF.

Methods: A total of 56 patients (30 female, 26 male) with Familial Mediterranean Fever (FMF) were enrolled in the study. They were diagnosed with FMF based on the Livneh diagnostic criteria (3). International Physical Activity Questionnaire - Short Form (IPAQ) was used to evaluate health-related physical activity. Patient-reported sleep quality was evaluated with the Pittsburgh Sleep Quality Index (PSQI). Hospital Anxiety and Depression Scale (HADS) was used to evaluate anxiety and depression in FMF patients. Patients who were 20-55 years old was included in the study.

Results: The mean age was 32.23±9.87 years. The mean disease duration of the patients was 12.24±7.61 years. The education level of 51.8% (n=29) of the participants was undergraduate and above. The rate of those who did not work was 32.1% (n=18) and 48.2% (n=27) of the participants were married. The mean of scores of IPAQ was 2333.99±2640.29, the mean of PSQI was 6.14±3.66, the mean of HADS-Anxiety was 7.89±5.03 and HADS-Depression was 7.01±4.44. The patients were classified according to physical activity categories as low (25.0%, n=14), moderate (41,1% n=23) and high (33.9%, n=19). Physical activity categories were not found associated with PSQI (p=0.437), HADS-Anxiety (p=0.363) and HADS-Depression (p=0.861). The relationships of scores of IPAQ, PSQI and HADS were demonstrated Table 1.

Conclusion: This study confirmed that patients with FMF suffer from sleep disturbances, anxiety and depression. In addition, sleep disturbances, anxiety and depression were not associated with physical activity category.

REFERENCES:

[1] Sokka, Tuulikki, et al. Physical inactivity in patients with rheumatoid arthritis: data from twenty-one countries in a cross-sectional, international study. Arthritis Care & Research: Official Journal of the American College of Rheumatology, 2008, 59.1: 42-50.

[2] Kucuksahin, Orhan, et al. Incidence of sleep disturbances in patients with familial Mediterranean fever and the relation of sleep quality with disease activity. International journal of rheumatic diseases, 2018, 21.10: 1849-1856.

[3] Bashardoust, Bahman. Familial Mediterranean fever; diagnosis, treatment, and complications. Journal of nephropharmacology, 2015, 4.1: 5.

Table 1. The correlations of IPAQ, PSQI and HADS scores.

		HADS-Depression	HADS-Anxiety	PSQI
IPAQ	r	-0.091	-0.142	-0.002
	p	0.505	0.295	0.990
PSQI	r	0.689	0.615	
	p	0.001	0.001	
HADS-Anxiety	r	0.681		
	p	0.001		

-Pearson Correlation

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1290

AB0861-HPR

MENTAL DISORDERS AND GASTROINTESTINAL SYMPTOMS IN RHEUMATIC DISEASES: A CROSS-SECTIONAL STUDY

F. S. Iaquinta[1], R. Spagnuolo[2], S. Naty[3], P. Doldo[2], R. D. Grembiale[3]. [1]*University "Magna Graecia" of Catanzaro, Rheumatology Research Unit, Department of Health Sciences, Catanzaro, Italy*; [2]*University "Magna Graecia" of Catanzaro - AOU Mater Domini - Gastroenterology Unit, Department of Experimental and Clinical Medicine, Catanzaro, Italy*; [3]*University "Magna Graecia" of Catanzaro, Rheumatology Research Unit, Department of Health Sciences, Catanzaro, Italy*

Background: Several studies agree that patients with chronic diseases are more likely to have mental health problems. Moreover, Rheumatic Diseases (RD) patients may show gastrointestinal symptoms as result of primary inflammation, secondary involvement or as treatment consequences. A better understanding of the potential association among such symptoms can help to improve treatment and quality of life.

Objectives: The aim of this study was to evaluate the impact of gastrointestinal symptoms (GI) on mental and social health in RD patients.

Methods: We performed a cross-sectional study of 69 RD patients with primarily osteoarticular symptoms. Patients completed questionnaires on GI symptoms (belly pain, constipation, diarrhea, disrupted swallowing, gas and bloating, nausea and vomiting, gastroesophageal reflux) and psychosocial changes (anxiety, depression, fatigue, sleep disturbance, pain interference, physical function, satisfaction with participation in social roles), of the Patient-Reported Outcomes Measurement Information System (PROMIS).

Results: Among 69 patients, 34 (49.3%) had a diagnosis of Rheumatoid Arthritis; 35 (50.7%) had axial spondyloarthritis (i.e. Psoriatic arthritis and Ankylosing Spondylitis). Median disease duration was 7,6±4 years and over one-third (36.2%) of patients had active disease. Most patients reported psychosocial changes and GI symptoms, as shown in Table 1. More specifically, figure 1 (A-G) shows that fatigue was associated with belly pain and bloating ($p<0.001$), and with constipation, diarrhea, disrupted swallowing and gastroesophageal reflux ($p<0.01$). Anxiety was related to disrupted swallowing and gastroesophageal reflux ($p<0.01$) whereas depressive symptoms were associated with belly pain ($p<0.001$), bloating and gastroesophageal reflux ($p<0.01$). Moreover, all gastrointestinal symptoms affected sleep quality. Finally, such symptoms significantly affected patients' social domain especially regarding satisfaction with participation in social roles ($p<0.05$ for belly pain and diarrhea, $p<0.01$ for bloating and disrupted swallowing) and physical functions ($p<0.001$ for belly pain, diarrhea, disrupted swallowing; $p<0.01$ for constipation, bloating and nausea and vomiting; $p<0.05$ for gastroesophageal reflux).

Table 1.

N = 69	Yes	Median *t*-Score ± SD
Mental and social Health PROMIS		
Anxiety, *n* (%)	48(69,6)	55,2±10
Depression, *n* (%)	40(58)	51,8±10
Fatigue, *n* (%)	52(75,4)	57,7±10
Sleep Disturbance, *n* (%)	44(63,8)	52±10
Pain interference, *n* (%)	62(89,9)	60,9±8
Physical Function, *n* (%)	64(92,8)	39,4±8
Satisfaction with participation in social roles, *n* (%)	21 (30,4)	45,2±10
GI-PROMIS		
Belly pain, *n* (%)	35(50,7)	50,6±14
Constipation, *n* (%)	36(52,2)	51,2±10
Diarrhea, *n* (%)	20(29)	45,2±8
Disrupted Swallowing, n (%)	31(44,9)	51±10
Gas and Bloating, *n* (%)	54(78,3)	55,5±8
Nausea and Vomiting, *n* (%)	32(46,4)	49,9±8
Gastroesophageal Reflux, *n* (%)	27(39,1)	49,1±11

Continuous variables are expressed as median and standard deviation. Categorical variables are expressed as number and proportion. GI and psychosocial changes scores were dichotomized for the use of categorical variables.

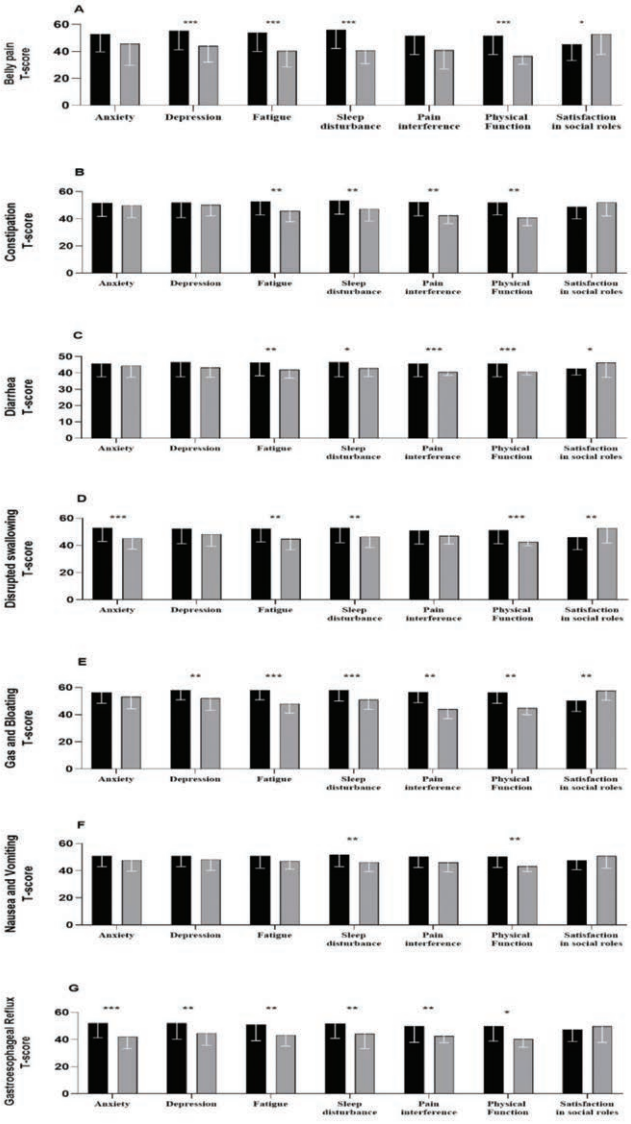


Figure 1. A–G: GI symptoms in RD patients across dichotomized psychosocial symptoms (Yes in Black/No in grey). The overall *p*-value was calculated by the Mann–Whitney non-parametric test for independent samples.

Conclusion: This study highlights the association between GI symptoms and psychosocial changes in RD patients. The use of validated Patients-Reported Outcomes, especially in clinical practice, may help to better define the impact of such symptoms on patients' quality of life and then evaluate patients' needs in a global dimension.

REFERENCES:

[1] P. T. Kröner, O. A. Tolaymat, A. W. Bowman, A. Abril, e B. E. Lacy, Gastrointestinal Manifestations of Rheumatological Diseases, Am. J. Gastroenterol., 2019.

[2] Mancina RM et al. Gastrointestinal Symptoms of and Psychosocial Changes in Inflammatory Bowel Disease: A Nursing-Led Cross-Sectional Study of Patients in Clinical Remission. Medicina (Kaunas). 2020 Jan 20;56(1):45.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1919

AB0862-HPR

THE RELATIONSHIP BETWEEN ANAEROBIC EXERCISE CAPACITY AND LOWER EXTREMITY FUNCTIONALITY IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

M. E. Acar[1], D. Bayraktar[2], S. Gucenmez[3], D. C. Saraç[2], N. Buker[2], U. Z. Kocak[2], D. Solmaz[4], S. Akar[4]. [1]*Izmir Katip Celebi University, Institute of Health Sciences, Department of Physiotherapy and Rehabilitation, Izmir, Turkey*; [2]*Izmir Katip Celebi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Izmir, Turkey*; [3]*Izmir Katip Celebi University,*

Ataturk Education and Research Hospital, Rheumatology Clinic, Izmir, Turkey; *[4]Izmir Katip Celebi Unviersity, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Izmir, Turkey*

Background: Familial Mediterranean fever (FMF) is an auto-inflammatory disease commonly affects people from Mediterranean basin. It is characterized by acute self-limiting inflammatory attacks of serous membranes. The disease is commonly associated with musculoskeletal symptoms of lower extremities such as arthritis, exercise induced leg pain, as well as protracted febrile myalgia. The term of anaerobic exercise capacity describes the ability of performing quick and explosive tasks such as stair climbing and brisk walking. It is well known that anaerobic exercise capacity is closely related to functional status.
Objectives: To assess the relationship between anaerobic exercise capacity and lower extremity functionality in patients with FMF.
Methods: Twenty-eight FMF patients (57% female) were included in the study. Median age was 33.5 (IQR 25/75: 23.3/44.3) years, median body mass index was 24.3 (IQR 25/75: 21.0/27.8) kg/m^2 median time since symptom onset was 20.0 (IQR 25/75: 11.5/24.5) years, median time since diagnosis was 10.0 (IQR 25/75: 3.75/17.5) years, and median colchicine dosage was 1.5 (IQR 25/75: 1.0/1.5) mg/day. Anaerobic exercise capacity was measured with Wingate Anaerobic Test by using a cycle ergometer. Peak power (watt/kg) and average power (watt/kg) were calculated. Stair climbing, standing from a chair, and walking were assessed by using 9-step stair climb test, 10-repetition chair stand test, and 6-minute walking distance, respectively. Spearman's rank-order correlation test was used to analyse the relationships between anaerobic exercise capacity and lower extremity functional tests.
Results: The results of the anaerobic exercise capacity and lower extremity functional test scores of patients with FMF were summarized in table 1. Moderate relationships were found between both peak and average anaerobic exercise capacities and lower extremity functional status tests (Table 1, p<0.05). Six-minute walking distance has the strongest association with both peak (rho: .672, p<0.001) and average (rho: .689, p<0.001) anaerobic exercise capacity.

Table 1. Anaerobic exercise capacity scores and lower extremity functionality as well as the relationships between anaerobic capacity and functional tests in patient with familial Mediterranean fever.

Characteristics	Median (IQR 25/75) (n:28)	The correlation results, rho, p values	
		Peak Power (watt/kg)	Average Power (watt/kg)
9-step stair climb test (seconds)	5.7 (5.1/6.4)	**-.590* p:0.001**	**-.648* p: 0.001**
10-repetition chair stand test (seconds)	16.6 (13.7/18.7)	**-.493* p:0.008**	**-.476* p:0.010**
6-minute walking distance (meters)	594.1 (551.1/643.3)	**.672* p<0.001**	**.689* p<0.001**
Peak power (watt/kg)	5.8 (4.1/7.9)		
Average power (watt/kg)	4.6 (3.1/5.9)		

IQR 25/75: Interquartile range between 25th and 75th percentiles; kg: kilograms, *Spearman's rank-order correlation test, p<0.05.

Conclusion: According to our results, anaerobic exercise capacity is related to lower extremity functional status in patients with FMF. Improving anaerobic capacity by using optimal rehabilitation programs including speed and agility exercises may help to improve anaerobic exercise capacity, and consequently lower extremity functionality in those patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2380

AB0863-HPR FUNCTIONAL STATUS ASSESSMENT THROUGH SELF-REPORTED QUESTIONNAIRES IN RHEUMATIC DISEASES

P. Herrera-Sandate[1], D. Vega-Morales[1], A. L. De-Leon-Ibarra[1], P. Valdes-Torres[2], L. A. Chavez-Alvarez[1], A. Limon-del Toro[1], I. D. J. Hernandez-Galarza[1], R. Pineda-Sic[1], D. Á. Galarza-Delgado[1]. *[1]Hospital Universitario Dr. José Eleuterio González, Rheumatology Service, Monterrey, Mexico*; *[2]Hospital Universitario Dr. José Eleuterio González, Sports Medicine and Physical Rehabilitation Department, Monterrey, Mexico*

Background: Health and disease status assessment is of paramount importance in rheumatic diseases. Self-report functional status questionnaires provide a cost and time-efficient means of systematic evaluation for physicians. The Health Assessment Questionnaire (HAQ) is one of the most utilized comprehensive measures of outcome, and is divided in 8 sections of activity domains, namely, dressing, arising, eating, walking, hygiene, reach, grip and outside activities. Other disease-specific instruments such as the Western Ontario and McMaster Osteoarthritis Index (WOMAC) share most of the functional domains evaluated by HAQ, whereas Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and WOMAC share domains mostly regarding pain and stiffness. Here, we present the results of the application of self-administered surveys in a third-level reference center in Mexico.
Objectives: Determine the functional status and most affected activity domains of patients with rheumatic diseases measured by generic (HAQ) and disease-specific (WOMAC and BASDAI) questionnaires in a reference center of northeastern Mexico.
Methods: We carried out a cross-sectional study in Rheumatology consultation in University Hospital "Dr. José Eleuterio González" in Monterrey, Mexico from August 2019 to December 2020. Nursery personnel systematically applied self-reported questionnaires HAQ, WOMAC and BASDAI in patients during their medical follow-up. Patient-reported outcomes were categorized by HAQ activity domains and/or pain and stiffness symptoms in WOMAC and BASDAI. Demographical characteristics were retrieved as well.
Results: Demographic characteristics are shown in Table 1. HAQ showed a higher prevalence of difficulty performing daily activities in the Grip domain. WOMAC question regarding heavy domestic duties had the higher degree of difficulty, as well as pain ascending stairs and stiffness after awakening. Fatigue was the most severe symptom in BASDAI, followed by pain in areas tender to touch and pressure and stiffness after awakening.
Conclusion: Disease activity and functional status impact is present on a mild-moderate level in self-reported questionnaires in the Rheumatology consultation of a northeastern center of reference in Mexico. The most affected domain in patients with rheumatic diseases is Grip domain, the most affected daily activities to perform are heavy domestic duties and the most prevalent symptoms are pain ascending stairs and stiffness after awakening as measured by HAQ, WOMAC and BASDAI, respectively.
REFERENCES:
[1] Ferreira, P. L., Gonçalves, S. P., Ferreira, L. N., Pereira, L. N., Antunes, P., Gouveia, N., Rodrigues, A., Canhão, H., & Branco, J. (2016). Assessing quality of life of self-reported rheumatic patients. Rheumatology international, 36(9), 1265–1274. https://doi.org/10.1007/s00296-016-3517-0.

Table 1. Clinical and demographic characteristics of self-reported questionnaires HAQ, WOMAC and BASDAI.

HAQ	n = 293
Female, n (%)	53.96 (95.6%)
Age in years, mean (SD)	51.96 (14.2)
Mean score	0.8
WOMAC	n = 59
Female, n (%)	56 (94.9%)
Age in years, mean (SD)	61.64 (9.19)
Mean score	35.6%
BASDAI	n = 8
Male, n (%)	5 (62.5%)
Age in years, mean (SD)	42.12 (14.77)
Mean score	4.98

HAQ, Health Assessment Questionnaire; WOMAC, Western Ontario and McMaster Osteoarthritis Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; SD, standard deviation.

Figure 1. HAQ, WOMAC and BASDAI questions arranged by HAQ activity domains and/or symptoms showing the prevalence of difficulty degree per activity.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2781

AB0864-HPR INFLUENCE OF THE TYPE OF PAIN SYNDROME ON THE SEVERITY OF ANXIETY-DEPRESSIVE DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Egorova[1], N. Nikitina2, A. Rebrov[1]. *[1]Saratov State Medical University name of V.I. Razumovsky Ministry of Health of Russia, Hospital Therapy,*

Saratov, Russian Federation; [1]*Saratov State Medical University name of V.I. Razumovsky Ministry of Health of Russia, Hospital Therapy, Saratov, Russian Federation*

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that leads to joint damage and deformation. Pain syndrome, along with functional limitations, causes the emergence of anxiety-depressive disorders. The patient's psycho-emotional characteristics affect the patient's quality of life and the effectiveness of the therapy. The aim: to assess the severity of anxiety and depression in women with rheumatoid arthritis, depending on the type of the pain syndrome.
Objectives: The study included 163 women with RA according to the EULAR / ACR 2010 criteria (age 53,9 ± 10,15 years, RA duration - 10 [4; 14] years, DAS28 – 5,03 [4,35; 5,8]).
Methods: We used the Hospital Depression and Anxiety Scale (HADS) questionnaire: 0-7 points were assessed as the absence of significant symptoms of anxiety and depression, 8-10 points - subclinically expressed anxiety and depression, more than 11 points - clinically expressed anxiety and depression. The severity of pain was determined by the VAS: no pain (0-4 mm), mild pain (5-44 mm), moderate pain (45-74 mm), severe pain (75-100 mm). Assessment of the type of pain (identification of the neuropathic component of pain) was carried out using the DN4 questionnaire: a sum of 4 or more points indicated the presence of a neuropathic component of pain (NCP). Statistical processing was performed using the STATISTICA 10,0 program.
Results: The frequency of occurrence of anxiety-depressive disorders in RA patients was determined: clinically pronounced anxiety was detected in 35 (21,4%) patients, depression - in 34 (20,9%); subclinically expressed anxiety - in 42 (25,8%), depression - in 44 (27%) patients; absence of reliably pronounced symptoms of anxiety - in 86 (52,8%) patients, depression - in 85 (52,1%) patients.
Severe pain according to VAS was noted in 57 (35%) patients, moderate pain - in 75 (46%), in 31 (19%) patients the pain syndrome was mild. In 81 (49,7%) patients a neuropathic component of pain was revealed.
The relationship was established between the presence of NCP and the severity of anxiety ($r = 0,27$, $p < 0,05$), depression ($r = 0,31$, $p < 0,05$). The relationship was revealed between the presence of NCP and the severity of pain according to the VAS ($r = 0.32$, $p < 0.05$).
To explain the relationship between the presence of NCP and anxiety-depressive disorders, the patients were divided into two groups depending on the presence of NCP, comparable in age, the main clinical characteristics of RA, and basic therapy. The level of anxiety in women with NCP (9,5 [7; 13]) was significantly higher than in patients without NCP (6.1 [4; 9]) ($p = 0.01$). The severity of depression in women with NCP was 8,55 [6; 11], in patients without NCP – 5,15 [3; 6] ($p = 0.005$).
Conclusion: Thus, every fifth patient with RA had clinically significance anxiety and depression, subclinical anxiety and depression were found in 26% of RA patients. Most of the patients (81%) had moderate or severe pain, half of the patients had signs of neuropathic pain. The relationship between the severity of anxiety and depression with the intensity of pain and the presence of a neuropathic component was revealed.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2795

AB0865-HPR FREQUENCY OF DEPRESSION IN SYSTEMIC LUPUS ERYTHEMATOSUS

L. Cano Garcia[1], S. Manrique Arija[1], F. Godoy-Navarrete[1], A. M. Cabezas-Lucena[1], G. Diaz-Cordobes[1], N. Mena-Vázquez[1]. [1]*Hospital Regional Universitario de Málaga, Rheumatology, Málaga, Spain*

Objectives: Cross-sectional observational study of a series of SLE patients selected from the Rheumatology consultations.
Methods: age ≥18 years with SLE (ACR 1997 criteria) capable of understanding and willing to take the questionnaires. Protocol: All patients with SLE undergoing follow-up in the rheumatology clinic are recorded in a database. A telephone call was made to all the patients included in the database and those patients who responded to the call and gave their verbal consent for the collection of data from their clinical history and completed the Goldberg questionnaire were finally included. The nurse was in charge of explaining the questionnaire to the patients. Variables: the main outcome variable was depression assessed by Goldberg (≥2 depression) and other variables were: previous diagnosis of depression, Charlson index, polypharmacy, psychiatric medication, referral to mental health or primary care, SLEDAI and SLICC. Descriptive, bivariate statistical analysis and multivariate logistic regression analysis (VD: Goldberg depression).
Results: 89 patients with SLE were included (95.5% women, mean age 49.44 ± 13.2 years and 18.28 ± 9.19 years of disease). The mean (SD) of the Goldberg scale in all the patients was 3.2 ± 2.9 and a total of 45 patients (50.4%) met criteria of depression according to Goldberg's screening, of which 19 (21.3%) patients had a previous diagnosis of depression. Only 9 patients (10.1%) had had a mental health follow-up and 22 patients (24.7%) were being followed by the family doctor. A total of 87 patients (97.8%) presented polypharmacy: severe polypharmacy 59 (66.3%) and 33 (37.1%) psychiatric medication. The most used psychiatric medication was: 7 (7.8%) bromazepam, 6 (6.7%) citalopram, 5 (5.6%) diazepam. Regarding comorbidities, the Charlson index was 1.82 ± 1.21, also highlighting that 34 (27%) of the sample had Sjögren syndrome. In the multivariate analysis, polypharmacy (OR, 1.8 [95% CI, 1.0-3.1]) and Sjogren's syndrome (OR, 3.8 [95% CI, 1.0-10.7]) were independently associated with depression by Goldberg.
Conclusion: Depression is underdiagnosed and undertreated in patients with SLE. Depression is associated with polypharmacy and the perception of patients with SLE of being ill. It is important to correctly treat depression in the context of SLE comorbidity due to its great impact on quality of life.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3204

HPR Epidemiology and public health (including prevention)

AB0866-HPR INPATIENT RHEUMATOLOGY HEALTHCARE IN A TERTIARY REFERRAL ACADEMIC HOSPITAL

C. M. Gamboa-Alonso[1], G. Figueroa-Parra[1], A. L. De-Leon-Ibarra[1], J. Díaz-Angulo[1], G. Serna-Peña[1], D. Vega-Morales[1], D. Á. Galarza-Delgado[1]. [1]*Universidad Autónoma de Nuevo León, Reumatología e Inmunología Clínica, Monterrey, Mexico*

Background: Diagnosis of autoimmune diseases (AD) has been increasing in recent years, with a prevalence of 3- 5% worldwide. The causes that lead to an inpatient approach in patients with suspicion or a confirmed rheumatic disease (RD) vary widely.
RD are at higher risk of infectious, cardiovascular and other comorbidities due to immunosuppression, a continuous inflammatory state and an altered immune response, increasing morbidity and mortality rates.
Objectives: Describe hospitalized patients who required a rheumatology consultation due to a preexistent or a new RD.
Methods: A descriptive, observational study was performed during a three year follow up (March 2017 -February 2020) in a University Hospital in Mexico. We included patients with definite or suspicion of a RD who received a rheumatologic evaluation. Demographic and clinical characteristics, length of stay and complications such as infection, readmission, use of mechanical ventilation and mortality were registered. Descriptive statistics were used. Binary regression models were applied to find association between clinical factors and infection/mortality in RD hospitalized patients, SPSS v20 was used to perform statistical analysis. A $P < 0.05$ was considered statistically significant.
Results: A total of 642 hospitalized patients received a rheumatologic evaluation. Of the evaluated patients, 315 (49.1%) had a history of a confirmed RD, of these, 237 (75.2%) were hospitalized due to a complication associated to the underlying RD and 78 were hospitalized for other non-rheumatic nor related disorder and were omitted for the rest of the analysis; 327 (50.9 %) patients were evaluated for the first time, 147 (45.0%) of them being diagnosed with a new RD; Systemic Lupus Erythematosus (SLE) 55 (37.4%) was the most frequent diagnosis. Figure 1
Of the 642 evaluated patients, 384 (59.81%) patients with a previous (237) or new (147) rheumatic cause of hospitalization were studied. Table 1A

Factors associated to infection and mortality in the 384 patients are shown in Table 1B.

Conclusion: Inpatient rheumatologic evaluation is a major concern of healthcare due to the severity and prognosis of these diseases. SLE was found to be the most common diagnosis in patients evaluated for the first time. Infection is an important cause of hospitalization and mortality, being the use of steroids and immunosuppression some of the main risk factors of these outcomes.
REFERENCES:
[1] O'Sullivan O, Bateman J, Jobanputra P. 172 Acute Rheumatology Referrals are Increasing: A Service Evaluation of more than 1000 Consecutive Acute Inpatient Referrals from a Tertiary Centre. Rheumatology. 1 de abril de 2016;55(suppl_1):i131-2.

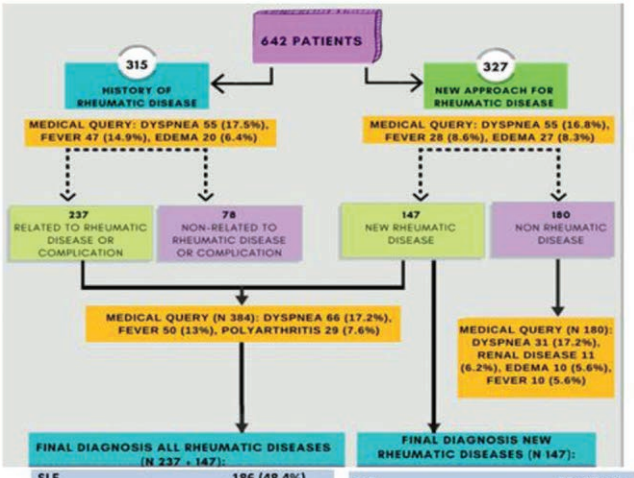


Table 1A. Descriptive analysis of patients receiving a Rheumatology evaluation

	Total evaluated patients	Rheumatic cause of hospitalization	New rheumatic disease
	n=642	n=384	n=147
Age (SD) Mean	39 (25-53)	40 (25-53)	40.56 (16-89)
Sex			
Female	462 (72%)	285 (74.2%)	94 (63.9%)
Median days of follow up	6 (4-11)	6 (3-11)	7 (2-11)
Previous immuno-supression	225 (35%)	156 (40.6%)	16 (10.9%)
Previous steroid use	197 (30.7%)	132 (34.4%)	12 (8.2%)
Mechanical ventilation	60 (9.3%)	26 (6.8%)	11 (7.5%)
Infection	248 (38.6%)	148 (38.5%)	51 (34.7%)
Mortality	59 (9.2%)	39 (10.2%)	13 (8.8%)
Readmission	106 (16.5%)	89 (23.2%)	14 (9.5%)

Table 1B. Association between clinical factors and infection/mortality

Infection	Univariate	Multivariate
	β (95 % CI)	β (95 % CI)
Age	1.02 (1-1.02)	1.02 (1.01-1.03)
Use of mechanical ventilation	4.82 (1.97-11.77)	4.28 (1.67-10.97)
Previous use of steroids	1.55 (1.01-2.39)	1.33 (0.74-2.4)
Previous use of immunosupression	1.37 (0.9-2.07)	1.16 (0.65-2.04)
Readmission	1.76 (1.02-3.02)	1.4 (0.76-2.56)
Mortality		
Age	0.71 (0.99-1.02)	0.99 (0.98-1.02)
Use of mechanical ventilation	7.09 (2.95-17.04)	8.54 (2.89-25.23)
Previous use of steroids	1.95 (1-3.8)	0.97 (0.39-2.39)
Previous use of immunosupression	2.58 (1.31-5.1)	3.06 (1.21-7.72)
Infection	3.66 (1.81-7.37)	2.96 (1.41-6.23)
Readmission	1.33 (0.58-3.05)	0.42 (0.14-1.24)

p <0.05 *

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1022

AB0867-HPR

VIOLENCE IN PREGNANT AND POSTPARTUM MEXICAN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES

L. G. Espinosa Banuelos[1], M. E. Corral Trujillo[1], C. M. Skinner Taylor[1], L. Pérez Barbosa[1], A. Y. Lujano Negrete[1], R. A. Rodriguez Chavez[1], R. Moyeda Martinez[1], A. Cárdenas[1], D. Á. Galarza-Delgado[1]. [1]*Hospital Universitario Dr. José Eleuterio González, Servicio de Reumatología, Monterrey, Mexico*

Background: Gender violence is a prevalent issue worldwide. In Mexico, four out of ten women suffer any kind of violence. The factors that make women even more vulnerable to domestic violence are pregnancy, socioeconomic status, educational level, and the presence of chronic health problems. Violence represents a major risk factor for depression, anxiety, poor adherence to medical treatment, and obstetric adverse events.

Objectives: The aim of this study is to determine the frequency of domestic violence in pregnant and postpartum women with autoimmune rheumatic diseases (ARD) and to compare with childbearing age women with ARD.

Methods: Pregnant and postpartum women (PPW) with rheumatic disease evaluated at the Pregnancy and Rheumatic Diseases Clinic from the University Hospital "Dr. José E. González" in Monterrey, México from August to October 2020 were invited to participate. To compare, we enrolled childbearing age women with ARD without previous pregnancies. The Spanish validated version of the Hurt, Insulted, Threatened with Harm, Screamed scale (HITS) was applied via telephonic interview. The HITS scale evaluates in 4 questions the presence and frequency of violence by their intimate partners in the last 12 months. A score ≥ 10 points is considered as positive for violence.

Results: A total of 48 women were included, 24 patients each group. The pregnant-postpartum group was divided in 6 (25) pregnant and 18 (75) postpartum women. Most of them were housewives (54.1%) with >10 years of education and with not formalized marital status 41% (common-law marriage). In the childbearing age group, most of them were employees (70.8), with >10 years of education with a current marital status of single (66.6%). The HITS scale was positive in the pregnant-postpartum group in 4 women (16.6%). Two of them had been victims of sexual assault and 2 reported physical/verbal violence. While in childbearing age group only 1 (4.16) reported physical/verbal violence.

Conclusion: The 16% of the pregnant-postpartum group in our sample were suffering from domestic violence by their intimate partners, in contrast to the childbearing age group with only 1 patient reported violence. We found that postpartum and pregnancy women had more prevalence of violence. Screening for domestic violence followed by counseling and early referral are necessary to mitigate the physical and psychological consequences of domestic violence.

References: Moreira DN, Pinto da Costa M. The impact of the Covid-19 pandemic in the precipitation of intimate partner violence. Int J Law Psychiatry. 2020;71:101606. doi:10.1016/j.ijlp.2020.101606.

Jackson CL, Ciciolla L, Crnic KA, Luecken LJ, Gonzales NA, Coonrod DV. Intimate partner violence before and during pregnancy: related demographic and psychosocial factors and postpartum depressive symptoms among Mexican American women. J Interpers Violence. 2015;30(4):659-679. doi:10.1177/0886260514535262.

Table 1. Sociodemographic characteristics and scale results

	Postpartum and pregnancy women n= 24	Childbearing age women n= 24
Age, years, mean	27.5	27.08
Occupation, n (%)		
Housewive	13 (54.1)	5 (20.8)
Employee	7 (29.1)	17 (70.8)
Student	4 (16.6)	2 (8.3)
Education years, n (%)		
Less than 10 years	11 (45.8)	7 (29.1)
More than 10 years	13 (54.1)	17 (70.8)
Marital status, n (%)		
Common-law marriage	10 (41.6)	-
Married	8 (33.3)	8 (33.3)
Single	6 (24.9)	16 (66.6)
Status, n (%)		
Postpartum	18 (75)	-
Pregnancy	6 (25)	-
Results of the HITS scale	5.37	4.37
Total, mean		
Score per ranges, n (%)		
0 – 9 points	20 (83.3)	23 (95.8)
10 – 20 points	4 (16.6)	1 (4.1)

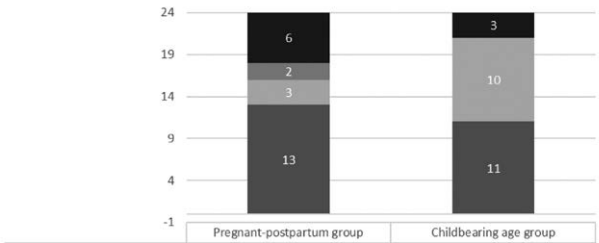


Figure 1. Autoimmune rheumatic diseases diagnosis per group

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1217

AB0868-HPR ADHERENCE TO DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN RHEUMATIC DISEASES DURING COVID-19 PANDEMIC

I. A. Moreno-Arquieta[1], G. G. Sánchez Mendieta[1], D. E. Flores Alvarado[1], J. A. Esquivel Valerio[1], D. Á. Galarza-Delgado[1]. [1]*Dr. José Eleuterio González (Gonzalitos) 235, Rheumatology, Monterrey, Mexico*

Background: The pandemic COVID-19 has set a new challenge in adherence to treatment in patients with rheumatic diseases. Prior studies in Latin America had reported adherence of 16.4% on Rheumatoid Arthritis (RA) and 45.9% in Systemic Lupus Erythematous (SLE). There is evidence that these patients believe their treatment increases the risk and gravity of COVID-19 and therefore, suspending the treatment could reduce this risk. It has been shown that a "Good adherence" is associated to a better survival.
Objectives: Describe the adherence to DMARDs in patients with Rheumatic diseases during COVID-19.
Methods: Descriptive, cross-sectional, self-report study conducted in rheumatology outpatient clinic of University Hospital in Monterrey, México. Consecutive patients with RA, SLE, Inflammatory Myopathies and Systemic Sclerosis, were approached during their routine appointments, March 2020 to December 2020 period during COVID-19 pandemic. They were asked how many days of the month they took the DMARD indicated in the previous appointment, with Based on this, adherence was classified into four categories: Good 100-75% (> 21 days), Regular 74-50% (21-15 days), Bad 49-25% (14-8 days) and Null <25% (<7 days). Data was obtained from our internal electronic patient record registry and analyzed with SPSS V.22.
RESULTS:

	n (DMARDs)	Good	Regular	Bad	Null
		n (%)	n (%)	n (%)	n (%)
Rheumatoid Arthritis	302	255 (84.4)	13 (4.3)	20 (6.6)	14 (4.6)
Systemic Lupus Erithematous	126	111 (88)	3 (2.3)	8 (6.3)	4 (3.1)
Inflammatory Myopathies	11	10 (90.9)	0 (0)	1 (9)	0 (0)
Systemic Sclerosis	30	27 (90)	2 (6.6)	1 (3.3)	0 (0)
TOTAL	469				

Conclusion: Despite what it is believed, patients are not changing therapeutic regimes. The adherence found in this group of patients was good, for the definition used in this study. It should be considered that the self-report method may overestimate adherence, so the data found must be correlated with objective methods in the future.
REFERENCES:
[1] Resende Prudente L, Souza Diniz J, Matteucci Ferreira TXA, Marçal Lima D, Antônio Silva N, Saraiva G, et al. Medication adherence in patients in treatment for rheumatoid arthritis and systemic lupus erythematosus in a university hospital in Brazil. Patient Preference and Adherence. 2016:10 863–870.
[2] Michaud K, Wipfler K, Shaw Y, et al. Experiences of patients with rheumatic diseases in the United States during early days of the COVID-19 pandemic. ACR Open Rheumatol 2020. doi:10.1002/acr2.11148.
[3] Waimann ChA, Marengo MF, de Achaval S, Cox VL, Garcia-Gonzalez A, Reveille JD. Electronic Monitoring of Oral Therapies in Ethnically Diverse and Economically Disadvantaged Patients With Rheumatoid Arthritis. Arthritis & Rheumatism. 2013:6 1421-1429.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2131

AB0869-HPR HOW TO IMPROVE THE QUALITY-OF-LIFE IN PATIENTS WITH OSTEOPOROSIS?

A. Lammert[1], S. Lezhenina[1], N. Shuvalova[2], N. Andreeva[1], E. Guryanova[3]. [1]*I.N. Ulianov Chuvash State University, Departament of Healthcare Management and Economics, Cheboksary, Russian Federation*; [2]*I.Ya.Yakovlev Chuvash Pedagogical State University, Department, Cheboksary, Russian Federation*; [3]*I. N. Ulianov Chuvash State University, Department Internal Diseases, Cheboksary, Russian Federation*

Background: This paper is an assessment of quality-of-life for patients living with osteoporosis. It employs special questionnaires and scales to allow for more detailed observation of the patient both during initial treatment and in dynamics. This allows us to establish the effectiveness of the therapy, to assess the need to correct the treatment and rehabilitation program, and to compare the effectiveness of various treatment methods and determine disease prognosis.
Objectives: to assess quality-of-life in patients with osteoporosis for further development of treatment and rehabilitation programs.
Methods: To assess the quality-of-life in patients with osteoporosis, HRQOL and SF-36 scale were used. The study was conducted from January to December 2019, at the Republican Clinical Hospital of the Chuvash Republic. The study involved 70 patients (n = 70) with a diagnosis of osteoporosis with a pathological fracture. Of the 70 patients included in the study, 35 women aged 67 ± 1.2 years and 35 men aged 60 ± 1.2 years. The results were statistically processed using MS Office Excel programs.
Results: According to the analysis carried out by the HRQOL method, more than half of the patients (52.13%) experienced daily back pain, which worsens their mood and well-being. When assessing the degree of pain, almost half of the patients (48.73%) rated their pain by VAS as moderate. Moreover, most of the respondents experienced a "significant" (46.51%) or "moderate" (34.29%) decrease in social activity due to pain syndrome associated with osteoporosis. In connection with this, 44.51% rated their satisfaction with their lives as "average degree of satisfaction".
When analyzing the quality-of-life indicators according to the SF-36 scales, we determined that the mental component of health predominates for women (The Short Form-36: MH=68,6±3,45 (Men: MH=48,5±2,85)). In men, high quantitative values of the scales "physical" and "role physical functioning" (The Short Form-36: PF=62,5±3,33; RP=58,4±3,81) indicate a more pronounced nature of changes in somatic status, which has a significant impact on the quality-of-life. The intensity of pain was perceived to be higher by men (The Short Form-36: BP=75,6±4,06) than by women (The Short Form-36: BP=35,7±1,86). This confirms that osteoporosis and its complications negatively affect the human psyche and can significantly worsen the quality-of-life.
Conclusion: Analysis of quality-of-life indicators using the SF-36, HRQOL method contributes to a more correct choice of effective strategy for specialized medical care and rehabilitation for patients with osteoporosis. This choice should be developed individually, taking into account the age, gender characteristics, the severity of structural and functional disorders and the psychological state of the patient. It must also take into account the presence and severity of concomitant diseases, which will require additional research and discussion at different levels of the organization of medical care.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2160

AB0870-HPR GLOBAL TRENDS IN PRP AND OSTEOARTHRITIS: A BIBLIOMETRIC AND VISUALIZED STUDY

Y. Qiu[1], Y. Zhang[1], L. Wen[1]. [1]*Beijing Hospital, National Center of Gerontology, Deparment of Orthopedic, Beijing, China*

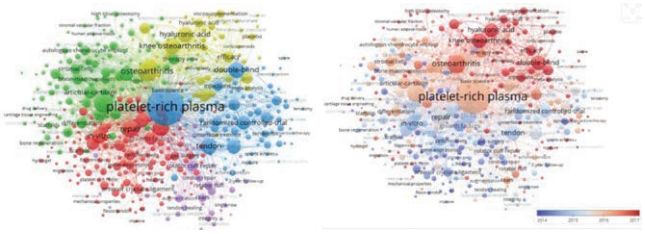
Background: Osteoarthritis (OA) is a serious disease, which is one of the main causes of joint pain and body dysfunction, raising serious economic and social burden. In recent years, there are tremendous articles on the treatment of osteoarthritis, platelet rich plasma (PRP) is one of the new trends in the treatment of osteoarthritis.
Objectives: The purpose of this study is to explore the development trend of PRP related osteoarthritis study and grasp the hot spots and directions in this field.
Methods: Publications focusing on PRP related osteoarthritis research from 2001 to 2020 were retrieved from Web of Science (WoS) and Science Citation Index-Expanded (SCIE) database. The retrieving methods were as follow: (theme = platelet rich plasma arthritis OR theme = platelet rich plasma osteoarthritis OR theme = platelet rich plasma cartilage OR theme = platelet rich plasma knee OR theme = platelet rich plasma orthopedic OR theme = platelet rich plasma orthopaedic OR theme = platelet rich plasma articular OR theme = platelet rich plasma joint OR theme = platelet rich plasma tendon). Publications were analyzed only when type is articles or reviews. The VOS viewer was used for the generation of bibliographic coupling and visualized study.

Results: A total of 2847 publications were retrieved, including 2636 articles and reviews. Before 2000, there were only 15 relevant papers, which were not included in the specific analysis. It is clear that the number of publications on PRP related OA study is increasing every year, a total of 398 articles or reviews were published in 2020. The United States is the leading country in this field, with a number of 932 publications (35.4%), followed by Italy (304 publications, 11.5%) and China (294 publications, 11.2%). The most prevalent areas of PRP related OA research were orthopedics (1013 papers, 38.4%), sports science (651 papers, 24.7%) and surgery (475 papers,18.0%). The top 3 journal that published the most PRP related OA study is American Journal of Sports Medicine (153 papers, 5.8%), Arthroscopy: The Journal of Arthroscopic & Related Surgery (95 papers, 3.6%), Journal of Orthopaedic Research (83 papers, 3.1%). The Harvard University (96 papers, 3.6%), Hospital for Special Surgery (83 papers, 3.1%) and University of London (75 papers, 2.8%) is the top 3 institution that published the most articles or reviews. Filardo G from Italy published the most articles or reviews (52, 2.0%) in this area, followed by Maffulli N from the UK (49 publications, 1.9%) and Kon E from Italy (46, 1.7%). PRP related OA study can be divided into five categories: intra-articular treatment study, clinical trials related study, soft tissue repairment study, gene and molecular biology study, regeneration and implantation study.

Conclusion: Publications on PRP related OA study is increasing according to the analysis on current global trends. The United States is now the leading country in this field, with the largest number and the highest quality of publications. Among the five cluster of PRP related OA studies, "intra-articular treatment study" and "regeneration and implantation study" are considered to be the current research hotspots in the PRP related OA field.

REFERENCES:

[1] Foster T E, Puskas B L, Mandelbaum B R, et al. Platelet-rich plasma: from basic science to clinical applications.[J]. American Journal of Sports Medicine, 2009, 37(11):2259-2272.



Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2849

AB0871-HPR

WOMEN IN RHEUMATOLOGY: BARRIERS, LIMITATIONS, AND GENDER INEQUALITY

G. Serna-Peña[1], I. J. Colunga-Pedraza[1], D. Á. Galarza-Delgado[1], N. Guajardo-Jauregui[1], D. Alpizar-Rodriguez[2], C. F. Pacheco Tena[2]. *[1]Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico*; *[2]Colegio Mexicano de Reumatología, Rheumatology, Ciudad de México, Mexico*

Background: In the last decades there has been a great progress towards gender equality in medicine, and this can be reflected in the proportion of women in Rheumatology, which has been on the rise recently. However, there continues to be a need for women to be able to succeed on equal opportunities with men (1).

Objectives: The aim of this study was to recognize the professional limitations and barriers that Mexican female rheumatologists must face.

Methods: Female rheumatologists were invited to participate. An online survey was applied anonymously, consisting of questions regarding demographic characteristics, professional, academic and research activities, as well as perceptions of gender discrimination and limitations of their profession.

Results: A total of 127 female rheumatologists voluntarily answered the electronic survey. Most of them were aged between 30 and 35 years (40.9%) and had 1-5 years of professional practice (40.2%) (Table 1); 52% have children and 42.4% of them consider that motherhood has had a negative impact on their professional life; 75.6% of female rheumatologists do not work on research activities and only 20.5% have participated in international congresses in the last 5 years; 80.5% report not participating in medical colleges (as leaders or board members). The three main reasons female rheumatologists refer as limitations on their profession are: having other priorities (34.6%), lack of time (32.3%) and lack of support from their peers/bosses (23.6%). Almost half women (45.7%) consider not being discriminated because of their gender in their profession, while the rest of them consider that they are or may be.

Table 1. Demographic characteristics.

Age, n (%)	
Younger than 35 years	52 (40.9%)
From 35 to 40 years	29 (22.8%)
From 40 to 45 years	16 (12.6%)
From 45 to 50 years	12 (9.4%)
Older than 50 years	18 (14.2%)
Marital status, n (%)	
Married	66 (52%)
Single	38 (29.9%)
Free union	13 (10.2%)
Divorced	8 (6.3%)
Widowed	2 (1.6%)
Years of professional practice, n (%)	
From 1 to 5 years	51 (40.2%)
From 5 to 10 years	31 (24.4%)
From 10 to 15 years	16 (12.6%)
From 15 to 20 years	10 (7.9%)
More than 20 years	19 (15%)

Conclusion: We found that most female rheumatologists are young and with a few years of professional practice, which coincides with the recent increase in the proportion of women in Rheumatology; and perhaps this is the reason why there is low participation in research activities and medical colleges. It is relevant that almost half of them perceive their gender as a reason of discrimination in their professional life. We consider that initiating the conversation of gender equality in Rheumatology, in national and international forums, and to actively search for a strategy to support and encourage our colleagues, are priorities at this moment.

REFERENCES:

[1] Andreoli L, Ovseiko PV, Hassan N, et al. Gender equity in clinical practice, research and training: Where do we stand in rheumatology? *Joint Bone Spine* 2019;86(6):669-72. doi: 10.1016/j.jbspin.2019.05.005.
[2] Colunga-Pedraza IJ, Arvizu-Rivera RI, Serna-Pena G, et al. Women's journey in Mexican rheumatology. Comment on 'Gender gap in rheumatology: speaker representation at annual conferences' by Monga et al. *Ann Rheum Dis* 2020 doi: 10.1136/annrheumdis-2020-218541.

Acknowledgements: We have no acknowledgements to declare.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3429

HPR Interventions (educational, physical, social and psychological)

AB0872-HPR

IMPACT OF COVID-19 ON A PHYSICAL ACTIVITY FEASIBILITY PILOT STUDY: THE PIPPRA EXPERIENCE

L. Larkin[1], A. Moses[1], S. Gallagher[2], A. Fraser[3,4], B. A. Esbensen[5,6], J. Green[1], L. Glynn[7], N. Kennedy[1]. *[1]University of Limerick, School of Allied Health and Health Research Institute, Limerick, Ireland*; *[2]University of Limerick, Department of Psychology and Health Research Institute, Limerick, Ireland*; *[3]University of Limerick, School of Medicine, Limerick, Ireland*; *[4]University Hospitals Limerick, Department of Rheumatology, Limerick, Ireland*; *[5]Rigshospitalet, Center for Rheumatology and Spine Diseases, Copenhagen, Denmark*; *[6]University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark*; *[7]University of Limerick, School of Medicine and Health Research Institute, Limerick, Ireland*

Background: The PIPPRA (Physiotherapist-led Intervention to Promote Physical Activity in Rheumatoid Arthritis) project is a feasibility project examining the impact of a physical activity behaviour change intervention in people who have rheumatoid arthritis (RA). The PIPPRA study recruitment commenced in October 2019, with participant assessment and intervention commencing in November 2019. In the Republic of Ireland people who have RA are categorised as high risk category for Covid-19, due to immunosuppression [1], although this categorisation contrasts with EULAR's provisional recommendations [2].

Objectives: To examine the impact of the Covid-19 pandemic and public health restrictions on a pilot randomised controlled feasibility study in 2020.

Methods: Participants (aged 18 years+, diagnosis of RA, independently mobile and low levels of physical activity [3]) were recruited from a rheumatology clinic at an urban hospital. Target recruitment was four participants per month for one year (N=48). Assessments were planned at baseline, eight and twenty-four weeks (N=144). Participants were randomised to intervention group or control group. The intervention group received four 1:1 sixty minute sessions with a physiotherapist (N=96). The intervention was delivered over eight weeks. Intervention and control groups received a physical activity information leaflet.

Results: The Covid-19 pandemic and associated public health restrictions forced the study to be formally paused in April 2020 and the study formally resumed

in August 2020. N=48 participants were recruited between October 2019 and March 2020 (six months). N=20 participants have commenced in the study, N=16 are awaiting baseline assessment, N=6 withdrew and N=6 were lost to follow-up prior to baseline. Trial protocol planned for the delivery of N=55 assessments and N=36 intervention sessions for participants who had commenced in the study. N=22 assessments and N=26 intervention sessions were delivered between November 2019 and March 2020. N=5 assessments and N=6 intervention sessions were conducted between August and October 2020. No assessment or intervention delivery occurred in November-December 2020 due to participant hesitancy in attending for assessment and/or intervention with increased public health restrictions. The impact of Covid-19 restrictions resulted in N=33 (60%) deviations from assessment protocol and N=10 (27%) deviations from intervention delivery protocol (Figure 1).

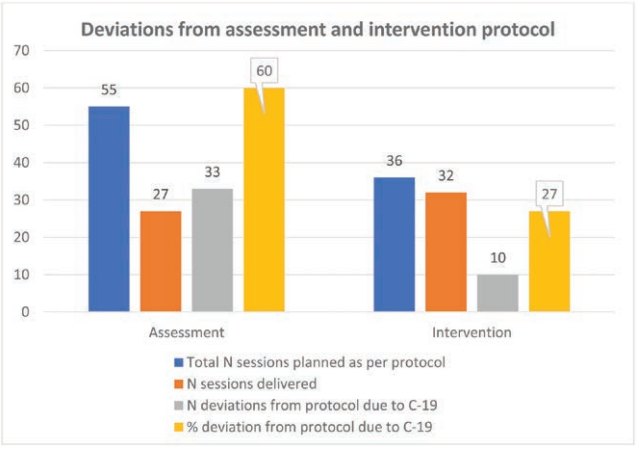


Figure 1. Deviations from assessment and intervention protocol in the PIPPRA study

Conclusion: The Covid-19 pandemic has had a significant impact on the delivery of the PIPPRA study. Feasibility study outcomes, including participant retention rate, and study delivery as per protocol, have been affected due to the Covid-19 pandemic. Participant reluctance to attend face-to-face sessions demonstrates the need to consider alternative methods of delivery, e.g. virtual delivery of interventions, where attending in person is not acceptable to participants [4], in future studies.

REFERENCES:

[1] Health Service Executive. (2019). *People at higher risk from COVID-19.* Accessed 5th Jan 2020 https://www2.hse.ie/conditions/coronavirus/people-at-higher-risk.html.

[2] Landewé RB et al (2020). EULAR provisional recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2. *Annals of the Rheumatic Diseases* 79:851-858.

[3] Godin, G. (2011). The Godin-Shephard leisure-time physical activity questionnaire. The Health & Fitness Journal of Canada, 4(1):18-22.

[4] Inan, OT et al. (2020). Digitizing clinical trials. *npj Digit. Med*. 3:10.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.162

AB0873-HPR

EFFECTIVENESS AND COST-EFFECTIVENESS OF LONGSTANDING EXERCISE THERAPY VERSUS USUAL CARE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS OR RHEUMATOID ARTHRITIS: THE PROTOCOLS OF TWO PARALLEL RANDOMIZED CONTROLLED TRIALS

M. A. T. van Wissen[1], M. Teuwen[1], C. Van den Ende[2,3], T. P. M. Vliet Vlieland[1], A. Den Broeder[2,3], W. Van den Hout[4], W. Peter[1], D. Van Schaardenburg[5], A. Van Tubergen[6,7], M. G. J. Gademan[1], S. Van Weely[1]. [1]*Leiden University Medical Center, Department of Orthopaedics, Rehabilitation and Physical Therapy, Leiden, Netherlands*; [2]*Radboud University Medical Center, Department of Rheumatology, Nijmegen, Netherlands*; [3]*Sint Maartenskliniek, Departement of Rheumatology, Nijmegen, Netherlands*; [4]*Leiden University Medical Center, Department of Biomedical Data Sciences, Leiden, Netherlands*; [5]*Reade, Center for Rehabilitation and Rheumatology, Amsterdam, Netherlands*; [6]*Maastricht University Medical Center, Department of Rheumatology, Maastricht, Netherlands*; [7]*Maastricht University, The Netherlands and Care and Public Health Research Institute (CAPHRI), Maastricht, Netherlands*

Background: Axial SpondyloArthritis (axSpA) and Rheumatoid Arthritis (RA) are chronic rheumatic diseases with an often progressive course, defined by chronic inflammation. With respect to exercise therapy, in axSpA and RA, multiple systematic reviews concluded that supervised exercise therapy is an effective and safe treatment option, resulting in small to modest improvements in pain, disease activity, functional ability and axial mobility. In general, most of the studies included in these reviews concerned programs of a relatively short duration (<12 weeks) and the studies mostly concerned patients with stable disease, without co-morbid conditions and relatively favorable functional ability (1-5). The group of patients with active disease, irreversible joint damage, multiple joint replacements and/or severe comorbidity hampering participation in exercise therapy programs and in need for individualized, longstanding therapy is therefore likely to be underrepresented in research so far. Consequently, cost-effectiveness studies on longstanding physical therapy are also lacking in these specific subgroups.

Objectives: We aim to evaluate the effectiveness and cost-effectiveness of longstanding exercise therapy compared to usual care in the subgroup of patients with axSpA or RA and severe limitations in functioning.

Methods: In two separate, parallel randomized controlled trials, the effectiveness and cost-effectiveness of longstanding, active exercise therapy (52 weeks) compared with usual care (1:1) will be evaluated (Figure 1). The longstanding, active exercise therapy will focus on improving individual limitations in daily activities and participation, and will be given by a trained physical therapist in the vicinity of the participant. For each diagnosis, 215 patients with severe limitations in activities and participation will be included. Assessments are performed at baseline, 12, 26, and 52 weeks. The primary outcome measure of effectiveness is the individual level of functioning (activities and participation), as measured with the Patient-Specific Complaints instrument at 52 weeks. For cost-effectiveness analyses, the EuroQol (EQ-5D-5L) and questionnaires on healthcare use and productivity will be administered. The economic evaluation will be a cost-utility analysis from a societal perspective. After 52 weeks, the patients in the usual care group are offered longstanding, active exercise therapy as well. Follow-up assessments are done at 104, 156 and 208 weeks.

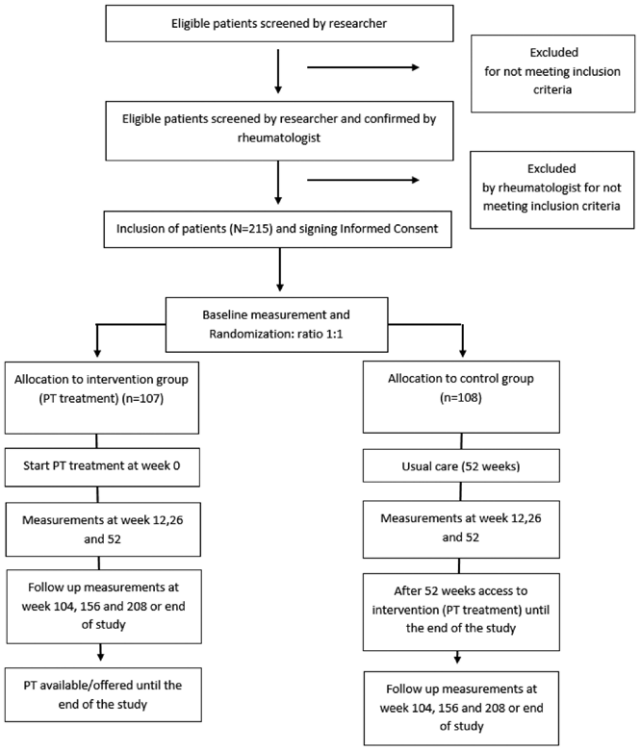


Figure 1. Study flowchart

Results: The results of these studies will provide insights in the effectiveness and cost-effectiveness of longstanding exercise therapy in the subgroup of axSpA and RA patients with severe functional limitations.

REFERENCES:

[1] Mewes J, de Bekker P, Bossen D, Steuten L. 2016. Systematic review of supervised physical exercise therapy for patients with rheumatoid arthritis. *Panaxea.*

[2] Mewes J, de Bekker P, Bossen D, Steuten L. 2016. Systematic review of supervised phyiscal exercise therapy for patients with ankylosing spondylitis. *Panaxea.*

[3] Swardh E, Brodin N. 2016. Effects of aerobic and muscle strengthening exercise in adults with rheumatoid arthritis: a narrative review summarising a chapter in Physical activity in the prevention and treatment of disease (FYSS 2016). *Br J Sports Med* 50: 362-7.
[4] Sveaas SH, Smedslund G, Hagen KB, Dagfinrud H. 2017. Effect of cardiorespiratory and strength exercises on disease activity in patients with inflammatory rheumatic diseases: a systematic review and meta-analysis. *Br J Sports Med* 51: 1065-72.
[5] Regel A, Sepriano A, Baraliakos X, van der Heijde D, Braun J, Landewe R, Van den Bosch F, Falzon L, Ramiro S. 2017. Efficacy and safety of non-pharmacological and non-biological pharmacological treatment: a systematic literature review informing the 2016 update of the ASAS/EULAR recommendations for the management of axial spondyloarthritis. *RMD Open* 3: e000397.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.431

AB0874-HPR TELEMEDICINE CONSULTING IN RHEUMATOLOGY: IDENTIFIED PROBLEMS OF NEW TECHNOLOGY

O. Teplyakova[1], A. Sarapulova[1]. [1]*Ural State Medical University, Outpatients Department, Yekaterinburg, Russian Federation*

Background: A feature of healthcare in 2020 was the work in conditions of massive incidence of COVID-19, limited and redistribution of human resources. One of the right decisions in these conditions is to organize schools for patients, which allow simultaneous education and convey the necessary information to a large number of people. The key aspects of the organization of telemedicine schools for patients are presented.
Objectives: To assess the feasibility of telemedicine schools for patients as a technology of modern health care in rheumatology.
Methods: The work was carried out by the method of a one-stage cross-sectional study of the questionnaire survey of participants of education in rheumatology, conducted in an on-line mode. The number of participants in rheumatology schools was 197 people, the results of the questionnaire were received from 36 respondents. The questionnaire based on the Google platform.
Results: 10 key principles of organizing online patient education at the present stage were identified: the use of distance technologies, the interest of a medical institution administration, the team approach, the technical possibilities of implementing schools, adaptation of lecture material for patients, the role of a specialized specialist in the educational process, patient participation, measurement efficiency and timely correction, development and improvement of educational technology for patients, desire for cooperation and exchange of experience.
Conclusion: The emergence of new opportunities related to online health education of the population, including educational activities for patients, opens up new prospects for improving clinical care aimed at promoting health and preventing disease.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.506

AB0875-HPR NON-PHARMACOLOGICAL AND PHARMACOLOGICAL APPROACHES TO THE MANAGEMENT OF PATIENTS WITH OSTEOARTHRITIS AND LIPID METABOLISM DISORDERS

T. Rogatkina[1], O. Korolik[1], V. Polyakov[2], G. Kravtsov[2], Y. Polyakova[3]. [1]*Volgograd State Medical University, Hospital Therapy, Volgograd, Russian Federation*; [2]*Volgograd State Medical University, Therapeutic Physical Education, Volgograd, Russian Federation*; [3]*Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky», Treatment and Prevention of Joint Disease Laboratory, Volgograd, Russian Federation*

Background: Attention is drawn to the frequent combination of osteoarthritis (OA) with cardiovascular disease. Non-specific inflammation plays a significant role in the pathogenesis of OA and atherosclerosis. Limiting the physical activity of patients with OA is an additional important factor aggravating the course of cardiovascular disease (CVD). Chronic pain syndrome, causing a neuroendocrine response, is often the cause of the development of complications of atherosclerotic disease. Dyslipidemia is the main cause of atherosclerosis and vascular thrombosis.
Objectives: To study variants of lipid metabolism disorders in female and male patients of different age groups with osteoarthritis.
Methods: Case histories of 90 patients with OA were analyzed. The average age of patients was 63.27 ± 11.31 years. The average body mass index (BMI) is 39.8 ± 3.2. All patients underwent questionnaires, general clinical and biochemical blood tests with lipid profile determination, anthropometry, bioimpedansometry, and the main metabolic rate assessment using indirect calorimetry in dynamics (at the beginning of the study and after 3 months).
Results: Burdened heredity for obesity, arterial hypertension (AH), diabetes mellitus (DM) was revealed. AH was diagnosed in 76 patients (84.4%), type II diabetes in 17 (18.9%), dyslipidemia and hypercholesterolemia in 56 (62.2%). Statins were taken by 43 patients (47.8%) - group I patients, which is associated with low adherence to therapy, group II included patients who did not initially take statins or stopped taking them at least 6 months before inclusion in the study.
Against the background of diet therapy and physiotherapy exercises, BMI (R0.99; p <0.05), fat mass (R0.95; p <0.05) significantly decreased, lipid profile normalization was noted: total cholesterol (R0.66; p <0 .05), LDL (R0.69; p <0.05), HDL (R0.95; p <0.05), TG (R0.57; p <0.05), AST decreased (R0.64; p <0.05) and ALT (R0.76; p <0.05) in both groups of patients, regardless of lipid-lowering therapy. A decrease in fat mass correlated with TG levels (R0.51; p <0.05), an increase in skeletal muscle mass (R0.60; p <0.05), lean mass (R0.72; p <0.05), and active cell mass (R0.59; p <0.05). The lipid profile in the I group of patients was significantly better before and at the end of the study. Long-term effects have not been investigated due to the short duration of the study.
Conclusion: In patients with OA, a high frequency of concomitant diseases of the cardiovascular system, lipid metabolism disorders was found. Non-drug therapy has a positive effect on the lipid profile and the level of transaminases. The decrease in body weight due to loss of fat mass reliably correlates with the level of TG. Timely use of statins contributes to the normalization of the lipid profile, reduces the risk of cardiovascular disease in patients with OA. It is necessary to study lipid profile disorders in patients with OA with recommendations for lifestyle modification (diet, physical activity), and if necessary, prescribe lipid-correcting therapy.
REFERENCES:
[1] E. Simakova, B. Zavodovsky, L. Sivordova [et al]. Prognostic significance of lipid disorders markers determination in pathogenesis of osteoarthritis. Vestnik Rossijskoj voenno-medicinskoj akademii. 2013. No. 2 (42). P.29-32.
[2] Zavodovsky B.V., Sivordova L.E. Prognostic significance value of definition of leptin level determination in osteoarthritis. Siberian Medical Journal (Irkutsk). 2012; 115(8):069-072.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1421

AB0876-HPR NEUROFEEDBACK AND TEMPERATURE BIOFEEDBACK TRAINING IMPROVE MIRCOCIRCULATION IN PATIENTS WITH SYSTEMIC SCLEROSIS

R. Grekhoff[1]. [1]*Zborovsky' Research Institute for Clinical and Experimental Rheumatology, Rehabilitation Department, Volgograd, Russian Federation*

Background: Microcirculatory disorders including Raynaud's phenomenon are one of the most important clinical symptoms of systemic sclerosis (SS).
Objectives: We found it appropriate to evaluate the clinical efficacy of biofeedback (BFB) in the complex therapy of SS patients based on analysis of nailfold capillaroscopy.
Methods: The study included 70 SS patients. 94% of patients we examined were women and 6% were men. The average age of the patients = 38±3,3 years, duration of illness = 14±2,6 years. Raynaud's phenomenon (RP) was observed in all the patients and its severe form was seen in 80% of the patients. The effectiveness of BFB was analyzed by studying the dynamics of the measures from the nailfold capillaroscopy and comparing the data obtained from patients of the main and control groups.
Results: Dynamics of capillaroscopic signs of therapy efficiency in main and control groups are summarized in the table:

Analized signs	Main group (n=40)		Control group (n=30)	
	before the therapy	after the therapy	before the therapy	after the therapy
Skin score, M±SD	22,56±10,24	14,99±9,44*	21,04±12,01	20,01±9,88
Dilation of the capillaries, %	34 (85)	16 (40)*	24 (80)	17 (56,6)
Avascular fields, %	26 (65)	24 (60)	13 (43,3)	17 (56,6)
Morphological capillaries' changes, %	36 (90)	22 (55)*	22 (73,3)	10 (33.3)*
Hemorrhage, %	25 (62,5)	10 (25)*	12 (40)	7 (23.3)

*- p < 0,05

It was found that patients participated in BFB training, showed significant positive dynamics in the following signs of capillaroscopic picture: dilatation of the capillaries (x^2 = 9,643; p = 0,026), morphological changes of the capillaries (x^2 = 4,90; p = 0,027), and hemorrhage (x^2 = 4,514; p = 0,034).

Only one indicator of capillaroscopy showed significant change in the control group of patients, the presence of dilated capillaries (x^2 = 5,833 with p = 0,016).
Conclusion: These findings suggest that treatment results were significantly better in the main study group of SS patients.
We suggest that biofeedback may be a useful adjunctive treatment for Raynaud's syndrome in patients with SS.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1701

AB0877-HPR EXERCISE COMPLIANCE AND DISEASE STATUS IN PATIENTS WITH RHEUMATIC DISEASES DURING COVID-19 PANDEMIC

G. G. Pala[1], Z. Tuna[1], N. G. Tore[1], S. Bayram[1], F. Sarİ[1], M. A. Ozturk[2], D. Oskay[1]. [1]*Gazi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Ankara, Turkey*; [2]*Gazi University, School of Medicine, Division of Rheumatology, Department of Internal Medicine, Ankara, Turkey*

Background: The COVID-19 pandemic affects the whole world in many ways. In an effort to slow down the infection, physical distancing and isolation policies have been implemented in Turkey, likewise the rest of the world. Thereby, rheumatic diseases require to obey the self-isolation recommendations strictly due to general vulnerability to infections in those patients. Due to the precautions taken for isolation, the physical inactivity level of the patients which would affect the disease activity has increased (1).
Objectives: The primary purpose of this study was to assess the exercise compliance and clinical status of the patients with rheumatic diseases during the COVID-19 pandemic. The secondary aim of the study was to evaluate the physical activity level and quality of life of the patients during the pandemic.
Methods: The research is a cross-sectional study. Seventy-nine patients with various rheumatic diseases were included in the study. Standard questions were used to evaluate the exercise habits, the level of pain and morning stiffness and severity of exacerbations. Pain and morning stiffness levels and attack severity were scored on a numerical rating scale (NRS) (0-10; with 0 indicating no pain/stiffness and 10 severe pain/stiffness). Attack duration was recorded in number of exacerbated days. Parameters were compared before and after the pandemic with Paired Samples T Test. The International Physical Activity Questionnaire-Short Form (IPAQ) and Nottingham Health Profile (NHP) Questionnaire were filled to assess the physical activity level and quality of life.
Results: Twenty-eight percent of the patients were diagnosed with Familial Mediterranean Fever (FMF), 37% were Ankylosing Spondylitis (AS), 14% were Systemic Sclerosis (ScS) 14% were Systemic Lupus Erythematosus (SLE), 6% were Rheumatoid Arthritis, 1% were Primary Sjogren Syndrome (PSS). Less than half of the patients (46%) did continue exercising regularly during the pandemic and 30 (81%) of them performed only the exercises given by the therapist while 7 (9%) of them tried different exercise types from another source. The reason for discontinuation to exercising expressed by the incompliant patients were mostly "unwillingness" (17 of 37 patients). Pain, morning stiffness and number of attacks were better during the pandemic compared to before however, a statistically significant difference was found only for morning stiffness (p = .036). The results of IPAQ showed that the majority of the patients (n: 48) were physically inactive, while only 2 patients were active during the pandemic. The most deteriorated quality of life subcategory was energy level of the patients according to the NHP scores.
Conclusion: This study results showed that patients with rheumatic diseases stayed physically inactive during the pandemic and the disease status has also been affected negatively. As the duration of the pandemic prolongs, levels of physical inactivity would increase and the progressive physical inactivity is expected to worsen patients' symptoms more. However, as the pandemic appears to continue, face-to-face exercise therapy should still be avoided. For all those reasons above, alternative ways of therapy like tele-rehabilitation would come onto stage to cope with the increasing physical inactivity of the rheumatic patients.
REFERENCES:
[1] Pinto AJ, Dunstan DW, Owen N, Bonfá E, Gualano B. Combating physical inactivity during the COVID-19 pandemic. Nature Reviews Rheumatology. 2020; 16(7):1-2.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1746

AB0878-HPR EFFECT OF AQUATIC PHYSIOTHERAPY ON PAIN AND QUALITY OF LIFE IN ELDERLY WOMEN WITH FIBROMYALGIA

M. Antunes[1], M. Vertuan[2], A. Miquilin[2], A. Pasqual Marques[1], R. Morales[2]. [1]*University of São Paulo, Department of Physiotherapy, Speech Therapy and Occupational Therapy, São Paulo - SP, Brazil*; [2]*Cesumar University, Physiotherapy Department, Maringá - PR, Brazil*

Background: Fibromyalgia is defined as a chronic non-articular rheumatic disease, characterized by generalized, diffuse bilateral pain and the presence of tender points in specific anatomical regions. Its symptoms are characterized by a very varied picture and the etiology is considered multifactorial. Today, with difficult treatment, fibromyalgia has been a major challenge for healthcare professionals. Aquatic physiotherapy is currently one of the most commonly used forms of intervention in the management of fibromyalgia, and for this reason it has been used in interdisciplinary rehabilitation programs to promote health.
Objectives: To evaluate the effects of aquatic physiotherapy on pain and quality of life in patients with fibromyalgia.
Methods: This is an interventional, quasi-experimental study carried out at the Physiotherapy School Clinic of Universidade Cesumar in the city of Maringá, PR, Brazil. The study was approved by the Human Research Ethics Committee of Unicesumar under opinion No. 1,025,567. Participated in the study, elderly women aged 60 years, with clinical diagnosis of fibromyalgia. To assess the quality of life, the Medical Outcomes Study 36 - Item Short-Form Health Survey (SF-36) instrument was used and to verify the intensity of the pain, the Visual Analogue Scale was used. The aquatic physiotherapy intervention protocol was to perform 10 Watsu sessions, performed twice a week, lasting 40 minutes each. To perform the Watsu method, the following steps of the technique were followed: before starting, opening, delivering the water, dancing the breath in the water, breathing balance and to finish releasing the spine. For data analysis, the Shapiro-Wilk test was initially applied to verify the normality of the variables under study. As the data presented a normal distribution, mean, standard deviation, minimum and maximum were used to characterize the results. To compare the initial and final variables, the dependent student t test was used. The significance adopted was p <0.05.
Results: The study included 17 elderly women with a mean age of 67.5 ± 4.7 years. When comparing the evaluation and the reassessment, a statistically significant improvement was evidenced in the domains of quality of life: functional capacity (p=0.00445), limitation due to physical aspects (p=0.01347), pain (p=0.00861), vitality (p=0.00044), limitation due to emotional aspects (p=0.02019), mental health (p=0.00748). The domains that did not show statistical increase were the general health status (p=0.30663) and the social aspects (p=0.05037). The pain, on the other hand, was statistically less after the intervention (p=0.00059).
Conclusion: Aquatic physical therapy provided benefits in reducing pain and improving the quality of life of elderly women with fibromyalgia. It is important to encourage individuals with fibromyalgia to perform non-pharmacological interventions, such as aquatic physiotherapy, to promote their health and quality of life.
REFERENCES:
[1] Oliveira DV, Ferreira AAM, Oliveira DCD, Leme DEDC, Antunes MD, Nascimento Júnior JRAD. Association of the practice of physical activity and of health status on the quality of life of women with fibromyalgia. Journal of Physical Education. 2019;30(1): e3027. https://doi.org/10.4025/jphyseduc.v30i1.3027.
[2] Antunes MD, Vertuan MP. Miquilin A, Leme DEC, Morales RC, Oliveira DV. Efeitos do Watsu na qualidade de vida e quadro doloroso de idosas com fibromialgia. ConScientiae Saúde. 2016;15(4), 636-641. https://doi.org/10.5585/conssaude.v15n4.6756.
[3] Antunes M, Ferreira A, Oliveira D, Júnior JN, Bertolini S, Marques AP. There is association between the level of physical activity and quality of life of women with fibromyalgia?. Annals of rheumatic diseases. 2019;78(2)650-1. http://dx.doi.org/10.1136/annrheumdis-2019-eular.2835.
Acknowledgements: This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2691

AB0879-HPR MOTIVATION OF HEALTHCARE PROVIDERS DURING COVID19 PANDEMIC OUTBREAK

C. Cobilinschi[1], A. Constantinescu[1], I. Draniceanu[1], A. Balanescu[1], V. Bojinca[1], C. L. Constantinescu[1], L. Groseanu[1], S. Daia-Iliescu[1], I. Saulescu[1], D. Mazilu[1], M. Duna[1], D. Opris-Belinski[1], R. Ionescu[1]. [1]*Sf. Maria Clinical Hospital, Rheumatology and Internal Medicine, Bucharest, Romania*

Background: Since the beginning of 2020, the medical staff caring for patients with rheumatic disorders has been exposed to considerable emotional and physical stress due to the COVID19 pandemic outbreak. Newly-designed circuits were imposed to better manage chronic patient admissions.
Objectives: To assess the level of motivation in healthcare personnel caring for patients with rheumatic disorders and identify determinants that lead to dissatisfaction during the COVID19 spread.
Methods: A 15-item questionnaire was distributed among medical and paramedical staff looking after chronic rheumatic patients. Motivation factors were included in questions having five preset answers, ranging from "not al all", "to a small extent", "moderately", "to a large extent" and "to a very large extent". The final item was an open-type question, favoring personal suggestions and potential changes in local management.

Results: Out of a total of a 124 responders, 82 were doctors with various degrees in training (fellow trainees, specialists in Rheumatology, Head of Department), 37 medical assistants, 3 nurses, a physical therapist, one clinical psychologist. Mean age in the group was 38.3 years old with a strikingly female dominance (87.6%). Within the responders, the financial factor represented by monthly salary or bonuses had no or little impact on work motivation during the pandemic since more than 70% answered with "not al all / to a small extent / moderately". Regarding motivation through working hours, 26.7% responded either "not at all" or "to a small extent", 32.4% were moderately motivated while only 12.4% were more enthusiastic. More than half (53.4%) of the staff stated that motivation was not entirely affected by working conditions in the hospital. Answers were relatively equally divided referring to motivation by safety at their workplace (almost 20% for each statement), and 40.9% suffered some extent of demotivation due to risk of contamination while caring for COVID19 positive patients. 42% of the staff was only moderately motivated by hospital's measure to limit the spread of COVID throughout the personnel. Almost 75% of the healthcare workers were not motivated by news media. Around 54% said that personal motivation was not influenced by a larger work volume and 43% were very much motivated by work relationships with colleagues. 41% of the staff is only moderately satisfied with their work during the COVID outbreak while 18% are not at all satisfied. Finally, the last open-question confirmed that for some the pandemic period was a time to bring healthcare professionals together to a stronger bond. Other responders felt that chronic rheumatic patients were left aside, while caring mostly for COVID19 patients and only limited admissions for life-threatening conditions. Moreover, medical staff suggested that the lack of a more frequent testing throughout the personnel to avoid contamination was demotivating, while still living with families or relatives.

Conclusion: Motivation of the personnel is a process with great economic and social impact. This study challenged the level of healthcare staff in difficult times caused by medical crisis. Results of the enquiry showed that financial benefits had no impact on motivation. Harsher working conditions or larger volume did not negatively impact motivation of staff, but the fear of contamination was considerable. Apparently the media influence was not a motivator for medical staff during the outbreak. Medical teams should find their stamina until the end of pandemia.

REFERENCES:

[1] Barati, M, Bashirian, S et al, Factors associated with preventive behaviours of COVID-19 among hospital staff in Iran in 2020: an application of the Protection Motivation Theory, *Journal of Hospital Infection* 2020.

[2] Barati, M, Bashirian, S et al, Factors associated with preventive behaviours of COVID-19 among hospital staff in Iran in 2020: an application of the Protection Motivation Theory, *Journal of Hospital Infection* 2020.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3271

AB0880-HPR

FACTORS THAT INFLUENCE PREGNANCY DECISIONS IN WOMEN WITH RHEUMATIC DISEASES

J. E. Compeán-Villegas[1], D. Á. Galarza-Delgado[1], C. M. Skinner Taylor[1], L. Pérez Barbosa[1], R. Moyeda Martinez[1], R. A. Rodriguez Chavez[1], L. G. Espinosa Banuelos[1], A. Y. Lujano Negrete[1]. [1]*Hospital Universitario "Dr. José Eleuterio González", Rheumatology, Monterrey, Mexico*

Background: The reproductive capacity of women with rheumatic diseases (RD) could be affected by factors such as sexual dysfunction, reduced gonadal function, foetal losses, drugs, and personal choices [1]. Studies have suggested that women with RD may underestimate their reproductive capacity [2], which may be reflected in unplanned pregnancies and/or adverse outcomes. One study found that women with rheumatoid arthritis (RA) have longer time to pregnancy compared to those without RA, suggesting that a reduction in fertility may be involved [3]. Another study found that patients with RA have more subfertility related to medication [4]. Aspects of sexual and reproductive health are not routinely addressed, so they are areas of opportunity to improve quality in care and research.

Objectives: Identify demographic and clinical factors associated with pregnancy decision in women with RD.

Methods: A population study was carried out including women with RD who had their first obstetric event from September 2017 to November 2020. According to the onset of sexual life and the year of conception of the first pregnancy, two groups were formed, who conceived before and after 5 years elapsed. Demographic and clinical data were obtained from medical records. Categorical variables were assessed using χ^2 test and Fisher's exact test where appropriate. Student's t-test was used to assess continuous variables. A p value of 0.05 or less was considered significative.

Results: Data were collected from 28 women, the main diagnosis was rheumatoid arthritis (21, 75%), followed by systemic lupus erythematosus (7, 25%), 14 of them (50%) were pregnant in the first 5 years after starting sex life. There were no differences in age of onset of sex life (p = 0.362), or other clinical characteristic, but women with pregnancies in the first lustrum had lower percentages of marriage union (35% vs 42%), paid-work (21% vs 28%), and use of highly effective contraception (21% vs 28%).

Conclusion: Conclusions: No factors were identified for pregnancies in the first lustrum, but there is a tendency to occur in single women, non-employees, and users of non-highly effective contraceptives methods. Further studies with a larger population are necessary to find modifiable factors and improve outcomes.

Table 1. Clinical characteristics.

	Obstetric event before 5 years	Obstetric event after 5 years	p-value
Total	14	14	
Current average age	24.85 +/- 4.3	29.92 +/- 5.7	0.404
Age at the first obstetric event, years	20.92 +/- 2.9	28.00 +/- 5.9	0.05
Age at the onset of rheumatic disease, years	20.71 +/- 5.5	23.42 +/- 4.0	0.135
Average age of onset of sex life, n (%)	18.64 +/- 2.9	18.07 +/- 2.5	0.362
Alcoholism consumption, n (%)	3 (21.42)	4 (28.57)	0.663
Tobacco use, n (%)	3 (21.42)	3 (21.42)	
Diabetes mellitus, n (%)	0 (0)	1 (7.14)	0.309
Hypertension, n (%)	1 (7.14)	0 (0)	0.309
Depression, n (%)	3 (21.42)	1 (7.14)	0.280
Anxiety, n (%)	2 (14.28)	1 (7.14)	0.541
Pre-pregnancy medication			
Methotrexate, n (%)	3 (21.42)	5 (35.71)	0.403
Leflunomide, n (%)	1 (7.14)	2 (14.28)	0.541
Sulfasalazine, n (%)	3 (21.42)	2 (14.28)	0.622
Hydroxichloroquine, n (%)	6 (42.85)	4 (28.57)	0.430
Azathioprine, n (%)	1 (7.14)	0 (0)	0.309
Cyclophosphamide, n (%)	2 (14.28)	0 (0)	0.142
Glucocorticoids, n (%)	5 (35.71)	5 (35.71)	

NA: Not applicable.

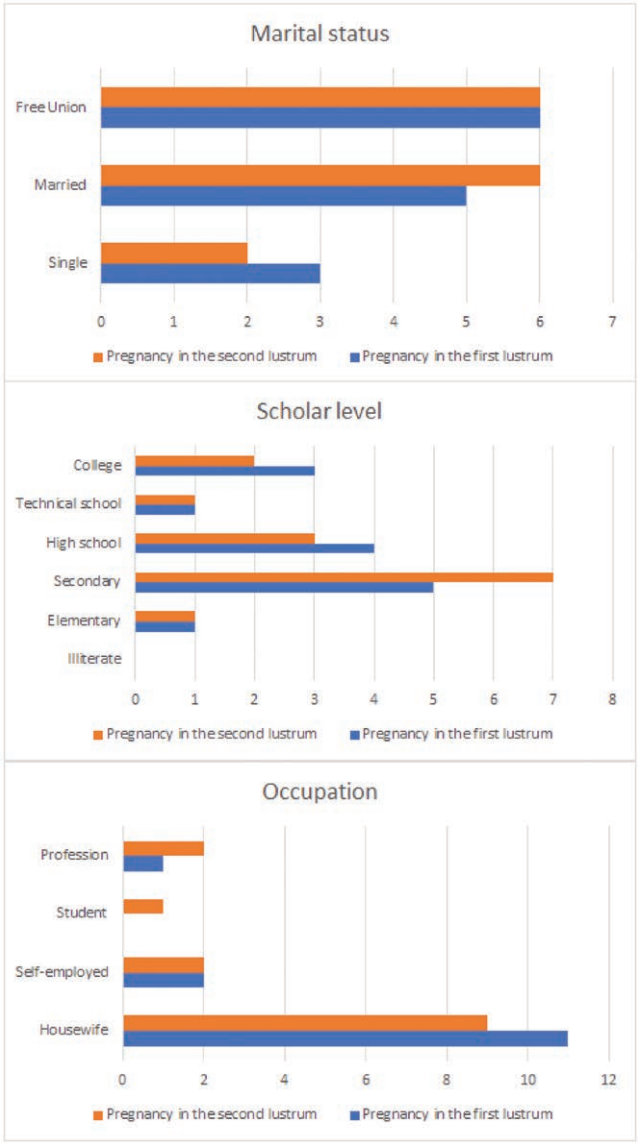


Image 1. Demographic characteristics.

REFERENCES:
[1] Østensen, M., 2017. Sexual and reproductive health in rheumatic disease. *Nature Reviews Rheumatology*, 13(8), pp.485-493.
[2] Birru Talabi, M., Clowse, M., Blalock, S., Switzer, G., Yu, L., Chodoff, A. and Borrero, S., 2019. Development of ReproKnow, a reproductive knowledge assessment for women with rheumatic diseases. *BMC Rheumatology*, 3(1).
[3] Jawaheer, D., Zhu, J., Nohr, E. and Olsen, J., 2011. Time to pregnancy among women with rheumatoid arthritis. *Arthritis & Rheumatism*, 63(6), pp.1517-1521.
[4] Brouwer, J., Fleurbaaij, R., Hazes, J., Dolhain, R. and Laven, J., 2017. Subfertility in Women With Rheumatoid Arthritis and the Outcome of Fertility Assessments. *Arthritis Care & Research*, 69(8), pp.1142-1149.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3348

AB0881-HPR EVALUATION OF NURSING CARE PLANS FOR RHEUMATOID ARTHRITIS PATIENTS: NURSING 2.0 PROJECT

L. Lopez Pedraza[1], M. Rodero[2], G. Candelas[2], C. Lajas[2], T. Mulero López[2], A. M. Perez Saez[1], L. León[1], Z. Rosales[2], B. Fernandez[2], L. Abasolo[1], L. Rodriguez Rodriguez[1]on behalf of Investigación de la Unidad de Gestión Clínica de Reumatología del Hospital Clínico San Carlos. *[1]Hospital Clínico San Carlos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Reumatología, Madrid, Spain*; *[2]Hospital Clínico San Carlos, Reumatología, Madrid, Spain*

Background: A better quality of care for chronic patients is only obtainable through multidisciplinary teams. In recent years, rheumatology nurses have been involved in the remote monitoring of aged Rheumatoid Arthritis (RA) patients, as their high levels of multi-morbidity and disability make routine contacts too complex for patients and caregivers. Nursing health care should be evidence-based and organized to optimize the professionals' time.
Objectives: To develop a pilot study of two Nursing Care Plans (NCP) in Rheumatology consultations for Rheumatoid arthritis patients, exploring the satisfaction, disease activity, adherence and quality of life of the patients.
Methods: This is a non-randomised interventional study. All the stablished RA patients attending our clinics were offered one of the care plans, based on clinic characteristics, functional status, social needs, social support, preferences and health literacy. They are focused on three fundamental axes: adaptation, adherence and safety of the patient. We evaluated the two NCP that were created: (1) Elderly established RA face to face/phone visit, (2) Active young established RA face to face/phone visit. The study included a first baseline visit and a second visit at six months. Outcomes were adherence to treatment: using the Morisky Green questionnaire, disease activity; through the erythrocyte sedimentation rate (ESR), patient satisfaction; using the LOPSS questionnaire and quality of life: using the EUROQOL 5D questionnaire, Visual analog scale of the attention received and Visual analog scale of the care received. Final visit were compared to baseline visit in both groups. The paired Wilcoxon or McNemar test were used.
Results: We included 48 patients, 16 from the NCP 1 and 32 from the NCP 2. All patients except one from the NCP 2 were followed-up and ended the study. The mean age of the participants was 56 years. 77.5% were women. 30.6% had an active smoking habit. 46% had universitary studies. 53.1 had an active labor situation. Regarding the main outcomes: a)Disease activity, a slight decrease in activity was observed between baseline and 6 months, but without statistically significant differences. b) Quality of life, we detected some improvement in all care plans in the EQ-index and in the Visual analog scale (VAE) but there were no statistically significant variations. c) Therapeutic adherence, we show the results in the Morinsky Green questionnaire. We obtained statistical significant decrease in the percentage of patients that forgot to take their prescribed medications after 6 months (p=0.04), and we also saw an increase in the percentage of patients taking medications at established times (up to 100% in all groups). d) Patient satisfaction with NCP obtained at the end of study, we used the LOPPS questionnaire. We obtained at six months a punctuation less than 1.5 (ordinal scale that 1 is good 5 is bad). e) Satisfaction of the care received by patients over the phone assessed at the end of study, it was almost 100%, being 75% of the patients scores 9 or over. f) Satisfaction with the care plans assessed at the end of study, the score given by patients was almost 90%, being 75% of the patients scores 8 or over.
Conclusion: After applying the NCP in both groups, we found positive results after 6 months and mainly regarding the therapeutic adherence. The program was well evaluated by the patients in terms of satisfaction of the care provided.
REFERENCES:
[1] Garner S, Lopatina E, Rankin JA, et al. Nurse-led care for patients with rheumatoid arthritis: A systematic review of the effect on quality of care. *J Rheumatol* 2017; 44: 757–765.
[2] Uthman I, Almoallim H, Buckley CD, et al. Nurse-led care for the management of rheumatoid arthritis: a review of the global literature and proposed strategies for implementation in Africa and the Middle East. *Rheumatology International* 2020; 1: 3.
[3] Bech B, Primdahl J, Van Tubergen A, et al. 2018 update of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. *Ann Rheum Dis* 2020; 79: 61–68.
Disclosure of Interests: Leticia Lopez Pedraza Grant/research support from: Pfizer, María Rodero Grant/research support from: Pfizer, Gloria Candelas Grant/research support from: Pfizer, Cristina Lajas Grant/research support from: Pfizer, Teresa Mulero López Grant/research support from: Pfizer, Ana María Perez Saez Grant/research support from: Pfizer, Leticia León Grant/research support from: Pfizer, Zulema Rosales Grant/research support from: Pfizer, Benjamin Fernandez Grant/research support from: Pfizer, Lydia Abasolo Grant/research support from: Pfizer, Luis Rodriguez Rodriguez Grant/research support from: Pfizer
DOI: 10.1136/annrheumdis-2021-eular.3538

AB0882-HPR ANCA-ASSOCIATED VASCULITIS: A CLINICAL PRACTICE ASSESSMENT

S. Mendly[1], G. Boutsalis[2]. *[1]Medscape Education Global, Medscape Education Global, London, United Kingdom*; *[2]Medscape Education Global, Medscape Education Global, New York, United States of America*

Background: AAV (ANCA-associated vasculitis) is a group of progressive, rare, severe autoimmune diseases[1,2]. AAV can affect blood vessels in different parts of the body resulting in damage to vital organs such as the lungs, kidneys, nervous system, gastrointestinal system, skin, eyes, and heart.[2] There are currently no approved therapies for remission-induction in patients with AAV. The current treatment armamentarium for AAV is comprised of various immunosuppressive therapies in combination with steroid treatment. Understanding clinical practice gaps in the management of AAV, can inform development of tools to improve physician practices.
Objectives: This medical education activity aims to assess physicians' knowledge on the various manifestations of antineutrophil cytoplasmic antibody-associated vasculitis (AAV), current guideline-recommended treatment strategies for remission induction in patients with AAV, as well as recent clinical trial data for combination therapies used for remission induction.
Methods: A 24-question survey consisting of multiple-choice knowledge and case-based questions was made available to nephrologists and rheumatologists without monetary compensation or charge. The questions were designed to evaluate knowledge regarding the various manifestations of AAV and the results from clinical trials that have compared the efficacy of combination therapies used for remission induction in patients with AAV. As well as application of guideline-recommended therapies and clinical trial data for remission induction in patients with AAV within clinical practice. The survey launched online on a website dedicated to continuous professional development. (www.medscape.org/viewarticle/920320) on July 15, 2020. Data were collected until October 1, 2020.
Results: 363 nephrologists and 190 rheumatologists completed the survey. Physicians demonstrated gaps in the following areas:

Topic	Incorrect Responses to Knowledge and Clinical Decision-Making Questions (%)	
	Nephrologists	Rheumatologists
Systemic diseases associated with AAV	59%	45%
How to confirm diagnosis of AAV	42%	25%
Therapy selection to induce remission that would be consistent with guidelines recommendations	71%	51%
Guideline-recommended therapy for patients that do not respond to the induction regimen	32%	34%
Definition of refractory disease	95%	94%
Most effective maintenance strategy for a patient once remission is achieved	80%	64%
Where would an emerging therapy such as a C5a receptor inhibitor fit into the therapeutic armamentarium of AAV?	62%	47%
What are the guideline-recommended therapies to reduce remission in patients without organ-threatening disease?	71%	51%
Most effective maintenance strategy for a patient once remission is achieved	80%	64%
Guideline-recommendations on length of time to continue maintenance therapy	31%	35%

Conclusion: This educational research on assessment of physicians' (nephrologists and rheumatologists) clinical practices yielded important insights into clinical gaps related to understanding of the disease pathophysiology and

progression of AAV, guideline recommendations on diagnosing and managing AAV with guideline-directed medical therapies (GDMTs), strategies for the management of relapsing and refractory disease in AAV and positioning of emerging therapies in the treatment paradigm.

REFERENCES:
[1] www.medscape.org/viewarticle/920320.
[2] Hutton HL, et al. Semin Nephrol 2017;37(5):418–35.
[3] Al-Hussain T, et al. Adv Anat Pathol 2017;24(4):226–34.

Disclosure of Interests: Sarah Mendly Grant/research support from: Supported by an independent educational grant from Vifor Pharma, George Boutsalis Grant/research support from: Supported by an independent educational grant from Vifor Pharma
DOI: 10.1136/annrheumdis-2021-eular.3684

AB0883-HPR CHRONIC RHEUMATIC DISEASE MANAGEMENT AND THE SELF-EFFICACY OF RHEUMATOID ARTHRITIS

Y. H. Xu[1], X. Zhang[1], C. Chen[1], Y. W. Zou[1], K. M. Yang[1], L. Dai[1]. [1]*Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Department of Rheumatology, Guangzhou, China*

Background: Rheumatoid arthritis (RA) is a common chronic disabling autoimmune disease, which cannot be cured completely at present, and patients need long-term medication treatment. The overall management of RA disease and patient self-management is important. Therefore, we built up a chronic rheumatic disease management team, formed by rheumatoid clinicians, clinical nurses and case managers, to provide "integrity continuity" disease management for RA by hospital on-site and WeChat APP. To this end, we used the arthritis self-efficacy scale-8 (ASES-8) to investigate the effect of the chronic disease management with RA.
Objectives: To explore the effect of chronic rheumatic disease management and the related factors of self-efficacy of RA patients.
Methods: Consecutive outpatients with RA who had been implemented chronic disease management were recruited from January 2019 to January 2020. A questionnaire survey of ASES-8 and clinical data were collected.
Results: 1. Among the 376 RA patients who have completed the survey, mean follow-up time of chronic disease management was 29 (8, 41) months, 35.4% patients in CDAI remission stage of disease activity, median ASES-8 score was 59(47,70), and 61.2% patients had medium or above medication adherence.
2. Patients with low ASES-8 had higher RA disease activity (including TJC28, SJC28, Pain VAS, PtGA, PrGA, ESR, CRP), more patients with dysfunction and lower medication adherence than those with high ASES-8 (all P<0.05).
3. Patients were divided into CDAI active RA group and in remission group, and those with low ASES-8 in remission group participated in chronic disease management for fewer months than those with high ASES-8 (median 20 vs. 32, P=0.033), and the HAQ-DI score was higher (P < 0.05). Active RA patients with low ASES-8 had higher disease activity, higher HAQ-DI (median 0.25 vs.0), fewer times of participating in patients' exchange meeting (median 0 vs.1), lower medication adherence (10.8% vs. 25.9%), and more anxiety or depression (57.6% vs. 31.8%) than those with high ASES-8 (all P < 0.05, Table 1 below).
Conclusion: The rheumatic chronic disease management team can help RA patients achieve a higher remission rate by continuous chronic disease management through hospital on-site and the Internet, and can help patients with good self-efficacy and medication adherence. In addition to disease control, we should pay attention to functional limitations and problems of back to work with RA patients in remission, while should pay attention to activity participation, medication adherence and emotional problems with active RA in further practice.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3785

Table 1. Comparison of ASES in different RA disease activity

Characteristics	CDAI remission			CDAI active		
	Low ASES (ASES≤59, *n*=36)	High ASES (ASES>59, n=97)	*P*	Low ASES (ASES≤59, *n*=158)	High ASES (ASES>59, n=85)	*P*
Female, n (%)	32 (88.9)	81 (83.5)	0.440	137 (86.7)	74 (87.1)	0.939
Age, yrs,± *s*	47.4±11.7	46.0±12.5	0.574	49.8±12.9	49.7±12.7	0.933
Disease duration, month, median (IQR)	48 (24,94)	60 (35,96)	0.560	75 (36,120)	72 (36,120)	0.625
Duration of chronic disease management, month, median (IQR)	20 (6,39)	32 (13,41)	**0.033**	29 (6,41)	29 (5,42)	0.766
Attend patients' exchange meeting, times, median (IQR)	6 (4,10)	8 (6,13)	0.673	0 (0,2)	1 (0,4)	**0.035**
Incapable to work, n (%)	11 (30.6)	15 (15.5)	0.051	46 (29.1)	18 (21.2)	0.180
Morisky medication adherence scale			0.857			**0.002**
Low adherence, n (%)	12 (33.3)	30 (30.9)		78 (49.4)	26 (30.6)	
Medium adherence, n (%)	15 (41.7)	38 (39.2)		63 (39.9)	37 (43.5)	
High adherence, n (%)	9 (25.0)	29 (29.9)		17 (10.8)	22 (25.9)	
28TJC, median (IQR)	0 (0,0)	0 (0,0)	0.148	3 (1,5)	1 (1,3)	**0.003**
28SJC, median (IQR)	0 (0,0)	0 (0,0)	0.734	1 (0,3)	1 (0,2)	**0.044**
PtGA, median (IQR)	0 (0,0)	0 (0,0)	0.302	4 (2,5)	2 (1,3)	**<0.001**
PrGA, median (IQR)	0 (0,0)	0 (0,0)	0.302	4 (2,5)	2 (1,3)	**<0.001**
Pain VAS, median (IQR)	0 (0,0)	0 (0,1)	0.800	3 (2,4)	2 (1,2)	**<0.001**
CRP, (mg/L), median (IQR)	3 (3,3)	3 (3,3)	0.833	3 (3,10)	3 (3,6)	0.422
HAQ-DI, median (P_5, P_{95})	0 (0,0.1625)	0 (0,0.0125)	**0.016**	0.25 (0,1.25)	0 (0,0.837)	**<0.001**
Anxiety or depression, n (%)	12 (33.3)	24 (24.7)	0.322	91 (57.6)	27 (31.8)	**<0.001**

HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

AB0884-HPR PERSONALISED TREATMENT GOALS IN PATIENTS WITH IMMUNE MEDIATED INFLAMMATORY DISEASE

S. Fadaei[1], H. Van Os-Medendorp[1], A. Sloeserwij[1], V. Sigurdsson[2], J. M. Van Laar[1], J. Spierings[1]. [1]*UMC Utrecht, Rheumatology & Clinical Immunology, Utrecht, Netherlands*; [2]*UMC Utrecht, Internal Medicine & Dermatology, Utrecht, Netherlands*

Background: Immune mediated inflammatory diseases (IMIDs) often have a chronic character and large impact on daily life of patients. In order to provide patient-centred care, insight in personal goals is a key issue.
Objectives: The aim of this study was to evaluate treatment goals of patients with IMIDs over time.
Methods: Patients with IMIDs were invited to complete a self-designed questionnaire about lifestyle, personal treatment goals and perceived care at their first visit to our centre and one year after referral. Clinical information was collected through the electronic patient record system.
Results: 41 (30%) patients of the 137 invited, completed both questionnaires. Participants had a mean age of 45.6 years (SD 13.4), N=35 (83%) was female, mean disease duration was 12.7 years (SD 12.7). Patients were diagnosed with connective tissue disease (CTD, n=19; 45%), antiphospholipid syndrome (APS, n=10; 24%), inflammatory arthritis (n=7; 17%) and psoriasis (n=7; 17%). We identified six categories of treatment goals: disease related, daily functioning, lifestyle, emotional wellbeing. Figure 1 shows the reported treatment goals at baseline and follow-up. Most frequently mentioned were goals related to disease, lifestyle and daily functioning. At follow-up we observed a vast increase in reported goals related to psychological wellbeing (from 5% to 16%). At baseline patients with APS chose lifestyle-related goals more often than other patients (RR=3.2; p=0.015). At follow-up patients with CTDs reported disease related-goals less often than other patients (RR=0.4; p=0.002). Patients did not report significant progress in reaching their goals on a Likert scale of 1-10. However, in 90% at first visit and in 83% of patients at follow-up, patients reported that the provided care was addressing issues they personally prioritized.
Conclusion: IMID patients' most frequent treatment goals relate to disease activity, lifestyle and daily functioning. Patients frequently change their treatment goals during the first year of treatment. Better understanding of

personal goals can help physicians providing targeted and personalised medicine.

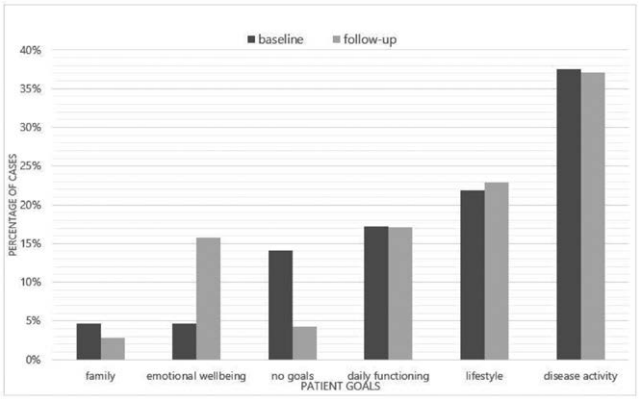


Figure 1. themes of treatment goals at baseline and follow-up

Acknowledgements: The researchers would like to thank all patients participating in this study and acknowledge the UMC Utrecht research program Infection and Immunity for supporting this initiative.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.259

AB0885-HPR SLEEP IN PATIENTS WITH RHEUMATOID ARTHRITIS

C. Andersen[1], K. M. Latocha2, B. A. Esbensen[1]. *[1]Rigshospitalet, Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Glostrup, Denmark*; *[1]Rigshospitalet, Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Glostrup, Denmark*

Background: Many patients with rheumatoid arthritis (RA) live with the consequences of arthritis in everyday life. Sleep disturbances, including insomnia, are highly prevalent and a complex issue that increases existing RA-related symptoms, such as pain, fatigue, and depressed mood. To our knowledge, only two studies have qualitatively investigated the patient perspective and experiences of sleep in people with RA (1-2).
Objectives: To investigate how people with RA and concomitant sleep disturbances describe their sleep and experience everyday life with poor sleep.
Methods: This study is a qualitative phenomenological study. In total, 14 people with RA and sleep disturbance were recruited from an RCT study (3) from the Center for Rheumatology and Spine Diseases at Rigshospitalet in 2012. Semi-structured interviews were performed after the last follow-up in the RCT. The analysis was based on Giorgis' descriptive phenomenological psychological analysis.
Results: For the characteristics of participants, see Table 1. We identified six essences; 1) "*When sleep is put into words*" covered that the participants described their poor sleep experiences simultaneously to their wishes for good sleep still existed. 2) "*The struggle to sleep*" included participants' descriptions of difficulties sleeping and how thoughts and worries could interfere with sleep at night. 3) "*Pain is a companion day and night*" included how pain affected sleep and how participants had problems with pain management. 4) "*To take sleep in their own hands*" described how the participants tried to create their framework for sleeping and how they also strove to reach out for help from, e.g. of professionals. 5) "*Everyday life in the shadow of sleep*" included the overwhelming fatigue, a need to rest during the day, and how social relationships were affected negatively. 6) "*Adapt to the circumstances*," which meant that the participants tried to seek shelter behind a facade, and at the same time tried to learn to live with the consequences of poor sleep in everyday life.
People with RA and sleep disturbances describe several challenges that affect their sleep, e.g., pain, thoughts at night, and many reasons for awakenings. Participants in this qualitative study were not aware of the difference between fatigue and poor sleep, both regarding reasons for occurring and management of the two highly prevalent consequences of RA. At the same time, they believed that health professionals lacked knowledge on sleep disturbances and management hereof in people with RA.
Conclusion: When people with RA and concomitant sleep disturbance describe their sleep, a struggle to sleep was most often described, characterized by pain, thoughts, difficulty falling asleep, and many and early awakenings. Everyday life experience with sleep disturbances was marked by fatigue and sleep deprivation, negative impact on social skills and relationships, and failure when they reached out for help.

Table 1. Characteristics of participants

	(N=8)
Age, median (range)	50 (44-60)
Sex, Women, n %	7 (77,8%)
RA-related	
Duration of RA, median (range)	14,75 (6-32)
DAS28-CRP, median (range)[1]	1,9 (1,62-3,03)
Physical function, HAQ, median (range)[1]	0,5 (0,000 – 2,13)
Sleep	
PSQI, median (range)[2]	9,5 (6-15)
Fatigue	
VAS fatigue, median (range)	33,4 (2-65)
BRAF-MDQ, median (range)[3]	25,5 (4-36)
Pain	
VAS pain, median (range)	25 (0-60)
Quality of Life	
VAS global, median (range)	45,6 (8-40)

[1] Disease activity score-28 C-reactive protein[2]Health Assessment Questionnaire, score 0-3 (Higher *score* indicates worse physical functioning.[2] Pittsburgh Sleep Quality Index, score 0-21 (score of 5 or more indicates sleep disturbances)[3] Visual Analog scale, score 0-100 (higher score is worse)[4] Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire score 0-70(higher score indicates more fatigue)

REFERENCES:

[1] Short V et al; Annals of the Rheumatic Diseases. 2017;76(Suppl 2):519.
[2] McKenna S, et al; EULAR. 2020; OP0267-HPR (2020).
[3] Løppenthin et al; BMC Musculoskeletal Disorders 2014, 15:49.

Disclosure of Interests: Camilla Andersen: None declared, Kristine Marie Latocha: None declared, Bente Appel Esbensen Speakers bureau: Bente Appel Esbensen has received speaking fees from Pfizer and Eli Lilly.
DOI: 10.1136/annrheumdis-2021-eular.332

AB0886-HPR ASSESSMENT OF SEASONAL VARIATIONS ON CHRONIC INFLAMMATORY RHEUMATISMS ACTIVITY

O. Hamdi[1], M. Sellami[1], S. Miladi[1], A. Fazaa[1], L. Souabni[1], K. Ouenniche[1], S. Kassab[1], S. Chekili[1], K. Ben Abdelghani[1], A. Laatar[1]. *[1]Mongi Slim Hospital, Rheumatology, Tunisia, Tunisia*

Background: Although rheumatoid arthritis (RA) and spondyloarthritis (SA) activities have been described to vary under the influence of several factors, little is known about the influence of seasonality on the activity of chronic inflammatory rheumatisms.
Objectives: To assess the influence of seasonality on the activity of chronic inflammatory rheumatisms.
Methods: We conducted a cross-sectional study involving patients with RA (2010 ACR/EULAR criteria) and SA (2009 ASAS criteria). Chronic inflammatory rheumatisms activity was assessed during the summer (June-September) and winter (December-February) using clinical parameters including the Patient's Global Assessment of disease activity (PGA), 10-cm Visual Analog Scale (VAS) pain score, morning stiffness, nocturnal awakenings, and joint count for RA (tender joint count (TJC) and swollen joint count (SJC)); biological parameters including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP); disease activity scores including the SDAI, CDAI and $DAS_{28}$for RA, BASDAI and $ASDAS_{CRP}$ for SA. An analysis of variance (ANOVA) was used to assess the statistical relationship between seasonality and rheumatisms activities.
Results: We enrolled 175 patients (100 RA and 75 SA) with a sex ratio of 0.5 and a mean age of 57.75 ± 10.53 years [23-83]. The mean chronic inflammatory rheumatisms duration was 12.38 ± 4.6 years. RA was erosive in 91% of cases. Rheumatoid factor and anti-citrullinated peptides antibodies were positive respectively in 84% and 85% of cases. Seventy-five percent of RA patients were on corticosteroids with a mean dose of 10.14 mg/day of prednisone equivalent and 79% of SA patients were on non-steroidal anti-inflammatory drugs. Eighty percent of our patients were treated with conventional synthetic DMARD and 44% with biological DMARD. Small joints were more affected than large joints regardless of the season in RA patients (p=0.05). The following parameters were higher in winter than in summer in RA patients: mean PGA 4.73 vs 4.64 (p=0.01); mean morning stiffness 1.6 vs 1.1 (p=0.01); mean SJC 8.7 vs 7.5 (p=0.01); mean DAS_{28} ESR 4.56 vs 3.99 (p= 0.05); mean DAS28 CRP 4.6 vs 3.41 (p= 0.05), mean SDAI 21.8 vs 19.5 (p= 0.05); mean CDAI 20.5 vs 18.75 (p= 0.01) and mean ESR 45.6mm/h vs 38.2 mm/h (p=0.01). As for SA, the following parameters were higher in winter than in summer: mean morning stiffness 2 vs 1.4 (p= 0.01); mean ASDASCRP 3.9 vs 3.1 (p= 0.01) and mean BASDAI 6.2 vs 4.9 (p= 0.05). However, we found no statistically significant

correlation between seasonal changes and VAS pain score, nocturnal awakenings, TJC, and CRP.
Conclusion: Chronic inflammatory rheumatisms activity was higher in winter. Health care professionals should take seasonal changes into account in order to improve therapeutic care.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.412

AB0887-HPR CHARLSON COMORBIDITY INDEX (CCI) IN RHEUMATOID ARTHRITIS: CLASSIFICATION AND CORRELATIONS

C. Flourou[1], S. Psarelis[2], A. Tofarides[3], E. Papanicolaou4, G. Papazisis[5]. *[1]Nicosia General Hospital, Internal Medicine Department, Nicosia, Cyprus*; *[2]Nicosia General Hospital, Rheumatology Department, Nicosia, Cyprus*; *[3]Nicosia General Hospital, Internal Medicine Department, Nicosia, Cyprus*; *[1]Nicosia General Hospital, Internal Medicine Department, Nicosia, Cyprus*; *[5]Aristotle University of Thessaloniki, Clinical Pharmacology, Thessaloniki, Greece*

Background: Charlson Comorbidity Index[1] is a tool including age and chronic diseases assessing the comorbidity burden. The age and the comorbidity burden in RA patients determine the morbidity and mortality.
Objectives: To assess and classification of CCI in RA patients with usage of the health-care system (outpatient clinics) in a real-world setting.
Methods: 327 patients with RA from a large outpatient service of a central hospital were retrospectively reviewed. Demographic characteristics, treatment for RA and comorbidities were recorded. Charlson Comorbidity Index (CCI) was measured and classified as low, intermediate and high score for 1-2, 3-4 and >=5 points, respectively. Its correlation with polypharmacy and necessity of biologic DMARDs was studied. Univariable and multivariable analyses were performed.
Results: Data from 327 RA patients (75,8% females, 24,2%males) with a mean±SD age of 63±11,8 years and disease duration 113±63 months, were recorded.
CCI was 3±1,2 points (mean±SD) and maximum score was observed at 7 points. High score (>=5points) was observed at 9,2% and in the majority the score was intermediate (3-4points) at 55%. All the RA patients with high score fulfilled the criteria of polypharmacy. Patients with high score had 9,7 times more probability of polypharmacy than the patients with low score (p=0.09, 1.4-2.5 95%CI).
70 patients were treated with biologic-DMARDs (21,7%), in the majority with TNFa inhibitors (16,5%). In RA patients receiving biologic-DMARDs was observed low or intermediate score of CCI. The most likely explanation is the severity of the disease that predominated, its complications and the possible overlap with other conditions.
Conclusion: The majority of RA patients had intermediate score of CCI. In patients with high score-meaning more comorbidities- polypharmacy was observed completely. Patients receiving biologic-DMARDs characterized with less comorbidities.
REFERENCES:
[1] Charlson E M et al. A new method of classifying prognostic comorbidity in longitudinal studies:development and validation. J Chronic Dis. 1987;40(5):373-83.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1103

AB0888-HPR EULAR SJOGREN'S SYNDROME PATIENT REPORTED INDEX-FATIGUE SCORE AND HADS-DEPRESSION SCORE MEDIATE IDENTITY SCORE OF ILLNESS PERCEPTION QUESTIONNAIRE IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

A. Kapusuz[1], K. Abacar[2], Y. Yenisoy[1], İ. Tatlı[3], E. N. Çakır[1], F. Türe-Özdemir[3], M. Yay[4], Ü. Karaçaylı[5], H. Direskeneli[2], N. Inanc[2], G. Mumcu[6]. *[1]Marmara University, Institute of Health Sciences, Istanbul, Turkey*; *[2]Marmara University Medical School, Department of Rheumatology, Istanbul, Turkey*; *[3]Marmara University Medical School, Department of Heamatology and Immunology, Istanbul, Turkey*; *[4]Mimar Sinan Fine Arts University, Department of Statistics, Istanbul, Turkey*; *[5]Health Sciences University, Department of Oral and Dental Surgery, Istanbul, Turkey*; *[6]Marmara University, Department of Health Management, Istanbul, Turkey*

Background: Dryness, fatigue, and pain are common clinical manifestations assessed by EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI)-Dryness, -Fatigue, -Pain scores in patients with primary Sjögren's syndrome (pSS). In addition, depression is also seen in these patients owing to the pattern of the chronic disease.
Objectives: The aim of the study was to assess the complex interactions among Depression status, Illness Perception, and prominent clinical manifestations evaluated by the ESSPRI (Dryness, Fatigue, and Pain) in patients with pSS.
Methods: In this cross-sectional study, 111 patients with pSS (M/F: 5/106; mean age: 52.9 ± 12.01 years) were included. The data were collected by clinical examination and a questionnaire regarding patient reported outcome measures (PROMs). Unstimulated (U-WSFR) and stimulated (S-WSFR) whole saliva flow rates of patients were calculated as ml/min. Hospital *Anxiety* and Depression Scale (*HADS*), Illness Perception Questionnaire-R (IPQ-R) and EULAR Sjogren's Syndrome Patient Reported Index were filled by patients. Increases in HADS score and subgroup scores of ESSPRI (Dryness, Fatigue and Pain) and IPQ-R dimensions regarding Identity, Consequences, and Emotional reflected poor conditions for patients. In addition, patients scored their disease activity (0: inactive-100: the worst activity) by using 100-mm visual analogue scale (VAS). After preliminary analysis, a mediation analysis was used to evaluate the relations among these variables.
Results: In the study, ESSPRI-Dryness score (6,27±2,79) was associated with U-WSFR (0,40±0,57) and S-WSFR (1,04±0,86),(r:-0,4 p=0.000; r:-0,3 p=0.004). Moreover, patients reported disease activity score (48,78±26,67) was related to U-WSFR (r: -0,3 p=0.026) as well as Consequence (19,12±5,47) and Emotional (19,54±7,02) scores of IPQ-R questionnaire (r: 0,3 p=0.035; r: 0,3 p=0.014).
In IPQ-R questionnaire, Identity score (8,04±3,1) reflecting number of symptoms that patients experienced due to their illness was correlated with scores of ESSPRI-Fatigue (5,29±2,97), ESSPRI-Pain (5,18±3,01), HADS-Anxiety (11,67±5,55), HADS-Depression (9,2±4,98) in the study (p<0.05).
In the mediation analysis, Identity score was directly mediated by ESSPRI-Fatigue score (p=0.0093) and indirectly mediated by HADS-Depression score (p=0.0011).
A bootstrap analysis with 5000 replications was applied to estimate mediation effect to generate 95% CI. Percentile bootstrap of HADS-Depression was found to be an effective mediator for Identity score based on 5000 bootstrap sample.
Conclusion: Both depression status and fatigue affected Identity score reflecting the number of symptoms poorly. Considering this complex relationship in disease activity assessment may positively affect disease outcomes.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1893

AB0889-HPR PERCEIVED SATISFACTION WITH CHRONIC PAIN CARE IN GERMAN PATIENTS WITH FIBROMYALGIA (FM)

M. Offenbächer[1], L. Toussaint[2], J. Hirsch[3], M. Weigl[4], N. Kohls[5], M. Vallejo[6], J. Rivera[7], F. Sirois[8], J. Dezutter[9]. *[1]Gasteiner Heilstollen, Medical Department, Bad Gastein, Austria*; *[2]Luther College, Psychology, Decorah, United States of America*; *[3]East Tennessee State University, Psychology, Johnson City, United States of America*; *[4]Klinikum Großhadern, Department of Orthopaedics, Physical Medicine and Rehabilitation, München, Germany*; *[5]Coburg University of Applied Sciences, Health Promotion, Coburg, Germany*; *[6]UNED, Psychology, Madrid, Spain*; *[7]Gregorio Marañón Hospital, Rheumatology, Madrid, Spain*; *[8]The University of Sheffield, Psychology, Sheffield, United Kingdom*; *[9]University of Leuven, School Psychology and Development in Context, Leuven, Belgium*

Background: In chronic pain care a multidimensional perspective with attention to patients' cognitions, emotions, and their ability to cope is needed (1). Previous studies are also pointing to the role of experiencing meaningfulness in life in the adjustment to disability.Therefore care should additionally focus on the existential domain of patients' lives to live up to a holistic care approach (2). However, there are only a few studies on how FM patients are satisfied with practitioners' attention to multiple aspects of life with a chronic pain condition.
Objectives: To assess perceived satisfaction with chronic pain care and its associations with health variables in a cohort of patients with FM.
Methods: We invited 18 FM self-help groups in Germany to participate anonymously in our survey and sent them in total 192 paper-and-pencil surveys. Sociodemographics, disease related variables (e.g. pain, general health) and psychological variables [e.g. depression, anxiety, hope, stress] were assessed with standardized instruments, including 5 items (answer format 1=very unsatisfied – 10=very satisfied) assessing subjective satisfaction with medical care in different domains with the following questions: How satisfied are you with the attention of your treatment team/physician at home for physiological aspects of your pain (Physio)/ the consequences of the pain on your physical functioning (Physical)/ on your psychological well-being (Mental)/ on your social life (Social)/ on your meaning in life (Meaning).
Results: In total 162 FM patients participated (=84% response rate). Their mean age was 58 years (SD=10), 84% (N=135) were female. Highest level of education was: Elementary School 29%, Junior High School 35%, High School 15%, College 12%, and other 10%. Duration of chronic pain was

18.2 years (SD=12.0). The satisfaction with care scale showed good internal consistency and measured one factor. The means of the subscale were: Physio 5.7 (SD=2.5)/ Physical 5.5 (SD=2.5)/ Mental 5.5 (SD=2.6)/ Social 5.0 (SD=2.5)/ Meaning 5.3 (SD=2.6). Correlations of the subscales are depicted in Table 1. There were no associations between pain variables and satisfaction with care, but satisfaction with care was associated with mental health, but not physical health, outcomes.

Table 1. Correlations of satisfaction of care with different health variables. Subscales physiological and physical aspects and HADS-anxiety were not significantly correlated. *<.05; **<.01; ns=not significant.

	Physio	Physical	Mental	Social	Meaning
HADS-depression	-.10 (ns)	-.12 (ns)	-.19*	-.16*	-.14 (ns)
General Health	.02 (ns)	.14 (ns)	.13 (ns)	.18*	.12 (ns)
Stress	-.15 (ns)	-.14 (ns)	-.17*	-.17*	-.13 (ns)
Hope	.18 (ns)	.18 (ns)	.26**	.26*	.22*

Conclusion: In this cohort of German FM patients the average satisfaction with care overall, as well as the specific aspects of care, was only moderate. Interestingly we found associations between satisfaction with care in mental, social and meaning in life aspects with psychological well-being pointing to the fact that care for chronic pain patients should also include those aspects in addition to just addressing biomedical aspects.

REFERENCES:

[1] Flor H and Turk D. Chronic pain: an integrated approach. Seattle, WA: IASP Press, 2011.

[2] Dezutter J, Casalin S, Wacholtz A, et al. Meaning in life: An important factor for the psychological well-being of chronically ill patients? Rehabilitat Psychol 2013; 58:334–341.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1993

AB0890-HPR

THE IMPACT OF GENDER ON PHYSICAL FUNCTION, FATIGUE, LONELINESS, DEPRESSION, AND SEXUAL FUNCTIONING IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH A SPECIAL FOCUS ON METHOTREXATE USAGE. A CROSS-SECTIONAL SINGLE-CENTRE STUDY

L. T. Bay[1], D. S. Nielsen[2], C. Flurey[3], A. Giraldi[4], S. Möller[5], C. Graugaard[6], T. Ellingsen[1]. [1]*Odense University Hospital, Rheumatology Research Unit, Department of Rheumatology, Odense, Denmark*; [2]*Odense University Hospital, Migrant Health Clinic & Department of Geriatrics, Odense, Denmark*; [3]*University of the West of England, Faculty of Health and Applied Sciences, Bristol, United Kingdom*; [4]*Copenhagen University, Sexological Clinic, Psychiatric Centre Copenhagen, Copenhagen, Denmark*; [5]*Odense University Hospital & University of Southern Denmark, OPEN, Odense, Denmark*; [6]*Aalborg University, Center for Sexology Research, Aalborg, Denmark*

Background: We lack knowledge of how gender, disease characterization, and measures of various Patient Reported Outcome Measures (PROMS) relate to Methotrexate (MTX) usage in patients with rheumatoid arthritis.

Objectives: To investigate the impact of gender on physical function, fatigue, depression, loneliness, and sexual functioning with a special focus on MTX usage.

Methods: A cross-sectional study design was used to collect data in a rheumatologic outpatient clinic. The following PROMs were applied: Changes in Sexual Functioning Questionnaire, UCLA Loneliness Scale, Beck´s Depression Inventory, Bristol Rheumatoid Arthritis Fatigue-Numeric Rating Scale, and the Health Assessment Questionnaire.

Results: Among 286 patients diagnosed with rheumatoid arthritis (69 men and 217 women), 67.8 % were defined as MTX-users one year after diagnosis.

Comparing women and men we found differences in PROMS, with significantly worse outcomes for women than men in physical functioning at diagnosis and in sexual functioning, depression, fatigue, physical functioning, and patient evaluation of disease burden at enrolment in the study.

There were only significant differences in the HAQ and loneliness score when comparing MTX-users with MTX-non-users in general (Table 1).

Conclusion: The results of this study show that women have more negative outcomes on the selected PROMs compared to men with RA. This difference between genders was also evident when comparing MTX-users with non-MTX-users, again with a poorer outcome on PROMs for women compared to men. This calls for attention in the clinical setting and further research in the used instruments and the importance of gender in the care and treatment of patients with RA.

Disclosure of Interests: Laila Twisttmann Bay: None declared, Dorthe S. Nielsen: None declared, Caroline Flurey: None declared, Annamaria Giraldi Speakers bureau: Astellas, Paid instructor for: Payment for lectures, Astellas, Consultant of: Ovaco Bio,Palatin Technologies, Futura Medical, Sören Möller: None declared, Christian Graugaard: None declared, Torkell Ellingsen: None declared

DOI: 10.1136/annrheumdis-2021-eular.2039

Table 1. Second column is adjusted for gender, patient age, years of education, and living alone, all other columns are not adjusted for gender. HAQ Health Assessment Questionnaire, VAS Visual Analog Scale, UCLA University of California Los Angeles, CSFQ Changes in Sexual Functioning Questionnaire, BDI Becks Depression Inventory, BRAF-NRS Bristol Rheumatoid Arthritis Fatigue Numeric Rating Scale

Adjusted analyses	*Comparing Women and men (overall)*		*Comparing MTX-users and non-MTX-users (overall)*		*Comparing women and men (MTX-user)*		*Comparing women and men (non-MTX-users)*		*Comparing male MTX-users and male non-MTX-users*		*Comparing female MTX-users and female non-MTX-users*	
	Coefficient (95% CI)	*p-value*	*Coefficient (95% CI)*	*p-value*	*Coefficient (95% CI)*	*p-value*	*Coefficient (95% CI)*	*p-value*	*Coefficient (95% CI)*	*p-value*	*Coefficient (95% CI)*	*p-value*
Physical functioning at diagnosis												
HAQ	0.42 (0.19; 0.66)	***<0.001***	-0.31 (-0.59; -0.04)	***0.024***	0.30 (0.04; 0.56)	***0.025***	1.09 (0.68; 1.51)	***<0.001***	0.25 (-0.14; 0.64)	0.205	-0.54 (-0.84; -0.24)	***<0.001***
Physical functioning at enrollment												
HAQ	0.38 (0.20- 0.55)	***<0.001***	-0.13 (-0.29- 0.03)	0.101	0.39 (0.19- 0.59)	***<0.001***	0.30 (-0.07- 0.66)	0.112	-0.21 (-0.57- 0.16)	0.274	-0.11 (-0.30- 0.07)	0.216
PROMs at enrollment												
Sexual dysfunction												
CSFQ	-12.16 (-14.80 - -9.52)	***<0.001***	-1.17 (-3.76- 1.41)	0.374	-13.30 (-16.27- 10.33)	***<0.001***	-9.20 (-14.90- -3.49)	***0.002***	1.99 (-3.45- 7.43)	0.473	-2.11 (-5.17- 0.95)	0.177
Loneliness												
UCLA	1.60 (-1.35 - 4.54)	0.288	4.15 (1.46- 6.85)	***0.003***	2.52 (-0.93- 5.98)	0.153	0.37 (-4.64- 5.38)	0.885	2.47 (-2.68- 7.61)	0.347	4.62 (1.50- 7.73)	***0.004***
Depression												
BDI	2.77 (1.04 - 4.50)	***0.002***	1.79 (-0.01- 3.58)	0.051	3.18 (1.07- 5.28)	***0.003***	2.14 (-0.50- 4.78)	0.112	0.98 (-1.58- 3.53)	0.454	2.01 (-0.15- 4.18)	0.068
Fatigue BRAF-NRS												
Severity	0.97 (0.31 - 1.63)	***0.004***	0.40 (-0.20- 1.00)	0.187	1.05 (0.30- 1.81)	***0.006***	0.87 (-0.50- 2.25)	0.212	0.26 (-1.13- 1.66)	0.713	0.44 (-0.24- 1.12)	0.201
Effect	1.06 (0.39 - 1.72)	***0.002***	0.25 (-0.38- 0.88)	0.442	1.07 (0.28- 1.86)	***0.008***	1.10 (-0.24- 2.44)	0.108	0.27 (-1.08- 1.63)	0.694	0.24 (-0.49- 0.98)	0.521
Coping	0.60 (-0.09- 1.28)	0.087	0.33 (-0.33- 0.99)	0.329	0.93 (0.13- 1.72)	***0.022***	-0.25 (-1.78- 1.28)	0.749	-0.60 (-2.17- 0.98)	0.457	0.58 (-0.15- 1.31)	0.120

AB0891-HPR

PATIENTS WITH RHEUMATIC DISEASE WHO WERE 'FEELING STRESSED' DURING THE SECOND WAVE COVID19 INFECTION

H. Baharuddin[1,2], S. L. Lim[2], S. S. Ch'ng[2], M. Mohd Zain[2], A. Rosman[2], H. Mohd Yusoof[2], A. K. B. Authar Singh[2], V. Y. Tay[2]. [1]*Universiti Teknologi MARA, Department of Internal Medicine, Sungai Buloh, Malaysia*; [2]*Selayang Hospital, Department of Medicine, Batu Caves, Malaysia*

Background: COVID-19 pandemic has been devastating not only medically but also socially and economically. Selangor, an urbanised state in Malaysia, has been severely affected by COVID19. There is concern that patients with rheumatic diseases (RD) may have higher risk of infection, with increased mortality[1].
Objectives: To investigate patients' characteristics which are associated with 'feeling stressed' among patients with RD during the second wave of COVID19 infection in Selangor.
Methods: This is a cross-sectional study conducted over 3 weeks during the second wave of COVID19 infection in Malaysia. Patients with RD, scheduled for rheumatology clinic appointment in a rheumatology referral centre were invited to participate in this study.
Personal and clinical data were collected by phone interview and from patients' medical records respectively. Patients were asked to grade their disease activity by giving a score from 0 (not active) to 10 (active). All patients were asked 'are you feeling stressed?' and the answer was recorded as yes or no. Reasons explored for a yes answer, included financial, social disruption, physical illness and future uncertainties. Categorical and continuous data were analysed using chi-squared test and student t-test, respectively. A p-value of <0.05 is considered statistically significant.
Results: Three hundred and sixty-one patients with various RD participated in this study. The mean age of these was 48.2 years (range between 16-80 years). More than half (54.3%) were Malay and other ethnicities were Chinese (25.5%), Indian (18.2%) and others (2%). A quarter of patients (24.7%) were not working (unemployed, retired and students) and a third of patients (32.1%) had unpaid work (mainly housewife). The other patients' characteristics are shown in Table 1.

Table 1. Characteristics of patients who were 'feeling stressed' and not 'feeling stressed' during the second wave of COVID19 infection.

Patients' characteristics		No of patients	Feeling stressed (n=83), no of patients (%)	Not feeling stressed (n=278), p-value no of patients (%)	
Age	<60	272	72 (26.5)	200 (73.5)	**0.006**
	≥60	89	11 (12.4)	78 (87.6)	
Gender	Male	61	16 (26.2)	45 (73.8)	0.510
	Female	300	67 (22.3)	233 (77.7)	
Ethnicity	Malay	196	38 (19.4)	158 (80.6)	0.076
	Others	165	45 (27.3)	120 (72.7)	
Relationship status	Married	275	59 (21.5)	216 (78.5)	0.215
	Unmarried	86	24 (27.9)	62 (72.1)	
Education level	Up to secondary	233	48 (20.6)	185 (79.4)	0.145
	Tertiary	128	35 (27.3)	93 (72.7)	
Work status	No work	89	13 (14.6)	76 (85.4)	**0.002**
	Unpaid work	116	20 (17.2)	96 (82.8)	
	Paid work	156	50 (32.1)	106 (67.9)	
Rheumatic disease	SLE	125	30 (23.8)	96 (76.2)	0.259
	RA	150	30 19.4)	125 (80,6)	
	Others	80	23 (28.8)	57 (71.3)	
Perceived disease activity			3.14 (2.4)	1.87 (2.1)	**<0.001**
Use biologics	Yes	25	7 (28)	18 (72)	0.537
	No	336	76 (22.6)	260 (77.4)	

Eighty-three (23%) admitted to 'feeling stressed' and the stressors identified were physical illness in 34 (40.9%), social disruption in 23 (27.7%), financial problems in 23 (27.7%) and future uncertainties in 19 (22.9%). Patients' characteristics that were significantly different between patients who were 'feeling stressed' and not 'feeling stressed' were age, employment status and perceived disease activity (Table 1).
Conclusion: The COVID19 pandemic has caused mental distress in a significant number of RD patients and associations were found with older age, having paid work and perceived disease activity. Issues that may influence patients' responses, including access to rheumatology care, medication and fear of getting infection were not explored in this study.
REFERENCES:
[1] Williamson EJ, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature, 2020; 584: 430–436.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2244

AB0892-HPR

PATIENT PERSPECTIVES ON PROVIDER PRACTICES LEADING TO AN AXIAL SPONDYLOARTHRITIS DIAGNOSIS: A QUALITATIVE STUDY

K. Lapane[1], C. Dubé[1], K. Ferrucci[2,3], S. Khan4, K. A. Kuhn[5], A. Ogdie[6], E. Yi[7], J. Kay[8,9], S. H. Liu[8,10]. [1]*University of Massachusetts Medical School, Population and Quantitative Health Sciences, Worcester, United States of America*; [2]*University of Massachusetts Medical School, Population and Quantitative Health Sciences, Worcester, United States of America*; [3]*University of Massachusetts Medical School, Clinical and Population Health Research Program, Graduate School of Biomedical Sciences, Worcester, United States of America*; [2]*University of Massachusetts Medical School, Population and Quantitative Health Sciences, Worcester, United States of America*; [5]*University of Colorado School of Medicine, Division of Rheumatology, Department of Medicine, Denver, United States of America*; [6]*Hospital of the University of Pennsylvania, Medicine, Philadelphia, United States of America*; [7]*Novartis Pharmaceuticals Corporation, HE&OR and Medical Access, East Hanover, United States of America*; [8]*University of Massachusetts Medical School, Division of Rheumatology, Department of Medicine, Worcester, United States of America*; [9]*UMass Memorial Medical Center, Rheumatology Center, Worcester, United States of America*; [10]*University of Massachusetts Medical School, Population and Quantitative Health Sciences, Worcester, United States of America*

Background: People with Axial Spondyloarthritis (axSpA) experience a diagnostic delay between 7 to 10 years. (1-5) This delay contributes to increased depression and desperation in searching for an appropriate diagnosis. (6) Consequently, people with axSpA experience impaired physical function, structural damage, and overall worsened quality of life than those who experience a timely diagnosis. (7)
Objectives: To gain knowledge and understand patients' experiences with healthcare providers in diagnosis of axSpA.
Methods: Using qualitative study design, we conducted six focus groups, with a total of 26 participants with a confirmed diagnosis of axSpA by rheumatologists from three different geographic locations: Worcester, MA, Aurora, CO and Philadelphia, PA. Focus groups were audio recorded and approximately 2 hours in duration. The focus groups were transcribed, deidentified, cleaned and stored in a secure location. NVivo software was used to code the data using a coding scheme which emerged from the focus group discussion topics. For intercoder reliability, two researchers coded the data and generated summary reports for data analysis.
Results: Patients described their frustrating journeys to diagnosis and attributed the lengthy diagnosis delays to a multitude of factors. These elements include, lack of definitive diagnostic test, disease characteristics, lack of primary care providers' awareness of axSpA, time, and trust. Patients felt that their physicians dismissed their complaints or would describe their symptoms as psychosomatic. The health care system also contributed to their diagnostic delays, including the lengthy referral process to a rheumatologist and the short clinical appointments. Patients believe that to reduce diagnostic delay, physicians must work with their patients; listening and believing their patients while allotting time for patients to discuss their experiences. In addition, patients believe earlier referral to a rheumatologist, and HLA-B27 genetic testing would decrease the diagnostic delay of axSpA.
Conclusion: In this study, patients desire definitive testing in clinical practice for earlier diagnosis of axSpA. Additionally, more education regarding the guidelines to diagnose axSpA and earlier referral to rheumatologists might be needed. Until this is feasible, patients seek clinicians who will work with them until a diagnosis is made, listening, and believing their experiences and symptoms.
REFERENCES:
[1] Deodhar A, Mease P, Reveille J, Curtis J, Karunaratne P, Malhotra K. Prevalence of axial spondyloarthritis among undiagnosed chronic back pain patients in the United States [abstract]. *Ann Rheum Dis.* 2014;73:198-199.
[2] Deodhar A, Mease PJ, Reveille JD, et al. Frequency of Axial Spondyloarthritis Diagnosis Among Patients Seen by US Rheumatologists for Evaluation of Chronic Back Pain. *Arthritis Rheumatol.* 2016;68(2326-5205 (Electronic)):1669–1676.
[3] Garrido-Cumbrera M, Poddubnyy D, Gossec L, et al. The European Map of Axial Spondyloarthritis: Capturing the Patient Perspective-an Analysis of 2846 Patients Across 13 Countries. *Curr Rheumatol Rep.* 2019;21(1534-6307 (Electronic)):19.
[4] Redeker I, Callhoff J, Hoffmann F, et al. Determinants of diagnostic delay in axial spondyloarthritis: an analysis based on linked claims and patient-reported survey data. *Rheumatology (Oxford)* 2019;58(1462-0332 (Electronic)):1634–1638.
[5] Strand V, Singh JA. Evaluation and Management of the Patient With Suspected Inflammatory Spine Disease. *Mayo Clin Proc* 2017;92(1942-5546 (Electronic)):555–564.

[6] Martindale J. The impact of delay in diagnosing ankylosing spondylitis/axial SpA. . *Rheumatology.* 2014;53.
[7] Yi EA-O, Ahuja A, Rajput T, George AT, Park Y. Clinical, Economic, and Humanistic Burden Associated With Delayed Diagnosis of Axial Spondyloarthritis: A Systematic Review. *Rheumatol Ther* 2020(2198-6576 (Print)):65-87.

Disclosure of Interests: Kate Lapane: None declared, Catherine Dubé Grant/research support from: Novartis, as personnel on such studies, Katarina Ferrucci: None declared, Sara Khan: None declared, Kristine A. Kuhn Consultant of: UCB, Eli Lilly, Novartis, Grant/research support from: Pfizer, Alexis Ogdie Consultant of: Abbvie, Amgen, BMS, Celgene, Corrona, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, Grant/research support from: Pfizer to Penn, Novartis to Penn, Amgen to Forward/NDB, Esther Yi Employee of: Novartis Pharmaceuticals, Jonathan Kay Consultant of: AbbVie, Inc.; Boehringer Ingelheim GmbH; Celltrion Healthcare Co. Ltd.; Jubilant Radiopharma; Merck & Co.,Inc.; Pfizer Inc.; Samsung Bioepis; Sandoz Inc.; Scipher Medicine; UCB, Inc., Grant/research support from: (paid to UMass Medical School) Gilead Sciences Inc.; Novartis Pharmaceuticals Corp.; Pfizer Inc., Shao-Hsien Liu Grant/research support from: Novartis
DOI: 10.1136/annrheumdis-2021-eular.2749

AB0893-HPR TREATMENT SATISFACTION, EXPECTATIONS, PATIENT PREFERENCES, AND CHARACTERISTICS IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA): TURKISH COHORT RESULTS OF THE SENSE STUDY

U. Kalyoncu[1], A. Kucuk[2], G. Sargin[3], F. Ozdener[4], S. Yolbaş[5], B. Yurttas[6], S. Turan[7], G. Kimyon[8], A. Sahin[9], S. Yilmaz[10], R. Mercan[11], H. Emmungil[6], M. Çınar[10], İ. Sezer[12], T. Kaşifoğlu[13], F. Cosan[4], T. Senturk[8], N. Inanc[14]. [1]*Hacettepe University – Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; [2]*Necmettin Erbakan University – Meram Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Kony, Turkey*; [3]*Aydin Adnan Menderes University – Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Aydin, Turkey*; [4]*Bahcesehir University – Faculty of Medicine, Department of Pharmacology, Istanbul, Turkey*; [5]*Inonu University – Turgut Ozal Medical Center Training and Research Hospital, Department of Internal Medicine, Division of Rheumatology, Malatya, Turkey*; [6]*Istanbul University Cerrahpasa – Cerrahpasa Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*; [7]*Trakya University – Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Edirne, Turkey*; [8]*Mustafa Kemal University – Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Hatay, Turkey*; [9]*Sivas Cumhuriyet University – Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Sivas, Turkey*; [10]*University of Health Sciences Turkey – Gulhane Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*; [11]*Namik Kemal University – Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Tekirdag, Turkey*; [12]*Akdeniz University – Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Antalya, Turkey*; [13]*Eskisehir Osmangazi University – Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Eskisehir, Turkey*; [14]*Marmara University – School of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey*

Background: Suboptimal control of RA may lead to severe and progressive articular damage, loss of function, and deterioration of the quality of life (QoL).
Objectives: To assess treatment satisfaction, sociodemographic, clinical, health care resource utilization, and QoL characteristics of patients with sub-optimally controlled RA and treated with conventional synthetic and/or biologic DMARDs.
Methods: This study was an international, multicenter, cross-sectional, non-interventional study. Adult RA patients with moderate to severe disease activity (DAS28>3.2) were enrolled. Patient satisfaction was evaluated with Treatment Satisfaction Questionnaire for Medication (TSQM, version 1.4) with a scale ranging from 0 (indicating poor satisfaction) to 100 (indicating perfect satisfaction). Patients were questioned regarding treatment adherence, patient preferences, and expectations. Workability was evaluated using Work Productivity and Activity Impairment Questionnaire-Rheumatoid Arthritis (WPAI-RA, version 2.0). Short Form 36 (V2) survey were performed to all patients.
Results: One hundred sixty-four patients were included in the study and most (78.0%) were female. The median age was 57.0 years, ranging between 22.0 and 84.0 years. Half of the patients (50.6%) were primary school graduates and 6.1% were unemployed due to RA and seeking work. Median time since RA diagnosis was 8.0 years and mean (±SD) DAS28-CRP score was 4.8 (±1.0). Mean total activity impairment was 54.9% (±27.4). In the past 3 months from enrollment, the mean number of healthcare professional and emergency room visits were 1.8 (±1.1) and 1.8 (±1.3), respectively. Mean number and length of hospitalizations in the previous 3 months were 1.1 (±0.3) times and 8.3 (±7.2) days, respectively. Mean TSQM scores were 53.5 (±21.4) for effectiveness, 86.0 (±26.7) for side effects, 67.8 (±16.5) for convenience, and 57.7 (±22.0) for global satisfaction. The leading expectation was 'lasting relief of RA symptoms' (mean score: 5.8). Preferred time until the effect of onset was 'up to 1 week' for 76.2% of the patients. Most of the patients (57.9%) preferred oral administrations and the most preferred frequency of administration was 'once per day' (46.3%). Mean physical and mental component summary scores for Short Form 36 (V2) survey were 37.9 (±8.3) and 40.1 (±10.7).
Conclusion: Two-thirds of the patients with RA who have suboptimal responses are not satisfied with their treatments. Moreover, oral and once-daily treatment approaches stand out in patient preferences. Finally, suboptimal control leads to deterioration in clinical characteristics, workability, and QoL of patients with RA.
Acknowledgements: The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the publication. All authors have received research funding for this study. The authors wish to thank B. Murat Ozdemir of Monitor CRO for medical editing and reviewing services of this manuscript. AbbVie provided funding to Monitor CRO for this work.
Disclosure of Interests: Umut Kalyoncu Speakers bureau: AbbVie, Pfizer, UCB, Novartis, and Janssen, Consultant of: AbbVie, Pfizer, UCB, Novartis, and Lilly, Grant/research support from: AbbVie, Pfizer, and Janssen, Adem Kucuk Speakers bureau: AbbVie, Gokhan Sargin: None declared, Fatih Ozdener Speakers bureau: UCB, Nutricia Advanced Medical Nutrition, Grant/research support from: Nutricia Advanced Medical Nutrition, Servet Yolbaş Speakers bureau: AbbVie, UCB, Pfizer, and MSD, Berna Yurttas: None declared, Sezin Turan: None declared, Gezmiş Kimyon Speakers bureau: AbbVie, Amgen, Pfizer, Novartis, UCB, MSD, Johnson and Johnson, and Celltrion, Consultant of: Amgen, and Pfizer, ALI SAHIN Speakers bureau: Roche, Pfizer, and AbbVie, Consultant of: Roche and Pfizer, Sedat Yilmaz Speakers bureau: UCB, Pfizer, AbbVie, MSD, Novartis, and Celltrion, Consultant of: Pfizer and Novartis, Rıdvan Mercan Speakers bureau: AbbVie, Novartis, MSD, Pfizer, UCB, Roche, Amgen, and Celltrion, Consultant of: Novartis, MSD, Pfizer, and Celltrion, Hakan Emmungil Speakers bureau: AbbVie, Pfizer, Novartis, and MSD, Muhammet Çınar Speakers bureau: AbbVie, Pfizer, Celltrion, UCB, Amgen, Novartis, and MSD, Grant/research support from: AbbVie, Pfizer, Celltrion, UCB, Amgen, Novartis, and MSD, İlhan Sezer Speakers bureau: AbbVie, Pfizer, MSD, Novartis, Celltrion, UCB, Amgen, and Abdi Ibrahim, Consultant of: AbbVie, Pfizer, MSD, Novartis, Celltrion, UCB, Amgen, and Abdi Ibrahim, Grant/research support from: AbbVie, Pfizer, MSD, Novartis, Celltrion, UCB, Amgen, and Abdi Ibrahim, Timuçin Kaşifoğlu Speakers bureau: AbbVie, Amgen, Roche, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Roche, MSD, Novartis, Pfizer, and UCB, Fulya Cosan Speakers bureau: AbbVie, Pfizer, Novartis, UCB, and MSD, Taskin Senturk: None declared, Nevsun Inanc Speakers bureau: AbbVie, UCB, Novartis, Pfizer, Roche, Lilly and MSD, Consultant of: Roche and Pfizer, Grant/research support from: Roche and Pfizer
DOI: 10.1136/annrheumdis-2021-eular.2846

AB0894-HPR THE JOURNEY OF PATIENTS WITH RHEUMATOID ARTHRITIS

M. Fusama[1], S. Oliver[2], H. Nakahara[3], Y. Van Eijk-Hustings[4], Y. Kuroe[5]. [1]*Takarazuka University, School of Nursing, Osaka, Japan*; [2]*Susan Oliver Associates, Nurse Consultant, Barnstaple, Devon., United Kingdom*; [3]*Osaka Yukioka College of Health Science, Department of Physical Therapy, Ibaragi, Japan*; [4]*Clinical Epidemiology and Medical Technology Assessment (KEMTA), Department of Patient&Care, Amsterdam, Netherlands*; [5]*Gifu College of Nursing, School of Nursing, hashima, Japan*

Background: The course of rheumatoid arthritis (RA) differs from patient to patient, and each patient has a unique story. The disease condition affects psychological and social aspects, greatly affecting the quality of life. The disease course is unpredictable, and each patient's story can be seen as a lifelong journey, full of ups and downs. Therefore, it is crucial to know what kind of support is required during the course of their life.
Objectives: The aim of this study is to examine the life story of patients with RA and clarify a common situation in their stories in order to consider what kind of support is needed.
Methods: This is a qualitative study using life story interview for patients with RA in Japan. Interview included disease history, patients' behaviors, effects on daily life, the patients' perspectives regarding psychological considerations and useful support. Data were analyzed using content analysis. This study was approved by the ethics committee and informed consent was obtained.
Results: Eight patients participated in this study. They were all females and the average age was 57 years old. As a result of the categorization, we extracted the following eight situations: (1) Emergence of symptom; patients thought joint pain would go away, however, the symptom did not improve and began to affect their daily life and work, (2) Choose a hospital to visit; pain and anxiety have continued and decided to visit a hospital, (3) Encounter with their doctors; patients expected their doctor to relieve their pain, while they were afraid of being told that they were suffering from a serious disease. (4) Diagnosis of RA; patients were

shocked when diagnosed and anxious about what would happen and wondered why they had such a disease, (5) Choice of treatment; patients were afraid of the side effects. They wanted to make a decision discussing with their doctor, but they could not understand the explanation about drugs well and, therefore, followed the doctor's opinion. (6) Change of treatment; a biological agent was often recommended. Patients were also worried about side effects and the financial burden. (7) Remission or stable phase; they felt better mentally too, however, they often felt anxiety about disease flare, side effect of drugs and financial burden, and (8) Flare and remission; patients felt shocked and disappointed when RA flared, and then, they noticed that patients with RA had alternating periods of relapse and remission and they had to live with RA.

These interviews revealed repeated worsening and improvement of symptoms and many similar repeated psychological reactions such as anxiety, shock, denial, conflict, acceptance, giving up and relief. To cope with these fluctuating disease and mental conditions, patients were supported by educational and psychological assistance, timely consultations, social life help from nurses and support from their family. The patients considered a trusting relationship with their doctors is necessary. The patients had also realized through their experience the importance of enhancing their own abilities, such as decision-making, prevention of infections and self-management skills. Moreover, they noticed that it is important to have their own goals including hobbies and work.

Conclusion: This study elucidated the common behaviors of patients with RA, the impact of RA on their psychological state and daily and social life, and the required support. The psychological condition and daily and social life also had a great influence on medical behavior. Therefore, psychosocial support and establishment of trust between healthcare professionals and patients are crucial. In addition, improving patients' self-management skills including self-efficacy and empowerment is also necessary. As patients with RA often feel anxious in various situations and expect nurses' support, nurses should listen to patients, pay attention to their concerns and anxieties, and show a solution-oriented attitude. In order for patients to feel at ease in their Patient Journey, nurses should sail with them while maintaining a patient-centered perspective.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3029

AB0895-HPR A MODERATED MEDIATION ANALYSIS FOR POOR ORAL HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH BEHÇET'S DISEASE

E. N. Çakır[1], Y. Yenisoy[1], A. Kapusuz[1], K. Abacar[2], F. Alibaz-Oner[2], M. Yay[3], Ü. Karaçaylı[4], N. Inanc[2], T. Ergun[5], H. Direskeneli[2], G. Mumcu[6]. *[1]Marmara University, Institute of Health Sciences, Istanbul, Turkey*; *[2]Marmara University, Division of Rheumatology, Istanbul, Turkey*; *[3]Mimar Sinan Fine Arts University, Department of Statistics, Istanbul, Turkey*; *[4]Health Sciences University, Department of Oral and Dental Surgery, Ankara, Turkey*; *[5]Marmara University, Department of Dermatology, Istanbul, Turkey*; *[6]Marmara University, Department of Health Management, Istanbul, Turkey*

Background: Since oral ulcer is a common clinical manifestation, oral health-related quality of life (OHRQoL) is affected by the presence of oral ulcer poorly in patients with Behcet's disease (BD).

Objectives: The aim of the study was to examine associated factors for poor OHRQoL status to improve treatment outcomes in patients with BD.

Methods: In this retrospective study, 339 BD patients (F/M: 179/160, mean age: 36,13±9,81 years) included. Data were collected by a structured questionnaire regarding treatment expectation, Oral Health Impact Profile-14 (OHIP-14) questionnaire for OHRQoL, oral ulcer activity, and disease severity score. Treatment expectation was coded by a 5-point Likert type scale (1: symptoms were completely cured vs 5: symptoms were worsened). OHIP-14 score was between "0 point (the best score)" and "56 points (the worst score)". The disease severity score was calculated according to the organ involvement. Then, patients were categorised as mucocutaneous involvement (n=181) and severe organ involvement (n=158). After preliminary analysis, a Moderated Mediation analysis was carried out.

Results: Oral ulcer activity was seen in 63,4% of the group (n=215). OHIP-14 score (22,05±16,47) was correlated with Treatment expectations (2,35±0,98) (r: 0,36 p=0.000) in the group. Poor scores of OHIP-14 and Treatment expectations were found in patients with active oral ulcers (mucocutaneous involvement: 27,56±14,55; 2,68±0,87, vs severe organ involvement: 28,51±17,25; 2,43±0,99) compared to those of inactive patients (mucocutaneous involvement: 13,38±12,23; 1,81±0,73 vs severe organ involvement: 8,79±10,19; 1,85±1,02) (p=0.000 for all). Patients with active oral ulcers were younger (35,09±9,52) than the others (39,57±10,06) in the mucocutaneous involvement group (p=0.0011) whereas a similar relation was not seen in the severe organ involvement (p=0.233).

In the moderated mediation analysis, it was found that OHIP-14 score was increased by the presence of oral ulcer in the direct path (p=0.0000) and the negative Expectation of the treatment as a first mediator (p = 0.0001) in the indirect path. Oral ulcer activity was associated with younger patients (p=0.0039). This effect was seen especially in patients with mucocutaneous involvement that had a moderator effect (p=0.0040). In addition, age was found to be a second mediator for the poor OHIP-14 score (p = 0.0053). Mediators and the moderator were found to effective for OHIP-14 score a bootstrap analysis with 5000 replications.

Conclusion: OHRQoL was affected by oral ulcer activity and poor treatment expectations. Age was also found to be another critical factor for OHRQoL.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3043

AB0896-HPR THE EVALUATION OF TYPE D PERSONALITY AND SELF-ESTEEM IN PATIENTS WITH FIBROMYALGIA

N. Gokcen[1], I. Coskun Benlidayi[2], L. Tamam[3], M. E. Demirkol[3], C. Yesiloglu[3], R. Guzel[2]. *[1]Cukurova University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Adana, Turkey*; *[2]Cukurova University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Adana, Turkey*; *[3]Cukurova University Faculty of Medicine, Department of Psychiatry, Adana, Turkey*

Background: Fibromyalgia (FM) is a condition characterized by chronic widespread pain, fatigue, sleep disturbances. Etiopathogenesis remains unclear; however, growing data regarding the effect of psychosocial factors on disease etiopathogenesis have drawn attention. Psychosocial elements such as type D personality and low level of self-esteem might increase disease burden (1). Accordingly, many researchers so far, have examined psychological parameters in FM and a limited number of studies focused on the personality type among patients with FM (2-5).

Objectives: The current study aimed to investigate type D personality and self-esteem in patients with FM.

Methods: Female patients with fibromyalgia and age-matched healthy controls were enrolled in this cross-sectional study. Type D personality was evaluated by using the type D scale (DS-14). The Rosenberg self-esteem scale (RSES) was used to assess self-esteem and psychosomatic symptoms. Psychological status was evaluated by the Beck Depression and Beck Anxiety Inventories. Fibromyalgia Impact Questionnaire (FIQ) was performed to assess functional impairment and health status in patients with FM. The potential confounders of type D personality were evaluated by binary logistic regression analysis.

Results: Seventy patients with FM and 60 controls were included. Type D personality was observed in 58.6% of the patients and in 21.7% of the control group (p<0.001). When compared to patients with non-type D personality, those with type D personality revealed lower self-esteem and poorer health status (p<0.05 for both), higher anxiety and depression scores (p<0.001 for both). According to binary logistic regression analysis, depression (β=1.178, CI 95% 1.055–1.316, p=0.004) and lower education level (β=0.818, CI 95% 0.682–0.982, p=0.031) were significantly related to type D personality in FM (Table 1).

Conclusion: Type D personality is more common in female patients with FM when compared to healthy women. Patients with type D personality have lower level of self-esteem when compared to those with non-type D personality. Depression and lower education level are potential confounders of type D personality in FM.

REFERENCES:

[1] Bazzichi L, Giacomelli C, Consensi A, Giorgi V, Batticciotto A, Di Franco M, Sarzi-Puttini P (2020) One year in review 2020: fibromyalgia. Clin Exp Rheumatol 38 Suppl 123(1):3-8.

[2] Conversano C, Marchi L, Ciacchini R, Carmassi C, Contena B, Bazzichi LM, Gemignani A (2018) Personality Traits in Fibromyalgia (FM): Does FM Personality Exists? A Systematic Review. Clin Pract Epidemiol Ment Health 14:263.

[3] Türkoğlu G, Selvi Y (2020) The relationship between chronotype, sleep disturbance, severity of fibromyalgia, and quality of life in patients with fibromyalgia. Chronobiol Int 37(1):68-81.

[4] Garip Y, Güler T, Bozkurt Tuncer Ö, Önen S (2019) Type D Personality is Associated With Disease Severity and Poor Quality of Life in Turkish Patients With Fibromyalgia Syndrome: A Cross-Sectional Study. Arch Rheumatol 35(1):13-19.

[5] Ablin JN, Zohar AH, Zaraya-Blum R, Buskila D (2016) Distinctive personality profiles of fibromyalgia and chronic fatigue syndrome patients. PeerJ 4:e2421.

Table 1. Binary logistic regression analysis for the evaluation of potential confounders of type D personality in patients with fibromyalgia.

	Wald	SE	β (95%CI)	p
Education (years)	4.664	0.093	0.818 (0.682–0.982)	0.031
Occupation duration (years)	0.116	0.037	1.013 (0.942–1.089)	0.733
Self-esteem scale (D1)	0.369	0.423	0.774 (0.338–1.771)	0.544
BDI	8.446	0.056	1.178 (1.055–1.316)	0.004
BAI	0.789	0.032	1.029 (0.966–1.095)	0.374

BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, SE: standard error, CI: confidence interval

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3155

AB0897-HPR EVALUATION OF ANXIETY AND DEPRESSION IN PATIENTS WITH KNEE OSTEOARTHRITIS USING THE HAD "HOSPITAL ANXIETY AND DEPRESSION SCALE"

M. Brahem[1], S. Abdellatif[1], H. Hachfi[1], A. Ben Salem[1], R. Sarraj[1], R. Ben Tekaya[1], Y. Mohamed[1]. [1]*Taher Sfar Hospital, Rhumatology, Mahdia,Tunisia*

Background: Knee osteoarthritis is considered to be one of the most common causes of functional impairment, which affects the quality of life of patients leading to severe mood disorders. Our goal is to evaluate the frequency of depression and anxiety in patients with knee osteoarthritis.
Objectives: Evaluate the frequency of depression and anxiety in patients with knee osteoarthritis.
Methods: This is a cross-sectional study over a period of 7 months from February to August 2016, including consecutively patients who consulted in the Rheumatology department at Mahdia university hospital for knee osteoarthritis. We evaluated for each patient a validated version of HAD "Hospital Anxiety and Depression scale". This score includes 14 items each one rated from 0 to 3 and two components including depression and anxiety.
Results: We included in our study 66 patients (56 women and 10 men) with an average age of 60.3 years [40-90 years]. Knee osteoarthritis was bilateral in 56.1% of cases. The examination found limited mobility of the knee in 45.5% and flessum in 13.8% of cases. Standard radiography showed stage 1 knee osteoarthritis in 4.5%, stage 2 in 31.8%, stage 3 in 56.1% and stage 4 in 7.6% of cases. All our patients were treated with analgesics, NSAIDs in 95.5%, local corticosteroid infiltrations in 43.9% and hyaluronic acid in 7.6% of cases.The mean visual analog scale(VAS)was 5.84 ±1.7 out of 10 [2-9]. The mean overall WOMAC index was 47.15±15.6 [12-82]. The average Lequesne index was 16.8±13.1, moderate disability was found in 3% of cases, significant disability in 6.1% of cases, very significant disability in 18.2% of cases and extreme disability in 72.7% of cases. The mean depression score was 9.3±2.6 [4-16], with 24.6% of the patients had no depressive symptomatology (score ≤7), 40% had doubtful depressive symptomatology (score between 8 and 10) and 35.4% of them had certain depressive symptomatology (score ≥11).The mean anxiety score was 8.88 ± 4 [0-19], 33.3% of patients had no anxiety symptoms (score ≤ 7), 34.8% had doubtful anxiety (score between 8 and 10) and 31.8% had certain anxiety (score ≥11). The statistical study found a significant correlation between the depression score and WOMAC score, but we did not find an association with age, sex, radiological stage, mobility limitation and VAS. Regarding anxiety, there was a correlation with age, WOMAC score and female gender. On the other hand, there was no correlation with VAS, Lequesne score, radiological stage and limitation of mobility.
Conclusion: Although knee osteoarthritis appears to be a benign pathology, its impact can be severe, including depression and anxiety, which are mainly influenced by the degree of functional disability. Hence psychological care is sometimes necessary in these chronic degenerative diseases.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3835

AB0898-HPR WICH FACTORS ARE RELATED TO PAINFUL EXPERIENCE IN PATIENTS AFFECTED BY CHRONIC INFLAMMATORY RHEUMATIC DISEASE DURING THE COVID-19 PANDEMIC?

T. El Joumani[1], H. Rkain[1,2], T. Fatima Zahrae[1], H. Kenza[3], R. Abouqal[4], N. Laila[5], S. Bahloul[1], E. A. Nada[1], T. Latifa[1], N. Hajjaj-Hassouni[6], F. Allali[1]. [1]*El Ayachi Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Department of Rheumatology B, Rabat, Morocco*; [2]*Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Physiology Laboratory, Rabat, Morocco*; [3] *Université Mohammed VI des Sciences de la Santé - UM6SS, Casablanca, Morocco., Ecole Internationale de Santé Publique, Rabat, Morocco*; [4]*Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Laboratory of Biostatistics, Rabat, Morocco*; [5]*Moroccan Association of Patients With Rheumatoid Arthritis and Spondyloarthritis, Rheumatology, Rabat, Morocco*; [6]*International University of Rabat, Rabat, Morocco, Rheumatology, Rabat, Morocco*

Objectives: To evaluate the effect of containment, during the Covid-19 pandemic, on the pain of patients with CIRD, and to analyze the factors associated with the experience of pain.
Methods: A cross-sectional study was conducted among patients with rheumatic diseases using a questionnaire providing information on patients and disease characteristics. Impact of COVID-19 on This is a cross-sectional study that consecutively included
Patients were asked to assess the global pain which they had experienced before and during the containment period, using a single Visual Analogue Scale (VAS) ranging from 0 (no pain) to 10 (greatest pain).
Statistical Analysis System IBM SPSS Statistics V20.0.0 was used to analyze the study data.
We performed univariate then multivariate analysis to search any related factors to pain perception during to quarantines. Qualitative values were analyzed by the chi2 test. Quantitative values were analyzed by the Student test when the measures were normally distributed or by nonparametric test (Mann–Whitney U) when the measures were not normally distributed (Kolmogorov–Smirnov test was used to test normality).
Results: Among the 350 patients who answered to the questionnaire online, rheumatoid arthritis represented 62.3%, spondyloarthropathy 34.3% and undifferentiated CIRD 3.4%.
Pain experience caused by the CIRD during the containment was reported by 79.1% of patients.
The level of pain, using the VAS of Pain increased significantly during the COVID-19 pandemic (4,6 ± 2,8 and 5,4 ± 3 before and during the containment; p<0.001).
In multivariate analysis, the factors implicated in pain were the negative impact of Coronavirus on access to rheumatologic care, discontinuation of therapeutic adherence, the disturbed quality of sleep and the negative psychological impact (table 1).
Table 1: Summarize multivariable analysis of factors associated with painful experience related to CIRD during containement.

Table 1. Multivariable analysis of factors associated with painful experience related to CIRD during containement

	P
Impact on monitoring	0.05
Impact on therapeutic adherence	<0.001
Quality of sleep disturbed	0.001
Negative psychological impact	0.02

Conclusion: This survey showed the that the COVID-19 pandemic have incresed painful experience in CIRD patients. Factors influencing painful experience should be taken into account to help patients to cope with their chronic rheumatism and this global health crisis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4073

AB0899-HPR THE IMPACT OF CORONAVIRUS (COVID-19) PANDEMIC ON THERAPEUTIC MAINTENANCE IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES

T. El Joumani[1], H. Rkain[1], T. Fatima Zahrae[1], H. Kenza[2], A. Radouan[3], N. Laila[4], S. Bahloul[1], E. A. Nada[1], T. Latifa[1], N. Hajjaj-Hassouni[5], F. Allali[1]. [1]*El Ayachi Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Department of Rheumatology B, Rabat, Morocco*; [2] *Université Mohammed VI des Sciences de la Santé - UM6SS, Casablanca, Morocco., Ecole Internationale de Santé Publique, Rabat, Morocco*; [3]*Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Laboratory of Biostatistics, Rabat, Morocco*; [4]*Moroccan Association of Patients With Rheumatoid Arthritis and Spondyloarthritis, Rheumatology, Rabat, Morocco*; [5]*International University of Rabat, Rabat, Morocco, Rheumatology, Rabat, Morocco*

Background: The Coronavirus pandemic caused many consequences on well being, access to care and therapeutic maintenance in patients with chronic diseases.
Objectives: To assess the impact of COVID-19 on therapeutic maintenance of patients with Chronic Inflammatory Rheumatic Diseases (CIRD) and to identify related factors to difficulties in access to rheumatologist care during the COVID-19 pandemic.
Methods: A cross-sectional study was conducted among patients with rheumatic diseases using a questionnaire providing information on patients and disease characteristics, impact of COVID-19 on access to rheumatologist care and therapeutic maintenance during the confinement. Reasons of therapeutic interruption and of diificulties in access to healthcare were precised.
Results: We received answers from 350 patients (female sex of 68%, mean age of 46,1 ± 14,4 years) suffering from Chronic Inflammatory Rheumatic Diseases (CIRD):rheumatic arthritis (RA) (62.3%), spondyloarthropathies (34.3%), and undifferentiated CIRD (3.4%). The global average disease evolution was 12,1 ± 9,7 years.
The patients were treated with conventional Disease-modifying anti-rheumatic drugs (cDMARDs) and biologic Disease-modifying anti-rheumatic drugs

(bDMARDs) in respectively 67.4% and 30.6% of cases. Corticosteroids and Non-steroidal Anti-Inflammatories (NSAIDs) intake was noted in 39.1 and 33.7% of patients.
Difficulties to access to rheumatologist care appointments were reported in 82.9% of the participants. Reasons of thoses difficulties are summurized in Figure 1.

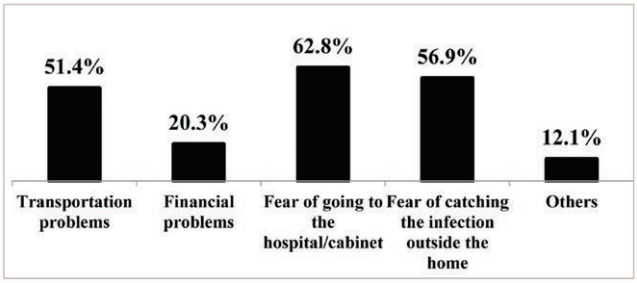


Figure 1. Causes of difficulties of access to Rheumatologist care during COVID-19 pandemic.

Half of patients declared that the pandemic had affected their therapeutic compliance. Discontinued drugs were in decreasing order: Synthetic antimalarials (68.4%), NSAIDs (45.8%), Methotrexate (43.8%), bDMARDs (25.2%), Sulfasalazine (18.2%) and Corticosteroids (10,2%).
Causes of treatments interruption are summarized in Table I.

Table 1. Causes of treatments interuption in patients with CIRD

Drugs	Not found in pharmacies	The pharmacy refuses to give me the treatment without a recent prescription	To avoid the decrease in immunity and therefore to avoid catching Covid-19	I stopped the follow-up, and so I stopped the treatment...	Other reasons
NSAIDS	0	27.8	74.1	44.4	27.8
Corticosteroids	0	14.3	92.9	57.1	50
Methotrexate	70.1	3	10.4	16.4	22.4
Sulfasalazine	0	12.5	25	75	100
Synthetic antimalarial	69.2	0	0	23.1	61.5
Leflunomide	0	0	0	0	0
bDMARDs	0	7.4	40.7	44.4	51.9

Conclusion: The COVID-19 pandemic impacted heavly on therapeutic maintenance in CIRD patients in our country. Patients expressed many difficulties in access to appropiate management. Facing to all thoses consequences, we need to devolopp as soon as possible adequate solutions adapted in such health crisis, especially therapeutic education and telemedecine.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4151

AB0900-HPR THE EXPECTATIONS AND EXPERIENCES OF PATIENTS WITH RHEUMATOID ARTHRITIS AFTER ENROLLING INTO AN EDUCATIONAL PROGRAM. RESULTS FROM A MIXED STUDY APPROACH

R. A. Castiblanco Montañez[1], A. Arevalo Velandia[1], J. D. Garzon Cepeda[1], F. Rodriguez-Florido[2], D. Buitrago-Garcia[1], G. Sánchez[1], P. Santos-Moreno[2]. *[1]Fundación Universitaria de Ciencias de la Salud FUCS. Sede Centro, Bogotá, Bogotá, Colombia*; *[2]Biomab IPS, Bogotá, Bogotá, Colombia*

Background: Rheumatoid arthritis (RA) is a high-cost disease, usually diagnosed at a productive age in life. RA brings significant changes in a patient's life. On an emotional level, the patient perceives a strong impact that generates disorientation, denial, depression, hopelessness, anger and fear due to the uncertainty of the development of the disease and the doubt of the turn that his life will take. However, each patient has different ways of coping with the disease and adapting to it (1,2). These changes require attention from health personnel. In this regard, different studies have reported the effect of educational, support and empowerment programs for patients on reducing the effects of the disease and the benefits are oriented towards improving lifestyles by improving self-care (3,4).
Objectives: To describe the experience of patients with rheumatoid arthritis, their perception and expectations about entering a multicomponent educational program in a specialized center in Bogotá - Colombia.
Methods: For this study a concurrent mixed design was used, in which quantitative and qualitative methods are applied simultaneously, we invited patients with rheumatoid arthritis who attended a specialized center in Bogotá - Colombia who enrolled in an education program called UNIVERSITAR. The quantitative phase included a descriptive analysis and the application of the expectations scale adapted from Borkovec and Nau (5); this scale collects information about the level of expectations and satisfaction of the program. The scale ranges from 0 (not at all) to 10 (very much). Immediately after the application of the scale, the participants were invited to a focus group that allowed the dialogue on the perception and expectations of the participants regarding the program, through a dynamic process in which the participants exchanged their ideas and opinions. A group interview script was used, aimed at identifying the patients' experiences with their diagnosis and their expectations regarding the program. Two focus groups were held with an average duration of one hour; the discussion was recorded on audio and transcribed in its entirely.
Results: We included 31 participants and were distributed in two focus groups. The median age of the participants was 60 years IQR (54-67), 92% were female. 77% of participants reported high scores for the satisfaction regarding the program. In the qualitative phase two categories emerged that speak of the experience of the participants with the disease. They highlighted the appearance of this disease in their lives in an unexpected way, the doubts and uncertainties that were generated from the diagnosis and the implications that this condition causes health in their everyday life. However, in the second category, the expectations and motivations of the participants towards the educational program are highlighted, and the factors that influence their participation and their motivation to train and empower themselves to make decisions and as expert patients, capable of educate, guide and support other patients with the same diagnosis.
Conclusion: The expectations and perceptions of the patients are of great importance, since through these the conditions with which these educational programs provide interventions and a better quality of life to these patients can be improved.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4160

AB0901-HPR SOCIAL AND PSYCHOLOGICAL IMPACT OF THE CONTAINEMENT DURING COVID-19 PANDEMIC ON PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES

T. El Joumani[1], H. Rkain[1], T. Fatima Zahrae[1], H. Kenza[2], A. Radouan[3], N. Laila[4], S. Bahloul[1], E. A. Nada[1], T. Latifa[1], N. Hajjaj-Hassouni[5], F. Allali[1]. *[1]El Ayachi Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Department of Rheumatology B, Rabat, Morocco*; *[2] Université Mohammed VI des Sciences de la Santé - UM6SS, Casablanca, Morocco., Ecole Internationale de Santé Publique, Rabat, Morocco*; *[3]Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Laboratory of Biostatistics, Rabat, Morocco*; *[4]Moroccan Association of Patients With Rheumatoid Arthritis and Spondyloarthritis, Rheumatology, Rabat, Morocco*; *[5]International University of Rabat, Rabat, Morocco, Rheumatology, Rabat, Morocco*

Background: Covid-19 pandemic had a worldwide impact on the population, global economy and health care systems.
Objectives: To evaluate the psychological state and social impact of patients with Chronic Inflammatory Rheumatic Diseases (CIRD) during this pandemic in order to understand how to optimize their quality of life.
Methods: It's a cross-sectional survey, where the data were collected through the online survey tool "google forms". A pilot test were conducted with the study committee members who analyzed the apparent validity of the questionnaire and identified issues that could lead to misunderstandings, and their suggestions were refined by a retest reliability until general agreement.
The social and psychological impacts were evaluated by 14 questions exploring the different effects of the containment on negative feelings, interest in the family, changes in daily activities and plans, quality of sleep, practice of physical activity before and during containment, as well as the impact of the Coronavirus on psychological health. Statistical Analysis System IBM SPSS Statistics V20.0.0 was used to analyze the survey data.
Results: 350 patients had participated in this online survey (mean age of 46,1 ± 14,4, 68% were women, 15.7% were illiterate, 45.7% were unemployed, rural residence in 11.7% of cases).
Patients reported that their mental health has been negatively affected by Coronavirus in 59.1% of cases. Table 1 summarizes the psychological events during the containment.

Table 1. Negative feelings during the containment

Negative feelings (%)	N = 350
Hopelessness	**23.7**
Anxiety	**55.4**
Fear	**29.7**
Frustration	**22.9**
Loneliness	**17.4**
Anger	**22.6**
Powerlessness	**24.3**

Patients reported that they paid more attention to their family in 87.1% during containment. Their daily lives and their life plans had changed because of

Coronavirus(in 89.7% and 81.4%). Sleep during the pandemic has been negatively affected in 72.6% of patients. Physical activity practice had significantly decreased during containment (26.6% vs 51.7%)
Conclusion: This study illustrates the social and psychological impact of COVID-19 pandemic on patients with CIRD. In the light of those results, we have lunched an awareness campaign to reinforce psychologic and social support of patients with CIRD during this global health crisis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4184

AB0902-HPR **COVID-19 PANDEMIC: KNOWLEDGE, BELIEVES AND FEARS IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES IN A DEVELOPING COUNTRY**

T. El Joumani[1], H. Rkain[1,2], T. Fatima Zahrae[1], H. Kenza[3], A. Radouan[4], N. Laila[5], S. Bahloul[1], E. A. Nada[1], T. Latifa[1], N. Hajjaj-Hassouni[6], F. Allali[1]. *[1]El Ayachi Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Department of Rheumatology B, Rabat, Morocco*; *[2]Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Laboratory of Physiology, Rabat, Morocco*; *[3] Université Mohammed VI des Sciences de la Santé - UM6SS, Casablanca, Morocco., Ecole Internationale de Santé Publique, Rabat, Morocco*; *[4]Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Laboratory of Biostatistics, Rabat, Morocco*; *[5]Moroccan Association of Patients With Rheumatoid Arthritis and Spondyloarthritis, Rheumatology, Rabat, Morocco*; *[6]International University of Rabat, Rabat, Morocco, Rheumatology, Rabat, Morocco*

Objectives: To investigate the knowledge, believes, and fears of patients with Chronic Inflammatory Rheumatic Diseases (CIRD) in Morocco regarding the Covid-19 pandemic.
Methods: COVID-19 related knowledge was evaluated through following items: clinical presentations, age of infection, transmission routes, self-reported preventive behaviors, patient's approach in case of suspicion of being infected by COVID-19 and vaccination. We also investigated the source of the patients' information.
Believes and fears of patients regarding COVID-19 was assessed using 2 items that explored participant's perception of the degree of threat to public health and their individual infection susceptibility compared to the general population.
Results: A cross-sectional study was conducted among patients with rheumatic diseases using a questionnaire providing information on patients and disease characteristics.
350 patients had participated in this online survey (mean age of 46,1 ± 14,4, 68% were women, 15.7% were illiterate, 45.7% were unemployed, rural residence in 11.7% of cases). The correct answer rates of the 6 questions of the knowledge section of the questionnaire were 53.4-100% with an average mean of 90.7%. The mean COVID-19 knowledge score was 5,43/6 (SD:0,48). Most participants (96.6%) correctly identified the age group concerned about Covid-19 infection. Remarkably 92.3% of the participants recognized 3 clinical features when 97.7% and 72.3% of the sample recognized perfectly modes of transmission and disease prevention measures. 87.4% of patients knew the recommended course of action to do if they have fever or cough and have recently been in contact with an infected patient. 64% of the study population thought that there was no vaccine available yet.
The sources of information on COVID-19 were in descending order: rheumatologist (56.6 %), personal research (on the internet or other) (43.4%), video broadcasts on national television channels (28%), other Awareness Video (24.2%).
Regarding the patients believes and fears toward COVID-19, 81.7% of patients believed that the pandemic is a serious threat for the public health and 80.6% thought that their CIRD makes them more exposed to the risk of contamination than general population.
Conclusion: The results of this survey show a high prevalence of patient concern about COVID-19. However, the majority of patients responded correctly on the mode of transmission and the means of protection for the COVID-19 infection. Those results could be explained by enormous awareness-raising efforts carried out by our differents departments of our government.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.4200

HPR Service developments, innovation and economics in healthcare

AB0903-HPR **DURATION OF TELEPHONE CONSULTATIONS AMONGST RHEUMATOLOGY PRACTITIONERS IN A DISTRICT GENERAL HOSPITAL - ADAPTING TO REMOTE CONSULTATION IN A COVID-19 PANDEMIC**

L. Parker[1], F. Coldstream[1]. *[1]University Hospitals Dorset NHS Foundation Trust, Rheumatology Department, Christchurch, United Kingdom*

Background: The Covid-19 pandemic has resulted in a rapid adoption of remote consultations in order to limit face to face clinical contact wherever appropriate, as recommended by the British Society for Rheumatology. The same clinic templates which existed for face-to-face encounters have been retrospectively adapted, without consideration of any potential difference in duration of consultations. Rheumatology practitioners from a variety of clinical backgrounds work alongside the rheumatology consultants, providing clinical care to patients with both inflammatory arthritis and connective tissue disease.
Objectives: To record the duration of all scheduled telephone consultations carried out by advances rheumatology practitioners in a 4-week period.
Methods: All scheduled telephone clinic encounters over a 4-week period were timed and the duration recorded in a spreadsheet. Data was collected in real time by all 8 rheumatology advanced practitioners working within the rheumatology department of a district general hospital, following each clinic episode.
Results: Data was recorded from a total of 337 clinic appointments. Of these, 317 (94%) were booked as routine, 3 (0.9%) as urgent, 4 (1.2%) were expedited following an advice line contact, and 13 (3.9%) no data was recorded. 28 (8%) of the patients did not answer when contacted. 80 (24%) clinic appointments lasted 15 minutes or less, 186 (55%) lasted 16 - 30 minutes, 37 (11%) lasted 31 - 45 minutes, and 6 (2%) lasted 46 - 60 minutes. The average duration was 22 minutes.
Conclusion: Within this department, remote consultations appear to have a similar duration when compared against the traditional clinic template for a fully face-to-face clinic, with some encounters lasting significantly longer than the planned duration. This would appear to differ to telephone consultations used in other settings, such as general practice where the duration is reportedly shorter[1]. This may be representative of the additional complexity and co-morbidity of a typical rheumatology patient, or due to the multi-faceted nature of a rheumatology follow-up appointment[2]. Although remote consultations are effective in limiting risk of exposure to Covid-19, they may not offer a quicker or more efficient service compared with the face-to-face model. Further study in this field is required to evaluate this widely adopted new pattern of working.
REFERENCES:
[1] Pinnock H, Bawden R, Proctor S, Wolfe S, Scullion J, Price D, Sheikh A. Accessibility, acceptability, and effectiveness in primary care of routine telephone review of asthma: pragmatic, randomised controlled trial. *BMJ*. 2003 Mar 1;326(7387):477-9. doi: 10.1136/bmj.326.7387.477. PMID: 12609944; PMCID: PMC150181.
[2] National Institute for Health and Care Excellence (NICE) (2018) rheumatoid arthritis in adults: management (NICE Guideline NG100). Available at https://www.nice.org.uk/guidance/ng100 [Accessed 05 January 2021].
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1282

AB0904-HPR **RHEUMATOLOGY NURSING AND COVID19: FIRST WAVE EXPERIENCES**

L. Cano Garcia[1], S. Garcia Diaz[2], S. P. Fernandez-Sanchez[3], C. Domínguez-Quesada[4], M. D. C. Ordoñez Cañizares[1], J. M. Martín Martín[5]on behalf of GTESER. *[1]Hospital Regional Universitario de Málaga, Rheumatology, Málaga, Spain*; *[2]Hospital Moises Broggi, Rheumatology, Barcelona, Spain*; *[3]Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*; *[4]Hospital Universitario Virgen Macarena, Rheumatology, Sevilla, Spain*; *[5]Hospital Universitario Virgen de la Candelaria, Rheumatology,Tenerife, Spain*

Objectives: To know the impact of the first wave of COVID19 (March to June 2020) in the nursing activity in rheumatology and explore improvements in patient care during the pandemic situation.
Methods: 2 surveys were sent to nurses working in the rheumatology area (Both in the Outpatient department and day care unit) during October 2020 in Spain. The first survey had 10 questions about what happened in the rheumatology units in the first wave of the COVID19 pandemic (March to June of 2020) and the second survey had 10 questions about the standards of quality of nursing care in times of pandemic. Google forms were used to collect and analyze data.
Results: 32 nurses completed the survey (30 women (93.8%)) with an average age of 49.6 ± 10.2 years. 93.8% work in the outpatient clinics and 2(6.2%) in day care units. The main results of the effects of the first wave of the pandemic are as follow: 4(12.5%) nurses were transferred to other areas of the hospital, 27(84.4%) showed changes in their care activity; and in 12(37,5%) of the surveyed centers, (slightly less than half of the medical staff) left their usual activity to care for covid-19 patients. In June 2020, at the end of the first wave, 17(53.1%) reported more decompensated patients and 22(68.8%) reported that they had both telephone and face-to-face consultations; 15(46.9%) reported that their clinical activity had increased.
Regarding the standards of quality during the pandemia: 27(84.4%) believed that rheumatology units should be strengthened,31(96.9%) reported the need to carry out COVID educational campaigns in rheumatic patients and 30(100%) stated that nursing education should lead that education; 31(96.7%) believed

that telephone consultation should be on demand and by telephone, 25 (78.1%) considered it necessary to include video calls and the possibility of receiving reports in non-face to face care and photos. Finally, 23(71.9%) centers recorded nursing and medical telephone consultations in their medical records.
Conclusion: The pandemic had a huge impact on nursing care for rheumatic patients, with difficulties associated with extra work load and changes in the dynamics of care. A readjustment of assistance has been necessary and audio-visual aids were necessary to improve telephone (non face to face) service.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1923

AB0905-HPR TELEMEDICINE IN RHEUMATOLOGY AT TIME OF COVID PANDEMIC

G. Cuomo[1], F. Masini[2], K. Gjeloshi[2], D. Lubrano[2], L. E. Adinolfi[2], C. Romano[2]. *[1]University of Campania Studies "Luigi Vanvitelli", Precision of Medicine, Napoli, Italy*; *[2]University of Campania Studies "Luigi Vanvitelli", Department of Medical and Surgical Sciences, Napoli, Italy*

Background: The outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has imposed considerable restrictions on people's mobility in order to limit infection transmission. Before the COVID -19 pandemic tele-rheumatology was proposed to patients living in remote areas. Currently, the use of telemedicine has increased significantly. We report on the implementation of a telemedicine program for the evaluation and treatment of patients with rheumatic diseases (1).
Objectives: The aim of the study is to evaluate telemedicine as a viable approach for routine follow-up and management of rheumatic disease.
Methods: Sixty-six patients were evaluated online by the remote rheumatologist in four weeks. The population of rheumatology patients was evaluated using a IARPLUS platform Information collected included demographic information consisting of age, gender, and primary rheumatologic diagnosis. Results: The average age of patients who were seen was 54 years and 85% of patients were women.
The most common disorders included rheumatoid arthritis (22, 33%), axial spondyloarthropathies (7, 11%), and psoriatic arthritis (15,23%), systemic sclerosis (13, 20%), lupus (6, 9%), UCTD (2,3%), Sjogren and fibromyalgia (1, 1.5%).
Results: All patients were given recommendations on COVID-19 vaccine administration. Therapy was remodeled in 13 patients (in particular in 5 patients with anemia intravenous iron infusion was scheduled; 1 started immunosuppressant therapy for proteinuria, 4 increased methotrexate for disease activity, 2 discontinued Methotrexate for adverse events (hypertransaminasemia), 1 suspended OH-chloroquine due to retinal accumulation; 2 biologic-naive patients, after a three-month of waiting due to inability to come to the hospital, started the biologic drug; 22 patients received a renewal of the therapeutic plan; 25 patients had a regular six-month follow up; 2 ticket exemption for illness; 13 consultations and/or laboratory tests (1 pneumological consultation, 1 ophthalmological consultation, 1 request for sacro-iliac MRI, 3 nailfold videocapillaroscopies, 3 FKT, 1 musculotendinous ultrasound, 1 antibodies for celiac disease, 2 antibodies anti Sars-CoV-2).
Conclusion: Telemedicine is becoming more prevalent. We report the successful use of this service in evaluation and management of rheumatic diseases in a period with limited access to rheumatologic care. We have shown that patients can be seen, evaluated, and successfully treated with a variety of medications, including biologic agents, and evaluated for both chronic inflammatory arthropaties and connective tissue diseases.
REFERENCES:
[1] Rheumatology Care Using Telemedicine Michael M. Rezaian; Telemedicine and e-Health, 2020.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2719

AB0906-HPR BENEFIT OF A NURSE-LED PROGRAM OF CARE FOR MANAGEMENT OF PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS: SYSTEMATIC LITERATURE REVIEW

P. Lois[1], L. Lopez Pedraza[1], G. Candelas[2], C. Lajas[2], M. Rodero[2], T. Mulero López[2], L. León[1], B. Fernandez[1], L. Rodriguez Rodriguez[1], L. Abasolo[1]on behalf of Departamento de Investigación de la Unidad de Gestión Clínica de Reumatología del Hospital Clínico San Carlos. *[1]Hospital Clínico San Carlos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Reumatología, Madrid, Spain*; *[2]Hospital Clínico San Carlos, Reumatología, Madrid, Spain*

Background: Nowadays, many countries experience an urgent demand for rheumatologists and greater cost-effectiveness. Thus, different alternatives to conventional outpatient physician-led follow-up have been investigated. The alternative of community-based service delivery systems is intended to meet emerging needs, reducing the costs of hospital care and morbidity. In patients with long-term conditions, such as Rheumatoid Arthritis (RA), nurses are seen as essential in the delivery of promotion in self-care and decision-making, favoring the empowerment of patients.
Objectives: To systematically investigate if the nurse led-care management (NLCM) education programs are beneficial in patients with RA.
Methods: This is a systematic literature research publication on the following bibliographic databases: Medline, Embase and the Cochrane Central register of Controlled Trials from the beginning until 2019.
Results: From a yield of 116 studies, 44 were included in the review. After quality assessment and exclusion of the lowest-ranked studies, 19 studies were analyzed. Outcomes were organized into six themes (1) disease activity; (2) adherence; (3)satisfaction; (4)treatment compliance, (5) depression and (6)quality of life. All studies had significant results in at least one of the outcomes.
Conclusion: According to our results, we can conclude that, clinicians could benefit from support conducted by nurse in the management of these patients in tasks such as metrology clinic, participation in enforcement, self-administration, the correct dosage and side effects of treatments, and link the patient and other professionals or entities. It would therefore be advisable to conduct further studies to draw more accurate and reliable conclusions in this context.
REFERENCES:
[1] Bech B, Primdahl J, Van Tubergen A, et al. 2018 update of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. *Ann Rheum Dis* 2020; 79: 61–68.
[2] Uthman I, Almoallim H, Buckley CD, et al. Nurse-led care for the management of rheumatoid arthritis: a review of the global literature and proposed strategies for implementation in Africa and the Middle East. *Rheumatology International* 2020; 1: 3.
[3] Garner S, Lopatina E, Rankin JA, et al. Nurse-led care for patients with rheumatoid arthritis: A systematic review of the effect on quality of care. *J Rheumatol* 2017; 44: 757–765.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3580

AB0907-HPR UNEXPECTED DIFFERENCE IN ACCEPTANCE OF TELECONSULTATION BETWEEN PATIENTS WITH LUPUS AND RHEUMATOID ARTHRITIS WHO UNDERWENT TO A DEVELOPED AND IMPLEMENTED TELEMEDICINE INNOVATIVE PROGRAM AFTER THE DECLARATION OF QUARANTINE DUE TO THE COVID-19 PANDEMIC IN COLOMBIA

S. M. Hernández-Zambrano[1], R. A. Castiblanco-Montañez[1], J. Chavez-Chavez[2], D. P. Rivera-Triana[2], A. Aza[3], L. Villarreal[3], M. Martinez[4], A. Rojas-Villarraga[2], P. Santos-Moreno[5]. *[1]Fundacion Universitaria de Ciencias de la Salud - FUCS, Nurse Department, Bogota, Colombia*; *[2]Fundacion Universitaria de Ciencias de la Salud - FUCS, Research Division, Bogota, Colombia*; *[3]Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, Administration, Bogota, Colombia*; *[4]Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, General Medicine, Bogota, Colombia*; *[5]Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, Rheumatology, Bogota, Colombia*

Background: The Covid-19 pandemic has generated restrictions in the mobility of people, affecting the face-to-face care of patients with chronic diseases, including autoimmune. The health emergency has created the need to establish follow-up alternatives, giving rise to telemedicine.
Objectives: To evaluate the level of attendance to teleconsultation and the face-to-face usual care in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) who underwent to a developed innovative telemedicine program after the declaration of quarantine due to the Covid-19 pandemic.
Methods: The present cross-sectional descriptive study reports retrospective data collected from patients with RA and SLE from March to June, 2020;. Since the beginning of March 2020 when Covid-19 was declared in Colombia as a health emergency establishing specific standards for outpatient care, our center has made the necessary legal and technical adjustments **to develop an innovative telemedicine service** to prevent the epidemiological risk. To all contacted patients were offered the option of teleconsultation or face-to-face consultation; a standardized protocol was set with clinimetry measures evaluated in both groups. Continuous variables were described using mean and standard deviation, and categorical variables were described using numbers and percentages. We performed chi-square tests of independence to determine differences between teleconsulting and conventional face-to-face consultation.
Results: A total of 5745 RA patients were followed-up, 5292 (92.1%) by teleconsulting and 453 (7.9%) by conventional face-to-face consultation; among the group of SLE patients, a total of 646 were assessed, of which there were 386 (60%) by teleconsultation and 260 (40%) by face-to-face consultation; this highlights an important difference in the level of acceptance of the teleconsultation

between patients with RA and SLE, being much lower in patients with SLE (*p value*< 0.0001). Regarding gender differences, in men, there were 33 (12.7%) SLE and 89 (19.6%) RA face-to-face consultations, while in women there were 227 (87.3%) SLE and 364 (80.4%) RA in a face-to-face consultation. Regarding patients who were attended through telemedicine, 45 (11.7%) SLE and 966 (18.3%) RA were men, while 341 (88.3%) SLE and 4326 (81.7%) RA were women; that means, in the RA cohort, a greater number of men prefer the face-to-face consultation than in the SLE cohort (*p value*< 0.0185). 10 RA patients were diagnosed with the Covid-19 in teleconsultation; in all cases, close contact with infected relatives was verified as the probable cause.

Table 1. Differences by gender in the level of teleconsultation acceptance and face-to-face assistance in patients with SLE and RA

RA Patients					
Gender		Teleconsulting (%[a])		Face-to-face consultation (%[a])	
Male	**1055**	**966**	**91,57%**	**89**	**8,43%**
Female	**4690**	**4326**	**92,23%**	**364**	**7,77%**
SLE Patients					
Gender		**Teleconsulting (%[a])**		**Face-to-face consultation (%[a])**	
Male	**78**	**45**	**57,69%**	**33**	**42,31%**
Female	**568**	**341**	**60,03%**	**227**	**39,97%**

[a] Total percentage of patients by gender. RA: Rheumatoid arthritis; SLE: Systemic lupus erythematosus.

Conclusion: Telemedicine may provide a viable option for the follow-up of patients with rheumatological diseases even beyond the pandemic. But unexpectedly, data showed an important difference in the acceptance of teleconsultation between patients with RA and SLE, being much higher in older and/or male patients with RA compared to patients with SLE; however, further studies are needed to support this conclusion.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3899

AB0908-HPR SIGNED, SEALED, DELIVERED: PHARMACISTS ACHIEVING BETTER CARE CLOSER TO HOME IN RHEUMATOLOGY HIGH COST DRUG MANAGEMENT DURING THE COVID-19 PANDEMIC

S. Gohil[1]. [1]*University Hospitals of Coventry and Warwickshire NHS Trust, Pharmacy, Coventry, United Kingdom*

Background: The Pharmacy High Cost Drug (HCD) and Homecare (HC) team, based at a large acute teaching hospital consists of a range of skilled pharmacists, technicians and administrative staff. The team act as a HCD liaison between the hospital and commissioners, working closely with an expanding variety of specialist clinical teams to manage prescription processing for the following patient groups; HC: 2238; Hospital FP10: 1060; Outsourced Subsidiary Pharmacy Model: 41. HCD management, particularly immunosuppressive biologic therapies for complex rheumatology conditions such as rheumatoid arthritis, has been challenging during the Covid-19 pandemic. The inelasticity in demand for better care closer to home and a functional Integrated Care Records system has intensified, as many patients are now shielding/self-isolating at home.[1] Frugal innovations have been key during this time – achieving value and simplicity in service re-design to deliver better patient care.

Objectives: This review explores the support provided by the Pharmacy HCD and HC team to the rheumatology service since March 2020 to aid in service improvements during the pandemic.

Methods: The Pharmacy HCD and HC team reviewed existing practice to better respond to the service changes required during the pandemic in regard to the following areas; identifying patients for Covid-19 shielding; responding to changes in HC service provision; communication with commissioners; remote staff working; reviewing HCD formulations and administration routes; changes in commissioning arrangements.

Results: i) Rapid development of patient datasets following identification of 1,623 immunosuppressive drug entries in line with BSR Covid-19 guidance (first published in March 2020), thus enabling social distancing/shielding guidance to be issued to patients via letters/virtual platforms.[2] ii) Swift re-routing of urgent new biologic HC registrants to a new hospital pharmacy home delivery provision when certain HC providers temporarily imposed restrictions on intake of new registrants. This hospital initiative was further enhanced to a hub and spoke model enabling patients to have easy access to their medications from their nominated local community pharmacy branch. iii) Providing assurance to commissioners that clinical follow up reviews could continue virtually, blood samples could be taken at an external hub and blueteq documentation would be completed covering NICE technology appraisal (TA) criteria. iv) A successful pilot utilising the lean PDSA (Plan, Do, Study, Act) quality improvement methodology, to enable remote working pharmacists and technicians to process HC prescriptions remotely in the absence of an electronic prescribing and medicines administration system. v) Reviewing potential plans to switch certain hospital day-case intravenous biosimilar infusions such as infliximab to subcutaneous administration via HC. vi) Business contingency development plans to protect fragile medication supply chains. vii) Clarifying implications for changes in contracting and payment arrangements announced by NHS England and NHS Improvement due to the pandemic.[3]

Conclusion: In summary, the role of the HCD Pharmacists during the pandemic in supporting rheumatology patients and the multidisciplinary team has been fundamental; ensuring signed prescriptions are securely processed to safely deliver medication to those in need.

REFERENCES:

[1] NHS. The NHS long term plan. 2019. [Online].
[2] British Society for Rheumatology (2020) Covid-19 - Identifying patients for shielding in England. [Online].
[3] NHS. Revised arrangements for NHS contracting and payment during the COVID-19 pandemic. 2020. [Online].

Acknowledgements: Mark Easter, UHCW and Interim Integrated Care System Chief Pharmacist, Hardeep Bagga, Deputy Chief Pharmacist, UHCW Pharmacy Homecare Team and UHCW Specialist Rheumatology Clinical Team.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3944

AB0909-HPR COVID 19 CRISIS: RAPID DEVELOPMENT OF REMOTE RHEUMATOLOGY MEDICATION CLINICS

R. Penford[1], E. Wren[1], K. Mackay[1]. [1]*Torbay Hospital, Rheumatology, Torquay, United Kingdom*

Background: We used to initiate DMARD(s) and Biologic therapies via nurse-led shared medical appointments (Group clinics) and could see up to 30 patients per week, with a maximum of 6 patients per group. We did this to start patients on their medications efficiently and safely and to manage the increase in workload.

However, with the onset of the COVID 19 pandemic, we had to stop these clinics immediately, but, we did not have capacity to start everyone on their medications in a timely manner by telephone. Telephoning each individual took > 9 hours per week, whereas previously it took 3-4 haours.

Objectives: We wanted to start patients on their all rheumatology medications safely and efficiently (within 10 days).

Methods: By April 2202, we had organised the filming of 10 short healthcare videos to give patients all the information they required to start a range of DMARDs and biologics.

We developed a new protocol (fig 1); patients are asked to view the relevant video, contact our department to confirm they understand the safety monitoring, risks, potential side effects, dose increases etc. As soon as they confirm by email they are happy to start treatment, a prescription is generated and emailed to the hospital outpatient pharmacy, where it is dispensed and delivered to the patient's home. We send a follow up reminder letter about blood test monitoring etc (copy to GP) and a 'shared care agreement' to GP. They are given the option to have a telephone clinic appointment with a specialist nurse if required.

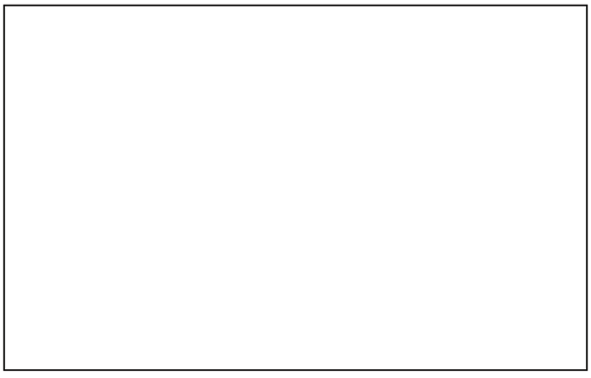


Figure 1.

Results: Of those requiring DMARDs, 62% reviewed the video, completed the checklist and confirmed by email they were happy to start treatment, within 24-hours. 88% had completed within 7 days.

Over half the patients (56%) were starting DMARDs for the first time, of those 8% requested a telephone consultation to discuss treatment further with the Rheumatology nurses. Of the 44% of patients already taking a DMARD and due to start a second medication 24% required a telephone clinic appointment.
As this is a new service, we asked for feedback, receiving replies from 34%, all scoring between 9/10 and 10/10.
We have released > 7 hours of specialist nurse time for telephone/helpline clinics.
Conclusion: The development of digital / remote medication clinics has been a success and we will continue with this approach. We have limited face-to-face appointments, started patients on rheumatology medications more quickly and efficiently than previously (but maintained safety), allowed the nursing staff time to spend more time working in our telephone clinics and have had excellent patient feedback. Although, we are aware, this is at a cost of no peer-to-peer interaction, which has been of value in the past.
Disclosure of Interests: Rian Penford: None declared, Elaine Wren: None declared, Kirsten Mackay Speakers bureau: I have been paid as a speaker for Roche within the last 12 months, Consultant of: I have worked as a paid consultant for Novartis, Janssen and Lilly within the last 12 moths, Grant/research support from: Novartis have assisted in the development of our Rheumatology App - Connect Plus - developed for rheumatology patients attending our department.
DOI: 10.1136/annrheumdis-2021-eular.4029

HPR Professional education, training and competencies

AB0910-HPR LEVELS OF DEPRESSION AND ANXIETY DURING COVID-19 PANDEMIC: AT WHAT DEGREE ARE HEALTH CARE WORKERS AFFECTED IN TUNISIA?

K. Ben Abdelghani[1], O. Hamdi[1], S. Miladi[1], M. Sellami[1], K. Ouenniche[1], L. Souabni[1], S. Kassab[1], S. Chekili[1], A. Fazaa[1], A. Laatar[1]. [1]*Mongi Slim Hospital, Rheumatology, Tunisia, Tunisia*

Background: Since December 2019, a novel pneumonia caused by coronavirus-19 (COVID-19) has been spreading internationally. Facing this critical pandemic, health care workers who are involved in treating these patients are at risk of developing psychological distress.
Objectives: To evaluate mental health outcomes among health care workers treating patients exposed to COVID-19.
Methods: This cross-sectional study collected demographic data and mental health measurements from health workers in different hospitals using an online questionnaire. Participants were divided in two groups: G1 included participants working in a COVID-19 unit and G2 included those who worked in a normal ward. Participants were asked to complete the 9-item Patient Health Questionnaire (PHQ-9) and the 7-item Generalized Anxiety Disorder scale (GAD-7). The total scores of these measurement tools were interpreted as follows: PHQ-9 normal (0-4), mild (5-9), moderate (10-14) and severe (15-21) depression; GAD-7 normal (0-4), mild (5-9), moderate (10-14) and severe (15-21) anxiety. We compared the two groups in terms of psychological distress using a Chi-square test.
Results: A total of 155 individuals with a mean age of 31.3 ± 25 years [26-45] and a sex-ratio of 0.3 completed the online questionnaire. Seventy-two participants (46%) worked in a COVID-unit. The mean number of nightshifts per month in the COVID-unit was 9.5 in G1 and 1.3 in G2 respectively. The mean number of work hours per day in the COVID unit was 5 hours in G1, and 0 in G2. G2 participants worked in COVID-units during nightshifts only. An increase in workload compared to the pre-epidemic was noted only in G1. Depression and anxiety scores were higher among participants of G1 compared to G2 (Table 1).

Table 1. Comparison of the participants according to the PHQ-9 and GAD-7 scores:

Score	G1	G2	p
Mild depression	33%	12%	0.001
Moderate depression	14%	9%	0.000
Severe depression	7%	0.9%	0.002
Mild anxiety	29%	17%	0.005
Moderate anxiety	18%	7.3%	0.002
Severe anxiety	8.4%	2.1%	0.001

G: Group

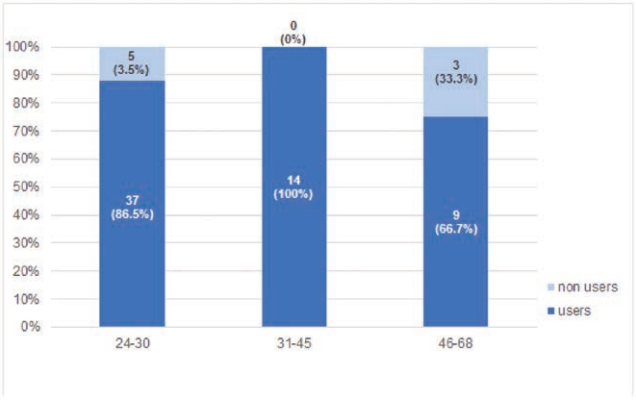
The need for psychological support was more frequent in G1 compared to G2 (38% vs 9%; p=0.005). Participants of G1 were diagnosed with depression (9 cases), anxiety (9 cases) and burn-out (3 cases). In G2, 4 participants were diagnosed with anxiety. The prescribed treatments were: antidepressants (5 cases), anxiolytic (10 cases), and psychotherapy (12 cases).
Conclusion: Individuals experience varying levels of distress during pandemics. In our study, health care workers in the frontline of COVID-units experienced high levels of anxiety and depression. Thus, necessary measures should be attached to psychological support strategies for health care workers.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.789

AB0911-HPR ROLE OF MOBILE APPLICATIONS IN RHEUMATOLOGY CARE: A MULTICENTRIC SURVEY

R. Bixio[1], A. Biglia[2], G. Virelli[1], A. Giollo[1], C. Montecucco[2], M. Rossini[1]. [1]*Università degli studi di Verona, Rheumatology, Verona, Italy*; [2]*Università degli studi di Pavia, Rheumatology, Pavia, Italy*

Background: Although mobile health applications (apps) are becoming increasingly popular across several medical specialties, no data are available in rheumatology. The aim of this study is to investigate whether apps are routinely used by rheumatologists.
Objectives: In our study we aim assess real-life use of mobile applications in rheumatology clinical activity and to evaluate mobile apps role in rheumatology training, in particular for residents, and clinical activity.
Methods: We invited a non-selected sample of rheumatologists (consultants, residents and medical students committed to begin rheumatology residency) to participate in an anonymous web-based survey. This survey investigated mobile application use in rheumatology care and issues and concerns about mobile device use in rheumatology.
Results: Sixty participants completed the survey (40% consultants, 48.3% residents, 11.7% students). 52/60 (86.7%) declared to use mobile apps during their work. More than 50% used apps at least once a day. Apps were mostly used for calculating clinical disease activity scores for chronic inflammatory arthritides. Most rheumatology residents stated that these apps could be a useful tool in medical training. However, using a smartphone during a clinical examination was deemed to be inappropriate by 26/60 (43.3%).
Conclusion: Mobile apps as clinical tools are widespread among rheumatologists.
REFERENCES:

[1] Newzoo Global Mobile Market Report 2019 | Light Version [Internet]. Newzoo. [cited 2021 Jan 23]. Available from: https://newzoo.com/insights/trend-reports/newzoo-global-mobile-market-report-2019-light-version/.
[2]eHealth WGO for. mHealth: new horizons for health through mobile technologies: second global survey on eHealth [Internet]. World Health Organization; 2011 [cited 2021 Jan 4]. Available from: https://apps.who.int/iris/handle/10665/44607.
[3] Grainger R, Townsley H, White B, Langlotz T, Taylor WJ. Apps for People With Rheumatoid Arthritis to Monitor Their Disease Activity: A Review of Apps for Best Practice and Quality. JMIR MHealth UHealth. 2017;5:e7.
[4]Salaffi F, Farah S, Di Carlo M. Smartphone APPlications in the clinical care and management of Rheumatic Diseases. Acta Bio Medica Atenei Parm. 2018;89:7–26.
[5] Maassen O, Fritsch S, Gantner J, Deffge S, Kunze J, Marx G, et al. Future Mobile Device Usage, Requirements, and Expectations of Physicians in German University Hospitals: Web-Based Survey. J Med Internet Res [Internet]. 2020 [cited 2021 Jan 23];22. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7781804/.
[6]Solomon DH, Rudin RS. Digital health technologies: opportunities and challenges in rheumatology. Nat Rev Rheumatol. Nature Publishing Group; 2020;16:525–35.
[7] Adami G, Giollo A, Rossini M, Orsolini G, Benini C, Viapiana O, et al. Different fracture risk profile in patients treated with anti-osteoporotic drugs in real-life. Reumatismo. 2020;72:71–4.
[8] Maurits M, Yuminaga H, Huizinga T, Knevel R. Mobile health applications in rheumatology: Could they improve our care and research? Int J Clin Rheumatol. Open Access Journals; 2019;14:44.



Acknowledgements: We thank prof. Punzi for helping to spread the survey among Rete Reumatologica Veneta

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3545

HPR Interdisciplinary research

AB0912-HPR AMIGOS DE FIBRO (FIBRO FRIENDS): EDUCATIONAL PROGRAM TO PROMOTE THE HEALTH OF PEOPLE WITH FIBROMYALGIA IN BRAZIL

M. Antunes[1], A. Schmitt[1], A. Pasqual Marques[1]. [1]*University of Sao Paulo, Department of Physiotherapy, Speech Therapy and Occupational Therapy, São Paulo - SP, Brazil*

Background: Health education is pointed out as the front line in non-pharmacological approaches in fibromyalgia.
Objectives: To develop an interdisciplinary educational program to promote the health of individuals with fibromyalgia in Brazil.
Methods: This is a qualitative study, through a focus group, carried out in a Basic Health Unit in the city of São Paulo, SP. The guiding questions were about the needs and demands exposed by patients with fibromyalgia and health professionals who work in primary health care. 12 individuals with fibromyalgia and 10 health professionals participated. The data were analyzed using the content analysis method proposed by Bardin, specifically the thematic content analysis.
Results: Amigos de Fibro (Fibro Friends) should be conducted through lectures, dynamics and conversation circles. The educational program must include 15 meetings with weekly frequency. The meetings are: 1st to present the program and socialization activities. 2nd: Doctor presents the concepts of fibromyalgia. 3rd: Nurse informs about practices and environments that favor self-care. 4th: Social Worker shows the importance of support. 5th: Physiotherapist shows the main body practices and physical activity. 6th: Nutritionist presents an adequate and healthy diet. 7: Psychologist shows mental health practices. 8th: Pharmacist informs about medicines. 9, 11 and 13: participants perform activities at home. 10: Naturologist presents integrative and complementary practices. 12th: Occupational Therapist encourages methods to save energy. Day 14: Speech therapist helps in the quality of sleep. 15: closing activity.
Conclusion: Amigos de Fibro is a program that presents interdisciplinary educational information for individuals with fibromyalgia, being considered a trend of care for the future. The next step is to conduct a clinical trial to verify the effect of this intervention and then implement it in the health service in Brazil. Fibro Friends was created from the conjunct action of patients and healthcare professionals, it can be an effective educational tool to be implemented at primary health attention centers, promoting the self-care, life quality and the promotion of health in individuals with Fibromyalgia. Fibro Friends is an excellent tool for patient education and counseling in Brazil.
REFERENCES:

[1] Antunes M, Ferreira A, Oliveira D, Júnior JN, Bertolini S, Marques AP. There is association between the level of physical activity and quality of life of women with fibromyalgia?. Annals of rheumatic diseases. 2019;78(2)650-1. http://dx.doi.org/10.1136/annrheumdis-2019-eular.2835.
[2] García-Ríos MC, Navarro-Ledesma S, Tapia-Haro RM, Toledano-Moreno S, Casas-Barragán A, Correa-Rodríguez M et al. Effectiveness of health education in patients with fibromyalgia: a systematic review. European Journal of Physical and Rehabilitation Medicine. 2019;55(2):301-13. https://doi.org/10.23736/S1973-9087.19.05524-2.
[3] Oliveira DV, Ferreira AAM, Oliveira DCD, Leme DEDC, Antunes MD, Nascimento Júnior JRAD. Association of the practice of physical activity and of health status on the quality of life of women with fibromyalgia. Journal of Physical Education. 2019;30(1): e3027. https://doi.org/10.4025/jphyseduc.v30i1.3027.
[4] Stuifbergen AK, Blozis SA, Becker H, Phillips L, Timmerman G, Kullberg V, et al. A randomized controlled trial of a wellness intervention for women with fibromyalgia syndrome. Clinical Rehabilitation. 2010;24(4):305-18. https://doi.org/10.1177/0269215509343247.

Acknowledgements: This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2598

Patient information and education

AB0913-PARE METHOTREXATE FOR RHEUMATOID ARTHRITIS: PATIENT PERSPECTIVES ON MONITORING IN PRIMARY CARE

R. de Barros Lopes[1], D. Murphy[1], F. Mclennan Battleday[2]. [1]*Royal Devon and Exeter NHS Foundation Trust, Rheumatology, Exeter, United Kingdom*; [2]*Royal Devon and Exeter NHS Foundation Trust, Medicine, Exeter, United Kingdom*

Background: Monotherapy with methotrexate (MTX) is one first-line option for newly diagnosed Rheumatoid Arthritis (RA)[1]. Although treatment is usually commenced by a specialist, repeat prescribing and monitoring responsibilities often lie with primary care. While inadequate monitoring is a safety concern, unnecessary duplication of monitoring invariably has cost implications for General Practice (GP).
Objectives: To ensure that patients in one South-West GP practice who are taking oral MTX for RA are appropriately monitored in line with current guidance from the British Society of Rheumatology (BSR). Current guidance recommends that once a stable MTX dose is maintained for six weeks, followed by monthly bloods for the next three months, that at least twelve weekly blood monitoring is sufficient from then on[1].
Methods: A randomised sample of 50 patients registered in one South-West GP practice that were taking a stable dose oral MTX for RA; for at least 6 months; was collected. The length of time between the patient's two most recent blood tests was recorded. A random selection of ten patients with more frequent monitoring than BSR guidance suggest were asked a series of questions to determine patient perspectives on reasons for monitoring frequency.
Results: 58% of patients had more frequent monitoring bloods than current BSR guidelines recommend. Within this group, the mode frequency of monitoring was four weeks, in line with the previous National guidance which was superseded in 2017[2].The most common themes in patient's perspectives on monitoring frequency were:
a.Previous abnormal blood results requiring close monitoring
b.Multiple disease modifying anti-rheumatoid drug (DMARD) regimes that included MTX
c.Patient preference
d.Unclear or unknown reason
The purported increased monitoring for multiple DMARD regimes were not in line with current national guidelines[1].
Conclusion: This audit demonstrates that over half of patients taking MTX for RA in one GP practice are having more frequent blood monitoring than BSR guidance suggests is necessary. Furthermore, it demonstrates that patient's understanding of their perceived need for increased monitoring is largely inaccurate or unclear to them. There is a clear deficit in patient education surrounding monitoring frequency which must be addressed in order to empower patients, as well as reducing unnecessary duplication of blood tests. As a result of this audit, patient education on MTX monitoring frequency was formally introduced as part of the RA annual patient review. An information sheet with these monitoring requirements was produced to aid practitioners in the education process.
REFERENCES:

[1] J, Ledingham et al | BSR/ BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs | Rheumatology 2017; 56: 865-8.
[2] Chakravarty K etc al | BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists | Rheumatology 2008; 47: 924–5.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3

AB0914-PARE INFORMATION PREFERENCES ABOUT TREATMENT OPTIONS IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS: A DELPHI CONSENSUS STUDY

J. Spierings[1,2], H. Nienhuis[3], E. Van Lieshout[1], J. M. Van Laar[1], A. Pieterse[4]. [1]*University Medical Centre Utrecht, Department of Rheumatology and Clinical Immunology, Utrecht, Netherlands*; [2]*Royal Free Hospital and University College London, Centre for Rheumatology and Connective Tissue Diseases and University College Medical School, London, United Kingdom*; [3]*University Medical Centre Utrecht, Department of Internal Medicine, Utrecht, Netherlands*; [4]*Leiden University Medical Centre, Department of Biomedical Data Sciences, Leiden, Netherlands*

Background: Diffuse cutaneous systemic sclerosis (dcSSc) has a high impact on quality of life and is associated with increased mortality. Several treatment options are available in dcSSc, including immunosuppressives, chemotherapy and hematopoietic stem cell transplantation. Shared decision making is key in choosing the appropriate treatment strategy. In earlier studies however, patients reported that the lack of accessible and reliable patient information about treatment options complicates decision making. In order to provide information that meets the needs of patients and addresses relevant benefits and harms, more insight in the preferences of patients is needed.
Objectives: The aim of this study was to identify and prioritize aspects that should be addressed when informing patients with dcSSc about treatment options, from a patient's perspective.
Methods: A three-round Delphi study was conducted with a panel of patients with dcSSc. The first questionnaire was based on a systematic literature search regarding benefits and harms of the four main treatments in dcSSc: methotrexate,

mycophenolate mofetil, cyclophosphamide, and stem cell transplantation. In the first round, patients were asked to indicate which information on the benefits and harms is essential for making a treatment decision; they could also add new items. In the second and third rounds, patients were asked to prioritize the items. After the third round, a live, online panel discussion was held in order to reach consensus. Consensus was defined as ≥75% agreement among panel members.

Results: Of the 36 patients invited, 67% (n=24) completed the first, 69% (n=25) the second and 75% (n=27) the third round. In the third round, median age of participants was 51 years (IQR 18), median disease duration was 4 years (IQR 5), 52% was female. Most patients had completed either an intermediate education level (59%) or high level of education (30%). Patients were or had been treated with mycophenolate mofetil (67%), methotrexate (44%), cyclophosphamide (41%), autologous stem cell transplantation (26%), rituximab (4%). Seven percent of patients were treatment-naïve. After the third round, eight patients joined the online panel discussion to reach final consensus. The panel reached consensus on seven benefits (prolonged progression-free survival, improved quality of life, improved daily functioning, improved pulmonary function, improved skin thickness, improved mobility and reduced fatigue) and four adverse events (treatment-related mortality, viral infections, cardiac damage, increased risk of cancer) as key themes for the decision making process (Table 1).

Conclusion: This study identified essential aspects of the four main treatment options for dcSSc. Our results can be used to develop effective patient information.

Table 1. Agreement on benefits and harms that should be addressed

Benefits	Agreement	Harms	Agreement
Improved pulmonary function	100%	Viral infections	88%
Improved skin thickness	100%	Cardiac damage	88%
Improved mobility	100%	Increased risk of cancer	88%
Prolonged progression-free survival	95%*	Treatment-related mortality	79%*
Improved quality of life	77%*	Flare or relapse of disease	63%
Improved daily functioning	77%*	Temporary increase in fatigue	25%
Reduced fatigue	75%	Temporary negative impact on social activities	25%
Improved hand function	25%	Nausea	25%
Improved mood	25%	Other autoimmune disease	13%
Improved cardiac function	13%	Hormonal imbalance	13%
Improved oesophageal function	7%	Concentration difficulty	13%
		Diarrhea	13%
		Erectile dysfunction	13%
		Depression	13%
		Infertility	13%
		Hair loss	13%

*Items on which consensus was reached in round 3

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.396

AB0915-PARE DEVELOPMENT AND USABILITY OF A WEB-BASED PATIENT-TAILORED TOOL TO SUPPORT ADHERENCE TO URATE-LOWERING THERAPY IN GOUT PATIENTS

R. te Kampe[1,2,3], A. Boonen[1,3], T. Jansen[2], J. M. Elling[3,4], M. Flendrie[5], Y. Van Eijk-Hustings[1], M. Janssen[2], C. Van Durme[1], H. De Vries[3,4]. *[1]Maastricht University Medical Center, Internal Medicine, Maastricht, Netherlands*; *[2]VieCuri Medical Center, Rheumatology, Venlo, Netherlands*; *[3]Maastricht University, Care and Public Health Research Institute (CAPHRI), Maastricht, Netherlands*; *[4]Maastricht University, Health Promotion, Maastricht, Netherlands*; *[5]Radboud University Nijmegen Medical Centre, Rheumatology, Nijmegen, Netherlands*

Background: Adherence to prescribed urate-lowering therapy (ULT) among gout patients is considered to be among the poorest of all chronic conditions. eHealth programs can be a possible opportunity to foster ULT adherence.

Objectives: This study describes the development and usability evaluation of a web-based tool to support ULT adherence among gout patients, specifically designed for a complement to usual care.

Methods: The Integrated Change (I-Change) model was used as theoretical basis for the development. The model combines various socio-cognitive theories and differentiates between three phases: a pre-motivational, a motivational, and a post-motivational phase. In practices, the I-Change gout tool contains three sessions, following the three phases of the I-Change model. Patients receive tailored feedback based on their answers in the form of animated videos and text messages after each session, and are prompted to set specific goals and action plans for their ULT adherence. The content and development of the I-Change gout tool was determined along an iterative process within a steering group of clinicians and researchers, supported by patient interviews and gout specific literature related to key aspects of medication adherence behavior. A cross-sectional mixed methods design was used to test usability of the support tool consisting of a think aloud method and a usability questionnaire.

Results: The steering group decided on the content of the three sessions of the I-Change gout tool. Depending on the intention to change ULT adherence behavior patients were navigated through the I-Change gout tool, patients with a low intention go through all 3 sessions and patients with a high intention go through the pre- and post-motivational session (figure 1). In total, the I-Change gout tool contains three sessions with 80 questions, 66 tailored textual feedback messages, and 40 tailored animated videos.

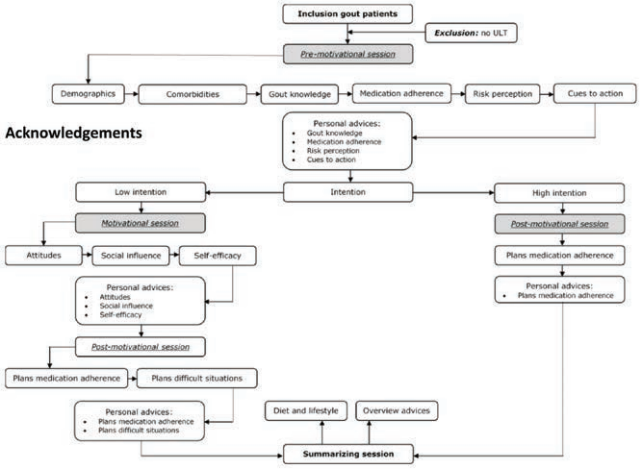


Figure 1. Flowchart of the computer-tailored I-Change gout tool for urate-lowering therapy adherence.

Twenty gout patients and seven healthcare professionals participated in the usability tests. The program end score rating for the gout tool was on average 8.4±0.9 (range 6-10) for patients and 7.7±1.0 (range 6-9) for healthcare professionals. Furthermore, participants reported a high intention to use and/or recommend the program in the future. Yet, participants identified some issues for further improvement of the systems user-friendliness by addressing barriers (e.g. more explicitly navigation) and weaknesses (e.g. technical and health literacy). The I-Change gout tool was updated according suggestions of improvements of the participants.

Conclusion: This study provides initial support for the usability by patients and healthcare professionals of a ULT adherence I-Change gout tool. Further studies need to be conducted to assess its efficacy and (cost-) effectiveness in daily practice.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1500

AB0916-PARE KNOWLEDGE OF DISEASE, DIAGNOSIS, ADHERENCE AND IMPACT OF RESEARCH IN PATIENTS WITH INFLAMMATORY ARTHRITIS

M. Canavan[1,2], V. Marzaioli[1,2], A. Donnelly[3], S. Wade[1,2], A. Fraser[4], T. O'sullivan[3], S. Harney[5], A. Ireland[6], D. Veale[2], U. Fearon[1,2]. *[1]Trinity College Dublin, Molecular Rheumatology, Dublin, Ireland*; *[2]St Vincent's University Hospital, Centre for Arthritis and Rheumatic Diseases, Dublin, Ireland*; *[3]Patient Advocate, Patient Advocate, Dublin, Ireland*; *[4]University of Limerick, UCL, Department of Rheumatology, Limerick, Ireland*; *[5]Cork University Hospital, UCC, Department of Rheumatology, Cork, Ireland*; *[6]Clanwilliam Square, Grand Canal Dock, Dublin, Ireland*

Background: The diagnosis and treatment of inflammatory arthritis has been transformed largely by the development of drugs that target specific molecules of the immune system. However, these changes have increased the complexity of the mechanisms of disease, its treatment and patients understanding. Patient education is needed in this area to facilitate decision making and to facilitate strong patient-partnerships in research.

Objectives: The aim of this study was to examine the level of understanding of inflammatory arthritis patients and the need for strong patient-partnership in research.

Methods: An online anonymous survey addressed questions about diagnosis, routine tests, medications and how they work, medication adherence, disease flare, heredity, pregnancy, and patient involvement in research.

Results: There were 1,873 respondents, 1416 of which had inflammatory arthritis (IA)-RA (65.8%) and PsA (34.2%). They were predominantly female (RA 86%,

PsA 85 %), aged 55±13 and 50±12. Less than 35% of patients had an understanding of diagnostic tests, what was measured and the implication for disease, with 75.5% also concerned about heredity. There was a high level of understanding of how specific medications treat inflammatory arthritis (72.9%). Adherence was also very high (>87%), with the main reasons for stopping medication without the advice of their clinician, 'feeling better' and 'side effects' however a significant proportion of patients (69.9%) reported a disease-flare following cessation of medication. Patients of childbearing age (69%) were also concerned that inflammatory arthritis reduced their chances of getting pregnant, with only 8% believing arthritis medications were safe to take during pregnancy. Finally, only 9% of patients had ever been asked to participate in a research study.

Conclusion: This study demonstrates a need for the development of stronger patient-partnerships with clinicians and researchers in relation to patient education and engagement with research, to create a platform where patients can have meaningful input and involvement in future research studies.

Acknowledgements: We wish to thank all the patients who contributed to this study

Disclosure of Interests: Mary Canavan: None declared, Viviana Marzaioli: None declared, Alex Donnelly: None declared, Siobhan Wade: None declared, Alexander Fraser: None declared, Tim O'Sullivan: None declared, Sinead Harney: None declared, Arthritis Ireland: None declared, Douglas Veale Speakers bureau: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Consultant of: Abbvie, Janssen, Novartis, MSD, Pfizer, UCB, Grant/research support from: Janssen, Abbvie, Pfizer, UCB, Ursula Fearon Speakers bureau: Abbvie, Grant/research support from: Janssen, Abbvie, Pfizer, UCB

DOI: 10.1136/annrheumdis-2021-eular.2085

AB0917-PARE KNOWLEDGE ON SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND ITS MANAGEMENT AMONG SLE PATIENTS ATTENDING RHEUMATOLOGY CLINIC AT NATIONAL HOSPITAL OF SRI LANKA

H. Perera[1], G. Kasthuriratna2. *[1]National Hospital of Sri Lanka, Rheumatology and Rehabilitation, Colombo, Sri Lanka*; *[1]National Hospital of Sri Lanka, Rheumatology and Rehabilitation, Colombo, Sri Lanka*

Background: Systemic Lupus Erythematosus (SLE) is a chronic relapsing and remitting multi-system involving autoimmune condition mainly affecting females of reproductive years. As any other chronic disease needing long term treatment and follow up, proper patient education and high level of patients' knowledge on their own diagnosis is mandatory for the optimum management. It is proven that poor patient awareness has led to poor compliance and catastrophic relapses. There were no Sri Lankan study to assess patients' knowledge on SLE and its management.

Objectives: To describe the demographic data, any exposure to patient education and to assess knowledge about their own diagnosis and its management among a group of already diagnosed patients with SLE attending rheumatology clinic in National Hospital of Sri Lanka.

Methods: A cross sectional descriptive study was carried out with convenience sampling and data were collected using interviewer administered questionnaire. All already diagnosed patients with Systemic Lupus Erythematosus attending the Rheumatology clinic during the data collection period were invited to participate in the study and total of 45 were enrolled with 100% response rate.

Results: Overall 45 participants were in the study and all were females. The mean age was 37 (±12.53) years and the average disease duration was 62 months. Considering the exposure to patient education 89.87% had at least one type of patient education and 10.1% had none. A significant proportion (84.4%) was aware about their own diagnosis and 82.2% was able to correctly mention their current medication. Overall knowledge about the disease and its management was moderate (68.7%) among this study population according to our scoring system. However, they had a poor knowledge (45%) relating to pregnancy and contraception.

Conclusion: The above study describes important demographic data, exposure to patient education and patients' knowledge about their own disease in population of Systemic Lupus Erythematosus patients attending National Hospital of Sri Lanka. Their overall knowledge regarding SLE, its management and complications were at a moderate level and awareness regarding pregnancy and contraception in a SLE patient was at a lower level. Therefore, clinicians should pay more attention in to patient education when managing conditions like SLE as it directly affect the patients' compliance and overall disease outcome.

REFERENCES:

[1] Cooper GS, Dooley MA, Treadwell EL, et al. Hormonal, environmental, and infectious risk factors for developing systemic lupus erythematosus. Arthritis Rheum 1998; 41:1714.

[2] Costenbader KH, Feskanich D, Stampfer MJ, Karlson EW. Reproductive and menopausal factors and risk of systemic lupus erythematosus in women. Arthritis Rheum 2007; 56:1251.

[3] Lahita RG. The role of sex hormones in systemic lupus erythematosus. Curr Opin Rheumatol 1999; 11:352.

[4] Hochberg MC. The incidence of systemic lupus erythematosus in Baltimore, Maryland, 1970-1977. Arthritis Rheum 1985; 28:80.

[5] Serdula MK, Rhoads GG. Frequency of systemic lupus erythematosus in different ethnic groups in Hawaii. Arthritis Rheum 1979; 22:328.

[6] Fernández M, Alarcón GS, Calvo-Alén J, et al. A multiethnic, multicenter cohort of patients with systemic lupus erythematosus (SLE) as a model for the study of ethnic disparities in SLE. Arthritis Rheum 2007; 57:576.

[7] Callahan LF, Pincus T. Associations between clinical status questionnaire scores and formal education level in persons with systemic lupus erythematosus. Arthritis Rheum 1990; 33:407.

[8] Petri M, Perez-Gutthann S, Longenecker JC, Hochberg M. Morbidity of systemic lupus erythematosus: role of race and socioeconomic status. Am J Med 1991; 91:345.

[9] Soe YM, Thant WLY, Sara Z, Nann Z, Oo PP, Kyaw PP, Lin KS, Aung KLL, Soe C. knowledge about their own disease among systemic erythematosus patients. Researchgate doi: 10.1111/1756 – 185x.13361.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2497

AB0918-PARE FAMILY PLANNING AND RMDS: A SURVEY

U. Viora[1], P. Grossi[2], F. Padovani[3], G. Mussi[4], S. Severoni[5], S. Tonolo[6], A. Verducci[7]. *[1]ANMAR Italia, Piemonte, ROMA, Italy*; *[2]ANMAR Italia, Toscana, ROMA, Italy*; *[3]ANMAR Italia, Abruzzo, ROMA, Italy*; *[4]ANMAR Italia, Liguria, ROMA, Italy*; *[5]ANMAR Italia, Lazio, ROMA, Italy*; *[6]ANMAR Italia, Veneto, ROMA, Italy*; *[7]ANMAR Italia, Umbria, ROMA, Italy*

Background: It is well known and universally aknowledged that RMDs are not related to old age, as those who are affected by these illness between 30 and 45 years old are a big number, perhaps the biggest one. Therefore, family planning and pregnancy are topics even more actual and their management is certainly one of the biggest source of distress and troubles in people affected by RMDs and their spouses.

Objectives: to define and deeply understand the problem's dimension, ANMAR made a survey according to the CAPIRE Observatory.

Methods: an pposite questionnaire was given to patients waiting for a rheumatological consultation, during 6 months in 2020.

Results: Over 300 women with an RMD fulfilled the questionnaire:
7 on 10 women are trying to become pregnant
51% of them did not notice it to their Rheumatologist.
57% of them has been already pregnant.

Conclusion: In Italy, women with RMDs are over 3.5 millions and the a lot of them are women of childbearing potential.
As therapies actually used are really effective, but may induce side effects on the reproductive system, it is absolutely needed to inform the Rheumatologist about the intent to procreate and to have suggestions about the correct chice of contracception models.
Communication between patient and Rheumatologist must be improoved, even in this important topic.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3040

AB0919-PARE WHAT DO OLD PEOPLE THINK OF THEIR RHEUMATOID ARTHRITIS TREATMENTS?

D. Khalifa[1], S. Belghali[1], M. Limam[2], N. Elamri[1], K. Baccouche[1], H. Zeglaoui[1], E. Bouajina[1]. *[1]Farhat Hached Hospital, Rheumatology, Sousse, Tunisia*; *[2]Farhat Hached Hospital, Preventive Medicine, Sousse, Tunisia*

Background: Managing chronic diseases such as rheumatoid arthritis (RA) is a challenge on a daily basis for rheumatologists and convincing our patients to properly take their medication may be difficult especially with elderly. First step comes with our patients' education and suppressing misbeliefs and misconceptions.

Objectives: To study beliefs of elderly RA patients on DMARDs and see what they really think of their treatments.

Methods: A cross-sectional study was conducted in a rheumatology clinic over a period of 4 months. Patients over the age of 65 having RA and being treated with conventional DMARDs or biologics were questionned about their medication. The belief about medicines questionnaire (BMQ) was used to assess different beliefs. It is a validated questionnaire of 18 items. Patients responded freely to each item using a Likert scale. The clinician later collected the data and 4 scores were calculated (concern (c), necessity (n), overuse and harm), thus classifying patients on 4 different groups as follows: accepting if n≥ 15 and c<15, ambivalent n≥ 15 and c≥15, indifferent if n< 15 and c <15 and skeptical if n<15 and c≥ 15.

Results: Forty elderly patients joined the study. The median of age was 66 years. They were mostly women (82.5%) with other comorbidities in 55% of the cases. The mean of DAS 28 score was 4.65± 1.77 and the mean of the VAS pain score was 5 out of 10. Only 17.5% of the patients were on remission or low disease activity. Radiological destructions were detected in 87.2% of the patients and deformities in 60% of them. Rheumatoid factor and/or citrullinated peptide antibodies were detected in 81.6% of the cases.95% of the patients were on methotrexate (MTX), 12.5% on Sulfasalazin and 12.5% on biotherapies. Corticosteroids were prescribed in 85% of the patients. Responses to the BMQ specific and general questionnaire are showed in table.1. The mean score of concern was 15.33±3.8, the mean score of harm was 13.44±2.9, the median of the necessity score was 18 and the median of the overuse score was 13.5. Analysing patients' beliefs, the majority of them were ambivalent towards their DMARDs (44.4%), 33.4% were accepting, 11.1% were skeptical and 11.1% were indifferent.

Table 1. BMQ responses

BMQ specific	Do not agree at all %	Do not agree %	Incertain %	Agree %	Agree very much %
My health at present depends on my RA medicines	5.6	22.2%	27.8	44.4	0
Having to take RA medication worries me	5.6	44.4	0	38.9	11.1
My life would be impossible without my RA medication	5.6	16.7	22.2	33.3	22.2
Without my RA medication i would be very ill	11.1	22.2	16.7	38.9	11.1
I sometimes worry about the long-term effects of my RA medication	27.8	11.1	11.1	44.4	5.6
My Ra medication is a mystery to me	5.6	33.3	5.6	50	5.6
My health in the future will depend on my RA medication	5.6	16.7	27.8	50	0
My RA medication disrupts my life	5.6	38.9	5.6	44.4	5.6
I sometimes worry about becoming too dependent to my RA medication	0	38.9	11.1	44.4	5.6
My RA medication protects me from becoming worse	0	16.7	5.6	61.1	16.7
BMQ general					
Doctors use too many medicines	0	16.7	27.8	44.4	11.1
People who take medicines should stop their treatment for a while every now and then	11.1	44.4	22.2	22.2	0
Most medicines are addictive	0	5.6	22.2	61.1	11.1
Natural remedies are safer than medicines	11.1	11.1	27.8	22.2	27.8
Medicines do more harm than good	11.1	27.8	27.8	27.8	5.6
All medicines are poisons	5.6	22.2	27.8	22.2	22.2
Doctors place too much trust on medicines	5.6	16.7	33.3	27.8	16.7
If doctors had more time with patients they would prescribe fewer medicines	0	11.1	22.2	33.3	33.3

Conclusion: Elderly RA patients should me more reassured about the safety of DMARDs and the importance of taking them and try to establish a better patient-doctor relationship.

REFERENCES:

[1] Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health* 1999; 14: 1–24.

[2] Aikens JE, Nease DE, Nau DP, et al. Adherence to Maintenance-Phase Antidepressant Medication as a Function of Patient Beliefs About Medication. *Ann Fam Med* 2005; 3: 23–30.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3274

AB0920-PARE WHAT WE LEARNED DURING COVID-19 PANDEMIC

J. Grygielska[1]. [1]*Polish Rheuma Federation 'REF', National Board, Warsaw, Poland*

Background: When the first official cases of pneumonia of unknown etiology in the city of Wuhan were reported by Chinese authorities to the World Health Organization (WHO) on 31st of December, 2019 nobody couldn't imagine that only month later new disease reached Europe and so fast change lives around the world. The first case of COVID-19 in Poland has been detected on 4th March 2020 and 16 days later Polish government introduced an epidemic state connected with new law regulations and with lockdown.

Objectives: Fast shared new coronavirus was a challenge for all. People with rheumatic and musculoskeletal diseases (RMDs) in very short time lost their sense of security. They received different information about COVID-19. One of the main information was that people with RMDs have higher risk of COVID-19. Providing real information in era of fake-news and giving of possible solutions during pandemic has become the goal of activities of patients organizations.

Methods: Lack of appropriate knowledge about new coronavirus forced different activities among entities acting for the benefit of patients. Our rheumatic patients organizations suspended group exercises and face to face meeting counting that it was only for 1-2 months. In social media from early March 2020 we support action "stay at home" like a warranty of safety. We tried to stay in contact with member organizations and in regional organizations with their members. We participated in action "Patient units us" organized by Minister for Patients Rights – during duty hours we had a chance to inform calling us people about different solutions connected with pandemic. Using our social media we inform people with RMDs about statement of EULAR and Polish Society for Rheumatology. After short break we are continuing works in Council of Patients Organization to the Minister for Patients Rights. Having contacts with RMDs patients we learn from them about their problems met in everyday lives.

Results: COVID-19 pandemic interrupted typical activities of our associations. After summer holidays we could organize group exercises and real meetings only during 2 months to new wave of coronavirus. Many members resigned from participation fear of infection. For the same reason people resigned from medical consultation and examination. Following confirmed information we could share it among our followers using websites and social media. Majority of medical consultations was remotely when physician calls to patient on time of appointed visit.

Conclusion: COVID-19 pandemic accelerated progress of e-health and of using of new technologies. On the one hand it give a challenge for people who didn't use it before to start to do it but on the other hand digital exclusion has deepened among people who never use Internet and stay alone in pandemic times. Virtual activities of associations give a chance to keep a contact with members, increase their knowledge, dispel doubts. Some changes forced by coronavirus infection are good and will stay among us like e-prescription, e-referral, internet patients account, virtual workshops and lectures. We are concerned that teleconsultations can replace medical examination in out-patient center. It can be danger for people with inflammatory arthritis. So long break in face to face meetings in associations can be a reason of lost of members especially older. Fast learning of using of new technology in medicine and in activities of associations give an opportunity for future but nothing can replace personal contact.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3304

AB0921-PARE PRACTICES AND BEHAVIORS DURING THE COVID-19 PANDEMIC IN PATIENTS WHO PARTIALLY ATTEND TO AN EDUCATIONAL PROGRAM ON RHEUMATOID ARTHRITIS. A CROSS-SECTIONAL SURVEY

F. Rodriguez[1], D. Buitrago-Garcia[2], G. Sánchez[3], P. Santos-Moreno[4]. [1]*Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, Educational Program for RA Patients UniversitAR, Bogota, Colombia*; [2]*Postgraduate Program in Clinical Epidemiology, Fundación Universitaria de Ciencias de la Salud-FUCS. Bogotá, Colombia., Epidemiology, Bogotá, Colombia*; [3]*Postgraduate Program in Clinical Epidemiology, Fundación Universitaria de Ciencias de la Salud-FUCS. Bogotá, Colombia., Epidemiology, Bogota, Colombia*; [4]*Biomab - Center for Rheumatoid Arthritis, Bogota, Colombia, Rheumatology, Bogota, Colombia*

Background: The new coronavirus disease has become a public health emergency that has not been seen for generations. Covid-19 disease leads to an extreme immune activation and cytokine response and constitutes a big risk and a challenge for patients with inflammatory conditions such as rheumatoid arthritis (RA). During the Covid-19 pandemic, rheumatologists and health-care professionals have faced many challenges to provide an adequate follow-up and treatment to RA patients; one of them, has been the establishment of lockdown for populations older than 60 years and the limitation of having face-to-face consultations, moving us to telemedicine activities. On the other hand, in our center an education program for patients with RA had been established in the second semester of 2019, which due to the epidemiological risk control measures, it was necessary to interrupt when we only had 5-6 months of a project that was planned for 2 years; it was mandatory to pause it and implement virtual education alternatives; this educational program for RA patients was also moved to virtual mode later.

Objectives: To describe possible changes in the practices and behaviors of patients with rheumatoid arthritis (RA) during the lockdown that started in March 2020 in Colombia due to the Covid-19 pandemic, who previously partially attended to an educational program on RA.

Methods: We included patients who attended previously a face-to-face educational program, that aims to teach and empower patients in all aspects related to RA. After the lockdown, the educational program had to stop abruptly while an online strategy was developed later; meanwhile the patients did not have any educational activity for 3-4 months. For this study, patients answered to a telephonic survey in July 2020; the survey included questions about their practices related to the Covid-19 pandemic, SARS-Cov-2 symptoms, adherence to rheumatoid arthritis treatment, virtual rheumatology consultations compliance and, the influence of news on their adherence.

Results: A total of 260 patients took part in the survey; mean age of the respondents was 60 years IQR (54-66), 93% were female. In July 2020 88% of patients had accessed a telemedicine-based and 12% a face-to-face rheumatology consultation; only 3.5% of patients reported having been less adherent to pharmacological therapy due to information received through media or social networks. Regarding the prevention measures taken during the pandemic, 98% reported to have stayed in their houses since the lockdown was stablished in Colombia, and have implemented or increased hand washing from one or none to more than three times per day. Also 8% of respondents lived with people who were at bigger risk of having SARS-CoV-2 (i.e. health care professionals, workers at public transportation, and supermarkets among others), the main measurement taken was to be completely separate from the person at risk to avoid contagion and maintaining hygiene measures and physical distancing (Fig 1). Only one patient was positive for SARS-CoV-2, due to a possible contagion from a relative at home and reported only flu-like symptoms without any complications. Patients highlighted the necessity to return to the educational on RA program agreeing to attend to an online modality. Patients highlighted the need for educational sessions focused on the relationship between rheumatoid arthritis, its treatment, and Covid-19.

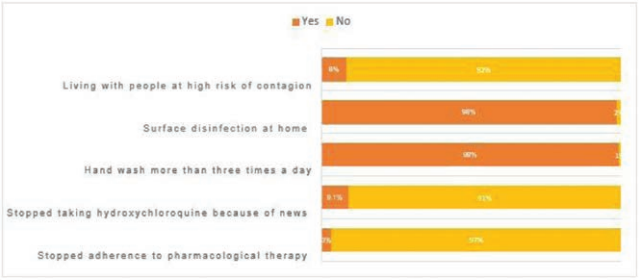


Figure 1. Behaviors, practices, and its changes due to Covid-19 pandemic

Conclusion: An educational on RA program shows to be helpful tool to maintain high adherence rates to the RA treatment despite of the new challenges associated to the pandemic and despite being incomplete due to lack of time; patient-centered education programs should continue to address the patient's concerns and beliefs about their disease and the Covid-19 issues.

Disclosure of Interests: Fernando Rodriguez: None declared, Diana Buitrago-Garcia: None declared, GUILLERMO SÁNCHEZ: None declared, Pedro Santos-Moreno Speakers bureau: Pedro Santos-Moreno has received fees for conferences from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi., Consultant of: Pedro Santos-Moreno has received fees for counseling and advisory boards from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi., Grant/research support from: Pedro Santos-Moreno has received esearch grants from: Abbvie, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi.

DOI: 10.1136/annrheumdis-2021-eular.3434

AB0922-PARE OSTEOPOROSIS AWARENESS LEVEL AS A METHOD FOR IMPROVING PRIMARY PREVENTION

S. Lezhenina[1], A. Lammert2, N. Shuvalova[3], E. Guryanova[4]. *[1]I. N. Ulianova Chuvash State University, Departament of Healthcare Management and Economics, Cheboksary, Russian Federation*; *[1]I. N. Ulianova Chuvash State University, Departament of Healthcare Management and Economics, Cheboksary, Russian Federation*; *[3]I.Ya.Yakovlev Chuvash Pedagogical State University, Department, Cheboksary, Russian Federation*; *[4]I. N. Ulianova Chuvash State University, Department internal diseases, Cheboksary, Russian Federation*

Background: Having complete information about osteoporosis is a prerequisite for preventive behavior, which determines the conscious adherence to the principles of a healthy lifestyle.

Objectives: To assess the level of awareness of osteoporosis among women.

Methods: A survey was conducted of 750 female respondents aged 15 to 55 years in the Chuvash Republic. The survey was conducted from January to December 2019. The questionnaire consisted of 30 questions. One point was awarded for each correct answer. The minimum score for passing the test was 75% correct answers. The questions addressed both general knowledge about osteoporosis and the relationship between disease onset and diet, physical activity, vitamin D, cigarette smoking, excessive alcohol consumption, and being overweight. The respondents were divided into two groups: group A (n = 375) - females from 15 to 35 years old and group B (n = 375) - females from 36 to 55 years old. Survey data was processed in Statistical Analysis Software 15.0. Statistical significance was calculated using Analysis of Variation.

Results: We obtained the following results for the Main Aspects of the survey: 1. Osteoporosis is a rare condition that occurs primarily in women (Awareness level: Group A - 47%; Group B - 67,5%; Analysis of Variation > 0,05). 2. Postmenopausal women are more at risk of osteoporosis (Awareness level: Group A - 73,5%; Group B - 70,4%; Analysis of Variation > 0,05). 3. Prevention of osteoporosis is impossible (Awareness level: Group A - 78,8%; Group B - 89%; Analysis of Variation > 0,05). 4. Vitamin D is synthesized by direct exposure to UV radiation on the skin (Awareness level: Group A - 53,1 %; Group B - 69,1%; Analysis of Variation > 0,05). 5. Effective prevention of osteoporosis are: I. Balanced diet; II. Absence of bad habits; III. Occupation with health-improving physical culture. IV. Reduction of excess body weight (Awareness level: Group A - 69,2%; Group B - 47,1%; Analysis of Variation > 0,05). 6. Increased consumption of table salt, sugar and excessive consumption of protein foods, vegetarianism negatively affects the quality of bone tissue (Awareness level: Group A - 56,7%; Group B - 70,4%; Analysis of Variation > 0,05).

Conclusion: The conducted survey shows that the level of awareness of osteoporosis and its prevention is low among women in different age groups. In some cases, it is even a cause for concern. We believe that respondents' statements that osteoporosis cannot be effectively prevented are the most important findings of our study. Starting from adolescence, women should be well aware of the main risk factors for the development of osteoporosis, the mechanisms of its development and its consequences. This knowledge will help substantiate why it is necessary to lead a healthy lifestyle, which will help to prevent the development of this disease in the future. The concept of prevention of osteoporosis should include the following recommendations for the general population: to maintain a physically active lifestyle and to spend sufficient time under the influence of sunlight, avoid smoking and drinking large amounts of alcohol, ensure that dietary calcium intake is in line with the recommended level in the area, and maintain an appropriate body weight.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3856

Building patient led organisations

AB0923-PARE WHAT IS THE IMPACT ON THE QUALITY OF LIFE (QOL) OF PEOPLE LIVING WITH SPONDYLOARTHRITIS (SPA*)?

S. Patenaude[1], W. Gerhart[2]. *[1]Canadian Spondylitis Association, Intern, Phelpston, Canada*; *[2]Canadian Spondylitis Association, Executive Director, Phelpston, Canada*

Background: SpA describes a group of chronic inflammatory arthritic diseases with common features including inflammation of the spine, eyes, skin and gastrointestinal tract. These conditions can be painful and debilitating for many. Delayed diagnosis and treatment can lead to irreversible damage to the spine and other joints. Diagnosis of these conditions can take, on average, 7 years or more. We don't know what causes SpA and there is no cure. The onset of symptoms can be in early childhood and expands throughout one's lifespan. It affects children, women and men worldwide.

Objectives: To understand how living with SpA impacts QOL (including relationships, work and day-to-day life) and what is important to patients in order to help the CSA** prioritize advocacy focus and resource development.

Methods: The CSA surveyed the community virtually from 11/19/19 to 01/21/20. The results of 838 respondents were analyzed after the survey closed.

Results: 66% of respondents had been diagnosed with Ankylosing Spondylitis and 24% with Psoriatic Arthritis. 22% were diagnosed with more than one form of SpA.

Over 70% reported their day-to-day life was negatively impacted by SpA. Only 7% indicated no impact on their daily life and 22% said it was somewhat impacted. Ability to remain in the workplace was impacted and 16% reported being on long-term disability and 4% on short-term disability. There were 7% who retired early due to their disease.

Sleep loss/interruption was reported by 89% and 74% said they avoid social events. 41% of participants are highly restricted by SpA when it comes to tasks like outdoor yard work. Other highly restricted tasks include exercise (36%) and cleaning (31%). Tasks of medium restriction include preparing meals (31%) and engaging in intimate relations (30%).

Upon diagnosis and disease progression, many reported less frequent participation in exercise, travel, intimate relationships, social outings and family activities. Some even said they stopped participating in these all together.

When asked to rank what was most important regarding QOL, most ranked living with no/reduced pain as most important, followed by improved sleep/no fatigue. The least important were returning to work and going out with friends.

Conclusion: SpA conditions have a negative impact on QOL and are a burden causing patients to constantly assess their situation, worry about tomorrow and adjust different aspects of their lives. Results confirmed every aspect of life is impacted, both physically and mentally, leaving people feeling hopeless and without a purpose. Many can no longer work or do their favorite hobbies which leads to emotional and mental difficulties. People struggle with maintaining social and intimate relationships, intensifying social isolation and low self-confidence. Many indicated that their loved ones have difficulties understanding chronic pain and illness, making patients feel like a burden. This may be attributed to general lack of knowledge about SpA. The unpredictability of the disease impacts QOL leaving patients hesitant to make social plans in advance. Even those who are undergoing successful treatment and have improved QOL worry about the future. QOL can be improved with proper treatment, management and support.

Many expressed frustrations of being limited by their disease and indicated that it is often the chronic pain that causes these limits. It is clear that by living with less pain, patients can improve all aspects of their lives and be happier.

The CSA is committed to educating, supporting and advocating on behalf of Canadians impacted by SpA to improve health outcomes and QOL.

It doesn't have to be visible to be real. Together we are stronger!

Footnotes:

*SpA conditions include: Ankylosing Spondylitis, Psoriatic Arthritis, non-radial SpA, Axial and Peripheral Spondyloarthritis, Enteropathic Arthritis, Reactive Arthritis and Juvenile Onset Arthritis

**The Canadian Spondylitis Association (CSA) is a national non-profit patient association supporting and advocating for those living with SpA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1615

Arthritis research

AB0924-PARE

EXPERIENCES AND PERCEPTIONS OF PATIENTS WITH PSORIATIC ARTHRITIS PARTICIPATING IN A TRIAL OF FAECAL MICROBIOTA TRANSPLANTATION: A NESTED QUALITATIVE STUDY

M. Skov Kragsnaes[1], S. Theodor Sødergren[1], J. Kjeldsen[2], H. C. Horn[1], H. L. Munk[1], J. K. Pedersen[3], C. Schufri Klinkby[1], M. De Wit[4], N. Gram Ahlmark[5], T. Tjørnhøj-Thomsen[5], T. Ellingsen[1]. *[1]Odense University Hospital, Department of Rheumatology, Odense, Denmark*; *[2]Odense University Hospital, Department of Medical Gastroenterology, Odense, Denmark*; *[3]Svendborg Hospital OUH, Section of Rheumatology, Department of Medicine, Svendborg, Denmark*; *[4]Amsterdam, Patient Research Partner, Amsterdam, Netherlands*; *[5]University of Southern Denmark, National Institute of Public Health, Copenhagen, Denmark*

Background: Patients' first-hand experiences of faecal microbiota transplantation (FMT) performed in a rheumatological care-setting have yet to be elucidated.

Objectives: The objectives were to explore participants' perceptions of being part of an FMT trial thereby identifying potential trial participation effects and enlightening the patient perspective on the outlook for future FMT trials in rheumatic diseases.

Methods: In a qualitative study nested within a double-blind, randomised, placebo-controlled trial (RCT) testing FMT as a potential new anti-rheumatic treatment,[1] semi-structured telephone interviews were conducted following the trial participants' final 26-week visit. The RCT was conducted at a Danish rheumatology university outpatient clinic with nationwide inclusion. The qualitative study included ten patients with psoriatic arthritis (PsA) who completed the final 26-week trial visit and were unaware of their treatment allocation (one gastroscopic-guided FMT or sham transplantation into the duodenum), see table 1. Qualitative researchers, who did not take part in the RCT, performed the interviews and the primary analysis. The experiences explored related to the conduct of the RCT and changes in the participants' everyday life. The analysis was carried out using a thematic approach. There was sufficient repetition of ideas in data to conclude data saturation.

Table 1. Characteristics of the participants.

Characteristic	Total (n = 10)
Female sex, no. (%)	7 (70%)
Age, yr.	53.9 (11.3)
Time since diagnosis, yr.[a]	7.4 (4.2, 12.8)
Rheumatoid factor IgM negative, no. (%)	10 (100%)
Anti-citrullinated peptide antibody negative, no. (%)	10 (100%)
HLA-B27 negative, no. (%)	8 (80%)
C-reactive protein, mg/L	4.5 (3.6)
HAQ-DI[b]	1.09 (0.40)
Swollen joint 66 count	7.4 (3.8)
Tender joint 68 count	22.8 (7.9)
SPARCC enthesitis index[c]	
Score ≥1, no. (%)	10 (100%)
Score in patients with a score ≥1	8.7 (4.0)

Data are mean (SD) or n (%) unless otherwise stated. [a] Time since diagnosis of psoriatic arthritis is presented as median and interquartile range (IQR).[b] Scores on the Health Assessment Questionnaire Disability Index (HAQ-DI) range from 0 to 3, with higher scores indicating greater disability. [c] Spondyloarthritis Research Consortium of Canada (SPAARC) Enthesitis Index range from 0 to 16, with higher scores indicating more severe disease.

Results: Participation in the RCT influenced the patients' understanding of PsA and induced positive changes in their everyday life. Renewed hopes for the future in addition to a feeling of enhanced care contributed to significant trial participation effects.[2] We identified several factors related to the RCT that may have promoted these effects (figure 1). FMT was deemed acceptable and safe, and all participants supported more research into the field of microbiota-targeted interventions in rheumatic diseases.

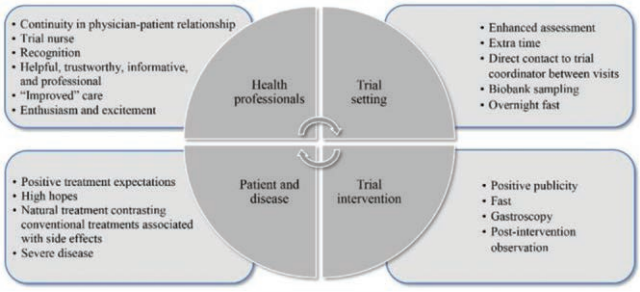


Figure 1. Factors related to the RCT that may have promoted trial participation effects.

Conclusion: Discrepancies between the clinical and the research setting should be considered when discussing the clinical relevance of the results of the RCT. Overall, patients with PsA who have participated in an RCT testing FMT find the treatment acceptable and safe encouraging more research into the field of microbiota-targeted interventions in rheumatic diseases. Further research into the potential beneficial and adverse effects of FMT in addition to exploring the magnitude and mechanisms behind FMT trial participation effects in the rheumatological setting are highly needed.

REFERENCES:

[1] Kragsnaes MS, Kjeldsen J, Horn HC, et al. Efficacy and safety of faecal microbiota transplantation in patients with psoriatic arthritis: protocol for a 6-month, double-blind, randomised, placebo-controlled trial. BMJ open 2018;8:e019231.

[2] McCambridge J, Kypri K, Elbourne D. Research participation effects: a skeleton in the methodological cupboard. *J Clin Epidemiol* 2014;67:845-9.

Acknowledgements: The authors thank the patient advisers and all the participants who shared their experiences with us.

Disclosure of Interests: Maja Skov Kragsnaes Grant/research support from: Novartis 2017 (unrestricted research grant) to cover 3 months PhD salary in relation to the study., Shaun Theodor Sødergren: None declared, Jens Kjeldsen: None declared, Hans Christian Horn: None declared, Heidi Lausten Munk: None declared, Jens Kristian Pedersen: None declared, Camilla Schufri Klinkby: None declared, Maarten de Wit: None declared, Nanna Gram Ahlmark: None declared,

Tine Tjørnhøj-Thomsen: None declared, Torkell Ellingsen Grant/research support from: Novartis 2017 (unrestricted research grant)
DOI: 10.1136/annrheumdis-2021-eular.2076

AB0925-PARE **A NARRATIVE REVIEW ASSESSING THE ROLE OF DIETARY SALT AS AN ENVIRONMENTAL RISK FACTOR FOR THE ONSET AND SEVERITY OF RHEUMATOID ARTHRITIS**

S. Ahmed[1], E. Nikiphorou[2,3], J. Bayliss[4]. [1]*Colchester Hospital, Rheumatology, Colchester, United Kingdom*; [2]*Kings College London, Centre for Rheumatic Diseases, London, United Kingdom*; [3]*Kings College London, Rheumatology Department, London, United Kingdom*; [4]*East Suffolk and North Essex NHS Foundation Trust, Library & Learning Resources, Ipswich, United Kingdom*

Background: The role of dietary salt consumption in the etiopathogenesis of Rheumatoid Arthritis (RA), and autoimmune disease in general, has received renewed interest. This has been fueled by the increased prevalence of autoimmune disease worldwide correlating with western diets and heightened consumption of salt rich foods and also studies at the cellular level demonstrating induction of IL 17 producing T helper cells (Th17) by dietary salt.
Objectives: To conduct a narrative review of observational studies and clinical trials on the role of dietary salt as an environmental risk factor for the onset and development of RA.
Methods: A comprehensive search was done of the literature from 2010 to 2021, using the search terms dietary salt and RA; the native interfaces EBSCO and Ovid were used. Databases searched included Pubmed, Embase, EMCare, Medline and CINAHL using a Population, Exposure and Outcome framework; the MESH terms RA, risk factors, nutrition and salt were used. Data was extracted by an independent reviewer.
Results: Out of the 72 studies initially identified, 50 were included in this review. Studies in murine models have demonstrated that high concentrations of sodium chloride promote the differentiation of T helper lymphocytes, via the serum- and glucocorticoid- inducible kinase 1 (SGK1) mediator towards the proinflammatory Th17 driven immune response. Six studies were carried out in human subjects. Study design ranged from cross sectional observational to nested case control studies. Sodium intake amongst participants characterized as having high intake, or being placed in the higher quartiles, ranged from 4.5-5grams per day. 5 out of 6 studies demonstrated that increased dietary salt consumption is associated with earlier onset RA. One study suggested an association between high salt intake and erosive disease at diagnosis and the development of anti-citrullinated protein antibodies (ACPA), although evidence was weak and from a single study only. Another study found that increased consumption of salt was only associated with risk of RA in smokers, highlighting the need to explore confounding variables further.
Conclusion: This narrative review of the literature provides some evidence that supports a role of excess dietary salt consumption as a risk factor for the onset and severity of RA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.2972

Psychosocial support

AB0926-PARE **IMPACT OF COVID 19 PANDEMIC ON TUNISIAN SPA PATIENTS: PSYCHOLOGICAL STATE AND TREATMENT ADHERENCE**

M. Rachdi[1], A. Feki[2], Z. Gassara[3], S. Ben Jemaa[4], M. Ghali[4], M. Ezzeddine[4], M. H. Kallel[4], H. Fourati[4], R. Akrout[4], S. Baklouti[4]. [1]*Hedi Chaker Hospital Sfax, Rheumatology, Sfax,Tunisia*; [2]*Hedi Chaker Hospital, Rheumatology, Sfax, Tunisia*; [3]*Hedi Chaker Hospital, Rheumatology, Sfax,Tunisia*; [4]*Hedi Chaker Hospital, Rheumatology, Sfax,Tunisia*

Background: The challenge posed by the COVID-19 pandemic may represent an overwhelmingly stressful event for ankylosing spondylitis (SpA) patients and impact their treatment adherence. In response to the COVID-19 pandemic, Tunisia,have adopted community containment to manage the spread of the virus. However, COVID-19 restrictions can alter psychological wellbeing and limit access to treatment for SpA patients.
Objectives: This study aimed to evaluate the impact of COVID-19 pandemic on psychological health and treatment adherence on Tunisian SpA patients.
Methods: This is a cross sectional study including patients with SpA (ASAS criteria). A survey comprising questions about adherence to stay home warnings; the obligation to go outside for work; satisfaction with the medical support or information received for COVID-19; showing up to medical check-ups, proper use of the medications; medications that the patient stopped taking.
Anxious and depressive symptoms were assessed using the Arabic version of Hospital Anxiety and Depression Scale (HADS) questionnaire.
Results: We included thirty patients. the average age was: 39,7 years-old and the sex ratio was: 13,3. 75 % of patients were married. The SpA was axial in 25%, peripheral in 20%, and both in 55 %. Most patients had a moderate activity and the mean activity scores were: BASDAI = 2.60, ASDAScrp:2.65
38% of patients were on biologics, 36 % on sulfasalazine and NSAIDs and 26 % on NSAIDs only.
It seemed that significant number of patients strictly adhered to stay home warnings (>89%) only 11% were obliged to go out for work during general lockdown while only 24 % adhered to it after general lockdown.
Most of the patient 78 % were not satisfied with the medical support or information about COVID 19. 88% of patients requested information from TV while 10 % requested it from social media and 2 % from relatives and friends working in health care field.
After the outbreak, 23% of the patients who had a scheduled chek-up visit attended the appointment as it was before.The remaining either 'did not want to come' (43%), wanted to come but could not contact anyone in the hospital (11%), was advised to postpone their visits (10%), or couldn't find means of transport (13%).A significant number of patients decreased or skipped their dose (69%), while only 13% continued their medications and 16%stopped taking NSAIDs.
Biological DMARDs(anti-TNF agents) were the most frequent drugs which patients decreased their dose, skipped or stopped taking 33%. sulfasalazine and NSAIDs were least likely 17% to be skipped or stopped.
43% of patients Had a HADS anxiety level more than or equal to 11: 87 % women and 13 % men. The highest anxiety scores were found among patients aged less than 45 years old (87%) married with children .32% of patients had a HADS depression level more than or equal to 11: 54 % women and 44 % men. the highest depression scores were found among patients aged less than 45 years old married with children.
No significant relationship was found between anxiety and depression levels regarding biologic treatment.
Conclusion: Our results suggest that patients with SpA were less likely to comply strictly to 'stay home' restrictions, most probably due to the male predominance and relatively younger age. Additionally, we noticed that SpA patients treated with anti-TNF agents were the patients that regular drug use had been considerably disrupted.
COVID 19 pandemic has heightened the need to care for patients with SpA in an increasingly virtual environment.
Additionally, we found that being female, having a lower level of education, having a child, living in a crowded family is correlated to higher levels of anxiety and depression.
REFERENCES:
[1] Smarr KL, Keefer AL. Measures of depression and depressive symptoms: Beck Depression Inventory-II (BDI-II),Hospital Anxiety and Depression Scale (HADS), and Patient Health Questionnaire-9 (PHQ-9) Arthritis care.
Acknowledgements: I would like to express my special thanks of gratitude to Rheumatology department of Hedi Chaker Hospital Sfax.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.3950

Work and rehabilitation

AB0927-PARE **WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN PATIENTS WITH SAPHO SYNDROME**

L. Gong[1], C. Li[2]. [1]*Peking Union Medical College Hospital, Institute of Clinical Medicine, Beijing, China*; [2]*Peking Union Medical College Hospital, Department of Traditional Chinese Medicine, Beijing, China*

Background: Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare disease, characterized by osteoarticular and cutaneous manifestations. Osteitis and hyperostosis are regarded as the core pathophysiological changes of SAPHO syndrome [1], which may lead to bone pain and loss of motor function. The Work Productivity and Activity Impairment (WPAI) questionnaire is an instrument to measure the impact of the disease on work productivity and activity, subsequently adapted for ankylosing spondylitis [2], rheumatoid arthritis [3], irritable bowel syndrome [4], and other chronic diseases [5]. However, no study has investigated the work productivity of patients with SAPHO syndrome.
Objectives: The purpose of this study is to give an overview of work productivity loss in SAPHO patients through the work productivity and activity impairment (WPAI) questionnaire and investigate the relationship between the WPAI and other disease-related indicators.

Methods: Patients for this cross-sectional study were recruited from Peking Union Medical College Hospital (Beijing, China). The questionnaires incorporating the WPAI were administered, along with demographic data, disease-specific measures, and general health variables. The construct validity of WPAI was evaluated by the correlations between WPAI outcomes and other measures. Wilcoxon rank-sum tests and non-parametric Kruskal-Wallis tests were used for comparison of WPAI outcomes between known-groups.

Results: A total of 376 patients were included and 201 patients (53.5%) were employed. The median (interquartile range [IQR]) of absenteeism, presenteeism, work productivity loss and activity impairment were 0% (0-13%), 20% (0-40%), 20% (0-52%) and 30% (0-50%), respectively. All WPAI outcomes showed moderate to strong correlations to other generic and disease-specific measures (|r| =0.43-0.75), except for absenteeism. Increasing disease activity and worse health status are significantly associated with higher impairment of work productivity and activity.

Conclusion: This study highlights the negative effects of SAPHO syndrome on patients' work productivity and activity, indicating a good construct validity and discriminative ability of WPAI. For reducing the economic burden, it is important to improve the patients' work productivity and daily activity with active intervention.

REFERENCES:

[1] Liu S, Tang M, Cao Y, Li C. Synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome: review and update. *Therapeutic advances in musculoskeletal disease.* 2020;12:1759720x20912865.

[2] Reilly MC, Gooch KL, Wong RL, Kupper H, van der Heijde D. Validity, reliability and responsiveness of the Work Productivity and Activity Impairment Questionnaire in ankylosing spondylitis. *Rheumatology (Oxford, England).* 2010;49(4):812-819.

[3] Zhang W, Bansback N, Boonen A, Young A, Singh A, Anis AH. Validity of the work productivity and activity impairment questionnaire--general health version in patients with rheumatoid arthritis. *Arthritis research & therapy.* 2010;12(5):R177.

[4] Frandemark A, Tornblom H, Jakobsson S, Simren M. Work Productivity and Activity Impairment in Irritable Bowel Syndrome (IBS): A Multifaceted Problem. *The American journal of gastroenterology.* 2018;113(10):1540-1549.

[5] Enns MW, Bernstein CN, Kroeker K, Graff L, Walker JR, Lix LM, et al. The association of fatigue, pain, depression and anxiety with work and activity impairment in immune mediated inflammatory diseases. *PloS one.* 2018;13(6):e0198975.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.484

Author Index

A T., 1160 (AB0268)
Aaløkken T. M., 104 (OP0174)
Aaltonen K., 82 (OP0140), 133 (OP0222)
Aarrestad Provan S., 82 (OP0140), 133 (OP0222)
Aas E., 119 (OP0198-HPR)
Aasvold A. M., 92 (OP0153-HPR)
Abacar K., 1028 (POS1486-HPR), 1467 (AB0888-HPR), 1471 (AB0895-HPR)
Abalo A. I., 576 (POS0667), 1196 (AB0342)
Ábalos-Aguilera M. C., 0020 (OP0038), 0751 (POS0970)
Abalos-Aguilera M. D. C., 426 (POS0394), 469 (POS0475), 1317 (AB0562)
Abasolo L., 896 (POS1225), 908 (POS1251), 910 (POS1253), 1464 (AB0881-HPR), 1475 (AB0906-HPR)
Abbas L., 730 (POS0933), 1377 (AB0689)
Abbes M., 1147 (AB0244)
Abbruzzese A., 1003 (POS1437)
Abd el-Khalek A. M., 477 (POS0490)
Abd Rahman R., 1177 (AB0302)
Abdalla A., 789 (POS1034)
Abdel Jaber M., 51 (OP0093)
Abdelhafiz D., 1081 (AB0105)
Abdelkarim E., 871 (POS1179), 1359 (AB0654)
Abdellaoui S., 1092 (AB0126), 1092 (AB0127)
Abdellatif A., 840 (POS1122)
Abdellatif S., 525 (POS0585), 1063 (AB0064), 1111 (AB0169), 1193 (AB0337), 1194 (AB0339), 1472 (AB0897-HPR)
Abdelli M. N., 975 (POS1385)
Abdelmoula L., 481 (POS0497), 768 (POS1000), 856 (POS1155), 1106 (AB0158), 1119 (AB0190), 1285 (AB0517), 1341 (AB0611), 1358 (AB0650), 1395 (AB0730), 1396 (AB0731), 1396 (AB0732)
Abdul Razzack A., 600 (POS0701)
Abdul Razzack S., 600 (POS0701)
Abdulahad W., 33 (OP0062)
Abdulaziz S., 855 (POS1153)
Abdulganieva D., 1253 (AB0452), 1269 (AB0484), 1283 (AB0513)
Abedallatif S., 1120 (AB0192)
Abhishek A., 841 (POS1124), 845 (POS1132), 846 (POS1133)
Abidi J., 9 (OP0015)
Abignano G., 163 (OP0269), 387 (POS0319), 906 (POS1246)
Abisror Jeannin N., 181 (OP0295), 261 (POS0103)
Abobului M., 164 (OP0270), 681 (POS0854), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690)
Abouqal R., 992 (POS1417), 1148 (AB0246), 1270 (AB0486), 1430 (AB0811), 1472 (AB0898-HPR)
Abraham L., 275 (POS0128)
Abraham Y., 403 (POS0348)
Abramkin A., 1088 (AB0118)
Abreu G., 75 (OP0131), 592 (POS0691), 1171 (AB0289)
Abreu M., 625 (POS0747), 909 (POS1252), 999 (POS1430), 1448 (AB0848)
Abreu P., 354 (POS0263)
Abrignani S., 229 (POS0048)
Abril A., 655 (POS0805)
Absher D., 192 (OP0314)
Abu Jbara M., 361 (POS0275-HPR), 1080 (AB0104)
Abud-Mendoza C., 624 (POS0745)
Abu-Zaid M. H., 832 (POS1104)
Acar M. E., 1454 (AB0862-HPR)
Accogli E., 105 (OP0176)
Acer Kasman S., 959 (POS1354), 961 (POS1359), 1016 (POS1462-HPR)
Acharya S., 192 (OP0314)
Achemlal L., 992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811)
Achenbach S., 56 (OP0102), 322 (POS0210)
Achikyan V., 709 (POS0903)
Acierno C., 1399 (AB0739)
Ackermann F., 388 (POS0323)
Ackermann S., 398 (POS0341)
Acosta Felquer M. L., 730 (POS0933), 759 (POS0984), 1377 (AB0689)
Acosta M. E., 296 (POS0167), 1042 (AB0015)
Acosta-Colman I., 1042 (AB0015), 1106 (AB0159)
Adaily N., 1219 (AB0383)
Adami G., 62 (OP0112), 106 (OP0178), 326 (POS0218), 560 (POS0644), 831 (POS1102), 867 (POS1173)
Adams D., 716 (POS0912), 720 (POS0918)
Adams L., 155 (OP0254)
Adamsson Eryd S., 1000 (POS1432)
Adan A., 32 (OP0060), 952 (POS1340)
Adarmouch L., 358 (POS0269-HPR)
Addison J., 544 (POS0614), 1126 (AB0204)
Adelsten T., 234 (POS0056), 865 (POS1170)
Adinolfi A., 845 (POS1132), 846 (POS1133), 850 (POS1141), 1348 (AB0629)
Adinolfi L. E., 907 (POS1248), 1475 (AB0905-HPR)
Adler G., 1274 (AB0494)
Adnan Z. A., 1425 (AB0802)
Adolf D., 1153 (AB0255)
Adrovic A., 247 (POS0079), 934 (POS1304)
Adsuara de Sousa L. F., 699 (POS0887)
Aelion J., 64 (OP0115), 138 (OP0228), 568 (POS0655)
Aeschlimann C., 635 (POS0763), 874 (POS1186)
Aeschlimann F., 872 (POS1183)
Af Klint E., 87 (OP0146)
Afari E., 1127 (AB0205)
Afif W., 993 (POS1420)
Afonso C., 293 (POS0162), 830 (POS1100), 1424 (AB0799)
Afreixo V., 738 (POS0950)
Aga A. B., 934 (POS1305), 1392 (AB0722)
Agacfidan A., 191 (OP0313)
Agafonova E., 337 (POS0233), 709 (POS0903), 761 (POS0987), 1262 (AB0470), 1276 (AB0498)
Agape E., 229 (POS0048)
Agargun B. F., 191 (OP0313), 912 (POS1257)
Agarwal P., 316 (POS0200), 782 (POS1026), 784 (POS1028), 1300 (AB0538)
Agarwal V., 1041 (AB0013)
Agati L., 903 (POS1240)
Agca R., 324 (POS0213)
Aggarwal A., 1163 (AB0276)
Aggarwal R., 4 (OP0008)
Aggelakos M., 631 (POS0757), 632 (POS0759), 635 (POS0764)
Aghamuradov S., 191 (OP0313), 913 (POS1259)
Agmon-Levin N., 892 (POS1217)
Agolli A., 600 (POS0701)
Agolli O., 600 (POS0701)
Agosti M., 254 (POS0090)
Agostoni C. V., 935 (POS1307)
Agrawal A., 1043 (AB0019)
Aguado Henche S., 946 (POS1328)
Agudo-Bilbao M., 1225 (AB0396), 1412 (AB0771)
Aguiar C., 242 (POS0071)
Aguiar Castellanos M., 904 (POS1242)
Aguiar R., 738 (POS0950)
Águila Maldonado R., 0730 (POS0933)
Águila Maldonado R., 1377 (AB0689)
Aguilar-Hurtado M. C., 323 (POS0211)
Aguilera S., 303 (POS0180)
Aguirre M. A., 20 (OP0038)
Aguirre-Zamorano M. Á., 469 (POS0475), 1245 (AB0432)
Agular B., 379 (POS0307)
Ahid S., 992 (POS1417), 1148 (AB0246), 1270 (AB0486), 1430 (AB0811)
Ahlers J., 528 (POS0591)
Ahlman M., 653 (POS0802)
Ahlquist P., 6 (OP0010)
Ahmad H. A., 794 (POS1040)
Ahmad M. M., 1134 (AB0215)
Ahmad N., 34 (OP0063)
Ahmad Y., 602 (POS0705)
Ahmed Abdi B., 702 (POS0893)
Ahmed K., 869 (POS1177)
Ahmed Narikkoottungal S., 869 (POS1177)
Ahmed S., 1484 (AB0925-PARE)
Ahomaa E., 752 (POS0973)
Aiello V., 906 (POS1246)
Aighobahi E., 468 (POS0473)
Aigner T., 120 (OP0200)
Aili K., 1330 (AB0586)
Aimeur C., 843 (POS1127)
Airaldi M., 979 (POS1393)
Airò P., 51 (OP0093), 166 (OP0273), 232 (POS0054), 384 (POS0316), 386 (POS0318), 387 (POS0321), 389 (POS0324), 530 (POS0593), 685 (POS0861), 701 (POS0891)
Airoldi C., 730 (POS0933), 771 (POS1005), 1377 (AB0689)
Aissopou E., 656 (POS0807)
Ait Bellabas K., 1147 (AB0243)
Aitken D., 307 (POS0186), 365 (POS0280)
Ajerouassi A., 1266 (AB0477)
Ajlani H., 481 (POS0497), 923 (POS1280), 926 (POS1288), 1272 (AB0490), 1273 (AB0492)
Ajmone-Marsan N., 675 (POS0843)
Akan O., 286 (POS0146)
Akar S., 131 (OP0220), 722 (POS0922), 727 (POS0929), 731 (POS0935), 861 (POS1165), 1140 (AB0229), 1255 (AB0456), 1266 (AB0479), 1317 (AB0561), 1366 (AB0669), 1454 (AB0862-HPR)
Akdemir U. O., 1077 (AB0097)
Akdoğan A., 518 (POS0568), 648 (POS0793), 728 (POS0931), 770 (POS1004), 814 (POS1070), 971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1299 (AB0535)
Akdogan N., 1327 (AB0579)
Akebo H., 492 (POS0516)
Akgul S., 1398 (AB0737)
Akhtari S., 132 (OP0221), 812 (POS1068)
Akhverdyan Y., 297 (POS0169), 455 (POS0451), 487 (POS0509), 1437 (AB0827)
Akil M., 602 (POS0705)
Akimova A., 43 (OP0080), 1045 (AB0023)
Akizuki S., 401 (POS0345)
Akkoc N., 217 (POS0027)
Akmaev V., 478 (POS0492), 1096 (AB0138), 1097 (AB0140)
Akpabio A., 2 (OP0006), 173 (OP0286)
Akrout R., 922 (POS1277), 1276 (AB0497), 1281 (AB0508), 1484 (AB0926-PARE)
Aktas I., 905 (POS1244)
Aktay Ayaz N., 201 (LB0004)
Akula M., 12 (OP0022)
Akyildiz Tezcan E., 1323 (AB0572)
Akyol A., 249 (POS0082)
Al Emadi S., 2 (OP0006), 173 (OP0286), 175 (OP0288), 361 (POS0275-HPR), 1080 (AB0104)
Al Khayyat S. G., 669 (POS0832), 746 (POS0963)
Al Mossawi H., 17 (OP0032)

Al Naqbi K., 1379 (AB0692)
Al Nokhatha S., 1230 (AB0404)
Alagündüz H., 1184 (AB0318)
Alam E., 361 (POS0275-HPR), 1080 (AB0104)
Alammari Y., 282 (POS0140), 462 (POS0462)
Alandejani A., 997 (POS1427)
Alani M., 572 (POS0660), 792 (POS1037), 792 (POS1038), 801 (POS1049), 1155 (AB0259)
Alarcin C., 28 (OP0054)
Alarcon G. S., 173 (OP0286), 177 (OP0289)
Alase A., 78 (OP0134)
Alasti F., 475 (POS0485)
Alataris K., 1158 (AB0264)
Al-Attar M., 757 (POS0980), 949 (POS1334)
Alazmi M., 1320 (AB0566)
Alba P., 875 (POS1188), 1194 (AB0338), 1196 (AB0342)
Albayrak Gezer I., 1323 (AB0572)
Al-Bazy S., 95 (OP0159-HPR)
Albiero E., 1133 (AB0214)
Albiero J. A., 1194 (AB0338), 1196 (AB0342)
Albrecht I., 528 (POS0591)
Albrecht K., 216 (POS0026), 990 (POS1414)
Albrechtsen T., 95 (OP0159-HPR)
Albuquerque C., 909 (POS1252), 1448 (AB0848)
Alburquerque Sendin F., 920 (POS1272)
Alcañiz Escandell C., 296 (POS0167), 857 (POS1157), 964 (POS1365), 1278 (AB0502)
Alcaraz-Clariana S., 920 (POS1272)
Alciati A., 190 (OP0310)
Alcivar Navarrete J., 730 (POS0933), 1377 (AB0689)
Alcorta Lorenzo N., 1141 (AB0230)
Aldasoro V., 34 (OP0064), 35 (OP0065), 960 (POS1355), 1132 (AB0211)
Alderaan K., 1320 (AB0566)
Alegre Sancho J. J., 685 (POS0861)
Alegre-Sancho J. J., 296 (POS0168), 1427 (AB0806)
Aleixo A., 1236 (AB0415), 1236 (AB0416), 1236 (AB0417)
Alekberova Z., 1072 (AB0085), 1072 (AB0086), 1409 (AB0764), 1409 (AB0765)
Aleksandrov A., 160 (OP0263-HPR), 225 (POS0040), 1059 (AB0053), 1110 (AB0167), 1423 (AB0797)
Aleksandrov V., 160 (OP0263-HPR), 225 (POS0040), 1059 (AB0053)
Aleksandrova E., 1442 (AB0837)
Aleksandrova N., 160 (OP0263-HPR), 225 (POS0040), 1110 (AB0167), 1423 (AB0797)
Aleksankin A., 1064 (AB0068)
Aleksanyan K., 187 (OP0306)
Alekseeva L., 118 (OP0197), 275 (POS0127), 276 (POS0130), 827 (POS1094), 1336 (AB0599), 1337 (AB0603), 1338 (AB0604)
Alekseeva O., 977 (POS1388), 1421 (AB0792)
Alenius G. M., 130 (OP0218), 864 (POS1169)
Alessandri C., 588 (POS0685), 645 (POS0783), 893 (POS1219), 902 (POS1238), 1069 (AB0079), 1073 (AB0087), 1143 (AB0234)
Alessandri E., 686 (POS0862), 908 (POS1250), 1247 (AB0438)
Alessandro R., 22 (OP0042)
Alessi H., 653 (POS0802)
Aletaha D., 70 (OP0126), 71 (OP0127), 255 (POS0092), 284 (POS0145), 475 (POS0485), 566 (POS0653), 725 (POS0926), 1005 (POS1441), 1306 (AB0547)
Alex G., 700 (POS0889)
Alexander S. A., 476 (POS0487)
Alexander T., 207 (POS0010), 623 (POS0744)
Alexandrova E., 772 (POS1008)
Alexeeva E., 100 (OP0166), 201 (LB0004), 247 (POS0079), 250 (POS0085), 934 (POS1304), 938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Alexopoulos H., 1381 (AB0697)
Alexovits S., 833 (POS1105)
Alexseev D., 1400 (AB0743)
Alfares E., 1230 (AB0404)
Alfranca M. A., 1241 (AB0427)
Alfredsson L., 53 (OP0096), 145 (OP0236), 206 (POS0009), 459 (POS0457), 474 (POS0484), 1059 (AB0054)
Alghamdi M., 1320 (AB0566)
Alghanim N., 1320 (AB0566)
Alhazmi A., 1320 (AB0566)
Ali A., 1052 (AB0039)
Ali I., 477 (POS0489), 1093 (AB0130)
Ali M., 566 (POS0653)
Ali O., 67 (OP0120)
Alia F., 522 (POS0577)
Alibaz-Oner F., 1471 (AB0895-HPR)
Alioto S., 1050 (AB0034)
Aliste Fernandez M., 1060 (AB0055)
Aliyeva N., 191 (OP0313), 913 (POS1259), 1251 (AB0448), 1359 (AB0653)
Alkan G., 522 (POS0576)
Alkan Melikoglu M., 959 (POS1354), 961 (POS1359)
Alkan O., 191 (OP0313)
Alkenaris H., 405 (POS0350)
Alkhadhrawi N., 1320 (AB0566)
Alkindi F., 1379 (AB0692)
Alkutobi Z., 834 (POS1107)
Allaart C., 259 (POS0097), 273 (POS0123), 351 (POS0258), 466 (POS0470), 471 (POS0479), 675 (POS0843), 932 (POS1300), 1107 (AB0160), 1365 (AB0667)
Allali F., 992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811), 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Allanore Y., 101 (OP0170), 105 (OP0175), 162 (OP0266), 163 (OP0269), 232 (POS0054), 384 (POS0316), 385 (POS0317), 386 (POS0318), 387 (POS0321), 419 (POS0378), 534 (POS0600), 681 (POS0855), 685 (POS0861), 694 (POS0877), 897 (POS1228), 1244 (AB0431), 1364 (AB0665)
Alle G., 875 (POS1188)
Allen C., 1008 (POS1449)
Allen Jr J. C., 1419 (AB0787)
Allenbach Y., 388 (POS0323)
Allendörfer J., 209 (POS0015)
Alleyrat C., 358 (POS0270-HPR)
Allez M., 901 (POS1236), 901 (POS1237)
Almodovar R., 32 (OP0060), 743 (POS0958), 766 (POS0996), 976 (POS1387)
Almohideb M., 1320 (AB0566)
Almquist J., 253 (POS0089)
Almutairi K., 55 (OP0100-HPR), 373 (POS0297), 1079 (AB0103)
Aloe' T., 1372 (AB0679)
Alonso C. G., 874 (POS1186)
Alonso Castro S., 1280 (AB0505)
Alonso Lecue P., 1046 (AB0026)
Alonso Valdivieso J. L., 1208 (AB0366)
Alonso-Pérez A., 1048 (AB0030)
Alonzo H., 1280 (AB0506)
Aloui M., 1417 (AB0784)
Alp G., 722 (POS0922), 861 (POS1165), 1255 (AB0456), 1366 (AB0669)
Alpa M., 601 (POS0704)
Alperi-López M., 1280 (AB0505)
Alperovich G., 138 (OP0228)
Alpizar-Rodriguez D., 559 (POS0642), 904 (POS1242), 905 (POS1245), 1428 (AB0808), 1450 (AB0852), 1459 (AB0871-HPR)
Alqutami F., 881 (POS1198), 895 (POS1223)
Alrayes H., 1320 (AB0566)
Alseiari K., 1379 (AB0692)
Alserawan L., 666 (POS0827)
Alshevskaya A., 482 (POS0500)
Alten R., 108 (OP0180), 194 (OP0318), 453 (POS0447), 533 (POS0599), 1127 (AB0205), 1128 (AB0207), 1157 (AB0261)
Altıntaş D., 959 (POS1354), 961 (POS1359)
Altobelli A., 1160 (AB0269)
Altomare A., 701 (POS0891), 1379 (AB0691)
Altulea D., 33 (OP0062)
Altun B., 648 (POS0793), 1198 (AB0347)
Alunno A., 39 (OP0074), 41 (OP0077), 175 (OP0287), 231 (POS0052), 630 (POS0755), 829 (POS1099), 1359 (AB0652)
Alvarado K., 559 (POS0642)
Alvarado-Cardenas M., 1241 (AB0426)
Álvarez Castro C., 1171 (AB0290), 1321 (AB0568)
Álvarez D., 1213 (AB0374)
Alvarez de Cienfuegos A., 820 (POS1081), 1231 (AB0405), 1231 (AB0406)
Alvarez G., 856 (POS1156)
Alvarez Hernandez E., 905 (POS1245), 1386 (AB0709)
Álvarez Hernandez M. P., 0908 (POS1251), 0910 (POS1253)
Álvarez M. P., 0896 (POS1225)
Álvarez Troncoso J., 0693 (POS0875)
Álvarez Troncoso J., 1192 (AB0333)
Álvarez Vega J. L., 1303 (AB0542)
Álvarez-Reguera C., 0050 (OP0091), 0091 (OP0152), 0220 (POS0030), 0621 (POS0740), 0899 (POS1231), 0953 (POS1342), 0960 (POS1357), 1002 (POS1436)
Álvarez-Reguera C., 1226 (AB0397), 1227 (AB0399), 1377 (AB0688), 1436 (AB0825)
Alvarez-Rivas N., 34 (OP0064), 1208 (AB0366)
Alvaro Gracia J. M., 984 (POS1403), 1385 (AB0706), 1397 (AB0734)
Alvaro-Gracia J. M., 233 (POS0055), 523 (POS0579), 658 (POS0812), 1117 (AB0185), 1239 (AB0422)
Alves C., 353 (POS0261), 1209 (AB0367), 1214 (AB0375)
Alves M., 101 (OP0170), 162 (OP0266), 384 (POS0316), 671 (POS0835), 674 (POS0840), 681 (POS0855), 1244 (AB0431)
Alves V., 182 (OP0297)
Alzahrani H., 977 (POS1389), 1391 (AB0720)
Alzahrani Y., 977 (POS1389), 1391 (AB0720)
Alzahrani Z. A., 1320 (AB0566)
Amano H., 589 (POS0687)
Amano K., 255 (POS0092)
Amano N., 689 (POS0868), 1096 (AB0136)
Amara K., 429 (POS0400)
Amaral T., 1255 (AB0457)
Amarilyo G., 928 (POS1294), 929 (POS1295)
Amarnani R., 448 (POS0440)
Amatucci A., 1347 (AB0628)
Ambery P., 1000 (POS1432)
Amengual Guedan M. J., 1060 (AB0055)
Ameni D., 1101 (AB0148)
Amer Y. A., 922 (POS1276)
Amiar O., 419 (POS0378)
Amigo Castañeda M. D. C., 1386 (AB0709)
Amikishiyev S., 191 (OP0313), 913 (POS1259), 1251 (AB0448)
Amin S., 389 (POS0325)
Amirdzhanova V., 1109 (AB0165), 1160 (AB0267), 1162 (AB0272)
Amit Rahat M., 543 (POS0613)
Amit Vazina M., 892 (POS1217)
Amital H., 64 (OP0115)
Ammitzbøll C., 866 (POS1171)
Ammitzbøll_Danielsen M., 352 (POS0260)
Amnahliza A. R., 459 (POS0457)
Amoura Z., 1186 (AB0323)
Amouzougan A. S., 1164 (AB0277)
Amri K., 925 (POS1287), 926 (POS1289), 926 (POS1290), 1417 (AB0784)
Amsler J., 33 (OP0061), 1161 (AB0270)
Amylidi-Mohr S., 649 (POS0794)
An J. X., 77 (OP0133)
An J., 188 (OP0307), 427 (POS0396)
An Y., 218 (POS0028)
Anagnostopoulos C. D., 15 (OP0029)
Anagnostopoulos Z., 1299 (AB0537)
Anand G., 1160 (AB0268)
Ananieva L. P., 387 (POS0321)
Ananieva L., 1400 (AB0743)
Ananyeva L. P., 371 (POS0291), 681 (POS0853), 683 (POS0857), 683 (POS0858), 684 (POS0860), 899 (POS1232), 1239 (AB0423), 1248 (AB0439), 1248 (AB0440), 1249 (AB0444), 1253 (AB0453), 1254 (AB0454), 1254 (AB0455)
Ananyeva L., 104 (OP0173)
Anatale-Tardiff L., 26 (OP0049)
Anca B., 519 (POS0569)
Ancer Rodríguez P. R., 1360 (AB0657)
Ancona S., 97 (OP0161)
Ancuta C., 489 (POS0512), 519 (POS0569), 1116 (AB0181), 1380 (AB0695)
Ancuta E., 1116 (AB0181), 1380 (AB0695)

Ancuta I., 519 (POS0569)
Andel P., 1009 (POS1451), 1218 (AB0381), 1418 (AB0785)
Andersen C., 1466 (AB0885-HPR)
Andersen J. B., 866 (POS1171)
Andersen V., 6 (OP0010), 9 (OP0017)
Anderson A. E., 1044 (AB0021)
Anderson A., 18 (OP0033), 1046 (AB0025)
Anderson E., 165 (OP0271)
Anderson J., 16 (OP0030), 143 (OP0233), 433 (POS0407), 788 (POS1032), 790 (POS1035), 805 (POS1054)
Anderson K., 581 (POS0672), 1155 (AB0259)
Andersson H., 104 (OP0174)
Andersson K. M., 12 (OP0022), 14 (OP0026), 192 (OP0315), 428 (POS0397)
Andersson M., 197 (OP0322-HPR), 994 (POS1423), 1330 (AB0586)
Andev R. S., 34 (OP0063)
Andrade L., 904 (POS1242)
Andrea G., 229 (POS0048)
Andréasson K., 339 (POS0237)
Andreeva N., 1458 (AB0869-HPR)
Andreica I., 233 (POS0055), 376 (POS0301), 1375 (AB0684), 1435 (AB0823)
Andreoli L., 39 (OP0074), 470 (POS0476), 519 (POS0569), 600 (POS0702), 612 (POS0724), 619 (POS0737), 628 (POS0751), 633 (POS0760), 635 (POS0764), 1435 (AB0822)
Andreou A., 1037 (AB0004)
Andres Cerezo L., 424 (POS0388), 850 (POS1142), 1233 (AB0410)
Andrés M., 282 (POS0141), 841 (POS1124)
Andréu Sánchez J. L., 34 (OP0064), 35 (OP0065), 610 (POS0721), 892 (POS1218), 967 (POS1371)
Andreu-Suárez Á., 283 (POS0143), 807 (POS1058), 946 (POS1327)
Andrews J., 449 (POS0442), 450 (POS0443), 460 (POS0459), 994 (POS1422)
Andrews K., 600 (POS0701)
Andrews M. R., 1019 (POS1468-HPR)
Andrews R., 402 (POS0346)
Anelli M. G., 1003 (POS1437), 1260 (AB0467)
Ang D. L. M., 459 (POS0457)
Ang L. W., 827 (POS1095)
Ángel Torres M. J., 0179 (OP0292)
Angelelli C., 150 (OP0246), 445 (POS0433), 873 (POS1185)
Angelini O., 1217 (AB0380)
Angermair S., 887 (POS1209)
Angevare S., 1373 (AB0681)
Anghel D., 1267 (AB0480)
Anić B., 1199 (AB0348), 1199 (AB0349)
Anic B., 694 (POS0877)
Anikin S., 275 (POS0127), 276 (POS0130), 1338 (AB0604)
Anino-Fernández J., 755 (POS0977), 977 (POS1390), 986 (POS1407), 1065 (AB0070)
Anniccherico F. J., 960 (POS1355)
Anno S., 1086 (AB0115)
Añón Oñate I., 323 (POS0211), 1317 (AB0562)
Anouk M., 1181 (AB0312)
Anoun J., 1219 (AB0383)
Ansari G., 1157 (AB0262)
Ansboro S., 241 (POS0069)
Antao J., 820 (POS1083)
Antignac M., 1009 (POS1450)
Antinozzi C., 1074 (AB0089)
Antivalle M., 254 (POS0090), 335 (POS0230)
Antolí A., 1 (OP0004)
Anton J., 98 (OP0164), 245 (POS0076), 247 (POS0079), 934 (POS1304)
Antonakopoulos N., 1299 (AB0537)
Antonelli A., 906 (POS1246)
Antonio Pereira Delgado Alves J., 1282 (AB0510)
Antoniol N., 1196 (AB0342)
Antonopoulou K., 238 (POS0064-PARE), 889 (POS1213), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Antonucci M., 630 (POS0755)
Anton-Vicente A., 699 (POS0886)
Antony A., 876 (POS1189)
Antony B., 276 (POS0129), 309 (POS0190), 362 (POS0276), 365 (POS0280)
Antony J., 981 (POS1397), 1143 (AB0235), 1413 (AB0773)
Antovic A., 87 (OP0146), 693 (POS0874), 898 (POS1230), 1184 (AB0318)
Antunes M., 1462 (AB0878-HPR), 1478 (AB0912-HPR)
Anwar S., 1313 (AB0557)
Anyanwu S., 72 (OP0128), 328 (POS0220), 329 (POS0222), 569 (POS0656)
Anzola Alfaro A. M., 610 (POS0721), 984 (POS1403), 1385 (AB0706), 1397 (AB0734)
Aouad K., 343 (POS0243), 818 (POS1078)
Aouba A., 397 (POS0338), 669 (POS0831), 954 (POS1343)
Aoyagi K., 998 (POS1429)
Apáthy Á., 1321 (AB0569)
Apaydın H., 1182 (AB0314)
Apparailly F., 39 (OP0074)
Appenzeller S., 100 (OP0167), 247 (POS0079), 934 (POS1304), 943 (POS1323), 1255 (AB0457), 1405 (AB0754)
Aprile M. L., 1135 (AB0217), 1135 (AB0218)
Aquilina N., 1068 (AB0077)
Aquino J. L. B. D., 1423 (AB0798)
Aragon M., 232 (POS0053)
Aramaki T., 581 (POS0674)
Aranda-Valera I. C., 740 (POS0952), 751 (POS0970), 920 (POS1272)
Aranguren Redondo M. A., 1141 (AB0230)
Aranow C., 177 (OP0289), 181 (OP0296)
Araújo F., 692 (POS0872)
Araujo F., 871 (POS1180)
Araújo G., 208 (POS0013)
Araújo N., 909 (POS1252), 1448 (AB0848)
Arayssi T., 361 (POS0275-HPR), 1080 (AB0104)
Arboleya Rodríguez L., 819 (POS1080)
Arbuzova A., 326 (POS0217)
Arca B., 34 (OP0064)
Arcarese L., 1260 (AB0467)
Archer A. M., 1203 (AB0357)
Arden N., 274 (POS0125)
Ardhaoui M., 1063 (AB0064), 1193 (AB0337), 1194 (AB0339)
Ardizzone M., 170 (OP0282)
Ardourel D., 21 (OP0039)
Arefeva L., 420 (POS0380)
Arefieva A., 249 (POS0083)
Arenas Torrado H. F., 479 (POS0493)
Arends E. J., 585 (POS0680)
Arends S., 24 (OP0046), 74 (OP0130), 221 (POS0031), 223 (POS0034), 769 (POS1002), 775 (POS1014), 1071 (AB0082), 1257 (AB0462)
Arevalo de Guillen I., 1042 (AB0015)
Arévalo M., 342 (POS0242)
Arevalo Salaet M., 1060 (AB0055)
Arevalo Velandia A., 1473 (AB0900-HPR)
Arfa S., 955 (POS1345), 1193 (AB0337), 1194 (AB0339), 1393 (AB0723), 1410 (AB0768), 1415 (AB0776), 1415 (AB0778)
Argiro R., 1418 (AB0786)
Argunova V., 930 (POS1297)
Argyriou A., 38 (OP0072)
Argyris A., 656 (POS0807)
Argyropoulou O., 15 (OP0029), 656 (POS0807), 668 (POS0829)
Ariani A., 388 (POS0322), 1326 (AB0578)
Arias de la Rosa I., 20 (OP0038), 426 (POS0394), 469 (POS0475), 769 (POS1001), 1317 (AB0562)
Arıcı M., 350 (POS0255), 648 (POS0793), 1198 (AB0347)
Arici Z. S., 968 (POS1372)
Arida A., 703 (POS0894)
Aries P. M., 528 (POS0591), 1263 (AB0472)
Arikan D., 64 (OP0115)
Aringer M., 69 (OP0124), 544 (POS0615), 617 (POS0733), 635 (POS0764)
Aringhieri G., 642 (POS0778)
Aritomi T., 1094 (AB0132)
Ariyurek M., 817 (POS1076)
Ark R., 488 (POS0511), 1339 (AB0607)
Arkfeld D., 208 (POS0012), 348 (POS0252), 965 (POS1366)
Arkhipova A., 1331 (AB0589)
Armagan B., 1105 (AB0157), 1124 (AB0200), 1124 (AB0201), 1182 (AB0314), 1299 (AB0535)
Armann J., 882 (POS1199)
Armentaro G., 936 (POS1308), 1374 (AB0683)
Armiraglio E., 940 (POS1315)
Armstrong A., 795 (POS1042), 810 (POS1063), 1293 (AB0528)
Arnalich Fernández F., 693 (POS0875), 1192 (AB0333)
Arnau Bartes A., 891 (POS1215)
Arnaud L., 181 (OP0296), 632 (POS0758), 877 (POS1190)
Arnold J., 30 (OP0057), 1173 (AB0293)
Aronova E., 465 (POS0467), 1131 (AB0209), 1138 (AB0225), 1147 (AB0245), 1158 (AB0263), 1363 (AB0663)
Arora P., 1406 (AB0756), 1451 (AB0854)
Arous Y., 1417 (AB0784)
Arriga Torres M. J. R., 1078 (AB0098)
Arsenyeva S., 249 (POS0083), 918 (POS1267), 948 (POS1332), 1394 (AB0726)
Artim-Esen B., 282 (POS0142), 602 (POS0706), 604 (POS0710), 636 (POS0766), 912 (POS1257), 913 (POS1259), 951 (POS1339), 1006 (POS1445), 1191 (AB0331), 1210 (AB0369), 1251 (AB0448), 1359 (AB0653), 1409 (AB0766)
Arzu Sağlam E., 648 (POS0793), 1198 (AB0347)
Asai S., 1142 (AB0233)
Aschwanden M., 655 (POS0806)
Ascoli Marchetti A., 1418 (AB0786)
Aseeva E., 614 (POS0729), 1168 (AB0284), 1180 (AB0309), 1180 (AB0310), 1184 (AB0319), 1185 (AB0320)
Ashraf A., 381 (POS0310), 527 (POS0589), 574 (POS0663)
Asif R., 862 (POS1167)
Asif S., 381 (POS0310), 527 (POS0589), 574 (POS0663), 1075 (AB0093), 1298 (AB0533), 1328 (AB0581)
Asimakopoulou F., 193 (OP0317-PARE)
Askanase A., 177 (OP0289)
Askari A., 540 (POS0608)
Askelson M., 245 (POS0076)
Askling J., 63 (OP0114), 68 (OP0122), 82 (OP0140), 130 (OP0218), 133 (OP0222), 145 (OP0236), 217 (POS0027), 474 (POS0484), 535 (POS0601), 864 (POS1169), 939 (POS1313), 1090 (AB0122)
Aslam A., 30 (OP0057)
Aslam F., 535 (POS0602)
Aslanidis S., 620 (POS0738)
Asnagli H., 18 (OP0034)
Asnal C., 138 (OP0228)
Assadi R., 371 (POS0292), 1433 (AB0819), 1438 (AB0828), 1438 (AB0829)
Assaraf M., 662 (POS0818)
Assassi S., 1234 (AB0413)
Assing M., 529 (POS0592)
Assmus J., 397 (POS0339)
Assudani D., 779 (POS1022)
Assunção H., 481 (POS0496), 606 (POS0713), 1101 (AB0147)
Astbury C., 253 (POS0089), 1000 (POS1432)
Astegiano M., 335 (POS0230)
Aston J., 989 (POS1412)
Ata E. B., 817 (POS1076)
Atagündüz P., 731 (POS0935), 1266 (AB0479)
Atakan N., 1327 (AB0579)
Atalay E., 117 (OP0195)
Atanes-Sandoval A., 32 (OP0060)
Atarshchikov D., 14 (OP0027)
Atas N., 733 (POS0940)
Atay L. O., 1077 (AB0097)
Ates A., 532 (POS0597), 949 (POS1335)
Ateş A., 69 (OP0125), 731 (POS0935)
Ateş O., 1182 (AB0314)
Atheymen R., 1162 (AB0273)
Athimni S., 1341 (AB0611)
Atienza-Mateo B., 32 (OP0060), 490 (POS0513), 531 (POS0595), 955 (POS1346), 1046 (AB0026), 1076 (AB0094), 1076 (AB0096), 1208 (AB0365), 1208 (AB0366), 1243 (AB0430)

Atreya R., 996 (POS1426)
Atsumi T., 596 (POS0697), 687 (POS0863), 1150 (AB0249)
Attar S., 855 (POS1153), 1259 (AB0465), 1320 (AB0566)
Atteno M., 907 (POS1248)
Atzeni F., 190 (OP0310), 324 (POS0214), 1389 (AB0716)
Atzinger A., 165 (OP0272)
Au D., 374 (POS0298)
Aubin F., 1322 (AB0570)
Audo R., 19 (OP0035)
Auger I., 1061 (AB0058)
Aurrecoechea E., 610 (POS0721)
Austin J., 885 (POS1205)
Auteri S., 704 (POS0896)
Authar Singh A. K. B., 1469 (AB0891-HPR)
Avanoglu Guler A., 733 (POS0940), 878 (POS1193), 1077 (AB0097), 1176 (AB0300), 1235 (AB0414), 1266 (AB0479)
Avcin T., 39 (OP0074), 242 (POS0072), 247 (POS0079), 934 (POS1304), 941 (POS1318)
Avdeeva A., 464 (POS0465), 542 (POS0611), 1134 (AB0216)
Averinova S., 840 (POS1123)
Averkieva J., 277 (POS0131), 1344 (AB0621), 1416 (AB0780), 1443 (AB0838)
Avetisov K., 717 (POS0913)
Avetisov S., 717 (POS0913)
Avgustidis N., 184 (OP0299), 523 (POS0580), 733 (POS0941)
Avik A., 1 (OP0003)
Avila G., 1042 (AB0015), 1106 (AB0159)
Aviña A., 22 (OP0043), 377 (POS0303)
Avolio J., 584 (POS0678)
Avouac J., 172 (OP0284), 331 (POS0225), 360 (POS0274-HPR), 419 (POS0378), 534 (POS0600), 662 (POS0818), 1364 (AB0665)
Avramovska A., 66 (OP0119), 880 (POS1196)
Avril J., 843 (POS1129)
Avrusin I., 931 (POS1299)
Avsic-Zupanc T., 242 (POS0072), 941 (POS1318)
Ayala-Lugo A., 1042 (AB0015)
Ayala-Terrados L., 1215 (AB0376)
Ayan G., 518 (POS0568), 648 (POS0793), 728 (POS0931), 770 (POS1004), 814 (POS1070), 817 (POS1076), 971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1250 (AB0446), 1299 (AB0535), 1327 (AB0579)
Ayari R., 925 (POS1287), 926 (POS1289), 926 (POS1290), 1417 (AB0784)
Aydemir H., 1355 (AB0644)
Aydin S., 183 (OP0298), 224 (POS0037), 1213 (AB0373)
Aydogan M., 1191 (AB0331)
Ayish D. M., 855 (POS1153)
Aykac K., 908 (POS1249)
Aykara I., 676 (POS0844), 1054 (AB0044)
Ayko A., 361 (POS0275-HPR), 1080 (AB0104)
Ayoub S., 843 (POS1127), 876 (POS1189)
Ayral X., 1364 (AB0665)
Aza A., 1475 (AB0907-HPR)
Azevedo S., 293 (POS0162), 773 (POS1010), 830 (POS1100), 1424 (AB0799)
Azevedo V. F., 1287 (AB0522)
Azimi M., 92 (OP0153-HPR)
Azmillah R., 53 (OP0096)
Azoulay L. D., 1186 (AB0323)
Azova M., 1397 (AB0735)
Azpiri-Diaz H., 463 (POS0463), 478 (POS0491), 510 (POS0552), 511 (POS0553), 978 (POS1392), 984 (POS1404), 1189 (AB0329)
Azpiri-López J. R., 463 (POS0463), 473 (POS0482), 473 (POS0483), 478 (POS0491), 510 (POS0552), 511 (POS0553), 515 (POS0562), 816 (POS1074), 978 (POS1392), 983 (POS1402), 984 (POS1404), 1087 (AB0117), 1189 (AB0329)
Azuma K., 1181 (AB0311)
Azuma N., 1181 (AB0311)
Azzolina D., 878 (POS1192)
Azzouqah O., 1205 (AB0360)
Azzouzi H., 295 (POS0166), 519 (POS0570), 1162 (AB0274)

Babajanians A., 228 (POS0047)
Babak V., 899 (POS1232), 1367 (AB0670)
Babaoglu H., 733 (POS0940)
Babini A. M., 1196 (AB0342)
Babu A S S., 700 (POS0889)
Bacchiega A. B., 909 (POS1252), 1448 (AB0848)
Bacco B., 628 (POS0751)
Baccouch K., 858 (POS1160)
Baccouche C., 525 (POS0585), 1120 (AB0192)
Baccouche K., 472 (POS0481), 520 (POS0572), 521 (POS0573), 526 (POS0588), 837 (POS1116), 838 (POS1117), 923 (POS1279), 924 (POS1283), 1099 (AB0144), 1142 (AB0232), 1345 (AB0623), 1346 (AB0625), 1480 (AB0919-PARE)
Bachiller-Corral J., 884 (POS1204), 914 (POS1260)
Badot V., 884 (POS1203)
Badsha H., 361 (POS0275-HPR), 1080 (AB0104)
Bae S. C., 177 (OP0289), 218 (POS0028)
Bae Y., 1123 (AB0198)
Baecklund E., 864 (POS1169)
Baek H. J., 1152 (AB0253)
Baer A., 74 (OP0130)
Baerlecken N. T., 528 (POS0591)
Baert I., 828 (POS1096)
Baeuerle T., 165 (OP0272)
Baez R., 874 (POS1186)
Bagby S., 369 (POS0288)
Bagel J., 787 (POS1031)
Baglan Yentur S., 522 (POS0576)
Baglin A., 343 (POS0243)
Bagnasco F., 98 (OP0164), 947 (POS1330)
Bağrıaçık C., 191 (OP0313)
Baharuddin H., 459 (POS0457), 1346 (AB0626), 1469 (AB0891-HPR)
Bahaz N., 1144 (AB0237)
Bahiri R., 481 (POS0497), 992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811)
Bahlas S., 187 (OP0304-PARE), 579 (POS0670), 832 (POS1104)
Bahloul S., 1270 (AB0486), 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Bahrami S., 404 (POS0349)
Bai M., 1318 (AB0564)
Baildam E., 927 (POS1292)
Bairwa D., 701 (POS0890)
Bajhammoh W., 855 (POS1153)
Bajocchi G., 190 (OP0310), 1389 (AB0716)
Baker M., 1158 (AB0264), 1406 (AB0756)
Bakewell C., 136 (OP0226), 311 (POS0194)
Bakhashwain E., 855 (POS1153)
Bakhle D., 533 (POS0598), 537 (POS0604)
Bakır F., 733 (POS0940)
Bakirov B., 890 (POS1214)
Bakker M. M., 198 (OP0324-PARE), 374 (POS0299)
Bakker T., 1153 (AB0254)
Baklacioglu H. S., 959 (POS1354), 961 (POS1359)
Bakland G., 543 (POS0612), 934 (POS1305), 1245 (AB0433), 1392 (AB0722)
Baklouti S., 837 (POS1115), 856 (POS1155), 922 (POS1277), 1109 (AB0164), 1276 (AB0497), 1281 (AB0508), 1358 (AB0650), 1484 (AB0926-PARE)
Bakshi A., 9 (OP0015)
Bakulev A., 796 (POS1043), 1298 (AB0534), 1302 (AB0540)
Balakhonova T., 493 (POS0520)
Balan B., 1360 (AB0656)
Balan S., 915 (POS1262), 948 (POS1331)
Balandraud N., 900 (POS1234), 1061 (AB0058)
Balanescu A., 164 (OP0270), 183 (OP0298), 519 (POS0569), 681 (POS0854), 773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690), 1462 (AB0879-HPR)
Balarini L., 582 (POS0676)
Balbir-Gurman A., 386 (POS0318), 691 (POS0871), 753 (POS0974), 892 (POS1217)
Balboa-Barreiro V., 403 (POS0347)
Balcı A., 627 (POS0750)
Balci Peynircioglu B., 971 (POS1378)
Baldassi F., 1206 (AB0361)
Baldi C., 573 (POS0661), 669 (POS0832), 746 (POS0963), 1252 (AB0450)
Baldini C., 78 (OP0135), 178 (OP0291), 642 (POS0778), 644 (POS0782)
Baldissera E. M., 30 (OP0056)
Baldissera E., 348 (POS0253), 955 (POS1347), 1206 (AB0361)
Baldivieso J. P., 560 (POS0645), 719 (POS0917), 1241 (AB0427)
Baldock D., 862 (POS1166), 1330 (AB0587)
Balduzzi S., 51 (OP0093)
Balevi Batur E., 1323 (AB0572)
Balfour A., 1130 (AB0208)
Balik Z., 1398 (AB0737)
Ball E., 161 (OP0265-HPR), 1243 (AB0429), 1410 (AB0767)
Ballesteros J. G., 1139 (AB0227)
Balogun S., 365 (POS0280)
Baloun J., 1051 (AB0038), 1062 (AB0063)
Balsa A., 546 (POS0617), 1047 (AB0027), 1101 (AB0149)
Bamford R., 458 (POS0456)
Bande J. M., 635 (POS0763), 771 (POS1005)
Bandi L., 1007 (POS1447)
Bandini G., 105 (OP0176)
Bandyopadhyay S., 1137 (AB0223)
Banerjee I., 1050 (AB0034)
Banerjee S., 137 (OP0227), 314 (POS0198), 795 (POS1042)
Bang H., 206 (POS0009)
Baniandrés O., 1385 (AB0706)
Bankole A., 297 (POS0170)
Bannert B., 108 (OP0180), 453 (POS0447), 533 (POS0599), 1128 (AB0207)
Banneville B., 172 (OP0284)
Bannon P., 654 (POS0804)
Bannour I., 1415 (AB0776)
Bansal N., 476 (POS0487)
Bansal P., 655 (POS0805)
Banshhikova N., 1045 (AB0023)
Banz Y., 649 (POS0795)
Bao C., 574 (POS0664), 1258 (AB0463)
Bao W., 797 (POS1044), 803 (POS1051)
Bao Y., 646 (POS0787)
Bär J., 676 (POS0844)
Baraf H. S. B., 580 (POS0671)
Baraff A., 369 (POS0287)
Baraliakos X., 83 (OP0141), 135 (OP0225), 152 (OP0250), 153 (OP0251), 155 (OP0253), 189 (OP0309), 221 (POS0032), 222 (POS0033), 224 (POS0038), 233 (POS0055), 332 (POS0226), 334 (POS0229), 338 (POS0235), 340 (POS0239), 344 (POS0245), 376 (POS0301), 525 (POS0584), 707 (POS0900), 712 (POS0907), 714 (POS0910), 720 (POS0918), 720 (POS0919), 728 (POS0930), 752 (POS0973), 851 (POS1145), 1262 (AB0471), 1263 (AB0472), 1289 (AB0524), 1375 (AB0684), 1435 (AB0823)
Baranov A., 1095 (AB0135)
Baranova M., 854 (POS1151), 855 (POS1152)
Barata Cavaleiro A. J., 161 (OP0264-HPR)
Baratella E., 1002 (POS1435)
Baravalle M., 1133 (AB0214)
Barawi A., 1052 (AB0039)
Barbagli S., 190 (OP0310), 1389 (AB0716)
Barbaglia A. L., 382 (POS0312)
Barbarroja Puerto N., 20 (OP0038), 426 (POS0394), 469 (POS0475), 769 (POS1001), 1065 (AB0070), 1317 (AB0562)
Barbati C., 1069 (AB0079), 1073 (AB0087)
Barbazan C., 523 (POS0579)
Barbazán C., 760 (POS0985)
Barber C. E. H., 377 (POS0303)
Barbey C., 597 (POS0698), 598 (POS0699)
Barbhaiya M., 607 (POS0715)
Barbich T., 887 (POS1208)
Barbosa Camacho J., 1139 (AB0227)
Barbosa Campanholo C., 139 (OP0229)
Barbosa J., 627 (POS0749), 1192 (AB0335), 1193 (AB0336)

Barbulescu A., 68 (OP0122)
Barcelo Bru M., 929 (POS1296)
Barcelos A., 131 (OP0220), 217 (POS0027), 738 (POS0950), 820 (POS1083)
Barcelos F., 593 (POS0692)
Barcenilla-Wong A., 358 (POS0269-HPR)
Barchuk W., 83 (OP0141)
Barcomb L., 1315 (AB0559)
Bardan I., 934 (POS1305), 1392 (AB0722)
Bardelli M., 573 (POS0661), 669 (POS0832), 746 (POS0963)
Bardet C., 228 (POS0046)
Bardin T., 841 (POS1124)
Barguil Macedo M., 826 (POS1093)
Baribaud F., 790 (POS1036)
Barile A., 954 (POS1344), 957 (POS1349), 1105 (AB0156)
Barington T., 419 (POS0377)
Barinotti A., 298 (POS0172), 1039 (AB0008), 1073 (AB0088)
Barinova A., 14 (OP0027), 204 (POS0004)
Barisione E., 1372 (AB0679)
Barloco L., 382 (POS0312)
Barnetche T., 1261 (AB0469)
Barnhill J., 607 (POS0715)
Baron M., 1237 (AB0419)
Barone F., 78 (OP0135)
Barragán-Garfías A., 904 (POS1242), 905 (POS1245)
Barreira-Hernández D., 144 (OP0234)
Barreiro-de-Acosta M., 916 (POS1264)
Barrera M. J., 303 (POS0180)
Barrett C., 166 (OP0274-PARE)
Barrett J., 289 (POS0152-HPR)
Barriga-Maldonado E., 1439 (AB0830), 1445 (AB0843)
Barros R., 644 (POS0781)
Barroso García N., 1324 (AB0574)
Barroso T., 1282 (AB0510)
Barsotti S., 906 (POS1246), 1232 (AB0407)
Bartholmai B., 389 (POS0325)
Bartlett S. J., 159 (OP0262-HPR), 356 (POS0267-HPR), 1014 (POS1459-HPR)
Bartnicka-Masłowska K., 1123 (AB0198)
Bartoletti A., 1 (OP0003)
Bartoli F., 546 (POS0618), 1032 (POS1495-HPR), 1154 (AB0256)
Bartoloni A., 897 (POS1228)
Bartoloni Bocci E., 211 (POS0019), 324 (POS0214), 594 (POS0693), 630 (POS0755)
Barton A., 403 (POS0348), 467 (POS0471)
Bartz-Bazzanella P., 1274 (AB0494)
Barua I., 104 (OP0174), 1245 (AB0433)
Basaran Ö., 908 (POS1249)
Basch A., 571 (POS0659)
Bashkinov R., 1352 (AB0636)
Bashkova I., 1095 (AB0135), 1335 (AB0596)
Basnayake B., 218 (POS0028)
Basnet A., 1305 (AB0545)
Basoski N., 238 (POS0063-PARE)
Bass A., 367 (POS0285)
Bastón I., 916 (POS1264)
Basu N., 1159 (AB0265)
Basualto S., 1448 (AB0848)
Bata-Csorgo Z., 4 (OP0008)
Batalov A., 732 (POS0938)
Batalov Z., 835 (POS1109)
Bateman J., 5 (OP0009-PARE), 903 (POS1241)
Batheesh A., 131 (OP0219)
Batlle-López A., 1436 (AB0825)
Batool S., 381 (POS0310), 527 (POS0589), 574 (POS0663), 1298 (AB0533), 1328 (AB0581)
Battagliotti C., 247 (POS0079), 934 (POS1304)
Batterham R., 374 (POS0299)
Batteux F., 534 (POS0600)
Batticciotto A., 190 (OP0310), 284 (POS0145), 1319 (AB0565), 1389 (AB0716)
Battista S., 292 (POS0160-HPR)
Baudoin P., 1107 (AB0160)
Bauer E., 170 (OP0282)
Bauer L., 334 (POS0229), 704 (POS0896), 705 (POS0897)
Bauer P., 673 (POS0838)
Baumeister H., 943 (POS1321)
Bautista-Molano W., 24 (OP0047), 1296 (AB0531)
Bay L. T., 1468 (AB0890-HPR)
Bayat S., 88 (OP0148), 979 (POS1394), 1275 (AB0495)
Baygul A., 532 (POS0597)
Bayindir O., 861 (POS1165), 1255 (AB0456), 1366 (AB0669)
Bay-Jensen A. C., 444 (POS0431), 468 (POS0473), 742 (POS0955), 748 (POS0966), 1064 (AB0067)
Bayliss J., 1484 (AB0925-PARE)
Baymeeva N., 465 (POS0467), 1158 (AB0263)
Baynton E., 862 (POS1166), 1330 (AB0587)
Bayrakci B., 908 (POS1249)
Bayraktar D., 1366 (AB0669), 1454 (AB0862-HPR)
Bayram D., 1182 (AB0314)
Bayram S., 1462 (AB0877-HPR)
Bays A., 994 (POS1422)
Baysal S., 532 (POS0597), 949 (POS1335)
Bazzani C., 530 (POS0593)
Bazzarelli M., 382 (POS0312)
Bazzichi L., 190 (OP0310), 1389 (AB0716)
Bdewi M., 777 (POS1020)
Beaart- van de Voorde L., 87 (OP0147)
Bean S., 1171 (AB0289)
Beauvais C., 1009 (POS1450)
Becce F., 278 (POS0134), 841 (POS1124), 845 (POS1132), 846 (POS1133)
Beccia A., 1022 (POS1474-HPR)
Becciolini A., 1326 (AB0578)
Bechman K., 744 (POS0959), 1357 (AB0649)
Beck C., 366 (POS0283), 824 (POS1089), 1050 (AB0035)
Beck D., 49 (OP0090)
Beck M., 1383 (AB0701)
Becker B., 1316 (AB0560)
Becker M. O., 694 (POS0877)
Beckmann I., 4 (OP0008)
Bečvář R., 384 (POS0316), 677 (POS0846), 1233 (AB0410)
Becvar V., 424 (POS0388)
Bedaiwi M., 1320 (AB0566)
Bedina S., 424 (POS0389), 1056 (AB0048), 1057 (AB0049), 1062 (AB0061), 1108 (AB0163), 1444 (AB0841)
Beesley R., 168 (OP0278-PARE), 1373 (AB0681)
Beggio M., 392 (POS0329)
Begum J., 1024 (POS1478-HPR), 1028 (POS1488-HPR)
Behanova M., 848 (POS1137)
Behar C., 1127 (AB0205)
Behning C., 91 (OP0151), 846 (POS1134), 920 (POS1271)
Behrens F., 135 (OP0225), 137 (OP0227), 311 (POS0194), 314 (POS0198), 373 (POS0296), 797 (POS1044), 806 (POS1055), 1288 (AB0523), 1289 (AB0524), 1306 (AB0547), 1311 (AB0553), 1315 (AB0559)
Beidas R., 810 (POS1063)
Beider S., 1186 (AB0322), 1385 (AB0707)
Beirão T., 1236 (AB0415), 1236 (AB0416)
Bejia I., 466 (POS0469), 1051 (AB0037), 1390 (AB0718), 1395 (AB0728), 1414 (AB0775)
Beketova T., 899 (POS1232), 1367 (AB0670)
Bekhtereva I., 647 (POS0790)
Bekis R., 627 (POS0750)
Bektaş E., 602 (POS0706)
Bektas M., 191 (OP0313), 912 (POS1257)
Bektaş M., 282 (POS0142), 602 (POS0706), 913 (POS1259), 951 (POS1339), 1327 (AB0579), 1409 (AB0766)
Belén Bravo S., 1048 (AB0030)
Belettato C., 168 (OP0277-PARE)
Belevonis G., 646 (POS0786)
Belghali S., 472 (POS0481), 1480 (AB0919-PARE)
Belhaj W., 1332 (AB0590), 1333 (AB0592), 1333 (AB0593)
Belkhiri M., 955 (POS1345), 1393 (AB0723), 1410 (AB0768)
Bellando Randone S., 105 (OP0176), 385 (POS0317), 387 (POS0321), 675 (POS0842), 906 (POS1246), 1032 (POS1495-HPR)
Bellando-Randone S., 355 (POS0264), 546 (POS0618), 897 (POS1228), 1192 (AB0334)
Belletti L., 1416 (AB0781)
Bellis E., 985 (POS1406)
Bellisai F., 669 (POS0832), 1252 (AB0450)
Bello-Gualtero J. M., 483 (POS0501)
Belloli L., 685 (POS0861)
Bellomio V. I., 635 (POS0763), 1196 (AB0342)
Bellone F., 838 (POS1119)
Belot A., 872 (POS1183)
Belousova E., 14 (OP0027), 1283 (AB0513)
Belov B., 614 (POS0729), 854 (POS1151), 855 (POS1152), 1180 (AB0309), 1180 (AB0310), 1363 (AB0663), 1406 (AB0757), 1407 (AB0759)
Belsack V., 589 (POS0687)
Beltai A., 379 (POS0306)
Beltrami M., 355 (POS0265)
Beltrán E., 32 (OP0060), 755 (POS0978), 952 (POS1340), 1225 (AB0396), 1303 (AB0542), 1412 (AB0771)
Belvisi M., 253 (POS0089)
Belvivere L., 1418 (AB0786)
Bély M., 1321 (AB0569)
Belyaeva I., 191 (OP0311)
Belyakova E., 647 (POS0790)
Belzunegui Otano J. M., 1141 (AB0230), 1279 (AB0503), 1303 (AB0542)
Bemark M., 14 (OP0026)
Ben Abdallah H., 975 (POS1385)
Ben Abdelghani K., 292 (POS0159-HPR), 481 (POS0497), 522 (POS0577), 835 (POS1110), 1030 (POS1491-HPR), 1113 (AB0173), 1113 (AB0174), 1117 (AB0184), 1118 (AB0188), 1277 (AB0499), 1332 (AB0590), 1333 (AB0592), 1333 (AB0593), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1368 (AB0672), 1368 (AB0673), 1381 (AB0698), 1390 (AB0717), 1397 (AB0736), 1411 (AB0770), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Ben Abderrazek Y., 1116 (AB0182)
Ben Aissa R., 290 (POS0155-HPR), 856 (POS1155), 1358 (AB0650)
Ben Ali K., 1066 (AB0071)
Ben Ammar L., 1090 (AB0123), 1097 (AB0139)
Ben Brahim M., 1198 (AB0346)
Ben Chehida R., 1414 (AB0775)
Ben Chekaya N., 923 (POS1281), 1225 (AB0395), 1395 (AB0730), 1396 (AB0731), 1396 (AB0732), 1415 (AB0777)
Ben Fredj F., 1219 (AB0383)
Ben Hassine I., 1219 (AB0383)
Ben Jemaa S., 837 (POS1115), 922 (POS1277), 1109 (AB0164), 1276 (AB0497), 1281 (AB0508), 1484 (AB0926-PARE)
Ben Majdouba M., 1147 (AB0244), 1272 (AB0490), 1273 (AB0492)
Ben Ncib D., 1400 (AB0744)
Ben Nessib D., 1101 (AB0148), 1112 (AB0171), 1286 (AB0520)
Ben Nsib D., 921 (POS1274), 1095 (AB0133), 1102 (AB0150), 1118 (AB0187)
Ben Rejeb B., 1193 (AB0337), 1194 (AB0339)
Ben Saidane O., 1396 (AB0732)
Ben Salem A., 525 (POS0585), 1063 (AB0064), 1111 (AB0169), 1120 (AB0192), 1193 (AB0337), 1194 (AB0339), 1472 (AB0897-HPR)
Ben Salem M., 1061 (AB0059)
Ben Slimen B., 975 (POS1385)
Ben Tekaya A., 481 (POS0497), 768 (POS1000), 1106 (AB0158), 1119 (AB0190), 1285 (AB0517), 1341 (AB0611), 1395 (AB0730), 1396 (AB0731), 1396 (AB0732)
Ben Tekaya R., 525 (POS0585), 1063 (AB0064), 1111 (AB0169), 1193 (AB0337), 1194 (AB0339), 1472 (AB0897-HPR)
Ben Ticha R., 664 (POS0822)
Ben Youssef S., 1061 (AB0059)
Benamar S., 54 (OP0098), 518 (POS0566)
Benavent D., 304 (POS0181), 750 (POS0969), 1277 (AB0500)
Benavidez F., 382 (POS0312)
Benaziez.Boutaleb R., 1144 (AB0237)
Bendahan D., 367 (POS0284), 1078 (AB0099)
Bendahmane C., 857 (POS1158), 858 (POS1159)
Bendzuck G., 1013 (POS1458-HPR)

Benegas M., 730 (POS0933), 771 (POS1005), 1377 (AB0689)
Benesova K., 372 (POS0293), 467 (POS0472)
Bengana B., 843 (POS1127)
Bengeri S., 1050 (AB0034)
Bengtsson K., 115 (OP0192)
Benhamou Y., 612 (POS0724)
Benini C., 867 (POS1173)
Benitez A., 382 (POS0312), 771 (POS1005)
Bennell K., 291 (POS0157-HPR)
Benoy S., 880 (POS1197)
Ben-Shachar R., 458 (POS0456)
Bentivegna M., 190 (OP0310), 1389 (AB0716)
Bentlage A., 1044 (AB0020)
Benveniste O., 196 (OP0321), 388 (POS0323)
Benvenuti F., 594 (POS0693)
Benzaquen N., 1196 (AB0342)
Benzin P., 1312 (AB0554)
Beranger M., 1009 (POS1450)
Berardi V., 585 (POS0681)
Berardicurti O., 954 (POS1344), 957 (POS1349), 1105 (AB0156)
Berbotto G., 875 (POS1188)
Berdal G., 92 (OP0153-HPR)
Berenbaum F., 109 (OP0181), 170 (OP0282), 230 (POS0051), 258 (POS0095), 417 (POS0373), 829 (POS1099), 1368 (AB0674)
Berendes R., 883 (POS1202), 936 (POS1309)
Berends S., 241 (POS0070)
Beresford M., 927 (POS1292)
Beretta G. B., 940 (POS1316)
Beretta G., 935 (POS1307), 941 (POS1317)
Bergaoui N., 466 (POS0469), 856 (POS1155), 1051 (AB0037), 1198 (AB0346), 1358 (AB0650), 1390 (AB0718), 1395 (AB0728), 1414 (AB0775)
Berger C., 655 (POS0806)
Berger J., 983 (POS1401)
Berghea F., 164 (OP0270), 681 (POS0854), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690)
Bergier H., 877 (POS1190)
Bergkamp S., 937 (POS1311), 1070 (AB0081)
Bergman M., 446 (POS0436), 579 (POS0670), 1311 (AB0553)
Bergmann C., 165 (OP0272), 391 (POS0328), 1075 (AB0091)
Bergmans P., 140 (OP0230), 142 (OP0232), 778 (POS1021), 799 (POS1046), 1295 (AB0530)
Bergner R., 846 (POS1134)
Bergö M., 12 (OP0022)
Bergsten U., 1350 (AB0633)
Bergstra S. A., 256 (POS0093), 259 (POS0097), 466 (POS0470), 471 (POS0479), 932 (POS1300)
Berking C., 996 (POS1426)
Berkun Y., 872 (POS1183)
Berli M., 11 (OP0020)
Berman H., 1196 (AB0342)
Berman J., 1309 (AB0551)
Berman M., 1309 (AB0551)
Bermudez Bermejo P. E., 853 (POS1149), 1386 (AB0709)
Bermúdez E., 1081 (AB0106)
Bernabei I., 226 (POS0041)
Bernabéu P., 820 (POS1081), 1208 (AB0366)
Bernal J. A., 610 (POS0721)
Bernal S., 1093 (AB0129)
Bernardes M., 260 (POS0100), 318 (POS0204), 476 (POS0488), 483 (POS0502), 718 (POS0914), 812 (POS1067), 833 (POS1106), 836 (POS1113), 919 (POS1270), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1299 (AB0536), 1339 (AB0608), 1432 (AB0816), 1441 (AB0835)
Bernardi S., 1391 (AB0719)
Bernardo A., 836 (POS1113), 1265 (AB0476)
Bernatsky S., 10 (OP0018), 173 (OP0285), 173 (OP0286), 177 (OP0289), 230 (POS0050), 235 (POS0058-PARE), 918 (POS1268), 993 (POS1420)
Berner Hammer H., 47 (OP0087), 1090 (AB0122)
Berni E., 1000 (POS1432)
Bernini C., 1201 (AB0354)
Bernstein E., 1234 (AB0413)
Berntson L., 247 (POS0079), 934 (POS1304)
Berriche O., 955 (POS1345), 1193 (AB0337), 1194 (AB0339), 1393 (AB0723), 1410 (AB0768), 1415 (AB0776), 1415 (AB0778)
Berry M., 275 (POS0128)
Bertani A., 355 (POS0265)
Bertero T., 628 (POS0751)
Bertheussen H., 139 (OP0229)
Berti A., 345 (POS0248), 1213 (AB0373)
Bertoldo E., 62 (OP0112), 106 (OP0178), 560 (POS0644), 867 (POS1173)
Bertoldo F., 831 (POS1102)
Bertoli A., 875 (POS1188)
Bertolini E., 355 (POS0265)
Bertolo M., 582 (POS0676)
Bertrand D., 356 (POS0266-HPR), 375 (POS0300), 484 (POS0503), 545 (POS0616), 1001 (POS1433), 1001 (POS1434), 1083 (AB0109)
Bertrand J., 120 (OP0200), 226 (POS0041)
Bertsias G., 11 (OP0019), 39 (OP0074), 181 (OP0296), 184 (OP0299), 523 (POS0580), 631 (POS0757), 632 (POS0759), 635 (POS0764), 733 (POS0941)
Bes C., 69 (OP0125), 731 (POS0935)
Besbes S., 1119 (AB0189)
Besbes Y., 1119 (AB0189)
Besisik B., 191 (OP0313)
Besısık S. K., 191 (OP0313)
Beskri O., 1095 (AB0134)
Bessette L., 84 (OP0143), 159 (OP0262-HPR), 251 (POS0087), 328 (POS0220), 336 (POS0232), 712 (POS0907), 800 (POS1047), 1014 (POS1459-HPR), 1312 (AB0555), 1313 (AB0557), 1314 (AB0558)
Bessonova I., 1403 (AB0750)
Besutti G., 37 (OP0069)
Besuyen R., 70 (OP0126), 83 (OP0141), 255 (POS0092), 569 (POS0657), 570 (POS0658), 792 (POS1037), 792 (POS1038), 801 (POS1049)
Betelli M., 105 (OP0175)
Bettaieb H., 1399 (AB0740), 1399 (AB0741), 1400 (AB0742)
Bettencourt P., 637 (POS0767), 1195 (AB0340)
Betteridge N., 101 (OP0169-PARE)
Bettiol A., 889 (POS1212)
Betz M., 45 (OP0083)
Beyaztaş L., 1021 (POS1471-HPR)
Beynon H., 1230 (AB0403)
Bhadauria N., 1411 (AB0769)
Bhana S., 2 (OP0006), 173 (OP0286), 175 (OP0288)
Bhandari J., 21 (OP0039)
Bharadwaj A., 1157 (AB0262)
Bhargava V., 1043 (AB0018)
Bhatraju P., 192 (OP0314)
Bhattoa H. P., 226 (POS0043)
Bi L., 574 (POS0664)
Bialik E., 1329 (AB0585), 1388 (AB0714)
Bialik V., 1329 (AB0585), 1388 (AB0714)
Bianchi D., 909 (POS1252)
Bianchi G., 833 (POS1105), 1007 (POS1447), 1216 (AB0379), 1271 (AB0488)
Bianciardi E., 1434 (AB0821)
Biancone L., 335 (POS0231)
Biard L., 37 (OP0068)
Biasi G., 190 (OP0310), 1389 (AB0716)
Bibulatova F., 275 (POS0127)
Bica B., 247 (POS0079), 625 (POS0747), 909 (POS1252), 934 (POS1304), 999 (POS1430), 1448 (AB0848)
Bica P. F., 1372 (AB0679)
Biddle K., 879 (POS1195)
Bienicka M., 470 (POS0477)
Bierma-Zeinstra S. M. A., 61 (OP0111), 1372 (AB0678)
Biesen R., 156 (OP0256), 305 (POS0183), 623 (POS0744)
Biggers S., 279 (POS0135)
Biggioggero M., 229 (POS0048)
Biglia A., 24 (OP0047), 1477 (AB0911-HPR)
Bijlsma H., 101 (OP0169-PARE), 199 (LB0002)
Bilberg A., 811 (POS1064)
Bilge A. K., 1251 (AB0448)
Bilgen Ş. A., 518 (POS0568), 648 (POS0793), 659 (POS0813), 728 (POS0931), 770 (POS1004), 814 (POS1070), 971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1250 (AB0446), 1299 (AB0535)
Bilgin E., 69 (OP0125), 347 (POS0251), 350 (POS0255), 518 (POS0568), 648 (POS0793), 728 (POS0931), 770 (POS1004), 814 (POS1070), 971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1299 (AB0535)
Bilginer Y., 100 (OP0168), 117 (OP0195), 243 (POS0074), 908 (POS1249), 930 (POS1298), 1398 (AB0737)
Bilia S., 906 (POS1246)
Bilici Salman R., 733 (POS0940), 878 (POS1193), 1077 (AB0097), 1176 (AB0300)
Biljan A., 723 (POS0924), 734 (POS0943)
Bilukha A., 811 (POS1065), 1320 (AB0567)
Bindee K., 173 (OP0285), 230 (POS0050)
Bingham C., 356 (POS0267-HPR), 539 (POS0607), 1014 (POS1459-HPR)
Binutti M., 878 (POS1192), 883 (POS1201)
Birch L., 18 (OP0034)
Bird P., 89 (OP0149), 153 (OP0252), 547 (POS0619), 794 (POS1040)
Birlik M., 627 (POS0750), 1247 (AB0437), 1256 (AB0459), 1386 (AB0708)
Birt J., 561 (POS0646)
Bismuth K., 417 (POS0373)
Bisoendial R., 1296 (AB0531)
Bistoni O., 630 (POS0755)
Biswas P., 584 (POS0678)
Bitsadze V., 619 (POS0737)
Bitzogli K., 1381 (AB0697)
Bixio R., 326 (POS0218), 1477 (AB0911-HPR)
Bizid S., 975 (POS1385)
Bjarnason H., 951 (POS1338)
Bjørngaard H., 951 (POS1337), 995 (POS1424)
Bjursten S., 112 (OP0186)
Blachley T., 26 (OP0049), 446 (POS0435), 530 (POS0594), 538 (POS0606)
Black R. J., 1441 (AB0834)
Black R., 1098 (AB0142)
Black S., 527 (POS0590), 539 (POS0607)
Blagojevic J., 163 (OP0269), 1032 (POS1495-HPR)
Blair J., 742 (POS0955)
Blake J., 1057 (AB0051)
Blanchard M., 120 (OP0199)
Blanco A., 967 (POS1371), 1225 (AB0396), 1412 (AB0771)
Blanco E. S., 382 (POS0312)
Blanco F. J., 306 (POS0185), 366 (POS0282), 403 (POS0347), 418 (POS0375), 425 (POS0392), 1051 (AB0036)
Blanco J. M., 68 (OP0123), 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Blanco R., 32 (OP0060), 34 (OP0064), 35 (OP0065), 50 (OP0091), 91 (OP0152), 138 (OP0228), 220 (POS0030), 490 (POS0513), 531 (POS0595), 563 (POS0649), 601 (POS0703), 610 (POS0721), 621 (POS0740), 707 (POS0900), 730 (POS0934), 755 (POS0977), 899 (POS1231), 952 (POS1340), 953 (POS1342), 955 (POS1346), 960 (POS1357), 963 (POS1362), 966 (POS1370), 967 (POS1371), 970 (POS1376), 977 (POS1390), 986 (POS1407), 1002 (POS1436), 1018 (POS1467-HPR), 1046 (AB0026), 1065 (AB0070), 1076 (AB0094), 1076 (AB0096), 1208 (AB0365), 1208 (AB0366), 1225 (AB0396), 1226 (AB0397), 1227 (AB0399), 1243 (AB0430), 1287 (AB0522), 1324 (AB0574), 1377 (AB0688), 1412 (AB0771), 1436 (AB0825)
Blanco-Madrigal J. M., 1076 (AB0096)
Blank N., 50 (OP0092), 670 (POS0834), 971 (POS1379), 972 (POS1380)
Blasco Santana L., 1192 (AB0333)
Blauvelt A., 795 (POS1042), 1130 (AB0208), 1297 (AB0532)
Blavnsfeldt A. B., 451 (POS0444)
Bleckwedel-Rolack L., 420 (POS0381)
Blettery M., 735 (POS0945)
Bley O., 528 (POS0591)
Bliddal S., 382 (POS0313)
Blizzard L., 276 (POS0129), 309 (POS0190), 365 (POS0280)
Bloch-Queyrat C., 52 (OP0094)
Blockmans D., 655 (POS0806)
Bloem H., 351 (POS0257), 978 (POS1391)

Blomberg A., 743 (POS0957)
Blomberg N., 1045 (AB0022)
Blonk A., 603 (POS0708), 604 (POS0709)
Blüml S., 475 (POS0485)
Blundell A., 879 (POS1195)
Blüthgen C., 90 (OP0150)
Blyszczuk P., 394 (POS0333)
Bø I., 92 (OP0153-HPR)
Bobbio Pallavicini F., 1260 (AB0467)
Bobirca F., 519 (POS0569)
Boboshko T., 916 (POS1263), 917 (POS1266)
Bobrikova D., 1095 (AB0135)
Bodnár N., 226 (POS0043)
Bodoki L., 226 (POS0043)
Boedecker J., 465 (POS0468)
Boehncke W. H., 787 (POS1031), 1291 (AB0526), 1300 (AB0538)
Boel A., 26 (OP0050), 339 (POS0236), 341 (POS0240), 735 (POS0944), 741 (POS0954)
Boers M., 114 (OP0189), 136 (OP0226), 314 (POS0197), 324 (POS0213), 1107 (AB0160)
Boffini N., 134 (OP0223)
Bogatyreva A., 1049 (AB0033)
Bogdan D., 890 (POS1214)
Bogdanos D., 1299 (AB0537)
Bogdanova S., 1393 (AB0724)
Bogdanova-Petrova S., 896 (POS1224), 1138 (AB0224)
Bogunia-Kubik K., 9 (OP0017)
Bohl-Buehler M., 135 (OP0225)
Bohmat L., 1401 (AB0745), 1403 (AB0750)
Bohne-Japiassu K., 393 (POS0331)
Bohórquez C., 610 (POS0721)
Böhringer S., 273 (POS0123)
Boiardi L., 37 (OP0069)
Boileau C., 258 (POS0095), 1127 (AB0205)
Boire G., 159 (OP0262-HPR), 1014 (POS1459-HPR)
Boisson M., 1364 (AB0665)
Boisvert A., 1043 (AB0019)
Bojinca M., 519 (POS0569), 773 (POS1009)
Bojinca V., 164 (OP0270), 681 (POS0854), 773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690), 1462 (AB0879-HPR)
Bokarewa M. I., 12 (OP0022), 14 (OP0026), 192 (OP0315), 428 (POS0397)
Bolce R., 333 (POS0228), 707 (POS0901), 710 (POS0904), 713 (POS0908), 714 (POS0909), 716 (POS0912), 718 (POS0915), 798 (POS1045), 1034 (POS1499-PARE), 1262 (AB0471), 1301 (AB0539)
Bolek E. C., 518 (POS0568), 648 (POS0793), 659 (POS0813), 728 (POS0931), 770 (POS1004), 814 (POS1070), 971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1299 (AB0535)
Boletis J. N., 635 (POS0764)
Boleto G., 345 (POS0248), 1213 (AB0373)
Bolstad N., 185 (OP0301)
Bolt H., 186 (OP0303-HPR)
Bolt J. W., 425 (POS0391)
Bomba D., 595 (POS0695)
Bombaci M., 229 (POS0048)
Bombardier C., 107 (OP0179), 452 (POS0445), 454 (POS0448), 454 (POS0449)
Bombardieri M., 7 (OP0011), 74 (OP0130), 79 (OP0136)
Bonazza S., 190 (OP0310), 1389 (AB0716)
Bond S., 168 (OP0277-PARE)
Bondt A., 1044 (AB0020)
Bonek K., 822 (POS1086)
Bonella F., 670 (POS0834)
Bonfa E., 909 (POS1252)
Bongenaar M., 1058 (AB0052)
Bonifati C., 1318 (AB0563)
Bonilla G., 610 (POS0721), 914 (POS1260)
Bonilla Gonzalez-Leganá C., 914 (POS1260)
Bonora A., 1222 (AB0389)
Boone N. W., 540 (POS0609)
Boone N., 911 (POS1256)
Boonen A., 101 (OP0169-PARE), 193 (OP0316), 198 (OP0324-PARE), 273 (POS0123), 340 (POS0238), 374 (POS0299), 484 (POS0503), 739 (POS0951), 751 (POS0971), 1479 (AB0915-PARE)
Boonstra M., 203 (POS0001)
Booth N., 1307 (AB0548)
Boots A., 33 (OP0062), 36 (OP0066), 657 (POS0809)
Bootsma H., 74 (OP0130), 78 (OP0135), 189 (OP0308), 221 (POS0031), 775 (POS1014), 1071 (AB0082), 1257 (AB0462)
Boquet M. D., 34 (OP0064)
Borah M., 1043 (AB0019)
Borangiu A., 164 (OP0270), 681 (POS0854), 773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690)
Borba E., 909 (POS1252)
Borg A., 260 (POS0101), 1068 (AB0077)
Borges I., 1282 (AB0510)
Borgiani P., 1038 (AB0006)
Borie R., 258 (POS0095), 897 (POS1227)
Borisova A., 1180 (AB0308), 1364 (AB0664)
Borjesson O., 898 (POS1230)
Bork C. S., 215 (POS0025)
Borlu M., 1327 (AB0579)
Borné Y., 372 (POS0295)
Borner U., 649 (POS0795)
Borocco C., 939 (POS1314)
Borodina I., 37 (OP0070)
Borrell Paños H., 1158 (AB0264)
Borrelli R., 335 (POS0230)
Bort S., 21 (OP0039)
Borte M., 50 (OP0092), 882 (POS1199), 972 (POS1380)
Borthakur S., 1043 (AB0019), 1050 (AB0034)
Bortolotti R., 51 (OP0093)
Bortoluzzi A., 134 (OP0223), 233 (POS0055), 470 (POS0476), 594 (POS0693), 607 (POS0716), 628 (POS0751), 1435 (AB0822)
Borucki R., 383 (POS0315)
Borzova E., 1414 (AB0774)
Bos R., 775 (POS1014), 805 (POS1053), 1107 (AB0160)
Boscarino J., 824 (POS1089)
Bosch P., 189 (OP0309), 261 (POS0102)
Bosello F., 1222 (AB0389)
Bosello S. L., 163 (OP0269), 370 (POS0289), 687 (POS0864), 701 (POS0891)
Bosio G., 650 (POS0797), 658 (POS0811)
Boteanu A., 610 (POS0721), 914 (POS1260), 946 (POS1327)
Botelho R., 582 (POS0676)
Both C., 540 (POS0608)
Botson J., 1348 (AB0630)
Bottaro L. C., 1007 (POS1447)
Böttcher J., 1422 (AB0796)
Botticella G., 833 (POS1105)
Bottois C., 360 (POS0273-HPR), 1364 (AB0665)
Bouagina E., 856 (POS1155), 1358 (AB0650)
Bouajina E., 472 (POS0481), 520 (POS0572), 521 (POS0573), 526 (POS0588), 837 (POS1116), 838 (POS1117), 858 (POS1160), 923 (POS1279), 924 (POS1283), 1099 (AB0144), 1142 (AB0232), 1345 (AB0623), 1346 (AB0625), 1480 (AB0919-PARE)
Bouali R., 975 (POS1385)
Bouaziz I., 1162 (AB0273)
Bouaziz M., 526 (POS0586), 526 (POS0587), 1112 (AB0171), 1117 (AB0186), 1119 (AB0191), 1278 (AB0501)
Boubaker F., 1415 (AB0776)
Boucly A., 52 (OP0094)
Bouden S., 768 (POS1000), 1106 (AB0158), 1119 (AB0190), 1285 (AB0517), 1341 (AB0611), 1395 (AB0730), 1396 (AB0731), 1396 (AB0732)
Bougault C., 431 (POS0404)
Boughoula K., 975 (POS1385)
Bouhedja N., 169 (OP0279-PARE), 1362 (AB0659)
Bouhnik Y., 544 (POS0614)
Boukabous A., 843 (POS1127)
Boulanger C., 240 (POS0067)
Boulestreau J., 417 (POS0374)
Boumans D., 1209 (AB0367), 1214 (AB0375)
Boumier P., 109 (OP0181)
Boumpas D., 11 (OP0019), 21 (OP0040), 631 (POS0757), 632 (POS0759), 635 (POS0764), 646 (POS0786)
Bounas A., 1299 (AB0537)
Bourdin A., 671 (POS0835)
Bourguiba R., 954 (POS1343)
Bourne T., 18 (OP0034)
Bournia V. K., 703 (POS0894)
Bourtseva T., 930 (POS1297)
Boussaa H., 1112 (AB0171), 1113 (AB0173), 1113 (AB0174), 1118 (AB0188), 1379 (AB0693), 1381 (AB0698), 1399 (AB0741), 1400 (AB0742)
Boussaid S., 290 (POS0155-HPR), 372 (POS0294), 856 (POS1155), 923 (POS1280), 926 (POS1288), 1090 (AB0123), 1097 (AB0139), 1144 (AB0236), 1144 (AB0238), 1145 (AB0240), 1147 (AB0244), 1272 (AB0490), 1273 (AB0492), 1358 (AB0650), 1421 (AB0793)
Boussoualim K., 1164 (AB0277)
Boussougou V. F., 1387 (AB0711)
Boutaibi H., 1162 (AB0274)
Boutemy J., 669 (POS0831)
Boutron-Ruault M. C., 7 (OP0012), 471 (POS0478)
Boutsalis G., 1464 (AB0882-HPR)
Boutzios G., 668 (POS0829)
Bouzid S., 1281 (AB0507)
Bowen C., 1426 (AB0803)
Bower H., 535 (POS0601), 864 (POS1169)
Bowes J., 8 (OP0014), 467 (POS0471)
Bowman S. J., 74 (OP0130), 79 (OP0136), 593 (POS0692)
Bowness P., 17 (OP0032)
Boxberger E., 1238 (AB0420)
Boyle S., 43 (OP0079)
Bozyczko M., 808 (POS1060)
Bozzao F., 1002 (POS1435), 1391 (AB0719)
Bozzolo E., 348 (POS0253), 594 (POS0693), 613 (POS0726)
Brådland S., 821 (POS1085), 1009 (POS1451), 1218 (AB0381), 1418 (AB0785)
Bradley A., 725 (POS0926)
Brahem M., 525 (POS0585), 923 (POS1281), 1063 (AB0064), 1111 (AB0169), 1120 (AB0192), 1193 (AB0337), 1194 (AB0339), 1415 (AB0777), 1472 (AB0897-HPR)
Brahim M., 1225 (AB0395)
Bran C., 1380 (AB0695)
Branco J., 1041 (AB0014), 1402 (AB0747)
Brandi M. L., 835 (POS1111)
Brandolino F., 29 (OP0055), 347 (POS0250)
Brandt H. C., 342 (POS0241), 456 (POS0453), 813 (POS1069)
Brandt H., 1020 (POS1470-HPR)
Brandt L., 112 (OP0185)
Brandt-Juergens J., 337 (POS0234), 342 (POS0241), 456 (POS0453), 706 (POS0899), 714 (POS0910), 780 (POS1023), 813 (POS1069)
Brandy-Garcia A., 967 (POS1371)
Braner A., 50 (OP0092)
Brantner C., 828 (POS1097)
Bratis K., 1172 (AB0291)
Braun J., 152 (OP0250), 155 (OP0253), 222 (POS0033), 224 (POS0038), 344 (POS0245), 373 (POS0296), 376 (POS0301), 525 (POS0584), 707 (POS0900), 714 (POS0910), 716 (POS0912), 752 (POS0973), 851 (POS1145), 1375 (AB0684), 1435 (AB0823)
Braun M., 892 (POS1217)
Braun R., 649 (POS0794)
Braun-Moscovici Y., 685 (POS0861), 691 (POS0871), 892 (POS1217)
Bravo B., 1208 (AB0366)
Bravo-Lee I., 1386 (AB0709)
Breban M., 343 (POS0243)
Brecht T., 446 (POS0436)
Breda M., 166 (OP0273), 389 (POS0324)
Bredemeier M., 582 (POS0676)
Bregman B., 54 (OP0099), 214 (POS0024)
Breillat P., 388 (POS0323)
Brekke L. K., 397 (POS0339)
Bremander A., 159 (OP0261-HPR), 197 (OP0322-HPR), 994 (POS1423), 1024 (POS1479-HPR), 1330 (AB0586)
Brennan A., 617 (POS0734)
Brenol C., 582 (POS0676)
Bressem K. K., 155 (OP0254)
Brett A., 450 (POS0443)
Breuer G., 892 (POS1217)
Breuil V., 367 (POS0284)
Brewster G. S., 299 (POS0173)
Bricman L., 880 (POS1196)
Bridges J., 192 (OP0314)

Bridges S. L., 1081 (AB0107)
Bridgewater S., 1441 (AB0834)
Bridgewood C., 433 (POS0408)
Briel A., 988 (POS1410)
Brigante A., 874 (POS1186), 1196 (AB0342)
Briggs A., 617 (POS0734)
Briki M., 120 (OP0199)
Brinkhaus M., 1044 (AB0020)
Brinkman D. M. C., 932 (POS1300)
Briolay A., 431 (POS0404)
Briones-Figueroa A., 946 (POS1327)
Brisslert M., 12 (OP0022)
Brites L., 481 (POS0496), 1101 (AB0147)
Brito D., 909 (POS1252), 1448 (AB0848)
Brittelli R., 906 (POS1246)
Brizuela L., 431 (POS0404)
Brkic A., 145 (OP0238)
Brkic Z., 308 (POS0189)
Broadwell A., 527 (POS0590)
Brocq O., 199 (LB0002)
Brodavka M., 892 (POS1217)
Broderick L., 621 (POS0739)
Broen J., 378 (POS0305), 880 (POS1197)
Brogan P., 947 (POS1330)
Broide M., 928 (POS1294), 929 (POS1295)
Brolin S., 1023 (POS1476-HPR)
Broll A., 1196 (AB0342)
Brom M., 1133 (AB0214)
Brossart P., 91 (OP0151), 842 (POS1126), 920 (POS1271), 1103 (AB0152), 1446 (AB0846), 1447 (AB0847)
Brouwer E., 33 (OP0062), 36 (OP0066), 221 (POS0031), 655 (POS0806), 657 (POS0809), 992 (POS1418), 1209 (AB0367), 1211 (AB0370), 1257 (AB0462)
Brown C., 168 (OP0277-PARE)
Brown E., 1033 (POS1497-PARE)
Brown M., 1000 (POS1432)
Brown P., 18 (OP0033), 403 (POS0348)
Broyde A., 200 (LB0003)
Brucato A., 105 (OP0175), 628 (POS0751)
Bruce I. N., 78 (OP0134), 177 (OP0289), 181 (OP0296), 586 (POS0683), 602 (POS0705), 617 (POS0734), 626 (POS0748)
Bruce I., 1172 (AB0291)
Bruce T., 87 (OP0147)
Bruchfeld A., 1 (OP0003), 898 (POS1230)
Brueck N., 244 (POS0075)
Brun M. K., 185 (OP0301)
Brunborg C., 232 (POS0054)
Brunetta E., 594 (POS0693)
Bruni C., 105 (OP0176), 355 (POS0264), 385 (POS0317), 387 (POS0321), 675 (POS0842), 681 (POS0855), 685 (POS0861), 897 (POS1228), 1032 (POS1495-HPR), 1154 (AB0256), 1234 (AB0413)
Bruni S., 1416 (AB0781)
Brunier L., 735 (POS0945)
Brunner B., 95 (OP0158-HPR)
Brunner F., 45 (OP0083), 46 (OP0085)
Brunner H., 201 (LB0004), 245 (POS0076)
Brunner J., 247 (POS0079), 882 (POS1199), 934 (POS1304)
Brunner M., 90 (OP0150), 688 (POS0866)
Bruno F., 380 (POS0308), 954 (POS1344), 957 (POS1349), 1105 (AB0156)
Bruno R., 833 (POS1105)
Brusasco M., 1326 (AB0578)
Brusi V., 906 (POS1246)
Bruzelius M., 1184 (AB0318)
Bryant A., 446 (POS0436)
Brzosko I., 1434 (AB0820)
Brzosko M., 1434 (AB0820)
Bu X., 251 (POS0087), 312 (POS0196), 568 (POS0655)
Bubnov R., 924 (POS1284)
Buch M. H., 70 (OP0126), 108 (OP0180), 251 (POS0086), 255 (POS0092), 453 (POS0447), 533 (POS0599), 569 (POS0657), 570 (POS0658), 579 (POS0670), 1128 (AB0207)
Buchanan R., 117 (OP0194), 629 (POS0753), 655 (POS0806), 1212 (AB0371)
Buchbinder R., 374 (POS0299)
Bucknall M., 158 (OP0259-HPR)
Buckner J., 1081 (AB0107)
Budoff M., 58 (OP0104), 325 (POS0215), 325 (POS0216), 520 (POS0571)
Buehring B., 752 (POS0973), 1375 (AB0684), 1435 (AB0823)
Bueno A., 976 (POS1387)
Bugatti S., 521 (POS0575), 913 (POS1258)
Bugdayli K., 652 (POS0800)
Buijs J., 911 (POS1256)
Buitrago-Garcia D., 1473 (AB0900-HPR), 1481 (AB0921-PARE)
Buker N., 1454 (AB0862-HPR)
Bukhari M., 488 (POS0511), 1081 (AB0105), 1339 (AB0607)
Bulbul Baskan E., 1327 (AB0579)
Bulimbašić S., 1199 (AB0348), 1199 (AB0349)
Bullock G., 274 (POS0125)
Bułło-Piontecka B., 1434 (AB0820)
Bulut S., 815 (POS1071)
Bundy C., 239 (POS0065-PARE), 343 (POS0244), 744 (POS0960), 745 (POS0961), 762 (POS0988), 762 (POS0989), 763 (POS0990)
Bungartz C., 1263 (AB0472)
Buoli M., 858 (POS1161), 869 (POS1176), 1363 (AB0661)
Burcet G., 699 (POS0886)
Burchett S., 1031 (POS1493-HPR)
Burden A. M., 59 (OP0106), 207 (POS0011), 255 (POS0091), 272 (POS0122), 323 (POS0212), 462 (POS0461), 974 (POS1383), 1128 (AB0206)
Burger S., 1280 (AB0505)
Burgess J., 276 (POS0129), 309 (POS0190)
Burgess S., 372 (POS0295)
Burgos-Vargas R., 24 (OP0047), 314 (POS0197), 853 (POS1149)
Burkard T., 59 (OP0106), 207 (POS0011), 272 (POS0122), 323 (POS0212), 974 (POS1383), 1128 (AB0206)
Burke M., 951 (POS1338)
Burkhardt H., 528 (POS0591)
Burmester G. R., 69 (OP0124), 72 (OP0128), 101 (OP0169-PARE), 199 (LB0002), 207 (POS0010), 255 (POS0092), 305 (POS0183), 328 (POS0220), 342 (POS0241), 456 (POS0453), 544 (POS0615), 567 (POS0654), 572 (POS0660), 623 (POS0744), 789 (POS1033), 813 (POS1069), 983 (POS1401), 1157 (AB0261), 1287 (AB0522)
Burn E., 58 (OP0105), 232 (POS0053)
Burón M. I., 426 (POS0394)
Burroughs J., 383 (POS0315)
Burry T., 431 (POS0405)
Bursi R., 211 (POS0019)
Burska A., 23 (OP0044), 78 (OP0134), 300 (POS0175), 302 (POS0179)
Burston J., 402 (POS0346)
Bursuc R. A., 1267 (AB0480)
Busch H., 149 (OP0244)
Buschiazzo E., 730 (POS0933), 1377 (AB0689)
Bushmakin A. G., 146 (OP0239)
Busquets N., 68 (OP0123)
Busso N., 226 (POS0041), 426 (POS0393)
Butbul Y., 187 (OP0305), 928 (POS1294), 929 (POS1295), 945 (POS1326)
Butcher B., 711 (POS0906)
Bütikofer L., 33 (OP0061)
Butink M., 101 (OP0169-PARE)
Buttel T., 358 (POS0269-HPR), 358 (POS0270-HPR)
Buttgereit F., 64 (OP0115), 191 (OP0312), 567 (POS0654), 575 (POS0665), 1048 (AB0029), 1049 (AB0031), 1052 (AB0040), 1107 (AB0160)
Buttgereit T., 305 (POS0183), 1048 (AB0029), 1049 (AB0031)
Buzzegoli T., 1404 (AB0752)
Bykerk V., 66 (OP0118), 159 (OP0262-HPR), 356 (POS0267-HPR), 530 (POS0594), 1014 (POS1459-HPR), 1081 (AB0107)
Bylsma J., 320 (POS0207)
Bythell M., 989 (POS1412)

C. Romão V., 644 (POS0781), 690 (POS0870)
Caballero Motta L. R., 658 (POS0812), 984 (POS1403), 1385 (AB0706), 1397 (AB0734)
Cabezas-Lucena A. M., 344 (POS0246), 1456 (AB0865-HPR)
Cabrera-Alarcón J. L., 1101 (AB0149)
Cabrera-Serrano A. J., 9 (OP0017)
Cabrera-Villalba S., 1042 (AB0015), 1106 (AB0159), 1120 (AB0193)
Cabri M., 1449 (AB0850)
Çabuk Çelik N., 0966 (POS1368)
Çabuk Çelik N., 1380 (AB0694)
Cacciapaglia F., 324 (POS0214), 701 (POS0891), 1003 (POS1437), 1217 (AB0380)
Cáceres Martín L., 0614 (POS0728)
Cacheda A. P., 755 (POS0978)
Cacoub P., 37 (OP0068), 233 (POS0055)
Cadar M., 150 (OP0246), 445 (POS0433)
Cadena-Trejo C., 1428 (AB0808)
Caeiro-Aguado M., 1326 (AB0577)
Caetano J., 1282 (AB0510)
Cafaro G., 211 (POS0019), 324 (POS0214), 809 (POS1061)
Cagan M., 659 (POS0813)
Çağatay A. A., 0191 (OP0313)
Çağlar E., 1329 (AB0584)
Çağlayan Ş., 0249 (POS0082), 0871 (POS1181), 0942 (POS1319)
Cailliau E., 1258 (AB0464)
Çakır B., 0733 (POS0940)
Çakır E. N., 1028 (POS1486-HPR), 1467 (AB0888-HPR), 1471 (AB0895-HPR)
Cakir O., 702 (POS0892)
Calabrese L., 328 (POS0220), 457 (POS0454)
Calabuig I., 282 (POS0141)
Calamia V., 306 (POS0185)
Calcagni M., 46 (OP0085), 151 (OP0248)
Calderaro D., 1448 (AB0848)
Calderón-Goercke M., 35 (OP0065), 1018 (POS1467-HPR)
Çalgüneri M., 1124 (AB0200), 1124 (AB0201), 1299 (AB0535)
Calin N., 519 (POS0569)
Caliskan E. B., 662 (POS0819), 663 (POS0820)
Cáliz Cáliz R., 0009 (OP0017)
Callahan L., 358 (POS0270-HPR)
Callahuara N., 730 (POS0933), 1377 (AB0689)
Calle M., 1008 (POS1449), 1448 (AB0849)
Callegher S. Z., 134 (OP0223), 618 (POS0735)
Callejas-Rubio J. L., 179 (OP0292), 350 (POS0256), 987 (POS1408), 987 (POS1409), 1182 (AB0315), 1183 (AB0316), 1208 (AB0366), 1231 (AB0406)
Callhoff J., 216 (POS0026), 990 (POS1414)
Calligaro A., 619 (POS0737), 1174 (AB0295), 1308 (AB0549)
Callis-Duffin K., 139 (OP0229)
Calvacchi S., 630 (POS0755)
Calvet Fontova J., 1060 (AB0055)
Calvet J., 342 (POS0242)
Calviño C., 916 (POS1264)
Calviño J., 1076 (AB0096)
Calvo Gutierrez J., 1109 (AB0166), 1245 (AB0432), 1253 (AB0451)
Calvo I., 201 (LB0004), 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Calvo J., 523 (POS0579)
Calvo M. E., 874 (POS1186)
Calvo R., 1133 (AB0214)
Calvo Sanz L., 946 (POS1327)
Calvo-Alén J., 610 (POS0721)
Calvo-Aranda E., 1354 (AB0643)
Calvo-Río V., 32 (OP0060), 730 (POS0934), 755 (POS0977), 952 (POS1340), 960 (POS1357), 977 (POS1390), 986 (POS1407), 1018 (POS1467-HPR), 1225 (AB0396), 1324 (AB0574), 1412 (AB0771)
Calza S., 628 (POS0751)
Camacho O., 1219 (AB0384)
Camellino D., 655 (POS0806), 833 (POS1105), 1201 (AB0354), 1216 (AB0379)
Camilleri S., 1078 (AB0099)
Camilo Estrella P., 1280 (AB0506)
Caminal Montero L., 1076 (AB0096)

Caminiti M., 906 (POS1246)
Caminiti R., 906 (POS1246)
Camp H., 72 (OP0128), 328 (POS0220), 569 (POS0656)
Campanaro F., 190 (OP0310), 1319 (AB0565)
Campanilho-Marques R., 690 (POS0870), 1250 (AB0445)
Campochiaro C., 232 (POS0054), 655 (POS0806), 906 (POS1246), 950 (POS1336), 953 (POS1341), 955 (POS1347), 1206 (AB0361)
Campos Costa F., 481 (POS0496), 1101 (AB0147), 1236 (AB0415), 1236 (AB0416)
Campos Esteban J., 892 (POS1218)
Campos Fernández C., 34 (OP0064), 35 (OP0065)
Can Bostan Ö., 347 (POS0251)
Can G., 627 (POS0750), 1247 (AB0437), 1256 (AB0459), 1327 (AB0579), 1386 (AB0708)
Can M. G., 604 (POS0710)
Cañada Martinez A. J., 1278 (AB0502)
Cañal J., 1225 (AB0396), 1412 (AB0771)
Canavan C., 847 (POS1136)
Canavan M., 14 (OP0025), 15 (OP0028), 205 (POS0007), 423 (POS0387), 1043 (AB0018), 1479 (AB0916-PARE)
Canbek S., 933 (POS1302)
Cancio Fanlo J. J., 1141 (AB0230)
Candelas G., 1464 (AB0881-HPR), 1475 (AB0906-HPR)
Candia L., 1296 (AB0531)
Cañete J. D. D., 0183 (OP0298)
Canhão H., 9 (OP0017)
Cano Garcia L., 494 (POS0521), 1453 (AB0859-HPR), 1456 (AB0865-HPR), 1474 (AB0904-HPR)
Cánovas Olmos I., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Cantagrel A., 109 (OP0181)
Cantarini L., 51 (OP0093), 573 (POS0661), 669 (POS0832), 746 (POS0963), 957 (POS1349), 1217 (AB0380)
Cantatore F. P., 582 (POS0675), 701 (POS0891), 1003 (POS1437), 1260 (AB0467), 1379 (AB0691)
Cantero-Nieto L., 1231 (AB0405), 1231 (AB0406)
Canti V., 619 (POS0737)
Canzoni M., 134 (OP0223)
Capacci A., 190 (OP0310), 1389 (AB0716)
Capelozzi V., 444 (POS0432)
Capelusnik D., 382 (POS0312), 739 (POS0951), 740 (POS0953)
Capocotta D., 888 (POS1210), 1260 (AB0467)
Caporali R., 108 (OP0180), 229 (POS0048), 284 (POS0145), 378 (POS0305), 453 (POS0447), 521 (POS0575), 533 (POS0599), 582 (POS0675), 619 (POS0737), 858 (POS1161), 869 (POS1176), 870 (POS1178), 872 (POS1182), 1128 (AB0207), 1363 (AB0661), 1374 (AB0683)
Caporossi D., 1074 (AB0089)
Capozzi A., 902 (POS1238)
Cappelleri J. C., 146 (OP0239), 704 (POS0895)
Cappelli A., 190 (OP0310), 1319 (AB0565), 1389 (AB0716)
Cappello C., 100 (OP0167)
Capurso G., 974 (POS1382)
Caputo M., 392 (POS0329)
Caracciolo J. A., 635 (POS0763)
Caracuel-Ruiz M. A., 366 (POS0282), 523 (POS0579)
Caramella D., 642 (POS0778)
Carames B., 418 (POS0375)
Carapellucci A., 224 (POS0037)
Carballo N., 991 (POS1416), 1132 (AB0212)
Carbo M., 24 (OP0046), 775 (POS1014)
Cárdenas A., 0463 (POS0463), 0473 (POS0482), 0473 (POS0483), 0478 (POS0491), 0510 (POS0552), 0511 (POS0553), 0515 (POS0562), 0816 (POS1074), 0893 (POS1220), 0978 (POS1392), 0983 (POS1402), 0984 (POS1404), 1085 (AB0113), 1087 (AB0117), 1189 (AB0329), 1360 (AB0657), 1361 (AB0658), 1444 (AB0842), 1457 (AB0867-HPR)
Cardinale G., 1271 (AB0488)
Cardinaletti P., 594 (POS0693)
Carey J., 859 (POS1162)
Cariddi A., 348 (POS0253)
Carletto A., 726 (POS0927), 1099 (AB0143)
Carlevaris L., 874 (POS1186)
Carli L., 630 (POS0756), 647 (POS0789)
Carlier H., 720 (POS0918)
Carlson N. S., 299 (POS0173)
Carmisciano L., 524 (POS0583), 679 (POS0850)
Carmona E., 652 (POS0801)
Carmona L., 2 (OP0006), 173 (OP0286), 175 (OP0288), 199 (LB0002), 304 (POS0181), 345 (POS0248), 889 (POS1213), 1089 (AB0120), 1213 (AB0373), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Carmona R., 224 (POS0037)
Carnevale A., 985 (POS1406)
Carpio K., 1239 (AB0422)
Carrara G., 134 (OP0223), 335 (POS0230), 470 (POS0476), 1435 (AB0822)
Carrasco Molina S., 693 (POS0875)
Carreira P., 232 (POS0054), 384 (POS0316)
Carrillo Vazquez S. M., 899 (POS1233)
Carrilo S., 559 (POS0642)
Carrino J., 943 (POS1323)
Carrión Barberà I., 1197 (AB0344)
Carroll H., 597 (POS0698), 598 (POS0699)
Carron P., 89 (OP0149), 136 (OP0226), 153 (OP0252)
Carruthers M., 1406 (AB0756)
Carstens M. N., 1245 (AB0433)
Carter L. M., 78 (OP0134), 626 (POS0748)
Cartin-Ceba R., 1220 (AB0386)
Carubbi F., 189 (OP0309), 190 (OP0310), 619 (POS0737), 630 (POS0755), 1359 (AB0652), 1389 (AB0716)
Carvajal Alegria G., 258 (POS0095)
Carvajal P., 303 (POS0180)
Carvalho H., 582 (POS0676)
Carvalho P., 340 (POS0238)
Carvidi A., 911 (POS1255)
Casabella A., 908 (POS1250), 1247 (AB0438)
Casademont J., 1365 (AB0666)
Casado E., 1060 (AB0055)
Casafont-Solé I., 490 (POS0513), 531 (POS0595)
Casali M. I., 37 (OP0069)
Casalla L., 771 (POS1005), 875 (POS1188)
Casasola J. C., 559 (POS0642)
Casciano G., 882 (POS1200)
Casciaro S., 294 (POS0163)
Cascino M. D., 648 (POS0792)
Casey E., 824 (POS1089)
Caso F., 906 (POS1246), 957 (POS1349), 1284 (AB0515)
Caspi D., 1049 (AB0032)
Castañeda Martínez D. D., 1085 (AB0113)
Castañeda S., 35 (OP0065), 393 (POS0331), 490 (POS0513), 531 (POS0595), 560 (POS0645), 700 (POS0888), 719 (POS0917), 755 (POS0977), 967 (POS1371), 977 (POS1390), 986 (POS1407), 1065 (AB0070), 1071 (AB0083), 1076 (AB0096), 1208 (AB0366), 1225 (AB0396), 1241 (AB0427), 1412 (AB0771)
Castañeda-Martínez M. M., 1085 (AB0113)
Castaño J. P., 20 (OP0038)
Castaño M. S., 887 (POS1208)
Castaños S., 1133 (AB0214)
Castellani C., 1143 (AB0234), 1160 (AB0269)
Castellano V., 572 (POS0660)
Castellanos-Moreira R., 542 (POS0610)
Castellví I., 685 (POS0861), 700 (POS0888), 1093 (AB0129), 1365 (AB0666), 1426 (AB0804)
Castiblanco Montañez R. A., 1473 (AB0900-HPR)
Castiblanco-Montañez R. A., 1475 (AB0907-HPR)
Castiglia A., 805 (POS1053)
Castillo D., 1365 (AB0666)
Castillo Ortiz A., 559 (POS0642), 904 (POS1242), 905 (POS1245)
Castrejón Fernández I., 1239 (AB0422)
Castrejon I., 68 (OP0123), 233 (POS0055), 658 (POS0812), 1117 (AB0185)
Castrignanò P., 672 (POS0837), 1241 (AB0425)
Castro A., 1205 (AB0360)
Castro B., 970 (POS1376)
Castro C., 635 (POS0763)
Castro Coello V. V., 874 (POS1186), 887 (POS1208), 1196 (AB0342)
Castro G., 582 (POS0676)
Castro Guardiola A., 856 (POS1156)
Castro I., 303 (POS0180)
Castro S., 952 (POS1340)
Castro Z., 1078 (AB0098), 1200 (AB0350)
Castro-Corredor D., 755 (POS0977), 977 (POS1390), 986 (POS1407), 1065 (AB0070)
Castro-Santamaria P., 1173 (AB0294)
Catalano A., 838 (POS1119)
Catanozi S., 444 (POS0432)
Catanzaro S., 46 (OP0085)
Caterson H., 654 (POS0804)
Catma Y., 191 (OP0313)
Catrina A., 87 (OP0146), 87 (OP0147), 206 (POS0009), 429 (POS0400), 1005 (POS1441)
Catrina S. B., 429 (POS0400)
Cattelan F., 1372 (AB0679)
Caturano A., 1446 (AB0844)
Cauli A., 134 (OP0223), 582 (POS0675), 632 (POS0758), 1260 (AB0467)
Cauvet A., 419 (POS0378)
Cavagna L., 985 (POS1406)
Cavalheiro Do Espírito Santo R., 0909 (POS1252)
Cavalli G., 0051 (OP0093), 0190 (OP0310), 0950 (POS1336), 0953 (POS1341), 0955 (POS1347), 1389 (AB0716)
Cavazzana I., 0906 (POS1246)
Cavedoni M., 1416 (AB0781)
Caversaccio M. D., 0649 (POS0795)
Cavigli E., 0897 (POS1228)
Caviglia G., 0335 (POS0230)
Cavuto C. C., 1423 (AB0798)
Caxaria S., 0120 (OP0200), 1052 (AB0039)
Cazenave T., 0136 (OP0226)
Cebanu M., 1337 (AB0601)
Cebon J., 0117 (OP0194)
Ceccarelli F., 0583 (POS0677), 0588 (POS0685), 0594 (POS0693), 0628 (POS0751), 0645 (POS0783), 0893 (POS1219), 1069 (AB0079), 1073 (AB0087), 1143 (AB0234), 1160 (AB0269), 1384 (AB0704)
Cecchetti R., 0906 (POS1246)
Cecchi I., 0298 (POS0172), 1039 (AB0008), 1073 (AB0088)
Cederholm S., 0098 (OP0164), 0947 (POS1330)
Cederlund A., 0260 (POS0101)
Cefle A., 0702 (POS0892), 0727 (POS0929), 1140 (AB0229), 1202 (AB0356), 1204 (AB0359), 1206 (AB0362)
Çekiç Ş., 1404 (AB0751)
Celano A., 0044 (OP0082-PARE)
Celia A. I., 0645 (POS0783), 1073 (AB0087)
Çelik B., 0282 (POS0142)
Çelik Z. B., 1040 (AB0012)
Cella D., 0146 (OP0239)
Cendes F., 1255 (AB0457)
Cene E., 0636 (POS0766)
Cengiz A. B., 0908 (POS1249)
Cengiz A. K., 1040 (AB0012)
Centurion O., 1106 (AB0159)
Cepeda-Ayala O. A., 0463 (POS0463), 0478 (POS0491), 0510 (POS0552), 0511 (POS0553), 0978 (POS1392), 0984 (POS1404), 1189 (AB0329)
Cercone S., 1260 (AB0467)
Cerda D., 1219 (AB0384)
Cere A., 0697 (POS0882), 1247 (AB0438)
Cerf-Payrastre I., 0857 (POS1158), 0858 (POS1159)
Ceribelli A., 0152 (OP0249)
Cerón-Carrasco J. P., 1048 (AB0030)
Cerqueira C., 0196 (OP0321), 0697 (POS0883)
Cerqueira M., 1003 (POS1438), 1424 (AB0799)
Cervantes-Rosete D., 0904 (POS1242), 0905 (POS1245)
Cervera R., 0181 (OP0296), 0637 (POS0767), 1195 (AB0340)
Cesareo M., 0980 (POS1395)
Ceseñas-Falcón L. Á., 1177 (AB0301)
Cesta A., 0107 (OP0179), 0452 (POS0445), 0454 (POS0448), 0454 (POS0449)
Cetin C., 0191 (OP0313), 0602 (POS0706), 0604 (POS0710), 0636 (POS0766), 0951 (POS1339), 1359 (AB0653), 1409 (AB0766)
Ceyhan M., 0908 (POS1249)
Ch'ng S. S., 1346 (AB0626), 1469 (AB0891-HPR)
Cha H. S., 0124 (OP0206), 0280 (POS0137), 0281 (POS0138), 0752 (POS0972), 1210 (AB0368)

Cha U. C., 0731 (POS0936)
Chaabene I., 1225 (AB0395)
Chaabo K., 0479 (POS0494)
Chakhalian M., 1402 (AB0748)
Chakieva D., 1095 (AB0135)
Chakr R., 0582 (POS0676)
Chakravarthy C H R., 1396 (AB0733)
Chakravarty S. D., 0783 (POS1027), 1289 (AB0524), 1291 (AB0526)
Chakravorty M., 0989 (POS1412)
Chalcev B., 0196 (OP0320), 0608 (POS0717), 0896 (POS1226), 1116 (AB0183), 1185 (AB0321)
Chalmeta Verdejo I., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Chamberlain J., 0847 (POS1136)
Chamizo Carmona E., 1303 (AB0542)
Chammakhi M., 0857 (POS1158), 0858 (POS1159)
Chamurlieva M., 1325 (AB0576)
Chan C. W. S., 0147 (OP0240), 0225 (POS0039), 0775 (POS1015)
Chan D., 0273 (POS0124)
Chan E., 0479 (POS0494)
Chan J., 0224 (POS0037)
Chan K. L., 0298 (POS0171), 0638 (POS0769), 0640 (POS0772)
Chan M., 0218 (POS0028)
Chandran V., 0132 (OP0221), 0431 (POS0405), 0432 (POS0406), 0812 (POS1068), 1313 (AB0557)
Chandrasekaran V., 0428 (POS0397)
Chang H., 0530 (POS0594)
Chang M. J., 0111 (OP0184), 0315 (POS0199), 0616 (POS0732), 0623 (POS0743), 0677 (POS0847), 0684 (POS0859), 0888 (POS1211)
Chang S. H., 0512 (POS0555), 0516 (POS0563), 0516 (POS0564)
Chang Y. J., 0116 (OP0193)
Chang Y., 1374 (AB0682)
Chao C. W., 0023 (OP0045)
Chao W. C., 1082 (AB0108)
Chapman D., 0450 (POS0443), 1148 (AB0247)
Charca Benavente L. C., 1280 (AB0505), 1397 (AB0734)
Charfi S., 1061 (AB0059)
Charles A. L., 0151 (OP0247), 0694 (POS0876)
Charles-Schoeman C., 0004 (OP0008), 0072 (OP0128), 0449 (POS0442), 0569 (POS0656), 0572 (POS0660)
Charlot A., 0149 (OP0243)
Charlotte A., 0559 (POS0641)
Charneca S., 0484 (POS0504)
Charnley M., 0042 (OP0078)
Chartier M., 0108 (OP0180), 0453 (POS0447), 0533 (POS0599), 1128 (AB0207)
Charuel J. L., 0388 (POS0323)
Chary Valckenaere I., 0170 (OP0282)
Chasnyk V., 0201 (LB0004), 0247 (POS0080), 0930 (POS1297), 0937 (POS1310), 0944 (POS1324), 1402 (AB0748)
Chatelain R., 0910 (POS1254), 1383 (AB0702)
Chatelus E., 0681 (POS0855), 0877 (POS1190)
Chatham W., 0192 (OP0314)
Chattopadhyay A., 1305 (AB0545)
Chatzidionysiou K., 0012 (OP0021), 0068 (OP0122), 0093 (OP0156-HPR), 0535 (POS0601), 0864 (POS1169), 1005 (POS1441)
Chatzigeorgiou M., 0193 (OP0317-PARE)
Chatziioannou M., 0193 (OP0317-PARE)
Chatzikrystallis I., 0193 (OP0317-PARE)
Chatzis L., 0022 (OP0041), 0178 (OP0291), 0180 (OP0294), 0370 (POS0290), 1381 (AB0697)
Chatzittofis A., 0605 (POS0711)
Chau J., 0139 (OP0229)
Chaudier A., 0877 (POS1190)
Chauhan D., 0621 (POS0739)
Chauhan K., 0318 (POS0205)
Chaussain C., 0228 (POS0046)
Chavan P. P., 0242 (POS0071)
Chavatza K., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764), 0646 (POS0786)
Chávez N., 0568 (POS0655)
Chavez-Alvarez L. A., 1007 (POS1446), 1455 (AB0863-HPR)
Chavez-Chavez J., 1475 (AB0907-HPR)
Chazerain P., 0172 (OP0284)
Cheah J. T. L., 1441 (AB0834)
Chebysheva S., 0187 (OP0306)
Chehab G., 1195 (AB0341)
Chekili S., 0292 (POS0159-HPR), 0835 (POS1110), 1030 (POS1491-HPR), 1113 (AB0173), 1113 (AB0174), 1117 (AB0184), 1118 (AB0188), 1277 (AB0499), 1332 (AB0590), 1333 (AB0592), 1333 (AB0593), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1368 (AB0672), 1368 (AB0673), 1381 (AB0698), 1390 (AB0717), 1397 (AB0736), 1411 (AB0770), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Cheldieva F., 0605 (POS0712), 0643 (POS0780), 1177 (AB0303), 1180 (AB0308)
Chemin K., 0001 (OP0003), 0038 (OP0072), 0196 (OP0321), 0203 (POS0003), 0206 (POS0008)
Chen C. K., 0116 (OP0193)
Chen C. W., 0121 (OP0201), 0391 (POS0327)
Chen C., 0456 (POS0452), 0690 (POS0869), 0698 (POS0884), 0853 (POS1148), 1091 (AB0125), 1465 (AB0883-HPR)
Chen H. H., 1082 (AB0108)
Chen H., 0307 (POS0187), 0657 (POS0810), 0661 (POS0815)
Chen J., 0188 (OP0307), 0574 (POS0664), 0619 (POS0736)
Chen L. F., 1091 (AB0125), 1225 (AB0394)
Chen L., 0307 (POS0187), 0312 (POS0196), 1122 (AB0197), 1288 (AB0523)
Chen M. H., 0023 (OP0045)
Chen M., 0349 (POS0254), 0667 (POS0828)
Chen R., 0661 (POS0816), 0661 (POS0817)
Chen S. T., 0023 (OP0045)
Chen S., 0064 (OP0115), 0670 (POS0833), 0698 (POS0885), 1354 (AB0642)
Chen T., 0646 (POS0788)
Chen W. H., 0621 (POS0739)
Chen X., 1053 (AB0042)
Chen Y. F., 0563 (POS0649)
Chen Y. H., 0218 (POS0028), 0564 (POS0651), 0622 (POS0741)
Chen Y. M., 0622 (POS0741)
Chen Y., 0191 (OP0312), 1048 (AB0029), 1049 (AB0031)
Chen Z., 0574 (POS0664), 1061 (AB0060)
Cheng C. F., 0599 (POS0700)
Cheng C., 0645 (POS0785)
Cheng I. T., 0257 (POS0094), 0818 (POS1079), 0860 (POS1164), 0895 (POS1222), 1323 (AB0571)
Cheng J. E., 0648 (POS0792)
Cheng L., 0460 (POS0458), 0622 (POS0742), 0678 (POS0848), 0680 (POS0851), 1037 (AB0005)
Cheng Q., 1053 (AB0042)
Cheng S., 0349 (POS0254), 0667 (POS0828)
Cheng T. T., 1152 (AB0253)
Cheng T., 0188 (OP0307), 0729 (POS0932), 0888 (POS1211)
Cheng Y. Z., 1346 (AB0626)
Cheour E., 0923 (POS1280), 0926 (POS1288), 1090 (AB0123), 1097 (AB0139), 1144 (AB0238), 1145 (AB0240), 1421 (AB0793)
Cherin P., 1186 (AB0323)
Cherkasova M., 0464 (POS0465), 0515 (POS0561), 0605 (POS0712), 0613 (POS0727), 0614 (POS0729), 0681 (POS0853), 0854 (POS1151), 1066 (AB0072), 1072 (AB0085), 1179 (AB0306), 1180 (AB0309), 1180 (AB0310), 1249 (AB0444), 1363 (AB0663), 1403 (AB0749)
Chernikova A., 1388 (AB0714)
Cherny K., 0840 (POS1122)
Chernykh E., 0581 (POS0673)
Chernyschova N., 1326 (AB0578)
Chernysheva T., 0514 (POS0558), 1328 (AB0582)
Chessa E., 0632 (POS0758)
Chevet B., 0662 (POS0818)
Chevret S., 0024 (OP0047)
Chia Y. L., 0587 (POS0684), 0590 (POS0688), 0592 (POS0690)
Chiarello S., 0985 (POS1406)
Chiarini G., 0530 (POS0593)
Chiarotto A., 1006 (POS1444)
Chiba S., 1028 (POS1487-HPR)
Chibisova K., 0100 (OP0166)
Chibnell-Smith A. L., 0168 (OP0278-PARE)
Chibnell-Smith S., 0168 (OP0278-PARE)
Chiche L., 0214 (POS0024)
Chickermane P. R., 0948 (POS1331)
Chickermane P., 0915 (POS1262)
Chighizola C., 0619 (POS0737), 0936 (POS1308)
Chikili S., 0522 (POS0577)
Chikina M., 0849 (POS1139), 0849 (POS1140), 0963 (POS1363), 1353 (AB0640)
Chikova I., 0931 (POS1299), 0937 (POS1310), 1402 (AB0748)
Chilukuri B., 0981 (POS1397), 1143 (AB0235), 1413 (AB0773)
Chimenti M. S., 0335 (POS0231), 0726 (POS0927), 1038 (AB0006), 1271 (AB0488), 1284 (AB0515), 1434 (AB0821)
Chin C., 0458 (POS0456)
Chinnadurai S., 0981 (POS1397), 1143 (AB0235), 1413 (AB0773)
Chinoy H., 0369 (POS0288)
Chiodin T., 0985 (POS1406)
Chiorrini R., 0517 (POS0565)
Chipping J., 0110 (OP0183), 0210 (POS0018)
Chirieac R., 1116 (AB0181), 1380 (AB0695)
Chiu Y. H., 0993 (POS1419), 1430 (AB0812)
Cho J., 0218 (POS0028)
Choe J. Y., 0512 (POS0555), 0516 (POS0563), 0516 (POS0564)
Chohan M., 1313 (AB0557)
Choi H., 0002 (OP0005), 0122 (OP0202), 0122 (OP0203), 0144 (OP0235), 0841 (POS1124), 0845 (POS1132), 0846 (POS1133), 0853 (POS1148), 0854 (POS1150), 0867 (POS1174), 0997 (POS1428)
Choi I. A., 0124 (OP0207), 1152 (AB0253)
Choi J., 0617 (POS0734), 1316 (AB0560)
Choi S., 0321 (POS0209)
Choi Y. J., 1072 (AB0084)
Chomakhidze A., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Chong D., 0022 (OP0042)
Chongpinitchai P., 0146 (OP0239)
Choquette D., 0107 (OP0179), 0256 (POS0093), 0454 (POS0448)
Chorin F., 0367 (POS0284)
Chouk M., 0748 (POS0967), 0793 (POS1039), 1159 (AB0266), 1279 (AB0504)
Chourabi C., 1116 (AB0182)
Chow A., 0084 (OP0143)
Chow E., 0257 (POS0094), 0860 (POS1164), 0895 (POS1222)
Chowdhury F., 0079 (OP0136)
Chowdhury K., 0074 (OP0129)
Choy E., 0072 (OP0128), 0402 (POS0346), 0569 (POS0656)
Christ L., 0033 (OP0061), 0649 (POS0795)
Christen L., 0239 (POS0065-PARE), 0343 (POS0244), 0744 (POS0960), 0745 (POS0961), 0762 (POS0988), 0762 (POS0989), 0763 (POS0990), 0868 (POS1175), 0889 (POS1213), 1277 (AB0500), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Christensen J., 0215 (POS0025)
Christensen R., 0006 (OP0010), 0095 (OP0159-HPR)
Christensen S., 0038 (OP0072)
Christians U., 0421 (POS0383)
Christiansen S. N., 0131 (OP0220), 0217 (POS0027)
Christides C., 0052 (OP0094)
Christopoulos P., 0372 (POS0293)
Chtourou L., 1162 (AB0273)
Chu A., 0085 (OP0144), 0710 (POS0905)
Chudakov D., 0014 (OP0027)
Chudinov A., 0191 (OP0311)
Chui E. T. F., 0225 (POS0039)
Chumasova O., 0482 (POS0500)
Chun K. H., 0030 (OP0056)
Chung C. H., 1072 (AB0084)
Chung C., 1450 (AB0853)
Chung H. Y., 0147 (OP0240), 0225 (POS0039), 0775 (POS1015)
Chung L., 1234 (AB0413)
Chung S., 0994 (POS1422)

Chung Y. K., 0639 (POS0771)
Chuo C. Y., 0648 (POS0792)
Ciaffi J., 0675 (POS0843)
Ciancarella C., 1073 (AB0087)
Cianci M., 1043 (AB0019), 1050 (AB0034)
Ciardi M. R., 0903 (POS1240)
Ciardo D., 0294 (POS0163)
Ciccacci C., 1038 (AB0006)
Ciccia F., 0022 (OP0042), 0301 (POS0177), 0338 (POS0235), 0390 (POS0326), 0594 (POS0693), 0778 (POS1021), 0888 (POS1210), 1165 (AB0279), 1259 (AB0465), 1260 (AB0467), 1271 (AB0488)
Cici D., 1379 (AB0691)
Ciciriello S., 0330 (POS0223), 1015 (POS1461-HPR)
Cicuttini F., 0009 (OP0015), 0118 (OP0196), 0276 (POS0129), 0362 (POS0276), 0365 (POS0280), 0832 (POS1103)
Cid M. C., 0031 (OP0059), 0272 (POS0121), 1211 (AB0370)
Ciechomska M., 0822 (POS1086)
Ciesla M., 0309 (POS0191)
Cifrián-Martínez J. M., 1046 (AB0026), 1076 (AB0094)
Cigarrán S., 1076 (AB0096)
Ciliento M. S., 0586 (POS0682)
Cimaz R., 0051 (OP0093), 0240 (POS0068), 0247 (POS0079), 0628 (POS0751), 0934 (POS1304), 0935 (POS1307), 0936 (POS1308), 0940 (POS1315), 0940 (POS1316), 0941 (POS1317), 0958 (POS1352)
Cimmino M. A., 0655 (POS0806), 1201 (AB0354)
Cinakli H., 0722 (POS0922), 0861 (POS1165), 1255 (AB0456), 1366 (AB0669)
Çınar M., 0727 (POS0929), 0731 (POS0935)
Çınar M., 1470 (AB0893-HPR)
Cincinelli G., 0284 (POS0145), 0870 (POS1178), 0872 (POS1182), 0941 (POS1317), 1374 (AB0683)
Cioffi G., 0326 (POS0218)
Cipolletta E., 0123 (OP0205), 0125 (OP0209), 0463 (POS0464), 0517 (POS0565), 0811 (POS1066), 0850 (POS1141)
Cipriani P., 0954 (POS1344), 0957 (POS1349), 1105 (AB0156)
Çıracı M. Z., 1086 (AB0114)
Circiumaru A., 0087 (OP0146), 0087 (OP0147), 0429 (POS0400), 1005 (POS1441)
Cirillo M., 1389 (AB0716)
Citera G., 0382 (POS0312), 0579 (POS0670), 0740 (POS0953), 0782 (POS1025), 1133 (AB0214), 1148 (AB0247)
Citeroni N., 0573 (POS0662)
Citriniti G., 0355 (POS0265)
Ciurea A., 0217 (POS0027), 0863 (POS1168)
Ciurtin C., 0008 (OP0013), 0300 (POS0174), 0625 (POS0746)
Civi Karaaslan T., 1389 (AB0715), 1453 (AB0860-HPR)
Civit De Garignani E. E., 1133 (AB0214)
Claire D., 0227 (POS0045)
Clark D., 0879 (POS1195)
Clark K., 0078 (OP0135)
Clark N., 0374 (POS0298)
Clark Y., 1057 (AB0051)
Clarke A. E., 0173 (OP0286), 0177 (OP0289), 0617 (POS0734)
Claudepierre P., 0027 (OP0052), 0172 (OP0284), 0317 (POS0201)
Claudia F., 1183 (AB0317)
Clavel C., 0206 (POS0009), 1061 (AB0058)
Clavijo Cornejo D., 1348 (AB0629)
Cleaton N., 0903 (POS1241)
Clément C., 0227 (POS0045)
Clemente D., 0872 (POS1183)
Clemente Garulo D., 0914 (POS1260)
Clewell J., 0353 (POS0262)
Clodi E., 0004 (OP0008)
Clouser Roche A., 0844 (POS1130)
Clowse M., 0213 (POS0022)
Cluckley D., 1050 (AB0034)
Cluzel P., 1186 (AB0323)
Coarse J., 0779 (POS1022)
Coassy A., 1164 (AB0277)
Coates L. C., 0039 (OP0074), 0135 (OP0224), 0139 (OP0229), 0140 (OP0230), 0183 (OP0298), 0338 (POS0235), 0728 (POS0930), 0779 (POS1022), 0781 (POS1024), 0785 (POS1029), 0789 (POS1034), 0792 (POS1037), 0792 (POS1038), 0797 (POS1044), 0801 (POS1049), 0803 (POS1051), 0821 (POS1084), 1301 (AB0539), 1308 (AB0550), 1316 (AB0560)
Coath F., 0744 (POS0959)
Cobelo C., 1076 (AB0096)
Cobilinschi C., 0164 (OP0270), 0681 (POS0854), 0773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1462 (AB0879-HPR)
Cobo-Ibáñez T., 0610 (POS0721)
Cobos-Villanueva F., 0904 (POS1242)
Cobra J., 0194 (OP0318)
Codd Y., 0291 (POS0156-HPR)
Codes H., 1093 (AB0129), 1365 (AB0666)
Codner D., 0431 (POS0405), 0432 (POS0406)
Codreanu C., 0131 (OP0220), 0217 (POS0027), 0256 (POS0093)
Codullo V., 0685 (POS0861), 0906 (POS1246)
Coe A., 0291 (POS0156-HPR)
Coenen M. J. H., 0009 (OP0017)
Coffey C., 0128 (OP0213), 0213 (POS0023), 0673 (POS0838)
Coffy A., 0379 (POS0306)
Cogo A. K., 0874 (POS1186)
Cohen A., 0131 (OP0219), 0286 (POS0147)
Cohen F., 1186 (AB0323), 1412 (AB0772)
Cohen S. B., 0328 (POS0220), 0563 (POS0650), 0564 (POS0651), 1149 (AB0248)
Cohen S., 1096 (AB0138), 1097 (AB0140)
Cohen Solal M., 0365 (POS0281)
Colaci M., 0388 (POS0322), 0906 (POS1246), 1135 (AB0217), 1135 (AB0218)
Colaco K., 0132 (OP0221), 0812 (POS1068)
Coladonato L., 1217 (AB0380)
Colafrancesco S., 0893 (POS1219), 1183 (AB0317)
Colagrande S., 0355 (POS0264), 0897 (POS1228)
Colak S., 0731 (POS0935)
Colaklar A., 0532 (POS0597), 0949 (POS1335)
Colasanti T., 1073 (AB0087)
Colatutto D., 0878 (POS1192)
Coldstream F., 1474 (AB0903-HPR)
Cole B., 0363 (POS0277)
Colella F., 0019 (OP0036)
Coleman M., 1175 (AB0298)
Colia R., 1379 (AB0691)
Colic A., 0234 (POS0056), 0865 (POS1170)
Colic J., 0693 (POS0874)
Colin E., 1209 (AB0367), 1214 (AB0375)
Collaboration of Rheumatologists C., 0807 (POS1057)
Collado L., 0425 (POS0392)
Collado P., 1076 (AB0096)
Collado Rodríguez L., 0306 (POS0185)
Collantes Estevez E., 0009 (OP0017), 0020 (OP0038), 0426 (POS0394), 0469 (POS0475), 0737 (POS0948), 0740 (POS0952), 0743 (POS0958), 0747 (POS0965), 0751 (POS0970), 0769 (POS1001), 0920 (POS1272), 1259 (AB0465), 1317 (AB0562)
Collantes-Estevez E., 0736 (POS0946), 0763 (POS0991), 0764 (POS0992), 0765 (POS0993), 0765 (POS0994)
Collantes-Estévez E., 0746 (POS0962)
Collet G., 0664 (POS0822)
Colli-Cortés M. B., 1386 (AB0709)
Collier D., 0066 (OP0118)
Collins F., 0019 (OP0036)
Collins G., 0274 (POS0125)
Collins T., 0157 (OP0258-HPR), 0228 (POS0047)
Colmegna I., 0010 (OP0018), 0918 (POS1268)
Colmenero Camacho M. A., 1341 (AB0612)
Colombo B., 1190 (AB0330)
Colombo F., 0319 (POS0206)
Colombres F., 0382 (POS0312)
Colomer J. I., 0896 (POS1225), 0908 (POS1251), 0910 (POS1253)
Colston E., 0795 (POS1042)
Colton C., 0843 (POS1128), 0844 (POS1130)
Colunga-Pedraza I. J., 0463 (POS0463), 0473 (POS0482), 0473 (POS0483), 0478 (POS0491), 0510 (POS0552), 0511 (POS0553), 0515 (POS0562), 0816 (POS1074), 0978 (POS1392), 0983 (POS1402), 0984 (POS1404), 1087 (AB0117), 1189 (AB0329), 1450 (AB0852), 1459 (AB0871-HPR)
Colwell H. H., 1203 (AB0357)
Coman I., 1112 (AB0172), 1246 (AB0435)
Combe B., 0019 (OP0035), 0028 (OP0053), 0054 (OP0098), 0080 (OP0138), 0085 (OP0144), 0109 (OP0181), 0110 (OP0183), 0128 (OP0214), 0258 (POS0095), 0379 (POS0306), 0380 (POS0308), 0518 (POS0566), 0567 (POS0654), 0569 (POS0657), 0570 (POS0658), 0770 (POS1003), 0789 (POS1033), 0820 (POS1082), 0902 (POS1239), 1273 (AB0493)
Combier A., 1364 (AB0665)
Comduehr S., 0395 (POS0335)
Cometi L., 0105 (OP0176), 1032 (POS1495-HPR), 1154 (AB0256)
Commisso C., 1326 (AB0578)
Compeán-Villegas J. E., 0893 (POS1220), 1463 (AB0880-HPR)
Conaghan P. G., 0089 (OP0149), 0093 (OP0155-HPR), 0136 (OP0226), 0153 (OP0252), 0275 (POS0128), 0311 (POS0194), 0314 (POS0197), 0450 (POS0443), 0468 (POS0474), 0625 (POS0746), 0707 (POS0901), 0794 (POS1040), 0919 (POS1269), 0943 (POS1323), 1334 (AB0594)
Concha J., 0383 (POS0315)
Conde Aranda J., 0418 (POS0376)
Condell J., 0740 (POS0952)
Conesa A., 0952 (POS1340)
Conesa-Zamora P., 0009 (OP0017)
Confalonieri M., 0897 (POS1228), 1002 (POS1435)
Conforti A., 0954 (POS1344), 1105 (AB0156)
Conforti M. L., 1032 (POS1495-HPR)
Conigliaro P., 0335 (POS0231), 0619 (POS0737), 0628 (POS0751), 0980 (POS1395), 1038 (AB0006), 1284 (AB0515), 1434 (AB0821)
Conings T., 0545 (POS0616)
Conlon N., 1230 (AB0404)
Connell C. A., 0565 (POS0652)
Connelly M., 1029 (POS1490-HPR)
Connolly S., 0108 (OP0180), 0794 (POS1040), 1127 (AB0205)
Connolly-Strong E., 0478 (POS0492), 1096 (AB0138)
Conort O., 0360 (POS0273-HPR), 0534 (POS0600)
Consolaro A., 0097 (OP0161)
Constantin A., 0258 (POS0095), 0559 (POS0641), 0869 (POS1177)
Constantine S., 0102 (OP0171), 0383 (POS0315)
Constantinescu A., 1462 (AB0879-HPR)
Constantinescu C. L., 0164 (OP0270), 0681 (POS0854), 0773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690), 1462 (AB0879-HPR)
Conti F., 0445 (POS0433), 0582 (POS0675), 0583 (POS0677), 0588 (POS0685), 0594 (POS0693), 0619 (POS0737), 0645 (POS0783), 0778 (POS1021), 0873 (POS1185), 0893 (POS1219), 0902 (POS1238), 0903 (POS1240), 1017 (POS1464-HPR), 1069 (AB0079), 1073 (AB0087), 1143 (AB0234), 1160 (AB0269), 1384 (AB0704)
Conticini E., 0573 (POS0661), 0669 (POS0832), 0746 (POS0963)
Contreras G., 0591 (POS0689)
Contreras R., 1042 (AB0015)
Conversano F., 0294 (POS0163)
Conway R., 0230 (POS0051), 0859 (POS1162), 1230 (AB0404), 1368 (AB0674)
Cook C., 0867 (POS1174), 0997 (POS1428)
Cook R., 0132 (OP0221), 0173 (OP0285), 0230 (POS0050), 0812 (POS1068)
Cope A., 0403 (POS0348), 1357 (AB0649)
Coppa G., 0668 (POS0830)
Coppes T., 0547 (POS0620)
Coral Alvarado P., 0479 (POS0493), 1081 (AB0106)
Corallo C., 0392 (POS0330)
Corbella X., 0001 (OP0004)
Cordeiro A., 0692 (POS0872)

Cordeiro I., 0690 (POS0870), 0692 (POS0872), 1250 (AB0445)
Corder R., 0120 (OP0200)
Cordero-Coma M., 0032 (OP0060), 0952 (POS1340), 1225 (AB0396), 1412 (AB0771)
Cordes M., 0165 (OP0272)
Cordingley L., 1029 (POS1490-HPR)
Cordtz R. L., 0215 (POS0025)
Cordtz R., 0382 (POS0313)
Ćorić M., 1199 (AB0348), 1199 (AB0349)
Corica F., 0838 (POS1119)
Cornalba M., 0199 (LB0002)
Cornelio A., 1187 (AB0325), 1188 (AB0326), 1351 (AB0635)
Cornell T., 0041 (OP0076)
Cornillie A., 1358 (AB0651)
Corominas H., 0277 (POS0132), 0655 (POS0806), 0666 (POS0827), 1093 (AB0129), 1158 (AB0264), 1219 (AB0384), 1365 (AB0666), 1426 (AB0804)
Coronel P., 0366 (POS0282)
Corp N., 0139 (OP0229)
Corradi F., 0628 (POS0751)
Corrado A., 0701 (POS0891), 1379 (AB0691)
Corral Trujillo M. E., 1361 (AB0658), 1457 (AB0867-HPR)
Corrales A., 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1018 (POS1467-HPR), 1046 (AB0026), 1065 (AB0070), 1076 (AB0094)
Corrêa B., 0208 (POS0013)
Correa Rodríguez M., 1182 (AB0315), 1183 (AB0316)
Correa-Fernández J., 0239 (POS0065-PARE), 0744 (POS0960), 0745 (POS0961), 0746 (POS0962), 0762 (POS0988), 0765 (POS0993), 0765 (POS0994), 0868 (POS1175), 0889 (POS1213), 1277 (AB0500), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Corte G., 0979 (POS1394)
Cortese G., 0897 (POS1228)
Cortet B., 0364 (POS0279), 0662 (POS0818), 0835 (POS1111)
Corwin E. J., 0299 (POS0173)
Cosan F., 1470 (AB0893-HPR)
Cosatti M., 0730 (POS0933), 0887 (POS1208), 1377 (AB0689)
Coscia M. A., 1165 (AB0279)
Cosentino M., 0635 (POS0763)
Cosentino V., 0730 (POS0933), 0771 (POS1005), 1377 (AB0689)
Cosenza M. E., 1167 (AB0282)
Coşkun B. N., 0069 (OP0125), 0731 (POS0935)
Coskun Benlidayi I., 1471 (AB0896-HPR)
Coşkuner T., 0249 (POS0082), 0871 (POS1181), 0942 (POS1319)
Cosma C., 0894 (POS1221)
Cossmann A., 1385 (AB0707)
Cosso R., 1216 (AB0379)
Cossu B., 0833 (POS1105)
Costa C., 0161 (OP0264-HPR)
Costa E., 0354 (POS0263), 0690 (POS0870), 0692 (POS0872), 1003 (POS1438), 1424 (AB0799)
Costa L., 0260 (POS0100), 0318 (POS0204), 0476 (POS0488), 0483 (POS0502), 0718 (POS0914), 0812 (POS1067), 0833 (POS1106), 0836 (POS1113), 0919 (POS1270), 0957 (POS1349), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1191 (AB0332), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1271 (AB0488), 1284 (AB0515), 1299 (AB0536), 1339 (AB0608), 1432 (AB0816), 1441 (AB0835)
Costa M., 1402 (AB0747)
Costa Moya E., 1060 (AB0055)
Costa N., 0182 (OP0297)
Costa Reis P., 0247 (POS0079), 0934 (POS1304)
Costache N. O., 1267 (AB0480)
Coste B., 0518 (POS0566), 0770 (POS1003), 0820 (POS1082)
Costecalde C., 0877 (POS1190)
Costedoat-Chalumeau N., 0181 (OP0295), 0181 (OP0296), 0182 (OP0297), 0612 (POS0724), 0968 (POS1373)
Costello R. E., 0872 (POS1183)
Costello W., 0002 (OP0006), 0115 (OP0191-PARE), 0173 (OP0286), 0175 (OP0288), 1373 (AB0681)
Costi S., 0935 (POS1307), 0936 (POS1308), 0940 (POS1315)
Coto-Hernández R., 0700 (POS0888)
Cots F., 0991 (POS1416)
Cottencin O., 1011 (POS1454-HPR)
Cougnaud Murail R., 0534 (POS0600)
Coumbe B. G. T., 1230 (AB0403)
Coupal L., 0107 (OP0179), 0454 (POS0448)
Courvoisier D., 0058 (OP0105), 0256 (POS0093), 0577 (POS0668)
Coury-Lucas F., 0571 (POS0659)
Couto M., 0692 (POS0872)
Coviello M., 1434 (AB0821)
Cowan M. P., 0771 (POS1005)
Cox C., 1050 (AB0034)
Cox P., 0844 (POS1131)
Cozzi F., 0386 (POS0318), 0392 (POS0329), 0906 (POS1246)
Cozzi G., 0894 (POS1221), 1308 (AB0549)
Cozzi M., 0979 (POS1393)
Cracowski J. L., 0331 (POS0225)
Crane D. A., 0609 (POS0719)
Crespo Espindola M. E., 1194 (AB0338)
Crespo J., 0970 (POS1376)
Crespo-Golmar A., 1048 (AB0030)
Crestani B., 0054 (OP0099), 0258 (POS0095)
Creus-Vila L., 0891 (POS1215)
Crijns H. J. M. J., 0317 (POS0202)
Crisafulli F., 0051 (OP0093), 0470 (POS0476), 0600 (POS0702), 0619 (POS0737), 0633 (POS0760), 1435 (AB0822)
Cristaudo A., 1318 (AB0563)
Cristina N., 0164 (OP0270)
Cristovão Maiorano A., 0625 (POS0747), 0999 (POS1430)
Cron R., 0192 (OP0314)
Croot L., 1451 (AB0854)
Cros M., 1148 (AB0247)
Cross M., 0358 (POS0269-HPR), 0358 (POS0270-HPR)
Crowson C. S., 0056 (OP0102), 0106 (OP0177), 0128 (OP0213), 0129 (OP0216), 0213 (POS0023), 0219 (POS0029), 0322 (POS0210), 0380 (POS0309), 0381 (POS0311), 0389 (POS0325), 0652 (POS0801), 0654 (POS0803), 0655 (POS0805), 0672 (POS0836), 0673 (POS0838), 0795 (POS1041), 0951 (POS1338)
Croxford R., 0173 (OP0285), 0230 (POS0050)
Cruz Y., 1187 (AB0325), 1188 (AB0326), 1351 (AB0635)
Cruz-Caparrós M., 1183 (AB0316)
Cruz-Domínguez M. D. P., 0904 (POS1242)
Crylov I., 1285 (AB0516)
Cuande E., 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Cubuk C., 0007 (OP0011)
Cucchiaro N., 0875 (POS1188), 1194 (AB0338), 1196 (AB0342)
Cucnik S., 1069 (AB0080), 1201 (AB0352)
Cuenca-Vera O., 1208 (AB0365)
Cuende E., 1103 (AB0151)
Cuevas Orta E., 0624 (POS0745)
Cui A., 0374 (POS0298)
Cui X., 0661 (POS0817)
Culver E. L., 0907 (POS1247)
Cumbo E., 0858 (POS1161)
Cunha A. R., 0179 (OP0293), 0738 (POS0950)
Cunha M., 0354 (POS0263)
Cunha Rodrigues K., 0991 (POS1415)
Cunha Santos F., 0354 (POS0263), 0773 (POS1010)
Cuomo G., 0778 (POS1021), 0906 (POS1246), 0907 (POS1248), 1446 (AB0844), 1475 (AB0905-HPR)
Cura Yayla B. C., 0908 (POS1249)
Curraj E., 0880 (POS1196)
Currie C., 1000 (POS1432)
Curtis J. R., 0328 (POS0220), 0356 (POS0267-HPR)
Curtis J., 0066 (OP0118), 0255 (POS0092), 0316 (POS0200), 0369 (POS0287), 0458 (POS0456), 0530 (POS0594), 0539 (POS0607), 0782 (POS1026), 0784 (POS1028), 1034 (POS1499-PARE)
Curtis P., 0591 (POS0689)
Cusa A., 0576 (POS0667)
Cush J., 0580 (POS0671)
Cutolo M., 0190 (OP0310), 0392 (POS0330), 0524 (POS0583), 0679 (POS0850), 0686 (POS0862), 0697 (POS0882), 0908 (POS1250), 1060 (AB0057), 1107 (AB0160), 1190 (AB0330), 1201 (AB0354), 1247 (AB0438), 1372 (AB0679), 1389 (AB0716)
Cutter G., 0279 (POS0135)
Cuttica R., 0245 (POS0076)
Czirják L., 0387 (POS0321)
Czókolyová M., 0421 (POS0383), 0425 (POS0390)

D'agostino M. A., 0136 (OP0226), 0314 (POS0197), 0370 (POS0289), 0687 (POS0864), 0845 (POS1132), 0846 (POS1133), 0850 (POS1141), 1273 (AB0493), 1348 (AB0629)
D'alessandro R., 0746 (POS0963), 1252 (AB0450)
D'amico M. E., 0586 (POS0682)
D'andréa Greve J. M., 0699 (POS0887)
D'angelo S., 0722 (POS0923), 0809 (POS1061), 0906 (POS1246), 1260 (AB0467)
D'antonio A., 0335 (POS0231), 1284 (AB0515), 1418 (AB0786)
D'cruz D., 0596 (POS0696), 0625 (POS0746), 1215 (AB0377)
D'haens G., 0359 (POS0271-HPR)
D'Onofrio B., 0521 (POS0575)
D'onofrio B., 0913 (POS1258)
D'silva K., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0867 (POS1174)
D'urso M., 0756 (POS0979)
Da Rocha Castelar Pinheiro G., 0582 (POS0676)
Da Silva J. A. P., 0179 (OP0293), 0233 (POS0055), 0606 (POS0713), 0695 (POS0878), 1101 (AB0147), 1107 (AB0160)
da Silva J. A. P., 0481 (POS0496)
Da Z., 0387 (POS0320)
Daada S., 1198 (AB0346), 1225 (AB0395)
Dadalova A., 0776 (POS1017), 0777 (POS1019), 1095 (AB0135), 1285 (AB0516), 1387 (AB0712)
Dadashova R., 0224 (POS0037)
Dadoun S., 0343 (POS0243), 0360 (POS0274-HPR)
Dagan A., 0892 (POS1217)
Dagan N., 0928 (POS1294)
Dagna L., 0037 (OP0068), 0051 (OP0093), 0190 (OP0310), 0348 (POS0253), 0613 (POS0726), 0694 (POS0877), 0809 (POS1061), 0897 (POS1228), 0906 (POS1246), 0907 (POS1247), 0950 (POS1336), 0953 (POS1341), 0955 (POS1347), 0960 (POS1356), 0974 (POS1382), 1206 (AB0361), 1211 (AB0370), 1260 (AB0467), 1389 (AB0716)
Daher A., 0361 (POS0275-HPR), 1080 (AB0104)
Dai F., 0852 (POS1146), 1040 (AB0011), 1067 (AB0075), 1252 (AB0449)
Dai L., 0456 (POS0452), 1091 (AB0125), 1174 (AB0296), 1225 (AB0394), 1227 (AB0398), 1465 (AB0883-HPR)
Dai X., 0657 (POS0810)
Daia S., 0164 (OP0270), 0681 (POS0854), 1112 (AB0172), 1246 (AB0435)
Daia-Iliescu S., 0773 (POS1009), 1378 (AB0690), 1462 (AB0879-HPR)
Daien C., 0019 (OP0035), 0054 (OP0098), 0128 (OP0214), 0518 (POS0566), 0770 (POS1003), 0820 (POS1082), 0902 (POS1239), 1148 (AB0247)
Daikeler T., 0655 (POS0806)
Dakkak Y., 0212 (POS0021)
Dal Pozzolo L., 0612 (POS0724)
Dal Pra Wendt A., 1440 (AB0833)
Dalakas M., 1381 (AB0697)
Dalbeni A., 0326 (POS0218)
Dalbeth N., 0281 (POS0139), 0841 (POS1124), 0845 (POS1132), 0846 (POS1133)
Daldoul C., 0526 (POS0588), 0837 (POS1116), 0838 (POS1117), 0858 (POS1160), 1346 (AB0625)
Dale J., 1159 (AB0265)
Dalkılıç E., 1140 (AB0229)
Dall'era M., 0595 (POS0694)
Dallagiacoma G., 1404 (AB0752)
Dallas J., 0165 (OP0271)
Dallegi A., 1102 (AB0150), 1118 (AB0187)

Dallos T., 0242 (POS0071)
Dalmao-Fernandez A., 0403 (POS0347)
Dalsgaard Nielsen B., 0036 (OP0066), 0657 (POS0809)
Damadoğlu E., 0347 (POS0251)
Damak J., 0837 (POS1115)
Damann N., 0806 (POS1055)
Damdimopoulos A., 0428 (POS0397)
Damerau A., 0191 (OP0312), 1049 (AB0031), 1052 (AB0040)
Damian L., 0638 (POS0768), 1360 (AB0656)
Damiani A., 0546 (POS0618)
Damjanov N., 0039 (OP0074), 0385 (POS0317), 0693 (POS0874)
Dan D., 0863 (POS1168)
Danebod K., 0234 (POS0056), 0865 (POS1170)
Daniello L., 0372 (POS0293)
Daniels J., 1021 (POS1472-HPR)
Daniels M., 0596 (POS0697)
Danielsen C., 1196 (AB0342)
Dapeña J. M., 0635 (POS0763)
Daridon C., 0567 (POS0654)
Darmant N., 1022 (POS1475-HPR)
Dasgupta B., 0396 (POS0337), 1211 (AB0370)
Dashkevich E., 0970 (POS1377)
Dass S., 0030 (OP0057), 1173 (AB0293)
Dau J., 0853 (POS1148), 0854 (POS1150)
Daures J. P., 0109 (OP0181), 0379 (POS0306)
Davenport E., 0808 (POS1060)
Davergne T., 0360 (POS0274-HPR)
David N., 0625 (POS0747), 0999 (POS1430)
David T., 1172 (AB0291)
Davidian S., 0709 (POS0903)
Davidson B., 1175 (AB0298), 1233 (AB0409)
Davidson T., 0654 (POS0804)
Davies J., 0167 (OP0275-PARE)
Davies R., 0148 (OP0241)
Davila-Jimenez J. A., 0463 (POS0463)
Davis C., 0278 (POS0134), 0374 (POS0298)
Davis III J. M., 0056 (OP0102), 0128 (OP0213), 0129 (OP0216), 0213 (POS0023), 0322 (POS0210), 0380 (POS0309), 0381 (POS0311)
Davydova A., 1095 (AB0135)
Dawes M., 0377 (POS0303)
Dawson J., 1441 (AB0834)
Day J., 0135 (OP0224), 0697 (POS0883), 0821 (POS1084)
De Abajo F., 0144 (OP0234)
DE Abreu Trigueros P., 1106 (AB0159)
De Agustin J. J., 1158 (AB0264)
De Angelis R., 0906 (POS1246)
De Argila D., 1076 (AB0096)
De Baere K., 0275 (POS0126)
De Bandt M., 0735 (POS0945)
De Bari C., 0019 (OP0036), 1052 (AB0039)
de Barros Lopes R., 1478 (AB0913-PARE)
De Benedetti F., 0098 (OP0164)
De Benedittis G., 1038 (AB0006)
De Blasi M., 0031 (OP0058)
De Boer P., 0932 (POS1300)
De Bono S., 0588 (POS0686)
De Boysson H., 0397 (POS0338), 0669 (POS0831)
De Bresser J., 0606 (POS0714)
de Buck P. D., 0471 (POS0479)
De Buck P. D., 0978 (POS1391)
De Carolis C., 0619 (POS0737)
De Ciuceis C., 0530 (POS0593)
De Cobelli F., 0897 (POS1228)
De Cock D., 0256 (POS0093), 0304 (POS0181), 0356 (POS0266-HPR), 0375 (POS0300), 0484 (POS0503), 0545 (POS0616), 0884 (POS1203), 1001 (POS1433), 1001 (POS1434), 1083 (AB0109)
De Diego Sola A., 1141 (AB0230)
De Dios J. R., 0034 (OP0064), 0035 (OP0065)
De Dios-Jiménez Aberásturi J., 0952 (POS1340)
De Francesco M., 0644 (POS0782)
de Hooge M., 0041 (OP0077)
De Hooge M., 0153 (OP0251)
De Inocencio J., 0098 (OP0164)
De Jong E., 0680 (POS0852)
De Jong P., 0992 (POS1418), 0993 (POS1419), 1087 (AB0116), 1430 (AB0812)
De Jong S., 0805 (POS1053)
De Jong T., 0012 (OP0021)
de Jong T., 0425 (POS0391)
De Jonge R., 0012 (OP0021), 1151 (AB0251)
De Jongh J., 0114 (OP0189)
De la Macorra J., 0560 (POS0645)
De la Rubia Navarro M., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
De La Torre I., 1157 (AB0261)
De la Torre M. L., 1196 (AB0342)
De la Torre N., 0892 (POS1218), 0914 (POS1260)
De Langhe E., 0196 (OP0321)
De Leeuw K., 0189 (OP0308), 1071 (AB0082)
De Lorenzis E., 0370 (POS0289), 0687 (POS0864), 0701 (POS0891)
De Luca G., 0232 (POS0054), 0906 (POS1246), 0950 (POS1336), 0953 (POS1341), 0955 (POS1347)
De Lucia O., 0134 (OP0223), 0284 (POS0145), 0935 (POS1307), 1331 (AB0588), 1374 (AB0683)
De Macedo Dos Santos L., 0699 (POS0887)
De Marchi G., 0594 (POS0693), 0878 (POS1192)
De Marco G., 0089 (OP0149), 0153 (OP0252), 0175 (OP0287), 0231 (POS0052)
De Martinis M., 1246 (AB0434)
De Meulemeester K., 0828 (POS1096)
De Miguel E., 0034 (OP0064), 0399 (POS0342), 0664 (POS0821), 0755 (POS0978), 0760 (POS0986), 0766 (POS0996), 0976 (POS1387), 1208 (AB0366), 1216 (AB0378), 1218 (AB0382)
De Montjoye S., 0066 (OP0119), 0880 (POS1196)
De Mutsert R., 0999 (POS1431)
De Oliveira R., 1405 (AB0754)
De Pablo P., 0216 (POS0026)
De Paulis A., 0594 (POS0693), 0897 (POS1228)
De Peyrecave N., 0332 (POS0226), 0720 (POS0919)
De Pietro F., 1246 (AB0434)
De Pinto M., 0672 (POS0837), 1241 (AB0425)
De Ribains G., 0018 (OP0034)
De Sandre P., 1099 (AB0143)
De Santis M., 0152 (OP0249), 0232 (POS0054), 0906 (POS1246)
de Silva N. L., 0485 (POS0505)
De Silva T., 0876 (POS1189)
De Slegte R., 0351 (POS0258)
De Souza V., 0909 (POS1252), 1448 (AB0848)
De Stefano G., 0882 (POS1200), 1399 (AB0739)
De Stefano L., 0521 (POS0575), 0913 (POS1258)
De Taeye S., 1044 (AB0020)
De Toro Santos J., 0540 (POS0608)
De Veras B., 0625 (POS0747), 0999 (POS1430)
De Vicente-Delmás A., 1324 (AB0574)
De Vita S., 0009 (OP0017), 0078 (OP0135), 0178 (OP0291), 0284 (POS0145), 0593 (POS0692), 0594 (POS0693), 0618 (POS0735), 0628 (POS0751), 0809 (POS1061), 0878 (POS1192), 0883 (POS1201), 1224 (AB0392)
De Vlam K., 0142 (OP0232), 0707 (POS0901), 0712 (POS0907), 0713 (POS0908), 0799 (POS1046), 0800 (POS1047), 1295 (AB0530)
De Vries C., 0996 (POS1425)
De Vries H., 1479 (AB0915-PARE)
De Vries-Bouwstra J., 0203 (POS0001), 0385 (POS0317), 0675 (POS0843), 0694 (POS0877)
De Wit M., 0006 (OP0010), 0139 (OP0229), 0183 (OP0298), 0198 (OP0324-PARE), 0374 (POS0299), 1483 (AB0924-PARE)
de Wolff L., 0074 (OP0130)
De Wolff L., 1257 (AB0462)
De Zwart A., 0291 (POS0157-HPR)
Deakin C., 0330 (POS0223), 0369 (POS0288), 0547 (POS0619), 1015 (POS1461-HPR)
Deary V., 0157 (OP0258-HPR)
Debacker E., 0275 (POS0126)
Debattista J., 1068 (AB0077)
Debbaruah P., 1041 (AB0013)
Debray M. P., 0258 (POS0095)
Debrut L., 0149 (OP0243), 0694 (POS0876)
Dębska-Ślizień A., 1434 (AB0820)
Decarriere G., 0128 (OP0214)
Decavele L., 0275 (POS0126)
Decianu R., 0773 (POS1009)
Dedeoglu F., 0165 (OP0271)
Deely D., 0241 (POS0069)
Dees C., 0165 (OP0272), 0391 (POS0328)
Degroote P., 1229 (AB0401)
Dehlin M., 0115 (OP0192), 0125 (OP0208), 0372 (POS0295), 1350 (AB0633)
Dejaco C., 0189 (OP0309), 1213 (AB0373), 1216 (AB0379), 1404 (AB0752)
Dejcman D., 1103 (AB0152)
Dekate P., 0900 (POS1235), 1242 (AB0428)
Deken V., 1011 (POS1454-HPR)
Dekker J., 0291 (POS0157-HPR), 1020 (POS1470-HPR)
Del Frate G., 0883 (POS1201)
Del Galdo F., 0163 (OP0269), 0385 (POS0317), 0387 (POS0319), 1074 (AB0089), 1244 (AB0431)
Del Papa N., 0232 (POS0054)
Del Rio A. P., 1255 (AB0457)
Del Río Martínez P. S., 0760 (POS0986)
Del Ross T., 0619 (POS0737), 1174 (AB0295), 1308 (AB0549)
Del Val del Amo N., 0960 (POS1355)
Delacour M., 0662 (POS0818)
Delavega M., 0489 (POS0512), 0874 (POS1186)
Delavenne X., 1164 (AB0277)
Delcoigne B., 0063 (OP0114), 0145 (OP0236), 0535 (POS0601), 0864 (POS1169), 0939 (POS1313)
Delemarre E. M., 1430 (AB0812)
De-Leon-Ibarra A. L., 1007 (POS1446), 1166 (AB0281), 1455 (AB0863-HPR), 1456 (AB0866-HPR)
Delepine T., 1258 (AB0464)
Delev N., 0076 (OP0132)
Delgado Beltrán C., 0967 (POS1371)
Delgado de la Poza J. F., 1060 (AB0055)
Delgado Sanchez M., 1208 (AB0366)
Delgado Tellez de Cepeda L., 0892 (POS1218)
Delgado-Domínguez C. J., 0239 (POS0065-PARE), 0343 (POS0244), 0744 (POS0960), 0745 (POS0961), 0762 (POS0988), 0762 (POS0989), 0763 (POS0990)
Dell'accio F., 0120 (OP0200), 1052 (AB0039)
Dell'isola A., 0292 (POS0160-HPR), 1372 (AB0678)
Della Paolera S., 0948 (POS1333)
Della Porta R., 1002 (POS1435)
Della Rossa A., 0906 (POS1246), 1232 (AB0407)
Della Torre E., 0907 (POS1247), 0950 (POS1336), 0960 (POS1356), 0974 (POS1382)
Dellamaria G., 0742 (POS0956)
Delle Sedie A., 0778 (POS1021), 1260 (AB0467)
Delolmo-Romero S., 1182 (AB0315)
Delphine W. V., 0719 (POS0916)
Delplace S., 0431 (POS0404)
Delrue N., 0828 (POS1096)
Delva Y., 0866 (POS1172)
Del-Val N., 0610 (POS0721), 1132 (AB0211)
Delvino P., 0029 (OP0055), 0347 (POS0250), 0668 (POS0830)
Demailly F., 0664 (POS0822)
Demasi R., 0566 (POS0653)
Demetres M., 0828 (POS1097)
Demetrio-Pablo R., 0050 (OP0091), 0220 (POS0030), 0621 (POS0740), 0960 (POS1357), 0977 (POS1390), 1225 (AB0396), 1226 (AB0397), 1227 (AB0399), 1412 (AB0771)
Demetriou C., 0859 (POS1162)
Demidova N., 1084 (AB0111)
Demin N., 0493 (POS0519), 0673 (POS0839), 0674 (POS0841), 1104 (AB0154), 1342 (AB0613), 1422 (AB0795)
Demina A., 0761 (POS0987), 1264 (AB0473), 1264 (AB0474), 1276 (AB0498), 1284 (AB0514)
Demir A., 1191 (AB0331)
Demir F., 0229 (POS0049), 0249 (POS0082), 0871 (POS1181), 0933 (POS1302), 0942 (POS1319)
Demir S., 0117 (OP0195), 0243 (POS0074)
Demirci Yıldırım T., 1386 (AB0708)
Demirkaya E., 0942 (POS1320), 0958 (POS1352), 0968 (POS1372), 0969 (POS1375)
Demirkol M. E., 1471 (AB0896-HPR)
Demmelmaie I., 0093 (OP0156-HPR)
Demonte D., 0021 (OP0039)
Demougeot C., 1062 (AB0062), 1067 (AB0073), 1159 (AB0266)
Demoulin D., 0128 (OP0214)

Den Broeder A., 0009 (OP0017), 0310 (POS0193), 0399 (POS0343), 0880 (POS1197), 1023 (POS1477-HPR), 1027 (POS1485-HPR), 1460 (AB0873-HPR)
den Broeder A., 0478 (POS0492)
Den Broeder N., 0310 (POS0193), 0399 (POS0343)
Denefle P., 0417 (POS0373)
Deneux-Tharaux C., 0181 (OP0295)
Deng W., 0278 (POS0133), 0847 (POS1135), 1057 (AB0050), 1354 (AB0642), 1355 (AB0645), 1421 (AB0791)
Denisova E., 0948 (POS1332)
Denisova R., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Deniz G., 0522 (POS0576)
Deniz R., 0191 (OP0313), 1006 (POS1445)
Dennison E., 0835 (POS1111)
Denson J., 0198 (LB0001)
Denton C., 0101 (OP0170), 0102 (OP0171), 0163 (OP0269), 0387 (POS0321), 0685 (POS0861), 0897 (POS1228), 1229 (AB0402), 1244 (AB0431)
Deodhar A., 0085 (OP0144), 0137 (OP0227), 0143 (OP0233), 0314 (POS0198), 0332 (POS0226), 0338 (POS0235), 0707 (POS0900), 0708 (POS0902), 0710 (POS0905), 0712 (POS0907), 0716 (POS0912), 0720 (POS0919), 0734 (POS0943), 0785 (POS1029), 0789 (POS1033), 0798 (POS1045), 0801 (POS1048), 1262 (AB0471), 1290 (AB0525), 1291 (AB0526), 1292 (AB0527)
Deparis N., 1009 (POS1450)
Depascale R., 0630 (POS0755)
Deppe D., 0156 (OP0256)
Deprez X., 0114 (OP0190), 1258 (AB0464)
Deprouw C., 0360 (POS0274-HPR)
Derakhshan M. H., 1159 (AB0265)
Derin M. E., 0966 (POS1368), 1380 (AB0694)
Derksen V., 1366 (AB0668)
Derman O., 1398 (AB0737)
Dernis E., 0080 (OP0138), 0183 (OP0298)
Dertkgil R., 0100 (OP0167)
Dertkigil S., 0100 (OP0167), 1255 (AB0457)
Descamps E., 1364 (AB0665)
Descamps V., 0901 (POS1236), 0901 (POS1237)
Deshani V., 1354 (AB0641)
Deshayes S., 0397 (POS0338), 0669 (POS0831), 0954 (POS1343)
Deshmukh V., 0060 (OP0108), 0416 (POS0372)
Deshpande G. A., 0753 (POS0975)
Deshpande S., 1340 (AB0610)
Desinova O., 0104 (OP0173), 0681 (POS0853), 0683 (POS0857), 0683 (POS0858), 0684 (POS0860), 0899 (POS1232), 1239 (AB0423), 1248 (AB0439), 1248 (AB0440), 1249 (AB0444), 1253 (AB0453), 1254 (AB0454), 1254 (AB0455), 1451 (AB0855)
Desjeux G., 0054 (OP0099), 0214 (POS0024)
Desmarets M., 1322 (AB0570)
Despert V., 0939 (POS1314)
Dessì M., 0324 (POS0214)
Destro Castaniti G. M., 0811 (POS1066)
Desvages A., 0114 (OP0190), 1427 (AB0807)
Devauchelle-Pensec V., 0214 (POS0024), 0662 (POS0818), 0939 (POS1314), 1204 (AB0358)
Devaux M., 0172 (OP0284)
Dey M., 1357 (AB0649)
Dezutter J., 1027 (POS1484-HPR), 1467 (AB0889-HPR)
Dgetluck N., 0102 (OP0171), 0383 (POS0315)
Dghaies A., 0925 (POS1287), 0926 (POS1289), 0926 (POS1290), 1417 (AB0784)
Dghais A., 1341 (AB0611)
Dhahri R., 0774 (POS1012), 0925 (POS1287), 0926 (POS1289), 0926 (POS1290), 1066 (AB0071), 1095 (AB0134), 1116 (AB0182), 1281 (AB0507), 1281 (AB0509), 1285 (AB0518), 1286 (AB0519), 1417 (AB0784), 1442 (AB0836), 1443 (AB0840)
Dhainaut A., 1245 (AB0433)
Dhawan V., 1163 (AB0276)
Dheir H., 1382 (AB0700)
Dhillon B., 0575 (POS0666)
Dhir V., 0584 (POS0679), 1163 (AB0276)
Dhouibi R., 1061 (AB0059)
DI Battista J., 0123 (OP0205)
Di Battista J., 0517 (POS0565)
Di Battista M., 1232 (AB0407)
DI Benedetto P., 0957 (POS1349)
DI Carlo M., 0190 (OP0310), 0811 (POS1066)
Di Carlo M., 0517 (POS0565), 1389 (AB0716)
DI Cola I., 0954 (POS1344), 1105 (AB0156)
DI Colo G., 0960 (POS1356)
Di Donato E., 1326 (AB0578)
DI Franco M., 0047 (OP0086), 0190 (OP0310), 0893 (POS1219), 1016 (POS1463-HPR), 1017 (POS1464-HPR), 1143 (AB0234), 1389 (AB0716)
DI Giuseppe D., 0082 (OP0140), 0130 (OP0218), 0131 (OP0220), 0133 (OP0222), 0864 (POS1169), 1059 (AB0054)
Di Giuseppe D., 0535 (POS0601)
Di Liberto D., 0301 (POS0177)
DI Liberto D., 0390 (POS0326)
DI Luigi L., 1074 (AB0089)
DI Maggio A., 1135 (AB0217), 1135 (AB0218)
Di Mattei V., 0613 (POS0726)
DI Matteo A., 0125 (OP0209), 0811 (POS1066)
Di Matteo A., 0463 (POS0464), 0482 (POS0499), 0517 (POS0565)
DI Natale M., 1239 (AB0422)
DI Nuzzo S., 1326 (AB0578)
Di Paolo J. A., 0331 (POS0224)
DI Poi E., 0628 (POS0751)
DI Santostefano R., 0096 (OP0160-HPR)
DI Sibio A., 0954 (POS1344)
DI Taranto R., 0858 (POS1161), 0869 (POS1176), 1363 (AB0661), 1374 (AB0683)
DI Vico C., 0888 (POS1210)
Diamandopoulos A., 1009 (POS1451), 1218 (AB0381)
Diamantino Saraiva F. M., 0029 (OP0055), 0644 (POS0781)
Diamantopoulos A., 0145 (OP0238), 0543 (POS0612)
Diana H., 1350 (AB0632)
Díaz J. A., 1429 (AB0810)
Diaz J., 1205 (AB0360)
Díaz Valle D., 0032 (OP0060)
Díaz-Angulo J., 1166 (AB0281), 1456 (AB0866-HPR)
Diaz-Cordobes G., 0946 (POS1328), 1456 (AB0865-HPR)
Díaz-Cordoves G., 1076 (AB0096)
Diaz-Coronado J. C., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336), 1200 (AB0351)
Díaz-Llopis M., 0032 (OP0060), 1225 (AB0396), 1412 (AB0771)
Diaz-Torne C., 0277 (POS0132), 1354 (AB0643)
Díaz-Torné C., 0666 (POS0827), 1093 (AB0129), 1365 (AB0666), 1426 (AB0804)
Dibnah B., 1057 (AB0051)
Dibrov D., 1451 (AB0855)
Didriksen H., 0689 (POS0867), 1245 (AB0433)
Diebold L., 0900 (POS1234)
Diego C., 0546 (POS0617)
Dieguez C., 0887 (POS1208)
Diehl A., 0251 (POS0086), 0563 (POS0650), 0564 (POS0651), 1149 (AB0248)
Diekhoff T., 0156 (OP0256)
Diekmann L., 0372 (POS0293), 0467 (POS0472)
Dieli F., 0390 (POS0326)
Diels J., 1313 (AB0556)
Diemel T., 0223 (POS0034)
Diercks G., 0189 (OP0308)
Dierckx S., 0066 (OP0119), 0880 (POS1196)
Dierssen-Sotos T., 1018 (POS1467-HPR)
Dieudé P., 0002 (OP0006), 0054 (OP0099), 0109 (OP0181), 0173 (OP0286), 0258 (POS0095), 0897 (POS1227)
Diez Álvarez E., 0628 (POS0752), 1171 (AB0290)
Diez Alvarez E., 0967 (POS1371), 1165 (AB0278), 1189 (AB0328), 1321 (AB0568)
Diez Vallejo C., 0856 (POS1156)
Diez-Perez A., 0835 (POS1111)
Dik W. A., 0308 (POS0189)
Dikovec C., 0374 (POS0299)
Dilbaryan A., 0081 (OP0139), 0155 (OP0253)
Diller M., 1054 (AB0043)
Dillon S. R., 0021 (OP0039)
Dimachkie M., 0004 (OP0008)
Dimauro I., 1074 (AB0089)
Dimitrov S., 0896 (POS1224), 1138 (AB0224)
Dimova D., 1108 (AB0162)
Dina O., 0146 (OP0239), 0704 (POS0895)
Ding C., 0276 (POS0129), 0309 (POS0190)
Ding T., 0427 (POS0396), 0771 (POS1006)
Ding X., 0121 (OP0201)
Dinis de Freitas J., 1101 (AB0147)
Dinis S. P., 0773 (POS1010)
Diot E., 0181 (OP0295), 0261 (POS0103)
Dipla K., 0620 (POS0738)
Direskeneli H., 1028 (POS1486-HPR), 1213 (AB0373), 1467 (AB0888-HPR), 1471 (AB0895-HPR)
Distler J. H. W., 0121 (OP0201), 0148 (OP0242), 0150 (OP0245), 0165 (OP0272), 0391 (POS0327), 0391 (POS0328), 0671 (POS0835), 0681 (POS0855), 0685 (POS0861), 1075 (AB0091), 1233 (AB0410), 1238 (AB0420)
Distler O., 0009 (OP0016), 0011 (OP0020), 0045 (OP0083), 0046 (OP0085), 0090 (OP0150), 0102 (OP0171), 0151 (OP0248), 0163 (OP0269), 0165 (OP0272), 0232 (POS0054), 0384 (POS0316), 0385 (POS0317), 0386 (POS0318), 0387 (POS0321), 0391 (POS0328), 0393 (POS0332), 0394 (POS0333), 0671 (POS0835), 0681 (POS0855), 0685 (POS0861), 0688 (POS0866), 0689 (POS0867), 0694 (POS0877), 1233 (AB0411), 1234 (AB0413), 1244 (AB0431), 1245 (AB0433)
Ditto M. C., 0254 (POS0090), 0335 (POS0230), 0676 (POS0845), 0904 (POS1243)
Dixon W., 0041 (OP0076), 0757 (POS0980), 1006 (POS1444)
Djossou H. J., 0170 (OP0282)
Dkhili W., 0926 (POS1290), 1442 (AB0836), 1443 (AB0840)
Do H., 0367 (POS0285)
Do S., 0077 (OP0133)
Dobashi H., 0395 (POS0336), 0513 (POS0556), 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1249 (AB0443), 1437 (AB0826)
Dobrota R., 0694 (POS0877)
Dobrovolskaya O., 0294 (POS0164), 0493 (POS0518), 0493 (POS0519), 0673 (POS0839), 0674 (POS0841), 1104 (AB0154), 1342 (AB0613)
Dogan I., 1124 (AB0200), 1124 (AB0201), 1299 (AB0535)
Dogra S., 1305 (AB0545)
Doherty M., 0185 (OP0302-HPR), 0841 (POS1124)
Dohey A., 0431 (POS0405), 0432 (POS0406)
Dokoupilova E., 0312 (POS0196), 0707 (POS0900)
Dokukina E., 0890 (POS1214)
Dolcini G., 0047 (OP0086), 1016 (POS1463-HPR)
Doldo P., 1012 (POS1457-HPR), 1454 (AB0861-HPR)
Dolhain R., 0127 (OP0211), 0127 (OP0212), 0186 (OP0303-HPR), 0317 (POS0202), 1044 (AB0020), 1058 (AB0052)
Dolscheid-Pommerich R., 0091 (OP0151), 0842 (POS1126)
Domanico A., 0105 (OP0176)
Domingo P., 1365 (AB0666)
Dominguez C., 0469 (POS0475)
Domínguez L., 1018 (POS1467-HPR), 1225 (AB0396), 1412 (AB0771)
Domínguez-Quesada C., 1474 (AB0904-HPR)
Dominici M., 1241 (AB0425)
Domjan A., 0226 (POS0043)
Domont F., 0172 (OP0284)
Donadini M. P., 1319 (AB0565)
Donado Gómez J. H., 1139 (AB0227)
Donaghy B., 0378 (POS0305)
Donati V., 0642 (POS0778), 0644 (POS0782)
Donato H., 1402 (AB0747)
Dong C., 0039 (OP0073), 0634 (POS0761), 0645 (POS0785), 1100 (AB0146), 1196 (AB0343)
Dong L., 0574 (POS0664)
Dong Z. R., 1040 (AB0011), 1067 (AB0075), 1252 (AB0449)
Donini L. M., 1183 (AB0317)
Donnelly A., 1479 (AB0916-PARE)
Donnelly S., 1427 (AB0805)
Doody D. R., 0609 (POS0719)
Dooley M. A., 0177 (OP0289)
Doornbos- van der Meer B., 1071 (AB0082)
Doré C., 0074 (OP0129)
Dorgham I., 0925 (POS1287), 0926 (POS1289), 0926 (POS1290)

Doria A. S., 0943 (POS1323)
Doria A., 0179 (OP0293), 0181 (OP0295), 0181 (OP0296), 0182 (OP0297), 0386 (POS0318), 0387 (POS0321), 0588 (POS0686), 0594 (POS0693), 0600 (POS0702), 0630 (POS0755), 0634 (POS0762), 0635 (POS0764), 0694 (POS0877), 0726 (POS0927), 0742 (POS0956), 0894 (POS1221), 0906 (POS1246), 1308 (AB0549)
Dorjée A. L., 0426 (POS0395)
Dörner T., 0076 (OP0132), 0406 (POS0351), 0588 (POS0686), 0593 (POS0692), 0623 (POS0744)
Dos Santos Beserra F., 0625 (POS0747), 0999 (POS1430)
Doskaliuk B., 0866 (POS1172), 1074 (AB0090)
Dos-Santos R., 0466 (POS0470), 0524 (POS0581), 0524 (POS0582), 0692 (POS0873), 0916 (POS1264), 0935 (POS1306), 1173 (AB0294)
Dostanko N., 1039 (AB0009)
Dougados M., 0024 (OP0047), 0109 (OP0181), 0193 (OP0316), 0308 (POS0188), 0332 (POS0226), 0340 (POS0239), 0342 (POS0242), 0360 (POS0273-HPR), 0379 (POS0306), 0544 (POS0614), 0716 (POS0912), 0720 (POS0919), 0739 (POS0951), 0747 (POS0965), 0750 (POS0969), 0753 (POS0975), 0766 (POS0995)
Douglas K., 0353 (POS0262), 1294 (AB0529), 1306 (AB0547)
Douma S., 0620 (POS0738)
Doumas S., 0011 (OP0019)
Doumen M., 0356 (POS0266-HPR), 0375 (POS0300), 0484 (POS0503), 0545 (POS0616), 1001 (POS1433), 1001 (POS1434), 1083 (AB0109)
Dourado E., 0484 (POS0504), 0690 (POS0870), 0692 (POS0872), 1250 (AB0445)
Downie B., 0452 (POS0446)
Doyle T., 0494 (POS0522)
Draniceanu I., 1462 (AB0879-HPR)
Drennan J., 0293 (POS0161-HPR)
Drescher E., 0486 (POS0508), 0786 (POS1030)
Dressler F., 0099 (OP0165), 0244 (POS0075), 0932 (POS1301), 0933 (POS1303), 0936 (POS1309), 0945 (POS1325), 0971 (POS1379)
Dreyer L., 0082 (OP0140), 0215 (POS0025), 0256 (POS0093), 0382 (POS0313)
Drivelegka P., 0115 (OP0192)
Drobinski P., 0468 (POS0473)
Drogomeretska O., 0866 (POS1172)
Drosos A., 0879 (POS1194), 1107 (AB0161)
Druce K., 0039 (OP0074)
Drucker A., 0173 (OP0285), 0230 (POS0050)
Drude B., 0983 (POS1401)
Drumez E., 0172 (OP0284), 0897 (POS1227)
Druyan A., 0753 (POS0974)
Dryglewska M., 0309 (POS0191)
Du F., 0574 (POS0664)
Du J. H., 0077 (OP0133)
Du S., 0794 (POS1040)
Du W., 0022 (OP0042)
Du Y., 1053 (AB0042)
Dua A., 0538 (POS0606)
Duan X., 0629 (POS0754)
Duan Y., 1288 (AB0523)
Duarte A., 0582 (POS0676), 0909 (POS1252), 1448 (AB0848)
Duarte C., 0481 (POS0496), 1101 (AB0147)
Duarte M., 1042 (AB0015), 1106 (AB0159)
Duarte V., 0730 (POS0933), 0759 (POS0984), 1377 (AB0689)
Duarte-Garcia A., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Duarte-Salles T., 0232 (POS0053)
Dubé C., 1022 (POS1474-HPR), 1469 (AB0892-HPR)
Dubey S., 0034 (OP0063)
Dubief B., 0843 (POS1129)
Dubinin A., 0259 (POS0098)
Dubinina T., 0084 (OP0142), 0726 (POS0928), 0761 (POS0987), 0962 (POS1360), 1264 (AB0473), 1264 (AB0474), 1276 (AB0498)
Dubinsky D., 0874 (POS1186)
Dubko M., 0247 (POS0080), 0931 (POS1299), 0937 (POS1310), 1402 (AB0748)
Dubnovitsky A., 0206 (POS0008)
Duboeuf F., 0431 (POS0404)
Dubois M., 0877 (POS1190)
Duboski V., 0824 (POS1089)
Duclos M., 1022 (POS1475-HPR)
Dudam R., 0900 (POS1235), 1242 (AB0428)
Dudek A., 1123 (AB0198)
Dudli S., 0045 (OP0083), 0046 (OP0085)
Duenas A., 0681 (POS0855)
Duffy C., 0210 (POS0017)
Duftner C., 1019 (POS1468-HPR)
Duggan A. M., 0136 (OP0226), 0314 (POS0197)
Duhamel A., 0897 (POS1227)
Dukatz P., 0344 (POS0245)
Dumas S., 0360 (POS0273-HPR), 0534 (POS0600)
Dumitru A., 1348 (AB0629)
Dumont A., 0669 (POS0831)
Dumoulin G., 1322 (AB0570)
Dumoulin Q., 0130 (OP0217)
Dumusc A., 0991 (POS1415)
Duna M., 0164 (OP0270), 0773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1462 (AB0879-HPR)
Dunga S. K., 0696 (POS0880)
Dunlap K., 0446 (POS0436), 0575 (POS0666)
Dunogue B., 0388 (POS0323)
Duong S., 0381 (POS0311), 0951 (POS1338)
Dupont A., 1229 (AB0401)
Duque Zapata N., 1139 (AB0227)
Duquenne L., 0463 (POS0464), 0482 (POS0499)
Durak Ediboglu E., 0722 (POS0922), 0727 (POS0929), 0731 (POS0935), 0861 (POS1165), 1255 (AB0456), 1366 (AB0669)
Durak G., 0191 (OP0313)
Duran Barragan S., 0559 (POS0642), 0904 (POS1242), 0905 (POS1245)
Duran E., 0347 (POS0251), 0350 (POS0255), 0518 (POS0568), 0648 (POS0793), 0728 (POS0931), 0770 (POS1004), 0814 (POS1070), 0971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1299 (AB0535)
Duran G., 1366 (AB0669)
Duran X., 0991 (POS1416), 1132 (AB0212), 1197 (AB0344)
Durán-Sotuela A., 0403 (POS0347)
Durek P., 0207 (POS0010)
Dures E., 1021 (POS1472-HPR), 1426 (AB0803), 1441 (AB0834)
Duret P. M., 0170 (OP0282), 0736 (POS0947)
Durez P., 0020 (OP0037), 0066 (OP0119), 0199 (LB0002), 0240 (POS0067), 0251 (POS0087), 0880 (POS1196), 0884 (POS1203), 1408 (AB0761)
Durhan G., 0817 (POS1076)
Durheim M., 0104 (OP0174)
Durmaz M. S., 1323 (AB0572)
Duruöz M. T., 0024 (OP0047), 0167 (OP0275-PARE), 0358 (POS0269-HPR), 0959 (POS1354), 0961 (POS1359), 1016 (POS1462-HPR)
Duteil D., 0151 (OP0247)
Duttenhofer G., 0962 (POS1361)
Dutton K., 0625 (POS0746)
Dvoryakovskaya T., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Dydykina I., 0834 (POS1108)
Dykhoff H. J., 0128 (OP0213), 0213 (POS0023)
Dyo A., 1095 (AB0135)
Dzekan O., 1338 (AB0605)
Dzhus M., 1401 (AB0746)
Dziedzic K., 0119 (OP0198-HPR)

Ea H. K., 0841 (POS1124)
Eaddy M., 0595 (POS0694)
Eades L., 0876 (POS1189)
Ebata N., 0275 (POS0128)
Ebbo M., 0907 (POS1247)
Ebrahim A., 0450 (POS0443)
Ebstein E., 0258 (POS0095)
Ecker T., 0120 (OP0199)
Eder L., 0132 (OP0221), 0139 (OP0229), 0173 (OP0285), 0183 (OP0298), 0230 (POS0050), 0565 (POS0652), 0812 (POS1068)
Eduarda Porto Raposo A., 0354 (POS0263)
Edwardes M., 1126 (AB0203)
Edwards C. J., 0602 (POS0705), 0625 (POS0746)
Edwards J., 0983 (POS1400)
Edwards L., 1050 (AB0034)
Eells J., 0779 (POS1022)
Efraimidou M., 1417 (AB0782)
Efremova A., 0294 (POS0164), 0493 (POS0518), 0493 (POS0519), 0673 (POS0839), 0674 (POS0841), 1104 (AB0154), 1342 (AB0613)
Egeli B., 0165 (OP0271), 0966 (POS1369), 0974 (POS1381)
Egorova E., 1455 (AB0864-HPR)
Egorova O., 0977 (POS1388), 1406 (AB0757), 1407 (AB0759)
Egües C. A., 1141 (AB0230)
Eguia Bernal M., 1085 (AB0113)
Ehirchiou D., 0426 (POS0393)
Ehlers L., 0191 (OP0312)
Ehrchen J., 0670 (POS0834)
Ehrenstein M., 0074 (OP0129), 0448 (POS0440), 1136 (AB0220)
Eibel H., 1383 (AB0701)
Eichbauer-Sturm G., 0320 (POS0208)
Eidner T., 0216 (POS0026)
Eis S., 1013 (POS1458-HPR)
Eisen S., 1092 (AB0128)
Ekici R., 1105 (AB0157)
Eklund K., 0131 (OP0220)
El Amri N., 0472 (POS0481), 0520 (POS0572), 0521 (POS0573), 0526 (POS0588), 0837 (POS1116), 0838 (POS1117), 0858 (POS1160), 0923 (POS1279), 0924 (POS1283), 1099 (AB0144), 1142 (AB0232), 1345 (AB0623), 1346 (AB0625)
El Aoufy K., 0105 (OP0176), 1032 (POS1495-HPR), 1192 (AB0334)
El Aroussy N., 0187 (OP0304-PARE)
El Bouchti I., 0992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811)
El Euch M., 0290 (POS0155-HPR), 1358 (AB0650)
El Fani N., 0856 (POS1154), 0925 (POS1286)
El Gaafary M., 0187 (OP0304-PARE), 0832 (POS1104)
El Joumani T., 1148 (AB0246), 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
EL Maghraoui A., 0992 (POS1417), 1270 (AB0486), 1430 (AB0811)
El Maghraoui A., 1148 (AB0246)
El Mahou S., 0172 (OP0284)
EL Moutaouakil H., 0817 (POS1077)
El Moutaouakil H., 1375 (AB0685)
El Ouali Z., 1375 (AB0685), 1422 (AB0794), 1433 (AB0819), 1438 (AB0828), 1438 (AB0829)
Elalouf O., 0200 (LB0003), 0885 (POS1206), 1181 (AB0312)
El-Am E., 0672 (POS0836)
Elamri N., 1480 (AB0919-PARE)
Elbez Y., 0108 (OP0180), 0453 (POS0447), 0533 (POS0599), 1127 (AB0205), 1128 (AB0207)
Eldred A., 0138 (OP0228), 1315 (AB0559)
Eldridge R. C., 0299 (POS0173)
Eldridge S., 0120 (OP0200), 1052 (AB0039)
Elefante E., 0628 (POS0751), 0630 (POS0756), 0647 (POS0789)
Eleftheriou D., 0247 (POS0079), 0934 (POS1304)
Elejalde J. I., 0960 (POS1355)
Eleuch M., 0372 (POS0294)
Elezoglou A., 0646 (POS0786), 1299 (AB0537)
Elghali M., 1198 (AB0346)
Elhai M. D., 0685 (POS0861)
El-Hajj J., 0340 (POS0239)
Elhem C., 1144 (AB0236)
Elia F., 1318 (AB0563)
Elia G., 0906 (POS1246)
Elias M., 0200 (LB0003), 0286 (POS0147), 0543 (POS0613), 0753 (POS0974)
Elias V., 0444 (POS0432)
Eliasson B., 0811 (POS1064)
Eliopoulos E., 0405 (POS0350), 1037 (AB0004)
Elisei I., 1112 (AB0172)
Eliseev M., 0849 (POS1139), 0849 (POS1140), 0963 (POS1363), 1350 (AB0631), 1353 (AB0640)

Elizondo-Plazas A., 1439 (AB0830)
Elkayam O., 0200 (LB0003), 0256 (POS0093), 0753 (POS0974), 0885 (POS1206), 0892 (POS1217), 1049 (AB0032), 1181 (AB0312), 1309 (AB0551)
Elkebir A., 1422 (AB0794)
Ellegaard K., 0283 (POS0144)
Elleuch M., 0856 (POS1155), 0923 (POS1280), 0926 (POS1288), 1090 (AB0123), 1097 (AB0139), 1144 (AB0238), 1145 (AB0240), 1147 (AB0244), 1272 (AB0490), 1273 (AB0492), 1421 (AB0793)
Elling J. M., 1479 (AB0915-PARE)
Elling-Audersch C., 0197 (OP0323-PARE)
Ellingsen T., 0006 (OP0010), 1468 (AB0890-HPR), 1483 (AB0924-PARE)
Elliott I., 1010 (POS1453)
Ellis J., 0170 (OP0281)
Elmaghraoui A., 1270 (AB0485)
El-Miedany Y., 0187 (OP0304-PARE), 0832 (POS1104)
Elnagar M., 0389 (POS0325)
Elndari N., 0862 (POS1167)
Elrefi M., 1068 (AB0076)
Elsaman A., 0977 (POS1389), 1391 (AB0720), 1420 (AB0790)
Elshawaf W., 0645 (POS0784)
Eltoraby E. E., 0477 (POS0490)
Emamikia S., 0260 (POS0101)
Emara N., 1175 (AB0297)
Embleton-Thirsk A., 0074 (OP0129)
Emeanuru K., 0530 (POS0594), 0538 (POS0606)
Emelyanov N., 1069 (AB0078), 1083 (AB0110), 1419 (AB0788)
Emelyanova O., 1069 (AB0078), 1083 (AB0110), 1419 (AB0788)
Emersic N., 0242 (POS0072), 0941 (POS1318)
Emery P., 0030 (OP0057), 0066 (OP0118), 0079 (OP0136), 0110 (OP0182), 0163 (OP0269), 0463 (POS0464), 0482 (POS0499), 0625 (POS0746), 1173 (AB0293)
Emir B., 0366 (POS0283)
Emmel J., 0175 (OP0287), 0231 (POS0052)
Emmi G., 0051 (OP0093), 0594 (POS0693), 0600 (POS0702), 0628 (POS0751), 0889 (POS1212), 1217 (AB0380)
Emminger W., 0883 (POS1202)
Emmungil H., 0731 (POS0935), 1470 (AB0893-HPR)
Enein A. F., 0477 (POS0490)
Enejosa J., 0486 (POS0508)
Engedal K., 0047 (OP0087)
Engel S., 0234 (POS0056), 0865 (POS1170)
Engelhardt B., 0805 (POS1054)
Enghard P., 0207 (POS0010), 0623 (POS0744)
Engin B., 1327 (AB0579)
Englbrecht M., 0096 (OP0160-HPR), 1274 (AB0494)
Englund M., 0292 (POS0160-HPR), 1372 (AB0678)
Engström M., 0429 (POS0400)
Enman Y., 0260 (POS0101)
Eom S. Y., 0124 (OP0207)
Eow L. H., 1015 (POS1460-HPR)
Eppeland S., 0092 (OP0153-HPR)
Epstein J., 0358 (POS0269-HPR), 0358 (POS0270-HPR)
Eraslan E., 1176 (AB0300)
Ercan Z., 0522 (POS0576)
Erdem Gürsoy D., 0959 (POS1354), 0961 (POS1359)
Erdem Y., 0648 (POS0793), 1198 (AB0347)
Erden A., 0069 (OP0125), 1105 (AB0157), 1124 (AB0200), 1124 (AB0201), 1182 (AB0314), 1299 (AB0535)
Erdes S., 0084 (OP0142), 0337 (POS0233), 0709 (POS0903), 0726 (POS0928), 0761 (POS0987), 1040 (AB0010), 1066 (AB0072), 1261 (AB0468), 1262 (AB0470), 1276 (AB0498), 1284 (AB0514)
Erdogan A., 1259 (AB0465)
Erdoğan B., 1086 (AB0114)
Erdogan S., 0014 (OP0026)
Erdugan M., 1006 (POS1445)
Erelel M., 0191 (OP0313)
Eremeeva A., 0084 (OP0142), 0726 (POS0928), 0796 (POS1043), 1298 (AB0534), 1302 (AB0540)
Erez Y., 0627 (POS0750), 1247 (AB0437), 1256 (AB0459), 1386 (AB0708)
Erezanu A., 0882 (POS1200), 1399 (AB0739)
Ergun T., 1471 (AB0895-HPR)
Eriksson G., 0596 (POS0696)
Eriksson K. K., 0398 (POS0341)
Erikstrup C., 0866 (POS1171)
Erkantarcı Levent E., 0347 (POS0251), 0350 (POS0255)
Erkorkmaz Ü., 1382 (AB0700)
Erlandsson M. C., 0012 (OP0022), 0428 (POS0397)
Erlandsson M., 0014 (OP0026), 0192 (OP0315)
Ermachenkova T., 0247 (POS0080)
Ernestam S., 0474 (POS0484)
Ernst D., 1186 (AB0322), 1385 (AB0707)
Ernst M., 0095 (OP0158-HPR)
Erpek E., 0722 (POS0922), 0861 (POS1165), 1255 (AB0456), 1366 (AB0669)
Erraoui K., 0965 (POS1367)
Erre G. L., 0324 (POS0214)
Ersözlü D., 0731 (POS0935)
Erten S., 1105 (AB0157), 1182 (AB0314)
Ertenli A. İ., 0069 (OP0125), 0350 (POS0255), 0518 (POS0568), 0648 (POS0793), 0728 (POS0931), 0731 (POS0935), 0770 (POS1004), 0814 (POS1070), 0971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1299 (AB0535)
Erul E., 1250 (AB0446)
Eryomushkin M., 0209 (POS0016), 0239 (POS0066-PARE)
Esatoglu S. N., 0660 (POS0814), 0662 (POS0819), 0663 (POS0820), 0958 (POS1351), 1207 (AB0364)
Esbensen B. A., 0095 (OP0159-HPR), 1459 (AB0872-HPR), 1466 (AB0885-HPR)
Escoffier L., 1078 (AB0099)
Escudero Contreras A., 0009 (OP0017), 0426 (POS0394), 0469 (POS0475), 0769 (POS1001), 1109 (AB0166), 1245 (AB0432), 1253 (AB0451), 1317 (AB0562)
Escudero Tepale E. M., 1078 (AB0098)
Esdaile J., 0022 (OP0043), 0377 (POS0303)
Esen F., 0191 (OP0313)
Esen I., 0036 (OP0066)
Eshed I., 0089 (OP0149), 0153 (OP0251), 0153 (OP0252), 0156 (OP0256), 0831 (POS1101)
Eskild T., 0281 (POS0139)
Eskitzis A., 0184 (OP0299), 0523 (POS0580), 0733 (POS0941)
Esparcia Pinedo. L., 1241 (AB0427)
Espasa G. V., 0635 (POS0763)
Esperança Almeida D., 0293 (POS0162), 0773 (POS1010), 0830 (POS1100), 1003 (POS1438), 1424 (AB0799)
Espígol-Frigolé G., 0272 (POS0121)
Espildora F., 0323 (POS0211)
Espinosa Banuelos L. G., 0893 (POS1220), 1360 (AB0657), 1361 (AB0658), 1439 (AB0830), 1444 (AB0842), 1445 (AB0843), 1457 (AB0867-HPR), 1463 (AB0880-HPR)
Espinosa G., 0350 (POS0256), 0637 (POS0767), 0967 (POS1371), 0987 (POS1408), 0987 (POS1409), 1195 (AB0340)
Espinosa M., 0020 (OP0038), 0892 (POS1218)
Espinoza V. R., 0326 (POS0217)
Espitia O., 0037 (OP0068)
Esquius Rafat M., 0891 (POS1215)
Esquivel Valerio J. A., 0445 (POS0434), 1018 (POS1466-HPR), 1425 (AB0801), 1458 (AB0868-HPR)
Essayan D., 1167 (AB0282)
Essex M., 0017 (OP0031)
Estadella M., 0760 (POS0985)
Esteban-Ortega M. D. M., 1225 (AB0396), 1412 (AB0771)
Estevez A., 0576 (POS0667), 1196 (AB0342)
Estrada P., 1219 (AB0384)
Etcheverry M., 1196 (AB0342)
Eulert S., 0872 (POS1183), 0882 (POS1199), 0943 (POS1321)
Eun Y. H., 0752 (POS0972), 1210 (AB0368)
Eun Y., 0062 (OP0113), 0124 (OP0206), 0280 (POS0137), 0281 (POS0138)
Evangelatos G., 0815 (POS1073)
Evans E., 0289 (POS0152-HPR)
Evans J., 1010 (POS1453)
Evans L. S., 0021 (OP0039)
Evans M., 0065 (OP0117)
Evans S., 0087 (OP0147)
Everett C., 0079 (OP0136)
Eviatar T., 0200 (LB0003), 0885 (POS1206), 0892 (POS1217), 1181 (AB0312)
Ewald H., 0655 (POS0806)
Exarchou S., 0130 (OP0218), 0339 (POS0236), 0741 (POS0954)
Expósito L., 0610 (POS0721)
Expósito R., 1065 (AB0070)
Exposito-Molinero M. R., 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Eyre S., 0008 (OP0014), 0009 (OP0016)
Ezeanuna M., 0476 (POS0487)
Ezzeddine M., 0922 (POS1277), 1276 (AB0497), 1281 (AB0508), 1484 (AB0926-PARE)

Fabacher T., 0736 (POS0947)
Fabbris T., 0229 (POS0048)
Faber C., 1202 (AB0355)
Fabre C., 0170 (OP0282)
Fabris B., 1002 (POS1435), 1391 (AB0719)
Facorat O., 0028 (OP0053)
Fadaei S., 1465 (AB0884-HPR)
Fagan N., 0589 (POS0687)
Fagart A., 0664 (POS0822)
Fagerli K. M., 0026 (OP0050), 0131 (OP0220), 0339 (POS0236), 0741 (POS0954), 0934 (POS1305), 1392 (AB0722)
Faggioli P., 0594 (POS0693)
Fagni F., 0889 (POS1212)
Fahem N. A. A., 0816 (POS1075)
Failli V., 0988 (POS1410)
Fain O., 0037 (OP0068)
Faiq M., 1075 (AB0093)
Fajardo Hermosillo L. D., 0491 (POS0515), 1169 (AB0286)
Fakhfakh R., 0520 (POS0572), 0521 (POS0573), 1099 (AB0144)
Fakhouri W., 1157 (AB0261)
Fakih O., 0748 (POS0967), 1275 (AB0496)
Falahee M., 0096 (OP0160-HPR), 1026 (POS1483-HPR)
Fallahi P., 0906 (POS1246)
Fallanca F., 1206 (AB0361)
Falleroni D., 0067 (OP0120)
Fallon L., 0704 (POS0895), 1286 (AB0521)
Falloon J., 0067 (OP0120)
Faloutsos M., 0943 (POS1322)
Falsetti P., 0573 (POS0661), 0669 (POS0832), 0746 (POS0963), 1252 (AB0450)
Falzon L., 0189 (OP0309), 0304 (POS0181)
Famulla K., 0567 (POS0654), 1153 (AB0255)
Fan A., 1022 (POS1475-HPR)
Fan H., 0564 (POS0651)
Fan X., 0301 (POS0176)
Fan Y., 1166 (AB0280)
Fana V., 0352 (POS0260), 1202 (AB0355)
Fang F., 0031 (OP0059), 0198 (LB0001)
Fang J., 0337 (POS0234)
Fani N., 0925 (POS1285)
Fanlo P., 0179 (OP0292), 0350 (POS0256), 0952 (POS1340), 0987 (POS1408), 0987 (POS1409)
Fanouriakis A., 0011 (OP0019), 0631 (POS0757), 0632 (POS0759), 0635 (POS0764), 0646 (POS0786)
Fantini D., 0588 (POS0686)
Faquetti M. L., 0255 (POS0091)
Faquih T., 0822 (POS1087)
Farah S., 0190 (OP0310), 1389 (AB0716)
Farber D. M., 0742 (POS0956)
Farewell V., 0602 (POS0705)
Farhat M. M., 1011 (POS1454-HPR)
Faria D., 0293 (POS0162), 0773 (POS1010), 0830 (POS1100), 1424 (AB0799)
Farih S., 0992 (POS1417), 1430 (AB0811)
Farina N., 0613 (POS0726), 0953 (POS1341), 0955 (POS1347)
Farisoğulları B., 0518 (POS0568), 0648 (POS0793), 0728 (POS0931), 0749 (POS0968), 0770 (POS1004), 0814 (POS1070), 0971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1250 (AB0446), 1272 (AB0491), 1299 (AB0535)
Farrelly E., 0595 (POS0694)
Farrow S., 0869 (POS1177)

Farrukh S., 1328 (AB0581)
Farshad M., 0045 (OP0083)
Farshad-Amacker N., 0045 (OP0083)
Fasano S., 0594 (POS0693), 0888 (POS1210), 1165 (AB0279)
Fasshauer M., 0244 (POS0075)
Fassio A., 0062 (OP0112), 0106 (OP0178), 0326 (POS0218), 0560 (POS0644), 0831 (POS1102), 0867 (POS1173)
Fatikhova A., 1253 (AB0452)
Fatima T., 0372 (POS0295)
Fatima Zahrae T., 1270 (AB0485), 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Fatma R., 1147 (AB0243)
Fattal E., 0393 (POS0331)
Faustini F., 0203 (POS0003), 0305 (POS0184)
Fautrel B., 0052 (OP0094), 0109 (OP0181), 0110 (OP0183), 0172 (OP0284), 0233 (POS0055), 0258 (POS0095), 0340 (POS0238), 0358 (POS0269-HPR), 0358 (POS0270-HPR), 0360 (POS0274-HPR), 0378 (POS0305), 0529 (POS0592), 0544 (POS0614), 0563 (POS0649), 0751 (POS0971), 0818 (POS1078), 1157 (AB0261), 1412 (AB0772)
Favalli A., 0229 (POS0048)
Favalli E. G., 0229 (POS0048), 0582 (POS0675)
Favalli E., 0521 (POS0575), 0809 (POS1061), 0870 (POS1178), 0872 (POS1182), 1271 (AB0488)
Favaro M., 0619 (POS0737), 1174 (AB0295), 1308 (AB0549)
Favero M., 0742 (POS0956)
Favre J., 1053 (AB0041)
Fayed F., 0871 (POS1179), 1359 (AB0654)
Fayet F., 1009 (POS1450), 1022 (POS1475-HPR)
Fayyaz H., 1450 (AB0853)
Fazaa A., 0292 (POS0159-HPR), 0481 (POS0497), 0835 (POS1110), 1030 (POS1491-HPR), 1113 (AB0173), 1113 (AB0174), 1117 (AB0184), 1118 (AB0188), 1277 (AB0499), 1332 (AB0590), 1333 (AB0592), 1333 (AB0593), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1368 (AB0672), 1368 (AB0673), 1381 (AB0698), 1390 (AB0717), 1397 (AB0736), 1411 (AB0770), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Fearon U., 0014 (OP0025), 0015 (OP0028), 0205 (POS0007), 0241 (POS0069), 0423 (POS0387), 0462 (POS0462), 0470 (POS0477), 0747 (POS0964), 0891 (POS1216), 1043 (AB0018), 1479 (AB0916-PARE)
Fedenko A., 0371 (POS0291)
Fedorov E., 0243 (POS0073), 0918 (POS1267), 0962 (POS1360), 1393 (AB0725), 1403 (AB0749), 1414 (AB0774)
Fedorov V., 0481 (POS0498)
Fedorovych K., 0866 (POS1172)
Feese M., 0279 (POS0135)
Fehres C., 0203 (POS0001)
Fehri W., 1116 (AB0182)
Feiskhanova L., 1283 (AB0511)
Feist E., 0528 (POS0591)
Feki A., 0922 (POS1277), 1109 (AB0164), 1276 (AB0497), 1281 (AB0508), 1484 (AB0926-PARE)
Feklistov A., 0294 (POS0164), 0493 (POS0518), 0493 (POS0519)
Feld J., 0200 (LB0003), 0543 (POS0613), 0753 (POS0974)
Feldhamer I., 0131 (OP0219), 0286 (POS0147)
Feldman B., 0247 (POS0079), 0934 (POS1304)
Feldt-Rasmussen U., 0382 (POS0313)
Felea I., 0638 (POS0768), 1360 (AB0656)
Felfeliyan B., 1334 (AB0594)
Felicetti M., 0742 (POS0956), 0809 (POS1061)
Felipe Díaz O. J., 1139 (AB0227)
Felloni P., 1229 (AB0401)
Fellous S., 0992 (POS1417), 1270 (AB0486), 1430 (AB0811)
Feltelius N., 0864 (POS1169)
Felten R., 0074 (OP0130), 0170 (OP0282), 0632 (POS0758), 0736 (POS0947), 0877 (POS1190)
Feng B., 0353 (POS0262)
Feng D., 0788 (POS1032), 0790 (POS1035), 0800 (POS1047), 1294 (AB0529), 1308 (AB0550)
Feng F., 1355 (AB0645)
Feng G., 0645 (POS0785)
Feng R., 0383 (POS0315)
Feng S., 0460 (POS0458), 0622 (POS0742), 0678 (POS0848), 0680 (POS0851), 1037 (AB0005)
Feng Z., 1063 (AB0066)
Fenoglio R., 0601 (POS0704)
Feriz A., 1187 (AB0325), 1188 (AB0326), 1351 (AB0635)
Ferjani H., 0526 (POS0586), 0526 (POS0587), 0774 (POS1013), 0776 (POS1018), 0921 (POS1274), 1091 (AB0124), 1095 (AB0133), 1101 (AB0148), 1102 (AB0150), 1112 (AB0171), 1117 (AB0186), 1118 (AB0187), 1119 (AB0189), 1119 (AB0191), 1278 (AB0501), 1283 (AB0512), 1286 (AB0520), 1379 (AB0693), 1399 (AB0740), 1399 (AB0741), 1400 (AB0742), 1400 (AB0744)
Ferkal S., 0027 (OP0052)
Ferl J., 0988 (POS1410)
Fernandes B. M., 0260 (POS0100), 0318 (POS0204), 0476 (POS0488), 0483 (POS0502), 0690 (POS0870), 0692 (POS0872), 0718 (POS0914), 0812 (POS1067), 0833 (POS1106), 0836 (POS1113), 0919 (POS1270), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1299 (AB0536), 1339 (AB0608), 1432 (AB0816), 1441 (AB0835)
Fernandes Lourenco M. H., 0690 (POS0870), 0692 (POS0872), 1402 (AB0747)
Fernandes P., 1405 (AB0754)
Fernandes S., 1170 (AB0288)
Fernandes V., 0582 (POS0676), 0625 (POS0747), 0999 (POS1430)
Fernandez B. F., 1052 (AB0039)
Fernandez B., 0896 (POS1225), 0908 (POS1251), 0910 (POS1253), 1464 (AB0881-HPR), 1475 (AB0906-HPR)
Fernandez C., 0079 (OP0136)
Fernandez D., 0139 (OP0229)
Fernández D., 0636 (POS0765)
Fernández de la Fuente Bursón L., 1075 (AB0092), 1132 (AB0213), 1145 (AB0239), 1420 (AB0789)
Fernández Fernández D., 0692 (POS0873), 0935 (POS1306), 1173 (AB0294)
Fernández López S., 1436 (AB0825)
Fernandez O., 1103 (AB0151), 1104 (AB0153), 1111 (AB0170)
Fernández Puente P., 0306 (POS0185)
Fernández Ramón R., 1226 (AB0397)
Fernández Reboul Fernández A., 1145 (AB0239)
Fernández S., 0819 (POS1080), 0967 (POS1371)
Fernandez-Bertolin S., 0232 (POS0053)
Fernández-Carballido C., 0755 (POS0977), 0760 (POS0986), 0766 (POS0996), 0952 (POS1340), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070), 1208 (AB0366), 1279 (AB0503)
Fernandez-Codina A., 0103 (OP0172), 0907 (POS1247)
Fernández-Díaz C., 0490 (POS0513), 0531 (POS0595), 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1208 (AB0366)
Fernández-Dominguez L., 1326 (AB0577)
Fernández-Fernández E., 0399 (POS0342), 0664 (POS0821), 1216 (AB0378), 1218 (AB0382)
Fernandez-Garcia V., 1428 (AB0808)
Fernández-Llanio N., 1208 (AB0366)
Fernández-López C., 0034 (OP0064), 1208 (AB0366)
Fernández-Maeztu Palacín I. M., 1145 (AB0239), 1420 (AB0789)
Fernández-Melón J., 1303 (AB0542)
Fernandez-Moreno M., 0403 (POS0347), 1051 (AB0036)
Fernandez-Nebro A., 0323 (POS0211), 0469 (POS0475), 0494 (POS0521), 0610 (POS0721), 0760 (POS0986), 1076 (AB0096)
Fernández-Ramón R., 0050 (OP0091), 0220 (POS0030), 0621 (POS0740), 0963 (POS1362)
Fernandez-Sanchez S. P., 1365 (AB0666), 1426 (AB0804), 1474 (AB0904-HPR)
Fernando D., 0485 (POS0505)
Fernezlian S., 0444 (POS0432)
Ferraccioli G., 0582 (POS0675)
Ferrada M., 0049 (OP0090), 0968 (POS1373)
Ferraioli M., 0335 (POS0231)
Ferrández-Quirante O., 0991 (POS1416), 1132 (AB0212)
Ferrara R., 0953 (POS1341)
Ferrari G., 0686 (POS0862), 1190 (AB0330), 1201 (AB0354)
Ferrari S. M., 0906 (POS1246)
Ferrari T., 0906 (POS1246)
Ferraz-Amaro I., 0032 (OP0060), 0490 (POS0513), 0531 (POS0595), 0614 (POS0728), 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070), 1225 (AB0396), 1412 (AB0771)
Ferreira E., 0637 (POS0767), 1195 (AB0340)
Ferreira G., 0909 (POS1252), 1448 (AB0848)
Ferreira J. F., 0354 (POS0263), 0773 (POS1010)
Ferreira R. J. O., 0161 (OP0264-HPR)
Ferreira R., 0836 (POS1113), 1191 (AB0332)
Ferreiro R., 0916 (POS1264)
Ferrer Galván M., 1075 (AB0092)
Ferrer González M. Á., 0009 (OP0017)
Ferreyra L., 0759 (POS0984)
Ferri C., 0906 (POS1246), 1359 (AB0652)
Ferrigno S., 0335 (POS0231), 0980 (POS1395), 1284 (AB0515)
Ferro F., 0630 (POS0756), 0642 (POS0778), 0644 (POS0782), 0647 (POS0789)
Ferro M., 0484 (POS0504), 0601 (POS0704)
Ferrucci K., 1022 (POS1474-HPR), 1469 (AB0892-HPR)
Fetisova A., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Feuchtenberger M., 0194 (OP0318)
Feurstein J., 0848 (POS1137)
Fguiri E., 0835 (POS1110)
Fianyo E., 0776 (POS1016), 0927 (POS1291)
Field E., 0918 (POS1268)
Field R., 1239 (AB0421)
Fields T., 0278 (POS0134)
Figgie M., 0367 (POS0285)
Figuereido C., 0194 (OP0318)
Figueroa-Parra G., 0445 (POS0434), 0893 (POS1220), 1031 (POS1494-HPR), 1166 (AB0281), 1177 (AB0301), 1345 (AB0624), 1425 (AB0801), 1439 (AB0830), 1445 (AB0843), 1456 (AB0866-HPR)
Figus F., 0134 (OP0223)
Filatova E., 1109 (AB0165), 1162 (AB0272), 1336 (AB0599)
Filhol E., 0518 (POS0566), 0770 (POS1003), 0820 (POS1082), 0902 (POS1239)
Filia A., 0011 (OP0019), 0021 (OP0040)
Filion K., 0993 (POS1420)
Filipescu I., 0009 (OP0017), 0638 (POS0768), 1360 (AB0656)
Filipović M., 0226 (POS0042)
Filippi E., 1259 (AB0465)
Filippini M., 0470 (POS0476), 0633 (POS0760), 1435 (AB0822)
Filippou G., 0841 (POS1124), 0845 (POS1132), 0846 (POS1133), 0850 (POS1141), 1335 (AB0598), 1348 (AB0629)
Filippucci E., 0123 (OP0205), 0125 (OP0209), 0517 (POS0565), 0811 (POS1066), 0850 (POS1141)
Filocamo G., 0935 (POS1307)
Finckh A., 0256 (POS0093), 0323 (POS0212), 0462 (POS0461), 0465 (POS0468), 0577 (POS0668), 0863 (POS1168), 1128 (AB0206)
Fineo A., 0882 (POS1200)
Finglas A., 0168 (OP0277-PARE)
Finnern H., 1033 (POS1497-PARE)
Finzel S., 0194 (OP0318), 1383 (AB0701)
Fioravanti A., 1331 (AB0588)
Fiore S., 0530 (POS0594), 0538 (POS0606)
Fiori G., 0546 (POS0618), 1032 (POS1495-HPR), 1154 (AB0256)
Fischer A., 0018 (OP0034)
Fischer P., 0588 (POS0686), 0767 (POS0997)
Fischer-Betz R., 0213 (POS0022), 1195 (AB0341), 1263 (AB0472)
Fischetti F., 0190 (OP0310), 1002 (POS1435), 1389 (AB0716), 1391 (AB0719)
Fisher B. A., 0593 (POS0692)

Fito Manteca M. C., 0960 (POS1355)
Fito-Manteca C., 1132 (AB0211), 1303 (AB0542)
Fitzgerald G., 0766 (POS0995)
Fitzgerald J., 0828 (POS1097), 0841 (POS1124)
Fitzgerald O., 0135 (OP0224), 0139 (OP0229), 0226 (POS0043), 0777 (POS1020), 0790 (POS1036), 1294 (AB0529), 1296 (AB0531), 1328 (AB0581)
Fiumicelli E., 0211 (POS0019)
Fjellstad C. P., 0236 (POS0060-PARE)
Flake D., 0457 (POS0454), 0458 (POS0456)
Fleck M., 0194 (OP0318)
Flegar D., 0226 (POS0042)
Fleischmann R., 0251 (POS0086), 0251 (POS0087), 0566 (POS0653)
Fleishaker D., 0704 (POS0895), 0777 (POS1020)
Flendrie M., 1023 (POS1477-HPR), 1351 (AB0634), 1479 (AB0915-PARE)
Fleurinck C., 0332 (POS0226), 0720 (POS0919)
Fliedner G., 0544 (POS0615)
Flipo R. M., 0054 (OP0099), 0108 (OP0180), 0109 (OP0181), 0114 (OP0190), 0172 (OP0284), 0258 (POS0095), 0453 (POS0447), 0533 (POS0599), 0662 (POS0818), 1128 (AB0207), 1258 (AB0464)
Flood R., 0282 (POS0140), 0859 (POS1162)
Flores Alvarado D. E., 0816 (POS1074), 0983 (POS1402), 1018 (POS1466-HPR), 1458 (AB0868-HPR)
Florescu A. T., 0519 (POS0569)
Flores-Fernández E., 0296 (POS0168), 1427 (AB0806)
Florica B., 0336 (POS0232)
Floris A., 0632 (POS0758)
Flouda S., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Floudas A., 0014 (OP0025), 0205 (POS0007), 0241 (POS0069), 0423 (POS0387)
Flouri I., 0184 (OP0299), 0523 (POS0580), 0733 (POS0941)
Flourou C., 1467 (AB0887-HPR)
Flurey C., 0291 (POS0158-HPR), 1468 (AB0890-HPR)
Fockens E., 0900 (POS1234)
Foddai S. G., 0298 (POS0172), 1039 (AB0008), 1073 (AB0088)
Fodili F., 0259 (POS0097)
Foekens T., 0238 (POS0063-PARE)
Foeldvari I., 0050 (OP0092), 0201 (LB0004), 0244 (POS0075), 0245 (POS0076), 0247 (POS0079), 0387 (POS0321), 0932 (POS1301), 0934 (POS1304), 0943 (POS1321), 0945 (POS1325), 0971 (POS1379)
Foell D., 0244 (POS0075), 0945 (POS1325)
Foerger F., 0767 (POS0997)
Fogel O., 0228 (POS0046), 1364 (AB0665)
Foley C., 0241 (POS0069)
Foley P., 0787 (POS1031)
Folle L., 0086 (OP0145)
Foltz V., 0089 (OP0149), 0153 (OP0252)
Fomicheva O., 0493 (POS0520)
Fomina D., 0890 (POS1214)
Fong W., 0989 (POS1411), 0990 (POS1413)
Fongen C., 0092 (OP0154-HPR)
Fonollosa A., 1225 (AB0396), 1412 (AB0771)
Fonollosa Pla V., 0350 (POS0256), 0987 (POS1408), 0987 (POS1409)
Fonseca D., 0260 (POS0100), 0318 (POS0204), 0476 (POS0488), 0483 (POS0502), 0718 (POS0914), 0812 (POS1067), 0833 (POS1106), 0836 (POS1113), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1236 (AB0415), 1236 (AB0416), 1236 (AB0417), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1299 (AB0536), 1432 (AB0816), 1441 (AB0835)
Fonseca J. E., 0007 (OP0011), 0009 (OP0017), 0029 (OP0055), 0484 (POS0504), 0644 (POS0781), 0690 (POS0870), 1250 (AB0445)
Font Ramos B., 0755 (POS0978)
Fontes Baptista A., 0699 (POS0887)
Fonti G. L., 0726 (POS0927), 0980 (POS1395), 1038 (AB0006), 1434 (AB0821)
Fontova Garrofe R., 0380 (POS0308)
Fonturenko A., 1352 (AB0636)
Font-Urgelles J., 0891 (POS1215)
Fonzetti S., 0642 (POS0778), 0644 (POS0782)
Foo S., 0241 (POS0069)
Ford K., 0530 (POS0594), 0538 (POS0606)
Ford M., 0005 (OP0009-PARE)
Förger F., 0213 (POS0022), 0649 (POS0794)
Fornaro M., 0324 (POS0214), 0701 (POS0891), 1003 (POS1437), 1217 (AB0380)
Forsblad-D'elia H., 0013 (OP0024), 0068 (OP0122), 0743 (POS0957), 0811 (POS1064), 0864 (POS1169)
Forslund S., 0017 (OP0031)
Forster A., 0108 (OP0180), 0453 (POS0447), 0533 (POS0599), 1128 (AB0207)
Förster M., 1422 (AB0796)
Fort J., 0877 (POS1190)
Fortin P., 0177 (OP0289)
Fossati-Jimack L., 0007 (OP0011), 0079 (OP0136)
Foster A., 0621 (POS0739)
Foster H., 0927 (POS1292)
Foster J., 0279 (POS0135)
Foti R., 0232 (POS0054), 0582 (POS0675), 0726 (POS0927), 0778 (POS1021), 0906 (POS1246), 1260 (AB0467), 1271 (AB0488)
Fotiadis D., 0178 (OP0291), 0180 (OP0294), 0370 (POS0290)
Fountaine R. J., 0823 (POS1088)
Fouodo C. J. K., 0149 (OP0244)
Fourati H., 0837 (POS1115), 0922 (POS1277), 1109 (AB0164), 1276 (AB0497), 1281 (AB0508), 1484 (AB0926-PARE)
Fourie N., 0198 (LB0001)
Fourmy J., 1024 (POS1478-HPR), 1028 (POS1488-HPR)
Fousteri G., 0960 (POS1356)
Fox N. L., 1170 (AB0288)
Fox R., 0593 (POS0692)
Fracassi E., 1099 (AB0143)
Fragío Gil J. J., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Fragou E., 0011 (OP0019)
Fragoulis G. E., 0161 (OP0264-HPR), 0815 (POS1073), 1159 (AB0265)
Fraj A., 0955 (POS1345), 1393 (AB0723), 1410 (AB0768), 1415 (AB0776), 1415 (AB0778)
Franca-Berthon P., 0365 (POS0281)
Franceschini F., 0051 (OP0093), 0166 (OP0273), 0389 (POS0324), 0470 (POS0476), 0530 (POS0593), 0594 (POS0693), 0600 (POS0702), 0612 (POS0724), 0619 (POS0737), 0628 (POS0751), 0633 (POS0760), 0650 (POS0797), 0658 (POS0811), 0906 (POS1246), 1271 (AB0488), 1435 (AB0822)
Francesco M., 1406 (AB0756)
Franchimont N., 0597 (POS0698), 0598 (POS0699)
Franchini R., 0294 (POS0163)
Francioni A., 1432 (AB0817)
Francioso F., 0811 (POS1066)
Francisco F., 0032 (OP0060), 1225 (AB0396), 1412 (AB0771)
Francisco R., 0168 (OP0277-PARE)
Francisco V., 0418 (POS0376)
Francis-Sedlak M., 0839 (POS1121)
Franck-Larsson K., 0098 (OP0164)
Franco T., 0666 (POS0827)
Franco-Jarava C., 1158 (AB0264)
Franco-Trepat E., 1048 (AB0030)
Frank Bertoncelj M., 0009 (OP0016), 0011 (OP0020)
Frank C., 1408 (AB0761)
Franklin K., 0743 (POS0957)
Franks A., 0009 (OP0015)
Frantz C., 1364 (AB0665)
Frasca L., 0150 (OP0246)
Fraser A., 0859 (POS1162), 1459 (AB0872-HPR), 1479 (AB0916-PARE)
Frassi M., 0051 (OP0093)
Frauenfelder T., 0090 (OP0150), 0688 (POS0866)
Frauman A., 0117 (OP0194)
Frech T., 0102 (OP0171)
Frederic M., 0719 (POS0916)
Fredi M., 0470 (POS0476), 0594 (POS0693), 0600 (POS0702), 0619 (POS0737), 0628 (POS0751), 0633 (POS0760), 1435 (AB0822)
Frediani B., 0573 (POS0661), 0669 (POS0832), 0746 (POS0963), 0957 (POS1349), 1252 (AB0450), 1260 (AB0467), 1271 (AB0488)
Freeman L., 0462 (POS0462)
Freeman T., 1015 (POS1461-HPR)
Freire González M., 0068 (OP0123), 0610 (POS0721), 1208 (AB0366)
Freire M., 0350 (POS0256), 0987 (POS1408), 0987 (POS1409)
Freitas P., 0481 (POS0496)
Freitas R., 0690 (POS0870), 0692 (POS0872)
Freites D., 0910 (POS1253)
Freschi M., 1255 (AB0457)
Fresko I., 0660 (POS0814), 0662 (POS0819), 0663 (POS0820), 0958 (POS1351)
Fretheim H., 0090 (OP0150), 0104 (OP0174), 0689 (POS0867), 1245 (AB0433)
Freudensprung U., 0544 (POS0614), 1126 (AB0204)
Fridman I., 0927 (POS1293)
Friedman A., 0486 (POS0508), 0568 (POS0655)
Frigerio D., 0809 (POS1061)
Frigui E., 1342 (AB0614), 1342 (AB0615)
Frisell T., 0068 (OP0122), 0535 (POS0601), 0864 (POS1169)
Fritsch-Stork R., 0320 (POS0208), 1019 (POS1468-HPR)
Frittoli R., 1255 (AB0457)
Frommer K., 0676 (POS0844), 1054 (AB0044)
Frontuto M., 0882 (POS1200), 1399 (AB0739)
Frostegård J., 1065 (AB0069)
Fruth M., 0224 (POS0038)
Fu Q., 0698 (POS0885)
Fu T., 0634 (POS0761)
Fu X., 0867 (POS1174), 1063 (AB0066)
Fuchs M., 0391 (POS0328)
Fuentes-Silva Y., 0877 (POS1190)
Fuerst T., 0794 (POS1040)
Fujieda Y., 0687 (POS0863)
Fujii T., 1150 (AB0249)
Fujikawa K., 0581 (POS0674)
Fujino Y., 0329 (POS0221)
Fujio K., 1168 (AB0285)
Fuke S., 0697 (POS0881)
Fukui N., 0275 (POS0128)
Fukui S., 0753 (POS0975), 1408 (AB0763)
Fukuse S., 1063 (AB0065)
Fuller R., 0826 (POS1093)
Fulvio G., 0642 (POS0778), 0644 (POS0782)
Funada M., 1094 (AB0132)
Furer V., 0200 (LB0003), 0753 (POS0974), 0885 (POS1206), 1049 (AB0032), 1181 (AB0312), 1309 (AB0551)
Furie R., 0075 (OP0131), 0076 (OP0132), 0586 (POS0683), 0587 (POS0684), 0589 (POS0687), 0590 (POS0688), 0591 (POS0689), 0592 (POS0690), 0592 (POS0691), 0595 (POS0695), 0597 (POS0698), 0598 (POS0699)
Furini F., 0607 (POS0716)
Furlan F., 0540 (POS0608), 1130 (AB0208)
Furniss D., 0207 (POS0011), 0274 (POS0125), 0974 (POS1383)
Furst D., 0072 (OP0128), 0102 (OP0171), 0232 (POS0054), 0385 (POS0317), 0387 (POS0321), 1123 (AB0198)
Furtner D., 0447 (POS0437), 1258 (AB0463), 1290 (AB0525)
Furukawa T., 1181 (AB0311)
Furuta S., 0395 (POS0336)
Furuya H., 1063 (AB0065)
Fusama M., 1470 (AB0894-HPR)
Fusaro E., 0254 (POS0090), 0335 (POS0230), 0582 (POS0675), 0676 (POS0845), 0778 (POS1021), 0904 (POS1243)
Fusta Novell X., 0891 (POS1215)

G U., 0533 (POS0598)
Gaarden T. L., 0047 (OP0087)
Gaber T., 0191 (OP0312), 1048 (AB0029), 1049 (AB0031), 1052 (AB0040)
Gabrie S., 1078 (AB0099)
Gabrielli A., 0232 (POS0054), 0384 (POS0316), 0385 (POS0317), 0386 (POS0318), 0387 (POS0321), 0594 (POS0693), 0681 (POS0855), 0685 (POS0861), 1234 (AB0413)

Gabrusskaya T., 0247 (POS0080)
Gabrys H., 0090 (OP0150), 0688 (POS0866)
Gademan M. G. J., 1460 (AB0873-HPR)
Gaelle T., 0020 (OP0037)
Gaffney K., 0223 (POS0035), 0235 (POS0059-PARE), 0337 (POS0234), 0720 (POS0919), 0744 (POS0959), 1126 (AB0204)
Gafner M., 0928 (POS1294)
Gaggiano C., 0051 (OP0093)
Gaggiano E., 0888 (POS1210), 1165 (AB0279)
Gahlemann M., 1033 (POS1497-PARE)
Gaidar E., 0247 (POS0080), 0931 (POS1299), 0937 (POS1310), 0944 (POS1324), 1402 (AB0748)
Gaillez C., 0136 (OP0226), 0311 (POS0194), 0314 (POS0197), 0797 (POS1044), 0802 (POS1050), 0803 (POS1051)
Gainullina G., 1283 (AB0513)
Gaisina D., 1253 (AB0452)
Gaitán-Valdizán J. J., 0050 (OP0091), 0220 (POS0030), 0621 (POS0740)
Galanopoulou V., 1090 (AB0121)
Galant C., 0020 (OP0037), 0240 (POS0067), 1408 (AB0761)
Galarza-Delgado D. Á., 0445 (POS0434), 0463 (POS0463), 0473 (POS0482), 0473 (POS0483), 0478 (POS0491), 0510 (POS0552), 0511 (POS0553), 0515 (POS0562), 0816 (POS1074), 0893 (POS1220), 0978 (POS1392), 0983 (POS1402), 0984 (POS1404), 1007 (POS1446), 1018 (POS1466-HPR), 1031 (POS1494-HPR), 1085 (AB0113), 1087 (AB0117), 1166 (AB0281), 1177 (AB0301), 1189 (AB0329), 1345 (AB0624), 1360 (AB0657), 1361 (AB0658), 1425 (AB0801), 1439 (AB0830), 1444 (AB0842), 1445 (AB0843), 1450 (AB0852), 1455 (AB0863-HPR), 1456 (AB0866-HPR), 1457 (AB0867-HPR), 1458 (AB0868-HPR), 1459 (AB0871-HPR), 1463 (AB0880-HPR)
Galarza-Molina R., 1450 (AB0852)
Galetti I., 1033 (POS1497-PARE)
Galfo G., 1271 (AB0488)
Galiero R., 1446 (AB0844)
Galindez E., 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070), 1076 (AB0096), 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Galíndez-Agirregoikoa E., 0034 (OP0064), 0035 (OP0065)
Galindo M., 0179 (OP0292)
Galindo Zavala R., 0946 (POS1328)
Galindo-Feria A. S., 0206 (POS0008), 0697 (POS0883)
Galindo-Izquierdo M., 0610 (POS0721), 1149 (AB0248)
Galisteo C., 1060 (AB0055)
Gall S., 0376 (POS0301)
Gallagher P., 0015 (OP0028), 0027 (OP0051), 0462 (POS0462), 0738 (POS0949), 0747 (POS0964), 1043 (AB0018)
Gallagher S., 1459 (AB0872-HPR)
Gallego A., 0034 (OP0064), 0755 (POS0978), 0952 (POS1340)
Galli E., 0037 (OP0069)
Galli R., 1007 (POS1447)
Gallipoli S., 0878 (POS1192)
Gallo G., 0707 (POS0901), 0789 (POS1033)
Gallo R., 0875 (POS1188)
Galloway J., 0070 (OP0126), 0255 (POS0092), 0479 (POS0494), 0573 (POS0662), 0744 (POS0959), 1008 (POS1448), 1357 (AB0649)
Galluccio F., 1331 (AB0588)
Galluzzo C., 1416 (AB0781)
Galozzi P., 0392 (POS0329)
Galushko E., 0518 (POS0567)
Gálvez Elkin M. S., 0730 (POS0933), 0887 (POS1208), 1377 (AB0689)
Gálvez-Ruiz D., 0762 (POS0989), 0763 (POS0990)
Gamal S., 0340 (POS0239)
Gamba M. J., 0576 (POS0667), 0730 (POS0933), 0771 (POS1005), 0875 (POS1188), 1377 (AB0689)
Gamboa-Alonso C. M., 1031 (POS1494-HPR), 1166 (AB0281), 1177 (AB0301), 1345 (AB0624), 1456 (AB0866-HPR)
Gancheva R., 1356 (AB0646)
Gandhi M., 0989 (POS1411), 0990 (POS1413)
Gandia Martinez M., 0032 (OP0060)
Gandjbakhch F., 0089 (OP0149), 0153 (OP0252)
Ganz F., 0143 (OP0233), 0338 (POS0235), 0710 (POS0905), 0722 (POS0923), 0723 (POS0924)
Gao D., 1025 (POS1481-HPR), 1166 (AB0280)
Gao T., 0143 (OP0233), 0338 (POS0235), 0710 (POS0905), 0712 (POS0907), 0722 (POS0923), 0723 (POS0924)
Garabajiu M., 1337 (AB0601)
Garaffoni C., 0607 (POS0716)
Garaiman A., 0694 (POS0877), 1233 (AB0411)
Garantziotis P., 0011 (OP0019), 0207 (POS0010)
Garassino M., 0953 (POS1341)
García A., 0034 (OP0064)
García C., 1103 (AB0151), 1104 (AB0153), 1111 (AB0170)
Garcia Cañas I. E., 0624 (POS0745)
García Castañeda N., 1065 (AB0070)
García Ciccarelli A., 1133 (AB0214)
Garcia de Vicuna R., 0560 (POS0645), 0700 (POS0888), 0719 (POS0917), 1241 (AB0427)
García de Yébenes M. J., 1089 (AB0120)
Garcia Diaz S., 1474 (AB0904-HPR)
García Fernández A., 0884 (POS1204), 0914 (POS1260), 0946 (POS1327)
Garcia Garcia C., 0486 (POS0508)
García García V., 0283 (POS0143), 0807 (POS1058)
Garcia Gomez C. L., 1376 (AB0686)
Garcia Gonzales E., 1252 (AB0450)
Garcia Hernandez I., 1024 (POS1480-HPR)
García Hernández I., 1056 (AB0047), 1075 (AB0092), 1145 (AB0239)
Garcia Kutzbach A., 1280 (AB0506)
Garcia L., 0635 (POS0763)
Garcia Llorente J. F., 0523 (POS0579)
García M., 0635 (POS0763), 0875 (POS1188), 1196 (AB0342)
Garcia Manrique de Lara M., 1060 (AB0055)
García Martos A., 0952 (POS1340)
García Morillo S., 1208 (AB0366)
Garcia Perez J., 1071 (AB0083)
Garcia Perez S., 0960 (POS1355), 1132 (AB0211)
Garcia S., 0260 (POS0100), 0318 (POS0204), 0476 (POS0488), 0483 (POS0502), 0692 (POS0872), 0718 (POS0914), 0812 (POS1067), 0833 (POS1106), 0836 (POS1113), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1299 (AB0536), 1432 (AB0816), 1441 (AB0835)
Garcia Salinas R., 0730 (POS0933), 1133 (AB0214), 1377 (AB0689)
García Vivar M. L., 0755 (POS0977), 0760 (POS0985), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070), 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Garcia-Alzorriz Morral E., 0991 (POS1416)
García-Aparicio Á., 0952 (POS1340)
García-Arellano G., 0983 (POS1402)
Garcia-Bournissen F., 0958 (POS1352)
García-Carazo S., 1047 (AB0027)
Garcia-Castañeda N., 0986 (POS1407)
Garcia-Cirera S., 1060 (AB0055)
García-García M. J., 0970 (POS1376)
García-Gómez J. A., 1231 (AB0405), 1231 (AB0406)
García-González J., 0068 (OP0123)
García-Guillén A., 0666 (POS0827), 1426 (AB0804)
Garcia-Gullien A., 0277 (POS0132)
Garcia-Heredia A., 0463 (POS0463)
García-Lledó A., 0144 (OP0234)
García-López H., 0922 (POS1275)
García-Luque L., 0920 (POS1272)
Garcia-Monco C., 0976 (POS1387)
García-Montes N., 0283 (POS0143), 0922 (POS1275), 1215 (AB0376)
Garcia-Montoya L., 0463 (POS0464), 0482 (POS0499)
García-Porrúa C., 1326 (AB0577)
García-Vadillo A., 0144 (OP0234), 0560 (POS0645)
García-Valle A., 0034 (OP0064), 0035 (OP0065), 0952 (POS1340)
Gardiner P., 0740 (POS0952)
Gardner G., 0994 (POS1422)
Garen T., 0104 (OP0174), 0689 (POS0867)
Garg A., 0139 (OP0229)
Garg M., 1334 (AB0595)
Garg N., 0318 (POS0205), 0774 (POS1011)
Gargani L., 0675 (POS0842)
Garimella R., 0600 (POS0701)
Garipova N., 0931 (POS1299)
Garrido Courel L., 0960 (POS1355), 1132 (AB0211)
Garrido-Castro J. L., 0737 (POS0948), 0740 (POS0952), 0743 (POS0958), 0920 (POS1272)
Garrido-Cumbrera M., 0239 (POS0065-PARE), 0343 (POS0244), 0744 (POS0960), 0745 (POS0961), 0746 (POS0962), 0762 (POS0988), 0762 (POS0989), 0763 (POS0990), 0763 (POS0991), 0764 (POS0992), 0765 (POS0993), 0765 (POS0994), 0868 (POS1175), 0889 (POS1213), 1277 (AB0500), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Garrido-González C., 0737 (POS0948), 0743 (POS0958), 0920 (POS1272)
Garrood T., 0479 (POS0494)
Garufi C., 0583 (POS0677), 0645 (POS0783), 1160 (AB0269), 1384 (AB0704)
Garvey T., 0654 (POS0803)
Garyfallos A., 1299 (AB0537)
Garza Acosta A. C., 0473 (POS0483), 0515 (POS0562), 0983 (POS1402)
Garza Elizondo M. A., 0445 (POS0434), 1085 (AB0113), 1425 (AB0801)
Garzanova L., 0104 (OP0173), 0681 (POS0853), 0683 (POS0857), 0683 (POS0858), 0684 (POS0860), 0899 (POS1232), 1239 (AB0423), 1248 (AB0440), 1253 (AB0453), 1254 (AB0454), 1254 (AB0455)
Garzon Cepeda J. D., 1473 (AB0900-HPR)
Gaspar C., 0695 (POS0878)
Gassara Z., 1276 (AB0497), 1281 (AB0508), 1484 (AB0926-PARE)
Gastelum-Strozzi A., 1428 (AB0808)
Gateva A., 1332 (AB0591)
Gatt K., 1068 (AB0077)
Gattamelata A., 1017 (POS1464-HPR), 1183 (AB0317)
Gatti D., 0062 (OP0112), 0106 (OP0178), 0326 (POS0218), 0560 (POS0644), 0831 (POS1102), 0867 (POS1173)
Gattinara M., 0936 (POS1308)
Gatto M., 0112 (OP0186), 0594 (POS0693)
Gattorno M., 0947 (POS1330)
Gaudio A., 0838 (POS1119)
Gaud-Listrat V., 1009 (POS1450)
Gaudreau A. J., 1313 (AB0557)
Gaujoux-Viala C., 0054 (OP0098), 0379 (POS0306), 0518 (POS0566), 0571 (POS0659), 0770 (POS1003), 0820 (POS1082), 0902 (POS1239)
Gauler G., 1274 (AB0494)
Gaur R., 0433 (POS0408)
Gautier M., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Gavali M., 0024 (OP0047)
Gavigan K., 0169 (OP0280-PARE), 0237 (POS0062-PARE), 1034 (POS1499-PARE)
Gavín C., 0366 (POS0282)
Gaydukova I., 0084 (OP0142), 0183 (OP0298), 0726 (POS0928), 0796 (POS1043), 1285 (AB0516), 1298 (AB0534), 1302 (AB0540), 1352 (AB0636)
Gaylis N., 1130 (AB0208)
Gazar Y., 0923 (POS1278), 1068 (AB0076)
Gazi S., 1299 (AB0537)
Gazitt T., 0131 (OP0219), 0200 (LB0003), 0286 (POS0147), 0543 (POS0613), 0753 (POS0974)
Ge X., 0009 (OP0016), 0430 (POS0401), 0646 (POS0788)
Gebhard C., 0694 (POS0877)
Geçmez G., 0514 (POS0560)
Gedikli M. A., 1380 (AB0694)
Geenen R., 0878 (POS1191)
Géher P., 0024 (OP0047)
Gehin J. E., 0185 (OP0301)
Gehring I., 1090 (AB0122)
Gehring K., 1064 (AB0067)
Geifman N., 0097 (OP0162)
Geijer M., 0339 (POS0237), 0743 (POS0957)
Geikowski T., 0933 (POS1303)
Geirsson A. J., 0082 (OP0140), 0217 (POS0027)

Gelfand J., 0810 (POS1063)
Gellert L., 0769 (POS1002)
Gellett A., 0789 (POS1033)
Gellis S., 0165 (OP0271)
Genç A. C., 0223 (POS0036), 0732 (POS0939)
Genc Kaya L., 0223 (POS0036)
Gendreau J. F., 0210 (POS0017)
Gendreau R. M., 0210 (POS0017)
Generali E., 0906 (POS1246)
Geneus V. J., 0333 (POS0228)
Geneva-Popova M., 1272 (AB0489)
Geng Y., 1166 (AB0280)
Genovese M. C., 1158 (AB0264)
Genre F., 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1046 (AB0026), 1065 (AB0070), 1076 (AB0094), 1076 (AB0096)
Gensler L. S., 0156 (OP0255), 0332 (POS0226), 0334 (POS0229), 0710 (POS0904), 0722 (POS0923), 0911 (POS1255)
Gentileschi S., 0573 (POS0661)
Gentzel-Jorczyk A., 1157 (AB0261)
Geny B., 0149 (OP0243), 0151 (OP0247), 0694 (POS0876), 1373 (AB0680)
Geoffroy M., 0170 (OP0282), 0227 (POS0045)
Georgantzoglou N., 0015 (OP0029)
George P., 0018 (OP0034)
Georgiadis A., 1107 (AB0161)
Georgiev T., 0896 (POS1224), 1138 (AB0224), 1332 (AB0591)
Georgin-Lavialle S., 0172 (OP0284), 0954 (POS1343)
Georgiou P., 1299 (AB0537)
Georgountzos A., 1299 (AB0537)
Gérard M., 0669 (POS0831)
Gerardi M. C., 0470 (POS0476), 0600 (POS0702), 0633 (POS0760), 1435 (AB0822)
Gerasimenko A., 1403 (AB0749)
Gerasimova D., 1049 (AB0033), 1155 (AB0257)
Gerasimova E., 0493 (POS0520), 1049 (AB0033), 1064 (AB0068), 1084 (AB0111), 1155 (AB0257)
Gerçik Ö., 0727 (POS0929)
Gerganov G., 0896 (POS1224), 1138 (AB0224)
Gerhart W., 0167 (OP0275-PARE), 0237 (POS0061-PARE), 1482 (AB0923-PARE)
Gerli R., 0190 (OP0310), 0211 (POS0019), 0594 (POS0693), 0630 (POS0755), 1389 (AB0716)
Germino R., 0565 (POS0652), 1286 (AB0521)
Gerogianni T., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Gerosa J., 0960 (POS1356)
Gerosa M., 0594 (POS0693), 0619 (POS0737), 0628 (POS0751)
Gerriets T., 0209 (POS0015)
Gerstner C., 0038 (OP0072)
Gertel S., 1049 (AB0032)
Gerus P., 0367 (POS0284)
Gervais E., 0939 (POS1314)
Gerwien J., 0725 (POS0926)
Geurts G., 0680 (POS0852)
Geurts J., 0120 (OP0199)
Gezer H. H., 0959 (POS1354), 0961 (POS1359), 1016 (POS1462-HPR)
Ghaffar U., 0951 (POS1338)
Ghalandari N., 0317 (POS0202)
Ghaleb B., 0027 (OP0052)
Ghali M., 1414 (AB0775), 1484 (AB0926-PARE)
Ghandehari H., 0363 (POS0278)
Ghanem S., 0923 (POS1278)
Ghang B., 0321 (POS0209)
Gharabaghtsyan M., 0931 (POS1299)
Gharsallah I., 0774 (POS1012), 0856 (POS1155), 0925 (POS1287), 0926 (POS1289), 0926 (POS1290), 1066 (AB0071), 1095 (AB0134), 1116 (AB0182), 1281 (AB0507), 1281 (AB0509), 1285 (AB0518), 1286 (AB0519), 1358 (AB0650), 1417 (AB0784), 1442 (AB0836), 1443 (AB0840)
Ghazouani E., 0926 (POS1290), 1066 (AB0071), 1442 (AB0836), 1443 (AB0840)
Gheorghe I. R., 0773 (POS1009)
Gheorghiu A. M., 0385 (POS0317), 0685 (POS0861)
Gheyle L., 0792 (POS1037), 0792 (POS1038), 0801 (POS1049)
Ghiatau A., 1267 (AB0480)
Ghini M., 0190 (OP0310), 1389 (AB0716)
Ghirardello A., 0630 (POS0755)
Ghorasaini M., 0416 (POS0371), 0822 (POS1087)
Ghori V., 1121 (AB0195)
Ghose S., 0943 (POS1322)
Ghosh N., 1441 (AB0834)
Ghozlani I., 0992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811)
Ghuman P., 0374 (POS0298)
Giacomelli R., 0190 (OP0310), 0301 (POS0177), 0390 (POS0326), 0957 (POS1349), 1260 (AB0467), 1389 (AB0716)
Giambalvo S., 0607 (POS0716)
Giancane G., 0098 (OP0164), 0947 (POS1330)
Gianfrancesco M., 0002 (OP0006), 0065 (OP0117), 0173 (OP0286), 0175 (OP0288)
Giani T., 0935 (POS1307), 0936 (POS1308), 0940 (POS1315), 0940 (POS1316), 0941 (POS1317)
Giannakopoulou I. I., 0646 (POS0786)
Giannini C., 0980 (POS1395)
Giannini M., 0149 (OP0243), 0151 (OP0247), 0694 (POS0876), 1373 (AB0680)
Giardina F., 1017 (POS1464-HPR), 1143 (AB0234), 1183 (AB0317)
Giardino A. M., 1260 (AB0467)
Giardullo L., 1379 (AB0691)
Gibofsky A., 0446 (POS0436), 0575 (POS0666)
Gibson K., 0218 (POS0028)
Giera M., 0416 (POS0371), 0822 (POS1087)
Gigante L., 0370 (POS0289), 0687 (POS0864)
Gigliotti P., 0906 (POS1246)
Gigliucci G., 1331 (AB0588)
Gil M., 0144 (OP0234)
Gilbert A., 1033 (POS1497-PARE)
Gilbert B., 0577 (POS0668), 0863 (POS1168)
Gilbert E., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Giles J. T., 0072 (OP0128), 0569 (POS0656)
Gilio M., 0882 (POS1200), 1399 (AB0739)
Gillard L., 1412 (AB0772)
Gilles L., 0083 (OP0141)
Gillet-van Dongen H., 0675 (POS0843)
Gil-Vila A., 0699 (POS0886), 0898 (POS1229), 1241 (AB0426)
Gilyarov M., 0890 (POS1214)
Gimeno M., 0366 (POS0282)
Gimeno-Torres L., 1197 (AB0344)
Ginaldi L., 1246 (AB0434)
Giner García M., 1341 (AB0612)
Ginosyan K., 1417 (AB0782)
Ginzler E. M., 0177 (OP0289)
Gioia C., 0047 (OP0086), 0190 (OP0310), 1016 (POS1463-HPR), 1017 (POS1464-HPR), 1389 (AB0716)
Giollo A., 0062 (OP0112), 0106 (OP0178), 0232 (POS0054), 0326 (POS0218), 0384 (POS0316), 0560 (POS0644), 0685 (POS0861), 0867 (POS1173), 1222 (AB0389), 1477 (AB0911-HPR)
Giorgi Rossi P., 0037 (OP0069)
Giorgi V., 0190 (OP0310), 1367 (AB0671), 1389 (AB0716)
Giorgis P., 0771 (POS1005)
Gioti O., 0635 (POS0764), 0646 (POS0786)
Giovale M., 1007 (POS1447)
Giovannini I., 0134 (OP0223), 0284 (POS0145), 0618 (POS0735)
Giraldi A., 1468 (AB0890-HPR)
Giraldo Herrera C. L., 1139 (AB0227)
Girard Bosch P., 0730 (POS0933), 0771 (POS1005), 1377 (AB0689)
Girasole G., 0833 (POS1105), 1216 (AB0379)
Giraud N., 1279 (AB0504)
Girgin S., 0648 (POS0793), 1198 (AB0347)
Girolimetto N., 0355 (POS0265), 0726 (POS0927)
Girschick H., 0246 (POS0077), 0882 (POS1199)
Giryes S., 0892 (POS1217)
Gismondo M. R., 1367 (AB0671)
Giudici F., 1002 (POS1435)
Giuggioli D., 0672 (POS0837), 0906 (POS1246), 1241 (AB0425)
Giusti A., 0833 (POS1105), 1007 (POS1447), 1216 (AB0379)
Gjeloshi K., 1475 (AB0905-HPR)
Gjertsson I., 0112 (OP0186), 0811 (POS1064)
Gkaliagkousi E., 0620 (POS0738)
Gkelaki M. C., 0344 (POS0245)
Gladman D. D., 0132 (OP0221), 0139 (OP0229), 0177 (OP0289), 0316 (POS0200), 0431 (POS0405), 0432 (POS0406), 0784 (POS1028), 0792 (POS1037), 0792 (POS1038), 0797 (POS1044), 0798 (POS1045), 0801 (POS1049), 0802 (POS1050), 0803 (POS1051), 0812 (POS1068), 1294 (AB0529), 1308 (AB0550), 1311 (AB0553), 1313 (AB0557)
Glaubitz S., 1167 (AB0283)
Glazyrina A., 1397 (AB0735)
Glerup M., 0098 (OP0164)
Glikmann-Johnston Y., 0616 (POS0731)
Glintborg B., 0009 (OP0017), 0063 (OP0114), 0082 (OP0140), 0126 (OP0210), 0131 (OP0220), 0133 (OP0222), 0217 (POS0027), 0234 (POS0056), 0865 (POS1170)
Gloor A., 0398 (POS0341)
Glukhova S., 0196 (OP0320), 0310 (POS0192), 0681 (POS0853), 0754 (POS0976), 0815 (POS1072), 0834 (POS1108), 1088 (AB0118), 1138 (AB0225), 1147 (AB0245), 1158 (AB0263), 1177 (AB0303), 1239 (AB0423), 1253 (AB0453), 1254 (AB0454), 1254 (AB0455), 1264 (AB0473), 1264 (AB0474), 1303 (AB0541), 1306 (AB0546), 1325 (AB0575), 1325 (AB0576), 1350 (AB0631), 1363 (AB0663)
Głuszko P., 0822 (POS1086), 1434 (AB0820)
Glynn L., 1459 (AB0872-HPR)
Glynn R., 0327 (POS0219)
Gnanapragasam J., 1432 (AB0817)
Gobbi C. A., 1194 (AB0338)
Gobbi C., 0874 (POS1186), 1133 (AB0214), 1196 (AB0342)
Godinho F., 0692 (POS0872)
Godoy-Navarrete F., 0323 (POS0211), 0344 (POS0246), 1453 (AB0859-HPR), 1456 (AB0865-HPR)
Godsave C., 0841 (POS1124), 0989 (POS1412)
Godzenko A., 0717 (POS0913)
Goekoop R., 0127 (OP0211), 0127 (OP0212), 0466 (POS0470), 0675 (POS0843)
Goekoop-Ruiterman Y., 0259 (POS0097)
Goel N., 0139 (OP0229)
Goetz T. I., 0165 (OP0272)
Goh W. R., 0273 (POS0124)
Gohil S., 1476 (AB0908-HPR)
Goizueta C., 0875 (POS1188), 1196 (AB0342)
Gok K., 1105 (AB0157), 1182 (AB0314)
Gokcen N., 1471 (AB0896-HPR)
Goker B., 0733 (POS0940), 0878 (POS1193), 1077 (AB0097), 1176 (AB0300)
Gold D., 0251 (POS0086)
Gold R., 0525 (POS0584)
Goldberg O., 0929 (POS1295)
Goldblatt F., 0218 (POS0028)
Golder V., 0218 (POS0028), 0616 (POS0731), 0629 (POS0753)
Goldin J., 0162 (OP0267), 0163 (OP0268)
Goldmann K., 0007 (OP0011), 0079 (OP0136)
Goletti D., 1003 (POS1437)
Goleva O., 0927 (POS1293)
Goll G. L., 0185 (OP0301)
Goloeva R., 1072 (AB0085), 1072 (AB0086), 1409 (AB0764), 1409 (AB0765)
Golovina O., 0196 (OP0320), 0896 (POS1226)
Gomes Correia A. M., 1003 (POS1438)
Gomez A., 0260 (POS0101)
Gómez Bahamonde R., 0418 (POS0376)
Gomez Centeno A. D., 1060 (AB0055)
Gomez de la Fuente F. J., 1208 (AB0365)
Gómez de la Torre R., 0967 (POS1371), 1208 (AB0366)
Gomez G., 0635 (POS0763), 1196 (AB0342)
Gómez García I., 0751 (POS0970), 0769 (POS1001), 1317 (AB0562)
Gomez H. M., 0589 (POS0687)
Gomez R., 0576 (POS0667), 0771 (POS1005)
Gómez R., 1048 (AB0030)
Gómez S., 0782 (POS1025)
Gómez Vaquero C., 0184 (OP0300)
Gomez-Centeno A., 0523 (POS0579), 0569 (POS0657), 0570 (POS0658)

Gomez-Garberi M., 0282 (POS0141)
Gómez-Puerta J. A., 0199 (LB0002)
Gómez-Reino J. J., 0542 (POS0610)
Gómez-Román J., 0393 (POS0331)
Gómez-Ruiz C., 0853 (POS1149)
Gomez-Vieites C., 0935 (POS1306)
Gomides A. P., 0909 (POS1252), 1448 (AB0848)
Gonçalves D. R., 0919 (POS1270), 1339 (AB0608)
Gonçalves N., 0692 (POS0872), 0871 (POS1180)
Goncharova R., 1036 (AB0003), 1039 (AB0009)
Gong L., 0574 (POS0664), 1484 (AB0927-PARE)
Gong Q., 0255 (POS0092), 1155 (AB0259)
Gönüllü E., 0223 (POS0036), 0731 (POS0935), 0732 (POS0939), 1382 (AB0700)
Gonzalez A., 0306 (POS0185)
Gonzalez C., 0916 (POS1264), 1385 (AB0706)
Gonzalez Chiappe S., 1222 (AB0388)
González Fernández I., 0628 (POS0752), 0692 (POS0873), 0935 (POS1306), 1165 (AB0278), 1171 (AB0290), 1173 (AB0294)
González L. A., 0636 (POS0765), 0639 (POS0770)
Gonzalez Lucero L., 0382 (POS0312), 0875 (POS1188)
González M. J., 0303 (POS0180)
González Márquez K. I., 1085 (AB0113)
Gonzalez Mazario R., 0857 (POS1157)
Gonzalez P., 0771 (POS1005)
Gonzalez Puig L., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
González S., 0303 (POS0180)
González Sánchez E., 0393 (POS0331), 1071 (AB0083)
Gonzalez V., 0419 (POS0378)
González-Alvarez B., 1208 (AB0366)
González-Álvaro I., 0403 (POS0348), 0719 (POS0917), 1089 (AB0120)
González-Colominas E., 1132 (AB0212)
González-Gay M. A., 0032 (OP0060), 0034 (OP0064), 0035 (OP0065), 0418 (POS0376), 0490 (POS0513), 0531 (POS0595), 0614 (POS0728), 0755 (POS0977), 0899 (POS1231), 0952 (POS1340), 0953 (POS1342), 0955 (POS1346), 0960 (POS1357), 0970 (POS1376), 0977 (POS1390), 0986 (POS1407), 1002 (POS1436), 1018 (POS1467-HPR), 1046 (AB0026), 1065 (AB0070), 1076 (AB0094), 1076 (AB0096), 1208 (AB0365), 1208 (AB0366), 1225 (AB0396), 1227 (AB0399), 1231 (AB0405), 1243 (AB0430), 1324 (AB0574), 1377 (AB0688), 1412 (AB0771)
González-Gay M. Á., 0050 (OP0091), 0091 (OP0152), 0220 (POS0030), 0393 (POS0331), 0601 (POS0703), 0621 (POS0740), 0730 (POS0934), 0963 (POS1362), 0966 (POS1370), 0967 (POS1371), 1226 (AB0397), 1436 (AB0825)
González-Mazón I., 0050 (OP0091), 0220 (POS0030), 0399 (POS0342), 0621 (POS0740), 0730 (POS0934), 0755 (POS0977), 0952 (POS1340), 0960 (POS1357), 0963 (POS1362), 0967 (POS1371), 0970 (POS1376), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070), 1218 (AB0382), 1225 (AB0396), 1324 (AB0574), 1412 (AB0771)
Gonzalez-Navas C., 0737 (POS0948), 0740 (POS0952), 0920 (POS1272)
González-Reyes J. A., 0426 (POS0394)
González-Rodríguez M., 0418 (POS0376)
Gonzalez-Sans D., 0699 (POS0886)
Gonzalez-Traves P., 0331 (POS0224)
Gooderham M., 0795 (POS1042)
Goodman S., 0367 (POS0285), 0472 (POS0480), 0828 (POS1097), 1441 (AB0834)
Goodspeed W., 0049 (OP0090)
Goodyear C., 0403 (POS0348)
Gopalakrishnan S., 0805 (POS1054)
Gopalakrishnapillai Syamala N., 1415 (AB0779)
Göpfert J., 0308 (POS0189)
Gorbunova Y., 0514 (POS0559), 0515 (POS0561), 1422 (AB0795)
Gordeev A., 0518 (POS0567)
Gordeev I., 0890 (POS1214)
Gordon C., 0043 (OP0081), 0074 (OP0129), 0177 (OP0289), 0181 (OP0296), 0602 (POS0705), 0626 (POS0748)
Gordon J., 0102 (OP0171)
Gorecki P., 0141 (OP0231), 0804 (POS1052)
Gori V., 0546 (POS0618)
Göricke B. M., 1167 (AB0283)
Gorla R., 0470 (POS0476), 0582 (POS0675), 0633 (POS0760), 1435 (AB0822)
Gorman A., 0462 (POS0462)
Gorodensky J., 0993 (POS1420)
Gorodetskiy V., 1116 (AB0183), 1406 (AB0757), 1414 (AB0774)
Gorostiza I., 1103 (AB0151), 1104 (AB0153), 1376 (AB0686)
Gossec L., 0002 (OP0006), 0039 (OP0074), 0054 (OP0098), 0140 (OP0230), 0142 (OP0232), 0173 (OP0286), 0175 (OP0288), 0183 (OP0298), 0199 (LB0002), 0233 (POS0055), 0343 (POS0243), 0360 (POS0274-HPR), 0728 (POS0930), 0778 (POS1021), 0779 (POS1022), 0781 (POS1024), 0782 (POS1025), 0790 (POS1035), 0799 (POS1046), 0818 (POS1078), 1009 (POS1450), 1292 (AB0527), 1294 (AB0529), 1295 (AB0530), 1308 (AB0550), 1316 (AB0560)
Gosselt H., 0012 (OP0021)
Goswami H., 1443 (AB0839)
Got J., 0576 (POS0667)
Gotelli E., 0392 (POS0330), 0524 (POS0583), 0679 (POS0850), 0686 (POS0862), 0697 (POS0882), 0908 (POS1250), 1060 (AB0057), 1190 (AB0330), 1201 (AB0354), 1247 (AB0438), 1372 (AB0679)
Gottenberg J. E., 0074 (OP0130), 0170 (OP0282), 0199 (LB0002), 0736 (POS0947), 0877 (POS1190)
Gottlieb A. B., 0783 (POS1027), 1293 (AB0528), 1300 (AB0538), 1304 (AB0544), 1448 (AB0849)
Goulenok T., 0199 (LB0002), 0261 (POS0103)
Goules A., 0015 (OP0029), 0022 (OP0041), 0178 (OP0291), 0180 (OP0294), 0370 (POS0290), 0656 (POS0807)
Goulielmos G., 0405 (POS0350), 1037 (AB0004)
Goulvestre C., 0534 (POS0600)
Goupille P., 0027 (OP0052), 0080 (OP0138), 0109 (OP0181), 0311 (POS0194), 0797 (POS1044), 1287 (AB0522)
Gouverneur A., 0331 (POS0225)
Governato G., 0642 (POS0778), 0644 (POS0782)
Govoni M., 0190 (OP0310), 0586 (POS0682), 0594 (POS0693), 0607 (POS0716), 0628 (POS0751), 0985 (POS1406), 1260 (AB0467), 1389 (AB0716)
Goyanka P., 0136 (OP0226), 0314 (POS0197)
Gozzoli D. S., 0655 (POS0806)
Graceffa D., 1318 (AB0563)
Gracia Tello B., 0350 (POS0256), 0987 (POS1408), 0987 (POS1409)
Gracia-Arechiga T. S., 1085 (AB0113)
Grader-Beck T., 0593 (POS0692)
Grados Canovas D., 0184 (OP0300)
Graef E., 0230 (POS0051), 1368 (AB0674)
Graell E., 1060 (AB0055)
Graf J., 0460 (POS0459)
Graf M., 0305 (POS0183)
Graham J., 0824 (POS1089)
Grainger R., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0230 (POS0051), 0859 (POS1162), 1368 (AB0674)
Gram Ahlmark N., 1483 (AB0924-PARE)
Graña J., 0967 (POS1371)
Granath F., 0126 (OP0210)
Grange L., 0889 (POS1213), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Granger B., 0258 (POS0095)
Grant E., 0331 (POS0224)
Grapton X., 0169 (OP0279-PARE), 1362 (AB0659)
Gräslund S., 0196 (OP0321)
Grassa R., 0923 (POS1279), 0924 (POS1283), 1142 (AB0232)
Grasshoff H., 0395 (POS0335)
Grassi D., 1359 (AB0652)
Grassi M., 1367 (AB0671)
Grassi W., 0123 (OP0205), 0125 (OP0209), 0811 (POS1066)
Grasso G., 0301 (POS0177)
Gratacos Masmitjà J., 1060 (AB0055)
Gratacos-Masmitja J., 0342 (POS0242), 0746 (POS0962), 0755 (POS0978), 0760 (POS0986), 0763 (POS0991), 0764 (POS0992), 0765 (POS0993), 0765 (POS0994), 0797 (POS1044), 0976 (POS1387), 1303 (AB0542)
Grateau G., 0954 (POS1343)
Grau García E., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Grau S., 0991 (POS1416)
Grau-Cerrato S., 1132 (AB0212)
Graugaard C., 1468 (AB0890-HPR)
Gravallese E., 0867 (POS1174)
Graver J. C., 0033 (OP0062)
Grayson P., 0049 (OP0090), 0653 (POS0802), 0968 (POS1373)
Grazio S., 1296 (AB0531)
Grčević D., 0226 (POS0042)
Grech Meli J. A., 1068 (AB0077)
Green J., 1459 (AB0872-HPR)
Green Y., 0596 (POS0696)
Greenwood M., 1136 (AB0220)
Greese J., 0156 (OP0256)
Gregorc V., 0953 (POS1341)
Gregori D., 0878 (POS1192)
Gregory W. J., 0757 (POS0980), 1031 (POS1493-HPR)
Grekhoff R., 1461 (AB0876-HPR)
Grembiale R. D., 0809 (POS1061), 1012 (POS1457-HPR), 1260 (AB0467), 1454 (AB0861-HPR)
Gremese E., 0142 (OP0232), 0190 (OP0310), 0217 (POS0027), 0324 (POS0214), 0582 (POS0675), 0594 (POS0693), 0778 (POS1021), 0799 (POS1046), 1260 (AB0467), 1295 (AB0530), 1389 (AB0716)
Gridneva G., 0465 (POS0467), 1131 (AB0209), 1147 (AB0245), 1158 (AB0263), 1363 (AB0663)
Grieb S., 0139 (OP0229)
Griep E. N., 1107 (AB0160)
Grifantini R., 0229 (POS0048)
Griffith J. F., 0257 (POS0094)
Griffiths B., 0602 (POS0705)
Griffiths C. E. M., 1293 (AB0528), 1297 (AB0532)
Griffiths H., 0108 (OP0180), 0330 (POS0223), 0453 (POS0447), 0533 (POS0599), 0547 (POS0619), 0711 (POS0906), 1015 (POS1461-HPR), 1128 (AB0207)
Griger Z., 0004 (OP0008)
Grigor'eva I., 0647 (POS0790)
Grigoriadou S., 0079 (OP0136)
Grima B., 1282 (AB0510)
Grinnell-Merrick L., 0808 (POS1060)
Grisoni F., 0255 (POS0091)
Grivas A., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Grivegnee C., 1358 (AB0651)
Grobelski J., 1447 (AB0847)
Grom A., 0245 (POS0076)
Gromov A., 1392 (AB0721), 1394 (AB0727)
Gromova M., 0840 (POS1123)
Gronenschild M., 0911 (POS1256)
Grönwall C., 0206 (POS0009), 0429 (POS0400)
Groseanu L., 0164 (OP0270), 0681 (POS0854), 0773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690), 1462 (AB0879-HPR)
Grosjean A., 0991 (POS1415)
Grossi P., 1480 (AB0918-PARE)
Grosso M., 0908 (POS1250), 1372 (AB0679)
Grove V., 0210 (POS0018)
Gruben D. C., 0565 (POS0652), 0782 (POS1025), 1286 (AB0521)
Grulich-Henn J., 0943 (POS1321)
Gruppen M., 0937 (POS1311)
Grygielska J., 1481 (AB0920-PARE)
Grygorieva N., 0836 (POS1112)
Grzechnik K., 1424 (AB0800)
Gu J., 0024 (OP0047)
Gu L., 0641 (POS0776)
Gu X., 0039 (OP0073), 0203 (POS0002), 0634 (POS0761), 1196 (AB0343)
Gu Z., 0039 (OP0073), 0430 (POS0401), 0634 (POS0761), 0645 (POS0785), 0646 (POS0787), 0646 (POS0788), 1100 (AB0146), 1196 (AB0343), 1353 (AB0639)
Guaglianone D., 0874 (POS1186)
Guaglione D., 1196 (AB0342)
Guajardo-Jauregui N., 0463 (POS0463), 0473 (POS0482), 0473 (POS0483), 0478 (POS0491),

0510 (POS0552), 0511 (POS0553), 0515 (POS0562), 0816 (POS1074), 0978 (POS1392), 0983 (POS1402), 0984 (POS1404), 1087 (AB0117), 1189 (AB0329), 1450 (AB0852), 1459 (AB0871-HPR)
Gualillo O., 0418 (POS0376), 1065 (AB0070)
Guan H., 0056 (OP0101)
Guan S., 0449 (POS0442)
Guan Z., 1052 (AB0039)
Gubar E., 0310 (POS0192), 0754 (POS0976), 0815 (POS1072), 1303 (AB0541), 1325 (AB0575), 1325 (AB0576), 1327 (AB0580)
Gucenmez S., 0722 (POS0922), 0861 (POS1165), 1255 (AB0456), 1366 (AB0669), 1454 (AB0862-HPR)
Guck J., 1238 (AB0420)
Guckenberger M., 0090 (OP0150)
Güçlü E., 1382 (AB0700)
Gudbjornsson B., 0082 (OP0140), 0126 (OP0210), 0131 (OP0220), 0133 (OP0222), 0217 (POS0027)
Gudgeon C., 0021 (OP0039)
Gudkevich K., 0970 (POS1377)
Gudu T., 1296 (AB0531)
Guellec D., 0939 (POS1314)
Guenther C., 0670 (POS0834)
Guerra Batista G., 1280 (AB0506)
Guerra M., 1236 (AB0415), 1236 (AB0416), 1236 (AB0417)
Guerra-Vázquez J. L., 1326 (AB0577)
Guerra-Zarama S., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Guerrero E., 1111 (AB0170)
Guerrero F., 0559 (POS0642)
Guerrero R., 0376 (POS0302)
Guerrero Zamora P., 1056 (AB0047)
Guerreschi P., 1011 (POS1454-HPR)
Guettrot Imbert G., 0181 (OP0295), 0261 (POS0103)
Guggino G., 0022 (OP0042), 0190 (OP0310), 0301 (POS0177), 0390 (POS0326), 0778 (POS1021), 1260 (AB0467), 1271 (AB0488), 1389 (AB0716)
Guiducci C., 0204 (POS0006)
Guiducci S., 0105 (OP0176), 0190 (OP0310), 0385 (POS0317), 0546 (POS0618), 0675 (POS0842), 0897 (POS1228), 0906 (POS1246), 1032 (POS1495-HPR), 1192 (AB0334), 1331 (AB0588), 1389 (AB0716)
Guiga A., 0526 (POS0588)
Guillán-Fresco M., 1048 (AB0030)
Guillemin F., 0358 (POS0269-HPR), 0358 (POS0270-HPR), 0380 (POS0308)
Guillén del Castillo A., 0898 (POS1229)
Guillén-Astete C., 0283 (POS0143), 0807 (POS1058), 0922 (POS1275), 1215 (AB0376)
Guillén-Del-Castillo A., 0350 (POS0256), 0987 (POS1408), 0987 (POS1409)
Guimarães F., 0293 (POS0162), 0692 (POS0872), 0773 (POS1010), 0830 (POS1100), 1424 (AB0799)
Guinsburg M., 0771 (POS1005), 0874 (POS1186)
Guis S., 0367 (POS0284), 1078 (AB0099)
Gül A., 0191 (OP0313), 0282 (POS0142), 0602 (POS0706), 0604 (POS0710), 0636 (POS0766), 0912 (POS1257), 0913 (POS1259), 0951 (POS1339), 1006 (POS1445), 1210 (AB0369), 1251 (AB0448), 1359 (AB0653), 1409 (AB0766)
Gul A., 1191 (AB0331)
Gul H., 0110 (OP0182)
Guldberg-Møller J., 0283 (POS0144)
Gulle S., 0627 (POS0750), 1247 (AB0437), 1256 (AB0459), 1386 (AB0708)
Gullick N., 0337 (POS0234)
Gulseren U. A., 0191 (OP0313)
Gulyás K., 0226 (POS0043), 0421 (POS0383), 0425 (POS0390)
Gun S. C., 0053 (OP0096), 0459 (POS0457), 1015 (POS1460-HPR)
Gunaydin C., 1040 (AB0012)
Gunderson T., 0106 (OP0177), 0128 (OP0213), 0213 (POS0023), 0380 (POS0309)
Gunnarsson I., 0001 (OP0003), 0203 (POS0003), 0206 (POS0009), 0305 (POS0184), 0643 (POS0779), 0898 (POS1230), 1023 (POS1476-HPR)
Gunnarsson R., 0104 (OP0174)
Gunver M. G., 0191 (OP0313)
Guo D., 0301 (POS0176)
Guo J., 0729 (POS0932), 1100 (AB0146)
Guo N., 0454 (POS0449)
Guo W., 0561 (POS0647)
Guo X., 1063 (AB0066)
Guo Y., 0430 (POS0401)
Gupta R., 1163 (AB0276)
Gupta S., 0844 (POS1131)
Gur M., 0522 (POS0576)
Guralnik L., 0691 (POS0871)
Gurel E., 0636 (POS0766)
Gürlevik S., 0908 (POS1249)
Gurtovaya O., 0581 (POS0672)
Guryanova E., 1458 (AB0869-HPR), 1482 (AB0922-PARE)
Guseva I., 0243 (POS0073), 1040 (AB0010)
Gustafson A., 0810 (POS1063)
Gut O., 0576 (POS0667)
Gutierrez C., 0377 (POS0304)
Gutiérrez J. M., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Gutierrez M., 0841 (POS1124), 0845 (POS1132), 0846 (POS1133), 1348 (AB0629)
Gutiérrez Polo R., 1132 (AB0211)
Gutierrez R., 0960 (POS1355)
Gutierrez-Herrera R. F., 0445 (POS0434), 1425 (AB0801)
Gutiérrez-Rodríguez F., 0560 (POS0645)
Gutin A., 0458 (POS0456)
Güven S. C., 1105 (AB0157), 1182 (AB0314)
Güz G. T., 0733 (POS0940)
Guzel F., 0968 (POS1372), 0969 (POS1375)
Guzel R., 1471 (AB0896-HPR)
Guzelant Ozkose G., 0974 (POS1381)
Guzey D. Y., 0912 (POS1257)
Gvozdenovic E., 0801 (POS1049)
Gwinnutt J., 0110 (OP0183), 0829 (POS1099)
Györfi A. H., 0165 (OP0272), 0391 (POS0328), 1075 (AB0091), 1238 (AB0420)

Ha Y. J., 0512 (POS0555), 0516 (POS0563), 0516 (POS0564)
Haaland D., 1288 (AB0523), 1306 (AB0547)
Haas F., 1153 (AB0255)
Haas J. P., 0099 (OP0165), 0882 (POS1199), 0936 (POS1309), 0945 (POS1325)
Haase I., 1013 (POS1458-HPR), 1195 (AB0341)
Haavardsholm E. A., 0123 (OP0204), 0185 (OP0301), 0281 (POS0139)
Haavardsholm E., 0219 (POS0029), 0795 (POS1041), 1090 (AB0122)
Habechi M., 1112 (AB0171)
Habu D., 1012 (POS1456-HPR)
Hachaichi S., 0540 (POS0608)
Hachfi H., 0525 (POS0585), 0923 (POS1281), 1063 (AB0064), 1111 (AB0169), 1120 (AB0192), 1193 (AB0337), 1194 (AB0339), 1415 (AB0777), 1472 (AB0897-HPR)
Hachim M. Y., 0881 (POS1198), 0895 (POS1223)
Hachulla E., 0172 (OP0284), 0199 (LB0002), 0385 (POS0317), 0612 (POS0724), 0681 (POS0855), 0685 (POS0861), 0897 (POS1227), 1011 (POS1454-HPR), 1229 (AB0401)
Hacker S., 0363 (POS0277)
Hackett K., 0157 (OP0258-HPR)
Hadad A., 0753 (POS0974)
Haddad A., 0131 (OP0219), 0200 (LB0003), 0286 (POS0147), 0543 (POS0613), 1309 (AB0551)
Haddouche A., 1147 (AB0243)
Haddouche E., 0481 (POS0497)
Haefliger L., 1053 (AB0041)
Haehle A., 0758 (POS0983)
Hafirassou H., 1144 (AB0237)
Hagan G., 0043 (OP0081)
Hagelskjær A., 0382 (POS0313)
Hagen E., 0346 (POS0249)
Hagen K. B., 0092 (OP0154-HPR), 0119 (OP0198-HPR)
Hagen M., 0194 (OP0318), 0461 (POS0460)
Hägg M., 0236 (POS0060-PARE)
Haglund E., 1330 (AB0586)
Hagman J., 0145 (OP0236)
Haibel H., 0080 (OP0137), 0081 (OP0139), 0155 (OP0253), 0155 (OP0254), 0342 (POS0241), 0456 (POS0453), 0756 (POS0979), 0813 (POS1069), 0887 (POS1209)
Haili S., 0157 (OP0257)
Haji Y., 1408 (AB0763)
Hajjaj-Hassouni N., 0024 (OP0047), 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Hajji H., 0774 (POS1013), 1101 (AB0148), 1283 (AB0512)
Hak A. E., 0937 (POS1311)
Hakroush S., 0345 (POS0247), 0611 (POS0722), 1228 (AB0400)
Halabi H., 0361 (POS0275-HPR), 1080 (AB0104), 1320 (AB0566)
Haladyj E., 0563 (POS0649)
Halbac A., 1360 (AB0656)
Halidou A. R., 1343 (AB0617)
Hall J., 0824 (POS1089), 0885 (POS1205)
Hall M., 0185 (OP0302-HPR)
Hall S., 0329 (POS0222), 0707 (POS0900)
Hallemans A., 0828 (POS1096)
Hallén J., 0150 (OP0245)
Haller M., 0883 (POS1202)
Hally K., 0383 (POS0315)
Halperin T., 0885 (POS1206)
Halse A. K. H., 1245 (AB0433)
Halvey P., 1043 (AB0019), 1050 (AB0034)
Hama S., 1187 (AB0324), 1249 (AB0442)
Hamad Saied M., 0872 (POS1183)
Hamann F., 0806 (POS1055)
Hamann S. E., 1202 (AB0355)
Hamar A., 0226 (POS0043), 0421 (POS0383), 0425 (POS0390)
Hamaui A., 0874 (POS1186)
Hamdan H., 0862 (POS1166)
Hamdi O., 0292 (POS0159-HPR), 1030 (POS1491-HPR), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Hamdi W., 0526 (POS0586), 0526 (POS0587), 0774 (POS1013), 0776 (POS1018), 0856 (POS1155), 0921 (POS1274), 1091 (AB0124), 1095 (AB0133), 1101 (AB0148), 1102 (AB0150), 1112 (AB0171), 1117 (AB0186), 1118 (AB0187), 1119 (AB0189), 1119 (AB0191), 1278 (AB0501), 1283 (AB0512), 1286 (AB0520), 1358 (AB0650), 1379 (AB0693), 1399 (AB0740), 1399 (AB0741), 1400 (AB0742), 1400 (AB0744)
Hamdulay S., 0233 (POS0055)
Hamdy Abdellatif Mohammed R., 1175 (AB0297), 1220 (AB0385)
Hamdy F., 0477 (POS0490)
Hamijoyo L., 0218 (POS0028)
Hamilton C. B., 0374 (POS0298)
Hamilton J., 0167 (OP0276-PARE)
Hamilton L., 0223 (POS0035), 0989 (POS1411)
Hammami S., 1061 (AB0059), 1162 (AB0273), 1198 (AB0346), 1225 (AB0395)
Hammel L., 0758 (POS0983)
Hammer A., 0596 (POS0696), 0596 (POS0697)
Hammer H. B., 0123 (OP0204), 0281 (POS0139), 0379 (POS0307)
Hamrani W. F., 1147 (AB0243)
Hamuryudan V., 0660 (POS0814), 0662 (POS0819), 0663 (POS0820), 0875 (POS1187), 0958 (POS1351), 1327 (AB0579)
Han C., 0316 (POS0200), 0782 (POS1026), 0784 (POS1028), 0785 (POS1029), 0801 (POS1048), 1292 (AB0527)
Han J., 0651 (POS0799), 0656 (POS0808), 1126 (AB0203)
Han K. D., 0062 (OP0113), 0124 (OP0206), 0281 (POS0138)
Han W. H., 0816 (POS1075)
Han X., 0401 (POS0344), 1125 (AB0202)
Hanafy M., 1068 (AB0076)
Hanène A., 1061 (AB0059), 1162 (AB0273)
Hanlon M., 0015 (OP0028), 0041 (OP0077)
Hanly J., 0177 (OP0289)
Hannawi H., 1110 (AB0168)

Hannawi S., 0881 (POS1198), 0895 (POS1223), 1110 (AB0168)
Hannech E., 0774 (POS1012)
Hanni F., 1147 (AB0243)
Hanova P., 0136 (OP0226)
Hansen G., 0204 (POS0006)
Hansen R. L., 1312 (AB0554)
Hansildaar R., 0495 (POS0523)
Hansmann S., 0246 (POS0077), 0943 (POS1321)
Hansson M., 0206 (POS0009), 0425 (POS0392)
Hao Y., 0218 (POS0028), 1166 (AB0280)
Happle C., 1385 (AB0707)
Haque U., 0356 (POS0267-HPR)
Hara S., 0956 (POS1348), 1407 (AB0760)
Haraoui B., 0251 (POS0086), 0336 (POS0232), 0580 (POS0671)
Haraoui P., 0066 (OP0118)
Harari S., 0897 (POS1228)
Harel L., 0247 (POS0079), 0928 (POS1294), 0929 (POS1295), 0934 (POS1304)
Hargreaves B., 0018 (OP0033)
Harifi G., 0361 (POS0275-HPR), 1080 (AB0104)
Harigai M., 0113 (OP0187), 0218 (POS0028), 0395 (POS0336), 0510 (POS0551), 0511 (POS0554), 0536 (POS0603), 0615 (POS0730)
Harney S., 1479 (AB0916-PARE)
Haroche J., 1186 (AB0323)
Haroon M., 0381 (POS0310), 0527 (POS0589), 0574 (POS0663), 1075 (AB0093), 1298 (AB0533), 1328 (AB0581)
Haroon N., 0173 (OP0285), 0230 (POS0050), 0723 (POS0924), 0766 (POS0995), 0943 (POS1323)
Harris J., 1170 (AB0288)
Harrold L., 0056 (OP0101), 1125 (AB0202)
Hartman L., 1107 (AB0160)
Hartmann F., 1030 (POS1492-HPR)
Hartmann M., 0246 (POS0077)
Hartung W., 1447 (AB0847)
Harui A., 0163 (OP0268)
Harvey P., 0132 (OP0221), 0812 (POS1068)
Harzy T., 0992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811)
Hasbal Akkuş C., 0229 (POS0049), 0249 (POS0082)
Haschka J., 0194 (OP0318), 0848 (POS1137)
Hascsi Z., 0425 (POS0390)
Hasegawa J., 0455 (POS0450), 1094 (AB0131), 1137 (AB0222)
Hashimoto M., 0401 (POS0345), 1025 (POS1482-HPR)
Hashimoto N., 0603 (POS0707)
Hashimoto T., 0603 (POS0707), 1181 (AB0311)
Hashmi F., 0381 (POS0310), 0527 (POS0589), 0574 (POS0663), 1298 (AB0533)
Hass M., 0842 (POS1126)
Hass S., 0808 (POS1060)
Hassan F., 1313 (AB0556)
Hassan N., 0039 (OP0074)
Hassan R., 0922 (POS1276)
Hassan S. U., 0023 (OP0044), 0300 (POS0175)
Hassan S., 0600 (POS0701)
Hassan W., 0832 (POS1104)
Hassayoun M., 1063 (AB0064), 1193 (AB0337), 1194 (AB0339)
Hassel J., 0372 (POS0293)
Hasseli R., 0171 (OP0283), 0209 (POS0015), 0915 (POS1261), 1054 (AB0043)
Hassen N., 0997 (POS1427)
Hassikou H., 0992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811)
Hata A., 0398 (POS0340)
Hatachi S., 0689 (POS0868), 1096 (AB0136)
Hatano M., 1168 (AB0285)
Hatemi G., 0349 (POS0254), 0660 (POS0814), 0662 (POS0819), 0663 (POS0820), 0667 (POS0828), 0727 (POS0929), 0958 (POS1351), 1207 (AB0364), 1327 (AB0579)
Hatta K., 0492 (POS0516)
Hattori K., 0455 (POS0450), 1094 (AB0131)
Hauge E. M., 0036 (OP0066), 0451 (POS0444), 0657 (POS0809), 0866 (POS1171)
Haugeberg G., 0048 (OP0089), 0145 (OP0238), 0543 (POS0612), 0821 (POS1085), 1009 (POS1451), 1135 (AB0219), 1218 (AB0381), 1418 (AB0785)
Haugen I. K., 0047 (OP0087), 0983 (POS1401)
Hausmann J., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Hawker G. A., 0358 (POS0269-HPR), 0358 (POS0270-HPR)
Hawkins E., 1017 (POS1465-HPR), 1136 (AB0220)
Hawrot-Kawecka A., 1434 (AB0820)
Hawtin R., 0452 (POS0446)
Hayashi H., 0398 (POS0340)
Hayashi Y., 1249 (AB0442)
Hayata A. L. S., 0582 (POS0676)
Haye M., 0875 (POS1188)
Haymann J. P., 0954 (POS1343)
Hazes J., 0127 (OP0212), 0289 (POS0151), 0353 (POS0261), 1087 (AB0116)
Haziqah Itqan A., 0459 (POS0457)
Hazlewood G., 0159 (OP0262-HPR), 1014 (POS1459-HPR)
Haznedaroglu S., 0733 (POS0940), 0878 (POS1193), 1077 (AB0097), 1176 (AB0300)
He D., 0574 (POS0664)
He J., 1440 (AB0831)
He M., 1100 (AB0146)
He P. F., 0111 (OP0184), 0315 (POS0199), 0460 (POS0458), 0616 (POS0732), 0619 (POS0736), 0622 (POS0742), 0623 (POS0743), 0677 (POS0847), 0678 (POS0848), 0680 (POS0851), 0684 (POS0859), 0888 (POS1211), 1037 (AB0005), 1436 (AB0824)
He X., 0280 (POS0136)
He Y. X., 1040 (AB0011), 1067 (AB0075)
Hebeisen M., 0272 (POS0122)
Hebing R., 0548 (POS0621), 0578 (POS0669), 1151 (AB0251)
Hecht R., 1153 (AB0255)
Hecker R., 0528 (POS0591)
Heckert S., 0259 (POS0097)
Heckmann B., 0148 (OP0242)
Hecquet S., 1062 (AB0062), 1067 (AB0073)
Hedenstierna L., 0474 (POS0484)
Hedström A. K., 0474 (POS0484)
Heegaard Brahe C., 0457 (POS0454)
Heegaard S., 1202 (AB0355)
Heeringa P., 0033 (OP0062), 0036 (OP0066), 0657 (POS0809)
Heesterbeek P., 0359 (POS0272-HPR)
Heggli I., 0045 (OP0083), 0046 (OP0085)
Heidecke H., 0149 (OP0244)
Heidenreich S., 0681 (POS0855)
Heijstek M. W., 0346 (POS0249), 1221 (AB0387)
Heil S., 1151 (AB0251)
Heimann N., 0209 (POS0015)
Heinrich F., 0207 (POS0010)
Heitmann S., 0386 (POS0318)
Hejazi E., 0383 (POS0315)
Hejbøl E. K., 0419 (POS0377)
Held U., 0685 (POS0861), 0694 (POS0877)
Hellgren K., 0126 (OP0210)
Helling-Bakki A., 0244 (POS0075)
Helliwell P., 0135 (OP0224), 0139 (OP0229), 0777 (POS1020), 0781 (POS1024), 0785 (POS1029), 0787 (POS1031), 0792 (POS1037), 0792 (POS1038), 0801 (POS1048), 0801 (POS1049), 1289 (AB0524), 1292 (AB0527), 1300 (AB0538)
Hellman U., 0013 (OP0024)
Hellmich B., 1211 (AB0370)
Helmus N., 0247 (POS0079), 0934 (POS1304)
Hemkens L., 0655 (POS0806)
Hemmig A., 0655 (POS0806)
Henao Y. K., 0984 (POS1403)
Henckaerts L., 0655 (POS0806)
Hendricks O., 0234 (POS0056), 0865 (POS1170)
Hendrikx T., 0083 (OP0141)
Henes J., 0194 (OP0318), 0670 (POS0834), 0694 (POS0877), 0971 (POS1379), 0972 (POS1380)
Henig N., 0595 (POS0695)
Hennessey A., 0166 (OP0274-PARE)
Henrickson M., 0245 (POS0076)
Henriksen M., 0283 (POS0144)
Henriques C., 0182 (OP0297), 0634 (POS0762)
Henrohn D., 1149 (AB0248)
Henrotin Y., 0365 (POS0281)
Henry J., 0199 (LB0002), 0662 (POS0818)
Henry-Blake C., 0983 (POS1400)
Henson F., 1052 (AB0039)
Hensor E., 0078 (OP0134), 0625 (POS0746), 0919 (POS1269)
Hensvold A., 0038 (OP0072), 0087 (OP0146), 0087 (OP0147), 0206 (POS0009), 1005 (POS1441)
Hercilla Vasquez L., 0198 (LB0001)
Heredia S., 1219 (AB0384)
Herger N., 0045 (OP0083), 0046 (OP0085)
Heřmánková B., 0677 (POS0846), 0678 (POS0849), 1233 (AB0410), 1234 (AB0412)
Hermann J., 0261 (POS0102)
Hermann K. G., 0156 (OP0256)
Hermann W., 1054 (AB0043)
Hermassi M., 0955 (POS1345), 1393 (AB0723), 1410 (AB0768)
Hermes T., 0595 (POS0694)
Hermida Gómez T., 1051 (AB0036)
Hernan P., 0037 (OP0068)
Hernández A., 0766 (POS0996), 1303 (AB0542)
Hernandez Beriain J. A., 0610 (POS0721)
Hernandez E., 0058 (OP0104), 0325 (POS0215), 0325 (POS0216), 0520 (POS0571)
Hernández F., 1444 (AB0842), 1445 (AB0843)
Hernandez I., 0910 (POS1253)
Hernández J. L., 0952 (POS1340)
Hernández-Breijo B., 0546 (POS0617)
Hernández-Cruz B., 0068 (OP0123), 1132 (AB0213), 1145 (AB0239), 1341 (AB0612)
Hernández-Esteban P., 0366 (POS0282)
Hernandez-Galarza I. D. J., 1007 (POS1446), 1455 (AB0863-HPR)
Hernandez-Garduno A., 1428 (AB0808)
Hernández-Garfella M., 0032 (OP0060), 0952 (POS1340)
Hernandez-Gonzalez M., 0898 (POS1229)
Hernández-Hernández V., 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070)
Hernández-Negrín H., 0609 (POS0720), 1178 (AB0304)
Hernandez-Parra D., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336), 1200 (AB0351)
Hernández-Rodríguez J., 0272 (POS0121)
Hernández-Zambrano S. M., 1475 (AB0907-HPR)
Hernanz Rodríguez I., 0952 (POS1340)
Herold M., 0320 (POS0208)
Herregods N., 0943 (POS1323)
Herrem C., 0724 (POS0925)
Herrera López M. G., 1360 (AB0657)
Herrera S., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336), 1200 (AB0351)
Herrera Van Oostdam D. A., 0624 (POS0745)
Herreras J. M., 0032 (OP0060)
Herrera-Sandate P., 0445 (POS0434), 1007 (POS1446), 1085 (AB0113), 1425 (AB0801), 1455 (AB0863-HPR)
Herrero-Morant A., 0091 (OP0152), 0601 (POS0703), 0730 (POS0934), 0899 (POS1231), 0960 (POS1357), 0963 (POS1362), 0966 (POS1370), 0967 (POS1371), 1226 (AB0397), 1227 (AB0399), 1377 (AB0688)
Herrick A., 0674 (POS0840)
Herron A., 1243 (AB0429)
Hertzberg-Nyquist K., 0093 (OP0156-HPR)
Heslinga M., 0495 (POS0523)
Hetland M. L., 0009 (OP0017), 0063 (OP0114), 0082 (OP0140), 0126 (OP0210), 0131 (OP0220), 0133 (OP0222), 0217 (POS0027), 0234 (POS0056), 0457 (POS0454), 0865 (POS1170)
Heusdens K., 0828 (POS1096)
Hewitt S., 0320 (POS0207)
Hiba B. A., 0372 (POS0294), 0522 (POS0577)
Hibino T., 0537 (POS0604)
Hidaka N., 0195 (OP0319), 0491 (POS0514), 0492 (POS0517), 1431 (AB0813)
Hidalgo C., 0034 (OP0064), 0035 (OP0065), 1208 (AB0366)
Hidalgo L., 0001 (OP0004)
Hidayatulloh S., 1425 (AB0802)
Hiepe F., 0207 (POS0010), 0305 (POS0183), 0623 (POS0744)

Higashida-Konishi M., 1099 (AB0145), 1187 (AB0324), 1249 (AB0442)
Higazi N., 0200 (LB0003)
Higginson-Scott N., 0013 (OP0023), 1043 (AB0019), 1050 (AB0034), 1167 (AB0282)
Higgs J., 0983 (POS1400)
Hilberdink B., 0038 (OP0071-HPR)
Hilkens C., 1046 (AB0025)
Hill C., 0362 (POS0276), 0852 (POS1147), 1098 (AB0142), 1441 (AB0834)
Hill D., 0806 (POS1056)
Hill J., 1307 (AB0548)
Hill T., 1376 (AB0687)
Hilliquin S., 0228 (POS0046)
Hillson J., 0021 (OP0039)
Himelein C., 1034 (POS1499-PARE)
Hingorani V., 0843 (POS1128), 0844 (POS1130)
Hinze A., 0389 (POS0325)
Hirano Y., 0455 (POS0450), 1094 (AB0131), 1137 (AB0222), 1142 (AB0233)
Hirata A., 0981 (POS1396)
Hirata S., 1152 (AB0253)
Hirose T., 0564 (POS0651)
Hirsch J., 1027 (POS1484-HPR), 1467 (AB0889-HPR)
Hisashi Y., 0537 (POS0604)
Hissink Muller P. C. E., 0302 (POS0178), 0932 (POS1300), 0937 (POS1311)
Hitchon C., 0159 (OP0262-HPR), 1014 (POS1459-HPR)
Hitraya E., 0458 (POS0456)
Hittinger A., 0227 (POS0045)
Hives F., 0114 (OP0190)
Hizmetli S., 0959 (POS1354), 0961 (POS1359)
Hlais S., 0340 (POS0239)
Hmaier E., 1111 (AB0169)
Hmamouchi I., 0992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811)
Ho C., 0640 (POS0773)
Ho G., 0854 (POS1150)
Ho L. Y., 0298 (POS0171), 0638 (POS0769), 0639 (POS0771), 0640 (POS0772)
Hobson B., 0377 (POS0303)
Hočevar A., 0650 (POS0796), 0664 (POS0823), 0666 (POS0826), 1201 (AB0352), 1201 (AB0353)
Hodin S., 1164 (AB0277)
Hodosi K., 0226 (POS0043), 0425 (POS0390)
Hoegh Matre K., 0094 (OP0157-HPR)
Hoens A., 0377 (POS0303)
Hoentjen F., 0359 (POS0271-HPR), 0548 (POS0621), 0578 (POS0669)
Hoeper J. R., 0158 (OP0260-HPR)
Hoeper K., 0158 (OP0260-HPR), 0758 (POS0983), 1385 (AB0707)
Hoepken B., 0334 (POS0229), 0704 (POS0896), 0705 (POS0897)
Hoes J., 0238 (POS0063-PARE)
Hoese G., 0216 (POS0026)
Hofer M., 0098 (OP0164)
Hoff P., 0191 (OP0312)
Hoffman D., 1015 (POS1461-HPR)
Hoffman P., 0049 (OP0090)
Hoffmann T., 0040 (OP0075), 1422 (AB0796)
Hoffmann-Vold A. M., 0090 (OP0150), 0101 (OP0170), 0104 (OP0174), 0162 (OP0266), 0232 (POS0054), 0384 (POS0316), 0385 (POS0317), 0386 (POS0318), 0387 (POS0321), 0681 (POS0855), 0685 (POS0861), 0689 (POS0867), 0694 (POS0877), 1234 (AB0413), 1245 (AB0433)
Hofman-Bang C., 0643 (POS0779)
Hofmann M. W., 0544 (POS0615)
Hofmann N., 0244 (POS0075)
Hogg M., 0157 (OP0258-HPR)
Höhenrieder P., 0910 (POS1254), 1383 (AB0702)
Höhne E., 1446 (AB0846)
Hoi A., 0218 (POS0028), 0616 (POS0731), 0629 (POS0753)
Hoinoiu E. M., 1267 (AB0480)
Hokkanen A. M., 0217 (POS0027)
Holden S., 0045 (OP0084)
Holdsworth E., 0378 (POS0305), 0885 (POS1205), 1136 (AB0221)
Holl R., 0943 (POS1321)
Holland C., 1153 (AB0255)
Holm Nielsen S., 0742 (POS0955), 0748 (POS0966)
Holmberg D., 0059 (OP0106), 0207 (POS0011), 0974 (POS1383)
Holst A. D., 0528 (POS0591)
Holt H. M., 0006 (OP0010)
Holz A., 1385 (AB0707)
Holzkaemper T., 1157 (AB0261), 1307 (AB0548)
Honda T., 1028 (POS1487-HPR)
Hong C. M., 0258 (POS0096)
Hong C., 1419 (AB0787)
Hong J., 0569 (POS0657), 0570 (POS0658)
Hong X., 0391 (POS0328)
Honglin Z., 0121 (OP0201), 0391 (POS0328)
Hoon E. A., 1441 (AB0834)
Hope L., 0584 (POS0678)
Hoppenreijs E., 0302 (POS0178)
Höppner C., 0756 (POS0979)
Horcada L., 0960 (POS1355), 1132 (AB0211)
Horch R., 0391 (POS0328)
Horibata S., 0689 (POS0868)
Horie K., 0449 (POS0441)
Horita T., 0395 (POS0336)
Horn H. C., 0006 (OP0010), 1483 (AB0924-PARE)
Horne A., 0939 (POS1313)
Horneff G., 0050 (OP0092), 0098 (OP0163), 0099 (OP0165), 0244 (POS0075), 0247 (POS0079), 0882 (POS1199), 0883 (POS1202), 0932 (POS1301), 0933 (POS1303), 0934 (POS1304), 0936 (POS1309), 0945 (POS1325), 0971 (POS1379)
Hörstermann J., 0246 (POS0077), 0936 (POS1309), 0943 (POS1321)
Horton M., 0457 (POS0454)
Horuluoglu B., 0196 (OP0321), 0206 (POS0008), 0697 (POS0883)
Horváth Á., 0226 (POS0043)
Horvath B., 1071 (AB0082)
Horváth C., 0226 (POS0043)
Horwath-Winter J., 0261 (POS0102)
Hoshiba R., 0956 (POS1348), 1407 (AB0760)
Hosonuma M., 1063 (AB0065)
Hospach T., 0098 (OP0163), 0099 (OP0165), 0244 (POS0075), 0882 (POS1199), 0883 (POS1202), 0932 (POS1301), 0945 (POS1325)
Hotsaniuk O., 0866 (POS1172)
Hou X., 1063 (AB0066)
Houssiau F., 0181 (OP0296), 0591 (POS0689), 0592 (POS0690), 0635 (POS0764)
Houtman M., 0009 (OP0016), 0011 (OP0020)
Houvenagel E., 0662 (POS0818), 1258 (AB0464)
Houzou P., 0776 (POS1016), 0927 (POS1291)
Hove Jaconsen S. E., 0009 (OP0017)
Howard R., 0167 (OP0275-PARE)
Hoxha A., 0628 (POS0751), 1099 (AB0143), 1174 (AB0295)
Hoyer B. F., 0171 (OP0283), 0915 (POS1261)
Hristova M., 1356 (AB0646)
Hristova S., 0896 (POS1224), 1138 (AB0224)
Hriz A., 0922 (POS1277), 1109 (AB0164)
Hsia E. C., 0312 (POS0195), 0316 (POS0200), 0447 (POS0437), 0708 (POS0902), 0781 (POS1024), 0782 (POS1026), 0783 (POS1027), 0784 (POS1028), 0785 (POS1029), 0787 (POS1031), 0801 (POS1048), 1258 (AB0463), 1291 (AB0526), 1292 (AB0527), 1293 (AB0528), 1300 (AB0538)
Hsieh C. I., 0116 (OP0193)
Hsieh C. W., 0622 (POS0741)
Hsieh S. C., 0599 (POS0700), 1440 (AB0832)
Hsieh T. Y., 0622 (POS0741)
Hsu P. N., 1152 (AB0253)
Hsu T., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0867 (POS1174)
Hsu V., 0681 (POS0855)
Hsueh C. H., 0581 (POS0672)
Hu F., 1055 (AB0046)
Hu J., 1122 (AB0197)
Hu L., 0721 (POS0921), 1025 (POS1481-HPR)
Hu X., 0403 (POS0348)
Hu Y., 0619 (POS0736)
Hua C., 0379 (POS0306), 0518 (POS0566), 0770 (POS1003), 0820 (POS1082), 0902 (POS1239)
Huang C. M., 1152 (AB0253)
Huang F., 0721 (POS0921), 0724 (POS0925), 1025 (POS1481-HPR)
Huang H. T., 0599 (POS0700)
Huang H., 0287 (POS0148), 1098 (AB0141)
Huang I., 0994 (POS1422)
Huang J., 0257 (POS0094)
Huang L., 0645 (POS0785), 0698 (POS0885)
Huang M. C., 0121 (OP0201)
Huang M., 0393 (POS0332)
Huang Q., 0227 (POS0044), 0278 (POS0133), 0428 (POS0399), 0851 (POS1144), 1005 (POS1443), 1057 (AB0050), 1354 (AB0642), 1421 (AB0791), 1446 (AB0845)
Huang W. N., 0622 (POS0741)
Huang W., 0494 (POS0522)
Huang X., 0227 (POS0044), 0597 (POS0698), 0598 (POS0699), 0851 (POS1144), 1092 (AB0128)
Huang Y. Q., 0280 (POS0136), 0852 (POS1146), 1040 (AB0011), 1252 (AB0449)
Huang Y., 0227 (POS0044), 0248 (POS0081), 0278 (POS0133), 0428 (POS0399), 0847 (POS1135), 0851 (POS1144), 1005 (POS1443), 1057 (AB0050), 1354 (AB0642), 1355 (AB0645), 1421 (AB0791), 1446 (AB0845)
Huang Z., 0227 (POS0044), 0248 (POS0081), 0428 (POS0399), 0848 (POS1138), 1005 (POS1443), 1354 (AB0642), 1446 (AB0845), 1446 (AB0845)
Huaylla Quispe A. V., 0296 (POS0167), 0964 (POS1365), 1278 (AB0502)
Hudock K., 0198 (LB0001)
Hudry C., 0343 (POS0243), 0360 (POS0274-HPR)
Hudson M., 0010 (OP0018), 0918 (POS1268)
Hueber A., 0040 (OP0075), 0088 (OP0148), 0194 (OP0318), 0420 (POS0381), 1030 (POS1492-HPR), 1275 (AB0495)
Hueber W., 0593 (POS0692)
Huegle B., 0932 (POS1301)
Hufnagel M., 0201 (LB0004), 0244 (POS0075), 0883 (POS1202), 0971 (POS1379)
Hugelius A., 0898 (POS1230)
Hughes C., 0806 (POS1056), 1323 (AB0573)
Hughes D., 0844 (POS1131)
Hughes M., 0385 (POS0317), 0885 (POS1205), 0897 (POS1228)
Hughes V., 1372 (AB0678)
Hügle M., 0465 (POS0468)
Hügle T., 0059 (OP0106), 0112 (OP0185), 0120 (OP0199), 0226 (POS0041), 0272 (POS0122), 0426 (POS0393), 0465 (POS0468), 0991 (POS1415), 1128 (AB0206), 1161 (AB0270)
Hühn R., 0882 (POS1199)
Hühne J., 0420 (POS0381)
Huijser E., 0308 (POS0189)
Huisingh C., 0886 (POS1207)
Huitema M. G., 0657 (POS0809)
Huizinga T., 0087 (OP0147), 0203 (POS0001), 0259 (POS0097), 0403 (POS0348), 0422 (POS0384), 0423 (POS0386), 0426 (POS0395), 0466 (POS0470), 0471 (POS0479), 0603 (POS0708), 0604 (POS0709), 0606 (POS0714), 0675 (POS0843), 1045 (AB0022), 1365 (AB0667), 1366 (AB0668)
Hukara A., 0394 (POS0333)
Hulejova H., 0424 (POS0388), 0850 (POS1142)
Humbert M., 0052 (OP0094)
Humby F., 0419 (POS0377)
Hummers L., 0102 (OP0171)
Hung V. W., 0257 (POS0094)
Hung W. T., 0622 (POS0741)
Hunt P., 1000 (POS1432)
Hunter D., 0358 (POS0269-HPR), 0358 (POS0270-HPR), 0853 (POS1148)
Hunter T., 0333 (POS0228), 0710 (POS0904), 1034 (POS1499-PARE)
Hunzelmann N., 0386 (POS0318), 0670 (POS0834), 0681 (POS0855), 0685 (POS0861)
Hur P., 0808 (POS1060)
Hurson C., 0015 (OP0028), 1043 (AB0018)
Huschek D., 0058 (OP0105)
Huscher D., 0384 (POS0316), 0386 (POS0318)
Husni M. E., 0139 (OP0229), 0183 (OP0298), 0802 (POS1050), 0808 (POS1060)

Hussain R. I., 0150 (OP0245)
Hussein H., 0053 (OP0096)
Hutchinson M., 0163 (OP0269)
Hwang M., 0710 (POS0904)
Hwang W., 0301 (POS0176)
Hyde C., 0449 (POS0442)
Hyrich K., 0002 (OP0006), 0058 (OP0105), 0097 (OP0162), 0110 (OP0183), 0148 (OP0241), 0173 (OP0286), 0175 (OP0288), 0199 (LB0002), 0256 (POS0093), 0872 (POS1183), 0927 (POS1292)
Hysa E., 0524 (POS0583), 0697 (POS0882), 1201 (AB0354), 1247 (AB0438)
Hyun-Sook K., 0758 (POS0982)

Iaccarino L., 0182 (OP0297), 0594 (POS0693), 0600 (POS0702)
Iachim V., 1267 (AB0480)
Iacono D., 0888 (POS1210)
Iafrate S., 0957 (POS1349)
Iagnocco A., 0134 (OP0223), 0284 (POS0145), 0841 (POS1124), 0845 (POS1132), 0846 (POS1133), 0850 (POS1141), 1348 (AB0629)
Iannone A., 1241 (AB0425)
Iannone C., 0030 (OP0056)
Iannone F., 0051 (OP0093), 0131 (OP0220), 0190 (OP0310), 0217 (POS0027), 0256 (POS0093), 0582 (POS0675), 0685 (POS0861), 0701 (POS0891), 0778 (POS1021), 0906 (POS1246), 1003 (POS1437), 1217 (AB0380), 1260 (AB0467), 1389 (AB0716)
Iannuccelli C., 0047 (OP0086), 1016 (POS1463-HPR), 1017 (POS1464-HPR)
Iaquinta F. S., 1012 (POS1457-HPR), 1454 (AB0861-HPR)
Iaremenko O., 0612 (POS0725)
Ibáñez S., 0024 (OP0047)
Ibañez-Costa A., 0020 (OP0038)
Ibarguengoitia O., 0610 (POS0721), 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Ibata L., 1146 (AB0242), 1163 (AB0275)
Ibn Hadj Amor H., 1111 (AB0169)
Ichchou L., 1270 (AB0485)
Ichikawa N., 0753 (POS0975)
Ichinose K., 0608 (POS0718)
Idborg H., 0305 (POS0184)
Idolazzi L., 0134 (OP0223), 0284 (POS0145), 0326 (POS0218), 0778 (POS1021), 0867 (POS1173)
Igawa T., 0608 (POS0718)
Ignacio Vargas J., 0486 (POS0508)
Ihan A., 0242 (POS0072), 0941 (POS1318)
Ikari Y., 1063 (AB0065)
Ikawa T., 1329 (AB0583)
Ikeda K., 0563 (POS0649), 1152 (AB0253)
Ikeda Y., 1408 (AB0763)
Ikić Matijašević M., 0226 (POS0042)
Ilbay S., 0908 (POS1249)
Ilenia R., 0190 (OP0310), 0211 (POS0019), 1389 (AB0716)
Ilinykh E., 1264 (AB0473), 1264 (AB0474), 1350 (AB0631)
Iliopoulos A., 0815 (POS1073)
Ilizaliturri Guerra O., 0816 (POS1074), 0983 (POS1402)
Illei G., 0067 (OP0120)
Illes A., 1121 (AB0195)
Illiano A., 0306 (POS0185)
Ilyinskii P., 0001 (OP0002)
Imabayashi K., 0449 (POS0441)
Imfeld S., 0655 (POS0806)
Inagaki K., 1063 (AB0065)
Inamova O., 0191 (OP0311), 1352 (AB0636)
Inanc M., 0177 (OP0289), 0282 (POS0142), 0602 (POS0706), 0604 (POS0710), 0636 (POS0766), 0912 (POS1257), 0913 (POS1259), 0951 (POS1339), 1006 (POS1445), 1191 (AB0331), 1210 (AB0369), 1251 (AB0448), 1327 (AB0579), 1359 (AB0653), 1409 (AB0766)
Inanc N., 0256 (POS0093), 1028 (POS1486-HPR), 1140 (AB0229), 1266 (AB0479), 1317 (AB0561), 1467 (AB0888-HPR), 1470 (AB0893-HPR), 1471 (AB0895-HPR)
Ince B., 0191 (OP0313), 0282 (POS0142), 0912 (POS1257), 0913 (POS1259), 0951 (POS1339), 1210 (AB0369), 1409 (AB0766)
Inchaurbe A. R., 1103 (AB0151), 1104 (AB0153), 1376 (AB0686)
Inderjeeth C., 0052 (OP0095), 0055 (OP0100-HPR), 0250 (POS0084), 0373 (POS0297), 0852 (POS1147), 1079 (AB0103), 1224 (AB0393)
Ines C., 0774 (POS1013), 1283 (AB0512)
Inês L., 0179 (OP0293), 0182 (OP0297), 0606 (POS0713), 0634 (POS0762)
Ines L., 1219 (AB0383)
Ingallinera T., 0204 (POS0006)
Ingegnoli F., 0858 (POS1161), 0869 (POS1176), 0870 (POS1178), 0872 (POS1182), 0906 (POS1246), 1363 (AB0661), 1374 (AB0683)
Inglese F., 0606 (POS0714)
Iñíguez C. L., 0035 (OP0065), 1326 (AB0577)
Ink B., 0779 (POS1022)
Inness S., 0396 (POS0337)
Inoue E., 0113 (OP0187), 0510 (POS0551), 0511 (POS0554), 0536 (POS0603)
Inoue Y., 0329 (POS0221), 0981 (POS1396)
Insua S., 0032 (OP0060)
Intriago M., 0376 (POS0302)
Intxaurbe A. R., 1111 (AB0170)
Inui K., 0465 (POS0466), 0808 (POS1059), 1012 (POS1456-HPR), 1086 (AB0115), 1329 (AB0583)
Invernizzi A., 0979 (POS1393)
Ioan-Facsinay A., 0416 (POS0371), 0822 (POS1087)
Ioannou Y., 0008 (OP0013)
Ionescu R., 0131 (OP0220), 0164 (OP0270), 0217 (POS0027), 0681 (POS0854), 0685 (POS0861), 0773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690), 1462 (AB0879-HPR)
Iordache C., 1116 (AB0181)
Ippoliti A., 1418 (AB0786)
Iqbal K., 0042 (OP0078)
Irace R., 0385 (POS0317), 0387 (POS0321)
Iraheta I., 0771 (POS1005)
Irastorza Larburu M. B., 1141 (AB0230)
Irazoque-Palazuelos F., 0559 (POS0642), 0904 (POS1242), 0905 (POS1245)
Ireland A., 1479 (AB0916-PARE)
Irvine A., 0161 (OP0265-HPR)
Irvin-Sellers O., 0705 (POS0897)
Irwin S., 0889 (POS1213), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Isaacs J. D., 0018 (OP0033), 0403 (POS0348), 1044 (AB0021), 1046 (AB0025)
Isabelle C., 0227 (POS0045)
Isaeva K., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Isailovic N., 0152 (OP0249)
Isakov O., 1309 (AB0551)
Isca C., 1241 (AB0425)
Isenberg D., 0008 (OP0013), 0074 (OP0129), 0177 (OP0289), 0181 (OP0296), 0300 (POS0174), 0586 (POS0683), 0602 (POS0705), 0625 (POS0746), 0626 (POS0748)
Ishibashi Y., 1055 (AB0045)
Ishida K., 1055 (AB0045)
Ishii S., 1063 (AB0065), 1168 (AB0285)
Ishii T., 1150 (AB0249), 1152 (AB0253)
Ishikawa K., 1063 (AB0065)
Ishikawa T., 1028 (POS1487-HPR)
Ishimaru H., 0492 (POS0516)
Ishimori M., 0710 (POS0904)
Ishizaki J., 0395 (POS0336)
Işık E. G., 1210 (AB0369)
Iskandar S. M., 0320 (POS0207)
Ismail A., 0185 (OP0302-HPR)
Isnardi C. A., 0382 (POS0312), 0874 (POS1186), 0875 (POS1188), 0887 (POS1208), 1133 (AB0214)
Isomäki P., 1150 (AB0250)
Isomura Y., 1246 (AB0436)
Isozaki T., 1063 (AB0065)
Israelsson L., 0206 (POS0009)
Issayeva B., 1184 (AB0319), 1185 (AB0320)
Isupova E., 0247 (POS0080), 0931 (POS1299), 0937 (POS1310), 0944 (POS1324), 1402 (AB0748)
Ito H., 1025 (POS1482-HPR)
Ito K., 0956 (POS1348), 1407 (AB0760)
Ito T., 1408 (AB0763)
Iturbe-Fernández D., 1046 (AB0026), 1076 (AB0094)
Iudici M., 0384 (POS0316), 1165 (AB0279)
Iuliano A., 0619 (POS0737)
Ivanoskiy S., 0930 (POS1298)
Ivković V., 1199 (AB0348), 1199 (AB0349)
Ivorra Cortés J., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Iwamoto N., 0581 (POS0674), 0608 (POS0718)
Iwasaki T., 0401 (POS0345), 0603 (POS0707)
Iwasaki Y., 1168 (AB0285)
Iyengar K. P., 1376 (AB0687)
Izadi Z., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Izaguirre P., 1196 (AB0342)
Izci M., 0286 (POS0146)
Izumi K., 1099 (AB0145), 1187 (AB0324), 1249 (AB0442)
Izutsu M., 0787 (POS1031), 1293 (AB0528)
Izzetti R., 0642 (POS0778), 0644 (POS0782)
Izzo R., 1183 (AB0317)

Jaafar S., 0279 (POS0135)
Jabonka A., 1385 (AB0707)
Jabrayilov J., 0648 (POS0793), 1198 (AB0347)
Jacklin C., 0889 (POS1213), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Jackman J., 0289 (POS0152-HPR)
Jackson J., 0275 (POS0128), 0275 (POS0128), 0396 (POS0337)
Jacob J., 1008 (POS1449)
Jacobs J. W. G., 0878 (POS1191)
Jacobsen S., 0177 (OP0289)
Jacobsohn L., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Jacobsson L. T. H., 0082 (OP0140), 0115 (OP0192), 0125 (OP0208), 0130 (OP0218), 0372 (POS0295), 0513 (POS0557), 1350 (AB0633)
Jacques C., 0417 (POS0373)
Jadon D., 0139 (OP0229), 1126 (AB0204)
Jadoon K., 1354 (AB0641)
Jafery S. A. O., 1417 (AB0783)
Jagger C., 0158 (OP0259-HPR)
Jagiello P., 0337 (POS0234)
Jahaj E., 1381 (AB0697)
Jahnsen J., 0185 (OP0301)
Jaimes F., 0636 (POS0765)
Jain S., 0584 (POS0679), 0584 (POS0679), 1163 (AB0276), 1163 (AB0276)
Jaïs X., 0052 (OP0094)
Jajić Z., 0226 (POS0042)
Jakobsen B., 0951 (POS1337), 0995 (POS1424)
Jakobsen U., 0982 (POS1398)
Jakuszko K., 1434 (AB0820)
Jala D., 0476 (POS0487)
Jambus A., 1167 (AB0283)
Jamil A., 0611 (POS0723)
Jan Wu Y. J., 0218 (POS0028)
Janak J., 0530 (POS0594), 0538 (POS0606)
Janani S., 0371 (POS0292), 0767 (POS0998), 0817 (POS1077), 0965 (POS1367), 1266 (AB0477), 1336 (AB0600), 1343 (AB0617), 1344 (AB0619), 1344 (AB0620), 1363 (AB0662), 1375 (AB0685), 1387 (AB0711), 1398 (AB0738), 1422 (AB0794), 1433 (AB0819), 1438 (AB0828), 1438 (AB0829)
Janarthanan M., 0247 (POS0079), 0934 (POS1304)
Janda A., 0050 (OP0092)
Jandova I., 0670 (POS0834)
Jankowska-Polańska B., 1121 (AB0194)
Jannat-Khah D., 0472 (POS0480)
Jans L., 0943 (POS1323)
Jansen G., 0012 (OP0021), 1151 (AB0251)
Jansen I., 0198 (OP0324-PARE)
Jansen J., 0547 (POS0620), 0562 (POS0648), 1122 (AB0196)
Jansen M., 0825 (POS1091), 0825 (POS1092)
Jansen S., 0308 (POS0189)
Jansen T., 0805 (POS1053), 0841 (POS1124), 1479 (AB0915-PARE)
Janssen M., 1479 (AB0915-PARE)
Janta I., 0984 (POS1403)
Jara D., 0303 (POS0180)
Jaramillo Arroyave D., 1213 (AB0374)
Jaramillo Gallego J. F., 0759 (POS0984)

Jardon S., 0349 (POS0254), 0667 (POS0828), 1310 (AB0552)
Jaremko J. L., 0089 (OP0149), 0153 (OP0252), 0831 (POS1101), 0943 (POS1323), 1334 (AB0594)
Jasim M., 0005 (OP0009-PARE), 0560 (POS0643)
Jast R., 1375 (AB0684)
Javed F., 1450 (AB0853)
Javier R. M., 0694 (POS0876), 0877 (POS1190)
Jaworski J., 1123 (AB0198)
Jayatilleke A., 0230 (POS0051), 1368 (AB0674)
Jayne D., 0398 (POS0340), 0589 (POS0687), 0592 (POS0690), 0635 (POS0764)
Jeffery R., 1450 (AB0853)
Jégo P., 0037 (OP0068)
Jeka S., 1123 (AB0198)
Jeleniewicz R., 1434 (AB0820)
Jelley J., 1313 (AB0557)
Jemmali S., 0290 (POS0155-HPR), 0372 (POS0294), 0923 (POS1280), 0926 (POS1288), 1090 (AB0123), 1097 (AB0139), 1144 (AB0238), 1145 (AB0240), 1147 (AB0244), 1272 (AB0490), 1273 (AB0492), 1421 (AB0793)
Jemni S., 0856 (POS1154), 0925 (POS1285), 0925 (POS1286)
Jenkins K., 0432 (POS0406)
Jenkins-Jones S., 1000 (POS1432)
Jennum P., 0095 (OP0159-HPR)
Jensen D. V., 0234 (POS0056), 0865 (POS1170)
Jensen G., 0123 (OP0204)
Jensen H., 0095 (OP0159-HPR)
Jensen M., 0428 (POS0397)
Jeria Navarro S., 0277 (POS0132), 0666 (POS0827), 1093 (AB0129), 1354 (AB0643), 1365 (AB0666), 1426 (AB0804)
Jerome D., 0559 (POS0641)
Jese R., 0650 (POS0796), 1201 (AB0352), 1201 (AB0353)
Jessen H., 0444 (POS0431)
Jessurun N., 0359 (POS0271-HPR), 0547 (POS0620), 0562 (POS0648), 0578 (POS0669), 1122 (AB0196), 1153 (AB0254)
Jesus D., 0179 (OP0293), 0182 (OP0297), 0634 (POS0762)
Ji B., 0596 (POS0696)
Ji J., 0039 (OP0073), 0634 (POS0761), 0645 (POS0785), 0646 (POS0787), 0646 (POS0788), 1063 (AB0066)
Ji L., 1166 (AB0280)
Ji X., 0721 (POS0921), 1025 (POS1481-HPR)
Ji Z., 0307 (POS0187), 0657 (POS0810), 0661 (POS0817), 1057 (AB0050)
Jia B., 0406 (POS0351), 0561 (POS0646), 0563 (POS0649), 0588 (POS0686)
Jian G. L., 0280 (POS0136), 0852 (POS1146)
Jiang D., 0070 (OP0126), 0572 (POS0660)
Jiang H., 0642 (POS0777)
Jiang L., 0307 (POS0187), 0574 (POS0664), 0657 (POS0810), 0661 (POS0815), 0661 (POS0816), 0661 (POS0817)
Jiang Y., 0781 (POS1024), 0783 (POS1027), 0785 (POS1029), 1040 (AB0011), 1067 (AB0075), 1291 (AB0526)
Jiang Z., 0690 (POS0869), 0698 (POS0884), 1122 (AB0197)
Jiaxi L., 0975 (POS1384)
Jiemy W. F., 0033 (OP0062)
Jiménez J. L., 0363 (POS0277)
Jimenez Jimenez X., 0904 (POS1242), 0905 (POS1245)
Jimenez Moreno M. D., 1341 (AB0612)
Jiménez-Moleón I., 0610 (POS0721)
Jiménez-Núñez F. G., 0323 (POS0211), 0494 (POS0521), 1453 (AB0859-HPR)
Jimenez-Soto R., 0853 (POS1149), 1386 (AB0709)
Jin A., 0827 (POS1095)
Jin X., 0657 (POS0810), 0661 (POS0817)
Jin Y., 0430 (POS0401), 0646 (POS0788), 0651 (POS0798), 1196 (AB0343)
Jing J., 0456 (POS0452)
Jirout F., 0819 (POS1080)
Jo H., 1149 (AB0248)
Jobanputra A., 0383 (POS0315)
Jofra T., 0960 (POS1356)
Johannesson M., 0087 (OP0147), 0403 (POS0348)
Johnson M., 0366 (POS0283)
Johnson S., 0173 (OP0285), 0230 (POS0050), 0247 (POS0079), 0674 (POS0840), 0934 (POS1304)
Johnston E., 0823 (POS1088)
Jolie V., 1042 (AB0015)
Joly J., 0356 (POS0266-HPR), 0484 (POS0503), 0545 (POS0616), 1083 (AB0109)
Jomaa O., 0466 (POS0469), 0923 (POS1279), 0955 (POS1345), 1051 (AB0037), 1142 (AB0232), 1393 (AB0723), 1395 (AB0728), 1410 (AB0768), 1415 (AB0776), 1415 (AB0778)
Jonasdottir A., 0001 (OP0003)
Jonell C., 0112 (OP0186)
Jones A., 0049 (OP0090), 0478 (POS0492), 1097 (AB0140)
Jones D., 0381 (POS0311)
Jones G. T., 0217 (POS0027)
Jones G., 0118 (OP0196), 0276 (POS0129), 0307 (POS0186), 0309 (POS0190), 0362 (POS0276), 0365 (POS0280), 0832 (POS1103)
Jones H. N., 0565 (POS0652)
Jones M., 0356 (POS0267-HPR)
Jones N., 0648 (POS0792)
Jones T., 0834 (POS1107)
Jones-Leone A., 0591 (POS0689)
Jonkers I., 1337 (AB0602)
Jonmundsson T., 0133 (OP0222)
Jonsen A., 0177 (OP0289)
Jonsson C., 0112 (OP0186), 0811 (POS1064)
Jonsson I. M., 0012 (OP0022)
Joo Y. B., 0641 (POS0774)
Joos L., 1222 (AB0388)
Jordan K., 0372 (POS0293)
Jordan S., 0685 (POS0861), 1233 (AB0411)
Jordhani M., 1360 (AB0655), 1381 (AB0696)
Jorge-Mora A., 1048 (AB0030)
Jørgensen C. M., 0866 (POS1171)
Jorgensen C., 0417 (POS0374)
Jørgensen K. K., 0185 (OP0301)
Joseph A., 1092 (AB0128)
Joseph K. L., 0092 (OP0154-HPR)
Joshi A., 0002 (OP0005), 0122 (OP0202), 0122 (OP0203), 0144 (OP0235)
Joshi V., 1432 (AB0817)
Joshua V., 0429 (POS0400)
Jouneau S., 0431 (POS0403), 0674 (POS0840)
Jovani V., 0820 (POS1081), 0952 (POS1340)
Joven-Ibáñez B., 0142 (OP0232), 0766 (POS0996), 0799 (POS1046), 1295 (AB0530)
Jover J. A., 0896 (POS1225)
Jriri S., 1147 (AB0244), 1345 (AB0623)
Ju S., 0010 (OP0018)
Juan-Mas A., 0034 (OP0064), 0766 (POS0996)
Juanola X., 0725 (POS0926), 0760 (POS0985), 1279 (AB0503)
Juanola-Roura X., 0766 (POS0996)
Juarez C., 0666 (POS0827)
Juarez M., 1101 (AB0149)
Juarez V., 1194 (AB0338)
Juche A., 0670 (POS0834)
Juengel A., 0011 (OP0020), 0045 (OP0083), 0046 (OP0085), 0151 (OP0248)
Juge P. A., 0054 (OP0099), 0258 (POS0095), 0897 (POS1227), 1127 (AB0205)
Juhász B., 0226 (POS0043)
Juhl Pedersen S., 0089 (OP0149), 0153 (OP0251), 0153 (OP0252), 0221 (POS0032), 0742 (POS0955), 0831 (POS1101), 1296 (AB0531)
Julià A., 1042 (AB0015)
Julien H., 0360 (POS0273-HPR)
Julio P., 1405 (AB0754)
Jun J. B., 0102 (OP0171)
Junge G., 0593 (POS0692)
Jurado Quijano G., 1132 (AB0213), 1145 (AB0239), 1420 (AB0789)
Jurado Zapata S., 0403 (POS0348)
Juras V., 0363 (POS0277)
Jurčić V., 0664 (POS0823)
Jurić D., 0120 (OP0199)
Jurisica I., 0432 (POS0406)
Jury E., 0008 (OP0013), 0300 (POS0174)
Just S. A., 0006 (OP0010), 0419 (POS0377), 0982 (POS1398)

K C S., 0700 (POS0889)
Kabadayi G., 0722 (POS0922), 0727 (POS0929), 0731 (POS0935), 0861 (POS1165), 1255 (AB0456), 1366 (AB0669)
Kabakchieva P., 1332 (AB0591)
Kachakova D., 0522 (POS0578)
Käding H., 0342 (POS0241), 0456 (POS0453), 0813 (POS1069)
Kadıyoran C., 1355 (AB0644)
Kadoba K., 0401 (POS0345)
Kaeley G. S., 0311 (POS0194)
Kaeley G., 0295 (POS0165), 1088 (AB0119), 1343 (AB0618)
Kafaja S., 0102 (OP0171)
Kaffel D., 0526 (POS0586), 0526 (POS0587), 0774 (POS1013), 0776 (POS1018), 0921 (POS1274), 1091 (AB0124), 1095 (AB0133), 1101 (AB0148), 1102 (AB0150), 1112 (AB0171), 1117 (AB0186), 1118 (AB0187), 1119 (AB0189), 1119 (AB0191), 1278 (AB0501), 1283 (AB0512), 1286 (AB0520), 1379 (AB0693), 1399 (AB0740), 1399 (AB0741), 1400 (AB0742), 1400 (AB0744)
Kafka S., 0527 (POS0590), 0539 (POS0607), 0708 (POS0902), 1300 (AB0538)
Kagan S., 0928 (POS1294), 0929 (POS1295)
Kagtagiri T., 0981 (POS1396)
Kahlenberg C., 0828 (POS1097)
Kahlenberg J. M., 0075 (OP0131)
Kaidar K., 0928 (POS1294)
Kaiser D., 0247 (POS0079), 0934 (POS1304)
Kakati S., 1041 (AB0013), 1443 (AB0839)
Kakkar R., 1167 (AB0282)
Kakkar V., 0387 (POS0319)
Kakoullis L., 1356 (AB0647)
Kakpovi K., 0776 (POS1016), 0927 (POS1291)
Kalashnikova E., 0246 (POS0078)
Kalashnikova O., 0247 (POS0080), 0937 (POS1310), 0944 (POS1324), 1402 (AB0748)
Kalavri E., 0646 (POS0786)
Kaleda M., 0249 (POS0083), 0918 (POS1267), 0948 (POS1332), 1038 (AB0007), 1393 (AB0725), 1394 (AB0726), 1403 (AB0749)
Kalika L., 0924 (POS1284)
Kalın S., 0229 (POS0049)
Kalinina E., 1095 (AB0135)
Kallel M. H., 0922 (POS1277), 1276 (AB0497), 1281 (AB0508), 1484 (AB0926-PARE)
Kallinich T., 0050 (OP0092), 0099 (OP0165), 0246 (POS0077), 0247 (POS0079), 0305 (POS0183), 0623 (POS0744), 0882 (POS1199), 0934 (POS1304), 0943 (POS1321), 0971 (POS1379), 0972 (POS1380)
Kalogiannaki E., 0184 (OP0299), 0523 (POS0580), 0733 (POS0941)
Kaltsonoudis E., 0879 (POS1194)
Kalunian K. C., 0177 (OP0289)
Kalunian K., 0586 (POS0683), 0597 (POS0698), 0598 (POS0699)
Kalus S., 0528 (POS0591)
Kalweit G., 0465 (POS0468)
Kaly L., 0543 (POS0613)
Kalyoncu U., 0069 (OP0125), 0183 (OP0298), 0489 (POS0512), 0518 (POS0568), 0648 (POS0793), 0727 (POS0929), 0728 (POS0931), 0731 (POS0935), 0749 (POS0968), 0770 (POS1004), 0814 (POS1070), 0815 (POS1071), 0817 (POS1076), 0971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1272 (AB0491), 1299 (AB0535), 1327 (AB0579), 1470 (AB0893-HPR)
Kambas K., 0015 (OP0029)
Kameda H., 0724 (POS0925), 0981 (POS1396), 1152 (AB0253)
Kameda T., 0513 (POS0556), 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1249 (AB0443), 1437 (AB0826)
Kamen D. L., 0177 (OP0289)
Kamenov Z., 1332 (AB0591)
Kamerling S., 0585 (POS0680)
Kamiya M., 0252 (POS0088), 1151 (AB0252)

Kammoun S., 1117 (AB0184)
Kamp Felbo S., 0287 (POS0149)
Kamphuis S., 0098 (OP0164), 0302 (POS0178), 1070 (AB0081)
Kampman A., 0024 (OP0046)
Kampstra A. S. B., 0422 (POS0384), 0423 (POS0386)
Kan S. L., 1451 (AB0856)
Kanagaratnam L., 0227 (POS0045)
Kaname S., 0753 (POS0975)
Kanayama Y., 0059 (OP0107), 1142 (AB0233)
Kanbur N., 1398 (AB0737)
Kandane-Rathnayake R., 0616 (POS0731)
Kandane-Rathnayake1 R., 0218 (POS0028)
Kandhasamy S., 0462 (POS0461)
Kane D., 0282 (POS0140), 0291 (POS0156-HPR), 0859 (POS1162)
Kaneko H., 1224 (AB0391)
Kaneko Y., 0753 (POS0975), 1099 (AB0145), 1152 (AB0253), 1362 (AB0660)
Kaneva M., 0247 (POS0080), 0937 (POS1310), 1052 (AB0039), 1402 (AB0748)
Kaneva R., 0522 (POS0578)
Kang E. H., 0512 (POS0555), 0516 (POS0563), 0516 (POS0564)
Kang K. Y., 1260 (AB0466)
Kang S. W., 0204 (POS0005)
Kang S. Y., 0124 (OP0206), 0280 (POS0137), 0281 (POS0138), 0752 (POS0972), 1210 (AB0368)
Kang Y. M., 0258 (POS0096)
Kania G., 0151 (OP0248), 0393 (POS0332), 0394 (POS0333), 0689 (POS0867)
Kanie T., 1408 (AB0763)
Kanıtez N. A., 0731 (POS0935)
Kannengiesser C., 0258 (POS0095)
Kantemirova M., 1397 (AB0735)
Kanyılmaz Turgut S., 0286 (POS0146)
Kao J. H., 0599 (POS0700), 1440 (AB0832)
Kapetanovic M. C., 0372 (POS0295)
Kappanayil M., 0915 (POS1262)
Kapsala N., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Kapsogeorgou E., 0015 (OP0029), 0022 (OP0041), 0668 (POS0829)
Kapusuz A., 1028 (POS1486-HPR), 1467 (AB0888-HPR), 1471 (AB0895-HPR)
Kara H., 1323 (AB0572)
Karaahmetoğlu F. S., 1086 (AB0114)
Karabay O., 1382 (AB0700)
Karabulut Y., 0957 (POS1350), 1382 (AB0699)
Karacanoglu D., 0908 (POS1249)
Karaçaylı Ü., 1028 (POS1486-HPR), 1467 (AB0888-HPR), 1471 (AB0895-HPR)
Karadag O., 0347 (POS0251), 0350 (POS0255), 0518 (POS0568), 0648 (POS0793), 0659 (POS0813), 0727 (POS0929), 0728 (POS0931), 0731 (POS0935), 0749 (POS0968), 0770 (POS1004), 0814 (POS1070), 0971 (POS1378), 0974 (POS1382), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1250 (AB0446), 1272 (AB0491), 1299 (AB0535)
Karadeniz H., 0733 (POS0940), 0878 (POS1193), 1077 (AB0097), 1176 (AB0300), 1317 (AB0561)
Karageorgas T., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Karagianni P., 0879 (POS1194)
Karakas A., 0627 (POS0750), 1247 (AB0437), 1256 (AB0459), 1386 (AB0708)
Karakaş B., 0966 (POS1368), 1380 (AB0694)
Karakaş Ö., 1105 (AB0157), 1182 (AB0314)
Karakaya J., 0815 (POS1071), 0908 (POS1249)
Karakitsiou M., 0649 (POS0794)
Karakostas P., 0842 (POS1126), 0920 (POS1271), 1103 (AB0152), 1447 (AB0847)
Karandyszowska N., 1184 (AB0318)
Karatas A., 0522 (POS0576), 1266 (AB0479), 1317 (AB0561)
Karataş B., 0966 (POS1368), 1380 (AB0694)
Karatas D., 0223 (POS0036), 0732 (POS0939)
Karataş D., 1382 (AB0700)
Karateev A., 1095 (AB0135), 1109 (AB0165), 1160 (AB0267), 1162 (AB0272), 1388 (AB0714)
Karateev D., 0916 (POS1263), 0917 (POS1266), 1384 (AB0705), 1442 (AB0837)
Karatza E., 0015 (OP0029)
Karberg K., 0342 (POS0241), 0456 (POS0453), 0813 (POS1069), 1274 (AB0494)
Karis E., 0056 (OP0101), 0066 (OP0118)
Karkouri M., 1422 (AB0794)
Karlsson M. L., 0093 (OP0156-HPR)
Karmani M., 1219 (AB0383)
Karner M., 1404 (AB0752)
Karoliussen L. F., 0281 (POS0139)
Karoliussen L., 0123 (OP0204)
Karonitsch T. M., 1060 (AB0056)
Karpouzas G., 0058 (OP0104), 0325 (POS0215), 0325 (POS0216), 0520 (POS0571)
Karr D., 0204 (POS0006)
Karsdal M., 0444 (POS0431), 0468 (POS0473), 0742 (POS0955), 0748 (POS0966), 1064 (AB0067)
Karstensen J. K., 0994 (POS1423)
Kart-Bayram G. S., 1182 (AB0314)
Karyekar C., 0140 (OP0230), 0377 (POS0304), 0781 (POS1024)
Karzakova L., 0969 (POS1374), 1331 (AB0589), 1388 (AB0713)
Kasama T., 1063 (AB0065)
Kasapcopur O., 0201 (LB0004), 0247 (POS0079), 0934 (POS1304), 0942 (POS1320), 0969 (POS1375)
Kasap-Cuceoglu M., 0100 (OP0168), 0117 (OP0195), 1398 (AB0737)
Kasem S., 0131 (OP0219)
Kashevarova N., 0275 (POS0127), 0276 (POS0130), 0827 (POS1094), 1336 (AB0599), 1337 (AB0603), 1338 (AB0604)
Kashkadayeva A., 0840 (POS1123)
Kasiem F. R., 0289 (POS0151)
Kaşifoğlu T., 0731 (POS0935), 1470 (AB0893-HPR)
Kasifoglu T., 0878 (POS1193)
Kasliwal R., 0213 (POS0022)
Kasraoui A., 0776 (POS1018)
Kassab S., 0292 (POS0159-HPR), 0522 (POS0577), 0835 (POS1110), 1030 (POS1491-HPR), 1113 (AB0173), 1113 (AB0174), 1117 (AB0184), 1118 (AB0188), 1277 (AB0499), 1332 (AB0590), 1333 (AB0592), 1333 (AB0593), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1368 (AB0672), 1368 (AB0673), 1381 (AB0698), 1390 (AB0717), 1397 (AB0736), 1411 (AB0770), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Kastbom A., 0068 (OP0122), 0206 (POS0009), 0864 (POS1169)
Kasthuriratna G., 1480 (AB0917-PARE)
Kastner D., 0049 (OP0090)
Kästner P., 0706 (POS0899), 0780 (POS1023)
Katavić V., 0226 (POS0042)
Kataxaki E., 1299 (AB0537)
Katayama M., 0689 (POS0868), 1096 (AB0136)
Kathrin K., 0670 (POS0834)
Katlan B., 0908 (POS1249)
Kato K., 0016 (OP0030), 0433 (POS0407), 0786 (POS1030), 0790 (POS1035), 0800 (POS1047), 1203 (AB0357), 1288 (AB0523)
Kato M., 0513 (POS0556), 0687 (POS0863), 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1249 (AB0443), 1437 (AB0826)
Katona G., 0428 (POS0397)
Katsifis G., 1299 (AB0537)
Katsikas M., 0247 (POS0079), 0934 (POS1304)
Katsimpari C., 0646 (POS0786)
Katsimpri P., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764), 1299 (AB0537)
Katsuhiko I., 0510 (POS0551), 0511 (POS0554)
Katsumata Y., 0218 (POS0028), 0395 (POS0336)
Katsuyuki Shinjo S., 0699 (POS0887)
Katz A., 0139 (OP0229)
Katz P., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0911 (POS1255)
Kaufman I., 0200 (LB0003)
Kautonen M., 0236 (POS0060-PARE)
Kav T., 0749 (POS0968), 1272 (AB0491)
Kavadichanda C., 0696 (POS0880), 0701 (POS0890)
Kavanagh M., 1406 (AB0756)
Kavanagh P., 1427 (AB0805)
Kavanagh R., 0859 (POS1162)
Kavanaugh A., 0139 (OP0229), 0329 (POS0222), 0566 (POS0653), 0797 (POS1044), 0821 (POS1085), 1286 (AB0521), 1292 (AB0527), 1294 (AB0529), 1301 (AB0539), 1306 (AB0547), 1311 (AB0553)
Kavvadias A., 0879 (POS1194)
Kawaai S., 0753 (POS0975), 1408 (AB0763)
Kawahara H., 0956 (POS1348)
Kawahata K., 0368 (POS0286)
Kawakami A., 0423 (POS0386), 0489 (POS0512), 0581 (POS0674), 0608 (POS0718), 0959 (POS1353), 0998 (POS1429), 1028 (POS1487-HPR)
Kawano M., 0956 (POS1348), 1407 (AB0760)
Kawasaki T., 0753 (POS0975)
Kawashiri S. Y., 0423 (POS0386), 0608 (POS0718), 0998 (POS1429), 1028 (POS1487-HPR)
Kawka L., 0877 (POS1190)
Kay J., 1022 (POS1474-HPR), 1123 (AB0198), 1469 (AB0892-HPR)
Kaya Akca U., 0100 (OP0168), 0117 (OP0195), 0908 (POS1249), 0930 (POS1298)
Kaya Z. N., 0223 (POS0036)
Kayani A., 0396 (POS0337)
Kazuyoshi S., 1094 (AB0132)
Kearsley-Fleet L., 0058 (OP0105), 0148 (OP0241), 0872 (POS1183), 0927 (POS1292)
Keavney B., 1172 (AB0291)
Kechida M., 1225 (AB0395)
Keck S., 1047 (AB0028)
Kedra J., 0258 (POS0095)
Keeling S., 0224 (POS0037)
Keen C., 0253 (POS0089)
Keen H., 0052 (OP0095), 0055 (OP0100-HPR), 0250 (POS0084), 0362 (POS0276), 0373 (POS0297), 0845 (POS1132), 0846 (POS1133), 0850 (POS1141), 0852 (POS1147), 1079 (AB0103), 1224 (AB0393), 1348 (AB0629)
Keenan A. M., 0039 (OP0074)
Keime C., 0149 (OP0243)
Keiserman M., 0312 (POS0196), 1156 (AB0260), 1315 (AB0559)
Kelava T., 0226 (POS0042)
Keller K. K., 0451 (POS0444)
Keller M., 1046 (AB0024)
Kellerhals S., 1161 (AB0270)
Kellner H., 0373 (POS0296), 0540 (POS0608), 0544 (POS0615)
Kelly A., 0204 (POS0006)
Kelly C., 0069 (OP0124)
Kelly N., 1017 (POS1465-HPR)
Kelly S., 1125 (AB0202)
Kelty E., 0852 (POS1147)
Kemiche F., 0857 (POS1158), 0858 (POS1159)
Kemik F., 0191 (OP0313), 0602 (POS0706)
Kemper E., 0317 (POS0202)
Kench J., 0654 (POS0804)
Kennedy A., 1033 (POS1497-PARE)
Kennedy N., 0115 (OP0191-PARE), 1459 (AB0872-HPR)
Kennedy S., 0363 (POS0278)
Kenza H., 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Kerekes G., 0421 (POS0383), 0425 (POS0390)
Keret S., 0691 (POS0871)
Kern M., 0824 (POS1089)
Kernder A., 1013 (POS1458-HPR)
Kerola A., 0219 (POS0029), 0795 (POS1041)
Kerr G., 0476 (POS0487)
Kerschbaumer A., 0071 (OP0127)
Kerstein-Staehle A., 0028 (OP0054)
Kersten B., 1248 (AB0441)
Kerstens F., 0962 (POS1361)
Kerzberg E., 0730 (POS0933), 1377 (AB0689)
Kesavan M., 1010 (POS1453)
Kesavan S., 0915 (POS1262)
Keser G., 0727 (POS0929)
Kesici S., 0908 (POS1249)
Keskin O., 0749 (POS0968), 1272 (AB0491)
Kessler J., 0793 (POS1039)
Kessouri M., 0571 (POS0659)

Keystone E. C., 0329 (POS0222)
Keystone E., 0107 (OP0179), 0159 (OP0262-HPR), 0452 (POS0445), 0454 (POS0448), 0462 (POS0461), 0564 (POS0651), 1014 (POS1459-HPR), 1123 (AB0198)
Keyszer G., 0670 (POS0834)
Khadzhynova Y., 1401 (AB0745)
Khaled Z., 1162 (AB0273)
Khalfalli H., 1379 (AB0693)
Khalid M., 0378 (POS0305), 1354 (AB0641)
Khalid S., 1345 (AB0622)
Khalifa D., 0472 (POS0481), 0856 (POS1154), 0923 (POS1281), 0925 (POS1285), 0925 (POS1286), 1415 (AB0777), 1480 (AB0919-PARE)
Khamashta M., 0602 (POS0705)
Khan A., 1075 (AB0093), 1411 (AB0769)
Khan N., 0072 (OP0128), 0251 (POS0087), 0486 (POS0508), 0568 (POS0655)
Khan O., 0012 (OP0022)
Khan S., 1022 (POS1474-HPR), 1469 (AB0892-HPR)
Khanna D., 0101 (OP0170), 0102 (OP0171), 0279 (POS0135), 0681 (POS0855), 0897 (POS1228), 1234 (AB0413), 1244 (AB0431), 1245 (AB0433)
Khanna P., 0279 (POS0135)
Khapsirokova M., 1261 (AB0468)
Kharit S., 0927 (POS1293)
Kharouf F., 0200 (LB0003), 0892 (POS1217)
Kharrat L., 0768 (POS1000), 1066 (AB0071), 1281 (AB0509), 1285 (AB0517), 1442 (AB0836), 1443 (AB0840)
Khaychuk V., 0108 (OP0180), 0453 (POS0447), 0468 (POS0474), 0533 (POS0599), 1125 (AB0202), 1128 (AB0207)
Khayrutdinov V., 0796 (POS1043), 1298 (AB0534), 1302 (AB0540)
Khayyat S. G., 0573 (POS0661)
Khehra K., 0374 (POS0298)
Khelkovskaia-Sergeeva A., 1249 (AB0444), 1254 (AB0454)
Khizroeva J., 0619 (POS0737)
Khmelinskii N., 0029 (OP0055), 0233 (POS0055), 0644 (POS0781), 0690 (POS0870), 1250 (AB0445)
Kholopova I., 0647 (POS0790)
Khosroshahi A., 0299 (POS0173)
Khoury G., 1273 (AB0493)
Khoury V., 1280 (AB0506)
Khoy K., 0669 (POS0831)
Khraishi M., 0084 (OP0143), 0336 (POS0232), 1312 (AB0555), 1314 (AB0558)
Khramov A., 0259 (POS0098), 1172 (AB0292)
Khrypov S., 0931 (POS1299)
Khubchandani R., 0242 (POS0071), 0247 (POS0079), 0934 (POS1304)
Khullar A., 1163 (AB0276)
Khvan J., 0196 (OP0320), 0608 (POS0717), 0896 (POS1226), 1116 (AB0183), 1185 (AB0321)
Kiadaliri A., 1372 (AB0678)
Kibbi L., 0361 (POS0275-HPR), 1080 (AB0104)
Kıcasık B., 0727 (POS0929), 1124 (AB0200), 1124 (AB0201)
Kido T., 0458 (POS0455)
Kidoguchi G., 1408 (AB0763)
Kiefer D., 0752 (POS0973), 1375 (AB0684)
Kiely P., 0480 (POS0495), 0806 (POS1056)
Kieskamp S., 0221 (POS0031), 0775 (POS1014), 1268 (AB0481)
Kihira D., 0455 (POS0450), 1094 (AB0131)
Kikuchi J., 0218 (POS0028)
Kildemand M., 0234 (POS0056), 0865 (POS1170)
Kilian A., 0230 (POS0051), 1368 (AB0674)
Kılıç L., 0347 (POS0251), 0518 (POS0568), 0648 (POS0793), 0659 (POS0813), 0728 (POS0931), 0770 (POS1004), 0814 (POS1070), 0971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1250 (AB0446), 1299 (AB0535)
Kilic S. S., 1404 (AB0751)
Killeen O., 0241 (POS0069)
Kilpatrick R., 0886 (POS1207)
Kiltz U., 0024 (OP0047), 0039 (OP0074), 0183 (OP0298), 0337 (POS0234), 0344 (POS0245), 0376 (POS0301), 0706 (POS0899), 0714 (POS0910), 0716 (POS0912), 0752 (POS0973), 0758 (POS0983), 0780 (POS1023), 1153 (AB0255), 1375 (AB0684), 1435 (AB0823)
Kim D. H., 0062 (OP0113)
Kim D., 0349 (POS0254), 0667 (POS0828)
Kim G., 0162 (OP0267), 0163 (OP0268)
Kim H. R., 0758 (POS0981)
Kim H. S., 0758 (POS0981)
Kim H., 0062 (OP0113), 0124 (OP0206), 0280 (POS0137), 0281 (POS0138), 0752 (POS0972), 1210 (AB0368)
Kim I. Y., 0124 (OP0206), 0281 (POS0138)
Kim J. S., 0758 (POS0982)
Kim J., 0124 (OP0207), 0204 (POS0005), 0314 (POS0198), 1152 (AB0253)
Kim L., 0708 (POS0902)
Kim M. H., 0682 (POS0856)
Kim M. U., 0512 (POS0555), 0516 (POS0563), 0516 (POS0564)
Kim M., 0334 (POS0229)
Kim S. H., 1123 (AB0198)
Kim S., 0452 (POS0446), 0651 (POS0798), 0716 (POS0911), 0886 (POS1207)
Kim T. H., 0085 (OP0144), 0716 (POS0911)
Kim T. J., 0024 (OP0047)
Kim T., 1123 (AB0198)
Kimble L. P., 0299 (POS0173)
Kimbrough A., 0652 (POS0801)
Kimpton J., 1136 (AB0220)
Kimyon G., 0069 (OP0125), 0731 (POS0935), 1470 (AB0893-HPR)
Kinarty A., 0543 (POS0613)
Kinch C., 0565 (POS0652)
King L., 0358 (POS0270-HPR)
Kinggaard Holm D., 0006 (OP0010)
Kingsbury D., 0245 (POS0076)
Kingsbury S., 0093 (OP0155-HPR), 0919 (POS1269)
Kınıklı G., 0532 (POS0597), 0727 (POS0929), 0949 (POS1335)
Kinnunen A., 1150 (AB0250)
Kiracı M., 0971 (POS1378)
Kiraz S., 0069 (OP0125), 0347 (POS0251), 0518 (POS0568), 0648 (POS0793), 0728 (POS0931), 0731 (POS0935), 0770 (POS1004), 0814 (POS1070), 0971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1299 (AB0535), 1327 (AB0579)
Kirby C., 0282 (POS0140)
Kirchler C., 1019 (POS1468-HPR)
Kirchner M., 1052 (AB0040)
Kirichenko T., 1049 (AB0033)
Kirillova E., 1253 (AB0452), 1283 (AB0513)
Kirillova I., 0493 (POS0520), 0514 (POS0559)
Kirilov N., 1340 (AB0609)
Kirilova E., 1340 (AB0609)
Kirk C., 0595 (POS0695)
Kirkham B., 0479 (POS0494)
Kirkham L. B., 1323 (AB0573)
Kirkhus E., 0943 (POS1323)
Kiryukhina N., 1095 (AB0135)
Kishikawa R., 1168 (AB0285)
Kishimoto K., 0001 (OP0002)
Kishimoto M., 0024 (OP0047), 0085 (OP0144), 0750 (POS0969), 0753 (POS0975), 0786 (POS1030), 1288 (AB0523)
Kisliak O., 0840 (POS1123)
Kissel T., 1044 (AB0020), 1366 (AB0668)
Kisten Y., 0087 (OP0146)
Kis-Toth K., 0013 (OP0023), 1043 (AB0019), 1050 (AB0034), 1167 (AB0282)
Kitagori K., 0401 (POS0345)
Kittler J., 1042 (AB0016)
Kivitz A., 0137 (OP0227), 0138 (OP0228), 0314 (POS0198), 0332 (POS0226), 0486 (POS0508), 0538 (POS0606), 0707 (POS0900)
Kiyan E., 1191 (AB0331)
Kjeken I., 0092 (OP0153-HPR), 0094 (OP0157-HPR)
Kjeldsen J., 0006 (OP0010), 1483 (AB0924-PARE)
Klaasen R. A., 0185 (OP0301)
Klaasen R., 0346 (POS0249), 1107 (AB0160), 1221 (AB0387)
Klaff J., 0486 (POS0508), 0568 (POS0655)
Klajn D. S., 0635 (POS0763)
Klareskog L., 0053 (OP0096), 0087 (OP0147), 0145 (OP0236), 0206 (POS0009), 0403 (POS0348), 0425 (POS0392), 0459 (POS0457), 0474 (POS0484), 0864 (POS1169), 1059 (AB0054)
Klausch T., 1107 (AB0160)
Klavdianou K., 0646 (POS0786), 1304 (AB0543)
Klawitter J., 0421 (POS0383)
Klefter O. N., 1202 (AB0355)
Klein A., 0098 (OP0163), 0099 (OP0165), 0244 (POS0075), 0882 (POS1199), 0883 (POS1202), 0932 (POS1301), 0933 (POS1303)
Klein K., 0009 (OP0016), 0011 (OP0020)
Klein M., 0678 (POS0849)
Kleinert S., 0194 (OP0318), 1274 (AB0494)
Kleinman J., 0607 (POS0715)
Kleist K., 0021 (OP0039)
Klementeva V., 1328 (AB0582)
Klemm P., 0040 (OP0075), 0676 (POS0844), 1013 (POS1458-HPR), 1030 (POS1492-HPR)
Klersy C., 0668 (POS0830)
Klescheva E., 0014 (OP0027)
Kleyer A., 0040 (OP0075), 0060 (OP0109), 0086 (OP0145), 0087 (OP0147), 0088 (OP0148), 0194 (OP0318), 0420 (POS0381), 0979 (POS1394), 0996 (POS1426), 1013 (POS1458-HPR), 1030 (POS1492-HPR), 1275 (AB0495)
Klii R., 1225 (AB0395)
Klika K., 0467 (POS0472)
Klimets A., 0772 (POS1008)
Klimiuk P., 1123 (AB0198)
Klingberg E., 0130 (OP0218), 0811 (POS1064), 1350 (AB0633)
Klinge B., 0996 (POS1425)
Klingelhöfer J., 0150 (OP0245)
Klokkeide A., 0092 (OP0153-HPR)
Klokkeide Å., 0094 (OP0157-HPR)
Kloppenburg M., 0273 (POS0123), 0304 (POS0182), 0351 (POS0258), 0416 (POS0371), 0603 (POS0708), 0604 (POS0709), 0606 (POS0714), 0822 (POS1087), 0999 (POS1431)
Klopsch T., 0528 (POS0591)
Klose-Jensen R., 0451 (POS0444)
Klotsche J., 0099 (OP0165), 0246 (POS0077), 0247 (POS0079), 0305 (POS0183), 0623 (POS0744), 0934 (POS1304), 0936 (POS1309), 0945 (POS1325)
Klumb E., 0909 (POS1252), 1448 (AB0848)
Klyachkin Y., 1311 (AB0553)
Kmar O., 0522 (POS0577)
Knagenhjelm J., 0592 (POS0690)
Knevel R., 0087 (OP0147), 0403 (POS0348), 0420 (POS0379), 0675 (POS0843)
Knežević T., 1199 (AB0348), 1199 (AB0349)
Knitza J., 0087 (OP0147), 0165 (OP0272), 0979 (POS1394), 1013 (POS1458-HPR), 1030 (POS1492-HPR), 1275 (AB0495)
Knoop J., 0291 (POS0157-HPR), 1020 (POS1470-HPR)
Knothe A., 1054 (AB0043)
Ko S., 1099 (AB0145)
Ko T. M., 1082 (AB0108)
Kobalava Z., 0326 (POS0217)
Kobayashi S., 0753 (POS0975)
Kobylinski T., 0376 (POS0301)
Koç N. S., 0648 (POS0793), 1198 (AB0347)
Koca N., 0191 (OP0313), 0912 (POS1257), 0913 (POS1259), 0951 (POS1339), 1006 (POS1445), 1409 (AB0766)
Koca S. S., 0522 (POS0576), 0731 (POS0935), 1140 (AB0229), 1266 (AB0479), 1317 (AB0561)
Kocaer S. B., 1386 (AB0708)
Kocak U. Z., 1454 (AB0862-HPR)
Kocasoy-Orhan E., 1191 (AB0331)
Kochbati S., 0856 (POS1155), 1358 (AB0650)
Kochkar R., 0926 (POS1290)
Kocijan R., 0848 (POS1137)
Kodric M., 1002 (POS1435)
Koehn C. L., 0167 (OP0275-PARE), 0374 (POS0298), 0377 (POS0303)
Koehner M., 0165 (OP0272)
Koeleman C., 1044 (AB0020)
Koessel H., 0244 (POS0075)
Koether V., 1229 (AB0401)
Koetter I., 0685 (POS0861)

Koffi-Tessio V. E. S., 0776 (POS1016), 0927 (POS1291)
Koga T., 0608 (POS0718), 0959 (POS1353)
Koh D. R., 0990 (POS1413)
Koh E. M., 0124 (OP0206), 0280 (POS0137), 0281 (POS0138), 0752 (POS0972), 1210 (AB0368)
Koh W. P., 0827 (POS1095)
Kohan M. P., 0382 (POS0312)
Kohler M., 0841 (POS1124), 0854 (POS1150)
Kohls N., 1027 (POS1484-HPR), 1467 (AB0889-HPR)
Koido A., 1408 (AB0763)
Koike T., 0465 (POS0466), 0492 (POS0517), 0808 (POS1059), 1012 (POS1456-HPR), 1086 (AB0115)
Koilubaeva G., 1184 (AB0319), 1185 (AB0320)
Kojima T., 1142 (AB0233), 1152 (AB0253)
Kok M. R., 0127 (OP0211), 0127 (OP0212), 0289 (POS0151), 0374 (POS0299), 1087 (AB0116), 1107 (AB0160)
Kok M., 0807 (POS1057)
Kok P., 0127 (OP0211), 0127 (OP0212)
Koksvik H. S., 0951 (POS1337), 0995 (POS1424)
Kolarov Z., 0522 (POS0578)
Kolarz B., 0309 (POS0191)
Kolb M., 0069 (OP0124), 1008 (POS1449)
Koletsos N., 0620 (POS0738), 1090 (AB0121)
Koliadenko D., 0612 (POS0725)
Kolkhidova Z., 0249 (POS0083), 0918 (POS1267), 1261 (AB0468), 1394 (AB0726)
Kollert F., 0033 (OP0061), 0649 (POS0795)
Kollmeier A., 0312 (POS0195), 0316 (POS0200), 0781 (POS1024), 0782 (POS1026), 0783 (POS1027), 0784 (POS1028), 0785 (POS1029), 0787 (POS1031), 0801 (POS1048), 1289 (AB0524), 1290 (AB0525), 1291 (AB0526), 1292 (AB0527), 1293 (AB0528), 1300 (AB0538)
Kolm I., 0046 (OP0085)
Koltakova A., 0014 (OP0027), 0204 (POS0004), 0371 (POS0291)
Koltsova E., 0731 (POS0937), 1084 (AB0111), 1095 (AB0135), 1146 (AB0241), 1265 (AB0475), 1383 (AB0703)
Komagata Y., 0395 (POS0336), 0753 (POS0975)
Komarc M., 0678 (POS0849), 1233 (AB0410)
Komech E., 0014 (OP0027), 0204 (POS0004)
Komuro I., 1168 (AB0285)
Kondo Y., 1362 (AB0660)
Kondrateva L., 0515 (POS0561), 0613 (POS0727), 1179 (AB0306), 1179 (AB0307)
Koné-Paut I., 0098 (OP0164), 0872 (POS1183), 0939 (POS1314)
Koneva O., 0104 (OP0173), 0681 (POS0853), 0683 (POS0857), 0683 (POS0858), 0684 (POS0860), 0899 (POS1232), 1239 (AB0423), 1248 (AB0440), 1253 (AB0453), 1254 (AB0454), 1254 (AB0455)
Kong T., 0460 (POS0458), 0622 (POS0742), 0678 (POS0848), 0680 (POS0851), 1037 (AB0005)
Kong X., 0657 (POS0810), 0661 (POS0817)
König I., 0149 (OP0244)
Konig M., 0230 (POS0051), 1368 (AB0674)
Konishi N., 1063 (AB0065)
Kono M., 0687 (POS0863)
Kononov A., 0944 (POS1324)
Konst Z., 0204 (POS0006)
Kontny E., 0822 (POS1086)
Koolvisoot A., 1139 (AB0228)
Koopman-Keemink Y., 0932 (POS1300)
Kopec J., 0997 (POS1427)
Kopitar A. N., 0242 (POS0072)
Koppert T., 0878 (POS1191)
Korendovych V., 1237 (AB0418), 1433 (AB0818)
Korendowych E., 0789 (POS1034)
Korez M. K., 1323 (AB0572)
Kori N., 0611 (POS0723)
Korish S., 0076 (OP0132)
Korkosz M., 0048 (OP0089), 1135 (AB0219)
Kornishina T., 0937 (POS1310)
Korochina I., 1328 (AB0582)
Korochina K., 1328 (AB0582)
Korolev M., 0043 (OP0080), 1045 (AB0023)
Koroleva M., 0277 (POS0131), 1344 (AB0621), 1416 (AB0780), 1443 (AB0838)
Korolik O., 1461 (AB0875-HPR)
Korotaeva T., 0014 (OP0027), 0142 (OP0232), 0204 (POS0004), 0310 (POS0192), 0754 (POS0976), 0796 (POS1043), 0799 (POS1046), 0815 (POS1072), 1295 (AB0530), 1296 (AB0531), 1298 (AB0534), 1302 (AB0540), 1303 (AB0541), 1306 (AB0546), 1325 (AB0575), 1325 (AB0576), 1327 (AB0580)
Korpak A., 0369 (POS0287)
Korsakova Y., 0754 (POS0976), 0815 (POS1072), 1303 (AB0541), 1325 (AB0575), 1325 (AB0576), 1327 (AB0580)
Korsten P., 0611 (POS0722), 0665 (POS0825), 0670 (POS0834), 1167 (AB0283), 1237 (AB0418), 1433 (AB0818)
Kortekaas M., 0273 (POS0123), 0351 (POS0258)
Kortus-Goetze B., 0050 (OP0092), 0971 (POS1379)
Korva M., 0242 (POS0072)
Kose M., 0191 (OP0313)
Koshak B., 0811 (POS1065)
Kosheleva N., 0614 (POS0729), 1180 (AB0309), 1180 (AB0310)
Koskela J., 0004 (OP0007)
Kosmetatou M., 0635 (POS0764)
Kosmin A., 0246 (POS0078), 1036 (AB0001)
Kosse L., 0359 (POS0271-HPR), 0548 (POS0621), 1122 (AB0196)
Kostareva O., 0948 (POS1332)
Koster M., 0651 (POS0799), 0652 (POS0800), 0652 (POS0801), 0654 (POS0803), 0655 (POS0805), 0951 (POS1338)
Kostik M., 0246 (POS0078), 0247 (POS0079), 0247 (POS0080), 0927 (POS1293), 0930 (POS1297), 0930 (POS1298), 0931 (POS1299), 0934 (POS1304), 0937 (POS1310), 0944 (POS1324), 1036 (AB0001), 1402 (AB0748)
Kostine M., 1261 (AB0469)
Kostopoulou M., 0635 (POS0764)
Kosturkova M., 1036 (AB0002)
Kosugiyama H., 0455 (POS0450), 1094 (AB0131)
Kotanidou A., 1381 (AB0697)
Kotecha P., 0573 (POS0662)
Kötter I., 0670 (POS0834)
Kougkas N., 0184 (OP0299), 0523 (POS0580), 0733 (POS0941)
Koumpouros Y., 0238 (POS0064-PARE)
Koushesh S., 0879 (POS1195)
Koutsianas C., 1304 (AB0543)
Koutsogianni K., 0193 (OP0317-PARE)
Koutsoviti S., 0646 (POS0786)
Kovačić N., 0226 (POS0042)
Kovalenko P., 0834 (POS1108)
Kovalevskaya O., 1088 (AB0118), 1180 (AB0308)
Kovshik A., 0772 (POS1008)
Kowal-Bielecka O., 0694 (POS0877)
Kowalski S., 0582 (POS0676)
Koyama M., 1099 (AB0145)
Koyama T., 1025 (POS1482-HPR)
Koyama Y., 0697 (POS0881)
Kozaci L., 0727 (POS0929)
Kozhevnikov A., 1393 (AB0724)
Kozhevnikova P., 0834 (POS1108)
Kozhukh G., 0206 (POS0008)
Krabbe S., 0089 (OP0149), 0153 (OP0252)
Kraev K., 1272 (AB0489)
Krafft V., 0095 (OP0158-HPR)
Krajewska-Wlodarczyk M., 1123 (AB0198)
Kramarič J., 1201 (AB0352), 1201 (AB0353)
Kranenburg - van Koppen L. J., 0238 (POS0063-PARE)
Krasselt M., 0421 (POS0382)
Kräter M., 1238 (AB0420)
Kraus F. V., 1047 (AB0028)
Krause A., 0171 (OP0283), 0915 (POS1261)
Krauß P. L., 0191 (OP0312), 1048 (AB0029), 1049 (AB0031)
Kravarik K., 0038 (OP0072)
Kravchenko D., 0846 (POS1134)
Kravtsov G., 0420 (POS0380), 1461 (AB0875-HPR)
Kravtsov V., 0420 (POS0380)
Krekeler M., 0851 (POS1145)
Krekhova E., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Kremer J. M., 0446 (POS0435)
Kremer J., 0538 (POS0606)
Kretchikova D., 1095 (AB0135)
Kreuter A., 0670 (POS0834)
Kreuter M., 0101 (OP0170), 0670 (POS0834)
Krichevskaya O., 1264 (AB0473), 1264 (AB0474)
Kricorian G., 0066 (OP0118)
Krijbolder D., 0978 (POS1391)
Krijthe B., 0127 (OP0211), 0127 (OP0212)
Krishan P., 0774 (POS1011)
Krishna S., 0879 (POS1195)
Krishna V., 0205 (POS0007), 0423 (POS0387)
Krishnamurthy A., 0429 (POS0400)
Krishnan V., 0707 (POS0901)
Kristensen L. E., 0283 (POS0144), 0339 (POS0237), 1312 (AB0554), 1315 (AB0559)
Kristensen S., 0215 (POS0025), 0382 (POS0313)
Kristiansen K., 0006 (OP0010)
Kristianslund E., 0133 (OP0222), 0217 (POS0027), 0256 (POS0093), 0934 (POS1305), 1392 (AB0722)
Kristyanto H., 1045 (AB0022)
Kriulin I., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Kriulina T., 1394 (AB0727)
Krivolapov Y., 0647 (POS0790)
Krivotulova I., 0514 (POS0558)
Kroegler B., 1418 (AB0786)
Kroese F. G. M., 0074 (OP0130), 0189 (OP0308)
Krogias C., 0525 (POS0584)
Krogulec M., 1123 (AB0198)
Krol R., 0346 (POS0249), 1221 (AB0387)
Kronbergs A., 0713 (POS0908), 0718 (POS0915), 0720 (POS0918), 0789 (POS1033)
Kronenberg D., 0226 (POS0041)
Krönke G., 0086 (OP0145), 0088 (OP0148), 0996 (POS1426), 1042 (AB0016)
Kronzer V., 0002 (OP0006), 0128 (OP0213), 0129 (OP0216), 0173 (OP0286), 0213 (POS0023), 0322 (POS0210), 0380 (POS0309)
Kroon F., 0273 (POS0123), 0304 (POS0182), 0351 (POS0258), 0416 (POS0371), 0822 (POS1087)
Krueger K., 0194 (OP0318), 0528 (POS0591), 1153 (AB0255)
Krueger W., 0860 (POS1163), 0886 (POS1207)
Krusche M., 0305 (POS0183), 1013 (POS1458-HPR)
Kruzikas D., 0734 (POS0943)
Krylov M., 0243 (POS0073), 1038 (AB0007), 1040 (AB0010)
Krylova A., 1285 (AB0516)
Ksouda K., 1061 (AB0059), 1162 (AB0273)
Kubo S., 0329 (POS0221)
Kubomoto S., 0228 (POS0047)
Kuca-Warnawin E., 0822 (POS1086)
Kucharz E., 1434 (AB0820)
Kuchinskaya E., 0246 (POS0078)
Kück F., 0665 (POS0825)
Kucuk A., 1355 (AB0644), 1470 (AB0893-HPR)
Küçük H., 0878 (POS1193), 1077 (AB0097), 1176 (AB0300)
Küçükşahin O., 0069 (OP0125), 0731 (POS0935), 1105 (AB0157), 1182 (AB0314)
Kucybała I., 0743 (POS0958)
Kudinsky D., 0276 (POS0130), 1421 (AB0792)
Kudryashov S., 0969 (POS1374), 1331 (AB0589), 1388 (AB0713)
Kudryavtseva A., 0465 (POS0467), 1131 (AB0209), 1147 (AB0245), 1158 (AB0263)
Kuemmerle-Deschner J. B., 0050 (OP0092), 0882 (POS1199), 0971 (POS1379), 0972 (POS1380)
Kuemmerle-Deschner J., 0244 (POS0075), 0883 (POS1202)
Kühl H., 1385 (AB0707)
Kühn A., 0224 (POS0038), 0883 (POS1202)
Kuhn C., 1274 (AB0494)
Kuhn K. A., 0748 (POS0966), 1022 (POS1474-HPR), 1469 (AB0892-HPR)
Kühnis A., 0688 (POS0866)
Kuijper J., 0021 (OP0039)
Kuijper M., 0353 (POS0261), 1087 (AB0116)
Kuijpers T., 0937 (POS1311)
Kulakova P., 0772 (POS1008)

Kulig P., 1046 (AB0024)
Kulikov A., 0709 (POS0903)
Kulyk M., 1401 (AB0746)
Kumagai S., 0689 (POS0868), 1096 (AB0136)
Kumar A., 0013 (OP0024)
Kumar R., 0001 (OP0003)
Kumar S., 0218 (POS0028)
Kumke T., 0213 (POS0022), 0334 (POS0229), 0704 (POS0896), 0705 (POS0897)
Kümmerle-Deschner J., 0945 (POS1325)
Kundaki B., 0841 (POS1124)
Kundu S., 0795 (POS1042)
Kundurdzhiev A., 1356 (AB0646)
Kundurzhiev T., 1356 (AB0646)
Kundzer A., 0084 (OP0142), 0726 (POS0928), 0796 (POS1043), 1298 (AB0534), 1302 (AB0540)
Künstner A., 0149 (OP0244)
Kunz J., 0372 (POS0293)
Kunz M., 0391 (POS0328)
Kuo C. F., 0116 (OP0193), 1152 (AB0253)
Kuo H. C., 0279 (POS0135)
Kupper H., 0064 (OP0115)
Kur J., 0377 (POS0303)
Kural A., 1086 (AB0114)
Kuraş S., 1086 (AB0114)
Kurbanmagomedov M., 1284 (AB0514)
Kurbanova S., 1397 (AB0735)
Kuriakose M., 0948 (POS1331)
Kurmann R., 0056 (OP0102), 0389 (POS0325), 0672 (POS0836)
Kurochkina Y., 0043 (OP0080), 0581 (POS0673), 1045 (AB0023)
Kuroe Y., 1470 (AB0894-HPR)
Kurose A., 1055 (AB0045)
Kurose R., 1055 (AB0045)
Kurrasch R., 1170 (AB0288)
Kurttila A., 1150 (AB0250)
Kuru O., 0286 (POS0146)
Kurut Aysin İ., 0861 (POS1165), 1255 (AB0456), 1366 (AB0669)
Kuryata O., 1452 (AB0858)
Kur-Zalewska J., 1434 (AB0820)
Kurzeja D., 0702 (POS0893)
Kusevich D., 0827 (POS1094), 1131 (AB0210), 1139 (AB0226), 1337 (AB0603)
Kushnareva I., 1172 (AB0292)
Kushnir I., 1095 (AB0135)
Kuster S., 0685 (POS0861)
Kutlubay Z., 0660 (POS0814), 0662 (POS0819)
Kuuliala A., 1150 (AB0250)
Kuuliala K., 1150 (AB0250)
Kuvardin E., 0647 (POS0790)
Kuwana M., 0102 (OP0171), 0685 (POS0861), 0897 (POS1228), 1150 (AB0249), 1152 (AB0253), 1246 (AB0436)
Kuwert T., 0165 (OP0272)
Kuznetsov G., 1328 (AB0582)
Kuznetsova N., 0754 (POS0976), 0815 (POS1072), 1325 (AB0575), 1325 (AB0576)
Kuznetsova T., 1384 (AB0705)
Kvien T. K., 0047 (OP0087), 0123 (OP0204), 0133 (OP0222), 0185 (OP0301), 0219 (POS0029), 0256 (POS0093), 0281 (POS0139), 0795 (POS1041), 0934 (POS1305), 1392 (AB0722)
Kvlividze T., 1437 (AB0827)
Kwan Z., 0816 (POS1075)
Kwekkeboom J., 0422 (POS0384)
Kwok Y. K., 0257 (POS0094)
Kyburz D., 0655 (POS0806), 1161 (AB0270)
Kyriakou A., 0605 (POS0711)
Kyung-Ann L., 0758 (POS0982)
Kyurkchiev D., 1432 (AB0815)

L'andolina M., 0906 (POS1246)
La Barbera L., 0390 (POS0326)
La Gamba F., 0363 (POS0277)
La Paglia G., 0254 (POS0090)
La Rocca G., 0642 (POS0778), 0644 (POS0782)
La Rosa A., 1099 (AB0143), 1135 (AB0217), 1135 (AB0218)
Laataoui S., 0526 (POS0588), 0837 (POS1116), 0858 (POS1160), 1346 (AB0625)
Laatar A., 0292 (POS0159-HPR), 0481 (POS0497), 0522 (POS0577), 0835 (POS1110), 0856 (POS1155), 1030 (POS1491-HPR), 1113 (AB0173), 1113 (AB0174), 1117 (AB0184), 1118 (AB0188), 1277 (AB0499), 1332 (AB0590), 1333 (AB0592), 1333 (AB0593), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1358 (AB0650), 1368 (AB0672), 1368 (AB0673), 1381 (AB0698), 1390 (AB0717), 1397 (AB0736), 1411 (AB0770), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Labbene E., 0526 (POS0586), 0526 (POS0587), 1117 (AB0186), 1119 (AB0191), 1278 (AB0501)
Labrador-Sánchez E., 0035 (OP0065)
Labreuche J., 1011 (POS1454-HPR), 1229 (AB0401)
Lacaille D., 0374 (POS0298), 0377 (POS0303), 0997 (POS1427)
Lacaze P., 0009 (OP0015)
Lacerda M., 0909 (POS1252)
Lachmann H. J., 0947 (POS1330)
Lackner A., 0261 (POS0102)
Ladehesa Pineda M. L., 0736 (POS0946), 0737 (POS0948), 0743 (POS0958), 0747 (POS0965), 0751 (POS0970), 0755 (POS0977), 0766 (POS0996), 0769 (POS1001), 0920 (POS1272), 0977 (POS1390), 0986 (POS1407), 1109 (AB0166), 1317 (AB0562)
Ladjouze-Rezig A., 0843 (POS1127)
Lafeber F., 0012 (OP0021), 0825 (POS1091), 0825 (POS1092)
Lafforgue P., 0900 (POS1234), 1061 (AB0058)
Lafyatis R., 0393 (POS0332)
Laganà A., 0676 (POS0845), 0904 (POS1243)
Laganović M., 1199 (AB0348), 1199 (AB0349)
Lages L., 1003 (POS1438)
Lago F., 0418 (POS0376)
Lagová M., 0058 (OP0105)
Lagunes-Galindo I., 0328 (POS0220), 0489 (POS0512), 0567 (POS0654)
Lagunova N., 0930 (POS1298)
Laheru D., 0139 (OP0229)
Lahmar K., 1281 (AB0507)
Lahmar W., 1116 (AB0182)
Lahoz C., 1218 (AB0382)
Lahrichi S., 0767 (POS0998), 1336 (AB0600), 1363 (AB0662), 1433 (AB0819), 1438 (AB0828), 1438 (AB0829)
Lai M., 0042 (OP0078)
Laila D., 0834 (POS1107)
Laila N., 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Laíño Piñeiro M. C., 1132 (AB0211)
Laitinen T., 0004 (OP0007)
Laiz A., 1093 (AB0129), 1365 (AB0666), 1426 (AB0804)
Lajas C., 1464 (AB0881-HPR), 1475 (AB0906-HPR)
Laliberté M. C., 0084 (OP0143), 0336 (POS0232), 1312 (AB0555), 1314 (AB0558)
Lally C., 1093 (AB0130)
Lam S. H. M., 0818 (POS1079)
Lam T. O., 0057 (OP0103)
Lam T., 0257 (POS0094)
Lamarao F., 0625 (POS0747), 0999 (POS1430)
Lamb J., 0369 (POS0288)
Lambers W., 0189 (OP0308), 1071 (AB0082)
Lambert C., 1022 (POS1475-HPR)
Lambert M., 0612 (POS0724)
Lambert R. G., 0089 (OP0149), 0153 (OP0251), 0153 (OP0252), 0221 (POS0032), 0224 (POS0037), 0831 (POS1101), 0943 (POS1323)
Lambert R., 1334 (AB0594)
Lambova S., 1256 (AB0460), 1257 (AB0461)
Lamers-Karnebeek F., 0880 (POS1197), 1366 (AB0668)
Lamkhanat O., 0295 (POS0166), 0519 (POS0570), 1162 (AB0274)
Lammert A., 1458 (AB0869-HPR), 1482 (AB0922-PARE)
Lammertsma A. A., 0114 (OP0189)
Lamoreaux B., 0839 (POS1121), 1347 (AB0628), 1348 (AB0630)
Lamorte S., 1326 (AB0578)
Lampa J., 0260 (POS0101)
Lampe C., 0168 (OP0277-PARE)
Lamprecht P., 0028 (OP0054)
Lan T. Y., 0599 (POS0700), 1440 (AB0832)
Lanchbury J., 0458 (POS0456)
Lande R., 0150 (OP0246)
Landete L., 0296 (POS0168)
Landewé R. B. M., 0024 (OP0047), 0083 (OP0141), 0152 (OP0250), 0153 (OP0251), 0221 (POS0032), 0222 (POS0033), 0334 (POS0229), 0340 (POS0238), 0540 (POS0609), 0751 (POS0971), 0911 (POS1256)
Landgren A., 1350 (AB0633)
Landgren E., 1024 (POS1479-HPR)
Landini N., 0355 (POS0264), 0675 (POS0842), 0897 (POS1228)
Landis J., 0794 (POS1040)
Landolfi G., 0335 (POS0230)
Landsittel D., 0584 (POS0678)
Lane J., 0207 (POS0011), 0974 (POS1383)
Lane M., 0786 (POS1030), 1306 (AB0547)
Lane N., 0072 (OP0128), 0569 (POS0656)
Lane R., 0018 (OP0034)
Lang A., 1052 (AB0040)
Langdahl B., 0451 (POS0444)
Lange U., 0040 (OP0075), 0383 (POS0314), 0676 (POS0844), 1030 (POS1492-HPR), 1054 (AB0043)
Langenfeld H., 0652 (POS0801), 0655 (POS0805)
Langer H. E., 0910 (POS1254), 1383 (AB0702)
Langholff W., 0527 (POS0590), 0539 (POS0607)
Langley R., 1293 (AB0528)
Langlois V., 0172 (OP0284)
Langrish C., 1406 (AB0756)
Lanna C. C., 0909 (POS1252)
Lannes B., 0149 (OP0243)
Lanni S., 0935 (POS1307)
Lanyon P., 0602 (POS0705), 0989 (POS1412)
Lanzillotta M., 0907 (POS1247), 0950 (POS1336), 0960 (POS1356), 0974 (POS1382)
Lao S. M., 1357 (AB0648)
Lao V., 0687 (POS0865)
Laouani C., 1219 (AB0383)
Lapadula G., 0582 (POS0675)
Lapane K., 1022 (POS1474-HPR), 1469 (AB0892-HPR)
Lapin S., 0647 (POS0790)
Lapkina N., 1095 (AB0135)
Lapshina S., 1283 (AB0511)
Larco Rojas X. E., 0628 (POS0752), 1189 (AB0328), 1321 (AB0568)
Lard L. R., 0978 (POS1391)
Laria A., 0594 (POS0693)
Larid G., 1061 (AB0058)
Larkin L., 0115 (OP0191-PARE), 1017 (POS1465-HPR), 1459 (AB0872-HPR)
Larkins N., 1051 (AB0036)
Laroca Skare T., 0909 (POS1252), 1448 (AB0848)
Larosa M., 0181 (OP0295), 0182 (OP0297), 0261 (POS0103)
Larsen P. V., 0419 (POS0377)
Larsen T. R., 0982 (POS1398)
Larsson A., 0305 (POS0184)
Larsson I., 0197 (OP0322-HPR), 0811 (POS1064), 1024 (POS1479-HPR)
Lasa A., 1093 (AB0129)
Lascaro N., 1217 (AB0380)
Laska M. J., 0404 (POS0349)
Laslett L., 0362 (POS0276)
Lassoued S., 0571 (POS0659)
Lataoui S., 0923 (POS1279), 0924 (POS1283), 1142 (AB0232), 1345 (AB0623)
Lateef A., 0218 (POS0028)
Latella J., 0139 (OP0229)
Latifa T., 0992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811), 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Latini A., 1038 (AB0006)
Latocha K. M., 0095 (OP0159-HPR), 1466 (AB0885-HPR)
Latour S., 0018 (OP0034)
Latourte A., 0841 (POS1124)
Lau C. S., 0147 (OP0240), 0218 (POS0028), 0225 (POS0039), 0775 (POS1015)

Lau I. S., 0053 (OP0096), 0459 (POS0457), 0837 (POS1114)
Lau S. L., 0257 (POS0094), 0860 (POS1164), 0895 (POS1222)
Lau T. C., 0990 (POS1413)
Laughton D., 0018 (OP0034)
Launay D., 1011 (POS1454-HPR), 1229 (AB0401)
Lauper K., 0041 (OP0077), 0058 (OP0105), 0148 (OP0241), 0256 (POS0093), 0577 (POS0668), 0863 (POS1168)
Laura C., 1241 (AB0425)
Laura P. S., 0020 (OP0038), 1208 (AB0366)
Laurent D., 0211 (POS0020), 0363 (POS0277)
Laurent M. D. B., 1408 (AB0761)
Laurent-Chabalier S., 0518 (POS0566), 0770 (POS1003), 0820 (POS1082), 0902 (POS1239)
Laurie M., 1092 (AB0128)
Laurindo I., 0582 (POS0676)
Lauwerys B., 0020 (OP0037), 0213 (POS0022), 0240 (POS0067), 1408 (AB0761)
Laverny G., 0149 (OP0243), 0151 (OP0247)
Lavi I., 0131 (OP0219), 0286 (POS0147)
Lawrence W. R., 0993 (POS1421)
Lawson-Tovey S., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0199 (LB0002), 0872 (POS1183)
Lazarevic D., 0247 (POS0079), 0934 (POS1304)
Lazaridis A., 0620 (POS0738)
Lazarini A., 0646 (POS0786)
Lazaris A. C., 0015 (OP0029)
Lazaro E., 0052 (OP0094), 0181 (OP0295)
Lazaro M. A., 0382 (POS0312), 0874 (POS1186)
Lazzari C., 0953 (POS1341)
Lazzaroni M. G., 0166 (OP0273), 0232 (POS0054), 0387 (POS0319), 0389 (POS0324), 0470 (POS0476), 0619 (POS0737), 0633 (POS0760), 0701 (POS0891), 1435 (AB0822)
Le Brun F. O., 0792 (POS1037), 0792 (POS1038), 0801 (POS1049)
Le Corvoisier P., 0027 (OP0052), 0317 (POS0201)
Le Cozannet R., 0365 (POS0281)
Le Gouellec N., 0664 (POS0822)
Le Guern V., 0181 (OP0295), 0182 (OP0297), 0261 (POS0103), 0612 (POS0724)
Lea.Savey@aphp.Fr>; L. S. F., 0954 (POS1343)
Leach C., 0237 (POS0062-PARE)
Leal Rodriguez S., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Leamy K., 0859 (POS1162)
Leandro-Merhi V. A., 1423 (AB0798)
Leatherwood C., 0070 (OP0126), 0255 (POS0092)
Lebedev Y., 0204 (POS0004)
Leblond A., 0419 (POS0378)
Lebwohl M., 0787 (POS1031), 1293 (AB0528), 1304 (AB0544)
Leccese P., 1217 (AB0380)
Lechtenboehmer C., 0272 (POS0122)
Lederballe Gron K., 0063 (OP0114)
Ledingham J., 0744 (POS0959)
Lee A. P. W., 0818 (POS1079), 1323 (AB0571)
Lee C. H., 1072 (AB0084)
Lee C. K., 1156 (AB0260)
Lee C., 0639 (POS0771), 0640 (POS0773)
Lee D. H., 0062 (OP0113)
Lee D. Y., 0062 (OP0113)
Lee E. B., 0102 (OP0171), 0682 (POS0856), 0976 (POS1386)
Lee E. K., 1072 (AB0084)
Lee E. Y., 0321 (POS0209), 0512 (POS0555), 0516 (POS0563), 0516 (POS0564)
Lee H. R., 0204 (POS0005)
Lee H., 0651 (POS0798)
Lee J. J. W., 0257 (POS0094)
Lee J. M., 0257 (POS0094)
Lee J. S., 0512 (POS0555), 0512 (POS0555), 0516 (POS0563), 0516 (POS0563), 0516 (POS0564), 0516 (POS0564), 0731 (POS0936)
Lee J. Y. E., 0235 (POS0058-PARE)
Lee J., 0062 (OP0113), 0124 (OP0206), 0280 (POS0137), 0281 (POS0138), 0752 (POS0972), 1210 (AB0368)
Lee K. A., 0132 (OP0221), 0758 (POS0981), 0812 (POS1068)
Lee K. H., 1015 (POS1460-HPR)
Lee K., 0124 (OP0206), 0251 (POS0086)
Lee M. L., 0640 (POS0773)
Lee M. S., 1072 (AB0084)
Lee M. Y., 0640 (POS0773)
Lee M., 1008 (POS1448)
Lee R., 1006 (POS1444), 1029 (POS1490-HPR)
Lee S. H., 0758 (POS0981)
Lee S. J., 0258 (POS0096), 0731 (POS0936), 1123 (AB0198)
Lee S. S., 0716 (POS0911)
Lee S. Y., 0758 (POS0981)
Lee S., 0124 (OP0206), 0280 (POS0137), 0281 (POS0138), 0752 (POS0972), 1210 (AB0368)
Lee V. W., 0257 (POS0094)
Lee Y. A., 0512 (POS0555), 0516 (POS0563), 0516 (POS0564)
Lee Y. H., 1124 (AB0199)
Lee Y. J., 1152 (AB0253)
Leeb B., 0256 (POS0093), 0320 (POS0208)
Leff R., 0595 (POS0695)
Lefkir S., 0843 (POS1127), 1092 (AB0126), 1092 (AB0127)
Legendre P., 0388 (POS0323)
Legger E., 0947 (POS1330)
Legkobyt A., 1452 (AB0858)
Leguizamón M. L., 0635 (POS0763), 1196 (AB0342)
Lehman T., 0137 (OP0227), 0247 (POS0079), 0934 (POS1304), 1316 (AB0560)
Lehovec R., 0363 (POS0277)
Lei A., 0253 (POS0089)
Lei G., 0307 (POS0186)
Leicht J. D., 0752 (POS0973)
Leila S., 0522 (POS0577)
Leipe J., 0372 (POS0293)
Leirisalo-Repo M., 1150 (AB0250)
Leishangthem B., 1163 (AB0276)
Lejon K., 0013 (OP0024)
Lema L., 1196 (AB0342)
Lemelle I., 0939 (POS1314)
Lemesle P., 0169 (OP0279-PARE), 1362 (AB0659)
Lemke L., 1130 (AB0208)
Lemmers J., 1248 (AB0441)
Lempp H., 0161 (OP0264-HPR)
Lems W., 0114 (OP0189), 0226 (POS0043), 0324 (POS0213), 1107 (AB0160), 1151 (AB0251)
Lena A., 0665 (POS0825)
Lenderking W., 0146 (OP0239)
Lendrem D., 0403 (POS0348), 1057 (AB0051)
Lendvai A., 0038 (OP0072)
Leng M., 0163 (OP0268)
Leng X., 0629 (POS0754)
Lennips N., 1268 (AB0481)
Lentini V. L., 0301 (POS0177)
León L., 0896 (POS1225), 0908 (POS1251), 0910 (POS1253), 1464 (AB0881-HPR), 1475 (AB0906-HPR)
Leon Luque M., 1076 (AB0096)
León P., 0053 (OP0097)
Leonardo M., 1076 (AB0096)
Leone G., 0940 (POS1316), 0941 (POS1317)
Leprevost J., 0001 (OP0002)
Lepri G., 0385 (POS0317), 0675 (POS0842), 1192 (AB0334)
Lequerre T., 0571 (POS0659)
Lera-Gómez L., 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1046 (AB0026), 1065 (AB0070), 1076 (AB0094), 1076 (AB0096)
Lerang K., 0078 (OP0135)
Lercara A., 1247 (AB0438)
Leroux A. C., 0669 (POS0831)
Lertratanakul A., 0016 (OP0030), 0312 (POS0196), 0338 (POS0235), 0433 (POS0407), 0788 (POS1032), 1287 (AB0522), 1294 (AB0529), 1306 (AB0547), 1308 (AB0550)
Lespessailles E., 0337 (POS0234), 0364 (POS0279)
Lesser E., 0026 (OP0049), 0790 (POS1035), 1287 (AB0522)
Lester S., 1098 (AB0142)
Letaeva M., 0277 (POS0131), 1344 (AB0621), 1416 (AB0780), 1443 (AB0838)
Letarouilly J. G., 1258 (AB0464)
Letyagina E., 0043 (OP0080), 1045 (AB0023)
Leuchten N., 0617 (POS0733)
Leung J., 0117 (OP0194), 1212 (AB0371)
Leung M. C., 0640 (POS0773)
Leung Y. Y., 0139 (OP0229), 0183 (OP0298), 0273 (POS0124), 0827 (POS1095), 0989 (POS1411), 0990 (POS1413), 1290 (AB0525), 1296 (AB0531)
Levartovsky D., 0200 (LB0003), 0885 (POS1206), 1049 (AB0032), 1181 (AB0312)
Levendoglu F., 1323 (AB0572)
Levin M., 0112 (OP0186)
Levin S., 0021 (OP0039)
Levine T., 0004 (OP0008)
Levinsky Y., 0928 (POS1294), 0929 (POS1295)
Levitch R., 0211 (POS0020)
Levy C., 0192 (OP0314)
Levy D. A., 0694 (POS0876)
Levy D., 1373 (AB0680)
Levy R., 0621 (POS0739)
Levy Y., 0102 (OP0171)
Lewis K. E., 0021 (OP0039)
Lewis M., 0007 (OP0011), 0079 (OP0136)
Lezhenina S., 1458 (AB0869-HPR), 1482 (AB0922-PARE)
Li A., 0654 (POS0804)
LI B. C., 0771 (POS1006)
Li C., 1484 (AB0927-PARE)
LI D., 0810 (POS1062)
LI E. K., 1323 (AB0571)
Li E., 0257 (POS0094)
LI E., 0818 (POS1079)
Li G., 1166 (AB0280)
Li H. G., 1174 (AB0296)
Li H., 0629 (POS0754)
LI H., 1419 (AB0787)
LI J., 0065 (OP0117)
Li J., 0387 (POS0320), 0561 (POS0647), 0574 (POS0664), 0670 (POS0833), 1136 (AB0221)
Li K. J., 0599 (POS0700)
LI K. J., 1440 (AB0832)
LI L., 0022 (OP0043)
LI M., 0178 (OP0290), 1323 (AB0571)
Li M., 0629 (POS0754), 0641 (POS0775)
LI N., 0163 (OP0268)
Li N., 0629 (POS0753)
LI P. H., 0147 (OP0240), 0775 (POS1015)
Li Q. H., 1174 (AB0296), 1225 (AB0394), 1227 (AB0398)
Li Q., 0431 (POS0405), 0432 (POS0406)
Li R., 1196 (AB0343)
LI T. K., 0257 (POS0094), 0818 (POS1079), 0860 (POS1164), 0895 (POS1222)
Li T. W., 0248 (POS0081), 0278 (POS0133), 0428 (POS0399), 1005 (POS1443), 1355 (AB0645)
LI T. W., 0847 (POS1135), 0851 (POS1144), 1057 (AB0050), 1354 (AB0642), 1421 (AB0791), 1446 (AB0845)
Li T., 0227 (POS0044), 1076 (AB0095)
LI T., 0848 (POS1138), 1440 (AB0831)
LI W., 0810 (POS1062)
Li X. F., 0427 (POS0396)
LI X. F., 0771 (POS1006)
LI X., 0107 (OP0179), 0111 (OP0184), 0888 (POS1211), 1037 (AB0005), 1408 (AB0762), 1436 (AB0824)
Li X., 0315 (POS0199), 0452 (POS0445), 0454 (POS0448), 0454 (POS0449), 0460 (POS0458), 0574 (POS0664), 0574 (POS0664), 0616 (POS0732), 0619 (POS0736), 0622 (POS0742), 0623 (POS0743), 0677 (POS0847), 0678 (POS0848), 0680 (POS0851), 0684 (POS0859), 0713 (POS0908), 0720 (POS0918), 0729 (POS0932)
Li Y. N., 0121 (OP0201), 0391 (POS0327), 1075 (AB0091)
LI Y., 0009 (OP0017), 0010 (OP0018), 0251 (POS0087), 0888 (POS1211)
Li Y., 0315 (POS0199), 0486 (POS0508), 0568 (POS0655), 0574 (POS0664), 0584 (POS0678), 0729 (POS0932)
LI Z., 0218 (POS0028)
Li Z., 0227 (POS0044), 0428 (POS0399), 0574 (POS0664), 0574 (POS0664)
Liang K., 0584 (POS0678)

Liang M., 0690 (POS0869), 0698 (POS0884)
Liang R., 0121 (OP0201)
Liao X., 1122 (AB0197)
Liao Y. W., 0622 (POS0741)
Liau S. M., 1015 (POS1460-HPR)
Lidar M., 0892 (POS1217)
Lieb S., 0714 (POS0910), 0758 (POS0983)
Liebel C., 0121 (OP0201)
Lieberman A., 0810 (POS1063)
Liedl D., 0106 (OP0177)
Liem S., 0203 (POS0001), 0675 (POS0843)
Liew D., 0117 (OP0194), 1212 (AB0371)
Liew J., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0230 (POS0051), 0476 (POS0487), 0859 (POS1162), 0994 (POS1422), 1368 (AB0674)
Likhacheva E., 1011 (POS1455-HPR)
Likhacheva T., 0247 (POS0080), 0931 (POS1299), 0937 (POS1310), 1402 (AB0748)
Lila A., 0275 (POS0127), 0276 (POS0130), 0371 (POS0291), 0465 (POS0467), 0515 (POS0561), 0518 (POS0567), 0605 (POS0712), 0613 (POS0727), 0643 (POS0780), 0815 (POS1072), 0834 (POS1108), 1072 (AB0085), 1095 (AB0135), 1109 (AB0165), 1138 (AB0225), 1177 (AB0303), 1178 (AB0305), 1179 (AB0306), 1179 (AB0307), 1184 (AB0319), 1185 (AB0320), 1306 (AB0546), 1336 (AB0599), 1337 (AB0603), 1338 (AB0604), 1364 (AB0664), 1422 (AB0795)
Liljefors L., 0206 (POS0009)
Lilleoere Rom A., 0126 (OP0210)
Lim A. L., 1451 (AB0856)
Lim C. S. E., 0223 (POS0035)
Lim F., 0301 (POS0176)
Lim N., 0173 (OP0286)
Lim S. L., 1469 (AB0891-HPR)
Lim S. S., 0177 (OP0289)
Lima A., 0377 (POS0303)
Lima J., 0695 (POS0878)
Limam M., 0472 (POS0481), 1480 (AB0919-PARE)
Limaye N., 0020 (OP0037), 0240 (POS0067)
Limaye V., 0697 (POS0883)
Limon-del Toro A., 1455 (AB0863-HPR)
Lin A., 0077 (OP0133)
Lin C. Y., 0707 (POS0901), 0716 (POS0912), 1301 (AB0539)
Lin J., 0456 (POS0452), 0657 (POS0810), 1091 (AB0125), 1227 (AB0398)
Lin M., 0012 (OP0021), 1151 (AB0251)
Lin N. Y., 0121 (OP0201), 1075 (AB0091)
Lin S., 0203 (POS0002)
Lin X., 0022 (OP0042), 0801 (POS1048)
Linda I., 0295 (POS0166), 0519 (POS0570), 0992 (POS1417), 1148 (AB0246), 1162 (AB0274), 1270 (AB0486), 1430 (AB0811)
Lindblom J., 0260 (POS0101)
Lindegaard H. M., 0419 (POS0377)
Lindfors A., 0087 (OP0147)
Lindholm C., 0592 (POS0690), 0592 (POS0691)
Lindqvist D., 0947 (POS1330)
Lindqvist E., 0339 (POS0237), 0535 (POS0601), 0864 (POS1169), 1024 (POS1479-HPR)
Lindsay C., 0139 (OP0229)
Lindsay L., 0648 (POS0792)
Lindström U., 0026 (OP0050), 0068 (OP0122), 0082 (OP0140), 0115 (OP0192), 0130 (OP0218), 0217 (POS0027), 0535 (POS0601), 0864 (POS1169)
Lindtvedt Valaas H., 0092 (OP0153-HPR)
Linge A. D., 0092 (OP0153-HPR)
Lini D., 0470 (POS0476), 0619 (POS0737), 0633 (POS0760), 1435 (AB0822)
Linkova I., 0890 (POS1214)
Linn N., 0968 (POS1373), 1033 (POS1498-PARE)
Linzalone A., 0882 (POS1200)
Liossis S. N., 1299 (AB0537)
Lioté F., 0841 (POS1124)
Liphardt A. M., 0086 (OP0145), 0088 (OP0148), 0420 (POS0381)
Lippe R., 0712 (POS0907), 0786 (POS1030), 0800 (POS1047), 1287 (AB0522), 1288 (AB0523), 1294 (AB0529), 1306 (AB0547)
Lipsky P., 0076 (OP0132)
Lisbona Muñoz M., 0053 (OP0097)
Lisitsyna T., 1088 (AB0118), 1177 (AB0303), 1178 (AB0305), 1180 (AB0308), 1364 (AB0664)
Lisse J., 0333 (POS0228), 0710 (POS0904), 1034 (POS1499-PARE)
Litinsky I., 0200 (LB0003)
Littlejohn G., 0330 (POS0223), 0547 (POS0619), 0629 (POS0753), 0711 (POS0906), 1015 (POS1461-HPR)
Littlewood C., 0293 (POS0161-HPR)
Liu A., 1170 (AB0288)
Liu C., 0086 (OP0145)
Liu F., 0810 (POS1062)
Liu G. Y., 0111 (OP0184), 0315 (POS0199), 0616 (POS0732), 0619 (POS0736), 0623 (POS0743), 0684 (POS0859), 0888 (POS1211)
Liu H., 1122 (AB0197)
Liu J., 0245 (POS0076), 0328 (POS0220), 1100 (AB0146), 1122 (AB0197), 1207 (AB0363), 1287 (AB0522), 1288 (AB0523), 1429 (AB0809)
Liu K., 0083 (OP0141)
Liu Leage S., 0333 (POS0228), 0713 (POS0908), 0725 (POS0926), 0798 (POS1045), 1259 (AB0465), 1262 (AB0471)
Liu M., 0307 (POS0186), 1005 (POS1443), 1136 (AB0221), 1446 (AB0845)
Liu Q., 0561 (POS0647)
Liu S. H., 1022 (POS1474-HPR), 1469 (AB0892-HPR)
Liu T. H., 0280 (POS0136)
Liu T., 1212 (AB0372)
Liu X., 0561 (POS0647), 0729 (POS0932), 1122 (AB0197), 1136 (AB0221)
Liu Y., 0248 (POS0081), 0278 (POS0133), 0406 (POS0351), 0428 (POS0399), 0661 (POS0816), 0785 (POS1029), 0847 (POS1135), 0851 (POS1144), 0975 (POS1384), 1057 (AB0050), 1122 (AB0197), 1212 (AB0372), 1292 (AB0527), 1354 (AB0642), 1355 (AB0645), 1406 (AB0758), 1421 (AB0791)
Liu Z., 0076 (OP0132)
Liverakos S., 0985 (POS1405)
Livshits Y., 1029 (POS1489-HPR)
Ljung L., 0063 (OP0114), 0133 (OP0222), 0474 (POS0484)
Llao Guardia J., 0891 (POS1215)
Llop Vilaltella M., 0342 (POS0242), 1060 (AB0055)
Llorca J., 0614 (POS0728), 1065 (AB0070), 1076 (AB0096)
Llorente I., 0719 (POS0917), 1241 (AB0427)
Lo K. H., 0447 (POS0437), 0708 (POS0902), 1258 (AB0463)
Lo Muscio A., 0858 (POS1161)
Lo Pizzo M., 0022 (OP0042), 0301 (POS0177), 0390 (POS0326)
Lo V., 0257 (POS0094)
Lobbedez T., 0669 (POS0831)
Löber U., 0017 (OP0031)
Loberg M., 0087 (OP0146)
Lobo Prat D., 0666 (POS0827), 1093 (AB0129), 1365 (AB0666), 1426 (AB0804)
Lobo Rodríguez C., 1385 (AB0706)
Lobo V., 1196 (AB0342)
Lockshin M., 0607 (POS0715)
Locquet M., 0835 (POS1111)
Loddo S., 0838 (POS1119)
Loef M., 0416 (POS0371), 0822 (POS1087), 0999 (POS1431)
Loffroy R., 0843 (POS1129)
Loft A. G., 0131 (OP0220), 0217 (POS0027), 0234 (POS0056), 0865 (POS1170)
Loghin-Oprea N., 1337 (AB0601)
Loginova E., 0310 (POS0192), 0754 (POS0976), 0815 (POS1072), 1303 (AB0541), 1306 (AB0546), 1325 (AB0575), 1325 (AB0576), 1327 (AB0580)
Loh Y. L., 1015 (POS1460-HPR), 1176 (AB0299)
Lohse A., 0939 (POS1314)
Loibner E., 0320 (POS0208)
Loïs B., 0227 (POS0045)
Lois P., 1475 (AB0906-HPR)
Lois-Iglesias A., 1048 (AB0030)
Lojacono A., 0470 (POS0476), 0628 (POS0751), 0633 (POS0760), 1435 (AB0822)
Lojo Oliveira L., 0914 (POS1260)
Lomakin N., 0890 (POS1214)
Lomakina O., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Lombardi F. A., 0294 (POS0163)
Lombardozzi G., 1434 (AB0821)
Londe A. C., 1255 (AB0457)
Long L., 1406 (AB0756), 1429 (AB0809)
Loo W. Y., 0816 (POS1075)
Lopalco G., 0051 (OP0093), 1217 (AB0380)
Lopatina N., 1414 (AB0774)
Lopatnikova J., 0482 (POS0500)
Lopes Barreto D., 0353 (POS0261), 1087 (AB0116)
Lopez Antequera G., 0053 (OP0097)
Lopez Corbeto M., 0929 (POS1296)
López- Corbetó M., 0943 (POS1322)
Lopez de Recalde-Martorell M., 0891 (POS1215)
Lopez Dominguez L. M., 1141 (AB0230)
López Gloria K., 1117 (AB0185), 1397 (AB0734)
López I Gómez M., 0960 (POS1355)
Lopez Isac E., 0008 (OP0014)
Lopez J. D., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Lopez Lasanta M., 1158 (AB0264)
Lopez M., 1132 (AB0211)
López Montilla M. D., 0769 (POS1001), 1317 (AB0562)
Lopez Pedraza L., 0908 (POS1251), 0910 (POS1253), 1464 (AB0881-HPR), 1475 (AB0906-HPR)
López Robles A., 0628 (POS0752), 1165 (AB0278), 1189 (AB0328)
López-Aldabe K., 0001 (OP0004)
López-Fagúndez M., 1048 (AB0030)
López-González R., 0034 (OP0064)
Lopez-Hoyos M., 0955 (POS1346), 1243 (AB0430)
López-Longo F. J., 0685 (POS0861), 0984 (POS1403)
López-Medina C., 0024 (OP0047), 0193 (OP0316), 0340 (POS0239), 0341 (POS0240), 0342 (POS0242), 0360 (POS0273-HPR), 0469 (POS0475), 0735 (POS0944), 0736 (POS0946), 0737 (POS0948), 0739 (POS0951), 0747 (POS0965), 0750 (POS0969), 0751 (POS0970), 0753 (POS0975), 0755 (POS0977), 0766 (POS0995), 0769 (POS1001), 0920 (POS1272), 0977 (POS1390), 0986 (POS1407), 1245 (AB0432), 1253 (AB0451), 1317 (AB0562)
López-Mejías R., 1046 (AB0026), 1065 (AB0070), 1076 (AB0094), 1076 (AB0096)
López-Nevot M. Á., 0009 (OP0017)
Lopez-Pedrera C., 0020 (OP0038), 0426 (POS0394), 0469 (POS0475), 0769 (POS1001), 1317 (AB0562)
López-Romero P., 1157 (AB0261)
López-Uriarte G. A., 1439 (AB0830)
Løppenthin K., 0095 (OP0159-HPR)
Lora V., 1318 (AB0563)
Lord J., 1426 (AB0803)
Loredo Alanis S. A., 1085 (AB0113)
Loredo Martínez M., 0967 (POS1371)
Lorello A., 0873 (POS1185)
Lorenz H. M., 0171 (OP0283), 0194 (OP0318), 0372 (POS0293), 0467 (POS0472), 0670 (POS0834), 0915 (POS1261), 1047 (AB0028)
Lorenzin M., 0134 (OP0223), 0726 (POS0927), 0742 (POS0956), 0894 (POS1221), 1308 (AB0549)
Lorenzo I., 0418 (POS0375)
Lorenzo-Alvarez J., 1326 (AB0577)
Lorenzon M., 0618 (POS0735)
Loricera J., 0034 (OP0064), 0035 (OP0065), 0490 (POS0513), 1208 (AB0366)
Łosińska K., 0048 (OP0089)
Łosińska K., 1135 (AB0219)
Lotfy Fayed H., 1175 (AB0297)
Lotz M., 0418 (POS0375)
Lou Y., 0049 (OP0090)
Loubiri I., 0466 (POS0469)
Loughrey S., 1243 (AB0429)
Louis Sidney F., 0258 (POS0095)
Louis-Sidney F., 0735 (POS0945)
Loureiro M., 0820 (POS1083)
Lourido L., 0306 (POS0185), 0425 (POS0392)
Louthrenoo W., 0218 (POS0028)
Louzada P., 0582 (POS0676)
Louzir B., 0774 (POS1012), 1066 (AB0071), 1095 (AB0134), 1116 (AB0182), 1281 (AB0507), 1281 (AB0509), 1285 (AB0518), 1286 (AB0519), 1442 (AB0836), 1443 (AB0840)

Lovan C., 0786 (POS1030), 0788 (POS1032)
Love T., 0131 (OP0220)
Lovell D. J., 0201 (LB0004), 0245 (POS0076)
Lovik A., 0484 (POS0503), 1083 (AB0109)
Lovriha S., 1391 (AB0719)
Lövström B., 0001 (OP0003), 0898 (POS1230), 1023 (POS1476-HPR)
Low A., 0301 (POS0176), 0989 (POS1411), 0990 (POS1413)
Low C., 0470 (POS0477), 0859 (POS1162)
Low S., 0223 (POS0035)
Lowe J., 0167 (OP0275-PARE)
Löwe P., 0191 (OP0312)
Loyola Correa T., 1004 (POS1440)
Loza E., 0523 (POS0579)
Loza M. J., 0790 (POS1036)
Lozano Rivas N., 0610 (POS0721)
Lozenski K., 0108 (OP0180), 0453 (POS0447), 0468 (POS0474), 0533 (POS0599), 1127 (AB0205), 1128 (AB0207)
Lozinsky S., 0192 (OP0314)
Lu C. H., 0599 (POS0700), 1440 (AB0832)
Lu F., 1122 (AB0197)
Lu L., 0002 (OP0005), 0022 (OP0042), 0122 (OP0202), 0122 (OP0203), 0144 (OP0235)
Lu W., 1315 (AB0559)
Lu X., 1122 (AB0197)
Lubberts E., 1058 (AB0052)
Luber M., 0391 (POS0328)
Lubrano D., 1475 (AB0905-HPR)
Lubrano DI Scorpaniello E., 1271 (AB0488)
Lubrano E., 0139 (OP0229), 0183 (OP0298), 0726 (POS0927), 0786 (POS1030), 0906 (POS1246), 1307 (AB0548)
Lucas C., 0431 (POS0403)
Lucasson F., 0183 (OP0298)
Lucchesi D., 0079 (OP0136)
Lucchini G., 1326 (AB0578)
Lucchino B., 0047 (OP0086), 1016 (POS1463-HPR), 1017 (POS1464-HPR)
Luchetti M. M., 0809 (POS1061)
Luchikhina E., 0916 (POS1263), 0917 (POS1266), 1384 (AB0705), 1442 (AB0837)
Luciani A., 0027 (OP0052)
Lucioni E., 0985 (POS1406)
Lüders S., 0342 (POS0241), 0456 (POS0453), 0756 (POS0979), 0813 (POS1069)
Ludolph I., 0391 (POS0328)
Lueck A., 0165 (OP0272)
Lugo-Perez S., 0463 (POS0463), 0473 (POS0482), 0473 (POS0483), 0478 (POS0491), 0510 (POS0552), 0511 (POS0553), 0515 (POS0562), 0816 (POS1074), 0978 (POS1392), 0983 (POS1402), 0984 (POS1404), 1087 (AB0117), 1189 (AB0329)
Lui G., 0460 (POS0459)
Luime J., 0289 (POS0151), 0807 (POS1057)
Luis M., 0233 (POS0055), 0481 (POS0496), 0695 (POS0878), 1101 (AB0147)
Luis R., 0730 (POS0933), 1377 (AB0689)
Luissi A., 1196 (AB0342)
Lujano Negrete A. Y., 0893 (POS1220), 1345 (AB0624), 1360 (AB0657), 1361 (AB0658), 1439 (AB0830), 1444 (AB0842), 1445 (AB0843), 1457 (AB0867-HPR), 1463 (AB0880-HPR)
Luk T. H., 0687 (POS0865)
Lukač N., 0226 (POS0042)
Lukanova R., 0885 (POS1205)
Lukas C., 0019 (OP0035), 0028 (OP0053), 0054 (OP0098), 0080 (OP0138), 0128 (OP0214), 0379 (POS0306), 0380 (POS0308), 0518 (POS0566), 0559 (POS0641), 0770 (POS1003), 0820 (POS1082), 0902 (POS1239), 1148 (AB0247), 1273 (AB0493)
Lukic T., 0564 (POS0651)
Lukina G., 0256 (POS0093), 0731 (POS0937), 0772 (POS1008), 1084 (AB0111), 1131 (AB0209), 1146 (AB0241), 1147 (AB0245), 1265 (AB0475), 1383 (AB0703), 1442 (AB0837)
Lukyanov S., 0014 (OP0027)
Lukyanova E., 0709 (POS0903)
Lumetti F., 0906 (POS1246)
Lumley M., 0878 (POS1191)
Lundberg I. E., 0093 (OP0156-HPR), 0196 (OP0321), 0206 (POS0008), 0697 (POS0883)
Lundberg K., 0206 (POS0009), 0996 (POS1425)
Lundquist C., 0014 (OP0026)
Lunt M., 0110 (OP0183), 0148 (OP0241)
Luo H., 0629 (POS0754)
Luo J., 0028 (OP0054), 0888 (POS1211)
Luo S. F., 0024 (OP0047), 0218 (POS0028)
Luo W. L., 0593 (POS0692)
Luo Y., 1063 (AB0066)
Lupo C., 0582 (POS0676)
Luppi F., 0897 (POS1228)
Luppino A. F., 0870 (POS1178), 0872 (POS1182)
Luqmani R., 0029 (OP0055), 0034 (OP0063), 0289 (POS0152-HPR), 1010 (POS1453)
Luque Huertas R. M., 0020 (OP0038)
Luque-Tévar M., 0020 (OP0038), 0426 (POS0394), 0469 (POS0475), 0769 (POS1001), 1317 (AB0562)
Lurier E., 1050 (AB0034)
Lutkova T., 0969 (POS1374)
Lutskii A., 0890 (POS1214)
Luttikhuis T., 0198 (OP0324-PARE)
Luursen-Masurel N., 1087 (AB0116)
Luyten F. P., 1337 (AB0602)
Luz K., 0198 (LB0001)
Lv C., 0387 (POS0320)
LV C., 0696 (POS0879)
LV P., 0657 (POS0810)
Ly K., 0397 (POS0338)
Lyall D., 0129 (OP0215)
Lybimova N., 0246 (POS0078), 0927 (POS1293)
Lydon H., 1052 (AB0039)
Lykkegaard J. J., 0352 (POS0260)
Lyman S., 0367 (POS0285)
Lynch M., 0158 (OP0259-HPR)
Lysunets T., 1452 (AB0858)
Lytkina K., 0731 (POS0937), 1146 (AB0241), 1265 (AB0475), 1383 (AB0703)

M N J., 0900 (POS1235)
MA D., 0022 (OP0042)
Ma J. D., 0456 (POS0452), 1091 (AB0125)
MA K. S. K., 0048 (OP0088), 0061 (OP0110), 0145 (OP0237), 0947 (POS1329)
Ma K. S. K., 0430 (POS0402), 0648 (POS0791)
Ma L., 0307 (POS0187), 0307 (POS0187), 0657 (POS0810), 0661 (POS0815), 0661 (POS0816), 0661 (POS0816), 0661 (POS0817)
MA N., 0157 (OP0257)
MA Y., 1025 (POS1481-HPR)
Maarseveen T., 0087 (OP0147)
Maas F., 0024 (OP0046), 0769 (POS1002)
Maas M., 1449 (AB0850)
Maassen J. M., 0466 (POS0470), 0471 (POS0479)
Maat B., 0238 (POS0063-PARE)
Maatallah K., 0526 (POS0586), 0526 (POS0587), 0774 (POS1013), 0776 (POS1018), 0921 (POS1274), 1091 (AB0124), 1095 (AB0133), 1101 (AB0148), 1102 (AB0150), 1112 (AB0171), 1117 (AB0186), 1118 (AB0187), 1119 (AB0189), 1119 (AB0191), 1278 (AB0501), 1283 (AB0512), 1286 (AB0520), 1379 (AB0693), 1399 (AB0740), 1399 (AB0741), 1400 (AB0742), 1400 (AB0744)
Maatoug F., 1095 (AB0134)
Maaty A., 0923 (POS1278)
Mabey B., 0458 (POS0456)
Mabrouk Y., 0526 (POS0586), 0526 (POS0587), 1117 (AB0186), 1119 (AB0189), 1119 (AB0191)
Maccarter D., 0845 (POS1132), 0846 (POS1133)
Macchioni P., 0355 (POS0265)
MacDermott E., 0241 (POS0069)
Maceiras F., 1303 (AB0542)
Maceiras-Pan F., 1326 (AB0577)
Macfarlane G., 0131 (OP0220), 0217 (POS0027)
Macgregor A., 0110 (OP0183), 0210 (POS0018), 0223 (POS0035)
MacGregor A., 0467 (POS0471)
Machado Escobar M., 0635 (POS0763), 0730 (POS0933), 1196 (AB0342), 1377 (AB0689)
Machado P. M., 0024 (OP0047), 0189 (OP0309), 0199 (LB0002), 0230 (POS0051), 0231 (POS0052), 0340 (POS0238), 1368 (AB0674)
Machado P., 0002 (OP0006), 0153 (OP0251), 0173 (OP0286), 0175 (OP0287), 0175 (OP0288), 0221 (POS0032), 0233 (POS0055), 0740 (POS0952), 0872 (POS1183)
Machet T., 0664 (POS0822)
Machlab K., 0320 (POS0207)
Macia L., 0019 (OP0035)
Macias M., 0904 (POS1242)
Macieira J. C., 0582 (POS0676)
Maciukiewicz M., 0011 (OP0020), 0090 (OP0150), 0688 (POS0866)
Mackay D., 0129 (OP0215)
Mackay J. W., 0825 (POS1091), 0825 (POS1092)
Mackay K., 1476 (AB0909-HPR)
Mackay M., 0177 (OP0289)
Mackie S., 1441 (AB0834)
Maclean M., 0768 (POS0999)
Macrae V., 1057 (AB0051)
Madan A., 0591 (POS0689)
Madeira N., 0354 (POS0263)
Madej M., 1434 (AB0820)
Madjid M., 0198 (LB0001)
Madrid García A., 0896 (POS1225), 0908 (POS1251), 0910 (POS1253)
Madsen C. M. T., 0159 (OP0261-HPR)
Madsen S. F., 0444 (POS0431), 0742 (POS0955), 1064 (AB0067)
Madureira P., 0812 (POS1067), 1299 (AB0536)
Madyanov I., 1335 (AB0596)
Maeda T., 0423 (POS0386), 0998 (POS1429)
Maejima Y., 0395 (POS0336)
Maeoka A., 1063 (AB0065)
Maestri Brittain J., 1202 (AB0355)
Magallares B., 0666 (POS0827), 1093 (AB0129), 1365 (AB0666), 1426 (AB0804)
Mageswaren E., 0053 (OP0096)
Maghraoui A., 0481 (POS0497)
Magira E., 1381 (AB0697)
Maglevaniy S., 0259 (POS0098), 1172 (AB0292)
Magnaguagno F., 0097 (OP0161)
Magnani L., 0672 (POS0837), 1241 (AB0425)
Magne D., 0431 (POS0404)
Magnusson K., 0047 (OP0087), 1372 (AB0678)
Magnusson M., 1184 (AB0318)
Magrey M., 0024 (OP0047), 0333 (POS0228), 0704 (POS0895), 0713 (POS0908), 0720 (POS0919), 0723 (POS0924), 0724 (POS0925), 1288 (AB0523)
Magri S., 1133 (AB0214)
Magro Checa C., 0911 (POS1256)
Magro F., 0919 (POS1270), 1339 (AB0608)
Magro R., 1068 (AB0077)
Maguire S., 0027 (OP0051), 0734 (POS0942), 0738 (POS0949), 0747 (POS0964), 0766 (POS0995), 0768 (POS0999)
Mahadevan S., 1396 (AB0733), 1415 (AB0779)
Mahadzir H., 1105 (AB0155)
Mahapatra R., 0239 (POS0065-PARE), 0343 (POS0244), 0744 (POS0960), 0745 (POS0961), 0762 (POS0988), 0762 (POS0989), 0763 (POS0990)
Mahbouba J., 0466 (POS0469), 1051 (AB0037), 1198 (AB0346), 1390 (AB0718), 1395 (AB0728), 1414 (AB0775)
Mahendrakar S., 1342 (AB0616)
Maher T., 0671 (POS0835), 1008 (POS1449)
Maheshwari R., 0981 (POS1397), 1143 (AB0235), 1413 (AB0773)
Maheu E., 0364 (POS0279)
Mahfoudhi H., 1116 (AB0182)
Mahler M., 0463 (POS0464)
Mahmoud Fahmy Mansour M., 0513 (POS0556), 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1249 (AB0443), 1437 (AB0826)
Mahmoud I., 0481 (POS0497), 0768 (POS1000), 1106 (AB0158), 1119 (AB0190), 1285 (AB0517), 1341 (AB0611), 1395 (AB0730), 1396 (AB0731), 1396 (AB0732)
Mahmoud K., 0300 (POS0175), 0625 (POS0746)
Mahmoud S., 1151 (AB0251)
Maho E., 0586 (POS0683)
Mahr A., 0349 (POS0254), 0667 (POS0828), 1222 (AB0388)
Mahroug M., 1162 (AB0274)

Mai T., 0590 (POS0688)
Maidana M., 1120 (AB0193)
Maier A., 0086 (OP0145)
Maigné G., 0397 (POS0338), 0669 (POS0831)
Maillefert J. F., 0358 (POS0270-HPR), 0843 (POS1129)
Mainuddin M., 0448 (POS0440)
Maioli G., 0229 (POS0048), 0284 (POS0145)
Maiorana A., 1241 (AB0425)
Maiz O., 0034 (OP0064), 0035 (OP0065), 0952 (POS1340), 0967 (POS1371)
Maiz-Alonso O., 0032 (OP0060), 1141 (AB0230), 1225 (AB0396), 1412 (AB0771)
Majdan M., 0309 (POS0191), 1424 (AB0800), 1434 (AB0820)
Majdoub F., 1277 (AB0499)
Majewski D., 0384 (POS0316)
Majima M., 0615 (POS0730)
Makarov M., 0259 (POS0098), 1172 (AB0292), 1329 (AB0585), 1388 (AB0714)
Makarov S., 0259 (POS0098), 1329 (AB0585), 1388 (AB0714)
Makatsariya A., 0619 (POS0737)
Makay B., 0942 (POS1320)
Makhloufi R., 0955 (POS1345), 1393 (AB0723), 1410 (AB0768)
Makhloufi-Dahou C., 1144 (AB0237)
Makol A., 0106 (OP0177), 0672 (POS0836), 0673 (POS0838)
Makri S., 0161 (OP0264-HPR), 0238 (POS0064-PARE), 0239 (POS0065-PARE), 0343 (POS0244), 0744 (POS0960), 0745 (POS0961), 0762 (POS0988), 0762 (POS0989), 0763 (POS0990), 0889 (POS1213), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Maksymowych W. P., 0024 (OP0047), 0083 (OP0141), 0085 (OP0144), 0089 (OP0149), 0153 (OP0251), 0153 (OP0252), 0221 (POS0032), 0224 (POS0037), 0704 (POS0896), 0720 (POS0918), 0831 (POS1101), 0943 (POS1323), 1334 (AB0594)
Malandrino D., 0889 (POS1212)
Malatestinic W., 1034 (POS1499-PARE)
Malatino L., 0388 (POS0322), 1135 (AB0217), 1135 (AB0218)
Malattia C., 0097 (OP0161)
Malayeri A., 0653 (POS0802)
Maldini C., 0875 (POS1188), 1196 (AB0342)
Maldonado F., 0874 (POS1186)
Maldonado Ficco H., 0382 (POS0312), 1133 (AB0214)
Maldonado G., 0376 (POS0302)
Maldonado M. A., 1081 (AB0107)
Maldonado-Cañón K., 0479 (POS0493), 1081 (AB0106)
Maldonado-Cocco J., 0024 (OP0047)
Malfait F., 0275 (POS0126)
Malhamé I., 0235 (POS0058-PARE)
Maliandi M. D. R., 0576 (POS0667)
Mallat Y., 0925 (POS1287), 0926 (POS1289), 0926 (POS1290), 1417 (AB0784)
Mallen C., 1026 (POS1483-HPR)
Malley T., 0289 (POS0152-HPR)
Mallick-Searle T., 0823 (POS1088)
Mallinson M., 0167 (OP0275-PARE)
Malliou N., 0238 (POS0064-PARE)
Malmberg C., 0617 (POS0734)
Malmhäll-Bah E., 0012 (OP0022)
Malmstrom H., 0098 (OP0164)
Malmström V., 0001 (OP0003), 0038 (OP0072), 0203 (POS0003), 0206 (POS0008), 0206 (POS0009), 0429 (POS0400)
Malvano Y. S., 0576 (POS0667)
Malyshenko O., 0277 (POS0131), 1344 (AB0621), 1416 (AB0780), 1443 (AB0838)
Mamadapur M., 1396 (AB0733), 1415 (AB0779)
Mammadova K., 1251 (AB0448)
Mammar N., 0529 (POS0592), 0571 (POS0659)
Mamoto K., 0465 (POS0466), 0808 (POS1059), 1012 (POS1456-HPR), 1086 (AB0115)
Mamus M., 0424 (POS0389), 1056 (AB0048), 1057 (AB0049), 1062 (AB0061), 1108 (AB0163), 1444 (AB0841)
Mamutova A., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Mancini P., 0134 (OP0223)
Mancuso G., 0907 (POS1247), 0960 (POS1356)
Mancuso P., 0037 (OP0069)
Mancuso S., 0583 (POS0677), 0902 (POS1238), 0903 (POS1240), 1160 (AB0269), 1384 (AB0704)
Mandai K., 0195 (OP0319), 0491 (POS0514), 0492 (POS0517), 0808 (POS1059), 1086 (AB0115), 1329 (AB0583), 1431 (AB0813)
Mande P., 1043 (AB0019)
Manderson S., 0289 (POS0152-HPR)
Mandl L. A., 0367 (POS0285)
Mandl P., 0314 (POS0197), 0850 (POS1141)
Mandl T., 0308 (POS0189)
Mandla R., 0236 (POS0060-PARE)
Maneiro J. R., 0766 (POS0996)
Manfrè V., 0618 (POS0735)
Manfredi A., 0030 (OP0056), 0324 (POS0214)
Mangat P., 1230 (AB0403)
Manger B., 0064 (OP0116), 0194 (OP0318)
Manger K., 0194 (OP0318)
Mangoni A. A., 0324 (POS0214)
Manh C. T., 0150 (OP0245)
Mani M., 0981 (POS1397), 1413 (AB0773)
Maniccia A., 0446 (POS0435), 0710 (POS0905), 0712 (POS0907), 0800 (POS1047), 0886 (POS1207)
Mankad R., 0056 (OP0102), 0672 (POS0836)
Mankia K., 0463 (POS0464), 0482 (POS0499)
Mann C., 0714 (POS0910)
Mann H., 0678 (POS0849), 1062 (AB0063), 1234 (AB0412)
Mannucci Walter P., 0568 (POS0655)
Manolache A., 1267 (AB0480)
Manolakou T., 0021 (OP0040)
Manoni M., 0292 (POS0160-HPR)
Manrique A., 0397 (POS0338)
Manrique Arija S., 0034 (OP0064), 0035 (OP0065), 0068 (OP0123), 0323 (POS0211), 0344 (POS0246), 0494 (POS0521), 1208 (AB0366), 1453 (AB0859-HPR), 1456 (AB0865-HPR)
Mansfield C., 0237 (POS0062-PARE)
Mansourian M., 0997 (POS1427)
Mantel E., 0012 (OP0021)
Mantha A., 0208 (POS0012), 0348 (POS0252), 0965 (POS1366)
Manzi S., 0177 (OP0289), 0586 (POS0683)
Manzo A., 0521 (POS0575), 0913 (POS1258)
Manzotti A., 1367 (AB0671)
Mao H. A., 0648 (POS0792)
Mao Z., 0430 (POS0401)
Mapelli C., 0940 (POS1316), 0941 (POS1317)
Maranini B., 0985 (POS1406)
Maraş Y., 1124 (AB0200), 1124 (AB0201), 1182 (AB0314)
Maravic M., 0901 (POS1236), 0901 (POS1237)
March L., 0276 (POS0129), 0358 (POS0269-HPR), 0358 (POS0270-HPR), 0362 (POS0276), 0654 (POS0804)
Marchenkova L., 0209 (POS0016), 0239 (POS0066-PARE), 0838 (POS1118), 0924 (POS1282), 1020 (POS1469-HPR), 1347 (AB0627)
Marchese M., 0026 (OP0049)
Marchesoni A., 0284 (POS0145), 0726 (POS0927), 0790 (POS1035), 1271 (AB0488), 1308 (AB0550)
Marchi I., 0985 (POS1406)
Marchisio E., 0229 (POS0048)
Marcos J., 0759 (POS0984)
Marcot C., 1373 (AB0680)
Marcus F., 0040 (OP0075), 1422 (AB0796)
Marder B., 0840 (POS1122)
Marelli L., 0940 (POS1316), 0941 (POS1317)
Marelli S., 0778 (POS1021), 0809 (POS1061), 1271 (AB0488)
Marenco J. L., 0469 (POS0475)
Marenco Maldonado J., 1200 (AB0351)
Marengo A., 0393 (POS0331)
Maresio E., 0878 (POS1192)
Margarida-de Castro A., 0601 (POS0703), 0966 (POS1370)
Maria A., 0172 (OP0284)
Maria Das Chagas Medeiros M., 0625 (POS0747), 0999 (POS1430)
Maria Kakehasi A., 0582 (POS0676), 0909 (POS1252), 1448 (AB0848)
Mariach C., 0576 (POS0667)
Marí-Alfonso B., 0350 (POS0256), 0987 (POS1408), 0987 (POS1409)
Mariampillai K., 0388 (POS0323)
Maricheva O., 1393 (AB0724)
Mariem S., 0835 (POS1110), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1368 (AB0672), 1368 (AB0673), 1390 (AB0717), 1397 (AB0736), 1411 (AB0770)
Mariette X., 0007 (OP0012), 0078 (OP0135), 0108 (OP0180), 0109 (OP0181), 0175 (OP0287), 0199 (LB0002), 0231 (POS0052), 0258 (POS0095), 0453 (POS0447), 0471 (POS0478), 0533 (POS0599), 0593 (POS0692), 1128 (AB0207)
Marin J., 0759 (POS0984)
Marin Zucaro N., 0759 (POS0984)
Marini R., 0100 (OP0167), 1405 (AB0754)
Marín-Jiménez I., 0916 (POS1264)
Marin-López M. A., 0184 (OP0300)
Marino N. G., 1389 (AB0716)
Marín-Sanz J. A., 0469 (POS0475)
Mariotte D., 0669 (POS0831)
Mariscal A., 1365 (AB0666)
Mariscal-Ocaña R., 1253 (AB0451)
Mariz H., 1448 (AB0848)
Markatseli T., 1107 (AB0161)
Markelova E., 0849 (POS1139), 1350 (AB0631)
Markert R., 0486 (POS0507)
Markéta K., 1238 (AB0420)
Markin A, 1049 (AB0033)
Markina Y., 1049 (AB0033)
Marko J., 0653 (POS0802)
Marko L., 0017 (OP0031)
Markova G., 0259 (POS0099), 0542 (POS0611)
Markova O., 0709 (POS0903)
Markovits D., 0892 (POS1217)
Marks J., 1239 (AB0421)
Marks M., 0009 (OP0016), 0011 (OP0020)
Marotte H., 0172 (OP0284), 0240 (POS0068), 0529 (POS0592), 1067 (AB0074), 1164 (AB0277)
Marozio L., 0628 (POS0751)
Marques A., 0161 (OP0264-HPR)
Marques C., 0909 (POS1252), 1448 (AB0848)
Marquez M., 1032 (POS1496-HPR)
Marquez O., 0904 (POS1242)
Marrakchi R., 1061 (AB0059)
Marrani E., 0247 (POS0079), 0628 (POS0751), 0934 (POS1304)
Mars N., 0004 (OP0007)
Marsal J., 0339 (POS0237)
Marsal S., 0108 (OP0180), 0380 (POS0308), 0453 (POS0447), 0533 (POS0599), 0943 (POS1322), 1042 (AB0015), 1128 (AB0207), 1149 (AB0248), 1158 (AB0264)
Marschall U., 0990 (POS1414)
Marshall M., 0983 (POS1400)
Marsman D., 0399 (POS0343)
Marson P., 1174 (AB0295)
Martín Amada M., 1183 (AB0316)
Martin C., 0417 (POS0373)
Martin Calderon L., 1237 (AB0419)
Martin H., 1062 (AB0062), 1067 (AB0073)
Martin Ibanez J., 1076 (AB0096), 1231 (AB0405), 1231 (AB0406)
Martin L., 0224 (POS0037), 0494 (POS0522), 0867 (POS1174)
Martin M., 0694 (POS0877), 1061 (AB0058)
Martín Martín J. M., 1474 (AB0904-HPR)
Martín Martín M., 1171 (AB0290)
Martin N., 0329 (POS0222), 0580 (POS0671), 1156 (AB0260)
Martin P., 0009 (OP0016)
Martín Pedraz L., 0946 (POS1328)
Martin R., 0797 (POS1044)
Martín-Domenech R., 0820 (POS1081)
Martínez A., 0904 (POS1242)
Martínez Cordellat I., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Martínez González O., 0760 (POS0986), 0952 (POS1340), 0967 (POS1371)
Martinez M., 1475 (AB0907-HPR)
Martinez Prada C., 0908 (POS1251)

Martínez Robles E., 0350 (POS0256), 0693 (POS0875), 0987 (POS1408), 0987 (POS1409), 1192 (AB0333)
Martinez S., 1146 (AB0242), 1163 (AB0275)
Martinez T., 1042 (AB0015), 1106 (AB0159)
Martínez-Barrio J., 0658 (POS0812), 1117 (AB0185), 1239 (AB0422)
Martinez-Costa L., 0032 (OP0060)
Martínez-Feito A., 0546 (POS0617), 1101 (AB0149)
Martínez-Ferrer À., 0296 (POS0168), 1427 (AB0806)
Martínez-Gómez X., 1241 (AB0426)
Martínez-López D., 0050 (OP0091), 0091 (OP0152), 0220 (POS0030), 0621 (POS0740), 0899 (POS1231), 0953 (POS1342), 0963 (POS1362), 0970 (POS1376), 1002 (POS1436), 1226 (AB0397), 1227 (AB0399), 1324 (AB0574), 1377 (AB0688)
Martínez-Martínez L., 1365 (AB0666)
Martínez-Martínez M. U., 0904 (POS1242), 0905 (POS1245)
Martínez-Rodríguez I., 1208 (AB0365)
Martínez-Valle F., 0907 (POS1247)
Martínez-Vidal M. P., 0755 (POS0977), 0820 (POS1081), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070)
Martin-Gutierrez L., 0300 (POS0174)
Martini A., 0201 (LB0004), 0245 (POS0076)
Martini F., 1216 (AB0379)
Martinis F., 0355 (POS0265)
Martin-Nares E., 0904 (POS1242), 0905 (POS1245)
Martinovic M., 0229 (POS0048)
Martín-Penagos L., 1076 (AB0096)
Martins A., 0260 (POS0100), 0318 (POS0204), 0476 (POS0488), 0483 (POS0502), 0718 (POS0914), 0812 (POS1067), 0833 (POS1106), 0836 (POS1113), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1191 (AB0332), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1299 (AB0536), 1432 (AB0816), 1441 (AB0835)
Martins F. R., 0260 (POS0100), 0318 (POS0204), 0476 (POS0488), 0483 (POS0502), 0690 (POS0870), 0718 (POS0914), 0812 (POS1067), 0833 (POS1106), 0836 (POS1113), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1299 (AB0536), 1432 (AB0816), 1441 (AB0835)
Martins P., 0388 (POS0323), 0690 (POS0870), 0692 (POS0872), 1250 (AB0445)
Martín-Varillas J. L., 0032 (OP0060), 0050 (OP0091), 0091 (OP0152), 0220 (POS0030), 0621 (POS0740), 0952 (POS1340), 0960 (POS1357), 0963 (POS1362), 0967 (POS1371), 1225 (AB0396), 1226 (AB0397), 1227 (AB0399), 1412 (AB0771)
Martire V., 0730 (POS0933), 0771 (POS1005), 0887 (POS1208), 1377 (AB0689)
Martusevitch N., 0970 (POS1377)
Martynova A., 1064 (AB0068)
Maruotti N., 1003 (POS1437), 1379 (AB0691)
Maruseac M., 0352 (POS0259)
Marusenko I., 1095 (AB0135)
Marx D., 0467 (POS0472)
Marzaioli V., 0014 (OP0025), 1043 (AB0018), 1479 (AB0916-PARE)
Marzo-Ortega H., 0089 (OP0149), 0153 (OP0252), 0724 (POS0925), 0725 (POS0926), 0728 (POS0930), 0868 (POS1175), 0889 (POS1213), 1277 (AB0500), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Mas A. J., 0610 (POS0721)
Masalova V., 0247 (POS0080), 0931 (POS1299), 0937 (POS1310), 1402 (AB0748)
Masaryk P., 1107 (AB0160)
Mascanfroni I., 1043 (AB0019)
Mascia M. T., 1416 (AB0781)
Masciocchi C., 0954 (POS1344), 0957 (POS1349), 1105 (AB0156)
Masetto A., 0224 (POS0037)
Mashaleh M., 0361 (POS0275-HPR), 1080 (AB0104)
Mashiach T., 0753 (POS0974)
Mashreghi M. F., 0207 (POS0010)
Masiak A., 1434 (AB0820)
Masieh D., 1028 (POS1488-HPR), 1340 (AB0610)
Masini F., 0906 (POS1246), 1475 (AB0905-HPR)
Maslyanskiy A., 0647 (POS0790)
Masneri S., 0530 (POS0593)
Mason A., 0372 (POS0295), 1175 (AB0298), 1233 (AB0409)
Mason J., 0030 (OP0056), 0810 (POS1063)
Mason L., 0175 (OP0287), 0231 (POS0052)
Masri B., 0361 (POS0275-HPR), 1080 (AB0104)
Masson M., 1261 (AB0469)
Mastbergen S., 0825 (POS1091), 0825 (POS1092)
Mastroberti G., 0882 (POS1200), 1399 (AB0739)
Mastroianni C. M., 0902 (POS1238), 0903 (POS1240)
Mat Husin N., 0459 (POS0457)
Mata Arnaiz M. C., 1227 (AB0399)
Mata C., 1065 (AB0070)
Mata-Arnaiz C., 0091 (OP0152)
Mata-Arnaiz M. C., 1226 (AB0397)
Matei A. E., 0121 (OP0201), 0165 (OP0272), 0391 (POS0328), 1238 (AB0420)
Mateus E., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0199 (LB0002), 0872 (POS1183), 0889 (POS1213), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Mathers D., 0330 (POS0223), 1015 (POS1461-HPR)
Mathew A. J., 0089 (OP0149), 0153 (OP0252)
Mathew J., 1205 (AB0360)
Mathew L., 1323 (AB0573)
Mathian A., 1186 (AB0323)
Mathias K., 0208 (POS0012), 0348 (POS0252), 0965 (POS1366)
Mathias L., 0173 (OP0286), 0208 (POS0012), 0348 (POS0252), 0965 (POS1366)
Mathias S., 1203 (AB0357)
Mathieu A., 0628 (POS0751)
Mathot R., 0241 (POS0070)
Mathsson-Alm L., 0206 (POS0009), 1090 (AB0122)
Mathur A., 0581 (POS0672)
Matin R. N., 1010 (POS1453)
Matiyashchuk I., 0612 (POS0725)
Matkava V., 0249 (POS0083), 0918 (POS1267), 1393 (AB0725), 1394 (AB0726)
Matloubian M., 0911 (POS1255)
Matos A., 0182 (OP0297), 0634 (POS0762)
Matsubara T., 0569 (POS0657), 0570 (POS0658)
Matsuda F., 0998 (POS1429)
Matsuda S., 1025 (POS1482-HPR)
Matsui K., 0753 (POS0975), 1181 (AB0311)
Matsui T., 0368 (POS0286)
Matsumoto S., 0536 (POS0603)
Matsumoto Y., 1012 (POS1456-HPR)
Matsuno H., 1150 (AB0249)
Matsushita S., 0492 (POS0516)
Matsuyama F., 0368 (POS0286)
Mattei J. P., 1078 (AB0099)
Matteson E., 0069 (OP0124), 0672 (POS0836), 0673 (POS0838)
Matthijssen X., 0130 (OP0217), 0212 (POS0021), 0259 (POS0097), 0420 (POS0379), 0448 (POS0438), 0486 (POS0506), 1155 (AB0258)
Mattioli I., 0889 (POS1212)
Mattli R., 0095 (OP0158-HPR)
Mattolini L., 0675 (POS0842)
Matucci Cerinic M., 0105 (OP0175), 0778 (POS1021)
Matucci-Cerinic M., 0102 (OP0171), 0105 (OP0176), 0163 (OP0269), 0232 (POS0054), 0355 (POS0264), 0385 (POS0317), 0386 (POS0318), 0387 (POS0321), 0546 (POS0618), 0675 (POS0842), 0694 (POS0877), 0897 (POS1228), 0906 (POS1246), 1032 (POS1495-HPR), 1154 (AB0256), 1157 (AB0261), 1192 (AB0334), 1260 (AB0467), 1331 (AB0588)
Matveychuk O., 1384 (AB0705)
Matz H., 1309 (AB0551)
Matza M., 0841 (POS1124)
Matzneller P., 1404 (AB0752)
Maugesten Ø., 0983 (POS1401)
Maumus M., 0417 (POS0374)
Maurer B., 0090 (OP0150), 0649 (POS0795), 0688 (POS0866), 1233 (AB0411)
Maurits M., 0087 (OP0147), 0403 (POS0348), 0420 (POS0379), 0675 (POS0843)
Mauro D., 0022 (OP0042), 0888 (POS1210)
Maurya S., 1163 (AB0276)
Mavragani C., 0180 (OP0294), 0370 (POS0290), 0656 (POS0807)
Mayana K., 0290 (POS0153-HPR)
Maya-Piña L. V., 0904 (POS1242)
Mayes M., 0162 (OP0266)
Maynard R., 0374 (POS0298)
Mazilu D., 0164 (OP0270), 0681 (POS0854), 0773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690), 1462 (AB0879-HPR)
Mazori D., 0165 (OP0271)
Mazur M., 1337 (AB0601)
Mazur-Nicorici L., 1337 (AB0601)
Mazurov V., 0084 (OP0142), 0191 (OP0311), 0726 (POS0928), 0776 (POS1017), 0777 (POS1019), 0796 (POS1043), 0890 (POS1214), 1095 (AB0135), 1285 (AB0516), 1298 (AB0534), 1302 (AB0540), 1352 (AB0636), 1387 (AB0712)
Mazzei M. A., 0746 (POS0963)
Mazzetti M., 0613 (POS0726)
Mazzoni M., 0097 (OP0161)
Mazzucchelli R., 0144 (OP0234), 0976 (POS1387)
Mazzuoccolo L., 0139 (OP0229)
Mcbeth J., 0757 (POS0980), 1006 (POS1444)
Mccabe C., 0291 (POS0158-HPR)
Mccarron M., 1410 (AB0767)
Mccarthy G., 0841 (POS1124), 0859 (POS1162), 1427 (AB0805)
Mccaskie A., 1052 (AB0039)
Mccaskill R., 0312 (POS0196), 0790 (POS1035), 1287 (AB0522)
Mccasland L., 1315 (AB0559)
McCormick N., 0002 (OP0005), 0122 (OP0202), 0122 (OP0203), 0144 (OP0235)
Mccormick N., 0853 (POS1148)
Mccourt C., 1410 (AB0767)
McCready J., 0157 (OP0258-HPR)
Mccrum C., 1031 (POS1493-HPR)
Mcdearmon-Blondell E., 0237 (POS0062-PARE), 0312 (POS0196), 0790 (POS1035), 1308 (AB0550)
Mcdermott G., 0494 (POS0522)
Mcdonagh J., 1029 (POS1490-HPR)
Mcdonald E. G., 0918 (POS1268)
Mcdonald R., 0139 (OP0229)
Mcgarry T., 0205 (POS0007)
McGarry T., 0423 (POS0387)
Mcgonagle D., 0175 (OP0287), 0231 (POS0052), 0284 (POS0145), 0311 (POS0194), 0721 (POS0920)
Mcgovern A., 0009 (OP0016)
Mcgrath S., 0112 (OP0186)
Mcharry K., 0198 (LB0001)
Mchenry M., 1243 (AB0429)
Mchugh N., 0135 (OP0224), 0369 (POS0288), 0602 (POS0705), 0789 (POS1034), 1426 (AB0803)
McInnes I., 0016 (OP0030), 0039 (OP0074), 0072 (OP0128), 0132 (OP0221), 0140 (OP0230), 0199 (LB0002), 0211 (POS0020), 0316 (POS0200), 0403 (POS0348), 0433 (POS0407), 0569 (POS0656), 0712 (POS0907), 0779 (POS1022), 0782 (POS1026), 0783 (POS1027), 0784 (POS1028), 0797 (POS1044), 0800 (POS1047), 0812 (POS1068), 1159 (AB0265), 1288 (AB0523), 1290 (AB0525), 1291 (AB0526), 1293 (AB0528), 1300 (AB0538)
McKee P., 0161 (OP0265-HPR)
Mckinnell J., 0204 (POS0006)
Mclean R., 0026 (OP0049)
McLean R., 0446 (POS0435)
Mclennan Battleday F., 1478 (AB0913-PARE)
Mcmahan Z., 0674 (POS0840), 1240 (AB0424)
Mcmaster C., 0117 (OP0194), 1212 (AB0371)
Mcmorrow F., 0369 (POS0288)
Mcneil J., 0009 (OP0015)
Mcquitty S., 0377 (POS0303)
Mcreynolds A., 0831 (POS1101)
Mcrorie E., 1134 (AB0215)
Mcveigh J., 0293 (POS0161-HPR)
Mcwilliams D., 0045 (OP0084)
MD Yusof M. Y., 0023 (OP0044), 0030 (OP0057), 0078 (OP0134), 0300 (POS0175), 0625 (POS0746), 1173 (AB0293)
Mease P. J., 0026 (OP0049), 0137 (OP0227), 0139 (OP0229), 0312 (POS0196), 0314 (POS0198), 0316

(POS0200), 0707 (POS0901), 0728 (POS0930), 0777 (POS1020), 0781 (POS1024), 0782 (POS1026), 0783 (POS1027), 0784 (POS1028), 0787 (POS1031), 0788 (POS1032), 0792 (POS1037), 0792 (POS1038), 0797 (POS1044), 0800 (POS1047), 0801 (POS1048), 0801 (POS1049), 0802 (POS1050), 0803 (POS1051), 0823 (POS1088), 1286 (AB0521), 1289 (AB0524), 1291 (AB0526), 1292 (AB0527), 1294 (AB0529), 1300 (AB0538), 1306 (AB0547), 1311 (AB0553), 1316 (AB0560)
Mechergui S., 1421 (AB0793)
Mechid F., 1144 (AB0237)
Mechlin M., 0278 (POS0134)
Medeiros A., 0582 (POS0676)
Medina M. A., 0635 (POS0763), 0730 (POS0933), 0771 (POS1005), 1377 (AB0689)
Meenakshi J., 0638 (POS0769)
Meert L., 0828 (POS1096)
Meerwein S., 1156 (AB0260)
Megat Mohamad Zainuddin P. A., 1346 (AB0626)
Mehl Eide R. E., 0094 (OP0157-HPR)
Mehmli T., 0774 (POS1012)
Mehta B., 0367 (POS0285), 0472 (POS0480)
Mehta N., 0810 (POS1063), 1304 (AB0544)
Meichtry A., 0095 (OP0158-HPR)
Meidan R., 0200 (LB0003), 1181 (AB0312)
Meier C., 0090 (OP0150), 0688 (POS0866)
Meier F., 0971 (POS1379)
Meinderink T., 0086 (OP0145), 0088 (OP0148), 1030 (POS1492-HPR)
Meisalu S., 0183 (OP0298)
Meisel C., 0305 (POS0183), 0623 (POS0744)
Meizlik P., 0596 (POS0696), 0596 (POS0697)
Mejdoub Y., 0837 (POS1115)
Mekinian A., 0037 (OP0068), 0172 (OP0284), 0232 (POS0054)
Mela C., 0585 (POS0681)
Melchiorre F., 0897 (POS1228)
Melchor S., 1208 (AB0366)
Melero R., 0034 (OP0064), 0035 (OP0065), 0490 (POS0513), 0531 (POS0595), 0967 (POS1371)
Meliconi R., 0906 (POS1246)
Melikoglu M., 0349 (POS0254), 0660 (POS0814), 0662 (POS0819), 0663 (POS0820), 0667 (POS0828), 0958 (POS1351), 1207 (AB0364)
Melis M. R., 1032 (POS1495-HPR), 1192 (AB0334)
Melissa P., 0586 (POS0682), 0619 (POS0737), 0628 (POS0751)
Melki I., 0872 (POS1183)
Melkumyan A., 1155 (AB0257)
Mellor A., 1044 (AB0021)
Mellors T., 0478 (POS0492), 1096 (AB0138), 1097 (AB0140)
Melnick J., 0279 (POS0135)
Melo A. K., 1448 (AB0848)
Melo A. T., 0690 (POS0870), 1250 (AB0445)
Melong Pianta Taleng C., 0863 (POS1168)
Melzer M., 0421 (POS0382)
Memlika E., 1360 (AB0655)
Mena-Vázquez N., 0323 (POS0211), 0344 (POS0246), 0469 (POS0475), 0494 (POS0521), 0946 (POS1328), 1453 (AB0859-HPR), 1456 (AB0865-HPR)
Menchen Viso L., 1385 (AB0706)
Mendel A., 0173 (OP0285), 0230 (POS0050), 0235 (POS0058-PARE)
Mendelsohn A. M., 1304 (AB0544)
Mendez Patarroyo P. A., 0479 (POS0493), 1081 (AB0106)
Mendiola-Jimenez A., 1085 (AB0113)
Mendizabal J., 0960 (POS1355), 1132 (AB0211), 1208 (AB0366)
Mendly S., 1464 (AB0882-HPR)
Mendonça J. A., 1423 (AB0798)
Mendoza Mendoza D. V., 1024 (POS1480-HPR)
Menegatti E., 0298 (POS0172), 1039 (AB0008)
Meng A., 0331 (POS0224)
Meng X., 0311 (POS0194), 0802 (POS1050)
Menon B., 1323 (AB0573)
Menor-Almagro R., 0610 (POS0721)
Mensah C., 0828 (POS1097)
Menter A., 1304 (AB0544)
Mentesidou L., 1090 (AB0121)
Menuet D., 0823 (POS1088)
Mera L. E., 0638 (POS0768)
Mera Varela A., 0418 (POS0376), 0524 (POS0581), 0524 (POS0582), 0692 (POS0873), 0935 (POS1306), 1173 (AB0294)
Meraj M., 0042 (OP0078)
Meran M., 1329 (AB0584)
Mercado Velasco D., 1386 (AB0709)
Mercan R., 0731 (POS0935), 0964 (POS1364), 1470 (AB0893-HPR)
Mercé A. L., 0635 (POS0763)
Mercedes Ferreira Caceres M., 0600 (POS0701)
Mercier G., 0128 (OP0214)
Merckaert P., 1127 (AB0205)
Merheb G., 0361 (POS0275-HPR), 1080 (AB0104)
Meric de Bellefon L., 0020 (OP0037), 0066 (OP0119), 0240 (POS0067)
Meridor K., 0200 (LB0003), 1049 (AB0032)
Meriem S., 0522 (POS0577)
Merino Bohóquez V., 1132 (AB0213)
Merkel P. A., 0345 (POS0248), 1213 (AB0373)
Merlo S., 0097 (OP0161)
Merola J. F., 0779 (POS1022), 0786 (POS1030), 1288 (AB0523), 1291 (AB0526), 1293 (AB0528), 1312 (AB0554)
Meroni P. L., 0619 (POS0737)
Merrill J. T., 0075 (OP0131), 0177 (OP0289)
Merrill J., 0076 (OP0132)
Merriman A., 0043 (OP0079)
Mertens J., 0680 (POS0852)
Mertz L., 0655 (POS0805)
Mertz P., 0149 (OP0243)
Mese S., 0191 (OP0313)
Mesnyankina A., 1168 (AB0284), 1184 (AB0319), 1185 (AB0320)
Messaoudi M., 0352 (POS0259)
Messaykeh J., 0361 (POS0275-HPR), 1080 (AB0104)
Messer L., 0170 (OP0282), 0736 (POS0947)
Messiniti V., 1165 (AB0279)
Metoui L., 0774 (POS1012), 0925 (POS1287), 0926 (POS1289), 0926 (POS1290), 1066 (AB0071), 1095 (AB0134), 1116 (AB0182), 1281 (AB0507), 1281 (AB0509), 1285 (AB0518), 1286 (AB0519), 1417 (AB0784), 1442 (AB0836), 1443 (AB0840)
Metzger D., 0149 (OP0243), 0151 (OP0247)
Meurot C., 0417 (POS0373)
Mevorach D., 0892 (POS1217)
Meyer A., 0149 (OP0243), 0151 (OP0247), 0694 (POS0876), 1373 (AB0680)
Meyer M., 0535 (POS0602), 1013 (POS1458-HPR)
Meyer S. E., 0158 (OP0260-HPR)
Meyer-Olson D., 0158 (OP0260-HPR), 0758 (POS0983)
Meyers A. B., 0943 (POS1323)
Meysami A., 1406 (AB0756)
Miarons-Font M., 0898 (POS1229)
Miccoli M., 0906 (POS1246)
Miceli Richard C., 0228 (POS0046), 0534 (POS0600)
Michalska M., 1126 (AB0203)
Michaud K., 0401 (POS0344), 0468 (POS0474)
Michaud M., 1204 (AB0358), 1412 (AB0772)
Michelsen B., 0063 (OP0114), 0082 (OP0140), 0126 (OP0210), 0131 (OP0220), 0133 (OP0222), 0217 (POS0027)
Micheroli R., 0462 (POS0461)
Michielsens C., 0310 (POS0193)
Micu M., 0519 (POS0569)
Middaugh N., 1125 (AB0202)
Middelkamp M., 0937 (POS1311)
Middelkoop H., 0603 (POS0708), 0604 (POS0709), 0606 (POS0714)
Midtbøll Ørnbjerg L., 0131 (OP0220), 0217 (POS0027)
Midtvedt Ø., 0104 (OP0174), 0689 (POS0867), 1245 (AB0433)
Miede C., 0101 (OP0170), 0162 (OP0266), 0674 (POS0840)
Miehlke G., 1385 (AB0707)
Miele V., 0897 (POS1228)
Mielke M., 0129 (OP0216), 0380 (POS0309), 0381 (POS0311)
Mielle J., 0019 (OP0035)
Mielnik P., 0934 (POS1305), 1392 (AB0722)
Migaw H., 0466 (POS0469)
Migliore A., 1331 (AB0588)
Migos M., 0879 (POS1194)
Migowa A., 1395 (AB0729)
Miguélez R., 0952 (POS1340)
Mihai C., 0232 (POS0054), 0519 (POS0569), 0694 (POS0877)
Mihailov C., 1380 (AB0695)
Mihaylova G., 1036 (AB0002)
Mijiyawa M., 0776 (POS1016), 0927 (POS1291)
Mikhnevich E., 1350 (AB0632)
Mikkelsen S., 0866 (POS1171)
Miladi S., 0292 (POS0159-HPR), 0481 (POS0497), 0522 (POS0577), 0835 (POS1110), 1030 (POS1491-HPR), 1113 (AB0173), 1113 (AB0174), 1117 (AB0184), 1118 (AB0188), 1277 (AB0499), 1332 (AB0590), 1333 (AB0592), 1333 (AB0593), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1368 (AB0672), 1368 (AB0673), 1381 (AB0698), 1390 (AB0717), 1397 (AB0736), 1411 (AB0770), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Milanesi A., 0029 (OP0055), 0347 (POS0250), 0668 (POS0830)
Milatz F., 0246 (POS0077), 0936 (POS1309)
Milene Cardozo F., 1440 (AB0833)
Miles S., 0210 (POS0018)
Milionis C., 1107 (AB0161)
Millán Arciniegas A. M., 0666 (POS0827), 1093 (AB0129), 1365 (AB0666), 1426 (AB0804)
Millar N. L., 0211 (POS0020)
Miller J., 0042 (OP0078)
Miller M., 0787 (POS1031), 1293 (AB0528), 1297 (AB0532)
Mills S., 0374 (POS0298)
Milnes L., 0235 (POS0057-PARE), 0290 (POS0154-HPR)
Min H. K., 1260 (AB0466)
Min M., 0165 (OP0271)
Minami Y., 1329 (AB0583)
Mina-Osorio P., 0585 (POS0681), 0595 (POS0694)
Minatsuki S., 1168 (AB0285)
Mindeholm L., 0211 (POS0020)
Minden K., 0099 (OP0165), 0244 (POS0075), 0246 (POS0077), 0247 (POS0079), 0882 (POS1199), 0883 (POS1202), 0932 (POS1301), 0934 (POS1304), 0936 (POS1309), 0943 (POS1321), 0945 (POS1325)
Minervina A., 0204 (POS0004)
Minet N., 0018 (OP0034)
Mingolla S., 0044 (OP0082-PARE), 0889 (POS1213), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Minguez M., 1208 (AB0366)
Mínguez S., 0891 (POS1215)
Minoda S., 0492 (POS0516)
Minoia F., 0940 (POS1316), 0941 (POS1317)
Min-Oo G., 0331 (POS0224)
Miquilin A., 1462 (AB0878-HPR)
Miranda D., 0559 (POS0642), 1078 (AB0098), 1200 (AB0350)
Miranda García M. J., 1341 (AB0612)
Miranda J., 0582 (POS0676)
Miranda-Carus M. E., 1047 (AB0027)
Miranda-Filloy J. A., 1076 (AB0096)
Miri S., 0774 (POS1013), 0776 (POS1018), 1102 (AB0150), 1118 (AB0187), 1283 (AB0512), 1285 (AB0518), 1286 (AB0519)
Miron M., 0312 (POS0195)
Mirrahimi M., 0011 (OP0020)
Mirza A., 0333 (POS0227)
Mirza S., 0367 (POS0285)
Misaki K., 0536 (POS0603)
Misasi R., 0902 (POS1238)
Miserocchi E., 0940 (POS1316), 0941 (POS1317)
Mishima K., 0449 (POS0441)
Mishra S., 0600 (POS0701)
Misko K., 1335 (AB0596)
Misse R. G., 0699 (POS0887)
Mistry P., 0078 (OP0135)
Mitchell C., 1050 (AB0034)
Mithal A., 0851 (POS1143)

Mitrovic S., 0052 (OP0094), 0360 (POS0274-HPR), 1412 (AB0772)
Miyagi T., 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1437 (AB0826)
Miyagishi H., 1152 (AB0253)
Miyamoto T., 1152 (AB0253)
Miyara M., 0388 (POS0323)
Miyazaki Y., 0329 (POS0221)
Mizokami A., 0581 (POS0674)
Mizukawa K., 0665 (POS0824)
Mizuki S., 0449 (POS0441)
Mizusaki M., 0961 (POS1358), 1169 (AB0287), 1223 (AB0390)
Mizushima I., 0956 (POS1348), 1407 (AB0760)
Mkinsi O., 0992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811)
Mlakar G., 0941 (POS1318)
Mo Y., 0456 (POS0452), 1091 (AB0125), 1174 (AB0296), 1225 (AB0394), 1227 (AB0398)
Moaaz M., 1197 (AB0345)
Moalla M., 1286 (AB0520)
Mobasheri A., 0418 (POS0376)
Mochizuki M., 0113 (OP0187)
Mockenhaupt L. M., 0091 (OP0151)
Moctezuma-Ríos J. F., 0904 (POS1242), 0905 (POS1245)
Modesto Dos Santos J. L., 0960 (POS1355)
Mody G., 1296 (AB0531)
Moeller B., 0131 (OP0220), 0323 (POS0212), 1296 (AB0531)
Moeller Pedersen F., 0006 (OP0010)
Moenkemoeller K., 0945 (POS1325)
Moes D. J., 0911 (POS1256)
Moezinia C., 0828 (POS1097)
Moga E., 0666 (POS0827)
Mogard E., 0339 (POS0237)
Mogensen M., 0283 (POS0144), 1312 (AB0554)
Moggi Pignone A., 0105 (OP0176), 0385 (POS0317), 0897 (POS1228), 1032 (POS1495-HPR)
Mohamed G., 0975 (POS1385)
Mohamed Hoesein F., 0993 (POS1419), 1430 (AB0812)
Mohamed M. E., 0805 (POS1054)
Mohamed Said M. S., 0053 (OP0096), 1177 (AB0302)
Mohamed Shehata R., 1197 (AB0345)
Mohamed Y., 0525 (POS0585), 1063 (AB0064), 1111 (AB0169), 1120 (AB0192), 1193 (AB0337), 1194 (AB0339), 1472 (AB0897-HPR)
Mohammadnezhad L., 0301 (POS0177)
Mohammed E., 1144 (AB0236)
Mohan S., 0651 (POS0799), 0656 (POS0808), 1126 (AB0203)
Mohannad N., 1197 (AB0345)
Mohd A., 1015 (POS1460-HPR)
Mohd Noor N., 0459 (POS0457), 1015 (POS1460-HPR)
Mohd R., 0611 (POS0723)
Mohd Yusoof H., 1469 (AB0891-HPR)
Mohd Zain M., 0459 (POS0457), 0837 (POS1114), 1346 (AB0626), 1469 (AB0891-HPR)
Mohd. Mokhtar A., 0053 (OP0096)
Moineddin R., 0943 (POS1323)
Moinzadeh P., 0670 (POS0834)
Moiseev S., 0004 (OP0008)
Moiseeva O., 0890 (POS1214)
Mok C. C., 0298 (POS0171), 0638 (POS0769), 0639 (POS0771), 0640 (POS0772), 0640 (POS0773)
Molberg Ø., 0104 (OP0174), 0689 (POS0867), 1245 (AB0433)
Molimard J., 0939 (POS1314)
Molina C., 0303 (POS0180)
Molina Collada J., 0658 (POS0812), 0984 (POS1403), 1117 (AB0185)
Moll M., 0247 (POS0079), 0934 (POS1304)
Molla Ismail Sali A., 0184 (OP0299), 0523 (POS0580), 0733 (POS0941)
Møller Døhn U., 0352 (POS0260), 1202 (AB0355)
Möller I., 0845 (POS1132), 0846 (POS1133)
Möller S., 0006 (OP0010), 1468 (AB0890-HPR)
Møller T., 0352 (POS0260)
Molloy E., 0747 (POS0964), 0891 (POS1216), 1211 (AB0370)
Molteni E., 0903 (POS1240), 1143 (AB0234), 1160 (AB0269)
Moltó A., 0024 (OP0047), 0181 (OP0295), 0308 (POS0188), 0343 (POS0243), 0360 (POS0273-HPR), 0534 (POS0600), 0736 (POS0946), 0753 (POS0975)
Monaghan M., 0015 (OP0028), 0205 (POS0007)
Monahan R., 0603 (POS0708), 0604 (POS0709), 0606 (POS0714)
Moncer R., 0856 (POS1154), 0925 (POS1286)
Monfort J., 0991 (POS1416), 1132 (AB0212)
Mongey A. B., 0891 (POS1216)
Mongin D., 0256 (POS0093), 0577 (POS0668)
Moñiz-Díez A., 0009 (OP0017)
Monjo I., 0399 (POS0342), 0546 (POS0617), 0664 (POS0821), 1047 (AB0027), 1216 (AB0378), 1218 (AB0382)
Monov S., 0522 (POS0578), 0873 (POS1184), 1108 (AB0162), 1432 (AB0815)
Monova D., 0873 (POS1184), 1108 (AB0162)
Monsalve S., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Monsberger B., 0725 (POS0926)
Monsef A., 0013 (OP0023), 1167 (AB0282)
Montagna P., 0392 (POS0330), 1060 (AB0057)
Montani D., 0052 (OP0094)
Monte M., 0878 (POS1192)
Monteagudo I., 1385 (AB0706), 1397 (AB0734)
Montecucco C., 0029 (OP0055), 0051 (OP0093), 0347 (POS0250), 0386 (POS0318), 0521 (POS0575), 0582 (POS0675), 0668 (POS0830), 0694 (POS0877), 0913 (POS1258), 1477 (AB0911-HPR)
Monteil J., 0397 (POS0338)
Montero D., 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Montero F., 0916 (POS1264)
Montero N., 0058 (OP0105)
Montes Pérez E., 0755 (POS0977), 0977 (POS1390), 0986 (POS1407)
Montesa M. J., 1208 (AB0366)
Monti R., 0954 (POS1344)
Monti S., 0029 (OP0055), 0051 (OP0093), 0345 (POS0248), 0347 (POS0250), 0668 (POS0830)
Monticielo O., 0625 (POS0747), 0909 (POS1252), 0999 (POS1430)
Montilla-Morales C. A., 0610 (POS0721), 0766 (POS0996)
Montini F., 0701 (POS0891)
Montoya García M. J., 1341 (AB0612)
Moon K. W., 0839 (POS1120)
Moore M., 0378 (POS0305)
Moosig F., 0544 (POS0615)
Moots R. J., 0593 (POS0692)
Moots R., 0452 (POS0446)
Mora A., 0892 (POS1218)
Morabito N., 0838 (POS1119)
Mora-Cuesta V. M., 1046 (AB0026), 1076 (AB0094)
Morad N., 0477 (POS0490)
Moragues Pastor C., 0184 (OP0300)
Morales L., 1133 (AB0214)
Morales R., 1462 (AB0878-HPR)
Morales-Águila M., 0344 (POS0246)
Morales-Ivorra I., 0184 (OP0300)
Morán Álvarez P., 0884 (POS1204)
Morana G., 0355 (POS0264)
Morand E. F., 0075 (OP0131), 0181 (OP0296), 0218 (POS0028), 0406 (POS0351), 0586 (POS0683), 0587 (POS0684), 0590 (POS0688), 0592 (POS0691), 0616 (POS0731), 0629 (POS0753), 0876 (POS1189)
Morati-Hafsaoui C., 0181 (OP0295), 0261 (POS0103)
Morbiducci J., 0635 (POS0763), 0887 (POS1208)
Morel J., 0019 (OP0035), 0028 (OP0053), 0054 (OP0098), 0080 (OP0138), 0128 (OP0214), 0518 (POS0566), 0559 (POS0641), 0770 (POS1003), 0820 (POS1082), 0902 (POS1239), 1148 (AB0247), 1273 (AB0493)
Morel N., 0181 (OP0295), 0261 (POS0103), 0612 (POS0724)
Moreland L., 0584 (POS0678)
Morella S. B., 0882 (POS1200), 1399 (AB0739)
Morell-Dubois S., 1011 (POS1454-HPR)
Morello R., 0669 (POS0831)
Moreno del Castillo C., 0853 (POS1149)
Moreno F., 0366 (POS0282)
Moreno J. A., 0426 (POS0394)
Moreno J., 0636 (POS0765)
Moreno L., 0376 (POS0302)
Moreno M., 0068 (OP0123), 0342 (POS0242), 0610 (POS0721), 0766 (POS0996), 0766 (POS0996)
Moreno Martinez Losa M., 0976 (POS1387)
Moreno Martinez-Losa M., 1060 (AB0055)
Moreno Ruzafa E., 0098 (OP0164), 0929 (POS1296)
Moreno-Arquieta I. A., 1018 (POS1466-HPR), 1458 (AB0868-HPR)
Moreno-Salinas A., 1031 (POS1494-HPR)
Moretti A., 1331 (AB0588)
Morf H., 1013 (POS1458-HPR)
Morgan A., 0018 (OP0033)
Mori M., 1152 (AB0253)
Mori S., 0252 (POS0088), 1151 (AB0252)
Moriano C., 0034 (OP0064), 0035 (OP0065), 0628 (POS0752), 0967 (POS1371), 1171 (AB0290), 1189 (AB0328), 1321 (AB0568)
Moriano Morales C., 1165 (AB0278)
Morikawa A., 1055 (AB0045)
Morillon D., 0735 (POS0945)
Morimoto M., 1181 (AB0311)
Morimoto S., 0998 (POS1429)
Morin F., 0078 (OP0135)
Morin I., 1121 (AB0195)
Morinobu A., 0401 (POS0345)
Morita M., 0753 (POS0975)
Moriwaki D., 1099 (AB0145)
Mørk C., 0185 (OP0301)
Moroni L., 0348 (POS0253), 0594 (POS0693), 0613 (POS0726)
Moros L., 0069 (OP0124)
Morosetti D., 1418 (AB0786)
Morovic-Vergles J., 0386 (POS0318)
Morozova M., 0890 (POS1214)
Morreale C., 0097 (OP0161)
Morris A., 0008 (OP0014)
Morrone A., 1318 (AB0563)
Morsel-Carlsen L., 0742 (POS0955)
Mortada M. A., 0922 (POS1276)
Mortensen A. S., 0382 (POS0313)
Morton A., 0839 (POS1121)
Morton F., 0403 (POS0348), 1159 (AB0265)
Morton S., 0876 (POS1189)
Mosca M., 0181 (OP0296), 0199 (LB0002), 0594 (POS0693), 0619 (POS0737), 0628 (POS0751), 0630 (POS0756), 0633 (POS0760), 0635 (POS0764), 0642 (POS0778), 0644 (POS0782), 0647 (POS0789), 1232 (AB0407)
Moscato P., 0778 (POS1021)
Moschetti L., 0600 (POS0702), 0612 (POS0724), 1435 (AB0822)
Moscioni E., 0811 (POS1066)
Moseng T., 0119 (OP0198-HPR), 0357 (POS0268-HPR)
Moses A., 0115 (OP0191-PARE), 1459 (AB0872-HPR)
Mosher D., 0224 (POS0037)
Mosor E., 1019 (POS1468-HPR)
Mosquera Martínez J. A., 1326 (AB0577)
Mostard R., 0911 (POS1256)
Mostaza J. M., 1218 (AB0382)
Mostova H., 1452 (AB0858)
Mota L., 0909 (POS1252), 1448 (AB0848)
Mothojakan N., 1342 (AB0616)
Motta F., 0152 (OP0249)
Mouamnia A., 1427 (AB0807)
Moulis G., 0968 (POS1373)
Mouna G., 1109 (AB0164), 1390 (AB0718), 1414 (AB0775)
Moura R. A., 0007 (OP0011)
Mourão A. F., 0871 (POS1180), 1402 (AB0747)
Mouriño C., 0610 (POS0721)
Moustakis S., 1435 (AB0823)
Mouterde G., 0128 (OP0214), 0850 (POS1141)
Mouthon L., 0385 (POS0317), 0388 (POS0323)
Moutsopoulos H. M., 0178 (OP0291), 0180 (OP0294), 0370 (POS0290)
Movahedi M., 0107 (OP0179), 0452 (POS0445), 0454 (POS0448), 0454 (POS0449)
Movshovich E., 0806 (POS1055)

Moya P., 0034 (OP0064), 0655 (POS0806), 0666 (POS0827), 0952 (POS1340), 1093 (AB0129), 1208 (AB0366), 1279 (AB0503), 1365 (AB0666), 1426 (AB0804)
Moyano S., 0887 (POS1208)
Moyeda Martinez R., 0893 (POS1220), 1345 (AB0624), 1360 (AB0657), 1361 (AB0658), 1439 (AB0830), 1444 (AB0842), 1445 (AB0843), 1457 (AB0867-HPR), 1463 (AB0880-HPR)
Moysidou G. S., 0635 (POS0764), 0818 (POS1078)
Mozgovaya E., 0424 (POS0389), 1056 (AB0048), 1057 (AB0049), 1062 (AB0061), 1108 (AB0163), 1444 (AB0841)
Mozo I., 1032 (POS1496-HPR)
Mozzani F., 0190 (OP0310), 1326 (AB0578), 1389 (AB0716)
Mrabet M., 0923 (POS1280), 0926 (POS1288)
Mroue' K., 0361 (POS0275-HPR), 1080 (AB0104)
Mrusek S., 0098 (OP0163), 0244 (POS0075), 0883 (POS1202), 0933 (POS1303)
Mtaoua S., 0925 (POS1285)
Mu R., 0447 (POS0437), 1004 (POS1439), 1076 (AB0095), 1440 (AB0831)
Mucenic T., 1170 (AB0288)
Muche B., 0025 (OP0048), 0155 (OP0254), 0342 (POS0241), 0456 (POS0453), 0756 (POS0979), 0771 (POS1007), 0813 (POS1069)
Mucientes A., 0908 (POS1251), 0910 (POS1253)
Mucke J., 1013 (POS1458-HPR), 1030 (POS1492-HPR)
Mudri S., 0021 (OP0039)
Mueller A. T., 0165 (OP0272)
Mueller A., 0867 (POS1174)
Mueller B. A., 0609 (POS0719)
Mueller H., 0069 (OP0124)
Muensterman E., 0805 (POS1054)
Mukerjee D., 1411 (AB0769)
Mukerji B., 0486 (POS0507)
Mukerji V., 0486 (POS0507)
Mukherjee S., 0245 (POS0076), 1081 (AB0107)
Mukhtar S., 0600 (POS0701)
Mulder M., 0288 (POS0150), 0310 (POS0193)
Mule' R., 1260 (AB0467)
Mulero López T., 1464 (AB0881-HPR), 1475 (AB0906-HPR)
Mulhearn B., 0170 (OP0281)
Mulherin D., 0005 (OP0009-PARE)
Mulkidzhan R., 0246 (POS0078), 1036 (AB0001)
Mullan R., 0014 (OP0025), 0015 (OP0028), 0241 (POS0069), 0282 (POS0140), 0291 (POS0156-HPR), 0859 (POS1162), 1043 (AB0018)
Müller A., 0028 (OP0054), 0149 (OP0244)
Muller I., 0012 (OP0021), 1151 (AB0251)
Muller P., 0074 (OP0129)
Muller R., 0112 (OP0185), 0465 (POS0468), 0577 (POS0668), 1161 (AB0270)
Müller-Ladner U., 0040 (OP0075), 0171 (OP0283), 0209 (POS0015), 0383 (POS0314), 0384 (POS0316), 0670 (POS0834), 0676 (POS0844), 0915 (POS1261), 1030 (POS1492-HPR), 1054 (AB0043), 1054 (AB0044), 1126 (AB0204)
Mulrooney E., 0047 (OP0087)
Mumba E., 0482 (POS0499)
Mumcu G., 1028 (POS1486-HPR), 1467 (AB0888-HPR), 1471 (AB0895-HPR)
Mundayat R., 0777 (POS1020)
Muñez E., 0892 (POS1218)
Munhoz G., 0909 (POS1252), 1448 (AB0848)
Munk H. L., 0006 (OP0010), 0234 (POS0056), 0865 (POS1170), 1483 (AB0924-PARE)
Muñoz C., 0639 (POS0770), 1213 (AB0374)
Muñoz Fernandez S., 1225 (AB0396), 1412 (AB0771)
Muñoz Jimenez. A., 1279 (AB0503)
Muñoz M., 0639 (POS0770)
Muñoz R., 1187 (AB0325), 1188 (AB0326), 1351 (AB0635)
Muñoz Reinoso P., 1024 (POS1480-HPR), 1056 (AB0047), 1075 (AB0092), 1132 (AB0213), 1145 (AB0239), 1420 (AB0789)
Muñoz-Callejas A., 0393 (POS0331), 1071 (AB0083)
Muñoz-Fernández S., 0523 (POS0579)
Muñoz-Monroy O. E., 0559 (POS0642)
Muntean L., 0024 (OP0047), 0638 (POS0768), 1360 (AB0656)
Murabe H., 0665 (POS0824)
Murakami K., 0401 (POS0345), 1025 (POS1482-HPR), 1055 (AB0045)
Murakawa Y., 0395 (POS0336)
Muram T., 0714 (POS0909)
Murata K., 1025 (POS1482-HPR)
Murata T., 0368 (POS0286)
Muratore F., 0037 (OP0069)
Muratore M., 0835 (POS1111)
Muraviev Y., 0465 (POS0467), 1158 (AB0263)
Muravyeva N., 0854 (POS1151), 0855 (POS1152)
Murdaca G., 0906 (POS1246)
Murgo A., 1331 (AB0588)
Murphy D., 1478 (AB0913-PARE)
Murphy G., 1017 (POS1465-HPR)
Murphy M., 1046 (AB0024)
Murray B., 0331 (POS0224)
Murray K., 0014 (OP0025), 0462 (POS0462), 0470 (POS0477), 0891 (POS1216)
Murtazalieva D., 1095 (AB0135)
Murtazalieva J., 1084 (AB0111)
Musa K., 1064 (AB0067)
Musaev G., 0890 (POS1214)
Musetescu A., 0519 (POS0569)
Musiał J., 1434 (AB0820)
Musselli C., 0597 (POS0698), 0598 (POS0699)
Mussi G., 1480 (AB0918-PARE)
Mustafa Ali S., 1006 (POS1444)
Mustafar R., 1177 (AB0302)
Muth J., 1238 (AB0420)
Muthusamy S., 1256 (AB0458)
Muzaffar S., 1170 (AB0288)
Myasoedova E., 0056 (OP0102), 0128 (OP0213), 0129 (OP0216), 0213 (POS0023), 0322 (POS0210), 0380 (POS0309), 0381 (POS0311)
Myers K., 0237 (POS0062-PARE)
Myklebust G., 1218 (AB0381)
Mylod E., 0470 (POS0477)
Myrup C., 0098 (OP0164)
Mysler E., 0251 (POS0087), 0565 (POS0652), 0566 (POS0653), 0592 (POS0690)
Mzabi A., 1219 (AB0383)

Naamane N., 1044 (AB0021)
Nacci F., 0190 (OP0310), 1032 (POS1495-HPR), 1154 (AB0256), 1260 (AB0467), 1389 (AB0716)
Nacef L., 0526 (POS0586), 0526 (POS0587), 1117 (AB0186), 1119 (AB0189), 1119 (AB0191)
Naclerio C., 0907 (POS1248)
Nada E. A., 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Naden R., 0841 (POS1124)
Naeem K., 1110 (AB0168)
Naessens D., 0377 (POS0304)
Nagpal S., 0015 (OP0028), 0205 (POS0007), 0423 (POS0387), 1043 (AB0018)
Nagy O., 0489 (POS0512)
Naidu G., 0584 (POS0679), 1163 (AB0276), 1305 (AB0545)
Naja M., 0300 (POS0174)
Najem C. E., 1203 (AB0357)
Nájera Herranz C., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Najm A., 0175 (OP0287), 0231 (POS0052), 0829 (POS1099), 1127 (AB0205)
Nakahara H., 1470 (AB0894-HPR)
Nakai T., 1408 (AB0763)
Nakajima A., 1150 (AB0249), 1150 (AB0249)
Nakajima S., 1224 (AB0391)
Nakajima T., 1028 (POS1487-HPR)
Nakamura H., 0465 (POS0466), 0492 (POS0517), 0608 (POS0718), 0808 (POS1059), 1086 (AB0115), 1431 (AB0813)
Nakamura K., 1094 (AB0132)
Nakamura M., 0911 (POS1255)
Nakano K., 0329 (POS0221)
Nakaoka Y., 0395 (POS0336), 0398 (POS0340)
Nakashima R., 0401 (POS0345)
Nakashima S., 0513 (POS0556), 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1249 (AB0443), 1437 (AB0826)
Nakayama Y., 0492 (POS0516)
Nakayamada S., 0329 (POS0221)
Nakazawa T., 0603 (POS0707)
Nakos-Bimpos M., 0021 (OP0040)
Nalesso G., 0120 (OP0200)
Nalli C., 0470 (POS0476), 0530 (POS0593), 0600 (POS0702), 0619 (POS0737), 0633 (POS0760), 1435 (AB0822)
Nam E. J., 0731 (POS0936)
Nam J., 0463 (POS0464), 0482 (POS0499)
Nandagudi A., 0834 (POS1107), 1157 (AB0262)
Naniwa T., 0395 (POS0336)
Nanni L., 1190 (AB0330)
Nannipieri V., 0647 (POS0789)
Narang T., 1305 (AB0545)
Narciso Resk Maklouf A. P., 0208 (POS0013)
Nardi C., 0355 (POS0264), 0897 (POS1228)
Naredo E., 0136 (OP0226), 0314 (POS0197), 0352 (POS0259), 0845 (POS1132), 0846 (POS1133)
Naretto C., 0601 (POS0704)
Narvaez J. A., 0184 (OP0300), 1158 (AB0264)
Narváez J., 0184 (OP0300), 0610 (POS0721), 0967 (POS1371), 1076 (AB0096), 1158 (AB0264), 1208 (AB0366)
Naryshkin E., 0259 (POS0098)
Nas K., 1016 (POS1462-HPR)
Nasadurai R., 1346 (AB0626)
Nash P., 0237 (POS0062-PARE), 0329 (POS0222), 0790 (POS1035), 0797 (POS1044), 0798 (POS1045), 1287 (AB0522), 1290 (AB0525), 1294 (AB0529), 1306 (AB0547), 1308 (AB0550), 1310 (AB0552)
Nasi S., 0226 (POS0041), 0426 (POS0393), 0730 (POS0933), 1377 (AB0689)
Nasonov E., 0464 (POS0465), 0514 (POS0559), 0515 (POS0561), 0542 (POS0611), 0613 (POS0727), 0754 (POS0976), 0815 (POS1072), 1011 (POS1455-HPR), 1084 (AB0111), 1088 (AB0118), 1095 (AB0135), 1131 (AB0210), 1134 (AB0216), 1139 (AB0226), 1179 (AB0306), 1179 (AB0307), 1180 (AB0308), 1325 (AB0575), 1325 (AB0576), 1364 (AB0664), 1421 (AB0792), 1422 (AB0795)
Nassar K., 0371 (POS0292), 0767 (POS0998), 0817 (POS1077), 0965 (POS1367), 1266 (AB0477), 1336 (AB0600), 1343 (AB0617), 1344 (AB0619), 1344 (AB0620), 1363 (AB0662), 1375 (AB0685), 1387 (AB0711), 1398 (AB0738), 1422 (AB0794), 1433 (AB0819), 1438 (AB0828), 1438 (AB0829)
Nassar M. K., 0645 (POS0784)
Nassar-Sheikh Rashid A., 0241 (POS0070), 0937 (POS1311)
Nast I., 0095 (OP0158-HPR)
Natalello G., 0370 (POS0289), 0687 (POS0864), 0701 (POS0891)
Natalucci F., 0588 (POS0685), 0645 (POS0783), 0903 (POS1240), 1073 (AB0087)
Nathan J., 1323 (AB0573)
Natur M., 0928 (POS1294)
Natvig B., 0119 (OP0198-HPR), 0357 (POS0268-HPR)
Naty S., 1012 (POS1457-HPR), 1454 (AB0861-HPR)
Navaneethan B., 1415 (AB0779)
Navarini L., 0957 (POS1349)
Navarra S., 0218 (POS0028), 0597 (POS0698), 0598 (POS0699), 0803 (POS1051)
Navarrete-Rouco M. E., 0991 (POS1416)
Navarro F., 0366 (POS0282)
Navarro N., 1060 (AB0055)
Navarro V., 1219 (AB0384)
Navarro-Compán V., 0024 (OP0047), 0146 (OP0239), 0239 (POS0065-PARE), 0342 (POS0242), 0343 (POS0244), 0546 (POS0617), 0704 (POS0895), 0722 (POS0923), 0744 (POS0960), 0745 (POS0961), 0746 (POS0962), 0750 (POS0969), 0762 (POS0988), 0762 (POS0989), 0763 (POS0990), 0763 (POS0991), 0764 (POS0992), 0765 (POS0993), 0765 (POS0994), 0766 (POS0996), 0868 (POS1175), 0889 (POS1213), 1277 (AB0500), 1307 (AB0548), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)

Navarro-Millan I., 1441 (AB0834)
Navarro-Zarza J. E., 0904 (POS1242)
Navrátilová A., 0424 (POS0388), 0850 (POS1142)
Nawata M., 1094 (AB0132)
Ndosi M., 0093 (OP0155-HPR), 0291 (POS0158-HPR), 1021 (POS1472-HPR), 1441 (AB0834)
Neale A., 1406 (AB0756)
Nebuloni M., 1367 (AB0671)
Neel T., 1067 (AB0074), 1164 (AB0277)
Neerinckx B., 0545 (POS0616)
Nees V., 0420 (POS0381)
Negi A., 0862 (POS1167)
Negi V., 0696 (POS0880), 0701 (POS0890)
Negrão Gonçalo Dias D., 0582 (POS0676)
Negru M. M., 0164 (OP0270), 0681 (POS0854), 0773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1267 (AB0480), 1378 (AB0690)
Negueroles Albuixech R., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Nekvindova L., 0532 (POS0596)
Nelson C., 1155 (AB0259)
Nelson-Piercy C., 0213 (POS0022)
Nemcova D., 0247 (POS0079), 0934 (POS1304)
Nemman V., 1196 (AB0342)
Nencioni A., 0833 (POS1105)
Neogi T., 0047 (OP0087), 0841 (POS1124), 0853 (POS1148)
Neri B., 0335 (POS0231)
Nerviani A., 0007 (OP0011)
Nesi C., 0980 (POS1395)
Nesterenko V., 1329 (AB0585), 1388 (AB0714)
Netea M., 0009 (OP0017)
Neto A., 1402 (AB0747)
Neto N., 0015 (OP0028), 0205 (POS0007)
Netzer C., 0120 (OP0199)
Neuhold M., 0140 (OP0230)
Neuman L. M., 1214 (AB0375)
Neumann E., 0209 (POS0015), 0676 (POS0844), 1054 (AB0043), 1054 (AB0044)
Neumann T., 1222 (AB0388)
Neurath M. F., 0996 (POS1426)
Neves J., 1003 (POS1438)
Nevo S., 0200 (LB0003), 0885 (POS1206)
Nevskaya T., 0103 (OP0172), 0320 (POS0207)
Newsome V., 1347 (AB0628)
Ng C. F., 1330 (AB0587)
Ng C. M., 1256 (AB0458)
Ng C. R., 1176 (AB0299), 1427 (AB0805)
Ng C. S., 1451 (AB0856)
Ng C. T., 0301 (POS0176)
Ng K. L., 0837 (POS1114)
Ng K., 0218 (POS0028)
Ng N., 0625 (POS0746)
Ng S. N., 0352 (POS0260)
Ng W. F., 0079 (OP0136), 1057 (AB0051)
Nguyen A., 1240 (AB0424)
Nguyen M., 0562 (POS0648), 1122 (AB0196)
Nguyen P., 0421 (POS0382)
Nguyen Y., 0007 (OP0012), 0471 (POS0478)
Ni X., 0646 (POS0788)
Niamane R., 0992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811)
Nicholls J., 1374 (AB0682)
Nicorescu I., 1046 (AB0025)
Niebusch N., 0611 (POS0722)
Niedermann Schneider K., 0095 (OP0158-HPR)
Niederreiter B., 1060 (AB0056)
Niehues S., 0155 (OP0254)
Nielsen C. H., 0382 (POS0313)
Nielsen C., 0419 (POS0377)
Nielsen D. S., 1468 (AB0890-HPR)
Nielsen S., 0247 (POS0079), 0934 (POS1304)
Niemantsverdriet E., 0130 (OP0217), 0212 (POS0021), 0351 (POS0257), 0420 (POS0379), 0486 (POS0506)
Nienhuis H., 1478 (AB0914-PARE)
Nierkens S., 1430 (AB0812)
Niesters M., 0273 (POS0123)
Nieters A., 1383 (AB0701)
Nieto González J. C., 0034 (OP0064), 0233 (POS0055), 0658 (POS0812), 0984 (POS1403), 1117 (AB0185), 1385 (AB0706), 1397 (AB0734)
Nieto R., 0730 (POS0933), 0875 (POS1188), 1196 (AB0342), 1377 (AB0689)
Niewerth M., 0099 (OP0165), 0246 (POS0077), 0882 (POS1199), 0936 (POS1309), 0943 (POS1321), 0945 (POS1325)
Nightingale P., 1026 (POS1483-HPR)
Nijish A., 1160 (AB0268)
Nikiphorou E., 0002 (OP0006), 0039 (OP0074), 0161 (OP0264-HPR), 0173 (OP0286), 0193 (OP0316), 0340 (POS0238), 0480 (POS0495), 0573 (POS0662), 0739 (POS0951), 0751 (POS0971), 0859 (POS1162), 1357 (AB0649), 1484 (AB0925-PARE)
Nikishina I., 0014 (OP0027), 0249 (POS0083), 0918 (POS1267), 0948 (POS1332), 1038 (AB0007), 1393 (AB0725), 1394 (AB0726), 1400 (AB0743)
Nikishina N., 1168 (AB0284), 1184 (AB0319), 1185 (AB0320)
Nikitin M., 0160 (OP0263-HPR), 1393 (AB0724)
Nikitina N., 0014 (OP0027), 1455 (AB0864-HPR)
Nikitina T., 0944 (POS1324), 1402 (AB0748)
Nikitinskaya O., 0294 (POS0164), 0493 (POS0518), 0493 (POS0519), 0673 (POS0839), 0674 (POS0841), 1104 (AB0154), 1342 (AB0613)
Nikolakis D., 0011 (OP0019)
Nikolenko M., 1084 (AB0111)
Nikolopoulos D., 0021 (OP0040), 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Nikolov M., 0835 (POS1109)
Nikolov N., 0835 (POS1109)
Nikpour M., 0218 (POS0028), 0629 (POS0753)
Nilsdotter A., 1330 (AB0586)
Nilsson P., 0425 (POS0392)
Ninaber M., 0675 (POS0843), 1365 (AB0667)
Ninagawa K., 0687 (POS0863)
Niolu C., 1434 (AB0821)
Nisa Hernandez L., 0649 (POS0795)
Nisar M. K., 0333 (POS0227), 1024 (POS1478-HPR), 1028 (POS1488-HPR), 1340 (AB0610), 1432 (AB0817)
Nishihata S. Y., 0608 (POS0718)
Nishikawa A., 1150 (AB0249)
Nishimi S., 1063 (AB0065)
Nishimura K., 0665 (POS0824)
Nishioka R., 0956 (POS1348), 1407 (AB0760)
Nishitani K., 1025 (POS1482-HPR)
Nissen M. J., 0112 (OP0185), 0131 (OP0220), 0217 (POS0027), 1161 (AB0270), 1259 (AB0465)
Nizhnik V., 0930 (POS1298)
Noack C., 0985 (POS1405)
Noblejas Mozo A., 0693 (POS0875), 1192 (AB0333)
Nochomovitz H., 0200 (LB0003)
Noel D., 0417 (POS0374)
Noel E., 0364 (POS0279)
Noel W., 0140 (OP0230), 0142 (OP0232), 0778 (POS1021), 0781 (POS1024), 0799 (POS1046), 1289 (AB0524), 1295 (AB0530), 1313 (AB0556)
Nogué E., 0080 (OP0138)
Nogueira-Recalde U., 0418 (POS0375)
Noguera-Pons J. R., 0820 (POS1081)
Nogués X., 0835 (POS1111)
Nolla J. M., 0032 (OP0060), 0184 (OP0300)
Nolla-Fontana C., 0898 (POS1229)
Nolte I. M., 0221 (POS0031)
Nomura A., 1408 (AB0763)
Nonaka F., 1028 (POS1487-HPR)
Noppakun K., 0589 (POS0687)
Norberg M., 0921 (POS1273)
Nordström D., 0082 (OP0140), 0133 (OP0222), 0217 (POS0027), 0256 (POS0093)
Nørgaard Agerbo J., 0234 (POS0056), 0865 (POS1170)
Norman M., 1067 (AB0074), 1164 (AB0277)
Norton S., 0110 (OP0183), 0479 (POS0494), 0744 (POS0959)
Noss E., 0460 (POS0459)
Nossent J., 0052 (OP0095), 0055 (OP0100-HPR), 0250 (POS0084), 0373 (POS0297), 0852 (POS1147), 1079 (AB0103), 1224 (AB0393)
Nossum R., 0094 (OP0157-HPR)
Nouicer S., 0372 (POS0294)
Novak A., 0018 (OP0034)
Novakovich E., 0653 (POS0802)
Novella-Navarro M., 0546 (POS0617), 1047 (AB0027), 1101 (AB0149)
Novik G., 1393 (AB0724)
Novikov A., 0772 (POS1008), 1442 (AB0837)
Novikov P., 0685 (POS0861)
Novikova A., 0849 (POS1139), 0849 (POS1140), 0963 (POS1363), 1353 (AB0640)
Novikova Y., 1397 (AB0735)
Noviski M., 0204 (POS0006)
Novosat T., 0824 (POS1089)
Nowak M., 0137 (OP0227), 0314 (POS0198), 1316 (AB0560)
Nowell W. B., 0169 (OP0280-PARE), 0237 (POS0062-PARE), 1034 (POS1499-PARE)
Nozal P., 0546 (POS0617), 0693 (POS0875)
Ntasiou E., 0525 (POS0584)
Ntourou A., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Nucci P., 0940 (POS1316), 0941 (POS1317)
Nucera V., 0324 (POS0214)
Nuez Zaragoza E., 1060 (AB0055)
Numeric P., 0735 (POS0945)
Nune A., 1376 (AB0687)
Nunes F., 1282 (AB0510)
Nunes H., 0388 (POS0323)
Núñez Cuadros E., 0946 (POS1328)
Nuñez-Conde A., 0699 (POS0886)
Nuño L., 0546 (POS0617), 0914 (POS1260), 1047 (AB0027), 1101 (AB0149)
Nur Aida Sabrina M. R., 0459 (POS0457)
Nurbaeva K., 1363 (AB0663)
Nuriakhmetova T., 1269 (AB0484)
Nurmohamed M. T., 0108 (OP0180), 0453 (POS0447), 0533 (POS0599), 1128 (AB0207)
Nurmohamed M., 0142 (OP0232), 0324 (POS0213), 0359 (POS0271-HPR), 0548 (POS0621), 0572 (POS0660), 0578 (POS0669), 0799 (POS1046), 1151 (AB0251), 1295 (AB0530)
Nurmukhametov M., 1329 (AB0585), 1388 (AB0714)
Nurudhin A., 1425 (AB0802)
Nurul-Aain A. F., 0053 (OP0096), 0459 (POS0457)
Nuruzzaman F., 0247 (POS0079), 0934 (POS1304)
Nyberg F., 0598 (POS0699)
Nygaard Dager T., 0092 (OP0153-HPR)
Nylander M., 1024 (POS1479-HPR)
Nys M., 0074 (OP0130), 0137 (OP0227)
Nzeusseu Toukap A., 0066 (OP0119), 0240 (POS0067), 0352 (POS0259)

O' Brien A., 0241 (POS0069)
O'brien E., 0728 (POS0930)
O'connell P., 0859 (POS1162)
O'leary H., 1017 (POS1465-HPR)
O'neill L., 0747 (POS0964), 0891 (POS1216)
O'neill S., 0218 (POS0028)
O'quinn S., 1171 (AB0289)
O'Rielly D., 0431 (POS0405), 0432 (POS0406)
O'rourke A., 0891 (POS1216)
O'shea A., 0293 (POS0161-HPR)
O'shea F. B., 0027 (OP0051), 0734 (POS0942), 0738 (POS0949), 0747 (POS0964), 0766 (POS0995), 0768 (POS0999)
O'sullivan D., 0139 (OP0229)
O'sullivan M., 1093 (AB0130)
O'sullivan T., 1479 (AB0916-PARE)
Oba P., 0959 (POS1354), 0961 (POS1359)
Obermeyer K., 0847 (POS1136), 1348 (AB0630)
Ocal M. L., 0282 (POS0142), 0951 (POS1339), 1006 (POS1445), 1191 (AB0331), 1210 (AB0369), 1409 (AB0766)
Ocampo D., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Occhipinti M., 0355 (POS0264)
Ochs W., 0194 (OP0318)
Oddis C. V., 0004 (OP0008)
Odhiambo R., 1395 (AB0729)
Odincova A., 1283 (AB0513)
Oelzner P., 0040 (OP0075), 1422 (AB0796)
Oesman J., 1184 (AB0318)
Offenbächer M., 1027 (POS1484-HPR), 1467 (AB0889-HPR)
Offer G., 1061 (AB0058)

Ogasawara K., 1055 (AB0045)
Ogawa N., 0395 (POS0336)
Ogbomo A., 0377 (POS0304)
Ogbonnaya A., 0595 (POS0694)
Ogdie A., 0026 (OP0049), 0139 (OP0229), 0141 (OP0231), 0237 (POS0062-PARE), 0804 (POS1052), 0810 (POS1063), 1022 (POS1474-HPR), 1280 (AB0506), 1311 (AB0553), 1316 (AB0560), 1469 (AB0892-HPR)
Ognibeni F., 0326 (POS0218)
Ogura T., 0981 (POS1396)
Oguz E., 1409 (AB0766)
Oh C., 0278 (POS0134)
Oh Y. J., 0839 (POS1120)
Oh Y., 0166 (OP0274-PARE)
Ohashi H., 1329 (AB0583)
Ohira Gazzeta M., 0582 (POS0676)
Ohldieck Fredheim G., 0092 (OP0153-HPR)
Ohmura K., 0401 (POS0345)
Ohrndorf S., 0983 (POS1401), 0988 (POS1410)
Ohtsuka N., 1081 (AB0107)
Oikonomoula E., 0238 (POS0064-PARE)
Okada A., 0581 (POS0674)
Okada M., 0753 (POS0975), 1408 (AB0763)
Okada N., 0398 (POS0340)
Okamoto N., 1150 (AB0249)
Okane D., 1410 (AB0767)
Okano T., 0465 (POS0466), 0492 (POS0517), 0517 (POS0565), 0725 (POS0926), 0808 (POS1059), 1012 (POS1456-HPR), 1086 (AB0115)
Okano Y., 1099 (AB0145), 1152 (AB0253), 1187 (AB0324), 1249 (AB0442)
Okawa J., 0383 (POS0315)
Okazaki T., 0395 (POS0336)
Okily M., 0591 (POS0689)
Okitsu S., 0305 (POS0184)
Oksum Solak E., 1327 (AB0579)
Oku K., 0687 (POS0863)
Okumuş G., 1251 (AB0448)
Oldroyd A., 0369 (POS0288)
Olech E., 1171 (AB0289)
Olejárova M., 0424 (POS0388)
Oliinyk M., 0481 (POS0498)
Olive A., 0380 (POS0308), 0967 (POS1371)
Oliveira de Oliveira I., 1004 (POS1440)
Oliveira Pinheiro F., 0260 (POS0100), 0318 (POS0204), 0476 (POS0488), 0483 (POS0502), 0718 (POS0914), 0812 (POS1067), 0833 (POS1106), 0836 (POS1113), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1299 (AB0536), 1432 (AB0816), 1441 (AB0835)
Oliver S., 1470 (AB0894-HPR)
Olivi P., 0062 (OP0112), 0831 (POS1102)
Olivieri G., 0588 (POS0685), 1073 (AB0087)
Olivo D., 0906 (POS1246)
Oller Rodríguez J. E., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Olmo Montes F. J., 1341 (AB0612)
Olofsson T., 0339 (POS0237)
Olsder W., 0139 (OP0229), 1296 (AB0531)
Olsen I. C., 1245 (AB0433)
Olsen I., 0185 (OP0301)
Olsen M., 0094 (OP0157-HPR)
Olsson P., 0308 (POS0189)
Olyunin Y., 1011 (POS1455-HPR), 1131 (AB0210), 1134 (AB0216), 1139 (AB0226)
Omarsdottir S., 0939 (POS1313)
Ombrello A., 0049 (OP0090)
Omelchenko V., 0043 (OP0080), 1045 (AB0023)
Ometto F., 0742 (POS0956)
Omma A., 1105 (AB0157), 1182 (AB0314)
Omoumi P., 0426 (POS0393), 1053 (AB0041)
Önal C., 0648 (POS0793)
Önal C., 1198 (AB0347)
Onen F., 0217 (POS0027), 0627 (POS0750), 1140 (AB0229), 1247 (AB0437), 1256 (AB0459), 1266 (AB0479), 1317 (AB0561), 1327 (AB0579), 1386 (AB0708)
Ong P. S., 0459 (POS0457)
Ong V., 1229 (AB0402)
Ong W. J., 0273 (POS0124)
Oniankitan O., 0776 (POS1016), 0927 (POS1291)
Oniankitan S., 0776 (POS1016)
Onken N., 0244 (POS0075)
Ono K., 0753 (POS0975)
Onofrio M., 0882 (POS1200)
Oñoro López C. M., 1192 (AB0333)
Oommen P. T., 0244 (POS0075)
Oommen P., 0050 (OP0092), 0972 (POS1380)
Ooms A., 0825 (POS1092)
Oon S., 0218 (POS0028)
Oortgiesen M., 0332 (POS0226), 0720 (POS0919)
Oparina N., 0014 (OP0026), 0192 (OP0315), 0428 (POS0397)
Opdam M., 0880 (POS1197), 1027 (POS1485-HPR)
Opris-Belinski D., 0164 (OP0270), 0681 (POS0854), 0773 (POS1009), 1107 (AB0160), 1112 (AB0172), 1378 (AB0690), 1462 (AB0879-HPR)
Opsahl Hetlevik S., 0247 (POS0079), 0934 (POS1304)
Oraa J., 1103 (AB0151)
Orange D., 0472 (POS0480)
Orbai A. M., 0183 (OP0298), 0777 (POS1020), 0785 (POS1029), 0802 (POS1050)
Orchard S., 0009 (OP0015)
Ordoñez Azuara Y. G., 0445 (POS0434), 1425 (AB0801)
Ordoñez Cañizares M. D. C., 1474 (AB0904-HPR)
Orefice V., 1069 (AB0079)
Oreiro N., 0403 (POS0347), 0418 (POS0375)
Orekhov A., 1049 (AB0033)
Orellana C., 1060 (AB0055)
Oren S., 0892 (POS1217)
Orenes Vera A. V., 0296 (POS0168), 1427 (AB0806)
Oreska S., 0677 (POS0846), 0678 (POS0849), 1233 (AB0410), 1234 (AB0412)
Origuchi T., 0608 (POS0718)
Orlandi M., 0355 (POS0264), 0385 (POS0317), 0388 (POS0322), 0675 (POS0842), 0897 (POS1228), 1192 (AB0334)
Ormseth S., 0058 (OP0104), 0325 (POS0215), 0325 (POS0216), 0520 (POS0571)
Ornetti P., 0843 (POS1129)
Orozco C., 0771 (POS1005)
Orozco D., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Orozco G., 0009 (OP0016)
Orozco Gonzalez C., 1139 (AB0227)
Orozco S., 1365 (AB0666)
Orozco-Galvez O., 0898 (POS1229), 0907 (POS1247)
Orquevaux P., 0181 (OP0295), 0261 (POS0103)
Orsi S., 0935 (POS1307)
Orsini F., 1374 (AB0683)
Orsolini G., 0106 (OP0178), 0326 (POS0218), 0594 (POS0693)
Ortega Castro R., 0323 (POS0211), 0469 (POS0475), 0747 (POS0965), 1065 (AB0070), 1109 (AB0166), 1245 (AB0432), 1253 (AB0451)
Ortega J., 0664 (POS0821), 1216 (AB0378)
Ortego N., 0350 (POS0256), 0967 (POS1371), 0987 (POS1408), 0987 (POS1409), 1076 (AB0096), 1182 (AB0315), 1183 (AB0316), 1208 (AB0366), 1225 (AB0396), 1231 (AB0405), 1231 (AB0406), 1412 (AB0771)
Ortiz A., 1133 (AB0214)
Ortiz M. A., 0277 (POS0132)
Ortiz Sanjuan F. M., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1208 (AB0366), 1278 (AB0502)
Ortiz Sanjuan F., 0531 (POS0595)
Ortiz-Sanjuán F., 0490 (POS0513)
Ortiz-Santamaria V., 0700 (POS0888)
Ortolan A., 0386 (POS0318), 0726 (POS0927), 0742 (POS0956), 0894 (POS1221), 1308 (AB0549)
Orwa J., 1395 (AB0729)
Oryoji K., 0449 (POS0441)
Osailan A., 0475 (POS0486)
Osborn T. G., 0672 (POS0836)
Osborne R., 0374 (POS0299)
Oshima H., 1099 (AB0145), 1187 (AB0324), 1249 (AB0442)
Osipyan M., 1417 (AB0782)
Osipyants R., 0326 (POS0217)
Oskay D., 1235 (AB0414), 1462 (AB0877-HPR)
Osman A., 0053 (OP0096)
Osmani Z., 0585 (POS0680)
Osmanova G., 0225 (POS0040)
Osorio P., 1146 (AB0242)
Osorio-Chavez J., 0953 (POS1342), 1002 (POS1436)
Ospelt C., 0009 (OP0016), 0011 (OP0020), 0039 (OP0074)
Ospina Cardona D., 0049 (OP0090)
Ostelo R., 0291 (POS0157-HPR), 1020 (POS1470-HPR)
Ostendorf L., 0207 (POS0010), 0623 (POS0744)
Osteras N., 0094 (OP0157-HPR), 0357 (POS0268-HPR)
Østerås N., 0119 (OP0198-HPR)
Østergaard M., 0083 (OP0141), 0089 (OP0149), 0095 (OP0159-HPR), 0131 (OP0220), 0153 (OP0251), 0153 (OP0252), 0217 (POS0027), 0221 (POS0032), 0234 (POS0056), 0287 (POS0149), 0450 (POS0443), 0457 (POS0454), 0720 (POS0918), 0725 (POS0926), 0742 (POS0955), 0794 (POS1040), 0865 (POS1170)
Østergaard M., 1334 (AB0594)
Østgård R., 0234 (POS0056), 0865 (POS1170)
Ostor A., 0085 (OP0144), 0138 (OP0228), 0143 (OP0233), 0338 (POS0235), 0567 (POS0654), 0710 (POS0905), 0712 (POS0907), 0722 (POS0923), 0800 (POS1047)
Ostrovrsnik J., 0666 (POS0826)
Ostrovski Souza Santos V. M., 0826 (POS1093)
Ostuzzi S., 0858 (POS1161)
Osullivan C., 0330 (POS0223), 0547 (POS0619), 0711 (POS0906), 1015 (POS1461-HPR)
Otahal P., 0362 (POS0276)
Otero F., 0524 (POS0581), 0524 (POS0582)
Othman A. A., 0581 (POS0672), 1155 (AB0259)
Othman M., 0053 (OP0096)
Otipoby K. L., 0013 (OP0023), 1043 (AB0019), 1050 (AB0034), 1167 (AB0282)
Otman Akat E., 0722 (POS0922), 0861 (POS1165), 1255 (AB0456), 1366 (AB0669)
Otobo T. M., 0943 (POS1323)
Ottaviani S., 0054 (OP0099)
Ouanes W., 0856 (POS1154), 0925 (POS1285), 0925 (POS1286)
Ouenniche K., 0292 (POS0159-HPR), 0835 (POS1110), 1030 (POS1491-HPR), 1113 (AB0173), 1113 (AB0174), 1117 (AB0184), 1277 (AB0499), 1332 (AB0590), 1333 (AB0592), 1333 (AB0593), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1368 (AB0672), 1368 (AB0673), 1381 (AB0698), 1390 (AB0717), 1397 (AB0736), 1411 (AB0770), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Oulehri W., 1373 (AB0680)
Ouyang Z. M., 1174 (AB0296), 1227 (AB0398)
Ovejero Crespo D., 0835 (POS1111)
Ovseiko P. V., 0039 (OP0074)
Ovsyannikov D., 1397 (AB0735)
Ovsyannikova O., 0104 (OP0173), 0681 (POS0853), 0683 (POS0857), 0683 (POS0858), 0684 (POS0860), 0899 (POS1232), 1239 (AB0423), 1248 (AB0440), 1253 (AB0453), 1254 (AB0454), 1254 (AB0455)
Owen A., 0009 (OP0015)
Owen C., 0117 (OP0194), 0655 (POS0806), 1212 (AB0371)
Oygar P. D., 0908 (POS1249)
Öz N., 0959 (POS1354), 0961 (POS1359)
Ozawa H., 1408 (AB0763)
Özcan Z. B., 1086 (AB0114)
Ozdede A., 0875 (POS1187), 1327 (AB0579)
Ozdel S., 0117 (OP0195)
Özdemir B., 1105 (AB0157), 1182 (AB0314)
Özdemir Işık Ö., 1140 (AB0229), 1202 (AB0356), 1204 (AB0359), 1206 (AB0362)
Ozdener F., 1470 (AB0893-HPR)
Ozdogan H., 0958 (POS1351)
Özen S., 0100 (OP0168), 0117 (OP0195), 0243 (POS0074), 0908 (POS1249), 0930 (POS1298), 0942 (POS1320)
Ozen S., 0201 (LB0004)
Özen S., 1398 (AB0737)
Ozer A., 0959 (POS1354), 0961 (POS1359)
Ozguler Y., 0660 (POS0814), 0662 (POS0819), 0663 (POS0820), 0958 (POS1351), 1207 (AB0364)
Özkan Z. G., 1210 (AB0369)

Ozmen M., 0722 (POS0922), 0727 (POS0929), 0861 (POS1165), 1255 (AB0456), 1366 (AB0669)
Özmen Süner K., 1382 (AB0700)
Ozsoy Adisen E., 1327 (AB0579)
Özsoy Z., 0518 (POS0568), 0648 (POS0793), 0728 (POS0931), 0770 (POS1004), 0814 (POS1070), 0971 (POS1378)
Özsoy Z., 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1299 (AB0535)
Ozsurekci Y., 0908 (POS1249)
Oztas M., 0875 (POS1187)
Oztaskin S., 0604 (POS0710)
Ozturk M. A., 0733 (POS0940), 0878 (POS1193), 1077 (AB0097), 1176 (AB0300), 1462 (AB0877-HPR)
Öztürk Z., 0223 (POS0036), 0732 (POS0939)
Öztürk Z., 1382 (AB0700)
Ozyazgan Y., 0660 (POS0814), 0662 (POS0819)
Ozyuncu O., 0659 (POS0813)

Paap D., 0775 (POS1014), 1268 (AB0481)
Paats A., 1106 (AB0159)
Pablo Sosa J., 0600 (POS0701)
Pablos J. L., 0366 (POS0282), 0760 (POS0985)
Paccou J., 0114 (OP0190), 0662 (POS0818)
Pachai C., 0794 (POS1040)
Pacheco Tena C. F., 0904 (POS1242), 0905 (POS1245), 1288 (AB0523), 1450 (AB0852), 1459 (AB0871-HPR)
Pacheco-Reyes A., 0898 (POS1229)
Pachera E., 0151 (OP0248), 0393 (POS0332)
Pachigolla S., 0297 (POS0170)
Pachkoria T., 0249 (POS0083)
Pachowsky M., 0060 (OP0109)
Pacini G., 0392 (POS0330), 0679 (POS0850), 0686 (POS0862), 0697 (POS0882), 1247 (AB0438)
Pacucci V. A., 0645 (POS0783)
Padin-Martín M. I., 0323 (POS0211)
Padjen I., 1199 (AB0348), 1199 (AB0349)
Padova H., 1181 (AB0312)
Padovani F., 1480 (AB0918-PARE)
Padula S., 0589 (POS0687)
Padyukov L., 0012 (OP0021), 0053 (OP0096), 0403 (POS0348), 0459 (POS0457)
Paez D., 0911 (POS1255)
Pafundi P. C., 1446 (AB0844)
Pagani S., 0319 (POS0206)
Pagano Mariano G., 0906 (POS1246)
Page D., 0377 (POS0303)
Pai V., 0584 (POS0679)
Paira S., 1133 (AB0214)
Pais-De-Barros J. P., 1062 (AB0062)
Paiva E., 0909 (POS1252), 1448 (AB0848)
Pala A. S., 0958 (POS1351)
Pala G. G., 1462 (AB0877-HPR)
Palamidas D., 0015 (OP0029)
Palanichamy A., 0790 (POS1036)
Palazuelos C., 0614 (POS0728)
Palazzo D., 0882 (POS1200), 1399 (AB0739)
Palazzo R., 0150 (OP0246)
Palermo A., 0889 (POS1212)
Palermo B. L., 0324 (POS0214), 0913 (POS1258)
Palese A., 0292 (POS0160-HPR), 0878 (POS1192), 1224 (AB0392)
Pallares Ferreres L., 0179 (OP0292)
Pallotti C., 0098 (OP0164)
Palmer D., 0187 (OP0304-PARE)
Palmou-Fontana N., 1018 (POS1467-HPR), 1324 (AB0574)
Palmowski A., 0575 (POS0665)
Palmqvist I., 1059 (AB0054)
Palmroth M., 1150 (AB0250)
Palmucci S., 0897 (POS1228)
Palomäki A., 0004 (OP0007)
Palominos P., 0183 (OP0298), 1306 (AB0547)
Palotie A., 0004 (OP0007)
Palshina S., 0608 (POS0717), 0962 (POS1360), 1116 (AB0183)
Paly V., 0617 (POS0734)
Pamfil C., 0638 (POS0768)
Pan F., 0118 (OP0196), 0832 (POS1103)
Panafidina T., 0613 (POS0727), 1179 (AB0306), 1179 (AB0307), 1422 (AB0795)
Panagakis P., 1304 (AB0543)
Panagiotopoulos A., 1304 (AB0543)
Panaro S., 1435 (AB0822)
Pancarte M., 1061 (AB0058)
Pandit H., 0275 (POS0128)
Panero Lamothe B., 0323 (POS0211)
Pang H. T., 0687 (POS0865)
Pangan A., 0312 (POS0196), 1288 (AB0523)
Paniagua Zudaire I., 0960 (POS1355), 1132 (AB0211)
Pano A., 0198 (LB0001)
Panopoulos S., 0703 (POS0894)
Panos G., 1356 (AB0647)
Panova A., 0948 (POS1332)
Pantano I., 0888 (POS1210)
Pantelidis D., 1090 (AB0121)
Paolini J. F., 0031 (OP0059), 0198 (LB0001), 1211 (AB0370)
Paolino S., 0392 (POS0330), 0679 (POS0850), 0686 (POS0862), 0697 (POS0882), 0908 (POS1250), 1060 (AB0057), 1107 (AB0160), 1190 (AB0330), 1201 (AB0354), 1247 (AB0438), 1372 (AB0679)
Papa R., 0098 (OP0164), 0947 (POS1330)
Papachristodoulou E., 1356 (AB0647)
Papadakis I., 0193 (OP0317-PARE)
Papadopoulos N., 0620 (POS0738), 1090 (AB0121)
Papageorgiou L., 0405 (POS0350)
Papagiannoulis E., 0863 (POS1168)
Papagoras C., 1299 (AB0537)
Papakonstantinou O., 0943 (POS1323)
Papamichail G., 1107 (AB0161)
Papanicolaou E., 1467 (AB0887-HPR)
Paparo S. R., 0906 (POS1246)
Papas A., 0593 (POS0692)
Papasidero S., 0635 (POS0763)
Papava M., 1238 (AB0420)
Papazisis G., 1467 (AB0887-HPR)
Papichev E., 0297 (POS0169), 0455 (POS0451), 0487 (POS0509), 1437 (AB0827)
Papoutsaki M., 1304 (AB0543)
Papp K., 0138 (OP0228), 0312 (POS0196), 0795 (POS1042), 1297 (AB0532), 1315 (AB0559)
Pappa A., 0238 (POS0064-PARE)
Pappa M., 0815 (POS1073)
Pappas D. A., 0446 (POS0435), 0530 (POS0594), 0538 (POS0606)
Parafioriti A., 0940 (POS1315)
Parameswaran V., 0276 (POS0129), 0309 (POS0190)
Paran D., 0200 (LB0003), 0885 (POS1206), 0892 (POS1217), 1181 (AB0312)
Pardo Campo E., 0819 (POS1080)
Parente H., 0293 (POS0162), 0690 (POS0870), 0773 (POS1010), 0830 (POS1100), 1424 (AB0799)
Parenti L., 0672 (POS0837)
Pariente A., 0331 (POS0225)
Parikh B., 0311 (POS0194), 0802 (POS1050)
Parikh N., 0169 (OP0280-PARE), 0449 (POS0442)
Parikh S., 0595 (POS0695)
Paris C., 0900 (POS1234)
Paris M., 0349 (POS0254), 0667 (POS0828)
Paris U. V., 0576 (POS0667)
Parisi S., 0134 (OP0223), 0254 (POS0090), 0335 (POS0230), 0676 (POS0845), 0904 (POS1243), 1331 (AB0588)
Park C. H., 0512 (POS0555), 0516 (POS0563), 0516 (POS0564)
Park E. A., 0976 (POS1386)
Park H. M. P., 0124 (OP0207)
Park H., 0666 (POS0827), 1093 (AB0129), 1354 (AB0643), 1426 (AB0804)
Park J. A., 0204 (POS0005)
Park J. K., 0682 (POS0856), 0976 (POS1386)
Park J. W., 0682 (POS0856)
Park S. H., 1125 (AB0202), 1152 (AB0253)
Park S. S. H., 0401 (POS0344), 0468 (POS0474)
Park S. Y., 0714 (POS0909), 0718 (POS0915), 0798 (POS1045)
Park W., 0716 (POS0911), 1156 (AB0260)
Park Y. J., 0641 (POS0774)
Park Y., 0512 (POS0555), 0516 (POS0563), 0516 (POS0564)
Parker A., 0018 (OP0034)
Parker B., 1172 (AB0291)
Parker L., 1175 (AB0298), 1233 (AB0409), 1239 (AB0421), 1474 (AB0903-HPR)
Parks M., 0367 (POS0285), 0828 (POS1097)
Parlak E., 0749 (POS0968), 1272 (AB0491)
Parma A., 0647 (POS0789)
Parmar S., 0983 (POS1400)
Parodis I., 0260 (POS0101), 0643 (POS0779)
Parperis K., 0161 (OP0264-HPR), 0605 (POS0711), 1356 (AB0647)
Parrulli S., 0979 (POS1393)
Parvaz M., 0074 (OP0129)
Pasa L., 0363 (POS0277)
Paşaoğlu H., 1077 (AB0097)
Pascart T., 0662 (POS0818), 0841 (POS1124), 0843 (POS1129)
Paschke J., 0089 (OP0149), 0153 (OP0252), 0221 (POS0032), 0224 (POS0037), 0831 (POS1101)
Pascual E., 0841 (POS1124), 1303 (AB0542)
Pascual-Salcedo D., 0546 (POS0617)
Pasechnik E., 0890 (POS1214)
Pasma A., 0238 (POS0063-PARE), 0289 (POS0151)
Pasqual Marques A., 1462 (AB0878-HPR), 1478 (AB0912-HPR)
Pasqual Pastor M., 0929 (POS1296)
Pasquale M. D., 0888 (POS1210)
Pasquali F., 0902 (POS1238)
Passey A., 0141 (OP0231), 0804 (POS1052)
Pastelín C. S., 1280 (AB0506)
Pastoor H., 0186 (OP0303-HPR)
Pastor J., 0128 (OP0214)
Pastore S., 0948 (POS1333)
Patanè M., 0524 (POS0583)
Patel B., 0049 (OP0090)
Patel H., 0789 (POS1033)
Patel J., 1357 (AB0648)
Patel R., 0156 (OP0255), 0994 (POS1422)
Patel S., 1323 (AB0573)
Patel V., 0228 (POS0047)
Patel Y., 0108 (OP0180), 0453 (POS0447), 0533 (POS0599), 1128 (AB0207)
Patenaude S., 0237 (POS0061-PARE), 1482 (AB0923-PARE)
Pateromichelaki K., 0184 (OP0299), 0523 (POS0580), 0733 (POS0941)
Paterson C., 0403 (POS0348), 1159 (AB0265)
Patiño-Trives A. M., 0020 (OP0038), 0426 (POS0394), 0469 (POS0475), 0769 (POS1001), 1317 (AB0562)
Patrícia Quereza e Silva Faria R., 0208 (POS0013)
Patrikeeva I., 0754 (POS0976), 0815 (POS1072), 1325 (AB0575), 1325 (AB0576)
Patwardhan A., 0242 (POS0071), 0247 (POS0079), 0934 (POS1304)
Paucar Loli L. M., 0934 (POS1305), 1392 (AB0722)
Paul H., 0112 (OP0185), 1161 (AB0270)
Paul M., 0240 (POS0068), 0317 (POS0201), 1067 (AB0074)
Paul S., 0240 (POS0068), 1067 (AB0074)
Pauling J., 0170 (OP0281)
Paulissen J., 0564 (POS0651)
Pavelka K., 0131 (OP0220), 0217 (POS0027), 0256 (POS0093), 0424 (POS0388), 0532 (POS0596), 0677 (POS0846), 0678 (POS0849), 0850 (POS1142), 1051 (AB0038), 1062 (AB0063), 1233 (AB0410), 1234 (AB0412)
Pávez Perales C., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Pavía M., 0892 (POS1218)
Pavia Pascual M., 0914 (POS1260)
Pavlova V., 0084 (OP0143), 1452 (AB0857)
Pavlych V., 0954 (POS1344), 1105 (AB0156)
Paz A., 0559 (POS0642)
Paz González R., 0306 (POS0185)
Pazmino S., 0356 (POS0266-HPR), 0375 (POS0300), 0484 (POS0503), 0545 (POS0616), 1001 (POS1433), 1001 (POS1434), 1083 (AB0109)
Pazos-Pérez A., 1048 (AB0030)
Pazzola G., 0594 (POS0693)
Pchelnikova P., 0916 (POS1263), 0917 (POS1266)
Pearce F., 0989 (POS1412)
Pearce-Fisher D., 0472 (POS0480), 0828 (POS1097), 1441 (AB0834)
Pearson M. E., 0575 (POS0666)

Pease C., 1173 (AB0293)
Peat G., 0983 (POS1400)
Peat-Fircak J., 0584 (POS0678)
Pechonkina A., 0070 (OP0126), 0255 (POS0092), 0569 (POS0657), 0570 (POS0658)
Peckham H., 0008 (OP0013), 0300 (POS0174)
Pecondon A., 0610 (POS0721)
Pedersen J. K., 0006 (OP0010), 0234 (POS0056), 0865 (POS1170), 1483 (AB0924-PARE)
Pedersen T. T., 0995 (POS1424)
Pedraz-Penalva M. T., 0820 (POS1081)
Pedrazzoni M., 0833 (POS1105)
Peeters I. R., 1023 (POS1477-HPR)
Peeters R., 0911 (POS1256)
Pegolo E., 0618 (POS0735)
Pego-Reigosa J. M., 0610 (POS0721)
Pehlivan Y., 0731 (POS0935), 1140 (AB0229), 1266 (AB0479), 1317 (AB0561)
Pehlivanturk-Kizilkan M., 1398 (AB0737)
Pei S., 0353 (POS0262)
Peichl P., 0108 (OP0180), 0453 (POS0447), 0533 (POS0599), 1128 (AB0207)
Peill J., 0482 (POS0499)
Peiteado D., 0546 (POS0617), 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1047 (AB0027), 1065 (AB0070), 1101 (AB0149)
Peitz J., 0246 (POS0077)
Peixoto D., 0293 (POS0162), 0830 (POS1100)
Peixoto Gu e Silva de Souza M., 0909 (POS1252)
Pekacova A., 1051 (AB0038), 1062 (AB0063)
Pel S., 0200 (LB0003), 0885 (POS1206)
Peláez-Ballestas I., 1428 (AB0808)
Pelechas E., 0879 (POS1194)
Peleg H., 0200 (LB0003)
Pellegrini R., 0906 (POS1246)
Pellegrino G., 0150 (OP0246), 0445 (POS0433), 0873 (POS1185), 0893 (POS1219), 0906 (POS1246)
Peloso P. M., 0840 (POS1122), 0841 (POS1125), 0847 (POS1136), 1348 (AB0630)
Peltomaa R., 1150 (AB0250)
Peña A., 0559 (POS0642)
Peña E., 0483 (POS0501)
Peña Sainz-Pardo E., 0952 (POS1340)
Peñalba A., 1076 (AB0096)
Pençe H. H., 1086 (AB0114)
Pendolino M., 0679 (POS0850)
Pendon G. P., 0730 (POS0933), 1377 (AB0689)
Penev B., 1432 (AB0815)
Penford R., 1476 (AB0909-HPR)
Peng J., 0008 (OP0013), 0300 (POS0174)
Peng Q., 1429 (AB0809)
Peng S. L., 0021 (OP0039)
Penkava F., 0017 (OP0032)
Penmetsa G., 0353 (POS0262)
Penn H., 0233 (POS0055)
Pennings Msc P., 0238 (POS0063-PARE)
Penso L., 0317 (POS0201)
Peon C., 0771 (POS1005)
Pepple S., 1173 (AB0293)
Pera M. A., 0635 (POS0763)
Pera M., 0874 (POS1186)
Perandones C., 1196 (AB0342)
Perdan-Pirkmajer K., 0666 (POS0826)
Perdriger A., 0431 (POS0403)
Perea-Fuentes I., 1215 (AB0376)
Pereira B., 1022 (POS1475-HPR)
Pereira D., 1255 (AB0457)
Pereira H., 0909 (POS1252), 1448 (AB0848)
Pereira I., 0582 (POS0676)
Pereira R. M., 0826 (POS1093)
Perera H., 1480 (AB0917-PARE)
Perez Alamino R., 0382 (POS0312), 0874 (POS1186), 1133 (AB0214), 1296 (AB0531)
Pérez Albaladejo L., 0323 (POS0211)
Pérez Barbosa L., 0893 (POS1220), 1360 (AB0657), 1361 (AB0658), 1439 (AB0830), 1444 (AB0842), 1445 (AB0843), 1457 (AB0867-HPR), 1463 (AB0880-HPR)
Perez C. E., 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Perez C., 0483 (POS0501)
Pérez C., 1132 (AB0212)
Pérez de Pedro I., 1208 (AB0366)
Perez Esteban S., 0914 (POS1260)
Pérez Galán M. J., 1317 (AB0562)
Perez Jaen A., 0856 (POS1156)
Perez L., 0204 (POS0006)
Perez N., 0635 (POS0763)
Pérez Ortega S., 0179 (OP0292)
Perez Pascual R., 0984 (POS1403)
Perez Saez A. M., 1464 (AB0881-HPR)
Perez Sandoval M. T., 0628 (POS0752), 1171 (AB0290)
Pérez Sandoval T., 1165 (AB0278), 1189 (AB0328), 1321 (AB0568)
p̈erez S., 1196 (AB0342)
Perez T., 1229 (AB0401)
Pérez Venegas J. J., 0469 (POS0475), 1024 (POS1480-HPR), 1056 (AB0047), 1075 (AB0092), 1132 (AB0213), 1145 (AB0239), 1341 (AB0612), 1420 (AB0789)
Pérez-Barquín R., 0601 (POS0703), 0966 (POS1370)
Perez-Chada L. M., 1312 (AB0554)
Pérez-Fernández R., 1046 (AB0026), 1076 (AB0094)
Perez-Garcia C., 0991 (POS1416), 1158 (AB0264)
Perez-Garcia L. F., 0127 (OP0211), 0127 (OP0212), 0186 (OP0303-HPR)
Perez-Onofre I., 1439 (AB0830)
Perez-Pampín E., 0009 (OP0017), 0034 (OP0064), 0035 (OP0065), 0068 (OP0123), 0306 (POS0185), 0524 (POS0581), 0524 (POS0582), 0692 (POS0873), 0916 (POS1264), 0935 (POS1306), 1173 (AB0294)
Perez-Ruiz F., 0841 (POS1124)
Perez-Sanchez C., 0020 (OP0038), 0426 (POS0394), 0469 (POS0475), 0769 (POS1001), 1317 (AB0562)
Perez-Sancristobal I., 0896 (POS1225), 0908 (POS1251), 0910 (POS1253)
Pérez-Veiga N., 0610 (POS0721)
Peries Reverter L., 0856 (POS1156)
Peroni C. L., 0676 (POS0845), 0904 (POS1243)
Perra L., 0901 (POS1236), 0901 (POS1237)
Perren A., 1342 (AB0616)
Perricone C., 0211 (POS0019)
Perricone R., 0335 (POS0231), 0619 (POS0737), 0778 (POS1021), 0980 (POS1395), 1038 (AB0006), 1260 (AB0467), 1284 (AB0515), 1418 (AB0786), 1434 (AB0821)
Perrier C., 0577 (POS0668)
Pertel P., 0707 (POS0900), 0724 (POS0925)
Pertuiset E., 0172 (OP0284), 0343 (POS0243), 0857 (POS1158), 0858 (POS1159)
Perurena-Prieto J., 0898 (POS1229)
Pesachov J., 0286 (POS0147)
Pesce E., 0229 (POS0048)
Pesce G., 1190 (AB0330)
Peschken C., 0177 (OP0289)
Pesonen M. E., 1245 (AB0433)
Petaipimol P., 0013 (OP0023), 1167 (AB0282)
Petciappan V., 1160 (AB0268)
Peter N., 1383 (AB0701)
Peter W., 1460 (AB0873-HPR)
Peterfy C., 0251 (POS0087), 1158 (AB0264)
Peterlik D., 0706 (POS0899), 0780 (POS1023)
Peters M., 0544 (POS0615)
Peters S., 1029 (POS1490-HPR)
Petersen M., 0065 (OP0117)
Peterson A., 0369 (POS0287)
Peterson J., 1348 (AB0630)
Peterson M., 0128 (OP0213), 0213 (POS0023)
Peterson S., 0316 (POS0200), 0782 (POS1026), 0784 (POS1028), 1313 (AB0556)
Pethö Z., 0226 (POS0043), 0421 (POS0383), 0425 (POS0390)
Pethoe-Schramm A., 0651 (POS0798)
Petit-Frere C., 1121 (AB0195)
Petrache O. G., 1267 (AB0480)
Petraglia F., 1192 (AB0334)
Petrariu L., 1380 (AB0695)
Petre A., 0681 (POS0854)
Petri M. A., 0177 (OP0289), 0181 (OP0296), 0377 (POS0304)
Petrova E., 1388 (AB0713)
Petrova M., 1352 (AB0636)
Pettersson S., 0093 (OP0156-HPR), 1023 (POS1476-HPR)
Pettiti G., 0906 (POS1246)
Petzold G., 1237 (AB0418)
Peyronnel C., 1062 (AB0062)
Peyruchaud O., 0431 (POS0404)
Pezoulas V., 0178 (OP0291), 0180 (OP0294), 0370 (POS0290)
Pfeiffenberger M., 0191 (OP0312), 1048 (AB0029), 1049 (AB0031), 1052 (AB0040)
Pfeiffer C., 0670 (POS0834)
Pfeiffer Jensen M., 0234 (POS0056), 0865 (POS1170)
Pfeifle R., 1042 (AB0016)
Pfeil A., 0040 (OP0075), 0171 (OP0283), 0915 (POS1261), 1030 (POS1492-HPR), 1422 (AB0796)
Pha M., 1186 (AB0323)
Pham M., 0535 (POS0602)
Pham T., 0172 (OP0284), 0900 (POS1234)
Philippe P., 0662 (POS0818), 1258 (AB0464)
Piantoni S., 0530 (POS0593), 1167 (AB0283)
Picaro F., 1399 (AB0739)
Picchi C., 0628 (POS0751)
Picchio M., 1206 (AB0361)
Picco E., 0875 (POS1188)
Picerno V., 0134 (OP0223), 1260 (AB0467)
Picot M. C., 0080 (OP0138)
Pierache A., 0114 (OP0190)
Piercy J., 0885 (POS1205)
Pierer M., 0421 (POS0382)
Pierobon E., 1326 (AB0578)
Pierre-Louis B., 1287 (AB0522)
Pieta A., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Pieterse A., 1478 (AB0914-PARE)
Pietromatera G., 0882 (POS1200)
Pietrowski W., 0383 (POS0314)
Piette Y., 0378 (POS0305)
Piga M., 0134 (OP0223), 0324 (POS0214), 0628 (POS0751), 0632 (POS0758)
Pigatto E., 0392 (POS0329), 0906 (POS1246)
Piguet V., 0132 (OP0221), 0812 (POS1068)
Pijnenburg L., 0877 (POS1190)
Pike V. C., 0278 (POS0134)
Pilar F. U., 0469 (POS0475), 0736 (POS0946), 0737 (POS0948)
Pilet S., 0901 (POS1236), 0901 (POS1237)
Pillet P., 0939 (POS1314)
Pillinger M. H., 0278 (POS0134)
Pimenta S., 0718 (POS0914), 1188 (AB0327), 1191 (AB0332), 1266 (AB0478)
Pimentel Dos Santos F., 0024 (OP0047), 1041 (AB0014), 1268 (AB0482), 1402 (AB0747)
Pin E., 0425 (POS0392)
Pina F., 0582 (POS0676)
Pina Vegas L., 0027 (OP0052), 0317 (POS0201)
Pinal-Fernandez I., 1241 (AB0426)
Pineda C., 0845 (POS1132), 0846 (POS1133), 0850 (POS1141), 1296 (AB0531), 1348 (AB0629)
Pineda Torra I., 0008 (OP0013)
Pineda Vidal S. I., 0874 (POS1186)
Pineda.Tamayo R., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336), 1200 (AB0351)
Pineda-Sic R., 1007 (POS1446), 1455 (AB0863-HPR)
Pinedo Gago M. C., 0872 (POS1183)
Pinheiro M., 0582 (POS0676), 0723 (POS0924), 0909 (POS1252), 1448 (AB0848)
Pinheiro Torres R., 1041 (AB0014), 1268 (AB0482), 1402 (AB0747)
Pinillos V., 0034 (OP0064)
Pink A., 1323 (AB0573)
Pinnell J., 1010 (POS1452)
Pino J., 0418 (POS0376)
Pino Martínez M., 1280 (AB0505)
Pinto A. S., 0354 (POS0263), 0692 (POS0872), 0773 (POS1010), 1424 (AB0799)
Pinto A., 1183 (AB0317)
Pinto P., 1236 (AB0415), 1236 (AB0416), 1236 (AB0417)
Pinto Tasende J. A., 0418 (POS0375), 0766 (POS0996), 1326 (AB0577)
Piovesan M., 0771 (POS1005)
Piper B., 0824 (POS1089)
Pires Da Rosa G., 0637 (POS0767), 1195 (AB0340)

Pirone C., 0583 (POS0677), 0645 (POS0783), 1069 (AB0079), 1073 (AB0087)
Pirrello J., 0031 (OP0059), 0198 (LB0001)
Pirronello S. M. G., 1002 (POS1435)
Pirson V., 0880 (POS1196)
Pisani P., 0294 (POS0163)
Piskin D., 0958 (POS1352), 0968 (POS1372), 0969 (POS1375)
Piskin G., 0962 (POS1361)
Piskin Sagir R., 1266 (AB0479), 1317 (AB0561)
Pisoni C., 0874 (POS1186), 1196 (AB0342)
Pistillo F., 1099 (AB0143)
Pistorio A., 0097 (OP0161), 0098 (OP0164)
Pitsigavdaki S., 0184 (OP0299), 0523 (POS0580), 0733 (POS0941)
Pitzalis C., 0007 (OP0011), 0079 (OP0136), 0120 (OP0200), 0319 (POS0206), 1052 (AB0039)
Pizarro C., 1103 (AB0152)
Pizzimenti M., 0149 (OP0243), 0694 (POS0876)
Pizzonia M., 0833 (POS1105)
Pizzorni C., 0392 (POS0330), 0679 (POS0850), 0686 (POS0862), 0697 (POS0882), 0908 (POS1250), 1190 (AB0330), 1247 (AB0438), 1372 (AB0679)
Plankar Srovin T., 0941 (POS1318)
Plant D., 0467 (POS0471)
Plasencia C., 0546 (POS0617), 0750 (POS0969), 0755 (POS0977), 0986 (POS1407), 1065 (AB0070), 1101 (AB0149), 1277 (AB0500)
Platt A., 0253 (POS0089)
Platzer A., 0475 (POS0485), 1060 (AB0056)
Plazuelo-Ramos P., 0343 (POS0244), 0762 (POS0988), 0762 (POS0989), 0763 (POS0990), 0763 (POS0991), 0764 (POS0992), 0765 (POS0993), 0765 (POS0994), 0889 (POS1213), 1277 (AB0500), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Plebani M., 0894 (POS1221)
Pleitavino F., 0833 (POS1105)
Plesa C. F., 1267 (AB0480)
Pleyer U., 0017 (OP0031)
Plüß M., 0611 (POS0722), 1167 (AB0283)
Pocovi-Gerardino G., 1182 (AB0315), 1183 (AB0316)
Poddubnyy D., 0017 (OP0031), 0025 (OP0048), 0080 (OP0137), 0081 (OP0139), 0153 (OP0251), 0155 (OP0253), 0155 (OP0254), 0156 (OP0256), 0221 (POS0032), 0239 (POS0065-PARE), 0332 (POS0226), 0342 (POS0241), 0343 (POS0244), 0373 (POS0296), 0456 (POS0453), 0707 (POS0900), 0710 (POS0905), 0713 (POS0908), 0722 (POS0923), 0744 (POS0960), 0745 (POS0961), 0750 (POS0969), 0756 (POS0979), 0762 (POS0988), 0762 (POS0989), 0763 (POS0990), 0769 (POS1002), 0771 (POS1007), 0798 (POS1045), 0813 (POS1069), 0887 (POS1209), 1259 (AB0465)
Poetzsch S., 0305 (POS0184)
Pogorelova O., 0493 (POS0520)
Pogozheva E., 1109 (AB0165), 1160 (AB0267), 1162 (AB0272)
Poiroux L., 1364 (AB0665)
Pok L. S. L., 0816 (POS1075)
Pokroy-Shapira E., 0892 (POS1217)
Polachek A., 0200 (LB0003), 0885 (POS1206), 1049 (AB0032), 1181 (AB0312)
Polanco Mora T., 1187 (AB0325), 1188 (AB0326), 1351 (AB0635)
Polekhina G., 0009 (OP0015)
Polido-Pereira J., 0329 (POS0222), 0644 (POS0781)
Polissidis A., 0021 (OP0040)
Polvent E., 0843 (POS1128), 0844 (POS1130)
Polyakov V., 0420 (POS0380), 1437 (AB0827), 1461 (AB0875-HPR)
Polyakova J., 0297 (POS0169), 0455 (POS0451), 0487 (POS0509)
Polyakova Y., 1437 (AB0827), 1461 (AB0875-HPR)
Pomar V., 1426 (AB0804)
Pombo M., 0542 (POS0610)
Pombo-Suarez M., 0131 (OP0220), 0217 (POS0027), 0256 (POS0093)
Pomirleanu C., 1380 (AB0695)
Ponchel F., 0110 (OP0182)
Pons Estel G., 0874 (POS1186)
Pons-Estel B., 0177 (OP0289), 0181 (OP0296)
Pons-Estel G., 0173 (OP0286), 0875 (POS1188), 0887 (POS1208), 1196 (AB0342)
Pontarini E., 0007 (OP0011), 0074 (OP0130), 0079 (OP0136)
Ponte C., 0029 (OP0055)
Pontikaki I., 0936 (POS1308)
Poon A., 0117 (OP0194)
Poorafshar M., 1090 (AB0122)
Pope J., 0103 (OP0172), 0159 (OP0262-HPR), 0320 (POS0207), 0468 (POS0474), 1014 (POS1459-HPR), 1237 (AB0419), 1251 (AB0447)
Popkova T., 0493 (POS0520), 0514 (POS0559), 0515 (POS0561), 0613 (POS0727), 0614 (POS0729), 1049 (AB0033), 1064 (AB0068), 1072 (AB0086), 1155 (AB0257), 1172 (AB0292), 1179 (AB0306), 1179 (AB0307), 1180 (AB0309), 1180 (AB0310), 1350 (AB0631), 1422 (AB0795)
Popov A., 0037 (OP0070), 0201 (LB0004)
Popov V., 0890 (POS1214)
Popova S., 1272 (AB0489)
Popp F., 1274 (AB0494)
Port H., 0742 (POS0955)
Porta F., 0850 (POS1141), 1335 (AB0598)
Porta S., 0875 (POS1188), 1196 (AB0342)
Porter D., 0403 (POS0348), 1159 (AB0265)
Portier E., 0308 (POS0188)
Portilla V., 0755 (POS0977), 0953 (POS1342), 0977 (POS1390), 0986 (POS1407), 1002 (POS1436), 1046 (AB0026), 1065 (AB0070), 1076 (AB0094)
Posio C., 0858 (POS1161), 0869 (POS1176), 1363 (AB0661)
Posthumus M. D., 0657 (POS0809)
Potapova A., 0977 (POS1388), 1406 (AB0757), 1407 (AB0759)
Potempa B. A., 0996 (POS1425)
Potempa J. S., 0996 (POS1425)
Potempa L. A., 0418 (POS0376)
Pothuru S., 0600 (POS0701)
Potretzke A., 0951 (POS1338)
Pou M. A., 1354 (AB0643)
Pouchot J., 0052 (OP0094), 0172 (OP0284), 1412 (AB0772)
Poudret M., 1164 (AB0277)
Poulain L., 0169 (OP0279-PARE), 1362 (AB0659)
Poulet B., 0120 (OP0200)
Poulsen A. E. F., 0089 (OP0149), 0153 (OP0252)
Pournara E., 0337 (POS0234), 0728 (POS0930)
Poveschenko O., 1045 (AB0023)
Povoroznyuk V., 0836 (POS1112)
Poyraz B. C., 0875 (POS1187)
Pozdeeva N., 1393 (AB0724)
Pozzi M. R., 0384 (POS0316)
Prabowo N. A., 1425 (AB0802)
Prabu A., 0602 (POS0705)
Prabu N., 1160 (AB0268)
Praciano L., 0208 (POS0013)
Pradel V., 0900 (POS1234), 1061 (AB0058)
Praestgaard J., 0211 (POS0020), 0363 (POS0277)
Praino E., 0726 (POS0927)
Prante O., 0165 (OP0272)
Prata A. R., 0481 (POS0496), 0606 (POS0713), 1101 (AB0147)
Prati C., 0331 (POS0225), 0719 (POS0916), 0748 (POS0967), 0793 (POS1039), 1067 (AB0073), 1159 (AB0266), 1275 (AB0496), 1279 (AB0504)
Pratsidou-Gertsi P., 0193 (OP0317-PARE)
Pratt A., 0018 (OP0033), 0403 (POS0348), 1044 (AB0021), 1046 (AB0025)
Prearo I., 1002 (POS1435)
Predeteanu D., 0164 (OP0270), 0681 (POS0854), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690)
Preedeekanit K., 1139 (AB0228)
Preen D., 0052 (OP0095), 0055 (OP0100-HPR), 0250 (POS0084), 0373 (POS0297), 0852 (POS1147), 1079 (AB0103), 1224 (AB0393)
Pregnolato F., 0940 (POS1315)
Premkuar A., 0828 (POS1097)
Preobrazhenskaia E., 1335 (AB0596)
Preuss P., 0920 (POS1271)
Price M., 0377 (POS0303)
Pricop L., 0201 (LB0004)
Pridgen W., 0210 (POS0017)
Prieto-Alhambra D., 0058 (OP0105), 0215 (POS0025), 0232 (POS0053), 0829 (POS1098)
Prieto-González S., 0272 (POS0121)
Prieto-Peña D., 0032 (OP0060), 0396 (POS0337), 0899 (POS1231), 0955 (POS1346), 1018 (POS1467-HPR), 1046 (AB0026), 1076 (AB0094), 1076 (AB0096), 1208 (AB0365), 1208 (AB0366), 1243 (AB0430), 1377 (AB0688)
Primdahl J., 0159 (OP0261-HPR), 0994 (POS1423)
Prince D., 0476 (POS0487)
Pringle S. A., 0189 (OP0308)
Prior Y., 0290 (POS0153-HPR)
Prior-Español Á., 0967 (POS1371)
Priori R., 0628 (POS0751), 0893 (POS1219), 0903 (POS1240), 1017 (POS1464-HPR), 1143 (AB0234), 1183 (AB0317)
Pripp A. H., 0048 (OP0089), 0543 (POS0612), 1135 (AB0219)
Prisco D., 0889 (POS1212)
Prisco L., 0494 (POS0522), 0867 (POS1174)
Probatova N., 1406 (AB0757)
Proderm Investigators A. T., 0004 (OP0008)
Proft F., 0017 (OP0031), 0025 (OP0048), 0080 (OP0137), 0081 (OP0139), 0155 (OP0254), 0156 (OP0256), 0342 (POS0241), 0456 (POS0453), 0750 (POS0969), 0756 (POS0979), 0771 (POS1007), 0813 (POS1069)
Prokhorova E., 0982 (POS1399)
Prothmann U., 1153 (AB0255)
Prothon S., 0253 (POS0089)
Protogerou A., 0656 (POS0807)
Protopopov M., 0025 (OP0048), 0080 (OP0137), 0081 (OP0139), 0155 (OP0254), 0342 (POS0241), 0456 (POS0453), 0756 (POS0979), 0771 (POS1007), 0813 (POS1069)
Protsenko D., 0890 (POS1214)
Proudman S., 0697 (POS0883)
Provan S. A., 0063 (OP0114)
Provenza J. R., 0909 (POS1252), 1448 (AB0848)
Pruner I., 0693 (POS0874)
Psachoulia K., 0586 (POS0683)
Psarelis S., 0161 (OP0264-HPR), 1356 (AB0647), 1467 (AB0887-HPR)
Psarras A., 0078 (OP0134)
Puche Larrubia M. Á., 0736 (POS0946), 0747 (POS0965)
Puchner R., 0320 (POS0208)
Puga Guzmán J. L., 0692 (POS0873)
Puig-Kröger A., 1047 (AB0027)
Pulito Cueto V., 1065 (AB0070)
Pulito-Cueto V., 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1046 (AB0026), 1076 (AB0094), 1076 (AB0096)
Punt N. C., 0540 (POS0609)
Punwaney R., 0078 (OP0135), 1170 (AB0288)
Pupim L., 0031 (OP0059), 0198 (LB0001), 1211 (AB0370)
Purgatorio M. A., 0882 (POS1200)
Pushkov A., 1392 (AB0721)
Pusztai A., 0226 (POS0043), 0421 (POS0383), 0425 (POS0390)
Putman M., 0230 (POS0051), 1368 (AB0674)
Putrik P., 0198 (OP0324-PARE), 0374 (POS0299)
Putro E., 1069 (AB0079)
Pype N., 0545 (POS0616)

Qi W., 0178 (OP0290), 0641 (POS0775), 0642 (POS0777)
Qiao J., 0111 (OP0184), 0315 (POS0199), 0616 (POS0732), 0619 (POS0736), 0623 (POS0743), 0677 (POS0847), 0684 (POS0859), 0888 (POS1211), 1436 (AB0824)
Qin L., 0257 (POS0094)
Qin Y., 1061 (AB0060)
Qing Y. F., 0280 (POS0136), 0852 (POS1146), 1040 (AB0011), 1067 (AB0075), 1252 (AB0449)
Qiu M. T., 0111 (OP0184), 0684 (POS0859)
Qiu V., 0260 (POS0101)
Qiu Y., 1458 (AB0870-HPR)
Qu J., 0629 (POS0754)
Quaglia M. I., 1194 (AB0338)
Quartier P., 0098 (OP0164)

Quartuccio L., 0009 (OP0017), 0878 (POS1192), 0883 (POS1201), 1224 (AB0392)
Quasny H., 0596 (POS0697), 1170 (AB0288)
Quattrocchio G., 0601 (POS0704)
Quebe A., 0561 (POS0646)
Queiró Silva R., 0819 (POS1080), 1280 (AB0505)
Queiroz Z., 0444 (POS0432)
Quéméneur T., 0664 (POS0822)
Quéré B., 0939 (POS1314)
Quereza e Silva Faria T., 0208 (POS0013)
Quesada-Masachs E., 0943 (POS1322)
Quesada-Masachs H., 0943 (POS1322)
Quevedo Vila V., 0610 (POS0721), 1326 (AB0577)
Quevedo-Abeledo J. C., 0614 (POS0728), 0755 (POS0977), 0766 (POS0996), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070)
Queyrel V., 0261 (POS0103)
Quiles Roger A., 0857 (POS1157)
Quinn K. A., 0345 (POS0248), 0653 (POS0802)
Quinn K., 1017 (POS1465-HPR)
Quinn S., 0747 (POS0964), 0891 (POS1216)
Quinn-Laurin V., 1334 (AB0594)
Quintana Lopez G., 0479 (POS0493), 1081 (AB0106), 1429 (AB0810)
Quintana R., 0874 (POS1186), 0875 (POS1188), 0887 (POS1208)
Quintero C., 0639 (POS0770)

R R., 1413 (AB0773)
Raad T., 0115 (OP0191-PARE)
Raadsen R., 0324 (POS0213), 0495 (POS0523)
Raaf N. B., 0843 (POS1127)
Rabelink T., 0585 (POS0680)
Rabensteiner D., 0261 (POS0102)
Racault A. S., 1121 (AB0195)
Rachdi M., 1484 (AB0926-PARE)
Radanova M., 1036 (AB0002)
Radawski C., 0096 (OP0160-HPR)
Radbruch A., 0207 (POS0010)
Rademacher J. G., 1237 (AB0418), 1433 (AB0818)
Rademacher J., 0017 (OP0031), 0025 (OP0048), 0080 (OP0137), 0081 (OP0139), 0155 (OP0254), 0342 (POS0241), 0756 (POS0979), 0769 (POS1002), 0771 (POS1007), 0813 (POS1069)
Rademakers J., 0198 (OP0324-PARE), 0374 (POS0299)
Radenska-Lopovok S., 0977 (POS1388), 1406 (AB0757)
Radin M., 0298 (POS0172), 1039 (AB0008), 1073 (AB0088)
Radmer Jensen M., 1202 (AB0355)
Radner H., 0475 (POS0485)
Radny F., 0156 (OP0256)
Radominski S., 1156 (AB0260)
Radouan A., 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Radstake T., 0064 (OP0115), 0721 (POS0920)
Radwan A., 0977 (POS1389), 1391 (AB0720), 1420 (AB0790)
Radwan Y., 0106 (OP0177), 0389 (POS0325), 0672 (POS0836), 0673 (POS0838)
Radziszewska A., 0008 (OP0013)
Raffayova H., 1296 (AB0531)
Raffeiner B., 0134 (OP0223), 0199 (LB0002), 1404 (AB0752)
Raggiunti M., 1246 (AB0434)
Raghunath S., 0616 (POS0731)
Ragusa F., 0906 (POS1246)
Rahal F., 1147 (AB0243)
Rahbar M., 0710 (POS0904)
Rahbari E., 0601 (POS0704)
Rahman A., 0177 (OP0289), 0181 (OP0296), 0602 (POS0705)
Rahman F., 0279 (POS0135)
Rahman P., 0316 (POS0200), 0431 (POS0405), 0432 (POS0406), 0707 (POS0901), 0714 (POS0909), 0781 (POS1024), 0782 (POS1026), 0783 (POS1027), 0784 (POS1028), 0801 (POS1048), 1292 (AB0527), 1293 (AB0528), 1300 (AB0538), 1313 (AB0557)
Rahmouni S., 1091 (AB0124), 1281 (AB0509)
Rai A., 1127 (AB0205)
Raimondo S., 0022 (OP0042)
Raimondo V., 0906 (POS1246)
Raio L., 0649 (POS0794)
Raithel E., 0363 (POS0277)
Raizada S., 0903 (POS1241)
Raja J., 1256 (AB0458)
Rajab I. M., 0418 (POS0376)
Rajagopala L., 0005 (OP0009-PARE)
Rajak R., 1342 (AB0616)
Rajalingham S., 0611 (POS0723), 1105 (AB0155)
Rakholiya J., 0655 (POS0805)
Rakkunedeth A., 1334 (AB0594)
Rakotozafiarison A., 0818 (POS1078)
Ramabhadran B., 1417 (AB0783)
Ramachandran P., 0787 (POS1031), 1293 (AB0528), 1300 (AB0538)
Ramakrishna Rao D. R., 1346 (AB0626)
Ramanan A., 0201 (LB0004)
Ramanathan S., 0847 (POS1136)
Ramazzotto F., 1435 (AB0822)
Rambojun A., 0789 (POS1034)
Rameev V., 1414 (AB0774)
Ramírez A., 0639 (POS0770)
Ramirez G. A., 0594 (POS0693), 0613 (POS0726), 0907 (POS1247)
Ramirez J., 1120 (AB0193)
Ramirez-Flores M. F., 1428 (AB0808)
Ramirez-Valle F., 0433 (POS0408)
Ramiro S., 0152 (OP0250), 0193 (OP0316), 0304 (POS0181), 0340 (POS0238), 0345 (POS0248), 0374 (POS0299), 0540 (POS0609), 0718 (POS0915), 0723 (POS0924), 0739 (POS0951), 0740 (POS0953), 0751 (POS0971), 0911 (POS1256), 1213 (AB0373)
Ramji D., 0402 (POS0346)
Ramming A., 0121 (OP0201), 0165 (OP0272), 0670 (POS0834), 0996 (POS1426), 1075 (AB0091)
Ramon A., 0843 (POS1129)
Ramonda R., 0026 (OP0050), 0339 (POS0236), 0726 (POS0927), 0741 (POS0954), 0742 (POS0956), 0809 (POS1061), 0841 (POS1124), 0894 (POS1221), 1308 (AB0549), 1331 (AB0588)
Ramoni V., 0105 (OP0175), 0628 (POS0751)
Ramos A., 0559 (POS0642)
Ramos Calvo A., 0967 (POS1371)
Ramos D. S., 0363 (POS0277)
Ramos E., 0350 (POS0256), 0987 (POS1408), 0987 (POS1409)
Ramos Ruperto L., 1192 (AB0333)
Ramos-Louro P., 0403 (POS0347)
Rampes S., 0573 (POS0662)
Rampoldi S., 1007 (POS1447)
Ramrattan L. A., 1088 (AB0119)
Ramsey-Goldman R., 0177 (OP0289)
Ramsubeik K., 1088 (AB0119)
Ramsundar N., 1432 (AB0817)
Rando S., 1007 (POS1447)
Ranganathan P., 1092 (AB0128)
Ranza R., 0143 (OP0233), 0338 (POS0235), 0582 (POS0676), 1308 (AB0550)
Ranzolin A., 0582 (POS0676)
Raposo B., 0001 (OP0003)
Rapp P., 1274 (AB0494)
Rapsomaniki P., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Rasero L., 1032 (POS1495-HPR)
Rasevich T., 1095 (AB0135)
Rashkov R., 0337 (POS0234)
Raskina T., 0277 (POS0131), 1344 (AB0621), 1416 (AB0780), 1443 (AB0838)
Rasmussen S. H., 0131 (OP0220), 0217 (POS0027), 0234 (POS0056), 0865 (POS1170)
Rassi J., 0340 (POS0239)
Rat A. C., 0054 (OP0098)
Raterman H., 0226 (POS0043), 1107 (AB0160)
Rath T., 0705 (POS0897)
Ratiu A., 0377 (POS0304)
Rato M., 0260 (POS0100), 0318 (POS0204), 0476 (POS0488), 0483 (POS0502), 0718 (POS0914), 0812 (POS1067), 0833 (POS1106), 0836 (POS1113), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1299 (AB0536), 1432 (AB0816), 1441 (AB0835)
Rattenbach R., 0417 (POS0373)
Rauch C., 0108 (OP0180), 0453 (POS0447), 0533 (POS0599), 1128 (AB0207)
Rauf A., 0806 (POS1056), 0915 (POS1262)
Raupach T., 1446 (AB0846)
Raupov R., 0246 (POS0078), 0247 (POS0080), 0931 (POS1299), 1036 (AB0001)
Ravelli A., 0097 (OP0161), 0201 (LB0004), 0242 (POS0071)
Ravelo J., 1387 (AB0710)
Rawstron A., 0030 (OP0057), 1173 (AB0293)
Ray N., 0074 (OP0130), 1081 (AB0107)
Raya E., 0034 (OP0064), 0967 (POS1371)
Raymond W., 0052 (OP0095), 0250 (POS0084), 0852 (POS1147), 1224 (AB0393)
Raza K., 0096 (OP0160-HPR), 1026 (POS1483-HPR)
Razumova I., 0717 (POS0913)
Reachel Varghese D., 0700 (POS0889)
Realle P., 0909 (POS1252), 1448 (AB0848)
Reategui Sokolova C., 0173 (OP0286)
Rebak J., 0874 (POS1186), 0887 (POS1208)
Rebrov A., 1455 (AB0864-HPR)
Recalchi S., 0902 (POS1238)
Rech J., 0050 (OP0092), 0088 (OP0148), 0194 (OP0318), 0420 (POS0381), 0461 (POS0460)
Recker F., 1446 (AB0846), 1447 (AB0847)
Recto R., 0589 (POS0687)
Recuero Diaz S., 0914 (POS1260)
Reddy M., 1406 (AB0756)
Redeker I., 0025 (OP0048), 0771 (POS1007), 1435 (AB0823)
Rednic S., 0338 (POS0235), 0638 (POS0768), 0685 (POS0861), 1360 (AB0656)
Redondo Costa J., 1003 (POS1438)
Redondo R., 0323 (POS0211), 1453 (AB0859-HPR)
Redondo Rodriguez R., 0344 (POS0246)
Rees F., 0560 (POS0643)
Reffstrup Christensen J., 0159 (OP0261-HPR), 0994 (POS1423)
Reggia R., 0633 (POS0760)
Regierer A., 0135 (OP0225), 0171 (OP0283), 0373 (POS0296), 0915 (POS1261)
Reginato A., 0841 (POS1124)
Regner E. H., 0748 (POS0966)
Regola F., 0530 (POS0593), 0594 (POS0693), 0650 (POS0797), 0658 (POS0811), 1435 (AB0822)
Rego-Perez I., 0403 (POS0347)
Rehart S., 1054 (AB0043), 1054 (AB0044)
Reich K., 0787 (POS1031)
Reichenbach S., 0033 (OP0061), 0272 (POS0122)
Reijnierse M., 0152 (OP0250), 0212 (POS0021), 0222 (POS0033), 0273 (POS0123), 0351 (POS0257), 0351 (POS0258), 0422 (POS0385), 0978 (POS1391), 0999 (POS1431)
Reimold A., 1205 (AB0360)
Reina D., 1219 (AB0384)
Reina-Sanz D., 1158 (AB0264)
Reis J., 0224 (POS0037)
Reis Neto E., 0909 (POS1252), 1448 (AB0848)
Reiser M., 0194 (OP0318)
Reiseter S., 0104 (OP0174)
Reitblat T., 0753 (POS0974), 0892 (POS1217)
Reji R., 0700 (POS0889)
Rekik S., 0290 (POS0155-HPR), 0372 (POS0294), 0923 (POS1280), 0926 (POS1288), 1090 (AB0123), 1097 (AB0139), 1144 (AB0238), 1145 (AB0240), 1147 (AB0244), 1272 (AB0490), 1273 (AB0492), 1421 (AB0793)
Relaño-Fernandez S., 0403 (POS0347)
Relas H., 0063 (OP0114), 0082 (OP0140), 0131 (OP0220), 0133 (OP0222)
Remesal A., 0098 (OP0164)
Remmelts H. H. F., 0346 (POS0249), 1221 (AB0387)
Remondino G., 1196 (AB0342)
Rempenault C., 0559 (POS0641)
Remuzgo Martinez S., 1046 (AB0026), 1076 (AB0094), 1076 (AB0096)
Remuzgo-Martínez S., 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070)
Remy J., 1229 (AB0401)
Remy-Jardin M., 1229 (AB0401)
Ren A., 0031 (OP0059)

Renaud P., 1408 (AB0761)
Repa A., 0184 (OP0299), 0523 (POS0580), 0733 (POS0941)
Repa E., 0193 (OP0317-PARE)
Resche-Rigon M., 0233 (POS0055)
Resende C., 0692 (POS0872)
Reshetnyak T., 0605 (POS0712), 0614 (POS0729), 0643 (POS0780), 1177 (AB0303), 1178 (AB0305), 1180 (AB0308), 1180 (AB0309), 1180 (AB0310)
Restrepo Vélez J., 0960 (POS1355)
Retamozo C., 0874 (POS1186)
Réthi B., 0429 (POS0400)
Reumaux H., 1412 (AB0772)
Reutfors J., 0939 (POS1313)
Reveille J. D., 0708 (POS0902), 0710 (POS0904), 0714 (POS0909), 0720 (POS0918)
Revenga M., 0034 (OP0064)
Revollo I., 0589 (POS0687)
Rexach Fumaña M., 0856 (POS1156)
Rexhaj E., 0649 (POS0794)
Reyes A. A., 0875 (POS1188), 0887 (POS1208)
Reyes G., 0904 (POS1242)
Reyes Soto M. A., 1450 (AB0852)
Reyes-Juárez J. L., 0699 (POS0886)
Reyna-de la Garza R. A., 1189 (AB0329)
Reynisdóttir G. B., 0133 (OP0222)
Reynolds A., 1051 (AB0036)
Reynolds G., 1008 (POS1448)
Reynolds J., 0043 (OP0081), 0078 (OP0134)
Reza Beigi D. M., 0873 (POS1185)
Rezaei H., 0087 (OP0146)
Rezniczek G., 1375 (AB0684)
Riahi H., 0526 (POS0586), 0526 (POS0587), 1112 (AB0171), 1117 (AB0186), 1119 (AB0191), 1278 (AB0501)
Riaz M., 0009 (OP0015)
Ribaldone D. G., 0335 (POS0230)
Ribeiro A. R., 1003 (POS1438)
Ribeiro S., 0208 (POS0013), 0909 (POS1252), 1448 (AB0848)
Ribi C., 0386 (POS0318)
Ricatte C., 0358 (POS0270-HPR)
Riccieri V., 0150 (OP0246), 0385 (POS0317), 0387 (POS0321), 0445 (POS0433), 0685 (POS0861), 0873 (POS1185), 0893 (POS1219), 0903 (POS1240), 0906 (POS1246), 1143 (AB0234)
Rice J. B., 0366 (POS0283)
Richards H., 0707 (POS0900)
Richards J. S., 0476 (POS0487)
Richards P., 0291 (POS0158-HPR), 1441 (AB0834)
Richer O., 0939 (POS1314)
Richette P., 0028 (OP0053), 0183 (OP0298), 0340 (POS0238), 0751 (POS0971), 0786 (POS1030), 0788 (POS1032), 0790 (POS1035), 0841 (POS1124), 0901 (POS1236), 0901 (POS1237)
Richez C., 0172 (OP0284), 0328 (POS0220), 0897 (POS1227), 1148 (AB0247), 1261 (AB0469)
Richter J., 0171 (OP0283), 0915 (POS1261), 1263 (AB0472)
Richter S., 0349 (POS0254), 0667 (POS0828), 1310 (AB0552), 1311 (AB0553)
Richter-Bastian K., 0383 (POS0314)
Riddell C., 0161 (OP0265-HPR), 1410 (AB0767)
Riddell V., 0369 (POS0288)
Ridker P., 0327 (POS0219)
Ridley A., 0017 (OP0032)
Riechers E., 0706 (POS0899), 0780 (POS1023), 1153 (AB0255)
Riegatorres J. C., 1177 (AB0301)
Riemekasten G., 0028 (OP0054), 0149 (OP0244), 0162 (OP0266), 0386 (POS0318), 0395 (POS0335), 0670 (POS0834), 1008 (POS1449)
Riera P., 1093 (AB0129)
Riesco Barcena C., 0296 (POS0167), 0964 (POS1365), 1278 (AB0502)
Rietschel C., 0246 (POS0077), 0883 (POS1202)
Rieu V., 0397 (POS0338)
Riggs R. J., 1033 (POS1497-PARE)
Rigopoulos D., 1304 (AB0543)
Riitano G., 0902 (POS1238)
Rillo O., 0771 (POS1005)
Rimoldi S. G., 1367 (AB0671)
Rincheval N., 0109 (OP0181), 0110 (OP0183)
Río L., 1132 (AB0212)
Rios C., 0376 (POS0302)
Rios D., 1043 (AB0019)
Ríos Fernández R., 1182 (AB0315), 1231 (AB0405)
Rios J. J., 0350 (POS0256), 0693 (POS0875), 0987 (POS1408), 0987 (POS1409), 1192 (AB0333)
Rios Rodriguez V., 0017 (OP0031), 0025 (OP0048), 0080 (OP0137), 0081 (OP0139), 0155 (OP0253), 0155 (OP0254), 0342 (POS0241), 0456 (POS0453), 0756 (POS0979), 0771 (POS1007), 0813 (POS1069)
Ríos-Fernández R., 1183 (AB0316)
Ríos-Garcés R., 0272 (POS0121)
Riou M., 1373 (AB0680)
Rischmueller M., 0580 (POS0671)
Risueño F., 0875 (POS1188)
Ritchlin C. T., 0016 (OP0030), 0312 (POS0195), 0433 (POS0407), 0779 (POS1022), 0781 (POS1024), 0785 (POS1029), 0790 (POS1035), 0790 (POS1036), 1290 (AB0525), 1291 (AB0526), 1293 (AB0528), 1300 (AB0538), 1308 (AB0550)
Ritis K., 0015 (OP0029)
Ritschl V., 0320 (POS0208)
Ritt P., 0165 (OP0272)
Rittner L., 1255 (AB0457)
Rius Rigau A., 0391 (POS0328)
Riva M., 1326 (AB0578)
Rivai Z. I., 0071 (OP0127)
Rivas J. L., 0563 (POS0650), 0564 (POS0651), 1148 (AB0247)
Rivellese F., 0007 (OP0011), 0041 (OP0077), 0079 (OP0136)
Rivera J., 1027 (POS1484-HPR), 1117 (AB0185), 1467 (AB0889-HPR)
Rivera M., 0559 (POS0642)
Rivera Teran V., 0559 (POS0642)
Rivera-Triana D. P., 1475 (AB0907-HPR)
Rivero W., 1146 (AB0242), 1163 (AB0275)
Rivero-Tirado M., 0970 (POS1376)
Rivière B., 0019 (OP0035)
Rixon M. W., 0021 (OP0039)
Riyazi N., 0273 (POS0123), 0351 (POS0258)
Rizzi M., 1383 (AB0701)
Rizzo A., 0022 (OP0042)
Rizzo Borges A., 1448 (AB0848)
Rizzo C., 0301 (POS0177)
Rizzo G., 0628 (POS0751)
Rizzoni D., 0530 (POS0593)
Rkain H., 0992 (POS1417), 1148 (AB0246), 1270 (AB0485), 1270 (AB0486), 1430 (AB0811), 1472 (AB0898-HPR), 1472 (AB0899-HPR), 1473 (AB0901-HPR), 1474 (AB0902-HPR)
Robbins D., 0204 (POS0006)
Roberts K., 0874 (POS1186), 0875 (POS1188), 0887 (POS1208), 1196 (AB0342)
Roberts-Toler C., 0538 (POS0606), 1125 (AB0202)
Robinson D. E., 0829 (POS1098)
Robinson G., 0008 (OP0013), 0300 (POS0174)
Robinson P., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0852 (POS1147), 0859 (POS1162)
Robinson R., 0366 (POS0283), 0824 (POS1089), 1050 (AB0035)
Robiony M., 0618 (POS0735)
Robles Marhuenda Á., 0179 (OP0292), 0693 (POS0875), 0700 (POS0888), 1192 (AB0333)
Robson J., 0291 (POS0158-HPR), 1021 (POS1472-HPR), 1441 (AB0834)
Rocamora G., 0001 (OP0004)
Roccatello D., 0298 (POS0172), 0601 (POS0704), 1039 (AB0008), 1073 (AB0088)
Rocha Castellanos D. M., 0600 (POS0701)
Rocha Jr L., 0909 (POS1252)
Rocha L., 0582 (POS0676)
Rocha Loureda B., 0306 (POS0185)
Rocha M., 0692 (POS0872)
Rodello J., 0636 (POS0765)
Röder E., 0127 (OP0211), 0127 (OP0212), 0186 (OP0303-HPR)
Rodere M., 1009 (POS1450), 1022 (POS1475-HPR)
Rodero M., 1464 (AB0881-HPR), 1475 (AB0906-HPR)
Rødevand E., 0543 (POS0612)
Rodionovskaya S., 0014 (OP0027)
Rodrigues J., 0293 (POS0162), 0830 (POS1100), 1424 (AB0799)
Rodrigues M., 0606 (POS0713)
Rodrigues Pereira Almeida M., 1405 (AB0755)
Rodrigues-de-Sousa D. P., 0920 (POS1272)
Rodrigues-Manica S., 1268 (AB0482)
Rodriguez Bautista E., 1187 (AB0325), 1188 (AB0326), 1351 (AB0635)
Rodriguez Carrio J., 1046 (AB0026)
Rodriguez Chavez R. A., 0893 (POS1220), 1360 (AB0657), 1361 (AB0658), 1439 (AB0830), 1444 (AB0842), 1445 (AB0843), 1457 (AB0867-HPR), 1463 (AB0880-HPR)
Rodriguez Cundin P., 1018 (POS1467-HPR)
Rodriguez F., 1481 (AB0921-PARE)
Rodriguez Gil G. F., 0887 (POS1208)
Rodríguez Herredia J. M., 0914 (POS1260)
Rodríguez Jiménez B., 1109 (AB0166)
Rodríguez Montero S., 0952 (POS1340)
Rodriguez Navarro S., 1060 (AB0055)
Rodriguez Rodriguez L., 0403 (POS0348), 0896 (POS1225), 0908 (POS1251), 0910 (POS1253), 1464 (AB0881-HPR), 1475 (AB0906-HPR)
Rodríguez-Alarcón A., 1132 (AB0212)
Rodríguez-Diez B., 0891 (POS1215)
Rodríguez-Escalera C., 0469 (POS0475)
Rodriguez-Florido F., 1473 (AB0900-HPR)
Rodriguez-García S. C., 0490 (POS0513), 0531 (POS0595), 0542 (POS0610), 1089 (AB0120)
Rodríguez-Heredia J. M., 0755 (POS0978)
Rodríguez-Lozano C., 0755 (POS0977), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070)
Rodriguez-Lozano C., 0760 (POS0985)
Rodriguez-Martin S., 0144 (OP0234)
Rodríguez-Miguel A., 0144 (OP0234)
Rodriguez-Muguruza S., 0380 (POS0308)
Rodriguez-Pla A., 0655 (POS0805), 1220 (AB0386), 1232 (AB0408)
Rodriguez-Pubto I., 0637 (POS0767), 0700 (POS0888)
Rodriguez-Reyne T. S., 0904 (POS1242), 0905 (POS1245)
Rodriguez-Romero A. B., 0463 (POS0463), 0473 (POS0482), 0473 (POS0483), 0478 (POS0491), 0510 (POS0552), 0511 (POS0553), 0515 (POS0562), 0816 (POS1074), 0978 (POS1392), 0983 (POS1402), 0984 (POS1404), 1087 (AB0117), 1189 (AB0329)
Rodriguez-Sanchez G. E., 1085 (AB0113)
Roelofs A., 0019 (OP0036), 1052 (AB0039)
Roennow A., 1033 (POS1497-PARE)
Roessinger O., 0120 (OP0199)
Roessler A., 1153 (AB0255)
Roest L., 0548 (POS0621)
Roetzer K., 0848 (POS1137)
Rogatkina T., 1461 (AB0875-HPR)
Roger K., 1079 (AB0103)
Roger V., 0056 (OP0102)
Rogier C., 0992 (POS1418)
Rohani-Montez C., 1008 (POS1449)
Rohekar S., 0224 (POS0037), 1296 (AB0531)
Rohr K., 0069 (OP0124)
Roig Vilaseca D., 1219 (AB0384)
Rojas E., 1120 (AB0193)
Rojas Tessel R., 0887 (POS1208)
Rojas Zuleta W. G., 1139 (AB0227)
Rojas-Giménez M., 0323 (POS0211), 0494 (POS0521), 1109 (AB0166), 1245 (AB0432), 1253 (AB0451)
Rojas-Gualdrón D., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336), 1200 (AB0351)
Rojas-Villarraga A., 1146 (AB0242), 1163 (AB0275), 1475 (AB0907-HPR)
Rojkovich B., 0064 (OP0115)
Rollefstad S., 0123 (OP0204), 0219 (POS0029), 0795 (POS1041)
Román Ivorra J. A., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Roman L., 1106 (AB0159), 1120 (AB0193)
Romano C., 0907 (POS1248), 1475 (AB0905-HPR)
Romano F., 0979 (POS1393)
Romano M., 0942 (POS1320), 0958 (POS1352), 0968 (POS1372), 0969 (POS1375)
Romanowska-Prochnicka K., 0685 (POS0861)

Román-Rodriguez C., 0769 (POS1001), 1317 (AB0562)
Romão V. C, 0007 (OP0011)
Rombaut L., 0275 (POS0126)
Romdhane W., 0955 (POS1345), 1393 (AB0723), 1410 (AB0768), 1415 (AB0778)
Romeo N., 0906 (POS1246)
Romero F., 0700 (POS0888)
Romero-Barco C. M., 0323 (POS0211), 0469 (POS0475)
Romero-Diaz J., 0177 (OP0289), 0589 (POS0687), 0597 (POS0698), 0598 (POS0699)
Romero-Gómez C., 1208 (AB0366)
Romero-Gómez M., 0469 (POS0475)
Romero-Yuste S., 0378 (POS0305), 0952 (POS1340), 0967 (POS1371), 1208 (AB0366)
Ronen I., 0606 (POS0714)
Rongyi C., 0661 (POS0815)
Ronneberger M., 0194 (OP0318), 1274 (AB0494)
Rönnelid J., 0206 (POS0009), 0459 (POS0457), 1090 (AB0122)
Ronsky J., 1334 (AB0594)
Roque-Dapresa Y., 0609 (POS0720)
Røren Nordén K., 0092 (OP0154-HPR)
Ros I., 1303 (AB0542)
Ros J., 1241 (AB0426)
Rosa J., 0759 (POS0984)
Rosa R. M., 1208 (AB0366)
Rosales Z., 1464 (AB0881-HPR)
Rosas J., 0366 (POS0282), 0766 (POS0996)
Rose E., 0049 (OP0090), 0968 (POS1373)
Rose T., 0305 (POS0183), 0623 (POS0744)
Rosen J., 0211 (POS0020)
Rosenberg D., 0200 (LB0003)
Rosendaal F., 0273 (POS0123), 0351 (POS0258), 0999 (POS1431)
Rosenthal A., 0841 (POS1124)
Rosina S., 0242 (POS0071)
Rosman A., 1469 (AB0891-HPR)
Rosner I., 0543 (POS0613)
Ross Terres J., 0588 (POS0686)
Rossi D., 0601 (POS0704)
Rossini C., 0530 (POS0593)
Rossini M., 0062 (OP0112), 0106 (OP0178), 0326 (POS0218), 0560 (POS0644), 0582 (POS0675), 0594 (POS0693), 0831 (POS1102), 0867 (POS1173), 1222 (AB0389), 1271 (AB0488), 1477 (AB0911-HPR)
Rossi-Semerano L., 0939 (POS1314)
Rotar Z., 0131 (OP0220), 0217 (POS0027), 0256 (POS0093), 0650 (POS0796), 0664 (POS0823), 0666 (POS0826), 1201 (AB0352), 1201 (AB0353)
Rotaru T., 1337 (AB0601)
Roth D., 0078 (OP0135), 0591 (POS0689), 0596 (POS0696), 0596 (POS0697), 1170 (AB0288)
Roth E., 0584 (POS0678)
Roth M., 0162 (OP0267), 0163 (OP0268)
Rothe K., 0421 (POS0382)
Rotondo C., 1379 (AB0691)
Røtterud J. H., 0119 (OP0198-HPR)
Rouabhia R., 1111 (AB0169)
Roubenoff R., 0211 (POS0020), 0363 (POS0277)
Roudier J., 1061 (AB0058)
Roukens A. H. E., 1366 (AB0668)
Rountree R., 0204 (POS0006)
Rouse T., 0587 (POS0684), 0590 (POS0688)
Rousselin C., 0664 (POS0822)
Roux C., 0308 (POS0188), 0360 (POS0273-HPR), 0367 (POS0284), 0662 (POS0818)
Rovere-Querini P., 0619 (POS0737)
Rovin B. H., 0591 (POS0689), 0592 (POS0690)
Rovito D., 0151 (OP0247)
Rowe M., 1043 (AB0019)
Roy C., 0001 (OP0002)
Rozier P., 0417 (POS0374)
Rozochkina E., 0731 (POS0937), 1265 (AB0475), 1383 (AB0703)
Rozza G., 0888 (POS1210)
Rozzo S., 1304 (AB0544)
Ruacho G., 0996 (POS1425)
Rua-Figueroa D., 0610 (POS0721)
Rua-Figueroa I., 0034 (OP0064)
Rúa-Figueroa I., 0610 (POS0721)
Ruaro B., 0897 (POS1228)
Ruban T., 0793 (POS1039)
Rubbert-Roth A., 0329 (POS0222), 0580 (POS0671), 1287 (AB0522)
Rubini E., 0298 (POS0172), 0601 (POS0704), 1039 (AB0008), 1073 (AB0088)
Rubio Muñoz P., 0952 (POS1340)
Rubio Romero E., 1208 (AB0366)
Rubio-Romero E., 0053 (OP0097), 1076 (AB0096)
Ruci D., 1360 (AB0655), 1381 (AB0696)
Ruci V., 1381 (AB0696)
Ruck T., 0209 (POS0015)
Ruderman E., 0790 (POS1035), 1287 (AB0522), 1296 (AB0531)
Rudin A., 0112 (OP0186)
Rudnik M., 0394 (POS0333)
Rudwaleit M., 0080 (OP0137), 0081 (OP0139), 0153 (OP0251), 0155 (OP0253), 0221 (POS0032), 0704 (POS0896), 0705 (POS0897), 0714 (POS0909), 0723 (POS0924)
Rueda-Gotor J., 0730 (POS0934), 0755 (POS0977), 0953 (POS1342), 0977 (POS1390), 0986 (POS1407), 1065 (AB0070)
Rueda-Medina B., 1182 (AB0315), 1183 (AB0316)
Ruediger C., 1441 (AB0834)
Rufer C. B., 0394 (POS0333)
Ruffalo L., 0584 (POS0678)
Ruffatti A., 0628 (POS0751), 1174 (AB0295)
Ruggiero A., 0888 (POS1210)
Rühlmann M., 0098 (OP0163), 0933 (POS1303)
Ruiz Bravo E., 1192 (AB0333)
Ruiz D., 0020 (OP0038), 0469 (POS0475), 0769 (POS1001), 1317 (AB0562)
Ruiz Jimeno T., 0766 (POS0996)
Ruiz M. E., 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Ruiz-Fernández C., 0418 (POS0376)
Ruiz-Irastorza G., 0177 (OP0289)
Ruiz-Lucea M. E., 0700 (POS0888)
Ruiz-Montesinos D., 0469 (POS0475), 0542 (POS0610), 1056 (AB0047), 1145 (AB0239), 1420 (AB0789)
Ruiz-Moreno O., 0032 (OP0060)
Ruiz-Romero C., 0306 (POS0185), 0425 (POS0392)
Ruiz-Simón S., 0282 (POS0141)
Rull-Gabayet M., 0904 (POS1242), 0905 (POS1245)
Rumiantceva D., 0709 (POS0903), 0761 (POS0987), 1262 (AB0470), 1276 (AB0498)
Rumsey D. G., 0943 (POS1323)
Rumyantseva O., 1084 (AB0111)
Runhaar J., 1372 (AB0678)
Ruperto N., 0098 (OP0164), 0201 (LB0004), 0245 (POS0076), 0947 (POS1330)
Rusanova O., 1069 (AB0078), 1083 (AB0110), 1419 (AB0788)
Ruscitti P., 0301 (POS0177), 0390 (POS0326), 0954 (POS1344), 0957 (POS1349), 1105 (AB0156)
Rush S., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Rusiñol M., 1060 (AB0055)
Rusinovich O., 0892 (POS1218)
Russ H., 1259 (AB0465)
Russell L., 0367 (POS0285)
Russell M., 0744 (POS0959)
Russell O., 1098 (AB0142)
Russo F., 1007 (POS1447)
Russo R., 1260 (AB0467)
Rutherford C., 0358 (POS0269-HPR), 0358 (POS0270-HPR)
Rutter M., 0989 (POS1412)
Rutter-Locher Z., 0479 (POS0494)
Ruyssen-Witrand A., 0110 (OP0183), 0183 (OP0298), 0360 (POS0274-HPR), 1148 (AB0247), 1261 (AB0469)
Růžičková O., 1051 (AB0038)
Ryan J., 0859 (POS1162)
Rybakova V., 1011 (POS1455-HPR), 1134 (AB0216)
Ryden L., 0996 (POS1425)
Rydholm M., 0513 (POS0557)

S R., 1396 (AB0733), 1415 (AB0779)
Saad H., 0923 (POS1278)
Saad S., 0361 (POS0275-HPR), 1080 (AB0104)
Saadaoui K., 1144 (AB0236), 1144 (AB0238), 1145 (AB0240)
Saadoun D., 0037 (OP0068), 0233 (POS0055), 0349 (POS0254)
Saag K., 0279 (POS0135), 0840 (POS1122), 0853 (POS1148)
Saas P., 1062 (AB0062)
Saavedra Chacón M. F., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Saavedra G., 0483 (POS0501)
Saavedra M. A., 1078 (AB0098), 1200 (AB0350)
Sabbah F., 0892 (POS1217)
Sabir Husin Athar S., 1346 (AB0626)
Sabo J., 0609 (POS0719), 0994 (POS1422)
Sabuzi F., 1418 (AB0786)
Saccon F., 0594 (POS0693), 0600 (POS0702)
Sacnun M., 1196 (AB0342)
Sada G., 0960 (POS1355), 1132 (AB0211)
Sada K. E., 0458 (POS0455)
Sada R., 0492 (POS0516)
Sadler R., 0711 (POS0906)
Sadosky A., 1050 (AB0035)
Sadovici-Bobeica V., 1337 (AB0601)
Saevarsdottir S., 0093 (OP0156-HPR), 0206 (POS0009), 0474 (POS0484), 1059 (AB0054)
Sáez-Comet L., 0350 (POS0256), 0700 (POS0888), 0987 (POS1408), 0987 (POS1409)
Saffore C., 0026 (OP0049), 0712 (POS0907), 0734 (POS0943)
Safieh M., 0543 (POS0613)
Safy-Khan M., 0253 (POS0089)
Sag E., 0100 (OP0168), 0117 (OP0195), 0243 (POS0074), 0930 (POS1298), 1398 (AB0737)
Sagard J., 0339 (POS0237)
Sagez F., 0632 (POS0758)
Şahin A., 0966 (POS1368)
Şahin A., 1380 (AB0694)
Sahin A., 1470 (AB0893-HPR)
Sahin Eroglu D., 0532 (POS0597), 0949 (POS1335)
Sahin N., 0959 (POS1354), 0961 (POS1359)
Sahin S., 0969 (POS1375)
Sahli H., 0290 (POS0155-HPR), 0372 (POS0294), 0923 (POS1280), 0926 (POS1288), 1090 (AB0123), 1097 (AB0139), 1144 (AB0236), 1144 (AB0238), 1145 (AB0240), 1147 (AB0244), 1272 (AB0490), 1273 (AB0492), 1421 (AB0793)
Sahlin-Ingridsson C., 0743 (POS0957)
Sahnoun R., 1162 (AB0273)
Sahraoui S., 1147 (AB0243)
Saidane O., 0768 (POS1000), 1106 (AB0158), 1119 (AB0190), 1285 (AB0517), 1341 (AB0611), 1395 (AB0730), 1396 (AB0731)
Sailer-Hoeck M., 0883 (POS1202)
Sainz Arnau E., 0891 (POS1215)
Sainz Comas L., 0666 (POS0827), 1093 (AB0129), 1365 (AB0666), 1426 (AB0804)
Sainz J., 0009 (OP0017)
Sainz L., 0277 (POS0132)
Saito A., 1168 (AB0285)
Saito T., 0689 (POS0868), 0998 (POS1429), 1096 (AB0136)
Sakai H., 1224 (AB0391)
Sakai N., 1063 (AB0065)
Sakai R., 0113 (OP0187), 0510 (POS0551), 0511 (POS0554), 0615 (POS0730)
Sakamoto A. P., 0247 (POS0079), 0934 (POS1304)
Sakamoto M., 0697 (POS0881)
Sakellariou G., 0134 (OP0223), 0284 (POS0145), 0324 (POS0214), 0850 (POS1141), 1335 (AB0598)
Saketkoo L. A., 0681 (POS0855)
Sakharova K., 1040 (AB0010), 1066 (AB0072), 1284 (AB0514)
Sakuraba K., 0429 (POS0400)
Salaffi F., 0190 (OP0310), 0517 (POS0565), 1260 (AB0467), 1367 (AB0671), 1389 (AB0716)
Salamaliki M., 0238 (POS0064-PARE)
Salaru V., 1337 (AB0601)
Salas E., 0610 (POS0721)
Saldana Pena L., 0289 (POS0152-HPR)
Saleh M., 1352 (AB0637)
Salgado Perez E., 0610 (POS0721)

Salgado-Pérez E., 0034 (OP0064), 0967 (POS1371), 1208 (AB0366)
Saliba W., 0131 (OP0219), 0286 (POS0147)
Salinas-Carmona M. C., 1085 (AB0113)
Sallés Lizarzaburu M., 0891 (POS1215)
Salliot C., 0007 (OP0012), 0471 (POS0478), 0571 (POS0659)
Salloum N., 0361 (POS0275-HPR), 1080 (AB0104)
Salman Monte T. C., 0179 (OP0292), 1197 (AB0344)
Salmon J. H., 0170 (OP0282), 0227 (POS0045), 1157 (AB0261)
Salnikova M., 0204 (POS0004)
Salnikova T., 1095 (AB0135)
Salugina S., 0243 (POS0073), 0918 (POS1267), 0962 (POS1360), 1393 (AB0725), 1403 (AB0749), 1414 (AB0774)
Salvador M. J., 0685 (POS0861), 0692 (POS0872), 0695 (POS0878)
Salvarani C., 0037 (OP0068), 0037 (OP0069), 0190 (OP0310), 0355 (POS0265), 0594 (POS0693), 0672 (POS0837), 0726 (POS0927), 1211 (AB0370), 1241 (AB0425), 1287 (AB0522), 1389 (AB0716)
Salvati L., 1359 (AB0652)
Salvatierra J., 1208 (AB0366)
Salviato Pileggi G., 0909 (POS1252), 1448 (AB0848)
Salyanova E., 1363 (AB0663)
Salzer U., 1383 (AB0701)
Samant M., 0031 (OP0059), 0198 (LB0001), 1211 (AB0370)
Samanta J., 1305 (AB0545)
Samarkina E., 0243 (POS0073), 0465 (POS0467), 1040 (AB0010), 1158 (AB0263)
Sambataro D., 0388 (POS0322)
Sambataro G., 0388 (POS0322), 0897 (POS1228)
Sambevski S., 0101 (OP0170)
Samec S., 1427 (AB0805)
Samhouri B., 0322 (POS0210)
Sami S., 0210 (POS0018)
Samia J., 1144 (AB0236)
Samigullina R., 0776 (POS1017), 0777 (POS1019), 1095 (AB0135), 1285 (AB0516), 1387 (AB0712)
Sammaritano L., 0607 (POS0715)
Sammel A., 0654 (POS0804)
Samões B., 0354 (POS0263), 0690 (POS0870), 0692 (POS0872), 1236 (AB0415), 1236 (AB0416), 1236 (AB0417)
Sampaio C., 0909 (POS1252)
Sampaio V., 0909 (POS1252)
Sampaio-Barros P. D., 0444 (POS0432)
Sampalis J. S., 1313 (AB0557)
Sampson E., 0013 (OP0023), 1167 (AB0282)
Samtsov A., 0796 (POS1043), 1298 (AB0534), 1302 (AB0540)
Samuelsson I., 0643 (POS0779)
Samuelsson S., 0253 (POS0089)
Şan S., 0702 (POS0892)
Şan S., 1202 (AB0356), 1204 (AB0359), 1206 (AB0362)
Sanabra C., 0755 (POS0978), 0760 (POS0985), 0760 (POS0986), 1279 (AB0503)
Sancar B., 0942 (POS1319)
Sánchez A. A., 1200 (AB0350)
Sanchez Alcover J., 1133 (AB0214)
Sanchez Alvarez J., 0960 (POS1355)
Sánchez G., 1473 (AB0900-HPR), 1481 (AB0921-PARE)
Sanchez Gonzalez A., 1200 (AB0350)
Sánchez J., 0032 (OP0060), 0034 (OP0064), 0035 (OP0065), 0967 (POS1371)
Sánchez Mendieta G. G., 1018 (POS1466-HPR), 1458 (AB0868-HPR)
Sanchez P., 0019 (OP0035)
Sanchez Perez J., 1076 (AB0096)
Sanchez Pernaute O., 0700 (POS0888), 0914 (POS1260)
Sanchez Rodríguez A., 0853 (POS1149), 1386 (AB0709)
Sánchez-Alonso F., 0068 (OP0123), 0542 (POS0610)
Sanchez-Andrade A., 0952 (POS1340)
Sanchez-Bautista J., 0636 (POS0765), 0639 (POS0770)
Sanchez-Bilbao L., 0034 (OP0064), 0035 (OP0065), 0050 (OP0091), 0091 (OP0152), 0220 (POS0030), 0621 (POS0740), 0755 (POS0977), 0899 (POS1231), 0952 (POS1340), 0960 (POS1357), 0963 (POS1362), 0970 (POS1376), 0977 (POS1390), 0986 (POS1407), 1225 (AB0396), 1226 (AB0397), 1227 (AB0399), 1324 (AB0574), 1377 (AB0688), 1412 (AB0771), 1436 (AB0825)
Sánchez-Bursón J., 0533 (POS0598)
Sánchez-Costa J. T., 0058 (OP0105)
Sanchez-Guerrero J., 0177 (OP0289)
Sánchez-Maldonado J. M., 0009 (OP0017)
Sanchez-Mateos P., 1239 (AB0422)
Sánchez-Mendoza L. M., 0426 (POS0394)
Sánchez-Piedra C., 0058 (OP0105), 0068 (OP0123), 0131 (OP0220), 0217 (POS0027), 0542 (POS0610)
Sanchez-Rodriguez A., 0904 (POS1242)
Sanchez-Salmón A., 1208 (AB0365)
Sanchez-Wonenburger M., 1173 (AB0294)
Sand J. M. B., 0444 (POS0431)
Sandal Uzun G., 0518 (POS0568), 0648 (POS0793), 0728 (POS0931), 0770 (POS1004), 0814 (POS1070), 0971 (POS1378), 1198 (AB0347)
Sandanger Ø., 0185 (OP0301)
Sander O., 1195 (AB0341)
Sanderson R., 0021 (OP0039)
Sandhu A., 0672 (POS0836), 0673 (POS0838)
Sandoval D., 0333 (POS0228), 0707 (POS0901), 0713 (POS0908), 0714 (POS0909), 0716 (POS0912), 0718 (POS0915), 0720 (POS0918), 0798 (POS1045), 1262 (AB0471), 1301 (AB0539)
Sandovici M., 0033 (OP0062), 0657 (POS0809)
Sandri G., 0355 (POS0265), 1416 (AB0781)
Sandrone A., 1408 (AB0761)
Sand-Svartrud A. L., 0092 (OP0153-HPR)
Sanges S., 1011 (POS1454-HPR)
Sangle S., 1215 (AB0377)
Sanguesa C., 0610 (POS0721)
Sankaralingam R., 0981 (POS1397), 1143 (AB0235), 1413 (AB0773)
Sanmartí R., 0108 (OP0180), 0533 (POS0599), 1128 (AB0207), 1158 (AB0264)
Sanmartin Martinez J. J., 0914 (POS1260)
Sanner H., 0098 (OP0164)
Sanpaolo E., 1379 (AB0691)
Sansom S., 0017 (OP0032)
Santacroce L., 0327 (POS0219)
Santamaria-Alza Y., 0636 (POS0765), 0639 (POS0770)
Santana N., 0559 (POS0642)
Santana Peralta J., 1187 (AB0325), 1188 (AB0326), 1351 (AB0635)
Santiago T., 0481 (POS0496), 0692 (POS0872), 0695 (POS0878), 1101 (AB0147)
Santilli D., 1326 (AB0578)
Santo L., 0726 (POS0927), 1260 (AB0467)
Santolini F., 0833 (POS1105)
Santopietro M., 0044 (OP0082-PARE)
Santos B., 0820 (POS1083)
Santos Filho A., 0444 (POS0432)
Santos M. J., 0131 (OP0220), 0173 (OP0286), 0217 (POS0027), 0247 (POS0079), 0256 (POS0093), 0692 (POS0872), 0738 (POS0950), 0934 (POS1304)
Santos Moreno P. I., 0483 (POS0501)
Santos Oliveira D., 0260 (POS0100), 0318 (POS0204), 0476 (POS0488), 0483 (POS0502), 0718 (POS0914), 0812 (POS1067), 0833 (POS1106), 0836 (POS1113), 1084 (AB0112), 1096 (AB0137), 1142 (AB0231), 1188 (AB0327), 1265 (AB0476), 1266 (AB0478), 1269 (AB0483), 1299 (AB0536), 1432 (AB0816), 1441 (AB0835)
Santos Ribeiro L., 0074 (OP0129)
Santos-Moreno P., 1146 (AB0242), 1163 (AB0275), 1473 (AB0900-HPR), 1475 (AB0907-HPR), 1481 (AB0921-PARE)
Sanz I., 0585 (POS0680)
Sanz J., 0766 (POS0996), 0892 (POS1218), 1279 (AB0503)
Sanz-Gómez S., 0239 (POS0065-PARE), 0343 (POS0244), 0744 (POS0960), 0746 (POS0962), 0763 (POS0991), 0764 (POS0992), 0868 (POS1175), 0889 (POS1213), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Saparbayeva M., 1184 (AB0319), 1185 (AB0320)
Sapart E., 0066 (OP0119), 0880 (POS1196)
Sara T., 0385 (POS0317)
Saraç D. C., 1454 (AB0862-HPR)
Saraiva J. F., 0198 (LB0001)
Saraiva L., 0179 (OP0293), 0481 (POS0496), 1101 (AB0147)
Sarapulova A., 1029 (POS1489-HPR), 1449 (AB0851), 1461 (AB0874-HPR)
Saraux A., 0109 (OP0181), 0258 (POS0095), 0379 (POS0306), 0567 (POS0654), 1261 (AB0469)
Sarbu A. C., 0033 (OP0061), 0649 (POS0795)
Sargin G., 0727 (POS0929), 1470 (AB0893-HPR)
Sarholz M., 0525 (POS0584)
Sarı A., 1124 (AB0200), 1124 (AB0201), 1299 (AB0535)
Sarİ F., 1462 (AB0877-HPR)
Sari İ., 0131 (OP0220), 0627 (POS0750), 0878 (POS1193), 1247 (AB0437), 1256 (AB0459), 1386 (AB0708)
Sari K., 0905 (POS1244)
Sarı S., 0191 (OP0313), 0951 (POS1339)
Sarıtas Nakip O., 0908 (POS1249)
Sarmiento Peña C., 1429 (AB0810)
Sarna V., 1245 (AB0433)
Sarraj R., 0525 (POS0585), 1063 (AB0064), 1111 (AB0169), 1120 (AB0192), 1193 (AB0337), 1194 (AB0339), 1414 (AB0775), 1472 (AB0897-HPR)
Sarrazadegan N., 0997 (POS1427)
Sarrot-Reynauld F., 0181 (OP0295), 0261 (POS0103)
Sartorelli S., 0348 (POS0253), 1206 (AB0361)
Sarzi Puttini P., 0254 (POS0090)
Sarzi-Puttini P., 0190 (OP0310), 0335 (POS0230), 0845 (POS1132), 0846 (POS1133), 0850 (POS1141), 0979 (POS1393), 1348 (AB0629), 1367 (AB0671), 1389 (AB0716)
Sasaki D., 0998 (POS1429)
Sasso E., 0457 (POS0454), 0458 (POS0456)
Sasso F. C., 1446 (AB0844)
Sastré C., 0746 (POS0962), 0755 (POS0978), 0760 (POS0985), 0760 (POS0986), 0763 (POS0991), 0764 (POS0992), 0765 (POS0993), 0765 (POS0994), 1279 (AB0503)
Satış H., 0069 (OP0125), 0733 (POS0940), 0878 (POS1193), 1077 (AB0097), 1176 (AB0300)
Sato E., 0909 (POS1252), 1448 (AB0848)
Sato S., 0394 (POS0334), 1152 (AB0253)
Sato Y., 0697 (POS0881), 1152 (AB0253)
Satoh T., 1055 (AB0045)
Satoh Y. I., 1055 (AB0045)
Satra Tzoufra F., 1299 (AB0537)
Sattar N., 0132 (OP0221), 0812 (POS1068)
Sattui S. E., 0230 (POS0051), 1368 (AB0674)
Saturansky E., 0730 (POS0933), 1377 (AB0689)
Satybaldyev A., 0259 (POS0099), 1084 (AB0111)
Sauer B., 0353 (POS0262)
Saulescu I., 0164 (OP0270), 0681 (POS0854), 0773 (POS1009), 1112 (AB0172), 1246 (AB0435), 1378 (AB0690), 1462 (AB0879-HPR)
Sauma M. D. F., 0582 (POS0676)
Saurit V., 1196 (AB0342)
Sauter W., 1033 (POS1497-PARE)
Sauvé M., 1033 (POS1497-PARE)
Savale L., 0052 (OP0094)
Savenkova N., 0772 (POS1008)
Savic S., 0030 (OP0057), 0049 (OP0090)
Sávio Nunes de Lima D., 0625 (POS0747), 0999 (POS1430)
Savio V., 0875 (POS1188), 1194 (AB0338), 1196 (AB0342)
Savostyanov K., 1392 (AB0721)
Sawada H., 0750 (POS0969)
Sawai T., 1055 (AB0045)
Sawhney S., 0247 (POS0079), 0934 (POS1304)
Sawyerr G., 0251 (POS0086), 0450 (POS0443)
Saxena A., 0585 (POS0681)
Saxer F., 0363 (POS0277)
Sbidian E., 0027 (OP0052), 0317 (POS0201)
Scabbia F., 0985 (POS1406)
Scafati J., 0887 (POS1208)
Scandling J., 0840 (POS1122)
Scanelli G., 1099 (AB0143)
Scanu A., 0845 (POS1132), 0846 (POS1133), 1348 (AB0629)
Scarafia S., 0382 (POS0312), 0730 (POS0933), 0771 (POS1005), 1377 (AB0689)
Scarpa M., 0168 (OP0277-PARE)

Scarpa R., 0906 (POS1246), 0957 (POS1349)
Scarpato S., 0594 (POS0693)
Scerri C., 1068 (AB0077)
Schaap C., 0346 (POS0249)
Schaefer M., 0058 (OP0105), 0064 (OP0116)
Schaeffer J., 0994 (POS1422)
Schaeverbeke T., 0109 (OP0181), 0331 (POS0225), 1261 (AB0469)
Schafer P., 0076 (OP0132)
Schäfer V., 0091 (OP0151), 0842 (POS1126), 0846 (POS1134), 0920 (POS1271), 1103 (AB0152), 1446 (AB0846), 1447 (AB0847)
Schally J., 0342 (POS0241), 0456 (POS0453), 0813 (POS1069)
Schänzer A., 0209 (POS0015)
Schatorjé E., 0302 (POS0178)
Schechtman J., 0527 (POS0590)
Scheel-Toellner D., 1044 (AB0021)
Scheepers L., 0362 (POS0276)
Scheicht D., 0920 (POS1271)
Scheinberg M., 1170 (AB0288)
Schenone C., 0392 (POS0330), 0686 (POS0862), 0908 (POS1250), 1201 (AB0354), 1247 (AB0438)
Schepman P., 0366 (POS0283), 0824 (POS1089), 1050 (AB0035)
Scherer A., 0465 (POS0468), 0863 (POS1168)
Scherer H. U., 0203 (POS0001), 1045 (AB0022)
Schers H. J., 1351 (AB0634)
Schessl J., 0004 (OP0008)
Schett G., 0039 (OP0074), 0040 (OP0075), 0060 (OP0109), 0086 (OP0145), 0087 (OP0147), 0088 (OP0148), 0121 (OP0201), 0135 (OP0225), 0136 (OP0226), 0140 (OP0230), 0165 (OP0272), 0194 (OP0318), 0211 (POS0020), 0311 (POS0194), 0314 (POS0197), 0373 (POS0296), 0391 (POS0327), 0391 (POS0328), 0420 (POS0381), 0461 (POS0460), 0790 (POS1036), 0848 (POS1137), 0979 (POS1394), 0996 (POS1426), 1030 (POS1492-HPR), 1042 (AB0016), 1075 (AB0091), 1238 (AB0420), 1275 (AB0495)
Scheuerle A., 0213 (POS0022)
Scheuerman O., 0929 (POS1295)
Schiaffino M. T., 1239 (AB0422)
Schick L., 0139 (OP0229)
Schieir O., 0159 (OP0262-HPR), 1014 (POS1459-HPR)
Schieker M., 0211 (POS0020), 0363 (POS0277)
Schiesaro M., 0392 (POS0329)
Schiff M. A., 0609 (POS0719)
Schilder A., 1107 (AB0160)
Schinke S., 0149 (OP0244)
Schinocca C., 0390 (POS0326)
Schiopu E., 0004 (OP0008), 1291 (AB0526)
Schiphof D., 0061 (OP0111), 0999 (POS1431)
Schjødt Jørgensen T., 0082 (OP0140), 0283 (POS0144), 1312 (AB0554)
Schleinitz N., 0052 (OP0094), 0907 (POS1247)
Schlicher L., 1046 (AB0024)
Schmajuk G., 0002 (OP0006), 0065 (OP0117), 0173 (OP0286), 0175 (OP0288)
Schmalzing M., 0540 (POS0608), 0670 (POS0834)
Schmeiser T., 0064 (OP0116), 0171 (OP0283), 0670 (POS0834), 0685 (POS0861), 0915 (POS1261)
Schmeller M., 1054 (AB0043)
Schmidkonz C., 0165 (OP0272)
Schmidt E. B., 0215 (POS0025)
Schmidt W. A., 0029 (OP0055)
Schmitt A., 1478 (AB0912-HPR)
Schmitt M., 0843 (POS1129)
Schmitt-Haendle M., 0194 (OP0318)
Schmok E., 1446 (AB0846)
Schneeberger E. E., 0382 (POS0312), 0740 (POS0953), 0771 (POS1005)
Schneider G., 0255 (POS0091)
Schneider M., 0181 (OP0296), 1195 (AB0341)
Schneider P., 0255 (POS0091)
Schneider T., 0887 (POS1209)
Schneider U., 0305 (POS0183), 0623 (POS0744)
Schnell A., 0192 (OP0314)
Schniering J., 0090 (OP0150), 0688 (POS0866)
Scholl J., 0548 (POS0621), 0562 (POS0648), 1122 (AB0196)
Scholz G., 0033 (OP0061)
Scholz H. M., 1054 (AB0044)
Schönau V., 0165 (OP0272)
Schonenberg D., 0247 (POS0079), 0934 (POS1304)
Schonenberg-Meinema D., 0241 (POS0070), 0302 (POS0178), 0932 (POS1300), 0937 (POS1311), 1070 (AB0081)
Schoof N., 0384 (POS0316), 0681 (POS0855)
Schoonen-Nuijten I., 0238 (POS0063-PARE)
Schoones J., 0573 (POS0662)
Schoonheim P., 1448 (AB0849)
Schramm U., 0211 (POS0020)
Schreiner J. K., 0920 (POS1271)
Schreurs M. W., 0308 (POS0189)
Schrijver B., 0308 (POS0189)
Schrøder H. D., 0419 (POS0377)
Schubert A., 1313 (AB0556)
Schuch F., 0194 (OP0318), 1274 (AB0494)
Schuetz C., 0050 (OP0092), 0972 (POS1380)
Schufri Klinkby C., 1483 (AB0924-PARE)
Schulert G., 0201 (LB0004), 0245 (POS0076)
Schulz B., 0337 (POS0234), 0728 (POS0930)
Schulze-Koops H., 0112 (OP0185), 0171 (OP0283), 0565 (POS0652), 0593 (POS0692), 0915 (POS1261), 1161 (AB0270)
Schumann A., 0149 (OP0244), 0395 (POS0335)
Schumann M., 0887 (POS1209)
Schüpbach R., 0045 (OP0083)
Schuster L., 0979 (POS1394), 1030 (POS1492-HPR)
Schwab J., 0854 (POS1150)
Schwabe C., 1121 (AB0195)
Schwarting A., 0031 (OP0058), 0596 (POS0697), 0985 (POS1405)
Schwartzman S., 0527 (POS0590)
Schwarz T., 0945 (POS1325)
Schweiger M., 1275 (AB0495)
Schweizer A., 0046 (OP0085)
Schweizer T. A., 0045 (OP0083)
Schwetje E., 0592 (POS0690), 1171 (AB0289)
Schymura Y., 0725 (POS0926), 1259 (AB0465), 1262 (AB0471)
Sciacca E., 0079 (OP0136)
Sciascia S., 0037 (OP0068), 0298 (POS0172), 0601 (POS0704), 1039 (AB0008), 1073 (AB0088)
Scirè C. A., 0029 (OP0055), 0134 (OP0223), 0189 (OP0309), 0233 (POS0055), 0335 (POS0230), 0470 (POS0476), 0845 (POS1132), 0850 (POS1141), 0872 (POS1183), 0985 (POS1406), 1348 (AB0629), 1435 (AB0822)
Scolieri P., 0134 (OP0223)
Scolnik M., 0875 (POS1188), 1196 (AB0342)
Sconfienza L. M., 0845 (POS1132), 0846 (POS1133)
Scorpiniti D., 0906 (POS1246)
Scott A., 0117 (OP0194)
Scott C. A., 0618 (POS0735)
Scott C., 0201 (LB0004)
Scotti C., 0363 (POS0277)
Scrivo R., 0183 (OP0298), 0893 (POS1219), 1143 (AB0234), 1160 (AB0269)
Sculco P., 0828 (POS1097)
Seaberg M. A., 0021 (OP0039)
Sebastian A., 0396 (POS0337)
Sebastiani G. D., 0619 (POS0737)
Sebastiani M., 0131 (OP0220), 0582 (POS0675)
Sebba A., 0561 (POS0646)
Sebbani M., 0358 (POS0269-HPR)
Secher A. E., 0126 (OP0210), 0352 (POS0260)
Seet A., 0002 (OP0006), 0173 (OP0286)
Seewordova L., 0297 (POS0169), 0420 (POS0380), 0455 (POS0451), 0487 (POS0509), 1437 (AB0827)
Sefik Bukilica M., 0693 (POS0874)
Segelov D., 1015 (POS1461-HPR)
Seguí Azpilcueta P., 0020 (OP0038)
Sehgal M., 0851 (POS1143)
Sehgal R., 0655 (POS0805)
Seidel M., 0398 (POS0341)
Seijas-López Á., 0967 (POS1371)
Seitz L., 0033 (OP0061)
Seleznev A., 0890 (POS1214)
Sellam J., 0170 (OP0282), 0360 (POS0274-HPR), 1009 (POS1450)
Sellami I., 0922 (POS1277), 1276 (AB0497), 1281 (AB0508)
Sellami M., 0292 (POS0159-HPR), 1030 (POS1491-HPR), 1113 (AB0173), 1113 (AB0174), 1117 (AB0184), 1118 (AB0188), 1277 (AB0499), 1332 (AB0590), 1333 (AB0592), 1333 (AB0593), 1381 (AB0698), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Sellas-Fernández A., 0782 (POS1025)
Selmi C., 0152 (OP0249), 0778 (POS1021), 0809 (POS1061)
Selvadurai S., 1015 (POS1460-HPR)
Selva-O'callaghan A., 0350 (POS0256), 0699 (POS0886), 0700 (POS0888), 0898 (POS1229), 0987 (POS1408), 0987 (POS1409), 1241 (AB0426)
Selvi E., 1252 (AB0450)
Semagina O., 1095 (AB0135)
Semashko A., 0518 (POS0567)
Semb A. G., 0123 (OP0204), 0219 (POS0029), 0795 (POS1041)
Semchenkova M., 1095 (AB0135)
Semenova O., 1384 (AB0705)
Semeraro A., 0726 (POS0927), 1003 (POS1437)
Semizarova I., 1095 (AB0135)
Semmelink J. F., 0425 (POS0391)
Semo Oz R., 0242 (POS0071)
Şen N., 0514 (POS0560), 0964 (POS1364)
Senba R., 0961 (POS1358), 1169 (AB0287), 1223 (AB0390)
Sendra-García A., 1427 (AB0806)
Şenel S., 1140 (AB0229), 1266 (AB0479), 1317 (AB0561)
Sener S., 1398 (AB0737)
Sengler C., 0882 (POS1199), 0883 (POS1202), 0943 (POS1321), 0945 (POS1325)
Sengupta R., 0235 (POS0059-PARE), 0720 (POS0919), 0744 (POS0959)
Senkal N., 1191 (AB0331)
Sennikov S., 0482 (POS0500)
Šenolt L., 0150 (OP0245), 0424 (POS0388), 0677 (POS0846), 0678 (POS0849), 0850 (POS1142)
Šenolt L., 1051 (AB0038), 1062 (AB0063), 1233 (AB0410), 1234 (AB0412)
Sensini F., 0954 (POS1344), 0957 (POS1349), 1105 (AB0156)
Senturk T., 0727 (POS0929), 1470 (AB0893-HPR)
Seo T., 0060 (OP0108), 0416 (POS0372)
Sephora B., 0360 (POS0273-HPR)
Sepriano A., 0039 (OP0074), 0041 (OP0077), 0152 (OP0250), 0222 (POS0033)
Seravina O., 1088 (AB0118), 1180 (AB0308)
Serban T., 0845 (POS1132), 0846 (POS1133), 1348 (AB0629)
Seredavkina N., 0605 (POS0712), 1177 (AB0303), 1178 (AB0305)
Seres T., 0421 (POS0383), 0425 (POS0390)
Sergeev V., 0924 (POS1282)
Sergey M., 0037 (OP0068)
Serling-Boyd N., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0867 (POS1174)
Serna Giraldo J. D., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Serna-Peña G., 1450 (AB0852), 1456 (AB0866-HPR), 1459 (AB0871-HPR)
Serone A., 0581 (POS0672)
Seror R., 0007 (OP0012), 0078 (OP0135), 0172 (OP0284), 0214 (POS0024), 0471 (POS0478)
Seroutou A., 0211 (POS0020)
Serrano E. R., 0635 (POS0763)
Serrano Morales R., 1194 (AB0338), 1196 (AB0342)
Serrano-Benavente B., 0658 (POS0812), 1117 (AB0185), 1239 (AB0422)
Serre G., 0206 (POS0009), 1061 (AB0058)
Servettaz A., 0172 (OP0284)
Sesin C., 0789 (POS1033)
Sestini S., 0168 (OP0277-PARE)
Sethi D., 0210 (POS0018)
Sethi V., 1334 (AB0595)
Setty Y., 1312 (AB0555), 1314 (AB0558)
Seven S., 0742 (POS0955)
Severoni S., 1480 (AB0918-PARE)
Sevilla B., 1076 (AB0096)
Sevim E., 0607 (POS0715)

Sewerin P., 1013 (POS1458-HPR), 1030 (POS1492-HPR), 1308 (AB0550)
Sexton J., 0092 (OP0153-HPR), 0185 (OP0301), 0219 (POS0029), 0795 (POS1041), 0934 (POS1305), 1392 (AB0722)
Seyahi E., 0660 (POS0814), 0662 (POS0819), 0875 (POS1187), 0958 (POS1351)
Seyman E., 1181 (AB0312)
Sezer İ., 1470 (AB0893-HPR)
Sezer S., 0949 (POS1335)
Sfar H., 1415 (AB0776), 1415 (AB0778)
Sfikakis P., 0142 (OP0232), 0337 (POS0234), 0656 (POS0807), 0703 (POS0894), 0799 (POS1046), 0815 (POS1073), 1295 (AB0530), 1299 (AB0537)
Sfontouris C., 0668 (POS0829)
Sfriso P., 0392 (POS0329)
Sgrò P., 1074 (AB0089)
Sha X., 0646 (POS0788)
Shadick N., 0457 (POS0454), 0494 (POS0522)
Shafieva I., 1095 (AB0135)
Shah C., 0533 (POS0598), 0537 (POS0604)
Shah J., 1395 (AB0729)
Shah K., 0274 (POS0125)
Shaharir S. S., 0611 (POS0723), 1105 (AB0155), 1177 (AB0302)
Shahbazian A., 0449 (POS0442)
Shaheen H. J., 0381 (POS0310), 0527 (POS0589), 0574 (POS0663)
Shahnaz M., 0053 (OP0096)
Shahril N. S., 0053 (OP0096), 0459 (POS0457)
Shahul A., 0948 (POS1331)
Shamsutdinova N., 1253 (AB0452)
Shan M., 0710 (POS0904)
Shan Y., 1125 (AB0202)
Shanmuganathan K., 1052 (AB0039)
Shapina M., 0014 (OP0027)
Shapiro A., 1148 (AB0247), 1149 (AB0248)
Shapovalenko A., 0918 (POS1267), 0948 (POS1332), 1393 (AB0725), 1394 (AB0726)
Sharapova E., 0275 (POS0127), 0276 (POS0130), 1336 (AB0599), 1337 (AB0603), 1338 (AB0604)
Shardina L., 0037 (OP0070)
Sharma A., 0513 (POS0557), 0584 (POS0679), 1163 (AB0276), 1305 (AB0545)
Sharma S. K., 0584 (POS0679), 1163 (AB0276)
Sharma S., 0467 (POS0471)
Sharma V., 1158 (AB0264)
Sharon O., 0200 (LB0003)
Sharp C., 0041 (OP0076)
Shataylo V., 0691 (POS0871)
Shaw T., 0072 (OP0128), 0566 (POS0653)
Shawi M., 0140 (OP0230), 0316 (POS0200), 0781 (POS1024), 0783 (POS1027), 0784 (POS1028), 0787 (POS1031), 1289 (AB0524), 1290 (AB0525), 1291 (AB0526), 1292 (AB0527), 1293 (AB0528), 1300 (AB0538)
Shayakhmetova R., 0104 (OP0173), 0681 (POS0853), 0684 (POS0860), 0899 (POS1232), 1239 (AB0423), 1248 (AB0440), 1249 (AB0444), 1253 (AB0453), 1254 (AB0454), 1254 (AB0455)
Shchendrigin I., 1095 (AB0135), 1325 (AB0576)
Sheeran T., 0005 (OP0009-PARE), 0540 (POS0608), 0903 (POS1241)
Shefer G., 0200 (LB0003)
Sheikh S., 1170 (AB0288)
Sheliabina O., 0849 (POS1139), 0849 (POS1140), 0963 (POS1363), 1353 (AB0640)
Shen C. Y., 0599 (POS0700), 1440 (AB0832)
Shen H. C., 0918 (POS1268)
Shen Y. K., 1297 (AB0532)
Shen Z., 0843 (POS1128), 0844 (POS1130)
Shenasan N., 0600 (POS0701)
Shenasan P., 0600 (POS0701)
Sheng S., 0781 (POS1024), 0783 (POS1027), 0785 (POS1029), 0787 (POS1031), 1290 (AB0525), 1291 (AB0526), 1293 (AB0528), 1300 (AB0538)
Shenker N., 0210 (POS0018)
Shenoy P., 0700 (POS0889)
Shephard A., 1069 (AB0080)
Sheriff I., 0377 (POS0303)
Sheriff M., 1313 (AB0557)
Shevchenko N., 1401 (AB0745), 1403 (AB0750)
Shevchuk S., 1270 (AB0487)
Shevnina J., 1269 (AB0484)
Shi G., 0460 (POS0458), 0622 (POS0742), 1037 (AB0005), 1436 (AB0824)
Shi H., 0251 (POS0086), 0563 (POS0650), 0661 (POS0817)
Shi J., 0619 (POS0736), 0629 (POS0754)
Shi L., 0257 (POS0094)
Shilova L., 0225 (POS0040), 1059 (AB0053)
Shimada H., 0513 (POS0556), 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1249 (AB0443), 1437 (AB0826)
Shimbo M., 1168 (AB0285)
Shimizu T., 0608 (POS0718)
Shin D. W., 0062 (OP0113)
Shin K., 1152 (AB0253)
Shin S., 0956 (POS1348), 1407 (AB0760)
Shingarova M., 0100 (OP0166)
Shipa M., 0074 (OP0129), 0448 (POS0440), 1136 (AB0220)
Shirai Y., 0685 (POS0861), 1246 (AB0436)
Shirinsky I., 0824 (POS1090)
Shirinsky V., 0824 (POS1090)
Shivacheva T., 0896 (POS1224), 1138 (AB0224)
Shkaruba N., 0482 (POS0500)
Shmidt E., 0014 (OP0027), 0204 (POS0004), 0731 (POS0937), 1146 (AB0241), 1265 (AB0475), 1383 (AB0703)
Shojania K., 0377 (POS0303)
Shoji A., 0510 (POS0551), 0511 (POS0554)
Shoji T., 0697 (POS0881)
Shoop-Worrall S., 0097 (OP0162), 1373 (AB0681)
Shu Q., 0561 (POS0647)
Shumilova A., 0643 (POS0780), 1177 (AB0303)
Shumnalieva R., 0522 (POS0578), 0873 (POS1184), 1108 (AB0162)
Shuvalova N., 1458 (AB0869-HPR), 1482 (AB0922-PARE)
Shwin K., 1205 (AB0360)
Sibata M., 1096 (AB0136)
Sibilia J., 0109 (OP0181), 0149 (OP0243), 0258 (POS0095), 0736 (POS0947), 0877 (POS1190)
Sicsik S., 0559 (POS0642)
Siddiqui A., 0869 (POS1177)
Siddiqui K., 1334 (AB0595)
Siddle H. J., 0039 (OP0074)
Siderius M., 0769 (POS1002)
Sidhu N., 0448 (POS0438), 0486 (POS0506)
Sidi S., 0997 (POS1427)
Sidiropoulos P., 0184 (OP0299), 0489 (POS0512), 0523 (POS0580), 0733 (POS0941), 1299 (AB0537)
Sidorov I., 0969 (POS1374)
Siebert S., 0129 (OP0215), 0142 (OP0232), 0312 (POS0195), 0799 (POS1046), 1159 (AB0265), 1295 (AB0530)
Siebuhr A. S., 0444 (POS0431)
Sieder C., 0714 (POS0910)
Siegel C., 0607 (POS0715)
Siegert E., 0385 (POS0317), 0386 (POS0318), 0387 (POS0321), 0670 (POS0834), 0685 (POS0861)
Sieghart D., 0403 (POS0348)
Siegmund B., 0017 (OP0031), 0887 (POS1209)
Sieiro Santos C., 1165 (AB0278), 1171 (AB0290), 1321 (AB0568)
Sieper J., 0024 (OP0047), 0025 (OP0048), 0080 (OP0137), 0081 (OP0139), 0085 (OP0144), 0153 (OP0251), 0155 (OP0253), 0221 (POS0032), 0341 (POS0240), 0373 (POS0296), 0756 (POS0979), 1262 (AB0471)
Sifuentes-Giraldo W. A., 0247 (POS0079), 0934 (POS1304)
Signori A., 0524 (POS0583)
Signorini V., 0630 (POS0756), 0647 (POS0789)
Sigurdardottir V., 0130 (OP0218)
Sigurdsson V., 1465 (AB0884-HPR)
Sikalo Y., 0481 (POS0498)
Sikora K., 0049 (OP0090)
Silano M., 0878 (POS1192)
Silberman A., 0200 (LB0003)
Sili Scavalli A., 0893 (POS1219)
Silk M., 0588 (POS0686)
Silke C., 1093 (AB0130)
Silman A., 0274 (POS0125)
Silva I., 1402 (AB0747)
Silva J., 1003 (POS1438)
Silva M., 0985 (POS1406)
Silva N. M., 0397 (POS0338), 0669 (POS0831)
Silvagni E., 0134 (OP0223), 0233 (POS0055), 0607 (POS0716)
Silvana D. R., 1408 (AB0761)
Silveira I., 0582 (POS0676)
Silvennoinen O., 1150 (AB0250)
Silverberg S., 1312 (AB0555)
Silverman S., 0366 (POS0283)
Silverthorne C., 1021 (POS1472-HPR), 1426 (AB0803), 1441 (AB0834)
Silvestri E., 0889 (POS1212)
Sim J., 0293 (POS0161-HPR)
Simanovich E., 0543 (POS0613)
Simão J., 0208 (POS0013)
Simard J., 0994 (POS1422)
Simeón-Aznar C. P., 0350 (POS0256), 0699 (POS0886), 0987 (POS1408), 0987 (POS1409)
Simon B., 1057 (AB0051)
Simon D., 0040 (OP0075), 0086 (OP0145), 0087 (OP0147), 0088 (OP0148), 0979 (POS1394), 0996 (POS1426), 1030 (POS1492-HPR), 1275 (AB0495)
Simon M., 0584 (POS0678)
Simon S. P., 0638 (POS0768), 1360 (AB0656)
Simone D., 0017 (OP0032)
Simonini G., 0628 (POS0751)
Simons G., 0096 (OP0160-HPR), 1026 (POS1483-HPR)
Simo-Perdigó M., 1241 (AB0426)
Simpson L., 0331 (POS0224)
Simsek I., 0363 (POS0278)
Sindi E. A., 0855 (POS1153)
Sinelnikova E., 0944 (POS1324)
Singer F., 0320 (POS0208)
Singer N., 1126 (AB0203)
Singh A., 0276 (POS0129), 0309 (POS0190), 1396 (AB0733)
Singh G., 0851 (POS1143)
Singh J., 0208 (POS0014), 0488 (POS0510), 0841 (POS1124)
Singh N., 0002 (OP0006), 0173 (OP0286), 0369 (POS0287), 0460 (POS0459), 0476 (POS0487), 0609 (POS0719), 0994 (POS1422)
Singh S., 0377 (POS0303), 1088 (AB0119)
Singhal A., 0568 (POS0655)
Singhal S., 0314 (POS0198)
Singleton M., 0994 (POS1422)
Siniauskaya E., 1039 (AB0009)
Sinigaglia L., 0190 (OP0310), 1389 (AB0716)
Sippl N., 0203 (POS0003), 0996 (POS1425)
Siqueira Afonso A., 1405 (AB0755)
Siracusano A., 1434 (AB0821)
Sirenko O., 1452 (AB0858)
Sirnes Hagland A., 0092 (OP0153-HPR)
Sirois F., 1027 (POS1484-HPR), 1467 (AB0889-HPR)
Sirotich E., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Sirotti S., 0845 (POS1132), 0846 (POS1133), 0850 (POS1141), 1348 (AB0629)
Sirufo M. M., 1246 (AB0434)
Šisl D., 0226 (POS0042)
Siste de Almeida Aoki I., 1423 (AB0798)
Sitbon O., 0052 (OP0094)
Siti-Aisyah A. A., 0053 (OP0096), 0459 (POS0457)
Siva A., 0660 (POS0814), 0662 (POS0819)
Sivadas S., 0915 (POS1262)
Sivera F., 0034 (OP0064), 0841 (POS1124), 0967 (POS1371)
Siwar B. D., 1106 (AB0158), 1119 (AB0190)
Sizikov A., 0482 (POS0500), 0581 (POS0673)
Sjöberg R., 0425 (POS0392)
Sjowall C., 0535 (POS0601), 0864 (POS1169)
Skana F., 1360 (AB0655)
Skeoch S., 0170 (OP0281), 0626 (POS0748)
Skinner Taylor C. M., 0893 (POS1220), 1345 (AB0624), 1360 (AB0657), 1361 (AB0658), 1439 (AB0830), 1444 (AB0842), 1445 (AB0843), 1457 (AB0867-HPR), 1463 (AB0880-HPR)
Skopouli F., 0178 (OP0291)
Skorpen C., 0951 (POS1337)

Skougaard M., 1312 (AB0554)
Skov Kragsnaes M., 0006 (OP0010), 1483 (AB0924-PARE)
Skov L., 0287 (POS0149)
Skowasch D., 1103 (AB0152)
Skrepnik N., 0363 (POS0278)
Slama M., 0466 (POS0469)
Slater H., 0293 (POS0161-HPR)
Slater V., 1057 (AB0051)
Sleglova O., 1051 (AB0038)
Sleptsova P., 0930 (POS1297)
Sletten T., 0711 (POS0906)
Slimani S., 0481 (POS0497), 1147 (AB0243)
Slobodnick A., 0278 (POS0134)
Sloeserwij A., 1465 (AB0884-HPR)
Slouma M., 0774 (POS1012), 0925 (POS1287), 0926 (POS1289), 0926 (POS1290), 1066 (AB0071), 1095 (AB0134), 1116 (AB0182), 1281 (AB0507), 1281 (AB0509), 1285 (AB0518), 1286 (AB0519), 1417 (AB0784), 1442 (AB0836), 1443 (AB0840)
Smedescu V. V., 1267 (AB0480)
Smeele H. T., 0127 (OP0211), 0127 (OP0212), 0317 (POS0202), 1058 (AB0052)
Smeets R., 0828 (POS1096), 1248 (AB0441)
Smerilli G., 0517 (POS0565), 0811 (POS1066)
Smirnov A., 1147 (AB0245), 1276 (AB0498), 1421 (AB0792)
Smith C., 1323 (AB0573), 1357 (AB0649)
Smith N., 0369 (POS0287)
Smith R., 1345 (AB0622)
Smith S., 0008 (OP0014), 0045 (OP0084)
Smith T., 0330 (POS0223), 0547 (POS0619), 0711 (POS0906), 1015 (POS1461-HPR)
Smith V., 0101 (OP0170), 0247 (POS0079), 0392 (POS0330), 0524 (POS0583), 0674 (POS0840), 0679 (POS0850), 0685 (POS0861), 0686 (POS0862), 0694 (POS0877), 0908 (POS1250), 0934 (POS1304), 0937 (POS1311), 1008 (POS1449), 1060 (AB0057), 1070 (AB0081), 1190 (AB0330), 1372 (AB0679)
Smiyan S., 0811 (POS1065), 1320 (AB0567)
Smolders J. M. H., 0359 (POS0272-HPR)
Smolen J. S., 0071 (OP0127), 0142 (OP0232), 0183 (OP0298), 0284 (POS0145), 0475 (POS0485), 0563 (POS0650), 0778 (POS1021), 0799 (POS1046), 1295 (AB0530), 1311 (AB0553)
Smolyarchuk E., 0890 (POS1214)
Smucrova H., 0677 (POS0846), 0678 (POS0849)
Snegireva L., 0247 (POS0080), 0931 (POS1299), 0937 (POS1310), 1402 (AB0748)
Snyder M., 0450 (POS0443)
So A., 0226 (POS0041), 0426 (POS0393), 0841 (POS1124)
So H., 0257 (POS0094), 0687 (POS0865), 0818 (POS1079), 0860 (POS1164), 0895 (POS1222)
Soare A., 0165 (OP0272), 1075 (AB0091)
Sobanski V., 1011 (POS1454-HPR)
Sockalingam S., 0218 (POS0028)
Sodin-Šemrl S., 1069 (AB0080)
Sofat N., 0879 (POS1195)
Sofianos I., 0646 (POS0786)
Soh H. C., 0654 (POS0804)
Sokol E., 0196 (OP0320), 0608 (POS0717), 0896 (POS1226), 1116 (AB0183), 1185 (AB0321)
Sokolova M. V., 0461 (POS0460)
Sokolova T., 0020 (OP0037), 0066 (OP0119), 0240 (POS0067), 0880 (POS1196)
Solanich X., 0001 (OP0004), 0700 (POS0888)
Solans-Laqué R., 1208 (AB0366)
Soldano S., 0392 (POS0330), 1060 (AB0057)
Soldati E., 1078 (AB0099)
Soliman A. M., 0138 (OP0228), 1315 (AB0559)
Solis C. V., 1085 (AB0113)
Söllner S., 0060 (OP0109)
Solmaz D., 0722 (POS0922), 0727 (POS0929), 0731 (POS0935), 0861 (POS1165), 1255 (AB0456), 1366 (AB0669), 1454 (AB0862-HPR)
Solomon D., 0056 (OP0101), 0327 (POS0219)
Solovyev S., 1184 (AB0319), 1185 (AB0320)
Solveig Dagfinrud H., 0047 (OP0087), 0092 (OP0154-HPR), 0357 (POS0268-HPR)
Someya K., 1094 (AB0132)
Sommerfleck F., 0730 (POS0933), 1377 (AB0689)
Son M. B., 0165 (OP0271)
Sondag M., 1279 (AB0504)
Song G. G., 1124 (AB0199)
Song I. H., 0085 (OP0144), 0251 (POS0087), 0329 (POS0222), 0338 (POS0235), 0566 (POS0653), 0712 (POS0907), 0721 (POS0920), 0722 (POS0923), 0723 (POS0924)
Song L., 0561 (POS0647)
Song M., 1297 (AB0532)
Song Q., 0015 (OP0028), 0312 (POS0195)
Song S., 0111 (OP0184), 0315 (POS0199), 0460 (POS0458), 0616 (POS0732), 0619 (POS0736), 0622 (POS0742), 0623 (POS0743), 0677 (POS0847), 0684 (POS0859), 0888 (POS1211), 1037 (AB0005), 1436 (AB0824)
Song Y. W., 0716 (POS0911), 0976 (POS1386)
Song Y., 0072 (OP0128), 0328 (POS0220), 0329 (POS0222), 0566 (POS0653), 0567 (POS0654), 0569 (POS0656), 0575 (POS0666), 0579 (POS0670), 0580 (POS0671), 0847 (POS1136)
Soni A., 0289 (POS0152-HPR)
Sonia R., 1144 (AB0236)
Soós B., 0421 (POS0383), 0425 (POS0390)
Sopala M., 0593 (POS0692)
Sordet C., 0877 (POS1190), 0939 (POS1314), 1009 (POS1450)
Sørensen C. M., 0234 (POS0056), 0865 (POS1170)
Sørensen I. J., 0287 (POS0149), 0742 (POS0955)
Sorensen S., 0009 (OP0017)
Soriano A., 0355 (POS0265)
Soriano E., 0139 (OP0229), 0376 (POS0302), 0759 (POS0984), 0875 (POS1188), 1133 (AB0214), 1294 (AB0529)
Sorice M., 0902 (POS1238)
Soriot-Thomas S., 0364 (POS0279)
Sornasse T., 0016 (OP0030), 0433 (POS0407), 0721 (POS0920)
Soroka N., 0084 (OP0142), 0726 (POS0928), 0796 (POS1043), 1298 (AB0534), 1302 (AB0540)
Sorokina L., 0247 (POS0080), 0930 (POS1297), 0931 (POS1299)
Sorotskaya V., 0754 (POS0976), 0815 (POS1072), 1095 (AB0135), 1325 (AB0576)
Sorrentino L., 0874 (POS1186), 1196 (AB0342)
Sosa J., 0382 (POS0312)
Sosyal O., 1266 (AB0479), 1317 (AB0561)
Soteriou D., 1238 (AB0420)
Sotirova M., 1108 (AB0162)
Soto Abánades C., 0693 (POS0875), 1192 (AB0333)
Soto L., 0786 (POS1030)
Sottile A., 0838 (POS1119)
Souabni L., 0292 (POS0159-HPR), 1030 (POS1491-HPR), 1113 (AB0173), 1113 (AB0174), 1117 (AB0184), 1118 (AB0188), 1277 (AB0499), 1381 (AB0698), 1431 (AB0814), 1466 (AB0886-HPR), 1477 (AB0910-HPR)
Soubrier M., 0170 (OP0282), 0183 (OP0298), 1022 (POS1475-HPR)
Souchaud-Debouverie O., 0261 (POS0103)
Souebni L., 0835 (POS1110), 1332 (AB0590), 1333 (AB0592), 1333 (AB0593), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1368 (AB0672), 1368 (AB0673), 1390 (AB0717), 1397 (AB0736), 1411 (AB0770)
Sousa Guerreiro C., 0484 (POS0504)
Sousa M., 0233 (POS0055), 0481 (POS0496), 0690 (POS0870), 1101 (AB0147)
Sousa-Pinto B., 0637 (POS0767), 1195 (AB0340)
Soussi B. G., 0215 (POS0025)
Southwood T., 0927 (POS1292)
Souto Vilas A., 0692 (POS0873), 0935 (POS1306), 1173 (AB0294)
Souto-Carneiro M., 0467 (POS0472), 1047 (AB0028)
Souza Muller C., 0384 (POS0316)
Soysal Gündüz Ö., 1140 (AB0229)
Sözeri B., 0201 (LB0004), 0229 (POS0049), 0249 (POS0082), 0871 (POS1181), 0933 (POS1302), 0942 (POS1319)
Spaethling-Mestekemper S., 1263 (AB0472), 1274 (AB0494)
Spaggiari L., 0037 (OP0069)
Spagnuolo R., 1012 (POS1457-HPR), 1454 (AB0861-HPR)
Sparks J., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0230 (POS0051), 0327 (POS0219), 0494 (POS0522), 0867 (POS1174), 1368 (AB0674)
Sparks M., 0327 (POS0219)
Specker C., 0171 (OP0283), 0544 (POS0615), 0915 (POS1261)
Spekking K., 0932 (POS1300)
Spellitz P., 0320 (POS0208)
Spertini F., 0385 (POS0317)
Speziali M., 0645 (POS0783), 1073 (AB0087)
Spielmann L., 0736 (POS0947)
Spiera R., 0102 (OP0171), 1406 (AB0756)
Spierings J., 0346 (POS0249), 0993 (POS1419), 1221 (AB0387), 1229 (AB0402), 1430 (AB0812), 1465 (AB0884-HPR), 1478 (AB0914-PARE)
Spiller L., 0025 (OP0048), 0155 (OP0254), 0771 (POS1007)
Spinella A., 0672 (POS0837), 0906 (POS1246), 1241 (AB0425)
Spinelli F. R., 0324 (POS0214), 0583 (POS0677), 0588 (POS0685), 0645 (POS0783), 0893 (POS1219), 0902 (POS1238), 0903 (POS1240), 1069 (AB0079), 1073 (AB0087), 1143 (AB0234), 1160 (AB0269), 1384 (AB0704)
Spinetto M. A., 0576 (POS0667)
Spirig J. M., 0045 (OP0083)
Špiritović M., 0677 (POS0846), 0678 (POS0849)
Špiritović M., 1233 (AB0410), 1234 (AB0412)
Spitsina S., 0424 (POS0389), 1056 (AB0048), 1057 (AB0049), 1062 (AB0061), 1108 (AB0163), 1353 (AB0638), 1444 (AB0841)
Spitz E., 0358 (POS0269-HPR), 0358 (POS0270-HPR)
Spoorenberg A., 0024 (OP0046), 0221 (POS0031), 0223 (POS0034), 0769 (POS1002), 0775 (POS1014), 1257 (AB0462), 1268 (AB0481)
Sprabery A. T., 0789 (POS1033), 1301 (AB0539)
Sproles A., 0245 (POS0076)
Spuls P., 0359 (POS0271-HPR), 0548 (POS0621)
Squizzato A., 1319 (AB0565)
Sreedharan S., 0629 (POS0753)
Staab D., 0943 (POS1321)
Stadler B., 0582 (POS0676), 1448 (AB0848)
Stagnaro C., 0630 (POS0756), 0647 (POS0789)
Stahly A., 0748 (POS0966)
Stainbrook T., 1347 (AB0628)
Stal R., 0152 (OP0250), 0222 (POS0033)
Stålesen R., 0203 (POS0003)
Stamm B., 0607 (POS0715)
Stamm T., 0101 (OP0169-PARE), 1019 (POS1468-HPR)
Stamp L., 0841 (POS1124)
Stan A., 1448 (AB0849)
Stanciu I., 0129 (OP0215)
Stanevicha V., 0247 (POS0079), 0934 (POS1304)
Stange R., 0226 (POS0041)
Staniland K., 0041 (OP0076)
Stanway J., 1046 (AB0025)
Stapleton T., 0291 (POS0156-HPR)
Starcevic D., 1251 (AB0447)
Starmans M., 0273 (POS0123), 0540 (POS0609)
Starovoytova M., 0104 (OP0173), 0681 (POS0853), 0683 (POS0857), 0683 (POS0858), 0684 (POS0860), 0899 (POS1232), 1239 (AB0423), 1248 (AB0439), 1248 (AB0440), 1249 (AB0444), 1253 (AB0453), 1254 (AB0454), 1254 (AB0455), 1451 (AB0855)
Stasiek M., 1434 (AB0820)
Stauder S., 0841 (POS1125)
Staurenghi G., 0979 (POS1393)
Stavropoulou M., 1304 (AB0543)
Steelandt A., 0419 (POS0378)
Steen Krogh N., 0063 (OP0114), 0234 (POS0056), 0865 (POS1170)
Steen Pettersen P., 0047 (OP0087)
Stefanantoni K., 0150 (OP0246), 0445 (POS0433), 0873 (POS1185)
Stefanidis D., 0533 (POS0598), 0537 (POS0604)
Stefanska A., 0707 (POS0900)
Steffen (née Harre) U., 0461 (POS0460)
Steffgen J., 0589 (POS0687)
Stegert M., 0655 (POS0806)

Steiger F., 1030 (POS1492-HPR)
Steigmiller K., 0685 (POS0861), 0694 (POS0877)
Steinkoenig I., 0139 (OP0229)
Stenger K., 1301 (AB0539)
Stenzel W., 0305 (POS0183)
Stephan J. L., 0240 (POS0068)
Stergiou I., 0180 (OP0294), 0370 (POS0290)
Stern M., 0076 (OP0132)
Sternad P., 0528 (POS0591), 1274 (AB0494)
Sterner K., 0149 (OP0244)
Stetter M., 0320 (POS0208)
Steup-Beekman G. M., 0603 (POS0708), 0604 (POS0709), 0606 (POS0714)
Stevenaert F., 1046 (AB0025)
Stevens R., 0602 (POS0705)
Stevens S., 0989 (POS1412)
Stevens W., 0102 (OP0171)
Stewart J., 1314 (AB0558)
Stiburkova B., 0850 (POS1142)
Sticherling M., 0996 (POS1426)
Stigler J., 0722 (POS0923)
Stimec J., 0943 (POS1323)
Stisen Z. R., 1312 (AB0554)
Stock C., 0671 (POS0835)
Stockert L., 0449 (POS0442)
Stoenoiu M., 0089 (OP0149), 0153 (OP0252), 0352 (POS0259)
Stoffel-Wagner B., 0091 (OP0151)
Stohl W., 1170 (AB0288)
Stoica V., 0519 (POS0569)
Stoika I., 0866 (POS1172)
Stok U., 1069 (AB0080)
Stolshek B., 0066 (OP0118)
Stone J. H., 0656 (POS0808), 1406 (AB0756)
Stones S., 0235 (POS0057-PARE), 0290 (POS0154-HPR), 1022 (POS1473-HPR)
Storck-Müller K., 0383 (POS0314)
Storey D., 1057 (AB0051)
Štorkánová H., 0150 (OP0245), 0677 (POS0846), 0678 (POS0849)
Štorkánová H., 1233 (AB0410), 1234 (AB0412)
Štorkánová L., 0150 (OP0245)
Stormly Hansen M., 1202 (AB0355)
Storoniak H., 1434 (AB0820)
Stout J. C., 0616 (POS0731)
Stouten V., 0484 (POS0503), 1001 (POS1434), 1083 (AB0109)
St-Pierre Y., 0617 (POS0734), 0993 (POS1420)
Strachan D., 0120 (OP0200), 1052 (AB0039)
Stradner M., 0261 (POS0102)
Strahm N., 0689 (POS0867)
Strand V., 0561 (POS0646), 0565 (POS0652), 0568 (POS0655), 0579 (POS0670), 0704 (POS0895), 1096 (AB0138), 1097 (AB0140)
Strangfeld A., 0002 (OP0006), 0058 (OP0105), 0064 (OP0116), 0135 (OP0225), 0171 (OP0283), 0173 (OP0286), 0175 (OP0288), 0199 (LB0002), 0256 (POS0093), 0373 (POS0296), 0872 (POS1183), 0915 (POS1261), 0990 (POS1414), 1263 (AB0472)
Stratigos A., 1304 (AB0543)
Stratton R., 0702 (POS0893), 1230 (AB0403)
Stratton S., 0853 (POS1148)
Strebkova E., 0118 (OP0197), 0275 (POS0127), 0276 (POS0130), 1084 (AB0111), 1338 (AB0604)
Strengholt S., 0572 (POS0660)
Strober B., 0788 (POS1032), 0795 (POS1042)
Stroeve S., 0046 (OP0085)
Strugariu G., 1380 (AB0695)
Strusberg I., 1133 (AB0214)
Stryker S., 0056 (OP0101)
Studart S., 0582 (POS0676)
Studenic P., 0403 (POS0348), 1005 (POS1441)
Stull D., 1171 (AB0289)
Su K., 0043 (OP0081)
Su R., 0771 (POS1006), 1043 (AB0017), 1408 (AB0762)
Su W., 1182 (AB0313)
Su Y., 1055 (AB0046), 1212 (AB0372), 1318 (AB0564), 1406 (AB0758)
Suárez Amorín G., 0091 (OP0152)
Suarez S., 1208 (AB0366)
Suárez-Amorín G., 1226 (AB0397), 1227 (AB0399)
Suárez-Ulloa V., 0403 (POS0347)
Subhi Y., 1202 (AB0355)
Subils G. C., 0887 (POS1208)
Suboticki J., 0579 (POS0670), 0580 (POS0671)
Šućur A., 0226 (POS0042)
Sudoł-Szopińska I., 0943 (POS1323)
Sudre L., 0417 (POS0373)
Sufka P., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0230 (POS0051), 1368 (AB0674)
Sugihara K., 0513 (POS0556), 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1249 (AB0443), 1437 (AB0826)
Sugihara T., 0395 (POS0336)
Sugimoto R., 0059 (OP0107)
Sugioka Y., 0465 (POS0466), 1012 (POS1456-HPR)
Sugitani N., 0113 (OP0187)
Sugiyama N., 0113 (OP0187), 0368 (POS0286), 0563 (POS0650), 0564 (POS0651)
Suh C. H., 0447 (POS0437), 0716 (POS0911)
Sui Y., 0085 (OP0144), 1156 (AB0260)
Sukalo A., 1036 (AB0003)
Sukhovyova O., 0187 (OP0306)
Sulli A., 0392 (POS0330), 0679 (POS0850), 0686 (POS0862), 0697 (POS0882), 0908 (POS1250), 1190 (AB0330), 1201 (AB0354), 1247 (AB0438), 1372 (AB0679)
Sumiyoshi R., 0608 (POS0718), 0959 (POS1353)
Summa L., 0148 (OP0242)
Sun H., 0824 (POS1089)
Sun J., 1353 (AB0639)
Sun L., 1122 (AB0197), 1207 (AB0363)
Sun M., 0429 (POS0400)
Sun S., 0847 (POS1135), 1057 (AB0050)
Sun X., 0460 (POS0458), 0622 (POS0742), 0678 (POS0848), 0680 (POS0851), 1037 (AB0005)
Sun Y., 0661 (POS0815), 0661 (POS0817)
Sun Z., 0561 (POS0647)
Sundel R., 0165 (OP0271)
Sundy J. S., 1167 (AB0282)
Sundy J., 0013 (OP0023)
Sung W. Y., 1152 (AB0253)
Suprun M., 1367 (AB0670)
Susok L., 0670 (POS0834)
Suspitsin E., 0246 (POS0078), 0247 (POS0080), 0930 (POS1298), 1036 (AB0001)
Süt N., 0875 (POS1187)
Sutcliffe N., 0079 (OP0136)
Suto T., 1060 (AB0056)
Suzuki T., 0581 (POS0674)
Suzuki Y., 0956 (POS1348), 1407 (AB0760)
Svanberg P., 0253 (POS0089)
Svanes Fevang B. T., 0397 (POS0339)
Svanteson S., 0087 (OP0147)
Svärd A., 0206 (POS0009)
Svensson M., 0014 (OP0026)
Svenungsson E., 0206 (POS0009), 0305 (POS0184), 0635 (POS0764), 0643 (POS0779), 0996 (POS1425), 1184 (AB0318)
Sverzellati N., 1326 (AB0578)
Svestkova N., 0872 (POS1183)
Swales C., 1021 (POS1472-HPR)
Swallow V., 0235 (POS0057-PARE), 0290 (POS0154-HPR)
Swart J. F., 0098 (OP0164)
Swearingen C., 0363 (POS0278), 0942 (POS1320)
Sweeney A. M. T., 0291 (POS0158-HPR)
Sweeney C., 0808 (POS1060)
Sweet K., 0312 (POS0195), 0790 (POS1036)
Świątoniowska-Lonc N., 1121 (AB0194)
Swierkot J., 0009 (OP0017), 0251 (POS0087), 0568 (POS0655)
Swift J., 1046 (AB0025)
Swingler L., 0235 (POS0059-PARE)
Swinnen T. W., 1337 (AB0602)
Sygyrta V., 0465 (POS0467), 1138 (AB0225), 1158 (AB0263)
Symons R., 0019 (OP0036)
Syngle A., 0318 (POS0205), 0774 (POS1011)
Syversen S. W., 0185 (OP0301)
Szamosi S., 0226 (POS0043), 0421 (POS0383), 0425 (POS0390)
Szántó S., 0226 (POS0043), 0421 (POS0383), 0425 (POS0390)
Szekanecz É., 0226 (POS0043), 0421 (POS0383), 0425 (POS0390)
Szekanecz Z., 0039 (OP0074), 0226 (POS0043), 0329 (POS0222), 0421 (POS0383), 0425 (POS0390), 1107 (AB0160)
Szentpetery A., 0226 (POS0043)
Szeto C. C., 0860 (POS1164), 0895 (POS1222)
Szilagyi I., 0061 (OP0111)
Szomolanyi P., 0363 (POS0277)
Sztajnbok F. R., 0247 (POS0079), 0934 (POS1304)
Szücs G., 0226 (POS0043), 0421 (POS0383), 0425 (POS0390)

T N T., 1396 (AB0733)
Tabak Ö. F., 0875 (POS1187)
Tabakov D., 0196 (OP0320)
Tabor Z., 0743 (POS0958)
Tada K., 0753 (POS0975)
Tada M., 0195 (OP0319), 0465 (POS0466), 0491 (POS0514), 0492 (POS0517), 1012 (POS1456-HPR), 1431 (AB0813)
Taddio A., 0948 (POS1333)
Taflan S. S., 0660 (POS0814), 1207 (AB0364)
Tagbor K., 0776 (POS1016), 0927 (POS1291)
Taghiyeva A., 0648 (POS0793), 0659 (POS0813), 1198 (AB0347)
Taglietti M., 0470 (POS0476), 0633 (POS0760), 1435 (AB0822)
Taguchi H., 1152 (AB0253)
Tahanan A., 0710 (POS0904)
Taib M. Z., 0459 (POS0457)
Takagi M., 1150 (AB0249)
Takagi Y., 0608 (POS0718)
Takahashi M., 0689 (POS0868)
Takahashi N., 1142 (AB0233), 1150 (AB0249)
Takahashi S., 0689 (POS0868), 1096 (AB0136)
Takahashi Y., 1224 (AB0391)
Takakura Y., 0981 (POS1396)
Takala R., 0402 (POS0346)
Takashima L., 0875 (POS1188)
Takei H., 1187 (AB0324), 1362 (AB0660)
Takeno M., 0349 (POS0254), 0667 (POS0828)
Takeuchi T., 0218 (POS0028), 0395 (POS0336), 0452 (POS0446), 0568 (POS0655), 0592 (POS0691), 1099 (AB0145), 1150 (AB0249), 1152 (AB0253), 1362 (AB0660)
Takizawa N., 0753 (POS0975)
Tal R., 0928 (POS1294), 0929 (POS1295)
Taliani G., 0897 (POS1228)
Talotta R., 0404 (POS0349)
Tam L. S., 0057 (OP0103), 0257 (POS0094), 0818 (POS1079), 0860 (POS1164), 0895 (POS1222), 1290 (AB0525), 1308 (AB0550), 1323 (AB0571)
Tamai H., 0458 (POS0455), 1152 (AB0253), 1362 (AB0660)
Tamai M., 0423 (POS0386), 0608 (POS0718), 0998 (POS1429)
Tamaki H., 1408 (AB0763)
Tamam L., 1471 (AB0896-HPR)
Tamas C., 1360 (AB0656)
Tamas M. M., 0638 (POS0768), 1360 (AB0656)
Tambiah J., 0363 (POS0278)
Tampe B., 0345 (POS0247), 0611 (POS0722), 0665 (POS0825), 1228 (AB0400)
Tamura M., 1181 (AB0311)
Tamura N., 0753 (POS0975), 1150 (AB0249)
Tan K., 0827 (POS1095)
Tan L. K., 0053 (OP0096), 0459 (POS0457)
Tan M., 0204 (POS0006)
Tan W., 0203 (POS0002), 0387 (POS0320), 0428 (POS0398), 0696 (POS0879)
Tan Y. K., 1419 (AB0787)
Tan Y., 0569 (POS0657), 0570 (POS0658)
Tanadini-Lang S., 0090 (OP0150), 0688 (POS0866)
Tanaka C., 0699 (POS0887)
Tanaka E., 0113 (OP0187), 0510 (POS0551), 0511 (POS0554), 0536 (POS0603), 0615 (POS0730)
Tanaka M., 0401 (POS0345), 1025 (POS1482-HPR)
Tanaka N., 0665 (POS0824)

Tanaka Y., 0218 (POS0028), 0251 (POS0087), 0328 (POS0220), 0329 (POS0221), 0395 (POS0336), 0537 (POS0604), 0566 (POS0653), 0579 (POS0670), 0586 (POS0683), 0592 (POS0691), 0694 (POS0877), 1094 (AB0132)
Tanculescu O., 1116 (AB0181)
Tang H., 1136 (AB0221)
Tang S., 0076 (OP0132)
Tang Y. K., 0640 (POS0773), 0687 (POS0865)
Tang Y. P., 0852 (POS1146), 1040 (AB0011), 1067 (AB0075), 1252 (AB0449)
Tani C., 0594 (POS0693), 0619 (POS0737), 0628 (POS0751), 0630 (POS0756), 0633 (POS0760), 0647 (POS0789)
Taniguchi A., 0753 (POS0975)
Taniguchi Y., 0753 (POS0975)
Taninaga T., 1152 (AB0253)
Tański W., 1121 (AB0194)
Tansley S., 0170 (OP0281), 0369 (POS0288)
Tantaoui H., 1344 (AB0620), 1398 (AB0738)
Tanten R., 0874 (POS1186), 0875 (POS1188)
Tanti G., 0594 (POS0693)
Tao Y., 0574 (POS0664)
Tappeiner C., 0033 (OP0061)
Tappuni A., 0079 (OP0136)
Tarakci E., 1389 (AB0715), 1453 (AB0860-HPR)
Tarantino G., 1434 (AB0821)
Tarasenko E., 1397 (AB0735)
Tarasova G., 0614 (POS0729), 1180 (AB0309), 1180 (AB0310)
Tardito S., 0392 (POS0330), 1060 (AB0057)
Tardugno M., 1446 (AB0844)
Targonska-Stepniak B., 1424 (AB0800)
Tariq M., 0396 (POS0337)
Tarn J., 1057 (AB0051)
Tarner I., 0383 (POS0314), 1054 (AB0043)
Tarnowski T., 1155 (AB0259)
Tas S., 0359 (POS0271-HPR), 0548 (POS0621), 0578 (POS0669)
Tascilar K., 0088 (OP0148), 0165 (OP0272), 0194 (OP0318), 0420 (POS0381), 0979 (POS1394), 0996 (POS1426), 1030 (POS1492-HPR), 1275 (AB0495)
Tashkin D., 0162 (OP0267), 0163 (OP0268)
Taskina E., 0275 (POS0127), 0276 (POS0130), 0827 (POS1094), 1336 (AB0599), 1337 (AB0603), 1338 (AB0604)
Tasset C., 0083 (OP0141)
Tasso M., 1284 (AB0515)
Tataru C., 0519 (POS0569)
Tateishi C., 0808 (POS1059)
Tatlı İ., 1028 (POS1486-HPR), 1467 (AB0888-HPR)
Tatsi A., 0646 (POS0786)
Tatsiana P., 1350 (AB0632)
Tatsiana R., 1350 (AB0632)
Tauman R., 1181 (AB0312)
Tavares-Costa J., 0293 (POS0162), 0830 (POS1100), 1424 (AB0799)
Tavoni A., 0906 (POS1246)
Tavor Y., 0892 (POS1217)
Tay V. Y., 1469 (AB0891-HPR)
Taylor J., 0581 (POS0672)
Taylor P. C., 0378 (POS0305), 0452 (POS0446), 0489 (POS0512), 0561 (POS0646), 0563 (POS0649), 0566 (POS0653), 0572 (POS0660)
Taylor W., 0841 (POS1124)
Taylor-Stokes G., 0885 (POS1205)
Tbini H., 0290 (POS0155-HPR)
Tchetina E., 0259 (POS0099), 0542 (POS0611)
Tchetverikov I., 0127 (OP0211), 0127 (OP0212), 0289 (POS0151), 0807 (POS1057)
te Kampe R., 1479 (AB0915-PARE)
Te Molder M., 0359 (POS0272-HPR)
Tedeschi S., 0651 (POS0798), 0841 (POS1124), 0845 (POS1132), 0846 (POS1133)
Tee M., 0598 (POS0699)
Tee Y. C., 0816 (POS1075)
Tegzová D., 0424 (POS0388), 1170 (AB0288)
Teh L. S., 0602 (POS0705), 0625 (POS0746)
Teixeira F., 0293 (POS0162), 0830 (POS1100), 1424 (AB0799)
Teixeira V., 0029 (OP0055)
Tejiozem Donfack K., 0665 (POS0825)
Tekaya R., 0360 (POS0274-HPR), 0768 (POS1000), 1106 (AB0158), 1119 (AB0190), 1120 (AB0192), 1285 (AB0517), 1341 (AB0611), 1395 (AB0730), 1396 (AB0731), 1396 (AB0732)
Tekgoz E., 0069 (OP0125), 0731 (POS0935)
Tektonidou M., 0703 (POS0894), 0815 (POS1073)
Tel A., 0618 (POS0735)
Tellenbach C., 0058 (OP0105)
Telyshev K., 0275 (POS0127), 0276 (POS0130), 1338 (AB0604)
Temiz Karadağ D., 0702 (POS0892)
Ten Cate R., 0932 (POS1300)
Ten Klooster P., 0562 (POS0648), 1122 (AB0196), 1153 (AB0254)
ten Kloster P., 0547 (POS0620)
Tenazinha M. C., 0644 (POS0781)
Tenbrock K., 0945 (POS1325)
Tenbusch M., 0996 (POS1426)
Teng L., 1310 (AB0552), 1311 (AB0553)
Teng Y. K. O., 0585 (POS0680), 1365 (AB0667)
Tennebø K., 0092 (OP0153-HPR)
Tenn-Mcclellan A., 0204 (POS0006)
Tenstad H., 0419 (POS0377)
Tenti S., 1331 (AB0588)
Tentolouris N., 0656 (POS0807)
Teodoro M. L. M., 1448 (AB0848)
Teodoro W., 0444 (POS0432)
Teplyakova O., 1029 (POS1489-HPR), 1449 (AB0851), 1461 (AB0874-HPR)
Ter Horst R., 0009 (OP0017)
Ter Wee M., 0114 (OP0189)
Terabe K., 1142 (AB0233)
Terao C., 0401 (POS0345)
Terizaki M., 0184 (OP0299), 0523 (POS0580)
Terkeltaub R., 0841 (POS1124)
Terpstra S., 0999 (POS1431)
Terreri M. T., 0247 (POS0079), 0934 (POS1304)
Terrier B., 0231 (POS0052)
Terroso G., 0260 (POS0100), 0833 (POS1106)
Terslev L., 0123 (OP0204), 0234 (POS0056), 0287 (POS0149), 0352 (POS0260), 0379 (POS0307), 0845 (POS1132), 0846 (POS1133), 0850 (POS1141), 0865 (POS1170), 1202 (AB0355), 1348 (AB0629)
Tesei G., 1154 (AB0256)
Tesser J., 1291 (AB0526)
Testa M., 0292 (POS0160-HPR)
Teuwen M., 1460 (AB0873-HPR)
Tezcan M. E., 0514 (POS0560), 0964 (POS1364)
Tezeghdenti A., 0926 (POS1290), 1066 (AB0071), 1442 (AB0836), 1443 (AB0840)
Thaçi D., 0795 (POS1042)
Thakkar S., 0366 (POS0283), 1050 (AB0035)
Thaler K., 1019 (POS1468-HPR)
Thanopoulou V., 1417 (AB0783)
Tharwat S., 0477 (POS0490), 0645 (POS0784), 0917 (POS1265), 1404 (AB0753)
Theander E., 0140 (OP0230), 0142 (OP0232), 0778 (POS1021), 0799 (POS1046), 1295 (AB0530)
Theja Reddy K., 0600 (POS0701)
Thejeel B., 1334 (AB0594)
Theodor Sødergren S., 1483 (AB0924-PARE)
Theodoridou A., 0337 (POS0234)
Theotikos E., 0646 (POS0786)
Therkildsen J., 0451 (POS0444)
Therkildsen P., 0036 (OP0066), 0657 (POS0809)
Thiel J., 1383 (AB0701)
Thiele L. E., 0031 (OP0058)
Thiele T., 1385 (AB0707)
Thilakarathne P., 1313 (AB0556)
Thomas B., 0120 (OP0200), 1052 (AB0039)
Thomas R., 0002 (OP0006), 0173 (OP0286)
Thomas T., 0172 (OP0284), 1164 (AB0277), 1261 (AB0469)
Thompson B., 0042 (OP0078)
Thompson J., 0169 (OP0280-PARE)
Thompson M., 1021 (POS1472-HPR)
Thomsen M. K., 0866 (POS1171)
Thomson W., 0008 (OP0014), 0097 (OP0162), 0927 (POS1292)
Thorne C., 0159 (OP0262-HPR), 1014 (POS1459-HPR), 1313 (AB0557)
Thornton S., 0245 (POS0076)
Thorup A. S., 0120 (OP0200), 1052 (AB0039)
Thota E., 0061 (OP0110)
Throup J., 0795 (POS1042)
Thumboo J., 0301 (POS0176), 0989 (POS1411), 0990 (POS1413), 1419 (AB0787)
Thurlings R. M., 0680 (POS0852)
Thway M., 1088 (AB0119)
Tiamiyu I., 0070 (OP0126), 0255 (POS0092), 0572 (POS0660)
Tian J., 0118 (OP0196), 0832 (POS1103)
Tian X., 0178 (OP0290), 0629 (POS0754), 0641 (POS0775)
Tierney A., 0115 (OP0191-PARE)
Tietz L. M., 0769 (POS1002)
Tieu J., 1441 (AB0834)
Tigrak S. N., 1404 (AB0751)
Tikly M., 0385 (POS0317)
Tiller J., 0009 (OP0015)
Tillett W., 0135 (OP0224), 0141 (OP0231), 0237 (POS0062-PARE), 0312 (POS0196), 0316 (POS0200), 0782 (POS1026), 0784 (POS1028), 0789 (POS1034), 0800 (POS1047), 0804 (POS1052), 0821 (POS1084), 1307 (AB0548), 1426 (AB0803)
Tillinger M., 0383 (POS0315)
Tin D., 0159 (OP0262-HPR), 1014 (POS1459-HPR)
Tinazzi I., 0134 (OP0223), 0284 (POS0145), 0355 (POS0265)
Tincani A., 0105 (OP0175), 0470 (POS0476), 0594 (POS0693), 0600 (POS0702), 0612 (POS0724), 0619 (POS0737), 0628 (POS0751), 0633 (POS0760), 0635 (POS0764), 1435 (AB0822)
Tipton C. M., 0585 (POS0680)
Tirelli F., 0232 (POS0054), 0393 (POS0332)
Tirosh I., 0929 (POS1295)
Tirri E., 0888 (POS1210), 1260 (AB0467), 1331 (AB0588)
Tissera Y., 0887 (POS1208), 1194 (AB0338), 1196 (AB0342)
Titton D., 0582 (POS0676)
Tiwari A., 0915 (POS1262), 0948 (POS1331)
Tjørnhøj-Thomsen T., 1483 (AB0924-PARE)
Tkachenko N., 0100 (OP0166)
Tłustochowicz W., 1434 (AB0820)
Tn T., 1415 (AB0779)
To C. H., 0639 (POS0771), 0640 (POS0772)
Tobar E., 0198 (LB0001)
Tobar Jaramillo M. A., 0759 (POS0984)
Toda T., 1099 (AB0145)
Todolí Parra J. A., 0350 (POS0256), 0987 (POS1408), 0987 (POS1409)
Todorov P., 0732 (POS0938)
Toes R., 0203 (POS0001), 0420 (POS0379), 0422 (POS0384), 0423 (POS0386), 0426 (POS0395), 1044 (AB0020), 1045 (AB0022), 1366 (AB0668)
Tofani L., 0105 (OP0176), 0355 (POS0264), 0385 (POS0317), 0675 (POS0842), 1154 (AB0256)
Tofarides A., 1467 (AB0887-HPR)
Toftegaard P., 0982 (POS1398)
Togawa D., 0252 (POS0088), 1151 (AB0252)
Togia K., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Togo K., 0275 (POS0128)
Tohma S., 0368 (POS0286)
Toker Dincer Z., 1389 (AB0715)
Tokunaga T., 1063 (AB0065)
Toledano K., 0892 (POS1217)
Toledano Martinez E., 1089 (AB0120)
Toledo-Coello M. D., 0469 (POS0475)
Tolend M., 0943 (POS1323)
Tomassetti S., 0897 (POS1228)
Tomasson G., 0345 (POS0248)
Tombetti E., 0030 (OP0056), 0105 (OP0175)
Tomčík M., 0150 (OP0245), 0677 (POS0846), 0678 (POS0849), 1234 (AB0412)
Tomcik M., 1233 (AB0410)
Tomé P., 0182 (OP0297)
Tomelleri A., 0396 (POS0337), 0655 (POS0806), 0950 (POS1336), 0953 (POS1341), 0955 (POS1347), 1206 (AB0361)
Tomero Muriel E., 0610 (POS0721), 0719 (POS0917)

Tomietto P., 1002 (POS1435), 1391 (AB0719)
Tomita T., 0716 (POS0912), 0753 (POS0975)
Tommasini A., 0948 (POS1333)
Toms A., 0223 (POS0035)
Tomsic M., 0131 (OP0220), 0217 (POS0027), 0650 (POS0796), 0664 (POS0823), 0666 (POS0826), 1201 (AB0352), 1201 (AB0353)
Tonello M., 0619 (POS0737), 0628 (POS0751), 1174 (AB0295)
Tonga E., 1021 (POS1471-HPR)
Toniati P., 0650 (POS0797), 0658 (POS0811)
Tonolo S., 1480 (AB0918-PARE)
Tony H. P., 0194 (OP0318), 0528 (POS0591), 0544 (POS0615), 0706 (POS0899), 0780 (POS1023)
Too C. L., 0053 (OP0096), 0459 (POS0457)
Toonen E., 0657 (POS0809)
Topal I., 0286 (POS0146)
Topaloglu R., 0117 (OP0195)
Topçuoğlu C., 1182 (AB0314)
Toplak N., 0242 (POS0071)
Toprover M., 0278 (POS0134)
Topuria I., 0446 (POS0436)
Tor Y. B., 0191 (OP0313)
Tordoff M., 0008 (OP0014)
Tore N. G., 1235 (AB0414), 1462 (AB0877-HPR)
Torfing T., 0419 (POS0377)
Torgashina A., 0196 (OP0320), 0608 (POS0717), 0896 (POS1226), 1116 (AB0183), 1168 (AB0284), 1185 (AB0321)
Torgutalp M., 0025 (OP0048), 0080 (OP0137), 0081 (OP0139), 0155 (OP0253), 0155 (OP0254), 0342 (POS0241), 0456 (POS0453), 0532 (POS0597), 0771 (POS1007), 0813 (POS1069), 0949 (POS1335)
Tornberg H., 0828 (POS1097)
Törnblom M., 1330 (AB0586)
Tornero C., 0766 (POS0996), 0976 (POS1387)
Torok K., 0247 (POS0079), 0934 (POS1304)
Toroptsova N., 0294 (POS0164), 0493 (POS0518), 0493 (POS0519), 0673 (POS0839), 0674 (POS0841), 1104 (AB0154), 1342 (AB0613)
Torp-Pedersen C., 0382 (POS0313)
Torre I., 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Torre J. C., 1303 (AB0542)
Torres L., 0811 (POS1064)
Torres Valdéz E., 0559 (POS0642)
Torre-Salaberri I., 0032 (OP0060), 0952 (POS1340), 0967 (POS1371), 1225 (AB0396), 1412 (AB0771)
Torres-Lopez E., 1085 (AB0113)
Torun E. S., 0191 (OP0313), 0602 (POS0706)
Tosounidou S., 0043 (OP0081), 0602 (POS0705), 1010 (POS1452)
Toss A., 1241 (AB0425)
Toth M., 0832 (POS1104)
Totoson P., 1062 (AB0062), 1067 (AB0073)
Toulgui E., 0856 (POS1154), 0925 (POS1285), 0925 (POS1286)
Touma Z., 0173 (OP0285), 0230 (POS0050)
Tournadre A., 0080 (OP0138), 0360 (POS0274-HPR), 1067 (AB0074)
Tournier M., 1062 (AB0062)
Toussaint L., 1027 (POS1484-HPR), 1467 (AB0889-HPR)
Toussirot E., 1204 (AB0358), 1322 (AB0570)
Touzi M., 0466 (POS0469), 1051 (AB0037), 1390 (AB0718), 1395 (AB0728), 1414 (AB0775)
Toyoizumi S., 0113 (OP0187), 0368 (POS0286)
Toyos Sáenz de Miera F. J., 0610 (POS0721), 1056 (AB0047), 1075 (AB0092)
Töyrä Silfverswärd S., 0192 (OP0315)
Trad N., 0975 (POS1385)
Traianos E., 1057 (AB0051)
Traksel R. A. M., 0880 (POS1197)
Tralice R., 0635 (POS0763)
Trallero-Araguás E., 0699 (POS0886), 0700 (POS0888), 0898 (POS1229), 1241 (AB0426)
Tramontano G., 1007 (POS1447)
Tran G., 0919 (POS1269)
Tran Manh C., 0121 (OP0201)
Tranah E., 1411 (AB0769)
Trandafir A., 1378 (AB0690)
Traore Y., 0358 (POS0269-HPR), 0358 (POS0270-HPR)
Trapnell B. C., 0198 (LB0001), 1211 (AB0370)
Trasieva T., 0592 (POS0690)
Trattnig S., 0363 (POS0277)
Trauzeddel R., 0246 (POS0077), 0883 (POS1202)
Traverson C., 0518 (POS0566), 0770 (POS1003), 0820 (POS1082), 0902 (POS1239)
Treadwell K., 0983 (POS1400)
Trefler J., 1123 (AB0198)
Trefond L., 0199 (LB0002)
Tremaskina P., 1306 (AB0546), 1327 (AB0580)
Tremblay A., 0431 (POS0403)
Treppo E., 0883 (POS1201), 1224 (AB0392)
Trespidi L., 0628 (POS0751)
Treutlein C., 0165 (OP0272)
Triaille C., 0020 (OP0037), 0240 (POS0067)
Triantafyllias K., 0031 (OP0058), 0985 (POS1405)
Triantafyllou A., 0620 (POS0738)
Triggianese P., 0335 (POS0231), 1038 (AB0006), 1284 (AB0515), 1418 (AB0786), 1434 (AB0821)
Trigueros-Vazquez M., 0899 (POS1231), 1377 (AB0688)
Trijau S., 0900 (POS1234)
Triki W., 0921 (POS1274), 1095 (AB0133), 1101 (AB0148), 1102 (AB0150), 1112 (AB0171), 1118 (AB0187), 1286 (AB0520), 1400 (AB0744)
Tringali G., 0985 (POS1406)
Trinh-Minh T., 0121 (OP0201), 0150 (OP0245), 0391 (POS0327)
Trivedi M., 0572 (POS0660), 0792 (POS1037), 0792 (POS1038), 0801 (POS1049)
Trives Folguera L., 0658 (POS0812), 1117 (AB0185), 1397 (AB0734)
Trofimenko A., 0424 (POS0389), 1056 (AB0048), 1057 (AB0049), 1062 (AB0061), 1083 (AB0110), 1108 (AB0163), 1419 (AB0788), 1444 (AB0841)
Troitskaya E., 0326 (POS0217)
Trojani M. C., 0367 (POS0284)
Trokovic N., 0063 (OP0114)
Troldborg A., 0866 (POS1171)
Tronnberg R., 0711 (POS0906)
Troum O., 0450 (POS0443)
Trouw L. A., 1085 (AB0113)
Truchetet M. E., 0331 (POS0225), 0681 (POS0855), 0685 (POS0861), 1261 (AB0469)
Truer T., 1307 (AB0548)
Truglia S., 0619 (POS0737), 0645 (POS0783), 0902 (POS1238), 0903 (POS1240)
Truillet R., 0365 (POS0281)
Trupin L., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Tsai W. C., 0447 (POS0437), 1152 (AB0253), 1258 (AB0463), 1290 (AB0525)
Tsang H. H. L., 0225 (POS0039)
Tsao Y. P., 0023 (OP0045)
Tsapis N., 0393 (POS0331)
Tschernatsch M., 0209 (POS0015)
Tse S. M., 0298 (POS0171), 0640 (POS0772), 0943 (POS1323)
Tsekoura K., 0238 (POS0064-PARE)
Tseng F. Y., 0023 (OP0045)
Tseng O., 0377 (POS0303)
Tseronis D., 0631 (POS0757), 0632 (POS0759), 0635 (POS0764)
Tsiami S., 0224 (POS0038), 0344 (POS0245), 0525 (POS0584), 0851 (POS1145), 1435 (AB0823)
Tsigarides J., 0210 (POS0018)
Tsirogianni A., 0668 (POS0829)
Tsitsami E., 0098 (OP0164)
Tsourouflis G., 0180 (OP0294)
Tsuge S., 1407 (AB0760)
Tsugihashi Y., 0492 (POS0516)
Tsuji S., 0312 (POS0196), 0753 (POS0975), 0788 (POS1032)
Tsuji Y., 0998 (POS1429)
Tsujimoto N., 1150 (AB0249)
Tsulukiya I., 0100 (OP0166), 0250 (POS0085), 0938 (POS1312), 1392 (AB0721), 1394 (AB0727)
Tsuritani K., 0536 (POS0603)
Tsurko V., 0840 (POS1123)
Tsuruta D., 0808 (POS1059)
Tuckwell K., 0648 (POS0792)
Tufan A., 0069 (OP0125), 0733 (POS0940), 0878 (POS1193), 1077 (AB0097), 1176 (AB0300), 1235 (AB0414)
Tugnet N., 0218 (POS0028)
Tukek B., 0660 (POS0814), 0662 (POS0819), 0663 (POS0820)
Tumakova A., 0930 (POS1298)
Tummala R., 0075 (OP0131), 0586 (POS0683), 0587 (POS0684), 0590 (POS0688), 0592 (POS0690), 0592 (POS0691), 1171 (AB0289)
Tuna Z., 1462 (AB0877-HPR)
Tundia N., 0446 (POS0435), 0446 (POS0436), 0575 (POS0666), 0579 (POS0670)
Turan S., 1470 (AB0893-HPR)
Türe-Özdemir F., 1028 (POS1486-HPR), 1467 (AB0888-HPR)
Turesson C., 0063 (OP0114), 0068 (OP0122), 0130 (OP0218), 0513 (POS0557), 0864 (POS1169)
Turgay T. M., 0532 (POS0597), 0949 (POS1335)
Turk J., 0462 (POS0462)
Turk M., 0462 (POS0462), 0891 (POS1216), 1251 (AB0447)
Turk S. M., 0223 (POS0036), 0732 (POS0939)
Türk S. M., 1382 (AB0700)
Turkiewicz A., 1372 (AB0678)
Turkoglu Genc F., 0223 (POS0036), 0732 (POS0939)
Turkstra F., 0273 (POS0123), 0962 (POS1361)
Turmezei T. D., 0825 (POS1091), 0825 (POS1092)
Turner A., 0918 (POS1268)
Turner D., 0885 (POS1206)
Turrent A., 0853 (POS1149), 1386 (AB0709)
Tveter A. T., 0092 (OP0154-HPR), 0094 (OP0157-HPR)
Tymms K., 0330 (POS0223), 0711 (POS0906), 1015 (POS1461-HPR)
Tzanis P., 0646 (POS0786)
Tzaribachev N., 0943 (POS1323)
Tzemach R., 1049 (AB0032)
Tzioufas A., 0015 (OP0029), 0022 (OP0041), 0178 (OP0291), 0180 (OP0294), 0370 (POS0290), 0656 (POS0807), 0668 (POS0829), 1299 (AB0537), 1381 (AB0697)

Überla K., 0996 (POS1426)
Ubiali T., 0594 (POS0693)
Ucar D., 0660 (POS0814), 0662 (POS0819)
Uçar M., 0733 (POS0940)
Ucci F., 1073 (AB0087)
Uceda J., 0469 (POS0475)
Uchida H. A., 0395 (POS0336)
Uchiyama S., 0603 (POS0707)
Ueeda K., 0961 (POS1358), 1169 (AB0287)
Uehara R., 1025 (POS1482-HPR)
Ueki Y., 0581 (POS0674)
Ueno K., 1329 (AB0583)
Ugarte-Gil M. F., 0002 (OP0006), 0173 (OP0286), 0177 (OP0289), 0877 (POS1190)
Ugarte-Gil M., 0181 (OP0296), 0230 (POS0051), 1368 (AB0674)
Ugurlu S., 0663 (POS0820), 0958 (POS1351), 0966 (POS1369), 0974 (POS1381), 1327 (AB0579), 1389 (AB0715), 1453 (AB0860-HPR)
Uhlig T., 0123 (OP0204), 0281 (POS0139)
Ullah S., 0381 (POS0310), 0527 (POS0589), 0574 (POS0663), 1298 (AB0533)
Ullmann M., 1121 (AB0195)
Ulrich N. H., 0045 (OP0083)
Ulu K., 0249 (POS0082), 0871 (POS1181), 0942 (POS1319)
Uludag O., 0636 (POS0766)
Umanzor C., 0621 (POS0739)
Umayahara T., 0697 (POS0881)
Umnova I., 0754 (POS0976), 0815 (POS1072), 1325 (AB0576)
Ünal E., 0815 (POS1071)
Ünal Ş., 0100 (OP0168)
Üner M., 0648 (POS0793)
Üner M., 1198 (AB0347)
Ungprasert P., 0652 (POS0800)
Unizony S., 0031 (OP0059), 0656 (POS0808), 1211 (AB0370)
Unlu Ozkan F., 0905 (POS1244)

Unterwalder N., 0305 (POS0183), 0623 (POS0744)
Unver B., 1329 (AB0584)
Upadhyaya S., 1251 (AB0447)
Upton L., 0230 (POS0051), 1368 (AB0674)
Urata Y., 0368 (POS0286)
Urban M. L., 0600 (POS0702), 0628 (POS0751), 0889 (POS1212)
Ureña I., 0323 (POS0211)
Uriarte Isacelaya E., 0610 (POS0721), 1141 (AB0230)
Uribe Luna A., 0856 (POS1156)
Urowitz M. B., 0177 (OP0289)
Urrego Callejas T., 0636 (POS0765), 1213 (AB0374)
Urrego-Laurín C., 0922 (POS1275)
Urruticoechea-Arana A., 0523 (POS0579), 0952 (POS1340), 0967 (POS1371), 1279 (AB0503), 1303 (AB0542)
Ursini F., 0906 (POS1246), 0957 (POS1349)
Urso L., 0701 (POS0891)
Uruha A., 0305 (POS0183)
Urumova M., 1262 (AB0470)
Urzainqui A., 0393 (POS0331), 1071 (AB0083)
Ushikubo M., 1249 (AB0442)
Ushio Y., 0513 (POS0556), 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1249 (AB0443), 1437 (AB0826)
Uslu A. U., 1355 (AB0644)
Usova E., 0277 (POS0131)
Usta B., 0749 (POS0968), 1272 (AB0491)
Üstün E. I., 1086 (AB0114)
Uy E., 0989 (POS1411)
Uyanik G., 0848 (POS1137)
Uygunoglu U., 0660 (POS0814), 0662 (POS0819)
Uziel Y., 0247 (POS0079), 0872 (POS1183), 0934 (POS1304), 1373 (AB0681)
Uzun C., 0949 (POS1335)
Uzun E., 1016 (POS1462-HPR)
Uzunhan Y., 0388 (POS0323)

V D., 0584 (POS0679)
Vacca A., 0387 (POS0321)
Vacchi C., 0324 (POS0214), 1241 (AB0425)
Vadillo C., 0910 (POS1253)
Vaghaiwalla Z., 0295 (POS0165), 1088 (AB0119), 1343 (AB0618)
Vagrecha A., 0192 (OP0314)
Vahldiek J. L., 0025 (OP0048), 0155 (OP0254), 0887 (POS1209)
Vahlyarskaya S., 0014 (OP0027)
Vaida-Voevod D. A., 0638 (POS0768)
Vaile J., 0468 (POS0474)
Valadares L. D. D. A., 1448 (AB0848)
Valderrama M., 0782 (POS1025)
Valdés Corona L. F., 0559 (POS0642)
Valdes-Torres P., 1007 (POS1446), 1455 (AB0863-HPR)
Valdez T., 1187 (AB0325), 1188 (AB0326), 1351 (AB0635)
Valdivieso J., 0693 (POS0875)
Valdivieso-Achá J. P., 0034 (OP0064)
Valeeva I. K., 1269 (AB0484)
Valencia O., 1032 (POS1496-HPR)
Valenciano A. C., 0760 (POS0985)
Valente C., 1053 (AB0041)
Valentini R., 0742 (POS0956)
Valenzuela-Almada M., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Valera-Ribera C., 0296 (POS0168), 1427 (AB0806)
Valerio V., 0918 (POS1268)
Valero C., 0719 (POS0917), 1241 (AB0427)
Valero O., 0380 (POS0308)
Valim V., 0582 (POS0676), 0909 (POS1252), 1448 (AB0848)
Valinotti V., 1042 (AB0015), 1106 (AB0159), 1120 (AB0193)
Vallejo M., 1027 (POS1484-HPR), 1467 (AB0889-HPR)
Vallejo Pascual M. E., 0628 (POS0752), 1171 (AB0290)
Vallejo-Yagüe E., 0323 (POS0212), 0462 (POS0461), 1128 (AB0206)
Vallerga C., 0061 (OP0111)
Valls-Pascual E., 0296 (POS0168), 0610 (POS0721), 1427 (AB0806)
Valois M. F., 0159 (OP0262-HPR), 1014 (POS1459-HPR)
Valor L., 0096 (OP0160-HPR), 0194 (OP0318), 0979 (POS1394), 1275 (AB0495)
Van ‘t Ende A., 0036 (OP0066)
van Baarsen L., 0425 (POS0391)
Van Beneden K., 0378 (POS0305)
Van Bentum R., 0705 (POS0897)
Van Berkel-de Joode W., 1020 (POS1470-HPR)
Van Bijnen S., 0880 (POS1197)
Van Bodegom-Vos L., 0038 (OP0071-HPR), 0119 (OP0198-HPR)
van Boheemen L., 0420 (POS0379)
Van Breda A., 0375 (POS0300), 1001 (POS1433)
Van Buchem M., 0606 (POS0714)
Van Caam A., 1248 (AB0441)
Van Criekinge T., 0828 (POS1096)
Van Daele P. L., 0078 (OP0135), 0308 (POS0189)
Van de Laar M., 0374 (POS0299)
Van de Sande M. G. H., 0026 (OP0050), 0131 (OP0220), 0217 (POS0027), 0707 (POS0900)
Van de Sande M., 0339 (POS0236), 0741 (POS0954)
Van de Stadt L., 0273 (POS0123), 0304 (POS0182), 0351 (POS0258)
Van Delft E., 0353 (POS0261)
Van den Akker E., 0403 (POS0348)
Van den Bemt B., 0359 (POS0271-HPR), 1027 (POS1485-HPR), 1351 (AB0634)
van den Bemt B., 0578 (POS0669)
Van den Berg J. M., 0241 (POS0070), 0302 (POS0178), 0932 (POS1300), 0937 (POS1311), 1070 (AB0081)
Van den Berg R., 0152 (OP0250), 0222 (POS0033)
Van den Bosch F., 0085 (OP0144), 0138 (OP0228), 0312 (POS0196), 0314 (POS0197), 0704 (POS0895), 0722 (POS0923), 0788 (POS1032), 0792 (POS1037), 0792 (POS1038), 0801 (POS1049)
Van den Dikkenberg, Msc M., 0238 (POS0063-PARE), 1087 (AB0116)
Van den Ende C. H. M., 1248 (AB0441)
Van den Ende C., 0359 (POS0272-HPR), 1460 (AB0873-HPR)
Van den Hoogen F., 0310 (POS0193), 0399 (POS0343)
Van den Hout W., 1460 (AB0873-HPR)
Van der Bijl A., 1366 (AB0668)
Van der Esch M., 0291 (POS0157-HPR)
Van der Geest K., 0396 (POS0337), 0657 (POS0809)
Van der Giesen F., 0038 (OP0071-HPR)
Van der Heijde D., 0024 (OP0047), 0026 (OP0050), 0085 (OP0144), 0137 (OP0227), 0152 (OP0250), 0153 (OP0251), 0221 (POS0032), 0222 (POS0033), 0304 (POS0182), 0314 (POS0198), 0332 (POS0226), 0339 (POS0236), 0340 (POS0238), 0341 (POS0240), 0351 (POS0258), 0720 (POS0918), 0735 (POS0944), 0741 (POS0954), 0751 (POS0971), 0753 (POS0975), 0783 (POS1027)
Van der Helm - van Mil A., 0127 (OP0211), 0127 (OP0212), 0130 (OP0217), 0351 (POS0257), 0353 (POS0261), 0978 (POS1391), 0992 (POS1418), 1005 (POS1442), 1155 (AB0258)
van der Helm - van Mil A., 0403 (POS0348), 0420 (POS0379), 0422 (POS0385), 0426 (POS0395), 0448 (POS0438), 0486 (POS0506)
Van der Helm-van Mil A., 0212 (POS0021)
Van der Horst-Bruinsma I., 0039 (OP0074), 0217 (POS0027), 0333 (POS0228), 0705 (POS0897)
van der Horst-Bruinsma I., 0142 (OP0232)
Van der Kaap J. H., 0127 (OP0211), 0127 (OP0212)
van der Kraan Y. M., 1268 (AB0481)
Van der Laken C. J., 0012 (OP0021), 0114 (OP0189), 1449 (AB0850)
Van der Leeden M., 0039 (OP0074), 0291 (POS0157-HPR)
Van der Maas A., 0399 (POS0343)
Van der Meulen A., 1365 (AB0667)
Van der Meulen C., 0273 (POS0123)
van der Tog C., 0478 (POS0492)
Van der Veer S., 1006 (POS1444)
Van der Velde J., 0999 (POS1431)
Van der Wee N., 0603 (POS0708), 0604 (POS0709)
Van der Windt D., 0139 (OP0229)
van der Woude D., 0422 (POS0384), 0423 (POS0386), 0426 (POS0395)
Van der Woude D., 1044 (AB0020), 1366 (AB0668)
Van Dijk A., 1248 (AB0441)
Van Dijk B., 0212 (POS0021), 0992 (POS1418)
van Dijk B., 0422 (POS0385)
Van Dongen C., 0911 (POS1256)
Van Dongen J. J. M., 0585 (POS0680)
Van Doorn M., 0289 (POS0151), 0359 (POS0271-HPR)
van Doorn M., 0548 (POS0621), 0578 (POS0669)
Van Durme C., 1479 (AB0915-PARE)
Van Dyke T., 0048 (OP0088), 0061 (OP0110)
Van Eijk-Hustings Y., 1470 (AB0894-HPR), 1479 (AB0915-PARE)
Van Exel J., 0186 (OP0303-HPR)
Van Gaalen F. A., 0024 (OP0047), 0026 (OP0050), 0152 (OP0250), 0222 (POS0033), 0339 (POS0236), 0341 (POS0240), 0735 (POS0944), 0741 (POS0954)
Van Gompel E., 0196 (OP0321)
Van Haren E., 0911 (POS1256)
Van Haren-Willems J., 1248 (AB0441)
Van Helden-Meeuwsen C. G., 0302 (POS0178), 0308 (POS0189)
Van Herwaarden N., 0680 (POS0852), 1023 (POS1477-HPR), 1351 (AB0634)
Van Hunsel F., 0578 (POS0669)
Van Kooten C., 0585 (POS0680)
Van Kuijk A., 0142 (OP0232)
Van Laar J. M., 0253 (POS0089), 0993 (POS1419), 1430 (AB0812), 1465 (AB0884-HPR), 1478 (AB0914-PARE)
Van Leeuwen N., 0203 (POS0001), 0675 (POS0843)
Van Leuven S., 1248 (AB0441)
Van Lieshout E., 1478 (AB0914-PARE)
Van Lingen C., 0168 (OP0277-PARE)
van Lint J., 0548 (POS0621), 0578 (POS0669)
Van Lint J., 0562 (POS0648), 1153 (AB0254)
Van Lunteren M., 0026 (OP0050), 0339 (POS0236), 0341 (POS0240), 0741 (POS0954)
Van Maurik A., 0078 (OP0135)
Van Mens L., 0039 (OP0074)
Van Meurs J., 0061 (OP0111)
van Mulligen E., 0422 (POS0385)
Van Nieuwland M., 1209 (AB0367), 1214 (AB0375)
Van Nimwegen J. F., 0074 (OP0130)
Van Onna M., 0937 (POS1311)
Van Onsem S., 0359 (POS0272-HPR)
van Oosterhout M., 0471 (POS0479)
Van Os-Medendorp H., 1465 (AB0884-HPR)
van Ouwerkerk L., 1365 (AB0667)
Van Puijenbroek E., 0359 (POS0271-HPR)
van Puijenbroek E., 0548 (POS0621), 0578 (POS0669)
Van Rossum M., 0932 (POS1300), 0943 (POS1323)
Van Schaardenburg D., 0114 (OP0189), 1460 (AB0873-HPR)
van Schaardenburg D., 0420 (POS0379)
van Schie K., 0422 (POS0384), 0423 (POS0386)
Van Schie K., 1044 (AB0020)
Van Sleen Y., 0036 (OP0066), 0655 (POS0806), 0657 (POS0809)
van Soest K., 0540 (POS0609)
Van Suijlekom-Smit L. W. A., 0932 (POS1300)
Van Tilburg S., 0302 (POS0178)
Van Tubergen A., 1460 (AB0873-HPR)
Van Vollenhoven R., 0076 (OP0132), 0177 (OP0289), 0328 (POS0220), 0588 (POS0686), 0597 (POS0698), 0598 (POS0699)
van Vollenhoven R., 0181 (OP0296), 0568 (POS0655)
Van Weely S., 0038 (OP0071-HPR), 1460 (AB0873-HPR)
van Wesemael T. J., 0426 (POS0395)
van Wissen M. A. T., 1460 (AB0873-HPR)
Van Zeben J., 0273 (POS0123), 0351 (POS0258)
Vanchieri C., 0897 (POS1228)
Vanderhoek L., 0320 (POS0207)
Vanegas-García A. L., 0639 (POS0770), 1213 (AB0374)
Vankova D., 0100 (OP0166)
Vanni K., 0327 (POS0219), 0867 (POS1174)
Vannier-Moreau V., 0054 (OP0099), 0214 (POS0024), 1127 (AB0205)
Vannuccini S., 1192 (AB0334)
Vanquaethem H., 0388 (POS0323)
Vanrenterghem J., 1337 (AB0602)
Varcasia G., 0906 (POS1246)
Vardanyan V., 1417 (AB0782)
Vargas Guerrero A., 0904 (POS1242)

Vasilenko A., 1325 (AB0575)
Vasilenko E., 0776 (POS1017), 0777 (POS1019), 1285 (AB0516), 1325 (AB0575), 1387 (AB0712)
Vasilev G., 1432 (AB0815)
Vasileva V., 0209 (POS0016), 0239 (POS0066-PARE), 0838 (POS1118), 0924 (POS1282), 1347 (AB0627)
Vasiliev V., 0608 (POS0717), 1116 (AB0183)
Vasko R., 0665 (POS0825), 1167 (AB0283)
Vasques J., 0484 (POS0504)
Vásquez G., 0636 (POS0765), 0639 (POS0770)
Vasquez-Canizares N., 0247 (POS0079), 0934 (POS1304)
Vassallo R., 0322 (POS0210), 0389 (POS0325)
Vassilaki M., 0129 (OP0216), 0380 (POS0309), 0381 (POS0311)
Vassilopoulos D., 1299 (AB0537), 1304 (AB0543)
Vastert S., 0098 (OP0164)
Vaughan-Sarrazin M., 0369 (POS0287)
Vaupel K., 0376 (POS0301)
Vautier M., 0233 (POS0055)
Vaux T., 0332 (POS0226), 0720 (POS0919)
Vaz C., 0318 (POS0204), 0354 (POS0263), 0476 (POS0488), 0773 (POS1010), 1096 (AB0137)
Vázquez Díaz M., 0884 (POS1204)
Vázquez Fuentes B. R., 0445 (POS0434), 1085 (AB0113), 1177 (AB0301), 1425 (AB0801)
Vázquez García J., 0403 (POS0347)
Vázquez Gómez M. A., 1341 (AB0612)
Vazquez M., 0559 (POS0642), 1042 (AB0015), 1120 (AB0193)
Vazquez Mellado J., 0853 (POS1149)
Vazquez Mosquera M. E., 0403 (POS0347)
Vazquez Perez-Coleman J. C., 0540 (POS0608)
Vazquez Rodriguez T. R., 0610 (POS0721)
Vázquez-Del Mercado Espinosa M., 0904 (POS1242), 0905 (POS1245)
Vázquez-Gómez I., 0296 (POS0168), 1427 (AB0806)
Veale D., 0014 (OP0025), 0015 (OP0028), 0205 (POS0007), 0241 (POS0069), 0423 (POS0387), 0462 (POS0462), 0470 (POS0477), 0747 (POS0964), 0891 (POS1216), 1043 (AB0018), 1479 (AB0916-PARE)
Vecellio M., 0152 (OP0249)
Veenstra E. C. A., 1268 (AB0481)
Veenstra F., 1351 (AB0634)
Vega Cornejo G., 0245 (POS0076)
Vega J., 0607 (POS0715)
Vega L., 1103 (AB0151), 1104 (AB0153), 1111 (AB0170), 1376 (AB0686)
Vega T., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Vega-Morales D., 0445 (POS0434), 0559 (POS0642), 0904 (POS1242), 0905 (POS1245), 1007 (POS1446), 1085 (AB0113), 1166 (AB0281), 1177 (AB0301), 1425 (AB0801), 1455 (AB0863-HPR), 1456 (AB0866-HPR)
Vegas-Revenga N., 1018 (POS1467-HPR), 1225 (AB0396), 1412 (AB0771)
Végh E., 0226 (POS0043), 0421 (POS0383), 0425 (POS0390)
Vehof J., 0074 (OP0130)
Veigl D., 0424 (POS0388)
Veillard E., 0199 (LB0002)
Vela-Casasempere P., 0034 (OP0064), 0760 (POS0986), 1208 (AB0366)
Velazco Zamora J. L., 0576 (POS0667)
Veldwijk J., 0096 (OP0160-HPR)
Velloso Feijoo M., 0323 (POS0211), 0610 (POS0721)
Velloso M. S., 1196 (AB0342)
Velmakin S., 0326 (POS0217)
Velosa A. P., 0444 (POS0432)
Veloso S., 1405 (AB0755)
Velozo E., 0771 (POS1005), 1133 (AB0214)
Velthuis K., 0547 (POS0620), 0562 (POS0648), 1122 (AB0196)
Veltishchev D., 1088 (AB0118), 1180 (AB0308), 1364 (AB0664)
Velvet A. J., 1172 (AB0291)
Vemuri P., 0381 (POS0311)
Vencovský J., 0004 (OP0008), 0072 (OP0128), 0424 (POS0388), 0677 (POS0846), 0678 (POS0849), 1051 (AB0038), 1062 (AB0063), 1233 (AB0410), 1234 (AB0412)
Venegas A., 0760 (POS0985)
Venerito V., 1217 (AB0380)
Venetsanopoulou A., 0178 (OP0291)
Venhoff N., 1383 (AB0701)
Venhuizen A. C., 1366 (AB0668)
Venkatachalam S., 0005 (OP0009-PARE), 0169 (OP0280-PARE)
Venn A., 0276 (POS0129), 0309 (POS0190)
Ventosa J. A., 1225 (AB0396), 1412 (AB0771)
Verano Castillo D. V., 0479 (POS0493)
Verardi L., 0370 (POS0289), 0687 (POS0864)
Verba M., 0080 (OP0137), 0081 (OP0139), 0155 (OP0253), 0342 (POS0241), 0456 (POS0453), 0756 (POS0979), 0769 (POS1002), 0813 (POS1069)
Verbraak F., 0705 (POS0897)
Verdiyeva A., 0034 (OP0063)
Verdonck T., 1001 (POS1434)
Verducci A., 1480 (AB0918-PARE)
Verhavert G., 1001 (POS1434)
Verhoef L. M., 0310 (POS0193), 0880 (POS1197), 1023 (POS1477-HPR), 1027 (POS1485-HPR)
Verhoeven F., 0719 (POS0916), 0748 (POS0967), 0793 (POS1039), 1062 (AB0062), 1067 (AB0073), 1159 (AB0266), 1275 (AB0496), 1279 (AB0504)
Verhoeven M., 0012 (OP0021)
Verikiou A., 0193 (OP0317-PARE)
Veris-van Dieren J., 0978 (POS1391)
Verma I., 0774 (POS1011)
Vermeer M., 1209 (AB0367), 1214 (AB0375)
Veroz Gonzalez R., 0952 (POS1340)
Versari A., 0037 (OP0069)
Verschueren P., 0356 (POS0266-HPR), 0375 (POS0300), 0484 (POS0503), 0545 (POS0616), 0884 (POS1203), 1001 (POS1433), 1001 (POS1434), 1083 (AB0109)
Verschueren S., 1337 (AB0602)
Versnel M., 0302 (POS0178), 0308 (POS0189)
Verstappen G. M., 0074 (OP0130)
Verstappen M., 0351 (POS0257), 0420 (POS0379), 0978 (POS1391), 1005 (POS1442), 1155 (AB0258)
Verstappen S., 0101 (OP0169-PARE), 0110 (OP0183), 0403 (POS0348), 0467 (POS0471), 1373 (AB0681)
Verstraete M., 0664 (POS0822)
Vertuan M., 1462 (AB0878-HPR)
Vervloesem C., 0375 (POS0300), 1001 (POS1433)
Vervullens S., 0828 (POS1096)
Verweij N. J. F., 0114 (OP0189)
Vesa S. C., 0638 (POS0768)
Vesel C., 0839 (POS1121)
Vesga Gualdrón J., 0483 (POS0501)
Vetters E., 0792 (POS1037)
Vettori S., 0671 (POS0835), 0685 (POS0861)
Vezzoli M., 0628 (POS0751)
Viapiana O., 0051 (OP0093), 0062 (OP0112), 0106 (OP0178), 0324 (POS0214), 0326 (POS0218), 0560 (POS0644), 0831 (POS1102), 0867 (POS1173), 1260 (AB0467)
Viatte S., 0467 (POS0471)
Vicens Bernabeu E., 0296 (POS0167), 0857 (POS1157), 0964 (POS1365), 1278 (AB0502)
Vicente-Rabaneda E. F., 0393 (POS0331), 0560 (POS0645), 0755 (POS0977), 0977 (POS1390), 1071 (AB0083), 1241 (AB0427)
Vidal S., 0277 (POS0132)
Vidal-Pedrola G., 1044 (AB0021)
Vidarsson G., 1044 (AB0020)
Videira T., 1236 (AB0415), 1236 (AB0416), 1236 (AB0417)
Vieira A., 0208 (POS0013)
Vieira M., 0233 (POS0055)
Vieira R., 1236 (AB0415), 1236 (AB0416), 1236 (AB0417)
Viers B., 0951 (POS1338)
Viktrup L., 0823 (POS1088)
Vila D., 0730 (POS0933), 1377 (AB0689)
Vilas J. P., 0354 (POS0263)
Villa-Blanco I., 0034 (OP0064), 0035 (OP0065)
Villalba J. M., 0426 (POS0394)
Villalva A., 0546 (POS0617), 1047 (AB0027), 1101 (AB0149)
Villar M. J., 1215 (AB0377)
Villarreal L., 1146 (AB0242), 1475 (AB0907-HPR)
Villarreal-Alarcón M. A., 1031 (POS1494-HPR)
Villarreal-Alarcón M. Á., 1166 (AB0281)
Villiger P., 0033 (OP0061), 0398 (POS0341)
Vils S. R., 0866 (POS1171)
Viñas Sague L., 0856 (POS1156)
Vincek K., 0941 (POS1318)
Vincent A., 0479 (POS0494)
Vincent E., 1121 (AB0195)
Vine S., 0651 (POS0798)
Vinet E., 0235 (POS0058-PARE), 0993 (POS1420)
Viney J. L., 1043 (AB0019)
Viney J., 0013 (OP0023), 1050 (AB0034), 1167 (AB0282)
Vinicki J. P., 0576 (POS0667)
Vinogradova I., 1095 (AB0135)
Vinokurova F., 0930 (POS1297)
Vinšová N., 0872 (POS1183)
Viola F., 0979 (POS1393)
Viola S., 0097 (OP0161)
Violeta V., 1378 (AB0690)
Viora U., 1480 (AB0918-PARE)
Virata A., 0652 (POS0801)
Virelli G., 1477 (AB0911-HPR)
Virščček A., 0650 (POS0796)
Virtanen A., 1150 (AB0250)
Vis M., 0289 (POS0151), 0805 (POS1053), 0807 (POS1057)
Visalli E., 0906 (POS1246)
Visman I., 0962 (POS1361)
Vissink A., 0074 (OP0130)
Visvanathan S., 0589 (POS0687)
Visweswaraiah J., 0013 (OP0023), 1167 (AB0282)
Vital E., 0023 (OP0044), 0030 (OP0057), 0078 (OP0134), 0300 (POS0175), 0302 (POS0179), 0625 (POS0746), 0626 (POS0748), 1173 (AB0293)
Vitale A., 0051 (OP0093), 0957 (POS1349)
Vitaloni M., 0358 (POS0269-HPR)
Vittecoq O., 0109 (OP0181), 0258 (POS0095)
Vivar-Pomiano N., 0087 (OP0146)
Vivekanantham A., 0232 (POS0053), 0829 (POS1098), 1010 (POS1453)
Vivero F., 1196 (AB0342)
Vizdoaga A., 1337 (AB0601)
Vlachakis D., 0405 (POS0350)
Vlachoyiannopoulos P., 0656 (POS0807), 0668 (POS0829), 1381 (AB0697)
Vladeva S., 1340 (AB0609)
Vleugels R., 0165 (OP0271)
Vliet Vlieland T. P. M., 0038 (OP0071-HPR), 0119 (OP0198-HPR), 1460 (AB0873-HPR)
Voclonová V., 0850 (POS1142)
Vodnala S., 1242 (AB0428)
Vohra S., 1172 (AB0291)
Vojinovic J., 0693 (POS0874)
Volkan Ö., 0514 (POS0560), 0964 (POS1364)
Volkmann E., 0101 (OP0170), 0162 (OP0267), 0163 (OP0268), 0671 (POS0835), 0674 (POS0840), 1240 (AB0424), 1245 (AB0433)
Volkov A., 0514 (POS0559), 0977 (POS1388), 1179 (AB0307), 1421 (AB0792)
Volkov M., 0422 (POS0384), 0423 (POS0386), 1044 (AB0020)
Voll R., 0171 (OP0283), 0915 (POS1261), 1383 (AB0701)
Volnukhin E., 0772 (POS1008)
Von Dalwigk K., 1060 (AB0056)
Von der Decken C. B., 1274 (AB0494)
von Hegedus J., 0416 (POS0371)
Von Hegedus J., 0822 (POS1087)
Von Loga I., 0863 (POS1168)
Von Richter O., 1130 (AB0208)
Von Stuckrad A. S. L., 0305 (POS0183), 0623 (POS0744)
Vonk M., 0162 (OP0266), 0232 (POS0054), 1248 (AB0441)
Vonkeman H., 0359 (POS0271-HPR), 0374 (POS0299), 0547 (POS0620), 0548 (POS0621), 0562 (POS0648), 0578 (POS0669), 1122 (AB0196), 1153 (AB0254)
Vontari S., 0900 (POS1235)

Voogdt-Pruis H., 0238 (POS0063-PARE)
Voorneveld H., 0374 (POS0299)
Voortman M., 0993 (POS1419), 1430 (AB0812)
Vorbrüggen W., 1274 (AB0494)
Vorobyova L., 1327 (AB0580)
Vos P., 0880 (POS1197)
Voskuyl A., 0114 (OP0189), 0181 (OP0296), 0324 (POS0213)
Vossen D., 1013 (POS1458-HPR)
Vosvotekas G., 1299 (AB0537)
Voulgarelis M., 0178 (OP0291), 0180 (OP0294), 0370 (POS0290)
Voulgari P., 0178 (OP0291), 0879 (POS1194), 1107 (AB0161), 1299 (AB0537)
Vounotrypidis P., 1299 (AB0537)
Vrablik M., 1234 (AB0412)
Vriezekolk J., 0288 (POS0150), 0359 (POS0272-HPR), 1027 (POS1485-HPR), 1351 (AB0634)
Vural M., 1086 (AB0114)
Vutcanu O., 0773 (POS1009)

Waarsing J. H., 0061 (OP0111)
Wachtlin D., 1244 (AB0431)
Waddington K., 0008 (OP0013)
Wade S., 0014 (OP0025), 0241 (POS0069), 1479 (AB0916-PARE)
Wadsworth II M. H., 0038 (OP0072)
Wagener P., 0806 (POS1055)
Wagner D. L., 0207 (POS0010)
Wagner L., 0168 (OP0277-PARE)
Wagner Poti Gomes K., 0909 (POS1252), 1448 (AB0848)
Wagner U., 0421 (POS0382), 0714 (POS0910)
Wahadat M. J., 0302 (POS0178), 1070 (AB0081)
Wähämaa H., 0429 (POS0400)
Wahinuddin S., 0053 (OP0096)
Wakabayashi K., 1063 (AB0065)
Wakefield R., 0463 (POS0464)
Waki D., 0458 (POS0455), 0665 (POS0824)
Wakiya R., 0513 (POS0556), 0961 (POS1358), 1169 (AB0287), 1223 (AB0390), 1249 (AB0443), 1437 (AB0826)
Walker J., 0353 (POS0262)
Walker U., 0272 (POS0122), 0465 (POS0468), 0681 (POS0855)
Walko S., 1287 (AB0522)
Wallace B., 0002 (OP0006), 0173 (OP0286)
Wallace D. J., 0177 (OP0289), 0588 (POS0686), 0596 (POS0697)
Wallace Z., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288), 0230 (POS0051), 0867 (POS1174), 0974 (POS1382), 0997 (POS1428), 1368 (AB0674)
Wallén H., 0643 (POS0779)
Wallenius M., 0951 (POS1337), 0995 (POS1424)
Wallman J. K., 0130 (OP0218), 0131 (OP0220), 0339 (POS0237)
Walls C., 0563 (POS0649)
Walsh D., 0045 (OP0084), 0540 (POS0608)
Walsh J. A., 0237 (POS0062-PARE), 0353 (POS0262), 0716 (POS0912), 0718 (POS0915), 0724 (POS0925), 1034 (POS1499-PARE), 1262 (AB0471), 1310 (AB0552)
Walther J., 0170 (OP0282)
Wan M. C., 0640 (POS0773)
Wan W., 0690 (POS0869), 0698 (POS0884)
Wang B., 0655 (POS0805)
Wang C., 0427 (POS0396), 0623 (POS0743), 0704 (POS0895), 0771 (POS1006), 1043 (AB0017), 1408 (AB0762)
Wang F., 0203 (POS0002), 0428 (POS0398), 0486 (POS0507), 0561 (POS0647)
Wang G., 0574 (POS0664)
Wang H., 0111 (OP0184), 1052 (AB0039)
Wang J. R., 1082 (AB0108)
Wang J., 0077 (OP0133), 0449 (POS0442), 0595 (POS0695), 0724 (POS0925), 0867 (POS1174)
Wang L. C., 0116 (OP0193)
Wang L. T., 0145 (OP0237), 0430 (POS0402), 0947 (POS1329)
Wang L., 0067 (OP0120), 0146 (OP0239), 0387 (POS0320), 0428 (POS0398), 0696 (POS0879), 0704 (POS0895)
Wang M., 1122 (AB0197)
Wang Q., 0616 (POS0732), 0629 (POS0754), 0641 (POS0776), 0677 (POS0847), 0678 (POS0848), 0680 (POS0851), 0888 (POS1211), 1122 (AB0197), 1436 (AB0824)
Wang R., 0021 (OP0039), 0670 (POS0833)
Wang T. S., 0198 (LB0001)
Wang X., 0085 (OP0144), 0188 (OP0307), 0189 (OP0308)
Wang Y. Y., 1043 (AB0017), 1408 (AB0762)
Wang Y., 0009 (OP0015), 0188 (OP0307), 0629 (POS0754), 0721 (POS0921), 0781 (POS1024), 1025 (POS1481-HPR), 1289 (AB0524)
Wang Z., 0138 (OP0228), 0365 (POS0280), 0975 (POS1384), 1315 (AB0559), 1318 (AB0564)
Wanivenhaus F., 0045 (OP0083)
Wanono S., 1364 (AB0665)
Wanten S. A. C., 1023 (POS1477-HPR)
Wanzenried A., 1233 (AB0411)
Ward M., 0181 (OP0296)
Warren D. J., 0185 (OP0301)
Warren R. B., 0779 (POS1022), 0795 (POS1042)
Warrington K. J., 0106 (OP0177), 0651 (POS0799), 0652 (POS0800), 0652 (POS0801), 0654 (POS0803), 0655 (POS0805), 0672 (POS0836), 0951 (POS1338), 1211 (AB0370)
Wasen C., 0014 (OP0026)
Wassenberg S., 0216 (POS0026)
Wasserman P., 0295 (POS0165)
Watanabe R., 0401 (POS0345), 1025 (POS1482-HPR)
Watson K., 0148 (OP0241)
Webb D., 0167 (OP0275-PARE), 0167 (OP0276-PARE), 0235 (POS0059-PARE), 0889 (POS1213), 1277 (AB0500), 1369 (AB0675), 1370 (AB0676), 1371 (AB0677)
Weber E., 0211 (POS0020)
Weber U., 0153 (OP0251), 0221 (POS0032), 0224 (POS0037), 0831 (POS1101)
Weber-Arden J., 0050 (OP0092), 0971 (POS1379), 0972 (POS1380)
Webers C., 0101 (OP0169-PARE)
Wedderburn L., 0097 (OP0162), 0369 (POS0288)
Wedrén S., 0130 (OP0218)
Weel A., 0238 (POS0063-PARE), 0353 (POS0261), 1087 (AB0116)
Wegrzyn L., 0860 (POS1163), 0886 (POS1207)
Wei B., 1166 (AB0280)
Wei H., 0387 (POS0320)
Wei J. C. C., 0704 (POS0895), 1170 (AB0288)
Wei L., 0137 (OP0227), 1316 (AB0560)
Wei W., 0629 (POS0754)
Wei X. N., 1174 (AB0296), 1227 (AB0398)
Weigl M., 1027 (POS1484-HPR), 1467 (AB0889-HPR)
Weill C., 0829 (POS1099)
Weinblatt M. E., 0457 (POS0454), 0847 (POS1136), 1348 (AB0630)
Weisman M., 0710 (POS0904)
Weiß A., 0135 (OP0225), 0373 (POS0296), 1263 (AB0472)
Weiss N., 0369 (POS0287)
Weiss P., 0943 (POS1323)
Weiswasser M., 0076 (OP0132)
Weits G., 0359 (POS0271-HPR)
Welcker M., 0528 (POS0591), 1274 (AB0494)
Welin E., 1023 (POS1476-HPR)
Welker P., 0988 (POS1410)
Weller-Heinemann F., 0050 (OP0092), 0099 (OP0165), 0244 (POS0075), 0932 (POS1301), 0936 (POS1309), 0943 (POS1321), 0945 (POS1325), 0971 (POS1379)
Welling J., 1033 (POS1497-PARE)
Wells A. F., 1311 (AB0553)
Wells I., 1026 (POS1483-HPR)
Wells K., 0049 (OP0090)
Welsch G., 0060 (OP0109)
Welsh C., 0431 (POS0405)
Welsh P., 0132 (OP0221), 0812 (POS1068)
Welsing P., 0012 (OP0021)
Wemeau Stervinou L., 0054 (OP0099)
Wen L., 1458 (AB0870-HPR)
Wendler J., 0194 (OP0318), 0806 (POS1055), 1274 (AB0494)
Wendling D., 0027 (OP0052), 0343 (POS0243), 0662 (POS0818), 0719 (POS0916), 0748 (POS0967), 0793 (POS1039), 1062 (AB0062), 1067 (AB0073), 1159 (AB0266), 1204 (AB0358), 1261 (AB0469), 1275 (AB0496), 1279 (AB0504), 1322 (AB0570)
Weng M. Y., 1152 (AB0253)
Wenink M., 0288 (POS0150), 0310 (POS0193)
Wennberg P., 0106 (OP0177)
Werdiningsih Y., 1425 (AB0802)
Werlen L., 0655 (POS0806)
Werlinrud J., 0419 (POS0377)
Wermskog L., 0167 (OP0275-PARE)
Werner M. L., 0887 (POS1208)
Werner S. G., 0910 (POS1254), 0983 (POS1401), 1383 (AB0702)
Werth V, 0383 (POS0315)
Werth V., 0075 (OP0131), 0076 (OP0132), 0597 (POS0698), 0598 (POS0699)
Westerlind H., 1059 (AB0054)
Westhovens R., 0356 (POS0266-HPR), 0375 (POS0300), 0484 (POS0503), 0545 (POS0616), 0884 (POS1203), 1001 (POS1433), 1001 (POS1434), 1083 (AB0109)
Westra J., 0189 (OP0308), 1071 (AB0082)
Wetterslev M., 0089 (OP0149), 0153 (OP0252)
Whalley S., 0167 (OP0276-PARE)
Whelan B., 1093 (AB0130)
Whelan S., 0201 (LB0004)
White A., 0366 (POS0283)
White B., 0102 (OP0171), 0383 (POS0315)
White D., 1315 (AB0559)
White R., 0728 (POS0930)
White W., 0590 (POS0688)
Whiteford J., 0120 (OP0200), 1052 (AB0039)
Wibetoe G., 0219 (POS0029), 0795 (POS1041)
Wichuk S., 0153 (OP0251), 0221 (POS0032), 0831 (POS1101)
Wicks I., 1211 (AB0370)
Widawski L., 0736 (POS0947)
Widdifield J., 0173 (OP0285), 0230 (POS0050)
Widding Hansen I. J., 0543 (POS0612)
Wiek D., 0101 (OP0169-PARE)
Wiencke A. K., 1202 (AB0355)
Wieser S., 0095 (OP0158-HPR)
Wiginder A., 0743 (POS0957)
Wigren E., 0196 (OP0321)
Wigston Z., 0023 (OP0044), 0078 (OP0134), 0300 (POS0175), 0302 (POS0179)
Wijethunga N., 0485 (POS0505)
Wijewantha S., 0485 (POS0505)
Wijewardena T., 0485 (POS0505)
Wijsenbeek M., 0101 (OP0170)
Wikström I., 0513 (POS0557)
Wiland P., 1123 (AB0198), 1130 (AB0208)
Wilhalme H., 0387 (POS0321)
Wilk M., 0048 (OP0089), 1135 (AB0219)
Wilkie R., 0158 (OP0259-HPR)
Wilkins K., 1021 (POS1472-HPR)
Willems M., 1337 (AB0602)
Willemsen- de Mey Msc G., 0238 (POS0063-PARE)
Williams B., 1171 (AB0289)
Williams N., 0828 (POS1097)
Williams R., 0161 (OP0264-HPR)
Wilsmann-Theis D., 1447 (AB0847)
Wilson A. G., 0072 (OP0128), 1427 (AB0805)
Wilson F., 0738 (POS0949)
Wilson L., 0049 (OP0090)
Wilson M., 0387 (POS0319)
Windschall D., 0098 (OP0163), 0099 (OP0165), 0244 (POS0075), 0883 (POS1202), 0932 (POS1301), 0936 (POS1309), 0943 (POS1321)
Winer R., 0132 (OP0221), 0812 (POS1068)
Wink F., 0024 (OP0046), 0223 (POS0034), 0769 (POS1002), 0775 (POS1014)
Winkler A., 0038 (OP0072), 0403 (POS0348)
Winthrop K., 0070 (OP0126), 0255 (POS0092), 0486 (POS0508), 0886 (POS1207), 1149 (AB0248), 1287 (AB0522)
Winzenrieth R., 1322 (AB0570)
Wipfler K., 0401 (POS0344)
Wirth T., 0900 (POS1234)
Wirz M., 0095 (OP0158-HPR)

Wise L., 0002 (OP0006), 0173 (OP0286), 0175 (OP0288)
Wisłowska M., 1434 (AB0820)
Wisniacki N., 0078 (OP0135)
Withers J., 0478 (POS0492), 1096 (AB0138), 1097 (AB0140)
Witsch-Baumgartner M., 0848 (POS1137)
Witte T., 0011 (OP0019), 0158 (OP0260-HPR), 1153 (AB0255), 1186 (AB0322), 1385 (AB0707)
Wittkowski H., 0882 (POS1199)
Wittmann M., 0078 (OP0134), 0302 (POS0179)
Wittoek R., 0275 (POS0126)
Wittstock K., 0401 (POS0344), 1125 (AB0202)
Wluka A., 0362 (POS0276)
Wohland H., 0617 (POS0733)
Wojciechowski R., 1123 (AB0198)
Wojciechowski W., 0743 (POS0958)
Wójciga J., 1121 (AB0194)
Wójcik K., 1434 (AB0820)
Wold O. M., 0092 (OP0154-HPR)
Woldeamanuel Y., 1220 (AB0385)
Wolf G., 0040 (OP0075), 1422 (AB0796)
Wolfson M. F., 0021 (OP0039)
Wolin D., 0808 (POS1060)
Wollenhaupt J., 1148 (AB0247)
Wollman J., 0200 (LB0003), 1181 (AB0312)
Wong C., 0433 (POS0408)
Wong D., 0911 (POS1256)
Wong E., 0579 (POS0670)
Wong P. C., 0818 (POS1079)
Wong P. S., 0702 (POS0893), 1230 (AB0403)
Wong R., 0245 (POS0076)
Wong T. L. V., 0687 (POS0865)
Woo S., 0640 (POS0773)
Wood K., 1057 (AB0051)
Woolf A., 0101 (OP0169-PARE)
Woolf R., 1323 (AB0573)
Worm M., 0670 (POS0834)
Worsch M., 0064 (OP0116)
Wortel C., 0203 (POS0001)
Wouters C., 1373 (AB0681)
Wouters F., 0130 (OP0217), 0351 (POS0257), 0420 (POS0379), 0422 (POS0385), 0448 (POS0438), 0486 (POS0506), 0978 (POS1391)
Woznicki J., 0593 (POS0692)
Wren E., 1476 (AB0909-HPR)
Wright E., 0824 (POS1089)
Wright G., 0575 (POS0666)
Wright K., 0056 (OP0102)
Wu B., 0661 (POS0817), 0718 (POS0915)
Wu C., 0794 (POS1040)
Wu H., 0191 (OP0312), 0574 (POS0664), 1053 (AB0042), 1122 (AB0197)
Wu J., 0387 (POS0320), 0589 (POS0687), 0704 (POS0895)
Wu L., 0629 (POS0754), 0670 (POS0833), 1122 (AB0197)
Wu M., 0387 (POS0320)
Wu R., 0427 (POS0396)
Wu T., 0456 (POS0452)
Wu W., 0300 (POS0174)
Wu Z., 0574 (POS0664), 0629 (POS0754)
Wuhrer M., 1042 (AB0016), 1044 (AB0020)
Wulffraat N., 0098 (OP0164), 0872 (POS1183), 1373 (AB0681)
Wurth P., 1274 (AB0494)
Wuyts W., 0101 (OP0170)
Wynne C., 1121 (AB0195)
Wysham K., 0460 (POS0459), 0994 (POS1422)

Xavier R., 0329 (POS0222), 0567 (POS0654), 0580 (POS0671), 0582 (POS0676), 0909 (POS1252)
Xavier T., 0880 (POS1196)
Xia Y., 0645 (POS0785)
Xian H., 1092 (AB0128)
Xiang L., 0989 (POS1411), 0990 (POS1413)
Xiao F. N., 0280 (POS0136), 0852 (POS1146)
Xiao F., 0022 (OP0042), 0670 (POS0833)
Xiao W., 0574 (POS0664)
Xiao Z., 0574 (POS0664)
Xibille Friedmann D. X., 0559 (POS0642), 0899 (POS1233), 0904 (POS1242), 0905 (POS1245)
Xie H., 0022 (OP0043)
Xie W., 0287 (POS0148), 1098 (AB0141)
Xie Z., 0307 (POS0186), 0450 (POS0443), 0641 (POS0775)
Xin X., 0989 (POS1411)
Xin Y., 0810 (POS1062), 0847 (POS1136)
Xingi E., 0015 (OP0029)
Xiong Q., 0280 (POS0136)
Xoxi B., 0913 (POS1258)
Xu A., 0997 (POS1427)
Xu C., 0327 (POS0219), 0429 (POS0400)
Xu D., 1004 (POS1439), 1076 (AB0095), 1440 (AB0831)
Xu J., 0574 (POS0664), 0574 (POS0664), 0629 (POS0754), 1122 (AB0197)
Xu L., 0696 (POS0879), 1055 (AB0046), 1318 (AB0564)
Xu S., 0527 (POS0590), 0539 (POS0607), 0708 (POS0902), 1289 (AB0524), 1290 (AB0525)
Xu W., 0067 (OP0120), 0789 (POS1033)
Xu X. L., 0312 (POS0195), 0781 (POS1024), 0783 (POS1027), 0785 (POS1029), 0787 (POS1031), 1289 (AB0524), 1291 (AB0526), 1293 (AB0528), 1300 (AB0538)
Xu X., 0121 (OP0201), 0391 (POS0327)
Xu Y. H., 1465 (AB0883-HPR)
Xue H., 0427 (POS0396)
Xue J., 1055 (AB0046), 1318 (AB0564)
Xue Z., 0634 (POS0761), 0646 (POS0787), 1196 (AB0343)
Xydis V., 1107 (AB0161)

Yacuzzi M. S., 0635 (POS0763)
Yağız B., 0069 (OP0125), 0731 (POS0935)
Yagur V., 1039 (AB0009)
Yagyu Y., 0458 (POS0455)
Yahya F., 0816 (POS1075)
Yalçın Dulundu B. Ç., 0191 (OP0313), 0913 (POS1259), 0951 (POS1339)
Yalçın İ., 0966 (POS1368), 1380 (AB0694)
Yalcinbayir O., 1404 (AB0751)
Yalçınkaya Y., 0282 (POS0142), 0602 (POS0706), 0604 (POS0710), 0636 (POS0766), 0912 (POS1257), 0913 (POS1259), 0951 (POS1339), 1006 (POS1445), 1191 (AB0331), 1210 (AB0369), 1251 (AB0448), 1359 (AB0653), 1409 (AB0766)
Yalici-Armagan B., 1327 (AB0579)
Yamada Y., 0195 (OP0319), 0465 (POS0466), 0491 (POS0514), 0492 (POS0517), 0808 (POS1059), 1086 (AB0115), 1431 (AB0813)
Yamagishi M., 0615 (POS0730)
Yamaguchi K., 1408 (AB0763)
Yamakido S., 0398 (POS0340)
Yamanaka H., 0113 (OP0187), 0536 (POS0603)
Yamaoka K., 0070 (OP0126), 0563 (POS0650)
Yamasaki M., 1162 (AB0271)
Yamasaki Y., 1246 (AB0436)
Yamashita H., 1224 (AB0391)
Yamashita K., 0398 (POS0340)
Yamazaki K., 0252 (POS0088), 1151 (AB0252)
Yamazaki Y., 1063 (AB0065)
Yan Q., 0698 (POS0885)
Yan R., 0843 (POS1128), 0844 (POS1130)
Yan S., 0843 (POS1128), 0844 (POS1130)
Yanagawa M., 0398 (POS0340)
Yanagida J., 1092 (AB0128)
Yanagihara K., 0998 (POS1429)
Yanai R., 0458 (POS0455)
Yang F., 0316 (POS0200), 0782 (POS1026), 0784 (POS1028)
Yang G., 1123 (AB0198)
Yang J., 0021 (OP0039), 0188 (OP0307), 0993 (POS1421)
Yang K. M., 1465 (AB0883-HPR)
Yang L. J., 1174 (AB0296)
Yang M., 0629 (POS0754), 0911 (POS1255)
Yang R., 0823 (POS1088)
Yang S., 0690 (POS0869), 0698 (POS0884)
Yang V., 1212 (AB0371)
Yang Y. W., 0787 (POS1031), 1293 (AB0528)
Yang Y., 0634 (POS0761)
Yap J., 0377 (POS0303)
Yaqub M., 0114 (OP0189)
Yardımcı G. K., 0518 (POS0568), 0648 (POS0793), 0659 (POS0813), 0728 (POS0931), 0749 (POS0968), 0770 (POS1004), 0814 (POS1070), 0971 (POS1378), 1124 (AB0200), 1124 (AB0201), 1198 (AB0347), 1250 (AB0446), 1272 (AB0491), 1299 (AB0535)
Yargucu F., 0727 (POS0929)
Yasar Bilge N. S., 0731 (POS0935)
Yaseen K., 0185 (OP0302-HPR)
Yasmine M., 0774 (POS1013), 0835 (POS1110), 0921 (POS1274), 1091 (AB0124), 1095 (AB0133), 1278 (AB0501), 1283 (AB0512), 1335 (AB0597), 1342 (AB0614), 1342 (AB0615), 1368 (AB0672), 1368 (AB0673), 1390 (AB0717), 1397 (AB0736), 1400 (AB0744), 1411 (AB0770), 1431 (AB0814)
Yasuoka H., 1152 (AB0253)
Yates D., 0166 (OP0274-PARE)
Yates M., 0744 (POS0959), 1008 (POS1448)
Yatskiu H., 1036 (AB0003)
Yatsyshyn R., 0866 (POS1172), 1074 (AB0090)
Yau V., 0651 (POS0798)
Yavuz S. Ş., 0191 (OP0313)
Yay M., 1028 (POS1486-HPR), 1467 (AB0888-HPR), 1471 (AB0895-HPR)
Yayla M. E., 0532 (POS0597), 0949 (POS1335)
Yayli S., 1327 (AB0579)
Yazdany J., 0002 (OP0006), 0065 (OP0117), 0173 (OP0286), 0175 (OP0288), 0230 (POS0051), 1368 (AB0674)
Yazici A., 0702 (POS0892), 1140 (AB0229), 1202 (AB0356), 1204 (AB0359), 1206 (AB0362), 1266 (AB0479), 1317 (AB0561)
Yazici H., 0660 (POS0814), 0662 (POS0819), 0663 (POS0820), 0958 (POS1351)
Yazici S., 1327 (AB0579)
Yazici Y., 0060 (OP0108), 0349 (POS0254), 0363 (POS0278), 0416 (POS0372), 0667 (POS0828), 0942 (POS1320)
Yazısız V., 0069 (OP0125), 0731 (POS0935)
Ybáñez-García D., 0296 (POS0168), 1427 (AB0806)
Ye J., 1316 (AB0560)
Ye L., 0070 (OP0126), 0255 (POS0092), 0572 (POS0660)
Ye W., 0821 (POS1084)
Ye Y., 0191 (OP0312), 0698 (POS0885), 0860 (POS1163), 0886 (POS1207)
Yee C. S., 0602 (POS0705), 0625 (POS0746), 0626 (POS0748)
Yee J., 0072 (OP0128)
Yeh L. T., 0843 (POS1128), 0844 (POS1130)
Yelnik C. M., 0612 (POS0724)
Yen P., 0066 (OP0118)
Yenisoy Y., 1028 (POS1486-HPR), 1467 (AB0888-HPR), 1471 (AB0895-HPR)
Yeo J., 0682 (POS0856), 0976 (POS1386)
Yeoh S. A., 0230 (POS0051), 0448 (POS0440), 1136 (AB0220), 1368 (AB0674)
Yesiloglu C., 1471 (AB0896-HPR)
Yessika Jackeline S., 0635 (POS0763)
Yeung J., 0224 (POS0037)
Yeung W. Y., 0147 (OP0240)
Yew J., 1015 (POS1460-HPR)
Yi E., 0808 (POS1060), 1022 (POS1474-HPR), 1469 (AB0892-HPR)
Yigla M., 0691 (POS0871)
Yildirim Cetin G., 1266 (AB0479), 1317 (AB0561)
Yıldırım T., 0350 (POS0255), 0648 (POS0793), 1198 (AB0347)
Yılmaz E., 1247 (AB0437)
Yilmaz I., 0969 (POS1375)
Yilmaz M., 0958 (POS1352), 0968 (POS1372)
Yılmaz Ş. R., 0648 (POS0793), 1198 (AB0347)
Yilmaz S., 0727 (POS0929), 1470 (AB0893-HPR)
Yılmaz S., 1140 (AB0229), 1266 (AB0479), 1317 (AB0561)
Yilmaz-Oner S., 0514 (POS0560), 0964 (POS1364)
Yim D. H., 0124 (OP0207)
Yim I. C., 0257 (POS0094)
Yin G., 0574 (POS0664)
Yin S., 0387 (POS0320)
Yin X. F., 0729 (POS0932)

Yin Z., 0569 (POS0657), 0570 (POS0658)
Yinh J., 0841 (POS1124)
Ymashita H., 0655 (POS0806)
Yndestad A., 1149 (AB0248)
Yokochi R., 0458 (POS0455)
Yokose C., 0002 (OP0005), 0122 (OP0202), 0122 (OP0203), 0144 (OP0235), 0841 (POS1124), 0853 (POS1148)
Yokota T., 0665 (POS0824)
Yolbaş S., 1470 (AB0893-HPR)
Yong S. S., 0816 (POS1075)
Yoo D., 0716 (POS0911)
Yoo J. E., 0062 (OP0113)
Yoo J., 1123 (AB0198)
Yoo S. J., 0204 (POS0005)
Yoo W. H., 1072 (AB0084)
Yoon S., 0990 (POS1413)
Yoosuf N., 0001 (OP0003)
Yorifuji K., 0689 (POS0868)
Yorio M., 1194 (AB0338)
Yoshida K., 0056 (OP0101), 0689 (POS0868), 0753 (POS0975), 1096 (AB0136)
Yoshida T., 0665 (POS0824), 1025 (POS1482-HPR)
Yoshifuji H., 0395 (POS0336), 0401 (POS0345)
Yoshii I., 0448 (POS0439), 0521 (POS0574), 1078 (AB0100), 1079 (AB0101), 1079 (AB0102), 1339 (AB0606)
Yoshii N., 0113 (OP0187)
Yoshikawa T., 1181 (AB0311)
Yoshinobu T., 0956 (POS1348), 1407 (AB0760)
You H., 0629 (POS0754)
You Y., 0787 (POS1031), 1293 (AB0528), 1297 (AB0532)
Younes M., 0856 (POS1155), 0923 (POS1281), 1358 (AB0650), 1415 (AB0777)
Young A., 0480 (POS0495)
Young F., 0462 (POS0462), 0470 (POS0477)
Young K., 0230 (POS0051), 1368 (AB0674)
Young L., 0166 (OP0274-PARE)
Young N., 0049 (OP0090)
Young P., 0777 (POS1020), 1286 (AB0521)
Youssef P., 0330 (POS0223), 1015 (POS1461-HPR)
Yu Q., 0460 (POS0458), 0622 (POS0742), 0677 (POS0847), 0678 (POS0848), 0680 (POS0851), 1037 (AB0005), 1436 (AB0824)
Yu S., 0670 (POS0833)
Yu X., 1122 (AB0197), 1408 (AB0762)
Yuan F., 0387 (POS0320)
Yuan J. M., 0827 (POS1095)
Yüce İnel T., 0878 (POS1193), 1386 (AB0708)
Yue X., 0860 (POS1163)
Yüksel K., 0117 (OP0195)
Yurdakul S., 0660 (POS0814), 0662 (POS0819), 0663 (POS0820), 0958 (POS1351)
Yurttas B., 0875 (POS1187), 0974 (POS1381), 1207 (AB0364), 1470 (AB0893-HPR)

Zabotti A., 0134 (OP0223), 0284 (POS0145), 0618 (POS0735), 0809 (POS1061), 0948 (POS1333)
Zacariaz J., 1133 (AB0214)
Zaccagnino E., 0156 (OP0255)
Zaccardelli A., 0867 (POS1174)
Zachariae C., 0287 (POS0149)
Zafeiridis A., 0620 (POS0738)
Zaffaroni A., 1319 (AB0565)
Zagainova V., 0824 (POS1090)
Zagato E., 0229 (POS0048)
Zagrebneva A., 0731 (POS0937), 1265 (AB0475)
Zahavi E., 0462 (POS0462)
Zaiats L., 1074 (AB0090)
Zajc Avramovic M., 0242 (POS0072), 0941 (POS1318)
Zakaria N., 1320 (AB0566)
Zaman M., 1342 (AB0616)
Zamora E., 0559 (POS0642), 0904 (POS1242), 0905 (POS1245)
Zamora L., 0218 (POS0028)
Zanardini C., 0633 (POS0760)
Zanatta E., 0232 (POS0054), 0384 (POS0316), 0386 (POS0318), 0685 (POS0861), 0906 (POS1246)
Zanetti A., 0134 (OP0223), 0335 (POS0230), 0470 (POS0476), 1435 (AB0822)
Zanframundo G., 0134 (OP0223), 0906 (POS1246), 0985 (POS1406)
Zapico I., 0819 (POS1080)
Zaralı S., 0912 (POS1257)
Zarco Montejo P., 0746 (POS0962)
Zarco-Montejo P., 0743 (POS0958), 0763 (POS0991), 0764 (POS0992), 0765 (POS0993), 0765 (POS0994), 0976 (POS1387)
Zarrar R., 0600 (POS0701)
Zatti S., 0470 (POS0476), 0628 (POS0751), 0633 (POS0760), 1435 (AB0822)
Zavada J., 0058 (OP0105), 0131 (OP0220), 0217 (POS0027), 0532 (POS0596), 0850 (POS1142)
Zavodovsky B., 0297 (POS0169), 0455 (POS0451), 0487 (POS0509), 1437 (AB0827)
Zayat A., 0625 (POS0746)
Zazueta B. E., 0904 (POS1242), 0905 (POS1245)
Zbinden A., 0767 (POS0997)
Zborovskaya I., 0225 (POS0040), 1062 (AB0061), 1444 (AB0841)
Zdrojewski Z., 1434 (AB0820)
Zegaloui H., 0526 (POS0588), 0837 (POS1116), 0838 (POS1117), 0858 (POS1160), 1346 (AB0625)
Zeglaoui H., 0472 (POS0481), 0520 (POS0572), 0521 (POS0573), 0923 (POS1279), 0924 (POS1283), 1099 (AB0144), 1142 (AB0232), 1345 (AB0623), 1480 (AB0919-PARE)
Zehender A., 1075 (AB0091)
Zehraoui N., 1144 (AB0237)
Zekre F., 0240 (POS0068)
Zelaya D., 0730 (POS0933), 1377 (AB0689)
Zemerova E., 0709 (POS0903)
Zen M., 0182 (OP0297), 0594 (POS0693), 0600 (POS0702), 0630 (POS0755), 1174 (AB0295)
Zeng A. Q., 1174 (AB0296)
Zeng J., 0993 (POS1421)
Zeng W. C., 1227 (AB0398)
Zeng X., 0178 (OP0290), 0629 (POS0754), 0641 (POS0775), 1122 (AB0197), 1156 (AB0260)
Zenz S., 0261 (POS0102)
Zepeda C., 0559 (POS0642)
Zerbi P., 1367 (AB0671)
Zerbini C., 0328 (POS0220)
Zervou M., 0405 (POS0350), 1037 (AB0004)
Zhai G., 0307 (POS0186)
Zhan F., 0629 (POS0754)
Zhan L., 1136 (AB0221)
Zhang D., 1196 (AB0343)
Zhang F., 0596 (POS0697)
Zhang H., 0561 (POS0646), 0574 (POS0664)
Zhang J. Q., 0111 (OP0184), 0684 (POS0859)
Zhang J., 0587 (POS0684), 0657 (POS0810), 0721 (POS0921)
Zhang L., 0022 (OP0042), 0307 (POS0187), 0478 (POS0492), 1096 (AB0138), 1097 (AB0140)
Zhang M., 0192 (OP0314), 0428 (POS0398), 0574 (POS0664), 0641 (POS0776)
Zhang Q. B., 0280 (POS0136), 0852 (POS1146), 1040 (AB0011), 1067 (AB0075), 1252 (AB0449)
Zhang Q., 1196 (AB0343)
Zhang S. X., 0111 (OP0184), 0188 (OP0307), 0315 (POS0199), 0460 (POS0458), 0616 (POS0732), 0619 (POS0736), 0622 (POS0742), 0623 (POS0743), 0677 (POS0847), 0678 (POS0848), 0680 (POS0851), 0684 (POS0859), 0729 (POS0932), 0888 (POS1211), 1037 (AB0005), 1436 (AB0824)
Zhang W., 0185 (OP0302-HPR)
Zhang X., 0039 (OP0073), 0456 (POS0452), 0634 (POS0761), 1091 (AB0125), 1166 (AB0280), 1212 (AB0372), 1465 (AB0883-HPR)
Zhang Y., 0138 (OP0228), 0148 (OP0242), 0315 (POS0199), 0367 (POS0285), 0616 (POS0732), 0617 (POS0734), 0623 (POS0743), 0677 (POS0847), 0684 (POS0859), 0729 (POS0932), 0853 (POS1148), 0867 (POS1174), 0888 (POS1211), 1353 (AB0639), 1436 (AB0824), 1458 (AB0870-HPR)
Zhang Z., 0218 (POS0028), 0287 (POS0148), 1098 (AB0141), 1166 (AB0280)
Zhao C., 0188 (OP0307), 0629 (POS0754)
Zhao D., 0574 (POS0664), 1156 (AB0260)
Zhao J. L., 0178 (OP0290), 0629 (POS0754), 0641 (POS0775), 1136 (AB0221)
Zhao J., 0574 (POS0664), 0642 (POS0777)
Zhao K., 0022 (OP0043)
Zhao L., 0840 (POS1122), 0847 (POS1136), 1348 (AB0630)
Zhao R., 0111 (OP0184), 0315 (POS0199), 0616 (POS0732), 0619 (POS0736), 0623 (POS0743), 0634 (POS0761), 0677 (POS0847), 0678 (POS0848), 0680 (POS0851), 0684 (POS0859), 0888 (POS1211), 1100 (AB0146), 1436 (AB0824)
Zhao S. S., 0193 (OP0316), 0235 (POS0059-PARE), 0480 (POS0495), 0739 (POS0951), 0844 (POS1131)
Zhao Y., 0629 (POS0754), 0642 (POS0777), 1136 (AB0221)
Zhao Z., 1406 (AB0758)
Zheludova E., 1397 (AB0735)
Zheng C., 0460 (POS0458), 0622 (POS0742), 0678 (POS0848), 0680 (POS0851), 1037 (AB0005)
Zheng D. H., 0456 (POS0452), 1091 (AB0125), 1174 (AB0296), 1225 (AB0394), 1227 (AB0398)
Zheng J. X., 0280 (POS0136), 0852 (POS1146)
Zheng J., 1040 (AB0011), 1067 (AB0075), 1252 (AB0449)
Zheng S., 0248 (POS0081), 0670 (POS0833)
Zheng W., 0646 (POS0788), 1207 (AB0363), 1353 (AB0639)
Zheng X., 0429 (POS0400)
Zhigulina K., 1353 (AB0638)
Zhilyaev E., 0731 (POS0937), 0982 (POS1399), 1084 (AB0111), 1146 (AB0241), 1265 (AB0475), 1383 (AB0703)
Zhilyaev G., 0982 (POS1399)
Zhogova O., 0930 (POS1298)
Zholobova E., 0187 (OP0306), 0201 (LB0004)
Zhong H., 1212 (AB0372), 1318 (AB0564)
Zhong Z., 0851 (POS1144), 1355 (AB0645), 1421 (AB0791)
Zhou B., 0801 (POS1048), 1300 (AB0538)
Zhou L., 0387 (POS0320), 0734 (POS0943)
Zhou T., 0031 (OP0059), 0198 (LB0001), 1211 (AB0370)
Zhou W., 1100 (AB0146)
Zhou Y., 0402 (POS0346), 0447 (POS0437), 0670 (POS0833), 1212 (AB0372), 1258 (AB0463)
Zhou Z., 0365 (POS0280)
Zhu D., 0333 (POS0228)
Zhu J., 0670 (POS0833), 0810 (POS1062), 1182 (AB0313)
Zhu W., 0876 (POS1189)
Zhu X., 0201 (LB0004)
Zhuang Y., 1182 (AB0313)
Zhukouskaya V., 0228 (POS0046)
Zhukova J., 0482 (POS0500)
Zhuo J., 0054 (OP0099), 0214 (POS0024), 1316 (AB0560)
Zhuravleva N., 0969 (POS1374), 1331 (AB0589), 1388 (AB0713)
Zhuravlyova L., 0481 (POS0498)
Ziade N., 0024 (OP0047), 0340 (POS0239), 0361 (POS0275-HPR), 0739 (POS0951), 1080 (AB0104)
Zickert A., 0643 (POS0779)
Ziegeler K., 0156 (OP0256)
Ziegler C., 0234 (POS0056), 0865 (POS1170)
Zielinska A., 1123 (AB0198)
Zigon P., 1069 (AB0080)
Zijlstra J., 0657 (POS0809)
Zimmer A., 0244 (POS0075)
Zindel B., 0095 (OP0158-HPR)
Zink A., 0064 (OP0116), 0216 (POS0026)
Zinke S., 0342 (POS0241), 0456 (POS0453), 0528 (POS0591), 0813 (POS1069)
Zinkernagel A. S., 0045 (OP0083)
Zinkina-Orihan A., 0890 (POS1214)
Ziouzina O., 0224 (POS0037)
Ziroldo Lopes J. V., 1448 (AB0848)
Zisapel M., 0200 (LB0003), 0885 (POS1206), 1181 (AB0312)
Zisman D., 0131 (OP0219), 0200 (LB0003), 0286 (POS0147), 0543 (POS0613), 0753 (POS0974), 0892 (POS1217), 1309 (AB0551)
Zisman L., 0543 (POS0613)
Zlei M., 0585 (POS0680)

Zobec F., 0878 (POS1192)
Zohdy S., 0917 (POS1265)
Zorkany B., 0024 (OP0047), 0340 (POS0239), 0361 (POS0275-HPR), 1080 (AB0104)
Zorn-Pauly L., 0305 (POS0183), 0623 (POS0744)
Zoshima T., 0956 (POS1348), 1407 (AB0760)
Zou H., 0690 (POS0869), 0698 (POS0884)
Zou Y. W., 1465 (AB0883-HPR)
Zou Y. Y., 0456 (POS0452), 1091 (AB0125)
Zouboulis C. C., 0349 (POS0254)
Zrinski Petrović K., 0226 (POS0042)
Zrour S., 0466 (POS0469), 1051 (AB0037), 1390 (AB0718), 1395 (AB0728), 1414 (AB0775)
Żuber Z., 201 (LB0004)
Zubiaur-Zamacola J., 0601 (POS0703), 0966 (POS1370)
Zubrzycka-Sienkiewicz A., 0064 (OP0115)
Zucchi D., 0619 (POS0737), 0630 (POS0756), 0633 (POS0760), 0647 (POS0789)
Zueger P., 0237 (POS0062-PARE), 0312 (POS0196), 0800 (POS1047), 1288 (AB0523)
Zuffada S., 0613 (POS0726)
Zuiani C., 0618 (POS0735)
Zulian F., 0393 (POS0332)
Zuluaga N., 0627 (POS0749), 1192 (AB0335), 1193 (AB0336)
Zuo X., 0574 (POS0664)
Zurita-Prada P., 0922 (POS1275)
Zverkova Sandström T., 0125 (OP0208)
Zviahina O., 1270 (AB0487)
Zvyagin I., 0014 (OP0027), 0204 (POS0004)
Zwerina J., 0320 (POS0208), 0848 (POS1137)
Zwezerijnen G. C. J., 0114 (OP0189)
Zybalova T., 1039 (AB0009)
Zybkova I., 0100 (OP0166)